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Quaternized amino functionalized cross-linked polyacrylamide as a new solid–liquid phase transfer catalyst in reduction of carbonyl compounds with $NaBH_4$

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Abstract—Poly[*N*-(2-aminoethyl)acrylamido]trimethyl ammonium chloride resin was developed as a new polymeric phase transfer catalyst. This quaternized polyacrylamide catalyzed the chemoselective reduction of aldehydes and ketones by $NaBH_4$ to give corresponding alcohols in high yields under mild conditions. © 2003 Elsevier Science Ltd. All rights reserved.

1. Introduction

In general, phase transfer catalysis has been widely accepted in industry and academia as a viable synthetic tool as depicted by the patent literature and the number of journal articles devoted to the topic.[1–3]

Insoluble polystyrene beads bearing quaternary ammonium or phosphonium salts have been widely used as phase transfer catalyst for liquid–liquid or solid–liquid heterogeneous organic synthesis.[4] On the other hand, it has been established that the nature of the polymeric support matrix has a significant role in the extent of its swelling and consequently on the efficiency of the supported species in the chemical reactions, with the polarity of the support material being the most important feature. Because of its physicochemical incompatibility with solvents and substrates, using a polystyrene support may often lead to low efficiency.[5] The design of synthetic polar polymeric supports like the polyacrylamide support is a significant advance and this holds promise for substantial improvements in the solid–liquid strategy.[6–9]

Sodium borohydride is a commonly used hydride transfer agent, which provides simple and convenient routes for the reduction of many organic compounds.[10] Polymer-bound borohydride offers several advantages over sodium borohydride. The primary advantage is the convenience of use of these materials and the minimal introduction of ionic species or organic by-product into treated bulk media. Simplified workup of reaction products is another advantage. Borohydride exchange resin (BER) was first reported in 1977 by Gibson and Baily,[11a] as a polymer supported borohydride reducing agent, to differ from sodium borohydride in reactivity and stability in alcoholic solvents and acidic solution and has been applied for different purposes.[11b,c]

Recently, we have reported the use of a quaternized amino functionalized cross-linked polyacrylamide as an efficient polymeric phase-transfer catalyst in the synthesis of halohydrins,[7] azidohydrins,[8] and also thiocyanohydrins.[9] This report describes the results of utilizing quaternized amino functionalized cross-linked polyacrylamide as an efficient polymeric phase transfer catalyst in the chemoselective reduction of aldehydes and ketones by sodium borohydride, in wet THF.

2. Results and discussion

Polyacrylamide cross-linked with divinylbenzene (DVB) (2%) was prepared by free radical solution polymerization of the monomer mixture in ethanol using $K_2S_2O_8$ as initiator. The resulting polymer was characterized by IR spectroscopy. The IR spectrum showed peaks at 3500 cm^{-1} (N–H amide), 1660 cm^{-1} (C=O amide), and 800 cm^{-1} (aryl group). Poly[*N*-(2-aminoethyl)acrylamide] was obtained by the transamidation reaction of cross-linked polyacrylamide with an excess amount of ethylenediamine (Scheme 1).

The amino resin was characterized by IR spectroscopy, and semi-quantitative ninhydrin reaction.[12] The resin gave a deep blue color on heating with ninhydrin reagent. The amino group capacity of the resin was determined by

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Keywords: polyacrylamide; $NaBH_4$; poly[*N*-(2-aminoethyl)acrylamide].

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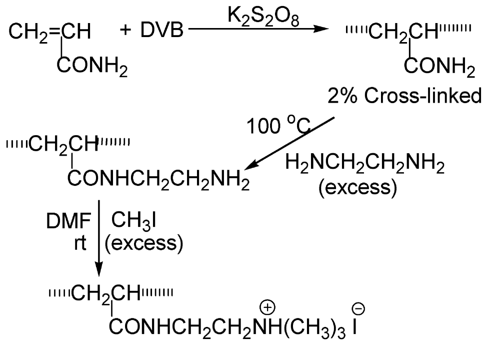


Scheme 1.

alkalimetric method to be 3.72 mmol/g of resin. Poly[*N*-(2-aminoethyl)acrylamido]trimethyl ammonium iodide was prepared by the reaction of poly[*N*-(2-aminoethyl)acrylamide] with an excess of methyl iodide in DMF at room temperature (Scheme 1). The resulting quaternized polymer was characterized by IR spectroscopy. The IR spectrum showed a peak at 1660 cm^{-1} (C=O, amide) and the intensity of the broad band of the N–H stretching was reduced considerably. The capacity of the quaternized resin was determined gravimetrically and by titration methods to be 3.21 and 3.06 mmol/g of resin, respectively.

The synthetic utility of this modified polymer was studied by examining the transformation of aldehydes and ketones to the corresponding alcohols with sodium borohydride using the polymer as a phase-transfer catalyst. The effect of solvent and molar ratio of the polymer on the reduction of aldehydes and ketones were investigated. The reactions were carried out in different solvents such as, absolute ethanol, ethanol (96%), methanol, dichloromethane, water, and wet THF, acetonitrile, benzene, and toluene (Table 1). Generally, the best solvent-system was wet THF. However, in some cases, wet benzene showed a better selectivity than wet THF. The optimum molar ratio of the polymeric catalyst to substrate was found to be 0.15–0.2:1. We observed that, there is a considerable difference between the reduction of carbonyl compounds in the presence and in the absence of the polymeric catalyst in wet THF (Table 2). Although, in the case of benzaldehyde and *p*-nitrobenzaldehyde, almost, no specified difference was observed in the absence or presence of the polymeric catalyst, however, for *p*-methoxybenzaldehyde, acetophenone and phenylacetophenone, the rate of reaction in the absence of the polymeric catalyst is very slow (entries 5–10). In the case of α,β-unsaturated carbonyl compound (entries 11, 12), in the absence of the polymeric catalyst, in addition to lower rate, no selectivity was observed and two products obtained.

Table 1. The effect of the solvent on the reduction with $NaBH_4$ using poly[*N*-(2-aminoethyl)acrylamido]trimethyl ammonium iodide as PTC

Entry	Substrate	Solvent	Time (h)	Conversion (%)[a]
1	Benzaldehyde	H_2O	1.5	86
2	Benzaldehyde	THF (dry)	1.5	35
3	Benzaldehyde	THF (wet)	0.5	100
4	Benzaldehyde	Acetonitrile (wet)	1.5	48
5	Benzaldehyde	Ethanol (abs.)	1.5	37
6	Benzaldehyde	Ethanol (96%)	1.5	90
7	Benzaldehyde	Methanol	1.5	85
8	Benzaldehyde	Benzene (wet)	1.5	67
9	Benzaldehyde	Toluene (wet)	1.5	56
10	Benzaldehyde	CH_2Cl_2	1.5	16
11	Acetophenone	H_2O	3	95
12	Acetophenone	THF (wet)	1.5	100
13	Acetophenone	Ethanol (96%)	4	56
14	Acetophenone	Methanol	4	74
15	Acetophenone	Benzene (wet)	4	8
16	Acetophenone	Toluene (wet)	4	5
17	Acetophenone	CH_2Cl_2	4	18

The molar ratio of $NaBH_4$: poly[*N*-(2-aminoethyl)acrylamido]trimethylammonium iodide: substrate was 0.5:0.2:1.

[a] Detected by GC.

Table 2. Reduction of aldehydes and ketones to their corresponding hydroxyl compounds with $NaBH_4$ in presence (+) and absence (−) of poly[*N*-(2-aminoethyl)acrylamido]trimethyl ammonium chloride resin as PTC in wet-THF

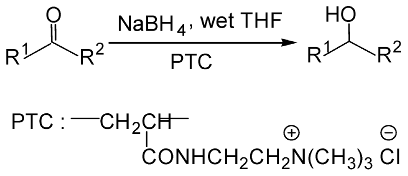
Entry	Substrate	The polymeric PTC	Time (min)	Conversion (%)
1	Benzaldehyde	+	30	100
2	Benzaldehyde	−	40	100
3	*p*-Nitrobenzaldehyde	+	15	100
4	*p*-Nitrobenzaldehyde	−	25	100
5	*p*-Methoxybenzaldehyde	+	200	100
6	*p*-Methoxybenzaldehyde	−	300	47
7	Acetophenone	+	90	100
8	Acetophenone	−	600	100
9	Phenylacetophenone	+	60	100
10	Phenylacetophenone	−	360	75
11	Benzalacetophonone	+	120	100
12	Benzalacetophonone	−	180	100[a]

[a] Two products were obtained.

The reduction of some representative aldehydes and ketones with sodium borohydride were carried out in the presence of this polymeric catalyst (Scheme 2). The results are listed in Table 3. Workup of the reaction was very easy and pure products were isolated without any purification. The filtered polymeric catalyst could be recovered several times and used without any loss in its capacity and efficiency.

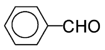
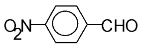
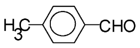
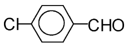
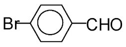
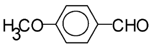
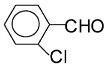
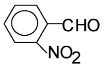
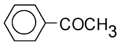
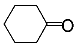
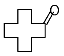
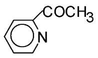
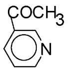
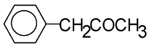
In addition to acting as a polymeric phase transfer catalyst, probably the reduction of carbonyl group is facilitated by hydrogen bonding between the oxygen of the carbonyl group and amidic hydrogen of the polymer. This fact is supported by our previous works with this polymeric phase transfer catalyst.[7–9] The rate of reduction of the carbonyl compound with $NaBH_4$ using this polymeric phase transfer catalyst in comparison with borohydride supported reagents is faster.[11] For example, the reaction times for the reduction of benzaldehyde and cyclohexanone with BER[11c] are 5 and 9 h, respectively, but with this catalytic system are 0.3 and 1 h (Table 3, entries 1 and 11). In addition, better selectivity between aldehydes and ketones in much shorter time is obtained using the catalytic system.

Allyl alcohols are important synthetic precursors. A regioselective reduction of α,β-unsaturated aldehydes and



Scheme 2.

Table 3. Reduction of aldehydes and ketones to their corresponding hydroxyl compounds with $NaBH_4$ in the presence of poly[*N*-(2-aminoethyl)acrylamido]trimethyl ammonium chloride resin as PTC

Entry	Substrate	Time (min)	Yield[a] (%)	Ref.[b]
1		20	95	18a
2		15	96	10a
3		60	94	10a
4		20	95	10a
5		20	96	10a
6		200	97	10a
7		10	95	10a
8		10	96	10a
9	$CH_3(CH_2)_4CHO$	10	96	10a
10		90	96	10a
11		60	96	18c
12		120	95	18c
13		45	95	10a
14		60	96	10a
15		30	94	13c
16	$PhCH_2COCH_2Ph$	60	95	13c
17	PhCH=CHCOPh	30	94[c]	18b
18	PhCH=CHCHO	30	95[c]	18a
19	CH_3CH=CHCHO	30	95[c]	13a
20	Citral	25	93[c]	18b

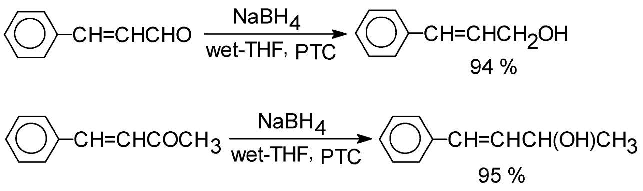
All of the reactions were carried out in presence of 0.2 M equiv. of the polymeric catalyst and in wet THF at room temperature. Products were identified by comparison of their IR and NMR spectra and/or physical data with the authentic samples.

[a] Yield refers to isolated product and also purity of products were determined by GC and physical data.

[b] For product.

[c] Only the carbonyl group was reduced.

ketones is an easy way to obtain these compounds. Therefore, this achievement is synthetically very important.[13] Specially, the reduction of α,β-unsaturated carbonyl compounds with $NaBH_4$ is highly solvent dependent and generally does not result in a useful regioselectivity.[14] Selective 1,2-reduction is usually achieved using modified hydride reagents, which are formed by the replacement of hydride with sterically bulky substituents or electron-withdrawing groups in order to discriminate between the structural or electron environments of the carbonyl functionality.[15,16]



Scheme 3.

As can be seen in Table 3 (entries 17–20), this system reduces unsaturated aldehydes and ketones to the corresponding unsaturated alcohols (Scheme 3).

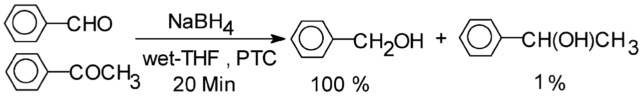
Selective reductions of one carbonyl group in the presence of other such groups is a frequent synthetic problem and various reagents have been developed for such selective reductions.[10,11] The chemoselectivity of the system was studied by competitively reducing the equimolar mixture of carbonyl compounds. As shown, this system generally reduces aldehydes much faster than ketones (Table 4, entries 1–3) (Scheme 4). The selectivity of this system is equal to or greater than that of previously reported selective reagents.[17] The data of entries 4–9 show a remarkable selectivity between aldehydes at room temperature. Thus aromatic aldehydes were preferentially reduced in the presence of aliphatic aldehydes with the high selectivity show by the 98:12 ratio between benzaldehyde and hexanal and the 100:11 ratio between *p*-nitrobenzaldehyde and hexanal.

More interesting chemoselectivity was observed in *para*-substituted benzaldehydes (Table 4, entries 6–9). We observed that, electron-withdrawing substituents enhanced the rate, whereas electron-donating substituents retarded the rate of the reductions. We also carried out chemoselective reductions with substituted benzaldehydes having more closely matched electron densities. The data of entries 7–11 show such selectivity. As shown, in these entries, the reaction is solvent dependent and using wet benzene gave a higher selectivity.

A very good selectivity was also observed between ketones (Table 4, entries 12 and 13). Thus, cyclohexanone was reduced much more quickly than hindered bicyclic ketones (Scheme 5), and 4-nitroacetophenone was reduced much more efficiently than acetophenone. However, in the case of substituted ketones having more closely matched electron density, no considerable difference observed for their chemoselective reductions in wet THF and also in wet benzene (Table 4, entries 14 and 15).

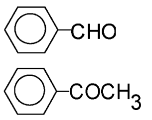
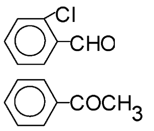
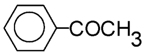
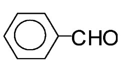
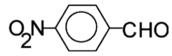
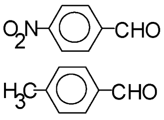
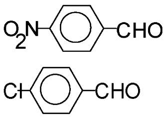
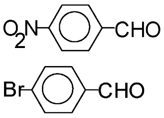
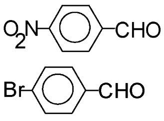
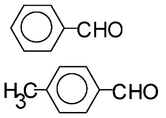
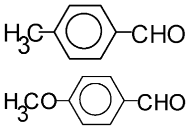
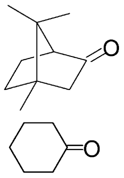
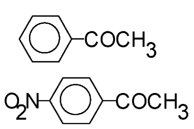
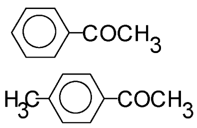
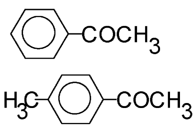
3. Conclusion

In conclusion poly[*N*-(2-aminoethyl)acrylamido]trimethyl ammonium halide resin proved to be a highly efficient polymeric phase transfer catalyst for the chemoselective reduction of aldehydes and ketones. In addition, the reduction of α,β-unsaturated aldehydes and ketones with this system is highly regioselective, resulting in the formation of the corresponding allylic alcohols. The



Scheme 4.

Table 4. Selective reduction of carbonyl compounds with $NaBH_4$ in the presence of poly[*N*-(2-aminoethyl)acrylamido]trimethyl ammonium chloride resin as PTC

Entry	Starting mixture[a]	Time (min)	Reduction[b] (%)
1		20	100
2		5	1 100
3	$CH_3(CH_2)_4CHO$ 	45	0 100
4	 $CH_3(CH_2)_4CHO$	20	0 98
5	 $CH_3(CH_2)_4CHO$	15	12 100
6		10	11 100
7		10	1 85
8		10	66 87
9[c]		15	75 100
10		30	2.5 89
11[c]		240	16 100
12		60	3 2
13		15	100 3
14		360	100 94
15[c]		360	93 89
			75

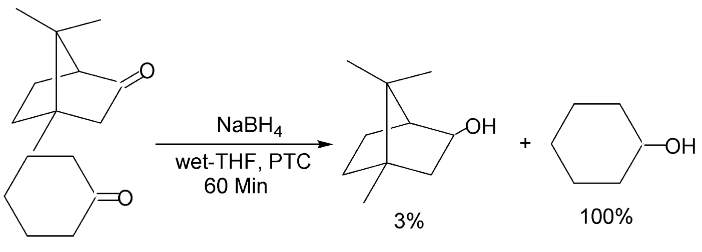
All of the reactions were carried out in presence of 0.2 M equiv. of the polymeric catalyst and in wet THF at room temperature.

[a] 1.0 mmol of each compound in 20 ml solvent.

[b] Determined by GC and ^1H NMR.

[c] The reaction was carried out in wet benzene.

reduction of carbonyl groups is probably facilitated by the hydrogen bonding between the oxygen of the carbonyl group and amidic hydrogen of the polymeric phase transfer catalyst. The resin has the inherent advantages of a solid phase transfer catalyst, including operational simplicity, filterability, and reusability.



Scheme 5.

4. Experimental

4.1. Materials and technique

Acrylamide was purchased from Fluka and was recrystallized from chloroform. DVB (55%) was also purchased from Fluka and was washed with sodium hydroxide solution (1%, 10 ml×2) and water (20 ml×3), to remove the inhibitor. Other reagents and solvents were used without further purification. Gas chromatography was recorded on a Shimadzu GC 14-A. IR spectra were run on a Perkin–Elmer IR-157-G Spectrophotometer. NMR spectra were recorded on a Bruker Avance DPX instrument (250 MHz). All products were characterized by comparison of their IR and NMR spectra and physical data with those of the authentic samples. All yields refer to the isolated products.

4.2. Preparation of poly[*N*-(2-aminoethyl)acrylamide]

DVB (3.9 g, 0.03 mol) and acrylamide (60.4 g, 0.85 mol) were dissolved in ethanol (250 ml). Benzoyl peroxide (350 mg, 1.4 mmol) was added and the mixture was heated while stirring at 70–75°C, for 5 h. The polymer formed was collected by filtration, washed several times with water, ethanol, benzene, and tetrahydrofuran, and dried at 60°C under reduced pressure. The IR spectrum of the polymer showed the characteristic absorption of amide (N–H) at 3200 and 3300 cm^{-1}, and carbonyl groups at 1660 cm^{-1}.

Polyacrylamide (10 g) was equilibrated with excess ethylenediamine (100 ml) for 12 h, and then the mixture was heated at 100°C for 12 h with stirring. The reaction mixture was poured into cold water (1 l). The resin was filtered and washed with NaCl solution (0.1 M) until the filtrate was free from ethylenediamine, as indicated by the absence of blue coloration with ninhydrin reagent. The gel was washed with water, methanol and then dried at 60°C under reduced pressure. The IR spectrum of the amino functionalized polyacrylamide showed the characteristic absorption of amino (N–H) group at 3500 cm^{-1}. The amino group content was determined by back titration and was found to be equal to 3.72 mmol/g.

4.3. Preparation of poly[*N*-(2-aminoethyl)acrylamido]-trimethyl ammonium iodide resin

Poly[*N*-(2-aminoethyl)acrylamide] (5 g) was equilibrated in DMF (100 ml) for 12 h. Methyl iodide (20 ml, 320 mmol) and NaOH (1 g, 25 mmol) was added and the reaction mixture stirred at room temperature for 48 h. The quaternized polymer was collected by filtration, washed several times with water and methanol until the filtrate was free from CH_3I, as indicated by absence of formation of AgI with $AgNO_3$. Finally the polymer was washed with ether and dried at 50°C under reduced pressure to afford the desired compound in a yield of 8.23 g. The capacity of quaternized resin was determined both gravimetrically and by titration. This was found to be 3.21 and 3.06 mmol/g of resin, respectively.

For the conversion of the iodide resin to other resin halides, the resin (5 g) was added to the metal halide aqueous solution (2 M, 100 ml), and the mixture was stirred for 12 h. The polymer sample was filtered, washed with distilled water, ether and dried at 50°C under reduced pressure.

4.4. Typical procedure for reduction of carbonyl compounds

A solution of a carbonyl compound (1 mmol) and $NaBH_4$ (0.5 mmol) in wet THF (20 ml) was added to the poly[*N*-(2-aminoethyl)acrylamido]trimethyl ammonium halide resin (~0.1 g) with stirring. Progress of the reaction was monitored by TLC and/or GC. After completion of the reaction, the resin was removed by filtration. A small amount of $NaBH_4$ which dissolved in wet THF was removed using a short silica-gel column. The organic solvent was dried with anhydrous Na_2SO_4. The corresponding pure product was obtained upon evaporation of solvent. The characterization of the product was performed with ^{1}H NMR, and IR techniques.

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References

1. Starks, C. M.; Liotta, C. L.; Halperm, M. *Phase Transfer Catalysis*, Chapman & Hall: New York, 1994.
2. Aglietto, M.; Chiellini, E.; Antone, S. D.; Ruggeri, G.; Solarv, R. *Pure Appl. Chem.* **1988**, *60*, 415, and the references cited therein.
3. Keller, W. E. *Phase Transfer Reaction*, Georg Thieme: Stuttgart, 1992; Vol. 3. Fluka-Compendium.
4. (a) Regen, S. L. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 421. (b) Tomoi, M.; Ford, W. T. In *Synthesis and Separation Using Functional Polymers*, Sherrington, D. C., Hodge, P., Eds.; Wiley: New York, 1988; pp 181–207.
5. (a) George, B. K.; Pillai, V. N. R. *Polymer* **1989**, *30*, 178. (b) Aiswaryakumari, K.; Sreekumar, K. *J. Appl. Polym. Sci.* **1996**, *59*, 2039.
6. (a) Atherton, E.; Harkiss, F. D.; Sheppard, R. C. *J. Chem. Soc., Chem. Commun.* **1978**, 538. (b) Mitra, S. S.; Sreekumar, K. *J. Polym. Sci. Part A: Polym. Chem.* **1997**, *35*, 1413.
7. Tamami, B.; Mahdavi, H. *Tetrahedron Lett.* **2001**, *42*, 8721.
8. Tamami, B.; Mahdavi, H. *React. Funct. Polym.* **2002**, *51*, 7.
9. Tamami, B.; Mahdavi, H. *Tetrahedron Lett.* **2002**, *43*, 6225.
10. (a) Firouzabadi, H.; Zeynizadeh, F. *Bull. Chem. Soc. Jpn* **1996**, *69*, 50630, and the references cited therein. (b) Hudlicky, M. *Reduction in Organic Chemistry*, Ellis Horwood: Chichester, 1984.
11. (a) Gibson, H. W.; Baily, F. C. *J. Chem. Soc., Chem. Commun.* **1977**, 815. (b) Hodge R. S. US Patent 4107099, 1978. (c) Yoon, N. M.; Park, B.; Gyaung, Y. S. *Tetrahedron Lett.* **1983**, *24*, 5367.
12. Spackman, D. H.; Stein, W. H.; Moore, S. *Anal. Chem.* **1958**, *30*, 1190.
13. (a) Johnson, M. R.; Rickborn, B. *J. Org. Chem.* **1970**, *35*, 1041. (b) Wilson, K. E.; Seinder, R. T.; Masamune, S. *J. Chem.*

Soc., Chem. Commun. **1970**, 213. (c) Sande, A. R.; Jagadale, M. H.; Mane, R. B.; Salunkhe, M. M. *Tetrahedron Lett.* **1984**, *25*, 3501.

14. Nutaitis, C. F.; Bernardo, J. E. *J. Org. Chem.* **1989**, *54*, 5629.
15. (a) Fujii, H.; Oshima, K.; Utimato, K. *Chem. Lett.* **1991**, 1847. (b) Fleet, G. W. J.; Harding, P. J. C. *Tetrahedron Lett.* **1981**, *22*, 675.
16. Firouzabadi, H.; Zeynizadeh, F. *Iranian J. Sci. Technol., Trans. A* **1995**, *19*, 103.
17. (a) Hutchins, R. O.; Kandasamy, D. *J. Am. Chem. Soc.* **1973**, *95*, 6131. (b) Brown, H. C.; Kulkarni, S. U. *J. Org. Chem.* **1977**, *42*, 4169. (c) Midland, M. M.; Tramontan, A. *J. Org. Chem.* **1978**, *43*, 1470. (d) Gribble, G. W.; Ferguson, D. C. *J. Chem. Soc., Chem. Commun.* **1975**, 538.
18. (a) Santaniello, E.; Ponti, F.; Manzocchi, A. *Synthesis* **1978**, 891. (b) Hutchins, R. O.; Kandasamy, D. *J. Org. Chem.* **1975**, *40*, 2530. (c) Yakabe, M.; Morimoto, T. *Can. J. Chem.* **1998**, *76*, 1916.