Organoboranes in Radical Reactions, Part 1

B-Alkylcatecholboranes as a Source of Radicals for Efficient Conjugate Additions to Unsaturated Ketones and Aldehydes

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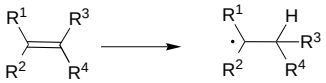
Abstract: Selective and efficient generation of alkyl radicals from alkenes as well as their addition to unsaturated ketones and aldehydes is reported. The method is based on a simple one-pot procedure involving the hydroboration of the alkene with catecholborane, followed by treatment with a catalytic amount of oxygen in the presence of DMPU and a radical trap. Examples of cyclization and cascade reactions are reported.

Keywords: boron · cascade reactions · domino reactions · Michael additions · radical reactions

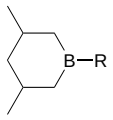
Introduction

Radical reactions are becoming an extremely useful tool for organic synthesis. The very rapid development of these reactions may be attributed to the emergence of very efficient ways to conduct them, such as the tin hydride approach,[1] the atom or group transfer reactions,[2–4] and the single-electron-transfer processes.[5, 6] However, alternative ways of generating radicals with high chemo-, regio- and eventually stereocontrol are still highly in demand. A particularly attractive process would be the direct generation of radicals from alkenes according to Equation (1). No efficient one-pot reaction of this type has yet been reported.



(1)

It is known from the pioneer work of Brown, that organoboranes are good radical precursors.[7–9] For instance, upon treatment with oxygen, trialkylboranes give rise to alkyl radicals that have been used for intermolecular radical additions to unsaturated ketones and aldehydes.[10, 11] This method of generating radicals has not been widely applied in synthesis with the exception of the systems with triethylborane-oxygen as the initiator for radical reactions.[12] One serious drawback of the trialkylborane approach is that only one out of the three alkyl groups is transferred, so the method is restricted to trialkylboranes obtained by hydroboration of easily available and cheap alkenes. A partial but limited solution to this problem was proposed by Brown and Negishi who used *B*-alkylboracyclanes.[8, 13] Borane **1** (R = H), the most efficient of the series, is prepared by the hydroboration of the expensive 2,4-dimethyl-1,4-pentadiene. An excess of alkene is required when **1** (R = H) is used as a hydroborating agent. With this system, a selective cleavage of the boron – alkyl bond was possible for secondary and tertiary alkyl groups. The resulting radicals could be trapped with highly reactive α,β-unsaturated carbonyl compounds bearing no substituents at the β position.[7] However, this method is not suitable for primary alkyl radicals (yield < 35 %) and for radical traps substituted at the β-position. Indeed, with these traps, addition of oxygen is necessary to run a chain reaction and the cleavage of the C–B bond is not selective anymore.[14]



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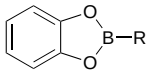
Results and Discussion

We demonstrate here that 2-alkylbenzo[*d*][1,3,2]dioxaborole (**2**; *B*-alkylcatecholboranes), easily obtained by hydroboration of olefins with the commercially available catecholborane, are excellent radical precursors and can be used for highly efficient radical additions to various α,β-unsaturated aldehydes and ketones.



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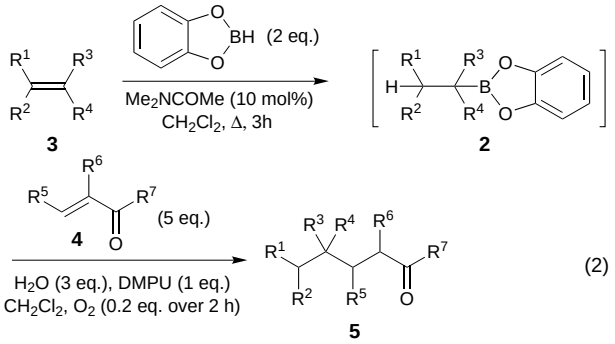
The hydroboration followed by radical reaction was examined for several model systems in accordance with Equation (2). The reaction conditions were optimized for the hydroboration of cyclohexene followed by radical addition to cyclohexenone. The best results were obtained when the hydroboration was conducted under conditions developed by Fu,[15] that is, reaction of the alkene with two equivalents of catecholborane catalyzed by *N*,*N*-dimethylacetamide (10 mol%) in dichloromethane. Water (3 equiv) was added



(2)

to destroy the excess of catecholborane followed by 1,3-dimethyl hexahydro-2-pyrimidinone (DMPU; 1 equiv) and the α,β-unsaturated carbonyl compound (5 equiv). Air was added to the system through a syringe pump over 2 h; the reaction requires only substoichiometric amounts of oxygen (0.2 equiv). Within 2 h, the reactions were complete. Results are summarized in Table 1 (see next page).

Hydroboration of cyclohexene **3a** followed by reaction with 1-penten-3-one **4a** led to **5aa** in excellent yield (entry 1, 94%). Reaction of the same cyclohexyl radical with β-substituted alkenones such as 4-hexen-3-one **4b**, cyclohexenone **4c** and cyclopentenone **4d** gave the ketones **5ab**, **5ac**, and **5ad** in 74, 79, and 86% yield, respectively (entries 2–4). Radical addition to methacrolein **4e** gave the adduct **5ae** in satisfactory yield (entry 5, 74% yield). However, addition to β-substituted α,β-unsaturated aldehydes such as crotonaldehyde **4f** gave the adduct **5af** in only modest yield (entry 6, 43%). Primary radicals resulting from the hydroboration of 1-octene **3b**, styrene **3c**, and methylenecyclohexane **3d** add efficiently to 1-penten-3-one **4a** (entries 7–9). In the two first cases, the hydroboration is not fully regioselective causing the formation of some isomeric products **5ba′** and **5ca′**. Addition of tertiary radicals generated from 2-thexylbenzo[*d*][1,3,2]-dioxaborole (obtained by the hydroboration of 2,3-dimethyl-2-butene **3e**) afforded the ketone **5ea** in 71% yield. We have also demonstrated that hydroboration of 1-substituted cycloalkenes followed by radical addition to 1-penten-3-one **4a** furnished the adducts **5fa**, **5ga**, and **5ha** in 80%, 88%, and 81% yield, respectively (entries 11–13). The *trans* isomers were formed preferentially in accordance with Giese's rules[16] for 2-substituted cyclic radicals. Finally, the reaction between **3a** and **4a** (entry 1) was repeated on a 30 mmol scale to demonstrate the preparative potential of the method. The ketone **5aa** was isolated in 83% yield after purification by distillation.

A plausible radical mechanism is presented in Figure 1 and is supported by the inhibition of the reaction observed with 2,2,6,6-tetramethylpiperidine-*N*-oxide (TEMPO) and galvinyl oxide, the stereoselectivity of the reactions with **3f–3h**,

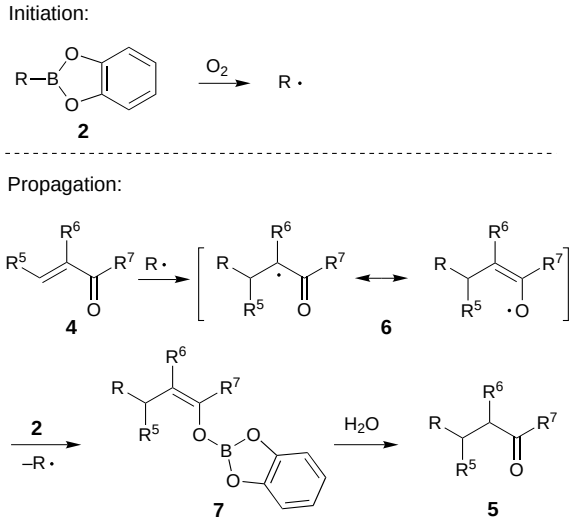


Figure 1. Possible mechanism for the formation of **5**.

and by the observation of typical radical rearrangements (see below). The alkyl radical R· is produced in an initiation step from the reaction of 2-(*R*)-benzo[*d*][1,3,2]dioxaborole with molecular oxygen. This radical then adds to the α,β-unsaturated carbonyl compound to give an enolate radical; this reacts with the borane **2** to give a boron enolate.[10] The exact role of water has not been proved, but it is expected to hydrolyse the excess of catecholborane and the formed boron enolate. This helps to avoid side reactions such as aldol condensations or conjugate additions. The presence of DMPU (1 equiv) is absolutely necessary to obtain good yields; however, its role is not yet understood.[17] Similar results were obtained with hexamethyl phosphoramide (HMPA) as the additive. Different attempts to use other types of radical traps such as methyl acrylate, phenylthioacrylate, *N*-phenylmaleimide, and vinyl phenyl sulfone have all failed. At the moment, the reaction is limited to α,β-unsaturated ketones and aldehydes. This suggests to us that the critical step in the chain reaction is the reaction of the enolate radical with the 2-alkylbenzo[*d*][1,3,2]dioxaborole, which liberates the alkyl radical R·. Enough spin density at the oxygen atom is present with ketones and aldehydes to render this step sufficiently

Abstract in French: *Nous décrivons une méthode sélective et efficace permettant d'engendrer des radicaux alkyles à partir d'alcènes et de les additionner sur des cétones et aldéhydes α,β-unsaturés. Une procédure expérimentale simple a été développée: l'hydroboration d'oléfines par le catecholborane fournit les B-alkylcatecholboranes qui sont immédiatement traités avec une quantité catalytique d'oxygène et la trappe à radicaux. Des exemples de cyclisations et de réactions en cascade viennent illustrer cette étude et confirmer la nature radicalaire de la réaction.*

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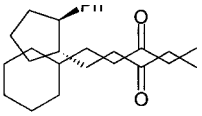
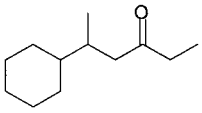
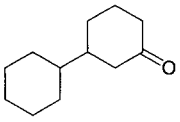
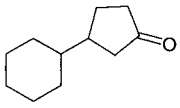
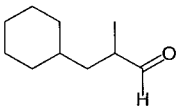
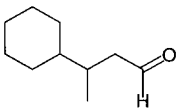
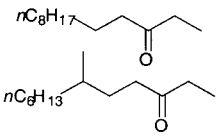
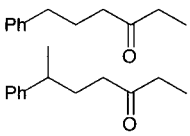
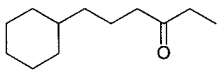
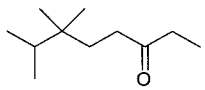
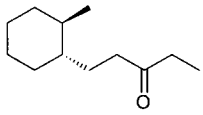
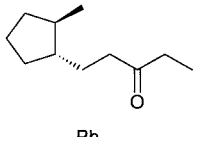
Table 1. Hydroboration of **3** followed by radical addition to **4** according to Equation (2).

	Alkene (**3**) Radical trap (**4**)	Product (**5**)		Yield [%]
13	1-phenyl-1-cyclopentene (**3h**)		**5ha**	81[e]
1	Cyclohexene (**3a**) 1-penten-3-one (**4a**)		**5aa**	94
2	cyclohexene (**3a**) 4-hexen-3-one (**4b**)		**5ab**	74
3	cyclohexene (**3a**) 2-cyclohexenone (**4c**)		**5ac**	79
4	cyclohexene (**3a**) 2-cyclopentone (**4d**)		**5ad**	86
5	cyclohexene (**3a**) methacrolein (**4e**)		**5ae**	74
6	cyclohexene (**3a**) *trans*-2-butenal (**4f**)		**5af**	43
7	1-octene (**3b**) 1-penten-3-one (**4a**)		**5ba** **5ba'**	60[a]
8	styrene (**3c**) 1-penten-3-one (**4a**)		**5ca** **5ca'**	70[b]
9	Methylenecyclohexane (**3d**) 1-penten-3-one (**4a**)		**5da**	69
10	2,3-dimethyl-2-butene (**3e**) 1-penten-3-one (**4a**)		**5ea**	71
11	1-Methyl-1-Cyclohexene (**3f**) 1-penten-3-one (**4a**)		**5fa**	80[c]
12	1-methyl-1-cyclopentene (**3g**) 1-penten-3-one (**4a**)		**5ga**	88[d]

[a] **5ba**/**5ba′** = 89:11. [b] **5ca**/**5ca′** = 78:22. [c] *cis*/*trans* = 20:80. [d] *cis*/*trans* = 9:91. [e] *cis*/*trans* = 5:95.

fast. However, this is not the case with ester, amide, and sulfone radical traps.

The utility of this approach to radical reactions is not limited to intermolecular reactions. Indeed, the chemoselectivity of the hydroboration allows us to devise intramolecular processes. A first example is depicted in Equation (3); selective hydroboration of the terminal alkene **8** followed by the addition of water (3 equiv), DMPU (1 equiv), and air (0.2 equiv O_2 over 2 h) gave the bicyclic ketone **9** in 45% yield as 95:5 *endo*/*exo* mixture.[18]

More complex reaction cascades are possible, the only requirement is that the last radical in the cascade has to be a ketone or aldehyde enolate radical in order to allow the propagation step (formation of a boron enolate). For instance, radical annulation starting from alkenylcyclopropanes has been examined. Hydroboration of (+)-2-carene followed by radical addition to pent-1-en-3-one **4a** afforded **10** in 40% yield [Scheme 1, Eq. (4)]. This process is highly stereoselective, since four new stereogenic centers are formed and only two diastereomers in a 66:34 ratio are formed. The complete reaction sequence is depicted in Scheme 1. The borane **11** gave the radical **12**, which in turn undergoes a cyclopropylalkyl ring opening (→**13**), an intermolecular addition to **4a** (→**14**), a 5-*exo*-cyclization (→**15**), and a second intermolecular addition to **4a** (→**16**). This reaction cascade is remarkable since it contains two distinct intermolecular C–C bond forming processes.

Conclusion

We have demonstrated that hydroboration with catecholborane followed by treatment with water/DMPU/oxygen represents an effective and simple one-pot procedure for performing radical addition to α,β-unsaturated ketones and aldehydes. For such transformations and because of its simplicity, our method is superior to the conjugate addition based on organometallic reagents. It is practicable on large scale and does not

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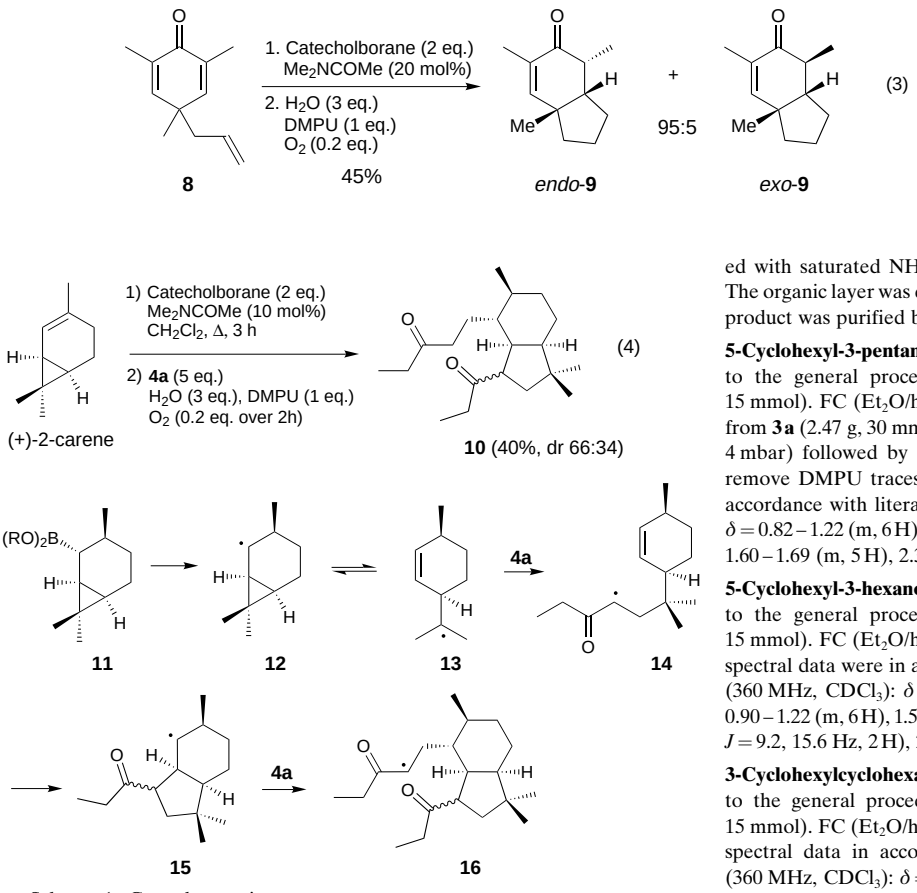

Scheme 1. Cascade reaction.

involve the handling of highly reactive and sensitive organometallic compounds. Moreover, application of this strategy to cyclization and annulation procedures prove the synthetic potential this approach. Efforts are currently being made in our laboratory to run complex reaction cascades as well as to develop an access to optically pure compounds by enantioselective hydroboration followed by radical reactions.

Experimental Section

General techniques: Flash column chromatography (FC) and filtration: Baker silica gel (0.063–0.200 mm), EtOAc, Et_2O, and hexane as eluents. Thin-layer chromatography (TLC): Baker silica gel 25 UV_{254} analytical plates; detection by spraying with a solution of $KMnO_4$ (3 g), K_2CO_3 (20 g), NaOH 5% (3 mL) in H_2O (300 mL) and subsequent heating. Gas chromatography (GC): Carlo Erba HRGC 5300, column Permabond SE-54 Macherey-Nagel (60→250 °C). IR spectroscopy: Perkin–Elmer 16PC. FT-IR spectroscopy: Mattson Unicam 5000. NMR spectroscopy: Bruker AM360 (^{1}H=360 MHz, ^{13}C = 90.5 MHz), Bruker avance DRX500 (^{1}H = 500.13 MHz, ^{13}C = 125.8 MHz); chemical shift in ppm relative to tetramethylsilane. MS: Vacuum Generators Micromass VG 70/70E and DS 11-250; CI (CH_4), EI (70 eV); m/z (%). High resolution mass spectra (HRMS) were recorded on a FTICR mass spectrometer Bruker 4.7T BioApex II. Elementary analysis: Ilse Beetz, Microanalytisches Laboratorium, D-8640 Kronach (Germany) and Ciba-Geigy, Mikrolabor, CH-1700, Fribourg-Marly (Switzerland).

General procedure: Catecholborane (0.64 mL, 6.0 mmol) was added dropwise at 0 °C to a solution of olefin **3** (3.0 mmol) and *N*,*N*-dimethylacetamide (28.0 μL, 0.3 mmol) in CH_2Cl_2 (2.0 mL), and the reaction mixture was heated under reflux for 3 h. Water (0.16 mL, 9.0 mmol) was added at 0 °C and the solution was stirred for 15 min at RT. CH_2Cl_2 (8.0 mL), DMPU (0.36 mL, 3.0 mmol), and the unsaturated ketone or aldehyde **4** (15.0 mmol) were successively added to this solution. Air (60.0 mL, 0.5 mmol O_2) was introduced over 2 h through a needle placed just above the reaction surface. After 2 h stirring at RT, the reaction mixture was treated with saturated NH_4Cl (10 mL) and extracted with Et_2O (3 × 20 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated. The crude product was purified by FC.

5-Cyclohexyl-3-pentanone (5aa): This compound was prepared according to the general procedure from **3a** (247 mg, 3 mmol) and **4a** (1.26 g, 15 mmol). FC (Et_2O/hexane 5:95) gave **5aa** (474 mg, 94%). Large scale: from **3a** (2.47 g, 30 mmol) and **4a** (12.6 g, 15 mmol), distillation (b.p. 87 °C/4 mbar) followed by filtration through silica gel (Et_2O/hexane 5:95) to remove DMPU traces (4.19 g, 83%). Physical and spectral data were in accordance with literature.[19] Colorless oil; ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 0.82–1.22$ (m, 6H), 1.04 (t, $J = 7.3$ Hz, 3H), 1.46 (dt, $J = 7.0$, 7.0 Hz, 2H), 1.60–1.69 (m, 5H), 2.38–2.45 (m, 4H).

5-Cyclohexyl-3-hexanone (5ab): This compound was prepared according to the general procedure from **3a** (247 mg, 3 mmol) and **4b** (1.47 g, 15 mmol). FC (Et_2O/hexane 3:97) gave **5ab** (402 mg, 74%). Physical and spectral data were in accordance with literature.[19] Colorless oil; ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 0.82$ (d, $J = 7.0$ Hz, 3H), 1.04 (t, $J = 7.3$ Hz, 3H), 0.90–1.22 (m, 6H), 1.59–1.74 (m, 5H), 1.87–1.94 (m, 1H), 2.44–2.14 (2dd, $J = 9.2$, 15.6 Hz, 2H), 2.37–2.47 (m, 2H).

3-Cyclohexylcyclohexanone (5ac): This compound was prepared according to the general procedure from **3a** (247 mg, 3.0 mmol) and **4c** (1.45 g, 15 mmol). FC (Et_2O/hexane 10:90) gave **5ac** (424 mg, 79%). Physical and spectral data in accordance with literature.[19] Colorless oil; ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 0.90–1.27$ (m, 6H), 1.35–1.43 (m, 1H), 1.52–1.76 (m, 7H), 1.82–1.90 (m, 1H), 2.02–2.12 (m, 2H), 2.18–2.28 (m, 1H), 2.31–2.41 (m, 2H).

3-Cyclohexylcyclopentanone (5ad): This compound was prepared according to the general procedure from **3a** (247 mg, 3 mmol) and **4d** (1.23 g, 15 mmol). FC (Et_2O/hexane 10:90) gave **5ad** (429 mg, 86%). Physical and spectral data were in accordance with literature.[19] Colorless oil; ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 0.89–1.02$ (m, 2H), 1.10–1.29 (m, 4H), 1.41–1.54 (m, 1H), 1.64–1.77 (m, 4H), 1.80–1.94 (m, 3H), 2.06–2.22 (m, 2H), 2.27–2.40 (m, 2H).

3-Cyclohexyl-2-methylpropanal (5ae): This compound was prepared according to the general procedure from **3a** (247 mg, 3 mmol) and **4e** (1.05 g, 15 mmol). FC (Et_2O/hexane 2:98) gave **5ae** (340 mg, 74%). Colorless oil**;** ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 0.80–0.95$ (m, 2H), 1.06 (d, $J = 6.7$ Hz, 3H), 1.14–1.36 (m, 5H), 1.56–1.71 (m, 6H), 2.44 (d sext, $J = 7.0$, 2.1 Hz, 1H), 9.58 (s, 1H); ^{13}C NMR (90.5 MHz, $CDCl_3$): $\delta = 13.8$, 26.3, 26.5, 33.1, 33.7, 35.1, 38.3, 43.8, 205.4; IR (neat): $\tilde{\nu} = 2923$, 2851, 2703, 1726, 1448 cm^{-1}; MS (CI, CH_4): *m*/*z* (%): 171 (15) [M^++CH_4], 155 (57) [M^++H], 137 (92), 125 (33), 95 (79), 81 (100), 69 (23), 55 (31); HRMS (CI, isobutane) $C_{10}H_{19}O$ [M^++H]: calcd 155.1435; found 155.1432.

3-Cyclohexylbutanal (5af): This compound was prepared according to the general procedure from **3a** (247 mg, 3 mmol) and **4f** (1.05 g, 15 mmol). FC (Et_2O /hexane 2:98) gave **5af** (200 mg, 43%). Colorless oil**;** ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 0.92$ (d, $J = 7.0$ Hz, 3H), 0.90–1.27 (m, 6H), 1.62–1.87 (m, 5H), 1.83–2.01 (m, 1H), 2.15–2.23 (m, 1H), 2.49–2.40 (m, 1H), 9.74 (s, 1H); ^{13}C NMR(90.5 MHz, $CDCl_3$): $\delta = 16.9$, 26.5, 26.6, 30.3, 33.1, 35.1, 42.8, 48.5, 203.2; IR (neat): $\tilde{\nu} = 2925$, 2852, 2710, 1727, 1448, 1381 cm^{-1}; MS (CI, CH_4): *m*/*z* (%): 155 (45) [M^++H], 137 (75), 111 (33), 110 (83), 95 (43), 81 (100), 69 (22), 55 (21); HRMS (CI, isobutane) $C_{10}H_{19}O$ [M^++H]: calcd 155.1435; found 155.1436.

3-Tridecanone and 6-methyl-3-dodecanone (5ba and 5b′a): This compound was prepared according to the general procedure from **3b** (337 mg, 3 mmol) and **4a** (1.26 g, 15 mmol). FC (Et_2O /hexane 5:95) gave **5ba/5b′a** (354 mg, 60%) as a 89:11 mixture not separable by chromatography. Colorless oil**;** GC: $t_r = 6.28$ min (**5b′a**), 6.62 min (**5ba**); ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 0.87$ (t, $J = 7.0$ Hz, 3H), 1.04 (t, $J = 7.3$ Hz, 3H), 1.24–1.26 (m, 14H), 1.53–1.72 (m, 2H), 2.38 (t, $J = 7.5$ Hz, 2H), 2.42 (q, $J = 7.4$ Hz, 2H);

^{13}C NMR (90.5 MHz, $CDCl_3$): $\delta = 7.8$, 10.9, 22.6, 23.9, 29.3, 29.4, 29.5, 29.6, 31.9 , 35.8, 42.4, 212.0; IR (neat): $\tilde{\nu} = 2925$, 2854, 1716, 1460, 1413, 1377, 1108 cm^{-1}; MS (70 ev, EI): *m*/*z* (%): 199 (29) [M^++1], 198 (2) [M^+], 169 (43), 126 (6), 109 (8), 95 (23), 85 (72), 72 (99), 57 (100); $C_{13}H_{26}O$ (182.16): calcd C 78.72, H 13.21; found C 78.73, H 13.59.

7-Phenyl-3-heptanone and 6-phenyl-3-heptanone (5ca and 5c′a): These compounds were prepared according to the general procedure from **3c** (312 mg, 3 mmol) and **4a** (1.26 g, 15 mmol). FC (Et_2O/hexane 10:90) gave **5ca/5c′a** (400 mg, 70%) as a 78:22 mixture not separable by chromatography. Colorless oil; GC: $t_r = 6.56$ min (**5c′a**), 7.11 min (**5ca**).

Compound **5ca**-major: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.04$ (t, $J = 7.3$ Hz, 3H), 1.59 – 1.63 (m, 4H), 2.40 (q, $J = 7.3$ Hz, 2H), 2.40 – 2.43 (m, 2H), 2.60 – 2.63 (m, 2H), 7.15 – 7.30 (m, 5H); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 7.8$, 22.5, 31.0, 35.9, 42.2, 125.7, 128.4, 142.5, 211.6; IR (neat): $\tilde{\nu} = 2936$, 1714, 1603, 1495, 1453, 1413, 1376, 1113, 748, 700 cm^{-1}; MS (70 ev, EI): *m*/*z* (%): 190 (31) [M^+], 161 (17), 143 (8), 129 (11), 118 (97), 105 (31), 91 (100), 85 (25), 72 (34), 57 (76); $C_{13}H_{18}O$ (190.13): calcd C 82.06, H 9.53; found C 82.12, H 9.58.

Compound **5c′a**-minor: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.99$ (t, $J = 7.3$ Hz, 3H), 1.25 (d, $J = 6.9$ Hz, 3H), 1.78 – 1.94 (m, 2H), 2.32 – 2.20 (m, 2H), 2.31 (q, $J = 7.3$ Hz, 3H), 7.15 – 7.30 (m, 5H); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta =$ 7.8, 23.6, 31.9, 35.7, 39.4, 40.5, 127.0, 126.1, 146.5, 211.6.

6-Cyclohexyl-3-hexanone (5da): This compound was prepared according to the general procedure from **3d** (289 mg, 3 mmol) and **4a** (1.26 g, 15 mmol). FC (Et_2O/hexane 10:90) gave **5da** (380 mg, 69%). Colorless oil**;** ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 0.83 – 0.90$ (m, 2H), 1.04 (t, $J = 7.3$ Hz, 3H), 1.10 – 1.25 (m, 6H), 1.53 – 1.70 (m, 7H), 2.37 (t, $J = 7.3$ Hz, 2H), 2.41 (q, $J = 7.3$ Hz, 2H); ^{13}C NMR(90.5 MHz, $CDCl_3$): $\delta = 7.8$, 21.3, 26.3, 33.3, 35.8, 37.0, 37.5 , 42.7, 211.8; IR (neat): $\tilde{\nu} = 2922$, 2850, 1717, 1449, 1414, 1376, 1111 cm^{-1}; MS (70 eV, EI): *m*/*z* (%): 183 (46) [M^++1], 182 (3) [M^+], 165 (14), 153 (66), 135 (100), 121 (12), 109 (12), 107 (9), 93 (19), 81 (24), 72 (44), 57 (87); $C_{12}H_{22}O$ (182.16): calcd C 79.06, H 12.16; found C 79.04, H 12.17.

6,6,7-Trimethyl-3-octanone (5ea): This compound was prepared according to the general procedure from **3e** (253 mg, 3 mmol) and **4e** (1.26 g, 15 mmol). FC (Et_2O/hexane 10:90) gave **5ea** (361 mg, 71%). Colorless oil**;** ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 0.79$ (s, 6H), 0.82 (d, $J = 7$ Hz, 6H), 1.06 (t, $J = 7.3$ Hz, 3H), 1.47 (sept, $J = 7.0$ Hz, 1H), 1.48 – 1.51 (m, 2H), 2.32 – 2.36 (m, 2H), 2.44 (q, $J = 7.3$ Hz, 2H); ^{13}C NMR(90.5 MHz, $CDCl_3$): $\delta = 7.9$, 17.4, 23.8, 33.9, 34.6, 35.4, 35.9, 37.4 , 212.3; IR (neat): $\tilde{\nu} = 2922$, 1715, 1463, 1378, 1113 cm^{-1}; MS (70 eV, EI): *m*/*z* (%): 171 (18) [M^++1], 170 (3) [M^+], 137 (8), 127 (50), 123 (20), 109 (31), 97 (10), 85 (32), 81 (14), 69 (15), 57 (100); $C_{11}H_{22}O$ (170.14): calcd C 77.58, H 13.02; found C 77.40, H 12.99.

1-(2-Methylcyclohexyl)-2-butanone (5fa): This compound was prepared according to the general procedure from **3f** (289 mg, 3 mmol) and **4a** (1.26 g, 15 mmol). FC (Et_2O/hexane 10:90) gave **5fa** (436 mg, 80%) as a *cis*/*trans* 20:80 mixture (GC and and ^{1}H NMR). Colorless oil**;** GC (140 °C): $t_r = 2.71$ min (*trans*-**5fa**), 2.99 min (*cis*-**5fa**).

cis-**5fa**: ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 0.82$ (d, $J = 7.0$ Hz, 3H).

trans-**5fa**: ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 0.89$ (d, $J = 7.0$ Hz, 3H), 0.85 – 1.06 (m, 3H), 1.04 (t, $J = 7.4$ Hz, 3H), 1.15 – 1.50 (m, 4H), 1.62 – 1.71 (m, 4H), 1.82 – 1.89 (m, 1H), 2.27 – 2.46 (m, 4H); ^{13}C NMR (90.5 MHz, $CDCl_3$): $\delta = 7.9$, 20.2, 26.5, 27.5, 31.6, 35.8, 36.8, 39.4 , 43.4, 212.3; IR (neat): $\tilde{\nu} = 2922$, 2853, 1716, 1447, 1377, 1113 cm^{-1}; MS (70 eV, EI): *m*/*z* (%): 183 (50) [M^++1], 182 (13) [M^+], 165 (17), 153 (20), 135 (81), 110 (68), 97 (35), 95 (42), 81 (41), 69 (42), 57 (92), 55 (100); $C_{12}H_{22}O$ (182.16): calcd C 79.06, H 12.16; found C 79.15, H 12.22.

1-(2-Methylcyclopentyl)-2-butanone (5ga): This compound was prepared according to the general procedure from **3g** (247 mg, 3 mmol) and **4a**(1.26 g, 15 mmol). FC (Et_2O/hexane 5:95) gave **5ga** (443 mg, 88%) as a *cis*/*trans* 9:91 mixture (GC and ^{1}H NMR), not separable by chromatography. Colorless oil; GC: $t_r = 8.11$ min (*trans*-**5ga**), 8.83 min (*cis*-**5ga**).

cis-**5ga**: ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 0.76$ (d, $J = 7.0$ Hz, 3H).

trans-**5ga**: ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 0.96$ (d, $J = 7.0$ Hz, 3H), 1.05 (t, $J = 7.3$ Hz, 3H), 1.03 – 1.23 (m, 3H), 1.28 – 1.35 (m, 1H), 1.38 – 1.42 (m, 1H), 1.51 – 1.57 (m, 2H), 1.75 – 1.85 (m, 3H), 2.33 – 2.46 (m, 4H); ^{13}C NMR (90.5 MHz, $CDCl_3$): $\delta = 7.8$, 19.3, 23.3, 28.7, 32.1, 34.7, 35.8, 40.5, 41.5, 47.2, 212.2; IR (neat): $\tilde{\nu} = 2949$, 2868, 1717, 1458, 1414, 1375, 1110 cm^{-1}; MS (70 eV, EI): *m*/*z* (%): 169 (84) [M^++1], 168 (15)[M^+], 151 (38), 139 (11), 121 (41), 95 (100), 93 (15), 81 (42), 69 (26), 57 (85); $C_{11}H_{20}O$ (168.15): calcd C 78.51, H 11.98; found C 78.45, H 11.94.

1-(2-Phenylcyclopentyl)-2-butanone (5ha): This compound was prepared according to the general procedure from **3h** (432 mg, 3 mmol) and **4a**(1.26 g, 15 mmol). FC (Et_2O/hexane 8:92) gave **5ha** (561 mg, 81%) as a *cis*/*trans* 5:95 mixture (GC and ^{1}H NMR), not separable by chromatography. Colorless oil**;** GC: t_r 7.35 min (*trans*-**5ha**), 8.29 min (*cis*-**5ha**); *trans*-**5ha**: ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 0.96$ (t, $J = 7.3$ Hz, 3H), 1.24 – 1.34 (m, 1H), 1.40 – 1.51 (m, 1H), 1.62 – 1.88 (m, 5H), 1.94 – 2.1 (m, 2H), 2.19 – 2.39 (m, 4H), 2.5 (q, $J = 9.7$ Hz, 1H), 7.15 – 7.30 (m, 5H); ^{13}C NMR (90.5 MHz, $CDCl_3$): $\delta = 7.8$, 24.1, 28.6, 32.4, 35.6, 35.8, 41.3, 47.5, 53.1, 125.9, 127.4, 128.3, 145.4, 211.5; IR (neat): $\tilde{\nu} = 2938$, 1717, 1600, 1492, 1451, 1373, 1111, 756, 700 cm^{-1}; MS (70 eV, EI): *m*/*z* (%): 230 (27) [M^+], 212 (15), 183 (15), 158 (39), 143 (12), 129 (25), 117 (35), 104 (64), 91 (99), 77 (15), 57 (100); $C_{16}H_{22}O$ (230.16): calcd C 83.43, H 9.63; found C 83.14, H 9.73.

2,4,6-Trimethylbicyclo[4.3.0]non-4-en-3-one (9): This compound was prepared according to the general procedure from **8** (530 mg, 3 mmol), which was prepared from 2,4,6-trimethylphenol by means of the procedure of Schmid[20] and Miller.[21] FC (Et_2O/hexane 5:95) gave **9** (241 mg, 45%) as a *endo*/*exo* 95:5 mixture (^{1}H NMR). Separation by further FC (Et_2O/hexane 2:98) was achieved. Colorless oil.

endo-**9**: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.10$ (d, $J = 6.9$ Hz, 3H), 1.23 (s, 3H), 1.20 – 1.28 (m, 1H), 1.39 – 1.47 (m, 1H), 1.51 – 1.62 (m, 2H), 1.71 (d, $J = 1.45$ Hz, 3H), 1.99 (ddt, $J = 2.2$, 4.6, 6.75 Hz, 1H), 2.70 (dq, $J = 6.8$, 4.6 Hz, 1H), 6.13 (s, 1H); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 13.4$, 16.0, 22.5, 24.0, 26.6, 40.4, 42.2, 44.6, 50.6, 133.2, 150.8, 202.2; IR (CH_2Cl_2): $\tilde{\nu} =$ 2953, 2869, 1676, 1446, 1373 cm^{-1}.

exo-**9**: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.14$ (d, $J = 6.9$ Hz, 3H), 1.16 (s, 3H), 1.50 – 1.61 (m, 2H), 1.66 – 1.77 (m, 3H), 1.75 (d, $J = 1.4$ Hz, 3H), 1.86 (dt, $J = 4.2$, 8.3 Hz, 1H), 1.98 – 2.05 (m, 1H), 2.28 (dq, $J = 6.9$, 1.6 Hz, 1H), 6.37 (s, 1H) ; ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 15.5$, 16.3, 23.1, 28.2, 30.7, 39.4, 43.6, 43.9, 51.9, 131.2, 151.3, 202.8; IR (CH_2Cl_2): $\tilde{\nu} = 2955$, 1674, 1455, 1372 cm^{-1}.

Mixture of *endo*-**9** and *exo*-**9**: MS (70 eV, EI): *m*/*z* (%):178 (75) [M^+], 163 (29), 150 (33), 135 (35), 122 (87), 109 (86), 107 (53), 93 (60), 83 (100), 67 (41), 55 (54); $C_{12}H_{18}O$ (178.13): calcd C 80.85, H 10.18; found C 80.85, H 10.60.

1-(1,1,5-Trimethyl-3-propionylperhydro-4-indenyl)-3-pentanone (10): This compound was prepared according to the general procedure from (+)-2-carene (409 mg, 3 mmol) and **4a** (1.26 g, 15 mmol). FC (Et_2O/hexane 5:95 then 10:90) gave **10** (366 mg, 40%) as a 34:66 mixture of two isomers (^{1}H NMR). Colorless oil.

Compound **10**-major: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.89$ (d, $J = 6.6$ Hz, 3H), 0.92 (s, 3H), 0.95 (s, 3H), 1.03 (2t, $J = 7.3$ Hz, 6H) 1.01 – 1.17 (m, 2H), 1.25 – 1.36 (m, 3H), 1.47 – 1.51 (m, 3H), 1.66 – 1.76 (m, 2H), 1.88 (dd, $J =$ 22.6, 14.0 Hz, 1H), 2.22 – 2.54 (m, 7H), 2.83 – 2.88 (m, 1H); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 7.9$, 8.1, 20.4, 21.4, 24.5, 28.9, 31.3, 32.1, 35.3, 36.0, 36.8, 41.6, 43.0, 45.7, 46.7, 47.0, 56.5, 212.2, 214.2; IR (CH_2Cl_2): $\tilde{\nu} = 2935$, 1710, 1457, 1374, 1114 cm^{-1}.

Compound **10**-minor: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.83$ (d, $J = 6.0$ Hz, 3H), 0.95 (s, 3H), 0.98 (s, 3H), 0.99 (t, $J = 7.2$ Hz, 3H), 1.04 (t, $J = 7.3$ Hz, 3H), 1.15 – 1.39 (m, 5H), 1.44 – 1.53 (m, 4H), 1.62 (q, $J = 7.6$, 1H), 1.81 (t, $J = 12.3$ Hz, 1H), 2.23 – 2.38 (m, 3H), 2.39 (q, $J = 7.4$ Hz, 2H), 2.48 (dq, $J =$ 7.2, 18.2 Hz, 1H), 2.66 (dq, $J = 7.2$, 18.2 Hz, 1H), 3.18 – 3.24 (m, 1H); ^{13}C NMR (125.8 MHz, $CDCl_3$): $\delta = 7.7$, 7.9, 20.2, 21.7, 26.1, 26.6, 30.7, 31.4, 33.1, 35.9, 37.7, 38.6, 39.3, 40.1, 43.7, 48.7, 49.1, 51.5, 211.8, 214.8.

Mixture of isomers of **10**: IR (CH_2Cl_2): $\tilde{\nu} = 2938$, 1709, 1456, 1373, 1111 cm^{-1}; MS (CI, CH_4): *m*/*z* (%): 307 (100) [M^++H], 306 (2) [M^+], 271 (19), 259 (4), 231 (27), 217 (10), 179 (9), 177 (14), 150 (25), 127 (19), 107 (7), 85 (3), 57 (21); $C_{20}H_{34}O_2$ (306.25): calcd C 78.38, H 11.18; found C 78.04, H 11.35.

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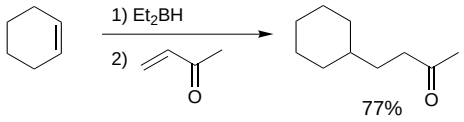

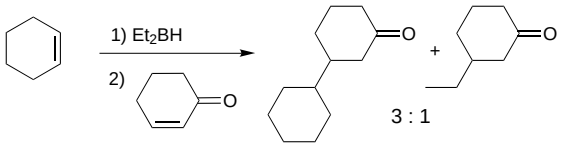

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