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An Efficient Radical Procedure for the Halogenation and Chalcogenation of *B*-Alkylcatecholboranes

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Dedicated to Professor Andreas Pfaltz on the occasion of his 60th birthday

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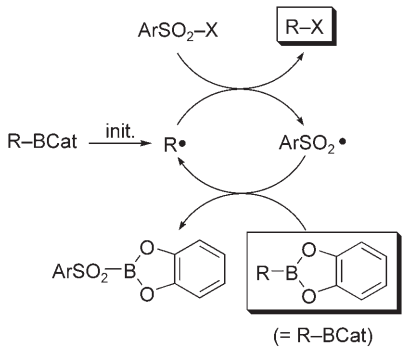
Abstract: An efficient formal anti-Markovnikov addition of HX (X = Cl, Br, I, SR and SeR) to olefins under mild reaction conditions is described. The procedure is based on the hydroboration of alkenes with catecholborane. The conversion of the intermediate *B*-alkylcatecholboranes to the corresponding halides, sulfides and selenides is based on a common process, i.e., generation of a radical from the alkylborane followed by abstraction of a heteroatom from an aromatic sulfonyl reagent. The efficiency of these radical reactions is remarkable. The mildness of the reaction conditions is well illustrated by the preparation of iodoalkanes. Despite the notorious reactivity of iodoalkanes under radical reaction conditions, no product degradation was observed.

Keywords: boranes; halogenation; radicals; selenides; sulfides; sulfonyl halides

Introduction

Organoboranes are very useful reagents for organic synthesis.[1] They are easily prepared by hydroboration of alkenes and are very efficiently converted into alcohols by oxidative treatment.[2] This reaction sequence represents one of the most efficient ways of achieving the anti-Markovnikov addition of water to alkenes. Extension of this chemistry to the formation of C–Cl,[3] C–Br,[4] and C–I[5] bonds by reaction of the organoboranes with halogenating agents has been reported. However, the high reactivity of the halogenating agent and/or the use of alkaline condition make these reactions only moderately attractive for synthetic applications. The formation of carbon-sulfur bonds has also been examined but is scarcely used for preparative purpose,[6] with the exception of the radical sulfurization process mediated by Barton esters.[7,8] The formation of a C–Se bond from organoboranes is limited to selenocyanates.[9] Recently, we discovered that *B*-alkylcatecholboranes are extremely useful radical precursors that can participate in efficient carbon-carbon[7,10–12] and carbon-oxygen[12,13] bond formation.[14] Chain reactions involving arenesulfonyl radicals and *B*-alkylcatecholboranes are particularly efficient as demonstrated by the allylation reaction with allylic sulfones.[11,15,16] In 1972 Davies and Roberts demonstrated that benzenesulfonyl bromide is a suitable reagent for the bromination of tri-*n*-butylborane.[17] They assumed that this reaction is a radical chain process in which a benzenesulfonyl radical displaces an alkyl radical from tri-*n*-butylborane. This interesting observation did not lead to any synthetic application. Here, we report on the free radical-mediated halogenation, sulfanylation and selanylation of alkylcatecholboranes using sulfonyl halides, sulfides and selenides as key reagents according to Scheme 1.[18,19]

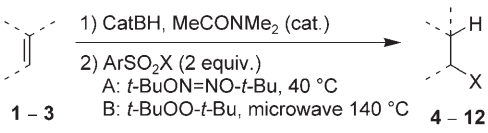


Scheme 1.

Results and Discussion

Halogenation

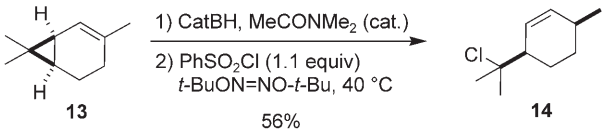
Different *B*-alkylcatecholboranes, prepared by hydroboration of olefins **1–3** under *N,N*-dimethylacetamide catalysis,[20] were allowed to react with arenesulfonyl halides according to Eq. (1) under either di-*tert*-butyl hyponitrite[21] initiation at 40 °C (method A) or di-*tert*-butyl peroxide at 140 °C using microwave heating (method B) [Eq. (1)]. Results are summarized in



(1)

Table 1. Primary (entries 1–6) and secondary (entries 7–9) chlorides, bromides and iodides were prepared in good to excellent yields. For chlorides and bromides, both reaction conditions could be used without significant change in yields. Microwaves heating allows us to reduce the reaction time down to 15 min. For the preparation of iodides, the reactions are run at 40 °C according to method A in order to avoid thermal decomposition of the products. Under these conditions, sensitive alkyl iodides are stable and can be obtained in good yields.

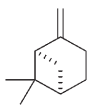
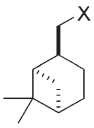
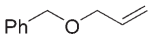
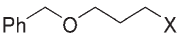
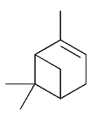
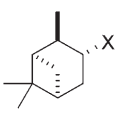
The radical nature of the halogenation process is supported by several observations. First, the stereoselectivity of the hydrohalogenation of α-pinene **3** (Table 1, entries 7–9) is characteristic for a radical process. An ionic process is expected to proceed with retention of configuration and to afford exclusively isopinocampheyl halides. However, traces (about 3%) of the pinocampheyl halides are detected by GC-MS analysis. A similar stereochemical outcome was obtained for the radical hydroallylation of α-pinene.[15] Secondly, a radical probe experiment was run with the cyclopropylcarbinyl radical derived from (+)-2-carene **13**. This radical is expected to rearrange with a rate constant higher than $10^9\ s^{-1}$.[22] The rate constants for the chlorination of primary and secondary alkyl radicals by $PhCH_2SO_2Cl$ have been measured by Chatgilialoglu to be $k = 1.2–1.3 \times 10^6\ M^{-1}s^{-1}$ at 25 °C.[23] These values are also expected to be valid for the reactions with $PhSO_2Cl$.[24] This assumption is confirmed by the recent report that $PhSO_2Cl$ reacts with the cyclohexyl radical at a rate constant $k = 1.2 \times 10^6\ M^{-1}s^{-1}$ at 18 °C.[25] These rates fit well with the observation that the reaction of (−)-2-carene **13** affords exclusively the ring-opened product **14** in 56% yield



(2)

[Eq. (2)]. A non-radical rearrangement could not explain the formation of this product, as it was established that no fragmentation occurs when the transformation proceeds *via* a polar mechanism or resulted from a concerted process.[26] In order to get a third insight into the reaction mechanism, the reaction was run in the absence of a radical initiator. However, we noticed that hydroboration of (+)-β-pinene **1** followed by reaction with benzenesulfonyl chloride at 40 °C proceeds even in the absence of di-*tert*-butyl hyponitrite and chloride **4** is isolated in similar yields. Traces of oxygen and/or homolytic cleavage the SO_2–

Table 1. Hydrohalogenation of alkenes according to Eq. (1).

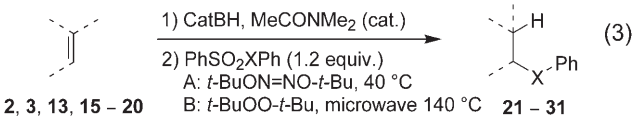
Entry	Alkene		Trap	Product		Method:[a] Yield[b]
1		**1**	$PhSO_2Cl$		**4**	A: 94%[c]
2			$PhSO_2Br$		**5**	A: 85%[c]
3			*p*-$TolSO_2I$		**6**	A: 88%[c]
4		**2**	$PhSO_2Cl$		**7**	B: 90%
5			$PhSO_2Br$		**8**	B: 90%
6			*p*-$TolSO_2I$		**9**	A: 77%
7		**3**	$PhSO_2Cl$		**10**	A: 83%[d]
8			$PhSO_2Br$		**11**	A: 90%[d]
9			*p*-$TolSO_2I$		**12**	A: 87%[d]

[a] Reactions were carried out on the 2.0 mmol scale.
[b] Yield of isolated product.
[c] 9:1 mixture of diastereomers (major isomer shown).
[d] Ratio of diastereomers $dr \geq 97:3$.

Cl bond are presumably initiating this efficient radical chain process.

Chalcogenation

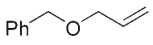
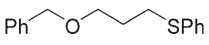
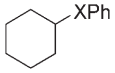
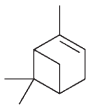
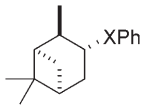
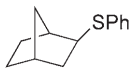
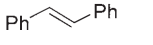
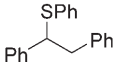
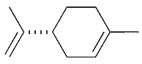
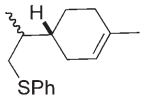
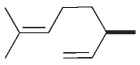
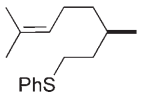
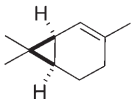
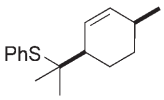
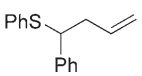
Extension of the reaction to the formation of carbon-sulfur and carbon-selenium bonds using commercially available *S*-phenyl benzenesulfonothioate and *Se*-phenyl benzenesulfonoselenoate was investigated next.[19] Reactions were run under the conditions developed for the halogenation process using initiation with either di-*tert*-butyl hyponitrite at 40 °C [Eq. (3), method A] or di-*tert*-butyl peroxide under microwave irradiation at 140 °C [Eq. (3), method B].[27] Both methods give clean and rapid reactions with a variety of substrates (Table 2). For instance, primary (entries 1,2) and secondary (entries 3–9) *B*-alkylcatecholboranes afford the expected sulfides and selenides **21–26** in good to excellent yields. Reaction at a benzylic position is also possible as demonstrated by the reaction with stilbene **17** affording **27** (Table 2, entry 10). Dienes, such as β-citronelene **18** (entry 11) and (*R*)-limonene **19** (entry 12) give the monosulfurized products **28** and **29** in good yields. In these two particular cases, the use of Wilkinson's catalyst for the hydroboration step leads to higher selectivities and yields.[28]



(3)

Reactions with (+)-2-carene **13** (entry 13) and 2-phenylmethylenecyclopropane **20** (entry 14) afford exclusively the products **30** and **31** resulting from the opening of the cyclopropane ring. These two reactions demonstrate again the radical nature of the process. Interestingly, the radical derived from (*R*)-limonene **18** (entry 11) and β-citronelene **19** (entry 12) are also expected to rearrange *via* 5-*exo*-trig and 6-*exo*-trig processes, respectively. Since the cyclization rate con-

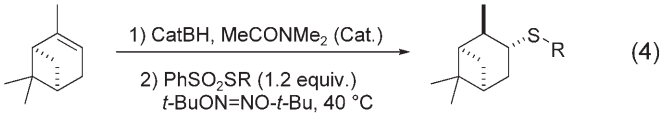
Table 2. Benzenesulfanylation and benzeneselanylation of alkenes according to Eq. (3).

Entry	Alkene		X	Product		Method:[a] Yield[b]
1		**2**	S		**21**	A: 64%
2		**2**	S		**21**	B: 80%
3		**15**	S		**22**	A: 73%
4		**15**	S		**22**	B: 98%
5		**15**	Se		**23**	A: 90%
6		**3**	S		**24**	A: 90%[c]
7		**3**	S		**24**	B: 92%[c]
8		**3**	Se		**25**	A: 93%[c]
9		**16**	S		**26**	A: 59%
10		**17**	S		**27**	A: 77%
11		**18**	S		**28**	A: 75%[d,e]
12		**19**	S		**29**	A: 92%[d]
13		**13**	S		**30**	A: 61%
14		**20**	S		**31**	A: 63%

[a] Reactions were carried out on 2.0 mmol scale.
[b] Yield of isolated product.
[c] Ratio of diastereomers *dr* ≥ 97:3.
[d] Hydroboration performed with $(Ph_3P)_3RhCl$ as a catalyst.
[e] 1:1 mixture of diastereomers.

stants are $k \leq 5 \times 10^5\ s^{-1}$ at 80 °C[29] and the concentration of $PhSO_2SPh$ is 1.2 M, the absence of cyclization products suggests a rate constant $k \geq 5 \times 10^6\ M^{-1} s^{-1}$ for the reaction of a primary alkyl radical with $PhSO_2SPh$. This rate constant is about one order of magnitude faster than the rate constant for the reaction of a primary alkyl radicals with diphenyl disulfide ($k = 2 \times 10^5\ M^{-1} s^{-1}$ at 80 °C[30]).

The sulfurization process is not limited to the introduction of an SPh group. Reagents for the introduction of *S*-alkyl residues can also be used. For instance, the organoborane derived from α-pinene **3** was treated with easily available *S*-methyl and *S*-benzyl benzenesulfonothioates[31] [Eq. (4)]. The corresponding sulfides **32** and **33** were obtained in good yields.



(4)

1

32 R = Me, 81% (*dr* = 97:3)
33 R = Bn, 84% (*dr* = 97:3)

Conclusions

Halogenation and chalcogenation of *B*-alkylcatecholboranes with $ArSO_2X$ reagents are mild and efficient procedures. The reactions can be carried out under conventional and microwave heating. Yields are comparable for both methods but reaction time is greatly reduced by using microwave conditions. Due to the exceptional reactivity of *B*-alkylcatecholboranes towards sulfonyl radicals, excellent yields are obtained with only 1.2 equivalents of the radical trap. The radical nature of the transformation is supported by experiments with radical probes and by stereochemical considerations. The halogenation and chalcogenation processes presented here compares favorably in term of yields and mildness of the reaction conditions with all known literature procedures.

Experimental Section

General Procedure A (conventional heating)

Catecholborane (0.639 mL, 6 mmol) was added dropwise at 0 °C to a solution of olefin (2.0 mmol) and *N,N*-dimethylacetamide (0.020 mL, 0.2 mmol) in CH_2Cl_2 (2.0 mL) under nitrogen. The reaction mixture was heated under reflux for 5 h. MeOH (0.200 mL, 4.8 mmol) was added at 0 °C and the solution was stirred for 15 min at room temperature. $PhSO_2X$ (2.4 mmol) was then added and the solution was warmed at reflux and di-*tert*-butyl hyponitrite (10 mg, 0.06 mmol) was added every 1 h. The reaction was monitored by GC-MS. At the end of the reaction time (typically 1–3 h), the solution turned black. The crude product was purified by flash chromatography.

General Procedure B (microwave heating)

Catecholborane (0.319 mL, 3 mmol) was added dropwise at 0 °C to a solution of olefin (1.5 mmol) and *N,N*-dimethylacetamide (0.014 mL, 0.15 mmol) in CH_2Cl_2 (2.0 mL) under nitrogen. The reaction mixture was heated under reflux for 5 h. MeOH (0.200 mL, 4.8 mmol) was added at 0 °C and the solution was stirred for 15 min at room temperature. The solvent was evaporated with a stream of nitrogen and the reaction mixture was transferred to a microwave reaction vessel containing either dichlorobenzene or DMF (4.0 mL), $PhSO_2X$ (1.8 mmol) and di-*tert*-butyl peroxide (25 mg, 0.15 mmol). The reaction vessel was closed and heated with microwave (600 W) at 140 °C for 15 min. The black reaction mixture was deposited onto a chromatography column and eluted with pentane to remove dichlorobenzene and with pentane/Et_2O (95:5) to elute the product. When *N,N*-dimethylformamide was used as solvent, the crude mixture was washed with water before flash chromatography.

General Procedure C (rhodium-catalyzed hydroboration)

Catecholborane (0.468 mL, 4.4 mmol) was added dropwise at 0 °C to a solution of alkene (2.0 mmol) and $(Ph_3P)_3RhCl$ (1 mol%, 18 mg) in CH_2Cl_2 (2.0 mL) under nitrogen. The reaction mixture was heated to reflux for 5 h. *t*-BuOH (0.24 mL, 2.5 mmol) was added at 0 °C and the solution was stirred for 15 min at room temperature. $PhSO_2X$ (2.4 mmol) was then added and the solution was warmed at reflux and di-*tert*-butyl hyponitrite (10 mg, 0.06 mmol) was added every 1 h. The reaction was monitored by GC-MS. At the end of the reaction time (typically 1–3 h), the solution turned black. The crude product was purified by flash chromatography.

General Procedure D (iodination)

Catecholborane (0.468 mL, 4.4 mmol) was added dropwise at 0 °C to a solution of alkene (2.0 mmol) and *N,N*-dimethylacetamide (0.020 mL, 0.2 mmol) in CH_2Cl_2 (2.0 mL) under nitrogen. The reaction mixture was heated to reflux for 5 h. *t*-BuOH (0.24 mL, 2.5 mmol) was added at 0 °C and the solution was stirred for 15 min at room temperature. After addition of freshly prepared *para*-toluenesulfonyl iodide[32] (846 mg, 30 mmol) at 0 °C. Air (60 mL, 0.5 mmol O_2) was introduced over 90 min through a needle placed just above the reaction surface. The reaction was monitored by GC-MS. The solution turned to dark yellow and black in 30 to 90 min. The organic phase was washed with a 10% aqueous $Na_2S_2O_3$ solution. The resulting organic layer was dried over $MgSO_4$. After evaporation of the solvent, the crude product was purified by flash chromatography.

Supporting Information

The detailed characterization of all compounds can be found in the Supporting Information.

Acknowledgements

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