Electrophilic Azides for Materials Synthesis and Chemical Biology

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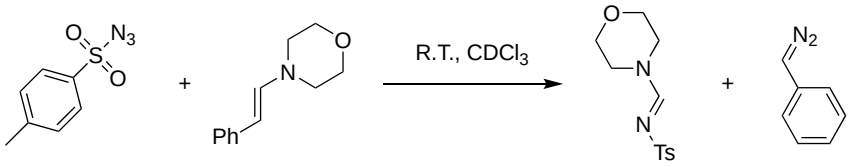
1. Cycloaddition reaction of sulfonyl azide and phenylacetaldehyde enamine

We carried out the cycloaddition reaction of sulfonyl azide with phenylacetaldehyde enamine under similar conditions ($CDCl_3$, room temperature) as in our earlier published paper for PFAAs.[1] The amidine product was isolated in 20-40% yields, accompanied by unanalyzable byproducts. Similar transformation was also reported in the literature.[2]

Below is a specific reaction between tosyl azide and styrylmorpholine (**Scheme S1**), together with the experimental details and NMR spectra (**Figs. S1**, **S2**) of the product.

2. Synthesis of 4-methyl-*N*-(morpholinomethylene)benzenesulfonamide



Scheme S1. Reaction of tosyl azide with styrylmorpholine.

To a solution of (*E*)-4-styrylmorpholine (1.0 mmol) in $CDCl_3$ (1.0 mL), a solution of tosyl azide (1.1 mmol) in $CDCl_3$ (1.0 mL) was added dropwise while stirring at room temperature. The reaction progress was monitored by NMR spectroscopy. After the completion of the reaction (~24 h), the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (EtOAc/hexanes = 1:9) to give the amidine product (R_f = 0.2) as a white powder (yield: 30%). ^{1}H NMR (500 MHz, DMSO-d_6): δ_H 2.36 (s, 3H, Ar-CH_3), 3.58 (m, 8H, morpholine H), 7.34 (d, 2H, Ar-H, J_{HH}= 8.1 Hz), 7.65 (dm, 1H, Ar-H, J_{HH}= 8.2 Hz), 8.29 (s, 1H, NC-*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.64, 44.31, 50.41, 66.04, 66.92, 126.69, 129.51, 139.21, 142.83, 157.69.

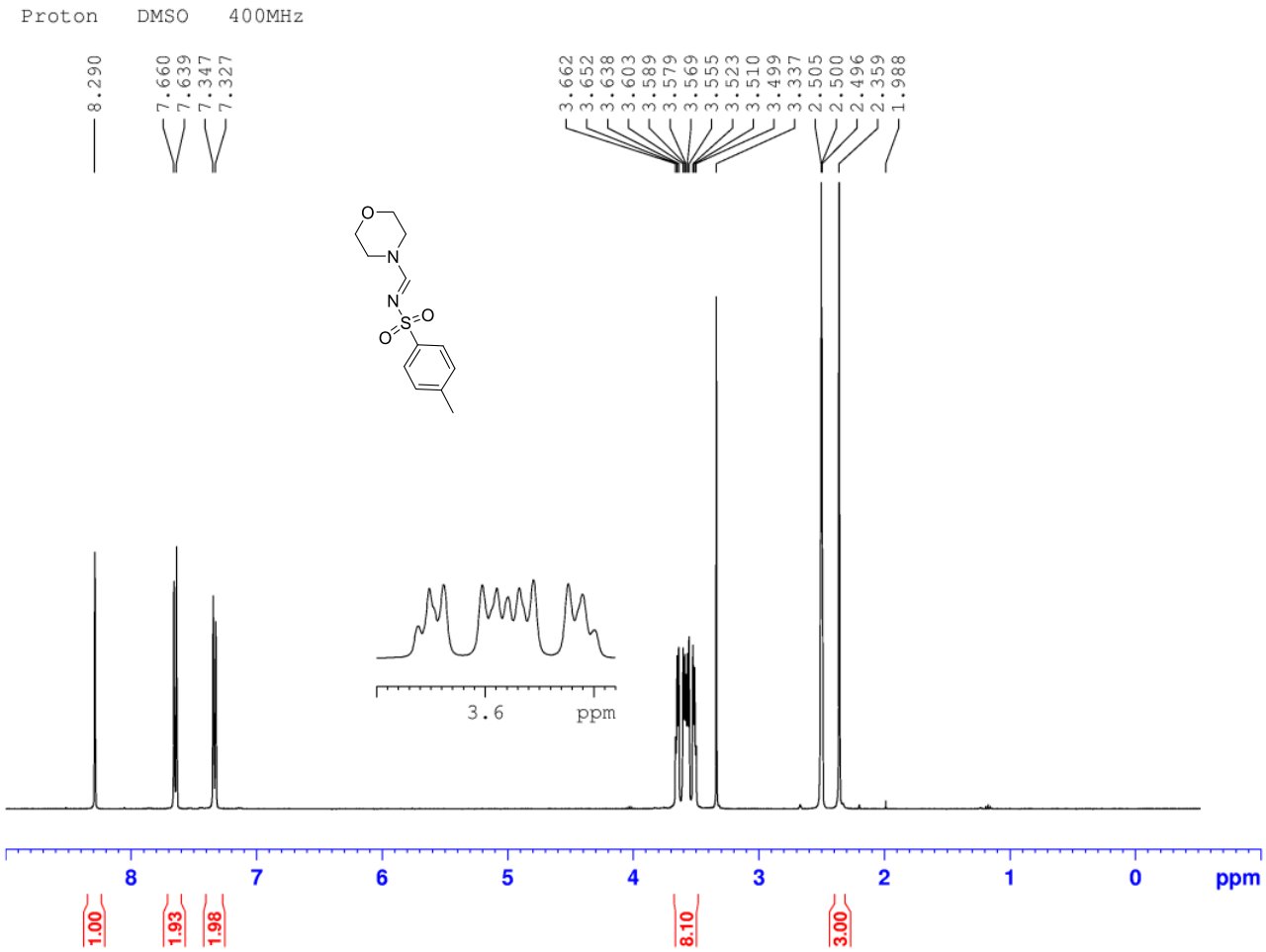


Figure S1. ^{1}H NMR spectrum of 4-methyl-*N*-(morpholinomethylene)benzenesulfonamide in DMSO-d_6.

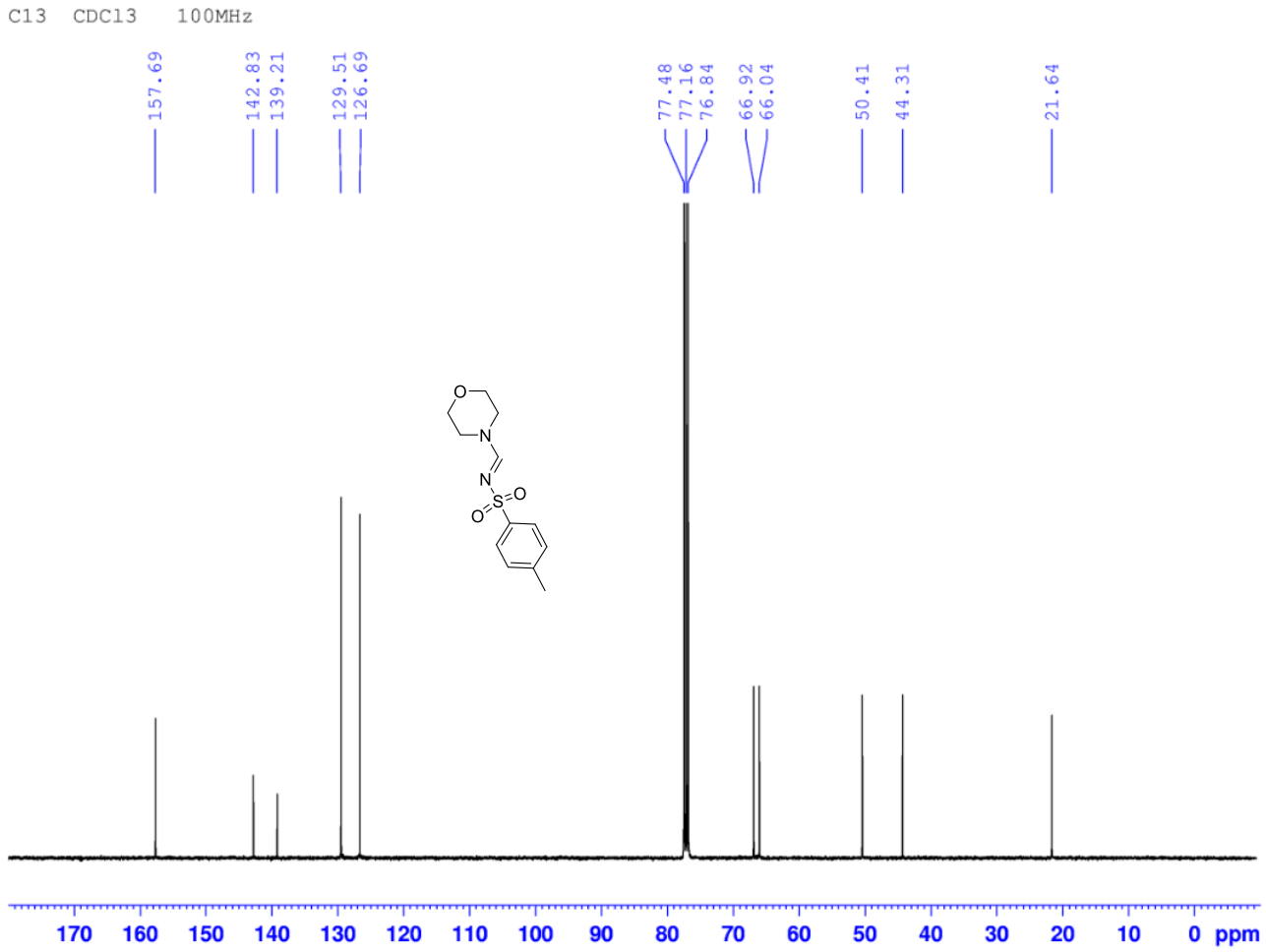


Figure S2. ^{13}C NMR spectrum of 4-methyl-*N*-(morpholinomethylene)benzenesulfonamide in $CDCl_3$.

References

1. Xie, S.; Lopez, S. A.; Ramstrom, O.; Yan, M.; Houk, K. N. 1,3-Dipolar cycloaddition reactivities of perfluorinated aryl azides with enamines and strained dipolarophiles. *J. Am. Chem. Soc.* **2015**, *137*, 2958-2966.
2. Efimov, I.; Bakulev, V.; Beliaev, N.; Beryozkina, T.; Knippschild, U.; Leban, J.; Zhi-Jin, F.; Eltsov, O.; Slepukhin, P.; Ezhikova, M.; Dehaen, W. Reactions of β-Azolylenamines with Sulfonyl Azides as an Approach to *N*-Unsubstituted 1,2,3-Triazoles and Ethene-1,2-diamines. *Eur. J. Org. Chem.* **2014**, 3684-3689.