## Experimental

**Wohl-Aue Reaction of *m*-Anisidine and *m*-Nitroanisole**—A mixture of *m*-anisidine (16.5 g.), *m*-nitroanisole (17 g.), and powdered KOH (40 g.) was boiled in toluene (150 cc.) under reflux in an oil bath for 3 hrs. After the reaction, toluene solution was removed by steam distillation. The crude crystalline substance deposited in the remaining aq. solution was filtered, dried, dissolved in benzene, and purified by chromatography on alumina. The first eluate contained no crystalline substance. From the next eluate yellow needles of m.p. 150~153° (from benzene) were obtained. Yield: 1.6 g. This was found to be identical with 1,8-dimethoxyphenazine (I) by mixed fusion. *Anal.* Calcd. for $C_{14}H_{12}O_2N_2$: C, 70.00; H, 5.00. Found: C, 69.81; H, 5.24.

From the last eluate 1,8-dimethoxyphenazine 5-N-oxide as yellow needles, m.p. 205~210° (from benzene), were obtained. Yield: 3.3 g. *Anal.* Calcd. for $C_{14}H_{12}O_3N_2$: C, 65.62; H, 4.68. Found: C, 65.24; H, 5.07.

**Deoxygenation of 1,8-dimethoxyphenazine 5-N-oxide**—A mixture of 1,8-dimethoxyphenazine 5-N-oxide (0.1 g.), zinc powder (0.1 g.), and glacial acetic acid (1 cc.) was warmed on a water bath for 15 mins. Water was added to this reaction mixture, the precipitate deposited was extracted with benzene, and purified on alumina. Yellow needles of m.p. 150~152° (from benzene) were obtained. Yield: 0.05 g. This was found to be identical with the authentic specimen of 1,8-dimethoxyphenazine by mixed melting point determination.

## Summary

*m*-Anisidine and *m*-nitroanisole were condensed by Wohl-Aue method and 1,8-dimethoxyphenazine and its 5-N-oxide were obtained.

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# Zen-ichi Horii, Teiji Tanaka, and Yuriko Murakami: Itaconic Acid in Organic Chemistry. I. Synthesis of 2-Methyl-1,4-naphthoquinone (Menadione).

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Until some years ago, itaconic acid was not easily obtainable but it is at the present time easily available because the economical preparation of this acid by fermentation of molasses has been found feasible. We noticed this acid useful as a starting material for synthetic organic chemistry, as its price was cheap and it had chemically interesting groups such as vinyl in its molecule. As an initial research of this series, we studied the preparation of menadione (2-methyl-1,4-naphthoquinone) from itaconic aicd. The reaction scheme adopted by us was as follows:

The hydrogenation of itaconic acid (I) to methylsuccinic aicd (II) was carried out according to the method of Dixon.[1] 2-Methyl-1-tetralone (VIII) was prepared by modification of the method of Alexander.[2] (V) was obtained by the Clemmensen reduction of 3-benzoyl-2-methylacrylic acid (VII), which was prepared by the reaction of itaconic anhydride and benzene in the presence of aluminum chloride.[1] The catalytic reduction of itaconic acid to methylsuccinic acid could be avoided by this method but the over-all yields (based on itaconic acid) of these methods were nearly the same.

Formerly, Sah[3] synthesized menadione (IX) by the chromium trioxide oxidation of 2-methylnaphthalene, which was prepared by the Clemmensen reduction of (VIII), followed

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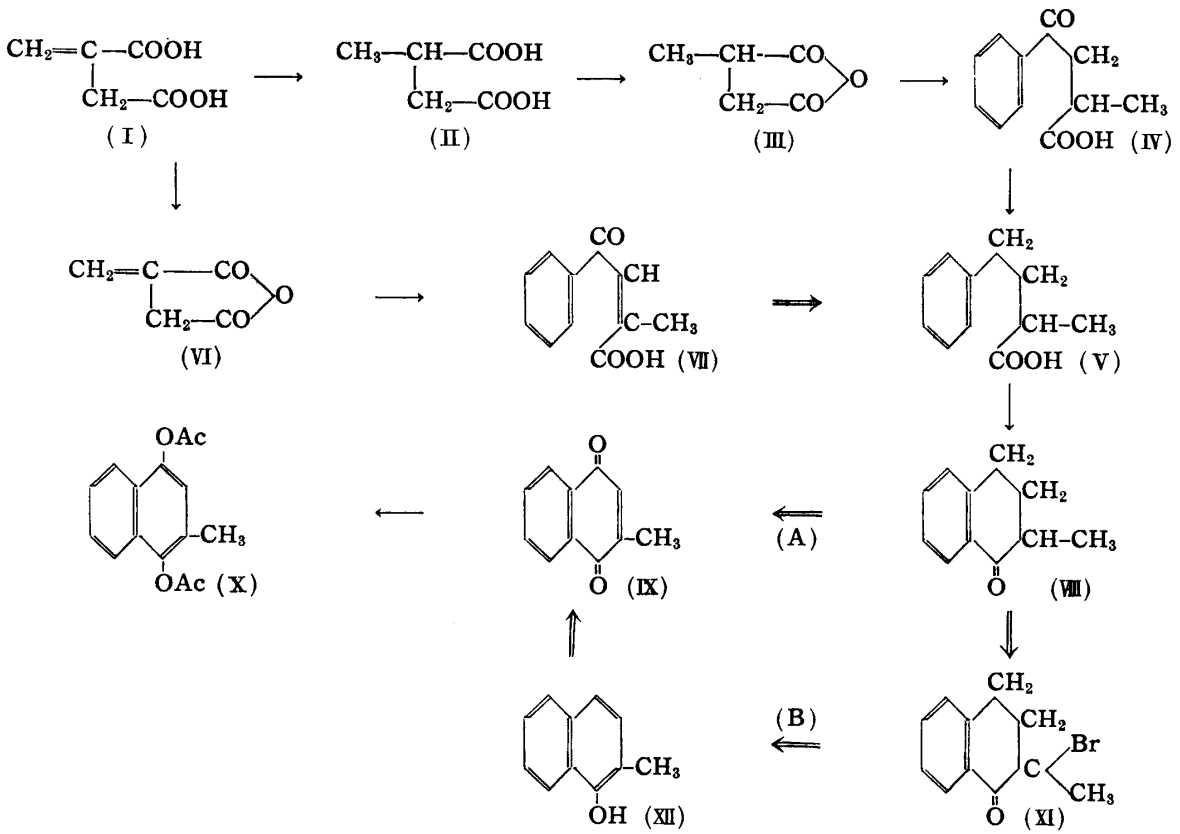
1) S. Dixon, H. Gregory, L. F. Wiggins: J. Chem. Soc., **1949**, 2139.
2) E. A. Alexander, A. Mudrak: J. Am. Chem. Soc., **72**, 3194(1950).
3) P. P. T. Sah, W. Bruell: Ber., **73**, 1430(1940).




(Steps indicated by shadowed arrows are new reactions)

by dehydrogenation with sulfur. The yield of the chromium trioxide oxidation of 2-methylnaphthalene was generally very poor, and though Sah did not report his yield, the yield reported by Fieser[4] was only 29%. The direct oxidation of (VIII) to (IX)(method A) gave a fairly good yield (30%). This method appears more convenient than that described by Sah in view of avoiding the processes of the tetralone derivative (VIII) to 2-methylnaphthalene. (IX) was also obtained by the method B, i.e. bromination of (VIII) gave 2-bromo derivative (XI), which was converted by reaction with 2,4,6-collidine to 2-methyl-1-naphthol (XII), followed by oxidation with chromium trioxide to (IX). Recently, Schmid[5] used lead tetraacetate as an oxidation agent in the oxidation of 2-methyl-5,7-dimethoxy-1-naphthol to the corresponding 1,4-naphthoquinone, but it was found that it could be

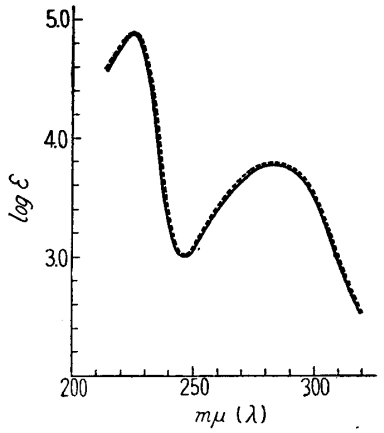



Fig. 1. 1,4-Diacetoxy-2-methylnaphthalene (menadiol diacetate)

—— (X): $\lambda_{max}$ 225 mμ (log ε 4.87), 284 mμ (log ε 3.79)

------ Authentic Sample: $\lambda_{max}$ 225 mμ (log ε 4.88), 284 mμ (log ε 3.78)

4) L.F. Fieser, W.P. Campbell, E.M. Fry, M.D. Gates, Jr.: J. Am. Chem. Soc., **61**, 3216(1939).
5) H. Schmid, A. Ebnoether, Th. M. Meijer: Helv. Chim. Acta, **35**, 910(1952).

effected by using chromium trioxide instead of lead tetraacetate in the similar reaction. Incidentally, after completion of this work, Shoji[6] published his result on the synthesis of menadione by direct oxidation of 2-methyltetralone with chromium trioxide in acetic acid. We are of the opinion, as with Shoji, that this reaction provides a convenient method for the preparation of menadione. From these experiments it was shown that itaconic acid was valuable as the starting material for the preparation of menadione.

## Experimental

**2-Methyl-1-tetralone (VIII)**—Prepared according to the method of Alexander, *et al.*[2]

**Clemmensen Reduction of 2-Methyl-3-benzoylacrylic Acid (VII)[1] to 2-Methyl-4-phenylbutyric Acid (V)**—A mixture of amalgamated Zn (prepared from mossy Zn (16 g.) and $HgCl_2$ (1.6 g.)),[7] in conc. HCl (14 cc.), water (6 cc.), toluene (8 cc.), glacial AcOH (0.4 cc.), and 2-methyl-3-benzoylacrylic acid (4.0 g.) was refluxed vigorously for 24 hrs. A 4-cc. portion of conc. HCl was added every 6 hrs. during this period. The reaction mixture was cooled to room temperature. The aqueous layer was separated and, after dilution with water, was extracted several times with ether. The combined ether and toluene solutions were washed with a little water and dried over anhyd. $Na_2SO_4$. The solvent was removed by distillation under diminished pressure and the residue was distilled. 2-Methyl-4-phenylbutyric acid was obtained as a colorless oil, $b.p_3$ 138~140°. Yield, 1.7 g. (43%).

**2-Methyl-1,4-naphthoquinone (IX)**—a) Method A : A solution of $CrO_3$ (12 g.) in 80% acetic acid (60 cc.) was added gradually to a stirred solution of 2-methyl-1-tetralone (6 g.) in glacial AcOH (60 cc.) at such a rate that the temperature did not exceed 20°. After 36 hrs.' standing at room temperature, the reaction mixture was poured into ice cold water, the yellow needles were collected, and recrystallized from MeOH, m.p. 104°. Yield, 1.8 g. (30%). *Anal.* Calcd. for $C_{11}H_8O_2$ : C, 76.73; H, 4.68. Found : C, 77.05; H, 4.47.

The diacetate of 2-methyl-1,4-naphthalenediol (X), prepared by reductive acetylation[4] of the quinone (IX) with AcONa, Zn powder, glacial AcOH, and $Ac_2O$, formed colorless prisms from MeOH, m.p. 111.5°. This compound was identified by comparing its m.p. and ultraviolet absorption spectrum with those of an authentic sample. *Anal.* Calcd. for $C_{15}H_{14}O_4$ : C, 69.75; H, 5.46. Found: C, 69.28; H, 5.22.

b) Method B : **2-Methyl-2-bromo-1-tetralone (XI)** : To a stirred solution of 2-methyl-1-tetralone (14.7 g.) in ether (200 cc.) was added bromine (16 g.) at such a rate that the temperature did not exceed 5°. After completion of the addition, stirring was continued for 1.5 hrs. The resulting solution was washed successively with water, $NaHCO_3$ solution, and water, and dried over anhyd. $Na_2SO_4$. After evaporation of ether, the residue was recrystallized from petr. ether and 2-methyl-2-bromo-1-tetralone was obtained as colorless plates, m.p. 66°. Yield, 17.5 g. (80%). *Anal.* Calcd. for $C_{11}H_{11}OBr$ : C, 55.23; H, 4.64. Fouud : C, 55.73; H, 4.88.

**2-Methyl-1-naphthol (XII)**—A solution of the 2-bromo derivative (1 g.) in 2,4,6-collidine (2.5 g.) was refluxed for 30 mins. After cooling, ether was added and the precipitated salt was removed by filtration. The filtrate was washed with dil. HCl and water, and dried over anhyd. $Na_2SO_4$. After removal of the solvent, the residue was purified from petr. ether and 2-methyl-1-naphthol was obtained as white needles, m.p. 61°. Yield, 0.5 g. (71%). *Anal.* Calcd. for $C_{11}H_{10}O$ : C, 83.50; H, 6.37. Found : C, 83.14; H, 6.24.

**Oxidation of 2-Methyl-1-naphthol (XII) to 2-Methyl-1,4-naphthoquinone (IX)**—To a stirred solution of 2-methyl-1-naphthol (XII) (1 g.) in glacial AcOH (10 cc.), a solution of $CrO_3$ (1.2 g.) in 80% AcOH (10 cc.) was added at such a rate that the temperature did not exceed 20°. After 48 hrs.' standing, the reaction mixture was poured into an ice water, the resulting yellow precipitate was collected, and purified from MeOH as (IX), m.p. 105°. Yield, 0.4 g. (37%). Diacetate of 2-methyl-1,4-naphthalenediol, m.p. 112°, undepressed on admixture with an authentic sample.

## Summary

Menadione was prepared from itaconic acid according to the reaction scheme described in the text. The direct oxidation of 2-methyl-1-tetralone to menadione (method A) appeared to be more convenient than that described by Sah[3] in view of avoiding the processes of the tetralone derivative to 2-methylnaphthalene. Method B was a little tedious but gave a good yield in each process. From these experiments, it could be concluded that itaconic acid is valuable as the staring material for the preparation of menadione.

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6) T. Shoji : J. Pharm. Soc. Japan, **76**, 1100(1956).
7) Org. Reactions, I, 163.