

POLYMERIC REAGENTS. IV. GENERATION OF SULFONIUM YLIDES ON INSOLUBLE RESINS BY PHASE
TRANSFER CATALYSIS

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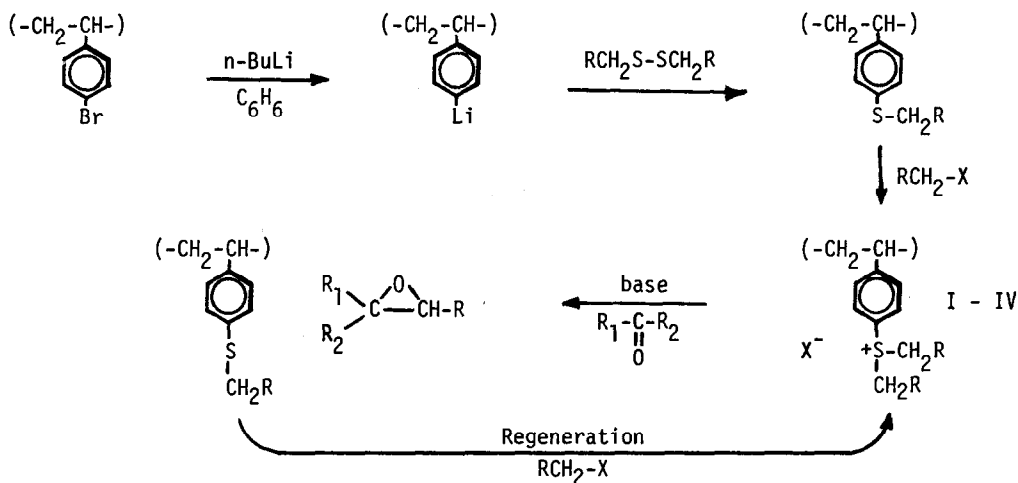
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A number of polymeric reagents¹ have been developed for use in simple processes such as oxidation^{2,3}, halogenation^{4,5}, epoxidation^{6,7}, acylation⁸ or Wittig reactions⁹. A polymeric reagent will provide an efficient and useful alternative to its low molecular weight counterpart if its design is such that it allows for an easier isolation of the desired product after reaction and if the polymeric by-product can be regenerated quantitatively to its former activity in simple fashion.

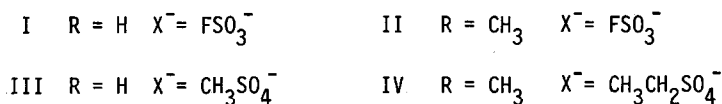
We report on the preparation of fully regenerable sulfonium salts anchored to insoluble polymers and on their use in the preparation of epoxides by reaction of their ylides with carbonyl compounds. A survey of the literature shows that two different polymeric sulfonium salts have been tested earlier^{10,11}. However, their application to the synthesis of epoxides met only with very limited success. In one instance¹⁰, the polymer contained two types of protons α to sulfur and its use resulted in loss of some sulfur from the polymer with concomitant formation of polymer-bound epoxide. In the second case¹¹, the polymer seemed to lack reactivity as shown by the very large excess which was required to obtain a 76% yield of epoxide by methylene transfer to benzaldehyde. In both cases the polymeric by-products could not be recovered quantitatively and the regenerated material was completely inactive.

Our polymeric sulfonium salts were prepared by chemical modification of crosslinked polystyrene via the corresponding sulfides in which approximately 30 to 35% of the aromatic rings carried the functional group. The reaction sequence we used involved the thallium III catalyzed bromination¹² of crosslinked polystyrene beads followed by lithiation¹² with n-butyl-lithium in benzene, reaction with excess disulfide¹², and alkylation of the resulting polymeric sulfide with an alkyl fluorosulfonate or a dialkyl sulfate. This reaction sequence was accomplished in good functional yield, and isolation of the reactive sulfonium salt was facilitated

greatly by its insolubility. In a typical reaction, 7.8 g. of a polystyrylethylsulfide containing 2.59 mequiv. of sulfur per gram¹³ were alkylated in 88% yield using 7 ml of ethyl fluorosulfonate in 70 ml of dichloromethane. The preparation, use, and regeneration of the sulfonium salts is outlined in scheme I below.



SCHEME I.



Reaction of the dimethylpolystyryl sulfonium fluorosulfonate with benzophenone using potassium tert-butoxide in DMSO gave a 90% conversion to the desired epoxide. After regeneration with methyl fluorosulfonate, a second reaction with benzophenone under the same conditions as above gave only a 60% conversion to epoxide. Attempted use of the regenerated polymer in a third reaction cycle gave almost no epoxide. Since this rapid loss of reactivity on repeated use would void the usefulness of the reagent, the reaction was attempted under milder conditions using a three phase system consisting of a suspension of the polymeric reagent in dichloromethane with an aqueous solution of sodium hydroxide and in the presence of a phase transfer catalyst such as tetrabutylammonium hydroxide or tetrabutylammonium iodide. The reaction was carried out at room temperature under vigorous stirring and a gradual change in the color of the polymer was observed. After 1-4 days of stirring, conversions into epoxide usually exceeded 98% for both methylene or ethylidene transfers¹⁴. Isolation of the epoxides from the reaction mixture was facilitated greatly by the insolubility of the polymeric sulfide which is produced in the reaction. The isolation and purification procedure amounted to a simple washing of the polymer with organic solvent followed by drying with magnesium sulfate and evaporation of the solvent.¹⁵ Typical results obtained using this procedure are shown in table I.

Recovery of the spent reagent after reaction was almost quantitative with only small mechanical losses occurring during transfers of the solid phase. After regeneration by alkylation

the recycled reagent was found to be as effective as the original material, and, after five successive reaction cycles, no appreciable loss of sulfur or decrease in reactivity could be observed. This result clearly indicates that phase transfer catalysis is the method of choice for the generation of ylides from these polymeric sulfonium salts. To our knowledge this is the first example of a reaction in which such a three phase system has been used to generate effectively a reactive intermediate.

Phase transfer catalysis has been used previously¹⁶ in the generation of sulfur ylides from soluble sulfonium salts; it is interesting to note that the yields of epoxides obtained from ketones under these conditions are sometimes low while the reaction involving polymeric sulfonium fluorosulfonates proceeds as well with ketones as it does with aldehydes. Two other advantages of the polymeric sulfonium salts are worthy of mention: the polymers are thermally stable and their sulfide by-products, being non-volatile, have no smell.

TABLE 1

Reaction of polymeric sulfonium fluorosulfonates with carbonyl compounds under phase transfer conditions.

Polymer	Carbonyl Compound	Product	Reaction time (days) ¹⁵	Yield (%)	
				VPC	isolated
I	Ph-CHO		3	100	97
I			1	100	94
I			1 4	86 >98	- 96
II	Ph-CHO		2 4	86 100	- -
II			0.8 4	89 >99	- 96

^a Product is a 1:1 mixture of cis and trans epoxides.

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13. This reaction was carried out on a polymeric sulfide prepared from Bio-beads SX-1 (Bio-Rad Laboratories) containing 8.3% S with a degree of functionalization of 0.32.
14. A typical reaction was carried out as follows: 2 g. of polymer I suspended in 15 ml dichloromethane containing 0.25 g. benzophenone were stirred with a solution of 1.3 g. NaOH in 2 ml water containing 0.16 g. of a 40% aqueous solution of tetrabutylammonium hydroxide. Analysis of the reaction mixture at regular time intervals gave the following results: 4 h, 54% conversion; 24 h, 86%; 48 h, 95%; 96 h, 98.3%. No other products were detected in the analysis by vapor phase chromatography. After filtration, washing, and evaporation of the solvent, 0.257 g. (96%) of epoxide were obtained. Satisfactory yields were also obtained using lower sulfonium salt/carbonyl compound ratios.
15. A shorter reaction time is required for the reaction to reach completion if a larger amount of phase transfer catalyst is used. However, the use of a large amount of phase transfer catalyst increases the work up required to obtain a pure product.
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