This article was downloaded by: [University of Maastricht] On: 27 October 2014, At: 13:02 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>

Studies on Bromination of Active Methylene by a Mixture of Hydrobromic Acid and Hydrogen Peroxide (or TBHP)

Vasudha H. Tillu^a, Popat D. Shinde^a, Ashutosh V. Bedekar^a & Radhika D. Wakharkar^a ^a Division of Organic Chemistry: Technology, National Chemical Laboratory, Pune, India Published online: 15 Aug 2006.

To cite this article: Vasudha H. Tillu, Popat D. Shinde, Ashutosh V. Bedekar & Radhika D. Wakharkar (2003) Studies on Bromination of Active Methylene by a Mixture of Hydrobromic Acid and Hydrogen Peroxide (or TBHP), Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 33:8, 1399-1403, DOI: 10.1081/SCC-120018701

To link to this article: http://dx.doi.org/10.1081/SCC-120018701

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



©2003 Marcel Dekker, Inc. All rights reserved. This material may not be used or reproduced in any form without the express written permission of Marcel Dekker, Inc.

SYNTHETIC COMMUNICATIONS[®] Vol. 33, No. 8, pp. 1399–1403, 2003

Studies on Bromination of Active Methylene by a Mixture of Hydrobromic Acid and Hydrogen Peroxide (or TBHP)

Vasudha H. Tillu, Popat D. Shinde, Ashutosh V. Bedekar, and Radhika D. Wakharkar*

> Division of Organic Chemistry: Technology, National Chemical Laboratory, Pune, India

ABSTRACT

Studies on bromination of active methylene with a mixture of hydrogen peroxide or *tert*-butylhydroperoxide (TBHP) and hydrobromic acid are discussed. Substituted acetophenones, benzocyclic ketones provide α -bromo-keto compounds in high yields under this reaction condition.

Key Words: Oxyhalogenation; Active methylene; H₂O₂; TBHP; HBr.

1399

DOI: 10.1081/SCC-120018701 Copyright © 2003 by Marcel Dekker, Inc. 0039-7911 (Print); 1532-2432 (Online) www.dekker.com

^{*}Correspondence: Radhika D. Wakharkar, Division of Organic Chemistry: Technology, National Chemical Laboratory, Pune 411008, India; Fax: +91-20-5893614; E-mail: rdw@dalton.ncl.res.in.

©2003 Marcel Dekker, Inc. All rights reserved. This material may not be used or reproduced in any form without the express written permission of Marcel Dekker, Inc.

1400

Tillu et al.

We have reported^[1] a simple and efficient protocol for the halogenation of arenes, alkenes, and alkynes using a combination of hydrohalic acid and hydrogen peroxide or *tert*-butylhydroperoxide (TBHP).

During the studies on the oxyhalogenation of variously substituted arenes using our protocol^[1] when acetophenone was subjected to bromination reaction, side chain bromination was preferred over aromatic bromination. The scope and generality of this observation is discussed in the present communication.

RESULTS AND DISCUSSION

Table 1 depicts the results of bromination of active methylenes (α - to keto group) in substituted acetophenones. It was found that they undergo α -bromination (Table 1, Entries 1–7) in high yields using hydrogen peroxide or TBHP as oxidants.

However, acetophenones with free hydroxyl function (phenolic, Entries 8 and 9) resulted into aromatic bromination, which is in agreement with our earlier^[1] observation. TBHP exhibited excellent selectivity for monobromination in case of cyclic ketones (Sch. 1) viz. indanone and tetralone (Entries 11 and 12) whereas H_2O_2 was required in large excess (Entry 10) for completion of reaction which furnished the dibrominated product as the single product in 89% yield. The reagent was found to be selective for bromination of active methylene as no bromination of benzylic positions was observed. Similar difference in the activity of the oxidants was observed and discussed in our previous publications. It is noteworthy that bromination of ethyl acetoacetate could be controlled (Entry 13) to obtain only monobrominated product in 99% yield in the presence of several vulnerable positions for bromination.

EXPERIMENTAL

General Procedure

Progress of reactions was monitored by TLC using Merck silica gel 60 F254 precoated plates and spots were visualized under UV light or on exposure to I_2 vapors. NMR spectra were recorded at 200 MHz in CDCl₃ using TMS as internal standard. Hydrogen peroxide (30% w/v) was procured from Asian chemicals, India and *tert*-butylhydroperoxide (TBHP, 70% w/v) was obtained from Aldrich Chemicals, India.

MARCEL DEKKER, INC. • 270 MADISON AVENUE • NEW YORK, NY 10016

©2003 Marcel Dekker, Inc. All rights reserved. This material may not be used or reproduced in any form without the express written permission of Marcel Dekker, Inc.

Bromination of Active Methylene by TBHP				1401
		Table 1.		
Entry	Substrate	Reaction condition	Product	% yield ^a
1		Dioxan HBr (1.5) HaQa (1.1)	₿r Br	95
2		Dioxan HBr (1.1) TBHP (1.1)	Br	85
3		Dioxan HBr (1.1) H ₂ O ₂ (1.1)	Br	93
4		Dioxan HBr (1.1) TBHP (1.1)	Br	87
5	O_N N_LO	Dioxan HBr (1.5) H ₂ O ₂ (1.1)	O ₂ N Br	75
6		Dioxan HBr (1.1) H ₂ O ₂ (1.1)	Cl O Br	94
7		Dioxan HBr (1.1) TBHP (1.1)	Cl O Br	90
8	но	Dioxan HBr (1.5) H ₂ O ₂ (1.1)	но Вг.	90
9	CI Me OH	Dioxan HBr (1.2) H_2O_2 (1.1)	CI Me OH	98
10		Methanol HBr (4.0) H ₂ O ₂ (4.0)	Br	89
11		Dioxan HBr (1.1) TBHP (1.1)	O Br	65
12		Dioxan HBr (1.1) TBHP (1.1)	D Br	64
13	COOC2H,	CH_2Cl_2 HBr (1.5) H_2O_2 (1.1)	BT→COOC2H3 COOC2H3	99

^aIsolated yield, characterized by usual spectral analysis.

©2003 Marcel Dekker, Inc. All rights reserved. This material may not be used or reproduced in any form without the express written permission of Marcel Dekker, Inc.

1402

Tillu et al.



Aqueous hydrobromic acid (47%) was purchased from S.D. Fine Chemicals, India.

Preparation of 2 Bromo-1-(4-methylphenyl)-l-ethanone (Table 1: Entry 4)

A solution of TBHP (70% aq. 0.25 mL 2 mmol) was added to a cooled mixture of HBr (48% aq. 0.34 mL, 2 mmol) in dioxan (5 mL) and the mixture stirred for 5 min. To this cold solution 4-methylphenyl-1-ethanone (0.268 g, 2 mmol) was added, stirred at same temperature for 30 min and then refluxed for 20 h. On completion of reaction (TLC) the solvent was evaporated and the product was taken in 5 mL water, extracted with EtOAc ($3 \times 10 \text{ mL}$) washed with water and brine, dried on sodium sulphate and concentrated on rotary evaporator to afford a yellowish solid. The product was purified by flash colum chromatography over silica gel to afford pure product (0.370 g, 86.85%). IR: ν 2991.83, 2922, 1659, 1583, 1171, 650 cm⁻¹, ¹H NMR: (CDCl₃) δ 2.4 (s, 3H) 4.4 (s, 2H), 7.22–7.27 (m, 2H), 7.84 (m, 2H). MS (*m*/*z*): 212 (M+), 164 (20), 119 (100), 105 (20), 91 (100), 77 (20), 65 (50). Elemental analysis: Calculated for C₉H₉BrO, C: 50.70, H: 4.22, Br: 37.08, Found C: 51.25, H: 4.29, Br: 37.06.

In conclusion we have demonstrated regioselective bromination of active methylene in high yields by applying a combination of hydrobromic acid and hydrogen peroxide or TBHP under mild reaction condition in high yield. This method provides simple work-up, easy purification and economical process for industrial applications.

ACKNOWLEDGMENT

A. V. B. and P. D. S. wish to thank CSIR New Delhi for the award of Pool Officership and Senior Research Fellowship, respectively.

©2003 Marcel Dekker, Inc. All rights reserved. This material may not be used or reproduced in any form without the express written permission of Marcel Dekker, Inc.

Bromination of Active Methylene by TBHP

1403

REFERENCE

 (a) Barhate, N.B.; Garjare, A.S.; Wakharkar, R.D.; and Bedekar. Simple and practicle halogenation of arenes, alkenes, and alkynes with hydrohalic acid/H₂O₂ (or TBHP). A.V. Tetrahedron 1999, 55, 11127; (b) Barhate, N.B.; Gajare, A.S.; Wakharkar, R.D.; Bedekar. Simple and efficient chlorination and bromination of aromatic compounds with aqueous TBHP (or H₂O₂) and a hydrohalic acid. A.V. Tetrahedron Lett. 1998, 39, 6349.

Received in the Netherlands June 5, 2002



©2003 Marcel Dekker, Inc. All rights reserved. This material may not be used or reproduced in any form without the express written permission of Marcel Dekker, Inc.