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Preparation of Trifluoromethyl-Substituted Alcohols from Allylsilanes and Trifluoroacetic Anhydride.

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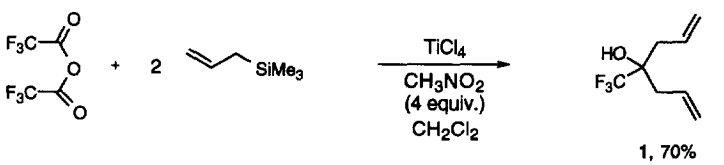
Abstract: The titanium tetrachloride-mediated addition of allyltrimethylsilane or 1,8-bis(trimethylsilyl)-2,6-octadiene and trifluoroacetic anhydride led to trifluoromethyl-diallylcarbinol or (*dl*)-1-trifluoromethyl-2,5-divinylcyclopentanol, respectively, in fair yields; this latter was further converted into several 1-trifluoromethyl-2-vinylcyclopentane derivatives.

The physical properties and chemical reactivities of organic molecules can be dramatically affected by fluorination. Hence, fluoro-organic compounds constitute a rather unique class of products. Among them, partially fluorinated compounds are highly useful for developing novel medicines, agricultural chemicals and new functional materials.[1]

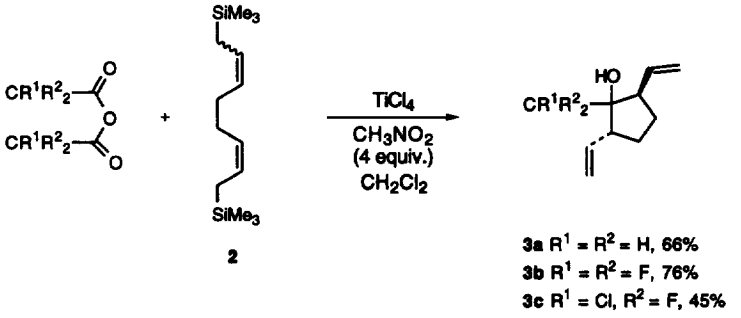
In recent years, the unique biological properties of fluorinated compounds have promoted the development of methods for their syntheses.[2]

It is well known that the Lewis acid-mediated reaction of acyl chlorides and allylsilanes gives rise to allylketones with allylic shift.[3] We have recently shown that the same reaction applied to anhydrides gives rise to diallylalkylcarbinols exclusively.[4] No trace of allylketone was detected. We herein report the condensation of allyltrimethylsilane to fluorinated anhydrides which leads to corresponding fluoromethyldiallylcarbinols.[5] For instance, the trifluoroacetylation of allyltrimethylsilane provides the alcohol **1** in 70% yield.



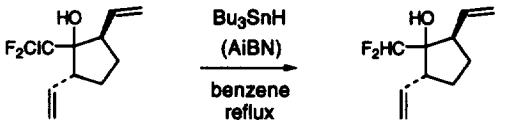
1, 70%

We also decided to condense anhydrides and 1,8-bis(trimethylsilyl)-2,6-octadiene (BISTRO). Electrophilic additions to the latter have already been shown to be an efficient strategy for the synthesis of 1,1-disubstituted-2,5-divinylcyclopentanes.[7] Acetylation, trifluoroacetylation or difluorochloroacetylation of BISTRO is a convenient route to functionalized cyclopentanols **3**. These reactions occur with high stereoselectivity since only the *d,l*-isomer is isolated in each case.



3a $R^1 = R^2 = H$, 66%
3b $R^1 = R^2 = F$, 76%
3c $R^1 = Cl$, $R^2 = F$, 45%

In the quest for preparing other fluorinated derivatives, compounds **3** were used in several reactions. Firstly, reduction of **3c** by tributyltin hydride afforded difluoromethylcyclopentanol **4** in quantitative yield.



3c **4**, 98%

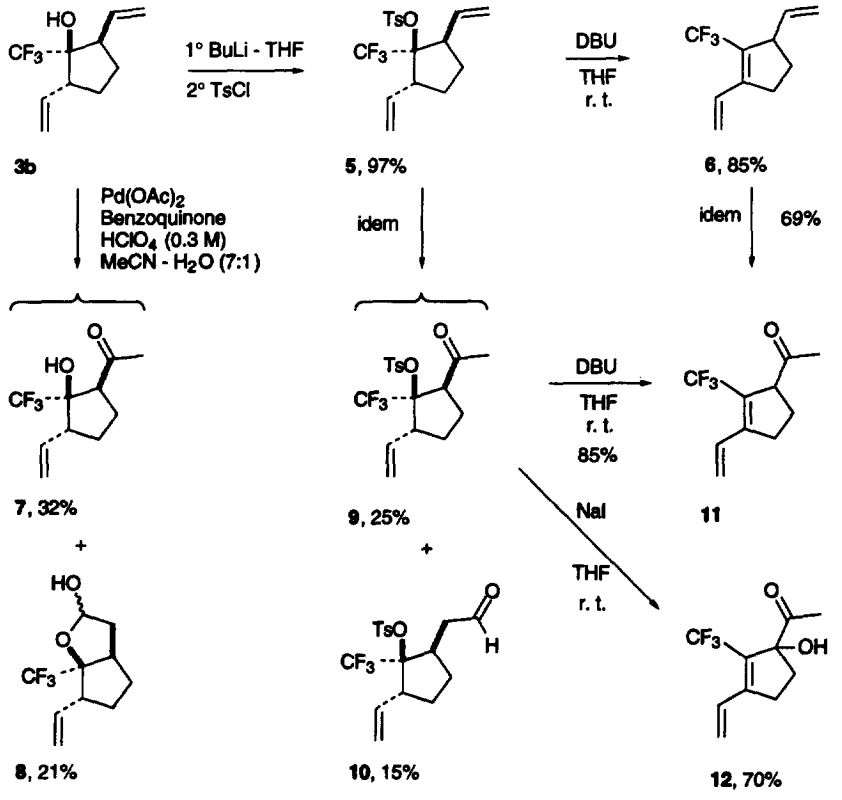
In a second time, the cyclopentanol **3b** was found to be readily converted to the corresponding tosylate **5** in near quantitative yield.

A DBU-promoted elimination of **5** was then performed leading to trifluoromethylcyclopentene **6**. Several attempts to add **6** to various dienophiles were unsuccessful.

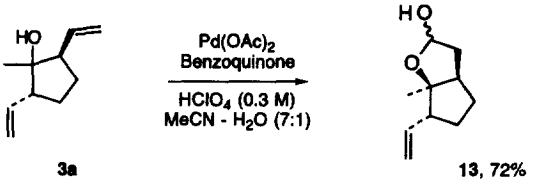
With the aim of obtaining acetyltrifluoromethylcyclopentane derivatives, alcohols **3a** and **3b**, tosylate **5** and triene **6** were submitted to a Wacker-type oxidation.[8]

In the cases of **3b** and **5**, we observed a selective oxidation of the vinyl group which is on the same side as the oxygenated function. Thus, acetylated compounds **7** and **9** were respectively formed from **3b** and **5**, along with the corresponding lactol **8** or aldehyde **10** resulting from an anti-Markovnikov hydration.

The regioselectivity of the reaction can be explained by postulating that palladium coordinates to the heteroatom. This phenomenon can also account for the anomalous anti-Markovnikov addition.[9]



The Wacker-process applied to the divinyl alcohol **3a** led only to the lactol **13**, the reaction proceeding rather slowly (47% of **3a** was recovered after three days).



Oxidation of triene **6** in the same conditions as before, led to dienic ketone **11**, which is obtained in four steps (43% overall yield) from trifluoroacetic anhydride (**2→3b→5→6→11**).

This ketone **11** can also be prepared by a DBU-treatment of tosylate **9** in 85% yield.

The fact that the treatment of the tosylate **9** by sodium iodide leads to the ketol **12** is puzzling.[10]

Several reactions involving **3** are being investigated in order to prepare other variously substituted fluoromethylcyclopentane derivatives which constitute building blocks for the synthesis of steroids.

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5 Anhydride (1 equiv.) was allowed to react with allyltrimethylsilane (3 equiv.) in CH_2Cl_2 solution in the presence of $TiCl_4$ (3 equiv.) and nitromethane (4 equiv.) at -85 °C for 2 h. The influence of the nitro group during the reaction of allylsilanes with various electrophilic compounds was previously discussed (cf. ref. 6).

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10 The ^1H and ^{13}C NMR data of compounds are as follows: **3b**, ^1H NMR (400 MHz, $CDCl_3$) δ 5.85 (m, 2H), 5.30 (d, J = 10.6 Hz, 1H), 5.25 (d, J = 17.4 Hz, 1H), 5.11 (d, J = 17.0 Hz, 1H), 5.06 (d, J = 10.2 Hz, 1H), 2.92 (q, J = 10.4 Hz, 1H), 2.75 (q, J = 8.0 Hz, 1H), 2.10-1.50 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 136.1, 134.6, 125.7 (q, J_{CF} = 286 Hz), 118.7, 115.9, 83.1 (q, J_{CF} = 27 Hz), 54.0, 47.2, 29.2, 27.8.

11, ^1H NMR (400 MHz, $CDCl_3$) δ 6.78 (dd, J = 17.0, J = 10.8 Hz, 1H), 5.383 (d, J = 17.0 Hz, 1H), 5.381 (d, J = 10.8 Hz, 1H), 3.84 (d, J = 9.7 Hz, 1H), 2.66 (m, 2H), 2.19 (d, J = 13.4, t, J = 9.7, d, J = 7.9 Hz, 1H), 2.11 (s, 3H), 1.91 (d, J = 13.4, quint., J = 4.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.0, 149.3 (q, J_{CF} = 4 Hz), 128.9, 126.2 (q, J_{CF} = 32 Hz), 123.0 (q, J_{CF} = 272 Hz), 121.9, 58.5, 32.2, 28.0, 26.0.

12, ^1H NMR (400 MHz, $CDCl_3$) δ 6.88 (dd, J = 17.4, J = 10.7 Hz, 1H), 5.59 (d, J = 17.4 Hz, 1H), 5.56 (d, J = 10.7 Hz, 1H), 4.49 (s, 1H), 2.99 (m, 1H), 2.72 (m, 1H), 2.32 (ddd, J = 14.5, J = 9.2, J = 4.3 Hz, 1H), 2.18 (s, 3H), 2.05 (ddd, J = 14.5, J = 9.6, J = 5.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.2, 151.7 (q, J_{CF} = 4 Hz), 129.1, 128.5 (q, J_{CF} = 30 Hz), 123.6, 122.7 (q, J_{CF} = 273 Hz), 90.3, 35.0, 30.8, 23.3.

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