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A General Method for the Preparation of 1,1-Bis(Trifluoromethyl)Substituted Olefins

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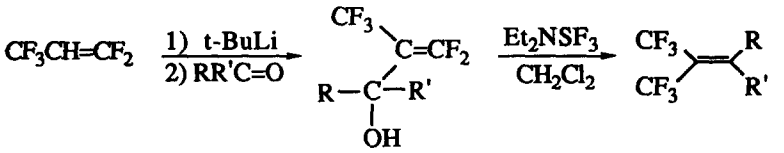
Abstract. The title compounds are prepared by treatment of 1,1-difluoro-2-trifluoromethyl-1-alken-3-ols (1) with diethylaminosulfur trifluoride (DAST) with high regioselectivity. The alcohols (1) are obtained by the reaction of 2-pentafluoropropenyllithium with aldehydes and ketones.

1,1-Bis-(trifluoromethyl)substituted olefins (2) are precursors of considerable interest in the synthesis of bis-(trifluoromethyl)analogues of the pyrethroids.[1] Due to the inductive effect of the geminal trifluoromethyl groups in 2, Michael addition reactions can be readily performed with this class of olefins to give useful compounds in high yields.[2]

Until now, only a few 1,1-bis(trifluoromethyl)substituted olefins have been prepared, mainly by the reactions of hexafluoroacetone with a corresponding phosphorous-ylide[3] or with phosphonate carbanions.[4] The *in situ* reaction[5] of triphenylphosphine with tetrakis(trifluoromethyl)-1,3-dithietane in the presence of aliphatic or aromatic aldehydes gives good to excellent yields of 1,1-bis(trifluoromethyl)substituted olefins. But a limitation of this method is the phosphonium ylide, which formed *in situ*, had too short of a life time to react with ketones. Recently, 2,2-dichlorohexafluoropropane was reacted with triphenylphosphine in an aprotic solvent under mild reaction conditions in the presence of aldehydes or ketones to give the corresponding bis(trifluoromethyl)substituted olefins.[6,7] Although this method gives reasonable yields of 1,1-bis(trifluoromethyl)substituted olefins when activated aldehydes are used as precursors, most ketones give low yields of the expected olefins. In this communication, we wish to report a new and practical method for the preparation of this class of compounds.

In previous work,[8] we described the preparation of an internal perfluorovinyllithium reagent, 2-pentafluoropropenyllithium, from commercially available 2-hydropentafluoropropene and *t*-butyllithium or LDA. We have now found that this vinyllithium reagent reacted with various aldehydes or ketones to give 1,1-difluoro-2-trifluoromethyl-1-alken-3-ols (1). Treatment of 1 with diethylaminosulfurtrifluoride (DAST) afforded 1,1-bis(trifluoromethyl)substituted

olefins in good yields. The results of this exploratory study are summarized in Table 1.



1 2

Table 1. The Formation of 1,1-Bis(trifluoromethyl)Substituted Olefins

No.	R	R'	Yield[a] of Alcohol 1 (%)	Yield[b,c] of Olefin 2 (%)
1	C_6H_5	H	86	70
2	$CH_3(CH_2)_6$	H	70	66
3	E-CH_3CH=CH	H	(63)	(53)
4	p-$CH_3OC_6H_4$	CF_3	83	91
5	m-$CF_3C_6H_4$	CF_3	80	84
6	E-C_6H_5CH=CH	CH_3	(93)	(66)
7	C_6H_5	CH_3	(70)[d]	(62)
8	-$CH_2CH_2CH_2CH_2CH_2$-		(74)	(57)
9	C_6H_5	C_6H_5	(68)[d]	(49)

[a]Isolated yield. Entries 3, 6, 7, 8 and 9 are ^{19}F NMR yields which were determined by using α,α,α-trifluorotoluene as an internal standard. [b]Isolated yields based on **1**. Isolated yield of entries 3, 6, 7, 8 and 9 are based on carbonyl compound. [c]All isolated alcohols and olefins gave satisfactory ^{19}F, ^{1}H, ^{13}C NMR, IR and GC-MS data. [d]In alcohol formation reaction, one equivalent of BF_3•Et_2O was added to the reaction mixture.

The alcohol formation reaction works well with a variety of aldehydes, such as benzaldehyde, aliphatic aldehydes, and α,β-unsaturated aldehydes. The reaction with ketones is also facile, and has been demonstrated for ketones containing a perfluoroalkyl or aryl group, as well as cyclic ketones. Although the reactions of benzophenone and acetophenone with 2-pentafluoropropenyllithium gave low conversion under normal conditions for aldehydes, these reactions gave reasonable yields with the addition of one equivalent of BF_3•Et_2O to the reaction mixture to activate the carbonyl group. The reaction of **1** with DAST gives regioselective

fluorination product 2 due to the high electronegativity of the difluoromethylene moiety in 1 which readily accepts nucleophilic attack by fluoride ion with concomitant deoxygenation.[9,10,11] Some fluorinated allylic alcohols, such as entries 6 and 9 in Table 1, were not thermally stable with respect to isolation. The crude products can be directly fluorinated with DAST without prior purification to produce the corresponding olefins (entries 3, 6, 7, 8 and 9).

In a typical experiment: A three-necked, round-bottomed flask equipped with a stir bar, a rubber septum port, a low temperature thermometer, and a Dry Ice/IPA condenser connected to a source of nitrogen was charged with 90 mL of dry ethyl ether. The ether was cooled to -78°C and 2-hydropentafluoropropene (4.5 g, 34.0 mmol) was condensed into the flask. The resultant solution was stirred vigorously at -78°C while a 1.7 M solution of *t*-butyllithium in pentane (20.0 mL, 34.0 mmol) was added dropwise *via* syringe. After the addition, the reaction mixture was stirred at -78°C for 0.5 hour. A solution of m-trifluoromethyl-2,2,2-trifluoroacetophenone (8.0 g, 33.1 mmol) in ether (6 mL) was then added *via* syringe in one portion. After the addition, the reaction mixture was stirred for one hour at -78°C and then was allowed to warm to -20°C over one hour. The reaction mixture was poured into a mixture of 5% sulfuric acid (40 mL) and ice (40 g). The organic layer of the resulting clear yellow solution was separated, washed sequentially with 5% aqueous sodium bicarbonate solution (30 mL) and twice with ice water (50 mL x 2) and dried over 4Å molecular sieves. The solvent was removed and the residue (12.0 g) was purified by column chromatography on silica gel (200-425 mesh, Fisher Scientific) with hexane/ether=9/1 (by volume) to give 1,1,1,4,4-pentafluoro-3-trifluoromethyl-2-(3-trifluoromethylphenyl)-3-buten-2-ol (9.8 g, 26.2 mmol, 79%) as a colorless liquid; Anal. Calcd (%) for $C_{12}H_5F_{11}O$; C, 38.50; H, 1.33; F, 55.88; Found (%) C, 38.75; H, 1.63; F, 55.35.

A three-necked, round-bottomed flask equipped with a stir bar, a rubber septum port, a low temperature thermometer, and a water condenser topped with a nitrogen source was charged with 5 mL of methylene chloride and 0.6 mL (4.5 mmol) of diethylaminosulfur trifluoride. The solution was cooled to -78°C and was stirred vigorously while a solution of $(m\text{-}CF_3C_6H_4)C(CF_3)(OH)C(CF_3)=CF_2$ (1.5 g, 4.0 mmol) in methylene chloride (1 mL) was added dropwise *via* syringe. After addition, the solution was stirred for 0.5 hour at -78°C and allowed to warm to room temperature over one hour. The reaction mixture was recooled to 0°C and a solution of 5% sodium bicarbonate (8 mL) was slowly added to the reaction mixture. The organic phase was separated, washed with ice water (10 mL x 2), and dried over 4Å molecular sieves. The solvent was removed and the residue was purified by column chromatography on silica gel, 40 g, (200-425 mesh, Fisher Scientific) with pentane as eluent to give 1,1,1,4,4,4-hexafluoro-3-trifluoromethyl-2-(3-trifluoromethylphenyl)-2-butene (1.3 g, 3.4 mmol, 84%) as a colorless liquid; (GLPC purity: > 99%). ^1H NMR ($CDCl_3$) δ 7.42 ppm

(d, J = 8 Hz, 1H), 7.53 ppm (s), 7.56 ppm (dd, J = 8, 8 Hz, 1H), 7.75 ppm (d, J = 8 Hz, 1H). ^{19}F NMR $CDCl_3$) δ -56.5 (q, J = 10 Hz, 3F), -58.6 (m, 3F), -59.7 (q, J = 15 Hz, 3F), -62.8 (s, 3F). ^{13}C NMR ($CDCl_3$) δ 120.6 (q, J = 277 Hz, 2 CF_3), 123.9 (q, J = 272 Hz, CF_3), 119.9 (q, J = 277 Hz, CF_3), 129.0 (m, $(CF_3)_2C=$), 145.5 (q, J = 36 Hz, $C=C(CF_3)_2$), 132.1 (s), 132.2 (q, J = 33 Hz), 131.2 (s), 129.5 (s), 127.7 (q, J = 4 Hz), 125.5 (s), (C_6H_4). HRMS: calcd. for $C_{12}H_4F_{12}$ 376.0121, found 376.0148. GC/MS m/z (relative intensity %) M^+ 376 (74.6), 357 (34.1), 337 (39.6), 307 (54.8), 287 (100), 268 (11.5), 237 (21.4), 219 (62.4), 195 (48.5), 187 (12.1), 169 (37.1), 99 (13.1), 75 (10.0), 69 (64.5). FTIR (CCl_4) cm^{-1} 1658w, 1442m, 1432w, 1343m, 1338m, 1335m, 1326vs, 1323m, 1318m, 1314m, 1311m, 1307m, 1302m, 1295m, 1277m, 1272m, 1270vs, 1267vs, 1099m, 1082m, 1079m, 1076m, 1012m, 917m, 910m, 864m, Anal. Calcd. (%) for $C_{12}H_4F_{12}$: C, 38.29; H, 1.06; F, 60.63; Found (%): C, 37.99; H, 1.35; F, 60.59.

By this newly developed general route, the title compounds not heretofore readily obtainable can be prepared in good yields from commercially available reagents in a simple two-step procedure starting from 2-hydropentafluoropropene and virtually any aldehyde or ketone.

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