CYCLIZATION OF THIOPHENEDICARBOXALDEHYDE WITH NITROMETHANE

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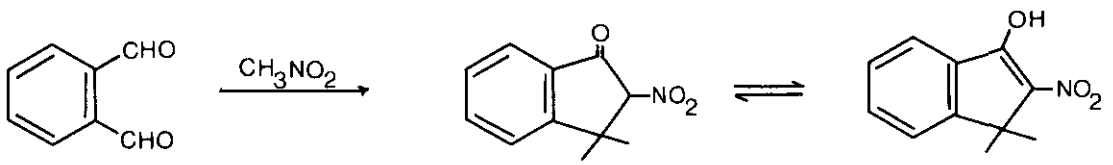
Abstract- The reaction of thiopheno[3,4-c]and[2,3-b]dicarboxaldehyde with nitromethane in alcoholic potassium hydroxide afforded the corresponding 5-nitro-4H-cyclopenta[c]thiophen-4-ol II and 5-nitro-4H-cyclopenta[b]thiophen-4-ol III, respectively.

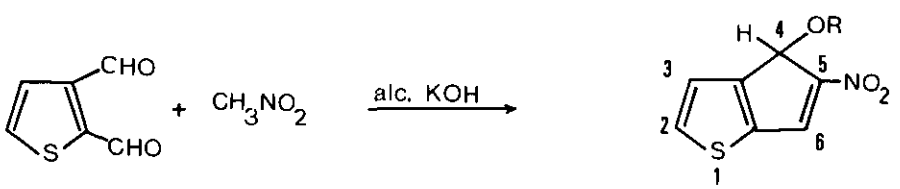
In the continuation to our study in the reaction of five membered heterocyclic o-dicarboxaldehydes[2-5], we wish to report the cyclization of thiophene-o-dicarboxaldehyde with nitromethane.

The reaction of o-phthaldehyde with nitromethane was studied by many authors[6-10]. Campbell et al[8]., reported that the product of the reaction was shown to be a tautomeric mixture, and the enol form was isolated in pure form.



Baer et al.[10] reported that the product of this reaction was 1-hydroxy-2-nitroindene, while Lichtenthler[9] reported that the product was 2-nitro-1-indenol, and he confirmed his result with ^1H nmr spectral study.

Firstly, we tried the reaction of thiopheno[2,3-b]dicarboxaldehyde I with nitromethane in alcoholic potassium hydroxide, to give, after acidification with HCl 5-nitro-4H-cyclopenta[b]-thiophen-4-ol II in fairly good yield.



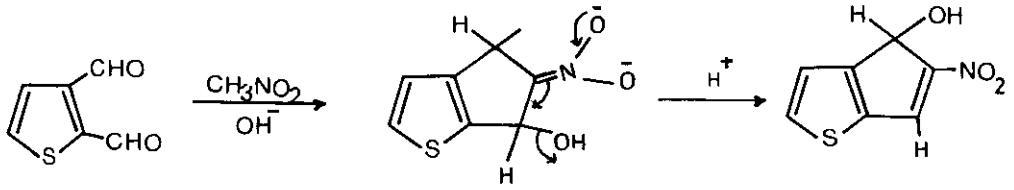
I

II

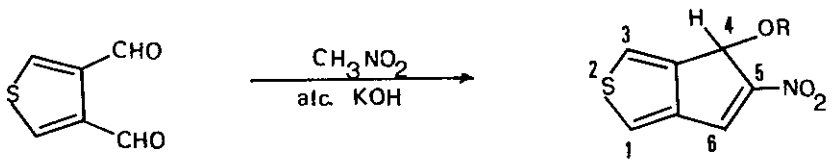
a, R=H b, R=CH_3

c, R=$COCH_3$

This result was in harmony with that obtained by Lichtenthler[9], according to the following mechanism.



Analogous treatment of thiopheno[3,4-c]dicarboxaldehyde with nitromethane gave the expected product 5-nitro-4H-cyclopenta[c]thiophen-4-ol in 12% yield.



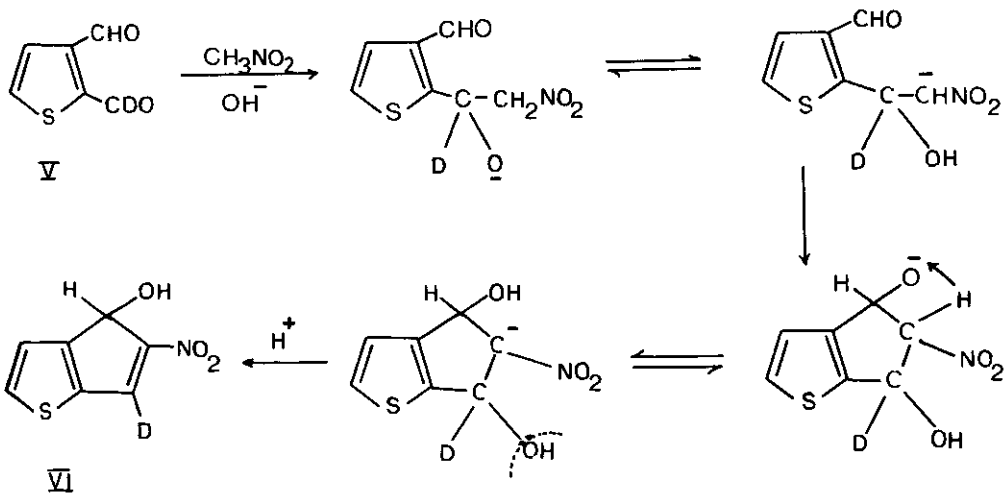
III

IV

a, R = H b, R = CH_3

c, R = $COCH_3$

The reaction of deuterated thiophenedicarboxaldehyde V with nitromethane was investigated in order to know about the mode of addition. The ^1H nmr spectrum of deuterated isomer VI displayed a marked decrease in the intensity of proton number 6, this is in favour that the reaction may be starts by initial addition of condensate anion of nitromethane on 2 position followed by cyclization with the other formyl group. The following mechanism is suggested.



V

VI

Table 1. Experimental data of compounds II, IV and VI.

Comp.	Eluent	Solvent	M.P. C°	Yield %	Mol.Formula (Mol.Weight)		Analyses % C	H	N	S
IIa	-	ET	139	53	$C_7H_5NO_3S$	Calcd.	45.90	2.73	7.65	17.48
					(183.10)	Found	45.62	2.51	7.30	17.91
IIb	E - H	C	154-155	49	$C_8H_7NO_3S$	Calcd.	48.73	3.55	7.10	16.24
	(3:1)				(197.11)	Found	48.28	3.27	7.33	16.49
IIc	E - H	B - H	114	63	$C_9H_7NO_4S$	Calcd.	48.00	3.11	6.22	14.22
	(2:1)	(2:1)			(225.03)	Found	48.27	3.39	6.49	14.42
IVa	-	ET	162-163	12	$C_7H_5NO_3S$	Calcd.	45.90	2.73	7.65	17.48
					(183.10)	Found	45.29	2.69	7.81	17.88
IVb	E - H	C	149-150	43	$C_8H_7NO_3S$	Calcd.	48.73	3.55	7.10	16.24
	(2:1)				(197.11)	Found	48.31	3.54	7.37	15.99
IVc	E - H	B - H	123	57	$C_9H_7NO_4S$	Calcd.	48.00	3.11	6.22	14.22
	(2:1)	(2:1)			(225.03)	Found	47.68	3.28	6.41	14.70
VI	-	ET	139	49	$C_7H_4NO_3SD$	Calcd.	45.66	2.71	7.60	17.41
					(184.10)	Found	45.42	2.60	7.35	17.19

B : Benzene; C: Cyclohexane; E: Ether; H: Hexane; ET: Ethyl alcohol.

Table 2. Spectroscopic data of compounds II, IV and VI.

Comp.	I.R. data cm^{-1}	^1H nmr data in ppm	Mass spectral data
IIa	3540(OH); 1572,1325 (NO_2).	7.18(d,H_2); 7.14(d,J=1.80,H_3); 5.68(s,H_4); 7.88(s,H_6).	M^+183(40%); m/e=182(100%), 137(21%).
IIb	1565,1328(NO_2).	7.2(d,H_2); 7.04(d,J=1.80,H_3); 5.68(s,H_4); 7.90(s,H_6); 3.25(s,CH_3).	
IIc	1740(C=O), 1582, 1321(NO_2).	7.20(d,H_2); 7.04(d,J=1.78,H_3); 5.66(s,H_4); 7.88(s,H_6); 2.18(s,CH_3).	M^+225, m/e=190(37%); 182 (100%); 166(27%).
IVa	3548(OH); 1574,	7.32(s, H_1&H_3); 5.64(s,H_4); 7.82 (s,H_6).	M^+183; m/e=182(100%); 153 (59%); 137(37%).
IVb	1568,1322(NO_2).	7.30(s,H_1&H_3); 5.64(s,H_4); 7.80 (s,H_6); 3.28(s,CH_3).	
IVc	17345C=O), 1572, 1328(NO_2).	7.32(s,H_1&H_3); 5.14(s,H_4); 7.8(s, H_6); 2.22(s,CH_3).	M^+225; 190(61%); 182(100%); 166(31%).
VI	3550(OH), 1580, 1325(NO_2).	7.20(d,H_2); 7.12(d,J=1.80,H_3); 5.66(s,H_4).	

EXPERIMENTAL

Compounds I,III and V were prepared according to the previously reported methods.[11,12] ^1H nmr spectra were recorded in a Varian A 60 in $CDCl_3$ using TMS as internal standard. Mass spectra were obtained on a Finnigan 3000(70 eV; 90°C). The melting points were taken on a Thomas-Hoover apparatus and are uncorrested. The prepared compounds were purified by column chromatography on silica G 60 (Merk). The experimental results are grouped in Table 1, and the spectral data are grouped in Table 2.

Condensation of thiophenedicarboxaldehyde with nitromethane (General method).
Thiophenedicarboxaldehyde 700 mg (0.005 mole) and nitromethane 305 mg (0.005 mole) were dissolved in 15 ml of methanol. To the ice cold solution was added with stirring 5 ml of cold solution of 10% alcoholic KOH at a fairly rapid drop rate. The reaction mixture was neutralized with 1N HCl. The colorless crystalline precipitate that appeared was isolated, washed with cold methanol, dried and crystallized from the proper solvent.

Alkylation of compounds II and IV.
A solution of 500 mg of compound II or IV in 10 ml of DMF was added dropwise to a suspension of 2 gm of NaH in 20 ml of DMF. The reaction mixture was stirred for 1 h, during this time the solution turned red. A solution of 2 ml of methyl iodide in 5 ml of DMF was added. The reaction mixture stirred for 2 h at room temperature, hydrolysed on water, extracted with methylene chloride, dried over $MgSO_4$ and evaporated at reduced pressure. The product was crystallized from the proper solvent.

Acetylation of compounds II and IV.[8]
A solution of 500 mg of compound II or IV in 5 ml of acetic anhydried containing a droplet of sulfuric acid was heated on a steam bath for 15 min, cooled, decomposed with ice and sodium bicarbonate. The reaction mixture was extracted with methylene chloride, washed with ice-cold sodium bicarbonate solution, dried and evaporated. The crude product was purified and crystallized from the proper solvent.

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