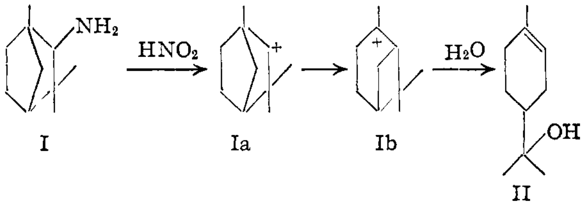
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA]

A Rearrangement of Camphenilone[1]

BY DONALD S. NOYCE

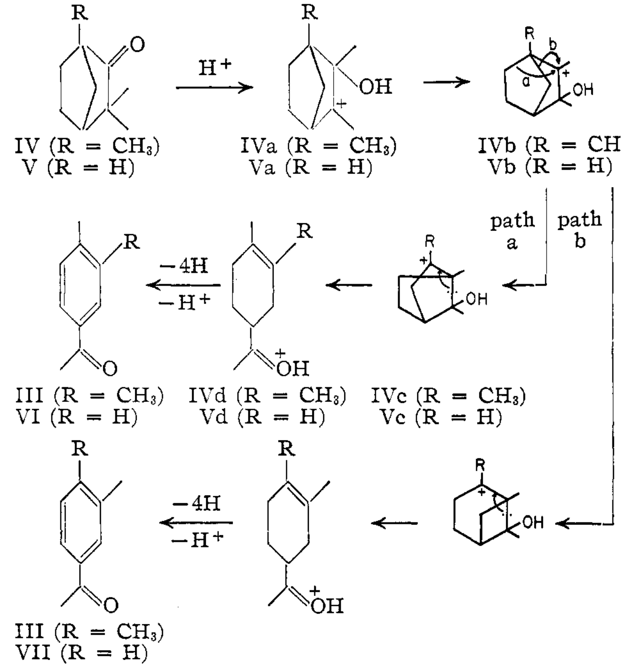
Among the many acid catalyzed rearrangements in the terpene series, there are several which seem to involve rearrangement of the camphane or fenchane skeleton to the pinane skeleton before subsequent reactions leading to the final observed products.

Hückel[2] has recently studied in detail the rearrangement undergone by fenchylamine (I) when treated with nitrous acid; one of the products is terpineol (II). Clearly, only initial migration of the intermediate fenchyl ion (Ia) to the pinyl ion (Ib) will explain the formation of II. Other cases are not so well defined.



Another rearrangement which may be explained on similar grounds is the formation of 3,4-dimethylacetophenone (III) (among other products) from camphor.[3] Fenchone (IV) is a likely intermediate in this reaction and, in fact, rearranges to III under similar conditions.[4] However, the rearrangement–dehydrogenation of IV is possible by two paths (Chart I), which both afford III. The present investigation was undertaken to determine with a reasonable degree of assurance which pathway represents the course of the reaction.

CHART I



The difference in the two paths lies in the position occupied by the 1-methyl group of fenchone (R in IV) in the final product. It was of interest therefore, to study the rearrangement of camphenilone (V, R = H) under similar conditions. Here the two pathways lead to two possible products, VI or VII, and one would expect to be able to distinguish the likely path for the reaction on the basis of the product obtained.

When camphenilone was heated with concentrated sulfuric acid under the conditions of Zaugg,[4b] a small amount of *p*-methylacetophenone (VI) was isolated, along with much recovered V. Under somewhat more drastic conditions (120°, one hour) a 15% yield of VI was obtained with very little unreacted V. Characterization of the semicarbazone, and hypobromite oxidation to *p*-toluic acid established that VI was the major product of the reaction. Careful examination failed to reveal any trace of the isomeric *m*-toluic acid from the hypobromite oxidation.

The steps in the proposed reaction sequence are all known individually. V is converted by acid to its salt, which undergoes a reverse pinacol-type rearrangement to Va, followed by migration to the isomeric ion Vb. Vb rearranges to Vc (compare camphene hydrochloride to isobornyl chloride) followed by ring cleavage (Vd). The final dehydrogenation of Vd is analogous to the aromatization mechanism which has been suggested by Doering and Beringer[5] for a similar reaction. The somewhat lower yields in the case of V compared with IV may well be due to a somewhat higher activation energy for the rearrangement process due to the necessity of the carbonium ion in the intermediate Vc being secondary rather than tertiary as in the case of IVc.

It thus seems probable that where two paths of essentially equal probability are open for rearrangement, migration to the pinane system is seldom observed. The rearrangement of cam-

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(1) Presented before the Division of Organic Chemistry, at the San Francisco Meeting of the American Chemical Society, March 30, 1949.

(2) (a) Hückel and Wolowski, *Chem. Ber.*, **80**, 39 (1947); (b) Wallach and Vivck, *Ann.*, **368**, 178 (1909).

(3) Armstrong and Kipping, *J. Chem. Soc.*, **63**, 76 (1893).

(4) (a) Marsh, *ibid.*, **75**, 1058 (1899); (b) Zaugg, THIS JOURNAL, **67**, 1861 (1945).

(5) W. E. Doering and F. M. Beringer, *ibid.*, **71**, 2221 (1949).

phorquinone to 2,2,3-trimethylcyclohexan-4-one-1-carboxylic acid is another case where it has recently been established that the product resulting from migration to the pinane system is not obtained.[6]

Experimental[7]

Camphenilone (V) was prepared by the method of Snitter[8] from camphene[9]; m. p. 36–37°, b. p. 191–193°.

Rearrangement of Camphenilone.—The fate of V under a variety of conditions is summarized in Table I.

TABLE I

Reagent	Temp., °C.	Time	Volatile, %	Recov. V, %	VI isolated, %
H_2SO_4	95–100	1 hr.	26	17	..
H_2SO_4	110	20 min.	15	7.5	7.5
H_2SO_4	120	1 hr.	18	2	14.5
Fum. sul. Ac_2O	R. T.	2 days	5	5	..

The best conditions are as follows: Sulfuric acid (40 ml.) was heated to 65° in a 3-neck, 200-ml. r. b. flask with stirrer, thermometer and exit tube for sulfur dioxide. V (13.8 g., 0.1 mole) was added all at once. The temperature rose to 75°, and there was appreciable darkening. The mixture was then heated to maintain a temperature of 110–120° for one hour, during which time there was a vigorous evolution of sulfur dioxide and considerable charring. After cooling to room temperature, the contents of the flask were poured into 250 ml. of water and steam distilled. The distillate was extracted three times with ether, the ethereal solution washed with 1 *N* sodium hydroxide, dried and concentrated. The yield of crude product was 2.50 g. (18.5%). Distillation afforded pure VI, b. p. 221°, n^{20}_{D} 1.5330.

A solution of 0.5 g. of the crude product in dilute ethanol was treated with semicarbazide hydrochloride and sodium acetate on the steam-bath. On cooling, *p*-methylacetophenone semicarbazone crystallized in 80% of the theoretical yield, m. p. 204.5–205.5°.[10] There was no depression of the m. p. of an authentic sample.

The mother liquors on standing overnight yielded a further crop of crystals (10%) which was largely camphenilone semicarbazone, m. p. 210–217°. Recrystallization gave camphenilone semicarbazone, m. p. and mixed m. p. 222–224°.[11]

Oxidation to *p*-Toluic Acid.—One gram of crude VI was treated with excess sodium hypobromite at room temperature. After destroying the excess hypobromite, the solution was steam distilled to remove a small amount of camphenilone and acidified with sulfuric acid. The precipitate which formed was filtered off and sublimed to yield 0.6 g. of *p*-toluic acid, m. p. and mixed m. p. 179–180°.[12] Various fractions of the sublimate showed no difference in m. p. behavior.

Summary

Camphenilone rearranges to *p*-methylacetophenone when heated with concentrated sulfuric acid. A possible reaction mechanism is discussed.

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[6] Chakravarti, *J. Chem. Soc.*, 1565 (1947).

[7] Analyses by the Micro Analytical Laboratories of The University of California. Melting points are corrected.

[8] Snitter, *Bull. Inst. Pin.*, 178 (1933) (*C. A.*, **28**, 139 (1934)).

[9] Generously supplied by The Glidden Company.

[10] Sorge, *Ber.*, **35**, 1070 (1902).

[11] Jagelki, *ibid.*, **32**, 1503 (1899).

[12] Fischli, *ibid.*, **12**, 615 (1879).

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[A CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

The Stobbe Condensation with 6-Methoxy-2-propionylnaphthalene. A Synthesis of Bisdehydrodoisynolic Acid[1]

BY WILLIAM S. JOHNSON AND ROBERT P. GRABER[2]

Bisdehydrodoisynolic acid, VI (R = H), which is one of the most potent estrogens known, was discovered by Miescher, Heer and Billeter[3] as a degradation product of the hormone equilenin. In the course of their brilliant study the Swiss workers also effected the total synthesis of this important acid, starting from 1-naphthylamine-6-sulfonic acid (Cleve's acid).[3,4] Since the conversion of the latter substance into the necessary intermediate, *viz.*, β-(6-methoxynaphthyl)-ethyl bromide, is quite laborious,[5] we were prompted to investigate a completely different approach, starting with 6-methoxy-2-propionylnaphthalene (I) which is readily available by Friedel–Crafts acylation of β-methoxynaphthalene.[6] The details of this new synthesis, which is depicted in the accompanying flow sheet, are reported herewith.[7]

The Stobbe condensation of the ketone I with diethyl succinate and potassium *t*-butoxide[8] or sodium hydride[9] gave in practically quantitative yield an oily mixture of half-esters which upon catalytic hydrogenation over platinum followed by saponification afforded a mixture which was easily separated into the desired dihydro acid III (R = H) melting at 165° (49% yield) and a crystalline dibasic acid (27% yield), m. p. 172°, which was shown (see below) to be a molecular compound between an unsaturated acid (VII) (R = H) melt-

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[3] Miescher, *Helv. Chim. Acta*, **27**, 1727 (1944); Heer, Billeter and Miescher, *ibid.*, **28**, 991, 1342 (1945).

[4] Anner and Miescher, *ibid.*, **29**, 586 (1946).

[5] See Wilds and Close, THIS JOURNAL, **69**, 3079 (1947), for best procedures.

[6] Haworth and Sheldrick, *J. Chem. Soc.*, 864 (1934).

[7] A preliminary account of this work appears in THIS JOURNAL, **70**, 2612 (1948).

[8] *Cf.* Johnson, Petersen and Schneider, *ibid.*, **69**, 74 (1947).

[9] Carried out by Guido H. Daub according to the procedure of Daub and Johnson, *ibid.*, **70**, 418 (1948).