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The Reaction of Dimethylalkynylaluminum Reagents with Trimethylsilyldiazomethane: Original Reactivity Leading to New α-Silylated Alkynyl Hydrazones

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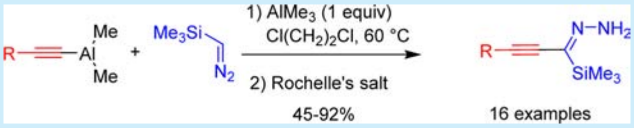
Ⓢ *Supporting Information*

ABSTRACT: Trimethylsilyl (TMS) diazomethane does not react as a homologating reagent but as a C-electrophilic species with dimethylalkynylaluminum reagents. This unprecedented reactivity enables a simple access to unusual α-silylated alkynyl hydrazones.



Diazoalkanes are useful synthetic reagents known to exhibit very diverse reactivity. They can act as free carbene or metal carbene precursors, leading to many important reactions such as insertions, cyclopropanations, 1,2-migrations, cross-couplings, and olefin metathesis. They can also behave as C-nucleophiles, 1,3-dipoles, or *N*-electrophiles.[1] This polyvalent reactivity can be illustrated by the reaction of diazoalkanes with organometallic compounds (Figure 1). Thus, transition metals are known to react with diazo compounds leading to metal carbenes of type **A**.[2] Organomagnesium and lithium compounds have been described to react with the *N*-terminal atom of diazoalkanes, leading to N-substituted hydrazones **B**.[3] More Lewis acidic, less nucleophilic compounds such as boranes[4] or alanes[5] are attacked by the C-terminus atom, leading to zwitterionic compounds **C** that can evolve by 1,2-migration reactions.

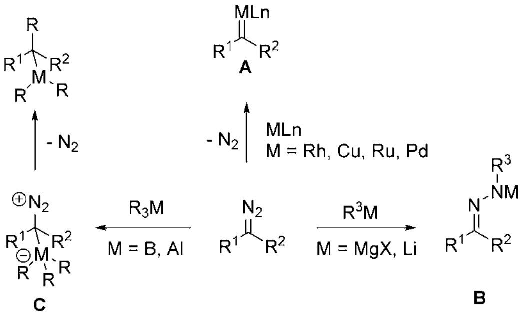


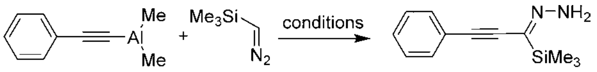
Figure 1. General reactivity of diazocompounds with organometallic reagents.

Despite a few reports on the reaction of diazomethane with several organoaluminum compounds, the reaction of diazocompounds with this class of organometallic reagents has been surprisingly much less investigated than with their borane homologues. The reaction of alkyl, alkenyl, or phenylaluminum reagents with diazomethane leads to intermediates of type **C** and eventually to homologated organoaluminum compounds under carefully controlled conditions to avoid the linear oligomerization (Aufbau) reaction.[5] This reaction is strongly dependent on the Lewis acidity of the reagents.[6]

In our ongoing work on the reactivity of mixed dimethylalkynyl aluminum reagents, we have recently shown that these reagents can act as nucleophiles,[7] but also formal dipolarophiles.[8] We were therefore interested in investigating their reactivity with trimethylsilyldiazomethane (TMS diazomethane), as this diazo compound is known to behave as a dipole reagent with alkynes[9] as well as a C-nucleophile with organoboron compounds, leading to intermediates of type **C**.[10]

Our first experiments with dimethylalkynylaluminum **1a** did not afford any of the expected products, but led to the formation of α-silylated hydrazone **2a** in 34% yield (Table 1, entry 1). The unprecedented electrophilic behavior of TMS diazomethane and the uniqueness of the product prompted us

Table 1. Optimization of the Reaction Conditions: Solvent and Additives[a]



1a **2a**

entry	solvent	temp (°C)	additive	time (h)	yield (%)
1	toluene	25	–	12	34
2	toluene	25	–	60	53
3	toluene	25	Et_3N[b]	48	0
4	toluene	25	$AlMe_3$[c]	48	65
5	toluene	60	$AlMe_3$	48	78
6	CH_2Cl_2	40	$AlMe_3$	24	71
7	DCE	60	$AlMe_3$	24	92

[a]Reaction conditions: **1** (1 mmol in solvent), TMS diazomethane (2 M in Et_2O, 1.5 mmol). [b]1 equiv of NEt_3. [c]1 equiv of $AlMe_3$ (2 M in toluene).

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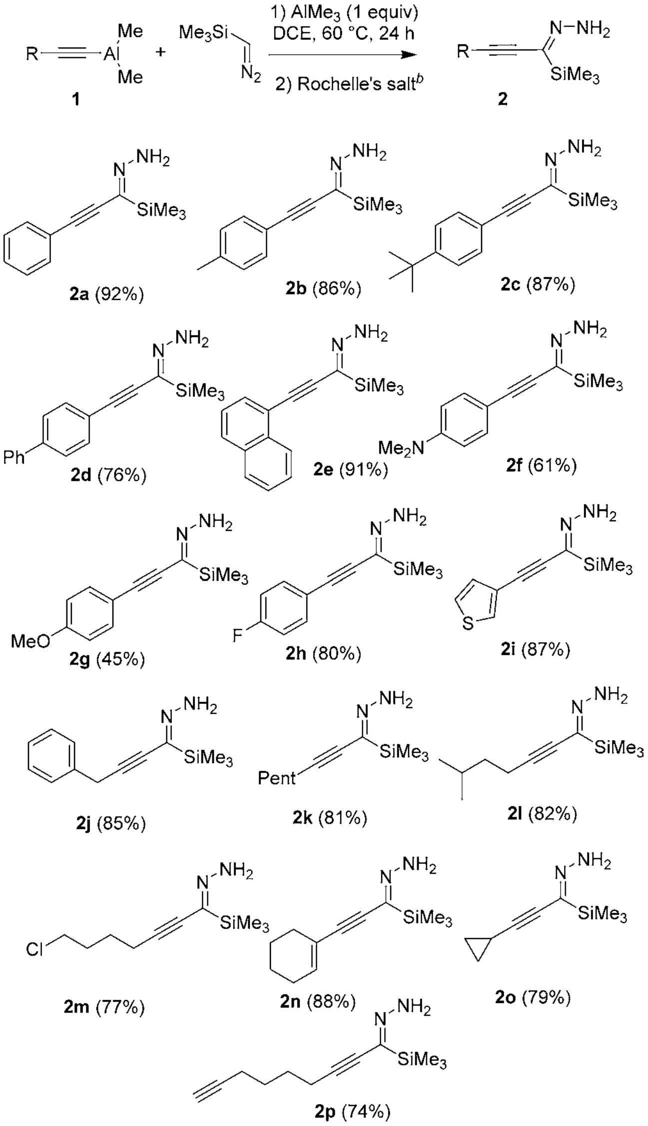
to investigate this reaction further. A longer reaction time led to an improved yield of 53% (Table 1, entry 2). Interestingly, the reaction was inhibited by the addition of 1 equiv of triethylamine (Table 1, entry 3).[7a] On the contrary, addition of 1 equiv of trimethylaluminum led to an improved chemical yield of 65% after 48 h (Table 1, entry 4).[11] The best conditions were obtained by heating the reaction mixture at 60 °C in 1,2-dichloroethane (DCE) for 24 h, leading to compound **2a** in 92% chemical yield (Table 1, entry 7).

The scope of this reaction was then investigated using optimized conditions with a large variety of dimethylaluminum alkynides (Scheme 1). In all the cases, the corresponding silylated hydrazone was obtained as the sole isolated product in yields ranging from 45% to 92%. The reaction tolerated both alkyl- (**2b**, **2c**) or heteroatom- (**2f**−**h**) substituted arylalkynyl groups, as well as heterocyclic (**2i**) or functional alkyl (**2m**), alkenyl (**2n**), or alkynyl (**2p**) moieties.

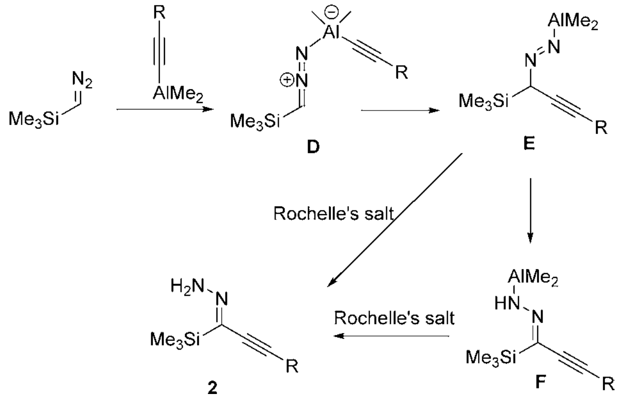
Scheme 1. Scope of the Reaction[a]



[a] All the dimethylalkynyl aluminum reagents have been prepared using a base-catalyzed terminal alumination of the corresponding alkynes.[7c] [b] All the reactions were quenched using a 2 M aqueous solution of Rochelle's salt (also named Seignette's salt). This potassium sodium tartrate enables a neutral treatment of the reaction and breaks up emulsions generally obtained by standard hydrolysis of organoaluminum species.

A plausible mechanism for the formation of **2** is depicted in Scheme 2. For steric and electronic reasons,[12] the reaction between **1** and TMS diazomethane does not lead to intermediate **C** but to N-coordinated species **D** which is activated toward nucleophilic attack, leading to intermediate **E**.[13] Isomerization before (intermediate **F**) or during the acidic quench of the reaction results in the formation of compound **2**.

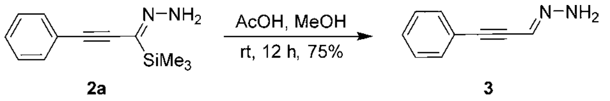
Scheme 2. Proposed Mechanism for the Formation of Silylated Hydrazones



Although acylsilanes are well-known reagents,[14] the corresponding hydrazone derivatives are much less documented.[15] To the best of our knowledge, unsubstituted α-silylated alkynyl hydrazones have never been described and their reactivity is unknown. A few synthetic applications of these species have been investigated.

A simple transformation of silylated alkynylhydrazones is the protodesilylation. These compounds proved to be quite sensitive to acid traces (they have to be purified on alumina) and can easily lead to the corresponding unsubstituted hydrazone **3** (Scheme 3). The preparation of **3** is not obvious since the condensation of hydrazine with 3-phenylpropiolaldehyde is hampered by the competitive formation of pyrazole.[16]

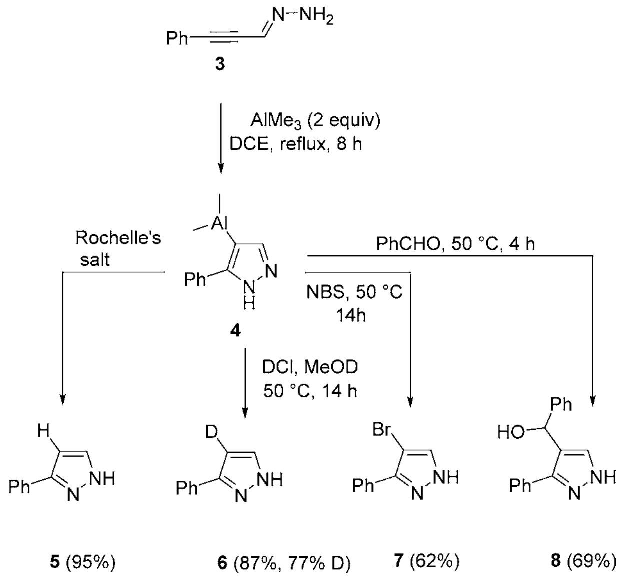
Scheme 3. Protodesilylation of Compound 2a



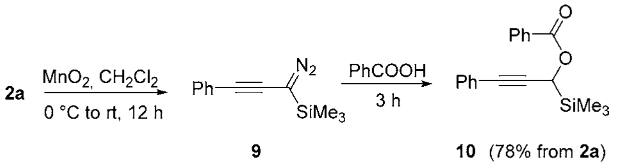
Compound **3** can serve as interesting starting material for new transformations, such as the intramolecular hydrazinoalumination, leading to substituted *N*−*H*-pyrazoles **5**−**8** after reaction with electrophiles (Scheme 4).[17]

More interestingly, compound **2a** can lead to the corresponding diazo **9** under oxidative conditions (Scheme 5).[15] Isolation and characterization of compound **9** in pure form proved to be difficult, but its formation was confirmed by its *in situ* reaction with benzoic acid,[18] leading to the α-benzoyl propargyl silane **10** in 78% overall isolated yield.[19] This example clearly outlines the potential of silylated alkynylhydrazones to be valuable precursors of α-alkynyl α'-trimethylsilyl diazomethane using a simple experimental procedure. Such

Scheme 4. Synthesis of NH-Pyrazoles from 3



Scheme 5. Synthesis of TMS Diazoalkyne 9 and Reaction with Benzoic Acid



diazo compounds have never been described, and their reactivity has to be investigated.[20]

In summary, we have reported the new reactivity of TMS diazomethane with dialkylalkynylaluminum reagents. This unprecedented reactivity enables the preparation of silylated alkynylhydrazones, a new class of reagents. Preliminary reactivity studies revealed that these compounds can be useful precursors to alkynylhydrazones, pyrazoles, and α-benzoyl propargyl silanes. We have also shown that starting from TMS diazomethane, it is possible to access TMS alkynyldiazomethane in only two steps. This new synthetic pathway enables the preparation of a new class of diazo compounds, whose reactivity is currently under investigation in our laboratory.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

General experimental procedures and analytical data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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