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SYNTHESIS AND PROPERTIES OF AZOLES AND THEIR DERIVATIVES. 57*. UNEXPECTED RESULTS OF 3-NITROPROPENE-1 [2+3] CYCLOADDITION TO C,C,N-TRIPHENYLNITRONE

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[2+3] Cycloaddition of 3-nitropropene-1 with C,C,N-triphenylnitrone leads to a mixture of 5-nitromethyl-2,3,3-triphenylisoxazolidine and 5-methyl-4-nitro-2,3,3-triphenylisoxazolidine. The results obtained can be explained assuming that 3-nitropropene-1 isomerizes to 1-nitropropene-1 under reaction conditions.

Keywords: [2+3] cycloaddition, nitrone, nitropropene, isomerization.

In previous papers of this series [1-4] we described the [2+3] cycloaddition of *trans*-R-substituted nitroethylenes (conjugated systems) with aryl nitrones. It was found that the reaction is entirely regioselective and leads to 4-nitro-5-R-isoxazolidines as the only reaction products. The present contribution is intended as an extension of our studies. In particular, it initiates investigations on the reactivity of unconjugated nitroalkenes in the reaction with aryl nitrones. For this purpose 3-nitropropene-1 (**1**) and C,C,N-triphenylnitrone (**2**) were chosen as model compounds. Theoretically [5,6], [2+3] cycloaddition of such reactants should lead to 5-nitromethyl-2,3,3-triphenylisoxazolidine (**3**).

The reaction was carried out in solvent-free conditions at room temperature using a tenfold molar excess of alkene. When the reaction was completed, the excess alkene was removed in vacuum and the semiliquid residue was tested by means of HPLC. Unexpectedly, it was found that the reaction yielded two products rather than one product as well as a small quantity of benzophenone. Their R_T were different from those of the starting compounds. Separation of the mixture by means of semipreparative HPLC produced compound **3** and 5-methyl-4-nitro-2,3,3-triphenylisoxazolidine (**4**) in molar ratio ca. 1:5 (Scheme 1).

It is interesting to note at this point that [2+3] cycloaddition of the same nitroalkene to aromatic nitrile N-oxides gave only 3-aryl-5-nitromethyl- isoxazolidines [7].

Despite this finding, which at first sight appears to be an unexplainable, it can be understood by assuming that under the reaction conditions nitropropene **1** isomerizes partially to *trans*-1-nitropropene-1 (**5**) by a [1,3]-sigmatropic shift. The possibility of such isomerization was reported some years ago [8, 9].

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* For Part 56, see [1].

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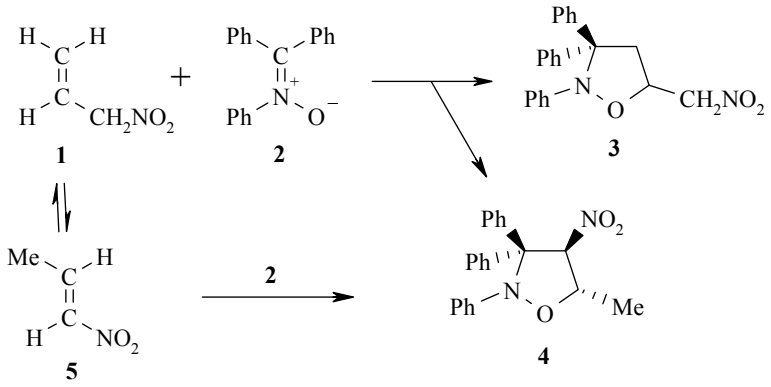
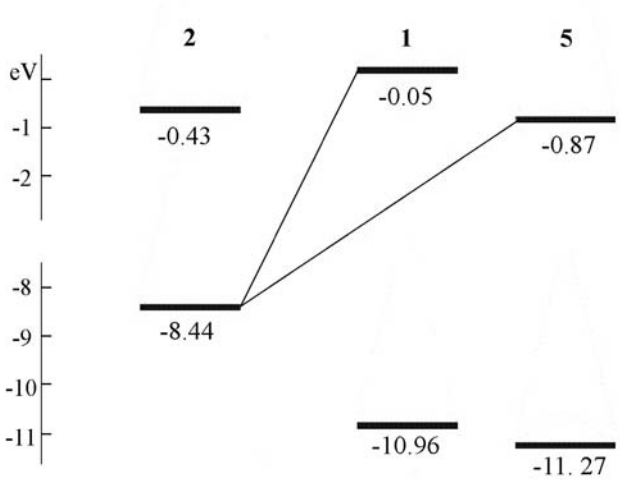
Scheme 1



Probably, the conjugated nitroalkene **5** reacts with nitrone **2** much faster than the unconjugated isomer **1**. This hypothesis is in agreement with an interaction diagram elaborated by us on the basis of FMO energies estimated for reactants **1**, **2** and **5** (Fig. 1). From the diagram it is evident that both cycloadditions are controlled by $HOMO_{nitrone}$–$LUMO_{alkene}$ interactions (ΔE_2–ΔE_1>1 eV). According to Sustmann's terminology [10] they are the normal electron demand reactions. However, the energy gap (ΔE_1) between LUMO of nitroalkene **5** and HOMO of nitrone **2** is smaller than that between LUMO of nitroalkene **1** and HOMO of nitrone **2**. Therefore, with regard to FMO theory [10, 11], the reaction leading to compound **4** should be preferred. Actually, by independent experiment it was proved that the [2+3] cycloaddition of nitropropene **5** with nitrone **2** in solvent-free conditions resulted in compound **4** with almost quantitative yield. Nevertheless, we are aware more rigorous investigations along similar lines are called for.



$$\Delta E_1 = |E_{\text{HOMO nitrone}} - E_{\text{LUMO alkene}}| \qquad 8.39 \qquad 7.57$$

$$\Delta E_2 = |E_{\text{HOMO alkene}} - E_{\text{LUMO nitrone}}| \qquad 10.53 \qquad 10.84$$

Fig. 1. FMO interaction diagram for [2+3] cycloaddition of C,C,N-triphenylnitrone **2** to nitropropenes **1,5** (data taken from AM1 calculations).

EXPERIMENTAL

Melting points were determined on the Boetius apparatus. ^{1}H NMR spectra were recorded on a Tesla BS-567C (80 MHz) spectrometer in $CDCl_3$ using TMS as an internal standard. IR spectra were recorded on a Bio-Rad-175C spectrometer in KBr discs. Mass spectra (70eV) were measured with a Varian MAT 112 spectrometer. HPLC analyses were carried out with a Knauer apparatus equipped with UV-VIS detector, using a Lichrospher 100RP column (4 × 240) and methanol–water (3:1 v/v) as an eluent at a flow rate of 1.3 cm^3/min. For separation of cycloadducts semipreparative HPLC was applied with a Lichrospher 100RP column (16 × 250) and methanol–water (3:1 v/v) as an eluent at a flow rate of 10 cm^3/min. 3-Nitropropene-1, *trans*-1-nitropropene-1 and C,C,N-triphenylnitrone were prepared according to the methods described in the literature [12-14].

[2+3] Cycloaddition of Triphenylnitrone with 3-Nitropropene-1. The reaction was carried out in the dark. A mixture of 3-nitropropene-1 (3.48 g, 0.04 mol) and C,C,N-triphenylnitrone (1.09 g, 0.004 mol) was stirred at room temperature for one week. Then the excess of nitroalkene was evaporated *in vacuo*, and the residue was separated by semipreparative HPLC. Evaporation of the eluent from the obtained fractions gave 5-nitromethyl-2,3,3-triphenylisoxazolidine (**3**) and 5-methyl-4-nitro-2,3,3-triphenylisoxazolidine (**4**) with R_T 9.8 and 16.3 min, respectively. The products were recrystallized from cyclohexane. Thus, 0.22 g (15%) of **3** (mp 107-109°C) and 1.08 g (75%) of **4** [mp 99-100°C (decomposition)] were obtained.

5-Nitromethyl-2,3,3-triphenylisoxazolidine (3). IR spectrum, ν, cm^{-1}: 1557, 1366 (NO_2), 1180, 958 (azolidine ring), 760, 695 (C_6H_5). ^{1}H NMR, δ, ppm (*J*, Hz): 2.46 (1H, dd, *J* = 8.8, *J* = 13.2, H-4); 3.79 (1H, dd, *J* = 12.8, *J* = 13.2, H-4); 4.10 (1H, dd, *J* = 5.0, *J* = 12.8, C$\underline{H}_2$NO$_2$); 4.81 (1H, dd, *J* = 7.7, *J* = 12.8, C$\underline{H}_2$NO$_2$); 5.25 (1H, m, *J* = 8.8, *J* = 12.8, *J* = 5.0, *J* = 7.7, H-5). Mass spectrum, *m/z* (I_{rel}, %): 360 $[M]^+$ (39), 257 $[(C_6H_5)_2C{=}NC_6H_5]^+$ (11), 253 $[M–C_6H_5NO]^+$ (50), 180 $[(C_6H_5)C{\equiv}NC_6H_5]^+$ (58), 91 $[C_6H_5N]^+$ (100). Found, %: C 73.46; H 5.52; N 7.81. $C_{22}H_{20}N_2O_3$. Calculated, %: C 73.32: H 5.59; N 7.77.

5-Methyl-4-nitro-2,3,3-triphenylisoxazolidine (4). IR, ν, cm^{-1}: 1559, 1369 (NO_2), 1181, 956, 925 (azolidine ring), 780, 693 (C_6H_5). ^{1}H NMR, δ, ppm (*J*, Hz): 1.66 (3H, d, *J* = 6.4, C$\underline{H}_3$); 5.18 (1H, dq, *J* = 8.1, *J* = 6.4, H-5); 5.75 (1H, d, *J* = 8.1, H-4). Mass spectrum, *m/z* (I_{rel}, %): 360 $[M]^+$ (40), 273 $[M–O_2NCHCHCH_3]^+$ (36), 257 $[(C_6H_5)_2C{=}NC_6H_5]^+$ (22), 180 $[(C_6H_5)C{\equiv}NC_6H_5]^+$, 91 $[C_6H_5N]^+$ (100). Found, %: C 73.41; H 5.58; N 7.78. $C_{22}H_{20}N_2O_3$. Calculated, %: C 73.32; H 5.59, N 7.77.

[2+3] Cycloaddition of Triphenylnitrone with *trans*-1-Nitropropene-1. A mixture of 1-nitropropene-1 (3.48 g, 0.04 mol) and C,C,N-triphenylnitrone (1.09 g, 0.004 mol) was shaken at room temperature for 15 min. When the reaction was completed, the excess of nitroalkene was evaporated to dryness *in vacuo*. The residue was tested by HPLC and then recrystallized from cyclohexane. In this manner 1.38 g (96%) of 5-methyl-4-nitro-2,3,3-triphenylisoxazolidine; mp 99-100°C (decomp.) was obtained.

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