1,3-Di(5-isoxazolyl)propane (1)

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In order to clarify some aspects of the behaviour towards alkali of polymers and copolymers of 5-vinylisoxazole (2) containing head-to-tail enchainment of 5-vinylisoxazole units, 1,3-di(5-isoxazolyl)propane has been synthesized and its reactions with alkali have been studied.

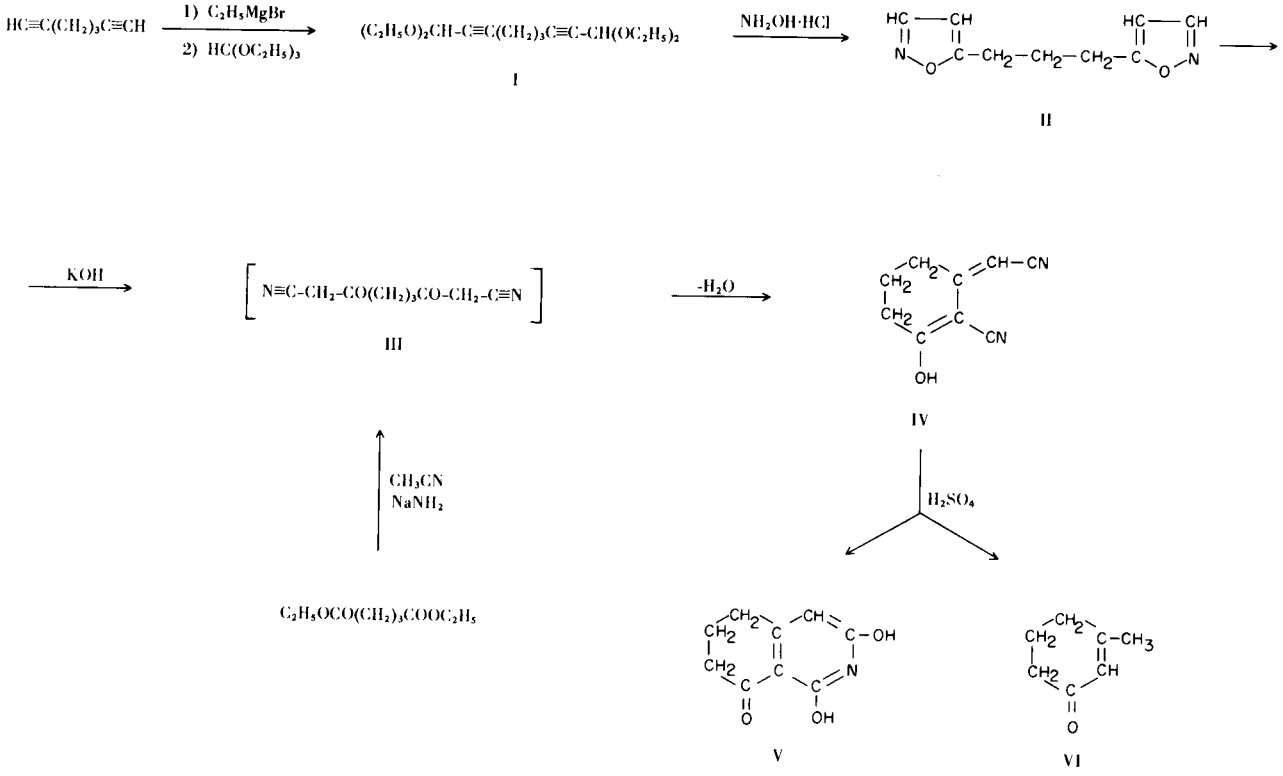
Reaction between 1,6-heptadiyne and ethyl magnesium bromide, followed by addition of ethyl orthoformate, gave 1,1,9,9-tetraethoxynona-2,7-diyne (I) (yield 45%) (Scheme 1). Compound I was separated by distillation and with no further purification was refluxed with hydroxylamine hydrochloride in aqueous-alcoholic solution to give 1,3-di(5-isoxazolyl)propane (II), (Scheme 1) whose molecular formula was determined by accurate mass measurement of the molecular ion under the conditions of the mass spectrum (Figure 1A).

The above described method of synthesis provided compound II free from 3-isoxazolyl substituted isomers, as shown by the nmr spectrum on neat liquid (3,4).

Compound II, as each 3-unsubstituted isoxazole derivative (5,6), reacted promptly with base; however, treatment with aqueous-methanolic potassium hydroxide, gave the 2-cyano-3-hydroxy-2-cyclohexene-1-ylidenacetonitrile (IV) in quantitative yield, instead of the expected 3,7-dioxoazelanitrile (III) (7).

Compound IV could be formed from III by reaction, in basic medium, between one of the two methylene groups, activated both by a carbonyl and a nitrile group, and the non-adjacent carbonyl group (Scheme 1). To support

SCHEME 1



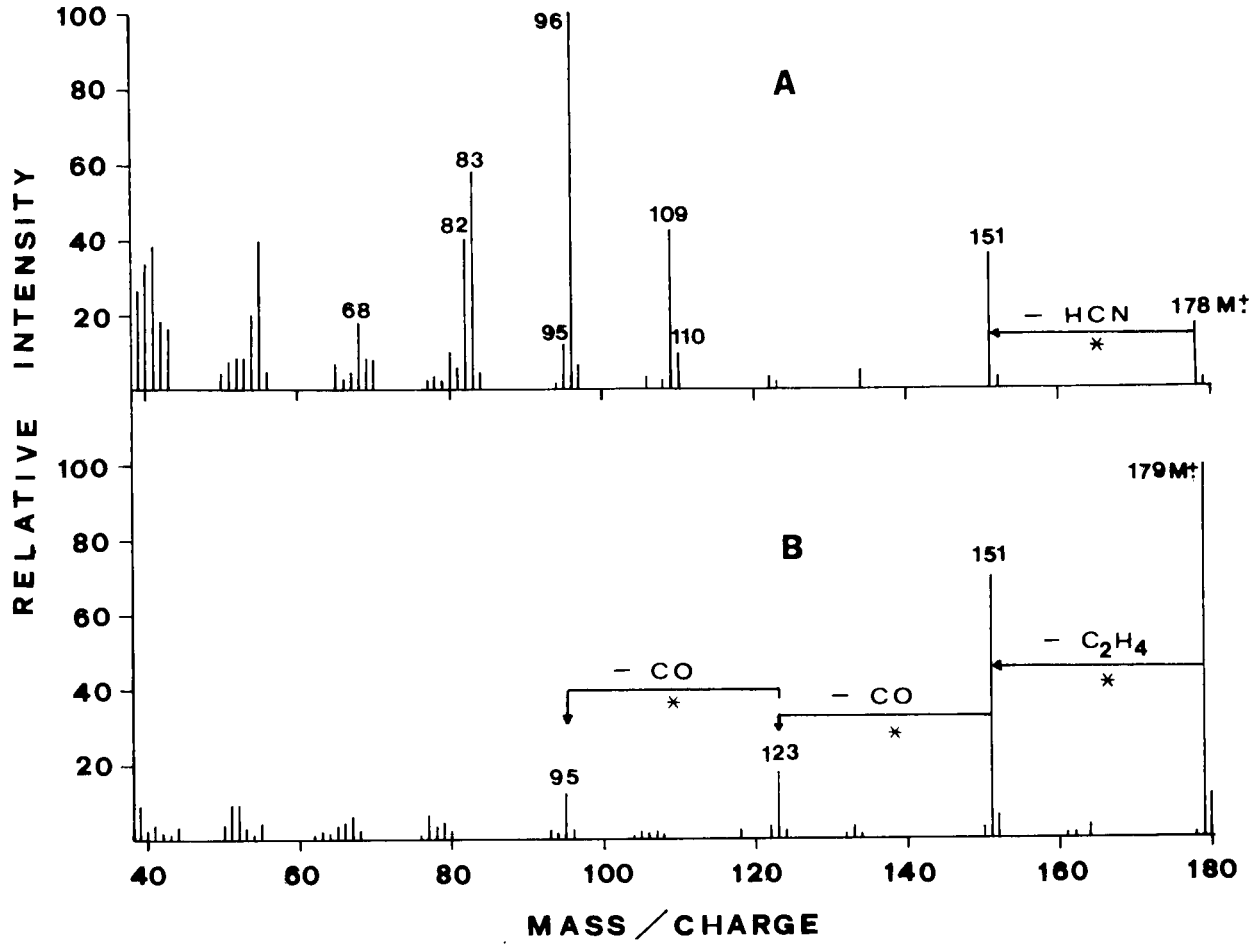


Figure 1. Mass Spectra. A is 1,3-di(5-isoxazolyl)propane; B is 1,3-dihydroxy-8-oxo-5,6,7,8-tetrahydroisoquinoline.

this hypothesis the reaction of II in alkaline medium has been investigated by uv spectra over a period of time: it appeared to take place through the formation of an intermediate compound having uv maximum (257 nm) in good agreement (8) with what is expected for compound III. Moreover the attempt to prepare the 3,7-dioxoazelanitrile (III) from diethyl glutarate and acetonitrile, according to the synthesis of the 3,8-dioxosebaconitrile (9) was unsuccessful, giving, probably through the previous formation of III, the compound IV in 95% yield (Scheme 1).

The structure of IV, suggested by elemental analysis and ir and nmr spectra, was established by treating IV with sulfuric acid (1:1). The reaction gave, with 86% yield, a mixture of 1,3-dihydroxy-8-oxo-5,6,7,8-tetrahydroisoquinoline (V) and 3-methyl-2-cyclohexen-1-one (VI) (10) in the molar ratio 27:73. The formation of V accords with the synthesis of 1,3-dihydroxyisoquinolines or 2,6-dihydroxypyridines from 1,5-dinitriles or esters (11,12).

Ir, nmr, and mass spectra as well as molecular formula by mass measurements and elemental analysis of V are entirely consistent with the assigned structure.

EXPERIMENTAL

Ir spectra were taken on a Perkin Elmer Model 225 spectrophotometer. Uv spectra were determined with a Hilgher Watts "Uvispek" H700 apparatus. Nmr spectra were run on a DA 60 IL Varian instrument. Mass spectra were recorded on a AEI MS-9 double focusing spectrometer operating at 70 eV.

1,1,9,9-Tetraethoxynona-2,7-diyne (I).

A solution of 8.40 g. of 1,6-heptadiyne in 50 ml. of ether was added with stirring to a solution of ethyl magnesium bromide prepared from 6.00 g. of magnesium and 27.30 g. of ethyl bromide in 200 ml. of ether. After standing overnight at room tempera-

ture, the reaction mixture was treated with 74.00 g. of ethyl orthoformate, refluxed for 42 hours with continuous stirring, then hydrolyzed with dilute hydrochloric acid and extracted with ether. The ether extracts, dried over anhydrous sodium sulfate, yielded after removal of the solvent by distillation, 12.19 g. of distilled I; b.p. 150-151°/0.5 Torr.

1,3-Di(5-isoxazolyl)propane (II).

A mixture of 5.95 g. of I dissolved in 50 ml. of ethanol, and 20.00 g. of hydroxylamine hydrochloride dissolved in 20 ml. of water was refluxed for 2 hours. Distillation of the reaction mixture under reduced pressure yielded II in the fraction boiling at 130-132°/0.6 Torr. The crude product was purified by treatment with aqueous-ethanolic solution of cadmium chloride: the white precipitate of the complex salt was filtered, dried under reduced pressure over phosphorus pentoxide to constant weight (6.42 g.), then suspended in water and extracted with isopropyl ether at about 60°. Removal of the solvent and distillation of the residue gave 2.05 g. of II, practically pure by gas-chromatographic analysis on 2 m butanediol succinate columns; b.p. 127-128°/0.52 Torr; $n_D^{25} = 1.5001$; uv λ max (water + methanol 4%) 218 nm (log $\epsilon = 4.10$); infrared (liquid film) cm^{-1}, 1593 (vs), 794 (s), 624 (m); nmr signals (δ in ppm; neat; TMS internal standard) 8.23 (doublet, two ring protons 3 position), 6.10 (doublet with hyperfine structure, two ring protons 4 position), 2.84 (triplet, 1 and 3 positioned CH_2), 2.03 (multiplet, 2 positioned CH_2); mass spectrum Figure 1A (direct inlet system at 100°).

Anal. Calcd. for $C_9H_{10}N_2O_2$: C, 60.66; H, 5.66; N, 15.72. Found: C, 60.56; H, 5.80; N, 15.57.

2-Cyano-3-hydroxy-2-cyclohexen-1-ylidenacetonitrile (IV).

(a) From 1,3-Di(5-isoxazolyl)propane.

A 0.420 g. sample of II was treated under stirring with 100 ml. of aqueous-methanolic (20% of methanol) solution of 1 *N* potassium hydroxide and allowed to stand overnight at room temperature. Acidification of the reaction mixture with hydrochloric acid, extraction with ether and removal of the solvent yielded 0.375 g. of IV, which was purified by recrystallization from benzene; m.p. 140-141°; uv λ max (0.1 *N* potassium hydroxide in water + 4% methanol) 319 nm (log $\epsilon = 4.53$); ir (potassium bromide) cm^{-1}, 3100 (s), 2227 (s), 2205 (s), 1616 (vs), 1588 (s); nmr signals (δ in ppm; solvent acetone-d_6; TMS internal standard) 9.65 (large singlet, OH), 5.17 (singlet with hyperfine structure, ylidenic CH), 2.63 (multiplet, 4 and 6 positioned CH_2), 1.87 (multiplet, 5 positioned CH_2).

Anal. Calcd. for $C_9H_8N_2O$: C, 67.48; H, 5.04; N, 17.49. Found: C, 67.61; H, 5.09; N, 17.44.

(b) From Diethyl Glutarate.

To a stirred solution of sodamide, prepared from 5.75 g. of sodium, in 300 ml. of liquid ammonia, was added 10.28 g. of acetonitrile, then 15.99 g. of diethyl glutarate dissolved in 25 ml. of ether. The mixture was stirred for 1 hour in presence of liquid ammonia and 1 hour more at room temperature after removal of the ammonia by dropwise addition of 200 ml. of ether. The reaction mixture, after hydrolysis with dilute hydrochloric acid, extraction with ether and removal of the solvent under reduced pressure, yielded 12.87 g. of IV; m.p. 140-141°. The ir and nmr spectra were superimposable with those of the product obtained by hydrolysis of II.

Hydrolysis of IV with Sulfuric Acid.

A 5.66 g. sample of IV, dissolved in 30 ml. of sulfuric acid (1:1), was distilled until a negative test of the distillate with 2,4-dinitrophenylhydrazine was obtained. The distillate, by extraction with ether and removal of the solvent, yielded 2.44 g. of distilled 3-methyl-2-cyclohexen-1-one (VI); b.p. 90-90.5°/20 Torr. Compound VI appeared to be identical with the product prepared from ethyl acetoacetate and paraformaldehyde, according to L. I. Smith *et al.* (10). From the residue of the distillation, by dilution with water to 150 ml. was precipitated 1.48 g. of 1,3-dihydroxy-8-oxo-5,6,7,8-tetrahydroisoquinoline (V); m.p. after crystallization from ethanol 267-268°; ir (potassium bromide) cm^{-1}, 3120 (m), 1665 (vs), 1610 (vs), 1576 (s); nmr signals (δ in ppm; solvent trifluoroacetic anhydride; TMS external standard) 5.53 (singlet, two OH), 3.62 (singlet with hyperfine structure, 4 positioned CH), 1.58 (triplet, 5 positioned CH_2), 1.37 (triplet, 7 positioned CH_2), 1.08 (multiplet, 6 positioned CH_2); mass spectrum Figure 1B (direct inlet system at 130°).

Anal. Calcd. for $C_9H_9NO_3$: C, 60.33; H, 5.06; N, 7.82. Found: C, 60.45; H, 5.04; N, 7.68.

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