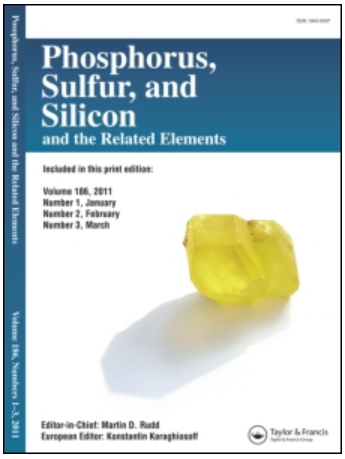

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Hexamethyldisilathiane in Novel Chemical Transformations: Concept of "Counterattack Reagent"

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Hexamethyldisilathiane in Novel Chemical Transformations: Concept of "Counterattack Reagent"

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Deliberate design on utilization of each moiety in the "counterattack reagent," $Me_3SiSSiMe_3$, allows it to accomplish multistep chemical transformations in one flask.

Keywords Bis-*O*-demethylation; carbonyl nitrile; counterattack reagent; hexamethyldisilathiane; oxime; thiohydroxamic acid

Hexamethyldisilathiane ($Me_3SiSSiMe_3$) is commonly used as a sulfur or silicon transfer reagent.[1,2] It can function as a reducing agent as well.[3] When the concept of "counterattack reagent" is applied to its use in organic reactions, intriguing multiple processes could be fulfilled in one flask.

A "counterattack reagent" can achieve at least two transformations *in situ* to give the desired product.[4,5] In the first transformation, this reagent is attacked by the other reactant to give a stable intermediate. In the second transformation, a moiety produced from this initially consumed reagent counterattacks that intermediate. Herein, we illustrate the multifunctions of hexamethyldisilathiane as a "counterattack reagent" in the following four topics.

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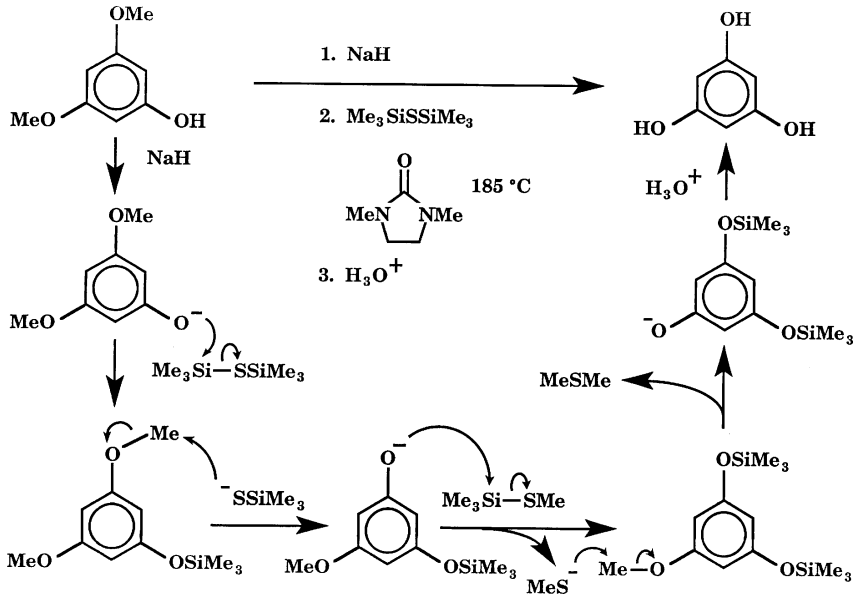
BIS-*O*-DEMETHYLATION OF ARYL METHYL ETHERS[6]

Difficulty exists in using nucleophilic reagents to accomplish sequential demethylation of dimethoxyarenes in one flask. This is due to the unfavorable generation of dianioic intermediates. We successfully solved this problem by applying $Me_3SiSSiMe_3$ for bis-*O*-demethylation. A representative example is shown in Scheme 1. Reaction of 3,5-dimethoxyphenol with 1.5 equiv of NaH and then 1.5 equiv of $Me_3SiSSiMe_3$ at 185°C in a sealed tube affords the corresponding triol in 75% yield. Both the nucleophilic centers (*i.e.*, S) and the electrophilic centers (i.e., Si) are allowed to react with intermediates in individual steps. In this bis-*O*-demethylation process, $Me_3SiSSiMe_3$ acts as an "electrophilic" counterattack reagent.



SCHEME 1

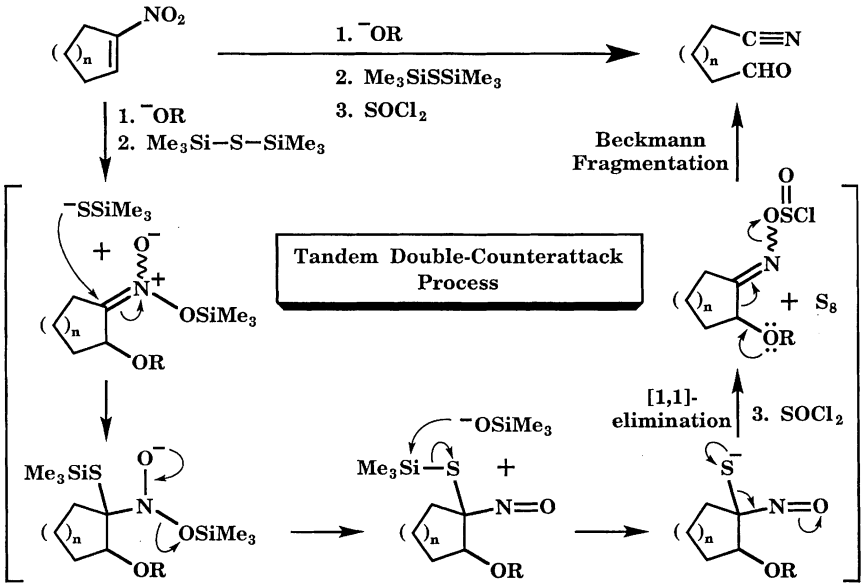
DOUBLE FUNCTIONAL GROUP TRANSFORMATION[7]

The sulfur- and silicon-containing reagent $Me_3SiSSiMe_3$ is also utilized for the performance of double functional group transformations, which are often regarded as arduous tasks to accomplish. The conversion of a nitroalkene to a carbonyl nitrile or an alkenyl nitrile with $Me_3SiSSiMe_3$ goes through a "tandem double-counterattack process." A representative example with a plausible reaction mechanism is illustrated in

Scheme 2. It involves a Michael addition, 1,2-addition, deoxygenation, 1,1-elimination, and Beckmann fragmentation. All of these steps are completed in one flask.

CONVERSION OF PRIMARY NITRO COMPOUNDS TO THIOHYDROXAMIC ACIDS AND THIOHYDROXIMATES[8]

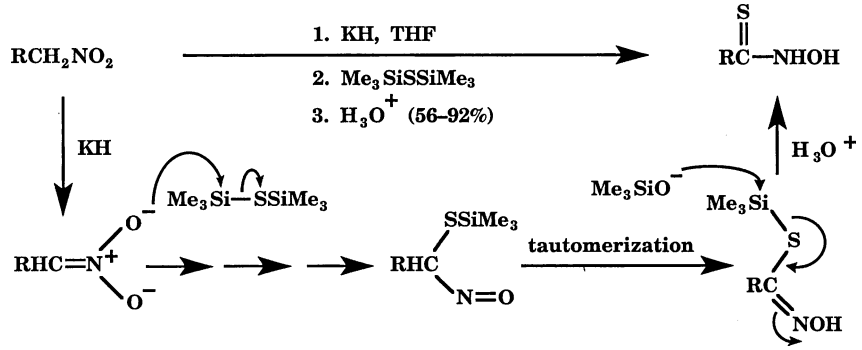
In analytical and biological chemistry, thiohydroxamic acids [RC(=S)NHOH] and thiohydroximates [RC(SR′)=NOH] play various roles. We have developed methods for the preparation of these compounds by application of the counterattack reagent concept. The procedures are experimentally simple and the applied reagents are cost-effective.



SCHEME 2

Treatment of primary nitro compounds with potassium hydride (KH) and $Me_3SiSSiMe_3$ in THF gives thiohydroxamic acids in 56–92% yields. By the same strategy, a thiohydroxamic acid can be obtained in 50% yield by treatment of *trans*-β-nitrostyrene with *i*-PrSLi in THF and then with $Me_3SiSSiMe_3$. Moreover, reaction of primary nitro compounds with *n*-BuLi and then with $MeSSiMe_3$ or $PhSSiMe_3$ (instead of $Me_3SiSSiMe_3$) produces the corresponding thiohydroximates in 61–78% yields. Various functional groups, including esters, acetals, arenes,

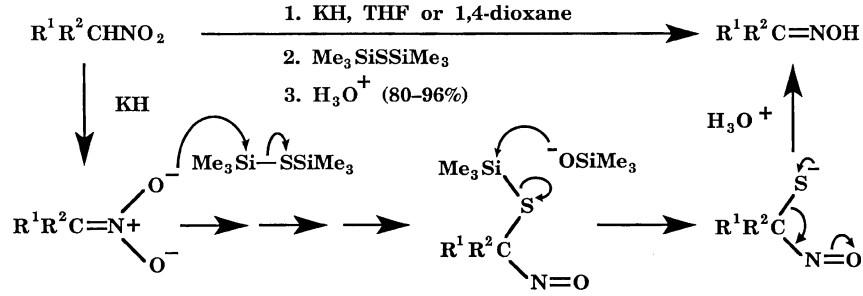
and sulfides, are stable to the reaction conditions. In these "one-flask" reactions, both thiosilanes $Me_3SiSSiMe_3$ and Me_3SiSR' act as counterattack reagents. The roles of $Me_3SiSSiMe_3$ are depicted in Scheme 3.



SCHEME 3

CONVERSION OF SECONDARY NITRO COMPOUNDS TO OXIMES[8]

Secondary nitro compounds, unlike the primary analogs, react with KH and then $Me_3SiSSiMe_3$ in THF or 1,4-dioxane to produce the corresponding oximes upon heating. The yields range from 80 to 96%. Because of lack of the second α proton in secondary nitro compounds, the nitroso intermediates in Scheme 4 cannot tautomerize (*cf.* Scheme 3). Finally, it goes through a 1,1-elimination of the sulfide center and generates oximes as the final products.



SCHEME 4

Use of $Me_3SiSSiMe_3$ as counterattack reagents allows the execution of complicated chemical conversions with minimal operations. Isolation of intermediates is no longer necessary. As a result, it often gives the desired products in appealing yields.

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