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Catalytic activity of magnetic Fe_3O_4@Diatomite earth and acetic acid for the N-acylation of sulfonamides

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ABSTRACT

The Brønsted and Lewis acidic promoted N-acylation of sulfonamides with acetic anhydride or benzoyl chloride has been achieved using glacial acetic acid and magnetic Fe_3O_4@Diatomite earth. Use of acetic acid as solvent omits the need for organic bases and permits the isolation of products by filtration and precipitation. Additionally, the magnetic composite Fe_3O_4@Diatomite acts as a conjugate proton super acid, enabling the acylation of sulfonamide compounds.

N-Acyl sulfonamides are best known as bacteriostatic and antimalarial agents[1] and are also present in a range of drugs possessing various pharmacological activities. Acylated sulfonamides are found in several recently developed therapeutic agents for Alzheimer's disease,[2] t-RNA synthesis inhibition,[3] antagonists of Angiotensin II,[4] prostaglandin Fla sulfonamides which may have use in the treatment of osteoporosis and Luekotriene D4-receptors.[5,6] The *N*-acyl sulfonamide group has shown significant potential for use in biological applications.[7–9] They are suitable carboxylic acid replacements and have been used as enzyme inhibitors due to their acidity and resistance to chemical and enzymatic hydrolysis.[10] Generally, *N*-acyl sulfonamides are synthesized by the acylation of easily accessible primary sulfonamides[11–13] using acid anhydrides, esters or acid chlorides in basic reaction media using trialkylamines, pyridine,[14,15] alkali hydroxides[16] or other bases.[17] The N-acylation of sulfonamides can also be performed under acidic conditions. For example, concentrated H_2SO_4 in acetonitrile has been used to promote the N-acylation of sulfonamides.[18] However, the use of highly acidic catalysts has potential problems relating to the corrosive acid waste of which handling presents undesirable economic and environmental issues and raises a number of health and safety issues.

Several Lewis acids, such as $BF_3{\cdot}Et_2O$, $ZnCl_2$, $MoCl_5$, $TiCl_4$, B$(C_6F_5)_3$, Sc$(OTf)_3$ and I_2, have been used to catalyze the N-acylation of sulfonamides.[19] Additionally, catalytic systems have been developed using solid Lewis acids, such as mesoporous aluminosilicas,[20,21] nanoclay,[22] zeolites and resin.[23] The use of porous materials such as zeolites is often limited by their pore size, which prevent larger molecules from reaching the active sites. Hence, there is still need for new catalysts which can overcome this problem. An ideal catalyst would act in a heterogeneous manner, be chemically and thermally stable, and easily available. Recently, researchers have focused their efforts on the application of metal or metal oxide nanoparticles as novel catalysts due to their high catalytic activities and improved selectivities.[24,25] Although nanocatalysts have several advantages over conventional catalyst systems, the isolation and recovery of these are difficult. To overcome this problem, the use of magnetically recoverable nanocatalysts which can be easily separated from reaction mixtures using an external magnetic field is of significant interest.[26] Amongst catalysts derived from heavy or rare metals, those featuring iron benefit from its high abundance and consequent lost cost. Hence, iron based catalysts, especially magnetic Fe_3O_4, have experienced increased use as metal-based reaction promoters, especially those that can be applied in catalytic amounts and/or are recyclable.[27,28]

Recently, attention has been focused on the utilization of mixed Lewis and Brønsted acids catalysts which can act as conjugate proton super acids.[29] In this research, magnetic Fe_3O_4@Diatomite earth composite, prepared by an in situ co-precipitation method with the assistance of ultrasound irradiation, was used as an efficient and easy separable catalyst for N-acylation and was compared with the catalytic activity of acetic acid (Scheme 1).

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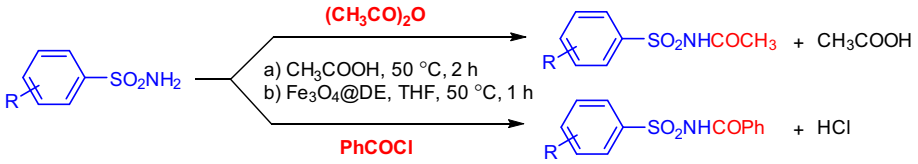
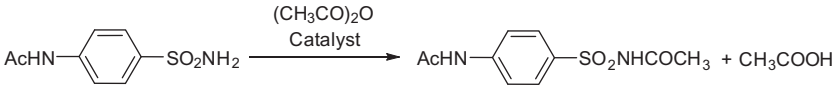
0040-4039/



Scheme 1. N-acylation of sulfonamides with acetic anhydride or benzoyl chloride.

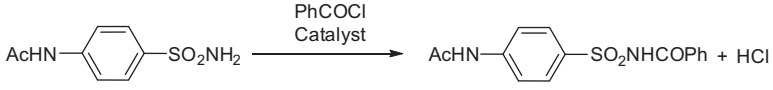
Table 1
N-acylation of *N*-(4-sulfamoylphenyl)acetamide with acetic anhydride using different catalysts[a]



Entry	Catalyst	Time (h)	*T* (°C)	Yield[b] (%)
1	—	8	rt	–
2	$FeCl_3{\cdot}6H_2O$	8	rt	Trace
3	Fe_2O_3	8	rt	Trace
4	Fe_3O_4	8	rt	53
5	$CoFe_2O_4$	8	rt	45
6	Diatomaceous Earth (DE)	8	rt	63
7	$CoFe_2O_4$@DE	8	rt	65
8	Fe_3O_4@DE	8	rt	78
9	Fe_3O_4@DE	2	rt	71
10	Fe_3O_4@DE	2	50	95
11	Fe_3O_4@DE	1	50	93

[a] Reactions conditions: THF (10 mL), sulfonamide (0.86 g, 4 mmol, 1 equiv), acetic anhydride (0.41 g, 4 mmol, 1 equiv), catalyst (3 mol %).
[b] Isolated yield.

Table 2
N-acylation of *N*-(4-sulfamoylphenyl)acetamide with benzoyl chloride using different catalysts[a]



Entry	Catalyst	Time (h)	*T* (°C)	Yield[b] (%)
1	—	8	rt	–
2	$FeCl_3{\cdot}6H_2O$	8	rt	32
3	Fe_2O_3	8	rt	37
4	Fe_3O_4	8	rt	48
5	$CoFe_2O_4$	8	rt	43
6	Diatomaceous Earth (DE)	8	rt	64
7	$CoFe_2O_4$@DE	8	rt	68
8	Fe_3O_4@DE	8	rt	75
9	Fe_3O_4@DE	2	rt	70
10	Fe_3O_4@DE	1	50	95

[a] Reactions conditions: THF (10 mL), sulfonamide (0.86 g, 4 mmol, 1 equiv), benzoyl chloride (0.56 g, 4 mmol, 1 equiv), catalyst (3 mol %).
[b] Isolated yield.

Initially, the model N-acylation reactions of *N*-(4-sulfamoylphenyl)acetamide with acetic anhydride and benzoyl chloride were examined. A comparison with the performance of some of the various heterogeneous catalysts clearly showed that the yields using Fe_3O_4@DE were higher (Tables 1 and 2). In addition, in the presence of Fe_3O_4@DE, the reactions were carried out using reduced times. An increase in the temperature up to 50 °C caused a significant increase in the efficiency of the reaction resulting in higher yields with short reaction times. Tables 1 and 2 clearly indicate that the Fe_3O_4 magnetic nanoparticles having Lewis acid character on the outer surfaces of the Diatomite earth help catalyze the N-acylation reaction. Having established optimized conditions, aryl sulfonamides containing different functional groups; –$NHCOCH_3$, –OMe, –Cl, –Br, –Me, –NO_2 and –COOH as well as methanesulfonamide were reacted with acetic anhydride and benzoyl chloride[30] under acetic acid or Fe_3O_4@DE catalysis and the results are summarized in Tables 3 and 4. The catalytic activities of both catalysts were good and in most cases, the heterogeneous catalyst gave better yields than the acetic acid solvent system (Tables 3 and 4). Excellent yields in the N-acylation reactions can be related to stabilization of the highly polar acylium intermediate with acetic acid as a polar solvent and Fe_3O_4@DE as a Lewis acid catalyst. The main advantages of using Fe_3O_4@DE as a heterogeneous catalyst compared to acetic acid as a homogeneous catalyst were the higher efficiencies and simple catalyst recycling at the end of the reaction. The desired sulfonamides were easily isolated in good yields and purities by

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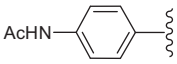
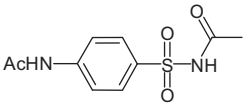
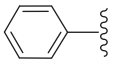
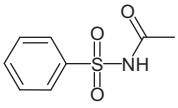
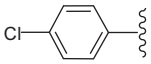
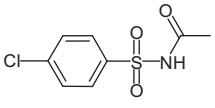
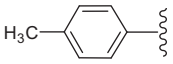
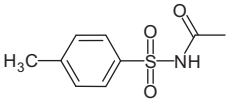
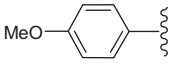
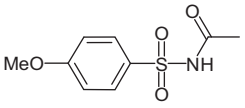
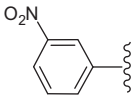
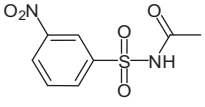
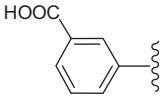
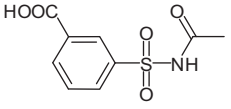
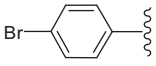
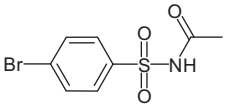
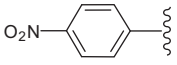
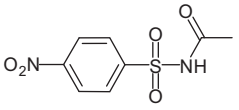
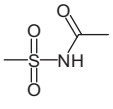
Table 3
N-acylation of sulfonamides with acetic anhydride

Entry	RSO_2NH_2	*N*-Acylsulfonamide	Yield[a] (%)	
			CH_3COOH[b]	Fe_3O_4@DE[c]
1		 **a1**	95	93
2		 **a2**	90	95
3		 **a3**	85	95
4		 **a4**	85	93
5		 **a5**	80	95
6		 **a6**	85	95
7		 **a7**	75	95
8		 **a8**	85	90
9		 **a9**	80	88
10		 **a10**	95	97

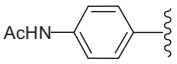
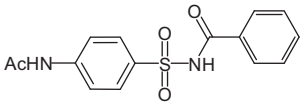
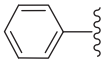
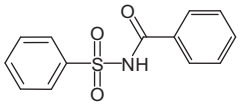
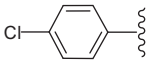
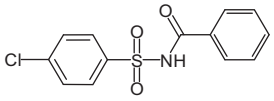
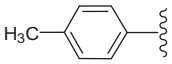
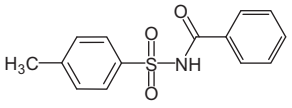
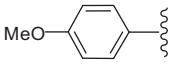
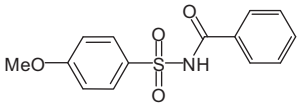
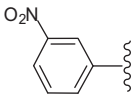
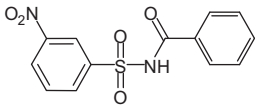
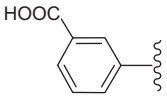
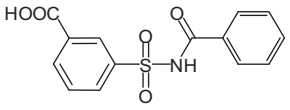
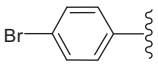
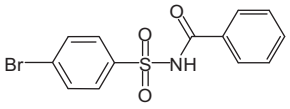
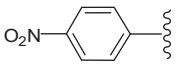
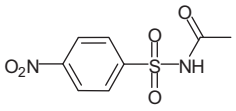
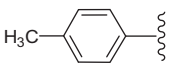
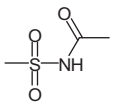
[a] Isolated yield.
[b] Reaction conditions: acetic acid (10 mL), sulfonamide (4 mmol, 1 equiv), acetic anhydride (0.41 g, 4 mmol, 1 equiv), 50 °C, 2 h.
[c] Reaction conditions: THF (10 mL), sulfonamide (4 mmol, 1 equiv), acetic anhydride (0.41 g, 4 mmol, 1 equiv), Fe_3O_4@DE (3 mol %), 50 °C, 1 h.

filtration of the precipitated solid from boiling water. This method eliminates the use of expensive organic solvents and amine bases, making the isolation and purification of the sulfonamide simple.

The magnetic catalyst has attractive properties, such as simple manipulation and reusability. The catalyst could be easily isolated by application of a magnetic field. The catalytic activity of the catalyst remained unchanged after five reaction cycles, with each cycle giving an excellent yield.[31]

In summary, we have demonstrated the glacial acetic acid and Fe_3O_4@DE composite promoted N-acylation reactions of primary

Table 4
N-acylation of sulfonamides with benzoyl chloride

Entry	RSO_2NH_2	*N*-Acylsulfonamide	Yield[a] (%)	
			CH_3COOH[b]	Fe_3O_4@DE[c]
1		 **b1**	95	95
2		 **b2**	80	96
3		 **b3**	90	95
4		 **b4**	80	95
5		 **b5**	90	95
6		 **b6**	70	95
7		 **b7**	80	95
8		 **b8**	80	93
9		 **b9**	85	95
10		 **b10**	95	99

[a] Isolated yield.
[b] Reaction conditions: acetic acid (10 mL), sulfonamide (4 mmol, 1 equiv), benzoyl chloride (0.56 g, 4 mmol, 1 equiv), 50 °C, 2 h.
[c] Reaction conditions: THF (10 mL), sulfonamide (4 mmol, 1 equiv), benzoyl chloride (0.56 g, 4 mmol, 1 equiv), Fe_3O_4@DE (3 mol %), 50 °C, 1 h.

sulfonamides. These procedures have the advantages of mild reaction conditions, high yields, clean reactions, short reaction times, and operational simplicity and recyclability, which make them useful and attractive for the syntheses of *N*-acylated sulfonamide derivatives.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2015.12.044.

References and notes

1. Albala, D. M.; Prien, E. L.; Galal, H. A. *J. Endourol.* **1994**, *8*, 401–403.
2. Hasegawa, T.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 423–428.
3. Banwell, M. G.; Crasto, C. F.; Easton, C. J.; Forrest, A. K.; Karoli, T.; March, D. R.; Mensah, L.; Nairn, M. R.; O'Hanlon, P. J.; Oldham, M. D.; Yue, W. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 2263–2266.
4. Chang, L. L.; Ashton, W. T.; Flanagan, K. L.; Chen, T. B.; O'Malley, S. S.; Zingaro, G. J.; Siegl, P. K.; Kivlighn, S. D.; Lotti, V. J.; Chang, R. S. *J. Med. Chem.* **1994**, *37*, 4464–4478.
5. Wang, Y.; Soper, D. L.; Dirr, M. J.; Delong, M. A.; De, B.; Wos, J. A. *Chem. Pharm. Bull.* **2000**, *48*, 1332–1337.
6. Musser, J. H.; Kreft, A. F.; Bender, R. H. W.; Kubrak, D. M.; Grimes, D.; Carlson, R. P.; Hand, J. M.; Chang, J. *J. Med. Chem.* **1990**, *33*, 240–245.
7. Heidler, P.; Link, A. *Bioorg. Med. Chem.* **2005**, *13*, 585–599.
8. Singh, S. K.; Vobbalareddy, S.; Kalleda, S. R.; Casturi, S. R.; Mullangi, R.; Ramanujam, R.; Yeleswarapu, K. R.; Iqbal, J. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 3921–3926.
9. Huang, S.; Connolly, P. J.; Lin, R.; Emanuel, S.; Middleton, S. A. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 3639–3641.
10. Johnson, D. C.; Widlanski, T. S. *Tetrahedron Lett.* **2001**, *42*, 3677–3679.
11. Singh, D. U.; Singh, P. R.; Samant, S. D. *Tetrahedron Lett.* **2004**, *45*, 4805–4807.
12. Wang, Y.; Sarris, K.; Sauer, D. R.; Djuric, S. W. *Tetrahedron Lett.* **2007**, *48*, 5181–5184.
13. Fu, S.; Lian, X.; Ma, T.; Chen, W.; Zheng, M.; Zeng, W. *Tetrahedron Lett.* **2010**, *51*, 5834–5837.
14. Kondo, K.; Sekimoto, E.; Nakao, J.; Murakami, Y. *Tetrahedron* **2000**, *56*, 5843–5856.
15. Kondo, K.; Sekimoto, E.; Miki, K.; Murakami, Y. *J. Chem. Soc. Perkin Trans. 1* **1998**, 2973–2974.
16. Ishizuka, N.; Matsumura, K.; Hayashi, K.; Sakai, K.; Yamamori, T. *Synthesis* **2000**, *6*, 784–788.
17. Shanguann, N.; Katukojvala, S.; Greenberg, R.; Williams, L. J. *J. Am. Chem. Soc.* **2003**, *125*, 7754–7755.
18. Martin, M. T.; Roschangar, F.; Eaddy, J. F. *Tetrahedron Lett.* **2003**, *44*, 5461–5463.
19. Reddy, C. R.; Mahipal, B.; Yaragorla, S. R. *Tetrahedron Lett.* **2007**, *48*, 7528–7532.
20. Haldar, S.; Koner, S. *J. Org. Chem.* **2010**, *75*, 6005–6008.
21. Chiu, J. J.; Pine, D. J.; Bishop, S. T.; Chmelka, B. F. *J. Catal.* **2004**, *221*, 400–412.
22. Singh, D. U.; Singh, P. R.; Samant, S. E. *Tetrahedron Lett.* **2004**, *45*, 4805–4807.
23. Rueping, M.; Raja, S.; Núñez, A. *Adv. Synth. Catal.* **2011**, *353*, 563–568.
24. Nagai, M.; Isoe, R.; Ishiguro, K.; Tominaga, H.; Shimizu, M. *Chem. Eng. J.* **2012**, *207*, 938–942.
25. Tamaddon, F.; Sabeti, M. R.; Jafari, A. A.; Tirgir, F.; Keshavarz, E. *J. Mol. Catal. A: Chem.* **2011**, *351*, 41–45.
26. Hoseini, S. J.; Nasrabadi, H.; Azizi, M.; Salimi Beni, A.; Khalifeh, R. *Synth. Commun.* **2013**, *43*, 1683–1691.
27. Bolm, C.; Legros, J. L.; Zani, L. *Chem. Rev.* **2004**, *104*, 6217–6254.
28. Maleki, A. *Tetrahedron* **2012**, *68*, 7827–7833.
29. Jasra, R. V. *Bull. Catal. Soc. India* **2003**, *2*, 157–183.
30. General procedure for N-acylation: *N*-(4-Sulfamoylphenyl) acetamide (0.86 g, 4 mmol) was treated with acetic anhydride (0.41 g, 4 mmol) in glacial acetic acid (10 mL). The mixture was stirred at 50 °C for 2 h and progress of the reaction was monitored by TLC. After completion, the precipitate was collected by filtration and washed with water. The impure precipitate was dissolved in an aqueous solution of sodium carbonate (50 mL, pH = 8.0) and filtered. Acetic acid was added dropwise to precipitate the product (pH = 5.0) which was collected by filtration to afford *N*-(4-acetamidophenylsulfonyl)acetamide **a1** as a white solid (0.97 g, 95%). The catalytic activities of the heterogeneous catalysts were determined by the reaction with acetic anhydride or benzoyl chloride. For example: *N*-(4-sulfamoylphenyl) acetamide (4 mmol) was treated with acetic anhydride (4 mmol) in the presence of catalyst (3 mol %) in THF (10 mL). After reaction completion, the catalyst was separated with an external magnetic field and the solvent removed by a rotary evaporator. The precipitate was dissolved in an aqueous solution of sodium carbonate (50 mL, pH = 8.0) and filtered. Acetic acid was added dropwise to precipitate the product (pH = 5.0) which was collected by filtration and was washed with distilled water to afford *N*-(4-acetamidophenylsulfonyl)acetamide as a white solid. All *N*-acylsulfonamides except compound **b7** are known compounds and are further characterized using mp, ^{1}H NMR, ^{13}C NMR, IR, MS and CHN analysis (see ESI for complete details). 3-(*N*-Benzoylsulfamoyl)benzoic acid (**b7**); $C_{14}H_{11}NO_5S$; MW: 305; mp: 153–155 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 7.59–7.89 (m, 3H), 8.05 (m, 3H), 8.38 (d, 2H, J = 6.4 Hz), 9.12 (s, 1H), 10.33 (br s, 1H), 10.68 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ(ppm): 122.4, 122.9, 130.2, 135.5, 136.1, 137.7, 141.4, 143.9, 145.1, 155.7, 169.9, 170.1; IR $\bar{\nu}$(cm^{-1}): 684, 755, 871, 992, 1114, 1238, 1360, 1440, 1599, 1713, 2882, 2934, 3070, 3241, 3373; Anal. Calcd: C, 55.08; H, 3.63; N, 4.59. Found: C, 55.17; H, 3.71; N, 4.65.
31. The reusability of the catalyst was investigated in the N-benzoylation of *N*-(4-sulfamoylphenyl)acetamide. At the end of the reaction, the catalyst was recovered by applying a magnetic field and the collected solid was washed with THF (3 × 10 mL), dried at 50 °C for 6 h and reused for the next reaction. The catalyst was used for 5 reactions without any significant decrease in activity (95%, 93%, 93%, 92% and 91% for the 1st, 2nd, 3rd, 4th and 5th run, respectively).