NEW THIAPYRIDINOPHANES

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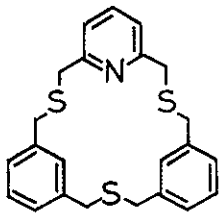
Syntheses, some spectral and chemical properties of new 18-membered trithiapyridinophane 1 and 13-membered dithiapyridinophane 2 are described.

Although a number of thiapyridinophanes has been known,[2] little attention has been paid to thiapyridinophanes containing one pyridine ring and two benzene rings in the molecules. We were interested in such thiapyridinophane systems which are useful precursors of pyridinophanes. This paper is concerned with syntheses, and some spectral and chemical properties of 2,11,20-trithia-[3]metacyclo[3]metacyclo[3](2,6)pyridinophane (1) and 2,17-dithia[3]orthocyclo-[0]orthocyclo[3](2,6)pyridinophane (2).



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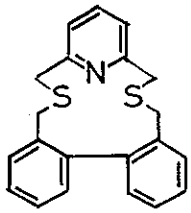

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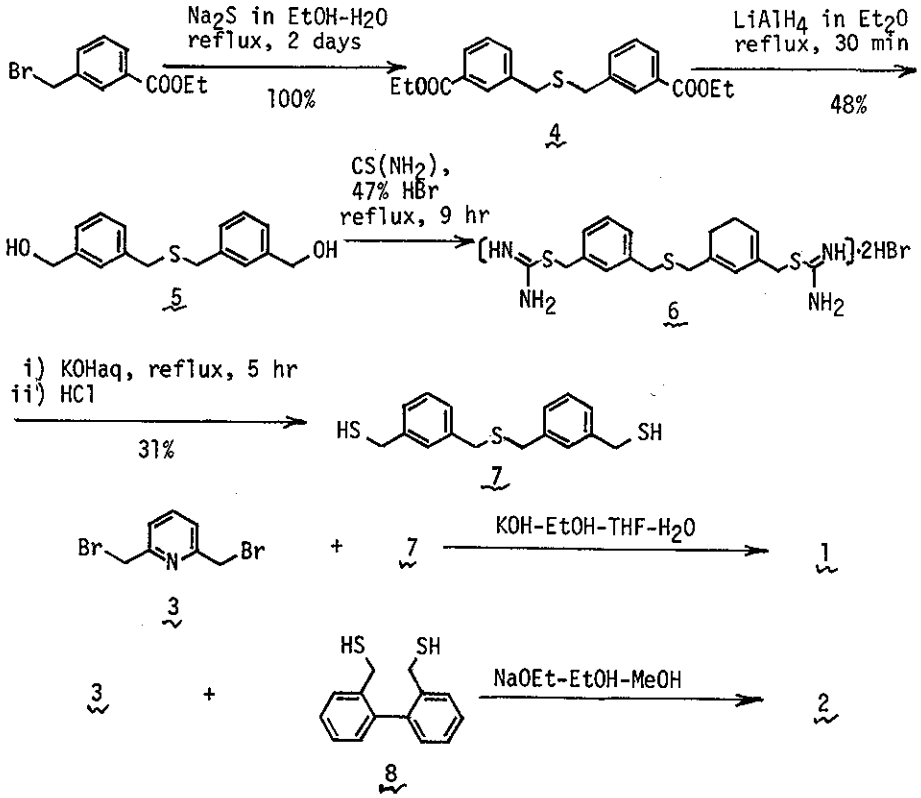
The 18-membered and 13-membered heterocycles, 1 and 2, were prepared by

condensations of 2,6-bisbromomethylpyridine (3)[3] and bis(m-mercaptomethylbenzyl)sulfide (7), and of 3 and 2,2'-bis(mercaptomethyl)diphenyl (8)[4] respectively. Dithiol 7 was prepared via diisothiouronium salt 6 starting from ethyl m-bromomethylbenzoate as illustrated in Scheme 1. Structural elucidation of bis(m-ethoxycarbonylbenzyl)sulfide (4), bis(m-hydroxymethylbenzyl)sulfide (5), and dithiol 7 were accomplished on the basis of spectral data.[5]

4: viscous oil; ir (neat) 1720 cm^{-1} (CO); nmr (CCl_4) δ 1.4 (6H, t, $CH_2\underline{CH_3}$), 3.6 (4H, s, $SC\underline{H_2}$), 4.35 (4H, q, $C\underline{H_2}Me$), 7.2-8.2 (8H, m, aromatic protons).

5: mp 56-57°C, colorless prisms; ir (KBr) 3260 cm^{-1} (OH); nmr ($CDCl_3$) δ 2.75



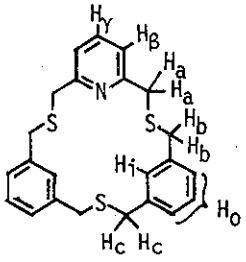
Scheme 1

(2H, br, OH, exchanged with D_2O), 3.58 (4H, s, SCH_2), 4.59 (4H, s, OCH_2), 7.23 (8H, m, aromatic protons).

7: colorless oil; ir (neat) 2560 cm^{-1} (SH); nmr ($CDCl_3$) δ 1.72 (2H, t, SH, J=8 Hz, exchanged with NaOD-D_2O), 3.52 (4H, s, SCH_2), 3.62 (4H, d, $HSCH_2$, J=8 Hz, changed to a singlet when treated with NaOD-D_2O), 7.15 (8H, m, aromatic protons).

When dibromide 3 was allowed to react with dithiol 7 in the presence of aqueous potassium hydroxide solution in a solution of ethanol-tetrahydrofuran under high dilution conditions, the expected 18-membered heterocycle 1, mp 178-179°C, as colorless prisms was obtained in 51% yield. In a similar reaction of 3 with dithiol 8, 13-membered heterocycle 2, mp 197-198°C, as colorless prisms was formed in 65% yield. The spectral data supported well the assigned structures for 1 and 2.

Table I. Nmr Spectral Data of 1 and 9



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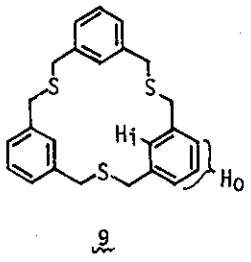

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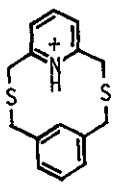
	Solvent	H_a	H_b	H_c	H_i	H_o	H_β	H_γ
1	$CDCl_3$	3.66	3.62	3.49	7.22(2H)	7.32(8H)		7.64
		(each 2H, s)			(apparent s)			(1H, dd)
1	CF_3COOH	4.16	3.87	3.61	7.04(2H)	7.34(6H)	7.75	8.35
		(each 2H, s)			(apparent s)		(2H, dd)	(1H, dd)
9	$CDCl_3$	3.52(12H, s, CH_2),			7.09(3H, s, H_i),		7.29(9H, apparent d, H_o)	

The nmr spectral data of 1 and cyclophane 9[6] are shown in Table I. The mass spectrum of 1 displayed a parent ion (M^+, rel. intensity 34.5%) at m/e 409, together with fragment ions at m/e 274 (100%), 243 (59%), 138 (36%), 135 (28%), and 107 (34%). The possible structure for the base ion of mass 274 would be 10, which would be formed by the elimination of thioformylbenzyl radical from M^+.



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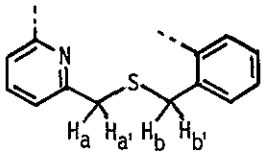
The nmr spectra of 2 were measured in various solvents, and temperature dependence of the nmr signals of the methylene groups in $C_6D_5NO_2$ was examined (Table II). In most cases all the methylene protons appeared as AB doublets; this clearly indicates that 2 exists as a preferred conformer. The assignment of the methylene protons at the α-position of the pyridine ring was on the

Table II Nmr Spectral Data of Methylene Groups in 2

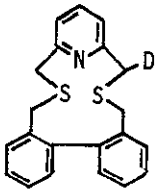


Solvent	Temp. °C	δ, ppm H_a-C-$H_{a'}$		H_b-C-$H_{b'}$		$J_{aa'}$ Hz	$J_{bb'}$ Hz
$CDCl_3$	34	3.39	3.69	3.56	4.08	14	17
C_6D_6	34	3.08	3.50	3.48	4.27	14	17
$C_6D_5NO_2$	34	3.42[a]		3.42	4.11	—	17
〃	50	3.30	3.56	3.46	4.11	14	16
〃	100	3.29	3.57	3.43	4.02	14	16
CF_3COOH	34	4.25[a]		3.71	4.13	—	13

a) Apparent singlet.

basis of the nmr spectrum of 2-d_1 (11). After 2 was treated with n-butyl-

lithium in a solution of n-hexane-THF under nitrogen at -70°C, the treatment of the resulting red solution of a carbanion of 2 with D_2O afforded a mixture of 2 (26%) and 11 (74%), whose composition was determined by the mass spectroscopy. In the mass spectrum an ion assignable to 2,6-lutidine-d_1 ion appeared as a base ion at m/e 108. In the nmr spectrum of the mixture in $CDCl_3$, the doublets at δ 3.39 and 3.69 decreased in intensity.



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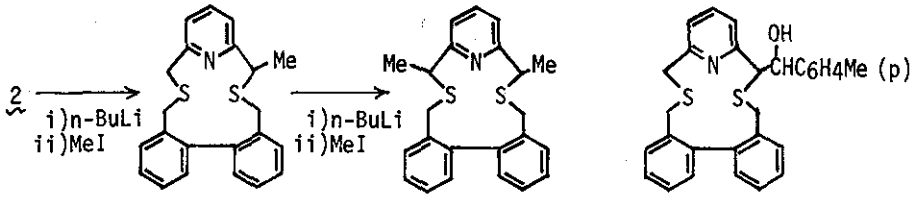
The mass spectrum of 2 exhibited a parent ion (rel. intensity 70%) at m/e 349, together with major ions at m/e 316 (15%), 211 (21%), 197 (15%), 178 (28%), 165 (25%), 152 (12%), 138 (28%), and 107 ([2,6-lutidine]$^+$, 100%).

The reaction of the carbanion of 2 mentioned above with methyl iodide gave a monomethyl derivative 12, mp 128-129°C, as colorless prisms in 54% yield.[7] A similar reaction of a carbanion of 12 which generated from 12 and n-butyllithium, with methyl iodide afforded a dimethyl derivative 13, mp 102-104°C, as colorless prisms in 37% yield. Structural elucidation of 12 and 13 were accomplished on the basis of spectral data.

12: nmr ($CDCl_3$) δ 1.51 (3H, d, CH_3, J=8 Hz, changed to a singlet when irradiated at δ 3.86), 3.3-4.2 (7H, complex m, $3CH_2$+ CH, a singlet appeared at δ 3.86 when irradiated at δ 1.51), 6.8-8.1 (11H, aromatic protons); mass spectrum m/e



12 13 14

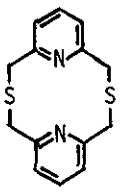
Scheme 2

363 (M^+, rel. intensity 100%), 348 (M^+ - Me, 9%), 330 (M^+ - SH, 18%), 211 (348^+ - $MeC_5H_3NCH{=}S$, 24%), 210 (14%), 209 (20%), 197 (211^+ - CH_2, 30%), 178 (211^+ -SH, 28%), 165 (30%), 152 (34%), 151 (38%), 150 (28%), 121 ([2-ethyl-6-methylpyridine]$^+$, 99%), 119 (121^+ - H_2, 54%).

13: nmr ($CDCl_3$) δ 1.65 (6H, apparent d, CH_3), 3.38 (2H, apparent d, CH), 3.69 (4H, s, CH_2), 6.8-8.2 (11H, aromatic protons); mass spectrum m/e 377 (M^+, rel. intensity 51%), 211 (23%), 197 (8%), 178 (15%), 165 (15%), 164 (42%), 135 ([2,6-diethylpyridine]$^+$, 28%), 133 [135^+ - H_2, 100%).

In the reaction of the carbanion of 2 with p-tolualdehyde an alcohol 14, mp 96-98°C, as colorless prisms was formed in 36% yield [14: ir (KBr) 3480 cm^{-1} (OH); nmr ($CDCl_3$) δ 2.27 (3H, s, CH_3), 3.4-4.3 (6H, m, CH_2), 3.96, 5.25 (each 1H, d, CH, J=5 Hz), 4.45 (1H, br, OH, exchanged with D_2O), 6.9-8.0 (15H, aromatic protons); mass spectrum m/e 469 (M^+)].

It has been reported that oxidation of dithiapyridinophane 15 with peracid



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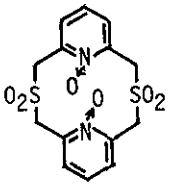

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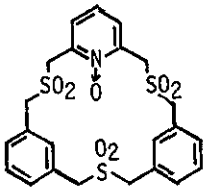

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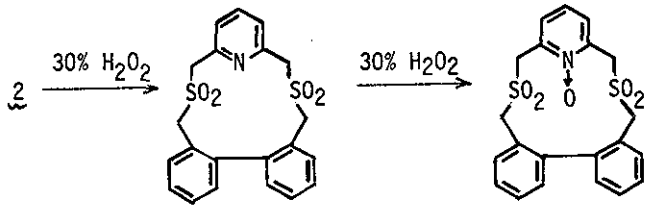


18 19

Scheme 3

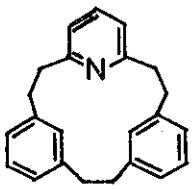
afforded bis-sulfone-bis-N-oxide 16 in moderate yield.[8]

When 1 was heated with 30% hydrogen peroxide in acetic acid-benzene under reflux for 2 hr, tris-sulfone-N-oxide 17, mp > 300°C, was formed quantitatively. On the other hand, a similar treatment of 2 afforded bis-sulfone 18, mp > 300°C, almost quantitatively. Further oxidation of 18 with 30% hydrogen peroxide in refluxing acetic acid for 1 hr gave a mixture of 18 and bis-sulfone-N-oxide 19, whose elemental analysis showed the intermediate values between those of 18 and 19. However, 18 and 19 could not be isolated. The oxidation rate of 2 is slower than that of 1; this seems to be due to a crowd structure of 2.[9]

17: ir (KBr) 1120, 1315 (SO_2), 1250 cm^{-1} (N→O); nmr (DMSO-d_6) δ 4.19, 4.78, 5.08 (each 4H, apparent s, CH_2), 7.0-8.0 (11H, m, aromatic protons).

18: ir (KBr) 1120, 1320 cm^{-1} (SO_2); nmr (DMSO-d_6) δ 4.39, 4.87 (each d, CH_2, J=17 Hz), 4.45 (apparent s, CH_2) (total 8H), 7.1-8.3 (11H, m, aromatic protons).

Recently, it has been reported that irradiation of dithiacyclophanes in the presence of trialkyl phosphite gives the corresponding cyclophanes in good yield.[10, 11] However, attempts to prepare cyclophanes, 20 and 21, by photochemical extrusion of sulfur from 1 and 2 were unsuccessful. Further investigation is in progress.



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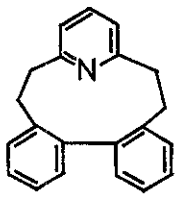

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