Synthesis of Methano-bridged Tetradehydrodiaza[22]annulene and Related Compounds

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Synthesis of 9,22-diethoxy-13,18-dimethyl-14,15,16,17-tetradehydro-2,7-methano-1,8-diaza[22]-annulene (9,22-diethoxy-13,18-dimethyl-2,7-methano-1,8-diazacyclodocosa-2,4,6,8,10,12,18,20,-22-nonaene-14,16-diyne), is described. Examination of ^{1}H NMR and electronic spectra indicates that the diaza[22]annulene shows no ring current effect but does show polyolefinic character despite the potential diatropic 22π-electron system. Attempts to prepare the higher analogues, diaza[24]- and -[26]annulenes are also described.

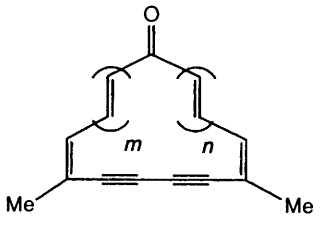
In previous papers, we have reported the synthesis of a series of monocyclic tetradehydroaza-annulenes **2**, higher vinylogues of pyridine, starting from a series of the tetradehydro-annulenones **1**,[1] and showed the alternation of the tropic nature between [4*n* + 2]π- and [4*n*]π-electron systems in compounds **2** with 14- to 22-membered rings.[2]

The systematic synthesis of aza-annulenes **2** starting from the annulenones **1** involved essentially (i) preparation of the corresponding oximes, (ii) Beckmann rearrangements to lactams, and finally (iii) *O*-alkylation of the lactams with Meerwein's reagent. This successful sequence of reactions led us to expect that starting from appropriate annulenediones, diaza-annulenes, the higher analogues of pyrimidine or pyrazine might be prepared. We have now realized this expectation in practice. Since the methano-bridge had been found to contribute to keeping the annulene perimeter planar in our studies upon methano-bridged tetradehydroannulenes[3] and thia-annulenes,[4] the methano-bridged annulenediones **3**–**5**, of which preparations were reported only very recently, as well as their higher analogues,[5] appeared to be the desirable starting materials for synthesis of diaza-annulenes. The methano-bridged diaza[22]annulene **8** thus obtained is the largest heteroannulene with two heteroatoms so far obtained in which both heteroatoms replace carbon atoms of the annulene perimeter.[6]

Results and Discussion

Synthesis.—Treatment of the tetradehydromethano[20]annulenedione **3**[5] with an excess of hydroxylamine hydrochloride in methanol, tetrahydrofuran (THF) and water gave the dioxime **6** in 88% yield. The appearance of only one singlet for the hydroxy protons seemed to suggest that compound **6** existed as a single isomer, but the configuration was not clear at this stage. Treatment of compound **6** with phosphorus pentachloride in tetrahydrofuran (THF) caused double Beckmann rearrangements to give the dilactam **7** (28%). The structure of compound **7** was assigned as indicated on the basis of its ^{1}H NMR spectrum (see below). Thus both amide nitrogens were directly bound to the cycloheptatriene ring. Since the Beckmann rearrangement usually proceeds so that the substituent *anti* to the hydroxy group moves from C to N,[7] the OH configurations of the dioxime **6** should be those indicated.

The dioxime **9** (51%), obtained from the tetradehydro-



1
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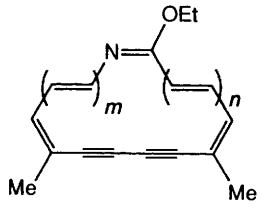
n = 1–3



2
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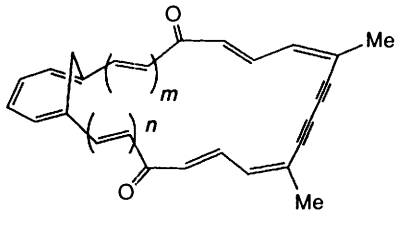
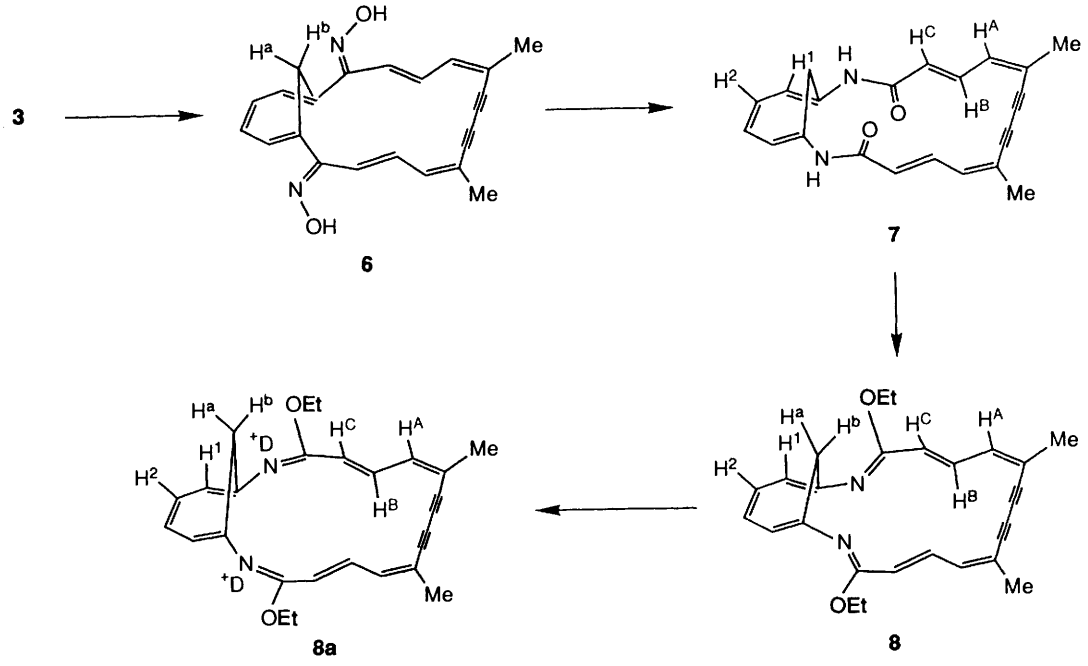


[20]-**3**: *m* = *n* = 0
[24]-**4**: *m* = *n* = 1
[26]-**5**: *m* = 1, *n* = 2



methano[24]annulenedione **4**,[5] consisted of an inseparable mixture of stereoisomers, as judged from the appearance of three hydroxy proton signals (see Experimental section). Beckmann rearrangement of the mixture gave the dilactam **10** (67%) as a sole isolable product. The ^{1}H NMR spectrum of compound **10** indicated that it possessed the geometry shown. Therefore the unsymmetrical structure **9** could be assigned to the main isomer of the precursor dioxime.

Similarly, the dioxime **11** (77%), which was obtained from the tetradehydromethano[26] annulenedione **5**,[5] was converted into the dilactam **12** in poor yield (18%). The ^{1}H NMR spectrum of **12** showed that **12** consisted of only one regioisomer shown by the formula, in which the two amide moieties again had opposite orientations.

The reaction of the dilactam **7** with Meerwein's reagent was slow and did not proceed to completion. The dilactam **7** reacted with a large excess of triethyloxonium tetrafluoroborate in dichloromethane for 3 days at room temperature to afford the desired tetradehydromethanodiaza[22]annulene **8** in a poor yield (9%) with a large recovery of the substrate **7**.

The tetradehydromethanodiaza[22]annulene **8** thus obtained is relatively stable as a solid and in solution.

The conversions of both dilactams **10** and **12** to the corresponding diaza[26]- and -[28]annulenes, respectively, as before were attempted under several different conditions by changing the reaction temperature and reactime time. However, the reactions of compounds **10** and **12** with a large excess of triethyloxonium tetrafluoroborate did not proceed and resulted in decomposition of the substrates due to instability of both compounds **10** and **12** under the reaction conditions.

It is noted that recrystallisation of the dioxime **6** and the dilactam **7** from acetone and of the dilactam **12** from methanol gave crystals containing solvent of crystallisation in a molar ratio of 1:1, respectively, as evidenced from ^{1}H NMR spectroscopy and elemental analyses (see Experimental section).

^{1}H *and* ^{13}C *NMR Spectra.*—Chemical shift assignments (see Experimental section) of the olefinic protons in dilactams **7**, **10** and **12** were made as follows. Broad doublet signals were assigned to the protons adjacent to a methyl group, because the broadening was due to allylic coupling to the methyl protons as revealed by decoupling experiments, while sharp doublets were assigned to the protons adjacent to a carbonyl group or the cycloheptatriene ring. Protons adjacent to nitrogens were easily assigned because these protons showed coupling with the NH protons. Then the proton sequence along the polyene moiety was determined by successive decoupling experiments.

All the –CH=CH– moieties showed J_{vic} 15–16 Hz indicating an *E* configuration while =CH–CH= moieties had J_{vic} 10–11 Hz indicating the *s-trans* conformation.[8] Irradiation of the methyl signals caused an intensity enhancement (NOE) of the doublet signals due to the respective adjacent olefinic protons H^A (and $H^{A'}$), clearly indicating that H^A (and $H^{A'}$) is located outside of the macrocyclic ring. The geometries of compounds **7**, **10** and **12** were therefore determined as shown by the structural formula.

The 500 MHz ^{1}H NMR spectrum of the tetradehydromethanodiaza[22]annulene **8** taken in $CDCl_3$ at 26 °C is shown in Fig. 1(*a*).

Owing to the potential 22π-aromatic system of compound **8**, diatropicity was expected, which would afford the signals of the inner protons (H^B and the methano bridge protons) at a higher field than their normal positions and of the outer protons at a lower field. Contrary to this expectation, the H^B signal appears at the lowest field, although this may partly be ascribed to the deshielding anisotropy effect of the diyne moiety. All other protons have normal chemical shifts. These features suggest that compound **8** is atropic in nature. This is in sharp contrast with the behaviour of the closely related carbocyclic analogue **13**, which showed strong diatropicity with the signals of the methano bridge protons at δ 0.91 and of the methyl groups at δ 2.36.

Another remarkable feature is that the two protons of the methano bridge are diastereotopic affording an AB quartet signal and the methylene protons of the ethoxy groups are also diastereotopic. This indicates that the macrocyclic ring is nonplanar and the flipping of the methano bridge is slow on the NMR time scale at 26 °C.

The degree of dia- or para-tropicity of a heteroannulene has been found to be much smaller than that of the corresponding carbocyclic annulene,[6] and we found that the monoaza[22]annulene **14** showed diatropicity, though small, with the signals of the methyl groups adjacent to the diyne moiety at δ 2.10 and

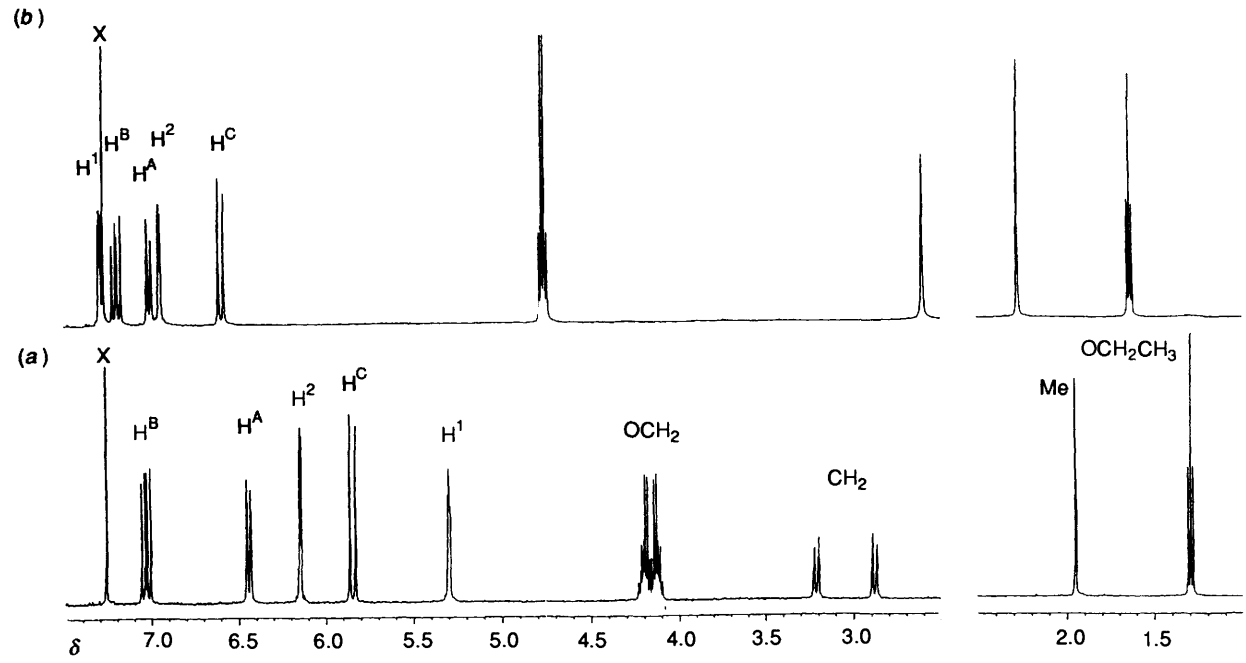
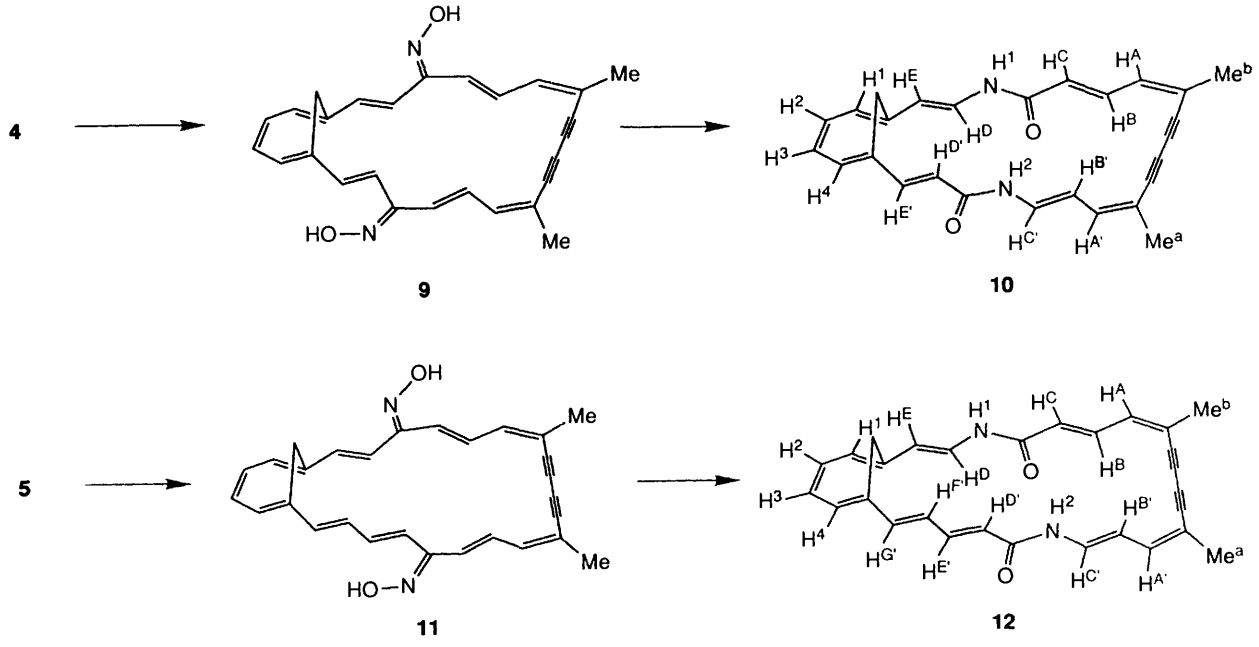


Fig. 1 500 MHz ^{1}H NMR spectrum of compound **8** at 26 °C: (*a*) in $CDCl_3$ (*b*) in $CDCl_3$–CF_3CO_2D (~ 2:1). The peak with × is due to $CHCl_3$



2.15.[2] Judging from the theoretical prediction that pyrimidine or pyrazine have similar resonance energies and thus similar tropicity to pyridine,[9] the present diaza compound **8** should show diatropicity to a similar extent as the monoaza compound **14**. Therefore, we consider that the atropic nature of compound **8** is not due to the introduction of two nitrogen atoms into the diatropic carbocyclic [22]annulene system **13**, but is attributable to the nonplanarity of the molecular skeleton. In compound **8**, the ethoxy groups must be located outside the macrocycle. Therefore compound **8** cannot assume a skeletal conformation similar to that of compound **13**, which would be more planar and thus more stable than the conformation which **8** is forced to adopt.

We have also studied ^{1}H NMR spectra of compound **8** in acidic media in order to obtain information on the effect of protonation on the geometry and tropicity of this compound. Addition of one-ninth volume of CF_3CO_2D to the $CDCl_3$ solution of compound **8** caused a dramatic change in the ^{1}H NMR spectrum. Further addition of CF_3CO_2D showed no further change in the spectrum, suggesting that compound **8** had been completely deuteriated, yielding the dicationic species **8a**. The ^{1}H NMR spectrum of **8** in $CDCl_3$–CF_3CO_2D (*ca.* 2:1) is shown in Fig. 1(*b*). The signals of all the protons except for those of the bridge methylene protons shift downfield. These results might be attributable to diminished π-electron density, arising from withdrawal of electrons by deuteriation and not to any change in tropicity, although the reason of the upfield shift of the bridged methylene protons is not clear.

The ^{13}C NMR spectrum of **8** in $CDCl_3$–CF_3CO_2D (*ca.* 2:1) shows an intriguing behaviour. Upon changing the solvent from $CDCl_3$ to $CDCl_3$–CF_3CO_2D, C-3/C-6, C-9/C-22 and C-11/C-20 show large downfield shifts (14.5, 13.3 and 11.6 ppm, respectively), while C-10/C-21 shifts strongly upfield (8.4 ppm) together with a small upfield shift of C-2/C-7 (3.9 ppm). This

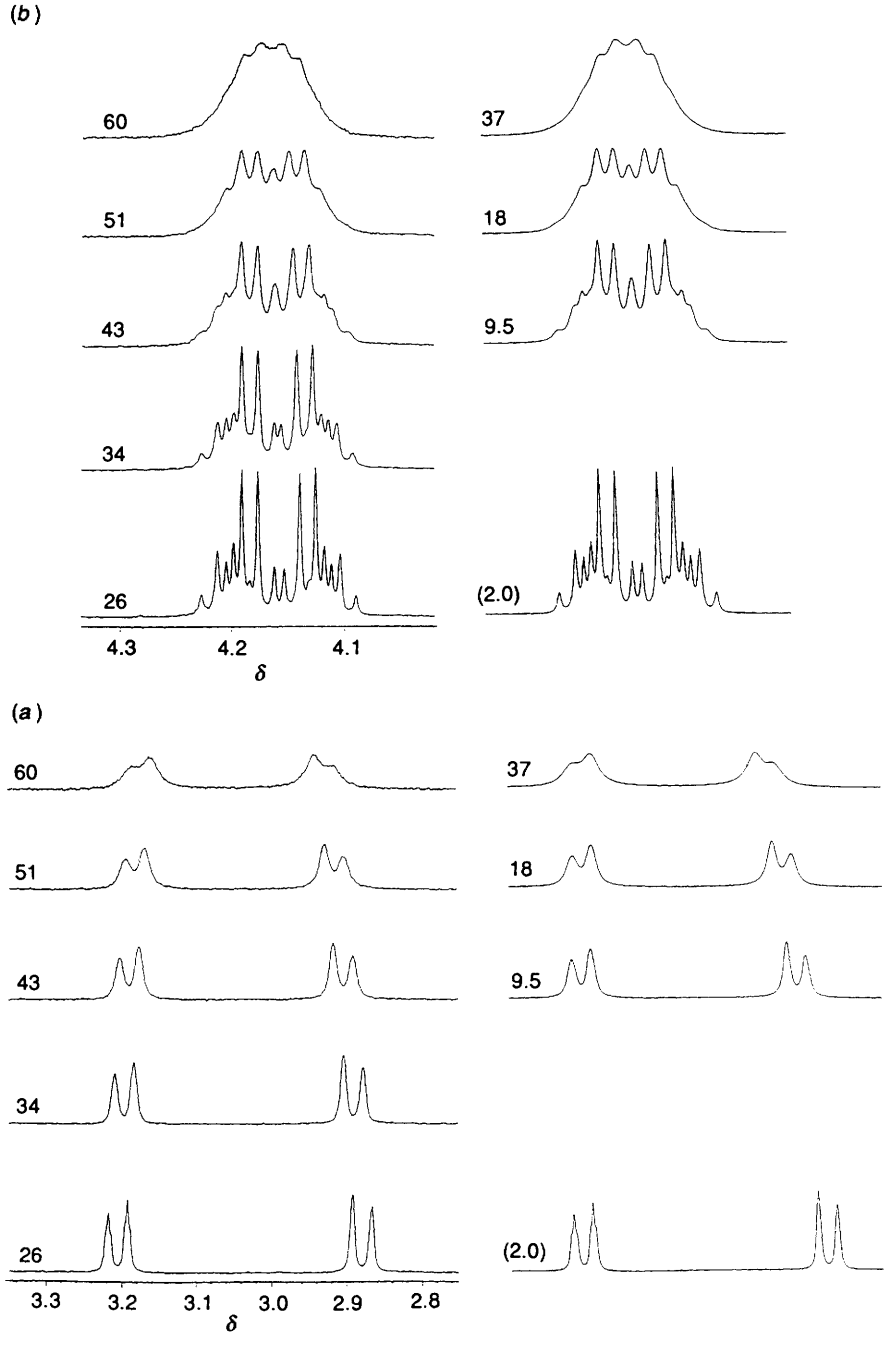


Fig. 2 Temperature-dependent ^{1}H NMR spectra of compound **8** in $CDCl_3$: (*a*) the methano bridge protons and (*b*) OCH_2 protons. On the left are the observed spectra at various temperatures (°C) and on the right are the calculated spectra with the best-fit rate constants (s^{-1})

clearly indicates that the electron density alternation occurs along the macrocyclic periphery. A similar behaviour has been observed previously in tetradehydro[15]annulenone derivatives.[10] The OCH_2 carbon shows a large downfield shift (11.2 ppm), probably due to charge density distribution on the oxygen atoms. The methano bridge carbon shows a large upfield shift (10.7 ppm), although the origin of this shift is not clear.

The bridge methylene protons of compound **8** in $CDCl_3$–CF_3CO_2D at 26 °C appeared as a singlet and the methylene protons of the ethoxy groups were also magnetically equivalent, suggesting that the flipping of the methano bridge was fast on the NMR timescale in this medium. This may be because the molecular skeleton in the species **8a** is more flexible than that of the neutral **8** presumably due to the increased single bond character of the original C=N bonds.

Flipping of the Methylene Bridge in Compound **8**.—In order to obtain information on the energy barrier to the flipping of the methano-bridge, a variable-temperature ^{1}H NMR study was performed for the diaza[22]annulene **8** in $CDCl_3$ in the temperature range 26–60 °C. These spectra are illustrated in Fig. 2 together with the calculated spectra using the DNMR3 program.[11] Rate constants were determined at three temperatures of 43, 51 and 60 °C so that both the methano bridge and OCH_2 signals gave the same best-fit value at each temperature. The free energy of activation for the flipping of the methano bridge is calculated to be 17.2 kcal mol^{-1},* while the enthalpy and entropy of activation are unreliable because of the narrow

* 1 cal = 4.184 J.

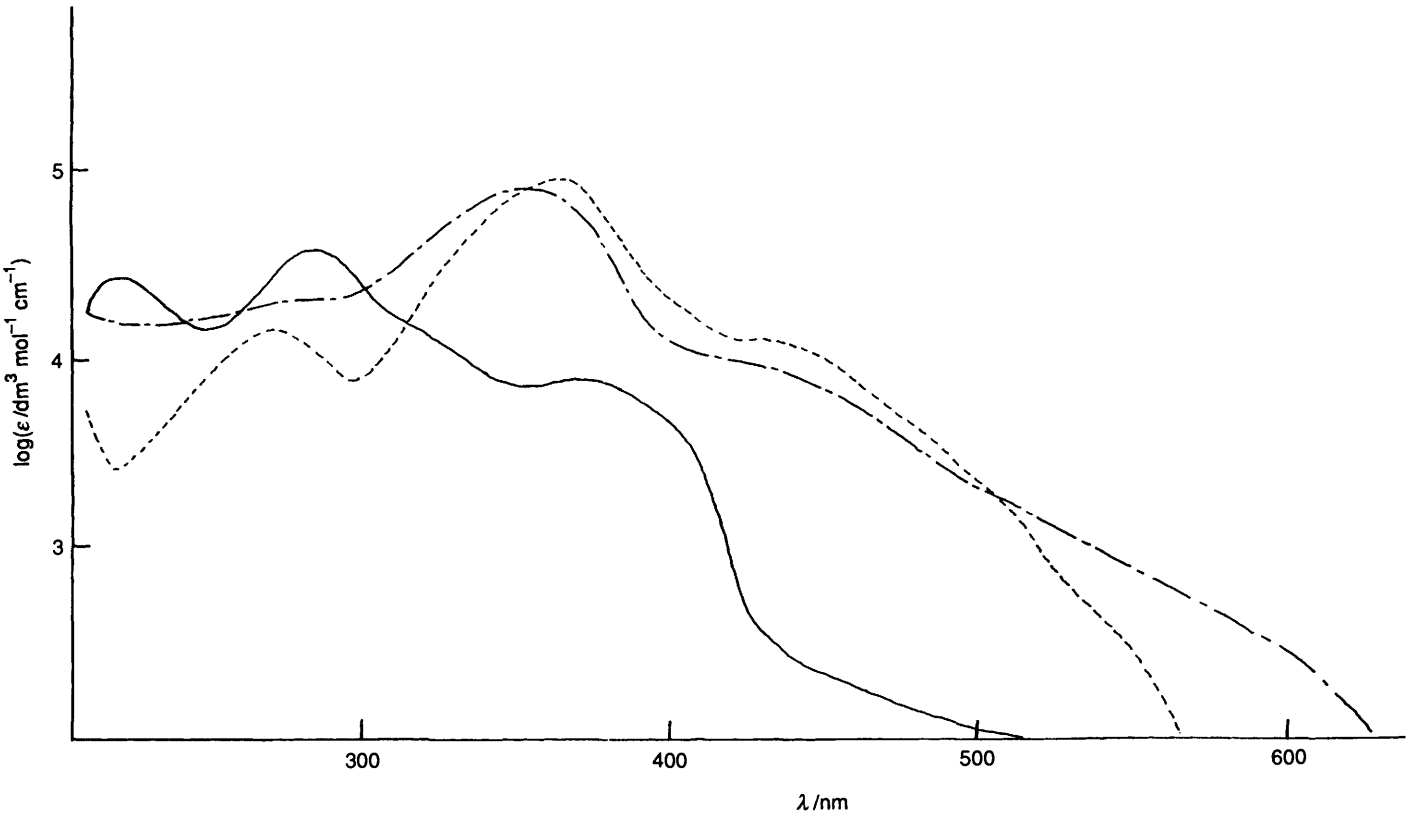
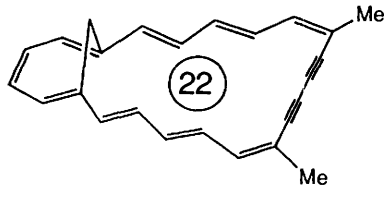


Fig. 3 Electronic absorption spectra of [22]annulene **13** (– – – –), aza[22]annulene **14** (— · — · —) and diaza[22]annulene **8** (——) in THF



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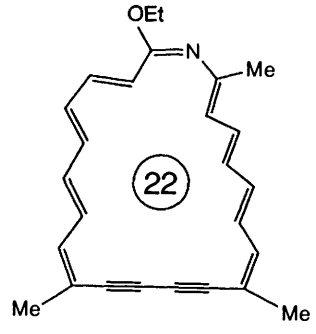


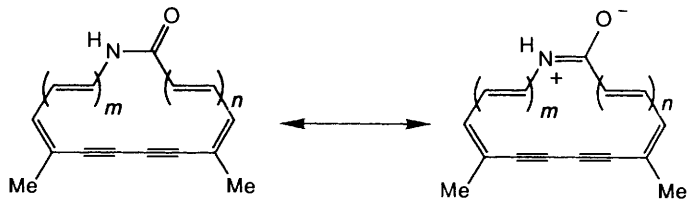
14

range of temperature and are not presented. The methylene bridge signal of the closely related carbocyclic [22]annulene **13** remained singlet down to −60 °C,[3b] and the activation energy for this process was estimated to be less than 12 kcal mol^{-1}. Thus, this fact might support the interpretation, described above, that the molecular skeleton of the diaza[22]annulene **8** is forced to be non-planar due to the presence of the ethoxy groups.

Elelectronic Spectra.—The electronic absorption spectrum, measured in THF, of the tetradehydromethanodiaza[22]-annulene **8** is illustrated in Fig. 3, together with those of the closely related compounds, the tetradehydromethano[22]annulene **13**[3b] and the tetradehydroaza[22]annulene **14**[2c] both of which have been confirmed to show diatropicity.

It is noted that these spectra are similar in shape to each other and show the three distinct absorption bands characteristic of $(4n + 2)\pi$-electron systems, as has been recognized in the spectra of carbocyclic $(4n + 2)\pi$-annulenes and dehydroannulenes.[12] This feature might be reasonably attributed to the fact that all of these compounds have 22π-electron perimeters. However, as is seen clearly from Fig. 3, all the bands of the diaza[22]annulene **8** are in shorter wavelengths by *ca.* 80 nm than the corresponding bands of the [22]annulene **13** and the aza[22]annulene **14**, indicating that **8** is atropic, while **13** and **14** are diatropic, which is consistent with the conclusion from ^{1}H NMR spectroscopy.

The series of the lactams **15**, the precursors of the aza-annulenes **2**, have been reported to show tropicity.[2c] In accordance with this result, their main (strongest) absorption maxima showed the same alternation in the wavelengths of the main absorption maxima between $(4n + 2)$ and $(4n)\pi$-systems, as has already been demonstrated for monocyclic annulenes and dehydroannulenes.[13] Here we can compare the main absorption maxima between the dilactams **10** ([26]-: 290 nm) and **12** ([28]-: 338 nm). Thus, it is evident that the main absorption maximum of $(4n + 2)\pi$-dilactam **10** is not at a longer wavelength than that of $(4n)\pi$-dilactam **12**, indicating that both of the dilactams **10** and **12** as well as the dilactam **7** are atropic, as revealed by ^{1}H NMR spectroscopy (see Experimental section).



15
m = 1–3
n = 1–3

Experimental

M.p.s were determined on a hot-stage apparatus and are uncorrected. IR spectra were taken with a Hitachi 260-50 spectrophotometer as KBr discs and were calibrated against polystyrene; only significant maxima are described. Electronic spectra were measured in tetrahydrofuran (THF) solution and run with a Hitachi 220A spectrophotometer. Mass spectra were recorded with a JEOL JMS-D 300 spectrometer operating at 75 eV using a direct-inlet system. ^{1}H NMR spectra at ambient temperature were recorded with a JEOL FX-90Q (90 MHz), GX-270 (270 MHz) or a Bruker AM-500 (500 MHz) spectrometer at 89.60, 270.16 or 500.14 MHz, respectively, $SiMe_4$ being used as an internal standard. *J*-Values are given in Hz. Assignments were clarified by the use of decoupling experiments where necessary. Variable-temperature ^{1}H NMR measurements were made on an AM-500 spectrometer and the temperatures were calibrated with an ethylene glycol sample. ^{13}C NMR spectra were recorded with a Bruker AM-500 spectrometer at 125.76 MHz, $SiMe_4$ being used as an internal standard. Chemical shifts of the protonated carbons were unambiguously assigned on the C–H COSY spectrum. Merck alumina (activity II–III) or Daiso Gel 1001 W was used for column chromatography.

Progress of all reactions was followed by TLC using Merck pre-coated silica gel. Dichloromethane was distilled over calcium hydride before use. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl under nitrogen atmosphere before use. Organic extracts with dichloromethane or chloroform were washed with saturated aq. sodium chloride and dried over anhydrous calcium chloride prior to removal of the solvent. Solvents were evaporated under water-pump pressure.

12,17-*Dimethyl*-2,7-*methanocycloicosa*-2,4,6,9,11,17,19-*heptaene*-13,15-*diyne*-1,8-*dione Dioxime* **6**.—To a stirred solution of the tetradehydromethano[20]annulenedione **3**[5] (2.50 g, 7.66 mmol) in methanol (20 cm^3) and THF (460 cm^3) was added in one portion a solution of hydroxylamine hydrochloride (20.0 g, 288 mmol) in water (40 cm^3) at room temperature and the mixture was stirred for 1 day at 48 °C. Then a further quantity of hydroxylamine hydrochloride (40 g) in water (40 cm^3) was added to the mixture and stirring was continued for a further 2 days at 48 °C. Then the mixture was poured into water and the aqueous layer was extracted with chloroform. The combined organic layers were washed with aq. sodium hydrogen carbonate, dried and concentrated. The residue was chromatographed on alumina (3.8 × 3.5 cm). The fractions eluted with 10–20% ethanol in chloroform afforded the *dioxime* **6** (2.39 g, 88%) as yellow needles, m.p. 168–170 °C (decomp.) (from hexane–acetone); *m*/*z* 356 (M^+, 17%) and 77 (100) (Found: M^+, 356.4); λ_{max}/nm 243 (ε/dm^3 mol^{-1} cm^{-1} 37 000), 274 (30 700), 324 (26 800) and 408sh (4600); ν_{max}/cm^{-1} 3200 (OH), 2190 (C≡C), 1605 (N=C), 980 and 960 [(*E*)-HC=CH]; δ_H[90 MHz; $(CD_3)_2SO$] 11.57 (2 H, s, OH), 6.94–6.44 (10 H, m, olefinic and 7-membered-ring H), 4.49 (1 H, d, *J* 12, H^b), 2.08 [6 H, s, $(CH_3)_2CO$], 1.85 (6 H, s, CH_3) and 1.64 (1 H, d, *J* 12, H^a) [Found: C, 75.4; H, 6.4; N, 6.5. $C_{23}H_{20}N_2O_2$·$(CH_3)_2CO$ requires C, 75.4; H, 6.3; N, 6.8%].

13,18-*Dimethyl*-2,7-*methano*-1,8-*diazacyclodocosa*-2,4,6,10,-12,18,20-*heptaene*-14,16-*diyne*-9,22-*dione* **7**.—A solution of phosphorus pentachloride (600 mg, 2.88 mmol) in dry THF (32 cm^3) was added dropwise to a stirred solution of dioxime **6** (109 mg, 0.31 mmol) in dry THF (20 cm^3) during 30 min at −12 °C, and stirring was continued for 5 h at room temperature. Then the solution was poured into aq. sodium hydrogen carbonate and the mixture was extracted with chloroform. The combined extracts were washed with brine and dried. The residue obtained after removal of the solvent was chromatographed on alumina (3.2 × 6 cm). The fractions eluted with 10% acetone in benzene afforded the *dilactam* **7** (39 mg, 28%) as red cubes, m.p. 264–265 °C (decomp.) (from hexane–acetone) (Found: M^+, 356.1521. $C_{23}H_{20}N_2O_2$ requires *M*, 356.1522); λ_{max}/nm 290 (ε 38 700), 342 (17 100) and 406sh (6900); ν_{max}/cm^{-1} 3260 (NH), 2180 (C≡C), 1650 (C=O), 985 and 970 [(*E*)-HC=CH]; δ_H(270 MHz; $CDCl_3$) 7.92 (2 H, s, NH), 7.29 (2 H, dd, *J* 15.6 and 11.0, H^B), 6.75 (2 H, m, H^2), 6.66 (2 H, d, *J* 11.0, H^A), 6.49 (2 H, m, H^1), 6.16 (2 H, d, *J* 15.6, H^C), 2.66 (2 H, s, CH_2), 2.17 [6 H, s, $(CH_3)_2CO$] and 2.04 (6 H, s, CH_3) [Found: C, 75.8; H, 6.1; N, 6.2. $C_{23}H_{20}N_2O_2$·$(CH_3)_2CO$ requires C, 75.4; H, 6.3; N, 6.8%].

9,22-*Diethoxy*-13,18-*dimethyl*-2,7-*methano*-1,8-*diazacyclodocosa*-2,4,6,8,10,12,18,20,22-*nonaene*-14,16-*diyne* **8**.—To a stirred solution of the dilactam **7** (137 mg, 0.38 mmol) in dry dichloromethane (10 cm^3) was added dropwise a solution of triethyloxonium tetrafluoroborate (1.90 g, 10.0 mmol) in dry dichloromethane (5 cm^3) during 5 min at room temperature under argon. After stirring for a further 21 h at room temperature, further portions of the oxonium salt (each 1.10 g/3 cm^3 of CH_2Cl_2) were added every 25 h. After stirring for a total of 3 days, the reaction was quenched by addition of 50% aqueous potassium carbonate (20 cm^3) during 10 min at 3 °C. Then the mixture was poured into water and extracted with dichloromethane. The combined extracts were evaporated and the residue was chromatographed on alumina (3.2 × 7 cm). The initial fractions eluted with benzene afforded the *diaza*[22]*annulene* **8** (15 mg, 9.0%) as brown needles, m.p. 149–150 °C (from hexane–benzene); *m*/*z* 412 (M^+, 100%) (M, 412.5); λ_{max}/nm 222 (ε 26 700), 285 (37 100), 372 (7700) and 397sh (6300) and see Fig. 3; ν_{max}/cm^{-1} 2170 (C≡C), 1635 (C=N), 1300, 1220, 1030 (–O–) and 960 [(*E*)-HC=CH]; δ_H(500 MHz; $CDCl_3$, 26 °C) 7.03 (2 H, dd, *J* 16.2 and 10.8, H^B), 6.44 (2 H, d, *J* 10.8, H^A), 6.14 (2 H, m, H^2), 5.84 (2 H, d, *J* 16.2, H^C), 5.29 (2 H, m, H^1), 4.19 (2 H, dq, *J* 10.9 and 7.1, CH_2CH_3), 4.12 (2 H, dq, *J* 10.9 and 7.1, CH_2CH_3), 3.21 (1 H, d, *J* 12.8, H^b), 2.88 (1 H, d, *J* 12.8, H^a), 1.95 (6 H, s, CH_3) and 1.29 (6 H, t, *J* 7.1, CH_2CH_3) and see Figs. 1(*a*) and 2; δ_H[500 MHz; $CDCl_3$–CF_3CO_2D (~2:1), 26 °C] 7.29 (2 H, m, H^1), 7.19 (2 H, dd, *J* 15.2 and 11.2, H^B), 7.00 (2 H, d, *J* 11.2, H^A), 6.94 (2 H, m, H^2), 6.58 (2 H, d, *J* 15.2, H^C), 4.75 (4 H, q, *J* 7.1, CH_2CH_3), 2.60 (2 H, s, CH_2), 2.27 (6 H, s, CH_3) and 1.63 (6 H, t, *J* 7.1, CH_2CH_3) and see Fig. 1(*b*); δ_C(125 MHz; $CDCl_3$) 158.3 (q, C-9 and C-22), 141.0 (q, C-2 and C-7), 138.3 (t, C-12 and C-19: C–H^A), 137.0 (t, C-11 and C-20: C–H^B), 124.7 (t, C-4 and C-5: C–H^2), 123.8 (q, C-13 and C-18), 120.0 (t, C-10

and C-21: C–H^C), 107.7 (t, C-3 and C-6: C–H^1), 82.8 and 81.2 (q, C≡C), 61.8 (s, CH_2CH_3), 43.8 (s, CH_2), 22.3 (p, CH_3) and 14.2 (CH_2CH_3); δ_C[125 MHz, $CDCl_3$–CF_3CO_2D (~2:1), 26 °C] 171.6 (q, C-9 and C-22), 148.6 (t, C-11 and C-20: C–H^B), 137.2 (t, C-12 and C-19: C–H^A), 137.1 (q, C-2 and C-7), 130.3 (t, C-4 and C-5: C–H^2), 122.7 (q, C-13 and C-18), 122.2 (t, C-3 and C-6: C–H^1), 111.6 (t, C-10 and C-21: C–H^C), 85.1 and 84.2 (q, C≡C), 73.0 (s, CH_2CH_3), 33.2 (s, CH_2), 23.0 (p, CH_3) and 14.1 (p, CH_2CH_3) (Found: C, 78.8; H, 6.7; N, 6.5. $C_{27}H_{28}N_2O_2$ requires C, 78.6; H, 6.8; N, 6.8%).

The latter fractions eluted with 10% acetone in benzene afforded the recovered dilactam **7** (103 mg).

16,21-*Dimethyl*-4,9-*methanocyclotetracosa*-2,4,6,8,10,13,15,-21,23-*nonaene*-17,19-*diyne*-1,12-*dione Dioxime* **9**.—To a stirred solution of the tetradehydromethano[24]annulenedione **4**[5] (1.10 g, 2.91 mmol) in methanol (30 cm^3) and THF (50 cm^3) was added in one portion a solution of hydroxylamine hydrochloride (12.1 g, 175 mmol) in water (20 cm^3) and the mixture was stirred for 4 h at 52 °C. Then the mixture was worked up as for the isolation of the compound **6**. The product was chromatographed on alumina (3.2 × 4.0 cm). The fractions eluted with 40–60% ethanol in chloroform afforded the *dioxime* **9** (623 mg, 51%) as yellow microcrystals, m.p. 143–145 °C (decomp.) (from hexane–chloroform); *m/z* 408 (M^+, 6%) and 51 (100) (Found: M^+, 408.4); λ_{max}/nm 230sh (ε 19 500), 270 (64 500), 285 (60 500), 358 (29 200) and 405sh (9330); ν_{max}/cm^{-1} 3180 (OH), 2180 (C≡C), 1600 (N=C) and 970 [(*E*)-HC=CH]; δ_H[90 MHz; $(CD_3)_2SO$] 11.58, 11.48, 11.45 (1:1:2) (2 H, s, OH), 6.93–6.42 (14 H, m, olefinic and 7-membered-ring H), 2.69 (2 H, br s, CH_2) and 1.91 (6 H, s, CH_3) (Found: C, 79.6; H, 6.0; N, 6.6. $C_{27}H_{24}N_2O_2$ requires C, 79.4; H, 5.9; N, 6.9%).

18,23-*Dimethyl*-5,10-*methano*-1,13-*diazacyclohexacosa*-3,5,-7,9,11,15,17,23,25-*nonaene*-19,21-*diyne*-2,14-*dione* **10**.—A solution of phosphorus pentachloride (1.17 g, 5.62 mmol) in dry THF (40 cm^3) was added dropwise to a stirred solution of the dioxime **9** (1.15 g, 2.82 mmol) in dry THF (360 cm^3) during 1 h at −18 to −15 °C. After stirring for 3 h at the same temperature, the mixture was stirred for a further 1.5 h at room temperature. Then the mixture was worked up as for the isolation of compound **7**. The product was chromatographed on Daiso gel (3.6 × 8.0 cm). The fractions eluted with benzene–dichloromethane (2:3) afforded the dilactam **10** (766 mg, 67%) as orange needles, m.p. 233–235 °C (decomp.) (from acetone–chloroform); *m/z* 408 (M^+, 85%) and 207 (100) (Found: M^+, 408.4); λ_{max}/nm 280sh (ε 45 700), 290 (46 300), 318sh (41 400) and 360 (38 600); ν_{max}/cm^{-1} 3250 (NH), 2180 (C≡C), 1660, 1620, 1600 (C=O, C=C) and 960 [(*E*)-HC=CH]; δ_H[500 MHz; $CDCl_3$–$(CD_3)_2SO$ (5:1)] 10.66 (1 H, d, *J* 10.0, NH^1), 8.41 (1 H, d, *J* 11.5, NH^2), 7.59 (1 H, d, *J* 15.4, $H^{E'}$), 7.50 (1 H, dd, *J* 15.2 and 11.5, H^B), 7.47 (1 H, dd, *J* 13.8 and 11.5, $H^{C'}$), 7.22 (1 H, dd, *J* 14.5 and 10.0, H^D), 6.85 (1 H, dd, *J* 10.5 and 6.2, H^2), 6.81 (1 H, d, *J* 11.5, H^A), 6.73 (1 H, d, *J* 11.2, $H^{A'}$), 6.73–6.70 (2 H, m, H^3 and H^4), 6.37 (1 H, d, *J* 15.2, H^C), 6.35 (1 H, d, *J* 6.2, H^1), 6.27 (1 H, d, *J* 14.5, H^E), 6.13 (1 H, d, *J* 15.4, $H^{D'}$), 6.06 (1 H, dd, *J* 13.8 and 11.2, $H^{B'}$), 3.40 (2 H, s, CH_2), 2.04 (3 H, s, Me^b) and 1.94 (3 H, s, Me^a) (Found: C, 79.4; H, 5.95; N, 6.6. $C_{27}H_{24}N_2O_2$ requires C, 79.4; H, 5.9; N, 6.9%).

18,23-*Dimethyl*-6,11-*methanocyclohexacosa*-2,4,6,8,10,12,15,17,23,25-*decaene*-19,21-*diyne*-1,14-*dione Dioxime* **11**.—To a stirred solution of the tetradehydromethano[26]annulenedione **5**[5] (1.42 g, 3.52 mmol) in methanol (40 cm^3) and THF (200 cm^3) was added in one portion a solution of hydroxylamine hydrochloride (4.60 g, 66 mmol) in water (8 cm^3) at room temperature. The mixture was stirred for 1 h at 52 °C, after which a further quantity of hydroxylamine hydrochloride (7.50 g, 107 mmol) in water (5 cm^3) was added and stirring was continued for a further 5 h at 52 °C. Then the mixture was worked up as for the isolation of the compound **6**. The product was chromatographed on alumina (3.8 × 2 cm). The fractions eluted with ethanol–dichloromethane (1:1) afforded the dioxime **11** (1.16 g, 77%) as yellow microcrystals, m.p. 164–165 °C (decomp.) (from hexane–chloroform); *m/z* 432 (M^+, 10%) and 83 (100) (Found: M^+, 434.5); λ_{max}/nm 261 (ε 50 300), 298 (82 000), 365 (29 000) and 401sh (17 800); ν_{max}/cm^{-1} 3185 (OH), 2180 (C≡C), 1600 (N=C) and 960 [(*E*)-HC=CH]; δ_H[90 MHz; $(CD_3)_2SO$] 11.40 (2 H, br s, OH), 7.08–6.22 (16 H, m, olefinic and 7-membered-ring H), 2.67 (2 H, s, CH_2) and 1.93 (6 H, s, CH_3) (Found: C, 80.1; H, 6.0; N, 6.2. $C_{29}H_{26}N_2O_2$ requires C, 80.2; H, 6.0; N, 6.45%).

20,25-*Dimethyl*-7,12-*methano*-1,15-*diazacyclooctacosa*-3,5,7,-9,11,13,17,19,25,27-*decaene*-21,23-*diyne*-2,16-*dione* **12**.—A solution of phosphorus pentachloride (220 mg, 1.12 mmol) in dry THF (10 cm^3) was added dropwise to a stirred solution of dioxime **11** (406 mg, 0.93 mmol) in dry THF (60 cm^3) during 10 min at −12 °C and the solution was stirred for 4 h at −4 °C. Then the mixture was worked up as for the isolation of compound **7**. The product was chromatographed on alumina (3.2 × 7 cm). The fractions eluted with chloroform afforded the dilactam **12** (73 mg, 18%) as red needles, m.p. 238–240 °C (decomp.) (from methanol); *m/z* 434 (M^+, 100%) (Found: M^+, 434.5); λ_{max}/nm 275 (ε 22 700) and 338 (67 400); ν_{max}/cm^{-1} 3240 (NH), 2180 (C≡C), 1660, 1620 (C=O, C=C), 990 and 950 [(*E*)-HC=CH]; δ_H[500 MHz; $CDCl_3$–$(CD_3)_2SO$] 8.90 (1 H, br d, *J* 11.0, NH^2), 8.13 (1 H, dd, *J* 14.8 and 11.4, H^B), 7.89 (1 H, dd, *J* 14.3 and 11.0, H^D), 7.22 (2 H, m, $H^{E'}$ and $H^{F'}$), 7.15 (1 H, d, *J* 11.0, NH^1), 7.06 (1 H, dd, *J* 13.6 and 11.0, $H^{C'}$), 6.97 (1 H, dd, *J* 13.6 and 11.4, $H^{B'}$), 6.76 (1 H, m, $H^{D'}$), 6.57 (1 H, m, $H^{G'}$), 6.54 (2 H, m, H^2 and H^3), 6.50 (1 H, d, *J* 11.4, $H^{A'}$), 6.36 (1 H, d, *J* 11.4, H^A), 6.33 (1 H, m, H^4), 6.12 (1 H, m, H^1), 5.94 (1 H, d, *J* 14.3, H^E), 5.81 (1 H, d, *J* 14.8, H^C), 2.87 (2 H, br s, CH_2), 1.98 (3 H, s, Me^b) and 1.83 (3 H, s, Me^a) (Found: C, 77.1; H, 6.6; N, 5.95. $C_{29}H_{26}N_2O_2$·CH_3OH requires C, 77.2; H, 6.5; N, 6.0%).

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