REACTION OF 2-FORMYL-1,3-CYCLANEDIONES WITH N,N'-SUBSTITUTED 1,1-DIAMINO-2-NITROETHYLENES

A. Ya. Strakov, M. V. Petrova, A. I. Gurkovskii, and O. Ya. Neiland

Reaction of 2-formyldimedone and 2-formyl-1,3-indanedione with 1,1-di(2-hydroxyethylamino)- and 1,1-di(4-morpholyl)-2-nitroethylenes produces 2-[3,3-di(2-hydroxyethylamino)-2-nitroprop-2-en-1-ylidene]- and 2-[3,3-di(4-morpholyl)-2-nitroprop-2-en-1-ylidene]-5,5-dimethyl-1,3-cyclohexanediones and the 1,3-indanediones, respectively. The reaction of the same 2-formyl-1,3-cyclanediones with 2-nitromethyleneimidazolidine yields 8,8-dimethyl-4-nitro-6-oxo-1,2,3,6,7,8-hexahydroimidazo[1,2-a]quinoline and 4-nitro-6-oxo-1,2-dihydro-6H-imidazo[1,2-c]-4-azafluorene.

N-Substituted 1,1-diamino-2-nitroethylenes react with compounds containing double bonds polarized by one or several electron-accepting groups to form products similar to those from the Mannich reaction or the aldol condensation [1-6]. The reaction of 2-formyldimedone (I) and 2-formyl-1,3-indanedione (II), the most reactive electrophilic center of which is the exocyclic carbon atom of the enol form [7], with 1,1-di(methylamino)-2-nitroethylene (IIIa) produces [1] 2-[3,3-di(methylamino)-2-nitroprop-2-enylidene]-5,5-dimethyl-1,3-cyclohexanedione (IVa) and -1,3-indanedione (Va).

In continuation of this work, reaction of the formyl derivatives I and II with 1,1-di(2-hydroxyethyl)- (IIIb) and 1,1-dimorpholyl- (IIIc) 2-nitroethylenes and with 2-nitromethyleneimidazolidine (IIId), prepared from 1,1-di(methylthio)-2-nitroethylene by the method [8] has been carried out.

The reaction of 2-formyl-1,3-cyclanediones I and II with 1,1-di(2-hydroxyethyl)-2-nitroethylene (IIIb) proceeds readily. Mixing methanolic or ethanolic solutions of I and II with equimolar amounts of IIIb leads to the corresponding condensation products IVb and Vb. Boiling the reaction mixtures and attempts at crystallization, as



I, IV A =
$$CH_2C(CH_3)_2CH_2$$
; II, V A = 1,2-C₆H₄; III - Va R = R² = H; R¹ = R³ = CH₃;
b R = R² = H; R¹ = R³ = CH₂CH₂OH; c RR¹ = R²R³ = (CH₂CH₂)₂O;
III d R = R² = H; R¹R³ = CH₂CH₂

Riga Technical University, Riga LV-1658, Latvia; e-mail: marina@osi.lanet.lv. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 330-333, March, 1999. Original article submitted June 30, 1998.

a rule, leads to formation of side products. Such behavior for IVb and Vb can be explained by the presence of functional groups (OH, NH, CO) that can participate both in intra- and intermolecular reactions. The reaction of I and II with 1,1-di(4-morpholyl)-2-nitroethylene (IIIc) is less sensitive to more vigorous reaction conditions. Products IVc and Vc can be recrystallized.

The structures of IVb,c and Vb,c were confirmed by IR and PMR spectra (see Experimental). The PMR spectra were more informative. They confirm the number and nature of all protons. The proton on the unsaturated atom $C_{(2)}$ has $\delta = 8.86$ (IVb), 8.84 (IVc), 8.24 (Vb), and 8.51 ppm (Vc). The protons of $C_{(4)}$ and $C_{(6)}$ methylene groups of IVb appear as one singlet at 2.31 ppm.

The strongly polar betaine structure VI is more likely for IVa-c by analogy with the IR and PMR spectral data [1].

The reaction of formyl derivatives I and II with 2-nitromethyleneimidazolidine (IIId) starts at 20°C and proceeds stepwise. Boiling equimolar quantities of I and IIId in ethanol for 10 min leads to a stable bright red product that does not change on further boiling. Dehydration of possible intermediate VIII formed by intramolecular addition leads to both IX and X or XI should be considered when discussing the structure of the red product.



The PMR spectrum of the product is characterized by a broad singlet for the exchangeable NH (or OH) proton (9.6 ppm), resonance absorption of the two conjugated =CH groups (4.66 and 7.57 ppm) as doublets with SSCCs through four bonds ${}^{4}J(H,H) = 1.4$ Hz, a multiplet for N(CH₂)₂N (3.8-4.0 ppm), and singlets for methyl (1.05 ppm) and methylene (2.33 ppm) groups. The spectral data is not confirm the structure XI, but structures IX and X are equally probable. However, observation of a homonuclear Overhauser effect between NH and NCH₂ protons (IX) and the lack of this effect between OH and =CH protons in structure X argues in favor of structure IX.

The presence of carbonyl and NH group is apparent in the IR spectrum (v_{CO} 1694 cm⁻¹, v_{NH} 3320 cm⁻¹). The ¹³C NMR spectra also are consistent with structure IX. A weak-field resonance signal observed at 194 ppm indicates the presence of carbonyl group as the signals for the C=O group of α , β -unsaturated carbonyl compounds are known to be characteristic and are observed in the range of 185-195 ppm [9].

Furthermore, at H/D isotopic exchange of the mobile NH proton the greatest isotope effect ($^{2}\Delta = 0.125$) is observed for N(D)CH₂-, which confirms that the proton is localized on the nitrogen atom and therefore, structure IX is confirmed. Isotope exchange is not observed for the low-field carbonyl signal at 194 ppm. This also confirms structure IX and excludes structure X.

Refluxing of 2-formyl-1,3-indanedione II and 2-nitromethyleneimidazolidine IIId in ethanol for 10 min results in the only possible dehydration of the intermediate VIII to produce compound XII, the structure of which was confirmed by IR and ¹H NMR spectra.

The quality of crystals of IX and XII enabled X-ray structural studies to confirm only the C-N-O skeleton of the molecules. The positions of the hydrogen atoms could not be determined.

Compound IX contains an unusual conjugated donor-acceptor system that includes diaminoethylene donor and two nitro- and carbonyl acceptor groups. This causes absorption to appear in the visible spectral region.

Compound XII, the structure of which is similar to IX, contains an acceptor indenone fragment and nitro group. The donor is the amidine fragment. These structural features are responsible for the intense absorption at \sim 440 nm in the visible region.

EXPERIMENTAL

IR spectra were recorded on a Specord 75-IR instrument as suspensions in vaseline oil (1800-1500 cm⁻¹) and in hexachlorobutadiene (3600-2000 cm⁻¹, frequencies of the C–H stretching vibrations at 3050-2800 cm⁻¹ are not included).

¹H NMR spectra were taken on Bruker WH 90/DS and Varian-Mercury spectrometers at 90 and 200 MHZ, respectively. ¹³C NMR spectra were recorded on a Varian-Mercury spectrometer at 50.03 MHz. The internal standard was HMDS.

Electronic absorption spectra were recorded on a Specord M-40 spectrophotometer for 10⁻⁵ M solutions.

2-[3,3-Di(2-hydroxyethylamino)-2-nitroprop-2-enylidene]-5,5-dimethyl-1,3-cyclohexanedione (IVb). Solution of 2-formyldimedione I (0.34 g, 2 mmol) in methanol (5 ml) was treated with an equimolar amount (0.38 g) of 1,1-di(2-hydroxyethylamino)-2-nitroethylene IIIb in methanol (20 ml) and left to stand for 72 h at 20°C. The yellow precipitate of IVb was filtered off. Yield 33%; mp 178-180°C. IR spectrum: 1670, 1640, 1596, 1568, 1522, 3480, 3260-3180 cm⁻¹. PMR spectrum (CDCl₃ + DMSO-d₆): 1.04 (6H, s, 2CH₃), 2.31 (4H, s, 2CH₂), 3.37-3.67 (8H, m, 2CH₂CH₂), 4.24 (1H, m, J = 6 Hz, OH), 5.07 (1H, t, J = 6 Hz, OH), 8.58 (1H, t, J = 6 Hz, NH), 8.86 (1H, s, =CH–), 8.89 ppm (1H, t, J = 6 Hz, NH). Found, %: C 52.60; H 6.80; N 12.12. C₁₅H₂₃N₃O₆. Calculated, %: C 52.78; H 6.79; N 12.31.

2-[3,3-Di(4-morpholyl)-2-nitroprop-2-enylidene]-5,5-dimethyl-1,3-cyclohexanedione (IVc). Mixture of I (0.34 g, 2 mmol) and 1,1-di(4-morpholyl)-2-nitroethylene (0.49 g, 2 mmol) in ethanol (20 ml) was boiled for 10 min. Half of the ethanol quantity was evaporated on a rotary evaporator. The solution was left for one day. The yellow precipitate of IVc was filtered off and recrystallized from ethanol. Yield 80%; mp 126-130°C. IR spectrum: 1650, 1584, 1518 cm⁻¹. PMR spectrum (CDCl₃): 1.04 (6H, s, 2CH₃), 2.33 (2H, s, CH₂), 2.42 (2H, s, CH₂), 3.51-3.76 [16H, m, N(CH₂CH₂)O], 8.84 ppm (1H, s, =CH–). Found, %: C 58.10; H 6.88; N 10.50. $C_{19}H_{27}N_3O_6$. Calculated, %: C 58.00; H 6.92; N 10.68.

2-[3,3-Di(2-hydroxyethylamino)-2-nitroprop-2-enylidene]-1,3-indanedione (Vb). Solution of IIIb (0.55 g, 2.9 mmol) in boiling methanol (15 ml) was added to boiling solution of 2-formyl-1,3-indanedione (0.50 g, 2.9 mmol) in methanol (10 ml). The yellow precipitate was filtered off after 24 h. Yield of Vb 0.64 g (70%); mp 214-215°C. IR spectrum: 1684, 1648, 1635, 1600, 1582, 1560, 3450, 3230-3200, 3125 cm⁻¹. PMR spectrum (DMSO-d₆): 3.18-3.51 (8H, m, 2CH₂CH₂), 4.71 (1H, t, J = 6 Hz, OH), 5.04 (1H, t, J = 6 Hz, OH), 7.67 (4H, center m, C₆H₄), 8.24 (1H, s, =CH–), 9.02 (1H, t, J = 6 Hz, NH), 9.47 ppm (1H, t, J = 6 Hz, NH). Found, %: C 55.15; H 4.90; N 12.02. C₁₆H₁₇N₃O₆. Calculated, %: C 55.33; H 4.93; N 12.10.

2-[3,3-Di(4-morpholyl)-2-nitroprop-2-enylidene]-1,3-indanedione (Vc). Mixture of compound IIb (0.30 g, 1.7 mmol) and IIId (0.42 g, 1.7 mmol) was boiled for 10 min in ethanol (20 ml). After 3 h the precipitate of Vd was filtered off and recrystallized from ethanol. Yield 0.30 g (46%) of yellow crystals; mp 206-209°C. IR spectrum: 1706, 1656, 1574, 1552, 1549 cm⁻¹. PMR spectrum (DMSO-d₆): 3.70 [16H, center m, $2N(CH_2CH_2)_2O$], 7.67-7.80 (4H, m, C₆H₄), 8.51 ppm (1H, s, =CH–). Found, %: C 60.03; H 5.30; N 10.40. C₂₀H₂₁N₃O₆. Calculated, %: C 60.14; H 5.30; N 10.52.

8,8-Dimethyl-4-nitro-6-oxo-1,2,3,6,7,8-hexahydroimidazo[1,2-a]quinoline (IX). Solutions of compound I (0.84 g, 5 mmol) in ethanol (10 ml) and IIIe (0.65 g, 5 mmol) in ethanol (15 ml) were mixed and boiled for 10 min. The mixture was cooled, bright red precipitate formed was filtered off and recrystallized from acetone. Yield of IX 0.78 g (60%); mp 248-249°C. IR spectrum: 1694, 1678, 1645, 1614, 1566, 3320 cm⁻¹. PMR spectrum (DMSO-d₆):

1.05 (6H, s, 2CH₃), 2.33 (2H, s, CH₂), 3.85 (4H, center m, CH₂CH₂), 4.66 (1H, d, J = 1.4 Hz, $=C_{(9)}H-$), 7.57 (1H, d, J = 1.4 Hz, $=C_{(5)}H-$), 9.53 ppm (1H, br. s, NH). ¹³C NMR spectrum (DMSO-d₆): 29.67, 32.95, 43.33, 44.98, 51.85, 106.03, 110.12, 114.53, 123.65, 131.85, 152.91, 194.12. UV spectrum in ethanol, λ_{max} , nm (log ϵ): 267 (4.15), 311 (3.58), 429 (4.14). Found, %: C 59.61; H 5.70; N 16.00. C₁₃H₁₅N₃O₃. Calculated, %: C 59.76; H 5.79; N 16.08.

4-Nitro-6-oxo-1,2-dihydro-6H-imidazo[1,2-c]-4-azafluorene (XII). Mixture of II (0.35 g, 2 mmol) and IIIe (0.26 g, 2 mmol) in ethanol (30 ml) was boiled for 1 h. The dark brown precipitate was filtered off, recrystallized from DMF, and dried first at 80°C and then in a vacuum desiccator over P₂O₅. Yield of XII 0.36 g (67%); mp 264-266°C. IR spectrum: 1698, 1654, 1607, 1582, 1573, 1535, 1522 cm⁻¹. PMR spectrum (DMSO-d₆): 4.24-4.62 (4H, m CH₂CH₂), 7.78-7.95 (4H, m, C₆H₄), 8.32 ppm (1H, s, =CH–). UV spectrum in CHCl₃, λ_{max} , nm (log ε): 256 (sh), 323 (4.07), 437 (4.56). Found, %: C 62.95; H 3.47; N 15.70. C₁₄H₉N₃. Calculated, %: C 62.92; H 3.39; N 15.72.

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