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A stereospecific anionic reduction of *gem*-bromohalocyclopropanes by the dimsyl anion

G.W. Wijsman, W.H. de Wolf and F. Bickelhaupt *

Scheikundig Laboratorium, Vrije Universiteit, De Boelelaan 1083, 1081 HV Amsterdam, The Netherlands
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Abstract. The reaction of several 2,2,3,3-tetrasubstituted-*gem*-bromohalocyclopropanes with *t*-BuOK in DMSO unexpectedly yielded the monohalocyclopropanes in good yield. A closer investigation revealed that this reaction must be initiated by a nucleophilic attack by the dimsyl anion ($CH_3SOCH_2^-$) on bromine with subsequent protonation of the carbenoid intermediate. The reaction occurs rapidly (within 2 minutes) and is not inhibited by radical scavengers or in the dark. Only bromine, and not chlorine, is reduced, and the intermediate cyclopropyl anion is configurationally stable under the reaction conditions.

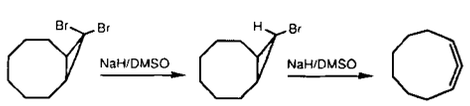
Introduction

The easy accessibility of *gem*-dihalocyclopropanes by dihalocarbene additions to alkenes has considerably enhanced our knowledge of the chemical transformations of these compounds[1a,b,c]. For example, the interesting stereochemical solvolysis of halocyclopropanes to (strained) allylsystems[1b,c,2,3], the base-induced elimination of HX to yield strained cyclopropenes[4] or the base-induced 1,4 elimations to give strained diene systems[5]. Thus, (di)halocyclopropanes cover a large area of chemistry[1b,c]. Monohalocyclopropanes can easily be prepared from their *gem*-dihalocyclopropane derivatives and dozens of reduction methods have been developed[1a,b,c].

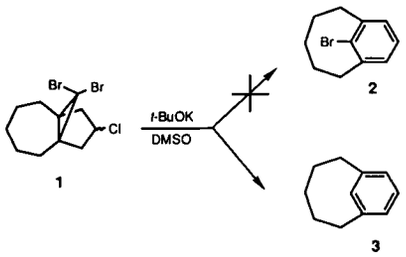
The reduction of a *gem*-dihalocyclopropane is not so difficult, and it is known that the reactivity of the leaving halide decreases in the series iodine > bromine > chlorine ≫ fluorine[1a]. For example, reduction of a 1,1-bromochlorocyclopropane always yields the chlorocyclopropane. For several reasons, it is desirable to have stereoselective reduction methods, but while reduction is easy, stereospecific reduction is not. For example, it is difficult to prepare a chlorocyclopropane from the corresponding stereochemically pure 1,1-bromochlorocyclopropane with retention of stereochemical integrity.

Most reductions are based on processes involving radical intermediates (R_3SnH[6]/R_3SiH[7]/$NaBH_4$[8]) and give mixtures of stereoisomers, because the intermediate halocyclopropylradical is not configurationally stable[1b,9]. Which isomer is formed preferentially is determined by the steric aspects in the hydrogen-transfer step to the radical. Exceptions to this rule are fluorocyclopropylradicals which are configurational stable, and thus 1,1-halofluorocyclopropanes can easily be reduced in a stereospecific way[9a,10]. Several reagents, however, can give reasonably stereospecific reduction, *e.g.* Zn/AcOH/EtOH; this reaction probably takes place via a radical anion[11]. Other reductions proceed via the cyclopropyl anion. Some older methods making use of metals, such as Mg or Li, or of derivatives of metals, *e.g.* Grignard reagents or RLi, are well known[1b]. But there are also some new, more elegant methods. It has been shown that phosphorus nucleophiles attack *gem*-halofunctions to yield reduction products[12], as well as some substituted cyclopropanes[13]. The first step in this reduction is a nucleophilic attack of phosphorus on the halide, which leads to extrusion of a cyclopropyl anion. This anion is then rapidly protonated to yield the halocyclopropane.

In 1965, *Gardner* and co-workers found that reaction of the methylsulphinyl methyl anion (= dimsyl anion) with a vicinal bromide yielded an unsubstituted alkene[14]; clearly, both a reduction and an elimination reaction were involved. In the same year, they found that the reaction of 9,9-dibromobicyclo[6.1.0]nonane with NaH/DMSO yielded the corresponding monobromide and, after prolonged reaction time, the cyclic allene (Scheme 1)[15]. They suggested that the dimsyl anion reacted with the dibromides in a nucleophilic attack at bromine, a carbanion acting as leaving group which was subsequently protonated. This protonation is reversible, and a second, apparently slower escape route of the highly energetic bromocyclopropyl anion gets a chance: it reacts as a carbenoid and irreversibly extrudes a bromide to yield a carbene, which then rearranges to the allene. Evidently the dimsyl anion is capable of reducing a dibromocyclopropane entity. This



Scheme 1.



Scheme 2.

reaction has been cited occasionally[1c,8,16-18], but has not been widely applied.

In our group[17,19,20], as well as in others[21], a variety of small and strained cyclophanes have been prepared[22]. In particular, [*n*]metacyclophanes ($n > 4$) can be synthesized via a convenient two-fold elimination and ring opening from propellane precursors[20-22]. In an attempt to obtain new derivatives of [5]metacyclophane, we prepared the dibromochloro[5.3.1]propellane **1**[2]. However, to our surprise, in the ensuing elimination step with *t*-BuOK/DMSO, the expected 11-bromo[5]metacyclophane **2** was not formed (by elimination of HCl and a 1,4 elimination of HBr with simultaneous cyclopropyl ring opening)[22], but the unsubstituted [5]metacyclophane **3** (Scheme 2)[23a]. This puzzling reduction caught our attention and recently, a few other examples have been encountered[17,23]. In this article, we report that this reduction is effected not by the added base *t*-BuOK, but by the dimsyl anion, it occurs very easily and stereoselectively in some systems.

Results and discussion

Preparative aspects

In recent years, we have focused our efforts on the synthesis of new halopropellane systems in order to prepare new and more strained cyclophanes. One of them, **4**, has been the precursor for the highly strained mono(Dewar-benzene) isomer of [1.1]metacyclophane **6** (Scheme 3)[17]. The other is the [3.3.1]propellane **8** (Scheme 4), which can serve as a precursor for the elusive [3]metacyclophane.

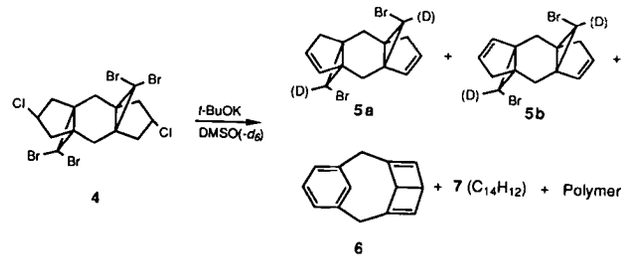
When **4** was treated with *t*-BuOK in DMSO, the products **5a**, **5b**, **6**, an isomeric $C_{14}H_{12}$ compound **7** and a yellow polymer were obtained (Scheme 3). We will not discuss the formation of the latter three, but focus our attention on the debromination which, in a very fast reaction, must have preceded the formation of **5**, **6** and **7**. The recovery of the products was reasonable, loss of material after longer reaction times being due to the instability of **6**. When the reaction was performed on a small scale in DMSO-d_6, a ^{1}H-NMR spectrum of the reaction mixture taken about 10 minutes after adding the *t*-BuOK, showed that **4** had been completely consumed. After prolonged reaction (1 hour) and the usual workup, **5a, b** were found to be dideuterated, as expected. We succeeded in obtaining a mixture of **5a, b** free from other products by crystallization from pentane, but separation of the two isomers was not possible, so a crystal structure could not be determined to establish the stereochemistry.

However, we were able to determine the stereochemistry of the two compounds by NMR techniques. From ^{1}H- and ^{13}C-NMR spectroscopy, it is clear that **5a** must have C_2 symmetry and **5b** C_i symmetry; **5a** shows eight ^{13}C resonances and **5b** seven. The protons of the central six-membered ring in **5a** give rise to two coinciding singlets at δ 2.21, implying that the two protons on each CH_2 group are equivalent, but the two CH_2 groups are not; note that there are two ^{13}C resonances (δ 21.7 and 30.9) which have a CH correlation with this singlet at 2.21 ppm. Compound **5b** shows an AB system with the intensity of four protons (δ 2.04 and 2.38, $^2J_{AB}$ 14.4 Hz), indicating that the two CH_2 groups are equivalent (one ^{13}C resonance at 26.3 ppm), but not symmetrical. Finally, NOE experiments proved that both bromines are *endo*, *i.e.*, directed towards the six-membered ring. Thus, the reduction had been highly regioselective, the nucleophilic attack from the dimsyl anion occurring from the presumably less hindered *exo* side. The difference between **5a** and **5b** is caused by the different direction of elimination of HCl in the five-membered ring; not surprisingly, there is no bias for either one, and **5a** and **5b** are formed in a 1:1 ratio.

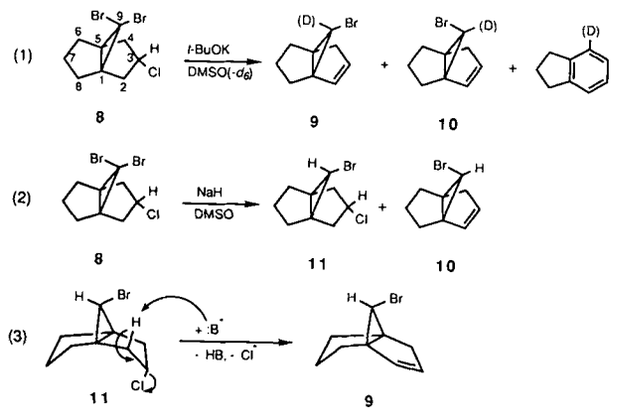
Another example of this reduction was found in the [3.3.1]propellane system **8** (Scheme 4). When **8** was treated with *t*-BuOK in DMSO (reaction 1 in Scheme 4), two isomeric reduced propellenes **9** and **10** were formed, along with indane (ratio 1:1:2). Again, the interesting formation of indane will not be discussed here. When the reaction was performed in DMSO-d_6, monodeuterated **9** and **10** were found, again in a 1:1 mixture. When the reaction was performed in the absence of the strong base *t*-BuOK, but with the dimsyl anion (reaction 2 in Scheme 4), only **10** and **11** were formed (ratio 1:1, along with a very small amount of **9**). The recovery was almost quantitative. The stereochemistry was assigned on the basis of several NOE experiments. Contrary to the *endo* specificity of **4**, there is no preference for reduction of the bromines above the two different five-membered rings. This can be rationalized by the rather symmetrical conformation of **8**. Both five-membered rings are slightly puckered down, pointing away from C9[24]. The chlorine has the *endo* position and is thus on the other side of the ring. The steric environment of both bromines is therefore almost equal, and the dimsyl anion can attack from both sides with equal ease.

A second remarkable feature apparent from Scheme 4 is the difference in the rates of the elimination reactions leading to **9** and **10**. The formation of **9** from the primary reduction product **11** is slower than the corresponding elimination leading to **10**: while the stronger proton base *t*-BuOK leads to rapid elimination in both cases (Eqn. 1), the weaker proton base dimsyl sodium cannot as easily achieve elimination of hydrogen chloride from **11**. As shown in Eqn. 3, this *trans*-diaxial elimination is hampered because the bulky bromine substituent hinders the attack of the base on the axial proton shown. Incidentally, this observation proves again the remarkable ease of the primary reduction step: it is faster than the rapid 1,2 elimination of hydrogen chloride leading to **9**, and this must also be true for the formation of **10**, where an intermediate corresponding to **11** was not observed, nor was the direct HCl elimination from **8**.

From the two reactions of Scheme 4 we conclude that it is the dimsyl anion which is responsible for the reduction of the *gem*-dibromocyclopropyl group. There are ample

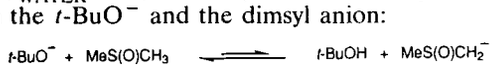


Scheme 3.



Scheme 4.

precedents in the literature that the *tert*-butoxide anion is capable to abstract a proton from DMSO and is thus responsible for the formation of the dimsyl anion[18], as *t*-BuOK is much more basic in DMSO [pK(DMSO) = 35 and pK(*t*-BuOK)$_{DMSO}$ = 32][25], than it is in water [pK(*t*-BuOK)$_{WATER}$ = 19)[26]. Thus, there is an equilibrium between the *t*-BuO$^-$ and the dimsyl anion:



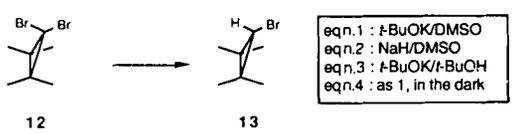
With this in mind one can understand that *t*-BuOK in DMSO is just another way of making a dimsyl anion in a low steady-state concentration. However, in this latter case, most of the *t*-BuOK is still available as a powerful base which promotes eliminations. This also implies that the exclusive reduction will only occur if no hydrogens β to the *gem*-bromohalo functionality are present, otherwise a 'simple' 1,2 elimination affording the strained cyclopropenes will occur[4]. Tetraalkyl-substituted *gem*-bromohalocyclopropanes (and thus our halopropellanes) fit these criteria and this may be the reason that this reduction has not been encountered more often. An interesting analogue in aromatic chemistry is the conversion of 1,2,4-tribromobenzene to 1,4-dibromobenzene with *t*-BuOK/DMSO![27].

We wish to point out that this easy reduction–elimination reaction is useful in the synthesis of strained cyclophanes, as it makes a separate reduction step (including purification) unnecessary; this is illustrated by the one-pot preparation of **3** and **6**.

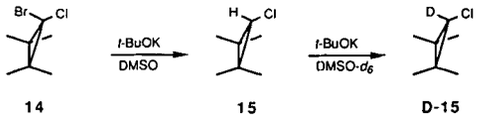
Mechanistic aspects

For preparative and mechanistic reasons, we were interested in the stereochemistry of the reduction. Therefore we synthesized and investigated some model systems.

These were chosen to fulfill several criteria. As mentioned before, the *t*-BuOK/DMSO system has the potential of making the dimsyl anion (which is responsible for the reduction) but, due to the presence of (large amounts of) *t*-BuOK, it is also a powerful eliminating medium. In order to prevent such eliminations, three tetraalkylcyclopropanes, *i.e.* 1-bromo-1-halo-2,2,3,3-tetramethylcyclopropane (**12**: halo = bromo, **14**: halo = chloro; Scheme 5 and 6) and 7-bromo-7-chloro-1,6-dimethylbicyclo[4.1.0]heptane (**16**; Scheme 7) were selected.



Scheme 5.



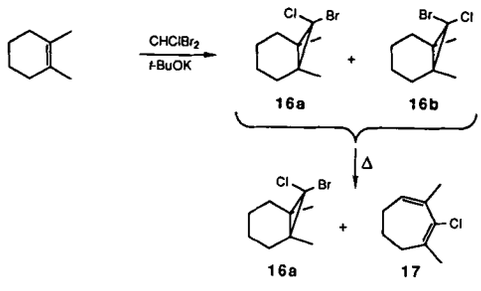
Scheme 6.

When **12**[28] was treated with *t*-BuOK in DMSO (Scheme 5, equation 1), only product **13**[6a] was obtained in good yield (88%). The reaction proceeds very quickly. Workup of a sample after a few minutes showed that only a trace of **12** was left. When the reaction mixture was stirred at elevated temperatures (4 h at 50°C), **13** was no longer recovered from the mixture; only unidentified volatile products (presumably bicyclobutane or allene derivatives) were formed, in analogy with the results of *Gardner* et al.[15]. When the dimsyl anion (NaH/DMSO; Scheme 5, equation 2) was used instead of the *t*-BuOK, essentially the same results were obtained. Clearly, *t*-BuOK in DMSO is preferable because it is experimentally more convenient. When the reaction was performed with *t*-BuOK in *t*-BuOH (Scheme 5, equation 3) no reaction took place; the recovery was almost quantitive. This supports our previous conclusion that it is the dimsyl anion and not the *t*-BuOK which is responsible for the reduction.

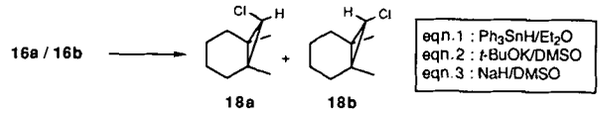
The reaction of **12** with *t*-BuOK/DMSO in the dark (Scheme 5, equation 4) gave the same results as equation 1. Similarly, reaction in the dark with a radical scavenger (1,3-dinitrobenzene) gave analogous results, although the yield of **13** was somewhat lower (68%). These results indicate that radicals are not involved. This leaves only the alternative that the debromination takes place via a polar S_N2 attack on bromine[27]. Later on, we will present some stereochemical evidence for this mechanism.

It was also of interest to investigate the behaviour of a 1,1-bromochlorocyclopropane. For this purpose, we synthesized compound **14**[29]; its reaction with *t*-BuOK/DMSO yielded only **15**[30] in high yield (96%, Scheme 6). As expected, the reduction of bromine, and not of chlorine occurred. When **15** was reacted with *t*-BuOK in DMSO-d_6, some deuterated **15** was detected by NMR and GC-MS analysis. This indicates that the carbanion (carbenoid), which is now obtained by a hydrogen abstraction, can indeed occur as an intermediate as postulated for the reduction reaction, and also that the proton abstraction is a reversible process.

To investigate the stereochemical aspects of the reaction we decided to synthesize the previously unknown compound **16** (Scheme 7). A bromochlorocarbene addition by the method of *Skattebøl*[31] to 1,2-dimethylcyclohexene yielded the isomers **16a** and **16b** in equal amounts. We were able to isolate one isomer by preparative gas chromatography in the following way. When the mixture of **16a, b** was injected, one isomer rearranged by opening of a cyclopropyl ring followed by loss of hydrogen bromide to give 2-chloro-1,3-dimethyl-1,3-cycloheptadiene (**17**); the other isomer was left in pure form. This thermal rear-



Scheme 7.



Scheme 8.

rangement is known to follow the Woodward–Hoffmann–de-Puy rules[32], which state that the leaving group must be *syn* to the six-membered ring. Therefore, it must be **16b** which rearranges to **17**. Hence, the unreactive, isolated isomer must be **16a**. Both stereoisomers of **16** could be unequivocally identified by their methyl signals in the ^{1}H-NMR spectrum (**16a**: δ 1.25 ppm; **16b**: δ 1.21 ppm).

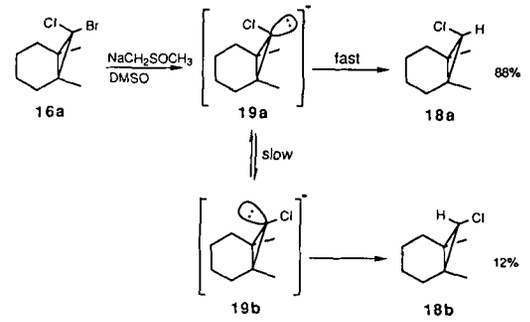
We performed several reduction reactions on the mixture of **16a, b** (Scheme 8; Table I), which yielded the monochloro compounds **18**. The assignment of the stereochemistry was checked by NOE measurements (positive NOE from the cyclopropyl proton on the methyl group for **18a**, no response for **18b**). Both compounds have a characteristic resonance signal for their cyclopropyl hydrogen (**18a**: δ 2.58 ppm; **18b**: δ 2.83 ppm).

Reduction of **16** with Ph_3SnH in Et_2O at 35°C for 2 hours yielded both isomers **18** in very good yield (98%) in the ratio **18a/18b** = 3/7 (Table I; entry 1). Thus, in the radical reduction, which involves a chlorocyclopropyl radical, rapid stereomutation occurs, and the ratio is apparently determined by steric factors governing the hydrogen transfer step.

A reduction with *t*-BuOK/DMSO in this system did not proceed satisfactorily. The total recovery was low. In addition to several unidentified products, some **18b** was found. Possibly, the system is not as inert as we had hoped, and the cyclopropyl ring opening occurred under these drastically basic conditions (Table I; entry 2).

The reaction with NaH/DMSO gave better results. This is not so much true for the prolonged reaction (30 min), which gave similar decomposition as in the *t*-BuOK/DMSO system, the only difference being that a trace of **18a** was still present (Table I; entry 3: ratio **18a/18b** = 1/9). With shorter reaction times, two minutes being the optimum, the ratio of **18a/18b** was almost 1/1 (Table I; entry 4). Apparently, **18a**, with the chlorine *syn* to the cyclohexane ring, is not very stable under the conditions, and reacts slowly to give unidentified products. This increased reactivity of **18a** is expected for a symmetry-controlled ring opening. Keeping the reaction time short suppresses this unwanted side reaction. A small drawback of this short reaction time is that some **16** remained unreacted.

When the reaction was performed on pure **16a** for 2 minutes, **18a** was the major compound with a ratio of **18a/18b** = 88/12 (Table I, entry 5). Thus, the isomer which is less favoured in the radical reaction, is formed in excess in this anionic reduction, in spite of its lower stability (*vide supra*). Even more importantly, the reduction occurs with a considerable degree of stereochemistry.



Scheme 9.

For the intermediate carbenoid **19a**, protonation is faster than inversion to the stereoisomeric carbenoid **19b** (Scheme 9). This can clearly be seen by examining Table I. In entry 5, a pure sample of **16a** gives mainly **18a**. This must be the kinetic and not the thermodynamic product. If it were the thermodynamic product, then entry 4 (with a 1:1 ratio of **16a, b**) would give the same results. This is not the case, and protonation of the carbenoid **19** is very fast under the reaction conditions. So we think that the inversion of the chlorocyclopropyl anion does not proceed very quickly under these reaction conditions, and, as the results show, most of the stereochemical information which is present in **16a**, is transferred to the product **18a**.

Conclusion

The reduction of a bromine from tetraalkyl-*gem*-bromohalocyclopropanes can easily be accomplished with *t*-BuOK in DMSO. The reaction is very rapid and occurs via a nucleophilic substitution of a dimsyl anion on the bromine, with subsequented protonation of the carbenoid intermediate. This protonation is very rapid and the cyclopropyl anion is reasonably configurationally stable under the reaction conditions. Only cyclopropanes without hydrogens vicinal to the *gem*-bromohalo functionality undergo this reduction as otherwise a 'simple' 1,2 elimination predominates. This easy reduction reaction is useful in the synthesis of small and strained cyclophanes[17,23a].

Experimental

The ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker WH-200 spectrometer at 200.1 and 50.29 MHz, respectively. NOE-difference experiments were performed on a Bruker WH-400 operating at 400 MHz. All NMR samples were measured in $CDCl_3$, with $CHCl_3$ as internal standard (δ 7.27 ppm). High-resolution mass spectra (HRMS) were measured on a Finnigan Mat-90 spectrometer operating at an ionization potential of 70eV, and GC-MS spectra were recorded on a HP-5971-MSD. (Preparative) Gas–liquid chromatography (GLC) was performed on an Intersmat P120 apparatus using a glass column (1.5 m × 1/4"; 15% SE-30 on Chromsorb WAW 60–80 mesh) with H_2 as carrier. The assignment of the signals is based on 2D-CH correlation, 2D-HH-COSY and NOE experiments.

Table I Reductions of a 1:1 mixture of **16a** *and* **16b**

Entry	Method	Solvent	Time (min)	Ratio [a] **18a/18b**	Unidentified products	Yield [b] (%)
1	Ph_3SnH	Et_2O	120	3:7	none	98
2	*t*-BuOK	DMSO	30	–:10	yes	low [c]
3	NaH	DMSO	30	1:9	yes	low [d]
4	NaH	DMSO	2	4.5:5.5	traces	65 [e]
5	NaH [f]	DMSO	2	9:1	traces	ca. 70

[a] Normalized to 10. [b] Yield of **18a** + **18b**. [c] Not determinable due to by-products; total recovery by weight about 18%. [d] Total recovery by weight about 24%. [e] Some **16** was still present, the yield of **18** was about 65%. [f] In this case, pure **16a** was used instead of the mixture.

Starting materials

endo,endo-5,11-Dichloro-13,13,14,14-tetrabromopentacyclo[7.3.1.$0^{1,9}$.$0^{3,7}$.$1^{3,7}$]tetradecane (**4**). To a cooled (0°C) solution of 5,11-dichlorotricyclo[7.3.0.$0^{3,7}$]dodeca-1(9),3(7)-diene[17] (0.45 g, 2.0 mmol) and $CHBr_3$ (3.60 g, 14.2 mmol) in anhydrous benzene (20 ml) under nitrogen was added *t*-BuOK (1.6 g, 14.2 mmol) over $\frac{1}{2}$ h. The reaction mixture was stirred for another h and then poured into a cold water/ether mixture. The resulting precipitate which was removed by filtration was the *endo,endo*-dichlorobiscarbene adduct **4**. The organic phase was treated again with $CHBr_3$ and *t*-BuOK. A standard workup provided a total of 630 mg of colourless crystals (55%), consisting of **4** and the two other isomers (*endo,exo*-dichloro- and *exo,exo*-dichloro-) of **4**.
Identification of **4** (*endo,endo*-dichloro-). ^{1}H NMR: δ 2.23, s, 4H; 2.73, AB part of A_2B_2X system; 2.50, $^2J_{HH}$ 15.3 Hz, $^3J_{HH}$ 6.0 Hz; 2.95, $^2J_{HH}$ 15.3 Hz, $^3J_{HH}$ 8.8 Hz, 8H; 4.29, X part of A_2B_2X system, tt, $^3J_{HH}$ 8.8 Hz, $^3J_{HH}$ 6.0 Hz, 2H. ^{13}C NMR: δ 29.9, t, J_{CH} 134 Hz, C2/8; 37.6, s, C1/3/7/9; 49.1, s, C13/14; 49.7, t, J_{CH} 133 Hz, C4/6/10/12, 56.6, d, J_{CH} 158 Hz, C5/11. HRMS ($C_{14}H_{14}{}^{79}Br_2{}^{81}Br_2{}^{35}Cl_2$ and two other isotopes) calcd.: 571.7163; found: 571.715.

9,9-Dibromo-endo-3-chlorotricyclo[3.3.1.0]nonane (**8**). The synthesis of **8** was performed in analogously to synthesis of **1**[2] and will be described elsewhere. The spectrometrical data are presented here. ^{1}H NMR: δ 1.83, m, 1H; 2.10, m, 3H; 2.30, m, 2H; 2.47, m, 4H; 4.53, m, 1H. ^{13}C NMR: δ 33.0, t, J_{CH} 133 Hz, C7; 36.2, t, J_{CH} 132 Hz, C6/8; 47.3, t, J_{CH} 134 Hz, C2/4; 53.5, s, C1/5; 58.2, s, C9; 69.5, d, J_{CH} 157 Hz, C3). HRMS ($C_9H_{11}{}^{79}Br_2{}^{35}Cl$) calcd.: 311.8916; found: 311.890.

Compounds **12** and **14** were prepared by addition of dibromo- or bromochlorocarbene to 2,3-dimethyl-2-butene, respectively, by the method described for the synthesis of **16** (*vide infra*). Purification was achieved by crystallization from EtOH.
1,1-Dibromo-2,2,3,3-tetramethylcyclopropane (**12**)[28]. ^{1}H NMR: δ 1.26, s, 12 H. M.P. 77°C (lit. 78°C).
1-Bromo-1-chloro-2,2,3,3-tetramethylcyclopropane (**14**)[29]. ^{1}H NMR: δ 1.23, s, 6H; 1.26, s, 6H. ^{13}C NMR: δ 18.7, Me; 21.9, Me; 29.5, s, C2/3; 69, s, C1.

7-Bromo-7-chloro-1,6-dimethylbicyclo[4.1.0]heptane (**16**). To a solution of 1,2-dimethylcyclohexene (1.2 g, 10 mmol) and $CHClBr_2$ (5.7 g, 27 mmol) in 100 ml of dry pentane, *t*-BuOK (3.0 g, 27 mmol) was slowly added over 2 h at 0°C. After stirring for 15 h at room temperature, the mixture was poured into 150 ml of cold water and extracted three times with pentane. The combined organic layers were washed with water and brine, dried on $MgSO_4$ and filtered. After removal of the pentane, a light yellow oil, being a 1:1 mixture of **16a, b**, remained, along with a small amount of unreacted $CHClBr_2$ and some polymer. Chromatography on a silica colomn with pentane, and removal of the $CHClBr_2$ under reduced pressure at 50°C yielded a clear oil consisting of **16a** and **16b** only (2.44 g, 9.5 mmol, 95%). Separation of isomers of **16** was achieved by preparative GLC at 140°C, which yielded **16a** (retention time 5 min) and **17** (retention time 2 min).
anti-7-Bromo-*syn*-7-chloro-1,6-dimethylbicyclo[4.1.0]heptane (**16a**). ^{1}H NMR: δ 1.25, s, 6H; 1.00–1.95, m, 8H. ^{13}C NMR: δ 21.1, t, J_{CH} 126 Hz; 22.9, q, J_{CH} 129 Hz, Me; 28.0, t, J_{CH} 126 Hz; 28.5, s, C1/6; 69.6, s, C7. HRMS ($C_9H_{14}{}^{79}Br^{35}Cl$) calcd.: 235.9968; found: 235.9980.
syn-7-Bromo-*anti*-7-chloro-1,6-dimethylbicyclo[4.1.0]heptane (**16b**). From the mixture of **16**, the signals of **16b** could be obtained by subtraction of those of **16a**. ^{1}H NMR: δ 1.21, s, 6H; 1.00–1.95, m, 8H. ^{13}C NMR: δ 19.8, 20.8, 29.0, C1/6; 30.4, 70.5, C7.
2-Chloro-1,3-dimethyl-1,3-cycloheptadiene (**17**). ^{1}H NMR: δ 1.80–2.00, m, 12H; 5.90, m, 1H. ^{13}C NMR: δ 20.3; 20.8; 25.2; 32.9; 35.4; 126, very low intensity; 129.5; 136.4; 136.7. HRMS ($C_9H_{13}{}^{35}Cl$) calcd.: 156.0706; found: 156.0696.

Preparation of dimsyl sodium. NaH (4.2 mmol, 0.17 g, 60% dispersion in mineral oil) was washed five times with pentane. Then 15 ml of dry DMSO was added. The mixture was heated to 80°C for 2 hours. The solution was cooled to room temperature.

Reaction of **4** *with t-BuOK / DMSO*

To a solution of **4** (186 mg, 0.32 mmol) in 35 ml of DMSO was added slowly under N_2 10 eq. (*ca.* 0.4 g) of *t*-BuOK at room temperature. After stirring for 15 min, the mixture was poured into cold water and extracted three times with pentane. The combined organic layers were twice washed with water, dried on $MgSO_4$, filtered and concentrated to give a yellow semi-crystalline residue, containing **5a, b, 6, 7** and a yellow polymer according to NMR and GC-MS. Purification was achieved by column chromatography on Al_2O_3 with pentane as eluent and several crystallizations of the residue from pentane at −20°C. This yielded a 1:1 mixture of **5a, b** as inseparable isomers.
endo,endo-13,14-Dibromopentacyclo[7.3.1.$0^{1,9}$.$0^{3,7}$.$1^{3,7}$]tetradeca-4,11-diene (**5a**). ^{1}H NMR: δ 2.21, two signals, s, 4H; 2.47, [AB part of ABXY system: δ(A) 2.42, $^2J_{HH}$ 17.5 Hz, $^3J_{HH}$ 2.1 Hz, $^4J_{HH}$ 2.1 Hz; δ(B) 2.52, $^2J_{HH}$ 17.5 Hz, $^3J_{HH}$ and $^4J_{HH}$ unres., 4H]; 2.64, s, 2H; 5.48, X part of ABXY system, *J* unres., 2H; 5.75, Y part of ABXY system, *J* unres., 2H.
endo,endo-13,14-Dibromopentacyclo[7.3.1.$0^{1,9}$.$0^{3,7}$.$1^{3,7}$]tetradeca-4,10-diene (**5b**). ^{1}H NMR: δ 2.22 (AB-system; δ 2.04 and δ 2.38, $^2J_{HH}$ 14.4 Hz, 4H); 2.46 [AB part of ABXY system: δ(A) 2.40, $^2J_{HH}$ 17.5 Hz, $^3J_{HH}$ 2.1 Hz, $^4J_{HH}$ 2.1 Hz; δ(B) 2.52, $^2J_{HH}$ 17.5 Hz, $^3J_{HH}$ and $^4J_{HH}$ unres., 4H]; 2.64, s, 2H; 5.48, X part of ABXY system, *J* unres., 2H; 5.75, Y part of ABXY system, *J* unres., 2H.
Mixture of **5**. ^{13}C NMR: δ 21.7, t, J_{CH} 129 Hz, **5a**; 26.3, t, J_{CH} 113 Hz, **5b**; 26.9, s; 27.7, s; 30.9, t, J_{CH} 128 Hz, **5a**; 35.4, s; 36.1, s; 40.2, d, J_{CH} 192 Hz; 40.3, d, J_{CH} 192 Hz; 44.0, t, J_{CH} 134 Hz; 44.2, t, J_{CH} 134 Hz; 129.3, t, J_{CH} 165 Hz; 129.5, t, J_{CH} 165 Hz; 135.6, t, J_{CH} 166 Hz; 135.7, t, J_{CH} 166 Hz; HRMS ($C_{14}H_{14}{}^{79}Br_2$) calcd.: 339.9461; found: 339.947.

Reaction of **8** *with t-BuOK / DMSO*

In a dry, N_2-flushed 10-ml flask, **8** (78 mg, 0.25 mmol) was allowed to react with 1.5 mmol sublimated *t*-BuOK in 3 ml dry DMSO (or DMSO-d_6). After 2 h at 40°C, the mixture was poured into 15 ml cold water and extracted four times with pentane. The organic layer was washed twice with water, dried on $MgSO_4$, filtered and concentrated under reduced pressure. The residue was a light yellow oil, yield 22 mg, containing three major products (indane, **9**, **10**) in a ratio of 2:1:1. Separation was achieved by preparative GLC at 130°C.
syn-9-Bromotricyclo[3.3.1.$0^{1,5}$]non-2-ene (**9**). ^{1}H NMR: δ 1.81–2.11, m, 6H; 2.42, m, 2H; 3.45, s, 1H; 5.51, m, 1H; 5.65, m, 1H. ^{13}C NMR: δ 28.2, t; 29.2, t; 31.8, t; 38.4, s; 40.8, s; 50.5, t; 130.1, d; 135.2, d; the intensity of C9 was too low to be observed.
In the deuterated compound, the signal at δ 3.45 was missing.
anti-9-Bromotricyclo[3.3.1.$0^{1,5}$]non-2-ene (**10**). ^{1}H NMR: δ 1.81–2.11, m, 6H; 2.42, m, 2H; 3.10, s, 1H; 5.41, m, 1H; 5.78, m, 1H. ^{13}C NMR: δ 27.6, t; 31.6, t; 32.6, t; 41.2, s; 41.6, s; 46.8, s, C9; 51.5, t; 132.9, d; 133.9, d.
In the deuterated compound, the signal at δ 3.10 was missing.

Reaction of **8** *with NaH / DMSO*

Dimsyl sodium (15 ml DMSO, 0.17 g NaH) was prepared as indicated above. To this solution was added **8** (0.5 mmol, 0.16 g) under N_2. After 2 h at 40°C, the mixture was poured into 25 ml of ice-water and extracted four times with pentane. The organic layer was washed twice with water, dried on $MgSO_4$, filtered and concentrated under reduced pressure, yielding 0.14 g of a light yellow oil (*ca.* 70%), containing **9**, **10** and **11** in a ratio of 1:11:12. Purification was achieved by preparative GLC (150°C). Compounds **9** and **10**, see above.
syn-9-Bromo-*endo*-3-chlorotricyclo[3.3.1.$0^{1,5}$]nonane (**11**). ^{1}H NMR: δ 1.82–2.02, m, 6H; 2.35 [AB part of A_2B_2X system: δ(A) 2.26, $^2J_{HH}$ 15.2 Hz, $^3H_{HH}$ 4.4 Hz; δ(B) 2.43, $^2J_{HH}$ 15.2 Hz, $^3J_{HH}$ 6.6 Hz, 4H]; 3.30, s, 1H; 4.59, X part of A_2B_2X system, tt, $^3J_{HH}$ 4.4 Hz, $^3J_{HH}$ 6.6 Hz, 1H. ^{13}C NMR: δ 29.5, t, C7; 33.0, t, C6/8; 40.3, d, C9; 42.7, t, C2/4; 43.9, C1/5; 67.9, d, C3. HRMS ($C_9H_{12}{}^{81}Br^{35}Cl$ or $C_9H_{12}{}^{79}Br^{37}Cl$) calc.: 235.9798, found: 235.980.

Reactions with **12**

Reaction 1 in Scheme 5. To *t*-BuOK (12 mmol, 1.3 g) dissolved in 30 ml of dry DMSO, **12** (3 mmol, 0.7 g) was added. The dark brown solution was stirred for 1 h at room temperature. The solution was poured into 50 ml cold water and extracted five times with pentane. The combined organic layers were washed twice with water and once with brine, dried on anhydrous $MgSO_4$, filtered and concentrated carefully under reduced pressure. The residue was 0.46 g (88%) of a light yellow oil, containing only **13**.
1-Bromo-2,2,3,3-tetramethylcyclopropane (**13**)[6a]. ^{1}H-NMR: δ 1.10, s, 6H; 1.14, s, 6H; 2.73, s, 1H.

Reaction 2 in Scheme 5. This reaction was performed with dimsylsodium (25 ml of DMSO, 6 mmol of NaH) and **12** (3 mmol) at room

temperature. The reaction time varied from 2 min to 5 h. The mixture was worked up as described before. Yield 0.44 g (84%), pure **13**.

Reaction 3 in Scheme 5. Potassium (*ca.* 0.25 g, 6 mmol) was allowed to react with 30 ml of dry *t*-BuOH. After dissolving all the potassium, **12** (3 mmol) was added and the mixture was stirred for 4 h at RT. After addition of cold water and several extractions with pentane, the organic layer was washed with water and brine, dried, filtered and concentrated, yielding 0.7 g of colourless crystals (99%), which appeared to be unreacted **12**.

Reaction 4 in Scheme 5. This reaction was performed as in reaction 1, with exclusion of light. Reaction time 15 h at room temperature. Yield 0.46 g (87%) of **13**.

Reaction in the dark with 1,3-dinitrobenzene. As reaction 4, with addition of 1 mmol *m*-dinitrobenzene. Reaction time 2 h. Yield 0.35 g (66%) of **13**.

Reaction of **14** *with t-BuOK / DMSO*

In a dry, N_2-flushed 25-ml flask, **14** (2 mmol, 0.42 g) was allowed to react with *t*-BuOK (6 mmol, 0.67 g) in 15 ml of dry DMSO. After 4 h at room temperature, the mixture was poured into 35 ml of cold water and extracted four times with pentane. The organic layer was washed twice with water, dried on $MgSO_4$, filtered and concentrated under reduced pressure. The residue was a colourless oil containing pure **15** (0.25 g, 96%).
1-Chloro-2,2,3,3-tetramethylcyclopropane (**15**)[30]. ^{1}H NMR: δ 1.08, s, 6H; 1.11, s, 6H; 2.67 s, 1H. ^{13}C NMR: δ 17.1, Me; 21.6 Me; 22.8, s, C2/3; 50.7, s, C1.

Reactions with **16**

Reaction with Ph_3SnH[6b]. To a 1:1 mixture of **16a, b** (0.29 g, 1.2 mmol) in anhydrous diethyl ether (15 ml) Ph_3SnH (0.46 g, 1.4 mmol) was added. The reaction mixture was stirred under reflux for 3 h. After cooling to room temperature, the diethyl ether was evaporated under reduced pressure, and pentane was added to the residue. The white precipitate formed was filtered and thoroughly washed with cold pentane. The pentane was then evaporated and the oily residue filtered through a 10-cm silica column, with pentane as eluent. After removal of the pentane, a colourless oil (0.20 g, 1.2 mmol, 98%) was obtained containing **18a** and **18b** in a 3:7 ratio (determined by ^{1}H-NMR).
syn-7-Chloro-1,6-dimethylbicyclo[4.1.0]heptane (**18a**). ^{1}H NMR: δ 1.03, s, 6H; 0.98–1.90, m, 8H; 2.58, s, 1H. ^{13}C NMR: δ 22.2; 22.3; 28.3; 52.1, s, C7, signal for C1/C6 is missing due to low intensity.
anti-7-Chloro-1,6-dimethylbicyclo[4.1.0]heptane (**18b**). ^{1}H NMR: δ 1.01, s, 6H; 0.98–1.90, m, 8H; 2.83, s, 1H. ^{13}C NMR: δ 17.5; 21.8; 31.6; 47.9, s, C7; signal for C1/C6 is missing due to low intensity.

Reaction with t-BuOK / DMSO. To 15 ml of anhydrous DMSO, *t*-BuOK (2.5 mmol, 0.28 g) and a 1:1 mixture of **16a, b** (1.4 mmol, 0.33 g) were added. The solution was stirred for 25 min at room temperature, then poured into 50 ml of cold water and extracted five times with pentane. The combined organic layers were washed twice with water and brine, dried on $MgSO_4$, filtered and concentrated carefully under reduced pressure. Yield *ca.* 0.05 g of a yellow, awful-smelling oil, containing unidentified by-products and **18b**.

Reaction with NaH / DMSO. The dimsyl sodium solution was prepared as described before. Then a 1:1 mixture of **16a, b** (0.33 g, 1.4 mmol) was added and the solution was stirred at room temperature. After 2 min (Table I, entry 4) or 30 min (entry 3), respectively, the reaction was broken off by pouring the mixture into cold water. The mixture was worked up as described above. Yield *ca.* 0.15 g (reaction time 2 min), mixture of **18a** and **18b** (ratio 4.5:5.5), some unreacted **16** and traces of unidentified products.

Reaction of **16a** *with NaH / DMSO*

Dimsylsodium was prepared as described above (0.17 g NaH/15 ml DMSO). In a 10-ml dry flask, containing 0.12 g (0.5 mmol) of pure **16a**, 5 ml of the dimsylsodium was added under N_2. The mixture was stirred for 2 min and worked up as described above. Yield *ca.* 0.06 g (70%) of a 9:1 mixture of **18a** and **18b**.

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