# Reaction of 2-(α-bromoacetyl)-phenoxathiin with substituted *o*-, *m*-, or *p*-formyl-aroxides

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**Abstract**

Solid sodium- or potassium aroxides with formyl and alkoxy substituents were reacted with 2-(α-bromoacetyl)-phenoxathiin **3** in the presence of crown ethers (15C5 or 18C6, respectively). When the formyl and hydroxy groups were in *meta*- or *para*- positions the resulting fluorescent compounds were 2-(α-formylaryloxyacetyl)-phenoxathiins **4a**–**d**; however, when these substituents were in the *ortho* position, the fluorescent products were benzo[*b*]furyl 2-phenoxathiinyl ketones **5e–h**, or naphtho[3,2-*b*]furyl 2-phenoxathiinyl ketone **8**. The chromatographic behavior of compounds **4a**–**d, 5e–h,** and **8** was investigated by TLC and reverse-phase-TLC (RP-TLC) for the hydrophobicity properties.

**Keywords:** 2-Formylaryloxy-(2-phenoxathiinyl)-1-ethanones, benzo[*b*]furyl-(2-phenoxathiine)-methanones; naphtho[*b*]furyl-(2-phenoxathiine)-methanones, RP-TLC

## Introduction

Phenoxathiin derivatives have recently gained attention owing to their fluorescent properties,[1–8] stability of cation-radicals,[9–11] and biological activities.[12–17] In a previous paper we have described the synthesis and properties of fluorescent 2-(α-aryloxyacetyl)-phenoxathiin derivatives on treating alkali aroxides with 2-(α-bromoacetyl)-phenoxathiin (**3**) in the presence of crown ethers.[1,18]

Duff formylation of corresponding phenols[19–21] afforded the substituted *o-*, *m-*, or *p*-formylphenols **1a** (vanillin), **1b** (ethylvanillin), **1c** (syringaldehyde), **1d** (isovanillin), **1e** (salicylaldehyde), **1f** (5-formylvanillin), **1g** (5-formylethylvanillin), **1h** (4,5-dihydroxy-isophthalaldehyde) and **6** (1-formyl-2-naphthol). They were converted into the corresponding alkali phenoxides (**2a**—**h** and **7**). In the present paper we report the synthesis of similar compounds (**4a**–**d**) having an extra formyl group, *via* an $S_N2$ substitution reaction of the bromine atom in **3**, when the starting phenols had a formyl group in the *meta* or *para* position (**1a**–**d**). However, when starting from *ortho*-formylphenols (**1e**–**h**) or from 1-formyl-2-naphthol (**6**) the resulting products were 2-benzo[*b*]furyl 2-phenoxathiinyl ketones (**5e**–**h**) and naphtho[3,2-*b*]furyl-2 2-phenoxathiinyl ketone (**8**), respectively. These products resulted from a dehydrative cyclization, *i.e*. aldolization followed by crotonization (similarly to the Rap–Stoermer reaction between salicylaldehyde and halomethyl-ketones by refluxing in alkaline medium,[22–25] which was applied earlier for obtaining thianthrenyl 2-benzo[*b*]furyl ketone).[26] Among the properties of the newly synthesized compounds (**4a**–**d**, **5e**–**h** and **8**), we describe the hydrophobic/hydrophilic balance based on the $R_f$ data from thin layer chromatography (TLC) on silica gel and a QSPR modeling of hydrophobicity. The electronic absorption and fluorescence spectral data will be reported in a separate paper.

## Results and Discussion

**Preparation of 2-(α-formylaryloxyacetyl)-phenoxathiin derivatives (4a–d)**

The solid alkaline phenoxides **2a**–**d** were prepared in high yield from the corresponding phenols **1a**–**d** (Table 1) using the conditions described earlier.[1,27,28] Then an excess of these aryloxide nucleophiles was reacted in dichloromethane with 2-(α-bromoacetyl)-phenoxathiin **3** in the presence of the suitable crown ether (C.E.) for complexing the cation of **2a**–**d**.[1,29,30]

The two-step synthesis of **4a**–**d** described by equations (1) and (2) involves the solubilization of the alkali phenoxide–crown ether complex in dichloromethane (eq. 1), followed by an $S_N2$ reaction at room temperature involving the haloketone (eq. 2, where PT is the 2-phenoxathiinyl moiety). Subscripts (*s*) and (*o*) indicate solid and organic phases, respectively.

$$ArO^-M^+_{(s)} + CE_{(o)} \rightleftharpoons [CE\text{-----}M]^+ArO^-_{(o)} \qquad \text{eq. 1}$$

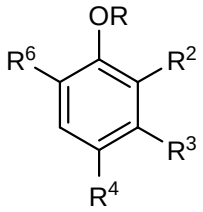
$$[CE\text{-----}M]^+ArO^-_{(o)} + PT\text{-}CO\text{-}CH_2Br_{(o)} \longrightarrow PT\text{-}CO\text{-}CH_2\text{-}OAr_{(o)} + [CE\text{-----}M]^+Br^-_{(o)} \qquad \text{eq. 2}$$

This reaction was monitored by TLC, both by following the formation of fluorescent compounds **4a**–**d** and by the disappearance of reactant **3**. The duration of the reaction differed according to the structure of the nucleophile, as will be seen in the Experimental Part. The organic solution was washed successively with aqueous acid and base, then concentrated, and the product (**4a**–**d**) was purified by preparative TLC. Yields are presented in Table 2.

**Preparations of 2-benzo[*b*]furyl 2-phenoxathiinyl ketones (5e–h) and naphtho[3,2-*b*]furyl-2,2-phenoxathiinyl ketone (8)**

The formylphenols **1e**–**h** (Table 1) and 1-formyl-2-naphthol (**6**) were prepared by Duff formylation of the corresponding phenols with urotropin.[31–33] Phenols **1e**–**h** and compound **6** were treated with alkali hydroxides. The solid formylphenoxides **2e**–**h** were thus prepared in the yields that are presented in Table 1. For the potassium naphthoxide **7** the yield was 56%. The reaction with the haloketone **3** was carried out as indicated in the preceding case, but the $S_N2$-product reacted further by intramolecular dehydration, affording furan derivatives. Whereas the Rap–Stoermer cyclization occurs under drastic conditions, in the present case the reaction proceeded at room temperature, probably due to the high nucleophilicity of the supramolecular complex. Table 3 presents the structures and yields for compounds **5e**–**h**.

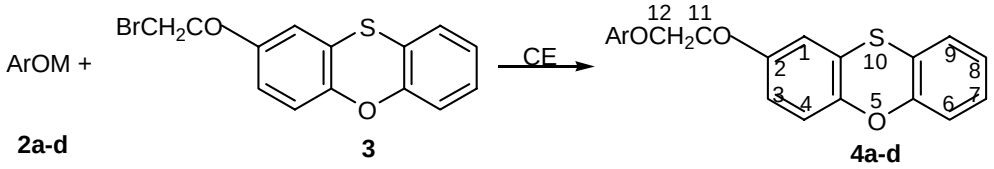
**Table 1**. Phenols **1a**–**h** (R = H) and the corresponding aroxides **2a**–**h** (R = M)




**1a-h, 2a-h**

| Compound | M | $R^2$ | $R^3$ | $R^4$ | $R^6$ | Yield % | C.E. |
|---|---|---|---|---|---|---|---|
| **a** | K | H | H | CHO | OMe | 90 | 18C6 |
| **b** | K | H | H | CHO | OEt | 80 | 18C6 |
| **c** | Na | OMe | H | CHO | OMe | 95 | 15C5 |
| **d** | K | H | CHO | H | OMe | 95 | 18C6 |
| **e** | K | H | H | H | CHO | 96 | 18C6 |
| **f** | Na | OMe | H | CHO | CHO | 72 | 15C5 |
| **g** | Na | OEt | H | CHO | CHO | 65 | 15C5 |
| **h** | K | OH | H | CHO | CHO | 91 | 18C6 |

**Table 2**. Structures and yields of 2-(α-formylaryloxyacetyl)-phenoxathiins (**4a**–**d**)



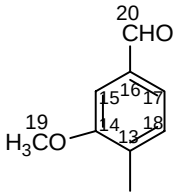
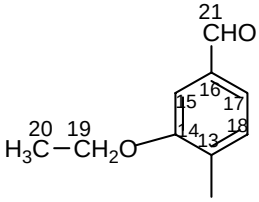
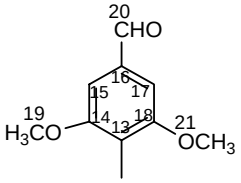
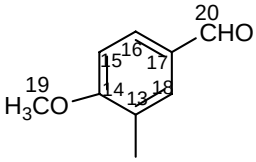
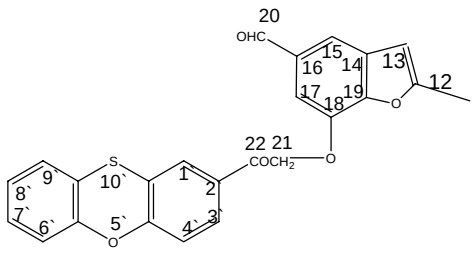

| Compound **4** | Ar in compound | Yield% |
|---|---|---|
| **a** |  | 38 |
| **b** |  | 85 |
| **c** |  | 46 |
| **d** |  | 76 |

**Table 3**. Yields and structures of compounds **5e**–**h** (Scheme 1)

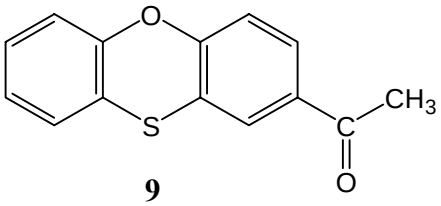
| Compound **5** | $R^1$ | $R^2$ | Yield % |
|---|---|---|---|
| **e** | H | H | 93 |
| **f** | CHO | $OCH_3$ | 33 |
| **g** | CHO | $OCH_2CH_3$ | 71 |
| **h** | CHO |  | 10 |

**NMR Spectra of compounds 4a–d**, **5e–h and 8.** Table 4 gives the $^{1}$H-NMR and $^{13}$C-NMR spectra of the new compounds **4a–d,** identifying the atoms in the phenoxathiin and phenyl rings, the aldehyde group, the alkoxy groups, and the ketone carbon. It is seen that the methylene C-12 group of compound **4c** is shifted about 2.5 ppm to lower field, probably because of the two neighboring methoxy groups. The quaternary carbons in $^{13}$C-NMR spectra are indicated as Cq.

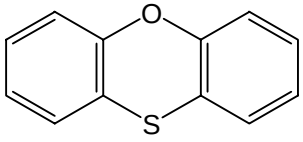
The $^{1}$H- and $^{13}$C- NMR data (Table 5) confirmed also the structures of the new compounds **5e–h** and **8** by identifying: (i) the presence of the phenoxathiin moiety; (ii) the presence of the benzo[*b*]furyl and naphtho[3,2-*b*]furyl ring, and of the substituents (CHO group for **8f–h** in C-16 position, MeO groups for **5f** in the C-18 position, an EtO group for **5g** in C-18 position); (iii) the presence of a carbonyl (C-11) group for **8e–h, 9** and a new carbonyl (C-22) group for **8h**; (iv) the presence of a methylene (C-21) group for **8h**.

**Hydrophobicity/hydrophilicity of compounds 4a–d, 5e–h and 8**

The hydrophobicity and hydrophilicity properties of compounds **4a–d, 5e–h** and **8** are important for their possible biomedical applications. They determine how substances interact with biomembranes and receptors, influencing their bioavailability and biospecificity. The octanol–water partition coefficient (*P*) and its logarithm (log*P*) are the usual parameters for estimating quantitatively these characteristics,[34] and they can be measured or computed. In our case, this property for compounds **4a–d, 5e–h** and **8** was studied experimentally by reversed phase TLC (RP-TLC)[1,18,35,36] and compared with the phenols **1a–h** (Table 1) and **6** (Scheme 2), with compounds **3**, with 2-(α-acetyl)-phenoxathiin **9,** and phenoxathiin **10**.




**9**




**10**

**Table 4**. $^{1}$H-NMR and $^{13}$C-NMR data of compounds **4a**–**d**

| Compound | NMR spectra in $CDCl_3$ [a,b] (δ, ppm, *J* Hz) |
|---|---|
| **4a** | **$^{1}$H**: 3.96 (s, 3H, H-19); 5.36 (s, 2H, H-12); 6.85 (d, 1H, H-18, 8.2); 6.99 (dd, 1H, H-6, dd, 2.3, 8.0); 7.10–7.01 (m, 3H, H-4, -8, -9); 7.15 (ddd, 1H, H-7, 2.4, 6.5, 8.0); 7.38 (dd, 1H, H-17, 1.9, 8.2); 7.44 (d, 1H, H-15, 1.9); 7.77 (d, 1H, H-1, 2.2); 7.78 (dd, 1H, H-3, 2.2, 9.1); 9.84 (s, 1H, H-20). **$^{13}$C**: 191.56 (C-12); 190.76 (C-20); 156.25 (Cq-4a); 152.66 (Cq-13); 150.81 (Cq-6a); 150.06 (Cq-16); 131.16 (Cq-14); 130.78 (Cq-2); 121.07 (Cq-1a); 118.23 (Cq-9a); 128.35 (CH); 128.12 (CH); 127.17 (CH); 126.79 (CH); 126.18 (CH); 125.31 (CH); 117.94 (CH); 117.91 (CH); 112.80 (CH); 109.96 (CH); 71.38 (C-12); 56.12 (C-19). |
| **4b** | **$^{1}$H**: 9.93 (s, 1H, H-21); 7.91 (dd, 1H, H-3, 2.1, 8.5); 7.88 (d, 1H, H-1, 2.1); 7.52 (d, 1H, H-15, 1.9); 7.46 (dd, 1H, H-17, 1.9, 8.1); 7.24 (ddd, 1H, H-7, 2.2, 6.8, 7.9); 7.19–7.08 (m, 4H, H-4, -6, -8, -9); 6.97 (d, 1H, H-18, 8.1); 5.44 (s, 2H, H-12); 4.27 (q, 2H, H-19, 7.0); 1.59 (t, 3H, H-20, 7.0). **$^{13}$C**: 192.08 (C-11); 190.56 (C-21); 156.27 (Cq-4a); 153.16 (Cq-14); 151.05 (Cq-6a); 149.76 (Cq-13); 131.64 (Cq-2); 131.31 (Cq-16); 121.07 (Cq-1a); 118.77 (Cq-9a); 128.66 (CH-3); 128.14 (CH-7); 127.44 (CH-1); 126.85 (CH-9); 125.75 (CH-17); 125.32 (CH); 117.97 (CH-4); 117.89 (CH-6); 114.17 (CH-18); 112.13 (CH-15); 72.15 (C-12); 64.95 (C-19); 14.77 (C-20). |
| **4c** | **$^{1}$H:** 9.87 (s, 1H, H-20); 7.84 (d, 1H, H-1, 2.1); 7.80 (dd, 1H, H-3, 8.4); 7.14 (ddd, 1H, H-7, 2.1, 6.9, 7.9); 7.13 (s, 2H, H-15, -17); 7.04 (d, 1H, H-4, 8.4); 6.99 (dd, 1H, H-6, 1.4, 7.9); 7.08–7.02 (m, 2H, H-8, -9); 5.25 (s, 2H, H-12); 3.89 (s, 6H, H-19). **$^{13}$C**:192.46 (C-11); 190.86 (C-20); 155.77 ($C_q$-4a); 153.03 (C-14, -18); 150.92 ($C_q$-6a); 141.67 (C-13); 131.90 (C-2); 131.34 (C-16); 120.51 ($C_q$-1a); 118.67 ($C_q$-9a); 128.42 (CH-3); 127.99 (CH-7); 127.37 (CH-1); 126.73 (CH-9); 125.13 (CH-8); 117.83 (CH-4); 117.700 (CH-6); 106.71 (C-15, -17); 74.80 (C-12); 56.27 (C-19). |
| **4d** | **$^{1}$H**: 9.81 (s, 1H, H-21); 7.77 (dd, 1H, H-3, 2.0, 8.9); 7.76 (d, 1H, H-1, 2.0); 7.50 (dd, 1H, H-16, 1.9, 8.2); 7.32 (d, 1H, H-18, 1.9); 7.14 (ddd, 1H, H-7, 2.2, 6.6, 8.1); 7.09–6.97 (m, 4H, H-4, -6, -8, -9); 7.02 (d, 1H, H-15, 8.2); 5.34 (s, 2H, H-12); 3.98 (s, 3H, H-19). **$^{13}$C**: 191.35 (C-11); 190.58 (C-20); 156.10 (Cq-4a); 154.92 (Cq); 150.80 (Cq-6a); 147.92 (Cq); 130.84 (Cq); 129.87 (Cq); 120.94 (Cq-1a); 118.51 (Cq-9a); 128.20 (CH); 128.05 (CH); 127.52 (CH); 127.02 (CH); 126.77 (CH); 125.23 (CH); 117.87 (CH); 111.57 (CH); 111.49 (CH); 111.14 (CH); 71.04 (C-12); 56.24 (C-19). |

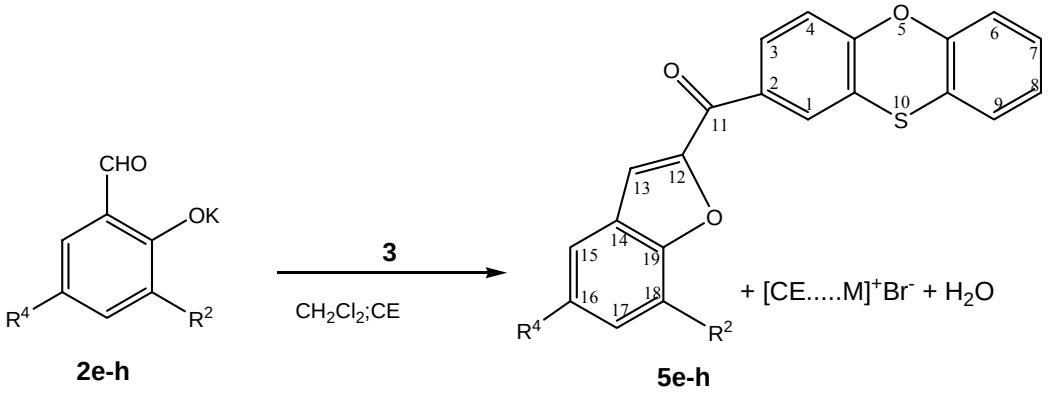
[a] At about 295K. [b] The atom numbering of compounds **4a**–**d** is as in Table 2.

**Table 5**. $^{1}$H- NMR and $^{13}$C- NMR data of compounds **5e**–**h** (Scheme 1) and **8** (Scheme 2).

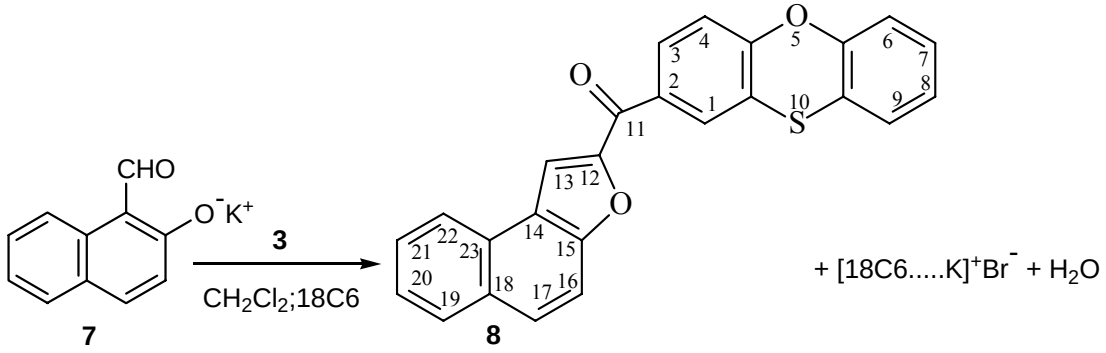
| Compound | NMR spectra in $CDCl_3$ [a,b] (δ, ppm, *J* Hz) |
|---|---|
| **5e** | **$^{1}$H-** 7.89 (dd, 1H, H-3, 2.1, 8.4); 7.83 (d, 1H, H-1, 2.1); 7.74 (ddd, 1H, H-15, 0.9, 1.2, 7.9); 7.64 (dq, 1H, H-18, 0.9, 1.2,); 7.54 (d, 1H, H-13, $^{5}J$($H^{13}$–$H^{18}$)=0.9) 7.51 (ddd, 1H, H-17, 1.2, 7.3, 8.4); 7.34 (ddd, 1H, H-16, 0.9, 7.3, 7.9); 7.15 (ddd, 1H, H-7, 2.1, 7.0, 8.7); 7.11 (d, 1H, H-6, 1.9); 7.09–7.00 (m, 3H, H-1, -8, -9). **$^{13}$C:** 181.97 (C-11); 155.94 (Cq-4a); 155.56 (Cq); 152.17 (Cq); 151.05 (Cq-6a); 133.45 (Cq); 126.92 (Cq); 120.63 (Cq-1a); 118.81 (Cq-9a); 129.77 (CH-3); 128.38 (CH-17); 128.33 (CH-1); 128.02 (CH-7); 126.80 (CH); 125.15 (CH); 124.03 (CH-16); 123.29 (CH-15); 117.89 (CH); 117.64 (CH-6); 116.11 (CH-13); 112.53 (CH-18); |
| **5f** | **$^{1}$H-** 10.03 (s, 1H, H-20); 7.95 (dd, 1H, H-3, 2.1, 8.5); 7.86 (d, 1H, H-1, 2.1); 7.85 (d, 1H, H-15, 1.5); 7.65 (s, 1H, H-13); 7.51 (d, 1H, H-17, 1.5); 7.16 (ddd, 1H, H-7, 2.2, 6.8, 7.9); 7.13–7.00 (m, 4H, H-4, -6, -8, -9); 4.09 (s, 3H, H-21). **$^{13}$C:** 191.20 (C-20); 181.06 (C-11); 155.81 (Cq-4a); 153.88 (Cq); 150.90 (Cq-6a); 148.83 (Cq); 146.89 (Cq); 134.35 (Cq); 132.81 (Cq); 128.37 (Cq); 120.78 (Cq-1a); 118.66 (Cq-9a); 129.99 (CH); 128.46 (CH); 128.05 (CH); 126.79 (CH); 125.21 (CH); 121.10 (CH); 117.89 (CH); 117.75 (CH); 115.93 (CH); 106.70 (CH); 56.27 (C-21). |
| **5g** | **$^{1}$H-** 10.02 (s, 1H, H-20); 7.93 (dd, 1H, H-3, 2.1, 8.5); 7.88 (d, 1H, H-1, 2.1); 7.82 (d, 1H, H-15, 1.5); 7.63 (s, 1H, H-13); 7.49 (d, 1H, H-17, 1.5); 7.15 (ddd, 1H, H-7, 2.2, 6.8, 7.9); 7.12–6.99 (m, 4H, H-4, -6, -8, -9); 4.35 (q, 2H, H-21, 7.0); 1.57(t, 3H, H-22, 7.0). **$^{13}$C:** 191.19 (C-20); 181.10 (C-11); 155.81 (Cq–4a); 153.80 (Cq); 150.95 (Cq–6a); 149.06 (Cq); 146.24 (Cq); 134.38 (Cq); 132.93 (Cq); 128.46 (Cq); 120.76 (Cq–1a); 118.71 (Cq–9a); 129.98 (CH); 128.53 (CH); 128.07 (CH); 126.81 (CH); 125.30 (CH); 120.77 (CH); 117.92 (CH); 117.75 (CH); 116.00 (CH); 107.85 (CH); 65.05 (C-21); 14.69 (C-22). |
| **5h** | **$^{1}$H-** 9.98 (s, 1H, H-20); 7.92 (dd, 1H, H-3, 2.2, 8.5); 7.88 (d, 1H, H-15, 1.3); 7.85 (d, 1H, H-1, 2.1); 7.77 (dd, 1H, H-3', 2.2, 8.5); 7.72 (d, 1H, H-1', 2.1); 7.65 (d, 1H, H-17, 1.3); 7.64 (s, 1H, H-13); 6.92–7.20 (m, 10H, H-4, H-6–9, H-4', H-6'÷9'); 5.55 (s, 2H, H-21). **$^{13}$C:** 191.13 (C-22); 190.62 (C-20); 183.41 (C-11); 156.81 (Cq); 156.08 (Cq–4a); 154.01 (Cq); 151.25 (Cq); 150.61 (Cq–6a); 148.36 (Cq); 144.99 (Cq); 138.46 (Cq); 134.14 (Cq); 132.63 (Cq); 128.62 (Cq); 121.18 (Cq); 120.85 (Cq–1a); 118.54 (Cq–9a); 117.88 (Cq); 129.88 (CH); 128.98 (CH); 128.36 (CH); 128.13 (CH); 127.99 (CH); 127.93 (CH); 127.62 (CH); 126.86 (CH); 126.40 (CH); 125.18 (CH); 121.08 (CH); 117.76 (CH); 117.72 (CH); 117.61 (CH); 117.58 (CH); 115.58 (CH); 109.56 (CH); 71.22 (C-21). |
| | **$^{1}$H-** 8.19 (d, 1H, H-22, 8.0); 7.74 (dd, 1H, H-19, 1.0, 9.1); 7.66 (ddd, 1H, |

| | |
|---|---|
| **8** | H-21, 1.3, 7.0, 8.2); 7.56 (ddd, 1H, H-20, 1.4, 7.0, 9.1); 8.03 (s, 1H, H-13); 7.86–8.00 (m, 3H, H-1, H-3, H-17); 7.01–7.19 (m, 6H, H-4, H-6, -7, -8, -9, H-16). **$^{13}$C:** 181.35 (C-11); 155.49 (Cq–4a); 154.51 (Cq); 152.01 (Cq); 151.12 (Cq–6a); 133.64 (Cq); 130.58 (Cq); 128.13 (Cq); 122.88 (Cq); 120.66 (Cq–1a); 118.89 (Cq–9a); 130.13 (CH); 129.77 (CH); 129.12 (CH); 128.33 (CH); 128.02 (CH); 127.49 (CH); 126.81 (CH); 125.63 (CH); 125.14 (CH); 123.41 (CH); 117.89 (CH); 117.66 (CH); 115.12 (CH); 112.81 (CH). |

[a] At about 295K.[b] The atom numbering of **5e**–**h** is as in Table 3, and of **8** as in Scheme 2.




**Scheme 1**. Synthesis of compounds **5e**–**h**.




**Scheme 2**. Synthesis of compound **8**.

Thus, $R_f$ values were measured, using precoated $C_{18}$-chain layers as stationary phases and various ethanol–water mixtures as mobile phases (Table 6). The molecular hydrophobicity, $R_{M0}$, determined as a result of experimental data depending on $R_{M0}$ values calculated with eqs. 3 and 4,[35–38] is the $R_M$ value extrapolated to zero concentration of organic component in the alcohol–water mixture; $b$ is the change in the $R_M$ value caused by increasing the concentration ($K$) of the

organic component in the mobile phase. Statistical analysis involved the correlation coefficient (*R*), the Fisher parameter[39–41] (*F*), and the standard deviation (*SD*) (Table 6).

$$R_M = \log(1/R_f - 1) \quad \text{eq. 3}$$

$$R_M = R_{M0} + bK \quad \text{eq. 4}$$

**Table 6.** $R_f$ values and hydrophobic characteristics ($R_{M0}$ and $b$) of the new compounds synthesized **4a–d, 5e–h, 8,** of phenols **1a–h** and **6** and of compounds **3, 9** and **10**. RP-TLC results for four ethanol–water mixtures (A–D) [a,b]

| Compound | $R_f$ | | | | Hydrophobicity characteristics | | Statistical parameters | | |
|---|---|---|---|---|---|---|---|---|---|
| | A | B | C | D | $R_{M0}$ | $b$ | $R$ | $F$ | $SD$ |
| **3** | 0.608 | 0.430 | 0.272 | 0.128 | 2.823 | -0.033 | -0.997 | 409.6 | 0.037 |
| **4a** | 0.721 | 0.556 | 0.405 | 0.179 | 2.694 | -0.034 | -0.990 | 103.0 | 0.076 |
| **4b** | 0.641 | 0.541 | 0.337 | 0.131 | 2.881 | -0.035 | -0.977 | 42.26 | 0.123 |
| **4c** | 0.666 | 0.583 | 0.391 | 0.210 | 2.300 | -0.029 | -0.984 | 62.85 | 0.083 |
| **4d** | 0.743 | 0.611 | 0.418 | 0.223 | 2.516 | -0.033 | -0.996 | 254.8 | 0.046 |
| **5e** | 0.384 | 0.222 | 0.135 | 0.052 | 3.264 | -0.034 | -0.994 | 180.1 | 0.056 |
| **5f** | 0.448 | 0.291 | 0.175 | 0.065 | 3.182 | -0.034 | -0.991 | 113.1 | 0.073 |
| **5g** | 0.397 | 0.194 | 0.121 | 0.052 | 3.327 | -0.034 | -0.994 | 183.2 | 0.057 |
| **5h** | 0.700 | 0.628 | 0.444 | 0.305 | 1.839 | -0.024 | -0.989 | 93.31 | 0.057 |
| **8** | 0.287 | 0.179 | 0.083 | 0.041 | 3.329 | -0.032 | -0.997 | 472.6 | 0.033 |
| **1a** | 0.891 | 0.848 | 0.810 | 0.794 | 0.108 | -0.011 | -0.970 | 32.48 | 0.043 |
| **1b** | 0.891 | 0.818 | 0.756 | 0.705 | -0.715 | -0.017 | -0.981 | 53.82 | 0.053 |
| **1c** | 0.864 | 0.848 | 0.810 | 0.794 | 0.108 | -0.011 | -0.970 | 32.48 | 0.043 |
| **1d** | 0.891 | 0.878 | 0.837 | 0.588 | 0.083 | -0.011 | -0.985 | 69.24 | 0.030 |
| **1e** | 0.810 | 0.772 | 0.675 | 0.588 | 0.823 | -0.016 | -0.991 | 117.3 | 0.033 |
| **1f** | 0.864 | 0.848 | 0.783 | 0.735 | 0.318 | -0.012 | -0.982 | 55.90 | 0.038 |
| **1g** | 0.851 | 0.818 | 0.729 | 0.661 | 0.682 | -0.016 | -0.991 | 115.1 | 0.033 |
| **1h** | 0.864 | 0.848 | 0.824 | 0.808 | -0.251 | -0.006 | -0.995 | 225.0 | 0.009 |
| **6** | 0.675 | 0.606 | 0.432 | 0.264 | 1.958 | -0.025 | -0.984 | 63.58 | 0.072 |
| **9** | 0.567 | 0.416 | 0.257 | 0.142 | 2.566 | -0.029 | -0.999 | 1093 | 0.020 |
| **10** | 0.500 | 0.333 | 0.181 | 0.0857 | 3.072 | -0.034 | -0.998 | 856.1 | 0.026 |

[a] Five determinations on silica gel RP-18$F_{254S}$ (Merck), with percent of ethanol in mixture ethanol–water: A = 90%, B = 80%, C = 70%, D = 60%.

[b] $R_{M0}$, $b$, $R$, $F$, and $SD$ are defined by the preceding text and eqs. 3 and 4.

In attempting to calculate log*P* values using fragmental constants,[34] a good correlation ($R$ =0.934) with experimental data for $R_{M0}$ was obtained for compounds **4a–d, 5e–h** and **8** (Figure

1). The 2-(α-acetyl)-phenoxathiin moiety is relatively hydrophobic, with log*P* = 1.08,[1] conferring hydrophobicity to compounds **4a**–**d, 5e**–**h** and **8**.

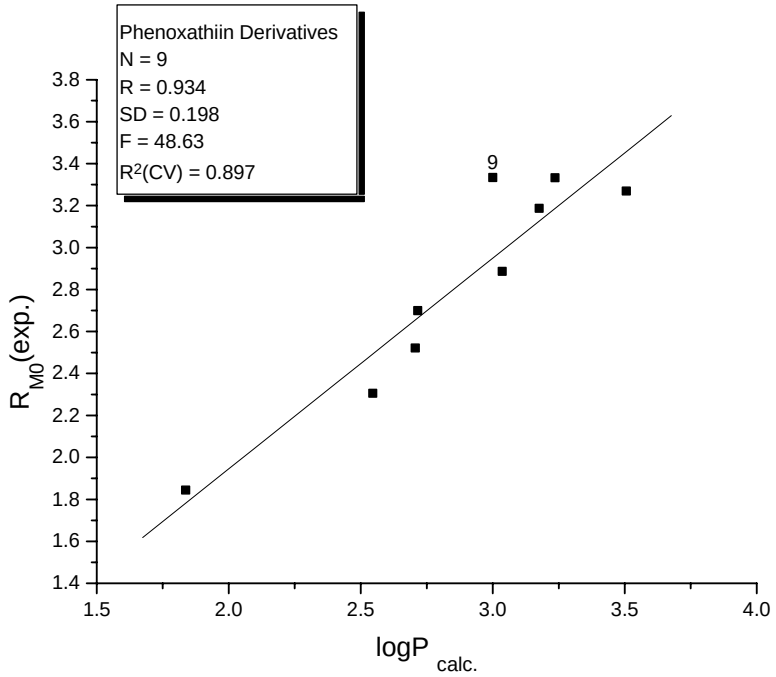



**Figure 1**. $R_{M0}$ *vs* log*P* for compounds **4a**–**d, 5e**–**h** and **8**.

The experimental results concerning the hydrophobic/hydrophilic character ($R_{M0}$ values, Table 6) allowed the following observations: (i) compared with phenols **1a**–**h,** compounds **4a**–**d** and **5e**–**h** are more hydrophobic (due to the acetylphenoxathiin moiety); (ii) the hydrophobicity of compounds **3, 4a**–**d, 5e**–**h**, **8, 9** and **10** decreases in the order: $R_{M0}$ **8**> $R_{M0}$ **5g** > $R_{M0}$ **5e**> $R_{M0}$ **5f**> $R_{M0}$ **10**> $R_{M0}$ **4b**> $R_{M0}$ **3**> $R_{M0}$ **4a**> $R_{M0}$ **9**> $R_{M0}$ **4d**> $R_{M0}$ **4c**> $R_{M0}$ **5h** (of course, the hydrophilicity increases in reverse order); (iii) the acetyl and bromoacetyl moieties reduce the hydrophobicity of the phenoxathiine, and the bromo- atom of the acetyl moiety increases the hydrophobicity ($R_{M0}$ **10**> $R_{M0}$ **3**> $R_{M0}$ **9)**; (iv) aside from the compound **5h** (with benzofuran and acetylphenoxathiin moieties present in molecule), due to the naphthofuran and benzofuran moieties, the compounds **5e**–**g** and **8** are more hydrophobic than the compounds **4a**–**d** (alone with acetylphenoxathiin moiety present in molecule), *i.e.*, $R_{M0}$ **8**> $R_{M0}$ **5e**–**g** > $R_{M0}$ **4a**–**d**> $R_{M0}$ **5h**.

**TLC behavior**

The TLC behavior was investigated because this characteristic has practical and theoretical importance. For this purpose we have chosen pure solvents (Table 7) with different values of the $E_T(30)$ (Dimroth–Reichardt`s) parameter.[42]

**Table 7.** TLC behavior ($R_f$) [a] of compounds **4a**–**d, 5e–h** and **8** on silica gel 60 $GF_{254}$ plates (Merck) with three mobile phases (solvents with different $E_T(30)$ values)[42]

| Compound | 1,2-Dichloroethane $E_T(30) = 41.9$ | Dichloromethane $E_T(30) = 41.1$ | Toluene $E_T(30) = 33.9$ |
|---|---|---|---|
| **4a** | 0.201 | 0.165 | 0.016 |
| **4b** | 0.354 | 0.299 | 0.100 |
| **4c** | 0.209 | 0.173 | 0.033 |
| **4d** | 0.322 | 0.314 | 0.066 |
| **5e** | 0.874 | 0.790 | 0.500 |
| **5f** | 0.393 | 0.362 | 0.083 |
| **5g** | 0.483 | 0.480 | 0.100 |
| **5h** | 0.372 | 0.363 | 0.065 |
| **8** | 0.963 | 0.818 | 0.486 |

[a] For five determinations.

The experimental results with pure solvents for compounds **4a**–**d, 5e**–**h** and **8** (Table 7) can be interpreted as follows: (i) the $R_f$ values depend on the solvent polarity ($E_T(30)$ values) and decrease in the following order: 1,2-dichloroethane > dichloromethane > toluene; (ii) irrespective of the mobile phases, the compounds with naphtho[*b*]furan or benzo[*b*]furan moieties have higher $R_f$ values comparatively with the formylaryloxy-phenoxathiin compounds ($R_f$ **8** > $R_f$ **5e**–**h** > $R_f$ **4a**–**d**); (iii) irrespective of the mobile phases, for compounds **5e–h** the formyl group decreases the $R_f$ values, the ethoxy group increases $R_f$ values and the acetylphenoxathiin moiety decreases the $R_f$ values ($R_f$ **5e** > $R_f$ **5g** > $R_f$ **5f** > $R_f$ **5h**); (iv) for formyl derivatives **4a**–**d**, the $R_f$ values depends on the mobile phases, on the number, nature and position of alkoxy groups present in the molecule (in 1,2-dichloroethane and toluene $R_f$ **4b** > $R_f$ **4d** > $R_f$ **4c** > $R_f$ **4a**, and in dichloromethane $R_f$ **4d** > $R_f$ **4b** > $R_f$ **4c** > $R_f$ **4a**).

**Formation of stable cation radicals**

The newly synthesized compounds **4a**–**d, 5e**–**h** and **8** have yellow fluorescence ($\lambda_{max}$ = 366 nm) both in solution and in the crystalline state. Due to the presence of the phenoxathiin moiety, all these compounds afford blue–violet cation-radicals on treatment with concentrated sulfuric acid.[9–11]

## Conclusions

New 2-(α-formylaryloxyacetyl)-phenoxathiin derivatives (**4a**–**d)**, 2-benzo[*b*]furyl 2-phenoxathiinyl ketones (**5e**–**h**), and naphtho[3,2-*b*]furyl-2,2-phenoxathiinyl ketone **8** were prepared by reacting the bromoketone derivative **3** with solid aroxides **2a**–**h** and **7** and a crown

ether in dichloromethane. The structures of the compounds **4a–d, 5e–h** and **8** were confirmed by analysis of $^{1}$H-NMR and $^{13}$C-NMR spectra. The hydrophobicity/hydrophilicity properties were investigated by means of reverse-phase thin-layer chromatography (RP-TLC), and a satisfactory correlation with calculated log*P* values was found. The TLC behavior was also investigated.

## Experimental Section

**General Procedures.** Starting compounds for synthesis: the phenols **1a–e**, phenoxathiine **10** and crown ethers (15C5 and 18C6) were from Aldrich. Formyl-phenols **1f–h**, 1-formyl-2-naphthol **6**, bromoketone **3**, and 2-(α-acetyl)-phenoxathiine **9**, were prepared according to literature data.[19–21,31–33,43–46] Silica gel plates 60 $GF_{254}$ (for TLC) and silica gel RP-18 $F_{254S}$ (for RP-TLC) were from Merck, Darmstadt. $^{1}$H-NMR and $^{13}$C-NMR spectra were recorded with a Varian Gemini 300 BB spectrometer (300 MHz for $^{1}$H-NMR and 75 MHz for $^{13}$C-NMR).

**Synthesis of phenoxides 2a–h and 7**

The solid aroxides were obtained as described previously,[1,27,28] in yields indicated in Table 1.

**Synthesis of compounds 4a–d, 5e–h, and 8. General procedure**

The solid aroxides **2a–h** and **7** were suspended in dichloromethane under stirring (25 mL for 1 g of aroxide), then the corresponding crown ether (Table 1), and finally 2-(α-bromoacetyl)-phenoxathiin **3** were added in the following molar ratio **2**:**3**:C.E.= 1.5:1:1.5 for the synthesis of **4a–d, 5e–g** and **8**; and 1:2.1:1.1 for compound **5h**. The reaction mixture rapidly became yellow, and was left at room temperature for 24 h for compounds **4a,b,d**; 48 h for **4c**; 72 h for **5e–g**; 192 h for **5h**. The course of the reaction was monitored by TLC, following the formation of fluorescent products and the disappearance of the bromoketone. The reaction mixture was washed three times by liquid/liquid extraction with 1N hydrochloric acid for removing the C.E., and then three times with aqueous 1N sodium hydroxide for removing unreacted phenols. The fluorescent organic layer (excitation at 366 nm) was dried on anhydrous sodium sulfate, and the solvent was removed by rotary evaporation. The crude products were purified by preparative TLC using silica gel plates 60$GF_{254}$ (with dichloromethane once for **5e–g**, twice for **4a** and **5h**, three times for **4b** and **4d**, five times for **4c**; and for **8** twice with toluene).

**2-(4-Formyl-2-methoxyphenyloxy)-(2-phenoxathiinyl)-ethan-1-one,** or **2-(α-(4-formyl-2-methoxyphenyloxy)acetyl)-phenoxathiin (4a).** Yellow solid, m.p. 168–170°C; (Found: C, 67.0; H, 4.00. $C_{22}H_{16}O_5S$ requires C, 67.33; H, 4.10).

**2-(2-Ethoxy-4-formylphenyloxy)-(2-phenoxathiinyl)-ethan-1-one,** or **2-(α-(2-ethoxy-4-formylphenyloxy)acetyl)-phenoxathiin (4b).** Yellow solid, m.p. 139–141°C. (Found: C, 67.50; H, 4.30. $C_{23}H_{18}O_5S$ requires C, 67.96; H, 4.46).

**2-(2,6-Dimethoxy-4-formylphenyloxy)-(2-phenoxathiinyl)-ethan-1-one,** or **2-(α-(2,6-dimethoxy-4-formylphenyloxy)acetyl)-phenoxathiin (4c).** Yellow solid, m.p. 152.5–154°C. (Found: C, 65.20; H, 4.10. $C_{23}H_{18}O_6S$ requires C, 65.39; H, 4.29).

**2-(3-Formyl-6-methoxyphenyloxy)-(2-phenoxathiinyl)-ethan-1-one,** or **2-(α-(3-formyl-6-methoxyphenyloxy)acetyl)-phenoxathiin (4d).** Yellow solid; m.p. 146–147°C. (Found: C, 67.28; H, 4.00. $C_{22}H_{16}O_5S$ requires C, 67.33; H, 4.10).

**2-Benzo[*b*]furyl 2-phenoxathiinyl methanone, or 2-benzo[*b*]furyl 2-phenoxathiinyl ketone (5e).** Dark-yellow solid, m.p. 150–151.5°C (Found: C, 73.18; H, 3.48. $C_{21}H_{12}O_3S$ requires C, 73.24; H, 3.51).

**2-(5-Formyl-7-methoxybenzo[*b*]furyl) 2-phenoxathiinyl methanone,** or **2-(5-formyl-7-methoxybenzo[*b*]furyl) 2-phenoxathiinyl ketone (5f).** Yellow solid, m.p. 171.5–172.5°C. (Found: C, 68.58; H, 3.45. $C_{23}H_{14}O_5S$ requires C, 68.64; H, 3.50).

**2-(7-Ethoxy-5-formylbenzo[*b*]furyl) 2-phenoxathiinyl methanone,** or **2-(7-ethoxy-5-formylbenzo[*b*]furyl) 2-phenoxathiinyl ketone (5g)**. Yellow solid, m.p. 149.5–151.5°C. (Found: C, 69.18; H, 3.80. $C_{24}H_{16}O_5S$ requires C, 69.21; H, 3.87).

**2-(2-(5-Formylbenzo[*b*]furyl 2-phenoxathiinyl methanone)-7-yl (2-phenoxathiinyl)-ethan-1-one,** or **2-(7-(2-(α-acetoxy)phenoxathiinyl)-5-formylbenzo[*b*]furyl) 2-phenoxathiinyl ketone (5h)**. dark-yellow solid, m.p. 168–169°C. Found: C, 68.70; H, 3.15. $C_{36}H_{20}O_7S_2$ requires C, 68.78; H, 3.20).

**Naphtho[2,1-*b*]-2-furyl 2-phenoxathiinyl methanone,** or **naphtho[2,1-*b*]-2-furyl 2-phenoxathiinyl ketone (8)**. 23% yield; yellow solid, m.p. 170–171°C. (Found: C, 78.45; H, 3.60. $C_{25}H_{14}O_3S$ requires C, 78.51; H, 3.69%.

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