## BF3•OEt2 PROMOTES FAST, MILD, CLEAN AND REGIOSELECTIVE DEHYDRATION OF TERTIARY ALCOHOLS

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Summary:  $BF_3$ •OEt<sub>2</sub> in methylene chloride at 25°C for 2 hours or less is shown to be effective for easy conversion of tertiary alcohols into the corresponding thermodynamically most stable alkenes.

Attempting to deprotect a tertiary alcohol *t*-butyldimethylsilyl ether,<sup>1</sup> we unexpectedly discovered that boron-trifluoride etherate<sup>2</sup> produced the corresponding alkene with excellent regiocontrol and in good yield (eq 1).<sup>3</sup> Subsequently we have found that 1-3 equivalents of BF<sub>3</sub>•OEt<sub>2</sub> in methylene chloride at 25°C converts also tertiary alcohols themselves into the corresponding alkenes. **These dehydrations are fast, mild, regioselective, and experimentally simple.** This BF<sub>3</sub>•OEt<sub>2</sub> procedure regularly gives cleaner dehydration products usually in higher yields than do established dehydrating agents such as the Burgess reagent,<sup>4</sup> thionyl chloride/triethylamine (a typical E<sub>2</sub> elimination),<sup>5</sup> or *p*-toluenesulfonic acid/benzene (a typical E<sub>1</sub> elimination),<sup>6</sup> and BF<sub>3</sub>•OEt<sub>2</sub> compares favorably also with many other dehydrating agents.<sup>7</sup> Results of this operationally convenient, gram-scale BF<sub>3</sub>•OEt<sub>2</sub> dehydrating procedure with 9 different tertiary alcohols are summarized in Table I.



Alcohol	Products	% Yie BF3·OEt2	eld (ratio of p TsOH/ PhH	roducts) using SOCl <sub>2</sub> / Et <sub>3</sub> N
RОН				
$R = CH_3(CH_2)_{15}$	R, H, R,	<b>90 %</b> ( <b>95:5</b> ) [ 10 min ] <sup>a</sup>	79 % (82:18)	74 % (28:72)
$R = 4-BrC_6H_4CH_2$		75 % (91:9) [2h]	24 % (92:8)	33 % (52:48)
Ph $R = H$	Ph Ph R	92% (99.6:0.4) [1h]	71 % (98:2)	64 % (94:6)
R = Me		<b>89 %</b> ( <b>91:9</b> ) [ 1 h ]	74 % (92:8)	24 % (97:3)
Ph	Ph Ph	85 % (91:9) [1h]	65 % (91:9)	50 % (96:4)
СХон		61 % (90:10) <sup>b</sup> [ 1.5 h ]	28 % (88:12)	18 % (72:28)
		<b>85 %</b> ( <b>85:4:5:6</b> ) <sup>b</sup> [ 30 min ]	42 % (93:2:5:0)	41 % (65:29:0:6)
2 HO 4 H HO 4 H	$\Delta^2$ , $\Delta^3$ , 3-exo CH <sub>2</sub>	<b>100 %</b> ( <b>95:5:0</b> ) [ 20 min ]	76 % (96:4:0)	- (72:26:2)
3β-ОН		100 % (95:5:0) [ 20 min ]	76 % (96:4:0)	_ (54:16:30)

Table I. BF<sub>3</sub>·OEt<sub>2</sub> Dehydration of 3° Alcohols at 25 °C in CH<sub>2</sub>Cl<sub>2</sub>.

a.  $BF_3 \cdot OEt_2$  reaction time. b. Reaction temperature was 0 °C.

A typical experimental procedure is as follows: An oven-dried 100 mL 1-necked round-bottomed flask was charged with 1-methyl-4-phenylcyclohexanol (1.186 g, 6.20 mmol) and methylene chloride (30 mL). The solution was cooled to 0°C and treated with freshly distilled BF<sub>3</sub>•OEt<sub>2</sub> (920  $\mu$ L, 7.50 mmol) via a gas-tight syringe. The reaction mixture was warmed to room temperature, stirred for one hour, and quenched with saturated NaHCO<sub>3</sub> solution (30 mL) at 0°C. The aqueous layer was separated and extracted twice with methylene chloride (20 mL x 2). The combined organic layers were washed with saturated NaCl solution (30 mL), dried over anhydrous MgSO<sub>4</sub>, filtered, and concentrated to afford a mixture of 1-methyl-4-phenylcyclohexane and 1-methylene-4-phenylcyclohexane (1.143 g, 100%) in 99.6:0.4 ratio as determined by analytical glc analysis. Short-path silica gel column chromatography with pentane and subsequent bulb-to-bulb distillation gave 1-methyl-4-phenylcyclohexene (0.983 g, 92%) with NMR characteristics identical to those reported;<sup>8</sup> <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  5.48 (m, 1H), 2.72 (m, 1H), 2.30-1.80 (m, 4H), 1.69 (s, 3H), 1.82-1.60 (m, 2H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  147.29, 133.97, 128.30, 126.88, 125.89, 120.83, 40.04, 33.58, 30.72, 30.07, 23.53.

Control experiments showed that secondary alcohols (e.g. cis- and trans-4-t-butylcyclohexanol) are stable to these BF<sub>3</sub>•OEt<sub>2</sub> reaction conditions. Other control experiments showed that BF<sub>3</sub>•OEt<sub>2</sub> under these conditions isomerized less stable to more stable alkenes (e.g. 1-methylene-4-phenylcyclohexane into 1-methyl-4phenylcyclohexene and 2-methyl-1-octadecene into 2-methyl-2-octadecene).<sup>9</sup> Dehydration and double bond isomerization of the tertiary decalol in Table I regioselectively into the corresponding bis-endocyclic octalin in good yield is noteworthy when compared with literature precedent.<sup>10</sup> The optimal reaction times, ranging from 10 minutes to 2 hours, were determined via tlc analysis of small aliquots of the BF3•OEt2 reaction mixtures; prolonged reaction times and higher reaction temperatures in the BF3. OEt2 reactions caused deterioration of the alkene products probably via carbocation intermediates. The ratios in Table 1 of alkene isomers produced by BF3•OEt2 were similar to the alkene isomer ratios formed by TsOH/benzene via a carbocation pathway, but the yields in the BF3•OEt2 dehydrations were consistently and considerably higher. Both BF3•OEt2 and TsOH/benzene converted axial and equatorial steroidal alcohols into the same ratio of alkenes, in contrast to the SOCl<sub>2</sub>/Et<sub>3</sub>N results (Table I). Neopentylic tertiary alcohols 1-3 as well as tertiary alcohols 4 and 5 that are prone to carbocation rearrangements or alkylation reactions gave unsatisfactory mixtures of products when exposed to BF3•OEt2; although Lewis basic diethyl ether in place of methylene chloride as solvent slowed the dehydration reaction, this ethereal solvent did not prevent skeletal rearrangement, for example, of spirobicyclic alcohol 3.



Despite its very broad appeal as a cheap, readily-available, and easily-handled Lewis acid,<sup>11</sup> surprisingly BF<sub>3</sub>•OEt<sub>2</sub> has not been used previously in a systematic way to convert tertiary alcohols into alkenes.<sup>2,3,12</sup> This report shows that many types of structurally different tertiary alcohols can be dehydrated rapidly, easily, and cleanly using BF<sub>3</sub>•OEt<sub>2</sub>. This simple procedure should be useful in many diverse applications.

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