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Thionin Oxide as a Possible Intermediate on Periodate Oxidation of 9-Thiabicyclo[6.1.0]nona-2,4,6-triene

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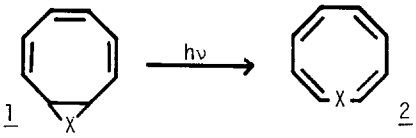
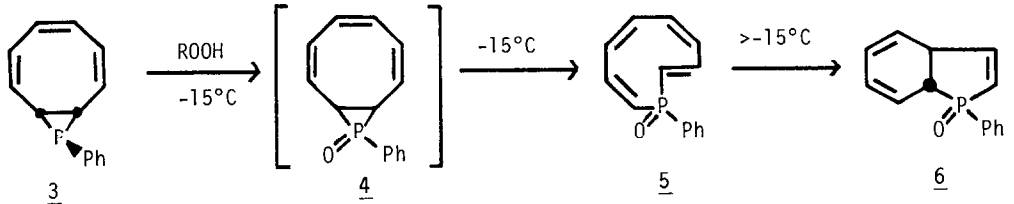
Abstract. 9-Thiabicyclo[6.1.0]nona-2,4,6-triene was oxidized at -15 to -20°C with sodium periodate in a methanol-water medium. The major isolated product was established as cis-3a,7a-dihydrobenzo[b]thiophene-cis-1-oxide, which is best explained as arising from intramolecular cycloaddition of a thionin oxide intermediate.

No synthetic method has yet been devised that opens access to the monocyclic thionin ring in spite of the interest attending it as a potentially aromatic, 10 π-electron system. Sulfoxide and sulfone derivatives of the thionins are also unknown. The method used successfully to prepare the N and O members (2) of the heteronin series involves the photochemical cleavage of the bridging bond in the 9-heterabicyclo[6.1.0]nona-2,4,6-triene system[1], but this method failed with the sulfur compound (1, X=S)[2].



1 2

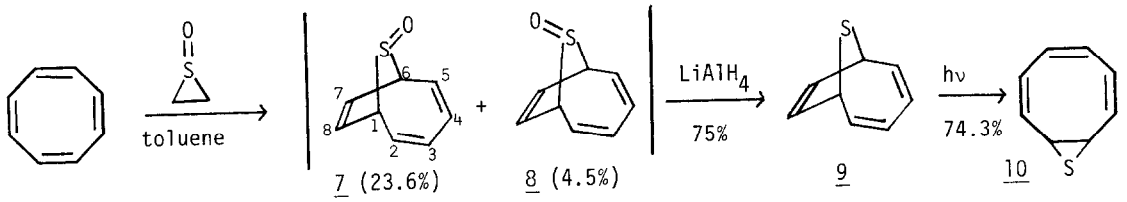
This procedure also failed[3] to provide the phosphonin system (2, X=PR), which still remains unknown[4]. However, we recently discovered a process that generates the P-oxide of a phosphonin with cis, cis, cis, trans geometry[5]; the oxide prepared (5) was stable enough at -15°C to permit its characterization by ^{31}P and ^{13}C NMR spectroscopy, although its half-life at 25°C was only 4 min with respect to an intramolecular cycloaddition to the trans-3a,7a-dihydrophosphindole system (6). The synthesis is based on the oxidation of 3 with peroxides at -15°C; apparently the initially formed P=O derivative 4 is unstable and spontaneously undergoes ring opening to the phosphonin oxide 5, whose geometry (trans-fusion) is predicted from orbital symmetry considerations[6].



3 4 5 6

It did not seem unreasonable to expect similar events on oxidation of the sulfur counterpart 10 of phosphine 3[7], thus opening a way to a thionin oxide, and we report here that we have evidence, from the isolation and full characterization of the intramolecular cycloadduct, supporting the concept that a thionin oxide is formed but is of low stability.

The sulfide 10 was prepared by a method described by Anastassiou[8]. All structures were confirmed by ^{13}C NMR analysis.



The mixture of sulfoxides 7 and 8 was first purified by flash chromatography (benzene, followed by ethyl acetate) and was separable by medium-pressure liquid chromatography (silica gel; ethyl acetate). They were characterized by ^{13}C NMR spectroscopy.

7, δ ^{13}C 59.0(C-1,6) 122.9(C-7,8), 128.1(C-3,4), 130.2(C-2,5)

8, δ ^{13}C 68.8(C-1,6), 120.3(C-7,8), 124.9(C-3,4), 126.9(C-2,5).

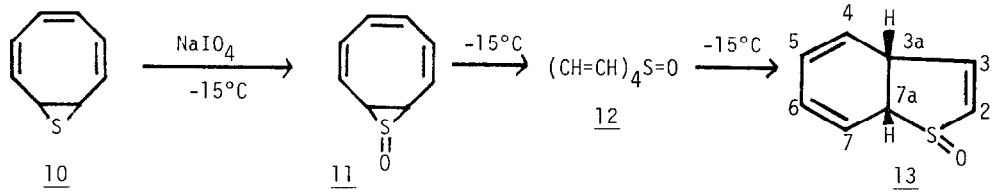
Phosphines related to these sulfoxides have very different ^{31}P NMR shifts (Δ δ 65 ppm[3]); since it is not known if ^{33}S NMR shifts are sensitive to similar structural influences, an attempt was made to characterize 7 and 8 by this technique. For 8, the ^{33}S NMR shift in toluene at 100°C was +320 ppm (downfield of CS_2 = 0). Unfortunately, no signal could be obtained for 7.

The 7-8 mixture was reduced with $LiAlH_4$, and sulfide 9 was then rearranged photochemically in hexane to 10. ^{13}C NMR spectra for both compounds were obtained.

9, δ ^{13}C 49.3(C-1,6), 120.3(C-7,8), 124.7(C-3,4), 138.2(C-2,5)

10, δ ^{13}C 51.0(C-1,8), 123.5(C-4,5), 128.6(C-2,7), 131.2(C-3,6)

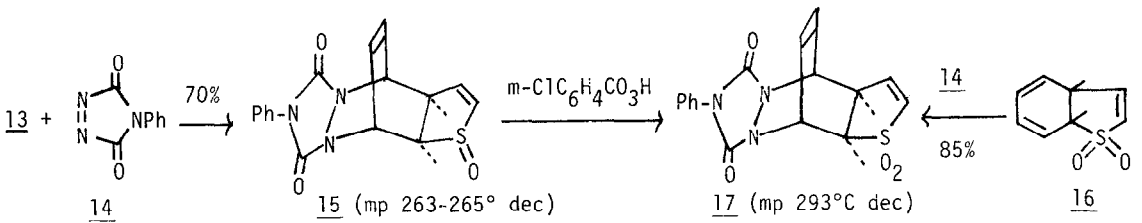
Thiirane 10 reacted with hydrogen peroxide to give only sulfoxide 7. However, treating a solution of 10 (0.5 g) in 50 ml of methanol at -15° to -20°C over a period of 2 hr with 1.1 g of $NaIO_4$ in 20 ml of water, followed by 2 hr stirring at this temperature, gave different results. Precipitated $NaIO_3$ was filtered off and methanol was evaporated at 0°C. The remaining aqueous solution was extracted with 5 x 25 ml of chloroform; the extracts (dried over $MgSO_4$) were separated by MPLC (ethyl acetate) to provide 80 mg of 7 (16%), 70 mg of 8 (14%) and 170 mg (34%) of a new compound identified as 3a,7a-dihydrobenzo[b]thiophene-1-oxide (13).



Compound 13, pure by NMR spectral analysis, was a non-crystallizing oil (mass spectrum, calcd for M^+, m/z 152.0296; found m/z 152.0297, 56%). The fragmentation pattern was relatively simple (M^+-OH, m/z 135, 100%; M^+-SO, m/z 104, 78%; $C_6H_6^+$, m/z 78, 67%; $C_7H_7^+$, m/z 91, 89%).

The ^{13}C NMR spectrum supported structure 13 (δ 43.8 (C-3a); 68.9 (C-7a); 142.5 (C-3); 134.3 (C-2); others 119.2, 122.2, 123.5, 125.0).

The 250 MHz ^1H NMR spectrum, employing the use of selective decoupling and computer simulation for interpretation, gave the parameters: H-2, δ 6.62, $J_{2,3}$ = 6.04, $J_{2,3a}$ = -3.09; H-3, δ 6.86, $J_{2,3}$ = 6.04, $J_{3,3a}$ = 2.48; H-3a, δ 4.33, $J_{3,3a}$ = 2.48, $J_{2,3a}$ = -3.09, $J_{3a,4}$ = 4.1, $J_{3a,5}$ = -3.1, $J_{3a,7a}$ = 10.88; H-4 δ 5.625 $J_{3a,4}$ = 4.1, $J_{4,5}$ = 9.5, $J_{4,6}$ = 0.9; H-5, δ 5.96, $J_{4,5}$ = 9.5, $J_{3a,5}$ = -3.1, $J_{5,6}$ = 6.00, $J_{5,7}$ = 0.9; H-6, δ 6.045, $J_{4,6}$ = 0.9, $J_{5,6}$ = 6, $J_{6,7}$ = 9.51, $J_{6,7a}$ = 2.8; H-7, δ 6.038, $J_{5,7}$ = 0.9, $J_{6,7}$ = 9.51, $J_{7,7a}$ = 5.58; H-7a δ 4.045, $J_{3a,7a}$ = 10.88; $J_{7,7a}$ = 5.58, $J_{6,7a}$ = 2.8 Hz. Of stereochemical significance is the relatively small value (10.9 Hz) for $^3J_{H\text{-}3a,H\text{-}7a}$, which indicates cis ring fusion (in other 1-heteradihydroindenes[8,9] and dihydroindene[10], J is 20-25 Hz for trans hydrogens, 12 Hz or less for cis hydrogens). This is the opposite stereochemical result from that observed with the phosphorus compound, but was confirmed chemically by the reaction sequence below.

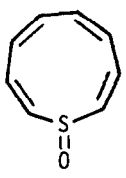


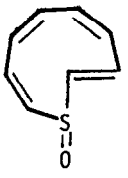
14 — 15 (mp 263-265° dec) — 17 (mp 293°C dec)

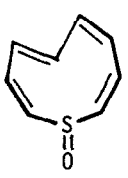
Since the sulfone 16 has known cis-fusion from its method of formation (dimerization of thiophene sulfone; loss of SO_2[11]), formation of the same P-TAD (14) adduct from sulfoxide 13 as indicated, confirmed by ^1H NMR and identical tracings (also on a mixture) on a differential scanning calorimeter, proves its stereochemistry.

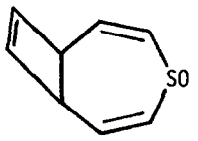
The final feature of the stereochemistry of 13, configuration at sulfur, was established with $Eu(thd)_3$ effects on the ^1H NMR spectrum (measured in $CDCl_3$ over the range 0.1 to 0.4 moles of complex per mole of 13: $\Delta\delta$/mole of complex H-7a, 2.10; H-3, 1.50; H-3a, 0.88; H-2, 0.73; H-7, 0.49; H-6, 0.38; H-4,5 negligible). Since H-7a was the most strongly affected signal, close proximity (cis orientation) to oxygen is established. The small effect on H-7 was consistent with this orientation of oxygen.

It now seems generally accepted[12] that isomerization of bicyclo[6.1.0]nonatrienes to dihydroindenes passes through 9-membered ring intermediates. This has also been established for a 9-aza derivative[13], and in our study of the 9-phospha compound, a phosphonin was observed to form and close to a dihydrophosphindole[5]. Also, it has been proposed that a silonin is an intermediate in the formation of a sila-dihydroindene on addition of a silylene to cyclooctatetraene[14]. We therefore interpret our observation of the formation of dihydrobenzothiophene oxide 13 on oxidation of sulfide 10 as evidence for the existence of a thionin oxide intermediate[15] (12a, 12b, or 12c), of low stability due to the ease of intramolecular cycloaddition.


12a


12b


12c



14

It is not possible at this time to select the proper structure on the basis of the cis-fusion in the isolated dihydrobenzothiophene product 13. cis-Fusion is frequently found after thermal isomerization of the bicyclo[6.1.0]nonatriene framework; various explanations have been discussed (e.g., ref. 12, 13, 16). A structure such as 14 may be another intermediate in the formation of the 9-membered ring.

Acknowledgement

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