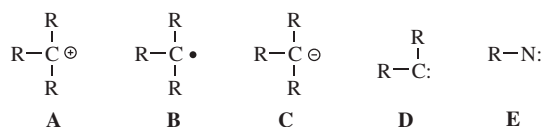


## Carbocations, Carbanions, Free Radicals, Carbenes, and Nitrenes

There are four types of organic species in which a carbon atom has a valence of only 2 or 3.<sup>1</sup> They are usually very short-lived, and most exist only as intermediates that are quickly converted to more stable molecules. However, some are more stable than others and fairly stable examples have been prepared of three of the four



types. The four types of species are *carbocations* (**A**), *free radicals* (**B**), *carbanions* (**C**), and *carbenes* (**D**). Of the four, only carbanions have a complete octet around the carbon. There are many other organic ions and radicals with charges and unpaired electrons on atoms other than carbon, but we will discuss only *nitrenes* (**E**), the nitrogen analogs of carbenes. Each of the five types is discussed in a separate section, which in each case includes brief summaries of the ways in which the species form and react. These summaries are short and schematic. The generation and fate of the five types are more fully treated in appropriate places in Part 2 of this book.

<sup>1</sup>For general references, see Isaacs, N.S. *Reactive Intermediates in Organic Chemistry*, Wiley, NY, **1974**; McManus, S.P. *Organic Reactive Intermediates*, Academic Press, NY, **1973**. Two serial publications devoted to review articles on this subject are *Reactive Intermediates* (Wiley) and *Reactive Intermediates* (Plenum).

## CARBOCATIONS<sup>2</sup>

### Nomenclature

First, we must say a word about the naming of **A**. For many years these species were called “carbonium ions,” although it was suggested<sup>3</sup> as long ago as 1902 that this was inappropriate because “-onium” usually refers to a covalency higher than that of the neutral atom. Nevertheless, the name “carbonium ion” was well established and created few problems<sup>4</sup> until some years ago, when George Olah and his co-workers found evidence for another type of intermediate in which there is a positive charge at a carbon atom, but in which the formal covalency of the carbon atom is five rather than three. The simplest example is the methanonium ion  $\text{CH}_5^+$  (see p. 766). Olah proposed<sup>5</sup> that the name “carbonium ion” be reserved for pentacoordinated positive ions, and that **A** be called “carbenium ions.” He also proposed the term “carbocation” to encompass both types. The International Union of Pure and Applied Chemistry (IUPAC) has accepted these definitions.<sup>6</sup> Although some authors still refer to **A** as carbonium ions and others call them carbenium ions, the general tendency is to refer to them simply as *carbocations*, and we will follow this practice. The pentavalent species are much rarer than **A**, and the use of the term “carbocation” for **A** causes little or no confusion.

### Stability and Structure

Carbocations are intermediates in several kinds of reactions.<sup>7</sup> The more stable ones have been prepared in solution and in some cases even as solid salts, and X-ray crystallographic structures have been obtained in some cases.<sup>8</sup> The X-ray of the

<sup>2</sup>For a treatise, see Olah, G.A.; Schleyer, P.v.R. *Carbonium Ions*, 5 vols., Wiley, NY, **1968–1976**. For monographs, see Vogel, P. *Carbocation Chemistry*, Elsevier, NY, **1985**; Bethell, D.; Gold, V. *Carbonium Ions*, Academic Press, NY, **1967**. For reviews, see Saunders, M.; Jiménez-Vázquez, H.A. *Chem. Rev.* **1991**, *91*, 375; Arnett, E.M.; Hofelich, T.C.; Schriver, G.W. *React. Intermed. (Wiley)* **1987**, *3*, 189; Bethell, D.; Whittaker, D. *React. Intermed. (Wiley)* **1981**, *2*, 211; Bethell, D. *React. Intermed. (Wiley)* **1978**, *1*, 117; Olah, G.A. *Chem. Scr.* **1981**, *18*, 97, *Top. Curr. Chem.* **1979**, *80*, 19, *Angew. Chem. Int. Ed.* **1973**, *12*, 173 (this review has been reprinted as Olah, G.A. *Carbocations and Electrophilic Reactions*, Wiley, NY, **1974**); Isaacs, N.S. *Reactive Intermediates in Organic Chemistry*, Wiley, NY, **1974**, pp. 92–199; McManus, S.P.; Pittman, Jr., C.U., in McManus, S.P. *Organic Reactive Intermediates*, Academic Press, NY, **1973**, pp. 193–335; Buss, V.; Schleyer, P.v.R.; Allen, L.C. *Top. Stereochem.* **1973**, *7*, 253; Olah, G.A.; Pittman Jr., C.U. *Adv. Phys. Org. Chem.* **1966**, *4*, 305. For reviews of dicarbocations, see Lammertsma, K.; Schleyer, P.v.R.; Schwarz, H. *Angew. Chem. Int. Ed.* **1989**, *28*, 1321; Pagni, R.M. *Tetrahedron* **1984**, *40*, 4161; Prakash, G.K.S.; Rawdah, T.N.; Olah, G.A. *Angew. Chem. Int. Ed.* **1983**, *22*, 390. See also, the series *Advances in Carbocation Chemistry*.

<sup>3</sup>Gomberg, M. *Berichte* **1902**, *35*, 2397.

<sup>4</sup>For a history of the term “carbonium ion,” see Traynham, J.G. *J. Chem. Educ.* **1986**, *63*, 930.

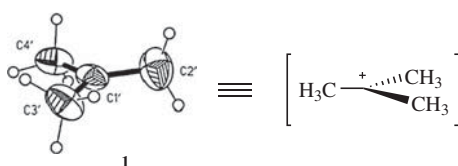
<sup>5</sup>Olah, G.A. *CHEMTECH* **1971**, *1*, 566; *J. Am. Chem. Soc.* **1972**, *94*, 808.

<sup>6</sup>Gold, V.; Loening, K.L.; McNaught, A.D.; Sehmi, P. *Compendium of Chemical Terminology: IUPAC Recommendations*, Blackwell Scientific Publications, Oxford, **1987**.

<sup>7</sup>Olah, G.A. *J. Org. Chem.* **2001**, *66*, 5943.

<sup>8</sup>See Laube, T. *J. Am. Chem.* **2004**, *126*, 10904 and references cited therein. For the X-ray of a vinyl carbocation, see Müller, T.; Juhasz, M.; Reed, C.A. *Angew. Chem. Int. Ed.* **2004**, *43*, 1543.

*tert*-butyl cation complexed with dichloromethane was reported,<sup>9</sup> for example, and is presented as **1** with the solvent molecules removed for clarity. An isolable dioxo-stabilized pentadienylium ion was isolated and its structure was determined by <sup>1</sup>H-, <sup>13</sup>C-NMR, mass spectrometry (MS), and IR.<sup>10</sup> A β-fluoro substituted 4-methoxyphenethyl cation has been observed directly by laser flash photolysis.<sup>11</sup> In solution, the carbocation may be free (this is more likely in polar solvents, in which it is solvated) or it may exist as an ion pair,<sup>12</sup> which means that it is closely associated with a negative ion, called a *counterion* or *gegenion*. Ion pairs are more likely in nonpolar solvents.



Among simple alkyl carbocations<sup>13</sup> the order of stability is tertiary > secondary > primary. There are many known examples of rearrangements of primary or secondary carbocations to tertiary, both in solution and in the gas phase. Since simple alkyl cations are not stable in ordinary strong-acid solutions (e.g., H<sub>2</sub>SO<sub>4</sub>), the study of these species was greatly facilitated by the discovery that many of them could be kept indefinitely in stable solutions in mixtures of fluorosulfuric acid and antimony pentafluoride. Such mixtures, usually dissolved in SO<sub>2</sub> or SO<sub>2</sub>ClF, are among the strongest acidic solutions known and are often called *super acids*.<sup>14</sup> The original experiments involved the addition of alkyl fluorides to SbF<sub>5</sub>.<sup>15</sup>



Subsequently, it was found that the same cations could also be generated from alcohols in super acid-SO<sub>2</sub> at -60°C<sup>16</sup> and from alkenes by the addition of a proton from super acid or HF-SbF<sub>5</sub> in SO<sub>2</sub> or SO<sub>2</sub>ClF at low temperatures.<sup>17</sup> Even alkanes give carbocations in super acid by loss of H<sup>-</sup>. For example,<sup>18</sup>

<sup>9</sup>Kato, T.; Reed, C.A. *Angew. Chem. Int. Ed.* **2004**, 43, 2908.

<sup>10</sup>Lüning, U.; Baumstark, R. *Tetrahedron Lett.* **1993**, 34, 5059.

<sup>11</sup>McClelland, R.A.; Cozens, F.L.; Steenken, S.; Amyes, T.L.; Richard, J.P. *J. Chem. Soc. Perkin Trans. 2* **1993**, 1717.

<sup>12</sup>For a treatise, see Szwarc, M. *Ions and Ion Pairs in Organic Reactions*, 2 vols., Wiley, NY, **1972–1974**.

<sup>13</sup>For a review, see Olah, G.A.; Olah, J.A., in Olah, G.A.; Schleyer, P.v.R. *Carbonium Ions*, Vol. 2, Wiley, NY, **1969**, pp. 715–782. Also see Fărcașiu, D.; Norton, S.H. *J. Org. Chem.* **1997**, 62, 5374.

<sup>14</sup>For a review of carbocations in super acid solutions, see Olah, G.A.; Prakash, G.K.S.; Sommer, J., in *Superacids*, Wiley, NY, **1985**, pp. 65–175.

<sup>15</sup>Olah, G.A.; Baker, E.B.; Evans, J.C.; Tolgyesi, W.S.; McIntyre, J.S.; Bastien, I.J. *J. Am. Chem. Soc.* **1964**, 86, 1360; Brouwer, D.M.; Mackor, E.L. *Proc. Chem. Soc.* **1964**, 147; Kramer, G.M. *J. Am. Chem. Soc.* **1969**, 91, 4819.

<sup>16</sup>Olah, G.A.; Sommer, J.; Namanworth, E. *J. Am. Chem. Soc.* **1967**, 89, 3576.

<sup>17</sup>Olah, G.A.; Halpern, Y. *J. Org. Chem.* **1971**, 36, 2354. See also, Herlem, M. *Pure Appl. Chem.* **1977**, 49, 107.

<sup>18</sup>Olah, G.A.; Lukas, J. *J. Am. Chem. Soc.* **1967**, 89, 4739.

isobutane gives the *tert*-butyl cation



No matter how they are generated, study of the simple alkyl cations has provided dramatic evidence for the stability order.<sup>19</sup> Both propyl fluorides gave the isopropyl cation; all four butyl fluorides<sup>20</sup> gave the *tert*-butyl cation, and all seven of the pentyl fluorides tried gave the *tert*-pentyl cation. *n*-Butane, in super acid, gave only the *tert*-butyl cation. To date, no primary cation has survived long enough for detection. Neither methyl nor ethyl fluoride gave the corresponding cations when treated with SbF<sub>5</sub>. At low temperatures, methyl fluoride gave chiefly the methylated sulfur dioxide salt (CH<sub>3</sub>OSO)<sup>+</sup> SbF<sub>6</sub><sup>−</sup>,<sup>21</sup> while ethyl fluoride rapidly formed the *tert*-butyl and *tert*-hexyl cations by addition of the initially formed ethyl cation to ethylene molecules also formed.<sup>22</sup> At room temperature, methyl fluoride also gave the *tert*-butyl cation.<sup>23</sup> In accord with the stability order, hydride ion is abstracted from alkanes by super acid most readily from tertiary and least readily from primary positions.

The stability order can be explained by the polar effect and by hyperconjugation. In the polar effect, nonconjugated substituents exert an influence on stability through bonds (inductive effect) or through space (field effect). Since a tertiary carbocation has more carbon substituents on the positively charged carbon, relative to a primary, there is a greater polar effect that leads to great stability. In the hyperconjugation explanation,<sup>24</sup> we compare a primary carbocation with a tertiary. It should be made clear that “the hyperconjugation concept arises solely from our model-building procedures. When we ask whether hyperconjugation is important in a given situation, we are asking only whether the localized model is adequate for that situation at the particular level of precision we wish to use, or whether the model must be corrected by including some delocalization in order to get a good enough description.”<sup>25</sup> Using the hyperconjugation model, it is seen that the

<sup>19</sup>See Amyes, T.L.; Stevens, I.W.; Richard, J.P. *J. Org. Chem.* **1993**, 58, 6057 for a recent study.

<sup>20</sup>The *sec*-butyl cation has been prepared by slow addition of *sec*-butyl chloride to SbF<sub>5</sub>–SO<sub>2</sub>ClF solution at −110°C [Saunders, M.; Hagen, E.L.; Rosenfeld, J. *J. Am. Chem. Soc.* **1968**, 90, 6882] and by allowing molecular beams of the reagents to impinge on a very cold surface [Saunders, M.; Cox, D.; Lloyd, J.R. *J. Am. Chem. Soc.* **1979**, 101, 6656; Myhre, P.C.; Yannoni, C.S. *J. Am. Chem. Soc.* **1981**, 103, 230].

<sup>21</sup>Peterson, P.E.; Brockington, R.; Vidrine, D.W. *J. Am. Chem. Soc.* **1976**, 98, 2660; Calves, J.; Gillespie, R.J. *J. Chem. Soc. Chem. Commun.* **1976**, 506; Olah, G.A.; Donovan, D.J. *J. Am. Chem. Soc.* **1978**, 100, 5163.

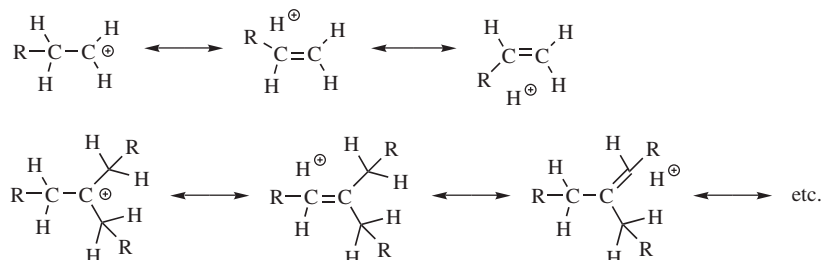
<sup>22</sup>Olah, G.A.; Olah, J.A., in Olah, G.A.; Schleyer, P.v.R. *Carbonium Ions*, Vol. 2, Wiley, NY, **1969**, p. 722.

<sup>23</sup>Olah, G.A.; DeMember, J.R.; Schlosberg, R.H. *J. Am. Chem. Soc.* **1969**, 91, 2112; Bacon, J.; Gillespie, R.J. *J. Am. Chem. Soc.* **1971**, 91, 6914.

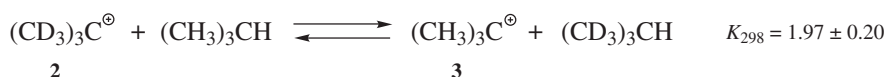
<sup>24</sup>For a review of molecular-orbital theory as applied to carbocations, see Radom, L.; Poppinger, D.; Haddon, R.C., in Olah, G.A.; Schleyer, P.v.R. *Carbonium Ions*, Vol. 5, Wiley, NY, **1976**, pp. 2303–2426.

<sup>25</sup>Lowry, T.H.; Richardson, K.S. *Mechanism and Theory in Organic Chemistry*, 3rd ed., HarperCollins, NY, **1987**, p. 68.

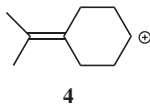
primary ion has only two hyperconjugative forms while the tertiary has six:



According to rule 6 for resonance contributors (p. 47), the greater the number of equivalent forms, the greater the resonance stability. Evidence used to support the hyperconjugation explanation is that the equilibrium constant for this reaction:



is 1.97, showing that **3** is more stable than **2**.<sup>26</sup> Due to a  $\beta$  secondary isotope effect, there is less hyperconjugation in **2** than in **3** (see p. 324 for isotope effects).<sup>27</sup>



There are several structural types of delocalization, summarized in Table 5.1.<sup>28</sup> The stabilization of dimethylalkylidene cation **4** is an example of double hyperconjugation.<sup>28,29</sup>

The field effect explanation is that the electron-donating effect of alkyl groups increases the electron density at the charge-bearing carbon, reducing the net charge on the carbon, and in effect spreading the charge over the  $\alpha$  carbons. It is a general rule that the more concentrated any charge is, the less stable the species bearing it will be.

The most stable of the simple alkyl cations is the *tert*-butyl cation. Even the relatively stable *tert*-pentyl and *tert*-hexyl cations fragment at higher temperatures to

<sup>26</sup>Meot-Ner, M. *J. Am. Chem. Soc.* **1987**, *109*, 7947.

<sup>27</sup>If only the field effect were operating, **2** would be more stable than **3**, since deuterium is electron-donating with respect to hydrogen (p. 23), assuming that the field effect of deuterium could be felt two bonds away.

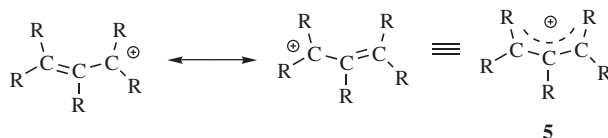
<sup>28</sup>Lambert, J.B.; Ciro, S.M. *J. Org. Chem.* **1996**, *61*, 1940.

<sup>29</sup>Alabugin, I.V.; Manoharan, M. *J. Org. Chem.* **2004**, *69*, 9011.

TABLE 5.1. Structural Types of Delocalization<sup>25</sup>

Valence Structures	Abbreviation	Name
	$\pi\pi$	Simple conjugation
	$\sigma\pi$	Hyperconjugation
	$\pi\sigma$	Homoconjugation
	$\sigma\sigma$	Homohyperconjugation
	$\sigma\pi/\pi\pi$	Hyperconjugation/ conjugation
	$\sigma\pi/\sigma\pi$	Double hyperconjugation

produce the *tert*-butyl cation, as do all other alkyl cations with four or more carbons so far studied.<sup>30</sup> Methane,<sup>31</sup> ethane, and propane, treated with super acid, also yield *tert*-butyl cations as the main product (see reaction **12-20**). Even paraffin wax and polyethylene give *tert*-butyl cation. Solid salts of *tert*-butyl and *tert*-pentyl cations (e.g.,  $\text{Me}_3\text{C}^+ \text{SbF}_6^-$ ) have been prepared from super acid solutions and are stable below  $-20^\circ\text{C}$ .<sup>32</sup>



In carbocations where the positive carbon is in conjugation with a double bond, as in allylic cations (the allyl cation is **5**,  $\text{R} = \text{H}$ ), the stability is greater because of increased delocalization due to resonance,<sup>33</sup> where the positive charge is spread over several atoms instead of being concentrated on one (see the molecular-orbital picture of this species on p. 41). Each of the terminal atoms has a charge of  $\sim \frac{1}{2}$  (the charge is exactly  $\frac{1}{2}$  if all of the R groups are the same). Stable cyclic and

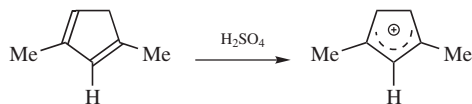
<sup>30</sup>Olah, G.A.; Lukas, J. *J. Am. Chem. Soc.* **1967**, 89, 4739; Olah, G.A.; Olah, J.A., in Olah, G.A.; Schleyer, P.v.R. *Carbonium Ions*, Vol. 2, Wiley, NY, **1969**, pp. 750–764.

<sup>31</sup>Olah, G.A.; Klopman, G.; Schlosberg, R.H. *J. Am. Chem. Soc.* **1969**, 91, 3261. See also, Hogeveen, H.; Gaasbeek, C.J. *Recl. Trav. Chim. Pays-Bas* **1968**, 87, 319.

<sup>32</sup>Olah, G.A.; Svoboda, J.J.; Ku, A.T. *Synthesis* **1973**, 492; Olah, G.A.; Lukas, J. *J. Am. Chem. Soc.* **1967**, 89, 4739.

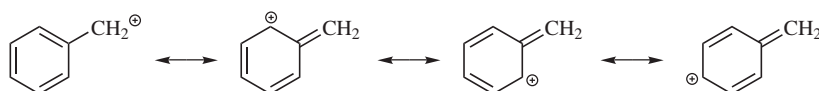
<sup>33</sup>See Barbour, J.B.; Karty, J.M. *J. Org. Chem.* **2004**, 69, 648; Mo, Y. *J. Org. Chem.* **2004**, 69, 5563 and references cited therein.

acyclic allylic-type cations<sup>34</sup> have been prepared by the solution of conjugated dienes in concentrated sulfuric acid, for example,<sup>35</sup>



Stable allylic cations have also been obtained by the reaction between alkyl halides, alcohols, or alkenes (by hydride extraction) and SbF<sub>5</sub> in SO<sub>2</sub> or SO<sub>2</sub>ClF.<sup>36</sup> Bis(allylic) cations<sup>37</sup> are more stable than the simple allylic type, and some of these have been prepared in concentrated sulfuric acid.<sup>38</sup> Arenium ions (p. 658) are familiar examples of this type. Propargyl cations (RC≡CCR<sub>2</sub><sup>+</sup>) have also been prepared.<sup>39</sup>

Canonical forms can be drawn for benzylic cations,<sup>40</sup> similar to those shown above for allylic cations, for example,



A number of benzylic cations have been obtained in solution as SbF<sub>6</sub><sup>-</sup> salts.<sup>41</sup> Diarylmethyl and triarylmethyl cations are still more stable. Triphenylchloromethane ionizes in polar solvents that do not, like water, react with the ion. In SO<sub>2</sub>, the equilibrium



has been known for many years. Both triphenylmethyl and diphenylmethyl cations have been isolated as solid salts<sup>42</sup> and, in fact, Ph<sub>3</sub>C<sup>+</sup> BF<sub>4</sub><sup>-</sup> and related salts are available commercially. Arylmethyl cations are further stabilized if they have

<sup>34</sup>For reviews, see Deno, N.C., in Olah, G.A.; Schleyer, P.v.R. *Carbonium Ions*, Vol. 2, Wiley, NY, **1970**, pp. 783–806; Richey Jr., H.G., in Zabicky, J. *The Chemistry of Alkenes*, Vol. 2, Wiley, NY, **1970**, pp. 39–114.

<sup>35</sup>Deno, N.C.; Richey, Jr., H.G.; Friedman, N.; Hodge, J.D.; Houser, J.J.; Pittman, Jr., C.U. *J. Am. Chem. Soc.* **1963**, 85, 2991.

<sup>36</sup>Olah, G.A.; Spear, R.J. *J. Am. Chem. Soc.* **1975**, 97, 1539 and references cited therein.

<sup>37</sup>For a review of divinylmethyl and trivinylmethyl cations, see Sorensen, T.S., in Olah, G.A.; Schleyer, P.v.R. *Carbonium Ions*, Vol. 2, Wiley, NY, **1970**, pp. 807–835.

<sup>38</sup>Deno, N.C.; Pittman, Jr., C.U. *J. Am. Chem. Soc.* **1964**, 86, 1871.

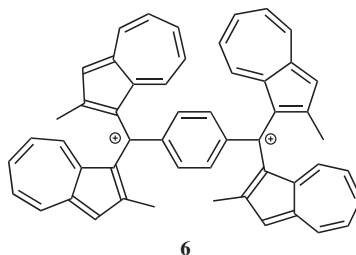
<sup>39</sup>Pittman, Jr., C.U.; Olah, G.A. *J. Am. Chem. Soc.* **1965**, 87, 5632; Olah, G.A.; Spear, R.J.; Westerman, P.W.; Denis, J. *J. Am. Chem. Soc.* **1974**, 96, 5855.

<sup>40</sup>For a review of benzylic, diarylmethyl, and triarylmethyl cations, see Freedman, H.H., in Olah, G.A.; Schleyer, P.v.R. *Carbonium Ions*, Vol. 4, Wiley, NY, **1971**, pp. 1501–1578.

<sup>41</sup>Olah, G.A.; Porter, R.D.; Jeuell, C.L.; White, A.M. *J. Am. Chem. Soc.* **1972**, 94, 2044.

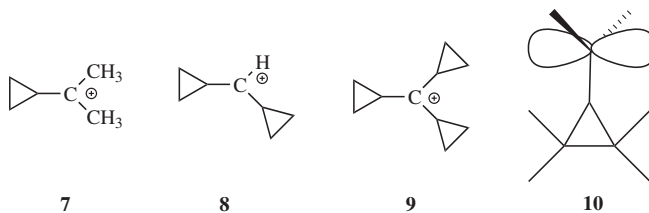
<sup>42</sup>Volz, H.; Schnell, H.W. *Angew. Chem. Int. Ed.* **1965**, 4, 873.

electron-donating substituents in ortho or para positions.<sup>43</sup> Dications<sup>44</sup> and trications are also possible, including the particularly stable dication (**6**), where each positively charged benzylic carbon is stabilized by two azulene rings.<sup>45</sup> A related trication is known where each benzylic cationic center is also stabilized by two azulene rings.<sup>46</sup>



6

Cyclopropylmethyl cations<sup>47</sup> are even more stable than the benzyl type. Ion **9** has been prepared by solution of the corresponding alcohol in 96% sulfuric acid,<sup>48</sup> and **7**, **8**, and similar ions by solution of the alcohols in  $\text{FSO}_3\text{H}-\text{SO}_2-\text{SbF}_5$ .<sup>49</sup> This special stability, which increases with each additional cyclopropyl group, is a



result of conjugation between the bent orbitals of the cyclopropyl rings (p. \$\$\$) and the vacant  $p$  orbital of the cationic carbon (see **10**). Nuclear magnetic resonance and other studies have shown that the vacant  $p$  orbital lies parallel to the C-2,C-3 bond of the cyclopropane ring and not perpendicular to it.<sup>50</sup> In this respect, the

<sup>43</sup>Goldacre, R.J.; Phillips, J.N. *J. Chem. Soc.* **1949**, 1724; Deno, N.C.; Schriesheim, A. *J. Am. Chem. Soc.* **1955**, 77, 3051.

<sup>44</sup>Prakash, G.K.S. *Pure Appl. Chem.* **1998**, 70, 2001.

<sup>45</sup>Ito, S.; Morita, N.; Asao, T. *Tetrahedron Lett.* **1992**, 33, 3773.

<sup>46</sup>Ito, S.; Morita, N.; Asao, T. *Tetrahedron Lett.* **1994**, 35, 751.

<sup>47</sup>For reviews, see, in Olah, G.A.; Schleyer, P.v.R. *Carbonium Ions*, Vol. 3, Wiley, NY, **1972**; Richey, Jr., H.G. pp. 1201–294; Wiberg, K.B.; Hess Jr., B.A.; Ashe III, A.H. pp. 1295–1345.

<sup>48</sup>Deno, N.C.; Richey, Jr., H.G.; Liu, J.S.; Hodge, J.D.; Houser, H.J.; Wisotsky, M.J. *J. Am. Chem. Soc.* **1962**, 84, 2016.

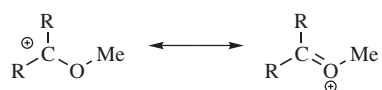
<sup>49</sup>Pittman Jr., C.U.; Olah, G.A. *J. Am. Chem. Soc.* **1965**, 87, 2998; Deno, N.C.; Liu, J.S.; Turner, J.O.; Lincoln, D.N.; Fruit, Jr., R.E. *J. Am. Chem. Soc.* **1965**, 87, 3000.

<sup>50</sup>For example, see Ree, B.; Martin, J.C. *J. Am. Chem. Soc.* **1970**, 92, 1660; Kabakoff, D.S.; Namanworth, E. *J. Am. Chem. Soc.* **1970**, 92, 3234; Buss, V.; Gleiter, R.; Schleyer, P.v.R. *J. Am. Chem. Soc.* **1971**, 93, 3927; Poulter, C.D.; Spillner, C.J. *J. Am. Chem. Soc.* **1974**, 96, 7591; Childs, R.F.; Kostyk, M.D.; Lock, C.J.L.; Mahendran, M. *J. Am. Chem. Soc.* **1990**, 112, 8912; Deno, N.C.; Richey Jr., H.G.; Friedman, N.; Hodge, J.D.; Houser, J.J.; Pittman Jr., C.U. *J. Am. Chem. Soc.* **1963**, 85, 2991.



geometry is similar to that of a cyclopropane ring conjugated with a double bond (p. 218). Cyclopropylmethyl cations are further discussed on pp. 459–463. The stabilizing effect just discussed is unique to cyclopropyl groups. Cyclobutyl and larger cyclic groups are about as effective at stabilizing a carbocation as ordinary alkyl groups.<sup>51</sup>

Another structural feature that increases carbocation stability is the presence, adjacent to the cationic center, of a heteroatom bearing an unshared pair,<sup>52</sup> for example, oxygen,<sup>53</sup> nitrogen,<sup>54</sup> or halogen.<sup>55</sup> Such ions are stabilized by resonance:



The methoxymethyl cation can be obtained as a stable solid,  $\text{MeOCH}_2^+ \text{SbF}_6^-$ .<sup>56</sup> Carbocations containing either  $\alpha$ ,  $\beta$ , or  $\gamma$  silicon atom are also stabilized,<sup>57</sup> relative to similar ions without the silicon atom. In super acid solution, ions such as  $\text{CX}_3^+$  ( $\text{X} = \text{Cl}, \text{Br}, \text{I}$ ) have been prepared.<sup>58</sup> Vinyl-stabilized halonium ions are also known.<sup>59</sup>

Simple acyl cations  $\text{RCO}^+$  have been prepared<sup>60</sup> in solution and the solid state.<sup>61</sup> The acetyl cation  $\text{CH}_3\text{CO}^+$  is about as stable as the *tert*-butyl cation (see, e.g., Table 5.1). The 2,4,6-trimethylbenzoyl and 2,3,4,5,6-pentamethylbenzoyl cations are especially stable (for steric reasons) and are easily formed in 96%  $\text{H}_2\text{SO}_4$ .<sup>62</sup> These

<sup>51</sup>Sorensen, T.S.; Miller, I.J.; Ranganayakulu, K. *Aust. J. Chem.* **1973**, 26, 311.

<sup>52</sup>For a review, see Hevesi, L. *Bull. Soc. Chim. Fr.* **1990**, 697. For examples of stable solutions of such ions, see Kabus, S.S. *Angew. Chem. Int. Ed.* **1966**, 5, 675; Dimroth, K.; Heinrich, P. *Angew. Chem. Int. Ed.* **1966**, 5, 676; Tomalia, D.A.; Hart, H. *Tetrahedron Lett.* **1966**, 3389; Ramsey, B.; Taft, R.W. *J. Am. Chem. Soc.* **1966**, 88, 3058; Olah, G.A.; Liang, G.; Mo, Y.M. *J. Org. Chem.* **1974**, 39, 2394; Borch, R.F. *J. Am. Chem. Soc.* **1968**, 90, 5303; Rabinovitz, M.; Bruck, D. *Tetrahedron Lett.* **1971**, 245.

<sup>53</sup>For a review of ions of the form  $\text{R}_2\text{C}^+-\text{OR}'$ , see Rakhmankulov, D.L.; Akhmatdinov, R.T.; Kantor, E.A. *Russ. Chem. Rev.* **1984**, 53, 888. For a review of ions of the form  $\text{R}'\text{C}^+(\text{OR})_2$  and  $\text{C}^+(\text{OR})_3$ , see Pindur, U.; Müller, J.; Flo, C.; Witzel, H. *Chem. Soc. Rev.* **1987**, 16, 75.

<sup>54</sup>For a review of such ions where nitrogen is the heteroatom, see Scott, F.L.; Butler, R.N., in Olah, G.A.; Schleyer, P.v.R. *Carbonium Ions*, Vol. 4, Wiley, NY, **1974**, pp. 1643–1696.

<sup>55</sup>See Allen, A.D.; Tidwell, T.T. *Adv. Carbocation Chem.* **1989**, 1, 1. See also, Teberekidis, V.I.; Sigalas, M.P. *Tetrahedron* **2003**, 59, 4749.

<sup>56</sup>Olah, G.A.; Svoboda, J.J. *Synthesis* **1973**, 52.

<sup>57</sup>For a review and discussion of the causes, see Lambert, J.B. *Tetrahedron* **1990**, 46, 2677. See also, Lambert, J.B.; Chelius, E.C. *J. Am. Chem. Soc.* **1990**, 112, 8120.

<sup>58</sup>Olah, G.A.; Heiliger, L.; Prakash, G.K.S. *J. Am. Chem. Soc.* **1989**, 111, 8020.

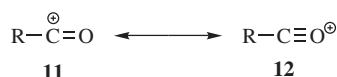
<sup>59</sup>Haubenstock, H.; Sauer, R.R. *Tetrahedron* **2004**, 60, 1191.

<sup>60</sup>For reviews of acyl cations, see Al-Talib, M.; Tashtoush, H. *Org. Prep. Proced. Int.* **1990**, 22, 1; Olah, G.A.; Germain, A.; White, A.M., in Olah, G.A.; Schleyer, P.v.R. *Carbonium Ions*, Vol. 5, Wiley, NY, **1976**, pp. 2049–2133. For a review of the preparation of acyl cations from acyl halides and Lewis acids, see Lindner, E. *Angew. Chem. Int. Ed.* **1970**, 9, 114.

<sup>61</sup>See, for example, Deno, N.C.; Pittman, Jr., C.U.; Wisotsky, M.J. *J. Am. Chem. Soc.* **1964**, 86, 4370; Olah, G.A.; Dunne, K.; Mo, Y.K.; Szilagy, P. *J. Am. Chem. Soc.* **1972**, 94, 4200; Olah, G.A.; Svoboda, J.J. *Synthesis* **1972**, 306.

<sup>62</sup>Hammett, L.P.; Deyrup, A.J. *J. Am. Chem. Soc.* **1933**, 55, 1900; Newman, M.S.; Deno, N.C. *J. Am. Chem. Soc.* **1951**, 73, 3651.

ions are stabilized by a canonical form containing a triple bond (**12**), although the positive charge is principally located on the carbon,<sup>63</sup> so that **11** contributes more than **12**.



The stabilities of most other stable carbocations can also be attributed to resonance. Among these are the tropylium, cyclopropenium,<sup>64</sup> and other aromatic cations discussed in Chapter 2. Where resonance stability is completely lacking, as in the phenyl ( $\text{C}_6\text{H}_5^+$ ) or vinyl cations,<sup>65</sup> the ion, if formed at all, is usually very short lived.<sup>66</sup> Neither vinyl<sup>67</sup> nor phenyl cation has as yet been prepared as a stable species in solution.<sup>68</sup> However, stable alkenyl carbocations have been generated on Zeolite Y.<sup>69</sup>

Various quantitative methods have been developed to express the relative stabilities of carbocations.<sup>70</sup> One of the most common of these, although useful only for relatively stable cations that are formed by ionization of alcohols in acidic solutions, is based on the equation<sup>71</sup>

$$H_R = \text{p}K_{R^+} - \log \frac{C_{R^+}}{C_{\text{ROH}}}$$

<sup>63</sup>Boer, F.P. *J. Am. Chem. Soc.* **1968**, *90*, 6706; Le Carpentier, J.; Weiss, R. *Acta Crystallogr. Sect. B*, **1972**, *1430*. See also, Olah, G.A.; Westerman, P.W. *J. Am. Chem. Soc.* **1973**, *95*, 3706.

<sup>64</sup>See Komatsu, K.; Kitagawa, T. *Chem. Rev.* **2003**, *103*, 1371. Also see, Gilbertson, R.D.; Weakley, T.J.R.; Haley, M.M. *J. Org. Chem.* **2000**, *65*, 1422.

<sup>65</sup>For the preparation and reactivity of a primary vinyl carbocation see Gronheid, R.; Lodder, G.; Okuyama, T. *J. Org. Chem.* **2002**, *67*, 693.

<sup>66</sup>For a review of destabilized carbocations, see Tidwell, T.T. *Angew. Chem. Int. Ed.* **1984**, *23*, 20.

<sup>67</sup>Solutions of aryl-substituted vinyl cations have been reported to be stable for at least a short time at low temperatures. The NMR spectra was obtained: Abram, T.S.; Watts, W.E. *J. Chem. Soc. Chem. Commun.* **1974**, 857; Siehl, H.; Carnahan, Jr., J.C.; Eckes, L.; Hanack, M. *Angew. Chem. Int. Ed.* **1974**, *13*, 675. The 1-cyclobutenyl cation has been reported to be stable in the gas phase: Franke, W.; Schwarz, H.; Stahl, D. *J. Org. Chem.* **1980**, *45*, 3493. See also, Siehl, H.; Koch, E. *J. Org. Chem.* **1984**, *49*, 575.

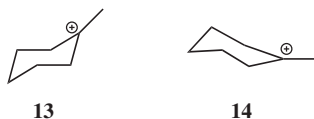
<sup>68</sup>For a monograph, see Stang, P.J.; Rappoport, Z.; Hanack, M.; Subramanian, L.R. *Vinyl Cations*, Academic Press, NY, 1979. For reviews of aryl and/or vinyl cations, see Hanack, M. *Pure Appl. Chem.* **1984**, *56*, 1819, *Angew. Chem. Int. Ed.* **1978**, *17*, 333; *Acc. Chem. Res.* **1976**, *9*, 364; Rappoport, Z. *Reactiv. Intermed. (Plenum)* **1983**, *3*, 427; Ambroz, H.B.; Kemp, T.J. *Chem. Soc. Rev.* **1979**, *8*, 353; Richey Jr., H.G.; Richey, J.M., in Olah, G.A.; Schleyer, P.v.R. *Carbonium Ions*, Vol. 2, Wiley, NY, **1970**, pp. 899–957; Richey Jr., H.G., in Zabicky, J. *The Chemistry of Alkenes*, Vol. 2, Wiley, NY, **1970**, pp. 42–49; Modena, G.; Tonellato, U. *Adv. Phys. Org. Chem.* **1971**, *9*, 185; Stang, P.J. *Prog. Phys. Org. Chem.* **1973**, *10*, 205. See also, Charton, M. *Mol. Struct. Energ.* **1987**, *4*, 271. For a computational study, see Glaser, R.; Horan, C. J.; Lewis, M.; Zollinger, H. *J. Org. Chem.* **1999**, *64*, 902.

<sup>69</sup>Yang, S.; Kondo, J.N.; Domen, K. *Chem. Commun.* **2001**, 2008.

<sup>70</sup>For reviews, see Bagno, A.; Scorrano, G.; More O'Ferrall, R.A. *Rev. Chem. Intermed.* **1987**, *7*, 313; Bethell, D.; Gold, V. *Carbonium Ions*, Academic Press, NY, **1967**, pp. 59–87.

<sup>71</sup>Deno, N.C.; Berkheimer, H.E.; Evans, W.L.; Peterson, H.J. *J. Am. Chem. Soc.* **1959**, *81*, 2344.

$pK_{R^+}$  is the  $pK$  value for the reaction  $R^+ + 2 H_2O \rightleftharpoons ROH + H_3O^+$  and is a measure of the stability of the carbocation. The  $H_R$  parameter is an early obtainable measurement of the stability of a solvent (see p. 371) and approaches  $pH$  at low concentrations of acid. In order to obtain  $pK_{R^+}$ , for a cation  $R^+$ , one dissolves the alcohol  $ROH$  in an acidic solution of known  $H_R$ . Then the concentration of  $R^+$  and  $ROH$  are obtained, generally from spectra, and  $pK_{R^+}$  is easily calculated.<sup>72</sup> A measure of carbocation stability that applies to less-stable ions is the dissociation energy  $D(R^+-H^-)$  for the cleavage reaction  $R-H \rightarrow R^+ + H^-$ , which can be obtained from photoelectron spectroscopy and other measurements. Some values of  $D(R^+-H^-)$  are shown in Table 5.2.<sup>75</sup> Within a given class of ion (primary, secondary, allylic, aryl, etc.),  $D(R^+-H^-)$  has been shown to be a linear function of the logarithm of the number of atoms in  $R^+$ , with larger ions being more stable.<sup>74</sup>

TABLE 5.2.  $R-H \rightarrow R^+ + H^-$  Dissociation Energies in the Gas Phase

Ion	$D(R^+-H^-)$		Reference
	kcal mol <sup>-1</sup>	kJ mol <sup>-1</sup>	
$CH_3^+$	314.6	1316	73
$C_2H_5^+$	276.7	1158	73
$(CH_3)_2CH^+$	249.2	1043	73
$(CH_3)_3C^+$	231.9	970.3	73
$C_6H_5^+$	294	1230	74
$H_2C=CH^+$	287	1200	74
$H_2C=CH-CH_2^+$	256	1070	74
Cyclopentyl	246	1030	74
$C_6H_5CH_2^+$	238	996	74
$CH_3CHO$	230	962	74

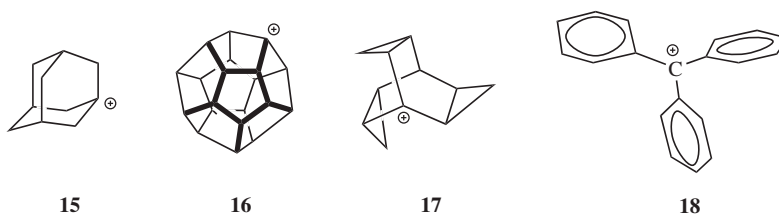
<sup>72</sup>For a list of stabilities of 39 typical carbocations, see Arnett, E.M.; Hofelich, T.C. *J. Am. Chem. Soc.* **1983**, *105*, 2889. See also, Schade, C.; Mayr, H.; Arnett, E.M. *J. Am. Chem. Soc.* **1988**, *110*, 567; Schade, C.; Mayr, H. *Tetrahedron* **1988**, *44*, 5761.

<sup>73</sup>Schultz, J.C.; Houle, F.A.; Beauchamp, J.L. *J. Am. Chem. Soc.* **1984**, *106*, 3917.

<sup>74</sup>Lossing, F.P.; Holmes, J.L. *J. Am. Chem. Soc.* **1984**, *106*, 6917.

<sup>75</sup>Hammett, L.P.; Deyrup, A.J. *J. Am. Chem. Soc.* **1933**, *55*, 1900; Newman, M.S.; Deno, N.C. *J. Am. Chem. Soc.* **1951**, *73*, 3651; Boer, F.P. *J. Am. Chem. Soc.* **1968**, *90*, 6706; Le Carpentier, J.; Weiss, R. *Acta Crystallogr. Sect. B*, **1972**, 1430. See also, Olah, G.A.; Westerman, P.W. *J. Am. Chem. Soc.* **1973**, *95*, 3706. See also, Staley, R.H.; Wieting, R.D.; Beauchamp, J.L. *J. Am. Chem. Soc.* **1977**, *99*, 5964; Arnett, E.M.; Petro, C. *J. Am. Chem. Soc.* **1978**, *100*, 5408; Arnett, E.M.; Pienta, N.J. *J. Am. Chem. Soc.* **1980**, *102*, 3329.

Since the central carbon of tricoordinated carbocations has only three bonds and no other valence electrons, the bonds are  $sp^2$  and should be planar.<sup>76</sup> Raman, IR, and NMR spectroscopic data on simple alkyl cations show this to be so.<sup>77</sup> In methylcyclohexyl cations, there are two chair conformations where the carbon bearing the positive charge is planar (**13** and **14**), and there is evidence that **14** is more stable due to a difference in hyperconjugation.<sup>78</sup> Other evidence is that carbocations are difficult to form at bridgehead atoms in [2.2.1] systems,<sup>79</sup> where they cannot be planar (see p. 435).<sup>80</sup> Bridgehead carbocations are known, however, as in [2.1.1]hexanes<sup>81</sup> and cubyl carbocations.<sup>82</sup> However, larger bridgehead ions can exist. For example, the adamantyl cation (**15**) has been synthesized, as the  $SF_6^-$  salt.<sup>83</sup> The relative stability of 1-adamantyl cations is influenced by the number and nature of substituents. For example, the stability of the 1-adamantyl cation increases with the number of isopropyl substituents at C-3, C-5 and C-7.<sup>84</sup> Among other bridgehead cations that have been prepared in super acid solution at  $-78^\circ\text{C}$  are the dodecahydryl cation (**16**)<sup>85</sup> and the 1-trishomobarrellyl cation (**17**).<sup>86</sup> In the latter



<sup>76</sup>For discussions of the stereochemistry of carbocations, see Henderson, J.W. *Chem. Soc. Rev.* **1973**, 2, 397; Buss, V.; Schleyer, P.v.R.; Allen, L.C. *Top. Stereochem.* **1973**, 7, 253; Schleyer, P.v.R., in Chirudoglu, G. *Conformational Analysis*; Academic Press, NY, **1971**, p. 241; Hehre, W.J. *Acc. Chem. Res.* **1975**, 8, 369; Freedman, H.H., in Olah, G.A.; Schleyer, P.v.R. *Carbonium Ions*, Vol. 4, Wiley, NY, **1974**, pp. 1561–574.

<sup>77</sup>Olah, G.A.; DeMember, J.R.; Commeyras, A.; Bribes, J.L. *J. Am. Chem. Soc.* **1971**, 93, 459; Yannoni, C.S.; Kendrick, R.D.; Myhre, P.C.; Bebout, D.C.; Petersen, B.L. *J. Am. Chem. Soc.* **1989**, 111, 6440.

<sup>78</sup>Rauk, A.; Sorensen, T.S.; Maerker, C.; de M. Carneiro, J.W.; Sieber, S.; Schleyer, P.v.R. *J. Am. Chem. Soc.* **1996**, 118, 3761.

<sup>79</sup>For a review of bridgehead carbocations, see Fort, Jr., R.C., in Olah, G.A.; Schleyer, P.v.R. *Carbonium Ions*, Vol. 4, Wiley, NY, **1974**, pp. 1783–1835.

<sup>80</sup>Della, E.W.; Schiesser, C.H. *J. Chem. Soc. Chem. Commun.* **1994**, 417.

<sup>81</sup>Ahman, J.; Somfai, P.; Tanner, D. *J. Chem. Soc. Chem. Commun.* **1994**, 2785.

<sup>82</sup>Della, E.W.; Head, N.J.; Janowski, W.K.; Schiesser, C.H. *J. Org. Chem.* **1993**, 58, 7876.

<sup>83</sup>Schleyer, P.v.R.; Fort, Jr., R.C.; Watts, W.E.; Comisarow, M.B.; Olah, G.A. *J. Am. Chem. Soc.* **1964**, 86, 4195; Olah, G.A.; Prakash, G.K.S.; Shih, J.G.; Krishnamurthy, V.V.; Mateescu, G.D.; Liang, G.; Sipos, G.; Buss, V.; Gund, T.M.; Schleyer, P.v.R. *J. Am. Chem. Soc.* **1985**, 107, 2764. See also, Kruppa, G.H.; Beauchamp, J.L. *J. Am. Chem. Soc.* **1986**, 108, 2162; Laube, T. *Angew. Chem. Int. Ed.* **1986**, 25, 349.

<sup>84</sup>Takeuchi, K.; Okazaki, T.; Kitagawa, T.; Ushino, T.; Ueda, K.; Endo, T.; Notario, R. *J. Org. Chem.* **2001**, 66, 2034.

<sup>85</sup>Olah, G.A.; Prakash, G.K.S.; Fessner, W.; Kobayashi, T.; Paquette, L.A. *J. Am. Chem. Soc.* **1988**, 110, 8599.

<sup>86</sup>de Meijere, A.; Schallner, O. *Angew. Chem. Int. Ed.* **1973**, 12, 399.

**TABLE 5.3.** The  $^{13}\text{C}$  Chemical Shift Values, in Parts Per Million from  $^{13}\text{CS}_2$  for the Charged Carbon Atom of Some Carbocations in  $\text{SO}_2\text{ClF-SbF}_5$ ,  $\text{SO}_2\text{-FSO}_3\text{H-SbF}_6$ , or  $\text{SO}_2\text{-SbF}_5$ <sup>90</sup>

Ion	Chemical Shift	Temperature, °C	Ion	Chemical Shift	Temperature, °C
$\text{Et}_2\text{MeC}^+$	-139.4	-20	$\text{C}(\text{OH})_3^+$	+28.0	-50
$\text{Me}_2\text{EtC}^+$	-139.2	-60	$\text{PhMe}_2\text{C}^+$	-61.1	-60
$\text{Me}_3\text{C}^+$	-135.4	-20	$\text{PhMeCH}^+$	-40 <sup>91</sup>	
$\text{Me}_2\text{CH}^+$	-125.0	-20	$\text{Ph}_2\text{CH}^+$	-5.6	-60
$\text{Me}_2\text{COH}^+$	-55.7	-50	$\text{Ph}_3\text{C}^+$	-18.1	-60
$\text{MeC}(\text{OH})_2^+$	-1.6	-30	$\text{Me}_2(\text{cyclopropyl})\text{C}^+$	-86.8	-60
$\text{HC}(\text{OH})_2^+$	+17.0	-30			

case, the instability of the bridgehead position is balanced by the extra stability gained from the conjugation with the three cyclopropyl groups.

Triarylmethyl cations (**18**)<sup>87</sup> are propeller shaped, although the central carbon and the three ring carbons connected to it are in a plane.<sup>88</sup> The three benzene rings cannot be all in the same plane because of steric hindrance, although increased resonance energy would be gained if they could.

An important tool for the investigation of carbocation structure is measurement of the  $^{13}\text{C}$  NMR chemical shift of the carbon atom bearing the positive charge.<sup>89</sup> This shift approximately correlates with electron density on the carbon. The  $^{13}\text{C}$  chemical shifts for a number of ions are given in Table 5.3.<sup>90</sup> As shown in this table, the substitution of an ethyl for a methyl or a methyl for a hydrogen causes a down-field shift, indicating that the central carbon becomes somewhat more positive. On the other hand, the presence of hydroxy or phenyl groups decreases the positive character of the central carbon. The  $^{13}\text{C}$  chemical shifts are not always in exact order of carbocation stabilities as determined in other ways. Thus the chemical shift shows that the triphenylmethyl cation has a more positive central carbon than diphenylmethyl cation, although the former is more stable. Also, the 2-cyclopropylpropyl and 2-phenylpropyl cations have shifts of -86.8 and -61.1, respectively, although we have seen that according to other criteria a cyclopropyl group is better

<sup>87</sup>For a review of crystal-structure determinations of triarylmethyl cations and other carbocations that can be isolated in stable solids, see Sundaralingam, M.; Chwang, A.K., in Olah, G.A.; Schleyer, P.v.R. *Carbonium Ions*, Vol. 5, Wiley, NY, **1976**, pp. 2427-2476.

<sup>88</sup>Sharp, D.W.A.; Sheppard, N. *J. Chem. Soc.* **1957**, 674; Gomes de Mesquita, A.H.; MacGillavry, C.H.; Eriks, K. *Acta Crystallogr.* **1965**, 18, 437; Schuster, I.I.; Colter, A.K.; Kurland, R.J. *J. Am. Chem. Soc.* **1968**, 90, 4679.

<sup>89</sup>For reviews of the nmr spectra of carbocations, see Young, R.N. *Prog. Nucl. Magn. Reson. Spectrosc.* **1979**, 12, 261; Farnum, D.G. *Adv. Phys. Org. Chem.* **1975**, 11, 123.

<sup>90</sup>Olah, G.A.; White, A.M. *J. Am. Chem. Soc.* **1968**, 90, 1884; **1969**, 91, 5801. For  $^{13}\text{C}$  NMR data for additional ions, see Olah, G.A.; Donovan, D.J. *J. Am. Chem. Soc.* **1977**, 99, 5026; Olah, G.A.; Prakash, G.K.S.; Liang, G. *J. Org. Chem.* **1977**, 42, 2666.

than a phenyl group at stabilizing a carbocation.<sup>91</sup> The reasons for this discrepancy are not fully understood.<sup>88,92</sup>

### Nonclassical Carbocations

These carbocations are discussed at pp. 450–455.

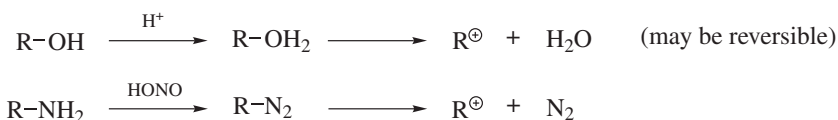
### The Generation and Fate of Carbocations

A number of methods are available to generate carbocations, stable or unstable.

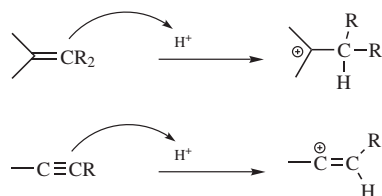
1. A direct ionization, in which a leaving group attached to a carbon atom leaves with its pair of electrons, as in solvolysis reactions of alkyl halides (see p. 480) or sulfonate esters (see p. 522):



2. Ionization after an initial reaction that converts one functional group into a leaving group, as in protonation of an alcohol to give an oxonium ion or conversion of a primary amine to a diazonium salt, both of which ionize to the corresponding carbocation:



3. A proton or other positive species adds to one atom of an alkene or alkyne, leaving the adjacent carbon atom with a positive charge (see Chapters 11, 15).

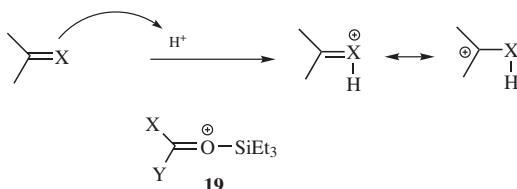


4. A proton or other positive species adds to one atom of a C=X bond, where X = O, S, N in most cases, leaving the adjacent carbon atom with a positive charge (see Chapter 16). When X = O, S this ion is resonance stabilized, as shown. When X = NR, protonation leads to an iminium ion, with the charge localized on the

<sup>91</sup>Olah, G.A.; Porter, R.D.; Kelly, D.P. *J. Am. Chem. Soc.* **1971**, 93, 464.

<sup>92</sup>For discussions, see Brown, H.C.; Peters, E.N. *J. Am. Chem. Soc.* **1973**, 95, 2400; **1977**, 99, 1712; Olah, G.A.; Westerman, P.W.; Nishimura, J. *J. Am. Chem. Soc.* **1974**, 96, 3548; Wolf, J.F.; Harch, P.G.; Taft, R.W.; Hehre, W.J. *J. Am. Chem. Soc.* **1975**, 97, 2902; Fliszár, S. *Can. J. Chem.* **1976**, 54, 2839; Kitching, W.; Adcock, W.; Aldous, G. *J. Org. Chem.* **1979**, 44, 2652. See also, Larsen, J.W.; Bouis, P.A. *J. Am. Chem. Soc.* **1975**, 97, 4418; Volz, H.; Shin, J.; Streicher, H. *Tetrahedron Lett.* **1975**, 1297; Larsen, J.W. *J. Am. Chem. Soc.* **1978**, 100, 330.

nitrogen. A silylated carboxonium ion, such as **19**, has been reported.<sup>93</sup>



Formed by either process, carbocations are most often short-lived transient species and react further without being isolated. The intrinsic barriers to formation and reaction of carbocations has been studied.<sup>94</sup> Carbocations have been generated in zeolites.<sup>95</sup>

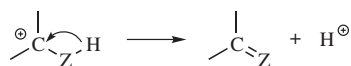
The two chief pathways by which carbocations react to give stable products are the reverse of the two pathways just described.

1. *The Carbocation May Combine with a Species Possessing an Electron Pair* (a Lewis acid–base reaction, see Chapter 8):



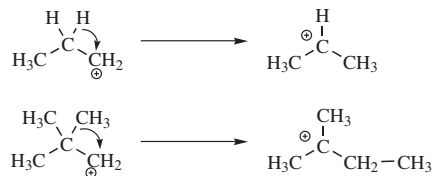
This species may be  $\text{OH}^-$ , halide ion, or any other negative ion, or it may be a neutral species with a pair to donate, in which case, of course, the immediate product must bear a positive charge (see Chapters 10, 13, 15, 16). These reactions are very fast. A recent study measured  $k_s$  (the rate constant for reaction of a simple tertiary carbocation) to be  $3.5 \times 10^{12} \text{ s}^{-1}$ .<sup>96</sup>

2. *The Carbocation May Lose a Proton* (or much less often, another positive ion) from the adjacent atom (see Chapters 11, 17):



Carbocations can also adopt two other pathways that lead not to stable products, but to other carbocations:

3. *Rearrangement.* An alkyl or aryl group or a hydrogen (sometimes another group) migrates with its electron pair to the positive center, leaving another positive charge behind (see Chapter 18):



<sup>93</sup>Prakash, G.K.S.; Bae, C.; Rasul, G.; Olah, G.A. *J. Org. Chem.* **2002**, 67, 1297.

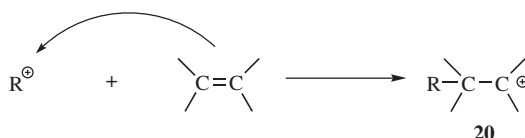
<sup>94</sup>Richard, J.P.; Amyes, T.L.; Williams, K.B. *Pure. Appl. Chem.* **1998**, 70, 2007.

<sup>95</sup>Song, W.; Nicholas, J. B.; Haw, J. F. *J. Am. Chem. Soc.* **2001**, 123, 121.

<sup>96</sup>Toteva, M.M.; Richard, J.P. *J. Am. Chem. Soc.* **1996**, 118, 11434.

A novel rearrangement has been observed. The 2-methyl-2-butyl-1- $^{13}\text{C}$  cation ( $^{13}\text{C}$ -labeled *tert*-amyl cation) shows an interchange of the inside and outside carbons with a barrier of  $19.5 (\pm 2.0 \text{ kcal mol}^{-1})$ .<sup>97</sup> Another unusual migratory process has been observed for the nonamethylcyclopentyl cation. It has been shown that “four methyl groups undergo rapid circumambulatory migration with a barrier  $< 2 \text{ kcal mol}^{-1}$  while five methyl groups are fixed to ring carbons, and the process that equalizes the two sets of methyls has a barrier of  $7.0 \text{ kcal mol}^{-1}$ .”<sup>98</sup>

4. *Addition.* A carbocation may add to a double bond, generating a positive charge at a new position (see Chapters 11, 15):



Whether formed by pathway 3 or 4, the new carbocation normally reacts further in an effort to stabilize itself, usually by pathway 1 or 2. However, **20** can add to another alkene molecule, and this product can add to still another, and so on. This is one of the mechanisms for vinyl polymerization.

## CARBANIONS

### Stability and Structure<sup>99</sup>

An *organometallic compound* is a compound that contains a bond between a carbon atom and a metal atom. Many such compounds are known, and organometallic chemistry is a very large area, occupying a borderline region between organic and inorganic chemistry. Many carbon–metal bonds (e.g., carbon–mercury bonds)

<sup>97</sup>Vrcek, V.; Saunders, M.; Kronja, O. *J. Am. Chem. Soc.* **2004**, 126, 13703.

<sup>98</sup>Kronja, O.; Kohli, T.-P.; Mayr, H.; Saunders, M. *J. Am. Chem. Soc.* **2000**, 122, 8067.

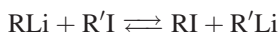
<sup>99</sup>For monographs, see Buncl, E.; Durst, T. *Comprehensive Carbanion Chemistry*, pts. A, B, and C; Elsevier, NY, **1980**, **1984**, **1987**; Bates, R.B.; Ogle, C.A. *Carbanion Chemistry*, Springer, NY, **1983**; Stowell, J.C. *Carbanions in Organic Synthesis*, Wiley, NY, **1979**; Cram, D.J. *Fundamentals of Carbanion Chemistry*, Academic Press, NY, **1965**. For reviews, see Staley, S.W. *React. Intermed. (Wiley)* **1985**, 3, 19; Staley, S.W.; Dustman, C.K. *React. Intermed. (Wiley)* **1981**, 2, 15; le Noble, W.J. *React. Intermed. (Wiley)* **1978**, 1, 27; Solov'yanov, A.A.; Beletskaya, I.P. *Russ. Chem. Rev.* **1978**, 47, 425; Isaacs, N.S. *Reactive Intermediates in Organic Chemistry*, Wiley, NY, **1974**, pp. 234–293; Kaiser, E.M.; Slocum, D.W., in McManus, S.P. *Organic Reactive Intermediates*, Academic Press, NY, **1973**, pp. 337–422; Ebel, H.F. *Fortchr. Chem. Forsch.* **1969**, 12, 387; Cram, D.J. *Surv. Prog. Chem.* **1968**, 4, 45; Reutov, O.A.; Beletskaya, I.P. *Reaction Mechanisms of Organometallic Compounds*, North Holland Publishing Co, Amsterdam, The Netherlands, **1968**, pp. 1–64; Streitwieser Jr., A.; Hammons, J.H. *Prog. Phys. Org. Chem.* **1965**, 3, 41. For reviews of nmr spectra of carbanions, see Young, R.N. *Prog. Nucl. Magn. Reson. Spectrosc.* **1979**, 12, 261. For a review of dicarbanions, see Thompson, C.M.; Green, D.L.C. *Tetrahedron* **1991**, 47, 4223.



are undoubtedly covalent, but in bonds between carbon and the more active metals the electrons are closer to the carbon. Whether the position of the electrons in a given bond is close enough to the carbon to justify calling the bond ionic and the carbon moiety a carbanion depends on the metal, on the structure of the carbon moiety, and on the solvent and in some cases is a matter of speculation. In this section, we discuss carbanions with little reference to the metal. In the next section, we will deal with the structures of organometallic compounds.

By definition, every carbanion possesses an unshared pair of electrons and is therefore a base. When a carbanion accepts a proton, it is converted to its conjugate acid (see Chapter 8). The stability of the carbanion is directly related to the strength of the conjugate acid. The weaker the acid, the greater the base strength and the lower the stability of the carbanion.<sup>100</sup> By stability here we mean stability toward a proton donor; the lower the stability, the more willing the carbanion is to accept a proton from any available source, and hence to end its existence as a carbanion. Thus the determination of the order of stability of a series of carbanions is equivalent to a determination of the order of strengths of the conjugate acids, and one can obtain information about relative carbanion stability from a table of acid strengths like Table 8.1.

Unfortunately, it is not easy to measure acid strengths of very weak acids like the conjugate acids of simple unsubstituted carbanions. There is little doubt that these carbanions are very unstable in solution, and in contrast to the situation with carbocations, efforts to prepare solutions in which carbanions, such as ethyl or isopropyl, exist in a relatively free state have not yet been successful. Nor has it been possible to form these carbanions in the gas phase. Indeed, there is evidence that simple carbanions, such as ethyl and isopropyl, are unstable toward loss of an electron, which converts them to radicals.<sup>101</sup> Nevertheless, there have been several approaches to the problem. Applequist and O'Brien<sup>102</sup> studied the position of equilibrium for the reaction



in ether and ether-pentane. The reasoning in these experiments was that the R group that forms the more stable carbanion would be more likely to be bonded to lithium than to iodine. Carbanion stability was found to be in this order: vinyl > phenyl > cyclopropyl > ethyl > *n*-propyl > isobutyl > neopentyl > cyclobutyl > cyclopentyl. In a somewhat similar approach, Dessy and co-workers<sup>103</sup> treated a

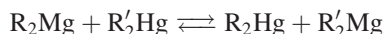
<sup>100</sup>For a monograph on hydrocarbon acidity, see Reutov, O.A.; Beletskaya, I.P.; Butin, K.P. *CH-Acids*; Pergamon: Elmsford, NY, **1978**. For a review, see Fischer, H.; Rewicki, D. *Prog. Org. Chem.* **1968**, 7, 116.

<sup>101</sup>See Gaul, S.T.; Squires, R.R. *J. Am. Chem. Soc.* **1988**, 110, 607; Schleyer, P.v.R.; Spitznagel, G.W.; Chandrasekhar, J. *Tetrahedron Lett.* **1986**, 27, 4411.

<sup>102</sup>Applequist, D.E.; O'Brien, D.F. *J. Am. Chem. Soc.* **1963**, 85, 743.

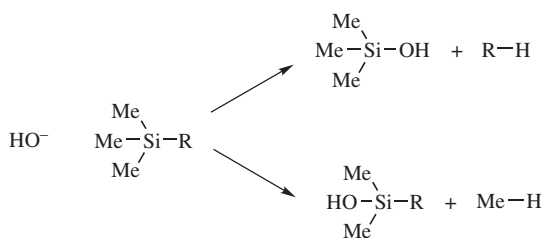
<sup>103</sup>Dessy, R.E.; Kitching, W.; Psarras, T.; Salinger, R.; Chen, A.; Chivers, T. *J. Am. Chem. Soc.* **1966**, 88, 460.

number of alkylmagnesium compounds with a number of alkylmercury compounds in tetrahydrofuran (THF), setting up the equilibrium



where the group of greater carbanion stability is linked to magnesium. The carbanion stability determined this way was in the order phenyl > vinyl > cyclopropyl > methyl > ethyl > isopropyl. The two stability orders are in fairly good agreement, and they show that stability of simple carbanions decreases in the order methyl > primary > secondary. It was not possible by the experiments of Dessy and co-workers to determine the position of *tert*-butyl, but there seems little doubt that it is still less stable. We can interpret this stability order solely as a consequence of the field effect since resonance is absent. The electron-donating alkyl groups of isopropyl result in a greater negative charge density at the central carbon atom (compared with methyl), thus decreasing its stability. The results of Applequist and O'Brien show that  $\beta$  branching also decreases carbanion stability. Cyclopropyl occupies an apparently anomalous position, but this is probably due to the large amount of *s* character in the carbanionic carbon (see p. 254).

A different approach to the problem of hydrocarbon acidity, and hence carbanion stability is that of Shatenshtein and co-workers, who treated hydrocarbons with deuterated potassium amide and measured the rates of hydrogen exchange.<sup>104</sup> The experiments did not measure *thermodynamic* acidity, since rates were measured, not positions of equilibria. They measured *kinetic* acidity, that is, which compounds gave up protons most rapidly (see p. 307 for the distinction between thermodynamic and kinetic control of product). Measurements of rates of hydrogen exchange enable one to compare acidities of a series of acids against a given base even where the positions of the equilibria cannot be measured because they lie too far to the side of the starting materials, that is, where the acids are too weak to be converted to their conjugate bases in measurable amounts. Although the correlation between thermodynamic and kinetic acidity is far from perfect,<sup>105</sup> the results of the rate measurements, too, indicated that the order of carbanion stability is methyl > primary > secondary > tertiary.<sup>104</sup>



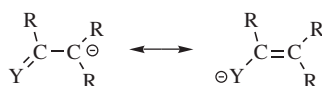
<sup>104</sup>For reviews, see Jones, J.R. *Surv. Prog. Chem.* **1973**, 6, 83; Shatenshtein, A.I.; Shapiro, I.O. *Russ. Chem. Rev.* **1968**, 37, 845.

<sup>105</sup>For example, see Bordwell, F.G.; Matthews, W.S.; Vanier, N.R. *J. Am. Chem. Soc.* **1975**, 97, 442.

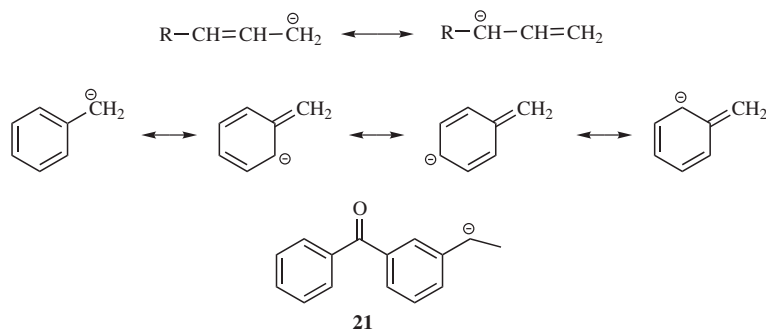
However, experiments in the gas phase gave different results. In reactions of  $^-OH$  with alkyltrimethylsilanes, it is possible for either R or Me to cleave. Since the R or Me comes off as a carbanion or incipient carbanion, the product ratio RH/MeH can be used to establish the relative stabilities of various R groups. From these experiments a stability order of neopentyl > cyclopropyl > *tert*-butyl > *n*-propyl > methyl > isopropyl > ethyl was found.<sup>106</sup> On the other hand, in a different kind of gas-phase experiment, Graul and Squires were able to observe  $CH_3^-$  ions, but not the ethyl, isopropyl, or *tert*-butyl ions.<sup>107</sup>

Many carbanions are far more stable than the simple kind mentioned above. The increased stability is due to certain structural features:

1. *Conjugation of the Unshared Pair with an Unsaturated Bond:*



In cases where a double or triple bond is located  $\alpha$  to the carbanionic carbon, the ion is stabilized by resonance in which the unshared pair overlaps with the  $\pi$  electrons of the double bond. This factor is responsible for the stability of the allylic<sup>108</sup> and benzylic<sup>109</sup> types of carbanions:



Diphenylmethyl and triphenylmethyl anions are still more stable and can be kept in solution indefinitely if water is rigidly excluded.<sup>110</sup>

<sup>106</sup>DePuy, C.H.; Gronert, S.; Barlow, S.E.; Bierbaum, V.M.; Damrauer, R. *J. Am. Chem. Soc.* **1989**, *111*, 1968. The same order (for *t*-Bu, Me, *i*Pr, and Et) was found in gas-phase cleavages of alkoxides (**12-41**): Tumas, W.; Foster, R.F.; Brauman, J.I. *J. Am. Chem. Soc.* **1984**, *106*, 4053.

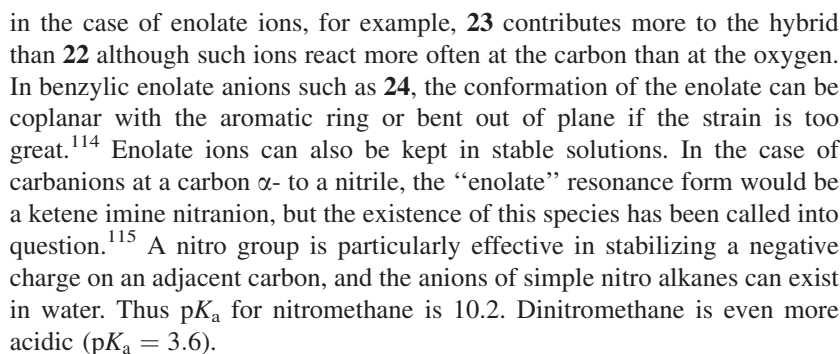
<sup>107</sup>Graul, S.T.; Squires, R.R. *J. Am. Chem. Soc.* **1988**, *110*, 607.

<sup>108</sup>For a review of allylic anions, see Richey, Jr., H.G., in Zabicky, J. *The Chemistry of Alkenes*, Vol. 2, Wiley, NY, **1970**, pp. 67–77.

<sup>109</sup>Although benzylic carbanions are more stable than the simple alkyl type, they have not proved stable enough for isolation so far. The benzyl carbanion has been formed and studied in submicrosecond times; Bockrath, B.; Dorfman, L.M. *J. Am. Chem. Soc.* **1974**, *96*, 5708.

<sup>110</sup>For a review of spectrophotometric investigations of this type of carbanion, see Buncel, E.; Menon, B., in Buncel, E.; Durst, T. *Comprehensive Carbanion Chemistry*, pts. A, B, and C, Elsevier, NY, **1980**, **1984**, **1987**, pp. 97–124.

Where the carbanionic carbon is conjugated with a carbon–oxygen or carbon–nitrogen multiple bond ( $Y = O$  or  $N$ ), the stability of the ion is greater than that of the triarylmethyl anions, since these electronegative atoms are better capable of bearing a negative charge than carbon. However, it is questionable whether ions of this type should be called carbanions at all, since



By combining a very stable carbanion with a very stable carbocation, Okamoto and co-workers<sup>117</sup> were able to isolate the salt **25**, as well as several

<sup>111</sup> Kinoshita, T.; Fujita, M.; Kaneko, H.; Takeuchi, K.-i.; Yoshizawa, K.; Yamabe, T. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 1145.

<sup>112</sup> Olmstead, M.M.; Power, P.P. *J. Am. Chem. Soc.* **1985**, *107*, 2174.

<sup>113</sup> Laferriere, M.; Sanrame, C.N.; Scaiano, J.C. *Org. Lett.* **2004**, *6*, 873.

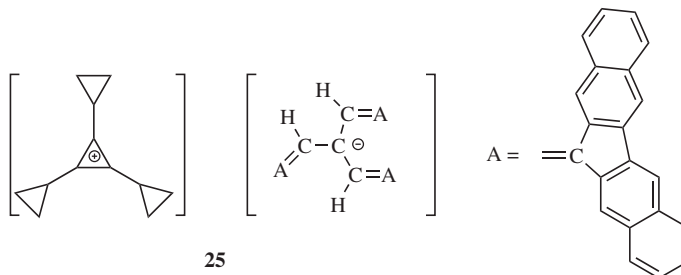
<sup>114</sup> Eldin, S.; Whalen, D.L.; Pollack, R.M. *J. Org. Chem.* **1993**, *58*, 3490.

<sup>115</sup> Abbotto, A.; Bradamanti, S.; Pagani, G.A. *J. Org. Chem.* **1993**, *58*, 449.

<sup>116</sup> Perkins, M.J.; Peynircioglu, N.B. *Tetrahedron* **1985**, *41*, 225.

<sup>117</sup> Okamoto, K.; Kitagawa, T.; Takeuchi, K.; Komatsu, K.; Kinoshita, T.; Aonuma, S.; Nagai, M.; Miyabo, A. *J. Org. Chem.* **1990**, *55*, 996. See also, Okamoto, K.; Kitagawa, T.; Takeuchi, K.; Komatsu, K.; Miyabo, A. *J. Chem. Soc. Chem. Commun.* **1988**, 923.

similar salts, as stable solids. These are salts that consist entirely of carbon and hydrogen.

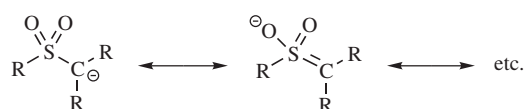


2. *Carbanions Increase in Stability with an Increase in the Amount of  $s$  Character at the Carbanionic Carbon.* Thus the order of stability is



Acetylene, where the carbon is  $sp$  hybridized with 50%  $s$  character, is much more acidic than ethylene<sup>118</sup> ( $sp^2$ , 33%  $s$ ), which in turn is more acidic than ethane, with 25%  $s$  character. Increased  $s$  character means that the electrons are closer to the nucleus and hence of lower energy. As previously mentioned, cyclopropyl carbanions are more stable than methyl, owing to the larger amount of  $s$  character as a result of strain (see p. 218).

3. *Stabilization by Sulfur<sup>119</sup> or Phosphorus.* Attachment to the carbanionic carbon of a sulfur or phosphorus atom causes an increase in carbanion stability, although the reasons for this are in dispute. One theory is that there is overlap of the unshared pair with an empty  $d$  orbital<sup>120</sup> ( $p\pi-d\pi$  bonding, see p. 52). For example, a carbanion containing the  $\text{SO}_2\text{R}$  group would be written



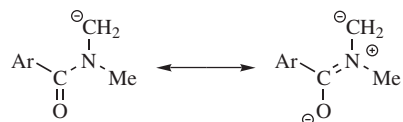
<sup>118</sup>For a review of vinylic anions, see Richey, Jr., H.G., in Zabicky, J. *The Chemistry of Alkenes*, Vol. 2, Wiley, NY, **1970**, pp. 49–56.

<sup>119</sup>For reviews of sulfur-containing carbanions, see Oae, S.; Uchida, Y., in Patai, S.; Rappoport, Z.; Stirling, C. *The Chemistry of Sulphones and Sulphoxides*, Wiley, NY, **1988**, pp. 583–664; Wolfe, S., in Bernardi, F.; Csizmadia, I.G.; Mangini, A. *Organic Sulfur Chemistry*, Elsevier, NY, **1985**, pp. 133–190; Block, E. *Reactions of Organosulfur Compounds*; Academic Press, NY, **1978**, pp. 42–56; Durst, T.; Viau, R. *Intra-Sci. Chem. Rep.* **1973**, 7 (3), 63. For a review of selenium-stabilized carbanions, see Reich, H.J., in Liotta, D.C. *Organoselenium Chemistry*, Wiley, NY, **1987**, pp. 243–276.

<sup>120</sup>For support for this theory, see Wolfe, S.; LaJohn, L.A.; Bernardi, F.; Mangini, A.; Tonachini, G. *Tetrahedron Lett.* **1983**, 24, 3789; Wolfe, S.; Stolow, A.; LaJohn, L.A. *Tetrahedron Lett.* **1983**, 24, 4071.

However, there is evidence against *d*-orbital overlap; and the stabilizing effects have been attributed to other causes.<sup>121</sup> In the case of a PhS substituent, carbanion stabilization is thought to be due to a combination of the inductive and polarizability effects of the group, and *d*-*p* $\pi$  resonance and negative hyperconjugation play a minor role, if any.<sup>122</sup> An  $\alpha$  silicon atom also stabilizes carbanions.<sup>123</sup>

4. *Field Effects.* Most of the groups that stabilize carbanions by resonance effects (either the kind discussed in 1 above or the kind discussed in paragraph 3) have electron-withdrawing field effects and thereby stabilize the carbanion further by spreading the negative charge, although it is difficult to separate the field effect from the resonance effect. However, in a nitrogen ylid  $R_3N^+-CR_2^-$  (see p. 54), where a positive nitrogen is adjacent to the negatively charged carbon, only the field effect operates. Ylids are more stable than the corresponding simple carbanions. Carbanions are stabilized by a field effect if there is any heteroatom (O, N, or S) connected to the carbanionic carbon, provided that the heteroatom bears a positive charge in at least one important canonical form,<sup>124</sup> for example,



5. *Certain Carbanions are Stable because they are Aromatic* (see the cyclopentadienyl anion p. 63, and other aromatic anions in Chapter 2).
6. *Stabilization by a Nonadjacent  $\pi$  Bond.*<sup>125</sup> In contrast to the situation with carbocations (see pp. 450–455), there have been fewer reports of carbanions stabilized by interaction with a nonadjacent  $\pi$  bond. One that may be mentioned is **17**, formed when optically active camphenilone (**15**) was treated with a strong base (potassium *tert*-butoxide).<sup>126</sup> That **17** was truly formed was

<sup>121</sup>Bernardi, F.; Csizmadia, I.G.; Mangini, A.; Schlegel, H.B.; Whangbo, M.; Wolfe, S. *J. Am. Chem. Soc.* **1975**, *97*, 2209; Lehn, J.M.; Wipff, G. *J. Am. Chem. Soc.* **1976**, *98*, 7498; Borden, W.T.; Davidson, E.R.; Andersen, N.H.; Denniston, A.D.; Epiotis, N.D. *J. Am. Chem. Soc.* **1978**, *100*, 1604; Bernardi, F.; Bottoni, A.; Venturini, A.; Mangini, A. *J. Am. Chem. Soc.* **1986**, *108*, 8171.

<sup>122</sup>Bernasconi, C.F.; Kittredge, K.W. *J. Org. Chem.* **1998**, *63*, 1944.

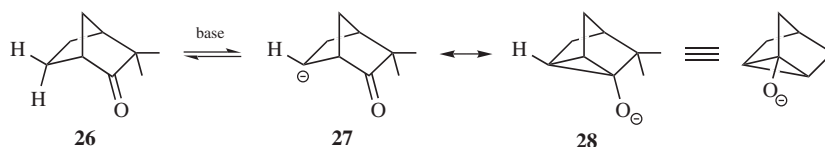
<sup>123</sup>Wetzel, D.M.; Brauman, J.I. *J. Am. Chem. Soc.* **1988**, *110*, 8333.

<sup>124</sup>For a review of such carbanions, see Beak, P.; Reitz, D.B. *Chem. Rev.* **1978**, *78*, 275. See also, Rondan, N.G.; Houk, K.N.; Beak, P.; Zajdel, W.J.; Chandrasekhar, J.; Schleyer, P.v.R. *J. Org. Chem.* **1981**, *46*, 4108.

<sup>125</sup>For reviews, see Werstiuk, N.H. *Tetrahedron* **1983**, *39*, 205; Hunter, D.H.; Stothers, J.B.; Warnhoff, E.W., in de Mayo, P. *Rearrangements in Ground and Excited States*, Vol. 1, Academic Press, NY, **1980**, pp. 410–437.

<sup>126</sup>Nickon, A.; Lambert, J.L. *J. Am. Chem. Soc.* **1966**, *88*, 1905. Also see, Brown, J.M.; Occolowitz, J.L. *Chem. Commun.* **1965**, 376; Grutzner, J.B.; Winstein, S. *J. Am. Chem. Soc.* **1968**, *90*, 6562; Staley, S.W.; Reichard, D.W. *J. Am. Chem. Soc.* **1969**, *91*, 3998; Miller, B. *J. Am. Chem. Soc.* **1969**, *91*, 751; Werstiuk, N.H.; Yeroushalmi, S.; Timmins, G. *Can. J. Chem.* **1983**, *61*, 1945; Lee, R.E.; Squires, R.R. *J. Am. Chem. Soc.* **1986**, *108*, 5078; Peiris, S.; Ragauskas, A.J.; Stothers, J.B. *Can. J. Chem.* **1987**, *65*, 789; Shiner, C.S.; Berks, A.H.; Fisher, A.M. *J. Am. Chem. Soc.* **1988**, *110*, 957.

shown by the following facts: (1) A proton was abstracted: ordinary



$\text{CH}_2$  groups are not acidic enough for this base; (2) recovered **26** was racemized: **28** is symmetrical and can be attacked equally well from either side; (3) when the experiment was performed in deuterated solvent, the rate of deuterium uptake was equal to the rate of racemization; and (4) recovered **26** contained up to three atoms of deuterium per molecule, although if **27** were the only ion, no more than two could be taken up. Ions of this type, in which a negatively charged carbon is stabilized by a carbonyl group two carbons away, are called *homoenolate ions*.

Overall, functional groups in the  $\alpha$  position stabilize carbanions in the following order:  $\text{NO}_2 > \text{RCO} > \text{COOR} > \text{SO}_2 > \text{CN} \sim \text{CONH}_2 > \text{Hal} > \text{H} > \text{R}$ .

It is unlikely that free carbanions exist in solution. Like carbocations, they usually exist as either ion pairs or they are solvated.<sup>127</sup> Among experiments that demonstrated this was the treatment of  $\text{PhCOCHMe}^- \text{M}^+$  with ethyl iodide, where  $\text{M}^+$  was  $\text{Li}^+$ ,  $\text{Na}^+$ , or  $\text{K}^+$ . The half-lives of the reaction were<sup>128</sup> for Li,  $31 \times 10^{-6}$ ; Na,  $0.39 \times 10^{-6}$ ; and K,  $0.0045 \times 10^{-6}$ , demonstrating that the species involved were not identical. Similar results<sup>129</sup> were obtained with Li, Na, and Cs triphenylmethides  $\text{Ph}_3\text{C}^- \text{M}^+$ .<sup>130</sup> Where ion pairs are unimportant, carbanions are solvated. Cram<sup>99</sup> has demonstrated solvation of carbanions in many solvents. There may be a difference in the structure of a carbanion depending on whether it is free (e.g., in the gas phase) or in solution. The negative charge may be more

<sup>127</sup>For reviews of carbanion pairs, see Hogen-Esch, T.E. *Adv. Phys. Org. Chem.* **1977**, *15*, 153; Jackman, L.M.; Lange, B.C. *Tetrahedron* **1977**, *33*, 2737. See also, Laube, T. *Acc. Chem. Res.* **1995**, *28*, 399.

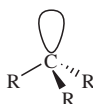
<sup>128</sup>Zook, H.D.; Gumby, W.L. *J. Am. Chem. Soc.* **1960**, *82*, 1386.

<sup>129</sup>Solov'yanov, A.A.; Karpyuk, A.D.; Beletskaya, I.P.; Reutov, O.A. *J. Org. Chem. USSR* **1981**, *17*, 381. See also, Solov'yanov, A.A.; Beletskaya, I.P.; Reutov, O.A. *J. Org. Chem. USSR* **1983**, *19*, 1964.

<sup>130</sup>For other evidence for the existence of carbanionic pairs, see Hogen-Esch, T.E.; Smid, J. *J. Am. Chem. Soc.* **1966**, *88*, 307, 318; **1969**, *91*, 4580; Abatjoglou, A.G.; Eliel, E.L.; Kuyper, L.F. *J. Am. Chem. Soc.* **1977**, *99*, 8262; Solov'yanov, A.A.; Karpyuk, A.D.; Beletskaya, I.P.; Reutov, V.M. *Doklad. Chem.* **1977**, *237*, 668; DePalma, V.M.; Arnett, E.M. *J. Am. Chem. Soc.* **1978**, *100*, 3514; Buncel, E.; Menon, B. *J. Org. Chem.* **1979**, *44*, 317; O'Brien, D.H.; Russell, C.R.; Hart, A.J. *J. Am. Chem. Soc.* **1979**, *101*, 633; Streitwieser, Jr., A.; Shen, C.C.C. *Tetrahedron Lett.* **1979**, 327; Streitwieser, Jr., A. *Acc. Chem. Res.* **1984**, *17*, 353.

localized in solution in order to maximize the electrostatic attraction to the counterion.<sup>131</sup>

The structure of simple unsubstituted carbanions is not known with certainty since they have not been isolated, but it seems likely that the central carbon is  $sp^3$  hybridized, with the unshared pair occupying one apex of the tetrahedron. Carbanions would thus have pyramidal structures similar to those of amines.



The methyl anion  $\text{CH}_3^-$  has been observed in the gas phase and reported to have a pyramidal structure.<sup>132</sup> If this is a general structure for carbanions, then any carbanion in which the three R groups are different should be chiral and reactions in which it is an intermediate should give retention of configuration. Attempts have been made to demonstrate this, but without success.<sup>133</sup> A possible explanation is that pyramidal inversion takes place here, as in amines, so that the unshared pair and the central carbon rapidly oscillate from one side of the plane to the other. There is, however, other evidence for the  $sp^3$  nature of the central carbon and for its tetrahedral structure. Carbons at bridgeheads, although extremely reluctant to undergo reactions in which they must be converted to carbocations, undergo with ease reactions in which they must be carbanions and stable bridgehead carbanions are known.<sup>134</sup> Also, reactions at vinylic carbons proceed with retention,<sup>135</sup> indicating that the intermediate **29** has  $sp^2$  hybridization and not the  $sp$  hybridization that would be expected in the analogous carbocation. A cyclopropyl anion can also hold its configuration.<sup>136</sup>



<sup>131</sup>See Schade, C.; Schleyer, P.v.R.; Geissler, M.; Weiss, E. *Angew. Chem. Int. Ed.* **1986**, 21, 902.

<sup>132</sup>Ellison, G.B.; Engelking, P.C.; Lineberger, W.C. *J. Am. Chem. Soc.* **1978**, 100, 2556.

<sup>133</sup>Retention of configuration has never been observed with simple carbanions. Cram has obtained retention with carbanions stabilized by resonance. However, these carbanions are known to be planar or nearly planar, and retention was caused by asymmetric solvation of the planar carbanions (see p. \$\$\$).

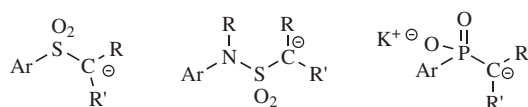
<sup>134</sup>For other evidence that carbanions are pyramidal, see Streitwieser, Jr., A.; Young, W.R. *J. Am. Chem. Soc.* **1969**, 91, 529; Peoples, P.R.; Grutzner, J.B. *J. Am. Chem. Soc.* **1980**, 102, 4709.

<sup>135</sup>Curtin, D.Y.; Harris, E.E. *J. Am. Chem. Soc.* **1951**, 73, 2716, 4519; Braude, E.A.; Coles, J.A. *J. Chem. Soc.* **1951**, 2078; Nesmeyanov, A.N.; Borisov, A.E. *Tetrahedron* **1957**, 1, 158. Also see, Miller, S.I.; Lee, W.G. *J. Am. Chem. Soc.* **1959**, 81, 6313; Hunter, D.H.; Cram, D.J. *J. Am. Chem. Soc.* **1964**, 86, 5478; Walborsky, H.M.; Turner, L.M. *J. Am. Chem. Soc.* **1972**, 94, 2273; Arnett, J.F.; Walborsky, H.M. *J. Org. Chem.* **1972**, 37, 3678; Feit, B.; Melamed, U.; Speer, H.; Schmidt, R.R. *J. Chem. Soc. Perkin Trans. 1* **1984**, 775; Chou, P.K.; Kass, S.R. *J. Am. Chem. Soc.* **1991**, 113, 4357.

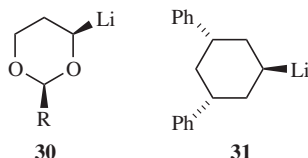
<sup>136</sup>Walborsky, H.M.; Motes, J.M. *J. Am. Chem. Soc.* **1970**, 92, 2445; Motes, J.M.; Walborsky, H.M. *J. Am. Chem. Soc.* **1970**, 92, 3697; Boche, G.; Harms, K.; Marsch, M. *J. Am. Chem. Soc.* **1988**, 110, 6925. For a monograph on cyclopropyl anions, cations, and radicals, see Boche, G.; Walborsky, H.M. *Cyclopropane Derived Reactive Intermediates*, Wiley, NY, **1990**. For a review, see Boche, G.; Walborsky, H.M., in Rappoport, Z. *The Chemistry of the Cyclopropyl Group*, pt. 1, Wiley, NY, **1987**, pp. 701–808 (the monograph includes and updates the review).



Carbanions in which the negative charge is stabilized by resonance involving overlap of the unshared-pair orbital with the  $\pi$  electrons of a multiple bond are essentially planar, as would be expected by the necessity for planarity in resonance, although unsymmetrical solvation or ion-pairing effects may cause the structure to deviate somewhat from true planarity.<sup>137</sup> Cram and co-workers showed that where chiral carbanions possessing this type of resonance are generated, retention, inversion, or racemization can result, depending on the solvent (see p. 759). This result is explained by unsymmetrical solvation of planar or near-planar carbanions. However, some carbanions that are stabilized by adjacent sulfur or phosphorus, for example,



are inherently chiral, since retention of configuration is observed where they are generated, even in solvents that cause racemization or inversion with other carbanions.<sup>138</sup> It is known that in THF,  $\text{PhCH}(\text{Li})\text{Me}$  behaves as a prochiral entity,<sup>139</sup> and **30** has been prepared as an optically pure  $\alpha$ -alkoxylithium reagent.<sup>140</sup> Cyclohexyllithium **31** shows some configurationally stability, and it is known that isomerization is slowed by an increase in the strength of lithium coordination and by an increase in solvent polarity.<sup>141</sup> It is known that a vinyl anion is configurationally stable whereas a vinyl radical is not. This is due to the instability of the radical anion that must be an intermediate for conversion of one isomer of vinylolithium to the other.<sup>142</sup> The configuration about the carbanionic carbon, at least for some of the  $\alpha$ -sulfonyl carbanions, seems to be planar,<sup>143</sup> and the inherent chirality is caused by lack of rotation about the C–S bond.<sup>144</sup>



<sup>137</sup>See the discussion, in Cram, D.J. *Fundamentals of Carbanion Chemistry*, Academic Press, NY, **1965**, pp. 85–105.

<sup>138</sup>Cram, D.J.; Wingrove, A.S. *J. Am. Chem. Soc.* **1962**, *84*, 1496; Goering, H.L.; Towns, D.L.; Dittmer, B. *J. Org. Chem.* **1962**, *27*, 736; Corey, E.J.; Lowry, T.H. *Tetrahedron Lett.* **1965**, 803; Bordwell, F.G.; Phillips, D.D.; Williams, Jr., J.M. *J. Am. Chem. Soc.* **1968**, *90*, 426; Annunziata, R.; Cinquini, M.; Colonna, S.; Cozzi, F. *J. Chem. Soc. Chem. Commun.* **1981**, 1005; Chassaing, G.; Marquet, A.; Corset, J.; Froment, F. *J. Organomet. Chem.* **1982**, *232*, 293. For a discussion, see Cram, D.J. *Fundamentals of Carbanion Chemistry*, Academic Press, NY, **1965**, pp. 105–113. Also see Hirsch, R.; Hoffmann, R.W. *Chem. Ber.* **1992**, *125*, 975.

<sup>139</sup>Hoffmann, R.W.; Rühl, T.; Chemla, F.; Zahneisen, T. *Liebigs Ann. Chem.* **1992**, 719.

<sup>140</sup>Rychnovsky, S.D.; Plzak, K.; Pickering, D. *Tetrahedron Lett.* **1994**, *35*, 6799.

<sup>141</sup>Reich, H.J.; Medina, M.A.; Bowe, M.D. *J. Am. Chem. Soc.* **1992**, *114*, 11003.

<sup>142</sup>Jenkins, P.R.; Symons, M.C.R.; Booth, S.E.; Swain, C.J. *Tetrahedron Lett.* **1992**, *33*, 3543.

<sup>143</sup>Boche, G.; Marsch, M.; Harms, K.; Sheldrick, G.M. *Angew. Chem. Int. Ed.* **1985**, *24*, 573; Gais, H.; Müller, J.; Vollhardt, J.; Lindner, H.J. *J. Am. Chem. Soc.* **1991**, *113*, 4002. For a contrary view, see Trost, B.M.; Schmuff, N.R. *J. Am. Chem. Soc.* **1985**, *107*, 396.

<sup>144</sup>Grossert, J.S.; Hoyle, J.; Cameron, T.S.; Roe, S.P.; Vincent, B.R. *Can. J. Chem.* **1987**, *65*, 1407.

### The Structure of Organometallic Compounds<sup>145</sup>

Whether a carbon–metal bond is ionic or polar-covalent is determined chiefly by the electronegativity of the metal and the structure of the organic part of the molecule. Ionic bonds become more likely as the negative charge on the metal-bearing carbon is decreased by resonance or field effects. Thus the sodium salt of acetoacetic ester has a more ionic carbon–sodium bond than methylsodium.

Most organometallic bonds are polar-covalent. Only the alkali metals have electronegativities low enough to form ionic bonds with carbon, and even here the behavior of lithium alkyls shows considerable covalent character. The simple alkyls and aryls of sodium, potassium, rubidium, and cesium<sup>146</sup> are nonvolatile solids<sup>147</sup> insoluble in benzene or other organic solvents, while alkyllithium reagents are soluble, although they too are generally nonvolatile solids. Alkyllithium reagents do not exist as monomeric species in hydrocarbon solvents or ether.<sup>148</sup> In benzene and cyclohexane, freezing-point-depression studies have shown that alkyllithium reagents are normally hexameric unless steric interactions favor tetrameric aggregates.<sup>149</sup> The NMR studies, especially measurements of <sup>13</sup>C–<sup>6</sup>Li coupling, have also shown aggregation in hydrocarbon solvents.<sup>150</sup> Boiling-point-elevation studies have been performed in ether solutions, where alkyllithium reagents exist in two- to fivefold aggregates.<sup>151</sup> Even in the gas phase<sup>152</sup> and in

<sup>145</sup>For a monograph, see Elschenbroich, C.; Salzer, A. *Organometallics*, VCH, NY, **1989**. For reviews, see Oliver, J.P., in Hartley, F.R.; Patai, S. *The Chemistry of the Metal–Carbon Bond*, Vol. 2, Wiley, NY, **1985**, pp. 789–826; Coates, G.E.; Green, M.L.H.; Wade, K. *Organometallic Compounds*, 3rd ed., Vol. 1; Methuen: London, **1967**. For a review of the structures of organodialkali compounds, see Grovenstein, Jr., E., in Buncl, E.; Durst, T. *Comprehensive Carbanion Chemistry*, pt. C, Elsevier, NY, **1987**, pp. 175–221.

<sup>146</sup>For a review of X-ray crystallographic studies of organic compounds of the alkali metals, see Schade, C.; Schleyer, P.v.R. *Adv. Organomet. Chem.* **1987**, 27, 169.

<sup>147</sup>X-ray crystallography of potassium, rubidium, and cesium methyls shows completely ionic crystal lattices: Weiss, E.; Sauermaun, G. *Chem. Ber.* **1970**, 103, 265; Weiss, E.; Köster, H. *Chem. Ber.* **1977**, 110, 717.

<sup>148</sup>For reviews of the structure of alkyllithium compounds, see Setzer, W.N.; Schleyer, P.v.R. *Adv. Organomet. Chem.* **1985**, 24, 353; Schleyer, P.v.R. *Pure Appl. Chem.* **1984**, 56, 151; Brown, T.L. *Pure Appl. Chem.* **1970**, 23, 447, *Adv. Organomet. Chem.* **1965**, 3, 365; Kovrizhnykh, E.A.; Shatenshtein, A.I. *Russ. Chem. Rev.* **1969**, 38, 840. For reviews of the structures of lithium enolates and related compounds, see Boche, G. *Angew. Chem. Int. Ed.* **1989**, 28, 277; Seebach, D. *Angew. Chem. Int. Ed.* **1988**, 27, 1624. For a review of the use of nmr to study these structures, see Günther, H.; Moskau, D.; Bast, P.; Schmalz, D. *Angew. Chem. Int. Ed.* **1987**, 26, 1212. For monographs on organolithium compounds, see Wakefield, B.J. *Organolithium Methods*, Academic Press, NY, **1988**, *The Chemistry of Organolithium Compounds*, Pergamon, Elmsford, NY, **1974**.

<sup>149</sup>Lewis, H.L.; Brown, T.L. *J. Am. Chem. Soc.* **1970**, 92, 4664; Brown, T.L.; Rogers, M.T. *J. Am. Chem. Soc.* **1957**, 79, 1859; Weiner, M.A.; Vogel, G.; West, R. *Inorg. Chem.* **1962**, 1, 654.

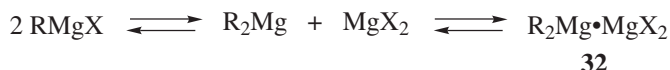
<sup>150</sup>Fraenkel, G.; Henrichs, M.; Hewitt, M.; Su, B.M. *J. Am. Chem. Soc.* **1984**, 106, 255; Thomas, R.D.; Jensen, R.M.; Young, T.C. *Organometallics* **1987**, 6, 565. See also, Kaufman, M.J.; Gronert, S.; Streitwieser, Jr., A. *J. Am. Chem. Soc.* **1988**, 110, 2829.

<sup>151</sup>Wittig, G.; Meyer, F.J.; Lange, G. *Liebigs Ann. Chem.* **1951**, 571, 167. See also, McGarrity, J.F.; Ogle, C.A. *J. Am. Chem. Soc.* **1985**, 107, 1805; Bates, T.F.; Clarke, M.T.; Thomas, R.D. *J. Am. Chem. Soc.* **1988**, 110, 5109.

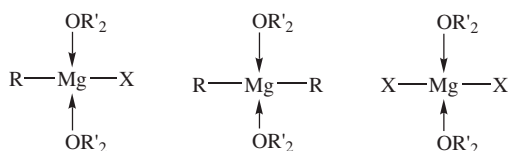
<sup>152</sup>Brown, T.L.; Dickerhoof, D.W.; Bafus, D.A. *J. Am. Chem. Soc.* **1962**, 84, 1371; Chinn, Jr., J.W.; Lagow, R.L. *Organometallics* **1984**, 3, 75; Plavšić, D.; Srzić, D.; Klasinc, L. *J. Phys. Chem.* **1986**, 90, 2075.

the solid state,<sup>153</sup> alkyl lithium reagents exist as aggregates. X-ray crystallography has shown that methyllithium has the same tetrahedral structure in the solid state as in ether solution.<sup>153</sup> However, *tert*-butyllithium is monomeric in THF, although dimeric in ether and tetrameric in hydrocarbon solvents.<sup>154</sup> Neopentyllithium exists as a mixture of monomers and dimers in THF.<sup>155</sup>

The C—Mg bond in Grignard reagents is covalent and not ionic. The actual structure of Grignard reagents in solution has been a matter of much controversy over the years.<sup>156</sup> In 1929, it was discovered<sup>157</sup> that the addition of dioxane to an ethereal Grignard solution precipitates all the magnesium halide and leaves a solution of R<sub>2</sub>Mg in ether; that is, there can be no RMgX in the solution since there is no halide. The following equilibrium, now called the *Schlenk equilibrium*, was proposed as the composition of the Grignard solution:



in which **32** is a complex of some type. Much work has demonstrated that the Schlenk equilibrium actually exists and that the position of the equilibrium is dependent on the identity of R, X, the solvent, the concentration, and the temperature.<sup>158</sup> It has been known for many years that the magnesium in a Grignard solution, no matter whether it is RMgX, R<sub>2</sub>Mg, or MgX<sub>2</sub>, can coordinate with two molecules of ether in addition to the two covalent bonds:



Rundle and co-workers<sup>159</sup> performed X-ray diffraction studies on solid phenylmagnesium bromide dietherate and on ethylmagnesium bromide dietherate, which they obtained by cooling ordinary ethereal Grignard solutions until the

<sup>153</sup>Dietrich, H. *Acta Crystallogr.* **1963**, *16*, 681; Weiss, E.; Lucken, E.A.C. *J. Organomet. Chem.* **1964**, *2*, 197; Weiss, E.; Sauermann, G.; Thirase, G. *Chem. Ber.* **1983**, *116*, 74.

<sup>154</sup>Bauer, W.; Winchester, W.R.; Schleyer, P.v.R. *Organometallics* **1987**, *6*, 2371.

<sup>155</sup>Fraenkel, G.; Chow, A.; Winchester, W.R. *J. Am. Chem. Soc.* **1990**, *112*, 6190.

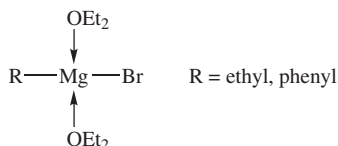
<sup>156</sup>For reviews, see Ashby, E.C. *Bull. Soc. Chim. Fr.* **1972**, 2133; *Q. Rev. Chem. Soc.* **1967**, *21*, 259; Wakefield, B.J. *Organomet. Chem. Rev.* **1966**, *1*, 131; Bell, N.A. *Educ. Chem.* **1973**, 143.

<sup>157</sup>Schlenk, W.; Schlenk Jr., W. *Ber.* **1929**, *62B*, 920.

<sup>158</sup>See Parris, G.; Ashby, E.C. *J. Am. Chem. Soc.* **1971**, *93*, 1206; Salinger, R.M.; Mosher, H.S. *J. Am. Chem. Soc.* **1964**, *86*, 1782; Kirrmann, A.; Hamelin, R.; Hayes, S. *Bull. Soc. Chim. Fr.* **1963**, 1395.

<sup>159</sup>Guggenberger, L.J.; Rundle, R.E. *J. Am. Chem. Soc.* **1968**, *90*, 5375; Stucky, G.; Rundle, R.E. *J. Am. Chem. Soc.* **1964**, *86*, 4825.

solids crystallized. They found that the structures were monomeric:



These solids still contained ether. When ordinary ethereal Grignard solutions<sup>160</sup> prepared from bromomethane, chloromethane, bromoethane, and chloroethane were evaporated at  $\sim 100^\circ\text{C}$  under vacuum so that the solid remaining contained no ether, X-ray diffraction showed *no*  $\text{RMgX}$ , but a mixture of  $\text{R}_2\text{Mg}$  and  $\text{MgX}_2$ .<sup>161</sup> These results indicate that in the presence of ether  $\text{RMgX} \cdot 2\text{Et}_2\text{O}$  is the preferred structure, while the loss of ether drives the Schlenk equilibrium to  $\text{R}_2\text{Mg} + \text{MgX}_2$ . However, conclusions drawn from a study of the solid materials do not necessarily apply to the structures in solution.

Boiling-point-elevation and freezing-point-depression measurements have demonstrated that in THF at all concentrations and in ether at low concentrations (up to  $\sim 0.1\text{ M}$ ) Grignard reagents prepared from alkyl bromides and iodides are monomeric, that is, there are few or no molecules with two magnesium atoms.<sup>162</sup> Thus, part of the Schlenk equilibrium is operating but not the other



part; that is, **32** is not present in measurable amounts. This was substantiated by  $^{25}\text{Mg}$  NMR spectra of the ethyl Grignard reagent in THF, which showed the presence of three peaks, corresponding to  $\text{EtMgBr}$ ,  $\text{Et}_2\text{Mg}$ , and  $\text{MgBr}_2$ .<sup>163</sup> That the equilibrium between  $\text{RMgX}$  and  $\text{R}_2\text{Mg}$  lies far to the left for “ethylmagnesium bromide” in ether was shown by Smith and Becker, who mixed  $0.1\text{ M}$  ethereal solutions of  $\text{Et}_2\text{Mg}$  and  $\text{MgBr}_2$  and found that a reaction occurred with a heat evolution of  $3.6\text{ kcal mol}^{-1}$  ( $15\text{ kJ mol}^{-1}$ ) of  $\text{Et}_2\text{Mg}$ , and that the product was *monomeric* (by boiling-point-elevation measurements).<sup>164</sup> When either solution was added little by little to the other, there was a linear output of heat until almost a 1:1 molar ratio was reached. Addition of an excess of either reagent gave no further heat output. These results show that at least under some conditions the Grignard reagent is largely  $\text{RMgX}$  (coordinated with solvent) but that the equilibrium can be driven to  $\text{R}_2\text{Mg}$  by evaporation of all the ether or by addition of dioxane.

<sup>160</sup>The constitution of alkylmagnesium chloride reagents in THF has been determined. See Sakamoto, S.; Imamoto, T.; Yamaguchi, K. *Org. Lett.* **2001**, 3, 1793.

<sup>161</sup>Weiss, E. *Chem. Ber.* **1965**, 98, 2805.

<sup>162</sup>Ashby, E.C.; Smith, M.B. *J. Am. Chem. Soc.* **1964**, 86, 4363; Vreugdenhil, A.D.; Blomberg, C. *Recl. Trav. Chim. Pays-Bas* **1963**, 82, 453, 461.

<sup>163</sup>Benn, R.; Lehmkühl, H.; Mehler, K.; Ruffńska, A. *Angew. Chem. Int. Ed.* **1984**, 23, 534.

<sup>164</sup>Smith, M.B.; Becker, W.E. *Tetrahedron* **1966**, 22, 3027.

For some aryl Grignard reagents it has proved possible to distinguish separate NMR chemical shifts for  $\text{ArMgX}$  and  $\text{Ar}_2\text{Mg}$ .<sup>165</sup> From the area under the peaks it is possible to calculate the concentrations of the two species, and from them, equilibrium constants for the Schlenk equilibrium. These data show<sup>165</sup> that the position of the equilibrium depends very markedly on the aryl group and the solvent but that conventional aryl Grignard reagents in ether are largely  $\text{ArMgX}$ , while in THF the predominance of  $\text{ArMgX}$  is less, and with some aryl groups there is actually more  $\text{Ar}_2\text{Mg}$  present. Separate nmr chemical shifts have also been found for alkyl  $\text{RMgBr}$  and  $\text{R}_2\text{Mg}$  in HMPA<sup>166</sup> and in ether at low temperatures.<sup>167</sup> When Grignard reagents from alkyl bromides or chlorides are prepared in triethylamine the predominant species is  $\text{RMgX}$ .<sup>168</sup> Thus the most important factor determining the position of the Schlenk equilibrium is the solvent. For primary alkyl groups the equilibrium constant for the reaction as written above is lowest in  $\text{Et}_3\text{N}$ , higher in ether, and still higher in THF.<sup>169</sup>

However, Grignard reagents prepared from alkyl bromides or iodides in ether at higher concentrations (0.5–1 *M*) contain dimers, trimers, and higher polymers, and those prepared from alkyl chlorides in ether at all concentrations are dimeric,<sup>170</sup> so that **32** is in solution, probably in equilibrium with  $\text{RMgX}$  and  $\text{R}_2\text{Mg}$ ; that is, the complete Schlenk equilibrium seems to be present.

The Grignard reagent prepared from 1-chloro-3,3-dimethylpentane in ether undergoes rapid inversion of configuration at the magnesium-containing carbon (demonstrated by NMR; this compound is not chiral).<sup>171</sup> The mechanism of this inversion is not completely known. Therefore, in almost all cases, it is not possible to retain the configuration of a stereogenic carbon while forming a Grignard reagent.

Organolithium reagents ( $\text{RLi}$ ) are tremendously important reagents in organic chemistry. In recent years, a great deal has been learned about their structure<sup>172</sup> in both the solid state and in solution. X-ray analysis of complexes of *n*-butyllithium with *N,N,N',N'*-tetramethylethylenediamine (TMEDA), THF, and 1,2-dimethoxyethane (DME) shows them to be dimers and tetramers [e.g.,  $(\text{BuLi}\cdot\text{DME})_4$ ].<sup>173</sup> X-ray analysis of isopropyllithium shows it to be a hexamer,

<sup>165</sup>Evans, D.F.; Fazakerley, V. *Chem. Commun.* **1968**, 974.

<sup>166</sup>Ducom, J. *Bull. Chem. Soc. Fr.* **1971**, 3518, 3523, 3529.

<sup>167</sup>Ashby, E.C.; Parris, G.; Walker, F. *Chem. Commun.* **1969**, 1464; Parris, G.; Ashby, E.C. *J. Am. Chem. Soc.* **1971**, 93, 1206.

<sup>168</sup>Ashby, E.C.; Walker, F. *J. Org. Chem.* **1968**, 33, 3821.

<sup>169</sup>Parris, G.; Ashby, E.C. *J. Am. Chem. Soc.* **1971**, 93, 1206.

<sup>170</sup>Ashby, E.C.; Smith, M.B. *J. Am. Chem. Soc.* **1964**, 86, 4363.

<sup>171</sup>Whitesides, G.M.; Witanowski, M.; Roberts, J.D. *J. Am. Chem. Soc.* **1965**, 87, 2854; Whitesides, G.M.; Roberts, J.D. *J. Am. Chem. Soc.* **1965**, 87, 4878. Also see, Witanowski, M.; Roberts, J.D. *J. Am. Chem. Soc.* **1966**, 88, 737; Fraenkel, G.; Cottrell, C.E.; Dix, D.T. *J. Am. Chem. Soc.* **1971**, 93, 1704; Pechhold, E.; Adams, D.G.; Fraenkel, G. *J. Org. Chem.* **1971**, 36, 1368; Maercker, A.; Geuss, R. *Angew. Chem. Int. Ed.* **1971**, 10, 270.

<sup>172</sup>For a computational study of acidities, electron affinities, and bond dissociation energies of selected organolithium reagents, see Pratt, L.M.; Kass, S.R. *J. Org. Chem.* **2004**, 69, 2123.

<sup>173</sup>Nichols, M.A.; Williard, P.G. *J. Am. Chem. Soc.* **1993**, 115, 1568.

(*i*PrLi)<sub>6</sub>],<sup>174</sup> and unsolvated lithium aryls are tetramers.<sup>175</sup>  $\alpha$ -Ethoxyvinyl lithium [CH<sub>2</sub>=C(OEt)Li] shows a polymeric structure with tetrameric subunits.<sup>176</sup> Aminomethyl aryllithium reagents have been shown to be chelated and dimeric in solvents such as THF.<sup>177</sup>

The dimeric, tetrameric, and hexameric structures of organolithium reagents<sup>178</sup> in the solid state is often retained in solution, but this is dependent on the solvent and complexing additives, if any. A tetrahedral organolithium compound is known,<sup>179</sup> and the X-ray of an  $\alpha,\alpha$ -dilithio hydrocarbon has been reported.<sup>180</sup> Phenyllithium is a mixture of tetramers and dimers in diethyl ether, but stoichiometric addition of THF, dimethoxyethane, or TMEDA leads to the dimer.<sup>181</sup> The solution structures of mixed aggregates of butyllithium and amino-alkaloids has been determined,<sup>182</sup> and also the solution structure of sulfur-stabilized allyllithium compounds.<sup>183</sup> Vinyl lithium is an 8:1 mixture of tetramer:dimer in THF at  $-90^{\circ}\text{C}$ , but addition of TMEDA changes the ratio of tetramer:dimer to 1:13 at  $-80^{\circ}\text{C}$ .<sup>184</sup> Internally solvated allylic lithium compounds have been studied, showing the coordinated lithium to be closer to one of the terminal allyl carbons.<sup>185</sup> A relative scale of organolithium stability has been established,<sup>186</sup> and the issue of configurational stability of enantio-enriched organolithium reagents has been examined.<sup>187</sup>

Enolate anions are an important class of carbanions that appear in a variety of important reactions, including alkylation  $\alpha$ - to a carbonyl group and the aldol (reaction 16-34) and Claisen condensation (reaction 16-85) reactions. Metal enolate anions of aldehydes, ketones, esters, and other acid derivatives exist as aggregates in ether solvents,<sup>188</sup> and there is evidence that the lithium enolate of

<sup>174</sup>Siemeling, U.; Redecker, T.; Neumann, B.; Stammer, H.-G. *J. Am. Chem. Soc.* **1994**, *116*, 5507.

<sup>175</sup>Ruhlandt-Senge, K.; Ellison, J.J.; Wehmschulte, R.J.; Pauer, F.; Power, P.P. *J. Am. Chem. Soc.* **1993**, *115*, 11353. For the X-ray structure of 1-methoxy-8-naphthyllithium see Betz, J.; Hampel, F.; Bauer, W. *Org. Lett.* **2000**, *2*, 3805.

<sup>176</sup>Sorger, K.; Bauer, W.; Schleyer, P.v.R.; Stalke, D. *Angew. Chem. Int. Ed.* **1995**, *34*, 1594.

<sup>177</sup>Reich, H.J.; Gudmundsson, B.O.; Goldenberg, W.S.; Sanders, A.W.; Kulicke, K.J.; Simon, K.; Guzei, I.A. *J. Am. Chem. Soc.* **2001**, *123*, 8067.

<sup>178</sup>For an *ab initio* correlation of structure with NMR, see Parisel, O.; Fressigne, C.; Maddaluno, J.; Giessner-Prettre, C. *J. Org. Chem.* **2003**, *68*, 1290.

<sup>179</sup>Sekiguchi, A.; Tanaka, M. *J. Am. Chem. Soc.* **2003**, *125*, 12684.

<sup>180</sup>Linti, G.; Rodig, A.; Pritzkow, H. *Angew. Chem. Int. Ed.* **2002**, *41*, 4503.

<sup>181</sup>Reich, H.J.; Green, D.P.; Medina, M.A.; Goldenberg, W.S.; Gudmundsson, B.Ö.; Dykstra, R.R.; Phillips, N.H. *J. Am. Chem. Soc.* **1998**, *120*, 7201.

<sup>182</sup>Sun, X.; Winemiller, M.D.; Xiang, B.; Collum, D.B. *J. Am. Chem. Soc.* **2001**, *123*, 8039. See also, Rutherford, J.L.; Hoffmann, D.; Collum, D.B. *J. Am. Chem. Soc.* **2002**, *124*, 264.

<sup>183</sup>Piffl, M.; Weston, J.; Günther, W.; Anders, E. *J. Org. Chem.* **2000**, *65*, 5942.

<sup>184</sup>Bauer, W.; Griesinger, C. *J. Am. Chem. Soc.* **1993**, *115*, 10871.

<sup>185</sup>Fraenkel, G.; Chow, A.; Fleischer, R.; Liu, H. *J. Am. Chem. Soc.* **2004**, *126*, 3983.

<sup>186</sup>Graña, P.; Paleo, M.R.; Sardina, F.J. *J. Am. Chem. Soc.* **2002**, *124*, 12511.

<sup>187</sup>Basu, A.; Thayumanavan, S. *Angew. Chem. Int. Ed.* **2002**, *41*, 717. See also, Fraenkel, G.; Duncan, J.H.; Martin, K.; Wang, J. *J. Am. Chem. Soc.* **1999**, *121*, 10538.

<sup>188</sup>Stork, G.; Hudrlik, P.F. *J. Am. Chem. Soc.* **1968**, *90*, 4464; Bernstein, M.P.; Collum, D.B. *J. Am. Chem. Soc.* **1993**, *115*, 789; Bernstein, M.P.; Romesberg, F.E.; Fuller, D.J.; Harrison, A.T.; Collum, D.B.; Liu, Q.Y.; Williard, P.G. *J. Am. Chem. Soc.* **1992**, *114*, 5100; Collum, D.B. *Acc. Chem. Res.* **1992**, *25*, 448.



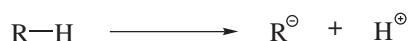
isobutyrophenone is a tetramer in THF,<sup>189</sup> but a dimer in DME.<sup>190</sup> X-ray crystallography of ketone enolate anions have shown that they can exist as tetramers and hexamers.<sup>191</sup> There is also evidence that the aggregate structure is preserved in solution and is probably the actual reactive species. Lithium enolates derived from esters are as dimers in the solid state<sup>192</sup> that contain four tetrahydrofuran molecules. It has also been established that the reactivity of enolate anions in alkylation and condensation reactions is influenced by the aggregate state of the enolate. It is also true that the relative proportions of (*E*) and (*Z*) enolate anions are influenced by the extent of solvation and the aggregation state. Addition of LiBr to a lithium enolate anion in THF suppresses the concentration of monomeric enolate.<sup>193</sup> *Ab initio* studies confirm the aggregate state of acetaldehyde.<sup>194</sup> It is also known that  $\alpha$ -Li benzonitrile [PhCH(Li)CN] exists as a dimer in ether and with TMEDA.<sup>195</sup> Mixed aggregates of *tert*-butyllithium and lithium *tert*-butoxide are known to be hexameric.<sup>196</sup>

It might be mentioned that matters are much simpler for organometallic compounds with less-polar bonds. Thus Et<sub>2</sub>Hg and EtHgCl are both definite compounds, the former a liquid and the latter a solid. Organocalcium reagents are also known, and they are formed from alkyl halides via a single electron-transfer (SET) mechanism with free-radical intermediates.<sup>197</sup>

### The Generation and Fate of Carbanions

The two principal ways in which carbanions are generated are parallel with the ways of generating carbocations.

1. A group attached to a carbon leaves without its electron pair:



The leaving group is most often a proton. This is a simple acid–base reaction, and a base is required to remove the proton.<sup>198</sup> However, other

<sup>189</sup>Jackman, L.M.; Szeverenyi, N.M. *J. Am. Chem. Soc.* **1977**, *99*, 4954; Jackman, L.M.; Lange, B.C. *J. Am. Chem. Soc.* **1981**, *103*, 4494.

<sup>190</sup>Jackman, L.M.; Lange, B.C. *Tetrahedron* **1977**, *33*, 2737.

<sup>191</sup>Williard, P.G.; Carpenter, G.B. *J. Am. Chem. Soc.* **1986**, *108*, 462; Williard, P.G.; Carpenter, G.B. *J. Am. Chem. Soc.* **1985**, *107*, 3345; Amstutz, R.; Schweizer, W.B.; Seebach, D.; Dunitz, J.D. *Helv. Chim. Acta* **1981**, *64*, 2617; Seebach, D.; Amstutz, D.; Dunitz, J.D. *Helv. Chim. Acta* **1981**, *64*, 2622.

<sup>192</sup>Seebach, D.; Amstutz, R.; Laube, T.; Schweizer, W.B.; Dunitz, J.D. *J. Am. Chem. Soc.* **1985**, *107*, 5403.

<sup>193</sup>Abu-Hasanayn, F.; Streitwieser, A. *J. Am. Chem. Soc.* **1996**, *118*, 8136.

<sup>194</sup>Abbotto, A.; Streitwieser, A.; Schleyer, P.v.R. *J. Am. Chem. Soc.* **1997**, *119*, 11255.

<sup>195</sup>Carlier, P.R.; Lucht, B.L.; Collum, D.B. *J. Am. Chem. Soc.* **1994**, *116*, 11602.

<sup>196</sup>DeLong, G.T.; Pannell, D.K.; Clarke, M.T.; Thomas, R.D. *J. Am. Chem. Soc.* **1993**, *115*, 7013.

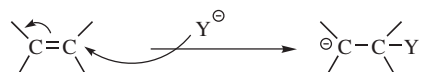
<sup>197</sup>Walborsky, H.M.; Hamdouchi, C. *J. Org. Chem.* **1993**, *58*, 1187.

<sup>198</sup>For a review of such reactions, see Durst, T., in Buncl, E.; Durst, T. *Comprehensive Carbanion Chemistry*, pt. B, Elsevier, NY, **1984**, pp. 239–291.

leaving groups are known (see Chapter 12):



2. A negative ion adds to a carbon–carbon double or triple bond (see Chapter 15):



The addition of a negative ion to a carbon–oxygen double bond does not give a carbanion, since the negative charge resides on the oxygen.

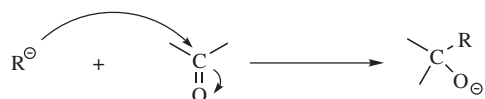
The most common reaction of carbanions is combination with a positive species, usually a proton, or with another species that has an empty orbital in its outer shell (a Lewis acid–base reaction):



Carbanions may also form a bond with a carbon that already has four bonds, by displacing one of the four groups ( $\text{S}_{\text{N}}2$  reaction, see Chapter 10):



Like carbocations, carbanions can also react in ways in which they are converted to species that are still not neutral molecules. They can add to double bonds (usually  $\text{C}=\text{O}$  double bonds; see Chapters 10 and 16),



or rearrange, although this is rare (see Chapter 18),



or be oxidized to free radicals.<sup>199</sup> A system in which a carbocation [ $\text{Ph}(p\text{-Me}_2\text{NC}_6\text{H}_4)_2\text{C}^+$ ] oxidizes a carbanion [ $(p\text{-NO}_2\text{C}_6\text{H}_4)_3\text{C}^-$ ] to give two free radicals, reversibly, so that all four species are present in equilibrium, has been demonstrated.<sup>200,201</sup>

<sup>199</sup>For a review, see Guthrie, R.D., in Buncl, E.; Durst, T. *Comprehensive Carbanion Chemistry*, pt. A, Elsevier, NY, **1980**, pp. 197–269.

<sup>200</sup>Arnett, E.M.; Molter, K.E.; Marchot, E.C.; Donovan, W.H.; Smith, P. *J. Am. Chem. Soc.* **1987**, *109*, 3788.

<sup>201</sup>Okamoto, K.; Kitagawa, T.; Takeuchi, K.; Komatsu, K.; Kinoshita, T.; Aonuma, S.; Nagai, M.; Miyabo, A. *J. Org. Chem.* **1990**, *55*, 996. See also, Okamoto, K.; Kitagawa, T.; Takeuchi, K.; Komatsu, K.; Miyabo, A. *J. Chem. Soc. Chem. Commun.* **1988**, 923.



Organometallic compounds that are not ionic, but polar-covalent behave very much as if they were ionic and give similar reactions.

## FREE RADICALS

### Stability and Structure<sup>202</sup>

A *free radical* (often simply called a *radical*) may be defined as a species that contains one or more unpaired electrons. Note that this definition includes certain stable inorganic molecules (e.g., NO and NO<sub>2</sub>), as well as many individual atoms (e.g., Na and Cl). As with carbocations and carbanions, simple alkyl radicals are very reactive. Their lifetimes are extremely short in solution, but they can be kept for relatively long periods frozen within the crystal lattices of other molecules.<sup>203</sup> Many spectral<sup>204</sup> measurements have been made on radicals trapped in this manner. Even under these conditions the methyl radical decomposes with a half-life of 10–15 min in a methanol lattice at 77 K.<sup>205</sup> Since the lifetime of a radical depends not only on its inherent stability, but also on the conditions under which it is generated, the terms *persistent* and *stable* are usually used for the different senses. A stable radical is inherently stable; a persistent radical has a relatively long lifetime under the conditions at which it is generated, although it may not be very stable.

Radicals can be characterized by several techniques, such as mass spectrometry<sup>206</sup> or the characterization of alkoxy carbonyl radicals by Step-Scan Time-Resolved Infrared Spectroscopy.<sup>207</sup> Another technique makes use of the magnetic moment that is associated with the spin of an electron, which can be expressed by a quantum number of  $\frac{1}{2}$  or  $-\frac{1}{2}$ . According to the Pauli principle, any two electrons occupying the same orbital must have opposite spins, so the total magnetic

<sup>202</sup>For monographs, see Alfassi, Z.B. *N-Centered Radicals*, Wiley, Chichester, **1998**; Alfassi, Z.B. *Peroxy Radicals*, Wiley, Chichester, **1997**; Alfassi, Z.B. *Chemical Kinetics of Small Organic Radicals*, 4 vols., CRC Press: Boca Raton, FL, **1988**; Nonhebel, D.C.; Tedder, J.M.; Walton, J.C. *Radicals*, Cambridge University Press, Cambridge, **1979**; Nonhebel, D.C.; Walton, J.C. *Free-Radical Chemistry*, Cambridge University Press, Cambridge, **1974**; Kochi, J.K. *Free Radicals*, 2 vols., Wiley, NY, **1973**; Hay, J.M. *Reactive Free Radicals*, Academic Press, NY, **1974**; Pryor, W.A. *Free Radicals*, McGraw-Hill, NY, **1966**. For reviews, see Kaplan, L. *React. Intermed. (Wiley)* **1985**, 3, 227; **1981**, 2, 251–314; **1978**, 1, 163; Griller, D.; Ingold, K.U. *Acc. Chem. Res.* **1976**, 9, 13; Huyser, E.S., in McManus, S.P. *Organic Reactive Intermediates*, Academic Press, NY, **1973**, pp. 1–59; Isaacs, N.S. *Reactive Intermediates in Organic Chemistry*, Wiley, NY, **1974**, pp. 294–374.

<sup>203</sup>For a review of the use of matrices to study radicals and other unstable species, see Dunkin, I.R. *Chem. Soc. Rev.* **1980**, 9, 1; Jacox, M.E. *Rev. Chem. Intermed.* **1978**, 2, 1. For a review of the study of radicals at low temperatures, see Mile, B. *Angew. Chem. Int. Ed.* **1968**, 7, 507.

<sup>204</sup>For a review of infrared spectra of radicals trapped in matrices, see Andrews, L. *Annu. Rev. Phys. Chem.* **1971**, 22, 109.

<sup>205</sup>Sullivan, P.J.; Koski, W.S. *J. Am. Chem. Soc.* **1963**, 85, 384.

<sup>206</sup>Sablier, M.; Fujii, T. *Chem. Rev.* **2002**, 102, 2855.

<sup>207</sup>Bucher, G.; Halupka, M.; Kolano, C.; Schade, O.; Sander, W. *Eur. J. Org. Chem.* **2001**, 545.

moment is zero for any species in which all the electrons are paired. In radicals, however, one or more electrons are unpaired, so there is a net magnetic moment and the species is paramagnetic. Radicals can therefore be detected by magnetic-susceptibility measurements, but for this technique a relatively high concentration of radicals is required.

A much more important technique is *electron spin resonance* (esr), also called *electron paramagnetic resonance* (epr).<sup>208</sup> The principle of esr is similar to that of nmr, except that electron spin is involved rather than nuclear spin. The two electron spin states ( $m_s = \frac{1}{2}$  and  $m_s = -\frac{1}{2}$ ) are ordinarily of equal energy, but in a magnetic field the energies are different. As in NMR, a strong external field is applied and electrons are caused to flip from the lower state to the higher by the application of an appropriate radio-frequency (rf) signal. Inasmuch as two electrons paired in one orbital must have opposite spins which cancel, an esr spectrum arises only from species that have one or more unpaired electrons (i.e., free radicals).

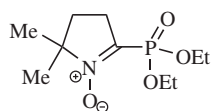
Since only free radicals give an esr spectrum, the method can be used to detect the presence of radicals and to determine their concentration.<sup>209</sup> Furthermore, information concerning the electron distribution (and hence the structure) of free radicals can be obtained from the splitting pattern of the esr spectrum (esr peaks are split by nearby protons).<sup>210</sup> Fortunately (for the existence of most free radicals is very short), it is not necessary for a radical to be persistent for an esr spectrum to be obtained. Electron spin resonance spectra have been observed for radicals with lifetimes considerably  $< 1$  s. Failure to observe an esr spectrum does not prove that radicals are not involved, since the concentration may be too low for direct observation. In such cases, the *spin trapping* technique can

<sup>208</sup>For monographs, see Wertz, J.E.; Bolton, J.R. *Electron Spin Resonance*; McGraw-Hill, NY, **1972** [reprinted by Chapman and Hall, NY, and Methuen, London, **1986**]; Assenheim, H.M. *Introduction to Electron Spin Resonance*, Plenum, NY, **1967**; Bersohn, R.; Baird, J.C. *An Introduction to Electron Paramagnetic Resonance*, W.A. Benjamin, NY, **1966**. For reviews, see Bunce, N.J. *J. Chem. Educ.* **1987**, *64*, 907; Hirota, N.; Ohya-Nishiguchi, H., in Bernasconi, C.F. *Investigation of Rates and Mechanisms of Reactions*, 4th ed., pt. 2, Wiley, NY, **1986**, pp. 605–655; Griller, D.; Ingold, K.U. *Acc. Chem. Res.* **1980**, *13*, 193; Norman, R.O.C. *Chem. Soc. Rev.* **1980**, *8*, 1; Fischer, H., in Kochi, J.K. *Free Radicals*, Vol. 2, Wiley, NY, **1973**, pp. 435–491; Russell, G.A., in Nachod, F.C.; Zuckerman, J.J. *Determination of Organic Structures by Physical Methods*, Vol. 3; Academic Press, NY, **1971**, pp. 293–341; Rassat, A. *Pure Appl. Chem.* **1971**, *25*, 623; Kevan, L. *Methods Free-Radical Chem.* **1969**, *1*, 1; Geske, D.H. *Prog. Phys. Org. Chem.* **1967**, *4*, 125; Norman, R.O.C.; Gilbert, B.C. *Adv. Phys. Org. Chem.* **1967**, *5*, 53; Schneider, F.; Möbius, K.; Plato, M. *Angew. Chem. Int. Ed.* **1965**, *4*, 856. For a review on the application of epr to photochemistry, see Turro, N.J.; Kleinman, M.H.; Karatekin, E. *Angew. Chem. Int. Ed.* **2000**, *39*, 4437. For a review of the related ENDOR method, see Kurreck, H.; Kirste, B.; Lubitz, W. *Angew. Chem. Int. Ed.* **1984**, *23*, 173. See also, Poole, Jr., C.P. *Electron Spin Resonance. A Comprehensive Treatise on Experimental Techniques*, 2nd ed., Wiley, NY, **1983**.

<sup>209</sup>Davies, A.G. *Chem. Soc. Rev.* **1993**, *22*, 299.

<sup>210</sup>For reviews of the use of esr spectra to determine structures, see Walton, J.C. *Rev. Chem. Intermed.* **1984**, *5*, 249; Kochi, J.K. *Adv. Free-Radical Chem.* **1975**, *5*, 189. For esr spectra of a large number of free radicals, see Bielski, B.H.J.; Gebicki, J.M. *Atlas of Electron Spin Resonance Spectra*; Academic Press, NY, **1967**.

be used.<sup>211</sup> In this technique, a compound is added that is able to combine with very reactive radicals to produce more persistent radicals; the new radicals can be observed by esr. Azulenyl nitrones have been developed as chromotropic spin trapping agents.<sup>212</sup> The most important spin-trapping compounds are nitroso compounds, which react with radicals to give fairly stable nitroxide radicals:<sup>213</sup>  $RN=O + R'^{\bullet} \rightarrow RR'N-O^{\bullet}$ . An *N*-oxide spin trap has been developed [33; 2(diethylphosphino)-5,5-dimethyl-1-pyrroline-*N*-oxide], and upon trapping a reactive free radical, <sup>31</sup>P NMR can be used to identify it.<sup>214</sup> This is an effective technique, and short-lived species such as the oxiranylmethyl radical has been detected by spin trapping.<sup>215</sup> Other molecules have been used to probe the intermediacy of radicals via SET processes. They are called SET probes.<sup>216</sup>



33

Because there is an equal probability that a given unpaired electron will have a quantum number of  $\frac{1}{2}$  or  $-\frac{1}{2}$ , radicals are observed as a single line in an esr spectrum unless they interact with other electronic or nuclear spins or possess magnetic anisotropy, in which case two or more lines may appear in the spectrum.<sup>217</sup>

Another magnetic technique for the detection of free radicals uses an ordinary NMR instrument. It was discovered<sup>218</sup> that if an nmr spectrum is taken during the course of a reaction, certain signals may be enhanced, either in a positive or negative direction; others may be reduced. When this type of behavior, called *chemically*

<sup>211</sup>For reviews, see Janzen, E.G.; Haire, D.L. *Adv. Free Radical Chem. (Greenwich, Conn.)* **1990**, 1, 253; Gasanov, R.G.; Freidlina, R.Kh. *Russ. Chem. Rev.* **1987**, 56, 264; Perkins, M.J. *Adv. Phys. Org. Chem.* **1980**, 17, 1; Zubarev, V.E.; Belevskii, V.N.; Bugaenko, L.T. *Russ. Chem. Rev.* **1979**, 48, 729; Evans, C.A. *Aldrichimica Acta* **1979**, 12, 23; Janzen, E.G. *Acc. Chem. Res.* **1971**, 4, 31. See also, the collection of papers on this subject in *Can. J. Chem.* **1982**, 60, 1379.

<sup>212</sup>Becker, D.A. *J. Am. Chem. Soc.* **1996**, 118, 905; Becker, D.A.; Natero, R.; Echegoyen, L.; Lawson, R.C. *J. Chem. Soc. Perkin Trans. 2* **1998**, 1289. Also see, Klivenyi, P.; Matthews, R.T.; Wermer, M.; Yang, L.; MacGarvey, U.; Becker, D.A.; Natero, R.; Beal, M.F. *Experimental Neurobiology* **1998**, 152, 163.

<sup>213</sup>For a series of papers on nitroxide radicals, see *Pure Appl. Chem.* **1990**, 62, 177.

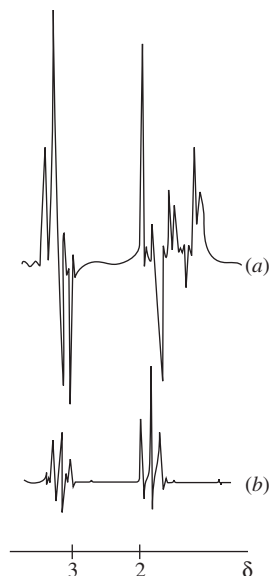
<sup>214</sup>Janzen, E.G.; Zhang, Y.-K. *J. Org. Chem.* **1995**, 60, 5441. For the preparation of a new but structurally related spin trap see Karoui, H.; Nsanzumuhire, C.; Le Moigne, F.; Tordo, P. *J. Org. Chem.* **1999**, 64, 1471.

<sup>215</sup>Grossi, L.; Strazzari, S. *Chem. Commun.* **1997**, 917.

<sup>216</sup>Timberlake, J.W.; Chen, T. *Tetrahedron Lett.* **1994**, 35, 6043; Tanko, J.M.; Brammer Jr., L.E.; Hervás, M.; Campos, K. *J. Chem. Soc. Perkin Trans. 2* **1994**, 1407.

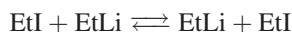
<sup>217</sup>Harry Frank, University of Connecticut, Storrs, CT., Personal Communication.

<sup>218</sup>Ward, H.R.; Lawler, R.G.; Cooper, R.A. *J. Am. Chem. Soc.* **1969**, 91, 746; Bargon, J.; Fischer, H.; Johnsen, U. *Z. Naturforsch., Teil A* **1967**, 22, 1551; Bargon, J.; Fischer, H. *Z. Naturforsch., Teil A* **1967**, 22, 1556; Lepley, A.R. *J. Am. Chem. Soc.* **1969**, 91, 749; Lepley, A.R.; Landau, R.L. *J. Am. Chem. Soc.* **1969**, 91, 748.



**Fig. 5.1** (a) The NMR spectrum taken during reaction between EtI and EtLi in benzene (the region between 0.5 and 3.5  $\delta$  was scanned with an amplitude twice that of the remainder of the spectrum). The signals at 1.0–1.6  $\delta$  are due to butane, some of which is also formed in the reaction. (b) Reference spectrum of EtI.<sup>221</sup>

*induced dynamic nuclear polarization*<sup>219</sup> (CIDNP), is found in the nmr spectrum of the product of a reaction, it means that *at least a portion of that product was formed via the intermediacy of a free radical*.<sup>220</sup> For example, the question was raised whether radicals were intermediates in the exchange reaction between ethyl iodide and ethyllithium (reaction 12-39):



Curve *a* in Fig. 5.1<sup>221</sup> shows an NMR spectrum taken during the course of the reaction. Curve *b* is a reference spectrum of ethyl iodide ( $\text{CH}_3$  protons at  $\delta = 1.85$ ;  $\text{CH}_2$  protons at  $\delta = 3.2$ ). Note that in curve *a* some of the ethyl iodide signals are

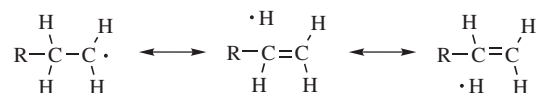
<sup>219</sup>For a monograph on CIDNP, see Lepley, R.L.; Closs, G.L. *Chemically Induced Magnetic Polarization*, Wiley, NY, 1973. For reviews, see Adrian, F.J. *Rev. Chem. Intermed.* **1986**, 7, 173; Closs, G.L.; Miller, R.J.; Redwine, O.D. *Acc. Chem. Res.* **1985**, 18, 196; Lawler, R.G.; Ward, H.R., in Nachod, F.C.; Zuckerman, J.J. *Determination of Rates and Mechanisms of Reactions*, Vol. 5, Academic Press, NY, **1973**, pp. 99–150; Ward, H.R., in Kochi, J.K. *Free Radicals*, Vol. 1, Wiley, NY, **1973**, pp. 239–273; *Acc. Chem. Res.* **1972**, 5, 18; Closs, G.L. *Adv. Magn. Reson.* **1974**, 7, 157; Lawler, R.G. *Acc. Chem. Res.* **1972**, 5, 25; Kaptein, R. *Adv. Free-Radical Chem.* **1975**, 5, 319; Bethell, D.; Brinkman, M.R. *Adv. Phys. Org. Chem.* **1973**, 10, 53.

<sup>220</sup>A related technique is called chemically induced dynamic electron polarization (CIDEP). For a review, see Hore, P.J.; Joslin, C.G.; McLauchlan, K.A. *Chem. Soc. Rev.* **1979**, 8, 29.

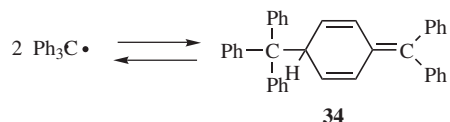
<sup>221</sup>Ward, H.R.; Lawler, R.G.; Cooper, R.A. *J. Am. Chem. Soc.* **1969**, 91, 746.

enhanced; others go below the base line (*negative enhancement*; also called *emission*). Thus the ethyl iodide formed in the exchange shows CIDNP, and hence was formed via a free-radical intermediate. Chemically induced dynamic nuclear polarization results when protons in a reacting molecule become dynamically coupled to an unpaired electron while traversing the path from reactants to products. Although the presence of CIDNP almost always means that a free radical is involved,<sup>222</sup> its absence does not prove that a free-radical intermediate is necessarily absent, since reactions involving free-radical intermediates can also take place without observable CIDNP. Also, the presence of CIDNP does not prove that *all* of a product was formed via a free-radical intermediate, only that some of it was. It is noted that dynamic nuclear polarization (DNP) enhance signal intensities in NMR spectra of solids and liquids. In a contemporary DNP experiment, a diamagnetic sample is doped with a paramagnet and the large polarization of the electron spins is transferred to the nuclei via microwave irradiation of the epr spectrum.<sup>223</sup> Dynamic nuclear polarization has been used to examine biradicals.<sup>224</sup>

As with carbocations, the stability order of free radicals is tertiary > secondary > primary, explainable by field effects and hyperconjugation, analogous to that in carbocations (p. 235):



With resonance possibilities, the stability of free radicals increases;<sup>225</sup> some can be kept indefinitely.<sup>226</sup> Benzylic and allylic<sup>227</sup> radicals for which canonical forms can be drawn similar to those shown for the corresponding cations



(pp. 239, 240) and anions (pp. 252) are more stable than simple alkyl radicals, but still have only a transient existence under ordinary conditions. However, the triphenylmethyl and similar radicals<sup>228</sup> are stable enough to exist in solution

<sup>222</sup>It has been shown that CIDNP can also arise in cases where para hydrogen ( $\text{H}_2$  in which the nuclear spins are opposite) is present: Eischmid, T.C.; Kirss, R.U.; Deutsch, P.P.; Hommeltoft, S.I.; Eisenberg, R.; Bargon, J.; Lawler, R.G.; Balch, A.L. *J. Am. Chem. Soc.* **1987**, 109, 8089.

<sup>223</sup>Wind, R.A.; Duijvestijn, M.J.; van der Lugt, C.; Manenschijn, A.; Vriend, J. *Prog. Nucl. Magn. Reson. Spectrosc.* **1985**, 17, 33.

<sup>224</sup>Hu, K.-N.; Yu, H.-h.; Swager, T.M.; Griffin, R.G. *J. Am. Chem. Soc.* **2004**, 126, 10844.

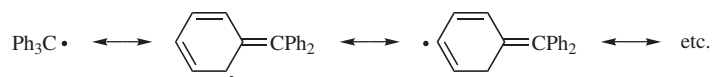
<sup>225</sup>For a discussion, see Robaugh, D.A.; Stein, S.E. *J. Am. Chem. Soc.* **1986**, 108, 3224.

<sup>226</sup>For a monograph on stable radicals, including those in which the unpaired electron is not on a carbon atom, see Forrester, A.R.; Hay, J.M.; Thomson, R.H. *Organic Chemistry of Stable Free Radicals*, Academic Press, NY, **1968**.

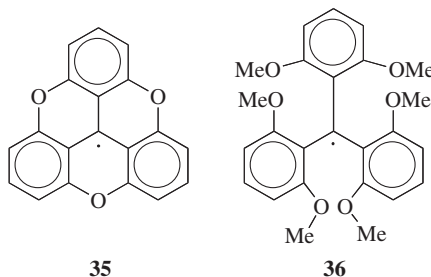
<sup>227</sup>For an electron diffraction study of the allyl radical, see Vajda, E.; Tremmel, J.; Rozsondai, B.; Hargittai, I.; Maltsev, A.K.; Kagramanov, N.D.; Nefedov, O.M. *J. Am. Chem. Soc.* **1986**, 108, 4352.

<sup>228</sup>For a review, see Sholle, V.D.; Rozantsev, E.G. *Russ. Chem. Rev.* **1973**, 42, 1011.

at room temperature, although in equilibrium with a dimeric form. The concentration of triphenylmethyl radical in benzene solution is  $\sim 2\%$  at room temperature. For many years it was assumed that  $\text{Ph}_3\text{C}\cdot$ , the first stable free radical known,<sup>229</sup> dimerized to hexaphenylethane ( $\text{Ph}_3\text{C}-\text{CPh}_3$ ),<sup>230</sup> but UV and NMR investigations have shown that the true structure is **34**.<sup>231</sup> Although triphenylmethyl-type radicals are stabilized by resonance:



it is steric hindrance to dimerization and not resonance that is the major cause of their stability.<sup>232</sup> This was demonstrated by the preparation of the radicals **35** and **36**.<sup>233</sup> These radicals are electronically very similar, but **35**, being planar, has much less steric hindrance to dimerization than  $\text{Ph}_3\text{C}\cdot$ , while **36**, with six groups in ortho positions, has much more. On the other hand, the planarity of **35** means that



it has a maximum amount of resonance stabilization, while **36** must have much less, since its degree of planarity should be even less than  $\text{Ph}_3\text{C}\cdot$ , which itself is propeller shaped and not planar. Thus if resonance is the chief cause of the stability of  $\text{Ph}_3\text{C}\cdot$ , **36** should dimerize and **35** should not, but if steric hindrance is

<sup>229</sup>Gomberg, M. *J. Am. Chem. Soc.* **1900**, 22, 757, *Ber.* **1900**, 33, 3150.

<sup>230</sup>Hexaphenylethane has still not been prepared, but substituted compounds [hexakis(3,5-di-*tert*-butyl-4-biphenyl)ethane and hexakis(3,5-di-*tert*-butylphenyl)ethane] have been shown by X-ray crystallography to be nonbridged hexaarylethanes in the solid state: Stein, M.; Winter, W.; Rieker, A. *Angew. Chem. Int. Ed.* **1978**, 17, 692; Yannoni, N.; Kahr, B.; Mislow, K. *J. Am. Chem. Soc.* **1988**, 110, 6670. In solution, both dissociate into free radicals.

<sup>231</sup>Lankamp, H.; Nauta, W.T.; MacLean, C. *Tetrahedron Lett.* **1968**, 249; Staab, H.A.; Brettschneider, H.; Brunner, H. *Chem. Ber.* **1970**, 103, 1101; Volz, H.; Lotsch, W.; Schnell, H. *Tetrahedron* **1970**, 26, 5343; McBride, J. *Tetrahedron* **1974**, 30, 2009. See also, Guthrie, R.D.; Weisman, G.R. *Chem. Commun.* **1969**, 1316; Takeuchi, H.; Nagai, T.; Tokura, N. *Bull. Chem. Soc. Jpn.* **1971**, 44, 753. For an example where a secondary benzylic radical undergoes this type of dimerization, see Peyman, A.; Peters, K.; von Schnering, H.G.; Rüchardt, C. *Chem. Ber.* **1990**, 123, 1899.

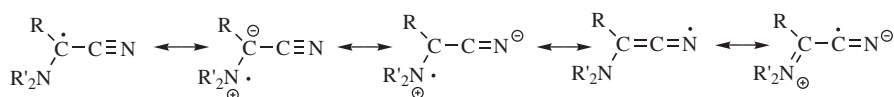
<sup>232</sup>For a review of steric effects in free-radical chemistry, see Rüchardt, C. *Top. Curr. Chem.* **1980**, 88, 1.

<sup>233</sup>Sabacky, M.J.; Johnson Jr., C.S.; Smith, R.G.; Gutowsky, H.S.; Martin, J.C. *J. Am. Chem. Soc.* **1967**, 89, 2054.

the major cause, the reverse should happen. It was found<sup>233</sup> that **36** gave no evidence of dimerization, even in the solid state, while **35** existed primarily in the dimeric form, which is dissociated to only a small extent in solution,<sup>234</sup> indicating that steric hindrance to dimerization is the major cause for the stability of triarylmethyl radicals. A similar conclusion was reached in the case of  $(\text{NC})_3\text{C}\cdot$ , which dimerizes readily although considerably stabilized by resonance.<sup>235</sup> Nevertheless, that resonance is still an important contributing factor to the stability of radicals is shown by the facts that (1) the radical  $t\text{-Bu}(\text{Ph})_2\text{C}\cdot$  dimerizes more than  $\text{Ph}_3\text{C}\cdot$ , while  $p\text{-PhCOC}_6\text{H}_4(\text{Ph})_2\text{C}\cdot$  dimerizes less.<sup>236</sup> The latter has more canonical forms than  $\text{Ph}_3\text{C}\cdot$ , but steric hindrance should be about the same (for attack at one of the two rings). (2) A number of radicals ( $p\text{-XC}_6\text{H}_4)_3\text{C}\cdot$ , with  $\text{X} = \text{F}, \text{Cl}, \text{O}_2\text{N}, \text{CN}$ , and so on do not dimerize, but are kinetically stable.<sup>237</sup> Completely chlorinated triarylmethyl radicals are more stable than the unsubstituted kind, probably for steric reasons, and many are quite inert in solution and in the solid state.<sup>238</sup>

Allylic radical are relatively stable, and the pentadienyl radical is particularly stable. In such molecules, (*E,E*)-(*E,Z*)-, and (*Z,Z*)-stereoisomers can form. It has been calculated that (*Z,Z*)-pentadienyl radical is  $5.6 \text{ kcal mol}^{-1}$  ( $23.4 \text{ kJ mol}^{-1}$ ) less stable than (*E,E*)-pentadienyl radical.<sup>239</sup> 2-Phenylethyl radicals have been shown to exhibit bridging of the phenyl group.<sup>240</sup> It is noted that vinyl radical have (*E*)- and (*Z*)-forms and the inversion barrier from one to the other increases as the electronegativity of substituents increase.<sup>241</sup> Enolate radicals are also known.<sup>242</sup>

It has been postulated that the stability of free radicals is enhanced by the presence at the radical center of *both* an electron-donating and an electron-withdrawing group.<sup>243</sup> This is called the *push-pull* or *captodative effect* (see also, pp. 185). The effect arises from increased resonance, for example:



<sup>234</sup>Müller, E.; Moosmayer, A.; Rieker, A.; Scheffler, K. *Tetrahedron Lett.* **1967**, 3877. See also, Neugebauer, F.A.; Hellwinkel, D.; Aulmich, G. *Tetrahedron Lett.* **1978**, 4871.

<sup>235</sup>Kaba, R.A.; Ingold, K.U. *J. Am. Chem. Soc.* **1976**, 98, 523.

<sup>236</sup>Zarkadis, A.K.; Neumann, W.P.; Marx, R.; Uzick, W. *Chem. Ber.* **1985**, 118, 450; Zarkadis, A.K.; Neumann, W.P.; Uzick, W. *Chem. Ber.* **1985**, 118, 1183.

<sup>237</sup>Dünnebacke, D.; Neumann, W.P.; Penenory, A.; Stewen, U. *Chem. Ber.* **1989**, 122, 533.

<sup>238</sup>For reviews, see Ballester, M. *Adv. Phys. Org. Chem.* **1989**, 25, 267, pp. 354–405, *Acc. Chem. Res.* **1985**, 18, 380. See also, Hegarty, A.F.; O'Neill, P. *Tetrahedron Lett.* **1987**, 28, 901.

<sup>239</sup>Fort Jr., R.C.; Hrovat, D.A.; Borden, W.T. *J. Org. Chem.* **1993**, 58, 211.

<sup>240</sup>Asensio, A.; Dannenberg, J.J. *J. Org. Chem.* **2001**, 66, 5996.

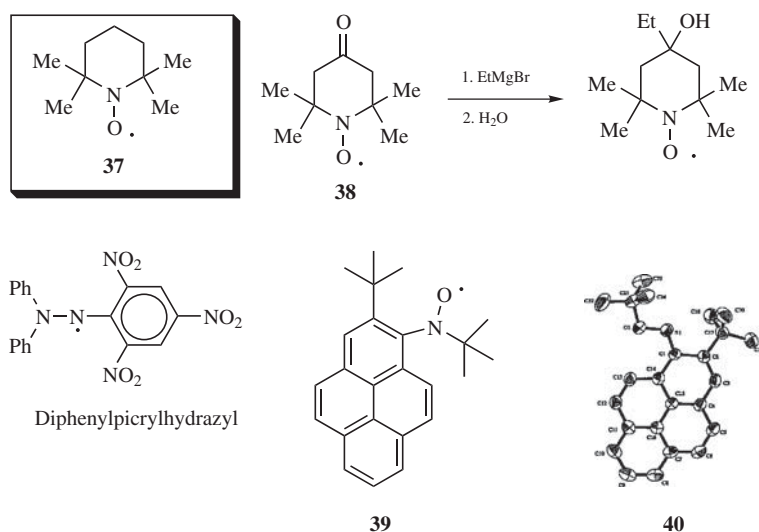
<sup>241</sup>Galli, C.; Guarnieri, A.; Koch, H.; Mencarelli, P.; Rappoport, Z. *J. Org. Chem.* **1997**, 62, 4072.

<sup>242</sup>Giese, B.; Damm, W.; Wetterich, F.; Zeltz, H.-G.; Rancourt, J.; Guindon, Y. *Tetrahedron Lett.* **1993**, 34, 5885.

<sup>243</sup>For reviews, see Sustmann, R.; Korth, H. *Adv. Phys. Org. Chem.* **1990**, 26, 131; Viehe, H.G.; Janousek, Z.; Merényi, R.; Stella, L. *Acc. Chem. Res.* **1985**, 18, 148.



There is some evidence in favor<sup>244</sup> of the captodative effect, some of it from esr studies.<sup>245</sup> However, there is also experimental<sup>246</sup> and theoretical<sup>247</sup> evidence against it. There is evidence that while  $\text{FCH}_2^\bullet$  and  $\text{F}_2\text{CH}^\bullet$  are more stable than  $\text{CH}_3^\bullet$ , the radical  $\text{CF}_3^\bullet$  is less stable; that is, the presence of the third F destabilizes the radical.<sup>248</sup>



Certain radicals with the unpaired electron not on a carbon are also very stable.<sup>249</sup> Radicals can be stabilized by intramolecular hydrogen bonding.<sup>250</sup>

<sup>244</sup>For a summary of the evidence, see Pasto, D.J. *J. Am. Chem. Soc.* **1988**, *110*, 8164. See also, Ashby, E.C. *Bull. Soc. Chim. Fr.* **1972**, 2133; *Q. Rev. Chem. Soc.* **1967**, *21*, 259; Wakefield, B.J. *Organomet. Chem. Rev.* **1966**, *1*, 131; Bell, N.A. *Educ. Chem.* **1973**, 143.

<sup>245</sup>See, for example, Korth, H.; Lommes, P.; Sustmann, R.; Sylvander, L.; Stella, L. *New J. Chem.* **1987**, *11*, 365; Sakurai, H.; Kyushin, S.; Nakadaira, Y.; Kira, M. *J. Phys. Org. Chem.* **1988**, *1*, 197; Rhodes, C.J.; Roduner, E. *Tetrahedron Lett.* **1988**, *29*, 1437; Viehe, H.G.; Merényi, R.; Janousek, Z. *Pure Appl. Chem.* **1988**, *60*, 1635; Creary, X.; Sky, A.F.; Mehrsheikh-Mohammadi, M.E. *Tetrahedron Lett.* **1988**, *29*, 6839; Bordwell, F.G.; Lynch, T. *J. Am. Chem. Soc.* **1989**, *111*, 7558.

<sup>246</sup>See, for example, Beckhaus, H.; Rüchardt, C. *Angew. Chem. Int. Ed.* **1987**, *26*, 770; Neumann, W.P.; Penenory, A.; Stewen, U.; Lehnig, M. *J. Am. Chem. Soc.* **1989**, *111*, 5845; Bordwell, F.G.; Bausch, M.J.; Cheng, J.P.; Cripe, T.H.; Lynch, T.-Y.; Mueller, M.E. *J. Org. Chem.* **1990**, *55*, 58; Bordwell, F.G.; Harrelson Jr., J.A. *Can. J. Chem.* **1990**, *68*, 1714.

<sup>247</sup>See Pasto, D.J. *J. Am. Chem. Soc.* **1988**, *110*, 8164.

<sup>248</sup>Jiang, X.; Li, X.; Wang, K. *J. Org. Chem.* **1989**, *54*, 5648.

<sup>249</sup>For reviews of radicals with the unpaired electron on atoms other than carbon, see, in Kochi, J.K. *Free Radicals*, Vol. 2, Wiley, NY, **1973**, the reviews by Nelson, S.F. pp. 527–593 (*N*-centered); Bentrude, W.G. pp. 595–663 (*P*-centered); Kochi, J.K. pp. 665–710 (*O*-centered); Kice, J.L. pp. 711–740 (*S*-centered); Sakurai, H. pp. 741–807 (Si, Ge, Sn, and Pb centered).

<sup>250</sup>Maki, T.; Araki, Y.; Ishida, Y.; Onomura, O.; Matsumura, Y. *J. Am. Chem. Soc.* **2001**, *123*, 3371.



Diphenylpicrylhydrazyl is a solid that can be kept for years, and stable neutral azine radicals have been prepared.<sup>251</sup> Nitroxide radicals were mentioned previously (p. 273),<sup>252</sup> and the commercially available TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl free radical, **37**) is a stable nitroxyl radical used in chemical reactions such as oxidations,<sup>253</sup> or as a spin trap.<sup>254</sup> Nitroxyl radical **38** is a nitroxide radical so stable that reactions can be performed on it without affecting the unpaired electron<sup>255</sup> (the same is true for some of the chlorinated triarylmethyl radicals mentioned above<sup>256</sup>). Several nitrogen-containing groups are known to stabilize radicals, and the most effective radical stabilization is via spin delocalization.<sup>257</sup> A number of persistent *N-tert*-butoxy-1-aminopyrenyl radicals, such as **39**, have been isolated as monomeric radical crystals (see **40**, the X-ray crystal structure of **39**),<sup>258</sup> and monomeric *N*-alkoxyarylaminyls have been isolated.<sup>259</sup>  $\alpha$ -Trichloromethylbenzyl(*tert*-butyl)aminoxyl (**41**) is extremely stable.<sup>260</sup> In aqueous media it is stable for >30 days, and in solution in an aromatic hydrocarbon solvent it has survived for more than 90 days.<sup>260</sup> Although the stable nitroxide radicals have the  $\alpha$ -carbon blocked to prevent radical formation there, stable nitroxide radicals are also known with hydrogen at the  $\alpha$ -carbon,<sup>261</sup> and long-lived vinyl nitroxide radicals are known.<sup>262</sup> A stable organic radical lacking resonance stabilization has been prepared (**42**) and its X-ray crystal structure was

<sup>251</sup>Jeromin, G.E. *Tetrahedron Lett.* **2001**, 42, 1863.

<sup>252</sup>For a study of the electronic structure of persistent nitroxide radicals see Novak, I.; Harrison, L.J.; Kovač, B.; Pratt, L.M. *J. Org. Chem.* **2004**, 69, 7628.

<sup>253</sup>See Anelli, P.L.; Biffi, C.; Montanari, F.; Quici, S. *J. Org. Chem.* **1987**, 52, 2559; Anelli, P.L.; Banfi, S.; Montanari, F.; Quici, S. *J. Org. Chem.* **1989**, 54, 2970; Anelli, P.L.; Montanari, F.; Quici, S. *Org. Synth.* **1990**, 69, 212; Fritz-Langhals, E. *Org. Process Res. Dev.* **2005**, 9, 577. See also, Rychnovsky, S.D.; Vaidyanathan, R.; Beauchamp, T.; Lin, R.; Farmer, P.J. *J. Org. Chem.* **1999**, 64, 6745.

<sup>254</sup>Volodarsky, L.B.; Reznikov, V.A.; Ovcharenko, V.I. *Synthetic Chemistry of Stable Nitroxides*, CRC Press: Boca Raton, FL, **1994**; Keana, J.F.W. *Chem. Rev.* **1978**, 78, 37; Aurich, H.G. *Nitroxides. In Nitrones, Nitronates, Nitroxides*, Patai, S., Rappoport, Z., (Eds.), Wiley, NY, **1989**; Chapt. 4.

<sup>255</sup>Neiman, M.B.; Rozantsev, E.G.; Mamedova, Yu.G. *Nature* **1963**, 200, 256. For reviews of such radicals, see Aurich, H.G., in Patai, S. *The Chemistry of Functional Groups, Supplement F*, pt. 1, Wiley, NY, **1982**, pp. 565–622 [This review has been reprinted, and new material added, in Breuer, E.; Aurich, H.G.; Nielsen, A. *Nitrones, Nitronates, and Nitroxides*, Wiley, NY, **1989**, pp. 313–399]; Rozantsev, E.G.; Sholle, V.D. *Synthesis* **1971**, 190, 401.

<sup>256</sup>See Ballester, M.; Veciana, J.; Riera, J.; Castañer, J.; Armet, O.; Rovira, C. *J. Chem. Soc. Chem. Commun.* **1983**, 982.

<sup>257</sup>Adam, W.; Ortega Schulte, C.M. *J. Org. Chem.* **2002**, 67, 4569.

<sup>258</sup>Miura, Y.; Matsuba, N.; Tanaka, R.; Teki, Y.; Takui, T. *J. Org. Chem.* **2002**, 67, 8764. For another stable nitroxide radical, see Huang, W.-I.; Chiarelli, R.; Rassat, A. *Tetrahedron Lett.* **2000**, 41, 8787.

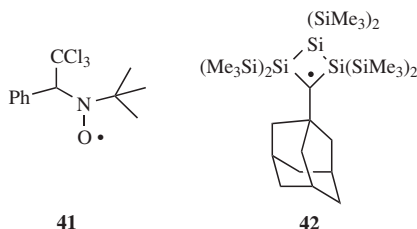
<sup>259</sup>Miura, Y.; Tomimura, T.; Matsuba, N.; Tanaka, R.; Nakatsuji, M.; Teki, Y. *J. Org. Chem.* **2001**, 66, 7456.

<sup>260</sup>Janzen, E.G.; Chen, G.; Bray, T.M.; Reinke, L.A.; Poyer, J.L.; McCay, P.B. *J. Chem. Soc. Perkin Trans. 2* **1993**, 1983.

<sup>261</sup>Reznikov, V.A.; Volodarsky, L.B. *Tetrahedron Lett.* **1994**, 35, 2239.

<sup>262</sup>Reznikov, V.A.; Pervukhina, N.V.; Ikorskii, V.N.; Ovcharenko, V.I.; Grand, A. *Chem. Commun.* **1999**, 539.

obtained.<sup>263</sup>



Dissociation energies ( $D$  values) of R—H bonds provide a measure of the relative inherent stability of free radicals R.<sup>264</sup> Table 5.4 lists such values.<sup>265</sup> The higher the  $D$  value, the less stable the radical. Bond dissociation energies have also been reported for the C—H bond of alkenes and dienes<sup>266</sup> and for the C—H bond in radical precursors XYZ—H, where X,Y can be H, alkyl, COOR, COR, SR, CN, NO<sub>2</sub>, and so on.<sup>267</sup> Bond dissociation energies for the C—O bond in hydroperoxide radicals (ROO•) have also been reported.<sup>268</sup>

**TABLE 5.4. The  $D_{298}$  Values for Some R—H Bonds.<sup>265</sup>**  
Free-radical Stability is in the Reverse Order

R	$D$	
	kcal mol <sup>-1</sup>	kJ mol <sup>-1</sup>
Ph• <sup>269</sup>	111	464
CF <sub>3</sub> •	107	446
CH <sub>2</sub> =CH•	106	444
Cyclopropyl <sup>270</sup>	106	444
Me•	105	438
Et•	100	419

<sup>263</sup>Apeloig, Y.; Bravo-Zhivotovskii, D.; Bendikov, M.; Danovich, D.; Botoshansky, M.; Vakulrskaya, T.; Voronkov, M.; Samoilova, R.; Zdravkova, M.; Igonin, V.; Shklover, V.; Struchkov, Y. *J. Am. Chem. Soc.* **1999**, *121*, 8118.

<sup>264</sup>It has been claimed that relative  $D$  values do not provide such a measure: Nicholas, A.M. de P.; Arnold, D.R. *Can. J. Chem.* **1984**, *62*, 1850, 1860.

<sup>265</sup>Except where noted, these values are from Kerr, J.A., in Weast, R.C. *Handbook of Chemistry and Physics*, 69th ed.; CRC Press: Boca Raton, FL, **1988**, p. F-183. For another list of  $D$  values, see McMillen, D.F.; Golden, D.M. *Annu. Rev. Phys. Chem.* **1982**, *33*, 493. See also, Tsang, W. *J. Am. Chem. Soc.* **1985**, *107*, 2872; Holmes, J.L.; Lossing, F.P.; Maccoll, A. *J. Am. Chem. Soc.* **1988**, *110*, 7339; Holmes, J.L.; Lossing, F.P. *J. Am. Chem. Soc.* **1988**, *110*, 7343; Roginskii, V.A. *J. Org. Chem. USSR* **1989**, *25*, 403.

<sup>266</sup>Zhang, X.-M. *J. Org. Chem.* **1998**, *63*, 1872.

<sup>267</sup>Brocks, J.J.; Beckhaus, H.-D.; Beckwith, A.L.J.; Rüchardt, C. *J. Org. Chem.* **1998**, *63*, 1935.

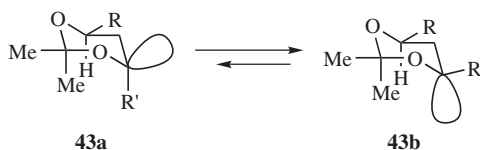
<sup>268</sup>Pratt, D.A.; Porter, N.A. *Org. Lett.* **2003**, *5*, 387.

<sup>269</sup>For the infra-red of a matrix-isolated phenyl radical see Friderichsen, A.V.; Radziszewski, J.G.; Nimlos, M.R.; Winter, P.R.; Dayton, D.C.; David, D.E.; Ellison, G.B. *J. Am. Chem. Soc.* **2001**, *123*, 1977.

<sup>270</sup>For a review of cyclopropyl radicals, see Walborsky, H.M. *Tetrahedron* **1981**, *37*, 1625. See also, Boche, G.; Walborsky, H.M. *Cyclopropane Derived Reactive Intermediates*, Wiley, NY, **1990**.

Me <sub>3</sub> CCH <sub>2</sub> •	100	418
Pr•	100	417
Cl <sub>3</sub> C•	96	401
Me <sub>2</sub> CH•	96	401
Me <sub>3</sub> C• <sup>271</sup>	95.8	401
Cyclohexyl	95.5	400
PhCH <sub>2</sub> •	88	368
HCO•	87	364
CH <sub>2</sub> =CH-CH <sub>2</sub> •	86	361

There are two possible structures for simple alkyl radicals.<sup>272</sup> They might have  $sp^2$  bonding, in which case the structure would be planar, with the odd electron in a  $p$  orbital, or the bonding might be  $sp^3$ , which would make the structure pyramidal and place the odd electron in an  $sp^3$  orbital. The esr spectra of  $\bullet\text{CH}_3$  and other simple alkyl radicals, as well as other evidence indicate that these radicals have planar structures.<sup>273</sup> This is in accord with the known loss of optical activity when a free radical is generated at a chiral carbon.<sup>274</sup> In addition, electronic spectra of the  $\text{CH}_3$  and  $\text{CD}_3$  radicals (generated by flash photolysis) in the gas phase have definitely established that under these conditions the radicals are planar or near planar.<sup>275</sup> IR spectra of  $\bullet\text{CH}_3$  trapped in solid argon led to a similar conclusion.<sup>276</sup>



Despite the usual loss of optical activity noted above, asymmetric radicals can be prepared in some cases. For example, asymmetric nitroxide radicals are known.<sup>277</sup> An anomeric effect was observed in alkoxy radical **43**, where the ratio of **43a**/**43b** was 1:1.78.<sup>278</sup>

<sup>271</sup>This value is from Gutman, D. *Acc. Chem. Res.* **1990**, *23*, 375.

<sup>272</sup>For a review, see Kaplan, L., in Kochi, J.K. *Free Radicals*, Vol. 2, Wiley, NY, **1973**, pp. 361–434.

<sup>273</sup>See, for example, Cole, T.; Pritchard, D.E.; Davidson, N.; McConnell, H.M. *Mol. Phys.* **1958**, *1*, 406; Fessenden, R.W.; Schuler, R.H. *J. Chem. Phys.* **1963**, *39*, 2147; Symons, M.C.R. *Nature* **1969**, 222, 1123, *Tetrahedron Lett.* **1973**, 207; Bonazzola, L.; Leray, E.; Roncin, J. *J. Am. Chem. Soc.* **1977**, *99*, 8348; Giese, B.; Beckhaus, H. *Angew. Chem. Int. Ed.* **1978**, *17*, 594; Ellison, G.B.; Engelking, P.C.; Lineberger, W.C. *J. Am. Chem. Soc.* **1978**, *100*, 2556. See, however, Paddon-Row, M.N.; Houk, K.N. *J. Am. Chem. Soc.* **1981**, *103*, 5047.

<sup>274</sup>There are a few exceptions. See p. \$\$\$.

<sup>275</sup> Herzberg, G.; Shoosmith, J. *Can. J. Phys.* **1956**, *34*, 523; Herzberg, G. *Proc. R. Soc. London, Ser. A* **1961**, *262*, 291. See also, Tan, L.Y.; Winer, A.M.; Pimentel, G.C. *J. Chem. Phys.* **1972**, *57*, 4028; Yamada, C.; Hirota, E.; Kawaguchi, K. *J. Chem. Phys.* **1981**, *75*, 5256.

<sup>276</sup> Andrews, L.; Pimentel, G.C. *J. Chem. Phys.* **1967**, *47*, 3637; Milligan, D.E.; Jacox, M.E. *J. Chem. Phys.* **1967**, *47*, 5146.

<sup>277</sup>Tamura, R.; Susuki, S.; Azuma, N.; Matsumoto, A.; Todda, F.; Ishii, Y. *J. Org. Chem.* **1995**, *60*, 6820.

<sup>278</sup>Rychnovsky, S.D.; Powers, J.P.; LePage, T.J. *J. Am. Chem. Soc.* **1992**, *114*, 8375.

Evidence from studies on bridgehead compounds shows that although a planar configuration is more stable, pyramidal structures are not impossible. In contrast to the situation with carbocations, free radicals have often been generated at bridgeheads, although studies have shown that bridgehead free radicals are less rapidly formed than the corresponding open-chain radicals.<sup>279</sup> In sum, the available evidence indicates that although simple alkyl free radicals prefer a planar, or near-planar shape, the energy difference between a planar and a pyramidal free radical is not great. However, free radicals in which the carbon is connected to atoms of high electronegativity, for example,  $\bullet\text{CF}_3$ , prefer a pyramidal shape;<sup>280</sup> increasing the electronegativity increases the deviation from planarity.<sup>281</sup> Cyclopropyl radicals are also pyramidal.<sup>282</sup> Free radicals with resonance are definitely planar, although triphenylmethyl-type radicals are propeller-shaped,<sup>283</sup> like the analogous carbocations (p. 245). Radicals possessing simple alkyl substituents attached to the radical carbon ( $\text{C}\bullet$ ) that have  $\text{C}^{sp^3}-\text{C}^{sp^3}$  bonds, and rotation about those bonds is possible. The internal rotation barrier for the *t*-butyl radical ( $\text{Me}_3\text{C}\bullet$ ), for example, was estimated to be  $\sim 1.4 \text{ kcal mol}^{-1}$  ( $6 \text{ kJ mol}^{-1}$ ).<sup>284</sup>

A number of diradicals (also called biradicals) are known,<sup>285</sup> and the thermodynamic stability of diradicals has been examined.<sup>286</sup> Orbital phase theory has been applied to the development of a theoretical model of localized 1,3-diradicals, and used to predict the substitution effects on the spin preference and S–T gaps, and to design stable localized carbon-centered 1,3-diradicals.<sup>287</sup> When the unpaired electrons of a diradical are widely separated, for example, as in  $\bullet\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\bullet$ ,

<sup>279</sup>Lorand, J.P.; Chodroff, S.D.; Wallace, R.W. *J. Am. Chem. Soc.* **1968**, *90*, 5266; Humphrey, L.B.; Hodgson, B.; Pincock, R.E. *Can. J. Chem.* **1968**, *46*, 3099; Oberlinner, A.; Rüchardt, C. *Tetrahedron Lett.* **1969**, 4685; Danen, W.C.; Tipton, T.J.; Saunders, D.G. *J. Am. Chem. Soc.* **1971**, *93*, 5186; Fort, Jr., R.C.; Hiti, J. *J. Org. Chem.* **1977**, *42*, 3968; Lomas, J.S. *J. Org. Chem.* **1987**, *52*, 2627.

<sup>280</sup>Fessenden, R.W.; Schuler, R.H. *J. Chem. Phys.* **1965**, *43*, 2704; Rogers, M.T.; Kispert, L.D. *J. Chem. Phys.* **1967**, *46*, 3193; Pauling, L. *J. Chem. Phys.* **1969**, *51*, 2767.

<sup>281</sup>For example, 1,1-dichloroalkyl radicals are closer to planarity than the corresponding 1,1-difluoro radicals, though still not planar: Chen, K.S.; Tang, D.Y.H.; Montgomery, L.K.; Kochi, J.K. *J. Am. Chem. Soc.* **1974**, *96*, 2201. For a discussion, see Krusic, P.J.; Bingham, R.C. *J. Am. Chem. Soc.* **1976**, *98*, 230.

<sup>282</sup>See Deycard, S.; Hughes, L.; Luszyk, J.; Ingold, K.U. *J. Am. Chem. Soc.* **1987**, *109*, 4954.

<sup>283</sup>Adrian, F.J. *J. Chem. Phys.* **1958**, *28*, 608; Andersen, P. *Acta Chem. Scand.* **1965**, *19*, 629.

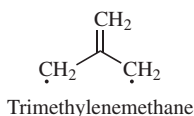
<sup>284</sup>Kubota, S.; Matsushita, M.; Shida, T.; Abu-Raqabah, A.; Symons, M.C.R.; Wyatt, J.L. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 140.

<sup>285</sup>For a monograph, see Borden, W.T. *Diradicals*, Wiley, NY, **1982**. For reviews, see Johnston, L.J.; Scaiano, J.C. *Chem. Rev.* **1989**, *89*, 521; Doubleday, Jr., C.; Turro, N.J.; Wang, J. *Acc. Chem. Res.* **1989**, *22*, 199; Scheffer, J.R.; Trotter, J. *Rev. Chem. Intermed.* **1988**, *9*, 271; Wilson, R.M. *Org. Photochem.* **1985**, *7*, 339; Borden, W.T. *React. Intermed. (Wiley)* **1985**, *3*, 151; **1981**, *2*, 175; Borden, W.T.; Davidson, E.R. *Acc. Chem. Res.* **1981**, *14*, 69; Salem, L.; Rowland, C. *Angew. Chem. Int. Ed.* **1972**, *11*, 92; Salem, L. *Pure Appl. Chem.* **1973**, *33*, 317; Jones II, G. *J. Chem. Educ.* **1974**, *51*, 175; Morozova, I.D.; Dyatkina, M.E. *Russ. Chem. Rev.* **1968**, *37*, 376. See also, Döhnert, D.; Koutecky, J. *J. Am. Chem. Soc.* **1980**, *102*, 1789. For a series of papers on diradicals, see *Tetrahedron* **1982**, *38*, 735.

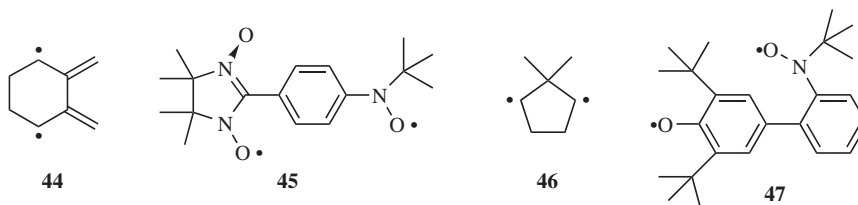
<sup>286</sup>Zhang, D.Y.; Borden, W.T. *J. Org. Chem.* **2002**, *67*, 3989.

<sup>287</sup>Ma, J.; Ding, Y.; Hattori, K.; Inagaki, S. *J. Org. Chem.* **2004**, *69*, 4245.

the species behaves spectrally like two doublets. When they are close enough for interaction or can interact through an unsaturated system as in trimethylenemethane,<sup>288</sup> they can have total spin numbers of +1, 0, or -1, since each



electron could be either  $\frac{1}{+2}$  or  $\frac{1}{-2}$ . Spectroscopically they are called *triplets*,<sup>289</sup> since each of the three possibilities is represented among the molecules and gives rise to its own spectral peak. In triplet molecules the two unpaired electrons have the same spin. Not all diradicals have a triplet ground state. In 2,3-dimethylecyclohexane-1,4-diyl (**44**), the singlet and triplet states were found to be almost degenerate.<sup>290</sup> Some diradicals, such as **45**, are very stable with a triplet ground state.<sup>291</sup> Diradicals are generally short-lived species. The lifetime of **46** was measured to be <0.1 ns and other diradicals were found to have lifetimes in the 4–316-ns range.<sup>292</sup> Diradical **47** [3,5-di-*tert*-butyl-3'-(*N*-*tert*-butyl-*N*-aminoxy)-4-oxybiphenyl] was found to have a lifetime of weeks even in the presence of oxygen, and survived brief heating in toluene up to ~60°C.<sup>293</sup> Radicals with both unpaired electrons on the same carbon are discussed under carbenes.



<sup>288</sup>For reviews of trimethylenemethane, see Borden, W.T.; Davidson, E.R. *Ann. Rev. Phys. Chem.* **1979**, *30*, 125; Bergman, R.G., in Kochi, J.K. *Free Radicals*, Vol. 1, Wiley, NY, **1973**, pp. 141–149.

<sup>289</sup>For discussions of the triplet state, see Wagner, P.J.; Hammond, G.S. *Adv. Photochem.* **1968**, *5*, 21; Turro, N.J. *J. Chem. Educ.* **1969**, *46*, 2. For a discussion of esr spectra of triplet states, see Wasserman, E.; Hutton, R.S. *Acc. Chem. Res.* **1977**, *10*, 27. For the generation and observation of triplet 1,3-biradicals see Ichinose, N.; Mizuno, K.; Otsuji, Y.; Caldwell, R.A.; Helms, A.M. *J. Org. Chem.* **1998**, *63*, 3176.

<sup>290</sup>Matsuda, K.; Iwamura, H. *J. Chem. Soc. Perkin Trans. 2* **1998**, 1023. Also see, Roth, W.R.; Wollweber, D.; Offerhaus, R.; Rekowski, V.; Lenmartz, H.-W.; Sustmann, R.; Müller, W. *Chem. Ber.* **1993**, *126*, 2701.

<sup>291</sup>Inoue, K.; Iwamura, H. *Angew. Chem. Int. Ed.* **1995**, *34*, 927. Also see, Ulrich, G.; Ziessel, R.; Luneau, D.; Rey, P. *Tetrahedron Lett.* **1994**, *35*, 1211.

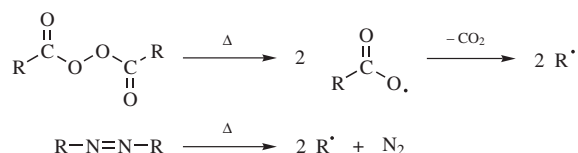
<sup>292</sup>Engel, P.S.; Lowe, K.L. *Tetrahedron Lett.* **1994**, *35*, 2267.

<sup>293</sup>Liao, Y.; Xie, C.; Lahti, P.M.; Weber, R.T.; Jiang, J.; Barr, D.P. *J. Org. Chem.* **1999**, *64*, 5176.

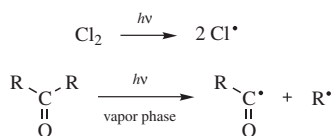
### The Generation and Fate of Free Radicals<sup>294</sup>

Free radicals are formed from molecules by breaking a bond so that each fragment keeps one electron.<sup>295,296</sup> The energy necessary to break the bond is supplied in one of two ways.

1. *Thermal Cleavage.* Subjection of any organic molecule to a high enough temperature in the gas phase results in the formation of free radicals. When the molecule contains bonds with  $D$  values or 20–40 kcal mol<sup>-1</sup> (80–170 kJ mol<sup>-1</sup>), cleavage can be caused in the liquid phase. Two common examples are cleavage of diacyl peroxides to acyl radicals that decompose to alkyl radicals<sup>297</sup> and cleavage of azo compounds to alkyl radicals<sup>298</sup>



2. *Photochemical Cleavage* (see p. 335). The energy of light of 600–300 nm is 48–96 kcal mol<sup>-1</sup> (200–400 kJ mol<sup>-1</sup>), which is of the order of magnitude of covalent-bond energies. Typical examples are photochemical cleavage of alkyl halides in the presence of triethylamine,<sup>299</sup> alcohols in the presence of mercuric oxide and iodine,<sup>300</sup> alkyl 4-nitrobenzenesulfonates,<sup>301</sup> chlorine, and of ketones:



The photochemistry of radicals and biradicals has been reviewed.<sup>302</sup>

<sup>294</sup>For a summary of methods of radical formation, see Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*; Pergamon: Elmsford, NY, **1986**, pp. 267–281. For a review on formation of free radicals by thermal cleavage, see Brown, R.F.C. *Pyrolytic Methods in Organic Chemistry*; Academic Press, NY, **1980**, pp. 44–61.

<sup>295</sup>It is also possible for free radicals to be formed by the collision of two nonradical species. For a review, see Harmony, J.A.K. *Methods Free-Radical Chem.* **1974**, 5, 101.

<sup>296</sup>For a review of homolytic cleavage of carbon–metal bonds, see Barker, P.J.; Winter, J.N., in Hartley, F.R.; Patai, S. *The Chemistry of the Metal-Carbon Bond*, Vol. 2, Wiley, NY, **1985**, pp. 151–218.

<sup>297</sup>Chateaufneuf, J.; Luszyk, J.; Ingold, K.U. *J. Am. Chem. Soc.* **1988**, 110, 2877, 2886; Matsuyama, K.; Sugiura, T.; Minoshima, Y. *J. Org. Chem.* **1995**, 60, 5520; Ryzhkov, L.R. *J. Org. Chem.* **1996**, 61, 2801. For a review of free radical mechanisms involving peroxides in solution, see Howard, J.A., in Patai, S. *The Chemistry of Peroxides*, Wiley, NY, **1983**, pp. 235–258. For a review of pyrolysis of peroxides in the gas phase, see Batt, L.; Liu, M.T.H. in the same volume, pp. 685–710.

<sup>298</sup>For a review of the cleavage of azoalkanes, see Engel, P.S. *Chem. Rev.* **1980**, 80, 99. For summaries of later work, see Adams, J.S.; Burton, K.A.; Andrews, B.K.; Weisman, R.B.; Engel, P.S. *J. Am. Chem. Soc.* **1986**, 108, 7935; Schmittle, M.; Rüchardt, C. *J. Am. Chem. Soc.* **1987**, 109, 2750.

<sup>299</sup>Cossy, J.; Ranaivosata, J.-L.; Bellosta, V. *Tetrahedron Lett.* **1994**, 35, 8161.

<sup>300</sup>Courtneidge, J.L. *Tetrahedron Lett.* **1992**, 33, 3053.

<sup>301</sup>Pasto, D.J.; Cottard, F. *Tetrahedron Lett.* **1994**, 35, 4303.

<sup>302</sup>Johnston, L.J. *Chem. Rev.* **1993**, 93, 251.

Radicals are also formed from other radicals, either by the reaction between a radical and a molecule (which *must* give another radical, since the total number of electrons is odd) or by cleavage of a radical<sup>303</sup> to give another radical, for example,



Radicals can also be formed by oxidation or reduction, including electrolytic methods.

Reactions of free radicals either give stable products (termination reactions) or lead to other radicals, which themselves must usually react further (propagation reactions). The most common termination reactions are simple combinations of similar or different radicals:



Another termination process is disproportionation:<sup>304</sup>

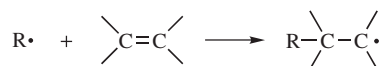
There are four principal propagation reactions, of which the first two are most common:



1. *Abstraction of Another Atom or Group, Usually a Hydrogen Atom* (see Chapter 14):

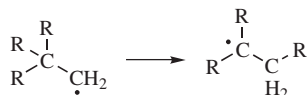


2. *Addition to a Multiple Bond* (see Chapter 15):



The radical formed here may add to another double bond and so on. This is one of the chief mechanisms for vinyl polymerization.

3. *Decomposition*. This can be illustrated by the decomposition of the benzyloxy radical (above).
4. *Rearrangement*:



<sup>303</sup>For a determination of activation barriers in the homolytic cleavage of radicals and ion radicals see Costentin, C.; Robert, M.; Saveant, J.-M. *J. Am. Chem. Soc.* **2003**, 125, 105.

<sup>304</sup>For reviews of termination reactions, see Pilling, M.J. *Int. J. Chem. Kinet.* **1989**, 21, 267; Khudyakov, I.V.; Levin, P.P.; Kuz'min, V.A. *Russ. Chem. Rev.* **1980**, 49, 982; Gibian, M.J.; Corley, R.C. *Chem. Rev.* **1973**, 73, 441.



This is less common than rearrangement of carbocations, but it does occur (though not when R = alkyl or hydrogen; see Chapter 18). Perhaps the best-known rearrangement is that of cyclopropylcarbinyl radicals to a butenyl radical.<sup>305</sup> The rate constant for this rapid ring opening has been measured in certain functionalized cyclopropylcarbinyl radicals by picosecond radical kinetics.<sup>306</sup> Substituent effects on the kinetics of ring opening in substituted cyclopropylcarbinyl radicals has been studied.<sup>307</sup> “The cyclopropylcarbinyl radical has found an important application as a radical clock.”<sup>308</sup> Various radical processes can be clocked by the competition of direct reaction with the cyclopropylcarbinyl radical ( $k_t$ ) and opening of that radical to the 1-buten-4-yl radical ( $k_r$ ) followed by trapping. Relative rates ( $k_t/k_r$ ) can be determined from yields of 4-X-1-butene and cyclopropylcarbinyl products as a function of the radical trap<sup>309</sup> (X–Y) concentration. Absolute rate constants have been determined for a number of radicals with various radical traps by laser flash photolysis methods.<sup>310</sup> From these absolute rate constants, reasonably accurate values of  $k_t$  can be estimated, and with the relative rate ( $k_t/k_r$ ), a value for  $k_r$  can be calculated. From the calibrated radical-clock reaction rate ( $k_r$ ), rates ( $k_t$ ) of other competing reactions can be determined from relative rate data ( $k_t/k_r$ ).”<sup>306</sup> Other radical clocks are known.<sup>311</sup>



Free radicals can also be oxidized to carbocations or reduced to carbanions.<sup>312</sup>

<sup>305</sup>For a discussion of radical vs. radical anion character see Stevenson, J. P.; Jackson, W. F.; Tanko, J. M. *J. Am. Chem. Soc.* **2002**, *124*, 4271.

<sup>306</sup>LeTadic-Biadatti, M.-H.; Newcomb, M. *J. Chem. Soc. Perkin Trans. 2* **1996**, 1467. See also, Choi, S.-Y.; Horner, J.H.; Newcomb, M. *J. Org. Chem.* **2000**, *65*, 4447. For determination of  $k$  for rearrangement and for competing reactions, see Cooksy, A. L.; King, H.F.; Richardson, W.H. *J. Org. Chem.* **2003**, *68*, 9441. For the ring opening of fluorinated cyclopropylcarbinyl systems see Tian, F.; Dolbier Jr., W.R. *Org. Lett.* **2000**, *2*, 835.

<sup>307</sup>Halgren, T.A.; Roberts, J.D.; Horner, J.H.; Martinez, F.N.; Tronche, C.; Newcomb, M. *J. Am. Chem. Soc.* **2000**, *122*, 2988.

<sup>308</sup>Griller, D.; Ingold, K.U. *Acc. Chem. Res.* **1980**, *13*, 317; Newcomb, M.; Choi, S.-Y.; Toy, P.H. *Can. J. Chem.* **1999**, *77*, 1123; LeTadic-Biadatti, M.-H.; Newcomb, M. *J. Chem. Soc., Perkin Trans. 2* **1996**, 1467; Choi, S.-Y.; Newcomb, M. *Tetrahedron* **1995**, *51*, 657; Newcomb, M. *Tetrahedron* **1993**, *49*, 1151; Newcomb, M.; Johnson, C.; Manek, M.B.; Varick, T.R. *J. Am. Chem. Soc.* **1992**, *114*, 10915; Nevill, S.M.; Pincock, J.A. *Can. J. Chem.* **1997**, *75*, 232.

<sup>309</sup>For an alkyl radical trap in aqueous medium see Barton, D.H.R.; Jacob, M.; Peralez, E. *Tetrahedron Lett.* **1999**, *40*, 9201.

<sup>310</sup>Choi, S.-Y.; Horner, J.H.; Newcomb, M. *J. Org. Chem.* **2000**, *65*, 4447; Engel, P.S.; He, S.-L.; Banks, J.T.; Ingold, K.U.; Luszyk, J. *J. Org. Chem.* **1997**, *62*, 1210; Johnston, L.J.; Luszyk, J.; Wayner, D.D.M.; Abeywickreyma, A.N.; Beckwith, A.L.J.; Scaiano, J.J.; Ingold, K.U. *J. Am. Chem. Soc.* **1985**, *107*, 4594; Chatgililoglu, C.; Ingold, K.U.; Scaiano, J.J. *J. Am. Chem. Soc.* **1981**, *103*, 7739.

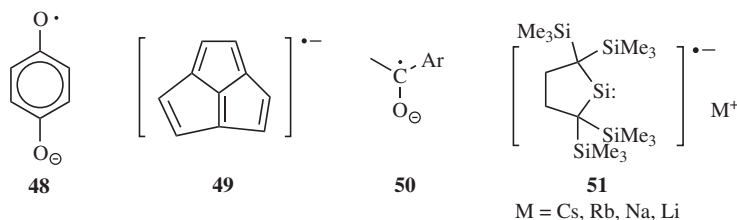
<sup>311</sup>For example, see Leardini, R.; Lucarini, M.; Pedulli, G.F.; Valgimigli, L. *J. Org. Chem.* **1999**, *64*, 3726.

<sup>312</sup>For a review of the oxidation and reduction of free radicals, see Khudyakov, I.V.; Kuz'min, V.A. *Russ. Chem. Rev.* **1978**, *47*, 22.

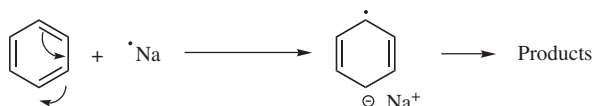


**Radical Ions<sup>313</sup>**

Several types of radical anions are known with the unpaired electron or the charge or both on atoms other than carbon. Examples include semiquinones<sup>314</sup> (**48**),



acepentalenes (**49**),<sup>315</sup> ketyls<sup>316</sup> (**50**) and the radical anion of the isolable dialkylsilylene **51**.<sup>317</sup> Reactions in which alkali metals are reducing agents often involve radical anion intermediates, for example, reaction **15-13**:



Several types of radical cation are also known.<sup>318</sup> Typical examples include alkyl azulene cation radicals (**52**),<sup>319</sup> trialkyl amine radical cations,<sup>320</sup>

<sup>313</sup>For a monograph, see Kaiser, E.T.; Kevan, L. *Radical Ions*, Wiley, NY, **1968**. For reviews, see Gerson, F.; Huber, W. *Acc. Chem. Res.* **1987**, *20*, 85; Todres, Z.V. *Tetrahedron* **1985**, *41*, 2771; Russell, G.A.; Norris, R.K., in McManus, S.P. *Organic Reactive Intermediates*; Academic Press, NY, **1973**, pp. 423–448; Holy, N.L.; Marcum, J.D. *Angew. Chem. Int. Ed.* **1971**, *10*, 115; Bilevitch, K.A.; Okhlobystin, O.Yu. *Russ. Chem. Rev.* **1968**, *37*, 954; Szwarc, M. *Prog. Phys. Org. Chem.* **1968**, *6*, 322. For a related review, see Chanon, M.; Rajzmann, M.; Chanon, F. *Tetrahedron* **1990**, *46*, 6193. For a series of papers on this subject, see *Tetrahedron* **1986**, *42*, 6097.

<sup>314</sup>For a review of semiquinones, see Depew, M.C.; Wan, J.K.S., in Patai, S.; Rappoport, Z. *The Chemistry of the Quinonoid Compounds*, Vol. 2, pt. 2, Wiley, NY, **1988**, pp. 963–1018. For a discussion of the thermodynamic stability of aromatic radical anions see Huh, C.; Kang, C.H.; Lee, H.W.; Nakamura, H.; Mishima, M.; Tsuno, Y.; Yamataka, H. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 1083.

<sup>315</sup>de Meijere, A.; Gerson, F.; Schreiner, P.R.; Merstetter, P.; Schüngel, F.-M. *Chem. Commun.* **1999**, 2189.

<sup>316</sup>For a review of ketyls, see Russell, G.A., in Patai, S.; Rappoport, Z. *The Chemistry of Enones*, pt. 1, Wiley, NY, **1989**, pp. 471–512. See Davies, A.G.; Neville, A.G. *J. Chem. Soc. Perkin Trans. 2* **1992**, 163, 171 for ketyl and thioketyl cation radicals.

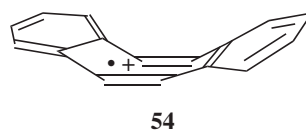
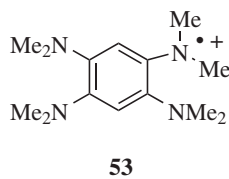
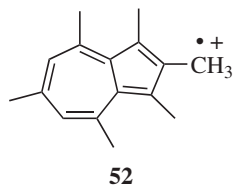
<sup>317</sup>Ishida, S.; Iwamoto, T.; Kira, M. *J. Am. Chem. Soc.* **2003**, *125*, 3212. For bis(tri-*tert*-butylsilyl)silylene: triplet ground state silylene see Sekiguchi, A.; Tanaka, T.; Ichinohe, M.; Akiyama, K.; Tero-Kubota, S. *J. Am. Chem. Soc.* **2003**, *125*, 4962.

<sup>318</sup>For reviews, see Roth, H.D. *Acc. Chem. Res.* **1987**, *20*, 343; Courtneidge, J.L.; Davies, A.G. *Acc. Chem. Res.* **1987**, *20*, 90; Hammerich, O.; Parker, V.D. *Adv. Phys. Org. Chem.* **1984**, *20*, 55; Symons, M.C.R. *Chem. Soc. Rev.* **1984**, *13*, 393; Bard, A.J.; Ledwith, A.; Shine, H.J. *Adv. Phys. Org. Chem.* **1976**, *13*, 155.

<sup>319</sup>Gerson, F.; Scholz, M.; Hansen, H.-J.; Uebelhart, P. *J. Chem. Soc. Perkin Trans. 2* **1995**, 215.

<sup>320</sup>de Meijere, A.; Chaplinski, V.; Gerson, F.; Merstetter, P.; Haselbach, E. *J. Org. Chem.* **1999**, *64*, 6951.

1,2-bis(dialkylamino)benzenes radical cations, such as **53**,<sup>321</sup> dimethylsulfoxonium cation radicals ( $\text{Me}_2\text{S}^+\bullet$ ),<sup>322</sup> *N*-alkyl substituted imine cation radicals ( $\text{Ph}_2\text{C}=\text{NEt}^+\bullet$ ),<sup>323</sup> dibenzo[*a,e*]cyclooctene (**54**, a nonplanar cation radical),<sup>324</sup> and [*n.n*]paracyclophane cation radicals.<sup>325</sup> A twisted radical cation derived from bicyclo[2.2.2]oct-2-ene has been reported.<sup>326</sup>



## CARBENES

### Stability and Structure<sup>327</sup>

*Carbenes* are highly reactive species, practically all having lifetimes considerably under 1 s. With exceptions noted below (p. 289), carbenes have been isolated only by entrapment in matrices at low temperatures (77 K or less).<sup>328</sup> The parent species  $\text{CH}_2$  is usually called *methylene*, although derivatives are more often named by the carbene nomenclature. Thus  $\text{CCl}_2$  is generally known as dichlorocarbene, although it can also be called dichloromethylene.

<sup>321</sup>Neugebauer, F.A.; Funk, B.; Staab, H.A. *Tetrahedron Lett.* **1994**, 35, 4755. See Stickley, K.R.; Blackstock, S.C. *Tetrahedron Lett.* **1995**, 36, 1585 for a *tris*-diarylamino benzene cation radical.

<sup>322</sup>Dauben, W.G.; Cogen, J.M.; Behar, V.; Schultz, A.G.; Geiss, W.; Taveras, A.G. *Tetrahedron Lett.* **1992**, 33, 1713.

<sup>323</sup>Rhodes, C.J.; Agirbas H. *J. Chem. Soc. Perkin Trans. 2* **1992**, 397.

<sup>324</sup>Gerson, F.; Felder, P.; Schmidlin, R.; Wong, H.N.C. *J. Chem. Soc. Chem. Commun.* **1994**, 1659.

<sup>325</sup>Wartini, A.R.; Valenzuela, J.; Staab, H.A.; Neugebauer, F.A. *Eur. J. Org. Chem.* **1998**, 139.

<sup>326</sup>Nelson, S.F.; Reinhardt, L.A.; Tran, H.Q.; Clark, T.; Chen, G.-F.; Pappas, R.S.; Williams, F. *Chem. Eur. J.* **2002**, 8, 1074.

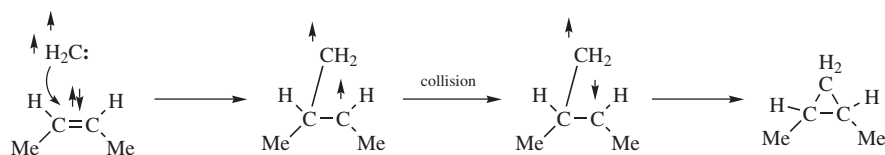
<sup>327</sup>For monographs, see Jones, Jr., M.; Moss, R.A. *Carbenes*, 2 vols., Wiley, NY, **1973–1975**; Kirmse, W. *Carbene Chemistry*, 2nd ed.; Academic Press, NY, **1971**; Rees, C.W.; Gilchrist, T.L. *Carbenes, Nitrenes, and Arynes*, Nelson, London, **1969**. For reviews, see Minkin, V.I.; Simkin, B.Ya.; Glukhovtsev, M.N. *Russ. Chem. Rev.* **1989**, 58, 622; Moss, R.A.; Jones, Jr., M. *React. Intermed. (Wiley)* **1985**, 3, 45; **1981**, 2, 59; **1978**, 1, 69; Isaacs, N.S. *Reactive Intermediates in Organic Chemistry*, Wiley, NY, **1974**, pp. 375–407; Bethell, D. *Adv. Phys. Org. Chem.* **1969**, 7, 153; Bethell, D., in McManus, S.P. *Organic Reactive Intermediates*, Academic Press, NY, **1973**, pp. 61–126; Closs, G.L. *Top. Stereochem.* **1968**, 3, 193; Herold, B.J.; Gaspar, P.P. *Fortschr. Chem. Forsch.*, **1966**, 5, 89; Rozantsev, G.G.; Fainzil'berg, A.A.; Novikov, S.S. *Russ. Chem. Rev.* **1965**, 34, 69. For a theoretical study, see Liebman, J.F.; Simons, J. *Mol. Struct. Energ.* **1986**, 1, 51.

<sup>328</sup>For example, see Murray, R.W.; Trozzolo, A.M.; Wasserman, E.; Yager, W.A. *J. Am. Chem. Soc.* **1962**, 84, 3213; Brandon, R.W.; Closs, G.L.; Hutchison, C.A. *J. Chem. Phys.* **1962**, 37, 1878; Milligan, D.E.; Mann, D.E.; Jacox, M.E.; Mitsch, R.A. *J. Chem. Phys.* **1964**, 41, 1199; Nefedov, O.M.; Maltsev, A.K.; Mikaelyan, R.G. *Tetrahedron Lett.* **1971**, 4125; Wright, B.B. *Tetrahedron* **1985**, 41, 1517. For reviews, see Zuev, P.S.; Nefedov, O.M. *Russ. Chem. Rev.* **1989**, 58, 636; Sheridan, R.S. *Org. Photochem.* **1987**, 8, 159, pp. 196–216; Trozzolo, A.M. *Acc. Chem. Res.* **1968**, 1, 329.

The two nonbonded electrons of a carbene can be either paired or unpaired. If they are paired, the species is spectrally a *singlet*, while, as we have seen (p. 278), two unpaired electrons appear as a *triplet*. An ingenious method of distinguishing



between the two possibilities was developed by Skell,<sup>329</sup> based on the common reaction of addition of carbenes to double bonds to form cyclopropane derivatives (15-51). If the singlet species adds to *cis*-2-butene, the resulting cyclopropane should be the *cis* isomer since the movements of the two pairs of electrons should



occur either simultaneously or with one rapidly succeeding another. However, if the attack is by a triplet species, the two unpaired electrons cannot both go into a new covalent bond, since by Hund's rule they have parallel spins. So one of the unpaired electrons will form a bond with the electron from the double bond that has the opposite spin, leaving two unpaired electrons that have the same spin and therefore cannot form a bond at once but must wait until, by some collision process, one of the electrons can reverse its spin. During this time, there is free rotation about the C—C bond and a mixture of *cis*- and *trans*-1,2-dimethylcyclopropanes should result.<sup>330</sup>

The results of this type of experiment show that CH<sub>2</sub> itself is usually formed as a singlet species, which can decay to the triplet state, which consequently has a lower energy (molecular-orbital calculations<sup>331</sup> and experimental determinations show that the difference in energy between singlet and triplet CH<sub>2</sub> is ~8–10 kcal mol<sup>-1</sup> or 33–42 kJ mol<sup>-1</sup><sup>332</sup>). However, it is possible to prepare triplet CH<sub>2</sub> directly by a

<sup>329</sup>Skell, P.S.; Woodworth, R.C. *J. Am. Chem. Soc.* **1956**, 78, 4496; Skell, P.S. *Tetrahedron* **1985**, 41, 1427.

<sup>330</sup>These conclusions are generally accepted though the reasoning given here may be oversimplified. For discussions, see Closs, G.L. *Top. Stereochem.* **1968**, 3, 193, pp. 203–210; Bethell, D. *Adv. Phys. Org. Chem.* **1969**, 7, 153, pp. 194; Hoffmann, R. *J. Am. Chem. Soc.* **1968**, 90, 1475.

<sup>331</sup>Richards, Jr., C.A.; Kim, S.-J.; Yamaguchi, Y.; Schaefer III, H.F. *J. Am. Chem. Soc.* **1995**, 117, 10104.

<sup>332</sup>See, for example, Hay, P.J.; Hunt, W.J.; Goddard III, W.A. *Chem. Phys. Lett.* **1972**, 13, 30; Dewar, M.J.S.; Haddon, R.C.; Weiner, P.K. *J. Am. Chem. Soc.* **1974**, 96, 253; Frey, H.M.; Kennedy, G.J. *J. Chem. Soc. Chem. Commun.* **1975**, 233; Lucchese, R.R.; Schaefer III, H.F. *J. Am. Chem. Soc.* **1977**, 99, 6765; Roos, B.O.; Siegbahn, P.M. *J. Am. Chem. Soc.* **1977**, 99, 7716; Lengel, R.K.; Zare, R.N. *J. Am. Chem. Soc.* **1978**, 100, 7495; Borden, W.T.; Davidson, E.R. *Ann. Rev. Phys. Chem.* **1979**, 30, 125, see pp. 128–134; Leopold, D.G.; Murray, K.K.; Lineberger, W.C. *J. Chem. Phys.* **1984**, 81, 1048.

photosensitized decomposition of diazomethane.<sup>333</sup> The CH<sub>2</sub> group is so reactive<sup>334</sup> that it generally reacts as the singlet before it has a chance to decay to the triplet state.<sup>335</sup> As to other carbenes, some react as triplets, some as singlets, and others as singlets or triplets, depending on how they are generated. There are, however, molecules that generate persistent triplet carbenes.<sup>336</sup> Indeed, remarkably stable diaryl triplet carbenes have been prepared.<sup>337</sup>

There is a limitation to the use of stereospecificity of addition as a diagnostic test for singlet or triplet carbenes.<sup>338</sup> When carbenes are generated by photolytic methods, they are often in a highly excited singlet state. When they add to the double bond, the addition is stereospecific; but the cyclopropane formed carries excess energy; that is, it is in an excited state. It has been shown that under certain conditions (low pressures in the gas phase) the excited cyclopropane may undergo cis-trans isomerization *after* it is formed, so that triplet carbene may seem to be involved although in reality the singlet was present.<sup>339</sup>

Studies of the IR spectrum of CCl<sub>2</sub> trapped at low temperatures in solid argon indicate that the ground state for this species is the singlet.<sup>340</sup> The geometrical structure of triplet methylene can be investigated by esr measurements,<sup>341</sup> since triplet species are diradicals. Such measurements made on triplet CH<sub>2</sub> trapped in matrices at very low temperatures (4 K) show that triplet CH<sub>2</sub> is a bent molecule, with an angle of ~136°.<sup>342</sup> Epr measurements cannot be made on singlet species, but from electronic spectra of CH<sub>2</sub> formed in flash photolysis of diazomethane it was concluded that singlet CH<sub>2</sub> is also bent, with an angle of ~103°.<sup>343</sup> Singlet CCl<sub>2</sub><sup>286</sup> and CBr<sub>2</sub><sup>344</sup> are also bent, with angles of 100 and 114°, respectively. It

<sup>333</sup>Kopecky, K.R.; Hammond, G.S.; Leermakers, P.A. *J. Am. Chem. Soc.* **1961**, *83*, 2397; **1962**, *84*, 1015; Duncan, F.J.; Cvetanović, R.J. *J. Am. Chem. Soc.* **1962**, *84*, 3593.

<sup>334</sup>For a review of the kinetics of CH<sub>2</sub> reactions, see Laufer, A.H. *Rev. Chem. Intermed.* **1981**, *4*, 225.

<sup>335</sup>Decay of singlet and triplet CH<sub>2</sub> has been detected in solution, as well as in the gas phase: Turro, N.J.; Cha, Y.; Gould, I.R. *J. Am. Chem. Soc.* **1987**, *109*, 2101.

<sup>336</sup>Tomioka, H. *Acc. Chem. Res.* **1997**, *30*, 315; Kirmse, W. *Angew. Chem. Int. Ed.* **2003**, *42*, 2117.

<sup>337</sup>Hirai, K.; Tomioka, H. *J. Am. Chem. Soc.* **1999**, *121*, 10213; Woodcock, H.L.; Moran, D.; Schleyer, P.v.R.; Schaefer III, H.F. *J. Am. Chem. Soc.* **2001**, *123*, 4331.

<sup>338</sup>For other methods of distinguishing singlet from triplet carbenes, see Hendrick, M.E.; Jones Jr., M. *Tetrahedron Lett.* **1978**, 4249; Creary, X. *J. Am. Chem. Soc.* **1980**, *102*, 1611.

<sup>339</sup>Rabinovitch, B.S.; Tschuikow-Roux, E.; Schlag, E.W. *J. Am. Chem. Soc.* **1959**, *81*, 1081; Frey, H.M. *Proc. R. Soc. London, Ser. A* **1959**, *251*, 575. It has been reported that a singlet carbene (CBr<sub>2</sub>) can add nonstereospecifically: Lambert, J.B.; Larson, E.G.; Bosch, R.J. *Tetrahedron Lett.* **1983**, *24*, 3799.

<sup>340</sup>Andrews, L. *J. Chem. Phys.* **1968**, *48*, 979.

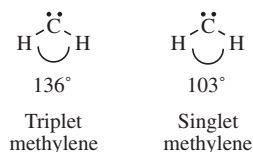
<sup>341</sup>The technique of spin trapping (p. 268) has been applied to the detection of transient triplet carbenes: Forrester, A.R.; Sadd, J.S. *J. Chem. Soc. Perkin Trans. 2* **1982**, 1273.

<sup>342</sup>Wasserman, E.; Kuck, V.J.; Hutton, R.S.; Anderson, E.D.; Yager, W.A. *J. Chem. Phys.* **1971**, *54*, 4120; Bernheim, R.A.; Bernard, H.W.; Wang, P.S.; Wood, L.S.; Skell, P.S. *J. Chem. Phys.* **1970**, *53*, 1280; **1971**, *54*, 3223.

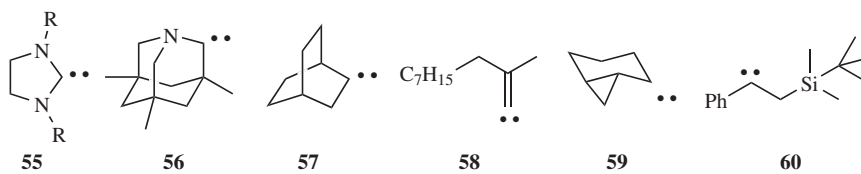
<sup>343</sup>Herzberg, G.; Johns, J.W.C. *Proc. R. Soc. London, Ser. A* **1967**, 295, 107, *J. Chem. Phys.* **1971**, *54*, 2276 and cited references.

<sup>344</sup>Ivey, R.C.; Schulze, P.D.; Leggett, T.L.; Kohl, D.A. *J. Chem. Phys.* **1974**, *60*, 3174.

has long been known that triplet aryl carbenes are bent.<sup>345</sup>



The most common carbenes are :CH<sub>2</sub> and CCl<sub>2</sub>,<sup>346</sup> but many others have been reported,<sup>347</sup> including heterocyclic carbenes, such as **55** (stabilized by the steric constraints of the ring geometry),<sup>348</sup> **56** (an aminocarbene without  $\pi$  conjugation),<sup>349</sup> bicyclo[2.2.2]octylidene, **57**,<sup>350</sup> alkylidene carbenes, such as **58**,<sup>351</sup> conformationally restricted cyclopropylcarbenes, such as **59**,<sup>352</sup>  $\beta$ -silylcarbenes, such as **60**,<sup>353</sup>  $\alpha$ -keto carbenes,<sup>354</sup> vinyl carbenes,<sup>355</sup> and chiral carbenoids.<sup>356</sup> In the case of **55** (R = Ph),<sup>357</sup> the precursor is a tetraaminoethylene, and when potassium hydride is present to preclude electrophilic catalysis, starting tetraaminoethylenes are recovered unchanged.



<sup>345</sup>Trozzolo, A.M.; Wasserman, E.; Yager, W.A. *J. Am. Chem. Soc.* **1965**, 87, 129; Senthilnathan, V.P.; Platz, M.S. *J. Am. Chem. Soc.* **1981**, 103, 5503; Gilbert, B.C.; Griller, D.; Nazran, A.S. *J. Org. Chem.* **1985**, 50, 4738.

<sup>346</sup>For reviews of halocarbenes, see Burton, D.J.; Hahnfeld, J.L. *Fluorine Chem. Rev.* **1977**, 8, 119; Margrave, J.L.; Sharp, K.G.; Wilson, P.W. *Fort. Chem. Forsch.* **1972**, 26, 1, pp. 3–13.

<sup>347</sup>For reviews of unsaturated carbenes, see Stang, P.J. *Acc. Chem. Res.* **1982**, 15, 348; *Chem. Rev.* **1978**, 78, 383. For a review of carbalkoxycarbenes, see Marchand, A.P.; Brockway, N.M. *Chem. Rev.* **1974**, 74, 431. For a review of arylcarbenes, see Schuster, G.B. *Adv. Phys. Org. Chem.* **1986**, 22, 311. For a review of carbenes with neighboring hetero atoms, see Taylor, K.G. *Tetrahedron* **1982**, 38, 2751.

<sup>348</sup>Denk, M.K.; Thadani, A.; Hatano, K.; Lough, A.J. *Angew. Chem. Int. Ed.* **1997**, 36, 2607; Herrmann, W.A. *Angew. Chem. Int. Ed.* **2002**, 41, 1290.

<sup>349</sup>Ye, Q.; Komarov, I.V.; Kirby, A.J.; Jones, Jr., M. *J. Org. Chem.* **2002**, 67, 9288.

<sup>350</sup>Ye, Q.; Jones, Jr., M.; Chen, T.; Shevlin, P.B. *Tetrahedron Lett.* **2001**, 42, 6979.

<sup>351</sup>Ohira, S.; Okai, K.; Moritani, T. *J. Chem. Soc. Chem. Commun.* **1992**, 721; Walsh, R.; Wolf, C.; Untiedt, S.; de Meijere, A. *J. Chem. Soc. Chem. Commun.* **1992**, 421, 422; Ohira, S.; Yamasaki, K.; Nozaki, H.; Yamato, M.; Nakayama, M. *Tetrahedron Lett.* **1995**, 36, 8843. For dimethylvinylidene carbene, see Reed, S.C.; Capostoli, G.J.; Zhu, Z.; Modarelli, D.A. *J. Org. Chem.* **2001**, 66, 287. For a review of alkylidenecarbenes, see Knorr, R. *Chem. Rev.* **2004**, 104, 3795.

<sup>352</sup>Fernamberg, K.; Snoonian, J.R.; Platz, M.S. *Tetrahedron Lett.* **2001**, 42, 8761.

<sup>353</sup>Creary, X.; Butchko, M.A. *J. Org. Chem.* **2002**, 67, 112.

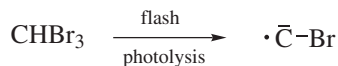
<sup>354</sup>Bonnichon, F.; Richard, C.; Grabner, G. *Chem. Commun.* **2001**, 73.

<sup>355</sup>Zuev, P.S.; Sheridan, R.S. *J. Am. Chem. Soc.* **2004**, 126, 12220.

<sup>356</sup>Topolski, M.; Duraisamy, M.; Rachoń, J.; Gawronski, J.; Gawronska, K.; Goedken, V.; Walborsky, H.M. *J. Org. Chem.* **1993**, 58, 546.

<sup>357</sup>See Wanzlick, H.-W.; Schikora, E. *Angew. Chem.* **1960**, 72, 494.

Flash photolysis of  $\text{CHBr}_3$  produced the intermediate  $\text{CBr}$ .<sup>358</sup>

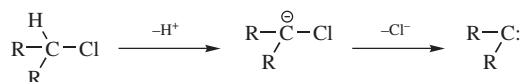


This is a *carbyne*. The intermediates  $\text{CF}$  and  $\text{CCl}$  were generated similarly from  $\text{CHFBr}_2$  and  $\text{CHClBr}_2$ , respectively.

### The Generation and Fate of Carbenes<sup>359</sup>

Carbenes are chiefly formed in two ways, although other pathways are also known.

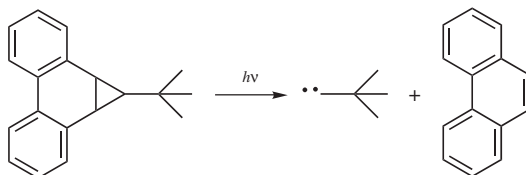
1. In  $\alpha$  elimination, a carbon loses a group without its electron pair, usually a proton, and then a group with its pair, usually a halide ion:<sup>360</sup>



The most common example is formation of dichlorocarbene by treatment of chloroform with a base (see reaction **10-3**) and geminal alkyl dihalides with  $\text{Me}_3\text{Sn}^-$ ,<sup>361</sup> but many other examples are known, such as

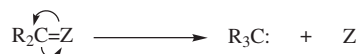


Ref. 362



Ref. 363

2. Disintegration of compounds containing certain types of double bonds:



<sup>358</sup>Ruzsicska, B.P.; Jodhan, A.; Choi, H.K.J.; Strausz, O.P. *J. Am. Chem. Soc.* **1983**, *105*, 2489.

<sup>359</sup>For reviews, see Jones Jr., M. *Acc. Chem. Res.* **1974**, *7*, 415; Kirmse, W., in Bamford, C.H.; Tipper, C.F.H. *Comprehensive Chemical Kinetics*, Vol. 9; Elsevier, NY, **1973**, pp. 373–415; Ref. 327. For a review of electrochemical methods of carbene generation, see Petrosyan, V.E.; Niyazymbetov, M.E. *Russ. Chem. Rev.* **1989**, *58*, 644.

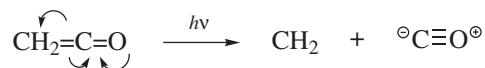
<sup>360</sup>For a review of formation of carbenes in this manner, see Kirmse, W. *Angew. Chem. Int. Ed.* **1965**, *4*, 1.

<sup>361</sup>Ashby, E.C.; Deshpande, A.K.; Doctorovich, F. *J. Org. Chem.* **1993**, *58*, 4205.

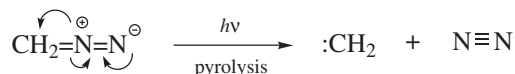
<sup>362</sup>Wagner, W.M. *Proc. Chem. Soc.* **1959**, 229.

<sup>363</sup>Glick, H.C.; Likhotovik, I.R.; Jones Jr., M. *Tetrahedron Lett.* **1995**, *36*, 5715; Stang, P.J. *Acc. Chem. Res.* **1982**, *15*, 348; *Chem. Rev.* **1978**, *78*, 383.

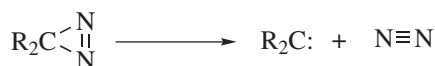
The two most important ways of forming  $\text{:CH}_2$  are examples: the photolysis of ketene



and the isoelectronic decomposition of diazomethane.<sup>364</sup>



Diazirines<sup>365</sup> (isomeric with diazoalkanes) give carbenes,<sup>366</sup> but arylmethyl radicals have also been generated from diazirines.<sup>367</sup> In a different study, thermolysis of diaryloxydiazirines gave the anticipated carbene products, but photolysis gave both carbenes and aryloxy radicals by  $\alpha$ -scission.<sup>368</sup>



Because most carbenes are so reactive, it is often difficult to prove that they are actually present in a given reaction. The lifetime of formylcarbene was measured by transient absorption and transient grating spectroscopy to be 0.15–0.73 ns in dichloromethane.<sup>369</sup> In many instances where a carbene is *apparently* produced by an  $\alpha$  elimination or by disintegration of a double-bond compound there is evidence that no free carbene is actually involved. The neutral term *carbenoid* is used where it is known that a free carbene is not present or in cases where there is doubt.  $\alpha$ -Halo organometallic compounds,  $\text{R}_2\text{CXM}$ , are often called carbenoids because they readily give an elimination reactions<sup>370</sup> (e.g., see **12-39**).

The reactions of carbenes are more varied than those of the species previously discussed in this chapter. Solvent effects have been observed in carbene reactions. The selectivity of certain carbenes is influenced by the nature of the solvent,<sup>371</sup> the distribution of rearrangement products (see below) from *tert*-butylcarbene<sup>372</sup> are

<sup>364</sup>For a review, see Regitz, M.; Maas, G. *Diazo Compounds*, Academic Press, NY, **1986**, pp. 170–184.

<sup>365</sup>For syntheses, see Martinu, T.; Dailey, W.P. *J. Org. Chem.* **2004**, *69*, 7359; Likhovtsov, I.R.; Tae, E.L.; Ventre, C.; Platz, M.S. *Tetrahedron Lett.* **2000**, *41*, 795.

<sup>366</sup>For a treatise, see Liu, M.T.H. *Chemistry of Diazirines*, 2 vols., CRC Press, Boca Raton, FL, **1987**. For reviews, see Liu, M.T.H. *Chem. Soc. Rev.* **1982**, *11*, 127; Frey, H.M. *Adv. Photochem.* **1966**, *4*, 225.

<sup>367</sup>Moss, R.A.; Fu, X. *Org. Lett.* **2004**, *6*, 3353.

<sup>368</sup>Fede, J.-M.; Jockusch, S.; Lin, N.; Moss, R.A.; Turro, N.J. *Org. Lett.* **2003**, *5*, 5027.

<sup>369</sup>Toscano, J.P.; Platz, M.S.; Nikolaev, V.; Cao, Y.; Zimmt, M.B. *J. Am. Chem. Soc.* **1996**, *118*, 3527.

<sup>370</sup>For a review, see Nefedov, O.M.; D'yachenko, A.I.; Prokof'ev, A.K. *Russ. Chem. Rev.* **1977**, *46*, 941.

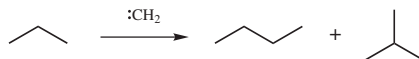
<sup>371</sup>Tomioka, H.; Ozaki, Y.; Izawa, Y. *Tetrahedron* **1985**, *41*, 4987.

<sup>372</sup>Moss, R.A.; Yan, S.; Krogh-Jespersen, K. *J. Am. Chem. Soc.* **1998**, *120*, 1088.; Krogh-Jespersen, K.; Yan, S.; Moss, R.A. *J. Am. Chem. Soc.* **1999**, *121*, 6269.



influenced by changes in solvent.<sup>373</sup> It is known that singlet methylene forms a charge-transfer complex with benzene.<sup>374</sup> Solvent interactions for chlorophenylcarbene and fluorophenylcarbene, however, are weak.<sup>375</sup>

1. Additions to carbon-carbon double bonds have already been mentioned. Carbenes also add to aromatic systems, but the immediate products rearrange, usually with ring enlargement (see **15-65**). Additions of carbenes to other double bonds, such as C=N (**16-46** and **16-48**), and to triple bonds have also been reported.
2. An unusual reaction of carbenes is that of insertion into C-H bonds (**12-21**). Thus,  $\text{:CH}_2$  reacts with methane to give ethane and with propane to give



*n*-butane and isobutane, as shown. Elimination to give an alkene is a competing side reaction in polar solvents, but this is suppressed in nonpolar solvents.<sup>376</sup> Simple alkyl carbenes, such as this, are not very useful for synthetic purposes, but do illustrate the extreme reactivity of carbene. However, carbenoids generated by rhodium catalyzed decomposition of diazoalkanes are very useful (p. 803) and have been used in a variety of syntheses. Treatment in the liquid phase of an alkane, such as pentane with carbene formed from the photolysis of diazomethane, gives the three possible products in statistical ratios<sup>377</sup> demonstrating that carbene is displaying no selectivity. For many years, it was a generally accepted principle that the lower the selectivity the greater the reactivity; however, this principle is no longer regarded as general because many exceptions have been found.<sup>378</sup> Singlet  $\text{CH}_2$  generated by photolysis of diazomethane is probably the most reactive organic species known, but triplet  $\text{CH}_2$  is somewhat less reactive, and other carbenes are still less reactive. The following series of carbenes of decreasing reactivity has

<sup>373</sup>Ruck, R.T.; Jones Jr., M. *Tetrahedron Lett.* **1998**, 39, 2277.

<sup>374</sup>Khan, M.I.; Goodman, J.L. *J. Am. Chem. Soc.* **1995**, 117, 6635.

<sup>375</sup>Sun, Y.; Tippmann, E.M.; Platz, M.S. *Org. Lett.* **2003**, 5, 1305.

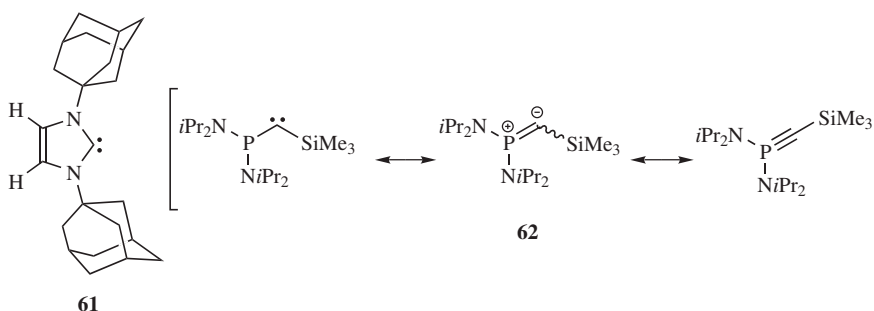
<sup>376</sup>Ruck, R.T.; Jones Jr., M. *Tetrahedron Lett.* **1998**, 39, 2277.

<sup>377</sup>Doering, W. von E.; Buttery, R.G.; Laughlin, R.G.; Chaudhuri, N. *J. Am. Chem. Soc.* **1956**, 78, 3224; Richardson, D.B.; Simmons, M.C.; Dvoretzky, I. *J. Am. Chem. Soc.* **1961**, 83, 1934; Halberstadt, M.L.; McNesby, J.R. *J. Am. Chem. Soc.* **1967**, 89, 3417.

<sup>378</sup>For reviews of this question, see Buncel, E.; Wilson, H. *J. Chem. Educ.* **1987**, 64, 475; Johnson, C.D. *Tetrahedron* **1980**, 36, 3461; *Chem. Rev.* **1975**, 75, 755; Giese, B. *Angew. Chem. Int. Ed.* **1977**, 16, 125; Pross, A. *Adv. Phys. Org. Chem.* **1977**, 14, 69. See also, Ritchie, C.D.; Sawada, M. *J. Am. Chem. Soc.* **1977**, 99, 3754; Argile, A.; Ruasse, M. *Tetrahedron Lett.* **1980**, 21, 1327; Godfrey, M. *J. Chem. Soc. Perkin Trans. 2* **1981**, 645; Kurz, J.L.; El-Nasr, M.M.S. *J. Am. Chem. Soc.* **1982**, 104, 5823; Srinivasan, C.; Shunmugasundaram, A.; Arumugam, N. *J. Chem. Soc. Perkin Trans. 2* **1985**, 17; Bordwell, F.G.; Branca, J.C.; Cripe, T.A. *Isr. J. Chem.* **1985**, 26, 357; Formosinho, S.J. *J. Chem. Soc. Perkin Trans. 2* **1988**, 839; Johnson, C.D.; Stratton, B. *J. Chem. Soc. Perkin Trans. 2* **1988**, 1903. For a group of papers on this subject, see *Isr. J. Chem.* **1985**, 26, 303.

been proposed on the basis of discrimination between insertion and addition reactions:  $\text{CH}_2 > \text{HCCOOR} > \text{PhCH} > \text{BrCH} \sim \text{ClCH}$ .<sup>379</sup> Dihalocarbenes generally do not give insertion reactions at all. Insertion of carbenes into other bonds has also been demonstrated, although not insertion into C–C bonds.<sup>380</sup>

Two carbenes that are stable at room temperature have been reported.<sup>381</sup> These are **61** and **62**. In the absence of oxygen and moisture, **61** exists as stable crystals with a melting point of 240–241°C.<sup>382</sup> Its structure was proved by X-ray crystallography.



3. It would seem that dimerization should be an important reaction of carbenes



but it is not, because the reactivity is so great that the carbene species do not have time to find each other and because the dimer generally has so much energy that it dissociates again. Apparent dimerizations have been observed, but it is likely that the products in many reported instances of “dimerization” do not arise from an actual dimerization of two carbenes but from attack by a carbene on a molecule of carbene precursor, for example,



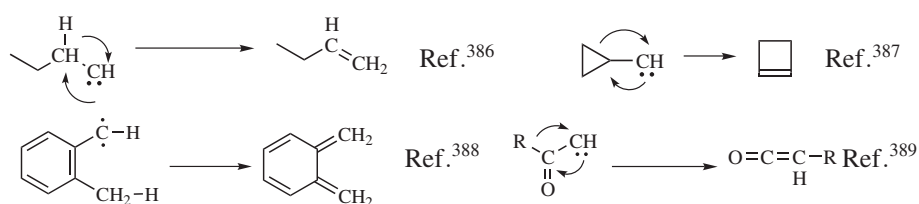
<sup>379</sup>Closs, G.L.; Coyle, J.J. *J. Am. Chem. Soc.* **1965**, 87, 4270.

<sup>380</sup>See, for example, Doering, W. von E.; Knox, L.H.; Jones, Jr., M. *J. Org. Chem.* **1959**, 24, 136; Franzen, V. *Liebigs Ann. Chem.* **1959**, 627, 22; Bradley, J.; Ledwith, A. *J. Chem. Soc.* **1961**, 1495; Frey, H.M.; Voisey, M.A. *Chem. Commun.* **1966**, 454; Seyferth, D.; Damrauer, R.; Mui, J.Y.; Julia, T.F. *J. Am. Chem. Soc.* **1968**, 90, 2944; Tomioka, H.; Ozaki, Y.; Izawa, Y. *Tetrahedron* **1985**, 41, 4987; Frey, H.M.; Walsh, R.; Watts, I.M. *J. Chem. Soc. Chem. Commun.* **1989**, 284.

<sup>381</sup>For a discussion, see Regitz, M. *Angew. Chem. Int. Ed.* **1991**, 30, 674.

<sup>382</sup>Arduengo III, A.J.; Harlow, R.L.; Kline, M. *J. Am. Chem. Soc.* **1991**, 113, 361.

4. Alkylcarbenes can undergo rearrangement, with migration of alkyl or hydrogen.<sup>383</sup> Indeed these rearrangements are generally so rapid<sup>384</sup> that additions to multiple bonds and insertion reactions, which are so common for CH<sub>2</sub>, are seldom encountered with alkyl or dialkyl carbenes. Unlike rearrangement of the species previously encountered in this chapter, most rearrangements of carbenes directly give stable molecules. A carbene intermediate has been suggested for the isomerization of cyclopropane.<sup>385</sup> Some examples of carbene rearrangement are



The rearrangement of acylcarbenes to ketenes is called the Wolff rearrangement (reaction **18-8**). A few rearrangements in which carbenes rearrange to other carbenes are also known.<sup>390</sup> Of course, the new carbene must stabilize itself in one of the ways we have mentioned.

<sup>383</sup>For a probe of migratory aptitudes of hydrogen to carbenes see Locatelli, F.; Candy, J.-P.; Didillon, B.; Niccolai, G.P.; Uzio, D.; Basset, J.-M. *J. Am. Chem. Soc.* **2001**, *123*, 1658. For reviews of carbene and nitrene rearrangements, see Brown, R.F.C. *Pyrolytic Methods in Organic Chemistry*, Academic Press, NY, **1980**, pp. 115–163; Wentrup, C. *Adv. Heterocycl. Chem.* **1981**, *28*, 231; *React. Intermed. (Plenum)* **1980**, *1*, 263; *Top. Curr. Chem.* **1976**, *62*, 173; Jones, W.M., in de Mayo, P. *Rearrangements in Ground and Excited States*, Vol. 1, Academic Press, NY, **1980**, pp. 95–160; Schaefer III, H.F. *Acc. Chem. Res.* **1979**, *12*, 288; Kirmse, W. *Carbene Chemistry*, 2nd ed., Academic Press, NY, **1971**, pp. 457–496.

<sup>384</sup>The activation energy for the 1,2-hydrogen shift has been estimated at 1.1 kcal mol<sup>-1</sup> (4.5 kJ mol<sup>-1</sup>), an exceedingly low value: Stevens, I.D.R.; Liu, M.T.H.; Soundararajan, N.; Paike, N. *Tetrahedron Lett.* **1989**, *30*, 481. Also see, Pezacki, J.P.; Couture, P.; Dunn, J.A.; Warkentin, J.; Wood, P.D.; Luszytk, J.; Ford, F.; Platz, M.S. *J. Org. Chem.* **1999**, *64*, 4456.

<sup>385</sup>Bettinger, H.F.; Rienstra-Kiracofe, J.C.; Hoffman, B.C.; Schaefer III, H.F.; Baldwin, J.E.; Schleyer, P.v.R. *Chem. Commun.* **1999**, 1515.

<sup>386</sup>Kirmse, W.; Doering, W. von E. *Tetrahedron* **1960**, *11*, 266. For kinetic studies of the rearrangement: Cl-CH-CHR<sub>2</sub> → ClCH=CR<sub>2</sub>, see Liu, M.T.H.; Bonneau, R. *J. Am. Chem. Soc.* **1989**, *111*, 6873; Jackson, J.E.; Soundararajan, N.; White, W.; Liu, M.T.H.; Bonneau, R.; Platz, M.S. *J. Am. Chem. Soc.* **1989**, *111*, 6874; Ho, G.; Krogh-Jespersen, K.; Moss, R.A.; Shen, S.; Sheridan, R.S.; Subramanian, R. *J. Am. Chem. Soc.* **1989**, *111*, 6875; LaVilla, J.A.; Goodman, J.L. *J. Am. Chem. Soc.* **1989**, *111*, 6877.

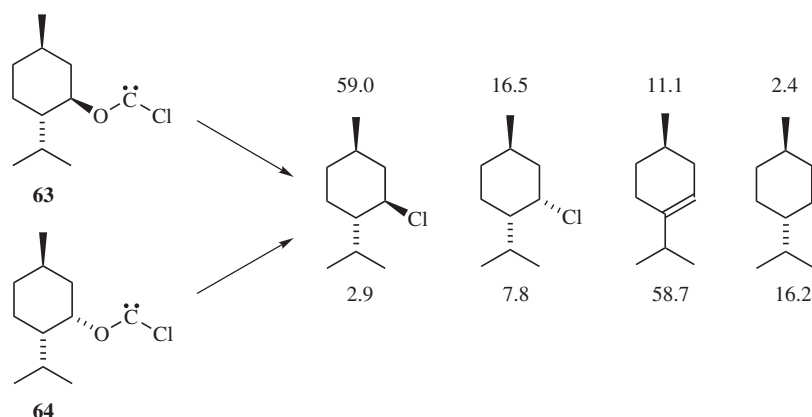
<sup>387</sup>Friedman, L.; Shechter, H. *J. Am. Chem. Soc.* **1960**, *82*, 1002.

<sup>388</sup>McMahon, R.J.; Chapman, O.L. *J. Am. Chem. Soc.* **1987**, *109*, 683.

<sup>389</sup>Friedman, L.; Berger, J.G. *J. Am. Chem. Soc.* **1961**, *83*, 492, 500.

<sup>390</sup>For a review, see Jones, W.M. *Acc. Chem. Res.* **1977**, *10*, 353.

5. The fragmentation reactions of alicyclic oxychlorocarbenes such as **63** and **64**<sup>391</sup> give substitution and elimination products. Menthylloxychlorocarbene, **63**, gave primarily the substitution product, whereas neomenthylloxychlorocarbene, **64**, gave primarily the elimination product, as shown. In this case, the substitution product is likely due to rearrangement of the chlorocarbene.<sup>392</sup> It is known that fragmentation of nortricycloxychlorocarbene in pentane occurs by an S<sub>N</sub>i-like process to give nortricycyl chloride.<sup>393</sup> In more polar solvents, fragmentation leads to nortricycyl cation–chloride anion pair that gives nortricycyl chloride and a small amount of *exo*-2-norbornenyl chloride. Fragmentation can also lead to radicals.<sup>394</sup>



6. Triplet carbenes can abstract hydrogen or other atoms to give free radicals, for example,



This is not surprising, since triplet carbenes are free radicals. But singlet carbenes can also give this reaction, although in this case only halogen atoms are abstracted, not hydrogen.<sup>395</sup>

<sup>391</sup>Moss, R.A.; Johnson, L.A.; Kacprzynski, M.; Sauers, R.R. *J. Org. Chem.* **2003**, *68*, 5114.

<sup>392</sup>A rearrangement product was noted for adamantylchlorocarbenes, possibly due to rearrangement of the chlorine atom from a chlorocarbene. See Yao, G.; Rempala, P.; Bashore, C.; Sheridan, R.S. *Tetrahedron Lett.* **1999**, *40*, 17.

<sup>393</sup>Moss, R.A.; Ma, Y.; Sauers, R.R.; Madni, M. *J. Org. Chem.* **2004**, *69*, 3628.

<sup>394</sup>Mekley, N.; El-Saidi, M.; Warkentin, J. *Can. J. Chem.* **2000**, *78*, 356.

<sup>395</sup>Roth, H.D. *J. Am. Chem. Soc.* **1971**, *93*, 1527, 4935, *Acc. Chem. Res.* **1977**, *10*, 85.

## NITRENES

Nitrenes,<sup>396</sup> R–N, are the nitrogen analogs of carbenes, and most of what we have said about carbenes also applies to them. Nitrenes are too reactive for isolation under ordinary conditions,<sup>397</sup> although *ab initio* calculations show that nitrenes are more stable than carbenes with an enthalpy difference of 25–26 kcal mol<sup>–1</sup> (104.7–108.8 kJ mol<sup>–1</sup>).<sup>398</sup>



Alkyl nitrenes have been isolated by trapping in matrices at 4 K,<sup>399</sup> while aryl nitrenes, which are less reactive, can be trapped at 77 K.<sup>400</sup> The ground state of NH, and probably of most nitrenes,<sup>401</sup> is a triplet, although nitrenes can be generated in both triplet<sup>402</sup> and singlet states. In additions of EtOOC–N to C=C double bonds two species are involved, one of which adds in a stereospecific manner and the other not. By analogy with Skell's proposal involving carbenes (p. 284) these are taken to be the singlet and triplet species, respectively.<sup>403</sup>

The two principal means of generating nitrenes are analogous to those used to form carbenes.

1. *Elimination.* An example is



<sup>396</sup>For monographs, see Scriven, E.F.V. *Azides and Nitrenes*, Academic Press, NY, **1984**; Lwowski, W. *Nitrenes*, Wiley, NY, **1970**. For reviews, see Scriven, E.F.V. *React. Intermed. (Plenum)* **1982**, 2, 1; Lwowski, W. *React. Intermed. (Wiley)* **1985**, 3, 305; **1981**, 2, 315; **1978**, 1, 197; *Angew. Chem. Int. Ed.* **1967**, 6, 897; Abramovitch, R.A., in McManus, S.P. *Organic Reactive Intermediates*, Academic Press, NY, **1973**, pp. 127–192; Hünig, S. *Helv. Chim. Acta* **1971**, 54, 1721; Belloli, R. *J. Chem. Educ.* **1971**, 48, 422; Kuznetsov, M.A.; Ioffe, B.V. *Russ. Chem. Rev.* **1989**, 58, 732 (*N*- and *O*-nitrenes); Meth-Cohn, O. *Acc. Chem. Res.* **1987**, 20, 18 (oxycarbonylnitrenes); Abramovitch, R.A.; Sutherland, R.G. *Fortsch. Chem. Forsch.*, **1970**, 16, 1 (sulfonyl nitrenes); Ioffe, B.V.; Kuznetsov, M.A. *Russ. Chem. Rev.* **1972**, 41, 131 (*N*-nitrenes).

<sup>397</sup>McClelland, R.A. *Tetrahedron* **1996**, 52, 6823.

<sup>398</sup>Kemnitz, C.R.; Karney, W.L.; Borden, W.T. *J. Am. Chem. Soc.* **1998**, 120, 3499.

<sup>399</sup>Wasserman, E.; Smolinsky, G.; Yager, W.A. *J. Am. Chem. Soc.* **1964**, 86, 3166. For the structure of CH<sub>3</sub>–N:, as determined in the gas phase, see Carrick, P.G.; Brazier, C.R.; Bernath, P.F.; Engelking, P.C. *J. Am. Chem. Soc.* **1987**, 109, 5100.

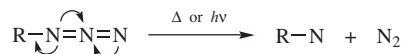
<sup>400</sup>Smolinsky, G.; Wasserman, E.; Yager, W.A. *J. Am. Chem. Soc.* **1962**, 84, 3220. For a review, see Sheridan, R.S. *Org. Photochem.* **1987**, 8, 159, pp. 159–248.

<sup>401</sup>A few nitrenes have been shown to have singlet ground states. See Sigman, M.E.; Autrey, T.; Schuster, G.B. *J. Am. Chem. Soc.* **1988**, 110, 4297.

<sup>402</sup>For the direct detection of triplet alkyl nitrenes in solution via photolysis of  $\alpha$ -azidoacetophenones see Singh, P.N.D.; Mandel, S.M.; Robinson, R.M.; Zhu, Z.; Franz, R.; Ault, B.S.; Gudmundsdottir, A.D. *J. Org. Chem.* **2003**, 68, 7951.

<sup>403</sup>McConaghy, Jr., J.S.; Lwowski, W. *J. Am. Chem. Soc.* **1967**, 89, 2357, 4450; Mishra, A.; Rice, S.N.; Lwowski, W. *J. Org. Chem.* **1968**, 33, 481.

2. *Breakdown of Certain Double-Bond Compounds.* The most common method of forming nitrenes is photolytic or thermal decomposition of azides,<sup>404</sup>



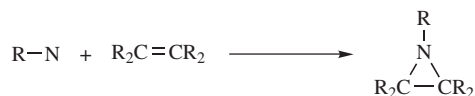
The unsubstituted nitrene NH has been generated by photolysis of or electric discharge through  $\text{NH}_3$ ,  $\text{N}_2\text{H}_4$ , or  $\text{HN}_3$ .

The reactions of nitrenes are also similar to those of carbenes.<sup>405</sup> As in that case, many reactions in which nitrene intermediates are suspected probably do not involve free nitrenes. It is often very difficult to obtain proof in any given case that a free nitrene is or is not an intermediate.

1. *Insertion* (see reaction 12-13). Nitrenes, especially acyl nitrenes and sulfonyl nitrenes, can insert into C—H and certain other bonds, for example,



2. *Addition to C=C Bonds* (see reaction 15-54):



3. *Rearrangements.*<sup>383</sup> Alkyl nitrenes do not generally give either of the two preceding reactions because rearrangement is more rapid, for example,



Such rearrangements are so rapid that it is usually difficult to exclude the possibility that a free nitrene was never present at all, that is, that migration takes place at the same time that the nitrene is formed<sup>406</sup> (see p. 1606). However, the rearrangement of naphthyl nitrenes to novel bond-shift isomers has been reported.<sup>407</sup>

<sup>404</sup>For reviews, see Dyall, L.K., in Patai, S.; Rappoport, Z. *The Chemistry of Functional Groups, Supplement D*, pt. 1, Wiley, NY, **1983**, pp. 287–320; Dürr, H.; Kober, H. *Top. Curr. Chem.* **1976**, 66, 89; L'Abbé, G. *Chem. Rev.* **1969**, 69, 345.

<sup>405</sup>For a discussion of nitrene reactivity, see Subbaraj, A.; Subba Rao, O.; Lwowski, W. *J. Org. Chem.* **1989**, 54, 3945.

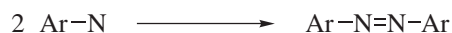
<sup>406</sup>For example, see Moriarty, R.M.; Reardon, R.C. *Tetrahedron* **1970**, 26, 1379; Abramovitch, R.A.; Kyba, E.P. *J. Am. Chem. Soc.* **1971**, 93, 1537.

<sup>407</sup>Maltsev, A.; Bally, T.; Tsao, M.-L.; Platz, M.S.; Kuhn, A.; Vosswinkel, M.; Wentrup, C. *J. Am. Chem. Soc.* **2004**, 126, 237.

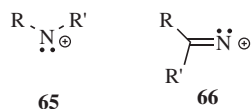
4. *Abstraction*, for example,



5. *Dimerization*. One of the principal reactions of NH is dimerization to diimide  $\text{N}_2\text{H}_2$ . Azobenzenes are often obtained in reactions where aryl nitrenes are implicated:<sup>408</sup>



It would thus seem that dimerization is more important for nitrenes than it is for carbenes, but again it has not been proved that free nitrenes are actually involved.



At least two types of *nitrenium ions*,<sup>409</sup> the nitrogen analogs of carbocations, can exist as intermediates, although much less work has been done in this area than on carbocations. In one type (**65**), the nitrogen is bonded to two atoms (R or R' can be H)<sup>410</sup> and in the other (**66**) to only one atom.<sup>411</sup> When R = H in **65** the species is a protonated nitrene. Like carbenes and nitrenes, nitrenium ions can exist in singlet or triplet states.<sup>412</sup>

<sup>408</sup>See, for example, Leyva, E.; Platz, M.S.; Persy, G.; Wirz, J. *J. Am. Chem. Soc.* **1986**, *108*, 3783.

<sup>409</sup>Falvey, D.E. *J. Phys. Org. Chem.* **1999**, *12*, 589; Falvey, D.E., in Ramamurthy, V., Schanze, K. *Organic, Physical, and Materials Photochemistry*, Marcel Dekker, NY, **2000**; pp. 249–284; Novak, M.; Rajagopal, S. *Adv. Phys. Org. Chem.* **2001**, *36*, 167; Falvey, D.E., in Moss, R.A., Platz, M.S., Jones, Jr., M. *Reactive Intermediate Chemistry*, Wiley-Interscience: Hoboken, NJ, **2004**; Vol. 1, pp. 593–650.

<sup>410</sup>Winter, A.H.; Falvey, D.E.; Cramer, C.J. *J. Am. Chem. Soc.*, **2004**, *126*, 9661.

<sup>411</sup>For reviews of **65**, see Abramovitch, R.A.; Jeyaraman, R., in Scriven, E.F.V. *Azides and Nitrenes*, Academic Press, NY, **1984**, pp. 297–357; Gassman, P.G. *Acc. Chem. Res.* **1970**, *3*, 26. For a review of **66**, see Lansbury, P.T., in Lwowski, W. *Nitrenes*, Wiley, NY, **1970**, pp. 405–419.

<sup>412</sup>Gassman, P.G.; Cryberg, R.L. *J. Am. Chem. Soc.* **1969**, *91*, 5176.