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Practical and Efficient Methods for Sulfonylation of Alcohols Using Ts(Ms)Cl / Et3N and Catalytic Me3N·HCl as Combined Base: Promising Alternative to Traditional Pyridine

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Abstract Several alcohols were smoothly and practically tosylated by two methods A and B. Method A uses the TsCl / Et3N (1.5-2.5 equiv) / cat. Me3N·HCl (0.1-1.0 equiv) reagent. Compared with the traditional Py-solvent method, the method A has merits of its much higher reaction rate, operational simplicity, economy in the use of the amine, and circumvention of the undesirable side reaction from R-OTs to R-Cl. Method B uses TsCl / KOH [or $Ca(OH)_2$] / cat. Et3N (0.1 equiv) / cat. Me3N·HCl (0.1 equiv) as the reagent, which will be suited for practical and large scale production for primary alcohols. On both methods A and B, a clear joint action of Et3N and Me3N·HCl catalysts was observed. ^1H NMR measurements support the proposed mechanism of the catalytic cycle. Related methanesulfonylation using Et3N and cat. Me3N·HCl *in toluene* solvent also successfully proceeded, wherein the clear joint action was also observed.

p-Toluenesulfonylation (tosylation) of alcohols is well recognized as a fundamental unit process in various fields of organic syntheses, especially for the reliable transformation of alcohols into their alkylating agents. Among a number of tosylation methods,[1] TsCl/Py (Ts=*para*-toluenesulfonyl, Py=pyridine) reagent has been traditionally and routinely employed. However, this method has three major problems.

One is that undesirable and concomitant loss of the tosylates into their chlorides is liable to occur during the tosylation; the Py·HCl by-product acts as the Cl-nucleophile. This side reaction frequently takes place when *excess amounts* of Py solvent are used and/or when the reaction temperature is elevated. The second is that *more than equimolar amounts* (ca. 10 equiv) of Py are generally required for completing the tosylation. The third is that the reaction time for unreactive alcohols generally requires relatively long time (over 10 h). Taking these backgrounds into consideration, we now report a couple of efficient methods (A and B) for the tosylation of various alcohols employing combined amine bases, Et3N and catalytic Me3N·HCl, which show a joint action. Related methanesulfonylation using Et3N and cat. Me3N·HCl is also described.

Method A involves the tosylation using the TsCl / Et3N / catalytic Me3N·HCl as the reagent. Table 1 summarizes these typical results which indicate that primary and secondary alcohols smoothly underwent the tosylation. The salient features are as follows. (1) Initial optimization was guided by the reaction of 3-octanol (entry 1) and screening of solvents revealed that dichloromethane, 1,2-dichloroethane, benzotrifluoride,[2] acetonitrile, and toluene, were also suitable.[3] (2) Several alcohols were smoothly tosylated at 0 - 5 °C within 1 h. (3) 1.5-2.5 equiv of Et3N and 0.1-1.0 equiv of Me3N·HCl was sufficient for the tosylation. (4) The absence of Me3N·HCl catalyst dramatically retarded the tosylation (entry 1-j): a clear joint action of Et3N and catalytic Me3N·HCl was observed. (5) In the case of 3-octanol replacement of Et3N for Py and the conventional Py-solvent method resulted in lower yields under identical conditions (entries 1-k, -l, -m). Catalytic use of DMAP (4-dimethylaminopyridine, an efficient acylating catalyst) in the place of

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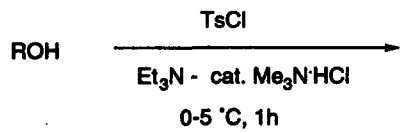
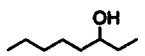
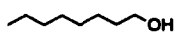
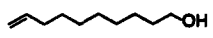
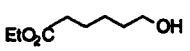
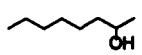
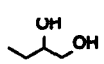
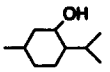
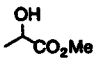
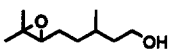
Me_3N·HCl was not so effective (entry 1-n). (6) Even unreactive 3,3-dimethylbutan-2-ol underwent the tosylation within 5 h (entry 9). Therefore, compared with conventional Py-solvent method, method A showed significantly higher reaction velocity.

Table 1. Tosylation of Alcohols Using TsCl / Et_3N / cat. Me_3N·HCl Reagent (Method A)



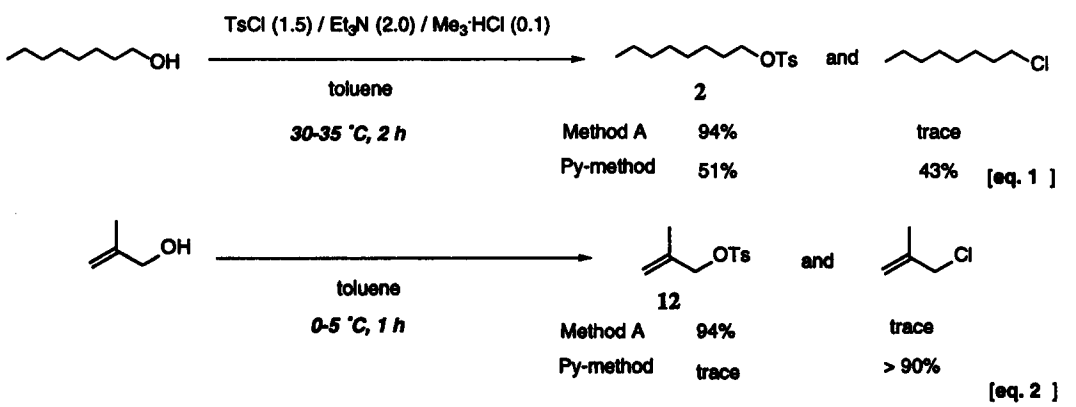
		equiv					
entry	alcohol	TsCl	Et_3N	Me_3N·HCl	solvent	tosylate	yield, %
1-a		1.5	1.5	0.1	CH_2Cl_2	1	83
-b					EDC[a]		86
-c					BTF[b]		82
-d					CH_3CN		42
-e					acetone		28
-f					toluene		48
-g		1.5	2.5	1.0	CH_2Cl_2		93
-h					CH_3CN		92
-i					toluene		91
-j		1.5	1.5	none	CH_2Cl_2 or toluene		<10
-k		1.5	2.5 (Py)	1.0	CH_2Cl_2		38[c]
-l		1.5	2.5 (Py)	1.0	toluene		trace[c]
-m		1.5	11 (Py)	none	------		40[d]
-n		1.5	1.5	0.1 (DMAP[e])			25
2-a		1.5	2.0	0.1	toluene	2	98
-b		1.2	2.0	0.1	toluene		90
3-a		1.5	2.0	0.1	CH_3CN	3	96
-b					toluene		92
4-a		1.5	2.0	0.1	CH_3CN	4	90
-b					toluene		90
5-a		1.5	2.0	0.1	CH_3CN	5	97
-b		1.5	2.5	1.0	toluene		87
6		3.0	3.0	0.2	CH_3CN	6	92

7-a		1.5	2.0	0.1	CH_3CN	7	92
-b		1.5	2.5	1.0	toluene		94
8		1.5	2.0	0.1	CH_3CN	8	95
9		1.5	2.0	0.1	CH_2Cl_2	9	92[f]
					CH_3CN		73[g]
		1.5	2.5	1.0	CH_3CN		90[f]
10		1.5	2.0	0.1	CH_3CN	10	93
11		1.5	2.0	0.1	toluene	11	93

a) 1,2-Dichloroethane. b) Bezotrifluoride. c) Py was used in the place of Et_3N. d) Conventional Py-solvent (11 equiv. *vs.* 3-octanol) method. e) 4-Dimethylaminopyridine. f) Reaction time is 3 h. g) Reaction time is 5 h.

It is also worth noting that method A significantly circumvented the side undesirable chlorination (from R-OTs to R-Cl) exemplified by the following two set of comparable experiments (Scheme 1). 1-Octanol was safely tosylated under identical conditions at 30-35 °C for 2 h [eq. 1]. Moreover, the reaction of methallyl alcohol, a labile allylic substrate, successfully proceeded in contrast to the Py-solvent method at 0-5 °C for 1 h [eq. 2]. These results indicate much lower nucleophilicity of $Et_3N{\cdot}HCl$ salt compared with the Py·HCl salt.

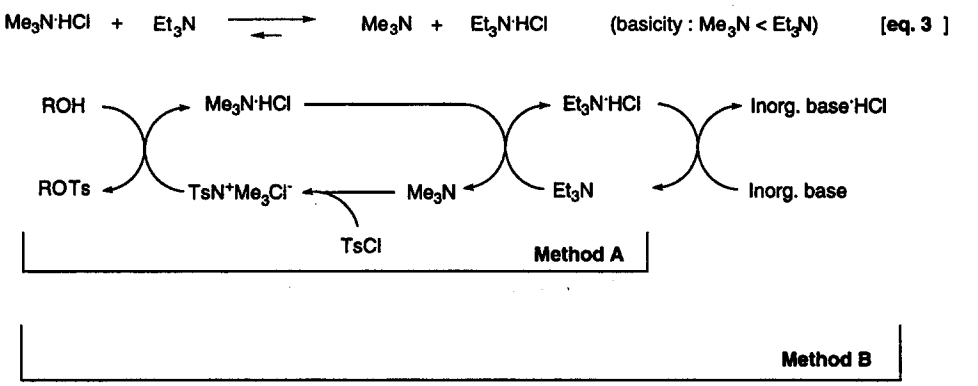
Consequently, method A will adequately replace the Py-method with respect to (1) its higher reaction rate; (2) safety for preparing tosylates; (3) operational simplicity; (4) economy in the use of the amine.



Scheme 1

Plausible mechanism of the Method A is illustrated in Scheme 2 (including Method B, *vide infra*). Because Et3N is stronger base than Me3N, Et3N neutralizes Me3N·HCl to give Me3N, namely, the equilibrium of eq. 3 lies so far to the right. ^{1}H NMR (90 MHz) measurement in CDCl3 revealed that equimolar mixture of Et3N (δ 1.05, 9H, t; 2.50 6H, q) and Me3N·HCl (δ 2.85, 9H, s) was immediately and totally transformed into Et3N·HCl (δ 1.35, 9H, t; 3.10, 6H, q) and Me3N (δ 2.50, 9H, s). In contrast, Py in the place of Et3N failed to generate Me3N due to the lower basicity of Py; no ^{1}H NMR spectrum change was observed.

Thus, Me3N generated *in situ* in turn forms the adduct with TsCl to give $TsN^+Me3{\cdot}Cl^-$, a strong tosylation reagent, which smoothly converts alcohols into the corresponding tosylates. ^{1}H NMR measurement (400 MHz) of the mixture of Et3N, Me3N·HCl, and TsCl in CDCl3 suggested the formation of $TsN^+Me3{\cdot}Cl^-$ (δ ca. 2.9, 9H, s)[4]. Presumably, such sterically unhindered Me3N smoothly forms the reactive sulfoniumammonium salt with TsCl in situ. All the ^{1}H NMR characterization would rationally accounted for the joint action of the combined bases, Et3N and Me3N·HCl and coincides with the results of Table 1, entries 1-g, -j, -k.

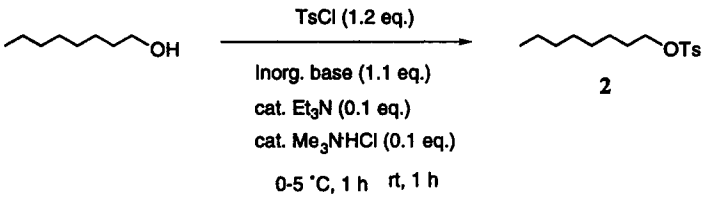


Scheme 2

Method B involves the tosylation using TsCl / Inorganic base / cat. Et3N (0.1 equiv) / cat. Me3N·HCl (0.1 equiv) - as the reagent. Based on the recent environmental and ecological concerns, the decrease of amounts of the amine-base will be desirable, because of its large quantity of BOD (biochemical oxygen demand) or COD (chemical oxygen demand). Since our earlier report described that 2-alkenyl and 2-alkynyl alcohols were safely tosylated using cat. amine and K2CO3,[1g] we applied its analogous protocol coupled with Method A to normal primary alcohols. As the main inorganic base, cheap and available KOH, K2CO3, Ca(OH)2, CaO, Mg(OH)2, and MgO were examined and 1-octanol was used for the initial optimization under fixed conditions (0-5 °C, 1 h; rt, 1 h) (Table 2). The salient features are as follows. (1) KOH and Ca(OH)2 were superior than the other inorganic bases, and the use of Mg(OH)2, and MgO resulted in <20%

conversion. (2) Similar to the Method A, the joint action of Et_3N and $Me_3N{\cdot}HCl$ was observed in 8 typical cases and the absence of $Me_3N{\cdot}HCl$ catalyst significantly retarded the tosylation. (3) Compared with the case of relatively acidic 2-alke(y)nyl alcohols using K_2CO_3 base,[1g] strong bases [KOH and $Ca(OH)_2$] should be naturally favored for the tosylation of normal primary alcohols.

Table 2. Tosylation of 1-Octanol Using TsCl / Inorganic base / cat. Et_3N / cat. $Me_3N{\cdot}HCl$ (Method B)



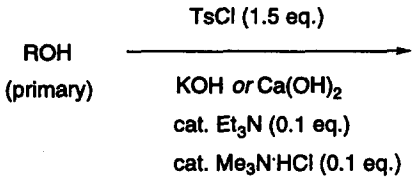
solvent \ Inorg. base	KOH	K_2CO_3	$Ca(OH)_2$	CaO
toluene	74 (68[a], 56[b])	57 (41[a], ~5[b])	33	18
CH_3CN	87 (74[a], 45[b])	43	77 (58[a], ~5[b])	66 (58[a], 24[b])
CH_2Cl_2	86 (83[a], 62[b])	39	87 (83[a], 57[b])	70 (56[a], 33[b])

a) Without Et_3N. b) Without $Me_3N{\cdot}HCl$.

Based on this optimization, tosylations of several primary alcohols were examined (Table 3). Reactions of secondary alcohols such as 2-octanol and 3-octanol, however, did not finished (< ca. 50%) even prolonged reaction time (0-5 °C, 1 h and rt, 10 h). Proposed mechanism of the Method B is also illustrated in Scheme 2. The inorganic main base would work to recycle cat. Et_3N chiefly and/or cat. Me_3N to some extent. Although the reaction velocity is significantly inferior to Method A, Method B will allow the practical and large scale production of primary tosylates.[5]

Finally, the related methanesulfonylation (mesylation) was examined. Usual mesylations are carried out in halogenated solvents (eg. CH_2Cl_2) or ether solvents (eg. ethers, THF) because of their high reaction verocity. Taking into account a recent experimental requirement, especially, for industrial productions, the reaction *in toluene* solvent should be desirable. In fact, 1.5 equiv of Et_3N and 0.1 equiv of $Me_3N{\cdot}HCl$ was found to be a good candidate for the mesylation *in toluene* as shown in Table 4. In the case of 3-octanol, independent use of Et_3N was markedly ineffective.

Table 3. Tosylation of Primary Alcohols Using TsCl / Inorganic base / cat. Et_3N and cat. Me_3N·HCl Reagent (Method B).



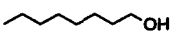
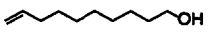
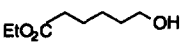
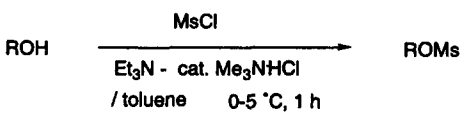
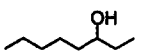
entry	alcohol	inorg. base (equiv)	conditions	solvent	tosylate	yield, %
1-a		KOH (1.5)	0-5 °C, 1 h; rt, 3 h	CH_3CN	**2**	92
-b		KOH (1.5)		toluene		90
-c		$Ca(OH)_2$ (1.5)		toluene		82
2-a		KOH (1.5)	0-5 °C, 1 h; rt, 5 h	toluene	**3**	89
-b						
3-a		$Ca(OH)_2$ (1.5)	0-5 °C, 1 h; rt, 3 h	CH_2Cl_2	**4**	97
-b				CH_3CN		74
4-a		$Ca(OH)_2$ (3.0)	0-5 °C, 1 h; rt, 3 h	CH_2Cl_2	**11**	97
-b				CH_3CN		74

Table 4. Mesylation of Alcohols in Toluene Using MsCl / Et_3N and cat. Me_3N·HCl Reagent.



		equiv			
entry	alcohol	Et_3N	Me_3N·HCl	mesylate	yield, %
1-a		2.5	1.0	**13**	92
-b		1.5	0.1		94
-c		1.5	none		<10
		1.5 (Py)	0.1		trace
		1.5	0.1 (DMAP[a])		87
2		1.5	0.1	**14**	91[b]

a) 4-Dimethylaminopyridine. b) Reaction time is 5 h.

In conclusion, we propose efficient, convenient, economical, environmentally harmonious tosylation methods A and B, which will be a promising improvement over the Py-method. In addition, the related methanesulfonylation *in toluene* was also performed.

Experimental

Melting points were determined on a hot stage microscope apparatus (Yanagimoto) and were uncorrected. ^{1}H NMR spectra were recorded on a JEOL EX-90 (90 MHz) and/or JEOL α (400 MHz) spectrometer in $CDCl_3$ using a TMS internal standard. IR spectra were recorded on a JASCO FT/IR-8000 spectrophotometer. Silica-gel column chromatography was performed on a Merck Art. 7734 and/or 9385. Commercial TsCl was recrystallized from EtOAc prior to use. Commercial Me_3N·HCl was dry up for several min. under reduced pressure.

General procedure of Method A. TsCl (1.2-1.5 mmol) in solvent (1.0 ml) was added to a stirred solution of an alcohol (1.0 mmol), Et_3N (1.5-2.5 mmol) and Me_3N·HCl (0.1 *or* 1.0 mmol) in solvent (1.0 ml) at 0-5 °C, and the mixture was stirred for 1 h. To decompose an excess TsCl, *N,N*-dimethylethylenediamine (ca. 130 mg) was added to the mixture, which was stirred for 10 min. (This procedure is not always necessary, if TsCl is easily separated off by column chromatography). Water was added to the mixture, which was extracted with EtOAc. The organic phase was washed with water and brine, dried (Na_2SO_4) and concentrated. The obtained crude product was purified by silica-gel column chromatography (hexane/ether = 30~10:1) to give the desired tosylate.

General procedure of Method B. TsCl (1.5 mmol) in solvent (1.0 ml) was added to a stirred suspension of an alcohol (1.0 mmol), inorganic base (1.5-3.0 mmol), Et_3N (10 mg, 0.1 mmol) and Me_3·HCl (10 mg, 0.1 mmol) in solvent (1.0 ml) at 0-5 °C, and the mixture was stirred for 1 h and at room temp. for 3-5 h. Aqueous 1M HCl was added to the mixture, which was extracted with EtOAc. A similar work up and purification of Method A gave the desired tosylate.

Note: Pellet KOH was refluxed in toluene for ca. 0.5 h to change into dispersion, which was used. High granules $Ca(OH)_2$ was used.

Mesylation of alcohols using MsCl / Et_3N and cat. Me_3N·HCl. MsCl (172 mg, 1.5 mmol) in toluene (0.5 ml) was added to a stirred solution of an alcohol (1.0 mmol), Et_3N (1.5 *or* 2.0 mmol), and Me_3N·HCl (0.1 *or* 1.0 mmol) in toluene (1.0 ml) at 0-5 °C, and the mixture was stirred for 1 h. A similar workup and purification by silica-gel column chromatography (hexane/EtOAc = 5:1) gave the desired mesylate.

Reaction of 1-octanol in the Py solvent method at 30 °C for 2 h (Scheme 1). TsCl (286 mg, 1.5 mmol) was added to a stirred solution of 1-octanol (130 mg, 1.0 mmol) in pyridine (0.87 ml) at 0-5 °C, and the mixture was stirred at 30 °C for 2 h. Usual work up of this method gave a crude product (275 mg), which contained 1-octyl tosylate (51%) and 1-chlorooctane (43%) by the estimation of ^{1}H NMR (400 MHz).

Reaction of methallyl (2-methyl-2-propenyl) alcohol in the Py solvent method at 0-5 °C for 2 h (Scheme 1). TsCl (286 mg, 1.5 mmol) was added to a stirred solution of tosylate (130 mg, 1.0 mmol) in pyridine (0.87 ml) at 0-5 °C, and the mixture was stirred for 1 h. Usual work up of this method gave a crude product (45 mg), which contained trace amounts of methallyl tosylate and mainly recovered TsCl.

3-Octyl *p*-Toluenesulfonate (1).[6] Colorless oil: ^{1}H NMR (90 MHz, $CDCl_3$) δ 0.80 (3H, t, J = 7.7 Hz), 1.01-1.82 (13H, m), 2.42 (3H, s), 4.38-4.62 (1H, m), 7.22-7.48 (2H, m), 7.71-7.89 (2H, m); IR (film) 2957, 2934, 2864, 1597, 1460, 1364, 1188, 1177, 1098, 910 cm^{-1}.

1-Octyl *p*-toluenesulfonate (2).[7] Colorless oil: ^{1}H NMR (90 MHz, $CDCl_3$) δ 0.87 (3H, t, J = 7.2 Hz), 1.08-1.82 (12H, m), 2.44 (3H, s), 4.03 (2H, t, J = 6.9 Hz), 7.24-7.49 (2H, m), 7.72-7.91 (2H, m); IR (film) 2928, 2857, 1599, 1466, 1362, 1177, 1098, 949, 910 cm^{-1}.

9-Decene-1-yl *p*-toluenesulfonate (3).[8] Colorless oil; ^{1}H NMR (90 MHz, $CDCl_3$) δ 0.78-2.18 (14H, m), 2.44 (3H, s), 4.02 (2H, t, J = 7.7 Hz), 4.81-5.12 (2H, m), 5.58-6.04 (1H, m), 7.22-7.44 (2H, m), 7.72-7.91 (2H, m); IR (film) = 2928, 1639, 1599, 1362, 1177, 937 cm^{-1}.

Ethyl 6-(*p*-toluenesulfonyloxy)hexanoate (4).[9] Colorless oil: ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.24 (3H, t, J = 7.7 Hz), 1.34-1.83 (6H, m), 2.25 (2H, t, J = 7.7 Hz), 2.45 (3H, s), 3.91-4.28 (4H, m), 7.23-7.44 (2H, m), 7.70-7.92 (2H, m); IR (film) 2942, 1734, 1458, 1360, 1177, 1030, 951 cm^{-1}.

2-Octyl *p*-Toluenesulfonate (5).[10] Colorless oil: ^{1}H NMR (90 MHz, $CDCl_3$) δ 0.82 (3H, t, J = 7.2 Hz), 0.99-1.69 (13H, m), 2.41 (3H, s), 4.41-4.79 (1H, m), 7.20-7.42 (2H, m), 7.68-7.89 (2H, m); IR (film) 2932, 2861, 1599, 1460, 1362, 1175, 1098, 914 cm^{-1}.

Bis(*p*-toluenesulfonyloxy)butane (6). Colorless crystals: mp 57.5-58.5 °C; ^{1}H NMR (90 MHz, $CDCl_3$) δ 0.82 (3H, t, J = 7.7 Hz), 1.48-1.81 (2H, m), 2.47 (6H, s), 4.02 (2H, d, J = 6.8 Hz), 4.40-4.71 (1H, m), 7.19-7.48 (4H, m), 7.59-7.91 (4H, m); IR (KBr) = 2976, 1597, 1460, 1362, 1194, 1179, 909 cm^{-1}. Anal. Calcd for $C_{16}H_{22}O_6S_2$: C, 54.25; H, 5.56. Found: C, 54.0; H, 5.4.

***l*-Menthyl *p*-toluenesulfonate (7).**[11] Colorless crystal: mp 92.5-93.5 °C; ^{1}H NMR (90 MHz, $CDCl_3$) δ 0.52 (3H, d, J = 6.4 Hz), 0.70-2.27 (15H, m), 2.42 (3H, s), 4.23-4.56 (1H, m), 7.23-7.43 (2H, m), 7.71-7.91 (2H, m); IR (film) 2963, 2936, 1599, 1454, 1358, 1179, 1098, 943, 910 cm^{-1}.

Methyl 2-(*p*-toluenesulfonyloxy)propionate (8).[12] Colorless oil: ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.52 (3H, d, J = 7.7 Hz), 2.44 (3H, s), 3.68 (3H, s), 4.98 (1H, q, J = 7.7 Hz), 7.22-7.43 (2H, m), 7.74-7.92 (2H, m); IR (film) 2957, 1761, 1451, 1370, 1190, 1179, 1084, 926 cm^{-1}.

3,3-Dimethylbutan-2-yl *p*-toluenesulfonate (9).[13] Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84 (9H, s), 1.21 (3H, d, J = 6.8 Hz), 2.44 (3H, s), 4.39 (1H, q, J = 6.4 Hz), 7.31-7.33 (2H, m), 7.78-7.80 (2H, m); IR (film) 2971, 1599, 1480, 1362, 1177, 1074, 901 cm^{-1}.

3,7-Dimethyl-6,7-epoxyoctyl *p*-toluenesulfonate (10). Colorless oil: ^{1}H NMR (90 MHz, $CDCl_3$) δ 0.85 (3H, d, J = 7.0 Hz), 1.25 (3H, s), 1.29 (3H, s), 1.10-1.80 (7H, m), 2.45 (3H, s), 2.65 (1H, t, J = 7.0 Hz), 4.10 (2H, d, J = 7.0 Hz), 7.20-7.45 (2H, m), 7.70-7.90 (2H, m); IR (film) 2961, 1360, 1177, 1098 cm^{-1}. Anal. Calcd for $C_{17}H_{26}O_4S$: C, 62.55; H, 8.03. Found: C, 62.3; H, 7.7.

2-Hexyn-1-ol *p*-toluenesulfonate (11). Colorless oil: ^{1}H NMR (90 MHz, $CDCl_3$) δ 0.90 (3H, t, J = 7.0 Hz), 1.20-1.65 (2H, m), 1.90-2.30 (2H, m), 2.45 (3H, s), 4.70 (2H, s), 7.20-7.45 (2H, m), 7.70-7.90 (2H, m); IR (film) 2967, 2240, 1364, 1175, 1098 cm^{-1}. Anal. Calcd for $C_{13}H_{16}O_3S$: C, 61.88; H, 6.39. Found: C, 61.6; H, 6.1.

Methallyl (2-Methyl-2-propenyl) *p*-toluenesulfonate (12).[1g] Colorless oil: ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.70 (3H, s), 2.45 (3H, s), 4.45 (2H, s), 4.89-5.06 (2H, m), 7.21-7.47 (2H, m), 7.70-7.91 (2H, m); IR (film) 2980, 2949, 1599, 1360, 1171, 934, 816 cm^{-1}.

3-Octyl methanesulfonate (13).[6] Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (3H, t, J = 7.2 Hz), 0.99 (3H, t, J = 7.2 Hz), 1.22-1.81 (10H, m), 3.03 (3H, s), 4.64-4.72 (1H, m); IR (film) 2938, 2872, 1350, 1175, 918 cm^{-1}.

3,3-Dimethylbutan-2-yl methanesulfonate (14).[13] Colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99 (9H, s), 1.40 (3H, d, J = 7.2 Hz), 3.01 (3H, s), 4.51 (1H, q, J = 7.2 Hz); IR (film) 2969, 2878, 1350, 1175, 905 cm^{-1}.

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3. Under identical conditions in Table 1 entry 1-a, DME, dioxane, THF, methyl isobutyl ketone were much inferior.
4. The chemical shifts of three independent experiments with three molar ratios (Et_3N : Me_3N·HCl : TsCl = 1.0 : 1.0 : 2.0, 1.0, and 0.5) were δ 2.85, 2.90, and 2.92, respectively. This progressive upfield shifts is considered to be average values between Me_3N and $TsN^+Me_3 \cdot Cl^-$ caused by rapid equilibrium in $CDCl_3$.
5. A phase transfer method was reported: Szeja, W. *Synthesis* **1979**, 822. However, when 1-octanol was examined in this method, some trials in our hands failed to obtain the desired tosylate **1a** in practical yields (<10%).
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