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Silver(I) oxide-mediated facile and practical sulfonylation of alcohols

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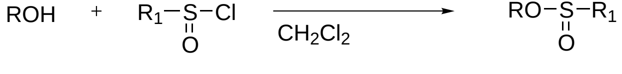
Abstract—Primary and secondary alcohols were efficiently sulfonylated in the presence of silver(I) oxide and potassium iodide in dichloromethane. The sulfonylation occurs under mild, neutral reaction conditions. The ease of isolation of the final product presents a marked advantage over the known methodologies.

The sulfonates are very important intermediates in organic synthesis. They are usually prepared by condensing the corresponding alcohols with sulfonating agents using pyridine or triethylamine[1] as a base. Recently, tetramethylalkyldiamine was reported to be an efficient base for sulfonylation reactions.[2] Other sulfonylations were achieved in aqueous sodium hydroxide[3] when the alcohols are sufficiently hydrophilic. Ring opening of dibutylstannylene acetal with sulfonyl chloride is another method for the monosulfonylation of diols.[4]

Silver(I) oxide (Ag_2O) is a well known reagent for the alkylation of alcohols in the presence of alkyl halide.[5,6] However, sulfonylation of alcohols with Ag_2O was yet to be reported in the literature. Herein, we would like to report that Ag_2O is an excellent reagent to promote sulfonylation of alcohols and diols in the presence of sulfonyl chloride and a catalytic amount of potassium iodide (KI) (Scheme 1).

The Ag_2O promoted sulfonylation described herein presents several advantages over the known methods. For instance, the reaction proceeds in neutral media and necessitates no work-up. Moreover, the reaction does not produce any chloride by-product[2] and the sulfonates are often isolated pure after a simple filtration; if purification is required, a short column suffices to yield a clean product.



Scheme 1.

General method for the sulfonylation of alcohols with Ag_2O: To a stirred solution of alcohol (1 mmol) in CH_2Cl_2 (4 mL) was added freshly prepared Ag_2O[6] (1.5–2.0 mmol), TsCl (1.1–2.0 mmol) and KI (0.2–2 mmol). The mixture was then stirred at room temperature or at 40°C until complete consumption of the alcohol (Table 1, conditions A, B and C). The reaction was filtered and the solvent evaporated. The product was further purified by flash chromatography. The results are summarized in Table 1.

In the absence of KI, the alcohols react very slowly with the sulfonating agent and the yields are generally low. For example, the methoxyethanol, when treated with tosyl chloride (TsCl) and Ag_2O in dichloromethane, the corresponding tosylate was isolated, after 36 h, in only 42% yield.[‡] However, when a catalytic amount of KI was added to the reaction medium, the yield increased to 60% within 5 h (entry 1, condition A). The KI accelerates the reaction rate by converting in situ the tosyl chloride into the much more reactive tosyl iodide.[§] The yield was significantly improved when the reactions were heated at 40°C (con-

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[‡] No reaction took place in the absence of Ag_2O.

[§] In addition to its role as an insoluble base and as a halide acceptor, Ag_2O probably facilitated the Finklestein-like reaction with KI; only starting material was recovered from the reaction of TsCl with KI in CH_2Cl_2 after 2 days. However, addition of Ag_2O to a mixture of TsCl and KI resulted in the disappearance of starting material

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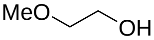
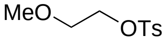
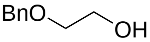
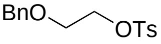
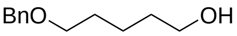
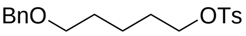
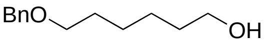
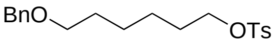
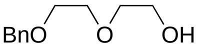
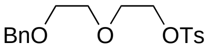
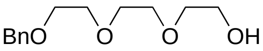
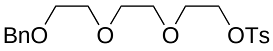
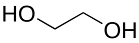
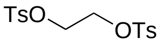
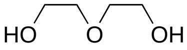
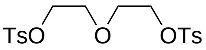
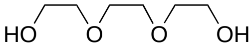
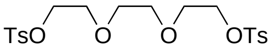
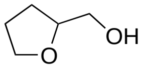
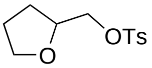
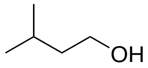
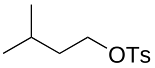
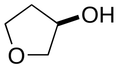
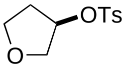
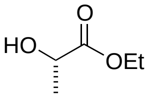
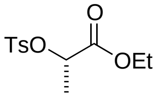
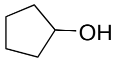
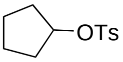
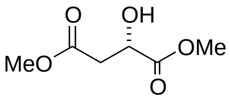
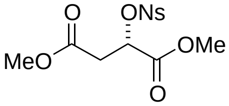
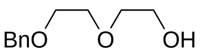
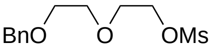
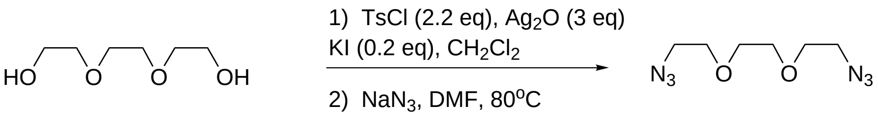
Table 1. Ag_2O-mediated sulfonylation of alcohols

Entry	Alcohol	Conditions[a]	Sulfonate	Yield
1		A B		60% 94%
2		C		95%
3		A B C		12% 56% 96%
4		C		90%
5		A		94%
6		A		99%
7		C[b]		92%
8		A[b]		91%
9		A[b]		98%
10		C		91%
11		C		88%
12		C		89%
13		B		93%
14		C		66%
15		A[c]		92%
16		A[c]		91%

[a] Conditions: A: Ag_2O (1.5 equiv.), TsCl (1.1 equiv.), KI (0.2 equiv.), 20°C, B: Ag_2O (1.5 equiv.), TsCl (1.1 equiv.), KI (0.2 equiv.), 40°C, C: Ag_2O (2.0 equiv.), TsCl (2.0 equiv.), KI (2.0 equiv.), 40°C. [b] Reagent quantities of condition A were doubled. [c] NsCl and MsCl were used as sulfonating agent.

dition B). In some case as in entry 3, the use of 2 equiv. of reagent afforded high yields of the sulfonate (conditions C). On the other hand, condition A was enough to convert oligoethylene glycols to their corresponding tosylates in excellent yields (entries 5–9). Secondary tosylates (entries 12–14) were also obtained in high yields. Other sulfonating agents such as *para*-nitrobenzenesulfonyl chloride (NsCl) and methanesulfonyl chloride (MsCl) gave excellent yield of the corresponding sulfonate (entries 15 and 16).

Since the reaction does not require any aqueous work-up, the transformation of hydroxyl groups into other functionalities can be achieved straightforward without isolating the intermediates. For example, treatment of triethylene glycol under the present conditions followed



Scheme 2.

by an S_N2 displacement of the ditosylate with sodium azide afforded the corresponding diazide in 85% overall yield (Scheme 2).

In conclusion, silver(I) oxide combined with potassium iodide is an efficient reagent system to mediate sulfonylation of alcohols in high yield under mild reaction conditions. A key merit of the present method is its applicability in neutral conditions. Thus, base- or acid-sensitive substrates are sulfonylated without detecting any side-products during the course of the reaction. All compounds were characterized by NMR, IR and MS and are consistent with the assigned structures.[7]

Acknowledgements

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6. Tanabe, M.; Peters, R. H. *Org. Synth. Coll. Vol. VII* **1990**, 386.
7. Selected spectral data for the product of entry 13: ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.21 (t, $J=7.5$ Hz, 3H), 1.51 (d, $J=6.0$ Hz, 3H), 2.44 (s, 3H), 4.11 (q, $J=7.7$ Hz, 2H), 4.30 (q, $J=6.0$ Hz, 1H), 7.34 (d, $J=7.5$ Hz, 2H), 7.82 (d, 7.5 Hz, 2H); ^{13}C NMR (65 MHz, $CDCl_3$): δ 13.9, 18.4, 21.65, 61.8, 74.1, 128.0, 129.8, 133.4, 145.1, 169.0.