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

Optical Rotatory Dispersion Studies. LXIV.[1] Detection of Conformational Changes Caused by Equatorial Methyl Groups[2]

BY CARL DJERASSI, E. LUND AND A. A. AKHREM[3]

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By using the molecular amplitude of the Cotton effect of (+)-3-methylcyclohexanone as a standard value for an equatorial methyl group β to the carbonyl group in a cyclohexane ring and combining this value with the molecular amplitude of a 3-keto-5α-steroid (III) or its bicyclic analog V, a calculated Cotton effect amplitude is obtained which differs considerably from the experimentally observed value for II or IV. This difference is ascribed to conformational distortion of the cyclohexanone ring caused by steric interaction between the newly introduced equatorial methyl group (in II or IV) and a suitably located hydrogen atom (C-11 in 3-keto steroids; *peri*-hydrogen atom in the decalone) in another ring. Confirmation of these views could be provided by the synthesis of (−)-3,9-dimethyl-*trans*-1-decalone (XII), where the equatorial group is not disturbed by any such hydrogen interactions and where the calculated and observed rotatory dispersion amplitudes coincide. A similar observation was also made with the corresponding (−)-3-*t*-butyl-9-methyl-*trans*-1-decalone (XIII).

One of the most important applications of our rotatory dispersion measurements of cyclohexanones[4] has been in the field of conformational analysis, because of the peculiar sensitivity of this method to very subtle conformational alterations. Frequently gross changes (*e.g.*, inversion of sign of Cotton effect) in the rotatory dispersion curve can be used to good advantage, as has for instance been done recently in the assignment of boat-like conformations to ring A of various steroid ketones.[5] A different rotatory dispersion approach involves the collection of standard values[6] of rotatory contributions (in terms of molecular amplitudes) of various substituents (*e.g.*, halogens, methyl, etc.) to the Cotton effect of a cyclohexanone. Comparison of calculated and observed values can lead to very instructive conclusions, as has been shown recently[7] in the recognition of a twist conformation in *cis*-2-*t*-butyl-5-methylcyclohexanone. We should now like to record another instance where this rotatory dispersion approach has led to the detection of a subtle conformational change.

The rotatory dispersion curve of (+)-3-methylcyclohexanone (I) in methanol solution has been measured several times in our laboratory[8] and an acceptable average value for the molecular amplitude *a* (molecular rotation of peak minus molecular rotation of trough divided by 100) is (+25). This becomes the standard value for the rotatory contribution of an equatorial methyl group β to the carbonyl group of a chair[9] cyclohexane ring. The recent availability[10] of 1β- and 1α-methyl-3-keto steroids made possible the experimental measurement of the Cotton effect of such substances and as an example we may cite the molecular amplitude *a* (+72) for 1β-methyldihydrotestosterone acetate (II). In order to obtain a calculated value for the molecular amplitude of II, all that is necessary is to subtract[11] (+25), the contribution of an equatorial methyl group (see I), from *a* (+54), which represents the experimentally observed molecular amplitude of the Cotton effect of dihydrotestosterone acetate (III) itself. Provided that such additivity of rotatory contributions is permissible—a point which will be proved below—then the gross divergence between the observed value (+72) and the calculated one (+29) must indicate some type of conformational distortion of ring A in II presumably due to the steric interference between the equatorial 1β-methyl and the 11α-hydrogen atom. Inspection of Dreiding models[12] shows immediately that such non-bonded interaction is readily relieved by converting ring A from a perfect chair toward a twist[13] conformation. Such an intermediate form would be expected[6] to show a strong positive Cotton effect and while it is impossible at this stage to indicate quantitatively the extent of this conformational change, there is little doubt that its existence is herewith demonstrated for the first time.

A second example where this type of analysis seems applicable is (−)-4,10-dimethyl-*trans*-2-decalone (IV)[14] with a negative Cotton effect of molecular amplitude (−49). The rotatory dispersion curve of the corresponding analog V with-

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[1] Paper LXIII, C. S. Barnes and C. Djerassi, *Chemistry & Industry*, 177 (1962).

[2] Supported by grant No. CRTY-5061 from the National Cancer Institute of the National Institutes of Health, U. S. Public Health Service.

[3] Visiting investigator from the N. D. Zelinski Institute of Organic Chemistry, Soviet Academy of Sciences, Moscow, USSR, under the Bronk–Nesmeyanov exchange agreement of the U. S. National Academy of Sciences and the USSR Academy of Sciences.

[4] C. Djerassi, "Optical Rotatory Dispersion: Applications to Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, chapters 4–9.

[5] *Inter al.*, (a) C. Djerassi, N. Finch, R. C. Cookson and C. W. Bird, *J. Am. Chem. Soc.*, **82**, 5488 (1960), (b) F. Sondheimer, Y. Klibansky, Y. M. Y. Haddad, G. H. R. Summers and W. Klyne, *J. Chem. Soc.*, 767 (1961); (c) D. T. Cropp, B. B. Dewhurst and J. S. E. Holker, *Chemistry & Industry*, 209 (1961).

[6] See for instance C. Djerassi and W. Klyne, *J. Chem. Soc.*, in press (1962), and references cited therein.

[7] C. Djerassi, E. J. Warawa, J. M. Berdahl and E. J. Eisenbraun, *J. Am. Chem. Soc.*, **83**, 3334 (1961).

[8] *E.g.*, C. Djerassi and G. W. Krakower, *ibid.*, **81**, 237 (1959).

[9] This is only an approximation, because in solution probably 10–20% of the substance exists in a conformation other than the chair form I. However, for the type of calculations performed at present, this is satisfactory (see for instance ref. 7).

[10] For starting materials see A. Popper, German Patent 1,023,764 (to Schering, A. G.), and R. Wiechert and E. Kaspar, *Ber.*, **93**, 1710 (1960). We are indebted to Dr. Horst Witzel of Schering, A. G., Berlin for a gift of II.

[11] Subtraction, rather than addition, is required because the 1β-methyl group lies in a negative octant in the perfect chair conformation of II; for details of the octant rule, see W. Moffitt, R. B. Woodward, A. Moscowitz, W. Klyne and C. Djerassi, *J. Am. Chem. Soc.*, **83**, 4013 (1961).

[12] A. Dreiding, *Helv. Chim. Acta*, **42**, 1339 (1959).

[13] For definition see W. S. Johnson, V. J. Bauer, J. L. Margrave, M. A. Frisch, L. H. Drieger and W. N. Hubbard, *J. Am. Chem. Soc.*, **83**, 606 (1961).

[14] L. H. Zalkow, F. X. Markley and C. Djerassi, *ibid.*, **82**, 6354 (1960).

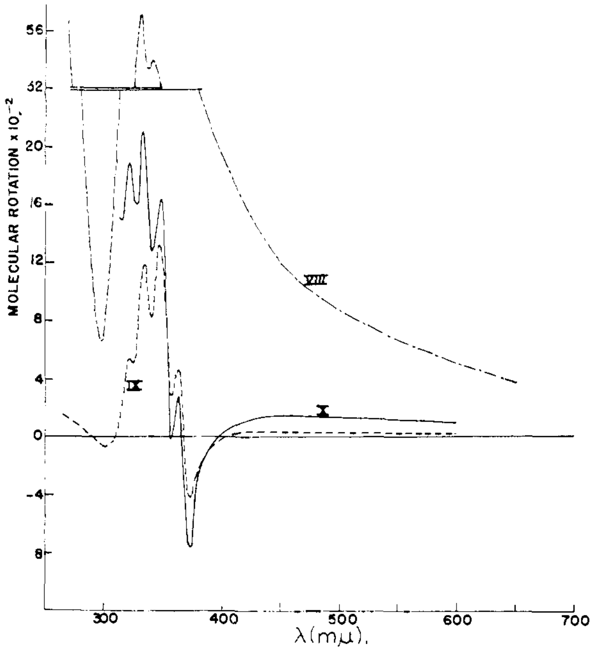

Fig. 1.—Optical rotatory dispersion curves (dioxane solution of (+)-4-methoxy-10-methyl-*trans*-$\Delta^{3,6}$-hexalone-3 (VIII), (+)-3,9-dimethyl-*trans*-$\Delta^{2,6}$-hexalone-1 (IX) and (+)-3-*t*-butyl-9-methyl-*trans*-$\Delta^{2,6}$-hexalone-1 (X).

out the equatorial methyl group had been determined earlier[15] in dioxane solution and repeat measurements in methanol now gave *a* (−51). Introduction of the extra equatorial methyl group (*a* = 25) into a positive octant leads to a predicted amplitude (−26) for the ketone IV, which again differs from the observed one (−42), although the discrepancy is not as large as in the steroid II. We believe that the simplest explanation for this difference is to assume a deformation from the ideal all-chair conformation, most likely caused by the equatorial hydrogen atom situated in the *peri* position at C-5, although possible interference with some of the hydrogens of the angular methyl group cannot be excluded at this time.

If discrepancies between observed and calculated rotatory dispersion amplitudes are to be used as criteria of conformational alterations, then it is necessary to demonstrate good agreement between these values in a substance where no conformationally disturbing factors enter into play. For this purpose, we have selected 3,9-dimethyl-*trans*-1-decalone (XII), where the equatorial methyl group in the C-3 position should be completely undisturbed, and its synthesis is described below.

Since optically active material was required, we started with the (+)-antipode[16] of 3-methoxy-9-methyl-*trans*-$\Delta^{2,6}$-hexalone-1 (VI)[17] of known[16] absolute configuration. This was cleaved with sulfuric acid to the previously described[16] diketone VII and then methylated with diazomethane.[18] The resulting mixture of enol ethers VI and VIII[19] was separated readily and the new enol ether VIII was treated successively with methyllithium[20] and sulfuric acid to afford (+)-3,9-dimethyl-*trans*-$\Delta^{2,6}$-hexalone-1 (IX), the rotatory dispersion curve of which is reproduced in Fig. 1. The ultraviolet, infrared and n.m.r. spectral properties of this α,β-unsaturated ketone were fully consistent with the formulation IX and the homogeneity of the liquid ketone was established by gas phase chromatography, thin-layer chromatography[21] and preparation of a sharp-melting 2,4-dinitrophenylhydrazone with the expected[22] ultraviolet absorption maximum at 387 mμ. Just as was observed[14] earlier with *trans*-4,10-dimethyl-$\Delta^{3,6}$-hexalone-2 (XV), catalytic hydrogenation of IX with a palladium–calcium carbonate catalyst in the presence of alkali reduced only the conjugated double bond of IX to afford (−)-3,9-dimethyl-*trans*-Δ^{6}-octalone-1 (XI). This ketone also proved to be homogeneous by the above-mentioned criteria and it seems safe to assume—as had been established[14] in the hydrogenation of the isomer XV—that hydrogenation occurred from the opposite side of the angular methyl group to generate an equatorially oriented C-3 methyl group. Complete hydrogenation of the isolated double bond in the octalone XI was effected with palladized charcoal catalyst giving the desired (−)-3,9-dimethyl-*trans*-1-decalone (XII). Its negative Cotton effect (methanol solution) was characterized by a molecular amplitude of *a* (−52), while *trans*-9-methyl-1-decalone (XIV) exhibited *a* (−27).[23] Addition of (−25), the rotatory contribution of the equatorial methyl group (see I) in a negative octant, leads to a predicted amplitude (−52) for XIV, which is in exact agreement with the experimentally observed one. These results confirm the validity of our earlier discussed conclusions and support the assumption that an equatorial methyl group in the C-3 position of a *trans*-1-decalone is not subject to any steric interaction. Alternatively, one can state that the difference between the molecular amplitudes of XII and XIV offers another means of arriving at the standard value of (25) for the rotatory contribution of an equatorial methyl group located β to the ketone function in a cyclohexane chair.

The above reaction sequence opened the way to determine the effect of a very bulky substituent, the *t*-butyl moiety, and for that purpose the enol ether VIII was treated with *t*-butylmagnesium chloride followed by acid cleavage to yield (+)-3-*t*-

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

[16] A. J. Speziale, J. A. Stephens and Q. E. Thompson, *J. Am. Chem. Soc.*, **76**, 5011 (1954). We are deeply indebted to Dr. William S. Knowles of the Monsanto Chemical Co. for a generous gift of this material.

[17] R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler and W. M. McLamore, *J. Am. Chem. Soc.*, **74**, 4223 (1952).

[18] See C. Tamm, *Helv. Chim. Acta*, **43**, 1700 (1960), for the diazomethane methylation of cholestane-1,3-dione.

[19] The rotatory dispersion curves of the two isomeric enol ethers proved to be very distinct; see Fig. 1 of present paper (R. D. curve of VIII in dioxane) and Fig. 5 in C. Djerassi, R. Riniker and B. Riniker, *J. Am. Chem. Soc.*, **78**, 6377 (1956).

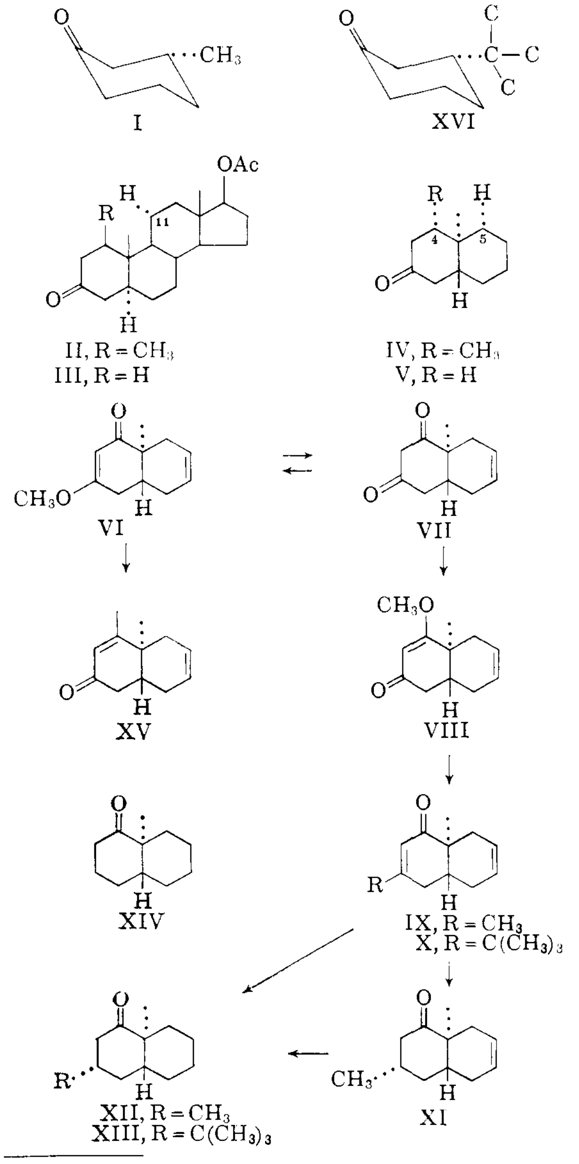
[20] A similar conversion of the enol ether VI to XV has already been reported in an earlier paper from this Laboratory (ref. 14) in connection with synthetic work in the eremophilone series.

[21] The isomeric enol ethers VI and VIII as well as IX and its position isomer XV (ref. 14) are readily separable on silica gel plates with the system hexane (or benzene)–10% ethyl acetate.

[22] C. Djerassi and E. Ryan, *J. Am. Chem. Soc.*, **71**, 1000 (1949).

[23] This value is based on new measurements conducted in methanol solution since the earlier data (ref. 15) pertained to dioxane.

butyl-9-methyl-*trans*-$\Delta^{2,6}$-hexalone-1 (X).[24] Hydrogenation of both double bonds was achieved with palladized charcoal catalyst leading to the required (−)-3-*t*-butyl-9-methyl-*trans*-1-decalone (XIII) with a negative Cotton effect (*a* = −66). Since the rotatory dispersion curve of (+)-3-*t*-butylcyclohexanone (XVI) has already been measured[25] in methanol solution, its *a*-value (37) need only be added to that (−27) of *trans*-9-methyl-1-decalone (XIV) to arrive at a calculated molecular amplitude of (−64) for (−)-3-*t*-butyl-9-methyl-*trans*-1-decalone (XIII), which is in very reasonable agreement with the observed one (−66). It follows, therefore, that there does not seem to exist any conformational distortion in the decalone XIII, a conclusion which was not necessarily self-evident because of possible interaction between one of the *t*-butyl methyl groups and the axial hydrogen atoms at positions 2 and 4.



I

XVI

II, R = CH3
III, R = H

IV, R = CH3
V, R = H

VI

VII

XV

VIII

XIV

IX, R = CH3
X, R = C(CH3)3

XII, R = CH3
XIII, R = C(CH3)3

XI

Experimental[26]

(+)-4-Methoxy-10-methyl-*trans*-$\Delta^{3,6}$-hexalone-3 (VIII).—A mixture of 11.6 g. of the enol ether VI[16] (m.p. 91–93°, $[\alpha]_D$ +58.6°), 6.7 cc. of sulfuric acid, 42 cc. of water and 57 cc. of dioxane was permitted to stand at room temperature overnight and was then processed as described[16] for its antipode. The resulting diketone VII (yield 9.2 g., m.p. 184–189°, $[\alpha]_D$ +151° in methanol) was suspended in 100 cc. of ether and stirred overnight at room temperature with a solution of 4 g. of distilled diazomethane in 200 cc. of ether. Evaporation of the solvent *in vacuo* and crystallization of the residue from petroleum ether (b.p. 60–68°) afforded 2.9 g. of the enol ether VI, m.p. 91–94°. Evaporation of the filtrate left 6.9 g. of yellow oil, which was chromatographed on 900 g. of Merck neutral alumina (activity I–II), the composition of the eluates being monitored by thin-layer chromatography,[21] VI being more mobile than VIII. Elution was accomplished with benzene containing 16% of ether. The first fractions provided an additional 1.8 g. of the enol ether VI (m.p. 91–94°), while the later eluates gave 4.0 g. of the desired enol ether VIII as a yellowish thick oil. Distillation at 160° (0.5 mm.) afforded a distillate which crystallized immediately, m.p. 49–50°, λ_{max}^{EtOH} 249 mμ, log ϵ 4.17, $\lambda_{max}^{CHCl_3}$ 6.10 and 6.28 μ, $[\alpha]^{30}_D$ +313° (*c* 5.0 in chloroform); R.D. (*c* 0.11 in dioxane) reproduced in Fig. 1: $[\alpha]_{589}$ +290°, $[\alpha]_{332}$ +2980°, $[\alpha]_{298}$ +339°, $[\alpha]_{270}$ +2940°. The n.m.r. spectrum (deuteriochloroform) showed signals[27] at 1.12 (angular methyl group), 3.70 (methoxyl), 5.30 (C-3 hydrogen) and 5.70 p.p.m. (C-6 and C-7 hydrogens).

Anal. Calcd. for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39; O, 16.65; OCH_3, 16.12. Found: C, 74.87; H, 8.22; O, 16.70; OCH_3, 15.82.

(+)-3,9-Dimethyl-*trans*-$\Delta^{2,6}$-hexalone-1 (IX).[28]—A solution of the enol ether VIII in 6 cc. of anhydrous ether was added slowly in an atmosphere of nitrogen to methyllithium prepared from 0.16 g. of lithium, 1.3 cc. of methyl iodide and 6 cc. of ether. After stirring at room temperature for 20 hr., the mixture was poured into ice-water, extracted with ether and the solvent evaporated. The oily residue, dissolved in 20 cc. of dioxane, 12 cc. of water and 2.2 cc. of sulfuric acid, was stirred for 3 hr. at room temperature, the product was isolated with ether and purified by chromatography on 10 g. of neutral alumina (activity II). Elution with benzene and distillation at a bath temperature of 110–130° (0.1 mm.) furnished 0.30 g. of hexalone IX as a colorless oil, which gave a single peak on gas phase chromatography at 190° using a 15% phenyldiethanolamine succinate on Chromosorb column; thin-layer chromatography on silica gel[21] showed a single spot with R_f 0.4. The ketone exhibited λ_{max}^{EtOH} 234 mμ, log ϵ 4.11, $\lambda_{max}^{CHCl_3}$ 6.05 μ (strong peaks at 7.60, 9.05, 9.90 and 11.85 μ serve to distinguish it from the isomer XV) and its R.D. curve (*c* 0.14 in dioxane) is shown in Fig. 1: $[\alpha]_{589}$ +15°, $[\alpha]_{373}$ −239°, $[\alpha]_{362}$ +262°, $[\alpha]_{357}$ +160°, $[\alpha]_{347}$ +743°, $[\alpha]_{340}$ +469°, $[\alpha]_{334}$ +671°, $[\alpha]_{326}$ +292°, $[\alpha]_{322}$ +306°, $[\alpha]_{265}$ +88°. The n.m.r. spectrum ($CDCl_3$) contained signals[27] at 1.00 (angular methyl group), 1.95 (methyl group attached to double bond), 5.63 (C-6 and C-7 protons) and 5.80 p.p.m. (C-2 proton).

Anal. Calcd. for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.38; H, 9.18.

The red 2,4-dinitrophenylhydrazone of IX was recrystallized from ethanol, whereupon it showed m.p. 186–187°, $\lambda_{max}^{CHCl_3}$ 387 mμ, log ϵ 4.45.

Anal. Calcd. for $C_{18}H_{20}N_4O_4$: C, 60.66; H, 5.66; N, 15.72. Found: C, 60.62; H, 5.77; N, 15.96.

(−)-3,9-Dimethyl-*trans*-Δ^6-octalone-1 (XI).—A 210-mg. sample of the above hexalone IX was hydrogenated with

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(24) The rotatory dispersion curve of X closely resembles that of its lower homolog IX as illustrated in Fig. 1.

(25) C. Djerassi, E. Warawa, R. E. Wolff and E. J. Eisenbraun, *J. Org. Chem.*, **25**, 917 (1960).

(26) All melting points were determined on the Kofler block. We are indebted to Mrs. Ruth Records for the rotatory dispersion measurements, to Dr. Lois Durham for the n.m.r. spectra and to Mr. E. Meier for the microanalyses.

(27) Reported in p.p.m. as δ-values (c.p.s. (relative to tetramethylsilane)/60); see C. Djerassi, T. Nakano, A. N. James, L. H. Zalkow, E. J. Eisenbraun and J. N. Shoolery, *J. Org. Chem.*, **26**, 1192 (1961).

(28) Attempts to synthesize this ketone by 1,4-addition of methylmagnesium iodide (in the presence of cuprous chloride) to the enol ether VI were abortive, the products being unreacted VI, cleavage product VII and 1,2-addition product XV.

120 mg. of 2% palladium–calcium carbonate catalyst in 10 cc. of 2% ethanolic potassium hydroxide solution. Hydrogen consumption stopped after 3 hr., whereupon the catalyst was filtered, the filtrate neutralized with dilute hydrochloric acid and the product isolated with ether. The oily octalone XI did not contain any α,β-unsaturated ketone as demonstrated by its infrared ($\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.88 μ) and ultraviolet ($\lambda_{\max}^{\mathrm{EtOH}}$ 288 mμ, log ε 1.47) spectra. Gas phase and thin layer chromatography indicated the homogeneity of the material, but mass spectral analysis[29] demonstrated the presence of a small amount (less than 10%) of the completely saturated decalone (XII); R.D. (*c* 0.05 in dioxane): $[\alpha]_{589}$ −14°, $[\alpha]_{315}$ −1865°, $[\alpha]_{270}$ +2285°, $[\alpha]_{250}$ +1815°.

The yellow **2,4-dinitrophenylhydrazone** exhibited m.p. 125–127° (recrystallized from methanol); $\lambda_{\max}^{\mathrm{CHCl_3}}$ 367 mμ, log ε 4.45.

Anal. Calcd. for $C_{18}H_{22}N_4O_4$: C, 60.32; H, 6.19; N, 15.63. Found: C, 60.34; H, 6.32; N, 15.62.

(−)-3,9-Dimethyl-*trans*-1-decalone (XII).—Hydrogenation of the isolated double bond of 90 mg. of the octalone XI was effected in 1 hr. with 100 mg. of 5% palladized charcoal catalyst and 5 cc. of ethanol. The resulting oil was homogeneous as determined by gas phase and thin-layer chromatography as well as by mass spectral analysis.[29] The decalone exhibited the following spectral properties: infrared ($CHCl_3$) band at 5.88 μ, ultraviolet (EtOH) maximum at 285 mμ, log ε 1.52, and n.m.r. signals[27] ($CDCl_3$) at 1.08 (angular methyl group) and doublet at 0.90 and 1.07 due to the C-3 methyl function; no peaks corresponding to olefinic protons could be detected; R.D. (*c* 0.10 in methanol): $[\alpha]_{589}$ −108°, $[\alpha]_{309}$ −1767°, $[\alpha]_{271}$ +1108, $[\alpha]_{256}$ +745°.

Anal. Calcd. for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.89; H, 11.14.

The yellow **2,4-dinitrophenylhydrazone of XII** melted at 133–135° after recrystallization from ethanol; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 369 mμ, log ε 4.48.

Anal. Calcd. for $C_{18}H_{24}N_4O_4$: C, 59.98; H, 6.71; N, 15.55. Found: C, 60.07; H, 6.49; N, 15.48.

(+)-3-*t*-Butyl-9-methyl-*trans*-$\Delta^{2,6}$-hexalone-1 (X).—To a solution of *t*-butylmagnesium chloride prepared from 2.5 g. of magnesium turnings and 13.5 cc. of *t*-butyl chloride in 10 cc. of ether was added 3.0 g. of the enol ether VIII and the mixture stirred at room temperature for 40 hr. After pouring into ice-water, extracting with ether, and removing the solvent, the residue was stirred overnight with 60 cc. of 50% aqueous dioxane containing 3 cc. of sulfuric acid. Sodium hydroxide was added until the mixture was slightly basic, the product was isolated with ether and chromatographed on 200 g. of neutral alumina. Elution was effected with hexane, hexane–benzene mixtures and benzene, the desired product (0.48 g.) being isolated from the benzene fractions. A small amount of impurity was separated by preparative gas phase chromatography at 180° with a Megachrom instrument using a SE-30 column (retention time 7.8 min.). Redistillation at 110–120° (0.1 mm.) provided 0.215 g. of colorless solid (m.p. 25–30°) of the hexalone X, $\lambda_{\max}^{\mathrm{EtOH}}$ 233 mμ, log ε 4.02, $\lambda_{\max}^{\mathrm{CHCl_3}}$ 6.02 and 6.08 μ; n.m.r. signals[27] ($CDCl_3$) at 1.01 (angular methyl), 1.14 (*t*-butyl methyl groups), 5.80 (C-2 proton) and 5.67 p.p.m. (C-6 and C-7 protons); R.D. (*c* 0.12 in dioxane) reproduced in Fig. 1: $[\alpha]_{589}$ +45°, $[\alpha]_{373}$ −350°, $[\alpha]_{363}$ +123°, $[\alpha]_{357}$ −17°, $[\alpha]_{348}$ +750°, $[\alpha]_{341}$ +584°, $[\alpha]_{334}$ +967°, $[\alpha]_{328}$ +734°, $[\alpha]_{322}$ +867°, $[\alpha]_{314}$ +685°.

Anal. Calcd. for $C_{15}H_{22}O$: C, 82.51; H, 10.16. Found: C, 82.21; H, 10.06.

The dark orange **2,4-dinitrophenylhydrazone** was recrystallized from methanol; m.p. 156–158°, $\lambda_{\max}^{\mathrm{CHCl_3}}$ 386 mμ, log ε 4.43.

Anal. Calcd. for $C_{21}H_{26}N_4O_4$: C, 63.30; H, 6.58; N, 14.06. Found: C, 63.33; H, 6.46; N, 14.38.

(−)-3-*t*-Butyl-9-methyl-*trans*-1-decalone (XIII).—The catalytic hydrogenation of both double bonds of the hexalone X (100 mg.) was accomplished in 1 hr. in ethanol solution with 100 mg. of 5% palladized charcoal catalyst. The resulting oil exhibited a single, symmetrical peak in a gas phase chromatogram and showed $\lambda_{\max}^{\mathrm{CHCl_3}}$ 5.88 μ, $\lambda_{\max}^{\mathrm{EtOH}}$ 287 mμ, log ε 1.60; n.m.r. signals[27] ($CDCl_3$) at 0.80 (*t*-butyl methyl groups), 0.98 (angular methyl group) and no signals corresponding to olefinic protons; R.D. (*c* 0.12 in methanol): $[\alpha]_{589}$ −76°, $[\alpha]_{310}$ −1685°, $[\alpha]_{273}$ +1270, $[\alpha]_{240}$ +730°.

Anal. Calcd. for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 80.69; H, 11.66.

The yellow **2,4-dinitrophenylhydrazone** showed m.p. 208–209° after recrystallization from methanol; $\lambda_{\max}^{\mathrm{CHCl_3}}$ 368 mμ, log ε 4.36.

Anal. Calcd. for $C_{21}H_{30}N_4O_4$: C, 62.66; H, 7.51; N, 13.92. Found: C, 62.28; H, 7.71; N, 13.92.

1β-Methylandrostan-17β-ol-3-one (1β-methyldihydrotestosterone) acetate (II),[10] R.D. (*c* 0.10 in methanol): $[\alpha]_{589}$ +68°, $[\alpha]_{308}$ +1325°, $[\alpha]_{260}$ −760°, $[\alpha]_{255}$ −662°. In the presence of hydrochloric acid[30] the peak occurred at $[\alpha]_{308}$ +552°, while the trough was found at $[\alpha]_{265}$ −319°.

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[29] We are indebted to Dr. Herbert Budzikiewicz for this determination.

[30] C. Djerassi, L. A. Mitscher and B. J. Mitscher, *J. Am. Chem. Soc.*, **81**, 947 (1959).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF DELAWARE, NEWARK, DEL.]

Mechanisms of Chromic Acid Oxidation. III.[2] The Oxidation of Diols

BY HAROLD KWART,[1a] J. A. FORD, JR.,[1b] AND G. C. COREY[1a,c]

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The earlier interpretations[3,4] of the rates of chromic acid oxidation of diols are found to be misleading, in view of conformational and structural effects which are shown here to govern reactivity. The occurrence of cyclic chromate esters as intermediates in the oxidation of certain diol structures but not of others has been inferred from rate data obtained for a variety of bicyclic, alicyclic and acyclic 1,2- and 1,3-diols. In this fashion, also, the geometric requirements for such cyclic chromate ester formation have been found to be similar to those deduced earlier for boric acid complexing with diols. It is suggested that the formation of esters by interaction of chromic acid with alcohols is quite analogous to ester formation with boric rather than sulfuric acid, as claimed previously.[3]

This investigation was prompted by diverse observations in the literature concerning the oxidation of diols with chromic acid. Roček[3] has reported that ethylene glycol shows a reduced rate of oxidation compared to ethanol and has interpreted this as a failure of the chromate ester mechanism, reasoning that a cyclic chromate ester should have been formed in greater amounts at equilibrium than

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[1] (a) Supported by the National Science Foundation under Grant NSF-G 6037. (b) Eastman Kodak Co., Rochester, N. Y. (c) Part of this work is abstracted from the Master's degree thesis of G. C. Corey presented to the University of Delaware, June, 1960.

[2] Previous papers in this series: (a) H. Kwart and P. F. Francis, *J. Am. Chem. Soc.*, **77**, 4907 (1955); (b) **81**, 2116 (1959); (c) H. Kwart, *Suomen. Kemi.*, **34A**, 173 (1961).

[3] J. Roček, *Coll. Czech. Chem. Comm.*, **25**, 1052 (1960).