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FACILE AND EFFICIENT SYNTHESIS OF ALKYL THIOTOSYLATES USING ANION EXCHANGE RESIN

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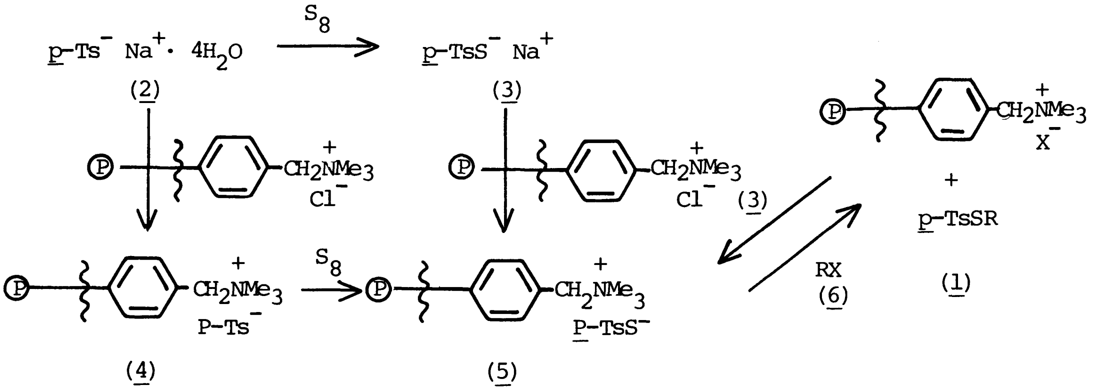
Facile and efficient synthesis of alkyl thiotosylates (1a-h) has been developed using anion exchange resin.

Although thiotosylates (1) have been shown to be highly useful reagents in versatile synthetic purposes,$^{1)}$ various difficulties associated with preparation and purification avoid further extensive use. We report here a facile and efficient synthesis of these reagent using an anion exchange resin which is able to eliminate the major difficulties encountered in the conventional method$^{2)}$ (Scheme).



Scheme

Sodium thiotosylate (3) 136.0^{g}, prepared in 92% yield from commercially available sodium p-toluenesulfinate tetrahydrate (2) and an equivalent amount of elemental sulfur in pyridine (RT, 48h) by a slight modification of the known method,$^{3)}$ is treated with Amberlyst A-26 (Cl$^-$ form) 390^{g} in water (600^{ml}) (RT, 18h) to give the resin supported thiotosylate (5) 368.5g (97%, capacity$^{4)}$ $1.57^{mmol}/g$) after washing throughly with water and acetone. The same resin supported thiotosylate (5) can also be prepared from the resin supported sulfinate (4),$^{5)}$ prepared from sodium p-toluenesulfinate (2) and Amberlyst A-26 (Cl$^-$ form), on treatment with an excess of elemental sulfur in boiling toluene (16h) though some of the sulfinate form (4) remains unchanged (ca. 10%).$^{6)}$ Conversion to the alkyl thiotosylates (1) can be simply carried out by treating the resin supported thiotosylate (5) with an appropriate alkyl halide (6a-j: excess for a, one equiv. for b-e, and two half equiv. for f, g) in boiling benzene for several hours.$^{7)}$ The alkyl thiotosylates (1a-h) isolated after removal of the resin and the solvent are practically pure (Table) and the resin recovered can be reconverted into the thiotosylate form (5) on treatment with aqueous sodium thiotosylate (3).[8)]

Table

entry	R-X 6	reaction time [h]	RSTs-*p* 1	yield [%] of 1	m.p. or b.p.	^{1}H-N.M.R.(CDCl$_3$) [ppm]
1	a. Me-I	19	Me- (1a)	96.6	55.5-56.5°C (57.5-58.5°C[9)])	2.45(s,3H), 2.48(s,3H), 7.32 (d,2H,9Hz), 7.80(d,2H,9Hz)
2	b. Et-I	18	Et- (1b)	96.0	156-158°C(0.03mmHg)	1.28(t,3H,7.2Hz), 2.45(s,3H), 3.00(q,2H,7.2Hz), 7.30(d,2H, 8.4Hz), 7.80(d,2H, 8.4Hz)
3	c. Bz-Br	24	Bz- (1c)	100.0	56°C	2.42(s,3H), 4.22(s,2H), 7.00-7.45(m,7H), 7.70(d,2H,8Hz)
4	d. Bz-Cl	24	Bz- (1c)	100.0		
5	e. Ph(CH$_2$)$_2$Br	25	Ph(CH$_2$)$_2$-(1d)	93.8	oil (non-distillable)	2.43(s,3H), 2.70-3.47(m,4H), 6.93-7.32(m,7H), 7.80(d,2H,8Hz)
6	f. Br(CH$_2$)$_2$Br	20	-(CH$_2$)$_2$- (1e)	89.0	74.0-74.5°C (75-76°C[2)])	2.45(s,6H), 3.25(s,4H),7.33 (d,2H, 8.4Hz), 7.83(d,2H,8.4Hz)
7	g. Br(CH$_2$)$_3$Br	20	-(CH$_2$)$_3$- (1f)	91.0	65.0°C(66-67°C[2)])	2.05(quint,2H,7Hz), 2.46(s, 6H), 3.03(t,4H,7Hz), 7.35(d, 2H,9Hz), 7.83(d, 2H,9Hz)
8	h. *i*-Pr-I	20	*i*-Pr- (1g)	61.0	168-170°C(0.03mmHg)	1.32(d,6H,7.4Hz), 2.45(s,3H), 3.52(hept,1H,7.4Hz), 7.33(d, 2H,8Hz), 7.83(d,2H,8Hz)
9	i. *i*-Pr-Br	25	*i*-Pr- (1g)	63.0		
10	j. allyl-Br	16	allyl- (1h)	98.6	125°C(0.03mmHg)	2.44(s,3H), 3.69(d,2H,6.4Hz), 5.00-6.17(m,3H), 7.32(d,2H, 8.4Hz), 7.81(d,2H,8.4Hz)

References

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2. R. B. Woodward, I. J. Pachter, and M. Scheinbaum, Org. Synth., 54, 33 (1974).
3. R. Sato, T. Goto, Y. Takikawa, and S. Takizawa, Synthesis, 1980, 615.
4. Optimal ratio between (3) and Amberlyst A-26 (Cl$^-$ form) as well as average capacity of (5) is deduced in terms of repeated experiments to yield methyl thiotosylate (1a) by treating the resin (5) prepared from (3) in a various ratios with an excess methyl iodide.
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6. Deduced by ^{1}H-NMR spectrum after treating the resin (5) with methyl iodide ((1a)(s, 3H, 2.45ppm) vs. methyl *p*-tolyl sulfone(s, 3H, 3.03ppm)).
7. Most of the experiments are carried out in 0.10-0.15 molar scale using the resin (5) prepared from sodium thiotosylate (3) and Amberlyst A-26 (Cl$^-$ form). The all new alkyl thiotosylates (1) exhibit satisfactory analytical data (C, H, S, ±0.3%).
8. Methyl thiotosylate (1a) is obtained in nearly quantitative yield by treating the regenerated resin (5) with an excess methyl iodide in boiling benzene.
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