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# Scope and Mechanism of Intramolecular Aziridination of Cyclopent-3-enyl-methylamines to 1-Azatricyclo[2.2.1.0<sup>2,6</sup>]heptanes with Lead Tetraacetate

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## Abstract

A series of seven cyclopent-3-en-1-ylmethylamines bearing one, two, or three methyl substituents at the C2, C3, C4, or C<sub>α</sub> positions, including the unsubstituted parent, was accessed by ring-closing metatheses of  $\alpha,\alpha$ -diallylacetonitrile (or methallyl variants) and  $\alpha,\alpha$ -diallylacetone followed by hydride reductions, or by Curtius degradations of  $\alpha,\alpha$ -dimethyl- and 2,2,3-trimethylcyclopent-3-enylacetic acids. Oxidation of the primary amines with Pb(OAc)<sub>4</sub> in CH<sub>2</sub>Cl<sub>2</sub>, CHCl<sub>3</sub> or benzene in the presence of K<sub>2</sub>CO<sub>3</sub> effected efficient intramolecular aziridinations, in all cases except the  $\alpha$ -methyl analogue (**16**), to form the corresponding 1-azatricyclo[2.2.1.0<sup>2,6</sup>]heptanes, including the novel monoterpene analogues, 1-azatricyclene and the 2-azatricyclene enantiomers. The cumulative rate increases of aziridination reactions observed by <sup>1</sup>H NMR spectroscopy in CDCl<sub>3</sub> resulting from the presence of one or two methyl groups on the cyclopentene double bond, in comparison to the rate of the unsubstituted parent amine (1 : 17.5 : >280), indicate a highly electrophilic intermediate as the nitrene donor and a symmetrical aziridine-like transition state. A mechanism is outlined in which the amine displaces an acetate ligand from Pb(OAc)<sub>4</sub> to form a lead(IV) amide intermediate RNHPb(OAc)<sub>3</sub> proposed as the actual aziridinating species.

## Introduction

Protonated aziridines (pK<sub>a</sub> 8.0)<sup>1</sup> are nitrogen analogues of protonated cyclopropanes and protonated epoxides (Fig. 1), species commonly invoked as initiating groups in polyene cyclizations, or in the former case as carbocation intermediates in biosynthetic mechanisms leading to isoprenoid natural products.<sup>2,3</sup> The obvious structural similarities have stimulated the synthesis and evaluation of many isoprenoid aziridines as inhibitors of terpene biosynthesis. For example, 2,3-epiiminosqualene, the aziridine analogue of 2,3-oxidosqualene, is an effective inhibitor of oxidosqualene cyclases.<sup>4</sup> Sterol analogues bearing an aziridine ring in the side chain at the 24, 25 position are potent inhibitors of cholesterol biosynthesis in rat hepatoma cells,<sup>5a</sup> and they block sterol methyl transferase activity essential for plant development<sup>5b</sup> and fungal cell growth.<sup>5c,5d</sup> The epiimino analogue of 24,28-epoxyfucosterol, an intermediate in phytosterol side chain cleavage, retards the growth and development of the

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**Supporting Information Available:** General aspects, instrumentation, preparative procedures, and characterization data for cyanocyclopentenenes, cyclopentenylmethylamines, and related intermediates (**4–6** and **8–16**); *N*-(cyclopentenyl)methylhydroxylamines (**33 – 35**); cyclopentenyl tosylate (**17**) and  $\alpha,\alpha$ -dimethylcyclopentenylacetic acid (**18**); and campholenic acids **22** and **23**; and <sup>1</sup>H and <sup>13</sup>C NMR spectra of most compounds reported. This material is available free of charge via the Internet at <http://pubs.acs.org>

silk worm, *Bombyx mori*.<sup>5c</sup> Aziridine analogues of the Cecropea juvenile hormones (JH) potentiate the JH activity of the natural epoxide metamorphosis regulators.<sup>6</sup>

The cyclopropane rings frequently found in terpene natural products<sup>7</sup> (eg presqualene diphosphate and cycloartenol) and marine steroid side chains (eg gorgosterol)<sup>8</sup> are presumably formed by proton eliminations from various types of protonated cyclopropanes or related bridged carbocation intermediates. In accord with this analogy, aziridine analogues of presqualene diphosphate were found to be inhibitors of squalene synthase at low micromolar concentrations.<sup>9</sup> The pentacyclic aziridine aza-trachylobane in the presence of inorganic pyrophosphate is a potent competitive inhibitor (IC<sub>50</sub> 0.02  $\mu$ M) of recombinant kaurene synthase from *Arabidopsis thaliana*.<sup>10</sup> These isoprenoid aziridines presumably exert their inhibitory effects by selective binding in the active sites and by specific interactions with catalytic residues. Since aziridinium ions are potential electrophiles, they may also undergo covalent reactions with active site residues. These transition state mimics have applications as active site probes and aids to assist crystallization of recombinant terpene synthases and to locate the active sites in co-crystals with these enzymes.<sup>11</sup>

We became interested in the synthesis of 1-azatricyclo[2.2.1.0<sup>2,6</sup>]heptanes<sup>12</sup> as aziridinium analogues of bridged ions in Wagner-Meerwein rearrangements that occur in biosynthetic mechanisms leading to bicyclic and tricyclic monoterpenes (Fig 2),<sup>2b, 13</sup> and in the evaluation of the bridged aziridines as active site probes for monoterpene synthases. In this paper we explore the scope of the intramolecular aziridination of methyl-substituted cyclopent-3-enylmethylamines to the corresponding methyl-bearing 1-azatricyclo[2.2.1.0<sup>2,6</sup>]heptanes, including the aza-tricyclenes, by means of lead tetraacetate oxidations.<sup>14</sup> The rates of the cyclizations afford insights into the mechanism and structure of the nitrenoid intermediate in the reactions.

Considerable current interest in the synthesis, reactions, and applications of aziridines is evident from numerous recent reviews<sup>15, 16</sup> and a monograph on aziridines and epoxides.<sup>17</sup> In principle bicyclic aziridines might be accessible by intramolecular reactions of unsaturated nitrenes or nitrenium ions.<sup>18,19</sup> However, a more practical approach for intramolecular aziridination involves the cyclization of nitrene equivalents bearing electron-withdrawing groups generated by oxidation of amides and sulfonamides, either presence or absence of Cu and Rh mediators.<sup>20</sup> Although oxidations of *N*-amino quinazolones and *N*-amino phthalimide with Pb(OAc)<sub>4</sub> or PhI(OAc)<sub>2</sub> generate nitrenoids capable of intermolecular aziridination of C=C double bonds,<sup>15,21,22</sup> these approaches are not readily adaptable to intramolecular aziridinations. A homologue of azatricylene **2** (1,3,3-trimethyltricyclo[2.2.2.0<sup>2,6</sup>]octane) was prepared by reaction of terpinylamine with NBS in acetone.<sup>23</sup> We decided to apply Nagata's direct synthesis of bridged, polycyclic aziridines by Pb(OAc)<sub>4</sub> oxidation of unsaturated primary amines,<sup>14</sup> as reported previously by Portoghesi and Sepp for the parent 1-aza-nortricyclene,<sup>12</sup> and employed previously in the synthesis of azatrachylobane.<sup>10</sup>

## Synthesis of Cyclopentenylmethylamines

The parent amine (**6**)<sup>12</sup> was obtained from diallylacetonitrile (**4**)<sup>24</sup> by ring-closing metathesis (RCM) using Grubbs' 1st-generation ruthenium catalyst,<sup>25a</sup> followed by LiAlH<sub>4</sub> reduction of cyclopentenyl nitrile **5** as summarized in Scheme 1. Similar metatheses of  $\alpha$ -allyl- $\alpha$ -methallylacetonitrile and bis-( $\alpha$ -methallyl)acetonitrile using the Grubbs 2nd-generation ruthenium catalyst (**8**  $\rightarrow$  **9** and **11**  $\rightarrow$  **12**)<sup>25b</sup> and subsequent hydride reductions afforded the homologues bearing one and two methyl groups on the cyclopentene double bond (**10** and **13**). The modest 31% yield of **12** reflects the slower, incomplete ring-closing metathesis at the low concentration necessary to minimize the competing polymerization. The two methallyl acetonitrile derivatives (**8** and **11**) were prepared by alkylations of the corresponding

cyanoacetate precursors (ethyl  $\alpha$ -allylcyanoacetate (**7**) and ethyl cyanoacetate) with methallyl chloride followed by chloride-induced de-ethylation-decarboxylations (NaCl, DMSO, 150 °C).<sup>26</sup>

The syntheses of substrates bearing one or two methyl substituents on the exocyclic aminomethyl position (**16** and **20**) are outlined in Scheme 2. De-ethylation-decarboxylation (LiCl, DMF, reflux) of  $\alpha,\alpha$ -diallylacetate gave  $\alpha,\alpha$ -diallylacetone (**14**, 44%) which underwent metathesis and reductive amination<sup>27</sup> to 1-(cyclopenten-3-yl)ethylamine (**15**  $\rightarrow$  **16**). The low purity of the crude product necessitated purification by conversion to the t-Boc derivative followed by TFA hydrolysis-decarboxylation (35% over 3 steps). Alkylation of the lithium enolate of methyl isobutyrate with homoallylic cyclopentenyl tosylate **17**<sup>28</sup> in THF and subsequent hydrolysis of the resulting methyl ester intermediate gave  $\alpha$ -cyclopentenyl isobutyric acid **18** in high overall yield. Curtius rearrangement with diphenylphosphoryl azide, <sup>29</sup> conversion of the resulting isocyanate to the carbamate **19** (An = *p*-anisyl) with *p*-methoxybenzyl alcohol, and alkaline hydrolysis afforded geminal dimethyl analogue **20**.

The long known retro-Prins fragmentation of (*S*)-(+)-camphorsulfonic acid (**21**) by KOH fusion at 200–220 °C for 5 min afforded (+)- $\alpha$ -campholenic acid **22**, in accord with the literature procedures<sup>30</sup> (Sch 3). The intermediacy of the expected exocyclic isomer (+)-isocampholenic acid (**23**), observed as a trace impurity (ca 2%) in **22**, was verified by interrupting the fusion reaction after 1 min, at which time mixtures of **22** and **23** were present. Selective epoxidation of the former in a 2:1 isomer mixture and chromatographic separation of the relatively polar epoxide enabled isolation of pure **23** having optical rotation and NMR spectral data matching the literature values.<sup>31</sup> The exo/endo ratios varied from 1:1 to 1:9 (yields 75–90%) in 10 runs differing in the proportion of water (0–30%) added to 85% KOH in preparation of the fusion reagent. Nor-campholenyl amine **25** was obtained by Curtius rearrangement<sup>29</sup> of acid **22**, carbamate derivatization (**24**, An = *p*-anisyl), and alkaline hydrolysis as described previously for the  $\alpha,\alpha$ -dimethyl amine **20** in Scheme 2. The same reaction sequence with (*R*)-(-)-camphorsulfonic acid (*ent*-**21**) provided (-)- $\alpha$ -campholenic acid (*ent*-**22**), the related carbamate intermediate *ent*-**24**, and the enantiomeric nor-campholenyl amine *ent*-**25** bearing the three ring methyl groups.

## Intramolecular Aziridinations

The preparative aziridination reactions with the seven cyclopentenylmethylenamines were conducted with 1–2 equivalents of Pb(OAc)<sub>4</sub> in CH<sub>2</sub>Cl<sub>2</sub> at room temp in the presence of anhydrous K<sub>2</sub>CO<sub>3</sub> as base to neutralize the acetic acid released according to similar procedures described by Nagata, Portoghese and their co-workers. (See Sch 4 and Table 1).<sup>10,12,14</sup> The reactions were terminated by addition of satd aq K<sub>2</sub>CO<sub>3</sub>, and the aziridines were extracted into ether and converted to the stable trifluoroacetate (TFA) salts, at which point yields were calculated. The free aziridine bases were later liberated as needed for characterization by reactions with solid K<sub>2</sub>CO<sub>3</sub> in CH<sub>2</sub>Cl<sub>2</sub>, CDCl<sub>3</sub>, or other solvents. The aziridines proved to be stable in dilute solutions (CH<sub>2</sub>Cl<sub>2</sub>, CDCl<sub>3</sub>, frozen benzene) at –20 °C. However, as noted previously,<sup>10,12,14</sup> the strained heterocycles decomposed readily as pure liquids, presumably undergoing polymerization to insoluble, uncharacterized material.

The proton and carbon-13 NMR chemical shifts for the aziridine ring protons and carbons, the C-7 N-CH<sub>2</sub>, and C-CH<sub>3</sub> attached to the aziridines in the free base and TFA salt forms are collected in Table 2. The assignments are based on chemical shift trends, and in some cases on the carbon multiplicities from DEPT experiments.

Some interesting trends are apparent from the data in Table 2. The chemical shifts for the aziridine ring C-H protons are consistently in the range 2.03 to 2.22 ppm, and they are shifted downfield ( $\Delta\delta$  = +1.48 to +1.63 ppm) in the protonated forms, reflecting the positive charge

and hybridization changes in the internal C-N bonds. The values for the C-7 N-CH<sub>2</sub> moieties are spread over a considerable range,  $\delta_{\text{H}}$  2.11–2.80 ppm. A shift to lower field is evidently caused by CH<sub>3</sub> substitution on the aziridine ring carbons. In contrast downfield shifts arising from N-protonation are reasonably consistent at  $\Delta\delta = 0.49$ – $0.74$  ppm. The higher field position of aziridine C-CH<sub>3</sub> in aza-tricyclene **32** ( $\delta_{\text{H}}$  1.16) as compared to the aziridine ring methyl derivatives **27** and **28** ( $\delta_{\text{H}}$  1.35 and 1.38) is attributable to C-C bond anisotropy arising from the adjacent CH<sub>3</sub> groups. The protonation shifts for the ring CH<sub>3</sub> vary from  $\Delta\delta +0.36$  (**27**) to  $\Delta\delta +0.27$  ppm (**28**).

The <sup>13</sup>C NMR chemical shifts for the aziridine ring carbons (C-2 and C-6) move from 31.8 (**26**) to 38.4 or 39.1 for one CH<sub>3</sub> (**27**) and to 45.1 for the dimethyl case (**28**), and they undergo downfield shifts by  $\Delta\delta +5.5$  to  $+10.7$  ppm in the corresponding TFA salts. In contrast the aziridine ring methyl resonances ( $\delta_{\text{C}}$  16.0 and 12.5 ppm) appear at higher field positions in the TFA salts ( $\Delta\delta -4.2$  to  $-2.9$  ppm for **27** and **28**). Similar protonation shieldings for carbons  $\beta$  to nitrogen in acyclic amines (generally  $\Delta\delta -3$  to  $-5$  ppm) are attributed to "electric field effects and C-H bond polarizations."<sup>32b,c</sup>

First-order rates for the aziridinations reactions were determined by integration of <sup>1</sup>H NMR spectra carried out in NMR tubes with the free amines and 2 equivalents of Pb(OAc)<sub>4</sub> in CDCl<sub>3</sub> (Table 1). An initial "burst phase" apparent in the slower reactions is attributed to warming resulting from the exothermic interactions of the amines with Pb(OAc)<sub>4</sub>. The proton NMR peaks for the  $\alpha$ -methyl groups of **16** and **20** immediately moved somewhat downfield upon addition of Pb(OAc)<sub>4</sub> ( $\Delta\delta_{\text{H}}$  +0.118 and +0.156 ppm, respectively). Reaction progress was monitored by the consistent decrease in the vinyl proton integrations, or in the case of **13** by the integration changes accompanying conversion of the vinyl CH<sub>3</sub> to aziridine CH<sub>3</sub>. Log plots (Fig 3 below) were linear over approximately 0.5 to 1 half-lives.

The proton NMR spectra acquired during oxidation of  $\alpha$ -methylamine **16** showed extraneous peaks considered to be impurities formed competitively with aziridine **29**. We suppose that these byproducts arise from competing dehydrogenation to the ketimine and its subsequent condensation and/or oxidations of the enamine tautomers.<sup>33a</sup> Although the presence of aziridine **29** was evident from its characteristic <sup>1</sup>H NMR signals (eg new methyl peak  $\delta_{\text{H}}$  1.18 (d,  $J = 6.5$  Hz, 3H)), the numerous impurities present after high conversions prevented isolation of the aziridine TFA salt in pure form, and the isolated yield was not determined in this case. The intramolecular aziridination of amine **13** bearing two CH<sub>3</sub> groups on the double bond was essentially complete within 4 min, and the half-life in this case could only be estimated to be  $< 1$  min. The half-lives varied approximately  $\pm 15\%$  in duplicate runs, and were independent of the amount of Pb(OAc)<sub>4</sub> reagent added.

The rates of several aziridinations in the same heterogeneous medium used in the preparative reactions, ie TFA salts in the presence of 5 equivalents of solid K<sub>2</sub>CO<sub>3</sub>, were also measured by NMR analyses. The reactions of the TFA amine salts bearing methyl groups on the cyclopentene double bond proceeded considerably more slowly (**13**·TFA  $t_{1/2}$  9 min vs  $< 1$  min, and **10**·TFA 95 min vs 16 min), whereas the rate of the parent cyclopentenylmethylamine (**6**) TFA salt was unchanged. Evidently liberation of the free amines **13** and **10** from the TFA salts becomes the rate-limiting step under these heterogeneous conditions.

The oxidative aziridination with  $\alpha,\alpha$ -dimethyl amine **20** was also effected with 2 equivalents of PhI(OAc)<sub>2</sub> **21** in CH<sub>2</sub>Cl<sub>2</sub> with a half-life of 6 h, ie about 3 times more slowly than the reaction with Pb(OAc)<sub>4</sub>. In this case the methyl singlet shifted from 1.058 to 1.176 and then to 1.252 over 30 min, and remained at 1.252 as the peaks for the aziridine grew more intense.

The solubility and stability of Pb(OAc)<sub>4</sub> in many organic solvents<sup>33</sup> provided an opportunity to evaluate the effects of additives and medium on the aziridination process. No reaction

occurred with 2 equiv of  $\text{Pb}(\text{OAc})_4$  and  $\alpha, \alpha$ -dimethylamine **20** in  $\text{CD}_3\text{CN}$  after 10 days or in  $\text{CD}_3\text{CO}_2\text{H}$  after 2 days, and the aziridination was very slow in  $\text{CD}_3\text{OH}$ . The aziridination with **20** proceeded ca 4 times more slowly in benzene- $d_6$  ( $t_{1/2}$  530 min vs 125 min in  $\text{CDCl}_3$ ). No aziridine formation was observed when 2 equiv of the sterically hindered tertiary amine base diisopropylethylamine was present in  $\text{CDCl}_3$ , although shifts of the NMR peaks for the *N*-isopropyl and *N*-ethyl groups were noticeable. The aziridination rate with the TFA salt of **10** was about the same ( $t_{1/2}$  16 and 15 min) when effected by 1.1 or 2.0 equivalents of  $\text{Pb}(\text{OAc})_4$ , 2 equiv of pyridine, and 3 equiv of  $\text{K}_2\text{CO}_3$ . Much faster rates were observed in aziridinations conducted with free amines **6**, **10**, and **20** and 2 equiv of  $\text{Pb}(\text{OAc})_4$  in pyridine- $d_5$  ( $t_{1/2}$  <15 min vs 280 min, ca 6 min vs 16 min, and <2 min vs 125 min, respectively). However, the product from the unsubstituted amine **6** was a 1:1 mixture of aziridine **26** and nitrile **5** resulting from double dehydrogenation. The oxidation of primary amine to nitriles with  $\text{Pb}(\text{OAc})_4$  has been reported.<sup>34</sup>

## Scope and Mechanism of Aziridinations

The intramolecular aziridinations proceeded in satisfactory to high yields (65 – 88%) with all amines except  $\alpha$ -methyl amine **16**, despite the large ring strain of the 1-azatricyclo[2.2.1.0<sup>2,6</sup>]heptane products estimated to be in the neighborhood of 47 kcal/mol. This figure is based on the known strain energy of nortricyclene (47.0 kcal/mol)<sup>35a</sup> together with the very similar values recorded for cyclopropane (27.5 and 28.13 kcal/mol)<sup>35a</sup> and aziridine (27.1 kcal/mol).<sup>35b</sup> We presume that our inability to isolate aziridine **29** is attributable to competing dehydrogenation to a labile ketimine and its relatively rapid oxidation and/or self-condensation to a mixture of amine by-products having properties similar to those of the aziridine. The various tricyclo[3.2.1.0<sup>2,7</sup>]octanes prepared in Nagata's pioneering investigation of aziridinations with  $\text{Pb}(\text{OAc})_4$  are further indications of the scope of this little used reaction.<sup>14</sup>

The increased rates ( $k_{\text{rel}}$  2.8 and 2.2) observed with amines bearing one or two  $\alpha$ -methyl groups (**16** and **20**) clearly indicates the insensitivity of the aziridination reaction to steric hindrance around the nitrogen center. In fact the cyclization reactions of all methyl-substituted derivatives proceeded faster than that of the parent amine **6**. The rates of these formal [2+1] heterocycloadditions increased dramatically and cumulatively with one or two methyl groups situated on the cyclopentenyl double bond (**10**  $k_{\text{rel}}$  17.5 and **13**  $k_{\text{rel}}$  280), demonstrating that aziridination is the slow step in the mechanism, and revealing the highly electrophilic nature of the nitrenoid intermediate and the apparent symmetry of the transition state.

A wide range of mechanisms and types of nitrenoid intermediates has been considered for the well-known aziridinations of olefins with *N*-amino heterocycles (primarily *N*-aminophthalimides and *N*-aminoquinazolones).<sup>21a, 22</sup> Plausible intermediates include *N*-acetoxyamines, nitrenes, nitrenium ions, aminyl radicals, hypervalent iodine (III) species (amino- or imino-iodinanes) with  $\text{PhI}(\text{OAc})_2$  as oxidant, and in the case of  $\text{Pb}(\text{OAc})_4$  lead (IV) species (lead amides or lead imines). Although Atkinson advocated the intermediacy of *N*-acetoxyamino heterocycles,<sup>22</sup> the selectivity variations with  $\text{Pb}(\text{OAc})_4$  and  $\text{PhI}(\text{OAc})_2$  as oxidant are considered inconsistent with a common intermediate.<sup>21a, 21b</sup>

We decided to test the possibility of an *N*-acetoxy intermediate by independent synthesis of the hydroxylamino ester **35** from the parent cyclopentenylmethylamine **6** as shown in Scheme 5.<sup>36</sup> However, the reaction of **35** with  $\text{Pb}(\text{OAc})_4$  under the usual conditions with monitoring by  $^1\text{H}$  NMR spectroscopy proceeded slowly with the development of numerous peaks, of which none were the characteristic signals of aziridine **26**. No evidence for a detectable buildup of the characteristic NMR absorptions for **35** could be seen in spectra taken during the kinetic runs of **6** with  $\text{Pb}(\text{OAc})_4$ . Furthermore the 3-fold faster aziridination of  $\alpha, \alpha$ -dimethylamine



**20** observed with  $\text{Pb}(\text{OAc})_4$  as oxidant ( $t_{1/2}$  125 min) compared to that with  $\text{PhI}(\text{OAc})_2$  ( $t_{1/2}$  360 min) is inconsistent with a common intermediate.

It seems reasonable to expect the amines to undergo ligand substitution with  $\text{Pb}(\text{OAc})_4$  to generate lead(IV) amides (**36**) or possibly lead imines (**37** and **38**) by the equilibrations shown in Scheme 6. One driving force for the exchange would be the subsequent formation of an acetate salt between the remaining amine and the equivalent of acetic acid released. The slight exotherm observed upon adding  $\text{Pb}(\text{OAc})_4$  to the amine as well the slight downfield of the proton NMR signals for the geminal methyls in **20** are attributable to the exchange process. Although the Pb(IV)-N bond is very weak ( $E_D$  Pb-N  $\sim$  20–30 kcal/mol),<sup>37</sup> many trialkyllead amides (eg  $\text{Et}_3\text{PbNEt}_2$ ) and trityllead amides and imides were reported in the literature by 1980.<sup>37</sup> A similar exchange equilibrium was proposed as the first step in the Steglitz rearrangement of tritylamine to benzophenone *N*-phenylimine ( $\text{Pb}(\text{OAc})_4$ , benzene, reflux).<sup>38</sup>

We propose that the aziridinations effected with  $\text{Pb}(\text{OAc})_4$  occur by intramolecular electrophilic attack of lead(IV) amides onto the ring double bonds with simultaneous formation of the aziridinium acetate salt (**41**) and  $\text{Pb}(\text{OAc})_2$  as depicted in the mechanism **39**  $\rightarrow$  **40**  $\rightarrow$  **41** (Sch 7). The large and cumulative rate-accelerating effects of methyl groups on the double bonds (**10**  $k_{\text{rel}}$  17.5 and **13**  $k_{\text{rel}}$   $>$  280,  $k_{10}/k_{13}$   $>$  16) clearly signify substantial and symmetrical positive charge accumulation at carbon in the transition state. Major driving forces for this formal [2+1]cycloaddition are the exchange of the weak Pb-N bond and for the stronger C-N bonds in the product, as well as the exothermic Pb(IV)  $\rightarrow$  Pb(II) 2-electron reduction ( $E^\circ$  at 25  $^\circ\text{C}$ ,  $\text{Pb}^{+4} + 2 e^- = \text{Pb}^{+2}$  1.65V).<sup>39</sup> This mechanism is similar to that proposed by Richardson et al<sup>21a</sup> for intermolecular aziridinations of olefins with *N*-aminoheterocycles and aryl iodine  $\text{ArI}(\text{OAc})_2$  in the absence of transition metal catalysts. Transition state [**40**] bears a resemblance to one proposed for the  $\text{Pb}(\text{OAc})_4$ -induced Steglitz rearrangement of tritylamines mentioned above.<sup>38</sup>

The transition state proposed for the intramolecular aziridinations [**40**] is similar to those associated with peroxy acid epoxidations of C=C double bonds (**42**  $\rightarrow$  [**43**]  $\rightarrow$  **44**)<sup>40, 41</sup> and with the solvolytic cyclizations of cyclopentenylethyl sulfonates to symmetrically-bridged norbornyl carbonium ions (**45**  $\rightarrow$  [**46**]  $\rightarrow$  **47**)<sup>42</sup> as illustrated in Scheme 7. The cumulative, rate-enhancing effects of alkyl substituents on olefin epoxidations (ca 10–20 times per alkyl substituent),<sup>43</sup> and the accelerating influence of one and two methyl groups on the cyclopentenyl double bond of **45** (increases of 7 and 38.5 times)<sup>42</sup> are taken to indicate analogous transition structures [**43**] and [**46**] having substantial positive charge accumulation simultaneously at both C=C carbons.

Transition state **40** may be likened to an intramolecular  $S_N2$  reaction taking place at nitrogen, with the C=C double bond as nucleophile and  $\text{Pb}(\text{OAc})_2$  as the leaving group. This analogy suggests aziridination via lead imine **38** would be disfavored by the presumed  $\text{sp}^2$  hybridization at the C=N nitrogen, in accord with the highly suppressed rates of  $S_N2$  substitutions at vinylic carbon. Furthermore, to our knowledge lead(IV) imines of this type are unknown in the literature.

The solvent effects observed on the aziridinations seem generally consistent with the mechanism and transition state in Scheme 6 and Scheme 7. The somewhat faster rates observed in  $\text{CDCl}_3$  compared to those in  $\text{C}_6\text{D}_6$  are attributable to transition state stabilization by the dipole of the former. However, the slower rates in  $\text{CD}_3\text{CN}$  and  $\text{CD}_3\text{OH}$  can be rationalized by competing ligation of Pb(IV) with the excess solvents. The rate suppression observed in  $\text{CD}_3\text{CO}_2\text{H}$  is probably caused by formation of an ammonium acetate salt and the resulting reduced concentration of free amine. Similarly the faster rates in pyridine probably arise from

the scavenging of acetic acid, and the resulting higher concentrations of free amine and key intermediate **36**.

## Conclusion

This work has established the generality of the  $\text{Pb}(\text{OAc})_4$ -induced intramolecular aziridination of cyclopentenylmethylamines to 1-azatricyclo[2.2.1.0<sup>2,6</sup>]heptanes<sup>12</sup> and has provided evidence indicating the highly electrophilic nature of the key nitrene donor **39** and a symmetrical aziridine-like transition state **40**. The strained, bridged aziridine products, or their *N*-alkyl or *N*-acyl aziridinium derivatives, and others available by analogous intramolecular aziridinations of related types of unsaturated primary amines,<sup>14</sup> would undergo predictable nucleophilic and electrophilic ring cleavage reactions,<sup>12, 15–17,44</sup> affording access to various heterocyclic structures. A noteworthy distinction of the intramolecular aziridinations with  $\text{Pb}(\text{OAc})_4$ <sup>12,14</sup> is the use of unsaturated primary amines lacking the commonly employed *N*-acyl or *N*-sulfonyl linkages.<sup>15–17, 45</sup> The compatibility of  $\text{Pb}(\text{OAc})_4$  with a wide range of functional groups and solvents,<sup>33</sup> together with the many synthetic approaches to unsaturated amines, point to a broad generality for the intramolecular aziridination-ring opening route to nitrogen heterocycles.

The azatricyclenes reported are novel aza analogues of the bridged bornyl carbonium ion (Fig 2) and potentially useful transition state inhibitors and active site probes for monoterpene cyclases. The enantiomeric 2-aza-tricyclenes ((+)-**32** and (–)-**32**) provide a means to evaluate the stereoselectivity of interactions with the biosynthetic enzymes that produce enantiomeric monoterpenes, eg (+)- and (–)-bornyl diphosphate synthases, and (+)- and (–)-pinene cyclases.<sup>2b,13</sup> Furthermore, ring opening reactions of the azatricyclenes afford a simple route to aza-monoterpenes such as 6-azaborneol and 2-azacamphane.<sup>46</sup>

## Experimental Section

### 4-Methoxybenzyl 2-(Cyclopent-3-en-1-yl)prop-2-ylcarbamate (**19**)

In the same manner as described below for urethane **24**, compound **19** was prepared from acid **18** (2.8 g, 18.18 mmol). Carbamate **19** (4.2 g, 80%) was obtained as an oil: <sup>1</sup>H-NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.30 (d, 2H,  $J$  = 8.8 Hz), 6.89 (d, 2H,  $J$  = 8.8 Hz), 5.65 (s, 2H), 4.97 (br s, 2H), 4.64 (br s, 1H), 3.81 (s, 3H), 2.70 (app quintet, 1H,  $J_{\text{app}}$  = 8.4 Hz),<sup>47</sup> 2.36 (br dd, 2H,  $J$  = 14.8, 9.6 Hz), 2.18 (br dd, 2H,  $J$  = 14.8, 8.5 Hz), 1.30 (br s, 6H). <sup>13</sup>C NMR ( $\text{CDCl}_3$ , 100.6 MHz)  $\delta$  159.7, 159.3, 130.2, 129.6, 128.9, 114.1, 71.6, 66.0, 55.5, 46.5, 34.1, 24.6; HRMS (ESI)  $m/z$  calcd for  $\text{C}_{17}\text{H}_{27}\text{NO}_3$  ( $M + H$ )<sup>+</sup> 290.1756, found: 290.1752.

### 2-(Cyclopent-3-en-1-yl)propan-2-amine (**20**)

As described below for amine **25**, carbamate **19** (4.2 g, 14.53 mmol) was hydrolyzed by refluxing in 40% methanolic KOH (25 mL). Amine **20** (1.75 g, 98%) was obtained as a colorless liquid: <sup>1</sup>H NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  5.66 (s, 2H), 2.40–2.26 (m, 3H), 2.16 (br dd, 2H,  $J$  = 13.5, 8. Hz), 1.06 (s, 6H); <sup>13</sup>C NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  129.6, 50.9, 49.5, 34.0, 28.6; HRMS (ESI)  $m/z$  calcd for  $\text{C}_8\text{H}_{15}\text{N}$  ( $M + H$ )<sup>+</sup> 125.1205, found: 125.1202.

### (+)-(1S)-4-Methoxybenzyl (2,2,3-Trimethylcyclopent-3-enyl)methylcarbamate ((+)-**24**)

Yamada's modified procedure<sup>29</sup> for the Curtius rearrangement was followed. A solution of acid (+)-**22** (3.0 g, 17.9 mmol) and  $\text{Et}_3\text{N}$  (4.2 mL, 3.0 g, 30.1 mmol) in 1,2-dichloroethane (40 mL) was stirred under  $\text{N}_2$  as neat diphenylphosphoryl azide (3.9 mL, 5.0 g, 18.1 mmol) was added. The solution was heated at reflux for 100 min, *p*-methoxybenzyl alcohol (3.7 mL, 4.1 g, 30.0 mmol) was added *via* syringe, and heating was resumed for 12 h. The solution was concentrated under reduced pressure, and the resulting yellow, oily residue was purified by



flash chromatography using a gradient of 5–10% EtOAc/hexane to give 4.5 g (83%) of urethane (+)-**24** as a colorless oil, which crystallized at  $-15^{\circ}\text{C}$ . Data for crystalline (+)-**24**: TLC  $R_f$  0.75 (10% EtOAc-hexane); mp  $43\text{--}44^{\circ}\text{C}$ ;  $[\alpha]_D^{25} +5.67^{\circ}$  ( $c$  1.1,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz) as a 5:2 mixture of two rotamers:  $\delta$  7.30 (d, 2H,  $J = 8.5$  Hz), 6.88 (d, 2H,  $J = 8.5$  Hz), 5.20 (s, 1H), 5.03 (s, 2H), 4.68 (br s, 1H), 3.80 (s, 3H), 3.36 (m, 1H), 3.15 (m, 1H), 2.30 (m, 1H), 1.94 (m, 2H), 1.58 (s, 3H), 1.03 (s, 3H), 0.83 (s, 3H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  159.7(s), 156.7(s), 148.5 (s), 130.2 (d, 2C), 128.9 (s), 121.4 (d), 114.1 (d, 2C), 66.6 (t), 55.4 (q), 49.7 (d), 46.6 (s), 42.4 (t), 34.3 (t), 26.5 (q), 19.9 (q), 12.5 (q); HRMS (ESI)  $m/z$  calcd for  $\text{C}_{18}\text{H}_{26}\text{NO}_3$  ( $M + H$ ) $^{+}$  304.1913, found: 304.1910.

**(–)-(1*R*)-4-Methoxybenzyl (2,2,3-Trimethylcyclopent-3-enyl)methylcarbamate ((–)-24)**

Crystalline urethane *ent*-**22** (6.2 g, 84%) was prepared as described above for (+)-**22** starting from (–)- $\alpha$ -campholenic acid (–)-*ent*-**22** (4.1 g, 24.4 mmol): mp  $42\text{--}44^{\circ}\text{C}$ ;  $[\alpha]_D^{25} -5.23^{\circ}$  ( $c$  2.9,  $\text{CHCl}_3$ ); the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of (–)-**24** were identical to those previously recorded for carbamate (+)-**24**; HRMS (ESI)  $m/z$  calcd for  $\text{C}_{18}\text{H}_{26}\text{NO}_3$  ( $M + H$ ) $^{+}$  304.1913, found: 304.1912.

**(±)-4-Methoxybenzyl (2,2,3-Trimethylcyclopent-3-enyl)methylcarbamate ((±)-24)**

Urethane (±)-**24** (oil, 2.7 g, 83%) was prepared as described above for (+)-**24** starting from (±)- $\alpha$ -campholenic acid (±)-**22** (1.8 g, 10.7 mmol). The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of compound (±)-**24** were identical to those previously recorded for carbamate (+)-**24**; HRMS (ESI)  $m/z$  calcd for  $\text{C}_{18}\text{H}_{26}\text{NO}_3$  ( $M + H$ ) $^{+}$  304.1913, found: 304.1910.

**(+)-(1*S*)-(2,2,3-Trimethylcyclopent-3-enyl)methylamine ((+)-25)**

Hydrolysis of the (*S*)-carbamate (+)-**24** was accomplished following a literature procedure.<sup>48</sup> A solution of (+)-**24** (4.0 g, 13.20 mmol) and KOH (10.0 g, 178.6 mmol) in 30 mL of 95% EtOH (4%  $\text{H}_2\text{O}$ ) was heated at reflux for 2.5 h, cooled to  $0^{\circ}\text{C}$ , and acidified with concd HCl. The solution was partially concentrated under reduced pressure, diluted with water (150 mL), and extracted with  $\text{CH}_2\text{Cl}_2$  ( $2 \times 25$  mL). The aq phase was cooled again to  $0^{\circ}\text{C}$ , basified with KOH pellets, and extracted with  $\text{CH}_2\text{Cl}_2$  ( $3 \times 15$  mL). The combined organic extracts were dried ( $\text{K}_2\text{CO}_3$ ) and evaporated at atmospheric pressure to yield 1.7 g (93%) of amine (+)-**25** as a clear oil: TLC  $R_f$  0.24 (alumina, 1% MeOH- $\text{CHCl}_3$ );  $[\alpha]_D^{25} +9.11^{\circ}$  ( $c$  1.1,  $\text{CHCl}_3$ );  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  5.21 (br s, 1H), 2.84 (dd, 1H,  $J = 12, 4.5$  Hz), 2.62 (dd, 1H,  $J = 12, 10$  Hz), 2.37 (m, 1H), 1.93–1.79 (m, 2H), 1.58 (br s, 3H), 1.49 (br s, 2H), 1.02 (s, 3H), 0.77 (s, 3H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  48.7, 121.5, 53.6, 46.6, 43.3, 34.5, 26.6, 19.9, 12.5.

**(–)-(1*R*)-[2,2,3-Trimethylcyclopent-3-enyl]methylamine ((–)-25)**

Hydrolysis of urethane (–)-**24** (4.2 g, 13.86 mmol) following the procedure described above for (+)-**25**, gave the enantiomeric amine *ent*-**25** (1.8 g, 93%). Data for (–)-**25**:  $[\alpha]_D^{25} -9.16^{\circ}$  ( $c$  3.8,  $\text{CHCl}_3$ ). The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of (–)-**25** were identical to those previously recorded for (+)-**25**.

**(±)-[2,2,3-Trimethylcyclopent-3-enyl]methylamine ((±)-25)**

Hydrolysis of urethane (±)-**24** (2.2 g, 7.26 mmol) following the procedure described above for (+)-**25**, gave the racemic amine (±)-**25** (0.91 g, 89%). The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of (±)-**25** were identical to those previously recorded for (+)-**25**.

## Aziridination Reactions

### 1-Azatricyclo [2.2.1.0<sup>2,6</sup>]heptane (26)

A suspension of anhyd K<sub>2</sub>CO<sub>3</sub> (460 mg, 3.33 mmol) in a solution of amine **6** as its trifluoroacetic acid (TFA) salt (129 mg, 0.611 mmol) in 40 mL of dry CH<sub>2</sub>Cl<sub>2</sub> was stirred magnetically as 580 mg (1.27 mmol) of solid Pb(OAc)<sub>4</sub> was added according to literature procedures<sup>10, 12, 14</sup> except that CH<sub>2</sub>Cl<sub>2</sub> was used as solvent instead of benzene. TLC analyses (CHCl<sub>3</sub> : MeOH = 10 : 1) showed complete reaction after 13 h. Satd aq K<sub>2</sub>CO<sub>3</sub> (20 mL) was added, and the product was extracted with ether (2 × 15 mL). The organic layers were combined, dried with MgSO<sub>4</sub>, and treated with TFA (90 mg, 0.79 mmol). Evaporation of the solvent provided the pure TFA salt of 1-azatricyclo [2.2.1.0<sup>2,6</sup>]heptane (**26**) as a yellow oil: yield, 83.0 mg (0.406 mmol, 67%); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)<sup>47</sup> δ 10.30–11.30 (m, 1H), 3.70 (s, 2H), 2.92 (s, 2H), 2.72 (s, 1H), 1.89 (app d, 2H, *J*<sub>app</sub> = 12.4 Hz), 1.74 (app dd, 2H, *J*<sub>app</sub> = 13.2, 1.6 Hz); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ 161.0 (q, *J* = 38.4 Hz), 115.8 (q, *J* = 286.6 Hz), 51.0, 38.1, 31.0, 29.1. Free aziridine: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)<sup>47</sup> δ 2.22 (s, 2H), 2.18 (s, 2H), 2.08 (s, 1H), 1.34 (app d, 2H, *J*<sub>app</sub> = 11.2 Hz), 1.21 (app dd, 2H, *J*<sub>app</sub> = 11.2, 1.2 Hz); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ 55.8, 31.8, 31.5, 28.5; IR (NaCl): 3027, 2924, 1446, 1393; HRMS (ESI-HRMS) *m/z* calcd for (M + H<sup>+</sup>) 96.0813, found 96.0717.

The following preparative aziridinations were conducted as described above for the unsubstituted 1-azatricyclo [2.2.1.0<sup>2,6</sup>]heptane (**26**).

### 2-Methyl-1-azatricyclo [2.2.1.0<sup>2,6</sup>]heptane (27)

Amine **10** as the TFA salt (105 mg, 0.47 mmol), K<sub>2</sub>CO<sub>3</sub> (350 mg, 2.5 mmol), CH<sub>2</sub>Cl<sub>2</sub> (20 mL), Pb(OAc)<sub>4</sub> (440 mg, 1.00 mmol), time (2 h), TFA (70 mg, 0.61 mmol), yield of aziridine **27** TFA salt (81 mg, 78%): <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)<sup>47</sup> δ 10.50–11.00 (m, 1H), 3.63 (s, 1H), 3.05 and 2.91 (ABdd, *J*<sub>AB</sub> = 9.2 Hz, 2H), 2.67 (s, 1H), 1.90 (app ABd1, *J*<sub>app</sub> = 12.4 Hz, 1H), 1.85 (app ABXdd1, *J*<sub>app</sub> = 12.4, 1.2 Hz, 1H), 1.78 (app ABd2, *J*<sub>app</sub> = 12.4 Hz, 1H), 1.71 (app ABXdd2, *J*<sub>app</sub> = 12.4, 1.2 Hz, 1H), 1.71 (s, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ 159.5 – 162.0 (m), 112.0 – 123.0 (m), 112.0 – 123.0 (m), 51.6, 49.8, 43.9, 36.4, 32.4, 31.1, 11.8. Free aziridine: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz)<sup>47</sup> δ 2.39 and 2.25 (app ABdd, *J*<sub>app</sub> = 9.9 Hz, 2H), 2.00–2.11 (br m, 1H), 2.08 (s, 1H), 1.32–1.40 (m, 2H), 1.35 (s, 3H), 1.16–1.24 (m, 2H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz) δ 56.7, 39.1, 38.5, 37.0, 33.1, 31.6, 16.0; IR (NaCl): 3289, 2960, 1557, 1455, 1377; HRMS (ESI-HRMS) *m/z* calcd for (M + H<sup>+</sup>) 110.0970, found: 110.0968.

### 2,6-Dimethyl-1-Azatricyclo [2.2.1.0<sup>2,6</sup>]heptane (28)

Amine **13** TFA salt (100 mg, 0.42 mmol), K<sub>2</sub>CO<sub>3</sub> (310 mg, 2.24 mmol), CH<sub>2</sub>Cl<sub>2</sub> (20 mL), Pb(OAc)<sub>4</sub> (380 mg, 0.84 mmol), time 1 h, TFA (60 mg, 0.53 mmol), yield of aziridine **28** TFA salt (80 mg, 81 %): <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz)<sup>47</sup> δ 10.30–10.70 (m, 1H), 3.01 (s, 2H), 2.60 (s, 1H), 1.83 (app dd, *J*<sub>app</sub> = 13.0, 1.0 Hz, 2H), 1.79 (app dd, *J*<sub>app</sub> = 12.5, 1.5 Hz, 2H), 1.65 (s, 6H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz) δ 160.9 (q, *J* = 38.1 Hz), 116.0 (q, *J* = 287.9 Hz), 53.2, 52.2, 37.8, 31.4, 9.6. Free aziridine: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) δ 2.53 (s, 2H), 2.16 (s, 1H), 1.35–1.44 (m, 4H), 1.38 (s, 6H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz) δ 56.3, 45.1, 38.4, 32.3, 12.5; IR (NaCl): 3252, 2949, 1557, 1455, 1386; HRMS (ESI-HRMS) *m/z* calcd for (M + H<sup>+</sup>) 124.1126, found: 124.1121.

### 7,7-Dimethyl-1-azatricyclo[2.2.1.0<sup>2,6</sup>]heptane (30) and its Methiodide Salt (31)

Following Nagata's procedure for the synthesis of bridged aziridines.<sup>14</sup> To a stirred suspension of primary amine **20** (894 mg, 7.3 mmol) and anhyd K<sub>2</sub>CO<sub>3</sub> (4.02 g, 29 mmol) in 150 mL of CH<sub>2</sub>Cl<sub>2</sub> was added Pb(OAc)<sub>4</sub> (6.45 g, 14.5 mmol) in 2-g portions. After 20 h, the solids were filtered, and the resulting filtrate was passed through a small column of basic alumina (Aldrich,

50.0 g, 150 mesh, 58 Å) under vacuum. The column was washed using a gradient of 1–2% MeOH/CH<sub>2</sub>Cl<sub>2</sub> as eluent. Fractions containing the aziridine (TLC alumina, 1% MeOH/CH<sub>2</sub>Cl<sub>2</sub> single spot at *R<sub>f</sub>* 0.7 when visualized with I<sub>2</sub> vapors) were combined and washed with 10% aq HCl. The aq layer was cooled to 0 °C, basified with NaOH pellets, extracted with Et<sub>2</sub>O (total volume 250 mL), and dried over anhyd K<sub>2</sub>CO<sub>3</sub>. For characterization purposes, a small portion of this solution was evaporated (0 °C) using a stream of nitrogen to give aziridine **30** as a colorless and highly volatile liquid: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) δ 2.19 (s, 2H), 1.79 (d, 2H, *J* = 11 Hz), 1.59 (s, 1H), 1.13 (d, 2H, *J* = 11 Hz), 1.02 (s, 6H). Methyl iodide (905 μL, 14.5 mmol) was added to the above dry ethereal solution. After 20 h at room temp, the white crystals that formed were filtered, washed with ether, and recrystallized from EtOH-Et<sub>2</sub>O to afford the methiodide salt **31** (1.3 g, 68% over two steps). Data for recrystallized **31**: mp 278–280 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) δ 4.51 (s, 2H), 3.34 (s, 3H), 2.45 (d, 2H, *J* = 13 Hz), 2.34 (s, 1H), 1.77 (d, 2H, *J* = 13 Hz), 1.40 (s, 6H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz) δ 49.3, 39.8, 34.7, 30.7, 19.8, 8.7; HRMS (ESI) calcd for *m/z* C<sub>9</sub>H<sub>16</sub>N 138.1283, found, 138.1282.

**(+)-2,3,3-Trimethyl-1-azatricyclo[2.2.1.0<sup>2,6</sup>]heptane ((+)-2-Azatricyclene, (+)-32)**

A suspension of primary amine (+)-**25** (308 mg, 2.2 mmol) and K<sub>2</sub>CO<sub>3</sub> (1.23 g, 8.9 mmol) in 150 mL of CH<sub>2</sub>Cl<sub>2</sub> was stirred and cooled in an ice bath as Pb(OAc)<sub>4</sub> (1.97 g, 4.44 mmol) was added in 0.5-g portions over 5 min. After 20 min, the solids were removed by filtration, and the resulting filtrate was passed through basic alumina (Aldrich, 50.0 g, 150 mesh, 58 Å) under vacuum using a gradient of 1–2% MeOH/CH<sub>2</sub>Cl<sub>2</sub> as eluent. Fractions containing aziridine (+)-**32** (TLC alumina *R<sub>f</sub>* 0.6, using 1% MeOH-CHCl<sub>3</sub>, single yellow spot when visualized with I<sub>2</sub> vapors) were combined and washed with 10% aq HCl (3 × 25 mL). The aq layer (containing the HCl salt of the aziridine) was cooled at 0 °C, basified with NaOH pellets, extracted with Et<sub>2</sub>O (3 × 100 mL), and dried over anhyd K<sub>2</sub>CO<sub>3</sub>. For characterization purposes, a small portion of this solution was evaporated using a stream of nitrogen to give aziridine (+)-**32** as a colorless and volatile liquid: [α]<sub>D</sub><sup>25</sup> +3.67° (*c* 0.33, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 2.80 (d, 1H, *J* = 10 Hz), 2.11 (d, 1H, *J* = 10 Hz), 2.03 (s, 1H), 1.74 (dt, 1H, *J* = 12, 1.6 Hz), 1.62 (s, 1H), 1.24 (d, 1H, *J* = 12 Hz), 1.16 (s, 3H), 0.93 (s, 3H), 0.91 (s, 3H); <sup>1</sup>H-NMR (D<sub>2</sub>O, 500 MHz) δ 2.64 (d, 1H, *J* = 10 Hz), 2.10 (s, 1H), 1.96 (d, 1H, *J* = 10 Hz), 1.67 (d, 1H, *J* = 12 Hz), 1.60 (s, 1H), 1.11 (d, 1H, *J* = 12 Hz), 0.99 (s, 3H), 0.74 (s, 3H), 0.73 (s, 3H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ 54.1, 45.2, 42.4, 41.2, 40.0, 30.1, 19.7 (2C), 10.5. HRMS (ESI) *m/z* calcd for C<sub>9</sub>H<sub>16</sub>N (M + H)<sup>+</sup> 138.1283, found: 138.1281. The dry ethereal solution thus obtained was filtered and kept at –20 °C for storage. The aziridine readily polymerizes when stored as a neat liquid.

**(+)-2,3,3-Trimethyl-1-azatricyclo[2.2.1.0<sup>2,6</sup>]heptane ((+)-2-Azatricyclene, (+)-32), Trifluoroacetate Salt**

To a cold (0 °C) and stirred solution of aziridine (+)-**32** (152.1 mg, 1.1 mmol) in 150 mL of ether was added TFA (122.8 mg, 83 μL, 1.11 mmol). Removal of the solvents under reduced pressure afforded the aziridinium TFA salt of (+)-**32** (246 mg, 88% for two steps) as an oil. A small sample was crystallized from ether/pentane. Data for the recrystallized salt: mp 117–118 °C; [α]<sub>D</sub><sup>25</sup> +1.26° (*c* 1.35, CHCl<sub>3</sub>); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) δ 3.66 (1H, s), 3.43 (d, 1H, *J* = 10 Hz), 2.85 (d, 1H, *J* = 10 Hz), 2.22 (s, 1H), 2.17 (d, 1H, *J* = 13.2 Hz), 1.79 (d, 1H, *J* = 13.2 Hz), 1.55 (s, 3H), 1.14 (s, 3H), 1.05 (s, 3H); <sup>13</sup>C-NMR (CDCl<sub>3</sub>, 125 MHz) δ 160.6 (q, *J* = 39.6 Hz), 115.4 (q, *J* = 288.2 Hz), 55.3, 49.6, 45.5, 43.6, 40.1, 29.5, 18.4, 18.3, 7.0; <sup>19</sup>F NMR (376 MHz) δ –76.01 (br s).

**(–)-2,3,3-Trimethyl-1-azatricyclo[2.2.1.0<sup>2,6</sup>]heptane ((–)-2-Azatricyclene, (–)-32)**

Pb(OAc)<sub>4</sub> oxidation of amine (–)-**25** (540 mg, 3.88 mmol) following the procedure given above for (+)-**25** gave the bridged aziridine *ent*-**32**, [α]<sub>D</sub><sup>25</sup> –3.52° (*c* 0.8, CHCl<sub>3</sub>). The <sup>1</sup>H and <sup>13</sup>C

NMR spectra of (–)-**32** were identical to those previously recorded for the enantiomer (+)-**32**. HRMS (ESI)  $m/z$  calcd for  $C_9H_{16}N$  ( $M + H$ )<sup>+</sup> 138.1283, found: 138.1280.

**(–)-2,3,3-Trimethyl-1-azatricyclo[2.2.1.0<sup>2,6</sup>]heptane [(–)-2-Azatricyclene] TFA Salt**

The TFA salt of *ent*-**25** (386 mg, 80% for two steps), prepared as described for (+)-**32**, showed mp 116–117 °C;  $[\alpha]_D^{25} -1.31^\circ$  (*c* 1.6,  $CHCl_3$ ). The <sup>1</sup>H, <sup>13</sup>C and <sup>19</sup>F NMR spectra of the TFA salt were identical to those previously recorded for the salt of the enantiomeric (+)-**32**.

**(±)-2,3,3-Trimethyl-1-azatricyclo[2.2.1.0<sup>2,6</sup>]heptane ((±)-2-Azatricyclene, (±)-**32**) and its Picrate Salt**

Pb(OAc)<sub>4</sub> oxidation of racemic amine (±)-**25** (122 mg, 0.86 mmol) following the procedure given above for (+)-**25** gave the bridged aziridine (±)-**32**. The <sup>1</sup>H and <sup>13</sup>C NMR spectra of (±)-**32** were identical to those previously recorded for aziridine (+)-**32**. HRMS (ESI)  $m/z$  calcd for  $C_9H_{16}N$  ( $M + H$ )<sup>+</sup> 138.1283, found: 138.1282.

The picrate salt of (±)-2-azatricyclene ((±)-**32**) was prepared by adding a solution of amine (±)-**32** (55.1 mg, 0.40 mmol) in 1 mL of 95% ethanol to a warm solution of picric acid (91.0 mg, 0.40 mmol) in 1 mL of 95% EtOH. Recrystallization from absolute ethanol gave the picrate salt (133 mg, 93%): mp 234–236 °C; <sup>1</sup>H NMR ( $CDCl_3$ , 500 MHz)  $\delta$  8.88 (s, 2H), 3.49 (s, 1H), 3.48 (d, 1H, *J* = 10 Hz), 2.93 (d, 1H, *J* = 10 Hz), 2.23 (s, 1H), 2.19 (d, 1H, *J* = 13.5 Hz), 1.81 (d, 1H, *J* = 12 Hz), 1.59 (s, 3H), 1.17 (s, 3H), 1.07 (s, 3H); <sup>13</sup>C NMR ( $CDCl_3$ , 125 MHz)  $\delta$  161.5, 141.8, 126.5 (4C), 54.4, 49.9, 44.8, 43.7, 40.2, 29.7, 18.9, 18.6, 7.3.

**(±)-2,3,3-Trimethyl-1-azatricyclo[2.2.1.0<sup>2,6</sup>]heptane ((±)-2-Azatricyclene) TFA Salt**

The TFA salt of (±)-**32** (18.5 mg, 83% over two steps), prepared as described for (+)-**32**, showed mp 111–113 °C. The <sup>1</sup>H, <sup>13</sup>C and <sup>19</sup>F NMR spectra were identical to those previously recorded for TFA salt of (+)-**32**.

## Representative Procedures and Data for Kinetic Runs

3-Methylcyclopent-3-enylmethylamine (**10**) was liberated from its TFA salt (15.8 mg, 0.0702 mmol) by reaction with excess anhyd  $K_2CO_3$  in  $CDCl_3$  (0.70 mL), the supernatant solution was transferred to an NMR tube, and solid Pb(OAc)<sub>4</sub> (60.0 mg, 0.138 mmol) was added. The progress of the aziridination reaction (**10** → **27**) was monitored by integration of the vinyl  $CH_3$  signal in <sup>1</sup>H NMR spectra taken at 5- and 3-minute intervals. Figure 3 (orange circles) shows a plot of  $-\ln[(\text{integral } \mathbf{10})/(\text{integral } \mathbf{10} + \mathbf{27})]$  at each time point. The half-life for this run was 19 min. Spectra taken at shorter times indicate faster conversion to the aziridine owing to warming of the solution caused by the initial exothermic reaction of Pb(OAc)<sub>4</sub> with the amine.

The kinetics of the other aziridination reactions were conducted similarly by NMR monitoring of  $CH_3$  signals, or in the case of the unsubstituted amine (**6**), by integration of the vinyl protons. The plots from three other kinetic run are shown in Figure 3. No peaks for side products were observed in the NMR spectra, except after extended time in aziridination **16** → **29**. The half-lives and relative rates are collected in Table 1.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgment

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## References

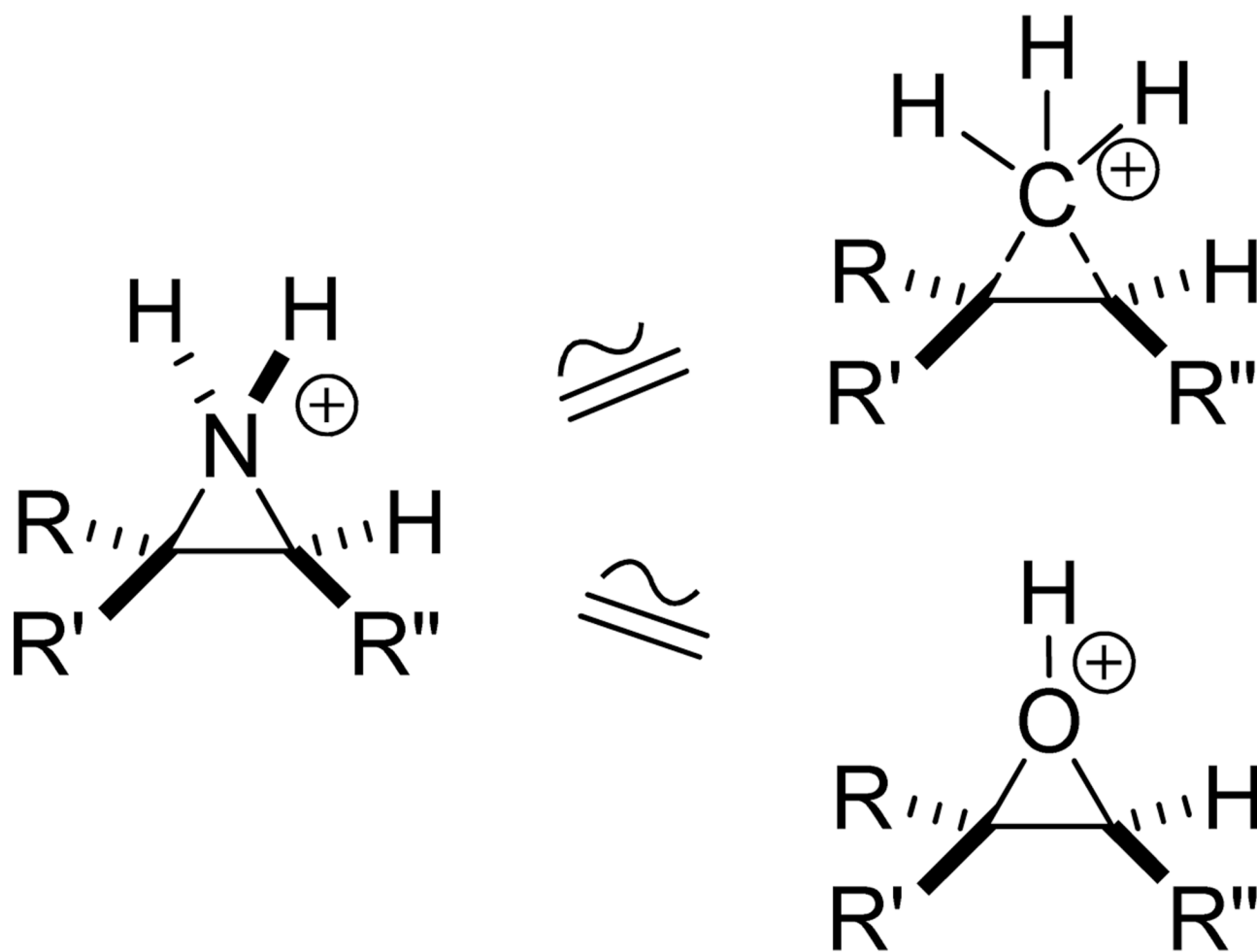
1. (a) Lange's Handbook of Chemistry. Vol. 15th Ed.. New York: McGraw-Hill; 1992. Table 8.8 (b) Kallies B, Mitzner R. J. Phys. Chem. B 1997;101:2959–2967.
2. (a) Porter, JW.; Spurgeon, SL., editors. Biosynthesis of Isoprenoid Compounds. Vol. Vol 1. New York: Wiley; 1983. (b) Davis EM, Croteau R. Top. Curr. Chem 2000;209:53–95.
3. Barton, D.; Nakanishi, K.; Meth-Cohn, O., editors. Comprehensive Natural Product Chemistry. Oxford: Elsevier Science; 1999. Cane DE. Isoprenoids Including Carotenoids and Steroids Vol. 2
4. Corey EJ, Ortiz de Montellano PR, Lin K, Dean PDG. J. Am. Chem. Soc 1967;89:2797–2798. [PubMed: 6043808]
5. (a) Popjak G, Meenan A, Parish EJ, Nes WD. J. Biol. Chem 1989;264:6230–6238. [PubMed: 2703486] (b) Nes WD, Janssen GG, Norton RA, Kalinowska M, Crumley FG, Tal B, Bergenstrahle A, Jonsson L. Biochem. Biophys. Res. Commun 1991;177:566–574. [PubMed: 2043140] (c) Nes WD, Hanners PK, Parish EJ. Biochem. Biophys. Res. Commun 1986;139:410–415. [PubMed: 3767970] (d) Maia C, Attias M, Urbina J, Gilbert I, Magaraci F, De Souza W. Biochem. Biophys. Res. Commun 2007;363:310–316. [PubMed: 17870055] (e) Fujimoto Y, Morisaki M, Ikekawa N, Horie Y, Nakasone S. Steroids 1974;24:367–375. [PubMed: 4416033]
6. (a) Corey EJ, Riddiford LM, Ajami AM, Yamamoto H, Anderson JE. J. Am. Chem. Soc 1971;93:1815–1816. (b) Anderson RJ, Henrick CA, Siddall JB. J. Org. Chem 1972;37:1266–1268.
7. (a) Dev, S., editor. CRC Handbook of Terpenoids. Boca Raton, FL: CRC Press; p. 1982-1989. (b) Nakanishi, K.; Goto, T.; Ito, S.; Natori, S.; Nozoe, S., editors. Natural Products Chemistry. Vol. Vols 1 and 3. Tokyo: Kodansha; 1974 and 1983. (c) Connolly, JD.; Hill, RA. Dictionary of Terpenoids. Vol. Vols 1–3. London: Chapman & Hall; 1991. (d) Glasby, JS. Encyclopedia of the Terpenoids. Vol. Vols. 1 and 2. Chichester: Wiley; 1982. 1982(e) Buckingham, J., editor. Dictionary of Natural Products. London: Chapman and Hall; 1994. (f) Buckingham, J. Dictionary of Natural Products (on-line web edition). London: Chapman & Hall/CRC Press; 2002.
8. (a) Giner JL, Djerassi C. Acta Chem. Scand 1992;46:678–679. [PubMed: 1419436] (b) Ling NC, Hale RL, Djerassi C. J. Am. Chem. Soc 1970;92:5281–5282. [PubMed: 5432671]
9. Koohang A, Coates RM, Owen D, Poulter CD. J. Org. Chem 1999;64:6–7. [PubMed: 11674074]
10. Roy A, Roberts FG, Wilderman PR, Zhou K, Peters RJ, Coates RM. J. Am. Chem. Soc 2007;129:12453–12460. [PubMed: 17892288]
11. Christianson DW. Chem. Rev 2006;106:3412–3442. [PubMed: 16895335]
12. Portoghese PS, Sepp DT. Tetrahedron 1973;29:2253–2256.
13. In ref <sup>2a</sup> Croteau R. Biosynthesis of Monoterpenes :225–282. Chap. 5 In ref <sup>3</sup> Wise ML, Croteau R. Monoterpene Biosynthesis :97–153. Chap. 2.05
14. (a) Nagata W, Hirai S, Kawata K, Aoki T. J. Am. Chem. Soc 1967;89:5045–5046. (b) Narisada M, Watanabe F, Nagata W. Synth. Commun 1972;2:21–26. (c) Nagata W, Wakabayashi T, Haga N. Synth. Commun 1972;2:11–19.
15. (a) Duan P-W, Chiu C-C, Lee W-D, Pan LS, Venkatesham U, Tzeng Z-H, Chen K. Tetrahedron: Asymmetry 2008;19:682–690. (b) Watson IDG, Yu L, Yudin AK. Acc. Chem. Res 2006;39:194–206. [PubMed: 16548508] (c) Padwa A, Murphree SS. Ark. Kemi 2006:6–33. (d) Halfen JA. Curr. Org. Chem 2005;9:657–669. (e) Müller P, Fruit C. Chem. Rev 2003;103:2905–2919. [PubMed: 12914485] (f) Dahanukar VH, Zavialov IA. Curr. Opin. Drug Dis. Dev 2002;5:918–927. (g) McCoull W, Davis FA. Synthesis 2000:1347–1365. (h) Mitchinson A, Nadin A. J. Chem. Soc., Perkin Trans 2000;1:2862–2892. (i) Osborn HMI, Sweeney J. Tetrahedron: Asymmetry 1997;8:1693–1715. (j) Li A-H, Dai L-X, Aggarwal VK. Chem. Rev 1997;97:2341–2372. [PubMed: 11848902] (k) Tanner D. Angew. Chem. Int. Ed. Engl 1994;33:599–619.
16. Padwa, A. Aziridines and Azirines: Monocyclic. In: Katritzky, AR.; Ramsden, CA.; Scriven, EFV.; Taylor, RJK., editors. Comprehensive Heterocyclic Chemistry III. Vol. Vol. 1. Amsterdam: Elsevier; 2008. p. 1-104.



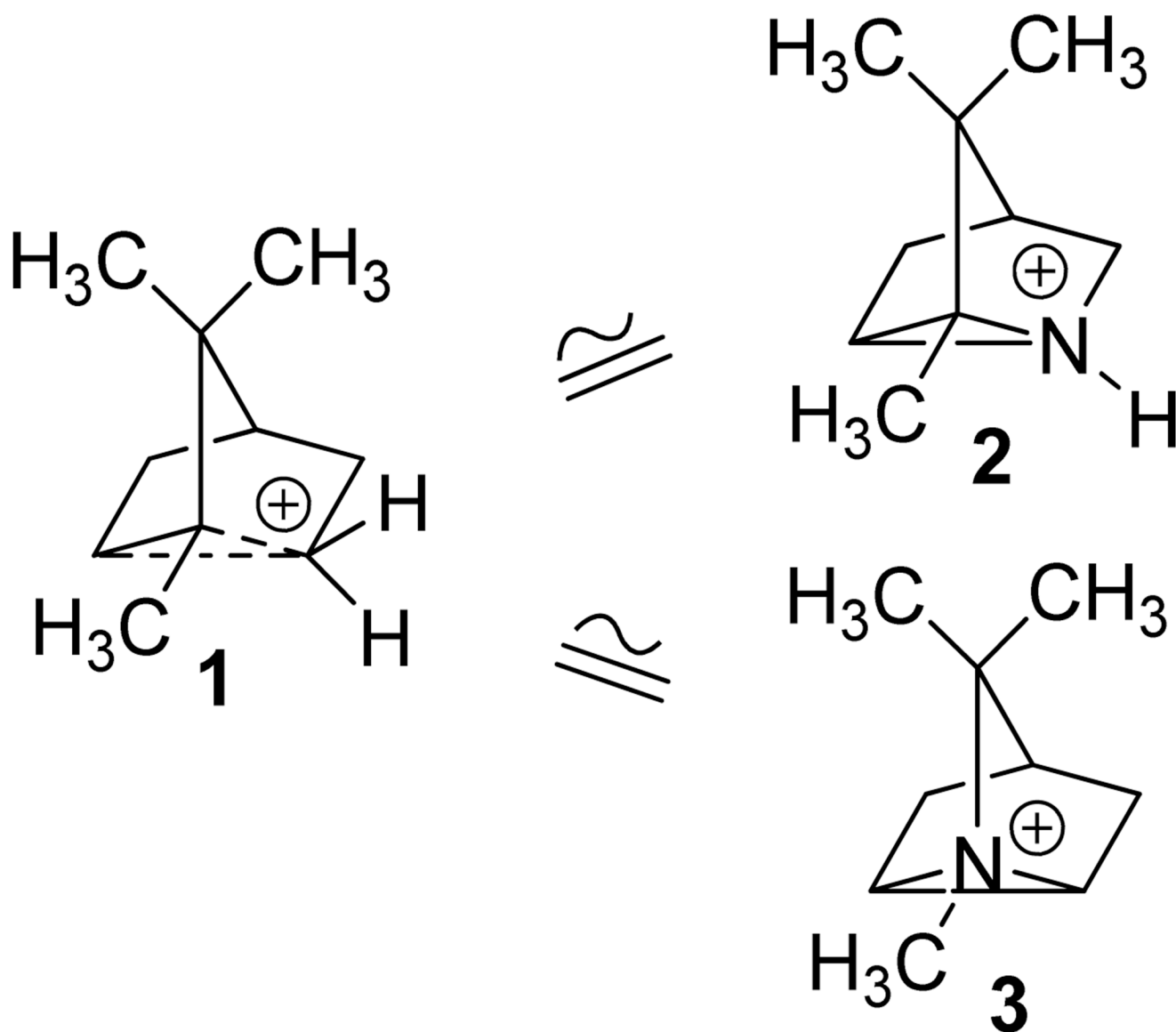
17. Yudin, AK., editor. Aziridines and Epoxides in Organic Synthesis. Weinheim: Wiley-VCH; 2006.
18. Moss, RA.; Platz, MS.; Jones, M., Jr, editors. Reactive Intermediate Chemistry. Hoboken, NJ: Wiley-Interscience; 2004. p. 501-650. Chaps 11–13
19. Moody, CJ.; Whitham, GH. Reactive Intermediates. Oxford UK: Oxford University Press; 1992.
20. (a) Padwa A, Flick AC, Leverett CA, Stengel T. J. Org. Chem 2004;69:6377–6386. [PubMed: 15357598] (b) Lebel H, Lectard S, Parmentier M. Org. Lett 2007;9:4797–4800. [PubMed: 17944479] (c) Liu R, Herron SR, Fleming SA. J. Org. Chem 2007;72:5587–5591. [PubMed: 17595136]
21. (a) Richardson RD, Desaize M, Wirth T. Chem. Eur. J 2007;13:6745–6754. (b) Li J, Chan PWH, Che C-M. Org. Lett 2005;7:5801–5804. [PubMed: 16354070]
22. Atkinson RS. Tetrahedron 1999;55:1519–1559.
23. Carman RM, Derbyshire RPC. Aust. J. Chem 2003;56:319–322.
24. Lin QJ, Zhang YM, Zhang CR, Song WZ, Qiu Q. Chin. Chem. Lett 1991;2:517–520.
25. (a) Kirkland TA, Grubbs RH. J. Org. Chem 1997;62:7310–7318. [PubMed: 11671845] (b) Berlin JM, Campbell K, Ritter T, Funk TW, Chlenov A, Grubbs RH. Org. Lett 2007;9:1339–1342. [PubMed: 17343392]
26. Ergün Y, Patir S, Okay G. J. Heterocycl. Chem 2002;39:315–317.
27. Miriyala B, Bhattacharyya S, Williamson JS. Tetrahedron 2004;60:1463–1471.
28. (a) Winstein S, Allred EL, Sonnenberg J. J. Am. Chem. Soc 1959;81:5833. (b) Allred EL, Sonnenberg J, Winstein S. J. Org. Chem 1960;25:26–29.
29. (a) Shioiri T, Ninomiya K, Yamada S-i. J. Am. Chem. Soc 1972;94:6203–6205. [PubMed: 5054412] (b) Kedrowski BL. J. Org. Chem 2003;68:5403–5406. [PubMed: 12816509] (c) Shioiri T, Yamada S-i. Org. Synth 1990;Vol. 7:206–207. Coll
30. (a) Bredt J, Houben J, Levy P. Chem. Ber 1902;35:1286–1292. (b) Sauers RR. J. Am. Chem. Soc 1959;81:925–927. (c) Crist BV, Rodgers SL, Lightner DA. J. Am. Chem. Soc 1982;104:6040–6045.
31. Hutchinson JH, Money T, Piper SE. Can. J. Chem 1986;64:854–860.
32. (a) Olah GA, Szilagyi PJ. J. Am. Chem. Soc 1969;91:2949–2955. (b) Breitmaier, E.; Voelter, W. Carbon-13 NMR Spectroscopy. Weinheim: VCH; 1987. p. 236-237. (c) Sarneski JE, Surprenant HL, Molen FK, Reilly CN. Anal. Chem 1975;47:2116–2124.
33. (a) Butler RN. Chem. Rev 1984;84:249–276. (b) Mihailović, MLj; Čecović, Ž. "Lead (IV) Acetate, ". In: Paquette, LA., editor. Encyclopedia of Reagents for Organic Synthesis. Vol. Vol. 5. Chichester: Chief; Wiley; 1995. p. 2949-2954.
34. (a) Mihailović, MLj; Stojiljković, A.; Adrejević, V. Tetrahedron Lett 1965;6:461–464. (b) Stojiljković A, Adrejević V, Mihailović MLj. Tetrahedron 1967;23:721–732.
35. (a) Osawa E, Szalontai G, Tsurumoto A. J. Chem. Soc., Perkin Trans 1983;2:1209–1216. (b) Banks HD. J. Org. Chem 2006;71:8089–8097. [PubMed: 17025297]
36. (a) Phanstiel O, Wang QX, Powell DH, Ospina MP, Leeson BA. J. Org. Chem 1999;64:803–806. [PubMed: 11674150] (b) Eriksson C, Sjödin K, Schlyter F, Högberg H-E. Tetrahedron: Asymmetry 2006;17:1074–1080. (c) Cheng Y-S, Lupo AT Jr, Fowler FW. J. Am. Chem. Soc 1983;105:7696–7703.
37. Lappert, MF.; Power, PP.; Sanger, AR.; Srivastava, RC. Metal and Metalloid Amides. Chichester, UK: Ellis Horwood; 1980. p. 271-272. 352–355
38. Sisti AJ, Milstein SR. J. Org. Chem 1974;39:3932–3936.
39. Dean, JA. Lange's Handbook of Chemistry, 15th Ed. New York: McGraw-Hill; 1999. p. 8-129. Table 8.27
40. Bartlett PD. Rec. Chem. Progr 1950;11:47–51.
41. (a) Swern, D. Organic Peroxides. Vol. Vol. II. New York: Wiley; 1971. Chap. V (b) Dryuk VG. Tetrahedron 1976;32:2855–2866. (c) Finn, MG.; Sharpless, KB. Asymmetric Synthesis. Morrison, JD., editor. Vol. Vol. 5. Orlando, FL: Academic Press; 1985. Chap. 8 (d) Bach RD, Canepa C, Winter JE, Blanchette PE. J. Org. Chem 1997;62:5191–5197. (e) Bach RD, Glukhovtsev MN, Gonzalez C, Marquez M, Estevez CM, Baboul AG, Schlegel HB. J. Phys. Chem. A 1997;101:6092–6100. (f) And relevant references cited in (a) – (e).
42. Bartlett PD, Sargent GD. J. Am. Chem. Soc 1965;87:1297–1307.
43. Swern D. J. Am. Chem. Soc 1947;69:1692–1698.



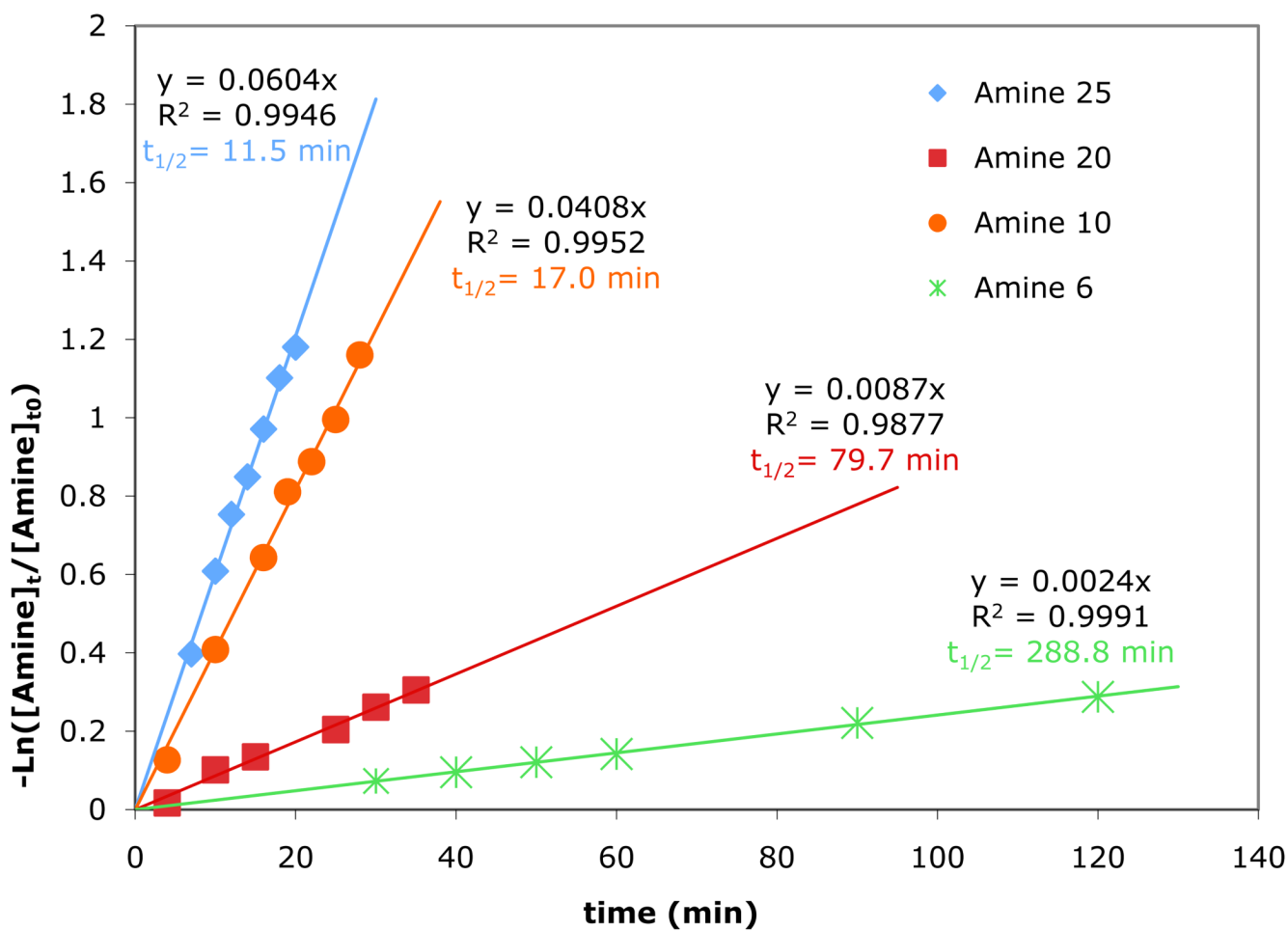
44. (a) Stamm H. J. Prakt. Chem., Chem. Ztg 1999;341:319–331. (b) Hu XE. Tetrahedron 2004;60:2701–2743. (c) Watson IDG, Yudin AK. J. Org. Chem 2003;68:5160–5167. [PubMed: 12816471] (d) Goujon J-Y, Gueyrard D, Compain P, Martin OR, Ikeda K, Kato A, Asano N. Bioorg. Med. Chem 2005;13:2313–2324. [PubMed: 15727880]
45. The intramolecular aziridination (77%) of a *t*-alkyl primary amine with 1 equiv of NBS in acetone has been reported (see Introduction).<sup>23</sup> However the scope of this potential alternative method is unclear
46. Faraldos JA, Coates RM. unpublished results
47. The abbreviation "app" (apparent) in NMR data means that the interpretation was based on a first-order analysis of the multiplet in question, and the data give the appearance, positions, and spacings of the signals. If the multiplet is actually part of a second-order spin system, the "apparent" chemical shift(s), multiplicity, and J values reported may be different than the true values
48. Angle SR, Arnaiz DO. Tetrahedron Lett 1989;30:515–518.



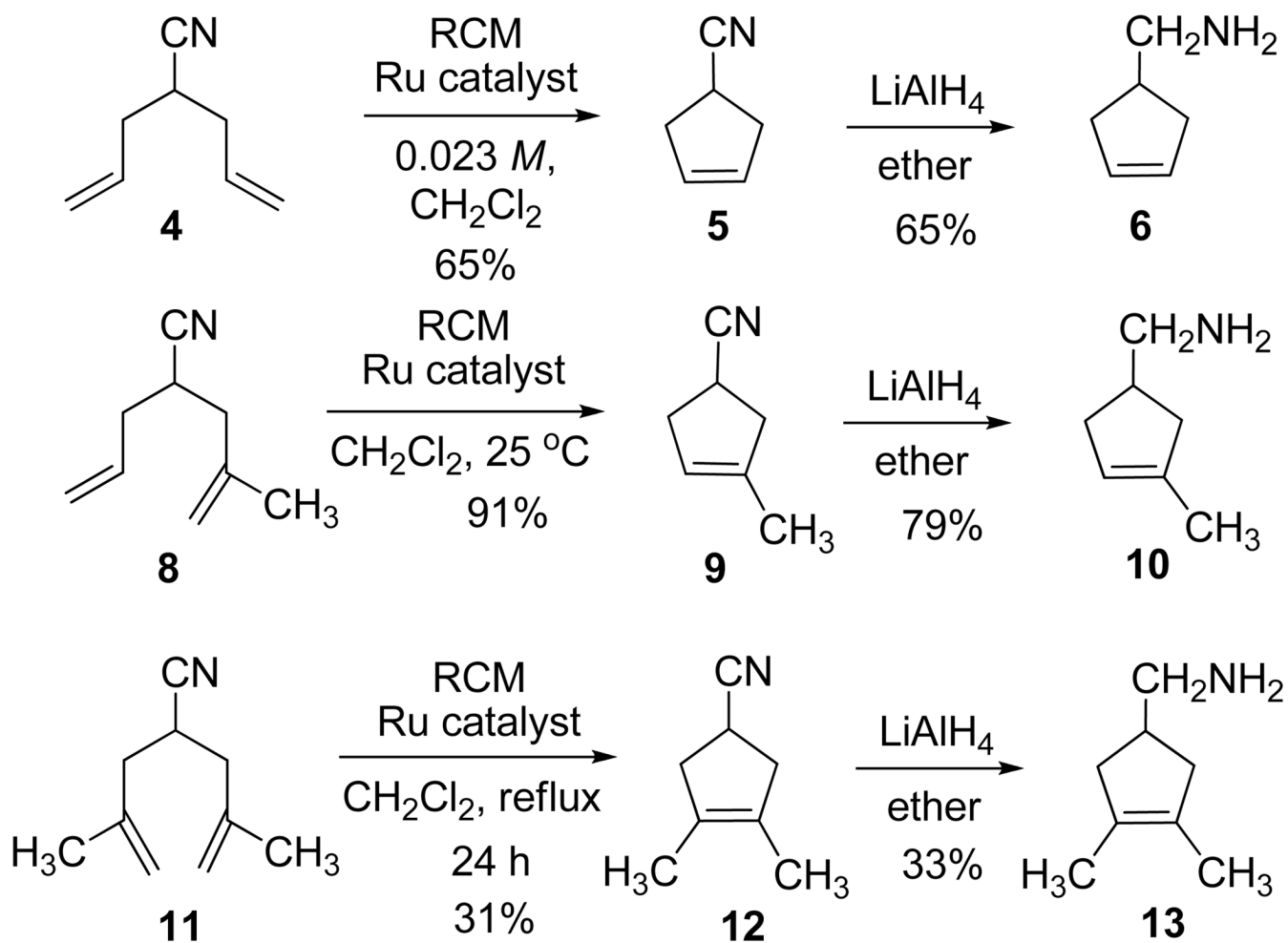
**Figure 1.**  
Illustration of the structural similarity of a generic protonated aziridine to protonated cyclopropanes and protonated epoxides.



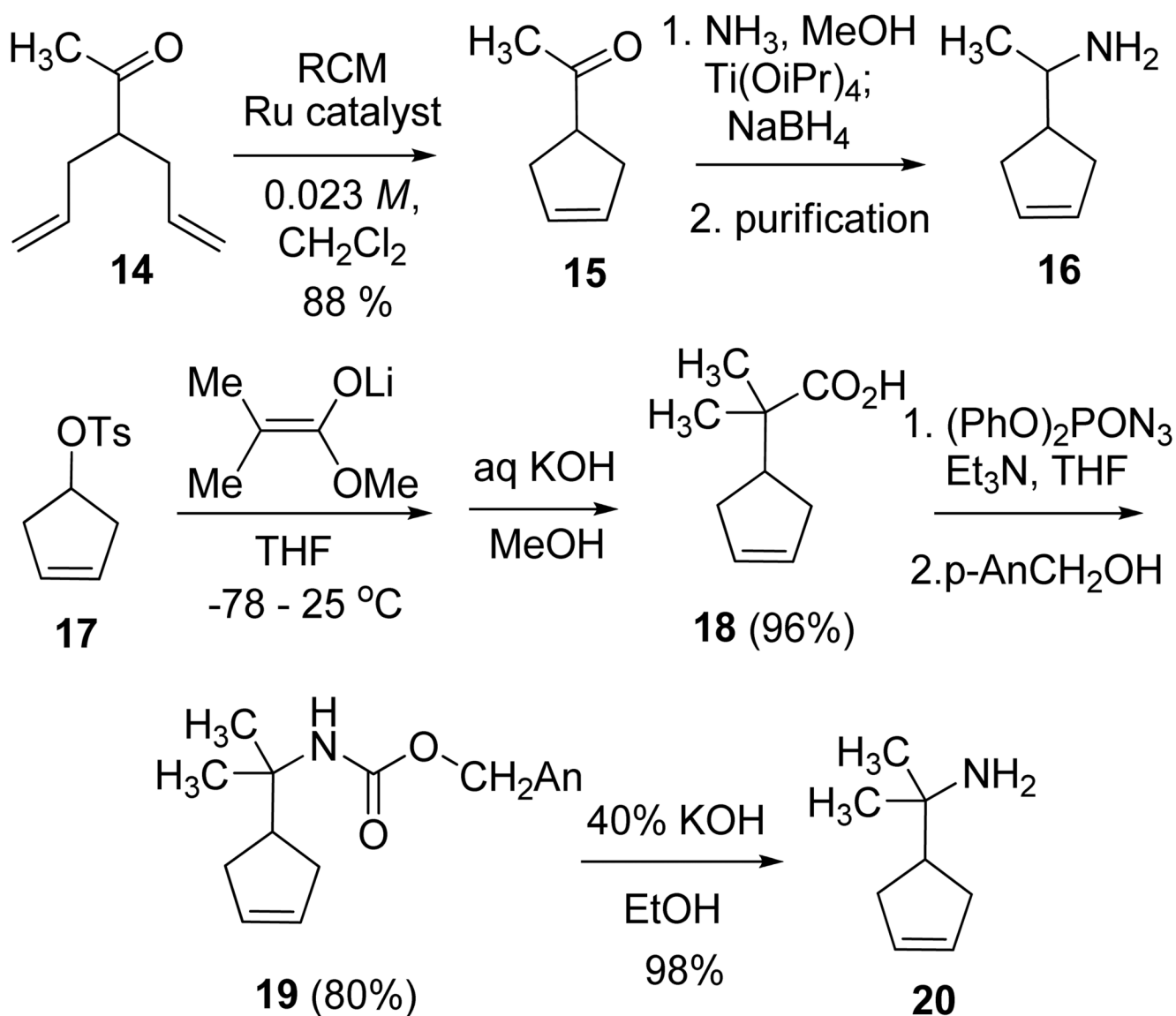
**Figure 2.**  
Non-classical bridged bornyl carbonium (**1**) and its azatricyclo[2.2.1.0<sup>2,6</sup>]heptane (azatricyclene) analogues **2** and **3**.



**Figure 3.** Pseudo first-order kinetic plots ( $t_{1/2} - \ln(2)/k$ ) for  $\text{Pb}(\text{OAc})_4$  oxidations of cyclopentenyl amines 6, 10, 20, and 24 by  $^1\text{H}$  NMR integrations of peaks for the corresponding aziridine products 26, 27, 30, and 32.

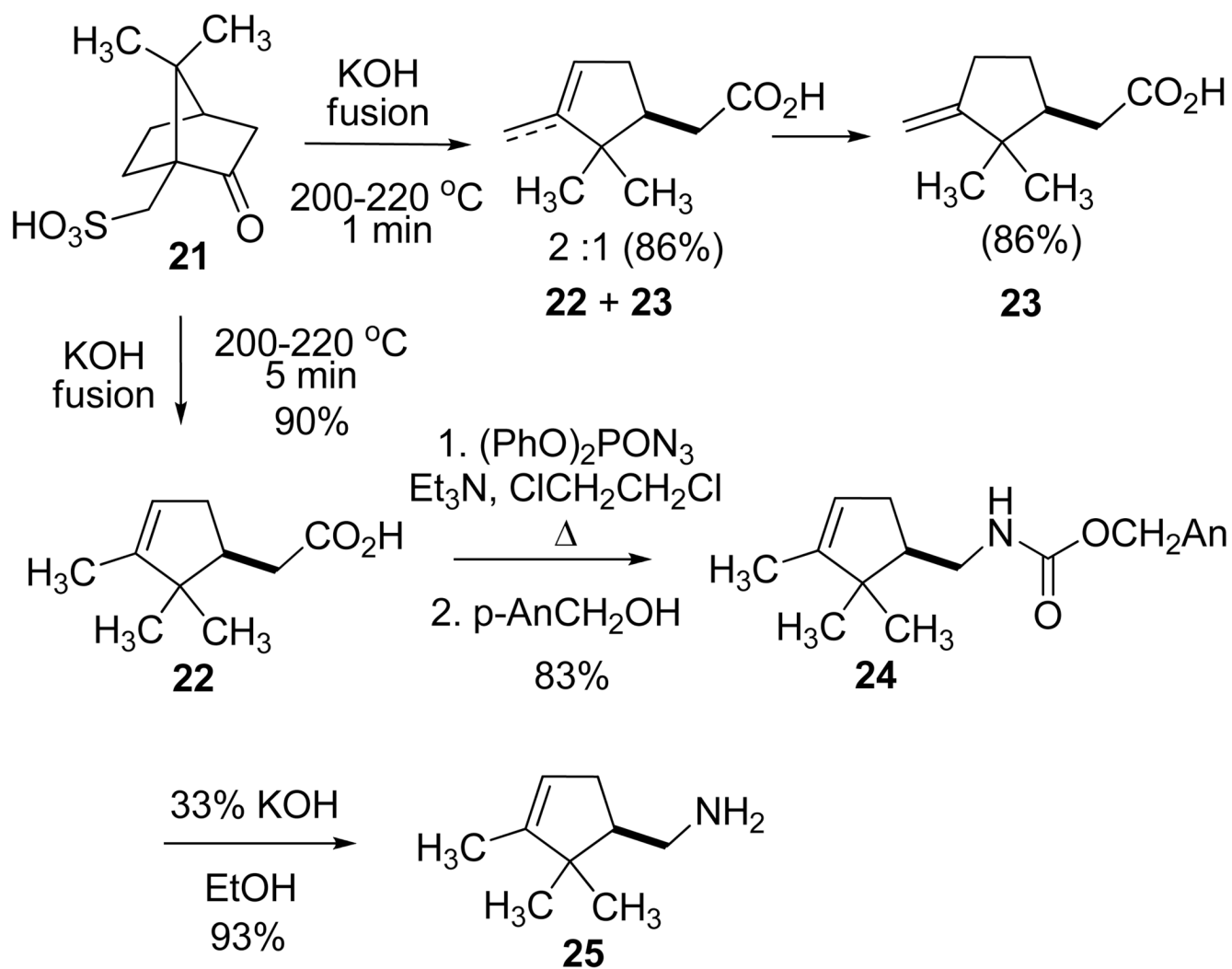


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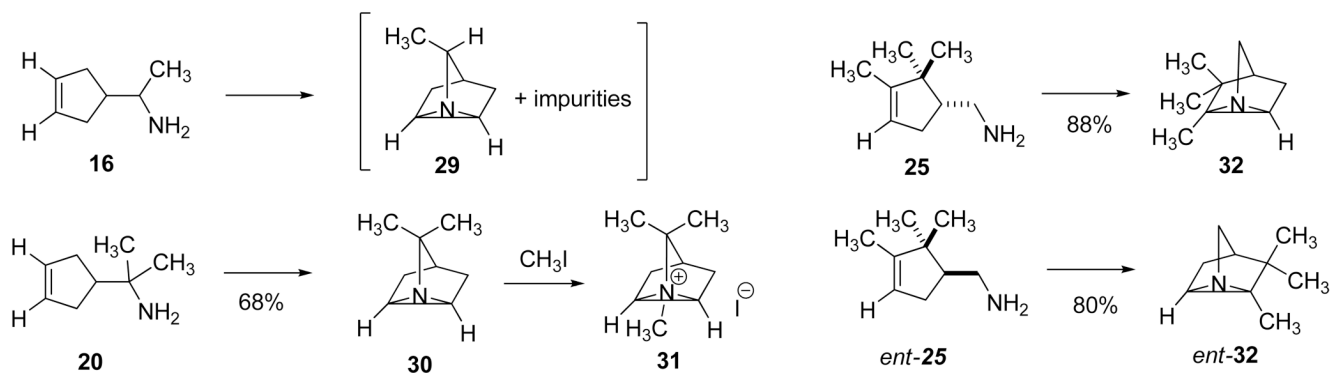
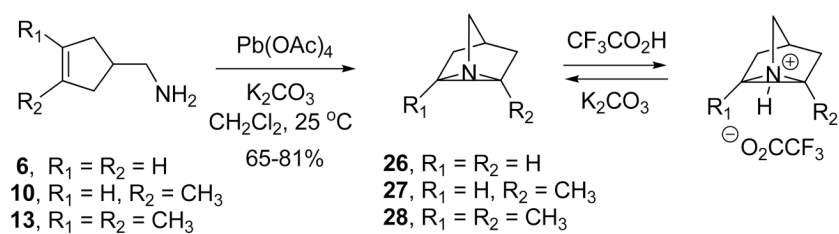


scheme 2.

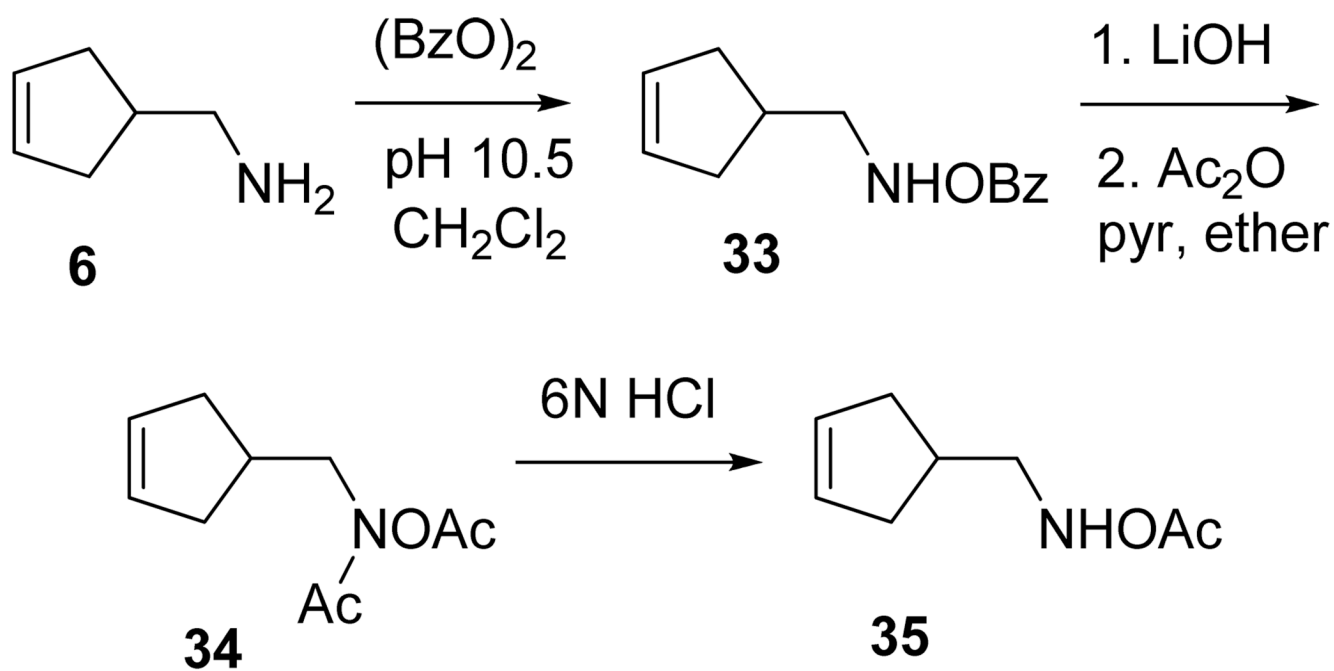




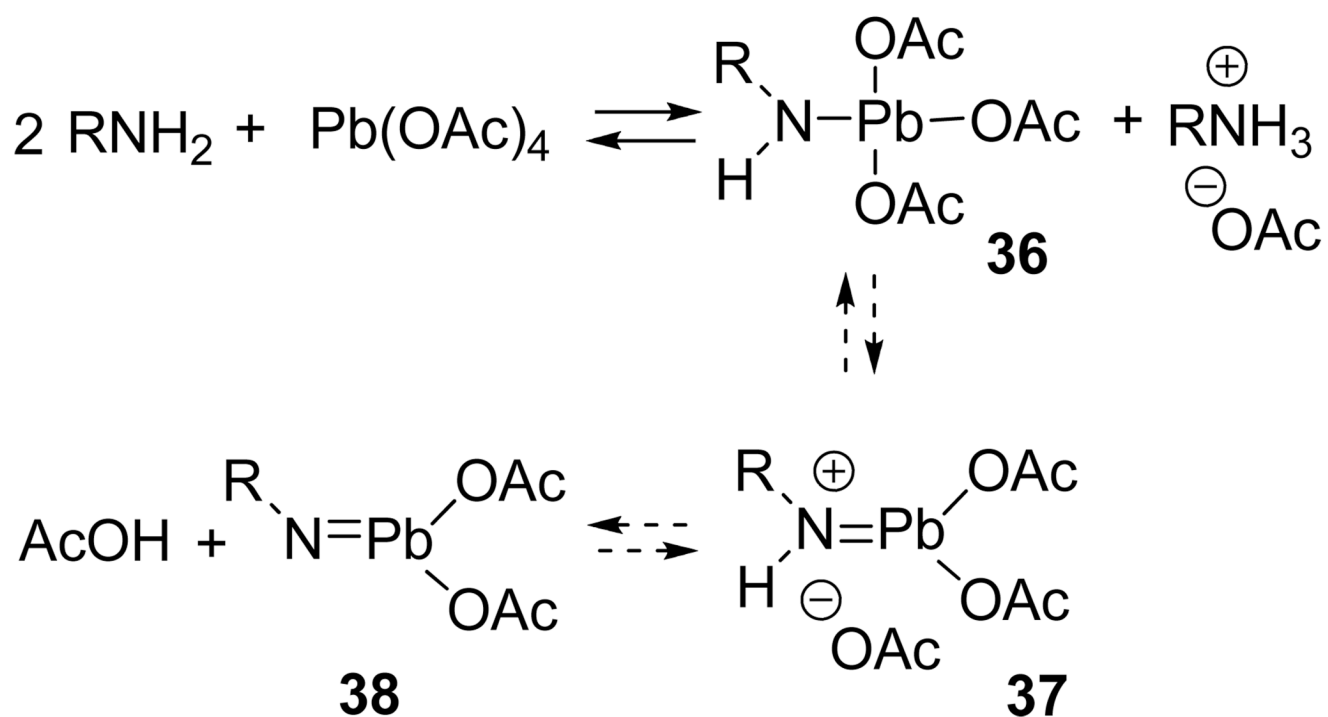
scheme 3.



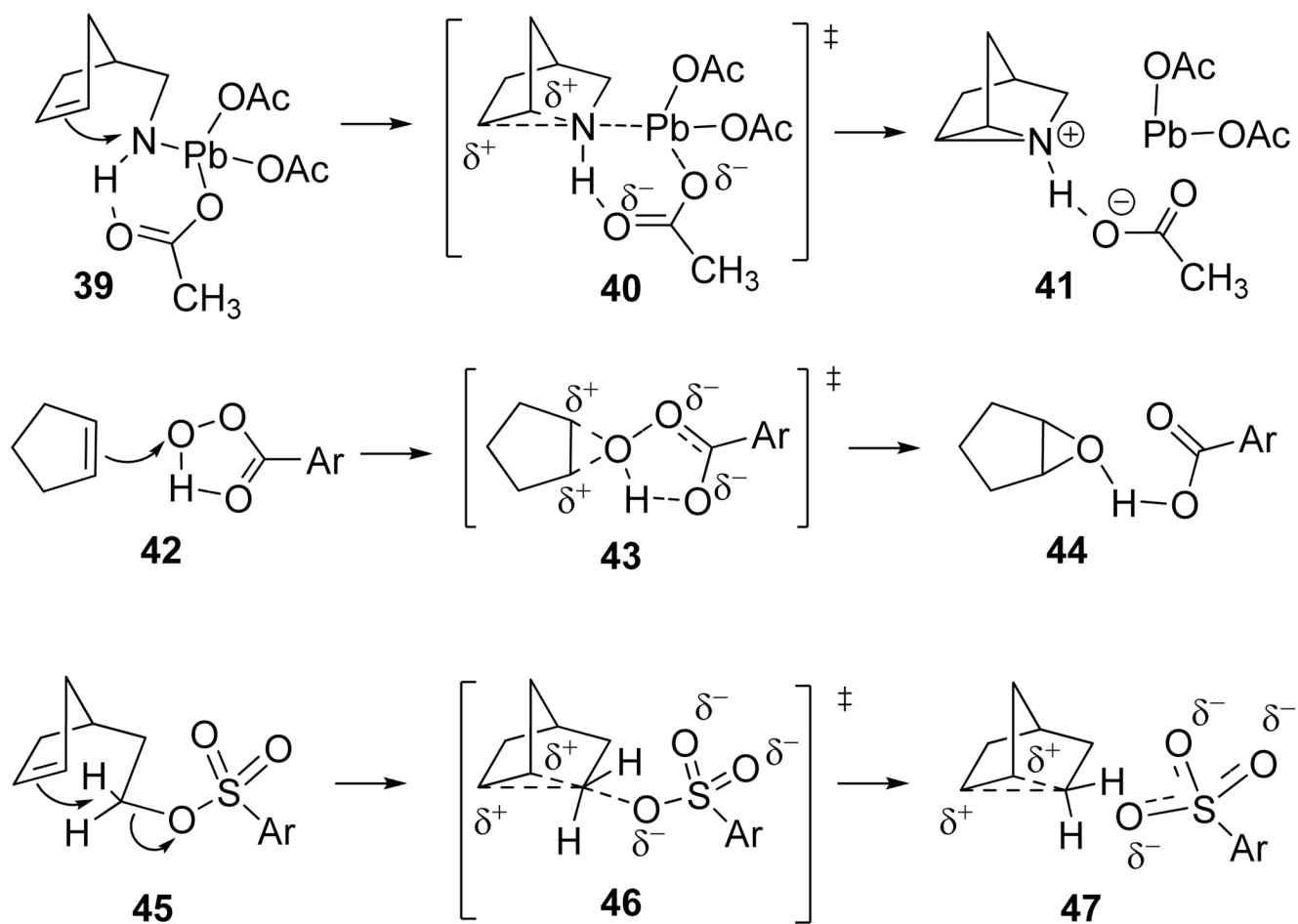
scheme 4.



scheme 5.



scheme 6.



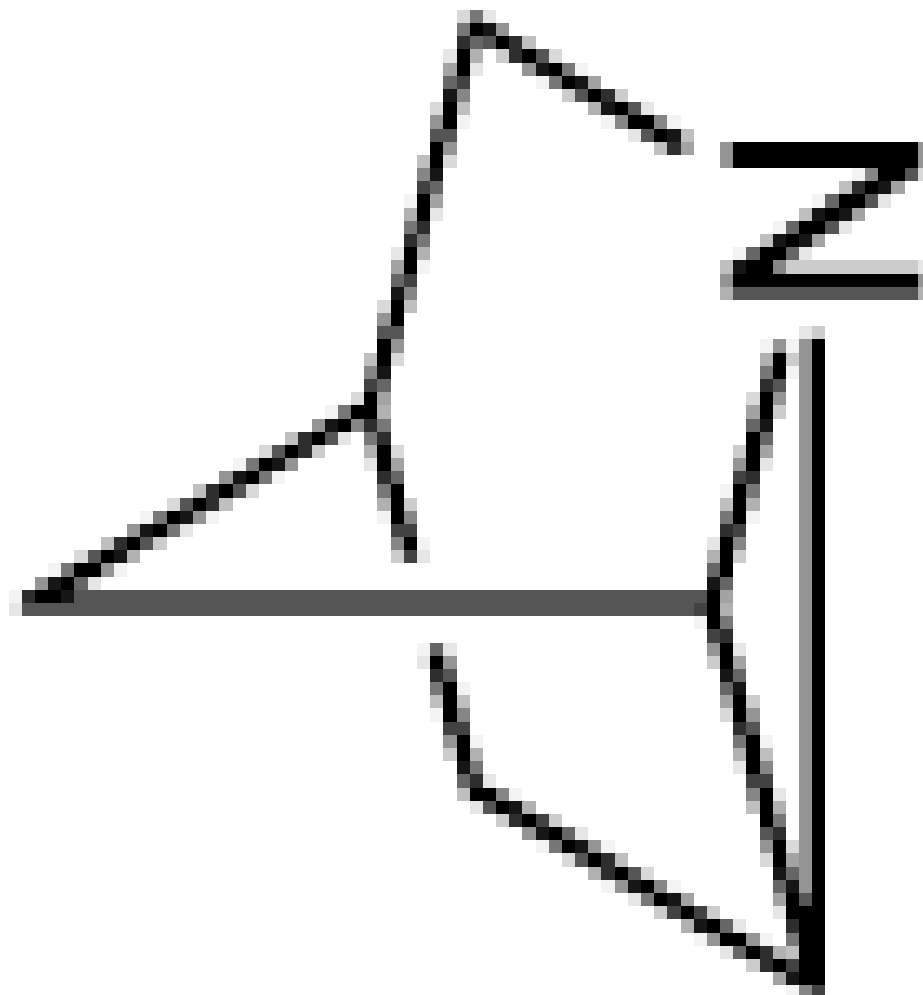
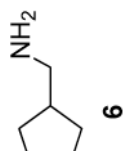
scheme 7.

## Table 1



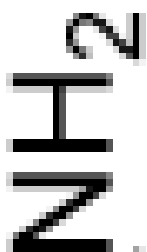
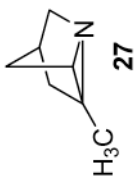
Effects of Intramolecular Aziridination of 3-Cyclopentenylmethylamine (6) and its Methyl Derivatives (see Runs) or  $\text{CDCl}_3$  (kinetic Runs) at 25 °C.

Amine No.	Aziridine No.	Yield <sup>d</sup> (%)	$t_{1/2}$ (min, ave)	$k_{\text{rel}}$ (1.0)
6		65	280	(1.0)

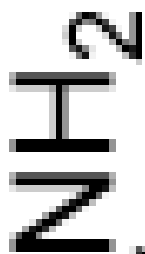
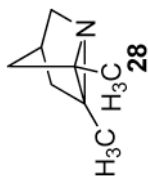


65


Amine No.	Aziridine No.	Yield <sup>d</sup> (%)(min, ave)	t <sub>1/2</sub>	k <sub>rel</sub>
10	27	78	16, 19 (17.5)	17.5



Amine No.	Aziridine No.	Yield <sup>d</sup> (%)	t <sub>1/2</sub> (min, ave)	k <sub>rel</sub>
		81	< 1 <sup>b</sup>	> 280



13

Amine No.	Aziridine No.	Yield <sup>d</sup> (%)(min, ave)	t <sub>1/2</sub>	k <sub>rel</sub>
		ND <sup>c</sup>	100 <sup>e</sup>	2.8

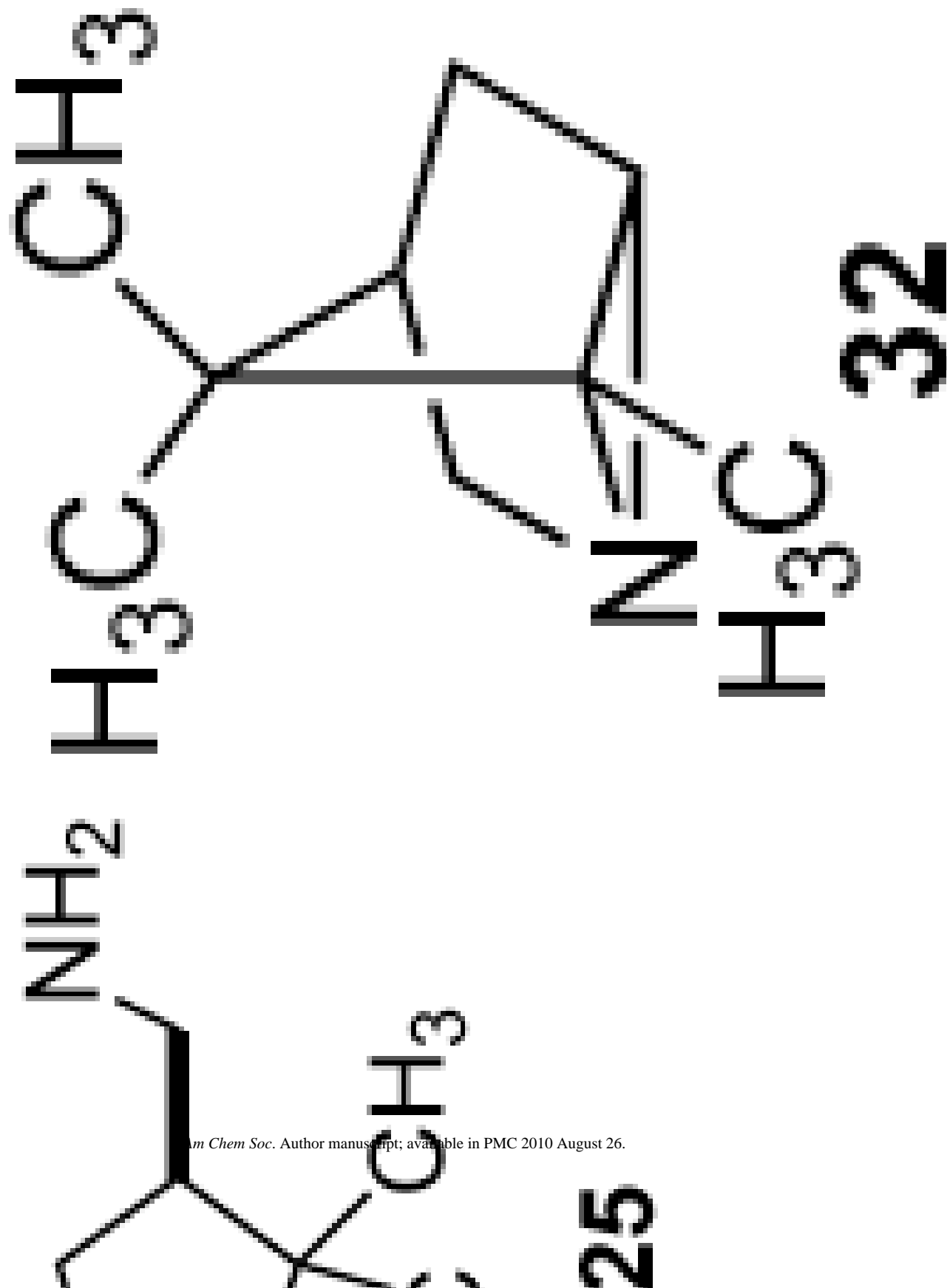
29

Amine No.	Aziridine No.	Yield <sup>d</sup> (%)(min, ave)	t <sub>1/2</sub>	k <sub>rel</sub>
		68 <sup>d</sup>	125	2.2



30

Amine No.	Aziridine No.	Yield <sup>d</sup> (%)	t <sub>1/2</sub> (min, ave)	k <sub>rel</sub>
25	32	88	8.11 (9.5)	29






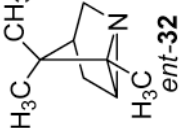
Amine No.		Aziridine No.	Yield <sup>d</sup> (%)(min, ave)	<i>t</i> <sub>1/2</sub>	<i>k</i> <sub>rel</sub>
t-25		 <i>ent</i> -32	80	ND <sup>c</sup>	ND <sup>c</sup>

Table 2

Selected Proton and Carbon-13 NMR Chemical Shifts for 1-Azabicyclo[2.2.2.0<sup>2,6</sup>]heptanes and Their Trifluoroacetate (TFA) Salts in CDCl<sub>3</sub>.

Aziridine No.	CH <sub>3</sub> substituents	Aziridine N-C-H	Aziridine N-C-CH <sub>3</sub>	C-7 N-CH <sub>2</sub> (CH)	C-8 N-C-CH <sub>3</sub>
<b>26</b>	none	$\delta_H$ 2.22 $\delta_C$ 31.8	—	2.18 55.8	—
<b>26 • TFA</b>	none	$\delta_H$ 3.70 $\delta_C$ 38.1	—	2.92 51.0	—
<b>27</b>	2-CH <sub>3</sub>	$\delta_H$ 2.10 $\delta_C$ 38.4, 39.1	1.35 16.0	2.25, 2.39 56.7	—
<b>27 • TFA</b>	2-CH <sub>3</sub>	$\delta_H$ 3.63 $\delta_C$ 43.9, 49.8	1.71 11.8	2.92, 3.05 51.6	—
<b>28</b>	2,6-(CH <sub>3</sub> ) <sub>2</sub>	$\delta_H$ — $\delta_C$ 45.1	1.38 12.5	2.53 56.3	—
<b>28 • TFA</b>	2,6-(CH <sub>3</sub> ) <sub>2</sub>	$\delta_H$ — $\delta_C$ 53.2	1.65 9.6	3.01 52.2	—
<b>30<sup>a</sup></b>	7,7-(CH <sub>3</sub> ) <sub>2</sub>	$\delta_H$ 2.19 $\delta_C$ 36.8	—	45.4	1.02 22.9
<b>30 • TFA<sup>a</sup></b>	7,7-(CH <sub>3</sub> ) <sub>2</sub>	$\delta_H$ 3.72 $\delta_C$ 39.1	—	—	1.37 20.6
<b>32</b>	2,3,3-(CH <sub>3</sub> ) <sub>3</sub>	$\delta_H$ 2.03 $\delta_C$ 41.2, 45.2	1.16 19.7	45.2 2.11, 2.80	—
<b>32 • TFA</b>	2,3,3-(CH <sub>3</sub> ) <sub>3</sub>	$\delta_H$ 3.66 $\delta_C$ 45.5, 49.6	1.55 7.0	52.2 2.85, 3.43 55.3	—

<sup>a</sup>Peaks from impurities appear in the <sup>13</sup>C NMR spectrum.