

REACTIONS OF NITROSOPHENOLS. VI.*

PREPARATION OF SOME HYDROXYPHENOXAZONES

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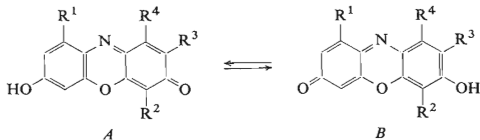
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The preparation of 2,4-dimethyl-7,9-dihydroxy-3-phenoxazone, 2,4-dimethyl-7-hydroxy-3-phenoxazone-9-carboxylic acid, and 9-hydroxy-5-benzo[*a*]phenoxazone-11-carboxylic acid by the reaction of corresponding nitrosophenols with phloroglucinol or 3,5-dihydroxybenzoic acid in ethylene glycol solutions is described. The tautomerism in the prepared compounds is discussed on the basis of their acetylation and IR and PMR spectra.

This paper describes the preparation and properties of 2,4-dimethyl-7,9-dihydroxy-3-phenoxazone (*I*), 2,4-dimethyl-7-hydroxy-3-phenoxazone-9-carboxylic acid (*II*) and 9-hydroxy-5-benzo[*a*]phenoxazone-11-carboxylic acid (*III*). Compounds *I* and *II* were prepared by a reaction of 2,6-dimethyl-4-nitrosophenol with phloroglucinol and 3,5-dihydroxybenzoic acid, respectively, and compound *III* was obtained by a reaction of 1-nitroso-2-naphthol with 3,5-dihydroxybenzoic acid.

Similarly to other 7-hydroxy-3-phenoxazones¹ and 9-hydroxy-5-benzo[*a*]phenoxazones, the question of the existence of the compounds *I*, *II* and *III* in the possible tautomeric forms *A* and *B* is interesting.



- I*, $R^1 = \text{OH}$; $R^2 = R^3 = \text{CH}_3$, $R^4 = \text{H}$
II, $R^1 = \text{COOH}$, $R^2 = R^3 = \text{CH}_3$, $R^4 = \text{H}$
III, $R^1 = \text{COOH}$; $R^2 = \text{H}$; $R^3, R^4 = \text{benzo}[a]\text{phenoxazone}$

According to the PMR-spectrum, the compound *I* exists in the form *A*. The high value of the chemical shift (δ) of the proton in position 1 indicates the presence of a strongly electron-accepting group $\text{C}=\text{O}$ in the neighbourhood of electron-donat-

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ing methyl groups in this nucleus. Further, the existence of long-range spin-spin interaction (across 4 bonds) between protons of the methyl group in the position 2 and aromatic proton in the position 1 and the relatively high value of the spin-spin coupling constant point to the presence of a well developed double bond between atoms $C_{(1)}$ and $C_{(2)}$. The tautomerism in the compound *III* was studied using its IR-spectrum. On the basis of a study of a series of phenoxazine dyes, Butenandt and coworkers² showed that the intensive band in the 710 cm^{-1} region is characteristic for benzo[*a*]phenoxazines. In the spectrum of compound *III*, this band is at 702 cm^{-1} . A comparison of intensity of this band in the spectrum of compound *III* with that of other benzo[*a*]phenoxazines leads to a qualitative conclusion that also this compound exists, under conditions of measurement, predominantly in the form *A*.

EXPERIMENTAL

The melting points were taken on a Bötetius block, the chromatography was carried out on silica gel CH (Lachema). UV- and visible spectra were measured on a Unicam SP 800 spectrophotometer in 1 cm cells in $5\text{--}6 \cdot 10^{-5}\text{M}$ methanolic solutions. The infrared spectra were taken on a spectrophotometer UR-20 (Zeiss) in nujol, the NMR measurements were carried out on a Varian T-60 instrument in hexadeuteriodimethylsulphoxide at room temperature. The chemical shift is given in p.p.m. relative to tetramethylsilane.

2,4-Dimethyl-7,9-dihydroxy-3-phenoxazine (*I*)

A mixture of 2,6-dimethyl-4-nitrosophenol³ (0.35 g) and phloroglucinol (0.75) g was dissolved in ethylene glycol (20 ml) at 105°C . After cooling to 85°C , four drops of 96% sulphuric acid were added under stirring, and the mixture was heated to 105°C . The red solution was cooled, poured into water (100 ml), the precipitate was filtered off, washed with water, dried, washed several times with ether, and crystallized from ethanol. This procedure afforded a red compound (60 mg) which does not melt till 350°C and which is soluble in alcohols and acetone. 2,4-Dimethyl-7,9-dihydroxy-3-phenoxazine resulted also in the reaction of 2,6-dimethyl-4-nitrosophenol with phloroglucinol-carboxylic acid in ethylene glycol solution in the presence of sulphuric acid (6 h stirring at 40°C). Decarboxylation⁴ of the phloroglucinolcarboxylic acid took probably place under these conditions. Ultraviolet and visible spectrum: 228 nm ($\log \epsilon = 4.38$), 263 (4.22), 282 (3.92), 464 (4.33), 587 (3.30). IR-spectrum (cm^{-1}): 1655 $\nu(\text{C}=\text{C})$, 1625 $\nu(\text{C}=\text{O})$, 1590, 1570 $\nu(\text{C}=\text{C}$ aromatic), 1490 $\nu(\text{C}=\text{N})$, 1470 ($\nu\text{C}=\text{C}$ aromatic), 1375 ($\nu\text{C}-\text{C}$), 1300 ($\nu\text{C}-\text{phenyl}$), 1150 ($\nu\text{C}-\text{O}$), 996 ($\delta\text{C}-\text{H}$), 845, 775, 750 ($\gamma\text{C}-\text{H}$). PMR-spectrum: 1.90 p.p.m. singlet, 3 H (4- CH_3); 2.00 p.p.m. doublet $J = 1.2\text{ Hz}$, 3 H (2- CH_3); 6.21 p.p.m. quartet $J = 2.4\text{ Hz}$, 2 H, (aromatic protons in positions 6 and 8; 7.17 p.p.m. quartet $J = 1.2\text{ Hz}$, 1 H (aromatic proton in position 1); 10.55 p.p.m. and 10.65 p.p.m. singlets, 1 H, removed on addition of D_2O (hydroxylic protons). For $\text{C}_{14}\text{H}_{11}\text{NO}_4$ (257.2) calculated: 65.40% C, 4.27% H, 5.44% N; found: 65.17% C, 4.40% H, 5.23% N.

Acetylation: Acetic anhydride (10 ml) was added to a solution of compound *I* (200 mg) in pyridin (10 ml). After 6 h the separated crystals were filtered and washed with ether. The filtrate on concentration by vacuum distillation afforded further amount of product, the total yield being 140 mg. Thin layer chromatography on silica gel (benzene-acetone 10 : 1) showed a spot, R_F 0.4 and a weak spot at R_F 0.3. Preparative chromatography on loose silica gel layer afforded only the compound R_F 0.4 which melted at $191\text{--}192^\circ\text{C}$. The orange-red compound $R_F = 0.3$ deacetylates readily, and attempts to isolate this compound failed. The obtained acetyl derivative is soluble in benzene, methanol, ethanol and acetone. For $\text{C}_{18}\text{H}_{15}\text{NO}_6$ (341.2) calculated: 63.55% C, 4.41% H, 4.11% N; found: 63.14% C, 4.68% H, 4.33% N.

2,4-Dimethyl-7-hydroxy-3-phenoxazone-9-carboxylic Acid (II)

A mixture of 3,5-dihydroxybenzoic acid (0.35 g), 2,6-dimethyl-4-nitrosophenol (0.35 g) and ethylene glycol (20 ml) was heated slowly to 105°C. The solution was cooled to 85°C and 4 drops of concentrated sulphuric acid were added under stirring. The stirred mixture was heated to 105°C for 10–15 min till a deep red solution was formed, then cooled and poured into 500 ml of water. The precipitate was filtered off, washed with water, dried, washed with ether till the filtrate was colourless, crystallized from ethanol and dried *in vacuo*, yielding thus 45 mg of the compound II, soluble in methanol, ethanol, sparingly soluble in acetone, and not melting till 350°C. UV- and visible spectrum: 228 nm ($\log \epsilon$ 4.94), 243 nm (4.88), 298 nm (3.61), 367 nm (3.83), 547 nm (4.19), 568 nm (4.18), 586 nm (sh) (4.13). IR-spectrum (cm^{-1}): 1735 ($\nu\text{C}=\text{O}$), 1640 sh ($\nu\text{C}=\text{C}$), 1630 ($\nu\text{C}=\text{O}$), 1600, 1560 ($\nu\text{C}=\text{C}$ arom.), 1500 ($\nu\text{C}=\text{N}$), 1465, 1460 ($\nu\text{C}=\text{C}$ arom.), 1380 ($\nu\text{C}-\text{C}$), 1315 (νC -phenyl), 1155 ($\nu\text{C}-\text{O}$), 1000 ($\delta\text{C}-\text{H}$), 860, 775, 750 ($\gamma\text{C}-\text{H}$). For $\text{C}_{15}\text{H}_{11}\text{NO}_5$ (285.2) calculated: 63.11% C, 3.85% H, 4.91% N; found: 62.92% C, 4.10% H, 4.69% N.

9-Hydroxy-5-benzo[a]phenoxazone-11-carboxylic Acid (III)

A mixture of 1-nitroso-2-naphthol (0.35 g), 3,5-dihydroxybenzoic acid (0.3 g) and ethylene glycol (50 ml) was refluxed till the mixture was homogeneous. Concentrated nitric acid (60%) (0.2–0.3 ml) was then added dropwise under stirring, the solution was allowed to cool, stirred 30 min and poured into 300 ml of water. The precipitate was filtered off, washed with water, dried and washed with ether. Thin layer chromatography (acetone–ammonia 19 : 2) of the crude product exhibits 3 spots, one of which is violet with red fluorescence. Repeated chromatography on loose layer of silica gel using the same solvent afforded the red-brown ammonium salt which was dissolved in water. Acidification with hydrochloric acid afforded the acid which was filtered off and crystallized from glacial acetic acid, giving thus a red compound (60 mg) not melting till 350°C, readily soluble in acetone, less soluble in methanol and ethanol. UV- and visible spectrum: 230 nm ($\log \epsilon$ 4.23), 248 nm (4.28), 282 sh (4.01), 290 nm (3.82), 460 (4.14), 550 (3.62). IR-spectrum 1740, 1722 sh, 1710 sh ($\nu\text{C}=\text{O}$), 1630 sh ($\nu\text{C}=\text{C}$), 1620 ($\nu\text{C}=\text{O}$), 1580, 1558 ($\nu\text{C}=\text{C}$ arom.), 1505 ($\nu\text{C}=\text{N}$), 1450 ($\nu\text{C}=\text{C}$ arom.), 1354 ($\nu\text{C}-\text{C}$), 1303 (νC -phenyl), 1186 ($\nu\text{C}-\text{O}$), 998 ($\delta\text{C}-\text{H}$) 850, 780 ($\gamma\text{C}-\text{H}$), 702 (skeletal vibration of benzo[a]phenoxazones). For $\text{C}_{17}\text{H}_8\text{NO}_5$ (307.2) calculated: 66.48% C, 3.95% H, 4.55% N; found: 66.45% C, 3.32% H, 4.27% N.

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