



Short Communication

Use of solid supported reagent in organic synthesis

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Abstract

The use of solid supported reagents is increasing, due to their tremendous potential to offer green chemical technologies. Now-a-days, silica supported acid catalysts have gained much importance due to their high activity. Moreover, silica-supported reagents are easy to handle, less toxic, can be easily separated and reused, due to which they may play important role both in academia and industries. Silicas generally require no pre-swelling, which makes their use far simpler. As oxidative bromination of alkenes is very important in synthesizing biologically and synthetically important dibromocompounds, a simple, efficient and cost effective method has been used for the bromination of alkenes by using SiO_2 - H_2SO_4 as solid heterogeneous catalyst.

Keywords: Solid supported reagents, oxidative bromination, alkenes, dibromocompounds, heterogeneous conditions.

Introduction

Bromination is a useful reaction in organic synthesis as these compounds are very important particularly in the preparation of different β -blocker, such as adrenoceptor agonists SR-58611A, denopamine, tembamide, formoterol, salmetrol etc. and in the manufacture of dyes, flame retardants, pharmaceuticals and agrochemicals¹⁻³. Brominated organic substrates are known to possess potent antitumour, antifungal, antibacterial, antineoplastic and antiviral activities⁴. Dibromoalkanes have also been used as precursors of pesticides, gasoline additives and synthetic building blocks⁵.

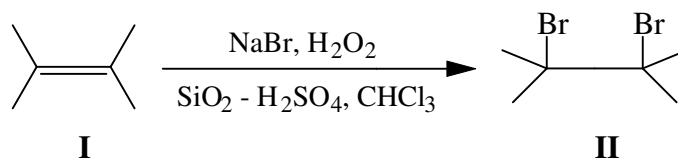
These have been used to synthesise alkynes, which are useful functional groups in organic reactions⁶⁻¹¹.

Bromination with molecular bromine is one of the most widely and extensively studied reactions. Molecular Bromine is very toxic and has corroding nature. One bromine atom is obtained in product whereas the other bromine atom forms HBr which is corroding in nature and has to be neutralized¹²⁻¹⁴. Thus, bromination with molecular bromine may be qualified as environmentally unfriendly reaction¹⁵. Environment friendly bromination protocols have been developed in place of use of bromine¹⁶.

Various reagents have been reported for the bromination of alkenes such as $\text{V(V)}\text{-H}_2\text{O}_2$, LiBr and CuBr, silica-pyridinium hydrobromide perbromide, tetrabutylammonium tribromide (TBATB), zinc bromide and leadtetracetate, benzyl trimethylammonium tribromide (BTMA Br_3), bromine and tetraethyl ammonium bromide, sodium bromide in the presence of sodium perborate¹⁷⁻²⁵.

However, some of these methods suffer from various drawbacks like insolubility of the metal bromides and the oxidising agents in non-aqueous solvents, long reaction times, polymerization of the alkene with the reagents and limited application to alkenes that are not affected by acids and aqueous media.

Now-a-days, silica-supported reagents have gained much importance due to their high activity. Moreover, silica-supported reagents are easy to handle, less toxic, can be easily separated and reused, hence, they may play important role both in academia and industries. So silica materials are probably the most studied and commonly used porous solids²⁶. As oxidative bromination of alkenes is very important in synthesizing dibromocompounds, a simple, efficient and cost-effective method has been used for the bromination of alkenes using SiO_2 - H_2SO_4 as solid heterogeneous catalyst (Scheme-1).



IIa: 1,2-Dibromodecane, **IIb:** 1,2-Dibromo-2-methoxypropane, **IIc:** 1,2-Dibromo-2,3-dichlorobutane, **IId:** 2,3-Dibromo-3-phenylpropanoic acid, **IIe:** 2,3-Dibromo-3(4-methoxyphenyl)propanoic acid.

Methodology

SiO_2 - H_2SO_4 as solid catalyst: To conc. H_2SO_4 (95%, 6g), SiO_2 (12g), diethyl ether (70mL) were added. The mixture was stirred for 30min. at room temperature. The diethylether was removed

and the residue obtained was warmed at 100°C for 5h under vacuum to get SiO₂-H₂SO₄ as a free flowing powder.

General method for the synthesis of vicinal dibromoalkanes with NaBr and H₂O₂ using SiO₂-H₂SO₄: Alkene (1 mmol), NaBr (1mmol) and H₂O₂ (2mL, 30%) were mixed in a pestle. SiO₂-H₂SO₄ (0.2g) was added and the mixture was grinded by using mortar (2min). The reaction mixture was then transferred to a round-bottomed flask (100mL) using chloroform (5mL) and stirred at 70°C in a pre-heated oil-bath for an appropriate time (Table-1). The reaction was monitored by TLC, and as the reaction completed, the catalyst was filtered off by triturating the reaction mixture with chloroform (3x10mL). The solvent was removed and the product obtained was crystallized by using pet. ether: EtOAc.

The structures of the products were confirmed by spectral analysis and using the literature data.

Table-1: Synthesis of vicinal dibromoalkanes^a from alkenes with NaBr and H₂O₂ using SiO₂-H₂SO₄ as catalyst.

Entry	Time (h)	Yield ^b (%)	MP ^c or BP ^c (°C)
IIa	3	98	BP 94-96 ²⁷
IIb	4	96	liq.
IIc	5	84	liq.
IId	2	89	MP 198-201
IIE	2	87	MP 152-154

a. Reaction conditions: alkene (1mmol), NaBr (1mmol), H₂O₂ (2 mL, 30%), SiO₂-H₂SO₄ (0.2g), CHCl₃ (5mL) and 70°C as the reaction temperature. b. Isolated yield, c. Melting Point or Boiling Point

Spectral data of synthesized compounds (IIa – IIE): 1,2-Dibromodecane (IIa): IR (ν_{\max} in cm⁻¹, KBr) : 2926, 400. ¹H NMR (DMSO-d₆): δ 0.90 (t, 3H), 1.30 (bs, 8H), 1.40-1.60 (m, 2H), 1.70-1.90 (m, 2H), 2.10-2.20 (m, 2H), 3.60 (t, 1H), 3.80 (dd, 1H), 4.10-4.20 (m, 1H). MS: m/z (M⁺): 300, 221, 207.

1,2-Dibromo-2-methoxypropane (IIb): IR (ν_{\max} in cm⁻¹, KBr) : 2920, 1265, 405. ¹H NMR (DMSO-d₆) : δ 2.04 (s, 3H), 3.24 (s, 2H), 4.00 (s, 3H). MS: m/z (M⁺): 153, 73, 69.

1,2-Dibromo-2,3-dichlorobutane (IIc): IR (ν_{\max} in cm⁻¹, KBr) : 2920, 756, 496. ¹H NMR (DMSO-d₆) : δ 1.59 (d, 3H), 4.00 (s, 2H), 4.36 (q, 1H). MS: m/z (M⁺): 286, 206, 192.

2,3-Dibromo-3-phenylpropanoic acid (IId): IR (ν_{\max} in cm⁻¹, KBr): 3066, 2829, 1686, 482. ¹H NMR (DMSO-d₆): δ 5.01 (d, 1H), 5.50 (d, 1H), 7.27-7.50 (m, 5H, H_{arom}), 8.01 (s, OH).

2,3-Dibromo-3(4-methoxyphenyl)propanoic acid (IIE): IR (ν_{\max} in cm⁻¹, KBr): 3026, 2832, 1685, 1222, 482. ¹H NMR (DMSO-d₆): δ 3.73 (s, 3H), 4.80 (d, 1H), 5.45 (d, 1H), 8.11 (s, OH).

Results and discussion

To develop a green and cost effective method for the oxidative bromination of alkenes, SiO₂-H₂SO₄ was chosen as the solid acid catalyst. Since hydrogen peroxide is considered as the green oxidizing agent, so the test reaction was carried out with hydrogen peroxide as oxidant and NaBr as the brominating agent in the presence of SiO₂-H₂SO₄ as solid acid catalyst. To optimize the reaction conditions, cinnamic acid was selected as the test substrate and at different temperatures, different set of reactions were made to carry out. The solvent and catalyst in varied quantities were tried. The amount of the catalyst used was found to be important to proceed the reaction quickly and in an environment-friendly method. Different amounts of the catalyst were tried and found that 0.2g of the catalyst for 1 mmole of the test substrate was sufficient to proceed the reaction in quantitative yield. For the selection of appropriate solvent, different solvents like methylene chloride, acetonitrile and chloroform were tried. Among these, chloroform was found to be the best solvent as with methylene chloride and acetonitrile, the reaction was not complete even after 20h of stirring at 70°C. Thus, the optimum conditions selected for the oxidative bromination of alkenes are: alkene (1mmol), NaBr (1mmol), H₂O₂ (2mL, 30%), SiO₂-H₂SO₄ (0.2g), CHCl₃ (5mL) and 70°C as the appropriate reaction temperature.

All the reactions were carried out under similar conditions. To show the versatility of the developed protocol, different alkenes were subjected to oxidative bromination and good results were produced under selected conditions (Table-1).

Conclusion

To conclude a simple, efficient and cost-effective procedure has been used for the bromination of alkene using non-toxic NaBr and H₂O₂ in liquid phase. Moreover, the yields are excellent and work-up procedure is very simple.

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