

1 h. After 7 h the mixture was allowed to warm to room temperature, and it was then concentrated to 25 mL and extracted with five 25-mL portions of propylene carbonate. The pentane layer was evaporated to give a white solid, mp 90–92 °C. The spectral properties of this material are reported in Table I.

Preparation of Pentabenzoyloxyphosphorane (26). Neither benzyl benzenesulfonate nor tribenzyl phosphite could be distilled without decomposition. These materials were prepared in the usual manner and used as obtained. Their spectral properties are recorded in Table I.

A solution of 0.216 g (0.001 mol) of benzyl benzenesulfonate in a few milliliters of carbon tetrachloride was added at 0 °C to a solution of 0.176 g (0.0005 mol) of tribenzylphosphite in a few milliliters of carbon tetrachloride. The ³¹P NMR spectrum of the reaction mixture 30 min after mixing showed two major absorptions in a 1:1 ratio at δ 0 and +69. The first absorption is due to phosphite and the second is due to phosphorane. After 3 days the phosphorane had completely decomposed.

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Reaction of 1,4-Diiodonorbornane, 1,4-Diiodobicyclo[2.2.2]octane, and 1,5-Diiodobicyclo[3.2.1]octane with Butyllithium. Convenient Preparative Routes to the [2.2.2]- and [3.2.1]Propellanes¹

Kenneth B. Wiberg,*^{2a} William E. Pratt,^{2a} and William F. Bailey*^{2b}

Contribution from the Department of Chemistry, Yale University, New Haven, Connecticut 06520, and the Department of Chemistry, University of Connecticut, Storrs, Connecticut 06268. Received September 20, 1976

Abstract: The reactions of 1,4-diiodobicyclo[2.2.2]octane and 1,5-diiodobicyclo[3.2.1]octane with *tert*-butyllithium provide convenient synthetic routes to the [2.2.2]- and [3.2.1]propellanes. The corresponding reaction of 1,4-diiodonorbornane gave 1-*tert*-butyl-4-iodonorbornane as a major product. Whereas 1,4-dibromonorbornane did not react with *tert*-butyllithium, 1-bromo-4-iodonorbornane did react and again gave 1-*tert*-butyl-4-iodonorbornane. The replacement of bromine rather than iodine indicates that both halogens are involved in the reaction and suggests that the [2.2.1]propellane may be an intermediate.

The intriguing properties of small-ring propellanes,³ a class of compounds in which all four bonds to a carbon atom are constrained to lie on one side of a plane, have stimulated considerable synthetic and theoretical interest. Although elegant synthetic approaches to a number of small-ring propellanes have been reported,³ most syntheses are limited in that they are not generally applicable to the synthesis of other highly strained propellanes. For this reason, we have been investigating routes to this class of tricyclic hydrocarbons which involve reduction of a suitably bridgehead–bridgehead di-

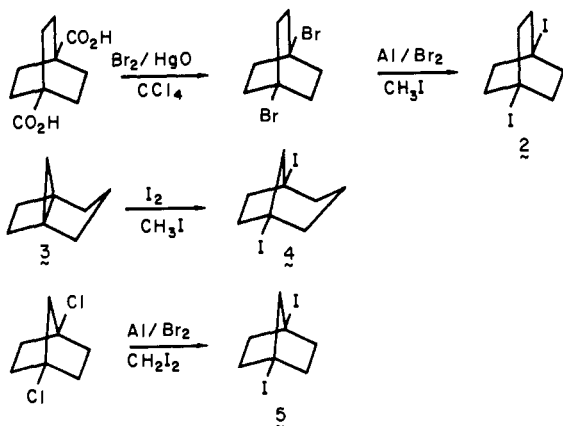
substituted bicyclic hydrocarbon. Our initial goal was the preparation of the elusive [2.2.1]propellane⁵ (1).

Whereas the electrochemical reduction of 1,5-dibromobicyclo[3.2.1]octane⁶ and 1,4-dibromobicyclo[2.2.2]octane⁷ led to the formation of the corresponding propellanes, the analogous reduction of 1,4-dibromonorbornane failed to give the [2.2.1]propellane (1) or any monomeric product which could unambiguously be attributed to the intermediacy of the [2.2.1]propellane.⁸ In a search for other methods by which the conversion might be effected, the reaction of bridgehead–

bridgehead dihalides with butyllithium reagents was examined. A precedent for this approach is found in the report by Pincock⁹ that substituted 1,3-dehydroadamantanes (derivatives of the [3.3.1]propellane) could be prepared from 1,3-dibromoadamantanes by dehalogenation with *n*-butyllithium.

Lansbury and Sidler have shown that the reaction of *tert*-butyllithium with 1-iodonorbornane affords essentially quantitative conversion to 1-norbornyllithium.^{10,11} For this reason, the iodides were used in the metal-halogen exchange reactions. The diiodo compounds were prepared as shown in Scheme I. The Hunsdiecker reaction used to prepare 1,4-

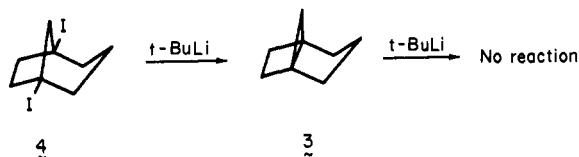
Scheme I



dibromobicyclo[2.2.2]octane proceeded in moderate yield. The conversion of this dibromide to 2 was effected in high yield using a reaction medium prepared¹² from aluminum foil and a catalytic amount of bromine in methyl iodide. A pure sample of 4 was most conveniently obtained by addition of iodine to the [3.2.1]propellane (3).^{13,14} The conversion of the readily obtained 1,4-dichloronorbornane¹⁵ to 5 has already been described.^{8,12}

The reduction of 4 with *tert*-butyllithium (Scheme II)

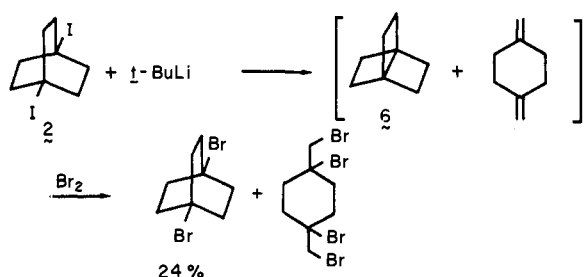
Scheme II



proceeds rapidly to afford a 59% yield of the [3.2.1]propellane (3). In accord with the predictions of Stohrer and Hoffmann concerning the stability of 3 in the presence of base,¹⁶ this propellane is inert to the action of *tert*-butyllithium at room temperature. The limiting factor to the synthesis of large quantities of 3 would appear to be the availability of the precursor diiodide 4.

In the reaction of 2 with *tert*-butyllithium, the isolation of the [2.2.2]propellane¹⁷ (6) was avoided because of its thermal instability.^{18,19} The reaction mixture was treated with bromine at -77°C and 1,4-dibromobicyclo[2.2.2]octane was isolated in 24% yield based on starting diiodide (Scheme III). The re-

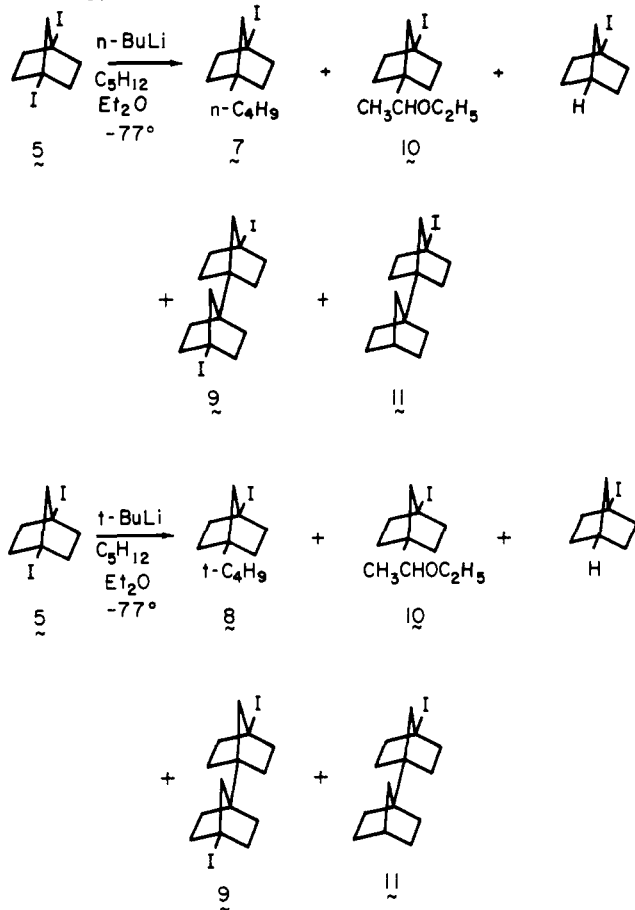
Scheme III



mainder of the product was 1,4-bis(bromomethyl)-1,4-dibromocyclohexane,²⁰ derived from 1,4-dimethylenecyclohexane. Although some Grob fragmentation product was obtained,^{16,21} this reductive dehalogenation is clearly an effective way in which to prepare the [2.2.2]propellane.

The reaction of 5 with an alkylolithium would be expected to proceed in analogous fashion. It is known, for example, that 1-iodonorbornane reacts with *tert*-butyllithium to give 1-norbornyllithium^{10,11} and, under the conditions used to prepare 3 and 6, this reaction is virtually quantitative. However, the course of the reaction of 5 with either *n*-butyllithium or *tert*-butyllithium proved to be quite different than that of the analogous dihalides discussed above. It was found that treatment of 5 with these alkylolithium reagents (Scheme IV) affords

Scheme IV



either 1-*n*-butyl-4-iodonorbornane (7) or 1-*tert*-butyl-4-iodonorbornane (8) as the major product. In both reactions, 4,4'-diiodobisnorbornane (9) was a major product along with smaller amounts of 1-(1'-ethoxyethyl)-4-iodonorbornane (10), 4-iodobisnorbornane (11), and 1-iodonorbornane. The possibility that some of these products were the result of subsequent reactions of long-lived norbornyllithium intermediates was investigated in a series of quenching experiments using both carbon dioxide and deuterium oxide. No evidence for the existence of such intermediates was found. It is also significant that no 1,3-dimethylenecyclopentane⁸ was detected in any of the reactions of 5 with butyllithium, although, a priori, the diene could have been formed either by the thermal cleavage of 1 (if produced) or via a Grob fragmentation of 5.^{16,21}

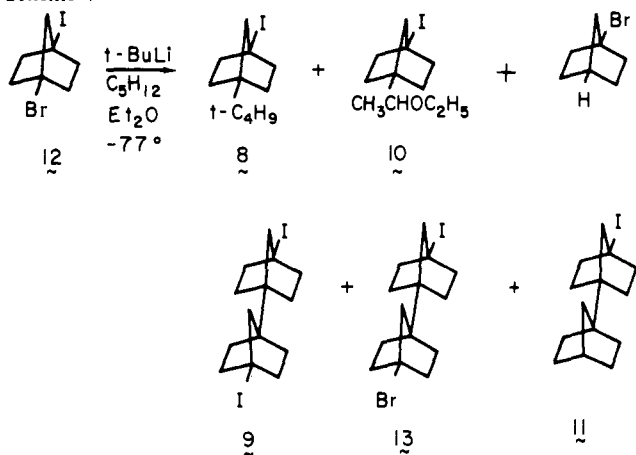
The predominant formation of products formally analogous to those which would arise from Wurtz-type coupling upon treatment of 5 with butyllithium must be considered in contradistinction to the fact that the metal-halogen interchange product, 1-norbornyllithium, is formed exclusively in the reaction of 1-iodonorbornane with *tert*-butyllithium.²² Clearly,

products **7**, **8**, **9**, and **11** (Scheme IV) could not have been formed by a simple nucleophilic displacement of iodide by a substituted 1-norbornyllithium. Moreover, while it is tempting to attribute formation of the products shown in Scheme IV to long-lived radical intermediates, such a rationale is inconsistent with the body of evidence which demonstrates that, whereas the 1-norbornyl radical is relatively *unstable*,²³ the 1-norbornyl anion appears to possess unusual stability.^{10,11}

It seemed important to establish the role of the second halogen in these reactions since, as noted above, the monoiodide undergoes a normal metal-halogen interchange.²² The second bridgehead halogen could serve to modify the stabilities of intermediates²⁴ in the metal-halogen interchange or it could actively participate in the reaction. Since we have observed that neither 1,4-dibromonorbornane nor 1-bromonorbornane reacts with *tert*-butyllithium under the conditions employed in the reactions of **5** with alkylolithiums, we felt that 1-bromo-4-iodonorbornane (**12**) would be useful in distinguishing between these possibilities. If only one halogen actively participates in the reaction, the iodine should be lost from **12** and 1-*tert*-butyl-4-bromonorbornane should be formed. On the other hand, if both halogens are actively involved in the reaction, **8** may be formed with the apparent loss of bromide as will be shown below.

It was possible to prepare the bromoiodide, **12**, by the reaction of 1,4-dichloronorbornane¹⁵ with the reagent formed from aluminum foil and a mixture of dibromo- and diiodomethane containing a small amount of bromine. The reaction of **12** with *tert*-butyllithium (Scheme V) gave essentially the

Scheme V

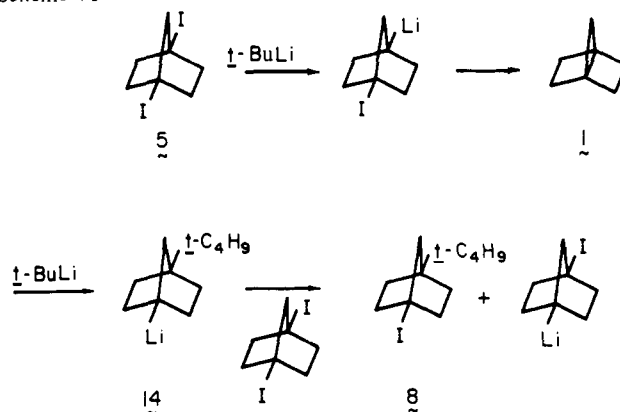


same products as those formed from **5** (Scheme IV). The only bromine containing compounds which were isolated were 1-bromonorbornane²⁵ and 4-bromo-4'-iodobisnorbornane (**13**).

If one concurs with the commonly accepted view that radical anions formed by adding an electron to an alkyl halide have very short lifetimes ($\sim 10^{-7}$ s), then the reactions would appear to proceed largely through the [2.2.1]propellane, **1**, as an intermediate (Scheme VI). With about 20 kcal/mol greater strain than the [3.2.1]propellane,¹⁴ **1** may well add *tert*-butyllithium^{26,27} giving **14**. A second metal-halogen interchange with the starting material would give the observed product, **8**. This proposal requires that **14** be more reactive toward **5** than is *tert*-butyllithium.²⁸

The principal difficulty with this reaction scheme arises from the formation of more 4,4'-diiodobisnorbornane (**9**) than 4-bromo-4'-iodobisnorbornane (**13**) when 1-bromo-4-iodonorbornane (**12**) was used (Scheme V). While a number of explanations are possible, all are highly speculative.^{26,27} The formation of minor amounts of **10** is consistent with abstraction of the α hydrogen in diethyl ether by alkylolithium and reactions of this intermediate²⁶ with the [2.2.1]propellane. Recent in-

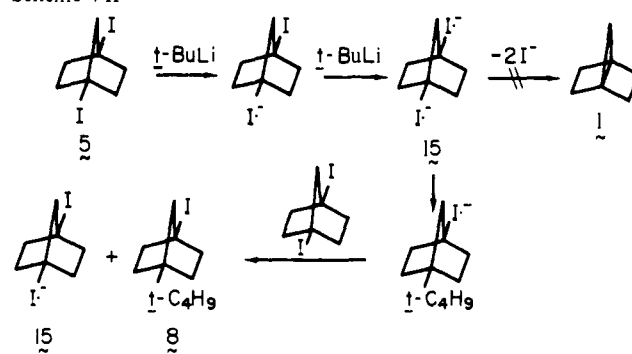
Scheme VI



vestigations of the Wittig rearrangement of ethers^{11,29} indicate that the initial step of this reaction involves abstraction of the α hydrogen by strong base. The carbanionic intermediate thus formed from diethyl ether may be expected to add to the strained [2.2.1]propellane to give the small quantities of **10** isolated in these reactions.

If the radical anion which may be formed via one-electron transfer between the halide and alkylolithium as the first step of the interchange reaction^{24,27} has a significant lifetime, another set of reactions may also be considered (Scheme VII).

Scheme VII



The second electron transfer may now go to the other halogen, giving the dianion-radical **15**. In the case of most 1,3- or 1,4-dihalides, the ring closed product could arise from a concerted reaction of such species. If the energetics of the reaction forming propellane, **1**, are unfavorable, one of the halogens may be lost as halide ion and be replaced by *tert*-butyl. The remaining electron could then be transferred to 1,4-diiodonorbornane, a reaction which could be expected to be exothermic. While this rationale is consistent with the reaction of the diiodide (**5**), it does not appear to be a reasonable explanation for the reactivity of 1-bromo-4-iodonorbornane (Scheme V). Since neither 1,4-dibromonorbornane nor 1-bromonorbornane reacts with *tert*-butyllithium, it seems highly unlikely that an electron would be transferred to the bromine atom of **12** to give the observed loss of bromine (cf. Scheme V).

Thus, of all the possibilities presented, Scheme VI, involving the intermediacy of the [2.2.1]propellane (**1**), best explains the results which have been obtained.

Experimental Section

Melting points were determined on a Hoover-Thomas melting point apparatus and are uncorrected. Boiling points are uncorrected. Proton magnetic resonance spectra were recorded on Jeol-MH-100, Perkin-Elmer R-32, or Bruker XH-270 instruments and shifts are referenced with respect to internal Me₄Si. Carbon magnetic resonance spectra were obtained on either a Varian CFT-20 or Bruker XH-270 spectrometer, and shifts are referenced with respect to internal Me₄Si.

Preparative GLC was effected with an Aerograph A-90-P chromatograph equipped with 0.25 in. aluminum and stainless-steel columns. High-resolution mass spectra were obtained on an AEI-MS-902 mass spectrometer at 70 eV. Microanalyses were performed by Atlantic Microlab, Inc.

The preparation of 1,4-diiodonorbornane (**5**) has been described.^{8,12} We are grateful to Dr. J. C. Kauer (E. I. du Pont de Nemours and Co.) for a generous gift of bicyclo[2.2.2]octane-1,4-dicarboxylic acid.^{30,31} The concentration of commercial alkyllithium solutions (Ventron) was determined immediately before use by the method of Watson and Eastham.³²

1,4-Dibromobicyclo[2.2.2]octane. A mixture of 3.80 g (19.2 mmol) of bicyclo[2.2.2]octane-1,4-dicarboxylic acid,^{30,31} 6.73 g (31.0 mmol) of red mercuric oxide, and 4.80 g (40.0 mmol) of magnesium sulfate in 150 mL of dry 1,2-dibromoethane was heated, with stirring, to 75 °C, and a solution of 6.40 g (40.0 mmol) of bromine in 60 mL of dry 1,2-dibromoethane was added dropwise to the stirred mixture. After addition was complete, the mixture was heated, with stirring, at 75 °C overnight. The reaction mixture was cooled and filtered through Celite, and the filtrate was washed successively with two 100-mL portions of saturated aqueous sodium bicarbonate and 100 mL of brine. After drying (MgSO₄), the extract was concentrated at reduced pressure to give a solid mass which was recrystallized from hot acetone to afford 2.1 g (40%) of the dibromide, mp 252–253.5 °C (lit.¹² mp 251 °C, lit.³¹ mp 256.6–258.0 °C); ¹H NMR (CDCl₃) δ 2.40 (s).

1,4-Diiodobicyclo[2.2.2]octane (2). Following the general procedure of McKinley, Pincock, and Scott,¹² narrow strips of common aluminum foil (522 mg, 19.5 mmol) were placed in a 250-mL round-bottomed flask filled with a magnetic stirrer, reflux condenser with drying tube, and an immersion thermometer. To this flask was added 75 mL of methyl iodide and 200 μL (3.90 mmol) of bromine. The mixture was heated at reflux for 3 h during which time the aluminum foil reacts to give an opaque orange-yellow suspension. This mixture was cooled to room temperature and 1.57 g (5.86 mmol) of 1,4-dibromobicyclo[2.2.2]octane was added at once. Stirring was continued at room temperature for 8.5 min before the contents of the flask were poured into 75 mL of cold water. The organic phase was separated, the aqueous layer was washed with two 20-mL portions of ether, and the combined organic extracts were washed successively with two 20-mL portions of 10% aqueous sodium bicarbonate, 20 mL of water, and 20 mL of brine. After drying (Na₂SO₄), the solvent was removed at reduced pressure to afford a pale-yellow solid which was recrystallized from methylene chloride–pentane (1:1) by slow evaporation of the solvent to give 1.69 g (81%) of the diiodide as needles, mp 245–246 °C (lit.¹² 240 °C, lit.³¹ 245–246 °C); ¹H NMR (CDCl₃) δ 2.60 (s).

The diiodide was also prepared from 1,4-dichlorobicyclo[2.2.2]octane in an analogous manner, as described by McKinley, Pincock, and Scott.¹² However, preparation of the dichloride precursor from bicyclo[2.2.2]octane-1,4-dicarboxylic acid using a modified Kochi reaction³³ resulted in a low yield (ca. 20%) of product.

1,5-Diiodobicyclo[3.2.1]octane (4). A solution of 2.00 g (18.5 mmol) of tricyclo[3.2.1.0^{1,5}]octane¹⁴ (**3**) in 20 mL of methyl iodide containing 100 mg of anhydrous potassium carbonate was cooled, under argon to –70 °C. To this solution was added 5.0 g of iodine (20 mmol) in 15 mL of methyl iodide over the course of 10 min at –70 °C. The reaction mixture was allowed to warm to room temperature and washed successively with two 15-mL portions of 10% aqueous sodium thiosulfate, 10 mL of water, and 10 mL of brine. After drying (MgSO₄), the solvent was removed at reduced pressure to afford an oil which was purified by elution from a short neutral alumina column with pentane to give 5.46 g (82%) of the diiodide as a clear oil. An analytical sample was prepared by preparative GLC on a 5-ft, 1.5% OV-101 on Anakrom ABS (80–100 mesh) column at 200 °C: IR (neat) 1250 (s), 800 (s), 730 (s) cm⁻¹; ¹H NMR (CDCl₃) δ 1.29–1.34 (m, 1 H), 1.73–1.79 (m, 1 H), 2.13–2.53 (m, 8 H), 2.67 (B portion of ABX₂, J_{AB} = 11.0 Hz, J_{BX} ≈ 0 Hz, 1 H), 3.08 (A portion of ABX₂, J_{AB} = 11.0 Hz, J_{AX} = 0.21 Hz, 1 H). Anal. (C₈H₁₂I₂): C, H, I.

1,4-Bis(bromomethyl)-1,4-dibromocyclohexane. The procedure of Lautenschlager and Wright was followed in the bromination of 1,4-dimethylenecyclohexane,²⁰ prepared from cyclohexane-1,4-dione using a modified Wittig reaction.³⁴ As described,²⁰ the reaction afforded an isomerically pure tetrabromide: mp 134–136 °C (lit.²⁰ mp 134–135 °C; ¹H NMR (CDCl₃) δ 2.1–3.1 (tightly coupled A₂A₂'-B₂B₂', 8 H), 4.50 (s, 4 H).

1-Bromo-4-iodonorbornane (12). To a mixture of 69 mL (0.84 mol)

of diiodomethane and 31 mL (0.42 mol) of dibromomethane, under nitrogen, was added 1.20 g (0.40 mol) of common aluminum foil and 0.50 mL of bromine. The mixture was heated at 110 °C for 30 min during which time the aluminum reacts to give a deep red-black suspension. To this suspension was added 4.52 g (25.8 mmol) of 1,4-dichloronorbornane¹⁵ and stirring was continued at 110 °C for 1.1 h. After cooling to room temperature, the contents of the flask were diluted with 300 mL of pentane–ether (1:1) and washed successively with three 50-mL portions of 10% aqueous sodium thiosulfate, 20 mL of water, and two 20-mL portions of brine. After drying (MgSO₄), the solvent was removed at reduced pressure to afford a black oil which was bulb-to-bulb distilled [ca. 150 °C (0.1 mm)] to give a yellow oil contaminated with diiodomethane.

The combined crude oil from three reactions run as described above (ca. 12–16 mL) was shaken with a solution of silver nitrate (10 g) in water (50 mL) until colorless. The oil was taken up in ether, dried (MgSO₄), and concentrated at reduced pressure to give a light-brown mass which was found, by analytical GLC on a 10-ft, 30% SE-30 on Anakrom A (60/80 mesh) column at 150 °C, to contain (in order of elution): 1,4-dibromonorbornane⁸ (40%), 1-bromo-4-iodonorbornane (47%, vide infra), and 1,4-diiodonorbornane (12.5%). Pure 1-bromo-4-iodonorbornane was isolated by preparative GLC on a 3-m, 3/4 in. o.d. "bi-wall" column packed with 20% FFAP on Anakrom A (50/60 mesh) at 180 °C. The combined yield from three runs was 1.64 g of product (14% yield based on 47% conversion); mp 64.5–65 °C; ¹H NMR (CDCl₃) δ 2.25–3.00 (m, 8 H), 2.87 (s, 2 H). Anal. (C₇H₁₀BrI): C, H, Br, I.

Tricyclo[3.2.1.0^{1,5}]octane (3). A solution of 742.2 mg (2.00 mmol) of 1,5-diiodobicyclo[3.2.1]octane in 20 mL of dry pentane–ether (3:1) was cooled to –77 °C under argon. To this stirred solution was added 4.20 mL of 0.50 M *tert*-butyllithium in pentane. The mixture was stirred for 3 min at –77 °C, during which time a precipitate formed, and the cooling bath was removed. After warming to room temperature, water (5 mL) and brine (2 mL) were added to the reaction mixture. The organic layer was separated, washed with two 10-mL portions of water and 10 mL of brine, dried (MgSO₄), and concentrated by distillation of the solvent under argon to give a 59% yield of the tricyclooctane (determined by analytical GLC). Preparative GLC on a 12-ft, 20% DC-710 on Anakrom U (60–80 mesh) column at 120 °C afforded pure product identical with authentic [3.2.1]propellane:¹⁴ ¹³C NMR³⁵ (CD₂Cl₂) δ 22.3, 24.2, 25.0 [C (1, 5)], 29.9, 32.9.

Tricyclo[2.2.2.0^{1,4}]octane (6). Preparation and Trapping. A solution of 686 mg (1.9 mmol) of 1,4-diiodobicyclo[2.2.2]octane (prepared from 1,4-dichlorobicyclo[2.2.2]octane) in 64 mL of dry pentane–ether (3:1) was cooled to –77 °C. To this stirred suspension was added 3.90 mL of 0.50 M *tert*-butyllithium in pentane. The resulting mixture was stirred for 11 min at –77 °C before the addition of 1.3 mL (ca. 20 mmol) of bromine. After warming to room temperature, the excess bromine was discharged by washing with 10% aqueous sodium thiosulfate, and a known quantity of adamantane was added as an internal standard. The organic extract was then washed with two 15-mL portions of water and 15 mL of brine and dried (MgSO₄). Analysis of the solution by GLC on a 10-ft, 20% SE-30 on Anakrom U (60–80 mesh) column at 140 °C revealed that the reaction had afforded 24 ± 2% 1,4-dibromobicyclo[2.2.2]octane and 76 ± 2%, isomerically pure, 1,4-bis(bromomethyl)-1,4-dibromocyclohexane.²⁰

In an independent experiment, the dehalogenation was run as described above, and the dry organic extract was concentrated at reduced pressure to give a white, crystalline solid. Isomerically pure 1,4-bis(bromomethyl)-1,4-dibromocyclohexane, mp 134–136 °C (lit.²⁰ mp 134–135 °C), was isolated by fractional crystallization from ligroin–ether (2:1) by slow evaporation. Pure 1,4-dibromobicyclo[2.2.2]octane, mp 252–253 °C (lit.¹² mp 251 °C, lit.³¹ mp 256.6–258.0 °C), was isolated from the mother liquor concentrate by preparative GLC on a 10-ft, 20% SE-30 on Anakrom U (60–80 mesh) column at 150 °C.

Reaction of 1-Iodonorbornane with *tert*-Butyllithium. Preparation of 1-(1'-Norboryl)ethanol. A solution of 1.00 g (4.5 mmol) of 1-iodonorbornane¹¹ in 28 mL of dry pentane–ether (1:3) was cooled to –77 °C under nitrogen. To this stirred solution was added 6.13 mL of 0.74 M *tert*-butyllithium in pentane. The resulting mixture was stirred for 30 min at –77 °C before the addition of 0.3 mL (ca. 8 mmol) of acetaldehyde. The cooling bath was removed and the mixture was allowed to warm, with stirring, to room temperature and partitioned between 25 mL of ether and 10 mL of 10% aqueous hydrochloric acid. The ethereal layer was separated and washed suc-

cessively with 10 mL of saturated aqueous sodium bicarbonate and 10 mL of brine. After drying (MgSO_4), the solvent was removed at reduced pressure to afford a virtually quantitative yield of 1-(1'-norbornyl)ethanol. An analytical sample was prepared by GLC on a 14-ft Carbowax 20M on Anakrom ABS column at 180 °C: $^1\text{H NMR}$ (CDCl_3) δ 1.04–1.68 (m, 16 H) with a 3 H doublet centered at 1.17 (CH_3 , $J = 6.4$ Hz), 2.20 (m, 1 H, bridgehead), 3.91 (q, 1 H, $J = 6.4$ Hz); IR (neat) 3100–3660 (OH), 2965, 2890, 1085 cm^{-1} . Mass spectrometric molecular weight, calcd for $\text{C}_9\text{H}_{16}\text{O}$: 140.120 19; found: 140.120 10.

Under the same conditions, 1-bromonorbornane²⁵ did not react with *tert*-butyllithium.

Treatment of 1,4-Dibromonorbornane with *tert*-Butyllithium. A solution of 1.27 g (5.0 mmol) of 1,4-dibromonorbornane^{8,12} in 27 mL of dry pentane-ether (1:3) was cooled to -77 °C under nitrogen. To this stirred suspension was added 3.85 mL of 1.3 M *tert*-butyllithium in pentane. The resulting mixture was stirred for 30 min at -77 °C before the addition of 0.34 mL (ca. 9 mmol) of acetaldehyde. The cooling bath was removed, and the mixture was allowed to warm to room temperature and partitioned between 25 mL of ether and 10 mL of 10% aqueous hydrochloric acid. The ethereal layer was separated and washed successively with 10 mL of saturated aqueous sodium bicarbonate and 10 mL of brine. After drying (MgSO_4), the solvent was removed at reduced pressure to afford a virtually quantitative recovery of 1,4-dibromonorbornane, mp 73 °C (lit.⁸ mp 73.5–74 °C, lit.¹² mp 73 °C).

Reaction of 1,4-Diiodonorbornane (5) with *tert*-Butyllithium. In these experiments, pentane-ether solvent mixtures of both 1:3 and 3:1 (volume:volume) were used with completely analogous results (vide infra). Less starting material was recovered (more nearly complete conversion was observed) when the pentane-ether (1:3) solvent system was employed.

A solution of 1.05 g (3.03 mmol) of 1,4-diiodonorbornane in 56 mL of dry pentane-ether (1:3) was cooled to -77 °C under nitrogen. To this stirred suspension (**5** was not completely soluble at -77 °C) was added 5.00 mL of 0.61 M *tert*-butyllithium in pentane. After stirring the resulting mixture for 30 min at -77 °C, 5 mL of water was added and the cooling bath was removed. When stirring was continued for only 10 min prior to the addition of water, the only substantive difference in the course of the reaction (vide infra) was the isolation of larger amounts of unreacted **5**.

After warming to room temperature, 5 mL of brine was added to the reaction mixture. The organic layer was separated, washed with two 10-mL portions of water and 10 mL of brine, dried (MgSO_4), and concentrated by evaporation of the solvent under a stream of dry nitrogen. The product mixture was analyzed, and the component fractions were separated by GLC on either a 14-ft, 30% SE-30 on Anakrom U (60–80 mesh) column at 140 °C, 12-ft, 20% OV-17 on Anakrom ABS (50–60 mesh) column at 150 °C (both for volatile components), or a 5-ft, 1.5% OV-101 on Anakrom ABS (80–100 mesh) column from 150 to 250 °C (manually increased). The major volatile component, identified by comparison with an authentic sample (IR, ms, $^1\text{H NMR}$), was 1-iodonorbornane¹¹ (7% relative area ratio). No 1,3-dimethylenecyclopentane⁸ was detected. The following compounds, identified on the basis of their physical and spectral properties (vide infra), were eluted by progressively increasing the oven temperature (relative, uncorrected area ratios in parentheses): 1-*tert*-butyl-4-iodonorbornane (**8** 47%), unreacted **5** (13%), 1-(1'-ethoxyethyl)-4-iodonorbornane (**10**, 5%), 4-iodobisnorbornane (**11**, 2%), and 4,4'-diiodobisnorbornane (**9**, 27%).

An analytical sample of 1-*tert*-butyl-4-iodonorbornane (**8**) was prepared by sublimation at 35–40 °C (10–15 mm): mp 44–45.5 °C; $^1\text{H NMR}$ (CDCl_3) δ 0.90 (s, 9 H), 1.2–1.3 (m, 4 H), 1.86 (apparent s, 2 H), 1.7–2.4 (m, 4 H); $^{13}\text{C NMR}$ (CDCl_3) δ 26.6 ($-\text{C}(\text{CH}_3)_3$), 31.3 ($-\text{C}(\text{CH}_3)_3$), 32.4 (C(2,6)), 38.3 (C(1) or C(4)), 44.2 (C(3, 5)), 50.7 (C(7)), 52.2 (C(4) or C(1)). Anal. ($\text{C}_{11}\text{H}_{19}\text{I}$): C, H, I. Mass spectroscopic molecular weight, calcd for $\text{C}_{11}\text{H}_{19}\text{I}$: 278.0535; found: 278.0535.

1-(1'-Ethoxyethyl)-4-iodonorbornane (10). $^1\text{H NMR}$ (CDCl_3) δ 1.07 (d, $J = 6.5$ Hz, 3 H, $\text{CH}_3\text{CH}-$), 1.16 (X portion of ABX_3 , $J_{\text{AX}} = J_{\text{BX}} = 6.9$ Hz (apparent triplet)), 3 H, ($\text{CH}_3\text{CH}_2\text{O}-$), 3.37 (B portion of ABX_3 , $J_{\text{AB}} = 9.3$ Hz, $J_{\text{BX}} = 6.9$ Hz, 1 H, $\text{CH}_3(\text{H})\text{CHO}-$), 3.43 (q, $J = 6.5$ Hz, 1 H, $\text{CH}_3\text{CH}-$), 3.60 (A portion of ABX_3 , $J_{\text{AB}} = 9.3$ Hz, $J_{\text{AX}} = 6.9$ Hz, 1 H, $\text{CH}_3(\text{H})\text{CHO}-$). Anal. ($\text{C}_{11}\text{H}_{19}\text{OI}$): C, H.

4-Iodobisnorbornane (11). Mass spectroscopic molecular weight, calcd for $\text{C}_{14}\text{H}_{21}\text{I}$: 316.0691; found: 316.0679.

4,4'-Diiodobisnorbornane (9). Mp 169–170 °C; $^1\text{H NMR}$ (CDCl_3) δ 2.15 (m, 4 H), 2.03 (m, 4 H), 1.83 (s, 4 H), 1.67 (m, 4 H), 1.31 (m, 4 H); mass spectroscopic molecular weight, calcd for $\text{C}_{14}\text{H}_{20}\text{I}_2$: 441.9663; found: 441.9661.

In an attempt to trap any norbornyllithiums which may have been present in the reaction mixture, the reaction of **5** with *tert*-butyllithium was repeated as described above. After stirring at -77 °C for 5 min, an excess of solid dry carbon dioxide was added to the reaction mixture. After acidification, the neutral and acidic fractions were separated. Analysis of the neutral fraction revealed the presence of the products described above. The acidic fraction contained only small amounts of high molecular weight, iodine containing carboxylic acid (apparently derived from **9**). No mononorbornane carboxylic acids were detected. Moreover, when D_2O (rather than H_2O) was added to the reaction mixture at -77 °C, the 1-iodonorbornane produced was not enriched in deuterium.

Reaction of 1,4-Diiodonorbornane (5) with *n*-Butyllithium. A suspension of 350 mg (1.00 mmol) of 1,4-diiodonorbornane in 30 mL of dry pentane-ether (3:1) was cooled to -77 °C under helium. To this stirred mixture was stirred for 10 min at -77 °C, 5 mL of water was added, and the cooling bath was removed. After warming to room temperature, 5 mL of brine was added to the reaction mixture. The organic layer was separated, washed with two 10-mL portions of water and 10 mL of brine, dried (MgSO_4), and concentrated by evaporation of the solvent under a stream of dry nitrogen. The product mixture was analyzed, and the component fractions were separated, as described above for the analogous reaction with *tert*-butyllithium. Products are shown in Scheme IV. As above, no 1,3-dimethylenecyclopentane was detected, and no mononorbornanecarboxylic acids were detected when the reaction mixture was quenched with carbon dioxide.

1-*n*-Butyl-4-iodonorbornane (7). $^1\text{H NMR}$ (CDCl_3) δ 0.92 (distorted triplet, 3 H), 1.1–1.7 (m, 10 H), 1.83 (apparent singlet, 2 H), 1.9–2.5 (m, 4 H). Anal. ($\text{C}_{11}\text{H}_{19}\text{I}$): C, H, I.

Reaction of 1-Bromo-4-iodonorbornane (12) with *tert*-Butyllithium. A solution of 1.10 g (3.6 mmol) of 1-bromo-4-iodonorbornane in 28 mL of dry pentane-ether (1:3) was cooled to -77 °C under nitrogen. To this solution was added 3.20 mL of 1.24 M *tert*-butyllithium in pentane. The resulting mixture was stirred for 30 min at -77 °C before the addition of 0.3 mL (ca. 8 mmol) of acetaldehyde. The cooling bath was removed, the mixture allowed to warm, with stirring, to room temperature and partitioned between 25 mL of ether and 10 mL of 10% aqueous hydrochloric acid. The ethereal layer was separated, washed successively with 10 mL of saturated aqueous sodium bicarbonate and 10 mL of brine, dried (MgSO_4), and concentrated. The product mixture was analyzed, and the component fractions were separated by GLC as described above in the reaction of **5** with *tert*-butyllithium. The following compounds were identified on the basis of their physical and spectral properties (relative, uncorrected area ratios in parentheses): 1-bromonorbornane (14%) identical by IR, $^1\text{H NMR}$, and ms to an authentic sample,²⁵ 1-*tert*-butyl-4-iodonorbornane (**8**, 39%), unreacted **12** (20%), 1-(1'-ethoxyethyl)-4-iodonorbornane (**10**, 3%), 4-iodobisnorbornane (**11**, 2%), 4-bromo-4'-iodobisnorbornane (**13**, 6%), 4,4'-diiodobisnorbornane (**9**, 16%).

4-Bromo-4'-iodobisnorbornane (13). Mass spectroscopic molecular weight, calcd for $\text{C}_{14}\text{H}_{20}\text{BrI}$: 393.9797; found: 393.9792.

Treatment of Tricyclo[3.2.1.0^{1,5}]octane (3) with *tert*-Butyllithium. A solution of 550 mg (5.1 mmol) of tricyclo[3.2.1.0^{1,5}]octane in 15 mL of dry pentane-ether (3:1) was cooled to -77 °C under argon and 9 mL of 0.74 M *tert*-butyllithium in pentane was added via syringe. After stirring for 30 min at -77 °C, the cooling bath was removed, and the solution was allowed to warm to room temperature. After standing 2 h at room temperature, 10 mL of water was added, and the dried organic phase was analyzed by GLC on a 12-ft, 20% DC-710 on Anakrom U (60–80 mesh) column at 120 °C. Only starting material could be detected. Evaporation of the solvent under a stream of argon afforded virtually quantitative recovery of tricyclo[3.2.1.0^{1,5}]octane.

References and Notes

- (1) (a) This investigation was supported by Grant No. MPS74-19380 from the National Science Foundation and in part by Grant No. 350344 from the Research Foundation of the University of Connecticut. Acknowledgment is also made to the Donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

- (b) This investigation was supported in part (270-mHz NMR) by National Institutes of Health Research Grant No. 1-P07-PR00798 from the Division of Research Resources.
- (2) (a) Yale University; (b) University of Connecticut.
- (3) The propellane nomenclature has been introduced (ref 4) to describe tricyclic compounds whose three rings share a common bond. For recent reviews, see: D. Ginsburg, "Propellanes", Verlag Chemie, Weinheim/Bergstr., Germany, 1975; D. Ginsburg, *Acc. Chem. Res.*, **5**, 249 (1972).
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- (26) It is by no means clear that the actual attacking species is an anion. The nature of reactions of strained propellanes with various reagents remains virtually unexplored (see ref 3 for a recent review). Thus, whereas the reaction of 1,3-dehydroadamantane (a [3.3.1]propellane) with bromine is clearly ionic in nature (see ref 9), it has been reported that the analogous reaction of the [3.3.1]propellane with bromine occurs via a radical pathway [P. Warner, R. LaRose, and T. Schlesinger, *Tetrahedron Lett.*, 1409 (1974)].
- (27) Detailed understanding of the reactions reported in the body of this paper is intimately related to fundamentally important questions concerning the nature of alkyllithium reactions. Unfortunately, there appears to be a dearth of detailed knowledge in this area (see ref 26). In particular, although the metal-halogen interchange has been widely exploited to synthetic advantage, the detailed nature of this reaction remains somewhat obscure. Evidence supporting the intermediacy of radical species in the metal-halogen interchange reaction has been obtained (see ref 24 for a recent review) but it is not clear whether this reaction occurs via a predominantly homolytic process or through some more complex pathway [see, for example, T. L. Brown, *Pure Appl. Chem.*, **23**, 447 (1970)].
- (28) In an experiment to determine the feasibility of this proposal, preformed 1-norbornyllithium was added to **5** under the conditions employed for the reactions in Schemes IV and V. The major products were 1-iodonorbornane, 4-iodobisnorbornane (**11**), and 4,4'-diiodobisnorbornane (**9**). This result is consistent with reaction Scheme VI (or Scheme VII) since it demonstrates that metal-halogen interchange does occur. Unfortunately, it does not demonstrate that this reaction occurs more rapidly than the corresponding reaction of **5** with *tert*-butyllithium.
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Biogenesis of Lung-Toxic Furans Produced during Microbial Infection of Sweet Potatoes (*Ipomoea batatas*)

Leo T. Burka,*^{1a,b} Lee Kuhnert,^{1b} Benjamin J. Wilson,^{1b} and Thomas M. Harris^{1a}

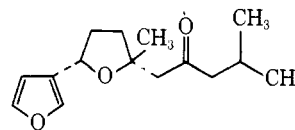
Contribution from the Department of Chemistry and Center in Environmental Toxicology, Vanderbilt University, Nashville, Tennessee 37232. Received October 21, 1976

Abstract: Certain pathogenic fungi are able to convert a furanosesquiterpenoid stress metabolite of the sweet potato, 4-hydroxymyoporone (**6**), to the lung-toxic furans **2–5**. Isolation of radioactive **2** and **3** from incubations of ¹⁴C-**6** with the fungus *F. solani* demonstrated that **6** can serve as a precursor to the lung toxins. A closely related fungus, *F. oxysporum*, could also convert **6** to **2–5** but less effectively. Compounds **2–5** could not be detected when *C. fimbriata*, another common fungal contaminant of sweet potatoes, was incubated with **6**.

Introduction

The discovery that the aflatoxins are frequent causative agents in toxicoses related to infection of food and feeds by the fungus *Aspergillus flavus* has led to increased concern about the effects of fungal contamination of foodstuffs.^{2a} The possibility that the host plant may be producing potentially toxic phytoalexins or stress metabolites in response to fungal infection is also apparent.^{2b} Stress metabolites produced by the sweet potato (*Ipomoea batatas*) have been subjects of investigation for many years. These include a group of furanosesquiterpenes, the classic example being ipomeamarone (**1**).^{2c}

The toxicity of **1** and similar furanosesquiterpenes is directed primarily toward the liver. The LD₅₀ values in mice for the hepatotoxic compounds are in the 200–300 mg/kg range;^{2c} neither the site of attack nor the potency of these toxins is ex-



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ceptional. Another group of more toxic furan compounds, **2–5**, has been isolated from mold-damaged sweet potatoes. Not only are these compounds more potent toxins than **1** (LD₅₀ 20–70 mg/kg), but they are unusual in that they exhibit a striking toxicity for the lungs characterized primarily by severe pulmonary edema.³ Lung-toxic effects of this sort have been noted in disease outbreaks in which cattle were fed culled sweet potatoes infected with fungi.⁴

As part of our investigation of these toxins we have been