Synthesis of Silica Bromide as Heterogeneous Reagent and its Application to Conversion of Alcohols to Alkyl Bromides

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Abstract: Silica bromide as heterogeneous reagent is prepared from the reaction of silica gel with PBr_3 as a non-hydroscopic, filterable, cheap, and stable yellowish powder that can be stored for months. The results show that the silica bromide is a suitable and efficient reagent for conversion of alcohols to alkyl bromides under mild conditions at room temperature. The easy availability of this reagent makes this simple procedure attractive and a practical alternative to the existing methods.

Keywords: Alkyl bromides, bromination, heterogeneous reagent, silica bromide.

INTRODUCTION

Deliberately performing chemical reactions in heterogeneous rather than homogeneous media was suggested by R. B. Merrifield [1] for use in polypeptide synthesis and by R. L. Letsinger [2] for polynucleotide synthesis. The classical idea was presented that chemical reactions should be performed in a completely homogeneous medium was not necessarily correct and that reactions can be accomplished even if one of the substrates was insoluble in the reaction media. The methodology of some organic synthesis has been revolutionized by this idea. In that the normal procedures associated with the workup of a chemical reaction are obviated and replaced by a simple filtration step [1, 2], this general advantage of solid-phase synthesis has been particularly exploited in polypeptide synthesis [3], where a polypeptide is synthesized in a repetitive sequential manner on the solid phase and the final products are only liberated from the polymer in a final cleavage reaction. Another approach to using polymer supports in organic synthesis was outlined by Fridkin, Patchornik, and Katchalski [4], who showed that a polymer-bound reagent could be used in heterogeneous reaction in such a way that excess reagents or by-products remain attached to the insoluble resin. These unwanted materials are then removed by filtration and the pure product is isolated from the filtration [5].

Many specific advantages of using insoluble resins such as supports, reagents, or catalysts have been reviewed [6], which include the simulation of high-dilution [7] or pseudodilution [8] conditions, the fishhook and concentration principle [9], selective intrapolymeric reactions [10], bulk and steric effects of the polymer backbone in asymmetric synthesis [11], the stabilization of reactive substances [12], and the elimination of volatile malodorous reagents [13].

Transformation of an alcohol function to a bromide function is one of the most described transformations in organic synthesis. Many reagents are commonly used to carry out this transformation [14]. The most widely used reagents are phosphorus tribromide [15], thionyl bromide [16], brominated Villsmeier salt [17], $Br_3CCOCBr_3/PPh_3$ and Br_3CCO_2Et/PPh_3, and tertiary phosphines with different sources of bromide [18]. Thus, an efficient and practical protocol for the preparation of alkyl bromides would be valuable. There are relatively few conditions for the conversion of alcohols into bromides. Previous examples include highly toxic reagents such as HBr gas and Br_2 or coupling reagents like CBr_4/PPh_3, Br_2 /PPh_3 and Br_2PPh_3 but HBr is always a by-product and high temperatures are often required [4]. Silica chloride [19] as the heterogeneous reagent is very closely to silica bromide in a functional group transformation.

RESULTS AND DISCUSSION

Herein, we report the synthesis and use of silica bromide for the mild and selective bromination of alcohols under mild conditions (Scheme **1**).

In order to select the best supporting bed and condition for preparation of a suitable silica bromide, we first reacted different types of silica with different amount of phosphorus tribromide in refluxing toluene under dry atmosphere. The results obtained are shown in Table **1**.

From all these reactions, the reagent which was obtained after filtration washing with dry dioxane and dry dichloromethane and drying showed a suitable weight increase. The amount of bromosilyl group was determined by a standard method [18]. The analysis of bromide on silica was identical

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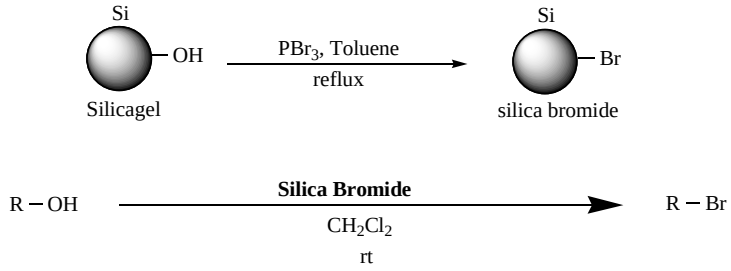


Scheme 1. Synthesis and use of silica bromide for synthesis of alkyl bromides.

Table 1. Using of Different Support to Synthesis of Silica Bromide.

Entry	Type of Silica Gel[a]	Reaction Time (h)	Amount of PBr_3 (g)	Amount of Bromide (mmole)
1	Column	24	15	1.8
2	Activated plate[b]	24	15	2.3
3	Dried plate	24	15	2.3
4	Plate	24	15	2.3
5	Plate	24	12	2.3
6	Plate	24	10	2.2
7	Plate	24	8	2.2
8	Plate	24	5	1.9
9	Plate	20	10	2.2
10	Plate	18	10	2.2
11	Plate	15	10	2.0

[a]Plate silica gel (Merck Darmestadt, type 60, 15-40 mm, 5 g) and column silica gel (Merck Darmestadt, type 60, 63-200 mm, 5 g) was used.

Table 2. Different Conditions for the Reaction of Benzyl Alcohol (1 mmol) with Different Quantities of Silica Bromide at Room Temperature in CH_2Cl_2 for 5 min.

Entry	Silica Bromide (mmol)	Conversion (%) to Benzyl Bromide
1	1	52
2	1.5	73
3	1.7	81
4	2.2	100
5	2.4	100
6	2.7	100

with that used for bromide in McDaniel's papers [20]. As demonstrated in Table **1**, the amount of bromosilyl group in the cases of using plate silica gel is considerably higher. Activation and drying of plate silica gel did not lead to a considerable difference in the capacity of obtained reagent. The reagent which was obtained under this condition converted benzyl alcohol to benzyl bromide quantitatively after 3 min in CH_2Cl_2 at room temperature.

Since the introduced filterable silica bromide showed excellent reactivity for the conversion of benzyl alcohol to benzyl bromide and provided a very simple and practical isolation of the product, we decided to study its applicability as a general reagent for the conversion of different classes of alcohols into alkyl bromides. We optimized the conditions for the conversion of benzyl alcohol to benzyl bromide using different ratio of silica bromide (Table **2**).

We then applied the optimized conditions for the reaction of structurally different alcohols, and found that they can be conveniently converted to the corresponding alkyl bromides under effective conditions and in high yields ranging from 81 to 99%. Functionality of compounds such as that of alkene, ether, acetate, and nitro proved to be stable under the reaction conditions. Reaction of 1,2-diols with silica bromide gave a mixture of isomers. For example, 2-bromo-1-phenylethanol and 2-bromo-2-phenylethanol was obtained from reaction of silica bromide with 1-phenyl-1,2-ethanediol (Table **3**, entry 18).

Table 3. Conversion of Alcohols to Bromides.

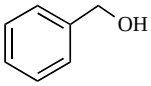
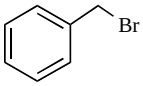
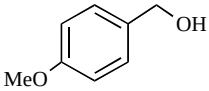
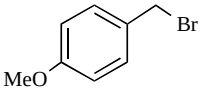
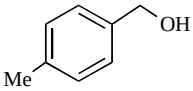
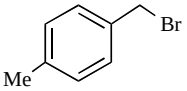
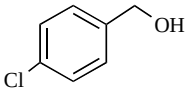
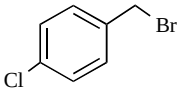
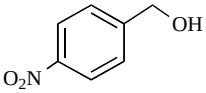
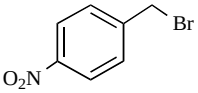
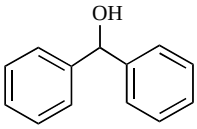
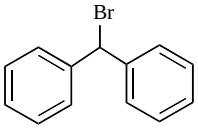
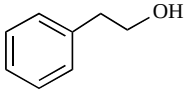
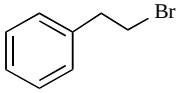
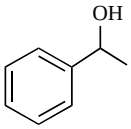
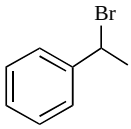
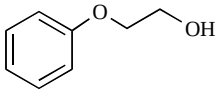
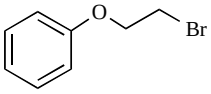
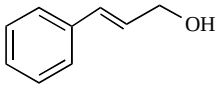
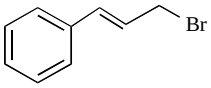
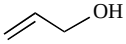
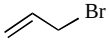
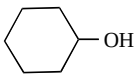
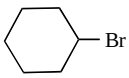
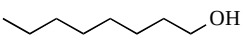
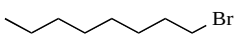
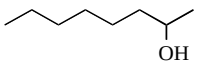
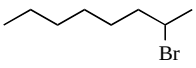
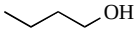
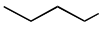
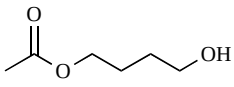
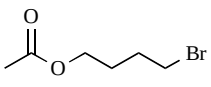
Entry	Substrate	Product	Time[a] (min)	Yield[b] (%)
1			3	98
2			3	99
3			3	96
4			3	96
5			5	90
6			5	96
7			10	94
8			7	96
9			10	95
10			5	93
11			5	91
12			10	81
13			10	92
14			10	85
15			10	90
16			10	89

Table 3. contd…

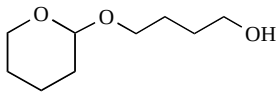
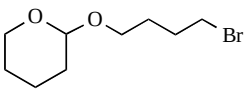
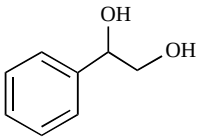
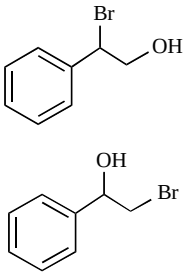
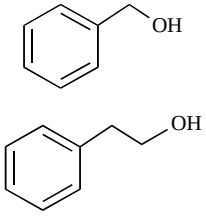
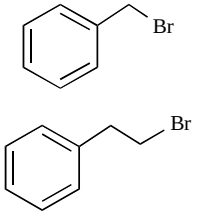
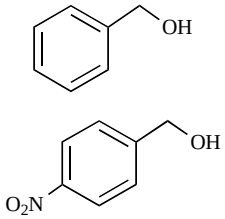
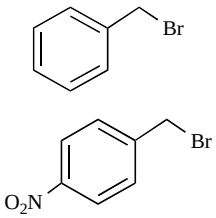
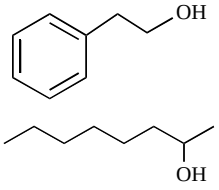
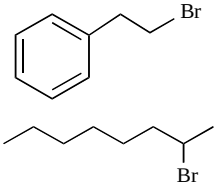
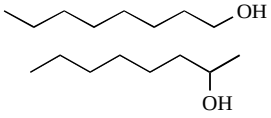
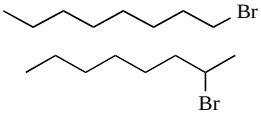
Entry	Substrate	Product	Time[a] (min)	Yield[b] (%)
17			10	88
18			3	82 18

Table 4. Competitive Reaction of Different Binary Mixture with Silica Bromide[a].

Entry	Binary Mixture of Alcohols[b]	Alkyl Bromide[c, d]	Conversion (%)
1			80 20
2			93 7
3			100 0
4			90 10

[a]2.2 Equivalent moles of silica bromide. [b]1 Equivalent mole of each of alcohols.
[c]GC yields using *n*-octane as an internal standard. [d]The time of reaction was 5 min.

In order to have more insight into the applicability of this method, some competitive reactions were performed between structurally different alcohols in binary mixtures. The results which are tabulated in Table **4** show high selectivity between 1° aliphatic and 1° benzylic alcohols, benzyl alcohol and 4-nitrobenzyl alcohol, and also between 1° and 2° alcohols.

CONCLUSION

In conclusion, we described in this paper an original reagent (silica bromide) for the bromination of primary and secondary hydroxyl groups. This reagent is prepared from the reaction of silica gel with PBr_3 as a non-hydroscopic, filterable, cheap, and stable yellowish powder that can be stored for months. The reactions are very fast without the

production of side-products. Moreover, the isolation of the products from the heterogeneous mixture is easy and not time-consuming.

EXPERIMENTAL

Procedure for Preparation of Silica Bromide

To silica gel (40 g) and dry toluene (80 mL) in a round bottomed flask equipped with a condenser and a drying tube, was added phosphorus tribromide (75 g, 0.21 mol) and refluxed for 18 h. After cooling, the product was filtered and washed, first with dry 1,4-dioxane (2 x 20 mL) and then with dichloromethane (2 x 20 mL). The yellowish product was kept in dessicator. The amount of bromosilyl group (2.2 mmole of Br/ g silica) was determined by a standard method [18, 20].

A Typical Procedure for the Conversion of Benzyl Alcohol to Benzyl Bromide

To a round bottom flask contain a stirring mixture of silica bromide (1 g, 2.2 mmol Br/ g silica) in dry CH_2Cl_2 (10 mL) at room temperature, was added benzyl alcohol (0.108 g, 1 mmol). After 3 min, GC analysis showed the completion of the reaction. The reaction mixture was filtered and the solvent was evaporated under vacuum. Benzyl bromide was obtained as a colorless liquid (0.167 g, 97%, bp 195-196.5 ^{o}C, lit.[20] bp 196-198 ^{o}C).

^{1}H NMR data for selected compounds

Product (**Table 3, entry 1**): ^{1}H NMR 200 MHz, $CDCl_3$): δ 4.28-4.29 (s, 2H), 7.25-7.39 (m, 5H).

2H), 6.87-7.18 (m, 4H).

Product (**Table 3, entry 3**): ^{1}H NMR 200 MHz, $CDCl_3$): δ 2.17 (s, 3H), 4.26 (s, 2H), 7.32-7.39 (m, 4H).

Product (**Table 3, entry 4**): ^{1}H NMR 200 MHz, $CDCl_3$): δ 4.26 (s, 2H), 7.45-7.48 (m, 4H).

Product (**Table 3, entry 5**): ^{1}H NMR 200 MHz, $CDCl_3$): δ 4.28 (s, 2H), 7.34-8.05 (m, 4H).

Product (**Table 3, entry 6**): ^{1}H NMR 200 MHz, $CDCl_3$): δ 6.28 (s, 1H), 7.23-7.47 (m, 10H).

Product (**Table 3, entry 7**): ^{1}H NMR 200 MHz, $CDCl_3$): δ 3.19-3.22 (t, 2H), 3.59-3.63 (t, 2H), 7.25-7.38 (m, 5H).

Product (**Table 3, entry 8**): ^{1}H NMR 200 MHz, $CDCl_3$): δ 2.09-2.10 (d, 3H), 5.24-5.28 (q, 1H), 7.29-7.50 (m, 5H).

Product (**Table 3, entry 9**): ^{1}H NMR 200 MHz, $CDCl_3$): δ 3.55-3.58 (t, 2H), 4.09-4.11 (t, 2H), 6.94-7.02 (m, 5H).

Product (**Table 3, entry 10**): ^{1}H NMR 200 MHz, $CDCl_3$): δ 3.71-3.77 (d, 2H), 6.55-6.57 (d, 1H), 7.16-7.19 (tt, 1H), 7.32-7.74 (m, 5H).

Product (**Table 3, entry 11**): ^{1}H NMR 200 MHz, $CDCl_3$): δ 3.70-3.72 (d, 2H), 4.99-5.02 (m, 1H), 7.01-7.06 (m, 1H).

Product (**Table 3, entry 12**): ^{1}H NMR 200 MHz, $CDCl_3$): 1.40-1.58 (m, 4H), 1.80-1.89 (m, 6H), 4.05-4.09 (m, 1H).

Product (**Table 3, entry 13**): ^{1}H NMR 200 MHz, $CDCl_3$): δ 0.82-0.87 (t, 3H), 1.23-1.29 (m, 12H), 3.23-3.27 (t, 2H).

Product (**Table 3, entry 14**): ^{1}H NMR 200 MHz, $CDCl_3$): δ 0.82-0.87 (t, 3H), 1.24-1.29 (m, 8H), 1.40-1.45 (md, 3H), 1.62-1.67 (t, 2H), 3.71-3.79 (m, 1H).

Product (**Table 3, entry 15**): ^{1}H NMR 200 MHz, $CDCl_3$): δ 3.19-3.22 (t, 2H), 3.59-3.63 (t, 2H), 7.25-7.38 (m, 5H).

Product (**Table 3, entry 16**): ^{1}H NMR 200 MHz, $CDCl_3$): δ 0.9-0.95 (t, 3H), 1.41-1.55 (m, 4H), 3.35-3.42 (t, 2H).

Product (**Table 3, entry 17**): ^{1}H NMR 200 MHz, $CDCl_3$): δ 1.51-1.58 (m, 3H), 1.75-1.90 (m, 7H), 3.31-3.33 (t, 2H), 3.57-3.58 (t, 2H), 3.60-3.75 (m, 2H), 4.68 (dd, 1H).

Product (**Table 3, entry 18**): ^{1}H NMR 200 MHz, $CDCl_3$): δ 3.43-3.68 (d, 2H), 4.61-4.67 (t, 1H), 7.43-7.47 (m, 5H).

CONFLICT OF INTEREST

The author(s) confirm that this article content has no conflicts of interest.

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