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POLYMER - BOUND TOSYL AZIDE

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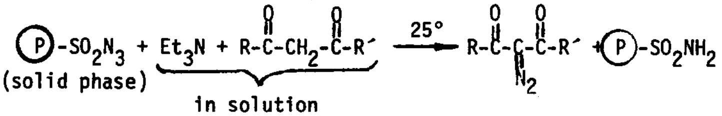
The remarkably simple phase separations afforded by insoluble polymeric supports have been exploited in many chemical systems. Ion exchange, peptide synthesis and affinity chromatography are general applications; specific organic reagents have also been developed. The undesirable solubility properties of triphenyl phosphine oxide and NN dicyclohexyl urea, byproducts in Wittig and peptide synthesis respectively, have resulted in polymeric reagents on which these byproducts remain covalently bound at the end of the reaction.[2] Herein we describe a polymeric tosyl azide which has similar advantages with respect to the monomeric reagent.

Polymeric tosyl chloride is prepared by treatment of Amberlite XE 305[3] with $ClSO_3H$ (70°, 30 min) followed by brief (30 min) refluxing with CCl_4.[4] The chloride is displaced by overnight stirring with aqueous, ethanolic dioxane containing excess NaN_3 to give the reagent; i.r. 2135 cm^{-1}, 1365 cm^{-1}. Combustion analysis indicates 3.7 meq. azide per gram of resin prepared in this manner. The resin decomposes rapidly when placed in an oil bath at 200°, but unlike tosyl azide, it fails to detonate on shock treatment and appears to be stable indefinitely at room temperature.

Diazo transfer reactions of the reagent with several β-dicarbonyl compounds were investigated.



$$\underset{\text{(solid phase)}}{\text{Ⓟ-}SO_2N_3} + \underbrace{Et_3N + R\text{-}\overset{O}{\overset{\|}{C}}\text{-}CH_2\text{-}\overset{O}{\overset{\|}{C}}\text{-}R'}_{\text{in solution}} \xrightarrow{25^\circ} R\text{-}\overset{O}{\overset{\|}{C}}\text{-}\underset{N_2}{\underset{\|}{C}}\text{-}\overset{O}{\overset{\|}{C}}\text{-}R' + \text{Ⓟ-}SO_2NH_2$$

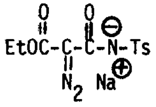
	R=	R'=	Solvent	reaction time(hrs)	yield(isolated)
1	C_6H_5	C_6H_5	EtOH	7	97%
2	"	CH_3	"	3 1/2	96
3	CH_3	"	"	3	73
4	EtO	"	MeCN	2 1/2	96
5	EtO	OEt	EtOH	42	91
6 ‡	"	"	"	17	68
7*	EtO	CH_2-CO_2Et	"	2	90

‡ NaOEt used as the base.

* All other products have been previously described.[5] This product was characterized as a greenish yellow liquid, i.r. 2160 cm^{-1}; nmr 3.7 δ (s) methylene, and nonequivalent ethyl esters.

Typically .05 M solutions of the substrate containing 6 eq. triethyl amine were stirred with 2 eq. of the polymeric reagent at ambient temperature. Optimal reaction times were established by monitoring the supernatant by nmr and workup consisted of mere filtration and solvent evaporation. As the table indicates, the polymer provides a vehicle by which these diazo transfers can be driven to completion and allows facile separation of excess reagent from product.

One qualitative difference between the polymeric reagent and tosyl azide in solution was noted. Diethylmalonate/sodium ethoxide (entry 6) has been reported to give I (97% yield) in solution with tosyl azide.[5] While the recovered polymer from entry 6 showed some carbonyl i.r. absorption, the steric bulk of the polymeric reagent apparently suppresses the formation of polymer-bound I.



$$\mathrm{EtO\overset{\overset{\displaystyle O}{\|}}{C}-\underset{\underset{\displaystyle N_2}{\|}}{C}-\overset{\overset{\displaystyle O}{\|}}{C}-\overset{\ominus}{N}-Ts}\quad \mathrm{Na}^{\oplus}$$

I

Since this polymeric reagent is scarcely more difficult to prepare than its monomeric counterpart, its advantages of safety, handling ease and improved yields should result in its preferential use for diazo transfer reactions.

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