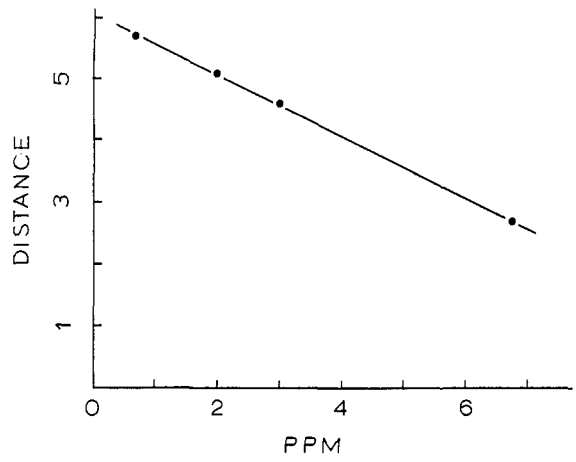

Figure 1. A plot of the ^{7}Li chemical shift of fluorenyllithium in various solvents *vs.* the estimated distance (ångstroms) separating the two ions.

form of solvent-separated ion pairs. It occurred that the ^{7}Li chemical shifts of IV could still be a result of the lithium cation being located above the π cloud of the fluorenyl anion if the distance between the two ions were changing with solvent.[11]

While the number of solvent layers separating the two ions in the solvent-separated ion pair is not known exactly, conductance studies of IV in THF[12] and DME[13] suggest an average of approximately one solvent layer. Furthermore, previous work[1] has shown that when fluorenyllithium is prepared in either THF or DME and the solvent removed by vacuum, at least three THF molecules or one DME molecule remain coordinated to IV. We have estimated the distance by assuming that there is an average of one solvent molecule separating the cation and anion in the solvent-separated ion pair. The distance separating the two ions in the contact ion pair (ether) was taken to be the sum of the ionic radius of the fluorenyl anion (2.1 Å)[12] and the ionic radius of the lithium cation (0.6 Å).[14] For the solvent-separated ion pairs the distance was taken to be that in the contact ion pair plus that of a solvent molecule as estimated from several measurements on Drieding models.[15] The ^{7}Li shifts for fluorenyllithium are plotted *vs.* the distance separating the two ions in Figure 1. An excellent linear relationship is obtained.[16] Therefore, the large range of ^{7}Li chemical shifts observed for IV with solvent is a direct result of solvent affecting the distance separating the fluorenyl and lithium ions. The suggestion that the lithium cation is located above the π cloud of certain planar aromatic anions is a valid description. Caution should be exercised, however, in using ^{7}Li shifts for structural studies since the above data show that a large upfield shift is not a necessary requirement for lithium being located above the π cloud of an aromatic anion. The ^{7}Li shift will also depend upon the type of ion pair formed and more specifically on the distance separating the two ions.

The results (Table I) for the effect of solvent on the ^{7}Li shifts of I–III are somewhat surprising in view of the cation-solvating ability of these solvents. It is well known that the order of cation-solvating ability of these solvents is DME > THF > *p*-dioxane.[17] Since I–III form contact ion pairs[6,7] it might have been expected that their ^{7}Li shifts in DME would have been downfield from that in THF. DME should solvate the ion pair better and, hence, disperse the cationic charge and weaken the coulombic interactions in the ion pair. The results indicate that we are probably observing a medium effect not related to the solvating ability of the solvents but due to some other bulk property of the solvent similar to the results reported[3] for LiBr and $LiClO_4$.

Acknowledgment. Partial support of this work by a grant from the Petroleum Research Foundation administered by the American Chemical Society is gratefully acknowledged.

(11) The shielding experienced by the lithium ion as a result of its being located above the plane of the aromatic anion decreases as the distance separating the two ions increases: C. E. Johnson, Jr., and F. A. Bovey, *J. Chem. Phys.*, 29, 1012 (1958).

(12) J. E. Hogen-Esch and J. Smid, *J. Amer. Chem. Soc.*, 88, 318 (1966).

(13) T. Ellingsen and J. Smid, *J. Phys. Chem.*, 73, 2712 (1969).

(14) L. Pauling, "The Nature of the Chemical Bond," 3rd ed, Cornell University Press, Ithaca, N. Y., 1960, p 514.

(15) Measurements were made assuming the oxygen atoms of the solvent to be coordinated with the cation.

(16) Although the shielding of a nucleus located above the π cloud of a benzene ring is not strictly linear with distance,[11] it is linear to a first approximation from a distance of 2.8–4.0 Å.

(17) J. F. Garst, R. A. Klein, D. Walmsley and E. R. Zabolotny, *J. Amer. Chem. Soc.*, 87, 4080 (1965).

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New Heteroaromatic Compounds. XXXIII.[1] 5,1,3,4-Boratriazaroles[2]

Sir:

Previous papers of this series[1,3] have described numerous compounds derived from "normal" aromatic systems by replacing a pair of adjacent carbon atoms by the isoelectronic BN combination; the boron-nitrogen bonds in many of these show remarkable resistance to chemical attack, implying that they are aromatic, a conclusion supported by their other physical and chemical properties. On this basis it seems likely that medicinally valuable compounds might be obtained by analogous replacement of pairs of carbon atoms in the aromatic rings of biologically active materials. There is therefore an incentive to prepare analogs of "biological" aromatic rings such as benzene, pyrrole, and imidazole.

Unfortunately the benzene analog, borazarene (I), seems to be rather unstable, judging by the ease with which its derivatives resinify,[4] while the compounds so far prepared in which boron forms part of a five-membered ring undergo hydrolysis with great ease.[3] Recently it has been shown that derivatives of 3,2-

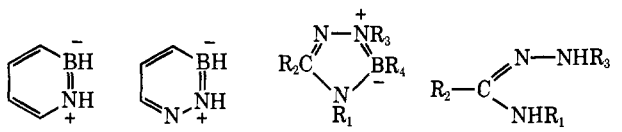
(1) Part XXXII: F. A. Davis, M. J. S. Dewar, R. Jones, and S. D. Worley, *J. Amer. Chem. Soc.*, 91, 2094 (1969).

(2) This work was supported by the Air Force Office of Scientific Research through Contract No. F44620-70-C-0121, the National Institutes of Health through Grant No. 1F02 GM-45321-01, and the Robert A. Welch Foundation.

(3) For reviews and nomenclature, see M. J. S. Dewar, *Progr. Boron Chem.*, 1, 235 (1964); *Advan. Chem. Ser.*, No. 42, 227 (1964).

(4) K. M. Davies, M. J. S. Dewar, and P. Rona, *J. Amer. Chem. Soc.*, 89, 6294 (1967).

borazaropyridine (II) are chemically very stable,[5] unlike those of I; this suggested that five-membered heteroaromatic rings containing boron might also be stabilized by additional heteroatoms. We wish to report a new synthesis of such a system, 5,1,3,4-boratriazarole (III), which seems to show stability of a high order and which can be regarded as an analog of imidazole or pyrazole.



I II III IV

One derivative of III had been reported previously, *i.e.*, the tetraphenylboratriazarole (III, $R_1 = R_2 = R_3 = Ph$) which was obtained in 5% yield by pyrolysis of a mixture of 2,5-diphenyltetrazole with the pyridine adduct of 2,5-diphenylboron azide.[6] We have now found that compounds of this type can be prepared quite generally and in good yield by heating a boronic acid derivative (RBX_2, where X = Cl, OCH_3, OC_2H_5, OH, or NMe_2) with the corresponding acid amidrazone (IV) in boiling benzene. Volatile products (HCl, $NHMe_2$) were removed by passing dry nitrogen through the reaction mixture while liquid ones (H_2O, ROH) were eliminated with a Dean-Stark moisture trap. The structures of the products were indicated by elemental analysis,[7] by the method of synthesis, and by the identity of the tetraphenyl derivative, as indicated by its melting point and infrared spectrum, with the compound prepared by Paetzold.[6] The mass spectra showed in each case a very strong peak corresponding to the mass number expected for the molecular ion from III. The compounds so far prepared are listed in Table I with their melting points.

Table I. 5,1,3,4-Boratriazaroles

	R_1	R_2	R_3	R_4	Mp, °C[a]	% yield[b]
IIIa	H	CH_3	H	C_6H_5	147–149	63
b	H	CH_3	CH_3	C_6H_5	130–131	64
c	C_6H_5	H	H	C_6H_5	149–150	59
d	H	2-Pyridyl	H	C_6H_5	166–167	81
e	C_6H_5	H	C_6H_5	C_6H_5	164–165	35
f	C_6H_5	C_6H_5	H	C_6H_5	222–223	95
g	C_6H_5	C_6H_5	C_6H_5	C_6H_5	198–200	65
h	C_6H_5	C_6H_5	H	*n*-Bu	107	50

[a] In sealed capillary, under nitrogen; uncorrected. [b] Based on starting amidrazone; reported yields before preparation of analytical samples.

While these boratriazaroles are destroyed by boiling with strong acid or alkali (*e.g.*, 10% HCl or NaOH) they are stable to hydrolysis under milder conditions. Thus contrary to the statement by Paetzold,[6] IIIg is unchanged by prolonged (2 weeks) exposure to air and is recovered unchanged on addition of water to a solution of it in ethanol. Moreover, IIId is formed by heating a dilute aqueous solution of the amidrazone and phenylboronic acid, a remarkable tribute to its stability; we know of no other case where an aminoborane has been formed by reaction of an amine with a boronic acid in aqueous solution. Several of these compounds are recovered on solution in acid followed by neutralization; this last observation suggests, however, that they may in fact have undergone reversible hydrolysis.

The aromatic nature of these compounds is further indicated by their mass spectra in which 99% of the total ionization is concentrated in the peak corresponding to the parent molecular ion; a relatively large peak was also observed corresponding to the doubly charged molecular ion, a feature which seems to be characteristic of "borazaromatic" compounds.[8] Since acid amidrazones (IV) can be prepared readily by procedures which allow introduction of an almost arbitrary selection of substituents,[9] the way seems open to the synthesis of a wide variety of compounds of possible biological interest.

We also tried to synthesize hydroxy analogs of III (*i.e.*, with $R_2 = OH$) by heating phenylboron dichloride with derivatives of semicarbazide. While products were obtained which showed mass spectra compatible with the expected 2-hydroxy-5,1,3,4-boratriazaroles, their instability to hydrolysis by traces of water or alcohol has so far prevented their isolation in a state pure enough for elemental analysis. The infrared spectrum of the triphenyl derivative showed a strong carbonyl band, indicating that it exists as the amide tautomer.

(5) J. Namtvedt and S. Gronowitz, *Acta Chem. Scand.*, 22, 1373 (1968).
(6) P. I. Paetzold, *Z. Anorg. Allg. Chem.*, 326, 64 (1963).
(7) All new compounds gave satisfactory elemental analyses.
(8) M. J. S. Dewar and P. Rona, unpublished work.
(9) D. G. Neilson, R. Roger, J. W. M. Heattie, and L. R. Newlands, *Chem. Rev.*, 70, 151 (1970).
(10) National Institutes of Health Postdoctoral Fellow.

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The Total Synthesis of (±)-Vindorosine

Sir:

Pentacyclic, highly functionalized *Aspidosperma* alkaloids are of special interest because two representatives, namely, vindoline and 1-demethyl-1-formylvindoline, are structural components of the oncolytic double alkaloids vincaleukoblastine and leurocristine. Vindorosine[1] which cooccurs with the two antitumor agents in *Vinca rosea* Linn. does not seem to have been detected in double alkaloids yet. It was proposed[1] to be 11-demethoxyvindoline (**1**), based mainly on comparison of its nmr and ORD spectra with those of vindoline (**2**).[2]

Outlined below is a synthesis of vindorosine (**1**) confirming its structure which should be applicable also to the preparation of related alkaloids.

Condensation of 1-methyltryptamine with 1-chloro-3-ketobutene-1 in ethanol solution containing triethylamine provided the liquid hydrogen bonded *cis*-enamino ketone **3** (92%): ir ($CHCl_3$) 3000, 1640, 1560 cm^{-1};

(1) B. K. Moza and J. Trojánek, *Collect. Czech. Chem. Commun.*, **28**, 1427 (1963).
(2) The correct gross structure of vindoline was determined by M. Gorman, N. Neuss, and K. Biemann (*J. Amer. Chem. Soc.*, **84**, 1058 (1962)) while the correct stereoformula follows from the X-ray analysis of leurocristine methiodide performed by J. W. Moncrief and W. N. Lipscomb (*Acta Crystallogr.*, 21, 322 (1966)).