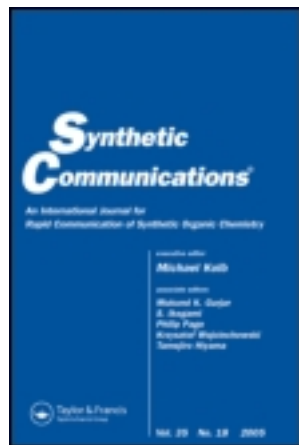


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ABSTRACT

One-pot borontrifluoride etherate promoted transformation of nitriles to esters was achieved by heating in corresponding alcohol as a reactant and solvent.

Key Words: Borontrifluoride; One-pot conversion; Nitriles; Esters; Alcohols.

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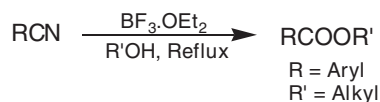
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The extensive uses of $\text{BF}_3 \cdot \text{OEt}_2$ in many organic transformations like acetylation,^[1] alkylation, cyclization,^[2] polymerization,^[3] cleavage of ethers^[4] & epoxides^[5] and dehydration are well known in literature. $\text{BF}_3 \cdot \text{OEt}_2$ catalyzed hydration and condensation of nitriles,^[6] and the conversion of nitrile to ester via hydrolysis to carboxylic acid have been reported in the literature.^[1,7] Using mineral acids in a dry alcohol^[1,7] and polyphosphate esters in methanol^[8] for the transformation of nitriles to esters are known in literature. In this report, we described the usage of $\text{BF}_3 \cdot \text{OEt}_2$ in an alcohol for the direct, simple and clean conversion of nitriles to the variety of corresponding esters (Sch. 1).

While we have been engaged with $\text{BF}_3 \cdot \text{OEt}_2$ catalyzed functional group transformations, the usage of $\text{BF}_3 \cdot \text{OEt}_2$ was found in the formation of esters directly from the corresponding nitriles and alcohols. It was confirmed by conducting the experiments on the reaction of benzonitrile with refluxing ethyl alcohol and water separately in presence of $\text{BF}_3 \cdot \text{OEt}_2$, which lead to ethyl benzoate and benzamide respectively. When we performed the same reaction of benzonitrile in refluxing ethyl alcohol in the absence of $\text{BF}_3 \cdot \text{OEt}_2$ for seven days, we did not observe any change in starting material and it was recovered quantitatively. Apart from the advantage of one-pot conversion of nitriles to esters, this conversion has the possibility of desired ester formation by selecting the appropriate alcohol as reactant and solvent. To generalize these observations, several experiments were conducted by utilizing various substituted aromatic nitriles, and aliphatic alcohols like methanol, ethanol, and *iso*-propanol and the results were tabulated based on some variants (Table 1).

The study was extended to the aliphatic substrate (malononitrile), which is more reactive than the aromatic substrates. To generalize our findings on this conversion, the catalytic studies were done on malononitrile with various alcohols under similar conditions for converting the aliphatic nitrile to aliphatic monoesters and diesters (Sch. 2). For example, malononitrile was heated in refluxing ethanol in presence of $\text{BF}_3 \cdot \text{OEt}_2$ to obtain ethyl cyanoacetate as major and ethyl malonate as minor products. The results of other reactions were tabulated as above (Table 2). Spectral data of all compounds are satisfied as in literature.



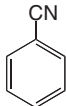
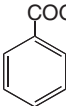
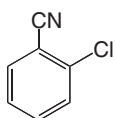
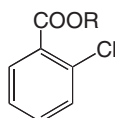
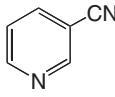
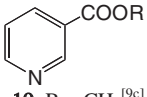
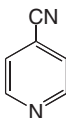
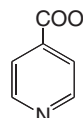
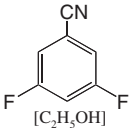
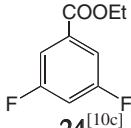
Scheme 1.



Borontrifluoride Etherate

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Table 1.

S. no.	Substrate [solvent]	Product	Time	Ratio	
				Substrate: BF ₃ .OEt ₂	Yield ^a (%)
					
1	[CH ₃ OH]	13 , R = CH ₃ ^[9a]	23 h ^b	1:4.0	82
2	[C ₂ H ₅ OH]	14 , R = C ₂ H ₅ ^[9b]	20 h	1:4.0	91
3	[(CH ₃) ₂ CHOH]	15 , R = ⁱ Pr ^[10a]	62 h	1:4.0	76
					
4	[CH ₃ OH]	16 , R = CH ₃ ^[10b]	6.5d ^b	1:4.0	43
5	[C ₂ H ₅ OH]	17 , R = C ₂ H ₅ ^[10b]	8.0d	1:6.7	67
6	[(CH ₃) ₂ CHOH]	18 , R = ⁱ Pr	23 h	1:6.5	83
					
7	[CH ₃ OH]	19 , R = CH ₃ ^[9c]	7.0d	1:6.0	43
8	[C ₂ H ₅ OH]	20 , R = C ₂ H ₅ ^[9d]	6.0d	1:6.0	67
					
9	[CH ₃ OH]	21 , R = CH ₃ ^[9e]	4.5d	1:4.0	63
10	[C ₂ H ₅ OH]	22 , R = C ₂ H ₅ ^[9f]	5.0d	1:4.0	40
11	[(CH ₃) ₂ CHOH]	23 , R = ⁱ Pr	3.5d	1:4.0	54
					
12	[C ₂ H ₅ OH]	24 ^[10c]	3.6d	1:4.4	54

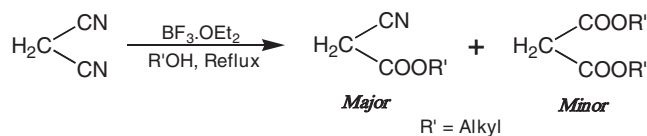
^aIsolated yields.^bd = days; h = hours.

In conclusion, the borontrifluoride etherate complex promoted direct conversion of nitriles to the corresponding esters (alkyl/aryl-alkyl) had been successfully achieved by using excess of an appropriate alcohol. The step-wise process through acids or amides to esters was



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Scheme 2.

Table 2. Reaction of malononitrile and alcohol.

S. no.	Alcohol	$\text{H}_2\text{C} \begin{array}{l} \diagup \text{CN} \\ \diagdown \text{COOR}' \end{array}$ Mono ester ^a	$\text{H}_2\text{C} \begin{array}{l} \diagup \text{COOR}' \\ \diagdown \text{COOR}' \end{array}$ Diester ^b	Time (h)	Ratio
					Substrate: $\text{BF}_3 \cdot \text{OEt}_2$
1	EtOH	90%; R' = Et ^[11a]	4% ^[11b]	24	1:2.1
2	EtOH	100%; R' = Et	Not formed	36	1:1.3
3	MeOH	68%; R' = Me ^[11c]	28% ^[11d]	68	1:2.1
4	<i>n</i> -BuOH	75%; R' = Bu ^[11e]	20% ^[12]	21	1:2.0

^aIsolated yields.

avoided by adopting this direct conversion of nitriles. Malononitrile was selectively converted into monoester (major) and diester (minor) by varying the molarity of $\text{BF}_3 \cdot \text{OEt}_2$ and reaction time (Table 2). The studies for finding a more efficient catalyst for the above transformation and the scope of utilization of this observation i.e., desymmetrization by selective functional group transformation in dinitriles are under progress.

EXPERIMENTAL

General Procedure

In a round bottom flask (50 mL) fitted with a reflux condenser was taken benzonitrile (1 g, 9.71 mmol) in ethanol (10 mL). A freshly distilled $\text{BF}_3 \cdot \text{OEt}_2$ (5.51 g, 38.82 mmol) was introduced into the reaction vessel and then the resulting mixture was refluxed under N_2 atm for 20 h. The solvent was removed under reduced pressure, washed with water (2×15 mL) and extracted with DCM (3×30 mL). DCM layer was dried over anhy. Na_2SO_4 , the solvent was removed in vacuo and the crude product was purified through silica gel column using Petroleum ether–Ethyl acetate (9.8:0.2) as eluent to obtain compound **14** as a colorless liquid.

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Compound 15. $R_f = 0.70$ (EtOAc–Pet.ether, 1:49); IR (Neat, ν_{\max}) cm^{-1} : 1715; $^1\text{H NMR}$ (200 MHz, CDCl_3/TMS) ppm: δ 1.40 (d, $J = 6.75$ Hz, 6H, $-(\text{CH}_3)_2$), 5.25 (p, $J = 6.75$ Hz, 1H, $-\text{CH}-$), 7.50 (d, $J = 6.75$ Hz, 2H, ArH), 7.55 (dd, $J = 6.75$ Hz, 1H, ArH), 7.85 (d, $J = 6.75$ Hz, 2H, ArH); MS (m/e): 164 (M^+).

Compound 18. $R_f = 0.81$ (EtOAc–Pet.ether, 1:4); IR (neat, ν_{\max}) cm^{-1} : 1720; $^1\text{H NMR}$ (400 MHz, CDCl_3/TMS) ppm: δ 1.25 (d, $J = 8.7$ Hz, 6H, $-(\text{CH}_3)_2$), 4.25 (p, $J = 8.7$ Hz, 1H, $-\text{CH}-$), 7.25–7.35 (m, 3H, ArH), 7.65 (d, $J = 8.7$ Hz, 1H, ArH); MS (m/e): 198, 200 (M^+).

Compound 20. $R_f = 0.56$ (EtOAc–Pet.ether, 1:3); IR (Neat, ν_{\max}) cm^{-1} : 1718; $^1\text{H NMR}$ (200 MHz, CDCl_3/TMS) ppm: δ 1.40 (t, $J = 8.1$ Hz, 3H, $\text{COOCH}_2\text{CH}_3$), 4.40 (q, $J = 8.1$ Hz, 2H, $\text{COOCH}_2\text{CH}_3$), 7.40 (dd, $J = 10.8$ Hz, 1H, ArH), 8.30 (d, $J = 10.8$ Hz, 1H, ArH), 8.75 (d, $J = 10.8$ Hz, 1H, ArH), 9.20 (s, 1H, ArH); MS (m/e): 151 (M^+).

Compound 23. $R_f = 0.40$ (EtOAc–Pet.ether, 1:4); IR (Neat, ν_{\max}) cm^{-1} : 1717; $^1\text{H NMR}$ (400 MHz, CDCl_3/TMS) ppm: δ 1.45 (d, $J = 6.6$ Hz, 6H, $-(\text{CH}_3)_2$), 5.30 (p, $J = 6.6$ Hz, 1H, $-\text{CH}-$), 7.85 (d, $J = 8.8$ Hz, 2H, ArH), 8.80 (d, $J = 8.8$ Hz, 2H, ArH); MS (m/e): 165 (M^+).

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