

# Preparation and properties of some 3-phenoxazone derivatives

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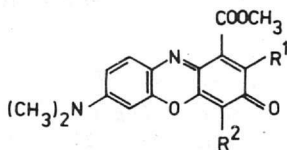
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The reaction of aromatic amines with some derivatives of 1-carboxy-7-dimethylamino-3-phenoxazone has been studied. Preparation and properties of seven 2-arylamino derivatives are described; the proposed structures are supported by u.v., i.r., and p.m.r. spectral data.

Была изучена реакция ароматических аминов с некоторыми производными 1-карбоксо-7-диметиламино-3-феноксазона. В работе описываются синтез и свойства семи 2-ариламинопроизводных; предлагаемая структура обоснована УФ, ИК, и  $^1\text{H}$ -ЯМР спектрами.

The amination of substances related to phenoxazine has been studied extensively [1—7]. For this purpose aromatic amines, mainly aniline, have been most often used. Rules according to which the arylamination takes its course [5] and the mechanism of the reaction have been established [7].

The present work describes the preparation and properties of some 2-arylamino-1-methoxycarbonyl-7-dimethylamino-3-phenoxazones. The structure of the prepared substances was confirmed by spectral methods.



I	$\text{R}^1 = \text{NHC}_6\text{H}_5$	$\text{R}^2 = \text{H}$
II	$\text{R}^1 = \text{NHC}_6\text{H}_4\text{OCH}_3$ ( <i>o</i> -)	$\text{R}^2 = \text{H}$
III	$\text{R}^1 = \text{NHC}_6\text{H}_4\text{OCH}_3$ ( <i>p</i> -)	$\text{R}^2 = \text{H}$
IV	$\text{R}^1 = \text{NHC}_6\text{H}_4\text{OCH}_3$ ( <i>m</i> -)	$\text{R}^2 = \text{H}$
V	$\text{R}^1 = \text{NHC}_6\text{H}_4\text{CH}_3$ ( <i>p</i> -)	$\text{R}^2 = \text{H}$
VI	$\text{R}^1 = \text{NHC}_6\text{H}_5$	$\text{R}^2 = \text{OCH}_3$
VII	$\text{R}^1 = \text{NHC}_6\text{H}_4\text{OCH}_3$ ( <i>o</i> -)	$\text{R}^2 = \text{OCH}_3$

## Experimental

The starting phenoxazine dyes, 1-methoxycarbonyl-7-dimethylamino-3-phenoxazine (*VIII*) and 1-methoxycarbonyl-4-methoxy-7-dimethylamino-3-phenoxazine (*IX*), were prepared as described [8, 9]. The aromatic amines were commercial products of reagent grade purity. The content of  $^{15}\text{N}$  in aniline (product of VEB, Berlin, GDR), used for the preparation of *I*, was 95%.

Thin-layer chromatography and column chromatography was performed on silica gel using benzene—acetone (3:1) mixture.

Absorption spectra in the u.v. and visible region were obtained for the solutions in 96% ethanol ( $c = 5 \times 10^{-5}$  M,  $d = 1$  cm) with Specord UV VIS spectrometer. The i.r. spectra were measured for compounds in potassium bromide pellets using UR-20 instrument; calibration was performed using a polystyrene film and indene. The p.m.r. spectra were measured in chloroform-*d* (internal standard tetramethylsilane) solutions with a 60 MHz spectrometer JNM-3H-60 (Jeol).

### *Arylamino derivatives I—VII*

Compound *VIII* or *IX* (0.6 g;  $\sim 5$  mmoles) was dissolved in ethanol (50 ml) and the aromatic amine ( $\sim 10$ — $15$  mmoles) was added. The mixture was heated on a water bath under a reflux condenser for 2—5 h while air was bubbled through. A half of the volume of the solvent was distilled off, the reaction mixture was cooled, the separated material was collected by filtration and washed with ethanol. A further crop of the solid was obtained after dilution of the filtrate with water. The purity of the crude product was checked by t.l.c.; it was purified by column chromatography if necessary. The eluted substances were recrystallized from chloroform. They were obtained as green lustrous crystalline substances well soluble in organic solvents (ethanol, chloroform, acetone, benzene, ether) but poorly soluble in water. For further properties of the compounds under investigation see Tables 1—3.

## Discussion

The substances *I—V* are easy to prepare; they separate readily from the reaction mixtures as crystalline, chromatographically almost pure solids. Only compounds *III* and *V* had to be isolated by means of chromatography. The preparation of 2-arylamino derivatives of *IX* was somewhat more difficult. While compounds *VI* and *VII*, formed from aniline and *o*-anisidine, could be isolated analytically pure, the reaction mixtures involving *m*- and *p*-anisidine, *o*- and *p*-toluidine, and dimethyl-*p*-phenylenediamine, as showed by t.l.c., contained several products. The isolation of analytically pure products from these reactions was abandoned. However, the chromatographic properties and the colour of the spots suggest that 2-arylamino derivatives were formed also in these reactions. The similarities of

Table 1

## Properties of the studied substances

Compound	Formula	M	Calculated/found			Yield %	M. p. °C	Absorption maxima $\lambda$ , nm (log $\epsilon$ )
			% C	% H	% N			
I	C <sub>22</sub> H <sub>19</sub> O <sub>4</sub> N <sub>3</sub>	389.4	67.86	4.92	10.97	64	243	213(4.35)—238(4.45)
			67.22	5.05	9.98			289(4.18)—569(4.50)
II	C <sub>23</sub> H <sub>21</sub> O <sub>5</sub> N <sub>3</sub>	419.4	65.86	5.05	10.02	54	245—246	213(4.40)—238(4.49)
			65.08	5.07	9.50			289(4.25)—569(4.58)
III	C <sub>23</sub> H <sub>21</sub> O <sub>5</sub> N <sub>3</sub>	419.4	65.86	5.05	10.02	40	214—215	213(4.22)—241(4.33)
			65.67	5.12	9.80			294(4.15)—569(4.51)
IV	C <sub>23</sub> H <sub>21</sub> O <sub>5</sub> N <sub>3</sub>	419.4	65.86	5.05	10.02	50	220—222	213(4.03)—238(4.16)
			65.60	5.15	9.50			294(3.92)—569(4.29)
V	C <sub>23</sub> H <sub>21</sub> O <sub>4</sub> N <sub>3</sub>	403.4	68.74	5.25	10.42	45	230—233	213(4.26)—241(4.41)
			68.28	5.38	10.08			293(4.20)—569(3.39)
VI	C <sub>23</sub> H <sub>21</sub> O <sub>5</sub> N <sub>3</sub>	419.4	65.86	5.05	10.02	49	223	215(4.32)—255(4.32)
			65.23	5.23	9.48			563(4.53)
VII	C <sub>24</sub> H <sub>23</sub> O <sub>6</sub> N <sub>3</sub>	449.4	64.14	5.12	9.35	62	210—212	214(4.61)—248(4.38)
			65.54	5.31	8.98			561(4.53)

Table 2

## IR spectral data for I—VII

Compound	$\bar{\nu}$ , $\text{cm}^{-1}$
I	3312 m, 3058 m, 2955 sh, 2927 s, 2815 w, 1728 s, 1642 s, 1621 s, 1588 m, 1575 s, 1523 s, 1507 sh, 1454 m, 1436 m, 1369 s, 1313 m, 1291 m, 1260 m, 1206 m, 1195 m, 1177 m, 1150 m, 1122 s, 1012 m, 1000 sh, 906 w, 895 w, 848 sh, 842 m, 825 w, 808 w, 787 m, 767 m, 744 sh, 720 w, 693 m, 657 m, 607 w, 508 m, 442 w
II	3341 m, 3075 w, 3018 w, 2949 m, 2930 m, 2843 m, 2814 w, 1732 s, 1643 s, 1611 s, 1578 s, 1583 sh, 1522 s, 1503 sh, 1486 s, 1464 s, 1437 s, 1368 s, 1311 m, 1264 m, 1243 s, 1212 m, 1196 m, 1180 m, 1162 m, 1152 m, 1126 s, 1064 w, 1049 m, 1017 m, 1000 m, 910 m, 902 sh, 854 m, 837 m, 828 w, 817 s, 782 m, 768 m, 757 m, 747 m, 714 w, 653 m, 636 m, 606 m, 583 w, 543 w, 530 w, 473 m, 441 m
III	3280 m, 2960 m, 2933 m, 2862 m, 1734 s, 1646 m, 1617 s, 1589 s, 1521 s, 1503 m, 1438 m, 1416 w, 1368 s, 1323 w, 1297 m, 1249 m, 1217 m, 1193 m, 1175 w, 1162 w, 1124 s, 1032 w, 997 m, 954 w, 908 w, 841 m, 819 s, 805 w, 779 m, 745 m, 706 w, 632 m, 607 w, 597 w, 567 w, 545 m, 520 m, 473 w, 443 m
IV	3309 m, 3073 w, 2955 w, 2930 m, 2860 m, 2815 w, 1739 s, 1645 m, 1612 m, 1602 s, 1573 s, 1520 sh, 1508 s, 1482 s, 1458 m, 1435 s, 1370 s, 1312 m, 1286 m, 1275 sh, 1231 m, 1205 sh, 1195 s, 1175 m, 1160 sh, 1150 m, 1123 m, 1082 w, 1040 m, 1016 m, 954 m, 897 m, 855 m, 838 m, 824 w, 817 m, 791 m, 766 w, 755 m, 743 m, 695 m, 656 w, 606 m, 590 m, 556 m, 535 w, 495 m, 467 m, 440 w
V	3305 m, 2950 m, 2930 m, 2863 m, 2815 w, 1725 s, 1643 s, 1619 s, 1600 s, 1570 s, 1560 sh, 1519 s, 1500 m, 1456 w, 1436 s, 1416 m, 1367 s, 1318 s, 1285 m, 1261 m, 1195 s, 1184 sh, 1152 m, 1123 s, 1063 w, 1010 m, 1000 m, 910 w, 900 m, 858 sh, 848 m, 818 m, 808 w, 788 m, 771 w, 745 m, 703 m, 635 m, 605 m, 597 sh, 532 m, 507 m, 477 w, 440 m
VI	3263 s, 2947 sh, 2931 m, 2860 m, 2813 w, 1730 s, 1641 s, 1615 sh, 1605 s, 1588 s, 1568 s, 1560 sh, 1518 s, 1508 s, 1496 sh, 1444 s, 1425 s, 1368 s, 1338 s, 1315 s, 1242 m, 1232 m, 1214 m, 1200 m, 1173 m, 1133 sh, 1120 s, 1103 m, 1075 w, 1057 m, 1005 s, 960 m, 926 m, 905 m, 875 m, 817 m, 798 m, 763 m, 751 m, 731 w, 693 m, 630 w, 603 m, 585 w, 506 s, 440 m
VII	3310 m, 2940 m, 2865 m, 2814 w, 1720 s, 1647 s, 1618 sh, 1608 s, 1595 sh, 1578 s, 1522 s, 1495 s, 1447 s, 1430 m, 1368 s, 1342 s, 1317 s, 1270 m, 1230 m, 1218 m, 1200 m, 1177 m, 1124 s, 1100 m, 1060 w, 1050 m, 1033 m, 1007 m, 962 m, 930 m, 903 m, 880 w, 858 w, 818 m, 798 m, 781 w, 763 m, 748 s, 731 m, 714 w, 605 m, 578 w, 548 w, 490 m, 477 m, 440 m, 418 w

s – strong, m – medium, w – weak, sh – shoulder.

I—VII to the analogous arylamino derivatives of 1-methoxycarbonyl-4-hydroxy-7-dimethylamino-3-phenoxazone [6, 7] suggest that the reaction studied in the present work is also governed by the bimolecular mechanism. The nucleophilic amino group is introduced at the position 2 activated by the neighbouring methoxycarbonyl group; the leuco form of the dye is an intermediate of the reaction.

The i.r. absorption band assignments (Table 2) were made in analogy with the published spectra of phenoxazine dyes [10—13], by studying the effect of the media upon the position of certain bands, and by comparison of the obtained spectra with those of  $^{15}\text{N}$  analogue of 1-methoxycarbonyl-2-phenylamino-7-dimethylamino-3-phenoxazone containing  $^{15}\text{N}$  in the bridge between the phenyl and phenoxazone part of the molecule. In addition to the absorption bands characteristic of phenoxazines ( $\nu(\text{C}=\text{C})$  and  $\nu(\text{C}=\text{N})$  at  $1650\text{—}1450\text{ cm}^{-1}$ ) the following bands were identified:  $\nu(\text{N—H})$  at  $3341\text{—}3263\text{ cm}^{-1}$  (in the case of the  $^{15}\text{N}$  derivative the  $\nu(\text{N—H})$  was shifted by  $9\text{ cm}^{-1}$  to the lower frequencies),  $\nu(\text{C}=\text{O})$  of the methoxycarbonyl group at  $1739\text{—}1720\text{ cm}^{-1}$ ,  $\nu(\text{C}=\text{O})$  of the phenoxazone ring at  $1621\text{—}1605\text{ cm}^{-1}$ ,  $\nu(\text{N—C}_6\text{H}_5)$  at  $1285\text{—}1260\text{ cm}^{-1}$  (in the case of the  $^{15}\text{N}$  derivative this band was shifted by  $2\text{ cm}^{-1}$  to the lower frequencies), and  $\delta(\text{CNH})$  at  $1523\text{—}1518\text{ cm}^{-1}$ . The low intensity band at  $\sim 2815\text{ cm}^{-1}$  and the intense band at  $\sim 1370\text{ cm}^{-1}$  reflect the presence of the dimethylamino group. A shift to the lower frequency values (by  $2\text{ cm}^{-1}$ ) of the medium intensity band at  $\sim 1160$  and  $770\text{ cm}^{-1}$  was observed in the spectra of the  $^{15}\text{N}$  analogues. The former band was assigned to the stretching vibration of the bond between the atoms of nitrogen and carbon of the phenoxazone ring; its appearance at low frequency values shows that, unlike for C—N bond of aromatic amines, no increase of the order of this bond occurs in the studied derivatives. The band at  $\sim 770\text{ cm}^{-1}$  may have appeared as a result of a rocking deformative vibration in the NH group [13].

The p.m.r. spectra of substances related to those of studied herein have not been described as yet. Therefore, for comparison, p.m.r. spectra (Table 3) of compounds VIII and IX were also measured. As a result of the strong effect of the  $-\text{N}(\text{CH}_3)_2$ ,  $-\text{COOMe}$  and  $\text{C}=\text{O}$  groups upon the aromatic protons all signals appearing in the spectra could be assigned. The signal of the NH proton was not visible in the spectrum. The following coupling constants were observed:  $J_{8,9} = 8.3\text{ Hz}$ ,  $J_{8,6} = 3.4\text{ Hz}$ , and  $J_{2,4} = 2.3\text{ Hz}$ . It is worth mentioning that the signal of the protons of the methoxycarbonyl group were shifted by 0.6 p.p.m. upfield, as a result of the introduction of the arylamino group into the position 2. This occurs obviously owing to the formation of an intramolecular hydrogen bond between NH and CO groups, resulting in hindered free rotation around the C—C bond between the methoxycarbonyl group and C-1. Thus, the protons of the methoxycarbonyl group become shielded exclusively by the C=N bond. The pronounced magnetic

Table 3

PMR data of some 3-phenoxazones

Compound	I	II	V	VII	VIII	IX	Intensity	Assignment
Chemical shift	3.13	3.08	3.13	3.08	3.13	3.14	6H	—N(CH <sub>3</sub> ) <sub>2</sub>
$\delta$ (p.p.m.)	3.23	3.25	3.30	3.23	3.88	3.95	3H	COOCH <sub>3</sub>
	—	3.83	—	3.83	—	—	3H	OCH <sub>3</sub> (anisidine)
	—	—	—	4.03	—	4.01	3H	OCH <sub>3</sub> [4]
	—	—	2.37	—	—	—	3H	CH <sub>3</sub> —C <sub>6</sub> H <sub>5</sub>
	6.49	6.42	6.40	—	6.22	—	1H	H [4]
	6.52	6.45	6.48	6.32	6.58	6.47	1H	H [6]
	6.73	6.80	6.62	6.82	6.65	6.63	1H	H [8]
	—	—	—	—	6.90	6.89	1H	H [2]
	7.63	7.58	7.54	7.50	7.54	7.52	1H	H [9]

anisotropy of this bond shows itself also by the high value of the chemical shift of the proton at the position 9 which lies in the direction of this bond and, consequently, is magnetically deshielded. As a result of the substitution of the hydrogen atom in the position 2 with the arylamino group the H-2 signal at 6.9 p.p.m. is no more present in the spectra of the respective substances. Another consequence of this substitution is the degradation of the H-4 doublet ( $J = 2.3$  Hz) to a singlet.

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