# The Use of 3,5-Dimethyl-4-nitroisoxazole for the Preparation of α,β-Unsaturated Aromatic Acids



*P. Sarti-Fantoni, D. Donati, M. Fiorenza, E. Moschi and V. Dal Piaz (1)*

Centro di studio del CNR sulla chimica e la Struttura dei Composti Eterociclici e loro Applicazioni, c/o Istituto di Chimica Organica, Via G. Capponi, 9 50121 Firenze, Italy

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A series of α,β-unsaturated aromatic acids were prepared by alkaline hydrolysis of 3-methyl-4-nitro-5-styrylisoxazoles.

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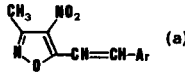
*Sir:*

The reactivity of 3,5-dimethyl-4-nitroisoxazole towards aromatic aldehydes, leading to 3-methyl-4-nitro-5-styryl-isoxazoles, was studied by Quilico and Musante (2). This reaction, reviewed by Kochetkov, *et al.*, was described as occuring in presence of organic bases only when the methyl group in the 5 position is activated by a nitro group in the 4 position in the isoxazole ring (3). Alkaline alkoxides were used (4) to catalyze the condensation reactions between benzaldehyde and 5-methylisoxazoles with substituents in the 4 position other than a nitro group. Recently 3,5-dimethylisoxazole was found to give addition reactions (5) with carbonyl compounds when treated with lithium or sodium amide. The importance of substituted isoxazoles as intermediates for the preparation of α,β- (6) and 1,4-diketones (7) was reported.

During the early study (2), the yellow 3-methyl-4-nitro-5-styrylisoxazole (I) was converted to a colourless photodimer with cyclobutane structure, when exposed to sunlight in the solid state. Later the photobehaviour of I was reinvestigated and the photodimer was shown to have α-truxillic type structure (8). The photoreactivity of I in benzene solution (9) gave the same photodimer obtained from the solid state and two dimers with δ-truxinic and ε-truxillic type structures together with a dimer resulting from cycloaddition on the exocyclic double bond on the 4,5-isoxazole positions. The structures of the above diphenyl cyclobutane dimers were clarified by spectroscopic data (nmr, ir and uv) and by the alkaline ring opening of isoxazole, followed by cleavage which lead to the corresponding diphenylcyclobutanedicarboxylic acids. In addition the *trans*-structure of monomer was determined by the $J_{AB}$ value of -CH=CH- in the nmr spectrum and again following the alkaline hydrolysis of I, which after acidification, gave *trans*-cinnamic acid.

On the basis of the above results we found it interesting to extend this hydrolysis reaction to other styrylisoxazoles substituted in the phenyl ring, to study if the reaction could be used as an alternative route for the preparation of α,β-unsaturated aromatic acids. For this purpose, a

Table 1




(a) HOOC-CH=CH-Ar (b)

| Ar | M.p. °C | $J_{AB}$ Hz | Uv (Methanol) λ max/nm (log ε) | Yield % (c) | M.p. °C Found | M.p. °C Lit. |
|---|---|---|---|---|---|---|
| $C_6H_5$ | 153 | 16 | 244 sh (4.04), 265 (4.13), 352 (4.36) | 65 | 133 | 133 (12) |
| *p*-Cl-$C_6H_4$ | 172-173 | 16 | 245 (3.96), 266 (4.04), 360 (4.20) | 67 | 246-247 | 247 (12) |
| *o*-Cl-$C_6H_4$ | 163-164 | 16 | 248 (4.04), 262 sh (4.02), 350 (4.27) | 90 | 200-202 | 200 (12) |
| *m*-Cl-$C_6H_4$ | 153-154 | (d) | 247 (4.11), 262 (4.11), 346 (4.31) | 90 | 165 | 165 (13) |
| 2,4-diCl-$C_6H_3$ | 164-165 | 16 | 252 (4.09), 262 sh (4.07), 350 (4.31) | 81 | 231-232 | 231-232 (14) |
| *p*-$CH_3$-$C_6H_4$ | 161-162 | 16 | 250 sh (3.92), 265 (3.95), 357 (4.20) | 96 | 196-197 | 196 (12) |
| *p*-$CH_3O$-$C_6H_4$ | 163-164 (2) | 15 | 252 (4.02), 280 (4.05), 387 (4.39) | 70 | 172; 187 (e) | 172.1; 187.3 (e) (12) |

(a) 3-Methyl-4-nitro-5-styrylisoxazoles were prepared as reported in reference 3. Analytical results for C,H,N were in agreement with the expected values. (b) Substituted *trans*-cinnamic acids were prepared according to the following procedure used for the hydrolysis of I leading to *trans*-cinnamic acid (*cf.* 9). Compound I (1 g.) was refluxed with sodium hydroxide (1*N*, 30 ml.) for 6 hours. Water (50 ml.) was then added to the cold mixture and the unreacted I was filtered (19 mg.). The solution, acidified with hydrochloric acid (6*N*) gave *trans*-cinnamic acid (354 mg.). Vacuum evaporation of the acid solution left a solid which was treated with ethanol and filtered. An additional amount of *trans*-cinnamic acid was recovered (57 mg.) by alkaline-acid treatment of the solid obtained by vacuum evaporation of the alcoholic solution. (c) Based on the consumed product. (d) Undetermined value. (e) Liquid crystal (172-187° mesomorphic state).

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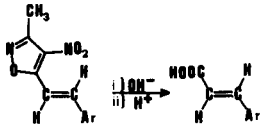
series of 3-methyl-4-nitro-5-styrylisoxazoles was prepared and hydrolysed in alkali (1*N* aqueous sodium hydroxide) according to the following Scheme.



Ar = $C_6H_5$ ; p-Cl-$C_6H_4$ ; o-Cl-$C_6H_4$ ; m-Cl-$C_6H_4$ ;
p-$CH_3$-$C_6H_4$ ; p-$OCH_3$-$C_6H_4$ ; 2,4-di Cl-$C_6H_3$

The data reported in Table 1 show that this procedure gives good results for the preparation of $\alpha,\beta$-unsaturated aromatic acids with two more carbon atoms with respect to the aldehydes used.

Nmr data concerning $J_{AB}$ of -CH=CH- for the condensation products (3-methyl-4-nitro-5-styrylisoxazoles) were in agreement for *trans*-structures, which are also maintained in the $\alpha,\beta$-unsaturated aromatic acids (substituted *trans*-cinnamic acids) resulting from alkaline hydrolysis followed by acidification.

This type of chemical behaviour of 3-methyl-4-nitro-5-styrylisoxazoles in alkali leading to $\alpha,\beta$-unsaturated aromatic acids may be considered an extention of the previous explanation of the solubility of 3,5-dimethyl-4-nitroisoxazole in alkali (2). In some cases the products resulting from mild alkaline ring opening of isoxazoles have been isolated (10,11).

Additional work is in progress to identify all the products resulting from the above hydrolysis and to extend the study of the title compound towards others reactives.

## REFERENCES AND NOTES

(1) Istituto di Chimica Farmaceutica dell 'Universitá di Firenze Via G. Capponi, 9 -50121 Firenze.

(2) A. Quilico, C. Musante, *Gazz. Chim. Ital.*, **72**, 399 (1942).

(3) N. K. Kochetkov, S. D. Sokolov and V. M. Luboshnikova, *Zh. Obshch. Khim.*, **32**, 1778 (1962).

(4) G. Renzi, V. Dal Piaz and S. Pinzauti, *Gazz. Chim. Ital.*, **99**, 753 (1969).

(5) C. Kashima, M. Uemori, Y. Tsuda and Y. Omote, *Bull. Chem. Soc. Japan*, **49**, 2254 (1976).

(6) C. Kashima, Y. Yamamato and Y. Tsuda, *J. Org. Chem.*, **40**, 526 (1975).

(7) A. Barco, S. Benetti, G. P. Pollini, P. G. Baraldi, M. Guarnieri and C. B. Vicentini, *J. Org. Chem.*, **44**, 105 (1979).

(8) D. Donati, M. Fiorenza, E. Moschi and P. Sarti-Fantoni, *J. Heterocyclic Chem.*, **14**, 951 (1977).

(9) D. Donati, M. Fiorenza and P. Sarti-Fantoni, *ibid.*, **16**, 253 (1979).

(10) V. Dal Piaz, S. Pinzauti and P. Lacrimini, *Synthesis*, 664 (1975).

(11) V. Dal Piaz and G. Renzi, *Gazz. Chim. Ital.*, **98**, 667 (1968).

(12) W. J. Hickinbottom and M. F. Ansell, in "Chemistry of Carbon Compounds", E. H. Rodd, Ed., Vol. III, Part B, Elsevier, London, 1956, chapter 15.

(13) F. Böck, G. Lock and K. Schmidt, *Monatsh. Chem.*, **64**, 399 (1934).

(14) F. P. Doyle, J. H. C. Naylor, U. S. Patent 3,470,151; *Chem. Abstr.*, **72**, 21682a (1970).