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The carboxyl derivatives of 6,8-di-(*tert.*-butyl)phenoxazine: Synthesis, oxidation reactions and fluorescence

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ABSTRACT

New carboxyl-containing *o*-aminophenols and phenoxazines were synthesized by condensation of 3,5-di-(*tert.*-butyl)-quinone with *p*-aminobenzoic and anthranilic acids. Oxidative transformations of the *o*-aminophenols and intermediate *o*-iminoquinones occur with the formation of the ESR detected phenoxazinyl radicals, which furthermore transform to phenoxazines or the dimeric products emerged through the radical attack at the C1 carbon of a formed phenoxazine. Molecular structure of the dimer obtained by oxidation of methyl ester of 4-[3,5-di-(*tert.*-butyl)-1-(2′-hydroxyphenyl)amino]benzoic acid was X-ray determined. Reaction of 4-[3,5-di-(*tert.*-butyl)-1-(2′-hydroxyphenyl)amino]benzoic acid with thionyl chloride gives rise to the formation of a derivative of 2-oxido-3H-benzo[d,j][1,2,3]oxathiazol system, the structure of which was established using X-ray crystallography. Solutions of methyl-6,8-di-(*tert.*-butyl)-10H-phenoxazine-3-carboxylate solvents display intense fluorescence covering a broad spectral region in the range of 400–600 nm.

1. Introduction

Phenoxazine and its derivatives have been long recognized as the important class of heterocyclic compounds exhibiting diverse biological activities [1], serving as sources of dyes for solid state solar cells [2,3] and light-emitting diodes [4], efficient scaffolds for radical-trapping antioxidants [5] and redox-active ligands of a broad variety of transition metal complexes of interest in catalysis and spintronics applications [6]. Special attention has also been given to the unique properties of phenoxazines as lipophilic stains and fluorescent chromophores for labeling biomolecules [7–9]. To be utilized as labels/probes of biomolecules, phenoxazines should usually be properly functionalized to ensure their coupling to targeted biologically important macromolecules. It has been previously shown that an efficient way of binding phenoxazine-based molecules to proteins and DNA consists in the side-chain carboxylation of phenoxazinium dyes or in the use of their easily hydrolyzed esters [10]. In this regard, of interest may be derivatives of phenoxazine containing carboxylic and alkoxycarbonyl groups directly linked to its aromatic rings. Two of four possible phenoxazine carboxylic acids, 10H-phenoxazine-1-carboxylic acid [11–13] and 10H-phenoxazine-2-carboxylic acid [14], had been previously synthesized and their derivatives showed manifold biological (antiinflammatory, antitumor, antimigraine and other) activities. At the same time no information is available in literature on spectroscopic and fluorescent properties of these acids and their derivatives as well as on the synthesis of derivatives of other, 10H-phenoxazine-3 and 10H-phenoxazine-4-carboxylic acids. Therefore, the main goals of the present work consisted in development of a facile procedure for the preparation of first derivatives of the former acid, its extention to 1-carboxy analogues and gaining insight into their fluorescent characteristics and oxidation reactions. Phenoxazines are not particularly fluorescent compounds and to exhibit sufficiently intense fluorescence, the molecules of phenoxazines, benzophenoxazines and phenoxazinium salts must bear both strong electron withdrawing and releasing substituents

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[5,7,9]. A rare example of a phenoxazine displaying strong fluorescence, while having in its molecule a single electron withdrawing substituent, is given by 1-cyano-7,9-di-(*tert.*-butyl) phenoxazine [9]. The alkyl groups in the aryl ring help to increase solubility of the polar heterocyclic compound in nonpolar solvents and enhance its fluorescence. These findings enable one to expect that structurally similar carboxyl and alkoxycarbonyl phenoxazines can manifest fluorescent properties.

2. Results and discussion

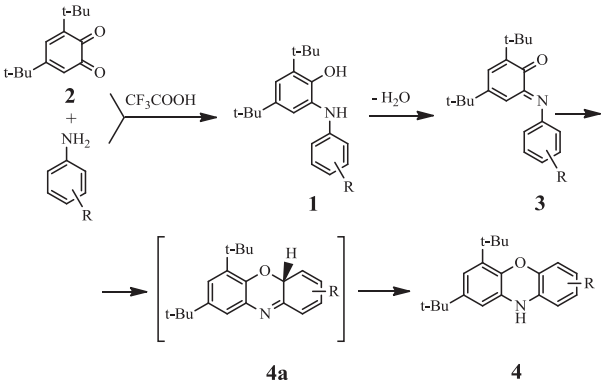
Within the broad range of synthetic routes to derivatives of phenoxazine (see Refs. [15,16] for reviews), the simplest one consists in the condensation of *o*-aminophenols (or their precursors) with vicinal dihalo [13] or dihydroxy [17] arenes. We have suggested that sterically shielded *o*-aminophenol derivatives **1** well soluble in nonpolar solvents and readily prepared by the reaction of 3,5-di-(*tert.*-butyl)-catechol with various aromatic and heterocyclic amines [18,19] can also serve as good precursors to the properly functionalized, particularly containing carboxyl substituents, phenoxazines.

Another conceivable route to *o*-aminophenols **1** involves replacement of 3,5-di-(*tert.*-butyl)-catechol by an accessible product of its oxidation, *o*-quinone **2** (Scheme 1). Condensation of quinone **2** with arylamines proceeds at mild conditions via its less hindered carbonyl group and, when being performed at aerobic conditions, do not usually comes to rest at the primary addition product **1**, but affords corresponding quinone imines **3**, which in their turn readily cyclize to phenoxazines **4** through the formation of the intermediate metastable 4a*H*-phenoxazines **4a** [20,21]. It may, therefore, be anticipated that by retarding or inhibiting the elimination water stage **1** → **3** one can isolate *o*-N-arylaminophenols as the final reaction products and use these as precursors to the targeted carboxyphenoxazines. On the other hand, the transformations shown in Scheme 1 may be regarded as an expedient direct way to these compounds.

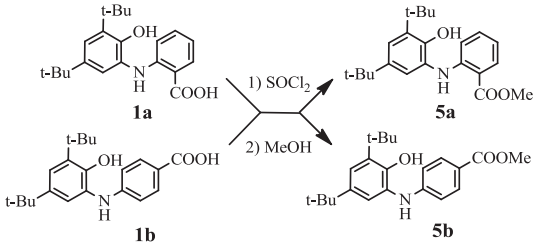
In the present work, we succeeded to show that the carboxyl containing *o*-N-arylaminophenols **1** (R = COOH) can be prepared by carrying out the reaction depicted in Scheme 1 in the presence of catalytic amounts of trifluoroacetic acid which blocks elimination of water from the primarily formed *o*-aminophenols. The reaction proceeds at aerobic conditions under prolonged heating of benzene or toluene solutions of *o*-quinone **2** with an excessive (one-and-a-half) amount of *o*- or *p*-aminobenzoic acids. The synthesized *o*-aminophenols **1a, 1b** were purified by column chromatography and fully characterized by elemental analysis, MS, ^{1}H NMR and IR spectroscopy. Methyl esters **5a,b** of the prepared *o*-N-arylaminophenols, were obtained in high yields either by a two-step reaction including conversion of **1a,b** to the chloranhydrides and their subsequent treatment with methanol (Scheme 2), or a direct condensation of methylaminobenzoates with 3,5-di-(*tert.*-butyl)-*o*-benzoquinone **2** (Scheme 1, R = COOMe).

An interesting ramification of the two-step esterification process presented in Scheme 2 has been found in the case of the reaction with *o*-N-phenylaminophenol **1b**. When using an excessive (~1:2) amount of thionyl chloride converting the carboxylic acid into the corresponding acid chloride its second molecule interacts with the hydroxyl and imine groups of the *o*-aminophenol to close the five-membered oxathiazol ring. The formed heterocyclic acid chloride readily reacts with arylamines (Scheme 3). The X-ray determined structure of one of thus prepared arylamides is shown in Fig. 1. The envelope conformation of **6** with the substantial deviation of the O1X atom from the S1XN18C19C32O33 plane are typical for the 1,2,3-oxathiazol cycles [22].

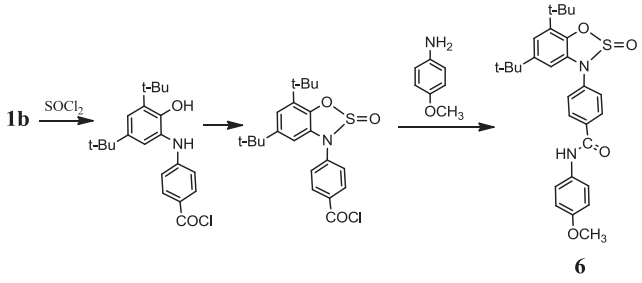
The proneness of *o*-iminoquinones **3** to oxidation reactions is manifested by the formation of phenoxazines occurring under prolonged reflux of toluene solutions of methylbenzoates **5** (or the initial components for their formation), as exemplified by the case of 6,8-di-(tert.-butyl)-3-methoxycarbonyl-10H-phenoxazine **7** shown in Scheme 4. Under treatment of **7** with a mild oxidant



Scheme 1. Synthesis of *o*-N-arylaminophenols **1** and phenoxazines **4** by the reaction of *o*-quinone **2** with arylamines.



Scheme 2. Preparation of methyl[3,5-di-*tert.*-butyl)-(2′-hydroxyphenyl)amino] benzoates.



Scheme 3. Formation of 2-oxido-3H-benzo[d,j] [1–3]oxathiazol-3-yl system in the reaction of *o*-N-phenylaminophenol **1b** with thionyl chloride.

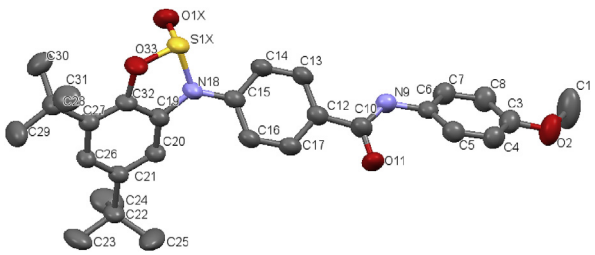
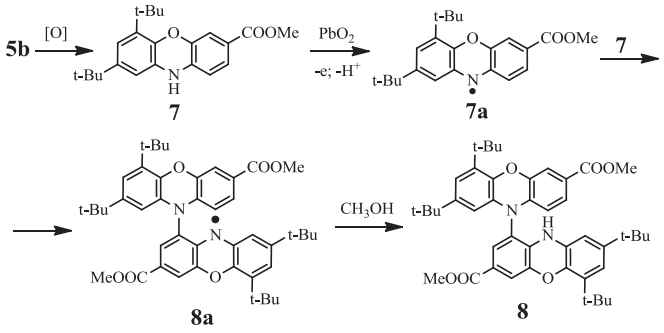


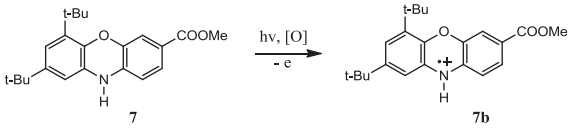
Fig. 1. Molecular structure of 4-(5,7-di-*tert.*-butyl-2-oxido-3H-benzo[d,j] [1–3]oxathiazol-3-yl)-N-(4-methoxyphenyl) benzamide **6**. The main crystallographic parameters and bond of distances are given in SI (Tables S1 and S2).



Scheme 4. Oxidation of **5b** leading to the formation of dimer **8**.

(PbO_2, toluene, 293 K) it becomes possible to detect the formation of the intermediate stable radicals (Scheme 4) established by ESR spectroscopy. A number of stable phenoxazinyl radicals similar to **7a** had been previously registered as the intermediates appearing in the oxidation of the primary products of condensation of *o*-benzoquinones with arylamines [21,23]. Under the conditions of the reaction (see experimental part), **7a** reacts with the formed phenoxazine **7** to give the radical **8a** (Fig. 2) converted then into the dimer **8** whose structure was established by X-ray crystallography (Fig. 3). Alkaline hydrolysis of the 6,8-di-(tert.-butyl)-3-methoxycarbonyl-10H-phenoxazine **7** leads, instead of the expected 6,8-di-*tert*-butyl-10H-phenoxazine-3-carboxylic acid, to a dimer **8** with a quantitative yield. In **8**, the two virtually planar phenoxazine rings are twisted by the angle close to 90°. It is worth of noting that formation of dimers of the parent phenoxazine under its oxidation had been first described by H. Musso in 1959 [24], who correctly assigned the structure of the major product of the reaction of phenoxazine with kalium and bromine to the 1,10 (4,9′ in the original nomenclature) type of bound monomers based on exclusively UV–Vis spectra of the compounds.

Stable character of radicals **7a**, **8a** formed under oxidation of **7** and other previously studied phenoxazine-containing radicals [20,21] is ensured by the presence in their molecules of two bulky *tert.*-butyl groups. We have found that a stable radical-cation **7b** is readily formed at aerobic conditions under UV (365 nm) irradiation of chloroform solution of **7** (Scheme 5). The ESR spectrum of **7b** is shown in Fig. 4. Fig. 5 illustrates kinetics of gradual accumulation of the radical-cation **7b** with increase in time of illumination of the solution. 6,8-Di-(*tert.*-butyl-10H-phenoxazine-1-carboxylic acid **9** (**4**, R = 1-COOH, Scheme 1) has been obtained by the reaction of 3,5-di-(*tert.*-butyl)-*o*-quinone **2** with anthranilic acid performed in solution of isopropyl alcohol and catalyzed by trifluoroacetic acid (Scheme 6). Under the action of a mild oxidant (PbO_2, 293 K, toluene) **9** affords a stable radical **10** identified by its ESR spectrum (Fig. 6).



Scheme 5. Formation of a stable radical-cation **7b** under irradiation of chloroform solution of 6,8-di-(*tert.*-butyl)-3-methoxycarbonyl-10H-phenoxazine **7**.

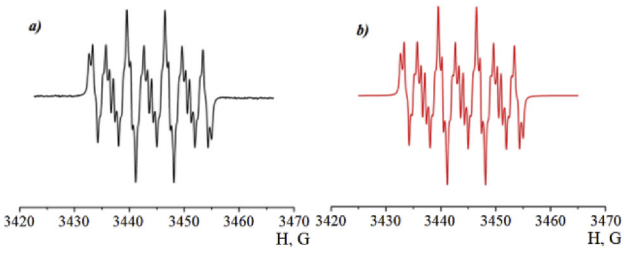


Fig. 2. The experimental (*a*) and simulated (*b*) ESR spectra of radical **8a** (PbO_2, toluene, 298 K) g = 2.00; $\alpha_{(N)} = 6.95$ G; $\alpha_{1(H)} = 3.75$ G; $\alpha_{3(H)} = 2.4$ G; $\alpha_{12,14(H)} = 0.7$ G.

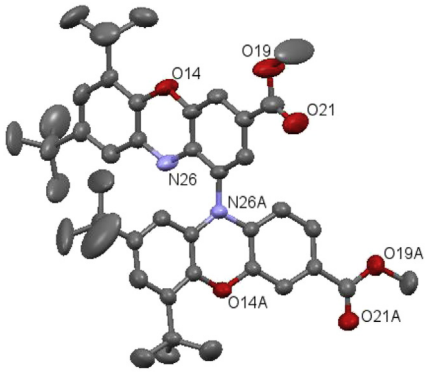


Fig. 3. Molecular structure of 6,6′-dimethyl-8,8′-di-(*tert.*-butyl)-10H-[1,10′-bisphenoxazin]-3,3′-dicarboxylate **8**. The main crystallographic parameters and bond of distances are given in SI (Tables S1 and S3).

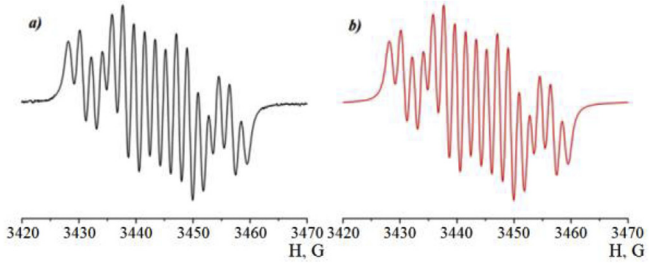


Fig. 4. The experimental (*a*) and simulated (*b*) ESR spectra of cation-radical **7b** formed under UV-irradiation of chloroform solution of **7** (~60 s, $CHCl_3$, 298 K): g = 2.00; $\alpha_{(N)} = 7.45$ G; $\alpha_{1(H)} = 3.79$ G; $\alpha_{3(H)} = 2.10$ G; $\alpha_{7(H)} = 7.45$ G; $\alpha_{11(H)} = 1.77$ G; $\alpha_{12,14(H)} = 0.55$ G.

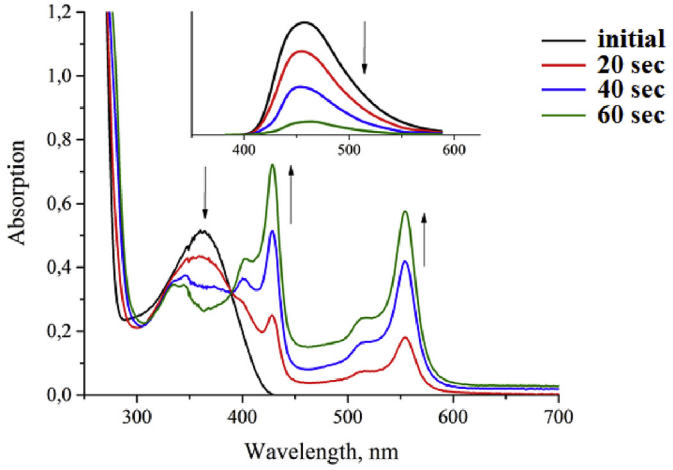
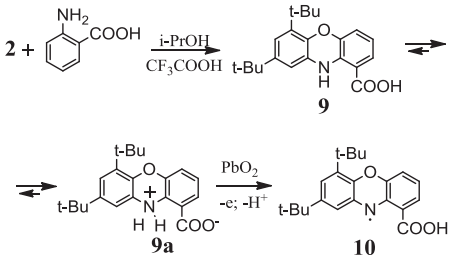


Fig. 5. UV–Vis absorption and emission (*incut*) spectra of chloroform solution ($C = 5.6 \times 10^{-5}$ M, 293 K) of 6,8-di-(*tert.*-butyl)-3-methoxycarbonyl-10H-phenoxazine **7** manifesting appearance and gradual accumulation of radical-cation **7b** under irradiation of the solution with the light of 365 nm: before irradiation (*black*) and after irradiation (*colour*) for 20, 40 and 60 s.



Scheme 6. Synthesis of 6,8-di-(*tert.*-butyl)-10H-phenoxazine-1-carboxylic acid **9**.

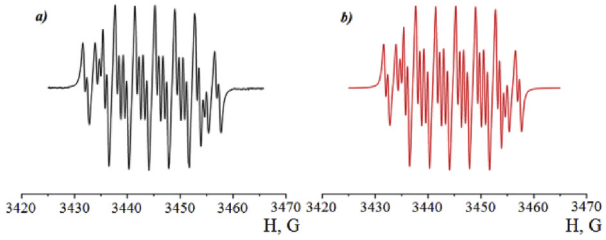
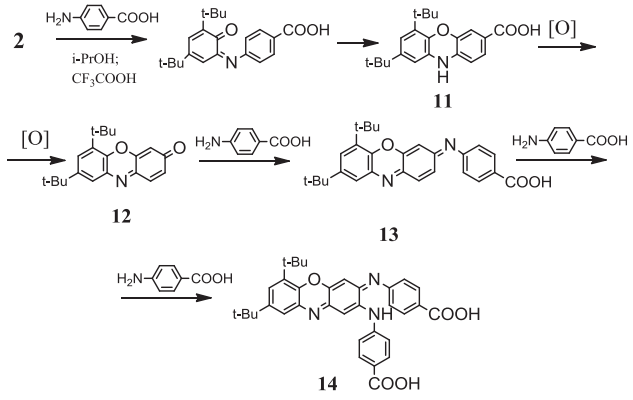


Fig. 6. The experimental (*a*) and simulated (*b*) ESR spectra of radical **10** (PbO_2, toluene, 298 K) g = 2.00; $\alpha_{(N)}$ = 7.55 G; $\alpha_{1,14(H)}$ = 3.75 G; $\alpha_{3(H)}$ = 2.31 G; $\alpha_{12(H)}$ = 0.7 G.

Formation of the cation-radical **7b** has also been registered by cyclic voltammetry (Fig. S1). The values of electrochemical parameters of first oxidation wave of **7**–**9** are given in SI (Table S4).

The course of the transformations shown in Scheme 1 strongly depends on the solvent. While no 10H-phenoxazine-1-carboxylic acid **9** (**4**, R = 1-COOH) was isolated as a product of the reaction carried out in benzene or toluene solution, performance of the reaction in the solution of isopropyl alcohol affords **9** obtained in moderate yield. More complicated is the reaction of **2** with *p*-aminobenzoic acid, which does not terminate at the formation of the targeted 10H-phenoxazine-3-carboxylic acid **11** and being performed at aerobic conditions involves its rapid oxidation to the intermediate di-(*tert*-butyl)phenoxazin-3-one **12** eventually transformed to 6,8-di-(*tert*-butyl)-N-(4-carboxyphenyl)-3-(4-carboxyphenyl)imine)-3H-phenoxazine-2-amine **14** (Scheme 7). This mechanism is fully analogous to that suggested and testified by X-ray structural determination of the product for the reaction of **2** with *p*-anisidine [23].

A distinguished feature of the prepared *o*-N-arylaminophenols and derivatives of 6,8-di-(*tert.*-butyl)phenoxazine is the bright fluorescence observed under UV irradiation (290–360 nm) of their



Scheme 7. Reaction of 3,5-di-(*tert.*-butyl)-*o*-quinone **2** with anthranilic and *p*-aminobenzoic acid.

solutions. The absorption and emission spectra of *o*-N-arylaminophenols **5** pictured in Fig. 7 demonstrate substantial batochromic shift of their longest wavelength absorption band and the corresponding fluorescence on passing from nonpolar (hexane) to polar (acetonitrile) solvent.

Particular emphasis is to be placed upon the rather high quantum efficiency of the fluorescence exhibited by methyl-4-[3,5-di-tert.-butyl)-(2′-hydroxyphenyl)amino] benzoate **5b** sharply and unexpectedly contrasted with low fluorescence of its isomer **5a** (Table 1). **5b** has low solubility in water, but it is much better soluble in water base. Same type solvatochromic behavior is inherent also in phenoxazines **7**–**9** (Fig. 8) displaying higher quantum efficiency of the fluorescence (Table 1). Both absorption and emission spectra of the acid **9** are notably shifted to the red region of the spectrum, which is, apparently, due to its specific dipolar structure **9a** (Scheme 6) strongly stabilized in the solution of polar acetonitrile. The quantum yield of fluorescence shown by **9** is significantly lower than those of **7** and **8**, which fact can be explained as the consequence of self-quenching in face-to-face aggregates typical of phenoxazine-containing dyes [7]. At the same time the acid **9**

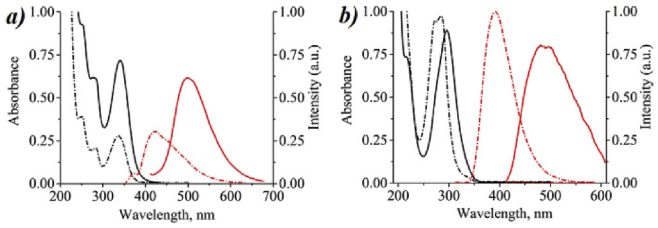


Fig. 7. UV–Vis absorption (*black*) and emission (*red*) spectra of methyl-2-[3,5-di-tert.-butyl)-(2′-hydroxyphenyl)amino] benzoate **5a** (*a*) and methyl-4-[3,5-di-tert.-butyl)-(2′-hydroxyphenyl)amino] benzoate **5b** (*b*) in acetonitrile (*solid*) and hexane (*dash and dot*).

Table 1
UV–Vis absorption and emission spectra of *o*-N-arylaminophenols and derivatives of 6,8-di-(*tert.*-butyl)phenoxazine: positions of maxima of the longest wavelength absorption (λ_{max}) and emission (λ^{fl}_{max}) band, Stokes shifts (η) and quantum yields of fluorescence (Φ_{fl}). A picture of Fig. S2 (SI) shows changes in colour of hexane solutions **5b**, **7** and **8** before and after irradiation with UV light (365 nm).

Compound	λ_{max}, nm		λ^{fl}_{max}, nm		η, nm		Φ_{fl}	
	CH_3CN	C_6H_{14}	CH_3CN	C_6H_{14}	CH_3CN	C_6H_{14}	CH_3CN	C_6H_{14}
1a	341	342	398	383	57	41	<0.01	<0.01
1b	296	289	469	405	173	116	<0.01	<0.01
5a	341	337	498	422	157	85	<0.01	<0.01
5b	296	284	489	391	193	107	<0.01	0.31
7	358	348	465	404	107	56	0.49	0.55
8	348	346	471	431	123	85	0.19	0.51
9	646	663[a]	763	786[a]	117	123[a]	<0.01	<0.01[a]

[a] In toluene.

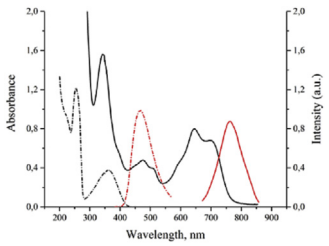


Fig. 8. UV–Vis absorption (*black*) and emission (*red*) spectra for methyl-6,8-di-*tert*-butyl-10H-phenoxazine-3-carboxylate **7** (*dash and dot*) and 6,8-di-*tert*-butyl-10H-phenoxazine-1-carboxylic acid **9** (*solid*) in acetonitrile.

intensely fluoresce in the spectral region substantially red-shifted compared to that covered by fluorescent spectra of the thoroughly studied Nile Red and Nile Blue phenoxazine dyes [7,25].

The water-solubility of Nile Red is extremely poor, but in other solvents its fluorescence maxima and intensity are good indicators of the dye's environment-polarity mentioned above, this solvatochromic effect is such that polar media cause a red-shift but decreased fluorescence intensity. This decreased fluorescence intensity is probably due to self-quenching of the dye in face-to-face aggregates. Consequently, this dye is particularly useful for studying lipids and events that involve impregnation of the dye in a polar media. Surprisingly, very few water-soluble analogues of Nile Red have been reported, and only limited fluorescence data have been given for those.

3. Conclusions

The carboxyl containing *o*-N-arylaminophenols **1** (R = COOH) can be prepared by the condensation of 3,5-di-(*tert*.-butyl)-*o*-quinone **2** with *p*-aminobenzoic and anthranilic acids in the presence of catalytic amounts of trifluoroacetic acid which blocks elimination of water from the primary products of the condensation. Oxidation reactions of the *o*-N-phenylaminocarboxyphenols **1** and their esters **5** leading to the formation of 10H-phenoxazine derivatives readily occur at mild conditions involving the formation of stable radicals registered by their ESR spectra. The compounds display intense fluorescence at reasonably long wavelengths in solutions of both polar and nonpolar solvents (Fig. 8, Table 1). The prepared 6,8-di-(*tert*.-butyl)-10H-phenoxazine-1-carboxylic acid **9** exists in polar in solvents as the inner salt and fluoresce at the spectral region substantially red shifted (to 650–850 nm) compared with other *o*-N-arylaminophenols **1** (R = COOH) and phenoxazine derivatives **7**, **8**. The acid **9** intensely fluoresce in the spectral region substantially red-shifted compared to that covered by fluorescent spectra of the thoroughly studied Nile Red and Nile Blue phenoxazine dyes [7,25]. The phenoxazines **7**–**9** are low soluble in water, but are well soluble in hexane, benzene and toluene. In combination with their pronounced fluorescent properties, good solubility of these compounds in nonpolar solvents solubility can be useful for studying lipids.

4. Experimental section

4.1. Materials and methods

All reagents and solvents were purchased from commercial sources (Aldrich) and used without additional purification. The compounds were characterized by ^{1}H NMR, mass spectra, elemental analysis, ESR, IR-, UV–Vis absorption spectra and cyclic voltammetry. ^{1}H NMR spectra were recorded on Bruker Avance spectrometer (600 MHz) in DMSO-d_6 or $CDCl_3$ solutions, the signals were referred with regard to the signals of residual protons of deutero-solvents (7.24 and 2.50 ppm, respectively), δ values were measured with precision 0.01 ppm. The mass spectra (electron impact, 70 eV, direct sample injection) were obtained on a Shimadzu GCMSQP2010SE instrument. Elemental analysis was performed by the classical microanalysis method. Melting points were determined using a PTP (M) apparatus and were left uncorrected. Control on the progress of the reactions and the individuality of products of the reactions was accomplished using thin layer chromatography with Silufol UV-245 wafers (benzene and methylene dichloride as eluents and iodine as developer). ESR spectra were recorded on X-band Bruker EMX spectrometer. The theoretical spectrum was calculated using the Bruker WinEPR Simfonia v.1.25 program. IR spectra were recorded on a Varian Excalibur 3100 FT-IR instrument using the attenuated total internal reflection technique (ZnSe crystal). Electronic absorption and emission spectra were recorded on Cary Scan 100 (Varian) and Cary Eclipse (Varian) spectrophotometers. Quantum yields of fluorescence were determined by the Parker – Rees method [26,27] with the use of methanol solution of cresyl violet acetate ($\Phi_{fl} = 0.54$) as the standard ($\lambda_{excitation} = 508$ nm). The cyclic voltammetry of **7**–**9** was measured with the use of three-electrode configuration (glassy-carbon working electrode, Pt counter electrode, Ag/Ag^+ reference electrode (0.01 M $AgNO_3$ in CH_3CN)) and potentiostat – galvanostat Elins P-45X.

The datasets of reflections from single crystals of compounds **6** and **8** were obtained on an automated diffractometer Smart Apex II CCD (MoKα, graphite monochromator, ω-scanning). The structure was solved by direct methods (SHELXTL 6.14) and refined by the full-matrix least-squares procedure in anisotropic approximation for non-hydrogen atoms (SHELXL-2014/7). Positions of hydrogen atoms were calculated geometrically and included in the refinement as riding groups. CCDC 1865077, 1842671 contain the supplementary crystallographic data for **6** and **8**. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk.

4.2. Compounds

4.2.1. 2-[3,5-di-tert.-butyl)-1-(2′-hydroxyphenyl)amino] benzoic acid (**1a**)

Benzene solution (10 mL) of 880 mg (0.004 mol) of 3,5-di-(*tert*.-butyl)-1,2-benzoquinone and 850 mg (0.0062 mol) of 2-aminobenzoic acid contained 0.03 mL of trifluoroacetic acid was refluxed for 8 h. The reaction mixture was partially evaporated and passed through a SiO_2 chromatographic column (l = 15 cm, d = 2.5 cm, CH_2Cl_2), to select the fraction with $R_f > 0.5$. The solvent was evaporated and the precipitate crystallized from hexane and then from methanol to give 690 mg (51%) of the amorphous colorless substance, m.p. 229–230°C. IR (KBr, ν, cm^{-1}): 3455 (O-H, C(O)O-H), 3335 (N–H), 2950–2866 (C–H), 1663 (C=O). ^{1}H NMR (δ, ppm., DMSO-d_6): 12.79 s (1H, COOH), 9.13 s (1H, NH), 8.28 s (1H, OH), 7.85 d (J = 7.9 Hz, 1H, C6), 7.28 d (J = 7.1 Hz, 1H, C4), 7.07 d (J = 2.2 Hz, 1H, C6′), 7.03 d (J = 2.2 Hz, 1H, C4′), 6.71–6.60 m (2H, C3-5), 1.38 s (9H, C3′-*t*-Bu), 1.23 s (9H, C5′-*t*-Bu); m\z: 341 (100%) [M$^+$]; Found: C, 73.85; H, 7.99; N, 4.08. $C_{21}H_{27}NO_3$ requires C, 73.87; H, 7.97; N, 4.10. The data on IR, ^{1}H NMR, mass-, UV–Vis and emission spectra are collected in SI (Figs. S3–S9).

4.2.2. 4-[3,5-di-tert.-butyl)-1-(2′-hydroxyphenyl)amino]benzoic acid (**1b**)

Prepared using the procedure described for the synthesis of **1a**. In chromatographic purification, the fraction exhibiting bluish-green fluorescence with R_f = 0.15–0.75 was selected. Pale pink crystals, m.p. 223–225°C. The yield = 68%. IR (KBr, ν, cm^{-1}): 3384 (O-H, C(O)O-H), 3353 (N–H), 2995–2868 (C–H), 1650 (C=O). ^{1}H NMR (δ, ppm, DMSO-d_6): 12.07 s (1H, COOH) 8.15 s (1H, NH), 7.80 s (1H, OH), 7.69 d (J = 8.7 Hz, 2H, 2-C2,6), 7.05 d (J = 2.2 Hz, 1H, C6′), 7.00 d (J = 2.2 Hz, 1H, C4′), 6.67 (d, J = 8.7 Hz, 2H, 2-C3,5), 1.38 s (9H, C3-*t*-Bu), 1.22 s (9H, C5-*t*-Bu); m\z: 341 (100%) [M$^+$]; Found: C, 73.88; H, 7.96; N, 4.10. $C_{21}H_{27}NO_3$ requires C, 73.87; H, 7.97; N, 4.10. The data on IR, ^{1}H NMR, mass-, UV–Vis and emission spectra are collected in SI (Figs. S10–S16).

*4.2.3. Methyl-2-[3,5-di-tert.-butyl)-(2′-hydroxyphenyl)amino] benzoate (**5a**)*

Benzene solution (30 mL) of 1.1 g (5.0 mmol) of 3,5-di-(*tert.*-butyl)-1,2-benzoquinone and 1.1 mL (7.5 mmol) of methyl ester of 2-aminobenzoic acid contained 0.05 mL of trifluoroacetic acid was refluxed for 2 h and then for 12 h using Dean-Stark apparatus. The reaction mixture was purified by passing through a SiO_2 chromatographic column (l = 25 cm, d = 3.0 cm, benzene) to select a bright yellowish-green fraction (лл 380 nm) with R_f 0.75. The syrup-like product gradually crystallized at room temperature during 2–3 days and was recrystallized from methanol to give 1.35 g (76%) of yellow crystals of **7a** with m.p. 106–108°C. IR (KBr, ν, cm^{-1}): 3402 (O-H), 3330 (N–H) 2953, 2866 (C–H), 1677 (C = O). ^{1}H NMR (δ, ppm, DMSO-d_6): 8.88 s (1H, NH), 8.33 s (1H, OH), 7.86 d (*J* = 8.0, 1.5 Hz, 1H, C6), 7.32 m (1H C4), 7.09 d (*J* = 2.2 Hz, 1H, C6′), 7.04 d (*J* = 2.2 Hz, 1H, C4′), 6.71–6.61 m (2H, C3-5), 2.50 m (3H, COOMe), 1.39 s (9H, C3′-*t*-Bu), 1.23 s (9H, C5′-*t*-Bu); m\z: 355 (100%) [M^+]; Found: C, 74.34; H, 8.25; N, 3.92. $C_{22}H_{29}NO_3$ requires C, 74.33; H, 8.22; N, 3.94. The data on IR, ^{1}H NMR, mass-spectra are collected in SI (Figs. S17–S19).

*4.2.4. Methyl-4-[3,5-di-tert.-butyl)-(2′-hydroxyphenyl)amino] benzoate (**5b**)*

Toluene solution of 150 mg (0.44 mmol) of acid **1b** and 0.2 mL (1.0 mmol) of thionyl chloride was refluxed for 2 h until emission of HCl was extinguished. The solution was diluted with 2 mL of methanol and was allowed to stand at room temperature for 5–6 h. The precipitated crystals were filtered off and crystallized from acetonitrile to give 140 mg (89%) of **7b**. Light yellow crystals, m.p. 218–220°C. IR (KBr, ν, cm^{-1}): 3501 (O-H), 3312 (N–H), 2953–2855 (C–H), 1694 (C = O). ^{1}H NMR (δ, ppm, DMSO-d_6): 8.19 s (1H, NH), 7.90 s (1H, OH), 7.72 d (*J* = 8.8 Hz, 2H, C2,6), 7.06 d (*J* = 2.2 Hz, 1H, C6′), 7.00 d (*J* = 2.2 Hz, 1H, C4′), 6.69 (d, *J* = 8.8 Hz, 2H, C3,5), 2.49 m (3H, COOMe), 1.38 s (9H, C6-*t*-Bu), 1,22 s (9H, C8-*t*-Bu); m\z: 355 (100%) [M^+]; Found: C, 74.30; H, 8.21; N, 3.93. $C_{22}H_{29}NO_3$ requires C, 74.33; H, 8.22; N, 3.94. The data on IR, ^{1}H NMR, mass-spectra are collected in SI (Figs. S20–S22).

*4.2.5. 4-(5,7-di-tert-butyl-2-oxido-3H-benzo[d][1,2,3]oxathiazol-3-yl)-N-(4-methoxyphenyl) benzamide (**6**)*

340 mg (1 mmol) of 4-(3,5-di-(*tert.*-butyl)-2-hydroxyphenylamino)benzoic acid **1b** was dissolved in 15 mL of toluene and thionyl chloride (0.2 mL, 2.8 mmol) was added dropwise. The solution was heated to boiling. The end of the reaction was monitored for the isolation of hydrogen chloride. The solution of 150 mg (1.2 mmol) of *p*-anisidine in 5 mL of toluene then was added to the reaction mixture. The reaction mass was boiled for an additional 2 h (until the completion of the HCl excretion). The reaction mass was left overnight, the precipitated crystals were filtered and recrystallized from toluene. White crystalline powder, m.p.: 200–202 °C. Yield: 380 mg (82%). IR (KBr, ν, cm^{-1}): 3312 (N–H), 2953–2870 (C–H), 1691 (C = O), 1174 (S=O). ^{1}H NMR ($CDCl_3$): 8.20 d (2H, *J* = 8.5 Hz, 4-H), 8.01 s (1H, NH), 7.76–7.78 t (4H, *J* = 6.7 Hz), 7.28 d (1H, *J* = 1.9 Hz, 1-H), 7.12–7.14 dd (2H, *J* = 2.3 Hz, *J* = 6.8 Hz, 6-H), 7.07 d (1H, *J* = 1.9 Hz, 2-H), 4.03 s (3H, OCH_3), 1.68 s (9H, *t*-Bu), 1.50 s (9H, *t*-Bu); m\z: 492 (100%) [M^+]; Found: C, 68.28; H, 6.59; N, 5.67. $C_{28}H_{32}N_2O_4S$ requires C, 68.27; H, 6.55; N, 5.69. The data on IR, ^{1}H NMR, mass-spectra are collected in SI (Figs. S23–S25).

*4.2.6. Methyl-6,8-di-tert-butyl-10H-phenoxazine-3-carboxylate (**7**)*

A solution of 1.1 g (5.0 mmol) of 3,5-di-(*tert.*-butyl)-1,2-benzoquinone and 1.13 g (7.5 mmol) of 4-aminobenzoic acid methyl ester in 30 mL of benzene was boiled with the reverse in the presence of 0.05 mL (0.1 mol-equivalents) of trifluoroacetic acid for 2 h. Then, it was boiled for another 6 h with a Dean-Stark nozzle. The reaction mass was chromatographed on an Al_2O_3 column (l = 20 cm, d = 3.0 cm, benzene), selecting a fraction with a blue fluorescence (380 nm) and R_f 0.45–0.55. The isolated product was crystallized first from acetone, then from methanol. 970 mg (55%) of light yellow crystals were obtained, m.p. 246–248 °C. IR (KBr, ν, cm^{-1}): 3310 (N–H), 2953–2870 (C–H), 1681 (C = O). ^{1}H NMR (δ, ppm, DMSO-d_6): 8.70 s (1H, NH), 7.39 dd (*J* = 8.2, 1.2 Hz, 1H, C^2), 7.10 d (*J* = 1.2 Hz, 1H, C^4), 6.64 d (*J* = 2.0 Hz, 1H, C^9), 6.50 d (*J* = 8.2 Hz, 1H, C^1), 6.44 d (*J* = 2.0 Hz, 1H, C^7), 3.76 s (3H, COOMe), 1.20 s (9H, C^6-tBu), 1,33 s (9H, C^8-tBu) m\z: 353 (100%) [M^+]; Found: C, 74.73; H, 7.73; N, 3.95. $C_{22}H_{27}NO_3$ requires C, 74.76; H, 7.70; N, 3.96. The data on IR, ^{1}H NMR, mass-, UV–Vis and emission spectra are collected in SI (Figs. S26–S30).

*4.2.7. Dimethyl-6,6′,8,8′-tetra-tert-butyl-10H-[1,10′-bisphenoxazine]-3,3′-dicarboxylate (**8**)*

a) Prepared using the procedure described for the synthesis of **7.** The mixture was refluxed in toluene for 20 h. The crude product was purified by column chromatorgaphy (Al_2O_3, l = 20 cm, d = 3.0 cm, benzene), selecting the fraction with blue-green fluorescence (380 nm) and R_f 0.65–0.75, crystallized from methanol. 340 mg (18%) of light yellow crystals were obtained, m.p. 308–310 °C. IR (KBr, ν, cm^{-1}): 3327 (N–H), 2916–2854 (C–H), 1717 (COOMe), 1702 (C = O). ^{1}H NMR (δ, ppm, $CDCl_3$): 7.51 d (*J* = 1.6 Hz, 1H, C^4), 7.45 d (*J* = 1.7 Hz, 1H, $C^{4'}$), 7.42 m (2H, $C^{2-2'}$), 6.88 d (*J* = 2.0 Hz, 1H, C^9), 6.78 d (*J* = 2.0 Hz, 1H, C^7), 6.36 d (*J* = 2.0 Hz, 1H, $C^{9'}$), 6.13–6.10 m (2H, $C^{7'-1'}$), 5.88 s (1H, NH), 3.84 (2s, 6H, 2-COOMe), 1.47, 1.43, 1.20, 1.14 (4s, 36H, 4-tBu); Found: C, 74.95; H, 7.44; N, 3.95. $C_{44}H_{52}N_2O_6$ requires C, 74.97; H, 7.44; N, 3.97.

b) 353 mg (1 mmol) of 6,8-di-(tert.-butyl)-3-methoxycarbonyl-10H-phenoxazine **7** was dissolved in 15 mL i-PrOH and KOH (56 mg, 1 mmol) was added. The solution was heated to boiling for 15 min. Then the solution was cooled, the precipitate dimethyl-6,6′,8,8′-tetra-*tert*-butyl-10H-[1,10′-bisphenoxazine]-3,3′-dicarboxylate (**8**) was filtered off, recrystallized from methanol. Yield: 302 mg (86%). The data on IR, ^{1}H NMR spectra are collected in SI (Figs. S31–S32).

*4.2.8. 6,8-di-tert-butyl-10H-phenoxazine-1-carboxylic acid, (**9**)*

880 mg (4 mmol) of 3,5-di-(*tert.*-butyl)-1,2-benzoquinone **2** and 820 mg (6 mmol) of anthranilic acid were dissolved in 20 mL of isopropyl alcohol. The solution heated at reflux during 12 h, periodically adding catalytic amounts of trifluoroacetic acid. The reaction mixture was evaporated. Formed precipitate was dissolved in 50 mL of 0.1 N NaOH. The solution was cooled and filtered from the insoluble precipitate. Then the mother liquor was neutralized with concentrated HCl, the resulting dark colored precipitate was filtered off, washed with water and dried. Black crystalline powder, m.p.: 238–240 °C. Yield: 760 mg (56%). IR (KBr, ν, cm^{-1}): 3452 (COO–H), 3332 (N–H), 2953–2854 (C–H), 1667 (C = O). ^{1}H NMR (DMSO-d_6): 12.85–13.10 s (1H, COOH), 9.14 s (1H, NH), 8.33 s (1H, 9-H), 7.84 d (1H, *J* = 7.8 Hz, 7-H), 7.25–7.31 t (1H, *J* = 7.8 Hz, 2-H), 7.02–7.06 dd (1H, *J* = 2.1 Hz, *J* = 8.6 Hz, 4-H), 6.62–6.67 t (1H, *J* = 8.4 Hz, 3-H), 1.37 s (9H, *t*-Bu), 1.22 s (9H, *t*-Bu); Found: C, 74.31; H, 7.40; N, 4.15. $C_{21}H_{25}NO_3$ requires C, 74.31; H, 7.42; N, 4.13. The data on IR and UV–Vis spectra are collected in SI (Figs. S33–S36).

*4.2.9. (Z)-4-((6,8-di-tert-butyl-2-((4-carboxyphenyl)amino)-3H-phenoxazin-3-ylidene)amino)benzoic acid (**14**)*

A solution of 220 mg (1 mmol) of 3,5-di-(*tert*.-butyl)-1,2-benzoquinone and 411 mg (3 mmol) of 4-aminobenzoic acid contained 0.01 mL of trifluoroacetic acid in 10 mL i-PrOH was refluxed for 6 h. The reaction mixture was evaporated. Precipitate was dissolved in 25 mL 0.1 N NaOH. The red-brown aqueous solution was filtered and neutralized with concentrated HCl. Precipitate was filtered off, dried and recrystallized from i-PrOH. 433.5 mg (77%) of red-brown prisms was obtained, m.p. 211–212 °C. IR (KBr, ν, cm^{-1}): 3285 cm^{-1} (N–H), 2921–2854 cm^{-1} (C–H), 1680 cm^{-1} (C = O). ^1H NMR ($CDCl_3$): 1.31 s (9H, *t*-Bu), 1.37 s (9H, *t*-Bu), 6.15–8.04 m (12H), 9.06 s (1H, NH), 12.80 s (1H, COOH); Found: C, 72.47; H, 5.88; N, 7.47. $C_{34}H_{33}N_3O_5$ requires C, 72.45; H, 5.90; N, 7.46. The data on IR, ^1H NMR, UV–Vis and emission spectra are collected in SI (Figs. S37–S41).

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tet.2018.12.047.

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