

1-METHYL-2-AZATHIABENZENE 1-OXIDE: SYNTHESIS AND SOME PROPERTIES

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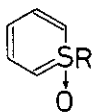
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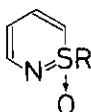
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Abstract — Synthesis and some properties (^1H - and ^{13}C -NMR spectra, deuteration, nitration, and cycloaddition) of 1-methyl-2-azathiabenzene 1-oxide are described.

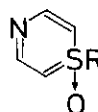
The chemistry of thiabenzene 1-oxides (1)¹ and their aza-analogues (2)² and (3)³ is of particular interest because they form a rather unique class of the six-membered unsaturated heterocycles, in which the six π -electrons cannot be fully delocalized over the six-membered ring due to the presence of the $-\text{S}(\text{O})\text{R}-$ group. All spectroscopic and chemical evidence suggest that they are not aromatic but of ylide in nature. In order to understand the physical and chemical properties of these ring systems, the synthesis of the hitherto unknown parent compounds is highly desirable. In this paper we wish to report the synthesis and some properties (^1H - and ^{13}C -NMR spectra, deuteration, nitration, and cycloaddition) of 1-methyl-2-azathiabenzene 1-oxide (8).



1

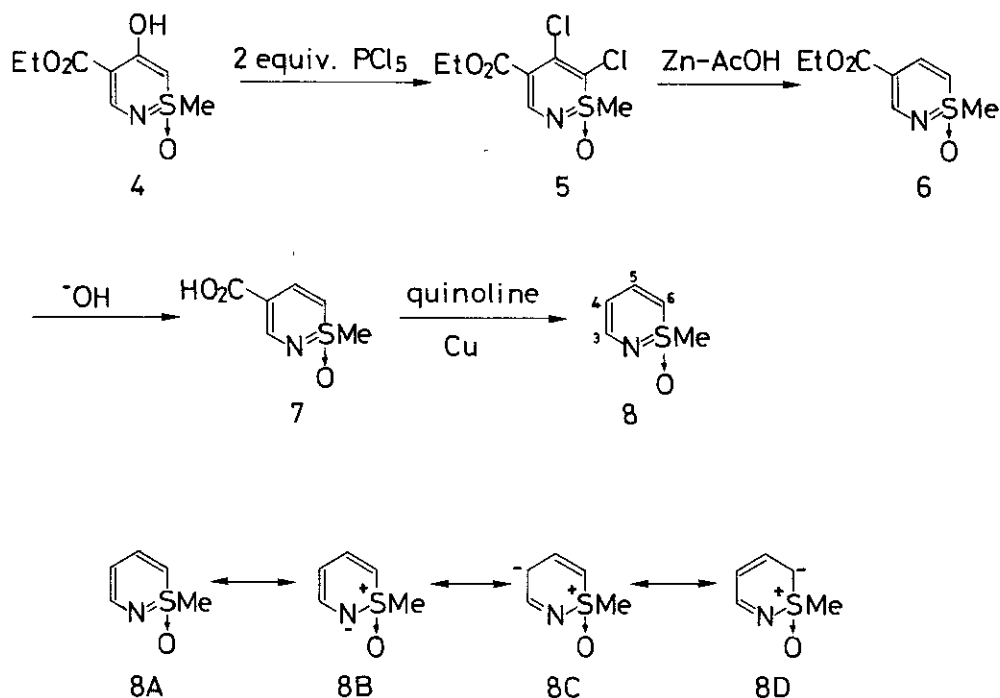


2



3

Synthesis — The synthetic route is illustrated in Scheme 1. Refluxing the previously reported ester (4)^{2b} with two molar equiv. of phosphorus pentachloride⁴ in methylene chloride gave the oily 5,6-dichloro derivative (5) in 69% yield. Reduction of (5) with zinc in refluxing acetic acid afforded (6), mp 78-79°C, in 63% yield, which was hydrolyzed with sodium hydroxide to the carboxylic acid (7), mp 187-189°C, in 84% yield. Decarboxylation of (7) was achieved by refluxing in quinoline in the presence of copper to give the oily compound (8) in 30% yield.



Scheme 1

Properties — The ¹H- and ¹³C-NMR spectra of (8) are summarized in Tables 1 and 2. For comparison, the spectral data of (6) are also included in the Tables. The results clearly indicate that the signals of the hydrogen and carbon atoms at the 4- and 6-positions occurred at much higher magnetic fields than those at the 3- and 5-positions, suggesting the higher electron density at the former positions (see resonance structures 8A-D). This was reflected by the following electrophilic reactions of (8).

Table 1. $^1\text{H-NMR}$ spectral data (δ values in CDCl_3) for the 2-azathiabenzene 1-oxides (J values in Hz)

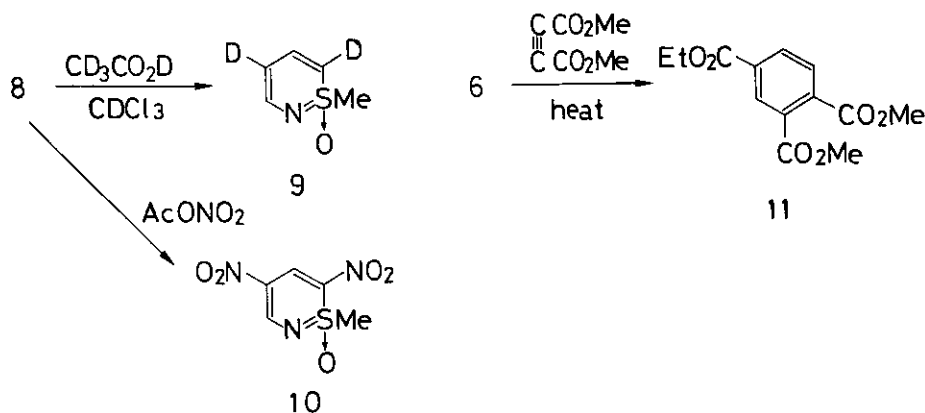
compd	3-H	4-H	5-H	6-H	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{4,6}$	$J_{3,5}$	$J_{3,6}$	others
(8)	7.38 (dd)	5.69 (dd)	7.10 (ddd)	5.90 (dd)	7	6	10	1	2	a	3.34 (1-CH_3)
(6)	8.33 (dd)	-	7.82 (dd)	5.97 (dd)	-	-	10	-	2	1.5	1.33 (CH_2CH_3) 3.39 (1-CH_3) 4.24 (CH_2CH_3)

^a Not determined.

Table 2. $^{13}\text{C-NMR}$ spectral data (δ values in CDCl_3) for the 2-azathiabenzene 1-oxides

compd	3-C	4-C	5-C	6-C	others
(8)	146.2	100.5	137.7	96.2	48.6 (1-CH_3)
(6)	152.9	104.7	138.5	96.1	14.4 (CH_2CH_3), 47.0 (1-CH_3), 60.3 (CH_2CH_3), 165.3 (C=O)

Deuteration of (8) in deuteriochloroform containing acetic acid- d_4 at 35°C proceeded slowly at both the 4- and 6-positions to give (9). Nitration of (8) with excess acetyl nitrate at -5°C afforded the 4,6-dinitro derivative (10), mp $110\text{--}111^\circ\text{C}$, only in 18% yield.



Scheme 2

Finally, it should be noted that (8) did not react with dimethyl acetylene-dicarboxylate under the conditions we employed (refluxing in bromobenzene). This behavior is in contrast to the case of (6) which underwent a [4+2] cycloaddition with dimethyl acetylenedicarboxylate⁵ in refluxing bromobenzene to give dimethyl 4-ethoxycarbonylphthalate (11).⁶

REFERENCES AND NOTES

1. (a) A. G. Hortmann, J. Am. Chem. Soc., 1965, 87, 4972; A. G. Hortmann and R. L. Harris, ibid., 1971, 93, 2471; (b) Y. Kishida and J. Ide, Chem. Pharm. Bull., 1967, 15, 360; C. Tamura, S. Seto, and Y. Kishida, Tetrahedron Lett., 1968, 2739; (c) T. M. Harris, C. M. Harris, and J. C. Cleary, Tetrahedron Lett., 1968, 1427; C. M. Harris, J. C. Cleary, and T. M. Harris, J. Org. Chem., 1974, 39, 72; (d) B. Holt, J. Howard, and P. A. Lowe, Tetrahedron Lett., 1969, 4937; (e) Y. Tamura, T. Miyamoto, H. Taniguchi, K. Sumoto, and M. Ikeda, Tetrahedron Lett., 1973, 1729; Y. Tamura, H. Taniguchi, T. Miyamoto, M. Tsunekawa, and M. Ikeda, J. Org. Chem., 1974, 39, 3519; T. Fujiwara, T. Hombu, K. Tomita, Y. Tamura, and M. Ikeda, J. Chem. Soc. Chem. Commun., 1978, 197; (f) M. Watanabe, T. Kinoshita, and S. Furukawa, Chem. Pharm. Bull., 1975, 23, 258; M. Watanabe, M. Matsuno, K. Kinoshita, and S. Furukawa, Heterocycles, 1977, 6, 1781; (g) L. Weber, C. Kruger, and Y. -H. Tsay, Chem. Ber., 1978, 111, 1709; L. Weber and D. Wewers, ibid., 1983, 116, 1327.
2. (a) T. R. Williams and D. J. Cram, J. Am. Chem. Soc., 1971, 93, 7333; J. Org. Chem., 1973, 38, 20; (b) Y. Tamura, M. Tsunekawa, T. Miyamoto, and M. Ikeda, J. Org. Chem., 1977, 42, 602; (c) A. C. Bares, P. D. Kennewell, and J. B. Taylor, J. Chem. Soc. Chem. Commun., 1973, 776; A. C. Barnes, P. W. Hairsine, S. S. Matharu, P. J. Ramm, and J. B. Taylor, J. Med. Chem., 1979, 22, 418; (d) M. Watanabe, M. Minohara, K. Masuda, T. Kinoshita, and S. Furukawa, Heterocycles, 1976, 4, 1875.
3. H. König, H. Metzger, and K. Seelert, Chem. Ber., 1965, 98, 3724.
4. Use of 1 molar equiv. of phosphorus pentachloride gave a mixture of (5) (21%) and 6-chloro-4-ethoxycarbonyl-5-hydroxy-1-methyl-2-azathiabenzene 1-oxide (42%).
5. The first example of a [4+2] cycloaddition in the 2-azathiabenzene 1-oxide derivatives was reported by M. Watanabe et al.^{1f}
6. A. K. Bahl and W. Kemp, J. Chem. Soc. (C), 1971, 2268.

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