

When a methoxyl group is present in the 6'-position the predominant product is a benzalcoumarone.

2. A mechanism is suggested to account for

these results, and an analogy is drawn between this reaction and the ring closure of 2'-hydroxychalcone dibromides with alkali.

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The Action of Alkali on Cyclohexanones

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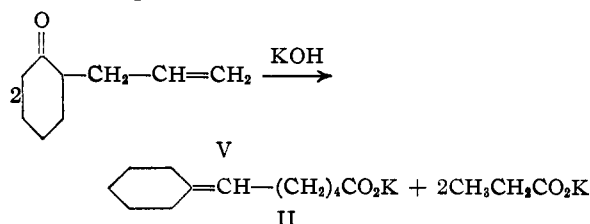
The cleavage of certain ketones by alkali with the formation of acids is well known for aromatic,¹ aralkyl,² and activated ketones such as β -keto acids. Relatively little work has been done with simple aliphatic ketones. This paper reports the results of an investigation of the nature of the products formed when cyclohexanone and one of its 2-substituted derivatives are treated with molten alkali. Other workers have shown that acids of unknown structure along with large amounts of neutral condensation products resulted when cyclohexanone was heated with potassium hydroxide at 180–190° for twenty-four hours.³

Three distinct types of reactions between cyclohexanone and potassium hydroxide have now been found, depending on the temperature used. The results can best be explained on the basis of the series of changes involving (1) formation of cyclohexylidenecyclohexanone (I), (2) cleavage of the ketone ring to a cyclohexylidenecaproic acid (II) and (3) migration of the double bond and degradation of the intermediate α,β -unsaturated acid to cyclohexanebutyric acid (IV). These transformations are shown in the accompanying equations and are discussed below.

At temperatures up to 220° the addition of cyclohexanone to molten potassium hydroxide resulted in the formation of a white crystalline solid which yielded only neutral products when treated with water. In the temperature range 250–280° a similar white precipitate formed momentarily but was very rapidly converted by an exothermic

in the acid from II was not established but no doubt exists concerning the carbon skeleton since this product yielded cyclohexanecaproic acid when hydrogenated. Prolonged treatment of II with molten alkali resulted eventually in a saturated 10-carbon acid identified as cyclohexanebutyric acid (IV). This transformation may involve the migration of the double bond of II into the α,β -position (III) followed by a retrograde aldol reaction to give cyclohexanebutyraldehyde which in turn would be converted by the alkali to IV. Support for the mechanism as pictured above is found in the fact that cyclohexylidenecyclohexanone yielded II when heated with molten potassium hydroxide.

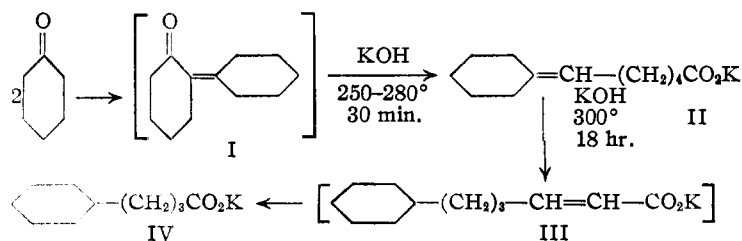
In the case of 2-allylcyclohexanone (V) an unusual cleavage took place with the formation of the potassium salts of propionic acid and the acid II, derived from cyclohexanone, in accordance with the equation



The fact that propionic acid, and not acrylic acid, was isolated indicates that this change may involve the migration of the double bond in the allyl side chain into conjugation with the carbonyl group and hydrolytic removal of this residue with the formation first of propionaldehyde and then of propionic acid.

Experimental⁴

Action of Potassium Hydroxide on Cyclohexanone (280°—thirty minutes).—Two hundred twenty-five (225) grams of solid potassium hydroxide was fused in a heavy-walled glass tube in an atmosphere of nitrogen. To this was added, with vigorous agitation, 43.6 g. of cyclohexanone over a period of thirty minutes while the temperature was maintained between 260 and 280°. The mixture was cooled and dissolved in water to form a clear solution with



reaction to a yellow oil (II). When cooled, this yellow oil solidified and, after solution in water and acidification, a 12-carbon unsaturated acid was obtained. The position of the double bond

(1) Bachmann, *THIS JOURNAL*, **57**, 737 (1935).

(2) Lock and Bock, *Ber.*, **70B**, 916 (1937).

(3) Wallach and Behnke, *Ann.*, **369**, 99 (1909).

(4) We are indebted to Dr. J. W. Stillman of these laboratories, under whose supervision the microanalyses reported here were carried out.

no evidence of any alkali-insoluble material. After acidification with concentrated hydrochloric acid and cooling, the solution was extracted with two portions of diethyl ether. The ether extract was then dried over anhydrous sodium sulfate, filtered, and the ether removed by distillation. The resulting residue, on distillation, yielded 14.7 g. of an acid (corresponding to II) boiling at 145–153° (2–3 mm.), n_D^{20} 1.4385.

Anal. Calcd. for $C_{12}H_{20}O_2$: neut. equiv., 196. Found: neut. equiv., 205.3.

This acid was found to be soluble in aqueous sodium bicarbonate, giving a solution which reduced potassium permanganate. It rapidly absorbed bromine with the evolution of hydrogen bromide and the formation of an oily derivative.

The ethyl ester prepared from this unsaturated 12-carbon acid had the properties: b. p. 131° (5 mm.); n_D^{25} 1.4642; d_4^{25} 0.9365.

Anal. Calcd. for $C_{14}H_{24}O_2$: C, 74.96; H, 10.78; sap. equiv., 224.3; *MR*, 65.87 (from atomic refractivity constants given in Lange, "Handbook of Chemistry," 3rd Edition, 1939, p. 855). Found: C, 75.22, 75.59; H, 10.52, 10.97; sap. equiv., 223.9; *MR*, 66.12 (R. Lorentz and H. Lorenz formula).

Hydrogenation of the acid in the presence of Raney nickel catalyst at 125° and 120 atm. hydrogen pressure for three hours yielded cyclohexanecaproic acid, from which was obtained a solid *p*-bromophenacyl ester identical with the *p*-bromophenacyl ester of an authentic sample of cyclohexanecaproic acid.⁵

Action of Potassium Hydroxide on Cyclohexanone (300°—eighteen hours).—A stainless steel bomb was charged with 125 g. of cyclohexanone and 250 g. of potassium hydroxide, the air was flushed out with nitrogen, and the mixture heated with agitation at 300° for eighteen hours. At the end of this time, the mixture was cooled and the grayish solid which separated was removed and discarded. The remaining oily product was extracted with water and the aqueous extract acidified with hydrochloric acid to yield an oily, water-insoluble acid. This acid on distillation gave a fraction amounting to 25 g. boiling at 160–180° (10 mm.). Redistillation of this product yielded cyclohexanebutyric acid boiling at 136–139° (4 mm.), m. p. 26.5–28.5°.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.55; H, 10.65;

(5) Supplied through the courtesy of the Dow Chemical Company. See also Hiers and Adams, *THIS JOURNAL*, **48**, 2385 (1926).

neut. equiv., 170.2. Found: C, 70.52; H, 10.34; neut. equiv., 178.5.

The *p*-bromophenacyl ester of this acid was found to melt at 76–77° and showed no depression in melting point when mixed with a sample of the *p*-bromophenacyl ester of an authentic sample of cyclohexanebutyric acid.

2-Allylcyclohexanone.—This was prepared by the method of Cornubert⁶ using allyl chloride instead of allyl iodide, b. p. 80–87° (13–15 mm.), n_D^{20} 1.4662 to 1.4669.^{6,7}

Action of Potassium Hydroxide on 2-Allylcyclohexanone.—In an atmosphere of nitrogen 20 g. of 2-allylcyclohexanone was added with stirring to 75 g. of potassium hydroxide at 240–250°. After twenty minutes the mixture was cooled, and the upper layer of yellowish solid was separated mechanically from the lower layer of potassium hydroxide and dissolved in water. Neutral products were removed from the aqueous layer by extraction with ether, and the aqueous layer was then acidified with the formation of a yellow oil. After separation and drying of the oil, it yielded, upon distillation, two fractions, the first (2 g.), boiling at 33–34° (5 mm.), and the second (4 g.) boiling at 157–170° (5 mm.).

The first fraction was demonstrated to be propionic acid: neut. equiv. Calcd. for $C_3H_6O_2$: 74.1. Found: 75.5, 75.6.

The *p*-bromophenacyl ester, m. p. 57.5–59°, showed no depression in melting point when mixed with the ester of an authentic specimen of propionic acid. The *p*-bromophenacyl ester of acrylic acid melted at 67.5–68° and mixtures of this ester with that of the ester in question melted at 53.5–56.5°.

The second, high-boiling fraction was shown to yield cyclohexanecaproic acid when hydrogenated.

Summary

1. Treatment of cyclohexanone with molten potassium hydroxide at 250–280° yields a 12-carbon unsaturated acid, and at 300° cyclohexanebutyric acid.

2. 2-Allylcyclohexanone is converted by molten potassium hydroxide at 250° to the same 12-carbon unsaturated acid; the allyl side chain appears as propionic acid.

(6) Cornubert and Maurel, *Bull. soc. chim.*, **49**, 1498 (1931).

(7) Cope, Hoyle and Heyl, *THIS JOURNAL*, **63**, 1843 (1941).

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p-Toluenesulfonates of 20-Hydroxypregnanes

BY LEWIS HASTINGS SARETT

The conversion of pregnane-3(α),20-diol 3-acetate 20-tosylate to Δ^{17} -pregnene-3(α)-ol by treatment with pyridine has been described.¹ The present work reports some additional applications of this useful procedure for the preparation of substituted ethylenes from secondary alcohols.²

Pregnane-3(α),12(α),20-triol 3,12-diacetate³ (I), was prepared by catalytic reduction of pregnane-

(1) Hirschmann, *J. Biol. Chem.*, **140**, 797 (1941).

(2) See, for example, *inter alia*, Ferns and Lapworth, *J. Chem. Soc.*, **101**, 273 (1912); Barnett and Reichstein, *Helv. Chim. Acta*, **21**, 426 (1938); v. Euw and Reichstein, *Helv. Chim. Acta*, **29**, 654 (1946).

(3) The configuration of the C-12 hydroxyl group in desoxycholic acid is taken as α , in accordance with the proofs of Gallagher and Long, *J. Biol. Chem.*, **162**, 495 (1946), and of Sorkin and Reichstein, *Helv. Chim. Acta*, **29**, 1218 (1946).

3(α),12(α)-diol-20-one diacetate.⁴ With *p*-toluenesulfonyl chloride I yielded a diacetate tosylate, which on refluxing with collidine gave a crystalline mixture of Δ^{17} - and Δ^{20} -pregnene-3(α),12(α)-diol diacetate (IIa and IIb). From the mixture obtained by hydroxylation of II, a readily crystalline 3(α),12(α),17,20-tetrol (III) could be separated. Periodate cleavage then yielded *etio*-cholane-3(α),12(α)-diol-17-one, isolated as the diacetate (IV).⁵ Oxidation of the amorphous glycol mixture which remained gave some *etio*-desoxycholic acid (V).

(4) Hoehn and Mason, *THIS JOURNAL*, **60**, 1493 (1938).

(5) We are indebted to Dr. L. F. Fieser of Harvard University for an authentic sample of this compound for comparison.