Synthesis of *NN'*-Dimethyl[2,2](2,5)pyrrolophane from 1,4,7,10-Cyclododecanetetraone

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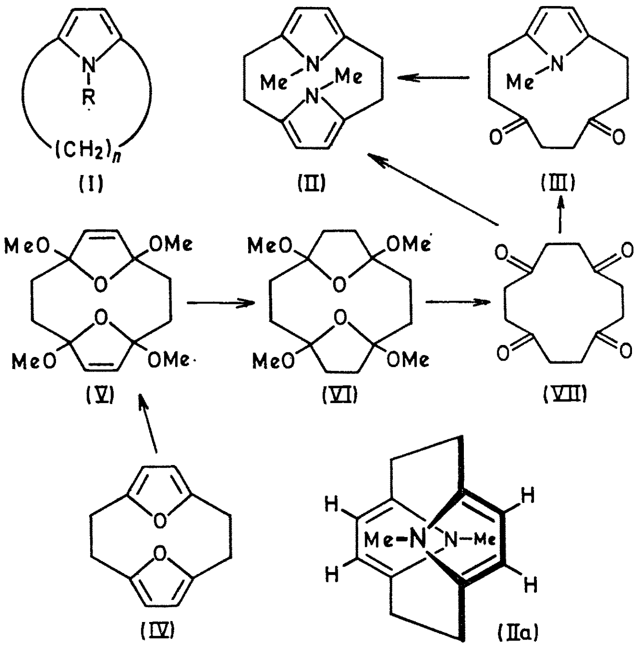
Summary The preparation of 1,4,7,10-cyclododecanetetraone {from [2,2](2,5)furanophane} and its conversion into [2,2](2,5)pyrrolophane is described.

WE report the preparation of *NN'*-dimethyl[2,2](2,5)-pyrrolophane (II), a member of a new class of hetero-cyclophanes, from the cyclic tetraketone (VII). While earlier workers have succeeded in forming[2,5] pyrrolophanes of type (I), where $n = 4$[1] and $n = 8$,[2] bipyrrole derivatives analogous to the well-known [2,2](2,5)furanophane (IV) have not previously been described.

The synthetic sequence involved in the conversion of (IV) into (II) is shown below. Formation of the unsaturated and saturated acetals (V) and (VI) by high pressure hydrogenation has been previously described by Winberg.[3] We have now found that hydrolysis of (VI) with $0{\cdot}2$N-HCl for 4 hr. at room temperature leads to the tetraone (VII) in good yield (95%). Compound (VII) may be crystallized from acetone as needles, m.p. 129—130°.† It shows a single carbonyl band in the i.r. (KBr) at 1710 cm^{-1} and has a sharp singlet (16H) in the n.m.r. at τ ($CDCl_3$) $7{\cdot}31$.

A solution of (VII) in glacial acetic acid, warmed to 80° under nitrogen, was treated with anhydrous methylamine for 30 min. The resulting mixture was made basic to pH 10 with ammonium hydroxide and extracted with chloroform. The chloroform solution was then washed with water to remove *N*-methylacetamide and the solvent removed by evaporation. Chromatography of the residue on silica gel, and elution with chloroform yielded the pyrrolophane (II)



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† All new compounds gave satisfactory analytical results and had the expected spectral properties.

which was crystallized from acetone as prisms, (42%) m.p. 144—145°:† i.r. (KBr) 2945 and 3005 cm^{-1}. The mass spectrum shows a parent peak at *m/e* 214 and an expected peak at 107 corresponding to the symmetrical cleavage of the molecule at the ethylene bridges. The bipyrrole is both light-sensitive and air-sensitive when slightly impure, but becomes more stable after purification by sublimation.

The n.m.r. spectrum of (II) is in excellent accord with the assigned structure, showing sharp singlets at τ ($CDCl_3$) 3·90 (4H, pyrrole C-*H*), 6·95 (6H, N–CH_3), and 7·16 (8H, ethylene bridge protons). The appearance of the β-protons on the pyrrole ring at normal positions[4] (*ca.* τ 3·90) suggests that the pyrrolophane has the *anti*-configuration shown in (IIa) where there is a minimum of transannular shielding by the aromatic rings.[5]

When the reaction of (VII) with methylamine was interrupted after only 10 min., the intermediate *N*-methyl-3,6-di-oxo-[8](2,5)pyrrolophane (III) was isolated. This material crystallized as prisms (72%) from ether m.p. 97—98°:† M^+ 219; i.r. (KBr) 1705 cm^{-1}; τ ($CDCl_3$) 4·00 (s, 2H, pyrrole C-*H*), 6·98 (s, 3H, N–CH_3), 7·08—8·50 (m, 12H). Further treatment of (III) with methylamine yielded (II) (95%).

The availability of the cyclic tetraone (VII) now provides a means of preparing a variety of [2,2](2,5)heterocyclophanes. We are investigating this and other aspects of the chemistry of (VII).

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