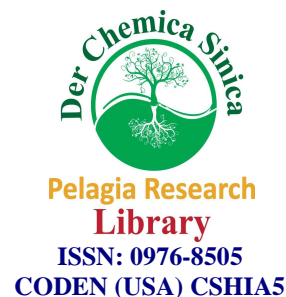




Pelagia Research Library

Der Chemica Sinica, 2012, 3(5):1140-1145



New Applications of Poly (*N*-bromoacrylamide) in Organic Synthesis: Highly Efficient and Regioselective Transformation of Alkenes into Bromohydrins, Bromoethers and Bromoacetates

Farzaneh Ebrahimzadeh^{*1,2}

¹Department of Chemistry, Science and Research Branch, Islamic Azad University, Fars, 7348113111, Iran

²Young Researchers Club, Islamic Azad University, Fars Science and Research Branch, Marvdasht, Iran

ABSTRACT

Crosslinked polyacrylamide was prepared from acrylamide and *N,N*-methylenebisacrylamide by free radical polymerization. Crosslinked Poly (*N*-bromoacrylamide) (PNBA) was synthesized by the bromination of polyacrylamide with KBr/Oxone in aqueous conditions. The capacity of PNBA measured by iodometric and gravimetric methods was 5.6 mmol per gram. PNBA as a bromine-containing polymer supported reagent was found efficient and well organized for the synthesis of high yielding bromohydrins, bromoethers and bromoacetates in presence of nucleophilic solvents (MeOH, EtOH, *i*-PrOH, AcOH and a mixture of H₂O–acetone) at 40°C. The spent polymeric reagent could be regenerated and reused for several times without appreciable loss in efficiency. PNBA reagent offers several advantages including, long shelf life, high efficiency, regioselectivity, elimination of hazards related to bromine containing compounds, and regeneration.

Key words: Poly (*N*-bromoacrylamide), Polymer supported reagent, Electrophilic addition, Esters, Ethers

INTRODUCTION

The vicinal functionalization of alkenes is an important process in synthetic organic chemistry and several methodologies are described in the literature.[1]

The electrophilic bromination of alkenes via a bromonium ion in presence of nucleophilic solvent is a very useful technique to prepare vicinal difunctionalized compounds regioselectively.[2] Vicinal halohydrins, haloethers, and haloesters are versatile synthetic intermediates that provide access to an array of functional groups.[3]

Sources of electrophilic halogen species (halonium ions) are of enormous interest from both mechanistic and green synthesis points of view. *N*-Haloimides are useful reagents for the halogenation of organic compounds; Halogen in these compounds has a greater electrophilic character than in X₂ and fewer corrosive and toxic. They are also easy to manipulate and produce the corresponding imides as by-products, which are less toxic and corrosive than HX (X = Cl, Br, I), generated when elementary halogen is used. [4] In the literature, some compounds such as NBS, [5,6] NBSac, [6,7] TBCA, [8] and *N*-bromoacetamide, [9] Bromamine-T[10] *N,N*-dibromobenzene sulphonamide, [11] have been reported for transformation of alkenes to vicinal 1,2-bromoethers, bromoesters and bromohydrins.

These reactions suffer from several disadvantages such as the use of stoichiometric amounts of corrosive X_2 / N -haloimide or the formation of great amounts of organic and inorganic wastes. [12] So heterogeneous N -halo-compounds can be improved these problems

In synthesis and applications of various polymeric species of N -halo compounds have been reported. [13] However there are a limited number of reports on polymers or copolymers containing N -haloamide. [14] With our knowledge, there is no systematic work in the literature on the utilization of Poly (N -bromoacrylamide) as a cohalogenating reagent, and we now communicate our results in this area. Therefore, we wish to introduce the synthesis of poly(N -bromoacrylamide) with different crosslinking density and its applications in synthesis of high yielding bromohydrins, bromoethers and bromoacetates in presence of nucleophilic solvents (MeOH, EtOH, *i*-PrOH, AcOH and a mixture of H_2O -acetone) .

MATERIALS AND METHODS

All chemicals were supplied by either Merck or Fluka. The progress of the reactions was followed with TLC, using silica gel SILG-UV 254 plates. Silica gel 60 was used for column chromatography. The identities of products were determined by comparison of their physical and spectral data with those reported in the literature. FT-IR spectra were recorded on a Shimadzu DR-8001 spectrometer. NMR spectra were recorded on a Bruker Avance DPX 250MHz instrument.

Procedure for preparation of poly (N -bromoacrylamide)

Crosslinked polyacrylamides (PNBA) using various percentage of N,N -methylenebisacrylamide (2%, 3%, 5%, 10%, 15% and 20%) were synthesized. The sample with 5% N,N -methylene bisacrylamide was good enough for handling and further reaction. Thus, acrylamide (5gr 0.069 mol) , potassium persulphate(0.4 gr,0.00136 mol), and N,N -methylenebisacrylamide (0.56gr, 0.0036mol) were dissolved in EtOH (10ml), heated for 6h at 60-70⁰C and then cooled, and the white polymer was filtered and washed with excess volume of EtOH to give the crosslinked polymer in almost quantitative yield. To a stirred suspension of polyacrylamide (5 gr), NaOH (70 mmol, 2.8 gr), Na_2CO_3 (105 mmo, 11.13gr) and KBr (75 mmol, 12.5gr) in H_2O (180 mL) cooled in an ice bath was added dropwise a solution of Oxone® (75 mmol, 46.05gr) in H_2O (150 mL). Solid precipitate was found during the addition of the oxidant solution, forming a dense suspension, which was stirred for 24 h. The product was isolated by filtration, washed with cold H_2O and dried in an air oven at 60 °C to afford 8.8 gr of poly (N -bromoacrylamide) as orange granules (Yield 83%). The capacity of polymer was 5.6 mmol per gram determined by iodometrically.

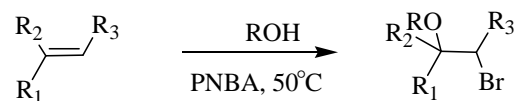
General Procedure for reaction of Alkene with PNBA and Nucleophilic Solvent

To a stirred solution of the alkene (1 mmol) in 5 mL nucleophilic solvent (MeOH, EtOH, PrOH, H_2O /Aceton(4:1) or AcOH) was added PNBA (2.5 mmol, 0.5 gr) at 40°C in small portions. After completion of the reaction, polyacrylamide was filtered off and CH_2Cl_2 (10 mL) was added. The aqueous phase was washed with CH_2Cl_2 (2 ×10 mL) and the combined organic layer was dried over anhyd Na_2SO_4 . After evaporation of the solvent on a rotary evaporator, the product was collected. Further purification has been archived with column chromatography. We can regenerate polymer by filtrations after completion the reaction and bromination of polyacrylamide by Oxone /KBr and reused it again.

RESULTS AND DISCUSSION

Cross-linked polyacrylamide was prepared from acrylamide monomer and N,N -methylene bisacrylamide (AC) by free radical polymerization.^{14f, 15} The IR spectra of PNBA showed those characterization peaks of polyacrylamide with the intensity of the broad band in the region 3100-3500 cm^{-1} decreasing considerably. The capacity of PNBA was determined iodometrically and gravimetrically to be 5.6 mmol of bromine per gram of the polymer with 5% crosslinking with N,N -methylene bisacrylamide. This polymeric reagent was obtained as an orange powder and was stable and did not lose bromine under laboratory conditions and could be stored for a long time. In order to develop a new method of preparation of bromohydrins, bromoethers and bromoacetates, we applied PNBA as source of Br^+ in the presence of oxygenated nucleophiles.

The reaction of PNBA with alkenes in presence of nucleophilic solvents (MeOH, *i*-PrOH, AcOH and a mixture of H_2O -acetone, 1:5) led to the correspond- ing β -bromoethers, β -bromoacetates and β -bromohydrins, in high regioselectivity and good yields (73–98%).(Scheme 1).



R₁=Ph,alkyl R=H,Me,Pr, Ac

R₂=H, Me

R₃=alkyl, phenyl, H

Scheme 1.

In this study styrene, α -methylstyrene, stilbene, allyl benzene and inden were used as substrates and methanol, isopropanol, acetic acid and water (H₂O–acetone, 1:4) as nucleophilic solvents. These results are summarized in Table 1.

The reactions were carried out stirring together 1mmol of the alkene with 3 mmol of PNBA in nucleophilic solvent at 40° C and after workup, the corresponding product were obtained in moderate to excellent yields. The products were characterized by spectroscopic methods.

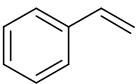
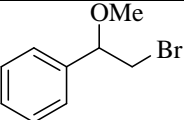
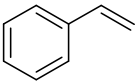
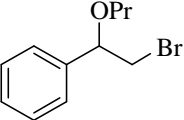
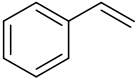
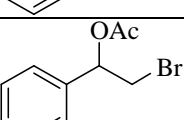
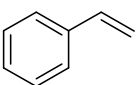
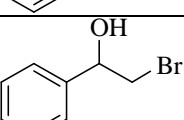
After work up, polyacrylamide was filtered off and the corresponding products were obtained in moderate to excellent yields.

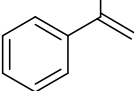
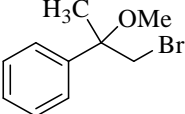
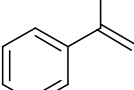
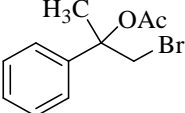
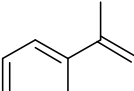
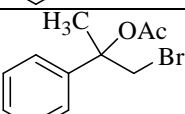
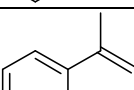
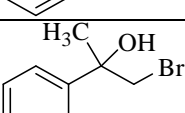
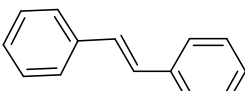
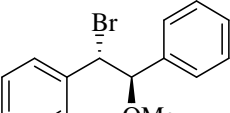
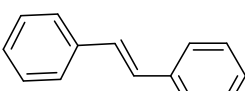
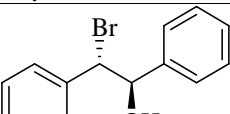
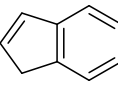
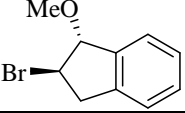
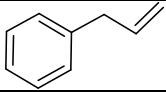
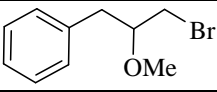
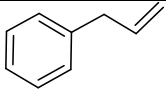
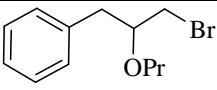
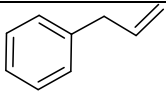
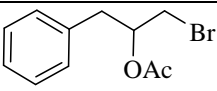
Bromination of styrene and allylbenzene with PNBA (Table 1) in the presence of acetic acid, alcohols (MeOH and i-PrOH) and water resulted on the respective β -bromoacetates, β -bromoethers and bromohydrins in good yields and high regioselectivity, also forming products from *trans*-addition following the Markownikoff's rule.

Also, this polymer are very gorgeous from Green Chemistry point of view, once they are easily handled stable solids and efficient source of electrophilic bromonium ions (Br⁺) that can brominated organic compounds without using Br₂.

The regioselectivity was extremely high forming products from *trans*-addition following the Markownikoff's law and no regioisomers were detected by the analytical procedures used (FTIR, GC mass, ¹H NMR and ¹³C NMR spectroscopy).

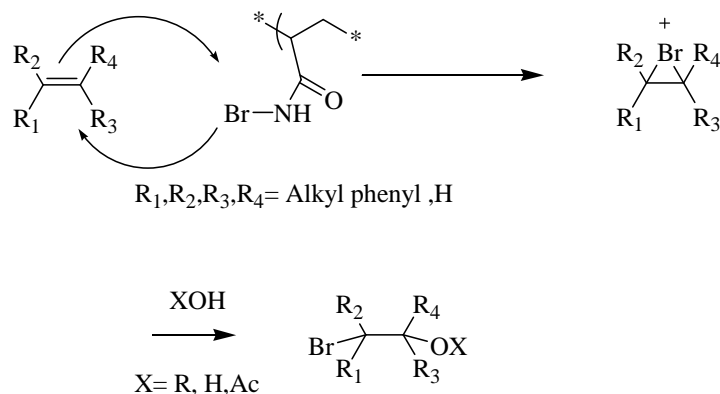
Table 1: Preparation of β -bromohydrine, β -bromoethers and β -bromoacetates of Alkenes with PNBA and Water, Alcohols or Acetic Acid

Entry	Alkene	Solvent	Product	Time	Yield ^{a,b}
1		MeOH		1h	95
2		PrOH		3h	70
3		AcOH		5h	65
4		H ₂ O		2h	70

5		MeOH		5h	80
6		PrOH		8h	70
7		AcOH		10h	80
8		H ₂ O		3h	75
9		MeOH		2h	60
10		H ₂ O		10h	80
11		MeOH		1h	60 ^b
12		MeOH		2h	80
13		PrOH		3h	60
14		AcOH		3h	65
<p>a) Isolated yield based on alkene b) All product characterized and compared and by FTIR, H NMR, CNMR and GC mass with known compound c) Trans product</p>					

As it seen, no diol arising from Prévost-Woodward reaction, was detected on the crude reaction mixture.

A proposed mechanism goes through formation of a bromonium ion intermediate from PNBA followed by ring opening promoted by the nucleophilic solvent. A proposed pathway is shown in Scheme 2.



Scheme 2: Proposed mechanism for reaction of alkene with nucleophilic solvent with PNBA

In resonance terms the bromonium ion created from styrene is in equilibrium with a carbocation form which is stabilized by conjugation.

The exhausted polymeric catalyst from different experiments was combined, washed with chloroform and dried overnight in a vacuum oven. It was rebrominated with oxone/KBr and reused again.

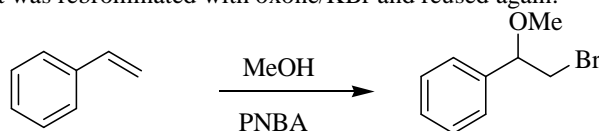


Table 2: Recycling of PNBA after regeneration

Run	Time	Conversion (%)
1st regeneration	1h	100
2nd regeneration	1h	90
3rd regeneration	100min	86
4rd regeneration	2h	80

CONCLUSION

In conclusion, the reaction of alkenes with PNBA is a simple method to prepare β -bromohydrins, β -bromoethers, and β -bromoacetates from alkenes. The reaction conditions are mild, the work up process is very simple and the method is easier than the usual routes employed to synthesize these compounds from alkenes. Furthermore, the PNBA as heterogeneous polymeric reagent is stable, safe and of easy handling, and the by-product for these reactions is polyacrylamide that can be filtrate, regenerate and reused. These reactions are no need of special techniques and conditions. Due to environmental problems involved in the manipulation of hazardous, toxic and corrosive halogens as well as the not readily available alternative reagents used in such transformation, our method becomes very useful and consistent with green chemistry principles.

Acknowledgement

The authors are thankful to the Research Councils of Shiraz University for its partial support of this work.

REFERENCES

- [1]. Smith M. B. ; March, J. March's Advanced Organic Chemistry. Reactions, Mechanism, and Structure; Wiley-Interscience: New York, 5 th ed., **2001**, 1043.
- [2]. Larock, R.C.; Comprehensive Organic Transformations: A Guide to Functional Group Preparation, 2nd ed, Wiley-VCH: New York, **1999**, p. 630
- [3]. (a) Stamatov, S. D.; Stawinski, J. *Eur. J. Org. Chem.* **2008**, 2635 (b) Minakata, S. ; Hayakawa J. *Chem. Commun.*, **2011**, 47, 1905.

- [4].(a)Mare, D. L, P. B. Electrophilic Halogenation; Cambridge University Press: Cambridge, **1976**, Chap. 5 and 7.(b) Ahmad, S. M.; Braddock, D. C.; Cansell, G.; Hermitage, S. A.; Redmond, J. M.; White, A. J. P. *Tetrahedron Lett.* **2007**, 48, 5948. and references therein.(c) Agrawal, M. K.; Adimurthy, S.; Ganguly, B.; Ghosh, P. K. *Tetrahedron***2009**, 65 , 2791(d) Parimala S. Vajjyanthi, P.S ;Mathiyalagan, N.*Pelagia Research Library , Der Chemica Sinica*, **2011**, 2 , 41.(d) Sinha,U. B.*Der Chemica Sinica*, **2012**, 3, 569.
- [5]. (a) Younes, M. R.; Chaabouni M. M. ; Bakloutia , A.*Tetrahedron Letters***2003**, 44 ,5263 .(b) Zhu, M.; Lin, S.; Zhao,G-L; Sun, J, Córdova, A. *Tetrahedron Letters*, **2010**, 51, 2708.(c) Shao, L.-X.; Shi, M. *Synlett***2006**, 1269 (d) Taber, D.F. ; Liang, J. L. *J. Org. Chem.* **2007**, 72, 431.(f) Hajra,S. Sinha, D. Bhowmick, M. *Tetrahedron Letters***2006**, 47, 7017.
- [6]. (a)de Souza, A. V. A .da Silva, J. F. M. de Mattos, M. C. S. *J. Braz. Chem. Soc.*, **2003**, 14, 832 .(b) de Souza, A. V. A ;Mendonça, G. F.; Bernini, R. B.; de Mattos M. C. S. *J. Braz. Chem. Soc***2007**, 18, 1575.
- [7].(a) Urankar, D.; Rutar, I.; Modec, B.; Dolenc, D. *Eur. J. Org. Chem.* **2005**, 2349.(b) Rezaiian, N. Vahedi,H. Massoudi, A. *Der Chemica Sinica*, **2011**, 2 , 86.
- [8].(a)Almeida, L. S. de.; Esteves, P. M.; Mattos, M. C. S. de. *Synlett.* **2006**, 1515.(b) Mendonça, G. F.; Sanseverino, A. M.; Mattos, M. C. S de. *Synthesis***2003** , 45.
- [9].(a)Schmidt, E. Knilling W. A. *Ascherl, Ber.***1926**, 59, 1279. (b) Winstein S. Lucas, H. J. *Ascherl, Ber.*, **1939**, 61, 1576 (b) Winstein, S.*Ascherl, Ber.* **1942**, 64, 2780.
- [10].(a)Xia,J. J; Wu, X- L; Wang G-W;*ARKIVOC***2008**, 22. (b)Wu, X- L. ; Wang G-WJ. *Org. Chem.* **2007**, 72, 9398.(c) Wang G-W; Wu, X- L; Adv. *Synth. Catal.* **2007**, 349, 1977.
- [11]. (a)Yoshida, M.; Mochizuki, H.; Suzuki, T.; Kamigata, N. *Bull. Chem. Soc. Jpn.* **1990**, 63, 3704. (b) Phukan, P.; Chakraborty, P.; Katakai, D. J. *J. Org. Chem.***2006**, 71, 7533.
- [12]. (a)Hajra,S.; Karmakar,A.; Bhowmick,M.;*Tetrahedron*, **2005**61,2279 (b) Hajra, S.; Bhowmick, M.; Karmakar, A.*Tetrahedron Lett*, **2005**, 46, 3073.(c)Abubshait, H.*Der Pharmacia Sinica*, **2012**, 3, 278.
- [13]. such as; (a)Schuttenberg, H.; Klump, G. ;Kaczmar, U. ;Turner, S. R.; Schulz, R. C. *J. Macromol. Sci., Chem.*, **1973**, 1085. (b)Frechet, J.M. J. unpublished work reported by P. Hodge, in: *Polymer-Supported Reactions in Organic Synthesis*. John Wiley and Sons, Ltd., **1980**, 103.(c)Sun, Y.; Sun,G. *Ind. Eng. Chem. Res.***2004**, 43, 5015.
14. (a)Mitra, S. S. ; Sreekumar, K.; *J. Polym. Sci. A: Polym. Chem.*, **1997**,35, 1413
(b)Okawara, M.; Shinokara, H. *Kogyo Kagaku Zasshi* **1957**, 60, 75 (c) Yanagisawa, Y.; Akiyama, M.; Okawara, M. *Kogyo Kagaku Zasshi* **1969**, 72, 1399. (d)George, B. K.; Pillai, V. N. R. *Eur. Polym. J.***1989**, 25, 1099.(e) Pillai, V. N. R. *Macromolecule*, **1988**, 21, 1867 (f) George, B. K. ;Pillai, V. N. R. *J. Polym. Sci. Polym. Chem.*,**1990**, 28, 2585.(g)Solichi M. M . *Reactive & Functional Polymers***1997**, 33, 247(h) Tamami, B.;Nasrollahi,A.; Ebrahimzadeh,F. *Iranian Polymer Journal*, **2009**, 18, 957.
15. Tamami, B.; Firouzabadi, H. ;Ebrahimzadeh,F.;Fadavi, A.*J. Iran. chem .Soc.***2009**, 6, 722.