Tetrahedron Letters 52 (2011) 6971–6973

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Polymer bromide-DMSO: novel reagent system for the oxidation of alcohols to carbonyl compounds

T.S.R. Prasanna, K. Mohanaraju *

Synthetic Polymer Laboratory, Department of Polymer Science & Tech, Sri Krisnadevaraya University, Anantapur 515055, India

ARTICLE INFO

Article history:
Received 11 August 2011
Revised 15 October 2011
Accepted 17 October 2011
Available online 21 October 2011

Keywords:
Polymer bromide
Oxidations
Benzylic alcohols
Carbonyl compounds

ABSTRACT

A novel method for the oxidation of alcohols to aldehydes is described using polymer bromide-DMSO at room temperature. The condition described enables clean and fast conversion to desired carbonyl compounds and a broad range of substrates are tolerated. The resin recovery and recyclability make the protocol more ecofriendly.

The ever-increasing demand for the efficient synthesis of novel organic compounds and environment conscious chemical processes has led to the development of novel techniques in organic synthesis. Use of polymer bound reagents introduce several advantages in organic synthesis including removing excess reagents and byproducts by simple filtration and reducing the effort required in workup and purification of the crude reaction mixture in several cases. Polymer assisted solution phase synthesis, a widely developed area in organic synthesis enables the chemist to prepare libraries of compounds more quickly and efficiently.[1] This line of chemistry has resulted in the development of a number of useful polymer-supported reagents which are finding increasing utility in organic synthesis.[2]

Oxidation of alcohols to carbonyl compounds is an important reaction in organic chemistry and various reagents have been developed to effect this transformation. These include (a) chromium-based reagents, such as Collins reagent ($CrO_3{\cdot}Py_2$), PDC or PCC[3] (b) activated DMSO,[4] resulting from the reaction of DMSO with electrophiles such as oxalyl chloride (Swern oxidation), carbodiimide (Pfitzner–Moffatt oxidation) or the complex $SO_3{\cdot}Py$ (Parikh–Doering oxidation) (c) hypervalent iodine compounds,[5] such as Dess–Martin periodinane or 2-iodoxybenzoic acid (d) catalytic TRAP in the presence of excess of NMO (Ley-Oxidation)[6] and (e) catalytic TEMPO in the presence of excess bleach (NaOCl).[7] Several other methods employing different reagents and modifications to the above methods have been reported.[8] However many of these protocols use harsh reagents where acid-sensitive functional groups are not tolerated, prolonged reaction time, cumbersome work-up procedures and isolation, and using poisonous and bad smelling liquids as reagents. Developing suitable reagents which exclude these limitations in the oxidation of alcohols to carbonyl compounds in the context of green chemistry appears to be a welcome goal.

In continuation of our research interest in developing novel methodologies in organic synthesis using polymer bound reagents[9] we became interested in Amberlyst A 26-Br_3^-. It is a source of Br^{3-} ions, the properties of which are different from those of molecular bromine. In particular, it is much less electrophilic and less reactive toward aromatic rings. Amberlyst A 26-Br_3^- is used in various transformations including selective *para*-bromination of phenols,[10] α-bromination of ketones,[11] regioselective bromomethoxylation of alkenes[12] etc. However to the best of our knowledge we found no reports employing polymer bromide in the bromination of benzylic alcohols. If the same can be achieved using polymer bromide in dimethyl sulfoxide (DMSO) the benzyl bromide formed will be oxidized in situ to a carbonyl compound. This will eventually serve two purposes, a one pot synthesis of carbonyl compounds with DMSO as the terminal oxidant and recovery and the recyclability to ensure that the process will meet the current requirements of green chemistry.

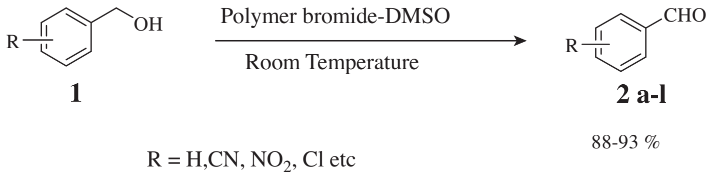
Herein, we wish to report the results of our investigation of using polymer bromide in the oxidation of benzylic alcohols to the corresponding carbonyl compounds with DMSO as the terminal oxidant (Scheme 1).

In initial studies we took 4-chlorobenzyl alcohol (1 equiv) and polymer bromide (1 equiv) in 10 volumes of DMSO and stirred at room temperature and the course of the reaction was monitored

---

* Corresponding author. Tel.: +91 08554 255655.
E-mail address: kmohanaraju@gmail.com (K. Mohanaraju).

0040-4039/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2011.10.086



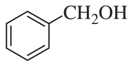
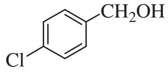
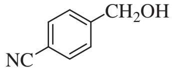
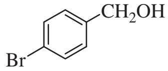
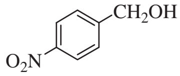
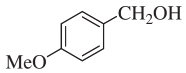
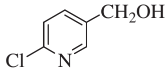
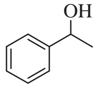
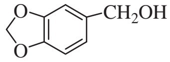
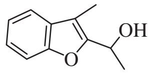
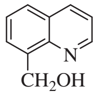
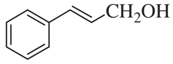
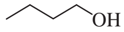
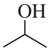
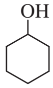
Scheme 1. Oxidation of alcohols to carbonyl compounds using polymer bromide-DMSO at room temperature.

by thin layer chromatography. Interestingly a nonpolar spot formed after 6 h and the starting material disappeared and the TLC plate that was dipped in 2,4-DNP solution developed a brown color. Analysis of the reaction mixture in GCMS showed the corresponding aldehyde mass. It is interesting to note that the reaction was clean and no purification was required after an aqueous work-up. Encouraged by the result the reaction was performed using benzyl alcohol and different alcohols containing various functional groups. Representative examples are shown in Table 1 (entries 1, 3–5) and the corresponding aldehydes were obtained in excellent yields. It is noteworthy to mention that there was no ring bromination with any of the substrate alcohols. The generality of the methodology was further confirmed by applying the same to heterocyclic alcohols (Table 1, entries 7, 11) and cinnamyl alcohol (Table 1, entry 12). In all the cases the reactions went into completion within the time reported. When the reaction was performed on 4-methoxy benzyl alcohol we observed 25% of the demethylated product and to circumvent the problem we tried to reduce the amount of catalyst and it was observed that the reaction did not go to completion after prolonged stirring. When we were thinking of neutralizing agents which can absorb the liberated HBr we came across a procedure which employs phenyl trimethyl ammonium tribromide for the α-bromination of arylalkyl ketones with anhydrous tetrahydrofuran (THF) as the buffer which reacts with liberated HBr.[13] An equal ratio of DMSO and anhydrous THF did the job in the case of acid-sensitive methoxy group containing benzyl alcohols and the demethylation could be reduced to less than 5%.

Then we turned our attention toward benzylic secondary alcohols (Table 1, entries 8, 10). By employing the nonTHF condition used for 4-chlorobenzyl alcohol both benzylic and heterocyclic secondary alcohols could be converted to the corresponding ketones in good yield. With the same method we wanted to see whether the carbonyl compounds can be obtained when aliphatic alcohols are employed. However the reaction did not yield the corresponding aldehydes when aliphatic primary and secondary alcohols were used (Table 1, entries 13–15). This may be presumably because polymer bromide is efficient only in converting highly reactive alcohols like benzylic and allylic to the corresponding bromides under the reaction conditions which are oxidized by DMSO to the corresponding carbonyl compounds and in the case of aliphatic alcohols where such reactivity is not present, the corresponding bromides are not formed. Based on the above observations the optimized condition for alcohols not containing acid-sensitive groups employs 1 equiv of polymer bromide in DMSO. For the alcohols containing acid-sensitive groups, 1 equiv of polymer bromide in equal ratio of DMSO/THF serves the purpose.

A tentative mechanism for the oxidation of alcohols to carbonyl compounds based on the above facts is represented below. (Scheme 2)

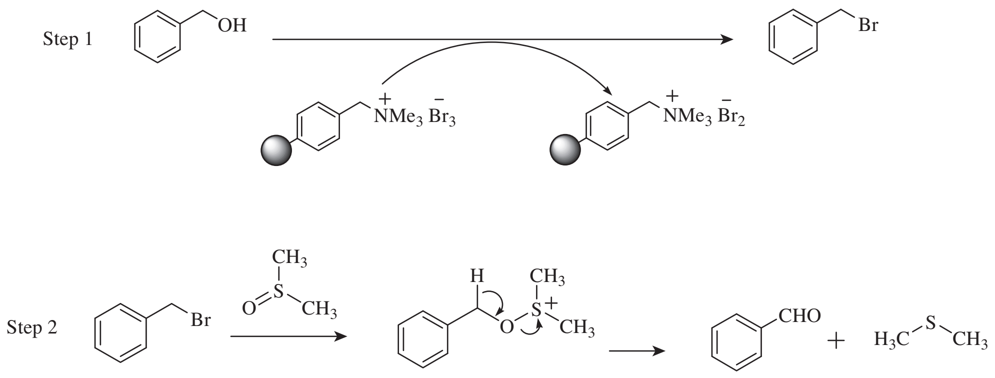
Table 1
Conversion of alcohols to aldehydes using polymer bromide-DMSO

Entry	Alcohol	Product	Product time[a] (h)	Yield[b] (%)
1		**2a**	4	92[c]
2		**2b**	6	95[c]
3		**2c**	4	91[c]
4		**2d**	5	92[c]
5		**2e**	6	93[c]
6		**2f**	5	90[d]
7		**2g**	6	94[c]
8		**2h**	5	90[c]
9		**2i**	5	89[d]
10		**2j**	6	88[c]
11		**2k**	4	91[c]
12		**2l**	5	90[c]
13		**2m**	5	No reaction[c]
14		**2n**	5	No reaction[c]
15		**2o**	5	No reaction[c]

[a] Reactions were monitored by GC–MS.
[b] Yields refer to pure products.
[c] Ref. 14i.
[d] Ref. 14ii.

Recovery and reusability of the catalyst

With the objective of reducing the cost, especially when intending to carry out large scale reaction, the catalyst reusability is also checked by recovering the resin. After the reaction is over the decolorized resin was filtered and converted into tribromide by the addition of bromine.[10] Reuse of the same using the optimized conditions (Ref. 14), with 4-chlorobenzyl alcohol as the model substrate gave the corresponding 4-chlorobenzaldehyde with yields almost comparable. The resin could be recovered without much loss in quantity and its reuse checked up to four cycles and the corresponding yields obtained in each cycle are tabulated in Table 2.



Scheme 2. Proposed mechanism for the oxidation of alcohols to carbonyl compounds using polymer bromide-DMSO.

Table 2
Recovery and reusability of polymer bromide in the conversion of 4-chlorobenzyl alcohol to 4-chlorobenzaldehyde

Entry	Cycles	Recovery of resin (wt %)	Yield of product[a,b] (%)
1	I	96	93
2	II	95	91
3	III	94	90
4	IV	94	90

[a] Isolated yields.
[b] Ref. 14i.

This makes the resin reusability possible eliminating the drawback of the cost factor.

In summary we have developed and demonstrated a novel use of polymer tribromide, amberlyst A 26-Br_3^- for the oxidation of benzylic alcohols to the corresponding carbonyl compounds. When compared to the previously reported procedures our method offers several advantages. The reaction is done at room temperature, a broad range of substituents are tolerated, and the recovery and reusability of the resin makes the entire protocol economical and environment friendly. Although the protocol is similar to Corey–Kim oxidation, the amount of bad smelling, volatile and poisonous dimethyl sulfide released into the environment is only stoichiometric which is far less than the amount required by Corey–Kim oxidation where the amount of dimethyl sulfide employed varies from 2.5 to 5 equiv. Taken together, the use of polymer tribromide for the oxidation of benzylic alcohols to carbonyl compounds represents an approach suitable for practicing green chemistry and thus should find wide application in organic synthesis.

References and notes

1. (a) Shuttleworth, S. J.; Allin, S. M.; Wilson, R. D.; Nasturica, D. *Synthesis* **2000**, 1035; (b) Bhalay, G.; Dunstan, A.; Glen, A. *Synlett* **2000**, 1846.
2. For a review of polymer-supported reagents, see: (a) Ley, S. V.; Baxendale, I. R.; Bream, R. N.; Jackson, P. S.; Leach, A. G.; Longbottom, D. A.; Nesi, M.; Scott, J. S.; Storer, R. I.; Taylor, S. J. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3815 (special review issue); (b) Petchmanee, T.; Ploypradith, P.; Ruchirawat, S. *J. Org. Chem.* **2006**, *71*, 782; (c) Flowers, R. A.; Xu, X.; Timmoons, C.; Li, G. *Eur. J. Org. Chem.* **2004**, 2988; (d) Pennington, T. E.; Kardiman, C.; Hutton, C. A. *Tetrahedron Lett.* **2004**, *45*, 6657; (e) Chiang, G. C. H.; Olsson, T. *Org. Lett.* **2004**, *6*, 3079; (f) Tashino, Y.; Togo, H. *Synlett* **2004**, 2010; (g) Jaunzems, J.; Kashin, D.; Schonberger, A.; Kirschning, A. *Eur. J. Org., Chem.* **2004**, 3435.
3. Collins, J. C.; Hess, W. W.; Frank, F. J. *Tetrahedron Lett.* **1968**, *9*, 3363.
4. (a) Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651; (b) Pfitzner, K. E.; Moffatt, J. G. *J. Am. Chem. Soc.* **1963**, *85*, 3027; (c) Parikh, J. R.; Doering, W. E. *J. Am. Chem. Soc.* **1967**, *89*, 5505.
5. Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155.
6. Ley, S. V.; Norman, J.; Griffith, W. P.; Marsden, S. P. *Synthesis* **1994**, 639.
7. (a) Anelli, P. L.; Biffi, C.; Montanari, F.; Quici, S. *J. Org. Chem.* **1987**, *52*, 2559; (b) Rozantsev, E. G.; Sholle, V. D. *Synthesis* **1971**, 190; (c) Leanna, M. R.; Sowin, T. J.; Morton, H. E. *Tetrahedron Lett.* **1992**, *33*, 5029.
8. (a) Uyanik, M.; Akakura, M.; Ishihara, K. *J. Am. Chem. Soc.* **2009**, *131*, 251; (b) Surendra, K.; Srilakshmi, K. N.; Arjun Reddy, M.; Nageswar, Y. V. D.; Rama Rao, K. *J. Org. Chem.* **2003**, *68*, 2058; (c) Bolm, C.; Magnus, A. S.; Hildebrand, J. P. *Org. Lett.* **2000**, *2*, 1173; (d) Park, H. J.; Lee, J. C. *Synlett* **2009**, 79; (e) Gheorghe, A.; Chinnusamy, T.; Cuevas-Yañez, E.; Hilgers, P.; Reiser, O. *Org. Lett.* **2008**, *10*, 4171; (f) Vatèle, J. M. *Synlett* **2006**, 2055; (g) Jiang, N.; Ragauskas, A. J. *J. Org. Chem.* **2007**, *72*, 7030; (h) Kim, S. S.; Jung, H. C. *Synthesis* **2003**, 2135; (i) Yang, G.; Wang, W.; Zhu, W.; An, C.; Gao, X.; Song, M. *Synlett* **2010**, 437.
9. An improved procedure for 2-amino-5-nitro-4,6-diarylcyclohex-1-ene-1,3,3-tricarbonitriles; Carbonate on polymer support (Amberlyst A-26 $NaCO_3^-$) as mild and reusable catalyst. Prasanna. T.S.R.; Mohanraju. K. Paper accepted in Journal of Korean Chemical Society 2011 (K-11-OC-034-A).
10. Smith, K.; James, M.; Matthews, I.; Bye, M. R. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1877.
11. (a) Cacchi, S.; Caglioti, L. *Synthesis* **1979**, 64; (b) Ployrpradith, P.; Kagan, R. K.; Ruchirwat, S. *J. Org. Chem.* **2005**, *70*, 5119.
12. Gopalakrishnan, G.; Kasinath, V.; Pradeep Singh, N. D.; Santhana Krishnan, V. P.; Anand Soloman, K.; Rajan, S. S. *Molecules* **2002**, *7*, 412.
13. Jacques, J.; Marquet, J. *Organic Synthesis* **1988**, *6*, 175.
14. *General Procedure for the oxidation of alcohols to carbonyl compounds.*
(i) Procedure for alcohols not containing acid-sensitive groups.
To a mixture of alcohol in dry DMSO (10 volume) was added 1 equiv of polymer bromide and the reaction mixture was stirred at room temperature for a given period of time (Table 1). After the completion of the reaction, the reaction mixture was filtered and the polymer bed washed with DMSO. Combined DMSO layers were quenched with ice–water mixture and extracted with ether. The ether layer was given water wash, brine wash, dried over anhydrous sodium sulphate, and concentrated to get the pure carbonyl compounds. All the products were characterized by NMR and MS analysis.
(ii) Procedure for alcohols containing acid-sensitive groups.
To a mixture of alcohol in dry DMSO/THF (10 volume, 50:50 mixture) was added 1 equiv of polymer bromide and the reaction mixture was stirred at room temperature for a given period of time (Table 1). After completion of the reaction, the reaction mixture was filtered and the polymer bed was washed with THF. Combined DMSO/THF layers were quenched with ice–water mixture and extracted with ether. The ether layer was given water wash, brine wash, dried over anhydrous sodium sulphate, and concentrated to get the pure carbonyl compounds.
Selected spectral data
4-bromobenzaldehyde (**3b**)
Mp: 59–60 °C, ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.6 (m, 4H), 9.9 (s, 1H). ^{13}C NMR ($CDCl_3$ 400 MHz); δ 129.5, 131.8, 132.3, 135.0 and 190.8. Analysis: C_7H_5BrO requires C: 45.44, H: 2.72, Br: 43.18; found C: 45.44, H: 2.70, Br: 43.18.
4-nitrobenzaldehyde (**4b**)
Mp: 105–106 °C, ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.6 (d, 2H, $J = 9$ Hz), 8.37 (d, 2H, $J = 9$ Hz). ^{13}C NMR ($CDCl_3$, 400 MHz); δ 123.5, 130.8, 139.3, 150.0 and 190.8. Analysis: $C_7H_5NO_3$ requires C: 55.63, H: 3.34, N: 9.26 found; C: 55.62, H: 3.33, Br: 9.26.