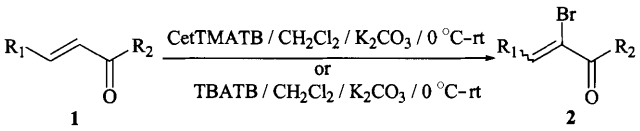
A Convenient and Useful Method of Preparation of α-Bromo Enones from the Corresponding Enones Using Organic Ammonium Tribromide (OATB)[1]

Gopal Bose, Pankaj M. Bujar Barua, Mihir K. Chaudhuri, Dipak Kalita, and Abu T. Khan*
Department of Chemistry, Indian Institute of Technology, Guwahati 781039, Assam, India

(Received December 19; CL-001140)

Various acyclic α-bromo enones **2** as well as cyclic α-bromo enones **4** can be prepared from the corresponding acyclic enones **1** and cyclic enones **3** respectively, in a one-pot procedure by employing organic ammonium tribromide, such as cetyltrimethylammonium tribromide (CetTMATB) or tetrabutylammonium tribromide (TBATB) in presence of K_2CO_3 in dichloromethane at 0 °C to room temperature under very mild conditions in good yields.[2]

The preparation of α-bromo enone has some considerable interest to the synthetic chemist for natural[3] and non-natural product[4] synthesis. It also serves as an essential precursor for generating α-keto vinyl anion equivalent for further use in organic synthesis.[5] For instance, α-bromo cyclopentenone (**4a**) has been used for the preparation of α-hydroxymethylcyclopentenone, which is a valuable starting material for natural products synthesis.[6] In addition, some of the α-bromo enones are also found in nature.[7] Although the preparation of these compounds are well known in literature,[8] still there is a need to find out much milder and better alternatives. The existing methods[8] are available so far i) bromination of enones with elemental bromine followed by dehydrobromination, using a suitable base such as triethylamine[3a,5] or sodium hydrogencarbonate[3b]; ii) reaction of enones with excess phenylselenium bromide, followed by treatment with a base pyridine[8c]; iii) epoxidation of enones using dimethyldioxirane, followed by epoxide ring opening with alkali metal bromide such as sodium bromide, and consequent dehydration.[8d] All these present methods have some drawbacks, such as molecular bromine is hazardous, difficult to maintain stiochiometric ratio and difficult to handle. On the other hand, the reagent phenylselenium bromide is toxic, expensive, and it also requires much longer reaction time to obtain the product. Sometimes it is failed to obtain β-substituted cyclic α-bromo enones by using elemental bromine.[8b] Therefore, a clean preparation of α-bromo enone is highly desirable. In an endeavour to change gradually the current working practices with greener alternatives, an enviroumentally favorable synthesis of organic ammonium tribromides (OATB), and some of its application is recently disclosed.[9] In the course of these studies, our attention is drawn to the problems of bromination of enones as highlighted above. Due to potentiality of organic ammonium tribromide (OATB) as a brominating agent,[10] it is expected to be possible to get an easy access to α-bromo enones from the bromination of enones with this type of reagents. The results of our successful attempts are reported in this communication. Thus, the reaction of *trans*-4-phenyl-3-buten-2-one (**1a**) with CetTMATB in CH_2Cl_2 at 0–5 °C, followed by treatment with K_2CO_3 at room temp gave *E/Z* (28/72) mixture of 3-bromo-4-phenyl-3-buten-2-one (**2a**) in a very good yield (Method A). The compound **2a** is also prepared from compound **1a** using TBATB in similar solvent system (Method B) at 0 °C–rt (Scheme 1). It may be noted that no bromination took place at C-1 position of **1a**. The *E/Z* ratio is ascertained by GC and ^{1}H NMR. Likewise, the reaction of 4-(4-methoxyphenyl)-3-buten-2-one (**1b**) with CetTMATB or TBATB, under exactly similar reaction conditions afforded 3-bromo-4-(4-methoxyphenyl)-3-buten-2-one (**2b**) as *E/Z* mixture (Scheme 1). When R_1 is phenyl present in the substrate then base K_2CO_3 is usually added after 3.5 h, otherwise it is added after 45 min exactly. Similarly, the substrates **1c**, **1d**, **1e**, and **1f** are sucessfully converted into the corresponding α-bromoenones **2c**, **2d**, **2e**, and **2f** respectively at 0 °C to room temperature (Table 1). Also, the reaction of an α,β-unsaturated ester, viz., methyl cinnamate **1g**, with CetTMATB or TBATB followed by treatment with K_2CO_3, provided α-bromo-α,β–unsaturated ester **2g**. α-Bromo-α,β–unsaturated esters are usually prepared[11] via arsonium ylides.



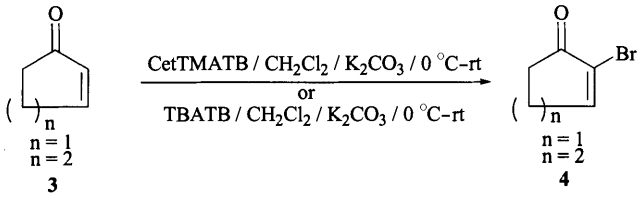
Scheme 1.

Table 1. Bromination of various acyclic enones by organic ammonium tribromides (OATB).

Entry	Substrate	Method	Time (h)	Product[a]	Yield[b] / %	[*E/Z*][c]
1a	R_1 = Ph, R_2 = Me	A	6.0	**2a**	68	28:72
		B	6.5		71	30:70
1b	R_1 = 4-OMePh, R_2 = Me	A	4.0	**2b**	70	15:85
		B	3.0		75	10:90
1c	R_1 = Ph, R_2 = Ph	A	8.0	**2c**	70	10:90
		B	6.0		72	10:90
1d	R_1 = 4-OMePh, R_2 = Ph	A	9.5	**2d**	85	20:80
		B	7.5		88	15:85
1e	R_1= Ph, R_2= $CH(Me)_2$	A	9.0	**2e**	69	22:78
		B	8.0		70	20:80
1f	R_1 = 4-OMePh, R_2= $CH(Me)_2$	A	9.0	**2f**	78	28:72
		B	7.5		81	30:70
1g	R_1 = Ph, R_2 = OMe	A	55	**2g**	68	50:50
		B	50		70	50:50

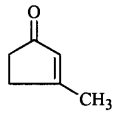
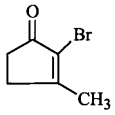
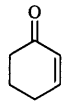
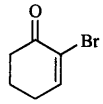
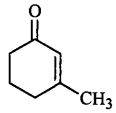
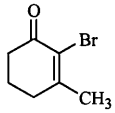
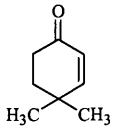
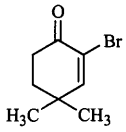
[a]Products have been characterized by IR, ^{1}H NMR, ^{13}C NMR and mass spectra. [b]Isolated yield. [c]*E/Z* ratio is determined by GC and ^{1}H NMR analysis.

Similarly, various cyclic enones (**3a–e**) reacted[12] with CetTMATB or TBATB in presence of K_2CO_3 at 0 °C–rt to provide readily the cyclic α-bromo enones (**4a–e**) in good yields (Scheme 2, Table 2). The generation of α-bromo enones can be explained by the initial formation of dibromo ketones, followed by readily dehydrobromination by a base such as K_2CO_3.



Scheme 2.

Table 2. Bromination of various cyclic enones by organic ammonium tribromides.

Entry	Substrate	Method	Time (min)	Product[a]	Yield[b] / %
3a		A	40		70
		B	15		65
3b		A	240		68
		B	180		72
3c		A	140		80
		B	120		75
3d		A	150		72
		B	120		75
3e		A	150		65
		B	120		68

[a]Products have been characterized by IR, ^{1}H NMR, ^{13}C NMR and mass spectra. [b]Isolated yield.

In conclusion, we have devised a simple and useful method for the synthesis of α-bromo enones from enones by employing organic ammonium tribromide, such as cetyltrimethylammonium tribromide or tetrabutylammonium tribromide as brominating agent under mild and environmentally favorable conditions. In addition, we have also achieved the preparation of β-substituted cyclic α-bromo enones. Owing to its operational simplicity, generality and efficacy, this method is expected to have wide utility for the synthesis of α-bromo enones. A similar transformation might be possible also with other organic ammonium tribromides, which is under investigation.

The authors are thankful for the financial support from Council of Scientific and Industrial Research, New Delhi [Grant No. 01(1541)/98/EMR-II to A.T.K] and the referees valuable comments.

References and Notes

1 This paper is dedicated to Professor Richard R. Schmidt, Universitaet Konstanz, Germany on the occasion of his 65th birthday.

2 This work was presented by A. T. Khan at the 13th International Conference on Organic Synthesis at Warsaw in Poland, July 1–5, 2000.

3 a) P. A. Wender, C. L. Hillemaun, and M. J. Szymoniika, *Tetrahedron Lett.*, **21**, 2205 (1980). b) C. G. M. Janssen, L. H. J. G. Simons, and E.F. Godefroi, *Synthesis*, **1982**, 389.

4 a) G. L. Dunn, V. J. DiPasquo, and J. R. E. Hoover, *J. Org. Chem.*, **33**, 1454 (1968). b) S. Arai, K. Nakayama, T. Ishida, and T. Shioiri, *Tetrahedron Lett.*, **40**, 4215 (1999).

5 A. B. Smith, III, S. J. Branca, M. A. Guactaro, P. M. Wovkulich, and A. Korn, in "Org. Synth. Coll. Vol.", John Wiley & Sons Inc., New York (1990), Vol. VII, p. 271.

6 A. B. Smith, III, in "Strategies and Tactics in Organic Synthesis," ed. by T. Lindberg, Academic Press Inc., San Diego (1994), Vol. 1 , pp. 239–243.

7 G. W. Gribble, in "Progress in the Chemisty of Organic Natural Products," ed. by W. Herz, G. W. Kirby, R. E. Moore, W. Steglich, and C. Tamm, Springer-Verlag, Vienna (1996), pp. 17–22 and references cited therein.

8 a) R. C. Larock "Comprehensive Organic Transformations," Wiley-VCH, New York (1999), p. 638. (b) C. J. Kowalski, A. E. Weber, and K. W. Fields, *J. Org. Chem.*, **47**, 5088 (1982). c) S. V. Ley and A. J. Whittle, *Tetrahedron Lett.*, **22**, 3301 (1981). d) G. Righi, P. Bovicelli, and A. Sperandio, *Tetrahedron Lett.*, **40**, 5889 (1999).

9 M. K. Chaudnuri, A. T. Khan, B. K. Patel, D. Dey, W. Kharmawophlang, T. R. Lakshmiprabha, and G. C. Mandal, *Tetrahedron Lett.*, **39**, 8163 (1998).

10 S. Kajigaeshi and T. Kakinami, *J. Synth. Org. Chem. Jpn.*, **51**, 366 (1993).

11 Z. Huang, L.Wu, L. Zhu, and X. Huang, *Synth. Commun.*, **26**, 677 (1996).

12 Method A: To a stirred solution of 2-cyclopenten-l-one (**3a**) (0.410 g, 5 mmol) in CH_2Cl_2 (10 mL) are added cetyltrimethylammonium tribromide (2.62 g, 5 mmol) and K_2CO_3 (2.07 g, 15 mmol) at 0–5 °C. Stirring is continued for 20 min at the same temperature, and then it is brought slowly to room temperature. The reaction is completed within 40 min as monitored by TLC. Then, the white solid is filtered off and the solid residue was washed with 10 mL of dichloromethane. The combined filtrate is concentrated in rotavapor and the crude product is purified by chromatography on silica gel (60–120 mesh). The compound is eluted with ethyl acetate–hexane mixture(1:9) and the product **4a** is obtained as a gummy liquid in 70 % yield (0.564 g). Method B: The compound **4a** is also prepared from **3a** using TBATB at 0–5 °C following the identical procedure as above.