

// NEUE KLASSE VON REAGENZIEN FÜR DIE ALKYNIERUNG UND CYANYLIERUNG & NBSP;

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HINTERGRUND

Scientists from the University of Göttingen developed novel reagents to attach terminal C-C or C-N triple bonds to organic molecules. These novel, sulfur based reagents have two striking advantages over the widely used EBX based reagents: They do not suffer from being potentially explosive but still show high alkylation rates with yields up to 90% and the reduced reactivity allows for selection of alkylation sites in one molecule.

PROBLEMSTELLUNG

The chemical versatility of the carbon-carbon triple bond is of high importance for the synthesis of fine chemicals. Therefore, reagents to facilitate alkylation (the introduction of a carbon-carbon triple bond) are highly desirable, not only for industrial chemistry but also for biological and medical applications. The first alkylation-reagent described in literature was based on ethynylbenziodoxolone (EBX) and could be used for gold-catalyzed alkylation of indoles, pyrroles, thiophenes, and furans. But there is an inherent drawback of EBX-based reagents, they are potentially explosive. An enormous effort was undertaken in industry and science, to reduce their tendency to explode. This led to safer alkylation reagents, but this came along with a reduction of the alkylation yields. Thus, especially for industrial purposes there is a strong need for safe and efficient alkylation reagents. The inventors accepted the challenge and developed 5-(alkynyl)benzothiothiophenium triflates, which fill this gap.

LÖSUNG

The inventors used transition-metal catalysis to perform electrophilic alkylation, using the backbone of the Umemoto reagent (a dibenzothiophene). They developed a new class of alkylation reagents, the 5-(alkynyl)dibenzothiophenium triflates, which can be synthesized with high efficiency (Figure1).

In contrast to EBX-based reagents, they do not have the inherent tendency to



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ENTWICKLUNGSSTAND

Prototyp

PATENTSITUATION

PCT anhängig
DE anhängig

CATEGORIES

//Chemie //Synthesen und
Verfahrenstechnik //Neue Substanzen

explode, show an improved chemoselectivity for thiols and they can transfer alkyne groups to Amides.

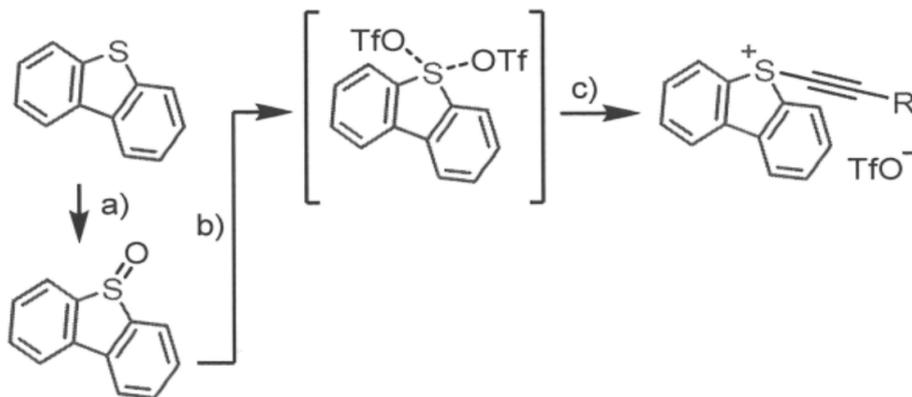


Figure 1) Synthesis of 5-(Alkynyl)benzothiofophenium triflates: (a) TfOH, H₂O₂, (1:2 equivalents), 0-->50°C, for 1h --> 47% yield. (b) Tf₂O (1 equivalents), 50°, 1h --> not isolated. (c) TMS alkyne (1 equiv.) --> R = Ph: 87%, R = p-(CF₃)Ph 97%, R = TIPS 70%.

VORTEILE

- very good alkylation efficiency
- intramolecular selection of alkylation sites is possible
- in contrast to EBX-based reagents there is no inherent tendency to explode
- broad substrate scope and high functional group tolerance
- easy synthesis
- cost effective production as a result of easy synthesis and no tendency to explode

These properties of 5-(Alkynyl)benzothiofophenium triflates makes them a n in many cases superior alternative to the currently preferred EBX-alkynylation reagents.

ANWENDUNGSBEREICHE

Terminal alkynes, are valuable in the synthesis of of fine chemicals in industry as well as for scientific and medical applications. As a result of not beeing explosive, the synthesis of these alkylation reagents can be upscaled. Reagents to attach alkyne-groups to chemicals are needed as basis for complex synthesis and could

be used universally. The increased selectivity allows for selective transfer of alkyne-groups, even in makromolecules.

PUBLIKATIONEN & VERWEISE

Publication Waldecker et al. (<https://doi.org/10.1002/anie.201807418>)

Homepage of Prof. Alcarazo:

(<https://www.uni-goettingen.de/de/forschung/569682.html>)
