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Sol-Gel Entrapped Pyridinium Hydrobromide Perbromide as a Recyclable Bromination Agent: Its Application to a One-Pot Bromination and Dehydrobromination Process

Yevgenia Levin,[a] Khalil Hamza,[a] Raed Abu-Reziq,[b] and Jochanan Blum*[a]

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Silica sol-gel encaged pyridinium hydrobromide perbromide can be used for clean, odorless bromination of a variety of substrates, including alkenes, ketones, and arenes. The used heterogenized bromination reagent can be recharged with bromine and recycled. In the presence of sol-gel entrapped 1,5,7-triazabicyclo[4.4.0]dec-5-ene, dibromides are dehydrobrominated to give vinyl monobromides and/or alkynes. Encapsulation of the pyridinium derivative and the guanidine base within separate sol-gel matrices enables the use of both opposing reagents in one-pot reactions without their mutual destroying each other.

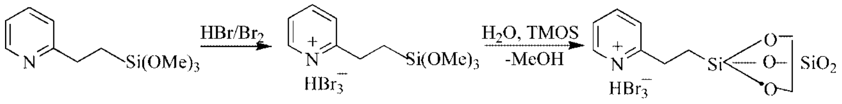
Introduction

In the course of our studies on the application of sol-gel technology to catalytic one-pot processes with opposing chemicals,[1] we have demonstrated that by entrapment of each of the reaction components within a separate ceramic matrix it is possible to carry out such catalyses without the mutual destruction of the reacting species. We were able to perform (i) rhodium-, ruthenium-, and mixed-metal-catalyzed hydrogenations and hydroformylations in the presence of catalyst poisons and inhibitors,[2] (ii) simultaneous acid- and base-promoted processes,[3] (iii) catalyses with oxidants and reductants,[4] enzymatic reactions in the presence of enzyme-destroying organometallics,[5] and (iv) combination of the catalytic Heck coupling with interfering photochemistry.[6] We have now extended our research to include a couple of opposing reactions which do not involve catalysts namely bromination and dehydrobromination. The bromination reagent of choice was a silylated modification of the well-known pyridinium hydrobromide perbromide[7] and as the hydrodebromination agent, we chose a glycidylated derivative of the strong base 1,5,7-triazabicyclo[4.4.0]dec-5-ene[8] that under homogeneous conditions inactivates completely the bromination reagent.

Results and Discussion

The silica sol-gel entrapped bromination reagent was prepared as described in the Exp. Sect. by treatment of commercially available 2-[2-(trimethoxysilyl)ethyl]pyridine with concentrated hydrobromic acid and bromine followed by hydrolysis and co-condensation with tetramethoxysilane (TMOS), as shown in Scheme 1.

The heterogenized pyridinium hydrobromide perbromide (PHPB@s.g.) formed after drying over P_2O_5 under reduced pressure, proved to act between 50 and 65 °C as a versatile bromination reagent. Examples given in Table 1 indicate that the reagent adds bromine to alkenes to form dibromides, it turns ketones into α-bromo ketones, brominates toluene to give benzyl bromide and converts phenol to ring-brominated phenols. The addition of bromine to the double bond of 4-methylstyrene takes place in preference to the substitution of a methyl hydrogen atom (see Entry 3), and the bromination of the CH_3 group of toluene is preferred to the ring bromination (Entry 7). Only in the case of the phenol, the ring is affected at the *ortho* and *para* positions (Entry 8). It is also notable that, unlike the bromination of



Scheme 1.

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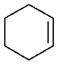
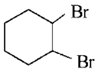
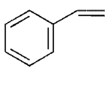
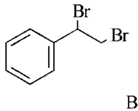
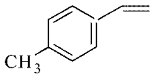
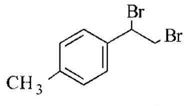
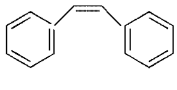
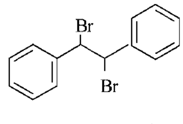
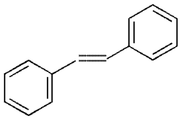
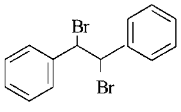
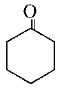
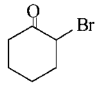
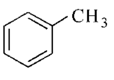
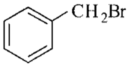
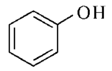
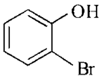
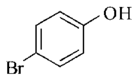
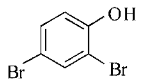
[a] Department of Organic Chemistry, The Hebrew University,
Jerusalem 91904, Israel
Fax: +972-2-6513832
E-mail: jblum@chem.ch.huji.ac.il
[b] Centre for Catalysis, Research and Innovation, University of Ottawa,
10 Marie Curie, Ottawa, Ontario K1N 6N5, Canada

Table 1. Bromination of various substrates by sol-gel entrapped pyridinium hydrobromide perbromide.[a]

Entry	Substrate	Reaction time, h	Products	Yield in the first run, %[b]
1		7		90[c]
2		8		78
3		8		89
4		8		61
5		6		33
6		7		78
7		8		85
8		8		7
				49
				3

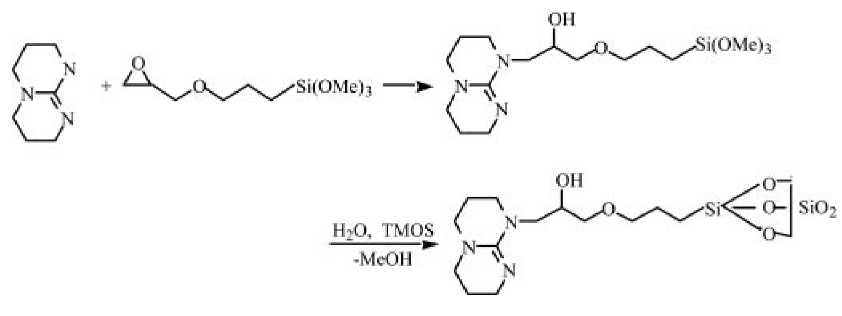
[a] Reaction conditions (except for Entry 8): 1.5 mmol of substrate in *n*-hexane (10 mL) was stirred under N_2 at 65 °C with 3 mmol of PHPB@s.g. In Entry 8, 2.25 mmol of the bromination reagent was used. [b] Average of at least 2 experiments that did not differ by more than ±3%. Analyses of the reaction mixtures indicated only the presence of the bromination products and the unreacted substrates. [c] If the reagent was not dried completely, the product was contaminated with varying amounts of 2-bromocyclohexanol.

the isomeric stilbenes by non-heterogenized pyridinium hydrobromide perbromide that transforms the (*Z*) and (*E*) compounds to *dl*- and *meso*-dibromides, respectively,[9] the entrapped reagent converts both stilbenes solely into the *meso* product. This phenomenon may be associated with the ability of the silica-bound reagent to reversibly interconvert the isomeric stilbenes.

Upon completion of the reaction, the used heterogenized pyridinium residue can be recharged with bromine and recycled. When the bromination reagent, that had been used in the experiments of Table 1 (6 mmol), was washed with CH_2Cl_2 (3 × 10 mL) and sonicated followed by treatment with Br_2 and removal of the excessive halogen, the bromination ability of the reagent was renewed. For example, the recycled PHPB@s.g., that was used under the conditions of Table 1 for the bromination of cyclohexene, afforded in the second, third and fourth runs of 7 h, 91, 92, and 88% of 1,2-dibromocyclohexane, respectively. Likewise, we brominated toluene with used and recharged agent and obtained in the first four cycles of 7 h, 75, 74, 77, and 74% of benzyl bromide.

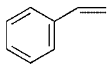
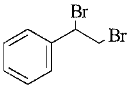
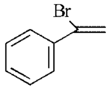
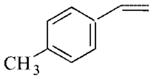
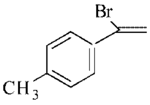
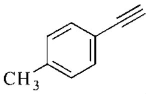
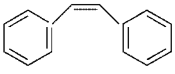
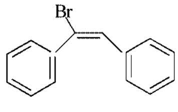
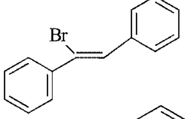
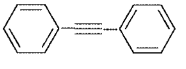
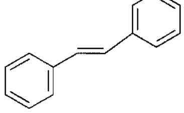
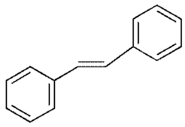
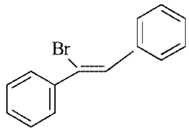
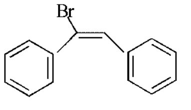
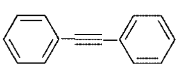
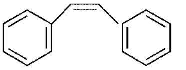
Some of the bromination products (e.g., the dibromides) could be dehydrobrominated by strong bases. Under homogeneous conditions, this operation could be carried out only after completion of the bromination process and isolation of the dibromides. A one-pot combined reaction is not possible because strong bases destroy the bromination reagent. This shortcoming could be overcome by entrapment of the base within a silica sol-gel matrix. The strong guanidine base 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) was modified with (3-glycidoxypropyl)trimethoxysilane, hydrolyzed and co-condensed with TMOS as shown in Scheme 2.[2b]

Application of the entrapped base TBD@s.g., does not destroy the heterogenized reagent, PHPB@s.g., and permits to carry out the bromination and hydrobromination in one pot. Representative results are summarized in Table 2. Vinyl bromides and/or acetylenes are formed in the first place during the dehydrobromination. It seems however, that the unsaturated products are re-brominated. Elimination of HBr may form an olefin with a different stereochemistry than the starting alkene. Indeed, the bromination of (*Z*)-stilbene (Table 2, Entry 3) forms during a reaction period of 15 h at 65 °C 47% of (*E*)-stilbene [only 2% of the (*Z*) isomer remains]. Likewise, (*E*)-stilbene affords under the same conditions 13% of (*Z*)- together with 20% of "unchanged" (*E*)-stilbene. Thus, unlike under homogeneous



Scheme 2.

Table 2. One-pot bromination and hydrodebromination of some unsaturated compounds.[a]

Entry	Substrate	Reaction time, h	Products (yields, %)[b]
1		12	 (13)  (75)
2		12	 (54)  (44)
3		15	 (25)  (15)  (10)  (47)
4		15	 (43)  (16)  (6.5)  (13)

[a] Reaction conditions: 1.5 mmol of substrate in 30 mL of *n*-hexane was stirred under N_2 at 65 °C (50 °C in Entry 2), with 3 mmol of PHPB@s.g. and 3 mmol of DBN@s.g. [b] The yields refer to isolated products. They are the average of at least 2 experiments that did not differ by more than ±3%. Analyses of the reaction mixtures indicated only the presence of the products listed in the table und the unreacted substrates.

conditions, the sol-gel entrapped base can enhance (indirectly) also the bromination process.

Experimental Section

Preparation of Sol-Gel Entrapped Pyridinium Hydrobromide Perbromide (PHPB@s.g.): To a solution of 2-[2-(trimethoxysilyl)ethyl]-pyridine (6 mmol, ABCR GmbH) in *n*-hexane (2.5 mL) was added with stirring 48% hydrobromic acid (7 mmol). After 10 min, elemental bromine (6 mmol) was added and the stirring was continued at 0 °C for 2 h. The mixture was then treated with tetramethoxysilane (5 mL, 33.9 mmol) and triply distilled water (4 mL, 222 mmol). Within a period of 12–16 h at room temperature, the mixture turned into a gel which was left to age for 24 h and dried with P_2O_5 at 1 Torr for another 24 h. The orange ceramic material was then sonicated in boiling *n*-hexane (3 × 10 mL), redried at room temperature at 1 Torr for 5 h to give 2.8 g of the entrapped bromination reagent.

General Procedure for the Bromination Process: Typically, a solution of the substrate (3 mmol) and the heterogenized bromination reagent (PHPB@s.g., 6 mmol) in *n*-hexane (20 mL) was stirred at 65 °C for 6 h. The ceramic material was filtered off and the filtrate concentrated, chromatographed on silica gel and worked up in the usual manner. The resulting products were separated either by GC or HPLC and their NMR and mass spectra compared with those of authentic samples.

Recharging of the Bromination Reagent: The filtered used bromination reagent was sonicated in warm (30 °C) CH_2Cl_2 (3 × 10 mL). Then CH_2Cl_2 (15 mL) was added and the agitated system cooled to 0 °C. Bromine (9 mmol) was added and the agitation at that temperature was continued for 3 h. The liquid was decanted and the ceramic residue dried at 1 Torr for 12 h, sonciated in *n*-hexane (3 × 10 mL) and redried at 1 Torr for 5 h before reapplication in a second run.

One-Pot Bromination and Dehydrobromination Processes: A mixture of the unsaturated substrate (1.5 mmol), the heterogenized bromination agent, PHPB@s.g. (3 mmol), the sol-gel entrapped base, DBN@s.g. (3 mmol, prepared by a modification of the published procedure, in which TMOS was used instead of tetraethoxysilane[2b]) and *n*-hexane (30 mL) was agitated at 65 °C for a period of 12–15 h. The ceramic material was filtered off, the filtrate was concentrated and separated by column chromatography on silica gel. The identity of the resulting compounds was determined by comparing the retention times of the gas chromatograms and the IR, NMR and mass spectra with those of authentic samples.

Acknowledgments

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