

Stobbe Condensation Involving Diethyl- β,β -dimethylglutarate III

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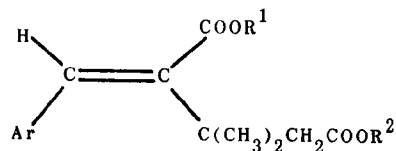
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Summary: Diethyl- β,β -dimethylglutarate condenses with 3,5-dimethyl-, 3,5-dimethoxy-, and 3,5-dichlorobenzaldehyde in presence of sodium hydride to give predominantly the (Z)-half ester (1a-c) together with small amounts of the (E)-half ester (2a-c). The structure and configuration of half-esters have been established on the basis of chemical and spectroscopic evidence.

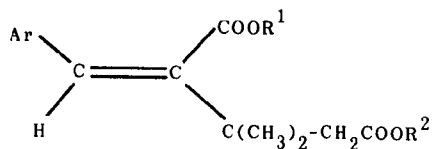
Recently, we reported that Stobbe condensation succeeded with diglycolic esters, [1-3], which are oxa analogues of the glutarates. A possible factor for this different behaviour might be that the crucial lactonisation step is influenced by the differences in the COC bond angle of the diglycollates and the corresponding CCC angle of the glutarates. It appeared reasonable to us that a gem-dimethyl effect at the 3-carbon might modify the central bond angle in favour of lactonisation; and in fact

the present work proves the validity of this structural variation. Also, recently diethyl- β,β -dimethylglutarate condenses with some aromatic aldehydes [4]. In the present work 3,5-dimethyl, 3,5-dimethoxy- and 3,5-dichlorobenzaldehyde were condensed with diethyl- β,β -dimethylglutarate in the presence of sodium hydride to give predominantly oily (Z)-half esters (1a-c) of which only the 3,5-dichlorophenyl half-ester (1c) were obtained in crystalline state; whereas the 3,5-dimethylphenyl

and 3,5-dimethoxyphenyl half-ester (1a,b) were obtained in the form of the corresponding (Z)-dibasic acids (1d,e). In all cases smaller amounts of the crystalline (E)-half-ester (2a-c) were isolated.



1



2

Ar R¹

a, 3,5-(CH₃)₂C₆H₃	C₂H₅
b, 3,5-(CH₃O)₂C₆H₃	C₂H₅
c, 3,5-Cl₂C₆H₃	C₂H₅
d, 3,5-(CH₃)₂C₆H₃	H
e, 3,5-(CH₃O)₂C₆H₃	H

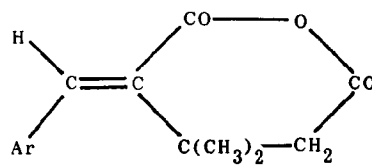
R²	Ar	R¹	R²
H	f; 3,5-Cl₂C₆H₃	H	H
H	g; 3,5-(CH₃)₂C₆H₃	H	H
H	h, 3,5-(CH₃O)C₆H₃	H	C₂H₅
H	i, 3,5-Cl₂C₆H₃	H	C₂H₅
H			

Chemical and spectroscopic evidence can be cited as strong support for the structure and configuration of the above half-esters. The structure of the solid (E)-half-esters (1a-c) and the solid (Z)-half-ester (1c) were supported by their infrared absorption spectra which exhibit absorption at 1695 and 1710 cm⁻¹ for α,β-unsaturated ester and non-conjugated carboxyl group [5] respectively.

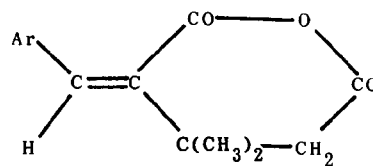
Saponification of the solid half-ester (2a-c) and (1c) gave the corresponding dibasic acids, (2d-f) and (1f) in pure crystalline state. The oily (Z)-half esters (1a,b) after saponification gave high yields of their corresponding dibasic acids (1d,e) in pure

crystalline form. All crystalline dibasic acids show νCO at 1690 and 1715 cm⁻¹ which corresponds to α,β-unsaturated and non-conjugated carboxyl groups respectively [5].

When the pure (Z) and (E) acids were treated with acetyl chloride, they were converted to their corresponding (Z) and (E) cyclic anhydrides (3a-c) and (4a-c) which were obtained in a pure crystalline form. The infrared spectra of these compounds are in agreement with their structure, since they show two absorption bands at 1795, 1740 cm⁻¹ characteristic of six-membered ring anhydrides [5].



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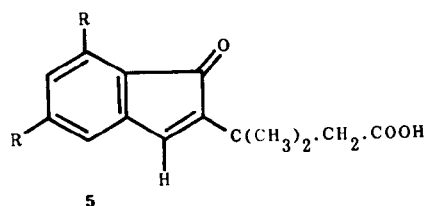


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a, Ar = 3,5-(CH₃)₂C₆H₃;
b, Ar = 3,5-(CH₃O)₂C₆H₃,
c, Ar = 3,5-Cl₂·C₆H₃

Refluxing the anhydride (3a-c) and (4a-c) with ethanol cleaves the ring at the non-conjugated carbonyl to give the corresponding 4-carboxyl half-esters (1g-i and 2g-i) in Ca 80%. The appearance of νCO at 1760, 1720 cm⁻¹ agrees with non-conjugated ester and α,β-unsaturated acids, and is considered as a further proof for the structure of the anhydrides.

The (E) configuration assigned to compounds (2a-c) is supported by the ring closure of their corresponding anhydrides (4a-c) under the influence of anhydrous aluminium chloride in nitrobenzene to 5,7-disubstituted 2-(β,β-dimethyl propionic) indene-1,3-one (5a-c) respectively.



a, R = CH₃, b, R = OCH₃, c, R = Cl

The structure of these cyclization products is based on: (i) their elemental analysis, (ii) their solubility in aqueous Na₂CO₃, (iii) their yellow colour, (iv) the formation of 2,4-dinitrophenylhydrazone derivative, (v) the appearance of an absorption at 1715, 1700 cm⁻¹ in their i.r. spectra which may be attributed to ν_{CO} for ring ketone and carboxyl groups, beside a sharp absorption band at 895 cm⁻¹ can be correlated for the isolated aromatic hydrogen [5], and (vi) the position of maxima in their electronic spectra (λ_{max} at 246-250, 294-296; ε_{max} Ca 34,000 - 41,000, 33,000 and 38,000) closely resemble to those of analogous compounds [1]. The longer wavelength bands extends well into the violet region thus reflecting the yellow colour of these compounds.

When the (Z)-anhydrides (3a-c) were subjected to the same cyclization reaction, they failed to cyclise, and the sole isolable product were their corresponding dibasic acids (1d-f).

Experimental

Melting points are not corrected, infrared (KBr) were measured on a Unicam Sp 1200 infracord, electronic spectra on a Unicam Sp 1800 Spectrophotometer.

(E)- and (Z)-5-aryl-3,3-dimethyl-4-ethoxycarbonyl pent-4-enoic acids (1a-c) and 2c by Stobbe condensation:

Diethyl-β,β-dimethylglutarate, the aldehyde and sodium hydride (1.5 : 1 : 1.5 mol) in excess dry benzene were stirred on water-bath for 20-25 hrs, and the reaction mixture was worked up as usual [1].

3,5-Dimethyl benzaldehyde:

(13.4 g) (stirred for 20 hrs) gave a half-ester mixture (17.2 g, 56% yield), which was dissolved in benzene-light petroleum (b.p. 90-100°) whereby it could be separated into two fractions: (i) the less soluble (E)-half-ester 1a (3.8 g) (cf. Table 1), (ii) the more soluble fraction (13.4 g). The latter was obtained as an oil and its composition revealed by sapanofication (see later).

3,5-Dimethoxybenzaldehyde (16.6 g):

Stirring for 20 hrs, gave a half-ester mixture (16.8 g, 50% yield), which was dissolved in ben-

Table 1: (Z)- and (E)-aryl-3,3-dimethyl-4-ethoxycarbonyl-pent-4-enoic acids 1c and 2a-c.

No.	M.p.(°C) Solvent of cryst. ^a	Formula Mol.wt.)	Analysis (%)		
			Calcd / Found		
			C	H	Cl
1c	123-25 bz	C ₁₆ H ₁₈ Cl ₂ O ₄ (345)	55.65	5.21	20.58
			55.80	5.40	20.80
2a	136-38 L.P. 80	C ₁₈ H ₂₄ O ₄ (304)	71.10	7.89	
			71.40	8.10	
2b	149-51 L.P.80	C ₁₈ H ₂₄ O ₆ (336)	64.22	7.11	
			64.50	7.30	
2c	168-70 L.P. 100	C ₁₆ H ₁₈ Cl ₂ O ₄ (345)	55.65	5.21	20.58
			55.90	5.50	20.90

(a) bz = benzene L.P. 80 = light petroleum (b.p. 80-100°C L.P. 100 = light petroleum (b.p. 100-120°C)

Table 2: (Z)- and (E)-5-aryl-3,3-dimethyl-4-carboxypent-4-enoic acids (1d-f) & (2d-f) and their corresponding anhydrides (3a-c) & (4a-c).

No.	M.p.(°C) Solvent of cryst. ^a	Formula (Mol.wt.)	Analysis (%)		
			C	Calcd / Found H	Cl
1d	156-58 bz	C ₁₆ H ₂₀ O ₄ (276)	69.56	7.24	
			69.80	7.40	
1e	175-77 bz	C ₁₆ H ₂₀ O ₆ (308)	62.33	6.49	
			62.50	6.80	
1f	111-13 L.P. 80	C ₁₄ H ₁₄ Cl ₂ O ₄ (317)	52.99	4.41	22.39
			53.20	4.60	22.60
2d	183-85 bz	C ₁₆ H ₂₀ O ₄ (276)	69.56	7.24	
			69.70	7.50	
2c	194-96 bz	C ₁₈ H ₂₀ O ₆ (308)	62.33	6.49	
			62.60	6.70	
2f	142-44 L.P.80	C ₁₄ H ₁₄ Cl ₂ O ₃ (317)	52.99	4.41	22.39
			53.30	4.50	22.70
3a	112-14 L.P. 80	C ₁₆ H ₁₈ O ₃ (258)	74.49	6.97	
			74.60	7.10	
3b	133-35 L.P. 80	C ₁₆ H ₁₈ O ₅ (290)	66.20	6.20	
			66.50	6.50	
3c	99-101 L.P. 60	C ₁₄ H ₁₂ Cl ₂ O ₃ (299)	56.18	4.01	23.74
			56.40	4.20	23.90
4a	155-57 L.P. 100	C ₁₆ H ₁₈ O ₃ (258)	74.49	6.97	
			74.70	7.30	
4b	171-73 bz	C ₁₆ H ₁₈ O ₅ (290)	66.20	6.20	
			66.40	6.30	
4c	118-20 L.P. 80	C ₁₄ H ₁₂ Cl ₂ O ₃ (299)	56.18	4.01	23.74
			56.20	4.10	23.80

(a) bz = benzene, L.P. 100 = light petroleum (b.p. 100-120°C), L.P. 80 = light petroleum (b.p. 80-100°C)
L.P. 60 = light petroleum (b.p. 60-80°C).

zene-light petroleum (b.p. 60-80 g, 50% yield), whereby it could be separated into two fractions: (i) the less soluble (E)-half-ester 1b (4.2 g) (cf. Table 1), (ii) the more soluble fraction (14.6 g). The latter was obtained as an oil whose composition was revealed by saponification (see later).

3,5-Dichlorobenzaldehyde (17.3 g):

Stirring for 23 hrs gave a half-ester mixture (22.1 g, 64% yield) which was separated by fractional crystallisation from benzene-light petroleum

(b.p. 60-80°C) to give: (I) the less soluble (E)-half-ester (1c) (5.1 g) and (ii) the more soluble (Z)-half-ester 2c (17.0 g) (cf. Table 1).

Saponification of the half-esters:

The half ester was refluxed with 10% aqueous sodium hydroxide (10 ml per gram ester) for 3 hrs (cf. Table 2).

The crystalline (E)-dimethyl half-ester 1a (2 g) gave the (E)- dimethyl dibasic acid 1d (1.5 g,

Action of aluminium chloride upon the cyclic anhydrides:

Aluminium chloride (1.2 mol) and a solution of the (E)-anhydride (1 mol) in nitrobenzene (15 ml per g anhydride) were stirred for 6 hrs and left overnight at room temperature. The acidic reaction product (75-80% yield) was obtained as yellow crystals, for details (cf. Table 3).

When the (Z)-anhydrides (4a-c) were subjected to the same procedure the corresponding dibasic acids were recovered in considerably high yield.

References

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