tion of 5.0 g. of *o*-nitrobiphenyl in 75 ml. of 95% ethanol. After thorough mixing, 5 g. of zinc amalgam was added and the mixture refluxed and stirred vigorously for 45 min. Thereupon 50 ml. of water was added, the solution filtered and the residue washed with 100 ml. of ether. The aqueous filtrate was extracted with three 50-ml. portions of ether. All ether solutions were combined, washed with saturated brine solution, filtered through anhydrous sodium sulfate and evaporated under vacuum. The orange semi-solid residue was dissolved in hot petroleum ether. Cooling led to 3.4 g. of yellow granular crystals, m.p. 63–69°, which on crystallization from petroleum ether changed to 2.8 g. of colorless crystals of *o*-hydroxylaminobiphenyl, m.p. 69–71°.

Anal. Calcd. for $C_{12}H_{11}ON$: C, 77.81; H, 5.99; N, 7.56. Found: C, 77.79; H, 6.11; N, 7.54.

Rearrangements of *o*-Hydroxylaminobiphenyl (VIc). (a) Pyrolytic Reactions.—A solution of 4.00 g. of *o*-hydroxylaminobiphenyl in 100 ml. of toluene was refluxed under a nitrogen atmosphere for 12 hr. It then was extracted with 10% hydrochloric acid solution. The acid extract was neutralized with sodium hydroxide and extracted with ether. The solvent of the organic extract then was evaporated, the residue dissolved in pyridine and treated with 15 ml. of acetic anhydride and the solution allowed to stand for 12 hr. The solution was poured into water. The resulting precipitate was washed with saturated sodium carbonate solution and water, dissolved in ethanol and decolorized with Norite and crystallized from aqueous ethanol. It yielded 800 mg. of *o*-acetamidobiphenyl, m.p. 118–120° (lit.[12] m.p. 119°), identical with an authentic sample.

The initial toluene solution was washed with saturated brine solution, filtered through dry sodium sulfate and chromatographed on alumina. Elution with petroleum ether yielded 120 mg. of *o*-azobiphenyl (VId), m.p. 136–139° (lit.[13] m.p. 144.5°), identical with an authentic sample. Further elution with benzene–ether gave 850 mg. of *o*-azoxybiphenyl (XI), m.p. 160–163° (lit.[13] m.p. 158°) after crystallization from aqueous acetone, identical with an authentic sample.

Anal. Calcd. for $C_{24}H_{18}ON_2$: C, 82.26; H, 5.18; N, 8.00. Found: C, 82.56; H, 5.47; N, 8.07.

A similar pyrolysis was carried out with a solution of 1.00 g. of *o*-hydroxylaminobiphenyl in 20 ml. of anhydrous benzene. The solution was placed into a nitrogen-swept Carius tube, sealed and heated at 270° for 24 hr. The identical work-up as above led to 150 mg. of *o*-acetamidobiphenyl, 50 mg. of *o*-azobiphenyl and 600 mg. of *o*-azoxybiphenyl.

(b) Acid-catalyzed Reactions.—A solution of 1.00 g. of *o*-hydroxylaminobiphenyl in 20 ml. of 20% sulfuric acid was heated on a steam-bath for 2 hr. After dilution of the cooled dark mixture with water it was extracted with ether and chloroform. Evaporation of the organic extracts to dryness and chromatography of the residue on alumina yielded 610 mg. of *o*-azoxybiphenyl (XI), m.p. 158–161°. Basification of the aqueous acid solution with 5% sodium hydroxide solution, extraction with ether and chloroform and evaporation of the organic extracts gave a residue, which was dissolved in pyridine, treated with 2 ml. of benzoyl chloride and heated on the steam-bath for 10 min. The cooled pyridine solution then was poured into water, and the resulting precipitate filtered and crystallized from benzene. This afforded 300 mg. of *o*-benzamidobiphenyl, m.p. 84–86°, identical with the specimen above. Adjustment of the basic aqueous solution of the initial reaction mixture to *p*H 7 and exhaustive extraction with ether and chloroform led to no more products.

A solution of 1.00 g. of *o*-hydroxylaminobiphenyl and of 1.00 g. of *p*-toluenesulfonic acid in 20 ml. of water was placed into a nitrogen-swept Carius tube, sealed and heated at 270° for 24 hr. The identical work-up as above yielded 75 mg. of *o*-azobiphenyl (VId), 550 mg. of *o*-azoxybiphenyl (XI) and 170 mg. of *o*-benzamidobiphenyl.

A solution of 4.00 g. of *o*-hydroxylaminobiphenyl and 4.00 g. of *p*-toluenesulfonic acid in 50 ml. of water was refluxed for 4 hr. under a nitrogen atmosphere. To the cooled reaction mixture there were added 50 ml. of 10% sulfuric acid solution, and the mixture was worked up as before, except that the basic products were acetylated rather than benzoylated. This run afforded 685 mg. of *o*-acetamidobiphenyl and 1.10 g. of *o*-azoxybiphenyl (XI). Ether–acetone elution of the chromatogram and crystallization from aqueous acetone gave 600 mg. of unrecognized black glistening crystals.

α-Phenylcyclohexanone Oxime 3,5-Dinitrobenzoate.—3,5-Dinitrobenzoyl chloride, 7.00 g., was added to a solution of 5.00 g. of α-phenylcyclohexanone oxime (IIa) in 20 ml. of anhydrous pyridine. After the initial heat of the reaction had subsided, the mixture was heated gently on the steam bath for 2 min. It then was cooled and poured with vigorous stirring into 200 ml. of cold water. The separating oil was allowed to settle and solidify. After decantation of the supernatant liquid the residue was washed with 10% hydrochloric acid and with water, dissolved in ethanol, decolorized with Norite and crystallized. Recrystallization from ethanol yielded 10.5 g. of white needles of the desired ester, m.p. 116–117°.

Anal. Calcd. for $C_{19}H_{17}O_6N_3$: C, 59.54; H, 4.43; N, 10.96. Found: C, 59.51; H, 4.92; N, 10.83.

A solution of 3.70 g. of the ester and 4 ml. of commercial triethylamine in 75 ml. of anhydrous benzene was refluxed for 48 hr. The wine-red reaction mixture was evaporated under vacuum, redissolved in benzene and extracted with water, 5% sodium hydroxide and 10% hydrochloric acid solutions. Acidification of the basic extract with 10% hydrochloric acid, extraction with ether, evaporation of the organic extract and crystallization of the residue from aqueous ethanol yielded 1.15 g. of 3,5-dinitrobenzoic acid, m.p. 204–207°, identical with an authentic sample. Chromatography of a concentrate of the initial benzene solution of alumina gave 25 mg. of tetrahydrocarbazole (IV), m.p. 116–120°, on elution with petroleum ether, 125 mg. of ethyl 3,5-dinitrobenzoate, m.p. 95–97° (lit.[12] m.p. 96°) (identical with an authentic sample), on elution with cyclohexane and crystallization from aqueous ethanol, and 1.15 g. of α-phenylcyclohexanone oxime, m.p. 168–171°, on elution with ether and crystallization from petroleum ether.

(12) F. Bell, *J. Chem. Soc.*, 2773 (1928).

(13) G. Friebel and B. Rassow, *J. prakt. Chem.*, **63**, 453 (1901).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, IOWA STATE UNIVERSITY, AMES, IOWA]

A New Synthesis of the Hydrophenanthrene Nucleus

BY ERNEST WENKERT, R. D. YOUSSEFYEH AND RONALD G. LEWIS

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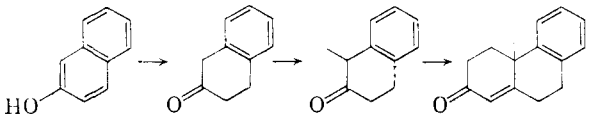
Reactions of the dry sodium salts of β-naphthol and its various α-alkyl derivatives with different alkyl halides and the three-step conversion of a resulting naphthalenone to a hydrophenanthrone are described.

A common feature of the recent large number of total syntheses of steroids, diterpenes and triterpenes is the extensive use of the Robinson cyclohexenone synthesis. Its application in the field of diterpene synthesis has meant invariably the construction of a hydrophenanthrene nucleus,[1] derivatives of I, by a route similar, although not identical in detail, to that employed by Cornforth and Rob-

(1) *Cf.* (a) G. Stork and J. W. Schulenberg, THIS JOURNAL, **78**, 250 (1956); (b) P. N. Rao and K. Raman, *Tetrahedron*, **4**, 294 (1958); (c) R. B. Turner, E. G. Herzog, R. B. Morin and A. Riebel, *Tetrahedron Letters*, 7 (1959).

inson[2] in their synthesis of a steroid intermediate. Three basic operations, reduction of a β-naphthyl system to a β-tetralone derivative and two alkylations thereof, have led always to the tricyclic nucleus,[3] *e.g.*

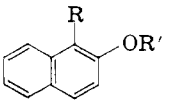


I

Recently it was demonstrated that the heretofore rigid sequence of steps in a Robinson hydrophenanthrone synthesis could be altered to permit the alkylations to precede the reduction.[4] The major significance of this modification was the portrayal, for the first time, of the fact that phenols (at least, β-naphthols) can serve as nucleophilic substrates in place of the customary ketones (or enols) in the Michael condensation, one of the two crucial alkylation steps, even if the site of alkylation is already mono-alkylated and, hence, the aromatic nucleus is converted to a hydroaromatic system. It now became of interest to ascertain whether similarly constituted phenols could be alkylated as their salts by alkyl halides with similar consequences. For this reason the C-alkylability of β-naphthol and 1-alkyl-2-naphthols came under investigation.[5]

While methylation of the dry sodium salt of β-naphthol (IIa) with methyl sulfate gave exclusively the methyl ether IIb, alkylation with methyl iodide in toluene led preponderantly to 1-methyl-2-naphthol (IIc). Under the latter conditions sodium β-naphthoxide and *n*-butyl bromide gave both O- and C-alkyl products in a 1.4:1 ratio. The ether IId was identical with the product of *n*-butylation of sodium β-naphthoxide in aqueous methanol, while the phenolic product (IIe) was shown to be identical with the product of Wolff–Kishner reduction of the ketophenol IIf, itself obtained by the base-catalyzed condensation of β-naphthol and methyl vinyl ketone.[6]

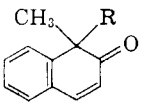
α-Alkylation of already alkylated naphthols proved to be a much higher-yielding process than alkylation of β-naphthol itself. Thus, a reaction of dry sodium 1-methyl-2-naphthoxide and methyl



II

a, R = R′ = H
b, R = H, R′ = Me
c, R = Me, R′ = H
d, R = H, R′ = *n*-Bu
e, R = *n*-Bu, R′ = H
f, R = $(CH_2)_2COCH_3$, R′ = H
g, R = R′ = Me
h, R = Me, R′ = *n*-Bu
i R = *n*-Bu, R′ = Me
j, R = $(CH_2)_2COCH_3$, R′ = Me
k, R = $(CH_2)_2CH(OH)CH_3$, R′ = H
l, R = $(CH_2)_2CH(OH)CH_3$, R′ = Me

iodide gave a 88% yield of unsaturated ketone IIIa, identified by its spectral properties and conversion to the known 1,1-dimethyl-2-tetralone 2,4-dinitrophenylhydrazone,[7] and only a 4% yield of the ether IIg.[8] Interaction of the same dry salt with *n*-butyl iodide gave a 50% yield of ketone IIIb and a 29% yield of ether IIh, while treatment of dry sodium 1-(*n*-butyl)-2-naphthoxide with methyl iodide gave a similar ratio of products, 59% of ketone IIIb and 30% of ether IIi.[9]



III

a, R = Me
b, R = *n*-Bu
c, R = CH_2Cl
d, R = CH_2I
e, R = $CHCl_2$
f, R = $(CH_2)_2COCH_3$
g, R = $(CH_2)_2CH(OH)CH_3$

The reactivity of sodium 1-methyl-2-naphthoxide toward polyhalomethanes was of interest for comparison with its above methylation and in connection with another investigation. As a consequence the salt was treated with methylene chloride, methylene iodide as well as chloroform, each for the same length of reaction time as in the methyl iodide reaction but at the reflux temperature of each individual halide. The salt proved inert toward methylene chloride, although it could be converted in a sealed tube reaction to the ketone IIIc and ether IV, the former highly predominating in yield. The reaction with methylene iodide was also sluggish despite the high reflux temperature of the halide but yielded some products, mostly IIId and some IV. Finally, chloroform treatment of the salt gave again a high product yield (of IIIe).[10] It is noteworthy in connection with the last reaction

(2) J. W. Cornforth and R. Robinson, *J. Chem. Soc.*, 676 (1946); 1855 (1949).

(3) A Folkers modification of the Robinson scheme [W. F. Newhall, S. A. Harris, F. W. Holly, E. L. Johnston, J. W. Richter, E. Walton, A. N. Wilson and K. Folkers, THIS JOURNAL, **77**, 5646 (1955)] has resulted recently in a synthesis of I itself (E. Wenkert and B. G. Jackson, unpublished data). Its first synthesis, however, was described in 1956[4] and was followed soon by a second one [K. E. Zwahlen, W. J. Horton and G. I. Fujimoto, THIS JOURNAL, **79**, 3131 (1957)].

(4) E. Wenkert and T. E. Stevens, *ibid.*, **78**, 2318 (1956).

(5) At the time this study was initiated only a few instances of C-alkylation of phenol salts by organic halides of other than alkyl or benzyl types were on record [J. Herzig and B. Erthal, *Monatsh.*, **32**, 501 (1901), and preceding papers; A. C. Jain and T. R. Seshadri, *Proc. Indian Acid. Sci.*, **42A**, 279 (1955) [*C. A.*, **50**, 8518 (1956)]; D. Y. Curtin and R. R. Frazer, *Chemistry & Industry*, 1358 (1957)]. While this state of affairs has not changed, a large amount of data on the mechanism of the reaction has been accumulated during the last three years [V. A. Zagorevsky, *J. Gen. Chem.* (*U.S.S.R.*), **27**, 488 (1958); D. Y. Curtin and R. R. Frazer, THIS JOURNAL, **80**, 6016 (1958), and preceding papers; N. Kornblum and A. P. Lurie, *ibid.*, **81**, 2705 (1959)].

(6) S. A. Miller and R. Robinson, *J. Chem. Soc.*, 1535 (1934).

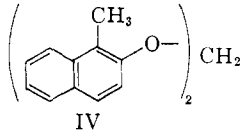
(7) M. D. Soffer, R. A. Stewart, J. C. Cavagnol, H. E. Gellerson and E. A. Bowler, THIS JOURNAL, **72**, 3704 (1950).

(8) K. Fries and E. Hubner, *Ber.*, **39**, 435 (1906).

(9) While the heterogeneity of the reactions and the insufficient number of cases studied prevent the formulation of rigorous conclusions, it is worthy of note that increasing the steric requirements of the reaction site in either the electrophile or nucleophile decreased the C/O alkylation ratio.

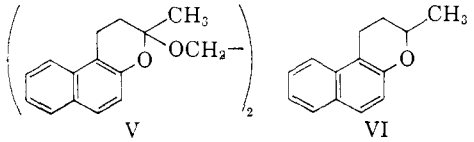
(10) While, again, the heterogeneity of each of the halomethane reactions warrants caution in their interpretation, the similarity of the discontinuity in the expected diminution of their rates (with increasing halogen content of the halomethanes) with that observed for reactions with other nucleophiles [P. Petrenko-Kritshenko and V. Opotsky, *Ber.*, **59B**, 2131 (1926)] may be more than coincidence. It suggests that the reaction with chloroform proceeds by a mechanism other than direct displacement, possibly by a carbene mechanism [*cf.* J. Hine, THIS JOURNAL, **72**, 2438 (1950); H. Wynberg, *ibid.*, **76**, 4998 (1954)]. Most recently the carbene pathway has been proved to be the mechanism of the Reimer–Tiemann reaction in homogeneous solution [J. Hine and J. M. van der Veen, *ibid.*, **81**, 6446 (1959)].

that from an experimental point of view the dry salt method may be the most efficient procedure for carrying out Reimer–Tiemann reactions, which are expected to lead to hydroaromatic ("abnormal") products.



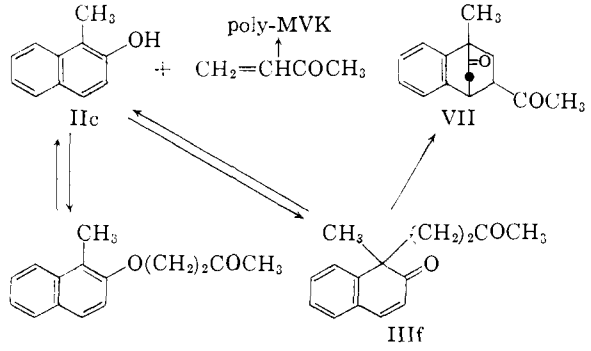
IV

By now, the preliminary survey of the α-alkylability of β-naphthols had yielded enough favorable results to permit the pursuance of the initial goal, a new hydrophenanthrone synthesis. As a consequence, the methylation of the dry sodio salt of 1-(γ-ketobutyl-)-2-naphthol (IIf) was studied. Unfortunately, this reaction led to a mixture, in which the desired naphthalenone (IIIf) could be recognized, but which also contained, alongside an O-methyl compound IIj, the fragmentation products 1-methyl-2-naphthol (IIc) and its methyl ether IIg. Since, as will be shown later, the sidechain carbonyl group was responsible for the anomalous behavior of the naphthol IIf, it had to be masked. When attempted ketalation of the keto group with ethylene glycol yielded the unusable ketal V, the carbonyl compound was reduced to the phenolic alcohol IIk with lithium aluminum hydride. Methylation of the sodio salt of IIk gave only C- and O-alkyl products, IIIg and III, respectively (in an over 2:1 ratio). The latter was identified by its ready acid hydrolysis to a mixture of starting naphthol IIk and VI.



V VI

Chromic acid oxidation of IIIg led to the diketone IIIf, whose behavior toward alkaline reagents was of theoretical interest. In a previous study of the Michael condensation of 1-methyl-2-naphthol

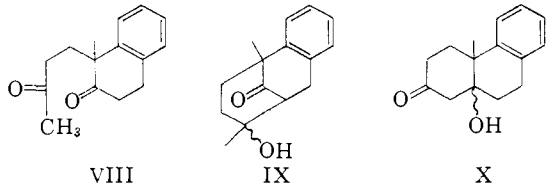


and methyl vinyl ketone, a reaction in which IIIf would be expected to be a crucial intermediate or the product, it had been shown that only starting naphthol was obtained by sodium ethoxide catalysis and a low yield of VII was the consequence of potassium *t*-butoxide catalysis. When, now, IIIf was treated with these bases similar results were observed. It thus appears that competitive high rates of *retro*-Michael processes and probably formation of methyl vinyl ketone polymer (poly-MVK) are the most important features of the various equilibria of the Michael reaction.

Discovery of the ease of the *retro*-Michael conversion of IIIf also permitted an interpretation of the aforementioned anomalous methylation of the sodio salt of 1-(γ-ketobutyl)-2-naphthol (IIf). Naphthoxide-induced reverse Michael reaction of IIIf, the major methylation product, can be envisaged to have given the sodio salt of 1-methyl-2-naphthol (IIc). The latter, in turn, was partly methylated, hence finally yielding a mixture of IIc and IIg.

Since the diketone VIII was the next desired compound, the reduction of the double bond of enedione IIIf and of the ketol IIIg (as well as chromic acid oxidation of the latter's reduction product) came under scrutiny. Unfortunately, catalytic hydrogenation, even under mild conditions, gave mostly over-reduced compounds and only low yields of dihydro products.[11] After some trial and error the most efficient procedure for the formation of VIII was found to be reduction of the ketol IIIg by lithium in liquid ammonia and chromic acid oxidation of the resultant mixture of diastereomeric saturated diols without their prior separation and characterization.

Mild base treatment of VIII led to a ketol, IX or X, whose physical properties proved it to be different from a previously reported ketol (X),[4,12] while stronger conditions yielded the tricyclic ketone I.



VIII IX X

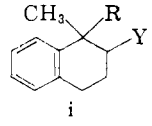
With completion of the present hydrophenanthrone synthesis complete operational flexibility has been introduced into the Robinson scheme of *proto*-terpenoid synthesis.

Acknowledgment.—Financial support by the National Science Foundation (research grant NSF-G6226) and partly by Ciba Pharmaceutical Products, Inc., is acknowledged most gratefully.

Experimental

Synthesis of 1-Alkyl-2-naphthols (II).—All dry sodium salts of β-naphthols were prepared by the dissolution of the β-naphthol in an absolute methanolic solution of an equimolar quantity of dry sodium methoxide, evaporation of the solution to dryness, addition of dry benzene and re-evaporation. The salts thus formed were used for alkylation without further purification.

(11) A detailed study of the palladium-induced hydrogenation of the acetate of IIIg revealed the undesired substances to be ia (Y = OH) and ib (Y = H). Furthermore, their formation must have been a consequence of the hydrogenation of the carbonyl group of the unsaturated ketone prior to the reduction of its double bond, since VIII proved inert to hydrogenation under identical reaction conditions.



i

(12) *Cf.* W. S. Johnson, J. J. Korst, R. A. Clement and J. Dutta, THIS JOURNAL, **82**, 614 (1960).

A heterogeneous mixture of sodium β-naphthoxide, from 5.0 g. of β-naphthol (IIa), and 20 ml. of distilled methyl sulfate was refluxed gently for 3 hr. The cooled mixture was poured into 30 ml. of 10% sodium hydroxide solution and stirred for 2 min. It then was extracted with ether and dried. The solvent and excess methyl sulfate were removed by vacuum distillation. Crystallization of the residue from 95% ethanol yielded 4.8 g. (88%) of methyl β-naphthyl ether (IIb), m.p. 73–74°, identical in all respects with an authentic sample.

A heterogeneous mixture of sodium β-naphthoxide, from 10 g. of β-naphthol (IIa), 20 ml. of methyl iodide in 50 ml. of dry toluene was refluxed for 18 hr. The cooled mixture was acidified with dilute hydrochloric acid solution and extracted with ether. The extract was dried and evaporated to dryness. The residue was chromatographed on alumina. Elution with petroleum ether yielded first 2.57 g. (25%) of methyl β-naphthyl ether (IIb), m.p. 73–74°, and then 4.00 g. (39%) of 1-methyl-2-naphthol (IIc), m.p. 110–111°, identical in all respects with an authentic sample.

A mixture of sodium β-naphthoxide, from 10.0 g. of β-naphthol (IIa), 20 g. of *n*-butyl bromide and 50 ml. of dry toluene was refluxed for 20 hr. The solvent then was reduced to a volume of 10 ml. and the mixture extracted with 25% sodium hydroxide solution. The latter was acidified with concentrated hydrochloric acid to *p*H 3 and extracted with ether. The extract was dried, evaporated and the residue chromatographed on 100 g. of alumina. Elution with petroleum ether gave 5.0 g. of a solid phenol, while 9:1 petroleum ether–benzene yielded 0.2 g. (2%) of starting β-naphthol (IIa). The remaining toluene solution was dried, evaporated and the residue also chromatographed on 100 g. of alumina. Elution with petroleum ether first yielded 7.9 g. of a neutral oil and then 0.6 g. more of the above solid phenol.

The oily product (7.9 g., 57% yield) was distilled under vacuum, b.p. 108°(22 mm.), leading to solid *n*-butyl β-naphthyl ether (IId), m.p. 33–35°.

Anal. Calcd. for $C_{14}H_{16}O$: C, 84.00; H, 8.06. Found: C, 83.96; H, 7.98.

The identity of IId was established by the following preparation of an authentic sample. The sodium salt of 10.0 g. of β-naphthol, made and left in 50 ml. of methanol, was mixed with 20 g. of *n*-butyl bromide in 50 ml. of water and 70 ml. of methanol. The resulting homogeneous solution was refluxed for 24 hr., at the end of which time it had separated into two layers. After addition of 50 ml. of 10% sodium hydroxide solution, it was extracted with ether. The extract was dried, evaporated and the residue chromatographed on alumina. Elution with petroleum ether led to 12.0 g. (86%) of *n*-butyl β-naphthyl ether (IId), b.p. 108° (25 mm.), m.p. 33–35°.

Crystallization of the solid phenol (5.6 g., 40% yield) from petroleum ether–chloroform yielded 1-*n*-butyl-2-naphthol (IIe), m.p. 79–81° (lit.[13] 80–81°). It was identified by comparison with an authentic sample prepared in the following manner. A mixture of 1.00 g. of 1-(γ-ketobutyl)-2-naphthol (IIf), prepared by a slight modification of the Robinson procedure[6] in 72% yield, 4 g. of potassium hydroxide, 6 ml. of 95% hydrazine and 20 ml. of ethylene glycol was refluxed for 1 hr. The mixture then was heated without reflux condenser to remove excess hydrazine, whereupon it was refluxed for 2 hr. The cooled mixture then was diluted with water, acidified with 2 *N* hydrochloric acid and extracted with ether. Drying of the extract over magnesium sulfate and removal of the solvent led to 0.92 g. (99%) of solid, which on crystallization from petroleum ether–chloroform gave 1-*n*-butyl-2-naphthol (IIe), m.p. 79–81°.

A solution of 2.00 g. of 1-(γ-ketobutyl)-2-naphthol (IIf) in 30 ml. of tetrahydrofuran was added slowly to a mixture of 3.5 g. of lithium aluminum hydride and 30 ml. of tetrahydrofuran. The mixture was stirred for 3 hours under nitrogen, ethyl acetate added for the decomposition of excess hydride and the mixture acidified with 1 *N* hydrochloric acid. The aqueous layer was extracted with ether, and the combined organic solutions washed with water, until the washings were neutral to litmus. Drying of the organic extracts over magnesium sulfate and removal of the solvent led to 1.92 g. (94%) of a solid which on crystallization from ether yielded 1-(γ-hydroxybutyl)-2-naphthol (IIk), m.p. 136–137° (lit.[14] 136–137°).

Ketalation of 1-(γ-Ketobutyl)-2-naphthol (IIf).—A mixture of 2.0 g. of 1-(γ-ketobutyl)-2-naphthol (IIf), 75 mg. of *p*-toluenesulfonic acid monohydrate, 16 ml. of ethylene glycol and 90 ml. of toluene was distilled slowly for 6 hours. The volume of the mixture was kept constant by the addition of fresh toluene every half-hour. After cooling the mixture, washing with saturated sodium bicarbonate solution and then with water, and drying over anhydrous magnesium sulfate, the solvent was removed under vacuum. Crystallization of the oily residue from methanol gave a solid which after alumina chromatography and elution with petroleum ether amounted to 1.4 g. (33%). Crystallization from methanol gave the ketal V, m.p. 200–201°; spectra; ultraviolet (95% ethanol), λ_{max} 232 mμ (ε 69,200), 280 mμ (ε 5030); λ_{min} 250 mμ (ε 4880), 300 mμ (ε 1980); infrared (CCl_4), C=C, 6.20(m), 6.30(m)μ.

Anal. Calcd. for $C_{30}H_{30}O_4$: C, 79.27; H, 6.65. Found: C, 79.15; H, 6.82.

Evaporation of the mother liquor from the first crystallization gave 0.6 g. of an unidentified oil; infrared spectrum (CCl_4), OH 2.78(m)μ, C=C 6.18(m), 6.29(m)μ.

Alkylations of 1-Methyl-2-naphthol (IIc).—Freshly distilled methyl iodide (30 ml.) was added to the sodium salt, derived from 1.00 g. of 1-methyl-2-naphthol (IIc), and the mixture refluxed for 4 hr. Upon cooling, 30 ml. of water was added and the mixture extracted with two 25-ml. portions of chloroform. Drying over magnesium sulfate and vacuum removal of the solvent gave a residue which was chromatographed over alumina. Elution with petroleum ether yielded first 12 mg. of an impure unidentified solid, m.p. 267–270°, and then 40 mg. (4%) of methyl 1-methyl-2-naphthyl ether (IIg), m.p. 38–39° after crystallization from petroleum ether (lit.[8] 39°). Elution with 5:1 petroleum ether–benzene produced 0.94 g. (88%) of oily 1,1-dimethyl-2(1H)-naphthalenone (IIIa), b.p. 60°(1.5 mm.); spectra: ultraviolet (95% ethanol), λ_{max} 230 mμ (ε 24,000) and 310 mμ (ε 5640), λ_{min} 255 mμ (ε 1300); infrared(CCl_4), C=O, 6.03(s)μ; C=C, 6.20(m)μ.

Anal. Calcd. for $C_{12}H_{12}O$: C, 83.69; H, 7.02. Found: C, 83.61; H, 7.21.

Its red 2,4-dinitrophenylhydrazone was crystallized from ethanol–ethyl acetate, m.p. 230–231°.

Anal. Calcd. for $C_{18}H_{16}O_4N_4$: C, 61.37; H, 4.58; N, 15.90. Found: C, 61.20; H, 4.61; N, 16.17.

Freshly distilled methylene iodide (30 ml.) was added to the sodio salt of 1.00 g. of 1-methyl-2-naphthol (IIc) and the mixture refluxed for 4 hr. After the same work-up as above 0.66 g. of the oily product was chromatographed on alumina. Elution with petroleum ether and crystallization of the eluate from ether gave 30 mg. (3%) of the ether IV, m.p. 146–147°; spectra: ultraviolet (95% ethanol), λ_{max} 222 mμ (ε 35,300), 234 mμ (ε 54,000) and 280 mμ (ε 4750); $\lambda_{shoulder}$ 270 mμ (ε 2900) and 290 mμ (ε 2440); λ_{min} 225 mμ (ε 35,200), 250 mμ (ε 2480) and 305 mμ (ε 1080); infrared (CCl_4), C=C, 6.20 (m) and 6.30 (w)μ.

Anal. Calcd. for $C_{23}H_{20}O_2$: C, 84.12; H, 6.12. Found: C, 84.27; H, 5.84.

Further elution with 5:1 petroleum ether–benzene gave 0.55 g. (29%) of 1-methyl-1-iodomethyl-2(1H)-naphthalenone (IIId) as an oil, b.p. 84°(1.5 mm.); spectra: ultraviolet (95% ethanol), λ_{max} 232 mμ (ε 30,000) and 310 mμ (ε 7450); λ_{min} 255 mμ (ε 2250); infrared(CCl_4), C=O, 6.05 (s)μ, C=C, 6.21(m)μ.

Anal. Calcd. for $C_{12}H_{11}OI$: I, 42.58. Found: I, 42.04.

A mixture of 50 mg. of IV in 15 ml. of 95% alcohol and 5 ml. of 2 *N* hydrochloric acid was heated for 15 min. and left standing for 24 hr. at room temperature. After extraction with ether, drying of the extract and vacuum removal of the solvent, the crude product, 35 mg., was chromatographed on alumina. Elution with 5:1 petroleum ether–benzene yielded 20 mg. of 1-methyl-2-naphthol (IIc), m.p. 106–108°.

Methylene chloride, 30 ml., was added to the sodio salt of 1.00 g. of IIc in a Pyrex tube, the latter sealed and heated at 100° for 8 hr. Upon work-up of the contents of the tube in the manner described above 0.85 g. of a crude solid was obtained, which on alumina chromatography and elution

(13) K. Ch. Gulati, S. R. Seth and K. Venkataraman, *J. prakt. Chem.*, **137**, 47 (1933).

(14) F. J. McQuillin and R. Robinson, *J. Chem. Soc.*, 586 (1941).

with petroleum ether gave 0.10 g. (10%) of crystalline IV, m.p. 146–147° after crystallization from ether. Elution with 5:1 petroleum ether–benzene yielded 0.42 g. (32%) of 1-methyl-1-chloromethyl-2(1H)-naphthalenone (IIIc) as an oil; spectra: ultraviolet (95% ethanol), λ_{max} 232 mμ (ε 30,400) and 310 mμ (ε 8540), λ_{min} 255 mμ (ε 2160); infrared (CCl_4), C=O, 6.03(s)μ; C=C, 6.18(m)μ.

Anal. Calcd. for $C_{12}H_{11}OCl$: C, 69.74; H, 5.36. Found: C, 69.98; H, 5.71.

Its red 2,4-dinitrophenylhydrazone crystallized from ethanol–ethyl acetate, m.p. 184–185°.

A mixture of the sodio salt of 1.00 g. of IIc and 30 ml. of chloroform was refluxed for 4 hr. After the mixture was washed with water, the chloroform solution dried and the solvent removed, the crude residue was chromatographed on alumina. Elution with petroleum ether gave first 10 mg. of an unidentified substance, m.p. 220–235°, and then 0.90 g. (60%) of 1-methyl-1-dichloromethyl-2(1H)-naphthalenone (IIIe), m.p. 64–65° after crystallization from chloroform–petroleum ether (lit.[15] 65°).

A mixture of the sodio salt of 1.00 g. of IIc and 30 ml. of *n*-butyl iodide was refluxed for 4 hr. After a work-up as before, the crude product was chromatographed on alumina. Elution with petroleum ether yielded 0.36 g. (29%) of an oil which became crystalline on standing, m.p. 33–36°. Crystallization from petroleum ether gave *n*-butyl 1-methyl-2-naphthyl ether (IIh), m.p. 35–36°; spectra: ultraviolet (95% ethanol), λ_{max} 232 mμ (ε 65,300) and 282 mμ (ε 5500), $\lambda_{shoulder}$ 272 mμ (ε 4430) and 292 mμ (ε 4360), λ_{min} 252 mμ (ε 2220) and 305 mμ (ε 1430); infrared (CCl_4), C=C, 6.19(m), 6.31(m)μ.

Anal. Calcd. for $C_{15}H_{18}O$: C, 84.07; H, 8.47. Found: C, 84.13; H, 8.62.

Elution with 5:1 petroleum ether–benzene yielded 0.65 g. (50%) of 1-methyl-1-(*n*-butyl)-2(1H)-naphthalenone (IIIb) as an oil, b.p. 93–95°(1.3 mm.); infrared spectrum (CCl_4), C=O, 6.05(s)μ; C=C, 6.20(m)μ.

Anal. Calcd. for $C_{15}H_{18}O$: C, 84.07; H, 8.47. Found: C, 83.94; H, 8.86.

Its red 2,4-dinitrophenylhydrazone could be crystallized from ethanol, m.p. 125–126°.

Anal. Calcd. for $C_{21}H_{22}O_4N_4$: C, 63.94; H, 5.62; N, 14.21. Found: C, 63.64; H, 5.73; N, 14.4.

Methylation of 1-Alkyl-2-naphthols (II).—A mixture of the sodio salt of 1.00 g. of IIe and 30 ml. of freshly distilled methyl iodide was refluxed for 4 hr. After the usual work-up the crude product was chromatographed on alumina. Elution with petroleum ether yielded 0.32 g. (30%) of oily methyl 1-(*n*-butyl)-2-naphthyl ether (IIi), b.p. 120°(1.5 mm.); spectra: ultraviolet (95% ethanol), λ_{max} 232 mμ (ε 70,500) and 282 mμ (ε 6160), $\lambda_{shoulder}$ 272 mμ (ε 4640) and 295 mμ(ε 5310), λ_{min} 252 mμ (ε 2320) and 305 mμ (ε 1740): infrared(CCl_4), C=C, 6.19(m), 6.30(m)μ.

Anal. Calcd. for $C_{15}H_{18}O$: C, 84.07; H, 8.47. Found: C, 84.28; H, 8.54.

Elution with 5:1 petroleum ether–benzene gave 0.63 g. (59%) of oily 1-methyl-1-(*n*-butyl)-2(1H)-naphthalenone (IIIb); infrared and ultraviolet spectra identical with those of IIIb above; 2,4-dinitrophenylhydrazone, m.p. 125–126° after crystallization from ethanol, no depression on admixture with a sample above.

Alumina chromatography and elution with 1:1 petroleum ether–benzene of the crude products from a 4-hr. reflux of the sodio salt of 1.00 g. of 1-(γ-hydroxybutyl)-2-naphthol (IIk) and 30 ml. of methyl iodide led to a solid, which on crystallization from petroleum ether–carbon tetrachloride yielded 0.25 g. (23%) of methyl 1-(γ-hydroxybutyl)-2-naphthyl ether (III), m.p. 61–62°; spectra: ultraviolet (95% ethanol), λ_{max} 232 mμ (ε 109,000) and 282 mμ (ε 11,100), $\lambda_{shoulder}$ 270 mμ (ε 8830) and 295 mμ (8900), λ_{min} 252 mμ (ε 4150) and 305 mμ (ε 294 0); infrared(CCl_4), OH, 2.84 (m)μ; C=C, 6.20(m)μ.

Anal. Calcd. for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.53; H, 7.99.

Elution with benzene gave 0.58 g. (54%) of 1-methyl-(γ-hydroxybutyl)-2-(1H)-naphthalenone (IIIg) as an oil; spectra: ultraviolet (95% ethanol), λ_{max} 232 mμ (ε 62,000) and 300 mμ (ε 8150), λ_{min} 252 mμ (ε 1490); infrared (CCl_4), OH, 2.80(w)μ(shoulder), 2.90(m)μ; C=O, 6.07(s)μ; C=C, 6.20(m)μ.

Anal. Calcd. for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.35; H, 8.00.

Its 3,5-dinitrobenzoate was crystallized from carbon tetrachloride, m.p. 138–139°.

Anal. Calcd. for $C_{22}H_{20}O_7N_2$: C, 62.26; H, 4.75. Found: C, 62.18; H, 4.82.

A mixture of 200 mg. of the ether III and 0.5 ml. of concentrated hydrochloric acid in 30 ml. of 60% aqueous ethanol was refluxed for 3 hr. The mixture was extracted with ether, the extract washed with water, dried and the solvent evaporated. Alumina chromatography of the crude residue and elution with petroleum ether gave 82 mg. (48%) of 2-methyl-5,6-benzochroman (VI), m.p. 90–91° after crystallization from hexane (lit.[14] 90–91°); spectra: ultraviolet (95% ethanol), λ_{max} 234 mμ (ε 60,000) and 280 mμ (ε 4680), $\lambda_{shoulder}$ 270 mμ (ε 4130) and 290 mμ (ε 3770), λ_{min} 250 mμ (ε 2440) and 300 mμ (ε 992); infrared (CCl_4), C=C, 6.19(m), 6.28(m)μ. Elution with benzene first gave a solid, which after crystallization from CCl_4 proved to be starting material (45 mg., 22%), and secondly another solid, which on crystallization from ether yielded 12 mg. (6%) of demethylated 1-(γ-hydroxybutyl)-2-naphthol (IIk), m.p. 135–137°, identical in all respects with the sample above.

A mixture of 200 mg. of 1-(γ-ketobutyl)-2-naphthol (IIf), sodium methoxide, prepared by the dissolution of 20 mg. of sodium in 15 ml. of methanol, and 10 ml. of methyl iodide was refluxed for 2 hr. The cooled mixture was diluted with water and extracted with ether. The extract was washed with water, dried over magnesium sulfate and evaporated. The residue, 135 mg. (59%), was crystallized from hexane, yielding crystalline methyl 1-(γ-ketobutyl)-2-naphthyl ether (IIj), m.p. 54°; spectra: ultraviolet (95% ethanol), λ_{max} 232 mμ (ε 100, 500) and 280 mμ (ε 9600), $\lambda_{shoulder}$ 270 mμ (ε 7650) and 295 mμ (ε 7960), λ_{min} 252 mμ (ε 4550) and 305 mμ (ε 2440); infrared (CCl_4), C=O, 5.85(s)μ; C=C, 6.19(m), 6.31(m)μ.

Anal. Calcd. for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 78.93; H, 6.90.

Treatment of the dry sodio salt of 1-(γ-ketobutyl)-2-naphthol (IIf) with methyl iodide, under reaction conditions and subsequent work-up identical with the cases described above, led to a crude product which was chromatographed on alumina. Elution with petroleum ether gave a solid, which on crystallization from hexane proved to be methyl 1-methyl-2-naphthyl ether (IIg), m.p. and m.m.p. 37–38°; identical spectra with those of an authentic sample. Elution with 10:1 petroleum ether–benzene gave another solid, which after crystallization from hexane could be shown to be methyl 1-(α-ketobutyl)-2-naphthyl ether (IIj), m.p. and m.m.p. 54°; identical spectra with those of above sample of IIj. Further elution with the same solvent mixture yielded intimate oily mixtures of ketonic material, some fractions of which revealed an identical infrared spectrum with that of 1-methyl-1-(γ-ketobutyl)-2(1H)-naphthalenone (IIIf) (*vide infra*). Finally, elution with benzene afforded the phenolic products. A solid was shown to be starting material, m.p. 86–89° after one crystallization from petroleum ether–carbon tetrachloride. Evaporation of the mother liquor and sublimation of the residue yielded another solid, which on crystallization from the same solvent pair could be identified as 1-methyl-2-naphthol (IIc), m.p. 109–110°; infrared spectrum identical with that of an authentic sample.

1-Methyl-1-(γ-ketobutyl)-2(1H)-naphthalenone (IIIf).—A chromic acid solution, 250 mg. of chromic oxide dissolved in 1 ml. of water and 12 ml. of glacial acetic acid, was added to a solution of 0.50 g. of 1-methyl-1-(γ-hydroxybutyl)-2(1H)-naphthalenone (IIIg) in 13 ml. of glacial acetic acid, and the mixture allowed to stand at room temperature for 3 hr. The mixture then was diluted with water and extracted with ether, the extract washed with 2% sodium hydroxide solution and then with water, dried over magnesium sulfate and the solvent evaporated. The crude product was chromatographed on alumina. Elution with 5:1 petroleum ether–benzene gave 0.41 g. (82%) of the diketone IIIf as an oil; infrared spectrum (CCl_4), C=O, 5.81(s), 6.03(s)μ; C=C, 6.18(m)μ.

(15) (a) F. Bell and H. W. Hunter, *J. Chem. Soc.*, 2903 (1950); (b) R. M. Dodson and W. P. Webb, THIS JOURNAL, **73**, 2767 (1951); (c) E. Wenkert and T. E. Stevens, *ibid.*, **78**, 5627 (1956).

Anal. Calcd for $C_{16}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 80.20; H, 7.00.

Its orange *mono*-2,4-dinitrophenylhydrazone, m.p. 155–156° after crystallization from ethanol–ethyl acetate, exhibited no infrared peak for a saturated carbonyl group, but did reveal the conjugated C=O 6.03(s)μ, a C=N 6.18(s)μ and C=C 6.25(s)μ bands.

Anal. Calcd. for $C_{21}H_{20}O_5N_4$: C, 61.76; H, 4.94; N, 13.72. Found: C, 61.61; H, 5.27; N, 13.72.

A sodium ethoxide solution, 10 mg. of sodium in 20 ml. of dry ethanol, of 50 mg. of the diketone IIIf was kept at room temperature for 8 hr. The solution then was acidified with acetic acid, concentrated to reduced volume, diluted with water and extracted with ether. The extract was dried over magnesium sulfate, the solvent evaporated and the residue chromatographed on alumina. Elution with 10:1 petroleum ether–ether gave 30 mg. (85%) of 1-methyl-2-naphthol (IIc), m.p. and m.m.p. 109–110°; infrared spectrum identical with that of an authentic sample.

A potassium *t*-butoxide solution, 10 mg. of potassium in 10 ml. of *t*-butyl alcohol, of 100 mg. of the diketone IIIf was kept at room temperature for 10 hr. The mixture was diluted with water, neutralized with acetic acid and extracted with ether. The organic extract was washed with water, dried over anhydrous magnesium sulfate and evaporated to dryness. Alumina chromatography of the oily residue and elution with 20:1 petroleum ether–ether led to 25 mg. of an oil. Elution with 10:1 petroleum ether–ether yielded 55 mg. (78%) of 1-methyl-2-naphthol (IIc), as identified by m.p. and infrared and ultraviolet spectra. Rechromatography of the oily eluate on 50:50 Celite–silicic acid and elution with 10:1 petroleum ether–ether gave 8 mg. (8%) of diketone VII, m.p. 105–107° (lit.[4] 108–109°), identical infrared spectrum with that of an authentic specimen. Elution with 5:1 petroleum ether–ether produced 10 mg. of an unidentified solid, m.p. 176–179° after crystallization from petroleum ether–carbon tetrachloride.

Reductions of 1,1-Dialkyl-2(1H)-naphthalenones (III). (a) **Catalytic Hydrogenation.**—In every one of the following cases an ethanol solution of the unsaturated ketone was hydrogenated over 10% of its weight of 5% palladium-on-charcoal at room temperature and atmospheric pressure until hydrogen uptake ceased. After filtration of the catalyst and vacuum removal of the solvent, the residue was chromatographed on alumina.

1,1-Dimethyl-2(1H)-naphthalenone (IIIa), 0.50 g., was converted to 0.42 g. of crude material, whose chromatogram yielded 0.31 g. (62%) of oily 1,1-dimethyl-2-tetralone on elution with petroleum ether; infrared spectrum (CCl_4), C=O, 5.83(s)μ; its 2,4-dinitrophenylhydrazone, m.p. 139–140° after crystallization from ethanol (lit.[7] 140–141°).

Hydrogenation of 50 mg. of 1-methyl-1-(γ-ketobutyl)-2(1H)-naphthalenone (IIIf) led to 15 mg. of an unidentified solid on petroleum ether elution, m.p. 50–56° after crystallization with petroleum ether; spectra: ultraviolet (95% ethanol), λ_{max} 266 mμ (ϵ 760) and 272 mμ (ϵ 730), λ_{min} 248 mμ (ϵ 496) and 270 mμ (ϵ 595); infrared (CCl_4), no OH or C=O bands. Elution with 10:1 petroleum ether–benzene gave 8 mg. (16%) of 1-methyl-1-(γ-ketobutyl)-2-tetralone (VIII) as an oil; spectra: ultraviolet (95% ethanol), λ_{max} 265 mμ (ϵ 482) and 272 mμ(ϵ 480), λ_{min} 248 mμ (ϵ 322) and 270 mμ (ϵ 374); infrared (CCl_4), C=O, 5.83(s)μ (*vide infra*). Elution with benzene led to 20 mg. (40%) of the ketol IX-X, m.p. 147–149° after crystallization from hexane–carbon tetrachloride; infrared spectrum (CCl_4), OH, 2.79(w), 2.91(w)μ; C=O, 5.83 (s)μ.

Anal. Calcd. for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.39; H, 8.34.

Hydrogenation of 0.40 g. of 1-methyl-1-(γ-hydroxybutyl)-2(1H)-naphthalenone (IIIg) produced 0.38 g. of a reaction mixture, infrared spectrum (CCl_4), OH, 2.85(w)μ; C=O, 5.84(m)μ, which was used for oxidation without further purification.

(b) **Chemical Reduction.**—A solution of 120 mg. of 1-methyl-1-(γ-hydroxybutyl)-2(1H)-naphthalenone (IIIg) in 10 ml. of dry ethanol and 50 ml. of liquid ammonia was stirred while 500 mg. of lithium wire was added over a 15-min. period. After addition of 20 ml. of ether and the gradual fading of the blue color of the solution, the ammonia was allowed to evaporate, 150 ml. of water added, and the aqueous layer extracted with ether. The combined extracts were washed with saturated brine solution, dried over magnesium sulfate and evaporated to dryness. The resulting oily diol mixture was used for oxidation without further purification.

Chromic Acid Oxidations.—The procedure utilized for the synthesis of IIIf (*vide supra*) was followed for each of the following cases.

Chromic acid oxidation of 100 mg. of the reaction mixture from the hydrogenation of IIIg yielded 75 mg. of crude products which on alumina chromatography and elution with 10:1 petroleum ether–benzene gave 65 mg. (65%) of 1-methyl-1-(γ-ketobutyl)-2-tetralone (VIII); spectra identical with those of the samples described above and below.

Oxidation of the product mixture from the lithium reduction of IIIf yielded 99 mg. (82% over-all) of spectrally pure VIII (*vide supra*).

Anal. Calcd. for $C_{15}H_{18}O_4$: C, 78.23; H, 7.88. Found: C, 78.40; H, 8.10.

Its orange bis-2,4-dinitrophenylhydrazone was crystallized from ethanol, m.p. 181–182°.

Anal. Calcd. for $C_{27}H_{26}O_8N_8$: C, 54.92; H, 4.43. Found: C, 55.36; H, 4.39.

Tricyclic Ketones I and IX-X.—A sodium methoxide solution (from 10 mg. of sodium) of 25 mg. of 1-methyl-1-(γ-ketobutyl)-2-tetralone (VIII) in 15 ml. of dry methanol was kept in the refrigerator for 10 hr. After addition of water and ether the aqueous layer was extracted with ether. The combined extracts were dried over magnesium sulfate, whereupon the solvent was evaporated and the oily residue chromatographed on 1:1 Celite–silicic acid. Elution with 10:1 petroleum ether–ether yielded 12 mg. (48%) of a solid, m.p. 140–143°. Crystallization from hexane–carbon tetrachloride gave ketone IX-X, m.p. 147–149°; identical spectra with those of sample above.

A sodium methoxide solution (50 mg. of sodium in 30 ml. of dry methanol) of 100 mg. of VIII was refluxed for 4 hr. The solution then was acidified with acetic acid, the solvent removed under vacuum and the remaining oil dissolved in ether. The resultant solution was washed with water, dried over magnesium sulfate and evaporated to dryness. The crude residue, 76 mg., was chromatographed on alumina. Elution with 5:1 petroleum ether–benzene led to 65 mg. (70%) of tricyclic ketone I, m.p. and m.m.p. 89–90° after crystallization from hexane (lit.[4] 89–90°); spectra identical with those of an authentic sample.