COMMUNICATIONS

DE LA FACULTÉ DES SCIENCES
DE L'UNIVERSITÉ D'ANKARA

Série B : Chimie

TOME : 31 ANNÉE : 1985

STOBBE CONDENSATION INVOLVING DIETHYL DIGLYCOLLATE WITH FURAN 2-ALDEHYDE AND THIOPHENE-2-ALDEHYDE SYNTHESIS OF CYCLOPENTENO-FURAN AND CYCLOPENTENO-THIOPHENE DERIVATIVES

by

E.I. ENAYAT, F.A. EL-BASSIOUNY, H.A. ABDEE-HAMİT, F.S. SAYED

7

Faculté des Sciences de l'Université d'Ankara
Ankara, Turquie

Communications dé la Faculté dés Sciéncés
dé l'Univérsité d'Ankara

La Revue "Communications de la Faculté des Sciences de l'Université d'Ankara" est un organe de publication englobant toutes les diciplines scientifiques représentées à la Faculté des Sciences de l'Université d'Ankara.

La Revue, jusqu'à 1975 a l'exception des tomes, I, II, III etait composée de trois séries

Série A : Mathématiques, Physique et Astronomie,
Série B : Chimie,
Série C : Sciences Naturelles.

A partir de 1975 la Revue comprend sept séries:

Série A_1 : Mathématiques,
Série A_2 : Physique,
Série A_3 : Astronomie,
Série B : Chimie,
Série C_1 : Géologie,
Série C_2 : Botanique,
Série C_3 : Zoologie.

A partir de 1983 les séries de C_2 Botanique et C_3 Zoologie ont été réunies sous la seule série Biologie C et les numéros de Tome commencerons par le numéro 1.

En principe, la Revue est réservée aux mémoires originaux des membres de la Faculté des Sciences de l'Université d'Ankara. Elle accepte cependant, dans la mesure de la place disponible les communications des auteurs étrangers. Les langues Allemende, Anglaise et Française seront acceptées indifféremment. Tout article doit être accompagné d'un resumé.

Les articles soumis pour publications doivent être remis en trois exemplaires dactylographiés et ne pas dépasser 25 pages des Communications, les dessins et figures portés sur les feuilles séparées devant pouvoir être reproduits sans modifications.

Les auteurs reçoivent 25 extraits sans couverture.

l'Adresse : Dergi Yayın Sekreteri
Ankara Üniversitesi,
Fen Fakültesi,
Beşevler–Ankara
TURQUIE

STOBBE CONDENSATION INVOLVING DIETHYL DIGLYCOLLATE WITH FURAN-2-ALDEHYDE AND THIOPHENE-2-ALDEHYDE. SYNTHESIS OF CYCLOPENTENO-FURAN AND CYCLOPENTENO-THIOPHENE DERIVATIVES

E.I. ENAYAT, F.A. EL-BASSIOUNY, H.A. ABDEL-HAMID, F.S. SAYED

Chemistry Department, Faculty of Science, Ain Shams University, Cairo, Egypt.

Diethyl diglycollate condenses with furan -2-aldehyde and thiophene-2- aldehyde in presence of sodium hydride to give predominantly the (Z)-half ester (1a, b) together with small amounts of the (E)-half ester (2a, b). The structure of the (E)-half esters was based on their cyclization to cyclopenteno-furan and cyclopentenothiophene derivatives (5a, b) respectively, as well as on spectroscopic evidence.

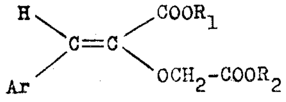
The ratio of isomers has been interpreted in terms of the relative ease of formation of the δ-lactone intermediates.

Diethyl diglycollate condenses with furan-2-aldehyde and thiophene -2-aldehyde in presence of sodium hydride to give predominantly the (Z) half ester (1a, b) together with small amounts of the (E)-half ester (2a, b). The structure of the (E)-half esters was based on their cyclization to cyclopenteno-furan and cyclopentenothiophene derivatives (5a, b) respectively, as well as on spectroscopic evidence.

The ratio of isomers has been interpreted in terms of the relative ease of formation of the δ-lactone intermediates.

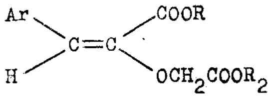
Recently diglycollic ester was shown to undergo Stobbe type condensation with some carbonyl compounds[1,2,3]). Besides extending the scope of the reaction, the present work was intended to investigate any possible dependence of isomer ratios upon structural variations in the carbonyl component. Also the aim of this investigation was the exploitation of the Stobbe condensation for the synthesis of substituted heterocyclic ring systems.

Furan-2-aldehyde and thiophene-2-aldehyde were condensed with diethyl-diglycollate in the presence of sodium hydride to give predominantly oily (Z)-half-esters (1a, b), which by saponification were converted to their corresponding dibasic acids (1c, d) in pure crystalline form. Smaller amounts of the crystalline (E)-half-esters (2a, b) were also isolated.



(1)

	Ar	R_1	R_2
a,	2-furyl	C_2H_5	H
b,	2-Thionyl	C_2H_5	H
c,	2-furyl	H	H



(2)

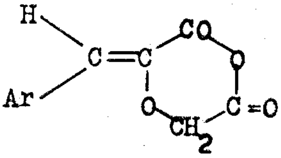
	Ar	R_1	R_2
d,	2-Thionyl	H	H
e,	2-furyl	H	C_2H_5
f,	2-Thionyl	H	C_2H_5

In the reported condensations involving heterocyclic aldehydes or ketones with succinic esters[4], only one isomeric half-ester could be isolated.

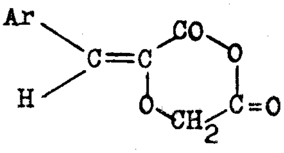
The structure of the solid half esters (2a, b) is supported by their infrared absorption spectra which exhibit absorption at 1695, 1715 cm^{-1} for α,β-unsaturated ester and non-conjugated carboxyl groups[5], respectively.

Saponification of the solid half-esters (2a, b) gave the corresponding dibasic acids (2c, d) in pure crystalline state. The oily (Z)-half-ester after saponification gave high yields of their corresponding dibasic acids in a pure crystalline form. All crystalline dibasic acids show $\nu C{=}O$ at 1700, 1720 cm^{-1} which corresponds to α, β-unsaturated and nonconjugated carboxyl groups[5] respectively.

When the pure (Z)- and (E)- acids were treated with acetyl chloride, they were converted to their corresponding (Z), and (E)-cyclic anhydrides (3a, b) and (4a, b) which were obtained in a pure crystalline form. The I.R. spectra of these compounds is in agreement with their structure since they show two absorption bands at 1800, 1745 cm^{-1} (characteristic of six membered ring anhydrides)[5].



(3)



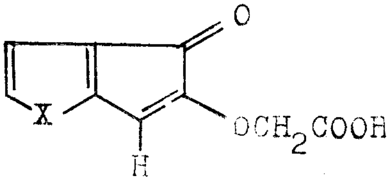
(4)

a, Ar = 2-furyl

b, Ar = 2-Thionyl

Refluxing the anhydrides (3a, b) and (4a, b) with ethanol cleaves the ring at the non-conjugated carbonyl to give the corresponding 4-carboxy-half-esters (1e,f) and (2e, f). The appearance of νC=O at 1760, 1720 cm^{-1} agrees with nonconjugated 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, b) is supported by the ring closure of their corresponding anhydrides (4a, b) under the influence of anhydrous aluminium chloride in nitrobenzene to cyclopentenofuran and cyclopentenothiophene derivatives (5a and b) respectively.



(5)

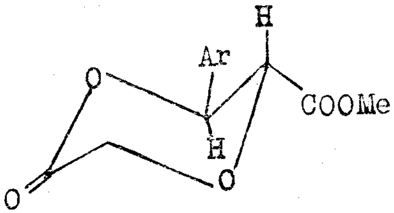
a, X = O

b, X = S

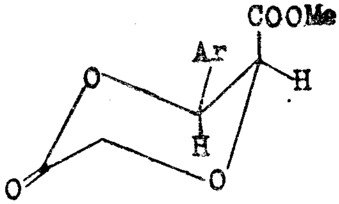
The structure of these cyclization products is based on: 1) their elemental analysis, ii) their solubility in sodium carbonate, iii) their yellow colour; iv) the formation of 2, 4-dinitrophenylhydrazone; v) the appearance of an absorption at 1715, 1700 cm^{-1} in their I.R. spectra which may be attributed to νC=O for ring ketonic and carboxyl groups[5]; vi) the positions of maxima in their electronic spectra (λ_{max} 244–246, 290–292, ϵ_{max} 29, 000–36,000, 31,000–37,000) resemble those for analogous compounds[1].

When the (Z)-anhydrides (3a, b) were subjected to the same cyclization reaction, they fail to cyclize, and the sole isolable product was their corresponding diacids (1c, d).

The predominance of the (Z)-half-esters in the condensation of heterocyclic aldehydes is in agreement with the reported observations[1,2,3] and can be interpreted in terms of the steric factors governing the relative ease of formation of the diastereomeric o-lactone intermediates (6 and 7) the formation of 6 is favoured by the presence of the two bulky groups (Ar and COOMe) in equatorial positions.



(6)



(7)

EXPERIMENTAL

Melting points are not corrected, infrared (KBr) spectra were measured on a Unicam SP 1200 Infracord; electronic spectra on a Unicam SP 1800 spectrophotometer.

(Z) and (E)-5-furyl (or thienyl)-4-methoxycarbonyl 1-3-oxa-pent-4-enoic acids (2a, b) by Stobbe condensation.

Diethyl diglycollate, the aldehyde and sodium hydride (1.5:1:1.5 mole) in excess dry benzene were stirred for 6 hrs at 60–70°C, and the reaction mixture was worked up as usual[1].

Furan-2-aldehyde: (9.6 g): (stirring for 6 hrs) gave a half-ester mixture (12 g, 50 % yield) which was dissolved in benzene-light petroleum (b.p. 80–100°) where by it could be separated into two fragments (i) the less soluble (E)-half ester 2a (4.3 g) (cf. Table 1), ii) the more soluble fraction (7.7 g). The latter was obtained as an oil and its composition revealed by saponification (see later).

Thiophene-2-aldehyde (9.6 g) (stirring for 3 hrs) gave a half-ester mixture (11.5 g, 45 % yieid) which was dissolved in benzene-light petroleum (b.p. 80–100°) whereby it could be separated into two fractions: i) the less soluble (E)-halfester 2b (3.9 g) (cf. Table 1) — ii) The more soluble fraction (7.6 g). The latter was obtained as an oil and its composition revealed by saponification (see later).

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 1).

The crystalline (E)-half-ester 2a (3 g) gave the (E)-dibasic acid 2c (2.1 g, 80 % yield). The oily half-ester mixture (7.7 g) gave upon saponification (6 g, 88 % yield) of an acidic product which was separated by fractional crystallization from benzene-light petroleum 100–120° into the less soluble (E)-dibasic acid 2c (1.1 g, 18 %) and the more soluble (Z)-dibasic acid 1c (4.9 g, 82 %).

The crystalline (E)-half-ester 2b (3 g) gave the (E)-dibasic acid 2d (2 g, 77 % yield). The oily half -ester fraction (7.6 g) gave (5.8 g, 86 % yield) of an acidic product which was separated as in 2a to the (E)-dibasic acid 2d (0.9 g, 15 % yield) and the (Z)-diacid 1d, (4.9 g, 85 % yield). Conversion of the dibasic acids (1c, d and 2 c, d) to the cyclic anhydrides (3a, b and 4a, b).

This was carried out by 3 hrs refluxing of the dibasic acid with acetyl chloride (10 ml per 1 g acid); (77–83 % yield). For details see Table 1.

Action of aluminium chloride upon the cyclic anhydries, (4a, b.).

Aluminium chloride (1.2 mol) and a solution of the (E) anhydride (4a, b) (1 mol) in nitrobenzene (15 ml per one g anhydride) were stirred

Table 1. (Z)- and (E)- furyl of (thienyl)-4- ethoxycarbonyl-3- oxapent -4- enoic acids (2a, b) and their corresponding diacids (1c, d) and (2 c, d) and anhydrides (3a,b) and (4a, b)

Nr.	M.p. (C) solvent of cryts. a)	Formula (Mol. wt.)	Analysis		
			Calcd. / Found		
			%C	%H	% S
2a	139—141 L.P. 80°	$C_{11}H_{12}O_6$ (240)	55.00 54.80	5.00 5.30	
2b	188—190 L.P. 100°	$C_{11}C_{12}O_5S$ (256)	51.56 52.10	4.68 4.90	12.50 12.60
1c	128—130 L.P. 80°	$C_9H_8O_6$ (212)	49.06 49.30	3.77 4.00	
1d	166—168 bz	$C_9H_8O_5S$ (228)	47.37 47.60	3.50 3.70	14.00 14.30
2c	156.-158 L.P. 100°	$C_9H_8O_5$ (212)	49.06 49.40	3.77 4.10	
2d	205—207 L.P. 100°	$C_9H_8O_5S$ (228)	47.37 47.50	3.50 3.80	14.00 14.20
3a	97— 99 L.P. 80°	$C_9H_8O_5$ (194)	55.66 55.90	3.01 3.30	
3b	149—151 bz	$C_9H_6O_4S$ (210)	51.42 51.70	2.85 3.10	15.23 15.60
4a	119—121 L.P. 100°	$C_9H_6O_5$ (194)	55.66 56.10	3.01 3.20	
4b	161—163 L.P. 100°	$C_9H_6O_4S$ (210)	51.42 51.60	2.85 3.10	15.23 15.50

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

for 6 hrs and left overnight at room temperature. The acidic reaction product (80–90 % yield) was obtained as yellow crystals and identified as (5a, b). For details c.f Table 2.

Table 2. Cyclopent-1-ene-3-oxo-[4,5-b] -furano (or thyano) -2-oxyacetic acid (5a-b) and their 2,4-dinitrophenylhydrazones

Nr.	M.p.°C cryst.a)	Formula (Mol.Wt	Analysis Calcd. / Found %C	%H	%S	2,4-Dinitrophenylhydrazones m.p.(°C) cryst.b)	Formula (Mol.Wt.)	Analysis Calc. /Found %N
5a	124–126	$C_9H_6O_5$	55.66	3.01		211–213	$C_{15}H_{10}O_8N_4$	14.97
	(bz)	(194)	56.00	3.00			(374)	15.10
5b	186–187	$C_9D_6O_4S$	51.42	2.85	15.23	232–234	$C_{15}H_{10}O_7SN_4$	11.80
	(bz)	(210)	51.60	3.10	15.40		(390)	12.10

a) bz = benzene b) Etyhl alcohol

When the (Z)-anhydride (3a, b) was subjected to the same reaction the corresponding dibasic acids were recovered in considerably high yield.

Conversion of the anhydrides (3 a, b — 4a, b) to the 4-carboxy half-ester (1e, f and 2e, f).

The anhydride was refluxed for 6 hrs with excess absolute ethanol (30 ml per 1g anhydride) to yield (67–75 % yield) of their position isomers (1e, f and 2e, f). For details cf. Table 3.

Table 3. Ethyl (Z)- and (E)-5- furyl or (Thienyl) -4- carboxy-3-oxa pent -4- enoates (1e, f) and (2e, f)

Nr	M.p. (°C) Solvent of cryst. a)	Formula (Mol. Wt.)	Analysis Calcd / Found %C	%H	%S
1e	111—113	$C_{11}H_{12}O_6$	55.0	5.0	
	(bz)	(240)	55.2	5.3	
1f	123—125	$C_{11}H_{12}O_5S$	51.56	4.88	12.50
	(bz)	(256)	52.30	4.90	12.80
2e	177—179	$C_{11}H_{12}O_6$	55.00	5.00	
	L.P. 80-bz	(240)	55.30	5.20	
2f	100—102	$C_{11}H_{12}O_5S$	51.56	4.88	12.50
	L.P. 100-bz	(256)	52.10	5.00	12.70

bz = benzene L.P. 80 = Light petroleum (b.p. 80–100°) L.P. 100 = Light petroleum (b.p. 100 120°)

REFERENCES

1. M.F. EL-NEWAIHY, M.R. SALEM, and F.A. EL-BASSIOUNY, Aust. J. Chem. 29, 223, (1976).
2. M.F. EL-NEWAIHY, M.R. SALEM, E.I. ENAYAT and F.A. EL-BASSIOUNY Aust. J. Chem. 32, 1159–63 (1979).
3. M.R. SALEM, E.I. ENAYAT, and A.A. KANDIL, J. Prakt. Chem. 321, 741 (1979).
4. N.R. EL-RAYYES, J. Prakt. Chem. 315, 295 (1973).
5. L.J. BELLAMY, The Infrared Spectra of Complex Molecules. Third Edition, Chapman and Hall, London 1975.