SOLID STATE PHOTODIMERIZATION OF (*E*)-1-(3-METHYL-4-NITROISOXAZOL-5-YL)-2-(2-THIENYL)ETHENE

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Abstract - Solid state irradiation of (*E*)-1-(3-methyl-4-nitroisoxazol-5-yl)-2-(2-thienyl)ethene (**1**) leads to (1α,2α,3β,4β)-1,3-bis(3-methyl-4-nitroisoxazol-5-yl)-2,4-bis(2-thienyl)cyclobutane (**2**) which is then oxidized to (1α,2α,3β,4β)-2,4-bis(2-thienyl)cyclobutane-1,3-dicarboxylic acid (**3**).

INTRODUCTION

In previous research[1] we studied the solid state photobehavior of 3-methyl-4-nitro-5-chlorostyrylisoxazoles which react through the double bond of the styryl portion to give centrosymmetric photodimers. The oxidation of the isoxazole rings of these dimers with potassium permanganate gave the corresponding chloro-α-truxillic acids. Similar behavior was found also for 3-methyl-4-nitro-5-styrylisoxazole.

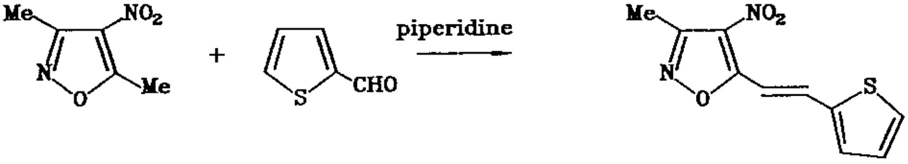
Owing to the easy preparation of 3-methyl-4-nitro-5-chlorostyrylisoxazoles and to the high yields of the photodimers obtained, the above procedure may be considered a good entry for the preparation of chloro-α-truxillic acids. The alternative direct irradiation of (*E*)-chloro-β-cinnamic acids led to chloro-β-truxinic acids.[2]

We now report the solid state photobehavior of the title compound **1** together with the configuration of the photoproduct obtained which in turn was used for the preparation of the (1α,2α,3β,4β)-2,4-bis(2-thienyl)cyclobutane-1,3-dicarboxylic acid.

RESULTS AND DISCUSSION

Compound **1** was obtained as a yellow solid by condensation reaction of 3,5-dimethyl-4-nitroisoxazole with 2-thiophenecarboxaldehyde in the presence of piperidine.

The (*E*) configuration of **1** follows from the ^{1}H-nmr spectrum which shows a coupling constant of 16.20 Hz for the ethylenic protons. Irradiation of solid compound **1** with glass filtered light of 250 W mercury lamp gave a colorless compound which was recognized as a dimer of **1** on the basis of elemental analysis, ^{1}H-, ^{13}C-nmr spectra and considering also the blue shift of the uv spectrum of the photoproduct with respect to that of **1**.



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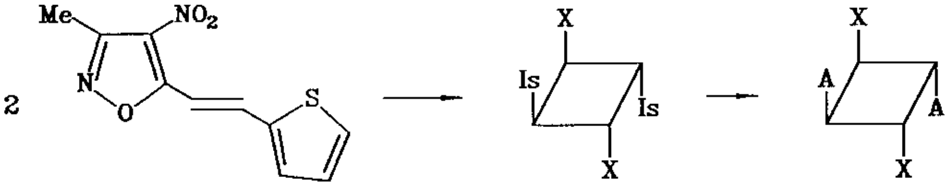
The configuration of the dimer was attributed by taking into account spectral evidence and chemical reactivity. In fact, the presence in the mass spectrum of this compound of a peak at m/z= 236 due to the $M^+/2$ fragment together with the absence of those at m/z=280 and m/z=192 is in agreement only with one of the five possible truxillic type structures. Among them, these results are consistent for a dimer derived from (*E*)-(*E*) [2+2] photocycloaddition of two molecules of **1** having α- or ε-truxillic type structure, as confirmed by ^{13}C-nmr data (Table 1). In fact, compound **2** shows nine lines (C-nitro was not observed) which, following the same considerations reported in Ref. 1, are in agreement for the above structures.

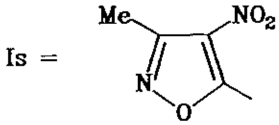


1

2

3 A=CO_2H

4 A=CO_2Me



However, the ^{1}H-nmr spectrum of the photoproduct shows one signal at δ 2.449 ppm for two 3-methyl groups which are shielded with respect to that of the monomer (2.595 ppm); this finding supports only the α-truxillic type structure for which the expected facing effect is operating.[1,3]

Oxidation of the photodimer with potassium permanganate gave a 2,4-bis(2-thienyl)cyclobutane-1,3-dicarboxylic acid for which the empirical formula $C_{14}H_{12}S_2O_4$ was consistent on the basis of elemental analysis and spectral data (^{1}H-, ^{13}C-nmr and mass spectra); we notice also that the ^{13}C-nmr signal for the carboxylic carbons (Table 1), shows the same chemical shift as that of C-5 atoms in the photodimer, thus suggesting the same electronic environment for both type of carbon atoms in these compounds.

Table 1. ^{1}H- and ^{13}C-nmr data of compounds 2 and 3

Compound	*^{1}H-nmr (δ, ppm)*	*^{13}C-nmr (δ, ppm)*
2	2.449 (s, 6H, 2x3-Me), 5.252 (m, AA'BB', 4H, cyclobutane ring), 6.850-7.200 (m, ABC,[a] 2x3H, thiophene ring)	11.434 (q, 3-Me), 38.642 (d, C-2), 45.032 (d, C-1), 125.646 (d), 126.112 (d), 127.303 (d), 139.053 (s, C-2'), 155.812 (s, C-3), 170.909 (s, C-5)
3[b]	4.175 (m, AA'BB', 4H, cyclobutane ring), 6.900-7.450 (m, ABC, 2x3H, thiophene ring), 12.310 (br s exch., 2H, 2xOH)	36.592(d, C-2), 49.304 (d, C-1), 124.647 (d), 125.322(d), 126.964 (d), 141.730 (s, C-2'), 171.913 (s, CO)

[a] Simulated spectrum gave $\delta_{H\text{-}5'} = 7.153$, $\delta_{H\text{-}4'} = 6.911$, and $\delta_{H\text{-}3'} = 6.882$ ppm; $J_{H5'\text{-}H4'} = 4.89$ Hz, $J_{H5'\text{-}H3'} = 1.20$ Hz, and $J_{H3'\text{-}H4'} = 3.71$ Hz. [b] Spectra recorded in DMSOd_6

The acid was then converted to the corresponding dimethyl ester which was recognized as dimethyl (1α,2α,3β,4β)-2,4-bis(2-thienyl)cyclobutane-1,3-dicarboxylate (**4**) by comparison of physical properties (mp and ^{1}H-nmr) with those reported in the literature[3] for this compound previously prepared by methanolysis of the photodimer obtained by solid state irradiation of (*E*)-β-2-thienylacrylamide.[3] From the above reported data it is also possible to attribute the configuration of both the photodimer and the acid which are (1α,2α,3β,4β)-1,3-bis(3-methyl-4-nitroisoxazol-5-yl)-2,4-bis(2-thienyl)cyclobutane (**2**) and (1α,2α,3β,4β)-2,4-bis(2-thienyl)cyclobutane-1,3-dicarboxylic acid (**3**), respectively.

It is worthy to note that whereas irradiation of (*E*)-β-2-thienylacrylic acid gives β-truxinic type structure dimer,[4] the above described route allows the preparation of the centrosymmetric (α-truxillic type) acid **3**.

EXPERIMENTAL

Melting points were determined on a Büchi 510 apparatus and are uncorrected. Infrared spectra were recorded with a Perkin-Elmer 283 instrument in potassium bromide pellets. Uv spectra were registered in methanol with a Cary-14 spectrophotometer. ^{1}H- And ^{13}C-nmr spectra were taken on a Varian VXR-300 instrument; chemical shifts are reported in ppm high frequency from tetramethylsilane as secondary reference standard, coupling constants in Hz. Mass spectra of compounds **1**, **3**, and **4** were registered with an Hewlett-Packard 5790 A instrument, whereas that of **2** was obtained at 20 eV by direct inlet (D.E.I.) of sample in a LKB 2091 spectrometer. Thin-layer chromatography (tlc) was carried out with Merck silica gel 60 F_{254} (benzene as eluent) and mineral light lamp (model UV SL-58) was used for revealing spots.

(*E*)-1-(3-Methyl-4-nitroisoxazol-5-yl)-2-(2-thienyl)ethene (**1**)

3,5-Dimethyl-4-nitroisoxazole (2 g, 14.1 mmol) and 2-thiophenecarboxaldehyde (1.58 g, 14,1 mmol) were dissolved in ethanol (15 ml) and refluxed under stirring for 30 min in the presence of piperidine (0.5 ml). The mixture was then cooled and yellow compound **1** was filtered and dried (2.526 g), mp 141-142 °C (from ethanol). Ir ν_{max}: 1620, 1505, and 1380 cm^{-1}; ^{1}H-nmr (δ, $CDCl_3$): 2.595 (s, 3H, 3-Me), 7.128 (dd, $J_{H4'-H3'} = 3.70$ Hz, $J_{H4'-H5'} = 5.10$ Hz, 1H, H-4'), 7.403 (d, $J_{H3'-H4'} = 3.70$ Hz, 1H, H-3'), 7.515 (d, $J_{H5'-H4'} = 5.10$ Hz, 1H, H-5'), 7.670 (AB system, J = 16.20 Hz, 2H, CH = CH); ^{13}C-nmr (δ, $CDCl_3$): 11.598 (q, 3-Me), 109.386 (d), 128.379 (d), 130.010 (d), 131.877 (d), 135.156 (d), 139.847 (s, C-2'), 155.876 (s, C-3), 166.648 (s, C-5); uv λ_{max} (log ε): 278 (4.06) and 384 (4.37); ms m/z (%): 236 (100) M$^+$, 137 (70), and 109 (67). Anal. Calcd for $C_{10}H_8N_2O_3S$: C, 50.84; H, 3.41; N, 11.86; S, 13.57. Found: C, 50.92; H, 3.45; N, 11.79; S, 13.70.

Tlc analysis of the mother liquor showed the presence of traces of starting materials together with other minor products; concentration of the solution precipitated a reddish solid (0.158 g) which was not further analyzed. Chromatographic separation allowed the recovery of additional **1** (0.023 g, overall yield 77%) and a solid (0.04 g) recognized as the Michael adduct of 3,5-dimethyl-4-nitroisoxazole to **1**.

(1α,2α,3β,4β)-1,3-Bis(3-methyl-4-nitroisoxazol-5-yl)-2,4-bis(2-thienyl)cyclobutane (**2**)

Compound **1** (0.15 g) was finely deposited between two borosilicate glass plates (20 x 20 cm) and irradiated with a mercury lamp (General Electric Company 250 W, 30 cm distance) for 3.5 h each side.

The irradiated solid was recovered with acetone; tlc of the mixture showed the presence of **1** (higher Rf), **2**, and traces of other products. Evaporation of solvent left a solid which was treated with ethanol and filtered to give the dimer **2** (0.108 g, yield 72%), mp 218-220 °C (from ethanol/acetone, 2:1 v/v). Ir ν_{max}: 1600, 1510, 1380, 1143, and 825 cm^{-1}; uv λ_{max} (log ε): 230 (4.52) and 268 (4.07); ms m/z (%): 236 (100) $M^+/2$. Anal. Calcd for $C_{20}H_{16}N_4O_6S_2$: C, 50.84; H, 3.41; N, 11.86; S, 13.57. Found: C, 50.91; H, 3.48; N, 11.92; S, 13.51.

(1α,2α,3β,4β)-2,4-Bis(2-thienyl)cyclobutane-1,3-dicarboxylic acid (3)

Compound **2** (3.251 g, 5.68 mmol) dissolved in acetone (250 ml) was added dropwise under stirring with a solution (360 ml, water-acetone, 1:3 v/v) of potassium permanganate (6.529 g). The mixture was kept at room temperature overnight, then the MnO_2 was filtered and the acetone was distilled off; the MnO_2 was then added to the solution and the mixture was treated with HCl (37%, 20 ml) and a 20% w/v aqueous solution (165 ml) of $Na_2SO_3.7H_2O$ to destroy MnO_2 and to precipitate the acid **3**. Purification of the solid by treatment with sodium hydrogencarbonate, charcoal, and re-precipitation with 6N HCl, gave compound **3** (1.178 g, yield 67%), mp 249-250 °C (after two crystallizations from ethanol-water, 1:2 v/v). Ir ν_{max}: 3000, 1700, 1430, and 600 cm^{-1}; ms m/z (%): 308 (1.6) M^+, 154 (100) $M^+/2$. Anal. Calcd for $C_{14}H_{12}O_4S_2$: C, 54.53; H, 3.92; S, 20.80. Found: C, 54.53; H, 4.07; S, 20.76.

Dimethyl (1α,2α,3β,4β)-2,4-bis(2-thienyl)cyclobutane-1,3-dicarboxylate (4)

Compound **3** (0.2 g, 0.649 mmol) was treated with thionyl chloride (3 ml) and refluxed for 15 min. The excess of thionyl chloride was then distilled off and the diacyl dichloride was refluxed with methanol (10 ml) for 15 min to give the dimethyl ester **4** (0.197 g, yield 90%), mp 162-163 °C (from methanol) [lit.[3] mp 158-160 °C (from petroleum ether)]. ^{1}H-Nmr (δ, $CDCl_3$): 3.481 (s, 6H, 2xOMe), 4.322 (m, AA'BB', 4H, cyclobutane ring protons), 6.960-7.320 (m, ABC, 6H, thiophene ring protons); ms m/z (%): 336 (0.2) M^+, 168 (100) $M^+/2$.

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