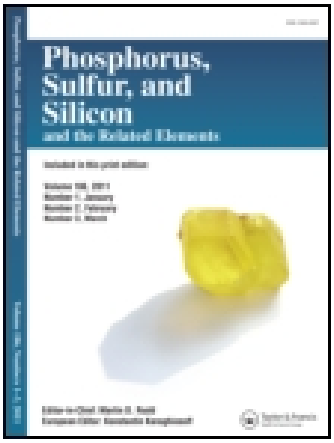


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gpss20

Solvent-Free, Efficient, and High Regioselective Conversion of Epoxides to Symmetrical and Unsymmetrical vic-Dihalides Using Chlorodiphenylphosphine and N-Halosuccinimides

Ghasem Aghapour [a] & Asieh Afzali [a]
[a] School of Chemistry , Damghan University , Damghan, Iran
Published online: 07 Mar 2011.

To cite this article: Ghasem Aghapour & Asieh Afzali (2011) Solvent-Free, Efficient, and High Regioselective Conversion of Epoxides to Symmetrical and Unsymmetrical vic-Dihalides Using Chlorodiphenylphosphine and N-Halosuccinimides, Phosphorus, Sulfur, and Silicon and the Related Elements, 186:3, 598-605, DOI: 10.1080/10426507.2010.509877

To link to this article: http://dx.doi.org/10.1080/10426507.2010.509877

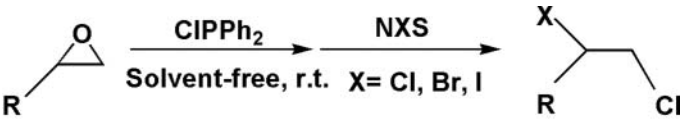
Phosphorus, Sulfur, and Silicon, 186:598–605, 2011

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426507.2010.509877

SOLVENT-FREE, EFFICIENT, AND HIGH REGIOSELECTIVE CONVERSION OF EPOXIDES TO SYMMETRICAL AND UNSYMMETRICAL *VIC*-DIHALIDES USING CHLORODIPHENYLPHOSPHINE AND N-HALOSUCCINIMIDES

Ghasem Aghapour and Asieh Afzali
School of Chemistry, Damghan University, Damghan, Iran

GRAPHICAL ABSTRACT



R= $PhOCH_2$, $C_4H_5O_2CH_2$, Ph, $^iPrOCH_2$, $C_3H_5OCH_2$, $C_{12}H_{25}$, *p*-Cl-$PhOCH_2$ or epoxide= cyclohexene oxide

65-97%

Abstract *A new method is described for the efficient and high regioselective conversion of epoxides to symmetrical and unsymmetrical* vic*-dihalides in high yields using chlorodiphenylphosphine and N-halosuccinimides under solvent-free and neutral conditions and at room temperature.*

Supplemental materials are available for this article. Go to the publisher's online edition of Phosphorus, Sulfur, and Silicon and the Related Elements *to view the free supplemental file.*

Keywords Chlorodiphenylphosphine; epoxide; N-halosuccinimide; solvent-free reaction; *vic*-dihalide

INTRODUCTION

Syntheticchemistry continues to develop various techniques for obtaining products with less environmental impact. One of the more promising approaches is solvent-free reactions.[1] The elimination of volatile organic solvents in organic syntheses is a most important goal in "green" chemistry. Furthermore, these reactions have some other advantages such as low costs, simplicity in process and handling, formation of cleaner products, enhanced selectivity, much improved reaction rates, and prevention of solvent wastes, hazards, and

Received 19 May 2010; accepted 18 July 2010.
We gratefully acknowledge the support of this work by the Damghan University Research Council.
Address correspondence to Ghasem Aghapour, School of Chemistry, Damghan University, Damghan 3671641167, Iran. E-mail: Gh_Aghapour@du.ac.ir

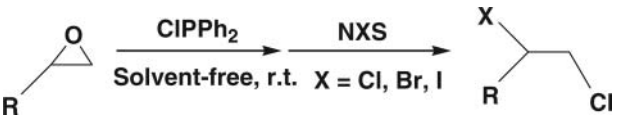
toxicity. These factors are especially important in industry. The development of solvent-free organic synthetic methods has thus become an important and popular research area.[1]

Additionally, epoxides are important intermediates in organic synthesis,[2] and, due to their particular polarity and strain in their three-membered ring, a large variety of nucleophiles are known to effect the ring opening of these compounds.[3,4] Although there are many methods reported for the conversion of epoxides into β-halohydrins,[5–8] their conversion to symmetrical or especially unsymmetrical *vic*-dihalides as other important halogenated compounds is rarely found in the literature. The use of reagents such as PPh_3/CCl_4,[9] PPh_3/X_2 (X = Cl, Br),[10a,b] and PPh_3/N-halo imides in acetonitrile under reflux conditions[7b] is reported for the preparation of symmetrical *vic*-dihalides and HCl/THF as highly acidic conditions in first step to produce chlorohydrin, followed by treatment with PPh_3/Br_2 in the second step[10b] and PPh_3/N-halo imides via a two-step procedure in acetonitrile under reflux conditions[7b] for the preparation of unsymmetrical *vic*-dihalides.

RESULTS AND DISCUSSION

Recently, we have reported on the application of PPh_3/DDQ/tetraalkylammonium halides in refluxing acetonitrile in the conversion of the epoxides to β-halohydrins and *vic*-dihalides,[11] and also the application of chlorodiphenylphosphine in the conversion of epoxides to chlorohydrins under mild and solvent-free conditions.[12] Also, we have shown additional abilities of trivalent phosphorus in organic synthesis,[13–16] including conversion of aldehydes and ketones to *gem*-dichlorides using chlorodiphenylphosphine/N-chlorosuccinimide ($ClPPh_2$/NCS).[17]

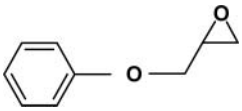
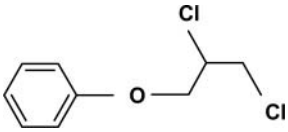
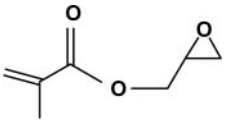
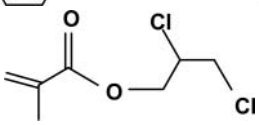
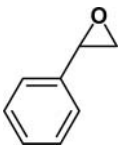
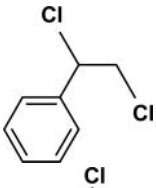
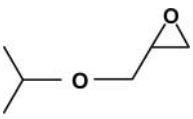
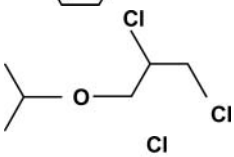
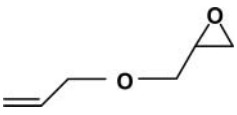
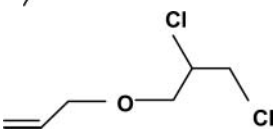
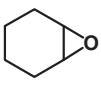
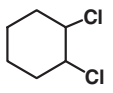
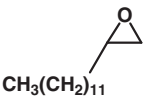
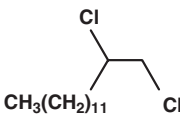
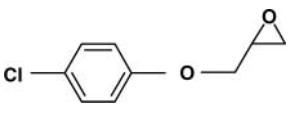
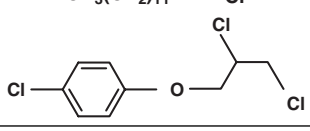
In continuation of this work, with respect to rarity of methods for preparation of symmetrical and especially unsymmetrical *vic*-dihalides from epoxides, and also the advantages of solvent-free reactions, we report in this article a new, more facile, and milder method for the efficient, regioselective, and solvent-free conversion of epoxides to symmetrical or unsymmetrical *vic*-dihalides using $ClPPh_2$ and N-halosuccinimides (NXS; X = Cl, Br, I) under neutral and one-pot conditions at room temperature in good to excellent yields (Scheme 1).



Scheme 1 Solvent-free conversion of epoxides to symmetrical and unsymmetrical *vic*-dihalides using chlorodiphenylphosphine and N-halosuccinimides ($ClPPh_2$ and NXS, X = Cl, Br, I) under neutral conditions at room temperature.

Initially we tried to convert glycidyl phenyl ether to 1,2-dichloro-3-phenoxy propane using $ClPPh_2$ and NCS under solvent-free conditions. In this connection, grinding of this epoxide with $ClPPh_2$ (1 eq.) alone for about 20 min gave 1-chloro-3-phenoxy-2-propanol, which was isolable by column chromatography.[12] We also found that the use of $ClPPh_2$ and NCS simultaneously is highly exothermic and vigorous for this purpose. Thus, for ease and mild performing of this transformation, first glycidyl phenyl ether was ground with $ClPPh_2$ (1 eq.) in a glass test tube until TLC showed the disappearance of the epoxide (20 min), and then NCS (1.2 eq.) was gradually added to the reaction mixture over a period of 3 min. The reaction mixture was magnetically agitated for 9.5 h so that TLC showed

Table 1 Solvent-free conversion of epoxides to *vic*-dichlorides using $ClPPh_2$ and NCS at room temperature[a,b]

Entry	Epoxides	*vic*-Dichlorides	Time (h)	Yield (%)[c]
1			9.85	90
2			10	87
3			9	85
4			10	83
5			5.25	97
6			4.5	70[d]
7			7.5	75
8			9.5	82

[a]Molar ratio 1:1:1.2 of epoxide:$ClPPh_2$:NCS was used in these reactions.

[b]First epoxide was ground with $ClPPh_2$ (1 eq.) in a glass test tube until TLC showed the disappearance of the epoxide (15–40 min), and then NCS was gradually added to the reaction mixture over a period of 3 min. The reaction mixture was magnetically agitated for appropriate time.

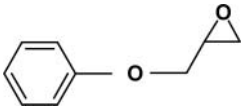
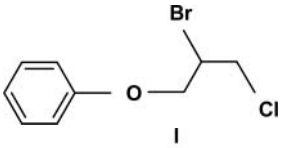
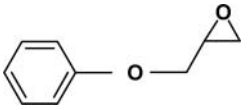
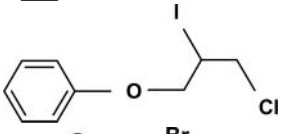
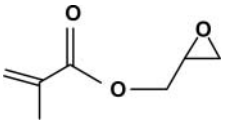
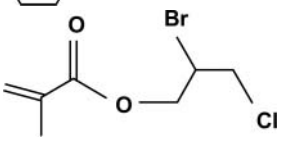
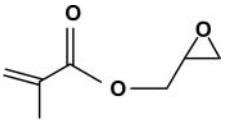
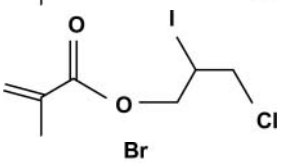
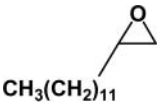
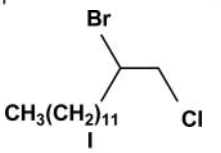
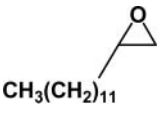
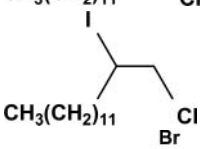
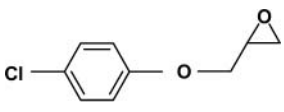
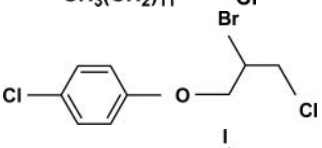
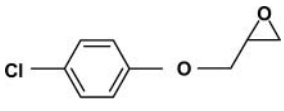
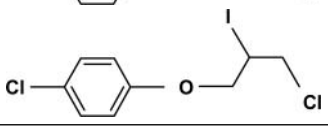
[c]Isolated yield.

[d]A mixture of cis:trans (1:2) was obtained in this case on the basis of NMR analysis.

the completion of the reaction. Column chromatography of the crude product afforded 1,2-dichloro-3-phenoxy propane in 90% yield. Then, we extended this procedure to other structurally different epoxides to obtain *vic*-dichlorides. The results of this investigation are shown in Table 1.

As shown in Table 1, epoxides are efficiently converted to their corresponding *vic*-dichlorides using $ClPPh_2$ and NCS in low molar ratio (1:1.2) under solvent-free conditions at room temperature. Under these reaction conditions, the activated aromatic ring,

Table 2 Solvent-free conversion of epoxides to unsymmetrical *vic*-halides using $ClPPh_2$ and NXS (X = Br, I) at room temperature[a,b]

Entry	Epoxides	Unsymmetrical *vic*-dihalides	Time (h)	Yield (%)[c]
1			10	65
2			12	73
3			9	70
4			15	72
5			14	83
6			15	92
7			17	69
8			15	75

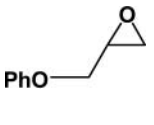
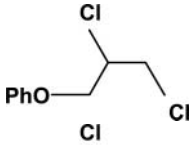
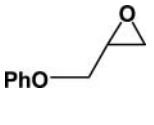
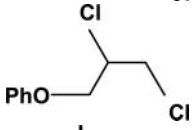
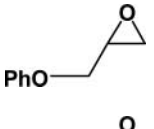
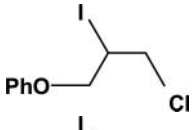
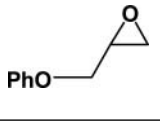
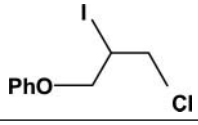
[a]Molar ratio 1:1:1.2 of epoxide:$ClPPh_2$:NXS was used in these reactions.

[b]First epoxide was ground with $ClPPh_2$ (1 eq.) in a glass test tube until TLC showed the disappearance of the epoxide (15–40 min), and then NXS was gradually added to the reaction mixture over a period of 3 min. The reaction mixture was magnetically agitated for the appropriate time.

[c]Isolated yield.

carbon–carbon double bonds, ester group, and ethereal bonds as functional groups that are present in the epoxide molecules remain intact. In addition, it is possible to obtain unsymmetrical *vic*-dihalides by exchanging NCS with N-bromosuccinimide (NBS) or N-iodosuccinimide (NIS) in the present method. The results of this exchange are shown in Table 2.

Table 3 Comparison of the efficiency of the presented method with our previously reported method based on using PPh_3/DDQ/tetraalkyl ammonium halide[11]

Entry	Epoxide	*vic*-Dihalide	Reagent (molar ratio)	Solvent	Temp. (°C)	Yield (%)[a]
1			$ClPPh_2$/NCS (1:1.2)	–	r.t.	90
2			PPh_3/DDQ/(*n*-butyl)$_4$NCl.H_2O (4:4:2.2)	CH_3CN	reflux	78[b]
3			$ClPPh_2$/NIS (1:1.2)	–	r.t.	73
4			PPh_3/DDQ/(*n*-butyl)$_4$NCl.H_2O/(*n*-butyl)$_4$NI (4:4:1.2:1.2)	CH_3CN	reflux	40[b]

[a]Isolated yield.

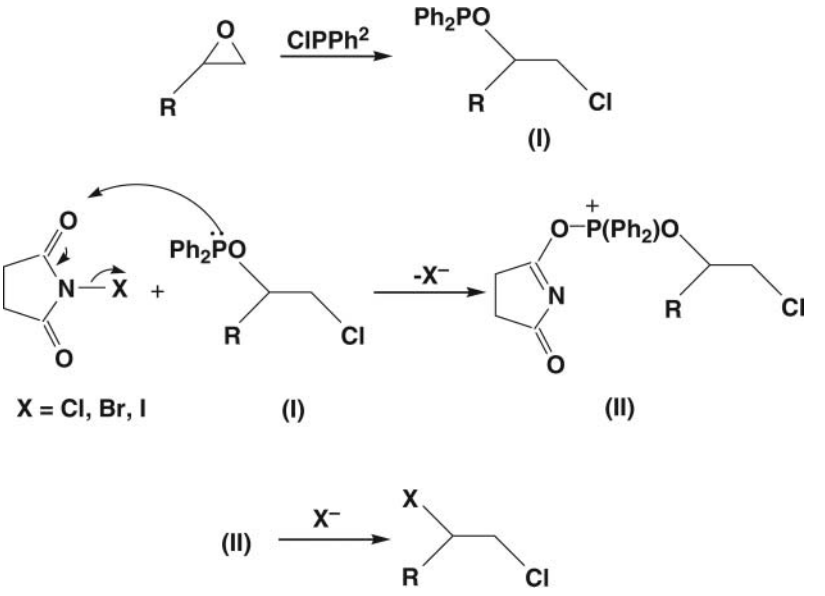
[b]In these reactions (entries 2 and 4), first the epoxide is treated with PPh_3:DDQ (1.2:1.2) in the presence of (*n*-butyl)$_4$NCl.H_2O producing *vic*-chloro alcohol. Then, the reaction mixture is transferred to another flask containing PPh_3:DDQ (2.8:2.8) alone or together with tetra alkyl ammonium iodide for obtaining symmetrical or unsymmetrical *vic*-dihalides, respectively.

As shown in Table 2, epoxides are efficiently converted to their corresponding *vic*-chlorohalides via a one-pot procedure using $ClPPh_2$ and then the appropriate NXS (X = Br, I) in low molar ratio (1:1.2) under solvent-free conditions at room temperature. In addition, in this transformation, it was observed that the epoxide ring is regioselectively opened from its less-hindered side due to steric factor by the reaction with $ClPPh_2$ so that the product contains a chlorine atom attached to a primary carbon atom and another halogen (Br or I) to a secondary one.

In order to obtain deeper insight into the advantages and merit of the current method compared to previously reported methods, we compared the efficiency of $ClPPh_2$ and NXS with, for example, triphenylphosphine/2,3-dichloro-5,6-dicyanobenzoquinone/tetra alkyl ammonium halide system (PPh_3/DDQ/R_4NX)[11] in this conversion. The results of this comparison are shown in Table 3.

As shown in Table 3, $ClPPh_2$ and NXS convert the epoxides to *vic*-dihalides in low molar ratio at room temperature in high yields under solvent-free conditions and in a one-pot manner. However, this conversion is operated using PPh_3/DDQ/R_4NX but in high molar ratio and in refluxing acetonitrile. In addition, the operation of this method is somewhat difficult, so that the first epoxide is treated with PPh_3/DDQ (1.2:1.2) in the presence of (*n*-butyl)$_4$NCl.H_2O producing *vic*-chloro alcohol. Then, the reaction mixture is transferred to another flask containing PPh_3/DDQ (2.8:2.8) alone or together with tetra alkyl ammonium iodide for obtaining symmetrical or unsymmetrical *vic*-dihalides, respectively.

Also, the use of PPh_3 and NXS (or *N*-halo saccharine = NXSac)[7b] for this conversion contains some disadvantages compared to the presented method, such as performing in



Scheme 2 Suggested mechanism for the conversion of epoxides to symmetrical and unsymmetrical *vic*-dihalides using $ClPPh_2$ and NXS (X = Cl, Br, I).

refluxing acetonitrile, the use of reagent in high molar ratio (up to 3.7:3.7), and the need to transfer the reaction mixture to the second reaction flask again for completion of the reaction. In addition, in the synthesis of chloroiodides using the present procedure, contrary to previous works,[7b,11] alkene formation is not an important competing pathway, and these products are obtained in good to excellent yields (Table 2, entries 2, 4, 6, and 8; Table 3, please compare entry 3 with entry 4).

Although the exact mechanism of these reactions is not clear, on the basis of the indicated mechanisms in this area,[7b,12] we may suggest that at first, the epoxide ring is regioselectively opened from its less-hindered side due to steric factor by reaction with $ClPPh_2$ affording adduct (**I**)[12] (Scheme 2). The addition of N-halosuccinimide to the reaction mixture converts the adduct (**I**) to the intermediate (**II**) with concomitant releasing of the halide anion.[7b] The desired symmetrical or unsymmetrical *vic*-dihalide is produced via attacking of the present halide anion to intermediate (**II**). This mechanism is in accordance with the formation of unsymmetrical *vic*-dihalides containing a chlorine atom attached to a primary carbon atom and bromine or iodine to a secondary one in the present method.

CONCLUSIONS

In conclusion, the present investigation has demonstrated that the use of $ClPPh_2$ and then NXS offers a solvent-free, simple, and convenient method, avoiding the use of molecular halogen[10a,b] with respect to its harsh handling and also halogenated hydrocarbon solvents such as dichloromethane, for the mild conversion of epoxides to their corresponding *vic*-dihalides. This method containing the ability of the synthesis of both symmetrical and unsymmetrical *vic*-dihalides, especially in a one-pot procedure, offers advantages such as commercial availability, ease of handling and inexpensiveness of the reagent, the use of

reagent in low molar ratio, reduced pollution, easy work up, excellent regioselectivity, high yields even for chloroiodides, and operation at room temperature in neutral media. Further studies toward the other applications of this reagent in organic synthesis are in progress in our laboratory.

EXPERIMENTAL

Solvents, reagents, and chemicals were obtained from Merck (Germany) and Fluka (Switzerland) chemical companies. The products are known compounds,[7b,11] and were characterized by comparison of their physical data, IR, NMR, and mass spectra with those prepared according to procedures reported in the literature. FT-IR spectra were recorded on a Perkin Elmer RXI spectrophotometer. Nuclear magnetic resonance spectra were recorded on a Brucker Avance DPX-250 or Brucker Avance DRX-500 spectrometers. Mass spectra were determined on a Shimadzu GCMS-QP 1000 EX at 70 ev. Thin layer chromatography was carried out on silica gel 254 analytical sheets obtained from Fluka.

General Procedure for the Conversion of Epoxides to Symmetrical or Unsymmetrical *vic*-Dihalides

Epoxide (1 mmol) was thoroughly mixed with $ClPPh_2$ (0.18 mL, 1 mmol) in a glass test tube. The resulting mixture was ground at room temperature for the appropriate time, which TLC showed complete disappearance of epoxide (15–40 min), and then NXS (X = Cl, Br, I) (1.2 mmol) was gradually added to the reaction mixture over a period of 3 min. The reaction mixture was magnetically agitated untile TLC showed the completion of the reaction. Column chromatography of the crude product gave pure symmetrical or unsymmetrical *vic*-dihalide in 70–97% and 65–92% yields, respectively (Tables 1 and 2).

The spectral data of some of the products can be found in the Supplemental Materials (available online).

REFERENCES

1. (a) Tanaka, K.; Toda, F. *Chem. Rev.* **2000,** *100*, 1025–1074; (b) Tanaka, K. *Solvent-Free Organic Synthesis*; Wiley-VCH Verlag: Weinheim, Germany, 2003.
2. Behrevs, C. H.; Ko, S. Y.; Sharpless, K. B.; Walker, F. J. *J. Org. Chem.* **1985,** *50*, 5687–5696.
3. Smith, J. G. *Synthesis* **1984**, 629–656.
4. Bonini, C.; Righi, G. *Synthesis* **1994**, 225–238.
5. (a) Stewart, C. A.; Vanderwerf, C. A. *J. Am. Chem. Soc.* **1954,** *76*, 1259–1264; (b) Chini, M.; Crotti, P.; Gardelli, C.; Macchia, F. *Tetrahedron* **1992,** *48*, 3805–3812; (c) Garrett, C. E.; Fu, G. C. *J. Org. Chem.* **1997,** *62*, 4534–4535; (d) Kotsuki, H.; Shimanouchi, T.; Ohshima, R.; Fujiwara, S. *Tetrahedron* **1998,** *54*, 2709–2722.
6. (a) Sharghi, H.; Naeimi, H. *Synlett* **1998,** 1343–1344; (b) Sharghi, H.; Eskandari, M. M. *Synthesis* **2002**, 1519–1522; (c) Sharghi, H.; Massah, A. R.; Eshghi, H.; Niknam, K. *J. Org. Chem.* **1998,** *63*, 1455–1461; (d) Salomon, C. J. *Synlett* **2001**, 65–68.
7. (a) Iranpoor, N.; Kazemi, F.; Salehi, P. *Synth. Commun.* **1997,** *27*, 1247–1258; (b) Iranpoor, N.; Firouzabadi, H.; Azadi, R.; Ebrahimzadeh, F. *Can. J. Chem.* **2006,** *84*, 69–75; (c) Betti, C.; Landini, D.; Maia, A. *Synlett* **2006**, 1335–1338.
8. (a) Roy, C. D. *Aust. J. Chem.* **2006,** *59*, 834–836; (b) Roy, C. D.; Brown, H. C. *Aust. J. Chem.* **2007,** *60*, 139–145; (c) Constantino, M. G.; Junior, V. L.; Invernize, P. R.; Filho, L. C. S.; Silva, G. V. J. *Synth. Commun.* **2007,** *37*, 3529–3539.

9. Isaacs, N. S.; Kirkpatrick, D. *Tetrahedron Lett.* **1972,** *13*, 3869–3870.
10. (a) Thakore, A. N.; Pope, P.; Oehlschlager, A. C. *Tetrahedron* **1971,** *27*, 2617–2626; (b) Sonnet, P. E.; Oliver, J. E. *J. Org. Chem.* **1976,** *41*, 3279–3283.
11. Iranpoor, N.; Firouzabadi, H.; Aghapour, G.; Nahid, A. *Bull. Chem. Soc. Jpn.* **2004,** *77*, 1885–1891.
12. Aghapour, G.; Afzali, A.; Salek, F. *Indian J. Chem.* **2009,** *48B*, 231–236.
13. Iranpoor, N.; Firouzabadi, H.; Aghapour, G.; Vaez zadeh, A. R. *Tetrahedron* **2002,** *58*, 8689–8693.
14. Iranpoor, N.; Firouzabadi, H.; Aghapour, G. *Synlett* **2001,** *7*, 1176–1178.
15. Iranpoor, N.; Firouzabadi, H.; Aghapour, G. *Synth. Commun.* **2002,** *32*, 2535–2541.
16. Aghapour, G.; Amirabadi, M. *Indian J. Chem. Sect. B* **2007,** *46*, 649–652.
17. Aghapour, G.; Afzali, A. *Synth. Commun.* **2008,** *38*, 4023–4035.