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Unexpected ring contraction in the barium-assisted cyclocondensation of 2,6-diformylpyridine and *N*,*N*-bis(2-aminoethyl)-2-phenylethylamine

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The cyclocondensation reaction between *N*,*N*-bis(2-aminoethyl)-2-phenylethylamine and 2,6-diformylpyridine in the presence of a barium template gave an unexpected 18-membered macrocyclic product in which a ring contraction at one side-arm has occurred to produce an imidazolidine ring.

We have previously reported[1] that the cyclocondensation reaction between *N*,*N*-bis(2-aminoethyl)-2-phenylethylamine (aepa) and 2,6-diacetylpyridine in the presence of silver(I) ions results in the isolation of an acyclic mononuclear silver(I) complex (Scheme 1) whereas the analogous reaction involving *N*,*N*-bis(3-aminopropyl)-2-phenylethylamine yields the expected pendant-arm Schiff-base macrocycle. The reaction between aepa and the more reactive dicarbonyl 2,6-diformylpyridine (dfp) has now been investigated with the aim of producing the corresponding 24-membered Schiff-base macrocycle. Herein we report the results of this interaction together with the crystal structure of a macrocyclic product resulting from an unexpected ring-contraction reaction.

The cyclocondensation reaction of aepa and dfp was attempted in the presence of silver(I) ions in methanol, acetonitrile or a mixture of both solvents. The ^{1}H NMR spectrum of the solid product isolated corresponded to a mixture of species whose separation proved unsuccessful. When the cyclocondensation was carried out in the presence of barium(II) perchlorate at room temperature with acetonitrile as solvent, two different products were isolated from separate attempts at the reaction.† One product corresponded to the expected 24-membered pendant-arm Schiff-base macrocycle $[BaL^1][ClO_4]_2$, while the other was identified as an 18-membered macrocycle $[BaL^2][ClO_4]_2$ (Scheme 2).

The IR spectrum of $[BaL^1][ClO_4]_2$ showed a band at 1654 cm^{-1} corresponding to the presence of imine bonds and two bands at 1108 and 624 cm^{-1} arising from non-co-ordinating perchlorate anions. The highest peak in the mass spectrum (*m*/*z* 850) was assigned to the cation $[BaL^1(ClO_4)]^+$. The ^{1}H and ^{13}C NMR data and elemental analysis are consistent with the above formulation.

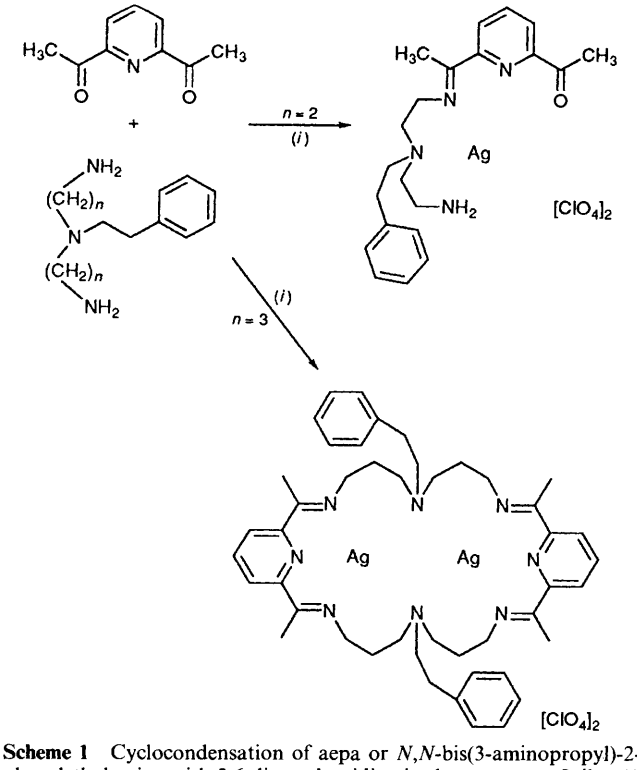
Vapour diffusion of diethyl ether into a solution of $[BaL^2][ClO_4]_2$ in acetonitrile afforded colourless crystals suitable for study by X-ray crystallography.‡ The molecular structure is shown in Fig. 1 together with the bond distances for the barium ion–donor interactions. The molecular dication comprises an 18-membered asymmetric macrocycle containing six nitrogen donors, all of which are within the normal bonding range of a co-ordinated barium atom. Bonds are formed to two pyridyl nitrogen atoms (3.01 and 2.80 Å), to their adjacent imine nitrogen atoms (2.91 and 2.90 Å) and to an intervening tertiary amine nitrogen atom (3.07 Å) which carries a pendant 2-phenylethyl substituent. The final bond to the macrocycle is to one of the nitrogens of an imidazolidine ring (3.00 Å); the second nitrogen atom of the ring, which carries a second pendant 2-phenylethyl substituent, is more remotely positioned (3.22 Å). The co-ordination of the barium(II) ion is completed by a rather linear, unidentate perchlorate anion (Ba–O 2.84 Å, Ba–O–Cl 162°), and an asymmetrically bidentate perchlorate anion (Ba–O 2.83 and 3.19 Å). The two pyridinyl rings are planar (root mean square deviations 0.009 and 0.011 Å, displacements of the barium 0.334 and 0.356 Å respectively), as are the phenyl rings (root mean square deviations 0.004 and 0.016 Å). The conformation of the macrocycle is 'crown-like' with the carbon skeleton bent back so as to present the ring of nitrogen atoms to the barium. Consequently the co-ordination environment of the barium is asymmetric with the six nitrogen atoms in one hemisphere and the two (or three) oxygen atoms of the perchlorate anions in the other. Not surprisingly the

† A solution of 2,6-diformylpyridine[2] (1 mmol) in acetonitrile (15 cm^3) was added dropwise to a solution of *N*,*N*-bis(2-aminoethyl)-2-phenylethylamine[1] (1 mmol) and barium(II) perchlorate (0.55 mmol) in acetonitrile (40 cm^3). After stirring at room temperature for 24 h the solution was concentrated using a rotary evaporator and then the product precipitated as a cream powder *via* the addition of diethyl ether. **CAUTION**: Although no problems were encountered during the course of this work attention is drawn to the potentially explosive nature of perchlorates.

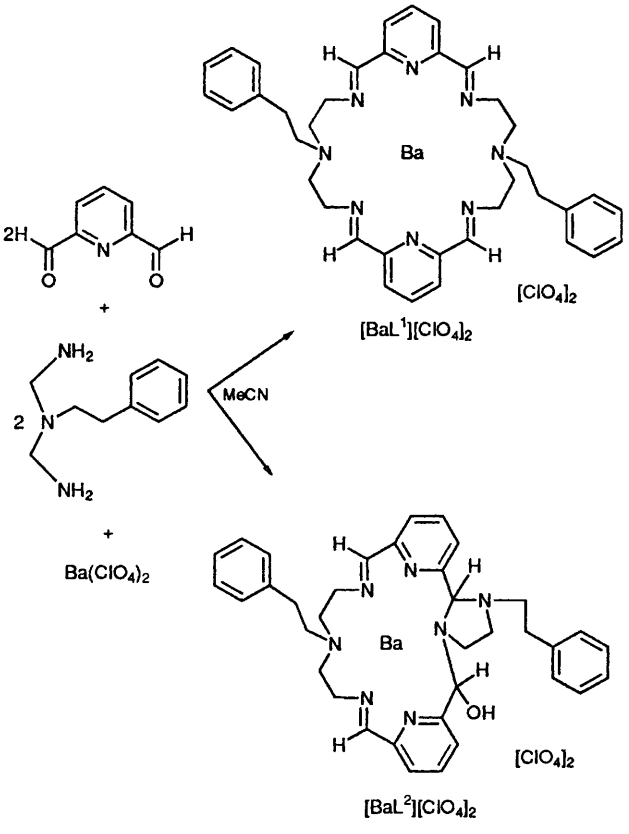
$[BaL^1][ClO_4]_2$: Yield 0.285 g, 60% (Found: C, 46.85; H, 5.05; N, 10.95; Cl, 6.90. Calc. for $C_{38}H_{44}BaCl_2N_8O_8{\cdot}2H_2O$: C, 46.35; H, 4.90; Cl, 6.90; N, 11.35%). IR (KBr disc): 1654 (C=N), 1108 and 624 cm^{-1} (ClO_4). NMR (CD_3CN): δ_H 8.35 (s, 4 H, imine), 8.20 (t, 2 H, pyridine), 7.75 (d, 4 H, pyridine), 7.24 (m, 10 H, phenyl), 3.72 (br, 8 H, CH_2) and 2.68 (m, 16 H, CH_2); δ_C 165.04, 154.0, 141.38, 141.33, 129.58, 129.31, 129.22, 126.82, 60.23, 57.65, 57.16 and 33.02. Mass spectrum (positive ion FAB): *m*/*z* 850 $[BaL^1(ClO_4)]^+$, 751 $[BaL^1]^+$.

$[BaL^2][ClO_4]_2{\cdot}0.5MeCN$: Recrystallised from acetonitrile–diethyl ether. Yield 0.055 g, 12% (Found: C, 47.20; H, 4.95; N, 10.30; Cl, 7.75. Calc. for $C_{36}H_{41}BaCl_2N_7O_9{\cdot}0.5MeCN$: C, 47.05; H, 4.55; Cl, 7.50; N, 11.10%). IR (KBr disc): 3427 (OH), 1656 (C=N), 1146, 1109, 1051, 1008, 755, 742, 703 and 624 cm^{-1} (ClO_4). NMR (CD_3CN): δ_H 8.53 (t, 1 H, imine), 8.50 (d, 1 H, imine), 8.10 (t, 1 H, pyridine), 8.04 (t, 1 H, pyridine), 7.81 (dt, 1 H, pyridine), 7.75 (m, 2 H, pyridine), 7.65 (dt, 1 H, pyridine), 7.24 (m, 10 H, phenyl), 5.17 (d, 1 H, CH), 4.98 (d, 1 H, OH), 4.51 (s, 1 H, CH), 4.29 (t, 1 H, CH_2), 3.96 (m, 1 H, CH_2), 3.86 (m, 1 H, CH_2), 3.59 (m, 2 H, CH_2), 3.22 (m, 5 H, CH_2) and 2.74 (m, 10 H, CH_2); δ_C 163.91, 161.73, 158.48, 154.66, 153.20, 141.12, 141.04, 140.80, 140.75, 129.77, 129.70, 129.50, 129.31, 129.27, 127.99, 127.34, 127.04, 127.0, 125.05, 83.38, 80.05, 58.10, 57.49, 55.60, 54.18, 52.99, 52.05, 50.15, 39.34, 34.25 and 27.20. Mass spectrum (positive ion FAB): *m*/*z* 823 $[BaL^2(ClO_4)]^+$.

‡ Crystal data: $C_{36}H_{41}BaCl_2N_7O_9{\cdot}0.5MeCN$, M = 944.5, monoclinic, space group $P2_1/c$ (C_{2h}^5, no. 14), a = 14.73(2), b = 16.943(11), c = 18.591(11) Å, β = 104.17(8)°, U = 4497(7) Å^3, Z = 4, D_c = 1.395 Mg m^{-3}, $F(000)$ = 1916, Mo-Kα radiation, $\bar{\lambda}$ = 0.710 69 Å, μ(Mo-Kα) = 1.058 mm^{-1}, crystal dimensions 0.65 × 0.40 × 0.20 mm. Three-dimensional, room temperature X-ray data were collected in the range $3.5 < 2\theta < 45°$ on a Nicolet R3 diffractometer by the ω scan method. The 3287 independent reflections (of 6352 measured) for which $|F|/\sigma(|F|) > 4.0$ were corrected for Lorentz and polarisation effects, but not for absorption. The structure was solved by direct methods and refined by blocked-cascade least-squares methods. Hydrogen atoms were included in calculated positions and refined in riding mode. Refinement converged at a final R = 0.0632 (R' = 0.0953, 503 parameters, mean and maximum δ/σ 0.000, 0.002), with allowance for the thermal anisotropy of all non-hydrogen atoms [with the exception of C(37)]. Minimum and maximum final electron density −0.85 and 0.71 e Å^{-3}. A weighting scheme $w^{-1} = \sigma^2(F) + 0.0021(F)^2$ was used in the latter stages of refinement. Complex scattering factors were taken from ref. 3 and from the program package SHELXTL-PC[4] as implemented on the Viglen 486dx computer. Complete atomic coordinates, thermal parameters and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre. See Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1996, Issue 1.



Scheme 1 Cyclocondensation of aepa or *N*,*N*-bis(3-aminopropyl)-2-phenylethylamine with 2,6-diacetylpyridine in the presence of silver(I) ions. (*i*) $AgNO_3$, reflux; $NaClO_4$



Scheme 2 Two different products isolated from the cyclocondensation of 2,6-diformylpyridine with aepa in the presence of barium(II) perchlorate

co-ordination geometry of the barium ion does not resemble any regular co-ordination polyhedron.

The presence of the HO–C–N group is confirmed and a hydrogen bond is formed from the pendant hydroxyl O(9) to either of two of the non-co-ordinated oxygens of the unidentate

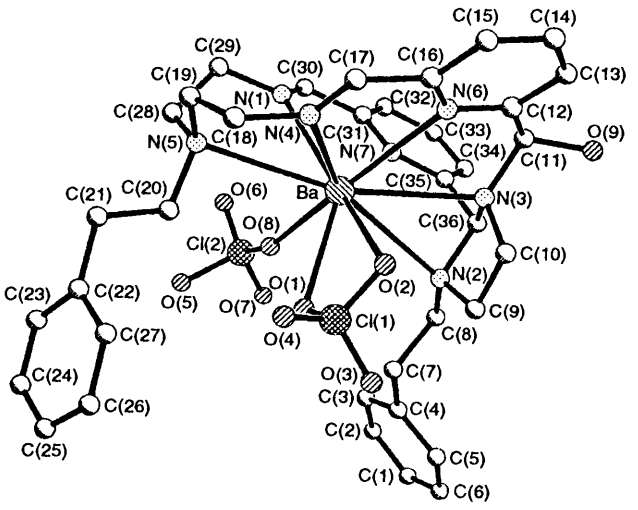


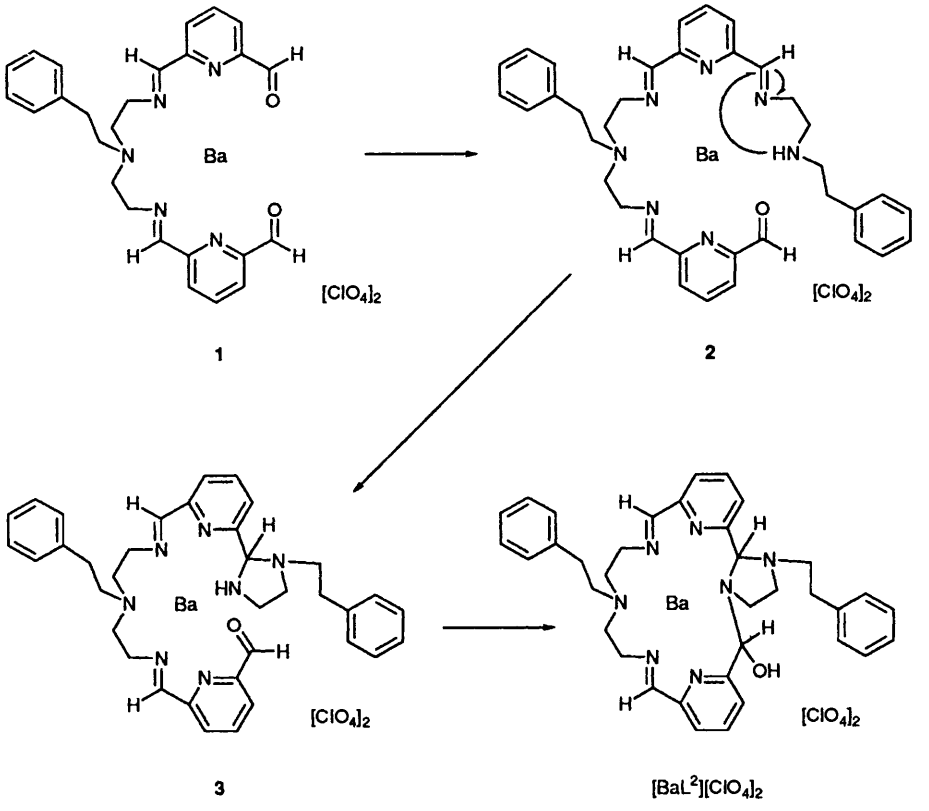
Fig. 1 Molecular structure of $[BaL^2][ClO_4]_2$. Barium–donor atom bond lengths (Å): Ba–N(1) 2.908(11), Ba–O(1) 2.834(10), Ba–N(2) 3.219(12), Ba–O(2) 3.194(11), Ba–N(3) 2.995(11), Ba–O(8) 2.836(11), Ba–N(4) 2.900(12), Ba–N(5) 3.07(14), Ba–N(6) 3.010(11), Ba–N(7) 2.799(10)

perchlorate anion in a molecule related by the screw operation $[1 - x, -0.5 + y, 0.5 - z]$ (O ··· O 2.96 and 3.08 Å, H ··· O 2.13 and 2.48 Å): the hydrogen was positioned along the shorter of these two interactions to give a good hydroxyl geometry. The asymmetric unit is completed by a half-occupancy acetonitrile of solvation which is disordered adjacent to a crystallographic inversion centre.

The IR spectrum of $[BaL^2][ClO_4]_2$ shows a band at 3427 cm^{-1} assignable to the hydroxyl group and at 1656 cm^{-1} corresponding to the imine bonds. The ν_3 and the ν_4 bands of the mono- and bi-dentate perchlorate anions are split giving rise to the signals 1146, 1109, 1051 and 1008 cm^{-1} (ν_3) and 755, 742, 703 and 624 cm^{-1} (ν_4). The highest peak in the mass spectrum of the complex (*m*/*z* 823) corresponds to the cation $[BaL^2(ClO_4)]^+$. The unambiguous assignment of the ^1H and ^{13}C NMR spectra for $[BaL^2][ClO_4]_2$ is difficult due to the asymmetric nature of the macrocycle. Inequivalence of all the methylene protons leads to significant overlap in the ^1H NMR spectrum between the separate phenyl environments and similarly between the separate methylene environments. The integrals for these regions, however, are appropriate for the 18-membered macrocycle L^2. Two imine signals were observed in the ^1H NMR spectrum at δ 8.50 and 8.53 and a signal at δ 4.98 was identified as the hydroxyl proton *via* a D_2O exchange experiment.

Ring contractions have been reported to occur for Schiff-base macrocycles as a consequence of nucleophilic addition of a secondary amine across an adjacent imine bond.[5–7] For example Nelson and co-workers[5] have reported a ring contraction in the reaction of 2-azapentane-1,5-diamine with 2,6-diacetylpyridine in which barium ions mediated a ring contraction from a 24- to an 18-membered macrocycle with accompanying expulsion of two imidazolidine rings. This leads to the suggestion that the isolation of two different macrocyclic complexes from this reaction arises from the presence of some *N*-(2-aminoethyl)-2-phenylethylamine in the aepa starting material. This could have arisen *via* the monoalkylation of 2-phenylethylamine by *N*-tosylaziridine, during the synthesis of aepa. Attempts to isolate *N*-(2-aminoethyl)-2-phenylethylamine *via* the reaction of an excess of 2-phenylethylamine with *N*-tosylaziridine, employing reduced reaction times, resulted in the isolation of either unreacted starting materials or aepa and so it has not been possible to test this pathway in isolation.

The two products could therefore be formed by similar mechanisms that differ at one particular stage. The complex



Scheme 3 Mechanism for the formation of $[BaL^2][ClO_4]_2$

$[BaL^1][ClO_4]_2$ would be expected to result from the normal reaction path for [2 + 2] tetraimine formation proposed by Nelson *et al.*[8] but the pathway for $[BaL^2][ClO_4]_2$ is less evident in light of the difficulty of reproducing the conditions of its formation. A mechanism is suggested in Scheme 3. It assumes that the first condensation reaction is between dfp and aepa and leads to a [2 + 1] diformyl product **1**. This could arise *via* initial formation of a [1 + 1] complex in a manner not dissimilar to the formation of an acyclic product in the reaction of aepa and 2,6-diacetylpyridine in the presence of silver(I), followed by addition of the second molecule of dfp to the pendant amine.[1] Intermediate **1** can then undergo a condensation reaction with *N*-(2-aminoethyl)-2-phenylethylamine to form intermediate **2**. This can then undergo an intramolecular addition of the secondary amine across the adjacent imine bond to yield the imidazolidine **3**. An internal cyclisation *via* reaction of the imidazolidine NH with the carbonyl group would then yield $[BaL^2][ClO_4]_2$.

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References

1 D. E. Fenton and P. C. Hellier, *Inorg. Chim. Acta*, 1992, **198–200**, 577.
2 P. Moore, N. W. Alcock, R. G. Kingston and C. Pierpoint, *J. Chem. Soc., Dalton Trans.*, 1984, 1941.
3 *International Tables for X-Ray Crystallography*, Kynoch Press, Birmingham, 1974, vol. 4.
4 G. M. Sheldrick, SHELXTL-PC, An integrated system for solving, refining and displaying crystal structures from diffraction data, Revision 4.1, Siemens plc, Germany, 1993.
5 M. G. B. Drew, J. Nelson and S. M. Nelson, *J. Chem. Soc., Dalton Trans.*, 1981, 1679.
6 R. Menif, A. E. Martell, P. J. Squattrino and A. Clearfield, *Inorg. Chem.*, 1990, **29**, 4723.
7 H. Adams, N. A. Bailey, D. E. Fenton, P. D. Hempstead and G. P. Westwood, *J. Inclusion Phenom. Mol. Recognit. Chem.*, 1991, **11**, 63.
8 S. M. Nelson, C. V. Knox, M. McCann and M. G. B. Drew, *J. Chem. Soc., Dalton Trans.*, 1981, 1669.

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