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Ring-opening of cyclic ethers with carbon–carbon bond formation by Grignard reagents

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ABSTRACT

The ring-opening of cyclic ethers with concomitant C–C bond formation was studied with a number of Grignard reagents. The transformation was performed in a sealed vial by heating to ~160 °C in an aluminum block or at 180 °C in a microwave oven. Good yields of the product alcohols were obtained with allyl- and benzylmagnesium halides when the ether was tetrahydrofuran or 3,3-dimethyloxetane. Lower yields were obtained with substituted tetrahydrofurans while no ring-opening was observed with tetrahydropyran. Only highly reactive allyl and benzyl Grignard reagents participated in the transformation while no reaction occurred with other alkylmagnesium halides.

1. Introduction

Formation of the carbon–carbon bond is at the cornerstone of organic synthesis and is often achieved by the reaction of a carbon nucleophile with a suitable electrophile. A number of functional groups can serve as the electrophile, but ethers (other than epoxides) are usually deemed too unreactive for this transformation. In fact, key nucleophilic substitution and addition reactions such as alkylations with lithium species, the Grignard reaction, the Wittig olefination, and reactions with organocopper reagents are often performed in ethereal solvents.[1] However, ethers are not always completely unreactive toward carbon nucleophiles.[2] Cyclic ethers larger than oxiranes undergo ring-opening with concomitant C–C bond formation with allylsilanes in the presence of a Lewis acid.[3] The same transformation can be carried out with organolithium reagents both in the presence and in the absence of a Lewis acid.[2a,4] Grignard reagents are also known to cleave ethers with formation of a C–C bond, but the reaction is sluggish and has found little synthetic use.[2b,5] The most successful example is the rather special reaction between tritylmagnesium bromide and THF, which produces 5,5,5-triphenylpentan-1-ol in 94% yield after reflux in benzene.[6] The transformation is presumably facilitated by the unusually strong coordination between the Grignard reagent and THF.[6]

Very recently, we conducted a study on the reversibility of the Grignard addition reaction.[7] By performing crossover experiments it was revealed that the addition of benzylmagnesium halides to ketones is in fact a reversible reaction.[7] The studies were performed at 140 °C in THF solution and small amounts of a byproduct from ring-opening of THF with the Grignard reagent were observed. Therefore, we decided to investigate this ring-opening in further detail in order to develop a more synthetically useful protocol. This transformation complements the established synthesis of primary alcohols from Grignard reagents and ethylene oxide.[8] Herein, we report a full account on the ring-opening of cyclic ethers with simultaneous C–C bond formation by Grignard reagents.

2. Results and discussion

p-Methylbenzylmagnesium chloride was chosen as the Grignard reagent for the initial studies and a 0.62 M solution in THF was prepared from *p*-methylbenzyl chloride and magnesium. Heating this solution to 140 °C in a sealed vial in an aluminum block produced the desired ring-opening product in a rather clean but also very slow reaction (Table 1, entry 1). To achieve a shorter reaction time the temperature was raised to 150 °C, which gave 79% isolated yield after 97 h (entry 2). Further increase in temperature resulted in a shorter reaction time, but without significantly improving the yield (entries 3 and 4). Several Lewis acids were investigated as additives in an attempt to improve this result, but in all cases a lower yield was obtained (entries 5–8). Other Lewis acids

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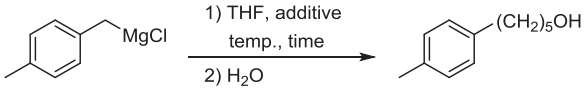
Table 1
Synthesis of 5-(*p*-methylphenyl)pentan-1-ol



Entry	Additive	Temp (°C)	Time (h)	Pressure[a] (bar)	Yield[b] (%)
1	—	140	260	—	82
2	—	150	97	—	79
3	—	160	41.5	—	70
4	—	170	41	—	82
5	CuI[c]	170	41	—	69
6	$MgBr_2 \cdot Et_2O$[c]	160	38.5	—	60
7	$BiCl_3$[c]	160	41.5	—	40
8	$CuBr_2$[c]	140	260	—	69
9[d]	—	180	16	13→16	60
10[d]	—	180	24	13→20	75
11[d]	Mesitylene[e]	180	16	11→14	36
12[d]	Decalene[e]	200	16	15→19	49
13[d]	Tetralene[e]	200	16	15→18	48
14[d]	Biphenyl[e]	200	16	15→20	60

[a] Values show start and final pressure.
[b] Isolated yield.
[c] 5% of the Lewis acid added.
[d] Performed in 10 mL sealed vial in a microwave oven with 2.5 mL of the Grignard solution in THF.
[e] 0.5 mL of the co-solvent added.

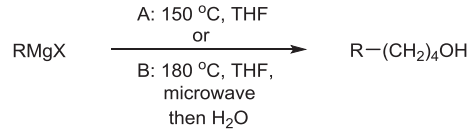
such as LiCl, $AlCl_3$, $TiCl_4$, CuBr, $FeCl_2$, $FeCl_3$, and $InCl_3$ gave inferior yields (results not shown).

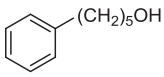
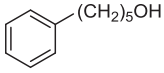
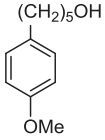
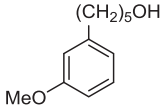
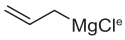
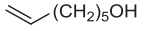
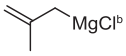
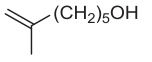
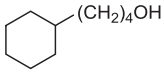
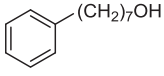
Since the transformation requires a high temperature in a closed vial it was also decided to perform the reaction in a microwave oven. Furthermore, the instrument allows for the internal pressure to be measured where a maximum of 20 bar is permitted. This gave a yield of 75% after heating to 180 °C for 24 h at which time the pressure limit was reached (entries 9 and 10). Attempts to improve the reaction by using high-boiling co-solvents and higher temperature only led to lower yields (entries 11–14). Thus, the ring-opening of THF with a Grignard reagent can be performed in good yield by using both conventional heating and a microwave oven. As a result, it was decided to study the substrate scope of the transformation under both conditions where a temperature of 150 °C was selected for the conventional heating and 180 °C under the microwave conditions.

The ring-opening of THF with benzylmagnesium bromide gave a moderate yield of 5-phenylpentan-1-ol (Table 2, entries 1 and 2). Notably, the yield increased significantly by using the corresponding chloride reagent (entries 3 and 4), which correlates with the known observation that alkylmagnesium chlorides are more reactive in the Grignard addition reaction than the bromide counterparts.[9] The experiment in entry 3 was performed with a manometer attached to the vial, which showed an internal pressure of 6 bar during conventional heating. An electron-donating group lowered the yield significantly especially when then the group was placed in the *para*-position (entries 5–8). Besides benzylic Grignard reagents, the ring-opening could also be performed with allylmagnesium chlorides (entries 9–11). On the contrary, alkyl Grignard reagents such as cyclohexyl- and 3-phenylpropylmagnesium bromide only furnished trace amounts of the desired product (entries 12 and 13). This observation is also in accordance with the previously observed reactivity difference between Grignard reagents since allyl- and benzylmagnesium halides are more reactive in the addition reaction than other alkyl reagents.[9,10] Overall, the best results are obtained with allyl- and benzylmagnesium chloride and in both cases similar yields are obtained for the two modes of heating.

Following these results it was then decided to investigate the ring-opening with other cyclic ethers. First, a 0.98 M solution of benzylmagnesium chloride was prepared in 2-

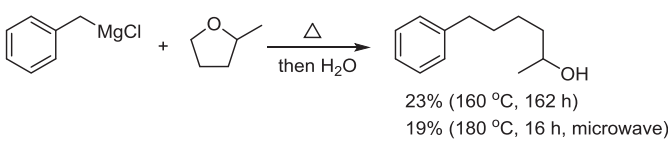
Table 2
Ring-opening of THF with Grignard reagents



Entry	RMgX	Method	Time (h)	Product	Yield[a] (%)
1	BnMgBr[b]	A	114		61
2		B	16		65
3	BnMgCl[c]	A	90		70
4		B	16		86
5	*p*-MeOBnMgCl[d]	A	95		40
6		B	24		35
7	*m*-MeOBnMgCl[d]	A	97		61
8		B	20		68
9		B	24		79
10[f]		A	66		34
11		B	24		50
12	CyMgBr[g]	A	237		~1
13	$Ph(CH_2)_3MgBr$[c]	A	233		~1

[a] Isolated yield.
[b] 0.49 M solution in THF.
[c] 0.68 M solution in THF.
[d] 0.25 M solution in THF.
[e] 2.3 M solution in THF.
[f] Heated at 120 °C.
[g] 1.13 M solution in THF.

methyltetrahydrofuran and the mixture was subjected to both conventional heating at 160 °C and microwave heating at 180 °C (Scheme 1). However, in both cases a poor yield was obtained although the transformation was regioselective for attack at the least substituted ether position. The same regioselectivity was observed in the ring-opening of 2-methyltetrahydrofuran by alkyllithium reagents.[4c]



Scheme 1. Ring-opening of 2-methyltetrahydrofuran.

Then, tetrahydropyran was investigated as a substrate and a 0.74 M solution of benzylmagnesium bromide was prepared in this solvent. However, no ring-opening occurred when this mixture was heated in an aluminum block at 170 °C. The lower reactivity of

tetrahydropyran was also observed in the reported ring-opening with alkyllithium reagents where a higher temperature was required for the six-membered ether than for THF.[4c] The benzyl Grignard solution in tetrahydropyran was also subjected to microwave heating, but due to the lower polarity of the solvent it was not possible to reach the desired temperature of 180 °C in this case. Consequently, tetrahydropyran is stable under the reaction conditions and it may therefore be possible to use this ether as a co-solvent for ring-opening of more valuable cyclic substrates.

To investigate this scenario, 2.5 mL of benzylmagnesium chloride in tetrahydropyran was mixed with 0.5 mL of 3,3-dimethyloxetane. It turned out that this mixture was sufficiently polar to be heated in a microwave oven at 180 °C. Due to the higher reactivity of the four-membered ether, the ring-opened product could now be obtained in only 4 h (Table 3, entry 1). With *p*-methylbenzylmagnesium chloride the same transformation proceeded in good yield in only 1 h (entry 2). Attempts to ring-open THF in the mixture with tetrahydropyran were less successful and only afforded 40% yield of 5-phenylpentan-1-ol (entry 3). Two other five-membered ethers were also studied and gave the ring-opening products in moderate yields (entries 4 and 5). The product stereochemistry in entry 4 indicates that the reaction proceeds by coordination of magnesium to oxygen followed by an S_N2 attack on carbon.[2] No reaction occurred with phthalan and *N*-methylpyrrolidinone at 200 °C (entries 6 and 7). As a result, the ring-opening in tetrahydropyran solution seems to be limited to highly reactive cyclic ethers such as 3,3-dimethyloxetane. This ether was also reacted with allylic Grignard reagents and the ring-opened products were isolated in good yields (entries 8 and 9). In these cases, the reaction could be performed with THF as the co-solvent and a more modest temperature of 120 °C.

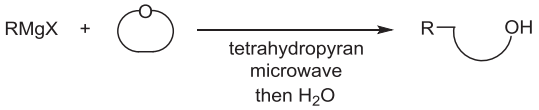
In summary, we have optimized the ring-opening of cyclic ethers with Grignard reagents to produce primary alcohols. Good yields were obtained with allyl- and benzylmagensium halides when the ether is THF or 3,3-dimethyloxetane. Neither alkyl Grignard reagents nor tetrahydropyran afforded any of the desired products while low to moderate yields were obtained with substituted tetrahydrofurans. The reactivity of the Grignard reagents in the transformation correlated with the reactivity in the Grignard addition reaction to ketones.

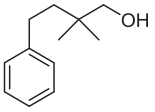
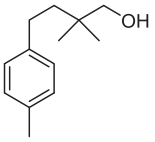
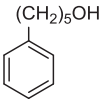
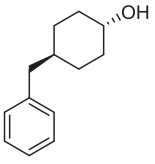
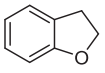
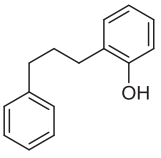
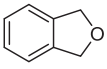
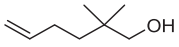
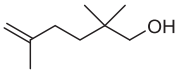
3. Experimental section

3.1. General methods

The allylic Grignard reagents were purchased from Sigma–Aldrich and used as received. The remaining Grignard reagents were prepared in a three-neck round-bottom flask by slow addition of the halide to a magnesium suspension in freshly distilled THF under an argon atmosphere. The base concentration was determined by quenching 1.0 mL of the solution in H_2O followed by addition of a few drops of phenolphthalein and then titrating with nitric acid until a color shift from pink to colorless occurred.[11] THF was distilled from sodium and benzophenone. Magnesium turnings were dried under high vacuum while glassware was dried in an oven at 185 °C. NMR spectra were recorded on a Varian Mercury 300 spectrometer with residual solvent signals as reference. Melting points were measured by Stuart SMP30 Melting Point Apparatus and are uncorrected. Mass spectrometry was performed by direct inlet on a Shimadzu GCMS-QP5000 instrument. Solvents used for chromatography were of HPLC grade. Thin layer chromatography was performed on aluminum plates coated with silica gel 60. Visualization was done by dipping into a solution of $KMnO_4$ (1%), K_2CO_3 (6.7%), and NaOH in H_2O, or a solution of H_2SO_4 (10%) in H_2O, followed by heating with a heatgun. Flash chromatography was performed with silica gel 60 (35–70 μm). Microwave heating was performed with a Personal Chemistry Emry Optimizer reactor. The pressure with conventional heating was measured by attaching a Keller LEO Record Monometer through a SyTracks H-cap spacer to the reaction vial. High resolution mass spectra were recorded on an Agilent 1100 LC system, which was coupled to a Micromass LCT

Table 3
Ring-opening of cyclic ethers with benzyl- and allylmagnesium halides[a]



Entry	Ether	Temp (°C)	Time (h)	Product	Yield[b] (%)
1[c]		180	4		69
2[d]		180	1		78
3[c]		190	24		40
4[c]		200	25		44
5[c]		200	24		49
6[c]		200	20	—	0
7[c]		200	20	—	0
8[e]		120	0.5		84
9[f]		120	0.5		67

[a] 2.5 mL of the Grignard reagent in tetrahydropyran was mixed with 0.5 mL of the ether and then heated in a microwave oven.
[b] Isolated yield.
[c] With 0.66 M solution of benzylmagnesium bromide in tetrahydropyran.
[d] With 0.62 M solution of *p*-methylbenzylmagnesium chloride in tetrahydropyran.
[e] With 2.3 M solution of allylmagnesium bromide in THF (instead of tetrahydropyran).
[f] With 0.48 M solution of methallylmagnesium bromide in THF (instead of tetrahydropyran).

orthogonal time-of-flight mass spectrometer equipped with a lock mass probe.

3.2. General procedure for ring-opening of THF by Grignard reagents with conventional heating

The solution of the Grignard reagent in THF (10.0 mL) was added to a screw-top heavy wall vial (20 mL) under an argon atmosphere and the vial was sealed. The reaction mixture was heated in an aluminum block with a lid to the indicated temperature for the time stated. The mixture was allowed to cool to ambient temperature, diluted with Et_2O and quenched with H_2O. The organic phase was washed with saturated aqueous NH_4Cl and H_2O. The organic layer was dried with $MgSO_4$, filtered, concentrated, and purified by flash column chromatography.

3.3. General procedure for ring-opening of THF by Grignard reagents with microwave heating

The solution of the Grignard reagent in THF (4.0 mL) was added to a microwave vial (10 mL) under an argon atmosphere and the vial was sealed. The reaction was heated by microwave irradiation to the indicated temperature for the time stated. The mixture was cooled to ambient temperature, diluted with Et_2O, and quenched with H_2O. The organic phase was washed with saturated aqueous NH_4Cl and H_2O. The organic layer was dried with $MgSO_4$, filtered, concentrated, and purified by flash column chromatography.

3.4. General procedure for ring-opening of cyclic ethers by Grignard reagents in tetrahydropyran

The solution of the Grignard reagent in tetrahydropyran (2.5 mL) was mixed with the cyclic ether (0.50 mL) in a microwave vial (10 mL) under an argon atmosphere and the vial was sealed. The reaction mixture was heated by microwave irradiation to the indicated temperature for the time stated. The mixture was cooled to ambient temperature, diluted with Et_2O, and quenched with H_2O. The organic phase was washed with saturated aqueous NH_4Cl and H_2O. The organic layer was dried with $MgSO_4$, filtered, concentrated, and purified by flash column chromatography.

3.5. 5-(*p*-Tolyl)pentan-1-ol (Table 1)[12]

Isolated as a colorless oil. R_f 0.21 (CH_2Cl_2); δ_H (300 MHz, $CDCl_3$) 7.14 (br s, 4H), 3.65 (t, J=6.6 Hz, 2H), 2.64 (t, J=7.6 Hz, 2H), 2.38 (s, 3H), 2.32 (s, 1H), 1.78–1.56 (m, 4H), 1.52–1.35 (m, 2H); δ_C (75 MHz, $CDCl_3$) 139.5, 135.0, 129.0, 128.3, 62.7, 35.5, 32.6, 31.5, 25.5, 21.0; ν_{max} (film) 3332, 3018, 2929, 2857, 1515, 1457, 1048, 804 cm^{-1}; MS m/z 178 [M^+]; HRMS (ESI) calcd for $C_{12}H_{17}$ [$M-H_2O+H]^+$ m/z 161.1325, found 161.1326.

3.6. 5-Phenylpentan-1-ol (Table 2, entries 1–4)

Isolated as a colorless oil. R_f 0.21 (CH_2Cl_2); δ_H (300 MHz, $CDCl_3$) 7.37–6.95 (m, 5H), 3.51 (t, J=6.6 Hz, 2H), 2.53 (t, J=7.7 Hz, 2H), 1.90 (s, 1H), 1.70–1.40 (m, 4H), 1.40–1.18 (m, 2H); δ_C (75 MHz, $CDCl_3$) 142.6, 128.5, 128.3, 125.7, 62.8, 36.0, 32.6, 31.3, 25.5; ν_{max} (film) 3333, 3026, 2931, 2857, 1603, 1585, 1495, 1453, 1050, 744, 696 cm^{-1}; MS m/z 164 [M^+]. NMR data are in accordance with literature values.[13]

3.7. 5-(*p*-Methoxyphenyl)pentan-1-ol (Table 2, entries 5 and 6)

Isolated as a colorless oil. R_f 0.29 (EtOAc/heptane 1:2); δ_H (300 MHz, $CDCl_3$) 7.10 (d, J=8.5 Hz, 2H), 6.83 (d, J=8.5 Hz, 2H), 3.79 (s, 3H), 3.62 (t, J=6.5 Hz, 2H), 2.56 (t, J=6.5 Hz, 2H), 1.69 (s, 1H), 1.68–1.53 (m, 4H), 1.45–1.33 (m, 2H); δ_C (75 MHz, $CDCl_3$) 157.7, 134.8, 129.3, 113.8, 62.9, 55.3, 35.0, 32.7, 31.6, 25.4; ν_{max} (film) 3337, 2931, 2856, 1612, 1510, 1462, 1299, 1242, 1176, 1034, 810 cm^{-1}; MS m/z 194 [M^+]; HRMS (ESI) calcd for $C_{12}H_{17}O$ [$M-H_2O+H]^+$ m/z 177.1279, found 177.1273. NMR data are in accordance with literature values.[14]

3.8. 5-(*m*-Methoxyphenyl)pentan-1-ol (Table 2, entries 7 and 8)

Isolated as a colorless oil. R_f 0.29 (EtOAc/heptane 1:2); δ_H (300 MHz, $CDCl_3$) 7.20 (dd, J=8.9, 7.6 Hz, 1H), 6.83–6.69 (m, 3H), 3.80 (s, 3H), 3.63 (t, J=6.6 Hz, 2H), 2.61 (t, J=7.7 Hz, 2H), 1.76–1.54 (m, 5H), 1.47–1.33 (m, 2H); δ_C (75 MHz, $CDCl_3$) 159.7, 144.4, 129.3, 121.0, 114.3, 111.0, 63.0, 55.3, 36.1, 32.8, 31.3, 25.5; ν_{max} (film) 3337, 2932, 2857, 1601, 1584, 1487, 1453, 1436, 1257, 1151, 1042, 776, 694 cm^{-1}; MS m/z 194 [M^+]. NMR data are in accordance with literature values.[15]

3.9. Hept-6-en-1-ol (Table 2, entry 9)

Isolated as a colorless oil. R_f 0.41 (Et_2O/pentane 1:2); δ_H (300 MHz, $CDCl_3$) 5.80 (ddt, J=16.9, 10.2, 6.7 Hz, 1H), 5.10–4.79 (m, 2H), 3.75–3.47 (m, 2H), 2.26–1.92 (m, 2H), 1.70–1.22 (m, 7H); δ_C (75 MHz, $CDCl_3$) 139.0, 114.5, 63.1, 33.8, 32.7, 28.8, 25.4; ν_{max} (film) 3331, 3077, 2929, 2858, 1641, 1458, 1053, 993, 908 cm^{-1}; MS m/z 115 [$M+H^+$]; HRMS (ESI) calcd for $C_7H_{15}O$ [$M+H]^+$ m/z 115.1117, found 115.1123. NMR data are in accordance with literature values.[16]

3.10. 6-Methylhept-6-en-1-ol (Table 2, entries 10 and 11)

Isolated as a colorless oil. R_f 0.30 (Et_2O/pentane 1:1); δ_H (300 MHz, $CDCl_3$) 4.83–4.52 (m, 2H), 3.64 (t, J=6.6 Hz, 2H), 2.02 (t, J=7.3 Hz, 2H), 1.80–1.25 (m, 9H); δ_C (75 MHz, $CDCl_3$) 146.1, 109.9, 63.1, 37.9, 32.8, 27.4, 25.5, 22.5; ν_{max} (film) 3331, 3074, 2932, 2859, 1649, 1449, 1374, 1052, 884 cm^{-1}; MS m/z 128 [M^+]; HRMS (ESI) calcd for $C_8H_{17}O$ [$M+H]^+$ m/z 129.1274, found 129.1278. NMR data are in accordance with literature values.[17]

3.11. 6-Phenylhexan-2-ol (Scheme 1)

Isolated as a colorless oil. R_f 0.23 (EtOAc/heptane 1:4); δ_H (300 MHz, $CDCl_3$) 7.32–7.15 (m, 5H), 3.79 (hex, J=6.2 Hz, 1H), 2.63 (t, J=7.7 Hz, 2H), 1.69–1.31 (m, 7H), 1.18 (d, J=6.2 Hz, 3H); δ_C (75 MHz, $CDCl_3$) 142.7, 128.5, 128.4, 125.8, 68.2, 39.3, 36.0, 31.6, 25.6, 23.6; ν_{max} (film) 3346, 3062, 3026, 2930, 2857, 1603, 1495, 1453, 1373, 1155, 1127, 1092, 1064, 930, 744, 697 cm^{-1}; MS m/z 178 [M^+]; HRMS (ESI) calcd for $C_{12}H_{17}$ [$M-H_2O+H]^+$ m/z 161.1325, found 161.1323. ^1H NMR data are in accordance with literature values.[18]

3.12. 2,2-Dimethyl-4-phenylbutan-1-ol (Table 3, entry 1)

Isolated as a colorless oil. R_f 0.33 (EtOAc/heptane 1:4); δ_H (300 MHz, $CDCl_3$) 7.42–7.07 (m, 5H), 3.38 (s, 2H), 2.71–2.44 (m, 2H), 1.67–1.52 (m, 2H), 1.50 (s, 1H), 0.97 (s, 6H); δ_C (75 MHz, $CDCl_3$) 143.3, 128.5 (3C), 128.4, 125.8, 71.9, 41.0, 35.4, 30.6, 23.9; ν_{max} (film) 3579, 3062, 3026, 2652, 2867, 1603, 1496, 1472, 1454, 1388, 1364, 1047, 1031, 762, 736, 697 cm^{-1}; MS m/z 178 [M^+]; HRMS (ESI) calcd for $C_{12}H_{17}$ [$M-H_2O+H]^+$ m/z 161.1325, found 161.1324. NMR data are in accordance with literature values.[19]

3.13. 2,2-Dimethyl-4-(*p*-tolyl)butan-1-ol (Table 3, entry 2)

Isolated as a colorless oil. R_f 0.29 (EtOAc/heptane 1:5); δ_H (300 MHz, $CDCl_3$) 7.11 (br s, 4H), 3.38 (d, J=4.8 Hz, 2H), 2.65–2.47 (m, 2H), 2.33 (s, 3H), 1.72–1.43 (m, 3H), 0.97 (s, 6H); δ_C (75 MHz,

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$CDCl_3$) 140.2, 135.2, 129.2, 128.3, 71.9, 41.2, 35.4, 30.1, 23.9, 21.1; ν_{max} (film) 3354, 3004, 2952, 2867, 1514, 1471, 1364, 1046, 1021, 808 cm^{-1}; MS *m/z* 192 [M^+]; HRMS (ESI) calcd for $C_{13}H_{19}$ [$M-H_2O+H]^+$ *m/z* 175.1487, found 175.1481. NMR data are in accordance with literature values.[19]

3.14. *trans*-4-Benzylcyclohexan-1-ol (Table 3, entry 4)

Isolated as a colorless oil. R_f 0.29 (EtOAc/heptane 1:2); δ_H (300 MHz, $CDCl_3$) 7.46–7.00 (m, 5H), 3.55 (ddd, *J*=10.7, 7.5, 3.3 Hz, 1H), 2.50–2.44 (m, 2H), 2.04–1.83 (m, 2H), 1.78–1.67 (m, 2H), 1.59–1.36 (m, 2H), 1.34–1.11 (m, 2H), 1.11–0.85 (m, 2H); δ_C (75 MHz, $CDCl_3$) 141.2, 129.2, 128.3, 125.9, 71.2, 43.4, 38.9, 35.6, 31.1; ν_{max} (film) 3259, 2924, 2852, 1450, 1369, 1083, 1043, 744, 697 cm^{-1}; MS *m/z* 190 [M^+]. NMR data are in accordance with literature values.[20]

3.15. 2-(3-Phenylpropyl)phenol (Table 3, entry 5)

Isolated as a colorless oil. R_f 0.25 (EtOAc/heptane 1:5); δ_H (300 MHz, $CDCl_3$) 7.36–6.90 (m, 7H), 6.79 (td, *J*=7.4, 1.2 Hz, 1H), 6.66 (dd, *J*=7.9, 1.0 Hz, 1H), 4.54 (s, 1H), 2.74–2.46 (m, 4H), 2.01–1.75 (m, 2H); δ_C (75 MHz, $CDCl_3$) 153.5, 142.4, 130.3, 128.6, 128.5, 128.2, 127.3, 125.9, 121.0, 115.4, 35.7, 31.3, 29.6; ν_{max} (film) 3530, 3061, 3026, 2932, 2858, 1591, 1495, 1453, 1328, 1235, 1170, 1096, 1043, 747, 697 cm^{-1}; MS *m/z* 212 [M^+]; HRMS (ESI) calcd for $C_{15}H_{17}O$ [$M+H]^+$ *m/z* 213.1274, found 213.1274. ^1H NMR data are in accordance with literature values.[21]

3.16. 2,2-Dimethylhex-5-en-1-ol (Table 3, entry 8)

Isolated as a colorless oil. R_f 0.32 (Et_2O/pentane 1:5); δ_H (300 MHz, $CDCl_3$) 5.81 (ddt, *J*=16.8, 10.1, 6.5 Hz, 1H), 5.00 (ddd, *J*=17.1, 3.5, 1.6 Hz, 1H), 4.95–4.88 (m, 1H), 3.30 (s, 2H), 2.15–1.92 (m, 2H), 1.69 (s, 1H), 1.42–1.21 (m, 2H), 0.87 (s, 6H); δ_C (75 MHz, $CDCl_3$) 139.6, 114.1, 71.9, 37.9, 35.2, 28.5, 23.9; ν_{max} (film) 3348, 3074, 2955, 2934, 2870, 1641, 1473, 1364, 1037, 992, 906 cm^{-1}; MS *m/z* 128 [M^+]; HRMS (ESI) calcd for $C_8H_{16}O$ [$M+H]^+$ *m/z* 129.1274, found 129.1273. ^1H NMR data are in accordance with literature values.[22]

3.17. 2,2,5-Trimethylhex-5-en-1-ol (Table 3, entry 9)

Isolated as a colorless oil. R_f 0.31 (Et_2O/pentane 1:5); δ_H (300 MHz, $CDCl_3$) 4.82–4.56 (m, 2H), 3.32 (s, 2H), 2.05–1.88 (m, 2H), 1.73 (s, 3H), 1.50 (s, 1H), 1.47–1.27 (m, 2H), 0.88 (s, 6H); δ_C (75 MHz, $CDCl_3$) 146.8, 109.5, 72.0, 36.8, 35.1, 32.2, 23.9, 22.8; ν_{max} (film) 3355, 3074, 2938, 2917, 2870, 1649, 1472, 1448, 1051, 1033, 883 cm^{-1}; MS *m/z* 142 [M^+]; HRMS (ESI) calcd for $C_9H_{19}O$ [$M+H]^+$ *m/z* 143.1430, found 143.1431. ^1H NMR data are in accordance with literature values.[23]

Supplementary data

^1H and ^{13}C NMR spectra of all compounds. Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2014.05.026.

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