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Synthesis and Some Properties of 2-Azathiabenzene 1-Oxides

MASAZUMI IKEDA,*[,a] HIDETSUGU TSUBOUCHI,[b] MASAYOSHI TSUNEKAWA,[b] HIROSHI KONDO,[b] and YASUMITSU TAMURA[b]

Kyoto Pharmaceutical University,[a] Misasagi, Yamashina, Kyoto 607, Japan and Faculty of Pharmaceutical Sciences, Osaka University,[b] 1–6 Yamada-oka, Suita, Osaka 565, Japan

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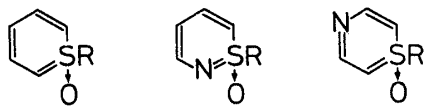
Syntheses of 1-methyl-2-azathiabenzene 1-oxide and its 5-methyl derivative are described. The physical (^{1}H-nuclear magnetic resonance (NMR) and ^{13}C-NMR spectra) and chemical properties (deuteration, bromination, and nitration) suggest that 1-methyl-2-azathiabenzene 1-oxides are best considered as cyclic sulfur ylides.

Keywords——2-azathiabenzene 1-oxide; sulfur ylide; cycloaddition; deuteration; nitration; bromination; thiabenzene 1-oxide

Thiabenzene 1-oxides **1**[1] and their aza-analogues **2**[1f,h,j,2] and **3**[3] form a rather unique class of six-membered fully unsaturated heterocycles, whose six π electrons cannot be fully delocalized over the ring because of the presence of the –S(O)R– group. X-Ray studies of some of these derivatives[1c,h,k] indicate that the heterocyclic rings have half-boat conformations with the apex at the sulfur atom. All other available evidence strongly suggests that they can best be regarded as cyclic sulfur ylides. In order to obtain more information about these unique ring systems the synthesis of the hitherto unknown parent compounds is highly desirable. In this paper we wish to report the preparation and some properties of the parent compound **9** of the 2-azathiabenzene 1-oxide series[4] and its 5-methyl derivative **11**. The cycloaddition reaction of the 4-acyl derivatives with dimethyl acetylenedicarboxylate is also described.



1 **2** **3**

Synthesis

The synthetic route used for **9** is illustrated in Chart 1. Heating of **4a**[2b] with 1 or 2 mol eq of phosphorus oxychloride in methylene chloride for 3 h gave only the 6-chloro derivative **5**. However, chlorination of **4a** with 2 mol eq of phosphorus pentachloride in methylene chloride gave the 5,6-dichloro derivative **6a** in 69% yield. Reduction of **6a** with zinc in acetic acid gave **7a** in 63% yield, and this was hydrolyzed with sodium hydroxide to the carboxylic acid **8a** in 84% yield. Decarboxylation of **8a** was achieved by heating it in quinoline in the presence of copper to give the desired **9** in 30% yield as an oil.

An attempt to synthesize the 1-phenyl derivative was unsuccessful. Thus, the same sequence of reactions was repeated from **4b**[2c] and the corresponding carboxylic acid **8b** was obtained, but in poor overall yield (4%). Unfortunately, decarboxylation of **8b** under the same reaction conditions as used for **8a** resulted in extensive decomposition.

The 1,5-dimethyl derivative **11** was easily obtained in 58% yield, along with the ester **12**

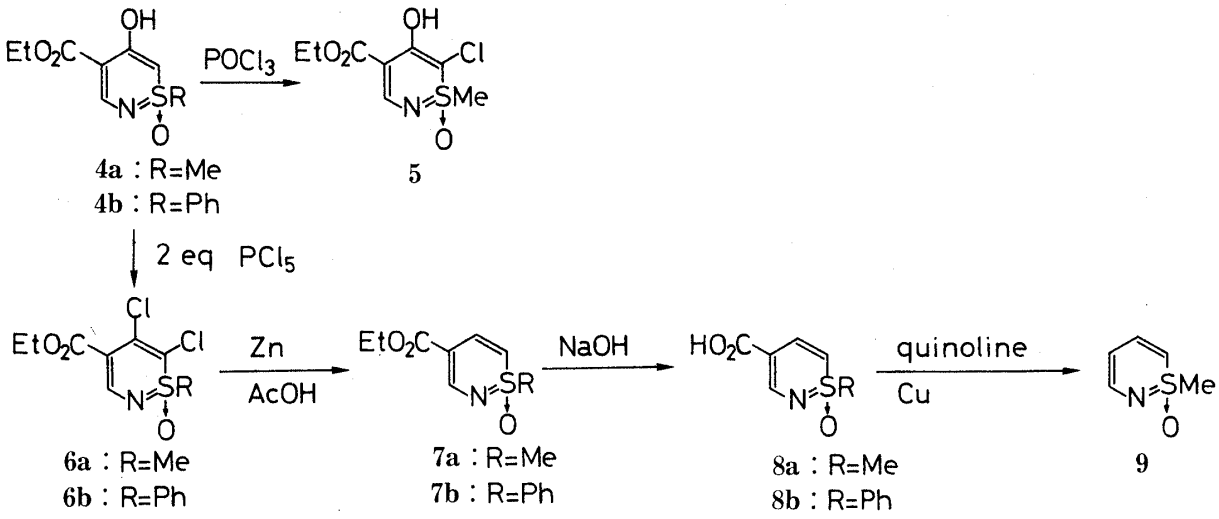


Chart 1

(23%), by refluxing the carboxylic acid **10**[2d] in ethanol in the presence of conc. sulfuric acid. The behavior of **10** is rather unusual, considering that esterification was the only observed reaction course when these conditions were applied to **8a**. A possible mechanism for the decarboxylation of **10** may involve an initial protonation at the 4-position to form an intermediate **13**, which may undergo decarboxylation. In fact, **10** and **8a** showed very different behavior in deuterium exchange experiments: **10** underwent deuterium exchange at the 6-position ($t_{1/2} = 48$ h) when a solution in deuteriochloroform containing trifluoroacetic acid-d_1 was allowed to stand at 35 °C, whereas no exchange took place with **8a** under the same conditions. The electronic effect of the 5-methyl group may be responsible for this abnormal behavior of **10**.

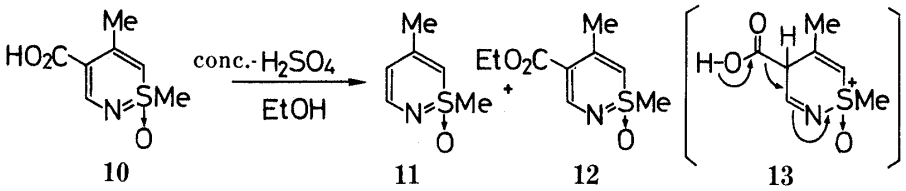


Chart 2

Properties

The ultraviolet (UV) absorption maxima of the 2-azathiabenzene 1-oxides **9** and **11** appeared at around 310 nm with an intensity of ε *ca.* 2100—2600. The position of the maximum was not affected by addition of 6 N hydrochloric acid.

The ^{1}H- and ^{13}C- nuclear magnetic resonance (NMR) spectra of **9** and related compounds are summarized in Tables I and II. It is very striking that the hydrogen and carbon atoms at the 4- and 6-positions appeared at much higher magnetic field than those at the 3- and 5-positions, indicating higher electron density at the former two positions (see resonance structures C and D). This was reflected in the electrophilic reactions of **9** and **11**.

Deuteration of **11** in deuteriochloroform containing acetic acid-d_4 at 35 °C proceeded slowly at both the 4- and 6-positions to give **15** ($t_{1/2} \approx 140$ h). On the other hand, deuteration of **9** under the same conditions proceeded at a much slower rate ($t_{1/2} \approx 700$ h) at both the 4- and 6-positions to give **14**.

Bromination of **11** with 1 mol eq of pyridine hydrobromide perbromide gave the

TABLE I. ^{1}H-NMR Spectral Data for the 2-Azathiabenzene 1-Oxides

Compd.	H-3	H-4	H-5	H-6	$J_{3,4}$	$J_{3,5}$	$J_{3,6}$	$J_{4,5}$	$J_{5,6}$	Others
9	7.40 (br d)	5.74 (dd)	7.16 (ddd)	5.95 (dd)	6	2	1	8	10	3.38 (1-Me) (s)
7a	8.36 (dd)	—	7.84 (dd)	5.97 (dd)	—	3	2	—	10	1.35, 4.26 (OEt) (t) (q) 3.39 (1-Me) (s)
11	7.30 (dd)	5.60 (dd)	—	5.74 (br)	7	—	1	—	—	2.12 (5-Me) (s) 3.30 (1-Me) (s)
12[2b]	8.43 (s)	—	—	5.80 (br)	—	—	—	—	—	1.33, 4.24 (OEt) (t) (q) 2.46 (5-Me) (s) 3.34 (1-Me) (s)

TABLE II. ^{13}C-NMR Spectral Data for the 2-Azathiabenzene 1-Oxides

Compd.	C-3	C-4	C-5	C-6	Others
9	146.2	100.5	137.7	96.2	48.6 (1-Me)
7a	152.9	104.7	138.5	96.1	14.4, 60.3 (OEt), 47.0 (1-Me) 165.3 (C=O)
11	145.4	102.8	149.8	94.5	22.7 (5-Me), 47.4 (1-Me)
12	152.1	105.6	154.3	95.2	14.4, 59.9 (OEt), 24.0 (5-Me), 46.9 (1-Me), 165.7 (C=O)

monobromide **16** (48%) and dibromide **17** (8%), and the use of 2 mol eq of the same brominating agent gave only the dibromide **17** in 86% yield. The preferential formation of the 4-bromo derivative **16** rather than the 6-bromo derivative with 1 mol eq of the brominating agent may be attributed to steric factors rather than the electronic character: the 6-position seems to be more hindered by the methyl group at the 5-position and the two substituents on the sulfur atom. Unfortunately, this was not confirmed because **9** gave only a resinous material under brominating conditions.

Nitration of **11** with excess of acetyl nitrate at -5 °C resulted in the formation of the 4,6-dinitro derivative **19** in 52% yield. Nitration of **9** proceeded very slowly but gave the 4,6-dinitro derivative **18** in 18% yield.

The structure assignments of these products were readily made on the basis of ^{1}H-NMR spectroscopy (see Experimental).

In summary, the 2-azathiabenzene 1-oxides can best be regarded as cyclic sulfur ylides

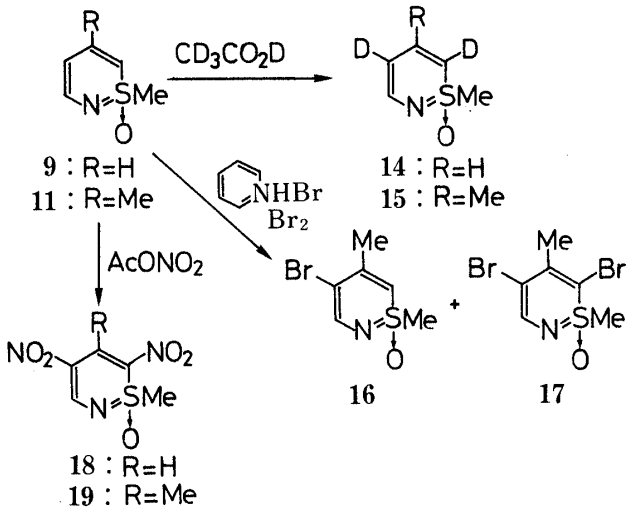


Chart 3

whose negative charge is delocalized over the azapentadienyl moiety and whose positive charge is localized on the sulfur atom (see resonance structures B-D). The stability of this ring system may be attributed to the $p\pi$–$d\pi$ bonding (resonance structures A and E). The electronic effect of the 5-methyl group is also significant.

Finally, we examined whether this ring system can function as a diene component in the Diels–Alder reaction. It was found that both **9** and **11** did not react with dimethyl acetylenedicarboxylate (DMAD) under various conditions. This is in contrast with the behavior of the 4-acyl derivatives **4a**, **7a**, **20**—**22**, which underwent a cycloaddition reaction with DMAD[5] in refluxing bromobenzene to give the corresponding phthalic esters **25**—**29** in good yields. The results are summarized in Table III.

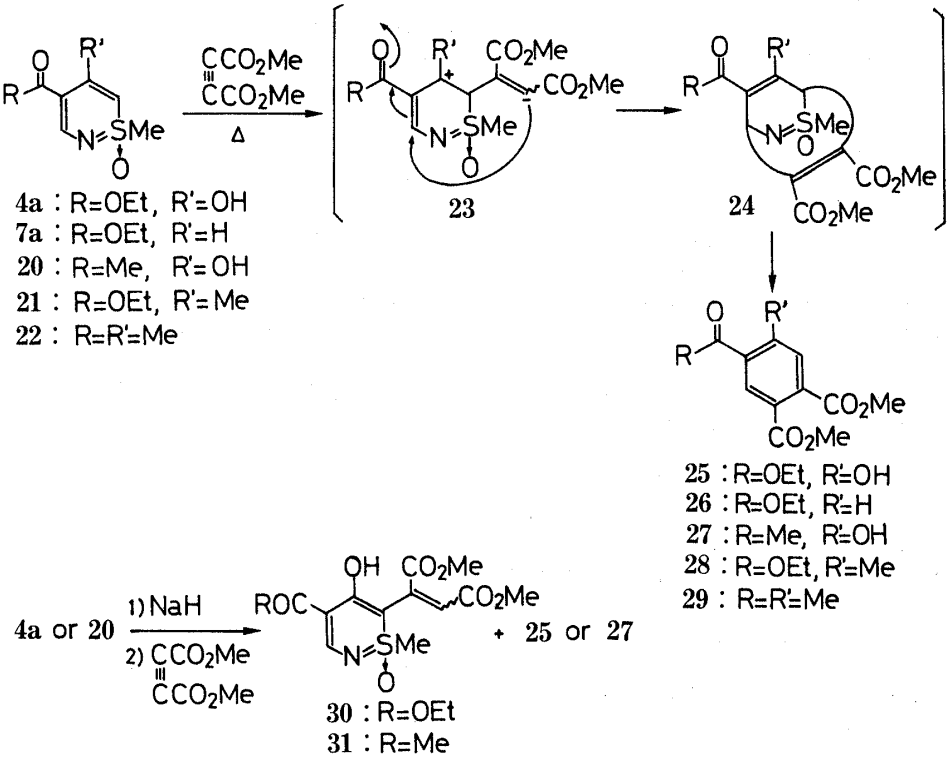


Chart 4

Table III. Cycloaddition of the 2-Azathiabenzene 1-Oxides with DMAD in Refluxing Bromobenzene

	Starting material R	R′	Reaction time (h)	Yield (%)	Product
22	Me	Me	4	65	**29**
21	OEt	Me	5	71	**28**
20	Me	OH	6	53	**27**
4a	OEt	OH	6	61	**25**
7a	OEt	H	24	44[a]	**26**

a) Unreacted starting material (41%) was recovered.

In principle, two mechanisms for the step of formation of the initial adducts **24** could be operative: (a) a concerted [4+2] cycloaddition process or (b) a stepwise "double Michael addition process" involving intermediates **23**. We prefer the latter mechanism for the following reasons: (1) the presence of the electron-withdrawing 4-acyl groups is essential for this cycloaddition (no reaction took place with **9** and **11**) and (2) the presence of the electron-donating group at the 5-position enhances the reactivity (compare the reactivities of **4a** or **21** and **7a**). In addition, we have found that **4a** or **20** reacted with DMAD under basic conditions (NaH in DMSO) at room temperature to give a mixture of **30** (40%) or **31** (27%) and **25** (25%) or **27** (16%).[6]

Experimental[7]

6-Chloro-4-ethoxycarbonyl-5-hydroxy-1-methyl-2-azathiabenzene 1-Oxide (5)——A solution of **4a**[2b] (217 mg, 1 mmol) and phosphorus oxychloride (306 mg, 2 mmol) in dry methylene chloride (3 ml) was refluxed for 3 h. The mixture was poured into ice-water and the organic layer was separated, washed with brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed (silica gel; ethyl acetate–*n*-hexane, 1 : 3) to give **5** (153 mg, 61%); oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2400—3200, 1670; ^{1}H-NMR ($CDCl_3$) δ: 1.42 (3H, t, J=8 Hz, $OCH_2\underline{CH_3}$), 3.53 (3H, s, 1-CH_3), 4.38 (2H, q, J=8 Hz, $OCH_2\underline{CH_3}$), 8.24 (1H, s, 3-H), 12.56 (1H, s, OH). Analysis was carried out by high-resolution mass spectrometry: Calcd for $C_8H_{10}ClNO_4$, 251.0020; Found, 251.0033.

Use of 1 mol eq of phosphorus oxychloride gave **5** in 42% yield.

5,6-Dichloro-4-ethoxycarbonyl-1-methyl-2-azathiabenzene 1-Oxide (6a)——A solution of **4a** (217 mg, 1 mmol) and phosphorus pentachloride (416 mg, 2 mmol) in dry methylene chloride (3 ml) was refluxed for 2 h. Work-up as described above gave **6a** (186 mg, 69%); oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720; ^{1}H-NMR ($CDCl_3$) δ: 1.32 (3H, t, J=7 Hz, $OCH_2\underline{CH_3}$), 3.55 (3H, s, 1-CH_3), 4.25 (2H, q, J=7 Hz, $OCH_2\underline{CH_3}$), 8.14 (1H, s, 3-H). Analysis was carried out by high-resolution mass spectrometry: Calcd for $C_8H_9Cl_2NO_3S$, 268.9679; Found 268.9679.

Use of 1 mol eq of phosphorus pentachloride in the above experiment gave a mixture of **5** (42%) and **6a** (21%).

4-Ethoxycarbonyl-1-methyl-2-azathiabenzene 1-Oxide (7a)——(A) From **6a**: A mixture of **6a** (1.5 g, 5.58 mmol) and zinc powder (3.5 g) in acetic acid (20 ml) was refluxed for 8 h. After cooling, the mixture was diluted with water and extracted with chloroform. The extract was washed with brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed (silica gel; benzene–ethyl acetate, 7 : 1) to give **7a** (706 mg, 63%); mp 78—79 °C (from ether); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1700. *Anal.* Calcd for $C_8H_{11}NO_3S$: C, 47.74; H, 5.51; N, 6.96. Found: C, 47.90; H, 5.42; N, 6.86.

(B) From **8a**: A solution of **8a** (87 mg, 0.5 mmol) in ethanol (2 ml) containing conc. H_2SO_4 (100 mg) was refluxed for 3 h. The mixture was concentrated, neutralized with 10% NaOH, and extracted with chloroform. The extract was washed with brine, dried ($MgSO_4$), and concentrated to give **7a** (70 mg, 70%).

4-Carboxy-1-methyl-2-azathiabenzene 1-Oxide (8a)——A solution of **7a** (201 mg, 1 mmol) and NaOH (120 mg) in ethanol (3 ml) was refluxed for 2 h. The mixture was concentrated, acidified with 10% HCl, and extracted wih chloroform. The extract was washed with water, dried ($MgSO_4$), and concentrated. The residual solid was recrystallized from ethyl acetate–*n*-hexane to give **8a** (145 mg, 84%); mp 187—189 °C; IR ν_{max}^{KCl} cm^{-1}: 2100—3000, 1660; ^{1}H-NMR (DMSO-d_6) δ: 3.55 (3H, s, 1-CH_3), 6.46 (1H, dd, J=10, 1 Hz, 6-H), 7.68 (1H, dd, J=10, 3 Hz, 5-H), 8.14 (1H, dd, J=1, 3 Hz, 3-H). *Anal.* Calcd for $C_6H_7NO_3S$: C, 41.61; H, 4.07; N, 8.09. Found: C, 41.48; H, 3.99; N, 8.04.

1-Methyl-2-azathiabenzene 1-Oxide (9)——A mixture of **8a** (173 mg, 1 mmol), quinoline (258 mg, 2 mmol), and

copper powder (25 mg) was refluxed for 30 min. After cooling of the mixture, chloroform was added and the whole was filtered on Celite. The filtrate was washed with 10% HCl and water, dried ($MgSO_4$), and concentrated. The residue was chromatographed (silica gel: benzene–ethyl acetate, 6 : 1) to give **9** (39 mg, 30%); oil; UV ν_{max}^{EtOH} nm (log ε): 313 (3.34). Analysis was carried out by high-resolution mass spectrometry: Calcd for C_5H_7NOS, 129.0248: Found, 129.0265.

5,6-Dichloro-4-ethoxycarbonyl-1-phenyl-2-azathiabenzene 1-Oxide (6b)——A solution of **4b**[2c] (279 mg, 1 mmol) and phosphorus pentachloride (520 mg, 2.5 mmol) in dry tetrachloroethane (5 ml) was heated for 2 h. Work-up gave a mixture of two products, which were separated by column chromatography (silica gel; benzene–ethyl acetate, 25 : 1) to give **6b** (83 mg, 25%) and an unidentified product (59 mg), mp 62—63 °C (from benzene–*n*-hexane).

Compound **6b**: mp 119—120 °C (from *n*-hexane–benzene); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720; ^{1}H-NMR ($CDCl_3$) δ: 1.40 (3H, t, J=7 Hz, $OCH_2\underline{CH_3}$), 4.36 (2H, q, J=7 Hz, $OC\underline{H_2}CH_3$), 7.45—7.9 (5H, br, aromatic protons), 8.38 (1H, s, 3-H). *Anal.* Calcd for $C_{13}H_{11}Cl_2NO_3S$: C, 47.00; H, 3.34; N, 4.22. Found: C, 47.04; H, 3.36; N, 4.18.

4-Ethoxycarbonyl-1-phenyl-2-azathiabenzene 1-Oxide (7b) and 6-Chloro-4-ethoxycarbonyl-1-phenyl-2-azathiabenzene 1-Oxide——A mixture of **6b** (996 mg, 3 mmol) and zinc powder (1.95 g) in acetic acid (20 ml) was refluxed for 24 h. Work-up gave a mixture of two products, which were separated by column chromatography (silica gel; benzene–ethyl acetate, 10 : 1) to give **7b** (165 mg, 21%) and its 6-chloro derivative (232 mg, 26%).

Compound **7b** was an oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1700; ^{1}H-NMR ($CDCl_3$) δ: 1.39 (3H, t, J=6 Hz, $OCH_2\underline{CH_3}$), 4.34 (2H, q, J=6 Hz, $OC\underline{H_2}CH_3$), 5.86 (1H, dd, J=10, 2 Hz, 6-H), 7.4—7.9 (5H, br, aromatic protons), 7.97 (1H, dd, J=10, 3 Hz, 5-H), 8.54 (1H, dd, J=3, 2 Hz, 3-H). Analysis was carried out by high-resolution mass spectrometry: Calcd for $C_{13}H_{13}NO_3S$, 263.0518; Found, 263.0628.

The 6-chloro derivative was an oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1700; ^{1}H-NMR ($CDCl_3$) δ: 1.34 (3H, t, J=7 Hz, $OCH_2\underline{CH_3}$), 4.31 (2H, q, J=7 Hz, $OC\underline{H_2}CH_3$), 7.3—7.9 (5H, br s, aromatic protons), 7.90 (1H, d, J=2 Hz, 5-H), 8.38 (1H, d, J=2 Hz, 3-H). Analysis was carried out by high-resolution mass spectrometry: Calcd for $C_{13}H_{12}ClNO_3S$, 297.0227; Found, 297.0227.

4-Carboxy-1-phenyl-2-azathiabenzene 1-Oxide (8b)——By using a similar procedure to that described for **8a**, **8b** (35 mg, 78%) was obtained from **7b** (50 mg): mp 171—172 °C (from ethyl acetate); IR ν_{max}^{KCl} cm^{-1}: 2200—3200, 1660; ^{1}H-NMR (DMSO-d_6) δ: 6.38 (1H, dd, J=10, 1 Hz, 6-H), 7.6—7.9 (5H, br s, aromatic protons), 7.84 (1H, dd, J=10, 2 Hz, 5-H), 8.32 (1H, br s, 3-H). *Anal.* Calcd for $C_{11}H_9NO_3S$: C, 56.16; H, 3.86; N, 5.95. Found: C, 56.69; H, 3.80; N, 5.88.

1,5-Dimethyl-2-azathiabenzene 1-Oxide (11)——A solution of **10**[2b] (187 mg, 1 mmol) in ethanol (5 ml) containing conc. H_2SO_4 (200 mg) was refluxed for 1 h. The mixture was concentrated, neutralized with 10% NaOH, and extracted with chloroform. The extract was washed with water, dried ($MgSO_4$), and concentrated to give a mixture of two products, which were separated by column chromatography (alumina; ethyl acetate–*n*-hexane, 1 : 3) to give **12** (49 mg, 23%); mp 70 °C (lit.[2b] 70 °C) and **11** (104 mg, 58%).

Compound **11** was an oil; UV ν_{max}^{EtOH} nm (log ε): 311 (3.20). Analysis was carried out by high-resolution mass spectrometry: Calcd for C_6H_9NOS, 143.0410: Found, 143.0405.

Deuterium Exchange Experiments——(A) **8a** and **10**: Trifluoroacetic acid-d_1 (1 drop) was added to a solution of a sample (0.1 mmol) in $CDCl_3$ (0.25 ml) at 35 °C. The exchange was followed by ^{1}H-NMR spectroscopy.

(B) **9** and **11**: Acetic acid-d_4 (3 drops) was added to a solution of a sample (0.1 mmol) in $CDCl_3$ (0.4 ml) at 35 °C. The exchange was followed by ^{1}H-NMR spectroscopy.

Bromination of 11——(A) A solution of **11** (143 mg, 1 mmol) and pyridine hydrobromide perbromide (384 mg, 1.2 mmol) in acetic acid (3 ml) was stirred at room temperature for 3 h. The mixture was diluted with water and extracted with chloroform. The extract was washed with saturated $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated. The residue was subjected to preparative thin-layer chromatography (TLC) on alumina (ethyl acetate–*n*-hexane, 1 : 3) to give 4-bromo-1,5-dimethyl-2-azathiabenzene 1-oxide (**16**) (106 mg, 48%), 4,6-dibromo-1,5-dimethyl-2-azathiabenzene 1-oxide (**17**) (24 mg, 8%), and unreacted **11** (19 mg, 13%).

Compound **16**: mp 114—115 °C (from benzene–*n*-hexane); ^{1}H-NMR ($CDCl_3$) δ: 2.21 (3H, s, 5-CH_3), 3.33 (3H, s, 1-CH_3), 5.90 (1H, s, 6-H), 7.58 (1H, s, 3-H). *Anal.* Calcd for C_6H_8BrNOS: C, 32.44; H, 3.63; N, 6.31. Found: C, 32.54; H, 3.58; N, 6.35.

Compound **17**: mp 81—82 °C (from benzene–*n*-hexane); ^{1}H-NMR ($CDCl_3$) δ: 2.42 (3H, s, 5-CH_3), 3.50 (3H, s, 1-CH_3), 7.43 (1H, s, 3-H). *Anal.* Calcd for $C_6H_7Br_2NOS$: C, 23.94; H, 2.34; N, 4.65. Found: C, 24.28; H, 2.40; N, 4.64.

(B) Use of 2 mol eq of pyridine hydrobromide perbromide gave only the dibromide **17** in 86% yield.

1,5-Dimethyl-4,6-dinitro-2-azathiabenzene 1-Oxide (19)——A solution of **11** (50 mg, 0.35 mmol) in acetic anhydride (1.4 ml) and acetic acid (0.6 ml) was added dropwise to a cooled solution of acetyl nitrate [prepared by adding 70% HNO_3 (0.25 ml) to acetic anhydride (1.7 ml) at −5 °C]. The reaction mixture was allowed to stand for 2 h at room temperature, then poured into ice-water. The mixture was extracted with chloroform and the extract was washed with a saturated $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated. The residual yellow solid was recrystallized from ethyl acetate–*n*-hexane to give **19** (42 mg, 52%); mp 150—151 °C; IR ν_{max}^{KCl} cm^{-1}: 1560, 1320; ^{1}H-NMR ($CDCl_3$) δ: 2.83 (3H, s, 5-CH_3), 3.88 (3H, s, 1-CH_3), 8.75 (1H, s, 3-H). *Anal.* Calcd for $C_6H_7N_3O_5S$: C, 30.91; H, 3.03; N, 18.02. Found: C, 31.11; H, 3.00; N, 17.69.

1-Methyl-4,6-dinitro-2-azathiabenzene 1-Oxide (18)——By using a similar procedure to that described above, except for the reaction time (5 d), **18** (39 mg, 18%) was obtained from **9** (129 mg, 1 mmol): mp 110—111 °C (from ether); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1555, 1320; ^{1}H-NMR ($CDCl_3$) δ: 3.95 (3H, s, 1-CH_3), 9.13 and 9.23 (1H each, AB q, J=2 Hz, 3- and 5-H). *Anal.* Calcd for $C_5H_5N_3O_5S$: C, 27.40; H, 2.30; N, 19.17. Found: C, 27.74; H, 2.29; N, 18.94.

General Procedure for Thermal Cycloaddition——A solution of the 1-azathiabenzene 1-oxide (**4a**, **7a**, **20**, **21**, and **22**) (1 mmol) and DMAD (2 mmol) in bromobenzene (2 ml) was refluxed under a nitrogen atmosphere. After removal of the solvent *in vacuo*, the residue was chromatographed (silica gel; benzene–ethyl acetate, 7 : 1). The reaction times and yields are given in Table III.

Dimethyl 4-ethoxycarbonyl-5-hydroxyphthalate (**25**): mp 33—34 °C [from petroleum ether (bp 30—60 °C)]; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3300—2800, 1730, 1680; ^{1}H-NMR ($CDCl_3$) δ: 1.44 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$), 3.88 (3H, s, OCH_3), 3.90 (3H, s, OCH_3), 4.46 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 7.08 (1H, s), 8.37 (1H, s), 11.29 (1H, s, OH). *Anal.* Calcd for $C_{13}H_{14}O_7$: C, 55.32; H, 5.00. Found: C, 54.94; H, 4.77.

Dimethyl 4-ethoxycarbonylphthalate (**26**)[8] was an oil.

Dimethyl 4-acetyl-5-hydroxyphthalate (**27**): mp 71 °C [from petroleum ether (bp 80—60 °C)]; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3200—2800, 1730, 1650; ^{1}H-NMR ($CDCl_3$) δ: 2.70 (3H, s, $COCH_3$), 3.89 (3H, s, OCH_3), 3.92 (3H, s, OCH_3), 7.06 (1H, s), 8.30 (1H, s), 12.62 (1H, s, OH). *Anal.* Calcd for $C_{12}H_{12}O_6$: C, 57.14; H, 4.80. Found: C, 56.84; H, 4.73.

Dimethyl 4-ethoxycarbonyl-5-methylphthalate (**28**) was an oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730; ^{1}H-NMR ($CDCl_3$) δ: 1.42 (3H, t, J=8 Hz, $OCH_2C\underline{H}_3$), 2.66 (3H, s, CH_3), 3.91 (6H, s, 2×OCH_3), 4.40 (2H, q, $OC\underline{H}_2CH_3$), 7.49 (1H, s), 8.30 (1H, s). Analysis was carried out by high-resolution mass spectrometry: Calcd for $C_{14}H_{16}O_6$, 280.0944; Found, 280.0926.

Dimethyl 4-acetyl-5-methylphthalate (**29**): mp 76.5 °C [from petroleum ether (bp 30—60 °C)]; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730, 1690; ^{1}H-NMR ($CDCl_3$) δ: 2.58 (3H, s, 5-CH_3), 2.62 (3H, s, $COCH_3$), 3.91 (6H, s, 2×OCH_3), 7.50 (1H, s), 8.07 (1H, s). *Anal.* Calcd for $C_{13}H_{14}O_5$: C, 62.39; H, 5.64. Found: C, 62.15; H, 5.83.

General Procedure for Base-Catalyzed Cycloaddition——Compound **4a** (218 mg, 1 mmol) was added portionwise to a solution of NaH (40 mg as a 60% oil dispersion) in DMSO (5 ml) at room temperature under a nitrogen atmosphere. The mixture was stirred for 30 min and then DMAD (143 mg, 1 mmol) was added. This mixture was refluxed for 8 h under a nitrogen atmosphere, diluted with ice-water, acidified with 10% HCl and extracted with CH_2Cl_2. The extract was washed with water, dried ($MgSO_4$), and concentrated. The residue was chromatographed (silica gel; benzene–ethyl acetate, 7 : 1) to give **30** (147 mg, 40%) and **25** (71 mg, 25%).

Compound **30** was an oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3200—2800, 1730, 1660; ^{1}H-NMR ($CDCl_3$) δ: 1.32 (1H, t, J=7 Hz, $OCH_2C\underline{H}_3$), 3.21 (3H, s, 1-CH_3), 3.70 (3H, s, OCH_3), 3.82 (3H, s, OCH_3), 4.28 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 7.16 (1H, s, olefinic proton), 8.30 (1H, s, 3-H), 11.1 (1H, s, OH). Analysis was carried out by high-resolution mass spectrometry: Calcd for $C_{14}H_{17}NO_8S$, 359.0630; Found, 359.0680.

Similarly, **20** gave **31** (27%) and **27** (16%).

Compound **31** was an oil; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3300—2800, 1730, 1675; ^{1}H-NMR ($CDCl_3$) δ: 2.49 (3H, s, $COCH_3$), 3.39 (3H, s, 1-CH_3), 3.59 (6H, s, 2×OCH_3), 7.22 (1H, s, olefinic proton), 8.74 (1H, s, 3-H), 13.52 (1H, s, OH). Analysis was carried out by high-resolution mass spectrometry: Calcd for $C_{13}H_{15}NO_7S$, 329.0568; Found, 329.0543.

A similar treatment of **32** with DMAD gave only the addition product **33** (59%), mp 121—122 °C (from ether–*n*-hexane); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3300—2500, 1730, 1640; ^{1}H-NMR ($CDCl_3$) δ: 1.33 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$), 3.54 (3H, s, 1-CH_3), 3.76 (3H, s, OCH_3), 3.83 (3H, s, OCH_3), 4.28 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 5.54 (1H, d, J=10 Hz, 2-H), 6.66 (1H, s, olefinic proton), 7.77 (1H, d, J=10 Hz, 3-H), 13.04 (1H, s, OH). *Anal.* Calcd for $C_{15}H_{18}O_8S$: C, 50.27; H, 5.06. Found: C, 50.24; H, 5.09.

References and Notes

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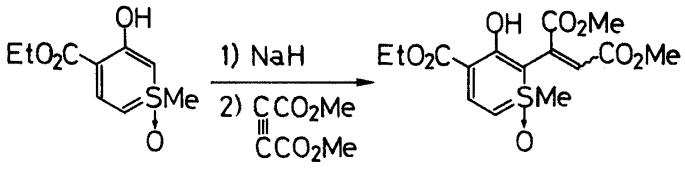
4) A part of this work has appeared as preliminary communication: M. Ikeda, H. Tsubouchi, M. Tsunekawa, H. Kondo, and Y. Tamura, *Heterocycles*, **20**, 2185 (1983).
5) The first example of a [4+2] cycloaddition in the 2-azathiabenzene 1-oxide derivatives was reported by Watanabe *et al.*[1j]
6) A similar treatment of 4-ethoxycarbonyl-5-hydroxythiabenzene 1-oxide (**32**) gave only the addition product **33** in 59% yield.



32 **33**

7) All melting points are uncorrected. ^{1}H-NMR spectra were determined with a Hitachi R-22 (90 MHz) spectrometer (with tetramethylsilane as internal standard) and ^{13}C-NMR spectra were obtained by Fourier transformation carried out on a Hitachi R-900 specrometer at 22.6 MHz. IR spectra were recorded with a JASCO IRA-1 spectrophotometer and UV spectra with a Hitachi 124 spectrophotometer. Low and high resolution mass spectra were obtained with a JMS-D-300 instrument at 70 eV.
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