Studies of Terpene Chemistry. I. The Acid-Catalyzed Dimerization of Citronellal[1]

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The bromination of citronellal gives a mixture of bromo ethers and bromo alcohols. The bromo alcohol mixture contains 8-bromomenthols which are dehydrobrominated to yield isopulegol. Debromination of the bromo ether mixture affords a dimeric unsaturated ether, $C_{20}H_{34}O$. The same unsaturated ether is obtained from the acid-catalyzed condensation of citronellal and isopulegol and from citronellal alone. We conclude that the products from the bromination of citronellal are formed by bromination of the acid-catalyzed cyclization and dimerization products. The dimeric unsaturated ether is shown to have structure 3 by degradative and spectroscopic studies.

In the course of studies of the synthesis of carbocyclic systems, the products from the bromination of citronellal have been examined. The bromination of citronellal was first reported by Wright[2] in 1874, and the first detailed description for the bromination was given by Kremers[3] in 1892. These authors described the bromination products of citronellal as unstable oils which could not be characterized. In our hands, the bromination products result from bromination of the acid-catalyzed cyclization and dimerization products of citronellal.

The bromination of citronellal in ether solution at 0° gives a mixture of bromo ethers and bromo alcohols in a ratio of 3:1. The bromination products showed signs of decomposition during storage at room temperature and we were not able to obtain satisfactory analytical data. All attempts at purification by crystallization or distillation met with failure.

Dehydrobromination of the bromo alcohols with hot collidine gave a mixture of isopulegols (1) which was identical with a commercial preparation. Oxidation of the isopulegol afforded isopulegone, characterized as the 2,4-dinitrophenylhydrazone, which could be isomerized to pulegone (2). Chromic acid oxidation of the bromo alcohol mixture afforded the corresponding bromo ketones which were converted to pulegone upon treatment with calcium carbonate in N,N-dimethylacetamide. These results indicate that the bromo alcohol fraction is a mixture of stereoisomers of 8-bromomenthol which may also contain some 8,9-dibromomenthols.

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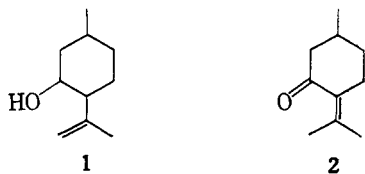
Treatment of the bromo ethers with lithium in liquid ammonia gave a mixture which showed three peaks on vapor phase chromatography. The major component, comprising about 76% of the mixture, was shown to be an olefinic ether, $C_{20}H_{34}O$, from combustion analyses, molecular weight determination, and spectroscopic data. The minor products had spectral characteristics similar to those of the main product, but they were not examined further. Treatment of the crude bromination product with zinc in ethanol afforded

isopulegol and the same mixture of unsaturated ethers. Hence, some of the bromines are vicinal. Analyses of the bromo ether fraction gave high values for bromine calculated on the basis of a tetrabromo ether and bromination of a sample of the total unsaturated ethers yielded a mixture of bromo ethers whose infrared spectrum was identical with the original mixture of bromo ethers. The same olefinic ether is obtained from the condensation of citronellal and isopulegol or citronellal alone in ether solution at room temperature in the presence of p-toluenesulfonic acid. Hence, it appears that the products from the bromination of citronellal, under the conditions used in the present investigation, arise from bromination of the acid-catalyzed cyclization and dimerization products of citronellal.

Microhydrogenation of the dimeric unsaturated ether indicated two double bonds and the infrared spectrum of this material shows no hydroxyl or carbonyl absorption, but peaks at 1650, 1100, and 900 cm.$^{-1}$ consistent with the presence of carbon–carbon double bonds and an ether. Structure 3 is proposed for the olefinic ether on the basis of degradative and spectroscopic evidence presented below.

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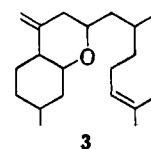
The proton magnetic resonance spectrum of the olefinic ether shows a one-proton triplet at δ 4.94 with $J = 5.0$ c.p.s. and broad singlet at δ 4.54 corresponding to two protons. The triplet at δ 4.94 is identical with the signal of the vinyl proton of citronellal. The signal at δ 4.54 is consistent with the presence of an *exo* methylene group as suggested by the 900-cm.$^{-1}$ band in the infrared spectrum.

Three fragments were identified from the ozonolysis of the unsaturated ether. Ozonolysis in methylene chloride afforded acetone in 70% yield isolated as the 2,4-dinitrophenylhydrazone. While it was not possible to isolate formaldehyde from ozonolysis in methylene chloride, ozonolysis in acetic acid followed by reductive work-up yielded formaldehyde in 25% yield as the dimedon derivative. Ozonolysis in methylene chloride followed by oxidative work-up furnished 1-acetyl-4-methylcyclohexene in 15% yield, characterized as the 2,4-dinitrophenylhydrazone. An authentic sample of 1-acetyl-4-methylcyclohexene was prepared by the ozonolysis of isopulegol followed by dehydration of the intermediate ketol. The 1-acetyl-4-methylcyclohexene is

(1) Supported by a Frederick Gardner Cottrell grant from the Research Corporation and the National Science Foundation, Grant GP-252.
(2) C. R. A. Wright, *Pharm. J.*, **5**, 233 (1874).
(3) E. Kremers, *Am. Chem. J.*, **14**, 203 (1892).

thought to be formed by alkaline cleavage of the ozonolysis product. The cleavage is viewed as a β-elimination followed by a reverse aldol. This degradation provides evidence regarding the position of the ether bridge.
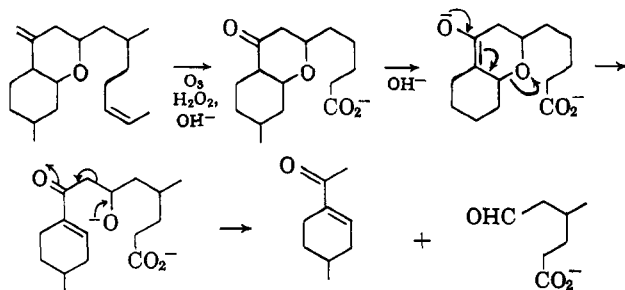
Dehydrogenation of the unsaturated ether gave a high yield of (6R)-2-(p-tolyl)-6,10-dimethyl-4-undecanone, obtained as an equimolar mixture of epimers at C-2. The structure of the ketone was suggested from its spectroscopic properties (see Experimental) and oxidation with potassium permanganate to yield dihydrocitronellic acid. The structure of the dehydrogenation ketone was confirmed by the synthesis outlined below.
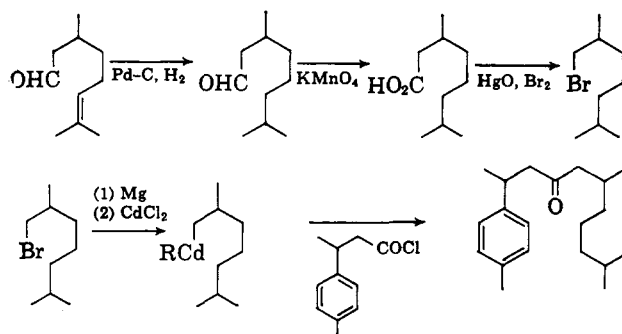

The synthesis proceeded smoothly and the final step, the reaction of the cadmium reagent from (2R)-2,6-dimethylheptyl bromide with racemic 3-(p-tolyl)butyryl chloride, afforded the desired ketone which was identical in all respects including rotation, with the dehydrogenation ketone. Since the synthetic ketone is almost certainly an equimolar mixture of epimers at C-2, we conclude that the dehydrogenation ketone is also a mixture of epimers.
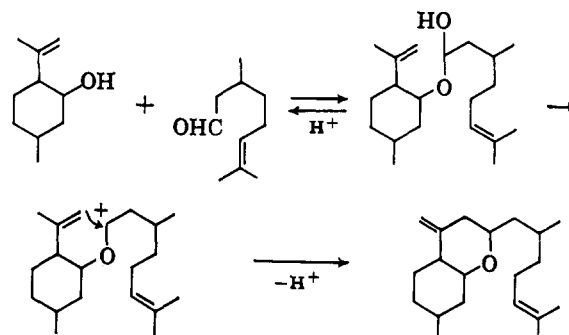
Since cleavage of the ether occurs without loss of any carbons, the ether linkage must be part of a ring. The protons adjacent to oxygen in the olefinic ether appear in the proton magnetic resonance spectrum as a multiplet at δ 3.33, but no reliable conclusions can be drawn about the size of the oxygen-containing ring. However, neither the vinyl protons nor the protons adjacent to oxygen are abnormally deshielded indicating that the ether bridge is not allylic. This conclusion is supported by the stability of the unsaturated ether to solutions of alkali metals in liquid ammonia.

Assuming no molecular rearrangement during dehydrogenation, the dehydrogenation indicates one site of attachment of the oxygen. The mechanism of formation of the dehydrogenation ketone requires further comment. It seems likely that the oxygen-containing ring is dehydrogenated first to yield the pyran. In the presence of a hydrogenation catalyst at

elevated temperatures, the pyran would be expected to be in equilibrium with the dienone, which would suffer aromatization to the observed product. There is ample analogy for the postulated isomerization of the pyran derivative to the dienone. The thermochromism of spiropyrans is ascribed to thermal interconversion of the pyran to the dienone.[4] It has also been found that enol ether of cis-β-ionone is isomerized to trans-β-ionone by iodine at room temperature or ultraviolet light.[5] In the present case, the dienone would be expected to aromatize with concomitant reduction of the isolated double bond in the presence of a hydrogenation catalyst. It is interesting to note that the tetrahydro ether, prepared by hydrogenation of the unsaturated ether, yields the same ketone upon dehydrogenation.
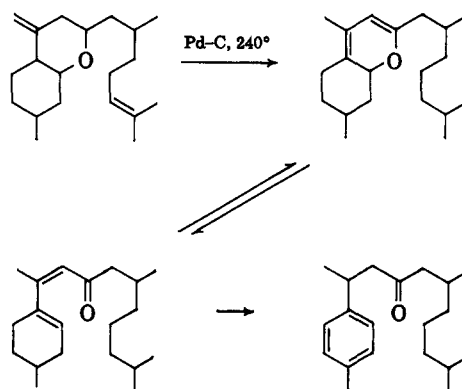
It seems quite certain that the dimeric bromo ethers obtained from the bromination of citronellal arise from the acid-catalyzed condensation of isopulegol and citronellal. The formation of 8-bromomenthol in the reac-

tion undoubtedly proceeds by the same carbonium ion which leads to isopulegol and there is little doubt that isopulegol is present in the reaction mixture. There are many analogies for the formation of pyran derivatives from the acid-catalyzed condensation of aldehydes and homoallylic alcohols.[6] It seems likely that there is ample hydrogen bromide present in the bromination mixture to catalyze the observed cyclizations since the bromine was not purified before use and a variety of side reactions would lead to additional hydrogen bromide.

(4) C. F. Koelsch, J. Org. Chem., 16, 1362 (1951).

(5) G. Büchi and N. C. Yang, J. Am. Chem. Soc., 79, 2318 (1957).

(6) A. T. Blomquist and J. Wolinsky, ibid., 79, 6025 (1957); L. J. Dolby and M. J. Schwarz, J. Org. Chem., 28, 1456 (1963); N. LeBel, R. N. Liesmer, and E. Melamedbasich, ibid., 28, 615 (1963); J. Cologne and P. Boisde, "Les Heterocycles Oxygenes." National Center of Scientific Research, Paris, 1962, p. 171.

Experimental[7]

Bromination of Citronellal.—A solution of (+)-citronellal (10 g., 0.07 mole) in 100 ml. of anhydrous ether was brominated by the dropwise addition of bromine (3.7 ml., 0.07 mole) over a period of 1 hr. at 0°. The ether solution was washed successively with water, 10% sodium bicarbonate solution, and the aqueous sodium thiosulfate. After drying over anhydrous magnesium sulfate, the solution was concentrated to a heavy yellow oil. This oil was chromatographed on grade III Woelm alumina (400 g.) to yield two fractions: fraction I, 15 g., eluted with 300 ml. of petroleum ether (30–60°); and fraction II, 5.0 g., eluted with 300 ml. of ethyl ether.

Fraction I was a heavy colorless oil, $[\alpha]^{25}$D −13.5° (c 1.356, chloroform), n^{25}D 1.5307, which was unstable to storage at room temperature; infrared: 1480, 1375, 1100, 815, and 770 cm.$^{-1}$. There was negligible absorption in the ultraviolet. The n.m.r. spectrum showed a complex multiplet at δ 4.00 and additional complex absorption in which there were evident two prominent singlets at δ 2.00 and 1.73 and a doublet at 0.97.

Fraction II was a colorless oil, $[\alpha]^{25}$D +3.33° (c 2.116, chloroform), n^{25}D 1.4961, which also decomposed on standing at room temperature; infrared: 3400, 2900, 1450, 1370, and 1100 cm.$^{-1}$.

Conversion of 8-Bromomenthol to Isopulegol.—A solution of 0.236 g. of 8-bromomenthols (from fraction II) in collidine (10 ml.) was refluxed for 15 min. The brown mixture was cooled and quenched in dilute sulfuric acid and ice and extracted with ether. The ether layer was washed with water and with saturated sodium bicarbonate solution and dried over anhydrous magnesium sulfate. The crude product was chromatographed on grade I Woelm alumina. The material (50 mg.), 30% yield, eluted from the column with 30% ethyl acetate–ethyl ether, was shown to be isopulegol by the gas chromatographic and infrared comparison with authentic isopulegol. Both the isopulegol obtained from dehydrobromination of fraction II and commercial isopulegol showed two peaks (3:1) upon gas chromatography using a TCEP column at 140°.

Isopulegone 2,4-Dinitrophenylhydrazone.—A sample of isopulegol (0.300 g., 0.0019 mole), obtained from fraction II, was oxidized by the method of Brown and Garg.[8] The crude ketone (0.200 g., 68%) gave an orange 2,4-dinitrophenylhydrazone, m.p. 136–137°, which did not depress the melting point of authentic isopulegone 2,4-dinitrophenylhydrazone, m.p. 140–141°. The ultraviolet spectrum (λ^{EtOH}_{max} 230 and 357 mμ) and the infrared spectrum (1755, 1650, 1460, 1360, 1100, and 900 cm.$^{-1}$) of this material were also identical with those of isopulegone 2,4-dinitrophenylhydrazone (m.p. 140–141°), prepared similarly from commercial isopulegol. The analytical sample melted at 140–141° after several crystallizations from 95% ethanol.[9]

Anal. Calcd. for $C_{16}H_{20}N_4O_4$: C, 57.82; H, 6.07; N, 16.86. Found: C, 57.71; H, 6.05; N, 17.08.

Isomerization of Isopulegone to Pulegone.—Isopulegone (0.500 g.) in 50 ml. of 0.1 N ethanolic sodium hydroxide was refluxed for 142 min. The reaction mixture was acidified and extracted with ether. The ether extracts were washed with sodium bicarbonate then water. The dried ether solution was concentrated and the residual oil gave a red 2,4-dinitrophenylhydrazone, m.p. 136–137° after crystallization from petroleum ether (30–60°). This material did not depress the melting point of authentic pulegone 2,4-dinitrophenylhydrazone, m.p. 139–140° (lit.[10] m.p. 142° from petroleum ether, m.p. 149–150° from

methanol), and the infrared spectra (KBr disk) were superimposable.

Chromic Acid Oxidation of 8-Bromomenthol.—The Brown and Garg[8] procedure was employed on 0.6 g. (0.0025 mole) of 8-bromomenthol. This gave a bromo ketone ($\nu^{CHCl_3}_{max}$ 1715 cm.$^{-1}$) which was used immediately in the following elimination reaction.

Conversion of 8-Bromomenthone to Pulegone.—A solution of 8-bromomenthone (0.062 g.) in N,N-dimethylacetamide (25 ml.) over 0.4 g. of calcium carbonate was refluxed for 30 min. Upon work-up, a ketonic product was obtained which gave a red 2,4-dinitrophenylhydrazone, m.p. 130–140°, which was identical with authentic pulegone 2,4-dinitrophenylhydrazone.

Lithium–Liquid Ammonia Debromination of the Bromo Ethers.—A solution of 2.14 g. (0.0034 mole) of I in anhydrous ether was added dropwise to a stirred solution of lithium metal (1.5 g., 0.21 g.-atom) in 100 ml. of anhydrous liquid ammonia. After 2 hr., the excess lithium was destroyed with ammonium chloride and the ammonia was allowed to evaporate. The usual work-up yielded 0.85 g. (85%) of a light yellow oil, b.p. 140–145° (4.5 mm.). Vapor phase chromatography on a 5-ft. column of Carbowax 20 M on firebrick showed three peaks. The first peak eluted comprised about 80% of the mixture. Material purified by preparative vapor phase chromatography[7] at 200° showed b.p. 142–144° (4.5 mm.), $[\alpha]^{25}$D −17.6° (c 0.393, ethyl acetate), n^{25}D 1.4905; infrared: 2980, 1650, 1383, 1225, 1102, 1090, 950, 890, 675, and 636 cm.$^{-1}$. Only end absorption was observed in the ultraviolet. The n.m.r. spectrum showed the following bands: δ 4.95 (t), 4.54 (s), 3.38 (m), 1.92 (m), 1.58 (d), 1.22 (m), and 0.85 (d).

Anal. Calcd. for $C_{20}H_{34}O$; C, 82.54; H, 11.80. Found: C, 82.30; H, 12.05.

Anal. Calcd. H_2 uptake for two double bonds in $C_{20}H_{34}O$: 146 mg./mmole of H_2. Found: 161 mg. of sample/mmole of H_2.

Zinc Reduction of the Bromination Products of Citronellal.—A solution of the crude bromination product from citronellal (200 g., 0.33 mole) in 2.0 l. of absolute ethanol was treated with 100 g. of zinc powder. This mixture was refluxed with stirring for 5 days. Portions of fresh zinc were added periodically. Addition of EDTA[11] to complex the zinc salts formed did not seem to influence the nature of the product, but it was added to the larger runs. The reaction mixture was filtered through a sintered-glass funnel, diluted with water, and extracted with ether. The ether extracts were dried over magnesium sulfate and the solvent was removed by flash distillation at atmospheric pressure. The residual oil was fractionally distilled to give 15 g. (15%) of isopulegol, and 50 g. (55%) of a mixture of olefinic ethers which was identical with the product obtained from the lithium–liquid ammonia debromination of fraction I.

Bromination of the Olefinic Ether Mixture.—A 1.8-g. (0.003 mole) sample of the bromo ethers was treated with zinc in refluxing ethanol with stirring for 3 days. The usual work-up gave 0.6 g. of the debromo ether (75% yield). The gas chromatogram of this material as well as the infrared spectrum were identical with those of the ether mixture from previous runs. This material was rebrominated in ether to yield 1.2 g. of bromo ethers. The infrared spectrum of this material and that of the original bromo ethers were found to be completely superimposable.

Attempted Cleavage of the Desbromo Ether with Sodium–Liquid Ammonia.—A solution of the olefinic ether (6.0 g., 0.020 mole) and sodium metal (3.0 g., 0.13 g.-atom) in 500 ml. of liquid ammonia was stirred for 5 hr. Only starting material could be isolated upon work-up.

Hydrogenation of the Olefinic Ether.—A solution of the olefinic ether (1.90 g.) in ethanol containing sufficient petroleum ether (30–60°) to make a homogeneous solution and one drop of 70% perchloric acid was hydrogenated over 100 mg. of 10% palladium-on-carbon catalyst in a low pressure hydrogenator. The product was a colorless oil, 1.80 g. (94%), b.p. 151–153° (4.0 mm.), n^{25}D 1.4679, $[\alpha]^{25}$D −7.88° (c 1.840, chloroform). The n.m.r. spectrum of the tetrahydro ether showed a two-proton multiplet at δ 3.38 and a doublet at 0.90.

Anal. Calcd. for $C_{20}H_{38}O$: C, 81.56; H, 13.01; mol. wt., 294.50. Found: C, 81.59; H, 12.77; mol. wt., 300.

Ozonolysis of the Olefinic Ether.—A solution of the unsaturated ether (1.0 g.) in methylene chloride (75 ml.) was ozonized at −80°

(7) All melting points and boiling points are uncorrected; distillations were carried out using a 65-cm. modified Podbielniak tantalum spiral column. A Wilkens Model A-90-P gas chromatograph and a Nester and Faust Prepko gas chromatograph with a commercial Carbowax 6000 column were used for vapor phase chromatography. Infrared spectra were determined with a Beckman IR-7 infrared spectrophotometer and ultraviolet spectra were measured with a Cary Model 11 spectrophotometer. Proton magnetic resonance spectra were determined in carbon tetrachloride solution using tetramethylsilane as internal standard with a Varian A-60 spectrometer. Microanalyses are by Micro-Tech Laboratories, Skokie, Ill.; Pascher and Pascher Laboratories, Bonn, Germany; and Berkeley Analytical Laboratories, Berkeley, Calif.

(8) H. C. Brown and C. P. Garg, *J. Am. Chem. Soc.*, **83**, 2952 (1961).

(9) The melting point of (+)-isoisopulegone 2,4-dinitrophenylhydrazone is recorded as 144–145°; the stereochemistry and purity of our preparation of isopulegone 2,4-dinitrophenylhydrazone are not certain [G. Ohloff, J. Osiecki, and C. Djerassi, *Ber.*, **95**, 1400 (1962)].

(10) (a) O. L. Brady, *J. Chem. Soc.*, 758 (1931); (b) W. Kuhn and H. Schinz, *Helv. Chim. Acta*, **36**, 161 (1953).

(11) Ethylenediaminetetraacetic acid tetrasodium salt.

until a blue color persisted. The solvent was carefully removed under vacuum at room temperature to give an oily ozonide. The ozonide was treated with 20 ml. of water and enough zinc powder to complete the decomposition. This mixture was allowed to stand for 2 hr. after which it was heated on a steam bath under nitrogen and the effluent gases were bubbled through a saturated solution of 2,4-dinitrophenylhydrazine in 2 N hydrochloric acid. This procedure gave acetone 2,4-dinitrophenylhydrazone (70%), m.p. 123–124°.

The ozonolysis of the olefinic ether (0.200 g.) in 20 ml. of glacial acetic acid was carried out at room temperature. The resulting solution was stirred with 10 ml. of water and zinc powder (0.5 g.) for 2 hr. and steam distilled. The steam distillate was treated with a solution of dimedon in water and the pH was adjusted to 3 with sodium acetate. A white precipitate (54 mg., 25%) was obtained which gave white needles, m.p. 190–192° after one recrystallization from ethanol. This material did not depress the melting point of an authentic sample of the dimedon derivative of formaldehyde. The infrared spectra of these two derivatives were superimposable.

Ozonolysis of the Olefinic Ether–Oxidative Procedure.—A solution of the desbromo ether (1.0 g., 0.003 mole) in 50 ml. of methylene chloride was ozonized at −70° until a blue color persisted. The solvent was removed under vacuum at room temperature. The oily residue was treated with 30 ml. of 20% sodium hydroxide and 20 ml. of 30% hydrogen peroxide solution. The reaction mixture was allowed to stand overnight at room temperature, after which it was heated on a water bath until oxygen evolution subsided. The reaction mixture was steam distilled and the steam distillate was extracted with ether. Evaporation of the ether gave 78 mg. (15%) of an oil which showed strong ultraviolet absorption at 238 mμ; infrared: 1660 and 1640 cm.$^{-1}$. A sample of this oil gave a crimson 2,4-dinitrophenylhydrazone, m.p. 205–207°. The ultraviolet spectrum of this derivative showed strong absorption at λ_{max}^{EtOH} 255 and 376 mμ.

Anal. Calcd. for $C_{15}H_{18}N_4O_4$: C, 56.47; H, 5.69; N, 17.56. Found: C, 56.2; H, 6.0; N, 17.8.

This material was identified as 1-acetyl-4-methylcyclohexene 2,4-dinitrophenylhydrazone by infrared and melting point comparison with an authentic sample.

2,4-Dinitrophenylhydrazone of 1-Acetyl-4-methylcyclohexene.—A solution of 0.200 g. (0.0012 mole) of isopulegol was ozonized in glacial acetic acid (50 ml.). The reaction mixture was stirred with zinc powder (2.0 g.) and 50 ml. of water for 2 hr. The usual work-up gave an oil, 0.194 g. (95%), which showed infrared absorption at 3400 and 1710 cm.$^{-1}$. This β-keto alcohol was treated with excess 2,4-dinitrophenylhydrazine reagent ·and heated to reflux for 15 min. The 2,4-dinitrophenylhydrazone of 1-acetyl-4-methylcyclohexene was isolated as a red crystalline solid, m.p. 205–207°, λ_{max}^{EtOH} 255 and 376 mμ.

Anal. Calcd. for $C_{15}H_{18}N_4O_4$: C, 56.47; H, 5.69; N, 17.56. Found: C, 56.66; H, 5.76; N, 18.00.

When the β-keto alcohol was refluxed with a 2% solution of p-toluenesulfonic acid, 1-acetyl-4-methylcyclohexene was obtained. The infrared spectrum of the crude ketone showed absorption at 1660 and 1640 cm.$^{-1}$. This material gave the same 2,4-dinitrophenylhydrazone as obtained in the direct treatment of the keto alcohol with refluxing 2,4-dinitrophenylhydrazine reagent.

The Acid-Catalyzed Condensation of Citronellal and Isopulegol.—An ether solution of citronellal (2.0 g., 0.013 mole) and isopulegol (2.0 g., 0.013 mole) was stirred overnight at room temperature. The infrared spectrum was measured immediately on mixing and again at the end of the stirring period. The second sample showed a new absorption at 1240 cm.$^{-1}$, a region characteristic of hemiacetals, and carbonyl absorption at 1710 cm.$^{-1}$. p-Toluenesulfonic acid (40 mg.) was added to this mixture and stirring was continued for 12 hr. The ether solution was washed with 10% sodium carbonate solution, sodium bisulfite solution, and water. Evaporation of the dried ether solution *in vacuo* gave 4.0 g. of an oil which was chromatographed on grade III Woelm alumina. Elution with petroleum ether (30–60°) afforded 2.0 g. (57%) of an oil. Vapor phase chromatography yielded the same olefinic ether obtained by debromination of the bromination products of citronellal. The same product could be obtained by treatment of citronellal alone with catalytic amounts of p-toluenesulfonic acid, whereas isopulegol alone did not give this product.

Dehydrogenation of the Olefinic Ether.—A mixture of 3.8 g. (0.013 mole) of the unsaturated ether and 30% palladium on charcoal (100 mg.) was heated under nitrogen at 240° for 36 hr. Subsequent runs were monitored by gas chromatography and it was shown that the reaction was essentially complete in 5–10 hr. Gas chromatographic assay of this product showed three major peaks. The retention times of these components were 16, 20.2, and 75 min. (Carbowax 20 M, 150°) in the ratio of 1:1:12. This mixture was fractionated carefully three times to yield an oil, b.p. 139–140° (0.75 mm.), n^{25}D 1.4834, [α]^{25}D +3.86° (c 1.550, chloroform), which was identical with an authentic sample of (6R)-2-(p-tolyl)-6,10-dimethyl-4-undecanone. This material showed infrared absorption at 1712 (ketonic carbonyl), aromatic overtone bands at 1900, strong absorption at 1500 and 817 cm.$^{-1}$ for 1,4-disubstituted benzene. The ultraviolet spectrum of this material showed λ_{max}^{EtOH} 277 (ϵ 425) and 285 mμ (425). The n.m.r. spectrum exhibited a singlet at δ 6.9 (aromatic C–H), a singlet at 2.20 (3 protons) ascribed to the toluene-type methyl, and a complex quartet at 3.17 ascribed to the proton at C-2. The C-3 protons were seen as a doublet at δ 2.50, J = 7 c.p.s., and the protons at C-5 appeared as a doublet at δ 2.05, J = 7 c.p.s. The same ketone was obtained from dehydrogenation of the tetrahydro ether under the same conditions.

Anal. Calcd. for $C_{20}H_{32}O$: C, 83.40; H, 11.16. Found: C, 83.72; H, 11.16.

Permanganate Oxidation of the Dehydrogenation Ketone.—A solution of the dehydrogenation ketone (1.2 g.) in acetone was treated with potassium permanganate (1.8 g.) and the mixture was heated at 40–50° with stirring for 4 hr. The carboxylic acids were isolated in the usual manner and esterified with methanol, 2,2-dimethoxypropane, and a trace of sulfuric acid. Vapor phase chromatography of the esters using a 5-ft. column of Carbowax 20-M on firebrick at 180° showed a peak at 3.8 min. identified as methyl dihydrocitronellate by comparing the retention time and infrared spectrum of the collected peak with those of an authentic sample.

(+)-Dihydrocitronellal.—A solution of 30.0 g. of citronellal (0.19 mole) in anhydrous ethyl acetate (300 ml.) and 0.5 g. of 10% palladium-on-carbon catalyst was hydrogenated with a Parr low-pressure hydrogenation apparatus. After 3 hr., the absorption of hydrogen ceased and the mixture was filtered. Evaporation of the solvent and fractional distillation yielded 23 g. (77%) of dihydrocitronellal, b.p. 83–88° (12 mm.), n^{25}D 1.4301, [α]^{25}D +7.49° (c 1.868, chloroform); lit.[12] b.p. 81.5–82° (13 mm.), n^{25}D 1.4273, [α]^{12}D +10.80°.

(+)-Dihydrocitronellic Acid.—The procedure of Ruhoff[13] was used to convert 37.0 g. (0.23 mole) of dihydrocitronellal to 29.0 g. (75%) of dihydrocitronellic acid, b.p. 139–145° (10 mm.), n^{25}D 1.4314, d^{25} 0.875, [α]^{25}D +4.25°; lit.[14] b.p. 139–141° (1.5 mm.), d^{17} 0.880, [α]^{25}D +4.2°.

(2R)-2,6-Dimethylheptyl Bromide.—The method of Cristol and Firth[15] was used to convert dihydrocitronellic acid to 2,6-dimethylheptyl bromide. From 49.4 g. (0.288 mole) of dihydrocitronellic acid, there was obtained 16.3 g. (29%) of (2R)-2,6-dimethylheptyl bromide, b.p. 87–90° (11 mm.), [α]^{25}D −1.25° (c 2.38, chloroform); lit.[14] b.p. 82.5° (12 mm.), [α]^{25}D −0.4°.

3-(p-Tolyl)butyryl chloride was prepared by refluxing 5.0 g. (0.028 mole) of 3-(p-tolyl)butyric acid, prepared by the method of Wotiz, Matthews, and Greenfield,[16] with excess thionyl chloride for 3 hr. This method afforded 5.1 g. (95%) of 3-(p-tolyl)-butyryl chloride, b.p. 133–137 (16 mm.), lit.[17] b.p. 125° (9 mm.).

(6R)-2-(p-Tolyl)-6,10-dimethyl-4-undecanone.—The Grignard reagent from (2R)-2,6-dimethylheptyl bromide (5.0 g., 0.024 mole) was prepared in anhydrous ether using 0.80 g. (0.025 g.-atom) of magnesium turnings and a small amount of 1,2-dibromoethane as an entraining agent. This reagent was converted to the corresponding cadmium reagent by the addition of anhydrous cadmium chloride (2.25 g., 0.012 mole) according to the method

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outlined by Cason and Prout.[18] A solution of 3-(p-tolyl)butyryl chloride (3.1 g., 0.015 mole) in benzene (30 ml.) was added dropwise to the cadmium reagent and resulting mixture was refluxed for 5 hr. The usual work-up followed by fractional

distillation gave 1.4 g. (28%) of ketone, b.p. 151–155° (1.1 mm.), n^{25}D 1.4843, $[\alpha]^{25}$D +4.38° (c 1.5860, chloroform).

Anal. Calcd. for $C_{20}H_{32}O$: C, 83.40; H, 11.16. Found: C, 83.45; H, 10.95.

The infrared spectrum, gas chromatogram, and n.m.r. spectrum of this ketone were found to be identical with those of the ketone obtained from dehydrogenation of the unsaturated ether.

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Friedel–Crafts Isomerization. VII.[1a] Aluminum Chloride Catalyzed Isomerization of the t-Butyltoluenes

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The isomerization of o-, m-, and p-t-butyltoluene with water-promoted aluminum chloride in excess of the t-butyltoluenes (heterogeneous system) and in nitromethane solution (homogenous system) was investigated. The isomer distributions were established using gas–liquid chromatography. The equilibrium isomer mixture starting from any of the isomers contains about 64% of the m- and 36% of the p-t-butyltoluene isomer.

Acid-catalyzed isomerization of the isomeric xylenes,[2] ethyltoluenes,[3] and cymenes[4] was investigated in considerable detail. Particularly the work of Allen established rate and equilibrium data of these three compound equilibrations.

The problem of aluminum chloride catalyzed isomerization of t-butyltoluenes was considered by Allen in the case of p-t-butyltoluene.[5]

This work was mainly concerned with the demonstration that intermolecular isomerization of neat p-t-butyltoluene is not possible and that the isomerization in aromatic hydrocarbon solvent (o-xylene), consequently, is entirely a dealkylation–alkylation process. It was concluded by Allen that the process is entirely intermolecular and involves only t-butylation of formed toluene, as p-t-butyltoluene can not be butylated.

Previous investigations have not considered the isomerization of m- and o-t-butyltoluene; neither was the equilibrium composition of the t-butyltoluenes established.

Results and Discussion

The isomerization of o-, m-, and p-t-butyltoluene with water-promoted aluminum chloride (heterogeneous system) and with aluminum chloride in nitromethane (homogeneous system) was investigated at room-temperature (~25°). The isomer distributions were established using gas–liquid chromatography.

Results of the rearrangement of p- and m-t-butyltoluene are presented in Tables I to IV. The equilibrium mixture contains about 63–64% m- and 36–37% p-t-butyltoluene with no *ortho* isomer present. Rearrangements in nitromethane solution are much slower than those of the neat compounds. Neat p-t-butyltoluene, for example, when isomerized with water-promoted aluminum chloride, reached equilibrium in

Table I

Isomerization of p-t-Butyltoluene with Water-Promoted Aluminum Chloride (Heterogeneous)

Time, min.	% meta	% para	% toluene	% 3,5-di-t-butyltoluene
1	14	86	6	5
2	21	79	8	7
4	37	63	12	8
6	44	56	13	9
10	54	46	13	10
15	61	39	15	11
25	60	40	17	12
40	59	41	17	11
60	63	37	18	12
90	62	38	22	15
150	64	36	20	15

about 60 min. (Table I), but over 20 hr. was needed in nitromethane solution (Table III). In the isomerization of the undiluted, neat isomers as well as in nitromethane solution, the main disproportionation products

Table II

Isomerization of m-t-Butyltoluene with Water-Promoted Aluminum Chloride (Heterogeneous)

Time, min.	% meta	% para	% toluene	% 3,5-di-t-butyltoluene
1	88	12	6	7
2	80	20	10	15
4	74	26	11	16
6	70	30	14	20
10	66	34	15	21
15	64	36	16	21
25	64	36	18	18
40	64	36	22	20
60	64	36	25	23
120	64	36	29	22
180	64	36	35	28

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are toluene and di-t-butyltoluenes which are found in very roughly the same molecular amounts. The total of disproportionation products increased with time and at equilibrium amounted to about 30–50 mole % of total aromatic.