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Cobalt-Induced C–N and C–C Bond Formation via Metal-Stabilized α-CF_3 Carbenium Ion

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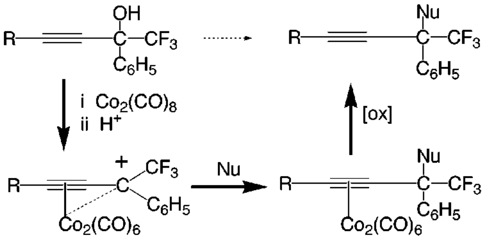
ABSTRACT



An α-CF_3-carbenium ion stabilized by a bimetallic [Co–Co] cluster was prepared and isolated in good yield, starting from the corresponding alcohol by action of HBF_4/Et_2O. C–N and C–C bonds with nitrogen and carbon nucleophiles could be easily formed. Subsequent decomplexation gave the free substituted *β*-CF_3 alkynes in good yields.

Trifluoromethyl alcohols are readily obtained by trifluoromethylation of carbonyl compounds using CF_3SiMe_3 as reagent.[1] However, their synthetic utility for introducing various functionalities α to a CF_3 group is limited because of difficult substitution by either S_N1 or S_N2 processes.[2] The electron-withdrawing character of the CF_3 group strengthens the C−O bond. Furthermore, in S_N2 processes, combination of steric and electronic repulsion of the incoming nucleophiles by fluorine atoms decrease the reaction rate, and harsh conditions are often required.[3] S_N1 processes are also limited by the high energy level of α-trifluoromethyl carbenium ions. However, the latter have been postulated as intermediates or generated under forcing conditions. In most cases they are stabilized by adjacent electron donor substituents such as aryl groups or heteroatoms.[4] In some rare cases they are sufficiently stabilized, for example by two electron-donating substituents, to be observable by NMR spectroscopy or in the gas phase.[5]

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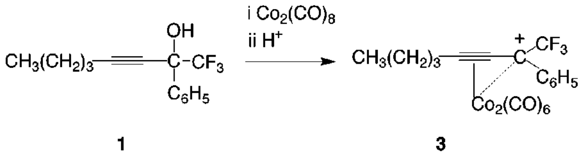
Bimetallic complexes of propargylium ions have been shown to be versatile agents for C−C, C−N, and C−S bond formation,[6] and we have previously reported that an α-CF_3-propargylium ion stabilized by a bimetallic [Co−Mo] cluster could be isolated.[7] This stimulated our interest in the reactivity of such α-CF_3-carbenium ions toward nitrogen and carbon nucleophiles. In addition, in these clusters the metal centers protect the triple bond functionality via coordination and allow an easy preparation of polyfunctional CF_3-substituted compounds which are very well-known as important intermediates in organic fluorine chemistry.

This paper is devoted to the synthesis and the reactivity of the α-CF_3-carbenium ion stabilized by a bimetallic [Co−Co] cluster, derived from the trifluoromethyl alcohol $CH_3(CH_2)_3C{\equiv}CC(C_6H_5)(CF_3)OH$ (**1**), obtained by action of the Grignard ($CH_3(CH_2)_3C{\equiv}CMgBr$) on α,α,α-trifluoracetophenone.

The dicobalt cluster $(Co_2(CO)_6)[CH_3(CH_2)_3C{\equiv}CC(C_6H_5)(CF_3)OH]$ (**2**) was prepared from the alcohol **1** and dicobalt octacarbonyl by the classical procedure.[8] Action of HBF_4/Et_2O on **2** in ethereal solution under argon afforded the carbenium ion **3** which appeared as an insoluble brown red oil (Scheme 1).

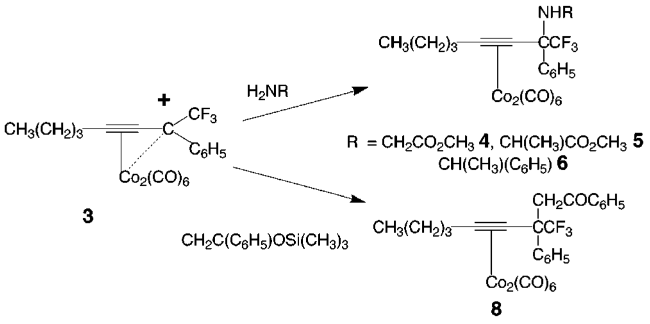
Scheme 1. Preparation of α-CF_3-Stabilized Carbenium Ion



After several washings with ether and quick drying under vacuum, the α-CF_3-propargylium ion **3** was placed in methylene chloride (CH_2Cl_2) to be used as electrophilic reagent. It is worth noting that this carbenium ion, substituted by a phenyl group, is stabilized enough by the [Co_2] cluster to be isolated, unlike the corresponding α-CH_3,α-CF_3-propargylium ion which required a [Co−Mo] cluster.[7] However, the lifetime of **3** was not long enough to allow complete characterization. In ^{19}F NMR, the CF_3 signal shifted from −73.9 ppm (alcohol **2**) to −58.5 ppm, and in ^1H NMR, the signal of the aromatic protons shifted from 7.5 to 9.5 ppm, which clearly indicates the carbocation formation. This latter readily reacted with water to give back the starting alcohol **2**.

We then investigated the reaction of **3** with amine derivatives (Scheme 2). In solution in CH_2Cl_2, at −10 °C, the carbenium ion **3** immediately reacted with glycine or L-alanine methyl esters and (*S*)-(+)-methylbenzylamine to provide the complexed amino derivatives **4**, **5**, or **6**, which could be isolated after purification on SiO_2 preparative plates, in 62%, 52%, and 54% yields, respectively, based on starting complexed alcohol **2** (compounds **5** and **6** were obtained as a mixture of diastereomers).

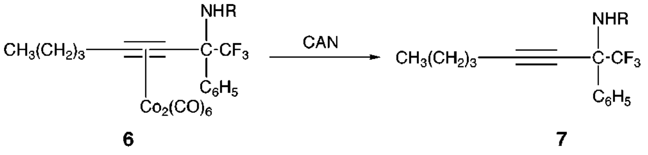
Scheme 2. Formation of C−N and C−C Bonds from Carbenium Ion **3**



In the case of **6**, the two diastereomers were separated by chromatography on silica gel, leading to **6a** and **6b** in increasing order of polarity, with $[\alpha]_D = +18.2$ ($c = 0.55$, CH_2Cl_2) and $[\alpha]_D = -14.5$ ($c = 0.55$, CH_2Cl_2) for **6a** and **6b**, respectively.

Decomplexation of **6a** and **6b** is readily obtained using ceric ammonium nitrate (CAN) in methanol solution (−78 °C),[9] leading to the free acetylenic compounds **7a** and **7b** in 83% and 87% yields, respectively (Scheme 3).

Scheme 3. Preparation of the Free Alkyne



Only a few examples of preparation of tertiary trifluoromethylamines are yet reported,[4e,10] and this method appears to be a new alternative.

These results prompted us to study the reactivity of the ion **3** with the silyl enol ether derived from the acetophenone. After 5 min at −10 °C, the adduct **8** was obtained as the

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sole product and could be isolated, after purification, in a 60% yield from the alcohol **2**. Decomplexation of **8** afforded the β-CF_3 alkyne **9** in a 90% yield. The triple bond can be used for further functionalizations.

In conclusion, we have shown that the hydroxyl groups of α-CF_3-propargyl alcohol can be easily substituted in good yields with nitrogen and carbon nucleophiles via the intermediate formation of α-CF_3-carbenium ions stabilized by a bimetallic [Co−Co] cluster. This application of the Nicholas reaction to fluoroalkyl substrates is of great interest in the synthesis of polyfunctional compounds containing a CF_3-substituted quaternary carbon.

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Supporting Information Available: Experimental procedures and full characterization (IR, ^{1}H, ^{13}C, ^{19}F NMR spectra and analysis) for compounds (**1**, **2**, **4**−**10**) are available free of charge via the Internet at http://pubs.acs.org.

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