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SYNTHESES OF NEW [2.2]PYRIDINOPHANES[1)]

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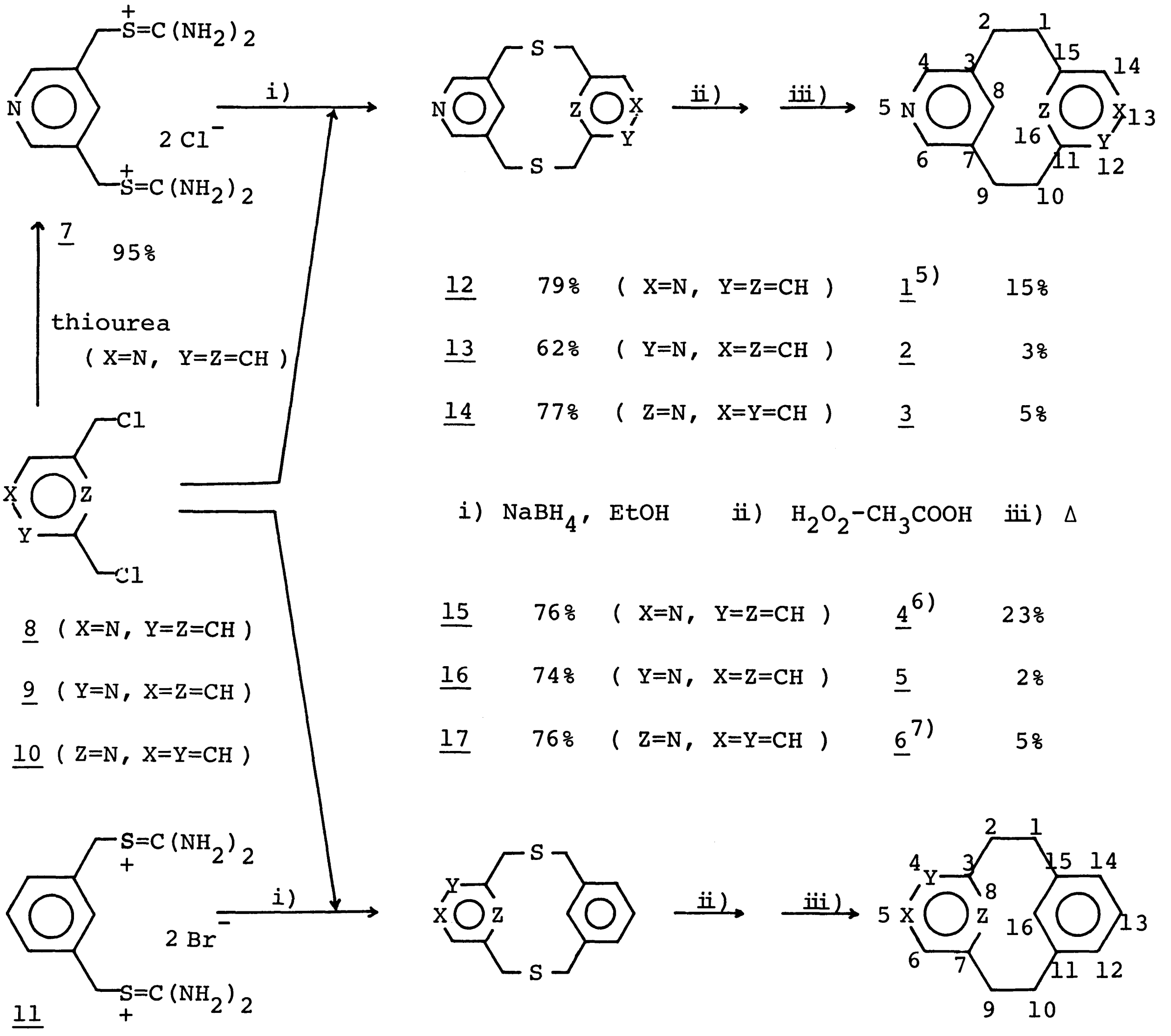
Six meta-bridged [2.2]pyridinophanes including three new compounds are synthesized successfully via the corresponding cyclic disulfides. Electronic effect of nitrogen atoms in pyridine rings constructed in a [2.2]metacyclophane-like stepped form is studied on the basis of their ^{1}H and ^{13}C NMR spectra.

We have previously described the synthesis of a novel analogue of methylviologen by the transannular reaction of [2.2](3,5)pyridinophane (1) under reductive conditions.2) The fact indicates that the meta-bridged [2.2](m,n)pyridinophanes are expected to be very efficient intermediates for preparing the condensed hetero aromatics. A few of such pyridinophanes have been known,3) but no (2,4)pyridinophane having [2.2]metacyclophane-like framework has been reported yet. Now we wish to report the syntheses of several pyridinophanes 1-6 involving (2,4)pyridinophanes and some spectral data of them.

Bis(chloromethyl)pyridines (8, 9, and 10) were prepared from the corresponding lutidines by the known method4) with some modification. The compounds 8 and 10 were purified by recrystallization but the chloride 9 was used without further purification because of its instability. Bis(isothiouronium) salts (7 and 11) were obtained from the corresponding halomethyl compounds by treatment with thiourea in 95% and 92% yields respectively. Direct coupling of 7 and 10 to cyclic disulfide (14) without isolation of intermediate dithiol was carried out with sodium borohydride in ethanol under high-dilution condition. After purification, the disulfide 14 was obtained as colorless plates from benzene-hexane in 77% yield. Other disulfides (12, 13, 15, 16, and 17) were also prepared from halides (8, 9, and 10) and isothiouronium salts (7 and 11) in a similar way to that used for 14. 2,11-Dithia[3.3](3,5)pyridinophane 12 was converted to the corresponding disulfone with H_2O_2-acetic acid in 81% yield and the disulfone was pyrolyzed at 700 °C /8×10^{-2}Torr to give the target cyclophane, [2.2](3,5)pyridinophane 1. The compounds 1 was purified by column chromatography on silica gel and recrystallization from chloroform-acetone (15% yield on 12) [1:[5] colorless prisms, mp 268-271 °C (in sealed tube)].



8 (X=N, Y=Z=CH)

9 (Y=N, X=Z=CH)

10 (Z=N, X=Y=CH)

12	79%	(X=N, Y=Z=CH)	1[5]	15%
13	62%	(Y=N, X=Z=CH)	2	3%
14	77%	(Z=N, X=Y=CH)	3	5%

i) $NaBH_4$, EtOH ii) H_2O_2-CH_3COOH iii) Δ

15	76%	(X=N, Y=Z=CH)	4[6]	23%
16	74%	(Y=N, X=Z=CH)	5	2%
17	76%	(Z=N, X=Y=CH)	6[7]	5%

Two different (3,5)pyridinophanes, [2.2](2,4)(3,5)pyridinophane (2) [2: colorless plates from benzene-hexane, mp 147-148 °C] and [2.2](2,6)(3,5)pyridinophane (3) [3: colorless needles from benzene-hexane, mp 164-166 °C] were synthesized in a quite similar manner as used for 1. The other disulfides (15, 16, and 17) were also treated with H_2O_2-acetic acid and the resulting disulfones were pyrolyzed at 500-

700 °C to give desired reference compounds, [2]metacyclo[2](3,5)pyridinophane (4) [4:6) colorless scales from ethanol, mp 164-165 °C], [2]metacyclo[2](2,4)pyridinophane (5) [5: colorless needles from hexane, mp 113-115 °C], and [2]metacyclo[2](2,6)pyridinophane (6) [6:7) colorless plates from hexane, mp 181-183 °C (in sealed tube)]. The structures of these pyridinophanes 1-6 were characterized by elemental analyses and NMR spectral data. (Tables 1 and 2)

Table 1. ^{1}H NMR data of pyridinophanes 1-6 (δ ppm in $CDCl_3$, 360 MHz)

Compd	H-4	H-5	H-8	H-13	H-14	H-16
1	8.386	———	4.549	———	8.386	4.549
2	8.318 or 8.365	———	4.510	8.529	6.990	4.355
3	8.349	———	4.600	7.630	7.129	———
4 8)	8.313	———	4.355	7.327	7.099	4.411
5	———	8.474	4.247	7.307	6.930 or 6.943	4.348
6	7.074	7.577	———	7.307	7.098	4.389

The aromatic inner protons (H-8 and H-16) of pyridinophanes 1-6 show marked upfield shift due to the magnetic anisotropy of the partially overlapped aromatic rings which are fixed in a stepped form as in [2.2]metacyclophane. The signal of H-16 proton of (3,5)pyridinophane 4 appears in the most lowfield (δ 4.411) among those of metacyclopyridinophanes 4-6. Similarly, C-16 carbon chemical shift (δ 138.34) of 4 is situated in somewhat lower field compared to that (δ 135.61) of (2,4)pyridinophane 5, which is comparable to δ 136.3 of [2.2]metacyclophane.9) The same tendency is observed between those of H-8 and C-16 of pyridinophanes 1 and 2. These facts indicate that electron density on inner carbon atom of pyridine ring

Table 2. ^{13}C NMR data of pyridinophanes 1-6 (δ ppm in $CDCl_3$, 90 MHz)

Compd	C-4	C-5	C-8	C-13	C-14	C-16
1	147.19	———	145.11	———	147.19	145.11
2	146.67 or 147.10	———	142.39	150.14	120.31	132.70
3	146.34	———	144.04	137.70	120.49	———
4	146.71	———	143.40	129.68	125.82	138.34
5	———	149.36	130.88	129.36	125.37 or 125.80	135.61
6	120.04	137.20	———	129.08	125.12	138.24

influences considerably on the electronic state of faced aromatic rings, especially of its inner carbon atoms, due to π-transannular interactions. In the case of (2,6)pyridinophanes, 3 and 6, on the other hand, high electron density on the inner pyridine nitrogen atoms induces more severe steric compression than in [2.2]metacyclophane to result in downfield shift of C-8 (3) and C-16 (6) absorptions in spite of the electronic effect.

The electronic spectra of pyridinophanes 1-6 are shown in Fig. 1. There are observed a little bathochromic shift and disappearance of fine structures on absorption bands as compared with those of the corresponding lutidines.10) It is probably due to some π-transannular interactions between chromophores as well as ring strain.

Further work is in progress and will be presented elsewhere.

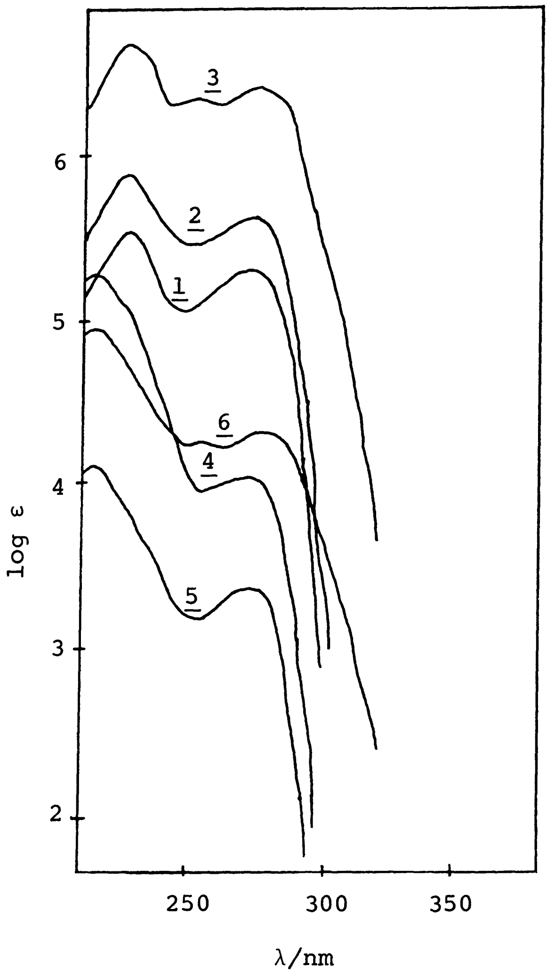


Fig. 1. UV spectra of pyridinophanes 1-6 in THF.11)

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11) The curves, except that of compound 5 at the bottom, have been displaced upward on the ordinate axis by 0.5 log ε unit increments from the curve immediately below.

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