SYNTHETIC COMMUNICATIONS, 25(15), 2203-2209 (1995)

BROMINATION OF VARIOUS UNSATURATED KETONES AND OLEFINS WITH POLY(4-METHYL-5-VINYLTHIAZOLIUM) HYDROTRIBROMIDE

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Abstract: Poly(4-Methyl-5-Vinylthiazolium) Hydrotribromide (P4M5VTHT) synthesis is reported; this polymer, incorporating 45% of bromine, was found to be a stable, regenerable and a successful brominating reagent for various organic unsaturations.

Among the numerous bromination methods available now in the chemical literature since the bromine discovery in 1826,¹⁻⁴ only two are based on thiazole matrices. Thus, Forlani has used 2,4-diamino and 4-amino-2-dimethylamino thiazolium hydrotribromides to halogenate in solution aryl and styryl methylene ketones and phenols⁵. In our hands, we have introduced and report herein an easy solid phase procedure using poly(4-methyl-5-vinylthiazolium) hydrotribromide.

The polymeric support utilized in this investigation was the product of the radical copolymerization of 4-methyl-5-vinylthiazole with styrene and

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divinylbenzene. Then the resulted poly(4-methyl-5-vinylthiazolium) containing 3,2 mmoles of thiazole per gram was functionalized in turn by aqueous hydrobromic acid and liquid bromine affording the corresponding hydrotribromide with 1,9 mmoles of Br_3^- per gram of beads.

Methylene chloride was retained as the best solvent for bromination reactions at room temperature. As to the substrates tested here, various olefins and ketones were chosen with different unsaturations (cf. Table) in order to study the selectivity of P4M5VTHT attack.

The bromination process is very simple: in a general procedure and on a millimolar scale, an excess of the reagent was gently stirred with the substrate according to the conditions mentioned in the experimental section and in the Table. The halogenation progress was monitored by capillary gas chromatography (CGC). At completion the hydrobromide resin and the solvent were taken off from the reaction mixture by filtration and evaporation respectively. CGC and GC-MS techniques were used for analysis and identification of the resulted bromocompounds. Yields were calculated by the usual chromatographic method.

The hydrobromide beads, previously filtered off, were thoroughly washed with usual organic solvents (CH₂Cl₂, MeOH, Acetone and ether), dried (if necessary) and reacted with a carbon tetrachloride solution of bromine at ambient temperature. An extraction using a Soxhlet apparatus allowed to eliminate the residual halogen and to finish the regeneration process of the brominating reagent. After each operation, we always found the P4M5VTHT bromine content equivalent to 45%.

From the Table, we noticed that in general, the molar ratio ($R = Br_3$ -/Substrate) has a great influence upon the reaction kinetics, the conversion percentage and the bromination selectivity. Interestingly for a given value of R, the reaction time has been optimized by chromatographic monitoring of the substrate consumption except for methylvinylketone and benzalacetone (runs 11, 14) which brominations were pursued overnight. It should be very interesting to carry out this work studying first the optimization of the molar ratio parameter.

These results show that alkenes were quantitatively and smoothly dibrominated; for instance cyclohexene was instantaneously consumed. As for

| Run | Substrate | Products yield + (%) ^b | Exp. conditions R ^c / Time (h) |
|--------|------------------------------------------------|-----------------------------------------------------------------------------------------|----------------------------------------------|
| 1 | Styrene | Dibromide (100) | 3/1,17 |
| 2 | Cyclohexene | Dibromide (100) | 2,5/ ^d |
| 3 | Trans-stilbene | Dibromide (100) | 3/2,5 |
| 4 | Acetone | 1-Bromo (80) + (20) | 2,5/2 |
| 5 | 2-Butanone | 1-Bromo (30) + 3-bromo (70) | 2,5/2 |
| 6 | 1-Phenyl-2-propanone | 1-Bromo (15) + 3-bromo (85) | 4/1 |
| 7 | Cyclohexanone | 2-Bromo (60) + 2,6-dibromo (40) | 3/0,17 |
| 8 9 | 2-Methylcyclohexanone 2-Methylcyclohexanone | 2-Bromo-2-Me (15) + (84) 2-Bromo-2-Me (100) | 0,4/1,5 3,5/0,8 |
| 10 | Acetophenone | Bromo (100) | 3/1,5 |
| 11 | Methylvinylketone | Dibromide (30) + (70) | 4/24 |
| 12 | Mesityl oxide | Bromomethyl (100) | 5/2 |
| 13 | β-Ionone | Bromomethyl (50) + (50) Bromomethyl (80) + (20) BromoMe (90) + 3,4-Dibr.(5) + (5) | 5/0,5 /1,33 -/2 |
| 14 | Benzalacetone | BromoMe (35) + (65) BromoMe (30) + 3,4-Dibr. (70) | AcOEt/3/0,75 /20 |
| 15 | Diethyl malonate | Bromo (30)+ (70) | 3/2,5 |
| 16 | Diethyl malonate | Bromo (50)+ (50) Bromo (80)+ (20) Bromo (100) | Reflux/3/0,5 /3/2 /3/3,5 |

Table. Brominations with poly(4-methyl-5-vinylthiazolium) hydrotribromide^a

^aUnless otherwise indicated, the bromination was performed in dichloromethane at room temperature. ^bRecovered starting material; yields were estimated by usual chromatographic method. ^cR = molar ratio (Br3⁻/Substrate); this parameter has not been optimized. ^dBromination was instantaneous.

ketones, unsymmetric ones were prevalently brominated at the most substituted carbon; α , β -unsaturated methylketones were mainly attacked at the methylic center except methylvinylketone which led only and partly to dibromide (run 11). However in the case of benzalacetone (entry 14), ethyl acetate was used in stead of dichloromethane in the hope of performing specifically the α -monobromination at the carbonyl group; in fact, within 45 minutes, only the bromomethylated derivative was formed (35%) but after then, the addition product was also obtained.

With diethyl malonate, temperature has further marked effect on the reaction; we had to reflux the solvent for 3,5 hours to reach the selective monobromination achievement.

No nucleophilic aromatic substitution, oxidation or allylic bromination products have been observed during this study. Also no gem-dibromides have been prepared neither with methylketones nor with diethyl malonate.

In conclusion, poly(4-methyl-5-vinylthiazolium) hydrotribromide reacts under mild experimental conditions as a good brominating agent for olefins and unsaturated ketones comparatively to liquid bromine and many of its analogues as NBS,⁶ pyridinium hydrotribromide,⁷ phenyltrimethylammonium tribromide,⁸ tetrabutylammonium tribromide,⁹ poly(4-vinylpyridinium) hydrobromide perbromide¹⁰ and Amberlyst A-26 Br₃⁻¹¹.

Nextly, we will report a comparative study on the bromination results and selectivity obtained with the hydrotribrominated thiazolic resins and other halogenating reagents.

EXPERIMENTAL

Commercial styrene was stirred with aqueous KOH, washed with water, dried over sodium sulfate and fractionated at reduced pressure in the presence of calcium hydride; divinylbenzene was also freshly distilled before use. All other chemicals were reagent grade (supplied from Aldrich and Janssen) and employed without further purification.

Chromatographic monitoring of the bromination course was performed using a fused silica capillary colomn SPB-1, SE 30 (30 m and 0,32 mm ID). GC-MS spectra were run on a Nermag R10-10C (70eV, chromatograph DI 700 Delsi, fused silica capillary colomn CPSILS (25 m and 0,25 mm ID). Microanalyses were carried out at the Service Central d'Analyse (CNRS) Vernaison, France. Infrared spectra were recorded as potassium bromide pellets on a Nicolet MX-S spectrophotometer.

Copolymerization of 4-methyl-5-vinylthiazole. This reaction, a twophase dispersion polymerization, was achieved by performing the aqueous phase and the monomer phase *separately*. The aqueous phase was done in a 500 ml three-necked round-bottom flask, equipped with a water-cooled condenser, a thermometer and a uniform speed stirrer (allowing constant stirring during the setting of the dispersion in order to preclude the size distribution disparity of the polymer particles). This phase was formed by two solutions A and B:

solution A: 80 g of water and 0,6 g of 10% aqueous NaOH,

solution B: 100 g of water, 0,46 g boric acid, 0,4 g of gelatin and 0,46 g of polyvinylpyrrolidon K25.

The monomer mixture was prepared in a beaker and consisted of 1,5 g of DVB (10%), 9 g of styrene (60%), 4,5 g of 4-methyl-5-vinylthiazole (30%), 15 ml of methylisobutylcarbinol as solvent and 1,2 g of azobisisobutyronitrile as radicals initiator. The AIBN was added to the monomers at $15^{\circ}C \pm 2^{\circ}C$ under manual stirring with a glass rod until it was dissolved.

4.8 g of solution A and 6 g of solution B were first charged in the reactor; the pH of the mixture should be 8,3 to 8,7 otherwise, it should be ajusted by adding small portions of boric acid or aqueous NaOH. Then, the monomer phase was introduced and the agitation was ajusted to 500 rpm. The mixture was subsequently heated to 90°C under nitrogen atmosphere for 5 hours. The resulted beads were filtered off, thoroughly washed with ether and dried. The

microanalyses of poly(4-methyl-5-vinylthiazole) gave 76.11% of Carbon, 7.43% of Hydrogen, 4.73% of Nitrogen and 10.2% of Soufre.

Preparation of P4M5VT Hydrotribromide: 1 g of resin (3,2 mmol of thiazole) was stirred in a 48% aqueous hydrobromic acid solution (10 mmol) for 2 hours at ambient temperature led to a polymeric hydrobromide which was washed by water and ether, dried and found to contain 53,52% C, 6% H, 3.42% N, 6.44% S and 22.72% Br. Its subsequent stirring in a CCl₄ (15 ml) solution of bromine (10 mmol) for 1 hour at room temperature gave the corresponding hydrotribromide. After thorough washings by CCl₄, acetic acid and CCl₄, this resin was submited to a Soxhlet extraction from a CCl₄/THF mixture for 6 hours and dried. The bromine content of the resulted hydrotribromide was 45%.

Bromination procedure: A solution of a substrate (3 mmol) was added to a stirred suspension of the hydrotribrominated resin under the appropriate experimental conditions reported in the Table (reactive bromine amount, solvent (30 ml), temperature and duration). The bromination progress was monitored by capillary gas chromatography (CGC) by injecting samples taken at regular intervals from the mixture. Then the polymer was simply isolated by filtration and the brominated products were recovered after solvent evaporation. Qualitative and quantitative analyses were performed as usual by capillary gas chromatography (CGC) and GC-MS techniques.

Regeneration of the brominating agent: Subsequent washings of the recovered hydrobrominated resin by usual organic solvents such as dichloromethane, methanol, acetone and ether (dried at 60° for 4 hours if necessary), followed by the treatment of the beads with a CCl4 solution of bromine for 2 hours at ambient temperature and extraction of the residual bromine in a Soxhlet apparatus, led to the regeneration of the reagent.

Also P4M5VTHT can be regenerated after several thorough washing of the previously filtered hydrobromide by aqueous sodium hydroxide until neutrality, followed by hydrotribrominating the resulted thiazolic resin as depicted above. Interestingly, its bromine content was kept constant to 45%.

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(Received in the UK 16 December 1994)