

An Eco-friendly and Simple Route to Synthesis of Acetanilide from Aniline

Sharda Pasricha

Department of Chemistry, Sri Venkateswara College, University of Delhi, New Delhi, India

ABSTRACT

Magnesium sulphate-glacial acetic acid system has been found to be a benign, eco-friendly and inexpensive catalyst for the synthesis of acetanilide from aniline. The method is simple, fast, green, avoids use of toxic acetic anhydride and involves catalysed reaction in line with the green chemistry principles. The method can be easily adopted at the undergraduate level and may find applications in the industrial scale acetylation of primary and secondary amines.

KEYWORDS: Lewis acid catalyst, Magnesium Sulphate heptahydrate, Acetylation, Undergraduate-Chemistry

How to cite this paper: Sharda Pasricha
"An Eco-friendly and Simple Route to
Synthesis of Acetanilide from Aniline"

Published in
International Journal
of Trend in
Scientific Research
and Development
(ijtsrd), ISSN: 2456-
6470, Volume-6 |
Issue-2, February
2022, pp.131-134, URL:
www.ijtsrd.com/papers/ijtsrd49128.pdf



IJTSRD49128

Copyright © 2022 by author(s) and
International Journal of Trend in
Scientific Research and Development
Journal. This is an
Open Access article
distributed under the
terms of the Creative Commons
Attribution License (CC BY 4.0)
(<http://creativecommons.org/licenses/by/4.0>)



INTRODUCTION

Acetylation of primary and secondary amines, alcohols and phenols is a simple nucleophilic acyl substitution reaction, which is conventionally carried out in the presence of an acidic [1] or basic [2] catalyst (Figure 1). The reaction finds extensive use in chemistry labs at undergraduate, post-graduate, research and industrial scale for protection of amino and hydroxy groups in a multistep synthesis of polyfunctional compounds [3, 4]. Conventionally, the acetylation reactions involve the use of acetyl chloride or acetic anhydride as acetylating agents. However, these reagents are corrosive and lachrymatory respectively, and therefore not ideal [5] for the acetylation reactions. Although a number of reagents and catalysts have been proposed for this reaction, there is a need for simple and efficient method, given the importance of this reaction.

Wang et al. [6] carried out acetylation of primary amines using glacial acetic acid. Acetylation reactions employing acetic acid for acetylation are slow since the carbonyl carbon in acetic acid is deactivated by the +R effect of the hydroxyl group [Figure 2]. If, however, the electrophilicity of the carbonyl carbon

in acetic acid can be increased, by using a suitable catalyst, the reaction may prove to be highly beneficial, since acetic acid is cheap and will involve only water as by-product. Acetylation with acetic acid is therefore environmentally benign and has 100% atom economy. Recently, Brahmachari et al. [5] reported use of zinc acetate/metal oxide and glacial acetic acid for N-acetylation of amines. Use of zinc salts is however discouraged due to potential toxicity of zinc. Several other reports of acetylation of amines, alcohols and phenols with acetic anhydride or Lewis-acid/acetic acid is known in literature [7-17]. These methods are however costly or use toxic solvents or generate toxic waste or require catalysts which are not readily available. Thus, a mild, cheap, simple and efficient method acetylation of amines is need of the hour.

Alkaline earth metals like magnesium (Mg) are abundant in earth. Using catalysts derived from abundant resources is vital for sustainable chemistry. Efficient reactions with Mg(II) based Lewis acid catalysts could offer a cheap yet practical synthetic route for acetylation of useful molecular skeletons.

Several examples of use of Mg(II) salts as Lewis acid catalyst are known till date[18-21].

Therefore, it is worthwhile to explore the use of magnesium salts as a viable reagent/catalyst in acetylation reaction of aniline. The current method

reports the use of magnesium sulphate heptahydrate-glacial acetic acid for a solvent-free, mild, cheap and benign route for the synthesis of acetanilide for aniline[Figure 3].

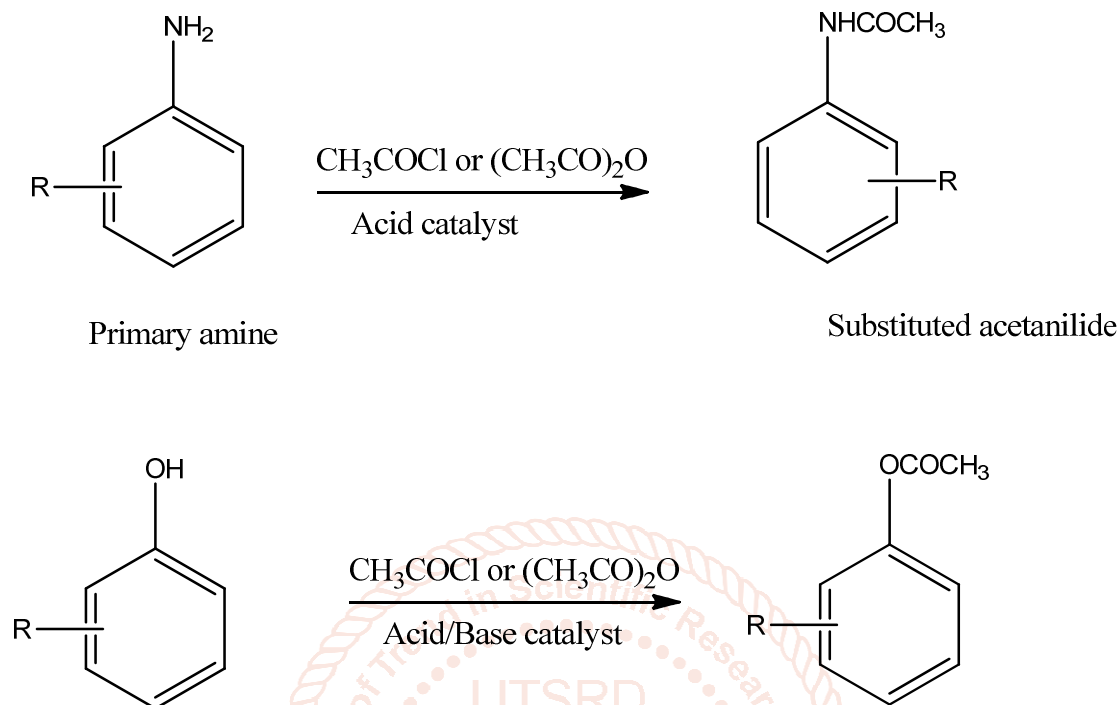


Figure 1: General route to acetylation of amines and phenols

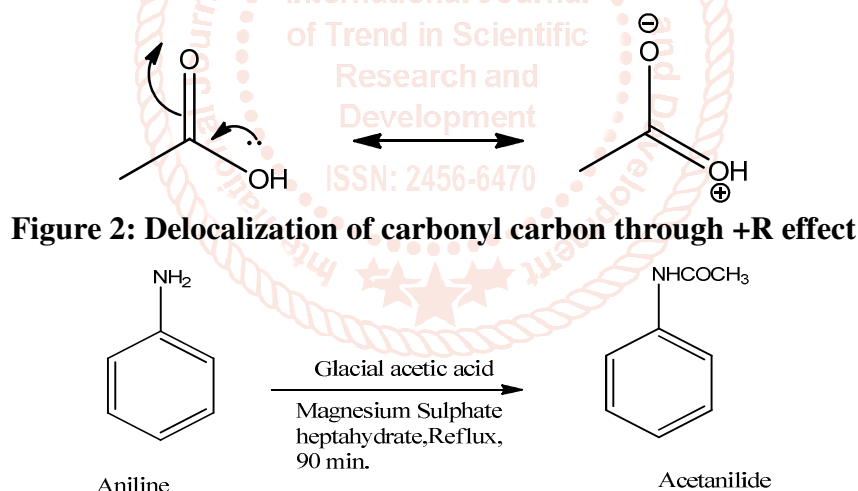


Figure 2: Delocalization of carbonyl carbon through +R effect

Figure 3: Acetylation of aniline with glacial acetic acid using magnesium sulphate heptahydrate as catalyst

Experimental

A mixture of magnesium sulphate heptahydrate (0.2 mmol), glacial acetic acid (3.0 mL) and aniline (1.0 mL, 10 mmol) was taken in a dry round-bottomed flask. 1-2 pumice stones were added and the reaction mixture was refluxed on a wire gauze for suitable time. Upon completion of the reaction (TLC), the contents were diluted with hot water (5.0 mL) and filtered hot. The filtrate was allowed to cool to room temperature and then cooled in an ice-water bath (100 mL). The sample was filtered at suction pump, washed well with minimum amount of ice-cold water, dried and weighed. A part of the crude sample was recrystallized from hot water. Melting point of the recrystallized sample was found to be 114°C.

Result and Discussion

A reaction of aniline (1.0 mL) with glacial acetic acid (3.0 mL) was carried out in the presence of magnesium sulphate heptahydrate (30 mg) as catalyst. It was found that the reaction proceeded to completion in 90 minutes to afford 80% yield of the desired product. No further increase in yield was observed on increasing the reaction

time. The yield was however found to decrease on reducing the reaction time[Table 1]. It was therefore concluded that 90 minutes is the optimum reaction time. Next, the reaction was carried out with varying amounts of magnesium sulphate heptahydrate (30, 40, 50----- 100 mg). It was found that the best yields(92%) was obtained when 50 mg of magnesium sulphate heptahydrate was used as catalyst[Table 2]. No further increase in yield of the desired product was obtained on increasing the amount of catalyst. The reaction in absence of catalyst gave poor yields of the desired product (60%). This strongly indicates the role of Lewis acid catalyst in catalysing the reaction [Figure 4].

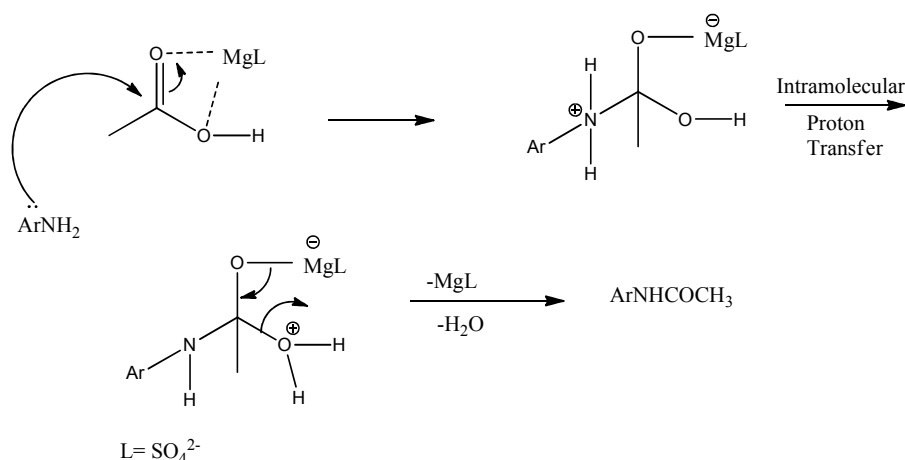


Figure 4: Mechanism of Lewis acid catalysed acetylation of aniline

Table 1: Effect of reaction time on the acetylation reaction

S. No.	Duration of reaction (minutes)	Yield Percentage (%)
1	45	50
2	60	70
3.	75	77
4	90	80

Conditions: Aniline (1.0 mL), glacial acetic acid (3.0 mL), 118°C, magnesium sulphate heptahydrate(30 mg),

Table 2: Effect of varying amounts of magnesium sulphate heptahydrate on the acetylation reaction

S. No.	Amount of Magnesium sulphate heptahydrate(mg)	Yield Percentage (%)
1	30	80
2	40	85
3.	50	92
3.	70	92
4	100	92

Conditions: aniline (1.0 mL), glacial acetic acid (3.0 mL), 118°C, 90 min.

Conclusion

Magnesium sulphate heptahydrate-glacial acetic acid system has proved to be a mild, cheap, simple, and benign catalyst for the synthesis of acetanilide from aniline. Lewis acid catalysis nucleophilic acyl substitution reaction by increasing the electrophilicity of the carbonyl group. The method may serve as a sustainable, inexpensive and green route for the acetylation of the primary amines.

References

- [1] J. Iqbal and R. R. Srivastava, *J. Org. Chem.*, 1992, 57, 2001; K. Ishihara, M. Kubota, H. Kurihara and H. Yamamoto, *J. Am. Chem. Soc.*, 117, 4413, 1995; J. Izumi, I. Shiina and T. Mukaiyama, *Chem. Lett.*, 141, 1995; A. G. M. Barret and D. C. Braddock, *Chem. Commun.*, 351, 1997; R. Ballini, G. Bosica, S. Carloni, L. Ciaralli, R. Maggi and G. Sartori, *Tetrahedron Lett.*, 39,6049, 1998.
- [2] T. Nishiguchi, K. Kawamine and T. Ohtsuka, *J. Org. Chem.*, 57, 312, 1992; Y. Kita, H. Maeda, K. Omori, T. Okuno and Y. Tamura, *J. Chem. Soc., Perkin Trans. 1*, 2999, 1993; J. Otera, *Chem. Rev.*, 93, 1449, 1993; A. Loupy, A. Petit, M. Ramdani, C. Yuanaeft, M. Majdoub, B. Labiad and D. Villemin, *Can. J. Chem.*, 71,90, 1993; G. W. Breton, *J. Org. Chem.*, 62, 8952, 1997; G. Hofle, V. Steglich and H. Vorbruggen, *Angew. Chem., Int. Ed. Engl.*, 17, 569, 1978.

- [3] T. W. Green and P. G. M. Wuts, Protective Groups in Organic Synthesis, 3rd edn, Wiley, New York, 1999.
- [4] L. Pearson, W.J. Roush, Handbook of reagents for organic synthesis: activating agents and protecting groups, John Wiley and Sons, Chichester, UK, pp 9–16, 1999.
- [5] G. Brahmachari, S. Laskar and S. Sarkar, Metal acetate/metal oxide in acetic acid: an efficient reagent for the chemoselective N-acetylation of amines under green conditions, *Journal of Chemical Research*, Volume 34, issue: 5, 288–295, 2010, <https://doi.org/10.3184/030823410X12746305905926>.
- [6] X. Wang, Qian Yang, F. Liu, Q., Microwave-Assisted Synthesis of Amide under Solvent-free Conditions, *Synthetic Communications*, 38:7, 1028–1035, 2008, DOI: 10.1080/00397910701860372.
- [7] S. Gowda, K.M. Lokanatha Rai Manganese (III) acetate as catalyst for the direct acetylation of alcohols with acetic acid, *Journal of Molecular Catalysis A: Chemical* 217, 27–29, 2004.
- [8] S. Jamwal, R. Dharela, R. Gupta, J. Ahn, G. S. Chauhan, Synthesis of cross linked lipase aggregates and their use in the synthesis of aspirin, *Chemical Engineering Research and Design*, Volume 97, 159–164, 2015. <https://doi.org/10.1016/j.cherd.2014.09.010>.
- [9] R. Biswas, A. Mukherjee, Introducing the Concept of Green Synthesis in the Undergraduate Laboratory: Two-Step Synthesis of 4-Bromoacetanilide from Aniline, *J. Chem. Educ.* 94, 9, 1391–1394, 2017. <https://doi.org/10.1021/acs.jchemed.6b00749>
- [10] K. V. V. K. Mohan, N. Narender, S. J. Kulkarni, Zeolite catalyzed acylation of alcohols and amines with acetic acid under microwave irradiation, *Green Chem.*, 8, 368–372, 2006. DOI: 10.1039/b600031b.
- [11] N. Narender, P. Srinivasu, S. J. Kulkarni, K. V. Raghavan, *Synth. Commun.*, 30, 1887, 2000; N. Narender, P. Srinivasu, S. J. Kulkarni and K. V. Raghavan, *Green Chem.*, 3, 104, 2000.
- [12] R. Alleti, M. Perambuduru, S. Samantha and V. Prakash Reddy, *J. Mol. Catal. A*, 226, 57, 2005.
- [13] T. N. Parac-Vogt, K. Deleersnyder and K. Binnemans, *Eur. J. Org. Chem.*, 1810, 2005.
- [14] S. Velusamy, S. Borpuzari and T. Punniyamurthy, *Tetrahedron*, 2005, 61, 2011.
- [15] R. Ghosh, S. Maiti and A. Chakraborty, *Tetrahedron Lett.*, 46, 147, 2005.
- [16] C. Li, M. Wang, X. Lu, L. Zhang, J. Jiang, & L. Zhang, *ACS Sustainable Chemistry & Engineering*, 8(11), 4353–4361, 2020.
- [17] S. M. Rafiaei, A. Kim, & M. Shokouhimehr, *Nanoscience and Nanotechnology Letters*, 6(4), 309–313, 2014.
- [18] D. E. Raup, B. Cardinal-David, D. Holte, and K. A. Scheidt, Cooperative Catalysis by Carbenes and Lewis Acids in a Highly Stereo selective Route to γ -Lactams, *Nat Chem. Sep*; 2(9), 766–771, 2010.
- [19] K. C. Ashalu, N. Rao, MgSO_4 catalyzed one-pot multi-component reaction: Synthesis of amidoalkylnaphthols. *Journal of Chemical and Pharmaceutical Research*, Volume 5, Issue 2, Pages 44–47, 2013.
- [20] B. Karami, S. Khodabakhshi, A facile synthesis of phenazine and quinoxaline derivatives using magnesium sulfate heptahydrate as a catalyst, *J. Serb. Chem. Soc.* 76 (9) 1191–1198, 2011.
- [21] D. Yang, L. Wang, D. Li, R. Wang, Magnesium Catalysis in Asymmetric Synthesis, *Chem* 5, 1108–1166, May 9, 2019.