

Synthesis of 3,3'-Methylenediisoxazoles

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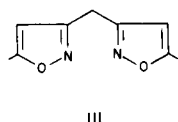
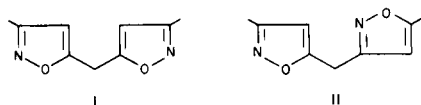
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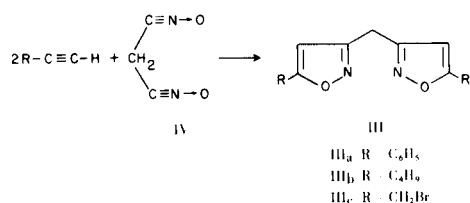
The synthesis of new 3,3'-methylene-diisoxazoles (III), from 1,3-dichloromalondioxime (IX) and acetylenic compounds is reported. We have studied the transformation of the chloronitroso compound (VII), obtained from malondioxime (V) in ether with gaseous chlorine at -70° , into IX. It was found that this was possible only by heating a DMSO solution. The characteristics of the compounds which are described are reported.

J. Heterocyclic Chem., 14, 159 (1977).

We recently examined the behavior of enamino ketones obtained from methylenediisoxazoles (I). Of the methylenediisoxazoles (I, II and III) capable of forming linear chains by hydrogenolysis, only III is still unknown (2).

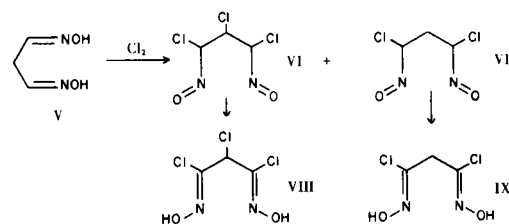


Among all possible schemes for the synthesis of diisoxazoles with structure III, we have assumed that the most valid synthesis is that involving the reaction between nitrile oxides and monosubstituted acetylenes (3). We therefore undertook the synthesis of malonodinitrile oxide (IV) starting from malondioxime *via* its still unknown 1,3-dichloro derivative.



Chlorination of malondioxime (V) leads to polychlorinated derivatives; however, under carefully controlled experimental conditions, the required product (VII) could be obtained, together with the trichlorinated product (VI).

As a matter of fact, by operating at low temperature



(-70°) in ether suspension, following the procedure described below, VII may be isolated. By treating VII with triethylamine at room temperature, very low yields of the corresponding diisoxazole (III) was obtained if the reaction was carried out in the presence of an acetylenic compound (4).

We therefore investigated the way in which to isomerize VII to IX, before the treatment with triethylamine. The chloronitroso derivative (VII) in ether, ethanol, benzene and toluene solution was quite stable even upon warming, provided the temperature was kept below the decomposition point; this is shown by the nmr spectrum that remains constant with time.

By heating the solution of VII in DMSO, a variation in the nmr spectrum is observed. If the temperature was brought to $80-90^{\circ}$, the nmr spectrum shows peak attenuation at 3.43 and 6.70 δ and the appearance of a signal at 3.78 δ . The nmr spectrum obtained was consistent with structure IX (5).

When the product obtained by thermal treatment of VII was allowed to react with monosubstituted acetylenic compounds in the presence of triethylamine, satisfactory yields of diisoxazoles (III) were provided.

EXPERIMENTAL

All melting points are uncorrected. Infrared spectra were measured with a "Perkin-Elmer" model 137 Infracord spectrometer. Nuclear magnetic resonance spectra were determined with a Varian Associates model A 60 spectrometer. Chemical shifts in δ ppm were measured with tetramethylsilane as the internal standard. Mass spectra were taken on a "Hitachi-Perkin-Elmer" RMU 6D single focusing spectrometer.

1,3-Dichloro-1,3-dinitrosopropane (VII) and 1,2,3-Trichloro-1,3-dinitrosopropane (VI).

A suspension of malondioxime (V) (3 g.) in distilled ether (300 ml.), was subjected at -70° to a chlorine stream (30 liters per hour for 2 minutes) by causing the chlorine absorption on the surface. After ether removal in the cold, a solid was obtained that was dissolved with ethanol (100 ml.). The undissolved fraction mainly consists of VI, m.p. 140° dec.; nmr δ ppm DMSO: 6.04 (1H, t); 6.95 (2H, d).

Anal. Calcd. for $C_3H_3Cl_3N_2O_2$: Cl, 51.77. Found: Cl, 51.94.

From ethanol solution, by solvent evaporation and after washing with ether a solid was obtained (1.5 g.), the analytical data of which correspond to the structure of 1,3-dichloro-1,3-dinitroso propane (VII), m.p. 98° dec.; nmr δ ppm DMSO: 3.43 (2H, t); 6.70 (2H, t).

Anal. Calcd. for $C_3H_4Cl_2N_2O_2$: Cl, 41.47. Found: Cl, 41.66.

1,3 Dichloromalondioxime (IX).

By heating 1.5 g. of VII dissolved in 20 ml. of DMSO at 90° for 45 minutes, 1 g. of crude IX was obtained.

3,3'-Methylenebis(5-phenylisoxazole) (IIIa).

Triethylamine (1.2 g.) was added under stirring at 0° to a mixture of IX (1 g.) and phenylacetylene (5 ml.); after one day at room temperature, water was added and ether extraction was performed. The extract was dried over sodium sulfate and the solvent was evaporated. Crystallization from hexane of the residue gave 1 g. of IIIa, yield 60%, m.p. 134° ; nmr (deuteriochloroform) δ ppm: 7.9-7.3 (10 H) m; 6.50 (2H) s; 4.22 (2H) s; MS: m/e 302 (M^+); 225, 197, 144, 105.

Anal. Calcd. for $C_{19}H_{14}N_2O_2$: C, 75.48; H, 4.67; N, 9.27. Found: C, 75.28; H, 4.60; N, 9.24.

3,3'-Methylenebis(5-n-butylisoxazole) (IIIb).

Triethylamine (1.2 g.) was added under stirring at 0° to a mixture of IX (1 g.) and hexane (5 ml.); after one day at room temperature, water was added and ether extraction was performed. The extract was dried over sodium sulfate and the solvent was evaporated. Tlc of the residue gave a liquid (IIIb), b.p. undetermined, yield 40%; nmr (deuteriochloroform) δ ppm: 5.95 (2H) s; 4.00 (2H) s; 2.70 (4H) m; 1.8-0.7 (14H) m; MS: m/e 262 (M^+); 233, 220, 177, 135.

Anal. Calcd. for $C_{15}H_{22}N_2O_2$: C, 68.67; H, 8.45; N, 10.68. Found: C, 68.52; H, 8.40; N, 10.66.

3,3'-Methylenebis(5-bromomethylisoxazole) (IIIc).

Triethylamine (1.2 g.) was added with stirring at 0° to a mixture of IX (1 g.) and propargyl bromide (5 ml.); after one day at room temperature, water was added and ether extraction was performed. The extract was dried over sodium sulfate and the solvent was evaporated. Crystallization from hexane of the residue gave 0.7 g. of IIIc, yield 35%, m.p. 62° ; nmr (deuteriochloroform) δ ppm: 6.28 (2H) s; 4.43 (4H) s; 4.10 (2H) s; MS: m/e 336 (M^+); 257, 241, 213, 134.

Anal. Calcd. for $C_9H_8Br_2N_2O_2$: C, 32.17; H, 2.40; N, 8.33; Br, 47.56. Found: C, 32.06; H, 2.36; N, 8.31; Br, 47.36.

REFERENCES AND NOTES

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- (2) S. Auricchio and A. Ricca, *Gazz. Chim. Ital.*, **103**, 37 (1973).
- (3) A. Quilico, "Isoxazoles," Interscience, New York, 1962.
- (4) It is known that chloronitroso derivatives isomerize easily to chlorooximes that, in the presence of bases, give rise to the corresponding nitrile oxides. Grundmann and Grunanger, "The Nitrile Oxides," Springer, Berlin, 1971.
- (5) Chloronitroso derivative VI shows the same behaviour.