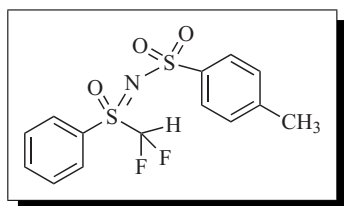


## N-[(Difluoromethyl)oxidophenyl- $\lambda$ 4-sulfanylidene]-4-methylbenzenesulfonamide



[1097192-99-8]  $C_{14}H_{13}F_2NO_3S_2$  (MW 345.38)  
 InChI = 1S/C14H13F2NO3S2/c1-11-7-9-13(10-8-11)22(19,20)  
 17-21(18,14(15)16)12-5-3-2-4-6-12/h2-10,14H,1H3  
 InChIKey = VALBQGJXIYHOGA-UHFFFAOYSA-N

(electrophilic difluoromethylating agent for sulfur, nitrogen, oxygen, and carbon nucleophiles<sup>1,2</sup>)

*Alternative Name:* N-tosyl-S-difluoromethyl-S-phenylsulfoximine.

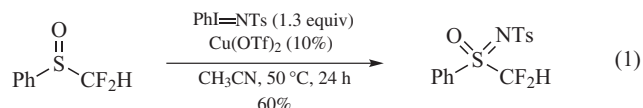
*Physical Data:* mp 96–98 °C.<sup>1</sup>

*Solubility:* sol acetonitrile, DMF, ethyl acetate, petroleum ether, DMSO,  $CH_2Cl_2$ ,  $CHCl_3$ .

*Form Supplied in:* crystalline solid; often prepared by copper-catalyzed oxidative imination of difluoromethyl phenyl sulfoxide ( $PhSOCF_2H$ ) with (tosylimino)phenyliodinane ( $PhI=NTs$ ).<sup>1</sup>

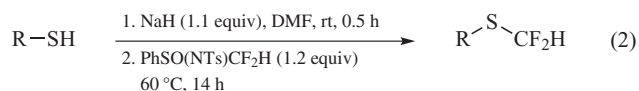
*Handling, Storage, and Precautions:* N-[(difluoromethyl)oxidophenyl- $\lambda$ 4-sulfanylidene]-4-methyl-benzenesulfonamide [ $PhSO(NTs)CF_2H$ ] has high reactivity with bases and reducing metals; store under anhydrous, neutral conditions; use in a fume hood.

**Preparation of N-[(difluoromethyl)oxidophenyl- $\lambda$ 4-sulfanylidene]-4-methyl-benzenesulfonamide [ $PhSO(NTs)CF_2H$ ].** Similar to many other sulfoximines,  $PhSO(NTs)CF_2H$  was prepared by oxidative imination of difluoromethyl phenyl sulfoxide ( $PhSOCF_2H$ ). Initially, the preparation of  $PhSO(NTs)CF_2H$  from  $PhSOCF_2H$  using hydrazoic acid (in situ generated from  $NaN_3$  and concentrated sulfuric acid or oleum) was unsuccessful.<sup>1</sup> However, it was later reported that the treatment of  $PhSOCF_2H$  with 1.3 equiv of (tosylimino)phenyliodinane ( $PhI=NTs$ ) in the presence of a catalytic amount (10 mol %) of copper(II) triflate gave the sulfoximine reagent  $PhSO(NTs)CF_2H$  in 60% yield (eq 1).<sup>1</sup> The  $PhSO(NTs)CF_2H$  reagent is a colorless crystalline solid, whose crystal structure has been determined.<sup>1</sup>

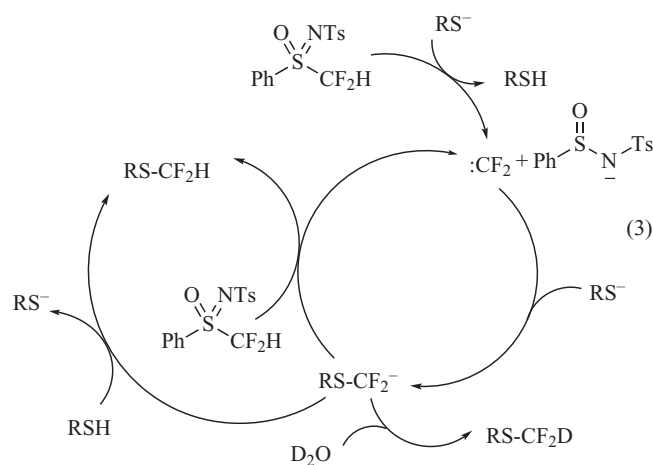
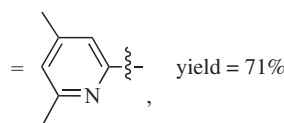


**Difluoromethylation of Sulfur Nucleophiles.** The  $PhSO(NTs)CF_2H$  reagent can be used as a difluoromethylating agent for a variety of structurally diverse thiols (eq 2).<sup>1</sup> Both aromatic and aliphatic thiols were treated with sodium

hydride to give sodium thiolates, and the latter species could successfully react with  $PhSO(NTs)CF_2H$  to give the corresponding difluoromethyl sulfides in good to excellent yields. Even the heteroaromatic thiols are also amenable with this difluoromethylation reaction (eq 2).<sup>1</sup> Although the reaction appears to be a typical  $S_N2$ -type transformation, deuterium-labeling experiments suggested that a difluorocarbene mechanism is formed in the process (eq 3).<sup>1</sup>

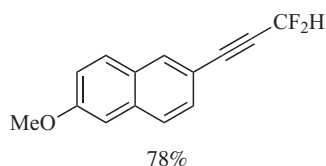
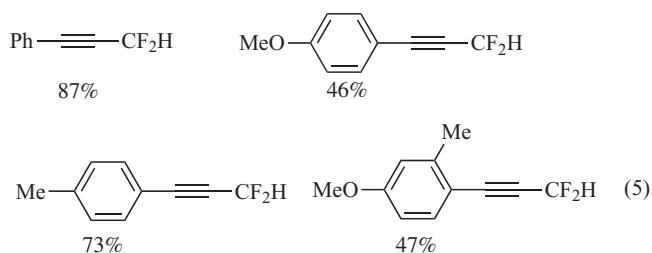
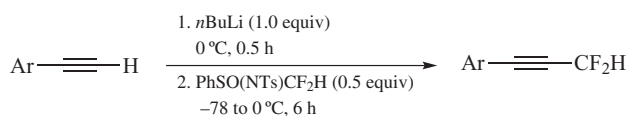
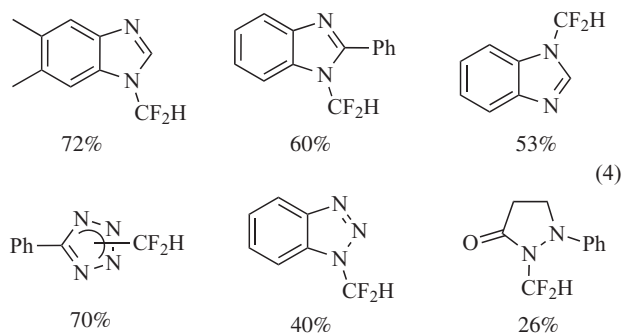
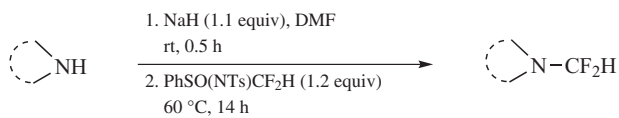


R = Ph, yield = 94%  
 =  $PhCH_2$ , yield = 57%

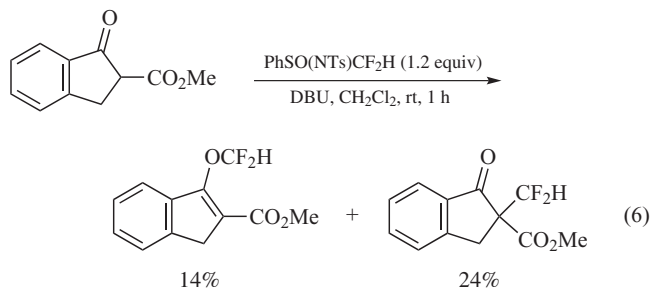


**Difluoromethylation of Nitrogen Nucleophiles.** The  $PhSO(NTs)CF_2H$  reagent can also facilitate the N-difluoromethylation of imidazole derivatives in moderate to good yields (eq 4).<sup>1</sup> Even the phenyltetrazole and benzotriazole can be N-difluoromethylated in 70 and 40% yield, respectively. However, when 1-phenyl-3-pyrazolidone was subjected to the same reaction, only a low yield (26%) of N-difluoromethylated product was obtained (eq 4).<sup>1</sup>

**Difluoromethylation of Carbon Nucleophiles.** The sulfoximine reagent  $PhSO(NTs)CF_2H$  is also able to undergo C-difluoromethylation of acetylene derivatives (eq 5).<sup>1</sup> It was found that the lithium acetylides smoothly reacted with  $PhSO(NTs)CF_2H$  to give the desired difluoromethylated alkynes in moderate to good yield (eq 5).<sup>1</sup>



**Difluoromethylation of Oxygen Nucleophiles.** The *O*-difluoromethylation with PhSO(NTs)CF<sub>2</sub>H is less explored. It was disclosed that when methyl *i*-indanone-2-carboxylate was used to react with PhSO(NTs)CF<sub>2</sub>H reagent, a mixture of 37:63 *O*/*C*-difluoromethylated products was obtained in 38% total yield (eq 6).<sup>2</sup> This indicates that during the difluoromethylation of 1,3-carbonyl compounds with PhSO(NTs)CF<sub>2</sub>H reagent, the *C*-difluoromethylation is preferred over the *O*-difluoromethylation.



1. Zhang, W.; Wang, F.; Hu, J., *Org. Lett.* **2009**, *11*, 2109.
2. Nomura, Y.; Tokunaga, E.; Shibata, N., *Angew. Chem., Int. Ed.* **2011**, *50*, 1885.

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