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Clay catalysed amidation of alcohols with nitriles in dry media

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Montmorillonite KSF catalyses the Ritter reaction in which several benzyl, allyl and tertiary alcohols are converted into amides in high yields, when heated with various nitriles in the absence of solvent. A comparative study of conventional *vs.* microwave irradiation for this clay catalysed reaction is presented.

The reaction of alcohols with nitriles in protic acid, popularly known as the Ritter reaction,[1] leads to amides. The carbonium ion formed by the reaction of a strong protic acid and alcohols or olefins reacts with nitriles to generate a nitrilium ion, which is subsequently trapped with water resulting in *N*-substituted amides. The classical method, which utilizes conc. H_2SO_4 (85–90%), is generally suitable for tertiary alcohols, but this strongly acidic medium limits its use, especially for acid sensitive substrates. In order to circumvent serious side reactions[2] in the sulfuric acid approach, several modifications and improvements have been attempted and the protic acid is often replaced by Lewis acids such as $AlCl_3$, $FeCl_3$ or $SnCl_4$ and the alcohols by alkyl halides.[3] $BF_3 \cdot OEt_2$[4] is used as a catalyst for selective amidation of benzyl alcohols; however, this method is not suitable for substrates bearing electron withdrawing groups (*e.g.*, 4-nitrobenzyl alcohols), 2° and 3° alcohols including aryl-alkyl carbinols and is inefficient in the case of α,β-unsaturated (cinnamyl) alcohols. Recently, rare earth exchanged HY-zeolite[5] has been utilized for the Ritter amidation of alcohols; however, the conversions were only partial even after 24 h of heating. Even though a clayfen (clay supported ferric nitrate) catalysed Ritter reaction has been reported[6] under conventional conditions, the method utilizes *tert*-alkyl halides as substrates and the yields reported are low and require long reaction times. In continuation of our work on eco-friendly organic transformations,[7] we present here a convenient Ritter amidation of alcohols catalysed by montmorillonite KSF under solvent-free conditions.

We first examined the reaction of a number of alcohols and nitriles under microwave heating by irradiating a mixture of clay and equimolar quantitites of the reactants in an open pyrex test tube and complete conversion was asertained by tlc monitoring. In order to precisely assess the efficiency of microwave heating, parallel experiments were conducted under conventional heating, by keeping the test tube containing the dry reaction mass immersed in a hot oil bath (preheated to 110–120 °C, analogous to the highest observed temperature during irradiation), with occasional mixing. From the results summerized in Table 1, it is evident that both modes of heating afford good yields of amides. Obviously with the microwave method conversions are faster (2–5 min), whereas the conventional mode of heating required much longer reaction times in order to attain comparable yields. Further, the clay catalysed Ritter reaction was found to be highly selective for benzylic, allylic and tertiary alcohols, yet general with regard to nitriles, which are the other reaction ingredients. Unlike Lewis acid catalysed Ritter amidation, our method is applicable to electron deficient benzyl alcohols, 2° and 3° aryl-alkyl carbinols and tertiary alcohols like *tert*-butanol and all these substrates formed amides in good yields. Furthermore, no appreciable thermal decomposition of the product was observed under either mode of heating.

Despite the possibilities for multiple reaction pathways in an overall conversion that proceeds through two high energy formally charged intermediates, the conversions in clay catalysed reactions were generally found to be clean. Different functional groups could tolerate these reaction conditions and no deallylation, dealkylation or debenzylation were observed, which are otherwise commonly encountered in any acid catalysed reaction. However, minor quantities (5–8%) of dimeric ethers were isolated along with the amides wherever primary benzyl or allyl alcohols were employed, which is in conformity with earlier reports.[8] Aryl-alkyl carbinols and tertiary alcohols also exclusively formed amides in high yields without any elimination by-products derived from alcohols. No reaction occurred in the case of primary aliphatic alcohols and no trace of acids derived from hydrolysis of nitriles were detected in the crude products. From these results, it is logical to presume that the selectivity observed during clay catalysed Ritter amidation may possibly be due to the stabilization of cationic intermediates in the interlamellar layers, as encountered in many clay catalysed reactions.[9]

The catalyst could be effectively reused for four cycles (after washing with methanol and drying at 120 °C for 5 h) without any apparent loss of activity; for example, the benzyl alcohol and benzyl cyanide combination under microwave irradiation[6] gave 82%, 80%, 80%, and 81% yields over 4 cycles. These results clearly show the advantages of our method over protic and Lewis acid catalysed Ritter reactions.

In conclusion the montmorillonite catalysed Ritter reaction presented in this paper is a convenient and high yielding method for the amidation of alcohols. Other merits such as inexpensive and reusable catalyst, solvent free reaction conditions and application of microwave for achieving quick and clean conversions, make our method eco-friendly and economical and hence it may find uses in organic synthesis.

Experimental

In a typical experiment 1-phenylethanol (1.2 g, 10 mmol) and 3-ethoxypropionitrile (1 g, 10 mmol) were admixed with KSF clay (1.2 g, w/w of alcohol) and subjected to microwave irradiation in a pyrex test tube for 3 min. Then the reaction mass was cooled to room temperature, charged on a short silica gel column (Merck, 200 mesh) and eluted (ethyl acetate–*n*-hexane, 2:8) to afford the pure amide as a pale yellow liquid (2.05 g, 93%). ^{1}H NMR ($CDCl_3$): δ 1.15 (t, 3H, $J = 7.5$ Hz), 1.45 (d, 3H, $J = 6.25$ Hz), 2.4 (t, 2H, $J = 6.25$ Hz), 3.5 (q, 2H, $J = 7.5$ Hz), 3.65 (t, 2H, $J = 6.25$ Hz), 5.15 (dd, 1H, $J = 7.5$ and 6.5 Hz), 6.85 (s br, 1H), 7.3 (m, 5H).

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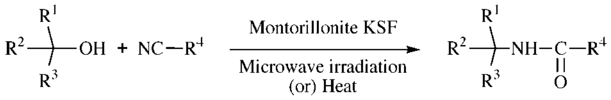
Table 1 Amidation of alcohols with nitriles[a]



R^1	R^2	R^3	R^4	Microwave[b] irradiation Time/min	Microwave[b] irradiation Yield[c]/%	Conventional heating Time/h	Conventional heating Yield[c]/%
H	H	Ph	$H_3CCH_2CH_2$	5	86(6)	10	74(5)
H	H	Ph	$PhCH_2$	4	83(5)	8	72(7)
H	H	Ph	Ph	4	80(8)	8	70(7)
H	H	$4\text{-}NO_2C_6H_4$	$PhCH_2$	6	75	12	68
H	CH_3	Ph	$EtOCH_2CH_2$	3	93	8	85
H	H	$4\text{-}MeOC_6H_4$	Ph	4	91	8	87
H	CH_3	Ph	$CH_2{=}CH$	3	84	6	73
H	H	$4\text{-}BnOC_6H_4$	$PhCH_2$	4	89	7	78
H	CH_3	Ph	$C(CH_3)_3$	4	87	5	75
H	Ph	Ph	CH_3	3	85	8	77
H	Ph	Ph	$Cl(CH_2)_2CH_2$	4	90	7	82
CH_3	CH_3	CH_3	$PhCH_2$	3	87	6	74
CH_3	CH_3	CH_3	Ph	3	83	6	72
CH_3	Ph	Ph	$CH_3CH_2CH_2$	3	85	8	76
CH_3	Ph	Ph	$ClCH_2$	4	88	7	80
H	H	$PhCH{=}CH$	$PhCH_2$	2	78(5)	5	67(6)
H	H	$PhCH{=}CH$	$CH_3CH_2CH_2$	3	80(8)	4	70(5)
H	H	$CH_3CH{=}CH$	$PhCH_2$	2	75(6)	5	65(8)
H	H	$CH_3CH{=}CH$	$CH_3CH_2CH_2$	3	77(6)	4	68(8)
H	H	$CH_3(CH_2)_6CH_2$	$CH_3CH_2CH_2$	No reaction			

[a] All products were characterised by IR, ^1H NMR, mass spectra and by comparison with known compounds. [b] Irradiations were carried out at an output of 650 W in a domestic microwave oven BPL BMO 700T (unoptimised). [c] Isolated yield after chromatography. Yields indicated in parentheses correspond to dimeric ethers.

References

1 (*a*) J. J. Ritter and P. P. Minier, *J. Am. Chem. Soc.*, 1948, **70**, 4045. (*b*) L. I. Krimen and D. J. Cota, *Org. React.* (*NY*), 1969, **17**, 213.

2 (*a*) S. Top and G. Jaouen, *J. Org. Chem.*, 1981, **46**, 78. (*b*) A. Garcia Martinez, R. Martinez Alvarez, E. Teso Vilar, A. Garcia Fraile, M. Hanack and L. R. Subramanian, *Tetrahedron Lett.*, 1989, **30**, 581. (*c*) T. Kiersznicki and R. Mazurkiewicz, *ROCZ Chem.*, 1977, **51**, 1021; *Chem. Abstr.*, 1978, **88**, 6504f. (*d*) D. H. R. Barton, P. D. Magnus and R. N. Young, *J. Chem. Soc., Chem. Commun.*, 1973, 331. (*e*) D. H. R. Barton, P. D. Magnus, J. A. Garbarino and R. N. Young, *J. Chem. Soc., Perkin Trans 1.*, 1974, **1**, 2101. (*f*) M. C. Cesa, US Pat. 5103055 A, 1992; *Chem. Abstr.*, 1992, **115**, 235100k. (*g*) Y. Takahashi, Y. Fukoaka, K. Sasaki and S. Senco, US Pat. 68–748165, 1968; *Chem. Abstr.*, 1973, **79**, 91627e. (*h*) Israel Min. Ind. Inst. Res. Develop., GB Pat. 1198680, 1970; *Chem. Abstr.*, 1970, **72**, 766833c.

3 H. Firouzabadi, A. R. Sardarian and H. Badparva, *Synth. Commun.*, 1994, **24**, 601.

4 M. Kacan and A. McKillop, *Synth. Commun.*, 1993, **23**, 2185.

5 A. R. A. S. Deshmukh, V. K. Gumaste and B. M. Bhawal, *Ind. J. Chem.*, 1997, **36B**, 369.

6 P. Eugenio, *Bull. Soc. Chim. Belg.*, 1985, **94**, 81.

7 (*a*) H. M. Sampath Kumar, P. K. Mohanty, M. S. Kumar and J. S. Yadav, *Synth. Commun.*, 1997, **27**, 1327. (*b*) H. M. Samapth Kumar, B. V. Subba Reddy, P. K. Mohanty and J. S. Yadav, *Tetrahedron Lett.*, 1997, **38**, 3619. (*c*) H. M. Sampath Kumar, B. V. Subba Reddy and J. S. Yadav, *Chem. Lett.*, 1998, 637. (*d*) H. M. Sampath Kumar, B. V. Subba Reddy, S. Anjaneyulu and J. S. Yadav, *Synth. Commun.*, 1998, **28**, 3811.

8 T. Li, H. Li, J. Guo and T. Jin, *Synth. Commun.*, 1996, **26**, 2497.

9 A. R. A. S. Deshmukh, V. K. Gumaste and B. M. Bhawal, *Synth Commun.*, 1995, **25**, 3939 and references cited therein.

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