14*H*-Naphtho[1',2':5,6]pyrano[2,3-*b*]quinoline Derivatives

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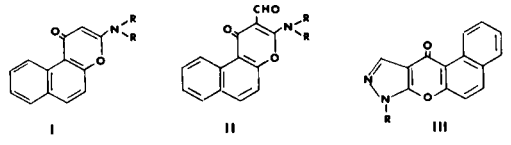
Reaction of (*N*-alkyl-*N*-phenyl)ethoxycarbonylacetamides with β-naphthol in the presence of phosphorus oxychloride afforded 1-oxo-3-(*N*-alkyl-*N*-phenyl)amino-1*H*-naphtho[2,1-*b*]pyrans. These compounds underwent reaction with *N*,*N*-dimethylformamide-phosphorus oxychloride at 95° yielding a mixture of 14*H*-naphtho[1',2':5,6]pyrano[2,3-*b*]quinoline derivatives and 1-oxo-2-formyl-3-(*N*-alkyl-*N*-phenyl)amino-9-oxy-1*H*-phenalene. When the same reaction was performed at 140°, only 14-oxo-14*H*-naphtho[1',2':5,6]pyrano[2,3-*b*]quinoline was obtained in a very good yield. The structures of such compounds were demonstrated by spectral data and by chemical transformations. On the other hand, the expected formylation in the 2 position was achieved when 1-oxo-3-(*N*-alkyl-*N*-benzyl)amino-1H-naphtho[2,1-*b*]pyrans reacted with *N*,*N*-dimethylformamide-phosphorus oxychloride.

In some previous papers, the synthesis of 1-oxo-3-dialkylamino-1*H*-naphtho[2,1-*b*]pyrans (I) and their chemical and pharmacological behavior have been described (1-7); the anticonvulsant, sedative or CNS depressant activities of some compounds I and of their 2-dialkylaminomethyl derivatives have been reported (3,4,6,7).

Moreover, reaction of compounds I with *N*,*N*-dimethylformamide in the presence of phosphorus oxychloride afforded the corresponding 2-formyl derivatives II which were useful intermediates for the synthesis of naphtho-[1',2':5,6]pyrano[2,3-*c*]pyrazole (8) derivatives III by treatment with hydrazine or monosubstituted hydrazines (9).

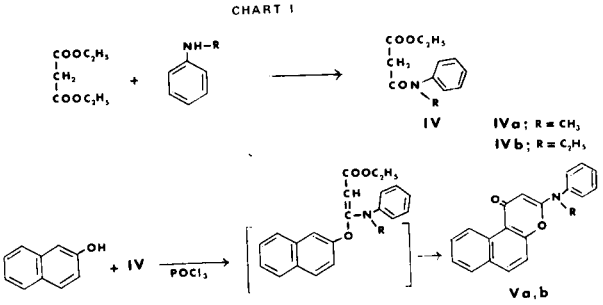


I II III

On continuing studies on the Vilsmeier-Haack reaction applied to compounds I, the reaction of *N*,*N*-dimethylformamide-phosphorus oxychloride with such compounds in which the substituent in position 3 was (*N*-alkyl-*N*-phenyl)amino (structure V) has now been investigated. Actually, the favourable position of the *N*-phenyl group in these compounds makes it available to be involved in the reaction, as it occurs, for instance, in the case of *N*-phenylanthranilic acids or their amides to afford acridines (10).

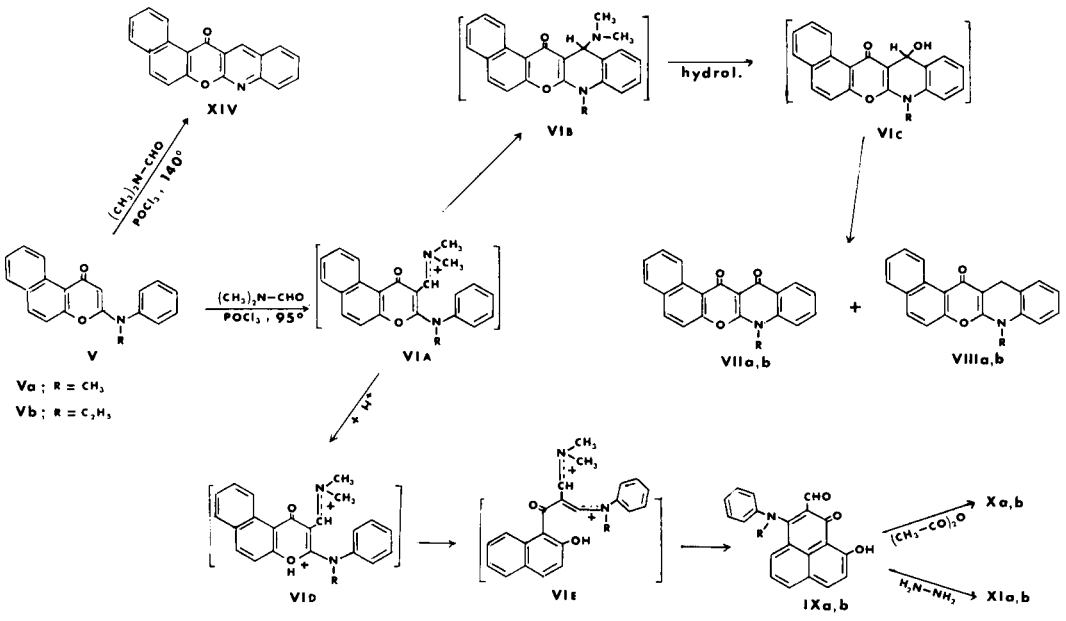
Therefore, the 1-oxo-3-(*N*-alkyl-*N*-phenyl)amino-1*H*-naphtho[2,1-*b*]pyrans (V) which were required were synthesized by condensations of (*N*-alkyl-*N*-phenyl)ethoxycarbonylacetamides (IV) with β-naphthol in the presence of phosphorus oxychloride, following a previously described procedure (1,2,3,6). Amide esters IV were prepared by reaction of *N*-alkylanilines with ethyl malonate (Chart I).

CHART I



When compounds V were treated with *N*,*N*-dimethylformamide-phosphorus oxychloride at 95°, no type II derivatives were formed. Instead, reaction occurred with the formation of products whose structure, elucidated by ir, nmr and mass spectra and by chemical transformations, demonstrated the important role of the *N*-phenyl group in this connection. Actually, the material obtained from the reaction was shown to be a mixture of 8-alkyl-13,14-dioxo-8*H*,13*H*,14*H*-naphtho[1',2':5,6]pyrano[2,3-*b*]-quinoline (VII), 8-alkyl-14-oxo-8*H*,13*H*,14*H*-naphtho-[1',2':5,6]pyrano[2,3-*b*]quinoline (VIII) and 1-oxo-2-formyl-3-(*N*-alkyl-*N*-phenyl)amino-9-oxy-1*H*-phenalene (IX). The formation of such compounds may be depicted in the following reaction pattern (Chart II).

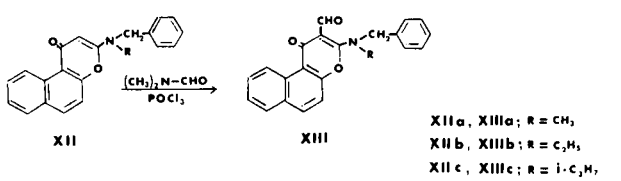
CHART II



Arising from the hydrolysis of the postulated intermediate VIB, which was formed by attack of the *N,N*-dimethylformamide-phosphorus oxychloride reactant in both the 2-position of the naphtho[2,1-*b*]pyran system and an *ortho* position of the *N*-phenyl group, the intermediate VIC disproportionated to a mixture of compounds VII and VIII. In a like manner, in the reaction of acridine with dimethyl sulfate and potassium hydroxide, intermediate 10-methyl-9-hydroxyacridan is reported to lead to the formation of 10-methyl-9-acridanone and 10-methylacridan (11,12).

On the other hand, single attack in the 2 position and γ-pyrone ring opening (VIE) followed by recyclization in the *peri* position, gave rise to the rearrangement into 1*H*-phenalene ring system derivatives (IX).

In this connection, ring opening, in the protonated intermediate VID, may be attributed to the electron withdrawing effect of the phenyl group, since a similar bulky 3-substituting group such as (*N*-alkyl-*N*-benzyl)-amino [compounds XII (3)], allowed the formation of the corresponding formyl derivatives XIII in very good yields.



No derivative of the naphtho[1′,2′:5,6]pyrano[2,3-*b*]-quinoline heterocyclic system is reported in the literature; only a few 8*H*-naphtho[1′,2′:5,6]pyrano[4,3-*b*]quinoline and 6*H*-naphtho[2′,1′:5,6]pyrano[4,3-*b*]quinoline derivatives are described (13).

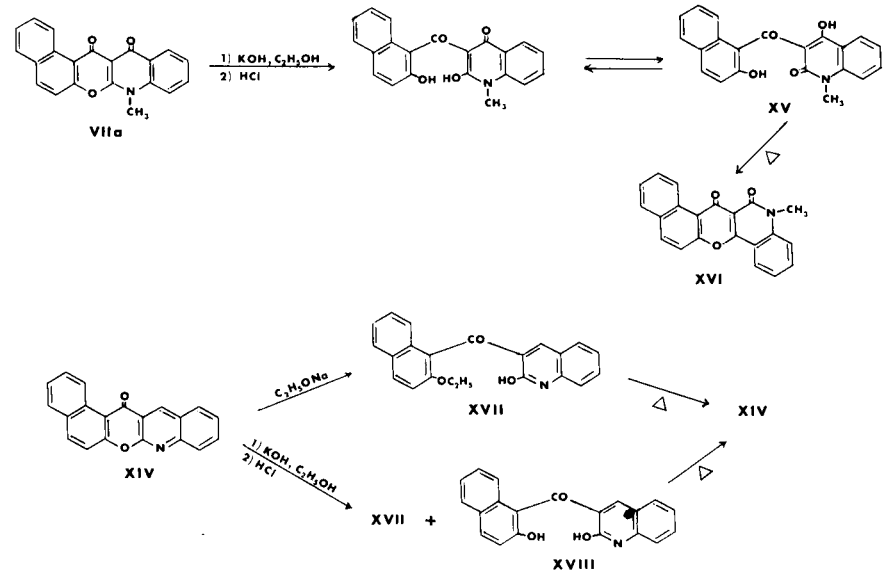
Compounds VII were white crystalline products whose elemental analyses, ir and nmr spectral data supported the proposed structure; the downfield H-1 signal [deshielding effect of 14-CO (14,1,2,3)], in nmr spectra, was a confirmatory evidence that the naphtho[2,1-*b*]-pyran moiety remained in the molecular constitution of VII. Moreover, the mass spectrum of VIIa showed the expected and molecular and fragment ions.

Chemical support for the structure VII was obtained by treating VIIa with alcoholic potassium hydroxide to afford 1,2-dihydro-1-methyl-2-oxo-3-(2′-oxy-1′-naphthoyl)-4-oxyquinoline (XV) which arose by γ-pyrone ring opening. This compound was yellow colored, easily soluble in dilute aqueous sodium hydroxide and insoluble in dilute hydrochloric acid.

Attempted crystallization of XV led to the formation of white crystalline 12,13-dihydro-12-methyl-13,14-dioxo-14*H*-naphtho[1′,2′:5,6]pyrano[3,2-*c*]quinoline (XVI) through the cyclization process depicted in Chart III.

Elemental analyses, ir and nmr spectral data were consistent with the proposed structures of the compounds XV and XVI. In particular, the nmr spectrum of XV no longer showed downfield signals [slight influence of

CHART III



side chain carbonyl group on the *peri* hydrogen (14)], whereas H-1 signal (τ = 0.30) appeared again in the spectrum of XVI (deshielding effect of 14-CO).

Facile loss of water and transformation into XVI occurred when XV was submitted to the melting point determination (see Experimental). In this connection, by elimination of water on vaporizing the sample, the mass spectrum of XV was identical with that of XVI.

The structure of the pale yellow crystalline compounds VIII was deduced from elemental analyses, ir, nmr and mass spectral data. Particularly, the nmr spectra showed signals for the 8-substituent and the heterocyclic system protons, among which were the downfield H-1 signal (deshielding effect of 14-CO) and the 13-CH_2 signal (singlet, relative intensity 2).

Confirmatory evidences of the structure of the compounds IX were yellow color and solubility in dilute aqueous sodium hydroxide due to the presence of a phenolic group, as well as elemental analyses, ir, nmr and mass spectral data. Actually, treatment of IX with acetic anhydride led to the formation of acetyl derivatives X; moreover, the easy formation of hydrazones XI supported the presence of a formyl group, since reaction of 1-oxo-1*H*-phenalene with usual ketone reagents is reported to be difficult (15).

Ir spectra of compounds IX showed, in particular, an OH stretching band, while the nmr spectra indicated the rearrangement of the molecular structure compared with that of the starting compounds V, since the downfield *peri* hydrogen signal, which was peculiar to these latter compounds, was no longer present. Furthermore, under a 30 eV electron impact, IXa gave, in addition to the significant fragment ions at m/e = 186 ($C_{11}H_8NO_2$), 143 ($C_{10}H_7O$) and 159 ($C_{10}H_9NO$), which were obtained at 70 eV, also the fragment ion at m/e = 171 ($C_{11}H_7O_2$), a most important result for the corroboration of the proposed structure. On the other hand, acetyl derivative Xa, in addition to the molecular ion at m/e = 371, showed all the same ion peaks.

An interesting result emerged by performing the reaction of 1-oxo-3-(*N*-alkyl-*N*-phenyl)amino-1*H*-naphtho-[2,1-*b*]pyrans (V) with *N*,*N*-dimethylformamide-phosphorus oxychloride at 140°. An analogous mechanism to that given for intermediate VIB (attack of the reactant on 2 and *N*-phenyl *ortho* positions) followed by dealkylation, gave rise to the formation of only one product, 14-oxo-14*H*-naphtho[1′,2′:5,6]pyrano[2,3-*b*]quinoline (XIV) (Chart II), in a very good yield.

Compound XIV was a white crystalline material, whose elemental analysis, ir, nmr and mass spectral data were consistent with the proposed structure; for instance, the nmr spectrum showed a downfield H-1 signal (deshielding effect of 14-CO) at τ = 0.32.

When compound XIV was treated with 30% alcoholic potassium hydroxide, γ-pyrone ring opening occurred and a mixture of 2-oxy-3-(2′-ethoxy-1′-naphthoyl)quinoline (XVII) and 2-oxy-3-(2′-oxy-1′-naphthoyl)quinoline (XVIII) was obtained. These compounds were yellow in color and only the latter was soluble in dilute aqueous sodium hydroxide.

The only formation of XVII was achieved when compound XIV was treated with sodium ethoxide.

Elemental analyses, ir, nmr and mass spectral data confirmed the structures of XVII and XVIII; for instance, the nmr spectra no longer showed the downfield signals except for the slight influence of the side chain carbonyl group on the *peri* hydrogen. Moreover, both XVII and XVIII afforded the starting compound XIV by loss of ethanol or water on heating.

EXPERIMENTAL

Melting points, determined with a Fisher-Johns (Electrothermal when above 300°) apparatus, and boiling points are uncorrected. Infrared spectra were obtained with a Perkin-Elmer 257 spectrophotometer (solid compounds in potassium bromide pellets). Nuclear magnetic resonance spectra were determined with a Perkin-Elmer R 12 spectrometer, using TMS as an internal standard (τ = 10). Mass spectra were recorded on a Varian CH7 mass spectrometer (70 eV). Analyses were performed by Laboratorio di Microanalisi, Istituto Carlo Erba per Ricerche Terapeutiche, Milano.

(*N*-Alkyl-*N*-phenyl)ethoxycarbonylacetamides (IV).

(*N*-Methyl-*N*-phenyl)ethoxycarbonylacetamide (IVa) was synthesized by heating 60.0 g. (0.37 mole) of ethyl malonate and 39.7 g. (0.37 mole) of *N*-methylaniline at 150° for 38 hours, with stirring, in a closed stainless steel high-pressure reaction vessel, following a previously described procedure (16,1,2,3). Distillation of the reaction mixture yielded 23.2 g. (28.3%) of the amide ester IVa, which was collected as a colorless liquid, b.p. 108-110° (0.09 mm.).

Anal. Calcd. for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.04; H, 6.75; N, 6.21.

(*N*-Ethyl-*N*-phenyl)ethoxycarbonylacetamide (IVb).

This compound was prepared in a manner similar to that for IVa using 60.0 g. (0.37 mole) of ethyl malonate and 44.8 g. (0.37 mole) of *N*-ethylaniline. The yield of colorless liquid IVb, b.p. 107-109° (0.1 mm.), was 23.8 g. (27.3%).

Anal. Calcd. for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28; N, 5.95. Found: C, 66.48; H, 7.23; N, 5.86.

1-Oxo-3-(*N*-methyl-*N*-phenyl)amino-1*H*-naphtho[2,1-*b*]pyran (Va).

Phosphorus oxychloride (11.5 g., 0.075 mole) was added dropwise with stirring to 12.2 g. (0.055 mole) of (*N*-methyl-*N*-phenyl)ethoxycarbonylacetamide (IVa) which was contained in a flask set in an ice bath and protected from atmospheric moisture with a calcium chloride tube. The mixture was then removed from the ice bath and held at room temperature for 30 minutes. A suspension of 7.2 g. (0.05 mole) of β-naphthol in 40 ml. of dichloroethane was added and the reaction mixture was refluxed for 6 hours.

After cooling, a solution of 68 g. of sodium acetate in 200 ml. of water was added and the mixture was refluxed for 2 hours. The layers were separated and the aqueous phase was extracted twice with dichloroethane. The combined organic portions were washed with water and evaporated under reduced pressure to give a dark oil which was shaken with a mixture of 2*N* aqueous sodium hydroxide and ether. On standing, white crystals separated out; crystallization from ethanol afforded 6.6 g. (43.8%) of pure Va, m.p. 170-171°; ir: 1627 cm^{-1} (CO), 1550 cm^{-1} (γ-pyrone C=C); nmr (deuteriochloroform) τ: 6.62 (s, 3, CH_3), 4.48 (s, 1, H-2), 2.90-2.01 (m, 10, H-5,6,7,8,9 plus N-C_6H_5), - 0.20 (mc, 1, H-10).

Anal. Calcd. for $C_{20}H_{15}NO_2$: C, 79.71; H, 5.02; N, 4.65. Found: C, 79.92; H, 4.93; N, 4.68.

1-Oxo-3-(*N*-ethyl-*N*-phenyl)amino-1*H*-naphtho[2,1-*b*]pyran (Vb).

This compound was prepared in the same manner as described for the (*N*-methyl-*N*-phenyl)amino derivative Va, using 11.5 g. (0.075 mole) of phosphorus oxychloride, 12.9 g. (0.055 mole) of (*N*-ethyl-*N*-phenyl)ethoxycarbonylacetamide (IVb) and 7.2 g. (0.05 mole) of β-naphthol. After crystallization of the crude product from cyclohexane, the resulting white crystals weighed 5.6 g. (35.5%) and melted at 141-142°; ir: 1630 cm^{-1} (CO), 1545 cm^{-1} (γ-pyrone C=C); nmr (deuteriochloroform): τ: 8.70 (t, J = 7 Hz, 3, CH_3), 6.12 (q, J = 7 Hz, 2, CH_2), 4.55 (s, 1, H-2), 2.90-1.92 (m, 10, H-5,6,7,8,9 plus N-C_6H_5), - 0.23 (mc, 1, H-10).

Anal. Calcd. for $C_{21}H_{17}NO_2$: C, 79.98; H, 5.43; N, 4.44. Found: C, 79.83; H, 5.28; N, 4.33.

The Reaction of 1-Oxo-3-(*N*-methyl-*N*-phenyl)amino-1*H*-naphtho-[2,1-*b*]pyran (Va) with *N*,*N*-Dimethylformamide.

Phosphorus oxychloride (0.92 g., 6 mmoles) was added dropwise to a stirred 2 ml. quantity of *N*,*N*-dimethylformamide which was contained in a flask cooled with an ice bath and protected from moisture with a calcium chloride tube.

Following the addition of the phosphorus oxychloride, the mixture was stirred for 30 minutes at room temperature; a suspension of 1.21 g. (4 mmoles) of Va in 8 ml. of *N*,*N*-dimethylformamide was then added slowly and the mixture was heated for 90 minutes at 95°, cooled and poured onto crushed ice. The resulting yellow-orange suspension was treated with excess saturated aqueous solution of sodium acetate and stirred for 2 hours at room temperature.

The dark green colored solid ultimately obtained was collected and washed with water; the material, 1.2 g., was a mixture of compounds VIIa, VIIIa and IXa which were separated according to the following procedure:

1) 8-Methyl-13,14-dioxo-8*H*,13*H*,14*H*-naphtho[1',2':5,6]pyrano-[2,3-*b*]quinoline (VIIa).

The reaction product described above was crystallized from pyridine affording 0.31 g. (23.7%) of a nearly pure white crystalline VIIa; m.p. 362-364° dec., after recrystallization from the same solvent; ir: 1658 cm^{-1} (CO); nmr (deuteriotrifluoroacetic acid) τ: 5.50 (s, 3, CH_3), 2.60-1.10 (m, 9, H-2,3,4,5,6,9,10,11,12), 0.38 (mc, 1, H-1); mass spectrum, m/e (relative intensity %): 327 (100), 312 (37), 310 (13), 299 (20), 284 (11), 256 (10).

Anal. Calcd. for $C_{21}H_{13}NO_3$: C, 77.05; H, 4.00; N, 4.28. Found: C, 76.99; H, 3.93; N, 4.26.

2) 8-Methyl-14-oxo-8*H*,13*H*,14*H*-naphtho[1',2':5,6]pyrano-[2,3-*b*]quinoline (VIIIa).

The pyridine filtrate was vacuum treated to remove the solvent and the resulting yellow solid was dissolved in chloroform and chromatographed on basic alumina. After evaporation of the chloroform eluant, the crude solid (0.35 g.) was crystallized from acetone yielding 0.20 g. (16.0%) of pale yellow crystalline VIIIa, m.p. 213-215°; ir: 1641 cm^{-1} (CO), 1555 cm^{-1} (γ-pyrone C=C); nmr (deuteriochloroform) τ: 6.70 (s, 3, CH_3), 6.00 (s, 13-CH_2), 3.40-2.10 (m, 9, H-2,3,4,5,6,9,10,11,12), - 0.20 (mc, 1, H-1); mass spectrum, m/e (relative intensity %): 313 (100), 312 (37), 298 (75), 284 (7), 269 (8), 240 (8), 142 (7).

Anal. Calcd. for $C_{21}H_{15}NO_2$: C, 80.49; H, 4.83; N, 4.47. Found: C, 80.40; H, 4.80; N, 4.48.

3) 1-Oxo-2-formyl-3-(*N*-methyl-*N*-phenyl)amino-9-oxy-1*H*-phenalene (IXa).

This product was recovered by treating the chromatography column, after washing with 40 ml. of ethanol, with 40 ml. of 2*N* aqueous sodium hydroxide and finally with water. The combined aqueous portions were acidified with concentrated hydrochloric acid and the nearly pure yellow crystalline IXa that separated (0.32 g., 24.3%) was crystallized from ethanol and melted at 234-235°; ir: 3120 cm^{-1}, broad (OH), 1655 and 1642 cm^{-1} (CO), 1570 cm^{-1} (C=C-N); nmr (DMSO-d_6) τ: 6.42 (s, 3, CH_3), 2.95-1.98 (m, 11, H-4,5,6,7,8 plus *N*-C_6H_5 plus OH), 1.67 (s, 1, CHO); mass spectrum (30 eV), m/e (relative intensity %): 329 (82), 328 (50), 312 (7), 301 (9), 300 (22), 284 (10), 186 (100), 171 (9), 159 (30), 143 (5), 130 (20), 115 (30), 103 (3), 89 (30), 77 (4).

Anal. Calcd. for $C_{21}H_{15}NO_3$: C, 76.58; H, 4.59; N, 4.25. Found: C, 76.64; H, 4.62; N, 4.19.

a) Acylation of IXa.

The suspension of 0.20 g. of IXa in 8 ml. of freshly distilled acetic anhydride was heated for one hour at 120-130° and poured onto crushed ice. Sodium bicarbonate was added and the yellow acetyl derivative Xa that separated was crystallized from benzene, m.p. 207-208°.

Anal. Calcd. for $C_{23}H_{17}NO_4$: C, 74.38; H, 4.61; N, 3.77. Found: C, 74.48; H, 4.64; N, 3.76.

b) Hydrazone Derivative of IXa.

The mixture of 0.27 g. of IXa, 0.07 g. of hydrazine hydrate and 10 ml. of ethanol was refluxed for 30 minutes. The white hydrazone XIa that separated upon cooling was crystallized from benzene and melted at 234-235° dec.

Anal. Calcd. for $C_{21}H_{17}N_3O_2$: C, 73.45; H, 4.99; N, 12.24. Found: C, 73.66; H, 5.00; N, 12.24.

The Reaction of 1-Oxo-3-(*N*-ethyl-*N*-phenyl)amino-1*H*-naphtho[2,1-*b*]pyran (Vb) with *N*,*N*-Dimethylformamide.

The reaction was carried out in the same manner as described for the methyl derivative Va using 1.26 g. (4 mmoles) of Vb. The solid recovered after hydrolysis with sodium acetate was a mixture of compounds VIIb, VIIIb and IXb which were separated according to the following procedure:

1) 1-Oxo-2-formyl-3-(*N*-ethyl-*N*-phenyl)amino-9-oxy-1*H*-phenalene (IXb).

The crude material described above was suspended in 2*N* aqueous sodium hydroxide and stirred for 4 hours; the residue was filtered and washed exhaustively with hot water. The combined aqueous portions were acidified with concentrated hydrochloric acid yielding the yellow compound IXb which was crystallized from ethanol (0.20 g.) and melted at 220-221°; ir: 3150 cm^{-1}, broad (OH), 1640 and 1632 cm^{-1} (CO), 1579 cm^{-1} (C=C-N); nmr (C_6H_5N-d_5) τ: 8.85 (t, J = 7 Hz, 3, CH_3), 5.75 (q, J = 7 Hz, 2, CH_2), 3.08-1.94 (m, 10, H-4,5,6,7,8 plus *N*-C_6H_5), 1.59 (s, 1, OH), 1.43 (s, 1, CHO).

Anal. Calcd. for $C_{22}H_{17}NO_3$: C, 76.95; H, 4.99; N, 4.08. Found: C, 76.78; H, 5.05; N, 4.18.

a) Acylation of IXb.

The procedure used for the acylation of IXa was followed using 0.5 g. of IXb and 10 ml. of acetic anhydride. Crystallization from benzene afforded the yellow acetyl derivative Xb which melted at 209-210°.

Anal. Calcd. for $C_{24}H_{19}NO_4$: C, 74.79; H, 4.97; N, 3.63. Found: C, 74.94; H, 5.08; N, 3.73.

b) Hydrazone Derivative of IXb.

This compound was prepared in the same manner as described for the hydrazone derivative of IXa, white crystals from benzene, m.p. 224-225°.

Anal. Calcd. for $C_{22}H_{19}N_3O_2$: C, 73.93; H, 5.36; N, 11.76. Found: C, 74.01; H, 5.32; N, 11.57.

2) 8-Ethyl-13,14-dioxo-8*H*,13*H*,14*H*-naphtho[1',2':5,6]pyrano-[2,3-*b*]quinoline (VIIb).

The residue from the treatment with aqueous sodium hydroxide and hot water was boiled with chloroform and the insoluble white material was collected and crystallized from pyridine giving 0.41 g. (30.0%) of pure VIIb, m.p. 323-324°; ir: 1664 cm^{-1} (CO); nmr (deuteriotrifluoroacetic acid) τ: 8.13 (t, J = 7 Hz, 3, CH_3), 4.86 (q, J = 7 Hz, 2, CH_2), 2.42-1.04 (m, 9, H-2,3,4,5,6,9,10,11, 12), 0.22 (mc, 1, H-1).

Anal. Calcd. for $C_{22}H_{15}NO_3$: C, 77.40; H, 4.43; N, 4.10. Found: C, 77.43; H, 4.43; N, 4.18.

3) 8-Ethyl-14-oxo-8*H*,13*H*,14*H*-naphtho[1',2':5,6]pyrano[2,3-*b*]-quinoline (VIIIb).

The chloroform filtrate obtained above was concentrated and chromatographed on basic alumina. After evaporation of the acetone eluant the crude solid was crystallized from this solvent affording 0.15 g. (11.5%) of pale yellow crystalline VIIIb, m.p. 207-209°; ir: 1640 cm^{-1} (CO), 1555 cm^{-1} (γ-pyrone C=C); nmr (deuteriochloroform) τ: 8.61 (t, J = 7 Hz, 3, CH_3), 6.02 (q, J = 7 Hz, 2, CH_2), 5.94 (s, 2, 13-CH_2), 3.26-1.95 (m, 9, H-2,3, 4,5,6,9,10,11,12), - 0.24 (mc, 1, H-1).

Anal. Calcd. for $C_{22}H_{17}NO_2$: C, 80.71; H, 5.23; N, 4.28. Found: C, 80.49; H, 5.13; N, 4.30.

A small quantity (0.03 g.) of IXb was recovered from the column following the same procedure as described for IXa (total yield 16.7%).

14-Oxo-14-naphtho[1',2':5,6]pyrano[2,3-*b*]quinoline (XIV).

The amounts of the different reactants and the procedure were the same as described for the reaction of Va with *N*,*N*-dimethylformamide. The variations were that the reaction mixture was heated for 2 hours at 140°, instead of 95°, cooled and poured onto crushed ice; the resulting mixture was then made basic by adding 2*N* aqueous sodium hydroxide.

The solid was collected by filtration and washed with water. Crystallization from benzene or pyridine afforded 1.0 g. (84.1%) of white crystalline XIV, m.p. 292-294°; ir: 1646 cm^{-1} (CO), other bands 1615, 1595 and 1577 cm^{-1}; nmr (deuteriotrifluoroacetic acid) τ: 2.50-1.30 (m, 9, H-2,3,4,5,6,9,10,11,12), 0.32 (mc, 1, H-1) - 0.05 (s, 1, H-13); mass spectrum, m/e (relative intensity %): 297 (100), 269 (25), 240 (41), 213 (14).

Anal. Calcd. for $C_{20}H_{11}NO_2$: C, 80.79; H, 3.73; N, 4.71. Found: C, 80.77; H, 3.76; N, 4.67.

When the reaction of Vb and *N*,*N*-dimethylformamide was carried out as above, there was obtained the same compound XIV in a similar yield. The identity of the material was established by ir spectra and by melting points.

1,2-Dihydro-1-methyl-2-oxo-3-(2'-oxy-1'-naphthoyl)-4-oxyquinoline (XV).

A suspension of 0.50 g. of VIIa in 20 ml. of 30% alcoholic

potassium hydroxide was refluxed for 3 hours and the dark orange colored solution ultimately obtained was poured onto crushed ice.

Removal of ethanol under reduced pressure and treatment with charcoal gave a solution which was made acid by the addition of concentrated hydrochloric acid. The yellow solid that separated was collected and washed with water; purification was achieved by dissolution of the material in dilute aqueous sodium hydroxide and by precipitation with dilute hydrochloric acid.

There was collected the yellow compound XV (0.46 g., 87.2%) which did not melt as such, but was converted into XVI upon heating; melting point behavior of XV: turned white at 170-175° and melted at 320-322°; ir: 3140 cm^{-1}, broad (OH), 1620 cm^{-1} (CO), other band, 1560 cm^{-1}; nmr (DMSO-d_6) τ: 6.63 (s, 3, CH_3), 2.93-2.00 (m, 10, H-5,6,7,8,3',4',5',6',7' plus OH), 1.83 (mc, 1, H-8'), 0.05 (bs, 1, OH).

Anal. Calcd. for $C_{21}H_{15}NO_4$: C, 73.03; H, 4.38; N, 4.06. Found: C, 72.90; H, 4.37; N, 4.02.

12,13-Dihydro-12-methyl-13,14-dioxo-14*H*-naphtho[1',2':5,6]-pyrano[3,2-*c*]quinoline (XVI).

Crystallization from ethanol or chloroform of a 0.30 g. sample of XV afforded 0.20 g. of white crystalline XVI which melted at 329-330°; this product was insoluble in 2*N* aqueous sodium hydroxide; ir: 1675 cm^{-1} (CO), other bands, 1628 and 1588 cm^{-1}; nmr (deuteriotrifluoroacetic acid) τ: 5.74 (s, 3, CH_3), 2.41-1.60 (m, 7, H-2,3,4,8,9,10,11), 1.34 and 1.16 (c, J = 8 Hz and dc, J = 8 Hz, 2, H-5,6), 0.30 (mc, 1, H-1); mass spectrum, m/e (relative intensity %): 327 (100), 312 (3), 298 (64), 284(2), 270 (7).

Anal. Calcd. for $C_{21}H_{13}NO_3$: C, 77.05; H, 4.00; N, 4.28. Found: C, 76.95; H, 3.98; N, 4.22.

2-Oxy-3-(2'-ethoxy-1'-naphthoyl)quinoline (XVII) and 2-Oxy-3-(2'-oxy-1'-naphthoyl)quinoline (XVIII).

a) The suspension of a 0.50 g. sample of XIV in 15 ml. of 30% alcoholic potassium hydroxide (by dissolving potassium hydroxide in 95% ethanol) was refluxed for 3 hours. The resulting solution was poured onto crushed ice and the yellow solid that separated was collected, washed with water and crystallized from ethanol. There was obtained 0.24 g. (41.6%) of XVII, m.p. 225-226°; melting point behavior of XVII: the melt solidified again at about 245° to a white solid which melted at 292-294°; ir: 1658 cm^{-1} (CO); nmr (DMSO-d_6) τ: 9.04 (t, J = 7 Hz, 3, CH_3), 5.90 (q, J = 7 Hz, 2, CH_2), 2.95-1.73 (m, 10, H-5,6,7,8,3',4'-5',6',7',8'), 1.57 (s, 1, H-4), - 1.91 (bs, 1, OH); mass spectrum, m/e (relative intensity %): 343 (40), 326 (9), 314 (16), 298 (100), 286 (15), 270 (20), 241 (2), 172 (55), 171 (32), 143 (12), 116 (29), 115 (36), 89 (23) (after treatment of the sample with deuterium oxide, the relative intensity of the fragment peak at m/e = 173 was found to be increased).

Anal. Calcd. for $C_{22}H_{17}NO_3$: C, 76.95; H, 4.99; N, 4.08. Found: C, 76.93; H, 4.96; N, 4.12.

The filtrate was vacuum treated to remove ethanol. A 0.13 g. quantity of starting compound XIV that separated was removed by filtration.

After addition of concentrated hydrochloric acid the resulting yellow precipitate was collected and washed with water; there was obtained 0.12 g. (22.6%) of XVIII which was crystallized from ethanol and melted at 238-242°. Melting point behavior of XVIII: the melt soon solidified to a white solid which melted at 292-294°; ir: 1656 cm^{-1} (CO); nmr (DMSO-d_6) τ: 3.04-2.00 (m, 10, H-5,6,7,8,3',4',5',6',7',8'), 1.75 (s, 1, H-4), - 0.30 (s, 1, 2'-OH), - 1.93 (bs, 1, 2-OH); mass spectrum, m/e (relative intensity %): 315 (100), 314 (90), 298 (42), 297 (48), 286 (26), 270 (11), 269 (10), 240 (10), 172 (86), 145 (21), 143 (13), 115 (25).

Anal. Calcd. for $C_{20}H_{13}NO_3$: C, 76.18; H, 4.16; N, 4.44. Found: C, 76.10; H, 4.20; N, 4.49.

b) To a suspension of 1.2 g. of XIV in 30 ml. of anhydrous ethanol, 40 ml. of a saturated solution of sodium ethoxide was added and the mixture was refluxed for 2 hours.

The resulting solution was poured onto crushed ice, ethanol was removed under reduced pressure and the solid that separated was collected by filtration. The material was boiled with ethanol and the insoluble starting compound XIV (0.37 g.) was removed by filtration. After concentration of the alcoholic solution, there was collected a solid (0.83 g., 59.9%) which was identical with XVII prepared according to method a).

Compound XIV from XVII.

A 0.2 g. sample of the compound XVII was heated for 20 minutes at 250-260°. After cooling, the solid was crystallized from benzene yielding XIV, m.p. 292-294°.

1-Oxo-2-formyl-3-(*N*-alkyl-*N*-benzyl)amino-1*H*-naphtho[2,1-*b*]-pyrans (XIII).

The general procedure described for the reaction of V with *N,N*-dimethylformamide was employed using 0.92 g. (6 mmoles) of phosphorus oxychloride, 2 ml. of *N,N*-dimethylformamide and 4 mmoles of 1-oxo-3-(*N*-alkyl-*N*-benzyl)amino-1*H*-naphtho[2,1-*b*]-pyrans (XII) (3) suspended in 8 ml. of *N,N*-dimethylformamide. The reaction mixture was heated for 90 minutes at 95° and poured onto crushed ice. The hydrolysis of the mixture was then accomplished by the addition of sodium carbonate and the white solid that separated was collected, washed with water and crystallized from ethanol.

By the above procedure, the following compounds (XIII) were prepared:

1-Oxo-2-formyl-3-(*N*-benzyl-*N*-methyl)amino-1*H*-naphtho[2,1-*b*]-pyran (XIIIa).

The yield of this compound was 71.2%, m.p. 130-131°; ir: 1663 cm^{-1} (CHO), 1626 cm^{-1} (CO), 1545 cm^{-1} (γ-pyrone C=C); nmr (deuteriochloroform) τ: 6.90 (s, 3, CH_3), 5.20 (s, 2, benzylic CH_2), 2.87-1.91 (m, 10, H-5,6,7,8,9 plus C_6H_5), 0.04 (mc, 1, H-10), - 0.30 (s, 1, CHO).

Anal. Calcd. for $C_{22}H_{17}NO_3$: C, 76.95; H, 4.99; N, 4.08. Found: C, 77.02; H, 4.96; N, 4.09.

1-Oxo-2-formyl-3-(*N*-benzyl-*N*-ethyl)amino-1*H*-naphtho[2,1-*b*]-pyran (XIIIb).

The yield of this compound was 87.4%, m.p. 134-135°; ir: 1664 cm^{-1} (CHO), 1624 cm^{-1} (CO), 1547 cm^{-1} (γ-pyrone C=C); nmr (deuteriochloroform) τ: 8.71 (t, J = 7 Hz, 3, CH_3), 6.36 (q, J = 7 Hz, 2, CH_2), 5.20 (s, 2, benzylic CH_2), 2.85-1.90 (m, 10, H-5,6,7,8,9 plus C_6H_5), 0.05 (mc, 1, H-10), - 0.28 (s, 1, CHO).

Anal. Calcd. for $C_{23}H_{19}NO_3$: C, 77.29; H, 5.36; N, 3.92. Found: C, 77.48; H, 5.26; N, 3.90.

1-Oxo-2-formyl-3-(*N*-benzyl-*N*-isopropyl)amino-1*H*-naphtho[2,1-*b*]-pyran (XIIIc).

The yield of this compound was 94.7%; m.p. 185-186°; ir: 1660 cm^{-1} (CHO), 1626 cm^{-1} (CO), 1536 cm^{-1} (γ-pyrone C=C) nmr (deuteriochloroform) τ: 8.54 (d, J = 7 Hz, 6, CH_3), 5.66 (mc, 1, CH), 5.29 (s, 2, benzylic CH_2(m, 2.94-1.95 (m, 10, H-5,6, 7,8,9 plus C_6H_5), 0.08 (mc, 1, H-10), - 0.23 (s, 1, CHO).

Anal. Calcd. for $C_{24}H_{21}NO_3$: C, 77.60; H, 5.70; N, 3.77. Found: C, 77.82; H, 5.73; N, 3.84.

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