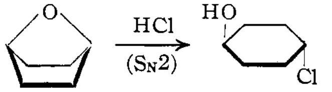
of these isomers has not been accomplished, but the phenylurethans of both forms have been described (m.p. 133–134°[1] and 99°[2]), the higher-melting derivative being regarded as the *trans*-compound. Attempts to prepare a stereochemically pure form of 4-chlorocyclohexanol by treatment of the pure *cis* or *trans* forms of the diol with hydrochloric acid have also led to mixtures from which neither isomer has been isolated in a pure condition.[2]

In view of the inversion which is generally observed to accompany the nucleophilic displacement reactions of epoxides,[3] it would be expected that the action of hydrogen chloride on the *cis*-ether, 1,4-epoxycyclohexane, should lead exclusively to *trans*-4-chlorocyclohexanol. When the addition of hydrogen chloride to this epoxide was carried out under conditions similar to those described for the preparation of tetramethylene chlorohydrin from tetrahydrofuran,[4] a waxy crystalline solid was obtained which melted at 82–83° after several recrystallizations from cyclohexane. This product gives a phenylurethan which melts at 132–133° and which is presumably identical with the phenylurethan of *trans*-4-chlorocyclohexanol described by Owen and Robins.[1] The α-naphthylurethan was also prepared to further characterize the compound.



Experimental[5]

1,4-Epoxycyclohexane.[6]—A mixture of 200 g. of hydroquinone and 200 ml. of methanol was hydrogenated over 20 g. of Raney nickel at 150° and 120 atmospheres until no more hydrogen was absorbed. Two hundred grams of freshly roasted activated alumina was added to the crude mixture of *cis*- and *trans*-1,4-cyclohexanediol which remained after evaporation of the methanol, and the mixture was heated at 240° under a 30-cm. Vigreux column for 5 hours. The distillate (b.p. 120–133°) thus obtained consisted of two layers which were separated and the lower aqueous layer was extracted several times with ether. The combined oil layer and ether extracts were dried over anhydrous magnesium sulfate and distilled through a 60-cm. Fenske column to give as the main fraction 87.0 g. (49% over-all yield) of the epoxide, b.p. 117–118° (uncor.).

***trans*-4-Chlorocyclohexanol.**—The epoxide (45.7 g.) was heated to the boiling point in a three-necked flask fitted with a reflux condenser, a thermometer dipping into the liquid, and a capillary tube through which a slow stream of gaseous hydrogen chloride was admitted near the bottom of the flask. The temperature rose gradually to *ca.* 150° over a period of 2 hours, after which the reaction was discontinued. On cooling, the contents of the flask crystallized to a greasy solid, which was taken up in hot benzene and recrystallized by the addition of petroleum ether; yield 42.8 g. (68%) of waxy crystals melting at 68–72°. After several recrystallizations from cyclohexane, the pure product was obtained in the form of colorless leaflets, m.p. 82–83°; b.p. 105° at 14 mm., 99° at 10 mm.

Anal. Calcd. for $C_6H_{11}ClO$: C, 53.54; H, 8.24. Found: C, 53.27; H, 8.14.

The **phenylurethan**, prepared in the usual way by heating the alcohol with phenyl isocyanate, melted at 132–133° after recrystallization from cyclohexane (lit.,[1] 133–134°).

The **α-naphthylurethan** was prepared by heating the alcohol with an equal weight of α-naphthyl isocyanate for 5 minutes and recrystallizing the solid product several times from cyclohexane. The pure derivative was obtained in the form of colorless needles melting at 157–158°.

Anal. Calcd. for $C_{17}H_{18}ClNO_2$: C, 67.18; H, 5.97. Found: C, 67.45; H, 5.85.

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RECEIVED JUNE 20, 1951

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[3] S. Winstein and R. B. Henderson, "Heterocyclic Compounds," edited by R. C. Elderfield, vol. I, John Wiley and Sons, Inc., New York, N. Y., 1950, p. 29.

[4] D. Starr and R. M. Hixon, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N Y., 1943, p. 571.

[5] Microanalyses were performed by the Clark Microanalytical Laboratory, Urbana, Illinois.

[6] *Cf.* R. C. Olberg, H. Pines and V. N. Ipatieff, THIS JOURNAL, **66**, 1096 (1944).

Preparation of an Intermediate for Synthesis of Lysine: ε-Bromocaproic Acid[1]

BY SIDNEY W. FOX, ERNEST H. POLAK, MILON W. BULLOCK AND YUTAKA KOBAYASHI

Successful conversion of cyclopentanone to δ-bromopentanoic acid[2] through an oxidation step with hydrogen peroxide has led to interest in the corresponding conversion of cyclohexanone to ε-bromocaproic acid in this Laboratory and in that of Heine and Jones.[3] In the present project, the ultimate goal has been the synthesis of lysine.

Experiences with this oxidation confirm the easy explosions recorded by Heine and Jones. The explosion problem has been overcome here by destroying the peroxides in the acidified aqueous solution of the lactone by addition of sufficient sodium sulfite to obtain a negative starch–iodide test, or by destroying the diethyl peroxides in the ether extracts by drying the ether solution over a mixture of sodium sulfate and sodium sulfite. As presented in the Experimental, the yields of bromoacid have been superior to those earlier recorded.

Attempts to isolate the lactone by distillation have been unfruitful. The product obtained was a mixture which distilled over a large range, and left a large residue. Apparently the lactone is polymeric and not readily purified by distillation. Oxidation of cyclohexanone with Caro's acid also has been shown to yield a product that cannot be purified by distillation,[4,5] although dehydration of ε-hydroxycaproic acid obtained in the production of hexamethylene glycol has given a distillable lactone.[6]

The ε-bromocaproic acid, directly prepared from the crude oxidation product, was converted to the α,ε-dibromocaproic acid by classical α-bromination as described by Merchant, Wickert and Marvel.[7] Although satisfactory aminations of α,ε-dibromo acid have not been carried out in these laboratories, conditions for this conversion have been reported.[8,9]

Experimental

ε-Bromocaproic Acid.—To 440 ml. of 20% sodium hydroxide solution in a three-liter flask equipped with an effi-

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[1] Journal Paper No. J-1941 of the Iowa Agricultural Experiment Station, Ames, Project 1110, Preparation of Chemicals for Agricultural Utility. This work was also supported by the Industrial Science Research Institute of Iowa State College.

[2] M. Fling, F. N. Minard and S. W. Fox, THIS JOURNAL, **69**, 2466 (1947).

[3] H. W. Heine and H. Jones, *ibid.*, **73**, 1361 (1951).

[4] R. Robinson and L. H. Smith, *J. Chem. Soc.*, 371 (1937).

[5] R. P. Linstead and H. N. Rydon, *ibid.*, 1995 (1934).

[6] F. J. Van Natta, J. W. Hill and W. H. Carothers, THIS JOURNAL, **56**, 455 (1934).

[7] R. Merchant, J. N. Wickert and C. S. Marvel, *ibid.*, **49**, 1828 (1927).

[8] D. C. Sayles and E. F. Degering, *ibid.*, **71**, 3161 (1949).

[9] E. F. Degering and L. G. Boatright, *ibid.*, **72**, 5137 (1950).

cient stirrer, thermometer and two dropping funnels, were added simultaneously 200 g. of cyclohexanone (Matheson) and 630 ml. of 30% hydrogen peroxide. The temperature of the reaction mixture was maintained at 50 ± 5° with the aid of a cold water-bath during the 70 min. required for the addition. The solution was extracted with two 150-ml. portions of ether to remove any unreacted cyclohexanone. The aqueous solution was acidified to congo red with concd. hydrochloric acid[10] and extracted with one 250-ml. and three 150-ml. portions of ether. The combined ether extracts were dried over sodium sulfate containing some sodium sulfite to remove diethyl peroxide from the ether.[11] Distillation of the ether on the steam-bath left 192 g. of crude ε-hydroxycaproic acid and its lactone which solidified on cooling.

To 218 g. of the crude acid and lactone, prepared as above, was added a cooled solution of 240 ml. of concentrated sulfuric acid in 1 l. of 48% hydrobromic acid. Much heat was evolved when the first portions of the acid solution were added to the mixture. The solution was left standing at room temperature two hours and then warmed on the steam-bath four hours. The solution was diluted with three liters of water, approximately 200 g. of ammonium sulfate was added and the ε-bromocaproic acid was extracted with 400 ml. and 200 ml. of ether. The combined ether extracts were dried over a mixture of sodium sulfate and sodium sulfite and distilled. Attempts to fractionate the residue through a 13-plate column at 10 mm. resulted in decomposition through the loss of hydrogen bromide; however, the product was readily distillable through a short Vigreux column at a lower pressure. The yield of product, b.p. 128–130° at 0.2 mm., was 113 g. (28% of the cyclohexanone).

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[10] When the acid and lactone were distilled, the peroxides were destroyed at this point by adding sodium sulfite to the hot acid solution until a negative starch–iodide test was obtained.

[11] The presence of diethyl peroxide in the ether is conveniently detected by a starch–iodide test. In one run in which no attempt was made to remove the peroxides a violent explosion occurred when the last traces of solvent were being distilled.

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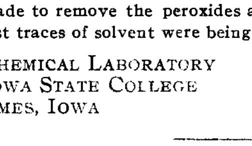
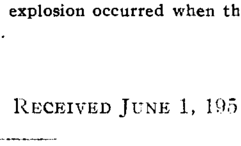
A Claisen Rearrangement of an Allyloxybenzophenone

BY REYNOLD C. FUSON AND FRANKLIN E. MUMFORD

The Claisen rearrangement of suitably constituted aromatic ethers appears to offer an attractive route to certain types of closely packed molecules, since the allyl group migrates by an intramolecular reaction.[1] In the triarylcarbinol series, for example, the rearrangement of the allyl group in 2,4-dimethyl-5-allyloxyphenylmesitylphenylcarbinol (I, R = mesityl) would yield a product (II, R = mesityl) in which two of the rings have the ortho positions occupied. Such a degree of crowding has not been achieved by addition of aryl organometallic compounds to substituted benzophenones.[2]

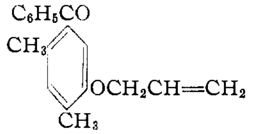


I

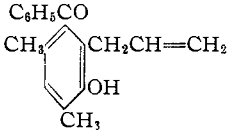


II

An approach to the synthesis of carbinols of type I has been made by way of the allyl ether (III) of 2,4-dimethyl-5-hydroxybenzophenone. The corresponding methyl ether had been prepared by benzoylation of 2,4-dimethylanisole in the presence of aluminum chloride.[3] By treatment with hydriodic acid the methyl ether was converted to the corresponding hydroxy ketone, which was allylated with allyl bromide in the presence of potassium carbonate. It is of interest that the keto ether (III) rearranged readily and in good yield to the allyl phenol (IV), for this confirms the surprising finding of Meisenheimer, Hanssen and Wächterowitz,[3] that the benzoyl group introduced into 2,4-dimethylanisole by the method of Friedel and Crafts is situated in a position meta to the methoxyl group. The rearrangement is unusual in that the aromatic nucleus involved bears a meta-directing group in a position meta to the allyloxyl group.[4]



III



IV

Condensation of the allyloxy ketone (III) with *o*-tolyl- and mesityllithium converted it to carbinols of type I in which R is, respectively, *o*-tolyl and mesityl. It was found, however, that the mesityl carbinol did not rearrange when heated at 200° for one hour. More drastic treatment converted it to resinous materials. It may be that the rearrangement fails because of steric factors, although models of the allylphenol (II, R = mesityl) indicate that it is capable of existence. Moreover, failure was met also with the carbinol in which R is *o*-tolyl, a molecule in which the space exigency is not great.

Experimental[5]

2,4-Dimethyl-5-allyloxybenzophenone (III).—This allyl ether was prepared by the method of Claisen and Eisleb.[6] A mixture of 6.79 g. of 2,4-dimethyl-5-hydroxybenzophenone, 4.36 g. of allyl bromide and 4.0 g. of potassium carbonate in 40 ml. of methyl ethyl ketone was heated under reflux for 12 hours. At the end of this period 100 ml. of water was added to dissolve the potassium bromide and excess potassium carbonate. The organic layer was removed, and the aqueous layer extracted exhaustively with ether. The extracts and organic layer were combined and washed successively with four 25-ml. portions of 10% potassium hydroxide solution and three 25-ml. portions of water. The ether boiled at 150–151° (0.07 mm.); n^{20}_D 1.5858. The yield of the light yellow liquid was 6.44 g. (80%).

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.09; H, 6.80.

2,4-Dimethyl-5-hydroxy-6-allylbenzophenone (IV).—The allyl ether (III) (1.06 g.) was heated at 220° for 90 minutes in an atmosphere of carbon dioxide. The brown reaction mass, when recrystallized from high-boiling petroleum ether, gave 0.89 g. (84%) of crude product; m.p. 120–128°. After two recrystallizations from a mixture of benzene and high-boiling petroleum ether, colorless crystals of the hydroxy ketone (IV) were obtained; m.p. 126–127°.

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.03; H, 6.92.

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(1) C. D. Hurd and M. A. Pollack, *J. Org. Chem.*, **3**, 550 (1939).

(2) (a) E. P. Kohler and L. W. Blanchard, Jr., THIS JOURNAL, **57**, 367 (1935); (b) R. C. Fuson, G. P. Speranza and R. Gaertner, *J. Org. Chem.*, **15**, 1155 (1950).

(3) J. Meisenheimer, R. Hanssen and A. Wächterowitz, *J. prakt. Chem.*, **119**, 315 (1928).

(4) See E. T. McBee and E. Rapkin, THIS JOURNAL, **73**, 2375 (1951).

(5) Infrared absorption data and interpretations by Miss Elizabeth Petersen.

(6) L. Claisen and C. Eisleb, *Ann.*, **401**, 21 (1913).