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A SIMPLE METHOD FOR THE PREPARATION OF UNSTABLE TOSYLATES

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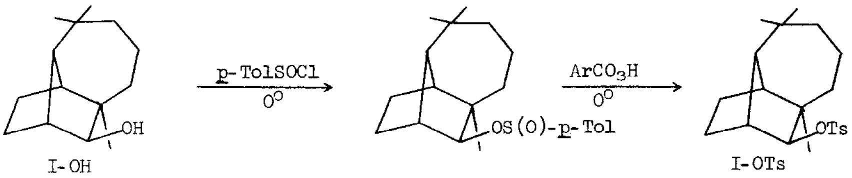
The p-toluenesulfonate (tosylate) group has served as a particularly useful leaving group in the initiation of carbonium ion reactions. In addition to possessing a reactivity comparable to the corresponding halide, the tosylate derivative has the advantage of generally being prepared from an alcohol without affecting the C-O bond, thus preserving the stereochemistry at the carbinyl position. Unfortunately the synthetic method most frequently employed for the preparation of tosylates, namely reaction of the alcohol with tosyl chloride in pyridine, is generally not suitable for either reactive or hindered structures. We have found that p-toluenesulfinate esters, which are more easily made and handled, may be converted by oxidation under mild conditions to the corresponding tosylate.

That sulfinates may be oxidized to sulfonates has been known for some time (1,2). However, the reagents commonly used [potassium permanganate/aqueous acetone (1), hydrogen peroxide in various protic solvents (2,3)] would clearly not be suitable for a reactive tosylate. We have found that treatment with m-chloroperbenzoic acid in methylene chloride suffices to convert the p-toluenesulfinate into the tosylate and that the method can be applied successfully to a variety of unstable and hindered tosylates. A good example is the preparation of I-OTs from longicamphenylol I-OH, a case in which tosyl chloride in pyridine (or several modifications) gives entirely hydrocarbon products. The results are summarized in Table I.



The p-toluenesulfinates were prepared according to the procedure of Wilt (4) with yields ranging from 67 to 84%. It is worth noting the facile sulfinylation of the hindered tertiary alcohols, t-butyl and 2-trifluoromethyl-2-propanol (5). The sulfinyl chloride would appear to have a reactivity comparable to an acid chloride.

Table I

RX	ROS(O)-p-Tol	ROTs
Cyclohexyl	84%	88%
Longicamphenylyl(I)	76%	84%
2-Bicyclo[3.1.1]heptyl(II)	80%	82%
t-Butyl	73%	- (10a)
2-Trifluoromethyl-2-propyl(III)	82%	75%
Benzyl	71% (4)	87%
p-Methoxybenzyl	67%	- (11)
α-Phenylethyl	73% (1)	72% (1,10a)
Benzhydryl	73% (12)	sulfone, 93% (10b)

The sulfinates were treated with about 1.4 equivalents of 85% m-chloroperbenzoic acid in methylene chloride at 0° for 1.5 hr. (24 hr. with III). The oxidations were generally successful, the exceptions being the very reactive derivatives: t-butyl, p-methoxybenzyl, and benzhydryl. In the last case the corresponding sulfone was obtained; thus internal rearrangement apparently exceeded the rate of oxidation.

A previous attempt to prepare 2-bicyclo[3.1.1]heptyl tosylate (II-OTs) by means of tosyl chloride/pyridine lead to the rearranged isomer endo-2-norbornyl tosylate (6). We have established that the unrearranged II-OTs was in fact obtained here by reductive cleavage (7) to the original alcohol in 58% isolated yield. After three days in solution at room temperature II-OTs had apparently rearranged to endo-2-norbornyl tosylate.

In addition to the examples cited in Table I 1-adamantanol has been converted to the corresponding tosylate in good yield (8). Previous attempts to prepare this tosylate by various methods gave at best material of 40% purity (9).

Owing to the unstable nature of many of these sulfonates only spectral characterization has been possible. Despite the close structural similarity of the sulfinates and tosylates, they can be readily distinguished spectroscopically. The $\Delta\tau$ (ortho-meta) for the sulfinates falls in the range -0.29 to -0.33 ppm; whereas the sulfonates show a regular downfield shift with $\Delta\tau$ (ortho-meta) -0.46 to -0.50 ppm. The $\Delta\Delta\tau$ for ROS(O)-p-Tol→ROTs is quite constant at -0.15 to -0.18 ppm. The shift of the carbinyl position is found to be -0.15 to -0.27 ppm. In the infrared spectra the sulfinates display the characteristic S=O stretch at 1120-1130 cm^{-1} (1150 cm^{-1} for III-OS(O)-p-Tol while the sulfonates have two bands at 1160-1185 cm^{-1} (sometimes a doublet) and 1345-1360 cm^{-1}.

Other methods which have been employed for the preparation of unstable tosylates are the reaction of the corresponding alkyl halide with silver tosylate (10) and the reaction of the sodium salt of the alcohol with tosyl chloride at low temperature (11). The former method has been successful in the generation of t-butyl, α-phenylethyl and benzhydryl tosylates. This approach depends upon the availability of the halide and has the disadvantage of stereochemical uncertainty. The second method has been used to prepare p-methoxybenzyl tosylate, but would seem to be limited to tosylates stable to elimination reactions. The present method retains the advantage of proceeding from alcohol to tosylate without C-O bond cleavage while generating the sulfonate under essentially neutral, aprotic conditions.

The procedure is illustrated below with the preparation of longicamphenylyl tosylate (I-OTs). Longicamphenylyl p-toluenesulfinate was prepared by the method of Wilt (4) from 3.0 g (17 mmole) p-toluenesulfinyl chloride and 3.5 g (17 mmole) of the alcohol in 35 ml of anhydrous ether containing one equivalent of pyridine at 0°. The crude product was purified by chromatography on silica gel (elution with 15% ether-hexane) affording 4.5 g (76%) of clear liquid, apparently a mixture of sulfinyl diastereomers: ν_{max}^{film} 1130 cm^{-1}, τ^{CDCl_3} 2.40 and 2.71 (2d, A_2B_2, J = 8 Hz), 6.27 and 6.33 (2S, ca. 1:1).

A solution of m-chloroperbenzoic acid (700 mg, 4 mmole) in 15 ml of methylene chloride was added dropwise to the p-toluenesulfinate (1.0 g, 2.8 mmole) in 20 ml of methylene chloride at 0°. The mixture (a white precipitate formed after 30 min) was stirred at 0° for 1.5 hr, then extracted with 5% potassium carbonate solution and water. The methylene chloride solution was dried (magnesium sulfate) and evaporated under reduced pressure in an ice-water bath. The resulting oil was crystallized from pentane at -8° (888 mg,84%): $\nu_{max}^{CHCl_3}$ 1165 cm^{-1}, 1350 cm^{-1}; τ^{CDCl_3} 2.25 and 2.72 (2d, A_2B_2, J = 8 Hz), 6.08 (S). The crystals decompose rapidly to a red-brown liquid at room temperature.

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