such as OH^- or SCN^-[20] and precisely in the same quantitative order as the E_s constants indicate. This could conceivably be the case but in the absence of powerful evidence to support it, the simple picture of "SN2-like" attack in electroreduction of alkyl bromides must be discarded.

Alternatively, the attack may be as Sease has proposed for bridgehead bromides,[21] "head-on" to the bromine resulting in displacement of the R *from* the bromine. But in this process of attack from the bromine side, no conventional steric effects by R groups should be noted in polarographic reduction of RBr compounds; the $E_{1/2}$ values of our alkyl bromides should lie on a line *vs.* σ^* prior to any correction for steric factors. Thus, frontal attack on bromine is at variance with the experimental results in this paper.

A third possibility for the geometry of the transition state could involve attack on the alkyl bromide by electrons from the DME in a direction perpendicular to the axis of the CBr bond.[22] Certainly, this would be spatially consistent with addition of an electron to the σ-antibonding orbital. In such a process not only would steric effects of nearby alkyl groups be present but they should be roughly as effective as in the hydrolysis process from which the Taft steric constants were derived. In hydrolysis, the incoming group also attacks perpendicularly to the axis of the (>C=O) bond. The quantitative success of the E_s parameters in correlating the polarographic behavior of these widely differing alkyl bromides provides support for a mechanism involving side attack on the CBr bond.

Work is planned to explore the mechanism of the involvement of distant groups in electroreductions including the use of *p*-methylthiophenoxyalkyl bromides to indicate the extent of radical character in the activated intermediate.[23]

Acknowledgments.—We gratefully acknowledge the essential support of the National Science Foundation under G11282 and GP-1438. We also thank Ralph W. Donaldson, Jr., for preliminary studies; Ted W. Reid, Jerry L. Kerkmeyer, and James P. Hardy for assistance in compound preparation or purification; and John E. Hiatt and David L. McFadden for hydrolytic kinetics under National Science Foundation Undergraduate Research Participation Programs.

[20] The *ad hoc* argument on p 5327 of ref 1b to explain the more negative reduction potentials of butyl and amyl bromides than propyl bromide invoked *more* hindrance to polarographic electron attack than SCN^- attack because the dominant importance of polar substituent effects was not then seen.

[21] J. W. Sease, P. Chang, and J. L. Groth, *J. Am. Chem. Soc.*, **86**, 3154 (1964).

[22] A possibility suggested by Professor A. Streitwieser, Jr., Gordon Research Conference on Electrochemistry, Santa Barbara, Calif., Jan 1965.

[23] A. Streitwieser, Jr., and C. Perrin, *J. Am. Chem. Soc.*, **86**, 4938 (1964).

Synthetic Experiments in the Eudalene Group of Bicyclic Sesquiterpenes. II[1]

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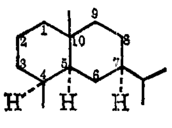
Department of Chemistry, University College, Cardiff, Wales, and Department of Chemistry, Clemson University, Clemson, South Carolina

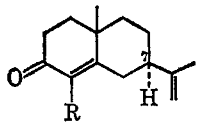
Received July 8, 1966

Some investigations on the application of the Robinson–Mannich annelation reaction to synthesis in the eudesmane group of sesquiterpenes are described. Epimerization at position 7 of the diketone XIV and the epoxide XV is easily effected by acid or base treatment. The possibility of using the major products of annelation reactions with (–)-dihydrocarvone in synthesis is thereby opened up.

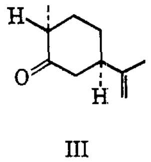
The Robinson–Mannich and related annelation reactions have featured prominently in syntheses in the terpene and steroid fields. We describe here some preliminary experiments designed to extend the application of the reaction in syntheses in the eudesmane (I) group of bicyclic sesquiterpenes. Our attention has been focussed in particular on the stereochemical problems[5] involved in the use of the reaction as a starting point in synthesis in this family.



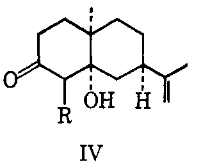
I



II



III



IV

In their synthesis of natural (+)-α-cyperone (II, R = CH_3) Howe and McQuillin[6] effected a Robinson–Mannich condensation between (+)-dihydrocarvone, of known absolute configuration[7] (III), and 1-diethylaminopentan-3-one methiodide. The major products were the ketol IV (R = CH_3) and the conjugated enone V (R = CH_3), in accordance with the established stereochemical course of the annelation reaction.[8] (+)-α-Cyperone (II, R = CH_3) was a minor product, but fortunately it was easily separated by chromatography and through the crystalline oxime. We anticipated that an analogous condensation of (+)-

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[1] Part I: A. R. Pinder and R. A. Williams, *J. Chem. Soc.*, 2773 (1963); *Chem. Ind.* (London), 1714 (1961).

[2] Abstracted from a thesis presented by D. C. Humber in partial fulfillment of the requirements for the Ph.D. Degree, University of Wales.

[3] Glaxo Research, Ltd., Greenford, Middlesex, England.

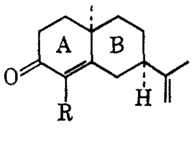
[4] To whom correspondence should be addressed, at Clemson University.

[5] For a review of stereochemical relationships among eudesmane sesquiterpenes see W. Cocker and T. B. H. McMurry, *Tetrahedron*, **8**, 181 (1960). We have used these authors' numbering.

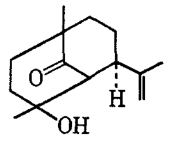
[6] R. Howe and F. J. McQuillin, *J. Chem. Soc.*, 2423 (1955).

[7] A. J. Birch, *Ann. Rept. Chem. Soc.*, **47**, 192 (1950), and references cited therein.

[8] (a) F. J. McQuillin, *J. Chem. Soc.*, 528 (1955); (b) T. A. Spencer, H. S. Neel, D. C. Ward, and K. L. Williamson, *J. Org. Chem.*, **31**, 434 (1966); (c) K. L. Williamson, L. R. Sloan, T. Howell, and T. A. Spencer, *ibid.*, **31**, 436 (1966); (d) T. A. Spencer, K. K. Schmiegel, and K. L. Williamson, *J. Am. Chem. Soc.*, **85**, 3785 (1963); (e) W. Cocker, *Ann. Rept. Chem. Soc.*, **51**, 210 (1954); (f) J. A. Marshall and W. I. Fanta, *J. Org. Chem.*, **29**, 2501 (1964).

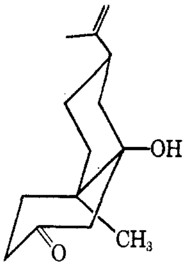


V

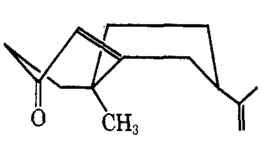


VI

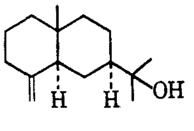
dihydrocarvone and 1-diethylaminobutan-3-one methiodide would lead to some II (R = H), with the correct stereochemistry for the synthesis under investigation. The condensation was effected, using sodium amide as base, and afforded the expected mixture of products II, IV, and V (R = H). Efforts to separate the first in a pure condition were only partially successful, though a variety of methods was tried. The other two products were easily separated and purified; the crystalline ketol is formulated as IV (R = H) because of the steric course of the annelation reaction and because its ORD curve and that of the analog IV (R = CH$_3$)[6] are virtually superimposable. The possibility of its having the bridged structure[9] (VI) is ruled out by the fact that its nmr spectrum shows only two singlet methyl signals, at 1.7 and 1.2 ppm. The ORD curve of this compound was quite unlike the mirror image of that of coprostan-3-one, in agreement with the expectation that it has nonsteroidal *cis*-fused rings,[8,10] as in VII (strong negative Cotton effect). The observed chemical shift of the angular methyl group (1.18 ppm, TMS = 0) is in agreement with this assignment of conformation.[8c,11]



VII



VIII

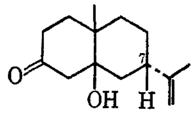


IX

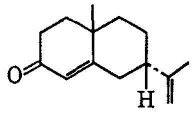
The major enone (V, R = H) was separated conveniently as its semicarbazone; it was also obtained by dehydration of ketol IV (R = H) under mild acid conditions. Its ORD curve bears a mirror image relationship to those of (+)-7-epi-α-cyperone[12] (II, R = CH$_3$, inverted at position 7) and 8-isotestosterone,[13] suggesting that in V (R = H) ring B has a boat conformation, as in these compounds. The ketone may therefore be more precisely formulated as VIII. The enantiomers of this ketone and of ketol IV (R = H) have been described very recently by Theobald.[14]

The minor enone II (R = H) was similarly isolated, in very poor yield, as its semicarbazone, which was cleaved with oxalic acid. Its ORD curve was almost superimposable upon that of (+)-α-cyperone (II, R = CH$_3$).[6] Despite the small amount of this ketone available, some progress toward the synthesis of β-eudesmol (IX) was made with it as starting point; this work will be described in a forthcoming paper.

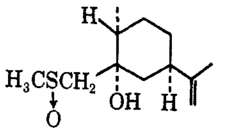
The principal products of an annelation reaction between (−)-dihydrocarvone and methyl vinyl ketone would be X and XI. Attention was next turned to the possibility of epimerizing these structures at position 7, so as to arrive at the desired eudesmane stereochemistry. Since we had the corresponding products derived from (+)-dihydrocarvone at hand we continued our studies in that series, *i.e.*, with IV and V (R = H), secure in the knowledge that any success could be reproduced with X and XI.



X



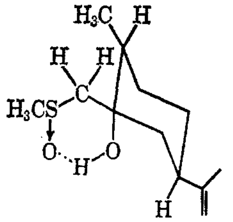
XI



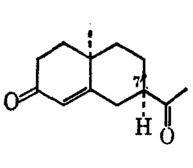
XII

The use of methylsulfinyl carbanion[15] as catalyst in the annelation reaction was more convenient. A complication was the formation of a small amount of aldol-type product XII, easily separable by chromatography.[15b] The structure of this by-product was settled by its hydrolysis to dimethyl sulfoxide and (+)-dihydrocarvone, by its ultraviolet spectrum [$\lambda_{\max}^{\text{EtOH}}$ 206 mμ (ε 2045)],[16] and by its infrared spectrum [bands at 3636 (free OH), 3472 (bonded OH), 1019 (S→O, H bonded[17]), and 891 cm^{-1} (C=CH$_2$)]. An interesting feature of its nmr spectrum was the presence of an AB quartet centered at 2.8 ppm (TMS = 0, 2 H, J = 12 cps), ascribed to the nonequivalence of the geminal protons of the CH$_2$SO group, adjacent to an asymmetric center.[18]

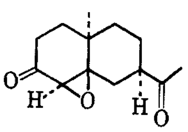
It is to be expected that the bulky methylsulfinyl group will be equatorial, so that the product can be formulated in more detail as XIII.



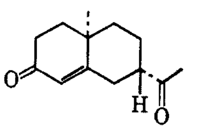
XIII



XIV



XV



XVI

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[9] W. S. Johnson, J. J. Korst, R. A. Clement, and J. Dutta, *J. Am. Chem. Soc.*, **82**, 614 (1960).

[10] *Cf.* R. Howe and F. J. McQuillin, *J. Chem. Soc.*, 1194 (1958); T. G. Halsall, D. W. Theobald, and K. B. Walshaw, *ibid.*, 1029 (1964); C. Djerassi, "Optical Rotatory Dispersion," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, p 185.

[11] W. G. Dauben, R. M. Coates, N. D. Vietmeyer, L. J. Durham, and C. Djerassi, *Experientia*, **21**, 565 (1965); D. R. Elliott, M. J. T. Robinson, and F. G. Riddell, *Tetrahedron Letters*, 1693 (1965).

[12] C. Djerassi, R. Riniker, and B. Riniker, *J. Am. Chem. Soc.*, **78**, 6362 (1956); R. Howe and F. J. McQuillin, *J. Chem. Soc.*, 1513 (1958); C. Djerassi, O. Halpern, V. Halpern, and B. Riniker, *J. Am. Chem. Soc.*, **80**, 4001 (1958).

[13] C. Djerassi, R. Riniker, and B. Riniker, *ibid.*, **78**, 6377 (1956).

[14] D. W. Theobald, *Tetrahedron Letters*, 969 (1966); *Tetrahedron*, **22**, 2869 (1966).

[15] (a) E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **84**, 866 (1962); (b) *ibid.*, **87**, 1345 (1965); see also G. G. Price and M. C. Whiting, *Chem. Ind.* (London), 775 (1963).

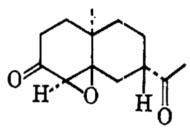
[16] H. P. Koch, *J. Chem. Soc.*, 2892 (1950); G. Leandri, A. Mangini, and R. Passerini, *ibid.*, 1386 (1957).

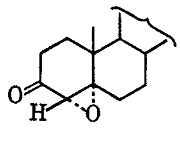
[17] T. Cairns, G. Eglinton, and D. T. Gibson, *Spectrochim. Acta*, **20**, 31 (1964).

[18] Compare, *inter alia*, H. R. Snyder, *J. Am. Chem. Soc.*, **85**, 2624 (1963); N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1964, pp 54–61, and references cited therein.

Ozonolysis of enone V (R = H) under neutral conditions, with work-up by steam distillation, afforded diketone XIV, accompanied by a small yield of the epoxy diketone XV. The ORD curve of XIV was very similar, in the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ regions of the enone chromophores, to that of starting enone V (R = H), and if it can be assumed that the 7-acetyl group makes no contribution to the Cotton effects (because of free rotation), it may be concluded that there has been no inversion at position 7 during the ozonolysis. Confirmation of configuration XIV was provided by treatment of the diketone with acid, which effected epimerization to enedione XVI. The ultraviolet absorption maximum of XVI appeared at 236 mμ (ethanol), while that of (XIV) was at 241 mμ. Howe and McQuillin[6] have observed that an epimerization of this type is accompanied by a hypsochromic shift of the absorption maximum in the case of (+)-7-epi-α-cyperone and (+)-α-cyperone. The ORD curve of XVI was very different in appearance from that of both V (R = H) and XIV in the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ regions of the enone chromophores, but a close resemblance was noted between it and the mirror image of that of cholest-4-en-3-one in the $n \rightarrow \pi^*$ region.[13,19]

The formation of epoxide XV (mp 104.5–106°) as a by-product of the ozonolysis is not unprecedented.[20] By way of confirmation of the stereochemistry at position 7, diketone XIV was epoxidized with alkaline hydrogen peroxide,[21] leading to a syrupy mixture of epoxides, from which XVII could be crystallized. An identical mixture was obtained by epoxidation of epimerized diketone XVI under the same conditions. The crystalline epoxide XVII (mp 61–62°) was also formed when epoxide XV was exposed to alkali for some hours at 0°. It is apparent that the two epoxides are C_7 epimerides, the alkaline hydrogen peroxide epoxidation of XIV having been accompanied by epimerization at position 7. Further, the configuration of the epoxy group is the same in both epoxy ketones. Previous work has shown that in the steroid series the formation of 4α,5α-epoxy-3-keto steroids from Δ^4-3-keto steroids is accompanied by a large negative ΔM_D,[22] and similarly 4β,5β-epoxidation results in a large positive value.[21a,22a,23] Table I shows that in the epoxidations under consideration the ΔM_D values are both strongly positive, and it is concluded that, since we are concerned with a system enantiomeric with the AB rings in steroids, the epoxides are in both cases 4β,5β. This configurational assignment is consistent with the observation[24] that 4α,5α-epoxycholestan-3-one (XVIII) shows a negative Cotton effect in its ORD curve; both our epoxy ketones showed strongly positive effects (XV, *a* +132; XVII, *a* +185, compared with XVIII, *a* −179),[24] in agreement with the enantiomeric relation between them and the steroidal epoxide. The signs of these Cotton effects in the $n \rightarrow \pi^*$ region of the cyclic keto groups are the same as those predicted on the basis of the reversed octant rule, the epoxide oxygen lying in the upper right (positive) octant in both structures.[25] The formation of epoxide XV during the ozonolysis could be prevented by effecting the reaction in the presence of pyridine.[26]


XVII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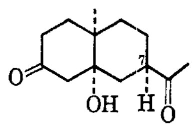
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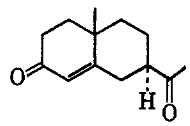
XX

TABLE I

Ketone	$M^K{}_D$, deg	Epoxide	$M^E{}_D$, deg	$\Delta M_D = M^E{}_D - M^K{}_D$, deg
XIV	−330	XV	−7	+323
XVI	−183	XVII	+164	+347

A superior route to diketone XIV was ozonolysis of crystalline ketol IV (R = H) to diketo alcohol XIX, the ORD curve of which was very similar to that of ketol IV (R = H). Evidently epimerization at C-7 had not occurred. Acid-catalyzed dehydration of XIX gave diketone XVI, with concomitant C-7 epimerization. It was also found convenient to ozonize the mixture of ketones II and V (R = H). This led to a mixture of diketones XIV and XX, separable by preparative thin layer chromatography. The latter, as expected, proved to be the enantiomer of "inverted" diketone XVI. The use of XX in the synthesis of β-eudesmol will be described in a forthcoming paper.[27] While this work was in progress a stereospecific synthesis of (±)-β-eudesmol was announced.[28]

Experimental Section[29]

(+)-Dihydrocarvone.—(−)-Carvone was reduced with zinc dust and alkali, essentially as described by Wallach and Schrader.[30] Pinacol formation was reduced to a minimum by carrying

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(19) A. E. Lippman, E. W. Foltz, and C. Djerassi, *J. Am. Chem. Soc.*, **77**, 4364 (1955).

(20) For other examples see P. S. Bailey, *Chem. Rev.*, **58**, 945 (1958).

(21) Compare (a) P. A. Plattner, H. Heusser, and A. Kulkarni, *Helv. Chim. Acta*, **31**, 1822 (1948); (b) R. L. Wasson and H. O. House, "Organic Syntheses," Coll. Vol. 4, John Wiley and Sons, Inc., New York, N. Y., 1963, p 552.

(22) (a) H. J. Ringold, E. Batres, O. Mancera, and G. Rosenkranz, *J. Org. Chem.*, **21**, 1432 (1956); (b) R. H. Bible, C. Placek, and R. D. Muir, *ibid.*, **22**, 607 (1957); (c) D. J. Collins, *J. Chem. Soc.*, 3919 (1959); (d) B. Camerino, B. Patelli, and A. Vercellone, *J. Am. Chem. Soc.*, **78**, 3540 (1956).

(23) E. P. Oliveto, C. Gerold, and E. B. Hershberg, *ibid.*, **79**, 3596 (1957).

(24) J. M. Coxon, M. P. Hartshorn, and D. N. Kirk, *J. Chem. Soc.*, 2461 (1964).

(25) C. Djerassi, W. Klyne, T. Norin, G. Ohloff, and E. Klein, *Tetrahedron*, **21**, 163 (1965).

(26) *Cf.* G. Slomp and J. L. Johnson, *J. Am. Chem. Soc.*, **80**, 915 (1958).

(27) For a preliminary account, see D. C. Humber and A. R. Pinder, *Tetrahedron Letters*, 353 (1966).

(28) J. A. Marshall and M. T. Pike, *ibid.*, 3107 (1965).

(29) Melting points and boiling points are uncorrected. Ultraviolet spectra were measured on a Unicam SP800, and infrared spectra were taken on Perkin-Elmer Infracords 137 and 237 and Unicam SP200G instruments. Nmr spectra were determined on a Perkin-Elmer R10 spectrometer at 60 Mc/sec, in deuteriochloroform solution, using tetramethylsilane as internal standard. ORD measurements were made by Professor W. Klyne and his associates on a Bellingham-Stanley/Bendix-Ericsson Polarmatic 62 spectropolarimeter. Glpc analyses were carried out on a Pye Argon chromatograph using a 20% PEGA on 100–200 mesh Celite column. Thin layer chromatography was effected with Merck silica gel G (0.03 cm thick), with location of spots with iodine. Preparative thin layer chromatography was on Merck silica gel HF 254 (0.2 cm thick) with location by ultraviolet light. Optical rotations are in chloroform at 25°. Petroleum ether refers to the fraction bp 60–80°.

(30) O. Wallach and H. Schrader, *Ann.*, **279**, 377 (1894); F. J. McQuillin, private communication.

out the reaction rapidly and by adding the aqueous potassium hydroxide to the hot, vigorously stirred mixture of zinc, ethanol, and carvone. A small improvement in yield was achieved by re-using the alcohol fraction of the steam distillation in subsequent runs.

Condensation of (+)-Dihydrocarvone with 1-Diethylaminobutan-3-one Methiodide. A.—(+)-Dihydrocarvone (29.3 g) in dry ether (130 ml) was stirred under nitrogen with sodium amide (8.7 g) suspended in dry ether (130 ml). 1-Diethylaminobutan-3-one methiodide (58 g) in dry pyridine (70 ml) was added rapidly and the mixture was stirred under dry nitrogen for 4 hr at 0°. Stirring was continued overnight at room temperature, and then at reflux temperature for 5 hr. Water was added to the cooled system and the ether layer was separated, washed with dilute hydrochloric acid, water, and sodium bicarbonate, dried, and concentrated. Distillation of the residue afforded a foreun of (+)-dihydrocarvone (10.5 g) followed by a main fraction, bp 110–115° (0.1 mm), 20.35 g, which solidified partially on keeping. Trituration with petroleum ether yielded (+)-**decahydro-5α-hydroxy-7β-isopropenyl-10α-methyl-3-oxonaphthalene** (IV, R = H, 9.35 g) which crystallized from petroleum ether in plates: mp 107.5–108°; $[\alpha]_D$ +54.6° (c 4.3); $\nu_{max}^{CCl_4}$ 3704 (OH), 1721 (C=O), 1645 and 895 cm^{-1} (C=CH$_2$); $\delta_{TMS}^{CCl_4}$ 1.18 (singlet, 3 H, C-10-CH$_3$), 1.68 (singlet, 3 H, =CCH$_3$), 2.11 (singlet, 1 H, OH), 2.44 (AB quartet, partly obscured, 2 H, J = 14 cps, CH$_2$ at position 4), and 4.65 ppm (broad singlet, 2 H, C=CH$_2$); ORD in methanol (400–200 mμ, c 0.16) $[\phi]_{400}$ +170°, $[\phi]_{303}$ −1130°, $[\phi]_{262}$ +4070° (shoulder), $[\phi]_{211}$ +8400°; a_{262}^{303} −52.

Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.57, 75.60; H, 9.75, 10.00.[31]

Redistillation of the noncrystalline part gave additional ketol (1.1 g); the residue was chromatographed on alumina (200 g). Elution with petroleum ether gave a pale yellow liquid: bp 92–96° (0.15 mm); 5.1 g; $[\alpha]_D$ −24.5° (c 4.5); ν_{max}^{film} 1677 (conjugated ketone C=O), 1613 (conjugated C=C), and 892 cm^{-1} (RR′C=CH$_2$), a mixture of ketones II and V (R = H).

Anal. Calcd for $C_{14}H_{20}O$: C, 82.35; H, 9.80. Found: C, 82.30; H, 9.80.

Continued elution with ethanol gave more ketol (2.8 g); total yield of ketol was 48%, based on unrecovered dihydrocarvone.

The ketone mixture was converted into its semicarbazone mixture, which was crystallized fractionally from pyridine. The less soluble semicarbazone (3.5 g) formed colorless, photochromic prisms: mp 221°, $[\alpha]_D$ −260° (c 0.45, pyridine).

Anal. Calcd for $C_{15}H_{23}N_3O$: C, 68.97; H, 8.81; N, 16.09. Found: C, 69.00; H, 8.95; N, 161.10.

The more soluble semicarbazone separated in irregular prisms (1.2 g): mp 211–211.5°, $[\alpha]_D$ +194.7° (c 0.53, pyridine). A further crystallization from ethanol gave rhombic prisms, mp 212–213°.

Anal. Found: C, 68.90; H, 8.60; N, 16.25.

The second semicarbazone (0.84 g), methanol (35 ml), water (15 ml), petroleum ether (12 ml), 40% aqueous formaldehyde (10 ml), and oxalic acid (2.0 g) were refluxed for 3 hr. Water was added, and the organic layer was separated, washed with water, dried, and distilled. The residue on chromatography on alumina, with elution with light petroleum gave (+)-**4-nor-α-cyperone** (II, R = H): 0.54 g; bp 85–86° (0.1 mm); n^{19}_D 1.5246; $[\alpha]_D$ +94.7° (c 0.80); λ_{max}^{MeOH} 243 mμ (ϵ 13,600); ν_{max}^{film} 1675 (conjugated ketone), 1616 (conjugated C=C), and 892 cm^{-1} (RR′C=CH$_2$).

Anal. Calcd for $C_{14}H_{20}O$: C, 82.35; H, 9.80. Found: C, 82.30; H, 9.91.

The **2,4-dinitrophenylhydrazone** after alumina chromatography, separated from ethanol as red needles: mp 165–166°, $[\alpha]_D$ +334° (c 0.29), $\lambda_{max}^{CHCl_3}$ 398 mμ (ϵ 28,800).

Anal. Calcd for $C_{20}H_{24}N_4O_4$: C, 62.50; H, 6.25; N, 14.58. Found: C, 62.12; H, 6.14; N, 14.30.

The oxime crystallized from petroleum ether (bp 40–60°) in feathery needles: mp 119.5–120°, $[\alpha]_D$ +133° (c 0.5, ethanol).

Anal. Calcd for $C_{14}H_{21}NO$: C, 76.71; H, 9.59; N, 7.39. Found: C, 76.64; H, 10.09; N, 6.63.

B.—Sodium methylsulfinyl carbanion was prepared under dry nitrogen, from powdered sodium hydride (5.0 g) and dry dimethyl sulfoxide (200 ml), essentially as described by Corey and Chaykovsky.[15] Freshly distilled (+)-dihydrocarvone (25.0 g) in dimethyl sulfoxide (35 ml) was added gradually at 25° with efficient stirring, during 1 hr and the mixture was stirred for 1 additional hr to ensure complete enolate formation. The methiodide prepared from diethylaminobutan-3-one (25.0 g) and methyl iodide (25.0 g)[32] was dissolved in dimethyl sulfoxide (100 ml) and added to the stirred enolate at 15° during 20 min. After 2 hr of stirring at room temperature, the mixture was poured into ice–water and the product was isolated with ether. Evaporation of the solvent was followed by a fraction, bp 120–140° (0.4 mm), 15.0 g, which crystallized partially on keeping. Trituration with petroleum ether, cooling, and filtration afforded ketol IV (R = H, 4.1 g), identical with that obtained under A.

Evaporation of the filtrate left an oily residue (10.9 g). A portion (5.0 g) of this, in petroleum ether was chromatographed on alumina (Peter Spence Type H, 100 g). Elution with benzene–petroleum ether mixture gave a yellow oil (2.7 g), shown by gas chromatography to be a mixture of the C-10 epimerides II and V (R = H) in the ratio 2:1. Ethanol elution gave a more strongly adsorbed fraction (2.0 g).

Repetition of the chromatography using silica gel (Davison, 100 g), with benzene–chloroform mixture elution, gave a yellow liquid (1.45 g), consisting of the same ketone mixture. Chloroform elution then gave an orange liquid (2.56 g) from which crystals (0.86 g) of ketol IV (R = H) separated. Continued chloroform elution yielded a yellow liquid (0.57 g) which crystallized from petroleum ether as needles (0.18 g) of aldol XII: mp 116.5°; $[\alpha]_D$ −124° (c 2.0); λ_{max}^{EtOH} 206 mμ (ϵ 2045);[16] $\nu_{max}^{CCl_4}$ 3636 (free OH), 3472 (bonded OH), 1650 and 891 (C=CH$_2$), and 1019 cm^{-1} (S→O, H bonded);[17] $\delta_{TMS}^{CCl_4}$ 0.98 (doublet, 3 H, >CHCH_3, J = 4 cps), 1.74 (singlet, 3 H, =CCH$_3$), 2.61 (singlet, 3 H, CH$_3$SO), 2.80 (AB quartet, 2 H, CH$_2$SO, J = 12 cps), 3.70 (broad singlet, 1 H, OH), and 4.70 ppm (singlet, 2 H, =CH$_2$).

Anal. Calcd for $C_{12}H_{22}O_2S$: C, 62.58; H, 9.63; S, 13.89. Found: C, 62.24; H, 9.58; S, 13.53.

Treatment of the product with hot 0.5 N alkali yielded (+)-dihydrocarvone, identified as its 2,4-dinitrophenylhydrazone, orange sheaves from ethanol; mp 146°, $[\alpha]_D$ +75.9° (c 0.3).[33]

Anal. Calcd for $C_{16}H_{20}N_4O_4$: C, 57.82; H, 6.07; N, 16.86. Found: C, 57.86; H, 6.15; N, 17.16.

Dehydration of Ketol IV (R = H).—(+)-Decahydro-5α-hydroxy-7β-isopropenyl-10α-methyl-3-oxonaphthalene (IV, R = H, 4.75 g) in ethanol (80 ml) was mixed with concentrated hydrochloric acid (8 ml) and kept for 8 days. Water and sodium bicarbonate were then added and the product was isolated with ether. Distillation of the residue after evaporation of the solvent afforded (−)-**7β-isopropenyl-10α-methyl-Δ^4-octalone-3** [V, R = H; 3.93 g; 90%; bp 83–84° (0.05 mm)]; n^{24}_D 1.5310; $[\alpha]_D$ −189° (c 4.8); λ_{max}^{MeOH} 243 mμ (ϵ 14,210); ν_{max}^{film} 1664 (conjugated ketone), 1616 (conjugated C=C), and 893 cm^{-1} (RR′C=CH$_2$), no OH band; $\delta_{TMS}^{CCl_4}$ 1.26 (singlet, 3 H, C-10—CH$_3$), 1.71 (singlet, 3 H, =CCH$_3$), 4.82 (multiplet, 2 H, C=CH$_2$), and 5.70 ppm (singlet, 1 H, >C=CHCO); ORD in methanol (c 0.19, 500–315 mμ, and 0.02, 315–265 mμ) $[\phi]_{500}$ −40°, $[\phi]_{400}$ −600°, $[\phi]_{352}$ −1230°, $[\phi]_{306}$ +1280°, $[\phi]_{265}$ +370°; a_{206}^{352} −25 (c 1.9 mg/ml, methanol).

Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 81.98; H, 9.87.

The **2,4-dinitrophenylhydrazone** crystallized from ethanol in bright red needles: mp 134–135°, $[\alpha]_D$ −402° (c 0.19), $\lambda_{max}^{CHCl_3}$ 395 mμ (ϵ 24,910).

Anal. Calcd for $C_{20}H_{24}N_4O_4$: C, 62.48; H, 6.29; N, 14.58. Found: C, 62.27; H, 6.15; N, 14.63.

The semicarbazone separated from methanol in prisms, mp 221°, which were photochromic, $[\alpha]_D$ −260° (c 0.5, pyridine).

Anal. Calcd for $C_{15}H_{23}N_3O$: C, 68.93; H, 8.87; N, 16.08. Found: C, 68.72; H, 8.90; N, 16.25.

The oxime was an oil: bp 115–120° (0.05 mm), $[\alpha]_D$ −209° (c 2.0, ethanol).

Anal. Calcd for $C_{14}H_{21}NO$: C, 76.66; H, 9.65; N, 6.39. Found: C, 76.02; H, 9.47; N, 6.22.

Theobald[14] records, for the enantiomer of this ketone, n^{20}_D 1.5353, $[\alpha]_D$ +185°, λ_{max} 241 mμ (ϵ 16,200), ν_{max} 1665, 1640, and 893 cm^{-1}; ORD (in methanol) a_{310}^{353} +24.5; 2,4-dinitrophenylhydrazone mp 139–140°; see also Marshall, *et al.*[31]

The same ketone was obtained by hydrolytic cleavage of the less soluble semicarbazone, mp 221°, described above.

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(31) The enantiomer of this compound has been described recently by D. W. Theobald[14] who records mp 110–111°, $[\alpha]_D$ −58°, ORD a_{265}^{301} +25, $\delta_{TMS}^{CCl_4}$ 1.2 and 1.7 ppm, and by J. A. Marshall, W. I. Fanta, and H. Roebke [*J. Org. Chem.*, **31**, 1016 (1966)], who give mp 106–107°.

(32) A. L. Wilds and C. H. Shunk, *J. Am. Chem. Soc.*, **65**, 469 (1943).

(33) G. Farges and A. Kergomard [*Bull. Soc. Chim. France*, 51 (1963)] give mp 146–147°.

Ozonolysis of Ketone V (R = H). **A.**—The ketone (3.0 g) in dry chloroform (20 ml) was ozonized at 0° for 23 hr. Water (100 ml) was added and the solvent steam-distilled off. The cooled residue was extracted thrice with chloroform and the extracts washed with aqueous sodium bicarbonate and water, dried and concentrated *in vacuo*. The viscous residue distilled at 144° (0.35 mm), 2.5 g, and solidified to a waxy solid, which crystallized from ether to give white prisms, mp 68–72°, raised to 70–75° (0.80 g) by a further crystallization from petroleum ether. Thin layer chromatography revealed the presence of two products with R_f values 0.48 and 0.62, which were separable by preparative thin layer chromatography. The former, **7β-acetyl-10α-methyl-Δ^4-octalone-3** (XIV), crystallized from petroleum ether (bp 40–60°)–ether in prisms: 0.35 g, mp 56–57.5°; $[\alpha]_D$ −160° (*c* 2.0); $\lambda_{\max}^{\mathrm{EtOH}}$ 641 mμ (ε 13,840); $\nu_{\max}^{\mathrm{CCl_4}}$ 1720 (C=O), 1680 (conjugated ketone C=O), and 1620 cm^{-1} (conjugated C=C); $\delta_{\mathrm{TMS}}^{\mathrm{CDCl_3}}$ 1.26 (singlet, 3 H, C-10—CH_3), 2.20 (singlet, 3 H, $COCH_3$), and 5.82 ppm (singlet, 1 H, C=CH); ORD in methanol (*c* 0.16, 500–300 mμ, and 0.03, 300–198 mμ) $[\phi]_{500}$ −310°, $[\phi]_{400}$ −580°, $[\phi]_{355}$ −940°, $[\phi]_{308}$ +6800°, $[\phi]_{258}$ −47,000° $[\phi]_{222}$ +11,600°, $[\phi]_{217}$ +11,200°, and $[\phi]_{198}$ +36,000°.

Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.56; H, 8.77.

The product with R_f 0.62 proved to be **7β-acetyl-4β,5β-epoxy-10α-methyldecalone-3** (XV); it crystallized from petroleum ether in plates: mp 104.5–106° (0.22 g); $[\alpha]_D$ −3.0° (*c* 2.0); no characteristic ultraviolet absorption; $\nu_{\max}^{\mathrm{CCl_4}}$ 1715 (C=O), 1260 and 925 cm^{-1} (epoxide);[34] $\delta_{\mathrm{TMS}}^{\mathrm{CDCl_3}}$ 1.12 (singlet, 3 H, C-10—CH_3), 2.20 (singlet, 3 H, $COCH_3$), and 3.09 ppm (singlet, 1 H, C-4—H); ORD in methanol (*c* 0.30) $[\phi]_{400}$ +320°, $[\phi]_{324}$ +4800°, $[\phi]_{281}$ −8400°, $[\phi]_{248}$ −5700°, and $[\phi]_{215}$ −7300°.

Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.09; H, 8.29.

B.—The ketone V (R = H, 2.0 g) in chloroform (20 ml) and pyridine (0.8 ml, 1 mole) was ozonized at 0° for 15 hr. Zinc dust was added and the mixture was shaken, with cooling, for 20 min, filtered, diluted with water (100 ml), and steam distilled to remove the solvents. The cooled residue was extracted thrice with chloroform, washed with water, and dried. Evaporation of the solvent *in vacuo* left a liquid bp 120–122° (0.05 mm) (1.7 g, 85%) which crystallized from petroleum ether (bp 40–60°)–ether in prisms, mp 55–56° (0.9 g), identical with the diketonic product obtained as described under A. Thin layer chromatography indicated that the product was homogeneous, no epoxide or possible alcoholic reduction product of the epoxide being encountered.

Epimerization of Diketone XIV.—The diketone (100 mg) in ethanol (2 ml) containing concentrated hydrochloric acid (0.2 ml) was kept for 24 hr at room temperature, then poured into ice–water and the mixture was extracted with ether. The extract was washed with sodium bicarbonate and water, dried, and concentrated *in vacuo*. The crystalline residue separated from petroleum ether to give **7α-acetyl-10α-methyl-Δ^4-octalone-3** (XVI) as needles: mp 107.5–108.5° (30 mg, 30%); $[\alpha]_D$ −89° (*c* 2.0); $\lambda_{\max}^{\mathrm{EtOH}}$ 237 mμ (ε 15,680); $\nu_{\max}^{\mathrm{CCl_4}}$ 1720 (C=O), 1680 (conjugated ketone C=O), and 1620 cm^{-1} (conjugated C=C); the infrared spectrum differed appreciably in the fingerprint region from that of the C-7-epimeric starting product; $\delta_{\mathrm{TMS}}^{\mathrm{CCl_4}}$ 1.26 (singlet, 3 H, C-10—CH_3), 2.12 (singlet, 3 H, $COCH_3$) and 5.62 ppm (singlet, 1 H, olefinic H); ORD in methanol (*c* 0.15, 500–300 mμ and 0.02, 300–217 mμ) $[\phi]_{500}$ −160°, $[\phi]_{400}$ −345°, $[\phi]_{350}$ 0°, $[\phi]_{332}$ +575°, $[\phi]_{319}$ 0°, $[\phi]_{252}$ −30,200°, $[\phi]_{236}$ 0°, $[\phi]_{220}$ 34,000°, and $[\phi]_{217}$ +31,100°.

Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.55; H, 8.82.

Epoxidation of Diketone XIV.—A solution of diketone XIV (206 mg) in methanol (5 ml) was kept at 0° and treated gradually with 30% hydrogen peroxide (0.3 ml), followed by aqueous 10% sodium hydroxide (0.2 ml), and set aside at 0° for 48 hr. Water was added and the product was isolated with ether in the usual manner. Evaporation afforded a viscous product, bp 120° (0.15 mm, 112 mg), which gave two spots on thin layer chromatography. **7α-Acetyl-4β,5β-epoxy-10α-methyldecalone-3** (XVII) crystallized preferentially when the product was dissolved in a little petroleum ether as needles: mp 61–62° (48 mg); $[\alpha]_D$ +73.8° (*c* 2.0); $\nu_{\max}^{\mathrm{CCl_4}}$ 1715 (C=O), 1260 and 925 cm^{-1} (epoxide);[34] the infrared spectrum differed appreciably from that of the C-7-epimer (XV); $\delta_{\mathrm{TMS}}^{\mathrm{CDCl_3}}$ 1.11 (singlet, 3 H, C-10—CH_3), 2.18 (singlet, 3 H, $COCH_3$), and 3.12 ppm (singlet, 1 H, C-4C—H); ORD in methanol (*c* 0.26) $[\phi]_{400}$ +950°, $[\phi]_{323}$ +7700°, $[\phi]_{275}$ −10,800°, $[\phi]_{240}$ −7500°, $[\phi]_{211}$ −11,400°.

Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.20; H, 8.00.

A cognate epoxidation of diketone XVI led to a similar mixture of epoxides, from which XVII crystallized.

Epimerization of Epoxide XV.—The epoxide (136 mg) in methanol (4 ml) was cooled to 0° and mixed with 10% aqueous sodium hydroxide (0.15 ml). After 48 hr at 0°, the mixture was worked up by dilution with water and ether extraction, yielding a yellow oil (119 mg), which on purification by preparative thin layer chromatography afforded the β-epoxide (XVII) as plates, mp 61–62°, from petroleum ether, identical with the product described above.

Ozonolysis of Ketol IV (R = H).—The ketol (3.0 g) in dry chloroform (20 ml) was ozonized at 0° for 19 hr. Water (100 ml) was added and the solvent removed by steam distillation. The residual liquid was extracted with chloroform; evaporation of the dried extract *in vacuo* gave **7β-acetyl-5α-hydroxy-10α-methyldecalone-3** (XIX, 2.9 g, 97%) which crystallized from petroleum ether–benzene (1:1) as needles: mp 140–141°; $[\alpha]_D$ +44° (*c* 2.0); $\nu_{\max}^{\mathrm{CHCl_3}}$ 3650 (OH) and 1715 cm^{-1} (C=O); $\delta_{\mathrm{TMS}}^{\mathrm{CHCl_3}}$ 1.20 (singlet, 3 H, C-10—CH_3), and 2.12 ppm (singlet, 3 H, $COCH_3$); ORD in methanol (*c* 0.15) $[\phi]_{400}$ +120° ,$[\phi]_{303}$ −1190°, $[\phi]_{263}$ +3490° (shoulder), and $[\phi]_{213}$ +7480°.

Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.47; H, 8.91.

Dehydration of Diketo Alcohol XIX.—The foregoing diketo alcohol (2.7 g) and benzene (40 ml) containing toluene-*p*-sulfonic acid (0.2 g) were refluxed for 30 min in a Dean–Stark apparatus, The cooled solution was washed with sodium bicarbonate and water and dried. Removal of the benzene *in vacuo* left a semicrystalline residue (2.3 g) which was dissolved in petroleum ether–benzene and chromatographed on silica gel (Davison, 60 g). Elution with benzene–methanol (9:1) afforded, after concentration, diketone XVI (1.4 g, 57%), mp 106–107°. Dehydration could also be effected with ethanolic hydrochloric acid at 0° for 7 days.

Ozonolysis of the Mixture of Ketones II and V (R = H).—The mixed ketones (0.45 g, $[\alpha]_D$ −80.1°, *c* 2.0) in dry chloroform (10 ml) and pyridine (0.2 ml) were ozonized at 0° for 5 hr. After zinc dust reduction the product was isolated in the usual manner, to give a liquid: bp 126–130° (0.1 mm); 0.38 g; $[\alpha]_D$ −60.7° (*c* 2.0); $\lambda_{\max}^{\mathrm{EtOH}}$ 240 mμ (ε 11,520); $\nu_{\max}^{\mathrm{CCl_4}}$ 1720 (saturated ketone), 1680 (conjugated ketone), and 1610 cm^{-1} (conjugated C=C). Thin layer chromatography revealed the presence of two components; one of these, diketone XX, crystallized preferentially, when the crude product was dissolved in petroleum ether–ether as needles: mp 107.5–108°; $[\alpha]_D$ +83° (*c* 2.0); $\lambda_{\max}^{\mathrm{EtOH}}$ 238 mμ (ε 16,080); $\nu_{\max}^{\mathrm{CCl_4}}$ 1716 (saturated ketone), 1679 (conjugated ketone), and 1620 cm^{-1} (conjugated C=C); $\delta_{\mathrm{TMS}}^{\mathrm{CCl_4}}$ 1.26 (singlet, 3 H, C-10—CH_3), 2.13 (singlet, 3 H, $COCH_3$), and 5.62 ppm (singlet, 1 H, =CH); ORD in methanol (*c* 0.074, 500–270 mμ and 0.024, 270–195 mμ) $[\phi]_{500}$ +190°, $[\phi]_{400}$ +310°, $[\phi]_{381}$ −290°, $[\phi]_{300}$ +2800°, $[\phi]_{270}$ +14,300°, $[\phi]_{249}$ +32,000°, $[\phi]_{218}$ −39,000°, and $[\phi]_{195}$ −31,400°. The ORD curve was the mirror image of that of XVI. The filtrate from the crystallization yielded, after evaporation and separation by preparative thin layer chromatography, diketone XIV, mp 53–55°.

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(34) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed, Methuen and Co., Ltd., London, 1958, p 118.