Unsaturated Ketone XXII and Hydrocarbon XXIII.—A solution of 18 mg. of sodium hydride in 1 ml. of dimethyl sulfoxide was added to a solution of 95 mg. of monotosylate from diol XIX in 1 ml. of dimethyl sulfoxide at 10° with stirring and under nitrogen; an immediate greenish brown coloration developed. After 15 min., the reaction mixture was worked up in the manner described above to give 45.4 mg. of a viscous liquid. The crude material in pentane was passed through a short column of 500 mg. of activity III neutral alumina, giving 29.5 mg. of unsaturated ketone XXII, purified by distillation *in vacuo* and then by v.p.c. on a 4-ft. 20% fluorosilicone column at 175° (retention time different from XXI; found: 8 min. at He flow 100 ml./min.). The product showed carbonyl absorption at 5.90 μ and differed clearly from XXI in the infrared.

Anal. Calcd. for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.48; H, 10.71.

Treatment of the ketone XXII with methylenetriphenylphosphorane in dimethyl sulfoxide as described above for XXI, and isolation also in the same way afforded a hydrocarbon (XXIII), v.p.c. retention time 19.6 min. using a 10-ft. 20% nitrile silicone column (He flow rate 60 ml./min.) which differed from isocaryophyllene (retention time under exactly the same conditions 17.4 min.). The v.p.c. retention time of XXIII happens to be the same as that of caryophyllene (I) under the same conditions. However, the infrared and n.m.r. spectra of XXIII are distinctly different from those of I or II.

The analytical specimen of XXIII was collected by v.p.c. on a 10 ft. 20% nitrile silicone column at 150° and He flow 55–60 ml./min.

Anal. Calcd. for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 87.75; H, 11.78.

Mono-*p*-toluenesulfonate of Diol XX.—To a solution of 80 mg. of diol XX in 0.3 ml. of dry pyridine and 1.0 ml. of methylene chloride was added 138 mg. (2 equiv.) of *p*-toluenesulfonyl chloride. The reaction mixture was stored at 0° for 30 min. and then at room temperature for 24 hr. under nitrogen. Several pieces of chopped ice were added and the mixture was stirred for 1 hr., during which period almost all of the methylene chloride had evaporated leaving an oil which gradually solidified. The solid was collected by filtration, washed thoroughly with water, and then dissolved in ether. Washing with saturated salt solution, followed by evaporation of the ether gave 125 mg. (93%) of pale yellow crystalline tosylate, m.p. 100.5–101.5°, the infrared spectrum of which showed two strong bands at 7.28 and 8.49 μ due to tosylate and "fingerprint" absorption clearly different from that of the monotosylate from XIX described above.

Unsaturated Ketone XXV.—A solution of excess sodium *t*-butoxide (140 mg. of sodium hydride and 1.1 ml. of *t*-butyl alcohol were used) in dimethyl sulfoxide (11 ml.) was added to a solution of 302 mg. of the monotosylate from diol XX in 2 ml. of dimethyl sulfoxide at 20° with stirring and under nitrogen; in this run no significant color change developed. The reaction mixture was stored at room temperature for 17 hr. and worked up by dilution with water and extraction in the usual manner to give a single unsaturated ketone XXV by v.p.c. analysis (nitrile silicone column) in essentially quantitative yield, infrared max. 5.89 μ. This product was clearly different from ketones XXI and XXII and also XXIV (see below) by both v.p.c. and infrared spectral measurements. The same product XXV was also obtained using methylsulfinylcarbanion followed by *t*-butyl alcohol as reagent with 20 hr. for isomerization of the ring fusion. The analytical specimen was collected by v.p.c.

Anal. Calcd. for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.42; H, 10.74.

***d,l*-Caryophyllene (I).**—The Wittig reagent methylenetriphenylphosphorane was prepared in dimethyl sulfoxide as described above for the synthesis of *d,l*-isocaryophyllene (II) and 5 equivalents (3 ml. of solution) were added to a solution of the ketone XXV (41 mg.) in 1 ml. of dimethyl sulfoxide. After 4 hr. at room temperature the product was isolated exactly as described for synthetic II. Evaporation of the washed pentane extracts left 44 mg. of liquid with v.p.c. retention time (only one peak) on a 10 ft. 20% TCEP column (He flow 55 ml./min.) of 27 min. at 125°, identical with a sample of natural I; with a 10-ft. 20% nitrile silicone column at 150° (He flow 55 ml./min.) the retention time was 20.3 min., again identical with natural I. Under the same v.p.c. conditions on the TCEP column isocaryophyllene has a retention time of 22 min. and is cleanly resolved from caryophyllene.[35] Thus the yield of synthetic *d,l*-I obtained was essentially quantitative. The infrared spectra of synthetic and natural I were absolutely identical.

Anal. Calcd. for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 88.04; H, 11.97.

Unsaturated Ketone XXIV.—A solution of sodium *t*-butoxide in dimethyl sulfoxide was prepared from 43 mg. of sodium hydride, 0.34 ml. (266 mg.) of *t*-butyl alcohol, and 3 ml. of dimethyl sulfoxide and 1.8 ml. of this solution was injected into a solution of 112 mg. of the monotosylate of XX in 3 ml. of dimethyl sulfoxide at 20° under nitrogen. The resulting brown solution was stored at room temperature for 4 hr. and 4.5 ml. of water was added with water cooling. The milky mixture was transferred into a separatory funnel with the aid of 15 ml. of water containing salt and a 2:1 pentane–ether mixture. The water layer was extracted with the same solvent four times and the combined extracts were washed with half-saturated (10 ml.) and saturated salt solution (10 ml.). Removal of the solvent gave a pale brown liquid in quantitative yield. This product consisted of two isomeric unsaturated ketones XXIV and XXV in ratio of about 3:2 which as determined by v.p.c. on a 10-ft. 20% nitrile silicone column showed two peaks at retention times of 23.2 min. (major) and at 25.8 min. (minor) (165° and He flow 60 ml./min.). The major unsaturated ketone XXIV was isomerized upon prolonged (15 hr.) treatment with sodium *t*-butoxide in dimethyl sulfoxide to the minor one XXV identical with the compound described above. Interestingly, this unstable *cis*-fused ketone XXIV did not react appreciably with the Wittig reagent in dimethyl sulfoxide under the conditions which completely transformed the isomeric ketones XXI, XXII, and XXV. An analytical sample was prepared by v.p.c., infrared max. 5.89 μ.

Anal. Calcd. for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.19; H, 10.73.

(35) The "natural caryophyllene" used in our studies was obtained from the Aldrich Chemical Co. and was labeled β-carophyllene. However, this material was a mixture of caryophyllene (I) and isocaryophyllene (II) in ratio 3:1 as shown clearly by v.p.c. The pure components were obtained by preparative v.p.c. The component of shorter retention time proved to be identical with a sample of pure isocaryophyllene provided by Dr. F. Sorm.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF STANFORD UNIVERSITY, STANFORD, CALIF.]

Optical Rotatory Dispersion Studies. XCI.[1] The Use of Low-Temperature Circular Dichroism Measurements for "Fingerprinting" of Steroidal Ketones[2]

BY KEITH M. WELLMAN,[3] R. RECORDS, E. BUNNENBERG, AND CARL DJERASSI

RECEIVED AUGUST 19, 1963

For purposes of locating a carbonyl group on a steroid skeleton, optical rotatory dispersion curves are generally more useful than circular dichroism curves, because the former exhibit characteristically different shapes (as well as signs) due to the operation of background rotation effects, which are absent in circular dichroism. It has now been noted that when circular dichroism measurements of such ketones are performed near the boiling point of liquid nitrogen (*ca.* −192°), vibrational fine structure is usually developed or intensified, which in many instances is characteristic of a carbonyl group in a given (bicyclic) environment and can thus be employed for purposes of "fingerprinting." Similar low-temperature measurements of the ultraviolet absorption spectrum in the $n \rightarrow \pi^*$ region are not as useful; vibrational fine structure is not as well developed as in the circular dichroism spectrum and furthermore larger amounts of material are required because of the low extinction.

In an earlier article,[4] where the relative advantages of the closely related phenomena optical rotatory dispersion (O.R.D.) and circular dichroism (C.D.) were compared, it was noted that for structural purposes, O.R.D. will often be preferable. This is due to the

(1) Paper XC: C. Djerassi, P. A. Hart, and C. Beard, *J. Am. Chem. Soc.*, **86**, 85 (1964).

(2) Supported by the National Science Foundation (Grant No. G-19905) and the National Cancer Institute (Grant No. 5T4-CA5061) of the National Institutes of Health, U. S. Public Health Service.

(3) National Institutes of Health Postdoctoral Research Fellow, 1962–1963.

(4) C. Djerassi, H. Wolf, and E. Bunnenberg, *J. Am. Chem. Soc.*, **84**, 4552 (1962).

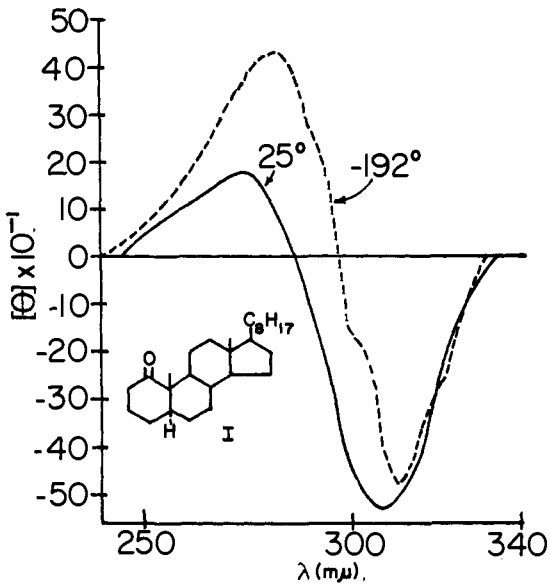


Fig. 1.—Circular dichroism (25 and −192°) of cholestan-1-one (I).

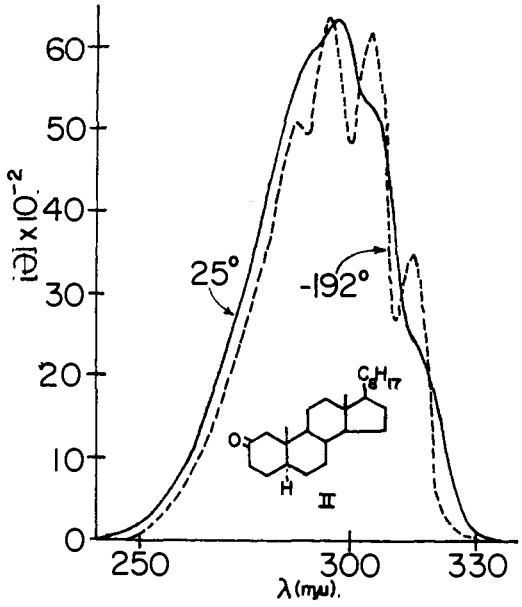


Fig. 2.—Circular dichroism (25 and −192°) of cholestan-2-one (II).

operation of background effects,[5] which can affect greatly the shape of Cotton effect curves, while C.D. curves can only be positive or negative and thus differ only quantitatively in terms of molecular ellipticity values. This latter feature is precisely the reason why C.D. lends itself more readily to quantitative evaluations of rotational strength than O.R.D.[6]

In a recent preliminary communication from this laboratory,[7] a technique was reported for measuring circular dichroism at low temperatures approaching that of liquid nitrogen, and its potential application to conformational mobility studies was indicated. Incidental to this work, it was noted that such circular dichroism curves often showed greatly increased fine structure. The initial work was performed with the carbonyl chromophore and it was felt that if this

(5) See also K. Mislow, E. Bunnenberg, R. Records, K. Wellman, and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 1342 (1963).

(6) See A. Moscowitz, *Tetrahedron*, **13**, 48 (1961), as well as Chapter 12 in ref. 21a.

(7) K. M. Wellman, E. Bunnenberg, and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 1870 (1963).

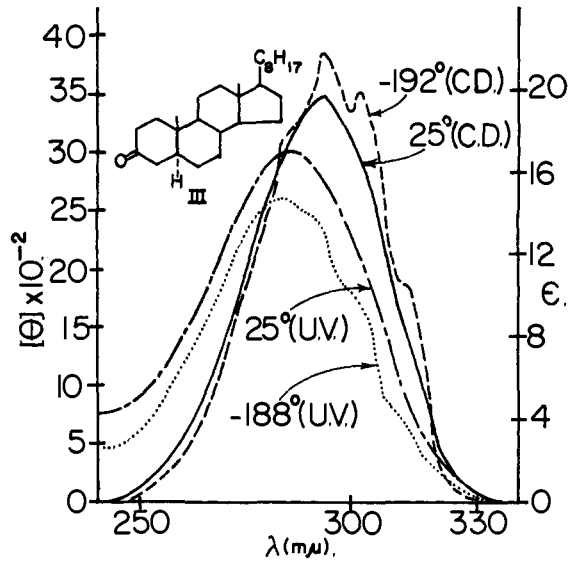


Fig. 3.—Circular dichroism (25 and −192°) and ultraviolet absorption (25 and −188°) of cholestan-3-one (III).

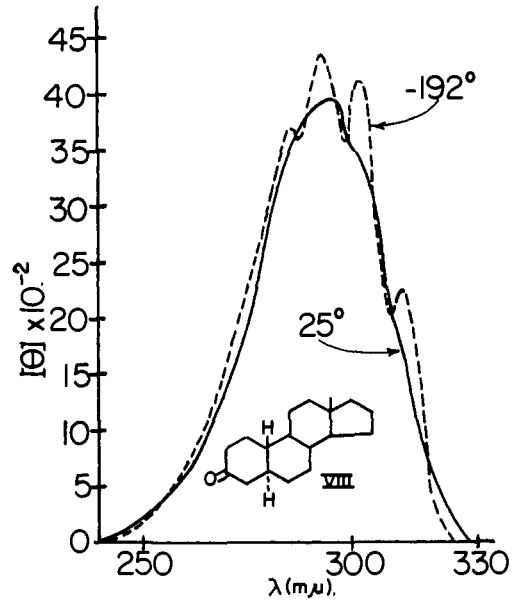


Fig. 4.—Circular dichroism (25 and −192°) of 19-nor-5α-androstan-3-one (VIII).

vibrational structure differed significantly for various keto steroids, low-temperature circular dichroism might be used similarly to optical rotatory dispersion[8] for locating a carbonyl group on a steroid skeleton. The experimental work outlined below supports this conclusion. All data are reported in an EPA solvent (5 vol. ether–5 vol. isopentane–2 vol. ethanol) at room temperature and at −192°.

1-Keto-5α-steroids, such as cholestan-1-one (I), represent an exception in that no particular vibrational structure develops upon measuring the circular dichroism at low temperature (see Fig. 1). They do, however, exhibit the very unique feature—hitherto noted[9] only among 4,4-dimethyl-3-ketones of the triterpene series—of two circular dichroism maxima of opposite sign and spaced nearly 30 mμ apart. We shall discuss elsewhere the possible physical significance of this most unexpected phenomenon; but for our present purposes, it suffices to note that this temperature- and solvent-

(8) C. Djerassi, W. Closson, and A. E. Lippman, *ibid.*, **78**, 3163 (1956).

(9) P. Witz, H. Herrmann, J.-M. Lehn, and G. Ourisson, *Bull. soc. chim. France*, 1101 (1963).

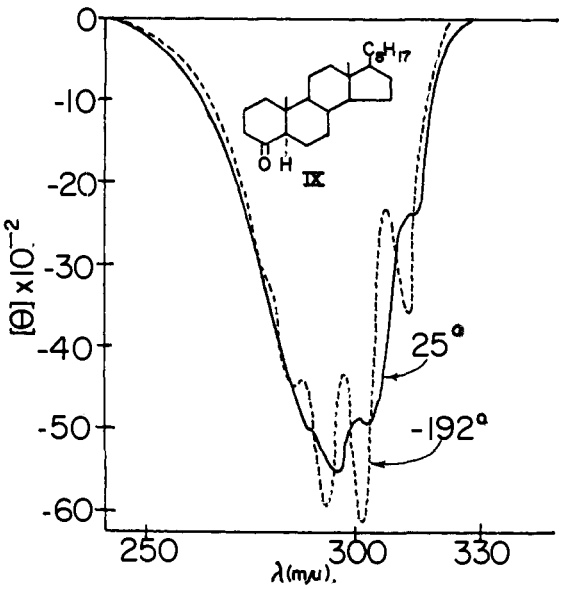


Fig. 5.—Circular dichroism (25 and −192°) of cholestan-4-one (IX).

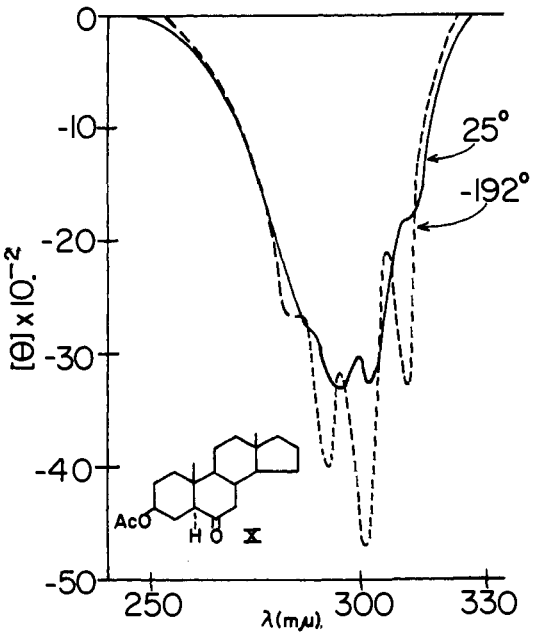


Fig. 6.—Circular dichroism (25 and −192°) of 5α-androstan-3β-ol-6-one acetate (X).

dependent feature, just like the unique O.R.D. curve[8] of 1-keto-5α-steroids, serves as an excellent criterion for recognizing a carbonyl group attached to position 1.

Attention has been directed previously[8] to the fact that the optical rotatory dispersion curves of 2- and 3- (*e.g.*, II and III) keto steroids are very similar (exhibiting rather symmetrical positive Cotton effects) and differ only quantitatively in amplitude. A more secure criterion of differentiation proved to be the detection of ketal formation[10] by O.R.D., since 2-keto steroids (II) hardly react under conditions where extensive ketal production (and hence a reduction in the amplitude of the Cotton effect) is observed with 3-keto steroids.

As demonstrated in Fig. 2 and 3, low-temperature circular dichroism curves provide a reasonably satisfactory and alternate way of differentiating between such isomeric keto steroids, the −192° C.D. curve

(10) C. Djerassi, L. A. Mitscher, and B. J. Mitscher, *J. Am. Chem. Soc.*; **81**, 947 (1959).

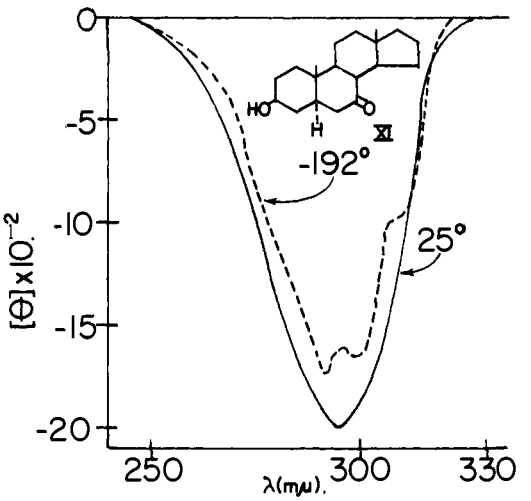
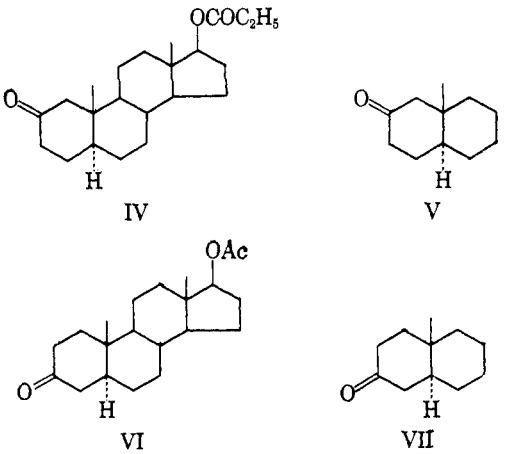


Fig. 7.—Circular dichroism (25 and −192°) of 5α-androstan-3β-ol-7-one (XI).

(Fig. 2) of cholestan-2-one (II) exhibiting four well-defined C.D. maxima,[11] with the two center ones being of nearly equal height.

In cholestan-3-one (III), only the two center maxima are well separated by a minimum, and of these two maxima the one situated at lower wave length is the more pronounced one. These diagnostic features—not discernible in the C.D. curves measured[12] at room temperature—are characteristic of the bicyclic environment of the carbonyl group. Thus, both 5α-androstan-17β-ol-2-one propionate (IV) and the bicyclic *trans*-9-methyl-2-decalone (V) show exactly the same C.D. pattern as cholestan-2-one (II, Fig. 2), while 5α-androstan-17β-ol-3-one acetate (VI) and *trans*-10-methyl-2-decalone (VII) exhibit low-temperature C.D. curves of the cholestan-3-one (III, Fig. 3) type. The structural requirements for such "fingerprinting" are, nevertheless, fairly specific and removal of the angular methyl group as in 19-nor-5α-androstan-3-one (VIII) yields a low-temperature C.D. curve (Fig. 4), which is much more reminiscent of the 2- (Fig. 2) rather than 3- (Fig. 3) keto steroid series.



A secure differentiation between 4- (*e.g.*, IX) and 6- (*e.g.*, X) 5α-keto steroids is not possible on the basis of O.R.D., both types exhibiting[8] negative Cotton effects. Similarly, C.D. measurements do not offer a satisfactory solution and, as noted in Fig. 5 and 6,

(11) For circular dichroism nomenclature see C. Djerassi and E. Bunnenberg, *Proc. Chem. Soc.*, in press.

(12) L. Velluz and M. Legrand, *Angew. Chem.*, **73**, 603 (1961), have recorded the room temperature circular dichroism curves in dioxane solution of nonconjugated monoketones in positions 3, 6, 7, 11, 12, 16, and 17 of the steroid framework.

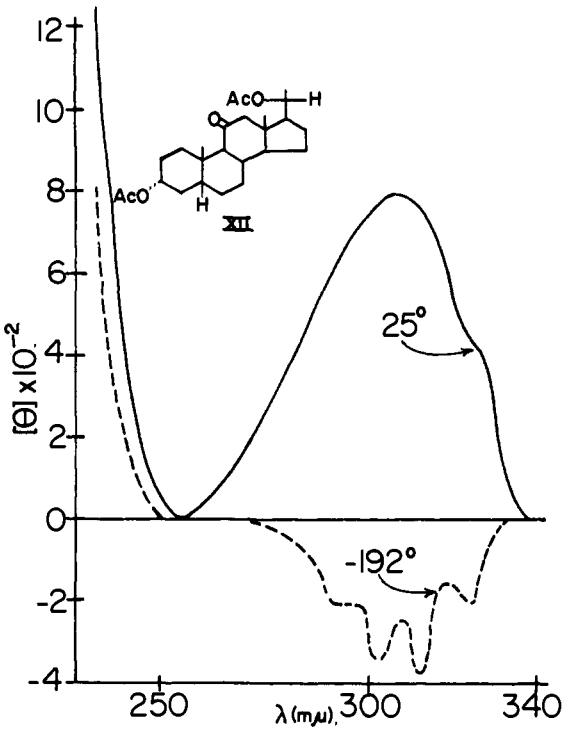
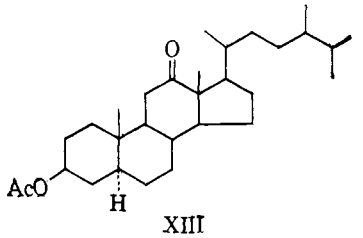


Fig. 8.—Circular dichroism (25 and −192°) of 5β-pregnane-3α,20β-diol-11-one diacetate (XII).

the fine structure already observable at room temperature becomes much sharper at −192° but is of essentially the same aspect in 4- and 6-ketones.

The situation is quite distinct among 7-keto-5α-steroids (*e.g.*, XI). Their circular dichroism curve (Fig. 7) at room temperature is devoid of fine structure, which does, however, become noticeable upon lowering the temperature to −192°. It differs from that (Fig. 1, 5, and 6) of the other six-membered ketones (5α-series) with a negative Cotton effect to such an extent that either this C.D. feature or the rather characteristic O.R.D. curve[8] (negative Cotton effect superimposed on negative background) can be employed for diagnostic purposes.

A dramatic effect is noted in the 11-keto series and is independent of the configuration at C-5. Thus, in our preliminary communication,[7] there was recorded the C.D. curve of 5α-androstan-11-one and it was noted that lowering of the temperature produced vibrational fine structure as well as an inversion in sign. A similar observation has been made in several other 11-mono ketones and, as demonstrated in Fig. 8, 11-keto steroids of the 5β-series (*e.g.*, XII) behave similarly. This unique feature, not observed with ketones in any other position of the steroid nucleus, now makes it a very simple matter to recognize the presence of the biologically important 11-ketone function. The beginning of a positive C.D. band below 250 mμ, noticeable in Fig. 8, appears to be associated with the 20-acetate group and is not observed in 11-ketones lacking that functionality.



XIII

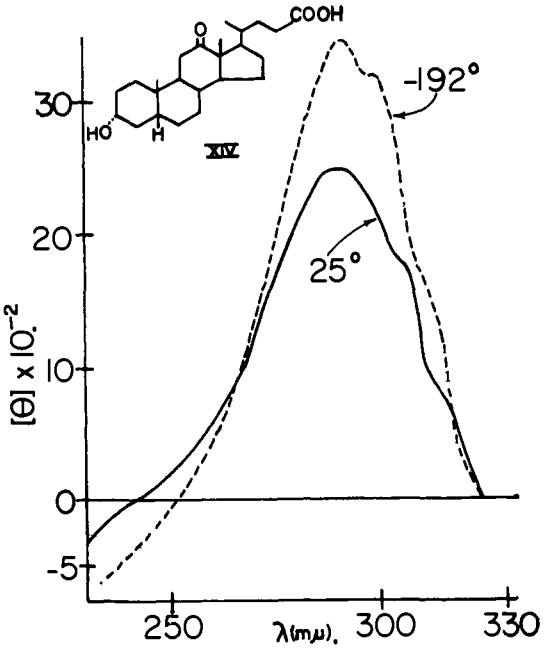


Fig. 9.—Circular dichroism (25 and −192°) of 3α-hydroxy-12 oxocholanic acid (XIV).

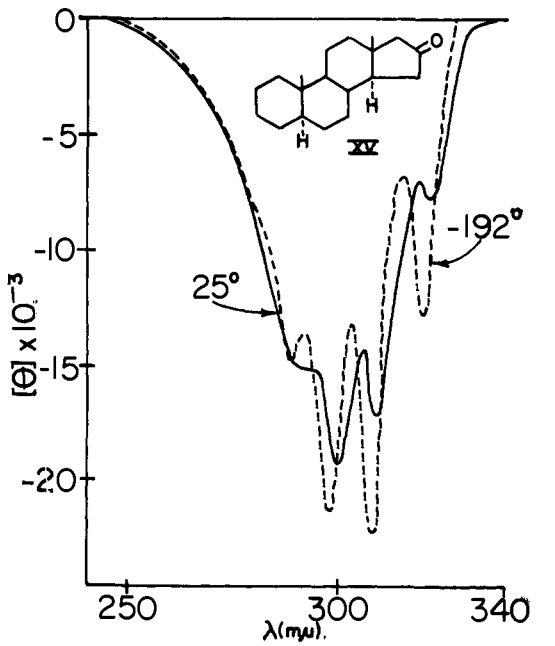


Fig. 10.—Circular dichroism (25 and −192°) of 5α-androstan-16-one (XV).

The C.D. curves (see Fig. 9) of 12-keto steroids, measured either at room temperature or at −192°, exhibit only an indication of fine structure, a characteristic which is independent of the configuration at C-5 (XIII or XIV) and which thus serves very well to differentiate a 12-ketone from any other six-membered ketone (C-2, C-3, C-11) of the steroid series with a positive Cotton effect.

Steroidal cyclopentanones represent a separate class, easily distinguishable from the other nuclear ketonic steroids by infrared spectroscopy, and the only problem to be faced is that of differentiating among them. The enormous negative Cotton effect, associated with a 16-keto grouping (14α-configuration), has already been commented upon in earlier O.R.D. studies[8,13] and places

(13) C. Djerassi, R. Riniker, and B. Riniker, *J. Am. Chem. Soc.*, **78**, 6362 (1956).

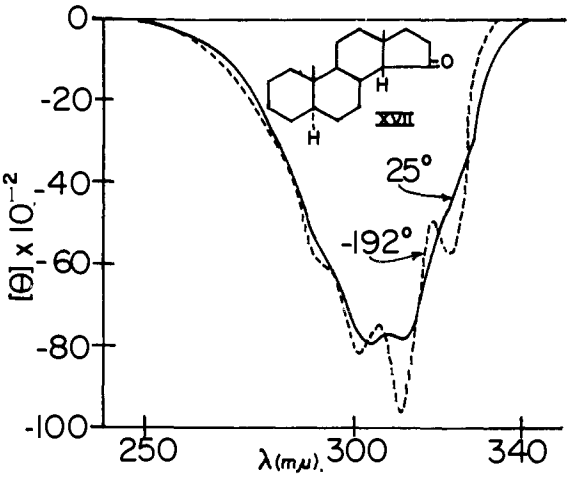


Fig. 11.—Circular dichroism (25 and −192°) of 5α,14β-androstan-15-one (XVII).

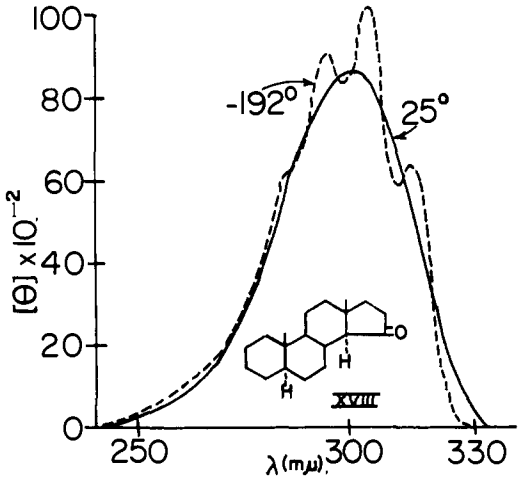
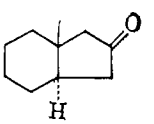


Fig. 12.—Circular dichroism (25 and −192°) of 5α,14α-androstan-15-one (XVIII)

this type of compound in a class by itself. Its circular dichroism (Fig. 10) is already characterized at room temperature by strong vibrational fine structure, which is simply sharpened somewhat upon lowering the temperature. An identical C.D. picture was obtained with its bicyclic analog XVI. The only other steroidal cyclopentanones which have been reported[13] to exhibit a negative Cotton effect are the 14β-15-ketones (*e.g.*, XVII). These can be differentiated from the 14α-16-ketones by virtue of the latter's much greater amplitude as well as by the differences (Fig. 11) in the C.D. fine structure.



XVI

15- (XVIII) and 17- (XIX) keto steroids of the 14α-series exhibit positive O.R.D. Cotton effects[8,13] which differ only slightly from a quantitative viewpoint. As noted in Fig. 12 and 13, their room temperature C.D. curves exhibit no fine structure, while that developed upon cooling to −192° is very similar in both types. It follows that neither O.R.D. nor C.D. can be used very effectively to differentiate between 15- (XVIII) and 17- (XIX) ketones with the C/D *trans* (14α) ring juncture. It should be recalled, however, that most 15-keto-14α-steroids (other than sterols) are readily isomerized with base—yielding a product

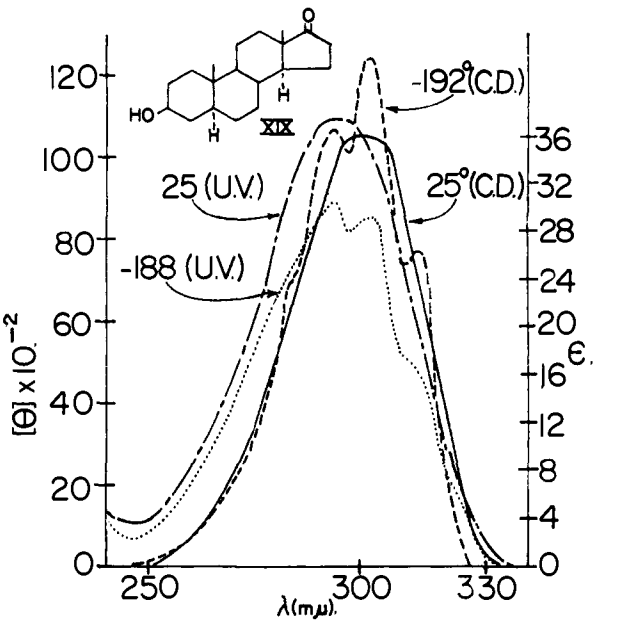


Fig. 13.—Circular dichroism (25 and −192°) and ultraviolet absorption (25 and −188°) of 5α-androstan-3β-ol-17-one (XIX).

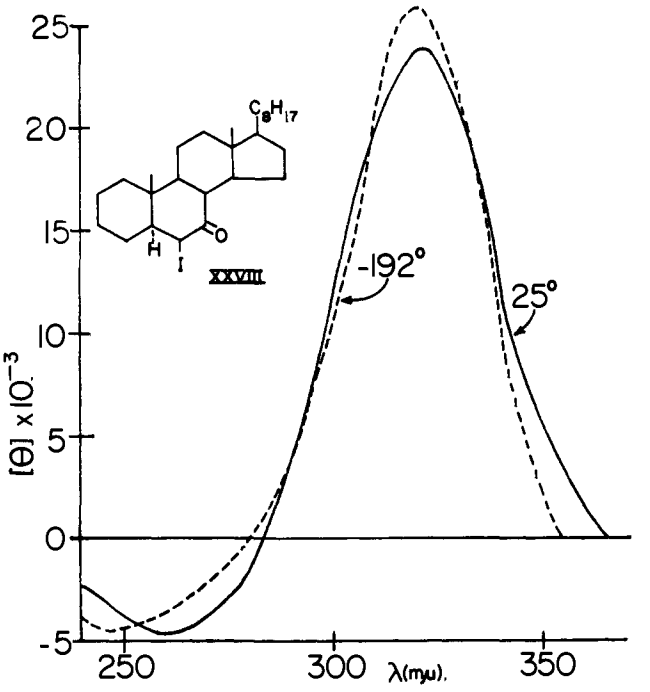


Fig. 14.—Circular dichroism (25 and −192°) of 6β-iodocholestan-7-one (XXVIII).

with a negative Cotton effect—so that O.R.D. or C.D. measurements before and after base treatment may offer diagnostic information.

In summary, it can be stated that for locating an isolated carbonyl group on a steroid skeleton, it is desirable to measure first the infrared spectrum—in order to determine the ring size—followed by O.R.D. and/or low-temperature C.D. measurements, a combination of all three being most desirable. Implicit in this conclusion is the previously documented observation that the presence of other "nonchromophoric" substituents in distant locations play no important role. There remains to be determined the effect of substituents adjacent to the carbonyl chromophore.

The effect upon the O.R.D. Cotton effect of chlorine,[14]

(14) C. Djerassi, J. Osiecki, R. Riniker, and B. Riniker, *J. Am. Chem. Soc.*, **80**, 1216 (1958).

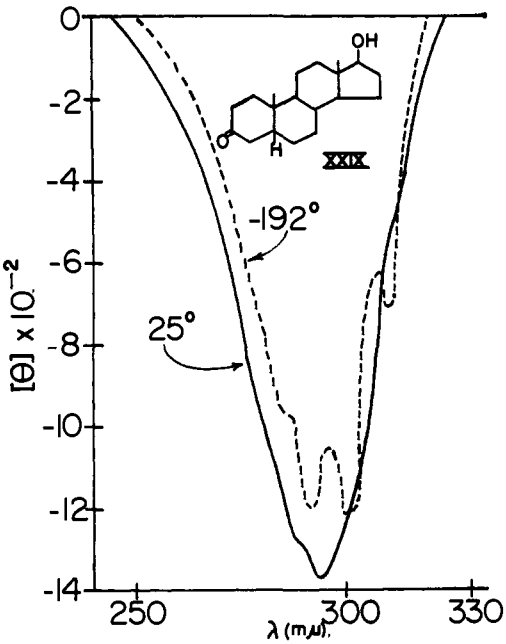
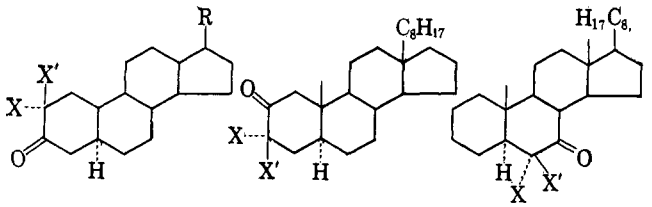


Fig. 15.—Circular dichroism (25 and −192°) of 5β-androstan-17β-ol-3-one (XXIX).

bromine,[14] fluorine,[14,15] and iodine[15,16] adjacent to a carbonyl group has already been studied in great detail and a few room temperature C.D. measurements have also been conducted.[16,17] The general conclusion was reached[14,18] that equatorial halogen atoms produce only a slight effect, while axially oriented halogens cause bathochromic shifts as well as possible inversions in sign of the Cotton effect. It was of interest, therefore, to determine whether the C.D. fine structure discussed in this paper would be affected by α-halogen substitution.

As a rule, introduction of an equatorial fluorine (XX), chlorine (XXI), bromine (XXIII), or iodine (XXVII) atom did not affect to any marked extent the vibrational fine structure in the low-temperature C.D. curves of the halogen-free parent ketones. However, insertion of an adjacent axial chlorine (XXII), bromine (XXIV), or iodine (XXVIII) atom obliterated completely any vestige of vibrational structure as is exemplified in the room temperature and −192° C.D. curves (Fig. 14) of 6β-iodocholestan-7-one (XXVIII).



XX, X = F, X′ = H, R = OAc
XXI, X = Cl, X′ = H, R = C_8H_{17}
XXII, X = Cl, X′ = Cl, R = C_8H_{17}
XXIII, X = H, X′ = Br
XXIV, X = Br, X′ = H
XXV, X = H, X′ = C_6H_5
XXVI, X = C_6H_5, X′ = H
XXVII, X = I, X′ = H
XXVIII, X = H, X′ = I

In the one case studied (cholestan-2-one (II)), introduction of an equatorial (XXV) or axial (XXVI) phenyl substituent did not affect the fine structure to any major extent, while attachment of a methyl group, as in 2α-methylcholestan-3-one, did produce some sharpening of vibrational structure, similar to the situation observed in going from an ordinary 3-keto steroid (*e.g.*, III in Fig. 3) to the 19-nor analog VIII (Fig. 4).

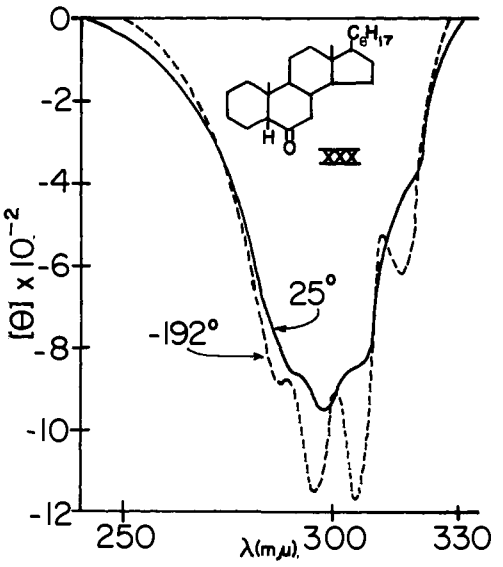


Fig. 16.—Circular dichroism (25 and −192°) of coprostan-6-one (XXX).

There remains to be considered the effect of stereochemical alterations in the ring skeleton. As noted above as well as in earlier O.R.D. studies,[8,19] stereochemical inversion at C-5 does not cause any important changes in the O.R.D. or C.D. behavior of 11- or 12-keto steroids. The situation is quite distinct, however, when the stereochemistry at that center is disturbed in ring A or B ketones. The explanation lies in the basic tenets of the octant rule[20] and need not be elaborated further at this stage, where only the effect upon vibrational fine structure is being considered.

In the 3-keto series, it is known[19] that inversion of the A/B ring juncture from 5α to 5β causes a reversal in sign of the Cotton effect and hence of the C.D. maximum. If one contrasts the low-temperature C.D. curve (Fig. 3) of a 5α-3-ketone (*e.g.*, III) with that (Fig. 15) of a 5β-3-ketone (XXIX), somewhat increased resolution can be noted in the latter. Of especial interest is a comparison of C-5 epimeric 6-keto steroids, since both exhibit[13,19] negative O.R.D. Cotton effects, with the 5β-isomer being much more intense. By comparing Fig. 6 (IX) and 16 (XXX), it can be seen that the relationship of the maxima at longest and shortest wave length—already noticeable in the room temperature C.D. curves—becomes very pronounced at −192° and can be used to good advantage in differentiating between 5α- and 5β-6-keto steroids.

In view of the close relationship[21] between the circular dichroism curve and the ultraviolet absorption spectrum of a given chromophore and the knowledge[22] that ultraviolet absorption spectra afford increased resolution at lower temperature, the question may be raised whether low-temperature ultraviolet spectros-

(15) C. Djerassi, I. Fornaguera, and O. Mancera, *J. Am. Chem. Soc.*, **81**, 2383 (1959).
(16) C. Djerassi, H. Wolf, and E. Bunnenberg, *ibid.*, **85**, 324 (1963).
(17) J.-M. Lehn and G. Ourisson, *Bull. soc. chim. France*, 1113 (1963).
(18) See also C. Djerassi and W. Klyne, *J. Am. Chem. Soc.*, **79**, 1506 (1957).
(19) C. Djerassi and W. Closson, *ibid.*, **78**, 3761 (1956).
(20) W. Moffitt, R. B. Woodward, A. Moscowitz, W. Klyne, and C. Djerassi, *ibid.*, **83**, 4013 (1961); C. Djerassi and W. Klyne, *J. Chem. Soc.*, 4929; 2390 (1963).
(21) (a) See C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, Chapters 1 and 12; (b) T. M. Lowry, "Optical Rotatory Power," Longmans, Green and Co., London, 1935, Chapter 11.
(22) See R. L. Sinsheimer, J. F. Scott, and J. R. Loofbourow, *J. Biol. Chem.*, **187**, 299 (1950).

copy in the n → π* region of the carbonyl chromophore may not also be used for the same type of fingerprinting among steroids. The answer is that low-temperature C.D. measurements are clearly preferable on two grounds.

First, at least two to three times as much material is required in ultraviolet spectrometry of such compounds because of the very low extinction, a drawback which may be quite serious with rare substances. Second, the resolution is not as satisfactory in the −188° absorption spectrum as compared to the C.D. curve measured at such low temperature. As examples, there are included both the room temperature and −188° absorption spectra of cholestan-3-one (III) and of 5α-androstan-3β-ol-17-one (XIX) in Fig. 3 and 13.

The appearance of and the variation in fine structure with changes in temperature and solvent have been attributed, *inter alia*, to the availability of low frequency vibrations and the nature of the solute–solvent interactions. Bayliss and McRae,[23] in particular, have discussed the fine structure of the long wave length n → π* carbonyl transition in terms of the solvent reorientation accompanying the redistribution of charge associated with the electronic promotion in the solute molecule. In terms of their model, the increased fine structure observed for many of the C.D. curves shown here might be attributed in part to a marked slowing down of solvent reorientation times at the lower temperatures in the now more viscous solvents. However, this can be at best only part of the explanation, since other mechanisms, such as the freezing out of low frequency vibrations, are undoubtedly also operative.

(23) N. S. Bayliss and E. G. McRae, *J. Phys. Chem.*, **58**, 1002, 1006 (1954).

Experimental

All measurements were performed in a mixture of ether–isopentane–ethanol in a ratio of 5:5:2 by volume using a Baird-Atomic/Jouan dichrograph operating with a photomultiplier voltage of 1.2 kv. and following the procedures and molecular ellipticity calculations outlined earlier.[4,5,11] A Cary Model 14 spectrophotometer was used for the ultraviolet measurements, using the normal programmed slit width.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, IOWA STATE UNIVERSITY OF SCIENCE AND TECHNOLOGY, AMES, IOWA]

Photoisomerization of 1-Aza-3,5,7-trimethylcyclohepta-4,6-dien-2-one[1]

BY O. L. CHAPMAN AND E. D. HOGANSON

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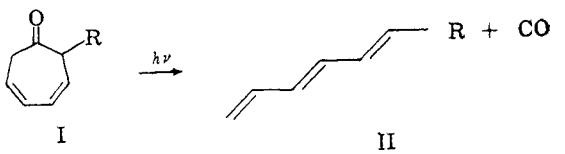
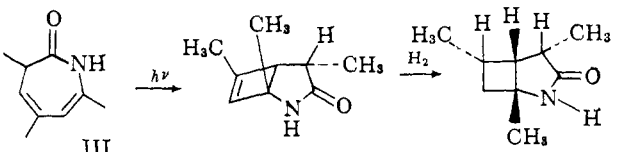
Irradiation of 1-aza-3,5,7-trimethylcyclohepta-4,6-dien-2-one (III) and its N-methyl derivative VII gives in each case a single photoisomer (two stereoisomers are possible) in 70% yield. The photoisomers are shown to be bicyclic valence tautomers by chemical transformations and spectroscopic absorption characteristics. The stereochemistry of the photoisomers is assigned on the basis of the spin coupling constant, J_{45}, and chemical equilibration. The photoisomerization provides a facile synthetic entry to a novel heterocyclic system. Unexpected spin–spin coupling between the C-6 methyl protons and the C-5 proton in IV is detected by double resonance. The N-methyl group of VIII appears as a doublet due to long range coupling to either the proton at C-4 or the proton at C-5.

A variety of conjugated cyclic and acyclic dienes photoisomerize smoothly to cyclobutene derivatives.[2,3] This photoisomerization is particularly useful for conjugated cycloheptadienes.[4,5] 3,5-Cycloheptadienone (I, R = H) and 2-methyl-3,5-cycloheptadienone (I, R = CH_3), however, undergo an anomalous photochemical reaction forming carbon monoxide and 1,3,5-hexatriene (II, R = H) and 1,3,5-heptatriene (II, R = CH_3).[5,6] The formal similarity between the dienelactam III and the 3,5-cycloheptadienones in placement of trigonal atoms within the seven-membered ring together with the possibility of facile formation of a novel heterocyclic system prompted a study of the photochemistry of III.



I II



III IV

Irradiation of ether solutions of III[7] with a mercury arc lamp encased in a quartz immersion well for 1 hr. gives after removal of the ether and sublimation of the product a single bicyclic photoisomer, m.p. 67–69°, in 70% yield. The photoisomer (osmometric molecular weight 142) shows infrared maxima at 3.15 and 3.27 (N–H), 3.38 and 3.43 (C–H), 5.94 (amide carbonyl), and 6.14 μ (C=C) but no ultraviolet maxima above 220 mμ. Catalytic reduction of the photoisomer gives a saturated dihydro derivative, m.p. 94–95°, 5.90 μ. The photoisomer thus must be bicyclic. Pyrolysis (430°) of the photoproduct gives the starting dienelactam III in 50% yield. This shows the photoprod-

(1) Part X of the photochemical transformations series. For part IX see O. L. Chapman, H. G. Smith, and P. A. Barks, *J. Am. Chem. Soc.*, **85**, 3171 (1963). Portions of this manuscript were taken from the M.S. thesis of E. Hoganson, Iowa State University of Science and Technology, 1963. Similar results have been obtained by L. A. Paquette, *J. Am. Chem. Soc.*, **86**, 500 (1964).

(2) O. L. Chapman, in "Advances in Photochemistry," Vol. I, W. A. Noyes, Jr., G. S. Hammond, and J. N. Pitts, Jr., Ed., Interscience Publishers, Inc., New York, N. Y., 1963.

(3) P. de Mayo and S. T. Reid, *Quart. Rev.* (London), **15**, 393 (1961).

(4) W. G. Dauben and R. L. Cargill, *Tetrahedron*, **12**, 186 (1961).

(5) O. L. Chapman and D. J. Pasto, *Chem. Ind.* (London), 54 (1961); O. L. Chapman, D. J. Pasto, A. A. Griswold, and G. W. Borden, *J. Am. Chem. Soc.*, **84**, 1220 (1962).

(6) O. L. Chapman and G. W. Borden, *J. Org. Chem.*, **26**, 4185 (1961).

(7) L. A. Paquette, *J. Am. Chem. Soc.*, **84**, 4987 (1962).