Reduction of Carboxylic Acids Using Esters of Benzotriazole as High-Reactivity Intermediates

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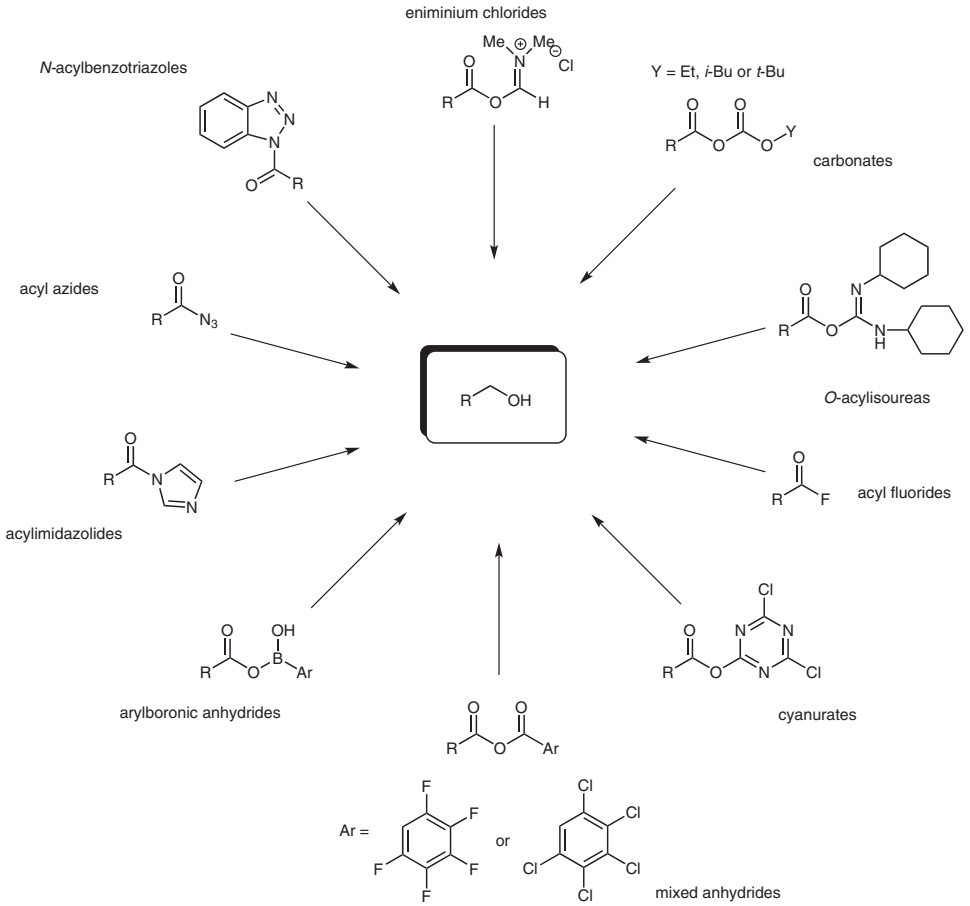
Abstract: Herein, we describe a simple and practical protocol for the reduction of carboxylic acids via the in situ formation of hydroxybenzotriazole esters followed by reaction with sodium borohydride to give the corresponding alcohols. The reaction proceeds with excellent yields in the presence of water.

Key words: alcohol, carboxylic acids, reduction, benzotriazole esters, carbodiimide

The reduction of carboxylic acids to alcohols is a useful and important transformation in synthetic organic chemistry. Although several methods of reduction are available, more efficient and convenient methods are continually being sought. In the years since Brown[1] reported that some acids can be reduced into alcohols in the presence of sodium borohydride and aluminum(III) chloride, diverse reduction strategies have been described, including the use of BH_3,[2] BH_3–$BF_3{\cdot}OEt_2$,[3] $BH_3{\cdot}SMe_2$–$BF_3{\cdot}OEt_2$,[4] $NaBH_4$ in combination with I_2,[5] $TiCl_4$,[6] $ZrCl_4$,[7] catechol–TFA,[8] H_2SO_4,[9] $BF_3{\cdot}OEt_2$,[10] $CaCl_2$,[11] diglyme,[12] and Br_2.[13] Carboxylic acids can also be reduced with $Zn(BH_4)_2$,[14] $Zr(BH_4)_4$,[15] the combination of KBH_4 with LiCl,[16]



Scheme 1 Reduction of carboxylic acids.

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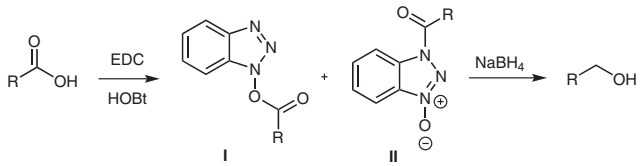
$ZnCl_2$,[17] $MgCl_2$,[18] or $HfCl_4$,[19] and $LiBH_4$ in presence of TMSCl.[20] Other important protocols include the use of $(i\text{-PrO})_2TiBH_4$,[21] $AlH_3{\cdot}NEt_3$,[22] Red-Al®,[23] SmI_2–$Sm(OTf)_3$,[24] $EtMe_2SiH$–triruthenium carbonyl clusters,[25] H_2–$[Rh(acac)(CO_2)]/[Mo(CO)_6]$,[26] and PMHS–TBAF.[27]

An alternative approach with more functional group tolerance is the transformation of the carboxylic acid into a highly reactive intermediate that can be reduced under mild reaction conditions (Scheme 1). Thus, alcohols can be obtained by the sodium borohydride reduction of carboxy methyleniminium chlorides,[28] carbonates,[29] *O*-acylisoureas,[30] fluorides,[31] cyanurates,[32] mixed anhydrides,[33] arylboronic anhydrides,[34] acylimidazolide,[35] acyl azides,[36] and *N*-acylbenzotriazoles.[37] In the same way, esters activated with 2-chloro-4,6-dimethoxy-1,3,5-triazine are reduced to give the corresponding alcohols with hydrogen and catalytic palladium on carbon.[38] McGeary et al.[39] reported the reduction of carboxylic acids via hydroxybenzotriazole esters prepared in situ from carboxylic acids and BOP reagents, while Katti et al.[40] described the reduction of the same intermediates, but obtained using 2-(6-nitro-1-oxybenzotriazol-3-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (NBTU).

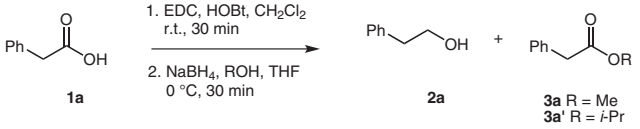


Scheme 2 Reduction of carboxylic acids.

With this background and our experience with benzotriazole esters in the synthesis of macrolactones[41] and esters,[42] we considered carrying out the same reaction employing 1-hydroxybenzotriazole (HOBt)/carbodiimide,[43] another classic coupling system in peptide chemistry, to furnish the same highly reactive benzotriazole esters[44] **I** and **II**, formed from dehydration of the carboxylic acid by means of the carbodiimide.[45] At first, we thought that a simple modification that employed HOBt/EDC [1-ethyl-3-(3-dimethylaminopropyl)carbodiimide] as the activation reagent, followed by reduction with sodium borohydride, would provide the same result as when the reaction is carried out with BOP or NBTU. However, the reaction did not progress when anhydrous tetrahydrofuran or other aprotic solvents were used.[39] These observations have given rise to the development of the present work, which pays special attention to the effect of solvent in the formation of side products. Herein we describe an efficient protocol for the conversion of carboxylic acids to alcohols using EDC and HOBt to form intermediates **I** and **II**. A representative example of the original process is depicted in Scheme 2.

Initially, we studied the reduction of phenylacetic acid (**1a**) in the presence of different amounts of sodium borohydride at 0 °C using dichloromethane or anhydrous tetrahydrofuran as the solvent (Table 1). We attempted the reaction in the absence of methanol or water, which are usually used as promoters in this type of reaction, and observed no formation of the desired product (entries 1 and 2). When the reaction was carried out in the presence of methanol, alcohol **2a** was obtained in low yield and the corresponding ester, methyl phenylacetate (**3a**) was detected as a side product (entries 3–6 and 9, 10). The use of propan-2-ol as the promoter of the reaction furnished the corresponding ester isopropyl phenylacetate (**3a′**) as the sole product (entries 7, 8 and 11, 12).

Table 1 Reduction of Phenylacetic Acid[a]



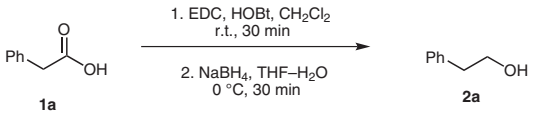
Entry	Solvent	$NaBH_4$ (equiv)	ROH	Yield[b] (%)	
				2a	**3a** or **3a′**
1	CH_2Cl_2	2	–	–	–
2	CH_2Cl_2	4	–	–	–
3	CH_2Cl_2	1	MeOH	20	–
4	CH_2Cl_2	2	MeOH	28	5
5	CH_2Cl_2	3	MeOH	35	8
6	CH_2Cl_2	4	MeOH	52	15
7	CH_2Cl_2	2	*i*-PrOH	–	5
8	CH_2Cl_2	4	*i*-PrOH	–	19
9	THF	2	MeOH	11	4
10	THF	4	MeOH	23	9
11	THF	2	*i*-PrOH	–	5
12	THF	4	*i*-PrOH	–	10

[a] Reaction conditions: 1. **1a** (1 mmol), EDC (1.1 mmol), HOBt (1.1 mmol), CH_2Cl_2 (15 mL), r.t., 30 min; 2. $NaBH_4$, solvent, ROH, 0 °C, 30 min.
[b] Yields of isolated product after chromatographic purification.

With these results in hand, we further explored the reaction, using the same system (EDC/HOBt) to activate the carboxylic acid in dichloromethane and then carry out the reduction with sodium borohydride in tetrahydrofuran at 0 °C, using water as a promoter. To our delight, the reduction reaction proceeded satisfactorily to give alcohol **2a** in good yields (Table 2). The scope of the reaction was evaluated employing 1–4 equivalents of sodium borohydride, and was monitored by TLC until the starting material was consumed. A short reaction time and two equivalents of sodium borohydride achieved the best reaction conditions (entry 2).

A variety of structurally diverse carboxylic acids **1a–i** and their derivatives were then studied using these experimental conditions to establish the generality of the present

Table 2 Reduction of Phenylacetic Acid[a]



Entry	$NaBH_4$ (equiv)	Time (h)	Yield[b] (%) of **2a**
1	1	0.5	49
2	2	0.5	75
3	3	0.5	78
4	4	0.5	78
5	2	2	75

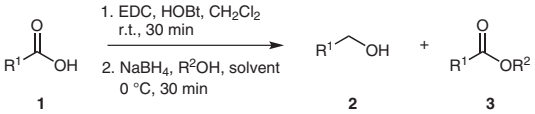
[a] Reaction conditions: 1. **1a** (1 mmol), EDC (1.1 mmol), HOBt (1.1 mmol), CH_2Cl_2 (15 mL), r.t., 30 min; 2. $NaBH_4$, THF (15 mL), H_2O (2 mL), 0 °C, 30 min.
[b] Yields of isolated product after chromatographic purification.

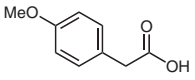
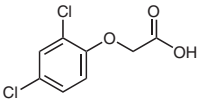
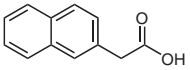
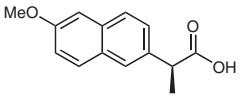
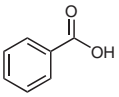
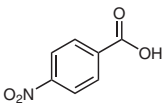
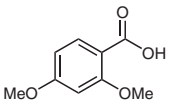
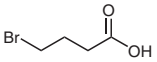
protocol and to examine the tolerance of the other functional groups present in the substrates (Table 3). Functional groups such as methoxy (entries 1, 4, and 7), phenoxy (entry 2), and nitro (entry 6), were tolerated in the reduction process. Phenylacetic acid substituted by electron-donating groups, such as methoxy **1b** (entry 1) was reduced in 80% yield. While derivatives **1c** and **1d** were reduced with lower yields (entries 2 and 3), naproxen **1e** furnished the corresponding alcohol **2d** in quantitative yield and with configuration retention (entry 4).[46] Benzoic acid (**1f**) (entry 5) and a derivative substituted by an electron-withdrawing group, such as nitro **1g** (entry 6) were reduced, but better yields than these were achieved with an electron-donating groups (entry 7). Finally, the reduction of an aliphatic carboxylic acid **1i** was carried out in quantitative yield (entry 8). It is important to note that when these reactions were carried out employing methanol or propan-2-ol as promoters, a low yield and significant formation of esters **3** were inevitable.

The amino alcohol moiety is a common structural component in a vast group of naturally occurring and synthetic molecules. A practical method for the synthesis of β-amino alcohols is the reduction of α-amino acids and their derivatives. In the present work, we demonstrate that our protocol is highly efficient towards that goal. The reduction of five amino acids **4a**–**e** (Ala, Phe, Ile, Ser, and Pro) was carried out in excellent yields to give the amino alcohols **5a**–**e** (Table 4). In all cases, the reaction conditions were compatible with the Boc protecting group, and neither racemization nor the formation of side products was observed.

In the last stage of our work, we paid attention to the reduction of α,β-unsaturated carboxylic acids **6**, which are often used to obtain allylic alcohols **7**. In general, the reaction scope was excellent results: the yields were high and the fully reduced alcohol **8** was always the minor product. As shown in Table 5, the reaction was carried out

Table 3 Conversion of Carboxylic Acids into the Corresponding Alcohol[a]



Entry	R^1CO_2H	R^2OH	Yield[b] (%)	
			2	**3**
1	 **1b**	MeOH	26	53
		i-PrOH	–	28
		H_2O	80	–
2	 **1c**	MeOH	9	14
		i-PrOH	2	10
		H_2O	55	–
3	 **1d**	MeOH	28	50
		i-PrOH	5	21
		H_2O	60	–
4	 **1e**	MeOH	71	20
		i-PrOH	22	5
		H_2O	99	–
5	 **1f**	MeOH	40	20
		i-PrOH	25	20
		H_2O	90	–
6	 **1g**	MeOH	10	20
		i-PrOH	5	20
		H_2O	60	–
7	 **1h**	MeOH	60	30
		i-PrOH	25	8
		H_2O	95	–
8	 **1i**	MeOH	75	22
		i-PrOH	50	25
		H_2O	99	–

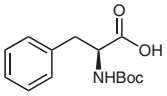
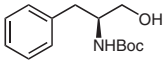
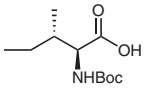
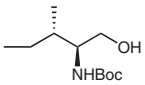
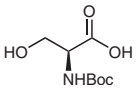
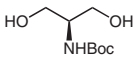
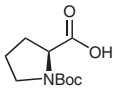
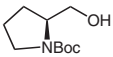
[a] Reaction conditions: 1. carboxylic acid **1** (1 mmol), EDC (1.1 mmol), HOBt (1.1 mmol), CH_2Cl_2 (15 mL), r.t., 30 min; 2. $NaBH_4$ (2 mmol), THF (15 mL), R^2OH (2 mL), 0 °C, 30 min.
[b] Yields of isolated product after chromatographic purification.

under Luche[47] conditions to minimize the complete reduction of the α,β-unsaturated system.

In conclusion, the present procedure provides a general, rapid, and convenient method for the reduction of carboxylic acids into alcohols. Its compatibility with a variety of normally reducible functional groups makes it useful for selective carboxylic acid reduction of polyfunctional molecules.

All reactions were conducted under a dried argon stream. All the chemicals were purchased from Aldrich Chemical Co and used without further purification unless stated otherwise. Yields refer to

Table 4 Conversion of Amino Acids into Amino Alcohols[a]

Entry	Acid	Alcohol	Yield[b] (%)
1	 **4a**	 **5a**	90
2	 **4b**	 **5b**	92
3	 **4c**	 **5c**	90
4	 **4d**	 **5d**	85
5	 **4e**	 **5e**	90

[a] Reaction conditions: 1. amino acids **4** (1 mmol), EDC (1.1 mmol), HOBt (1.1 mmol), CH_2Cl_2 (15 mL), r.t., 30 min; 2. $NaBH_4$ (2 mmol), THF (15 mL), H_2O (2 mL), 0 °C, 30 min.
[b] Yields of isolated product after chromatographic purification.

the chromatographically and spectroscopically (^1H and ^{13}C) homogeneous materials, unless otherwise stated. All glassware utilized was flame-dried before use. Reactions were monitored by TLC carried out on 0.25-mm E. Merck silica gel plates. Developed TLC plates were visualized under a short-wave UV lamp and by heating plates that were dipped in $Ce_2(SO_4)_3$. Flash column chromatography (FCC) was performed using silica gel (230–400) and employed a solvent polarity correlated with TLC mobility. NMR experiments were conducted on a Varian 300 MHz instrument using $CDCl_3$ (99.9% D) as the solvent referenced to internal standards $CDCl_3$ (δ = 7.26 ^1H, 77.00 ^{13}C) or TMS as internal reference (δ = 0.00). Mass spectra were recorded on Jeol JS102 high-resolution mass spectrometer.

2-Phenylethanol (2a); Typical Procedure

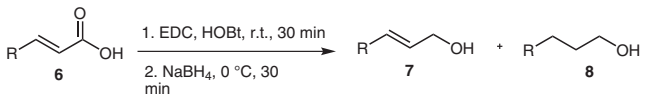
To a soln of **1a** (200 mg, 1.47 mmol) in CH_2Cl_2 (15 mL) was added HOBt (246 mg, 1.6 mmol) and EDC (308 mg, 1.6 mmol). The mixture was stirred for a total of 30 min and then concentrated in vacuo. The residue was dissolved in THF (15 mL) and cooled to 0 °C, and $NaBH_4$ (111 mg, 2.94 mmol) was added to the stirred mixture. This was followed by the addition of H_2O (1 mL). The resulting mixture was stirred at 0 °C for 30 min, and then quenched with MeOH (5 mL), and EtOAc (25 mL) was added. The organic phase was washed with 10% citric acid soln (2 × 10 mL), 10% $NaHCO_3$ soln (2 × 10 mL), 10% K_2CO_3 soln (2 × 10 mL), and brine (2 × 10 mL), dried (Na_2SO_4), and concentrated under vacuum. The crude product was purified by column chromatography (silica gel) to give **2a**; yield: 134 mg (75%).

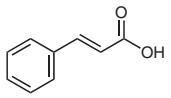
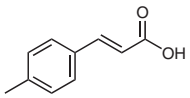
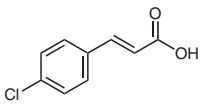
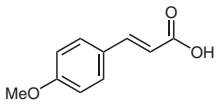
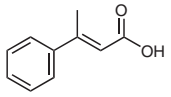
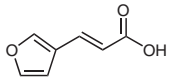
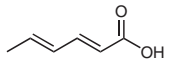
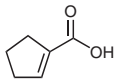
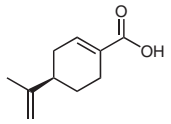
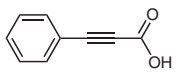
^1H NMR ($CDCl_3$): δ = 7.36–7.718 (m, 5 H), 3.84 (t, *J* = 6.4 Hz, 2 H), 2.86 (t, *J* = 6.4 Hz, 2 H), 1.62 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 138.4, 129, 128.5, 126.4, 63.6, 39.1.

MS (EI): *m*/*z* = 122.

Table 5 Reduction of α,β-Unsaturated Carboxylic Acids[a]



Entry	Acid	Yield[b] (%)	Ratio[c] (**7**/**8**)
1	 **6a**	99[d] 99[e]	91:9 95:5
2	 **6b**	94[d] 94[e]	87:13 94:6
3	 **6c**	80[d] 78[e]	85:15 91:9
4	 **6d**	93[d] 95[e]	87:13 95:5
5	 **6e**	73[d] 72[e]	76:24 83:17
6	 **6f**	90[d] 90[e]	80:20 94:6
7	 **6g**	70[d] 75[e]	95:5 100:0
8	 **6h**	99[d] 99[e]	86:14 92:8
9	 **6i**	92[d] 90[e]	100:0 100:0
10	 **6j**	92[d] 93[e]	82:18 90:10

[a] Reaction conditions: 1. carboxylic acids **6** (1 mmol), EDC (1.1 mmol), HOBt (1.1 mmol), CH_2Cl_2 (15 mL), r.t., 30 min; 2. $NaBH_4$ (2 mmol), THF (15 mL), H_2O (2 mL), 0 °C, 30 min.
[b] Yields of isolated product after chromatographic purification.
[c] Ratios were determined by NMR.
[d] With $CeCl_3$.
[e] Without $CeCl_3$.

2-(4-Methoxyphenyl)ethanol (2b)
[CAS Reg. No. 702-23-8]

^{1}H NMR ($CDCl_3$): δ = 7.13 (dd, *J* = 8.7, 2 Hz, 2 H), 6.84 (dd, *J* = 8.7, 2 Hz, 2 H), 3.8 (t, *J* = 6.6 Hz, 2 H), 3.78 (s, 3 H), 2.79 (t, *J* = 6.6 Hz, 2 H), 1.65 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 158.2, 130.5, 129.9, 113.9, 63.7, 55.2, 38.2.

MS (EI): *m*/*z* = 152.

2-(2,4-Dichlorophenoxy)ethanol (2c)
[CAS Reg. No. 120-67-2]

^{1}H NMR ($CDCl_3$): δ = 7.36 (d, *J* = 2.4 Hz, 1 H), 7.17 (dd, *J* = 8.7, 2.4 Hz, 1 H), 6.86 (d, *J* = 8.7 Hz, 1 H), 4.11 (t, *J* = 4.8 Hz, 2 H), 3.98 (t, *J* = 4.8 Hz, 2 H), 2.24 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 153, 130, 127.6, 126.3, 123.9, 114.6, 71, 61.1.

MS (EI): *m*/*z* = 206.

2-(Naphthalen-2-yl)ethanol (2d)
[CAS Reg. No. 1485-07-0]

^{1}H NMR ($CDCl_3$): δ = 7.82–7.77 (m, 3 H), 7.66 (s, 1 H), 7.49–7.40 (m, 2 H), 7.34 (dd, *J* = 8.4, 1.7 Hz, 1 H), 3.92 (t, *J* = 6.5 Hz, 2 H), 3.01 (t, *J* = 6.5 Hz, 2 H), 1.52 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 135, 133, 132, 128, 127.6, 127.4, 127.3, 126, 125, 63, 39.

MS (EI): *m*/*z* = 172.

(*S*)-6-(2-Methoxynaphthalen-2-yl)propan-1-ol (2e)
[CAS Reg. No. 26159-36-4]

^{1}H NMR ($CDCl_3$): δ = 7.70 (d, *J* = 8.4 Hz, 1 H), 7.69 (d, *J* = 8.7 Hz, 1 H), 7.59 (d, *J* = 0.9 Hz, 1 H), 7.33 (dd, *J* = 8.7, 1.8 Hz, 1 H), 7.14 (dd, *J* = 8.4, 2.4 Hz, 1 H), 7.11 (d, *J* = 2.4 Hz, 1 H), 3.90 (s, 3 H), 3.76 (d, *J* = 6.9 Hz, 2 H), 3.07 (sextet, *J* = 6.9 Hz, 1 H), 1.34 (d, *J* = 6.9 Hz, 3 H), 1.6 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 157, 138, 133, 129, 127, 126, 125, 118, 105, 68, 55, 42, 17.

MS (EI): *m*/*z* = 216.

Benzyl Alcohol (2f)
[CAS Reg. No. 100-51-6]

^{1}H NMR ($CDCl_3$): δ = 7.40–7.19 (m, 5 H), 4.95 (s, 2 H).

^{13}C NMR ($CDCl_3$): δ = 140.9, 128.3, 127.3, 126.9, 64.7.

MS (EI): *m*/*z* = 108.

4-Nitrobenzyl Alcohol (2g)
[CAS Reg. No. 619-73-8]

^{1}H NMR ($CDCl_3$): δ = 8.23 (d, *J* = 8.5 Hz, 2 H), 7.54 (d, *J* = 9.0 Hz, 2 H), 4.85 (d, *J* = 5.0 Hz, 2 H), 1.93 (t, *J* = 5.0 Hz, 1 H).

^{13}C NMR ($CDCl_3$): δ = 148.3, 147.5, 127.2, 124, 64.2.

MS (EI): *m*/*z* = 153.

2,4-Dimethoxybenzyl Alcohol (2h)
[CAS Reg. No. 7314-44-5]

^{1}H NMR ($CDCl_3$): δ = 7.15 (dd, *J* = 7.9, 1.0 Hz, 1 H), 6.43 (m, 2 H), 4.58 (d, *J* = 8.37 Hz, 2 H), 3.80 (m, 6 H), 2.51 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 157.8, 129.2, 119.5, 106.8, 106.6, 100.6, 58.2, 55.9.

MS (EI): *m*/*z* = 168.

4-Bromobutan-1-ol (2i)
[CAS Reg. No. 33036-62-3]

^{1}H NMR ($CDCl_3$): δ = 3.70 (t, *J* = 6.3 Hz, 2 H), 3.46 (d, *J* = 6.3 Hz, 2 H), 2.04–1.83 (m, 2 H), 1.81–1.65 (m, 2 H).

^{13}C NMR ($CDCl_3$): δ = 61.8, 33.6, 30.9, 29.1.

MS (EI): *m*/*z* = 152.

***N*-(*tert*-Butoxycarbonyl)-l-alaninol (5a)**
[CAS Reg. No. 79069-13-9]

^{1}H NMR ($CDCl_3$): δ = 5.0 (br s, 1 H), 3.57 (m, 1 H), 3.48 (m, 2 H), 1.39 (s, 9 H), 1.12 (d, *J* = 6.7 Hz, 3 H).

^{13}C NMR ($CDCl_3$): δ = 156.3, 79.5, 66.5, 48.4, 28.3, 17.2.

MS (EI): *m*/*z* = 175.

***N*-(*tert*-Butoxycarbonyl)-l-phenylalaninol (5b)**
[CAS Reg. No. 66605-57-0]

^{1}H NMR ($CDCl_3$): δ = 7.31–7.20 (m, 5 H), 4.83 (br s, 1 H), 3.86 (s, 1 H), 3.64 (dd, *J* = 11.0, 3.5 Hz, 1 H), 3.53 (dd, *J* = 10.7, 5.7 Hz, 1 H), 2.83 (d, *J* = 6.9 Hz, 2 H), 1.41 (s, 9 H).

^{13}C NMR ($CDCl_3$): δ = 156.1, 137.8, 129.3, 128.5, 126.5, 79.7, 64.2, 53.7, 37.4, 28.3.

MS (EI): *m*/*z* = 251.

***N*-(*tert*-Butoxycarbonyl)-l-isoleucinol (5c)**
[CAS Reg. No. 141321-50-8]

^{1}H NMR ($CDCl_3$): δ = 4.83 (br, 1 H), 3.67–3.52 (m, 2 H), 3.42–3.36 (m, 1 H), 2.78 (br, 1 H), 1.86–1.76 (m, 3 H), 1.44 (s, 9 H), 0.95–0.90 (m, 6 H).

^{13}C NMR ($CDCl_3$): δ = 156.9, 79.6, 63.8, 57.0, 36.2, 28.5, 25.5, 15.6, 11.6.

MS (EI): *m*/*z* = 217.

***N*-(*tert*-Butoxycarbonyl)-l-serinol (5d)**
[CAS Reg. No. 125414-41-7]

^{1}H NMR ($CDCl_3$): δ = 5.31 (br s, 1 H); 3.41–3.74 (m, 5 H), 3.30 (br s, 2 H), 1.42 (s, 9 H).

^{13}C NMR ($CDCl_3$): δ = 156.5, 79.9, 63.0, 53.2, 28.4.

MS (EI): *m*/*z* = 191.

***N*-(*tert*-Butoxycarbonyl)-l-prolinol (5e)**
[CAS Reg. No. 69610-40-8]

^{1}H NMR ($CDCl_3$): δ = 4.0–3.89 (m, 1 H), 3.68–3.24 (m, 4 H), 2.09–1.93 (m, 1 H), 1.88–1.73 (m, 2 H), 1.66–1.53 (m, 1 H), 1.47 (s, 9 H).

^{13}C NMR ($CDCl_3$): δ = 157.1, 80, 67, 59, 47, 28.7, 28.4, 23.

MS (EI): *m*/*z* = 201.

(*E*)-3-Phenylprop-2-en-1-ol (7a)
[CAS Reg. No. 4407-36-7]

^{1}H NMR ($CDCl_3$): δ = 7.44–7.38 (m, 2 H), 7.37–7.31 (m, 2 H), 7.30–7.24 (m, 1 H), 6.62 (d, *J* = 16 Hz, 1 H), 6.38 (dt, *J* = 16, 5.7 Hz, 1 H), 4.32 (dd, *J* = 5.7, 1.5 Hz, 2 H), 2.48 (br s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 137.2, 131.7, 129.1, 129.0, 128.2, 127.0, 64.3.

MS (EI): *m*/*z* = 134.

3-Phenylpropan-1-ol (8a)
[CAS Reg. No. 122-97-4]

^{1}H NMR ($CDCl_3$): δ = 7.34–7.28 (m, 2 H), 7.25–7.21 (m, 3 H), 3.70 (t, *J* = 6.5 Hz, 2 H), 2.74 (t, *J* = 7.9 Hz, 2 H), 2.02–1.89 (m, 2 H).

^{13}C NMR ($CDCl_3$): δ = 141.8, 128.5, 128.3, 125.9, 62.3, 34.2, 32.1.

MS (EI): *m*/*z* = 136.

(*E*)-3-*p*-Tolylprop-2-en-1-ol (7b)
[CAS Reg. No. 122058-30-4]

^{1}H NMR ($CDCl_3$): δ = 7.29 (d, *J* = 8.4 Hz, 2 H), 7.13 (d, *J* = 8.4 Hz, 2 H), 6.58 (d, *J* = 15.9 Hz, 1 H), 6.33 (dt, *J* = 15.9, 5.7 Hz, 1 H), 4.32 (d, *J* = 5.7 Hz, 2 H), 2.34 (s, 3 H), 1.50 (br s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 137.5, 132.3, 129.8, 129.1, 126.4, 123.9, 65.1, 24.3.

MS (EI): *m*/*z* = 148.

3-*p*-Tolylpropan-1-ol (8b)
[CAS Reg. No. 5406-39-3]

^{1}H NMR ($CDCl_3$): δ = 7.09 (br s, 4 H), 3.66 (t, *J* = 6.4 Hz, 2 H), 2.66 (t, *J* = 7.7 Hz, 2 H), 2.32 (s, 3 H), 1.91–1.83 (m, 2 H), 1.53 (br s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 138.7, 135.4, 129.1, 128.3, 62.4, 34.4, 31.7, 21.0.

MS (EI): *m*/*z* = 150.

(*E*)-3-(4-Chlorophenyl)prop-2-en-1-ol (7c)
[CAS Reg. No. 24583-70-8]

^{1}H NMR ($CDCl_3$): δ = 7.20–7.13 (m, 4 H), 6.45 (d, *J* = 15.9 Hz, 1 H), 6.21 (dt, *J* = 15.9, 5.4 Hz, 1 H), 4.26 (d, *J* = 5.4 Hz, 2 H), 3.97 (br s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 137.5, 132.3, 129.8, 129.1, 126.4, 123.9, 65.1, 24.3.

MS (EI): *m*/*z* = 168.

3-(4-Chlorophenyl)propan-1-ol (8c)
[CAS Reg. No. 6282-88-8]

^{1}H NMR ($CDCl_3$): δ = 7.24 (d, *J* = 8.5 Hz, 2 H), 7.12 (d, *J* = 8.5 Hz, 2 H), 3.61 (t, *J* = 7.3 Hz, 2 H), 2.67 (t, *J* = 7.3 Hz, 2 H), 1.92–1.78 (m, 2 H), 1.76 (br s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 140, 131.2, 129.5, 128.1, 61.3, 33.7, 31.1.

MS (EI): *m*/*z* = 170.

(*E*)-3-(4-Methoxyphenyl)prop-2-en-1-ol (7d)
[CAS Reg. No. 53484-50-7]

^{1}H NMR ($CDCl_3$): δ = 7.31 (d, *J* = 8.6 Hz, 2 H), 6.86 (d, *J* = 8.6 Hz, 2 H), 6.53 (d, *J* = 15.9 Hz, 1 H), 6.33 (dt, *J* = 15.9, 5.7 Hz, 1 H), 4.30 (d, *J* = 5.7 Hz, 2 H), 3.81 (s, 3 H).

^{13}C NMR ($CDCl_3$): δ = 138.7, 135.4, 129.1, 128.3, 62.4, 34.4, 31.7, 21.0.

MS (EI): *m*/*z* = 164.

3-(4-Methoxyphenyl)propan-1-ol (8d)
[CAS Reg. No. 5406-18-8]

^{1}H NMR ($CDCl_3$): δ = 7.10 (d, *J* = 8.5 Hz, 2 H), 6.82 (d, *J* = 8.5 Hz, 2 H), 3.77 (s, 3 H), 3.63 (t, *J* = 6.5 Hz, 2 H), 2.63 (t, *J* = 8.0 Hz, 2 H), 2.11 (br s, 1 H), 1.83 (m, 2 H).

^{13}C NMR ($CDCl_3$): δ = 159.6, 129.9, 128.1, 126.7, 126.1, 114.4, 64.2, 55.7.

MS (EI): *m*/*z* = 166.

(*E*)-3-Phenylbut-2-en-1-ol (7e)
[CAS Reg. No. 54976-38-4]

^{1}H NMR ($CDCl_3$): δ = 7.43–7.21 (m, 5 H), 5.96 (tq, *J* = 6.6, 1.0 Hz, 1 H), 4.35 (d, *J* = 6.6 Hz, 2 H), 2.06 (d, *J* = 0.6 Hz, 3 H), 1.91 (br s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 142.8, 137.7, 128.2, 127.2, 126.4, 125.7, 59.8, 15.9.

MS (EI): *m*/*z* = 148.

3-Phenylbutan-1-ol (8e)
[CAS Reg. No. 2722-36-3]

^{1}H NMR ($CDCl_3$): δ = 7.26 (m, 5 H), 3.62 (m, 2 H), 2.80 (m, 1 H), 1.87 (m, 2 H), 1.25 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR ($CDCl_3$): δ = 145.3, 127.3, 126.8, 126.2, 65.4, 40.3, 35.4, 21.7.

MS (EI): *m*/*z* = 150.

(*E*)-3-(Furan-3-yl)prop-2-en-1-ol (7f)
[CAS Reg. No. 54355-98-5]

^{1}H NMR ($CDCl_3$): δ = 7.40 (s, 1 H), 7.35 (s, 1 H), 6.51 (s, 1 H), 6.46 (d, *J* = 15.9 Hz, 1 H), 6.09 (td, *J* = 13.8, 5.9 Hz, 1 H), 4.25 (d, *J* = 5.9 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 143.6, 140.5, 128.1, 123.6, 121.2, 107.5, 63.6.

MS (EI): *m*/*z* = 124.

3-(Furan-3-yl)propan-1-ol (8f)
[CAS Reg. No. 56859-92-8]

^{1}H NMR ($CDCl_3$): δ = 7.34 (s, 1 H), 7.23 (s, 1 H), 6.27 (s, 1 H), 3.68 (t, *J* = 6.3 Hz, 2 H), 2.51 (t, *J* = 7.7 Hz, 2 H), 1.82 (q, *J* = 7.1 Hz, 2 H), 1.57 (br s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 142.8, 138.9, 124.4, 110.9, 62.3, 32.8, 21.0.

MS (EI): *m*/*z* = 126.

(2*E*,4*E*)-Hexa-2,4-dien-1-ol (7g)
[CAS Reg. No. 17102-64-6]

^{1}H NMR ($CDCl_3$): δ = 5.34 (m, 2 H), 6.21 (dd, *J* = 10 Hz, 1 H), 6.05 (dd, *J* = 9.5 Hz, 1 H), 5.72 (m, 2 H), 4.16 (d, *J* = 5.9 Hz, 2 H), 1.76 (d, *J* = 6.3 Hz, 3 H).

^{13}C NMR ($CDCl_3$): δ = 130.7, 129.2, 128.7, 125.7, 66.1, 17.1.

MS (EI): *m*/*z* = 98.

Hexan-1-ol (8g)
[CAS Reg. No. 928-92-7]

^{1}H NMR ($CDCl_3$): δ = 3.58 (t, *J* = 6.6 Hz, 2 H), 1.50–1.55 (m, 2 H), 1.24–1.32 (m, 6 H), 0.86 (t, *J* = 6.6 Hz, 3 H).

^{13}C NMR ($CDCl_3$): δ = 62.8, 32.6, 31.6, 25.4, 22.5, 13.9.

MS (EI): *m*/*z* = 102.

Cyclopent-1-enylmethanol (7h)
[CAS Reg. No. 1120-80-5]

^{1}H NMR ($CDCl_3$): δ = 5.62–5.59 (m, 1 H), 4.18 (m, 2 H), 2.39–2.27 (m, 4 H), 1.96–1.86 (m, 2 H), 1.46 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 144.2, 125.3, 62.0, 32.5, 32.3, 23.4.

MS (EI): *m*/*z* = 98.

Cyclopentylmethanol (8h)
[CAS Reg. No. 3637-61-4]

^{1}H NMR ($CDCl_3$): δ = 3.48 (d, *J* = 7.03 Hz, 2 H), 2.22 (br s, 1 H), 2.06 (septet, *J* = 7.47 Hz, 1 H), 1.71 (m, 2 H), 1.55 (m, 4 H), 1.22 (m, 2 H).

^{13}C NMR ($CDCl_3$): δ = 67.4, 42.2, 29.2, 25.6.

MS (EI): *m*/*z* = 100.

[(*R*)-4-(Prop-1-en-2-yl)cyclohex-1-enyl]methanol (7i)
[CAS Reg. No. 57717-97-2]

^{1}H NMR ($CDCl_3$): δ = 5.70 (m, 1 H), 4.73 (m, 2 H), 4.01 (m, 2 H), 2.15 (m, 4 H), 2.10 (br s, 1 H), 1.97 (m, 1 H), 1.87 (m, 1 H), 1.73 (m, 4 H).

^{13}C NMR ($CDCl_3$): δ = 148.9, 136.4, 121.6, 107.8, 66.4, 40.2, 29.5, 26.6, 25.2, 19.9.

MS (EI): *m*/*z* = 152.

3-Phenylprop-2-yn-1-ol (7j)
[CAS Reg. No. 1504-58-1]

^{1}H NMR ($CDCl_3$): δ = 7.45–7.43 (m, 2 H), 7.33–7.30 (m, 3 H), 4.50 (s, 2 H), 1.69 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 131.5, 128.3, 128.2, 122.5, 87.3, 85.3, 51.2.

MS (EI): *m*/*z* = 132.

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