

PII: S0040-4039(96)01045-3

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

Hélène Pellissier*, Serge Wilmouth and Maurice Santelli*

Lab. de Synthèse Organique, associé au CNRS n°1411, Faculté de St-Jérôme, 13397 Marseille (France) Fax: (33) 91 98 38 65; e-mail: m.santelli@lso.u-3mrs.fr

Abstract: The titanium tetrachloride-mediated addition of allyltrimethylsilane or 1,8bis(trimethylsilyl)-2,6-octadiene and trifluoroacetic anhydride led to trifluoromethyldiallylcarbinol or (dl)-1-trifluoromethyl-2,5-divinylcyclopentanol, respectively, in fair yields; this latter was further converted into several 1-trifluoromethyl-2-vinylcyclopentane derivatives. Copyright © 1996 Published by Elsevier Science Ltd

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.



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.



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.



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 $(2\rightarrow 3b\rightarrow 5\rightarrow 6\rightarrow 11)$.

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.

References and Notes

- (a) Fuchigami, T.; Konno, A.; Nakagawa, K.; Shimojo, M. J. Org. Chem. 1994, 59, 5937-5941. (b) Biggadike, K.; Borthwick, A. D. J. Chem. Soc., Chem. Comm. 1990, 1380-1382. (c) Puech, F.; Gosselin, G.; Imbach, J. L. J. Chem. Soc., Chem. Comm. 1989, 955-957. (d) Biomedical Aspects of Fluorine Chemistry, Filler, R., Kobayashi, Y., Eds; Kodansha & Elsevier Biomedical: Tokyo, 1982. (e) Welch, J. T.; Eswarakrishnan, S. Fluorine in Bioorganic Chemistry; Wiley: New York, 1991.
- (a) Mizutani, K.; Yamazaki, T.; Kitazume, T. J. Chem. Soc., Chem. Comm. 1995, 51-52. (b) Resnati, G. Tetrahedron 1993, 49, 9385-9445. (c) M^cClinton, M. A.; M^cClinton, D. A. Tetrahedron 1992, 48, 6555-6666. (d) Bégué, J. P.; Bonnet-Delpon, D. Tetrahedron 1991, 47, 3207-3258.
- 3 (a) Calas, R. J. Organomet. Chem. 1980, 200, 11-36. (b) Nakanishi, S.; Kumeta, K.; Otsuji, Y. Tetrahedron Lett. 1994, 35, 3727-3728. (c) Larock, R. C.; Lu, Y. J. Org. Chem. 1993, 58, 2846-2850 and ref. therein.
- 4 Pellissier, H.; Wilmouth, S.; Santelli, M. Bull. Soc. Chim. Fr. 1995, 132, 627-641.
- 5 Anhydride (1 equiv.) was allowed to react with allyltrimethylsilane (3 equiv.) in CH₂Cl₂ solution in the presence of TiCl₄ (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).
- 6 Tubul, A.; Ouvrard, Ph.; Santelli, M. Bull. Soc. Chim. Fr. 1992, 129, 265-269.
- (a) Tubul, A.; Santelli, M. Tetrahedron 1988, 44, 3975–3982. (b) Tubul, A.; Santelli, M. Synthesis 1991, 173–176. (c) Ouvrard, Ph.; Tubul, A.; Santelli, M. Tetrahedron Lett. 1992, 33, 7519–7520. (d) Michellys, P.-Y.; Pellissier, H.; Santelli, M. Tetrahedron Lett. 1993, 34, 1931–34. (e) Pellissier, H.; Toupet, L.; Santelli M. J. Org. Chem. 1994, 59, 1709-1713. (f) Pellissier, H.; Faure, R.; Santelli, M. J. Chem. Soc., Chem. Comm. 1995, 1847-1848.
- 8 Miller, D. G.; M. Wayner, D. D. J. Org. Chem. 1990, 55, 2924–2927.
- 9 Pellissier, H.; Michellys, P.-Y.; Santelli, M. Tetrahedron Lett. 1994, 35, 6481-6484.
- The ¹H and ¹³C NMR data of compounds are as follows: 3b, ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (50 MHz, CDCl₃) 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, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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.