A Novel Gallium/Samarium-mediated Coupling of Epoxides with Allyl Halides in Aqueous Media and Synthesis of Homoallylic Alcohols

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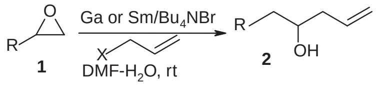
A mild and efficient protocol for the coupling of various substituted epoxides **1** with allylgallium reagent generated in situ in a Bu_4NBr–DMF–H_2O system have been developed. The coupling is also found to be equally effective when samarium is used in lieu of gallium and the corresponding homoallylic alcohols **2** were obtained in almost comparable yields.

Metal mediated reactions in aqueous media have recently found considerable application in organic synthesis as they offer significant advantages over conventional reactions using dry organic solvents.[1] The use of water as solvent can reduce or eliminate environmental damage by organic wastes.[2] Therefore, organic reactions in aqueous media have attracted great attention. Also, nucleophilic ring opening of epoxides with organometallic reagents has found widespread application in the formation of carbon–carbon σ-bonds.[3] Among the most common reagents employed are organomagnesium, organocopper, organozinc, organoaluminium and organoboron compounds.[4] In some cases the basicity of these reagents can promote undesired side reactions. A useful alternative, which often avoids these problems, is the Lewis acid-promoted addition of less basic carbon nucleophiles.[4b] Many reagents acting as Lewis acids have been used for the cleavage of epoxides and their conversion into 1,2-diamino, 1,2-halo-, 1,2-alkoxy-, and 1,2-diazido- alcohols,[5] but only a few methods are reported for the allylation of epoxides with allylmetal reagents.[6] In a report[7] it is stated that allylative ring opening of ethylene oxide can be performed smoothly with allylsilanes under the influence of $TiCl_4$. Introduction of methyl substituent, however, results in the formation of mixtures of products.[8] In another report, the successful allylation of alkenyloxiranes with allyltin reagents in the presence of $BF_3 \cdot OEt_2$ is described.[9] The allylative ring opening takes place at the site of the alkenyl substitution, which stabilize the incipient positive charge, so that it prevents the isomerization of oxiranes. Therefore, in view of the great utility of epoxides as synthetic intermediates in organic chemistry, it is worthwhile to explore the versatility of gallium metal on the epoxide-opening and its subsequent allylation for the synthesis of homoallylic alcohols. In continuation of our ongoing programme on metal mediated organic transformations,[10] we report herein the first example of gallium mediated ring-opening allylation of epoxides and synthesis of homoallylic alcohols under aqueous conditions using tetrabutylammonium bromide (TBAB) as an additive. In a very recent report[11] Lu and Li et al. have developed a InCl mediated coupling of epoxides with allylbromide catalyzed by mesoporous silica supported palladium (expensive nano Pd-26, nano Pd-6, $PdCl_2(PPh_3)_2$, $Pd(OAc)_2$, $[Pd(allyl)Cl]_2$, $Pd(PPh_3)_4$) to give homoallyl alcohols in 47–76% yields. In contrast we have investigated that various epoxides undergo allylation when reacted with stoichiometric-quantity of the allylgallium reagent generated in situ in a Bu_4NBr–DMF–H_2O system at room temperature to produce homoallylic alcohols **2** in high yields.

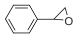
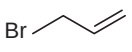
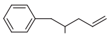
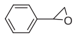
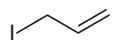
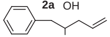
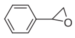
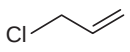
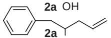
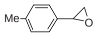
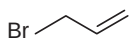
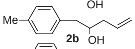
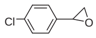
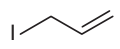
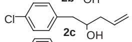
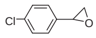
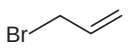
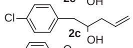
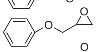
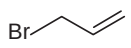
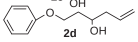
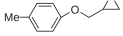
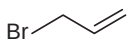
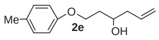
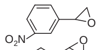
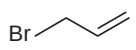
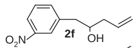
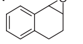
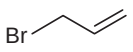
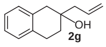
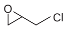
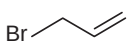
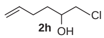
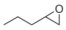
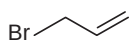
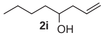
We paid particular attention to gallium, a soft low valent and comparatively less studied element of group IIIA; there have been only a few examples of synthetic reactions in the literature[12] using gallium, which belongs to the same group as the extensively studied boron, aluminium, and indium[13] metals. Previously, indium has been used for the allylation of epoxides in aprotic solvents.[14] After comparing the first ionization and reduction potentials of gallium with those of indium (Ga: FIP, 5.99 eV, E^o, $Ga^{+3}/Ga = -0.56$ V; In: FIP, 5.79 eV, E^o, $In^{+3}/In = -0.345$ V), Wang et al.[15] expected similar properties between the two metals. As in the case of indium, the reduction potential of gallium is not too negative, and thus it is not sensitive to water and does not form oxides readily in air.



Scheme 1.

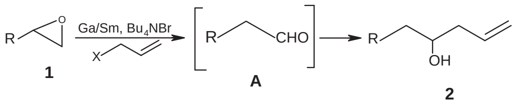
Treatment of styrene oxide with allylgallium reagent in the presence of 2 mol % tetrabutylammonium bromide (TBAB) afforded the corresponding 1-phenyl-4-penten-2-ol in 85% yield. Analysis of the crude mixture did not indicate the formation of any other regioisomer. Similarly various other substituted epoxides were reacted smoothly with allylgallium reagent in aqueous media to give the corresponding homoallyl alcohols in 75–85% yields. Even the sterically hindered cyclic epoxides showed good yields of the target products. The coupling also proceeds effectively when allylsamarium reagent was used and corresponding homoallylic alcohols were obtained in almost comparable yields (Table 1). The reactions are generally clean and no trace of side product could be detected in the NMR spectrum of the crude product. The structure of the homoallylic alcohols thus obtained were unambiguously identified on the basis of their spectral data (IR, NMR, MS) and finally by comparing with authentic samples.[10,16] The electron-donating or withdrawing groups at the aromatic ring did not seem to effect the reaction significantly either in terms of yields or the rate of the reaction. Similarly allylgallium or allylsamarium reagent reacted smoothly with epichlorohydrin (Entry 11) to give the corresponding 1-chloro-5-hexen-2-ol in 75 and 70%, yields, respectively without the formation of 1,3-dichloro-2-propanol. The results, as summarized in Table 1, reveal the generality of this methodology in terms of structural variations of the epoxides and regioselectivity; in each case homoallylic alcohols were isolated in high yields. Moreover, a nitro function was not reduced under the reaction condition. Thus 3-nitro styrene oxide was successfully allylated. Usually a nitro group is sensitive to reduction by metals and is not tolerated under Barbier conditions.[17] In this sense, the use of TBAB as an activating agent is superior to the use of Al, Fe, or $NaBH_4$ reported previously.[18] Also, allyl iodide was found to be as reactive as allyl bromide, but the reactivity of allyl chloride was found to be much less. The use of Bu_4NBr was found to be important, as the allylation did not proceed at all with gallium or samarium alone. It is obvious that activation of the metal is needed for this reaction to proceed. We tried other metal salts like KBr and $MgBr_2$ in aqueous media as additives in place of TBAB and found

Table 1. Allylation of epoxides in DMF-H_2O (3:1) by Ga/Sm-TBAB system

Entry	Epoxides **1**	Allyl halides	Products[a] **2**	Reaction time/h,Ga	Yields /%,Ga	Reaction time/h, Sm	Yields /%, Sm
1			 **2a**	3.5	85	4.0	80
2			 **2a**	3.5	83	4.0	80
3			 **2a**	6.0	75	7.0	70
4			 **2b**	4.0	86	4.5	82
5			 **2c**	4.0	87	4.5	80
6			 **2c**	4.5	81	5.0	80
7			 **2d**	4.5	80	5.0	76
8			 **2e**	4.0	82	5.0	76
9			 **2f**	4.5	80	4.0	75
10			 **2g**	4.5	78	4.5	75
11			 **2h**	3.5	75	4.5	70
12			 **2i**	4.0	76	4.5	72

[a] All the products were characterised by NMR, IR, and MS spectroscopy.

these to be ineffective or to give poor yields. Approximately 0.2 equiv. of Bu_4NBr was found to be sufficient for these reactions to proceed and the use of a large excess did not lead either to higher yields or faster reaction rates. It is also interesting to note that the nature of the solvent controlled the formation of homoallylated products. The reaction is not effective and various by-products are formed when acetonitrile or THF is used as the solvent. The reaction failed to produce any desired compound when DMF alone was used as the solvent. Also, no isolable product was formed when the reaction was run in water. After screening the reaction conditions, the optimum solvent for this coupling reaction was seen to be a 3:1 mixture of DMF–H_2O. Although the detailed mechanism of the reaction is not clear, it is likely that Bu_4NBr effects the generation of an active allylgallium or allylsamarium reagent,[19] and the epoxides undergo rearrangement to form the corresponding aldehydes A.[20] These in situ generated aldehydes reacts rapidly with organogallium or organosamarium reagents to afford the corresponding homoallylic alcohols (Scheme 2).[10,21]



Scheme 2.

In conclusion, this simple and easily reproducible coupling of epoxides with allyl halide[22] using samarium and gallium under aqueous conditions affords various homoallylic alcohols of potentially high synthetic utility in high yields, without the formation of any undesirable side products.

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22 General procedure for the regioselective cleavage of epoxides and synthesis of homoallylic alcohols: To a suspension of gallium (0.5 g, 2 mmol), allyl bromide (0.48 g, 4 mmol) and TBAB (0.064 g, 0.2 mmol) was taken in 15 mL DMF–H_2O (3:1) in a round bottom flask placed in an ice-bath. The mixture was then stirred for 15 min until all the metal dissolved to form a clear solution. To this mixture was then added a solution of styrene oxide 1 (Entry 1, 0.24 g, 2 mmol) in DMF (3 mL). The resulting mixture was stirred for 3 h at room temperature. After completion (monitored by tlc) the reaction mixture was quenched with NH_4Cl solution, extracted with ethyl acetate (3 × 20 mL) and washed with water and brine solution (3 × 20 mL). The combined ether extracts were dried over anhydrous sodium sulphate and the residue obtained thereafter on evaporation of the solvent was subjected to column chromatography using ethyl acetate-hexane (1:5) as eluent to afford the pure product 1-phenyl-4-penten-2-ol 2 in 85% yield. Similarly, other epoxides (Entries 2 to 12) were reacted with allylgallium reagent to get the corresponding homoallyl alcohols in high yields. Even the sterically hindered cyclic epoxides and styrene oxides or epichlorohydrin showed good yields of the target products. The reactions are generally clean and no trace of side product could be detected in the NMR spectra of the crude products. The reaction with samarium metal was carried out similarly and the corresponding homoallylic alcohols were isolated in comparable yields. All products were characterized by infrared and ^1H NMR spectroscopy, and finally by comparison with authentic samples. **2a**: (liquid), ^1H NMR ($CDCl_3$) δ: 1.48 (br, s, 1H, OH), 2.05–2.40 (m, 2H), 2.65–2.75 (m, 2H), 3.70–3.76 (m, 1H), 5.10–5.19 (m, 2H), 5.90 (m, 1H), 7.15–7.40 (m, 5H). IR ν_{max}/KBr/cm^{-1}: 3350, 2925, 1645, 1500, 1450, 1080, 1035, 945, 740. EIMS m/z 162 M^+, 121, 103, 92. Anal. Calcd for $C_{11}H_{14}O$: C, 81.48; H, 10.60. Found C, 81.55; H, 1052. **2g** liquid: ^1H NMR ($CDCl_3$) δ: 1.42–1.60 (m, 4H), 1.88 (br, s, 1H, OH), 2.48 (m, 2H), 2.95 (d, 2H, $j = 18$ Hz), 5.10 (dd, 1H, $j = 1.7$, 10 Hz), 5.18 (dd, 1H, $J = 1.7$, 18 Hz), 5,85–5.98 (m, 1H), 7.09–7.28 (m, 4H). IR ν_{max}/KBr/cm^{-1}: 3410, 2900, 1645, 1490, 1450, 1075, 1030, 945, 745. EIMS m/z 188 M^+, Anal. Calcd for $C_{13}H_{16}O$: C, 82.98; H, 8.51. Found C, 83.05; H, 8.61. **2i**: (liquid), ^1H NMR ($CDCl_3$) δ: 1.45–2.50 (m, 5H, –CH_2CH_2–, OH), 3.25–4.05 (m, 3H, –CH_2ClCH–), 4.70–6.20 (m, 3H, –CH_2=CH–). EIMS m/z 135 M^+, 100, 84, 43. Anal. Calcd for $C_6H_{11}OCl$: C, 53.55; H, 8.18; Found C, 53.61; H, 8.24.

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