

Amberlyst A-21 an Excellent Heterogeneous Catalyst for the Conversion of Carbonyl Compounds to Oximes

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Oximes can be efficiently obtained at room temperature by simply dissolving the appropriate carbonyl compounds and hydroxylamine hydrochloride, in ethanol, with Amberlyst A-21 as catalyst. Good yields of oximes are obtained, in very short reaction times, even with polyfunctionalized substrates.

Oximes are an important class of molecules because of their synthetic utility as protected forms of the carbonyl compounds and their ability to form other functionalities. In fact, besides the Beckmann rearrangement (oximes to amides), oximes can be conveniently converted into nitriles,¹ nitro compounds,² gem-halonitro compounds,³ isoxazolines,⁴ vinyl isonitriles,⁵ nitrones,⁶ primary⁷ or secondary⁸ amines, and stabilized carbanions.⁹

The standard method for preparing oximes is the reaction of an aldehyde or ketone with hydroxylamine hydrochloride in an alcoholic solution, under reflux temperature, and in the presence of sodium acetate or pyridine.¹⁰ The latter method is the most used, especially for the oximation of hardly soluble ketones¹¹ and steroidal ketones.¹² However, pyridine presents some limitations since this base is highly flammable, and harmful by inhalation and in contact with skin.

In recent years there has been a tremendous upsurge of interest in various chemical transformations mediated by heterogeneous catalysts after innumerable chemical reactions are facilitated by this catalyst, and associated literature is extensive.¹³

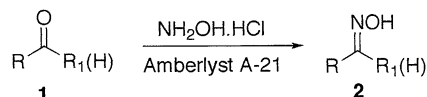
In connection with our studies on reactions carried out with heterogeneous conditions,¹⁴ we found that Amberlyst A-21, a macroreticular anionic resin with the $-N(CH_3)_2$ as functional group, is an excellent and far superior catalyst for the synthesis of oximes from carbonyl compounds.

Our method is carried out at room temperature by simply dissolving the appropriate carbonyl compound (1 mol) and hydroxylamine hydrochloride (2 mol), in ethanol, with Amberlyst A-21 (10 g for 0.05 mol of carbonyl), and leaving the mixture for 1 h (only for the compounds **1j** and **1l** longer reaction times were needed, 8–10 h).

Yields (Table 1) are high and work-up is exceedingly simple, only involving filtration, extractive work-up with diethyl ether, and evaporation to obtain the product in a high state of purity (at least 97%, as diastereomeric mixture); no further purification steps are required. Moreover, this catalyst does not affect labile functional group (ether, cyano, sulphone, nitro, hydroxyl, tetrahydropyranyl, (Z)-C-C double bond) and its mildness is demonstrated by the stability of α -nitrocyclohexanone **1h**, in the oximation process, vs the ring-cleavage process.¹⁵ The mono-oximation of the 1,3-diketone **1k** can be explained with the high enolization of this compound.

The advantage of the reported procedure over the previous methods is (i) to avoid reflux temperature and toxic base, (ii) short reaction times, (iii) the easy work-up, (iv) the high purity

Table 1.



	Carbonyl Compound 1	Oxime 2	Yield (%) of 2
a-d			2a R=Me 96
			2b R=OMe 78
			2c R=NO ₂ 97
			2d R=CN 97
e-g			2e n=1 100
			2f n=3 95
			2g n=7 96
h,i			2h R=H, R1=NO ₂ 91
			2i R=Ph, R1=H 86
j			2j 70
k			2k 87
l,m			2l n=0 85
			2m n=1 90
n			2n 88
o			2o 89
p			2p 96
q			2q 74
r			2r 96

of the products, (v) the high chemoselectivity, and (vi) the evident economical and ecological convenience due to the possibility of recuperating and recycling the catalyst, after regeneration.

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References and Notes

- 1 A. Carotti, F. Campagna, and R. Ballini, *Synthesis*, **1979**, 56; D. Dauzonne, P. Demerseman, and R. Royer, *Synthesis*, **1981**, 739; M. N. Rao, P. Kumar, and K. Garyali, *Org. Prep. Proc. Int.*, **21**, 230 (1989) and references cited therein; D. Villemain, M. Laloui, and A. B. Alloum, *Chem. & Ind.*, **1991**, 176.
- 2 E. J. Corey, and H. Estreicher, *Tetrahedron Lett.*, **1980**, 1117; R. Ballini, E. Marcantoni, and M. Petrini, *Tetrahedron Lett.*, **33**, 4835 (1992); G. A. Olah, P. Ramaiah, C.-S. Lee, and G. K. S. Prakash, *Synlett*, **1992**, 337; F. P. Ballistreri, E. Barbuzzi, G. A. Tomaselli, and R. M. Toscano, *Synlett*, **1996**, 1093; P. R. Dave, and F. Forohar, *J. Org. Chem.*, **61**, 8897 (1996).
- 3 A. Zaks, A. V. Yabannavar, D. R. Dodds, C. A. Evans, P. R. Das, and R. Malchow, *J. Org. Chem.*, **61**, 8692 (1996).
- 4 J. T. Pulkkinen, and J. J. Vepsalainen, *J. Org. Chem.*, **61**, 8604 (1996).
- 5 D. H. R. Barton, T. Bowles, S. Husinec, J. E. Forbes, A. Llobera, A. E. A. Porter, and S. Z. Zard, *Tetrahedron Lett.*, **29**, 3343 (1988).
- 6 E. Malamidov-Xenikaki, X. N. Stampelos, T. A. Charalambis, and C. C. Karapostolou, *Tetrahedron*, **53**, 747 (1997).
- 7 S. Itsuno, Y. Sakurai, and K. Ito, *Synthesis*, **1988**, 995; J. Ipaktschi, *Chem. Ber.*, **117**, 856 (1984); D. Carr, B. Iddon, H. Suchitzky, and R. T. Parfitt, *J. Chem. Soc., Perkin Trans 1*, **1980**, 2374; J. Herscovici, M.-J. Egrn, and K. Antonakis, *J. Chem. Soc., Perkin Trans 1*, **1988**, 1219; S. Negi, M. Matsukura, M. Mizuno, K. Miyake, and N. Minami, *Synthesis*, **1996**, 991.
- 8 S. Sasatani, T. Miyazak, K. Maruoka, and H. Yamamoto, *Tetrahedron Lett.*, **24**, 4711 (1983); K. Kotera, and K. Kitahonok, *Org. Synth.*, **48**, 20 (1968).
- 9 M. Bellassoued, F. Dardoize, Y. Frangin, and M. Gaudemar, *J. Organometallic Chem.*, **165**, 1 (1979); A. Hassner, and F. Naumann, *Chem. Ber.*, **53**, 3884 (1988).
- 10 S. Dayagi, and Y. Degani in "The Chemistry of the Carbon-Nitrogen Double Bond" ed by S. Patai, Interscience, New York (1970), p 61.
- 11 N. E. Bachmann, and C. H. Boatner, *J. Am. Chem. Soc.*, **58**, 2097 (1936).
- 12 Y. Sato, and H. Kaneko, *Steroids*, **5**, 279 (1965); G. Rosenkranz, O. Mancercz, F. Sondheimer, and C. Djerassi, *J. Org. Chem.*, **21**, 520 (1956).
- 13 G. H. Posner, *Angew. Chem., Int. Ed. Engl.*, **17**, 487 (1978); D. C. Baley, and S. H. Langer, *Chem. Rev.*, **81**, 109 (1981); J. A. Schwarz, *Chem. Rev.*, **95**, 477 (1995); B. C. Gates, *Chem. Rev.*, **95**, 511 (1995); D. W. Goodman, *Chem. Rev.*, **95**, 523 (1995); H. Hattori, *Chem. Rev.*, **95**, 537 (1995); M. Boudart, *Chem. Rev.*, **95**, 661 (1995).
- 14 G. Rosini, R. Ballini, and P. Sorrenti, *Synthesis*, **1983**, 1014; R. Ballini, M. Petrini, and G. Rosini, *Synthesis*, **1987**, 711; R. Ballini, M. Petrini, and V. Polzonetti, *Synthesis*, **1992**, 355; R. Ballini, G. Bosica, and P. Forconi, *Tetrahedron*, **52**, 1677 (1966); R. Ballini, P. Marziali, and A. Mozzicafreddo, *J. Org. Chem.*, **61**, 3209 (1996).
- 15 R. H. Fischer, and H. M. Weitz, *Synthesis*, **1980**, 261.