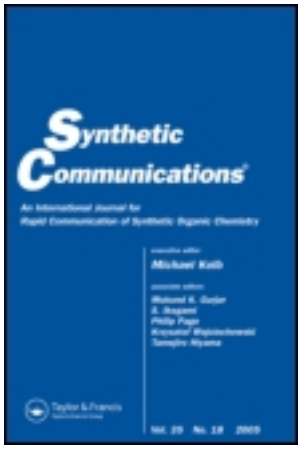
This article was downloaded by: [Pennsylvania State University]
On: 16 February 2013, At: 13:44
Publisher: Taylor & Francis
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Catalyst-Free, Direct, High Regio- and Chemoselective Conversion of Epoxides to Vicinal Haloesters Under Mild, Neutral, and Solvent-Free Conditions

Ghasem Aghapour [a] & Razieh Hatefipour [a]

[a] School of Chemistry, Damghan University, Damghan, Iran

Accepted author version posted online: 22 Feb 2012.Version of record first published: 07 Jan 2013.

To cite this article: Ghasem Aghapour & Razieh Hatefipour (2013): Catalyst-Free, Direct, High Regio- and Chemoselective Conversion of Epoxides to Vicinal Haloesters Under Mild, Neutral, and Solvent-Free Conditions, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 43:7, 1030-1040

To link to this article: http://dx.doi.org/10.1080/00397911.2011.621097

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.tandfonline.com/page/terms-and-conditions

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae, and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand, or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

Synthetic Communications®, 43: 1030–1040, 2013
Copyright © Taylor & Francis Group, LLC
ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397911.2011.621097

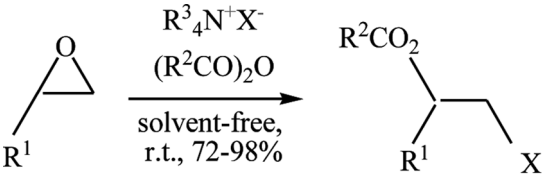
Taylor & Francis
Taylor & Francis Group

Downloaded by [Pennsylvania State University] at 13:44 16 February 2013

CATALYST-FREE, DIRECT, HIGH REGIO- AND CHEMOSELECTIVE CONVERSION OF EPOXIDES TO VICINAL HALOESTERS UNDER MILD, NEUTRAL, AND SOLVENT-FREE CONDITIONS

Ghasem Aghapour and Razieh Hatefipour
School of Chemistry, Damghan University, Damghan, Iran

GRAPHICAL ABSTRACT



R^1= $PhOCH_2$, CH_2=$CHCH_2OCH_2$, Ph, $ClCH_2$, $(CH_3)_2CHOCH_2$; or epoxide = cyclohexene oxide
R^2= CH_3, Ph; R^3= n-butyl, n-pentyl, n-hexyl;
X= Cl, Br, I

Abstract *A catalyst-free, high regio- and chemoselective method is described for the mild conversion of wide varieties of epoxides directly to their corresponding vicinal haloesters using quaternary ammonium halides $R_4N^+X^-$ (X equals; Cl, Br, I; R = n-butyl, n-pentyl, n-hexyl) in the presence of an aliphatic or aromatic carboxylic anhydride at room temperature under neutral and solvent-free conditions.*

Keywords Carboxylic anhydride; catalyst-free; epoxide; quaternary ammonium halide; vicinal haloester

INTRODUCTION

Epoxides are important intermediates in organic synthesis.[1] Their facile regio- and stereoselective ring-opening reactions with a wide variety of nucleophiles provide a powerful strategy in organic chemistry.[1–6] However, in most of the epoxide ring-opening reactions under acidic conditions, the formation of a mixture of regio-isomers and polymerization is observed. One of the useful nucleophilic reactions of epoxides is their conversion into their vicinal halohydrins,[7] important and

Received July 3, 2011.
Address correspondence to Ghasem Aghapour, School of Chemistry, Damghan University, Damghan 36715 364, Iran. E-mail: Gh_Aghapour@du.ac.ir

Downloaded by [Pennsylvania State University] at 13:44 16 February 2013

versatile synthons in organic synthesis. Many different reagents or catalysts have been introduced in various conditions for this purpose.[8,9]

Synthesis of esters has played a most important role in organic synthesis from its infancy.[10] This importance stemmed from the utility of esters in diverse fields both in the laboratory and in industry. Ester moieties, irrespective of whether acyclic or cyclic, constitute major backbones, as well as functional groups of chemical significance, in numerous natural products and synthetic compounds. Ester groups also play versatile temporary roles in organic synthesis for protection of carboxylic acids and hydroxy groups. In this connection, the acetylation of alcohols is one of the most widely used process for the protection of hydroxy groups, which is routinely carried out by acid anhydrides or acid chlorides in the presence of tertiary amines,[11] protic or Lewis acids,[12] or sometimes solid acid catalysts.[13] Many different reagents or catalysts have also been introduced in various conditions for the esterification reactions.[10]

Although there are several reports concerning the preparation of vicinal halohydrins from epoxides using different reagents or catalysts,[8,9] relatively little attention has been paid to the direct conversion of epoxides into *vic*-haloesters, although the latter are superior intermediates in the synthesis of structurally defined bioconjugates[14] of interest in membranology,[15] enzymology,[16] gene therapy,[17] and drug design.[18] In addition, these compounds containing two important functional groups (halogen and ester) have multiple modes of reactivity and represent an interesting and important subclass. In contrast to simple haloalkanols, which can be conveniently prepared by cleavage of oxirane derivatives with metal halides under acidic conditions,[4,19] preparation of the corresponding halohydrin esters always poses synthetic problems. The existing protocols, involving cleavage of the oxirane unit with acyl chlorides (alone[20] or in combination with CrO_2Cl_2,[21] $CoCl_2$,[22] a catalytic amount of Bu_2SnCl_2/Ph_3P,[23] hexaalkylguanidinium chloride,[24] $LiClO_4$ as a catalyst[25]) or related haloacylating system (e.g., $TiCl_4$/EtOAc/imidazole[26]) or with trimethylsilyl halide (TMSX) in the presence of pyridine and a mixture of carboxylic acid–trifluoroacetic anhydride (CA-TFAA) under argon at 80 °C[27] suffer from certain limitations such as competing side reactions, performance at high temperature and in acidic media, handling of the reagent, incompatibility with oxidation- / Lewis acid–sensitive substrates, and performance in harmful organic solvents such as $CHCl_3$, CH_3CN, or benzene. Another method based on epoxide ring opening is a SnX_2-promoted fission of 2,3-epoxy alcohol derivatives with TMSX, which after acylation affords O-acetylated vicinal halohydrins in rather erratic yields and mediocre regioselectivity.[28]

On the other hand, waste prevention and environmental protection are major requirements in an overcrowded world of increasing demands. Synthetic chemistry continues to develop various techniques for obtaining better products with less environmental impact. One of the more promising approaches is solvent-free organic synthesis.[29] These reactions have many advantages such as reduced pollution, low costs, and simplicity in process and handling. These factors are especially important in industry.[30]

Thus, on the basis of these descriptions, the development of simple and efficient methods for preparation of vicinal haloesters from epoxides especially in neutral and solvent-free conditions is desirable.

In continuation of our very recent works on the ring opening of epoxides,[31] especially such as conversion of epoxides to β-chlorohydrins[9d] and also to

Downloaded by [Pennsylvania State University] at 13:44 16 February 2013

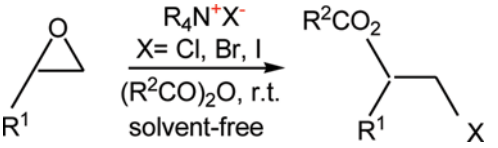
2-thiocyanatoalkyl alkanoates,[32] we now report a direct and catalyst-free method for the conversion of epoxides to vicinal haloesters using quaternary ammonium halides $R_4N^+X^-$ (X = Cl, Br, I; R = n-butyl, n-pentyl, n-hexyl) in the presence of an aliphatic or aromatic carboxylic anhydride $(R^2CO)_2O$ ($R^2 = CH_3$, Ph) at room temperature under neutral and solvent-free conditions (Scheme 1).

First, we took 2,3-epoxypropyl phenyl ether as an example and optimized the reaction conditions for its conversion to 1-chloro-3-phenoxypropan-2-yl acetate **1** using chloride anion in the presence of acetic anhydride $(CH_3CO)_2O$. In this connection, we found that no desired product **1** was formed using NH_4Cl and acetic anhydride in CH_3CN or CH_2Cl_2 as solvent or under solvent-free conditions, at room temperature or under reflux conditions. Thus, tetrahexylammonium chloride $(n\text{-Hexyl})_4N^+Cl^-$ was used in the presence of acetic anhydride (Ac_2O) in various conditions for this conversion. The results are shown in Table 1. In all of these catalyst-free reactions, first acetic anhydride was mixed with chloride salt, the reaction mixture was stirred for about 15 min, and then epoxide was added to it.

As shown in this table, this conversion was unsuccessful in the CH_2Cl_2 or CH_3CN as solvent at room temperature or under reflux conditions. In these cases, the desired product **1** was obtained in only 0–30% yields using $(n\text{-hexyl})_4N^+Cl^-$/ Ac_2O in 1:2 molar ratio after relatively long reaction times (Table 1, entries 6–9). Under solvent-free conditions, **1** was produced in good yield using $(n\text{-hexyl})_4N^+Cl^-$/ Ac_2O in 1.6:1.5 molar ratio at 60 °C after 1 h (Table 1, entry 5) and in poor yield by 1:0.5 molar ratio of this mixed reagent at room temperature after 22 h (Table 1, entry 1). The results were better with increasing the amount of acetic anhydride (Table 1, entries 2 and 3). Finally, the best result was obtained in the case of the entry 4 of this table so that **1** was produced in 95% yield using this mixed reagent (1:2) at room temperature after 6 h under solvent-free conditions.

We therefore used this conditions (Table 1, entry 4) for the conversion of other epoxides to their corresponding vicinal haloesters. In this connection, to develop the applicability of the present method, we exchanged the type of carboxylic anhydride and also quaternary ammonium halide to benzoic anhydride and tetrabutylammonium bromide or tetrapentylammonium iodide respectively in some cases. However, these quaternary ammonium halides (1.5 eq.) were used slightly more than tetrahexylammonium chloride for obtaining better results. The results are shown in Table 2.

As shown in this table, epoxides are directly and efficiently converted to vicinal haloesters in excellent yields by a mixture of $R_4N^+X^-/(RCO)_2O$ in 1–1.5:2 molar ratio at room temperature under mild, neutral, and solvent-free conditions and without a catalyst. Except for the case of styrene oxide, which produced two regio-isomers



Scheme 1. Direct and catalyst-free conversion of epoxides to *vic*-haloesters using $R_4N^+X^-$ (X = Cl, Br, I; R = n-butyl, n-pentyl, n-hexyl) / $(R^2CO)_2O$ ($R^2 = CH_3$, Ph) at room temperature under neutral and solvent-free conditions. (Figure is provided in color online.)

Table 1. Conversion of 2,3-epoxypropyl phenyl ether to 1-chloro-3-phenoxypropan-2-yl acetate (**1**) with a mixture of tetrahexylammonium chloride and acetic anhydride in various conditions and without using a catalyst

Entry	Solvent	Molar ratio[a]	Temp. (°C)	Time (h)	Yield (%)
1	—	1:1:0.5	Rt	22	30
2	—	1:1:1	Rt	7	75
3	—	1:1:1.5	Rt	6	80
4	—	1:1:2	Rt	6	95
5	—	1:1.6:1.5	60	1	60
6	CH_2Cl_2	1:1:2	Rt	8	0
7	CH_2Cl_2	1:1:2	Reflux	15	5
8	CH_3CN	1:1:2	Rt	21	5
9	CH_3CN	1:1:2	Reflux	21	30

[a]Molar ratio is related to epoxide: $(n\text{-hexyl})_4N^+Cl^-$/ Ac_2O.

Downloaded by [Pennsylvania State University] at 13:44 16 February 2013

(Table 2, entry 6), the reaction of other unsymmetrical epoxides occurred with high regioselectivity, and the halide anion attacked at the less-hindered side of the epoxide ring because of the combination of steric and electronic factors.

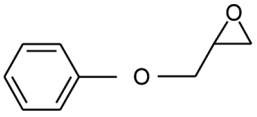
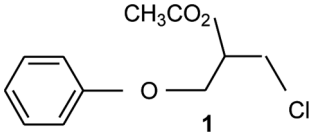
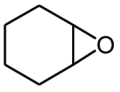
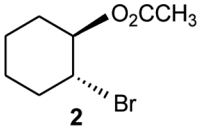
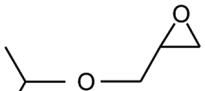
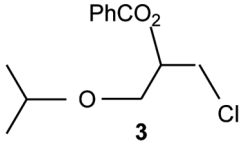
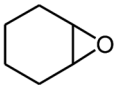
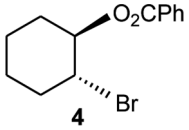
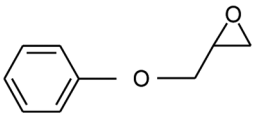
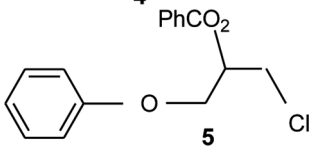
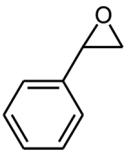
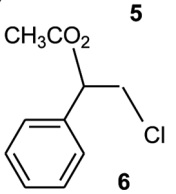
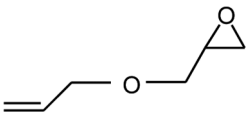
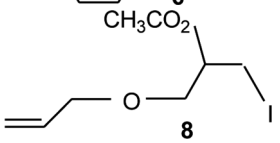
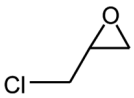
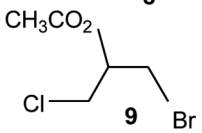
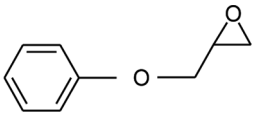
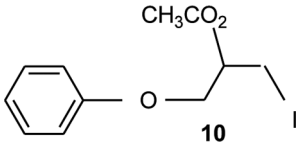
Under this reaction condition, the ethereal bonds, phenyl ring, carbon–carbon double bonds, and carbon–halogen bonds as functional groups that are present in the epoxide molecules remain intact.

To have more insight into the applicability, selectivity, and limitations of the present method, we studied the possibility of the conversion of 2,3-epoxypropyl phenyl ether to **1** in the presence of some other functional groups in binary mixtures. For this purpose a binary mixture of 2,3-epoxypropyl phenyl ether and another organic compound (1:1) was added to a flask containing a stirring mixture of $(n\text{-hexyl})_4N^+Cl^-/Ac_2O$ (1:2) at room temperature under solvent-free conditions. The conversion yields obtained for these selective reactions of different binary mixtures are shown in Scheme 2. In addition to the various selectivities mentioned, as shown in this scheme, epoxides can be efficiently converted to their corresponding vicinal haloesters in the presence of esters, carboxylic acids, aldehydes, amines, and amides with excellent selectivity using the present method. This excellent chemoselectivity is probably related to greater reactivity of epoxides compared to these functional groups in the present reaction medium, which contains both nucleophile (halide anion) and electrophile (carboxylic anhydride) because of their angle strain.

Although the exact mechanism of this reaction is not clear, it seems that epoxide ring concomitantly reacts with both halide anion and carboxylic anhydride from its less hindered carbon atom and oxygen atom, respectively, converting epoxide to vicinal haloester directly.

In conclusion, the present investigation has demonstrated that the use of a mixture of quaternary ammonium halides and an aliphatic or aromatic carboxylic anhydride offers a direct, simple, and efficient method, avoiding the use of a catalyst for the conversion of wide varieties of epoxides to their corresponding vicinal haloesters in good yields at room temperature under solvent-free conditions. This environmentally friendly method can be efficiently used for preparation of *vic*-haloesters even in the presence of many other functional groups with excellent chemoselectivity. Easy

Table 2. Catalyst-free conversion of epoxides to vicinal haloesters using a mixture of $R_4N^+X^-$ (1–1.5 eq.) (X = Cl, Br, I; R = n-butyl, n-pentyl, n-hexyl) and acetic anhydride or benzoic anhydride (2 eq.) at room temperature under neutral and solvent-free conditions[a]

Entry	Epoxide	vic-Haloesters	Time (h)	Yield (%)[b]
1		 **1**	6	95
2		 **2**	5	92
3		 **3**	6	98
4		 **4**	4	85
5		 **5**	7	97
6		 **6**	8	79 (19)[c, d]
7		 **8**	29	74
8		 **9**	7	72
9		 **10**	24	77

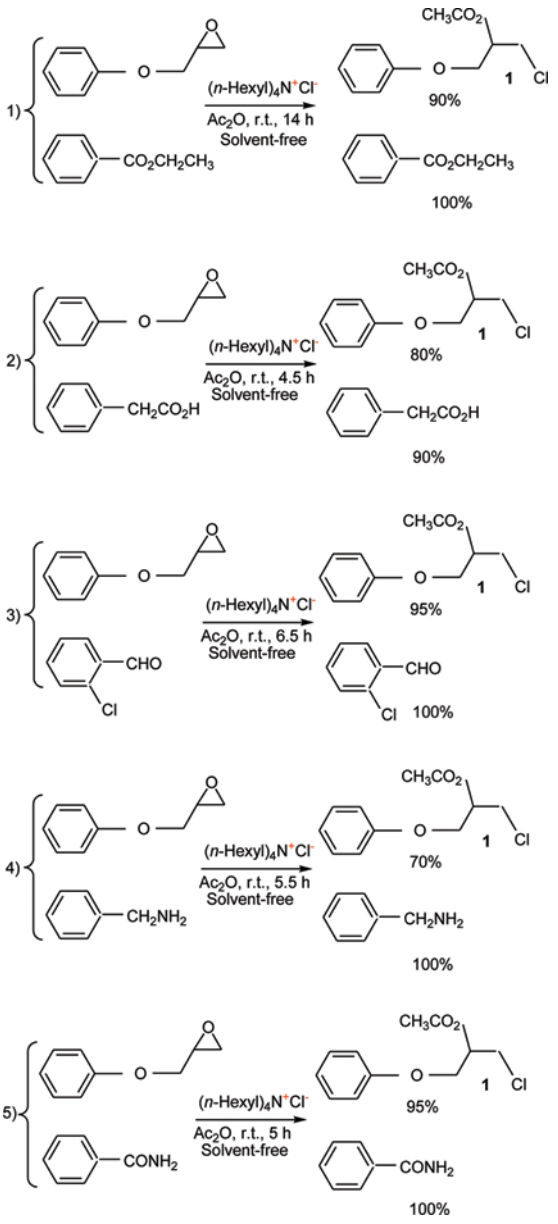
[a]In all of these reactions, first a mixture of halide salt and carboxylic anhydride was stirred for 15–30 min and then epoxide was added to it.

[b]Isolated yields.

[c]Yields are based on NMR analysis.

[d]The number in parentheses is related to 2-chloro-2-phenylethyl acetate as regioisomeric product.

Downloaded by [Pennsylvania State University] at 13:44 16 February 2013



Scheme 2. Chemoselectivities in the conversion of 2,3-epoxypropyl phenyl ether to **1** using (*n*-hexyl)4N+Cl-(1 eq.)/Ac_2O (2 eq.) at room temperature under solvent-free conditions. (Figure is provided in color online.)

workup, reduced pollution resulting from lack of using a catalyst and solvent, availability and ease of handling of reagents, excellent regioselectivity, and operation under mild and neutral conditions are other advantages of this method.

Downloaded by [Pennsylvania State University] at 13:44 16 February 2013

EXPERIMENTAL

Solvents, reagents, and chemicals were obtained from Merck (Germany) and Fluka (Switzerland) Chemical Companies. Products are known compounds and were characterized by their physical or spectral data. Fourier transform–infrared (FT-IR) spectra were recorded on a Perkin-Elmer RXI spectrophotometer. Nuclear magnetic resonance spectra were recorded on a Brucker Avance DRX-500 spectrometer. Thin-layer chromatography (TLC) was carried out on silica-gel 254 analytical sheets obtained from Fluka.

Typical Procedure for the Conversion of 2,3-Epoxypropyl Phenyl Ether to 1-Chloro-3-phenoxypropan-2-yl Acetate (1)[25] Using (*n*-Hexyl)$_4$N$^+$Cl$^-$ in the Presence of Acetic Anhydride

Acetic anhydride (2 mmol, 0.189 mL) was added to a flask containing tetrahexylammonium chloride (1 mmol, 0.39 g) at room temperature under solvent-free conditions. The reaction mixture was stirred until it changed to a homogeneous form (15 min). Then, 2,3-epoxypropyl phenyl ether (1 mmol, 0.12 mL) was added to the reaction mixture, and stirring was continued for 6 h so that TLC showed the completion of the reaction. The crude product was subjected to short column chromatography on silica gel using petroleum bezine as eluent, affording **1**, 0.222 g, 95% yield. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.13 (s, 3H), 3.78–3.82 (dd, 1H, $J = 11.67$, 5.3 Hz), 3.85–3.88 (dd, 1H, $J = 11.68$, 5.1 Hz), 4.14–4.20 (m, 2H), 5.32–5.36 (m, 1H), 6.92–7.01 (m, 3H), 7.29–7.32 (m, 2H) ppm; ^{13}C-NMR ($CDCl_3$, 125.77 MHz): δ 21.41, 42.96, 66.25, 71.53, 115.01, 121.89, 130.04, 158.60, 170.69 ppm; FT-IR (neat): 3063 (m), 3041 (m), 2961 (s), 2925 (s), 2851 (s), 1747 (s), 1599 (s), 1495 (s), 1222 (s), 1046 (s), 810 (s), 753 (s), 691 (s) cm^{-1}. Mass spectra *m/e*: 230 (M + 2, 0.9%), 228 (M, 3%), 137 (M + 2 – PhO, 22.68%), 135 (M – PhO, 68.83%), 43 (CH_3CO, 100%).

Spectral Data

1-Chloro-3-phenoxypropan-2-yl benzoate (5)[25]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.94–4.02 (m, 2H), 4.30–4.37 (m, 2H), 5.58–5.62 (m, 1H), 6.96–7.01 (m, 3H), 7.29–7.33 (m, 2H), 7.45–7.48 (m, 2H), 7.58–7.61 (m, 1H), 8.08–8.10 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$, 125.77 MHz): δ 43.14, 66.40, 72.01, 115.17, 121.92, 128.92, 129.94, 130.04, 130.34, 133.88, 158.73, 166.14 ppm; FT-IR (neat): 3063 (w), 3039 (w), 2960 (w), 2882 (w), 1723 (s), 1599 (m), 1588 (m), 1496 (m), 1267 (s), 1242 (s), 1110 (s), 813 (w), 754 (m), 710 (s), 690 (m) cm^{-1}.

1-Iodo-3-phenoxypropan-2-yl acetate (10). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.17 (s, 3H), 3.47–3.50 (dd, 1H, $J = 10.62$, 5.5 Hz), 3.56–3.59 (dd, 1H, $J = 10.63$, 5.7 Hz), 4.14–4.17 (dd, 1H, $J = 10.15$, 5.1 Hz), 4.23–4.26 (dd, 1H, $J = 10.14$, 4.9 Hz), 5.12–5.14 (m, 1H), 6.95–7.04 (m, 3H), 7.33–7.36 (m, 2H) ppm; ^{13}C-NMR ($CDCl_3$, 125.77 MHz): δ 3.80, 21.40, 68.42, 71.27, 115.14, 121.89, 130.00, 158.63, 170.49 ppm; FT-IR (neat): 3062 (w), 3040 (w), 2928 (w), 2876 (w), 1744 (s), 1599 (s), 1588 (m), 1495 (s), 1226 (s), 1172 (m), 1048 (m), 754 (s), 691 (m), 599 (w), 510 (w) cm^{-1}; mass spectra *m/e*: 320 (M, 22%), 261 (M – CH_3CO_2, 1.3%), 227 (M – PhO, 100%), 193 (M – I, 1.47%), 167 (M – PhO – CH_3CO_2H, 16%), 133 (M – I – CH_3CO_2H, 44%),

Downloaded by [Pennsylvania State University] at 13:44 16 February 2013

43 (CH_3CO, 100%). Anal. calcd. for $C_{11}H_{13}IO_3$ (320.13): C, 41.27; H, 4.09; I, 39.64. Found: C, 41.23; H, 4.06; I, 39.69.

1-Chloro-3-isopropyloxypropan-2-yl benzoate (3)[25]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.20–1.21 (d, 6H, $J = 6.07$ Hz), 3.66–3.71 (m, 1H), 3.75–3.79 (m, 2H), 3.86–3.89 (dd, 1H, $J = 11.67$, 5.24 Hz), 3.92–3.95 (dd, 1H, $J = 11.63$, 4.59 Hz), 5.36–5.41 (m, 1H), 7.47–7.50 (m, 2H), 7.60–7.63 (m, 1H), 8.10–8.12 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$, 125.77 MHz): δ 22.44, 43.68, 66.52, 72.86, 72.94, 128.83, 130.22, 130.25, 133.65, 166.17 ppm.

1-Allyloxy-3-iodopropan-2-yl acetate (8). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.12 (s, 3H), 3.33–3.37 (dd, 1H, $J = 10.47$, 5.55 Hz), 3.43–3.47 (dd, 1H, $J = 10.46$, 5.68 Hz), 3.57–3.60 (dd, 1H, $J = 10.42$, 5.01 Hz), 3.66–3.69 (dd, 1H, $J = 10.42$, 4.98 Hz), 4.02–4.05 (m, 2H), 4.90–4.92 (m, 1H), 5.21–5.24 (dd, 1H, $J = 10.40$, 1.42 Hz), 5.28–5.32 (dd, 1H, $J = 17.25$, 1.6 Hz), 5.86–5.93 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$, 125.77 MHz): δ 4.36, 21.44, 70.42, 71.79, 72.77, 117.96, 134.59, 170.47 ppm; FT-IR (neat): 3030 (w), 3013 (w), 2924 (w), 2856 (w), 1747 (s), 1636 (m), 1232 (s), 668 (w), 599 (w), 517 (w) cm^{-1}; mass spectra m/e: 284 (M, 0.3%), 241 (M – CH_3CO, 2.9%), 227 (M – C_3H_5O, 35.2%), 157 (M – I, 100%), 43 (CH_3CO, 100%). Anal. calcd. for $C_8H_{13}IO_3$ (284.09): C, 33.82; H, 4.61; I, 44.67. Found: C, 33.89; H, 4.63; I, 44.64.

***Trans*-1-acetoxy-2-bromocyclohexane (2).** Bp = 110–111 °C (12 mm.) [lit.[33] 109–110 °C (12 mm.)]; FT-IR (neat): 2930 (m), 2862 (m), 1743 (s), 1235 (s), 1038 (m), 696 (w), 602 (w) cm^{-1}.

***Trans*-1-benzoyloxy-2-bromocyclohexane (4)[34].** ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.36–1.39 (m, 1H), 1.47–1.53 (m, 2H), 1.75–1.83 (m, 3H), 2.22–2.32 (m, 2H), 4.01–4.06 (m, 1H), 5.04–5.08 (m, 1H), 7.41–7.45 (m, 2H), 7.53–7.57 (m, 1H), 8.03–8.07 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$, 125.77 MHz): δ 23.62, 24.80, 31.00, 35.08, 60.99, 76.77, 128.79, 130.12, 130.70, 133.43, 166.12 ppm; FT-IR (neat): 3069 (w), 3021 (w), 2973 (m), 2930 (w), 2873 (w), 1723 (s), 1602 (w), 1585 (w), 1451 (w), 1270 (s), 1111 (s), 1026 (w), 711 (s), 686 (w) cm^{-1}.

2-Chloro-1-phenylethyl acetate (6)[24]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.14 (s, 3H), 3.71–3.74 (dd, 1H, $J = 11.66$, 4.5 Hz), 3.77–3.81 (dd, 1H, $J = 11.66$, 8.05 Hz), 5.95–5.98 (dd, 1H, $J = 8.06$, 4.5 Hz), 7.33–7.42 (m, 5H) ppm; ^{13}C-NMR ($CDCl_3$, 125.77 MHz): δ 21.40, 46.93, 75.51, 127.09, 129.17, 129.25, 137.64, 170.30 ppm.

2-Chloro-2-phenylethyl acetate (7)[25]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.06 (s, 3H), 4.41–4.44 (dd, 1H, $J = 11.74$, 5.93 Hz), 4.45–4.49 (dd, 1H, $J = 11.74$, 7.81 Hz), 5.06–5.09 (dd, 1H, $J = 7.71$, 5.96 Hz), 7.33–7.42 (m, 5H) ppm; ^{13}C NMR ($CDCl_3$, 125.77 MHz): δ 21.15, 60.05, 68.30, 127.83, 129.23, 129.39, 138.06, 170.88 ppm.

1-Bromo-3-chloropropan-2-yl acetate (9)[25]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.16 (s, 3H), 3.62–3.64 (m, 2H), 3.78–3.80 (m, 2H), 5.18–5.20 (m, 1H) ppm; ^{13}C-NMR ($CDCl_3$, 125.77 MHz): δ 21.21, 30.71, 43.74, 71.79, 170.24 ppm; FT-IR (neat): 2962 (m), 2924 (m), 1748 (s), 1373 (m), 1228 (s), 1032 (m), 745 (w), 602 (w) cm^{-1}; mass spectra m/e: 181 (M + 4 – ^{37}Cl or M + 2 – ^{35}Cl, 1.5%), 179 (M + 2 – ^{37}Cl or M – ^{35}Cl, 1.5%), 167 (M + 4 – $CH_2{}^{37}Cl$ or M + 2 – $CH_2{}^{35}Cl$, 87%), 165 (M + 2 – $CH_2{}^{37}Cl$ or M – $CH_2{}^{35}Cl$, 82%), 158 (M + 4 – CH_3CO_2H, 12%), 156

Downloaded by [Pennsylvania State University] at 13:44 16 February 2013

(M + 2 – CH_3CO_2H, 51%), 154 (M – CH_3CO_2H, 38%), 137 (M + 4 – ^{81}Br or M + 2 – ^{79}Br, 4.5%), 135 (M + 2 – ^{81}Br or M – ^{79}Br, 15%), 123 (M + 4 – $CH_2{}^{81}Br$ or M + 2 – $CH_2{}^{79}Br$, 17.9%), 121 (M + 2 – $CH_2{}^{81}Br$ or M – $CH_2{}^{79}Br$, 55.2%), 77 (M + 4 – CH_3CO_2H – ^{81}Br or M + 2 – CH_3CO_2H – ^{79}Br, 32.8%), 75 (M + 2 – CH_3CO_2H – ^{81}Br or M – CH_3CO_2H – ^{79}Br, 98.6%), 43 (CH_3CO, 100%).

ACKNOWLEDGMENTS

We gratefully acknowledge the support of this work by the Damghan University Research Council.

Downloaded by [Pennsylvania State University] at 13:44 16 February 2013

REFERENCES

1. Behrens, C. H.; Ko, S. Y.; Sharpless, K. B.; Walker, F. J. Selective transformation of 2,3-epoxy alcohols and related derivatives: Strategies for nucleophilic attack at carbon-1. *J. Org. Chem.* **1985**, *50*, 5687–5696.
2. Nugent, W. A. Chiral Lewis acid catalysis: Enantioselective addition of azide to meso epoxides. *J. Am. Chem. Soc.* **1992**, *114*, 2768–2769.
3. Tokunaga, M.; Larrow, J. F.; Kakiuchi, F.; Jacobsen, E. N. Asymmetric catalysis with water: Efficient kinetic resolution of terminal epoxides by means of catalytic hydrolysis. *Science* **1997**, *277*, 936–938.
4. Bonini, C. R.; Righi, G. Regio- and chemoselective synthesis of halohydrins by cleavage of oxiranes with metal halides. *Synthesis* **1994**, 225–238.
5. Smith, J. G. Synthetically useful reactions of epoxides. *Synthesis* **1984**, 629–656.
6. Yamada, J.; Yumoto, M.; Yamamoto, Y. Aminolead compounds as a new reagent for regioselective ring opening of epoxides. *Tetrahedron Lett.* **1989**, *30*, 4255–4258.
7. (a) Konopelski, J. P.; Boehler, M. A.; Tarasow, T. M. Preparation of (1R,2S)- and (1S,2R)-2-chloro-1,2-diphenylethanol and other. β-halohydrins in enantiomerically pure form. *J. Org. Chem.* **1989**, *54*, 4966–4970; (b) Ueda, Y.; Maynard, S. C. Highly regioselective formation of bromohydrins by reaction of epoxy-azetidinones with $MgBr_2$: An alternative route to 4-bromomethylcarbonylmethyl-2-azetidinone, a key carbapenem precursor. *Tetrahedron Lett.* **1988**, *29*, 5197–5200.
8. (a) Iranpoor, N.; Firouzabadi, H.; Aghapour, G.; Nahid, A. Selective conversion of epoxides to *vic*-halo alcohols and symmetrical or unsymmetrical dihalides by triphenylphosphine/2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in the presence of quaternary ammonium halides. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 1885–1891; (b) Iranpoor, N.; Adibi, H. Iron(III) trifluoroacetate as an efficient catalyst for solvolytic and nonsolvolytic nucleophilic ring opening of epoxides. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 675–680; (c) Garrett, C. E.; Fu, G. C. π-Bound phosphorus heterocycles as catalysts: Ring opening of epoxides with TMSCl in the presence of a phosphaferrocene. *J. Org. Chem.* **1997**, *62*, 4534–4535; (d) Kotsuki, H.; Shimanouchi, T.; Ohshima, R.; Fujiwara, S. Solvent-free organic reactions on silica-gel supports: Facile transformation of epoxides to β-halohydrins with lithium halides. *Tetrahedron* **1998**, *54*, 2709–2722; (e) Kwon, D. W.; Cho, M. S.; Kim, Y. H. Samarium(III) iodide complex catalyzed regioselective cleavage of epoxides to iodohydrins: tandem epoxide opening–iodocyclization. *Synlett* **2003**, 959–962.
9. (a) Shaghi, H.; Eskandari, M. M. Conversion of epoxides to halohydrins with elemental halogen catalyzed by phenylhydrazine. *Synthesis* **2002**, 1519–1522; (b) Shaghi, H.; Massah, A. R.; Eshghi, H.; Niknam, K. Crown ethers as new catalysts in the highly regioselective halogenative cleavage of epoxides with elemental halogen. *J. Org. Chem.* **1998**,

63, 1455–1461; (c) Diaz, D.; Martin, T.; Martin, V. S. Stereocontrolled synthesis of unsaturated halohydrins from unsaturated epoxides. *J. Org. Chem.* **2001**, *66*, 7231–7233; (d) Aghapour, G.; Afzali, A.; Salek, F. Facile, high regio- and chemoselective conversion of epoxides to β-chlorohydrins using chloro diphenyl phosphine under solvent-free conditions. *Indian J. Chem.* **2009**, *48B*, 231–236.

10. Otera, J.*Esterification, Methods, Reactions, And Applications*; Wiley-VCH Verlag: Weinheim, 2003.
11. (a) Greene, T. W.; Wuts, P. G. M.*Protective Groups in Organic Synthesis*; Wiley: New York, 1991; (b) Kocienski, P. J. *Protecting Groups*; Thieme: Stuttgart, 1994.
12. Larock, R. C.*Comprehensive Organic Transformations*; VCH: New York, 1989; p. 980; For more references see: (a) Saravanan, P.; Singh, V. K. An efficient method for acylation reactions. *Tetrahedron Lett.* **1999**, *40*, 2611–2614; (b) Chandrasekhar, S.; Ramachander, T.; Takhi, M. Acylation of alcohols with acetic anhydride catalyzed by $TaCl_5$: Some implications in kinetic resolution. *Tetrahedron Lett.* **1998**, *39*, 3263–3266; (c) Damen, E. W. P.; Braamer, L.; Scheeren, H. W. Lanthanide trifluoromethanesulfonate–catalysed selective acylation of 10-deacetylbaccatin III. *Tetrahedron Lett.* **1998**, *39*, 6081–6082; (d) Orita, A.; Mitsutome, A.; Otera, J. Distannoxane-catalyzed highly selective acylation of alcohols. *J. Org. Chem.* **1998**, *63*, 2420–2421; (e) Breton, G. W. Selective monoacetylation of unsymmetrical diols catalyzed by silica gel–supported sodium hydrogen sulfate. *J. Org. Chem.* **1997**, *62*, 8952–8954; (f) Orita, A.; Sakamoto, K.; Hamada, Y.; Mitsutome, A.; Otera, J. Mild and practical acylation of alcohols with esters or acetic anhydride under distannoxane catalysis. *Tetrahedron* **1999**, *55*: 2899–2910.
13. (a) Li, T. S.; Li, A. X. Montmorillonite clay catalysis, part 10: K-10 and KSF-catalysed acylation of alcohols, phenols, thiols and amines: Scope and limitation. *J. Chem. Soc., Perkin Trans.* **1998**, *1*, 1913–1918; (b) Ballini, R.; Bosica, G.; Carloni, L.; Ciaralli, L.; Maggi, R.; Sartori, G. Zeolite HSZ-360 as a new reusable catalyst for the direct acetylation of alcohols and phenols under solventless conditions. *Tetrahedron Lett.* **1998**, *39*, 6049–6052; (c) Bhaskar, P. M.; Loganathan, D. Per-O-acetylation of sugars catalysed by montmorillonite K-10. *Tetrahedron Lett.* **1998**, *39*, 2215–2218.
14. (a) Williams, J. R.; Boehm, J. C. The syntheses of 3 beta-steroidal diacylglyceryl sulfides, sulfoxides, and sulfones. *Steroids* **1995**, *60*, 321–323; (b) Junk, T.; Pappalardo, G. C.; Irgolic, K. J. Synthesis and characterization of *rac*-1,2-bis(palmitoyloxy)-3-propyl (2-trimethylarsonioethyl)phosphonate, an arsenic-containing phosphonolipid. *Appl. Organomet. Chem.* **1990**, *4*, 103–109; (c) Lok, C. M. Versatile methods for the synthesis of mixed-acid 1,2-diacylglycerols. *Chem. Phys. Lipids* **1978**, *22*, 323–337; (d) Ali, S.; Bittman, R. Facile diacylation of glycidyl tosylate: Chiral synthesis of symmetric-chain glycerophospholipids. *J. Org. Chem.* **1988**, *53*, 5547–5549.
15. Prades, J.; Funari, S. S.; Escriba, P. V.; Barcelo, F. Effects of unsaturated fatty acids and triacylglycerols on phosphatidylethanolamine membrane structure. *J. Lipid Res.* **2003**, *44*, 1720–1727.
16. (a) Iwasaki, Y.; Yamane, T. Enzymatic synthesis of structured lipids. *J. Mol. Catal. B: Enzym.* **2000**, *10*, 129–140; (b) Pleiss, J.; Scheib, H.; Schmid, R. D. The *His gap* motif in microbial lipases: A determinant of stereoselectivity toward triacylglycerols and analogs. *Biochimie* **2000**, *82*, 1043–1052.
17. Ren, T.; Liu, D. Synthesis of cationic lipids from 1,2,4-butanetriol. *Tetrahedron Lett.* **1999**, *40*, 209–212.
18. (a) Kurz, M.; Scriba, G. K. E. Drug–phospholipid conjugates as potential prodrugs: Synthesis, characterization, and degradation by pancreatic phospholipase A_2. *Chem. Phys. Lipids* **2000**, *107*, 143–157; (b) Parang, K.; Wiebe, L. I.; Knaus, E. E. Novel approaches for designing 5′-*O*-ester prodrugs of 3′-azido-2′3′-dideoxythymidine (AZT). *Curr. Med. Chem.* **2000**, *7*, 995–1039.

Downloaded by [Pennsylvania State University] at 13:44 16 February 2013

19. Bajwa, J. S.; Anderson, R. C. A highly regioselective conversion of epoxides to halohydrins by lithium halides. *Tetrahedron Lett.* **1991**, *32*, 3021–3024.
20. Parfenov, E. A.; Serebrennikova, G. A.; Preobrazhenskii, N. A.*Zh. Org. Khim.* **1967**, *3*, 1951–1955.
21. (a) Sharpless, K. B.; Teranishi, A. Y.; Backvall, J. E. Chromyl chloride oxidations of olefins: Possible role of organometallic intermediates in the oxidations of olefins by oxo transition metal species. *J. Am. Chem. Soc.* **1977**, *99*, 3120–3128. (b) Backvall, J. E.; Young, M. W.; Sharpless, K. B. Vicinal acetoxychlorination of olefins by chromyl chloride in acetyl chloride. *Tetrahedron Lett.* **1977**, *18*, 3523–3526.
22. Iqbal, J.; Amin Khan, M.; Srivastava, R. R. Cobalt-catalysed regioselective cleavage of oxiranes with acylchlorides. *Tetrahedron Lett.* **1988**, *29*, 4985–4986.
23. Shibata, I.; Baba, A.; Matsuda, H. Regioselective ring cleavage of oxiranes catalyzed by organotin halide–triphenylphosphine complex. *Tetrahedron Lett.* **1986**, *27*, 3021–3024.
24. Gros, P.; Le Perchec, P.; Senet, J. P. Reaction of epoxides with chlorocarbonylated compounds catalyzed by hexaalkylguanidinium chloride. *J. Org. Chem.* **1994**, *59*, 4925–4930.
25. Azizi, N.; Mirmashhori, B.; Saidi, M. R. Lithium perchlorate–promoted highly regioselective ring opening of epoxides under solvent-free conditions. *Catal. Commun.* **2007**, *8*, 2198–2203.
26. Iranpoor, N.; Zeynizadeh, B. Efficient and regioselective conversion of epoxides into vicinal chloroesters with $TiCl_4$ and imidazole in ethyl acetate. *J. Chem. Res. Synop.* **1998**, 582–583.
27. Stamatov, S. D.; Stawinski, J. Efficient, highly regioselective, and stereospecific conversion of glycidol systems into C2-*O*-acylated vicinal halohydrins. *Tetrahedron Lett.* **2006**, *47*, 2543–2547.
28. Oriyama, T.; Ishiwata, A.; Hori, Y.; Yatabe, T.; Hasumi, N.; Koga, G. Highly regioselective tin-mediated ring opening of 2,3-epoxy alcohol derivatives with trimethylisilyl halide. *Synlett* **1995**, 1004–1006.
29. Tanaka, K. *Solvent-Free Organic Synthesis*; Wiley-VCH Verlag: Weinheim, 2003.
30. Tanaka, K.; Toda, F. Solvent-free organic synthesis. *Chem. Rev.* **2000**, *100*, 1025–1074.
31. (a) Aghapour, G.; Hatefipour, R. Catalyst-free, efficient, and facile conversion of epoxides to β-hydroxy thiocyanates under neutral conditions. *Synth. Commun.* **2009**, *39*, 1698–1707. (b) Aghapour, G.; Afzali, A. Solvent-free, efficient, and high regioselective conversion of epoxides to symmetrical and unsymmetrical *vic*-dihalides using chlorodiphenylphosphine and N-halosuccinimides. *Phosphorus, Sulfur Silicon Relat. Elem.* **2011**, *186*(3): 598–605.
32. Aghapour, G.; Hatefipour, R. Catalyst-free, direct, high regio-, and chemo-selective conversion of epoxides to 2-thiocyanatoalkyl alkanoates under neutral and solvent-free conditions. *Can. J. Chem.* **2010**, *88*(7), 598–604.
33. Winstein, S.; Buckles, R. E. The role of neighboring groups in replacement reactions, I: Retention of configuration in the reaction of some dihalides and acetoxyhalides with silver acetate. *J. Am. Chem. Soc.* **1942**, *64*, 2780–2786.
34. Taniguchi, Y.; Tanaka, S.; Kitamura, T.; Fujiwara, Y. Lanthanoid-catalyzed ring-opening reaction of epoxides with acyl halides. *Tetrahedron Lett.* **1998**, *39*, 4559–4560.

Downloaded by [Pennsylvania State University] at 13:44 16 February 2013