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HALOMETHYL—METAL COMPOUNDS

LXXIII*. GRIGNARD REAGENTS DERIVED FROM *gem*-DIBROMOCYCLOPROPANES. α-BROMOCYCLOPROPYLTIN COMPOUNDS AS PRECURSORS FOR α-BROMOCYCLOPROPYLLITHIUM REAGENTS BY TRANSMETALATION

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Summary

The reaction of isopropylmagnesium chloride in THF with *gem*-dibromocyclopropanes gave α-bromocyclopropylmagnesium chloride compounds. When the reaction is carried out at room temperature, these are unstable and carbene-derived products are obtained. At about —70° these reagents are stable and can be used in synthesis. Protolysis gives a mixture of *syn* and *anti* isomers when these are possible, but when these Grignard reagents are treated with trimethyltin chloride, only the isomer with the trimethylstannyl substituent in the *anti* position is obtained. Treatment of *syn*-7-bromo-*anti*-7-trimethylstannylnorcarane with n-butyllithium at —95° gave only *syn*-7-bromo-*anti*-7-lithionorcarane; stereospecific reactions of this reagent with CO_2 and hexachloroethane are described. In situ Grignard—Wurtz reactions were used to prepare 7,7- bis(trimethylsilyl)- and 7,7-bis(trimethylstannyl)norcarane.

Introduction

We have studied in some detail the formation, stability and reactions with (organo)metallic halides of α-bromocyclopropyllithium reagents [1]. To complement these investigations, we have examined the preparation and utilization in organometallic synthesis of analogous α-bromocyclopropylmagnesium compounds.

α-Halogenated Grignard reagents have been reviewed recently by Villieras

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* For part LXXII see ref. 1.

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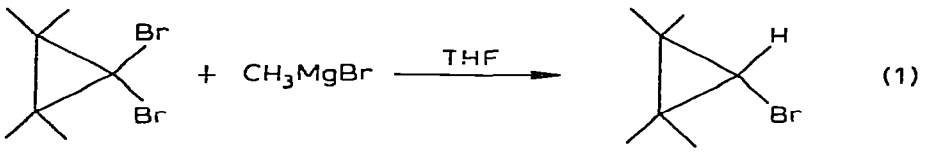
[2], but there had been no reports of stable α-halocyclopropyl Grignard compounds. The interaction of metallic magnesium with *gem*-dihalocyclopropanes had been found generally to result in formation of allenes [3] and some reactions of preformed Grignard reagents with *gem*-dibromocyclopropanes [4] and with ethyl phenyldichloroacetate [5] had been shown to give mono-reduced products (e.g., eqn. 1).



(1)

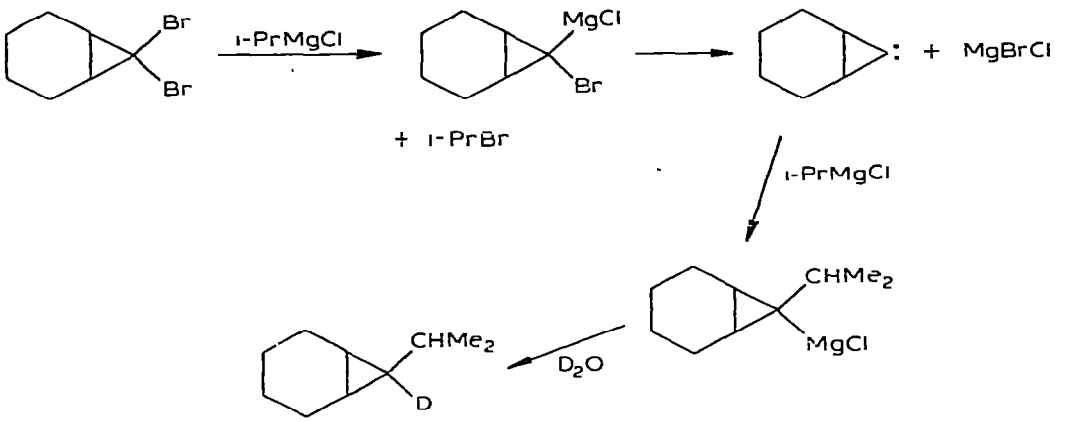
Results and discussion

α-Bromocyclopropyllithium reagents are stable only at low (−80 to −100°) temperatures, and it was expected that this also would be the case for α-bromocyclopropylmagnesium halides. However, in view of the known action of methylmagnesium bromide on *gem*-dibromocyclopropanes at room temperature [4], our initial work was devoted to such room temperature systems.

The room temperature reaction of CH_3MgBr with *gem*-dibromocyclopropanes [4] is characterized by an initial, variable induction period, often followed by a violent, at times uncontrollable, exotherm [6]. The use of a stronger organomagnesium base such as isopropylmagnesium chloride would be expected to be more effective if this reduction proceeded by way of an α-bromocyclopropyl Grignard reagent, and this point received our first attention. When 7,7-dibromonorcarane was added to an equimolar quantity of isopropylmagnesium chloride in THF at room temperature, an exothermic reaction commenced. After hydrolytic work-up of the reaction mixture, only a trace of 7-bromonorcarane could be detected by GLC. Instead, a large amount of unreacted 7,7-dibromonorcarane and two other major products, the *syn* and *anti* isomers of 7-isopropylnorcarane, were present. Repetition of this reaction, first with 2.4 molar equivalents of i-PrMgCl per equivalent of 7,7-dibromonorcarane, and then with 10 equivalents of i-PrMgCl, gave increased 7-isopropylnorcarane yields, 37 and 68%, respectively. The *anti/syn* isomer ratio in the 10/1 reaction was 1.4. The 7-H NMR signals of each isomer were identified by treating the reaction mixture with D_2O and noting the absence of the resonances at highest field. This D_2O-hydrolysis experiment, which resulted in deuterium incorporation, demonstrated that a Grignard intermediate was involved. A likely reaction course which will give the 7-isopropylnorcarane isomers involves initial magnesium—bromine exchange, followed by α-elimination of MgBrCl to give norcaranylidene. This carbene intermediate will then insert into the Mg—C bond of isopropylmagnesium chloride to form the *syn* and *anti* isomers of 7-bromo-7-norcaranylmagnesium chloride (Scheme 1). *anti*-7-Isopropylnorcarane was identified by its narrower (24 Hz), more complicated 7-H multiplet, compared with the broader (29 Hz) width of the corresponding signal in the NMR spectrum of the *syn* isomer. Such a comparison has been employed for characterization of 1-bromo-*cis*-2,3-dimethylcyclopropane [7].

A similar reaction carried out with a large excess of n-butylmagnesium

SCHEME 1

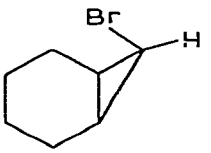
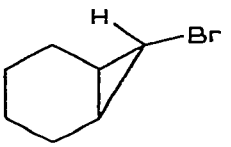
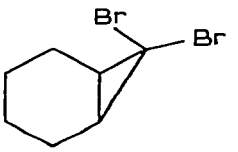
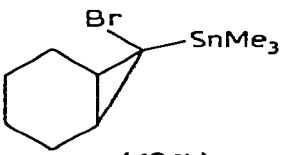


chloride gave, after hydrolytic work-up, a 1.3/1 ratio of the isomers of 7-n-butylnorcarane in 69% yield. The configuration of the isomers could not be assigned readily, but relative refractive indices and GLC retention times of the n-butyl- and isopropylnorcarane isomers suggests that the *anti*-7-n-butyl isomer was the major one produced in this reaction. In contrast to these results, when 1,1-dibromo-2-phenylcyclopropane was added to an excess of isopropylmagnesium chloride in THF the product was phenylallene (48%), not 1-isopropyl-2-phenylcyclopropane. This suggests that the insertion of a cyclopropylidene into the Mg—C bond requires that the ring be structurally constrained to prevent opening to an allene. The results of ref. 4 vs. those of ref. 3 bear on this point, although the exact Grignard intermediates probably are not strictly comparable. However, similar conclusions may be drawn from the results of the reactions of methyllithium with various *gem*-dibromocyclopropanes [8].

The results described above established that isopropylmagnesium chloride does indeed undergo Mg—Br exchange with *gem*-dibromocyclopropanes at room temperature, but that under these conditions the resulting α-bromocyclopropyl Grignard compounds are unstable. Accordingly, the exchange reactions were studied at lower temperatures. The 7,7-dibromonorcarane/i-PrMgCl system was of immediate interest and was examined first. The optimum exchange conditions were established by three reactions carried out at —65° for varying lengths of time (Table 1). It is apparent that a 6 h exchange time is adequate for a nearly complete exchange. However, increased reaction times also increased the yield of lower boiling impurities. The apparent initial *anti*-7-ClMg/*syn*-7-ClMg isomer ratio of 8/1 decreased with reaction time to 3.4/1. Treatment of such an i-PrMgCl/7,7-dibromonorcarane reaction mixture with one molar equivalent of trimethyltin chloride after 6 h gave only *syn*-7-bromo-*anti*-7-trimethylstannylnorcarane in 49% yield. The fact that the organotin product yield does not exceed the yield of the *anti* isomer of 7-bromonorcarane obtained in the hydrolysis reaction suggests that only the *syn*-7-bromo-*anti*-7-norcaranylmagnesium chloride isomer is reacting with trimethyltin chloride. Presumably the other isomer is too hindered to react with trimethyltin chloride at these low temperatures.

TABLE 1

REACTIONS OF ISOPROPYLMAGNESIUM CHLORIDE WITH 7,7-DIBROMONORCARANE IN THF (INITIAL MIXING AT −95°. FURTHER REACTION AT −65 ± 4°)

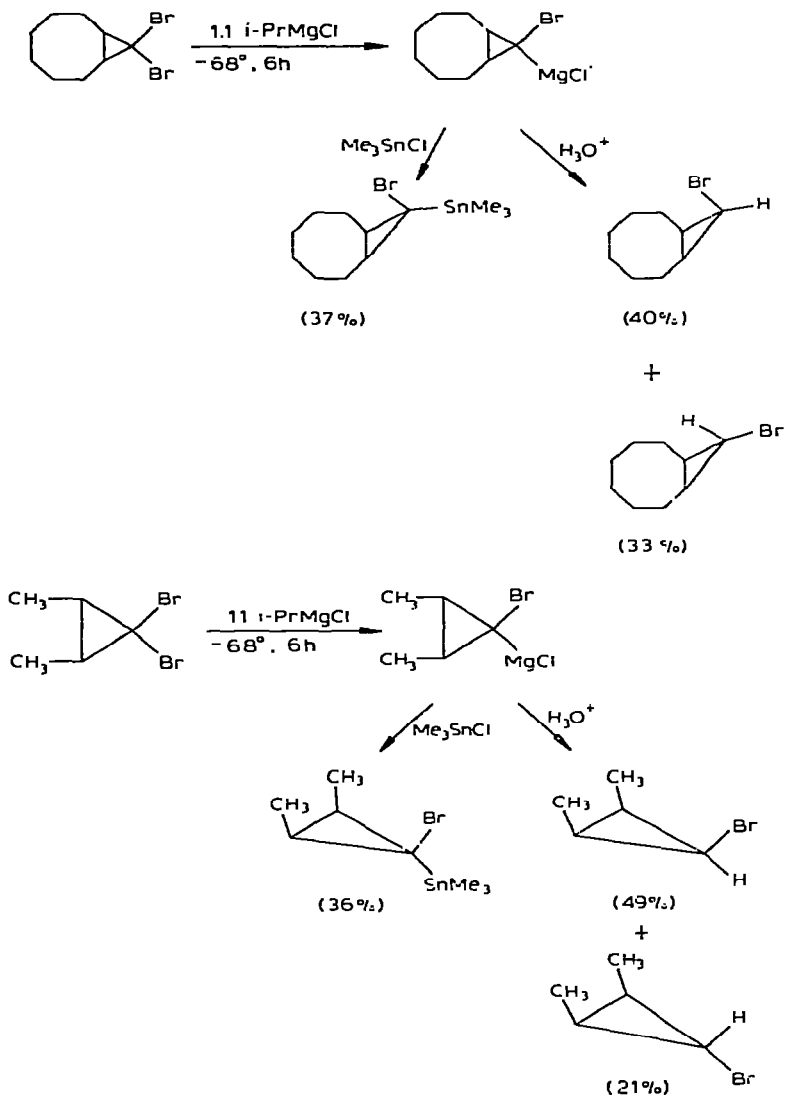
Reaction time (h)	Reactant (added at −95°)	Products		
				
0.5	H_3O^+	24%	3%	59%
3.0	H_3O^+	57%	16%	11%
6.0	H_3O^+	57%	17%	3%
6.0	Me_3SnCl	 (49%)		

Similar reactions were carried out with 9,9-dibromobicyclo [6.1.0]nonane and 1,1-dibromo-*cis*-2,3-dimethylcyclopropane (Scheme 2). The trends established with 7,7-dibromonorcarane were continued with these systems. First, formation of the Grignard reagent with the MgCl substituent in the less hindered *anti* position was favored, as shown by experiments in which these reaction mixtures were hydrolyzed. Secondly, reaction of each Grignard reagent isomer mixture with trimethyltin chloride gave only the isomer in which the trimethyltin group is in the *anti* position. The yields of the trimethyltin derivatives were high, based on the amount of the 7-*syn*-Br-7-*anti*-ClMg isomer formed as determined by the protolysis experiments. It was found that equally good yields could be obtained by adding only enough trimethyltin chloride to react with the amount of this Grignard isomer present.

Such isomerically exclusive reactions should be of considerable synthetic utility. Since the steric factor associated with trimethyltin chloride is generally considered not to be extreme, such selectivity of reaction of mixtures of α-bromocyclopropylmagnesium chloride isomers should obtain in the case of other modestly bulky substrates. This point is receiving further attention.

The selective formation of *anti*-7-bromo-*syn*-7-lithionorcarane by the reaction of n-butyllithium with a slight excess of 7,7-dibromonorcarane has been described in the preceding paper of this series [1]. The availability of *syn*-7-bromo-*anti*-7-trimethylstannylnorcarane from the experiment described above raised the interesting possibility that *syn*-7-bromo-*anti*-7-lithionorcarane might be obtained by selective reaction of this tin compound with n-butyllithium, thus making both organolithium isomers separately available for further studies. Both lithium—bromine exchange and lithium—tin exchange occur readily at low temperatures, but the generally high transmetalation reactivity

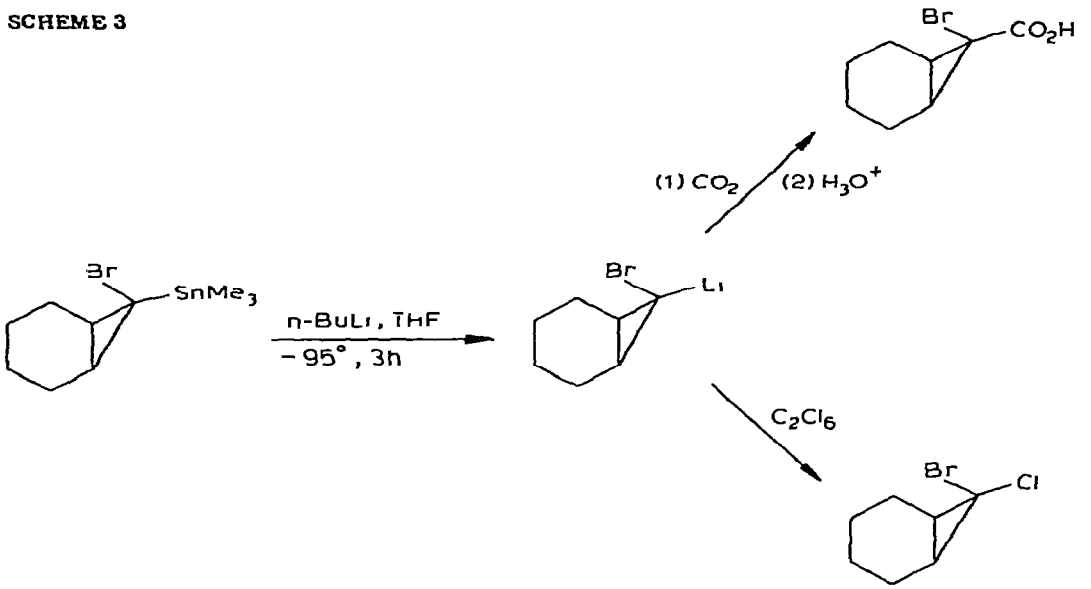
SCHEME 2



of organotin compounds might be expected to result in regioselective attack of n-butyllithium at tin rather than at bromine. This was indeed the case (Scheme 3), and, as indicated, this allowed the preparation of isomerically pure *syn*-7-bromo-*anti*-7-norcaranylcarboxylic acid and *syn*-7-bromo-*anti*-7-chloronorcarane. This general concept is capable of extension to other systems, e.g., to the tin compounds in Scheme 2 and their isomers [1].

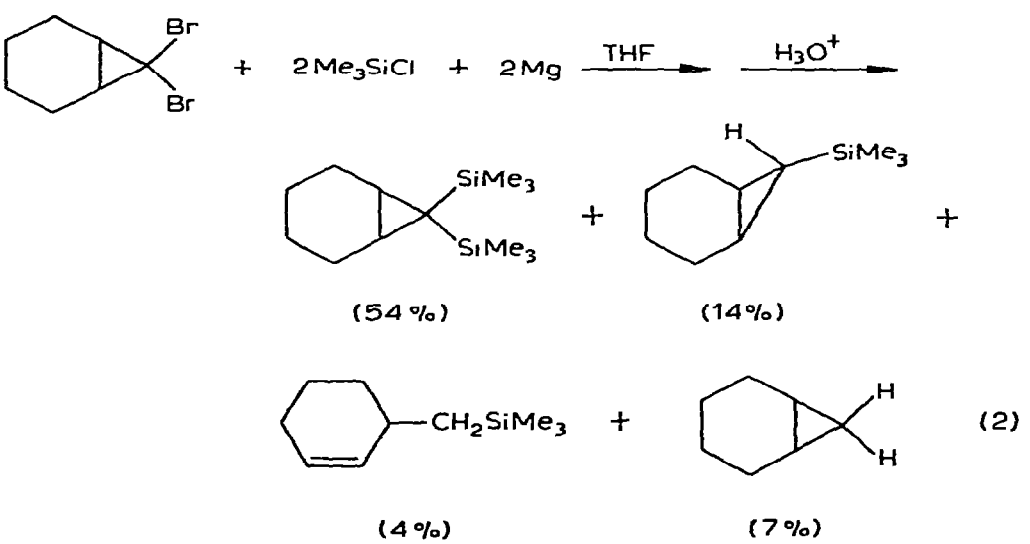
Also investigated during the course of this study were in situ coupling reactions of *gem*-dibromocyclopropanes and organometallic halides in the presence of magnesium. Such Grignard-Wurtz reactions have been widely used in the synthesis of main group organometallic compounds but had not been applied to cyclopropyl systems. The addition of 7,7-dibromonorcarane to magnesium (3 molar equiv.) and trimethylchlorosilane (2.6 molar equiv.) in THF

SCHEME 3



resulted in consumption of magnesium; after hydrolysis a mixture of products was obtained (eqn. 2), which included the desired 7,7-bis(trimethylsilyl)norcarane. An authentic sample of 3-trimethylsilylmethylcyclohexene was prepared by reaction of trimethylsilylmethylmagnesium chloride with 3-bromocyclohexene. A similar reaction of 7,7-dibromonorcarane, trimethyltin chloride and magnesium in THF gave 7,7-bis(trimethylstannyl)norcarane in 57% yield. In this case, by-products were not isolated. This procedure should be capable of generalization in its applications to other *gem*-dibromocyclopropanes.

In conclusion, we note that conversions of *gem*-dihalocyclopropanes of the type described in this and the previous [1] publication provide viable and



(2)

often superior alternatives to additions of functional carbenes (or carbenoids) to olefins. For instance, the organolithium and Grignard routes which we have developed make available α-halocyclopropyl-silanes and -tin compounds. The direct addition of trimethylsilylhalocarbenes to olefins via $(Me_3SiCCl_2)_2Hg/Ph_2Hg$ and $(Me_3SiCBr_2)_2Hg/Ph_2Hg$ does take place but is not easily effected [9]. Furthermore, the required organomercury compounds are difficult to prepare [10]. While addition of Me_3SnCCl to cyclohexene was shown to occur, the high temperature required to generate the carbene from $(Me_3Sn)_2CCl_2$ and $(Me_3Sn)_2CClBr$ also served to decompose the initial product, 7-chloro-7-trimethylstannylnorcarane, and only secondary products were obtained [11]. The organolithium route also is more advantageous in the preparation of α-halocyclopropanecarboxylic acids and of their esters. Organomercury reagents which transfer $XCCO_2R$ (X = Cl, Br) have been prepared, but their reactions with olefins require high temperatures and long reaction times and give good yields only in some cases [12]. Further investigations into the synthetic applications of α-halocyclopropyl-lithium and -magnesium reagents thus will be of some interest.

Experimental

General comments

The general comments of the previous paper of this series [1] are applicable.

Preparation of 7-isopropylnorcarane

A solution of isopropylmagnesium chloride was prepared in a 500 ml, three-necked flask from 14.0 g (0.57 mmol) of magnesium turnings, 70 ml of isopropyl chloride and 200 ml of THF. To this mixture was added a solution of 12.7 g (50 mmol) of 7,7-dibromonorcarane in 30 ml of THF during a 1-h period, which produced a mildly exothermic reaction. After the reaction mixture had cooled to ambient temperature, it was cautiously hydrolyzed with saturated ammonium chloride solution. The organic layer was decanted and the solid cake was extracted with 2 × 50 ml of hexane. The organic layers were combined and most of the solvents were removed by distillation through a 30 cm Vigreux column. The pot residue was trap-to-trap distilled (40°/0.02 mm Hg) and the distillate was fractionated through a short path head to yield 4.66 g (68%) of a fraction with b.p. 69-73°/25 mmHg. This fraction was analyzed by GLC (20% Apiezon L, 140°) and found to contain two components with approximate area ratio of 1.4/1.0, in order of elution. These were characterized as *anti*-7-isopropylnorcarane and *syn*-7-isopropylnorcarane, respectively, on the basis of the widths of the NMR resonances of the 7-protons.

1st eluted compound: n_D^{25} 1.4448. Anal. Found (mixed isomers): C, 86.55; H, 12.99. $C_{10}H_{18}$ calcd.: C, 86.87; H, 13.12%. NMR (CCl_4, $CHCl_3$): δ 2.0-1.0 (m, 8H, $(CH_2)_4$), 1.0-0.8 (broad d, 7H, $CH(CH_3)_2$), 0.7-0.4 (m, 2H, cyclopropyl H) and 0.3 to −0.1 ppm (m, 1H, isopropylcyclopropyl H of basal width 24 Hz).

2nd eluted compound: n_D^{25} 1.4586. NMR (CCl_4, $CHCl_3$): δ 2.1-0.6 (m, 17H, cyclohexyl and isopropyl, maxima at 1.30, 1.03, 0.94) and 0.28 ppm (d of t, 1H, *J* 7.0, 10.0 Hz, isopropylcyclopropyl H).

Preparation of 7-deuterio-7-isopropylnorcarane

The reaction and workup were carried out identically with the previous procedure, except that the reaction mixture was very cautiously treated with a solution of 20 g (1.0 mol) of deuterium oxide in 50 ml of THF and then hydrolyzed with saturated ammonium chloride solution. Distillation yielded 3.40 g (49%) of b.p. 62-66°/20 mmHg, which contained traces of 7-bromonorcarane. The isomers were separated by GLC (at 165°) and characterized by their NMR and IR spectra.

1st eluted compound: NMR (CCl_4, CH_2Cl_2): δ 2.0-1.0 (m, 8H, $(CH_2)_4$), 1.0-0.8 (broad, 7H, $CH(CH_3)_2$) and 0.7-0.5 ppm (m, 2H, cyclopropyl H), no resonance between 0.30 and −0.10 ppm.

2nd eluted compound: NMR (CCl_4, CH_2Cl_2): δ 2.3-0.6 ppm (m, all H, maxima at 1.30, 1.03, 0.97), no resonance above 0.6 ppm.

Preparation of 7-n-butylnorcarane

Following the previous procedure, a solution of 0.57 mol of n-butylmagnesium chloride was prepared in 200 ml of THF and treated with a solution of 12.7 g (50 mmol) of 7,7-dibromonorcarane in 30 ml of THF. Distillation of the trap-to-trap distillate yielded 5.25 g (69%) of 7-n-butylnorcarane of b.p. 93-96°/20 mmHg. The isomers were easily separated by preparative GLC (20% XE 60, 165°) and individually characterized. The area ratio was ca. 1.3/1.0 in the order of elution.

1st eluted compound: n_D^{25} 1.4530. Anal. Found: C, 86.91; H, 13.31. $C_{11}H_{20}$ calcd.: C, 86.76; H, 13.23%. NMR (CCl_4, $CHCl_3$): δ 2.2-0.9 ppm (m, all H, maxima at 1.65, 2.25, 1.87, 1.50).

2nd eluted compound: n_D^{25} 1.4623. Anal. Found: C, 86.43; H, 13.38. $C_{11}H_{20}$ calcd.: C, 86.76; H, 13.23%. NMR (CCl_4, $CHCl_3$): δ 2.2-0.4 ppm (m, all H, maxima at 1.70, 1.30, 1.20, 0.88).

Reaction of 1,1-dibromo-2-phenylcyclopropane with isopropylmagnesium chloride

A solution of isopropylmagnesium chloride was prepared from 2.6 g (107 mmol) of magnesium turnings and 75 ml of THF. Following the preceding general procedure, a solution of 13.8 g (50 mmol) of 1,1-dibromo-2-phenylcyclopropane in 20 ml of THF was added during a 1-h period. Distillation of the trap-to-trap distillation volatiles yielded 2.57 g (48%) of phenylpropadiene of b.p. 36-38°/1.5 mmHg (lit. [13] b.p. 64-65°/11 mmHg), which became yellow and more viscous after standing for a few days. The NMR spectrum was identical with that of a sample prepared by a known route [13].

NMR (CCl_4, ext. $CHCl_3$): δ 7.5-7.3 (broad s, 5H, C_6H_5), 6.35 (t, 1H, *J* 6.5 Hz, =C=CHPh) and 5.34 (d, 2H, *J* 6.5 Hz, =C=CH_2).

Reaction of isopropylmagnesium chloride with 7,7-dibromonorcarane; hydrochloric acid quench

In a 500 ml, three-necked flask a solution of isopropylmagnesium chloride was prepared from 1.5 g (59 mmol) of magnesium turnings, 10 ml (110 mmol) of isopropyl chloride and 80 ml of freshly distilled THF. After the preparation had been completed, the condenser was replaced with a low temperature

thermometer assembly. The reaction mixture was cooled to —95 ± 5° and then a solution of 12.7 g (50 mmol) of 7,7-dibromonorcarane in 30 ml of THF was added during a 2-min period. The mixture was then surrounded with a dry ice—acetone bath for a variable length of time (temperature of mixture was —65 ± 4°). The mixture was then cooled to —90 ± 5° and quenched with 4.0 ml (50 mmol) of concentrated hydrochloric aced, stirred for an additional 15 min, and then allowed to warm to room temperature. The mixture was hydrolyzed with saturated ammonium chloride solution and the organic layer was decanted and the solid cake was extracted with 50 ml of hexane. The combined organic layers were filter-dried through sodium sulfate and then concentrated by distilling away most of the solvents through a 30 cm Vigreux column. The pot residue was trap-to-trap distilled (50°/0.02 mmHg.) GLC yield analysis (10% Apiezon L, 140°) showed the following yields as a function of exchange of time: *syn*-7-bromonorcarane: 0.5 h, 11.9 mmol (24%); 3 h, 28.4 mmol (57%), 6 h, 28.5 mmol (57%); *anti*-7-bromonorcarane: 0.5 h, 1.7 mmol (3%); 3 h, 7.9 mmol (16%);·6 h, 8.4 mmol (17%); 7,7-dibromonorcarane: 0.5 h, 29.6 mmol (59%); 3 h, 5.3 mmol (11%); 6 h, 1.3 mmol (3%). There were also several peaks due to low boiling components noticed in the 6-h reaction.

Reaction of 7-bromo-7-norcaranylmagnesium chloride with trimethyltin chloride

In a 1 liter, three-necked flask was prepared a solution of isopropylmagnesium chloride from 13.4 g (0.55 mmol) of magnesium turnings, 80 ml (0.90 mol) of isopropyl chloride, and 600 ml of THF. After the preparation had been completed, the reflux condenser was replaced with a low temperature thermometer assembly and the mixture was cooled to —95 ± 3°. Then a solution of 127 g (0.50 mol) of 7,7-dibromonorcarane in 150 ml of THF was added during a 5-min period and the flask was surrounded with a dry ice—acetone bath. After the reaction mixture had been maintained at —67 ± 4° for 6 h, the mixture was cooled to ca. —90° and a solution of 70 g (0.35 mol) of trimethyltin chloride dissolved in 80 ml of THF was added. The mixture was then stirred overnight while being cooled by the dry ice—acetone bath. After 12 h, the temperature was —58°. The mixture was allowed to warm to room temperature and hydrolyzed with saturated ammonium chloride solution. The organic layer was decanted and the solvents were removed on a rotary evaporator. The pot residue after evaporation was trap-to-trap distilled (60°/0.01 mmHg) and the distillate was fractionated through a 20 cm Vigreux column to yield 81.6 g (69% based on Me_3SnCl, 85% based on a 57% formation of *syn*-7-bromo-*anti*-7-norcaranylmagnesium chloride, cf. previous experiment) of *syn*-7-bromo-*anti*-7-trimethylstannylnorcarane, b.p. 55-57°/0.02 mmHg, n_D^{25} 1.5396. Anal. Found: C, 38.82; H, 5.72; Br, 23.90. $C_{10}H_{19}BrSn$ calcd.: C, 35.55; H, 5.66; Br, 23.64%. NMR (CCl_4, $CHCl_3$): δ 2.3-0.7 (m, 10H, cyclohexyl) and 0.16 ppm (s, 9H, J ($^{117,119}Sn$—H) 52, 54 Hz, Me_3Sn).

Reaction of isopropylmagnesium chloride with 1,1-dibromo-cis-2,3-dimethylcyclopropane; hydrochloric acid quench

In a 500 ml, three-necked flask a solution of isopropylmagnesium chlor-

ide was prepared from 2.70 g (110 mmol) of magnesium turnings, 18 ml (210 mmol) of isopropyl chloride, and 150 ml of THF. Following the same procedure as above for the protolysis of 7-bromo-7-norcaranylmagnesium chloride, a solution of 22.8 g (100 mmol) of 1,1-dibromo-*cis*-2,3-dimethylcyclopropane in 50 ml of THF was added to the mixture at a temperature of −95°. After exchange at −67 ± 3° for 5 h, the mixture was treated with 10 ml (125 mmol) of concentrated hydrochloric acid at a reaction temperature of −95°. The mixture was stirred for 30 min before being allowed to warm to room temperature, and then it was hydrolyzed with saturated ammonium chloride solution. The organic layer was decanted and trap-to-trap distilled (40°/0.05 mmHg). The solvents were removed by distillation through a 20 cm Widmer column until almost all of the THF had been removed. The pot residue was then distilled through a fractionating short-path head to yield 10.4 g (70%) of 1-bromo-*cis*-2,3-dimethylcyclopropane. GLC analysis (10% UC-W98, 70°) showed a 1.0/2.4 ratio of the *anti/syn* isomers. A check of an aliquot of the trap-to-trap distillate showed that there had been no change in the isomer ratio during distillation. The isomers were separated by GLC (10% UC-W98, 70°) and identified by their characteristic NMR spectra [7].

Preparation of syn-7-bromo-anti-7-trimethylstannyl-cis-2,3-dimethylcyclopropane

By a procedure identical with the preceding one, a solution of 1-bromo-*cis*-2,3-dimethylcyclopropylmagnesium chloride was treated with a solution of 20.0 g (100 mmol) of trimethyltin chloride dissolved in 50 ml of THF and the resulting mixture was stirred overnight at a reaction temperature of −63 ± 3°. After warming the reaction mixture to room temperature, it was hydrolyzed; the organic layer was decanted and then it was trap-to-trap distilled (30°/0.05 mmHg). The distillate was concentrated by distillation through a 30 Vigreux column until the head temperature reached 70°. The pot residue was distilled through a fractionating short-path head to yield 11.19 g (36%) of *syn*-7-bromo-*anti*-7-trimethylstannyl-*cis*-2,3-dimethylcyclopropane of b.p. 61-63°/2.3 mmHg. There was a small forecut of b.p. 33-37°/2.3 mmHg which appeared to be unreacted starting material. The main product was identified by comparison of its NMR spectrum one of a known sample [1]. There was only one Me_3Sn resonance in the NMR at δ 0.10 ppm, indicative of only the one isomer being present.

Reaction of isopropylmagnesium chloride with 9,9-dibromobicyclo[6.1.0]-nonane; hydrochloric acid quench

By a procedure identical to the preceding one, 110 mmol of isopropylmagnesium chloride in 150 ml of THF was treated with 28.3 g (100 mmol) of 9,9-dibromobicyclo[6.1.0]nonane in 50 ml of THF at −67 ± 3° for 5 h. After protolysis with 10 ml (125 mmol) of concentrated hydrochloric acid at −95°, the mixture was stirred in the dry ice—acetone bath overnight. After workup in the usual manner, distillation through a 20 cm Vigreux column yielded 14.8 g (73%) of 9-bromobicyclo[6.1.0]nonane of b.p. 46-50°/0.3 mmHg. An isomer ratio of 1.0/1.2 of *anti/syn* was determined by GLC (10% UC-W98, 140°) and NMR [14].

Preparation of syn-9-bromo-anti-9-trimethylstannylbicyclo[6.1.0]nonane

By a procedure identical with the preceding one was prepared 226 mmol of isopropylmagnesium chloride in 200 ml of THF and it was treated with a solution of 56.4 g (200 mmol) of 9,9-dibromobicyclo[6.1.0]nonane in 50 ml of THF at −68 ± 4° for 6 h. Then the mixture was treated with a solution of 40 g (200 mmol) of trimethyltin chloride dissolved in 75 ml of THF. The reaction mixture was then stirred overnight with a dry ice—acetone cooling bath. The mixture was warmed up to room temperature, hydrolyzed, and the organic layer was decanted. Most of the THF was distilled through a 30 cm Vigreux column. The pot residue was distilled (short-path head) to yield 35.9 g of b.p. 70-81°/0.04 mmHg, mainly 76-79°/0.04 mmHg. The distillate was analyzed by GLC (10% UC-W98, 170°) and found to contain about 12% starting dibromide. NMR analysis indicated a 15% excess of aliphatic protons (relative to the trimethyltin resonance). The starting dibromide was removed as follows. The distillate was placed in a 500 ml standard low temperature reaction apparatus and dissolved in 100 ml of THF. After the mixture had been cooled to −95°, 65 ml (15 mmol) of 2.3 *M* n-butyllithium was added and the mixture was stirred for 15 min before protolysis with 2.0 ml (25 mmol) of concentrated hydrochloric acid. The mixture was stirred at −90° for 15 min and then it was warmed to room temperature. The solvents were removed by rotary evaporation and the residue was distilled through a fractionating short-path head to yield 27.1 g (37%) of *syn*-9-bromo-*anti*-9-trimethylstannylbicyclo-[6.1.0]nonane of b.p. 79-81°/0.07 mmHg, n_D^{25} 1.5348. Anal. Found: C, 40.09; H, 6.36; Br, 23.02. $C_{12}H_{23}BrSn$ calcd.: C, 39.39; H, 6.34; Br, 21.84%. NMR (CCl_4, $CHCl_3$): δ 2.0-0.7 (m, 14H, cyclooctyl H) and δ 0.15 (s, 9H, *J* ($^{117,119}Sn$—H) 52, 54 Hz).

Preparation of 1-bromo-2,2-dimethylcyclopropane

A solution of isopropylmagnesium chloride was prepared in a 500 ml, three-necked flask from 5.9 g (0.24 mol) of magnesium turnings, 30 ml (0.30 mol) of isopropyl chloride, and 250 ml of THF. Following the preceding procedure, the Grignard reagent was allowed to react with a solution of 46 g (0.20 mol) of 1,1-dibromo-2,2-dimethylcyclopropane while the reaction temperature was maintained at −69 ± 3°. Then the mixture was cooled to −95 ± 2° and quenched with 20 ml (0.25 mol) of concentrated hydrochloric acid. After stirring the mixture in a dry ice—acetone bath overnight, the mixture was allowed to warm to room temperature and it was further hydrolyzed with saturated ammonium chloride solution. The organic layer was decanted and concentrated by distillating most of the solvent through a 20 Widmer column. The pot residue was trap-to-trap distilled (room temp./0.01 mmHg) and the distillate was redistilled at reduced pressure to yield 22.4 g (75%) of 1-bromo-2,2-dimethylcyclopropane of b.p. 41-42°/60 mmHg (Lit. [14] 107-108°). An NMR spectrum agreed with the published data [14].

Preparation of 7,7-bis(trimethylsilyl)norcarane

Into a 500 ml, three-necked flask equipped with a mechanical stirrer, reflux condenser (nitrogen inlet tube), and a 30 ml constant rate addition funnel was placed 7.3 g (0.30 mol) of magnesium turnings and the apparatus

was flamed out. After the flask had cooled, 200 ml of THF and 34 ml (0.26 mol) of trimethylchlorosilane were added to the flask. The addition funnel was charged with a solution of 25.4 g (0.10 mol) of 7,7-dibromonorcarane in 10 ml of THF. The addition was carried out over a period of 2 h and the mixture was stirred for an additional 3-h period. The reaction mixture was hydrolyzed with saturated ammonium chloride solution, the organic layer was decanted and the residual solid was dissolved in a mixture of diethyl ether/ 1 *N* hydrochloric acid. The ether layers were combined and dried over anhydrous sodium sulfate. The solvents were distilled off through a 30 cm Vigreux column. The pot residue was trap-to-trap distilled (80°/ 0.2 mmHg) to yield 36.8 g of distillate, which was fractionated through a 20 cm Vigreux column at reduced pressure. Four fractions were obtained: 1, b.p. 24-35°/80 mmHg mostly THF; 2, b.p. 40-42/60 mmHg, mostly norcarane; 3, b.p. 66-92°/10 mmHg, predominantly $Me_3SiC_7H_{11}$; 4, b.p. 96-98°/3.5 mmHg almost pure 7,7-bis(trimethylsilyl)norcarane.

The four components were characterized by the following data: Fraction 2 (norcarane): A slightly impure sample had n_D^{25} 1.4562; the NMR spectrum and GLC retention time were identical to those of an authentic sample, n_D^{24} 1.4548. Fraction 3 was separated by GLC (20% carbowax 20 M at 150°) into two components, one of which was *anti*-7-trimethylsilylnorcarane, n_D^{25} 1.4558 (lit. [15] n_D^{25} = 1.4561). The NMR spectrum was identical with the reported data [15]. The second component was not the expected *syn* isomer. It compared identically with a compound which was later prepared and characterized as 3-(trimethylsilylmethyl)cyclohexene. Fraction 4 was characterized as 7,7-bis(trimethylsilyl)norcarane: b.p. 80-82°/0.5 mmHg, b.p. 96-98°/3.5 mmHg; n_D^{25} 1.4915. Anal. Found: C, 65.16; H, 11.69. $C_{13}H_{28}Si_2$ calcd.: C, 64.91; H, 11.73%. NMR (CCl_4, $CHCl_3$): δ 2.2-0.8 (m, 10H, cyclohexyl H), 0.15 (s, 9H, Me_3Si) and —0.03 ppm (s, 9H, Me_3Si). GLC yield analysis (10% Carbowax 20 M at 148°) showed the presence of norcarane, 7.1 mmol (7%), *anti*-7-trimethylsilylnorcarane, 13.6 mmol (14%), 3-(trimethylsilylmethyl)cyclohexene, 4.4 mmol (4%), and 7,7-bis(trimethylsilyl)norcarane, 54.4 mmol (54%).

Preparation of 3-(trimethylsilylmethyl)cyclohexene

Into a 100 ml, three-necked flask equipped with a magnetic stirring bar, reflux condenser (nitrogen inlet tube), and an addition funnel was placed 0.60 g (25 mmol) of magnesium turnings and the apparatus was flamed out. After the flask had cooled, 5 ml of Et_2O was added to it and the addition funnel was charged with 2.85 g (23.3 mmol) of chloromethyltrimethylsilane (Peninsular Chem. Research) and 20 ml of Et_2O. The solution was added dropwise after initiating the reaction with 70 μl of 1,2-dibromoethane. After the Grignard formation had been completed, a solution of 3.16 g (20 mmol) of 3-bromocyclohexene in 5 ml of Et_2O was added. A mildly exothermic reaction occured and the mixture was subsequently stirred at reflux for 2 h. The mixture was hydrolyzed with saturated ammonium chloride solution, the organic layer was decanted, and the solid was washed with 20 ml of fresh Et_2O. The combined organic solutions were dried over sodium sulfate and then distilled through a 20 cm Vigreux column to remove most of the Et_2O. The pot residue was trap-to-trap distilled (90°/20 mmHg) and the distillate

was analyzed by GLC (20% XE-60, 200°). There was only one major high boiling component, which was isolated and characterized as the expected 3-(trimethylsilylmethyl)cyclohexene, n_D^{25} 1.4596. Anal. Found: C, 71.61; H, 11.88. $C_{10}H_{10}Si$ calcd.: C, 71.34; H, 11.97%. NMR (CCl_4, $CHCl_3$): δ 5.9 (broad s, 2H, CH=CH), 2.8-1.3 (m, 7H, tetramethylene), 0.60 (d, 2H, *J* 7.0 Hz, $SiCH_2$) and 0.03 (s, 9H, Me_3Si).

Preparation of 7,7-bis(trimethylstannyl)norcarane

Into a 250 ml, single-necked flask equipped with a magnetic stirring bar and a reflux condenser topped with a constant rate addition funnel (nitrogen inlet tube) was placed 3.6 g (0.15 mol) of magnesium turnings. The apparatus was flamed out. After the flask had cooled, a solution of 20 g (0.10 mol) of trimethyltin chloride dissolved in 60 ml of THF was prepared in the flask. The addition funnel was charged with a mixture of 12.54 g (0.050 mol) of 7,7-dibromonorcarane and 20 ml of THF. After 15 drops of this solution had been added to the flask, the reaction was initiated by the addition of 0.30 ml of 1,2-dibromoethane. The rest of the solution was added during a 1.5-h period. The mixture was stirred for 2 h after the addition had been completed and then it was hydrolyzed. The organic layer was decanted, dried over sodium sulfate, and distilled to remove most of the THF. The pot residue was trap-to-trap distilled (90°/0.02 mmHg) and the distillate was redistilled through a short-path head to yield 12.0 g (57%) of 7,7-bis(trimethylstannyl)norcarane, b.p. 76-79°/0.02 mmHg. An analytical sample was obtained by preparative GLC (20% UC-W98, 240°) n_D^{25} 1.5323. Anal. Found: C, 36.80; H, 6.60. $C_{13}H_{28}Sn$ calcd.: C, 37.02; H, 6.68%. NMR (CCl_4, $CHCl_3$): δ 2.2-1.0 (m, 10H, cyclohexyl), 0.17 (s, 9H, *J* (^{117,119}Sn—H) 48, 51 Hz, Me_3Sn) and −0.02 ppm (s, 9H, *J* (^{117,119}Sn—H) 48,51 Hz, Me_3Sn).

Preparation of syn-7-bromo-anti-7-norcaranylcarboxylic acid

Into a flamed-out 500 ml standard low temperature reaction apparatus was placed 16.9 g (50 mmol) of *syn*-7-bromo-*anti*-7-trimethylstannylnorcarane and 100 ml of THF. After the mixture had been cooled to −95 ± 3°, 50 ml (80 mmol) of 1.6 *M* n-butyllithium was added and the mixture was stirred for 3 h. Then 50 g (1.1 mol) of finely crushed (granular) dry ice added at once. The mixture was stirred for 20 min and then it was treated with 7.0 ml of concentrated hydrochloric acid. Further work-up was identical to that described in the experiment above. The product, *syn*-7-bromo-*anti*-7-norcaranylcarboxylic acid, m.p. 95-99°, was obtained in 60% yield. An analytical sample was recrystallized twice from hexane to yield white plates of m.p. 98-99.5°. Anal. Found: C, 43.92; H, 5.04; Br, 36.58. $C_8H_{11}BrO_2$ calcd.: C, 43.86; H, 5.06; Br, 36.47%. NMR (CCl_4, $CHCl_3$): δ 2.6-0.6 ppm (m, all H, maxima at 1.95, 1.40).

The methyl ester was prepared by reaction with MeOH (H_2SO_4) in 84% yield: 7-bromo-*anti*-7-carbomethoxynorcarane of b.p. 73-74°/0.5 mmHg. This compound had IR and NMR spectra identical with those of a sample prepared via bromocarbomethoxycarbene [11]. An NMR spectrum of mixed pure isomers showed that proton resonance of each of the methoxy groups was slightly different; the *anti* carbomethoxy group has its resonance at 0.03 ppm higher field that the *syn* isomer.

Reaction of syn-7-bromo-anti-7-trimethylstannylnorcarane with n-butyllithium; hexachloroethane quench

Into a flamed-out 500 ml, standard low temperature reaction apparatus were placed 16.9 g (50 mmol) of *syn*-7-bromo-*anti*-7-trimethylstannylnorcarane and 100 ml THF. After the mixture had been cooled to −95 ± 2°, 40 ml (64 mmol) of 1.6 *M* n-butyllithium was added and the mixture was stirred for 1 h. Then the mixture was treated with a solution of 16.6 g (70 mmol) of hexachloroethane dissolved in 40 ml of THF, which was added as rapidly as possible (4 min) while maintaining the temperature below −95°. The mixture was stirred for an additional 30 min and then it was allowed to warm to room temperature. The mixture was treated with 50 ml of water and the organic layer was dried over anhydrous magnesium sulfate. The filtered solution was concentrated by distilling most of the solvents through a 20 cm Vigreux column. The clear pot residue was distilled at reduced pressure and the fraction of b.p. 45-60°/1.5 mmHg was heated gently under a reflux condenser (10 mmHg aspirator pressure) until no more solid would sublime. The liquid residue was redistilled through a short path head to yield ca. 7.0 g of liquid of b.p. 49-51°/1.0 mmHg. The distillate was analyzed by GLC (20% DC-200, 160°), and found to consist of two components of approximately equal areas. One component was identified as di-n-butyldimethyltin by comparison of its IR spectrum and retention time with those of an authentic sample. The other component was collected on a larger scale (same conditions) and identified as *syn*-7-bromo-*anti*-7-chloronorcarane, n_D^{25} 1.5286. IR (film): (unique bands in italics) 3010w, 2945vs, 2920s, 3000m, 2875m, 2860s, 1462m, 1456(sh), 1444s, 1435m, 1375w, 1350w, 1342m, 1333m, 1273w, 1257w, 1230m, 1178w, 1166m, 1128w, 1094m, 1082m, 1033m, 1023s, 972m, 910m, *842m*, 830m, *784vs*, 768vs, 747w, *643m*.

The IR spectra of the individual isomers as well as that of a 1/1 mixture are reproduced in ref. 1. The yield was estimated at 25% by relative GLC peak areas of the two components in the distilled mixture.

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