

# PROCEEDINGS OF THE CHEMICAL SOCIETY

OCTOBER 1964

---

## CHRISTMAS COMPETITION, 1964

### The Editor's Lament

READERS will be aware of the Publications Survey being carried out (*Proceedings*, 1963, 73) to determine the pattern of publications required to meet the present and future needs of Chemists. It will also have been noticed (*Proceedings*, 1964, 273) that, apart from this, changes are already being brought about in some of the Society's monthly periodicals.

It seems likely that readers may like to express their own views on the future of chemical publications, and are invited to submit them, as a contribution to the Christmas Competition, in the style of the rhyme:

“Ten little nigger boys went out to dine,  
One choked his little self and then there were nine”

Contributions may begin at any point and rise or descend the numerical scale (depending on the contributor's view of the future of publications). A prize (book token for two guineas) is offered for the best set of not less than three verses.

Entries must reach the Editor (The Chemical Society, 20—21 Cornwall Terrace, Regent's Park, London, N.W.1) not later than December 31st, 1964, and may be accompanied by a pseudonym for publication. It is hoped to issue a report in an early issue of *Chemistry in Britain*.

The Editor's decision will be final.

## CENTENARY LECTURE\*

## Applications of Optical Rotatory Dispersion and Circular Dichroism in Stereochemistry

By CARL DJERASSI

(STANFORD UNIVERSITY, STANFORD, CALIFORNIA, U.S.A.)

THE closely related phenomena<sup>1,2</sup> of optical rotatory dispersion (ORD) and circular dichroism (CD) are now sufficiently well known, so that an introductory discussion is unnecessary. The first observations<sup>1</sup> date to the early part of the nineteenth century, yet the real use and familiarity of these methods by the organic chemist is only about ten years old. This is perhaps most dramatically illustrated in Fig. 1 with the very rapid increase since 1955 in the number of publications concerned with applications of optical rotatory dispersion in organic chemistry. This rise coincided with the development in the early fifties of a commercially available spectropolarimeter<sup>3</sup> and the first publications from our laboratory (1955)<sup>4</sup> on organic chemical applications of ORD and from Harvard University (1956)<sup>5</sup> on ORD studies in the polypeptide and protein fields. In fact, the number of publications in the field have risen so rapidly that the figures for the last three years in Fig. 1 should only

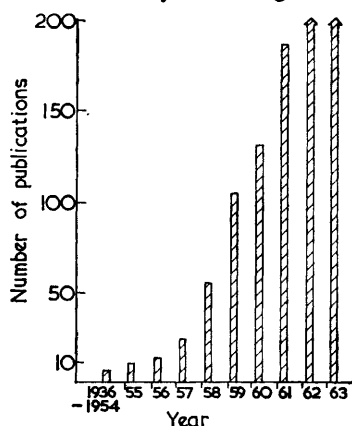


FIG. 1. Number of publications dealing with organic chemical application of optical rotatory dispersion (1936-1963).

be considered as approximate, as they are based only on my own perusal of the literature. Five years ago,<sup>4</sup> it was still feasible for me to present a complete coverage of the place that optical rotatory dispersion was occupying in organic chemistry. In the interim, over 700 relevant articles have appeared (see Fig. 1) and it is patently impossible to present even a cursory survey of the progress that has been made. On the other hand, a sufficient amount of time has elapsed so that the real role of optical rotatory dispersion and of circular dichroism in organic chemistry has now become clear.

The principal applications<sup>4</sup> are in the fields of structure determination (*e.g.*, location of carbonyl group in a steroid or triterpenoid), in analytical problems—notably those pertaining to mixtures of isomers,<sup>6</sup> in the detection of weak or hidden absorption bands and finally in stereochemistry. It is principally through its contributions to stereochemistry that optical rotatory dispersion (and hence circular dichroism) has passed the iron test of any new physical tool—does it provide information not already available from other sources or methods?—and has found a secure place among the relatively few physical methods which the organic chemist employs in the solution of his research problems. Therefore, I shall restrict myself largely to a survey of some of the stereochemical applications of optical rotatory dispersion and to point out what parallel or supplementary role circular dichroism fulfils. In view of the volume of work that has been published in recent years (Fig. 1), main emphasis will be placed on studies conducted at Stanford University.

The interplay<sup>2</sup> among the optical rotatory dispersion, circular dichroism, and ultraviolet absorption properties of a typical (colourless) organic substance, as well as the nomenclature commonly employed in ORD<sup>7</sup> and CD<sup>8</sup> studies, is illustrated

\* Delivered before the Chemical Society at The University, Glasgow on May 26th, 1964, at the Imperial College of Science and Technology, London, S.W.7 on June 11th, and elsewhere.

<sup>1</sup> For a detailed history see Lowry, "Optical Rotatory Power," Longmans, Green, and Co. Ltd., London, 1935.

<sup>2</sup> For a recent brief discussion of the relationship between absorption, circular dichroism and optical rotatory dispersion see Foss, *J. Chem. Educ.*, 1963, **40**, 592.

<sup>3</sup> Rudolph, *J. Opt. Soc. Amer.*, 1955, **45**, 50.

<sup>4</sup> For leading references see Djerassi, "Optical Rotatory Dispersion: Applications to Organic Chemistry," McGraw-Hill Book Co., New York, 1960.

<sup>5</sup> For leading references see Blout, chapter 17 in ref. 4.

<sup>6</sup> For some recent examples see: Nakano, Hasegawa, and Djerassi, *Chem. Pharm. Bull. (Tokyo)*, 1963, **11**, 465; Lablache-Combiere, Levisalles, Pete, and Rudler, *Bull. Soc. chim. France*, 1963, 1689; Djerassi and von Mutzenbecher, *Proc. Chem. Soc.*, 1963, 377.

<sup>7</sup> Djerassi and Klyne, *Proc. Chem. Soc.*, 1957, 55.

<sup>8</sup> Djerassi and Bunnenberg, *Proc. Chem. Soc.*, 1963, 299.

in Fig. 2 through the positive Cotton effect exhibited by the weak 264 m $\mu$  transition of the episulphide chromophore in 3 $\beta$ -hydroxycholestan-5 $\alpha$ ,6 $\alpha$ -episulphide.<sup>9</sup> This example also demonstrates a second point, which is discussed in more detail below, namely that frequently the sign of rotation in the visible (e.g.,  $[\alpha]_D$ ) is not the same as that of the compound's first Cotton effect (Fig. 2: positive ultra-

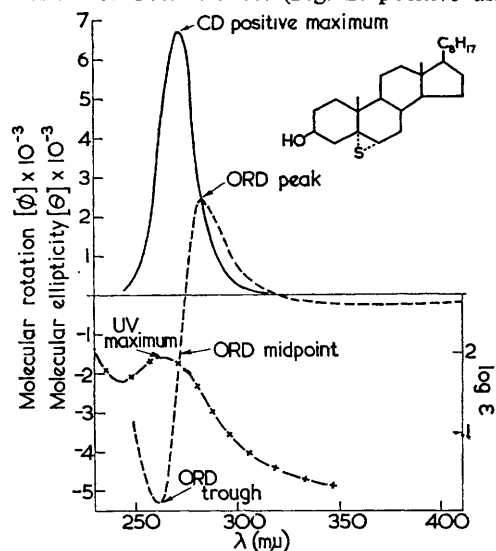


FIG. 2. Optical rotatory dispersion, circular dichroism and ultraviolet spectral curves of 3 $\beta$ -hydroxycholestan-5 $\alpha$ ,6 $\alpha$ -episulphide illustrating current nomenclature practice.

violet Cotton effect *versus* negative rotation in visible). The rotatory dispersion curves in this lecture are expressed in terms of molecular rotation ( $[\phi]$ ), while all circular dichroism curves are expressed in molecular ellipticity units ( $[\theta]$ ). As indicated earlier,<sup>8</sup> this system has the great advantage for the organic chemist that both properties of the molecule are expressed in terms of parameters which are of the same order of magnitude.

**Relative Advantages of Optical Rotatory Dispersion and Circular Dichroism.**—Prior to the renaissance in the nineteen-fifties, only a few rotatory dispersion

and circular dichroism measurements had been performed on organic substances in the ultraviolet region. The results, chiefly due to Lowry,<sup>1</sup> Kuhn,<sup>10</sup> and Mitchell,<sup>11</sup> have been summarised by Klyne.<sup>12</sup> While this classical work did not lead to any applications in organic chemistry—principally because insufficient examples were examined to permit any generalisation—it demonstrated the feasibility of performing such parallel ORD and CD measurements. The reason that the “new era”<sup>14</sup> concentrated initially only on optical rotatory dispersion was purely accidental and due to the availability<sup>3</sup> of a commercial spectropolarimeter. There is no doubt that if the first commercial instrument had instead been one for the measurement of circular dichroism, all of our early studies would have been performed with it. Fortunately, this was not the case, because it is unlikely that any of the subtleties of optical rotatory dispersion would then have been uncovered.

The success of these optical rotatory dispersion studies<sup>4,5</sup> stimulated the long dormant interest in improved instrumentation, both in terms of new spectropolarimeters<sup>13</sup> and of devices<sup>14</sup> for measuring circular dichroism. One of these circular dichroism instruments<sup>14c</sup> is in commercial production and a slightly modified version of it was employed in the work discussed below.

Now that instruments are available to measure either ORD or CD, the question naturally arises what, if any, advantage one tool has over the other. This question has been answered in some detail<sup>15</sup> and need only be covered briefly at this stage. For the vast majority of organic chemical applications, either method will provide the identical answer and information derived from ORD or CD may be employed interchangeably. An illustration is the recent circular dichroism measurements of some steroidal<sup>16</sup> and triterpenoid<sup>17</sup> ketones, work which essentially duplicates the earlier optical rotatory dispersion studies from our own laboratory on these substances.<sup>18,19</sup> While not providing any fundamentally new information, this repetition of earlier ORD work in terms of CD is useful in that it offers experimental support for the prediction that the resulting conclusions must be identical. Thus the octant

<sup>9</sup> Djerassi, Wolf, Lightner, Bunnenberg, Takeda, Komeno, and Kuriyama, *Tetrahedron*, 1963, **19**, 1547.

<sup>10</sup> *Inter al.*, Kuhn and Braun, *Z. phys. Chem. (Leipzig)*, 1930, (B) **8**, 445.

<sup>11</sup> Mitchell and Schwarzwald, *J.*, 1939, 889 and earlier papers.

<sup>12</sup> Klyne in (Raphael, Taylor, and Wynberg, eds.) “Advances in Organic Chemistry,” Interscience Publ., Inc., New York, 1960, Vol. I, pp. 258–260.

<sup>13</sup> For review see Carroll and Blei, *Science*, 1963, **142**, 200.

<sup>14</sup> (a) Mitchell, “Unicam Spectrovision,” 1958, No. 6, 6; (b) Badoz, Billardon, and Mathieu, *Compt. rend.*, 1960, **251**, 1477; (c) Grosjean and Legrand, *ibid.*, 2150; (d) Deen, D.Sc. Thesis, Leiden, 1961; (e) Holzwarth, Gratzner, and Doty, *J. Amer. Chem. Soc.*, 1962, **84**, 3194; (f) Mason, *J.*, 1962, 3285.

<sup>15</sup> Djerassi, Wolf, and Bunnenberg, *J. Amer. Chem. Soc.*, 1962, **84**, 4552.

<sup>16</sup> Velluz and Legrand, *Angew. Chem.*, 1961, **73**, 603.

<sup>17</sup> Witz, Herrmann, Lehn, and Ourisson, *Bull. Soc. chim. France*, 1963, 1101.

<sup>18</sup> Steroids: Djerassi, *et al.*, *J. Amer. Chem. Soc.*, 1955, **77**, 4354, 4359, 4364; 1956, **78**, 440, 3163, 3761, 6362, 6377.

<sup>19</sup> Triterpenoids: Djerassi, *et al.*, *J. Amer. Chem. Soc.*, 1958, **80**, 4001; 1959, **81**, 4587.

rule,<sup>20,21</sup> which was developed exclusively from a large body of optical rotatory dispersion measurements,<sup>4</sup> and which permits a prediction of the sign and often also of the approximate amplitude of the Cotton effect of a ketone, is *ipso facto* applicable to circular dichroism data.

Having pointed out the gross similarity of the two physical methods, it is now appropriate to draw attention to some of their specific advantages. The most distinguishing characteristic of ORD curves is the operation of background effects, *i.e.*, the rotational contribution of more distant absorption bands of the same chromophore or of other atoms in the same molecule, which may produce variations in shape which are not encountered in circular dichroism. The contrasting situation is illustrated in Figs. 3 and 4, which contain the ORD and CD

prostan-3-one (2) and cholestan-7-one (4) are much more meaningful, than their negative CD curves (Fig. 4), which show only some quantitative differences. In this particular group of steroid ketones, the background effect is presumably due to varying contributions associated with the  $\pi \rightarrow \pi^*$  absorption of the carbonyl group below 200 m $\mu$ . Such background effects have also been employed to good advantage among twisted biphenyls<sup>22</sup> and they are responsible for the observation (see Fig. 2) that at times the rotation in the visible spectral range is of opposite sign to that of the ultraviolet Cotton effect.

One may conclude, therefore, that for "fingerprinting" purposes, ORD is to be preferred over CD. In order to impart some distinguishing characteristic to the CD curve, measurements have been performed<sup>23</sup> near the boiling point of liquid nitrogen,

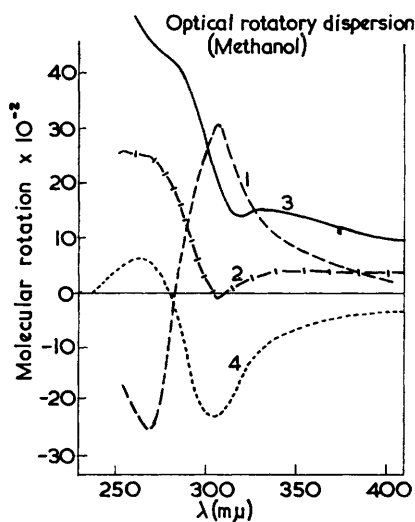


FIG. 3

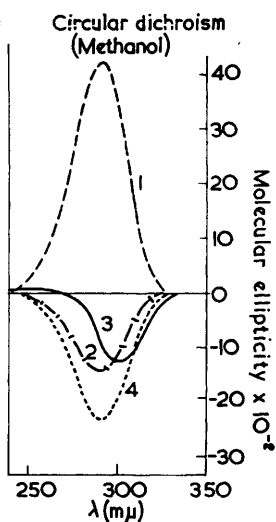


FIG. 4

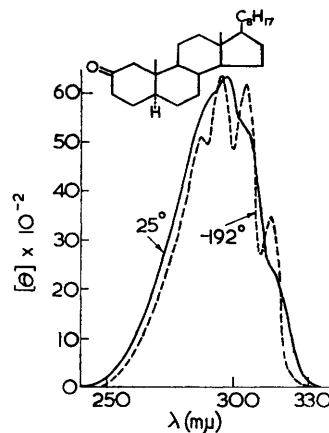


FIG. 5

FIG. 3. Optical rotatory dispersion curves (methanol) of cholestan-3-one (1), coprostan-3-one (2), cholestan-1-one (3), and cholestan-7-one (4).

FIG. 4. Circular dichroism curves (methanol) of cholestan-3-one (1), coprostan-3-one (2), cholestan-1-one (3), and cholestan-7-one (4).

FIG. 5. Circular dichroism curves (EPA) of cholestan-2-one at 25° and -192°.

curves of four isomeric steroid ketones. While the CD curves (Fig. 4) can only be positive or negative, the operation of background effects in the ORD curves (Fig. 3) lend sufficient "personality" to the curves that their characteristic shapes can be used without difficulty for characterisation purposes. Clearly, the differences in the ORD curves of co-

since such conditions have been shown<sup>24</sup> to produce increased vibrational structure in the CD curve. This approach shows considerable promise since the acquired fine structure (see for instance Fig. 5) differs in a diagnostically significant manner in several of the keto-steroids examined.

The existence of background effects in ORD and

<sup>20</sup> Moffitt, Woodward, Moscowitz, Klyne, and Djerassi, *J. Amer. Chem. Soc.*, 1961, **83**, 4013.

<sup>21</sup> Djerassi and Klyne, *J.*, 1962, 4929; 1963, 2390.

<sup>22</sup> Mislow, Bunnenberg, Records, Wellman, and Djerassi, *J. Amer. Chem. Soc.*, 1963, **85**, 1342.

<sup>23</sup> Wellman, Records, Bunnenberg, and Djerassi, *J. Amer. Chem. Soc.*, 1964, **86**, 492.

<sup>24</sup> Wellman, Bunnenberg, and Djerassi, *J. Amer. Chem. Soc.*, 1963, **85**, 1870.

their absence in CD is an advantage for structural work, but a disadvantage in calculations<sup>25</sup> of rotational strengths. While such calculations are generally not performed in standard organic chemical work, rotational strengths are of considerable interest for theoretical investigations and for such purposes, the CD curve is definitely to be preferred. In organic chemical studies, when it is desirable to express a Cotton effect in quantitative terms, and only the ORD curve is available, then instead of somewhat laborious calculations<sup>25</sup> of the rotational strengths, the molecular amplitude (difference in molecular rotation between peak and trough divided by 100) of the appropriate Cotton effect may be employed<sup>21</sup> to good effect.

Another area where CD may offer advantages over ORD may be in instances of overlapping absorption bands, of which a pertinent example is given in Fig. 6. Earlier ORD measurements<sup>26</sup> have

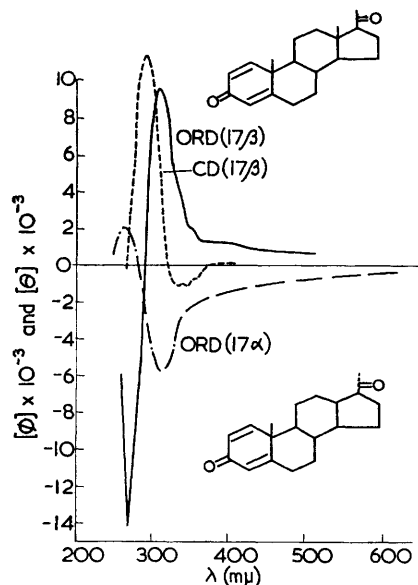


FIG. 6. Optical rotatory dispersion curves (dioxan) of 17 $\alpha$ - and 17 $\beta$ -pregna-1,4-diene-3,20-dione and circular dichroism curve (dioxan) of 17 $\beta$ -isomer.

shown that steroidal 1,4-dien-3-ones exhibit a very weak negative multiple Cotton effect in the 380–340 m $\mu$  region, which is also reflected in their CD curves.<sup>27</sup> Saturated steroidal 20-keto-steroids,<sup>28</sup> on the other hand, exhibit a powerful Cotton effect

(first extremum  $\sim 310$  m $\mu$ ), which is positive in the naturally occurring 17 $\beta$ -series, but of opposite sign in the 17 $\alpha$ -epimers. This characteristic ORD feature has been used<sup>29</sup> to good advantage in stereochemical assignments at C-17 of various 20-keto-steroids. Recently, a series of 17 $\alpha$ -20-keto-steroids became available<sup>30</sup> including 17 $\alpha$ -pregna-1,4-diene-3,20-dione and its 17 $\beta$ -epimer, the ORD curves of which are reproduced in Fig. 6. The oppositely signed Cotton effects in the 310 m $\mu$  region associated with the 20-keto-group dominate the picture and serve as secure means of stereochemical differentiation at C-17. The contribution in the 380–340 m $\mu$  range of the 1,4-dien-3-one chromophore, known to be weak,<sup>26</sup> is practically obliterated since it is hidden under the descending tail of the powerful 310 m $\mu$  Cotton effect. For comparison, the CD curve of the 17 $\beta$ -isomer is also included in Fig. 6, from which the presence of both chromophores is clearly recognisable. A similar situation has recently been encountered<sup>31</sup> in an ORD study of some C-13 epimeric androsta-1,4-diene-3,17-diones, where the Cotton effect of the cyclopentanone essentially swamped out the contribution of the 1,4-dien-3-one moiety.

It would be incorrect to assume that contributions from overlapping absorption bands are always more readily discerned by CD than by ORD. The opposite

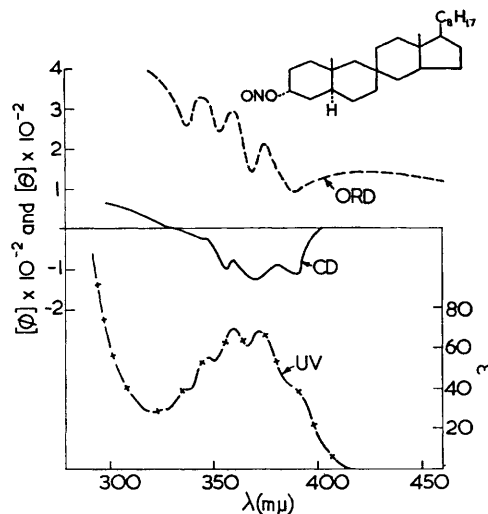


FIG. 7. Optical rotatory dispersion, circular dichroism and ultraviolet spectral curves of cholestan-3 $\alpha$ -ol nitrite in dioxan-pyridine (500:1).

<sup>25</sup> Moscovitz, chapter 12 in ref. 4.

<sup>26</sup> Djerassi, Riniker, and Riniker, *J. Amer. Chem. Soc.*, 1956, **78**, 6377.

<sup>27</sup> Tschesche, Mörner, and Snatzke, *Annalen*, 1963, **670**, 103.

<sup>28</sup> Djerassi, *Bull. Soc. chim. France*, 1957, 741; Djerassi, Halpern, Schindler, and Tamm, *Helv. Chim. Acta*, 1958, **41**, 250.

<sup>29</sup> Crabbé, *Tetrahedron*, 1963, **19**, 51.

<sup>30</sup> Rubin and Blosssey, *Steroids*, 1963, **1**, 453 and unpublished studies.

<sup>31</sup> Urech, Vischer, and Wettstein, *Helv. Chim. Acta*, 1963, **46**, 2788.



situation is encountered<sup>32</sup> in cholestan-3 $\alpha$ -ol nitrite (Fig. 7), where the multiple Cotton effect of the ORD curve is better defined than that of the corresponding CD curve.

Finally, a third problem of overlapping absorption bands should be noted, in which only CD will offer an unambiguous answer. An example is (+)-1,2-diselenane-3,6-dicarboxylic acid,<sup>15</sup> whose ultraviolet absorption, CD and ORD curves are reproduced in Fig. 8. The CD curve consists of three clearly recog-

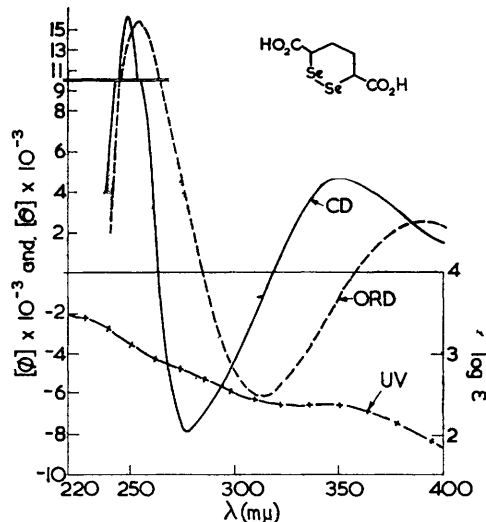


FIG. 8. Optical rotatory dispersion, circular dichroism and ultraviolet spectral curves of (+)-1,2-diselenane-3,6-dicarboxylic acid in dioxan.

nisable Cotton effects of alternating sign centred at 351, 277, and 249  $m\mu$ . The corresponding maxima in the ultraviolet spectrum are only very poorly defined, thus demonstrating the great advantage of CD for uncovering hidden absorption bands. If we now examine the corresponding ORD curve, we note that the first (positive Cotton effect) centred near 350  $m\mu$  is equally decisive as far as that particular transition of the diselenide is concerned. However, it is very difficult to determine whether the positive ORD extremum at 255  $m\mu$  is the peak of a positive Cotton effect corresponding to the 249  $m\mu$  transition, or of a negative Cotton effect centred at 277  $m\mu$ . If the latter is the case, then the troughs of the positive 351  $m\mu$  and negative 277  $m\mu$  Cotton effects must have collapsed into one negative extremum due to overlap. That this is actually the case is only clearly demonstrated by the CD curve. Similar difficulties have been encountered in *N*-phthalimido-derivatives of amines and amino-

acids, and resolved by appropriate CD measurements.<sup>33</sup>

In summary,<sup>15</sup> it can be stated that while for stereochemical purposes—notably for the establishment of absolute and relative configurations as discussed below—either ORD or CD alone can be used usually with equal effectiveness, parallel measurements of both parameters are to be preferred if more subtle information is desired. Some additional comments on this point will be made towards the end of this lecture.

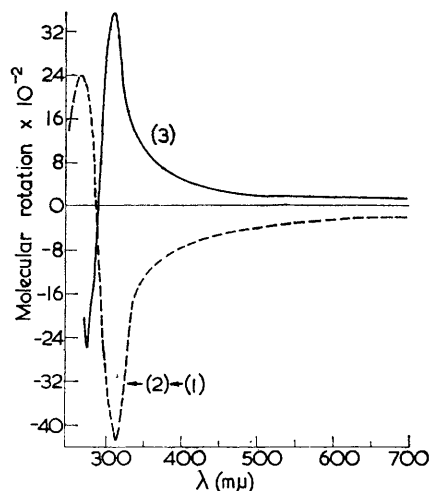


FIG. 9. Optical rotatory dispersion curves (methanol) of 4 $\alpha$ -ethylcholestan-3-one (3) and of degradation product (2) of cafestol (1).

**Some Recent Applications in Stereochemistry.**—(a) *Determination of Absolute Configuration.* The assignment of absolute configuration has always been an intriguing problem for the organic chemist. In recent years, notably in the natural products field, it has become essential, because of its direct pertinence to biosynthetic considerations. This is an area where optical rotatory dispersion has found immediate and widespread acceptance, because of the urgent need for new and rapid methods for the determination of absolute configuration.

The original work<sup>34</sup> concentrated on the carbonyl chromophore and was based on the experimentally documented fact that the sign of the Cotton effect of a given ketone was dominated by its immediate environment—in polycyclic systems the surrounding bicyclic framework. Provided no conformation changes are operative (*vide infra*), then all that is required is to compare the rotatory dispersion curve of a model ketone (*e.g.*, a steroid) of known absolute

<sup>32</sup> Djerassi, Wolf, and Bunnenberg, *J. Amer. Chem. Soc.*, 1963, **85**, 2835.

<sup>33</sup> Wolf, Bunnenberg, and Djerassi, *Chem. Ber.*, 1964, **97**, 533.

<sup>34</sup> Djerassi, Riniker, and Riniker, *J. Amer. Chem. Soc.*, 1956, **78**, 6362.

configuration and identical bicyclic environment as the unknown ketone, with the latter's dispersion curve.

The method has been used with telling success in a wide variety of instances<sup>35</sup> and a single example—the determination of the absolute configuration of cafestol<sup>34,36</sup> should suffice to illustrate its operation. The furan ring of cafestol (1, Fig. 9a) was trans-

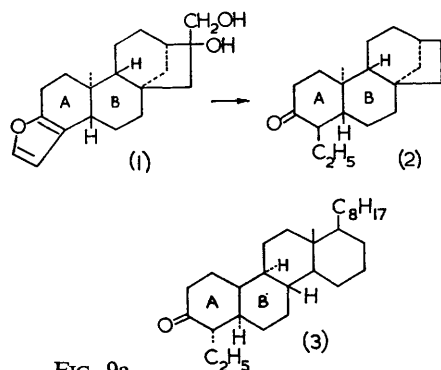


FIG. 9a

formed<sup>36</sup> into the ethyl ketone moiety of (2) and the latter's rotatory dispersion curve compared with that<sup>34</sup> of 4α-ethylcholestan-3-one (3). Since the two Cotton effect curves were of mirror image (Fig. 9) it follows that cafestol possesses the antipodal absolute stereochemistry of the A/B ring juncture, a result which was most unexpected although in the interval many other examples of such antipodal terpenoids have been uncovered by optical rotatory dispersion measurements. The simplicity of this approach should be contrasted with the difficulty which would have been encountered if this configurational problem would have had to be solved by classical chemical means. Since only the sign and approximate amplitude of the Cotton effect associated with the carbonyl chromophore is used as a guide, circular dichroism measurements can be employed with equal facility.

This approach is, of course, not limited to the carbonyl group. The only reason why this chromo-

phore was selected for much of our initial work<sup>4</sup> is that its  $n \rightarrow \pi^*$  absorption occurs in a convenient spectral range with low extinction; furthermore, it is one of the most common functional groups in organic chemistry, especially if one considers that alcohols are readily oxidised to the corresponding ketones.

In more recent years, we have developed the concept of "chromophoric derivatives" in which a "transparent"\* functional group is transformed into a derivative, which absorbs in a more accessible spectral range. Such work is of intrinsic interest, since it offers information on the optical and spectral behaviour of new chromophores, and it also serves to demonstrate whether their ORD or CD curves lend themselves to stereochemical conclusions. In Table 1 are listed the functional groups and chromophoric derivatives which have been investigated<sup>15,32,33,37-47</sup> in our laboratory, together with the

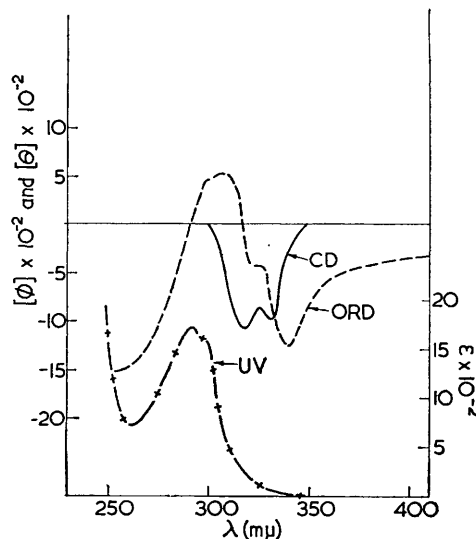


FIG. 10. Optical rotatory dispersion, circular dichroism, and ultraviolet spectral curves of N-phthaloyl-20β-amino-5α-pregnan-3β-ol in dioxan.

\* It should be recalled that "transparent" is a relative term and depends largely on the status of the instrumental art. Chromophores, such as the carboxyl group, which were considered "transparent" a few years ago, can now be shown (see Klyne, Scopes, and Jennings, XIX I.U.P.A.C. Congress, London, July, 1963, Abstracts, p. 110) to exhibit Cotton effect curves by using spectropolarimeters which can penetrate further into the ultraviolet.

<sup>35</sup> For leading references see chapter 10 in ref. 4 as well as Djerassi, *Pure and Appl. Chem.*, 1961, 2, 475.

<sup>36</sup> Djerassi, Cais, and Mitscher, *J. Amer. Chem. Soc.*, 1959, 81, 2386.

<sup>37</sup> Sjöberg, Fredga, and Djerassi, *J. Amer. Chem. Soc.*, 1959, 81, 5002.

<sup>38</sup> Djerassi, Lund, Bunnenberg, and Sheehan, *J. Org. Chem.*, 1961, 26, 4509.

<sup>39</sup> Djerassi, Lund, Bunnenberg, and Sjöberg, *J. Amer. Chem. Soc.*, 1961, 83, 2307.

<sup>40</sup> Djerassi, Undheim, Sheppard, Terry, and Sjöberg, *Acta Chem. Scand.*, 1961, 15, 903.

<sup>41</sup> Unpublished experiments with A. Kjaer (Copenhagen) and B. Sjöberg (Uppsala).

<sup>42</sup> Djerassi, Harrison, Zagneetko, and Nussbaum, *J. Org. Chem.*, 1962, 27, 1173.

<sup>43</sup> Sjöberg, Cram, Wolf, and Djerassi, *Acta Chem. Scand.*, 1962, 16, 1079.

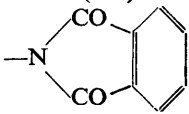
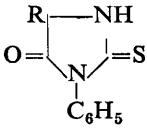
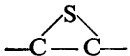
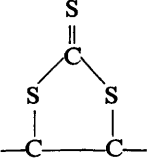
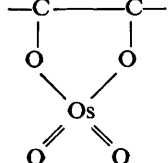
<sup>44</sup> See also Sjöberg, Karlen, and Dahlbom, *Acta Chem. Scand.*, 1962, 16, 1071.

<sup>45</sup> Djerassi, Undheim, and Weidler, *Acta Chem. Scand.*, 1962, 16, 1147.

<sup>46</sup> Unpublished experiments with J. Burakevich.

<sup>47</sup> Bunnenberg and Djerassi, *J. Amer. Chem. Soc.*, 1960, 82, 5953.

TABLE I.

Functional group	Chromophoric derivative	Absorpt. max. (m $\mu$ )	Ref.
$-\text{NH}_2^a$	$-\text{NHC}(=\text{S})\text{SR}$	330	15, 37
$-\text{NH}_2^a$		300	33, 38
$>\text{NH}$	NNO	370	39
$-\text{NHCOR}$	N(NO)COR	350—450	39
$\text{RCHCO}_2\text{H}$ $ \text{NH}_2$		310	15, 40
$\text{RCHCO}_2\text{H}$ $ \text{NH}_2$	$\text{RCHCO}_2\text{H}$ $ \text{NHC}(=\text{S})\text{OC}_2\text{H}_5$	280	15, 40
$\text{RCHCO}_2\text{H}$ $ \text{NH}_2$	$\text{RCHCO}_2\text{H}$ $ \text{NHC}(=\text{S})\text{C}_6\text{H}_5$	380, 290	41, 44
$\text{RCHCO}_2\text{H}$ $ \text{NH}_2$	$\text{RCHCO}_2\text{H}$ $ \text{NHC}(=\text{S})\text{CH}_2\text{C}_6\text{H}_5$	335, 270	41, 44
$-\text{OH}$	$-\text{OC}(=\text{S})\text{SR}$	350	15, 37, 42, 43
$-\text{OH}$	$-\text{ONO}$	325—390	32, 42
$-\text{CO}_2\text{H}$	$-\text{CONHC}(=\text{S})\text{NR}_2$	340	15, 45
$-\text{CO}_2\text{H}$	$-\text{C}(=\text{S})\text{NRR}'$	325—360	46
$-\text{C}=\text{C}-$		260	9
$-\text{C}=\text{C}-$		235, 305, 430	9
$-\text{C}=\text{C}-$		450, 550	47

<sup>a</sup> Also applicable to  $\alpha$ -amino-acids.



position of the optically active absorption band(s) of these derivatives. In most instances, the sign of the Cotton effect of the "chromophoric derivative" could be related to the absolute configuration of the adjacent asymmetric centre, in spite of the fact that free rotation is possible around the bond connecting the substituent to the asymmetric carbon atom. Further comment on this point will be made below in the section dealing with free rotational isomerism.

With the exception of the osmate complexes (last entry in Table 1), all the chromophores listed in Table 1 have been subjected to parallel ORD and CD measurements and as anticipated, the stereochemical conclusions were identical. Consequently, no particular advantage accrues to either method when employed for such stereochemical purposes. In a number of instances, the ORD and especially the CD measurements have uncovered hidden transitions, which were not detectable by ordinary ultraviolet spectroscopy. This subject is outside the scope of the present lecture, but one recent example may be cited in Fig. 10 in terms of the ultraviolet, ORD, and CD curves of *N*-phthaloyl-20 $\beta$ -amino-5 $\alpha$ -pregnan-3 $\beta$ -ol.<sup>53</sup> The ORD and especially the CD curves show two closely spaced negative Cotton effects at 332 and 318 m $\mu$ , which correspond to transitions that are completely hidden in the ultraviolet spectrum under the strong 293 m $\mu$  absorption band. Similar observations have been made in our laboratory in a number of instances while conducting ORD and CD studies on non-ketonic chromophores such as biaryls<sup>22,48-50</sup> and aporphines,<sup>51</sup> disulphides and diselenides,<sup>15,52</sup> trithiones,<sup>53,54</sup>  $\alpha$ -iodo-ketones,<sup>55</sup> aliphatic nitro-compounds,<sup>32</sup> azides,<sup>56</sup> thiocyanates,<sup>57</sup> ethylene thioketals,<sup>57</sup> and thiolacetates.<sup>57</sup> This uncovering of hidden or overlapping absorption bands

by means of ORD or CD is a profitable area of research, which is bound to expand considerably.<sup>58</sup>

Of even broader range for absolute configurational assignments is the octant rule<sup>20,21</sup> and some of its extensions,<sup>59,60</sup> since once the scope of the rule has been established, model compounds of known absolute configuration are not required any more. The rule predicts the sign of the rotational contribution of various substituents in a ketone and its qualitative use has been of great importance for absolute configurational work.<sup>61</sup> By establishing quantitative values for some of the more common substituents (e.g., methyl,<sup>62</sup> isopropyl,<sup>63</sup> *t*-butyl<sup>64</sup>) through the synthesis of appropriate model compounds, the amplitude of a given ketone's Cotton effect can frequently be predicted<sup>21</sup> and thus used for more subtle conformational conclusions (*vide infra*). Until now, the octant rule has been used only in ketones, but *a priori* there is no reason why similar generalisations cannot also be made for other chromophores (cf. ref. 56), where the geometry of the relevant transition is well understood

(b) *Applications to Conformational Analysis.* The birth and early development, in England, of conformational analysis in organic chemistry<sup>65</sup> make it particularly appropriate to consider in this lecture the role which ORD and CD play in this area of stereochemistry. The enormous potential of ORD in conformational analysis and the sensitivity of the method to even slight conformational alterations was recognised quite early in our work.<sup>19,26,34,66,67</sup> In the intervening years, so many papers have been published on the detection or description of conformational changes by means of optical rotatory dispersion, that it is impossible to provide even a cursory review of the subject within the confines of

<sup>48</sup> Mislow, Glass, Happs, Simon, and Wahl, *J. Amer. Chem. Soc.*, 1964, **86**, 1710.

<sup>49</sup> Mislow, Glass, O'Brien, Rutkin, Steinberg, Weiss, and Djerassi, *J. Amer. Chem. Soc.*, 1962, **84**, 1455.

<sup>50</sup> Bunnenberg, Djerassi, Mislow, and Moscowitz, *J. Amer. Chem. Soc.*, 1962, **84**, 2823, 5003.

<sup>51</sup> Djerassi, Mislow, and Shamma, *Experientia*, 1962, **18**, 53.

<sup>52</sup> Djerassi, Fredga, and Sjöberg, *Acta Chem. Scand.*, 1961, **15**, 417.

<sup>53</sup> Djerassi and Lüttringhaus, *Chem. Ber.*, 1961, **94**, 2305.

<sup>54</sup> Wolf, Bunnenberg, Djerassi, Lüttringhaus, and Stockhausen, *Annalen*, 1964, in the press.

<sup>55</sup> Djerassi, Wolf, and Bunnenberg, *J. Amer. Chem. Soc.*, 1963, **85**, 324.

<sup>56</sup> Unpublished experiments with K. Ponsold (Jena) and A. Moscowitz (Minneapolis).

<sup>57</sup> Unpublished experiments with D. A. Lightner and K. Takeda (Osaka).

<sup>58</sup> For recent illustrations see Weiss and Ziffer, *J. Org. Chem.*, 1963, **28**, 1248; Yang and Samejima, *J. Amer. Chem. Soc.*, 1963, **85**, 4039.

<sup>59</sup> Djerassi and Klyne, *J. Amer. Chem. Soc.*, 1957, **79**, 1506.

<sup>60</sup> Moscowitz, Mislow, Glass, and Djerassi, *J. Amer. Chem. Soc.*, 1962, **84**, 1945.

<sup>61</sup> For a typical example see Djerassi, Quitt, Mosettig, Cambie, Rutledge, and Briggs, *J. Amer. Chem. Soc.*, 1961, **83**, 3720.

<sup>62</sup> Beard, Djerassi, Sicher, Sipos, and Tichy, *Tetrahedron*, 1963, **19**, 919.

<sup>63</sup> Djerassi, Hart, and Beard, *J. Amer. Chem. Soc.*, 1964, **86**, 85.

<sup>64</sup> Djerassi, Hart, and Warawa, *J. Amer. Chem. Soc.*, 1964, **86**, 78.

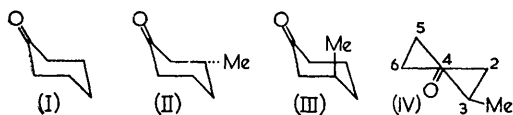
<sup>65</sup> *Inter al.*, Barton, *Experientia*, 1950, **6**, 316; *J.*, 1953, 1027; Barton and Cookson, *Quart. Rev.*, 1956, **10**, 44; Barton and Morrison in (Zechmeister, ed.) "Progress in the Chemistry of Organic Natural Products," Springer Verlag, Vienna, 1961, Vol. XIX, pp. 165-241.

<sup>66</sup> Djerassi and Marshall, *J. Amer. Chem. Soc.*, 1958, **80**, 3986.

<sup>67</sup> Djerassi and Geller, *Tetrahedron*, 1958, **3**, 319.

the present lecture. I shall therefore limit myself to a few selected examples, which should illustrate the scope and trend of current research in the field. If I were asked to specify the single most important contribution of optical rotatory dispersion (and hence also of circular dichroism), I would point to conformational studies as the answer. The justification is perhaps best given by a simple example.

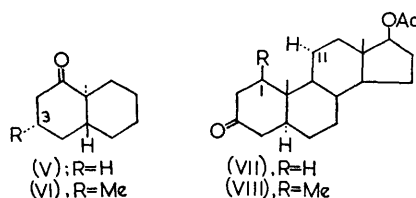
The carbonyl group in the chair form (I) of cyclohexanone is an intrinsically symmetric chromophore. (+)-3-Methylcyclohexanone (II) exhibits<sup>68</sup> a positive Cotton effect owing to asymmetric perturbation of the electrons involved in the  $n \rightarrow \pi^*$  transition of the symmetric carbonyl chromophore by the partially unshielded nuclei of the methyl substituent, which in the chair form (II) is situated in a positive octant.<sup>20</sup> In the alternate chair form (III), the only asymmetric substituent—the methyl group—is now located in a negative octant and a negative Cotton effect would be predicted. Finally, in the twist form (IV), the cyclohexanone ring itself becomes asymmetric and the additional contributions of carbon atoms 3 and 5, which reside in positive octants as does the methyl group, lead to the prediction<sup>69</sup> that IV should display a very much stronger positive Cotton effect than II.



Intermediate forms between the extremes encompassed by II, III, and IV, would then give Cotton effects differing either qualitatively (sign) or quantitatively (amplitude) from those of II, III, and IV, depending upon the relative juxtaposition of the various asymmetric atoms *vis-à-vis* the carbonyl chromophore. The same situation will be encountered in more complex molecules, except that the contribution of additional substituents has to be reckoned with. The effect of these additional asymmetric substituents decreases rapidly with distance and this explains why generally only the bicyclic environment around the carbonyl group in polycyclic systems needs to be taken into consideration in a qualitative prediction of the sign of the Cotton effect for absolute configurational purposes (*vide supra*). With this picture as a background we may now consider a few actual examples from the literature, where ORD and CD were employed in problems of conformational analysis.

The first example<sup>70</sup> shows the demonstration by means of ORD of an anticipated conformational change produced by an equatorial methyl group. The approximate rotatory contribution of an equatorial methyl substituent  $\beta$  to a carbonyl group in a cyclohexanone can be derived from the Cotton effect amplitude ( $a$ )<sup>21</sup> of (+)-3-methylcyclohexanone, which may be expected to exist largely in the chair form (II). This value  $a \sim 25$  when added to the experimentally determined value  $a = -27$  for (–)-*trans*-9-methyl-1-decalone (V) leads to a predicted amplitude of  $-52$  for (–)-3,9-dimethyl-*trans*-1-decalone (VI), which is in excellent agreement with the experimentally determined Cotton effect. We conclude, therefore, that introduction of an equatorial methyl group into the C-3 position of (V) does not produce conformational distortion.

However, when the same simple arithmetic operation is performed with 5 $\alpha$ -androstan-17 $\beta$ -ol-3-one acetate (VII) and its 1 $\beta$ -methyl homologue (VIII), a calculated value of  $a = +29$  is obtained for (VIII), which is in marked contrast to the observed amplitude of  $+72$ . The origin for this serious discrepancy appears to be the non-bonded interaction, easily seen from an inspection of models, between the equatorial 1 $\beta$ -methyl and 11 $\alpha$ -hydrogen substituents, which can relieve itself most readily by conformational distortion of ring A. Either a boat form (with C-2 and C-5 the prow and stern) of ring A or the corresponding twist form (with C-3 and C-10 the “points”<sup>69</sup>) would relieve this interaction and at the same time move the 1 $\beta$ -methyl group from a negative to a positive octant.



The second example<sup>71</sup> illustrates how rotatory dispersion measurements uncovered an unexpected conformational phenomenon, for which there existed no precedent. One of the long outstanding problems in conformational analysis is the conformation of the *cis*-2-decalones, for which two all-chair forms are feasible—the “steroid” conformation (IX) and the “non-steroid” form (X). Originally,<sup>72</sup> it had been

<sup>68</sup> French and Naps, *J. Amer. Chem. Soc.*, 1963, **85**, 2303; Djerassi and Krakower, *ibid.*, 1959, **81**, 237.

<sup>69</sup> Djerassi and Klyne, *Proc. Nat. Acad. Sci., U.S.A.*, 1962, **48**, 1093.

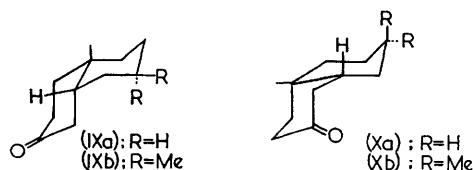
<sup>70</sup> Djerassi, Lund, and Akhrem, *J. Amer. Chem. Soc.*, 1962, **84**, 1249.

<sup>71</sup> Djerassi, Burakevich, Chamberlin, Elad, Toda, and Stork, *J. Amer. Chem. Soc.*, 1964, **86**, 465.

<sup>72</sup> Klyne, *Experientia*, 1956, **12**, 119.

suggested that *cis*-10-methyl-2-decalone exists in the "non-steroid" form (Xa), while the opposite conclusion was reached<sup>66</sup> from a comparison of the ORD curves of optically active *cis*-10-methyl-2-decalone and 5 $\beta$ -3-keto-steroids, which must exist in the "steroid" conformation because of the additional B/C ring juncture. In any event, the energy difference between IXa and IXb was predicted<sup>73</sup> to be quite small.

A much more unambiguous case seemed to be *cis*-7,7,10-trimethyl-2-decalone,<sup>73</sup> where an additional methyl-methylene interaction is introduced in the "steroid" form (IXb), which is absent in the "non-steroid" counterpart (Xb). The very reasonable conclusion was drawn<sup>73</sup> that the trimethyldecalone exists almost completely as Xb. This deduction can be tested easily in the optically active ketone by means of optical rotatory dispersion, since the octant rule<sup>20</sup> would predict a strong, positive Cotton effect for Xb—all substituents being in positive octants—while a very weak or negligible Cotton effect should be exhibited by the "steroid" conformation IXb, since virtually all contributions cancel out. When the optically active form of *cis*-7,7,10-trimethyl-2-decalone was synthesised,<sup>71</sup> the surprising observation was made that the substance showed only a very slight Cotton effect, which definitely rules out the anticipated<sup>73</sup> "non-steroid" conformation (Xb). While the ORD results would be compatible with the alternate "steroid" conformation (IXb), this can certainly be eliminated on energetic grounds, because of the unfavourable methyl-methylene interaction. Evidently, one or more flexible forms are involved—a conclusion which would not have been reached in the absence of ORD measurements.



A third example<sup>67,74</sup> covers the demonstration of conformational mobility in *trans*-2-chloro-5-methylcyclohexanone (XI) by ORD<sup>67,74</sup> and CD<sup>24,75</sup> measurements. The octant rule<sup>20,59</sup> predicts a positive Cotton effect for the diequatorial form (XIa) (Fig. 11) and a strongly negative one for the diaxial conformation (XIb) of *trans*-2-chloro-5-methylcyclohexanone. As shown in Fig. 11, the Cotton effect is

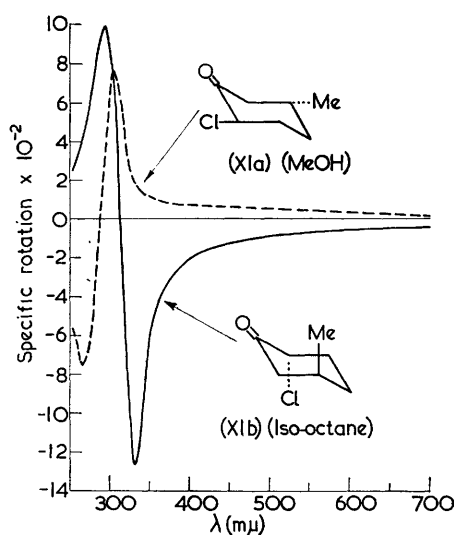


FIG. 11. Optical rotatory dispersion curves of *trans*-2-chloro-5-methylcyclohexanone (XI) in methanol and iso-octane.

indeed positive in the polar medium methanol, but becomes negative when iso-octane is employed as solvent. This result suggests the presence of an increased amount of the diaxial form (XIb) in the non-polar solvent in accord with prediction<sup>76</sup> about the effect of solvent polarity upon the conformer equilibrium in  $\alpha$ -halogenocyclohexanones. By estimating the quantitative contribution of an axial  $\alpha$ -chlorine atom from steroid models, it is possible to calculate<sup>74</sup> an approximate amplitude value for the pure diaxial form (XIb) and thus to determine the approximate percentage of the conformers in methanol (99% XIa) and iso-octane ( $\sim$  82% XIa).

The problem can also be attacked by circular dichroism measurements (Fig. 12), where changes in solvent polarity<sup>24</sup> or in temperature<sup>24,75</sup> affect the conformer equilibrium. In fact, it has been shown<sup>77</sup> that from the temperature-dependent CD measurements it is possible to calculate the relative conformer populations with a considerably greater degree of accuracy, thus showing that in methanol there is present  $97 \pm 2\%$  diequatorial isomer (XIa) compared to  $89 \pm 3\%$  in iso-octane solution. In spite of the fact that the two conformers XIa and XIb absorb over 20 m $\mu$  apart, the ultraviolet absorp-

<sup>73</sup> Halsall and Thomas, *J.*, 1956, 2431.

<sup>74</sup> Djerassi, Geller, and Eisenbraun, *J. Org. Chem.*, 1960, **25**, 1; Allinger, Allinger, Geller, and Djerassi, *ibid.*, 1961, **26**, 3521.

<sup>75</sup> Moscovitz, Wellman, and Djerassi, *Proc. Nat. Acad. Sci. U.S.A.*, 1963, **50**, 799.

<sup>76</sup> Allinger and Allinger, *Tetrahedron*, 1958, **2**, 64.

<sup>77</sup> Moscovitz, Wellman, and Djerassi, *J. Amer. Chem. Soc.*, 1963, **85**, 3515.

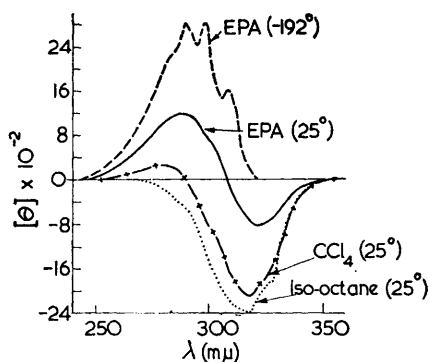
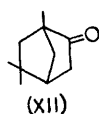


FIG. 12. Circular dichroism curves of *trans*-2-chloro-5-methylcyclohexanone (XI) in carbon tetrachloride (25°), iso-octane (25°), and EPA (25° and -192°).

tion spectrum of *trans*-2-chloro-5-methylcyclohexanone exhibits only a single broad hump (due to overlapping) in the 290  $m\mu$  region. The presence of the two species, however, is clearly discernible in the CD curve (Fig. 12) principally because the two contributions, though strongly overlapping, are of opposite sign.

A change in sign of the Cotton effect does not necessarily denote a conformational equilibrium. A number of conformationally rigid molecules (*e.g.*, isofenchone (XII)<sup>78</sup>) exhibit this phenomenon, which has been ascribed<sup>75,79</sup> to asymmetric solvation, *i.e.*, varying mixtures of solvated and non-solvated species. We may consider in some detail the case of (-)-menthone (XIII), where conformational mobility as well as asymmetric solvation can be shown<sup>80</sup> to operate.



In Fig. 13 are summarised some of the solvent-dependent circular dichroism measurements that have been performed with (-)-menthone (XIII). *A priori*, the very substantial difference in wavelength (ca. 30  $m\mu$ ) between the positive and negative maxima in any given solvent might be construed to mean that we are not dealing with a simple equilibrium between the unsolvated diequatorial form XIIIa (predicted<sup>63</sup> to be weakly positive) and the unsolvated diaxial chair (XIIIb) or twist (XIIIc) forms, both of which should show strong negative Cotton

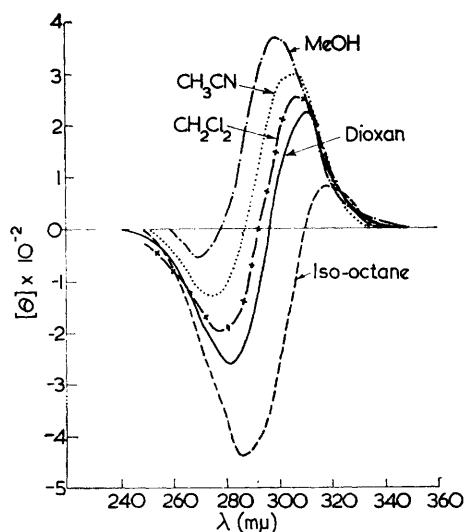
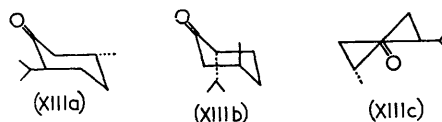


FIG. 13. Circular dichroism curves of (-)-menthone (XIII) in methanol, acetonitrile, methylene chloride, dioxan, and iso-octane.

effects.<sup>20,63</sup> The basis for such a conclusion would be that there exists no obvious reason why such a conformational change should cause such a large wavelength change; in fact a pair of equatorial-axial steroidal isomers (XVI vs. XVII<sup>63</sup>) exhibited a maximal difference in their individual CD maxima of only 3–5  $m\mu$ . However, a recent calculation<sup>80</sup> has shown that superposition of two oppositely signed CD bands differing in the location of the respective maxima by only 1  $m\mu$  can give rise to the type of "double-humped" curve seen in Fig. 13 in which the two maxima are separated by as much as 28  $m\mu$ . A consequence of this superposition is that the amplitude of the resulting double CD signal is very much weaker than that of the individual components. In other words, even two conformers differing in their CD maxima by a very small value ( $\sim 1 m\mu$ ) can cause the effect shown in Fig. 13, which, therefore, need not necessarily be associated with solvation.



If we now examine the temperature-dependent circular dichroism of (-)-menthone in a hydro-

<sup>78</sup> Gervais and Rassat, *Bull. Soc. chim. France.*, 1961, 743.

<sup>79</sup> Coulombeau and Rassat, *Bull. Soc. chim. France*, 1963, 2673.

<sup>80</sup> Unpublished experiments by Laur, Briggs, Moscovitz, Djerassi, and Wellman.

carbon mixture (5:1 isopentane-methylcyclohexane), we note (Fig. 14) a red shift upon lowering the

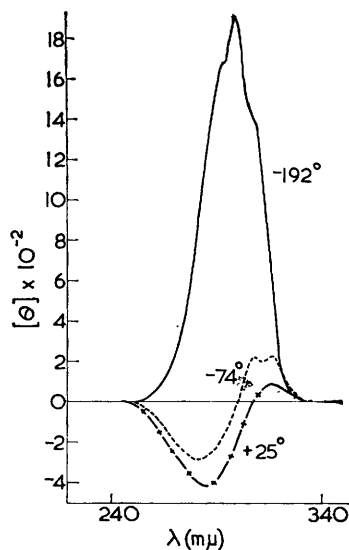


FIG. 14. Circular dichroism curves of (–)-menthone (XIII) in 5:1 isopentane-methylcyclohexane at  $25^\circ$ ,  $-74^\circ$ , and  $-192^\circ$ .

temperature to  $-192^\circ$  as well as a major increase in rotational strength in going from  $-74^\circ$  to  $-192^\circ$  as compared to the  $+25^\circ$  to  $-74^\circ$  range. This substantial increase in the positive CD curve upon drastic lowering of the temperature is in agreement with an increase in population of the diequatorial

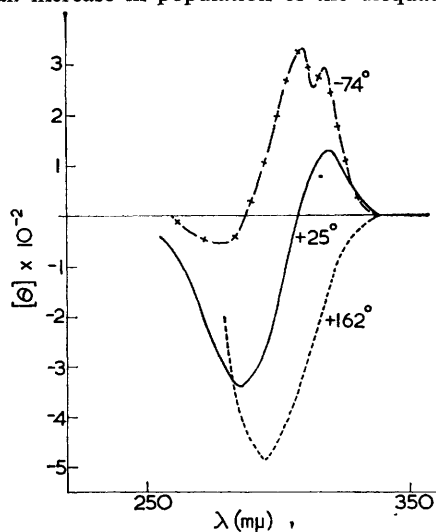


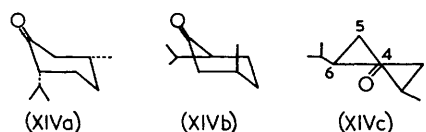
FIG. 15. Circular dichroism curves of (–)-menthone (XIII) in decalin at  $+162^\circ$ ,  $+25^\circ$ , and  $-74^\circ$ .

<sup>81</sup> Ohloff, Osiecki, and Djerassi, *Chem. Ber.*, 1962, **95**, 1400.

conformer XIIIa and at the same time is inconsistent with solvation playing the exclusive role, since the lower wavelength band should have increased on cooling.

An even wider temperature range was feasible<sup>80</sup> in decalin, where the range  $-74^\circ$  to  $+162^\circ$  could be covered. Particularly noticeable (Fig. 15) is the increase in the negative CD band upon raising the temperature, which is best interpreted in terms of an augmented contribution by a negatively rotating non-solvated conformer, such as (XIIIb) and/or (XIIIc).

The effect of temperature and solvent changes upon the circular dichroism<sup>80</sup> of (+)-isomenthone (XIV) will be reported elsewhere in detail, but it is pertinent to mention that the very strong positive Cotton effect, first noted in ORD measurements,<sup>81</sup> clearly eliminates<sup>63</sup> the possibility that the conformer XIVb with an equatorial isopropyl group plays an important role. A mixture of XIVa and XIVc is most consistent<sup>63</sup> with the observed ORD and CD results.



The existence of at least three different forms is demonstrated in a graphic manner in Fig. 16, which contains the CD curves of 2-oxo-1-p-menthanol (XV)

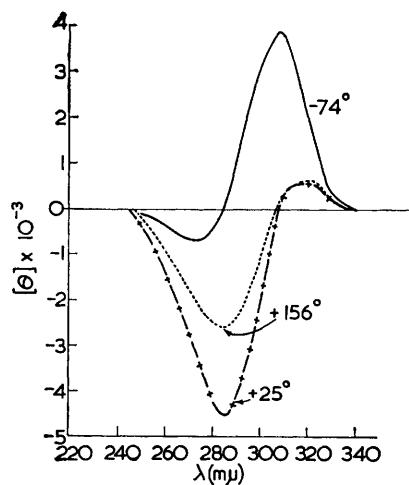
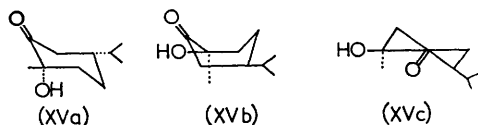


FIG. 16. Circular dichroism curves of 2-oxo-1-p-menthanol (XV) in decalin at  $+156^\circ$ ,  $+25^\circ$ , and  $-74^\circ$ .



(XV)<sup>82</sup> measured in decalin solution at  $-74^\circ$ ,  $+25^\circ$ , and  $+156^\circ$ . The evidence for the occurrence of at least three forms is clear since the rotational strength at room temperature is more negative than at  $+156^\circ$ , while a positive CD curve is obtained at low temperatures. The earlier<sup>83</sup> ORD measurements, conducted at room temperature in different solvents, showed a positive Cotton effect in polar media (*e.g.*, methanol, dimethyl sulphoxide), but a negative one in non-polar solvents (iso-octane, carbon tetrachloride). This was interpreted in terms of a conformational equilibrium between the chair form (XVa) (polar solvent) with an axial hydroxyl group incapable of intramolecular hydrogen bonding, and the alternate boat conformation (XVb),\* in which hydrogen bonding between the equatorial hydroxyl group and the carbonyl function is feasible. These conclusions were consistent with the predictions from the octant rule (positive Cotton effect for XVa, negative for XVb) as well as the observed<sup>83</sup> wavelength shifts. It should be noted that the alternate twist form (XVc) (carbon atoms 1 and 4 the "points" of the twist) is excluded, since it would display a strongly positive Cotton effect.

If we turn now to the CD results (Fig. 16) in decalin, we can interpret them at least qualitatively by assuming that the conformer population is changed at  $-74^\circ$  in the direction of (XVa) (positive Cotton effect, no intramolecular hydrogen bond), while at elevated temperatures (*e.g.*,  $+152^\circ$ ) we are dealing with increased quantities of (XVb) (negative Cotton effect), in which the intramolecular hydrogen bond has been broken and/or with the appearance of the positively rotating twist form (XVc). At room temperature, the hydrogen-bonded form of (XVb) enters into play.



The examples cited so far have all involved conformational changes of cyclic ketones, which were reflected in alterations in the Cotton effect (as measured by ORD or CD) because the relative positions of the various atoms in the appropriate octants differed in each conformer. The same effect can be produced by free rotational isomerism, which is usually much more difficult to measure, and some pertinent results<sup>80</sup> bearing on this point will now be given.

The rotational strength of 2α-isopropyl-19-nor-

5α-androstan-3-one (XVI)<sup>83</sup> increases considerably upon lowering the temperature as exemplified by circular dichroism data reproduced in Fig. 17. Pre-

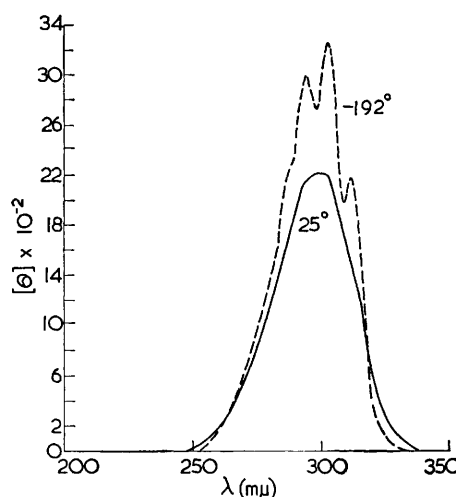


FIG. 17. Circular dichroism curves of 2α-isopropyl-19-nor-5α-androstan-3-one (XVI) in EPA at  $25^\circ$  and  $-192^\circ$ .

cisely the same situation is encountered<sup>24</sup> in 2α-isopropylcholestan-3-one (XVIII).<sup>83</sup> On the other hand, no change in rotational strength is observed<sup>80</sup> in 2β-isopropyl-19-nor-5α-androstan-3-one (XVII)<sup>83</sup> over the range  $+25^\circ$  to  $-192^\circ$ . These results are interpreted as meaning that in the two equatorially substituted isopropyl ketones (XVI and XVIII), one is dealing with a rotamer mixture at room temperature and that upon lowering the temperature to the boiling point of liquid nitrogen, free rotation is restricted and the proportion of the favoured rotamer enriched. In the axial isomer (XVII), on the other hand, there probably exists already at room temperature a great preponderance of one rotamer (XVIIa), in which the isopropyl group assumes the most favoured position, namely that in which the isopropyl hydrogen atom, rather than one of its methyl groups, is pointed towards the angular hydrogen atom. If such a condition obtains at  $+25^\circ$ , then no change would be expected upon lowering the temperature.

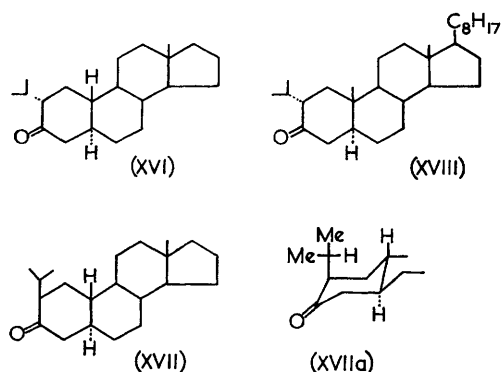
The rotational change illustrated in Fig. 17 was produced by leaving the geometry of the chromophore-containing portion of the molecule undisturbed and simply altering the relative population of the atoms of the isopropyl group in the various

\* The corresponding twist form with carbon atoms 2 and 5 the "points" of the twist (see ref. 69) is probably a more likely representation.

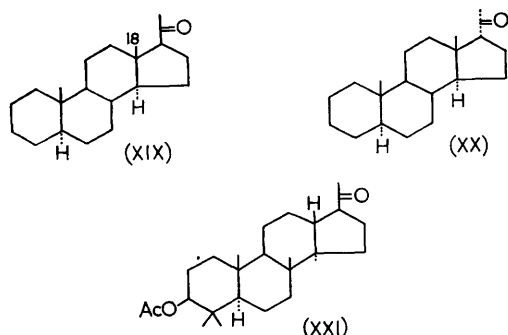
<sup>82</sup> Newhall, *J. Org. Chem.*, 1959, **24**, 1673.

<sup>83</sup> Djerassi, Records, and Bach, *Chem. and Ind.*, 1961, 258.





octants. The reverse can also be accomplished, namely to examine free rotation in a substance, where the carbonyl group is at liberty to move relative to the cyclic framework. In 5 $\alpha$ -pregnan-20-one (XIX) and its 17 $\alpha$ -isomer (XX), the acetyl group is theoretically free to rotate around C-17. In actual fact, free rotation is severely restricted—in the 17 $\beta$ -isomer (XIX) by the C-18 angular methyl group as well as the equatorial hydrogens at C-12 and C-16, and in the 17 $\alpha$ -isomer (XX) by the axial hydrogen atoms at C-12, C-14, and perhaps C-16. This restricted rotation manifests itself in the large amplitude<sup>28</sup> of the ORD Cotton effects of such 20-keto-steroids and in the observation that the rotational strength is affected to only a small extent over the range +25° to -192° as determined<sup>80</sup> by CD measurements. The situation is drastically altered in 3 $\beta$ -acetoxyhexanordammaran-20-one (XXI),<sup>84</sup> which for stereochemical purposes may be considered a 20-keto-steroid (XIX) analogue lacking the C-18 angular methyl group.



The ORD curve<sup>85</sup> of this ketone (XXI) is characterised by a weak negative Cotton effect, in marked contrast to the strongly positive Cotton effect of the 20-keto-steroid (XIX). This difference has been

ascribed<sup>85</sup> to relatively free rotation in the dammaran-20-one derivative (XXI) since the restraint imposed by the angular methyl group is now absent. A striking confirmation of this view is afforded by the temperature-dependent CD data collected in Fig. 18.

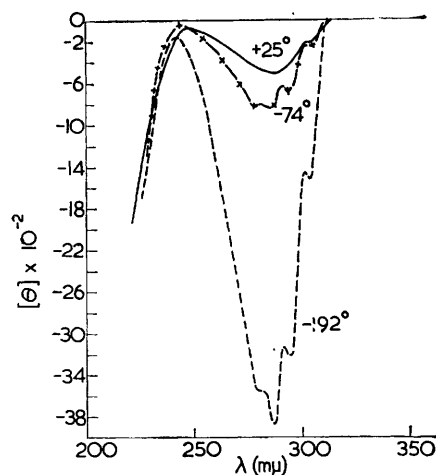


FIG. 18. Circular dichroism curves of 3 $\beta$ -acetoxyhexanordammaran-20-one (XXI) in EPA at +25°, -74°, and -192°.

It will be noted that the rotational strength changes only slightly in the range +25° to -74°, but then increases greatly upon cooling to -192°. Evidently, the energy difference between the various rotamers is so small that cooling to very low temperature is required before a meaningful preponderance of a preferred rotamer is reached.

In the previous discussion of "chromophoric derivatives," it was noted (see Table I) that many of the newly introduced chromophores are situated in portions of the molecule that are subject to free rotation. Nevertheless, in most instances a direct relation between the sign of the Cotton effect of that derivative and the absolute configuration of the nearest asymmetric centre was possible. The most likely explanation<sup>43,45</sup> is that the predominant rotamer composition is altered only slightly by changes around the asymmetric centre, which in general is some distance from the appropriate chromophore. Low-temperature CD studies of such substances are now under way in our laboratory to examine this question in greater detail.

All the work discussed so far has dealt with inherently symmetric chromophores—the optical activity being due to vicinal action by asymmetrically situated atomic substituents. In recent years, a second type of chromophore—the inherently dissymmetric

<sup>84</sup> Mills, J., 1956, 2196. For stereochemistry see Biellmann, Crabbé, and Ourisson, *Tetrahedron*, 1958, 3, 303.

<sup>85</sup> Djerassi, Mitscher, and Mitscher, *J. Amer. Chem. Soc.*, 1959, 81, 947.

one—has been studied in some detail,<sup>22,49,50,60,86–88</sup> and its bearing on some conformational problems will now be considered briefly. Inherently dissymmetric chromophores, as for instance the twisted biphenyls<sup>48–50</sup> or hexahelicene<sup>88</sup> possess an inherent chirality, which leads to optical activity irrespective of its molecular environment. The rotational strength of such chromophores is in general much greater than that of the asymmetrically disturbed, inherently symmetric chromophores. Interesting examples are  $\alpha\beta$ -unsaturated ketones.<sup>87</sup> When planar, they resemble closely their saturated analogues in terms of representing an inherently symmetric chromophore. However, when non-planarity enters, which is usually the case in cyclic systems, an inherent chirality is introduced and its sense (left-handed or right-handed) can be related to the sign of the Cotton effect, quite analogous to the situation in *cisoid* dienes,<sup>89</sup> whose  $\pi$ -system resembles that of  $\alpha\beta$ -unsaturated ketones.

This relationship between chirality and sign of Cotton effect applies to both the  $n \rightarrow \pi^*$  and  $\pi \rightarrow \pi^*$  absorption bands. While the original ORD studies<sup>18,26</sup> of  $\alpha\beta$ -unsaturated ketones were limited to the  $n \rightarrow \pi^*$  region, recent improvements in spectropolarimetric instrumentation have permitted penetration<sup>87</sup> through the high-intensity *K*-band. An

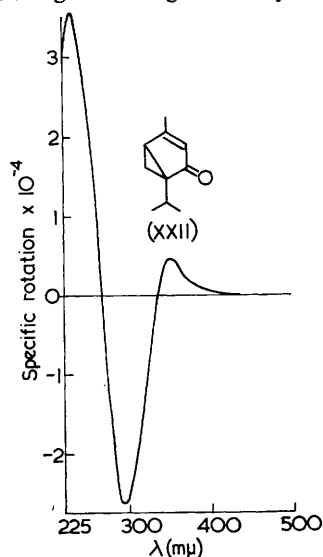


FIG. 19. Optical rotatory dispersion curve (methanol) of umbellulone (XXII).

<sup>86</sup> Mislow, Glass, Moscovitz, and Djerassi, *J. Amer. Chem. Soc.*, 1961, **83**, 2771.

<sup>87</sup> Djerassi, Records, Bunnenberg, Mislow, and Moscovitz, *J. Amer. Chem. Soc.*, 1962, **84**, 870.

<sup>88</sup> For further discussion see Moscovitz, *Tetrahedron*, 1961, **13**, 48; Mislow, *Ann. New York Acad. Sci.*, 1962, **93**, 457; Cookson and Hudec, *J.*, 1962, 429; Whalley, *Chem. and Ind.*, 1962, 1024.

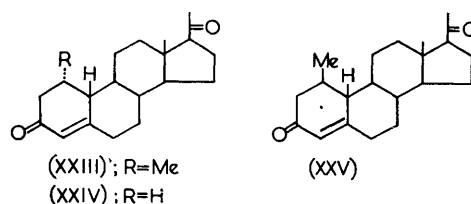
<sup>89</sup> Moscovitz, Charney, Weiss, and Ziffer, *J. Amer. Chem. Soc.*, 1961, **83**, 4461.

<sup>90</sup> Kuriyama, Kondo, and Tori, *Tetrahedron Letters*, 1963, 1485.

<sup>91</sup> Davies and Petrow, *Tetrahedron*, 1963, **19**, 1771. For n.m.r. studies of similar ketones see Collins, Hobbs, and Sternhell, *Austral. J. Chem.*, 1963, **16**, 1030.

illustration is offered in Fig. 19 with the ORD curve of umbellulone (XXII) measured with the Bendix-Ericsson spectropolarimeter; the positive Cotton effect associated with the  $n \rightarrow \pi^*$  transition as well as the powerful negative one due to the  $\pi \rightarrow \pi^*$  transition are clearly defined. The angle of skew in the non-planar,  $\alpha\beta$ -unsaturated carbonyl chromophore determines the extent to which the substance under examination behaves like an inherently dissymmetric chromophore. When this angle is small, the chirality contribution may be partially or completely offset by vicinal interaction of the type observed in asymmetrically perturbed, intrinsically symmetric chromophores. Furthermore, the handedness of the  $C=C=C=O$  chromophore is inverted in changing the conformation of a cyclohexanone ring and it is conceivable that the rotatory contribution of one conformer, though present in much smaller amount, may dominate the overall sign of the Cotton effect. Consequently, care must be exercised in interpreting the sign of the Cotton effect in terms of a given conformation. However, if a reference ORD or CD curve is available, departure in sign from it may be considered *prima facie* evidence for conformational distortion. Originally,<sup>26</sup> such Cotton effect anomalies were studied in C-6 substituted  $\Delta^4$ -3-keto-steroids and associated with distortions in ring B. The more recent studies,<sup>87</sup> interpreted in the light of the inherently dissymmetric chromophore concept for the  $\alpha\beta$ -unsaturated carbonyl moiety, show that distortion of ring A is involved.

Thus, 1 $\alpha$ -methyl-19-norprogesterone (XXIII) exhibits a Cotton effect similar to that of the lower homologue 19-norprogesterone (XXIV), while an inversion in sign is observed<sup>26,87</sup> in the 1 $\beta$ -methyl isomer (XXV), presumably due to interaction between the equatorial 1 $\beta$ -methyl group and the 11 $\alpha$ -hydrogen atom [see also earlier discussion of (VII) *versus* (VIII)]. Similar instances of conformational distortion in  $\Delta^4$ -3-keto-steroids, uncovered through ORD measurements on 2 $\beta$ -<sup>90</sup> and 6 $\beta$ -<sup>91</sup> substituted analogues, have been reported recently.



This sensitivity of  $\alpha\beta$ -unsaturated ketones towards very subtle interactions indicates that the Cotton effect of such substances should be employed with very great caution for absolute configurational deductions.

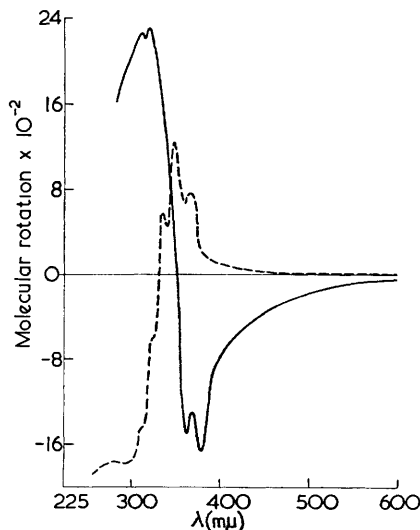


FIG. 20. Optical rotatory dispersion curve (dioxan) of  $\Delta^3$ -trans-10-methyloctal-2-one (XXIX) and  $\Delta^{10}$ -trans-1 $\beta$ -methylbicyclo(5,4,0)undecen-9-one (XXX).

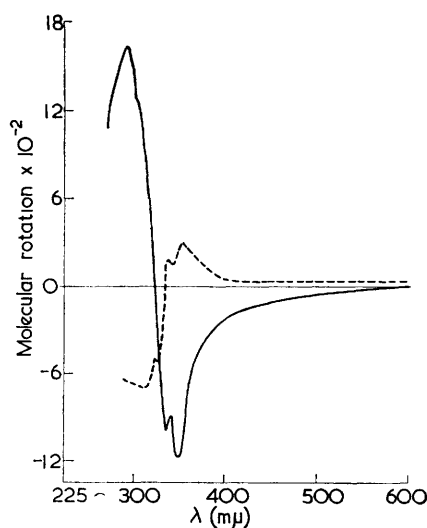
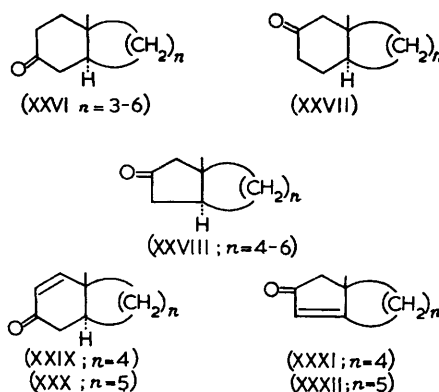


FIG. 21. Optical rotatory dispersion curves (dioxan) of  $\Delta^3(9)$ -8-methylhydrinden-2-one (XXXI) and  $\Delta^7$ -1 $\beta$ -methylbicyclo(5,3,0)decen-9-one (XXXII).

A striking illustration is afforded by the observation<sup>92</sup> that the saturated bicyclic ketones (XXVI), (XXVII), and (XXVIII) all exhibit positive Cotton effects, irrespective of the nature of the adjacent, non-ketonic ring, while inversions in sign are encountered in the  $\alpha\beta$ -unsaturated ketone pairs (XXIX) versus (XXX) (Fig. 20), and (XXXI) versus (XXXII) (Fig. 21). This inversion in the Cotton effect in the unsaturated ketones is only attributable to a conformational change imparted by the change in size of the adjacent ring, since the substances belong to the same absolute configurational series. These results have an obvious bearing on the utilisation of ORD and CD for absolute configurational assignments among perhydroazulenic terpenes.<sup>93</sup>



From the above discussion, it should be clear that while there is much overlap between optical rotatory dispersion and circular dichroism as far as organic chemical applications are concerned, the two methods do complement each other in several areas in a very desirable fashion. Studies in stereochemistry, notably in conformational analysis, have benefited greatly from the availability of these tools and much progress can still be anticipated. This is particularly true if improved instrumentation can keep pace with the demands and interests of the chemist.

In earlier reviews<sup>94,95</sup> I have emphasised the need for better spectropolarimeters with farther ultra-violet penetration as well as for a convenient instrument to measure circular dichroism. The recent improvements in spectropolarimetry<sup>96</sup> have to a large extent satisfied this demand; at present, penetration below 190 m $\mu$  is feasible and many chromophores, hitherto outside the range of standard spectropolarimetry, now yield interesting Cotton effect

<sup>92</sup> Djerassi and Gurst, *J. Amer. Chem. Soc.*, 1964, **86**, 1755.

<sup>93</sup> See Djerassi, Osiecki, and Herz, *J. Org. Chem.*, 1957, **22**, 1361.

<sup>94</sup> Djerassi, *Rec. Chem. Progress*, 1959, **20**, 141.

<sup>95</sup> Djerassi, *Tetrahedron*, 1961, **13**, 28.

<sup>96</sup> For a practical performance comparison of the four commercially available spectropolarimeters see ref. 54.

curves, which are amenable to theoretical interpretation and hence practical utilisation. The instrumentation situation is less bright in the circular dichroism field, simply because the present commercially available instrument does not reach as far into the ultraviolet<sup>97</sup> as several of the spectropolarimeters. This is a serious drawback<sup>98</sup> and since few laboratories will purchase both instruments because of the expense factor, the choice will generally be in favour of ORD owing to the present greater spectral penetration of spectropolarimeters.

What is really needed is to be able to measure both optical rotatory dispersion and circular dichroism down to 185 m $\mu$  with one single instrument. There is no practical reason why such a combined instrument cannot be constructed. When this is accomplished, the organic chemist as well as the theoretician interested in optical phenomena will have at their disposal the instrument of choice. In view of the past

level of excellence in the design of spectropolarimeters, I trust that this challenge to British ingenuity in instrumentation will not remain unheeded.

As can be seen from the many references, I owe to my students and other collaborators a debt, the extent of which cannot be expressed adequately in such an acknowledgment. Suffice it to say, that virtually none of the work presented here could have been accomplished without their most able assistance. I am especially indebted to Dr. E. Bunnenberg for many instrumental contributions, to Mrs. Ruth Records for practically operating during the past four years two instruments simultaneously and to Professor A. Moscovitz of the University of Minnesota for numerous stimulating discussions on theoretical points. Financial support was provided by the National Institutes of Health of the U.S. Public Health Service and by the National Science Foundation.

<sup>97</sup> For a typical example see Fig. 7 in ref. 33.

<sup>98</sup> A description of a research instrument with greater ultraviolet penetration has been published recently by M. Grosjean and M. Tari, *Compt. rend.*, 1964, **258**, 2034.

## COMMUNICATIONS

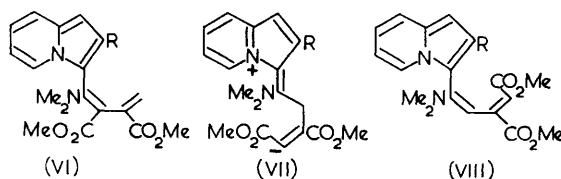
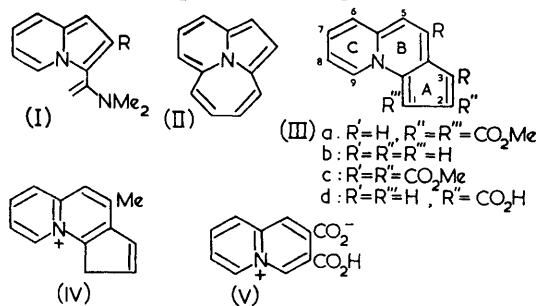
### The Formation of Cyclopenta[*c*]quinolizines from 3-1'-Dimethylaminovinylindolizines and Dimethyl Acetylenedicarboxylate

By W. K. GIBSON and D. LEAVER\*

WE investigated the reaction between dimethyl acetylenedicarboxylate and the enamines (I; R=Me, Ph, or CO<sub>2</sub>Me) with a view to synthesising derivatives of the hypothetical<sup>1</sup> cycl[4,3,2]azine (II). It is now clear, however, that the reaction, which when carried out in boiling toluene, is accompanied by loss of dimethylamine, leads to the cyclopenta[*c*]quinolizines (IIIa). The first indication that the products were not based on the ring system (II) was afforded by the presence of a low field absorption (between  $\tau$  -0.4 and 0.3) in their n.m.r. spectra which was attributable to the  $\alpha$ -pyridine proton (position 9 in III) since its multiplicity varied in a predictable manner with the position of methyl substitution in the pyridine ring.

Hydrolysis and decarboxylation of the orange diester (IIIa; R=Me) was effected by boiling hydrochloric acid, and the product (IIIb; R=Me) showed an ultraviolet spectrum, in acid solution, which was attributable to the ion (IV or its 3*H*-isomer) since it resembled closely, but was interposed in wavelength between, the spectra of the quinolizinium<sup>2</sup> and the benzo[*c*]quinolizinium<sup>3</sup> ion. Further evidence for the presence of a quinolizine nucleus

is shown by the presence of a quinolizine nucleus



\* Department of Chemistry, University of Edinburgh.

<sup>1</sup> Windgassen, Saunders, and Boekelheide, *J. Amer. Chem. Soc.*, 1959, **81**, 1459.

<sup>2</sup> Boekelheide and Gall, *J. Amer. Chem. Soc.*, 1954, **76**, 1832.

<sup>3</sup> Glover and Jones, *J.*, 1958, 3021.

was afforded by oxidation of the triester (IIIa;  $R=CO_2Me$ ), with nitric acid, to the known<sup>4</sup> betaine (V) which was identified by comparison with an authentic specimen.

Rings A and B of the cyclopenta[c]quinoline nucleus are iso- $\pi$ -electronic with azulene and, in accord with this structure, compounds (IIIb) readily undergo electrophilic substitution to give mono- and di-acyl, monoaryloxy, and mononitroso derivatives. Halogenation and nitration fail because of decomposition.

The formation of the 1,2-diester (IIIa) proceeded by way of the intermediate compounds (VI) which can be isolated by carrying out the reaction in a cold, aprotic solvent and which are converted into the cyclopenta[c]quinolizines by boiling toluene. Compounds (VI) are clearly formed by collapse of the zwitterion (VII), in the way established<sup>5</sup> for related reactions, to give a cyclobutene which isomerises to the butadiene (VI). By carrying out the initial addi-

tion reaction in methanol, however, the zwitterion can be intercepted by proton transfer to give the isomeric butadiene (VIII) which can be converted into the 2,3-diester (IIIc) by boiling xylene. The isomeric 1,2- and 2,3-diester (IIIa and IIIc;  $R=Ph$ ) were converted into the same monocarboxylic acid (IIId;  $R=Ph$ ) by partial hydrolysis and decarboxylation.

The very low  $\tau$  value of the 9-proton in the 1,2-diester (IIIa) is evidently partly due to a direct deshielding effect of the 1-methoxycarbonyl group since the decarboxylated compounds (IIIb) and the 2,3-diester (IIIc) show  $\tau$  values (1.2–1.6) more normal for  $\alpha$ -pyridine protons. The 9-protons in the mono- and di-benzoyl compounds also show very low  $\tau$  values (–0.8 and –0.2, respectively) and this is taken as evidence that acylation occurs first in the 1-position. The second acyl group is considered to enter the 3-position.

(Received, August 21st, 1964.)

<sup>4</sup> Bradsher and Barker, *J. Org. Chem.*, 1964, **29**, 452.

<sup>5</sup> Berchold and Uhlig, *J. Org. Chem.*, 1963, **28**, 1459; Brannock, Burpitt, and Thweatt, *ibid.*, p. 1462.

## The Reaction of Tosyl Derivatives of Inositols with Sodium Benzoate in Dimethylformamide

By S. J. ANGYAL and T. S. STEWART\*

THE reaction of sulphonyl derivatives of sugars and polyols with sodium benzoate in boiling dimethylformamide has recently acquired importance.<sup>1,2</sup> If the sulphonyl group is in a furanose or pyranose ring, the reported outcome<sup>3</sup> of the reaction is either displacement of the sulphonyloxy-group by a benzoate group with inversion, or recovery of unchanged starting material. Cyclitols being good model compounds for the behaviour of carbohydrates, we have studied this reaction with a number of tosylated inositols.

An unexpectedly great variety of reactions was observed. In only one instance did benzoate exchange with inversion occur, and only one of the compounds was recovered unchanged; all the other compounds reacted, however, and it was soon realised that their reactions took place even in the absence of sodium benzoate.

Three reactions were observed to occur, in the presence or absence of sodium benzoate, depending on the nature of the groups attached to the vicinal carbon atoms: (i) If there is a neighbouring acetoxyl

group in a *trans*-position [*e.g.*, 1,2,3,4-tetra-*O*-acetyl-5-*O*-methyl-6-*O*-tosyl(–)-inositol] and the solvent contains some water, inversion takes place through the initial formation of a cyclic acetoxonium ion. Similar reactions of acyclic polyols have recently been reported.<sup>3</sup> (ii) If the neighbouring group is hydroxyl in a *trans*-position [*e.g.*, 2-*O*-methyl-1-*O*-tosyl(–)-inositol], an epoxide, and the two products resulting from its subsequent opening, are formed. (iii) If there is a vicinal and *cis*-tosyloxy-group [3,4-di-*O*-benzyl-1,2-*O*-cyclohexylidene-5,6-di-*O*-tosyl(–)-inositol], elimination occurs with the formation of an enol tosylate. A similar instance has recently been described<sup>4</sup> involving a derivative of an acyclic polyol.

In the compound [1,2:5,6-di-*O*-isopropylidene-3-*O*-methyl-4-*O*-tosyl(+)-inositol] that displayed benzoate exchange with inversion, and in the compound [1,2:5,6-di-*O*-isopropylidene-3,4-di-*O*-tosyl(–)-inositol] that did not react, there are no neighbouring hydrogen atoms, acetoxyl, or hydroxyl groups in *trans*-relationship to the tosyl groups.

(Received, July 22nd, 1964.)

\* School of Chemistry, The University of New South Wales, Kensington, N.S.W.

<sup>1</sup> Reist, Goodman, and Baker, *J. Amer. Chem. Soc.*, 1958, **80**, 5775; Bukhari, Foster, Lehmann, and Webber, *J.*, 1963, 2287; Bukhari, Foster, Lehmann, Webber, and Westwood, *J.*, 1963, 2291; Baggett, Bukhari, Foster, Lehmann, and Webber, *J.*, 1963, 4157.

<sup>2</sup> Reist, Spencer, and Baker, *J. Org. Chem.*, 1959, **24**, 231; Foster, Harrison, Lehmann, and Webber, *J.*, 1963, 4471; Hill, Hough, and Richardson, *Proc. Chem. Soc.*, 1963, 346.

<sup>3</sup> Bukhari, Foster, Randall, and Webber, *J.*, 1963, 4167; Baker and Haines, *J. Org. Chem.*, 1963, **28**, 438.

<sup>4</sup> Bukhari, Foster, and Webber, *J.*, 1964, 2514.

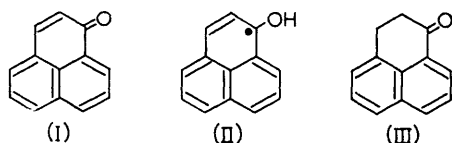


### The Photochemistry of Phenalen-1-one

By H. KÖLLER, G. P. RABOLD, K. WEISS\*, and T. K. MUKHERJEE†

IRRADIATION of aromatic ketones generally gives bimolecular reduction products,<sup>1</sup> whereas  $\alpha\beta$ -unsaturated ketones dimerise to cyclobutanes.<sup>2</sup> Dimerisation is still the preferred reaction if the double bond is conjugated with an aromatic ring. The combination of these structural features in phenalen-1-one (I) leads to unique behaviour.

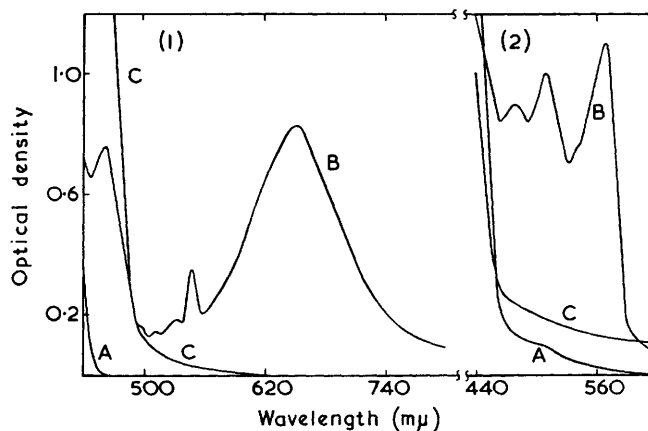
Although irradiation of ketone (I) in outgassed benzene, methylcyclohexane, or carbon tetrachloride (100-w mercury lamp, 20–75 hr.) results in only slight change, the solution in propan-2-ol becomes deep green after a few minutes (see Figure). Identical



absorption bands are produced in methanol, ethanol, ethyl acetate, and acetone. In propan-2-ol, the colour shows first-order decay in the dark ( $k = 4.1 \times 10^{-2} \text{ min}^{-1}$  at  $25^\circ$ ); in the other solvents, the decay is more complex. Oxygen or iodine immediately discharges the colour. In basic solution a deep orange-red colour is produced (see Figure), which is also oxygen-sensitive and decays more slowly ( $k = 3.2 \times$

$10^{-3} \text{ min}^{-1}$  at  $25^\circ$ ). Strong electron spin resonance (e.s.r.) signals are associated with the coloured solutions: a 24-line spectrum of six quartets (neutral) and a six-line spectrum (basic). We assign these spectra to the 1-hydroxyphenalen-1-yl radical (II) and its anion, respectively,<sup>3</sup> which have been previously detected by polarography.<sup>4</sup> However, the optical spectra shown in the Figure are not due to these radicals. This conclusion is based on (1) a faster e.s.r. signal decay ( $k = 0.18 \text{ min}^{-1}$ )<sup>3</sup> than optical decay, (2) the absence of transient colour in diphenylmethane solutions which show the 24-line e.s.r. spectrum, and (3) the approximate equality of the rate of colour formation observed by flash technique and the rate of radical decay.

In propan-2-ol and methanol, irradiation produces at least six compounds. 2,3-Dihydrophenalen-1-one (III) was isolated in both solvents in 13% yield [based on converted ketone (I)]. In diphenylmethane, the ketone (III) is the major product. This direct photochemical reduction of a double bond appears to be without precedent, although a sensitised reduction has been reported.<sup>5</sup> The propanol reaction also furnished two yellow compounds, which have analytical and spectral data consistent with their being diketonic dimers of ketone (I). No acetone was detected, and an attempt to trap



Spectra of intermediates from  $1 \times 10^{-3} \text{ M}$ -phenalen-1-one in (1) propan-2-ol, and (2) 0.1 M-NaOH (2:3:1 propan-2-ol-water): (A) before, (B) immediately after irradiation, (C) after admission of oxygen.

\* Department of Chemistry, Northeastern University, Boston 15, Mass., U.S.A.

† Energetics Branch, Air Force Cambridge Research Laboratories, Bedford, Mass., U.S.A.

<sup>1</sup> G. Porter and P. Suppan, *Proc. Chem. Soc.*, 1964, 191; J. N. Pitts, Jr., H. W. Johnson, Jr., and T. Kuwana, *J. Phys. Chem.*, 1962, **66**, 2456, and references cited therein.

<sup>2</sup> P. E. Eaton, *J. Amer. Chem. Soc.*, 1962, **84**, 2344; A. Mustafa, *Chem. Rev.*, 1952, **51**, 1.

<sup>3</sup> G. P. Rabold and K. Weiss, manuscript in preparation.

<sup>4</sup> H. Berg, Preprints Fifth Internat. Symp. on Free Radicals, Uppsala, 1961, paper 8; H. Beckmann, *Austral. J. Chem.*, 1961, **14**, 229; H. Beckmann and P. Silbermann, *Chem. and Ind.*, 1955, 1635.

<sup>5</sup> G. W. Griffin and E. J. O'Connell, *J. Amer. Chem. Soc.*, 1962, **84**, 4148.



HO-CMe<sub>2</sub>· radicals as terebinic acid by the addition of maleic acid<sup>6</sup> failed.

The transient colours are reminiscent of the intermediate in the photo-reduction of benzophenone in propan-2-ol, for which radical structures could not be confirmed by e.s.r. measurements.<sup>7</sup> Our results leave little doubt that the radicals generated by reaction of excited ketone with solvent are precursors of the coloured diamagnetic intermediates. The latter

appear to incorporate the solvent or a solvent-derived oxidation product. Significantly, solvents in which colour is observed either bear carbonyl groups or can give rise to them by oxidation. Although the sensitivity to oxygen and iodine may be an intrinsic property of the intermediate, it is more likely to be due to an equilibrium with radicals in which the diamagnetic molecule is heavily favoured.

(Received, August 5th, 1964.)

\* Cf. G. O. Schenck, G. Koltzenburg, and H. Grossmann, *Angew. Chem.*, 1957, **69**, 177.

<sup>7</sup> G. O. Schenck, W. Meder, and M. Pape, *Proc. Internat. Conf. Peaceful Uses At. Energy*, Geneva, 1958, **29**, 352; J. H. Sharp, T. Kuwana, A. Osborne, and J. N. Pitts, Jr., *Chem. and Ind.*, 1962, 508; J. N. Pitts, Jr., R. L. Letsinger, R. P. Taylor, J. M. Patterson, G. Recktenwald, and R. B. Martin, *J. Amer. Chem. Soc.*, 1959, **81**, 1068.

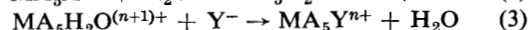
### Direct Substitution of I<sup>-</sup> by Cl<sup>-</sup> in Cr(H<sub>2</sub>O)<sub>5</sub>I<sup>2+</sup>

By MICHAEL ARDON\*

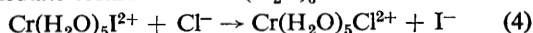
It has been generally assumed<sup>1</sup> that substitution reactions of octahedral complexes in which ligand X<sup>-</sup> is substituted by ligand Y<sup>-</sup> as in



proceed *via* an intermediate aquo (or hydroxo) complex



This generalization† is brought into serious question by the finding reported here that even in mono-substituted aquo-complexes, such as Cr(H<sub>2</sub>O)<sub>5</sub>I<sup>2+</sup>, direct substitution takes place without the intermediate formation of Cr(H<sub>2</sub>O)<sub>6</sub><sup>3+</sup>:



The iodopenta-aquochromic ion<sup>3</sup> is kinetically (as well as thermodynamically) much less stable to aquation than other halogenopenta-aquochromic ions and is aquated completely within a few hours in aqueous perchloric acid, at room temperature. When other ions are absent, the sole product is Cr(H<sub>2</sub>O)<sub>6</sub><sup>3+</sup>, but if Cl<sup>-</sup> is present a considerable quantity of Cr(H<sub>2</sub>O)<sub>5</sub>Cl<sup>2+</sup> is produced together with Cr(H<sub>2</sub>O)<sub>6</sub><sup>3+</sup>.

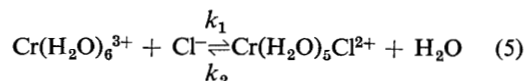
Cr(H<sub>2</sub>O)<sub>5</sub>I<sup>2+</sup> was prepared by oxidation of chromous perchlorate with iodine,<sup>3</sup> and purified by absorption on a cooled cation-exchange column (Dowex 50 4×) and elution with 0.4M-perchloric acid. This operation was carried out at 0.5°.

The rate of decomposition of CrI<sup>2+</sup> was measured spectrophotometrically (at 650 mμ) at 30° in 1M-perchloric and 1M-hydrochloric acid, respectively. The pseudo-first-order rate constant was determined

from the plot of log (D<sub>t</sub> - D<sub>∞</sub>) versus *t* (found: 0.0138 min.<sup>-1</sup> and 0.0147 min.<sup>-1</sup> in 1M-HClO<sub>4</sub> and 1M-HCl, respectively).

The solutions were kept at 30° for 7 hr. (~ 8 half lives) and were then absorbed on cation-exchange columns (Dowex 50 8×). The perchloric acid solution contained only the Cr(H<sub>2</sub>O)<sub>6</sub><sup>3+</sup> ion. In the hydrochloric acid solution a green band was observed below the blue hexaquo band and after elution with 1M-perchloric acid it was identified as Cr(H<sub>2</sub>O)<sub>5</sub>Cl<sup>2+</sup>. The ratio of CrCl<sup>2+</sup> to Cr(H<sub>2</sub>O)<sub>6</sub><sup>3+</sup> was 14.3:100 in this solution, and is considerably higher than the relative increase in decomposition rate observed in 1M-hydrochloric acid (6.5:100).

The chloro-complex could not be formed *via* the Cr(H<sub>2</sub>O)<sub>6</sub><sup>3+</sup> ion by a secondary reaction with Cl<sup>-</sup> as in



because this reaction is too slow: at 30° the rate constant *k*<sub>1</sub> is smaller than 1.6 × 10<sup>-7</sup> moles l<sup>-1</sup> sec.<sup>-1</sup>,<sup>4</sup> so that less than 0.5% of the complex could be formed by this reaction path. In order to check whether the reaction products of the aquation reaction of CrI<sup>2+</sup> do not catalyse the formation of CrCl<sup>2+</sup> by reaction (5) a control experiment was conducted in which the iodo-complex was aquated completely in dilute perchloric acid and was then added to a 1M-hydrochloric acid solution. This mixture was kept for 7 hr. at 30°C and analysed by ion-exchange chromatography—no trace of CrCl<sup>2+</sup> could be detected.

(Received, July 6th, 1964.)

\* Department of Inorganic and Analytical Chemistry, The Hebrew University of Jerusalem, Israel.

† The only reported exception concerns the azidopentacyanocobaltic anion, in which direct substitution of azide by thiocyanate takes place.<sup>2</sup>

<sup>1</sup> Stranks, "Modern Coordination Chemistry", Ed. Lewis and Wilkins, Interscience, 1960, p. 136.

<sup>2</sup> Haim and Wilmarth, *J. Inorg. Chem.*, 1962, **1**, 583.

<sup>3</sup> Taube and Myers, *J. Amer. Chem. Soc.*, 1954, **76**, 2103.

<sup>4</sup> Baltisberger and King, *J. Amer. Chem. Soc.*, 1964, **86**, 795.

Conformational Free-energy Differences in 3 $\beta$ -Substituted Steroids

By D. NEVILLE JONES and D. E. KIME\*

THE differences in free energy between a substituent axially and equatorially orientated in a cyclohexane ring ('conformational free-energy differences') have been adduced from investigations of monocyclic compounds.<sup>1</sup> These conformational free-energy differences are not always additive when applied to disubstituted monocyclic cyclohexane derivatives.<sup>1,2</sup>

cholestan-6-one (I; R = H) and 5 $\beta$ -cholestan-6-one (II; R = H) and then  $K_x$  was determined for various 3 $\beta$ -substituted derivatives of 5 $\alpha$ - and 5 $\beta$ -cholestan-6-one. Conformational analysis indicated that the introduction of a 3 $\beta$ -substituent X in these compounds should lead to values of  $K_x$  lower than  $K_H$ , since such substituents are equatorial in (I; R = X) and axial in (II; R = X).

Starting material	Method	$K$	$-\Delta G^\circ_x$ (kcal.)	$-\Delta G^\circ_H$ (kcal.)	$-(\Delta G^\circ_x - \Delta G^\circ_H)^*$ (kcal.)	Lit. values	Ref.
I; R = H	t	2.95		1.08†		0.9	3
II; R = H	t	2.57		0.95		1.2	4
I; R = H	c	4.95		1.12			
I; R = OH	t	4.83	1.57		0.5		
II; R = OH	t	4.65	1.54		0.5	0.4—0.9	1
I; R = OH	c	15.8	1.93		0.9		
I; R = OAc	t	6.12	1.80		0.7	0.4—0.7	1
II; R = OAc	t	5.55	1.72		0.6		
I; R = Cl	t	4.04	1.40		0.3		
II; R = Cl	t	3.97	1.37		0.3	0.3—0.5	1
I; R = Cl	c	7.26	1.39		0.3		
I; R = OMe	t	4.40	1.48		0.4	0.5—0.7	1

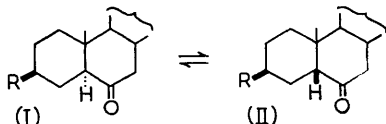
\* to the nearest 0.1 kcal.

† this value taken in further calculations.

t thermal equilibration at 230°.

c acid-catalysed equilibration in aqueous ethanol at 80°.

We have measured the free-energy differences between substituents axially and equatorially orientated at C-3 in steroids and found them to be in general agreement with values obtained in monocyclic compounds. Our method involved the equilibration of 3 $\beta$ -substituted 5 $\alpha$ -cholestan-6-ones with 3 $\beta$ -substituted 5 $\beta$ -cholestan-6-ones by heating them to 230° under nitrogen in a glass vessel for 3—5 hr. In each case equilibrium was approached



from both sides. The equilibrium constant  $K_H$  was first determined for the interconversion of 5 $\alpha$ -

Equilibrium constants were determined by direct isolation of each component by thin-layer chromatography. Then  $\Delta G^\circ_H$  was calculated for the equilibrium (I; R = H)  $\rightleftharpoons$  (II; R = H), and also  $\Delta G^\circ_x$  for the equilibrium (I; R = X)  $\rightleftharpoons$  (II; R = X). The conformational free-energy differences between C-3 axial and equatorial substituents was then given by  $\Delta G^\circ_x - \Delta G^\circ_H$  (see Table).

The conformational free-energy values recorded in the Table are reliable only to  $\pm 0.1$  kcal. at best, as in other methods of determination of free-energy values,<sup>1</sup> and our values are in general agreement with those obtained previously. The disparity in the values obtained for the hydroxyl group in the absence of solvent (thermal equilibration) and in the presence of ethanol (acid-catalysed equilibration) can be

\* Chemistry Department, Sheffield University.

<sup>1</sup> Eliel, *J. Chem. Educ.*, 1960, **87**, 126; "Stereochemistry of Carbon Compounds", McGraw-Hill, New York, 1962, p. 234.

<sup>2</sup> Eliel and Lukach, *J. Amer. Chem. Soc.*, 1957, **79**, 5986.

<sup>3</sup> Turner, *J. Amer. Chem. Soc.*, 1952, **74**, 2118.

<sup>4</sup> Allinger, Darooge, and Hermann, *J. Org. Chem.*, 1961, **26**, 3626.

attributed to the greater effective size of the hydroxy-group in the latter due to intermolecular hydrogen bonding.<sup>1</sup> The values obtained for the acetate group agree with that of Eliel and Gianni<sup>5</sup> (0.7) but not with that of Chapman and his co-workers<sup>6</sup> (1.5).

The agreement between the conformational free-energy differences obtained after thermal equilibration at 230°, and acid-catalysed equilibration at 80°, and the previously reported values obtained at various temperatures between 25° and 80°, indicate that the entropy changes involved in these equilibrations are very small.

It appears that conformational free-energy differ-

ences determined in monocyclic systems are applicable to 3 $\beta$ -substituted steroids. Conversely, conformational free-energy values can conveniently be determined by using the 3 $\beta$ -substituted cholestan-6-one system. The method is capable of considerable refinement since optical rotatory dispersion techniques can be used to determine the equilibrium constants accurately.<sup>4,7</sup> Previous equilibration methods, except that of Eliel and Rerick,<sup>8</sup> required that the group being investigated was itself epimerizable, and the kinetic techniques were applicable only to reactive groups. These requirements do not apply to the present procedure.

(Received, August 20th, 1964.)

<sup>5</sup> Eliel and Gianni *Tetrahedron Letters*, 1962, 97.

<sup>6</sup> Chapman, Parker, and Smith, *J.*, 1960, 3634.

<sup>7</sup> Djerassi, Riniker, and Riniker, *J. Amer. Chem. Soc.*, 1956, 78, 6362.

<sup>8</sup> Eliel and Rerick, *J. Amer. Chem. Soc.*, 1960, 82, 1367.

### The Quenching of Mercury 2537Å Resonance Radiation by Fluorinated Olefins

By A. R. TROBRIDGE and K. R. JENNINGS\*

ALTHOUGH the quenching of mercury 2537Å resonance radiation by hydrocarbons has received considerable attention,<sup>1-3</sup> there are very few values available in the literature of the quenching cross-sections of fluorinated compounds.<sup>4</sup> Gunning and Strausz<sup>2</sup> have suggested that the Hg 6<sup>3</sup>P<sub>1</sub> atom is electrophilic in nature, and it is therefore to be expected that if fluorine replaces hydrogen in a molecule, the quenching cross-section will decrease as a result of the strong inductive effect exerted by fluorine.

As part of a study of the reactions of fluorinated olefins in mercury-photosensitised systems, we have measured the quenching cross-sections of a number of olefins, and these together with relevant literature values, are given in the Table.

combustion in a copper oxide furnace and by mass spectrometry. A plot of  $1/\Phi_N$  against [olefin]/[N<sub>2</sub>O] was made in each case, and the method of least squares was used to evaluate the quenching cross-section of the olefin relative to that of nitrous oxide. The figures in the Table are based on a value of  $\sigma^2 = 18.0\text{Å}^2$  for nitrous oxide.<sup>1</sup>

The progressive reduction of the quenching cross-sections in the series C<sub>2</sub>H<sub>4</sub> → C<sub>2</sub>F<sub>4</sub> confirms the electrophilic nature of the Hg 6<sup>3</sup>P<sub>1</sub> atom. The two values quoted for the propenes show a similar trend and may be compared with  $\sigma^2 = 42.6\text{Å}^2$  for CH<sub>3</sub>-CH=CH<sub>2</sub>. The similarity in the quenching cross-sections of C<sub>2</sub>F<sub>4</sub> and C<sub>3</sub>F<sub>6</sub> suggests that the CF<sub>3</sub> group and the F atom deactivate the double bond by about the same amount. Further work is in

Molecule	C <sub>2</sub> H <sub>4</sub>	CH <sub>2</sub> =CHF	CH <sub>2</sub> =CF <sub>2</sub>	CHF=CF <sub>2</sub>	CF <sub>2</sub> =CF <sub>2</sub>	CF <sub>3</sub> -CF=CF <sub>2</sub>	CH <sub>3</sub> -CF=CH <sub>2</sub>
$\sigma^2$ (Å <sup>2</sup> )	31	29.8	27.2	19.7	10.6	10.9	36.6
this work							
$\sigma^2$ (Å <sup>2</sup> )	31 <sup>1</sup>		26.3 <sup>4</sup>		9.3 <sup>4</sup>		
literature							

These values were obtained in a circulating system at  $23 \pm 1^\circ\text{C}$ , the nitrous oxide technique developed by Cvetanovic being used.<sup>5</sup> Non-condensable gases were collected by a Toepler pump and analysed by

progress with the aim of determining the effect on the quenching cross-section of varying the position and degree of substitution in other fluorinated olefins.

(Received, September 16th, 1964.)

\* Department of Chemistry, The University, Sheffield, 10.

<sup>1</sup> R. J. Cvetanovic, "Progress in Reaction Kinetics," Vol. II, Pergamon, Ed. G. Porter, 1964.

<sup>2</sup> H. E. Gunning and O. P. Strausz, "Advances in Photochemistry," Vol. I, Wiley, Ed. W. A. Noyes, G. S. Hammond, and J. N. Pitts, 1963.

<sup>3</sup> Y. Rousseau and H. E. Gunning, *Canad. J. Chem.*, 1963, 41, 465.

<sup>4</sup> M. G. Bellas, Y. Rousseau, O. P. Strausz, and H. E. Gunning, *J. Chem. Phys.*, 1964, 41, 768.

<sup>5</sup> R. J. Cvetanovic, *J. Chem. Phys.*, 1955, 23, 1208.

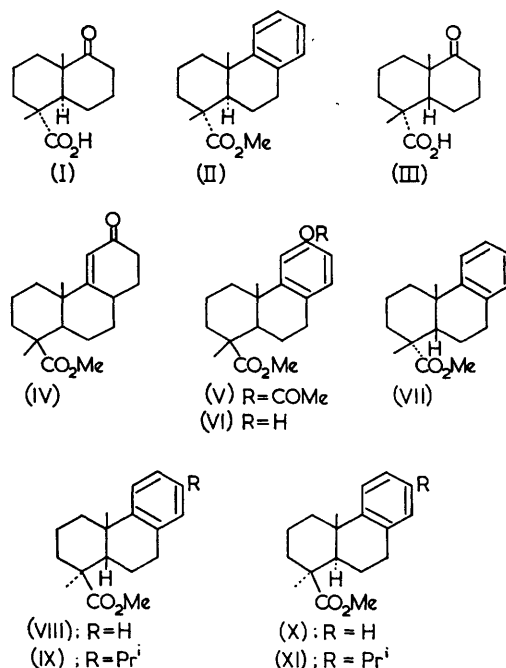
## Palladium-Charcoal Induced Isomerization of Diterpenoid Resin Acids\*

By C. T. MATHEW, Miss G. SEN GUPTA, and P. C. DUTTA†

IN an earlier communication,<sup>1</sup> the stereochemistry of a bicyclic keto-acid, m.p. 141°, was depicted as (I) because of its conversion into methyl dehydrodeisopropylabietate (II). Spencer,<sup>2</sup> reported the synthesis of an isomeric keto-acid, m.p. 184°, which he also converted into (II). It therefore became necessary to re-examine our previous results, and we are now able to report that our bicyclic acid is in fact (III) and that Spencer's acid is (I) as reported.<sup>2</sup> Discernibly the discrepancy arose during the dehydrogenation step involving heating with palladium-charcoal<sup>1,2</sup> leading to isomerization at the ring junction. Conversion of our acid into a known tricarboxylic compound (*e.g.*, VII) through processes not involving possibility of isomerization was envisaged as a solution to this problem. The ester (IV)<sup>1</sup> was converted into the enol acetate ( $\lambda_{\text{max}}$ . 268 m $\mu$ ,  $\log \epsilon$  3.8, in alcohol) by treatment with acetic anhydride, acetyl chloride, and pyridine.<sup>3</sup> Bromination with *N*-bromosuccinimide in carbon tetrachloride in the presence of fused potassium carbonate<sup>4</sup> followed by dehydrobromination with collidine produced (V) which on mild alkaline hydrolysis afforded the phenol (VI). The phenolic hydroxyl group was removed by diethyl phosphite followed by lithium and ammonia.<sup>5</sup> On concentration the product furnished (VII), m.p. 89–90°, [overall yield, *ca.* 20%, based on (IV)], the identity being established through mixed melting point with authentic material.<sup>6</sup> Our findings are thus more in confirmation of Johnson's generalizations<sup>7</sup> of axial attack in angular methylation than otherwise, as suggested earlier.<sup>1</sup>

That heating with palladium-charcoal had brought about isomerization of the *cis*-ester (VII) to (II), alteration having occurred at the ring junction next to the carboxyl group, was further verified. The *cis*-ester (VIII)<sup>8</sup> with palladium-charcoal (10%) at 235–240° for 1 hr. gave methyl *trans*-deoxypodocarpate (X) in about 60% yield.

Similarly (IX)<sup>9</sup> underwent conversion into the *trans*-form (XI). This type of isomerization differs from that brought about with aluminium chloride by Wenkert,<sup>10</sup> and Ohta and Ohmori,<sup>11</sup> in that the change occurs at the junction farther from the benzene ring, and the former evidently proceeds through ionic mechanism. Dreiding's<sup>12</sup> observations with  $\alpha$ -decalones in presence of palladium-charcoal obviously involve participation of radicals. Any direct participation of the benzene ring in effecting the change at the ring junction is a remote possibility as this has also been observed with a few 9-methyl-*cis*-decalins.<sup>13</sup>



(Received, July 31st, 1964.)

\* These results were presented (by P.C.D.) at the International Conference on the Chemistry of Natural Products, Kyoto, Japan, 1964.

† Department of Organic Chemistry, Indian Association for the Cultivation of Science, Calcutta-32, India.

<sup>1</sup> Mathew and Dutta, *Proc. Chem. Soc.*, 1963, 135.

<sup>2</sup> Spencer, Weaver, Schwartz, Greco, and Smith, *Chem. and Ind.*, 1964, 577; We thank Prof. Spencer for sending a copy of the manuscript of his communication before publication.

<sup>3</sup> Velluz, Goffinet, Warnant, and Amiand, *Bull. Soc. chim. France*, 1957, 1289.

<sup>4</sup> Corbett and Speden, *J. Chem. Soc.*, 1958, 3710.

<sup>5</sup> Kenner and Williams, *J. Chem. Soc.*, 1955, 522.

<sup>6</sup> Saha, Ganguly, and Dutta, *J. Amer. Chem. Soc.*, 1959, **81**, 3670.

<sup>7</sup> Johnson, Allen, Hindersinn, and Pappo, *J. Amer. Chem. Soc.*, 1962, **84**, 2181.

<sup>8</sup> Ghatak, Datta, and Ray, *J. Amer. Chem. Soc.*, 1960, **82**, 1728.

<sup>9</sup> Sharma, Ghatak, and Dutta, *Tetrahedron*, 1963, **19**, 985.

<sup>10</sup> Wenkert and Jackson, *J. Amer. Chem. Soc.*, 1958, **80**, 211.

<sup>11</sup> Ohta and Ohmori, *Pharm. Bull. Japan*, 1957, **5**, 91.

<sup>12</sup> Ross, Smith, and Dreiding, *J. Org. Chem.*, 1955, **20**, 905.

<sup>13</sup> G. Sen Gupta, D. Phil. Thesis, Calcutta Univ. 1964.



# On the Mechanism of the Solid-state *cis-trans*-Photoisomerisation of 1,2-Dibenzoyl ethylene

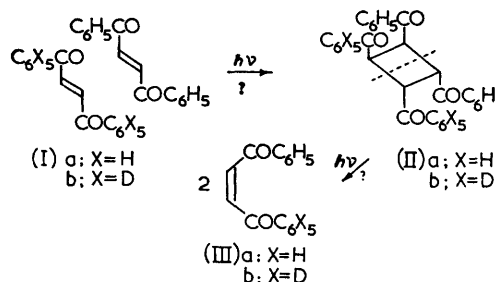
By G. W. GRIFFIN, E. J. O'CONNELL, and J. M. KELLIHER\*

THE recent detailed studies of sensitised<sup>1</sup> and unsensitised<sup>2</sup> *cis-trans*-photoisomerisation reactions have been restricted to the liquid phase, and no completely satisfying mechanistic description of this comparatively simple photochemical process appears yet to have been advanced.<sup>3</sup> Although the intimate details of the reaction remain to be clarified, it is generally conceded that isomerisation in solution proceeds through rotation in either an excited state or a vibrationally excited ground state.

Our work on the solid-state photochemistry of dimethyl fumarate and fumaronitrile<sup>4</sup> and earlier preliminary reports by G. M. J. Schmidt and his co-workers on the dimerisation of the  $\alpha$  and  $\beta$  crystal modifications of cinnamic acid<sup>5</sup> (which have since been extended to include other olefins)<sup>6</sup> suggest that stereochemical integrity is maintained during photodimerisations. The results to date confirm that the stereochemistry of the dimeric cyclobutanoid product is dictated by the crystal lattice geometry of the monomer, *i.e.*, direct bond formation occurs between nearest neighbour molecules in the lattice, and extensive isomerisation of the olefinic substrate and/or rotational equilibration during dimerisation is precluded.

It is noteworthy that *trans*-1,2-dibenzoyl ethylene (Ia) undergoes an exceedingly slow isomerisation to the colourless *cis*-modification (IIIa) on prolonged irradiation of the solid. In view of our earlier experience this transformation appeared unusual although it is not without analogy.<sup>7</sup> An inviting mechanism which avoids the necessity of invoking rotation in the solid consists of initial photodimerisation of (Ia) to *cis,trans,cis*-1,2,3,4-tetrabenzoylcyclobutane (IIa) which on subsequent irradiation under-

goes cleavage in the opposite sense (II; dotted line) to afford the *cis*-modification (IIIa).†



The validity of the suggested mechanism was investigated by irradiating an equimolar mixture of (Ia) and *trans*-1,2-di(pentadeuterobenzoyl)ethylene (Ib) which had been co-crystallised from methanol. The assumption that random distribution of (Ia) and (Ib) is attained appears eminently reasonable. The deuterated dibenzoyl ethylene was prepared by Friedel-Crafts acylation of deuterobenzene with fumaryl chloride and aluminium chloride in carbon disulphide. The mass spectrum of a sample of the co-crystallised mixture showed parent peaks of approximately equal intensity for the protio- and deuterio-components (*m/e* 236 and 246, Ia and Ib, respectively). After irradiation, the mixture was extracted with cyclohexane to remove preferentially the more soluble *trans*-form. The crude residual *cis*-isomer then was purified by elution chromatography on alumina followed by repeated recrystallisation. The mass spectrum of the purified *cis*-isomer also exhibited peaks at *m/e* 236 and 246. However, the peak at *m/e* 241 expected for (IIIb) was conspicuously absent. This result unequivocally excludes the

\* (E.J.O.C. and J.M.K.) Department of Chemistry, Yale University, New Haven, Conn.; (G.W.G.) Tulane University, New Orleans, La.

† The solid state isomerisations were conducted at 20° in sealed Pyrex ampoules. The olefin was deposited from solution on the inner surface of the ampoule by evaporation of solvent. A 250w photoflood lamp was employed as a light source and the irradiations were continued for a period of a week.

We had established earlier that (Ia) and (IIIa), unlike typical  $\alpha\beta$ -unsaturated carbonyl compounds, do not dimerise efficiently even in solution.<sup>3,7</sup> After prolonged irradiation of (Ia) in benzene with a 250w-cosmetic sun lamp only trace quantities of *trans,trans,trans*-1,2,3,4-tetrabenzoylcyclobutane (< 1%) could be isolated.

The photochemical cleavage of cyclobutane derivatives is well documented<sup>7</sup> and in fact the "*all-trans*"-isomer of (IIa) was shown to be photochemically unstable in solution. (See Griffin and Hager, *Rev. Chim. (Acad. R.P.R.)*, 1962, 7, 901.)

<sup>1</sup> Saltiel and Hammond, *J. Amer. Chem. Soc.*, 1963, **85**, 2515.

<sup>2</sup> Schulte-Frohlinde, *Annalen*, 1958, **615**, 114; Orlando, jun., Zimmerman, and Gianni, Abstracts, 147th National Meeting of the American Chemical Society, Philadelphia, Pennsylvania, April, 1964, p. 20N.

<sup>3</sup> Hammond and Turro, *Science*, 1963, **142**, 1541.

<sup>4</sup> Griffin, Basinski, and Velluro, *Tetrahedron Letters*, 1960, No. 3, 13; Griffin, Velluro, and Furukawa, *J. Amer. Chem. Soc.*, 1961, **83**, 2725; Griffin, Basinski, and Peterson, *J. Amer. Chem. Soc.*, 1962, **84**, 1012.

<sup>5</sup> Schmidt, *Acta Cryst.*, 1957, **10**, 793; Cohen and Schmidt, "Reactivity of Solids," de Boer, Ed., Elsevier Publishing Co., Amsterdam, 1951, p. 556; Bernstein and Quimby, *J. Amer. Chem. Soc.*, 1943, **65**, 1845.

<sup>6</sup> Sadeh and Schmidt, *J. Amer. Chem. Soc.*, 1962, **84**, 3970.

<sup>7</sup> Mustafa, *Chem. Rev.*, 1952, **51**, 5.

"crossover" mechanism envisioned for the *trans*-*cis*-isomerisation of solid 1,2-dibenzoyl ethylene, and is in accord with the observations made on benzylideneacetone in solution.†

One interpretation consistent with these results is that the solid-state dimerisations proceed *via* an excited species whose multiplicity differs from that involved in *trans*-*cis*-isomerisations. It is possible that dimerisation (which is essentially intramolecular in character in the solid matrix) could occur within

the short lifetimes associated with the singlet state. In contrast the inefficient rotational isomerisation in the solid may require lifetimes of the order expected for triplet species. It is noteworthy that no phosphorescence could be detected for (Ia) in methylcyclohexane-isopentane glass (5:1) at 77°K.<sup>8</sup> This, in conjunction with other evidence, suggests that intersystem crossing to the triplet state is not efficient.

(Received, June 22nd, 1964.)

† A similar mechanism has been advanced to explain the *trans*-*cis*-isomerisation of benzylideneacetone in solution (see House, *J. Org. Chem.*, 1959, **24**, 1374), and was rejected on the basis of convincing experimental data. However, in view of the rigidity inherent in the crystal lattice the possibility that such a mechanism could be operative in the solid appeared reasonable.

An X-ray crystallographic study has been initiated to establish if, in fact, *trans*-1,2-dibenzoyl ethylene does possess a lattice structure consistent with the suggested mechanism.

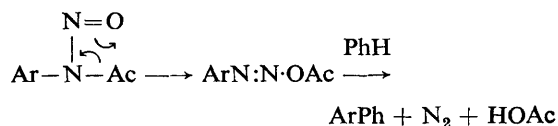
Mass spectral data were obtained on a modified C.E.C. 21-103A instrument.

<sup>8</sup> Griffin and O'Connell, *J. Amer. Chem. Soc.*, 1962, **84**, 4148.

## The Anomalous Decomposition of *o*-*t*-Butyl-*N*-nitrosoacetanilide: Evidence for the Participation of an Aryne

By J. I. G. CADOGAN and P. G. HIBBERT\*

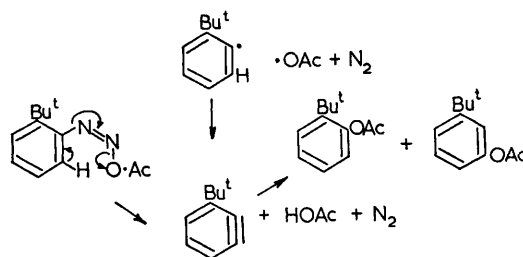
It is well known<sup>1</sup> that *N*-nitrosoacetylarylamines in aromatic solvents rearrange by way of four-membered intermediates to esters of diazoic acids, which arylate the solvent by way of aryl radicals to give the corresponding biaryl and acetic acid.



Certain aspects of the reactions have yet to be adequately explained however, *e.g.*, the formation of acetic acid in high yield, the very low accountability of methyl radicals and carbon dioxide (which would arise by decomposition of *free* acetyloxy-radicals), and absence of products (aryl acetates) of substitutions of the latter in the aromatic solvent.<sup>2</sup>

Cadogan, Hey, and Williams,<sup>3</sup> while noting that *p*-*t*-butyl-*N*-nitrosoacetanilide behaved normally on decomposition in benzene to give 4-*t*-butylbiphenyl, reported that the corresponding reaction of the *o*-isomer was anomalous in that the major product was an ester or mixture of esters believed to be the *t*-butylphenyl acetates. The anomalous nature of the reaction was subsequently confirmed by Rondstvedt and Blanchard,<sup>4</sup> neither group offered an explanation.

It is now possible to advance an explanation of the behaviour of the *o*-*t*-butyl derivative. In this case it is assumed that rearrangement of the nitroso-compound gives the *cis*-diazoate. Huisgen has shown that in certain cases the *trans*-diazoate is formed.<sup>5</sup> The formation of the *cis*-isomer, though less likely, cannot be precluded in the case of simple nitrosoacetylarylamines, however. Examination of scale models (Dreiding Stereomodels) shows that the presence of an *o*-*t*-butyl group greatly increases the possibility of formation of the *cis*-isomer. It is further assumed that the bulk *t*-butyl group constrains the intermediate diazoacetate in such a way that concerted decomposition occurs to give 3-*t*-butylbenzynes and acetic acid. It is not possible to distinguish between this and the alternative stepwise homolytic process:



\* St. Salvator's College, University of St. Andrews, St. Andrews, Fife.

<sup>1</sup> Williams, "Homolytic Aromatic Substitution," Pergamon Press, 1959; Huisgen, *Annalen*, 1951, **573**, 163.

<sup>2</sup> Cf. Rüchardt and Merz, *Tetrahedron Letters*, 1964, 2431.

<sup>3</sup> Cadogan, Hey, and Williams, *J.*, 1954, 3352.

<sup>4</sup> Rondstvedt and Blanchard, *J. Amer. Chem. Soc.*, 1955, **77**, 1771.

<sup>5</sup> Huisgen, *Annalen*, 1951, **574**, 171.



In either event the aryne and acetic acid, which are created in close proximity, would be expected to react to give a mixture of *o*- and *m*-*t*-butylphenyl acetates.

The presence in the nitrosoacetanilide of *ortho*-groups smaller than *t*-butyl would result in less constraint leading to the formation of the *trans*-diazote which would decompose in the normal fashion.

The decomposition of *o*-*t*-butyl-*N*-nitrosoacetanilide in benzene has now been reinvestigated in the light of the above considerations. In agreement with prediction the product has been shown (g.l.c. and n.m.r.) to contain *o*- and *m*-*t*-butylphenyl acetates (total yield 46%) in the ratio 2:1, the *p*-isomer being absent (0.03% would have been detected). Hydrolysis of the ester fraction gave a mixture of the correspond-

ing *t*-butylphenols. The g.l.c. results were checked by analyses on widely different column packings and with different conditions.

The formation of 3-*t*-butylbenzyl has been further confirmed by the isolation of 2-*t*-butyltritycene (9%) in addition to *o*- and *m*-*t*-butylphenyl acetate (20%) from the reaction of *o*-*t*-butyl-*N*-nitrosoacetanilide with anthracene in benzene. The structure of the 2-*t*-butyltritycene was confirmed by comparison of its n.m.r. and u.v. spectra with those of triptycene itself.

Examination of the ester fraction in the last experiment after removal of 2-*t*-butyltritycene reveals that the relative proportion of *o*-isomer is increased, thus indicating that only some of this isomer arises from a mechanism involving the aryne.

(Received, August 27th, 1964.)

### The Structure of Trisdiaminecobalt(III) Ion-pairs

By S. F. MASON and Miss B. J. NORMAN\*

WERNER's observation<sup>1</sup> that the molecular rotation of a dissymmetric metal complex ion is affected by the gegenion has been studied recently<sup>2,3</sup> in connection with outer-sphere co-ordination. The molecular rotation is the sum of contributions from the optically-active electronic transitions of the molecule, and it is now found that each circular dichroism band of (+)-Co(en)<sub>3</sub><sup>3+</sup> and of (+)- and (-)-Co(+pn)<sub>3</sub><sup>3+</sup> in aqueous solution is changed by the addition of polarizable anions (Figs. 1 and 2). The effects are larger the greater the charge of the anion, and they are qualitatively similar for trigonal and tetrahedral oxyanions at low concentration. In terms of the rotational strength, *R*, measured by the circular dichroism band area, the changes due to an increase in anion concentration consist in the case of (+)-Co(en)<sub>3</sub><sup>3+</sup> of a decrease in *R*(*E*<sub>a</sub>) and a compensating increase in *R*(*A*<sub>2</sub>), an enhancement of *R*(*E*<sub>b</sub>), and the development of a new circular dichroism band and unpolarized absorption in the 2600 Å region (Fig. 1). Analysis of the 2600 Å absorption by standard methods<sup>4</sup> indicates the formation of a 1:1 ion-pair. With (+)-Co(+pn)<sub>3</sub><sup>3+</sup>, but not (-)-Co(+pn)<sub>3</sub><sup>3+</sup>, quantitatively similar spectroscopic changes are observed. In the case of (-)-Co(+pn)<sub>3</sub><sup>3+</sup> the form of the variation of *R*(*E*<sub>a</sub>) + *R*(*A*<sub>2</sub>) with anion concentration is different (Fig. 2), the two bands being unresolved in this complex, and no circular

dichroism absorption is measurable at 2600 Å although an unpolarized band is found at that wave-

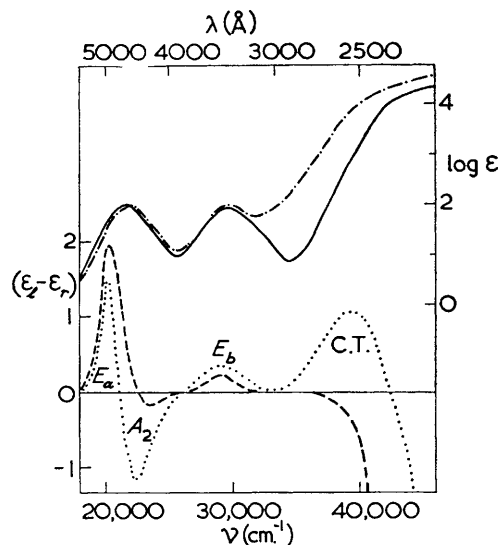


FIG. 1. The electronic spectrum of (+)-Co(en)<sub>3</sub>(ClO<sub>4</sub>)<sub>3</sub>; unpolarized absorption ——— in water, and — . — . in 0.05M-phosphate; circular dichroism ——— in water, and ..... in 0.05M-phosphate.

\* Chemistry Department, The University of Exeter. Present address: School of Chemical Sciences, University of East Anglia, Norwich.

<sup>1</sup> Werner, *Ber.*, 1912, **45**, 121.

<sup>2</sup> Albinak, Bhatnagar, Kirschner, and Sonnessa, *Canad. J. Chem.*, 1961, **39**, 2360.

<sup>3</sup> Larsson, *Acta Chem. Scand.*, 1962, **16**, 2267.

<sup>4</sup> Evans and Nancollas, *Trans. Faraday Soc.*, 1953, **49**, 363; Taube and Posey, *J. Amer. Chem. Soc.*, 1953, **75**, 1463; *ibid.*, 1956, **78**, 15.

length. The presence or absence of circular dichroism at 2600 Å indicates that an oxyanion and (+)-Co(en)<sub>3</sub><sup>3+</sup> or (+)-Co(+pn)<sub>3</sub><sup>3+</sup> but not (-)-Co(+pn)<sub>3</sub><sup>3+</sup> have a preferred mutual orientation in the ion-pair.

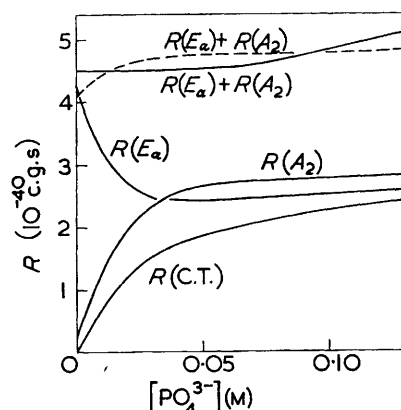
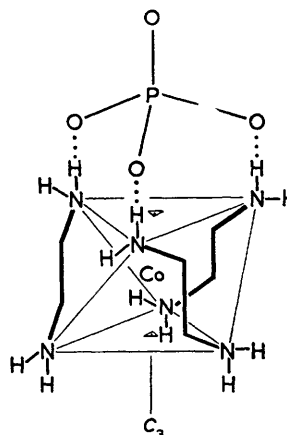


FIG. 2. The variation with phosphate-ion concentration of the rotational strengths  $R$  of the electronic transitions given by (+)-Co(en)<sub>3</sub><sup>3+</sup> (full lines) and by (-)-Co(+pn)<sub>3</sub><sup>3+</sup> (dashed line). The symmetry representations refer to the bands illustrated in Fig. 1.

The *lel* and *ob* conformations of the chelate rings are fixed in (+)- and (-)-Co(+pn)<sub>3</sub><sup>3+</sup>, respectively.<sup>5</sup> In the *lel* conformation, which is adopted by Co(en)<sub>3</sub><sup>3+</sup> in the crystals with known structures,<sup>6</sup> two sets of three N-H bonds have a polar direction nearly parallel to the three-fold axis ( $C_3$ ) and three sets of two N-H bonds are directed perpendicular to the  $C_3$  axis. In the *ob* conformation no two N-H bonds have a common orientation. Thus the probable structure of the ion-pair formed by oxyanions with (+)-Co(en)<sub>3</sub><sup>3+</sup> or (+)-Co(+pn)<sub>3</sub><sup>3+</sup> is (I) for the methyl groups of the latter complex ion would impede the formation of hydrogen bonds directed perpendicular to the  $C_3$  axis.

The absorption and circular dichroism bands of the ion-pair (I) at 2600 Å are due to the transfer of charge from the anion to the cation. The method<sup>7</sup> of Wolfsberg and Helmholz shows that the highest occupied orbital of trigonal and tetrahedral oxyanions with a closed shell has  $A$  symmetry in the  $C_3$  group of the ion-pair (I), consisting of an anti-bonding combination of oxygen 2p lone-pair

orbitals directed tangentially to the circle described by the radius vector from the  $C_3$  axis to the hydrogen-bonded oxygen atoms. The lowest unoccupied orbitals of Co(en)<sub>3</sub><sup>3+</sup> are the  $d_{\gamma}$  orbitals with  $E$  symmetry in the group  $C_3$ . Thus the charge transfer (C.T.) transition has moments directed perpendicular to the  $C_3$  axis and it mixes with other transitions of  $E$  symmetry. In particular, part of the magnetic moment of the  $E_a$  transition is borrowed and shared with the  $E_b$  transition, diminishing  $R(E_a)$ , enhancing  $R(E_b)$ , and giving a non-zero  $R(C.T.)$ . In the free randomly-orientated (+)-Co(en)<sub>3</sub><sup>3+</sup> ion  $R(E_a)$  and  $R(A_2)$ , which are opposed in sign, mutually cancel<sup>8</sup> to within 5%, so that the decrease in  $R(E_a)$  due to ion-pairing results in a commensurate increase in  $R(A_2)$ . By other mechanisms the exact compensation of the observed changes (Fig. 2) in  $R(E_a)$  and  $R(A_2)$  would not be generally expected.



At low concentrations the effect of sulphate and thiosulphate is similar to that of phosphate (Fig. 2), but with these anions at concentrations  $> 0.2M$  the previous changes are reversed and the circular dichroism spectrum of (+)-Co(en)<sub>3</sub><sup>3+</sup> reverts to that of the free cation, owing to the breakdown of the specific orientation of the ion-pair (I) in the denser ionic atmosphere. At the same time a small increase in the sum  $R(E_a) + R(A_2)$  is found, an effect observed additionally with halide and hydroxide at all concentrations. Perchlorate at any practicable concentration has virtually no effect upon the circular dichroism spectra of Co(III) complexes in aqueous solution.

(Received, August 12th, 1964.)

<sup>5</sup> Corey and Bailar, *J. Amer. Chem. Soc.*, 1959, **81**, 2620.

<sup>6</sup> Nakatsu, Saito, and Kuroya, *Bull. Chem. Soc. Japan*, 1956, **29**, 428; Nakatsu, Shiro, Saito, and Kuroya, *ibid.*, 1957, **30**, 158; Nakatsu, *ibid.*, 1962, **35**, 832.

<sup>7</sup> Wolfsberg and Helmholz, *J. Chem. Phys.*, 1952, **20**, 837.

<sup>8</sup> McCaffery and Mason, *Mol. Phys.*, 1963, **6**, 359.

## The Photochemical Formation of Trifluoromethoxyl Fluoride

By P. J. AYMONINO\*

TRIFLUOROMETHOXYL FLUORIDE (prepared<sup>1</sup> from methanol, or carbon monoxide, or carbonyl fluoride and fluorine) is one of the few thermally stable substances containing fluorine bonded to oxygen.

To determine whether fluorine atoms are able to react with carbonyl fluoride even at room temperature, we have photolysed fluorine molecules in the presence of carbonyl fluoride. Fluorine and carbonyl fluoride do not react in the dark at room temperature.

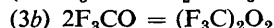
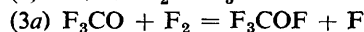
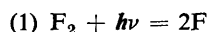
Carbonyl fluoride was prepared before each experiment in a quartz vessel by adding fluorine slowly to carbon monoxide.<sup>2</sup> Infrared spectroscopy spectra showed that carbon dioxide and traces of silicon tetrafluoride were the only impurities present in carbonyl fluoride so prepared.

Mixtures of carbonyl fluoride and an excess of fluorine (1:2 to 1:3) below atmospheric pressures were irradiated for several hours at 35°C with a mercury high-pressure quartz lamp in a quartz vessel immersed in a water-thermostat made of Pyrex glass (to cut off light of too-short wavelength). At the end of the reaction the pressure decrease was about 75%

of the value expected from the stoichiometry of the reaction:  $F_2CO + F_2 = F_3COF$ .

Trifluoromethoxyl fluoride was the main product. It was identified by i.r.-spectroscopy and gas density, after its separation by low-temperature distillation from small quantities of bistrifluoromethyl peroxide, carbon dioxide, silicon tetrafluoride, and traces of carbonyl fluoride and carbon tetrafluoride. Trifluoromethoxyl fluoride accounted for 80% of the original carbon monoxide, as determined iodometrically.<sup>1</sup>

As carbonyl fluoride does not absorb at the wavelength employed, fluorine atoms must be responsible for the formation of the trifluoromethoxyl fluoride and bistrifluoromethyl peroxide by schemes of the type:



Trifluoromethoxyl radicals are also produced by the photolysis of trifluoromethoxyl fluoride.<sup>3</sup>

(Received, February 10th, 1964.)

\* Instituto Superior de Investigaciones, Facultad de Química y Farmacia, Universidad Nacional de La Plata, La Plata, República Argentina.

<sup>1</sup> Kellogg and Cady, *J. Amer. Chem. Soc.*, 1948, **70**, 3986.

<sup>2</sup> Heras, Arvia, Aymonino, and Schumacher, *Z. phys. Chem.*, 1961, **28**, 250.

<sup>3</sup> Porter and Cady, *J. Amer. Chem. Soc.*, 1957, **79**, 5625; Allison and Cady, *Ibid.*, 1959, **81**, 1089; Pass and Roberts, *Inorg. Chem.*, 1963, **2**, 1016; and our own preliminary results.

## The Existence of Two Crystalline Forms of Anhydrous Copper(II) Nitrate

By N. LOGAN, W. B. SIMPSON, and S. C. WALLWORK\*

DURING the determination of the crystal structure of anhydrous copper(II) nitrate,<sup>1</sup> two types of single crystal X-ray photograph were recognised. Samples of the substance giving each type of photograph have now been studied more extensively. Since both substances gave correct analyses for copper(II) nitrate yet differed in their X-ray powder photographs and infrared spectra, they must simply be two different crystalline modifications. It is now realised that the published infrared data<sup>2</sup> and some e.s.r. measurements<sup>3</sup> relate to what is now termed the  $\beta$ -form, whereas the crystal structure work so far reported relates to the  $\alpha$ -form. We therefore give below some characteristic data by means of which the two forms may be distinguished.

$\alpha$ -Cu(NO<sub>3</sub>)<sub>2</sub>. This is obtained as a crystalline powder by heating the adduct Cu(NO<sub>3</sub>)<sub>2</sub>·N<sub>2</sub>O<sub>4</sub> *in vacuo* to about 100°. Attempts to recrystallise this form by sublimation have always resulted in a mixture of the two forms. The most significant feature of the infrared spectrum of the  $\alpha$ -form is the absence of any strong absorption bands above 1510 cm.<sup>-1</sup> and the appearance of a band at 1435 cm.<sup>-1</sup>. Lines in the X-ray powder pattern (*d* values in Å, and qualitative intensities; Cu-K $\alpha$  radiation,  $\lambda$  = 1.542Å) down to *d* = 1.70Å are as follows: 5.57vs; 4.31vs; 4.14s; 3.78w; 3.54w; 3.41m; 3.33w; 3.08mw; 2.99mw; 2.79s; 2.69w; 2.53m; 2.42m; 2.34m; 2.30m; 2.22m; 2.16ms; 2.08w; 2.04w; 2.01m; 1.95mw; 1.92w; 1.87mw; 1.83m; 1.77vw; 1.71m.

\* Department of Chemistry, The University, Nottingham.

<sup>1</sup> S. C. Wallwork, *Proc. Chem. Soc.*, 1959, 311; S. C. Wallwork and W. E. Addison, *J.*, in the press.

<sup>2</sup> C. C. Addison and B. M. Gatehouse, *J.*, 1960, 613.

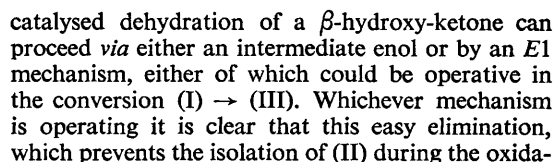
<sup>3</sup> S. J. T. Owen, K. J. Standley, and A. Walker, *J. Chem. Phys.*, 1964, **40**, 183; E. A. Boudreaux, private communication.

At room temperature both forms are stable for long periods in the absence of moisture but at elevated temperatures the  $\alpha$ -form is transformed into the  $\beta$ -form, very slowly at about 100° but rapidly at 150° and above. Details of the infrared spectra of both forms of copper(II) nitrate will be published separately,<sup>4</sup> as will the crystal structure of the  $\beta$ -form now under investigation.

<sup>4</sup> N. Logan and W. B. Simpson, to be published.

By P. J. BEYNON, P. M. COLLINS, and W. G. OVEREND\*

elimination of methanol in addition to oxidation. The structure of this compound was based on its elemental analysis, the physical evidence, liberation of benzaldehyde on acidification, decolorisation of permanganate, consumption of hydrogen (3.9 mol.) in the presence of palladium on charcoal, and on its formation from compound (II), with elimination of methanol, by heating it for 0.5 hr. in pyridine which is 0.1M in either perchloric acid or hydrochloric acid (in pyridine alone the initial material was recoverable). Noyce *et al.*<sup>5</sup> have shown that the acid-



\* Noyce and Reed, *J. Amer. Chem. Soc.*, 1958, **80**, 5539; Noyce, King, Lane, and Reed, *J. Amer. Chem. Soc.*, 1962, **84**, 1638.

tion of (I) with  $\text{CrO}_3\text{-C}_5\text{H}_5\text{N}$  does not occur if ruthenium tetroxide is the oxidant.

Examples of the oxidation of a hydroxyl group attached to a furanoid ring are limited.<sup>6</sup> Theander<sup>6c</sup> obtained a product in small yield from the oxidation of di-*O*-isopropylidene-D-glucufuranose. Oxidation occurred at C-3 with concomitant loss of the 5,6-*O*-isopropylidene residue. We find that di-*O*-isopropylidene-D-glucufuranose is oxidised, in 80% yield, cleanly, by ruthenium tetroxide to give 1,2:5,6-di-*O*-isopropylidene- $\alpha$ -D-ribo-3-hexulofuranose (IV) b.p.  $97^\circ/0.01$  mm.,  $[\alpha]_D + 107^\circ$  [hydrate, m.p.  $109\text{--}112^\circ$ ,  $[\alpha]_D + 45^\circ$ ; oxime, m.p.  $103\text{--}104^\circ$ ,  $[\alpha]_D +$

$180^\circ$ ]. This compound is noteworthy because (i) it affords D-allose<sup>7</sup> (70% crude, containing a small amount of glucose; 30% pure) on reduction with lithium aluminium hydride and subsequent acid hydrolysis; and (ii) D-ribo-3-hexulose has been claimed<sup>8</sup> as a constituent of a disaccharide found in *Agrabacterium tumefaciens*, a tumour-producing organism.

Unless otherwise stated  $[\alpha]_D$  refer to  $\text{CHCl}_3$  and infrared spectra were determined with KBr discs. Satisfactory analyses have been obtained for all crystalline compounds.

(Received, August 11th, 1964.)

\* See (a) Ishidate, Tamura, and Kinoshita, *Chem. Pharm. Bull. (Tokyo)*, 1962, **10**, 1258; (b) Oka and Wada, *Yakugaku Zasshi*, 1963, **83**, 890 (*Chem. Abs.*, 1964, **60**, 1825d); (c) Theander, *Acta Chem. Scand.*, 1963, **17**, 1751.

<sup>7</sup> Phelps and Bates, *J. Amer. Chem. Soc.*, 1934, **56**, 1250.

<sup>8</sup> Fukui and Hochster, *J. Amer. Chem. Soc.*, 1963, **85**, 1697.

## The Crystal Structure of the Photodimer of 1-Methyl-2-pyridone

By MICHAEL LAING\*

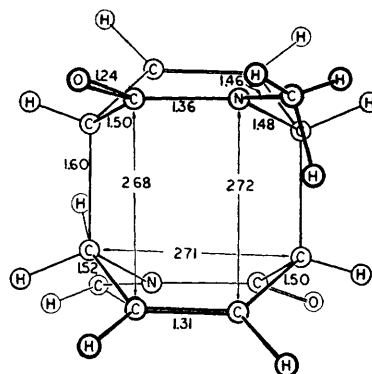
WHEN an aqueous solution of 1-methyl-2-pyridone is irradiated with ultraviolet light, a unique 1,4-dimer is formed.<sup>1</sup> The results of an n.m.r. study implied that this molecule is a centrosymmetric tricyclic octadiene derivative,<sup>2</sup> and inspection of a model indicated that some very short intramolecular non-bonded interactions should be present.

A sample of the material was supplied by Dr. L. A. Paquette, and needle-like crystals were obtained from ethyl acetate at  $0^\circ$ .  $\text{C}_{12}\text{H}_{10}\text{N}_2\text{O}_2$ ;  $M = 218$ ; monoclinic,  $a = 7.45$ ,  $b = 11.53$ ,  $c = 7.50$  Å,  $\beta = 127.95^\circ$ ;  $D_m = 1.425$ ;  $Z = 2$ ; space group  $P2_1/c$ , implying molecular symmetry is  $\bar{1}$ .

The structure was solved *via* the sharpened three-dimensional Patterson function, and refined anisotropically to an  $R$ -value of 0.089 for 487 observed reflections (1164 recordable with Cu- $K_\alpha$  radiation). The hydrogen atoms were located from a three-dimensional difference synthesis and were included in the later stages of refinement with isotropic temperature factors. The bond lengths, with standard deviations of about 0.015 Å are shown in the Figure which is a projection of the molecule down  $a$ .

The  $sp^3\text{C}\text{--}sp^3\text{C}$  bond of 1.60 Å is significantly stretched from the usual 1.54 Å. This increase is due to the strain caused by the very close contacts between the two pyridone rings; each of the values,

2.68, 2.71, and 2.72 Å is distinctly shorter than 3.4 Å which is the sum of the van der Waals radii for the pairs of atoms concerned. The remaining bond lengths are quite normal.





## NEWS AND ANNOUNCEMENTS

**Meetings for the Presentation of Communications.**

—The Council has agreed to provide opportunities for the presentation of Communications at scientific meetings. The proposal will be introduced on a small scale at the Anniversary Meetings in Glasgow on April 7–9th, 1965, to be followed by a further meeting to be held in Nottingham on September 21st–22nd, 1965. It is hoped that chemists in this country, and particularly those in the younger age groups, will welcome this opportunity of getting themselves and their work appreciated.

In the past formal meetings for the reading of papers have been held in London and occasionally in the provinces, but these have recently not been popular. It is believed, however, that one- or two-day meetings at which there will be an opportunity for the presentation and discussion of the most recent results, *i.e.*, the kind of work that would be published by the Society as Communications, will be welcomed by the chemical world generally. The selection of papers will be made as late as possible in order to give speakers an opportunity to include their latest work. There will be no direct publication from the meeting and authors will be free subsequently to publish as they wish.

Fellows who wish to submit a paper for the meeting in Glasgow should apply not later than Saturday, January 30th, 1965, on the forms available from the General Secretary. A short abstract will be required at this time to assist in the selection of papers, but those whose applications are accepted may, if they wish, substitute an amended abstract at any date up to Monday, March 1st, 1965. The circulated abstracts, distributed a few days before the meeting, will be reproduced directly by offset printing from the authors' own manuscripts which must, therefore, be carefully prepared to the specifications available with the application form.

**Local Representatives.**—The Council has approved the following changes of Local Representatives:

Canberra, Australia *Professor A. Albert* in place of  
*Professor G. M. Badger*  
Glasgow . . . . *Dr. D. W. A. Sharp* in place of  
*Dr. H. C. S. Wood*

**Election of New Fellows.**—40 Candidates were elected to the Fellowship in September, 1964.

**Deaths.**—We regret to announce the deaths of the following: *Mr. A. F. Allen* (2.8.64), a Fellow for over 50 years; *Mr. F. W. Edwards* (10.5.64), formerly Analytical and Consulting Chemist for the City of Westminster; *Dr. J. Farquharson* (22.8.64), a Consultant at Beecham Group Limited; *Professor F. H. Garner* (18.9.64), Emeritus Professor of Chemical Engineering at the University of Birmingham;

*Dr. R. N. Lacey* (31.7.64), of the British Petroleum Research Centre; *Dr. R. Lessing* (2.9.64), who was a Consulting Chemist and Chemical Engineer; *Mr. G. A. Turner* (26.3.64), of Worcester.

**Meldola Medal.**—This Medal is the gift of the Society of Maccabaeans and is normally awarded annually. The next award will be made early in 1965 to the chemist who, being a British subject and under 30 years of age at December 31st, 1964, shows the most promise as indicated by his or her published chemical work brought to the notice of the Council of the Royal Institute of Chemistry before December 31st, 1964.

No restrictions are placed upon the kind of chemical work or the place in which it is conducted. The merits of the work may be brought to the notice of the Council, either by persons who desire to recommend the candidate or by the candidate himself, by letter addressed to The President, The Royal Institute of Chemistry, 30 Russell Square, London, W.C.1, the envelope being marked "Meldola Medal".

The letter should be accompanied by six copies of a short statement on the candidate's career (date of birth, education and experience, degrees and other qualifications, special awards, etc., with dates) and a list of titles, with references, of papers or other works published by the candidate, independently or jointly. Candidates are also advised to forward one reprint of each published paper of which copies are available.

**The Beilby Medal and Prize, 1965.**—Awards from the Sir George Beilby Memorial Fund are made by the Administrators of the Fund, representing the Royal Institute of Chemistry, the Society of Chemical Industry, and the Institute of Metals. Sir George Beilby had been President of each of these three bodies, and they jointly sponsored the appeal for subscriptions whereby the Fund was raised as a memorial to him after his death in 1925.

The Beilby Medal and Prize, which consists of a gold medal and a substantial sum of money, is specified as being "For Advancement in Science and Practice". Such an award is now being offered annually.

The awards are made to British investigators in science in recognition of independent original work of exceptional merit, carried out continuously over a period of years and involving the development and application of scientific principles in any field related to the special interests of Sir George Beilby, *i.e.*, in chemical engineering, fuel technology, or metallurgy, in their modern interpretations. The awards are intended as an encouragement to younger men and women (preferably under age 40) who have done



distinguished work of practical significance in any of these fields.

Consideration will be given in due course to the making of an award from the Fund in 1965. Outstanding work of the nature indicated may be brought to the notice of the Administrators, either by persons who desire to recommend the candidate or by the candidate himself, not later than December 31st, 1964, by letter addressed to The Convener of the Administrators, Sir George Beilby Memorial Fund, The Royal Institute of Chemistry, 30 Russell Square, London, W.C.1.

The letter should be accompanied by nine copies of a short statement on the candidate's career (date of birth, education and experience, degrees and other qualifications, special awards, etc., with dates) and of a list of titles, with references, of papers or other works published by the candidate, independently or jointly. Photographic copies of these documents are acceptable. Candidates are also advised to forward one reprint of each published paper of which copies are available.

**American Chemical Society Publications.**—A long established reciprocal agreement allows Fellows of the Chemical Society, not being Members of the American Chemical Society, to subscribe to the publications of the latter Society at a discount of 10% from the non-members' rates. No discount is available on the Chemical Abstracts Service, however. Fellows wishing to take advantage of this concession should apply to the American Chemical Society, 1155 Sixteenth Street, N.W., Washington, D.C. 20036, U.S.A.

Fellows wishing to apply for membership of the American Chemical Society may obtain forms of application from the General Secretary.

**I.U.P.A.C. Committee on the Teaching of Chemistry.**—The International Union of Pure and Applied Chemistry has recently established a permanent Committee on the Teaching of Chemistry. The present membership consists of *Professor J. Benard*, *Professor J. A. Campbell*, *Professor W. A. Noyes Jr.*, *Professor M. Oki*, *Professor O. Reutov*, *Professor G. M. Schwab* with *Professor R. S. Nyholm* as Chairman and *Dr. P. Sykes* as Secretary. At its first meeting in Basle, the Committee defined its role as:

- To disseminate information concerning chemical education at all levels throughout the world.
- To offer advice, through public statements and by direct contact with interested bodies, on the kind of activity which it feels will ensue the development of a modern approach to the teaching of chemistry.

Towards these ends the Secretary would be pleased to hear of any activity which might be of interest to the members of the Committee. His address is the

University Chemical Laboratory, Lensfield Road, Cambridge.

**The Welwyn Hall Research Association.**—Whiting and Industrial Powders and Chalk Lime and Allied Industries have merged to form a new co-operative industrial research organisation. Mr. D. B. Jones will be the Chairman of the new Association, Mr. D. C. Soul, the first Director of Research, and Mr. G. E. Bessey, a consultant. Welwyn Hall Research Association will occupy the existing joint premises in Church Street, Welwyn, Hertfordshire, and during the next five years it aims to spend over £400,000 in serving its member firms. Further details of the new Association and its work can be obtained from the Secretary or the Technical Information Officer.

**Symposium.**—A Symposium on Oxidation in Organic Chemistry will be held in Manchester on March 23rd–24th, 1965. Further enquiries should be addressed to Dr. G. Holt, Department of Chemistry, Manchester College of Science and Technology, Manchester, 1.

**Personal.**—*Professor G. M. Badger* has been appointed Professor Emeritus in the Department of Chemistry, the University of Adelaide.

*Dr. J. Carnduff*, formerly of Harvard University, has taken up a Research Fellowship at the University of Strasbourg, Strasbourg, France.

*Mr. B. E. P. Clement* has been appointed Deputy Chemist and Bacteriologist to the North Bedfordshire Water Board, Bedford.

*Dr. B. R. James*, formerly of A.E.R.E., Harwell, has been appointed Assistant Professor in the Chemistry Department at the University of British Columbia, Canada.

*Dr. A. D. Jenkins* has been appointed to a Senior Lectureship in Chemistry in the University of Sussex.

The D.S.I.R. has made a grant of £1,450 to *Mr. N. Jones* and *Mr. E. Catterall*, of the Lanchester College of Technology, Coventry, for the purchase of a gas chromatography unit and accessories in connection with their investigations of Friedel–Crafts acylation of alkenes and cycloalkenes and studies of the stereoregular polymerisation of dienes and olefin oxides.

*Dr. V. E. Malpass* has been appointed Senior Research Chemist with the Marbon Chemical Division of Borg–Warner Corporation, West Virginia, U.S.A.

The title of Professor of Chemistry has been conferred on *Dr. D. J. Millen*, in respect of his post at University College.

*Dr. W. McCrae*, formerly Research Chemist at Lederle Laboratories, New York, U.S.A., has been appointed an Imperial Chemical Industries Research Fellow at the University of Cambridge.

*Mr. I. T. McWalter*, formerly Industrial Chemist at the Atomic Energy Research Establishment, Harwell, has been appointed Lecturer in Inorganic Chemistry at Robert Gordon's Technical College, Aberdeen.

*Dr. T. J. Painter*, has been appointed Lecturer in Biochemistry at the Royal Free Hospital School of Medicine, London, from April 1st, 1965.

*Professor G. W. Perold*, Professor of Chemistry at the University of South Africa, has been appointed to the Chair of Organic Chemistry at the University of the Witwatersrand as from January 1st, 1965. He will succeed Professor D. G. Backeberg who has been on the staff of the University for more than 40 years and was appointed Professor of Organic Chemistry and Head of the Department in 1955.

*Dr. S. K. Pradhan*, formerly of the Worcester Foundation for Experimental Biology, Shrewsbury, Massachusetts, has been appointed Head of the Chemistry Department, University of Shivaji, India.

*Dr. A. Robson*, formerly of the Wool Industries Research Association in Leeds, has been appointed Professor of Fibre Science at the University of Leeds.

*Dr. B. Rose* has been appointed to a Senior

Lectureship in Chemistry at the University of Nigeria.

*Dr. C. E. Stickings* has been appointed Senior Lecturer in the Department of Biochemistry at the Imperial College of Science and Technology, London.

*Dr. B. J. Wakefield*, has been appointed Lecturer in the Department of Chemistry and Applied Chemistry at the Royal College of Advanced Technology, Salford, Lancashire.

*Dr. S. Walker*, Reader in the Chemistry Department of the College of Advanced Technology, Birmingham, has been awarded the degree of D.Sc. by the University of London.

*Dr. H. Watts*, formerly Senior Lecturer in Applied Physical Chemistry at the South Australian Institute of Technology, has joined the Exploratory Research Laboratory of Dow Chemical of Canada Limited, Ontario, Canada.

*Dr. R. O. Williams*, formerly Technical Officer with Imperial Chemical Industries Limited, has been appointed Lecturer in Organic Chemistry at the Technical College at Portsmouth.

*Dr. C. J. Wormald* has been appointed Assistant Lecturer in Chemistry at the University of Bristol.

## FORTHCOMING SCIENTIFIC MEETINGS

### London

Thursday, November 19th, 1964, at 6 p.m.  
Discussion Meeting on Free Radicals. To be held in the Rooms of the Society, Burlington House, W.1.

### Aberdeen

Thursday, November 12th, 1964, at 8 p.m.  
Lecture, "The Chemistry of Oxidative Phosphorylation," by Dr. V. M. Clark, M.A. Joint Meeting with the University Chemical Society, to be held in the Chemistry Department, The University.

Tuesday, November 24th, at 8 p.m.  
Lecture, "The Substituent Effects of Positive Poles in Aromatic Nitration," by Dr. J. H. Ridd. Joint Meeting with the Royal Institute of Chemistry and the Society of Chemical Industry, to be held in the Biochemistry Lecture Theatre, Marischal College.

### Aberystwyth

Thursday, November 12th, 1964, at 5 p.m.  
Lecture, "Topographical Studies of Crystal Surfaces," by Dr. J. M. Thomas. Joint Meeting with the University College of Wales Chemical Society, to be held in the Edward Davies Chemical Laboratory.

### Birmingham

(Joint Meetings with the University Chemical Society, to be held in the Chemistry Department, The University.)

Friday, November 20th, 1964, at 4.30 p.m.  
Lecture, "Ways of Promoting Chemical Reactivity," by Dr. G. Baddeley.

Friday, December 4th, at 4.30 p.m.  
Lecture, "Synthetic Sex Hormones," by Professor A. J. Birch, D.Phil., F.R.S.

### Brighton

(Joint Meetings with the University Chemical Society, to be held in the Chemical Laboratory, The University of Sussex.)

Monday, November 9th, 1964, at 5.15 p.m.  
Lecture, "Optical Rotatory Dispersion," by Professor W. Klyne, M.A., Ph.D.

Monday, November 23rd, at 5.15 p.m.  
Lecture, "Fluoroalicyclic Compounds," by Professor J. C. Tatlow, Ph.D., F.R.I.C.

### Bristol

(Joint Meetings with the Society of Chemical Industry and the Royal Institute of Chemistry, to be

held in the Department of Chemistry, The University, unless otherwise stated.)

Thursday, November 19th, 1964, at 5.30 p.m.

Lecture, "Some Effects of Molecular Orientation in Gases and Liquids," by Dr. A. D. Buckingham, M.A. Also joint with the Student Chemical Society.

Thursday, November 26th, at 7.30 p.m.

Social Evening to be held at Cheltenham.

Thursday, December 3rd, at 6.30 p.m.

Lecture, "Aerosols—The Development of Pressurised Packaging," by Mr. P. Dyson, B.A., B.Sc.

### Cambridge

(Joint Meetings with the University Chemical Society, to be held in the University Chemical Laboratory, Lensfield Road.)

Friday, November 6th, 1964, at 8.30 p.m.

Lecture, "The Stabilisation of Low-valent States of Transition Metals by Tertiary Phosphines," by Professor J. Chatt, Sc.D., F.R.S.

Friday, November 20th, at 8.30 p.m.

Lecture, "Some Recent Studies on the Biosynthesis of Alkaloids," by Professor D. H. R. Barton, D.Sc., F.R.S.

### Cardiff

Monday, November 16th, 1964, at 5 p.m.

Lecture, "Some Applications of Electron Spin Resonance Spectroscopy in Elucidating Reaction Mechanisms," by Dr. R. O. C. Norman, B.A. To be given in the Department of Chemistry, University College, Cathays Park, Cardiff.

### Dublin

Friday, November 27th, 1964, at 7.45 p.m.

Lecture, "Dissociation of Energies, Ionisation Potentials and Electron Affinities of Molecules and Radicals," by Professor W. C. Price, F.R.S. Joint Meeting with the Werner Society, to be held in the Department of Chemistry, Trinity College.

### Durham

(Joint Meetings with the University Chemical Society, to be held in the Science Laboratories, South Road.)

Monday, November 9th, 1964, at 5 p.m.

Lecture, "Multiple Bonds in Inorganic Chemistry," by Dr. M. F. Lappert, F.R.I.C.

Monday, November 23rd, at 5 p.m.

Official Meeting and Lecture, "Chemical Methods of Attaining High Temperatures," by Professor P. Gray, M.A., Ph.D.

Monday, November 30th, at 5 p.m.

Lecture to be given by Dr. M. C. Whiting, M.A.

Wednesday, December 2nd, at 5.15 p.m.

Lecture, "Applications of Nuclear Magnetic Resonance Spectroscopy," by Dr. J. E. Page, F.R.I.C.

### Edinburgh

Tuesday, November 10th, 1964, at 4.30 p.m.

Lecture, "Stepwise Equilibria," by Dr. F. J. C. Rossotti, M.A. Joint Meeting with the University Chemical Society, to be held in the Department of Chemistry, The University.

Thursday, November 12th, at 7.30 p.m.

Lecture, "Modern Aspects of Structure Determination," by Professor W. D. Ollis, Ph.D. Joint Meeting with the Royal Institute of Chemistry and the Society of Chemical Industry, to be held in the Heriot-Watt College.

### Exeter

(Meetings to be held in the Washington Singer Laboratories, Prince of Wales Road.)

Friday, November 13th, 1964, at 5.15 p.m.

Lecture, "Some Aspects of Electrophilic Aromatic Substitutions," by Professor C. Eaborn, Ph.D., D.Sc.

Friday, December 4th, at 5.15 p.m.

Lecture, "Organic Semiconductors," by Professor D. D. Eley, O.B.E., F.R.S.

### Glasgow

Thursday, November 19th, 1964, at 4 p.m.

Lecture, "Atomic and Molecular Events at the Surfaces of Metals," by Professor F. C. Tompkins, Ph.D., F.R.S. Joint Meeting with the Alchemists' Club, to be held in the Chemistry Department, The University.

### Hull

(Joint Meetings with the University Students Chemical Society, to be held at the Lecture Theatre, The University.)

Thursday, November 12th, 1964, at 4 p.m.

Lecture, "Chemical Methods of Attaining High Temperatures," by Professor P. Gray, M.A., Ph.D.

Thursday, November 26th, at 4 p.m.

Lecture, "Some Aspects of the Chemistry of Titanium and Neighbouring Elements," by Dr. G. W. A. Fowles.

### Leicester

Thursday, November 12th, 1964, at 5 p.m.

Lecture, "Spectroscopic Aspects of Optical Rotary Power," by Professor S. F. Mason, M.A., D.Phil. Joint Meeting with the Chemical Society of Leicester College of Technology, to be given at the College of Technology.

**Liverpool**

Thursday, November 26th, 1964, at 5 p.m.

Lecture, "The Role of Organometallic Compounds in the Development of Co-ordination Chemistry," by Professor F. G. A. Stone, M.A., Sc.D. Joint Meeting with the Society of Chemical Industry, the Royal Institute of Chemistry, and the University Chemical Society, to be held in the Donnan Laboratories, The Chemistry Department, The University.

**Manchester**

Thursday, November 12th, 1964, at 6.30 p.m.

Lecture, "The Corrin Ring System," by Professor A. W. Johnson, M.A., Ph.D., A.R.C.S. To be given in Theatre R/H 10, Renold Building, Manchester College of Science and Technology.

**Northern Ireland**

Tuesday, November 3rd, 1964, at 7.45 p.m.

Lecture, "The Nature of Reactive Intermediates in Cationic Polymerisation," by Professor D. C. Pepper, M.A., Ph.D. Joint Meeting with the Royal Institute of Chemistry, the Society of Chemical Industry, and the Andrews Club, to be held in the Department of Chemistry, David Keir Building, Queen's University, Belfast.

**North Wales**

Thursday, November 19th, 1964, at 5.30 p.m.

Lecture, "Some Problems in Carbohydrate Chemistry," by Professor E. J. Bourne, D.Sc., F.R.I.C. Joint Meeting with the University College of North Wales Chemical Society, to be held in the Chemistry Department, University College, Bangor.

**Norwich**

(Meetings to be held in Lecture Room 2, The University of East Anglia, Wilberforce Road.)

Thursday, November 26th, 1964, at 5.30 p.m.

Tilden Lecture, "Experiments with Orientated Molecules," by Dr. A. D. Buckingham, M.A.

Thursday, December 3rd, at 7.45 p.m.

Lecture, "Metal to Metal Bonds in Inorganic Compounds," by Professor R. S. Nyholm, D.Sc., F.R.S. Joint Meeting with the Royal Institute of Chemistry.

**Nottingham**

(Joint Meetings with the University Chemical Society, to be held in the Large Lecture Theatre, the Department of Chemistry, The University.)

Tuesday, November 10th, 1964, at 5 p.m.

Lecture, "Some Aspects of Polyacetylene Chemistry," by Professor Sir Ewart Jones, D.Sc., F.R.S.

Tuesday, November 24th, at 5 p.m.

Lecture, "Symmetry, Structure, and Spectroscopy," by Professor A. D. Walsh, M.A., Ph.D.

**Oxford**

(Joint Meetings with the Alembic Club, to be held in the Inorganic Chemistry Laboratory.)

Monday, November 2nd, 1964, at 8.30 p.m.

Lecture, "Experiments with Orientated Molecules," by Dr. A. D. Buckingham, M.A.

Monday, November 16th, at 8.30 p.m.

Lecture, "Gastrin, a Peptide Hormone," by Professor G. W. Kenner, Ph.D., Sc.D.

**Reading**

Tuesday, November 17th, 1964, at 5.30 p.m.

Tilden Lecture, "Experiments with Orientated Molecules," by Dr. A. D. Buckingham, M.A. Joint Meeting with the Royal Institute of Chemistry and the University Chemical Society, to be held in the Large Chemistry Lecture Theatre, The University.

**Swansea**

(Joint Meetings with the Student Chemical Society, to be held in the Chemistry Lecture Theatre, University College.)

Monday, November 2nd, 1964, at 4.30 p.m.

Lecture, "Some Aspects of the Chemistry of Bacterial Cell Walls," by Professor J. Baddiley, Ph.D., D.Sc., F.R.S.

Monday, November 9th, at 4.30 p.m.

Lecture, "The Role of Organometallic Compounds in the Development of Co-ordinate Chemistry," by Professor F. G. A. Stone, M.A., Ph.D.

Monday, November 30th, at 5 p.m.

Lecture, "The Hydrogen Bond," by Dr. L. J. Bellamy. Also joint with the Royal Institute of Chemistry.

**Southampton**

Friday, November 6th, 1964, at 7 p.m.

Lecture, "The Compounds of the Inert Gases," by Dr. R. D. Peacock. To be given in Lecture Room H9, College of Technology, Portsmouth.

Friday, December 4th, at 5 p.m.

Lecture, "A Chemist at Sea," by Dr. L. H. N. Cooper, F.R.I.C. To be given in the Lecture Theatre, the Chemistry Department, the University.

**Tees-side**

(Please note that the Lecture by Professor A. Birch on Thursday, November 19th, has been postponed. A new date will be announced later.)