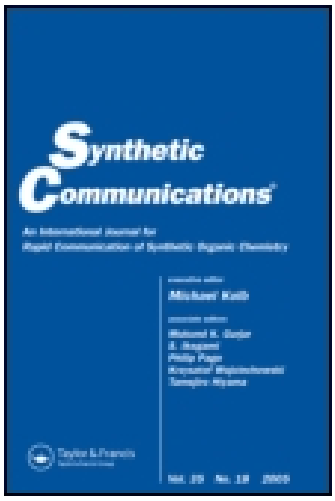

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Catalytic Friedel-Crafts Acylation of Alkoxy Benzenes by Ferric Hydrogensulfate

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Catalytic Friedel–Crafts Acylation of Alkoxy Benzenes by Ferric Hydrogensulfate

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ABSTRACT

Friedel–Crafts acylation of alkoxy benzenes is achieved efficiently by reaction with aliphatic acid anhydrides in the presence of catalytic amounts of ferric hydrogensulfate, $Fe(HSO_4)_3$, in nitromethane.

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Alkyl benzenes and aryl halides, as well as aromatic anhydrides, remain intact under these conditions.

Key Words: Friedel-Crafts; Acylation; Ferric hydrogensulfate; Catalysis; Alkoxy benzenes.

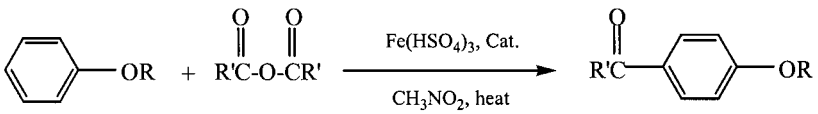
Friedel–Crafts acylation is one of the most important protocols for bringing about the formation of carbon–carbon bonds between aromatic rings and aliphatic moieties.[1] The traditional methods generally involve the use of stoichiometric amounts of aluminum chloride or sulfuric acid.[2] Various other Lewis acids have been used intensively.[3] Many of the classic catalysts such as metallic halides and Bronsted acids cause serious environmental problems and are corrosive.[4–9] Some of them suffer from unavailability, instability or hygroscopicity. Among the new reported reagents for Friedel–Crafts acylation are graphite,[10] zeolites,[11] activated zinc,[12] zirconium sulfate,[13] bismuth trifluoromethansulfonate,[14] and titanium chloride.[15] Recently the acylation reaction was also carried out in the absence of both solvent and catalyst.[16,17]

So, the development of heterogeneous solid acid catalysts to replace the use of strongly acidic, homogeneous, corrosive, and polluting reagents can be considered extensively.

We have already reported the application of iron(III) salts in the formation of carbon–nitrogen and carbon–oxygen bonds in organic compounds.[18–22] Herein we report a selective method for acylation of alkoxy benzenes with aliphatic acid anhydrides in the presence of 20 mol% of ferric ion as $Fe(HSO_4)_3$ in nitromethane (Sch. 1).

As shown in the Table 1, the catalytic acylation of alkoxy benzenes proceeded well with high position selectivity for the formation of *para*-acylated products in good yields. Among the common organic solvents that have been used for Friedel–Crafts acylation, we found that nitromethane is the solvent of choice for our reactions.

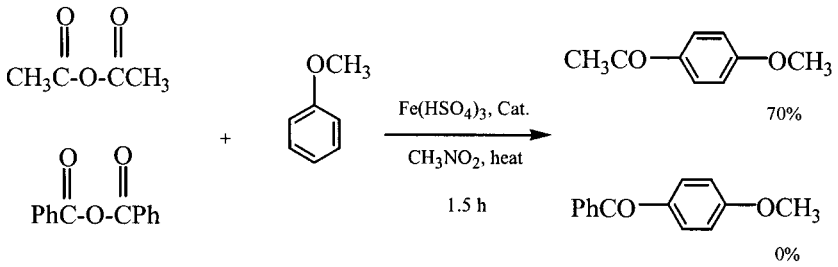
We also observed that the aromatic acid anhydrides react sluggishly under the same conditions. Therefore the competitive reaction between acetic anhydride and benzoic anhydride with anisole was studied and a high degree of chemoselectivity was observed (Sch. 2).



Scheme 1.

Table 1. Friedel–Crafts acylation of alkoxy benzenes by aliphatic anhydrides in the presence of $Fe(HSO_4)_3$.

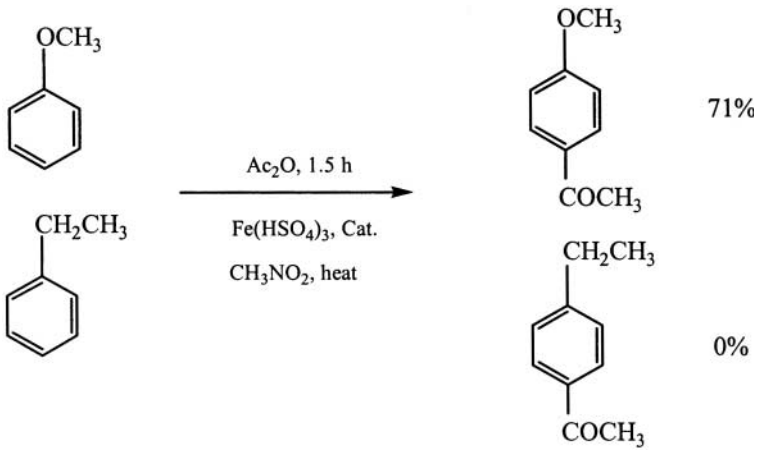
Entry	R	R'	Time (h)	$Fe(HSO_4)_3$/sub. (mole ratio)	Yield (%)
1	$-CH_3$	$-CH_3$	1.5	0.2	71
2	$-CH_2CH_3$	$-CH_3$	2.5	0.2	74
3	$-CH_2(CH_2)_2CH_3$	$-CH_3$	3.5	0.2	73
4	$-CH_2CH(CH_3)_2$	$-CH_3$	5	0.2	69
5	$-CH_2(CH_2)_4CH_3$	$-CH_3$	4	0.2	70
6	$-CH_3$	$-CH_2CH_3$	1.5	0.2	70
7	$-CH_2CH_3$	$-CH_2CH_3$	2.5	0.2	72
8	$-CH_2(CH_2)_2CH_3$	$-CH_2CH_3$	3	0.2	74
9	$-CH_2CH(CH_3)_2$	$-CH_2CH_3$	4.5	0.2	75
10	$-CH_2(CH_2)_4CH_3$	$-CH_2CH_3$	3.5	0.2	73



Scheme 2.

This method also permits us to conduct the selective acylation of alkoxy benzenes in the presence of the less reactive aromatic compounds such as arenes and aryl halides. For example ethylbenzene remained untouched in the competitive reaction with anisole in the presence of acetic anhydride and 20 mol% of the catalyst (Sch. 3).

In conclusion, ferric hydrogensulfate is an inexpensive, non-toxic, stable, efficient, and heterogeneous catalyst for the selective acylation of alkoxy benzenes. Although ferric chloride can also be used for this purpose, its hygroscopic nature limits its applications in the laboratory.[23] $Fe(HSO_4)_3$ is proposed as a very good successor for $FeCl_3$ in other organic reactions such as alcoholysis and hydrolysis of epoxides,[18] Beckmann rearrangement,[19] etherification, and transetherification reactions,[20,22] Biginelli reaction,[24] etc.



Scheme 3.

EXPERIMENTAL

Products are known compounds and were characterized by comparison of their spectral data (^{1}H NMR, IR) and physical properties with those reported in the literature. ^{1}H NMR spectra were run on a Bruker Avance 200 MHz spectrometer. IR spectra were obtained by a Shimadzu 470 spectrophotometer. Progresses of the reactions were followed by TLC using silica gel Polygrams SIL G/UV 254 Sheets. Melting points were determined in open capillaries with a Gallen-Kamp melting point apparatus and are corrected. All yields refer to isolated products.

General Procedure for the Acylation of Alkoxy Benzenes

Ferric hydrogensulfate (0.21 g, 0.6 mmol) was added to a solution of alkoxy benzene (3 mmol) and acid anhydride (6 mmol) in nitromethane (7 mL). The mixture was stirred magnetically at 75–80°C for the appropriate period of time (Table 1). The progress of the reaction was monitored by TLC (eluent: *n*-hexane/diethyl ether: 2/1). Then nitromethane was evaporated under reduced pressure and a solution of $NaHCO_3$ (5%, 20 mL) was added. The aqueous mixture was extracted with diethyl ether (3×20 mL). The organic layer was dried (Na_2SO_4) and concentrated. Final purification on a short silica gel column afforded the desired products in 69–75% yield.

Spectral and Physical Data of the Products

Entry 1. IR (KBr), ν (cm^{-1}): 3060 (w), 3000 (w), 2960 (m), 1665 (s), 1600 (s), 1470 (m), 1250 (s), 1020 (s), 830 (s); ^{1}H NMR ($CDCl_3$), δ (ppm): 7.9 (2H, d), 6.9 (2H, d), 3.8 (3H, s), 2.6 (3H, s); m.p. = 35°C (lit.[25] = 37°C), m.p. of semicarbazone derivative = 195–197°C (lit.[25] = 197–198°C).

Entry 2. IR (KBr), ν (cm^{-1}): 3050 (w), 2980 (m), 2910 (w), 1665 (s), 1600 (s), 1475 (m), 1250 (s), 1030 (m), 845 (m); ^{1}H NMR ($CDCl_3$), δ (ppm): 7.9 (2H, d), 6.9 (2H, d), 4.0 (2H, q), 2.6 (3H, s), 1.3 (3H, t); m.p. = 34°C (lit.[25] = 36–37°C), m.p. of semicarbazone derivative 178–180°C (lit.[25] = 179–180°C).

Entry 3. IR (neat), ν (cm^{-1}): 3060 (w), 2950 (s), 1675 (s), 1600 (s), 1470 (m), 1250 (s), 1020 (m), 830 (s); ^{1}H NMR ($CDCl_3$), δ (ppm): 7.9 (2H, d), 6.8 (2H, d), 4.0 (2H, t), 2.6 (3H, s), 0.9–1.5 (7H, m); m.p. = 23°C (lit.[26] = 22°C), m.p. of oxime derivative = 83°C (lit.[26] = 86°C).

Entry 4. IR (neat), ν (cm^{-1}): 3050 (w), 2950 (s), 1678 (s), 1600 (s), 1470 (m), 1250 (s), 1020 (m), 830 (m); ^{1}H NMR ($CDCl_3$), δ (ppm): 7.8 (2H, d), 6.8 (2H, d), 3.7 (2H, d), 2.6 (3H, s), 2.0 (1H, m), 1.2 (6H, d); m.p. of oxime derivative = 105–106°C (lit.[27] = 107°C).

Entry 5. IR (neat), ν (cm^{-1}): 3050 (w), 2940 (s), 1678 (s), 1600 (s), 1470 (m), 1250 (s), 1030 (m); ^{1}H NMR ($CDCl_3$), δ (ppm): 7.8 (2H, d), 6.8 (2H, d), 4.0 (2H, t), 2.5 (3H, s), 0.8–1.7 (11H, m); m.p. of oxime derivative = 77°C (lit.[27] = 78°C).

Entry 6. IR (neat), ν (cm^{-1}): 3050 (w), 2950 (s), 1675 (s), 1600 (s), 1470 (m), 1255 (s), 1220 (s), 1025 (s), 950 (m), 700 (s); ^{1}H NMR ($CDCl_3$), δ (ppm): 7.9 (2H, d), 6.9 (2H, d), 3.8 (3H, s), 2.9 (2H, q), 1.2 (3H, t); m.p. 25–27°C (lit.[25] = 26–27°C), m.p. of semicarbazone derivative = 170–172°C (lit.[25] = 171–172°C).

Entry 7. IR (neat), ν (cm^{-1}): 3050 (w), 2980 (s), 2910 (s), 1678 (s), 1600 (s), 1475 (w), 1250 (s), 1220 (s), 800 (m); ^{1}H NMR ($CDCl_3$), δ (ppm): 7.8 (2H, d), 6.9 (2H, d), 4.0 (2H, q), 3.0 (2H, q), 0.9–1.7 (6H, m); m.p. = 28–30°C (lit.[25] = 29–30°C), m.p. of semicarbazone derivative = 182°C (lit.[25] = 181–183°C).

Entry 8. IR (neat), ν (cm^{-1}): 3050 (w), 2950 (s), 2910 (s), 1680 (s), 1600 (s), 1460 (s), 1250 (s), 1220 (s), 950 (m), 795 (m); ^{1}H NMR ($CDCl_3$), δ (ppm): 7.8 (2H, d), 6.8 (2H, d), 4.0 (2H, t), 3.0 (2H, q), 0.9–1.8 (10H, m); m.p. = 27–29°C (lit.[28] = 28°C), m.p. of oxime derivative = 77°C (lit.[28] = 79°C).

Entry 9. IR (KBr), ν (cm^{-1}): 3050 (w), 2950 (s), 2910 (s), 1673 (s), 1600 (s), 1472 (m), 1255 (s), 1230 (s), 1020 (s), 795 (s); ^{1}H NMR ($CDCl_3$), δ (ppm): 7.9 (2H, d), 6.9 (2H, d), 3.8 (2H, d), 3.0 (2H, q), 2.1 (1H, m), 0.8–1.5 (9H, m); m.p. = 44°C, m.p. of 2,4-dinitrophenylhydrazone derivative = 155–157°C.

Entry 10. IR (neat), ν (cm^{-1}): 3050 (w), 2930 (s), 1675 (s), 1600 (s), 1460 (m), 1250 (s), 1220 (s), 795 (m); ^1H NMR ($CDCl_3$), δ (ppm): 7.8 (2H, d), 6.8 (2H, d), 3.9 (2H, t), 2.9 (2H, q), 0.7–1.6 (14H, m); m.p. of 2,4-dinitrophenylhydrazone derivative = 161–163°C.

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