75 ml. of ethanol, 0.30 g. of PtO_2 and 20 ml. of $0.1N$ base, hydrogen uptake was complete in 40 min., and upon distillation 43.5 g. (99% yield) of 3,5-dimethyl-2,3-hexanediol was obtained, b.p. 110–113° at 23 mm., n_D^{25} 1.4446.

1-(1'-Hydroxyethyl)cyclohexanol. Hydrogenation of 1-acetylcyclohexanol (42.6 g., 0.3 mole) using 75 ml. of ethanol, 0.30 g. of PtO_2, and 5 drops of $0.1N$ ethanolic NaOH took 30 min. (without base, 2 runs required 3 hr. each). Upon distillation there was obtained 41.7 g. (96% yield) of 1-(1'-hydroxyethyl)cyclohexanol, b.p. 75–85° at 0.8 mm., n_D^{25} 1.4828.

No phenylurethane or α-naphthylurethane could be prepared. However, esterification with 3,5-dinitrobenzoic acid using the method of Brewster[10] gave the monoester in 94% yield, m.p. 122–125° after one recrystallization from ethanol (lit.[4c] m.p. 122.5–123.5°).

2-Phenyl-2,3-butanediol. Hydrogenation of 25.3 g. (0.15 mole) of 3-hydroxy-3-phenyl-2-butanone in 50 ml. of ethanol using 0.20 g. of PtO_2 and 10 drops of $0.1N$ NaOH in ethanol required 1 hr. 40 min. and gave 19.9 g. (78% yield) of 2-phenyl-2,3-butanediol, b.p. 106–113° at 2.0 mm. When no base was used, hydrogenation required 5.5 hr. Because of the possibility of hydrogenolysis a sample was submitted for analysis.

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.90; H, 8.77.

Acknowledgments. The authors express their sincere thanks to Dr. C. O. Herman, Air Reduction Chemical Co., New York, and to Dr. F. E. Cislak, Reilly Tar and Chemical Co., Indianapolis, for generous gifts of acetylenic alcohols. Special thanks are due G. M. Maciak of the Lilly Research Laboratories, Indianapolis, for the analyses reported and to the Eli Lilly Co. for a fellowship award to E. J. W.

NOTRE DAME, IND.

---

[10] J. H. Brewster and C. J. Ciotti, Jr., *J. Am. Chem. Soc.*, **77**, 6214 (1955).

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF NOTRE DAME]

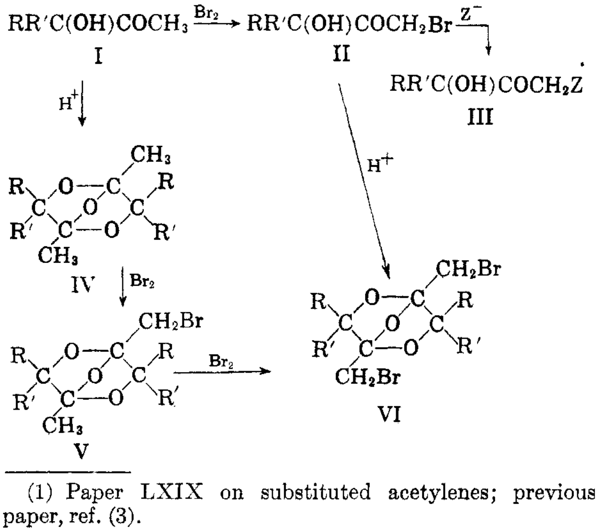
Reactions of α-Ketols Derived from Tertiary Acetylenic Carbinols. II. Bromination and Bimolecular Transannular Dehydration[1]

G. F. HENNION AND E. J. WATSON[2]

Received October 18, 1957

α-Ketols, RR'C(OH)$COCH_3$, derived from tertiary acetylenic carbinols, have been found to be susceptible to a bimolecular condensation reaction in the presence of acid leading to 1,4-dimethyl-3,3,6,6-tetraalkyl-2,5,7-trioxabicyclo[2.2.1]heptanes (IV). This reaction often intervenes seriously in the bromination of the ketones so that most of the bromination product is the corresponding 1,4-bis(bromomethyl)trioxabicycloheptane (VI) rather than the anticipated bromomethyl ketone (II).

Since a variety of α-ketols are readily accessible in high yield from commercially available tertiary acetylenic carbinols,[3] efforts are under way in this laboratory to develop syntheses from the ketols. One obvious approach to this end is provided by bromination followed by various nucleophilic displacement reactions, I → II → III, as shown below (Z = −OH, −OCOR, $-NR_2$, etc.) We wish to report now our experience with the bromination step, I → II.



At the outset of this work interest focused chiefly on dihydroxyacetone-type end products (III, Z = −OH; simple analogs of cortisone) since a significant amount of similar work had been reported by Billimoria and Maclagen,[4] especially in the case of 1-acetylcyclohexanol [I, R and R' = $-(CH_2)_5-$]. The latter compound was found to brominate readily in carbon tetrachloride solution. When the solvent was removed and the residue subjected to hydrolysis under mild conditions (with sodium formate in methanol), a crystalline product, m.p. 101–111°, was recovered. Several crystallizations raised the melting point to 115–118°, indicating immediately that the product was not 1-hydroxyacetylcyclohexanol,[4] m.p. 86–87°, but rather an unidentified dimeric bromination product mentioned by Billimoria.[4] This substance surpris-

---

[1] Paper LXIX on substituted acetylenes; previous paper, ref. (3).

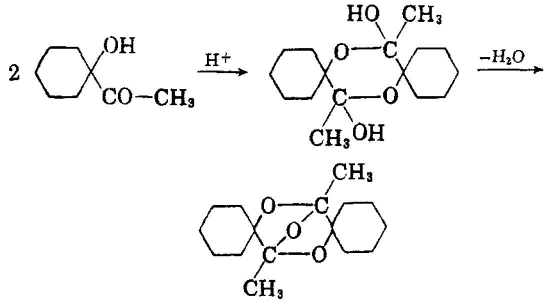
[2] Eli Lilly Co. Fellow, 1954–1956. Abstracted from a portion of the Ph.D. Dissertation of E. J. W.

[3] G. F. Hennion and E. J. Watson, *J. Org. Chem.*, **23**, 656 (1958).

[4] J. D. Billimoria and N. F. Maclagen, *J. Chem. Soc.*, 3067 (1951); 3257 (1954). See also D. Papa, H. F. Ginsberg, and F. J. Villani, *J. Am. Chem. Soc.*, **76**, 4441 (1954) and G. W. Stacy, R. A Mikulec, S. L. Razniak, and L. D. Starr, *J. Am. Chem. Soc.*, **76**, 524 (1954); **79**, 3587 (1957).

ingly showed no carbonyl or hydroxyl absorption in the infrared, contained bromine but was stable to alkaline hydrolysis, did not react with acetic anhydride or with semicarbazide, etc. This evidence, coupled with analysis and molecular weight determination, showed the product to be 1,4-bis-(bromomethyl) - 3,3,6,6 - bis(pentamethylene)-2,5,7-trioxabicyclo[2.2.1]heptane[5] (VI, R and R′ = $-(CH_2)_5$-).

In order to determine whether this product arose *via* II or IV, 1-acetylcyclohexanol in carbon tetrachloride was treated with HBr (also with HCl) and facile conversion to 1,4-dimethyl-3,3,6,6-bis(pentamethylene)-2,5,7-trioxabicyclo[2.2.1]heptane[6] (IV, R and R′ = $-(CH_2)_5$-) was observed. These findings are in accord with the fact that certain α-hydroxyketones spontaneously cyclize to 2,5-dihydroxy-1,4-dioxanes;[7a] subsequent transannular dehydration is, of course, possible[7b] in the instances cited above, for example:



Similar experiments were then carried out with 3-hydroxy-3-methyl-2-butanone (I, R = R′ = CH_3). Treatment with acids under mild conditions gave the known 1,3,3,4,6,6-hexamethyl-2,5,7-trioxabicyclo[2.2.1]heptane[8] (IV, R = R′ = CH_3) while bromination in carbon tetrachloride yielded the corresponding dibromo substitution product (VI, R = R′ = CH_3) previously prepared by Scheibler and Fischer.[9]

Bromination of 3-hydroxy-3-ethyl-2-pentanone (I, R = R′ = C_2H_5) in carbon tetrachloride, however, gave a 45% yield of the bromoketone (II, R R′ = C_2H_5) indicating that the cyclization reactions to IV and/or VI may be subject to steric hindrance by the groups R and R′. Other examples of the action of bromine and of acid on α-ketols are cited in the Experimental section. It will be noted that a monobromo derivative of the trioxabicycloheptane type (V, R = R′ = CH_3) was isolated from two of the experiments.

The influence of solvents on the bromination step (I → II) was examined in a preliminary manner and it was observed that the bromoketones (II) may be obtained, although not in high yield, when the reaction is carried out in acetic acid, in ether or along with dioxane in ether. In two instances cited in the Experimental section the bromoketones were hydrolyzed successfully to known dihydroxyacetone-type end products (III, Z = −OH).

EXPERIMENTAL

The α-ketols used were prepared from acetylenic carbinols as described in the previous paper.[3]

Bromination of 1-acetylcyclohexanol in CCl_4 and attempted hydrolysis. 1-Acetylcyclohexanol (44.0 g., 0.31 mole) and 250 ml. of CCl_4 were placed in a 500-ml. Erlenmeyer flask. Bromine (17 ml., 53 g., 0.33 mole) was added followed by 2 ml. of 48% HBr and 3 ml. of glacial acetic acid. HBr evolution began after 10 min. The flask was then placed in an ice bath. Bromination was complete in another 10 min. The clear, yellow solution was poured into a separatory funnel with an equal volume of ice water. The organic layer was separated and washed with $NaHCO_3$ solution until there was no more effervescence. The neutral reaction mixture was placed in a 1-l. flask with 35 g. (0.51 mole) of sodium formate and 150 ml. of methanol. The mixture was refluxed for 15 hr., then cooled in an ice-salt bath and filtered through a sintered glass funnel. Solvents were removed by distillation until solid began to settle out. The solid isolated was proved to be sodium formate, 3.42 g. The filtrate was placed in the refrigerator and a white solid crystallized slowly. When dry this second white solid weighed 11.2 g., m.p. 95–100°. After one recrystallization from ethanol it weighed 7.0 g., m.p. 101–111°. A second crop weighed 1.31 g., m.p. 99–103°. Three additional recrystallizations of the solid from ethanol raised the m.p. to 115–118°. This substance was identified as 1,4-bis(bromomethyl)-3,3,6,6-bis(pentamethylene)-2,5,7-trioxabicyclo[2.2.1]heptane[5] as explained above.

Anal. Calcd. for $C_{16}H_{24}Br_2O_3$: C, 45.30; H, 5.70; Br, 37.68. Found: C, 45.36; H, 5.75; Br, 37.58.

When the experiment was repeated with the omission of the attempted hydrolysis, 34.6 g. of product (53% yield) was obtained, m.p. 106–111°.

Bromination of 3-hydroxy-3-methyl-2-butanone in CCl_4. Bromine (13 ml., 40 g., 0.25 mole) in 100 ml. of CCl_4 was added in small portions to a solution of 12.8 g. (0.125 mole) of 3-hydroxy-3-methyl-2-butanone in 100 ml. of CCl_4. Bromination was rapid after a 5-min. induction period and the temperature rose to 45°. A small upper layer (water) appeared at the end of the reaction. The mixture was washed with ice water and neutralized with $NaHCO_3$ solution as above. The solvent was removed by distillation first at atmospheric pressure and finally at reduced pressure. The residue was dissolved in ethanol, cooled, and enough water added to cause an oil to separate. The oil was redissolved by heating and the solution cooled slowly yielding 18.1 g. (42% yield) of a white solid, m.p. 54–64°. Recrystallization from 40 ml. of 90% methanol gave 1,4-bis(bromomethyl)-3,3,6,6-tetramethyl-2,5,7-trioxabicyclo[2.2.1]heptane, m.p. 66–68° (lit.[9] m.p. 64–65°).

Anal. Calcd. for $C_{10}H_{16}Br_2O_3$: C, 34.91; H, 4.69; Br, 46.46. Found: C, 35.07; H, 4.87; Br, 46.63.

Bromination of 3-hydroxy-3-methyl-2-pentanone in CCl_4. In a 500-ml. Erlenmeyer flask was placed 58.1 g. (0.5 mole) of 3-hydroxy-3-methyl-2-pentanone in 100 ml. of CCl_4. A solution of 26 ml. (0.5 mole) of bromine in 75 ml. of CCl_4 was then added in small portions. Bromination was rapid at room

---

[5] Alternative name: 8,16-bis(bromomethyl)-8,16-epoxy-7,15-dioxadispiro[5.2.5.2]hexadecane.

[6] Alternative name: 8,16-dimethyl-8,16-epoxy-7,15-dioxadispiro[5.2.5.2]hexadecane.

[7] (a) J. C. Sheehan, R. C. O'Neill, and M. A. White, *J. Am. Chem. Soc.*, **72**, 3376 (1950). (b) I. Elphimoff-Felkin and B. Tchoubar, *Bull. soc. chim. France*, 551 (1952).

[8] G. F. Hennion and J. F. Froning, *J. Am. Chem. Soc.*, **62**, 653 (1940).

[9] H. Scheibler and A. Fischer, *Ber.*, **55**, 2903 (1922). Structures assigned by these authors have since been shown to be incorrect: see ref. (8) and I. N. Nazarov and A. N. Elizarova, *Bull. acad. sci. U.R.S.S., Classe sci. chim.*, 203 (1940); *Chem. Abstr.*, **36**, 744 (1942).

temperature. A cold water bath was used to hold the reaction temperature at about 35°. The reaction mixture was poured into a funnel containing 500 ml. of ice water. The layers were separated and the CCl_4 layer washed with water again, then with $NaHCO_3$ solution and finally with brine. After drying over anhydrous Na_2SO_4, the material was filtered into a flask and the CCl_4 removed by distillation at reduced pressure. A little MgO was added to the distilling flask and the residual liquid distilled to give 52.3 g. of a liquid, b.p. 113–120° at 0.7 mm., n_D^{25} 1.5050 (56% yield of 1,4-bis(bromomethyl)-3,6-dimethyl-3,6-diethyl-2,5,7-trioxabicyclo[2.2.1]heptane). This material was redistilled into six fractions: (*1*) b.p. 89–108° at 0.75 mm., 2.02 g., n_D^{25} 1.5018; (*2*) b.p. 108–112° at 0.75 mm., 2.21 g., n_D^{25} 1.5020; (*3*) b.p. 112° at 0.75 mm. to 114° at 0.35 mm., 4.58 g., n_D^{25} 1.5030; (*4*) b.p. 114–116° at 0.35 mm., 12.05 g., n_D^{25} 1.5049; (*5*) b.p. 116° at 0.35 mm., 12.84 g., n_D^{25} 1.5053; (*6*) b.p. 116–120° at 0.35 mm., 11.97 g., n_D^{25} 1.5058. Material from fractions (*4*), (*5*), and (*6*) was redistilled and a center cut taken for analysis, b.p. 114° at 0.7 mm., n_D^{25} 1.5058.

Anal. Calcd. for $C_{12}H_{20}Br_2O_3$: C, 38.73; H, 5.42; Br, 42.95. Found: C, 38.25; H, 5.35; Br, 44.14.

1-Bromo-3-hydroxy-3-methyl-2-pentanone. A. By bromination in acetic acid. In a one-liter Erlenmeyer flask was placed 85.8 g. (0.738 mole) of 3-hydroxy-3-methyl-2-pentanone in 100 ml. of glacial acetic acid and 25 ml. of water. A solution of 120 g. (0.75 mole) of bromine in 200 ml. of glacial acetic acid and 50 ml. of water was added to the ketol solution. About 2–3 ml. of 48% HBr was added and the reaction mixture heated to 50°. After about 4–5 hr. the reaction mixture was a clear, pale yellow color. The solution was poured into a separatory funnel containing 1 liter of ice water and 500 ml. of ether. The ether layer was separated and washed with 500 ml. of water. The two water layers were combined and extracted with 500 ml. of ether which was then combined with the original ether layer. The combined ethereal extract was treated with water to which solid $NaHCO_3$ was added until there was no more effervescence. The water layer was drained off, the ether layer was washed with brine, and then dried over Na_2SO_4. A little MgO was added as a stabilizer.

The ethereal solution was then filtered into a separatory funnel and gradually added to a heated Claisen flask so that ether could be removed by distillation. A little MgO was added to the residual liquid and it was distilled under reduced pressure into six fractions: (*1*) b.p. 29.5° at 1.5 mm. to 67° at 1.0 mm., 3.14 g., n_D^{25} 1.4490; (*2*) b.p. 67–74° at 0.9 mm., 4.0 g., n_D^{25} 1.4751; (*3*) b.p. 74° at 0.9 mm. to 82° at 0.85 mm., 15.37 g., n_D^{25} 1.4799; (*4*) b.p. 82° at 0.85 mm. to 85.5° at 0.75 mm., 52.6 g., n_D^{25} 1.4838; (*5*) b.p. 85.5–88° at 0.75 mm., 14.85 g., n_D^{25} 1.4885; (*6*) b.p. 88° at 0.75–0.8 mm., 9.42 g., n_D^{25} 1.4952. Combined weight of fractions *3,4,5*, and *6* was 92.2 g., a 64% yield of 1-bromo-3-hydroxy-3-methyl-2-pentanone. Redistillation gave 73.6 g., 45% yield, of material b.p. 73° at 0.55 mm. to 81° at 0.35 mm., n_D^{25} 1.4822 [lit.[10] b.p. 43–45° (oil bath temp.) at 0.005 mm., n_D^{25} 1.4831].

B. *By bromination with dioxane dibromide in ether.* In a 500-ml. flask was placed 50 ml. of dioxane. Bromine (22 ml., 0.43 mole) was added, the mixture cooled in an ice bath, and diluted with 200 ml. of ether. To the slurry thus formed was added a solution of 51.5 g. (0.44 mole) of 3-hydroxy-3-methyl-2-pentanone in 100 ml. of ether. Decolorization took 2–3 min. The mixture was washed and dried as usual and the ether was removed by distillation. The residual liquid was distilled giving: fraction (*1*), b.p. 32° at 3.5 mm. to 74° at 1.5 mm., 10.9 g., n_D^{25} 1.4619; fraction (*2*), b.p. 74° at 1.5 mm. to 84° at 1.3 mm., 37.4 g., n_D^{25} 1.4865. Fraction (*2*) represents a 45% yield of the bromoketol. This portion was redistilled into five fractions: (*1*) b.p. 78° at 2.6 mm. to 79° at 2.5 mm., 1.15 g., n_D^{25} 1.4760; (*2*) b.p. 79–83° at 2.5 mm., 4.40 g., n_D^{25} 1.4808; (*3*) b.p. 83–83.5° at 2.5 mm., 6.25 g., n_D^{25} 1.4820; (*4*) b.p. 83.5–81° at 2.5 mm., 8.14 g., n_D^{25} 1.4826; (*5*) b.p. 81–84° at 2.5 mm., 6.22 g., n_D^{25} 1.4830.

A sample of fraction (*4*) was analyzed.

Anal. Calcd. for $C_6H_{11}BrO_2$: C, 36.94; H, 5.69; Br, 40.97. Found: C, 36.42; H, 5.72; Br, 41.87.

Another experiment, identical with the above except that the bromine was added to a solution of dioxane in ether, gave a 48% yield of the bromoketol.

Bromination of 3-hydroxy-3-ethyl-2-pentanone. A. *In CCl_4.* One-half mole (65.1 g.) of 3-hydroxy-3-ethyl-2-pentanone was brominated in CCl_4 as described above. Distillation *in vacuo* provided three fractions: (*1*) b.p. 30° at 1.8 mm. to 55° at 1.2 mm., 7.4 g., n_D^{25} 1.4295; (*2*) b.p. 55° at 1.2 mm. to 74° at 1.0 mm., 12.4 g., n_D^{25} 1.4600; (*3*) b.p. 74° at 1.0 mm. to 86° at 1.3 mm., 47.7 g., n_D^{25} 1.4827; residue, 16.5 g. Fraction (*3*) represents a 45% yield of 1-bromo-3-hydroxy-3-ethyl-2-pentanone.

B. *In acetic acid.* The experiment was repeated in acetic acid as described above. Two distillations gave 36.5 g. (35% yield), b.p. 76–79° at 1.3 mm., n_D^{25} 1.4782 (lit.[11] b.p. 116–118° at 15 mm., n_D^{17} 1.4788).

Bromination of 3-hydroxy-3-methyl-2-butanone in ether followed by reaction with 10% NaOH. A two-liter, three-neck flask was fitted with a mercury-sealed, motor-driven stirrer, a reflux condenser, and a stopper bearing both an addition funnel and a thermometer. Ether (500 ml.) was added and the flask was cooled in an ice bath. Bromine (80 g., 0.5 mole) was added and stirring started. Then 51.1 g. (0.5 mole) of 3-hydroxy-3-methyl-2-butanone was added and the bromination conducted as above. In the funnel was placed 400 ml. of a 10% NaOH solution. About 180 ml. of this was added, in small portions, rather rapidly, the rate of the addition being determined by the ability of the cooling bath to prevent the ether from refluxing too vigorously. At this point several drops of phenolphthalein solution were added. The addition of NaOH solution was continued, the solution being allowed to discharge the pink color before more alkali was added. The neutral solution required about two days to separate into two distinct layers. The layers were separated, the ethereal layer dried and the ether removed by distillation. The yellowish residual liquid was distilled at reduced pressure to give 18.9 g. of a liquid, b.p. 117–126° at 22 mm., n_D^{25} 1.4655. The reaction was repeated and yielded another 23.03 g., b.p. 80–90° at 3.5 mm., n_D^{25} 1.4632–1.4676. The combined fractions were subjected to two more distillations and the product was finally collected in three fractions: (*1*) b.p. 111° at 15 mm., 11.68 g., n_D^{25} 1.4651; (*2*) b.p. 111–111.5° at 15 mm., 10.02 g., n_D^{25} 1.4649; (*3*) b.p. 111.5–112° at 15 mm., 12.45 g., n_D^{25} 1.4648.

The infrared spectrum and elementary analysis showed the product to be 1-bromomethyl-3,3,4,6,6-pentamethyl-2,5,7-trioxabicyclo[2.2.1]heptane (V, $R = R' = CH_3$).

Anal. Calcd. for $C_{10}H_{17}BrO_3$: C, 45.30; H, 6.46; Br, 30.14. Found: C, 45.81; H, 6.64; Br, 30.24.

This compound was also prepared as follows. In a 500-ml. flask was placed 250 ml. of ether to which was added 40 g. (0.25 mole) of bromine with cooling by an ice bath. After the solution had cooled to below 20°, 46.6 g. (0.25 mole) of 1,3,3,4,6,6-hexamethyl-2,5,7-trioxabicyclo[2.2.1]heptane was added. Decolorization was rapid. After the ethereal solution was washed, the ether was removed by distillation. The residual liquid was distilled into seven fractions: (*1*) b.p. 27° at 4.8 mm., to 37.5° at 3.7 mm., 7.69 g., n_D^{25} 1.4178; (*2*) b.p. 37.5° at 3.7 mm. to 40° at 4.5 mm., 4.11 g., n_D^{25} 1.4178; (*3*) b.p. 40° at 4.5 mm. to 78° at 3.9 mm., 1.64 g., n_D^{25} 1.4183 (total 13.44 g., 29% recovery of starting material); (*4*) b.p. 80–81° at 4.2 mm., 0.72 g., n_D^{25} 1.4572; (*5*) b.p. 81–85° at 4.2 mm., 13.06 g., n_D^{25} 1.4677; (*6*) b.p. 85° at 4.2 mm. to 86° at 4.5 mm., 12.09 g., n_D^{25} 1.4677; (*7*) b.p. 86° at 4.5 mm. to 91° at 4.0 mm., 8.13 g., n_D^{25} 1.4689 (total, fractions *5* to *7*, 33.28 g., 52% yield).

---

(10) G. W. Stacy, R. A. Mikulec, S. L. Razniak, and L. D. Starr, *J. Am. Chem. Soc.*, **79**, 3587 (1957).

(11) J. Colonge and L. Cumet, *Bull. soc. chim. France*, 842 (1947).

Preparation of 1,4-dimethyl-3,3,6,6-bis(pentamethylene)-2,5,7-trioxabicyclo[2.2.1]heptane.[6] A. *From 1-acetylcyclohexanol and HBr.* 1-Acetylcyclohexanol (28.4 g., 0.2 mole) in 100 ml. of CCl_4 was treated with HBr from a tank until the solution was saturated. After standing overnight, the mixture had an insoluble upper layer (water). The CCl_4 solution was washed with water and with $NaHCO_3$ solution until neutral and then dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure leaving a residue of oily solid. Methanol was added to take up the oil and the solid was recovered by filtration. White crystals were thus obtained, m.p. 101–108°. Recrystallization from a methanol-chloroform mixture gave 10.5 g. (40% yield), m.p. 104–109°.

B. *From 1-acetylcyclohexanol and HCl.* The above procedure was repeated on the same scale using HCl gas. The product weighed 17.3 g., m.p. 103.5–110°. An additional 3.1 g. was obtained by concentration of the filtrate and had m.p. 103.5–108.5°. Total weight was 20.4 g., 77% yield.

C. *From 1-acetylcyclohexanol and toluenesulfonic acid.* A mixture of 71.1 g. (0.5 mole) of 1-acetylcyclohexanol, 250 ml. of petroleum ether (Skellysolve F), and 2 g. of *p*-toluenesulfonic acid in a 500-ml. flask provided with a Dean-Stark trap and reflux condenser was subjected to heating for removal of water by azeotropic distillation in the usual way. After two days, 3.8 ml. of water had been removed (theory, 4.5 ml.). The solution was cooled, filtered through a 2.5 cm. layer of anhydrous K_2CO_3, and the petroleum ether was removed by distillation. A tan colored solid resulted, weight 64.5 g. (97% yield) which was recrystallized from methanol-chloroform to give a white, crystalline material, m.p. 105–109°.

Anal. Calcd. for $C_{16}H_{26}O_3$: C, 72.14; H, 9.84. Found: C, 72.25; H, 10.05.

Preparation of 1,3,3,4,6,6-hexamethyl-2,5,7-trioxabicyclo[2.2.1]heptane. A. *From 3-hydroxy-3-methyl-2-butanone and HCl.* A solution of 104.4 g. (1.02 moles) of 3-hydroxy-3-methyl-2-butanone in 200 ml. of CCl_4 was saturated with HCl gas. The reaction mixture soon became cloudy and a small upper layer of water subsequently appeared. The reaction mixture was neutralized with anhydrous K_2CO_3, enough being used to absorb the water. The mixture was filtered and the filtrate was dropped into a heated 200-ml. flask from a separatory funnel, the solvent being removed by distillation. The residual liquid was distilled at reduced pressure to give fraction (*1*), b.p. 53° at 29 mm. to 62° at 22 mm., 36.3 g., n_D^{25} 1.4158 and fraction (*2*), b.p. 62–64° at 22 mm., 31.7 g., n_D^{25} 1.4166. Fraction (2) represents a 33% yield of product.

B. *From 3-hydroxy-3-methyl-2-butanone and toluenesulfonic acid.* A mixture of 51.1 g. (0.5 mole) of 3-hydroxy-3-methyl-2-butanone, 200 ml. of petroleum ether (Skellysolve F), and 2 g. of *p*-toluenesulfonic acid was subjected to azeotropic distillation using a Dean-Stark trap as described above. After 24 hr., 4.0 ml. of water had been collected (theory, 4.5 ml.). After neutralization, filtration, and removal of solvent, the residue was distilled *in vacuo*, yielding 38 g. of product (82% yield), b.p. 60–66° at 22 mm., n_D^{25} 1.4168 (lit.[8] b.p. 81–82° at 50 mm., n_D^{20} 1.4199).

1,3,4,6-Tetramethyl-3,6-diethyl-2,5,7-trioxabicyclo[2.2.1]heptane. 3-Hydroxy-3-methyl-2-pentanone (58.1 g., 0.5 mole) was subjected to the azeotropic dehydration as described above. After 3 days, 2.8 ml. of water was collected (theory, 4.5 ml.). Distillation gave 13.0 g. (22.4%) of recovered ketol, b.p. 30–90° at 24 mm., n_D^{25} 1.4230 and 36.7 g. (68.5% yield) of product, b.p. 90–100° at 24 mm., n_D^{25} 1.4311. Redistillation gave material with b.p. 94.5–95° at 22 mm., n_D^{25} 1.4316.

Anal. Calcd. for $C_{12}H_{22}O_3$: C, 67.25; H, 10.35. Found: C, 67.44; H, 10.48.

1,3,4,6-Tetramethyl-3,6-diisobutyl-2,5,7-trioxabicyclo[2.2.1]heptane. 3-Hydroxy-3,5-dimethyl-2-hexanone (72.1 g., 0.5 mole) was subjected to the azeotropic dehydration as described above. After 3 days, the reaction mixture yielded 12.3 g. of recovered ketol, b.p. 74–120° at 14 mm., n_D^{25} 1.4259 and 41.8 g. (62% yield) of product, b.p. 120–126° at 14 mm., n_D^{25} 1.4388. Redistillation gave material with b.p. 131° at 21 mm., n_D^{25} 1.4390.

Treatment of the same ketol with HCl gave only a 23% of product with 56% recovered ketol.

Anal. Calcd. for $C_{16}H_{30}O_2$: C, 71.06; H, 11.18. Found: C, 71.49; H, 11.15.

Attempted reaction of 3-hydroxy-3-ethyl-2-pentanone with toluenesulfonic acid. When 3-hydroxy-3-ethyl-2-pentanone (65.1 g., 0.5 mole) was subjected to the azeotropic dehydration for one week, only the starting material was recovered, 56.2 g. (86%) b.p. 62–65° at 21 mm., n_D^{25} 1.4230.

Bromination of 1-acetylcyclohexanol in ether followed by reaction with 10% NaOH. 1-Acetylcyclohexanol (71.1 g., 0.5 mole) was treated with bromine in ether and then, without isolation of product, with 10% NaOH as described above. When the ether was removed by distillation, 1-hydroxyacetylcyclohexanol crystallized and was collected in the following fractions: (*1*) 15.1 g., m.p. 87–88.5°; (*2*) 4.9 g., m.p. 80–87°; (*3*) 11.3 g., m.p. 83–84°; (*4*) 2.6 g., m.p. 82–84°. Total weight was 33.9 g. (43% yield). The first three fractions were combined and recrystallized from ether to give 21.6 g., m.p. 88–89° (lit.[4] m.p. 86–87°).

1,3-Dihydroxy-3-methyl-2-pentanone. In a 500-ml. flask was placed 30.1 g. (0.47 mole) of KOH (C.P. analyzed, 87.9% KOH) and 150 ml. of absolute methanol. The solution was cooled and 37.7 g. (0.51 mole) of purified ethyl formate was added. The mixture was refluxed for 2 hr. At the end of this time, 73.5 g. (0.377 mole) of 1-bromo-3-hydroxy-3-methyl-2-pentanone was added. The reaction mixture was boiled under reflux for 17 hrs., cooled in an ice-salt bath and filtered through a Büchner funnel. When the solvent was removed by distillation some crystalline material was present. The oil was taken up in $CHCl_3$ and the solid filtered off. The $CHCl_3$ was removed and the residual liquid was distilled *in vacuo* into seven fractions: (*1*) b.p. 39° at 2.6 mm. to 81° at 2.0 mm., 0.80 g., n_D^{25} 1.4420; (*2*) b.p. 81° at 2.0 mm. to 82° at 1.75 mm., 3.29 g., n_D^{25} 1.4489; (*3*) b.p. 82° at 1.75 mm. to 82° at 1.5 mm., 6.39 g., n_D^{25} 1.4497; (*4*) b.p. 82° at 1.5 mm. to 84° at 1.4 mm., 10.46 g., n_D^{25} 1.4508; (*5*) b.p. 84–83.5° at 1.4 mm., 8.50 g., n_D^{25} 1.4520; (*6*) b.p. 82° at 2.6 mm. to 100° at 2.7 mm., 5.01 g., n_D^{25} 1.4541; (*7*) b.p. 100° at 2.7 mm. to 102° at 3.0 mm., 1.09 g., n_D^{25} 1.4754. Weight of fractions (*2*) through (*6*) is 33.65 g. (68% yield). When this material was redistilled there was obtained 26.36 g. (53%) of liquid b.p. 96° at 0.7 mm., n_D^{25} 1.4528–1.4531 (lit.[10] b.p. 25° (bath temp.) at 0.005 mm., 51–58° at 0.1–0.25 mm., n_D^{25} 1.4537).

Acknowledgments. The authors express their sincere thanks to G. M. Maciak, W. L. Brown, H. L. Hunter, and Miss G. Beckmann of the Lilly Research Laboratories, Indianapolis, for the analyses reported and to the Eli Lilly Co. for a fellowship award to E. J. W.

NOTRE DAME, IND.