Boron trifluoride monohydrate, a highly efficient catalyst for thioacetalization [1]

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Boron trifluoride monohydrate, an inexpensive superacid, was found to be an efficient catalyst for thioacetalization.

Keywords: Acid catalysis; boron trifluoride monohydrate; thioacetals

During our studies on fluorination of organic compounds, we needed to prepare a series of 1,3-dithiolanes. 1,3-dithiolanes have often been used as protected carbonyl groups in organic synthesis because of their stability under usual acidic or basic conditions [2]. 1,3-dithiolanes are also useful synthons as carbonyl anion equivalents [3]. Dithiolanes are usually prepared by acid catalyzed condensation of 1,2-ethanedithiol with carbonyl compounds. Various acids have been used, including concentrated HCl, $ZnCl_2$, $BF_3 \cdot Et_2O$, $AlCl_3$, $TiCl_4$, and $BF_3 \cdot 2CH_3CO_2H$, for this transformation [4].

Boron trifluoride monohydrate ($BF_3 \cdot H_2O$) is a nonoxidative strong acid with the acidity comparable to that of 100% sulfuric acid [5]. The applications of this acid in organic synthesis, however, are limited [6,7]. Recently we have found this acid in conjunction with nitric acid or potassium nitrate to be an excellent aromatic nitrating system [8]. Interested in further exploring the utility of boron trifluoride monohydrate in organic synthesis, we now report the highly efficient condensation of 1,2-ethanedithiol with carbonyl compounds catalyzed by boron trifluoride monohydrate.

To a vigorously stirred mixture of carbonyl compound (10 mmol) and 1,2-ethane dithiol (15 mmol) in methylene chloride (20 mL) at 0°C was added 1 mL of $BF_3:OH_2$ through a syringe. The reaction was usually complete in 15 to 30 minutes. After normal aqueous work-up and evaporation of the solvent, products were obtained in nearly quantitatively yields.

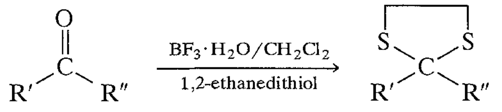
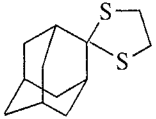
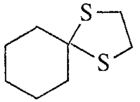
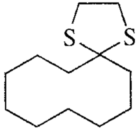
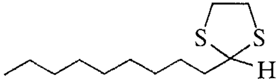
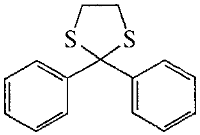
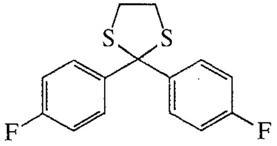
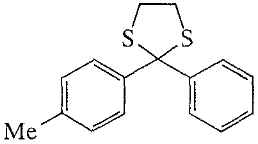
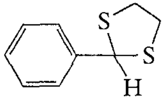
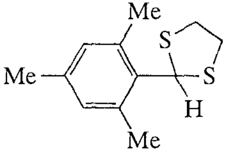
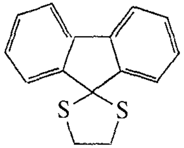
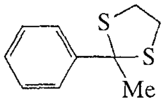


Table 1
Boron trifluoride monohydrate catalyzed thioacetalization

1,3-dithiolane	Yield [a] (%)	m.p.(°C) or b.p. (°C)/Torr.		^{13}C NMR [c] (ppm)	MS (m/e %)
		Found	Reported		
	98	54–55	55–55.5 [9a]	78.1, 42,2, 38.9 36.9, 26.4	226 (M^+, 45.9), 198 (100.0), 166 (26.3) 165 (25.3), 134 (13.8), 133 (76.8)
	90	96/3	107/5 [9b]	68.5, 42.6, 38.1, 25.9, 24.7	174 (M^+, 51.5), 146 (38.5), 131 (100) 114 (15.6), 81 (50.1)
	96 [b]	55–56	–	72.2, 38.7, 38.5, 26.7, 26.1, 24,4, 23.9	230 (M^+, 17.4), 202 (19.1), 187 (4.7) 169 (20.3), 145 (5.2), 131 (100), 118 (21.8), 105 (10.3), 92 (4.6)
	97	80/1	– [4c]	71.6, 43.3, 39.3, 31.9, 26.5, 22.5, 13.9	246 (M^+, 2.5), 185 (1.2), 175 (100) 143 (1.4), 131 (1.9), 119 (6.0) 105 (14.1)
	96 [b]	79/1	–	53.7, 39.2, 38.2, 31.7, 29.4, 29.2, 29.14, 29.09, 22.5, 14.0	232 (M^+, 6.8), 171 (1.1), 119 (2.2) 105 (100), 95 (1.5), 91 (1.4)
	98	103–104	104–105 [4c]	14.6, 128.2, 127.9 127.1, 76.8, 40.2	258 (M^+, 9.2), 230 (43.9), 229 (53.2) 198 (34.1), 197 (17.4), 187 (13.4) 181 (10.1), 165 (97.8), 121 (100), 77 (44.8)
	98 [b]	52–53		161.7 (d, $^1J = 247.8$ Hz), 140.1 (d, $J = 3.2$), 130.0 (d, $J = 8.4$), 114.6 (d, $J = 21.8$), 40.2	294 (M^+, 7.8), 266 (41.4), 265 (41.5) 247 (7.9), 234 (23.8), 201 (84.3) 188 (4.3), 181 (6.1), 171 (5.5) 139 (100), 95 (24.6)

	97	oil	– [9 d]	144.6, 141.6, 136.7, 128.4, 128.0, 128.0, 127.7, 127.0, 76.6, 39.9, 20.8	272 (M^+, 9.2), 244 (33.6), 243 (25.9) 229 (47.7), 212 (63.1), 211 (22.6) 197 (21.1), 179 (100), 178 (43.3) 165 (28.8), 152 (14.7), 135 (81.3) 91 (30.2), 77 (35.1)
	93	110/1	109.5/0.7 [9 c]	140.1, 128.2, 127.7, 56.0, 40.0	182 (M^+, 57.8), 154 (50.6), 153 (86.1) 135 (11.2), 122 (31.5), 121 (100) 105 (9.4), 91 (9.8), 77 (34.8)
	94	53–55	56–58 [4 e]	138.1, 137.2, 130.1, 128.4, 51.5, 40.1, 20.9, 20.8	224 (M^+, 3.0), 209 (0.6), 181 (19.5) 163 (100), 149 (12.5), 148 (24.9) 147 (13.4), 115 (7.8), 91 (7.2), 77 (5.7)
	99	124–125	123.5–124.5 [4 c]	150.4, 138.4, 128.2,128.2 125.1, 119.8, 68.5, 42.2	256 (M^+, 39.9), 228 (61.7), 227 (68.1) 196 (100), 195 (31.1), 165 (17.4) 163 (12.6), 152 (66.4)
	93	131/3	162–163.5/ 11 [9 b]	145.7, 127.8, 126.9, 126.6 68.4, 40.1, 33.7	196 (M^+, 31.6), 181 (70.5), 168 (38.1) 167 (61.9), 149 (6.3), 136 (30.3) 121 (100), 103 (83.0), 91 (12.3), 77 (45.3)

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[a] Isolated yields

[b] Satisfactory elemental analyses were obtained, C ± 0.5, H ± 0.2.

[c] In $CDCl_3$ at room temperature. Chemical shifts referenced to tetramethylsilane signal.

A variety of ketones and aldehydes were investigated (see table 1) and aromatic as well as aliphatic carbonyl compounds worked equally well. In case of aromatic carbonyl compounds, neither electron-withdrawing or electron-donating substituents on the ring did significantly affect the yield. The thioacetalization reaction is exothermic and proceeds very fast. Thus accurate measurement of reaction rates would be difficult under these conditions. It is well established that thioacetalization is an acid catalyzed reaction [4]. The high acidity of $BF_3:H_2O$ certainly enhances the reaction rate. Moreover, $BF_3:H_2O$ can function as a water scavenger further facilitating the dehydration.

In summary, $BF_3 \cdot H_2O$ is a highly efficient acid catalyst for preparation of 1,3-dithiolanes under very mild conditions with nearly quantitative yields. Furthermore, $BF_3 \cdot H_2O$ is inexpensive and can be easily prepared in the laboratory [7]. The presently developed procedure offers a most efficient route to the preparation of 1,3-ditholanes from carbonyl compounds.

All the carbonyl compounds and 1,2-ethanedithol were purchased from Aldrich, and used as such. Boron trifluoride was obtained from Matheson Gas products. $BF_3 \cdot H_2O$ was prepared according to a reported procedure [7].

NMR spectra were run on a Varian Associates Model VXR-200 NMR spectrometer. Mass spectra were obtained on a Finnigan Incos-50 GC-MS instrument. Gas chromatographic analyses were performed on a Varian (model 3700) gas chromatograph using a quartz column coated with DB-5.

TYPICAL METHOD OF PREPARATION OF 1,3-DITHIOLANES

To a vigorously stirred CH_2Cl_2 (20 mL) solution of the carbonyl compound (10 mmol) and 1,2-ethanedithol (15 mmol), 1 mL $BF_3 \cdot H_2O$ (20 mmol) was added dropwise through a syringe over a period of 5 min at 0°C. The reaction mixture was stirred for another 25 min, and quenched with 40 mL of ice water. The quenched mixture was extracted with CH_2Cl_2 (3×30 mL). The combined organic extracts were washed with aq. 10% $NaHCO_3$ solution to remove any acid, and dried over $MgSO_4$ followed by evaporation in a rotary evaporator under high vacuum. The product was further purified, if necessary, by either distillation or recrystalization and subjected to GC-MS and NMR analysis.

Acknowledgement

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