

## SHORT COMMUNICATION

### POLYVINYLPIRROLIDONE-BROMINE COMPLEX: AN EFFICIENT POLYMERIC REAGENT FOR SELECTIVE PREPARATION OF BENZYL BROMIDES IN THE PRESENCE OF HEXAMETHYLDISILANE

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**ABSTRACT.** Benzylic bromides were conveniently obtained in high yields via the reaction of the corresponding alcohols with crosslinked polyvinylpyrrolidone-bromine complex (PVPP-Br<sub>2</sub>)/hexamethyldisilane in chloroform at reflux condition. Selective conversion of benzyl alcohol to benzyl bromide in the presence of primary aliphatic alcohols, e.g. 2-phenylethanol was also achieved.

**KEY WORDS:** Polyvinylpyrrolidone-bromine, Benzyl bromide, Hexamethyldisilane, Selective bromination

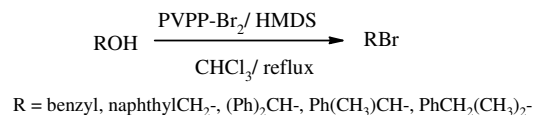
## INTRODUCTION

The transformation of benzyl bromide derivatives into valuable end products in supramolecular compounds such as fullerene precursor and dendrimer core is often utilized in organic syntheses [1, 2]. The traditional methods include highly toxic reagent such as HBr gas [3], BBr<sub>3</sub> [4, 5] and PBr<sub>3</sub> or combination of reagents like Br<sub>2</sub>/PPh<sub>3</sub> [6], CBr<sub>4</sub>/PPh<sub>3</sub> [7], and high temperatures are often required.

Some alternative reagents reported for this purpose are bromotrimethylsilane [8], HDMS/PyH<sup>+</sup>Br<sub>3</sub><sup>-</sup> [9], ClSiMe<sub>3</sub>/LiBr [9], Br<sub>3</sub>CCOCBr<sub>3</sub>/PPh<sub>3</sub> or Br<sub>3</sub>CCO<sub>2</sub>Et/PPh<sub>3</sub> [10] and silphos/X<sub>2</sub>[11]. However, most of the reagents introduced for the conversion of alcohols to bromides gave by-product, and are of limited selectivity.

The application of polymer supports as reagent and catalyst has received special attention in the past decades, due to the easy work up of reaction products and unique selectivity which are undoubtedly attractive features of this methodology. In addition, most of the polymer supported reagents can be recycled after use [12, 13]. Among the synthetic polymeric beds employed for this purpose, poly(vinylpyrrolidone) can act as safe carrier for a variety of compounds in the blood stream and has been used as a retardant for drugs and elimination of toxins [14]. It displays a strong binding affinity toward small molecules [15], its iodine complex, povidon-iodine, is widely used as an anti-infective agent in clinical treatments [16]. In our previous reports, we introduced crosslinked polyvinylpyrrolidone-bromine complex as an efficient reagent for the bromination of alkenes, oxidation of alcohols [17], and oxidative deprotection and selective deprotection of silyl ethers to the corresponding alcohols [18] and bromination of activated aromatic compounds [19]. To extend the synthetic utility of this reagent as a safe polymeric brominating agent, our effort has been directed toward conversion of alcohols to the corresponding bromides using crosslinked polyvinylpyrrolidone-bromine complex (PVPP-Br<sub>2</sub>) in the presence of HDMS (Scheme 1).

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Scheme 1

## EXPERIMENTAL

*Apparatus and reagents.* Crosslinked polyvinylpyrrolidone (PVPP) was purchased from Fluka. Other chemicals were purchased from Merck. Melting points were recorded on an electro thermal melting point apparatus. The NMR spectra were recorded in CDCl<sub>3</sub> with TMS as an internal standard on a Bruker Avance DRX 500 MHz spectrometer. IR spectra were determined on a SP-1100, P-UV-Com instrument. Purity determination of the products was accomplished by TLC on silica gel poly gram SIL G/UV 254 plates. Products identified by comparison IR, and <sup>1</sup>H NMR spectra, with those reported for authentic samples. In this study, the crosslinked PVPP-Br<sub>2</sub> complex is obtained according to our previous article [19].

*General procedure for bromination of benzylic alcohols.* To a suspension of PVPP-Br<sub>2</sub> (1 mmol, 0.35 g) and HMDS (3 mmol, 0.44 g) in a flask were added chloroform (5 mL) and stirred about 0.5 h at room temperature. Then a solution of benzyl alcohol (1 mmol) in chloroform (5 mL) was added drop-wise to the reaction mixture and stirred at reflux temperature for 1 h. The reaction mixture was monitored by TLC in hexane/ethylacetate (4:1) as eluent. Then, the spent resin was filtered and the residue washed with CH<sub>2</sub>Cl<sub>2</sub> (2 × 25 mL). The filtrate was poured into a 100 mL separating funnel, washed with water (2 × 25 mL). Finally, the organic layer was dried over sodium sulfate. Removal of the volatile materials from the dried extracts gave spectroscopically pure benzyl bromide. A similar procedure was employed in reactions with other alcohols (Table 1). Further purification performed through silica gel column chromatography. *Caution:* benzylic bromides can be powerful lachrymators and should be used with adequate ventilation and precautions against skin contact or ingestion.

*Regeneration of the PVPP-Br<sub>2</sub>.* One of the main aspects in the use of cross-linked polyvinylpyrrolidone supported bromine complex is the possibility of recycling and reuse of the polymer. The spent reagent collected from the bromination reactions was washed thoroughly with diethyl ether to remove any residual organic compounds. The resin was filtered and dried. For functionalization, the regenerated polymer was treated with dilute bromine solution in dichloromethane which was added drop wise using a separatory funnel and stirred for 0.5 h at room temperature. The resulting mixture was filtered and washed with dichloromethane (2 × 20 mL) and dried in desiccator.

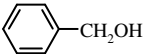
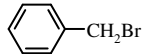
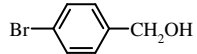
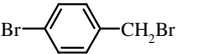
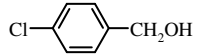
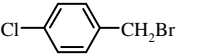
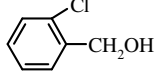
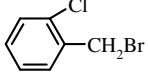
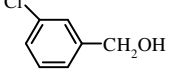
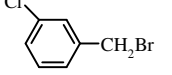
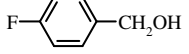
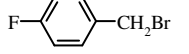
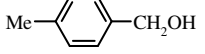
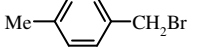
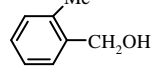
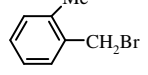
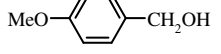
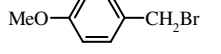
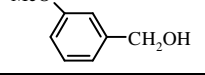
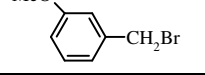
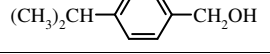
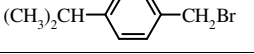
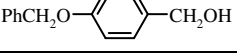
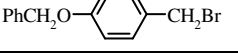
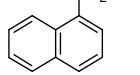
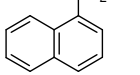
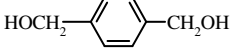
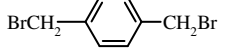
*3-Methoxybenzyl bromide (Table 1, entry 10).* <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 3.86 (s, 3H), 4.52 (s, 2H), 6.59-7.33 (m, 4H). IR (neat): 3055, 2987, 2870, 1509, 1465, 1421, 1271, 1156, 1155, 1035 cm<sup>-1</sup>.

*4-Pr<sup>i</sup>-Benzyl bromide (Table 1, entry 11).* <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 1.33-1.31 (d, J = 10 Hz, 6H), 2.95-3.01 (m, 1H), 4.56 (s, 2H), 7.27-7.40 (dd, J = 8 Hz, 4H). IR (neat): 3021, 2963, 2870, 1643, 1515, 1494, 1381, 1280, 1265, 1156, 1131, 1036 cm<sup>-1</sup>.

*4-Benzyloxybenzyl bromide (Table 1, entry 12).* <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 4.55 (s, 2H), 5.11 (s, 2H), 6.98-7.49 (m, 9H). IR (neat): 2933, 2867, 1613, 1572, 1456, 1380, 1300, 1224, 1128, 1006 cm<sup>-1</sup>.

*1-(2-Bromo-2-methylpropyl)benzene* (Table 1, entry 17).  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.82 (s, 6H), 3.26 (s, 2H), 7.30-7.37 (m, 5H); IR (neat): 3024, 2965, 1653, 1496, 1364, 1208, 1133, 1047  $\text{cm}^{-1}$ .

Table 1. Bromination of alcohols to the corresponding bromides with PVPP- $\text{Br}_2$ /HMDS.

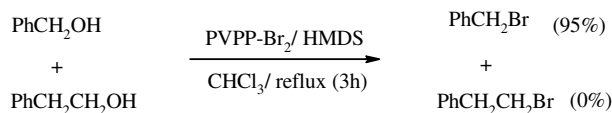
Entry	Substrate	Product <sup>a</sup>	Time (h)	Yield (%) <sup>b</sup>	Ref.
1			1	98	21-23
2			2	98	21-23
3			2.5	92	10
4			1.5	96	19-21
5			1.5	94	19-21
6			2.5	98	19-21
7			1	98	19-21
8			1.5	98	19-21
9			3	90	10
10			3	86	-
11			1.5	98	-
12			1.5	98	-
13			3.5	84	19-21
14			3	94	10

15			3	75	19-21
16	(Ph) <sub>2</sub> CHOH	(Ph) <sub>2</sub> CHBr	3.5	70	10
17			4	47	-

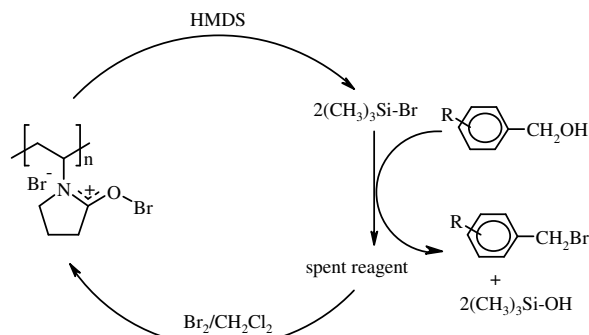
<sup>a</sup>All of the products were identified by comparing melting point and <sup>1</sup>H NMR with those of authentic samples reported in the literature. <sup>b</sup>Yields refer to isolated products.

## RESULTS AND DISCUSSION

The PVPP-Br<sub>2</sub> complex is insoluble, non-volatile polymeric reagent and retains its activity several months after its preparation. As shown in Table 1, a variety of benzylic alcohols was treated with PVPP-Br<sub>2</sub>/HMDS in chloroform as a solvent under reflux condition. Primary benzylic alcohols (Table 1, entries 1-14) were easily converted to the corresponding benzyl bromides in good to excellent yields. Secondary benzylic alcohols (Table 1, entries 15, 16) were converted to the corresponding bromides in good yields. In the case of 2-methyl-1-phenyl-2-propanol (entry 17) as a tertiary alcohol, the corresponding bromide is obtained in 47% yield. Surprisingly, the aromatic ring of the alcohols are not affected under the reaction conditions. Attempts to brominate primary and secondary aliphatic alcohols with addition of more reagent were unsuccessful even at longer time. Therefore, the selective conversion of benzylic alcohols to the corresponding bromides was achieved in the presence of primary and secondary aliphatic alcohols. In a typical experiment when equimolar amount of benzyl alcohol and 2-phenylethanol were treated with one equivalent of the polymeric reagent for 3 h in chloroform under reflux conditions, only benzyl alcohol was selectively converted to benzyl bromide and 2-phenylethanol was remained unchanged (Scheme 2).



Scheme 2



Scheme 3

It is reasonable to assume that the present reaction is initiated by the oxidative cleavage of the silicon-silicon bond in hexamethyldisilane to the corresponding bromotrimethylsilane in the presence of PVPP-Br<sub>2</sub> complex [20]. The in situ generated bromotrimethylsilane reacted with benzylic alcohols to afford benzyl bromide derivatives. The spent resin could be converted back to the starting polyvinylpyrrolidone complex after washing with organic solvent as depicted in (Scheme 3).

### CONCLUSIONS

In conclusion, crosslinked polyvinylpyrrolidone-bromine complex is stable, non-hygroscopic, easy to prepare and handle, and represent an efficient and selective brominating reagent for preparation of benzyl bromide derivatives in the presence of hexamethyldisilane.

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### REFERENCES

1. Newkome, G.R.; Moorefield, C.N.; Vogtle, F. *Dendrimers and Dendrons Concepts, Syntheses, Applications*, Wiley-VCH Verlag GmbH: Weinheim (Germany); **2001**, pp 195-204.
2. Mehta, G.; Srirama Sarma, P.V.V. *Tetrahedron Lett.* **2002**, 43, 9343.
3. Reid, E.E.; Ruhoff, J.R.; Burnett, R.E. *Organic Syntheses*, Collect. Vol. 2, Wiley: New York; **1943**, p 246.
4. Hudson, H.R.; Kinghorn, R.R.F.; Murphy, W.S. *J. Chem. Soc.* **1971**, 3593.
5. Madjabadi, A.A.; Pham, T.N.; Ashby, E.C. *Synthesis* **1989**, 614.
6. Wily, G.A.; Hershkowitz, R.L.; Rein, B.M.; Chung, B.C. *J. Am. Chem. Soc.* **1964**, 86, 964.
7. Wagner, A.; Hertz, M.P.; Mioskowski, C. *Tetrahedron Lett.* **1990**, 31, 3141.
8. Jung, M.E.; Hatfield, G.C. *Tetrahedron Lett.* **1978**, 19, 4483.
9. Olah, G.A.; Gupta, B.; Malhotra, R.; Narang, S.C. *J. Org. Chem.* **1980**, 45, 1638.
10. Iranpoor, N.; Firouzabadi, H.; Jamalian, A.; Kazemi, F. *Tetrahedron* **2005**, 61, 5699.
11. Tongkate, P.; Pluemanupat, W.; Chavasiri, W. *Tetrahedron Lett.* **2008**, 49, 1146.
12. Mathur, K.; Narang, C.K.; Williams, R.E. *Polymer as Aids in Organic Chemistry*, Academic Press: New York; **1980**.
13. Akelah, A.; Sherrington, D.S. *Chem. Rev.* **1981**, 81, 557.
14. Ader, A.W.; Paul, T.L.; Reinhardt, W.; Safran, M.; Pino, S.; Arthur, M.C.; Braverman, W.L.E. *J. Clin. Endocrinol Metab.* **1988**, 66, 632.
15. Liu, C.; Cui, S.; Wang, Z.; Zhang X. *J. Phys. Chem. B* **2005**, 109, 14807.
16. Oster, G.; Immergut, E.H. *J. Am. Chem. Soc.* **1954**, 76, 1393.
17. Lakouraj, M.M.; Tajbakhsh, M.; Mokhtary, M. *J. Chem. Res.* **2005**, 481.
18. Lakouraj, M.M.; Mokhtary, M. *Lett. Org. Chem.* **2007**, 4, 64.
19. Mokhtary, M.; Lakouraj, M.M. *Chin. Chem. Lett.*, **2011**, 22, 13.
20. Razuvaev, G.A.; Brevnova, T.N.; Semenov, V.V. *Russ. Chem. Rev.* **1986**, 55, 606.
21. Gremlich, H.U.; Pachler, K.G.R.; Matlok, F. *Merck FTIR Atlas; A Collection of FTIR Spectra*, VCH: Weinheim, Germany; **1988**.
22. Pouchert, C.J. *The Aldrich Library of Infrared Spectra*, VCH: Weinheim, Germany; **1981**.
23. Pouchert, C.J. *The Aldrich Library of NMR Spectra*, Aldrich Chemical Company Inc.: USA; **1983**.