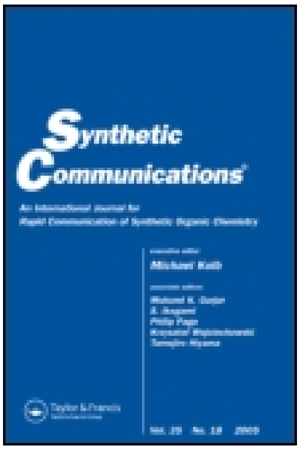
This article was downloaded by: [University of Glasgow]
On: 12 June 2013, At: 07:32
Publisher: Taylor & Francis
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



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

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

BENZYLTRIMETHYLAMMONIUM HYDROXIDE CATALYSED NITROALDOL CONDENSATION

Vivek J. Bulbule [a] , G. K. Jnaneshwara [a] , Ravindra R. Deshmukh [a] , Hanumant B. Borate [a] & Vishnu H. Deshpande [b]

[a] Division of Organic Chemistry, Technology, National Chemical Laboratory, Pune, 411 008, India

[b] Division of Organic Chemistry, Technology, National Chemical Laboratory, Pune, 411 008, India

Published online: 16 Aug 2006.

To cite this article: Vivek J. Bulbule , G. K. Jnaneshwara , Ravindra R. Deshmukh , Hanumant B. Borate & Vishnu H. Deshpande (2001): BENZYLTRIMETHYLAMMONIUM HYDROXIDE CATALYSED NITROALDOL CONDENSATION, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 31:23, 3623-3626

To link to this article: http://dx.doi.org/10.1081/SCC-100107010

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.tandfonline.com/page/terms-and-conditions

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.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae, and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand, or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

SYNTHETIC COMMUNICATIONS, 31(23), 3623–3626 (2001)

BENZYLTRIMETHYLAMMONIUM HYDROXIDE CATALYSED NITROALDOL CONDENSATION

Vivek J. Bulbule, G. K. Jnaneshwara,
Ravindra R. Deshmukh, Hanumant B. Borate,
and Vishnu H. Deshpande*

Division of Organic Chemistry, Technology,
National Chemical Laboratory,
Pune – 411 008, India

ABSTRACT

Benzyltrimethylammonium hydroxide is found to be a very efficient catalyst for nitroaldol condensation in a short time with excellent yield.

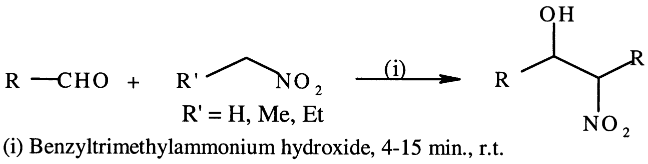
The nitroaldol condensation is a key reaction in the synthesis of several biologically active compounds.[1] The nitro group of nitroaldol products can be easily functionalised to amine,[2] can be converted into carbonyl compounds,[3] and easily denitrated by further functional group manipulations.[4] Several catalysts have been reported in literature to effect the Henry reaction e.g. alumina,[5] amberlyst A-21,[6(a)] Mg–Al–Hydrotalcite,[6(b)] KF on alumina,[7] NaOH with the surfactant catalyst hexadecyltrimethylammonium

---

*Corresponding author. Fax: +91 020 5893614.

www.dekker.com

chloride[8] etc. Recently TBAF hydrate[9] has been used, but the use of 1 to 2 equivalents suppresses its use in synthetic organic chemistry. The classical nitroaldol reaction, performed by using strong bases, often results in the formation of side products by the aldol condensation and Cannizzaro



Scheme 1.

Table 1. Benzyltrimethylammonium Hydroxide Catalyzed Preparation of Nitroalkanols[a]

Entry	R	Nitroalkane	Time (min)	Yield[b](%)
1	*p*-Chlorophenyl	Nitroethane[c]	10	91
		Nitroethane[d]	6	95
2	*p*-Nitrophenyl	Nitroethane[d]	4	98
3	*p*-Methoxyphenyl	Nitroethane[c]	12	90
		Nitroethane[d]	8	94
4	2-Furyl	Nitroethane[c]	8	81
		Nitroethane[d]	6	85
5	*o*-Chlorophenyl	Nitroethane[d]	10	94
6	*m*-Nitrophenyl	Nitroethane[d]	4	98
7	Phenyl	Nitroethane[c]	10	83
		Nitroethane[d]	6	88
8	*o*-Hydroxyphenyl	Nitroethane[c]	15	91
		Nitroethane[d]	12	86
9	3,4,5-Trimethoxyphenyl	Nitroethane[c]	10	82
		Nitroethane[d]	8	93
10	2-Chloro-3-quinolinyl	Nitroethane[d]	6	80
11	Isobutyl	Nitroethane[c]	8	78
		Nitroethane[d]	5	80
12	*m*-Nitrophenyl	Nitromethane[c]	8	92
		Nitromethane[d]	5	98
13	*m*-Nitrophenyl	Nitropropane	6	98

[a]All the nitroalkanols showed satisfactory spectroscopic data. [b]Isolated yield after column chromatographic purification. [c]1.1 equivalent of nitroalkane. [d]Nitroalkane used in excess.

reaction of aldehydes or olefin formation. In our continuing interest [6(b)] to explore the utility of various catalysts to effect the Henry reaction we have developed a convenient and quick method for the effective synthesis of nitroaldols using benzyltrimethylammonium hydroxide as a catalyst to give excellent yields of nitroaldols (Scheme 1) and we wish to report our results herein.

When aldehydes were stirred with 1.1 equivalent of nitroalkanes in water containing a few drops of THF,[10] in presence of catalytic amount of benzyltrimethylammonium hydroxide at room temperature the desired nitroaldol products were formed in excellent yields. The substrates containing electron withdrawing groups were found to undergo faster reaction (Entries 2, 6, 12 and 13) compared to electron rich substituted aromatic compounds and give almost quantitative yield. An aliphatic aldehyde also underwent nitroaldol condensation (Entry 11). Efforts were made to achieve quantitative yields by modifying reaction parameters. It was observed that instead of using a mixture of water and THF as solvent, when reactions were run using an excess of nitroalkane, various aldehydes underwent nitroaldol reactions in almost quantitative yields and in a short period of 4–15 min (Table 1).

In conclusion, we have demonstrated that benzyltrimethylammonium hydroxide can be used as an effective catalyst to prepare various nitroalkanols in excellent yields by nitroaldol condensation.

ACKNOWLEDGMENTS

VJB thanks LTMT Mumbai, JGK and RRD thank CSIR, New Delhi, for the award of senior research fellowship.

REFERENCES

1. (a) Koshinen, P.M.; Koshinen, A.M.P. Synthesis **1998**, 1975; (b) Rosini, G.; Ballini, R. Synthesis **1988**, 833; (c) Tsay, S.C.; Patel, V.H.; Hwu, J.R. Synlett **1998**, 939; (d) Ballini, R.; Bosica, G. Eur. J. O. Chem. **1998**, *2*, 355; (e) Scarpi, D.; Occhiato, E.G.; Guorna, A. J. Org. Chem. **1999**, *64*, 1727.
2. Barett, A.G.M.; Spilling, D.C. Tetrahedron Lett. **1988**, *29*, 5733.
3. (a) Ceccherelli, P.; Curini, M.; Marcotullio, M.C.; Epifano, F.; Rosati, O. Synthetic Comm. **1998**, *28*, 3057; (b) Adam, W.; Makosza, M.C.; Moller C.R.; Zhao, C.G. Synlett **1998**, 1335; (c) Ballini, R.; Papa, F.; Abate, C. Eur. J. O. Chem. **1999**, *1*, 87.

4. (a) Ono, N.; Kaji, A. Synthesis **1986**, 693; (b) Ballini, R.; Curini, M.; Epifano, F.; Marcotullio, M.C.; Rosati, O. Synlett **1998**, 1049 and references cited therein; (c) Rosini, G.; Ballini, R. Synthesis **1988**, 833.
5. Rosini, G.; Ballini, R.; Sorrenti, P. Synthesis **1983**, 1014.
6. (a) Ballini, R.; Petrini, M.; Rosini, G. Synthesis **1987**, 711; (b) Bulbule, V.J.; Deshpande, V.H.; Velu, S.; Sudalai, A.; Sivasanker, S.; Sathe, V.T. Tetrahedron **1999**, *55*, 9325.
7. Melot, J.M.; Texier-Boullet, F.; Foucraud, A. Tetrahedron Lett. **1986**, *7*, 493.
8. Ballini, R.; Bosica, G. J. Org. Chem. **1997**, *62*, 425.
9. Hanessian, S.; Devasthale, P. Tetrahedron Lett. **1996**, *37*, 987.
10. Experimental procedure: To a mixture of 3-nitrobenzaldehyde (500 mg, 3.31 mmole) and nitroethane (272 mg, 3.63 mmole) in water (5 ml) and THF (0.4 ml) was added 1 drop of benzyltrimethylammonium hydroxide (40% aq. solution) at room temperature. The mixture was stirred at room temperature for 4 min. After the reaction was complete (TLC), excess water was added and the aqueous layer was extracted with chloroform (2×20 ml). The combined organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography to afford 1-(3-nitrophenyl)-2-nitropropan-1-ol (734 mg, 98%); ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.40 (d, J = 7.3 Hz, 3H), 3.46 (d, J = 4 Hz, 1H, D_2O exchangeable), 4.70–4.85 (m, 1H), 5.22 (dd, J = 7.5 Hz, 4 Hz, 1H), 7.60 (t, J = 8.1 Hz, 1H), 7.70–7.80 (m, 1H), 8.15–8.30 (m, 2H); MS (*m*/*z* rel. intensity %) 226 M^+ (5), 179 (45), 151 (76), 150 (95), 149 (100), 135 (8), 121 (5), 115 (10), 105 (50), 90 (9) and 77 (52).

Received in the UK October 30, 2000

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

Downloaded by [University of Glasgow] at 07:32 12 June 2013

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.S. Copyright Office for information on Fair Use limitations of U.S. copyright law. Please refer to The Association of American Publishers' (AAP) website for guidelines on Fair Use in the Classroom.

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 Website User Agreement for more details.

Order now!

Reprints of this article can also be ordered at
http://www.dekker.com/servlet/product/DOI/101081SCC100107010