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4-Nitrophenyltriflate as a New Triflating Agent

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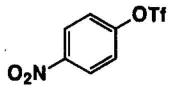
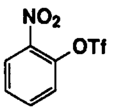
Abstract: Aryl triflates were prepared under mild conditions using 4-nitrophenyl triflate (1) as a stable, crystalline triflating agent. © 1997, Elsevier Science Ltd. All rights reserved.

Aryl triflates are very important synthetic intermediates and are usually prepared by treatment of the corresponding phenols with triflic anhydride in the presence of a base such as pyridine and triethylamine.[1] More convenient procedures using other reagents such as imidazole triflate,[2] *N*-phenyltriflimide[3] and *N*-(2-pyridyl)triflimide[4] have been proposed . We disclose herein an efficient method for introduction of the triflate group employing the readily prepared 4-nitrophenyl triflate (1) as a stable, crystalline [mp: 52-53°C (EtOAc/heptane), Lit[2] 53°C] new triflating reagent.



1



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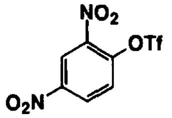
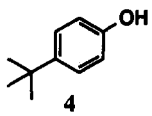
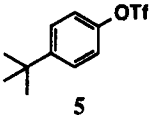
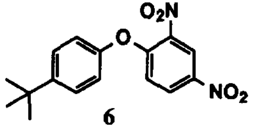
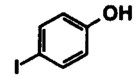
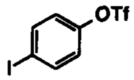
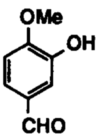
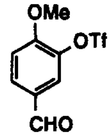
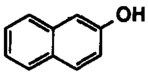
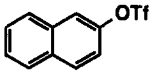
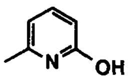
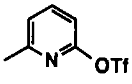


3

The known 4-nitrophenyltriflate (**1**), 2-nitrophenyltriflate (**2**) and 2,4-dinitrophenyltriflate (**3**)[1] were prepared in high yields by reacting the corresponding phenols with triflic anhydride under standard conditions. We first examined the reaction of 4-*t*-butylphenol (**4**) with reagents **1-3** (Table 1). In DMF at room temperature in the presence of 2 equivalents of K_2CO_3, the reaction of **1** or **2** with **4** gave 4-*t*-butylphenyl triflate (>80% yield) together with regeneration of the corresponding nitrophenol. Control experiments showed that **1** is more reactive than **2** as triflating agent. No biaryl ether resulting from the S_NAr reaction was detected in either experiments. A different reactivity profile was, however, observed for the 2,4-dinitrophenyltriflate (**3**). In this case, exclusive S_NAr reaction took place to give the coupling product (biaryl ether **6**, entry d) in analogy with Hamilton's observations using 2,6-dinitrophenyltosylate.[5] Based on these results, K_2CO_3-DMF were employed as standard conditions using **1** as triflating agent for other substrates. The results, depicted in table 1, show that both electron rich and poor arylphenols could be triflated in good to excellent yields. Naphthol (entry g) and heteroaromatic compound such as 2-hydroxy-6-methyl pyridine (entry h) can also be transformed into triflates under identical conditions.

It was found that the positive charge of **1** was largely located on sulfur atom rather than on carbon atom (polarity index $P = I_S/I_C = 12.1$ for **1**).[6] As a consequence, a low polarizable nucleophile such as phenoxide should attack preferentially on sulfur atom (S-O scission) in agreement with experimental observations. It is interesting to note that the reaction of **1** with soft nucleophiles such as secondary amines gave exclusively diaryl amines resulting from S_NAr reaction (C-O scission).[7]

Table 1. Preparation of Aryl Triflate Using Nitrophenyl Triflate as Triflating Agents

Entry	Phenols	Conditions^a	Product	Yield, %^{b}
a	 **4**	K_2CO_3, DMF, **1**, 4h	 **5**	83
b	**4**	CsF, MeCN, **1**, 22h,	**5**	88
c	**4**	K_2CO_3, DMF, **2**, 10h	**5**	89
d	**4**	K_2CO_3, DMF, **3**, 2h	 **6**	91
e	 **7**	K_2CO_3, DMF, **1**, 1.5h	 **8**	90
f	 **9**	K_2CO_3, DMF, **1**, 2h	 **10**	92
g	 **11**	K_2CO_3, DMF, **1**, 1h	 **12**	92
h	 **13**	K_2CO_3, DMF, **1**, 4h	 **14**	75

^{a} All reactions were performed on 0.5-1 mmol scale at room temperature; ^{b} Isolated yield.

In summary, 4-nitrophenyltriflate (**1**) is an excellent triflating agent. It is not hygroscopic and appears to be indefinitely stable. From the view point of atom economy,[8] **1** is superior to *N*-phenyltriflimide[3] and *N*-(2-pyridyl)triflimide[4] where one of the two triflate groups was wasted.

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