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BF_3-H_2O catalyzed Fries rearrangement of phenolic esters

G. K. Surya Prakash,* Chiradeep Panja, Thomas Mathew, and George A. Olah

Department of Chemistry, Loker Hydrocarbon Research Institute, University of Southern California, 837 Bloom Walk, Los Angeles, CA 90089-1661, USA

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BF_3-H_2O catalyzed Fries rearrangement is reported. Aliphatic and aromatic carboxylic acid esters of phenols react smoothly under mild conditions to provide the corresponding hydroxyketones in high yield, selectivity and purity.

KEY WORDS: BF_3 monohydrate; phenolic esters; Fries rearrangement; hydroxyketones; *para* selectivity.

1. Introduction

Hydroxyarylketones are synthetically and industrially important compounds. Many of them are used in perfumes, pharmaceuticals, paints and varnishes. They are also used in metallurgic and rubber industry. They also serve as important building blocks in organic synthesis. Several methods such as the Friedel-Crafts reaction, the Hoesch and Nencki reaction, Fries reaction etc. are available for the preparation of hydroxyaryl ketones [1]. Among these methods, the Fries rearrangement is the most widely used industrially.

Rearrangement of phenolic esters to *o*- or *p*-hydroxyphenylketones under acidic conditions is known as Fries rearrangement. The *ortho*/*para* ratio depends on various factors, such as temperature, solvent, amount of catalyst, etc. The reaction has been studied extensively and it has been well established that both Lewis and Brønsted acids [2] can promote the reaction with comparable efficiency. Varieties of Lewis acids such as $AlCl_3$, $HgCl_2$, $SnCl_4$, $FeCl_3$, and Brønsted acids such as TsOH, H_3PO_4, TfOH, HF, and Me_3SO_3H have been extensively employed [3]. Use of solid acids, such as Zeolites, Nafion-H and heteropoly acids for the Fries rearrangement have also been documented [4–6]. Extensive studies have been carried out to establish the mechanistic (intra or intermolecular) nature of the reaction [7]. However, no clear mechanistic conclusion can be drawn yet. The Fries rearrangement under photocatalytic conditions (Photo-Fries Rearrangement) [8], as well as the Fries rearrangement of thio and phosphorous esters [9,10] under regular and microwave conditions [11] have also been reported. To date, numerous modified versions of the Fries rearrangement have been patented for commercial purposes [12]. The Fries rearrangement is generally carried out in the presence or absence of a solvent with stoichiometric amount of acid in most cases. Solvents, such as nitrobenzene, dichloromethane, and chlorobenzene are commonly employed. Among the various catalysts mentioned earlier, $AlCl_3$ is the most widely used Lewis acid catalyst. A number of esters having different functional moieties on the acid part and phenolic part have been studied. However, studies have shown that similar to any aromatic electrophilic substitution reaction, the reactivity of the substrate is generally attenuated by the presence of electron withdrawing groups [13].

Recently, we have been exploring the use of BF_3-H_2O as a convenient substitute for expensive or hazardous superacidic systems, such as trifluoromethanesulfonic acid, HF, etc., which are required in many strong acid catalyzed synthetic transformations. During the course of our study, we found that BF_3-H_2O can be used as a strong Brønsted acid system for the Fries rearrangement under certain experimental conditions. Herein, we report the BF_3-H_2O catalyzed Fries rearrangement of phenolic esters.

2. Experimental

Unless otherwise mentioned, all chemicals were purchased from commercial sources. Some of the acid chlorides and esters were prepared following conventional procedures. BF_3-monohydrate was prepared by the method described (*vide infra*). ^1H, ^{13}C and ^{19}F NMR spectra were recorded on Varian NMR spectrometers at 400 MHz and 300 MHz, respectively. ^1H NMR chemical shifts were determined relative to internal tetramethylsilane at δ 0.0 ppm or to the signal of a residual protonated solvent in $CDCl_3$ (δ 7.24 ppm). ^{13}C NMR chemical shifts were determined relative to internal tetramethylsilane at δ 0.0 ppm or to the ^{13}C signal of $CDCl_3$ at δ 77.0 ppm. ^{19}F NMR chemical shifts were

*To whom correspondence should be addressed.
E-mail: gprakash@usc.edu

Table 1
Optimization of conditions for the Fries rearrangement of phenyl benzoate in BF_3-H_2O

Entry	BF_3-H_2O (eqv.)	Temp. (°C)	Time (h)	Conversion (%)	Phenol (%)	Ketone **2** (%)	Ketone **3** (%)
1	15	20	2	89	26	1	62
2	30	20	2	95	15	1	79
3	75	20	3	100	14	1	85
4	50	50	1	100	7	2	91
5	50	75	1	100	5	3	92
6[a]	50	80	1	100	2	3	95

[a] Preheated oil bath was used.

determined relative to internal $CFCl_3$ at δ 0.0 ppm. GC and Mass spectra were recorded on a Thermofinnigan Mass spectrometer.

A Typical procedure for the preparation of BF_3-H_2O (1:1) complex is as follows: BF_3 was passed carefully into a Nalgene bottle containing a weighed amount of distilled water (36 g, 2 mol) with efficient cooling[†] until a desired weight increase was observed. The amount of BF_3 absorbed was 134 g, which corresponds to a ratio of 1:1.01 in BF_3-H_2O. The complex was stored in a refrigerator.

Fries rearrangement was performed in a closed pressure tube (30 mL). The phenolic ester (1 mmol) was placed in a pressure tube to which BF_3-H_2O (50 mmol, 4.30 g) was added and the tube was closed. The tube was immediately immersed into a preheated (80 °C) oil bath and the reaction mixture was stirred at 80 °C for an hour. Then the mixture was cooled to room temperature and poured into ice-water in a 250 mL beaker. The tube was washed with ice-water and dichloromethane and extracted with dichloromethane (4 × 25 mL). The combined organic layer was washed with aqueous sodium bicarbonate solution (2 × 15 mL) followed by brine solution (1 × 15 mL). After drying over anhydrous sodium sulfate, the solvent was removed under reduced pressure to obtain the corresponding hydroxyketones in analytically pure form (by NMR). The isomeric ratio was determined using NMR and GCMS. The products were characterized by comparing their spectral data with those of the authentic samples. Spectral data of the products are listed subsequently. Some compounds were only partially soluble in $CDCl_3$ and a mixture of $CDCl_3$ and DMSO-D_6 were used in those cases for NMR analyses.

2.1. 1-(4-Hydroxyphenyl)ethanone (Table 2, entry 1)

^{1}H NMR: δ 2.59 (s, 3H), 6.96 (d, J = 8.97 Hz, 2H), 7.91 (d, J = 8.97 Hz, 2H), 8.45 (brs, 1H); ^{13}C NMR: δ 26.2, 115.6, 129.2, 131.3, 161.7, 199.1; MS (EI), m/z 135.7 ($M^{\cdot+}$), 93.8 ($M^{\cdot+}$-$COCH_3$).

[†]Caution! Highly exothermic, dry ice-acetone bath is recommended for cooling, when excessive heat is generated.

2.2. 1-(4-Hydroxyphenyl)-propan-1-one (Table 2, entry 2)

^{1}H NMR: δ 1.19(t, J = 7.32 Hz, 3H), 2.93 (q, J = 7.32 Hz, 2H), 6.88 (d, J = 8.98 Hz, 2H), 7.86 (d, J = 8.97 Hz, 2H), 9.63 (s, 1H); ^{13}C NMR: δ 8.2, 30.8, 115.0, 128.4, 130.0, 135.8, 161.6, 199.2; MS (EI), m/z 150.6 ($M^{\cdot+}$), 120.2 ($M^{\cdot+}$-CH_2CH_3).

2.3. 1-(4-Hydroxyphenyl)-2, 2-dimethylpropan-1-one (Table 2, entry 3)

^{1}H NMR: δ 1.05 (s, 9H), 2.84 (s, 2H), 6.98 (d, J = 8.79 Hz, 2H), 7.91 (d, J = 8.79 Hz, 2H), 8.70 (brs, 1H); ^{13}C NMR: δ 30.2, 31.8, 49.9, 115.5, 130.5, 131.4, 161.5, 201.7; MS (EI), m/z 192.5 ($M^{\cdot+}$), 135.2 ($M^{\cdot+}$-$(CH_3)_3C$), 120.2 ($M^{\cdot+}$- $(CH_3)_3CCH_2$).

2.4. 1-(4-Hydroxyphenyl)-2-methylpropan-1-one (Table 2, entry 4)

^{1}H NMR: δ 1.22 (d, J = 6.77 Hz, 6H), 3.57 (m,1H), 7.00 (d, J = 8.61 Hz, 2H), 7.93 (d, J = 8.62 Hz, 2H), 8.60 (brs, 1H); ^{13}C NMR: δ 19.4, 35.0, 115.7, 129.5, 131.2, 161.4, 205.7; MS (EI), m/z 163.4 ($M^{\cdot+}$), 120.2 ($M^{\cdot+}$- $(CH_3)_2CH$).

2.5. 1-(4-Hydroxyphenyl)-3-methylbutan-1-one (Table 2, entry 5)

^{1}H NMR: δ 0.99 (d, J = 6.59 Hz, 6H), 2.27 (m, 1H), 2.81 (d, J = 6.96 Hz, 2H), 6.97 (d, J = 8.98 Hz, 2H), 7.92 (d, J = 8.79 Hz, 2H), 8.16 (brs, 1H); ^{13}C NMR: δ 22.7, 25.8, 47.2, 115.6, 129.5, 131.1, 161.4, 201.2; MS (EI), m/z 177.6 ($M^{\cdot+}$), 135.3 ($M^{\cdot+}$-$(CH_3)_2CH$), 120.3 ($M^{\cdot+}$- $(CH_3)_2CHCH_2$).

2.6. 1-(4-Hydroxyphenyl)-2-phenylethanone (Table 2, entry 6)

^{1}H NMR: δ 4.20 (s, 3H), 6.85 (d, J = 8.60 Hz, 2H), 7.22–7.32 (m, 5H), 7.89 (d, J = 8.61 Hz, 2H), 9.80 (brs, 1H); ^{13}C NMR: δ 45.0, 115.6, 126.7, 128.3, 128.6, 129.5, 131.1, 135.3, 162.4, 196.2; MS (EI), m/z 211.1 ($M^{\cdot+}$), 120.6 ($M^{\cdot+}$- $PhCH_2$).

Table 2
Results for the Fries rearrangement of alkyl carboxylic acid esters of phenols

Entry	R_1	R_2	Yield (%)	Ortho/paraisomer ratio
1	CH_3	H	85	1:36.9
2	CH_3CH_2	H	93	1:8.0
3	$(CH_3)_3CCH_2$	H	96	1:11.6
4	$(CH_3)_2CH$	H	90	1:14.1
5	$(CH_3)_2CHCH_2$	H	91	1:21.0
6	Ph–CH_2	H	97	1:19.0
7	Ph–CH_2CH_2	H	82	1:1.7
8	Ph–$CH_2CH_2CH_2$	H	79	ortho only
9	Ph–$CH_2CH_2CH_2CH_2$	H	90	1:17.0
10	Tolyl-CH_2	H	99	1:24.0
11	CH_3	4-CH_3–Ph	81	ortho only

2.7. 1-(2-Hydroxyphenyl)-4-phenylbutan-1-one (Table 2, entry 8)

^{1}H NMR: δ 2.11 (quin, J = 6.31 Hz, 2H), 2.66 (t, J = 6.5 Hz, 2H), 2.94 (t, J = 6.14 Hz, 2H), 6.86–6.91(m, 3H), 7.19–7.25 (m, 3H), 7.27–7.31 (m, 1H), 7.46 (ddd, J = 7.51 Hz, J = 7.51 Hz, J = 1.47 Hz, 1H), 8.04 (dd, J = 7.88 Hz, J = 1.44 Hz, 1H); ^{13}C NMR: δ 23.1, 29.5, 39.0, 115.3, 120.2, 126.6, 127.2, 128.8, 129.5, 132.3, 133.7, 144.7, 156.0, 199.6; MS (EI), m/z, 146.2 ($M^{\cdot+}$-PhOH).

2.8. 1-(4-Hydroxyphenyl)-5-phenylpentan-1-one (Table 2, entry 9)

^{1}H NMR: δ 1.60–1.80 (m,4h), 2.63 (t, J = 7.32 Hz, 2H), 2.89 (t, J = 7.15 Hz, 2H), 6.88 (d, J = 8.79 Hz, 2H), 7.10–7.19 (m, 3H), 7.21–7.30 (m, 2H), 7.83 (d, J =8.79 Hz, 2H), 9.60 (s, 1H); ^{13}C NMR: δ 23.9, 30.8, 35.4, 37.5, 115.1, 125.3, 127.9, 128.0, 128.5, 130.2, 141.9, 161.6, 198.8; MS (EI), m/z 254.4 ($M^{\cdot+}$), 135.3 ($M^{\cdot+}$-Ph$(CH_2)_3$), 120.3 ($M^{\cdot+}$- $(CH_2)_4$Ph).

2.9. 1-(4-Hydroxyphenyl)-2-p-tolylethanone (Table 2, entry 10)

^{1}H NMR: δ 2.29 (s, 3H), 4.14 (s, 2H), 6.86 (d, J = 8.97 Hz, 2H), 7.08–7.14 (m, 4H), 7.89 (d, J = 8.79 Hz, 2H), 9.59 (s, 1H); ^{13}C NMR: δ 20.7, 44.4, 115.2, 128.1, 129.0, 129.2, 130.9, 131.7, 135.9, 161.9, 196.4; MS (EI), m/z 225.3 ($M^{\cdot+}$), 120.3 ($M^{\cdot+}$-CH_3PhCH_2).

2.10. 1-(2-Hydroxy-4-methylphenyl)ethanone (Table 2, entry 11)

^{1}H NMR: δ 2.28 (s, 3H), 2.58 (s, 3H), 6.86 (d, J = 8.42 Hz, 1H), 7.24–7.27 (m, 1H), 7.48 (d, J = 1.65 Hz, 1H), 12.12 (s, 1H); ^{13}C NMR: δ 20.3, 26.4, 118.0, 119.2, 128.0, 130.4, 137.5, 160.0, 204.6; MS (EI), m/z 151.8 ($M^{\cdot+}$), 134.7 ($M^{\cdot+}$-OH), 106.3 ($M^{\cdot+}$-$COCH_3$).

2.11. 1-(4-Hydroxyphenyl)-1-phenylmethanone (Table 3, entry 1)

^{1}H NMR: δ 6.92 (d, J = 8.79 Hz, 2H), 7.43–747 (m, 2H), 7.52–7.54 (m, 1H), 7.70–7.74 (m, 4H), 9.60 (brs, 1H); ^{13}C NMR: δ 114.7, 127.5, 128.0, 128.9, 131.1, 132.2, 137.8, 161.4, 195.0; MS (EI), m/z 197.0 ($M^{\cdot+}$), 120.2 ($M^{\cdot+}$-Ph).

2.12. 1-(4-Hydroxy-phenyl)-1-(2-methylphenyl) methanone (Table 3, entry 2)

^{1}H NMR: δ 2.28 (s, 3H), 6.87 (d, J = 8.79 Hz, 2H), 7.19–7.27 (m, 3H), 7.33–7.37 (m, 1H), 7.71 (d, J = 8.79 Hz), 8.79 (brs, 1H); ^{13}C NMR: δ 19.7, 115.6, 125.2, 127.8, 129.2, 130.1, 130.8, 133.2, 135.9, 138.6, 162.1, 199.5; MS (EI), m/z 212.3 ($M^{\cdot+}$), 119.9 ($M^{\cdot+}$-PhCH_3).

2.13. 1-(4-Hydroxyphenyl)-1- (4-methylphenyl) methanone (Table 3, entry 3)

^{1}H NMR: δ 2.43 (s, 3H), 6.90 (d, J = 8.97 Hz, 2H), 7.26 (d, J = 8.42 Hz, 2H), 7.64 (d, J = 8.06 Hz, 2H), 7.71 (d, J = 8.97 Hz, 2H), 9.61 (brs, 1H); ^{13}C NMR: δ 21.2, 114.9, 128.4, 128.7, 129.5, 132.3, 135.4, 142.0, 161.4, 195.1; MS (EI), m/z 212.5 ($M^{\cdot+}$), 195.6 ($M^{\cdot+}$-OH), 120.3 ($M^{\cdot+}$-PhCH_3).

2.14. 1-(4-Hydroxyphenyl)-1-(4-methoxyphenyl) methanone(Table 3, entry 4)

^{1}H NMR: δ 3.88 (s, 3H), 6.90 (d, J = 8.61 Hz, 2H), 6.96 (d, J = 8.79 Hz, 2H), 7.69 (d, J = 8.61 Hz, 2H), 7.76 (d, J = 8.97 Hz, 2H), 9.60 (brs, 1H); ^{13}C NMR: δ 54.9, 112.9, 114.7, 128.7, 130.3, 131.5, 131.9, 161.0, 162.1, 193.9; MS (EI), m/z 228.0 ($M^{\cdot+}$), 134 ($M^{\cdot+}$-PhOH), 120.2 ($M^{\cdot+}$-PhOCH_3).

2.15. 1-(4-Fluorophenyl)-1-(4-hydroxyphenyl) methanone (Table 3, entry 5)

^{1}H NMR: δ 6.91 (d, J = 8.79 Hz, 2H), 7.16 (t, J = 8.79 Hz, 2H), 7.69 (d, J = 8.79 Hz, 2H), 7.76 (dd, J = 6.50 Hz, J = 8.98 Hz, 2H), 9.90 (s, 1H); ^{13}C NMR: δ .114.4 (d, $^2J_{CF}$ = 21.36 Hz), 114.6, 127.6, 131.3 (d, $^3J_{CF}$ = 9.15 Hz), 131.8, 133.9 (d, $^4J_{CF}$ = 3.06 Hz), 161.3, 163.9 (d, $^1J_{CF}$ = 253.53 Hz), 193.1; ^{19}F NMR: δ −107.8 (m); MS (EI), m/z 215.4 ($M^{\cdot+}$), 120.3 ($M^{\cdot+}$- PhF).

2.16. 1-(4-Chlorophenyl)-1-(4-hydroxyphenyl) methanone (Table 3, entry 6)

^{1}H NMR: δ 6.91 (d, J = 8.97 Hz, 2H), 7.44 (d, J = 8.33 Hz, 2H), 7.67–7.71 (m, 4H), 9.78 (s, 1H); ^{13}C NMR: δ 115.1, 127.9, 128.0, 130.7, 132.3, 136.5, 137.5, 161.8, 193.9; MS (EI), m/z 232.5 ($M^{\cdot+}$), 195.6 ($M^{\cdot+}$-Cl), 120.3 ($M^{\cdot+}$-PhCl).

Table 3
Results for Fries rearrangement of aromatic carboxylic acid esters of phenols

Entry	R_1	R_2	Yield (%)	*Ortho*/*para* isomer ratio
1	Ph	H	81	1:31.7
2	2-Me–Ph	H	94	1:32.3
3	4-Me–Ph	H	95	1:62.7
4	4-MeO–Ph	H	98	1:52.7
5	4-F–Ph	H	71	1:15.8
6	4-Cl–Ph	H	90	1:9.2
7	3-Cl–Ph	H	88	1:26.8
8	3-Br–Ph	H	68	1:9.0
9	1-Naphthyl	H	90	1:42.7
10	2-Naphthyl	H	93	1:19.0

2.17. 1-(3-Chlorophenyl)-1-(4-hydroxyphenyl)methanone (Table 3, entry 7)

^{1}H NMR: δ 6.92 (d, J = 8.60 Hz, 2H), 7.41 (t, J = 7.95 Hz, 1H), 7.50–7.52 (m, 1H), 7.58 (td, J = 7.51 Hz, J = 1.65 Hz, 1H), 7.68 (t, J = 1.65 Hz, 1H), 7.71 (d, J = 8.61 Hz, 2H), 9.80 (brs, 1H); ^{13}C NMR: δ 115.0, 127.2, 127.6, 128.8, 129.1, 131.0, 132.3, 133.7, 139.8, 161.9, 193.4; MS (EI), m/z 232.4($M^{\cdot+}$), 195.9 ($M^{\cdot+}$-Cl), 120.0 ($M^{\cdot+}$-PhCl).

2.18. 1-(4-Bromophenyl)-1-(4-hydroxyphenyl)methanone (Table 3, entry 8)

^{1}H NMR: δ 6.91 (d, J = 8.59 Hz, 2H), 7.61 (s, 4H), 7.70 (d, J = 6.57 Hz, 2H), 9.78 (s, 1H); ^{13}C NMR: δ 115.1, 126.1, 127.9, 130.8, 131.0, 132.3, 136.9, 161.9, 194.0; MS (EI), m/z 278.2 ($M^{\cdot+}$ + 2), 196.4 ($M^{\cdot+}$-Br), 120.7 ($M^{\cdot+}$- PhBr).

2.19. 1-(4-Hydroxyphenyl)-1-(1-naphthyl)methanone (Table 3, entry 9)

^{1}H NMR: δ 6.87 (d, J = 8.79 Hz, 2H), 7.42–7.51 (m, 4H), 7.75 (d, J = 8.60 Hz, 2H), 8.86 (d, J = 7.69 Hz, 1H), 7.92 (d, J = 7.88 Hz, 1H), 7.96 (d, J = 8.24 Hz, 1H), 9.65 (s, 1H); ^{13}C NMR: δ 115.0, 124.0, 125.1, 125.8, 126.0, 126.4, 127.9, 129.1, 129.9, 130.2, 132.5, 133.0, 136.7, 162.2, 196.3; MS (EI), m/z 247.6 ($M^{\cdot+}$), 230.3 ($M^{\cdot+}$-OH), 126.6 ($M^{\cdot+}$-Ph(CO)OH).

2.20. 1-(4-Hydroxyphenyl)-1-(2-naphthyl)methanone (Table 3, entry 10)

^{1}H NMR: δ 6.94 (d, J = 8.70 Hz, 2H), 7.54–7.62 (m, 2H), 7.78 (d, J = 8.70 Hz, 2H) 7.83 (dd, J = 8.61 Hz, J = 1.65 Hz, 1H), 7.90–7.95 (m, 3H), 8.20 (s, 1H), 9.91 (s, 1H); ^{13}C NMR: δ 114.9, 126.9, 127.2, 127.2, 127.9, 128.3, 129.9, 131.3, 131.9, 133.9, 134.9, 161.3, 194.5; MS (EI), m/z 248.4 ($M^{\cdot+}$), 154.4 ($M^{\cdot+}$-(PhOH), 120.5 ($M^{\cdot+}$-Naphthyl).

3. Results and discussion

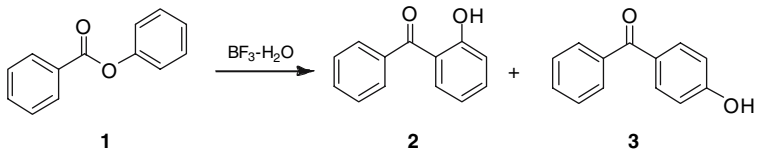
Meerwein [14] first indicated that BF_3 can be used as a Lewis acid catalyst for the Fries rearrangement and would be a suitable substitute for $AlCl_3$. However, no such study was carried out with it. Other studies showed that the reaction was sluggish when BF_3 alone was used as the acid catalyst. Later, complexes of BF_3, such as the BF_3-acetic acid, acetate or etherate have been used for the Fries rearrangement, especially for the acetate esters of naphthols [15]. In such cases, the acidic medium behaves as a Lewis acid and the reaction proceeds through the complexation of the boron atom of BF_3 with the oxygen atom of the esters. We have now explored the utility of BF_3-H_2O complex as a strong and effective Brønsted acid catalyst for the Fries rearrangement of phenolic esters.

Two water complexes are known with BF_3; the monohydrate (BF_3-H_2O) and the dihydrate (BF_3-$2H_2O$). The dihydrate complex is very stable and its acidity is close to that of 100% nitric acid. On the other hand, BF_3-H_2O 1:1 complex is a stronger acid system with the acidity close to that of 100% sulfuric acid ($-H_o \sim 12$) [16]. BF_3 monohydrate complex is a colorless fuming liquid with a density of 1.8 g/mL and melting point of 6.2 °C. Its non-oxidizing property, strong acidity and modest cost compared to that of trifluoromethanesulfonic acid, prompted us to study various acid catalyzed synthetic transformations with it [17].

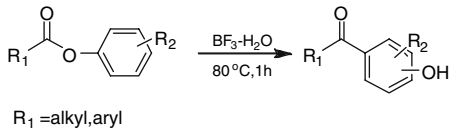
We performed first the Fries rearrangement of phenyl benzoate (neat) in BF_3-H_2O, at room temperature. We observed the formation of both *para* and *ortho*-hydroxybenzophenone along with a significant amount of phenol, under the reaction conditions. Subsequently, we optimized the reaction conditions (Scheme 1 and Table 1) and obtained the hydroxybenzophenone in high yield with high *para*-selectivity.

Using the optimized reaction conditions, we subsequently carried out the Fries rearrangement of various phenyl esters (Scheme 2). The corresponding *para*-hydroxyketones were obtained in high yields in the majority of the cases. Both alkyl and aromatic carboxylic acid esters of phenols undergo Fries rearrangement equally well, under the reaction conditions and the results are summarized in Tables 2 and 3. Interestingly, during the course of our study, we observed that the *para* selectivity decreases from phenylacetyl esters to phenylbutyric esters (Table 2, entry 6 to 9). Surprisingly, 4-phenylbutyrate gave the corresponding *ortho* product, exclusively. However, with further increase in chain length, the *para* selectivity increased. Thus, 5-phenylvaleryl ester provided the *para* derivative as the major product (Table 2, entry 9).

Next, we expanded our methodology for esters with substituted phenyl groups. However, the reaction in these cases was found to be highly substrate dependent. Most of the benzoate derivatives gave only hydrolysis



Scheme 1. Fries rearrangement of phenyl benzoate in BF_3-H_2O.



Scheme 2. Fries rearrangement of carboxylic acid esters of phenols.

product, phenols and no Fries rearrangement was observed under the reaction conditions. Some of the acetate esters, especially the halogen substituted phenyl esters of acetic acid, afforded the Fries rearrangement products, but a significant amount of the corresponding phenols were also formed. However, in the case of 4-methylphenyl acetate (Table 2, entry 11), phenol formation was minimum and the corresponding Fries product was obtained in good yield. We also found that the *para* selectivity is relatively higher when there are electron donating groups present in the carboxylic acid part of the phenolic esters studied (Table 3, entry 3, 4 and 9).

The significant feature of the present method is that there is no need for further purification of the product. Although in some cases, negligible amount of phenol was formed, but it could be removed by keeping the product under vacuum (by sublimation) for several hours, affording the desired product in high yield and purity.

We also explored the use of BF_3-$2H_2O$ for the Fries rearrangement of phenyl acetate under similar conditions. In this case, we observed the formation of hydroxyacetophenone and a large amount of phenol. Further, the selectivity towards the *para* isomer decreased. Even after several attempts, we were unable to find optimal conditions, wherein exclusive Fries rearrangement would take place. Possibly, in BF_3-$2H_2O$, due to its lower acidity, partial hydrolysis of the ester is preferred over the rearrangement path. Due to our interest in recycling BF_3-H_2O, we attempted the direct extraction of the product from the acidic media avoiding an aqueous workup, but the product was obtained in lower yield (40%). Possibly, the hydroxyketones being good Lewis bases, form complexes with BF_3 and excess water is needed to break them up and liberate the free ketones. We also scaled up the reaction of phenyl acetate by 10-fold without any significant decrease in the product yield and selectivity (80% yield and 98% *para* selectivity). It is also noteworthy to mention that the yields, selectivity and the amount of phenol formation depend on the temperature and the quality of the BF_3-H_2O used. The oil bath should be preheated to 80 °C and the pressure tube should be immersed into it immediately after the addition of the acid. Freshly prepared BF_3-H_2O always gave the best result in terms of selectivity, yield and minimum phenol formation.

4. Conclusion

In summary, a simple and useful method for the Fries rearrangement has been found using BF_3-H_2O. Aromatic and alkyl carboxylic acid esters of phenols react equally well to produce the corresponding hydroxy ketones in good to excellent chemical yields and high *para* selectivity. Simplicity, clean reaction, use of inexpensive acid, solvent free conditions and lack of elaborate purification processes (products are pure by NMR), make the presently developed Fries reaction more useful, economic and convenient.

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