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Recommended Citation
Matsnev, Andrej V.; Belina, Steven P.; Qing, Si-Yan; Berger, Kyle A.; Scavuzzo, Anthony R.; Dudzinski, Piotr; Dreier, Anna-Lena; Haufe, Günter; and Thrasher, Joseph S., "Recent Advances in the Synthesis and Application of SF5-Containing Organic Compounds" (2016). Chemistry Annual Research Symposium. 3.
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Recent Advances in the Synthesis and Application of SF₅-Containing Organic Compounds

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It is well known that fluorinated molecules play an important role in daily life. For example, organic molecules bearing either a fluorine atom itself or a short perfluorinated substituent such as mono- difluoro-, and trifluoromethyl groups, or pentafluoroethyly and perfluoroisopropyl groups are already widely used in medicinal and agricultural chemistry. In contrast, molecules with long perfluorinated chains have found vast application in materials science. Among the fluorne-containing moieties, the pentafluorosulfanyl (SF₅) substituent occupies a special place.¹ The pentafluorosulfanyl group brings unique properties to organic compounds and often improves their biological activities due to the group’s high chemical and metabolic stability, significant lipophilicity, substantial steric effect, unique geometry, and low surface energy. Here we present new routes towards SF₅-substituted aliphatic and heterocyclic compounds.

Synthesis of new SF₅-containing heterocyclic compounds

2-SF₅CF₂-substituted quinazolin-4(3H)-ones and quinazolines

Quinazolones often demonstrate biological activity and can be used as hypnotic, sedative, analgesic, antibacterial, and antitumor agents. Using pentafluorosulfanylfluoroacetic acid (3), we synthesized the corresponding amides 12, which upon refluxing in glacial acetic acid were transformed into quinazolines 13.

2-Pentafluorosulfanylfluoromethyl-4-chloroquinazoline (16) was synthesized by heating 13b with POCl₃. The halogen atom in compound 16 is reactive and easily undergoes nucleophilic substitution in anhydrous ammonia to produce the corresponding 2-pentafluorosulfanylfluoromethyl-4-aminoquinazoline (17).

Treatment of quinazoline 16 with hydrazine led to 18, which can be used for further cyclization.

2-SF₅CH₂-substituted quinazolin-4(3H)-ones and quinazolines

Using pentafluorosulfanylacetic acid (19),¹ we synthesized quinazoline 21, which upon heating with POCl₃ gave quinazoline 22 and with further reaction with ammonia gave quinazoline 23.

2-SF₅CF₂-substituted benzimidazoles

We successfully synthesized the SF₅CF₂-containing benzimidazole 25 from 4-Boc-protected α-phenylene-diamine 24 by acid catalyzed de-protection/cyclization reaction with trifluoroacetic acid.

References


Acknowledgements

We thank the National Science Foundation (NSF-ICC 1124859) and the Deutsche Forschungsgemeinschaft (Ha 2145/12-1, AOBB 5858/5) for financial support.

Chem. Matsnev, A. V.; Thrasher, J. S.
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Introduction

It is well known that fluorinated molecules play an important role in daily life. For example, organic molecules bearing either a fluorine atom itself or a short perfluorinated substituent such as mono-, difluoro-, and trifluoromethyl groups, or pentafluoroethyly and perfluoroisopropyl groups are already widely used in medicinal and agricultural chemistry. In contrast, molecules with long perfluorinated chains have found vast application in materials science. Among the fluorne-containing moieties, the pentafluorosulfanyl (SF₅) substituent occupies a special place.¹ The pentafluorosulfanyl group brings unique properties to organic compounds and often improves their biological activities due to the group’s high chemical and metabolic stability, significant lipophilicity, substantial steric effect, unique geometry, and low surface energy. Here we present new routes towards SF₅-substituted aliphatic and heterocyclic compounds.

Synthesis of SF₅CF₄(O)OH

Using the aforementioned methods we synthesized pentafluorosulfanyl-4-fluorooctanoic acid (2)² using the following procedure:

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