# STUDIES ON STOBBE CONDENSATION

# REACTIONS OF ALDEHYDES AND KETONES WITH DIMETHYL METHYLSUCCINATE

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## ABSTRACT

Benzaldehyde, *o*-methoxybenzaldehyde, *p*-chlorobenzaldehyde, benzophenone, and acetophenone are condensed with dimethyl methylsuccinate in the presence of potassium *tert*butoxide to give the corresponding  $\beta$ -half-esters. In the case of *o*-methoxybenzaldehyde the lactonic acid (IX) is also obtained. The  $\beta$ -half-esters are cyclized by sodium acetate and acetic anhydride to the corresponding acetoxynaphthoates which are converted into their methoxynaphthoates. Alkaline hydrolysis of the  $\beta$ -half-esters yields the corresponding itaconic acids, the anhydrides of which are converted to their  $\alpha$ -half-esters.

In a preliminary communication (1, 2) the reaction of two representative ketones, benzophenone and fluorenone, with diethyl methylsuccinate in the presence of sodium ethoxide was shown to proceed by a Stobbe condensation giving the expected half-esters in good yields. In the present work we are reporting an extension of this study on both aldehydes and ketones. Benzaldehyde, *o*-methoxybenzaldehyde, *p*-chlorobenzaldehyde, benzophenone, and acetophenone were condensed with dimethyl methylsuccinate in the presence of potassium *tert*-butoxide (3); from the products were formed anhydrides, half-esters, indones, and naphthalene derivatives. In all these reactions, exact parallels were found with the corresponding products previously obtained from ethyl succinate itself (3).

Good yields (60-72%) of the  $\beta$ -half-esters (II) were obtained from the condensation of benzaldehyde, *o*-methoxybenzaldehyde, benzophenone, and acetophenone. However, the yield was only poor, as expected, with *p*-chlorobenzaldehyde, but a shorter period of reflux was found to increase this yield slightly and minimize resinification. In the case of acetophenone, the isomeric  $\beta$ -half-ester (VI; R = CH<sub>3</sub>) was also obtained and separated.

The condensation of the aldehydes in general afforded, in addition to the expected half-esters, varying amounts of the corresponding itaconic acids.

o-Methoxybenzaldehyde gave also a small amount of an acidic non-ketonic substance, m.p. 217°, which was found to be the lactonic acid (IX). The constitution of (IX) as 2-o-anisyl-3-carboxy-4-o-methoxybenzylidene-3-methyl-5-oxotetrahydrofuran follows from the following observations: (a) the infrared spectrum (KBr) showed a strong band at 1 750 cm<sup>-1</sup>, characteristic of the stretching frequencies of carbonyl groups of  $\alpha,\beta$ unsaturated- $\gamma$ -lactones (4) and (b) alkaline hydrolysis of the substance gave the itaconic acid (II; R<sub>1</sub> = R<sub>3</sub> = R<sub>4</sub> = H, R<sub>2</sub> = CH<sub>3</sub>O) and o-methoxybenzaldehyde which was characterized as the 2,4-dinitrophenylhydrazone. Analogs of (IX) have frequently been observed in the condensations of ethyl succinate with aromatic aldehydes. The formation of this lactonic acid at high temperature is evidence for (a) the relative stability of the intermediate paraconic ester (3) towards the *tert*-butoxide ions; and (b) the comparative reactivity of o-methoxybenzaldehyde. When o-methoxybenzaldehyde was condensed with dimethyl methylsuccinate in the presence of sodium ethoxide at  $-15^\circ$ , the lactonic acid (IX) was obtained as the main product.

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Benzaldehyde and p-chlorobenzaldehyde also gave different amounts of benzoic acid and p-chlorobenzoic acid arising from a Cannizzaro reaction, a common side reaction in Stobbe condensations (3). The difference in the yields of this side reaction, was confirmed by treating p-chlorobenzaldehyde, benzaldehyde, and o-methoxybenzaldehyde with potassium *tert*-butoxide under the same conditions of the Stobbe experiment but in the absence of the succinic ester, where the yields of the resulting benzoic acids, as expected, were found to be 45, 22, and 5% respectively. This is in agreement with the electronic structures of these aldehydes where the -I effect of the Cl atom in p-chlorobenzaldehyde favors the side reaction (by the transfer of a hydranion) while the +T effect of the methoxyl group in o-methoxybenzaldehyde opposes it.



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Hydrolysis of the half-esters using 10% sodium hydroxide solution gave very good yields of the corresponding itaconic acids except that from *p*-chlorobenzaldehyde which

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gave a poor yield of the corresponding itaconic acid. This was improved by lowering the temperature of reflux (130°, oil bath) and by decreasing the concentration of the alkali (5%). The half-ester of benzaldehyde gave a purer product in higher yield when barium hydroxide was used. The two isomeric half-esters of acetophenone (II;  $R_1 = R_4 = CH_3$ ,  $R_2 = R_3 = H$  and VI;  $R = CH_3$ , separated by fractional crystallization after distillation, gave the corresponding itaconic acids which were found to be identical with those obtained from the hydrolysis of the crude undistilled mixture of the half-esters. This indicates that the two forms of the half-ester are stable to heat. The constitutions of the two isomeric itaconic acids of acetophenone as *cis*- and *trans*- $\alpha$ ,  $\gamma$ -dimethyl- $\gamma$ -phenylitaconic acid (II;  $R_1 = CH_3$ ,  $R_2 = R_3 = R_4 = H$  and VI; R = H respectively) were demonstrated in the usual way (3); (a) the two acids gave acetophenone on oxidation with alkaline permanganate, showing the absence of double bond migration and (b) cyclization of both itaconic acids (m.p.'s 139° and 178-180°) with concentrated sulfuric acid (5) at room temperature was successful only in the case of the acid of m.p. 178-180°, yielding the indoneacetic acid (VII) as a yellow, crystalline solid, m.p. 127° (2,4-dinitrophenylhvdrazone, m.p. 186-187°).

The structures and the *cis* configuration of the  $\beta$ -half-esters from the three aldehydes and benzophenone were confirmed in the usual way (3) by their cyclization with fused sodium acetate in acetic anhydride (6) to the corresponding methyl acetoxymethylnaphthoates (V) in good yields. Alkaline hydrolysis of the acetoxy esters gave the corresponding phenolic acids. Methyl 4-acetoxy-3-methyl-1-phenyl-2-naphthoate (V;  $R_1 =$  $C_6H_5$ ,  $R_2 = R_3 = H$ ,  $R_4 = CH_3$ ,  $R_5 = CH_3CO$ ) afforded in addition to the expected phenolic acid (V;  $R_1 = C_6H_5$ ,  $R_2 = R_3 = R_4 = R_5 = H$ ) a phenolic solid which was found to be the phenolic ester (V;  $R_1 = C_6H_5$ ,  $R_2 = R_3 = R_5 = H$ ,  $R_4 = CH_3$ ), as it showed bands in the infrared region (Nujol mull) at 3 500 (hydroxyl) and 1 715 cm<sup>-1</sup> (aryl esters). The phenolic ester and acids when treated with dimethyl sulfate and anhydrous potassium carbonate in acetone afforded the corresponding methoxy esters. Methyl 4-methoxy-3-methyl-2-naphthoate (V;  $R_1 = R_2 = R_3 = H$ ,  $R_4 = R_5 = CH_3$ ) was obtained as a liquid and identified in the form of its solid methoxy acid (V;  $R_1 =$  $R_2 = R_3 = R_4 = H$ ,  $R_5 = CH_3$ ). The itaconic acids were converted by acetyl chloride (7) into their anhydrides (III and VIII) in very good yields, except the itaconic acid from benzaldehyde (II;  $R_1 = R_2 = R_3 = R_4 = H$ ) which failed completely to dehydrate and was recovered unchanged. The anhydrides on boiling with methanol (8) gave the corresponding  $\alpha$ -half-esters (IV) in excellent yields. Thus in the formation of the  $\alpha$ - and  $\beta$ -half-esters, and in the reactions of the latter, exact parallels are found with the analogous compounds from ethyl succinate in which the positions of the ester groups have been rigorously proved (3).

#### EXPERIMENTAL\*

# Condensation of Aldehydes or Ketones with Dimethyl Methylsuccinate (General Procedure)

A solution of the aldehyde or ketone (0.1 mole) and dimethyl methylsuccinate (0.1 mole) in dry *tert*butanol (25 ml) was added under nitrogen atmosphere to a boiling solution of potassium *tert*-butoxide (from metallic potassium (0.12 mole) and *tert*-butanol (85 ml)). The addition took place in a period of 20 min, and the whole mixture was then refluxed under nitrogen for a further 45 min (the time of reflux was reduced to half an hour in case of *p*-chlorobenzaldehyde). The ice-cold mixture was acidified (litmus) with cold dilute hydrochloric acid. Distillation of alcohol under reduced pressure left a residue, which was diluted

\*All melting points and boiling points are uncorrected, unless otherwise stated, the melting range of analytical samples was less than 1°. All yields refer to the yields of crude material. Infrared spectra were recorded on a Perkin-Elmer Infracord 137 spectrophotometer with a sodium chloride prism. Microanalyses are carried out by A. Bernhardt, Max-Plank-Institute, Mulheim (Ruhr).

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with water and extracted with ether. The ethereal solution was washed with water and repeatedly extracted with sodium bicarbonate solution which was then acidified with cold dilute hydrochloric acid to give the reaction product.

Benzaldehyde (10.6 g) gave a brown viscous oil (15.5 g), which failed to solidify. This when subjected to distillation under reduced pressure (140-150° at 0.3 mm, oil bath) gave a trace of benzoic acid (0.5 g) and most of the residue started to resinify. Saponification of the product (1 g) with a saturated solution of barium hydroxide (15 ml, 4 h heating at 100°) gave a barium salt which after filtration, washing with ethanol, and acidification with dilute hydrochloric acid yielded  $cis - \alpha$ -methyl- $\gamma$ -phenylitaconic acid (II;  $R_1 = R_2 =$  $R_3 = R_4 = H$ ) as colorless solid (0.8 g, 85% yield), m.p. 194° (from methanol).

Anal. Calcd. for C<sub>12</sub>H<sub>12</sub>O<sub>4</sub>: C, 65.44; H, 5.49. Found: C, 65.44; H, 5.66.

When the above experiment was repeated but without the substituted succinic ester; benzoic acid, m.p. 122°, was obtained in about 22% yield.

o-Methoxybenzaldehyde (13.6 g) gave a viscous brown oil (25 g). Treatment of this oil with benzene in the cold, precipitated a solid (22 g) on standing. This solid after filtration was treated with boiling benzene in which it partly dissolved. The insoluble fraction (3.7 g) was found to be the itaconic acid (II;  $R_1 = R_3 =$  $R_4 = H$ ,  $R_2 = CH_3O$ ), m.p. 198–199° (from water). This melting point was undepressed on admixture with a specimen of cis- $\gamma$ -o-methoxyphenyl- $\alpha$ -methylitaconic acid obtained from the alkaline hydrolysis of the half-ester (II;  $R_1 = R_3 = H$ ,  $R_2 = CH_3O$ ,  $R_4 = CH_3$ ) as shown later. Evaporation of the benzene solution gave the soluble fraction as a solid (17.6 g, 66% yield) which was crystallized from benzene, m.p. 168-170°. This was identified as  $\beta$ -methyl- $\alpha$ -hydrogen cis- $\gamma$ - $\sigma$ -methoxyphenyl- $\alpha$ -methylitaconate (II;  $R_1 = R_3 = H$ ;  $R_2 = CH_3O, R_4 = CH_3).$ 

Anal. Calcd. for C14H16O5: C, 63.62; H, 6.10. Found: C, 63.80; H, 6.28.

The original benzene mother liquor on long keeping gave a small amount of a solid acid (2.5 g), m.p. 217° (from methanol), which failed to give a 2,4-dinitrophenylhydrazone. This substance was found to be 2-o-anisyl-3-carboxy-4-o-methoxybenzylidene-3-methyl-5-oxo-tetrahydrofuran (IX). Infrared spectrum (KBr): 1 750 cm<sup>-1</sup>.

Anal. Calcd. for C21H20O6: C, 68.47; H, 5.4; CH3O, 16.84; mol. wt. and equiv. wt., 368). Found: C, 68.59; H, 5.60; CH<sub>3</sub>O, 17.08; mol. wt., 346; equiv. wt., 360.

Alkaline hydrolysis of this substance (0.4 g, 2 h refluxing with 10% sodium hydroxide solution) gave acid and neutral products. The acid (0.25 g), m.p. 196–198 (from water), on admixing with the previous specimen of  $cis-\gamma$ -o-methoxyphenyl- $\alpha$ -methylitaconic acid (II;  $R_1 = R_3 = R_4 = H, R_2 = CH_3O$ ) gave no depression. The neutral semisolid (0.1 g) gave an orange 2,4-dinitrophenylhydrazone, m.p. 238° (from ethanol). This on admixing with an authentic specimen of o-methoxybenzaldehyde 2,4-dinitrophenylhydrazone (from B.D.H. o-methoxybenzaldehyde), m.p. 243-244° (from ethanol), gave no depression.

No o-methoxybenzoic acid was detected accompanying the Stobbe product. When the experiment was carried out under the same conditions, but in the absence of the methylsuccinic ester, o-methoxybenzoic acid (5% yield), m.p. 100°, was obtained and identified by its melting point and mixed melting point with a specimen of o-methoxybenzoic acid (B.D.H.).

Saponification of the half-ester (II;  $R_1 = R_3 = H$ ,  $R_2 = CH_3O$ ,  $R = CH_3$ ) (1 g) with 10% sodium hydroxide solution (15 ml, 2 h refluxing), gave a colorless solid (0.8, 84.5% yield), m.p. 198-199° (from water). This was identified as  $cis-\gamma-o$ -methoxyphenyl- $\alpha$ -methylitaconic acid (II;  $R_1 = R_3 = R_4 = H$ ,  $R_2 = CH_3O).$ 

Anal. Calcd. for C13H14O5: C, 62.39; H, 5.64. Found: C, 62.41; H, 5.66.

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### Alternative Preparation of 2-o-Anisyl-3-carboxy-4-o-methoxybenzylidene-3-methyl-5-oxotetrahydrofuran (IX)

A solution of o-methoxybenzaldehyde (12.1 g, 2 mole) and dimethyl methylsuccinate (4.4 g, 1 mole) in anhydrous ether (100 ml) was added dropwise with cooling  $(-15^{\circ})$  and shaking to a suspension of finally powdered alcohol-free sodium ethoxide (2 mole, from 1.12 g sodium in 50 ml dry ether). A precipitate rapidly separated. The mixture was kept for 2 days at  $-15^{\circ}$  and then at 0 for another 2 days. The ice-cold mixture was acidified (litmus) with cold dilute hydrochloric acid. The ethereal layer was separated and the aqueous layer was extracted with ether. The ethereal layer and extracts were washed with water then repeatedly extracted with sodium carbonate solution. This was acidified to give an oil which was taken into ether and dried (Na<sub>2</sub>SO<sub>4</sub>). Evaporation of the solvent gave a semisolid (9.5 g) which solidified completely under benzene, m.p. 215-220°. This was crystallized from methanol as colorless crystals, m.p. 219-221°, and on admixing with a sample of the lactonic acid (IX, m.p. 217°) gave no depression.

p-Chlorobenzaldehyde (14 g) gave a deep-brown resinified oil (15 g). This was partly solidified after the addition of a little amount of benzene and standing. The solid fraction (about 2 g) melted over a wide range indicating that it was a mixture. Treatment of this mixture with boiling water gave two substances. The soluble one (1.4 g), m.p. 240° (from benzene), was found to be *p*-chlorobenzoic acid, and identified by its melting point and mixed melting point with an authentic specimen of p-chlorobenzoic acid (B.D.H.). The insoluble colorless substance (0.5 g), m.p. 206° (from methanol), was found to be  $cis-\gamma-p$ -chlorophenyl- $\alpha$ methylitaconic acid (II;  $R_1 = R_2 = R_4 = H$ ,  $R_3 = Cl$ ) Anal. Calcd. for  $C_{12}H_{11}O_4Cl$ : C, 56.27; H, 4.32; Cl, 13.95. Found: C, 56.22; H, 4.17; Cl, 14.56.

The benzene solution gave, after evaporation, an oily residue (about 13 g). A part of this oil (4 g) was

refluxed with 5% sodium hydroxide solution at 130° (oil bath) for 4 h. The solid product obtained after acidification, was treated repeatedly with boiling water. The insoluble part (1.1 g, m.p. 206° from methanol) was identified as  $cis-\gamma-p$ -chlorophenyl- $\alpha$ -methylitaconic acid (II;  $R_1 = R_2 = R_4 = H$ ,  $R_3 = CI$ ) by its melting point and mixed melting point with the acid obtained directly from Stobbe reaction. The hot water washings gave after cooling a colorless solid (0.4 g, m p. 240°) which was found to be p-chlorobenzoic acid. When the Stobbe experiment was carried out normally but with no methylsuccinic ester; a solid acid, m.p. 240°, was obtained in about 45% yield and was identified as p-chlorobenzoic acid. Benzophenone (18 g) gave a solid product (22 g, 72% yield). This was crystallized from benzene as colorless

crystals, m.p. 152°, and identified as  $\beta$ -methyl- $\alpha$ -hydrogen- $\gamma_1\gamma$ -diphenyl- $\alpha$ -methylitaconate (II; R<sub>1</sub> = C<sub>6</sub>H<sub>5</sub>,  $R_2 = R_3 = H, R_4 = CH_3$ ).

Anal. Calcd. for C19H18O4: C, 73.53; H, 5.85. Found: C, 73.64; H, 5.73.

Saponification of this half-ester (1 g) resulted in the known  $\gamma,\gamma$ -diphenyl- $\alpha$ -methylitaconic acid (2) (II;  $R_1 = C_6H_5$ ,  $R_2 = R_3 = R_4 = H$ ) as colorless crystals, m.p. 178° (from water). Anal. Calcd. for  $C_{18}H_{16}O_4$ : C, 72.96; H, 5.44. Found: C, 73.29, H, 5.41.

Acetophenone (12 g) gave a brown viscous oil (19 g, 76.6% yield). On distillation a heavy, pale-yellow oil, b.p. 158° at 0.7 mm, was obtained (12.2 g, 64.5% yield) which was partially solidified. The solid was separated by decantation, washed with little cold benzene, and crystallized from methanol as colorless needles (4.5 g), m.p. 106-108°. This was found to be  $\beta$ -methyl  $\alpha$ -hydrogen cis- $\alpha$ , $\gamma$ -dimethyl- $\gamma$ -phenylitaconate (II;  $R_1 = R_4 = CH_3$ ,  $R_2 = R_3 = H$ ).

Anal Calcd. for C14H16O4: C, 67 73; H, 6.50. Found: C, 68.07; H, 6.11.

Saponification of this crystalline half-ester (1 g) gave a colorless solid (0.7 g) crystallizable from benzene, m.p. 139°, and was identified as  $cis-\alpha,\gamma$ -dimethyl- $\gamma$ -phenylitaconic acid (II;  $R_1 = CH_3, R_2 = R_3 = R_4 = H$ ). Anal. Calcd. for C15H14O4: C, 66.65; H, 6.02. Found: C, 66.99; H, 6.42.

Alkaline hydrolysis of the oil fraction (1 g from about 7.5 g) gave a colorless solid (0.65 g), m.p. 178-180° (from water). This was identified later as trans- $\alpha$ ,  $\gamma$ -dimethyl- $\gamma$ -phenylitaconic acid (VI; R = H).

Anal. Calcd. for C13H14O4: C, 66.65; H, 6.02. Found: C, 66.72; H, 6.16.

Saponification of the crude undistilled Stobbe product of acetophenone yielded a semisolid acid. This after treatment with charcoal gave colorless droplets of oil which solidified after cooling (42% yield), m.p. 124-157°, and was partly soluble in hot benzene. The insoluble fraction was found to be the acid (VI; R = H) of m.p. 178–180°, and the soluble fraction to be the acid (II;  $R_1 = CH_3$ ,  $R_2 = R_3 = R_4 = H$ ) of m.p. 139°.

### Oxidation of $\alpha, \gamma$ -Dimethyl- $\gamma$ -phenylitaconic Acids

 $\alpha,\gamma$ -Dimethyl- $\gamma$ -phenylitaconic acid (m.p. 139°, 0.5 g) was dissolved in 20% sodium carbonate solution (5 ml). Potassium permanganate solution (0.8 g in 45 ml water) was added dropwise with stirring until the color of permanganate persisted. The mixture was left for 2 h at room temperature, then extracted with ether. The ethereal layer after washing with water and drying (Na<sub>2</sub>SO<sub>4</sub>) was evaporated to give an oily residue (0.2 g). This oil gave a 2,4-dinitrophenylhydrazone, m.p. 229-230° (from ethanol), which on admixing with an authentic specimen of acetophenone 2,4-dinitrophenylhydrazone (from B.D.H. acetophenone) gave no depression. Repeating the above oxidation on the acid isomer (m.p. 178-180°) gave the same product.

Action of Concentrated Sulfuric Acid on the  $\alpha,\gamma$ -Dimethylitaconic Acids  $\alpha,\gamma$ -Dimethyl- $\gamma$ -phenylitaconic acid, m.p. 178–180°, (0.5 g) was treated with concentrated sulfuric acid (15 ml) at room temperature. The mixture was allowed to stand for 30 min, then poured on ice. 2-Methyl-2-(3-methyl-1-indone)-acetic acid (VII) was precipitated after cooling and crystallized from ether - petroleum ether (b.p. 40-60°) as long yellow needles (0.25 g), m.p. 127°. Infrared spectrum (Nujol mull): 1 790 and 1 740 cm<sup>-1</sup>.

Anal. Calcd. for C13H12O3: C, 72.21; H, 5.59. Found: C, 71.64; H, 5.52.

It gave a 2,4-dinitrophenylhydrazone as orange crystals, m.p. 186-187° (from ethanol).

Anal. Calcd. for C<sub>19</sub>H<sub>16</sub>O<sub>6</sub>N<sub>4</sub>: C, 57.57; H, 4.07; N, 14.14. Found: C, 57.73; H, 4.15; N, 13.89.

When the experiment was repeated on the acid isomer, m.p. 139°, a colorless solid was obtained which was found to be the starting material.

## Cyclization of the $\beta$ -Half-esters (General Procedure)

The  $\beta$ -half-ester (except that of p-chlorobenzaldehyde) (5g) and anhydrous sodium acetate (2g) in acetic anhydride (40 ml) were refluxed for 6 h, then worked up by removing the acetic anhydride under reduced pressure, adding water, then extracting the product with ether. The ethereal solution was washed with sodium bicarbonate solution and then water and dried (Na<sub>2</sub>SO<sub>4</sub>). Evaporation of the solvent left a neutral product.

The cis- $\beta$ -half-ester from benzaldehyde (II;  $R_1 = R_2 = R_3 = H$ ,  $R_4 = CH_3$ ) gave a solid, crystallizable from benzene as colorless crystals, m.p. 120°, (69% yield) and was found to be methyl 4-acetoxy-3-methyl-2naphthoate (V;  $R_1 = R_2 = R_3 = H$ ,  $R_4 = CH_3$ ,  $R_5 = CH_3CO$ ).

Anal. Calcd. for C15H14O4: C, 69.75; H, 5.46. Found: C, 70.33; H, 5.63.

Alkaline hydrolysis of this product (2 g, 2 h reflux in 10% sodium hydroxide solution, 50 ml) gave 4-hydroxy-3-methyl-2-naphthoic acid (V;  $R_1 = R_2 = R_3 = R_4 = R_5 = H$ ; 90% yield) as dirty needles, m.p. 237-238° (from methanol).

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Anal. Calcd. for C<sub>12</sub>H<sub>10</sub>O<sub>3</sub>: C, 71.28; H, 4.99. Found: C, 71.27; H, 5.26.

The cis- $\beta$ -half-ester from o-methoxybenzaldehyde (II;  $R_1 = R_3 = H$ ,  $R_2 = CH_3O$ ,  $R_4 = CH_3$ ) afforded a neutral solid (61% yield), crystallizable from methanol as colorless needles, m.p. 123–125°, and was identified as methyl 4-acetoxy-8-methoxy-3-methyl-2-naphthoate (V;  $R_1 = R_3 = H$ ,  $R_2 = CH_3O$ ,  $R_4 = CH_3$ ,  $R_{\mathfrak{s}} = C\dot{H_{\mathfrak{z}}}CO).$ 

Anal. Calcd. for C16H16O5: C, 66.66; H, 5.59; CH3O, 21.52; CH3CO, 14.93. Found; C, 67.03; H, 5.70; CH<sub>3</sub>O, 20.98; CH<sub>3</sub>CO, 15.52.

Saponification of this acetoxyester as usual gave a quantitative yield of 4-hydroxy-8-methoxy-3-methyl-2naphthoic acid (V;  $R_1 = R_3 = R_4 = R_5 = H$ ,  $R_2 = CH_3O$ ) as dirty crystals, m.p. 243-245° (from methanol).

Anal. Calcd. for C13H12O4: C, 67.23; H, 5.21. Found: C, 67.40; H, 5.27.

The cis- $\beta$ -half-ester from p-chlorobenzaldehyde (II;  $R_1 = R_2 = H$ ,  $R_3 = Cl$ ,  $R_4 = CH_3$ ) (4 g) and anhydrous sodium acetate (1.5 g) in a mixture of acetic anhydride (25 ml) and glacial acetic acid (25 ml) were heated at 130° (oil bath) for 3 h. The reaction mixture was then worked up as in the general procedure. The neutral product (3.8 g) as a brown viscous oil was saponified to give a semisolid product from which dirty crystals (20% yield) of 6-chloro-4-hydroxy-3-methyl-2-naphthoic acid (V;  $R_1 = R_2 = R_4 = R_5 = H$ ,  $R_3 = Cl$ ) were isolated, m.p. 275-276° (from aqueous methanol).

Anal. Calcd. for  $C_{12}H_{2}O_{3}Cl: C, 60.88; H, 3.80, Cl; 15.01.$  Found: C, 60.78; H, 3.88; Cl, 15.1. The  $\beta$ -half-ester from benzophenone (II;  $R = C_{6}H_{5}, R_{2} = R_{3} = H, R_{4} = CH_{3}$ ) proceeded normally with a quantitative yield of methyl 4-acetoxy-3-methyl-1-phenyl-2-naphthoate (V;  $R_1 = C_6H_5$ ,  $R_2 = R_3 = H_3$  $R_4 = CH_3$ ,  $R_5 = CH_3CO$  which was obtained as a colorless solid crystallizable from methanol, m.p. 137°. Anal. Calcd. for C<sub>21</sub>H<sub>18</sub>O<sub>4</sub>: C, 75.43; H, 5.43. Found: C, 75.28; H, 5.53.

This gave on alkaline hydrolysis a solid mixture which was dissolved in ether and the ethereal solution was extracted with sodium carbonate solution. The alkaline extract afforded a solid acid (40% yield) and light crystals, m.p. 232°, and identified as 4-hydroxy-3-methyl-1-phenyl-2-naphthoic acid (V;  $R_1 = C_6H_5$ ,  $R_2 = R_3 = R_4 = R_5 = H$ ).

Anal. Calcd. for C<sub>18</sub>H<sub>14</sub>O<sub>3</sub>: C, 77.68; H, 5.07. Found: C, 77.94; H, 5.48.

The phenolic solid was crystallizable from benzene as colorless needles, m.p. 155°, and its infrared spectrum and analysis fitted for methyl 4-hydroxy-3-methyl-1-phenyl-2-naphthoate (V;  $R_1 = C_6H_5$ ,  $R_2 = R_3 = R_5$ = H,  $R_4 = CH_3$ ). Infrared spectrum (Nujol mull): 3 500 and 1 710 cm<sup>-1</sup>.

Anal. Calcd. for C19H16O3: C, 78.06; H, 5.52. Found: C, 78.15; H, 5.43.

#### Methylation of Phenolic Acids (General Procedure)

The phenolic acid (1 g), dimethyl sulfate (3 g), and anhydrous potassium carbonate (4 g) in acetone (30 ml) were refluxed for 12 h on a water bath. Removal of acetone afforded a solid residue to which water was added to dissolve any inorganic material. The organic product was then filtered or extracted with ether.

4-Hydroxy-3-methyl-2-naphthoic acid (V;  $R_1 = R_2 = R_3 = R_4 = R_5 = H$ ) gave a colorless oil (87.5%) yield). This when refluxed with 10% sodium hydroxide solution (15 ml) for 2 h, afforded, after washing with ether and acidification with cold hydrochloric acid, 4-methoxy-3-methyl-2-naphthoic acid (V;  $R_1 =$  $R_2 = R_3 = R_4 = H$ ,  $R_5 = CH_3$ ) (92% yield) as colorless crystals, m.p. 207° (from benzene).

Anal. Calcd. for C13H12O3: C, 72.21; H, 5.59; CH3O, 14.35. Found: C, 72.29; H, 6.20; CH3O, 14.36.

4-Hydroxy-8-methoxy-3-methyl-2-naphthoic acid (V;  $R_1 = R_3 = R_4 = R_5 = H$ ,  $R_2 = CH_3O$ ) required a bigger amount of acetone (50 ml), and absolute methanol (20 ml) was added for its dissolution. The produced methyl 4,8-dimethoxy-3-methyl-2-naphthoate (V;  $R_1 = R_3 = H$ ,  $R_2 = CH_3O$ ,  $R_4 = R_5 = CH_3$ ) was separated as colorless needles (95% yield), m.p. 108-110° (from methanol).

Anal. Calcd. for C15H16O4: C, 69.21; H, 6.20. Found: C, 69.56; H, 6.25.

This after saponification as usual gave 4,8-dimethoxy-3-methyl-2-naphthoic acid (V;  $R_1 = R_3 = R_4 = H_1$  $R_2 = CH_3O$ ,  $R_5 = CH_3$ ) (87.7% yield) as a colorless solid, m.p. 209–211° (from acetic acid).

Anal. Calcd. for  $C_{14}H_{14}O_4$ : C, 68.28; H, 5.73; CH<sub>3</sub>O, 25.16. Found: C, 67.73; H, 5.74; CH<sub>3</sub>O, 24.22. 6-Chloro-4-hydroxy-3-methyl-2-naphthoic acid (V;  $R_1 = R_2 = R_4 = R_5 = H$ ,  $R_3 = Cl$ ) gave the corresponding methoxy ester (V;  $R_1 = R_2 = H$ ,  $R_3 = Cl$ ,  $R_4 = R_5 = CH_3$ ) as colorless needles (99% yield), m.p. 100-102° (from methanol).

Anal. Calcd. for C14H13O3Cl: C, 63.51; H, 4.9; Cl, 13.42. Found: C, 63.52; H, 4.89; Cl, 12.55.

4-Hydroxy-3-methyl-1-phenyl-2-naphthoic acid (V;  $R_1 = C_6H_5$ ,  $R_2 = R_3 = R_4 = R_5 = H$ ) gave methyl 4-methoxy-3-methyl-1-phenyl-2-naphthoate (V;  $R_1 = C_6H_5$ ,  $R_2 = R_3 = H$ ,  $R_4 = R_5 = CH_3$ ) (88% yield) as colorless crystals, m.p. 113–115° (from methanol). Anal. Calcd. for  $C_{20}H_{18}O_3$ : C, 78.41; H, 5.92. Found: C, 78.82; H, 5.99.

Methyl 4-hydroxy-3-methyl-1-phenyl-2-naphthoate (V;  $R_1 = C_6H_5$ ,  $R_2 = R_3 = R_5 = H$ ,  $R_4 = CH_3$ ) gave a neutral solid, m.p. 113-115 (from methanol). This on admixing with a specimen of the above methoxy ester (V;  $R_1 = C_6H_5$ ,  $R_2 = R_3 = H$ ,  $R_4 = R_5 = CH_3$ ) gave no depression.

#### Preparation of $\alpha$ -Half-esters (General Procedure)

The itaconic acid (1 g) was dissolved in the least amount of hot acetyl chloride (in case of the itaconic acid from p-chlorobenzaldehyde, a mixture of acetic anhydride and acetyl chloride was required). The mixture was refluxed for 2 h on a water bath and the excess acetyl chloride was then removed under reduced pressure

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to give a solid itaconic anhydride. This anhydride (0.5 g) was then refluxed in dry methanol (10 ml) for 3 h. After the removal of excess methanol under reduced pressure, a solid residue was obtained.

The itaconic acid from o-methoxybenzaldehyde (II;  $R_1 = R_3 = R_4 = H$ ,  $R_2 = CH_3O$ ) proceeded normally to give the anhydride (III;  $R_1 = R_3 = H, R_2 = CH_3O$ ) (0.8 g, 75% yield) as colorless needles, m.p. 149–150° (from benzene).

Anal. Calcd. for C13H12O4: C, 67.23; H, 5.21. Found: C, 66.66; H, 5.29.

Treatment of this anhydride with methanol gave the  $\alpha$ -half-ester (IV;  $R_1 = R_3 = H; R_2 = CH_3O$ ) (70%) yield) as colorless crystals, m.p. 162-163° (from methanol). Anal. Calcd. for  $C_{14}H_{16}O_5$ : C, 63.62; H, 6.10. Found: C, 63.38; H, 6.22.

The itaconic acid from p-chlorobenzaldehyde (II;  $R_1 = R_2 = R_4 = H$ ,  $R_3 = Cl$ ) (1 g) was dissolved in acetic anhydride (10 ml). Acetyl chloride (15 ml) was then added to the solution, and the experiment was carried out as usual to give the anhydride (III;  $R_1 = R_2 = H$ ,  $R_3 = Cl$ ) (0.9 g, 89% yield). This was separated in yellow crystals from acetic anhydride, m.p. 175-177°.

Anal. Calcd. for C12H3O3Cl: C, 60.88; H, 3.8; Cl, 15.01. Found: C, 60.34; H, 3.41; Cl, 16.15.

Treatment of this anhydride with methanol gave  $\alpha$ -methyl  $\beta$ -hydrogen  $cis-\gamma-p$ -chlorophenyl- $\alpha$ -methylitaconate (IV;  $R_1 = R_2 = H$ ,  $R_3 = Cl$ ) (80% yield) as pale-yellow crystals, m.p. 143–144° (from benzenebenzine, b.p. 40-60°).

Anal. Calcd. for  $C_{13}H_{13}O_4Cl$ : C, 58.1; H, 4.42; Cl, 13.2. Found: C, 58.23; H, 4.75; Cl, 13.68. *The itaconic acid from benzophenone* (III;  $R_1 = C_6H_5$ ,  $R_2 = R_3 = R_4 = H$ ), on dehydration, gave the known anhydride (1) (III;  $R_1 = C_6H_5$ ,  $R_2 = R_3 = H$ ) (0.7 g, 78% yield) as colorless crystals, m.p. 148° (from benzene).

Anal. Calcd. for C<sub>18</sub>H<sub>14</sub>O<sub>3</sub>: C, 77.68; H, 5.07. Found: C, 78.17; H, 5.07.

This anhydride when treated with methanol yielded the  $\alpha$ -half-ester (IV;  $R_1 = C_6H_5$ ,  $R_2 = R_3 = H$ ) (78% yield) as colorless solid crystallizable from ether – petroleum ether (b.p. 40-60°), m.p. 154-155°.

Anal. Calcd. for C<sub>19</sub>H<sub>18</sub>O<sub>4</sub>: C, 73.53; H, 5.85. Found: C, 74.11; H, 5.81.

 $cis-\alpha,\gamma$ -Dimethyl- $\gamma$ -phenylitaconic acid (II;  $R_1 = CH_3, R_2 = R_3 = R_4 = H$ ) gave on dehydration, cis- $\alpha,\gamma$ -dimethyl- $\gamma$ -phenylitaconic anhydride (III;  $R_1 = CH_3$ ,  $R_2 = R_3 = H$ ) (0.8 g, 92% yield) as colorless needles, m.p. 94-95° (from benzene).

Anal. Calcd. for C13H12O3: C, 72.21, H; 5.59. Found: C, 72.32; H, 5.68.

Treatment of this anhydride with methanol gave the  $\alpha$ -half-ester (IV;  $R_1 = CH_3$ ,  $R_2 = R_3 = H$ ) as a colorless solid (85.5% yield) crystallizable from methanol, m.p. 121-123°

Anal. Calcd. for C14H16O4: C, 67.73; H, 6.50. Found: C, 67.79; H, 6.70.

trans- $\alpha,\gamma$ -Dimethyl- $\gamma$ -phenylitaconic acid (VI; R = H) afforded, on dehydration, trans- $\alpha,\gamma$ -dimethyl- $\gamma$ phenylitaconic anhydride (VIII) (0.7 g, i.e. 84% yield) as colorless crystals, m.p. 89-90° (from benzene, petroleum ether, b.p. 40-60°).

Anal. Calcd. for C13H12O3: C, 72.21; H, 5.59. Found: C, 72.60; H, 5.58.

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