Catalytic Friedel–Crafts acylation of aromatic ethers using SmI_3

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10% mol SmI_3 catalysed the Friedel–Crafts acylation of aromatic ethers by acyl chlorides in acetonitrile with the yields of 48–82%. Reactions of various substituted aromatic ethers with acyl chloride were studied. The structures of compounds were established by IR and ^{1}H NMR. The main product obtained with anisole is the *para*-substituted compound with only a trace (<5 %) of *meta* and *ortho* substituted products. This shows that the acylation of aromatic ethers is highly regioselective in the presence of SmI_3, a pattern repeated with the other aromatic ethers used.

Keywords: Friedel–Crafts acylation, aromatic ethers, samarium triiodide

Since samarium diiodide was introduced into organic synthesis by Kagan,[1] there has been a widespread interest in the use of samarium reagents in organic synthesis.[2] Many new reactions have been found involving various samarium reagents such as samarium metal,[3-4] samarium diiodide[5-6] and triiodide,[7] and samarium/auxiliary systems.[8-9] For example, Cocellon and Huerta reported that α,β-unsaturated ketones can be obtained by reaction of α-chloro-β-hydroxy ketones catalysed by SmI_3.[7] In our group, we have reported the use of samarium triiodide.[10-15] Friedel–Crafts acylation is still a fundamental and useful reaction for introducing functional substituents onto aromatic rings.[16] Present industrial practice requires stoichiometric amounts of a soluble Lewis acid (*e.g.* $AlCl_3$) or strong mineral acids (*e.g.* HF), which results in a substantial amount of waste and in corrosion problems.[17] Though there are some metal triflate catalysts which can reduce these problems,[18] they are usually high cost and not available on an industrial scale. Herein we report another catalyst SmI_3 for this reaction which is easily obtained and is insensitive to water.

Using catalytic amounts of SmI_3(10%, mol) in the Friedel–Crafts acylation of aromatic ethers good yields of product are obtained (Table 1). Reaction steps are outlined in Scheme 1. The required aromatic ethers were made from the corresponding phenols via methylation with dimethyl sulfate and sodium hydroxide.

All of the acylated products are known compounds and the structures of the compounds were characterised by IR and ^{1}H NMR. We found that the main product of entry **2a** (and **2b** or **2c**) was the *para* position product with only a trace (<5 %) of *meta* and *ortho* position product in the presence of 10% mol SmI_3. The much higher yield of *para* position product than *ortho* position product was because of the size of methoxy group. The other aromatic ethers in Table 1 showed similar selectivity. Thus, SmI_3 gives highly regeoselective Friedel–Crafts acylation reactions. None of the solvents employed in the reaction were distilled and thus it is show that the catalyst is not as sensitive to water as $AlCl_3$. The coordination percentage of SmI_3 to ketones is low, so we consider that the reaction mechanism of aromatic ethers with acyl chloride in the presence of SmI_3 is similar to the mechanism for acylation catalysed by bismuth(III) triflate.[19] Compared to other "clean" Friedel–Crafts acylation catalysts (e.g. $Hf(OTf)_4$ and $Bi(OTf)_3$), SmI_3 is easy to prepare, insensitive to water and cheap. The advantages of this method are the rapid reactions, simple operation, and mild and neutral conditions.

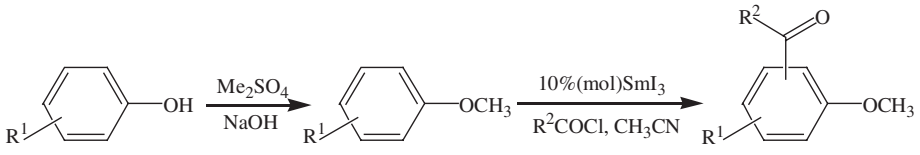
Table 1 Products and yields of reaction of acyl chloride with aromatic ethers

Entry	R^1	R^2	Temperature reaction time / °C	/h	Yield /%[a]
2a	H	CH_3	r.t.	3	82
2b	H	CH_3CH_2	r.t.	3	78
2c	H	Ph	45	4	61
2d	*m*-OCH_3	CH_3	r.t.	2	75
2e	*m*-OCH_3	CH_3CH_2	r.t.	2	70
2f	*m*-OCH_3	Ph	45	5	60
2g[b]	*p*-OCH_3	CH_3	r.t.	3	59
2h[b]	*p*-OCH_3	CH_3CH_2	r.t.	3	60
2i[b]	*p*-OCH_3	Ph	45	5	51
2j	*m*-CH_3	CH_3	r.t.	3	65
2k	*m*-CH_3	CH_3CH_2	r.t.	3	56
2l	*m*-CH_3	Ph	45	5	54
2m	*m*-Cl	CH_3	50	4	48

[a]Isolated yields based on aromatic ethers.
[b]Where R^2 group sited at the *o*-position.

Experimental

Chemicals were purchased from Fluka and Aldrich. Thin layer chromatography (TLC) on commercial plates of silica gel GF_{254} was used to monitor the progress of the reactions. Yields refer to isolated products after purification. Melting point were determined on a YANACO melting point apparatus and are uncorrected. Infrared (IR) spectra were taken on a Nicolet 230 FT-IR spectrophotometer. ^{1}H NMR spectra were recorded in $CDCl_3$ on a Bruker Avance 500 DMX spectrometer using TMS as internal standard.



1a-1e **2a-2m** yield: 48-82%

R^1= H, *m*-OCH_3, *p*-OCH_3, *m*-CH_3, *m*-Cl
R^2= CH_3, CH_3CH_2, Ph

Scheme 1

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Typical procedure for acylation

Samarium powder (0.15 g, 1.0 mmol) was placed in a three-necked round bottom flask with a magnetic stirring bar. Acetonitrile (10 ml) and iodine (0.38g, 3.0mmol) were added. After the mixture was stirred for 3 hours at room temperature, the substrate aromatic ether (10 mmol) was added and then the acyl chloride (10 mmol) was dropped into it. The resulting solution was stirred for 2–5 h, and the reaction was quenched with 2–3 ml of water. Then another 20 ml of water was added. The mixture was extracted with diethyl ether (2 × 30 ml). The ethereal extracts were combined and washed with saturated NaCl solution (15 ml), and dried over Na_2SO_4. After filtration and removal of the solvents, the crude product was purified by column chromatography (silica gel) using petroleum ether–ethyl acetate as eluent.

1-(4-Methoxyphenyl)ethanone **(2a)**: M.p.: 36–38 °C (lit.[20a], 36–39 °C); IR υ_{max}(KBr)/cm^{-1}: 3005, 2937, 1674, 1601, 1258cm^{-1}; ^{1}HNMR($CDCl_3$)δ_H:2.54(s,3H),3.86(s,3H),6.92(d,2H,*J*=7.2Hz),7.93 (d, 2H, *J* =7.3 Hz).

1-(4-Methoxyphenyl)propan-1-one **(2b)**: M.p.: 27–28 °C(lit.[20b], 27–29 °C); IR υ_{max}(KBr)/cm^{-1}: 3006, 2976, 2937, 1683, 1602, 1259cm^{-1}; ^{1}H NMR ($CDCl_3$) δ_H: 1.21(t, 3H, *J*=7.2 Hz), 2.92–2.98 (m, 2H), 3.86 (s, 3H), 6.93 (d, 2H, *J* =7.1 Hz), 7.95 (d, 2H, *J* =7.3 Hz).

(4-Methoxyphenyl)phenylmethanone **(2c)**: M.p.: 60–63 °C(lit.[20c], 58–63 °C); IR υ_{max}(KBr)/cm^{-1}: 3008, 2934, 1652, 1599, 1258; ^{1}H NMR ($CDCl_3$) δ_H: 3.88 (s, 3H), 6.96 (d, 2H, *J* =8.0 Hz), 7.47 (t, 2H, *J*=7.5 Hz), 7.56 (d, 1H, *J* =7.2 Hz), 7.76 (d, 2H, *J* =8.1 Hz), 7.83 (d, 2H, *J* =9.0 Hz).

1-(2,4-Dimethoxyphenyl)ethanone **(2d)**: M.p.: 39–40 °C(lit.[20d], 39–41 °C); IR υ_{max}(KBr)/cm^{-1}: 3002, 2943, 1663, 1599, 1258; ^{1}H NMR ($CDCl_3$) δ_H: 2.57 (s, 3H), 3.85 (s, 3H), 3.89 (s, 3H), 6.45 (s, 1H), 6.52 (d, 1H, *J* =8.3 Hz), 7.83 (d, 1H, *J* =9.2 Hz).

1-(2,4-Dimethoxyphenyl)propan-1-one **(2e)**: M.p.: 67–68 °C(lit.[20e], 67 °C); IR υ_{max}(KBr)/cm^{-1}: 3007, 2972, 2938, 1666, 1600, 1255; ^{1}H NMR ($CDCl_3$) δ_H: 1.16 (t, 3H, *J*=7.3 Hz), 2.94–2.98 (m, 2H), 3.85 (s, 3H), 3.88 (s, 3H), 6.45 (s, 1H), 6.52 (d, 1H, *J* =9.3 Hz), 7.81 (d, 1H, *J* =9.1 Hz).

(2,4-Dimethoxyphenyl)phenylmethanone **(2f)**: M.p.: 86–87 °C(lit.[20f], 87–88 °C); IR υ_{max}(KBr)/cm^{-1}: 3004, 2940, 1657, 1603, 1275; ^{1}H NMR ($CDCl_3$) δ_H: 3.70 (s, 3H), 3.87 (s, 3H), 6.50–6.56 (m, 2H), 7.38–7.43 (m, 3H), 7.50–7.52 (m, 1H), 7.77 (d, 2H, *J* = 6.5 Hz).

1-(2,5-Dimethoxyphenyl)ethanone **(2g)**: Oil(lit.[20g]); IR υ_{max}(film)/cm^{-1}: 3003, 2994, 2944, 1673, 1608, 1258; ^{1}H NMR ($CDCl_3$) δ_H: 2.61 (s, 3H), 3.79 (s, 3H), 3.87 (s, 3H), 6.91 (d, 1H, *J* =9.2 Hz), 7.03 (d, 1H, *J* =9.1 Hz), 7.29 (s, 1H).

1-(2,5-Dimethoxyphenyl)propan-1-one **(2h)**: Oil(lit.[20h]); IR υ_{max} (film)/cm^{-1}: 3008, 2999, 2938, 1674, 1609, 1277; ^{1}H NMR ($CDCl_3$) δ_H: 1.16 (t, 3H, *J*=7.2 Hz), 2.98–3.02 (m, 2H), 3.79 (s, 3H), 3.85 (s, 3H), 6.90 (d, 1H, *J* =9.3 Hz), 7.00 (d, 1H, *J* =9.2 Hz), 7.24 (s, 1H).

(2,5-Dimethoxyphenyl)phenylmethanone **(2i)**: M.p.: 50–51 °C(lit.[20i], 51 °C); IR υ_{max}(KBr)/cm^{-1}: 3005, 2939, 1661, 1599, 1272; ^{1}H NMR ($CDCl_3$) δ_H: 3.79 (s, 3H), 3.86 (s, 3H), 6.50–6.56 (m, 2H), 7.39–7.44 (m, 3H), 7.49–7.50 (m, 1H), 7.76 (d, 2H, *J* =6.5 Hz).

1-(4-Methoxy-2-methylphenyl)ethanone **(2j)**: Oil (lit.[20j], 12 °C); IR υ_{max}(film)/cm^{-1}: 3001, 2927, 1673, 1603, 1248; ^{1}H NMR ($CDCl_3$) δ_H: 2.54 (s, 3H), 2.56 (s, 3H), 3.83 (s, 3H), 6.74 (s, 1H), 6.76 (d, 1H, *J* =6.3 Hz), 7.75 (d, 1H, *J* =8.2 Hz).

1-(4-Methoxy-2-methylphenyl)propan-1-one **(2k)**: M.p.: 42–43 °C(lit.[20k], 43 °C); IR υ_{max}(KBr)/cm^{-1}: 3002, 2974, 2937, 1678, 1604, 1249; ^{1}H NMR ($CDCl_3$) δ_H: 1.18 (t, 3H, *J*=7.3 Hz), 2.55 (s, 3H), 2.88-2.93 (m, 2H), 3.84 (s, 3H), 6.74 (s, 1H), 6.75 (d, 1H, *J* =6.4 Hz), 7.73 (d, 1H, *J* =9.2 Hz).

(4-Methoxy-2-methylphenyl)phenylmethanone **(2l)**: Oil(lit.[20l]); IR υ_{max}(film)/cm^{-1}: 3001, 1655, 1603, 1273; ^{1}H NMR ($CDCl_3$) δ_H: 2.42 (s, 3H), 3.86 (s, 3H), 6.74 (d, 1H, *J* =11.1 Hz), 6.83 (s, 1H), 7.34 (d, 1H, *J* =9.4 Hz), 7.45 (t, 2H, *J*=7.6 Hz), 7.57 (t, 1H, *J*=7.5 Hz), 7.77 (d, 2H, *J* =7.3 Hz).

1-(2-chloro-4-methylphenyl)ethanone **(2m)**: Oil(lit.[20m]); IR υ_{max} (film)/cm^{-1}: 3005, 2941, 1687, 1598, 1251; ^{1}H NMR ($CDCl_3$) δ_H: 2.64 (s, 3H), 3.85 (s, 3H), 6.84 (d, 1H, *J* =9.3 Hz), 6.93 (s, 1H), 7.68 (d, 1H, *J* =9.1 Hz).

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