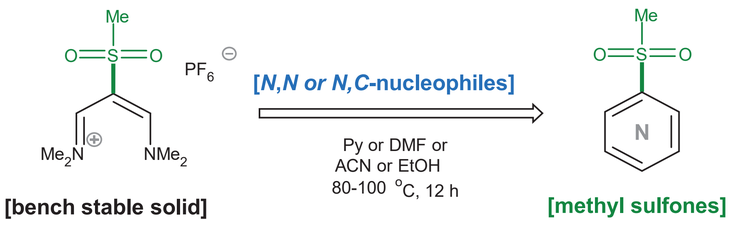
# Versatile Synthesis of Drug-like Methyl Sulfones For Medicinal Chemistry

Yaroslav Poplavskyi,[1] Vasyl Ripenko,[1,2] Sergei Bova,[1] Angelina Biitseva,[1] Yurii V. Dmitriv,[1,3] Andrei A. Tolmachev,[1] Iryna V. Sadkova,[1] Iryna Pishel,[4] Oleksii Grygorov,[4] Vo Quang Huy Phan,[5] H. V. Rasika Dias,[5] Olha Kolodiazhna,[1] Pavel K. Mykhailiuk[1,2]

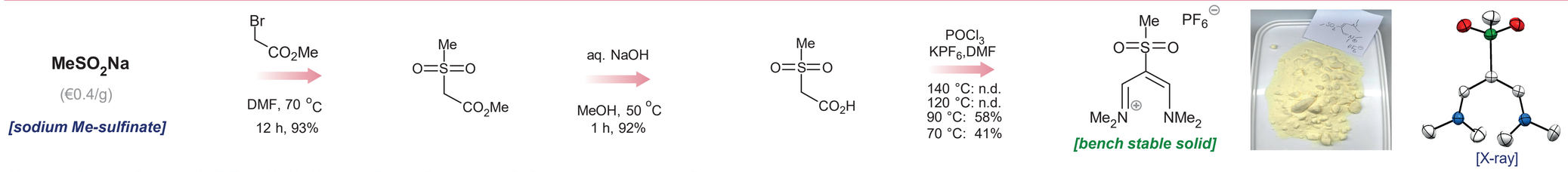
1. Enamine Ltd., Winston Churchill street 78, 02094, Kyiv, Ukraine
2. Chemistry Department, Taras Shevchenko National University of Kyiv, Volodymyrska st. 64, 01601 Kyiv (Ukraine).
3. National Technical University of Ukraine “Igor Sikorsky Kyiv Polytechnic Institute”, 03056 Kyiv (Ukraine).
4. Bienta; Winston Churchill Street 78, 02094 Kyiv (Ukraine).
5. Department of Chemistry and Biochemistry, The University of Texas at Arlington, Arlington, Texas 76019 (United States)

## Introduction and Aim

The methyl sulfone ($MeSO_2$) group is a well-established polar substituent in medicinal and agrochemical compounds, commonly used alongside methoxy, dimethylamino, acetyl, and acetoxy groups. A substructure search of the DrugBank database (accessed on March 14, 2024) identified 31 approved, veterinary-approved, or investigational drugs containing the $MeSO_2$ motif, underlining its relevance in bioactive molecules. 1,2 In this work, we report the development of a novel chemical reagent (compound 1) enabling direct access to methyl sulfones via reactions with a broad range of N,N- and N,C-bis-nucleophiles. This transformation provides previously unreported $MeSO_2$-containing scaffolds with high efficiency, and it is scalable from milligram to multigram quantities. All compounds were fully characterized, and their structural features suggest promising utility in medicinal chemistry, particularly in the design of novel pharmacophores and ligand frameworks for coordination chemistry. This work expands the synthetic toolkit for incorporating $MeSO_2$-based motifs into drug-like molecules.



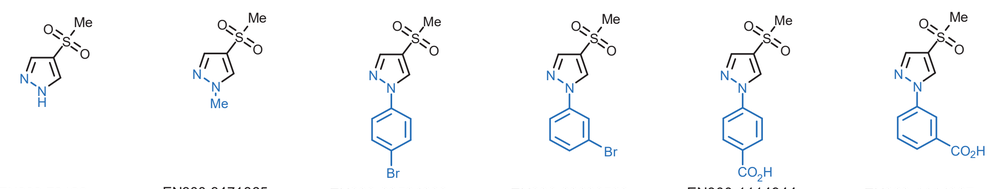

## Preparation of MeSO2-vinamidinium reagent



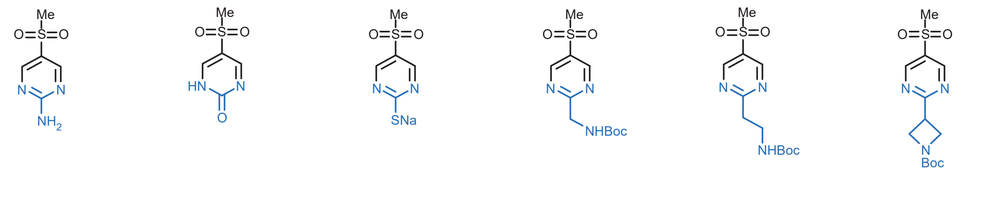

## Synthesis of MeSO2 substituted heterocycles


## Results

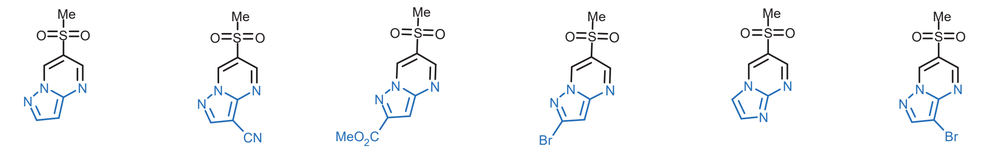
**1,2-*N-N* nucleophiles** (hydrazines)



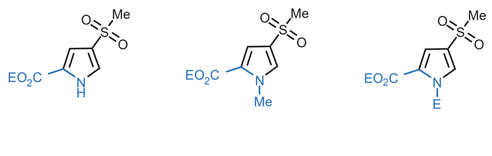

**1,3-*N-N* nucleophiles** (amidines)



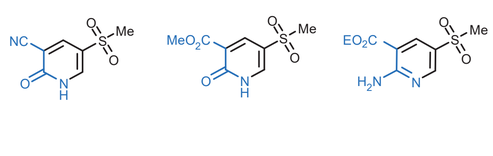

**1,3-*N-N* nucleophiles** (amino heterocycles)



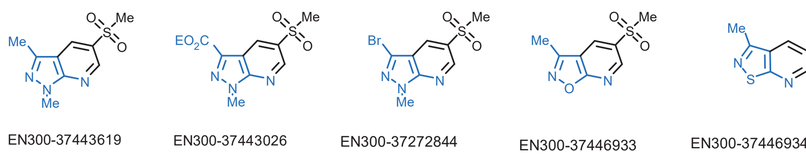

**1,2-*N-C* nucleophiles** (pyrrole synthesis)



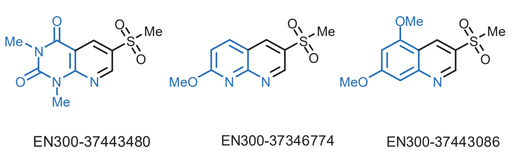

**1,3-*N-C* nucleophiles** (pyridine synthesis)



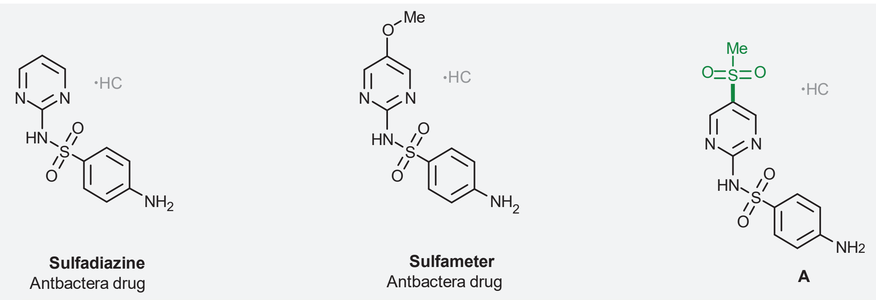

**1,3-*N-C* nucleophiles** (5-membered amino heterocycles)




***1,3-N-C nucleophiles*** (6-membered amino (hetero)aromatics)




## Physicochemical properties of model compounds

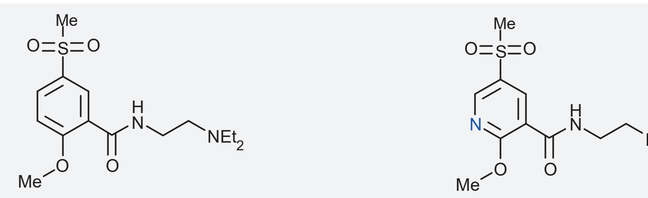



**Sulfadiazine**
Antbactera drug

**Sulfameter**
Antbactera drug

**A**

| Compound | Sol. | clogP | logD | $CL_n$ | $t_{12}$ |
|---|---|---|---|---|---|
| **Sulfadiazine** | 397 | 0.39 | -0.8 | 2* | 1073* |
| **Sulfameter** | 361 | 0.23 | -0.2 | 0* | 7565* |
| **A** | 391 | -0.8 | <-1 | 1* | 1519* |




**Tapride**
Neuroepcdrug

**B**

| Compound | Sol. | clogP | logD | $CL_n$ | $t_{12}$ |
|---|---|---|---|---|---|
| **Tiapride** | 394 | 0.46 | -1 | 0* | 6276* |
| **B** | 393 | -0.16 | -0.7 | 0* | 7257* |

## Contact

Pavel K. Mykhailiuk, Dr. Sci.
pavel.mykhailiuk@gmail.com, mykhailiukchem.org
Enamine Ltd, www.enamine.net
78 Winston Churchill St, 02094, Kyiv, Ukraine

## References

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2.R. Gianatassio, D. Kadish, *Org. Lett*,. **2019**, *21*, 2060–2063.
3.Oleksandr P. Datsenko et al., *Org. Lett.*, 2025.