

OXIDATIVE COUPLING OF 4a,9-DIAZA-1,2,4a,9a-TETRAHYDROFLUORENES.

1. SYNTHESIS OF MONONUCLEAR HETEROCYCLIC QUINONEDIIMINES

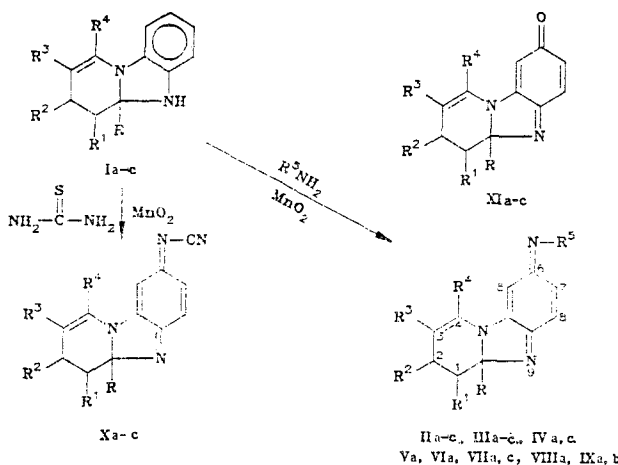
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UDC 547.567.5'781.3'678.3:541.634

Oxidative coupling of 4a,9-diaza-1,2,4a,9a-tetrahydro-9H-fluorene with primary amines and ammonia in the presence of MnO₂ gives the corresponding 6-aryl (or alkyl)imino-4a,9-diaza-1,2,4a,9a-tetrahydro-6H-fluorenes. Coupling with thiourea under these conditions affords 6-cyanoimino-4a,9-diaza-1,2,4a,9a-tetrahydro-6H-fluorenes.

4a,9-Diaza-1,2,4a,9a-tetrahydro-9H-fluorenes are readily oxidized by manganese dioxide to give polycyclic quinoneminoimines containing an enamine grouping attached to a quinoid structure [1]. It was of interest to obtain some new examples of the little-known enamino-quinonediimines, by oxidative coupling of the above-mentioned diazatetrahydrofluorenes with primary amines.

The formation of quinoneimines by oxidative coupling of aromatic amines with p-phenylenediamines and p-aminophenols is well known (for the synthesis of indamines and indophenols, see [2, p. 611]). Examples of the oxidative coupling of aromatic amines with other compounds containing a primary amino-group are much less frequent, and for the most part are concerned with the autocondensation of primary aromatic amines [3, 4]. The oxidatants usually employed are K₃Fe(CN)₆ and silver compounds. Manganese dioxide has not been used for this purpose.



I—XI a R+R¹=R³+R⁴=(CH₂)₄, R²=H; b R+R¹=(CH₂)₄, R²=R⁴=C₆H₅, R³=H;
 c R=R²=R⁴=C₆H₅, R¹=R³=H; II R⁵=C₆H₅, III R⁵=C₆H₄(COOH)-4, IV R⁵=C₆H₄SO₃H-4,
 V R⁵=C₆H₃(NO₂)₂-2,4, VI R⁵=C₆H₄(N=NC₆H₅)-4, VII R⁵=cyclo-C₆H₁₁, VIII R⁵=
 =4-(2,2,6,6-tetramethylpiperidyl), IX R⁵=H

We have examined the joint oxidation of the diazahydrofluorenes (Ia-c) and aromatic amines (aniline, 2,4-dinitroaniline, p-aminoazaobenzene, p-aminobenzoic acid, and sulfanilic acid), aliphatic amines (cyclohexylamine, 4-amino-2,2,6,6-tetramethylpiperidine), ammonia and thiourea, with manganese dioxide. The reaction with primary amines and ammonia gives the

Far Eastern State University, Vladivostok 690652. Translated from *Khimiya Geterotsiklicheskikh Soedinenii*, No. 11, pp. 1500-1504, November, 1989. Original article submitted February 2, 1988; revision submitted January 18, 1989.

TABLE 1. UV and IR Spectra of (II-X)

| Com- pound | λ_{\max} , nm (log ϵ) | IR spectrum, cm^{-1} | | | |
|---------------|--|---------------------------------|------|--------------|---------------------------|
| | | $\text{C}_{(3)}=\text{C}_{(4)}$ | C=N | C=C, quinone | others |
| IIa | 498 (4.17) | 1673 | 1634 | 1582, 1534 | — |
| IIb | 496 (4.06) | 1650 | 1631 | 1586, 1550 | — |
| IIc | 460 (4.15) | 1646 | 1630 | 1589, 1546 | — |
| IIIa | 506 (3.79) | 1672 | 1634 | 1580, 1520 | — |
| IIIb | 496 (4.06) | 1652 | 1634 | 1591, 1545 | 1705 (COOH) |
| IIIc | 466 (3.54) | 1643 | 1636 | 1587, 1523 | 1694 (COOH) |
| IVa | 542 (3.97) | 1634 | 1634 | 1565, 1508 | 3400 (SO ₂ OH) |
| IVc | 495 (3.87) | 1643 | 1635 | 1600, 1514 | 3388 (SO ₂ OH) |
| Va | 524 (4.08) | 1643 | 1630 | 1580, 1539 | 1338 (NO ₂) |
| VIa | 519 (4.23) | 1672 | 1634 | 1580, 1523 | — |
| VIIa | 466 (4.06) | 1671 | 1630 | 1588, 1527 | — |
| VIIc | 488 (4.01) | 1645 | 1636 | 1580, 1517 | — |
| VIIIa | 466 (4.21) | 1669 | 1631 | 1591, 1524 | — |
| IXa | 489 (3.58) | 1668 | 1632 | 1571, 1509 | 3300 (NH) |
| IXb | 445 (3.85) | 1649 | 1634 | 1596, 1530 | 3300 (NH) |
| Xa | 542 (4.05) | 1667 | 1631 | 1569, 1500 | 2172, 2155 (CN) |
| Xb | 518 (4.15) | 1651 | 1629 | 1574, 1520 | 2172 (CN) |
| Xc | 512 (4.02) | 1645 | 1629 | 1576, 1495 | 2175 (CN) |

mononuclear heterocyclic quinonediimines (II-IX) bearing the same substituent R⁵ as in the original amino-components; joint oxidation of (I) with thiourea results in the evolution of H₂S to give (X), which contain the N-cyanoimino-group.

N-Cyanoquinoneimines have recently been obtained [5] by condensation of quinones with bistrimethylsilylcarbodiimide in the presence of TiCl₄. A new method of introducing the N-cyanoimino-group into the quinoid structure has thus been found [6]. The reaction with phenylhydrazine and thiosemicarbazide is nonselective as a result of the rapid oxidation of these compounds by manganese dioxide, while acid amides and urea fail to react, apparently as a result of their low nucleophilicity, the products being the quinonemonoimines (XI). Joint oxidation of (I) and glycine gives the compounds (IX), probably as a result of the decomposition of the glycine by MnO₂ to acetaldehyde, CO₂, and ammonia [7], the latter also undergoing coupling.

The UV spectra of most of the quinonediimines (Table 1) show a bathochromic shift of the absorption maximum from the 2,4,9a-triphenyl compounds (c) to 2,4-diphenyl-1,9a-trimethylene compounds (b), then to the 1,9a,3,4-bistetramethylene derivatives (a). The introduction of a strong electron-acceptor group (N-cyanoimino or 2,4-dinitrophenyl) results in a marked bathochromic shift, while introduction of the azo-group (VIa) gives a moderate bathochromic shift as compared with (IIa).

In the IR spectra of the quinonediimines (Table 1), absorption for the C₍₃₎=C₍₄₎ enamine bonds, and for the quinoid C=N and C=C may be discerned. The absorption for the COOH carbonyl group is shifted to lower frequencies in the sequence (IIIc)-(IIIb)-(IIIa) (in the case of (IIIa), it overlaps the C₍₃₎=C₍₄₎ absorption), probably as a result of increased charge transfer, and consequently the donor effect on the COOH group in this sequence. The absorption for the CN group in the spectra of (X) corresponds to that reported for N-cyanoquinoneimines [5].

The structure of the signals for the 5-H, 7-H, and 8-H protons in the PMR spectra of the quinonediimines (Table 2) confirm the p-quinoid structure. In the ¹³C NMR spectrum of (Xa), the singlet signal for C₍₆₎ lies at 174.2 ppm, in accordance with the data for N-cyanoquinoneimines [5].

The mass spectral data for the molecular ions of all the quinonediimines (the spectrum of (IVa) could not be obtained as a result of its nonvolatility) corresponding to the calculated molecular masses. In most instances (part from (IIIc, IVc, VIIIa, and IXa), the molecular ion peak had the greatest intensity. In the spectra of compounds containing the 1,9a-tetramethylene group (a, b), peaks for the fragment [M - C₄H₉]⁺ were present, formed by elimination of this group, while the spectra of the 2,4,9a-triphenyl derivatives (c) did not show this peak, but a new, quite intense peak for the ion [M - C₆H₅]⁺ appeared, probably formed by cleavage of the angular phenyl group. In the mass spectra of the carboxy- (III)

TABLE 2. PMR Spectral Data for (II-X)

| Com- pound | Chemical shift, ppm (coupling const., Hz) | | | | | | Harom |
|---------------|---|--------------|--------------|-----------------------|---------------|---|-------|
| | 2-H | 3-H | 5-H | 7-H | 8-H, d (J=10) | | |
| IIa | 2.72 m | — | 5.60 s | —* | —* | 6.80...7.38 m | |
| IIb | 3.82 d, d (10; 3) | 5.40 d (3,0) | 4.59 d (2,0) | —* | —* | 6.59 (1H, d, 7.5); 6.92...7.45 m | |
| IIc | 3.36 q, d (12,00; 6,0; 2,5) | 5.40 d (2,5) | 4.80 d (1,8) | —* | —* | 6.60 (1H, d, 7.5); 6.90...7.50 m | |
| IIIa | 2.75 m | — | 5.65 s | 7.10 d (10,0) | 7.27 | 7.05 (2H, d 8,0); 8.10 (2H, d 8,0) | |
| IIIb | 3.85 d, d (10,0; 3,0) | 5.30 d (3,0) | 4.30 d (2,0) | —* | —* | 6.90...7.45 m | |
| IIIc | —** | 5.35 br. s | 4.46 s | 6.90 d (10,0) | 7.06 | 7.12...7.78 m | |
| IVa | —*** | — | 6.02 s | 7.29 d (10,0) | 7.37 | 6.88 (2H, d, 8-H); 7.78 (2H, d 8,0) | |
| Va | —*** | — | 5.34 d (2,0) | 6.97 d, d (10,0; 2,0) | 7.12 | 7.06 (1H, d, 9,0); 8.33 (1H, d, d ; 9,0; 2,5); 8.90 (1H, d 2,5) | |
| Vb | —*** | — | 5.70 s (1,5) | 7.47 d (10,0) | 7.49 | 7.10...7.40 m; 7.93 m | |
| VIIa | 2.6 m | — | 5.75 d (1,5) | 6.79 d, d (10,0; 1,5) | 6.88 | — | |
| VIIc | 3.48 m | 5.87 d (2,0) | 4.90 s | —* | 7.42 | 7.26...7.77 m | |
| VIIIa | 2.60 m | — | 5.81 s (1,5) | 6.80 d (10,0) | 6.89 | — | |
| IXa | 2.78 m | — | 6.36 d (2,0) | 7.52 d, d (10,0; 1,5) | 7.18 | — | |
| IXb | 3.89 d, d (10,0; 3,0) | 5.72 d (3,0) | 5.26 d (2,0) | 7.31 d, d (10,0; 2,0) | 7.82 | — | |
| Xa | 2.78 m | — | 6.38 d (2,0) | 6.85 d, d (10,0; 2,0) | 7.14 | — | |
| Xb | 3.82 d, d (10,0; 3,0) | 5.34 d (3,0) | 4.59 d (2,0) | —* | —* | 6.59 (1H, d, 7,5); 6.92...7.45 m | |
| Xc | 3.48 q, d (12,0; 6,0; 2,5) | 5.70 d (2,5) | 5.46 d (2,0) | 6.84 d, d (10,0; 2,0) | 7.19 | 7.23...7.73 m | |

*Overlaps the aromatic proton signals.

**Overlaps the DMSO signal.

***Overlaps the signals for the other aliphatic protons.

TABLE 3. Synthesis Conditions and Properties of Quinonedimines (II-X)

| Compound oxidized | Molar ratio of compounds oxidized | MnO ₂ modification | Solvent | Reaction time, h | Compound obtained | Empirical formula | mp, °C | Yield, % |
|--|-----------------------------------|-------------------------------|--------------|------------------|-------------------|---|----------------|----------|
| Ia+aniline | 1:3 | γ-MnO ₂ | Benzene | 1.5 | IIa | C ₂₅ H ₂₇ N ₃ | 191...193 | 98 |
| Ib+aniline | 1:1.5 | γ-MnO ₂ | Benzene | 1.0 | IIb | C ₃₃ H ₂₉ N ₃ | 205...207 | 89 |
| Ic+aniline | 1:1.5 | γ-MnO ₂ | Benzene | 2.0 | IIc | C ₃₅ H ₂₇ N ₃ | 212...213 | 100 |
| Ia+p-aminobenzoic acid | 1:2 | MnO ₂ inact | Ethanol | 0.5 | IIIa | C ₂₆ H ₂₇ N ₃ O ₂ | <360 (decomp.) | 62 |
| Ib+p-aminobenzoic acid | 1:1.5 | γ-MnO ₂ | Ethanol | 3.0 | IIIb | C ₃₄ H ₂₉ N ₃ O ₂ | <205 (decomp.) | 94 |
| Ic+p-aminobenzoic acid | 1:3 | γ-MnO ₂ | Ethanol | 1.5 | IIIc | C ₃₆ H ₂₇ N ₃ O ₂ | 234...235 | 86 |
| Ia+sulfanilic acid | 1:2 | MnO ₂ inact | Ethanol | 2.0 | IVa | C ₂₅ H ₂₇ N ₃ O ₃ S | <360 (decomp.) | 87 |
| Ic+sulfanilic acid | 1:2 | γ-MnO ₂ | Ethanol | 4.0 | IVc | C ₃₅ H ₂₇ N ₃ O ₃ S | <360 (decomp.) | 70 |
| Ia+2,4-dinitroaniline | 1:2 | MnO ₂ inact | Acetonitrile | 1.5 | Va | C ₂₅ H ₂₅ N ₅ O ₄ | 199...200 | 84 |
| Ia+p-aminoazobenzene | 1:1.5 | MnO ₂ inact | Benzene | 1.0 | VIa | C ₃₁ H ₃₁ N ₅ | 165 (decomp.) | 100 |
| Ia+cyclohexylamine | 1:2 | MnO ₂ inact | Ethanol | 2.0 | VIIa | C ₂₅ H ₃₃ N ₃ | 179...180 | 93 |
| Ic+cyclohexylamine | 1:2 | γ-MnO ₂ | Ethanol | 3.0 | VIIc | C ₃₅ H ₃₅ N ₃ | 172...174 | 72 |
| Ia+4-amino-2,2,6,6-tetramethylpiperidine | 1:2 | γ-MnO ₂ | Ethanol | 1.0 | VIIIa | C ₂₃ H ₄₀ N ₄ | 185...187 | 84 |
| Ia+ammonia | 1:10 | MnO ₂ inact | Ethanol | 2.0 | IXa | C ₁₉ H ₂₃ N ₃ | <360 (decomp.) | 67 |
| Ib+ammonia | 1:10 | γ-MnO ₂ | Ethanol | 4.0 | IXb | C ₂₇ H ₂₅ N ₃ | <150 (decomp.) | 57 |
| Ia+thiourea | 1:5 | γ-MnO ₂ | Ethanol | 4.0 | Xa | C ₂₀ H ₂₂ N ₄ | 212...213 | 80 |
| Ib+thiourea | 1:1.5 | γ-MnO ₂ | Ethanol | 4.0 | Xb | C ₂₈ H ₂₄ N ₄ | 239...241 | 95 |
| Ic+thiourea | 1:2.5 | γ-MnO ₂ | Ethanol | 7.0 | Xc | C ₃₀ H ₂₂ N ₄ | 173...174 | 42 |

and sulfo- (IV) derivatives, peaks were present for ions corresponding to fragmentation of the COOH and SO₃H groups. In the spectrum of (VIIIa), the strongest peak was that for the ion [M - CH₃]⁺.

In two instances, the spectral data indicate the coexistence of the syn- and anti-forms of the quinonediimines. In the PMR spectrum of (IIa), two signals are present for the 5a-H proton, at 5.60 and 5.97 ppm with an intensity ratio of 6:1, which we attribute to the anti- and syn-forms of this compound respectively, since the syn-isomer is sterically hindered. The location of the signal for the 5-H proton at lower field in the syn-form is probably due to the descreening of this proton by the syn-phenyl group; in such a case, this group should be coplanar with the quinoid ring. In the IR spectrum of (Xa), two bands are present for the CN group which are also clearly due to the presence of two stereoisomeric forms. However, the PMR spectrum of this compound did not show doubling of any of the signals for the quinoid protons (5-H, 7-H, and 8-H). There is clearly a rapid interchange between the two stereoisomeric forms, similar examples having been reported with N-cyanoquinoneimines [5].

EXPERIMENTAL

UV spectra were obtained on a Perkin-Elmer instrument, in chloroform, or in the case of (IIIa, b) in ethanol, IR spectra on a Specord IR-75 in chloroform and vaseline grease, and NMR spectra on a Bruker WM-250 (250 MHz) in CDCl₃ or DMSO-d₆, internal standard TMS. Mass spectra were obtained on an LKB-9000 instrument, ionizing voltage 70 eV, with direct sample introduction. The progress of the reactions and the purity of the products were checked by TLC on Silufol plates. The element analyses for (II-X) (C, H, and N) were in agreement with the calculated values.

9a-R-1-R¹-2-R²-3-R³-4-R⁴-6-Aryl(alkyl, or cyano)imino-4a,9-diaza-1,2,4a,9a-tetrahydro-6H-fluorenes (II-X) (Table 3). To a solution of the appropriate (I) (0.5-1.0 g) and the amino-component in 15-30 ml of solvent was added rapidly with stirring MnO₂ (I:MnO₂ = 1:15). The mixture was stirred at room temperature until all the (I) had reacted (TLC), the MnO₂ filtered off, and washed on the filter until the wash liquid was only faintly colored. In the synthesis of (IIIb) and (IIIc), washing was carried out with 3% NaOH, in the case of (VIIa, b), (VIIIa), and (IXa) with 5% HCl, and in the remaining cases, with the same solvent as that used in the reaction. Impurities were extracted from the basic and acidic solutions with ether, then the acidic extracts were basified with Na₂CO₃, and the basic extracts acidified with acetic acid, the reaction products being extracted with ether (or in the case of (IIIb, c), with chloroform). The solvent was usually removed at reduced pressure, except that in the case of (IXa) the ether was removed at room temperature as a result of the thermal instability of this compound. When isolating (IIIa), (Va), (VIc), and (Xa, c) the residue after removal of the solvent was chromatographed on silica gel, eluent hexane-ether; in the cases of (Va) and (VIc), in addition to the quinonediimines, the quinonemonoimines (XIa) and (XIc) were isolated in yields of 9 and 19% respectively. In the isolation of the remaining quinonediimines, the residue after removal of the solvent consisted of the almost pure product. The quinonediimines were obtained as crystalline solids, most of which were soluble in ethanol, acetone, chloroform, and DMSO, less so in ether, and sparingly soluble in hexane. Compounds (IIa, b) and (Xb, c) were recrystallized from a mixture of benzene and hexane, (IIc), (IIIa), (IVc), (Va), and (VIIa) from a mixture of acetone and hexane, (IIIc) and (IVa) from a mixture of ethanol and DMF, (VIa) and (Xa) from a mixture of ether and hexane, (IIIb) from a mixture of chloroform and hexane, and (VIIIa) from hexane. Compounds (VIc) and (IXa, b) could not be recrystallized..

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