citation, not observed, while the peaked vibrational distribution usually associated with reaction 9 was not evident.[4,5,7]

A final possibility, reactions of $(HI)_n$ with $n \geq 3$, cannot be completely excluded, as some trimers and tetramers were present, although they appeared to be much less common (by a factor of 5 to 20) than the dimers.

Reaction 2 was tried under a variety of beam conditions with $(Cl_2)_2$ concentrations as high as 10%, but no emission from HCl was observed. It is possible that not enough energy is imparted to the HCl to significantly populate the first vibrational level.

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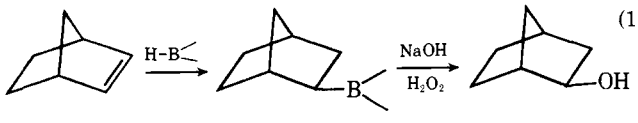
Consistent Inversion in the Base-Induced Reaction of Iodine with Organoboranes. A Convenient Procedure for the Synthesis of Optically Active Iodides

Sir:

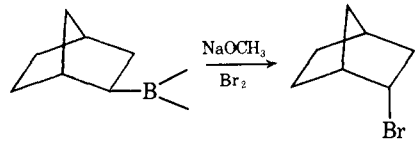
The base induced reaction of iodine with diisopinocampheyl-2-butylborane produces optically active 2-iodobutane of high optical activity with configuration opposite to that of the 2-butanol produced in the oxidation of the borane by alkaline hydrogen peroxide. Similarly, the products from the corresponding reactions of iodine with tri-*exo*-norbornylborane and *B*-methoxy-9-borabicyclo[3.3.1]nonane (B-MeO-9-BBN) reveal that the reaction involves inversion of configuration at carbon. It is therefore evident that this reaction, in contrast to the large majority of reactions of organoboranes, involves *substitution* of the boron–carbon bond with clean inversion.

The great majority of the reactions of organoboranes involving rupture of the carbon–boron bond proceed with retention[1] (eq 1). We recently observed that the reaction of



(1)

bromine with tri-*exo*-norbornylborane in the presence of sodium methoxide yielded a product that was predominantly *endo*-bromonorbornane[2] (eq 2).



(2)

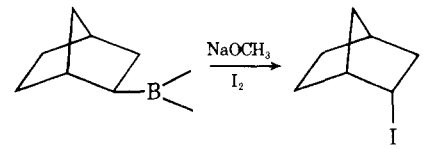
The question arose as to whether this unexpected stereochemistry of substitution was a consequence of some unique feature of the norbornyl system,[3,4] or a consequence of the exceptional tendency of bromine to engage in free radical reactions.[5] For example, we had previously observed that the apparent heterolytic reaction of bromine with organoboranes, $R_3B + Br_2 \rightarrow RBr + R_2BBr$, actually proceeds through a free radical bromination[6] (eq 3). Accordingly, we decided to investigate the reaction of iodine with organoboranes as a means of avoiding such ambiguities. Free-radical chain reactions involving iodine are rare.[7]

$$(CH_3CH_2)_3B + Br\cdot \longrightarrow CH_3\dot{C}HB(CH_2CH_3)_2 + HBr$$

$$CH_3\dot{C}HB(CH_2CH_3)_2 + Br_2 \longrightarrow CH_3\underset{\displaystyle Br}{\underset{|}{C}}HB(CH_2CH_3)_2 + Br\cdot \qquad (3)$$

$$CH_3\underset{\displaystyle Br}{\underset{|}{C}}HB(CH_2CH_3)_2 + HBr \longrightarrow CH_3CH_2Br + (CH_3CH_2)_2BBr$$

The reaction of iodine with tri-*sec*-alkylborane in the presence of sodium methoxide in methanol proceeds with the conversion of two of the three alkyl groups to the corresponding iodide.[8] Tri-*exo*-norbornylborane, obtained via the hydroboration of norbornene, behaves similarly, giving a 70% yield of 2-iodonorbornane. The product proved to be largely *endo*-norbornyl iodide in the initial stages of the reaction. However, with extended treatment, considerable isomerization to exo occurs. The hitherto unreported *endo*-norbornyl iodide could be obtained by running the reaction to the approximate utilization of one group, followed by removal of the small amount of exo isomer by selective solvolysis (eq 4). Consequently, the earlier result involving bromine[2] is not exceptional.

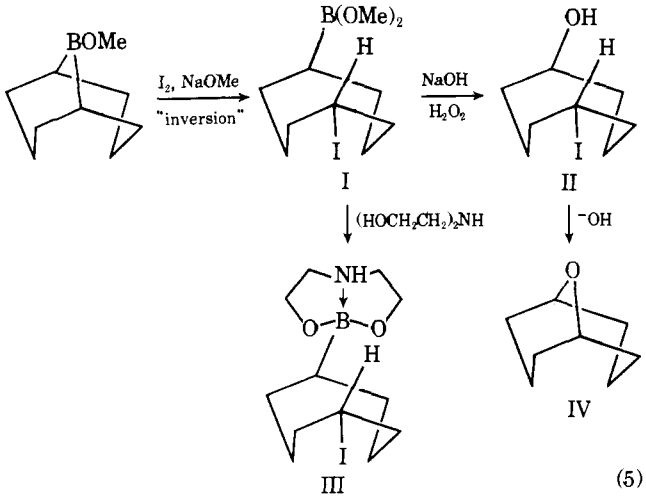


(4)

The following procedure is representative. A dry, nitrogen-flushed 400-ml flask with the usual accessories[9] was charged with 29.25 g of norbornene (0.300 mol) in 200 ml of dry tetrahydrofuran (THF) and hydroborated by the dropwise addition of 41 ml of 2.45 M borane–THF (0.100 mol) at 0°. After 1 h at 25°, 1 ml of methanol was added to destroy traces of residual hydride. The flask was wrapped in aluminum foil,[10] and cooled to 0°. Then 56 g of iodine (0.220 mol) was added (under nitrogen), followed by 46.5 ml of a 4.72 M solution of sodium methoxide in methanol over 10 min. Excess iodine was decolorized with 10 ml of saturated aqueous sodium thiosulfate. Extraction with pentane (3 × 50 ml) and distillation yielded 17.2 g (78% based on one norbornyl group) of 2-iodonorbornane (bp 54–55° at 1.8 mm). Analysis by ^1H NMR[11] revealed the mixture to be 80% *endo*- and 20% *exo*-iodonorbornane. Refluxing the isomeric mixture in 200 ml of 80% aqueous methanol (v/v) containing 5 g of potassium carbonate for 3 h selectively destroyed the exo isomer. Extraction with pentane and distillation gave 12.0 g of pure *endo*-iodonorbornane (bp 51.5–52.0° at 1.2 mm, $n^{20}D$ 1.5650).

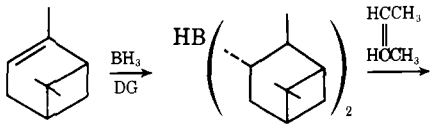
Treatment of B-MeO-9-BBN in the presence of methanolic sodium methoxide with iodine at 25° results in the disappearance of the iodine color over 1–2 h. Following oxidation by alkaline hydrogen peroxide, 9-oxabicyclo[3.3.1]nonane, IV, was formed in 60–85% yields by GLC analysis (eq 5). Oxidation of I must produce the *trans*-5-iodocyclooctanol II, readily converted into 9-oxabicyclo[3.3.1]nonane.[13] Indeed, it proved possible to isolate the postulated intermediate I as the crystalline diethanolamine derivative, III,[14] mp 148–153° dec.

Both B-MeO-9-BBN and tri-*exo*-norbornylborane in-

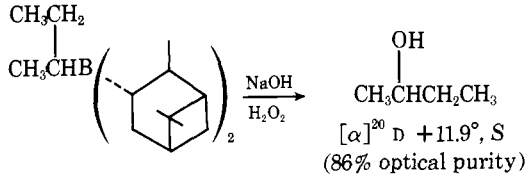


(5)

volve reaction of iodine at a bicyclic center. It was important to establish whether inversion would occur at a secondary center not involving this special structural feature. We selected diisopinocampheyl-2-butylborane[15] for study (eq 6). Note that the 2-butanol produced from (−)-α-pinene possesses the *S* configuration.



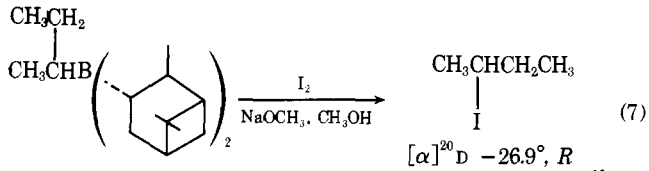
$[\alpha]_D$ −47.0°
(91% optical purity)



(6)

$[\alpha]^{20}_D$ +11.9°, *S*
(86% optical purity)

Treatment of the borane with iodine in the presence of sodium methoxide–methanol yields 2-iodobutane (*R*) with $[\alpha]^{20}D$ −26.9° (84% optical purity) (eq 7).



(7)

$[\alpha]^{20}_D$ −26.9°, *R*
(84% optical purity)[16]

α-Pinene ($[\alpha]_D$ −47.1°) was converted to diisopinocampheylborane in diglyme and the latter treated with *cis*-2-butene as previously described.[15,9] The product, 0.200 mol, was divided into two equal parts. One-half was oxidized with alkaline hydrogen peroxide, yielding 2-butanol with $[\alpha]^{20}D$ +11.9°, whereas the second was treated with iodine and sodium methoxide–methanol (2 h). A 49% yield of 2-iodobutane was obtained, $[\alpha]^{20}D$ −26.9°. The alcohol possesses the *S* configuration, whereas the iodide possesses the *R*.

Consequently, it is evident that the reaction of organoboranes with iodine, induced by sodium methoxide, proceeds generally with inversion of the carbon–boron bond. This development not only provides a new synthetic route to *endo*-norbornyl and similar bicyclic iodides, but it makes available a promising new route to optically active iodides.

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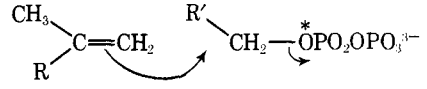
Application of Unreactive Analogs of Terpenoid Pyrophosphates to Studies of Multistep Biosynthesis. Demonstration That "Presqualene Pyrophosphate" Is an Essential Intermediate on the Path to Squalene

Sir:

Pyrophosphate monoesters play a dominating role in the biosynthesis of terpenoids, especially with reference to chain extension and ring formation.[1] The head-to-tail joining of isoprene units by carbon coupling, for example, involves intermolecular nucleophilic attack by a carbon–carbon double bond at a saturated carbon with displacement of a pyrophosphate leaving group:



Analogues of pyrophosphates in which the carbinol oxygen (O*, above) is replaced by methylene can reasonably be expected both to resist such enzymic C–C coupling and to function as selective enzyme inhibitors ("substrate analogue" type). In this communication we describe the synthesis of a series of these pyrophosphate analogues (C-substituted methylphosphonophosphates), the demonstration that they do inhibit biosynthetic processes involving pyrophosphate substrates as postulated, and an illustration of how this inhibition can be utilized to gain new information regarding multistep biosynthetic pathways.

Geranylmethylphosphonophosphate trilithium salt (**4**, R = geranyl) was synthesized starting with the reaction of geranyl bromide (**1**, R = geranyl) with 1 equiv of dimethyl lithiomethylphosphonate[2] in tetrahydrofuran (THF) at −78° to form phosphonic diester **2**[3] (60–70%). Cleavage of