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Straightforward conversion of alcohols into dibenzenesulfonimides

Emerson Giovanelli, Eric Doris* and Bernard Rousseau

Service de Marquage Moléculaire et de Chimie Bioorganique, DSV/DBJC, CEA/Saclay, 91191 Gif-sur-Yvette Cedex, France

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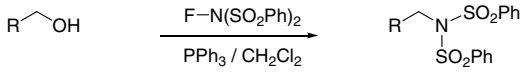
Abstract—The reaction of various alcohols with *N*-fluorodibenzenesulfonimide and triphenylphosphine leads to the corresponding dibenzenesulfonylated amines in high yields.

The conversion of oxygen- into nitrogen-containing compounds is a key transformation in organic synthesis.[1] Several methods have been developed for this purpose. For example, the synthesis of substituted amines from the corresponding alcohols is a well established transformation.[2] However, in most cases, a multi-step process is needed. Indeed, the classical method for O → N exchange requires activation of the hydroxyl group, followed by nucleophilic displacement of the activated oxygen by the nitrogen atom.[3] Direct transformation can nevertheless be achieved using the Mitsunobu reaction[4] and analogous variants.[5] Also, Odom et al. recently reported the titanium-mediated synthesis of allylic amines starting from alkenyl alcohols.[6]

In the present letter, we would like to report an alternative process for the nucleophilic substitution of alcohols by nitrogen derivatives (Scheme 1). Our method involves the utilization of a phosphine in combination with a fluorinated sulfonimide. The treatment in refluxing dichloromethane of various alcohols with 2.5 equiv of triphenylphosphine and an equimolar quantity of *N*-fluorodibenzenesulfonimide led to the corresponding dibenzenesulfonimides.

The scope and limitation of this novel reaction was assessed using a variety of alcoholic substrates. Results



Scheme 1.

are summarized in Table 1. The overall yields are in most cases excellent and the method has successfully been extended to diversely substituted alcohols. The reaction is high yielding with primary alcohol substrates such as 3-methylbutan-1-ol (entry 1) and *trans*-pent-2-en-1-ol (entry 3). It is noteworthy that in the latter case, only one product was observed, despite the propensity of allylic systems to participate in $S_{N'}$ pathways. In the case of a 1,2-diol (entry 4), a selective mono-substitution (>95:5) was obtained affording the corresponding amino-alcohol derivative in 90% yield. The process is equally efficient with benzylic (entry 2) and secondary alcohols (entries 5 and 6) although extended reaction time (15 h) and excesses of both reagents (3.5 equiv) were necessary in the case of entry 6 to obtain a good yield of isolated product. Our attempts to extend the abovementioned reaction to a tertiary alcohol (e.g., α,α-dimethylbenzenepropanol) were unsuccessful as the latter underwent facile β-elimination leading to a mixture of alkenes (entry 7). Taken together, the isolated yields of products indicate the following order of reactivity for the starting alcohols: primary ≈ benzylic > secondary ⋙ tertiary.

The stereochemical outcome of the process was also investigated. Accordingly, the reaction of (*S*)-(−)-1-phenylethanol with triphenylphosphine/*N*-fluorodibenzenesulfonimide afforded the expected dibenzenesulfonimide in high yield with inversion of configuration (entry 5). This is indicative of a predominant S_N2 type mechanism. However, the enantiomeric excess of the product dropped to 50%.[7] This partial loss of optical purity suggests either the emergence of a competing S_N1 mechanism or in situ racemization of the dibenzenesulfonimide product. However, the latter option was rejected as no loss of optical purity was detected when

* Corresponding author. Tel.: +33 169 08 80 71; fax: +33 169 08 79 91; e-mail: eric.doris@cea.fr

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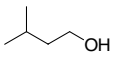
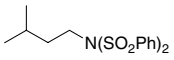
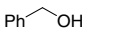
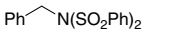
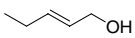
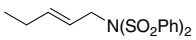
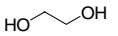
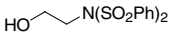
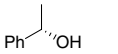
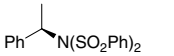
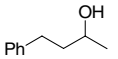
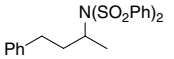
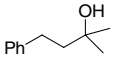
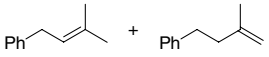
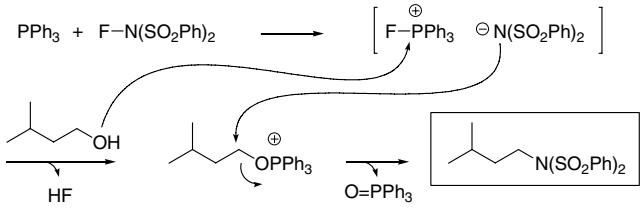
Table 1. Examples of alcohol substitution by dibenzenesulfonimide

Entry	Alcohol	Product(s)	Yield (%)
1			99
2			95
3			99
4			90
5			90
6			87
7			58[a]

[a] Products were obtained in a 3/2 ratio.



Scheme 2.

an authentic sample of (+)-*N*-(1-phenylethyl)dibenzenesulfonimide was subjected to the standard experimental conditions. Hence, the S_N1 mechanism is probably concurrently operative in this case due to the preferential stabilization of the benzylic carbocation.

A postulated reaction mechanism is illustrated in Scheme 2 for the synthesis of *N*-(3-methylbutyl)dibenzenesulfonimide. As *N*-fluorodibenzenesulfonimide is commonly used as synthetic 'F^{+}' equivalent,[8] we speculate that the initial step involves the reaction of the fluorinated reagent with electron-rich triphenylphosphine. The resulting phosphonium salt then undergoes reaction with the hydroxyl group of the substrate giving rise to an activated leaving group. The HF released during this step is most likely neutralized by the excess of the sulfonimide anion. Finally, the nucleophilic attack of anionic sulfonimide to the carbon atom adjacent to the oxygen affords the expected product along with triphenylphosphine oxide. In this process, *N*-fluorodibenzenesulfonimide plays a dual role, namely a reagent for the activation of PPh_3, and a pronucleophile whose reactivity is unmasked after the initial fluorine atom transfer.

In conclusion, we disclose here a new and efficient reaction for the conversion of alcohols to dibenzenesulfonimides. The process involves the utilization of triphenylphosphine together with *N*-fluorodibenzenesulfonimide. The latter reagent acts not only as an activator of the phosphine but also as the nucleophilic species.

A typical experimental procedure is given for the synthesis of N-(3-methylbutyl)dibenzenesulfonimide: Under N_2, 3-methylbutan-1-ol (30 μL, 0.275 mmol, 1 equiv) was diluted in 3 mL of anhydrous CH_2Cl_2 and *N*-fluorodibenzenesulfonimide (0.217 g, 2.5 equiv) was added in one portion. PPh_3 (0.180 g, 2.5 equiv) was added quickly in small portions and the reaction mixture was stirred under reflux for 4 h. The solvent was evaporated and the crude was purified by silica gel chromatography (cyclohexane/CH_2Cl_2: 3/2) to give 0.100 g (0.272 mmol, 99%) of a white solid.

^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.90 (d, $J = 6$ Hz, 6H), 1.54–1.64 (m, 3H), 3.75 (t, $J = 8$ Hz, 2H), 7.55 (m, 4H), 7.67 (m, 2H), 8.06 (d, $J = 8$ Hz, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 22.2, 25.9, 38.5, 48.2, 128.0, 129.0, 133.8, 140.0. IR (KBr): 3071, 2954, 2870, 1584, 1467, 1449, 1369, 1174 cm^{-1}. MS (ESI-TOF): 368 $[M+H]^+$, 406 $[M+K]^+$, 773 $[2M+K]^+$.

Acknowledgements

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7. Enantiomeric excesses were determined by chiral HPLC using a Chiracel AS 250 × 4.6 mm column, hexane/EtOH: 98/2, 1 mL/min, 35 °C, UV detection.
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