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Formation of homoallylic bromohydrins in indium-mediated allylation reactions of phenacyl bromides in aqueous solution

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ABSTRACT

A method is described for carrying out indium-mediated allylation reactions of phenacyl bromides in aqueous solution that form homoallylic bromohydrins. By employing subsequent base treatment, the homoallylic bromohydrins were converted to allylic epoxides. Finally, the process has been used as a key step in a concise sequence for the synthesis of 3-allylbenzofuran.

1. Introduction

Because water is readily available and environmentally benign, considerable attention has been given to its employment as a solvent for organic chemical reactions.[1] In particular, metal-mediated C–C bond forming reactions occurring in aqueous media have been intensively investigated.[2] While bromohydrins and their homoallylic counterparts are useful building blocks in synthetic organic chemistry,[3] only a few examples exist in which direct allylation reactions of α-bromocarbonyl compounds have been employed to form homoallylic bromohydrins in good yields.[4] Although indium-mediated aqueous allylation reactions of α-chlorocarbonyl compounds to form homoallylic chlorohydrins have been reported,[5] the scope of the reaction is limited by the low availability of the phenacyl chloride substrates. In contrast, phenacyl bromides are readily available and the formed homoallylic bromohydrins should be useful and versatile substrates in organic synthesis. The results of a previous effort showed that diallylation products are produced when indium is employed to mediate allylation reactions of α-bromocarbonyl compounds (phenacyl bromides) in THF.[6] The homoallylic bromohydrins can be obtained through indium-mediated allylation of α-diazocarbonyl compounds in THF.[7] However, when metals with high nucleophilicity such as zinc or magnesium are employed in allylation of α-bromocarbonyl compounds, epoxides are produced as major products.[8] To the best of our knowledge, a metal-mediated Barbier type process transforming α-bromoketones to homoallylic bromohydrins has not been described to date. In continuation of our efforts aimed at the development of C–C bond forming reactions in water,[9] we explored the use of phenacyl bromides as substrates in aqueous metal-mediated Barbier type allylation reactions that form highly functionalized homoallylic bromohydrins.

2. Results and discussion

This effort began with an investigation of metal-mediated allylation reactions of phenacyl bromide (**1a**) with allyl bromide, in which various metals were screened for their reactivity in aqueous solution. The conditions employed and the results of the reactions are presented in Table 1. The results showed that only indium is useful in promoting this process in an efficient and functional group tolerant manner.[10]

It has been reported that reaction of indium with allyl halides is easier than that with α-halo carbonyl compounds at rt.[2] Owing to concern about competitive reductive dehalogenation reactions, a minimum amount of indium was utilized in an exploratory effort probing solvent effects on the allylation reaction of phenacyl bromide (**1a**) with allyl bromide to form homoallylic bromohydrin **2a**. The results (Table 2) show that although **2a** was

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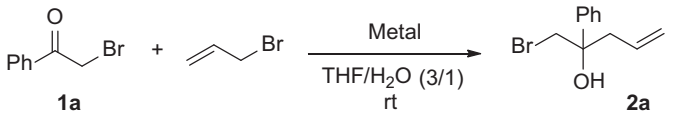
Table 1
Metal screening[a]



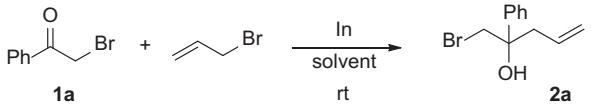
1a 2a

Entry	Metal	Reaction time (h)	Yield (%)
1	Indium	14	58
2	Zinc dust	8	0
3	Bismuth	12	0
4	Gallium	12	0
5	Aluminium	12	0

[a] Conditions: **1a** (1.0 mmol), allyl bromide (2.0 mmol) and indicated metal (1.0 mmol) in THF (1.5 mL)/water (0.5 mL) at rt.

formed when water was used as solvent, the process was sluggish and did not proceed to completion even after 8 h (Table 2, entry 1). Moreover, no reaction took place in THF[11] (Table 2, entry 2) but when a mixture of THF and water was employed as solvent, reaction took place to completely consume **1a** and form the desired product in moderate isolated yield (Table 2, entries 3 and 4). THF/H_2O (1:3) was found to be the optimum solvent system for the allylation reaction, which affords the desired product in good yield along with trace amounts of starting material and the reduction product, acetophenone (Table 2, entry 5). In contrast to Yadav's results giving diallylation product,[6] homoallylic bromohydrin **2a** was obtained as the only product in 80% when the optimum solvent system (THF/H_2O=1:3) was applied (Table 2, entry 6). It is likely that the nucleophilicity of the allylindium species generated in aqueous media differs from that in Yadav's condition.[12]

Table 2
Solvent optimization studies[a]



1a 2a

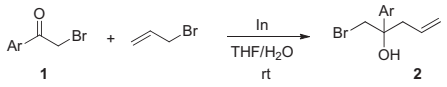
Entry	Solvent	Reaction time (h)	Yield (%)
1	H_2O	8	69[b]
2	THF[c]	8	0
3	THF/H_2O (1:1)	15	67
4	THF/H_2O (3:1)	14	58
5	THF/H_2O (1:3)	14	78
6[d]	THF/H_2O (1:3)	24.5	80

[a] Conditions: **1a** (1.0 mmol), allyl bromide (2.0 mmol) and indium metal (1.0 mmol) in solvent (2.0 mL) at rt.
[b] No isolation was performed and conversion (%) was given due to separation issues.
[c] Commercially available THF contains trace amount of water.
[d] Condition: **1a** (1.0 mmol), allyl bromide (2.5 mmol) and indium metal (2.5 mmol) in solvent (2.0 mL) at rt.

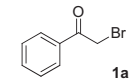
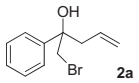
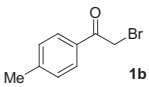
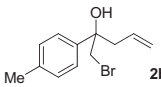
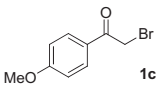
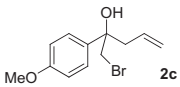
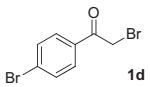
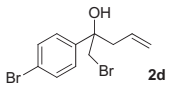
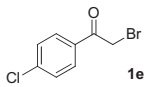
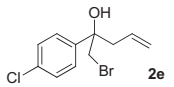
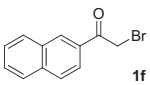
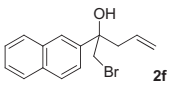
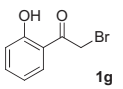
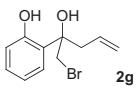
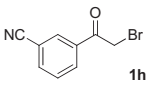
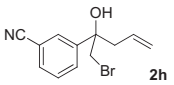
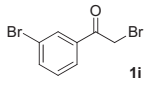
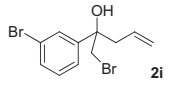
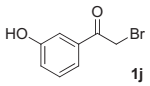
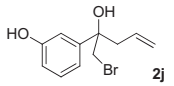
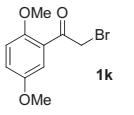
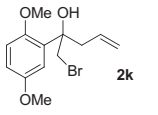
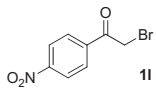
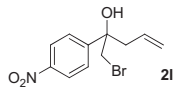
The results of an investigation exploring the scope of this indium promoted allylation process, show that under the optimized conditions a variety of aryl ring substituted phenacyl bromide derivatives are converted to the corresponding homoallylic bromohydrins in moderate to excellent yields (Table 3). It is worthy to note that none or trace amount of the reductive dehalogenation products are formed in all of the reactions in Table 3.

We also probed the outcome of this allylation process when it is followed by addition of aqueous sodium hydroxide to the crude reaction mixture. We observed that this one-pot operation produces even labile epoxides efficiently (Table 4).

Table 3
Indium-mediated allylation reactions of phenacyl bromides[a]

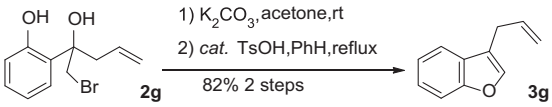


1 2

Entry	Substrate	Product	Yield[a] (%)
1	 1a	 2a	78
2	 1b	 2b	95
3	 1c	 2c	73
4	 1d	 2d	86
5	 1e	 2e	96
6	 1f	 2f	88
7	 1g	 2g	85
8	 1h	 2h	98
9	 1i	 2i	96
10	 1j	 2j	81
11	 1k	 2k	99
12	 1l	 2l	78

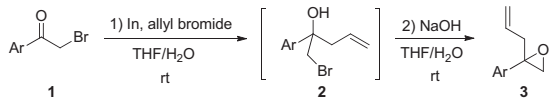
[a] Conditions: **1** (1.0 mmol), allyl bromide (2.0 mmol), and indium metal (1.0 mmol) in THF (0.5 mL)/water (1.5 mL) at rt.

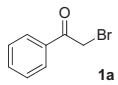
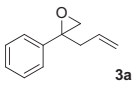
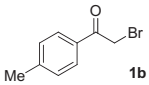
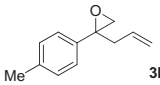
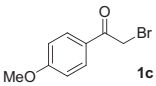
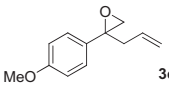
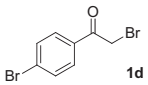
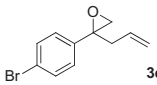
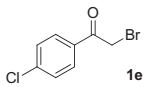
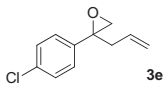
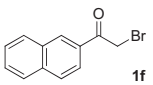
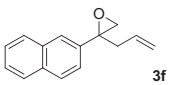
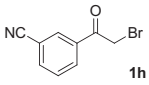
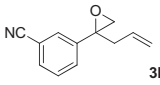
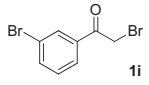
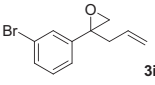
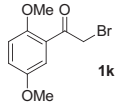
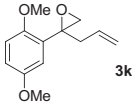
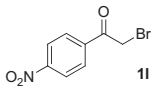
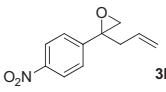
To demonstrate a synthetic application of the methodology, bromohydrin (**2g**), formed from *ortho*-hydroxyphenacyl bromide (**1g**), was converted to 3-allylbenzofuran (**3g**) in high yield via a two-step sequence involving sequential base and acid treatment (Eq. 1). Many substances containing the benzofuran motif are known to be biologically active. Preparation of 3-allylbenzofuran employing different approaches has been reported.[13] Thus, the method described above provides an alternative route to access 3-allylbenzofuran (**3g**).



(1)

Table 4
One-pot epoxide formation from phenacyl bromides[a]



Entry	Substrate	Product **3**	Yield[a] (%)
1	 **1a**	 **3a**	77
2	 **1b**	 **3b**	76
3	 **1c**	 **3c**	75
4	 **1d**	 **3d**	79
5	 **1e**	 **3e**	81
6	 **1f**	 **3f**	77
7	 **1h**	 **3h**	84
8	 **1i**	 **3i**	76
9	 **1k**	 **3k**	73
10	 **1l**	 **3l**	67

[a] The isolated yield was determined from phenacyl bromide **1**. Labile epoxides **3b** and **3c** would undergo rearrangement reaction during chromatography process to form aldehydes.

3. Conclusion

The investigation described above has led to the development of a method for the synthesis of homoallylic bromohydrins in an aqueous medium. In addition, we showed that the homoallylic bromohydrins can be directly converted to allylic epoxides and a 3-allylbenzofuran.

4. Experimental section

4.1. General

All commercially available chemicals were used without further purification. TLC analyses were run on a TLC glass plate (Silica gel 60 F_{254}) and were visualized using UV and a solution of phosphomolybdic acid in ethanol (5 wt %) or *p*-anisaldehyde stain. Flash chromatography was performed using silica gel (70–230 mesh). ^1H and ^{13}C NMR spectra were recorded on a 300 MHz spectrometer. Chemical shifts are reported relative to $CHCl_3$ [δ_H 7.24, δ_C (central line) 77.0]. Mass spectra were recorded under atmospheric pressure chemical ionization (APCI) or electron spray interface (ESI) conditions. High-resolution mass spectra were recorded by orbitrap mass spectrometer or electron spray interface (ESI) conditions with a magnetic sector analyzer.

4.2. Synthesis

4.2.1. General procedure for indium-mediated allylation reactions of α-bromoketones. A mixture of allyl bromide (2.0 mmol), indium powder (1.0 mmol), and α-bromoketone (1.0 mmol) in THF/H_2O (0.5 mL:1.5 mL) was stirred at ambient temperature. Reaction was monitored by TLC until no starting material was observed and normally the reaction mixture was stirred at rt overnight. The reaction mixture was then extracted with Et_2O (5 mL×2). The combined organic layers were washed with brine (3 mL×2), dried over $MgSO_4$, and concentrated in a rotary evaporator. The residue was purified by silica-gel chromatography using Et_2O/hexanes (1:20) as eluent to give the product.

*4.2.1.1. 1-Bromo-2-phenylpent-4-en-2-ol (**2a**).* Following the general procedure, the title compound was obtained (188 mg, 78%). An oil; TLC (Et_2O/hexanes (1:4)) R_f=0.45; ^1H NMR (300 MHz, $CDCl_3$) δ 2.55 (s, 1H), 2.72 (dd, *J*=6.6, 0.9 Hz, 2H), 3.75 (d, *J*=10.5 Hz, 1H), 3.77 (d, *J*=10.5 Hz, 1H), 5.05–5.14 (m, 2H), 5.50–5.64 (m, 1H), 7.25–7.39 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 44.5 (CH_2), 44.8 (CH_2), 74.6 (C), 119.6 (CH_2), 125.3 (CH×2), 127.4 (CH), 128.3 (CH×2), 132.4 (CH), 142.6 (C); APCI-MS *m*/*z* (rel intensity) 223 ($[M+H-H_2O]^+$, 23), 193 (36), 178 (65), 161 (100); HRMS $[M+H-H_2O]^+$ for $C_{11}H_{12}Br$: 223.0117, found 223.0124. These data are in agreement with those reported in the literature.[7]

*4.2.1.2. 1-Bromo-2-p-tolylpent-4-en-2-ol (**2b**).* Following the general procedure, the title compound was obtained (242 mg, 95%). An oil; TLC (Et_2O/hexanes (1:4)) R_f=0.50; ^1H NMR (300 MHz, $CDCl_3$) δ 2.34 (s, 3H), 2.56 (s, 1H), 2.72 (d, *J*=7.2 Hz, 2H), 3.72 (d, *J*=11.1 Hz, 1H), 3.76 (d, *J*=11.1 Hz, 1H), 5.07–5.29 (m, 2H), 5.52–5.66 (m, 1H), 7.18 (d, *J*=8.1 Hz, 2H), 7.30 (d, *J*=8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.9 (CH_3), 44.6 (CH_2), 44.8 (CH_2), 74.5 (C), 119.4 (CH_2), 125.2 (CH×2), 129.0 (CH×2), 132.6 (CH), 137.0 (C), 139.7 (C); APCI-MS *m*/*z* (rel intensity) 237 ($[M+H-H_2O]^+$, 50), 192 (20), 175 (100), 159 (57); HRMS $[M+H-H_2O]^+$ for $C_{12}H_{14}Br$: 237.0273, found 237.0281. These data are in agreement with those reported in the literature.[7]

*4.2.1.3. 1-Bromo-2-(4-methoxyphenyl)pent-4-en-2-ol (**2c**).* Following the general procedure, the title compound was obtained (198 mg, 73%). An oil; TLC (Et_2O/hexanes (1:4)) R_f=0.35; ^1H NMR (300 MHz, $CDCl_3$) δ 2.51 (s, 1H), 2.70 (dd, *J*=7.2, 0.9 Hz, 2H), 3.70 (d, *J*=10.5 Hz, 1H), 3.72 (d, *J*=10.5 Hz, 1H), 3.79 (s, 3H), 5.05–5.14 (m, 2H), 5.50–5.64 (m, 1H), 6.87 (d, *J*=8.1 Hz, 2H), 7.32 (d, *J*=8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 44.7 (CH_2), 44.8 (CH_2), 55.2 (CH_3), 74.4 (C), 113.6 (CH×2), 119.5 (CH_2), 126.6 (CH×2), 132.6 (CH), 134.7 (C), 158.8 (C); APCI-MS *m*/*z* (rel intensity) 255 (87), 253 ($[M+H-H_2O]^+$, 100), 208 (12), 191 (24); HRMS $[M+H-H_2O]^+$ for

$C_{12}H_{14}BrO$: 253.0223, found 253.0230. These data are in agreement with those reported in the literature.[7]

*4.2.1.4. 1-Bromo-2-(4-bromophenyl)pent-4-en-2-ol (**2d**).* Following the general procedure, the title compound was obtained (275 mg, 86%). An oil; TLC (Et_2O/hexanes (1:4)) R_f=0.45; ^1H NMR (300 MHz, $CDCl_3$) δ 2.58 (s, 1H), 2.68 (dd, J=7.2, 0.9 Hz, 2H), 3.68 (d, J=10.8 Hz, 1H), 3.72 (d, J=10.8 Hz, 1H), 5.06–5.12 (m, 2H), 5.48–5.62 (m, 1H), 7.27 (d, J=8.1 Hz, 2H), 7.47 (d, J=8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 44.0 (CH_2), 44.8 (CH_2), 74.5 (C), 120.0 (CH_2), 121.5 (C), 127.3 (CH×2), 131.4 (CH×2), 132.0 (CH), 141.8 (C); IR (neat) 3536, 2927, 1493 cm^{-1}; APCI-MS m/z (rel intensity) 305 (47), 303 (100), 301 ($[M+H-H_2O]^+$, 52); HRMS $[M+H-H_2O]^+$ for $C_{11}H_{11}Br_2$: 300.9222, found 300.9233.

*4.2.1.5. 1-Bromo-2-(4-chlorophenyl)pent-4-en-2-ol (**2e**).* Following the general procedure, the title compound was obtained (265 mg, 96%). An oil; TLC (Et_2O/hexanes (1:4)) R_f=0.42; ^1H NMR (300 MHz, $CDCl_3$) δ 2.57 (s, 1H), 2.68 (d, J=7.8 Hz, 2H), 3.68 (d, J=10.5 Hz, 1H), 3.72 (d, J=10.5 Hz, 1H), 5.07–5.13 (m, 2H), 5.48–5.62 (m, 1H), 7.29 (d, J=8.1 Hz, 2H), 7.34 (d, J=8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 44.1 (CH_2), 44.8 (CH_2), 74.5 (C), 120.0 (CH_2), 126.9 (CH×2), 128.4 (CH×2), 132.0 (CH), 133.3 (C), 141.3 (C); APCI-MS m/z (rel intensity) 261 (8), 259 (32), 257 ($[M+H-H_2O]^+$, 27), 177 (100); HRMS $[M+H-H_2O]^+$ for $C_{11}H_{11}BrCl$: 256.9727, found 256.9735. These data are in agreement with those reported in the literature.[4]

*4.2.1.6. 1-Bromo-2-(naphthalen-2-yl)pent-4-en-2-ol (**2f**).* Following the general procedure, the title compound was obtained (256 mg, 88%). An oil; TLC (Et_2O/hexanes (1:4)) R_f=0.42; ^1H NMR (300 MHz, $CDCl_3$) δ 2.70 (s, 1H), 2.80 (dd, J=7.8, 0.9 Hz, 2H), 3.83 (d, J=10.8 Hz, 1H), 3.86 (d, J=10.8 Hz, 1H), 5.05–5.17 (m, 2H), 5.52–5.66 (m, 1H), 7.45–7.51 (m, 3H), 7.81–7.93 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 44.4 (CH_2), 44.8 (CH_2), 74.9 (C), 119.7 (CH_2), 123.2 (CH), 124.7 (CH), 126.1 (CH), 126.2 (CH), 127.5 (CH), 128.1 (CH), 128.2 (CH), 132.4 (CH), 132.5 (C), 133.0 (C), 140.1 (C); APCI-MS m/z (rel intensity) 275 (80), 273 ($[M+H-H_2O]^+$, 88), 211 (100), 193 (54); HRMS $[M+H-H_2O]^+$ for $C_{15}H_{14}Br$: 273.0273, found 273.0287. These data are in agreement with those reported in the literature.[4]

*4.2.1.7. 2-(1-Bromo-2-hydroxypent-4-en-2-yl)phenol (**2g**).* Following the general procedure, the title compound was obtained (219 mg, 85%). An oil; TLC (Et_2O/hexanes (1:4)) R_f=0.12; ^1H NMR (300 MHz, $CDCl_3$) δ 2.83 (dd, J=7.8, 0.9 Hz, 2H), 3.28 (s, 1H), 3.72 (d, J=10.8 Hz, 1H), 3.91 (d, J=10.8 Hz, 1H), 5.14–5.21 (m, 2H), 5.60–5.74 (m, 1H), 6.80–6.88 (m, 2H), 6.99 (dd, J=7.8, 1.5 Hz, 1H), 7.15–7.21 (m, 1H), 8.73 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 42.6 (CH_2), 43.1 (CH_2), 77.8 (C), 118.1 (CH), 119.6 (CH), 120.4 (CH_2), 124.0 (C), 126.7 (CH), 129.7 (CH), 131.8 (CH), 156.2 (C); IR (neat) 3242, 2978, 1583 cm^{-1}; APCI-MS m/z (rel intensity) 241 (41), 239 ($[M+H-H_2O]^+$, 45), 177 (10), 159 (100); HRMS $[M+H-H_2O]^+$ for $C_{11}H_{12}BrO$: 239.0066, found 239.0072.

*4.2.1.8. 3-(1-Bromo-2-hydroxypent-4-en-2-yl)benzonitrile (**2h**).* Following the general procedure, the title compound was obtained (261 mg, 98%). An oil; TLC (Et_2O/hexanes (1:4)) R_f=0.20; ^1H NMR (300 MHz, $CDCl_3$) δ 2.68 (d, J=6.9 Hz, 2H), 2.82 (s, 1H), 3.71 (s, 2H), 5.04–5.10 (m, 2H), 5.49–5.58 (m, 1H), 7.24–7.63 (m, 3H), 7.73 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 43.3 (CH_2), 44.6 (CH_2), 74.4 (C), 112.0 (C), 118.6 (CH), 120.1 (CH_2), 128.9 (CH), 129.3 (CH), 129.9 (CH), 130.9 (CH), 131.3 (CH), 144.4 (C); IR (neat) 3468, 3075, 2229 cm^{-1}; APCI-MS m/z (rel intensity) 266 ($[M+H]^+$, 100), 248 (27), 186 (60), 168 (67); HRMS $[M+H]^+$ for $C_{12}H_{13}BrNO$: 266.0175, found 266.0185.

*4.2.1.9. 1-Bromo-2-(3-bromophenyl)pent-4-en-2-ol (**2i**).* Following the general procedure, the title compound was obtained (307 mg, 96%). An oil; TLC (Et_2O/hexanes (1:4)) R_f=0.50; ^1H NMR (300 MHz, $CDCl_3$) δ 2.57 (s, 1H), 2.68 (d, J=7.2 Hz, 2H), 3.71 (s, 2H), 5.08–5.14 (m, 2H), 5.49–5.63 (m, 1H), 7.19–7.32 (m, 2H), 7.39–7.42 (m, 1H), 7.58 (t, J=1.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 43.9 (CH_2), 44.8 (CH_2), 74.4 (C), 120.0 (CH_2), 122.7 (C), 124.0 (CH), 128.7 (CH), 129.8 (CH), 130.6 (CH), 131.9 (CH), 145.2 (C); IR (neat) 3543, 3080, 1562 cm^{-1}; APCI-MS m/z (rel intensity) 301 ($[M+H-H_2O]^+$, 5), 223 (93), 221 (100), 157 (38); HRMS $[M+H-H_2O]^+$ for $C_{11}H_{11}Br_2$: 300.9222, found 300.9223.

*4.2.1.10. 3-(1-Bromo-2-hydroxypent-4-en-2-yl)phenol (**2j**).* Following the general procedure, the title compound was obtained (208 mg, 81%). An oil; TLC (Et_2O/hexanes (1:4)) R_f=0.30; ^1H NMR (300 MHz, $CDCl_3$) δ 2.64 (s, 1H), 2.69 (d, J=7.2 Hz, 2H), 3.71 (s, 2H), 5.06–5.14 (m, 2H), 5.50–5.61 (m, 2H), 6.74 (d, J=8.1 Hz, 1H), 6.88–6.95 (m, 2H), 7.20 (d, J=8.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 44.2 (CH_2), 44.8 (CH_2), 74.7 (C), 112.7 (CH), 114.5 (CH), 117.6 (CH), 119.8 (CH_2), 129.6 (CH), 132.3 (CH), 144.6 (C), 155.7 (C); IR (neat) 3527, 3323, 1592 cm^{-1}; APCI-MS m/z (rel intensity) 241 ($[M+H-H_2O+2]^+$, 20), 239 ($[M+H-H_2O]^+$, 22), 177 (100), 159 (57); HRMS $[M+H-H_2O]^+$ for $C_{11}H_{12}BrO$: 239.0066, found 239.0072.

*4.2.1.11. 1-Bromo-2-(2,5-dimethoxyphenyl)pent-4-en-2-ol (**2k**).* Following the general procedure, the title compound was obtained (298 mg, 99%). An oil; TLC (Et_2O/hexanes (1:4)) R_f=0.35; ^1H NMR (300 MHz, $CDCl_3$) δ 2.67 (dd, J=13.8, 7.8 Hz, 1H), 2.99 (dd, J=13.8, 6.3 Hz, 1H), 3.32 (s, 1H), 3.75 (s, 3H), 3.79 (s, 3H), 3.83 (d, J=10.2 Hz, 1H), 4.03 (d, J=10.2 Hz, 1H), 5.00–5.11 (m, 2H), 5.55–5.68 (m, 1H), 6.74–6.82 (m, 2H), 7.06 (d, J=2.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 42.0 (CH_2), 42.8 (CH_2), 55.6 (CH_3), 55.7 (CH_3), 74.9 (C), 111.9 (CH), 112.8 (CH), 114.7 (CH), 118.5 (CH_2), 131.4 (C), 133.4 (CH), 150.0 (C), 153.3 (C); IR (neat) 3512, 2941, 1501 cm^{-1}; APCI-MS m/z (rel intensity) 285 ($[M+H-H_2O+2]^+$, 57), 283 ($[M+H-H_2O]^+$, 63), 221 (79), 203 (100); HRMS $[M+H-H_2O]^+$ for $C_{13}H_{16}BrO_2$: 283.0328, found 283.0337.

*4.2.1.12. 1-Bromo-2-(4-nitrophenyl)pent-4-en-2-ol (**2l**).* Following the general procedure, the title compound was obtained (223 mg, 78%). An oil; TLC (Et_2O/hexanes (1:4)) R_f=0.42; ^1H NMR (300 MHz, $CDCl_3$) δ 2.71 (d, J=7.2 Hz, 2H), 2.76 (s, 1H), 3.75 (d, J=10.5 Hz, 1H), 3.78 (d, J=10.5 Hz, 1H), 5.05–5.13 (m, 2H), 5.48–5.62 (m, 1H), 7.58 (d, J=9.6 Hz, 2H), 8.19 (d, J=9.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 43.3 (CH_2), 44.9 (CH_2), 74.9 (C), 120.4 (CH_2), 123.4 (CH×2), 126.6 (CH×2), 131.3 (CH), 147.1 (C), 150.2 (C); APCI-MS m/z (rel intensity) 286 ($[M+H]^+$, 19), 268 (37), 239 (51), 159 (100); HRMS $[M+H]^+$ for $C_{11}H_{13}BrNO_3$: 286.0073, found 286.0080. These data are in agreement with those reported in the literature.[6]

4.2.2. General procedure for indium-mediated allylation reactions of α-bromoketones to form epoxides in one-pot. A mixture of allyl bromide (2.0 mmol), indium powder (1.0 mmol), and α-bromoketone (1.0 mmol) in THF/H_2O (0.5 mL:1.5 mL) was stirred at ambient temperature. Reaction was monitored by TLC until no starting material was observed and normally the reaction mixture was stirred at rt overnight. NaOH (2 N) aqueous solution (2.5 mL) was then added to the reaction mixture and the mixture was stirred at rt for 2 h. The reaction mixture was then extracted with Et_2O (5 mL×2). The combined organic layers were washed with brine (3 mL×2), dried over $MgSO_4$, and concentrated in a rotary evaporator. The residue was purified by silica-gel chromatography using hexanes as eluent to give the product.

*4.2.2.1. 2-Allyl-2-phenyloxirane (**3a**).* Following the general procedure, the title compound was obtained (123 mg, 77%). An oil;

TLC (Et_2O/hexanes (1:4)) R_f=0.67; ^1H NMR (300 MHz, $CDCl_3$) δ 2.64 (dd, J=15.0, 7.2 Hz, 1H), 2.75 (d, J=5.4 Hz, 1H), 2.87 (dd, J=15.0, 7.2 Hz, 1H), 2.99 (d, J=5.4 Hz, 1H), 5.06–5.16 (m, 2H), 5.70–5.84 (m, 1H), 7.24–7.39 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 39.4 (CH_2), 54.7 (CH_2), 59.2 (C), 118.3 (CH_2), 125.8 (CH×2), 127.4 (CH), 128.2 (CH×2), 132.6 (CH), 139.9 (C). These data are in agreement with those reported in the literature.[8a]

*4.2.2.2. 2-Allyl-2-p-tolyloxirane (**3b**).* Following the general procedure, the title compound was obtained (132 mg, 76%). An oil; TLC (Et_2O/hexanes (1:4)) R_f=0.70; ^1H NMR (300 MHz, $CDCl_3$) δ 2.32 (s, 3H), 2.62 (dd, J=15.0, 7.5 Hz, 1H), 2.73 (d, J=5.4 Hz, 1H), 2.87 (ddt, J=15.0, 7.5, 1.5 Hz, 1H), 2.97 (d, J=5.4 Hz, 1H), 5.04–5.14 (m, 2H), 5.69–5.83 (m, 1H), 7.13 (d, J=7.8 Hz, 2H), 7.25 (d, J=7.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.0 (CH_3), 39.5 (CH_2), 54.8 (CH_2), 59.1 (C), 118.3 (CH_2), 125.8 (CH×2), 128.9 (CH×2), 132.8 (CH), 136.9 (C), 137.1 (C). These data are in agreement with those reported in the literature.[8a]

*4.2.2.3. 2-Allyl-2-(4-methoxyphenyl)oxirane (**3c**).* Following the general procedure, the title compound was obtained (143 mg, 75%). An oil; TLC (Et_2O/hexanes (1:4)) R_f=0.50; ^1H NMR (300 MHz, $CDCl_3$) δ 2.62 (dd, J=14.7, 7.5 Hz, 1H), 2.73 (d, J=5.4 Hz, 1H), 2.83 (ddt, J=14.7, 7.5, 1.2 Hz, 1H), 2.96 (d, J=5.4 Hz, 1H), 3.76 (s, 3H), 5.05–5.15 (m, 2H), 5.70–5.84 (m, 1H), 6.85 (d, J=8.7 Hz, 2H), 7.29 (d, J=8.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 39.5 (CH_2), 54.6 (CH_2), 55.0 (CH_3), 58.8 (C), 113.4 (CH×2), 118.1 (CH_2), 127.0 (CH×2), 131.8 (C), 132.8 (CH), 158.8 (C); IR (neat) 3048, 2938, 1518 cm^{-1}; EIMS m/z (rel intensity) 190 (M^+, 15), 161 (56), 135 (100), 121 (38); HRMS $[M]^+$ for $C_{12}H_{14}O_2$: 190.0994, found 190.0991.

*4.2.2.4. 2-Allyl-2-(4-bromophenyl)oxirane (**3d**).* Following the general procedure, the title compound was obtained (189 mg, 79%). An oil; TLC (Et_2O/hexanes (1:4)) R_f=0.62; ^1H NMR (300 MHz, $CDCl_3$) δ 2.57 (dd, J=15.0, 7.2 Hz, 1H), 2.66 (d, J=5.4 Hz, 1H), 2.83 (dd, J=15.0, 6.6 Hz, 1H), 2.95 (d, J=5.4 Hz, 1H), 5.05–5.13 (m, 2H), 5.65–5.79 (m, 1H), 7.21 (d, J=8.4 Hz, 2H), 7.41 (d, J=8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 38.9 (CH_2), 54.5 (CH_2), 58.5 (C), 118.5 (CH_2), 121.2 (C), 127.5 (CH×2), 131.1 (CH×2), 132.1 (CH), 138.9 (C). These data are in agreement with those reported in the literature.[8a]

*4.2.2.5. 2-Allyl-2-(4-chlorophenyl)oxirane (**3e**).* Following the general procedure, the title compound was obtained (158 mg, 81%). An oil; TLC (Et_2O/hexanes (1:4)) R_f=0.67; ^1H NMR (300 MHz, $CDCl_3$) δ 2.59 (dd, J=15.0, 7.2 Hz, 1H), 2.69 (d, J=5.4 Hz, 1H), 2.84 (ddt, J=15.0, 7.2, 1.2 Hz, 1H), 2.98 (d, J=5.4 Hz, 1H), 5.05–5.13 (m, 2H), 5.66–5.80 (m, 1H), 7.28 (br s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 39.2 (CH_2), 54.8 (CH_2), 58.7 (C), 118.6 (CH_2), 127.3 (CH×2), 128.4 (CH×2), 132.3 (CH), 133.2 (C), 138.4 (C). These data are in agreement with those reported in the literature.[8a]

*4.2.2.6. 2-Allyl-2-(naphthalen-2-yl)oxirane (**3f**).* Following the general procedure, the title compound was obtained (162 mg, 77%). An oil; TLC (Et_2O/hexanes (1:4)) R_f=0.57; ^1H NMR (300 MHz, $CDCl_3$) δ 2.73 (dd, J=15.0, 7.2 Hz, 1H), 2.84 (d, J=5.4 Hz, 1H), 3.00 (ddt, J=15.0, 7.2, 1.2 Hz, 1H), 3.07 (d, J=5.4 Hz, 1H), 5.06–5.19 (m, 2H), 5.74–5.88 (m, 1H), 7.43–7.50 (m, 3H), 7.80–7.85 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 39.2 (CH_2), 54.6 (CH_2), 59.3 (C), 118.3 (CH_2), 123.5 (CH), 124.8 (CH), 125.8 (CH), 126.0 (CH), 127.4 (CH), 127.7 (CH), 127.8 (CH), 132.5 (CH), 132.5 (C), 132.9 (C), 137.2 (C). These data are in agreement with those reported in the literature.[8a]

*4.2.2.7. 3-(2-Allyloxiran-2-yl)benzonitrile (**3h**).* Following the general procedure, the title compound was obtained (156 mg, 84%). An oil; TLC (Et_2O/hexanes (1:4)) R_f=0.35; ^1H NMR (300 MHz, $CDCl_3$) δ 2.60 (dd, J=15.0, 6.6 Hz, 1H), 2.70 (d, J=5.1 Hz, 1H), 2.87 (dd, J=15.0, 6.6 Hz, 1H), 3.02 (d, J=5.1 Hz, 1H), 5.07–5.14 (m, 2H), 5.64–5.78 (m, 1H), 7.42 (t, J=7.5 Hz, 1H), 7.52–7.64 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 38.7 (CH_2), 54.7 (CH_2), 58.3 (C), 112.3 (C), 118.4 (C), 119.0 (CH_2), 129.0 (CH), 129.4 (CH), 130.2 (CH), 130.9 (CH), 131.7 (CH), 141.5 (C); IR (neat) 3068, 2232, 1484 cm^{-1}; EIMS m/z (rel intensity) 185 (M^+, 3), 154 (15), 130 (100), 116 (39); HRMS $[M]^+$ for $C_{12}H_{11}NO$: 185.0841, found 185.0833.

*4.2.2.8. 2-Allyl-2-(3-bromophenyl)oxirane (**3i**).* Following the general procedure, the title compound was obtained (182 mg, 76%). An oil; TLC (Et_2O/hexanes (1:4)) R_f=0.75; ^1H NMR (300 MHz, $CDCl_3$) δ 2.59 (dd, J=15.0, 6.6 Hz, 1H), 2.70 (d, J=5.1 Hz, 1H), 2.85 (dd, J=15.0, 7.5 Hz, 1H), 2.98 (d, J=5.1 Hz, 1H), 5.07–5.15 (m, 2H), 5.66–5.79 (m, 1H), 7.15–7.39 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 39.1 (CH_2), 54.7 (CH_2), 58.6 (C), 118.8 (CH_2), 122.4 (C), 124.5 (CH), 128.9 (CH), 129.8 (CH), 130.5 (CH), 132.1 (CH), 142.3 (C); IR (neat) 3086, 2912, 1571 cm^{-1}; EIMS m/z (rel intensity) 239 (M^+, 5), 183 (100), 169 (28), 128 (83); HRMS $[M]^+$ for $C_{11}H_{11}BrO$: 237.9993, found 237.9988.

*4.2.2.9. 2-Allyl-2-(2,5-dimethoxyphenyl)oxirane (**3k**).* Following the general procedure, the title compound was obtained (161 mg, 73%). An oil; TLC (Et_2O/hexanes (1:4)) R_f=0.44; ^1H NMR (300 MHz, $CDCl_3$) δ 2.50 (dd, J=14.7, 7.5 Hz, 1H), 2.69 (d, J=5.1 Hz, 1H), 2.84 (dd, J=14.7, 7.5 Hz, 1H), 2.94 (d, J=5.1 Hz, 1H), 3.71 (s, 3H), 3.77 (s, 3H), 4.97–5.04 (m, 2H), 5.62–5.76 (m, 1H), 6.74 (s, 2H), 6.89 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 39.5 (CH_2), 53.0 (CH_2), 55.4 (CH_3), 55.5 (CH_3), 58.6 (C), 111.1 (CH), 113.3 (CH), 113.6 (CH), 117.7 (CH_2), 129.4 (C), 132.8 (CH), 150.8 (C), 153.1 (C); IR (neat) 2940, 2833, 1500 cm^{-1}; EIMS m/z (rel intensity) 220 (M^+, 43), 191 (24), 165 (100), 121 (41); HRMS $[M]^+$ for $C_{13}H_{16}O_3$: 220.1099, found 220.1093.

*4.2.2.10. 2-Allyl-2-(4-nitrophenyl)oxirane (**3l**).* Following the general procedure, the title compound was obtained (137 mg, 67%). An oil; TLC (Et_2O/hexanes (1:4)) R_f=0.37; ^1H NMR (300 MHz, $CDCl_3$) δ 2.62 (dd, J=15.0, 7.2 Hz, 1H), 2.72 (d, J=5.1 Hz, 1H), 2.93 (dd, J=15.0, 7.2 Hz, 1H), 3.05 (d, J=5.1 Hz, 1H), 5.08–5.15 (m, 2H), 5.65–5.79 (m, 1H), 7.51 (d, J=7.2 Hz, 2H), 8.16 (d, J=7.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 38.7 (CH_2), 54.9 (CH_2), 58.6 (C), 119.0 (CH_2), 123.3 (CH×2), 126.7 (CH×2), 131.6 (CH), 147.0 (C), 147.3 (C); EIMS m/z (rel intensity) 205 (M^+, 2), 164 (9), 150 (100), 128 (52); HRMS $[M]^+$ for $C_{11}H_{11}NO_3$: 205.0739, found 205.0743. These data are in agreement with those reported in the literature.[14]

4.3. 3-Allylbenzofuran (3g)

To a solution of **2g** (257 mg, 1 mmol) in acetone (4 mL) was added K_2CO_3 (414 mg, 3 mmol) at rt and the suspension was stirred at rt for 3 h. CH_2Cl_2 (5 mL) and 10% aq NH_4Cl (5 mL) were added. The mixture was transferred to a separatory funnel and the aqueous layer was extracted with CH_2Cl_2 (5 mL×2). The organic layers were combined, dried over $MgSO_4$, and concentrated in a rotary evaporator. The residue was dissolved in benzene (3.5 mL) and TsOH/H_2O (6 mg, 0.03 mmol) was added. The mixture was heated at reflux for 1 h and then the mixture was cooled to rt. Et_2O (5 mL) and 10% aq $NaHCO_3$ (5 mL) were added. The mixture was transferred to a separatory funnel and the aqueous layer was extracted with Et_2O (5 mL×2). The organic layers were combined, dried over $MgSO_4$, and concentrated in a rotary evaporator. The residue was purified by silica-gel chromatography using Et_2O/hexanes (1:10) as eluent to give the product **3g** (130 mg, 82%). An oil; TLC (hexanes) R_f=0.5; ^1H NMR (300 MHz, $CDCl_3$) δ 3.46 (d, J=7.8 Hz, 2H), 5.14–5.27 (m, 2H), 6.00–6.13 (m, 1H), 7.24–7.35 (m, 2H), 7.44–7.60 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.0 (CH_2), 111.3 (CH), 116.3 (CH_2), 118.3 (C), 119.7 (CH), 122.2 (CH), 124.1 (CH), 128.0 (C), 135.3 (CH), 141.5 (CH), 155.4 (C); EIMS m/z (rel intensity) 158 (M^+, 100), 131 (60), 113 (16), 77 (15); HRMS $[M]^+$ for $C_{11}H_{10}O$: 158.0732, found 158.0730. These data are in agreement with those reported in the literature.[13]

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2013.07.012.

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