twice from dilute hydrochloric acid, to give clusters of fine soft fibrous needles, melting sharply at 225–226° with slight previous sintering. Analysis showed conclusively that the hydrochloride is derived from a halogen-free amine.

Anal. Calcd. for $C_{19}H_{23}O_4N \cdot HCl$: C, 62.36; H, 6.33; N, 3.86; Cl, 9.69. Found: C, 62.17; H, 6.65; N, 3.98; Cl, 9.90.

The picrate recrystallized from ethanol in light yellow silky needles, m. p. 172–173°.

Anal. Calcd. for $C_{25}H_{26}O_{11}N_4$: N, 10.03. Found: N, 9.96.

N-Acetyl Derivative (VII).—To a solution of the above hydrochloride (95 mg.) in 4 cc. of dry pyridine, 5 drops of acetyl chloride was added cautiously with continuous swirling of the flask. The mixture was warmed gently until most of the precipitated pyridine hydrochloride had dissolved. After standing at room temperature for ten hours, it was evaporated in a stream of air, and the gummy residue, when rubbed with water, crystallized giving 74 mg. of the acetyl derivative, m. p. 178–179°, raised to 179.5° after two recrystallizations from aqueous methanol.

Anal. Calcd. for $C_{21}H_{25}O_5N$: C, 67.89; H, 6.78; N, 3.77. Found: C, 67.86; H, 6.83; N, 3.82.

The ultraviolet absorption spectrum was quite different from that of N-acetylcolchinol methyl ether, as shown in Fig. 1.

4-(4-Methoxyphenyl)-5,6,7-trimethoxyhydrindone-1 (V) by Cyclization of II.—β-2-(4,5,6,4′-Tetramethoxy)-biphenylpropionic acid (II, 1.10 g.) was cyclized by essentially the procedure described above, to yield 650 mg. (62%) of the crude ketone V, m. p. 85°; recrystallization from methanol gave glistening needles of m. p. 89°, which is the reported value.[2]

The *oxime* was obtained in 81% yield, melting at 215°; the reported value[2] is 217°.

1-Amino-4-(4-methoxyphenyl)-5,6,7-trimethoxyhydrindone (VI).—Reduction of the above oxime with hydrogen and Raney nickel by the procedure used on the bromo ketone oxime, gave 80% of the expected amine. There was no depression on mixed melting point of the hydrochlorides, picrates and acetyl derivatives of the amine derived from the oximes of the bromo ketone VIII and the bromine-free ketone V.

Diethyl 3,4,5-Trimethoxybenzoylmalonate.—3,4,5-Trimethoxybenzoyl chloride (12 g.) was added slowly to a well-stirred suspension of the sodio derivative of diethyl malonate in benzene (*ca.* 100 cc.), prepared by treating powdered sodium (2.3 g.) in benzene with diethyl malonate (16 g.). After stirring overnight, dilute hydrochloric acid was added, the benzene layer separated, and washed with aqueous sodium bicarbonate and water. The dried solution was evaporated under reduced pressure, giving a crystalline residue (16 g., 87%), m. p. 87°. After crystallization from ethanol–water the pure product had the m. p. 89–90°.

Anal. Calcd. for $C_{17}H_{22}O_8$: C, 57.62; H, 6.26. Found: C, 57.43; H, 5.77.

Reduction of this product with hydrogen and Raney nickel at low temperature and pressure, followed by hydrolysis with 10% sulfuric acid, did not yield β-(3,4,5-trimethoxyphenyl)-propionic acid. Instead, some 3,4,5-trimethoxybenzoic acid was obtained, and a neutral compound, of uncertain structure, which was insoluble in ether, and which melted, after several recrystallizations from benzene, at 201–202°.

Anal. Found: C, 66.6; H, 6.7.

Summary

β-2-(3-Bromo-4,5,6,4′-tetramethoxybiphenyl)-propionic acid is cyclized under Friedel–Crafts conditions to a hydrindone derivative, the bromine migrating during the reaction. The structure is proved by conversion to 1-acetamino-4-(4-methoxyphenyl)-5,6,7-trimethoxyhydrindone, which is an isomer of N-acetylcolchinol methyl ether, and which is also obtained from the ketone prepared by cyclization of β-2-(4,5,6,4′-tetramethoxybiphenyl)-propionic acid.

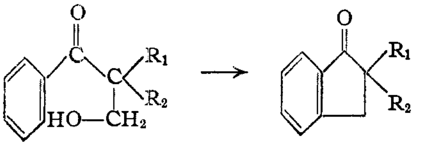
ROCHESTER, N. Y. RECEIVED JULY 19, 1948

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

2-Alkyl-1-indanones

BY J. H. BURCKHALTER[1] AND REYNOLD C. FUSON

The discovery that β-hydroxy-α-methylpropiophenone (Ia), when treated with sulfuric acid, underwent ring closure to yield 2-methyl-1-indanone (IIa)[2] suggested that this type of reaction might afford a superior method of preparation of compounds of this general class.



I II

	R_1	R_2
a	H	CH_3
b	H	C_2H_5
c	H	C_3H_7
d	CH_3	CH_3

The procedure has now been extended to ring closures of β-hydroxy-α-ethylpropiophenone (Ib) and β-hydroxy-α-propylpropiophenone (Ic), and although β-hydroxy-α,α-dimethylpropiophenone (Id) was reconverted by both sulfuric and phosphoric acids to isobutyrophenone, it was conveniently cyclized by phosphorus pentoxide to the desired 2,2-dimethyl-1-indanone (IId).

Despite success in obtaining from β-hydroxy ketones the four indanones whose synthesis has so far been attempted, the low yields in both steps render the method impractical. In a search for a more practical synthetic approach, the possibility of utilizing β-amino ketones instead of the isosteric β-hydroxy ketones was considered. Indeed β-dimethylaminopropiophenone (IIIa) has been made available by means of the Mannich reaction, and its hydrochloride has been degraded by steam distillation to acrylophenone (IVa) and dimethylamine hydrochloride.[3] The fact that acrylophenone can be so readily obtained from a Mannich base suggested the possibility of an extension of the method to the preparation of α-alkylacrylo-

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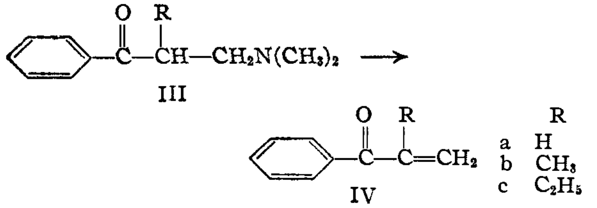
[1] Present address: Department of Pharmaceutical Chemistry, School of Pharmacy, University of Kansas, Lawrence, Kansas.

[2] Fuson, Ross and McKeever, THIS JOURNAL, 60, 2935 (1938).

[3] Mannich and Heilner, *Ber.*, 55, 356 (1922).

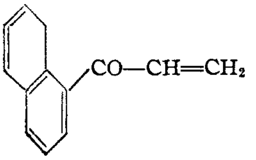
phenones (IV), which might be converted by ring closure to the desired 2-alkyl-1-indanones (II).



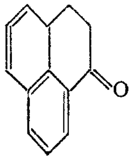
The hydrochlorides of β-dimethylamino-α-methylpropiophenone (IIIb), β-dimethylamino-α-ethylpropiophenone (IIIc) and β-dimethylamino-1-propionaphthone were prepared, respectively, in yields of 83, 60 and 95%. α-Methylacrylophenone (IVb) and α-ethylacrylophenone (IVc) were obtained in 70 and 68% yields, respectively, by steam distillation of the corresponding β-amino ketone hydrochlorides (III). Further, it was found that these α,β-unsaturated ketones (IVb and c), when treated with sulfuric acid, did undergo ring closure to form 2-methyl-1-indanone (IIa) and 2-ethyl-1-indanone (IIb), in yields of 88 and 49%, respectively.

The Mannich bases (IIIb and c) thus not only provide a convenient synthesis of certain 2-alkyl-1-indanones *via* the α,β-unsaturated ketones, but also a useful means is afforded of obtaining the desired α,β-unsaturated ketones as such.[4]

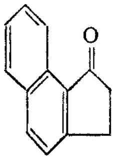
The ring closure experiments with acrylophenones (IV) aroused interest in finding out whether the analogous 1-acrylonaphthone (V) would cyclize to 7-perinaphthanone[5] (VI) or to 4,5-benzo-1-indanone (VII). 7-Perinaphthanone (VI) had been prepared previously as a yellow crystalline product (m. p. 85–86°) by ring closure of β-1-naphthylpropionic acid[6] while the indanone (VII) had been obtained as a white crystalline product (m. p. 102–103°) by ring closure of β-2-naphthylpropionic acid.[6,7] Treatment of 1-acrylonaphthone (V) with sulfuric acid actually resulted in the preparation of the white crystalline 4,5-benzo-1-indanone (VII), as shown by its melting point (102–103°) and elementary analysis. Because of polymerization, the intermediate 1-acrylonaphthone was obtained in very low yield from steam distillation of β-dimethylamino-1-propionaphthone hydrochloride.



V



VI



VII

Further studies in the synthesis of indanones are in progress and will be reported at a later date.

Experimental

Indanones from β-Hydroxy Ketones

2-Ethyl-1-indanone (IIb).—The procedure of Fuson, Ross and McKeever[2] for the preparation of 2-methyl-1-indanone (IIa) was applied in this experiment. From 106 g. of butyrophenone, 24 g. of paraformaldehyde and 11 g. of anhydrous potassium carbonate, 90 g. of butyrophenone was recovered unchanged, and 16 g. (13% yield) of yellow-colored β-hydroxy-α-ethylpropiophenone (Ib) was obtained by distillation at 150° (3.5 mm.); n^{20}_{D} 1.5273, d^{20}_{20} 1.080, M_D calcd. 50.92, found 50.70.

Four grams of β-hydroxy-α-ethylpropiophenone was cyclized with sulfuric acid according to the procedure of Fuson, Ross and McKeever.[2] One-half gram (14% yield) of light yellow-colored 2-ethyl-1-indanone boiled at 90° (3.5 mm.); $n^{20.5}_{D}$ 1.5448, d^{20}_{20} 1.031, M_D calcd. 47.20, found 48.90.[8]

The semicarbazone of 2-ethyl-1-indanone was prepared and recrystallized from alcohol; m. p. 199°.[9]

2,2-Dimethyl-1-indanone (IId).—Following the procedure described for the foregoing experiment, from 78.5 g. of isobutyrophenone 35 g. (37% yield) of the β-hydroxy-α,α-dimethylpropiophenone (Id) was obtained. Distilling range, 125–131° (3.5 mm.),[10] $n^{19.5}_{D}$ 1.5314, d^{20}_{20} 1.089, M_D calcd. 50.92, found 50.50. A fraction distilling at 131° (3.5 mm.) was collected separately and found to possess the same refractive index. On standing it solidified. When recrystallized from alcohol the hydroxy ketone, which had previously been described as a liquid,[10] melted at 79–81°.

The phenylurethan of β-hydroxy-α,α-dimethylpropiophenone melted at 87°.[11]

A solution of 6 g. of β-hydroxy-α,α-dimethylpropiophenone in 15 cc. of xylene was added to 3.5 g. of phosphorus pentoxide in 15 cc. of xylene, and the mixture refluxed for an hour. After removal of the xylene under reduced pressure, the residue was transferred to a smaller flask and distilled. Two and one-half grams (45% yield) of a liquid boiling at 95° (3.5 mm.)[12] was obtained. The refractive index, $n^{18.9}_{D}$ 1.5409, agreed closely with that in the literature,[8] $n^{18.9}_{D}$ 1.5408, for 2,2-dimethyl-1-indanone.

2-Propyl-1-indanone (IIc).—By the procedure outlined for 2-ethyl-1-indanone, 106 g. of valerophenone yielded only 7.5 g. (6% yield) of β-hydroxy-α-propylpropiophenone (Ic); b. p. 160° (3.5 mm.), n^{20}_{D} 1.525, d^{20}_{20} 1.040, M_D calcd. 55.58, found 56.50.

Anal.[13] Calcd. for $C_{11}H_{14}O_2$: C, 74.43; H, 8.39. Found: C, 74.74; H, 8.39.

Cyclization of 8 g. of β-hydroxy-α-propylpropiophenone with sulfuric acid yielded a gram of yellow-colored 2-propyl-1-indanone which distilled at 100° (3 mm.). All the indanone was used for the preparation of the semicarbazone. Recrystallized from alcohol, the derivative melted at 188–191°.

Anal. Calcd. for $C_{13}H_{17}N_3O$: C, 67.51; H, 7.41. Found: C, 67.10; H, 7.02.

β-Amino Ketones

β-Dimethylamino-α-methylpropiophenone Hydrochloride (IIIb).—The procedure of Mannich and Heilner[3] was

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(4) Kizhner [*J. Russ. Phys.-Chem. Soc.*, **46**, 1411 (1914); *C. A.*, **9**, 2066 (1915)], in an attempt to prepare α-methylacrylophenone by a different means actually obtained 2-methyl-1-indanone instead.

(5) For nomenclature, see Fieser and Hershberg, THIS JOURNAL, **60**, 1659 (1938).

(6) Mayer and Sieglitz, *Ber.*, **55**, 1844 (1922).

(7) Cook and Hewitt, *J. Chem. Soc.*, 1111 (1933).

(8) v. Auwers, *Ann.*, **415**, 161 (1918), accounts for an exaltation in the observed molecular refractivity of indanones through tension in the alicyclic ring. He found deviations of 1.32 and 1.56, respectively, for 2-methyl-1-indanone and 2,2-dimethyl-1-indanone.

(9) Leuchs and Kowalski, *Ber.*, **58**, 2822 (1925), found 200–203°.

(10) Blaise and Herman, *Ann. chim.*, [8] **23**, 524 (1911), found 152–153° (12 mm.).

(11) Blaise and Herman give a melting point of 89°.

(12) Haller and Bauer, *Compt. rend.*, **150**, 1475 (1910), found 118–119° (15 mm.).

(13) Analytical data in this paper furnished by Mr. Charles Beazley.

applied to 180 g. of propiophenone, 120 g. of dimethylamine hydrochloride and 42 g. of paraformaldehyde. After recrystallization from acetone, 251 g. (83% yield) of the white salt was obtained; m. p. 150–154°.[14]

Anal. Calcd. for $C_{12}H_{18}ClNO$: C, 63.27; H, 7.97; N, 6.15. Found: C, 63.19; H, 8.03; N, 6.24.

β-Dimethylamino-α-ethylpropiophenone Hydrochloride (IIIc).—The substitution of butyrophenone for propiophenone in the foregoing procedure resulted in a 60% yield of the desired product. However, it was found necessary to remove much of the solvent alcohol in order to induce crystallization of the crude product. Further, since recrystallization was difficult possibly because of the presence of dimethylamine hydrochloride, the crude material was dissolved in water and treated with an excess of 10% sodium hydroxide solution. The mixture was extracted with two portions of ether, which were combined and dried over anhydrous magnesium sulfate. A white crystalline hydrochloride was precipitated from the filtered solution, which, after recrystallization from acetone, melted at 140–141°.

Anal. Calcd. for $C_{13}H_{20}ClNO$: C, 64.56; H, 8.34. Found: C, 64.67; H, 8.09.

β-Dimethylamino-1-propionaphthone Hydrochloride.—From 52 g. of 1-acetonaphthone, 30 g. of dimethylamine hydrochloride and 12 g. of paraformaldehyde, 76 g. (95% yield) of the desired white crystalline salt was prepared. A portion recrystallized from acetone melted at 150–153°.[15]

Anal. Calcd. for $C_{15}H_{18}ClNO$: C, 68.28; H, 6.88. Found: 68.29; H, 6.84.

Indanones from α,β-Unsaturated Ketones

2-Methyl-1-indanone (IIa).—Steam was led into 141 g. of β-dimethylamino-α-methylpropiophenone hydrochloride and a pungent oil possessing a lachrymatory effect distilled with water. The distilling flask was also heated externally to keep a low volume. At the end of the distillation, the mixture was extracted with two portions of ether and the extracts were dried over anhydrous sodium sulfate. After removal of the ether, 63.5 g. (70% yield) of the straw colored α-methylacrylophenone (IVb) distilled at 60° (3 mm.); n^{20}_D 1.5354, d^{20}_{20} 1.024, M_D calcd. 44.33, found 44.25.

Anal. Calcd. for $C_{10}H_{10}O$: C, 82.15; H, 6.90. Found: C, 82.20; H, 7.10.

α-Methylacrylophenone rapidly added bromine, producing a more severe lachrymator. 1,3-Diphenyl-4-methyl-2-pyrazoline was prepared by boiling for a few minutes an alcoholic solution of equal weights of methylacrylophenone and phenylhydrazine. When recrystallized from alcohol, the light yellow-colored derivative melted at 119–121°.

Anal. Calcd. for $C_{16}H_{16}N_2$: C, 81.32; H, 6.83. Found: C, 81.43; H, 6.66.

Fifty-nine and one-half grams of α-methylacrylophenone was poured slowly with stirring into 100 cc. of concentrated sulfuric acid. The mixture became warm and darkened slightly. After the liquid had cooled to room temperature, it was poured with stirring into a liter of water. The cooled mixture was extracted with two portions of ether and the extracts dried over anhydrous sodium sulfate. After removal of the ether, 52.5 g. (88% yield) of 2-methyl-1-indanone was distilled at 90° (3 mm.); n^{20}_D 1.5543.[16] Its semicarbazone melted at 199°.[2]

2-Ethyl-1-indanone (IIb).—By the preceding procedure, 60 g. of β-dimethylamino-α-ethylpropiophenone hydrochloride was converted into 27 g. (68% yield) of light yellow-colored α-ethylacrylophenone (IVc); b. p. 85° (5 mm.), n^{20}_D 1.5267, d^{20}_{20} 0.998, M_D calcd. 48.93, found 49.00.

From a cyclizing experiment with sulfuric acid, 37% of pure α-ethylacrylophenone was recovered unchanged [b. p. 90° (6 mm.), n^{20}_D 1.5270], and a 49% yield of 2-ethyl-1-indanone was obtained [b. p. 108° (6 mm.), n^{20}_D 1.5455], thus accounting for 86% of the starting material. The semicarbazone melted at 203°[9]; a mixed melting point determination with the semicarbazone of 2-ethyl-1-indanone which was derived from β-hydroxy-α-ethylpropiophenone showed no depression.

4,5-Benzo-1-indanone (VII).—Steam distillation of 68 g. of β-dimethylamino-1-propionaphthone hydrochloride, in the manner of the preceding experiments, yielded 40 g. of a liquid from the benzene extracts which might have been crude 1-acrylonaphthone. However, distillation under reduced pressure produced 20 g. of 1-acetonaphthone and 20 g. of a clear, amber-colored, brittle polymeric material which was only slightly soluble in benzene.

An additional 44 g. of β-dimethylamino-1-propionaphthone hydrochloride was subjected to steam distillation. The distillate was extracted with ether and the extracts dried over anhydrous magnesium sulfate. Removal of the ether left only 6 g. of an oil. It was added directly with stirring to 50 cc. of concd. sulfuric acid. The solution was allowed to cool before it was poured into 600 cc. of water. Ether extracts of the resulting mixture were dried. Removal of the ether left an oil which readily crystallized. After four recrystallizations from dilute alcohol, 1 g. of white 4,5-benzo-1-indanone was obtained; m. p. 102–103°.[7]

Anal. Calcd. for $C_{13}H_{10}H_{10}O$: C, 85.68; H, 5.53. Found: C, 85.68; H, 5.57.

Summary

Several 2-alkyl-1-indanones have been synthesized by subjecting the appropriate β-hydroxy- or α,β-unsaturated ketone to ring closure.

It has been found that the Mannich bases derived from acylophenones afford a superior method of preparation of the unsaturated ketones.

4,5-Benzo-1-indanone rather than 7-perinaphthanone was obtained by ring closure of 1-acrylonaphthone.

URBANA, ILLINOIS RECEIVED AUGUST 9, 1948

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[14] Knott, *J. Chem. Soc.*, 1190 (1947), reports 142.5° and 81% yield.

[15] Knott reports 165° and 34% yield.

[16] Kizhner, ref. 4, found 136° (32 mm.), n^{20}_D 1.5543; v. Auwers, ref. 8, found 125° (18 mm.), n^{20}_D 1.5538.