This article was downloaded by: [Moskow State Univ Bibliote] On: 18 February 2014, At: 06:54 Publisher: Taylor & Francis Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information: <u>http://www.tandfonline.com/loi/lsyc20</u>

CALCINED Mg-AI HYDROTALCITE AS A HETEROGENEOUS BASE CATALYST FOR GEWALD AMINOTHIOPHENE SYNTHESIS

R. Rajagopal , T. M. Jyothi , Thomas Daniel , K. V. Srinivasan & B. S. Rao Published online: 16 Aug 2006.

To cite this article: R. Rajagopal , T. M. Jyothi , Thomas Daniel , K. V. Srinivasan & B. S. Rao (2001) CALCINED Mg-AI HYDROTALCITE AS A HETEROGENEOUS BASE CATALYST FOR GEWALD AMINOTHIOPHENE SYNTHESIS, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 31:20, 3113-3117, DOI: <u>10.1081/SCC-100105884</u>

To link to this article: http://dx.doi.org/10.1081/SCC-100105884

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at http://www.tandfonline.com/page/terms-and-conditions

SYNTHETIC COMMUNICATIONS, 31(20), 3113–3117 (2001)

CALCINED Mg-AI HYDROTALCITE AS A HETEROGENEOUS BASE CATALYST FOR GEWALD AMINOTHIOPHENE SYNTHESIS

R. Rajagopal, T. M. Jyothi, Thomas Daniel, K. V. Srinivasan, and B. S. Rao*

National Chemical Laboratory, Pune 411008, India

ABSTRACT

Calcined Mg-Al hydrotalcite (Mg/Al = 4) has been conveniently employed as a heterogeneous base catalyst in the synthesis of 2-amino-3-cyanothiophenes adopting a one pot Gewald aminothiophene methodology.

The Gewald reaction constitutes a very useful and versatile method for the synthesis of 2-aminothiophene with an electron withdrawing substituent in the 3-position and alkyl and/or aryl groups in the 4- and 5-positions.¹ Aminothiophenes found their way as very important diazo components for azo dyes which give exotic colours with high tinctorial strength. The development of Gewald reaction for the synthesis of 2-amino-3-cyano, 2-amino-3-carbethoxy and 2-amino-3-carbonyl substituted thiophenes has been made

3113

Copyright © 2001 by Marcel Dekker, Inc.

www.dekker.com

^{*}Corresponding author.

ORDER		REPRINTS
-------	--	----------

RAJAGOPAL ET AL.

possible the synthesis of an enormous number of thieno-fused heterocycles of great medicinal interest such as thienopyrimidines and thienodiazepines.

In one version of Gewald reaction aliphatic aldehydes, ketones or β -dicarbonyl compounds react with active nitriles and sulfur in presence of amines. Amines such as diethyl amine and morpholine have been employed as catalysts. Both one step and two step routes have been adopted with numerous ketones and aldehydes or their Knoevanagel – Cope condensation products (Scheme 1). In particular, cyclic and heterocyclic saturated ketones have been used extensively.



Herein we report our preliminary results on the application of calcined Mg-Al htdrotalcite as a heterogeneous catalyst in the Gewald aminothiophene synthesis. Hydrotalcites are interesting class of materials, which can be utilized as precursors for mixed metal oxides with pronounced basic properties. They can be efficiently used as basic heterogeneous catalysts in many organic transformations such as aldol and Knoevenagel condensations,² epoxidation,³ cyanoethylation⁴ and Meerwein–Ponndorf–Verley reduction.⁵ Mg-Al hydrotalcites having Mg:Al=4:1 was synthesized using the procedure reported by Miyata et al.⁶ Typical XRD, IR, TGA and DTA patterns have substantiated the formation of hydrotalcites.

We have chosen methyl ethyl ketone and three cyclic ketones viz. cyclopentanone, cyclohexanone and cylcoheptanone for condensation with malononitrile in presence of sulfur to yield 2-amino-3-cyano-thiophenes (Scheme 2).

Results of Gewald reaction of cyclic ketones with malononitrile and sulfur are summarized in Table 1. The lower yield of the product in the case of cycloheptanone is attributed to the increasing nonbonded repulsive interaction between methylene protons in the middle and large sized rings fused to a planar five membered ring.⁷

Copyright @ Marcel Dekker, Inc. All rights reserved



ORDER	<u> </u>	REPRINTS
-------	------------	----------

GEWALD AMINOTHIOPHENE SYNTHESIS



3115



Table 1. Gewald Aminothiophene Synthesis over Calcined Mg-Al (Mg/Al=4) Hydrotalcite Catalyst^a

Substrate	Reaction time (h)	Yield (%)	
Cyclopentanone	12	85	
Cyclohexanone	8	91	
Cycloheptanone	14	56	
Ethyl Methyl Ketone	8	61	
Cyclohexanone ^b	12	88	
Cyclohexanone ^c	14	86	
Cyclohexanone ^d	9	90	

^aReaction conditions: cyclic ketone (0.002 moles), malononitrile (0.002 moles), sulfur (0.003 moles) and ethanol (7 ml), catalyst calcined in air at 450°C for 6 h (50 mg). ^{b-c}Second and third recycling. ^dUsed catalyst reactivated in air at 450°C.

In the first step of the reaction, ketone reacts with malononitrile to form α , β -unsaturated nitrile by Knoevanagel – Cope condensation. In the second step, sulfur reacts with the intermediate compound formed in the first step to complete the cyclization (Scheme 3). To investigate the catalytic influence in detail, we separately carried out the reaction of cyclohexanone and malononitrile with hydrotalcite (first step). The condensed product formed was isolated and made to react with sulfur in presence of the catalyst under same experimental conditions (second step). We found that the first step of the reaction is completed in 3 h and no condensation takes place in the absence of catalyst. The second step of the reaction was very slow and never attained completion. From the rate of reaction of both the steps, it can be concluded that the reaction proceeds essentially through the intermediate A.

The reusability of the catalyst was examined by using the filtered catalyst for subsequent reactions. The catalyst was found to be reusable without appreciable loss in activity.

Copyright © Marcel Dekker, Inc. All rights reserved

Marcel Dekker, Inc.

270 Madison Avenue, New York, New York 10016

ORDER		REPRINTS
-------	--	----------



In conclusion, we have demonstrated that calcined Mg-Al hydrotalcite catalysts can be successfully employed to replace secondary amines in Gewald synthesis of aminothiophenes. Hope this will open new vistas in the field of recyclable heterogeneous base catalysis in heterocyclic synthesis.

EXPERIMENTAL

Preparation of Mg-Al Hydrotalcite Catalyst

To an aqueous solution containing $Mg(NO_3)_2 \cdot 6H_2O$ and $Al(NO_3)_3 \cdot 9H_2O$ mixed at the required ratio, an aqueous solution of NaOH and Na₂CO₃ was added dropwise with stirring, until the pH reached 10. The slurry was stirred at 313 K for 13 h, filtered and washed with deionised water to the neutral pH and dried at 373 K for 24 h. Finally the catalyst was calcined at 723 K in air for 12 h.

Characterization of Catalysts

The physico-chemical characterization of the catalysts has been done by XRD, thermogravimetry and BET surface area measurements. The ICPES method was adopted to estimate the ratio of M^{II} and M^{III} ions in calcined hydrotalcite.

Reaction Procedure

All the reactions were carried out batch wise in a 100 ml R.B. flask fitted with a reflux condenser with constant stirring. One equivalents of cyclic ketone (0.002 moles), malononitrile (0.002 moles) and 1.1 equivalents of sulfur (0.003 moles) and 7 ml ethanol as solvent were taken in a round bottom flask. 50 mg of freshly activated hydrotalcite catalyst was added to this suspension and temperature slowly raised to 60°C. Reaction was mon-

Copyright © Marcel Dekker, Inc. All rights reserved

Marcel Dekker, Inc.

270 Madison Avenue, New York, New York 10016

3116

ORDER		REPRINTS
-------	--	----------

itored by T.L.C. (eluent 10% ethylacetate in petroleum ether). After the reaction, the catalyst was filtered off, filtrate extracted with ethylacetate and finally purified by column chromatography. Physico-chemical characterization of the products were performed using NMR, MS, IR, elemental analysis and melting point determination. In the case of methyl ethyl ketone, the ketone itself was used as solvent instead of ethanol.

ACKNOWLEDGMENT

R.R. thanks CSIR, New Delhi for the award of Senior Research Fellowhip.

REFERENCES

- 1. Gewald, K.; Schinke, E.; Bottcher, H. Chem. Ber. 1966, 99, 94.
- Lakshmi Kantam, M.; Choudary, B.M.; Venkat Reddy, Koteswara Rao, K.; Figueras, F. Chem. Commun. 1998, 1033.
- Ueno, S.; Yamaguchi, K.; Yoshida, K.; Ebitani, K.; Kaneda, K. Chem. Commun. 1998, 295.
- Kumbhar, P.S.; Sanchez-valente, J.; Figueras, F. Chem. Commun. 1998, 1091.
- 5. Kumbhar, P.S.; Sanchez-valente, J.; Lopez, J.; Figueras, F. Chem. Commun. 1998, 535.
- 6. Miyata, S.; Kumura, T.; Shimada, M. U.S. Pat. 1975, 3, 879523.
- Rosowsky, A.; Chaykowsky, M.; Chan, K.K.N.; Lin, M.; Modest, E.J. J. Med. Chem. 1973, 16, 185.

Received in the Netherlands December 20, 2000

Downloaded by [Moskow State Univ Bibliote] at 06:54 18 February 2014



3117

Request Permission or Order Reprints Instantly!

Interested in copying and sharing this article? In most cases, U.S. Copyright Law requires that you get permission from the article's rightsholder before using copyrighted content.

All information and materials found in this article, including but not limited to text, trademarks, patents, logos, graphics and images (the "Materials"), are the copyrighted works and other forms of intellectual property of Marcel Dekker, Inc., or its licensors. All rights not expressly granted are reserved.

Get permission to lawfully reproduce and distribute the Materials or order reprints quickly and painlessly. Simply click on the "Request Permission/Reprints Here" link below and follow the instructions. Visit the <u>U.S. Copyright Office</u> for information on Fair Use limitations of U.S. copyright law. Please refer to The Association of American Publishers' (AAP) website for guidelines on <u>Fair Use in the Classroom</u>.

The Materials are for your personal use only and cannot be reformatted, reposted, resold or distributed by electronic means or otherwise without permission from Marcel Dekker, Inc. Marcel Dekker, Inc. grants you the limited right to display the Materials only on your personal computer or personal wireless device, and to copy and download single copies of such Materials provided that any copyright, trademark or other notice appearing on such Materials is also retained by, displayed, copied or downloaded as part of the Materials and is not removed or obscured, and provided you do not edit, modify, alter or enhance the Materials. Please refer to our <u>Website</u> User Agreement for more details.

Order now!

Reprints of this article can also be ordered at http://www.dekker.com/servlet/product/DOI/101081SCC100105884