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Modified *B*-Alkylcatecholboranes as Radical Precursors

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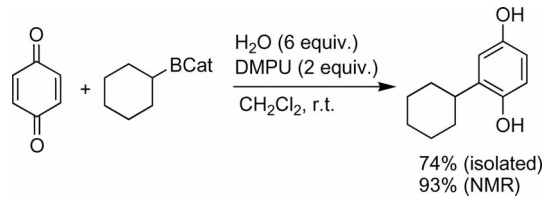
Generation of radicals from *B*-alkylcatecholboranes represents an efficient tin-free procedure for the generation of alkyl radicals. A modified version of this method has been developed. The simple catechol is replaced by a dihydroxylated tetrahydroisoquinoline, which can be separated from the reaction products by simple extraction with an aqueous acid solution. The modified alkyl radical precursors are easily prepared from alkenes by hydroboration with BH_3·Me_2S followed by treatment with the dihydroxytetrahydroisoquinoline. The new alkylboronates of this type are suitable radical precursors in a wide range of reactions such as sulfenylation, allylation, alkynylation, vinylation, and addition to quinones. This strategy is particularly useful when separation of reaction products from catechol residues is problematic, as illustrated by a radical addition to 1,4-benzoquinone leading to 2-alkyl-1,4-hydroquinones.

Introduction

Radical reactions have become a very useful synthetic tool and are routinely applied for the synthesis of natural products.[1] Industrial uses of radical reactions are, however, despite some important exceptions, rather scarce. A major reason for this is the fact that many radical processes are still based on the use of triorganotin reagents. These reagents are not only toxic, but they are also tedious to remove from the final products. Therefore, the demand for preparative tin-free radical reactions has been growing over the last decade.[2] Among the many strategies to avoid tin in radical reactions, it was found that the use of organoboranes as radical precursors is particularly promising. Indeed, they generate efficiently radicals, and they produce nontoxic boronic acid derivatives as byproducts.[3] Organoboranes can be employed for a wide range of radical reactions involving primary, secondary, and tertiary alkyl radicals. Recently, the readily available *B*-alkylcatecholboranes were shown to be unique precursors of alkyl radicals, and their efficiency for a broad range of reactions was demonstrated.[4] First, an efficient radical addition of in situ formed *B*-alkylcatecholboranes onto α,β-unsaturated enones and enals was reported.[5] This reaction represents a modified and improved version of the Brown–Negishi reaction.[6] More recently, this reaction was extended to the addition of radicals onto benzoquinones,[7] thus creating straightforward access to 2-substituted hydroquinones, which are common subunits in biologically active secondary metabolites (Scheme 1). *B*-Alkylcatecholborane-mediated radical reactions produce, after workup, nontoxic byproducts such as boronic acid derivatives and catechol. Reaction products are usually easily purified by filtration through silica gel. Filtration through a small pad of aluminum oxide (basic or neutral) is sufficient to remove all the boron- and catechol-derived byproducts. The removal of catechol derivatives by washing the crude products with an aqueous base is also possible. However, such purification strategies are inconvenient when slightly acidic or polar products are formed. In such cases, a large discrepancy between yields estimated by GC or NMR analysis of the crude products and isolated yields is observed as shown in the example depicted in Scheme 1.[7]



Scheme 1. Radical addition to 1,4-benzoquinone. Discrepancy between NMR yield determined by analysis of the crude product and isolated yield.

In view of these purification difficulties, a modified strategy that facilitates isolation of products exhibiting polarity and acidity similar to catechol was investigated. Modification of the catechol part of *B*-alkylcatecholboranes by introducing an amino group will deliver amino-substituted catechol-like byproducts that are expected to be easily removed by acidic workup. We report here the development of such modified *B*-alkylcatecholboranes and their applications in radical chemistry such as the radical addition to benzoquinones.

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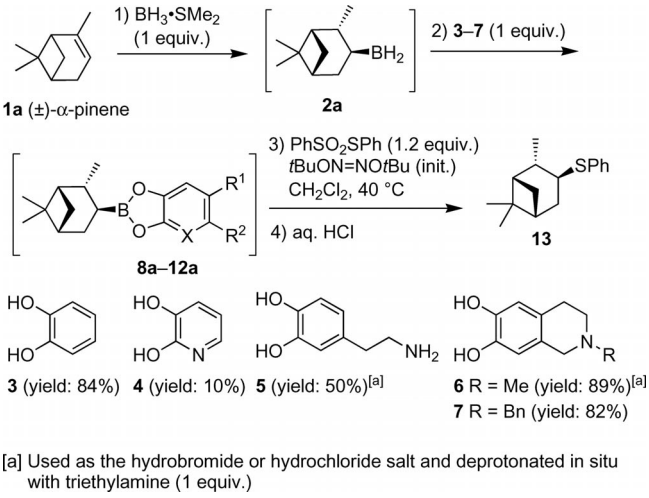
Results and Discussion

We started our investigations by testing different modified *B*-isopinocampheylcatecholborane analogues in the highly efficient radical sulfenylation reaction depicted in Scheme 2.[8] Desired organoboranes **8**–**12** are generated in a one-pot process involving hydroboration of α-pinene (**1a**) with a borane–dimethyl sulfide complex (1 equiv.) followed by reaction with modified catechols **3**–**7**.[9] The radical sulfenylation reaction with *S*-phenyl benzenethiosulfonate[10] was then run according to the procedure previously described by using di-*tert*-butyl hyponitrite (3 mol-%) as radical initiator in refluxing dichloromethane.[8] The reaction involving aminocatechols **4**–**7** was then washed with a 10% hydrochloric acid aqueous solution, which successfully removed **4**–**7** allowing an easy isolation of product **13**.

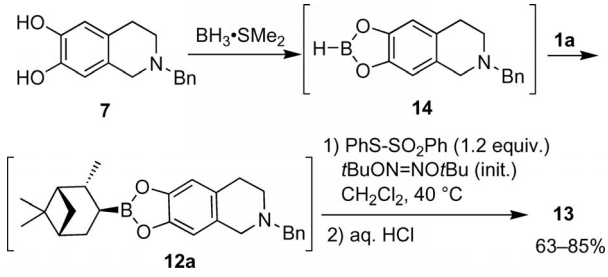


[a] Used as the hydrobromide or hydrochloride salt and deprotonated in situ with triethylamine (1 equiv.)

Scheme 2. Testing a selection of catechol analogues in the sulfenylation of *B*-isopinocampheylborane.

The use of catechol **3** affords desired product **13** in 84% yield, a yield close to that obtained when α-pinene is directly hydroborated with catecholborane according to the original procedure (90% yield).[8] 2,3-Dihydroxypyridine (**4**) gives a very low yield (10%) of **13**. The use of dopamine **5** leads to a modest yield of 50%. It was assumed that the intermediate organoboranes derived from **4** and **5** are hardly formed or are undergoing oligomerization, presumably due to disturbing B–N interactions. Indeed, it is known that boronic ester derivatives of **4** undergo macrocyclization through the formation of dative B–N bonds.[11] In contrast to these deceiving results, the overall one-pot sequences using tetrahydroisoquinolines **6** or **7** (82 and 89% yield) are as efficient as the corresponding reaction with catechol **3**. Tetrahydroisoquinolines **6** and **7** are synthesized from commercially available 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline hydrochloride in two steps via the HBr salt of the tertiary amine.[12] Because the isolation of *N*-methylated free amine **6** proved to be difficult, *N*-benzylated amine **7**, which was easily isolated due to its increased hydrophobicity, was kept for further investigations.

The generation of modified *B*-isopinocampheylcatecholborane **12a** from **1a** was examined in more detail. Our initial procedure (see Scheme 2) involves hydroboration with BH_3·Me_2S (1 equiv.) followed by reaction with **7**. Another approach involving direct hydroboration of α-pinene (**1a**) with modified catecholborane **14** should afford the same *B*-isopinocampheylcatecholborane **12a** (Scheme 3). To test this hypothesis, catechol **7** was transformed into catecholborane **14** by treatment with BH_3·Me_2S (1 equiv.). Unfortunately, presumably because of aggregation, borane **14** is only partly soluble and irreproducible yields are obtained for the hydroboration–sulfenylation of **1a**. All attempts to improve the solubility of **14** by varying the solvent did not increase the yield or reproducibility and this approach was abandoned. On the basis of these results, the formation of *B*-alkylcatecholboranes through hydroboration of alkenes with BH_3·Me_2S followed by reaction with tetrahydroisoquinoline **7** was selected for the rest of the work.

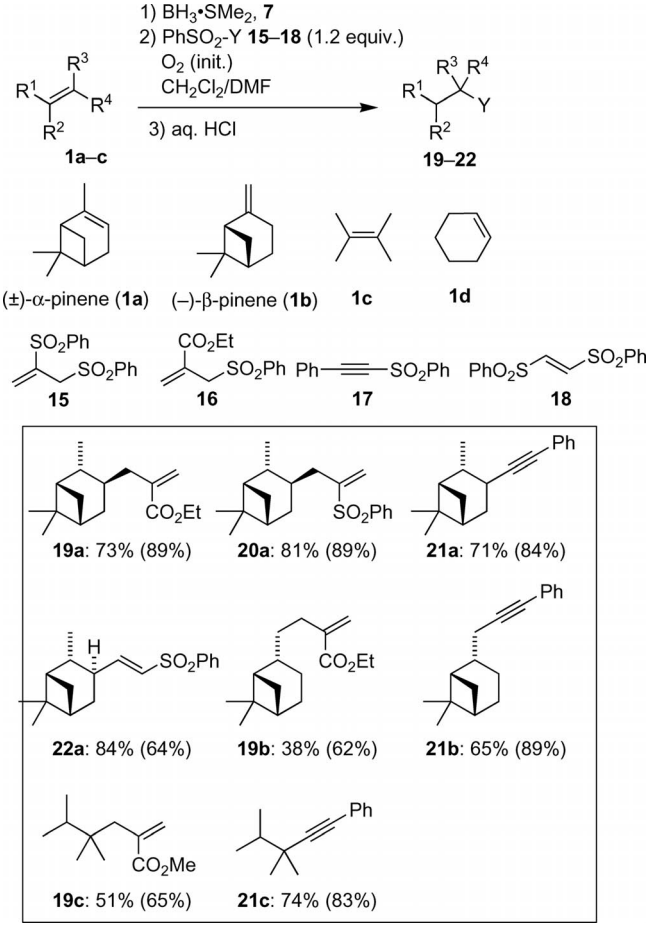


Scheme 3. Sulfenylation procedure involving generation of modified *B*-isopinocampheylcatecholborane **12a** through hydroboration with catecholborane **14**.

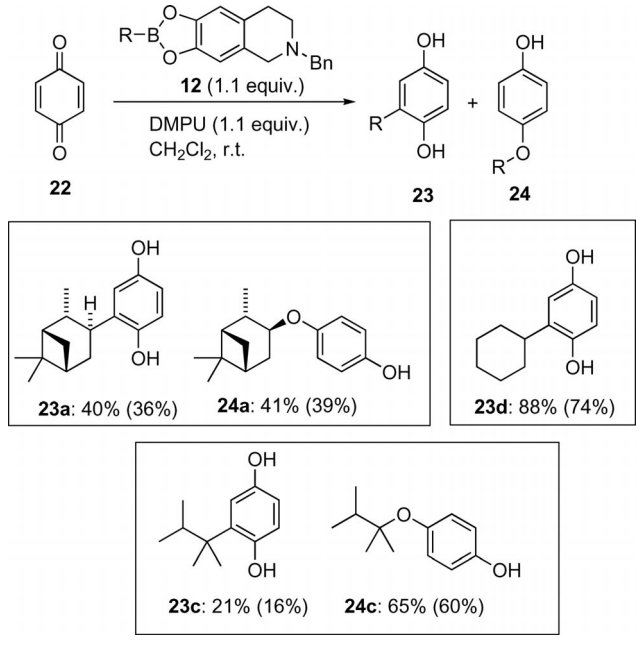
Extension of the use of *B*-alkylcatecholboranes of type **12** for allylation, alkynylation, and vinylation procedures was investigated (Scheme 4). Commercially available alkenes such as (–)-β-pinene (**1b**), (±)-α-pinene (**1a**), and 2,3-dimethyl-2-butene (**1c**) were selected for the generation of primary, secondary, and tertiary alkyl radicals, respectively. As radical traps, allyl sulfones **15** and **16**, alkynyl sulfone **17**, and vinyl sulfone **18** were chosen. Alkenes were hydroborated with BH_3·Me_2S, treated with **7**, and the in situ generated **12** was allowed to react with the different radical traps in a dichloromethane/*N*,*N*-dimethylformamide (DMF) solvent mixture at 40 °C. The radical process was initiated by a constant flow of air passing through the reaction vessel. A substoichiometric amount of oxygen (0.14 to 0.28 equiv.) was necessary to reach completion of the reactions. Better yields were obtained when DMF was used a as a cosolvent; this was partly due to the better solubility of the sulfone radical traps in the DMF-containing solvent mixture. Neither neat dichloromethane nor neat DMF led to equally good results. Deviations in concentration of the reaction mixture did not affect the yield, but the 2:1 ratio of CH_2Cl_2/DMF was the most efficient. Results depicted in Scheme 4 show that, despite some minor decreases in yield compared to the original method, consistently good results are obtained with secondary and tertiary radicals generated

from α-pinene (**1a**) and tetramethylethylene (**1c**) (**19a**–**22a**: 71–84%; **19c**: 51%, **21c**: 74%). The increase in yield from 64 to 84% for vinylated product **22a** is noteworthy. Reactions involving a primary radical derived from **1b** gave moderate yields. The moderate yields for **19b** (38%) and **21b** (65%) results probably from difficulties in the hydroboration step. Indeed, the hydroboration of unhindered alkenes does not stop at the monoalkylborane stage and terminal alkenes are known to proceed exclusively to the trialkylborane species.[13] We observed that hydroboration of **1b** with a substoichiometric quantity of a borane dimethyl sulfide complex in dichloromethane afforded the trialkylborane within 10 min at room temperature, which is in accordance with Brown's findings using hexane as the solvent.[14] Nevertheless, an older study by Brown showed that trialkylboranes can equilibrate to the monoalkylborane in the presence of a diborane solution.[15] We assumed that such an equilibration would occur between the boronic species derived from **1b** and the borane–dimethyl sulfide complex. In principle, trialkylboranes are also radical precursors, although they are less effective, as only one of the three alkyl groups is efficiently transformed into the product.[3b,3d] For organoboranes **12a/12c** prepared from **2a/2c**, the hydroboration step was less problematic. Indeed, Brown reported that monoisopinocampheylborane **2a** is best prepared indirectly from the diisopinocampheylborane[14,16] even if direct access by hydroboration of **1a** was reported.[17] The hydroboration of **1c** was performed according to a published procedure.[18]

In order to further illustrate the interest of generating radicals from modified *B*-alkylcatecholborane **12**, the radical addition onto 1,4-benzoquinone was investigated. Recently, we reported that alkyl radicals generated from *B*-alkylcatecholboranes add onto 1,4-benzoquinone at either the C-atom leading to substituted hydroquinones or at the O-atom resulting in aryl ethers.[7] It was shown that competing O-addition strongly depends on the bulkiness of the alkyl radical. The new reaction procedure with in situ generated modified *B*-alkylcatecholboranes **12** afforded the 1,4-conjugate addition products **23** and aryl ethers **24** in ratios comparable to the original method but with increased isolated yields (Scheme 5). This procedure involved the addition of a slight excess amount of **12** (1.1 equiv.) to 1,4-benzoquinone (**22**) in dichloromethane containing DMPU. Compared to the published procedure, the excess amount of *B*-alkylcatecholboranes could be reduced from 2 to 1.1 equiv. and the use of water as an additive was abandoned, as it does not bring any yield enhancement.[7] As anticipated, isolation and purification of the products is facilitated relative to the original method with type **8** organoboranes, as an acidic workup enabled facile and complete removal of **7** and all derivatives of **7**. For example, hydroquinone **23d**, which is formed in 93% NMR yield from **8d**, was only isolated in 74% yield (see Scheme 1). By using **12**, the 2-alkylated hydroquinone is now isolated in 88% yield.



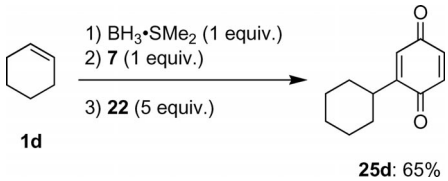
Scheme 4. Radical allylation, alkynylation, and vinylation of modified *B*-alkylcatecholboranes. Yields obtained by the previously published method using hydroboration with catecholborane are given in parentheses.[4]



Scheme 5. Radical addition of modified *B*-alkylcatecholboranes onto 1,4-benzoquinone.

As expected, purification is less tedious due to the absence of the typical black slurry stemming from polymerized catechol.

As already mentioned, a twofold excess of organoborane was required in the original procedure with **8** to prevent the oxidation of the hydroquinone products in the presence of benzoquinone.[7] In the current procedure with **12**, this excess amount could be reduced to 1.1 equiv. without observing the formation of 2-alkylated quinones. On the other hand, an efficient preparation of 2-substituted quinones is additionally possible by treating intermediate alkylboronate **12** with an excess amount of benzoquinone. As shown in Scheme 6, quinone **25d** was obtained in 65% yield from cyclohexene **1d** by using a fivefold excess of 1,4-benzoquinone.



Scheme 6. One-pot radical preparation of 2-substituted quinones.

Conclusions

A modified version of the method involving *B*-alkylcatecholboranes as radical precursors has been developed. The simple catechol has been replaced by dihydroxylated tetrahydroisoquinoline **7**, which can be separated from the reaction products by simple extraction with an aqueous acid solution. The modified alkyl radical precursors are generated in situ from alkenes by hydroboration with commercially available borane–dimethyl sulfide complex followed by treatment with modified catechol **7**. The new alkylboronates of type **12** are suitable radical precursors for a wide range of reaction such as sulfenylation, allylation, alkynylation, vinylation, and addition to quinones. This strategy is particularly useful when separation of reaction products form catechol residues is an issue.

Experimental Section

2-Benzyl-1,2,3,4-tetrahydroisoquinoline-6,7-diol (7): A mixture of 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline hydrochloride (50.4 g, 219.6 mmol), absolute ethanol (730 mL), and triethylamine (30.6 mL, 219.6 mmol) was stirred at room temperature for 1 h. Then, additional amounts of triethylamine (30.6 mL, 219.6 mmol) and benzyl bromide (26.1 mL, 219.6 mmol) were added, and the mixture was stirred at room temperature for 3.5 h. The cloudy orange solution was filtered to remove some precipitated Et_3N salt, and ethanol was removed under reduced pressure. The orange residue was dissolved in CH_2Cl_2 and washed with brine (2×). The organic layer was dried with Na_2SO_4 and filtered through a pad of silica gel, which was packed with a solution of 2% Et_3N in CH_2Cl_2. The product was washed through with *tert*-butyl methyl ether, and the solvents were removed under reduced pressure. The residue was triturated with pentane and 2-benzyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (39.2 g, 63%) was collected by filtration as a colorless solid. M.p. 89–90 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.28 (m, 5 H, arom. H), 6.60 (s, 1 H, arom. H), 6.49 (s, 1 H, arom. H), 3.84 (s, 3 H, MeO), 3.81 (s, 3 H, MeO), 3.69 (s, 2 H, NCH_2Ar), 3.55 (s, 2 H, NCH_2Ar), 2.85–2.81 (m, 2 H, NCH_2), 2.76–2.72 (m, 2 H, CH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.7, 147.4, 138.6, 129.2, 128.4, 127.2, 126.9, 126.4, 111.7, 109.7, 62.9, 56.0, 55.8, 50.9, 28.9 ppm. HRMS (ESI): calcd. for $C_{18}H_{21}NO_2Na$ 306.1469; found 306.1465. Further data are in accordance with the literature.[19] A mixture of 2-benzyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (47.3 g, 167 mmol) and HBr (48%, 600 mL) was heated under reflux for 3 h and then stirred overnight at room temperature, allowing the product to precipitate. The solid was filtered and washed with cold EtOH, affording hydrobromide salt **7**·HBr as a colorless solid (53.1 g, 95%). Salt **7**·HBr (15 g, 44.6 mmol) was suspended in water (700 mL). A 4 N NaOH solution (11.5 mL) was slowly added until basic pH and the initially white suspension turned yellow. Free amine **7** was collected by filtration and washed with cold water. Oven drying at 55 °C and 40 mbar for 60 h afforded **7** (10.2 g, 90%) as a bright yellow solid. M.p. 150–151 °C. ^{1}H NMR (400 MHz, DMSO): δ = 8.61 (s, 2 H, OH), 7.33–7.22 (m, 5 H, arom. H), 6.45 (s, 1 H, arom. H), 6.35 (s, 1 H, arom. H), 3.57 (s, 2 H, NCH_2Ar), 3.34 (s, 2 H, NCH_2Ar), 2.63–2.53 (m, 4 H, NCH_2CH_2Ar) ppm. ^{13}C NMR (100 MHz, DMSO): δ = 143.6, 143.3, 138.6, 128.7, 128.2, 126.9, 125.1, 124.3, 115.1, 113.1, 61.9, 55.1, 50.5, 28.0 ppm. IR (neat): $\tilde{\nu}$ = 3162 (br.), 2822 cm^{-1}. LRMS (EI): *m/z* (%) = 255 (79) $[M]^+$, 226 (50), 178 (54), 164 (67), 136 (81), 120 (75), 91 (100), 77 (43), 65 (73). HRMS (EI): calcd. for $C_{16}H_{17}NO_2$ 255.12593; found 255.12596. $C_{16}H_{17}NO_2$ (255.31): calcd. C 75.27, H 6.71, N 5.49; found C 75.35, H 6.74, N 5.52.

Phenyl(2,6,6-trimethylbicyclo[3.1.1]hept-3-yl)sulfane (13): A solution of (±)-α-pinene (**1a**; 159 μL, 1 mmol) and borane–dimethyl sulfide (90% in dimethyl sulfide, 105 μL, 1 mmol) in CH_2Cl_2 (1.0 mL) was heated under reflux for 3 h and cooled to room temperature afterwards. This solution was added by cannula to a suspension of catechol analogue **7** (255 mg, 1 mmol) in CH_2Cl_2 (2.0 mL) at 0 °C over a period of 15 min. Evolution of hydrogen was observed. More CH_2Cl_2 (1.0 mL) was added. and the reaction mixture was stirred for 1.5 h at room temperature. *S*-Phenyl benzenethiosulfonate (300 mg, 1.2 mmol), di-*tert*-butyl hyponitrite (5–9 mg, 0.03–0.05 mmol), and CH_2Cl_2 (0.5 mL) were added, and the mixture was heated under reflux. After 1 h, more di-*tert*-butyl hyponitrite (5–9 mg, 0.03–0.05 mmol) was added, and the mixture was heated for another hour under reflux. After allowing the reaction to stir overnight at room temperature, it was worked up. EtOAc (10 mL) and a 10% aqueous HCl solution (10 mL) were added, and some remaining precipitate was removed by filtration. The layers were separated, the aqueous layer was back-extracted with EtOAc (10 mL), and the organic layer was washed again with a 10% aqueous HCl solution (10 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography (pentane/Et_2O, 98:2) afforded **13** (202 mg, 82%) as an inseparable mixture with a minor quantity of side product PhSSPh. Data for **13**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.44–7.40 (m, 2 H, arom. H), 7.32–7.18 (m, 3 H, arom. H), 3.39 (ddd, *J* = 9.8, 7.2, 5.8 Hz, 1 H, CHS), 2.56–2.46 (m, 1 H), 2.32 (dtd, *J* = 9.8, 6.2, 2.2 Hz, 1 H), 2.14–2.04 (m, 2 H), 1.96–1.90 (m, 1 H), 1.83 (td, *J* = 6.0, 2.0 Hz, 1 H), 1.20 (s, 3 H, Me), 1.12 (d, *J* = 7.2 Hz, 3 H, Me), 1.02 (s, 3 H, Me), 0.98 (d, *J* = 9.8 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.8, 131.7, 128.9, 126.6, 48.2, 44.5, 42.2, 38.8, 37.8, 33.5, 27.9, 23.5, 21.6 ppm. Further data are in accordance with the literature.[8]

2,6,6-Trimethyl-3-[2-(phenylsulfonyl)allyl]bicyclo[3.1.1]heptane (20a): A solution of (±)-α-pinene (**1a**; 160 μL, 1 mmol) and borane–dimethyl sulfide (90% in dimethyl sulfide, 105 μL, 1 mmol) in CH_2Cl_2 (1.0 mL) was heated under reflux for 3 h and cooled to room temperature afterwards. This solution was added by cannula to a suspension of **7** (255 mg, 1 mmol) in CH_2Cl_2 (2.0 mL) at 0 °C over a period of 15 min, and the cannula was rinsed with CH_2Cl_2 (0.5 mL). Evolution of hydrogen was observed. The reaction mixture was then stirred for 1.5 h at room temperature while becoming a clear solution and changing color continuously from yellow to red. The solution was concentrated under a flow of N_2 to about 2 mL of solvent, resulting in a 0.5 M solution. Sulfone **15** (387 mg, 1.2 mmol) and DMF (1.0 mL) were added, and the reaction mixture was heated at 40 °C. Air (60 mL/h) was constantly bubbled into the mixture by syringe pump over a period of 2 h. After allowing the reaction mixture to stir overnight at room temperature, Et_2O and a 10% aqueous HCl solution were added, and some remaining precipitate was removed by filtration. The layers were separated, the aqueous layer was back-extracted with Et_2O, and the organic layer was washed again with a 10% aqueous HCl solution. The combined organic layers were washed with brine, dried with Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/TBME, 9:1) afforded **20a** (259 mg, 81%) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91–7.85 (m, 2 H, arom. H), 7.64–7.50 (m, 3 H, arom. H), 6.41 (s, 1 H, C=C*H*H), 5.79 (s, 1 H, C=CH*H*), 2.49 (dd, *J* = 15.4, 3.6 Hz, 1 H, C*H*H–C=C), 2.24 (dtd, *J* = 9.6, 6.2, 2.1 Hz, 1 H, CH*H*–C=C), 2.05 (dd, *J* = 15.0, 10.3 Hz, 1 H), 1.95–1.78 (m, 3 H), 1.73–1.68 (td, *J* = 5.8, 1.9 Hz, 1 H), 1.54 (quint.-like d, *J* = 7.0, 1.8 Hz, 1 H), 1.21 (ddd, *J* = 12.9, 5.6, 2.4 Hz, 1 H), 1.13 (s, 3 H, Me), 0.93 (d, *J* = 7.2 Hz, 3 H, Me), 0.85 (s, 3 H, Me), 0.61 (d, *J* = 9.7 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.5, 139.4, 133.5, 129.3, 128.4, 124.7, 48.1, 43.9, 41.8, 40.6, 38.7, 34.2, 34.1, 33.9, 28.1, 22.9, 21.4 ppm. IR (neat): $\tilde{\nu}$ = 2902 (br.), 1446, 1303, 1145, 1081 cm^{-1}. LRMS (EI): *m*/*z* (%) = 319 (7) $[M + H]^+$, 263 (11), 177 (70), 161 (48), 143 (62), 137 (87), 121 (78), 107 (77), 93 (83), 81 (90), 55 (90), 41 (100). Further data are in accordance with the literature.[4a]

2-(2,3-Dimethylbutan-2-yl)benzene-1,4-diol (23c) and 4-(2,3-Dimethylbutan-2-yloxy)phenol (24c): At 0 °C, 2,3-dimethyl-2-butene (**1c**, 195 μL, 1.65 mmol) was added to borane–dimethyl sulfide (90% in dimethyl sulfide, 175 μL, 1.65 mmol) and it was stirred for 2.5 h under neat conditions at 0 °C. The mixture was diluted with CH_2Cl_2 (0.5 mL), and it was slowly added by cannula to a suspension of **7** (421 mg, 1.65 mmol) in CH_2Cl_2 (4.0 mL) at 0 °C. Evolution of hydrogen was observed. The cannula was rinsed with CH_2Cl_2 (2.5 mL). The reaction mixture was stirred for 2 h at room temperature, while becoming a clear yellow solution. It was then diluted with CH_2Cl_2 (3 mL). DMPU (200 μL, 1.65 mmol) and 1,4-benzoquinone (**22**, 162 mg, 1.5 mmol) were successively added, and the solution was stirred at room temperature for 2 h. Et_2O and a 10% aqueous HCl solution were added, and some remaining precipitate was removed by filtration. The layers were separated, the aqueous layer was back-extracted with Et_2O, and the organic layer was washed again with a 10% aqueous HCl solution. The combined organic layers were washed with brine, dried with Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash chromatography (pentane/Et_2O, 4:1, 3:1) afforded **23c** (61 mg, 21%) as an off-white solid and **24c** (189 mg, 65%) as a yellowish solid. Data for **23c**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.73–6.71 (m, 1 H, arom. H), 6.53–6.52 (m, 2 H, arom. H), 4.40 (s, 1 H, OH), 4.36 (s, 1 H, OH), 2.60 (sept., *J* = 6.9 Hz, 1 H, C*H*Me$_2$), 1.29 (s, 6 H, Me), 0.76 (d, *J* = 6.9 Hz, 6 H, *Me*$_2$CH) ppm. Further data are in accordance with the literature.[7] Data for **24c**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.87–6.82 (m, 2 H, arom. H), 6.74–6.68 (m, 2 H, arom. H), 4.54 (s, 1 H, OH), 1.92 (sept., *J* = 6.8 Hz, 1 H, C*H*Me$_2$), 1.14 (s, 6 H, Me), 1.01 (d, *J* = 6.8 Hz, 6 H, *Me*$_2$CH) ppm. Further data are in accordance with the literature.[7]

2-Cyclohexylcyclohexa-2,5-diene-1,4-dione (25d): Cyclohexene (**1d**, 170 μL, 1.65 mmol) was added to a solution of borane–dimethyl sulfide (90% in dimethyl sulfide, 175 μL, 1.65 mmol) in CH_2Cl_2 (1.5 mL) at 0 °C. The mixture was stirred for 3 h at 0 °C, and a white precipitation was observed. A suspension of **7** (421 mg, 1.65 mmol) in CH_2Cl_2 (4.0 mL) was added slowly by dropping funnel to the organoborane mixture at 0 °C. Evolution of hydrogen was observed. The funnel was rinsed with CH_2Cl_2 (6.5 mL). The orange reaction mixture was stirred for 2 h at room temperature. DMPU (200 μL, 1.65 mmol) and 1,4-benzoquinone (**22**, 892 mg, 8.25 mmol) were successively added, and the solution was stirred at room temperature for 2 h. Et_2O and a 10% aqueous HCl solution were added, and some remaining precipitate was removed by filtration. The layers were separated, the aqueous layer was back-extracted with Et_2O, and the organic layer was washed again with a 10% aqueous HCl solution. The combined organic layers were washed with brine, dried with Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash chromatography (pentane/Et_2O, 95:5) afforded **25d** (204 mg, 65%) as a greenish-brown solid. M.p. 49–51 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.72 (d, *J* = 10.1 Hz, 1 H, CH=C*H*), 6.66 (dd, *J* = 10.1, 2.4 Hz, 1 H, C*H*=CH), 6.47 (dd, *J* = 2.3, 1.1 Hz, 1 H, C=CH), 2.71–2.61 (m, 1 H, C*H*–C=C), 1.82–1.71 (m, 5 H), 1.45–1.29 (m, 2 H), 1.24–1.07 (m, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 188.2, 187.2, 154.1, 137.1, 136.0, 130.9, 36.5, 32.1, 26.4, 26.1 ppm. IR (neat): $\tilde{\nu}$ = 2934, 2852, 1645, 1597, 1446, 1306 cm^{-1}. HRMS (ESI): calcd. for $C_{12}H_{14}O_2Na$ 213.0891; found 213.0896. Spectral data are in accordance with the literature.[20]

Supporting Information (see footnote on the first page of this article): Full experimental data and spectra of new compounds.

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[1] a) S. Z. Zard, *Radical Reactions in Organic Synthesis*, Oxford University Press, **2003**; b) A. Gansäuer, *Radicals in Synthesis I: Methods and Mechanisms*, Springer, **2006**; c) A. Gansäuer, *Topics in Current Chemistry Vol. 263: Radicals in Synthesis II: Complex Molecules*, Springer, **2006**; d) P. Renaud, M. P. Sibi, *Radicals in Organic Synthesis*, Wiley-VCH, Weinheim, **2001**, vols. 1 and 2.

[2] a) P. A. Baguley, J. C. Walton, *Angew. Chem. Int. Ed.* **1998**, *37*, 3073; b) A. Studer, S. Amrein, *Synthesis* **2002**, 835.

[3] a) P. Renaud, A. Beauseigneur, A. Brecht-Forster, B. Becattini, V. Darmency, S. Kandhasamy, F. Montermini, C. Ollivier, P. Panchaud, D. Pozzi, E. M. Scanlan, A. P. Schaffner, V. Weber, *Pure Appl. Chem.* **2007**, *79*, 223; b) V. Darmency, P. Renaud, *Top. Curr. Chem.* **2006**, *263*, 71; c) A. P. Schaffner, P. Renaud, *Eur. J. Org. Chem.* **2004**, 2291; d) C. Ollivier, P. Renaud, *Chem. Rev.* **2001**, *101*, 3415.

[4] a) A. P. Schaffner, P. Renaud, *Angew. Chem. Int. Ed.* **2003**, *42*, 2658; b) A. P. Schaffner, V. Darmency, P. Renaud, *Angew. Chem. Int. Ed.* **2006**, *45*, 5847.

[5] C. Ollivier, P. Renaud, *Chem. Eur. J.* **1999**, *5*, 1468.

[6] H. C. Brown, E. I. Negishi, *J. Am. Chem. Soc.* **1971**, *93*, 3777.

[7] E. Kumli, F. Montermini, P. Renaud, *Org. Lett.* **2006**, *8*, 5861.

[8] A. P. Schaffner, F. Montermini, D. Pozzi, V. Darmency, E. M. Scanlan, P. Renaud, *Adv. Synth. Catal.* **2008**, *350*, 1163.
[9] C. Cadot, J. Cossy, P. I. Dalko, *Chem. Commun.* **2000**, 1017.
[10] S. Cren, P. Renaud in *Electronic Encyclopedia of Reagents for Organic Synthesis* (e-EROS), Wiley, New York, **2007**.
[11] N. Christinat, R. Scopelliti, K. Severin, *Chem. Commun.* **2004**, 1158.
[12] E. E. Smissman, J. R. Reid, D. A. Walsh, R. T. Borchardt, *J. Med. Chem.* **1976**, *19*, 127.
[13] H. C. Brown, B. C. S. Rao, *J. Am. Chem. Soc.* **1959**, *81*, 6428.
[14] H. C. Brown, N. N. Joshi, *J. Org. Chem.* **1988**, *53*, 4059.
[15] H. C. Brown, A. Tsukamoto, D. B. Bigley, *J. Am. Chem. Soc.* **1960**, *82*, 4703.
[16] a) H. C. Brown, P. V. Ramachandran, *Pure Appl. Chem.* **1991**, *63*, 307; b) H. C. Brown, J. R. Schwier, B. Singaram, *J. Org. Chem.* **1978**, *43*, 4395.
[17] a) H. C. Brown, U. P. Dhokte, *J. Org. Chem.* **1994**, *59*, 2025; b) H. C. Brown, A. W. Moerikofer, *J. Am. Chem. Soc.* **1962**, *84*, 1478; c) J. V. B. Kanth, H. C. Brown, *Tetrahedron Lett.* **2000**, *41*, 9361.
[18] H. C. Brown, A. K. Mandal, S. U. Kulkarni, *J. Org. Chem.* **1977**, *42*, 1392.
[19] K. Mohri, K. Suzuki, M. Usui, K. Isobe, Y. Tsuda, *Chem. Pharm. Bull.* **1995**, *43*, 159.
[20] D. Niethammer, B. Kirste, H. Kurreck, *J. Chem. Soc. Faraday Trans.* **1990**, *86*, 3191.

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