

(refluxing for thirty minutes) and (b) hydroxylamine in methanol (refluxing for ten hours).

### Summary

1,4-Dimesityl-3-methyl-1,2,4-butanetrione enol has been synthesized from mesaconyl chloride.

Methylation with diazomethane gave all of the four possible methyl ethers. The *cis-trans* 2-enol methyl ethers were made in another way by the

action of sodium methoxide on bromodimesitylolethylene. The configurations were determined by interconversions and relative stability. The labile 4-enol methyl ether was obtained in a second way by acid catalytic methylation of the enol; and the stable 4-enol methyl ether, along with the carbon-methyl derivative, was obtained by alkylation of the silver enolate.

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[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY OF THE UNIVERSITY OF VIRGINIA]

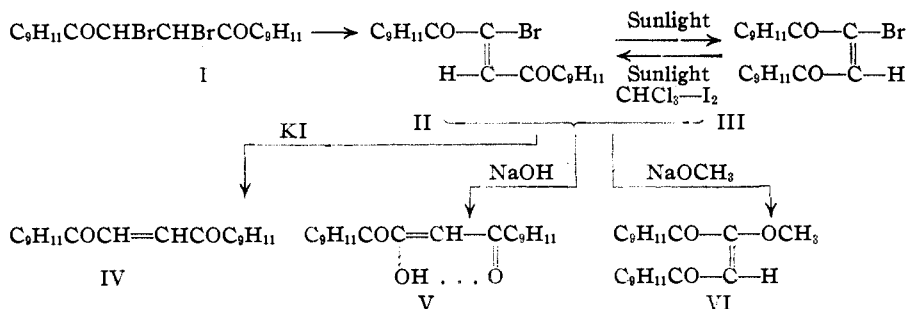
## The Stereoisomeric Bromo 1,4-Dimesityl Unsaturated 1,4-Diketones

BY ROBERT E. LUTZ AND DANIEL H. TERRY<sup>1</sup>

This report deals with the preparation of some halogen derivatives which were made in connection with the work on 1,4-dimesityl and 1,4-dimesityl-3-methyl 1,2,4-butanetrione enols.

### The 1,4-Dimesityl Series

The yellow *trans*-bromodimesitylolethylene (II) is made easily from dimesitylolethylene dibromide (I).<sup>2</sup> It is converted by the action of sunlight into a colorless isomer which, therefore, must be the *cis*-isomer (III). Conversion back into the *trans*-isomer was brought about by the action of sunlight on a chloroform solution containing a trace of iodine as a catalyst.



Both *cis*- and *trans*-isomers react with methanolic potassium hydroxide to give the triketone enol (V) and with sodium methoxide to give the *cis*-2-enol ether (VI). In the latter reaction no consistent stereochemical orientation is involved. 1,4-Addition probably occurs, but the intermediate 4-enolates, while theoretically capable of existing and maintaining individual configurations,

would hardly be expected to do so during this reaction under alkaline conditions.<sup>3</sup>

The action of potassium iodide on the bromo unsaturated diketones in both cases gave *trans*-dimesitylolethylene (IV), a somewhat surprising reaction which must be attributed to the fact that these compounds contain the conjugated  $\alpha$ -bromoketone system. The halogen in the corresponding dimesitylmethyl series is not reducible under the same conditions, however, due perhaps to an increase in the total steric hindrance by the substituted methyl group.

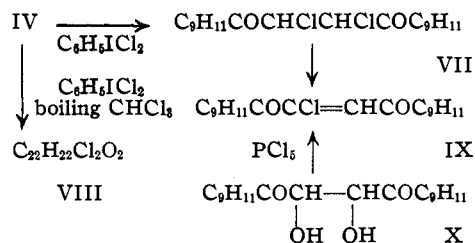
Chlorination of dimesitylolethylene (IV) was carried out to verify certain compounds and reactions which had been previously reported.<sup>2,4</sup> Phenyl iodochloride in cold chloroform converted the unsaturated diketone into the dichloride (VII) which had previously been isolated in extremely small amounts when free chlorine was used.<sup>2</sup> This dichloride when subjected to the action of boiling ethanol lost hydrogen chloride and gave the yellow *trans*-dimesitylolethylene (IX) which can be made by the action of hydrochloric acid on dimesitylolethylene oxide<sup>4</sup> and by the action of phosphorus pentachloride on dimesitylolethylene glycol (X).

(1) du Pont Fellow, 1939-1940; present location, Jackson Laboratory, E. I. du Pont de Nemours & Co., Wilmington, Del.

(2) Lutz, *THIS JOURNAL*, **48**, 2905 (1926).

(3) Cf. the facile rearrangement of the labile 4-enol ether [Lutz and Terry, *J. Org. Chem.*, **7**, 320 (1942)].

(4) Lutz and Wood, *THIS JOURNAL*, **60**, 229 (1938).

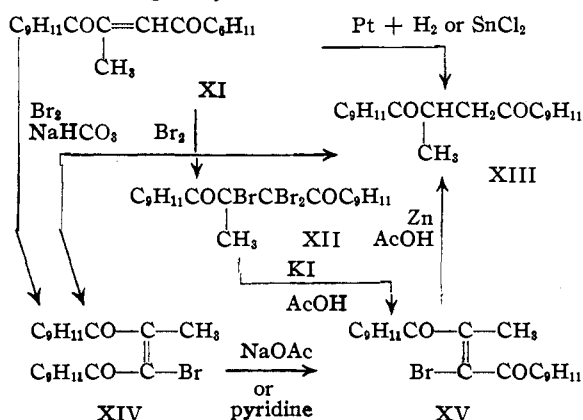


When dimesityloethylene was treated with phenyl iodochloride in boiling chloroform, a dichloro unsaturated diketone (VIII) was obtained which was shown to involve nuclear substitution, by the resistance toward reduction by zinc and acetic acid of at least one of the halogens. This compound evidently is a derivative of IX.

### The 1,4-Dimesityl-3-methyl Series

The unsaturated diketone of this series (XI) does not give a stable dibromide but reacts slowly in chloroform solution to give what appears to be the *cis*-bromo unsaturated diketone (XIV), along with two other products, the saturated diketone (XIII) and a tribromo compound which is believed to be XII. Possibly the unstable dibromide and hydrobromide are involved and, in the presence of hydrogen bromide generated during the reaction, act as  $\alpha$ -bromoketones to give up bromine and simultaneously to undergo reduction.<sup>5</sup>

In order to avoid complications due to secondary bromination the same reaction was carried out in the presence of an excess of powdered sodium bicarbonate to remove hydrogen bromide. Under these conditions the *cis*-bromo unsaturated diketone was obtained relatively free from by-products and in good yield.

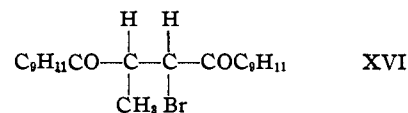


The structure of the *cis*-bromo unsaturated diketone (XIV) was proved by analysis and by the

(5) Cf. Couper and Lutz, *J. Org. Chem.*, **7**, 79 (1942).

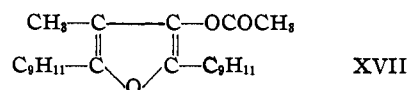
facile rearrangement under the influence of sodium acetate or pyridine into a stable isomer which consequently must be the *trans*-form (XV). The *trans*-compound was then reduced by means of zinc and acetic acid to the saturated diketone (XIII) which was obtained also by direct reduction of the unsaturated diketone (XI).

The conversion of the *trans*-unsaturated diketone (XI) to the labile *cis*-bromo unsaturated diketone (XIV) by bromination presumably involves the intermediate formation of an unstable dibromide. Obviously, in view of the production of the *labile*-stereoisomer under these circumstances this transformation is best interpreted as a *trans*-addition of bromine to give an unstable dibromide of the configuration (XVI), followed by *trans*-elimination of hydrogen bromide.



The structure of the tribromo derivative (XII) was deduced from analysis and the conversion by means of potassium iodide into the *trans*-bromo unsaturated diketone (XV).

Incidental to this work the acetoxyfuran (XVII) was made from the unsaturated diketone (XI). When the usual combination, acetic anhydride and sulfuric acid, was employed, there was produced a sulfur containing compound of empirical formula  $\text{C}_{23}\text{H}_{26}\text{O}_6\text{S}$ ; however, when acetyl chloride was substituted for acetic anhydride, as was done in the case of dimesityloethylene itself, the acetoxyfuran was then obtained without difficulty.



## Experimental

### The 1,4-Dimesityl Series

*trans*-2-Bromo-1,4-dimesityl-2-butanedione-1,4 (1,2-dimesitylbromoethylene) (II).—The best preparation has previously been reported.<sup>6</sup> The bromo compound has now been obtained in other ways as follows:

(a) A suspension of 5 g. of the dibromide of dimesityloethylene (I) and 1.5 g. of sodium benzoate in 75 cc. of absolute ethanol was refluxed for one and one-half hours. On cooling 0.85 g. of unchanged material separated. On diluting the filtrate with water 3.5 g. (84%) of crude products separated.

(b) A mixture of 5 g. of dibromide (I), 3 g. of freshly prepared silver benzoate, and 50 cc. of isopropyl ether was

(6) Conant and Lutz, *This Journal*, **47**, 881 (1925).

refluxed for eight hours and filtered. Evaporation gave 2.8 g. (55%) of II.

(c) A solution of 0.2 g. of the *cis*-isomer (III) in chloroform to which a crystal of iodine had been added, was exposed to sunlight for six hours; 0.05 g. of pure *trans*-isomer (II) was recovered and identified.

The following experiments were performed on the *trans*-compound (II):

(a) Treatment of 2.0 g. in 70% ethanol with 1 g. of potassium hydroxide under refluxing for one hour gave 1.6 g. (94%) of nearly pure enol (V).

(b) Treatment with a 30:5:3 concd. acetic acid-concd. hydrochloric acid-water mixture under refluxing for two hours was without result.

(c) Exposure of a solution of one gram in ethanol to sunlight for eight hours gave 0.8 g. of the *cis*-isomer.

(d) A solution of 0.15 g. in concd. acetic acid with potassium iodide reacted slowly on standing. Iodine was liberated. Upon diluting with water 0.1 g. of dimesityloethylene separated and was identified.

(e) Acetic anhydride and a small amount of concd. sulfuric acid at 100° for five minutes was without action.

(f) A solution of sodium methoxide was added under stirring to a methanol solution of 0.75 g. of II and the reaction was allowed to continue at room temperature for thirty minutes. Dilution with water gave 0.57 g. (62%) of nearly pure product which was recrystallized and identified as the *cis*-2-enol methyl ether (VI).

***cis*-2-Bromo-1,4-dimesityl-2-butenedione-1,4** (1,2-dimesitylbromoethylene) (III).—An ethanol solution of 1 g. of the *trans*-isomer (II) was bleached by exposure for eight hours to sunlight. Upon evaporation and crystallization 0.8 g. of colorless *cis*-isomer was isolated. After repeated crystallization from 70% ethanol it melted at 88–89°.

*Anal.* Calcd. for  $C_{22}H_{23}BrO_2$ : C, 66.2; H, 5.8. Found: C, 66.2; H, 6.1.

The action of 0.2 g. of potassium hydroxide in 30 cc. of 70% methanol on 0.3 g. of III (refluxing for one hour) gave 0.23 g. (92%) of nearly pure enol (V).

Potassium iodide in cond. acetic acid at 75° converted this compound in good yield into dimesityloethylene.

Acetic anhydride and a trace of concd. sulfuric acid at 100° for five minutes was without effect.

Sodium methoxide in methanol acting on 0.15 g. of III at room temperature for thirty minutes gave 0.11 g. (83%) of nearly pure *cis*-2-enol methyl ether (VI).

**2,3-Dichloro-1,4-dimesitylbutanedione-1,4** (Dimesityloethylene dichloride) (VII).—A solution of 2 g. of the *trans*-unsaturated diketone (IV) in 50 cc. of dry chloroform was treated with 1.8 g. of phenyliodochloride; the mixture was allowed to stand in a glass-stoppered flask for five days at room temperature, with occasional shaking. Evaporation of the resulting solution gave a colorless solid residue which was washed with ethanol; yield 0.94 g. (39%). Repeated crystallization from ethyl acetate brought the melting point to 209° (decomp.) (*cf.* ref. 2).

*Anal.* Calcd. for  $C_{22}H_{24}Cl_2O_2$ : C, 67.52; H, 6.18; Cl, 18.12. Found: C, 67.51, 66.52; H, 6.16, 5.71; Cl, 18.04.

***trans*-2-Chloro-1,4-dimesityl-2-butenedione-1,4** (Dimesitylochloroethylene) (IX).—The compound has been reported previously.<sup>4</sup> It may be obtained also as follows:

(a) A solution of 0.2 g. of the dichloro saturated diketone (VII) in 25 cc. of ethanol was refluxed for eight hours. The yellow solution was evaporated and 0.17 g. (95%) of nearly pure product was obtained. It was recrystallized and identified by mixture melting point with a sample prepared previously.<sup>4</sup>

(b) A solution of 0.3 g. of dimesityloethylene glycol (X) in dry chloroform was treated with 0.2 g. of phosphorus pentachloride. A vigorous reaction took place with evolution of hydrogen chloride. The chloroform was evaporated, water added and the organic material was extracted with ether. Upon evaporation and crystallization of the residual oil from ethanol 0.2 g. of the chloro unsaturated diketone was obtained in nearly pure condition. It was identified by mixture melting point.

**A Dichlorodimesityloethylene (VIII).**—A mixture of 10 g. of dimesityloethylene, 8.6 g. of phenyliodochloride and 50 cc. of dry chloroform was refluxed for three hours. Concentration under reduced pressure gave 0.4 g. of bright yellow solid which was purified by repeated crystallization from ethyl acetate; yellow needles; m. p. 209.5–210°.

*Anal.* Calcd. for  $C_{22}H_{22}Cl_2O_2$ : C, 67.84; H, 5.65. Found: C, 68.06, 68.08; H, 5.67, 5.44.

Reduction of a small sample by zinc dust and concd. acetic acid gave a new chlorine containing compound of m. p. 166–167° which was not purified or investigated further. This sufficed to show that at least one of the chlorines of VIII was in a mesityl nucleus.

#### The 1,4-Dimesityl-2-methyl Series

***trans*-1,4-Dimesityl-2-methyl-2-butenedione-1,4** (1,2-Dimesitylmethylethylene) (XI).—The following modification of the earlier procedure<sup>7</sup> was used. Thirty grams of mesaconyl chloride was added dropwise over two hours to a well-stirred mixture of 120 cc. of carbon disulfide, 60 g. of finely ground anhydrous aluminum chloride and 48 g. of mesitylene. The mixture was then warmed on a water-bath for twenty minutes and poured into ice and hydrochloric acid. The carbon disulfide layer was separated and distilled, and the residue crystallized from ethanol; yield 54.6 g. (91%) melting at 88–90°. Recrystallized material melting at 96° was used in succeeding experiments.

The action of sunlight (two days) on a methanol solution was without result. Bromination according to the earlier method<sup>8</sup> gave much non-crystalline material and small yields of solids which were mixtures. Attempts to isolate a dibromo compound failed and it appeared likely that this desired compound was unstable and easily converted into the unsaturated bromo diketone through loss of hydrogen bromide. A typical experiment is as follows: a chloroform solution (15 cc.) of 7.2 g. of bromine was added dropwise with mechanical stirring to a solution of 15 g. of (XI) in 20 cc. of chloroform at –10°. Copious evolution of hydrogen bromide was observed and the color of bromine was discharged slowly. After the addition the mixture was allowed to stand for fifteen minutes and was evaporated under reduced pressure. The solid which appeared was washed with petroleum ether and filtered (18 g. melting at 124–126°). A portion of this (0.5 g.) upon

(7) Lutz and Taylor, *THIS JOURNAL*, **55**, 1168 (1933).

(8) Taylor, Dissertation, University of Virginia, 1932.

distillation in the vacuum oven at 130° gave a crystalline deposit on the cold-finger condenser of 0.3 g. (m. p. 140–142°) which was identified as the *cis*-bromo unsaturated diketone (XIV). The residue from this distillation was crystallized from ethanol and gave 0.15 g. of colorless solid of m. p. 180–182°. This is described below as tribromodimesitylbutanedione (XII). Concentration of the petroleum ether washings of the crude product (above) gave an oil which contained little halogen. This material was finally induced to crystallize by vacuum distillation at 135° onto a cold-finger condenser, followed by manipulation and seeding of the distillate. This product (0.33 g.) melted at 58–60° and was identified as the saturated diketone (XIII).

Chlorination attempts, using phenyl iodochloride, were unsuccessful.

**1,4-Dimesityl-2-methylbutanedione-1,4 (XIII).**—A solution of 3 g. of the unsaturated diketone (XI) in 100 cc. of ethanol was hydrogenated using 0.15 g. of platinum oxide. One molecule was absorbed rapidly. Two drops of piperidine were added and the mixture was allowed to stand for six hours under hydrogen. Filtration and evaporation gave an oil, which, upon vacuum distillation onto a cold-finger condenser and manipulation in solvents, was finally induced to crystallize. Upon repeated recrystallization from ethanol it melted at 60.5°.

*Anal.* Calcd. for  $C_{23}H_{28}O_2$ : C, 82.14; H, 8.33. Found: C, 81.72; H, 8.49.

This same compound was obtained by reduction of the unsaturated diketone (XI) by means of stannous chloride in a 3:1 mixture of concd. acetic and hydrochloric acids, and also by reduction of the *trans*-bromo unsaturated diketone (XV) by means of zinc and concd. acetic acid.

Attempts to obtain a crystalline furan through the use of hydriodic acid (sp. gr. 1.7), or refluxing acetic acid continuously saturated with hydrogen chloride, were without success. The use of acetic anhydride and sulfuric acid led to a compound of m. p. 102–103° (crystallized from ligroin) which was shown not to be the furan by analyses. This was not studied further.

**2,2,3-Tribromo-1,4-dimesityl-3-methylbutanedione-1,4 (XII).**—The crude material obtained as described above was partially purified by vacuum evaporation of the impurities consisting of compounds containing less halogen, and was further purified by repeated crystallization from an ethanol-ethyl acetate mixture; m. p. 188°.

*Anal.* Calcd. for  $C_{23}H_{23}O_2Br_3$ : C, 48.17; H, 4.36. Found: C, 47.85; H, 4.42.

This compound was isolated in several experiments from mixtures obtained by brominations followed by manipulations in which sodium methoxide was used. This compound did not react and remained as an insoluble residue.

**Reduction of the tribromo compound (0.15 g.)** in concd. acetic acid by potassium iodide (warming to 70° and then allowing to cool slowly on standing for three hours) gave 0.06 g. of nearly pure *trans*-bromo unsaturated diketone (XV) which was purified by crystallization from ethanol and identified.

***cis*-2-Bromo-1,4-dimesityl-3-methyl-2-butenedione-1,4 (XIV).**—A chloroform solution of 4.8 g. of bromine was added dropwise to a mechanically stirred solution of 10 g. of

the unsaturated diketone (XI) in chloroform containing 1 g. of suspended powdered sodium bicarbonate. The temperature was maintained at 0°. The color of bromine disappeared within twenty minutes after the last addition. This solution was then washed in succession with aqueous sodium bisulfite and with water. Upon evaporation and crystallization of the residue from petroleum ether, 7.8 g. of fine colorless needles was obtained (77.7%). Repeated crystallizations from ethanol-ethyl acetate mixtures brought the melting point to 143.5–144°. From the filtrates 1.4 g. of starting material was recovered.

*Anal.* Calcd. for  $C_{23}H_{25}O_2Br$ : Br, 19.37. Found: Br, 19.55.

***trans*-2-Bromo-1,4-dimesityl-3-methyl-2-butenedione-1,4 (XV).**—A mixture of 3 g. of the *cis*-isomer (XIV), 3 g. of sodium acetate and 50 cc. of 95% ethanol was refluxed for two hours. Upon cooling and diluting with water 2.05 g. of product separated (m. p. 168–169°). Alternate crystallizations from ethanol and from ethyl acetate raised the melting point to 171–171.5°.

*Anal.* Calcd. for  $C_{23}H_{25}O_2Br$ : C, 66.85; H, 6.10. Found: C, 67.14; H, 6.14.

This compound was obtained also when sodium benzoate was substituted for sodium acetate; and it was obtained when a mixture of the *cis*-isomer and isopropyl ether and freshly precipitated silver benzoate was refluxed for twelve hours. The same transformation was effected by the action of a 1:1 mixture of pyridine and water under refluxing for one hour.

**Reduction of 0.5 g. of XV** by 25 cc. of concd. acetic acid and 1 g. of zinc dust under stirring for ninety minutes at room temperature gave an oil which finally was induced to crystallize after distillation in the vacuum oven at 133°. The yield was 0.16 g. and the m. p. 57–59°; it was identified by mixture melting point as the saturated diketone (XIII).

**3-Acetoxy-2,5-dimesityl-4-methylfuran (XVII).**—Two drops of concd. sulfuric acid were added to a suspension of 1.5 g. of dimesitylmethylethylene (XI) in 10 cc. of acetyl chloride. The suspended solid dissolved immediately with darkening. After warming for five minutes the mixture was hydrolyzed with ice-water and neutralized with sodium carbonate. Extraction with ether and subsequent evaporation gave 0.52 g. of almost pure product. Repeated crystallization from ethanol raised the melting point to 88°. Some starting material was recovered from the residual oils.

*Anal.* Calcd. for  $C_{25}H_{28}O_3$ : C, 79.84; H, 7.49. Found: C, 79.57; H, 7.75.

When acetic anhydride was used instead of acetyl chloride in the above experiment only unchanged material was obtained.

### Summary

*trans*-Bromodimesitylethylene has been converted into a *cis*-form. Reactions of the stereoisomers have been studied.

The chlorination of dimesitylethylene with phenyliodochloride gave the monochloro derivative in good yield.

Bromination of dimesitylmethylethylene gave a *cis*-monobromo derivative from which the *trans*-isomer was made by inversion. The use of sodium

bicarbonate in preventing secondary reactions during bromination is described.

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[CONTRIBUTION FROM NICHOLS LABORATORY, NEW YORK UNIVERSITY]

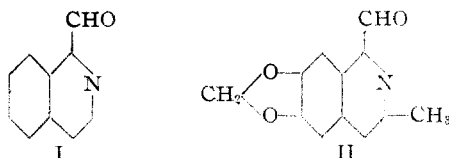
## Condensation Reactions of Isoquininaldehyde

BY ROBERT S. BARROWS AND H. G. LINDWALL

The successful use of lepidine as a source of cinchoninaldehyde<sup>1</sup> suggested that 1-methylisoquinoline might similarly be oxidized through the action of selenium dioxide to yield isoquininaldehyde (I). The method of Späth,<sup>2</sup> with modification, was used for the preparation of 1-methylisoquinoline. The modification involved the substitution of Raney nickel for platinized asbestos in the dehydrogenation of 1-methyl-3,4-dihydroisoquinoline. The 1-methylisoquinoline thus obtained was characterized by the preparation of several known derivatives.

The oxidation of 1-methylisoquinoline by selenium dioxide was carried out in dioxane solution with vigorous stirring; an excess of selenium dioxide was avoided. The product (I), which is volatile with steam, reacts with Tollens reagent, gives a sodium bisulfite addition product, and forms an oxime, a phenylhydrazone and a semicarbazone. The aldehyde (I) formed no hydrate.

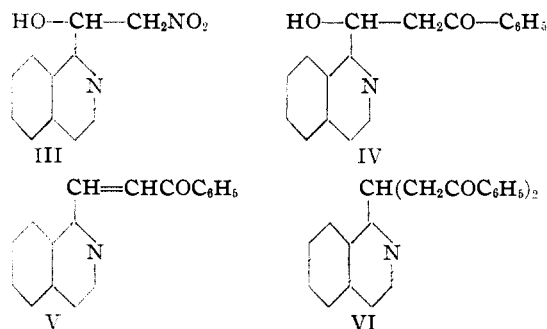
A similar oxidation of 1,3-dimethyl-6,7-methylenedioxyisoquinoline was carried out. The product, an aldehyde, formed a monoxime, and is tentatively assigned the structure 3-methyl-6,7-methylenedioxyisoquininaldehyde (II).



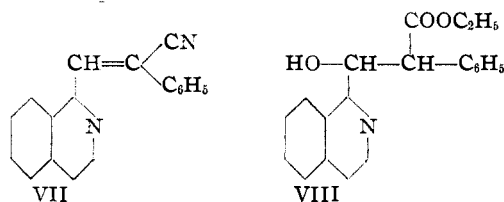
The condensation reactions of compound I with a series of "active methylene" compounds were studied. Condensation with nitromethane was accomplished readily to yield  $\alpha$ -nitro- $\beta$ -hydroxy- $\beta$ -(isoquinolyl-1)-ethane (III).

Initial attempts at condensation with acetophenone gave a mixture of products; with varied conditions, however, either IV, V, or VI could be obtained as the principal product. If the con-

densation of equimolecular quantities of isoquininaldehyde and acetophenone was carried out in the presence of sodium hydroxide for a short period of time, IV was obtained, but if longer time was allowed or if sodium ethylate was used, compound V resulted. With an excess of acetophenone and either sodium hydroxide or sodium ethylate, VI was the principal product.



No product could be obtained from isoquininaldehyde and phenylacetic acid under conditions of the Perkin condensation, but two derivatives of phenylacetic acid were condensed under other conditions. Phenylacetonitrile and compound I yielded VII in the presence of diethylamine or sodium ethylate; ethyl phenylacetate and I gave VIII when sodium ethylate was used as the catalyst.



### Experimental

**1-Methylisoquinoline.**—To 1-methyl-3,4-dihydroisoquinoline (15 g.) was added an excess of Raney nickel and the mixture was heated under reflux for fifteen to twenty minutes or until the temperature of the mixture had reached 248° (the boiling point of 1-methylisoquinoline); yield, 70–75%; boiling point 124–126° (at 10 mm.). **Melting points of derivatives:** picrate, 230–232°; sul-

(1) Kwartler and Lindwall, *THIS JOURNAL*, **59**, 524 (1937).

(2) Späth, Berger and Kuntara, *Ber.*, **63**, 134 (1930); Späth and Polgar, *Monatsh.*, **51**, 193 (1929).