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Systematic Series of Azacycl[3.3.3]azines of Varying Nitrogen Content: Nitrogen-15 Magnetic Resonance Spectra

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ABSTRACT

Nitrogen-15 NMR spectra were obtained for a systematic series of azacycl[3.3.3]azines: 1,3,4,6,7,9-hexaaza-,1,3,4,6,7-pentaaza-,1,3,4,6-tetraaza-, 1,3,4,6,8-pentaaza-, and 1,3,6-triazacycl[3.3.3]azine. The magnetic resonance data were compared with other physical and spectroscopic properties available for the series relative to the diminishing number of peripheral nitrogens in alternating positions. The properties of 1,3,4,6,8-pentaazacycl[3.3.3]azine, which has a peripheral 1,4-diazine-type nitrogen, are distinct from those of the rest of the series.

INTRODUCTION

High-resolution nitrogen-15 nuclear magnetic resonance spectroscopy [1] has provided detailed information on the shielding of nitrogen atoms in a series of cyclic azines and azolopyridines [2]. The effects of interaction between nitrogen atoms and of additional fused aromatic rings in mono- and polyazines were examined systematically. A 1,2-arrangement of nitrogen atoms in a diazine results in a large downfield shift of the ^{15}N resonance relative to that in a monoazine; a 1,4-arrangement results in a smaller downfield shift; and, by contrast, a 1,3-arrangement produces a large upfield shift [2]. Ring systems containing a bridgehead nitrogen atom between two or more six-membered rings have not yet been similarly examined.

RESULTS AND DISCUSSION

We have now investigated the ^{15}N NMR spectra of a systematic series of azacycl[3.3.3]azines, **1–5**. The term cyclazine denotes a fused conjugated ring system held planar by three covalent bonds to an internal nitrogen atom [3, 4], as in **1–5**, also **6** and **7**. 1,3,4,6,7,9-Hexaazacycl[3.3.3]azine [5] (**1**, also called tri-*s*-triazine) is the ultimate member of an alternating C,N azacycl[3.3.3]azine series in which cycl[3.3.3]azine [6], devoid of peripheral nitrogens, is the basic nucleus. There is considerable theoretical interest in the azacycl[3.3.3]azine series because of the 12π-electron periphery and the question of the involvement of the *n* electrons on the central N.

Systematic trends have already been noted in the comparative physical properties of a series such as **1**, **2**, **3**, **5** or **7**, and **6**, which has a diminishing number of peripheral N's in alternating positions. The colors of the crystalline azacycl[3.3.3]azines range from yellow (**1**) [5] to orange (**2**) [7], lavendar (**3**) [7–9], blue (**5**and **7**) [7, 10–12], and brown (**6**) [6]. The wavelength of the lowest energy transition,

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Dedicated to Professor Ernest Eliel on the occasion of his seventieth birthday.

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S_0–S_1, moves correspondingly from 443 nm (**1**, CH_3CN) [5] to 531 (**2**, CH_3CN) [7], 608 (**3**, CH_3CN) [7], 632(**5**, EtOH) [10], and 1290 (**6**, cyclohexane) [13, 14]. This band shows maximal absorption at 637 nm (CH_3CN) for the only 1,4-diazine-containing member of the series 1,3,4,6,8-pentaazacycl[3.3.3]azine (**4**), which is described as blue [7] or violet [15]. The difference of ~100 nm between the long-wavelength maxima of **4** and its position isomer, 1,3,4,6,7-pentaazacycl[3.3.3]azine (**2**), with all the peripheral nitrogens in alternating positions is noteworthy.

The position of the first absorption band is sensitive to inductive perturbations. Leupin and Wirz [13] provided an equation relating substitution in **6** by inductive acceptors, e.g., N for CH in alternating positions 1,3,4, and so on. Their plot of transition energies of azacycl[3.3.3]azines vs. the Hückel charge-density changes upon excitation agrees well with the documented positions of the first absorption band and has demonstrated [5, 16] predictive value. The photoelectron spectra of the azacycl[3.3.3]azines exhibit a well resolved band that arises from the HOMO. The π_1 ionization potentials decrease as the number of nitrogen atoms in alternating positions decreases in the series [7]: 9.16 eV (**1**), 8.52 (**2**), 7.90 (**3**), 7.36 (**5**), and 7.51 (**7**); and 5.86 (**6**) [17]. The ionization potential for compound **4**, 8.38 eV, is lower than that of its C,N-alternating isomer **2**.

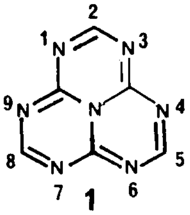
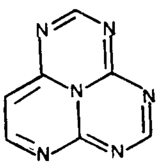
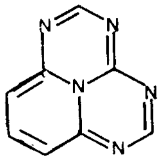
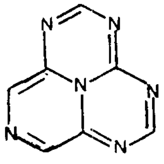
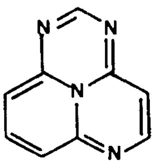
There is a substantial upfield shift in the ^1H NMR spectra for the protons as the C,N-alternating series is traversed. For example, 2-H progresses from δ 8.3 (**1**, $(CD_3)_2SO$) [5] through 7.8 (**2**) [7], 7.2 (**3**) [7], 6.85 (**7**,$CDCl_3$) [12], and 6.50 (**5**, $CDCl_3$) [10, 11] to 3.65 (**6**, $[(CH_3)_3Si]_2O$) [6a]. The 2-H signal for **4**, the isomer of **2**, is at δ 7.39 [15]. The exceptionally high degree of shielding in cycl[3.3.3]azine (**6**) is regarded as evidence of a paramagnetic ring current in the antiaromatic perimeter of 12 π-electrons [6]. A slight upfield shift in the ^{13}C NMR signals for C2 (and C5) was observed in the partial series **1–3**: δ 171 (**1**, $(CD_3)_2SO$), 169 (**2**), 167 (**3**), and 169 (**4**) [7]. The ^{15}N chemical shifts of compounds **1–5** obtained in the present investigation, along with their assignments, are listed in Table 1. The values for the azacycl[3.3.3]azines were obtained at the natural-abundance level in dimethyl sulfoxide over a four day period while the sample was maintained at room temperature.

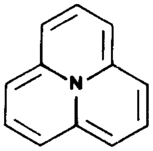
In the series of azacycl[3.3.3]azines **1–5**, a noteworthy trend is observed in the chemical shift for the central nitrogen. The value moves downfield with a decreasing number of nitrogen atoms in the alternating positions of the periphery. The resonance of the central ^{15}N shifts from + 189 ppm for **1** to 181.5 (**2**), 176.6 (**3**), and 172.1 (**5**); all compounds were measured in $(CH_3)_2SO$ and related to 1 M $H^{15}NO_3$ as an external standard. The order is consistent with the diminishing number of 1,3-nitrogen interactions for the series [2b, 18], but the magnitude of the differences in chemical shifts between adjacent members of the series is much less than that observed for mono- and bicyclic azines [2b]. The value of 172.9 for the central N or 1,3,4,6,8-pentaazacycl[3.3.3]azine (**4**) in comparison with that of 181.5 for the central N of the isomeric 1,3,4,6,7-pentaazacycl[3.3.3]azine (**2**) is consistent with the downfield shift expected [2b] for the 1,4-arrangement of nitrogens in the third ring of **4**. The shielding values for the central N, 189–172.1 ppm, are well above that observed for monocyclic *s*-triazine, 98.5[2b], but close to the value reported, 190.1, for indolizine in which the *n* electrons on the nitrogen are part of a 10 π-electron aromatic system [2c].

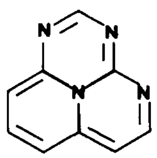
While the protons external to the periphery that supports a paramagnetic ring current are shifted upfield through the series of azacyclazines **1**, **2**, **3**, and **5**, the influence of the ring current on a central nitrogen that is internal to a 12 π-electron ring has not been established. The ring current is expected to modulate the ^{15}N resonance that has been described above to result from the difference in number and position of the nitrogens in the periphery. There are no models available at present that predict the effect of peri-fusion of an additional variant ring, e.g., triazine, pyrimidine, pyridine, pyrazine, upon the first and second rings of **1**, **2**, **3**, and **4**, respectively. It is surprising that, despite the large changes in optical absorption wavelengths for the C,N-alternating series **1**, **2**, **3**, and **5**, there are no corresponding large changes in central ^{15}N chemical shifts, such as are commonly observed for many substances where $n \rightarrow \pi^*$ optical transitions are important [19]. By contrast, the N8 resonance in compound **4**, 13.7, is shifted far downfield from the triazine nitrogens of **1** and the pyrimidine nitrogen of the third ring of **2**. If the N8 resonance is considered in relation to other pyrazines, however, the extent of deshielding is approximately 30 ppm greater than that observed for pyrazines previously studied [2b]. The large second-order paramagnetic effect may result from the mixing into the ground state of an electronic excited state that corresponds to an $n \rightarrow \pi^*$ transition at N8 [19].

As mentioned above, the first transition in the visible range for **4** is at lower energy than for **1**, **2**, or **3** (and is of higher probability) [7]. It had been found earlier [18] that there was almost a linear relationship between ^{14}N shifts and calculated π-charge densities at the nitrogen atoms for the series of pyridazine, pyrazine, pyridine, pyrimidine, triazine, whereas there was no correlation of chemical shifts with $n \rightarrow \pi^*$ transition energies. Calculations of π-charge densities for the series of compounds **1–5** reveal that the π-charge density on N8 is uniquely lower than the charge densities of all other nitrogens throughout the series [20]. The unique deshielding of N8 and its π-charge density are accordingly in qualitative agreement.

TABLE 1 ^{15}N NMR Data for Azacycl[3.3.3]azines

COMPOUND	SOLVENT AND CONCENTRATION(M)	NITROGEN ATOM	NITROGEN SHIELDING δ^{15}N(ppm from 1M H^{15}NO$_3$)
 **1**	DMSO (0.16)	peripheral N central N	138.0 189.0
 **2**	DMSO (0.43)	N7 N6 N3 or N4 N4 or N3 N1 central N	123.6 131.0 138.0 139.8 146.9 181.5
 **3**	DMSO (0.23)	N3,N4 N1,N6 central N	137.6 152.2 176.6
 **4**	DMSO (0.40), + 0.05M Cr(acac)$_3$	N8 N3,N4 N1,N6 central N	13.7 141.6 145.9 172.9
 **5**	DMSO (0.16)	N6 N3 N1 central N	126.5 142.0 161.3 172.1


6


7

The assignment of the chemical shift in the 189–172 ppm range to the central nitrogen throughout the series was straightforward because, in the proton-coupled ^{15}N spectra, the signal in this range showed no ^2J (^{15}N—^{1}H) coupling. We were aided in making the other assignments listed in Table 1 by a combination of factors including the ^2J (^{15}N—^{1}H) couplings in the ^{15}N spectra and the related ^3J (^1H—^1H) couplings in the ^1H spectra of those azacycl[3.3.3]azines with adjacent C—H's. The ^{15}N spectra of **1**, **3**, and **4** were simplified by the inherent symmetry of these structures. In the cases of **3** and **4**, the signals at higher field were assignable to the pairs of peripheral nitrogens located so as to experience the proximity shielding of the hydrogen on the adjacent ring [2b], i.e., N1 and N6. The signals that showed the least variance with changes in the third ring, namely, 138.0, 138.0 and 139.8, 137.6, and 141.6 for azacycl[3.3.3]azines **1**, **2**, **3**, and **4**, respectively, could be assigned to N3 and N4, the pair of nitrogens most distant from the third ring. The decision as to whether the ^{15}N resonance at 161.3 ppm for compound **5** corresponds to N1 or N6 was made on the basis of the difference in the number of 1,3-nitrogen interactions, one for N6 and three for N1, that produce an upfield shift [2]. The assignment is supported by the trend toward higher field for the signals at 138.0, 146.9, 152.2, and 161.3 corresponding to N1 in compounds **1**, **2**, **3**, and **5**, respectively. A missing nitrogen resonance for 1,3,4,6,8-pentaazacycl[3.3.3]azine (**4**) came into view when the spectrum was run in DMSO solution to which 0.05 M Cr(acac)$_3$ had been added. This relaxation reagent might have been added to DMSO solutions of each of the compounds studied, but it did not appear necessary until compound **4** was examined. The resonance at extremely low field, 13.7 ppm upfield from $H^{15}NO_3$, was assigned to the pyrazine nitrogen at N8 on the basis of the known deshielding effect of the 1,4-nitrogen interaction[2b]. There is a small net deshielding effect on the central nitrogen at the other end of the pyrazine third ring that is at least partially balanced by the shielding effect of the four 1,3-nitrogen interactions in the first and second triazine rings, as mentioned earlier.

The nitrogen-15 spectroscopic data support the original argument that Dewar and Trinajstić [21] advanced for cycl[3.3.3]azine (**6**). The azacycl[3.3.3]azines of the series **1–5** are aptly characterized as nitrogen-bridged antiaromatic [12] annulenes. The data are also consistent with the rule of topological charge stabilization of Gimarc [22] that predicts the greatest degree of stabilization when a peripheral methine is substituted by a nitrogen atom at the 1, 3, 4, 6, 7, and 9 positions, resulting in the following sequence of diminishing chemical stability: **1** > **2** > **3** or **4** > **5**.

EXPERIMENTAL

1,3,4,5,7,9-Hexaazacycl[3.3.3]azine (**1**), 1,3,4,6,7-pentaazacycl[3.3.3]azine (**2**), 1,3,4,6-tetraazacycl[3.3.3]azine (**3**), and 1,3,4,6,8-pentaazacycl[3.3.3]azine (**4**) were prepared from the appropriate intermediates by flash vacuum pyrolysis [5a–b, 7]. 1,3,6-Triazacycl[3.3.3]azine (**5**) was prepared as described by Ceder and Andersson [10,11]. The ^{15}N NMR spectrum of **1** was first obtained on a 250-MHz Fourier transform instrument operating at 25.37 MHz, and the ^{15}N NMR spectra of **2–5** were obtained on a Bruker WM-500 MHz spectrometer operating at 50.68 MHz. The spectra were obtained in dimethyl sulfoxide solutions with *N*,*N*-dimethylformamide as an internal standard for **1** and 1 M $H^{15}NO_3$ as an external standard for **2–5**. The reported chemical shifts are in parts per million upfield from the resonance of external $H^{15}NO_3$. The samples were run at about 30 °C using gated proton decoupling or no proton decoupling.

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