One-Pot Transformation of Olefins into α-Aminoalcohols Via Vic-Bromohydrins Catalyzed by Silica

Saadia Oubaassine[1], Brahim Boualy[2], Soufiane El Houssame[2], Mustapha Ait Ali[1] and Larbi El Firdoussi[1,*]

[1]*Equipe de Chimie de Coordination et Catalyse, Département de Chimie, Université Cadi Ayyad, Faculté des Sciences Semlalia, B.P 2390, 40001 Marrakech, Morocco*

[2]*Laboratoire de Chimie et Modélisation Mathématique, Université Hassan 1er, Faculté Polydisciplinaire de Khouribga, B.P 145, 25000 Khouribga, Morocco*

Abstract: Commercially available silica (SiO_2) was found to be highly effective catalyst for one-pot synthesis of α-aminoalcohols from olefins via bromohydrins using morpholine as nitrogen fragment donor. Furthermore, silica in the presence of easily accessible N-bromosuccimide (NBS) catalyzes a rapid and quantitative room temperature bromohydroxylation of simple olefins. Various olefins are easily converted to the corresponding vic-bromohydrins and in "one pot" to α-aminoalcohols in excellent yields and high selectivity. The reaction offers a simple and efficient method for the preparation of vic-bromohydrins and α-aminoalcohools.

Keywords: α-Aminoalcohol, Bromohydroxylation, Morpholine, Olefins, One-pot synthesis, Silica.

INTRODUCTION

Aminoalcohols are structural units present in many synthetic and natural products possessing potent biological activity [1]. Indeed, the 1,2-aminoalcohol's function is present in the widely consumed drug propanolol, a β-blocking agent and in the structure of serine protease inhibitors [2-4]. They have attracted more the attention of chemists with a number of different strategies being devised for their construction [5-7]. In an ongoing project in our laboratory, we were interested to the synthesis of 1,2-aminoalcohols derivatives via the ring opening of epoxides using amines as nucleophiles [8, 9]. This route, which is one of the most versatile and well established reactions of all 'click chemistry' protocols, is typically carried out in the presence of a catalyst and a large excess of amines at elevated temperatures. For this reason, non-conventional techniques, besides the most classical procedures, have been used to promote the reaction. Thus, we assume that vicinal halohydrins could be one of the better starting materials to prepare vicinal aminoalcohols.

In addition, vicinal halohydrins represent a valuable pathway to produce versatile starting materials that are widely used in synthetic organic chemistry [10, 11]. Generally, halohydrins, can be prepared directly by ring opening of epoxides using hydrogen halides [12-15] or by functionalization of alkenes [16]. However, it is still desirable to discover improved method to use efficiently these reagents for halohydroxylation of olefins under mild reaction conditions. Herein, we report an efficient novel methodology for the regioselective synthesis of 1,2-aminoalcohols from vicinal halohydrins prepared in-situ from alkenes. The optimization of these reactions was studied with methylstyrene, chosen as model substrate, in the presence of catalytic amount of SiO_2.

To the best of the authors' knowledge, the use of SiO_2 as catalyst in these transformations has not been reported.

EXPERIMENTAL SECTION

Materials

NMR studies were performed on a Bruker Avance 300 spectrometer in $CDCl_3$ solution, chemical shifts are given in ppm relative to external TMS and coupling constant (J) in Hz. The reaction mixtures were analyzed on a Trace GC Thermo Finnigan chromatograph equipped with FID, using capillary columns BP (25 m × 0.25 mm, SGE). Liquid chromatography was performed on silica gel (Merk 60, 220-440 mesh; eluent: hexane/ethyl acetate). All reagents and solvents used were purchased from commercial sources and used as received without further purification (Aldrich, Acros).

*Address correspondence to this author at the Equipe de Chimie de Coordination et Catalyse, Département de Chimie, Université Cadi Ayyad, Faculté des Sciences Semlalia, B.P 2390, 40001 Marrakech, Morocco; Tel: +212 524 434649; Fax: +212 524 437408;
E-mail: elfirdoussi@ucam.ac.ma

E-ISSN: 2408-9834/14 © 2014 Cosmos Scholars Publishing House

General Procedure for the Synthesis of Vic-Bromohydrins

To a suspension of olefin (0.5 g) in solvent (4 mL) and NBS (0.98 g) in water (1 mL), 0.04 g of SiO_2 was added. The mixture was stirred at room temperature for the indicated time. The reaction was monitored by GC. At the end of the reaction, the mixture was diluted with 50 mL of water and extracted 3 times with 25 mL of EtOAc. The organic layer was concentrated and the residue was purified by using silica gel column chromatography with Hexane-EtOAc as eluant. The obtained pure vic-bromohydrins were characterized by NMR analysis. All the isolated products analysis is compared to those in the literature.

General Procedure for the Preparation of α-Aminoalcohol *In Situ*

To a stirred solution of olefin (4 mmol) in 4 mL of solvent (THF or Acetone) and NBS (5 mmol) in water (1 mL) were added SiO_2 (0.04 g). After 10-30 min, 2 equivalents of morpholine were added and the resulted mixture was stirred at room temperature for the indicated time. The reaction mixture was diluted with 25 mL of water and extracted with EtOAc (3×15 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. Pure aminoalcohol was obtained by column chromatography over silica gel using Hexane/EtOAc as eluent and characterized by ^1H and ^{13}C NMR.

1c: ^{1}HNMR (300 MHz $CDCl_3$): δ= 7.21- 7.42 (m, 5H; -CH, Ar); 5.25 (s, 1H, OH); 3.64 (m, 4H; $-CH_2$,); 2.9 (2d, J= 7.8 Hz, $-CH_2$); 2.5 (m, 4H; $-CH_2$,); 1.5 (s, 3H, $-CH_3$). ^{13}CNMR ($CDCl_3$): δ: 148.05, 128,11 126.42, 124.78, 71.94, 69.96, 66.91, 55.12, 29.47

2c: ^{1}HNMR (300 MHz $CDCl_3$): δ= 7.1- 7.3 (m, 5H; -CH, Ar); 4.65 (s, 1H, -CH); 3.65 (m, 4H; $-CH_2$); 3.25 (s, 1H; -OH,); 2.65 (m, 2H, $-CH_2$). 2.35 (m, 4H, $-CH_2$); ^{13}CNMR ($CDCl_3$): δ: 128.05, 68.65, 66.96, 60.76, 49.97.

3c: ^{1}HNMR (300 MHz. $CDCl_3$): δ= 7.1- 7.4 (m, 5H; -CH, Ar); 4.25 (d, 1H, -CH); 3.6 (m, 4H; $-CH_2$,); 3.1 (s, 1H, OH); 2.95 (m, 1H, -CH); 2.35 (m, 4H; $-CH_2$,); 0.9; (d, 3H; $-CH_3$).^{13}CNMR ($CDCl_3$): δ: 136.43, 129.72, 128.13, 127.70, 75.65, 67.07, 64.39, 51.86, 19.63.

4c: ^{1}HNMR (300 MHz $CDCl_3$): δ= 3.5 (m, 4H; $-CH_2$,); 3.1 (s, 1H, -CH); 2.4 (s, 1H, -CH); 2 (m, 4H; $-CH_2$,); 3.5 (m, 8H; $-CH_2$,); ^{13}CNMR ($CDCl_3$): δ: 70.22, 68.12, 67.21, 48.55, 33.02, 25.2, 23.82, 22.02.

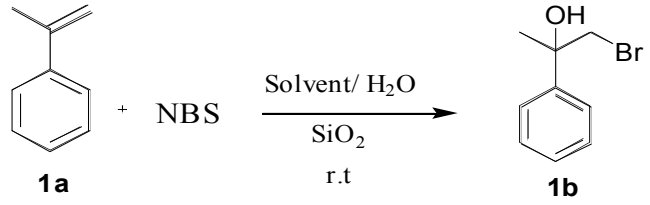
5c: ^{1}HNMR (300 MHz $CDCl_3$): δ= 3.8 (m, 4H; $-CH_2$); 3.45 (s, 1H, -CH); 2.6 (m, 2H; $-CH_2$,); 2.4(m, 4H, $-CH_2$); 2 (s, 1H; -OH,); 1.35(m, 8H, $-CH_2$); 1.35(m, 3H, $-CH_3$). ^{13}CNMR ($CDCl_3$): δ: 67.5, 65.95, 65.21, 53.6, 34.80, 31.67, 29.30, 25.41, 22.45, 13.95.

RESULTS AND DISCUSSION

Synthesis of Bromohydrins from Olefins

The vic-bromohydrins were prepared in a short sequence of straightforward reactions from alkenes in catalytic way. The reaction was carried out under mild conditions in the presence NBS using SiO_2 as heterogeneous and especially effective catalyst. The results show that olefins react regioselectively to form the vic-halohydrins in excellent yields.

In a preliminary step, the reaction of α-methylstyrene and N-Bromosuccinimide was conducted in the presence of catalytic amount of silica (SiO_2) (Scheme **1**). The influences of the nature of solvent and the amount of catalyst have been studied (Table **1**).



Scheme 1: Bromohydroxylation of α-methylstyrene **1a**.

Table 1: Bromohydroxylation of 1a using Different Amount of SiO_2 and Solvent Systems

Entry	Amount of SiO_2 (g)	Solvent	Time (min)	Yield [a] (%)
1	None	acetone/water	60	10
2	0.02	acetone/water	10	85
3	0.03	acetone/water	10	94
4	0.04	acetone/water	10	98
5	0.05	acetone/water	10	98
6	0.04	THF/water	15	97
7	0.04	CH_3CN/water	15	90
8	0.04	DME/water	15	78

Conditions: α-methylstyrene **1a** (0.5 g), NBS (0.98 g), catalytic amount of SiO_2, solvents (4/1), room temperature.
[a] Isolated yield after column chromatography.

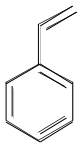
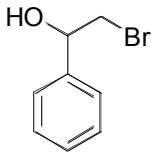
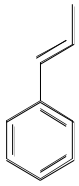
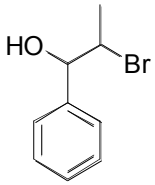
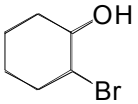
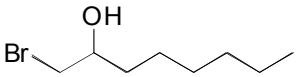
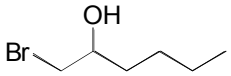
In the presence of a catalytic amount of SiO_2, bromohydroxylation of α-methylstyrene **1a** in a mixture

of acetone/water (4/1) as solvent, lead to the corresponding bromohydrin in 98% yield (Table **1**, Entry 4). The reaction was completed within 10 min at room temperature and no by-products were obtained. In order to confirm the role of SiO_2 as catalyst, a blank reaction was carried out at similar reaction conditions. The reaction occurs with 10% yield after 60 min (Table **1**, Entry 1). Decrease of catalyst loading has negative effect on the yield of the reaction (Table **1**, Entry 2).

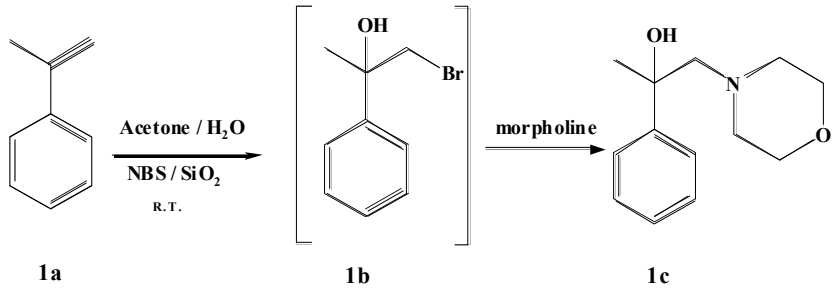
The reactions carried out in both THF/water and acetone/water combinations gave the corresponding bromohydrins in good yields (Table **1**, Entries 4, 6). However, the catalytic activity decreases slowly when the reaction was monitored in acetonitrile/water or DME/water combination (Table **1**, Entries 7, 8).

In order to extend the scope and limitation of the reaction, the protocol according to the bromohydroxylation of α-methylstyrene **1a** was then performed using representative olefins as substrates (Table **2**). In a similar manner, the styrene derivatives (**2a** and **3a**), cyclohexene **4a** and aliphatic olefins (**5a** and **6a**) reacted with NBS at room temperature in aqueous solution of acetone to give the corresponding vic-bromohydrins. As shown in Table **2**, all the reactions were completed within 10–30 min to give the desired products in a good to excellent yields (79–98%) (Table **2**, Entries 9-13). A high regioselectivity in favor

Table 2: Silica Catalyzed Bromohydroxylation of Representative Olefins

Entry	Olefins	Time (min)	Products	Yield [a] (%)
9	 **2a**	30	 **2b**	90
10	 **3a**	15	 **3b**	97
11	 **4a**	20	 **4b**	79
12	 **5a**	10	 **5b**	98
13	 **6a**	20	 **6b**	80

Conditions: olefin (0.5 g), NBS (0,98 g), Silica (0.04 g), Acetone/water (4/1), room temperature.
[a] Isolated yield after column chromatography.
NMR analyses of products **2b-6b** are compared to those in the literature [10, 17-19].



Scheme 2: One pot transformation of α-methylstyrene **1a** into α-aminoalcohol **1c**.

of attack of the bromine atom at the terminal carbon was observed and only a unique regioisomer was obtained.

Synthesis of α-Aminoalcohols

Under optimized reaction conditions, the amination was carried out in-situ and in the presence of SiO_2 as catalyst using morpholine as a nitrogen fragment donor. The reaction proceeds at room temperature in the presence of 2 equivalents of amine. The substrate is converted regioselectively to the corresponding aminoalcohol in excellent yield (95%).

A kinetic study was carried out using SiO_2 as catalyst. Figure **1**, which depicts the evolution of bromohydrin and aminoalcohol versus time, shows that the bromohydrin **1b** was formed at the early stage of the reaction and reached a maximum after 10 min and then disappeared. The formation of aminoalcohol took place and its amount increased rapidly and then much more slowly after 30 min. This observation proves that bromohydrin **1b** behaves in the presence of SiO_2 as an intermediate that reacts to give the aminoalcohol **1c**.

Conditions: α-methylstyrene (0.5 g), NBS (0.98 g), Silica (0.04 g), Acetone/water (4/1), morpholine (2 eq.), R.T.

We next planned to establish the generality of the SiO_2-catalyzed one-pot synthesis of α-aminalcohol with other olefins. Styrene derivatives (**2a** and **3a**), cyclohexene **4a** and aliphatic olefin **5a** were treated with NBS and morpholine at room temperature in aqueous solution of acetone using SiO_2 as catalyst (Table **3**). In each case, the corresponding α-aminalcohol was formed in a good to excellent yields (80–98%). Excellent regioselectivity, as in the case of bromohydroxylation, was observed.

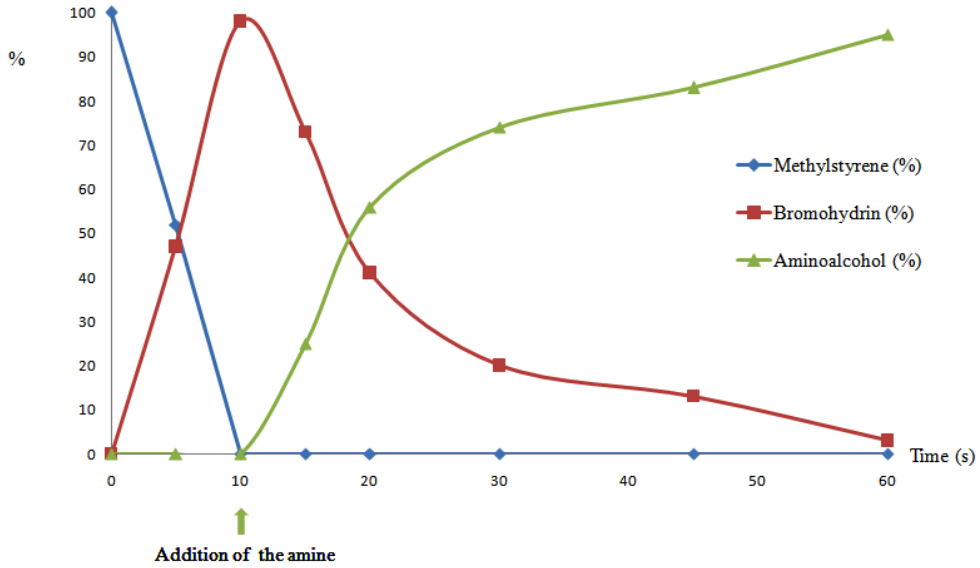
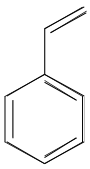
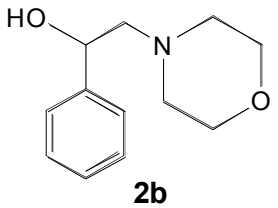
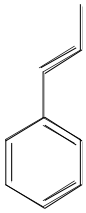
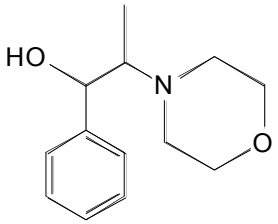
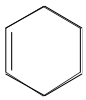
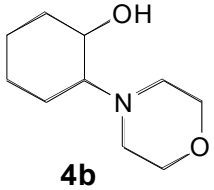
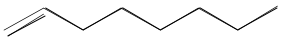
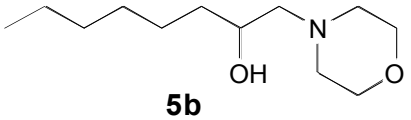


Figure 1: Synthesis of aminoalcohol fom α-methylstyrene via bromohydrin catalyzed by SiO_2; conversion and product distribution vs. time.

Table 3: Synthesis of α-Aminoalcohols using SiO_2 as Catalyst Under the Optimized Conditions

Try	Olefins	Time (h)	Products	Yield [a] (%)
14	 **2a**	1.5	 **2b**	90
15	 **3a**	1.5	 **3b**	97
16	 **4a**	2	 **4b**	80
17	 **5a**	2	 **5b**	98

Reactions conditions: olefin (0.5 g), NBS (1.3 eq.), Silica (0.04 g), morpholine (2eq.), Acetone/water (4/1), R.T.
[a] Isolated yield after column chromatography.

CONCLUSION

In summary, we have described for the first time, the use of commercially available SiO_2 as efficient catalyst for a simple synthesis of 1,2-aminoalcohols via vic-bromohydrins with easily accessible NBS as source of halogen. The conversion of various olefins has been successfully carried out under mild conditions. This novel methodology led to the corresponding aminoalcohols in a good to excellent yields and shows a high degree of regioselectivity.

REFERENCES

[1] Boukhari A, Blida R, Ismail F. C.R Chimie 2010; 13: 1440–1442.

[2] Genow M, Dimitrov V, Ivanova V. Tetrahedron Asymmetry 1997; 22: 3703-3706.

[3] Hayashi Y, Rohde JJ, Corey EJ. J Am Chem Soc 1996; 118: 5502-5503.

[4] Ager DJ, Prakash I, Schaad DR Chem Rev 1996; 96: 835-875.

[5] Barrett AGM, Seefeld MA, Williams DJ J Chem Soc Chem. Commun 1994; 9:1053-1054.

[6] Krepski LR, Jensen KM, Heilmann SM, Rasmussen JK.Synthesis 1986; 4: 301-303.

[7] Jackson WR, Jacobs HA, Matthews BR, Jayatilake GS. Tetrahedron Lett 1990; 31: 1447-1450.

[8] Outouch R, Boualy B, El Firdoussi L, Ait Ali M, Rizzoli C, Spannenberg A Z. Kristallogr. 2011; NCS 226: 279-280.

[9] Outouch R, Rauchdi M, Boualy B, El Firdoussi L, Roucoux A, Ait Ali M. Acta chimica Slovenica 2014; 61: 67-72

[10] Palmisano G, Tagliapietra S, Barge A, Binello A, Boffa L, Cravotto G. Synlett 2007; 12: 2041–2044.

[11] Manoj KA, Adimurthy S, Gangyly B, Ghosh PK. Tetrahedron 2009; 65: 2791-2797

[12] Charda DR, Herbert CB. Journal of Organometallic Chemistry 2007; 692: 1608-1613.

[13] Smith JG, Fieser M, Reagent for Organic Synthesis, vols. 1–12, John Wiley and Sons: New York; 1990.

[14] Bonini C, Righi G. Synthesis 1994; 25: 225-238.

[15] Majetich G, Hicks R, Reister S. J. Org. Chem. 1997; 62: 4321-4326.

[16] Ranu BC, Banerjee S. J. Org. Chem. 2005; 70: 4517-4520.

[17] Narender M, Reddy MS, Nageswar YVD, Rama Rao K. Journal of Molecular Catalysis A: Chemical 2006; 258: 10–14.

[18] Conte V, Di Furia F, Moro S. Tetrahedron Lett. 1996; 37: 8609-8612.

[19] Yadav JS. Reddy BVS, Baishya G, Harshavardhan SJ, Chary ChJ, Gupta MK. Tetrahedron Lett. 2005; 46: 3569–3572.

Received on 03-10-2014 Accepted on 24-10-2014 Published on 24-11-2014

http://dx.doi.org/10.15379/2408-9834.2014.01.02.02

© 2014 Oubaassine *et al.* ; Licensee Cosmos Scholars Publishing House.
This is an open access article licensed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/3.0/), which permits unrestricted, non-commercial use, distribution and reproduction in any medium, provided the work is properly cited.