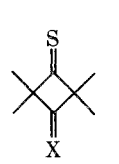
The Effect of Solvent on the Regioselectivity of Cycloaddition of Diazomethane to the Thione Group in Adamantanethione

Summary: The Δ^2-1,2,3-thiadiazoline to Δ^3-1,3,4-thiadiazoline product ratio for the cycloaddition of diazomethane to the thione group in adamantanethione is highly dependent on the reaction solvent.

Sir: The cycloaddition of diazomethane to each of the C=S groups in 1 (X = S, ethereal solution) proceeds regiospecifically to yield *cis*- and *trans*-bis-Δ^3-1,3,4-thiadiazolines **2**.[1] Treatment of 1 (X = O, ether solution) with an ethereal solution of diazomethane also leads to the regiospecific cycloadduct **3**.[2] On the other hand, cycloaddition of diazomethane to the C=S group in adamantanethione (4) in ether occurs in a regioselective manner. The Δ^3-1,3,4-thiadiazoline **5** to Δ^2-1,2,3-thiadiazoline **6** product ratio was found to be ~3 when the reaction was carried out in ether.[1]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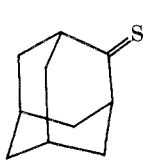
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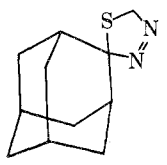
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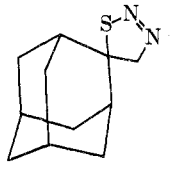
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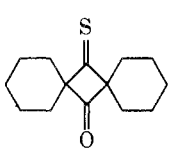
We now wish to report that the **5** to **6** product distribution found in the cycloaddition of diazomethane to the C=S group in 4 is highly dependent on the solvent which is used in the reaction. The results of this study are tabulated in Table I.

Table I
Diazomethane Cycloadditions to the C=S Group of 4 in Various Solvents

Solvent[a]	% Δ^3 (**5**)[b]	% Δ^2 (**6**)	E_T[c]
Petroleum ether	87	13	
Ether	80	20	34.6
Benzene	76	24	34.5
Methylene chloride	58	42	41.1
Ethanol[d]	41	59	51.9
Methylene chloride[e]	40	60	41.1
Acetonitrile[f]	32	68	46.0
Methanol[g]	30	70	55.5
Methanol[h]	22	78	55.5

[a] Solutions of **4** (0.12 *M*) were cooled to 0°. An alcohol-free ethereal solution of diazomethane was prepared from Diazald. The cold diazomethane solution was added dropwise to the orange thione solutions. The reaction appeared to be instantaneous. The solvent was removed under reduced pressure with cooling. The residue was dissolved in $CDCl_3$ and the pmr recorded. [b] Thiadiazolines **5** and **6** exhibit singlets at δ 5.8 and δ 5.0, respectively. The percentages are based on area integrations of these singlets. [c] Solvent polarity parameter; see C. Reichardt, *Angew. Chem., Int. Ed. Engl.*, **4**, 29 (1965). [d] A 0.03 *M* solution of **4** at 22° was treated with a cold, ethereal solution of diazomethane. [e] A 0.12 *M* solution of **4** was treated with a methylene chloride solution of diazomethane. [f] A 0.03 *M* solution of **4** at 0°. The reaction was also performed at room temperature and the same product ratio was found. [g] A 0.04 *M* solution of **4** at 0°. [h] A 0.03 *M* solution of **4** (0°) was treated with a methylene chloride solution of diazomethane.

Treatment of dithione **1** (X = S) in a methanol solution (0°) with an ethereal solution of diazomethane leads to the same isomeric mixture of thiadiazolines **2** as is obtained when the reaction is performed in ether as solvent. Similarly, treatment of the thione ketone **7** in ether or methanol as solvent (0°) leads only to the Δ^3-1,3,4-thiadiazoline **8**. No evidence for the other regioisomers could be found in the pmr spectra of the products from either of these compounds.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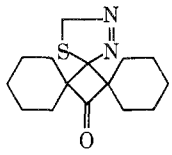
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The mechanistic aspects of 1,3-dipolar cycloadditions have been the subject of much debate[3,4] and theoretical treatment.[5]

As a dipolarophile the C=S bond exhibits high reactivity.[1-3] Other cycloadditions to substrates with C=S bonds such as aliphatic thiones,[6] thiobenzophenone,[7] thion esters,[6,8] dithio esters,[6,9] and phenyl isothiocyanate[10] have been reported.

The exclusive formation of Δ^3-1,3,4-thiadiazolines from 1 (X = S), 1 (X = O), and 7 (independent of solvent polarity) is perhaps due to steric control of approach of the diazomethane to the thione group.[1,3c] However, in 4 models seem to indicate a somewhat more accessible thione group. Either directional approach of the diazomethane is possible. The dominance of the Δ^2 isomer in polar solvents might be due to the fact that the alignment of dipoles for the transition state leading to this isomer has a greater overall moment than the alternative transition state.[11]

It is not clear to us whether the regiospecificity found in 1 (X = S), 1 (X = O), and 7 or the varying regioselectivity found in 4 as a function of the solvent could have been predicted *via* the HOMO-LUMO model recently proposed by Houk and coworkers.[5] The question must be asked as to whether other dipolar cycloadditions might show regioisomeric product variations which depend on solvent.[5c]

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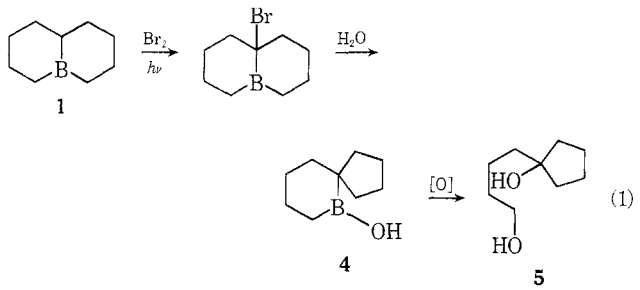
Synthetic Approach to New Organoborane Structures *via* the α-Bromination of Borapolycyclanes

Summary: The light-induced reaction of bromine with borapolycyclanes (**1**, **2**, **3**) in the presence of water provides an entry into polycyclic organoborane intermediates with interesting new structures and to the organic derivatives into which they may be converted.

Sir: A simple six-membered boracyclane can undergo ring contraction to produce a five-membered carbocyclic boron intermediate by photochemical reaction with bromine in the presence of water.[1] The reaction proceeds through a rapid, selective α-bromination, followed by a facile migration of the B–C bond from boron to carbon.[2] This development makes possible the synthesis of carbocyclic structures from the corresponding straight-chain dienes.

We now wish to report that the reaction is applicable to much more complex systems. Thus, its application to representative borapolycyclanes (**1**, **2**, **3**)[3] proceeds satisfactorily and provides an entry to interesting new organoborane structures (**4**, **6**, **8**) and to the organic derivatives into which such boron compounds can be converted (**5**, **7**, **9**).

For example, treatment of 9-boradecalin (**1**) with bromine in the presence of light and water provides 6-hydroxy-6-boraspiro[4.5]decane (**4**). The structure of **4** was confirmed by oxidation with alkaline hydrogen peroxide to 1-(4-hydroxybutyl)cyclopentanol[4] (eq 1), in an overall yield of 50%. It is evident that the α-bromination occurs selectively at the α tertiary hydrogen atom, rather than at the α secondary position.



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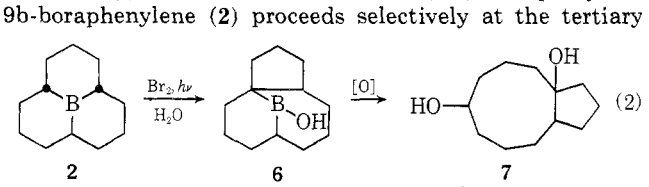
Similarly, the α-bromination of *cis,cis,trans*-perhydro-9b-boraphenylene (**2**) proceeds selectively at the tertiary

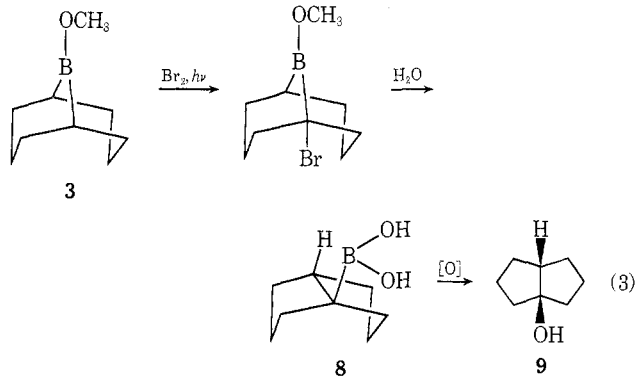


2 6 7 (2)

position. Hydrolysis–oxidation in the usual manner provides bicyclo[7.3.0]dodecane-1,5-diol[4] in 70% yield *via* the polycyclic borane intermediate, 13-hydroxy-13-boratricyclo[7.3.1.0^{1,5}]tridecane (**6**) (eq 2).

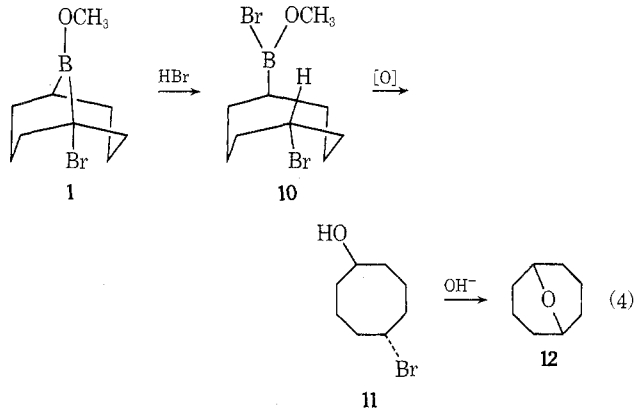
The case of 9-methoxy-9-borabicyclo[3.3.1]nonane (**3**) is of special interest. It was recently established that the α-bromination of *B*-isopropyl-9-borabicyclo[3.3.1]nonane occurs almost exclusively at the α position of the isopropyl group.[5] No significant attack occurs at the α bridgehead positions. Consequently, it was uncertain whether α-bromination in **3** would be feasible.

In fact the bromination, albeit somewhat more sluggish than the other cases, proceeds satisfactorily, producing the *cis*-bicyclo[3.3.0]octane-1-boronic acid (**8**), readily oxidized to *cis*-bicyclo[3.3.0]octan-1-ol[6] (**9**) in a yield of 65% (eq 3). Although the bromo intermediate was not isolated, it is evident that bridgehead substitution must have taken place in view of the structures of the products (**8**, **9**).



3 8 9 (3)

The reaction is accompanied by the formation of cyclooctane 1,5-epoxide[7] (**12**) in 22% yield. This product may arise from a competing attack of hydrogen bromide on the bromination intermediate to form **10** (eq 4). Pmr examination of the reaction mixture reveals the presence of a methine proton (4.05–4.50 ppm in CCl_4) assigned to **10**. The integral area ratio of the spectrum reveals that the reaction proceeds 70% through path 3 and 30% through path 4.



1 10 11 12 (4)

The following procedure for the preparation of *cis*-bicyclo[3.3.0]octan-1-ol is representative. A dry 300-ml flask, equipped with a septum inlet, thermometer well, pressure-equalizing dropping funnel, reflux condenser, and magnetic stirrer, was flushed with dry nitrogen and maintained under a positive nitrogen pressure. The flask was cooled to 0–5° and charged with 4.56 g (30 mmol) of pure 9-methoxy-9-borabicyclo[3.3.1]nonane,[8] 40 ml of methylene chloride, and 30 ml of water. Bromine (1.65 ml, 30 mmol) in 20 ml of methylene chloride was slowly added at 0–5° over 1.5 hr. After the bromine color disappeared, sodium hydroxide solution (6 *N*, 15 ml), ethanol (60 ml), and aqueous hydrogen peroxide (30%, 10 ml) were added at 0–5°. The mixture was then refluxed for 1 hr. The or-