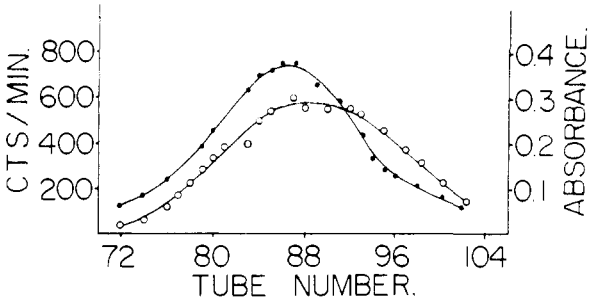

Fig. 1.—Resolution of D-arabinose-I-C^{14} and unlabeled D-arabinose in the all glass countercurrent apparatus of Craig and Post with upper and lower phase volumes of 10 ml. The solvent system was an equilibrated mixture of 2 parts of cyclohexane with 1 part 95% ethanol at 22 deg. The upper phase composition, by volume in per cent. of water, ethanol and cyclohexane, was 0.8, 15.5 and 84.5 as determined by matching spectra of synthetic mixtures of the components using the Perkin–Elmer infrared spectrophotometer, Model 21. The corresponding composition of water, ethanol and cyclohexane in the lower phase was 2.5, 48 and 49: ●, radioactivity, measured with an end window Geiger counter; ○, absorbance at 370 millimicrons of the arabinosylamine.[3] Twenty mg. of unlabeled D-arabinose mixed with 4 microcuries of labeled pentose constituted the sample for the 880 transfer distribution shown here.

= 0.14) were separated, even partially, from their unlabeled counterparts. Plots of log specific activity against tube number for xylose-1-C^{14} and D-ribose-1-C^{14}, linear and parallel to the abscissa.

Because arabinose-5-C^{14} did not show the isotope effect, it was unlikely that mass alone could account for the data. An isotope effect not dependent on mass alone has been reported previously by Piez and Eagle,[1] who observed that C^{14} on carbons 1 or 2 more than on carbons 3 or 4 decreased the rate of release of amino acids from Dowex 50 during pH gradient elution. These investigators attributed this isotope influence during ion exchange to an inductive effect, C^{14} being less electronegative than C^{12}. Thereby, the nearer the isotope was to the charged centers of the amino acid the less acid they became. If our reasoning is correct C^{14} on carbon 1 would be expected to alter the dipole moment of the sugar through an inductive effect and, as a consequence, the distribution coefficient in the cyclohexane system would be changed. Possibly several forms (for example the aldehyde and one or more chain forms) comprise the arabinose sample undergoing distribution, but arabinose 1-C^{14} contributes to the more slowly migrating components of the equilibria during countercurrent distribution. Since the isotope effect was not observed with similarly labeled xylose and ribose, it might be that the corresponding equilibria are too one sided for the effect to be discernible in countercurrent distribution in cyclohexane–ethanol. Differences in migration have suggested that at least two isomeric forms of a pure reducing sugar are present during dialysis through thin films.[2] In the studies reported here, the broader than theoretical distribution for the chemically pure unlabeled arabinose

(2) L. C. Craig and A. Pulley, *Biochemistry*, **1**, 89 (1962).

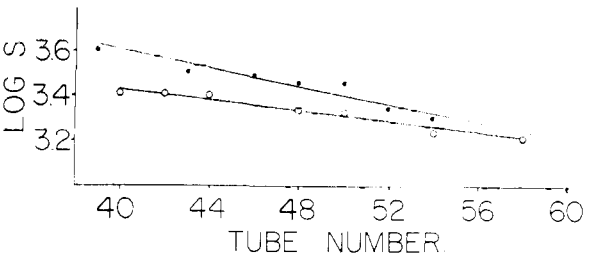

Fig. 2.—Plots of log specific activity, S, against tube number, X, in accordance with $\ln S = [(M_1 - M_2)X/\sigma^2] + [(M_2^2 - M_1^2)/2\sigma^2]$ derived from the ratio of two curves (absorbance, C^{14}-activity) assuming the normal distribution and that they have the same standard deviation σ, but M_1, the mean of the absorbance curve differs from M_2, the mean of the C^{14} activity curve; thus, the slope of the line is the index of resolution. Upper line plots D-arabinose-1-C^{14} mixed with unlabeled L-arabinose while the lower line compares the mobility of L-arabinose-1-C^{14} mixed with unlabeled D-arabinose. In each case there were 600 transfers in the solvent system described in Fig. 1.

(Fig. 1) and the deviations from linearity of the plots of log specific activity *versus* fraction number (Fig. 2) are consistent with such polymorphism.

The specific activity of the mixture of inert and labeled pentose, the sample for countercurrent distribution, was kept between 37 and 40 microcuries per millimole. Isotopic sugars were purchased from Calbiochem. The radiochemical purity of both D and L arabinose-1-C^{14} was found to be higher than 99% when mass calculated from observed characteristic absorbance and absorbance index[3] was compared with the mass computed from radioactivity and sample specific activity. In addition, isolated arabinose from tubes representing the peak, right or left side of the curve such as that in Fig. 1 moved more slowly, on redistribution, than the corresponding unlabeled pentose or unlabeled enantiomer. Although, for radiochemical impurities to account for the above data, similar impurities would be required to reside in both D-arabinose-1-C^{14} and L-arabinose-1-C^{14}; then, both enantiomers must, in addition, yield the above purity through the absorbance of their arabinosylamines and their specific activities.

(3) R. E. Timell, C. P. J. Glaudemans and A. L. Currie, *Anal. Chem.*, **28**, 1916 (1956).

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BORON-CONTAINING ANALOGS OF ISOQUINOLINE

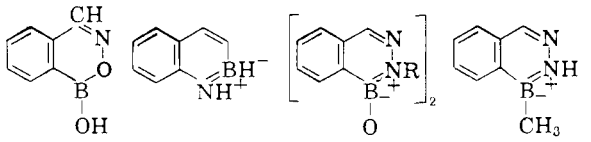
Sir:

Some years ago Snyder, Reedy, and Lennarz[1] prepared the cyclic oxime (I) as a derivative characteristic of *o*-formylphenylboronic acid. Since this ring system bears an obvious analogy to 2,1-borazaronaphthalene (II) which is known[2] to be aromatic, and since borazarophenanthrene is known

(1) H. R. Snyder, A. J. Reedy and W. J. Lennarz, *J. Am. Chem. Soc.*, **80**, 835 (1958).

(2) M. J. S. Dewar and R. Dietz, *Tetrahedron*, **15**, 26 (1961); *J. Org. Chem.*, **26**, 3253 (1961).

to be a more stable ring system than boroxarophenanthrene,[3] it seemed likely that aza analogs of I might show unusual properties. We now have prepared several derivatives of this novel ring system and find them to show typical aromatic stability.



I II III IV

a, R = H
b, R = Ph

Reaction at room temperature of *o*-formylphenylboronic acid in ether with anhydrous hydrazine in absolute ethanol yielded bis-(4,3-borazaro-4-isoquinolinyl) ether, IIIa, (80%) m.p. 234–234.5°; λ_{max}^{EtOH} 300, 280, 269 mμ (log ε = 3.64, 3.85, 4.26); ν_{max}^{KBr} (salient absorptions) 3340, 1603, 1563, 1502, 1445, 1382, 772 cm.$^{-1}$; *anal.* Calcd. for $C_{14}H_{12}B_2N_4O$: C, 61.39; H, 4.42; B, 7.90; N, 20.46. Found: C, 61.29; H, 4.48; B, 7.61; N, 20.22. This compound may be recovered after boiling for 2 hours in 15% potassium hydroxide or concentrated hydrochloric acid. Aliphatic hydrazones or aromatic boronic acids would be destroyed by this treatment. IIIa is not deboronated by bromine in refluxing acetic acid. To our knowledge this is the first example of a borazaro compound containing more than two heteroatoms that withstands such treatment.

When *o*-formylphenylboronic acid was added to an aqueous solution of phenylhydrazine hydrochloride, bis-(3-phenyl-4,3-borazaro-4-isoquinolinyl) ether (IIIb) (m.p. 196–186.5°) separated immediately as colorless needles in almost quantitative yield; λ_{max}^{EtOH} 303, 284 mμ (log ε = 4.38, 4.45); ν_{max}^{KBr} (salient absorptions) 3052, 1597, 1494, 1406, 1383, 1334, 893, 757, 695 cm.$^{-1}$; n.m.r. complex multiplet between 2.98 and 1.63 τ only; *anal.* Calcd. for $C_{26}H_{20}B_2N_4O$: C, 73.98; H, 4.78; B, 513; N, 12.33; mol. wt., 422. Found: C, 73.76; H, 4.74; B, 5.05; N, 12.50; mol. wt. (Rast), 399.

The spectra of these compounds and their hydrolytic stability suggest that the hetero ring is aromatic. The stability and ease of preparation of 4-methyl-4,3-borazaroisoquinoline (IV) provide additional evidence for this. Reaction of excess of methylmagnesium bromide with IIIa in ether at 0° yielded IV (60%), m.p. 97.0–97.5°; λ_{max}^{EtOH} 301, 290, 265, 210 mμ (log ε = 3.53, 3.46, 3.88, 4.55); ν_{max}^{KBr} (salient absorptions) 3280, 1597, 1557, 1494, 1430, 1315, 1211, 902, 764 cm.$^{-1}$; n.m.r., sharp singlet, 9.10 τ, multiplets 2.90 to 1.67 τ (relative areas 3:5); *anal.* Calcd. for $C_8H_9BN_2$: C, 66.73; H, 6.30; B, 7.51; N, 19.46; mol. wt., 144; found: C, 66.56; H, 6.35; B, 7.54; N, 19.75; mol. wt. (Rast), 136. This compound is recovered unchanged from boiling 10% hydrochloric acid or boiling 10% potassium hydroxide and may indeed be purified by extracting an aqueous solution of its hydrochloride with ether, followed by neutralization to precipitate the neutral compound. 4-Methyl-4,3-borazaroisoquinoline reacts with fuming nitric acid in acetic anhydride, at −30°, to yield a mixture of boron containing compounds, the infrared and n.m.r. spectra of which indicate that they are probably nitro isomers of IV with predominant retention of the B methyl group.

Snyder and his co-workers were unable to characterize the reaction product of *o*-formylphenylboronic acid and 2,4-dinitrophenylhydrazine.[1] It seems likely in this case that the destabilizing effect of an electron withdrawing group adjacent to boron in the molecule promotes hydration to form the acyclic 2,4-dinitrophenylhydrazone.[4]

We also have re-examined the boroxaroisoquinoline (I). If I is aromatic, it should behave as a protic acid, in contrast to non-aromatic boron compounds which behave as Lewis acids.[2] We found that the ultraviolet spectrum of I showed a small bathochromic shift on solution in alkali, unaffected by addition of mannitol. This implies that I is indeed a protic acid.[5] However, attempts to replace the hydroxyl group in I by methyl have so far failed, suggesting that I is less aromatic than the nitrogen analog (III) (*cf.* ref. 3).

In the light of our studies of I and III, amides of *o*-aminophenylboronic acid which have been reported as semianhydrides[6] may well be 4,3-boroxaroquinolines. If so, the corresponding 4,3-borazaroquinolines should be stable.

This work has been supported by a grant from the National Science Foundation.

(3) M. J. S. Dewar and R. Dietz, *J. Chem. Soc.*, 1344 (1960).

(4) Similar problems have been encountered in studies of 9,10-borazarophenanthrene (M. J. S. Dewar and P. M. Maitlis, *Tetrahedron*, **15**, 35 (1961).

(5) The ultraviolet spectrum of boronophthalide in ethanol shows a small hypsochromic shift on addition of alkali or mannitol and aromatic boronic acids behave likewise.

(6) C. G. Clear and G. E. K. Branch, *J. Org. Chem.*, **2**, 522 (1938); A. H. Soloway, *J. Am. Chem. Soc.*, **82**, 2442 (1960).

(7) Woodrow Wilson Fellow 1960–1961; National Science Foundation Predoctoral Fellow, 1961–1962.

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SUBSTITUENT EFFECTS. II. C^{13}-PROTON COUPLINGS IN CARBON sp^2 SYSTEMS[1]

Sir:

An additivity relation for C^{13}-proton couplings in substituted methanes was reported recently.[1] Gutowsky and Juan[2] have attempted to explain the additivity relation by means of a valence bond approach. These investigations, however, have been restricted to substituted sp^3 carbon atoms. The present communication reports some of our findings on substituted sp^2 carbon atoms.

For the substituted methanes, CHXYZ, the C^{13}-H coupling constants have been found[1] to obey the equation

$$J_{CH} = \Sigma\zeta_X. \qquad (1)$$

where ζ_X is a numerical constant associated with substituent X, the sum being taken over all the substituents except the proton in question. Zeta

(1) Part I, E. R. Malinowski, *J. Am. Chem. Soc.*, **83**, 4479 (1961).

(2) H. S. Gutowsky and C. S. Juan, *ibid.*, **84**, 307 (1962).