

A NEW SYNTHESIS OF 3-NITROISOXAZOLES

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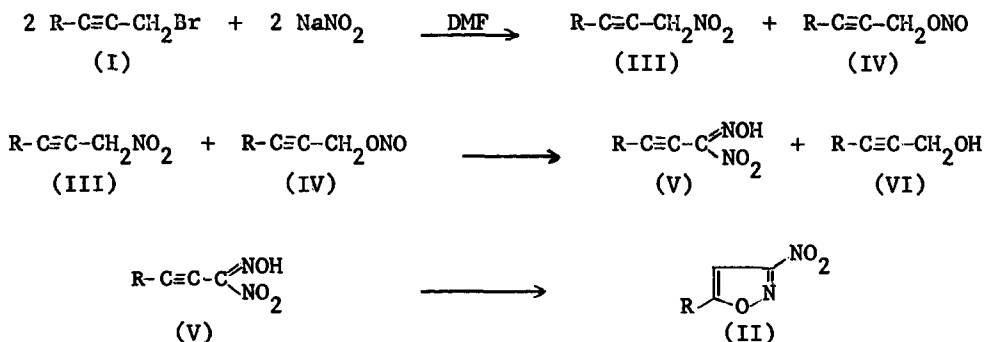
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As an extension of the studies carried out some years ago on the synthesis of β -nitroketones from β -halogenoketones^{1,2}, the reaction between methylenacetylenic bromides (I) and sodium nitrite in dimethylformamide has been investigated.

The reaction furnished 3-nitroisoxazoles (II) which were identified through elemental and spectroscopical (IR, NMR) analysis. For further identification, compounds (II) could also be converted into the corresponding amines by SnCl_2 reduction and into 3-isoxazolones by treatment with aqueous alkalis. Data related to compounds (II), of which only 3-nitro-5-phenylisoxazole had already been reported in literature³, are summarized in the Table 1.

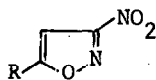
The described reaction can be considered as a new general method for the synthesis of compounds (II) whose formation can be interpreted as resulting from interaction of the primary nitroderivatives (III) with the corresponding nitrous esters (IV) originated by a nucleophilic attack of the nitrite ion, as previously described by Kornblum, Blackwood and Mooberry⁴, and affording the nitrolic acids (V) and the primary alcohols (VI). Formation of (II) from (V) follows the classical isoxazole cyclization scheme originally described by Claisen⁵ and Moureu^{6,7}.



Evidence supporting this interpretation was the isolation from the reaction mixtures of substantial quantities of alcohols (VI).

Studies on extensions of the reported reaction and on the chemical behaviour of 3-nitroisoxazoles are now in progress and will be published later.

TABLE 1

3-NITROISOXAZOLES^a

R-	b.p. (torr.)	m.p. ^b (solvent)	Yield %	Reaction time (hours)	References for intermediates I
H- ^c	101-3°/30mm	----	32	18	Commercially available
n-C ₄ H ₉ -	95-100°/2mm	----	30	18	8
C ₆ H ₅ - ³	---	108-9° (methanol)	63	4	9
CH ₃ OCO-	---	62-3° (benzene-hexane)	20	46	10
	---	174° (d)	28	14	11

a - Satisfactory elemental analyses were obtained for all reported compounds.

b - Not corrected.

c - NMR analysis in CDCl₃ (TMS as standard) showed a doublet at 7.16-7.2 ppm(δ).

d - Purified by sublimation.

General Reaction Procedure: 0.15 Moles of bromide (I) were added dropwise to a stirred solution of 0.3 moles of sodium nitrite in 100 ml of DMF at 15-20°C. Stirring was protracted at room temperature for some hours (as in Table 1) after heat evolution had subsided. The reaction mixture was diluted with water (300ml) and extracted with ethyl ether. The extracts, after drying on anhydrous sodium sulphate, were evaporated and the residue purified by conventional methods.

REFERENCES

1. R.Fusco, S.Rossi - Chem.Ind.(London) 1957, 1650
2. R.Fusco, S.Rossi - Ist.Lomb.(Rend.Sc.) A 93, 143 (1959)
3. P.Bravo, G.Gaudiano - Gazz.Chim.Ital. 96, 454 (1966)
4. N.Kornblum, R.K.Blackwood, D.D.Mooberry - J.Am.Chem.Soc. 78, 1501 (1956)
5. L.Claisen - Ber. 36, 3665 (1903)
6. C.Moureu, M.Brachin - Comp.Rend. 137, 795 (1903)
7. C.Moureu, M.Brachin - Bull.Soc.Chim.France 31, 343 (1903)
8. M.S.Newman, J.H.Wotiz - J.Am.Chem.Soc. 71, 1295 (1949)
9. Tchao Yin Lai - Bull.Soc.Chim.France 53, 1533 (1933)
10. H.B.Henbest, E.R.H.Jones, I.M.S.Walls - J.Chem.Soc. 1950, 3646
11. J.B.Armitage, M.C.Whiting - J.Chem.Soc. 1952, 2005