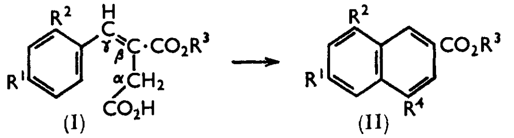
208. The Stobbe Condensation. Part I. The Cyclisation of Methyl Hydrogen cis-γ-o-Methoxyphenyl- and Methyl Hydrogen cis-γ-p-Methoxyphenyl-itaconate to the Corresponding Naphthalene Derivatives.

By A. M. El-Abbady and Lanson S. El-Assal.

Methyl hydrogen *cis*-γ-*o*-methoxyphenyl- and methyl hydrogen *cis*-γ-*p*-methoxyphenyl-itaconate have been isolated on Stobbe condensation of *o*- and *p*-methoxybenzaldehyde with methyl succinate. They are cyclised by acetic anhydride and sodium acetate to methyl 4-acetoxy-8- and -6-methoxy-2-naphthoate which are converted into 1 : 5- and 1 : 7-dimethoxynaphthalene, respectively.

The *cis*-β-half esters, methyl hydrogen *cis*-γ-*o*- (I*a*; $R^3 = Me$) and *cis*-γ-*p*-methoxyphenyl-itaconate (I*b*; $R^3 = Me$) are obtained in about 76% yield by Stobbe condensation of *o*- and *p*-methoxybenzaldehyde, respectively, with dimethyl succinate and *tert.*-butyl alcoholic potassium *tert.*-butoxide.[1] Condensation with ethanolic sodium ethoxide gave inferior results.[2,3] The structure and the *cis*-configuration of the products were confirmed by their cyclisation with sodium acetate in acetic anhydride [3] to methyl 4-acetoxy-8- and -6-methoxy-2-naphthoate (II*a* and *b*; $R^3 = Me$, respectively) in nearly quantitative yield, and this provides a new route for synthesis of naphthalene derivatives.



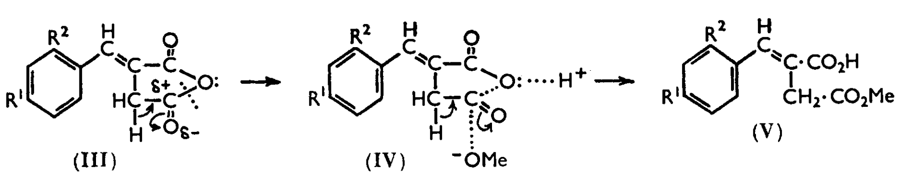
(I) (II)

	R¹	R²	R⁴
(I*a*)	H	OMe	—
(I*b*)	OMe	H	—
(II*a*)	H	OMe	OAc
(II*b*)	OMe	H	OAc

However, the parent itaconate (I; $R^1 = R^2 = H$, $R^3 = Me$) itself gave a very low yield, with much resin.

Alkaline hydrolysis of the acetoxy-esters gave 4-hydroxy-8- and -6-methoxy-2-naphthoic acid (as II), respectively. These phenolic acids were converted by methyl sulphate and potassium carbonate in acetone into the corresponding dimethoxy-esters which were hydrolysed to the dimethoxy-acids and then decarboxylated to give 1 : 5- and 1 : 7-dimethoxynaphthalene, respectively. The 1 : 5-compound was identical with an authentic specimen,[3a,4] but the 1 : 7-compound was an oil which was characterised as a dinitro-derivative.

Hydrolysis of the *cis*-β-half esters (I*a* and *b*; $R^3 = Me$) with boiling aqueous barium hydroxide gave the *cis*-itaconic acids, identical with those obtained by Baddar, El-Assal, Doss, and Shehab.[5] These were converted by acetyl chloride [2,3] into their *cis*-anhydrides



(III) (IV) (V)

a: $R^1 = H$, $R^2 = OMe$. *b*: $R^1 = OMe$, $R^2 = H$.

(III*a* and *b*, respectively). With boiling methanol [3b] these anhydrides gave the *cis*-α-half esters (V*a* and *b*) which were different from the *cis*-β-half esters (I*a* and *b*; $R^3 = Me$)

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[1] Cf. Johnson and Daub, "Organic Reactions," J. Wiley and Sons Inc., 1951, Vol. VI, p. 1.

[2] Johnson *et al.*, *J. Amer. Chem. Soc.*, 1947, **69**, 74; 1950, **72**, 511.

[3] Baddar, El-Assal, and Baghos, *J.*, (*a*) 1955, 1714; (*b*) 1958, 986.

[4] Naylor and Gardner, *J. Amer. Chem. Soc.*, 1931, **53**, 4109.

[5] Baddar, El-Assal, Doss, and Shehab, *J.*, 1959, 1016.

obtained by the Stobbe condensation. This adds evidence for the structures of the *cis*-β-half esters (I).

It has been noted[3b,6] that alcoholysis of anhydrides of type (III) always yields a half ester of type (V) and not that of type (I). This might be due to the attack of a proton on the cyclic oxygen atom of the anhydride, leading to a positive charge on the neighbouring carbon atom stabilised by hyperconjugation (cf. III); the anion MeO^- attacks this positive centre (see IV), which leads to the α-half ester (V).

EXPERIMENTAL

Methyl Hydrogen cis-γ-o-*Methoxyphenylitaconate* (I*a*; $R^3 = Me$).—A solution of *o*-methoxybenzaldehyde (13·6 g., 1 mol.) and methyl succinate (17·5 g., 1·2 mol.) in *tert.*-butyl alcohol (15 ml.) was added to a boiling solution of potassium *tert.*-butoxide [from metallic potassium (5·8 g.) in *tert.*-butyl alcohol (85 ml.)] during 15 min., and the whole refluxed for a further 45 min. The cold mixture was acidified (litmus) with concentrated hydrochloric acid. Evaporation under reduced pressure left a brown viscous oil which was treated with ice-water and extracted with ether. The ethereal solution was washed with water and repeatedly extracted with cold sodium hydrogen carbonate solution, then acidified. The product was filtered off, washed, dried (*ca.* 18·5 g.), and digested with boiling benzene, and the whole was filtered (residue *ca.* 1·6 g.). The benzene solution on concentration afforded a nearly colourless product which on repeated crystallisation from benzene gave *methyl hydrogen* cis-γ-o-*methoxyphenylitaconate* (*ca.* 13 g.), m. p. 138—140° (Found: C, 61·4; H, 5·6; OMe, 24·2. $C_{13}H_{14}O_5$ requires C, 62·4; H, 5·65; OMe, 24·8%. The low value for carbon is attributed to partial hydrolysis).

Evaporation of the benzene mother-liquor precipitated a semi-solid light brown product which is probably a mixture of the stereoisomeric half-esters of type (I).

Methyl 4-Acetoxy-8-methoxy-2-naphthoate (II*a*; $R^3 = Me$).—The above half ester (11 g.) and sodium acetate (3·5 g.) in acetic anhydride (50 ml.) were refluxed for 5 hr., then worked up as usual.[3] Evaporation left *methyl 4-acetoxy-8-methoxy-2-naphthoate* (*ca.* 11 g.), m. p. 124—127°, which after two crystallisations from benzene–light petroleum (b. p. 60—80°) formed needles, m. p. 128—129° (Found: C, 65·6; H, 5·2; OMe, 22·6. $C_{15}H_{14}O_5$ requires C, 65·7; H, 5·1; OMe, 22·6%).

This ester with 15% aqueous-alcoholic (v/v) potassium hydroxide (100 ml.) (2 hours' refluxing) gave pale-yellow *4-hydroxy-8-methoxy-2-naphthoic acid* in crystals (*ca.* 7·5 g.), m. p. 259—260° (from acetic acid) (Found: C, 65·8; H, 4·7; OMe, 14·0. $C_{12}H_{10}O_4$ requires C, 66·05; H, 4·6; 2OMe, 14·2%).

Methyl 4 : 8-Dimethoxy-2-naphthoate.—The above phenolic acid (5 g.), dimethyl sulphate (14·5 g.), and anhydrous potassium carbonate (19 g.) in acetone (150 ml.) were refluxed for 12 hr., affording *methyl 4 : 8-dimethoxy-2-naphthoate* (5·3 g.), plates (from methanol), m. p. 107—108° (Found: C, 68·8; H, 5·7; OMe, 37·6. $C_{14}H_{14}O_4$ requires C, 68·3; H, 5·7; 3OMe, 37·8%). Hydrolysis of this (4 g.) with 15% aqueous-alcoholic (v/v) potassium hydroxide solution (50 ml.) (2 hours' refluxing) as above gave the *dimethoxy-acid*, m. p. 214—215° (from acetic acid) (Found: C, 66·8; H, 5·3; OMe, 25·8. $C_{13}H_{12}O_4$ requires C, 67·2; H, 5·2; 2OMe, 26·7%).

1 : 5-*Dimethoxynaphthalene.*—The preceding acid (0·5 g.) was refluxed in quinoline (5 ml.) with copper-bronze (0·8 g.) for 2·5 hr., and then worked up as usual. The product (0·3 g.) crystallised from benzene, to give 1 : 5-dimethoxynaphthalene, m. p. 183—184°, undepressed on admixture with an authentic specimen.[3a,4]

Methyl Hydrogen cis-γ-p-*Methoxyphenylitaconate* (I*b*; $R^3 = Me$).—*p*-Methoxybenzaldehyde (13·6 g., 1 mol.) and methyl succinate (17·5 g., 1·2 mol.) in *tert.*-butyl alcohol (25 ml.) were added to a boiling solution of potassium *tert.*-butoxide [from metallic potassium (5·8 g.) and the alcohol (95 ml.)] during 30 min. and the whole was refluxed for a further 30 min., then worked up as described for the *o*-isomer. The solid product (*ca.* 19 g.) was digested in boiling benzene, and the solution was filtered from the insoluble residue (*ca.* 2 g.). The benzene solution on concentration afforded *methyl hydrogen* cis-γ-p-*methoxyphenylitaconate* which on repeated crystallisation from benzene had m. p. 119—120° (13 g.) (Found: C, 62·0; H, 5·85; OMe, 24·3. $C_{13}H_{14}O_5$ requires C, 62·4; H, 5·65; 2OMe, 24·8%).

Methyl 4-Acetoxy-6-methoxy-2-naphthoate (II*b*; $R^3 = Me$).—The preceding ester (5 g.) was

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[6] Johnson and Goldman, *J. Amer. Chem. Soc.*, 1944, **66**, 1030.

cyclised with sodium acetate (1·7 g.) in boiling acetic anhydride (30 ml.) (6 hr.) in the usual manner. The *naphthoate* (*ca.* 5·4 g.), on crystallisation from benzene–light petroleum (b. p. 40—60°), had m. p. 125—126° (Found: C, 65·6; H, 5·0; OMe, 21·9. $C_{15}H_{14}O_5$ requires C, 65·7; H, 5·1; 2OMe, 22·6%).

Hydrolysis of this ester (II*b*; R^3 = Me, as for its isomer (50 ml.) (2 hours' refluxing) gave 4-*hydroxy*-6-*methoxy*-2-*naphthoic acid* (*ca.* 4·5 g.), m. p. 200—201° (decomp.) (from dilute acetic acid) (Found: 60·75; H, 5·3; OMe, 12·5. $C_{12}H_{10}O_4,H_2O$ requires C, 61·0; H, 5·1; 2OMe, 13·1%). The analytical result was the same even when the acid had been heated at 60—70°/4 mm. for 3 hr. When the acid was crystallised from glacial acetic acid, its solution gradually darkened and gave light-brown and violet crystals. The former had m. p. 252—254°, and on crystallisation from glacial acetic acid became heterogeneous. Therefore, the crude acid was used in the next experiment.

Methyl 4 : 6-*Dimethoxy*-2-*naphthoate*.—The preceding crude phenolic acid (4 g.), methyl sulphate (12 g.), potassium carbonate (15 g.), and acetone (100 ml.) were refluxed for 10 hr., then worked up as usual, giving *methyl* 4 : 6-*dimethoxy*-2-*naphthoate* (~4·4 g.) in needles (from methanol), m. p. 104—105° (Found: C, 68·5; H, 5·9; OMe, 36·9. $C_{14}H_{14}O_4$ requires C, 68·3; H, 5·7; 3OMe, 37·8%). Hydrolysis of this (3 g.) with 15% aqueous-alcoholic (v/v) potassium hydroxide solution (50 ml.) gave the *dimethoxy-acid* (~2·8 g.), m. p. 262—263° (Found: C, 67·15; H, 5·3; OMe, 26·8. $C_{13}H_{12}O_4$ requires C, 67·2; H, 5·2; 2OMe, 26·7%).

1 : 7-*Dimethoxynaphthalene*.—The preceding acid (0·7 g.) and copper-bronze (0·5 g.) in quinoline (8 ml.) were heated at 205—210° (nitrobenzene-bath) for 1 hr. Further copper-bronze (0·5 g.) was added during a further hour with continuous heating and stirring, then the whole was worked up in the usual manner, affording a viscous brown oil. This oil was extracted with light petroleum (b. p. 40—60°), and the solution filtered from resin. Removal of the solvent gave 1 : 7-dimethoxynaphthalene as a pale brown oil. Nitric acid (*d* 1·42; 0·6 ml.) in acetic acid (5 ml.) was added to a stirred solution of the oil (0·55 g.) in acetic acid (10 ml.) during 30 min. at 30—35°, and then left overnight.[3b] The precipitated crystals (*ca.* 0·4 g.) recrystallised from acetic acid, to give a pale yellow *dinitro-derivative*, m. p. 212—213° (Found: C, 51·8; H, 3·85; N, 10·15; OMe, 22·1. $C_{12}H_{10}O_6N_2$ requires C, 51·8; H, 3·6; N, 10·1; 2OMe, 22·3%).

cis-γ-o-*Methoxyphenylitaconic Acid*.—The *cis*-β-half ester (I*a*; R^3 = Me) (6 g.) was hydrolysed with a concentrated barium hydroxide solution (100 ml.) (2 hours' refluxing), and the precipitated barium salt was filtered off, washed with water and with alcohol, and dried. Acidification with dilute hydrochloric acid liberated an acid which was filtered off, washed, and dried (*ca.* 6 g.). Crystallisation from dilute acetic acid gave *cis*-γ-*o*-methoxyphenylitaconic acid in pale yellow crystals,[5] m. p. 210—211°.

cis-γ-o-*Methoxyphenylitaconic Anhydride* (III*a*).—The above acid (5 g.) was boiled with acetyl chloride (6 ml.) for 2 hr. After evaporation the residue recrystallised from benzene, to give the *anhydride* (*ca.* 4·2 g.) in needles, m. p. 132—133° (Found: C, 66·0; H, 4·7; OMe, 13·9. $C_{12}H_{10}O_4$ requires C, 66·05; H, 4·6; 2OMe, 14·2%).

α-*Methyl* β-*Hydrogen* cis-γ-o-*Methoxyphenylitaconate* (V*a*).—The anhydride (1 g.) was refluxed in methanol (20 ml.) for 3 hr. Evaporation and crystallisation of the residue (1 g.) from benzene–light petroleum (b. p. 80—100°) gave α-*methyl* β-*hydrogen* cis-γ-o-*methoxyphenylitaconate* [3b] in needles, m. p. 128—130°, depressed on admixture with the isomeric ester (Found: C, 62·6; H, 5·75; OMe, 24·2. $C_{13}H_{14}O_5$ requires C, 62·4; H, 5·6; 2OMe, 24·8%).

cis-γ-*p*-*Methoxyphenylitaconic Acid* (I*b*; R^3 = H).—The β-half-ester was refluxed with concentrated barium hydroxide solution (200 ml.) for 6 hr., then worked up as described for its *o*-isomer. The *cis*-γ-*p*-methoxyphenylitaconic acid was obtained in lemon-yellow crystals,[5] m. p. 202—203°.

cis-γ-p-*Methoxyphenylitaconic Anhydride* (III*b*).—The preceding acid (I*b*; R^3 = H) (0·5 g.) with acetyl chloride (15 ml.) (3 hours' refluxing) gave the *itaconic anhydride* (*ca.* 0·4 g.), flakes (from benzene), m. p. 166—167° (Found: 66·1; H, 4·7; OMe, 13·65%).

α-*Methyl* β-*Hydrogen* cis-γ-p-*Methoxyphenylitaconate* (V*b*).—The anhydride (III*b*) (*ca.* 0·5 g.) in methanol (30 ml.) gave, as in the preceding case, α-*methyl* β-*hydrogen* γ-p-*methoxyphenylitaconate* (~0·5 g.), needles [from benzene–light petroleum (b. p. 50—60°)], m. p. 139—140°, depressed on admixture with the β-half-ester (Found: C, 62·3; H, 5·7; OMe, 24·1%).

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A'IN-SHAMS UNIVERSITY, CAIRO, EGYPT.

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