



An unusual synthesis of a spirothioxanthene derivative

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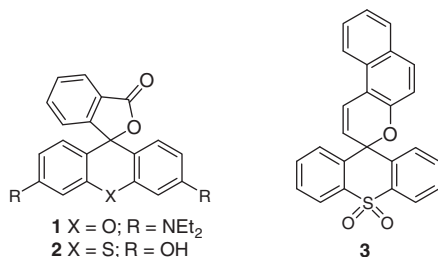
Spirolactone

ABSTRACT

The reaction of diphenyl sulfone with 2,3-dibromophthalazine-1,4-dione in the presence of *n*-butyllithium gave a spiro-9*H*-thioxanthene-10,10-dioxide derivative in 45% yield, the structure of which was proved by X-ray crystallography.

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Xanthenes and spiroxanthenes are important and versatile compounds in organic chemistry. Amongst them are, for example, rhodamine-based compounds such as **1** and its analogues, which are used as fluorescent chemosensors,¹ electrochromic materials,² photosensitisers³ and as sensitizers of photopolymer materials.⁴ The sulfur analogues, spirothioxanthenes, have also been widely described,³ including thiofluorescein (**2**)⁵ and the photochromic thioxanthene-10,10-dioxide derivative **3**,⁶ which was obtained by oxidation of the thioxanthene precursor. The spirothioxanthene skeleton is usually synthesised either starting from thioxanthone,⁵ or from diphenyl sulfide and phthalic anhydride.⁷ Herein, we report a novel route to the spirothioxanthene system, as exemplified by the synthesis of compound **6**.



In continuation of our studies on new diarylsulfone building blocks for conjugated oligomers,⁸ we reacted diphenyl sulfone (**4**) with 2,3-dibromophthalazine-1,4-dione (**5**), which was previously synthesised from phthalhydrazide and zinc bromide under the

mediation of lead(IV) acetate,⁹ in the presence of *n*-butyllithium.¹⁰ A single product was obtained in 45% yield, the structure of which we could not unambiguously assign based on NMR spectroscopic, mass spectrometric and IR spectroscopic data. X-ray analysis of a single crystal revealed the spirothioxanthene structure **6** (Fig. 1).¹¹

From directly comparable experiments using 1, 2, 4 and 10 equiv of *n*-butyllithium, the highest yield was obtained with 4 equiv. A possible mechanism for the formation of **6** is shown in Scheme 1. Lithiation of **4** and reaction with **5** followed by loss of bromide, as shown in **A**, would yield an intermediate which could undergo a second lithiation followed by spirocyclisation and loss of dinitrogen and bromide, as shown in **B**, to give the product **6**. The bromine substituents on **5** are necessary for the reaction to proceed, which is consistent with the mechanism postulated in Scheme 1. Using 2,3-dihydrophthalazine-1,4-dione, instead of **5**, gave no product; and unreacted starting materials were recovered.

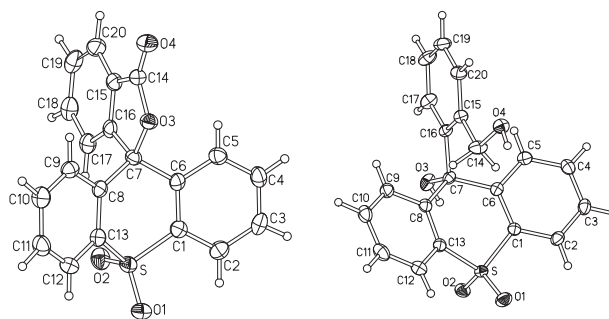
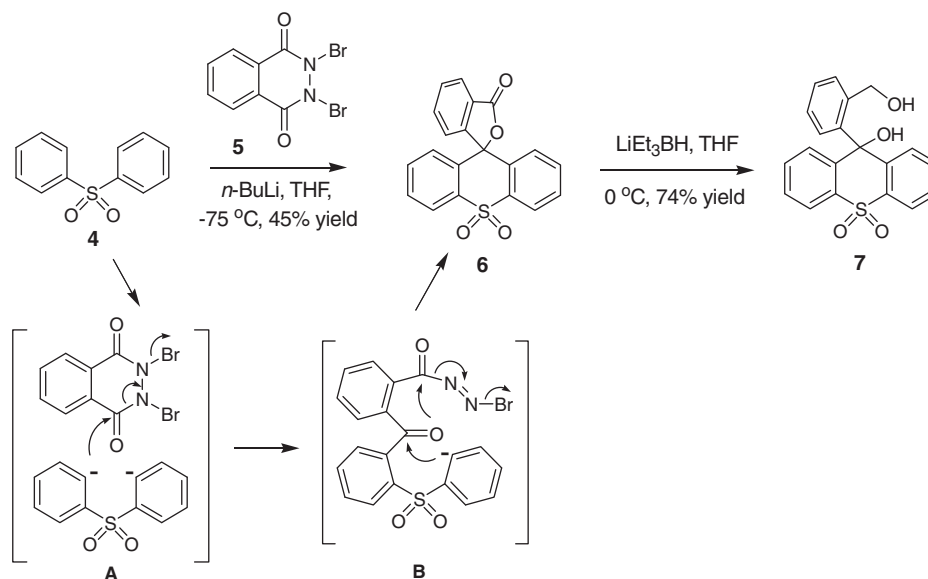


Figure 1. X-ray molecular structures of **6** (left) and **7** (right) (thermal ellipsoids at 50% probability level).

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Scheme 1. Postulated mechanism for the formation of compound **6**, followed by reduction to **7**.

The attempted reduction of **6** with lithium aluminium hydride gave exclusively the unreacted starting material. Trialkylborohydrides are more powerful reducing agents. Compound **6** was, therefore, treated with lithium triethylborohydride (Super-Hydride), which gave the diol product **7** in 74% yield.¹² Initial NMR spectroscopic and mass spectrometric data did not confirm the structure of product **7**. Only one of the two OH protons gave a visible signal in the ¹H NMR spectrum [δ_{H} 4.50 (s, 1H) exchanged with D₂O shake] and the highest observed mass peak was at m/z 334 (EI mode) which can be attributed to the loss of water from **7**. Subsequent mass spectra (ES mode) showed the $[M+Na]^+$ ion for **7**. For a reliable determination of the structure, crystals were grown for X-ray analysis (Fig. 1), which unambiguously proved the formation of compound **7**. This is in agreement with the work of Brown et al., who investigated reactions of trialkylborohydrides, in particular, lithium triethylborohydride, and showed that lactones rapidly react with up to 2 equiv of hydride and undergo reduction to the diol stage.¹³

Attempts to brominate spiro compound **6** with NBS and acetic acid, bromine and acetic acid or bromine and iron (III) bromide were unsuccessful and resulted only in the recovery of the starting material.

In summary, we have developed a new route to an interesting spiro derivative of the 9H-thioxanthene-10,10-dioxide system in a synthetically viable yield. There is clearly scope to explore the functional group tolerance in this process and to explore further reactions of **6**.

Acknowledgement

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Supplementary data

Supplementary data (copies of spectra of compounds **6** and **7**) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.10.048.

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- Preparation of spiro[isobenzofuran-1(3H),9'-thioxanthene]-3-one-10,10-dioxide (**6**): diphenyl sulfone (1.1 equiv) was placed in a flame-dried flask under argon and dissolved in dry THF (10 ml). The solution was cooled to -75 °C, *n*-butyllithium (4.0 equiv) was added dropwise and the mixture was stirred for 1 h keeping the temperature at -75 °C. Then, 2,3-dibromophthalazine-1,4-dione (**5**) (1.0 equiv) was added and the mixture allowed to warm to rt gradually overnight under argon. The reaction was quenched by adding H₂O (30 ml) and the aqueous phase extracted with CH₂Cl₂ (3 × 50 ml) and EtOAc (2 × 30 ml). The product precipitated from the aqueous phase, was filtered and dried to give **6** (45% yield) as a white solid. Crystals for X-ray analysis were obtained by slow recrystallisation from EtOH. Mp = 239.5–241.0 °C; ¹H NMR (700 MHz, CDCl₃): δ = 8.26 (dd, J = 7.8 Hz, J = 1.2 Hz, 2H), 8.02–7.98 (m, 2H), 7.62 (m, 4H), 7.58–7.49 (m, 4H); ¹³C NMR (176 MHz, CDCl₃): δ = 170.22, 153.24, 136.67, 135.84, 135.58, 133.42, 130.12, 129.95, 126.37, 126.12, 124.22, 123.88, 122.49, 82.00; HRMS (ASAP) m/z calcd for [C₂₀H₁₂O₄S+H]⁺: 349.0535, found: 349.0531; IR (KBr) (ν_{max} /cm⁻¹): 1782, 1596, 1467, 1300, 1244, 1167, 1147. X-ray experiment: Bruker SMART 6000 CCD area detector, Mo K α radiation (λ = 0.71073 Å), T = 120 K. Crystal data: C₂₀H₁₂O₄S, M = 348.36, monoclinic, space group *P*2₁/*c* (No. 14), a = 13.9202(7), b = 8.0866(4), c = 14.9348(8) Å, β = 114.34(1)°, U = 1531.7(2) Å³, Z = 4, μ = 0.24 mm⁻¹, 14,160 reflections with $2\theta \leq 50^\circ$, R_{int} = 0.070, R = 0.039 [2096 data with $I \geq 2\sigma(I)$], $wR(F^2)$ = 0.112 (all 2698 unique data). CCDC-781882.
- Preparation of 9-(2-hydroxyphenyl)-9H-thioxanthene-9-ol-10,10-dioxide (**7**): compound **6** (1 equiv) was dissolved in dry THF (10 ml) under argon and the solution was cooled to 0 °C. An excess of Super-Hydride solution (1 M in THF, 4 equiv) was added carefully. The mixture was kept under argon and stirred at rt overnight. EtOH (5 ml) was carefully added to quench the excess of Super-Hydride. CH₂Cl₂ (50 ml) was added and the organic phase washed with H₂O (3 × 50 ml). The mixture was purified by column chromatography on silica gel

eluting with EtOAc/petroleum ether (bp 40–60) in a 1:1 (v/v) ratio to give **7** (74% yield) as a white solid. Crystals for X-ray analysis were obtained by slow recrystallisation from a mixture of CH₂Cl₂ and hexane. Mp = 107.5–108.5 °C; ¹H NMR (400 MHz, CDCl₃): δ = 8.18 (dd, *J* = 7.7 Hz, *J* = 1.2 Hz, 2H), 7.98–7.88 (m, 1H), 7.61–7.52 (m, 4H), 7.49–7.47 (m, 4H), 7.15 (d, *J* = 7.9 Hz, 1H), 4.50 (s, 1H), 3.86 (d, *J* = 5.3 Hz, 2H), (1H not observed); ¹³C NMR (101 MHz, CDCl₃): δ = 188.56, 143.33, 139.51, 137.93, 136.38, 133.33, 129.62, 129.26, 129.08, 128.97, 128.26, 127.74, 123.69, 73.70, 62.97; HRMS (ES): *m/z* calcd

[C₂₀H₁₆O₄S+Na]⁺: 375.0667, found: 375.0663; IR (KBr) (*v*_{max}/cm⁻¹): 1442, 1289, 1160, 1146, 1003. X-ray experiment: Bruker SMART 1000 CCD area detector, Mo Kα radiation (λ = 0.71073 Å), *T* = 120 K. *Crystal data*: C₂₀H₁₆O₄S, *M* = 352.39, monoclinic, space group *P*2₁/*n* (No. 14), *a* = 7.679(1), *b* = 27.580(4), *c* = 7.951(1) Å, β = 108.01(1)°, *U* = 1601.3(4) Å³, *Z* = 4, μ = 0.23 mm⁻¹, 16,060 reflections with $2\theta \leq 57.5^\circ$, *R*_{int} = 0.044, *R* = 0.039 [3457 data with *I* ≥ 2σ(*I*)], *wR*(*F*²) = 0.099 (all 3838 unique data). CCDC-789461.

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