

# Mechanistic Definition of Trimethylstannylation of 1,4-Dihalobicyclo[2.2.2]octanes: A Labeling Experiment Excludes Intermediacy of [2.2.2]Propellane but Suggests a Novel Radical Chain Mechanism

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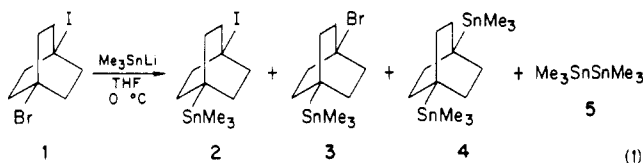
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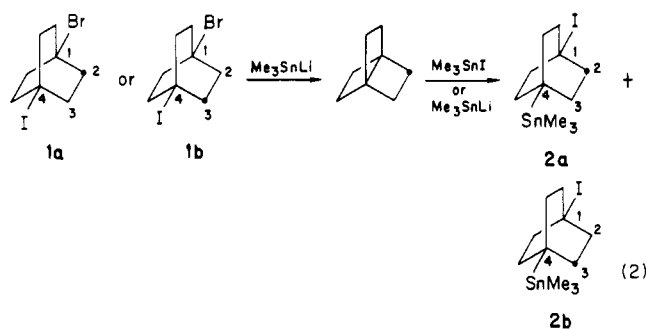
A specifically labeled  $^2\text{H}$  derivative of 1-bromo-4-iodobicyclo[2.2.2]octane has been synthesized and reacted with (trimethylstannyl)lithium. A full product and  $^2\text{H}$ -label profile has been established by  $^1\text{H}$ ,  $^2\text{H}$ ,  $^{13}\text{C}$ , and  $^{119}\text{Sn}$  NMR spectroscopy, and the intermediacy of [2.2.2]propellane can be disregarded. The results, along with others for additional 1,4-dihalobicyclo[2.2.2]octanes, are best accommodated by a chain mechanism (involving radical anions and free radicals) somewhat akin to the  $\text{S}_{\text{RN}}1$  mechanism for electron-transfer initiated aliphatic and aromatic nucleophilic substitutions.

Recently, we reported<sup>1</sup> that treatment of 1-bromo-4-iodobicyclo[2.2.2]octane (1) with  $\text{Me}_3\text{SnLi}$  (1.3 equiv; inverse addition) in THF at 0 °C yields a product mixture containing three stannanes (2, 3, and 4; eq 1), in the ratio



of 4:2:1, respectively, in the presence of substantial amounts of unreacted 1 (ca. 60%). Hexamethyldistannane (5) was also identified as a significant reaction product. Taken at face value, the result strongly infers an unprecedented halogen nucleofugality ( $\text{Br} > \text{I}$ )<sup>2</sup> for an halogen-metal exchange (HME) or electron-transfer (ET) initiated process. We proposed a tentative interpretation based on the predominance of carbanion formation (HME mechanism) which leads to [2.2.2]propellane<sup>3</sup> as a transient intermediate.<sup>4</sup>

We reasoned that if the aforementioned proposal is indeed valid then, based on symmetry considerations, stannylation of an appropriate isotopically labeled derivative of 1 (1a or 1b) should lead to two label isomers (or isotopomers) of 2 (2a and 2b; eq 2) in approximately equal amounts. In the case of a predominant direct replacement mechanism essentially only one isotopomer (2a or 2b) should be formed. Since a convenient precursor for in-



roducing deuterium is now readily available,<sup>5</sup> we decided to synthesize a deuterium derivative of 1 (1a; • designates label) and to examine its reaction with  $\text{Me}_3\text{SnLi}$  in the hope that the results of such a study would bear significantly on the overall mechanism of the reaction. In addition, we also report on the completion of a product analysis of the trimethylstannylation of a series of 1,4-dihalobicyclo[2.2.2]octanes. Herein we report the results of our study.

## Results and Discussion

**Synthesis of Isotopomer 1a.** The synthetic route is shown in Scheme I. Mass spectroscopic analysis established that the final product was a mixture containing 1 (ca. 50%) and its mono- and dideuterio derivatives (1a;  $37.5 \pm 1.0$  and  $13.4 \pm 1.6\%$ , respectively).  $^1\text{H}$  NMR of 1 + 1a (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.32 (5.12 H, m), 2.56 (6 H, m); 44% deuterium incorporation.  $^{13}\text{C}$  NMR of 1 + 1a (75.46 MHz,  $\text{CDCl}_3$ , relative to  $\text{Me}_4\text{Si}$ ):  $\delta$  58.24 (C1), 41.06 (C2), 43.36 (C3), 39.23 (C4). A characteristic pattern of one- and two-bond  $^2\text{H}/^1\text{H}$  isotope effects on the chemical shifts is observed.<sup>6</sup> Thus, a triplet upfield (ca.  $-0.40$  ppm,  $J_{\text{CD}} = 20.62$  Hz) of the C2 resonance due to the species bearing one deuterium is readily seen. Furthermore, signals upfield (ca.  $-0.07$ ,  $-0.13$  and  $-0.10$ ,  $-0.20$  ppm) of the C1 and C3 resonance, respectively, which arise from the mono- and

(1) Adcock, W.; Iyer, V. S.; Kok, G. B.; Kitching, W. *Tetrahedron Lett.* **1983**, 24, 5901.

(2) Competitive experiments in which equimolar mixtures of 1-bromo- and 1-iodobicyclo[2.2.2]octane and 1-bromo- and 1-iodo-4-methylbicyclo[2.2.2]octane were treated with a deficiency of  $\text{Me}_3\text{SnLi}$  established unequivocally that the iodide is ca. twice as reactive as the bromide.

(3) (a) Eaton, P. E.; Temme, G. H. *J. Am. Chem. Soc.* **1973**, 95, 7508. (b) Wiberg, K. B. *Acc. Chem. Res.* **1984**, 17, 379.

(4) (a) The chief objection to invoking the formation of [2.2.2]propellane is the propensity of (4-halobicyclo[2.2.2]oct-1-yl)lithium derivatives to undergo Grob fragmentation at  $-80$  °C to afford 1,4-dimethylenecyclohexane. Similar to the diiodide<sup>4b</sup> and fluoro iodide<sup>4c</sup>, we have found that treatment of an ethereal solution of 1-bromo- or 1-chloro-4-iodobicyclo[2.2.2]octane with 2 equiv of *tert*-butyllithium at  $-80$  °C followed, after 10 min, by the addition of  $\text{Br}_2$  afforded almost quantitative amounts of 1,4-bis(bromomethyl)-1,4-dibromocyclohexane. (b) Wiberg, K. B.; Pratt, W. E.; Maturro, M. G. *J. Org. Chem.* **1982**, 47, 2720. (c) Adcock, W.; Iyer, V. S. *J. Org. Chem.* **1985**, 50, 1538.

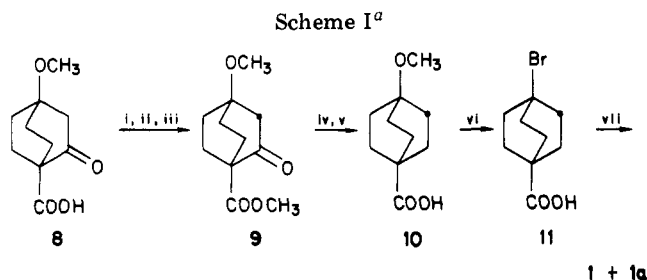
(5) Adcock, W.; Abeywickrema, A. N. *J. Org. Chem.* **1982**, 47, 2951.

(6) (a) Aydin, R.; Günther, H. Z. *Naturforsch. B. Anorg. Chem., Org. Chem.* **1979**, 34B, 528. (b) Aydin, R.; Günther, H. *J. Am. Chem. Soc.* **1981**, 103, 1301. (c) Jurlina, J. L.; Stothers, J. B. *J. Am. Chem. Soc.* **1982**, 104, 4677. (d) Aydin, R.; Wesener, J. R.; Günther, H.; Santillan, R. L.; Garibay, M. E.; Joseph-Nathan, P. *J. Org. Chem.* **1984**, 49, 3845.

**Table I. Chemical Shifts (ppm) of Stannanes (2, 3, and 4) in Product Mixture from Trimethylstannylation of Labeled Bromo Iodide (1 + 1a)**

compd	<sup>1</sup> H NMR (CDCl <sub>3</sub> ) <sup>a,b</sup>	<sup>2</sup> H NMR (CHCl <sub>3</sub> ) <sup>c-e</sup>	<sup>13</sup> C NMR (CDCl <sub>3</sub> ) <sup>b,f</sup>
2 <sup>g</sup>	1.87 (m, H3), 2.44 (m, H2), -0.66 (SnMe <sub>3</sub> )	2.44, 2.46 (D2)	48.95 (C1), 41.46 (C2), 33.83 (C3), 19.26 (C4), -12.57 (SnMe <sub>3</sub> )
3 <sup>h</sup>	1.87 (m, H3), 2.17 (m, H2), -0.47 (SnMe <sub>3</sub> )	2.17, 2.19 (D2)	65.55 (C1), 38.56 (C2), 33.29 (C3), 20.00 (C4), -12.46 (SnMe <sub>3</sub> )
4 <sup>i</sup>	1.70 (m, H2 and H3), -0.10 (SnMe <sub>3</sub> )	1.69, 1.71 (D2)	21.34 (C1), 31.32 (C2), 31.32 (C3), 21.34 (C4), -12.77 (SnMe <sub>3</sub> )

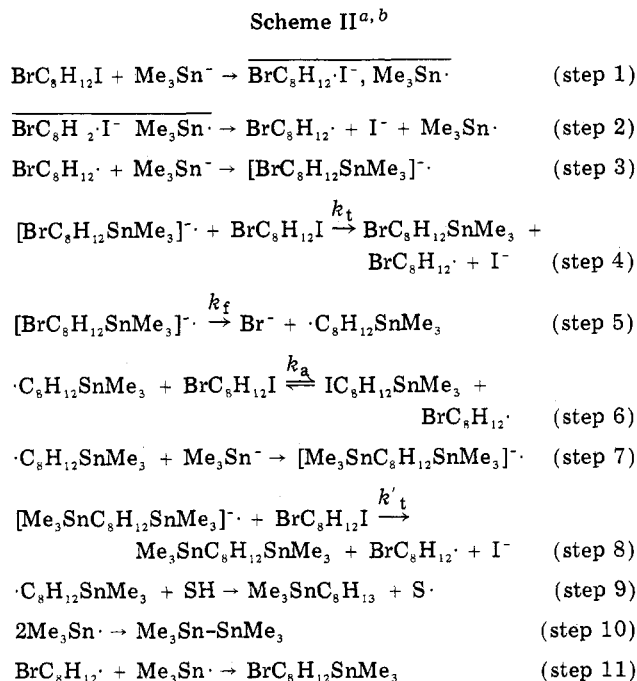
<sup>a</sup> 300 MHz. <sup>b</sup> Chemical shifts relative Me<sub>4</sub>Si. <sup>c</sup> 46.06 MHz. <sup>d</sup> Chemical shifts relative to CDCl<sub>3</sub> set at 7.24 ppm. <sup>e</sup> Resonance signals are overlapping absorptions for mono- and dideuterio species, respectively. <sup>f</sup> 75.46 MHz. <sup>g</sup> 1-Iodo-4-(trimethylstannyl)bicyclo[2.2.2]octane. <sup>h</sup> 1-Bromo-4-(trimethylstannyl)bicyclo[2.2.2]octane. <sup>i</sup> 1,4-Bis(trimethylstannyl)bicyclo[2.2.2]octane.



<sup>a</sup> Reagents and conditions: (i) 1 M NaOH, 20 °C. (ii) D<sub>2</sub>O/NaOCH<sub>3</sub>, 50 °C, 16 h; 1 M HCl. (iii) CH<sub>3</sub>N<sub>2</sub>/Et<sub>2</sub>O. (iv) HS(CH<sub>2</sub>)<sub>2</sub>SH/C<sub>6</sub>H<sub>5</sub>/p-TsOH, reflux, 16 h; Raney Nickel/EtOH, reflux, 48 h. (v) 0.5 M NaOH/50% aqueous EtOH, 20 °C, 16 h. (vi) 48% aqueous HBr/Ac<sub>2</sub>O, reflux, 120 h. (vii) Me<sub>3</sub>COI/Freon 113, hv/40-50 °C, 2 h.

dideuterio species, are clearly visible. No isotopic perturbation of C4 is observed. It should be noted that the relative intensities of the "multiplets" for C1 and C3 were in accord with expectations (ca. 4:3:1 and 21:3:1, respectively) based on the mass spectrometric determined composition of 1 + 1a (vide supra). <sup>2</sup>H NMR of 1 + 1a (46.06 MHz, CHCl<sub>3</sub>, relative to CDCl<sub>3</sub> (7.24 ppm): δ 2.31, 2.33 (overlapping signals for mono- and dideuterio species). This spectrum with no absorptions in the 2.5-2.6 ppm region, taken in conjunction with the corresponding <sup>1</sup>H NMR (vide supra), confirms that deuterium in the labeled mixture is located only at C2.

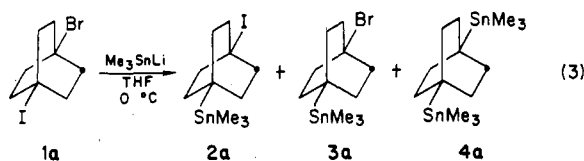
**Trimethylstannylation of Labeled Bromo Iodide Mixture 1 + 1a.** A sample of the labeled mixture of (1 + 1a, 500 mg, 0.00159 mol) was treated with Me<sub>3</sub>SnLi (2 equiv) in the usual manner to provide, after sublimation, a product mixture containing three stannanes (2, 3, and 4) uncontaminated with the precursor bromo iodides. The results of a detailed NMR analysis (<sup>1</sup>H, <sup>2</sup>H, and <sup>13</sup>C) of the stannane mixture are listed in Table I. Assignments for the <sup>1</sup>H and <sup>2</sup>H NMR spectra followed unambiguously from the corresponding spectra of the labeled bromo iodide mixture (1 + 1a, vide supra) as well as intensity considerations. It should be noted that the resonance signals of H3 for 2 and 3 are coincident. The <sup>13</sup>C chemical shifts for the various stannanes were readily assigned on the basis of substituent effects, intensities, and tin-carbon spin-spin coupling constants.<sup>7</sup> A comparison of the <sup>1</sup>H and <sup>2</sup>H NMR spectra reveals that, for the latter, there is only one set of deuterium resonances for each stannane in the product mixture. Hence, only one label isomer of each halo-stannane (2 and 3) is indicated and, moreover, the deuterium in each one is specifically located at C2. This interpretation is unambiguously confirmed by the pattern of two-bond <sup>2</sup>H/<sup>1</sup>H isotope effects on the <sup>13</sup>C chemical shifts of C1 and C3 for 2 and 3, which is identical with that observed (vide supra) for the labeled bromo iodide mixture 1 + 1a. No corresponding isotopic perturbation is observed



<sup>a</sup> Li<sup>+</sup> is understood to be present as the counter ion.

<sup>b</sup> For expedience, the formation of a radical-iodide anion adduct is understood to occur prior to steps 4 and 8.

on the <sup>13</sup>C chemical shifts of C2 and C4 for each halo-stannane (2 and 3). Thus, it is required that the stannylation of the labeled mixture 1 + 1a proceeds exclusively as shown in eq 3. All spectra (<sup>1</sup>H, <sup>2</sup>H, and <sup>13</sup>C NMR), including the <sup>119</sup>Sn NMR spectrum,<sup>8</sup> indicate that the stannanes (2, 3, and 4) are present in the product mixture in the ratio of 3:1:3, respectively.



**Mechanism of Trimethylstannylation.** The result of the labeling experiment excludes [2.2.2]propellane as a significant intermediate in the stannylation reaction of 1 (eq 1).<sup>1</sup> Moreover, it appears to preclude any mechanistic proposal which suggests that the bromine in 1 is replaced directly. We believe the most plausible mechanistic sequence which accounts for the remarkable result of the labeling experiment is that shown in Scheme II. It can be seen that this is a chain mechanism involving radical anions and free radicals as intermediates which is very similar to the so called S<sub>RN</sub>1 mechanism for electron-

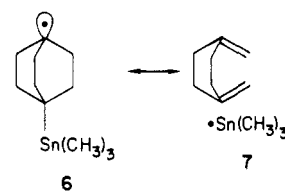
(7) Full details of the <sup>13</sup>C and <sup>119</sup>Sn NMR spectra of the (4-halo-bicyclo[2.2.2]oct-1-yl)stannanes will be presented in connection with other studies.<sup>8</sup>

(8) (a) Adcock, W.; Kok, G. B.; Abeywickrema, A. N.; Kitching, W.; Drew, G. M.; Olszowy, H. A.; Schott, I. *J. Am. Chem. Soc.* 1983, 105, 290. (b) Adcock, W.; Kok, G. B.; Iyer, V. S.; Kitching, W.; Drew, G. M., manuscript in preparation.

transfer initiated aliphatic<sup>9</sup> and aromatic<sup>10</sup> nucleophilic substitution reactions. The possibility of nucleophilic substitution at the bridgehead of polycyclic alkyl halides by the  $S_{RN}1$  mechanism has recently been demonstrated.<sup>11</sup> However, it differs from the usual  $S_{RN}1$  mechanism in two significant ways. Firstly, the initiation step in Scheme II involves the formation of a radical-halide ion adduct<sup>12</sup> and not a radical anion as the initial intermediate. Secondly, Scheme II has an additional propagation step 6 involving iodine atom transfer (or abstraction). This step 6 is demanded by the exclusive formation of a particular label isomer of **2** (eq 3). The key feature of the mechanism is the formation and subsequent fate of the bromo tin radical anion ( $[\text{BrC}_8\text{H}_{12}\text{SnMe}_2]^-$ ). It can be seen that this species decomposes by two competitive pathways (bimolecular electron transfer (step 4) and unimolecular fragmentation (step 5)) whose relative rates ( $k_t[\text{BrC}_8\text{H}_{12}\text{I}]$  vs.  $k_f$ , respectively), together with the relative rate of iodine atom abstraction ( $k_a[\text{BrC}_8\text{H}_{12}\text{I}]$ ), determine the overall course of the reaction.

A remarkable feature is the greater selectivity of the 4-trimethylstannylbicyclo[2.2.2]oct-1-yl radical (**6**) with respect to iodine (step 6) than toward bromine. However, there is some evidence to support this.<sup>13</sup> Noteworthy is the preference for iodine vs. hydrogen atom abstraction (step 6 vs. step 9) given that the solvent is THF. A detailed analysis of the crude stannylation product (2 equiv of  $\text{Me}_3\text{SnLi}$ ) revealed a significant amount (ca. 5% of reaction product) of  $\text{Me}_3\text{SnC}_7\text{H}_{13}$  (not present in the original sublimed product)<sup>1</sup> which must result from hydrogen abstraction from the solvent (step 9). When compared with information on the bicyclo[2.2.2]oct-1-yl radical,<sup>14</sup> our data indicate that the  $\text{Me}_3\text{Sn}$  substituent appears to have a profound stabilizing influence on this apparently highly reactive bridgehead radical species. This is not altogether surprising given that strong "through-bond" coupling of the bridgehead bond MOs in various 4-substituted bicyclo[2.2.2]oct-1-yltrimethylstannanes is strongly suggested by <sup>119</sup>Sn NMR substituent chemical shifts (SCS).<sup>8</sup> Furthermore, the <sup>19</sup>F NMR SCS of 1-fluoro-4-(trimethylstannyl)bicyclo[2.2.2]octane<sup>4c,15</sup> indicates that the  $\sigma_{\text{C-Sn}}$  and  $\sigma^*_{\text{C-F}}$  bond MOs are strongly coupled. In valence bond terms, the possible stabilization of the 4-(trimethylstannyl)bicyclo[2.2.2]oct-1-yl radical (**6**) by a delocalization mechanism may be denoted by the canonical structure **7** (depicted for only one of the three ethano bonds).

The mechanism in Scheme II is strengthened by our observation that as disubstitution increases (case of 2 equiv of  $\text{Me}_3\text{SnLi}$  vs. 1 equiv) there is a definite increase in the iodo tin (**2**)/bromo tin (**3**) ratio (ca. 2:1 to 3:1). This is consistent with a reduced rate for the bimolecular step (4) ( $k_t[\text{BrC}_8\text{H}_{12}\text{I}]$ ) compared with that of the unimolecular step (5) ( $k_f$ ) as the reaction progresses.



Confirmation that trimethylstannylation proceeds mainly by an electron-transfer mechanism is provided by the fact that stannylation (2 equiv of  $\text{Me}_3\text{SnLi}$ ) of **1** is largely suppressed in the presence of dicyclohexylphosphine. The latter compound is considered an excellent alkyl radical trap<sup>16</sup> and, hence, is able to divert the reaction from predominant substitution to mainly reduction products (1-bromo- (18%) and 1-iodobicyclo[2.2.2]octane (5%) and bicyclo[2.2.2]octane (77%)). Only a trace of the tin derivatives were detected. The detection of 1-iodobicyclo[2.2.2]octane is of interest since the results of the labeling experiment (complete absence of isotopomer **2b**) indicated no direct replacement of bromine. We are unable to offer an explanation for this apparent dichotomy.

**Trimethylstannylation of 1,4-Dihalobicyclo[2.2.2]octanes.** Further compelling support for Scheme II is that it enables several unusual observations on the stannylation of 1,4-dihalobicyclo[2.2.2]octanes in general to be rationalized. These are as follows: (i) Whereas the fluoro iodide leads only to fluoro stannane,<sup>5</sup> the chloro iodide leads to significant amounts of disubstitution as well as to the iodo and chloro stannanes (chloro tin:iodo tin:ditin = 7.2:1.4:1).<sup>1</sup> The apparent nucleofugal behavior of the chloro group contrasts markedly with the inability to replace chlorine in 1-chloro-4-methylbicyclo[2.2.2]octane with  $\text{Me}_3\text{SnLi}$ <sup>17</sup> and other bridgehead chlorides.<sup>16b,18</sup> The result for the fluoro iodide is explained by step 4 being very much greater than step (5) ( $k_t[\text{FC}_8\text{H}_{12}\text{I}] \gg k_f$ ), whereas for the chloro iodide step 4 is still greater than step 5 but the latter fragmentation is sufficiently competitive to allow disubstitution to occur without the intermediacy of  $\text{ClC}_8\text{H}_{12}\text{SnMe}_3$  which is unreactive toward  $\text{Me}_3\text{SnLi}$ . It is of interest to note that 1-chlorobicyclo[2.2.2]octane was detected as a minor product in the chloro iodide reaction. This must be the result of hydrogen abstraction from the solvent by the appropriate bridgehead radical. (ii) Treatment of the chloro bromide with 2 equiv of  $\text{Me}_3\text{SnLi}$  produces the chloro tin and ditin compounds in the ratio of 1:1.5 (<sup>13</sup>C NMR and GLPC), with the absence of bromo stannane. Compared with the result for the chloro iodide in i above, this result is remarkable. However, it is explicable in terms of a marked change in the relative rates of steps 4 and 5 on going from the iodide to the bromide. The rate of step 4 has been reduced as step 5 is constant for both cases. In addition, step 6 which would lead to the bromo tin compound, is not competitive. (iii) Stannylation (2 equiv of  $\text{Me}_3\text{SnLi}$ ) of the dibromide and diiodide leads to disubstitution for the former with only a trace of bromo tin, but for the latter both iodo tin and ditin are formed in the ratio of 4:1, respectively. Considerable amounts of unreacted precursor was present in each case. In terms of Scheme II, these results are understandable in terms of step 5 being greater than step 4<sup>19</sup> and step 6 being

(9) Kornblum, N. *Angew. Chem. Int. Ed. Engl.* 1975, 14, 734.

(10) (a) Bunnett, J. F. *Acc. Chem. Res.* 1978, 11, 413. (b) Rossi, R. A. *Acc. Chem. Res.* 1982, 15, 164.

(11) (a) Rossi, R. A.; Palacios, S. M.; Santiago, A. N. *J. Org. Chem.* 1982, 47, 4654. (b) Palacios, S. M.; Santiago, A. N.; Rossi, R. A. *J. Org. Chem.* 1984, 49, 4609.

(12) (a) Symons, M. C. R. *Pure Appl. Chem.* 1981, 53, 223 and references therein. (b) Bailey, W. F.; Gagnier, R. P.; Patricia, J. J. *J. Org. Chem.* 1984, 49, 2098 and references therein.

(13) (a) Halogen atom abstraction by radicals is known to be much more rapid for iodides than for bromides.<sup>13b-d</sup> (b) Evans, F. W.; Fox, R. J.; Szwarc, M. *J. Am. Chem. Soc.* 1960, 82, 6414. (c) Kosower, E. M.; Schwager, I. *J. Am. Chem. Soc.* 1964, 86, 5528. (d) Cooper, R. A.; Lawler, R. G.; Ward, H. R. *J. Am. Chem. Soc.* 1972, 94, 545 and 552.

(14) (a) Baker, F. W.; Holtz, H. D.; Stock, L. M. *J. Org. Chem.* 1963, 28, 514. (b) Engel, P. S.; Chae, W. K.; Baughman, S. A.; Marschke, G. E.; Lewis, E. S.; Timberlake, J. W.; Leudtke, A. E. *J. Am. Chem. Soc.* 1983, 105, 5030 and references therein.

(15) Adcock, W.; Abeywickrema, A. N. *J. Org. Chem.* 1982, 47, 2957.

(16) (a) Radical and anion trapping experiments<sup>16b,c</sup> with dicyclohexyl phosphine and *tert*-butylamine, respectively, on 1-bromo- and 1-iodobicyclo[2.2.2]octane indicate that the stannylation reaction in each case proceeds mainly by a free-radical process. (b) Smith, G. F.; Kuivila, H. G.; Simon, R.; Sultan, L. *J. Am. Chem. Soc.* 1981, 103, 833. (c) Alnejjar, M. S.; Kuivila, H. G. *J. Am. Chem. Soc.* 1985, 107, 416.

(17) Adcock, W.; Iyer, V. S., unpublished work.

(18) Koerner, G. S.; Hall, M. L.; Traylor, T. G. *J. Am. Chem. Soc.* 1976, 98, 6764.

competitive in the diiodide case but not for the dibromide.

Finally, we wish to point out that the formation of the halo tin radical anion (step 3) and its subsequent fragmentation (step 5) raises an intriguing question as to how the electron is transmitted across the bicyclo[2.2.2]octyl ring (intramolecular electron transfer by "through-bond" or "through-space"  $\sigma$ -electron delocalization<sup>20</sup> or an electron-tunnelling mechanism?<sup>21</sup>). Studies of appropriate model substrates are in progress in an attempt to further delineate this phenomenon.

### Experimental Section

**General Methods.** Melting points and boiling points are uncorrected. The broad-band proton-decoupled <sup>13</sup>C NMR spectra (22.53 and 75.46 MHz) were recorded in the pulse Fourier transform mode on JEOL FX-90Q and Bruker CXP-300 spectrometers, respectively. The latter instrument was employed for recording proton NMR spectra (300 MHz) and broad-band proton-decoupled <sup>2</sup>H NMR spectra (46.06 MHz). <sup>119</sup>Sn spectra were recorded at 37.08 MHz on a JEOL FX-100. Routine <sup>1</sup>H NMR spectra were measured with a Varian EM-360 (60 MHz). All spectra were obtained on CDCl<sub>3</sub> solutions.

Mass spectra were obtained on an AEI MS30 spectrometer with an ionizing energy of 70 eV. Analytical vapor-phase chromatographic analyses were performed on a Varian 1740 gas chromatograph with a 10 ft column of 5% SE-30 on 100/120 Chromosorb W and a 6 ft column of silicone-OV17 on 100/120 Chromosorb WHP.

Tetrahydrofuran was distilled from sodium benzophenone ketyl under an atmosphere of dry nitrogen. The trimethylstannylation reactions were performed under argon in flame-dried glassware. Chlorotrimethylstannane (Aldrich) and dicyclohexylphosphine (Strem Chemicals, Inc.), were obtained commercially and were used as received.

Several of the 1,4-dihalobicyclo[2.2.2]octanes (bromo iodide 1, chloro iodide, and diiodide) were available from other investigations.<sup>8,22</sup> 1,4-Dibromobicyclo[2.2.2]octane (<sup>13</sup>C NMR (CDCl<sub>3</sub>, relative to Me<sub>4</sub>Si)  $\delta$  58.86 (C1, 4), 40.18 (C2, 3)) was prepared from the diiodide in the manner recently described by Wiberg et al.<sup>4b</sup> (mp 250–251 °C (lit.<sup>4b</sup> mp 252–254 °C)).

**(Trimethylstannyl)lithium.** By use of the procedure of Tamborski et al.<sup>23</sup> freshly cut lithium shavings (0.23 g, 0.032 mol), which were washed with anhydrous hexane, were added to tetrahydrofuran (5 mL) under an atmosphere of argon. A solution of chlorotrimethylstannane (0.64 g, 0.0032 mol) in tetrahydrofuran (4 mL) was then added dropwise to the suspended lithium metal at 0 °C. The well stirred reaction mixture was maintained at this temperature for 5 h. The final dark-green mixture was filtered before immediate use.

**Trimethylstannylation of 1,4-Dihalobicyclo[2.2.2]octanes.** In a typical reaction, (trimethylstannyl)lithium (1 or 2 equiv) in tetrahydrofuran (prepared as above) was added dropwise to a well stirred solution of the 1,4-dihalobicyclo[2.2.2]octane (0.0033 mol) in THF (5 mL) maintained at 0 °C. After keeping the well stirred reaction mixture at 0 °C for 16 h, the reaction was carefully quenched with a saturated aqueous ammonium chloride solution and extracted with ether. The extract was dried over anhydrous magnesium sulfate and filtered, and the solvent evaporated to afford the reaction product mixture. The crude as well as the sublimed reaction product mixture was analyzed by GLPC and NMR (<sup>13</sup>C, <sup>119</sup>Sn, and <sup>1</sup>H) to determine the relative proportion

of products. The results from the various methods were mutually consistent.

**1-Bromo-4-chlorobicyclo[2.2.2]octane.** By use of the procedure of Wiberg et al.<sup>4b</sup> a solution of 1-chloro-4-iodobicyclo[2.2.2]octane<sup>8</sup> (1 g, 0.0037 mol) in anhydrous dichloromethane (35 mL) was treated with a solution of bromine (1.3 g) in dichloromethane (12 mL). After stirring the reaction mixture at room temperature for 2 h, a standard workup followed by sublimation (0.8 g, 97%) and recrystallization afforded white microcrystals: mp 242–244 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  2.3 (12 H, s, CH<sub>2</sub>CH<sub>2</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, relative to Me<sub>4</sub>Si)  $\delta$  59.88 (C1), 39.33 (C2), 38.75 (C3), 63.43 (C4). Anal. Calcd for C<sub>8</sub>H<sub>12</sub>ClBr: C, 42.99; H, 5.41. Found: C, 42.34; H, 5.19.

**Conversion of 8 to 9.** 4-Methoxy-2-oxobicyclo[2.2.2]octane-1-carboxylic acid<sup>5</sup> (8, 15.0g, 0.075 mol) was added to an aqueous solution of sodium hydroxide (1 M, 100 mL) and the mixture stirred vigorously for 1 h. The resulting solution was then evaporated to dryness in vacuo to yield the sodium salt of the carboxylic acid (8) quantitatively. The vacuum oven-dried sodium salt was then added to a solution of deuterium oxide (75 g, 3.75 mol) and freshly prepared sodium methoxide (0.2 g, 0.0033 mol). The resulting solution, kept under an atmosphere of dry nitrogen, was then heated to 50 °C and stirred vigorously at this temperature until <sup>1</sup>H NMR analysis indicated that hydrogen/deuterium exchange was essentially complete (ca. 6 h). The reaction mixture was cooled to room temperature and then carefully acidified by the addition of 2 M hydrochloric acid. The acidified solution was then allowed to stand in a refrigerator for 24 h and the precipitate obtained collected by filtration. Further acid was obtained by extraction of the filtrate with diethyl ether. The combined acid (13 g, 87%) was shown to have greater than 85% deuterium incorporation by <sup>1</sup>H NMR (integration of the pertinent resonance absorption at 2.57 ppm).<sup>5</sup>

A sample of the crude dry deuterated acid (11 g, 0.055 mol) was esterified in a standard way (diazomethane in ether)<sup>24</sup> without purification since a trial sublimation was found to lead to a significant loss of deuterium. Kugelrohr distillation of the ester (9) afforded a colorless oil (10 g, 0.046 mol, 85%): bp 104 °C (2.0 mm); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  1.83–2.00 (8 H, m, CH<sub>2</sub>CH<sub>2</sub>), 3.20 (3 H, s, OCH<sub>3</sub>), 3.73 (3 H, s, COOCH<sub>3</sub>). <sup>1</sup>H NMR indicated greater than 85% deuterium incorporation.

**Reduction and Hydrolysis of 9 to 10.** By use of the procedure of Djerassi et al.<sup>25</sup> a solution of 9 (10.6 g, 0.05 mol), ethanedithiol (6.95 g, 0.067 mol), and anhydrous *p*-toluenesulfonic acid (0.26 g) in dry benzene (250 mL) was heated under reflux for 18 h in a flask equipped with a Soxhlet extractor. The latter contained molecular sieves (50 g, Linde 3A) in order to remove water formed during the course of the reaction. After allowing the benzene solution to cool it was then washed with aqueous sodium bicarbonate and water, and dried before removal of the benzene by careful distillation to afford the ethylene dithioketal of 9.

The crude dithioketal was then added to ethanol (300 mL, 95%) containing Raney Nickel<sup>26</sup> (327 g) and the mixture was heated under reflux with vigorous stirring for 48 h.<sup>27</sup> Workup in the usual manner followed by Kugelrohr distillation gave the deuterated derivative of methyl 4-methoxybicyclo[2.2.2]octane-1-carboxylate<sup>5</sup> as a colorless liquid: 5.5 g (50%); bp 90–92 °C (1.0 mm); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  1.70–1.76 (11.2 H, m, CH<sub>2</sub>CH<sub>2</sub>), 3.13 (3 H, s, OCH<sub>3</sub>), 3.63 (3 H, s, COOCH<sub>3</sub>), ca. 40% deuterium incorporation.

The deuterated ester (5 g, 0.025 mol) was treated with aqueous ethanolic potassium hydroxide (2 g, 0.03 mol) in the manner previously described for the hydrolysis of methyl 4-fluorobicyclo[2.2.2]octane-1-carboxylate.<sup>5</sup> Sublimation afforded the deuterated derivative (10) of 4-methoxybicyclo[2.2.2]octane-1-carboxylic acid<sup>5</sup> as a white solid: 4 g (87%); mp 168–170 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  1.80–1.90 (11.3 H, m, CH<sub>2</sub>CH<sub>2</sub>), 3.23 (3 H, s, OCH<sub>3</sub>), 10.00–10.40 (1 H, broad s, COOH), ca. 35% deuterium incorporation.

(19) (a) Half-wave reduction potentials ( $E_{1/2}$  values)<sup>19b</sup> in DMF (vs. SCE) for the iodo tin (–2.22 V) and the diiodide (–1.95 V) compounds indicate that step 4 is thermodynamically favourable for the stannylation of the diiodide. (b) Adcock, W.; Kok, G. B.; Iyer, V. S.; Peters, D. G.; Lundy, K. M.; Kitching, W. *J. Org. Chem.*, in press.

(20) (a) Hoffman, R.; Imamura, A.; Hehre, W. J. *J. Am. Chem. Soc.* 1968, 90, 1499. Hoffman, R. *Acc. Chem. Res.* 1971, 4, 1. (b) Gleiter, R. *Angew. Chem., Int. Ed. Engl.* 1974, 13, 696. (c) Paddon-Row, M. N. *Acc. Chem. Res.* 1982, 15, 245.

(21) (a) Calcaterra, L. T.; Closs, G. L.; Miller, J. R. *J. Am. Chem. Soc.* 1983, 105, 670. (b) Miller, J. R.; Calcaterra, L. T.; Closs, G. L. *J. Am. Chem. Soc.* 1984, 106, 3047.

(22) Adcock, W.; Iyer, V. S., manuscript in preparation.

(23) Tamborski, C.; Ford, F. E.; Soloski, E. J. *J. Org. Chem.* 1963, 28, 237.

(24) Vogel, A. I. "Practical Organic Chemistry"; Longmans: London, 1970; pp 971–973.

(25) Djerassi, C.; Giorman, M. *J. Am. Chem. Soc.* 1953, 75, 3704.

(26) Pettit, G. R.; Van Tamelen, E. E. *Org. React.* 1944, 2, 356.

(27) Roberts, J. D.; Moreland, W. T.; Frazier, W. J. *J. Am. Chem. Soc.* 1953, 75, 637.

**Conversion of 10 to 11.** The deuterated derivative of 4-methoxybicyclo[2.2.2]octane-1-carboxylic acid (4 g, 0.022 mol) was treated with 48% aqueous hydrobromic acid in the manner previously indicated by Adcock and Kok<sup>28</sup> for the corresponding hydrogen analogue. After a similar workup, sublimation followed by recrystallization afforded colorless needles: 3.0 g (60%); mp 264–265 °C.

**Conversion of 11 to a mixture of 1 + 1a.** The bromo-carboxylic acid (11, 2 g, 0.0085 mol) was treated with *tert*-butyl hypoiodite and then irradiated in the same manner as previously

described for the preparation of 1-fluoro-4-iodobicyclo[2.2.2]octane from the corresponding acid.<sup>5</sup> A standard workup, followed by chromatography on alumina, afforded a mixture of 1-bromo-4-iodobicyclo[2.2.2]octane (1)<sup>8</sup> and its deuterium derivatives (1a) as a white solid after recrystallization: 2.0 g (74.6%); mp 224–226 °C; mass spectrum, *m/z* (*M*<sup>+</sup> - Br) (relative intensity) 187 (77.12), 188 (66.19), 189 (100), 190 (66.36), 191 (29.89), 192 (2.89). The results of the deuterium assay are given in the Results and Discussion section.

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(28) Adcock, W.; Kok, G. B. *J. Org. Chem.* 1985, 50, 1079.

## Thermal Decomposition of Geminal Diazidomalonic Acid Derivatives. An Intermolecular Process

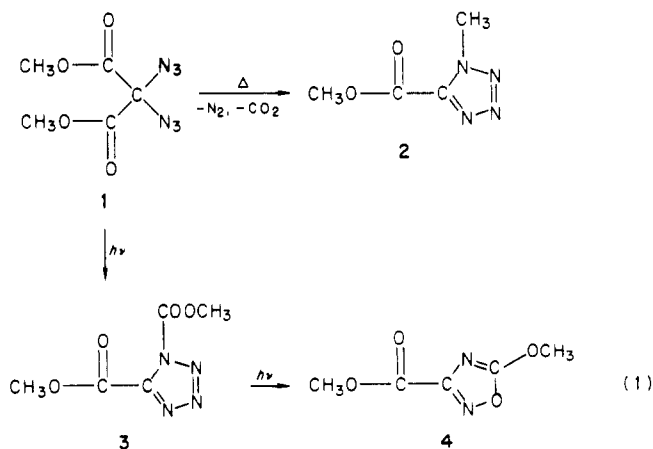
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Thermal decomposition of a 1:1 mixture of (CH<sub>3</sub>OCO)<sub>2</sub>C(N<sub>3</sub>)<sub>2</sub> and (CD<sub>3</sub>OCO)<sub>2</sub>C(N<sub>3</sub>)<sub>2</sub> to yield 1-methyl-5-carbomethoxytetrazole-*d*<sub>x</sub> proceeds with crossover of the isotope label, indicating an intermolecular pathway for this reaction. A chain mechanism involving tetrazolium nucleophiles is proposed. The thermal decomposition of diazidomalonamide (14) and *N,N'*-dimethyldiazidomalonamide (16) occurs analogously yielding 5-carbamoyltetrazole (15) and 5-(methylcarbamoyl)tetrazole (17), respectively. In order to test the mechanistic possibility that a tetrazolium intermediate plays a role in these decompositions, lithio-5-carbomethoxytetrazole was added in 10% molar concentration to dimethyl diazidomalonate (1) in dodecane. A similar experiment was carried out with diazidomalonamide (14). In both cases the reaction occurred at lower temperatures, and in each case the same products were observed as those obtained in the normal thermolysis.

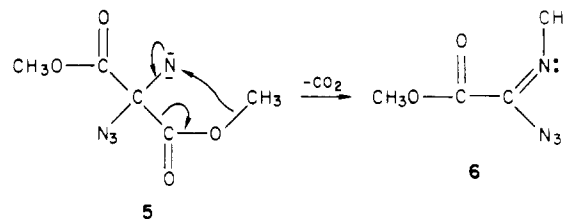
The thermal decomposition (140 °C, dodecane, 12 h) of dimethyl diazidomalonate (1) yields 2.<sup>1</sup> The photochemical decomposition of 1 (1% benzene solution, high-pressure lamp 0.5-W, 2800 Å, room temperature) yields 3.<sup>2</sup> Prolonged irradiation of 1 or separate irradiation of 3 yields 4 (eq 1).



The photochemical reaction is similar to that occurring in simpler systems, namely, loss of molecular dinitrogen upon irradiation and concomitant 1,2 group migration.<sup>3</sup> Whether a discrete nitrene intervenes is uncertain.<sup>4a,b</sup> Group migration could occur synchronously with loss of dinitrogen within the singlet manifold.<sup>4</sup> The ground-state

triplet nitrene has been well characterized spectroscopically and is a discrete reaction intermediate.<sup>5</sup>

The thermal reaction 1 → 2 is obviously more complicated than simple group migration since a fragmentative loss of carbon dioxide must occur. The loss of CO<sub>2</sub> and methyl group transfer intramolecularly via the arrangement depicted in 5 → 6 corresponds to a 5-endo-tet process and is accordingly stereoelectronically unfavorable.<sup>6</sup>



However, recently a mechanism for the decomposition of a geminal diazide appeared which pointed up the possibility of an alternative transfer. The specific example that was reported involved the rearrangement 7 → 8 → 9.<sup>7</sup>

(1) Moriarty, R. M.; Serridge, P. *J. Am. Chem. Soc.* 1971, 93, 1534.

(2) Moriarty, R. M.; Kliegman, J. M.; Shovlin, C. *J. Am. Chem. Soc.* 1967, 89, 5958.

(3) (a) Lwowski, W. "Nitrenes"; Interscience: New York, 1970. (b) March, J. "Advanced Organic Chemistry", 2nd ed.; McGraw-Hill: New York, 1977; pp 178–186. (c) Carey, F. A.; Sundberg, R. J. "Advanced Organic Chemistry"; Plenum Press: New York, 1977; Part B, pp 301–321.

(4) (a) Moriarty, R. M.; Reardon, R. C. *Tetrahedron* 1970, 26, 1379. (b) Pritzkow, W.; Timm, D. *J. Prakt. Chem.* 1966, 32, 178. (c) Lewis, F. D.; Saunders, W. H. *J. Am. Chem. Soc.* 1971, 93, 47.

(5) Wasserman, E.; Smolinsky, G.; Yager, W. A. *J. Am. Chem. Soc.* 1964, 86, 3166.

(6) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* 1976, 734.

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