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Stereoselective Sonochemical Reductive Silylation of Geminal Dibromocyclopropanes by Bulk Magnesium

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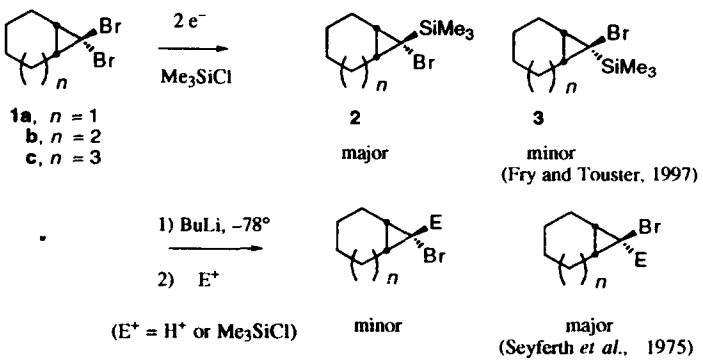
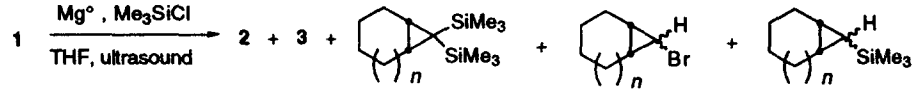
Abstract : Ultrasonic irradiation of a THF solution containing both trimethysilyl chloride and a bicyclic 1,1-dibromocyclopropane in the presence of bulk magnesium affords 1-trimethylsilyl-1-bromocyclopropanes in 72-93% yield. The sonochemical reactions proceed stereoselectively to afford as the major product the product in which the trimethylsilyl group is *cis* to the hydrogen atoms at the ring juncture.

We recently reported the electrochemical reductive silylation of several bicyclic 1,1-dibromocyclopropanes (**1**) (Eqn 1).[1] Of particular interest was our observation that such reactions proceed stereoselectively to afford as the major product monosilyl derivatives (**2**) whose stereochemistry is opposite to that of the major products (**3**) of successive treatment of **1** with a metallating agent (*n*-BuLi) and trimethylsilyl chloride (TMSCl) (Scheme 1).[2] A surprising discovery made in the course of the latter investigation was the apparent increase in current efficiency (up to 200%) when the mixture was subjected to the action of ultrasonic irradiation during electrolysis. This was traced to the use of a sacrificial magnesium anode in the undivided electrolysis cell.[1] When the magnesium rod was replaced with an inert substance or incorporated into a divided cell, the unusual ultrasonic effect disappeared. We postulated that, although the magnesium rod was essentially inert in an unsonicated electrolysis, sonication induced a rapid Grignard reaction with **1** to afford organomagnesium intermediates which could then react with TMSCl to afford **2** and **3**. In the present paper we confirm the rapid reaction between **1** and magnesium under the action of ultrasonication and demonstrate the significantly higher yields and stereoselectivity of the sonochemical process over the purely electrochemical reductive silylation of **1**.

Scheme 1



Dibromocyclopropanes **1a-c** were dissolved in anhydrous THF containing excess TMSCl and sonicated in a laboratory ultrasonic cleaning bath in a flask containing a bulk magnesium rod. A mixture consisting primarily of **2** and **3**, but also containing smaller amounts of disilyl compound **4**, monobromides **5**, and monosilyl compounds **6** was produced.(Table 1). The requirement for ultrasound to effect these conversions was demonstrated by a control experiment: in the absence of sonication, less than 2% reaction took place in four days, whereas most sonications were at least 50% complete in 15 minutes. The time course of a typical sonochemical reaction is shown in Fig. 1; note that the sum of the yields of **2** and **3** is plotted in this graph. In order to achieve rapid sonochemical conversion, it was necessary to control several experimental parameters, including proper placement of the reaction flask within the bath (directly above the ultrasonic transducer and at a height within the bath at which stirring by the ultrasonic energy was maximal, as judged visually).[1] Furthermore, since metal components in the bath tended to damp the ultrasonic energy, the copper coiling coil used to maintain the bath water near ambient temperature was located in the bath as far away from the reaction flask as possible and immersed only the minimum amount necessary to provide adequate cooling. The magnesium rod was supported by a hole bored in a rubber septum covering the top of the one-neck reaction flask, in such a manner that there was no direct contact between the magnesium rod and the glass flask.



4 5 6

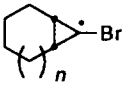
Table 1. Products of reductive silylation of bicyclic dibromocyclopropanes.

			Product Composition (%)[a]					
Run	Dibromide	Mode	**1**	**2** + **3**, (2:3)	**4**	**5**	**6**	Ref.
1	**1a**	Sonochemical	0	93 (88:12)	3	2	1	This work
2	**1a**	Electrochemical	6	58 (82:18)	2	6	16	1
3	**1b**	Sonochemical	3	80 (94:6)	9	3	2	This work
4	**1b**	Electrochemical	30	38 (63:38)	6	18	0	1
5	**1c**	Sonochemical	2	75 (94:6)	14	4	3	This work
6	**1c**	Sonochemical	2	72 (93:7)	11	6	4	This work
7	**1c**	Electrochemical	6	26 (68:32)	2	50	12	1
8	**9**	Sonochemical	2	82 (95:5)	8	3	2	This work
9	**1a**	Sonochemical	2	53 (95:5)	29	6	5	This work

[a] Mixture analyzed by gc and gc-ms.

Our previous work had demonstrated that **4** is produced by reductive silylation of **2** and **3**. We showed that **5** and **6** are formed by hydrogen abstraction by intermediate bromocyclopropyl and silylcyclopropyl radicals **7** and **8**, respectively, from the solvent.[1,3] **4** and **6** are formed by reduction of **2** and **3**; **5** is formed by reduction of **1**. Furthermore, reduction of **2** or **3** is significantly slower than reduction of **1** (Fig. 1). Run 9

produced the disilane **4a** in significantly higher amounts than obtained in the other runs. The concentrations of **1a** and TMSCl in this experiment were 4.5 times greater than the other runs, but it is not clear why this should affect the rate of conversion of **2a** and **3a** to **4a**. One might have guessed that the sonochemical reaction, being a heterogeneous process taking place on the (fixed area) magnesium surface, would be independent of the solution concentration of the other reactants. The sum of compounds **1-6** remains close to 100% throughout the sonication (Fig. 1), demonstrating that there are no other significant side reactions.



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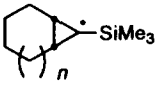

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There are very significant differences between the sonochemical and electrochemical silylations of **1.** The yields of bromosilanes **2** and **3** are considerably better in the sonochemical reaction than in the electrochemical silylations (see Table 1 and ref 1).There is also a substantially higher stereoselective preference for formation of **2** over **3**. The higher stereoselectivity of the sonochemical reaction over the corresponding electrochemical process (Table 1) is of interest in connection with potential applications relying on subsequent stereospecific transformations of **2**.[4-14] It may be that this improved stereoselectivity is due to closer contact between the dibromide and the metal surface at the point of electron transfer. Electrochemical reductions of alkyl halides exhibit a more modest stereoselectivity than do chemical reactions of similar substrates.[14] This implies that the alkyl halide is not in direct contact with the electrode surface; in fact, it might be up to a full molecular diameter distant from the surface at this point. This would considerably reduce its effective steric bulk. On the other hand, the alkyl halide probably has to be in contact with the magnesium surface for reaction to occur; if so, steric effects would be more significant. Another factor which might be of importance would be solvation of magnesium in the intermediate Grignard reagent, which would increase its intrinsic steric size. A bulky group should prefer the *exo* position, i. e., *cis* to the hydrogen atoms at the bridgehead.

Summary. Ultrasonic irradiation of a THF solution containing a chlorotrialkylsilane, bicyclic 1,1-dibromocyclopropane, and a bulk magnesium rod results in rapid formation of a mixture containing as major product a mixture of 1-trialkylsilyl-1-bromocyclopropanes (**2** and **3**). The reactions proceed with a substantial preference for formation of the isomer (**2**) in which the trialkylsilyl group is *cis* to the hydrogen atoms at the bridgehead of the bicyclic system. The stereoselective formation of **2** nicely complements the metallation-silylation sequence, which favors the epimer (**3**).[2]

Representative sonochemical reaction. A solution of 5 mmol of **1c** and 25 mmol of chlorotrimethylsilane in 10 mL of dry THF was placed in a 2.5 x 10 cm test tube. The test tube was sealed by a rubber septum through which was inserted a 7 mm diameter x 120 mm magnesium rod suspended above the bottom of the test tube. The tube was then placed in a Branson (Danbury, CT) 2200 ultrasonic bath maintained at *ca.* 10 °C by a copper cooling coil. Tube and coil were positioned so as to maximize the action of ultrasound on the magnesium rod.[1] Samples were taken periodically and quenched by addition of saturated aqueous $NaHCO_3$. The organic products were extracted with a few mL of hexane and the hexane solution, after washing with H_2O and drying over $MgSO_4$, was analyzed by gc and gc-mass spectrometry.

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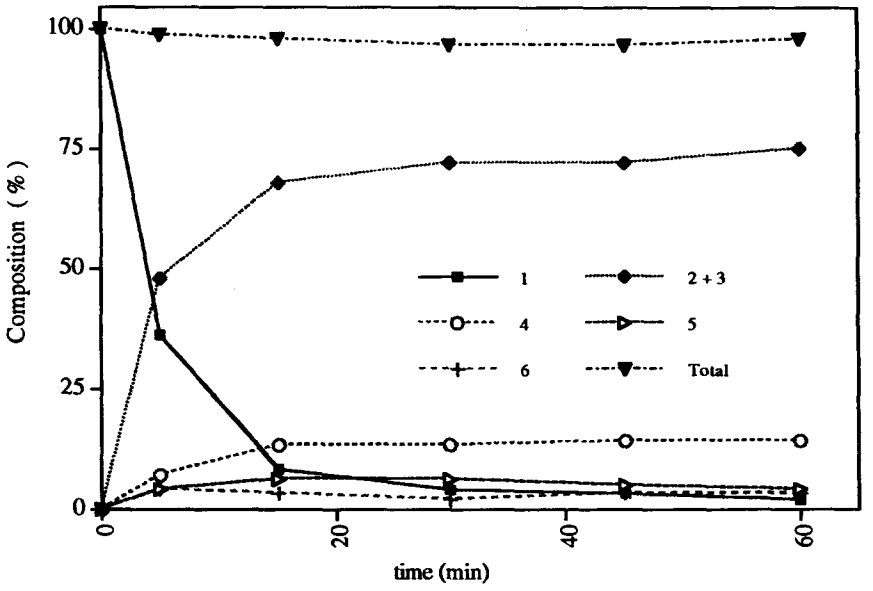

Figure 1. Composition of reaction mixture in run #5 as a function of sonication time.

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