An Efficient Organocatalyzed Interconversion of Silyl Ethers to Tosylates Using DBU and *p*-Toluenesulfonyl Fluoride

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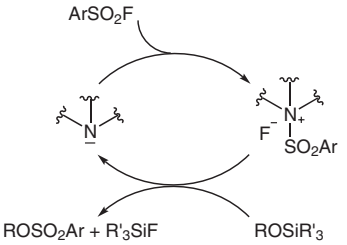
Abstract: A mild and efficient interconversion from silyl ethers to sulfonates esters is reported with good yields. This silyl-sulfonyl exchange proceeds readily in acetonitrile at room temperature in the presence of *p*-toluenesulfonyl fluoride and a catalytic amount of 1,8-diazabicyclo[5.4.0]undec-7ene (DBU). This method can be used with trimethysilyl (TMS), triethylsilyl (TES) and *tert*-butyldimethylsilyl (TBDMS) ethers.

Key words: organocatalysis, sulfonate ester, silyl ether, DBU, *p*-toluenesulfonyl fluoride

Alkylation is a fundamental reaction and powerful tool in organic synthesis. Among the numerous routes available in the literature, conversion of alcohols into halides or sulfonates is probably the most useful approach for the preparation of alkylating agents.[1] One of the most commonly employed leaving group is the *p*-toluenesulfonate ester. In the course of a multistep synthesis, the preparation of tosylates is often preceded by a silyl ether deprotection step.[2] The development of a 'one-pot' methodology would be therefore desirable in view of the fact that both steps are replaced by a single reaction. Despite obvious advantages offered by such an interconversion strategy, only one procedure using a catalytic heterogenous system ($FeCl_3$–Montmorillonite K-10) to convert aliphatic TMS ethers to sulfonate esters has been described in the literature.[3] We whish to report herein an efficient, mild, and high-yielding organocatalytic process to realize this useful interconversion.

Our laboratory has recently developed the transprotection of silyl ethers into benzoates by making use of benzoyl fluoride in the presence of a catalytic amount of 4-(dimethylamino)pyridine (DMAP).[4] To account for the good reactivity observed, a *N*-acylpyridinium fluoride salt is presumed to be formed and then to react smoothly with the silyl ether thanks to the high affinity of silicon for the fluoride ion.

By analogy with this work, in the presence of a nitrogen Lewis base, one can assume that an arylsulfonyl fluoride may possibly react with a silyl ether via the formation of an arylsulfonyl ammonium fluoride salt. This key intermediate should exert a specific activation on the silyl ether to promote the desired arylsulfonyl transfer (Scheme 1).

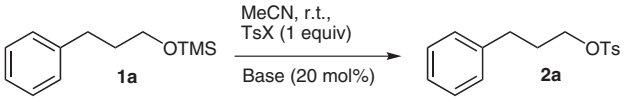


Scheme 1 Working hypothesis for the development of a new organocatalytic interconversion process of silyl ethers to arylsulfonates

On the basis of this working hypothesis, we first examined the reactivity of silyl ether[5] **1a** at room temperature in acetonitrile in the presence of a catalytic amount of various nitrogenous bases (20 mol%) and a stoichiometric amount of tosylating agents (Table 1).

Surprisingly, although no reaction took place with Hünigs base, 1,4-diazabicyclo[2.2.2]octane (DABCO), quinuclidine, DMAP, and *N*-methylimidazole (Table 1, entries 1–5), we were pleased to find out that DBU[6] gave the desired

Table 1 Nitrogen Lewis Bases and Tosylating Agents Screening



Entry	TsX	Base	Time (h)	Yield (%)[a]
1	TsF	DIEA	24	0
2	TsF	DABCO	24	0
3	TsF	Quinuclidine	24	0
4	TsF	DMAP	24	0
5	TsF	*N*-Methylimidazole	24	0
6	TsF	DBU	4	95
8	TsCl	DBU	3	0
9	Ts_2O	DBU	2	23
10	Ts_2O	DBU	20	61

[a] Isolated yields.

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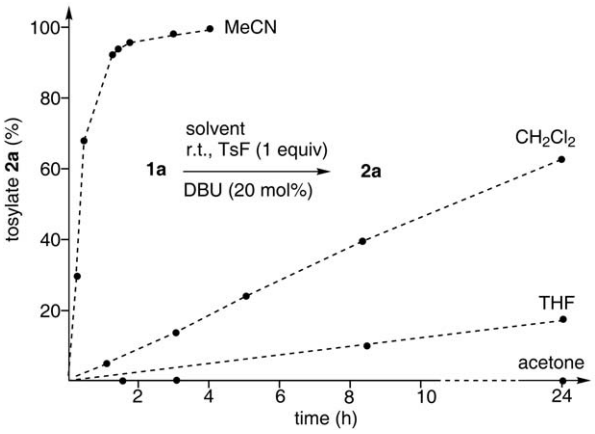


Figure 1 Solvents screening for the interconversion of TMS ether **1a** to tosylate **2a**

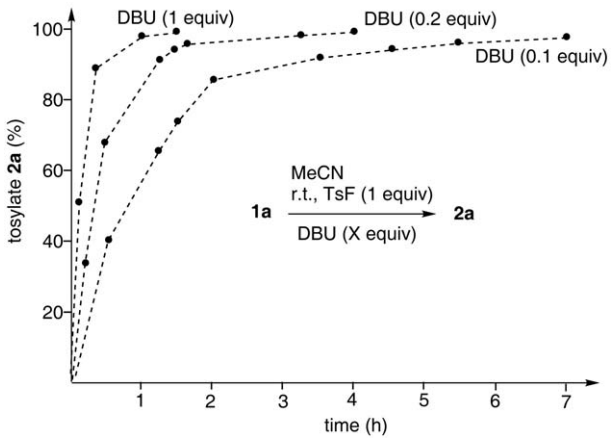
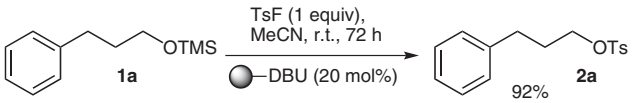


Figure 2 Influence of catalyst loading on the rate of reaction



Scheme 2 Interconversion of **1a** using polystyrene-supported DBU

product **2a** in high yield (Table 1, entry 6). The reaction conducted with *p*-toluenesulfonic anhydride led to incomplete conversion, even after prolonged reaction time (Table 1, entries 9, 10), while being completely unproductive with *p*-toluenesulfonyl chloride (Table 1, entry 8). This result points out the fluoride activation of the silyl ether as an important driving force in this interconversion process.

The DBU–*p*-toluenesulfonyl fluoride combination[7] having proved to be effective, we then examined the influence of the solvent on the reaction rate. Whereas acetonitrile revealed to be the best solvent furnishing the desired tosylate **2a** in 95% yield within four hours, dichloromethane and tetrahydrofuran gave rather poor results affording **2a** in 23% and 5% yield, respectively, while no reaction took place in acetone. The high reactivity of the silyl ether in acetonitrile may be ascribed to the good coordinating properties of that solvent with silicon (Figure 1).[8]

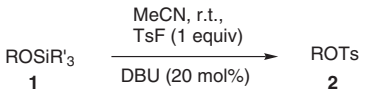
Attempts to reduce the catalyst loading from 20 mol% to 10 mol% resulted in a significant increase in the reaction time. However, complete and clean conversion into **2a** was observed within eight hours at room temperature, making these reaction conditions rather attractive for synthetic applications (Figure 2).

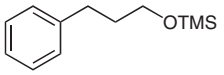
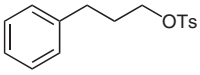
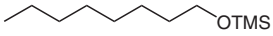
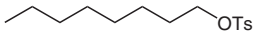
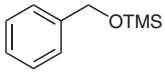
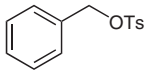
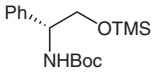
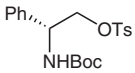
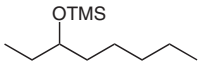
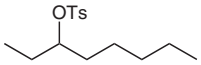
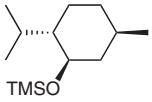
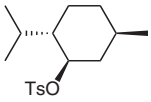
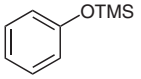
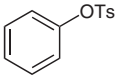
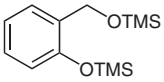
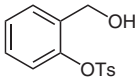
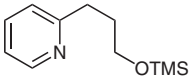
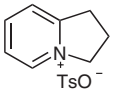
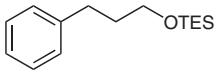
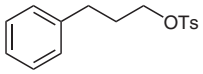
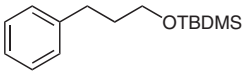
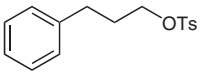
The synthetic potential of this catalytic transformation was then assessed with various silyl ethers **1a**–**k** (Table 2).[9,10] Some primary and secondary TMS ethers were first examined and underwent tosylation in excellent yields. At room temperature, the primary ethers **1a**–**d** were transformed in four hours (Table 2, entries 1–4), whereas 48 hours were required to ensure complete conversion with secondary TMS ethers **1e**,**f** (Table 2, entries 5, 6). It is interesting to note that decreasing the catalyst loading from 20 mol% to 10 mol% did not significantly affect the reaction rate when the reaction is conducted at reflux (Table 2, entries 1, 6). Phenolic TMS ethers **1g**,**h** proved to be highly reactive, providing tosylates **2g**,**h** within 30 minutes in excellent yields (Table 2, entry 7). The higher reactivity of phenolic TMS ethers was evidenced by the selective and clean conversion of the phenolic TMS ether in **1h**, while leaving untouched the primary TMS ether (Table 2, entry 8). Interestingly, tosylation of silyl ether **1i** was followed by the quaternization of the pyridine ring to provide the pyridinium salt **2i** in 90% yield (Table 2, entry 9). This last example highlights the attractive potential of this strategy in developing tandem interconversion–intramolecular ring-closure reactions. This methodology was also successfully applied to TES and TBDMS ethers **1j**,**k** (Table 2, entries 10 and 11). With TES ether **1j**, exchange reaction was completed at room temperature within eight hours (Table 2, entry10). While TBDMS ether **1k** remains unaffected after 24 hours at room temperature, the reaction occurred smoothly in refluxing acetonitrile for four hours to give tosylate **2k** in 95% yield (Table 2, entry11).

The silyl ether–tosylate interconversion could be also achieved in high yield, in the presence of polystyrene-supported DBU[11] at room temperature during 72 hours. Tosylate **2a** was isolated in a clear manner by simple filtration and evaporation of the filtrate, thus facilitating workup and catalyst recycling (Scheme 2).

To complete this study, we considered the selectivity of this transformation (Scheme 3). When a mixture of primary and secondary TMS ethers **1a** and **1f** (1:1) was subjected to the above-mentioned standard conditions, the primary tosylate **2a** was selectively obtained with good yield. An excellent selectivity was also found between TMS ether **1b** and TES (or TBDMS) ethers **1j** and **1k**. When a mixture of TMS ether **1b** and TES ether **1j** (1:1) was allowed to react with an equimolar amount of tosyl fluoride, only the TMS ether **1b** underwent tosylation in 90% yield without any trace of **2a**. These results clearly revealed that this methodology can be applied for the selective tosylation of primary silyl ethers in the presence of

Table 2 Scope of the Silyl Ether–Tosylate Interconversion



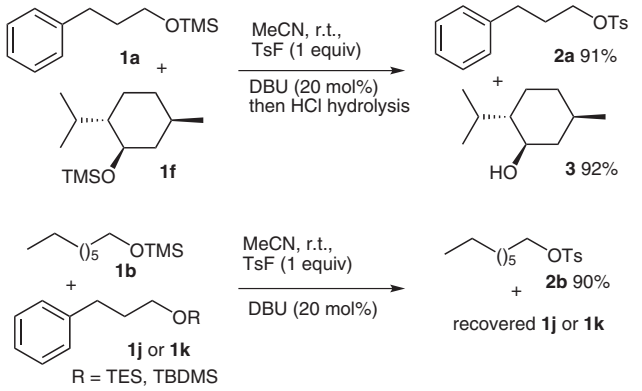
Entry	Silyl ether **1**	Tosylate **2**	Time (h)	Yield (%)[a]
1	 **1a**	 **2a**	4 4	96 95[b]
2	 **1b**	 **2b**	4	95
3	 **1c**	 **2c**	4	97
4	 **1d**	 **2d**	4	85
5	 **1e**	 **2e**	48	90
6	 **1f**	 **2f**	48 48	95 95[b]
7	 **1g**	 **2g**	0.5	96
8	 **1h**	 **2h**	0.5	90[c]
9	 **1i**	 **2i**	4	90
10	 **1j**	 **2a**	8	94
11	 **1k**	 **2a**	24 4	0 95[d]

[a] Isolated yields.
[b] Reaction performed at reflux with 10 mol% of DBU.
[c] Hydrolysis of the residual silyl ether protecting group occurred during the workup of the reaction.
[d] Reaction performed at reflux.

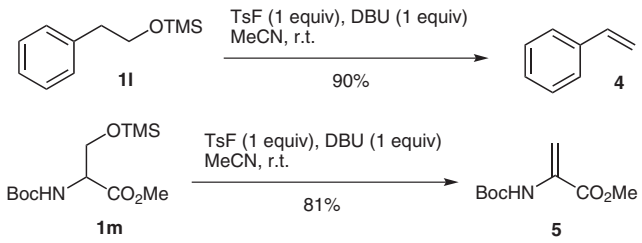
secondary silyl ethers and for the tosylation of TMS ethers in the presence of TES or TBDMS ethers.

Attempts to extent this procedure to silyl ethers bearing acidic protons in α position, led to subsequent elimination of the resulting tosylate. As a result, when the reaction was conducted with one equivalent of DBU to drive the reaction to completion, TMS ethers **1l** and **1m** afforded styrene **4** and amino acrylic ester **5** in good yields (Scheme 4).

In summary, the present methodology describes a simple, mild, and high-yielding organocatalytic procedure for the interconversion of silyl ethers to *p*-toluenesulfonate esters. Furthermore, this interconversion process revealed to be highly selective regarding the nature of the silyl ethers



Scheme 3 Examples of selective direct tosylation of silyl ethers



Scheme 4 Examples of tandem interconversion–elimination reactions

making possible interconversion of TMS ethers in the presence of an additional TES or TBDMS ether. A high selectivity was also observed between primary and secondary ethers.

Acknowledgment

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References and Notes

(1) (a) Selected recent references: Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed.; Wiley: New York, **1999**. (b) Kim, J.-G.; Jang, D. O. *Synlett* **2007**, 2501. (c) Kazemi, F.; Massah, A. R.; Javaherian, M. *Tetrahedron* **2007**, *63*, 5083. (d) Comagic, S.; Schirrmacher, R. *Synthesis* **2004**, 883.

(2) Selected recent references: (a) Honda, T.; Kaneda, K. *J. Org. Chem.* **2007**, *72*, 6541. (b) Prasad, K. R.; Chandrakumar, A. *J. Org. Chem.* **2007**, *72*, 6312. (c) Ojika, M.; Kigoshi, H.; Yoshida, Y.; Ishigaki, T.; Nisiwaki, M.; Tsukada, I.; Arakawa, M.; Ekimoto, H.; Yamada, K. *Tetrahedron* **2007**, *63*, 3138. (d) Watanabe, H.; Mori, N.; Itoh, D.; Kitahara, T.; Mori, K. *Angew. Chem. Int. Ed.* **2007**, *46*, 1512. (e) Lawhorn, B. G.; Boga, S. B.; Wolkenberg, S. E.; Boger, D. L. *Heterocycles* **2006**, *70*, 65.

(3) Movassagh, B.; Shokri, S. *Z. Naturforsch., B: Chem. Sci.* **2005**, *60*, 763.

(4) Poisson, T.; Dalla, V.; Papamicaël, C.; Dupas, G.; Marsais, F.; Levacher, V. *Synlett* **2007**, 381.

(5) **General Procedure for the Preparation of Silyl Ethers 1a–m**
To a solution of 3-phenylpropanol (139 mg, 1 mmol) and Et_3N (120 mg, 1.1 mmol) in CH_2Cl_2 (5 mL) was added TMSCl (115 mg, 1.05 mmol). The mixture was stirred at r.t. overnight. The solvent was removed under reduced pressure and the residue was diluted with pentane (10 mL). Simple filtration through a short pad of Celite® provided silyl ether **1a** in 93% yield which could be used in the silyl ether exchange reaction without further purification.

(6) For other examples in nucleophilic catalysis in which DBU is superior to other amine bases, see: (a) Aggarwal, V. K.; Mereu, A. *Chem. Commun.* **1999**, 2311. (b) Shieh, W.-C.; Dell, S.; Repič, O. *J. Org. Chem.* **2002**, *67*, 2188. (c) Yeom, C.-E.; Kim, H. W.; Lee, S. Y.; Kim, B. M. *Synlett* **2007**, 146. (d) Murtagh, J. E.; McCooey, S. H.; Connon, S. J. *Chem. Commun.* **2005**, 227.

(7) DBU (Sigma-Aldrich) and *p*-toluenesulfonyl fluoride 97% (Acros Organics) were used as received.

(8) (a) Olah, G. A.; Narang, S. C.; Gupta, B. G. B.; Malhotra, R. *J. Org. Chem.* **1979**, *44*, 1247. (b) Morita, T.; Okamoto, Y.; Sakurai, H. *J. Chem. Soc., Chem. Commun.* **1978**, 874. (c) Morita, T.; Okamoto, Y.; Sakurai, H. *Tetrahedron Lett.* **1978**, 2523. (d) Olah, G. A.; Narang, S. C. *Tetrahedron* **1982**, *38*, 2225.

(9) **General Procedure for the Interconversion of Silyl Ethers 1a–m**
To a solution of TMS ether **1a** (209 mg, 1 mmol) and TsF (179 mg, 1 mmol) in MeCN (2 mL) was added DBU (30 μL, 0.2 mmol). The mixture was stirred for 4 h at r.t. followed by addition of H_2O (4 mL). The aqueous phase was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with H_2O (10 mL) and brine (10 mL). After drying ($MgSO_4$) and concentration under vacuum, the residue was chromatographed on SiO_2 (cyclohexane–Et_2O, 9:1) affording tosylate **2a** (278 mg, 96% yield).

(10) **Spectral Data for Tosylate 2h**
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.77 (d, 2 H, *J* = 8.3 Hz), 7.51 (d, 1 H, *J* = 7.5 Hz), 7.36 (d, 2 H, 8.3 Hz), 7.29 (t, 1 H, *J* = 7.5 Hz), 7.21 (t, 1 H, *J* = 7.5 Hz), 6.86 (d, 1 H, *J* = 7.5 Hz), 4.58 (s, 2 H), 2.61 (s, 1 H), 2.48 (s, 3 H). ^{13}C (75 MHz, $CDCl_3$): δ = 146.9, 145.9, 134.6, 132.2, 130.3, 130.0, 128.8, 128.5, 127.6, 122.3, 59.6, 21.8. IR (KBr): ν_{max} = 3392, 1597, 1487, 1453, 1371, 1192, 1179, 1156, 1089, 1040.
Spectral Data for Tosylate 2d
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.66 (d, 2 H, *J* = 8.3 Hz), 7.35–7.17 (m, 7 H), 5.20–5.18 (m, 1 H), 4.93–4.89 (m, 1 H), 4.28–4.15 (m, 2 H), 2.43 (s, 3 H), 1.41 (s, 9 H). ^{13}C (75 MHz, $CDCl_3$): δ = 155.0, 145.0, 137.8, 132.4, 129.9, 128.8, 128.0, 127.9, 126.6, 80.1, 71.6, 28.3, 21.7. IR (KBr): ν_{max} = 3383, 1690, 1525, 1361, 1172, 1097, 1052, 964. Mp 123–124 °C.
Spectral Data for Tosylate 2i
^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.13 (d, 1 H, *J* = 6.0 Hz), 8.22 (t, 1 H, *J* = 7.7 Hz), 7.80 (d, 1 H, *J* = 7.7 Hz), 7.72 (t, 1 H, *J* = 6.9 Hz), 7.59 (d, 2 H, *J* = 8.1 Hz), 7.04 (d, 2 H, *J* = 8.1 Hz), 4.96 (t, 2 H, *J* = 7.7 Hz), 3.44 (t, 2 H, *J* = 7.7 Hz), 2.43–2.35 (m, 2 H), 2.27 (s, 3 H). ^{13}C (75 MHz, $CDCl_3$): δ = 158.4, 144.9, 144.1, 142.4, 139.2, 128.7, 126.0, 125.9, 124.6, 59.4, 32.5, 21.7, 21.4. IR (KBr): ν_{max} = 3434, 1628, 1505, 1190, 1129, 1039, 1012, 812, 691, 571. Mp 120–121 °C. All other synthesized compounds are in accordance with the literature data.

(11) Polystyrene-bound DBU (1.15 mmol/g loading, 1% cross-linked with DVB) was purchased from Aldrich.