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SULPHUR DIOXIDE EXTRUSION FROM DI-2-PYRIDYLMETHYL SULPHONES : SYNTHESIS OF TRANS-1,2-DI-2-PYRIDYLETHENE AND [2.2](2,6)PYRIDINOPHANE

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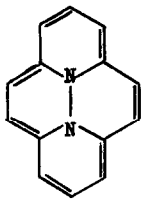
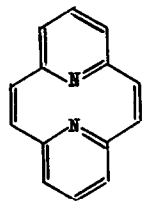
Recent work in the fields of cyclophanes[1] and cyclazines[2] has been particularly valuable in increasing our understanding of such important concepts as aromaticity, ring current phenomena, non-bonded and Transannular interactions. The interesting valence tautomeric system of 15,16-dihydro-15,16-diazapyrene (1) and [2.2](2,6)pyridinophane-1,9-diene (2) which bridges the gap between cyclophanes and cyclazines[3], was first reported thirteen years ago as the object of an unsuccessful synthetic attempt by Baker and coworkers[4]. Very recently, Boekelheide and Lawson[5] reported the preparation of the cyclophane 2 and presented preliminary evidence against its facile valence tautomerism to the cyclazine system 1. We would now like to record our work in this area.



1



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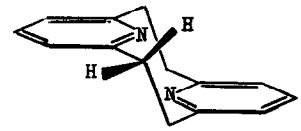
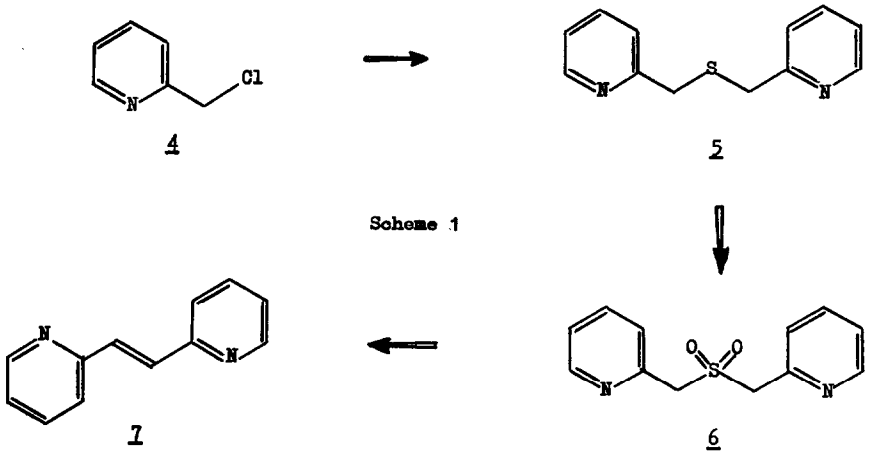


3

The failure of early attempts at the preparation of [2.2]metacyclophane-1,9-diene systems from the corresponding methylene bridged systems has been attributed to the geometry of such saturated bridged systems (see 3)[6] which prevents normal benzylic stabilisation of radical or ionic intermediates[7]. This bridging group reactivity problem should be avoided in a more flexible [3.3](2,6)pyridinophane system, which would, however, then require a ring contraction reaction to generate the desired [2.2](2,6)pyridinophane system. The elegant work of Paquette's and Bordwell's groups[8] on the Ramberg-Bäcklund reaction of α-halosulphones suggested this sulphur dioxide extrusion reaction as eminently suitable for such a ring contraction to give olefinic bridges. The anticipated ease of formation of the required dithia[3.3]metacyclophane system has been subsequently verified[9] and pyrolytic sulphur dioxide extrusion[9,10] established as a facile route to the corresponding [2.2]cyclophane systems.

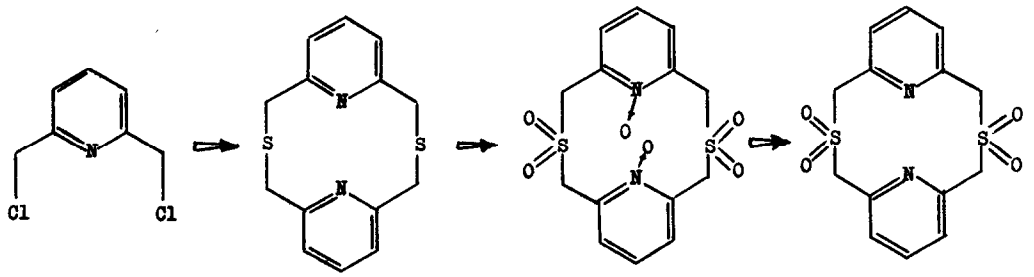
At the start of this work the required 2,11-dithia[3.3](2,6)pyridinophane (9) was unknown and since the choice of the base and solvent for the Ramberg-Bäcklund reaction appeared to be somewhat critical[8] and selective oxidation at sulphur in the presence of pyridine nitrogens was a potential problem, an investigation of a model system (see scheme 1) was undertaken.



Scheme 1

The reaction of 2-chloromethylpyridine (4)[11] with sodium sulphide in ethanol readily gave di-2-pyridylmethyl sulphide (5)[12] in excellent yield. Attempted monohalogenation of 5 using the usual reagents[13] failed to give satisfactory results. Oxidation with slightly less than two equivalents of meta-chloroperbenzoic acid, however, smoothly gave di-2-pyridylmethyl sulphone in good yield with no evidence of competitive N-oxidation. Attempted halogenation of the sulphone 6 under mildly basic conditions also failed to yield monohalogenated products but, using carbon tetrachloride and the vigorously basic conditions reported by Meyers et al[14], chlorination evidently occurred and was followed by a rapid base induced dehydrohalogenation - sulphur dioxide extrusion, i.e. Ramberg-Bäcklund reaction, to give in excellent yield trans-1,2-di-2-pyridylethene (7)[15].

Scheme 2



We then turned our attention to the cyclophane system (see scheme 2). As we were about to undertake the synthesis of 2,11-dithia[3.3](2,6)pyridinophane (9) its preparation was reported by Vogtle and Schunder[9] (and later by Boekelheide and Lawson[5]) from 2,6-bischloromethylpyridine (8)[16] and sodium sulphide under standard high dilution conditions. In our hands such reaction

yielded up to 19% of purified bis-sulphide 9 and 3% of the corresponding trimeric tris-sulphide. Oxidation of the bis-sulphide 9 with four equivalents of peracid unexpectedly gave the bis-sulphone-bis-N-oxide 10 in moderate yield as the sole isolated product. Attempts to protect the pyridine nitrogens from oxidation by protonation using trifluoroperacetic acid in excess trifluoroacetic acid or by trifluoroacetylation (CF_3CO_3H in $CF_3COOH/(CF_3CO)_2O$)[18] were ineffective. Some understanding of this unexpected oxidation pattern came after an examination of space-filling models of the probable initially formed intermediate bis-sulphoxide. In its preferred conformation further oxidation to the sulphone level is sterically retarded apparently sufficiently to allow N-oxidation to become competitive. Using excess oxidant, the yield of the sparingly soluble 10, which precipitated directly from the reaction mixture in high purity, was practically quantitative. Selective reduction of the pyridine N-oxide groups of 10 was effected by iron in refluxing trifluroacetic acid[19] giving in high yield the desired bis-sulphone 11. Application of the modified Ramberg-Bäcklund reaction of Meyers et al[14] failed to give satisfactory results due to the very low solubility of the bis-sulphone and the apparent instability of the expected product 2 to the vigorously basic (nucleophilic) conditions[5]. Sulphur dioxide extrusion under pyrolytic conditions (0.01 mm/680°C)[10], however, proceeded smoothly giving the stable saturated bridge pyridinophane 3 in 46% yield after purification.

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