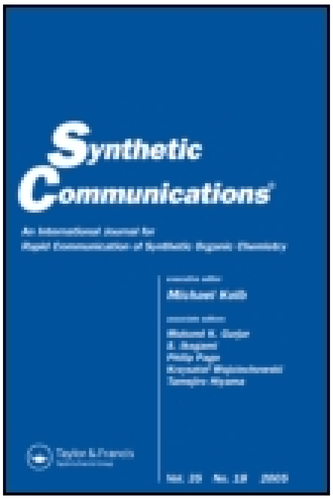
This article was downloaded by: [Monash University Library]
On: 04 December 2014, At: 00:06
Publisher: Taylor & Francis
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



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

Mukaiyama Aldol Reactions of Silyl Enolates Catalyzed by Iodine

Prodeep Phukan [a]
[a] Department of Chemistry , Gauhati University , Guwahati, 781014, Assam, India

Published online: 21 Aug 2006.

To cite this article: Prodeep Phukan (2004) Mukaiyama Aldol Reactions of Silyl Enolates Catalyzed by Iodine, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 34:6, 1065-1070, DOI: 10.1081/SCC-120028638

To link to this article: http://dx.doi.org/10.1081/SCC-120028638

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®
Vol. 34, No. 6, pp. 1065–1070, 2004

Mukaiyama Aldol Reactions of Silyl Enolates Catalyzed by Iodine

Prodeep Phukan*

Department of Chemistry, Gauhati University, Guwahati, Assam, India

ABSTRACT

Iodine catalyzed Mukaiyama aldol reaction of silyl enol ethers and silyl ketene acetal with aldehydes, ketones and acetals in good yield with preferential antiselectivity has been described.

Key Words: Iodine; Mukaiyama aldol; Silyl enol ether; Silyl keten acetal; Aldehydes; ketones.

The aldol addition reaction has long been considered as one of the most versatile carbon–carbon bond forming reactions in organic synthesis. In particular, cross aldol reactions of silyl enol ethers which proceed in a highly regioselective manner to afford adducts in high yield. Since the discovery of Mukaiyama aldol reaction[1] promoted by $TiCl_4$, a variety of catalysts have been used to activate this process.[2] Many catalysts are fraught with

---

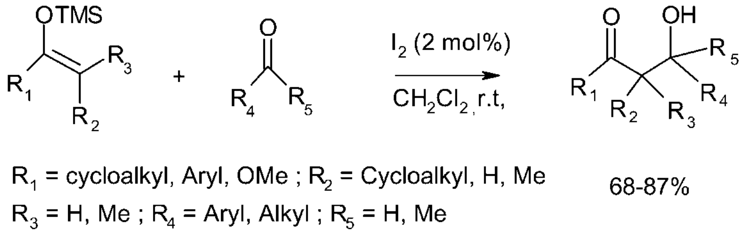
*Correspondence: Prodeep Phukan, Department of Chemistry, Gauhati University, Guwahati-781014, Assam, India; E-mail: pphukan@yahoo.com.

DOI: 10.1081/SCC-120028638
0039-7911 (Print); 1532-2432 (Online)

www.dekker.com

limitations such as the use of stoichiometric amount of catalyst, moisture sensitivity of the catalyst, expensive reagents etc. Although recent reports claimed significant improvement circumventing these drawbacks, new methods are still desirable. Recently, Li and co-workers reported[2k] the use of $Et_2O : MgI_2$ as a catalyst for aldol reactions, however this method suffers from a draw back related to stringent dry reaction medium. In recent times, iodine has been emerging as an effective catalyst for various organic transformations.[3] The advantages in the use of iodine are (1) mild neutral condition (2) inexpensive reagent (3) no stringent dry conditions required. We describe herein an efficient and convenient procedure for Mukaiyama aldol reactions in the presence of a catalytic amount of iodine (Sch. 1).

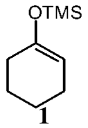
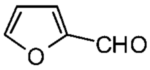
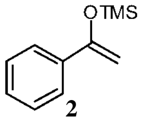
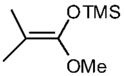
The catalytic effect of iodine was evaluated for three representative silyl enol ethers *viz.* 1-[(trimethylsilyl)oxy]-1-cyclohexene, 1-[(trimethylsilyl)oxy]-1-phenylethylene and 1-methoxy-2-methyl-1-(trimethylsilyloxy)-1-propene with various carbonyl compounds (Sch. 1). Reaction proceeds well with different carbonyl compounds such as aldehyde, ketones, and acetals with good yields (Table 1). The optimum amount of iodine needed to catalyze the reaction is only 2 mol% based on the electrophile used. Initially, the reaction was performed with 1-[(trimethylsilyl)oxy]-1-cyclohexene and banzaldehyde. In a typical procedure, the enol ether, electrophile and iodine were stirred in dichloromethane at room temperature for appropriate time. In general, the crude product contains alcohol in a major amount and the trimethyl silylolxy compound in a minor amount. After completion of the reaction, methanol was added to ensure complete deprotection of the silyl group.[4] Selectivity is temperature dependent as seen from the Table 1 (entry 2 and 3). The ratio of the stereo-isomers (syn/anti) was determined by comparing the intensities of the methine proton signal (—CH—O) in the ^{1}H-NMR spectrum of the crude product and matching the data reported[2] elsewhere. As expected, aromatic aldehydes react faster than aliphatic one. From the results, it could be observed that there is a general trend for antiselectivity, irrespective of the nature of aldehydes. The aldol reaction was



Scheme 1.

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

Table 1. Iodine catalysed Mukaiyama aldol reactions of different silyl enolates with electrophiles.

Entry	Enol ether	Electrophiles	Time (h)	Yield (%)[a]	Syn/anti[b,c]
1.	 **1**	PhCHO	1.5	84	24 : 76[d]
2.	**1**	PhCHO	1.5	84	30 : 70[e]
3.	**1**	PhCHO	2	87	48 : 52[f]
4.	**1**	*p*-MeO-PhCHO	1.5	78	28 : 72[g]
5.	**1**	*p*-NO_2-PhCHO	1.5	79	30 : 70[h]
6.	**1**	*p*-Cl-PhCHO	1.5	79	30 : 70[i]
7.	**1**		1.5	82	25 : 75[j]
8.	**1**	$(CH_3)_2CHCHO$	2	73	34 : 66[k]
9.	 **2**	PhCHO	1.5	87	—
10.	**2**	$(CH_3)_2CHCHO$	2	75	—
11.	**2**	$HCH(OMe)_2$	1.5	68	—
12.	**2**	$PhCH(OMe)_2$	1.5	78	—
13.	**2**	CH_3COCH_3	5	71	—
14.	**2**	$CH_3(CH_2)_2COC$	5	68	—
15.	 **3**	PhCHO	2.5	80	—
16.	**3**	*p*-NO_2-PhCHO	2.5	80	—
17.	**3**	*p*-Cl-PhCHO	2.5	77	—
18.	**3**	$(CH_3)_3CH_2CHO$	3	70	—

[a] Isolated yield after chromatographic purification.

[b] Products are characterized by ^1H, ^{13}C NMR, IR spectroscopy and mass spectrometry.

[c] Stereoisomer ratios are determined by ^1H NMR analysis.

[d] Ref.[1b,2b,2l,2m].

[e] Temp. 0°C.

[f] Temp. −78°C.

[g] Ref.[2g,2l].

[h] Ref.[2g,2l].

[i] Ref.[2g,2l].

[j] Ref.[2b,2m].

[k] Ref.[1b,2b].

also performed with acetal (Table 1, entry 11, 12) and ketones (Table 1, entry 13, 14). Reaction proceeds well with acetals as well as ketones in good yield.

Mechanism of the reaction is not yet studied. There are two mechanisms known[1b,5] in the literature in case of metal catalyzed aldol reaction. The most well accepted mechanism is the formation of a six-membered transition state at the intermediate stage.[1b] The second pathway was observed by Seto[5] which proceeds via an initial electron transfer from the enol-ether to the co-ordinated metal. In our case, the second pathway is most likely wherein the reaction proceeds via initial co-ordination of iodine with aldehyde and then electron transfer between silyl enol ether and iodine.

In conclusion, a simple process for aldol reactions catalyzed by iodine has been demonstrated.

EXPERIMENTAL

Iodine was purified by sublimation before use. ^{1}H NMR and ^{13}C NMR spectra were recorded in Bruker 400 MHz instrument in $CDCl_3$, using TMS as internal standard. IR spectra were recorded in Perkin-Elmer Spectrum RXI FT-IR spectrometer. Mass spectra were recorded on a Finnigan mass spectrometer using ionization energy of 70 eV and elemental analysis was carried out in Perkin-Elmer 2400 Series II elemental analyzer.

Typical Procedure

Silyl enol ether (1.1 mmol) in dichloromethane (1 mL) was added to a solution of aldehyde (1 mmol), and iodine (0.02 mmol) in dichloromethane (1 mL) and stirred at room temperature. After completion of reaction (TLC), of methanol (10 mL) was added and stirred for 1 hr. Sodium thiosulfate (20 mg) was added, the reaction mixture stirred for 10 min and evaporated. The residue was taken up in ether, washed with brine, dried (Na_2SO_4) and concentrated. Purification of the crude product by flash chromatography on silica gel (230–400 mesh) with petroleum ether −EtOAc as eluent gave the pure product (70–87%).

3-Hydroxy-3-methyl-1-phenyl-1-hexanone. IR (neat): 3492, 2960, 2933, 1670, 1597, 1449, 1374, 1213 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 0.91 (t, $J = 7.3$ Hz, 3H), 1.31–1.47 (m, 2H), 1.52–1.61 (m, 2H), 3.11 (dd, $J = 23.6$, 17.1 Hz), 4.1 (s, 1H), 7.45 (t, $J = 8.1$ Hz, 1H), 7.94 (d, $J = 7.3$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 14.57, 17.33, 27.03, 44.7, 46.9, 71.97, 128.04, 128.68, 133.56, 137.35, 202.06. MS: (m/z, % rel. intensity) 191(4), 163(31), 145(2), 129(5), 120(20), 105 (100), 91 (3), 77 (38), 71 (20), 43 (42).

Analysis: $C_{13}H_{18}O_2$ requires C, 75.69 and H, 8.79 %; found: C, 75.64 and H, 8.72%.

Methyl 3-hydroxy-2,2-dimethyl-3-(4-nitrophenyl)propanoate. Mp. 115–117°C (Lit[6] 114–116°C); IR ($CHCl_3$, cm^{-1}): 3461, 3055, 2986, 1732, 1606, 1523, 1470, 1435, 1349, 1265. ^1H NMR (400 MHz, $CDCl_3$): 1.11(s, 3H), 1.12(s,3H), 3.43 (bs, 1H), 3.72 (s, 3H), 4.99 (s, 1H), 7.47 (d, $J = 8.59$ Hz, 2H), 8.16 (d, $J = 8.84$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): 19.13, 22.74, 47.60, 52.36, 77.69, 122.9, 128.56, 174.23, 174.47, 177.74. MS: (m/z, % rel. intensity): 254 (68), 236 (77), 194 (2), 180 (6), 166 (8), 128 (4), 115 (11), 105 (26), 102 (100), 87 (34), 73 (24).

ACKNOWLEDGMENT

I am thankful to Dr. N. C. Barua of RRL, Jorhat, India, for constant encouragement and DST, New Delhi for financial support.

REFERENCES

1. (a) Mukaiyama, T.; Narasaka, K.; Banno, K. Chem. Lett. **1973**, 1011; (b) Mukaiyama, T.; Benno, K.; Narasaka, K. J. Am. Chem. Soc. **1974**, *96*, 7503.
2. (a) Ohki, H.; Wada, M.; Akiba, K. Tetrahedron Lett. **1988**, *29*, 4719; (b) Kawai, M.; Onaka, M.; Izumi, Y. Bull. Chem. Soc. Jpn. **1988**, *61*, 1237; (c) Sato, T.; Wakahara, Y.; Otera, J.; Nozaki, H. Tetrahedron **1991**, *47*, 9773; (d) Roux, C.L.; Itoughmane, H.G.; Dubac, J.; Jaud, J.; Vignaux, P. J. Org. Chem. **1993**, *58*, 1835; (e) Kobayashi, S.; Hachiya, I.; Ishitani, H.; Araki, M. Synlet **1993**, 472; (f) Ishihara, K.; Hananki, N.; Yamamoto, H. Synlett **1993**, 577; (g) Ranu, B.C.; Chakrabarty, R. Tetrahedron **1993**, *49*, 5333; (h) Reetz, M.T.; Fox, D.N.A. Tetrahedron Lett. **1993**, *34*, 1119; (i) Van de Weghe, P.; Collin, J. Tetrahedron Lett. **1993**, *34*, 3881; (j) Nakamura, H.; Matsuhashi, H.; Arata, K. Synlett **2000**, 668; (k) Li, W-D.Z.; Zhang, X-X. Org. Lett. **2002**, *4*, 3485; (l) Nakamura, E.; Shimizu, M.; Kuwajima, I.; Sakata, J.; Yokoyama, K.; Noyori, Y. J. Org. Chem. **1983**, *48*, 932; (m) Noyori, R.; Nishida, I.; Sakata, J. J. Am. Chem. Soc. **1983**, *105*, 1598.
3. (a) Yadav, J.S.; Reddy, B.V.S.; Rao, C.V.; Reddy, M.S. Synthesis **2003**, 247; (b) Karimi, B.; Golshani, B. Synthesis **2002**, 784; (c) He, Z.; Gao, G.; Hand, E.S.; Kispert, L.D.; Strand, A.; Liaaen-Jensen, S. J. Phys. Chem. A **2002**, *106*, 2520; (d) Xu, X.; Zhang, Y. Synth. Commun. **2002**, *32*, 2643; (e) Basu, M.K.; Samajdar, S.; Becker, F.F.; Banik, B.K. Syn. Lett. **2002**,

319; (f) Yadav, J.S.; Reddy, B.V.S.; Rao, C.V.; Rao, K.V. J. Chem. Soc. Perkin Trans. 1 **2002**, 1401; (g) Ramalinga, K.; Vijayalakshmi, P.; Kaimal, T.N.B. Tetrahedron Lett. **2002**, *43*, 879; (h) Yadav, J.S.; Chand, P.K.; Anjaneyulu, S. Tetrahedron Lett. **2002**, *43*, 3783; (i) Periana, R.A.; Mirinov, O.; Taube, D.J.; Gamble, S. Chem. Commun. **2002**, 2376; (j) Firouzabadi, H.; Iranpoor, N.; Sobhani, S. Tetrahedron Lett. **2002**, *43*, 3653; (k) Firouzabadi, H.; Iranpoor, N.; Hazarkhani, H.J. Org. Chem. **2001**, *66*, 7527; (l) Deka, N.; Sarma, J.C. J. Org. Chem. **2001**, *66*, 1947.

4. Vaino, A.R.; Szarek, W.A. Chem. Commun. **1996**, 2351.
5. Sato, T.; Wakahara, Y.; Otera, J.; Noyaki, H. J. Am. Chem. Soc. **1991**, *113*, 4028.
6. Creger, P.L. Tetrahedron Lett. **1972**, 79.

Received in India September 22, 2003

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

Downloaded by [Monash University Library] at 00:06 04 December 2014

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/ Order Reprints" 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.

Request Permission/Order Reprints

Reprints of this article can also be ordered at http://www.dekker.com/servlet/product/DOI/101081SCC120028638