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PYRROLE STUDIES PART 41.[1] REACTIVITY OF 3,4-DIFORMYL-2,5-DIMETHYLPYRROLE WITH DIAMINOALKANES. AN UNUSUAL FORMATION OF 2-AZAFULVENES

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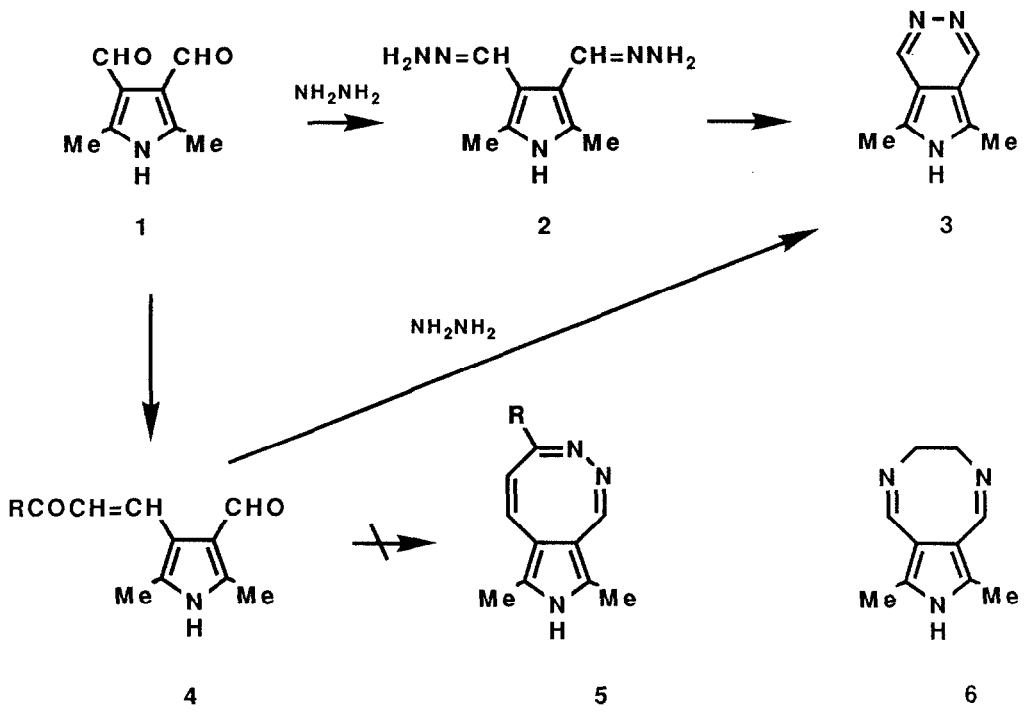
3,4-Diformyl-2,5-dimethylpyrrole (**1**) reacts with α,ω-diaminoalkanes, $NH_2(CH_2)_nNH_2$, to form either the potentially tautomeric 2:2 macrocyclic adduct (**7a**) ⇌ (**8**), when n = 2, or the potentially tautomeric 1:1 bicyclic adduct (**18**) ⇌ (**19**), when n = 4, 5, 6, and 12. ^1H and ^{13}C N.m.r. spectral data indicate that the 2-azafulvene structures predominate for both types of cycloadducts. Only polymeric material was obtained when n = 3.

It is well established that 3,4-diformyl-2,5-dimethylpyrrole (**1**) reacts with hydrazines to produce 6*H*-pyrrolo[3,4-*d*]pyridazines,[2] and there is sound evidence for the intermediate formation of the bis-hydrazone (**2**), which cyclises with the extrusion of hydrazine to yield (**3**).[3] It has also been demonstrated[4] that the monohydrazone of 1-(3-formyl-2,5-dimethylpyrrol-4-yl)-but-1-en-3-one (**4**, R = Me) cyclises *via* a Michael-type reaction, with the subsequent extrusion of propanone to yield the pyridazine (**3**) and does not undergo the intramolecular 1,2-condensation to form the bicyclic 8*H*-pyrrolo[3,4-*d*][1,2]diazocine (**5**).

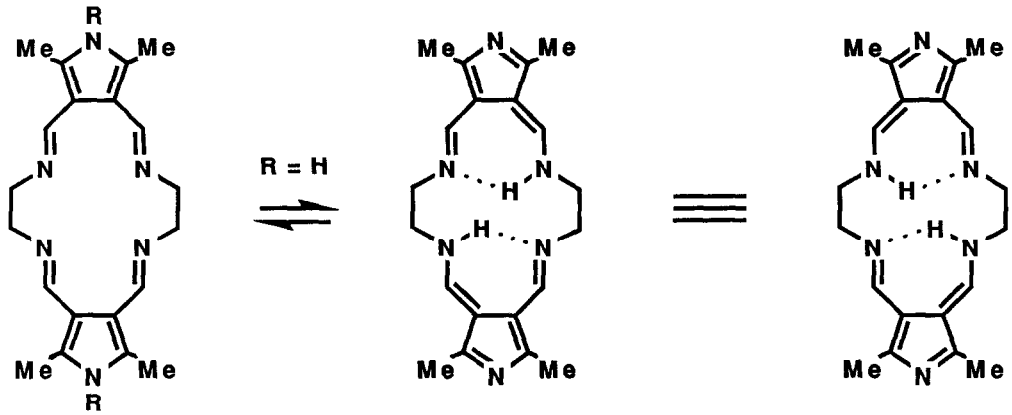
It was of interest, therefore, to explore the reactions of α,ω-diaminoalkanes with the 3,4-diformylpyrrole which, in the case of 1,2-diaminoethane, could lead to the formation of 6,7-dihydro-1,3-dimethyl-2*H*-pyrrolo[3,4-*c*]-[1,4]diazocine (**6**).

Infrared and ^1H n.m.r. spectral data and elemental analysis for the product, which was obtained in an 80% yield from the reaction of the



diformylpyrrole (**1**) with 1,2-diaminoethane, were compatible with the formation of a 1:1 adduct. Mass spectral data indicated, however, that unlike the analogous reaction of (**1**) with hydrazine, the product was not a bicyclic compound, but appeared to be the 2:2 macrocyclic adduct (**7a**). The exclusive formation of (**7a**) probably occurs as a result of severe ring strain and unacceptable steric interactions in the diazocine (**6**), which are absent in the macrocyclic system. It is significant, however, that no evidence was found for any formation of the polymeric condensation product (**9**, x = 2), or for a 2:1 adduct of the type (**10**).

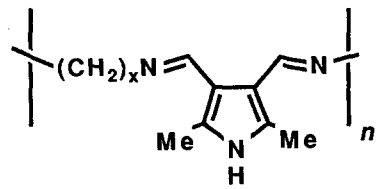
An unusual feature of the 100 MHz ^{1}H n.m.r spectrum of the 2:2 adduct, when measured in $CDCl_3$ at 20°C, was the appearance of two signals at 7.98 and 8.04 p.p.m., attributable to the -CH=N- system. The two signals coalesced at ca. 51°C and appeared as a sharp singlet at 8.00 p.p.m., when the temperature was increased to 60°C. Additionally, only one singlet was observed at 8.73 p.p.m., when the ^{1}H n.m.r spectrum of the compound was measured in trifluoroacetic acid. That these features did not result from two (or more) conformational forms of (**7a**) at equilibrium at 20°C was evident from the observation that the 400 MHz ^{1}H n.m.r. spectrum of the compound also showed two signals centred at 8.00 p.p.m. and 6Hz apart. Such signals could only



7
a R = H
b R = Me
c R = Et

8

8'



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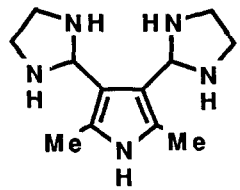

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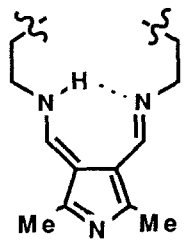
arise from a spin-spin interaction between the imine CH group and an NH group. In keeping with this postulate, the ^{1}H n.m.r spectrum of the 2:2 adduct, which had been subjected to H/D exchange, showed only a singlet at 8.00 p.p.m. The 6 Hz coupling is too large, however, to result from a five-bond interaction with the pyrrolyl NH group of (**7a**) and the most probable alternative explanation requires the macrocyclic system to adopt the doubly degenerate tautomeric form (**8**). The ^{13}C n.m.r. spectrum of the tautomeric system was found to exhibit two signals for the pyrrolyl ring carbons at 158.6 and 114.5 p.p.m., which are totally uncharacteristic of a 1H-pyrrole system,[5] but are compatible with the time-averaged spectral data expected of a symmetrical resonance stabilised 2-azafulvene system.[6] Additionally, in contrast with the spectral data for (**8**), the ^{1}H and ^{13}C n.m.r. spectra of the N-methyl and N-ethyl derivatives of the 1H-pyrrole tautomeric form, (**7b**) and (**7c**), which were prepared by alkylation of (**8**) or

by the reaction of the 1-alkyl derivative of (**1**) with diaminoethane, exhibited the expected signals for the imine system and the 1H-pyrrole ring system at ca. 8.6 and 159 p.p.m., and at ca. 117 and 130 p.p.m., respectively.



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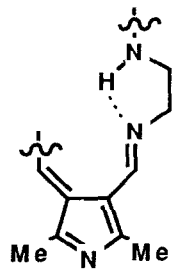

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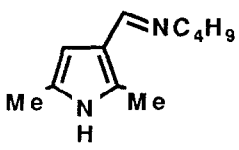

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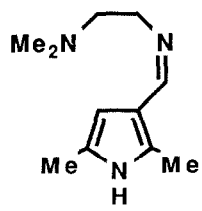

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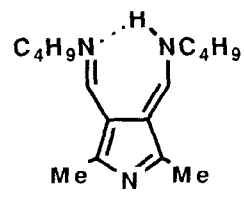

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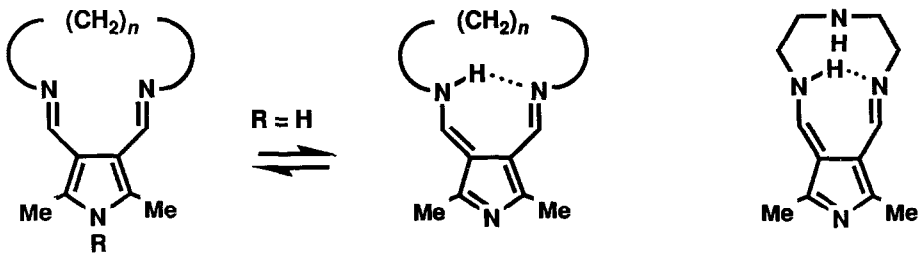
The enhanced stability of the 2-azafulvene system (**8**) is obviously derived from H-bonding within the macrocyclic system. This can occur in two directions, as shown in partial structures (**11**) and (**12**). An examination of the ^{13}C n.m.r. spectral data for the corresponding model systems (**14**) and (**15**) (Table 1) clearly shows that (**14**) exists a 1H-pyrrole, whereas (**15**) exists as the 2-azafulvene, indicating that it is probabaly H-bonding of type (**11**) which stabilises the 2-azafulvene tautomeric structure (**7a**) of the macrocycles.

For reference, the ^{1}H n.m.r.spectrum for the N-butyl imine (**13**), derived from 3-formyl-2,5-dimethylpyrrole, showed a singlet at 8.15 p.p.m., assignable to the imine group, while the ^{13}C n.m.r. spectrum exhibited signals at 103.9, 117.9, 127.7 and 131.2 p.p.m., and at 155.3 p.p.m., characteristic of the 1H-pyrrole ring system and the imine group,

common dicationic species. Again, the collapse of the $J_{CH,NH}$ coupling, observed for protonated (**8**), can be rationalised in terms of the increased mobility of the acidic protons between all four nitrogen atoms of the macrocyclic system. Further evidence for the formation of the common dications is provided by the electronic spectral data of the neutral and of the protonated forms of (**7a** ⇌ **8**) and (**7b**) (see Experimental Section).

The reaction of (**1**) with 1,2-diaminopropane also produced a 2:2 macrocylic adduct in high yield. An inseparable mixture of the three stereoisomers of the two positional isomers (**17a**) and (**17b**) were obtained, as indicated by the n.m.r. spectral data.

In a manner analogous to their rections with hydrazine, the α,β-unsaturated ketones (**4**, R = Me, Et) reacted with 1,2-diaminoethane to yield the 2:2 macrocyclic adduct (**8**), albeit in low yield (ca. 20%) indicating that, compared with the intermolecular Michael-type reaction and subsequent extrusion of the ketone leading to (**8**), both the intramolecular ring closure via a Michael type reaction with extrusion of the ketone to yield the diazocine, and the intramolecular condensation reaction with the ketonic carbonyl group to form the ten-membered ring are disfavoured reactions.



18 **19** **20**

a $n = 4$; **b** $n = 5$; **c** $n = 6$; **d** $n = 12$

In contrast with the formation of the macrocyclic system (**8**) from the reaction of (**1**) with 1,2-diaminoethane, the corresponding reactions α,ω-diaminoalkanes, where there are four or more carbon atoms in the alkane chain, produced the potentially tautomeric 1:1 bicyclic adducts (**18** ⇌ **19**) in high yield, while the reaction of (**1**) with 1,3-diaminopropane gave only the polymer (**9**, x = 3). The observed formation of the 2:2 and 1:1 adducts and the polymer, depending upon the number of carbon atoms in the alkane chain, can be rationalised in terms of a mechanism analogous to that postulated for the formation of the pyrrolopyridazine (**3**) with entropy and enthalpy factors

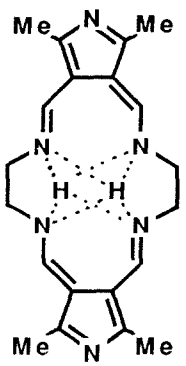
Table 1. ^{1}H and ^{13}C Spectral Data (p.p.m.) for the Potentially Tautomeric System (**7a** ⇌ **8**), the Model Systems (**14**) and (**15**), and Fixed Form Systems (**7b**) and (**7c**)

		-CH=N-		5-membered ring C atoms	
7a	**8**	8.00	155.8	114.6	158.7
14		8.19	156.3	103.9 118.0	127.4 131.0
15		7.92	154.6	114.8	155.9
7a		8.64	159.3	116.3	130.8
7b		8.67	159.4	116.7	129.9

respectively.

The coalescence of the imine ^{1}H n.m.r. signals at elevated temperatures is consistent with increased mobility of the tautomeric protons, such that they are effectively associated with all four nitrogen atoms of the macrocyclic system (**16**), analogous to the H-bonded porphin system. Under these conditions, the time-averaged coupling constant is effectively zero.

The ^{1}H and ^{13}C n.m.r. spectra of the potentially tautomeric systems (**7a** ⇌**8**), and of the N-alkylated 1H-pyrrole derivatives (**7b**) and (**7c**), when measured in trifluoroacetic acid, were compatible with the formation of a



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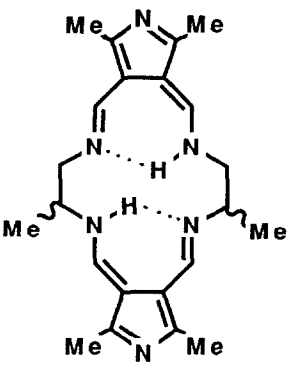
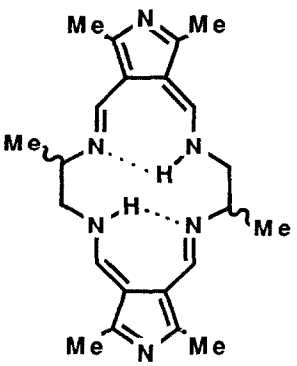


17a



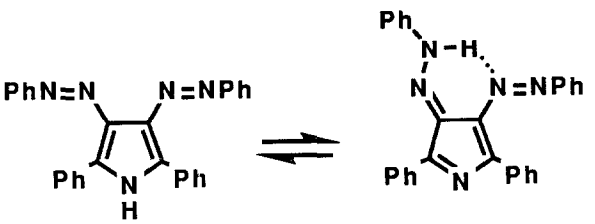
17b

controlling the formation of the three systems. Drieding models show that the 10-membered ring system (**18a** ⇌ **19a**), obtained from the reaction of (**1**) with 1,4-diaminobutane, is probably the smallest cyclic bis-imine which does not possess excessive steric internal interactions. It is remarkable, however, that even the reaction of 1,12-diaminododecane with (**1**) gave the 1:1 bicyclic adduct (**18d** **19d**) in 83% yield in preference to the polymeric system (**9**, x = 12).

As with the macrocyclic system (**8**), the ^{13}C n.m.r. spectra of the 1:1 bicyclic products indicates that they exist preferentially in the 2-azafulvene form (**19**) (see Experimental Section) and the Drieding models show that the imine-enamine nitrogen atoms are positioned virtually within their van der Waal distance of each other, which suggests that H-bonded system will be particularly stable. Bis(2-aminoethyl)amine reacted with (**1**) to give (**20**) in a 65% yield.

The reaction of 1-ethyl-3,4-diformyl-2,5-dimethylpyrrole with 1,6-diaminohexane gave the 1H-pyrrole bicyclic model system (**18c**, R = Et). The same compound could also be obtained by reaction of (**19c**) with triethyloxonium tetrafluoroborate, followed by treatment with aqueous potassium hydroxide.

It is noteworthy that, unlike (**8**) and (**19**), the diformylpyrrole (**1**) and the pyrrolopyridazine (**3**) exist in the 1H-pyrrole form. This reflects, in the first case, the greater acidity of the enolic OH of the 2-azafulvene form of (**1**), compared with that of the pyrrolyl NH of the 1H-pyrrole system (**1**), and, in the second case, the position of the equilibrium between the 2H- and 6H-pyrrolo[3,4-d]pyridazines is governed by the greater aromatic resonance stabilisation of the 6H-system. It has been reported,[7] however, that the 3,4-bis(phenylazo)pyrrole (**21**) exists predominantly as the 2-azafulvene (**22**) and, as with (**8**) and (**19**), it is possible that the system is stabilised by the strong intramolecular H-bonding.



21 22

Experimental:

Infrared spectra were obtained for Nujol mulls using a Perkin Elmer 577 spectrometer. The electronic spectra of compounds (**7a** ⇌ **8**) and (**7b**) were measured using a Pye-Unicam SP8-200 spectrophotometer. ^{1}H and ^{13}C N.m.r.

spectra were measured for ca. 30% solutions in $CDCl_3$, unless stated otherwise, at 100 and 25 MHz, respectively, using a JEOL JMN FX-100 spectrometer, or at 400 and 100 MHz, respectively, using a JEOL JNM GX-400 specrometer. All chemical shifts are reported relative to tetramethylsilane (δ = 0) and the deuterated solvent was used as as a lock signal for the ^{13}C n.m.r. spectra. A Kratos MS25 mass spectrometer produced the low resolution mass spectral data and high resolution mass spectral data were provided by Dr F.A. Mellon and Dr J. Egles of the Institute of Food Research, Norwich, using an AEI MS902 mass spectrometer.

General reaction of 3,4-diformyl-2,5-dimethylpyrrole (1) with diaminoalkanes. Method A.- The diformylpyrrole (**1**) (1.51 g, 0.01 mol) and the appropriate diaminoalkane (0.01 mol) in methanol (15 ml) were stirred at 25°C for 12 h in the presence of 4A molecular sieve. The precipitated product was collected, separated from the molecular sieve, washed with ice-cold methanol (2 x 5 ml) and recrystallised from ethanol. Method B.- Equimolar amounts (0.005 mol) of (**1**) and the diaminoalkane in methanol (20 ml) were stirred at 20°C for 5 min in the presence of 4A molecular sieve and then heated under reflux for ca. 15 min. The crude product was separated from the molecular sieve and recrystallised from methanol.

Using Method A, the reaction of (**1**) with 1,2-diaminoethane gave 5,6,7,14,15,16-hexahydro-1,3,10,12-tetramethyldipyrrolo[3,4-f][3',4'-n][1,4,-9,12]tetra-azacyclohexadecine (**8**) (80%), m.p. 300°C (Found: C, 68.2; H, 7.2; N, 23.8, M^+ 350 a.m.u. $C_{20}H_{26}N_6$ requires C, 68.5; H, 7.5; N, 24.0%). ν_{max} 3450 - 3300, 1655 cm^{-1}; λ_{max} (EtOH) 229.5 (log ε 480), 250sh (4.49), 296sh (4.41), 316 nm (4.45); (4N H_2SO_4) 217 (4.80), 251 (4.09), 311nm (4.57); δ_H 2.45 (s, 12H), 3.75 (s, 8H), 8.00 (d, 6 Hz, 4H) and 8.04 (s, 2H); δ_C 15.1 (q), 58.2 (t), 114.6 (s), 155.8 (d), 158.7 (s); δ_H (CF_3CO_2H) 2.56 (s, 12H), 4.32 (s, 8H), 8.73 (s, 4H).

The isomeric 5,6,7,14,15,16-hexahydro-1,3,6,10,12,15- and 1,3,6,10,12,16-hexamethyldipyrrolo[3,4-f][3',4'-n][1,4,9,12]tetra-azacyclohexadecines (**17a**) and (**17b**) (Found: C, 69.8; H, 8.2; N, 22.3, M^+ 375 a.m.u. $C_{22}H_{30}N_6$ requires C, 69.8; H, 8.0; N, 22.2%) were obtained using Method A, as an inseparable mixture (m.p. 300°C), in an overall yield of 78% from the reaction of (**1**) with 1,2-diaminopropane. δ_H (400 MHz) 1.22 - 1.31 [6H, three overlapping doublets, centred at 1.234, 1.268, 1.295 (ca. 1:2:1)], 2.45 (s, 12H), 3.40 - 3.60 (overlapping q, 2H), 3.94 (br s, 2H), 3.94 - 4.05 (m, 2H), 7.80 - 8.20 [4H, doublets centred at 7.85, 7.89, 7.94, 7.955, 8.01, 8.03, 8.06, 8.10 (ca. 1.5:1.0:2.7:1.0:1.0:3.6:1.4:1.95)]; δ_C 11.9 (q), 12.2 (q), 13.4 (q), 13.5 (q), 14.0 (q), 40.6 (t), 42.0 (t), 42.3 (t), 51.0 (t), 52.5 (t), 52.9 (t), 54.3 (t), 55.4 (t), 112.4 (s), 115.2 (s), 118.0 (s), 120.8 (s), 121.5 (s), 153.9 (s), 154.2 (s), 155.3 (s), 155.5 (s), 163.4 (d), 163.8 (d), 164.3 (d),

164.7 (d).

6,7,8,9-Tetrahydro-1,3-dimethyl-5H-pyrrolo[3,4-c][1,6]diazacyclodecine (**19a**), m.p. 285 - 287°C (Found: C, 70.6; H, 8.5; N, 20.5; M^+ 203 a.m.u. $C_{12}H_{17}N_3$ requires C, 70.9; H, 8.4; N, 20.7%) was obtained by Method A in 60% yield from (**1**) and 1,4-diaminobutane. ν_{max} 3450 - 3300, 1660 cm^{-1}; δ_H 1.79 (s, 4H); 2.43 (s, 6H); 3.58 (s, 4H), 7.94 (s, 2H); δ_C 15.0 (q), 29.1 (t), 55.6 (t), 114.7 (s), 155.1 (d), 157.0 (s).

6,7,8,9,10-Pentahydro-1,3-dimethyl-5H-pyrrolo[3,4-i][1,4,7]triazacycloundecine (**20**), m.p. 135 - 136°C (Found: C, 66.0; H, 8.1; N, 25.4. M^+ 218 a.m.u. $C_{12}H_{18}N_4$ requires C, 66.0; H, 8.3; N, 25.7%) was obtained in 65% yield, using Method A, from (**1**) and bis(2-aminoethyl)amine. ν_{max} 3200, 1660 cm^{-1}; δ_H 2.36 (s, 6H), 2.84 (t, 4H), 3.58 (t, 4H), 7.86 (s, 2H); δ_C 14.8 (q), 50.6 (t), 55.4 (t), 114.8 (s), 155.5 (d) 156.4, (s).

Using Method A, 6,7,8,9,10-Pentahydro-1,3-dimethyl-5H-pyrrolo[3,4-c][1,6]-diazacycloundecine (**19b**), m.p. 135 - 137°C, (Found: 71.7; H, 8.5; N, 19.2. M^+ 217 a.m.u. $C_{13}H_{19}N_3$ requires C, 71.9; H, 8.8; N, 19.4%) was obtained in 92% yield from (**1**) and 1,5-diaminopentane. ν_{max} 3400 - 3200, 1660 cm^{-1}; δ_H 1.66 (m, 6H), 2.42 (s, 6H), 3.54 (m, 4H), 7.96 (s, 2H); δ_C 14.6 (q), 31.1 (t), 49.8 (t), 55.1 (t), 114.7 (s), 155.0 (d), 156.0 (s).

6,7,8,9,10,11-Hexahydro-1,3-dimethyl-5H-pyrrolo[3,4-c][1,6]diazacyclododecine (**19c**), m.p. 158 - 160°C (Found: C, 72.7; H, 9.1; N, 18.1. M^+ 231 a.m.u. $C_{14}H_{21}N_3$ requires C, 72.7; H, 9.2; N, 18.2%) was obtained in 95% yield (Method B) from (**1**) and 1,6-diaminohexane. ν_{max} 3300, 1665 cm^{-1}; δ_H 1.50 (br t, 4H), 1.67 (br t, 4H), 2.41 (s, 6H), 3.51 (t, 4H), 7.91 (d, 6.6 Hz, 2H); δ_C 14.9 (q), 27.5 (t), 31.3 (t), 55.7 (t), 114.6 (s), 154.8 (d), 156.4 (s).

6,7,8,9,10,11,12,13,14,15,16,17-Dodecahydro-1,3-dimethyl-5H-pyrrolo[3,4-c]-[1,6]diazaoctacyclodecine (**19d**), m.p. 177- 179°C (Found: C, 76.0; H, 10.3; N, 13.0. M^+ 315 $C_{20}H_{33}N_3$ requires C, 76.1; H, 10.5; N, 13.3%) was obtained in 83% yield by Method B (57% by Method A) from (**1**) and 1,12-diaminododecane. ν_{max} 3325, 1670 cm^{-1}; δ_H 1.12 - 1.70 (m, 20H), 2.42 (s, 6H), 3.47 (t, 4H), 7.91 (d, 6 Hz, 2H). δ_C 15.0 (q), 27.5 (t), 29.6 (t), 29.8 (t), 30.0 (t), 31.5 (t), 55.4 (t), 114.8 (s), 154.6 (d), 156.3 (s).

Reaction of 3,4-diformyl-2,5-dimethylpyrrole with acylic methyl ketones: The appropriate ketone (0.01 mol) was added with stirring to (**1**) (1.51 g, 0.01 mol) and sodium hydroxide (1.5 g) in aqueous methanol (40% v/v, 35 ml) and the mixture was stirred at room temperature for 2 - 3 h. The deep red solution was diluted with water (30 ml) and extracted with dichloromethane (4 ($CaCl_2$), and evaporated to yield the α,β-unsaturated ketone (**4**).

1-(4-Formyl-2,5-dimethylpyrrol-3-yl)but-1-en-3-one (**4**, R = Me) (73%) had m.p. 201 - 202°C (Found: C, 68.9; H, 6.7; N, 7.4 $C_{11}H_{13}NO_2$ requires C, 69.1; H, 6.8; N, 7.3%). ν_{max} 3180, 1650, 1630 cm^{-1}; δ_H 2.58 (s, 3H), 2.68 (s, 3H),

7.31 (d, 16 Hz, 1H), 8.56 (d, 16 Hz, 1H), 6.69 (s, 1H).

1-(4-Formyl-2,5-dimethylpyrrol-3-yl)pent-1-en-3-one (**4**, R = Et) (78%) had m.p. 164 - 165°C (Found: C, 70.4; H, 7.4; N, 7.0. $C_{12}H_{15}NO_2$ requires C, 70.2; H, 7.4; N, 6.8%). ν_{max} 3195, 1655, 1625 cm^{-1}; δ_H 1.25 (t, 3H), 2.36 (s, 3H), 2.50 (s, 3H), 2.70 (q, 2H), 6.78 (d, 16.6 Hz, 1H), 8.05 (d, 16.6 Hz, 1H), 9.97 (s, 1H).

Reaction of 1-(4-formyl-2,5-dimethylpyrrol-3-yl)but-1-en-3-one (**4**, R = Me) and -pent-1-en-3-one (**4**, R = Et) with 1,2-diaminoethane: The appropriate α,β-unsaturated ketone (**4**) (0.01 mol) and 1,2-diaminoethane (2.0 g, 0.33 mol) in methanol (30 ml) were stirred at 25°C for 10 h. The yellow precipitate was collected, washed with cold methanol (10 ml), and recrystallised from ethanol to give the macrocycle (**8**), m.p. > 300°C (23% from **4**, R = Me; 21% from **4**, R = Et), which was identical in all respects with the product obtained from the reaction of (**1**) with 1,2-diaminoethane.

2,6,7,11,15,16-Hexahydro-1,2,3,10,11,12-hexamethyldipyrrolo[3,4-f][3',4'-n]-[1,4,9,12]tetraazacyclohexadecine (**7b**).- 3,4-Diformyl-1,2,5-trimethylpyrrole (0.57 g, 0.0035 mol in acetonitrile (25 ml) was refluxed with 1,2-diaminoethane (0.21 g, 0.0035 mol) in the presence of 4A molecular sieve for 3 h. The molecular sieve was removed by filtration of the hot solution and the reaction mixture was allowed to cool. The white crystalline product was collected and recrystallised from acetonitrile to give the 2,11-dimethyl derivative (**7b**) (0.73 g, 55%), which was isolated as a 1:1 complex with acetonitrile, m.p. 228°C (Found: C, 68.65; H, 7.9; N, 23.4 $C_{22}H_{30}N_6 + CH_3CN$ requires C, 68.7; H H, 7.9; N, 23.4%). M^+ 378; ν_{max} 1645 cm^{-1}; λ_{max} (EtOH) 230 (log ε 4.73), 254.5 (4.34), 300nm (4.63); (4N H_2SO_4) 216 (4.81), 250.5 (4.18), 307.5 (4.58); δ_H 2.30 (s, 12H), 3.23 (s, 6H), 3.86 (s, 8H), 8.64 (s, 4H), δ_C 10.9 (q), 29.8 (q), 62.0 (t), 116.3 (s), 130.8 (s), 159.3 (s).

2,11-Diethyl-2,6,7,11,15,16-hexahydro-1,3,10,12-tetramethyldipyrrolo[3,4-f]-[3'4'-t]-1,4,9,12-tetraazacyclohexadecine (**7c**).- Method A: 1,2-Diaminoethane (0.3 g, 0.005 mol) in acetonitrile (35 ml) was allowed to react with 1-ethyl-3,4-diformyl-2,5-dimethylpyrrole (1.0 g, 0.005 mol) [m.p. 106°C (Found: C, 66.7; H, 7.5; N, 7.8 $C_{10}H_{13}NO_2$ requires C, 67.0; H, 7.3; N, 7.8%) obtained by Vilsmeier-Haack formylation of 1-ethyl-2,5-dimethylpyrrole] in a manner analogous to that described above for the reaction of 3,4-diformyl-1,2,5-trimethylpyrrole to give the 2,11-diethyl derivative (**7c**) (1.49 g, 69%), m.p. 191 - 193°C (Found: C, 70.2; H, 8.5; N, 20.2. M^+ 406 a.m.u. $C_{24}H_{34}N_6$ requires C, 70.9 H, 8.4; N, 20.1%). ν_{max} 1635 cm^{-1}; δ_H 1.17 (t, 6H), 2.34 (s, 12H), 3.74 (q, 4H), 3.86 (s, 8H), 8.67 (s, 4H); δ_C 10.6 (q), 15.6 (q), 37.8 (t), 62.1 (t), 116.7 (s), 129.9 (s), 159.4 (d). Method B: Potassium hydroxide (1.12 g, 0.02 mol) in DMSO (20 ml) was stirred at 25°C

for 10 min and (8) (3.50 g, 0.01 mol) was added and the mixture stirred at 25°C for a further 15 min. Iodoethane (6.74 g, 0.04 mol) was added dropwise and the mixture heated at 60°C for 2 h and then cooled to 0°C. After 10h at 0°C, the precipitated product was collected and recrystallised from ethanol to give (**7c**) (2.12 g, 60%), m.p. 189 - 190°C. Method C: Triethyloxonium tetrafluoroborate (0.16 g, 0.0008 mol) was added with vigorous stirring to (**8**) (0.15 g, 0.0004 mol) in dichloromethane (20 ml). The solution was stirred for 15 min and then kept at 0°C for 5 h. The precipitated 2,11-diethyl tetrafluoroborate salt (0.15 g, 63%), m.p. 300°C, which was recrystallised from aqueous ethanol (Found: C, 48.3; H, 6.0; N, 14.3 $C_{26}H_{36}B_2F_8N_6$ requires C, 49.5; H, 6.2; N, 14.2%). δ_H (DMSO-d_6) 1.25 (t, 6H), 3.62 (s, 12H), 4.05 - 4.25 (overlapping q and br s, 12H), 8.79 (d, 7Hz, 4H). Treatment of the salt with aqueous potassium hydroxide (15%, 20 ml) and rapid filtration of the suspension gave (**7c**), which was contaminated with hydrolysed material.

2-Ethyl-6,7,8,9,10,11-hexahydro-1,3-dimethyl-2H-pyrrolo[3,4-c][1,6]diazacyclododecine (**18c**, R = Et).- Method A: 1-Ethyl-3,4-diformyl-2,5-dimethylpyrrole (0.75 g, 0.004 mol) in acetonitrile (25 ml) was allowed to react with 1,6-diaminohexane (0.46 g, 0.004 mol) in a manner analogous to that used for the corresponding reaction of the diformylpyrrole with 1,2-diaminoethane. The bicyclic compound (0.98 g, 94%) was recrystallised from acetonitrile, m.p. 222 - 224°C (Found: C, 73.8; H, 9.7; N, 15.8 Cl6H25N3 requires C, 74.1; H, 9.7; N, 16.2%). ν_{max} 1650 cm^{-1}; δ_H 1.25 (t, 3H), 1.00 - 2.00 (m, 8H), 2.40 (s, 6H), 2.43 (t, 4H), 3.80 (q, 2H), 8.60 (s, 2H). δ_C 10.5 (q), 15.2 (q), 27.2 (t), 31.4 (t), 38.1 (t), 62.3 (t), 116.4 (s), 131.3 (s), 156.8 (d). Method B: The 5H-pyrrolo[3,4-c][1,6]diazacyclododecine (**19c**) (0.38g, 0.0015 mol) and triethyloxonium tetrafluoroborate (0.29 g, 0.0015 mol) in dichloromethane (20 ml) were stirred vigorously for 15 min at room temperature and then kept at 0°C for 5 h. The precipitated 2-ethyl tetrafluoroborate salt (0.31 g, 89%), m.p. 215 - 217°C was collected. (Found: N, 12.1; M^+ 347 a.m.u. $C_{16}H_{26}BF_4N_3$ requires N, 12.1%; M^+ 347 a.m.u). ν_{max} 1650 cm^{-1}; δ_H (DMSO-d_6) 1.24 (3H, t), 1.3 - 1.5 (4H, br m), 1.5 - 16.5 (4H, br m), 2.53 (6H, s), 3.5 - 3.8 (4H, br m), 4.06 (2H, q), 8.67 (2H, d, 7.3 Hz); δ_C (DMSO-d_6) 9.9 (q), 14.5 (q), 26.7 (t), 29.9 (t), 55.1 (t), 113.5 (s), 143.3 (s), 158.6 (d). Treatment of the 2-ethyl salt with aqueous potassium hydroxide (15%, 20 ml) and rapid filtration of the suspension gave (**18c**, R = Et), which was contaminated with partially hydrolysed material.

General reaction of 3,4-diformyl-2,5-dimethylpyrrole and 3-formyl-2,5-dimethylpyrrole with aminoalkanes.- The formylpyrrole (0.005 mol) and an excess of the aminoalkane (0.01 mol) in acetonitrile (30 ml) were heated under reflux in the presence of A4 molecular sieve for ca. 8 h. The molecular sieve was removed and the excess aminoalkane and the solvent were removed

under reduced pressure (0.1 mm of Hg) to give the methyleneimine.

(2,5-Dimethyl-1H-pyrrol-3-yl)methylene(N-n-butyl)imine (**13**) (50%), m.p. 73 - 75°C, was obtained from 3-formyl-2,5-dimethylpyrrole and 1-aminobutane (Found: C, 74.0; H, 10.4; N, 15.5 $C_{11}H_{18}N_2$ requires C, 74.1; H, 10.2; N, 15.7%). ν_{max} 3250, 1680 cm^{-1}; δ_H 0.91 (t, 3H), 1.17 - 1.80 (m, 4H), 2.14 (s, 3H), 2.31 (s, 3H), 3.49 (t, 2H), 6.17 (s, 1H), 8.15 (s, 1H); δ_C 11.0 (q), 12.6 (q), 13.9 (q), 20.4 (t), 33.4 (t), 61.2 (t), 103.9 (d), 117.9 (s), 127.7 (s), 131.2 (s), 155.3 (d).

N-(2-Dimethylaminoethyl) (2,5-dimethyl-1H-pyrrol-3-yl)methyleneimine (**14**) (93%), m.p. 67 - 70°C was obtained from the monoformylpyrrole and 2-(dimethylamino)ethylamine. (Found: N, 21.4; M^+ 193.1589 a.m.u. $C_{11}H_{19}N_3$ requires N, 21.7% M^+ 193.1582 a.m.u.) ν_{max} 1628 cm^{-1}; δ_H 2.13 (s, 3H), 2.23 (s, 3H), 2.29 (s, 6H), 2.59 (t, 6.8 Hz, 2H), 3.64 (t, 6.8 Hz, 2H), 6.11 (s, 1H), 8.19 (s, 1H); δ_C 11.0 (q), 12.7 (q), 45.7 (q), 59.7 (t), 60.6 (t), 103.9 (d), 118.0 (s), 127.4 (s), 131.0 (s), 156.3 (d).

6-(n-Butylamino)-1,3-dimethyl-2-azafulven-4-yl methylene(N-n-butyl)imine (**15**) (83%) was obtained, as an unstable oil, from (**1**) and 1-aminobutane (Found: C, 73.5; H, 10.25; N, 16.1 $C_{16}H_{27}N_3$ requires C, 73.5; H, 10.4; N, 16.1%). ν_{max} 1640 and 1615 cm^{-1}; δ_H 1.75 (t, 6H), 1.65 - 1.85 (m, 8H), 2.41 (s, 6H), 3.48 (t, 4H), 7.92 (s, 2H); δ_C 13.8 (q), 14.9 (q), 20.2 (t), 33.6 (t), 54.6 (t), 114.8 (s), 154.6 (d), 155.9 (s).

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