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# An Expedient Synthesis of Allylic/Secondary Bromides from Dehydration of Tertiary-β-bromo Alcohols

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#### ABSTRACT

Tertiary- $\beta$ -bromo alcohols, derived from simple monoterpenes and olefins, react with BF<sub>3</sub>.OEt<sub>2</sub> in refluxing benzene in 1–2 h to afford the corresponding allylic/secondary bromides in 45–90% yield. In case of substrates containing olefinic or hydroxyl groups, formation of cyclic ethers was observed.

*Key Words:* Tertiary- $\beta$ -bromo alcohols; Dehydration; BF<sub>3</sub>·OEt<sub>2</sub>; Allylic bromides; Secondary bromides.

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Selective synthesis of allylic bromides and functionalized allylic halides plays an important role in organic synthesis.<sup>[1]</sup> They serve as useful precursors for allylic organometallic reagents<sup>[2]</sup> and oxygenated monoterpenes,<sup>[3]</sup> which are important flavor compounds. The allylic halides are generally obtained by direct halogenation with reagents viz., NBS, NCS, NIS,<sup>[4]</sup> and *t*-BuOCl.<sup>[5]</sup>Alternatively, electrophilic addition of halonium ion to olefins in polar solvents, referred to as co-halogenation reaction, leads to the formation of halohydrin derivatives.<sup>[6]</sup> Bromohydrins serve as useful intermediates for the functionalization of olefins to oxygenated compounds. The trans stereochemistry of halohydrins renders them useful intermediates for several applications in organic synthesis; mention may be made of, radical cyclization to lactones,<sup>[7]</sup> selective reduction with HSn(Bu)<sub>3</sub> to stereo-specific alcohols<sup>[8]</sup> and a tandem approach to generate reactive radical intermediate by cohalogenation and homolytic carbocyclization.<sup>[9]</sup> As a part of our continuing work on the funtionalization of monoterpenic hydrocarbons, we synthesized bromohydrins of monoterpenes and olefins (Table 1, 1a-f). These compounds have specific trans stereochemistry, described earlier in the stereo-specific synthesis of trans-\beta-terpineol from limonene.<sup>[10]</sup> To our knowledge, synthesis of reactive allylic halides from tertiary- $\beta$ -bromo alcohols is not reported in literature. On the other hand, dehydration of tertiary and benzylic alcohols has been reported by a number of catalysts.<sup>[11,12]</sup> Recently, we studied direct oxidation of bromohydrins.<sup>[13]</sup> In the present study, we investigated their dehydration with a view to obtaining allylic bromides.

In our studies, we found that of the several Lewis acid catalysts tried,  $BF_3 \cdot OEt_2$  effected dehydration of tertiary- $\beta$ -bromo alcohols. While these bromohydrins, **1a–1d**, under basic conditions gave internal cyclized epoxides, with catalytic quantity of  $BF_3 \cdot OEt_2$  (10 mol%) in refluxing benzene readily afforded allylic halides (Sch. 1) in good yields. Results of this reaction are summarized in Table 1. Interestingly, **1e** upon reaction with acidic catalysts gave exclusively *trans*-2-bromo-1,8-cineole (**2e**), a key intermediate for the synthesis of *trans*-2-acetoxy-1,8-cineole, a major aroma constituent of *Alpinia galanga* Willd.<sup>[14]</sup> This, apparently, results from the internal addition of hydroxyl moiety to the isopropenyl double bond between C-8 and C-9 carbons. Also, in case of bromohydrin **1f** the product was *trans*-2-bromo-1,8-cineole, which again could be due to cyclic ether formation between hydroxyl groups on C-1 and C-8 carbons.

In summary, dehydration of tertiary- $\beta$ -bromo alcohols by simple and inexpensive BF<sub>3</sub>·OEt<sub>2</sub> reagent in catalytic quantity is reported. These reactions take place rapidly and can be conveniently carried out on

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# Tertiary-β-bromo Alcohols

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*Table 1.* Reaction of tertiary- $\beta$ -bromo alcohols with BF<sub>3</sub>·OEt<sub>2</sub> in refluxing benzene.

Entry	Substrate 1	Product <sup>a</sup> 2	Yield <sup>b</sup> (%)	Reaction time (h)
A	OH	Br	60	1
В	<sup>1</sup> , OH ,,Br	Br	75	2
С	OHBr	Br	82°	2
D		Br	45	1.5
E	<sup>T</sup> OH Br	Br	90	1
F	OH OH OH	Br	50	2

<sup>a</sup>Characterized by <sup>1</sup>H, <sup>13</sup>C NMR, and mass spectra.

<sup>b</sup>Yield after purification by distillation under reduced pressure.

<sup>c</sup>Formation of 15% of vinylic halide was observed.



large scale to afford corresponding allylic bromides. The method adopted here to get the reactive halides from the corresponding olefins through bromohydrin intermediates provides a new synthetic methodology useful for the preparation of oxygenated terpene derivatives, which are important flavor constituents of several essential oils. YM4

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# General Procedure: Reaction of Tertiary-β-bromo Alcohols with BF<sub>3</sub>·OEt<sub>2</sub>

In a round-bottomed flask, a solution of tertiary- $\beta$ -bromo alcohol (Entry **1a–f**, 5 mmol) in dry benzene (10 mL) was taken. To this BF<sub>3</sub>·OEt<sub>2</sub> (10 mol%) was added, and the mixture was set for reflux. The reaction was monitored on GC (HP-1 Column,  $60^{\circ}/8^{\circ}/220^{\circ}$ C-5 min) by periodic injection of aliquot of worked-up sample for the disappearance of the bromohydrin. At the end of the reaction, the product was put into 5% NaHCO<sub>3</sub> (20 mL) and organic layer separated. It was washed with water (10 mL × 2) and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. Evaporation of solvent afforded crude product, which was distilled under reduced pressure to afford pure halide. The physical, spectral, and analytical data of products are given below. The optical rotations were recorded at Perkin-Elmer 243 digital polarimeter. NMR spectra were recorded at Bruker AMX-400 instrument. Mass spectra and elemental analysis were carried out at Shimadzu QP 5000 GC-MS and Elementar EL-III instruments respectively.

**6-Bromo-1-methyl-cyclohex-1-ene (2a).** B.p.  $62-64^{\circ}C/4.5$  Torr.  $[\alpha]_D^{20}$  +1.5° (c = 2, CHCl<sub>3</sub>). <sup>1</sup>H NMR  $\delta$  ppm = 1.79 (s, 3H), 1.33–1.65 and 1.94–2.23 (m, 6H), 4.63 (s, 1H), 5.55 (br, 1H). <sup>13</sup>C NMR: 134.3, 127.1, 54.7, 33.1, 25.2, 22, 17.4. MS (m/z): 176 (2.5), 174 (2.5), 161 (2), 159 (0.5), 149 (0.5), 147 (1.5), 135 (2), 133 (0.5), 121 (3), 119 (3), 96 (10), 95 (100), 79 (45), 77 (35), 67 (80), 55 (50), 41 (45). Anal. calcd. for C and H: 48.02 and 6.33. Found: 48.31 and 5.77 respectively.

**6-Bromo-1-methyl-4-(1-methylethyl)-cyclohex-1-ene(2b).** B.p. 78–80°C/ 1.5 Torr.  $[\alpha]_D^{20}$  +16° (c = 2, CHCl<sub>3</sub>). <sup>1</sup>H NMR  $\delta$  ppm = 0.86 (d, 6H, J = 3 Hz), 1.80 (s, 3H), 1.13–1.56 and 1.86–2.26 (m, 6H), 4.60 (s, 1H), 5.53 (br, 1H). <sup>13</sup>C NMR: 134.1, 127.3, 55.8, 36.5, 34.4, 31.7, 29, 21.4, 19.7, 19.4. MS (m/z): 218 (2), 216 (2), 203 (0.5), 201 (0.5), 175 (1), 173 (1), 138 (6), 137 (48), 95 (48), 93 (30), 81 (100), 79 (33), 67 (33), 41 (50). Anal. calcd. for C and H: 55.60 and 7.89. Found: 55.61 and 7.20 respectively.

**3-Bromo-2-phenyl-prop-1-ene (2c).** B.p.  $80-82^{\circ}$ C/1.5 Torr. <sup>1</sup>H NMR  $\delta$  ppm = 4.41 (s, 2H), 5.58 (s, 1H), 5.51 (s, 1H), 7.36–7.42 (m, 3H), 7.52–7.54 (m, 2H). <sup>13</sup>C NMR: 144.4, 128.5, 128.3, 127.8, 127.6, 126.2, 126, 117.2, 34.2. MS (*m*/*z*): 198 (22), 196 (22), 117 (100), 115 (75), 103 (8), 102 (6), 91 (30), 77 (10), 58 (35), 51 (22), 39 (18). Anal. calcd. for C and H: 54.85 and 4.60. Found: 54.85 and 4.62 respectively.

**6-Bromo-1-methyl-4-(1-methylethyl)-cyclohex-1-en-5-one (2d).** B.p. 96–98°C/1.5 Torr. <sup>1</sup>H NMR  $\delta$  ppm = 1.28 (d, J = 6.9 Hz, 6H), 2.17 (s, 1H), 2.29 (s, 3H), 1.86–2.05 (m, 2H), 3.18–3.27 (m 1H), 4.93 (br, 1H). <sup>13</sup>C NMR: 152.8, 126.2, 121.5, 52.7, 33.2, 26.8, 22.7, 22.4, 20.8, 20.6. MS

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#### Tertiary-β-bromo Alcohols

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(m/z): 232 (0.5), 230 (0.5), 217 (0.5), 215 (0.5), 204 (1), 202 (1), 190 (6), 188 (6), 152 (3), 151 (12), 135 (9), 121 (1), 109 (12), 107 (3), 82 (100), 69 (6), 54 (15), 41 (28). Anal. calcd. for C and H: 51.96 and 6.54. Found: 51.86 and 6.63 respectively.

**6-Bromo-1,3,3-trimethyl-2-oxabicyclo[2.2.2]-octane (2e).** B.p. 78–80°C/ 0.7 Torr.  $[\alpha]_D^{20}$  +8.6° (c = 3, CHCl<sub>3</sub>). <sup>1</sup>H NMR  $\delta$  ppm = 0.92 (s, 3H), 0.94 (s, 3H), 1.44 (s, 3H), 1.53–1.57 (m, 1H), 1.62–1.67 (m, 2H), 1.72–1.75 (m, 1H), 1.99–2.02 (m, 1H), 2.3–2.35 (m, 1H), 2.51–2.57 (m, 1H), 3.86 (br, 1H). <sup>13</sup>C NMR: 55.9, 56.8, 53.1, 22.8, 22, 21.7, 21.3, 21, 20.4, 19.8. MS (m/z): 234 (3), 232 (3), 219 (2), 217 (2), 191 (20), 189 (24), 153 (55), 135 (10), 109 (20), 95 (45), 82 (25), 71 (60), 55 (40), 43 (100), 41 (95). Anal. calcd. for C and H: 51.52 and 7.35. Found: 51.79 and 7.35 respectively.

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