

**SOLID STATE PHOTODIMERIZATION REACTION OF SOME 3-STYRYLISOXAZOLO-  
[3,4-d]PYRIDAZIN-7(6H)-ONES**

Stefano Chimichi,<sup>a</sup> Giovanna Ciciani,<sup>b</sup> Vittorio Dal Piaz,<sup>b</sup> Francesco De Sio,<sup>a</sup> Piero Sarti-Fantoni,<sup>\*a</sup> and Tomas Torroba<sup>c</sup>

<sup>a</sup> *Centro CNR sulla chimica e la struttura dei composti eterociclici e loro applicazioni, c/o Dipartimento di Chimica Organica, Via Gino Capponi 9, I-50121 Firenze, Italy,* <sup>b</sup> *Dipartimento di Scienze Farmaceutiche, Via Gino Capponi 9, I-50121 Firenze, Italy,* and <sup>c</sup> *Facultad de Veterinaria, Universidad de Extremadura, E-10071 Caceres, Spain*

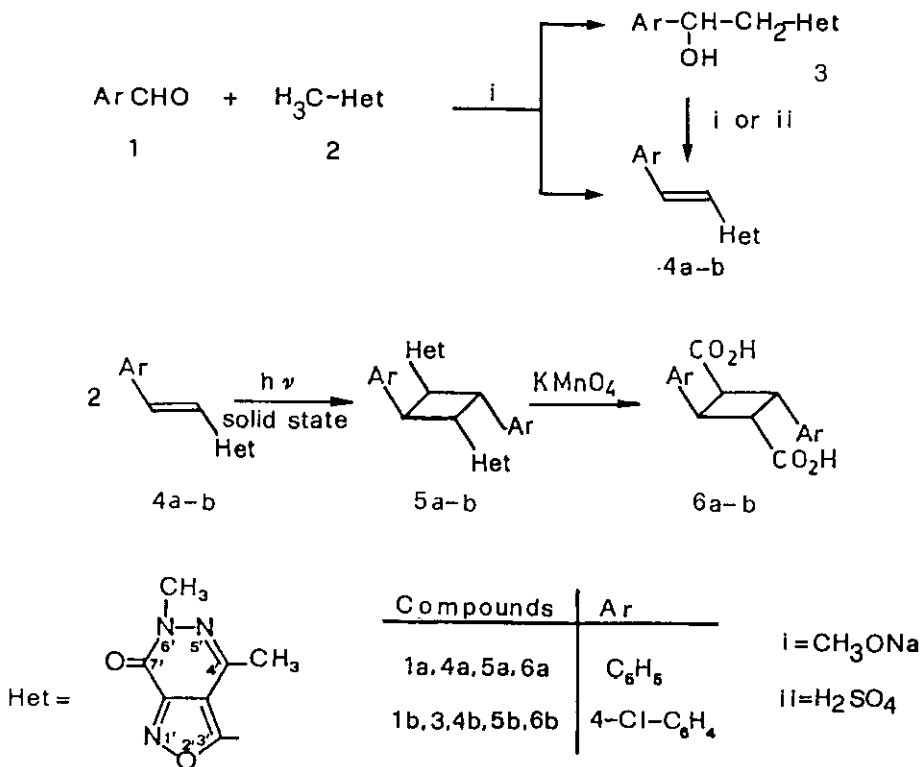
**Abstract**—The solid state irradiation of the title compounds 4a-b gave two colourless products which were recognized as the corresponding dimers 5a-b. The cyclobutane centrosymmetric structure of the dimers was demonstrated by taking into account the spectroscopic data and the nature of the oxidation products 6a-b.

3,4,6-Trimethylisoxazolo[3,4-d]pyridazin-7(6H)-one (2) reacted with aromatic aldehydes to give the corresponding 4,6-dimethyl-3-styrylisoxazolo[3,4-d]pyridazin-7(6H)-ones (4a-b) as yellow products.<sup>1</sup>

We have found that compound 4a turned colourless after irradiation with sunlight even upon standing in glass tubes. The presence of a styryl group in 4a strongly suggested that a cyclobutane photodimer was formed under the above conditions, through a photocycloaddition of ethylenic bonds of two molecules of 4a. In fact, it is well known that the solid state photoreactivity of organic compounds is correlated to the presence of particular groups which are involved in the photo-reactions under topochemical condition.<sup>2</sup> Thus, cinnamic acids<sup>3</sup> and substituted stilbenes<sup>4</sup> are known to give photodimers in the solid state. In addition even when the styryl group is bonded to heterocyclic systems such as thiophene<sup>4</sup> and isoxazole,<sup>5</sup> the same photoreaction takes place and dimers with a cyclobutane structure are formed.

Under this view, we now report a study on the solid state photobehaviour of compound 4a, with the aim to show that the dimer 5a ( $\alpha$ -truxillic acid type configuration) is obtained. The photobehaviour of the solid 4-chlorostyryl compound 4b is also investigated.

The studied compounds 4a-b<sup>1</sup> and 5a-b were prepared according to the following scheme:



The dimeric cyclobutane structures of compounds 5a-b were attributed by spectroscopic data and elemental analyses. In fact, the mass spectra of 5a-b show peaks at m/z (rel.intensity) 534 (5) and m/z 602 (2) which are in agreement for M<sup>+</sup> of dimers of 4a-b; in addition peaks at m/z 267 (100; M<sup>+</sup>/2 of 5a) and m/z 301 (100; M<sup>+</sup>/2 of 5b) are also present whereas those corresponding to Ar-CH=CH-Ar<sup>+</sup> or Het-CH=CH-Het<sup>+</sup> are absent. These results are in agreement with truxillic acid type structures and allow us to exclude the truxinic acid type ones. However, no conclusive assignment concerning the configuration of 5a-b is possible on the basis of the above data.

The <sup>1</sup>H-nmr chemical shifts of N-CH<sub>3</sub> and C-CH<sub>3</sub> for dimers 5a-b are very close to those of monomers 4a-b (Table). These findings suggest that the photoreaction involves only the ethylenic bond of 4a-b, leaving the heterocyclic systems unaltered.

Table. Spectroscopic data for compounds 4a-b and 5a-b

Compound	<sup>1</sup> H-nmr (δ, ppm, CDCl <sub>3</sub> )	Uv λ <sub>max.</sub> , nm, (log ε)
4a <sup>a</sup>	2.58(s, 3H, 4'-CH <sub>3</sub> ), 3.70(s, 3H, N-CH <sub>3</sub> ), 7.35-7.80(m, 5H, Ph), 7.48(AB system, 2H, J=16 Hz, CH=CH)	242sh (3.05), 302 (4.12), and 364 (4.27)
4b	2.58(s, 3H, 4'-CH <sub>3</sub> ), 3.72(s, 3H, N-CH <sub>3</sub> ), 7.35-7.65(AA'BB' system, 2H, J=17 Hz, CH=CH)	236 (3.98), 306 (3.98), and 366 (4.27)
5a	2.48(s, 6H, 2x4'-CH <sub>3</sub> ), 3.62(s, 6H, 2xN-CH <sub>3</sub> ), 5.12(s, 4H, cyclobutane ring protons), 7.15-7.40(m, 10H, 2xPh)	--
5b <sup>b</sup>	2.56(s, 6H, 2x4'-CH <sub>3</sub> ), 3.57(s, 6H, 2xN-CH <sub>3</sub> ), 5.28(brs, 4H, cyclobutane ring protons), 7.20-7.60(AA'BB' system, 8H, 2xArH <sub>4</sub> )	--

<sup>a</sup>This work. <sup>b</sup>Spectrum recorded in DMSO-*d*<sub>6</sub>

Further information was obtained by oxidizing 5a-b with potassium permanganate which allowed us to recover α-truxillic and 4,4'-dichloro-α-truxillic acids 6a-b respectively. Ir, <sup>13</sup>C-nmr, and <sup>1</sup>H-nmr spectra of 6a-b were superimposable with those of authentic samples.<sup>6</sup> In both cases <sup>13</sup>C-nmr of the crude acids 6a-b gave only one peak for the carboxylic carbons proving that other truxillic isomers are not formed during the oxidation. Thus, since the carboxylic carbons derive from the C-3' of the isoxazole systems, we assign the structure of the dimers 5a-b to trans-1,3-di-(4,6-dimethyl-7-oxoisoxazolo[3,4-d]pyridazin-3-yl)-cis-2-trans-4-diarylcyclobutane (centrosymmetric structure).

During the preparation of 4b we also isolated a colourless compound which, on the basis of elemental analysis and spectroscopic data was recognized as 2-(4,6-dimethyl-7-oxoisoxazolo[3,4-d]pyridazin-3-yl)-1-(4-chlorophenyl)-ethan-1-ol (3). This product was then converted into 4b by treatment with sulphuric acid or by refluxing with sodium methoxide.

## EXPERIMENTAL

Melting points were determined on a Büchi 510 melting point apparatus and are uncorrected. Infrared spectra were recorded either with a Perkin-Elmer 283 apparatus in KBr pellets or with a Perkin-Elmer 337 spectrometer for nujol mulls.  $^1\text{H}$ -nmr and  $^{13}\text{C}$ -nmr spectra were recorded on a Perkin-Elmer R32 and on a Varian FT 80-A spectrometers, respectively. All chemical shifts were reported in ppm downfield from tetramethylsilane as internal standard, coupling constants in Hz. Mass spectra were obtained by D.E.I. with a VG 70-70 EQ spectrometer. Uv spectra were registered in methanol with a Cary-14 spectrophotometer. Irradiation reactions were carried out by using a mercury lamp (G.E.C. 250 W). All new compounds gave satisfactory microanalytical results.

### Preparation of Compound 3

A suspension of 2 (1.1 g) and 4-chlorobenzaldehyde (1b) (1.7 g) in methanol (10 ml) was refluxed for 2 min with sodium methoxide prepared from sodium (0.14 g) and methanol (8 ml). Rapid refrigeration of the mixture afforded compound 3 as a colourless solid (yield 62%), mp 230°C (from acetic acid). Ir (nujol) 3310 and 1660  $\text{cm}^{-1}$ ;  $^1\text{H}$ -nmr ( $\text{DMSO-}d_6$ )  $\delta$  2.48(s, 3H, 4'- $\text{CH}_3$ ), 3.54(d,  $J=6.8$  Hz, 2H,  $\text{CH}_2$ ), 3.63(s, 3H,  $\text{NCH}_3$ ), 4.9-5.2(m, 1H, CH), 5.88(exch d,  $J=4$  Hz, OH), 7.40(s, 4H, ArH<sub>4</sub>);  $^{13}\text{C}$ -nmr ( $\text{DMSO-}d_6$ )  $\delta$  171.6(s, C=O), 152.5(s, C-3/C-7a), 151.2(s, C-7a/C-3), 142.8(s, C-4), 140.1(s), 131.8(s), 128.1(d), 127.6(d), 113.2(s, C-3a), 70.1(d, CHOH), 37.5(q, N- $\text{CH}_3$ ), 36.8(d,  $\text{CH}_2$ ), 18.3(q, C- $\text{CH}_3$ ).

### Preparation of Compounds 4a-b

Compounds 4a-b were prepared according to the procedure reported in Ref.1. Alternatively, 4b could also be obtained with method A or B.

A) Compound 3 (0.15 g) was refluxed for 5 min with sodium methoxide (Na 0.03 g, methanol 5 ml). The expected 4b was then recovered as yellow crystals (yield 52%), mp 260°C (lit.<sup>1</sup> 260°C).

B) Compound 3 (0.15 g) was treated with sulphuric acid (4 ml) and left at room temperature for 1 h. The solution was then added to ice-water to give a yellow solid which was worked up and recognized (mp and  $^1\text{H}$ -nmr spectrum) as 4b (yield 62%).

### Preparation of Compounds 5a-b

A solution of compound 4a (0.194 g) in hot ethanol (50 ml) was deposited on two glass plates (40 cm x 40 cm). After evaporation of the solvent the plates were covered with another two glass plates and the sandwiches were irradiated for 3 h

each side. The solid was then recovered by flushing the plates with acetone. Concentration of the solvent left the solid 5a (0.172 g, yield 92%), mp 270°C dec. (from dimethylformamide and sublimation at 190°C/10<sup>-2</sup>mmHg). By the same procedure compound 4b (0.204 g) in hot ethanol (100 ml), irradiated for 4h, gave the colourless dimer 5b (0.174 g, yield 85%), mp 285-286°C dec. (from dimethylformamide).

#### Oxidation Reactions of Compounds 5a-b

Compound 5a (1.945 g) suspended in water (12 ml) was treated with sodium hydroxide (1 N, 5 ml) and added dropwise with a solution of potassium permanganate (2.5% w/v, 20 ml). The mixture was stirred at 40°C for 40 h and filtered. The solid, containing manganese dioxide together with unreacted 5a was treated again in the same manner. The new solid was treated with sodium sulphite and concentrated hydrochloric acid to recover unreacted 5a (0.095 g); addition of dilute hydrochloric acid to the combined alkaline solutions gave a solid (0.251 g) which was worked up and recognized as 6a (<sup>13</sup>C-nmr, <sup>1</sup>H-nmr and ir spectra). Treatment of 5b (1.82 g) by the same procedure gave unreacted starting material (1.163 g) and a solid (0.195 g) which was recognized as 6b by <sup>13</sup>C-nmr, <sup>1</sup>H-nmr and ir spectra.

#### ACKNOWLEDGMENTS

We wish to acknowledge support by C.N.R., "Progetto Finalizzato Chimica Fine e Secondaria", during the years 1980-83.

#### REFERENCES

- 1) V. Dal Piaz, S. Pinzauti, and P. Lacrimini, *J. Heterocycl. Chem.*, 1976, 13, 409.
- 2) M. D. Cohen and G. M. J. Schmidt, *J. Chem. Soc.*, 1964, 1996.
- 3) M. D. Cohen, G. M. J. Schmidt, and F. I. Sonntag, *J. Chem. Soc.*, 1964, 2000.
- 4) B. S. Green and L. Heller, *J. Org. Chem.*, 1974, 39, 196 and references cited therein.
- 5) D. Donati, M. Fiorenza, E. Moschi, and P. Sarti-Fantoni, *J. Heterocycl. Chem.*, 1977, 14, 951.
- 6) A. Baracchi, S. Chimichi, F. De Sio, D. Donati, R. Nesi, P. Sarti-Fantoni, and T. Torroba, *Heterocycles*, in press.

Received, 29th July, 1986