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Stereoselective ultrasonically induced reductive monosilylation of geminal dibromonorcaranes. Steric effects

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Abstract

Sonochemical reductive silylation of 1-R-7,7-dibromonorcaranes (R = H, Me, Et, *i*-Pr) by magnesium produces in each case two 7-bromo-7-trialkylsilylnorcaranes (alkyl = methyl or ethyl). The major isomer is *exo* (the trialkylsilyl group is *cis* to the R substituent), but the stereoselectivity of silylation decreases as the alkyl group size at C-1 increases. 1-Phenyl-7,7-dibromonorcarane produced a mixture of phenylcycloheptadienes and monobromonorcaranes. © 1999 Elsevier Science S.A. All rights reserved.

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1. Introduction

Halocyclopropanes are useful synthetic intermediates [1–6] and have a long-established use as substrates for testing the stereochemical features of reaction mechanisms [7–9]. Recently silylcyclopropanes have emerged as versatile synthetic intermediates [10], particularly since many of their reactions occur with strictly defined stereochemistry [7–9,11]. A synthetic route to 1-halo-1-trialkylsilylcyclopropanes, incorporating both halogen and silane functionalities, would be of interest, but only if it proceeded in such a way as to place the two groups in well defined stereochemical relationship to other groups on the cyclopropane ring. In a recent study of the electrochemical reduction of several dibromocyclopropanes (**1**) in the presence of trimethylchlorosilane (TMS–Cl), we found that the substances **1** are converted to bromotrimethylsilylcyclopropanes (**2** and **3**) in fair-to-good yields (Scheme 1) [12]. The reactions were found to proceed with modest stereoselectivity. The major stereoisomer in the electrochemical reaction was found to be that in which the silyl group is in the *exo*-position (**2**), whereas a sequence involving metallation of the dihalide at low temperature, followed by addition of TMS–Cl, had previously been shown to afford the complementary *endo*-trimethylsilyl isomer **3**. [13]

This discovery was potentially useful in its own right. However, our interest was piqued by the incidental observation in the course of that study that dihalides **1** react readily with magnesium and trimethylchlorosilane (TMS–Cl) in a *non-electrochemical* reaction if the reaction vessel is subjected to *ultrasonic irradiation* during reaction. [14–16] The regioselectivity of the sonochemical reaction appeared to be superior to the electrochemical process [12]. The present study was carried out to further define the stereochemical course of the sonochemical reaction and to examine methods for improving its stereoselectivity.

2. Results and discussion

The 1-substituted-7,7-dibromonorcaranes (**4a–e**), prepared by addition of dibromocarbene to the corresponding cyclohexene [16], were chosen because they present an increasing degree of steric hindrance in the vicinity of the reaction site. A mixture of the dibromide and 1.2 molar equivalents of chlorotrimethylsilane (**5a**) was sonicated in dry THF containing a slight excess of

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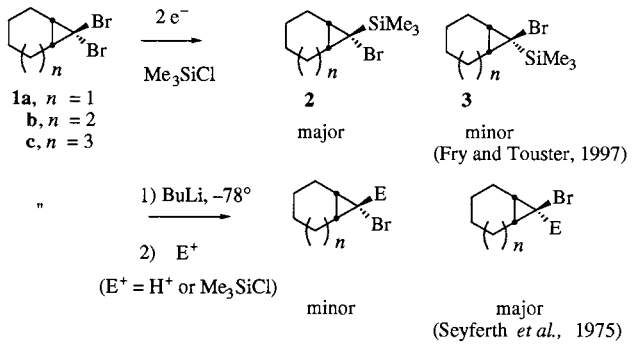
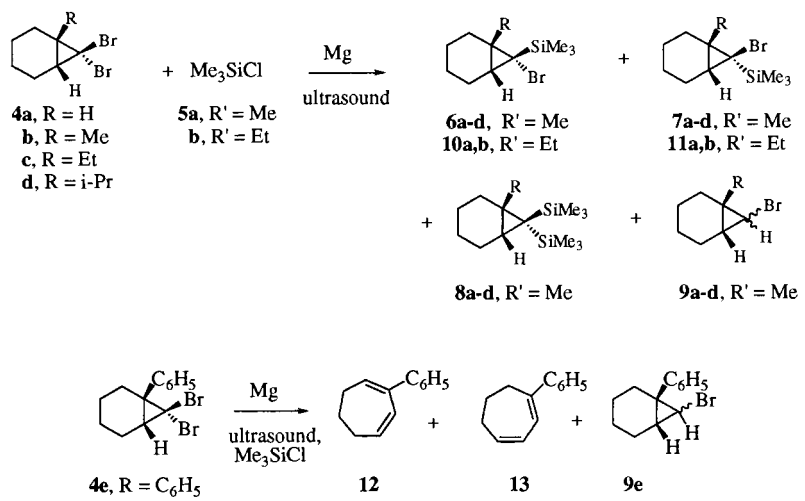


Scheme 1.

magnesium powder. Although longer irradiation was sometimes necessary, most reactions were complete in 0.5–3 h at 25°C (Scheme 2). Sonication is known to accelerate the reaction between alkyl halides and metals [14,15,17]. In control experiments, we found that only a few percent of the dihalide is consumed after several days when the suspension is stirred magnetically, whereas the dihalide is usually completely consumed within hours when the reaction vessel is immersed in an ultrasonic bath. Exact placement of the reaction flask within the ultrasonic bath is important to obtain reproducible results [12,18,19]. The bromosilanes **6** and **7** constitute the principal products from **4a**–**d** under these conditions; significantly for possible synthetic applications, little disilyl compound **8** is produced. This was of course insured by the use of less than two equivalents of magnesium, but in point of fact, monobromides **6** and **7** react with magnesium much more slowly than do the starting dibromides **4** [12]. Small amounts of the corresponding monobromonorcaranes (**9**) were also formed in each reaction (Table 1). After analysis of the mixture by gas chromatography (GC) and work-up, the major bromosilyl product (and the minor isomer when a sufficient quantity could be isolated) was isolated by preparative GC for subsequent spectral analysis. Dibromides **4a** and **4b** were also reacted with triethylchlorosilane (**5b**) to afford the corresponding bromotrialkylsilylcyclopropanes **10** and **11**. Reduction of 1-phenyl-7,7-dibromonorcarane (**4e**) under the usual silylation conditions afforded neither **6** nor **7**. Instead, a mixture of four compounds consisting of dienes (**12** [20] and **13** [21]) and two stereoisomeric monobromides (**9e**) was produced. The (inseparable) mixture of **12** and **13** was isolated by preparative GC and identified by mass and ^{1}H-NMR spectroscopy (four multiplets in the region d 5.9, 6.1, 6.2 and 6.4, four multiplets at 2.1, 2.4, 2.5 and 2.8, and an aromatic multiplet from 7.2 to 7.5).

2.1. NMR measurements

The dibromocyclopropanes and the major bromosilane isomer from each sonochemical reaction were subjected to careful analysis by a number of NMR techniques. The stereochemistry of the trialkylsilyl group was assigned as follows. Proton spin–lattice (T_1) relaxation times were first measured by the inversion-recovery method [22]. The bridgehead cyclopropyl proton(s) could be assigned because they have the largest T_1 of any protons in the molecule as a consequence of the rigidity of the cyclopropane ring. Spin decoupling experiments and the chemical shift of the cyclopropyl proton (at ca. δ 1 in the *exo*-trimethylsilyl isomers **6** and ca. δ 1.9 in the *exo*-bromo isomers **7**) supported the T_1 assignments. Nuclear Overhauser enhancement (n.o.e.) experiments were then carried out, irradiating the trialkylsilyl protons. *Exo*-trimethylsilyl compounds **6** exhibit a n.o.e. of the cyclopropyl bridge proton and the bridgehead alkyl group; *endo*-trimethylsilyl compounds **7** exhibit enhancement of two or more of the cyclohexyl ring resonances (those protons *syn* to the



Scheme 2.

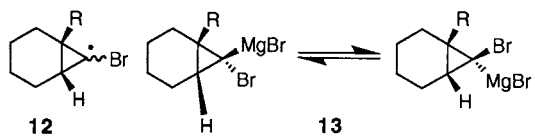
Table 1
Product composition from the sonochemical reduction of geminal dibromocyclopropanes bymagnesium in the presence of chlorotrimethylsilane

Run	Dibromide	Silylating agent	Unreacted dibromide, **4** (%)	Product mixture composition (%)		
				Bromosilanes **6** plus **7** or **10** plus **11** (%) (*exo*:*endo* ratio)	Disilane, **8** (%)	Monobromide **9** (%)
1	**4a**	**5a**	22	61 (94:6)	<1	17
2	**4a**	**5b**	20	66 (87:13)	0	14
3	**4b**	**5a**	9	73 (91:9)	0	10
4	**4b**	**5b**	15	75 (89:11)	1	10
5	**4c**	**5a**	17	78 (81:19)	0	5
6	**4d**	**5a**	5	85 (68:32)	1	9

trialkylsilyl group) [12]. Our assignments substantiate an earlier postulate [13] that *exo*-trimethylsilyl protons resonate at higher field than do those of the *endo* isomer.

Sonochemical reductive silylation clearly complements the two-step metallation–silylation sequence [13] for synthesis of 7-bromo-7-silylnorcaranes, since the latter reaction produces the *endo*-silyl isomer as the major product (Scheme 1), whereas the *exo*-silyl isomer is the predominant product from the sonochemical reaction. The sonochemical reaction is carried out at room temperature, proceeds in fair-to-good yields, and shows little or no tendency to proceed further to the corresponding disilyl compound. On the other hand, the tendency to form the *exo*-silyl isomer **6** decreases as the size of the bridgehead alkyl group increases.

There is general agreement that the reaction of alkyl halides with magnesium involves transient radicals which are coordinated to magnesium and more or less quickly reduced to carbanions [23–26]. Our results require that at least one intermediate in the overall process be capable of losing its stereochemical configuration. Cyclopropyl radicals are generally believed to invert relatively rapidly [7,27,28]. Cyclopropyl carbanions and the corresponding lithium compounds have been traditionally understood to maintain their stereochemical configuration [29,30] However, 7-lithio-7-bromonorcaranes, although configurationally stable at −78°C, lose configuration at temperatures closer to room temperature [9,31]. It is likely that the first step in the sonochemical reaction of dibromides **4** with magnesium is a single electron transfer to form a rapidly interconverting bromocyclopropyl radical (**12**). It is not possible therefore to determine whether the two bromine atoms of **4** are attacked selectively or with more or less equal facility. However, we showed earlier that electron transfer from an electrode surface occurs preferentially to the more sterically accessible halogen of a bicyclic geminal halide [32]. We favor a similar interpretation here, i.e. that the more readily accessible *exo* bromine atom of **4** is more reactive. The organomagnesium species (**13**), formed by reduction of the radical, may invert more or less rapidly; this is suggested by run # 2, in which the *exo*:*endo* stereoselectivity increases as the steric bulk of the silyl halide increases. A bulky silane is less likely to react from the *endo* face of **13**. By the same token, increased steric bulk on the *exo* face of **13** as the size of the R group increases will favor silylation from the *endo* direction.

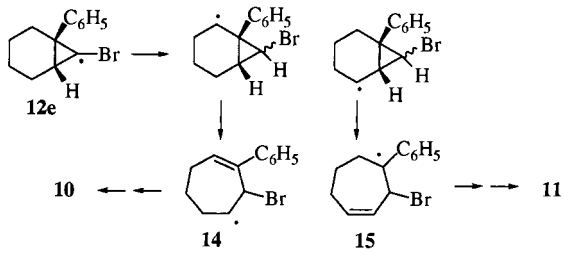


(3)

The initially formed bromonorcarane radicals **12** apparently have a finite lifetime under our conditions, since bromides presumably **9** arise by hydrogen abstraction by **12** from the solvent THF, a good hydrogen atom donor [33,34]. Our recent study of electrochemical reductive silylations [12] showed that such monobromides are formed even in scrupulously dried solvents, so it is unlikely that they arise by protonation of a carbanion or Grignard species **13**. The conversion of 1-phenyl-7,7-dibromonorcarane (**4e**) to dienes **10** and **11** provides further evidence for radical intermediates in these reactions. We propose that these dienes arise by intramolecular hydrogen atom abstraction and subsequent ring opening (Scheme 3). Conversion of rearranged radicals **14** and **15** to **10** and **11** could proceed by loss of bromine atom or by reduction to a carbanion by magnesium, followed by loss of bromide ion.

3. Experimental

^{1}H-NMR spectra were measured at 400 MHz in $CDCl_3$ on a Varian XL-400 spectrometer. GC-MS spectrometry was carried out using a Hewlett–Packard 5890/59988A GC-MS. Preparative GC was carried out on a Varian model 3300 GC using a $2 \times 1/8''$ 5% OV-101 on Chromosorb GHP column.



Scheme 3.

3.1. General procedure for synthesis of dibromocyclopropanes

A slurry of alkene and three to five equivalents of potassium *t*-butoxide was cooled in an ice bath. Three equivalents of bromoform were added drop-wise and the mixture was allowed to stir; total addition plus stirring time ranged from 4 to 7 h. Distilled water was then added. The aqueous layer was extracted with hexane; the organic layer was washed with water. The combined organic layers were dried over $MgSO_4$, solvent was evaporated, and the dibromide purified by fractional distillation. Dibromocyclopropanes **4a** [12], **4b** [35], **4d** [36] and **4e** [20] are known compounds.

3.2. 1-Ethyl-7,7-dibromonorcarane (**4c**)

B.p. 71–73°C/0.2 mm. ^{1}H-NMR ($CDCl_3$): δ 1.08 (t, 3H), 1.46 (dd, 1H), and 1.16–2.01 (m, 10H). MS m/e: 284, 282, 280 [M^+], 255, 253, 251 (100), 203, 201, 121.

3.3. 1-Phenyl-7,7-dibromonorcarane20 (**4e**)

Spectral data appear not to have been reported in the literature for this compound. B.p. 118°C/0.1 mm. ^{1}H-NMR ($CDCl_3$): δ 1.35 (m, 4H), 1.55 (m, 2H), 1.8 (m, 1H), 2.1–2.3 (m, 2H), 7.3 (m, 4 H), and 7.4 (t, 1H). MS m/e: 251 (63), 249 (63) [$M^+ - Br$], 169 (100), 141 (81), 91 (45).

3.4. Representative procedure for sonochemical reductive silylation

Dry THF (25 ml), magnesium powder (0.100 g, 4.1 mmol) dibromide **4a** (0.97 g, 3.8 mmol), and chlorosilane **5a** (0.51 g, 4.7 mmol) were added to a large flame-dried test tube which was then sealed with a rubber septum and flushed with nitrogen. The opaque gray suspension was immersed in a water-filled Bransonic 2200 ultrasonic bath and sonicated for 3 h, after which it was a clear yellow solution. Samples were removed periodically, quenched with aqueous $NaHCO_3$, extracted with ether and dried. The ether extract was analyzed by GC. The mixture was worked up as above when bromosilane formation was complete. The major product was isolated by preparative GC and analyzed by GC-MS and ^{1}H-NMR spectroscopy. Bromosilanes **6a** and **7a** have been described previously **12**. Structures of minor products were assigned from their mass spectra.

3.5. exo-7-Trimethylsilyl-endo-7-bromonorcarane (6a)

^{1}H-NMR ($CDCl_3$): δ 0.03 (s, 9H), 1.0 (m, 2H), 1.23 (m, 2H), 1.4 (m, 2H), 1.5 (m, 2H), 2.0 (m, 2H). MS m/e: 248, 246 [M^+], 206, 204, 139, 137 (100), 93.

3.6. endo-7-Trimethylsilyl-exo-7-bromonorcarane (**7a**)

^{1}H-NMR ($CDCl_3$): δ 0.25 (s, 9H), 1.2 (m, 4H), 1.45 (m, 2H), 1.7 (m, 2H), 1.9 (m, 2H). MS m/e: 248, 246 [M^+], 233, 231, 139, 137 (100), 93.

3.7. exo-7-Trimethylsilyl-endo-7-bromo-1-methylnorcarane (**6b**)

^{1}H-NMR ($CDCl_3$): δ 0.17 (s, 9H), 0.96 (dd, 1H), 1.2 (s, 3H), 1.26 (m, 2H), 1.46 (m, 3H), 1.66 (m, 1H), 1.84 (m, 1H), 2.00 (m, 1H). MS m/e: 262, 260 [M^+], 139, 137, 107, 93, 91, 73 (100).

3.8. exo-7-Trimethylsilyl-endo-7-bromo-1-ethylnorcarane (**6c**)

^{1}H-NMR ($CDCl_3$): δ 0.2 (s, 9H), 0.94 (t, 3H), 1.14–1.6 (m, 9H), 1.76 (t, 1H), 2.0 (m, 1H). MS m/e: 276, 274 [M^+], 248, 246, 139, 137, 107, 93, 91, 73 (100).

3.9. exo-7-Trimethylsilyl-endo-7-bromo-1-isopropylnorcarane (**6d**)

^{1}H-NMR ($CDCl_3$): δ 0.22 (s, 9H), 0.92 (dd, 1H), 0.96 (d, 3H), 0.97 (d, 3H), 1.2 (m, 2H), 1.4–1.6 (m, 5H), 1.89 (m, 1H), 2.02 (m, 1H). MS m/e: 290, 288 [M^+], 247, 245, 139, 137, 93, 91, 73 (100).

3.10. exo-7-Triethylsilyl-endo-7-bromo-norcarane (**10a**)

^{1}H-NMR ($CDCl_3$): δ 0.6 (q, 6H), 0.97 (t, 9H), 1.05 (dd, 2H), 1.26 (m, 2H), 1.41 (m, 2H), 1.55 (m, 2H), 2.0 (m, 2H). MS m/e: 290, 288 [M^+], 233, 231, 167 (100), 165 (100), 139, 137, 93, 91.

3.11. exo-7-Triethylsilyl-endo-7-bromo-1-methylnorcarane (**10b**)

^{1}H-NMR ($CDCl_3$): δ 0.67 (q, 6H), 0.97 (t, 9H),1.16 (s, 3H), 1.0–2.3 (m, 9 H). MS m/e: 275, 273, 167, 165 (100), 139, 137, 107, 93, 79.

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