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PRELIMINARY NOTE

A Convenient Synthesis of 1,1-Difluoroallenes from Trifluoromethylketones via the Shapiro Reaction Pathway

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SUMMARY

A number of 1,1-difluoroallenes have been conveniently synthesized by means of the Shapiro reaction. The requisite trifluoromethylketone 2,4,6-triisopropylbenzenesulfonylhydrazones were prepared by a simple condensation method. The geometric features relating to their reactivity towards the Shapiro reaction have been discussed.

1,1-Difluoroallenes have been shown to be very reactive species in cycloaddition reactions [1]. To our knowledge, only two compounds of this kind, 1,1-difluoroallene and 1,1-difluoro-3-methyl-1,2-butadiene, were known.The reaction of 1-trifluoromethyl-1-alkenyl bromides with n-BuLi has been employed for their synthesis [1b], though for one of them, some other very tedious methods exist [2]. In connection with our recent interest in looking for fluorine-containing building blocks, we have found that the Shapiro reaction [3] of trifluoromethylketone 2,4,6-triisopropylbenzenesulfonylhydrazones (trisylhydrazones) could serve as a convenient method for the preparation of 1,1-difluoroallenes. Thus, in view of the paucity of methods for their preparation and their potential utilities both as synthetic precursors for the construction of fluorine-containing molecules of biological interest [4] and as mechanistically

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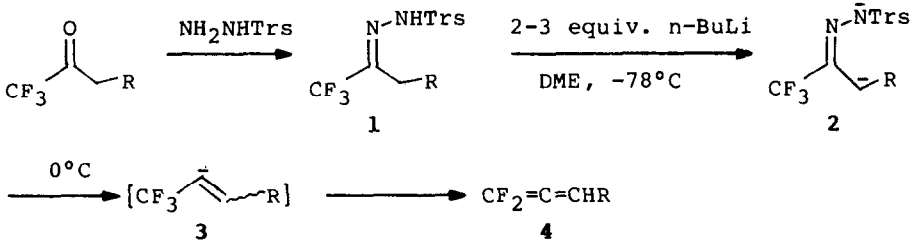
diagnostic reagents [1] for cycloaddition reactions, we have embarked on a study of this reaction. Herein, we wish to report the results of our investigation.

The reaction is believed to follow the typical Shapiro reaction pathway as shown in Scheme 1. In the case where there is no fluorine substituent, vinyl anions are usually obtained



Scheme 1

as a discrete intermediate which can be trapped by various electrophiles [3], but the trifluoromethyl substituted vinyl anion **3** is extremely labile and undergoes ready defluorination prior to trapping [5] to give 1,1-difluoroallene **4**. Although this lability of **3** has been noted earlier and has been utilized for a preparative purpose [1b], its accessibility appeared to be difficult because the previous method for generation of **3** required a 1-trifluoromethyl-1-alkenyl bromide as its precursor which was not readily obtainable. In contrast, the production of **3** by the pathway outlined in Scheme 1 has proved to be successful and synthetically applicable due to the ready availability of a variety of trifluoromethylketones [6].

In general, the fluoroallenes thus prepared (Table 1) are less stable than those without fluorine substituents but they still possess reasonable stability except **4e** which could not be isolated under the present condition and could only be detected during its formation by an evanesent ^{19}F NMR signal appearing within the known range of allenic fluorine absorptions. This anomalous unstability of **4e** was in agreement with the observation that some phenyl substituted haloallenes are quite prone to oligomerization [2].

TABLE 1

Synthesis of 1,1-difluoroallenes

Trisylhydrazones[a] of	n-BuLi(equiv.)	Allenes[b]	Yield[c] (%)
CF_3COCH_3 **1a**	2.2	$CF_2=C=CH_2$ **4a**	80[d]
$CF_3CO(CH_2)_3CH_3$ **1b**	2.5	$CF_2=C=CH(CH_2)_2CH_3$ **4b**	72[e]
$CF_3CO(CH_2)_5CH_3$ **1c**	3.0	$CF_2=C=CH(CH_2)_4CH_3$ **4c**	67
$CF_3COCH_2CH_2Ph$ **1d**	2.5	$CF_2=C=CHCH_2Ph$ **4d**	45
CF_3COCH_2Ph **1e**	2.2	$CF_2=C=CHPh$ **4e**	—f)

a Prepared by condensation of trifluoromethylketones with an equal molar amount of trisylhydrazide in methanol containing a few drops of conc. hydrochloric acid; yield, 81-93%.

b The IR and ^{19}F NMR data of **4a** were identical to that reported in literature [1b]. For **4b-4d**, satisfactory spectral data (IR, ^{19}F NMR, ^{1}H NMR and MS) were obtained and their elemental compositions were determined by HRMS.

c Isolated yield unless otherwise stated.

d Collected in a trap cooled at -78°C.

e Yield determined by ^{19}F NMR.

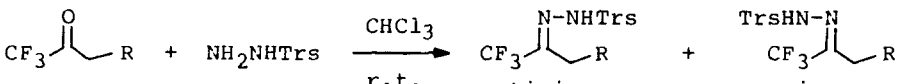
f Not stable enough to be isolated.

Regarding the intrinsic reactivity of these trifluoroketone trisylhydrazones towards the Shapiro reaction, we felt that it would be of benefit and interest to study their geometry which might have played an important role in making our method a successful one. It has been well established that the α-deprotonation in the Shapiro reaction exhibited a substantial preference for selective removal of an α-hydrogen which is syn to the trisylamido group [3], therefore, the ready formation of the dianion **2** in Scheme 1 may well be on account of the fact that the geometry of 1 might be a favorable one for the abstraction of an α-proton, i.e. the one with trifluoromethyl and trisylamido groups bearing an anti relationship as was indicated in Scheme 1. This supposition was unambiguously confirmed by ^{19}F NMR spectroscopy and by comparison with the known structural analogs.

As shown in Table 2, the ^{19}F NMR spectra of the initially (kinetically) formed trisylhydrazones show a substantial chemical shift difference between the syn and anti trifluoromethyl groups. The signal assignment for each pair of isomers was

TABLE 2

^{19}F NMR data and the anti/syn ratio of the Trisylhydrazones



Trisylhydrazones of	^{19}F NMR($CHCl_3$, δ)[a] anti	syn	anti/syn ratio initial[b]	equilibrium[c,d]
CF_3COCH_3	-5.3	-10.1	95/5	>97/3
$CF_3CO(CH_2)_3CH_3$	-7.3	-11.0	80/20	>97/3
$CF_3CO(CH_2)_5CH_3$	-7.2	-11.0	77/23	>97/3
$CF_3COCH_2CH_2Ph$	-7.3	-10.7	82/18	>97/3
CF_3COCH_2Ph	-7.6	-12.5	45/55	>97/3

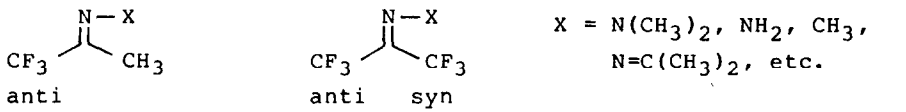
[a] TFA as external standard, downfield is negative.

[b] Measured after 2 h on mixing trifluoromethylketone with trisylhydrazide in $CHCl_3$ at room temperature.

[c] Measured after several days or after addition of a drop of conc. hydrochloric acid so that an equilibrium was reached

[d] No CF_3 signal corresponding to the syn-isomer was observed.

based on: a) the established exclusive anti geometry of various trifluoroacetone imine derivatives [7], b) the observation that among various hexafluoroacetone imine derivatives, the ^{19}F NMR signal of the syn-trifluoromethyl group always has a downfield shift as compared with that of the anti [7].



When the geometric isomers finally reached an equilibrium, the downfield signal corresponding to the syn-CF_3 collapsed in all cases, leading to the exclusive formation of the single anti isomer. Thus, the trifluoromethyl group has exerted a strong directing effect towards the trisylamido group possibly due to favourable electronic interactions which override steric repulsions, making trisylhydrazones ready for a syn hydrogen abstraction.

Finally, we have attempted to prepare a tetra-substituted 1,1-difluoroallene, (2,2-difluorovinylidene)cyclohexane, from trifluoromethylcyclohexylketone trisylhydrazone which carried only a tertiary α-hydrogen. However, the only product obtained was 2,2,2-trifluoro-1-cyclohexyl-diazoethane resulting from the related aprotic Bamford-Stevens reaction even when a stronger base, e.g. s-BuLi, was employed. This is not unexpected because in the Shapiro reaction, the formation of dianions by removal of a tertiary α-hydrogen has been proved to be fairly difficult [8], albeit in one case, it has been achieved [9].

In a typical experiment, trifluoromethylketone trisylhydrazone **1c**(5 mmol) was dissolved in DME(20 ml) and was cooled to -78°C; the orange coloured dianion **2c** was then generated by treatment of **1c** with 3 equivalents of n-BuLi in hexane at -78°C. The reaction mixture was stirred for a while at this temperature, and was then allowed to warm to 0°C. At this temperature, the fragmentation of **2c** occurred readily with the formation of the unstable anion **3c** which rapidly underwent defluorination to give **4c**. After usual workup, the product was isolated by column chromatography on silica gel eluting with pentane, yield, 67%; IR(neat) 2020 (C=C=C), 1200 (=C-F) cm^{-1}; ^{19}F NMR(CCl_4, δTFA) +25.3 (m); ^1H NMR(CCl_4, δ) 0.80 (t,3H), 0.95-1.55 (m, 6H), 2.13 (m, 2H), 6.26 (t-t, J_{HH}=6.5Hz, J_{HF}=2.6Hz, 1H); MS, m/z(relative intensity) 103 (10), 90 (100) ; exact mass calcd. for $C_8H_{12}F_2$: 146.0907, found: 146.0933.

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