Complexes of Ligands providing Endogenous Bridges. Part 2.[1] The Non-template Synthesis of Tetraimine Schiff Base Macrocycles derived from 1,3-Diamino-2-hydroxypropane[*]

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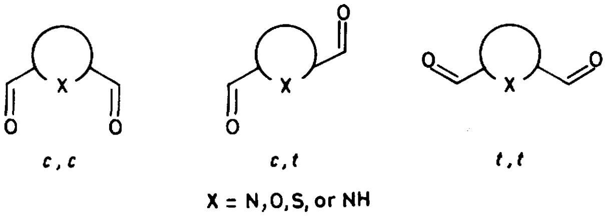
The synthesis of metal-free tetraimine Schiff base macrocycles derived from the (2 + 2) condensation of 1,3-diamino-2-hydroxypropane with pyrrole-2,5-dicarbaldehyde and with thiophene-2,5-dicarbaldehyde are described.

Tetraimine Schiff base macrocycles have generally been synthesised, as their metal complexes, through the (2 + 2) condensation of heterocyclic dicarbonyls and 1,*n*-diaminoalkanes in the presence of alkaline-earth, or main group, metals as template devices.[2] This technique is particularly applicable when pyridine, or furan, dicarbonyls are employed as the 'head' units for the macrocycle. Use of thiophene-2,5-dicarbaldehyde (tda) led to the synthesis of metal-free tetraimine Schiff-base macrocycles, and it was found that the use of a metal template was unnecessary.[3] We here report the non-template synthesis of related macrocycles containing potential endogenous bridging functions.

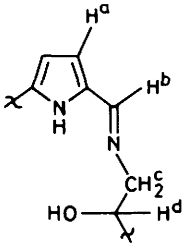
Results and Discussion

It has been noted[4] that there is an interesting coincidence concerning conformer distribution in heterocyclic dicarbonyls and the need for a metal template in condensation reactions to produce tetraimine macrocycles which, in spite of Curtin-Hammett principle,[5] may play a contributory role in the mechanism. The dicarbonyls may exist as *cis,cis* (*c,c*), *cis,trans* (*c,t*), and *trans,trans* (*t,t*) conformers (below). N.m.r. studies, usually in nematic phases, have revealed that for pyridine-2,6-dicarbaldehyde (pda) the only important conformer is *t,t*,[6] for furan-2,5-dicarbaldehyde (fdc) there is a 2:1:1 distribution of *c,t*:*t,t*:*c,c* conformers,[7] and for tda the distribution is 80:20 of *c,c*:*c,t*.[8] The dipole moments of pda and 2,6-diacetylpyridine, in benzene, have been interpreted as derived from a high proportion of *t,t* present with *ca.* 5% *c,t* and negligible *c,c*.[9] The structures of metal complexes of macrocycles[2,10] bearing these 'head' units, and of a free macrocycle,[3] show the macrocycles to have *c,c* arrangements.



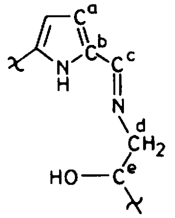
If it is the *c,c* conformer which leads most readily to macrocyclisation then only with tda is that conformer present in excess thus allowing a metal-free condensation to occur. For pda and fdc the metal-template procedure is required and the metal can be seen as redirecting conformer distribution to *c,c* through complexation prior to cyclisation. N.m.r. studies on pyrrole-2,5-dicarbaldehyde (pdc) have indicated[11] a *c,c*:*c,t* conformer ratio of 80:20 and this suggests that metal-free macrocycles should be available from this source.

Table. N.m.r. data for $L^1 \cdot H_2O$

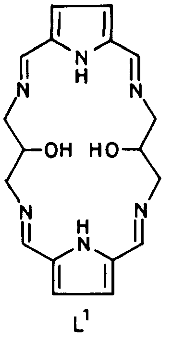


^1H N.m.r. [400 MHz, $(CD_3)_2SO$]	
a	6.54, s, 4 H
b	8.13, s, 4 H
c	3.68, d, 8 H
d	3.93, q, 2 H

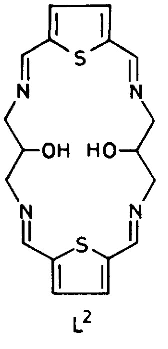
^{13}C N.m.r.* [63 MHz, $(CD_3)_2SO$]	
a	112.66
b	132.71
c	152.80
d	64.92
e	70.25



* All singlets.

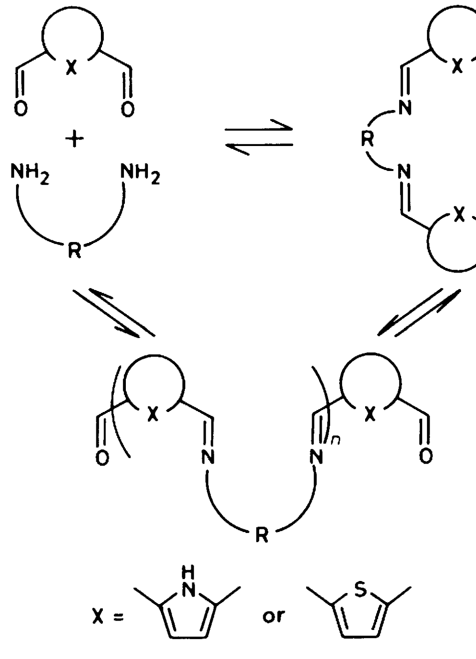


L^1



L^2

When equimolar amounts of pdc and 1,3-diamino-2-hydroxypropane (dhp) were refluxed together in dry ethanol for 1.5 h, $L^1 \cdot H_2O$ precipitated from solution as a very fine orange powder. It was, on occasion, necessary to filter the reaction mixture whilst hot in order to remove small amounts of a polymeric gum which formed during the reflux. $L^1 \cdot H_2O$ was isolated by centrifuging the suspension and decanting off the supernatant. The i.r. spectrum shows no absorptions due to unreacted carbonyl, or primary amine, functions but has bands at 3 375 (endogenous OH), 3 250 (pyrrole NH), and 1 640 cm^{-1} (imine CN). The mass spectrum has a parent peak at *m/e* 354 and the ^1H and ^{13}C n.m.r. confirm the integrity of the macrocycle in solution (Table). There is a peak of very low intensity at *m/e* 477 in the mass spectrum corresponding to an



R = —CH$_2$CH(OH)CH$_2$—

Scheme.

acyclic oligomer having composition pdc:dhp of 3:2; the ^{1}H n.m.r. shows a signal at 9.6 p.p.m. corresponding to a very small amount of carbaldehyde protons (*ca.* 2% compared with the imine protons from the macrocycle by integration). Free $L^1 \cdot H_2O$ was also isolated from reactions which were carried out in the presence of metal-template ions (Ba, Sr, Ca, or Pb).

The corresponding reaction between tda and dhp in dry ethanol under reflux for 1 h gave, on cooling, a white precipitate of $L^2 \cdot H_2O$. The i.r. spectrum gives no absorptions corresponding to free primary amine, or carbonyl, functions but has bands at 3 400 (endogenous OH) and 1 630 cm^{-1} (imine CN). The mass spectrum shows a parent ion peak at *m/e* 388. $L^2 \cdot H_2O$ was not sufficiently soluble to record a ^{1}H n.m.r. spectrum. The free ligand was also recovered when the above reaction was carried out in the presence of various metal-template ions (Ba, Sr, Ca, or Pb). As in the reaction to produce $L^1 \cdot H_2O$ this suggests that a non-template procedure predominates.

It is by no means certain that the role attributed to the conformer ratio is dominant. The products of the metal-free reaction are, in general, relatively insoluble in the reaction media. It is therefore likely that in any equilibrium system (Scheme) the facile precipitation of the product would displace the equilibrium towards cyclisation. In this context it is interesting to note that the employment of non-protic solvents such as tetrahydrofuran,[12] benzene,[13] or toluene[13] in reactions involving pda have led to isolated examples of metal-free macrocycles. This could have arisen through modified conformer ratios, or different product solubilities.

Experimental

Details of the physical measurements are given in ref. 1.

Preparation of $L^1 \cdot H_2O$.—Pyrrole-2,5-dicarbaldehyde[14] (5 mmol) and 1,3-diamino-2-hydroxypropane (5 mmol) were dissolved in dry ethanol (150 cm^3) and the resulting solution was heated at reflux for 1.5 h. If necessary a gummy precipitate was removed from the solutions by filtration of the reaction mixture when hot. On cooling, $L^1 \cdot H_2O$ precipitated from solution as a very fine orange powder and was isolated by centrifuging the suspension, decanting off the supernatant, and drying *in vacuo*. Yield 55%, m.p. 125—127 °C (Found: C, 58.2; H, 6.3; N, 22.0. $C_{18}H_{24}N_6O_3$ requires C, 58.1; H, 6.5; N, 22.6%). Mass spectrum: P^+ at *m/e* 354.

Preparation of $L^2 \cdot H_2O$.—Thiophene-2,5-dicarbaldehyde[15] (5 mmol) and 1,3-diamino-2-hydroxypropane (5 mmol) were dissolved in dry ethanol (100 cm^3) at reflux temperature and the resulting solution was refluxed for 1.5 h. On cooling, $L^2 \cdot H_2O$ precipitated from solution and was isolated by filtration and dried *in vacuo*. Yield 50%, m.p. 210 °C (decomp.) (Found: C, 53.2; H, 5.3; N, 13.5; S, 15.0. $C_{18}H_{22}N_4O_3S_2$ requires C, 53.2; H, 5.6; N, 13.8; S, 16.0%). Mass spectrum: P^+ at *m/e* 388.

Acknowledgements

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