

ordinary workup, ethyl 2-phenylglycidate was isolated by distillation in vacuo [99–107 °C (0.5 mmHg)] as a mixture of *E* and *Z* isomers (1:1 by GLC): yield 13.9 g, 72%.

References and Notes

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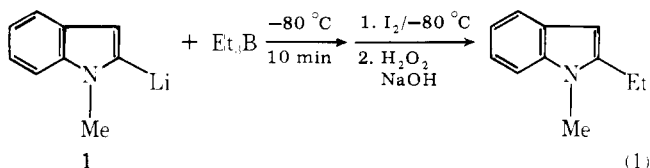
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Aromatic Substitution via Organoboranes. Regiospecific Formation of 2-Alkylindoles

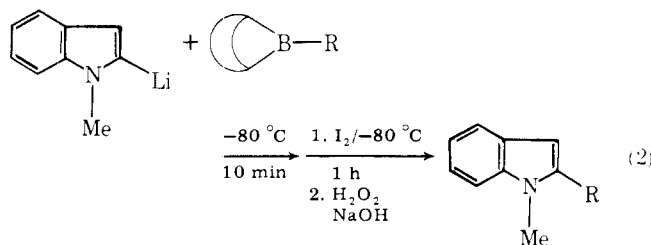
Summary: *N*-Substituted 2-lithioindoles react with trialkylboranes or *B*-alkyl-9-BBN derivatives to give, after iodination, 2-alkylindoles in yields ranging from 60 to 96%.

Sir: The pioneering work of Gilman¹ and others² has demonstrated that many aryllithium derivatives are available via either halogen–lithium exchange or proton abstraction. In particular, in heterocycles, many aryllithiums are available with the lithium attached at positions not easily substituted via electrophilic substitution reactions. Our recent interest in alkenyltrialkylborate salts³ and their use in organic synthesis has led us to begin an investigation of the related aryltrialkylborate salts. We now wish to report our results on the iodination of the aryltrialkylborate salts⁴ derived from *N*-substituted 2-lithioindoles.

When *N*-methyl-2-lithioindole⁵ (1) is treated at –80 °C with 1 equiv of triethylborane followed by iodination and the usual oxidative workup, a 79% yield of *N*-methyl-2-ethylindole⁶ is obtained (eq 1). Furthermore, treatment of 1 with



B-alkyl-9-BBN derivatives⁷ gives selective transfer of the alkyl group to the indole nucleus (eq 2).



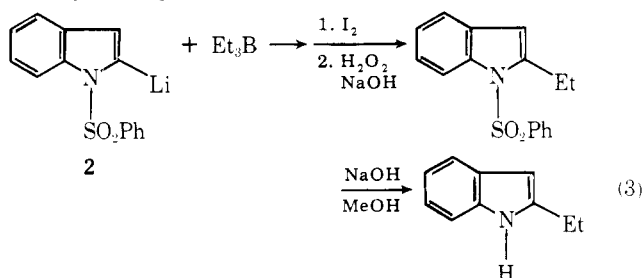
In general, electrophilic functionalization of the indole nucleus leads to regioselective formation of 3-substituted indoles.⁸ We have therefore undertaken an investigation of the scope of this reaction using a variety of organoboranes. The results are summarized in Table I.

Table I. The Reaction of the "Ate" Complex Derived from 1-Methyl-2-lithioindole^a and Trialkylboranes^b with Iodine^c for the Synthesis of *N*-Methyl-2-alkylindoles⁶

Organoborane	product	% yield ^e
triethylborane	<i>N</i> -methyl-2-ethylindole	79
triisobutylborane	<i>N</i> -methyl-2-isobutylindole	71
<i>B</i> -isobutyl-9-BBN ^d		85
tri- <i>sec</i> -butylborane	<i>N</i> -methyl-2- <i>sec</i> -butylindole	71
<i>B</i> - <i>sec</i> -butyl-9-BBN ^d		78
tricyclopentylborane	<i>N</i> -methyl-2-cyclopentylindole	79
<i>B</i> -cyclopentyl-9-BBN ^d		60
tricyclohexylborane	<i>N</i> -methyl-2-cyclohexylindole	96
<i>B</i> -cyclohexyl-9-BBN ^d		78

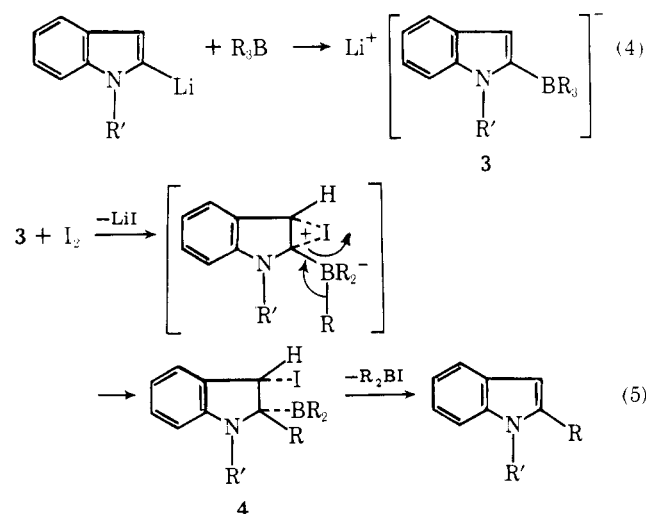
^a 5 mmol in 10 mL of ether. ^b 5 mmol added neat or as a 0.5–1.0 M solution in THF at –80 °C. ^c 5.25 mmol added in 5 mmol of THF. ^d Reactions involving *B*-alkyl-9-BBN derivatives were run on a 2.5-mmol scale. ^e Analysis by GLC vs. an internal standard.

While *N*-methylindoles include many biologically important indole alkaloids,⁹ any general methodology must allow for the direct substitution of the indole nucleus itself. The recent preparation of 2-lithio-*N*-benzenesulfonylindole (2)¹⁰ provides a potentially useful substrate. Thus, treatment of 2 with triethylborane and iodine leads to the 2-alkylated indole in 57% isolated yield. Subsequent hydrolysis with methanol/2 *N* NaOH (5:1, reflux, 48 h)¹⁰ gives 2-ethylindole in 85% isolated yield (eq 3).



Presumably, the mechanism of this reaction is analogous to the iodination of alkenylborate salts. Initial complexation of the lithium derivative with the borane leads to an "ate" complex (eq 4). Subsequent formation of an iodonium ion, followed by migration of an alkyl group from boron to carbon, leads to 4. β -Haloboranes similar to 4 are known to eliminate R_2BX under a variety of conditions.¹¹ Thus, a thermal syn elimination³ of R_2BI leads directly to the 2-alkylindole (eq 5).

In summary, the present development allows the regio-specific functionalization of the 2 position of the indole nu-



cleus via organoboranes. The use of *B*-alkyl-9-BBN derivatives makes this procedure superior to the S_N2 reaction for hindered alkyl groups. In addition, we have found that the formation of the "ate" complex activates the 3 position to attack by carbon electrophiles. These results, as well as applications to other aromatic systems, will be the subject of forthcoming publications.

The following procedure is representative.^{12,13} A dry 50-mL round-bottom flask equipped with a septum-capped side arm and reflux condenser was connected to an oil bubbler. The system was purged with nitrogen and maintained under nitrogen until after the oxidation. To this flask was added 5 mL of THF and 0.682 g (2.5 mmol) of *N*-benzenesulfonylindole.¹⁰ To this solution maintained at -12°C was added 1.60 mL (3 mmol) of *tert*-butyllithium. The flask was allowed to stir in air for 20 min, cooled to -80°C , and 0.428 mL (3.00 mmol) of triethylborane was added. The solution was stirred for 10 min, and 0.84 g of I_2 in 3 mL of THF was added. The solution was stirred for 1 h at -80°C and allowed to warm to room temperature. The residual borane was washed three times with 3 mL of 3 N NaOH then oxidized by addition of 2 mL of 3 N NaOH followed by the dropwise addition of 2 mL of 30% hydrogen peroxide. After stirring at room temperature for 1 h, the organic layer was diluted with ether, separated, washed with water, and dried (MgSO_4) and the solvent was removed under vacuum to give 0.62 g of a crude brown solid. Recrystallization from methanol gave 0.39 g (57%) of analytically pure 1-(benzenesulfonyl)-2-ethylindole (mp $95.0\text{--}96.5^\circ\text{C}$).

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References and Notes

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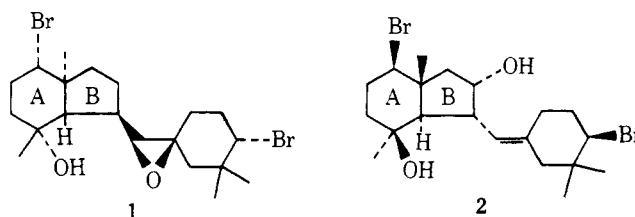
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Isolation and Structure of Angasiol¹

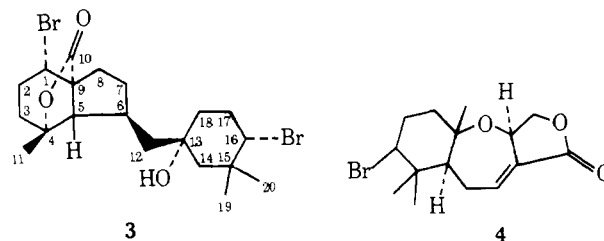
Summary: The structure and absolute configuration of a new dibromoditerpene designated angasiol has been determined by X-ray crystallographic techniques.

Sir: The seaweeds have developed very effective enzyme systems for utilizing halide ions in synthesis of halogenated terpenes.² Marine red algae (*Rhodophyta* phylum), especially members of the genera *Laurencia* and *Plocamium*, have proved to be quite adept at halogen atom incorporation.³ Certain mollusk herbivores consume such algae and accumulate some of the halogenated constituents for their chemical defense mechanism. A useful illustration is provided by the gastropod (subclass Opisthobranchia) *Aplysia californica* feeding on *Laurencia* and *Plocamium* seaweeds.⁴

Two new dibromoditerpenes, irieol A (1) and iriediol (2), were recently isolated from a Gulf of California *Laurencia* sp. by Fenical and colleagues,⁵ and X-ray crystallographic methods were used to derive structures 1 and 2. But assign-



ment of absolute configurations could not be made with certainty and structure 2 according to the crystallographic data should represent the A/B ring enantiomer of 1. We now wish to report that the South Pacific Ocean (East Australia) sea hare *Aplysia angasi* contains an apparently related dibromoditerpene designated angasiol (3), that accompanies the cytotoxic component aplysiastatin (4).⁶ The discovery of an-



gasiol provides the first evidence that some sea hares may store exogenous dibromoditerpenes of the new irieol A type for certain biosynthetic processes.⁷ After the absolute configuration of angasiol had been established by X-ray methods, comparison with irieol A (1) revealed the same absolute configuration at six chiral centers, according to the original tentative assignment for 1.^{1,2}

Angasiol (3) was isolated (Supplementary Material) from a chloroform-soluble fraction in turn obtained through a solvent-partitioning sequence applied to a 2-propanol extract of *Aplysia angasi*. Careful chromatography using a Merck size C prepacked column⁸ and elution with 9:1 ligroin-ethyl acetate led to angasiol (3, 0.007% yield, as needles from acetone-hexane, mp $189\text{--}191^\circ\text{C}$) corresponding to empirical formula $\text{C}_{20}\text{H}_{30}\text{Br}_2\text{O}_3$: mass spectrum m/e , 458/460/462 ($\text{M} - \text{H}_2\text{O}$), 379/381 ($\text{M} - \text{H}_2\text{O} - \text{Br}$), 378/380 ($\text{M} - \text{H}_2\text{O} - \text{HBr}$); ORD and CD in methanol gave positive plain curves; IR (KBr) 3500 (s), 1765, 1210, 1150, and 575 cm^{-1} . The broad band decoupled ^{13}C NMR spectrum⁹ of angasiol revealed the presence of 20 carbon atoms, and the off-resonance decoupled spectrum confirmed the molecular formula. The ^{13}C NMR spectra indicated the presence of a γ -lactone carbonyl (δ 176.56) and an associated tertiary alkoxy group (83.55), a tertiary alcohol (72.43), two quaternary carbon atoms without