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The Synthesis of 12-Ethoxy-4,9-methanoaza[12]annulene, a 12π-Electron Vinylogue of Pyridine

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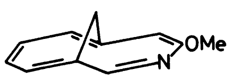
Synopsis. The title aza[12]annulene has been synthesized by Beckmann rearrangement of the oxime from the methano[11]annulenone, followed by alkylation of the resulting lactam. Examination of the ^{1}H NMR spectrum indicates that the aza[12]annulene is slightly paratropic.

Several diatropic methano-bridged aza[10]annulene derivatives (e.g. 1) were prepared previously.[1] Also, the bisdehydroaza[14]annulene **2** as well as its higher analogs was prepared and proved to sustain ring current.[2] Of these azaannulene family of pyridine type, the 12π-analogue is unknown. We have now synthesized the title aza[12]annulene derivative by the reaction sequence used to prepare **2**,[2] in order to discover whether the same alternation of tropicity between $(4n+2)\pi$- and $(4n)\pi$-electron systems occurs in the azaannulene series as has already been demonstrated in the carbocyclic annulene series.[3] This synthetic objective has been verified experimentally.



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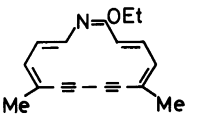
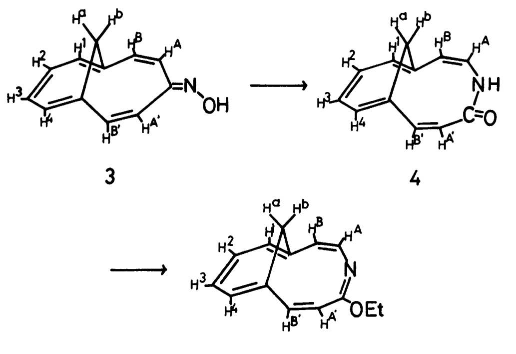


2

Although several attempts of rearrangement reactions with phosphorus pentachloride were fruitless, the oxime **3**, obtained from 4,9-methano[11]annulenone,[4] when heated with *p*-toluenesulfonyl chloride in pyridine,[5] gave Beckmann rearrangement product, the lactam **4**, in 26% yield. The alkylation of **4** with triethyloxonium tetrafluoroborate gave the desired aza[12]annulene **5** in 10% yield. The substance was unstable to diffused light and air.



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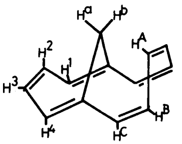

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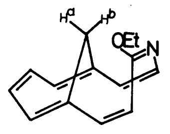

5a

The ^{1}H NMR chemical shifts of **5** are listed in Table 1, together with those of the closely related methano[12]annulene **6**. Table 1 shows that **5** is slightly paratropic as espected for a 12π-electron system, since the annulene outer protons resonate at relatively high field and the H^b proton of the bridged methylene group do at relatively low field, as compared with the usual olefinic and methylene protons. This also suggests that **5** exists in syn-form **5a** as similarly to the case of **6**.[6] However, comparison of the chemical shifts of the corresponding protons between **5** and **6** shows that the paratropicity of **5** is smaller than that of **6**, revealing that an incorporation of a nitrogen atom and a substitution of ethoxyl group into and upon the molecular perimeter of **6** hinder conjugation of π-electrons to some extent.

Variable-temperature ^{1}H NMR spectra of the aza[12]annulene **5** were run over the range from −60 to 60 °C, and the results show all the spectra to be essentially temperature-independent, ruling out a change in the conformation **5a** between these temperatures.

Experimental

All melting points are uncorrected. IR spectra were measured on Hitachi 260-50 spectrophotometer as KBr disk; only significant maxima are reported. UV spectra were taken on Hitachi 220A spectrophotometer and were recorded in nm, in tetrahydrofuran solution. ε-Values are given in parentheses, the shoulders being denoted by sh. Mass spectra were measured with JEOL JMS-200 spectrometer at 75 eV using a direct inlet system. ^{1}H NMR spectra were taken on JEOL FX-90Q (90 MHz) or GX-270 (270 MHz) spectrometer, and refer to solutions in $CDCl_3$, unless otherwise stated, in δ-values with TMS as an internal standard. The coupling constants (J) are given in Hz. Alumina (II—III) was used for column chromatography. Preparative TLC was carried out on 20×20 cm silica-gel plates (Merck, 0.5 mm thick). Dichloromethane was distilled over calcium hydride before use. Organic extracts were dried over anhyd sodium sulfate prior to solvent removal.

Table 1. ^{1}H NMR Chemical Shifts of Methanoaza[12]annulene **5** (270 MHz) and Methano-[12]annulene **6** (90 MHz) in $CDCl_3$ (δ Value: Internal Standard TMS)

Compd	H^2	H^3	H^4	H^1	H$^{B'}$	H$^{A'}$	H^C	H^B	H^A	H^b	H^a	-C$\underline{H}_2$CH$_3$	-CH$_2$C$\underline{H}_3$
5	6.56	6.41	6.13	5.97	6.41	5.09		—6.40—		5.39	1.62	4.35—4.05	1.36
6	6.28—6.22		5.86—5.77				5.59———5.52			7.10	2.35		

1-Hydroxyimino-4,9-methanocycloundeca-2,4,6,8,10-pentaene (3). To a stirred soln of the 4,9-methano[11]-annulenone[4] (586 mg, 3.44 mmol) in methanol (40 ml) and THF (10 ml) was added a soln of hydroxylamine hydrochloride (4.8 g) in water (10 ml) at 38 °C in one portion. After stirring for further 10 h at the same temp, further quantities of hydroxylamine hydrochloride (each 5.0 g in water (10 ml)) were added after every 40 h. After stirring for a total of 5 d at 38 °C, the soln was poured into water. The precipitates formed were filtered off under suction, giving **3** (444 mg, 70%). Recrystallization from chloroform afforded orange needles: Mp 196—197 °C; MS *m/z* 185, (M^+, 96%) and 141 100); mol wt 185.2; IR 3140 (OH), 1610 (C=N), and 680 cm^{-1} (cis C=C); UV λ_{max} 213 sh (9710), 229 (14400), 280 (36700), and 341 nm (3220); ^1H NMR (90 MHz, DMSO-d_6) δ=11.31 (s, 1H, OH, exchangeable with D_2O), 7.03—6.96 (m, 2H, H^2, H^3), 6.89 (d, 12, 1H, H^B), 6.71 (d, 12, 1H, $H^{B'}$), 6.69—6.59 (m, 2H, H^1, H^4), 6.09 (d, 12, 1H, $H^{A'}$), 5.86 (d, 12, 1H, H^A), 6.84 (d, 11, 1H, H^b), and 0.54 (d, 11, 1H, H^a).

Found: C, 77.89; H, 5.93; N, 7.40%. Calcd for $C_{12}H_{11}NO$: C, 77.81; H, 5.99; N, 7.56%.

5,10-Methanoazacyclododeca-3,5,7,9,11-pentaen-2-one (4). A soln of *p*-toluenesulfonyl chloride (1.75 g, 9.20 mmol) in pyridine (10 ml) was added to a stirred soln of the oxime **3** (340 mg, 1.84 mmol) in pyridine (50 ml). After stirring for 6 h at 90 °C, further quantities (1.5 g) of the chloride were added and stirring was continued for further 6 h at 90 °C. Then the mixture was poured onto water and extracted with benzene. The extracts were washed with 2M-hydrochloric acid (1 M=1 mol dm^{-3}), aq sodium hydrogencarbonate soln, and aq sodium chloride soln, and dried. The dark red semisolid obtained after solvent removal was chromatographed on alumina (4.3×8 cm). The fractions eluted with dichloromethane afforded the lactam **4** (87 mg, 26%). Recrystallization from hexane-benzene afforded yellow needles: Mp 146—147 °C; MS *m/z* 185 (M^+, 72%) and 156 (100); mol wt 185.2; IR 3140 (NH), 1640, and 1605 cm^{-1} (C=O, C=C); UV λ_{max} 249 (25300) and 344 nm (2300); ^1H NMR (270 MHz) δ=6.89 (d, 11.7, 1H, $H^{B'}$), 6.74—6.10 (m, 7H, H^1, H^2, H^3, H^4, H^A, H^B, NH), 5.98 (d, 11.7, 1H, $H^{A'}$), 3.08 (d, 13.5, 1H, H^b), and 2.18 (d, 13.5, 1H, H^a).

Found: C, 78.07; H, 6.02; N, 7.80%. Calcd for $C_{12}H_{11}NO$: C, 77.81; H, 5.99; N, 7.56%.

The following fractions eluted with 10% ethanol in dichloromethane gave the recovered oxime **3** (107 mg).

12-Ethoxy-4,9-methanoaza[12]annulene (5). To a stirred soln of the lactam **4** (50 mg, 0.27 mmol) in dry dichloromethane (14 ml) was added dropwise a soln of triethyloxonium tetrafluoroborate (1.54 g, 8.10 mmol) in dry dichloromethane (14 ml) during 40 min at room temp. After stirring for 5 h at room temp, the soln was cooled in an ice-bath and aq. 50% potassium carbonate soln (8 ml) was cautiously added. Then the mixture was poured into water and extracted with dichloromethane. The residue after solvent removal was chromatographed on alumina (4.2×8.5 cm). The fractions eluted with hexane gave a semisolid, which was further purified by preparative plate chromatography (dichloromethane-hexane (1 : 1) as eluent). The fast moving, yellow band gave the azaannulene **5** (6.0 mg, 10%). Recrystallization from hexane-benzene afforded yellow needles: Mp 67—68 °C; IR 1200 1120, and 1070 cm^{-1} (-O-); UV λ_{max} (ε) 252 (41900) and 310 nm sh (18600); ^1H NMR (270 MHz) δ=6.56 (dd, 10.5, 5.6, 1H, H^2), 6.41 (dd, 10.5, 5.6, 1H, H^3), 6.41 (d, 10, 1H, $H^{B'}$), 6.13 (d, 5.6, 1H, H^4), 6.04 (s, 2H, H^A, H^B), 5.97 (d, 5.6, 1H, H^1), 5.39 (d, 12.1, 1H, H^b), 5.09 (d, 10, 1H, $H^{A'}$), 4.35—4.23 (m, 1H, $-C\underline{H}_2CH_3$), 4.17—4.05 (m, 1H, $-C\underline{H}_2CH_3$), 1.62 (d, 12.1, 1H, H^a), and 1.36 (t, 7, 3H, $-CH_2C\underline{H}_3$).

HRMS: Found: *m/z* 213.1120. Calcd for $C_{14}H_{15}NO$: M, 213.1151.

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References

1) M. Schätter-Ridder, A. Wagner, M. Schwamborn, E. Schreiner, F. Devrout, and E. Vogel, *Angew. Chem.*, **90**, 894 (1978); H. J. Golz, J. W. Muchowski, and M. L. Maddox, *ibid.*, **90**, 896 (1978); W. J. Lipa, H. J. Crawford, P. C. Radlick, and G. K. Helmkamp, *J. Org. Chem.*, **43**, 3813 (1979).

2) J. Ojima, T. Nakada, E. Ejiri, and M. Nakamura, *J. Chem. Soc., Perkin Trans. 1*, **1986**, 933.

3) For reviews, a) F. Sondheimer, *Acc. Chem. Res.*, **5**, 81 (1972); b) M. Nakagawa, *Pure Appl. Chem.*, **44**, 885 (1975).

4) E. Vogel, "Topics in Nonbenzenoid Aromatic Chemistry," Hirokawa, Tokyo (1977), Vol. 2, pp. 243—281.

5) W. D. Burrow and R. H. Eastman, *J. Am. Chem. Soc.*, **79**, 3756 (1957).

6) E. Vogel, M. Mann, Y. Sakata, K. Müllen, and J. M. F. Oth, *Angew. Chem.*, **86**, 231 (1974); K. Yamamoto, S. Kuroda, Y. Nozawa, S. Fujita, and J. Ojima, *J. Chem. Soc., Chem. Commun.*, **1987**, 199.