SYNTHESIS AND PROPERTIES OF AZOLES AND THEIR DERIVATIVES

XXIV.* PREPARATION OF ISOXAZOLINES AND ISOXAZOLES CONTAINING ADAMANTYL RADICALS BY THE 1,3-DIPOLAR CYCLOADDITION REACTION

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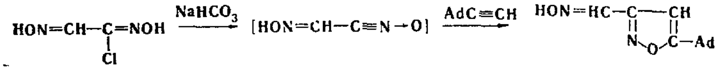
The 1,3-dipolar cycloaddition reaction of nitrile N-oxides, and also the thermal condensation of arylhydroxamic acid chlorides with unsaturated derivatives of the adamantane series leads to the corresponding 3,5-disubstituted isoxazolines and isoxazoles.

There is no information in the literature on the use in the 1,3-dipolar cycloaddition reaction of unsaturated adamantane derivatives as the dipolarophiles. In our work we have investigated the reaction of 1-vinyladamantane, 1-isopropenyladamantane, and 1-ethynyladamantane, with N-oxides of aromatic and aliphatic nitriles, leading to the formation of the isoxazolines (I-VI) and the isoxazoles (VII-IX). The constants and yields of the compounds obtained are given in Table 1.

It is known [2] that in the reaction of nitrile N-oxides with unsaturated compounds a large role is played by steric factors. Thus, in their reaction with monosubstituted olefins or acetylenes containing voluminous substituents, of the two possible isomeric azoles the one in which the substituent occupies position 5 is formed predominantly. This isoxazoline alone is formed as a result of reactions of nitrile N-oxide with 1,1-disubstituted olefins [3]. Since the adamantyl radical creates great steric hindrance, it could be expected that in our case isoxazolines and isoxazoles with the adamantyl radical in position 5 were formed.

The PMR spectrum of 5-adamantyl-3-phenylisoxazole has three groups of signals: a multiplet at about 2 ppm, characteristic for the protons of adamantane [4], a singlet at 6.12 ppm of the 4-H proton, and a complex group of signals at about 7.15 ppm of the phenyl ring. The PMR spectrum of 5-adamantyl-3-phenyloxazoline contains, in addition to the signals characteristic for the adamantane protons, an unsymmetrical doublet at 3 ppm (4-CH_2) and a triplet at 4.13 ppm (5-H). When mixtures of unsaturated adamantane derivatives and arylhydroxamic acid chlorides are boiled, a reaction takes place with the evolution of hydrogen chloride and the formation of compounds identical with the adducts obtained by the 1,3-dipolar cycloaddition reaction. However, in the case of thermal condensation the yields are lower because of the formation of byproducts which probably arise under the action of the hydrogen chloride liberated.

Adamantyl-substituted unsaturated compounds also take part in a 1,3-dipolar cycloaddition reaction with N-oxides of aliphatic nitriles: the hydroxyiminoacetonitrile N-oxide formed by the dehydrochlorination of antichloroglyoxime reacts with 1-ethynyladamantane with the formation of the isoxazole (X) (92 %).



X

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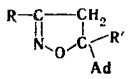
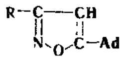
*For communication XXIII, see [1].

I. M. Gubkin Moscow Institute of the Petrochemical and Gas Industry. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 180-182, 1975. Original article submitted November 20, 1973.



I-VI



VII-IX

Compound	R	R′	mp, °C	Empirical formula	Found, %			Calculated, %			Yield, %
					C	H	N	C	H	N	
I	Phenyl	H	109—110	$C_{19}H_{23}NO$	81,0	8,7	4,9	81,3	9,0	5,0	96
II	p-Nitrophenyl	H	213—214	$C_{19}H_{22}N_2O_3$	70,2	7,1	8,5	70,0	6,9	8,6	98
III	5-Nitrofuryl	H	179—180	$C_{17}H_{22}N_2O_4$	64,5	6,3	8,9	64,6	6,4	9,0	80
IV	Phenyl	CH_3	95—96	$C_{20}H_{22}NO$	80,3	8,4	5,0	80,4	8,5	4,9	85,5
V	p-Nitrophenyl	CH_3	207—208	$C_{20}H_{21}N_2O_3$	70,4	7,1	8,1	70,7	7,2	8,2	88
VI	5-Nitrofuryl	CH_3	177—178	$C_{18}H_{19}N_2O_4$	65,5	6,7	8,4	65,4	6,8	8,6	68
VII	Phenyl		97—98	$C_{19}H_{21}NO$	81,5	7,6	5,1	81,7	7,5	5,0	93
VIII	p-Nitrophenyl		197—198	$C_{19}H_{20}N_2O_3$	70,2	6,3	8,7	70,4	6,2	9,0	95
IX	5-Nitrofuryl		136—137	$C_{17}H_{18}N_2O_4$	63,1	6,0	8,9	63,4	6,0	9,1	73

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*Solvent for crystallization: for (I, IV, VII) petroleum ether, for (II and VIII) C_3H_7OH, for (III and VI) C_2H_5OH, and for (V) CH_3OH.

EXPERIMENTAL

The PMR spectra were obtained on a JEOL 4H-100 instrument in CCl_4 with TMS as standard. The IR spectra were taken on a UR-10 spectrometer and the UV spectra on a Unicam SP 800A spectrophotometer. The purity of all the compounds obtained was checked by TLC on alumina of Brockmann activity grade 2 in the heptane–n-propanol system.

The N-oxides of aromatic nitriles were obtained by the dehydrochlorination of the chlorides of the corresponding hydroxamic acids by means of triethylamine [5] and were used without isolation. The chlorides of benzhydroxamic and p-nitrobenzhydroxamic acids were obtained by chlorinating the corresponding oximes with chlorine [6]; 5-nitrofurfural oxime was chlorinated with nitrosyl chloride [7]; hydroxyiminoacetonitrile N-oxide was obtained by the dehydrochlorination of anti-chloroglyoxime [8] with aqueous sodium bicarbonate. The unsaturated adamantane derivatives used as dipolarophiles were obtained by known methods: 1-vinyladamantane and 1-isopropenyladamantane by the dehydration of the corresponding alcohols [9, 10], and 1-ethynyladamantane by the dehydrobromination of 2-(adamant-1-yl)-1,1-dibromoethane [11].

1,3-Dipolar Cycloaddition Reaction. At room temperature with vigorous stirring, a solution of 0.01 mole of triethylamine in 20 ml of anhydrous ether was slowly added to a solution of 0.01 mole of hydroxamoyl chloride and 0.01 mole of dipolarophile in 80 ml of anhydrous ether. The reaction mixture was stirred at room temperature for 2-3 h, the precipitate was filtered off, washed with water to eliminate triethylamine hydrochloride, combined with the product obtained after the evaporation of the ethereal solution, and purified by recrystallization.

The IR spectra of the compounds obtained included the absorption bands characteristic for the adamantane structure: 2933, 2907, 2857, 1357, and 1017-1038 cm^{-1}, and frequencies assignable to the stretching vibrations of a C=N bond (1625-1600 cm^{-1}). UV spectrum, λ_{max}, nm: (VII) 277 (in heptane), 293 (in acetonitrile); (I) 283 (in heptane), 323 (in acetonitrile).

5-Adamant-1′-yl)-3-hydroxyiminoethylisoxazoles (X). The reaction was performed as described above using instead of triethylamine a solution of 0.01 mole of $NaHCO_3$ in 10 ml of water, which was added to a mixture of anti-chloroglyoxime and 1-ethynyladamantane at −10 to 0° C. This gave (X) with a yield of 92%, mp 155-156° C (from ethanol). Found: C 71.5; H 6.4; N 10.1%. $C_{14}H_{18}N_2O_2$. Calculated: C 71.6; H 6.5; N 10.2%. IR spectrum, cm^{-1}; 1580 (C=N of a hydroxyimine), 3300 (OH).

Thermal Condensation of Unsaturated Adamantane Derivatives with Arylhydroxamoyl Chlorides. A mixture of 0.01 mole of a hydroxamoyl chloride and 0.01 mole of an unsaturated compound in 50 ml of toluene was boiled until the evolution of hydrogen chloride ceased (25-30 h). The toluene was evacuated off in vacuum and the residue was purified by recrystallization.

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