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TRANSFORMATIONS OF NITRO-SUBSTITUTED DIHYDROISOINDOLES IN REACTIONS WITH ACTIVATED ALKYNES

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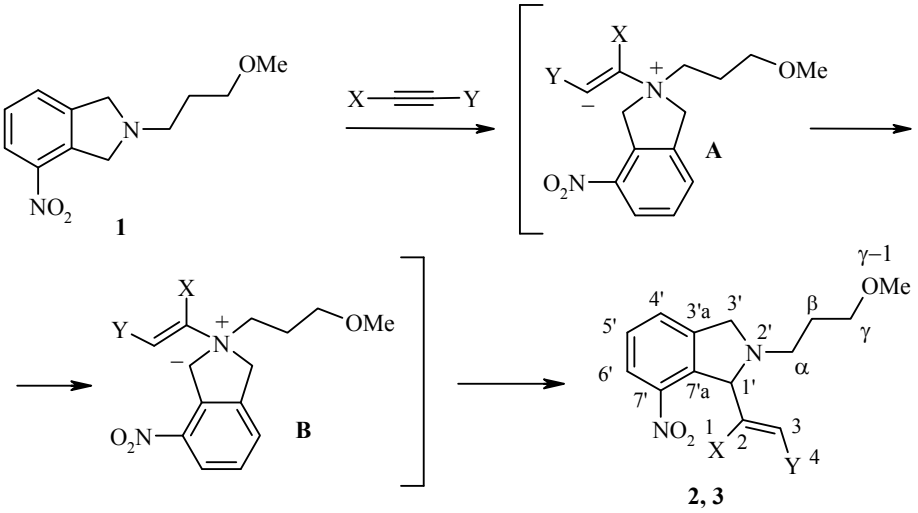
We have previously shown that the reaction of 4-hydroxymethyl-substituted dihydroisoindoles with activated alkynes at room temperature occurs *via* recyclization of a dihydropyrrole fragment to form 1,3-dihydroisobenzofurans [1]. Only in the case of carrying out the reaction with methyl propiolate at -20ºC were we able to record the formation of the product of expansion of the dihydropyrrole ring (i.e. the corresponding benzazepine [2]).



2 X = Y = CO_2Me; **3** X = H; Y = CO_2Me

It was of interest to study the behavior of dihydroisoindoles containing an electron-acceptor substituent in the aromatic ring under the action of activated alkynes. The dihydroisoindole **1** was synthesized using method [3].

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It was found that the introduction of a nitro group into the aromatic fragment of the isoindoline leads to a novel way of transforming this ring in the presence of electron-deficient alkynes.

Compound **1** reacts with methyl propiolate and dimethylacetylene dicarboxylate at room temperature to give good yields of the 1-vinyl-substituted dihydroisoindoles **2**, **3**, which are the products of a Stevens rearrangement of the intermediate ylide **B** (Scheme). It was interesting to note that the solvent did not prove to have a marked effect on the reaction course. In both acetonitrile and methanol the only reaction products were the dihydroisoindoles **2**, **3**.

The structure of the compounds obtained was confirmed by their overall spectroscopic data.

IR spectra were taken on an Infralum FT-801 Fourier spectrometer as KBr tablets. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker WP-400 instrument (400 and 100 MHz respectively) using $CDCl_3$ and with TMS as internal standard. Electrospray ionization mass spectra were obtained on an Agilent 1100 LC/MSD Trap System VL mass spectrometer.

Reaction of Dihydroindole 1 with Acetylenedicarboxylic Ester and Methyl Propiolate (General Method). The activated alkyne (0.8 mmol) was added to a solution of isoindoline **1** (0.4 mmol) in acetonitrile or methanol (10 ml). The product was stirred at room temperature for 5 days and the course of the reaction was monitored by TLC on Silufol UV-254 plates (revealed by UV radiation of wavelength 254 nm). The oil obtained after removal of solvent was flash chromatographed on a 60 Å silica gel column (150 mm×12 mm) using methanol in chloroform (1-5%) as eluent.

Dimethyl Ester of 2-[2-(3-Methoxypropyl)-7-nitro-2,3-dihydro-1H-isoindol-1-yl]-2-butenedioic Acid (2). Orange oil. Yield 60%. R_f 0.51 (Silufol, ethyl acetate–hexane, 5:3). IR spectrum, ν, cm^{-1}: 1737, 1655 ($COOCH_3$), 1579, 1349 (NO_2). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.71-1.79 (2H, m, β-CH_2); 2.73-2.81 (1H, m, α-CH_2); 2.88-2.93 (1H, m, α-CH_2); 3.26 (3H, s, γ-1-OCH_3); 3.39 (2H, td, *J* = 6.4 and 2.8, γ-CH_2); 3.48 (3H, s, 4-CO_2CH_3); 3.64 (3H, s, 1-CO_2CH_3); 3.90 (1H, d, *J* = 13.7, H-3'); 4.23 (1H, dd, *J* = 13.7 and 1.9, H-3'); 5.31 (1H, br. s, H-1'); 5.95 (1H, s, H-3); 7.39 (1H, t, *J* = 7.8, H-4'); 7.43-7.47 (1H, m, H-5'); 7.97 (1H, d, *J* = 8.1, H-6'). ^{13}C NMR spectrum, δ, ppm: 28.7, 49.3, 51.9, 52.1, 56.7, 58.6, 70,5, 72.3, 122.8, 122.9, 128.3, 129.4, 130.4, 134.8, 144.2, 146.4, 165.0, 167.5. Mass spectrum, *m/z* 379 $[M+1]^+$. Found, %: C 57.17; H 5.82; N 7.36. $C_{18}H_{22}N_2O_7$. Calculated, %: C 57.14; H 5.86; N 7.40.

Methyl (2*E*)-3-[2-(3-methoxypropyl)-7-nitro-2,3-dihydro-1H-isoindol-1-yl]acrylate (3). Orange oil. Yield 73%. R_f 0.6 (Silufol, ethyl acetate–hexane, 5:3). IR spectrum, ν, cm^{-1}: 1722 (CO_2CH_3), 1529, 1350 (NO_2). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.71-1.79 (2H, m, β-CH_2); 2.68-2.83 (2H, m, α-CH_2); 3.26 (3H, s, γ-1-OCH_3); 3.39 (2H, td, *J* = 6.2, *J* = 1.2, γ-CH_2); 3.63 (3H, s, 1-$CO_2C\underline{H}_3$); 3.99 (1H, d, *J* = 13.7, H-3'); 4.16 (1H, d, *J* = 13.7, H-3'); 5.26 (1H, d, *J* = 7.5, H-1'); 6.06 (1H, dd, *J* = 15.6, *J* = 1.2, H-2); 6.68-6.80 (1H, m, H-3); 7.34-7.41 (1H, d, H-5'); 7.48 (1H, d, *J* = 7.5, H-4'); 7.96 (1H, d, *J* = 8.1, H-6'). ^{13}C NMR spectrum, δ, ppm: 28.9, 49.8, 51.6, 56.7, 58.7, 69.2, 70.5, 118.1, 122.2, 123.0, 123.4, 128.7, 129.1, 143.5, 144.0, 166.6. Mass spectrum, *m/z* 321 $[M]^+$. Found, %: C 60.27; H 6.23; N 8.69. $C_{16}H_{20}N_2O_5$. Calculated, %: C 50.99; H 6.29; N 8.74.

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