Synthesis, Proton Magnetic Resonance, and Stereochemistry of Certain *o*-Tolylcyclohexanediols[1]

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The three new *o*-tolylcyclohexanediols, *trans*-2-*o*-tolyl-*cis*-4-hydroxycyclohexanol, *trans*-2-*o*-tolyl-*trans*-5-hydroxycyclohexanol, and *trans*-2-*o*-tolyl-*cis*-6-hydroxycyclohexanol, have been synthesized and their configurations and conformations have been established by n.m.r. Chemical proof of configurations is also given. The n.m.r. spectra, measured in deuteriochloroform, are consistent with chair conformations with the tolyl group in an equatorial orientation. Evidence is given for the deshielding effect of an axial hydroxyl group on an axial proton when in 1–3 diaxial spatial proximity. Complications resulting from virtual long-range coupling are observed and discussed.

As a part of the investigation of certain aryl-substituted cyclohexanols shown to possess cardio-inhibitory properties,[5-7] the availability of some cyclohexanediols of known stereochemistry was desired. The synthesis and stereochemical analysis of three new *o*-tolylcyclohexanediols are reported in this paper. Configurational and conformation assignments are made by nuclear magnetic resonance and chemical proof is given for the assigned configurations.

The compounds of this series were prepared by the methods shown in Chart I.

trans-4-Nitro-5-*o*-tolylcyclohexane (2) has been reported previously.[8] The Nef aldehyde and ketone synthesis was used to convert 2 to 2-*o*-tolyl-4-cyclohexen-1-one (3). The method has been described for analogous compounds.[9] 2-*o*-Tolyl-5-cyclohexen-1-one (4) was obtained quantitatively by the acid-catalyzed isomerization of 3.

Lithium aluminum hydride reduction of **3** afforded a mixture of *cis*- and *trans*-2-*o*-tolyl-4-cyclohexen-1-ol consisting of 80% *trans* (**5**) and 20% *cis* (**6**). The similar reduction of **4** yielded a mixture of *cis*- and *trans*-2-*o*-tolyl-5-cyclohexen-1-ol consisting of 60% *trans* (**7**) and 40% *cis* (**8**). Benzoylation of the two alcohol mixtures afforded *trans*-2-*o*-tolyl-4-cyclohexenyl benzoate (**9**) and *trans*-2-*o*-tolyl-5-cyclohexenyl benzoate (**10**), respectively. Pure **5** and **7** were obtained by the lithium aluminum hydride reduction of **9** and **10**, respectively. Pure **6** and **8** and their benzoates were never isolated.

The perbenzoic acid epoxidation of **9** and **10** was carried out essentially by the method described by Henbest and Nicholls[10] for the epoxidation of 3-cyclohexen-1-ol. Epoxidation of **9** afforded a mixture of *trans*-2-*o*-tolyl-*cis*-4,5-epoxycyclohexyl benzoate (**11**) and *trans*-2-*o*-tolyl-*trans*-4,5-epoxycyclohexyl benzoate (**12**). Similarly, epoxidation of **10** afforded a mixture of *trans*-2-*o*-tolyl-*trans*-5,6-epoxycyclohexyl benzoate (**13**) and *trans*-2-*o*-tolyl-*cis*-5,6-epoxycyclohexyl benzoate (**14**). The epoxides were separated by recrystallization.

Lithium aluminum hydride reduction of **11** and **12** afforded *trans*-2-*o*-tolyl-*cis*-4-hydroxycyclohexanol (**15**) and *trans*-2-*o*-tolyl-*trans*-5-hydroxycyclohexanol (**16**), respectively. Lithium aluminum hydride reduction of **13** and **14** afforded **16** and *trans*-2-*o*-tolyl-*cis*-6-hydroxycyclohexanol (**17**), respectively.[11] Since the nucleophilic opening of the epoxide ring in cyclohexane systems is known to proceed to give the *trans*-diaxial product, the configurations of the four isomeric epoxides were assigned on the basis of epoxides **12** and **13** both giving diol **16** upon reduction. The configurations of the diols, **15**, **16**, and **17**, were assigned on the basis that **16** was obtained from both epoxides **12** and **13**.

The use of nuclear magnetic resonance (n.m.r.) for configurational and conformational analysis of six-membered ring compounds is well established.[6,8,12] The method has proven especially useful for conformational and configurational analysis in fixed six-membered ring compounds where one or more vicinal hydrogens, isolated from the remainder of the ring hydrogens, exhibit simple first-order pattern.[6,8,12h-k,p] Of special importance is the fact that for compounds in the fixed chair conformation the spin–spin coupling between axial hydrogens on neighboring carbons is three to four times as great as between neighboring hydrogens in other orientations. As a direct result of the stronger axial–axial hydrogen couplings in such fixed systems, the signal half-width of hydrogens in an axial orientation when coupled with axial hydrogens on adjacent

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[3] Abstracted from the thesis submitted in partial requirement for the degree of Doctor of Philosophy, 1963.

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[5] A. C. Huitric, T. C. West, R. A. Durbin, and G. H. Bryan, *J. Am. Pharm. Assoc.*, **48**, 131 (1959).

[6] A. C. Huitric and J. B. Carr, *J. Org. Chem.*, **26**, 2648 (1961).

[7] Harold H. Smookler and John J. DeFeo, *J. Pharm. Sci.*, **51**, 736 (1962).

[8] W. F. Trager, F. F. Vincenzi, and A. C. Huitric, *J. Org. Chem.*, **27** 3006 (1962).

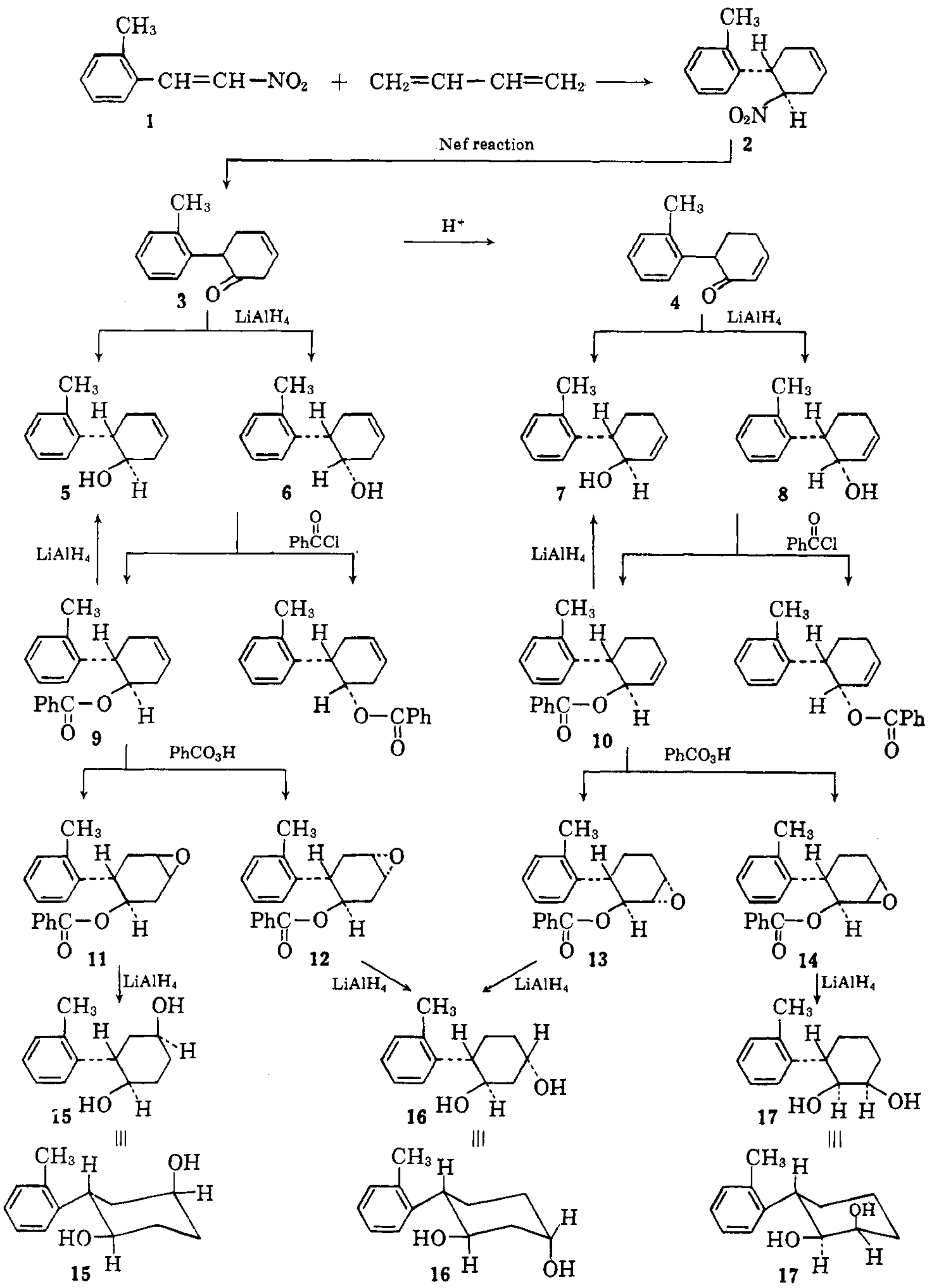
[9] A. C. Huitric, W. C. Clarke, Jr., K. Leigh, and D. C. Staiff, *ibid.*, **27**, 715 (1962).

[10] H. B. Henbest and B. Nicholls, *J. Chem. Soc.*, 4608 (1957).

[11] For clarity in the n.m.r. discussion later in this paper the diols have been considered as derivatives of *trans*-2-*o*-tolylcyclohexanol. The carbons of the cyclohexane ring have thus been numbered in a clockwise direction with the tolyl group attached at C-2.

[12] (a) R. U. Lemieux, R. K. Kullnig, H. J. Bernstein, and W. G. Schneider, *J. Am. Chem. Soc.*, **80**, 6098 (1958); (b) J. I. Musher, *ibid.*, **83**, 1146 (1961); (c) K. J. Williamson and W. S. Johnson, *ibid.*, **83**, 4623 (1961); (d) R. U. Lemieux, R. K. Kullnig, and R. Y. Moir, *ibid.*, **80**, 2237 (1958); (e) H. Finegold and H. Kwart, *J. Org. Chem.*, **27**, 2361 (1962); (f) G. E. McCasland, S. Furuta, L. F. Johnson, and J. N. Shoolery, *J. Am. Chem. Soc.*, **83**, 2335 (1961); (g) J. N. Shoolery, J. F. Johnson, S. Furuta, and G. E. McCasland, *ibid.*, **83**, 4243 (1961); (h) A. C. Huitric, W. G. Clark, Jr., K. Leigh, and D. C. Staiff, *J. Org. Chem.*, **27**, 715 (1962); (i) A. C. Huitric and W. F. Trager, *ibid.*, **27**, 1926 (1962); (j) A. C. Huitric, W. S. Stravropoulos, and B. J. Nist, *ibid.*, **28**, 1539 (1963); (k) D. C. Staiff and A. C. Huitric, *ibid.*, **28**, 3531 (1963); (l) F. J. Schmitz and W. S. Johnson, *Tetrahedron Letters*, **15**, 647 (1962); (m) R. J. Abraham and J. S. E. Holker, *J. Chem. Soc.*, 806 (1963); (n) B. B. Dewhurst, J. S. E. Holker, A. Lablache-Combier, and J. Levisalles, *Chem. Ind.* (London), 1667 (1961); (o) R. W. K. Woo, H. W. Dion, L. Durham, and H. S. Mosher, *Tetrahedron Letters*, **17**, 735 (1962); (p) A. C. Huitric, J. B. Carr, W. F. Trager, and B. J. Nist, *Tetrahedron*, **19**, 2145 (1963); this is by no means a complete list of examples.

Chart I



carbons is approximately three times the signal half-width of coupled hydrogens in other orientations.

The conformations and n.m.r. spectra of **15**–**17** are shown in Fig. 1. The spectra were measured in deuteriochloroform and the chemical shifts are expressed as τ-values relative to tetramethylsilane as an internal reference. In each spectra the signals of the aromatic protons of the tolyl group, occurring downfield owing to the deshielding resulting from the magnetic anisotropy of the benzene ring, are not shown.

The spectra of **15**–**17** are consistent with structures in which the cyclohexane ring exists in the chair conformation with the tolyl group in an equatorial orientation. The conformations can readily be assigned from the n.m.r. signals of the hydrogens attached to the carbons containing the tolyl and hydroxyl groups, since these signals are paramagnetically shifted from the signals of the remainder of the ring hydrogens. The signal of the 2-proton in each case, τ 6.71 in **15**, about 7.29 in **16**, and 6.78 in **17**, occurs as a broad multiplet of half-width in the order of 20 c.p.s., indicative of an axial proton coupled to adjacent axial protons. These values agree well with reported half-widths of 18.5[11b] and 22 c.p.s.[11a] for the signal of the axial 1-proton in *trans*-4-*t*-butylcyclohexanol. Similarly, the signal of the 1-proton in each case, τ 6.25 in **15**, about 5.88 in **16**, and 6.30 in **17**, is indicative of a proton in an axial orientation. The half-width of the 1-proton signal in **15** is approximately 20 c.p.s. In **16** the signal of the 1-proton, although overlapped with the signal of the equatorial 5-proton, appears to be a broad multiplet indicative of a proton in an axial orientation. In **17** the 1-proton signal occurs as a broad doublet, due to coupling with the adjacent axial 2-proton ($J_{1,2}$ = 10.9 c.p.s.), with unresolved minor splitting due to coupling with the adjacent equatorial 6-proton.

The signals of the remaining paramagnetically shifted proton in each isomer supports the assigned conforma-

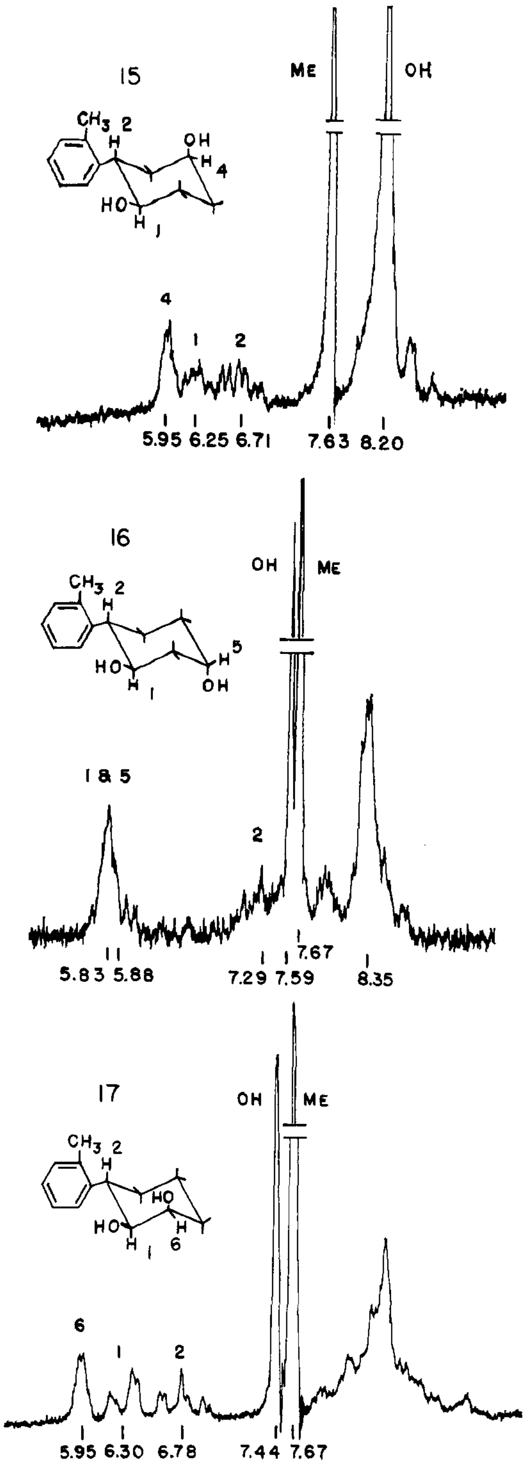


Fig. 1.—N.m.r. spectra of *trans*-2-*o*-tolyl-*cis*-4-hydroxycyclohexanol (**15**), *trans*-2-*o*-tolyl-*trans*-5-hydroxycyclohexanol (**16**), and *trans*-2-*o*-tolyl-*cis*-6-hydroxycyclohexanol (**17**); 60 Mc., about 1 M in deuteriochloroform at 23°.

tions. The signal of the 4-proton in **15**, at τ 5.95, occurs essentially as a singlet of half-width, 7.6 c.p.s. The 5-proton signal in **16**, at τ 5.83, has a half-width of only 10.6 c.p.s. Similarly, the signal of the 6-proton in **17**, at τ 5.95, has a half-width of 6.8 c.p.s. The slightly larger half-width value of the 5-proton signal in **16** can be accounted for by the overlapping of the 1- and 5-proton signals. These values agree well with the reported half-width value of 7 c.p.s. for the signal of the equatorial 1-proton in *cis*-4-*t*-butylcyclohexanol.[11a,b]

The occurrence of the 2-proton signal in **15** as a simple first-order six-peak multiplet is indicative that the coupling constant between the 2-proton and the axial 1-proton approximates the coupling constant between the 2-proton and axial 3-proton ($J_{2,1} \simeq J_{2,3a} \simeq$ 9.5–10 c.p.s.), resulting in a triplet which is further split by coupling with the equatorial 3-proton ($J_{2,3e} \simeq$ 4.7 c.p.s.). In contrast, the signal of the axial 1-proton in **15** cannot be treated by a simple first-order approximation. The existence of the 1-proton signal as a broad unresolved multiplet indicates that certain complications are occurring to increase the signal multiplicity. Under certain conditions, the multiplicity of a proton signal can be increased by virtual long-range coupling[13] by protons more than three bonds removed. In **15** the multiplicity of the 1-proton signal could be increased by virtual long-range coupling with the 5-protons. This virtual long-range coupling would occur if the strongly coupled axial 5- and 6-protons have a similar chemical shift. Since both the axial 5- and 6-proton signals appear as a part of the overlapping multiplet centered at approximately τ 8.20, the chemical shift of neither can be determined. However, due to the narrowness of the multiplet, it is probable that the axial 5- and 6-protons do have similar chemical shifts, and thus give rise to virtual long-range coupling which results in an increased multiplicity of the signal of the 1-proton. Similarly, the occurrence of the signal of the axial 2-proton in **16** as a broad unresolved multiplet indicates that a simple first-order treatment is not applicable. An increased multiplicity of the axial 2-proton signal would arise owing to virtual long-range coupling by the 4-protons if the strongly coupled axial 3- and 4-protons have similar chemical shifts. If the signals of the axial 3- and 4-protons are a part of the rather narrow multiplet centered at τ 8.35, virtual long-range coupling would occur to give rise to the increased multiplicity of the axial 2-proton. Selectively deuterated compounds have been prepared which substantiate these observations of virtual long-range coupling increasing the multiplicity of the 1-proton signal in **15** and the 2-proton signal in **16**. These results, along with other observations from selectively deuterated compounds, will be reported in a subsequent paper.

The paramagnetic shift of a proton or methyl group resulting from a spatial 1,3-interaction with a hydroxyl group has previously been shown to be useful in determining the position and configuration of hydroxyl groups relative to the proton or methyl group affected.[14–16] This long-range spatial deshielding of a proton by a hydroxyl group is clearly shown in **15**–**17**. With the cyclohexane ring existing in the chair conformation with the tolyl group equatorial, the axial 2-proton in **15** and **17** is in close spatial proximity with an axial 4- and 6-hydroxyl group, respectively. The axial 2-proton in **16**, however, is spatially proximate only to axial 4- and 6-protons. The signal of the 2-proton in **15** and **17** occurs at τ 6.71 and 6.78, respectively, compared with the 2-proton signal in **16** at τ 7.29. Similarly, in **16** the signal of the 1-proton, which

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[13] J. I. Musher and E. J. Corey, *Tetrahedron*, **18**, 791 (1962).

[14] J. N. Shoolery and M. T. Rogers, *J. Am. Chem. Soc.*, **80**, 5121 (1958).

[15] Y. Kawazoe, Y. Sato, M. Natsume, H. Hasegawa, T. Okamoto, and K. Tsuda, *Chem. Pharm. Bull.* (Tokyo), **10**, 338 (1962).

[16] T. Okamoto and Y. Kawazoe, *ibid.*, **11**, 643 (1963).

is spatially proximate to the axial 5-hydroxyl group, occurs at approximately τ 5.88, compared with the 1-proton signal at τ 6.25 in **15** and 6.30 in **17**. Although other factors may to some degree alter their chemical shifts, for the most part the deshielding of the 1-proton in **16** and the 2-proton in **15** and **17** is attributed to the spatial 1,3-interaction between the proton and the proximate axial hydroxyl group.

In contrast with the complex signal of the 2-proton in **16**, the 2-proton signal in **17** occurs as a simple first-order signal. This can be accounted for by the deshielding of the axial 4-proton in **17** by the axial 6-hydroxyl group. The deshielding of the axial 4-proton must result in sufficient separation of the signals of the axial 3- and 4-protons so as to prevent virtual long-range coupling of the axial 2-proton by the axial 4-proton.

Experimental[17]

2-*o*-Tolyl-4-cyclohexen-1-one (**3**).—This compound was obtained by a method previously used for analogous compounds.[9] To 20.0 g. (0.092 mole) of *trans*-4-nitro-5-*o*-tolylcyclohexene,[8] dissolved in 300 ml. of 95% ethanol, through which oxygen-free nitrogen had bubbled for 30 min., was added a basic solution prepared by adding 4.24 g. (0.184 g.-atom) of metallic sodium to 100 ml. of 95% ethanol. This mixture was added with stirring to a mixture of 480 ml. of water, 360 ml. of ethanol, 156 ml. of concentrated hydrochloric acid, and 9.60 g. of sodium bisulfite at 0° after oxygen-free nitrogen had bubbled through both mixtures for 2 hr. A blue color appeared upon addition and persisted throughout the addition. The mixture was stirred at 0° for 1 hr. during which time the blue color turned to light green. The mixture was poured into 1.8 l. of ice–water and extracted with ether; the ethereal extracts were washed with cold 5% sodium bicarbonate solution, and then with water to neutrality. The work-up was carried out at low temperature to minimize acid-catalyzed isomerization to **4**. The ethereal solution was dried by passage through anhydrous sodium sulfate and standing over anhydrous calcium sulfate (Drierite). The greenish color persisted throughout. Filtration, solvent removal, and recrystallization from hexane containing a small amount of absolute ethanol resulted in a 63% yield of white crystals, m.p. 46.5–47.5°; infrared, ν C=O 1705 cm.$^{-1}$ (KBr).

Anal. Calcd. for $C_{13}H_{14}O$: C, 83.83; H, 7.58. Found: C, 83.76; H, 7.68.

cis- **and** *trans*-**2-*o*-Tolyl-4-cyclohexen-1-ol.**—To 15 ml. of anhydrous ether was added, with stirring, 0.77 g. (0.02 mole) of lithium aluminum hydride. To this mixture was added slowly, with stirring, 7.60 g. (0.041 mole) of **3** in 35 ml. of anhydrous ether. Addition time was 30 min. The mixture was stirred for 1 hr., excess lithium aluminum hydride was destroyed by dropwise addition of water, and the resulting mixture was poured into 100 ml. of water. The mixture was made acidic with 10% hydrochloric acid, the ether layer was separated, and the aqueous layer was extracted with ether. The ethereal extracts were washed with 5% sodium bicarbonate solution and water until neutral, and dried by passage through anhydrous sodium sulfate and standing over Drierite. Filtration, solvent removal, and vacuum distillation afforded an 87% yield of colorless liquid, b.p. 100–101° at 0.49–0.50 mm. Vapor phase chromatography (v.p.c.) of the distillate on a 5-ft. column of 18% Carbowax 20M on 60–80-mesh Chromosorb W showed two components present in an 80 to 20% ratio. They were characterized as *trans* (**5**) and *cis* (**6**), respectively, as follows. Three-fourths of a gram (0.044 mole) of the distillate in 10 ml. of ethyl acetate was reduced catalytically over a palladium-on-carbon catalyst to a mixture of *cis*- and *trans*-2-*o*-tolylcyclohexanol.[6] Filtration, solvent removal, and vacuum distillation yielded a clear distillate, b.p. 98° at 0.53 mm. V.p.c. on a 5-ft. column of 18% Carbowax 20M on 60–80-mesh Chromosorb W showed the product ratio to be 80% *trans* and 20% *cis*.

trans-**2-*o*-Tolyl-4-cyclohexen-1-ol** (**5**).—Pure **5** was obtained by reduction of **9**. To 10 ml. of anhydrous ether was added, with stirring, 0.40 g. (0.011 mole) of lithium aluminum hydride. To this mixture was added slowly with stirring 1.50 g. (0.0051 mole) of **9** in 15 ml. of anhydrous ether. The mixture was stirred for 2 hr., excess lithium aluminum hydride was destroyed by dropwise addition of water, and the resulting mixture was made acidic with 10% hydrochloric acid. The ether layer was separated, and the aqueous layer was extracted with ether. The ethereal extracts were washed with 5% sodium bicarbonate solution, washed with water to neutrality, and dried by passage through anhydrous sodium sulfate and standing over Drierite. Filtration, solvent removal, and vacuum distillation yielded a low-boiling fraction of benzyl alcohol and a 70% yield of colorless liquid, b.p. 76–77° at 0.17 mm. Comparison of the v.p.c. emergence times with those of **5** and **6** using a 5-ft. column of 18% Carbowax 20M on 60–80-mesh Carbowax W verified that the distillate was **5**.

trans-**2-*o*-Tolyl-4-cyclohexyl Benzoate** (**9**).—A mixture of 9.70 g. (0.052 mole) of **5** and **6** (80% **5**, 20% **6**) and 9.05 g. (0.064 mole, 7.5 ml.) of benzoyl chloride was heated at 110–130° for 1.5 hr. The resulting mixture was poured into 100 ml. of water, 5.0 g. of sodium bicarbonate was added, and the resultant mixture was shaken vigorously. The mixture was extracted with ether; the ethereal extracts were washed with water to neutrality and dried by passage through anhydrous sodium sulfate and standing over Drierite. Filtration and solvent removal gave a crude reddish oil, which was taken up in hexane and treated with activated charcoal. Recrystallization from a hexane–benzene mixture afforded a 51% yield of white crystals, m.p. 54–55°. Lithium aluminum hydride reduction of **9** gave pure **5**. No effort was made to isolate the pure *cis* isomer.

Anal. Calcd. for $C_{20}H_{20}O_2$: C, 82.16; H, 6.90. Found: C, 82.46; H, 6.93.

trans-**2-*o*-Tolyl-*cis*-4,5-epoxycyclohexyl Benzoate** (**11**) **and** *trans*-**2-*o*-Tolyl-*trans*-4,5-epoxycyclohexyl Benzoate** (**12**).—These compounds were prepared by the epoxidation of **9** with perbenzoic acid according to the procedure described by Henbest and Nicholls.[10] A solution of 17.65 g. (0.06 mole) of **9** in 210 ml. of anhydrous ether containing 0.184 mole of perbenzoic acid (0.875 *M*) was stored at 0° for 15 days. The excess perbenzoic acid was removed by washing with a cold 10% sodium hydroxide solution. After one washing the ether layer was slightly basic and gave a negative peracid test with potassium iodide solution. The ether solution was washed with water to neutrality and dried by standing over Drierite. Filtration and solvent removal yielded a near quantitative yield of a mixture of **11** and **12**. The per cent composition of the mixture was not determined. Crystallization from petroleum ether yielded a white solid, m.p. 64–88°. Separation of **11** and **12** was accomplished by successive recrystallizations from a petroleum ether–benzene mixture: **11**, m.p. 80–81°; **12**, m.p. 117–118°.

Anal. Calcd. for $C_{20}H_{20}O_3$: C, 77.90; H, 6.54. Found for **11**: C, 77.72; H, 6.32. Found for **12**: C, 77.49; H, 6.44.

The perbenzoic acid solution was prepared by the method described in "Organic Syntheses,"[18] and standardized by the procedure described by Pierce, Haenisch, and Sawyer.[19]

2-*o*-Tolyl-5-cyclohexen-1-one (**4**).—A solution of 5.86 g. (0.03 mole) of **3**, 35 ml. of ethanol, and 30 ml. of concentrated hydrochloric acid was refluxed for 3 hr. and poured into 200 ml. of water; the resultant cloudy mixture was extracted with ether. The ethereal extracts were washed with 5% sodium bicarbonate solution, washed with water to neutrality, and dried by passage through anhydrous sodium sulfate and standing over Drierite. Filtration, solvent removal, and vacuum distillation gave an 83% yield of colorless liquid, b.p. 100° at 0.175 mm.; infrared, ν C=O 1670 cm.$^{-1}$. No analysis was obtained on this intermediate.

trans- **and** *cis*-**2-*o*-Tolyl-5-cyclohexen-1-ol.**—These compounds were prepared in a ratio of 60% *trans* (**7**) and 40% *cis* (**8**) by the lithium aluminum hydride reduction of **4** essentially as described for the preparation of **5** and **6**. A 30% Rochelle salt solution was used for hydrolysis. A 91% yield of colorless liquid, b.p.

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[17] All melting points were determined with a Kofler micro hot stage. Microanalyses were by Weiler and Strauss, Oxford, England. Infrared spectra were determined using a Beckman IR 5-A infrared spectrophotometer.

[18] M. Tiffeneau "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 422.

[19] W. C. Pierce, E. L. Haenisch, and D. T. Sawyer, "Quantitative Analysis," 4th Ed., John Wiley and Sons, Inc., New York, N. Y., 1961, p. 298.

123-124° at 1.38 mm., was obtained. Identification of isomers was made by catalytic reduction to a mixture of *cis*- and *trans*-2-*o*-tolylcyclohexanol[6] and subsequent v.p.c. as described for the identification of **5** and **6**.

trans-**2-*o*-Tolyl-5-cyclohexen-1-ol (7)**.—This compound was prepared in 76% yield by the lithium aluminum hydride reduction of **10** according to the procedure described for the preparation of **5** from **9**, b.p. 88-89° at 0.23-0.24 mm.

Anal. Calcd. for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 82.55; H, 8.42.

trans-**2-*o*-Tolyl-5-cyclohexenyl Benzoate (10)**.—A mixture of 15.10 g. (0.08 mole) of **7** and **8** (60% **7**, 40% **8**), 16.9 g. (0.120 mole) of benzoyl chloride, and 50 ml. of anhydrous pyridine were heated for 1.5 hr. at 140°. A white precipitate formed and heat was evolved upon addition of the benzoyl chloride to the pyridine. This precipitate dissolved upon heating. At the end of the heating, two layers were present. The mixture was hydrolyzed by pouring into 200 ml. of 10% hydrochloric acid. The resulting mixture was extracted with ether, and the ethereal extracts were washed with 10% hydrochloric acid, 5% sodium bicarbonate solution, and water. After drying by passage through anhydrous sodium sulfate and standing over Drierite, the solution was filtered and solvent was removed. The crude reddish product was treated with activated charcoal and recrystallized from a hexane-benzene mixture to give a 34% yield of white crystals, m.p. 81-81.5°. (The per cent yield was based on the amount of **7** in the starting material, 9.06 g.) Lithium aluminum hydride reduction of **10** gave pure **7**.

Anal. Calcd. for $C_{20}H_{20}O_2$: C, 82.16; H, 6.90. Found: C, 82.49; H, 6.92.

trans-**2-*o*-Tolyl-*trans*-5,6-epoxycyclohexyl Benzoate (13)** and *trans*-**2-*o*-Tolyl-*cis*-5,6-epoxycyclohexyl Benzoate (14)**.—These compounds were prepared by the epoxidation of **10** with perbenzoic acid as described for the preparation of **11** and **12** from **9**. Recrystallization from a hexane-benzene mixture resulted in the crystallization of two different crystal structures, one needles and the other rock-like. The different crystal structures were separated with forceps. Recrystallization afforded **13** as needles, m.p. 128.5-129.5°, and **14**, rock-like, m.p. 105-106°.

Anal. Calcd. for $C_{20}H_{20}O_3$: C, 77.90; H, 6.54. Found: **13**, C, 77.82; H, 6.64; **14**, C, 78.20; H, 6.47.

trans-**2-*o*-Tolyl-*cis*-4-hydroxycyclohexanol (15)**.—This compound was prepared by the lithium aluminum hydride reduction of **11**. To a stirred mixture of 0.75 g. (0.020 mole) of lithium aluminum hydride in 10 ml. of anhydrous ether was added slowly 3.12 g. (0.011 mole) of **11** in 30 ml. of anhydrous ether. Heat was evolved during the addition. The mixture was stirred for 1.5 hr., and hydrolyzed by pouring into 42 ml. of 30% Rochelle salt solution, and the ether layer separated. The aqueous layer was extracted with ether and the combined ethereal extracts were dried by passage through anhydrous sodium sulfate. Solvent removal afforded white crystals which were recrystallized from benzene, m.p. 149.5-150°.

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.55; H, 8.60.

trans-**2-*o*-Tolyl-*trans*-5-hydroxycyclohexanol (16)**.—This compound was prepared by the lithium aluminum hydride reduction of **12** and by the similar reduction of **13** as described for the preparation of **5** from **11**. The product from the reduction of **12** was isolated by elution chromatography over 10 g. of neutral alumina using 25-ml. portions of eluent. The eluents used were petroleum ether-benzene mixture (50:50) and benzene. Recrystallization from a benzene-petroleum ether mixture gave white crystals, m.p. 117-119°. The reduction of **13** gave a 72% yield, m.p. 118-119°. A mixture melting point of the two products showed no depression and their infrared spectra were identical. The analytical sample had m.p. 119-119.5°.

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.85; H, 8.72.

trans-**2-*o*-Tolyl-*cis*-6-hydroxycyclohexanol (17)**.—This compound was prepared by the lithium aluminum hydride reduction of **14** as previously described for the preparation of **15** from **11**. Recrystallization from a hexane-benzene mixture afforded white crystals, m.p. 116.8-117.3°.

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.38; H, 8.75.

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Ketenes. III. Cycloaddition of Ketenes to Acetylenic Ethers[1]

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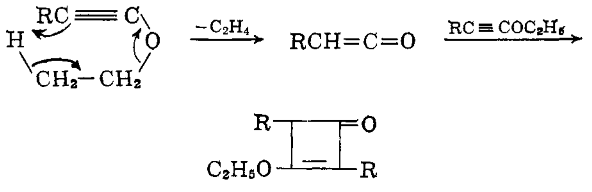
Dialkylketenes add to ethoxyacetylene to give 4,4-dialkyl-3-ethoxy-2-cyclobuten-1-ones and to 1-buten-3-ynyl methyl ether to give 4,4-dialkyl-3-(2-methoxyvinyl)-2-cyclobuten-1-ones. Some new reactions of these cyclobutenones are described.

The cycloaddition of ketenes to alkoxyacetylenes was first suggested by Nieuwenhuis and Arens,[3] whose interpretation of Ficini's earlier work[4] showed that pyrolysis of ethoxyacetylenes gave ethoxycyclobutenones. This reaction apparently involves a concerted elimination of an aldoketene from the ethoxyacetylene, followed by cycloaddition of the ketene and acetylenic ether.



Proof of this mechanism, by addition of diphenylketene to ethoxyacetylene, was obscured by the formation of rearrangement products,[5,6] and by a peculiar mode of addition involving a benzene nucleus of the diphenylketene.[7,8] Unequivocal evidence for the formation of a cyclobutenone has been presented,[9] however, and the addition of ketene to several acetylenic ethers has been described.[10,11]

Dimethylketene, presumably less reactive than di-

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[1] Paper II in this series: R. H. Hasek, P. G. Gott, and J. C. Martin' *J. Org. Chem.*, **29**, 1239 (1964).

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