

STOBBE CONDENSATION ON 1-ACETYL-2-METHOXY NAPHTHALENE

A. Essawy and A.Z.M. Heikal

Faculty of Science, Zagazig University, Zagazig, A.R. Egypt

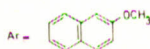
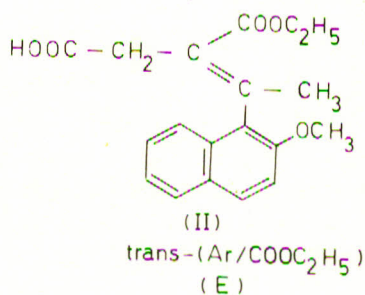
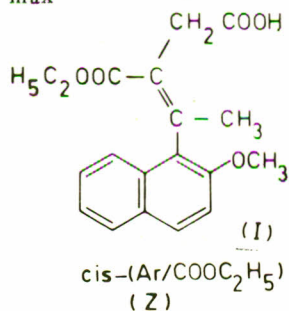
(Received September 30, 1979; revised May 7, 1980)

1-Acetyl-2-methoxy naphthalene was condensed with diethyl succinate in the presence of $(\text{CH}_3)_3\text{COK}$ it gave two stereoisomeric half esters (I) and (II). The structures of these isomers were proved by chemical reactions.

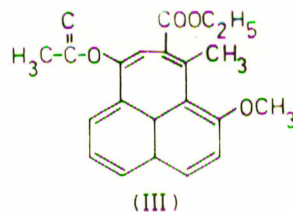
INTRODUCTION

The factors affecting the proportions of stereoisomers produced in the Stobbe condensation involving aldehydes and unsymmetrical ketones, were the subject of some recent investigations [1-3]. The available results indicate that both steric and polar effects are involved [4-8]. The present investigation is a study in which 1-acetyl-2-methoxy naphthalene has been used. The steric effect was varied by the introduction of 2-methoxy naphthyl group instead of phenyl and 3,4-disubstituted phenyl groups in acetophenone, 1-acetyl-2-methoxy naphthalene was condensed with diethyl succinate in the presence of potassium *t*-butoxide, and gave the two stereoisomeric half esters [3,4,7,8] (Z)-2-carbethoxy-3-(2-methoxy-1-naphthyl)pent-3-enoic acid (I, 70%) and (E)-2-carbethoxy-3-(2-methoxy-1-naphthyl)pent-3-enoic acid (II, 18%). The stereoisomeric half esters (I) and (II) were detected by TLC.

Position of the Double Bond. The position of the double bond in the two stereoisomeric half esters (I) and (II) was determined by oxidation with cold dil alkaline potassium permanganate. In each case, the neutral oxidation product was characterized as the original ketone, indicating that the half esters have the alkylidene structures as shown in (I) and (II). The IR spectrum of II showed strong absorption bands at 1742 cm^{-1} (ester group) and 1705 cm^{-1} (carboxylic acid group). Its UV absorption spectrum in CHCl_3 showed bands at $\lambda_{\text{max}} 255\text{ nm}$ ($\epsilon 25.8 \times 10^3$) and λ_{max} at 312 nm ($\epsilon 4.2 \times 10^3$).

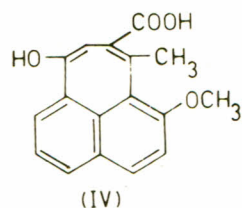


Cyclisation of the cis (Ar-CH₂COOH)-Configuration II. The *cis*-relationship of the aryl group to $-\text{CH}_2\text{COOH}$ in the crystalline half ester (II) was proved by its susceptibility to cyclisation yielding the corresponding acetoxy ester (III) [4] on heating with sodium acetate-acetic anhydride mixture.

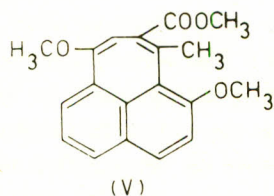


The UV absorption spectrum of acetoxy ester (III) in CHCl_3 showed $\lambda_{\text{max}} 277\text{ nm}$ ($\epsilon 108.35 \times 10^3$) and $\lambda_{\text{max}} 303\text{ nm}$ ($\epsilon_{\text{max}} 36.5 \times 10^3$). Its IR absorption spectrum exhibits two strong carbonyl absorptions at 1760 (aryl acetate) and 1720 cm^{-1} (aromatic carbethoxy group).

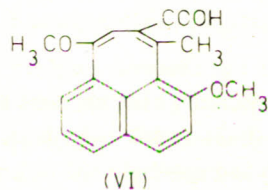
Saponification of the acetoxy ester (III) gave the corresponding phenolic acid (IV), which showed IR absorption typical for the phenolic and carbonyl groups-broad band at 3450 (phenolic hydroxyl group) bands at 2570 and 1700 cm^{-1} (carboxylic acid group). The UV absorption spectrum of the acid (IV) in CHCl_3 showed bands at $\lambda_{\text{max}} 265\text{ nm}$ ($\epsilon 13.8 \times 10^3$) and $\lambda_{\text{max}} 220\text{ nm}$ ($\epsilon 5.7 \times 10^3$).



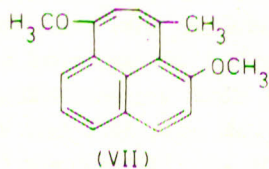
Absorption corresponding to phenolic (OH) in the IR spectrum disappeared upon complete methylation of the phenolic acid (IV) giving the methoxy ester (V), which showed carbonyl absorption at 1725 cm^{-1} (ester group).



Saponification of the methoxy ester (V) gave the corresponding acid (VI), its IR spectrum showed bands at 2560 and 1690 cm^{-1} (carboxylic acid group).

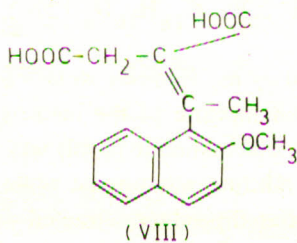


Decarboxylation of the methoxy acid (VI) gave the corresponding ether (VII).



The IR spectrum of (VII) showed the absence of carboxylic bands.

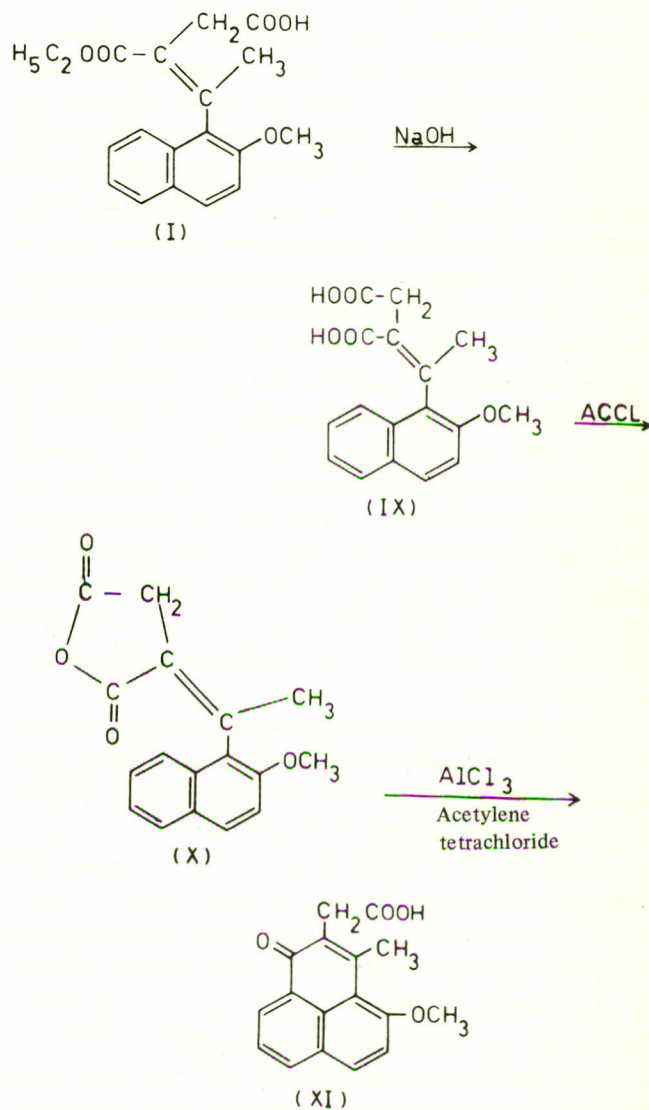
On the other hand, saponification of the *cis*-Ar-CH₂COOH (II) gave the corresponding dibasic acid (VIII). Its IR spectrum showed absorption bands at 3090 , 1735 (nonconjugated carboxylic acid group), 1701 (conjugated carboxylic acid group) and 1638 cm^{-1} ($\nu\text{ C}=\text{C}$). Its UV spectrum (CHCl₃) showed absorption at $\lambda_{\text{max}}\ 240\text{ nm}$ ($\epsilon\ 31.250 \times 10^3$).



The position of the double bond was determined by oxidation with alkaline potassium permanganate. The neutral oxidation product was characterised as the original ketone.

Proof for Trans (Ar-CH₂COOH). Saponification of the oily half ester fraction (I) gave dibasic acid (IX) which on treatment with acetyl chloride gave the corresponding cyclic anhydride (X). The IR absorption spectrum of anhydride (X) showed strong absorption bands at 1820 and 1765 cm^{-1} (due to mechanical coupling of five-membered anhydride ring). Its UV absorption spectrum (CHCl₃) showed bands at $\lambda_{\text{max}}\ 259\text{ nm}$ (34.368×10^3).

The IR spectrum of (IX) showed absorption bands at 1720 and 1705 cm^{-1} due to nonconjugated and conjugated carboxylic acid groups respectively.



The anhydride (X) was treated with aluminium chloride in acetylene tetrachloride [4] to give 2-cyclohexen-1-one acetic acid derivative (XI). Besides analytical data the

establishment of structure (XI) was based on the following data: (i) Solubility in sodium carbonate solution. (ii) The IR spectrum showed strong carbonyl absorption at 1700 and 1710 cm^{-1} respectively, which fall in the range expected for nonconjugated carboxylic acid groups and α,β -unsaturated six-membered ketones. (iii) The UV absorption spectrum (CHCl_3) showed bands at $\lambda_{\text{max}} 257\text{ nm}$ ($\epsilon 34.2 \times 10^3$), $\lambda_{\text{max}} 315\text{ nm}$ ($\epsilon 4.02 \times 10^3$) and $\lambda_{\text{max}} 390\text{ nm}$ ($\epsilon 0.4 \times 10^3$).

EXPERIMENTAL

IR absorption spectra were determined with an Unicam SP 1200 spectrophotometer using KBr wafer technique. UV absorption spectra were recorded with a Beckman model 25 spectrophotometer.

General Procedure for the Stobbe Condensation. A solution of the 1-acetyl-2-methoxy naphthalene (1 mole) in diethyl succinate (1.5 mole) was added dropwise to boiling stirred solution of potassium *t*-butoxide (1.1 mole) (25 ml of *t*-butanol/1 g potassium). The addition lasted half-an-hour; heating on a water-bath and stirring were then continued for 1 hr. Most of the alcohol was then removed under reduced pressure and the cooled residue was rendered slightly acidic with dilute hydrochloric acid. The organic substance was extracted into ether, washed several times with water, and then extracted with cold NaOH solution. The alkaline extract was cooled, acidified with HCl, and the precipitated material extracted with ether. Evaporation of the latter left the reaction product as an oily half ester (88% yield), in which crystalline material began to appear after standing for several days. By fractional crystallization, two components were separated. The first was (I) separated from light petrol (40–60°) as an oily substance (yield 70%). (Found: C 69.3, H 6.2%. $\text{C}_{19}\text{H}_{20}\text{O}_5$ (328) requires: C 69.5, H 6.14%).

The second component was *cis*-Ar- CH_2COOH (II), crystallized from light petrol (60–80°) as a yellow solid crystals, m.p. 74°, yield 18%. (Found: C 69.4, H 6.0%. $\text{C}_{19}\text{H}_{20}\text{O}_5$ (328) requires: C 69.5, H 6.14%).

Oxidation of the Half Esters I and II. To an ice-cold solution the half ester (2 g) in 3% sodium carbonate solution (200 ml), a cold 2% potassium permanganate solution (120 ml), was added portionwise while stirring. The reaction mixture was left at room temperature for 24 hr, treated with few drops of hydrogen peroxide, and the precipitated manganese dioxide filtered off. Both filtrate and precipitate were extracted with benzene. The organic extracts were dried (Na_2SO_4), evaporated. The resulting solids were characterized as the original ketone.

Cyclization of the Cis Half Ester: Formation of Com-

pound III. A mixture of the *cis* half ester (1 mole), freshly fused sodium acetate (1.2 mole) and acetic anhydride (excess), was refluxed for 8 hr. After the removal of acetic anhydride under reduced pressure, water was added and the organic material extracted with ether. The ethereal solution was successively washed with water, 5% sodium carbonate solution, cold 5% sodium hydroxide solution and finally with water. Evaporation of the dried ethereal solution gave the neutral cyclization product which was crystallized from ethanol to give (III) as yellowish brown crystals, m.p. 175°, yield 60%. (Found: C 71.6, H 5.6%. $\text{C}_{21}\text{H}_{20}\text{O}_5$ (352) requires: C 71.58, H 5.72%).

Saponification of the Acetoxy Ester (III): Formation of compound (IV). The acetoxy ester was refluxed with 10% NaOH (aq) (10 ml/1 g ester), for 5 hr. The solution (which darkened at the end of the reaction) was extracted with ether to remove the unsaponified material. The alkaline solution was cooled, acidified with dil HCl, and the solid material precipitated was taken up in ether, evaporation of the dried ethereal solution left the phenolic acid, which was crystallized from benzene–light petrol (40–60°) to give buffy crystals (IV), m.p. 190° (yield 80%). (Found: C 72.1, H 5.1%. $\text{C}_{17}\text{H}_{14}\text{O}_4$ (282) requires: C 72.3, H 5.00%).

Methylation of the Phenolic Acid (IV): Formation of Compound (V). A mixture of the phenolic acid (0.01 mole), dimethyl sulphate (0.04 mole), anhydrous potassium carbonate (0.04 mole) and acetone (100 ml), was refluxed for 20 hr on a water-bath. The solvent was then evaporated, water added, and the organic material extracted with ether. The ethereal solution was successively washed with water, 10% NaOH (aq) and finally with water. The ethereal solution was dried (MgSO_4) and evaporated to give the solid methoxy ester (V), which was recrystallized from ethanol to give brown crystals, m.p. 56°, yield 90%. (Found: C 73.6, H 5.8%. $\text{C}_{19}\text{H}_{18}\text{O}_4$ (310) requires: C 73.5, H 5.8%).

Saponification of the Methoxy Ester (V): Formation of Compound (VI). The methoxy ester was refluxed with 10% NaOH (aq) (10 ml/1 g ester) for 5 hr. The solution (which became dark at the end of the reaction) was cooled and extracted with ether. The alkaline solution cooled, acidified with HCl (dil), and the precipitated solid taken up in ether. The ethereal solution was dried and evaporated. The solid methoxy acid (VI) was recrystallized from methanol to give brown crystals, m.p. 225°, yield 80%. (Found: C 73.1, H 5.3%. $\text{C}_{18}\text{H}_{16}\text{O}_4$ (296) requires: C 72.96, H, 5.4%).

Decarboxylation of the Methoxy Acid (VI): Formation of Compound (VII). A mixture of the methoxy acid (1 g) copper-bronze (1 g) and quinoline (5 ml) was refluxed for 4 hr. The reaction mixture was poured while hot into dil HCl and the precipitated product extracted with benzene.

Table 1. Characterisation of compounds (VIII) and (IX).

Compound	M.p. (°C)	Solvent* yield (%)	Mol. formula Mol. wt.	Analysis (%)	
				Found	Required
VIII	115	M 60	C ₁₇ H ₁₆ O ₅ 300	C 68.1	68.0
				H 5.2	5.4
IX	160	B/P 70	C ₁₇ H ₁₆ O ₅ 300	C 67.9	68.0
				H 5.3	5.4

*M = methanol, B/P = benzene–light petrol (60–80°).

The organic extract was washed with dil HCl, water, sodium carbonate solution and water, dried (MgSO₄). The product obtained was crystallized from methanol to give (VII), m.p. 160°, yield 70%. (Found: C 80.7, H 6.2%. C₁₇H₁₆O₂ (252) requires: C 80.93, H 6.4%).

Saponification of the Half Esters (Compounds I and III): Formation of Compounds (VIII) and (IX) Respectively. The half esters were refluxed with 10% NaOH (aq) (8 ml/l g half ester) for a period of 5 hr. The alkaline solution was then cooled in ice, acidified with dil HCl and the precipitated material taken up in ether. The ethereal solution was washed with water, dried (Na₂SO₄), and evaporated. The results are listed in Table 1.

Conversion of the Dibasic Acid (IX) to the Anhydride (X). The dibasic acid (IX) (1 g) was refluxed with acetyl chloride (10 ml) for 3 hr. Excess of acetyl chloride was removed by distillation. The product was extracted with ether and the ethereal solution washed with 5% sodium carbonate solution and then by water. The ethereal solution was dried and evaporated. The solid obtained was recrystallized from benzene–light petrol (60–80°) to give yellow crystals (X), m.p. 173°, (yield 70%). (Found: C 72.2, H 5.0%. C₁₇H₁₄O₄ (282) requires: C 72.3, H 5.00%).

Action of Aluminium Chloride on the Anhydride (X): Formation of (XI). To a stirred ice-cold solution of the anhydride (X) (2.82 g), (0.01 mole) in acetylene tetrachloride

(50 ml/l g anhydride), anhydrous aluminium chloride (0.01 mole) was added in one portion and stirring was continued for 6 hr. The reaction mixture was left for two days at room temperature and then decomposed with ice-cold dil HCl. The acetylene tetrachloride was removed by steam-distillation and the reaction product extracted with ether. The ethereal solution was washed with water, extracted with 5% sodium carbonate and the alkaline solution was acidified. The acidic reaction product was then extracted with ether. The solid product obtained was recrystallized from ethanol to give (XI), m.p. 215°, (yield 70%). (Found: C 72.2, H 5.1%. C₁₇H₁₄O₄ (282) required: C 72.3, H 5.00%).

REFERENCES

1. W. Bersche, *et al.* *Annal*, **526**, 1 (1936).
2. F.G. Baddar, L.S. El-Assal and V.B. Baghos, *ibid*, **161**, 986 (1958).
3. F.G. Baddar, *et al.*, *J. Chem. Soc.*, **20**, 3332 (1971).
4. M.F. El-Newaihy and M.A. El-Hashash, *J. Chem. Soc.*, 2373 (1971).
5. Selim, *et al.*, *J. Bilharziasis*, **2**, 239 (1974).
6. E. Abbady, *et al.*, *Rev. Roum. Chem.*, **20**, 965 (1975).
7. Baddar, *et al.*, *J. Indian Chem. Soc.*, **52**, 1177 (1975).
8. Mouss, *et al.*, *Indian J. Chem.*, (Sec.B.), **48**, 707 (1976).