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NAPHTHINDOLES. 2*. NAPHTHO[2,3-e]INDOLE-4,9-DIONES AND NAPHTHO[2,3-f]INDOLE-5,10-DIONES

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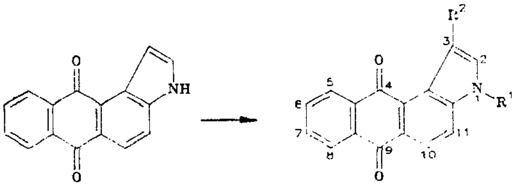
UDC 547.759.3'655.1.07

The reactivity of naphtho[2,3-e]indole-4,9-dione and naphtho[2,3-f]indole-5,10-dione towards electrophiles (acylation, azocoupling, and the Mannich and Vilsmeier reactions) has been examined.

In order to assess the reactivity of the previously-synthesized naphtho[2,3-e]indole-4,9-dione (I) and naphtho[2,3-f]indole-5,10-dione (II) [1], we have examined some electrophilic substitution reactions characteristic of indoles, namely acylation, azocoupling, and the Vilsmeier and Mannich reactions. A qualitative comparison of the physicochemical properties of (I) and (II) with indole and some electron-deficient tetracyclic pyrroles such as 3H-pyrrolo[2,3-c]acridine and 3H-pyrrolo[2,3-c]phenothiazine-11,11-dioxide has also been carried out.

The Vilsmeier reaction of (I) and (II) with N,N-dimethylformamide gives 3-formylnaphtho[2,3-e]indole-4,9-dione (III) and 3-formylnaphtho[2,3-f]indole-5,10-dione (IV) in lower yields (70%) than in the case of indole, but somewhat higher than in the case of pyrroloacridine and pyrrolophenothiazine dioxide [3, 4]. Aminomethylation of (I) and (II) with the crystalline Mannich reagent [5] in DMF at 75°C gives 3-N,N-dimethylaminomethylnaphtho[2,3-e]indole-4,9-dione (V) hydrochloride and 3-N,N-dimethylaminomethylnaphtho[2,3-f]indole-5,10-dione (VI) hydrochloride.



I

III, V, VII, IX, XI

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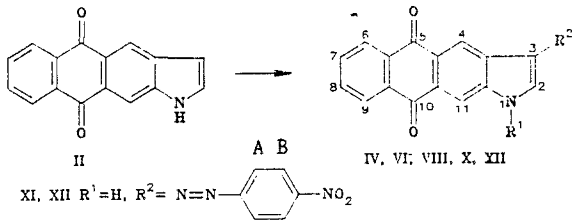
*For communication 1, see [1].

D. I. Mendeleev Institute for Chemical Technology, Moscow 115047. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 783-786, June, 1989. Original article submitted December 25, 1987.

0009-3122/89/2506-0646 $12.50



II

IV, VI; VIII, X, XII

XI, XII R^1=H, R^2= N=N–C_6H_4–NO_2

III, IV R^1=H, R^2=COH; V, VI R^1=H, R^2=$CH_2N(CH_3)_2$; VII R^1=R^2=$COCH_3$; VIII R^1=H. R^2=$COCH_3$; IX, X R^1=$COCH_3$, R^2=H

Examination of the behavior of (I) and (II) in Friedel–Crafts reactions showed that unlike indole, which undergoes resinification in the presence of Lewis acids, naphthoindolediones, like pyrrolophenothiazine dioxide [4], react readily. Acetylation with acetyl chloride in dichloroethane in the presence of anhydrous $AlCl_3$ gave 1,3-diacetylnaphtho[2,3-e]indole-4,9-dione (VII) and 3-acetylnaphtho[2,3-f]indole-5,10-dione (VIII). Acetylation on of (I) and (II) with acetic anhydride under the conditions described for indole afforded 1-acetylnaphtho[2,3-e]indole-4,9-dione (IX) and 1-acetylnaphtho[2,3-f]indole-5,10-dione (X) in yields of 42 and 50% respectively. Acetylation of indole under similar conditions gives a mixture of mono- and diacetyl compounds [6], but pyrroloacridine and pyrrolophenothiazine dioxide give quantitative yields of the monoacetyl derivatives [3, 4]. Vilsmeier acetylation with the N,N-dimethylacetamide–phosphoryl chloride complex did not take place, apparently as a result of the lower electrophilicity of the complex.

Azocoupling of the naphthoindolediones (I) and (II) with p-nitrobenzenediazonium chloride was carried out in aqueous dioxane at pH 6. The diazonium salt and the naphthoindoledione were reacted in proportions of 4:1. The yields of the angular (XI) and linear (XII) azocompounds were 64 and 38% respectively.

All the reaction products were identified by their PMR spectra by the absence of signals for the 3-H proton, and the presence of signals for the appropriate substituent. The electronic (and in many cases the anisotropic) effects of the substituents resulted in a low-field shift of the signals for the adjacent protons. The PMR spectral parameters for (I-VIII), (X), and (XI) in DMSO-D_6, for (IX) in acetone-D_6, and for (XII) in DMF-D_7 are given in Table 1. The chemical shifts of the benzene ring protons of the naphthomoiety (ABCD system) were seen at 7.8-8.3 ppm.

The IR spectra of (VII), (IX), and (X) showed no absorption for NH stretching vibrations, indicating the presence of a substituent at nitrogen. The appearance of additional absorption at 1640 cm^{-1} for (III) and (IV) is due to C=O stretching vibrations of the formyl group, and at 1730 cm^{-1} for (VIII) to stretching vibration of the acetyl C=O group.

EXPERIMENTAL

IR spectra were obtained on a UR-20 instrument in Vaseline grease. PMR spectra were recorded on a Bruker WP-200 SY, internal standard TMS. Mass spectra were obtained on a Varian MAT-311A, ionizing voltage 70 eV, cathode emission current 1 mA, accelerating voltage 3 kV. The evaporator temperature for the samples was programmed linearly from 30 to 300°C. The progress of the reactions was followed and the purity of the products checked by TLC on plates with bound layers of Silufol UV-254 silica gel. Preparative chromatography was carried out on silica gel, L 40/100 grade. The elemental analyses for C, H, and N were in agreement with the calculated values.

3-Formylnaphtho[2,3-e]indole-4,9-dione (III, $C_{17}H_9NO_3$). To 0.62 ml (8 mmole) of freshly-distilled DMF was added at -5°C with stirring 0.2 ml (2 mmole) of $POCl_3$. The resulting complex was stirred for 1 h at room temperature, cooled to -5°C, and a solution of 0.25 g (1 mmole) of (I) in 2 ml of DMF added. The mixture ws held for 1 h at 75°C, poured on to ice, and 10% KOH added to pH 7. The solid was filtered off, washed with water, and dried to give 0.20 g (71%) of product, mp 315°C (from ethyl acetate). IR spectrum: 1640, 1680 (C=O), 3180 cm^{-1} (N–H). Found: M 275. Calculated: M 275.

3-Formylnaphtho[2,3-f]indole-5,10-dione (IV, $C_{17}H_9NO_3$) was obtained as for (III). Yield 0.19 g (68%), mp 378°C (from alcohol). IR spectrum: 1640, 1680 (C=O), 3350 cm^{-1} (NH). Found: M 275. Calculated: M 275.

TABLE 1. Chemical Shifts and Coupling Constants in the PMR Spectra of (I-XII)

Compound	1-R	2-H	3-R	4-H	10-H	11-H	J, Hz
I	11,72 (1H, br.s)	7,72 (1H, d.d)	7,47 (1H, d.d)	—	8,03 (1H, d)	7,85 (1H, d)	$J_{1,2}=1,93$; $J_{2,3}=2,92$; $J_{1,3}=1,92$; $J_{10,11}=8,77$
II	11,86 (1H, br.s)	7,73 (1H, d.d)	6,81 (1H, d, d)	8,51 (1H, s)	—	8,29 (1H, s)	$J_{1,2}=2,50$; $J_{2,3}=3,29$; $J_{1,3}=1,83$
III	*	8,36 (1H, s)	10,77 (1H, s)	—	8,17 (1H, d)	8,01 (1H, d)	$J_{10,11}=8,04$
IV	*	8,98 (1H, s)	10,09 (1H, s)	8,57 (1H, s)	—	8,35 (1H, s)	—
V	12,49 (1H, br.s)	8,04 (1H, s)	4,78 (2H, s); 2,87 (6H, s)	—	8,15 (1H, d)	8,00 (1H, d)	$J_{10,11}=8,41$
VI	12,28 (1H, br.s)	8,01 (1H, s)	4,51 (2H, s); 2,73 (6H, s)	8,34 (1H, s)	—	8,75 (1H, s)	—
VII	2,77 (3H, s)	8,60 (1H, s)	2,50 (3H, s)	—	8,30 (1H, d)	8,85 (1H, d)	$J_{10,11}=8,77$
VIII	12,72 (1H, br s)	8,70 (1H, d)	2,54 (3H, s)	9,06 (1H, s)	—	8,29 (1H, s)	$J_{1,2}=2,19$
IX	2,75 (3H, s)	8,25 (1H, d)	7,70 (1H, s)	—	~8,3	8,82 (1H, d)	$J_{2,3}=3,66$; $J_{10,11}=8,77$
X	2,74 (3H, s)	8,18 (1H, d)	7,04 (1H, d.d)	8,51 (1H, s)	—	9,16 (1H, d)	$J_{2,3}=3,84$
XI	*	8,35 (1H, s)	8,05 (2H, d) (A); 8,42 (2H, d) (B)	—	8,20 (1H, d)	8,00 (1H, d)	$J_{10,11}=8,40$; $J_{AB}=9,14$
XII	*	8,49 (1H, s)	8,12 (2H, d) (A); 8,45 (2H, d) (B)	9,34 (1H, s)	—	8,81 (1H, s)	$J_{AB}=9,14$

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*No signal seen as a result of NH → ND exchange.

3-Dimethylaminomethylnaphtho[2,3-e]indole-4,9-dione Hydrochloride (V, $C_{19}H_{17}ClN_2O_2$. To 0.2 g (0.8 mmole) of (I), dissolved in 10 ml of DMF, was added 0.2 g (2.2 mmole) of the crystalline Mannich reagent, and the mixture stirred for 3 h at 75°C. The solid which separated was filtered off, washed with alcohol, and dried to give 0.23 g (84%) of product, mp 275°C (from alcohol). IR spectrum: 1670 (C=O), 3180 cm^{-1} (N—H). Found: M 304. Calculated: M 304

3-Dimethylaminomethylnaphtho[2,3-f]indole-5,10-dione Hydrochloride (VI, $C_{19}H_{17}ClN_2O_2$) was obtained as for (V), yield 0.27 g (88%), mp 288°C (from alcohol). IR spectrum: 1670 (C=O), 3230 cm^{-1} (N—H). Found: M 304. Calculated: M 304.

1,3-Diacetylnaphtho[3,2-e]indole-4,9-dione (VII, $C_{18}H_{11}NO_4$). To 0.4 g (3 mmole) of anhydrous $AlCl_3$ in 5 ml of dichloroethane was added 0.25 ml (3 mmole) of acetyl chloride at 0°C, the mixture stirred for 30 min, and 0.12 g (0.5 mmole) of (I) in 40 ml of dichloroethane added at 5°C. The mixture was stirred for 1 h at 40°C, poured into 150 ml of cold water, and the product filtered off, washed with water, and dried. Yield 0.07 g (44%), mp 252°C (from alcohol). IR spectrum: 1690, 1730 cm^{-1} (C=O). Found: M 331. Calculated: M 331.

3-Acetylnaphtho[2,3-f]indole-5,10-dione (VIII, $C_{18}H_{11}NO_3$) was obtained as for (VII). Yield 0.11 g (79%), mp 360°C (from alcohol; decomp.). IR spectrum: 1680 (C=O), 3220 cm^{-1} (N—H). Found: M 289. Calculated: M 289.

1-Acetylnaphtho[2,3-e]indole-4,9-dione (IX, $C_{18}H_{11}NO_3$). A mixture of 0.1 g (0.4 mmole) of (I) and 5 ml of acetic anhydride was boiled for 15 h. The acetic anhydride was then distilled off under reduced pressure, and the resulting (IX) purified by chromatography (silica gel L 40/100, benzene—acetone (9:1)). Yield 0.05 g (42%), mp 272°C (from alcohol). IR spectrum: 1680, 1730 cm^{-1} (C=O). Found: M 289. Calculated: M 289.

1-Acetylnaphtho[2,3-f]indol-5, 10-dione (X, $C_{18}H_{11}NO_3$) was obtained as for (IX). Yield 0.06 g (50%), mp 248°C (from alcohol). IR spectrum: 1680, 1715 cm^{-1} (C=O). Found: M 289. Calculated: M 289.

3-(4'-Nitrophenylazo)naphtho[2,3-e]indole-4,9-dione (XI, $C_{22}H_{12}N_4O_4$). To a solution of 0.5 g (2 mmole) of (I) in 100 ml of 1,4-dioxane and 10 ml of water was added at 0°C 8 mmole of p-nitrophenyldiazonium chloride, maintaining the pH of the solution at 6 by adding sodium acetate. The mixture was stirred for 8 h, filtered, the solid washed with water until neutral, and dried. Yield 0.51 g (64%), mp 276°C (from dioxane; decomp.). IR spectrum: 1680 (C=O), 3290 cm^{-1} (N—H).

3-(4'-Nitrophenylazo)naphtho[2,3-f]indole-5,10-dione (XII, $C_{22}H_{12}N_4O_4$) was obtained as for (XI). Yield 0.3 g (38%), mp 361°C (from dioxane; decomp.). IR spectrum: 1680 (C=O), 3360 cm^{-1} (N—H).

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