Preparation and Molecular Structure of Bridged Tetra-aza Macrocyclic Ligands

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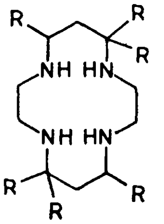
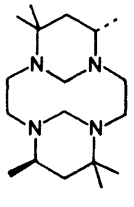
Three derivatives of geometric isomers of 1,4,8,11-tetra-aza-5,5,7,12,12,14-hexamethylcyclotetradecane have been prepared by coupling (a) the *meso*-isomer with formaldehyde and formic acid and (b) the *meso*- and racemic isomers with glyoxal. Their crystal structures have been determined from four-circle diffractometer data: 5,5,7,12,12,14-hexamethyl-1,4,8,11-tetra-azatricyclo[9.3.1.1^{4,8}]hexadecane (3) is triclinic, $P\bar{1}$, with a = 5.977(1), b = 11.276(2), c = 8.964(2) Å, α = 112.85(1), β = 115.54(1), γ = 91.28(1)°, R = 0.043 for 1 339 observed reflections [$I > 3\sigma(I)$]; *meso*-1,1,3,6,6,8-hexamethyl-3a,5a,8a,10a-tetra-azaperhydropyrene, isomer (4), is triclinic, $P\bar{1}$, with a = 6.219(2), b = 8.412(3), c = 19.397(7) Å, α = 94.62(3), β = 87.65(3), γ = 118.50(3)°, R = 0.049 for 1 371 observed reflections; and the racemic isomer (5) is monoclinic, $P2_1/c$, with a = 11.507(2), b = 11.964(2), c = 13.885(2) Å, β = 107.94(1)°, R = 0.041 for 2 128 observed reflections. The structures show that none have four aligned lone pairs, and thus are unlikely to function as quadridentate ligands to one metal ion. The conformation of (3) is standard, but (4) and (5) have *cis*-fusion at three of five junctions in their fused decalin system. This can be attributed to steric hindrance at an intermediate stage in the formation process.

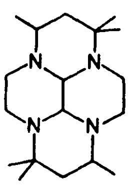
MACROCYCLIC, quadridentate, nitrogen-donor ligands have been investigated extensively in recent years, particularly in relation to their biological significance.[1] The fourteen-membered macrocyclic ligand, 1,4,8,11-tetra-azacyclotetradecane (1), known as cyclam, forms particularly stable complexes of the type *trans*-[M(L)X$_2$] [L = (1); X = anion] with divalent metal ions (M), in which the macrocycle has tertiary nitrogen-configurations *RSSR*;[2] the *N*-tetramethyl derivative of (1) (1,4,8,11-tetramethyl-1,4,8,11-tetra-azacyclotetradecane, known as TMC) forms six- and five-co-ordinate metal complexes of the type *trans*-[M(L)X$_2$] and [M(L)X]X (L = TMC) with nitrogen-configurations *RSSR* and *RSRS*, respectively. The structures of several such complexes have been investigated by n.m.r. methods and by *X*-ray crystallography.[1-5]



(1) R = H
(2) R = Me



(3)



(4) (*meso*)
(5) (*racemic*)

Synthesis of TMC from cyclam is usually achieved by methylation with a mixture of formaldehyde and formic acid.[3,6] However, attempts to methylate the *meso*-isomer of the related macrocycle 1,4,8,11-tetra-aza-5,5,7,12,12,14-hexamethylcyclotetradecane (2) by this route gave an unexpected product whose structure we have established by *X*-ray crystallography.[3] At the same time we have investigated the reaction between the *meso*- and racemic isomers of (2) with the bifunctional aldehyde glyoxal, and have established the structures of the products formed, again using crystallography.[4,5] In this way we could also investigate the feasibility of using these new macrocycles as quadridentate ligands. Parallel ^{13}C and ^{15}N n.m.r. investigations of the metal complexes of (2) and the products formed in this work are also under way, and will be reported at a later date.[7]

TABLE 1

Compound	(3)	(4)	(5)
Formula	$C_{18}H_{36}N_4$, 0.25H_2O	$C_{18}H_{34}N_4$	$C_{18}H_{34}N_4$
System	Triclinic	Triclinic	Monoclinic
Absences	None	None	$h0l$, $l \neq 2n$; $0k0$, $k \neq 2n$
Space group	$P\bar{1}$ (assumed)	$P\bar{1}$ (assumed)	$P2_1/c$
a/Å	5.977(1)	6.219(2)	11.507(2)
b/Å	11.276(2)	8.412(3)	11.964(2)
c/Å	8.964(2)	19.397(7)	13.885(2)
α(°)	112.85(1)	94.62(3)	90
β(°)	115.54(1)	87.65(3)	107.94(1)
γ(°)	91.28(1)	118.50(3)	90
U/Å^3	489.09(15)	888.8(6)	1 818.6(5)
Z	1	2	4
M	313.0	306.5	306.5
D_c/g cm^{-3}	1.06	1.15	1.12
R(final)	0.043	0.049	0.041

Radiation, Mo-K_α with graphite monochromator. λ = 0.71069 Å.

Scan, $\theta/2\theta$ at 1.0—29.3° min^{-1}, depending on the intensity of a 2 s pre-scan. Maximum 2θ = 50°. Background measurements taken for 1/4 of the scan time at each end of the scan; three standard reflections measured every 97 reflections, showing no significant alteration.

Scan range about α_1, α_2 positions	±1.0	±1.0	±0.85°
Reflections: all	2 255	2 648	3 482
with $I/\sigma(I) > 3.0$	1 339	1 371	2 128

EXPERIMENTAL

Preparation of meso- *and Racemic* 1,4,8,11-*Tetra-aza*-5,5,7,12,12,14-*hexamethylcyclotetradecane* (2).—This followed ref. 8 with two slight changes. The solution of [Ni(en)$_3$](ClO$_4$)$_2$ was refluxed with acetone for some hours, rather than being left for a week; the reduction employed NaBH$_4$ instead of Raney nickel, to increase the yield of *meso*-(2).

Preparation of 5,5,7,12,12,14-*Hexamethyl*-1,4,8,11-*tetra*-

TABLE 2

Atomic co-ordinates (× 10^4) with standard deviations in parentheses

Atom	X	Y	Z
Compound (3)			
N(1)	3 317(3)	3 823(1)	1 883(2)
N(2)	5 844(3)	6 569(1)	5 470(2)
C(1)	5 878(4)	4 666(2)	2 762(3)
C(2)	6 151(4)	6 150(2)	3 815(3)
C(3)	5 810(4)	7 988(2)	6 335(3)
C(4)	5 273(4)	8 203(2)	7 952(3)
C(5)	6 828(4)	7 592(2)	9 206(3)
C(6)	7 544(3)	6 143(2)	6 808(2)
C(7)	8 315(4)	8 940(2)	7 033(3)
C(8)	3 622(4)	8 295(2)	4 943(3)
C(9)	6 147(5)	7 815(2)	10 732(3)
O(1)	9 175(8)	5 116(5)	662(6)
H(11)	6 225(33)	4 561(17)	1 750(25)
H(12)	7 320(37)	4 369(19)	3 564(25)
H(21)	7 876(40)	6 563(21)	4 050(27)
H(22)	4 881(36)	6 450(20)	3 022(27)
H(41)	3 435(32)	7 818(17)	7 436(23)
H(42)	5 644(35)	9 162(19)	8 697(24)
H(51)	8 666(37)	8 039(20)	9 803(27)
H(61)	9 343(30)	6 710(16)	7 566(21)
H(62)	7 573(30)	5 259(16)	6 147(21)
H(71)	9 884(43)	8 848(24)	8 051(31)
H(72)	8 158(44)	9 790(23)	7 476(31)
H(73)	8 541(42)	8 780(22)	5 970(30)
H(81)	4 075(40)	8 359(22)	4 004(28)
H(82)	3 250(41)	9 120(22)	5 608(29)
H(83)	1 963(43)	7 650(24)	4 344(31)
H(91)	6 527(51)	8 653(28)	11 488(37)
H(92)	7 107(41)	7 305(22)	11 416(29)
H(93)	4 241(47)	7 470(25)	10 182(33)
H(101)	9 020(49)	4 212(25)	−615(35)
H(102)	10 795(78)	4 555(41)	622(58)
Compound (4)			
N(1)	5 536.5(36)	3 481.3(26)	3 214.1(10)
N(2)	5 811.1(34)	2 646.5(24)	1 758.7(10)
N(3)	6 862(3)	338(2)	2 050(1)
N(4)	3 102(3)	201(3)	2 987(1)
C(1)	4 255(5)	3 915(3)	2 706(1)
C(2)	5 687(5)	4 274(3)	2 043(1)
C(3)	7 137(4)	2 923(3)	1 084(1)
C(4)	7 327(5)	1 206(3)	855(1)
C(5)	8 340(4)	595(3)	1 416(1)
C(6)	4 376(4)	−1 161(3)	2 001(1)
C(7)	3 229(4)	−1 424(3)	2 706(1)
C(8)	1 837(5)	−72(4)	3 674(1)
C(9)	2 015(5)	1 746(4)	3 958(1)
C(10)	4 486(6)	3 415(4)	3 914(1)
C(11)	5 545(4)	1 796(3)	2 991(1)
C(12)	6 861(4)	2 017(3)	2 284(1)
C(13)	5 568(5)	3 156(4)	547(1)
C(14)	9 693(5)	4 565(3)	1 101(2)
C(15)	8 587(5)	−1 078(4)	1 182(2)
C(16)	2 877(6)	−808(4)	4 205(2)
C(17)	−865(5)	−1 411(4)	3 560(2)
C(18)	6 362(6)	3 674(4)	4 457(2)
H(11)	2 646(51)	3 053(38)	2 619(16)
H(12)	4 294(79)	5 072(58)	2 893(23)
H(21)	7 327(58)	5 187(43)	2 122(17)
H(22)	4 655(83)	4 540(62)	1 680(25)
H(41)	5 812(56)	368(41)	734(17)
H(42)	8 579(82)	1 419(60)	432(24)
H(51)	−3(60)	1 512(44)	1 548(18)
H(61)	4 600(76)	7 773(56)	1 882(23)
H(62)	3 442(62)	9 066(45)	1 693(18)
H(71)	4 311(68)	8 349(50)	3 036(20)
H(72)	1 629(69)	7 654(51)	2 669(21)
H(91)	860(61)	1 946(44)	3 696(18)
H(92)	1 350(76)	1 649(56)	4 404(23)
H(101)	4 176(81)	4 459(60)	3 971(24)
H(111)	6 717(54)	1 622(40)	3 295(16)
H(121)	8 622(56)	2 915(41)	2 377(17)
H(131)	3 855(68)	2 235(49)	573(20)
H(132)	6 265(93)	3 088(67)	130(27)
Compound (4)			
H(133)	5 845(96)	4 482(71)	609(28)
H(141)	863(68)	4 492(50)	1 420(22)
H(142)	750(86)	4 477(63)	719(27)
H(143)	9 563(78)	5 612(57)	1 141(23)
H(151)	7 052(71)	8 013(52)	1 019(21)
H(152)	9 273(72)	8 551(53)	1 540(22)
H(153)	9 944(72)	9 183(53)	825(21)
H(161)	4 566(72)	9 766(53)	4 230(21)
H(162)	2 349(74)	7 953(56)	4 075(22)
H(163)	2 033(97)	9 306(70)	4 654(29)
H(171)	8 416(71)	9 051(53)	3 189(22)
H(172)	8 949(70)	7 451(53)	3 453(21)
H(173)	8 151(85)	8 622(62)	3 974(25)
H(181)	7 950(94)	4 926(71)	4 426(27)
H(182)	7 171(84)	2 974(64)	4 359(24)
H(183)	5 566(107)	3 368(77)	4 864(32)
Compound (5)			
N(1)	9 798.4(5)	1 434.4(4)	3 467.2(4)
N(2)	7 483.8(5)	391.2(5)	3 326.8(4)
N(3)	7 470.4(5)	1 079.5(4)	1 673.6(4)
N(4)	9 925.8(5)	207.0(4)	2 101.9(4)
C(1)	9 193.0(6)	1 559.0(6)	4 248.7(5)
C(2)	7 825.0(7)	1 483.1(6)	3 815.0(6)
C(3)	6 141.3(7)	159.6(7)	2 972.5(6)
C(4)	5 534.3(7)	907.2(7)	2 065.8(7)
C(5)	6 141.7(6)	888.5(6)	1 236.7(6)
C(6)	8 068.0(7)	937.8(6)	891.8(5)
C(7)	9 440.2(6)	1 046.1(6)	1 308.7(5)
C(8)	11 287.8(6)	158.9(6)	2 498.6(5)
C(9)	11 760.8(6)	1 202.6(6)	3 131.1(6)
C(10)	11 142.6(6)	1 423.7(6)	3 937.9(6)
C(11)	9 399.6(6)	377.5(5)	2 919.2(5)
C(12)	8 004.4(6)	284.3(5)	2 498.2(5)
C(13)	5 940.6(8)	−1 081.5(7)	2 699.3(8)
C(14)	5 603.1(8)	373.1(9)	3 836.0(8)
C(15)	5 564.5(7)	1 773.3(8)	437.5(7)
C(16)	11 660.1(7)	−913.2(6)	3 117.2(6)
C(17)	11 819.3(7)	76.9(8)	1 613.7(6)
C(18)	11 582.3(7)	2 534.0(8)	4 469.6(7)
H(11)	9 394(6)	2 289(6)	4 564(5)
H(12)	9 514(7)	988(7)	4 813(6)
H(21)	7 503(8)	1 534(7)	4 393(6)
H(22)	7 479(7)	2 145(6)	3 321(6)
H(41)	4 673(9)	702(8)	1 749(7)
H(42)	5 545(8)	1 709(7)	2 307(7)
H(51)	6 008(7)	114(6)	920(5)
H(61)	7 845(7)	179(7)	561(6)
H(62)	7 764(7)	1 518(7)	362(6)
H(71)	9 794(8)	907(7)	735(7)
H(72)	9 644(5)	1 819(5)	1 545(5)
H(91)	11 628(7)	1 852(7)	2 685(6)
H(92)	12 637(8)	1 106(8)	3 463(7)
H(101)	11 368(6)	814(6)	4 463(6)
H(111)	9 673(7)	−264(6)	3 409(5)
H(121)	7 865(7)	−502(6)	2 217(6)
H(131)	5 061(10)	−1 273(9)	2 513(9)
H(132)	6 228(8)	−1 311(7)	2 123(7)
H(133)	6 417(9)	−1 539(9)	3 274(8)
H(141)	5 579(9)	1 188(8)	3 967(7)
H(142)	4 731(9)	113(9)	3 602(8)
H(143)	6 108(10)	−22(9)	4 507(8)
H(151)	4 701(9)	1 684(9)	267(8)
H(152)	5 794(8)	2 519(9)	744(7)
H(153)	5 823(10)	1 695(10)	−195(9)
H(161)	12 535(8)	−983(7)	3 295(6)
H(162)	11 423(9)	−933(8)	3 756(8)
H(163)	11 287(8)	−1 590(7)	2 682(7)
H(171)	11 759(8)	776(7)	1 268(7)
H(172)	12 715(10)	−116(9)	1 897(8)
H(173)	11 403(10)	−542(9)	1 140(8)
H(181)	12 497(10)	2 589(10)	4 644(9)
H(182)	11 240(9)	3 177(9)	3 997(8)
H(183)	11 380(9)	2 581(9)	5 130(8)

azatricyclo$[9.3.1.1^{4,8}]$*hexadecane* (3).—A solution containing 40% formaldehyde (2.5 cm^3) and 98% formic acid (2.5 cm^3) in methanol (50 cm^3) was added dropwise to a refluxing solution containing *meso*-(2) (2 g) in methanol (50 cm^3). The resulting solution was refluxed for 5 h, during which it changed from colourless to reddish brown. A sodium hydroxide solution in methanol was added in slight excess and all the solvents were removed. The brown residue was extracted with hexane and the extract was dried (Na_2SO_4) and filtered. Colourless solids were obtained on evaporation of hexane. The *product* (3) was recrystallised from light petroleum (yield 0.8 g), m.p. 116—117 °C (Found: C, 70.1; H, 11.8; N, 18.25. $C_{18}H_{36}N_4$ requires C, 70.05; H, 11.75; N, 18.15%).

Preparation of meso-(4) *and Racemic* 1,1,3,6,6,8-*Hexamethyl*-3a,5a,8a,10a-*tetra-azaperhydropyrene* (5).—Compound (2) (1.6 g) and glyoxal hydrate (0.5 g) were dissolved in

TABLE 3

Bond lengths (Å) and skeletal angles (°) with standard deviations in parentheses

Compound (3)

N(1)–C(1)	1.477(3)	C(2)–H(22)	0.96(2)
N(1)–C(5)	1.489(2)	C(4)–H(41)	1.00(2)
N(1)–C(6)	1.459(3)	C(4)–H(42)	0.98(2)
N(2)–C(2)	1.467(3)	C(5)–H(51)	1.00(2)
N(2)–C(3)	1.487(2)	C(6)–H(61)	1.01(2)
N(2)–C(6)	1.456(3)	C(6)–H(62)	0.95(2)
C(1)–C(2)	1.531(3)	C(7)–H(71)	1.03(2)
C(3)–C(4)	1.547(4)	C(7)–H(72)	0.91(2)
C(3)–C(7)	1.544(3)	C(7)–H(73)	0.97(3)
C(3)–C(8)	1.529(3)	C(8)–H(81)	1.02(3)
C(4)–C(5)	1.527(3)	C(8)–H(82)	0.98(2)
C(5)–C(9)	1.522(4)	C(8)–H(83)	1.00(2)
C(1)–H(11)	0.98(3)	C(9)–H(91)	0.87(3)
C(1)–H(12)	1.02(2)	C(9)–H(92)	1.01(3)
C(2)–H(21)	1.02(3)	C(9)–H(93)	1.02(3)
C(1)–N(1)–C(5)	112.5(2)	N(2)–C(3)–C(8)	109.5(2)
C(1)–N(1)–C(6)	113.6(1)	C(4)–C(3)–C(7)	110.2(2)
C(5)–N(1)–C(6)	106.4(2)	C(4)–C(3)–C(8)	107.9(2)
C(2)–N(2)–C(3)	115.2(2)	C(7)–C(3)–C(8)	108.6(2)
C(2)–N(2)–C(6)	113.6(2)	C(3)–C(4)–C(5)	115.3(2)
C(3)–N(2)–C(6)	112.4(1)	C(4)–C(5)–C(9)	112.2(2)
N(1)–C(1)–C(2)	115.8(2)	C(4)–C(5)–N(1)	111.2(1)
N(2)–C(2)–C(1)	116.4(2)	C(9)–C(5)–N(1)	113.2(2)
N(2)–C(3)–C(4)	107.1(2)	N(1)–C(6)–N(2)	112.5(1)
N(2)–C(3)–C(7)	113.4(2)		

Compounds (4) and (5)

	(4)	(5)
N(1)–C(1)	1.467(5)	1.466(1)
N(1)–C(10)	1.478(4)	1.482(1)
N(1)–C(11)	1.450(4)	1.474(1)
N(2)–C(2)	1.472(4)	1.469(1)
N(2)–C(3)	1.496(4)	1.496(1)
N(2)–C(12)	1.490(4)	1.457(1)
N(3)–C(5)	1.474(4)	1.479(1)
N(3)–C(6)	1.458(3)	1.463(1)
N(3)–C(12)	1.447(4)	1.470(1)
N(4)–C(7)	1.467(4)	1.468(1)
N(4)–C(8)	1.496(4)	1.494(1)
N(4)–C(11)	1.468(3)	1.456(1)
C(1)–C(2)	1.510(4)	1.505(1)
C(3)–C(4)	1.534(5)	1.527(1)
C(3)–C(13)	1.552(5)	1.532(1)
C(3)–C(14)	1.522(3)	1.532(1)
C(4)–C(5)	1.520(5)	1.520(1)
C(5)–C(15)	1.519(5)	1.530(1)
C(6)–C(7)	1.503(4)	1.511(1)
C(8)–C(9)	1.538(5)	1.527(1)
C(8)–C(16)	1.555(6)	1.530(1)
C(8)–C(17)	1.518(4)	1.535(1)
C(9)–C(10)	1.521(4)	1.524(1)
C(10)–C(18)	1.543(5)	1.528(1)
C(11)–C(12)	1.552(4)	1.534(1)
C(1)–H(11)	0.87(3)	0.971(8)
C(1)–H(12)	1.07(6)	1.020(8)
C(2)–H(21)	0.93(3)	0.984(10)
C(2)–H(22)	1.09(5)	1.043(7)
C(4)–H(41)	0.87(2)	0.983(9)
C(4)–H(42)	1.11(4)	1.015(9)
C(5)–H(51)	0.94(2)	1.017(7)
C(6)–H(61)	1.06(5)	1.014(8)
C(6)–H(62)	0.93(5)	0.994(8)
C(7)–H(71)	1.02(4)	1.014(10)
C(7)–H(72)	0.94(3)	0.985(6)
C(9)–H(91)	0.99(4)	0.976(8)
C(9)–H(92)	1.03(5)	0.978(9)
C(10)–C(101)	1.03(6)	1.007(7)
C(11)–H(111)	1.05(5)	1.009(7)
C(12)–H(121)	1.01(3)	1.012(7)
C(13)–H(131)	0.97(3)	0.991(11)
C(13)–H(132)	0.89(5)	0.993(11)
C(13)–H(133)	1.18(5)	0.984(10)
C(14)–H(141)	0.97(4)	0.993(10)
C(14)–H(142)	1.02(4)	1.004(10)
C(14)–H(143)	0.96(5)	1.046(10)
C(15)–H(151)	0.92(3)	0.954(10)
C(15)–H(152)	0.95(4)	0.989(10)
C(15)–H(153)	1.04(4)	1.015(13)
C(16)–H(161)	0.91(3)	0.964(9)
C(16)–H(162)	0.93(3)	1.006(12)
C(16)–H(163)	1.14(6)	1.022(9)
C(17)–H(171)	1.06(5)	0.964(9)
C(17)–H(172)	0.90(4)	1.006(12)
C(17)–H(173)	1.02(5)	1.022(9)
C(18)–H(181)	1.03(4)	1.007(12)
C(18)–H(182)	0.99(7)	1.010(10)
C(18)–H(183)	0.91(4)	1.015(12)
C(1)–N(1)–C(10)	111.2(3)	110.1(1)
C(1)–N(1)–C(11)	110.0(2)	109.1(1)
C(10)–N(1)–C(11)	111.8(2)	109.7(1)
C(2)–N(2)–C(3)	112.1(2)	114.8(1)
C(2)–N(2)–C(12)	109.8(2)	109.0(1)
C(3)–N(2)–C(12)	112.3(2)	111.0(1)
C(5)–N(3)–C(6)	115.1(2)	109.9(1)
C(5)–N(3)–C(12)	109.7(2)	110.5(1)
C(6)–N(3)–C(12)	111.2(2)	108.9(1)
C(7)–N(4)–C(8)	111.8(2)	114.6(1)
C(7)–N(4)–C(11)	110.6(2)	109.6(1)
C(8)–N(4)–C(11)	113.7(2)	111.0(1)
N(1)–C(1)–C(2)	108.1(3)	112.0(1)
N(2)–C(2)–C(1)	110.6(2)	109.7(1)
N(2)–C(3)–C(4)	108.7(2)	109.1(1)
N(2)–C(3)–C(13)	107.1(3)	108.8(1)
N(2)–C(3)–C(14)	114.4(2)	109.7(6)
C(4)–C(3)–C(13)	107.7(2)	111.6(1)
C(4)–C(3)–C(14)	109.8(3)	110.8(1)
C(13)–C(3)–C(14)	109.0(2)	106.8(1)
C(3)–C(4)–C(5)	112.6(2)	114.6(1)
N(3)–C(5)–C(4)	110.3(3)	110.2(1)
N(3)–C(5)–C(15)	112.1(2)	110.7(1)
C(4)–C(5)–C(15)	112.5(2)	110.0(1)
N(3)–C(6)–C(7)	109.1(2)	112.4(1)
N(4)–C(7)–C(6)	111.2(2)	109.9(1)
N(4)–C(8)–C(9)	108.6(2)	109.2(1)
N(4)–C(8)–C(16)	113.9(3)	108.7(1)
N(4)–C(8)–C(17)	108.6(2)	109.8(1)
C(9)–C(8)–C(16)	109.7(3)	112.0(1)
C(9)–C(8)–C(17)	107.4(3)	110.7(1)
C(16)–C(8)–C(17)	108.6(3)	106.5(1)
C(8)–C(9)–C(10)	116.9(3)	113.6(1)
N(1)–C(10)–C(9)	110.9(2)	109.7(1)
N(1)–C(10)–C(18)	109.5(3)	110.5(1)
C(9)–C(10)–C(18)	115.6(3)	110.2(1)
N(1)–C(11)–N(4)	113.8(3)	112.6(1)
N(1)–C(11)–C(12)	108.6(2)	112.4(1)
N(4)–C(11)–C(12)	113.0(2)	109.3(1)
N(2)–C(12)–N(3)	112.1(2)	112.5(1)
N(2)–C(12)–C(11)	112.4(3)	109.2(1)
N(3)–C(12)–C(11)	109.3(2)	112.8(1)

methanol (20 cm^3)–acetonitrile (20 cm^3). For (4) the *meso*-form of (2) and for (5) the racemic form was used. The solution was refluxed for 1 h, during which it changed from colourless to orange-brown. On removal of the solvent, a coloured residue was obtained. It was extracted with light petroleum and the extract was dried (Na_2SO_4) and filtered. Colourless *plates* were obtained on slow evaporation of the solvent. The yield of (4) was 0.6 g, m.p. 97—98 °C; of (5), 0.5 g, m.p. 96—97 °C [Found: for (4) C, 70.5; H, 11.35; N, 18.15. For (5) C, 70.5; H, 11.45; N, 17.9. $C_{18}H_{34}N_4$ requires C, 70.5; H, 11.2; N, 18.3%].

Crystallographic Study.—Crystal data for (3)—(5) are in Table 1, with details of intensity measurements. Data were collected with a Syntex $P2_1$ diffractometer, which was used also for determination of unit cell parameters by a least squares fit to the reflecting positions of 15 strong reflections in each case.

Structure solution for all compounds followed identical patterns. Solution by direct methods (SHELX) revealed groups of atoms in cyclohexane-like geometry, but these failed to refine satisfactorily, and were implausibly placed relative to the centres of symmetry. Relaxation of the space groups to $P1$, and the application of Fourier methods enabled the fragments to be expanded to the full molecules, after which the centres of symmetry could be relocated correctly.

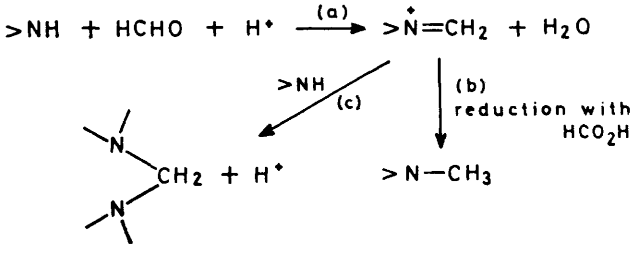
Final refinement was by full matrix least-squares methods with anisotropic temperature factors for all atoms. Weights were taken as 1.0 or $\sin\theta/0.25$ for $\sin\theta < 0.25$. For (3) a difference Fourier synthesis suggested the presence of a partial water molecule, and this was included with 25% occupancy. Scattering factors from ref. 9 were used, in the analytical form. The *X*-Ray 76 programs [10] were used, on a Burroughs B6700 computer.

Table 2 contains atomic co-ordinates, and Table 3 bond lengths and angles. Structure factors and temperature factors are listed in Supplementary Publication No. SUP 22771 (38 pp.).* There are no features of particular note in the packing, and this is not further discussed.

DISCUSSION

The product of the reaction between a mixture of formaldehyde and formic acid with *meso*-(2) was found to have structure (3), in which methylene bridges across two pairs of adjacent nitrogen-atoms have formed. Similarly, (4) and (5) produced from the reactions of glyoxal with *meso*- and racemic isomers of (2) have the structure shown, with a single C_2 bridge between all four nitrogen atoms.

For the reaction between an amine and formaldehyde-formic acid, two stages, (a) and (b), might be expected (Scheme). However, in the presence of a second amine, pathway (c) can compete with pathway (b) to give a methylene-bridged species, as observed in the formation of (3). Pathway (b) is clearly more important than (c) for reactions of (1), and the question arises as to why (1) and (2) behave so differently. The most plausible explanation lies in kinetic factors affecting either or both pathways (b) and (c). One possibility is steric interference from the methyl groups with the attack of formic acid on the $>\overset{+}{N}=CH_2$ group. However, this is perhaps unlikely as it could be approached from both sides, and it is more probable that the methyl groups change the preferred conformation of cyclam, making pathway (c) easier. It may well be that cyclam itself can take up an everted conformation in which the nitrogen atoms are distant one from another. It is also worth noting that step (c) but not (b) should be reversible, and therefore more forcing conditions, perhaps with additional acid, might produced the tetra-*N*-methyl derivative.



SCHEME

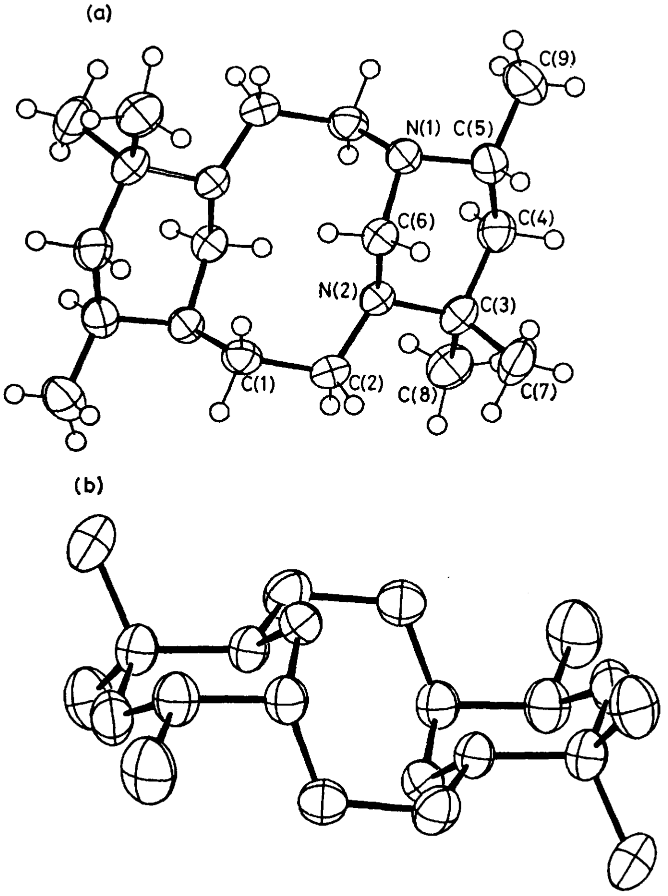


FIGURE 1 Two views of the molecule of (3): (a) with the crystallographic atomic numbering and including hydrogen atoms, (b) to show the conformation of the central ring. The hydrogen atoms are numbered according to the carbon atom to which they are attached

Of the overall conformation of (3) (Figure 1), not much need be said. The two six-membered rings are in chair form with the single methyl groups equatorial. The

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* For details, see Notices to Authors, No. 7, *J.C.S. Perkin II*, 1979, Index issue.

central ten-membered ring (with an internal centre of symmetry) achieves reasonably staggered conformations about each bond. The lone pairs of the nitrogen atoms are aligned in pairs, but the two sets point in opposite directions. Thus they could donate to two metal ions, but it seems unlikely that the central ring could twist to let them point towards a single central metal ion.

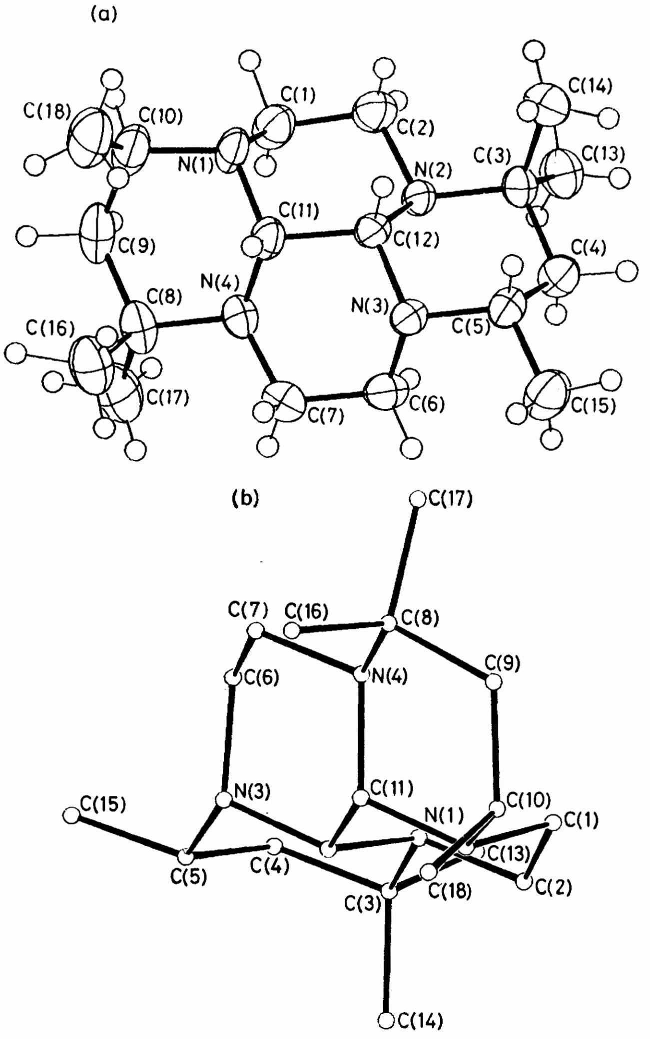

FIGURE 2 Two views of the molecule of (4): (a) with the crystallographic numbering and including hydrogen atoms, (b) to show the ring conformation. Compound (5) is identical except that C(18) is equatorial, not axial

The conformations of (4) and (5) are more interesting (Figure 2). Both consist of fused decalins, for which the thermodynamically favoured conformation must be all *trans* [as in Figure 3(a)]. However, that actually found has *cis*-fusion for three of the five junctions. In particular, the central C_2H_4 bridge is *cis*, as is one each of the C-N links from it [N(1)-C(11) and N(3)-C(12)]. The result is that there are pairs of rings at 90° to each other [Figure 2(b), Figure 3(b)]. A reason for this can be suggested from the intermediate stage in the reaction when one pair of nitrogen atoms have coupled but the others have not. The two conformations that would lead respectively to Figures 3(a) and (b) are shown in Figures 3(c) and (d), and it will be seen that the central region of (c) is severely crowded, while flexing of the more open part of (d), lying on the angle between the two parts of the molecule, would be quite possible, making this intermediate relatively more stable. Thus there will be powerful kinetic control leading to the structure of Figure 3(b) instead of 3(a).

There is no difference in the structures of (4) and (5) apart from that stemming from the original substitution pattern. Isomer (4) has one axial and one equatorial methyl group, but in (5) both are equatorial. The latter should therefore be slightly more stable.

Although the conformation of (4) and (5) produces a fold into which a metal atom might fit, unfortunately it simultaneously forces two of the lone pairs to point out of this cleft. Only if N(1) and N(3) were to invert would this molecule be likely to form a good ligand, and this would also affect the overall geometry. The only route likely to produce rigid ligands isomeric to (3)—(5) and better adapted for co-ordination will be formation in a template reaction, already co-ordinated to a metal atom. This investigation is now in progress.

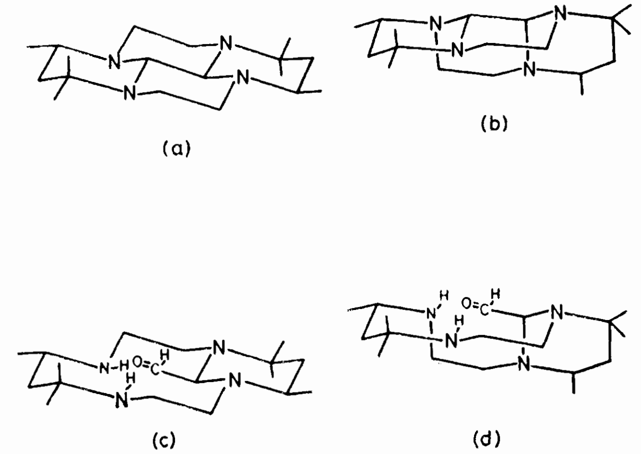

FIGURE 3 (a) All *trans*-conformation for (5); (b) actual conformation for (5); (c) intermediate for all *trans*-conformation; (d) intermediate for actual conformation

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