Synthesis of anthraoxaza- and anthradioxaphosphorine derivatives

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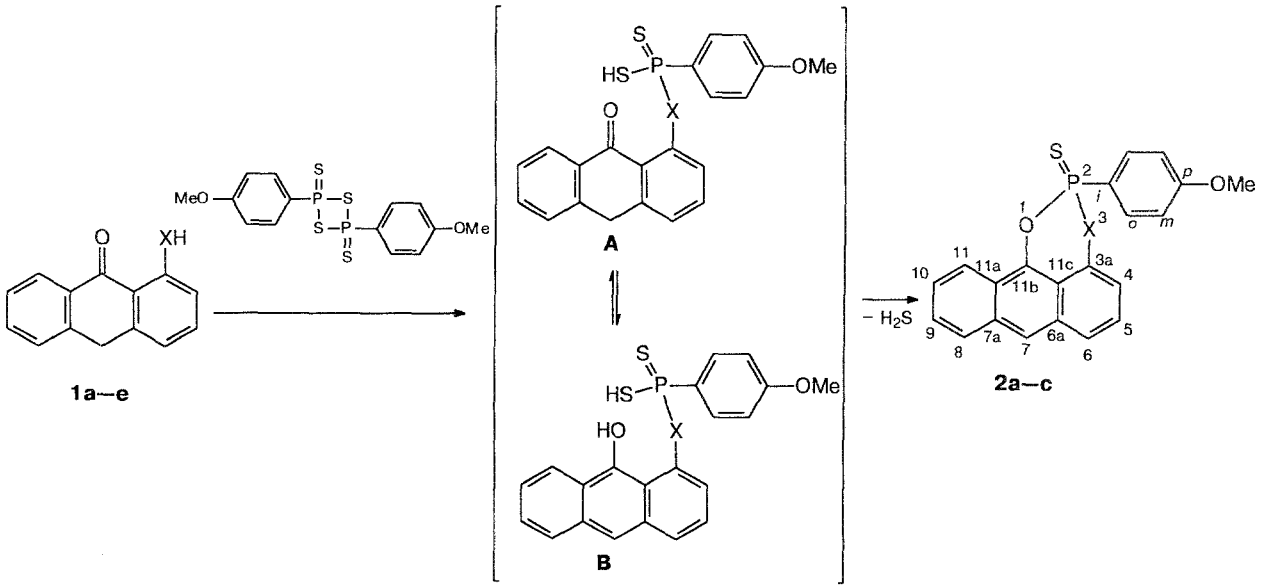
Anthraoxaza- and anthradioxaphosphorine sulfides were obtained by treatment of 1-amino- and 1-hydroxy-9-anthrones with Lawesson's reagent.

Key words: 1-amino-9-anthrone, 1-hydroxy-9-anthrone, Lawesson's reagent, cyclization; anthraoxazaphosphorine sulfide, anthradioxaphosphorine sulfide.

Lawesson's reagent, 2,4-bis(*p*-methoxyphenyl)-1,3-dithiadiphosphetane-2,4-disulfide, is an efficient thionating reagent for carbonyl compounds. When amino or hydroxy groups are present at positions adjacent to the carbonyl group, cyclization with inclusion of Lawesson's reagent occurs to give phosphacyclanes.[1,2] For example, β-oxoamides[3] for β-aminovinylketones[4] undergo thionation of the carbonyl group along with formation of oxa(or thia)azaphosphorine sulfides.

We have studied for the first time the reaction between Lawesson's reagent and 1-amino- and 1-hydroxyanthrones (**1**) to give derivatives of anthraoxaza- and anthradioxaphosphorine sulfides (**2**), respectively. When aminoanthrone **1a** and Lawesson's reagent (1 : 1) were boiled in toluene for a short time, the reactants dissolved and the reaction mixture became yellowish-green. Chromatography on SiO_2 gave anthraoxazaphosphorine-2-sulfide **2a** in 68 % yield. 1-Methylaminoanthrone (**1b**) and 1-hydroxyanthrone (**1c**) react with Lawesson's reagent more slowly than anthrone **1a** (the reaction takes 2—3 h) to give anthraoxazaphosphorine-2-sulfide **2b** and anthradioxaphosphorine-2-sulfide **2c**, respectively (Scheme 1, Table 1). Attempts to isolate and characterize similar cyclization products formed in the reaction of *N*-phenyl- and *N*-acetylaminoanthrones (**1d,e**) with Lawesson's reagent failed because complex mixtures of insufficiently stable compounds were produced.

Scheme 1



X = NH (**a**), NMe (**b**), O (**c**), NPh (**d**), NCOMe (**e**)

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Table 1. Characteristics of the compounds synthesized

Compound	Yield (%)	M.p./°C (chloroform—methanol)	Mol. weight, found calculated	Molecular formula
2a	68	187—191	377.0592 377.0639	$C_{21}H_{16}NO_2PS$
2b	59	145—147.5	391.0805 391.0796	$C_{22}H_{18}NO_2PS$
2c	55	186—188	378.0479 378.0480	$C_{21}H_{15}PS$
3	50	197—202	455.9601 455.9585	$C_{21}H_{14}BrO_3PS$

Probably, nucleophilic attack by an amino or hydroxy group of anthrone **1** on the P atom of the monomeric form of Lawesson's reagent[1] gives rise to an intermediate, a derivative of 4-methoxyphenyldithiophosphonic acid (**A**), whose enol form (**B**) abstracts an H_2S molecule and undergoes intramolecular cyclization to give compound **2** (see Scheme 1).

Anthraoxaza- and anthradioxaphosphorine sulfides **2** are yellow crystalline compounds, which fluoresce when dissolved in organic solvents. These compounds have low stability in alkaline media and are transformed into amino- or hydroxyanthraquinones. Electrophilic reagents attack the C atom at position 7 in anthradioxaphosphorines. For instance, compound **2c** reacts with bromine at room temperature to give the 7-bromo-derivative **3**. Alkylation of anthraoxazaphosphorine **2a** with dimethyl sulfate in the benzene—NaOH (40 %)—TEBA-Cl system at ~20 °C gave the *N*-methyl-derivative **2b**.

The structures of the compounds synthesized were established based on the mass-, NMR, and IR spectral data and from the electronic absorption spectra (Table 2). The IR spectra of phosphorine sulfides **2** do not contain the characteristic vibration frequencies of C=O, NH_2, or O—H groups. The spectrum of compound **2a** contains an absorption band of an NH group (3280 cm^{-1}),

Table 2. Spectral parameters of the compounds synthesized

Compound	^1H NMR, δ (*J*/Hz)	^{13}C NMR, δ (*J*/Hz)	Electronic spectrum, λ_{max}/nm (log ε)
2a	3.58 (s, 3 H, OCH_3); 6.37 (d, 1 H NH, $^2J_{H,P}$ = 13.5); 6.64 (m, 2 H, H_m, $^4J_{H,P}$ = 3.5); 6.71 (d, 1 H, H(4), $^3J_{H,H}$ = 7.0); 7.21 (m, 1 H, H(5)); 7.40—7.49 (m, 3 H, H(6), H(9), H(10)); 7.71 (m, 2 H, H_o, $^3J_{H,P}$ = 13.5); 7.84 (m, 1 H(8)); 8.00 (s, 1 H, H(7)); 8.37 (m, 1 H, H(11))	55.03 (OCH_3); 108.50 (C(4), $^3J_{C,P}$ = 8.3); 113.90 (C_m, $^3J_{C,P}$ = 11.4); 120.60 (C(11a)); 120.80 (C(10)); 121.30 (C(7)); 121.60 (C(11)); 125.40 (C(9)); 125.68 (C_i, $J_{C,P}$ = 142.5); 125.90 (C(5)); 126.40 (C(6)); 127.50 (C(8)); 131.70 (C(6a)); 132.30 (C_o, $^2J_{C,P}$ = 13.2); 132.60 (C(7a)); 134.70 (C(3a)); 162.50 (C_p)*	244.6 (4.85), 261.0 (4.87), 356.1 sh (3.60), 375.4 (3.90), 401.9 (3.88), 418.1 sh (3.80)
2b	3.27 (d, 3 H, NCH_3, $^3J_{H,P}$ = 12.0); 3.75 (s, 3 H, OCH_3); 6.75 (d, 1 H, H(4), $^3J_{H,H}$ = 7.5); 6.84 (m, 2 H, H_m, $^4J_{H,P}$ = 3.5); 7.36 (m, 1 H, H(5)); 7.45 (m, 2 H, H(9), H(10)); 7.54 (d, 1 H, H(6), $^3J_{H,H}$ = 8.5); 7.78 (m, 2 H, H_o, $^3J_{H,P}$ = 14.0); 7.90 (m, 1 H, H(8)); 8.08 (s, 1 H, H(7)); 8.34 (m, 1 H, H(11))	32.12 (NCH_3, $^2J_{C,P}$ = 6.5); 55.25 (OCH_3); 105.60 (C(4), $^3J_{C,P}$ = 5.2); 114.06 (C_m, $^3J_{C,P}$ = 16.5); 112.00 (C(11c), $^3J_{C,P}$ = 8.0); 120.70 (C(7), C(8)); 120.80 (C(11a), $^3J_{C,P}$ = 6.5); 121.72 (C(11)); 124.00 (C_i, $^1J_{C,P}$ = 142.5); 125.26 (C(9)); 126.09 (C(5)); 126.49 (C(6)); 127.40 (C(8)); 131.84 (C(6a)); 132.50 (C(7a)); 133.30 (C_o, $^2J_{C,P}$ = 14.0); 138.59 (C(3a)); 142.60 (C(11b), $^3J_{C,P}$ = 9.4); 163.06 (C_p, $^4J_{C,P}$ = 3.1)	244.6 (4.92), 259.9 (4.92), 356.1 sh (3.68), 373.1 (4.00), 396.8 (4.01), 418.1 (3.94)
2c	3.78 (s, 3 H, OCH_3); 6.90 (m, 2 H, H_m, $^4J_{H,P}$ = 3.6); 7.07 (d, 1 H, H(4), $^3J_{H,H}$ = 7.2); 7.37 (m, 1 H, H(5)); 7.52—7.48 (m, 2 H, H(9), H(10)); 7.70 (d, 1 H, H(6), $^3J_{H,H}$ = 8.5); 7.94 (m, 2 H, H_o, $^3J_{H,P}$ = 15.0); 7.95 (m, 1 H, H(8)); 8.16 (s, 1 H, H(7)); 8.33 (m, 1 H, H(11))	55.33 (OCH_3); 111.00 (C(4), $^3J_{C,P}$ = 7.2); 111.36 (C(11s), $^3J_{C,P}$ = 14.1); 114.12 (C_m, $^3J_{C,P}$ = 17.2); 120.80 (C(11a), $^3J_{C,P}$ = 6.2); 121.04 (C(7)); 121.22 (C(11)); 121.32 (C_i, $^1J_{C,P}$ = 157.9); 123.49 (C(6)); 125.90 (C(9), C(10)); 126.71 (C(5)); 127.83 (C(8)); 131.70 (C(6a)); 132.80 (C(7a)); 131.61 (C_o, $^2J_{C,P}$ = 14.6); 141.68 (C(11b), $^2J_{C,P}$ = 7.3); 145.97 (C(3a), $^2J_{C,P}$ = 7.6); 163.68 (C_p, $^4J_{C,P}$ = 3.2)	256.7 (5.08), 344.3 sh (3.50), 352.1 sh (3.60), 362.3 (3.83), 368.7 (3.82), 382.3 (3.97), 401.9 (3.90)
3	3.82 (s, 3 H, OCH_3); 6.98 (m, 2 H, H_m, $^4J_{H,P}$ = 3.8); 7.16 (d, 1 H, H(4), $^3J_{H,H}$ = 7.0); 7.55 (m, 1 H, H(10)); 7.57 (m, 1 H, H(5)); 7.66 (m, 1 H, H (9)); 7.95 (m, 2 H, H_o, $^3J_{H,P}$ = 14.8); 8.23 (d, 1 H, H(6), $^3J_{H,H}$ = 8.0); 8.37 (m, 1 H, H(11)); 8.48 (m, 1 H, H(8))		261.0 (5.04), 358.2 sh (3.63), 377.6 (3.93), 399.4 (4.02), 420.9 (3.93)

* The C(11b) and C(11c) atoms were not detected due to the low signal/noise ratio.

which disappears after methylation (compound **2b**). A characteristic feature of the ^{13}C NMR spectra is the absence of signals in the weak-field region (~180 ppm) and the presence of spin-spin interaction between the C and P atoms. The highest coupling constant (142.5—157.9 Hz) is observed for the neighboring C_i and P atoms, while $^2J_{C,P}$ and $^3J_{C,P}$ (from ~5 to ~17 Hz) and $^4J_{C,P}$ (~3 Hz) have lower values. A similar correlation is evident in the ^1H NMR spectra for the coupling constants of the P and H atoms. The electronic spectra of compounds **2** display several well-resolved absorption bands in the region of 350—450 nm typical of peri-fused anthracene derivatives.

Experimental

IR spectra were recorded in KBr pellets on a UR-20 spectrophotometer. Electronic spectra were obtained in ethanol ($1 \cdot 10^{-4}$ mol L^{-1}) on a Specord UV-Vis spectrometer. The molecular weights of the compounds synthesized and their elemental compositions were determined from the exact mass numbers of the molecular ions on a GC/MC Finnigan MAT-8200 instrument. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 30 °C on Bruker AM-200 and Bruker AM-400 spectrometers. The signals were assigned using selective double $^{13}C\{^1H\}$ resonance data. Chromatography was carried out on silica gel using benzene as the eluent.

The data of elemental analyses with respect to C, H, N, P, and S in the compounds synthesized agree with the calculated values (see Table 1).

1-Amino-9-anthrone (1a) was obtained by reduction of 1-aminoanthraquinone with sodium hydrosulfite in an alkaline medium by the known method.[5]

Anthrones **1b—d** were synthesized in a similar way. Anthrone **1d** undergoes gradual transformation into 1-phenylaminoanthraquinone when kept in air; therefore, a freshly-prepared sample was used. ^1H NMR of **1d**, δ: 4.17 (s, CH_2); 6.60 (dd, H(2)); 6.92—7.45 (m, H(3), H(4), H(5), H(6), H(7), Ph); 8.08 (m, H(8)); 11.17 (s, NH). The small inconsistency in the integral intensities of the signals and the presence of additional low-intensity signals around δ 7—8 may indicate that the sample contains 1-phenylaminoanthraquinone. The mass spectrum of the sample contains molecular ion peaks corresponding to anthrone **1d** (*m/z* 285) and 1-phenylaminoanthraquinone (*m/z* 299).

1-Acetylamino-9-anthrone (1e) was obtained by the acetylation of anthrone **1a** according to the procedure reported previously.[5]

2-(4-Methoxyphenyl)-2,3-dihydroanthra[1,9-*de*][1,3,2]-oxazaphosphorine-2-sulfide (2a). A suspension of anthrone **1a** (0.5 g, 2.4 mmol) and Lawesson's reagent[2] (1.0 g, 2.5 mmol) in dry toluene (10 mL) was boiled for 2—3 min. The reaction mixture was cooled and chromatographed to give compound **2a** (0.68 g).

Anthraoxazaphosphorine **2b** and 2-(4-methoxyphenyl)-2*H*-anthra[1,9-*de*][1,3,2]dioxaphosphorine-2-sulfide (**2c**) were synthesized in a similar way (the reaction times were 2 and 3 h, respectively).

2-(4-Methoxyphenyl)-7-bromo-2*H*-anthra[1,9-*de*][1,3,2]-dioxaphosphorine-2-sulfide (3). A solution of compound **2c** (0.3 g, 0.8 mmol) and bromine (0.06 mL, 1.17 mmol) in chloroform (15 mL) was kept for 24 h at ~20 °C, washed with water, concentrated to a small volume, and chromatographed. The yield of compound **3** was 0.18 g.

Methylation of anthraoxazaphosphorine sulfide 2a. A mixture of compound **2a** (0.15 g, 0.3 mmol), dimethyl sulfate (0.05 g, 0.3 mmol), NaOH (0.4 g, 10 mmol), TEBA-Cl (0.03 g, 0.1 mmol), water (0.5 mL), and benzene (15 mL) was stirred for 30 min at ~20 °C, washed with dilute HCl and water, chromatographed, and recrystallized from chloroform containing methanol. The yield of compound **2b** was 0.22 g (13 %).

The characteristics of the compounds synthesized are presented in Table 1. The ^1H and ^{13}C NMR and electronic spectroscopy data are given in Table 2.

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