Practical and Safe Sulfonylation of 2-Alkynyl and 2-Alkenyl Alcohols Using the Combined Bases of a Catalytic Amount of Tertiary Amine and Potassium Carbonate

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Several 2-alkynyl and 2-alkenyl alcohols were effectively sulfonylated with methanesulfonyl chloride or *p*-toluenesulfonyl chloride using the combined bases of a catalytic amount of tertiary amine and potassium carbonate. The reaction was conducted with reliable safety and while avoiding the disposal of wasted amines. The mesylation of 2-propyn-1-ol proceeded on a large scale (more than 20 kg) without a substantial production of explosive 3-chloro-1-propyne. The choice of the catalysts was important, and sterically unhindered tertiary amines, such as trimethylamine, *N,N*-dimethylbenzylamine, and triethylamine, were effective. Without these catalysts the reactions were significantly retarded. The reaction was so mild that it could be applied to complex and optically active 4-hydroxy-3-methyl-2-(2-propynyl)-2-cyclopenten-1-one, which is an important alcohol moiety of synthetic pyrethroids.

The methanesulfonylation (mesylation) and *p*-toluenesulfonylation (tosylation) of alcohols are well recognized as being fundamental and useful processes in various fields of organic synthesis, especially as for reliable transformations of alcohols into alkylating agents. These sulfonylations are conventionally carried out by treating alcohols with sulfonyl chlorides in the presence of tertiary amine as an acid binder.

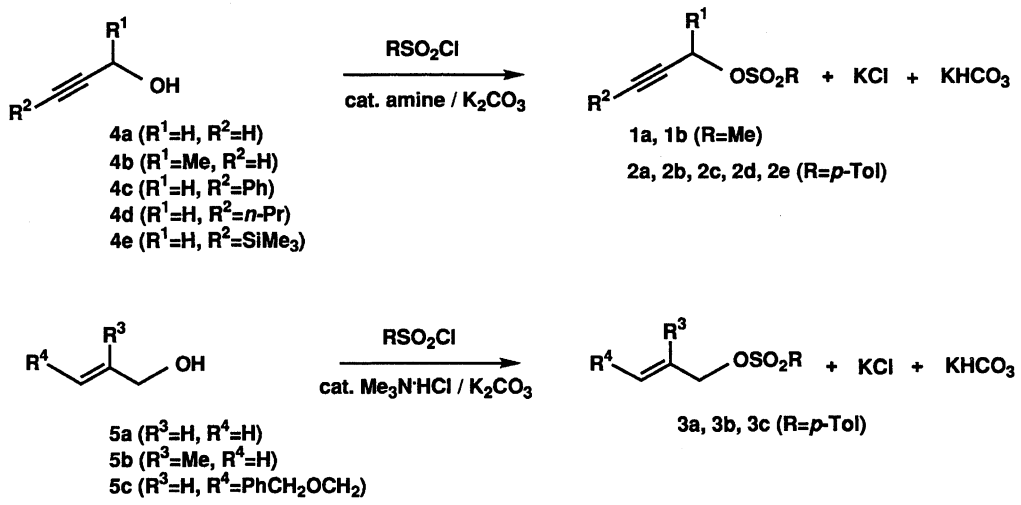
Since it was pointed out that 2-propynyl halides, similar alkylating reagents, possess explosive characteristics,[1,2] 2-propynyl methanesulfonates (mesylates) **1a** and **1b**, or *p*-toluenesulfonates (tosylates) **2a** and **2b**, should be replaced for these 2-propynyl halides as soon as possible, particularly for bulky scale syntheses. However, the aforementioned sulfonylation of synthetically important 2-alkynyl and 2-alkenyl alcohols, **4** and **5**, often requires special care. The reactive sulfonates are liable to change into the corresponding halides (including the undesirable 2-propynyl halides) in situ, due to the action of the relatively reactive ammonium halides as the by-products. To evade this problem, several techniques using lithium,[3] sodium,[4] and the silver salts[5] of alcohols, or a careful use of triethylamine,[6] have been reported. However, these reactions often required rather tedious procedures and/or expensive reagents for large-scale preparation. We report here on a practical, useful and safe method for preparing both 2-alkynyl mesylates, **1** or tosylates **2**, and 2-alkenyl tosylates **3**, using the combined bases of a catalytic amount of tertiary amine (0.05—0.10 molar amount) and potassium carbonate (K_2CO_3; 1.00—1.20 molar amount), as shown in Scheme 1.

In addition, the method would have other merits during industrial-scale production from both economical and ecological standpoints. After preparing of the usual method, an equimolar amount of amine may need to be recycled from the ammonium salts or the acidic water phase. Otherwise, the wasted amines would require a large quantity of BOD (biochemical oxygen demand) or COD (chemical oxygen demand).

The 2-propynyl mesylates, **1a** and **1b**, are important as synthetic intermediates, for example, of pyrethroid insecticide[7] and phthalimide-type herbicides.[8,9]

Results and Discussion

First, the mesylation of 2-propyn-1-ol (propargyl alcohol, **4a**) was found to proceed using a catalytic amount (0.05 molar amount) of triethylamine combined with an equimolar amount of K_2CO_3, giving an excellent yield of methanesulfonate **1a**, which was conducted on a large scale using no less than 20 kg of **4a**. Thus, the undesirable side formation of an explosive 3-chloro-1-propyne (propargyl chloride) was significantly suppressed by the present method. The use of other inorganic bases, such as NaOH, KOH, and $KHCO_3$, in the place of K_2CO_3 gave lower yields of 85, 59, and 15%, respectively. Without triethylamine, the yield clearly decreased. The usual method using equimolar triethyl-

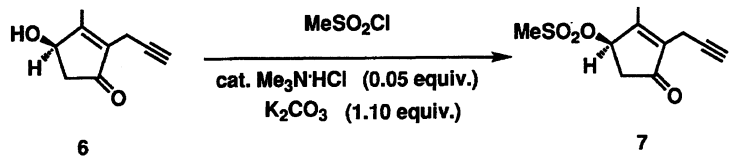


Scheme 1.

Table 1. Mesylation or Tosylation of 2-Alkyn-1-ols Using Cat. Tertiary Amine/K_2CO_3 Systeme[a)]

Entry	Alcohol	R^1	R^2	R	Catalyst(Molar amount)	Solvent	Product	Yield/%[b)]
1	**4a**	H	H	Me	Et_3N (0.05)	MIBK[c)]	**1a**	93 (95[d)])
2	**4a**	H	H	Me	Et_3N (0.05)	Toluene	**1a**	93[d)]
3	**4a**	H	H	Me	No catalyst	MIBK	**1a**	54[d)]
4	**4a**	H	H	*p*-Tol[e)]	Me_3N·HCl (0.10)	MIBK	**2a**	91
5	**4a**	H	H	*p*-Tol	No catalyst	MIBK	**2a**	57
6	**4b**	Me	H	Me	Et_3N (0.05)	Toluene	**1b**	77[d)]
7	**4b**	Me	H	Me	Me_3N·HCl (0.05)	Toluene	**1b**	91[d)]
8	**4b**	Me	H	Me	*N*,*N*-Dimethylbenzylamine (0.10)	Toluene	**1b**	93[d)]
9	**4b**	Me	H	Me	No catalyst	Toluene	**1b**	8[d)]
10	**4b**	Me	H	*p*-Tol	Me_3N·HCl (0.10)	Toluene	**2b**	59
11	**4c**	H	Ph	*p*-Tol	Me_3N·HCl (0.10)	CH_2Cl_2	**2c**	84
12	**4d**	H	*n*-Pr	*p*-Tol	Me_3N·HCl (0.10)	CH_2Cl_2	**2d**	83
13	**4e**	H	Me_3Si	*p*-Tol	Me_3N·HCl (0.10)	CH_2Cl_2	**2e**	62

a) The reaction was carried out at 0—5 °C. Molar ratio of alcohol : sulfonyl chloride : K_2CO_3 is 1.00 : 1.20 : 1.00 (Et_3N) or 1.10 (Me_3N·HCl). b) Isolated yield unless otherwise noted. c) Methyl isobutyl ketone. d) Based on GLC-IS method described in experimental section. e) *p*-Toluenesulfonyl.



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Scheme 2.

amine showed a gradual formation of propargyl chloride as a by-product to the extent of 5—10% from a careful GLC analysis, if the reaction time was prolonged.

Next, in the case of 3-butyn-2-ol (**4b**), a catalytic amount of trimethylamine hydrochloride and *N*,*N*-dimethylbenzylamine were found much more effective than triethylamine. To study the structure and reactivity relationship, several amines were examined: *N*,*N*-Diisopropylethylamine (21%), pyridine (19%), 4-(dimethylamino)pyridine (26%), and imidazole (24%) had a slight accelerating effect, but *N*,*N*-diethylaniline was almost ineffective. A reaction without the amine catalyst also gave a poor yield. The tosylation of propargyl alcohol (**4a**) could also be carried out using similar conditions. Several 2-alkynyl alcohols, such as 3-phenyl-2-propyn-1-ol (**4c**), 2-hexyn-1-ol (**4d**), and 3-trimethylsilyl-2-propyn-1-ol (**4e**), could be subjected to the present tosylation. These above-mentioned results are all summarized in Table 1. Of note is that the usual tosylation of **4c** using an equimolar amount of triethylamine in CH_2Cl_2 or using pyridine solvent as the compared experiment under similar conditions gave a tosylate **2c** in poor yields (45% and ca. 10%, respectively).

After due consideration of the high reactivity of trimethylamine hydrochloride, the tosylation of allyl alcohol (**5a**) and 2-methyl-2-propen-1-ol (methallyl alco-

hol, **5b**) was also applied. In this case, triethylamine was inferior to trimethylamine hydrochloride; the use of only K_2CO_3 (equimolar amount) was not effective at all, as shown in experimental section. The reactions of 3-phenyl-2-propen-1-ol (cinnamyl alcohol) with *p*-toluenesulfonyl chloride,[10] however, did not give the desired sulfonate at all with an almost recovery of these alcohols (ca. 80%), along with a small amount of complex mixtures including 3-chloro-1-phenyl-1-propene (cinnamyl chloride). The tosylation of 3,7-dimethyl-2,5-octadien-1-ol (geraniol) was attempted, because the tosylate had been prepared only in situ;[11] however, 3-chloro-3,7-dimethyl-1,6-octadiene was obtained as the main product in about 20% yield. These chlorides formed via the intermediary sulfonates, although with a little conversion, it was presumably due to the inherent high reactivity of these intermediary sulfonates.

The present reaction possibly proceeded as follows: a catalytic amine initially formed a reactive sulfonylammonium salt, which, in turn, reacted with an alcohol to give the sulfonates and the ammonium chloride; then, the ammonium chloride was neutralized by K_2CO_3, which changed into KCl and $KHCO_3$ accompanying the reproduction of the catalytic amine. Accordingly, the choice of tertiary amine was critical for the reaction. Sterically unhindered tertiary amines, such as trimethylamine, *N*,*N*-dimethylbenzylamine, and triethylamine, were effective because they are liable to form reactive sulfonylammonium salts.[12]

Finally, the reaction of a 4-hydroxy-3-methyl-2-(2-propynyl)-2-cyclopenten-1-one (**6**), which is an important alcohol moiety of synthetic pyrethroids,[13] occurred as shown in Scheme 2. This mesylation is an important industrial process for the optically active cyclopentanoide **6**.[14] These methods will allow the industrial production of 2-alkynyl or 2-alkenyl sulfonates, with reliable safety and while avoiding the disposal of wasted amines.

Experimental

Apparatus and Materials. Analytical GLC was performed on an HP-5980II with an HR-Thermon 3000B capillary column (30 m) and/or on a Shimadzu GC9A with a 5% PEG packed column (1m). NMR spectra were recorded on a JEOL EX-90 spectrometer in $CDCl_3$ using a TMS internal standard. IR spectra were recorded on a Hitachi 270-30 spectrophotometer. All of the reagents and solvents were of commercial grade and were used without further purification, i,e., as technical grades. Silica-gel column chromatography was performed on a Merck Art. 7734.

Large Scale Preparation of 2-Propynyl Methanesulfonate (1a).[15] (Table 1, Entry 1) To a suspension of 2-propyn-1-ol (propargy alcohol; **4a**, 21.0 kg, 374.6 mol), Et_3N (1.9 kg, 18.8 mol), and K_2CO_3 (51.8 kg, 374.6 mol) in 4-methyl-2-pentanone (methyl isobutyl ketone; MIBK) (150.0 kg) was added methanesulfonyl chloride (51.5 kg, 449.5 mol) with sufficient stirring at 0—5 °C for 8 h using a 500 dm^3 glass-lined reactor. After the mixture was stirred for 2 h, water (170.0 kg) was added at 20 °C. The separated water phase was back extracted with MIBK (50.0 kg) and the combined organic extracts were washed with 3% aqueous Na_2SO_4. The obtained solution was analyzed by GLC (capillary column) using ethyl benzoate as an internal standard to give the sulfonate **1a** in 95% yield. Using 10.00 g of **4a**, 22.25 g of **1a** (93%) was isolated by silica-gel column chromatographic purification (hexane/ethyl acetate=5 : 1). Colorless liquid; IR (film) 2140, 1350, and 1180 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.70 (1H, t, J=2.0 Hz), 3.15 (3H, s), 4.85 (2H, d, J=2.0 Hz).

Preparation of 2-Propynyl *p*-Toluenesulfonate (2a).[15] (Table 1, Entry 4) To a stirred suspension of propargyl alcohol (**4a**, 5.60 g, 0.10 mol) and K_2CO_3 (15.20 g, 0.12 mol) in MIBK (50.00 ml) was added Me_3N·HCl (0.96 g, 0.01 mol) at 0—5 °C. After 5 min, *p*-toluenesulfonyl chloride (20.97 g, 0.12 mol) in MIBK (50.0 ml) was added at 0—5 °C for an hour. After the mixture was stirred for an hour, water (100 g) was added at 20 °C. The separated water phase was back extracted with MIBK (20.0 ml) and the combined organic extracts were first washed with water, and then, saturated aqueous NaCl, dried (Na_2SO_4), concentrated, and purified by column chromatography (hexane/EtOAc=10 : 1) giving 19.13 g (91%) of the sulfonate **2a**. Colorless liquid; IR (film) 2150, 1370, and 1180 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.45 (3H, s), 2.45 (1H, d, J=2.0 Hz), 4.70 (2H, d, J=2.0 Hz), 7.35 (2H, d, J=9.0 Hz), 7.85 (2H, d, J=9.0 Hz).

Preparation of 1-Methyl-2-propynyl Methanesulfonate (1b).[16] (Table 1, Entry 7) To a stirred solution of 3-butyn-2-ol (**4b**, 4.21 g, 0.060 mol) in toluene (39 ml) was added K_2CO_3 (9.54 g, 0.069 mol) and trimethylamine hydrochloride (0.29 g, 3.0 mmol). After 10 min., methanesulfonyl chloride (8.25 g, 0.072 mol) was added with vigorous stirring at 0—5 °C for one hour; the mixture was then stirred for one hour. Then, water (55.74 g) was added at 20 °C and the organic phase was washed with 5% aqueous Na_2SO_4 and dried (Na_2SO_4). After filtration, the obtained solution was analyzed by GLC (capillary column) using ethyl benzoate as an internal standard to give the sulfonate (**1b**) in 91% yield. Colorless liquid; IR (film) 2150, 1370, and 1180 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.65 (3H, d, J=8 Hz), 2.70 (1H, d, J=2 Hz), 3.15 (3H, s), 5.30 (1H, dd, J=8 and 2 Hz).

1-Methyl-2-propynyl *p*-Toluenesulfonate (2b).[17] Colorless liquid; IR (film) 2130, 1360, and 1180 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.60 (3H, d, J=8 Hz), 2.40 (1H, d, J=2 Hz), 2.45 (3H, s), 5.20 (1H, dd, J=8 and 2 Hz), 7.30 (2H, d, J=9.0 Hz), 7.85 (2H, d, J=9.0 Hz).

3-Phenyl-2-propynyl *p*-Toluenesulfonate (2c). Colorless crystals; mp 78—80 °C (lit,[10] decomp); IR (Nujol) 1370, and 1180 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.35 (3H, s), 4.90 (2H, s), 7.20—7.45 (5H, m) 7.30 (2H, d, J=9.0 Hz), 7.85 (2H, d, J=9.0 Hz).

2-Hexynyl *p*-Toluenesulfonate (2d).[18] Colorless liquid; IR (film) 1370 and 1170 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.90 (3H, t, J=7.0 Hz),1.15—1.60 (2H, m), 1.95—2.20 (2H, m), 2.45 (3H, s), 4.70 (2H, t, J=2.5 Hz), 7.30 (2H, d, J=9.0 Hz), 7.85 (2H, d, J=9.0 Hz).

3-Trimethylsilyl-2-propynyl *p*-Toluenesulfonate (2e).[19] Colorless liquid; IR (film) 1370 and 1170 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.10 (9H, s), 2.45 (3H, s), 4.70 (2H, s), 7.35 (2H, d, J=9.0 Hz), 7.85 (2H, d, J=9.0 Hz).

Preparation of Allyl *p*-Toluenesulfonate (3a).[20]

Similar to the procedure for preparing **2a** using allyl alcohol (**5a**), **3a** was obtained at a yield of 81% (Me_3N·HCl catalyst), 41% (Et_3N catalyst), and a trace amount (without a catalyst). Colorless liquid; IR (film) 1600, 1370, and 1180 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.45 (3H, s), 4.45—4.65 (2H, m), 5.15—5.45 (2H, m), 5.60—6.10 (1H, m), 7.35 (2H, d, J=9.0 Hz), 7.80 (2H, d, J=9.0 Hz).

Preparation of 2-Methyl-2-propenyl *p*-Toluenesulfonate (3b).[21] Similar to the procedure for preparing of **2a** using 2-methyl-2-propen-1-ol (methallyl alcohol; **5a**), **3b** was obtained in 81% yield. Colorless liquid; IR (film) 1600, 1370, and 1180 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.70 (3H, s), 2.45 (3H, s), 4.40 (2H, s), 4.85—5.05 (2H, m), 7.35 (2H, d, J=9.0 Hz), 7.80 (2H, d, J=9.0 Hz).

***cis*-4-Benzyloxy-2-buten-1-yl *p*-Toluenesulfonate (3c).** Yield 52%. Colorless liquid; IR (film) 1600, 1370, and 1180 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.45 (3H, s), 4.00 (2H, d, J=6.0 Hz), 4.50 (2H, s), 4.65 (2H, d, J=6.0 Hz), 5.40—6.00 (2H, m), 7.10—7.50 (5H, m), 7.35 (2H, d, J=9.0 Hz), 7.85 (2H, d, J=9.0 Hz). Found: C, 64.70; H, 5.91%. Calcd for $C_{18}H_{20}O_4S$: C, 64.98; H, 6.02%.

Preparation of (*R*)-2-Methyl-4-oxo-3-(2-propynyl)-2-cyclopentenyl Methanesulfonate (7).[22] Using the same procedure as that for preparing of **1b**, allyl alcohol **6** was used as a starting substance in place of 3-butyn-2-ol (**4b**). Yield 88%. Yellow crystals; mp 73—75 °C; $[\alpha]_D^{21}$ −18.0 (*c* 1.18, $CHCl_3$); IR (Nujol) 2120, 1705, 1370, and 1170 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.05 (1H, t, J=3.0 Hz), 2.25 (3H, s), 2.55 (1H, dd, J=18.0 and 6.0 Hz), 3.00 (1H, dd, J=18.0 and 6.0 Hz), 3.10 (3H, s; $C\underline{H}_3SO_2$-), 3.15 (2H, d, J=3.0 Hz), 5.60 (1H, br). Found: C, 55.20%; H, 5.21%. Calcd for $C_{10}H_{12}O_4S$: C, 55.26%; H, 5.30%.

Sulfonates **1a**, **1b**, **2a**, **2b**, **2c**, **2d**, **2e**, **3a**, and **3b**, are known: CAS registry Nos. are **1a**, [16156-58-4]; **1b**, [59967-06-5]; **2a**, [6165-76-0]; **2b**, [53487-52-8]; **2c**, [21541-60-6]; **2d**, [51721-35-8]; **2e**, [71321-16-9]; **3a**, [41411-59-0]; **3b**, [20443-62-3].

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References

1) N. I. Sax, "Dangerous Properties of Industrial Materials," 7th ed, Von Nostrand Reinhold, New York (1987).
2) L. Bretherick, "Handbook of Reactive Chemical Hazards," 4th ed, Butterworths, London (1990).
3) H. C. Brown, R. Bernheimer, C. J. Kim, and S. E. Sheppele, *J. Am. Chem. Soc.*, **99**, 370 (1967).
4) J. K. Kochi and G. B. Hammond, *J. Am. Chem. Soc.*, **75**, 3443 (1953).
5) H. M. R. Hoffman, *J. Chem. Soc.*, **1965**, 6748.
6) R. K. Crossland and K. L. Servis, *J. Org. Chem.*, **35**, 3195 (1970).
7) N. Itaya and M. Hirano, U. S. Patent 4176189 (1979); *Chem. Abstr.*, **90**, 186946z (1979).
8) E. Nagano, T. Haga, R. Sato, and K. Morita, U. S. Patent 4640707 (1987); *Chem. Abstr.*, **105**, 56350t (1986).
9) E. Nagano, S. Hashimoto, R. Yoshida, H. Matsumoto, and K. Kamoshita, U. S. Patent 4484941 (1984); *Chem. Abstr.*, **98**, 71924p (1983).
10) P. H. Boyle, J. H. Coy, and H. N. Dobbs, *J. Chem. Soc., Perkin Trans. 1*, **1972**, 1617; C. R. Johnson and G. A. Dutra, *J. Am. Chem. Soc.*, **95**, 7777 (1973).
11) M. Hajime and E. Negishi, *J. Org. Chem.*, **47**, 4161 (1982); C. D. Poulter and D. S. Mautz, *J. Am. Chem. Soc.*, **113**, 4895 (1991).
12) J. F. King, E. A. Luinstra, and D. R. K. Harding, *J. Chem. Soc., Chem. Commun*, **1972**, 1313; J. F. King and J. R. du Manoir, *J. Am. Chem. Soc.*, **97**, 2566 (1975).
13) T. Matsuo, T. Nishioka, M. Hirano, Y. Suzuki, K. Tsushima, N. Itaya, and H. Yoshioka, *Pestic. Sci.*, **11**, 202 (1980).
14) S. Mitsuda, T. Umemura, and H. Hirohara, *Appl. Microbiol. Biotech.*, **29**, 310 (1988).
15) K. Zeile and H. Meyer, *Ber. Dtsch. Chem. Ges. B*, **75B**, 356 (1942).
16) L -I. Olsson and A. Claesson, *Acta Chem. Scand., Ser B*, **B33**, 679 (1979).
17) U. K -Pomeranz, H. J. Hansen, and H. Schmid, *Helv. Chem. Acta*, **56**, 2981 (1973).
18) L. Pop, I. Oprean, A. Barabas, and F. Hodosan, *J. Prackt. Chem.*, **328**, 867 (1986).
19) H. Westmijize and P. Vermeer, *Synthesis*, **1979**, 390.
20) H. Gilman and N. J. Beaber, *J. Am. Chem. Soc.*, **47**, 518 (1925).
21) O. A. Prib and M. S. Malinovskii, *Ukr. Khim. Zh.*, **30**, 198 (1964); *Chem. Abstr.*, **60**, 13175d (1964).
22) H. Danda, Y. Furukawa, and T. Umemura, *Synlett*, **1991**, 441.