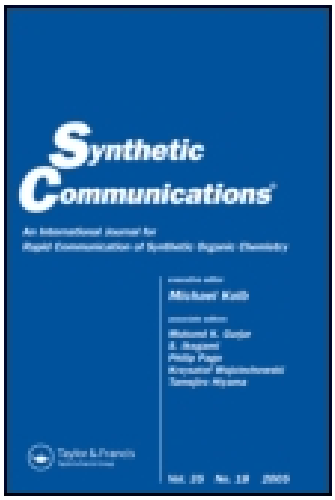

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High Yield Regioselective Ring Opening of Epoxides Using Samarium Chloride Hexahydrate

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High Yield Regioselective Ring Opening of Epoxides Using Samarium Chloride Hexahydrate

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ABSTRACT

Epoxides were converted to the corresponding β-azidohydrins and β-iodohydrins using $SmCl_3 \cdot 6H_2O/NaN_3$ in DMF and $SmCl_3 \cdot 6H_2O$/NaI in acetonitrile respectively. The reactions were highly regioselective, efficient, and gave excellent yields under mild and neutral conditions.

Key Words: Samarium chloride; Azidohydrins; Iodohydrins; Epoxides.

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INTRODUCTION

The ring opening reactions of epoxides are intriguing research area that can still be considered interesting. *vic*-Azidohydrins and halohydrins are of considerable importance in the synthesis of natural products and in many organic transformations. 1,2-Azidoalcohols are interesting intermediates for the synthesis of chiral aziridines[1] as well as precursors of vicinal amino alcohols that occur widely in nature and often constitute the moiety in structures of biologically active compounds,[2,3] natural products,[4,5] cardiovascular agents,[6,7] antibiotics,[8] immunostimulants,[9] and chiral ligands for asymmetric catalysis.[10] They are also important in the chemistry of carbohydrates and nucleosides.

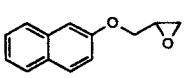
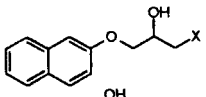
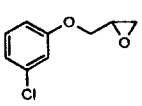
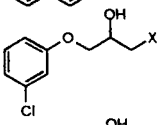
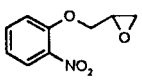
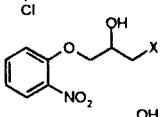
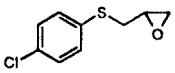
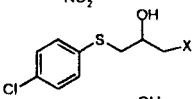
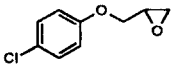
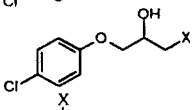
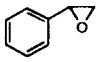
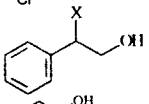
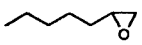
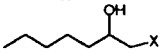
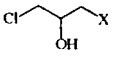
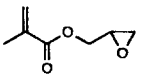
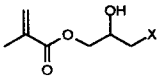
There are several reports on synthesis of azidohydrins and halohydrins. 1,2-Azidoalcohols can be synthesized by ring opening of epoxides using $Ti(OiPr)_4/TMSN_3$,[11] $V(OiPr)_3/TMSN_3$,[12] $Yb(OiPr)_3/TMSN_3$,[13] $Cr(salen)_2/TMSN_3$,[14] Lewis acid/$TMSN_3$,[15] PTC/$TMSN_3$,[16] $NaN_3/M(NO_3)_2$, [M=Cu, Co, Ni, Zn, Zr],[17] $NaN_3/Mg(ClO_4)_2$,[20f] $NaN_3/SnCl_2{\cdot}2H_2O$–MgI_2 in THF,[18] NaN_3/LiOTf,[20f] NaN_3/Clay/Zeolite,[19] NaN_3/NH_4Cl,[20] HN_3 with DIPEA,[21] $Al(N_3)_3$,[22a] $Bu_2Sn(N_3)_2$[23] in DMF at 60 °C, $Ti(N_3)_4$[22b] in organic solvent, polymer supported azide[24] systems. Many of these reactions are complicated by isomerization, epimerization, and the rearrangement products. Conventionally, epoxides are transformed to halohydrins by electrophilic cleavage with hydrogen halide[25] but it requires harsh reaction conditions with often low regioselectivity. Competing reagents and side reactions with other acid-sensitive functionalities limit the use of strong Lewis acids, such as BF_3.[26] The hydrophobic nature of LiI[27] limits its use to iodohydrin formation. Iodohydrins can also be prepared by iodomethylation of carbonyl compounds with CH_2I_2 in presence of SmI_2[28] and elemental iodine,[29] however all such methods require excess reagents. Other methods include MgI_2 in ether,[30] TMSCl/NaI[30b] in acetonitrile, NaI(aq) (pH 2),[31] $InCl_3$/NaI,[31] $CeCl_3{\cdot}7H_2O$/NaI,[32] $Ti(OiPr)_4$/NaI,[33] triphenylphosphonium iodide,[34] and others.[35] Most of these reactions give poor yield and less regioselectivity and longer reaction time. Therefore, there is a scope for new reaction systems.

The use of lanthanides based reaction systems are our current interest. In the present work we describe the use of samarium(III) chloride hexahydrate as a catalyst for the regioselective ring opening of epoxides to get azidohydrins and iodohydrins. Azidohydrin formation in acetonitrile was very slow and even after 24 h of reaction time no significant transformation was observed and all the starting epoxide was

recovered unreacted. The reaction was complete within 5–6 h at room temperature in DMF, however iodohydrin formation was complete within 10–20 min in acetonitrile. All the reactions were carried out in laboratory grade solvent without further drying.

Except the reaction of epoxides, styrene oxide (Table 1, Entry 6) and heptene oxide (Table 1, Entry 8) which produce a small percentage of

Table 1. Regioselective ring opening of epoxides[a] using $SmCl_3 \cdot 6H_2O$.

Entry	Epoxide	Major product[b]	X	Isolated yield[c] (%)
1			N_3	90
			I	95
2			N_3	91
			I	94
3			N_3	92
			I	96
4			N_3	90
			I	95
5			N_3	92
			I	96
6			N_3	91 (10:1)
			I	95 (11:1)
7			N_3	94
			I	97
8			N_3	89 (9:1)
			I	92 (10:1)
9			N_3	93
			I	98
10			N_3	92
			I	97

[a]All the reactions were carried out at room temperature.
[b]Structure and regiochemical ratios determined for the products by proton-NMR.[36]
[c]Yields refer to the isolated product and figures in the bracket indicate ratio of regioisomers wherein observed.

other regioisomer, the reaction of other epoxides were found to be highly regioselective and only one isomer was obtained. The high regioselectivity of glycidyl ethers (Table 1, Entries 1–5) could be attributed to metal chelation and the attack of the nucleophile at C-3, a less hindered position. As expected in case of styrene oxide 2-azido- and 2-iodo-2-phenylethanols (Table 1, Entry 6) were obtained as the major products due to formation of stabilized benzylic cation during the reaction. It is noteworthy that there was no formation of any Michael addition product in the case of glycidyl methacrylate (Table 1, Entry 10).

In conclusion, we have demonstrated a highly efficient, regioselective conversion of epoxides to azidohydrins and iodohydrins under mild and neutral conditions. It has several advantages such as very less reaction time, easy handling, room temperature reaction, and no need of dry solvent.

EXPERIMENTAL

^{1}H-NMR spectra were recorded in $CDCl_3$ on FT–NMR JEOL (60 MHz) instrument using TMS as internal standard. IR spectra were recorded in $CHCl_3$ using BUCK SCIENTIFIC 500 instrument. All solvents were obtained commercially and were used without further purification. All substrates were purified before use.

Typical Procedure for Azidohydrin Formation of Glycidyl Methacrylate

To a slurry of $SmCl_3{\cdot}6H_2O$ (1.28 g, 3.51 mmol) and DMF (35 mL), glycidyl methacrylate (0.5 g, 3.51 mmol) in DMF (6 mL) was added and stirred at room temperature for 1 min. Then, NaN_3 (0.25 g, 3.85 mmol) was added to it and stirred. The reaction was monitored by TLC (reaction was complete within 5 h). On completion, solution was filtered and solvent was removed under reduced pressure and the crude product was purified by silica gel (60–120 mesh) column chromatography using ethyl acetate and hexane (9:1 by volume) to yield a viscous oil. The product, 3-azido-2-hydroxypropyl methacrylate (0.60 g, 92%) obtained was characterized by ^{1}H-NMR, IR spectral data. ^{1}H-NMR ($CDCl_3$): δ 1.89 (s, 3H), 3.09–4.23 (m, 6H), 5.53 (s, 1H), 6.06 (s, 1H). IR ($CHCl_3$): 3366, 2924, 2860, 2099, 1714, 1660, 1439, 1168 cm^{-1}.

Typical Procedure for Iodohydrin Formation of Glycidyl Methacrylate

To a slurry of $SmCl_3 \cdot 6H_2O$ (1.28 g, 3.51 mmol) and acetonitrile (35 mL), glycidyl methacrylate (0.5 g, 3.51 mmol) in acetonitrile (6 mL) was added and stirred at room temperature for 1 min. Then, NaI (0.58 g, 3.87 mmol) was added to it, and the reaction mixture stirred. The reaction was monitored by TLC (reaction was complete within 15 min). On completion, solution was filtered and solvent was removed under reduced pressure and the crude product was purified by silica gel (60–120 mesh) column chromatography using ethyl acetate and hexane (9:1 by volume). The product, 3-iodo-2-hydroxypropyl methacrylate (0.92 g, 92%) obtained was an oil and characterized by ^{1}H-NMR, IR spectral data. ^{1}H-NMR ($CDCl_3$): δ 1.87 (s, 3H), 3.25 (m, 2H), 3.85–4.12 (m, 4H), 5.54 (s, 1H), 6.06 (s, 1H). IR ($CHCl_3$): 3416, 2964, 1716, 1700, 1634, 1162 cm^{-1}.

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35. (a) Smith, J.G. Synthesis **1984**, 629–656; (b) Larock, R.C. *Comprehensive Organic Transformations*, 2nd Ed.; Wiley-VCH: New York, 1999; 1038–1041.
36. IR values are expressed in cm^{-1} and ^{1}H-NMR values are expressed in δ scale in ppm. **Entry 1.** 1-Azido-3-(2-naphthyloxy-2-propanol. ^{1}H-NMR ($CDCl_3$). δ 2.58 (m, 1H), 3.69–3.72 (m, 2H), 4.12 (m, 3H), 6.98–7.73 (m, 7H). IR ($CHCl_3$): 3360, 2921, 2867, 2099, 1597, 1388, 1257. 1-Iodo-3-(2-naphthyloxy)-2-propanol. ^{1}H-NMR ($CDCl_3$): δ 2.33 (m, 1H), 3.28–3.37 (m, 2H), 3.90–4.02 (m, 3H), 7.02–7.68 (m, 7H). IR ($CHCl_3$): 3405, 3044, 2917, 1460, 1392, 1257, 1216. **Entry 2.** 1-Azido-3-(3-chlorophenoxy)-2-propanol. ^{1}H-NMR ($CDCl_3$): δ 2.81 (m, 1H), 3.37–3.68 (m, 2H), 3.93–3.99 (m, 3H), 6.64–7.27 (m, 4H). IR ($CHCl_3$): 3374, 3050, 2921, 2871, 2099, 1591, 1475, 1241. 1-Iodo-3-(3-chlorophenoxy)-2-propanol. ^{1}H-NMR ($CDCl_3$): δ 2.80 (m, 1H), 3.26–3.64 (m, 2H), 3.91 (m, 3H), 6.41–7.25 (m, 4H). IR ($CHCl_3$): 3380, 3035, 2918, 2866, 1582, 1478, 1244. **Entry 3.** 1-Azido-3-(2-nitrophenoxy)-2-propanol. ^{1}H-NMR ($CDCl_3$): δ 3.08 (m, 1H), 3.68–3.84 (m, 2H), 4.20 (m, 3H), 6.90–7.88 (m, 4H). IR ($CHCl_3$): 3350, 3041, 2921, 2877, 2101, 1603, 1520, 1352, 1281, 1254. 1-Iodo-3-(2-nitrophenoxy)-2-propanol. ^{1}H-NMR ($CDCl_3$): δ 3.17 (m, 1H), 3.23–3.42 (m, 2H), 3.99–4.22 (m, 3H), 6.88–7.87 (m, 4H). IR ($CHCl_3$): 3504, 3050, 2938, 2872, 1602, 1518, 1349, 1281, 1253. **Entry 4.** 1-Azido-3-(4-chlorothiophenoxy)-2-propanol. ^{1}H-NMR ($CDCl_3$): δ 2.74 (m, 1H), 4.01–4.09 (m, 2H), 4.39–4.49 (m, 3H), 7.09–7.24 (d, 2H), 7.52–7.66 (d, 2H). IR ($CHCl_3$): 3356, 2923,

2870, 2100, 1591, 1489, 1234. 1-Iodo-3-(4-chlorothiophenoxy)-2-propanol. ^{1}H-NMR ($CDCl_3$): δ 2.30–2.32 (m, 1H), 3.33–3.41 (m, 2H), 3.97 (m, 3H), 6.70–6.87 (d, 2H), 7.14–7.29 (d, 2H). IR ($CHCl_3$): 3378, 2917, 2877, 1589, 1489, 1233. **Entry 5.** 1-Azido-3-(4-chlorophenoxy)-2-propanol. ^{1}H-NMR ($CDCl_3$): δ 2.84 (m, 1H), 4.01–4.09 (m, 2H), 4.39–4.49 (m, 3H), 7.09–7.24 (d, 2H), 7.52–7.66 (d, 2H). IR ($CHCl_3$): 3356, 2923, 2870, 2100, 1591, 1489, 1242. 1-Iodo-3-(4-chlorophenoxy)-2-propanol. ^{1}H-NMR ($CDCl_3$): δ 2.34–2.37 (d, 1H), 3.33–3.41 (m, 2H), 3.97 (m, 3H), 6.70–6.87 (d, 2H), 7.14–7.29 (d, 2H). IR ($CHCl_3$): 3378, 2917, 2877, 1589, 1489, 1241. **Entry 6.** 2-Azido-2-phenylethanol. ^{1}H-NMR ($CDCl_3$): δ 2.23 (s, 1H), 3.84–4.10 (m, 2H), 5.10 (m, 0.09H, minor), 5.20–5.27 (m, 0.91H, major), 7.40 (m, 5H). IR ($CHCl_3$): 3368, 3020, 2980, 2870, 1249, 1063. 2-Iodo-2-phenylethanol. ^{1}H-NMR ($CDCl_3$): δ 2.22 (s, 1H), 3.85–4.04 (m, 2H), 5.05–5.10 (m, 0.08H, minor), 5.11–5.29 (m, 0.92H, major), 7.36 (m, 5H). IR ($CHCl_3$): 3368, 3020, 2980, 2870, 2101, 1249, 1063. **Entry 7.** 1-Azido-2-cyclohexanol. ^{1}H-NMR ($CDCl_3$): δ 0.96–1.82 (m, 8H), 2.65 (s, 1H), 3.26–3.27 (m, 2H). IR ($CHCl_3$): 3380, 2921, 2868, 2100, 1460, 1257, 1094. 1-Iodo-2-cyclohexanol. ^{1}H-NMR ($CDCl_3$): δ 0.95–1.79 (m, 8H), 2.62 (s, 1H), 3.23–3.25 (m, 2H). IR ($CHCl_3$): 3376, 2962, 2851, 1458, 1016. **Entry 8.** 1-Azido-2-heptanol. ^{1}H-NMR ($CDCl_3$): δ 0.90 (m, 3H), 0.92–1.38 (m, 8H), 2.71 (s, 1H), 3.19–3.35 (m, 2.7H, major), 3.36–3.63 (m, 0.3H, minor). IR ($CHCl_3$): 3384, 2970, 2872, 2098, 1460, 1257, 1094. 1-Iodo-2-heptanol. ^{1}H-NMR ($CDCl_3$): δ 0.89 (s, 3H), 0.91–1.36 (m, 8H), 2.60 (s, 1H), 3.11–3.33 (m, 2.73H, major), 3.35–3.67 (m, 0.27H, minor). IR ($CHCl_3$): 3363, 2956, 2920, 2851, 1458, 1017. **Entry 9.** 1-Azido-3-chloro-2-propanol. ^{1}H-NMR ($CDCl_3$): δ 2.58 (s, 1H), 3.72–3.74 (m, 4H), 4.10–4.08 (m, 1H). IR ($CHCl_3$): 3379, 2970, 2868, 2098, 1460, 1258, 1092. 3-Chloro-1-iodo-2-propanol. ^{1}H-NMR ($CDCl_3$): δ 2.54 (s, 1H), 3.71–3.73 (m, 4H), 4.06–4.08 (m, 1H). IR ($CHCl_3$): 3360, 2922, 2860, 1458, 1258, 1017.