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# REACTION OF 1,2-DIAMINO-4-NITROBENZENE WITH 1,5-DIKETONES. SYNTHESIS AND OXIDATIVE REACTIONS OF NITROBENZIMIDAZOLES

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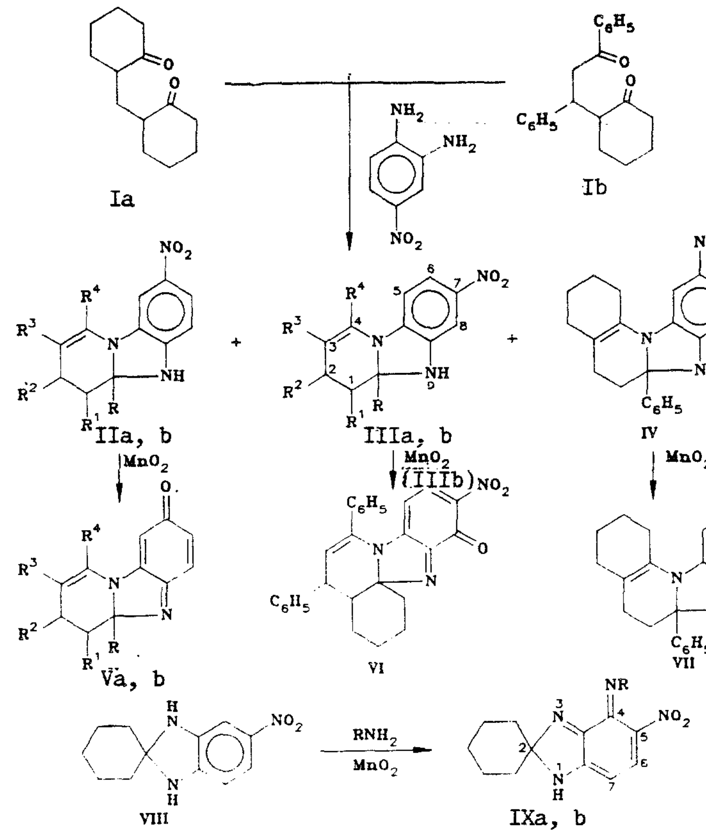
*Reaction of 1,5-diketones with 1,2-diamino-4-nitrobenzene gave a mixture of the 6- and 7-nitro derivatives of 4a,9-diaza-1,2,4a,9a-tetrahydrofluorene. Oxidation of the 6-nitro derivatives with $MnO_2$ gives para-quinone imines with elimination of the nitro groups. Oxidation of the 7-nitro derivative and oxidative conjugation of 5-nitro-2,2-pentamethylene-1,2-dihydrobenzimidazole with primary amines in the presence of $MnO_2$ gives nitro ortho-quinone imines.*

1,5-Diketones react readily with o-phenylenediamine to form 4*a*,9-diaza-1,2,4*a*,9*a*-tetrahydro-9H-fluorenes containing a 1,2,2-trisubstituted benzimidazole fragment [1]. In the presence of $MnO_2$ this is oxidized to para-quinoids [2-4]. The reaction



II, III, V a $R+R^1=R^3+R^4=(CH_2)_4$, $R^2=H$; b $R+R^1=(CH_2)_4$, $R^2=R^4=C_6H_5$, $R^3=H$;
IX a $R=cyclo\text{-}C_6H_{11}$; b R=4-(2,2,6,6-tetramethylpiperidyl)

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TABLE 1. Parameters for Compounds Synthesized

| Compound | Empirical formula | mp, °C | IR spectrum, ν, cm$^{-1}$ | | | PMR spectrum, ppm (spin-spin coupling constant, Hz)* | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | C=C enamine | NH | quinoid nucleus | 2-H | 3-H, d | 5-H, d | 6-H | 7-H | 8-H, d | HN br. s |
| IIa | $C_{19}H_{23}N_3O_2$ | 178 . . . 180 | 1665 | 3500 | — | — | — | 7,37 (2) | | 7,61 dd (8; 2) | 6,30 (8) | 5,15 |
| IIb | $C_{27}H_{25}N_3O_2$ | 226 . . . 228 | 1645 | 3434 | — | 3,66 dd (10; 3,5) | 5,40 (3,5) | 6,36** | | 7,62 dd (8; 2) | 6,36** | 5,17 |
| IIIa | $C_{19}H_{23}N_3O_2$ | 180 . . . 184 | 1677 | 3550 | — | — | — | 6,54 (8) | 7,65 dd (8; 2) | — | 7,23 (2) | 4,48 |
| IIIb | $C_{27}H_{25}N_3O_2$ | 204 . . . 207 | 1649 | 3420 | — | 3,64 dd (10,5; 3,5) | 5,45 (3,5) | 5,54 (8) | *** | — | *** | 4,56 |
| IV | $C_{27}H_{25}N_3O_2$ | 128 . . . 132 | 1654 | 3450 | — | — | — | *** | — | 7,12 dd (8; 2) | 6,28 (8) | 4,72 |
| VI | $C_{27}H_{25}N_3O_3$ | 220 . . . 222 | 1640 | — | 1670, 1570 | 4,01 dd (10; 3) | 5,82 (3) | 4,57 (9) | 8,40 d (9) | — | — | — |
| VII | $C_{27}H_{24}N_2O$ | 102 . . . 104 | 1660 | — | 1625, 1578, 1534 | 3,28 q (6) | — | 6,00 (1,5) | — | 6,63 dd (10; 1,5) | 7,12 (10) | — |
| IXa | $C_{18}H_{24}N_4O_2$ | 172 . . . 174 | — | 3200 | 1638, 1580, 1567 | — | — | — | 8,08 d (10) | 6,49 d (10) | — | 7,48 |
| IXb | $C_{21}H_{30}N_5O_2$ | 152 . . . 154 | — | 3300 | 1638, 1575, 1566 | — | — | — | 7,96 d (10) | 6,53 d (10) | — | 7,60 |

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*PMR spectra: IXa, 5.08 (1H, m, CH–N=); IXb, 1.22 (6H, s, $2CH_3$); 1.38 (6H, s, $2CH_3$); 5.87 ppm (1H, m, CH–N=).

**Signals for 5-H and 8-H give a two-proton multiplet.

***Obscured by the aromatic proton signals.

of 1,5-diketones with substituted o-phenylenediamines has not been investigated. The interest in analogous reactions is connected with their regiodirectionality and the effect of substituents on the oxidative reactivity of the compounds obtained.

We have studied the reaction of 1,2-diamino-4-nitrobenzene with the alicyclic diketone Ia and the half cyclic diketone Ib. The reaction occurs readily but not regioselectively with relation to the amino component and leads to mixtures of 6- and 7-nitro-4*a*,9-diaza-1,2,4*a*,9*a*-tetrahydrofluorenes.

The symmetrical diketone Ia gives the 6-nitro (IIa) and 7-nitro derivatives (IIIa) in the ratio 1:1.3. The nonsymmetric diketone Ib theoretically can give four diazahydrofluorenes. In practice, refluxing in xylene gives three of these, viz., the 6-nitro derivatives IIb and IV and the 7-nitro derivative IIIb in the ratio IIb:IIIb:IV = 1:1:0.7. Under milder conditions (refluxing in ethanol) virtually only IIb and IIIb (in approximately equal amounts) are formed with traces of IV. Thus, in this case, regioselectivity is observed with respect to the diketone although to a lower degree than that in the reaction of diketone Ib and analogs with unsubstituted o-phenylenediamine. Formation of IV type diazahydrofluorenes is not observed, probably because of their lower thermodynamic stability [1]. Observation of IV is probably explained by a significant decrease in the stability of the alternative IIb on account of the steric repulsion of the nitro group and the phenyl radical ($R^4$). At the same time, formation of a 7-nitro type IV compound was not observed (an alternative to IIIb in which analogous repulsion is absent).

Oxidation of the 6-nitro derivatives IIa, b and IV with $MnO_2$ leads to elimination of the nitro group and formation of the p-quinone monoimines Va, b (described earlier [2]) and VII. Upon oxidation of nitro derivative IIa, compound Va is only one of a complex mixture of products. If one carries out a combined oxidation of IIa and malononitrile in the presence of $MnO_2$ there is formed a mixture of only two compounds, viz., Va and the product of oxidative conjugation with malononitrile 6-dicyanomethylene-4*a*,9-diaza-1,2,4*a*,9*a*-tetrahydro-6H-fluorene (X) which has been described before [3]. Its formation also involves oxidative elimination of a nitro group. Oxidation of the 7-nitro derivative IIIa with $MnO_2$ gives a complex mixture of products but not including Va. At the same time, oxidation of IIIb forms VI in quantitative yield. In contrast to the products of oxidation of diazafluorenes not containing a nitro group [2], it is an o-quinone monoimine. A similar orienting effect of electron acceptors was noted [5] for the reaction of nucleophiles with 2H-benzimidazoles. For 5-arylsulfonyl-2H-benzimidazoles, nucleophilic attact is oriented to position 4 and not 6 as in the case of 2H-benzimidazoles not having electron-acceptor substituents in position 5.

With these data in mind we carried out conjugative oxidation of 5-nitro-2,2-pentamethylene-1,2-dihydrobenzimidazole VIII [6] with the primary amines cyclohexylamine and 4-amino-2,2,6,6-tetramethylpiperidine and obtained the corresponding quinone diimines. These were assigned the structures IXa, b (and not the amino 2H-benzimidazoles) by analogy with the products of treating 5-phenylsulfonyl-2,2-pentamethylene-2H-benzimidazole with primary amines [5]. We have previously studied the conjugative oxidation [4] of diazatetrahydrofluorenes (not containing a nitro group) with primary amines which led to formation of p-quinone diimines. Thus, in this series, introduction of a nitro group into the benzimidazole fragment changes the orientation of the oxidative conversion to the formation of ortho-quinonoid structures.

The structures of the synthesized compounds were confirmed by IR and PMR spectral data. In particular, the PMR spectra of the ortho-quinonoid compounds VI and IXa, b showed signals for the quinoid protons (5-H and 6-H in VI, 6-H and 7-H in IXa, b) as 10 Hz spin-coupled doublets. In the alternative para-isomers these signals occur as singlets. The PMR spectrum of the p-quinoid VII is analogous to the spectra of diazahydrofluorene p-quinone monoimines [2].

## EXPERIMENTAL

IR spectra were recorded on a Specord IR-75 instrument for $CHCl_3$ solutions, PMR spectra on a Bruker WM-250 in $CDCl_3$ with TMS internal standard, and mass spectra on an MX-1320 with direct sample introduction and an ionization intensity of 70 eV.

Elemental analytical data and molecular weights (mass spectrometric) agreed with those calculated. Parameters for the compounds synthesized are given in Table 1.

**Reaction of 1,5-Diketones with 1,2-Diamino-4-nitrobenzene. A.** A mixture of diamine (6.4 g, 0.04 mole), diketone Ia or Ib (0.04 mole), and p-toluenesulfonic acid (0.2 g) was refluxed in ethanol (150 ml) for 5 h (Ia) or 9 h (Ib). For Ia the ethanol was evaporated under reduced pressure, the residue chromatographed on a silica gel column (100/250, 150 g), eluting with hexane–ethyl acetate (3:1) to give IIIa (1.6 g), a mixture of IIa and IIIa (4.1 g), and IIa (1.8 g). The overall yield of IIa and IIIa was 7.5 g (59%). For compound Ib the reaction mixture was cooled, the precipitated solid filtered off, and the filtrate evaporated to one third volume and an additional amount of precipitate filtered off to give a mixture of IIb and IIIb (13.8 g, 82%). This mixture was chromatographed on a silica gel column (100/250, 300 g) eluting with hexane–ethyl acetate to give IIIb (1.3 g) and IIb (3.3 g).

**B.** A mixture of diketone Ib (12 g, 0.04 mole) the diamine (6.4 g, 0.04 mole), and p-toluene sulfonic acid (0.3 g) was refluxed in xylene (200 ml) for 5 h with a Dean and Stark trap. Xylene was evaporated under reduced pressure and the residue chromatographed on silica gel (100/250, 300 g) using hexane–ethyl acetate (ratio varying from 5:1 to 3:1) to give IIIb (1.3 g), a mixture of IIIb and IV (2.2 g), IV (1.1 g), a mixture of IV and IIb (1.4 g), and IIb (1.5 g). The overall yield of isomers IIb, IIIb, and IV was 7.5 g (45%). The isomer ratios in the mixtures were determined by PMR spectroscopy and the compounds were recrystallized from ethanol.

**Oxidation of Nitro Derivatives of 4*a*,9-Diaza-1,2,4*a*,9*a*-tetrahydrofluorene. A.** A tenfold excess of $MnO_2$ was added with stirring to a solution of the nitro derivatives (IIb, IIIb, IV, 0.2-0.5 g) in acetone (IIIb, IV) or benzene (IIb) (15-30 ml). The mixture was stirred for 2-4 h and the $MnO_2$ filtered off, washed on the filter with reaction solvent, and the combined filtrate evaporated to remove solvent. Quinone imines Vb, VI, VII were separated by preparative TLC on unbonded silica gel plates (100/160, 30 × 24 cm) in corresponding yields of 30 (eluent chloroform–ether 5:1), 71 (ether–hexane 2:1), and 15% (hexane–ethyl acetate, 1.5:1). Compound Vb was identified by mixed melting point with a known sample and by IR spectroscopy.

**B.** $\gamma$-$MnO_2$ (0.25 g, 3 mmoles) was added with stirring to a solution of IIa (0.1 g, 0.3 mmole) and malononitrile (0.05 g, 0.8 mmole) in acetone (10 ml) and stirred for 2 h. The products Va and X were identified in the reaction mixture by TLC in three systems: hexane–ethyl acetate (2:1), chloroform, and hexane–ether (1:1).

**Oxidative Conjugation of 5-Nitro-2,2-pentamethylene-1,2-dihydrobenzimidazole with Primary Amines.** $\gamma$-$MnO_2$ (2.5 g, 37 mmoles) was added with stirring to a solution of VIII (0.3 g, 1.3 mmoles) and the amine [0.3 g, cyclohexylamine (A) or 4-amino-2,2,6,6-tetramethylpiperidine (B)] in ethanol (15 ml) and stirred for 1 h. The $MnO_2$ was filtered off and washed on the filter with ethanol in case B and in ethanol and then acetone in case A. For A the acetone filtrate was evaporated, the ethanol diluted with water, and the precipitated solid filtered off. From both filtrates pure compound IXa was obtained (overall yield 78%). For B ethanol was distilled off under reduced pressure and the residue recrystallized from a mixture of benzene–hexane to give IXb in 77% yield.

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