It was shown that no correction was needed for material in the gas phase during equilibration by equilibrating one sample with seven times as much free space as the other samples. The composition of this sample was identical with the others equilibrated at the same temperature. It was also shown that the method could be adapted to a smaller scale by equilibrating a sample of pure *cis*- and a sample of pure *trans*-hydrindane using 0.10 ml. of hydrindane and 20 mg. of 10% palladium-on-charcoal in 4-mm. Pyrex tubing. The results of these small scale runs were identical with those on a larger scale at the same temperature.

DETROIT 2, MICH.

[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

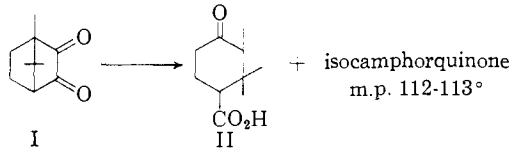
The Structure of Isocamphorquinone

BY SAMUEL G. LEVINE[1,2]

RECEIVED SEPTEMBER 26, 1959

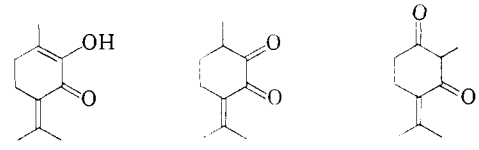
Isocamphorquinone has been shown to have the structure V.

Isocamphorquinone was first described by Manasse and Samuel[3] as an easily resinified product, $C_{10}H_{14}O_2$, resulting from the action of a cold fuming sulfuric acid mixture on camphorquinone (I). Also produced in this reaction was a keto-carboxylic acid, $C_{10}H_{16}O_3$, which has since been clearly identified[4] as 2,2,3-trimethyl-4-keto-cyclohexanecarboxylic acid (II).



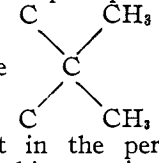
I II

Isocamphorquinone was found[5] to yield a urethan and a benzoate as well as an oxime and a phenylhydrazone—the derivatives, in each case, resulting from condensation with a single equivalent of reagent. In addition, the compound could be titrated as a mono-acid and gave various positive tests indicating olefinic, enolic and reducing properties. Based on these and certain other experiments (*vide infra*), Manasse and Samuel[5] assigned the dienolone structure III to isocamphorquinone[6]; the corresponding diketo modification IV was proposed by Bredt[7] during the same period. In the present communication it is shown that isocamphorquinone is in fact a tautomer of 2-methyl-6-isoproylidene-cyclohexane-1,3-dione (V).

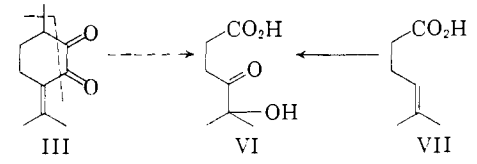


III IV V

The early ascription of a monocyclic carbon skeleton to isocamphorquinone resulted from its ease of oxidation by cold, dilute permanganate solution. The main product of this reaction was a keto-acid, m.p. 97–98° (semicarbazone, m.p. 199–200°), formulated by Bredt as 5-hydroxy-5-methyl-4-ketohexanoic acid (VI). Although this assignment originally rested only on the simultaneous isolation of succinic acid and acetone as "further decomposition products," its correctness has been shown by later work. Thus, Staudinger and co-workers[8] have prepared 5-methyl-Δ^4-hexenoic acid (VII) which, on permanganate oxidation, produced acetone, succinic acid and a hydroxyketo-acid $C_7H_{12}O_4$, m.p. 97° (semicarbazone, m.p. 198–200°), in close agreement with Bredt's data. The above experiment led, then, to the suggestion[7a] that the dimethylcarbinyl bridge of camphorquinone is broken in isocamphorquinone for, were it still present, the



stable moiety should have been found intact in the permanganate oxidation product. That this grouping is here the precursor of an isopropylidene function (as in III or IV) was early inferred from the production of acetone, in high



III VI VII

(1) U. S. Public Health Service pre-doctoral fellow 1952–1953. Present address: Eastern Regional Research Laboratory, U. S. Department of Agriculture, Philadelphia 18, Pa.

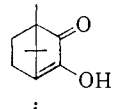
(2) Abstracted from the Ph.D. Thesis of Samuel G. Levine, Harvard University, December, 1953. The author is happy to acknowledge with thanks the guidance of Professor R. B. Woodward during the course of this research.

(3) (a) O. Manasse and E. Samuel, *Ber.*, **30**, 3157 (1897); (b) **31**, 3258 (1898).

(4) R. N. Chakravarti, *J. Chem. Soc.*, 1565 (1947).

(5) O. Manasse and E. Samuel, *Ber.*, **35**, 3829 (1902).

(6) It may be of interest that the first structure assigned (ref. 3b) by these authors was i, the hypothetical enolic form of isocamphorquinone.



i

Their later rejection (ref. 5) of this prohibitively strained structure was due to the failure of isocamphorquinone to yield camphor glycol on reduction.

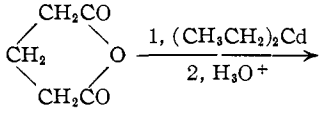
(7) (a) J. Bredt, F. Rochussen and J. Monheim, *Ann.*, **314**, 389 (1901). (b) Isocamphorquinone is represented as Bredt's structure (IV) in J. L. Simonsen, "The Terpenes," Vol. II, Cambridge University Press, Cambridge, 1939, p. 469, and in E. H. Rodd, "The Chemistry of Carbon Compounds," Vol. II, part B, Elsevier Publishing Co., New York, N. Y., 1953, p. 613.

(8) H. Staudinger, W. Kreis and W. Schilt, *Helv. Chim. Acta*, **5**, 743 (1922).

yield, on acidic hydrolysis of isocamphorquinone.[9] The other product of this reaction—and one of especial structural significance—is a $C_7H_{12}O_3$ carboxylic acid (VIII), m.p. 51–52°.

In our view, the production of a carboxylic acid on acidic hydrolysis of isocamphorquinone cannot be satisfactorily explained in terms of the previous structural proposals. Furthermore, the reported[5] failure of the substance to yield a quinoxaline derivative (on treatment with *o*-phenylenediamine[10]) seemed, likewise, anomalous for the putative 1,2-dione system and prompted us to re-examine the chemistry of this compound.

Repetition of the preparation of isocamphorquinone, essentially by the published method, gave the expected product, m.p. 112–113°, which formed the known phenylhydrazone, m.p. 170–172°, and oxime, m.p. 119–121°. On treatment with diazomethane in methanol-ether, a crystalline product $C_{11}H_{16}O_2$ (methyl ether), m.p. 83–85°, was obtained. By heating isocamphorquinone in dilute sulfuric acid, we were able to verify its conversion to acetone (isolated as the 2,4-dinitrophenylhydrazone) and a carboxylic acid, m.p. 52°. *Although the German authors considered this compound to be a hydroxy-acid, our product could be established as a keto-acid by conversion to an oxime, m.p. 116–118°, and a semicarbazone, m.p. 186–188° dec.* These properties were found to be in general agreement with those recorded for 5-ketoheptanoic acid.[11] An authentic



$CH_3CH_2COCH_2CH_2CH_2COOH$

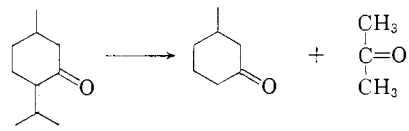
sample of this acid, prepared from glutaric anhydride and diethylcadmium, yielded corresponding derivatives of identical melting points, not depressed on admixture. The equation for the hydrolytic cleavage of isocamphorquinone may now be given as

$$C_{10}H_{14}O_2 + 2H_2O \xrightarrow{H^+} CH_3COCH_3 + CH_3CH_2CO(CH_2)_3COOH$$

VIII

The structural significance of these degradation products was further advanced by finding that they are also obtained by alkaline hydrolysis of isocamphorquinone. This similarity of reaction course at either *p*H extreme led us to expect that the relationship between isocamphorquinone and these cleavage products is a simple one, involving no rearrangement but only simple hydrolytic processes.

(9) The hydrolytic cleavage of pulegone (ii) to acetone and 3-



ii

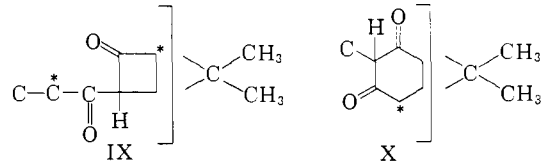
methylcyclohexanone had been discovered a few years earlier; O. Wallach, *Ann.*, **289**, 337 (1896).

(10) The product of this reaction, $C_{16}H_{20}ON_2$, corresponds to condensation with loss of only one molecule of water.

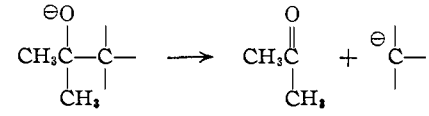
(11) E. E. Blaise and M. Maire, *Bull. soc. chim.*, [4] **3**, 424 (1908).

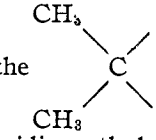
There are several $C_{10}H_{14}O_2$ structures which, on acidic as well as alkaline hydrolysis, could yield acetone and 5-ketoheptanoic acid. Most of these hypothetical isocamphorquinone formulations are not, however, compatible with Bredt's permanganate oxidation product VI. In particular, one need consider only those condensed systems which include a dimethylcarbinyl group to account for the dimethylcarbinol system found in VI. Furthermore, since no such grouping—actual or potential—obtains in 5-ketoheptanoic acid, it follows that the three carbon atoms involved must be those which appear as acetone on hydrolysis.

It is pertinent now to consider the likely manner by which the carboxyl group of 5-ketoheptanoic acid (VIII) originates[12] on hydrolysis of isocamphorquinone. We regard the generation of this function under acidic as well as alkaline conditions from a highly enolic starting substance to be, in all, strongly indicative of a 1,3-dione precursor system. These conditions would be satisfied by assigning to isocamphorquinone one of the part structures IX or X. *Indeed, all alternative β-diketone types are ruled out by their lack of the required intact dimethylcarbinyl group.*

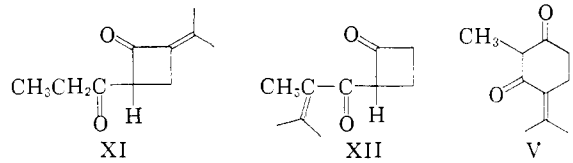


The location of this three-carbon moiety in IX or X is evidenced by its hydrolytic conversion to acetone which (*e.g.*, under alkaline conditions) likely involves the process



Thus, the  group must be attached to one

of the acidic methylene groups (*) in the above part structures.[13] Three specific $C_{10}H_{14}O_2$ formulations for isocamphorquinone may, in this way, be derived.



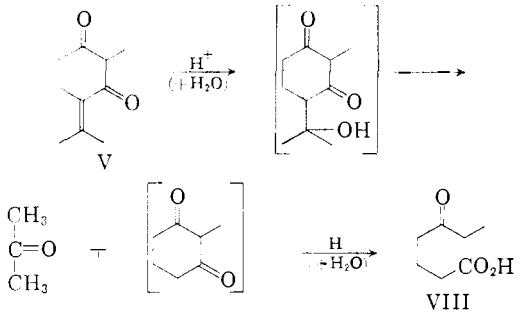
Further, since neither XI nor XII would be expected to yield the ketol-carboxylic acid VI on permanganate oxidation, we propose V (and its tautomers)[14] as the structure of isocamphorquinone.

(12) That no carboxyl function is initially present in this compound can be concluded from the lack of infrared absorption bands between 5.5 and 6.0μ in the spectrum of isocamphorquinone methyl ether.

(13) The acidic *tertiary* positions of IX and X must, of course, be maintained to allow for the highly enolic nature of isocamphorquinone.

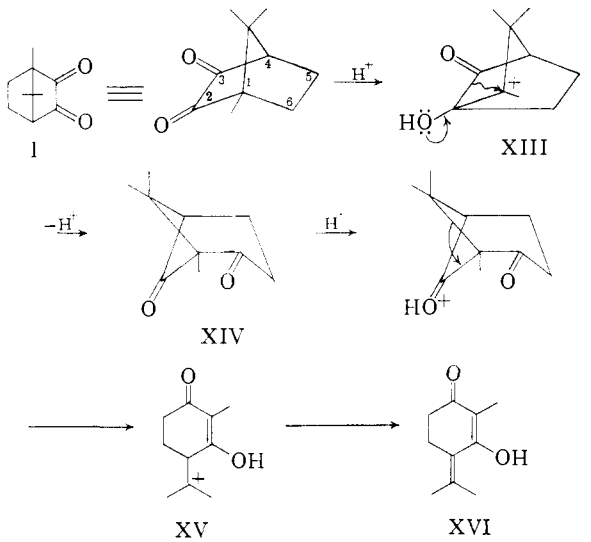
(14) Spectral measurements indicate that the dione V, in chloroform solution, is converted to an equilibrium mixture involving enolic tautomers; see Experimental.

The course of hydrolysis (*e.g.*, acid catalyzed) of isocamphorquinones can now be detailed as a reverse aldol condensation followed by β-diketone cleavage.



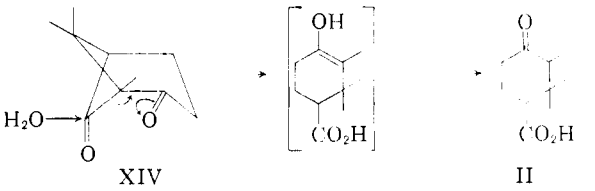
V VIII

Turning again to the *formation* of isocamphorquinone, we may propose a rational path by which this unusual rearrangement might be thought to occur. A solution of camphorquinone (I) in fuming sulfuric acid could undergo protonation at the C(2) carbonyl group with rearrangement to the oxygenated camphene-hydro cation[15] XIII.[16] The ensuing semipinacolic shift gives rise to an electrically neutral intermediate, the (3,1,1)bicycloheptane derivative XIV. Protonation of XIV at the C(3) carbonyl and heterolysis of the C(1)–C(7) bond leads to the tertiary carbonium ion XV which, in turn, is simply related by proton loss to an enol form (XVI) of isocamphorquinone.



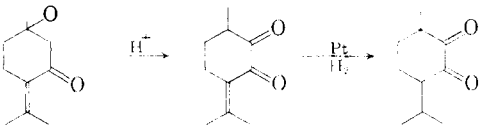
I XIII XIV XV XVI

Manasse and Samuel have found that, on treatment with concentrated (instead of fuming) sulfuric acid, camphorquinone is converted *predominantly* to the keto-carboxylic acid II. This product could result from attack of water on the protonated form of the intermediate bicyclic dione XIV with resulting β-diketone cleavage, leading to the enolate of II.



XIV II

In conclusion, it is interesting to draw attention to a recent paper[17] concerning the properties of a new terpene ketone $C_{10}H_{14}O_2$ (XVII) from the oil of *Mentha rotundifolia*. This substance, on steam distillation from dilute sulfuric acid, gave an isomeric, highly enolic product, m.p. 74.5°, formulated by the author as an enol form[18] of IV, the previously accepted structure for isocamphorquinone.



XVII (IV) diosphenol m.p. 83–83.5°

Experimental[19]

Isocamphorquinone (V).—A mixture[20] of concentrated sulfuric acid (175 ml., 98% H_2SO_4) and fuming sulfuric acid (42 ml., 30% SO_3) was protected from atmospheric moisture and cooled to −3° in a salt–ice-bath. Camphorquinone[21] (15 g.) was added inthree portions at about 30-second intervals with rapid stirring. A temporary rise in temperature of a few degrees with observed and within 20 minutes all of the diketone had dissolved in the acid mixture. The cold solution was then mixed with about 1000 g. of ice, stirred vigorously, and set aside at 5° for 4 hours. At that time the white, flocculent precipitate was collected, washed well with water, and dried *in vacuo* over concentrated sulfuric acid. The yield of crude, dry product varied from 5 to 9 g. (33 to 60%). Recrystallization of this material from methanol–water or benzene–cyclohexane gave isocamphorquinone as colorless prisms, m.p. 113–114°; ultraviolet spectrum: λ_{max} 294 (ε 12,800); infrared spectrum: bands at 2.8, 3.0–3.1, 5.81, 5.94 and 6.2μ. Freshly prepared solutions in chloroform had very little absorption in the 5.5–6.0μ region but gave rise to a very intense, poorly resolved band at 6.1–6.2μ. This absorption decreased in intensity on standing while that at 5.81 and 5.94μ increased. This phenomenon is likely due to the isomerization of isocamphorquinone from a completely enolic structure to an equilibrium mixture containing the dione form IV.

Isocamphorquinone oxime and isocamphorquinone phenylhydrazone were prepared by the procedure of Manasse and Samuel.[5] Our products had m.p. 119–121° and 171–172°, respectively. The German authors give m.p. 122–123° and 169–170°. The oxime had λ_{max} 252 mμ (ε 10,000); infrared spectrum: bands at 2.8, 3.0, 5.92 and 6.2 μ.

Isocamphorquinone Methyl Ether.—A solution of isocamphorquinone (1.66 g.) in ether (25 ml.) and methanol (15 ml.) was treated with a cooled solution of diazomethane (from 2.8 g. of nitrosomethylurea) in 100 ml. of 50% ether–methanol and kept at 5° for 3 days. Evaporation of solvent *in vacuo* left a clear green oil which was dissolved in benzene (100 ml.) and percolated through a short column of neutral

(15) See S. Winstein, *et al.*, THIS JOURNAL, **74**, 1127 (1952) and earlier references cited therein.

(16) Other examples of 1,2-shifts initiated by the conjugate acid of a carbonyl group occur in the rearrangement of hexamethyl acetone (S. Barton, F. Morton and C. R. Porter, *Nature*, **169**, 373 (1952)) and in the aldehyde-ketone rearrangement (L. W. Kendrick, B. M. Benjamin and C. J. Collins, THIS JOURNAL, **80**, 4057 (1958)).

(17) R. H. Reitsema, *ibid.*, **78**, 5022 (1958).

(18) The predominant tautomer was considered to be the fully conjugated 3,8(9)-*p*-menthadiene-3-ol-2-one.

(19) Melting points were determined with a Kofler micro melting point apparatus and are uncorrected. Ultraviolet spectra were takeu in 95% ethanol and infrared spectra were measured in chloroform solution. Microanalyses were performed by Dr. S. M. Nagy and his associates at the microchemical laboratory of the Massachusetts Institute of Technology.

(20) The ratio of fuming to concentrated sulfuric acid given here was found to result in maximum yields of isocamphorquinone.

(21) Prepared by the procedure of W. C. Evans, J. M. Ridgion and J. L. Simonsen, *J. Chem. Soc.*, 137 (1934).

alumina. The benzene eluate was washed with 20 ml. of 10% aqueous potassium hydroxide (0.25 g. of isocamphorquinone recovered on acidification), then with water, and dried over sodium sulfate. Evaporation of solvent left a partly crystalline residue which was triturated with light petroleum ether and recrystallized from cyclohexane. The methyl ether was obtained as needle crystals (0.3 g., 19%), m.p. 83–85°; ultraviolet spectrum: λ_{max} 293 mμ (ε 16,400) with an inflection at 258 mμ (ε 7,500); infrared spectrum, high intensity bands at 6.10 and 6.20μ.

Anal. Calcd. for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.09; H, 8.95.

5-Ketoheptanoic Acid VIII. (a) By Alkaline Hydrolysis of Isocamphorquinone.—A solution of isocamphorquinone (0.50 g.) and potassium hydroxide (5.0 g.) in water (25 ml.) was heated under gentle reflux while the system was swept by a slow stream of nitrogen. The effluent gas was bubbled through an alcoholic solution of 2,4-dinitrophenylhydrazine reagent causing the accumulation, over five hours, of a voluminous yellow-orange precipitate. The solid was collected and, after recrystallization from methanol, had m.p. 123–124° alone or admixed with authentic acetone 2,4-dinitrophenylhydrazone.

The cooled, alkaline reaction solution was washed with ether, concentrated *in vacuo* to 10-ml. volume, cautiously acidified (cooling) to *p*H 3, and extracted with 50 ml. of ether in five portions. After washing with saturated, aqueous sodium chloride, the dried ethereal solution was concentrated *in vacuo* and the residue crystallized from ether–hexane at 0°. The keto acid, 0.203 g. (47%), was thus obtained as fine needle crystals, m.p. 51–52°.

The semicarbazone, crystallized once from ethanol, had m.p. 186–188° alone or admixed with an authentic sample (part c).

The oxime, crystallized once from water, had m.p. 116–118° alone or admixed with an authentic sample (part c).

(b) **By Acidic Hydrolysis of Isocamphorquinone.**—Isocamphorquinone was heated under reflux with dilute sulfuric acid according to the procedure of Manasse and Samuel.[5] The acidic product was directly converted to the semicarbazone and the oxime. Melting point and mixture melting point observations were identical with those recorded above.

(c) **Synthesis from Glutaric Anhydride.**—Ethylmagnesium bromide (0.15 mole) in ether (150 ml.) was treated with cadmium chloride (15.6 g., 0.08 mole) according to de Benneville's procedure[22] for conversion to the dialkyl cadmium reagent. To the resulting ethereal solution was added powdered glutaric anhydride (9.1 g., 0.08 mole) at 0° and with stirring over a period of 15 minutes; reaction was then continued for one hour at reflux temperature. The cooled reaction mixture was treated with 73 ml. of cold 10% hydrochloric acid and the aqueous layer extracted with 150 ml. of ether in three portions. The combined ether solutions were extracted with saturated aqueous sodium bicarbonate; the aqueous layer was separated, carefully acidified, and repeatedly extracted with ether. The combined extracts were washed with water, dried and evaporated at reduced pressure yielding 8.0 g. (69%) of crude, partly oily product which was directly converted to the oxime, m.p. 116–118°, and the semicarbazone, m.p. 186–188°d.

(22) P. L. deBenneville, *J. Org. Chem.*, **6**, 462 (1941).

CAMBRIDGE, MASS.

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

Ring Interconversion by Transacylation in the Benzofluorenone and Benzanthrone Series[1]

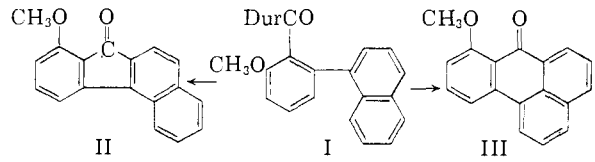
BY REYNOLD C. FUSON, WILLIAM A. HILLS AND BRUNO VITTIMBERGA

RECEIVED SEPTEMBER 8, 1959

Duryl 6-methoxy-2-(α-naphthyl)-phenyl ketone reacts in the presence of polyphosphoric acid to give 8- and 10-methoxyfluorenones and the corresponding 8- and 10-methoxybenzanthrones. Under mild conditions only the 8-methoxyfluorenone and the 8-methoxybenzanthrone are formed. Drastic conditions afford only the two benzanthrones. When heated with polyphosphoric acid the 8-methoxyfluorenone isomerizes to the 10-methoxy derivative, which in turn forms the 10-methoxybenzanthrone. It appears that the formation of the fluorenones is rate controlled and that that of the benzanthrones is equilibrium controlled.

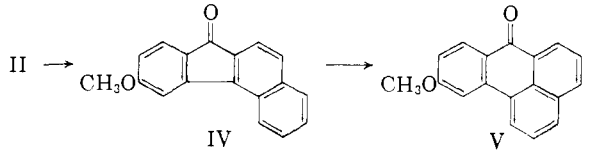
Acid-catalyzed cleavage of diaryl ketones and subsequent use of the resulting carboxylic acids as acylating agents makes possible transcarbonylation processes, *i.e.*, the formation of one ketone from another.[2] The cleavage, best accomplished with polyphosphoric acid, occurs easily with many ketones having an aryl radical of the hindered type. When the ketone carries in addition a suitable aryl radical in an *o*-position, cyclization may occur to produce a fluorenone.[3]

In the present study this cleavage–cyclization procedure was applied to duryl 6-methoxy-2-(α-naphthyl)-phenyl ketone (I), which offers the interesting possibility of forming a fluorenone or a benzanthrone, depending, respectively, on whether the acylation takes place at the adjacent β-position or in such a manner as to form a *peri*-bridge. Experiment has shown that both types of ring closure occur.



II I III

When the ketone was kept for 10 hr. in polyphosphoric acid at room temperature, the fluorenone II was formed in 13.3% yield and the benzanthrone III in a yield of 7.6%, most of the original ketone being recovered. Under more drastic reaction conditions the 10-methoxyfluorenone IV and the 10-methoxybenzanthrone V were produced also. It was observed too that the 8-methoxyfluorenone II, when heated with polyphosphoric acid, rearranged to the 10-methoxy isomer IV and this fluorenone, in turn, was isomerized by similar treatment to the 10-methoxybenzanthrone V.



IV V

(1) This investigation was supported in part by a grant from the Office of Ordnance Research, U. S. Army (Contract No. DA-11-022-ORD-874).

(2) R. C. Fuson, G. R. Bakker and B. Vittimberga, THIS JOURNAL, **81**, 4858 (1959).

(3) R. C. Fuson and J. J. Miller, *ibid.*, **79**, 3477 (1957).