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Fe-exchanged montmorillonite K10—the first heterogeneous catalyst for acylation of sulfonamides with carboxylic acid anhydrides

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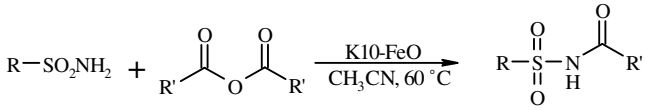
Abstract—Fe-exchanged montmorillonite K10 catalyzes a highly efficient reaction between sterically and electronically diverse sulfonamides and carboxylic acid anhydrides to furnish *N*-acylsulfonamides in excellent yield and high selectivity. The catalyst can also be reused several times.

In drug synthesis, the *N*-acyl sulfonamide moiety has emerged as an important feature for biological activity. Several recently developed drugs, including therapeutic agents for Alzheimer's disease,[1] inhibitors for tRNA synthetase as antibacterial agents[2] and prostaglandin Fla sulfonamides for the potential treatment of osteoporosis,[3] incorporate this moiety. In addition, *N*-acyl-*N*-(2,3,4,5,6-pentafluorophenyl)methane sulfonamides function as chemoselective *N*-acylating reagents.[4]

The majority of reports describe the preparation of the *N*-acyl derivatives using basic reaction media. For instance, the target compounds have been obtained by coupling sulfonamides with acid chlorides or anhydrides in the presence of trialkylamines or pyridine,[4,5] or alkali hydroxides.[6] Another approach utilizes carboxylic acids along with coupling agents like EDC, DCC or carbonyl diimidazole,[2,3] the by-product of which must subsequently be removed from the reaction mixture. Morisawa et al. has used concd H_2SO_4 in the carboxylic acid anhydride itself taken as a solvent; whereas Martin et al. has used concd H_2SO_4 in acetonitrile.[7]

In recent years, the use of solid acidic catalysts, such as clays and zeolites, has received considerable attention in different areas of organic synthesis, because of their environmental compatibility, reusability, greater selectivity, operational simplicity, nontoxicity, noncorrosiveness, low cost and ease of isolation. In particular, clay catalysts make a reaction convenient, more economic and environmentally benign. They act as both Brønsted and Lewis acids in their natural and ion-exchanged forms.[8] We have recently reported the high activity of Fe-exchanged montmorillonite clays for the Friedel–Crafts benzylation of arenes with benzyl chlorides,[9a,b,c] the Beckmann rearrangement[9d] and nitrile formation.[9e]

The present paper describes a selective and highly efficient procedure for the synthesis of *N*-acyl sulfonamides using an inexpensive and reusable Fe-exchanged montmorillonite K10 catalyst (K10-FeO) (Scheme 1).



R = CH_3, C_6H_5, *p*-$CH_3C_6H_4$, *p*-$MeOC_6H_4$, *p*-ClC_6H_4
R' = CH_3, C_6H_5, CF_3

Scheme 1. *N*-acylation of sulfonamides with carboxylic acid anhydrides.

Keywords: Fe-exchanged montmorillonite; Sulfonamides; Carboxylic acid anhydrides.

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The catalyst was prepared by treating Mont. K10 clay with anhyd $FeCl_3$ in acetonitrile solution as described earlier.[9a] The catalyst was activated at 120 °C for 5 h prior to use.

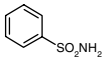
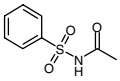
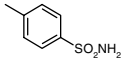
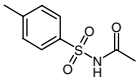
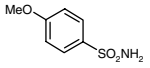
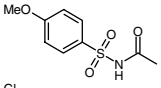
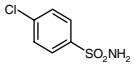
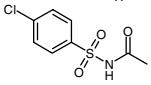
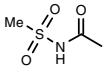
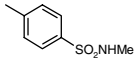
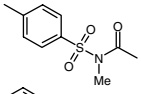
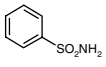
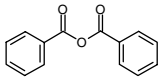
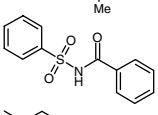
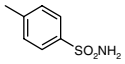
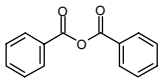
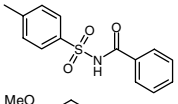
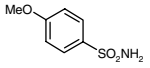
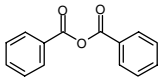
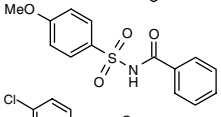
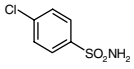
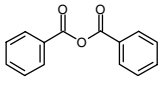
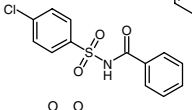
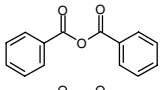
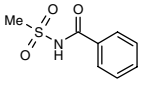
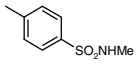
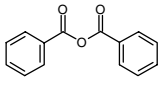
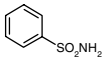
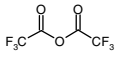
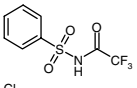
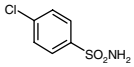
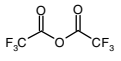
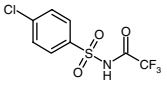
The reaction of benzenesulfonamide with acetic anhydride was carried out in different solvents in the presence of K10-FeO (Table 1). Based on this, acetonitrile was selected as the solvent for further study. These results can be attributed to the ability of the solvent to stabilize the acylium intermediate.[7] The reaction was carried out in CH_3CN in the presence of different Fe-based catalysts viz. K10-FeO, K10-FeA,[9a] K10-FePLS,[9c] Fe-PILC[10] and also K10. K10-FeO was superior to all the other Fe-based heterogeneous catalysts tested. It should be noted that a blank reaction without any catalyst gave no product even after 5 h under identical conditions. Thus, it was observed that K10-FeO was the best catalyst for the reaction. Using this catalyst, different sulfonamides, primary as well as secondary were reacted with three

Table 1. *N*-Acylation of benzenesulfonamide with acetic anhydride in different solvents using K10-FeO catalyst

Entry	Solvent	Time (min)	Yields (%)[a]
1	Acetonitrile	15	92
2	Ethyl acetate	30	88
3	Tetrahydrofuran	45	94
4	Chloroform	45	90

[a] Isolated yield.

Table 2. *N*-Acylation of arene sulfonamides with different acid anhydrides in acetonitrile in the presence of K10-FeO[a]

Entry	Sulfonamide **1**	Carboxylic acid anhydride **2**	*N*-Acylsulfonamide[b] **3**	Time (min)	Yield[c] (%)
a				15	92
b				15	95
c				15	91
d				5	98
e	$MeSO_2NH_2$			15	82
f				15	92
g				120	74
h				120	72
i				120	67
j				120	78
k	$MeSO_2NH_2$			120	62
l			No reaction	120	—
m				30	62
n				30	66

[a] Sulfonamide: 5 mmol; carboxylic acid anhydride: 5 mmol; catalyst: 0.5 g; CH_3CN: 5 mL.
[b] All products were characterized by ^1H NMR and IR spectroscopy.
[c] Isolated and unoptimized yield.

anhydrides viz. acetic anhydride, benzoic anhydride and trifluoroacetic anhydride (Table 2).[11,12] Acetic anhydride was found to be more reactive than trifluoroacetic anhydride and benzoic anhydride. The reactions proceeded smoothly with acetic anhydride, whereas the reactions with benzoic anhydride took longer times. The reaction of *N*-methyl-*p*-toluenesulfonamide with benzoic anhydride (Table 2, entry l) did not proceed even after 2 h. This may be due to unfavourable steric and electronic effects of both the sulfonamide and benzoic anhydride.

Recyclability of the catalyst, K10-FeO, was also studied. After each cycle the used catalyst was filtered and activated at 120 °C before using for the next cycle. The activity of the catalyst was unaffected even after five cycles.

In summary, we have demonstrated that K10-FeO is a superior heterogeneous acidic catalyst for the *N*-acylation of primary and secondary sulfonamides with carboxylic anhydrides. The procedure has the advantages of mild reaction conditions, high yields of products, cleaner reactions with greater selectivity, short reaction times, operational simplicity and recyclability, which makes it useful and attractive for the synthesis of *N*-acylated sulfonamide derivatives.

Acknowledgements

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References and notes

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10. Fe-pillared bentonite clay (Fe-PILC) was prepared as reported in Rightor, E. G.; Tzou, M. S.; Pinnavaia, T. J. *J. Catal.* **1991**, *130*, 29–40.
11. *Typical experimental procedure*: A mixture of benzenesulfonamide **1a** (5 mmol), acetic anhydride **2a** (5 mmol) and K10-FeO (0.5 g) in acetonitrile (5 mL) was stirred at 60 °C for an appropriate time (Table 2). After complete conversion, as indicated by TLC, the catalyst was filtered off and water (10–15 mL) was added dropwise to precipitate the product. The resultant mixture was stirred for 10–15 min. The solid was filtered-off and purified by column chromatography on silica gel (Merck, 60–120 mesh, EtOAc–hexane, 3:7) to afford the pure product **3a**.
12. All the new products obtained in this study were characterized by ^{1}H NMR and IR.
N-Acetyl benzenesulfonamide ***3a***: Solid: mp 122–124 °C, IR (KBr): 3127, 2915, 1704, 1472, 1356, 1245, 1169, 861 cm^{-1}, ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.08$ (s, 3H), 7.54 (t, $J = 7.2$ Hz, 2H), 7.66 (t, $J = 6$ Hz, 1H), 8.06 (d, $J = 6$ Hz, 2H), 8.95 (br s, 1H, NH). Anal. Calcd for $C_8H_9NSO_3$: C, 48.23; H, 4.55; N, 7.03; S, 16.09. Found: C, 48.35; H, 4.57; N, 7.10; S, 16.01.
N-Acetyl-p-toluenesulfonamide ***3b***: Solid: mp 138–140 °C, IR (KBr): 3264, 1726, 1504, 1445, 1337, 1269, 1160, 1026 cm^{-1}, ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.07$ (s, 3H), 2.45 (s, 3H), 7.35 (d, $J = 7.8$ Hz, 2H), 7.94 (d, $J = 8.4$ Hz, 2H), 8.2 (br s, 1H, NH). Anal. Calcd for $C_9H_{11}NSO_3$: C, 50.69; H, 5.20; N, 6.57; S, 15.04. Found: C, 50.51; H, 5.23; N, 6.66; S, 14.98.
N-Acetyl-p-chlorobenzenesulfonamide ***3d***: Solid: mp 192–194 °C, IR (KBr): 3291, 3069, 1701, 1459, 1426, 1341, 1183, 1064 cm^{-1}, ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.07$ (s, 3H), 7.54 (d, $J = 6.9$ Hz, 2H), 8.0 (d, $J = 8.7$ Hz, 2H), 8.2 (br s, 1H, NH). Anal. Calcd for $C_8H_8ClNSO_3$: C, 41.12; H, 3.45; Cl, 15.17; N, 5.99; S, 13.72. Found: C, 41.24; H, 3.47; Cl, 15.23; N, 6.1; S, 13.67.
N-Benzoyl-p-toluenesulfonamide ***3h***: Solid: mp 147–149 °C, IR (KBr): 3121, 2905, 1699, 1474, 1429, 1357, 1239, 1166, 1090, 860 cm^{-1}, ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.44$ (s, 3H), 7.35 (d, $J = 8.4$ Hz, 2H), 7.43 (t, $J = 7.8$ Hz, 2H), 7.55 (t, $J = 7.5$ Hz, 1H), 7.8 (d, $J = 7.2$ Hz, 2H), 8.04 (d, $J = 6.9$ Hz, 2H), 9.22 (br s, 1H, NH). Anal. Calcd for $C_{14}H_{13}NSO_3$: C, 61.08; H, 4.76; N, 5.09; S, 11.65. Found: C, 60.86; H, 4.77; N, 5.14; S, 11.58.
N-Benzoyl-p-chlorobenzenesulfonamide ***3j***: Solid: mp 185–186 °C, IR (KBr): 3246, 2939, 1780, 1475, 1370, 1308, 1237, 1166, 892 cm^{-1}, ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.5$ (m, 5H), 7.78 (d, $J = 7.2$ Hz, 2H), 8.1 (d, $J = 7.8$ Hz, 2H), 8.94 (br s, 1H, NH). Anal. Calcd for $C_{13}H_{10}ClNSO_3$: C, 52.8; H, 3.41; Cl, 11.99; N, 4.74; S, 10.84. Found: C, 52.62; H, 3.42; Cl, 12.13; N, 4.78; S, 10.94.