Unexpected Formation of 3,3,3-Trifluoropropyltriphenylphosphonium Bromide and Subsequent Wittig-Olefination

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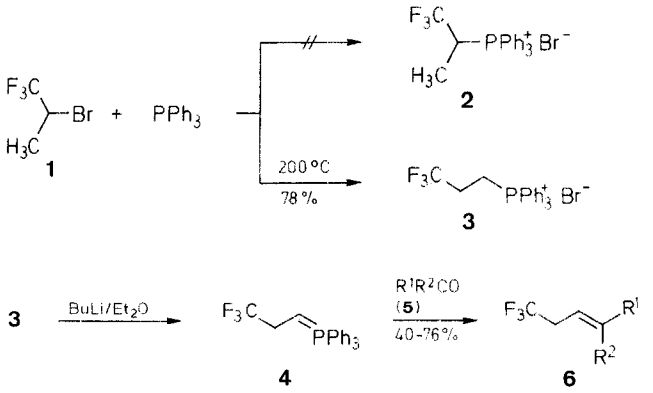
An unusual rearrangement during the reaction of 1,1,1-trifluoroisopropyl bromide with triphenylphosphine leads to 3,3,3-trifluoropropyltriphenylphosphonium bromide, rendering the corresponding olefins accessible.

Trifluoromethyl-substituted olefins are important synthetic intermediates in the synthesis of a variety of organofluorine compounds. We recently described the synthesis of bis(trifluoromethyl)-substituted olefins,[1] and now report the synthesis of olefins containing a 3,3,3-trifluoropropylidene unit. Only a few examples of this type of olefin have been prepared. Three principal methods have been used:

- the reaction of trifluoromethyl or trifluoroethyl copper with substituted allylbromides,[2] or β-bromostyrene[3,4] respectively;
- the coupling of 1-iodo-2,2,2-trifluoroethane with 1-phenyl-2-tributylstannylethene, catalyzed by tetrakis(triphenylphosphine) palladium;[5] and
- the dehydroiodination of trifluoroiodoalkanes, which generally leads to isomeric olefins.[6]



5,6	R^1	R^2
a	C_2H_5	C_2H_5
b	C_4H_9	C_4H_9
c	Ph	Ph
d	CH_2Cl	CH_2Cl
f	$-(CH_2)_5-$	
g	$-CH_2CH_2OCH_2CH_2-$	
h	$-CH_2CH_2N(C_3H_7)CH_2CH_2-$	

Our approach to these compounds is based on the reaction of 1,1,1-trifluoroisopropyl bromide **(1)** with triphenylphosphine. The reaction, considerably hindered, only takes place if both components are heated without solvent at 200°C, to form unambiguously 3,3,3-trifluoropropylphosphonium bromide **(3)**; no traces of the isomeric 1,1,1-trifluoroisopropylphosphonium bromide **(2)** are found.

The mechanism of this rearrangement is not yet clear, but three possibilities may be considered:

- nucleophilic attack of triphenylphosphine on the methyl group of **1**, hydride shift to the secondary carbon atom, and elimination of a bromide ion; or
- nucleophilic attack of triphenylphosphine on the bromine atom, activated by the neighbouring electron-withdrawing trifluoromethyl group, separation of a bromotriphenylphosphonium ion, followed by a proton shift (from the methyl group to the secondary carbon atom), and addition of the bromotriphenylphosphonium ion; or
- dehydrobromination of **1** to 3,3,3-trifluoropropene, which adds triphenylphosphoniumbromide, formed from triphenylphosphine and hydrogen bromide.

Interestingly the reaction of triphenylphosphine with either isopropyl bromide[7] or ethyl 2-bromopropanoate[8] yields the non-rearranged phosphonium salts.

Hence, this reaction provided a novel and convenient method for the preparation of olefins containing a 3,3,3-trifluoropropylidene unit. Treatment of 3,3,3-trifluoropropyltriphenylphosphonium bromide **(3)** with butyllithium generates 3,3,3-trifluoropropylidenephosphorane **(4)**, which can be reacted with aldehydes or ketones. The ylid **4** is sufficiently reactive that ketones e.g. benzophenone will also yield olefins. The prepared olefins **6** are listed in the Table.

Sodium bases, e.g. sodium amide which are frequently used to convert phosphonium salts into ylids, failed to generate **4**. This excludes a *cis*-selective olefination of **4** with aldehydes according

Table. Physical data for Compounds **3** and **6**

Product	Yield (%)	Molecular Formula[a]	IR (film)[b] ν (cm^{-1})	^{1}H-NMR ($CDCl_3$) δ, J (Hz)	^{13}C-NMR ($CDCl_3$) δ, J (Hz)
3	78	$C_{21}H_{19}BrF_3P$ (439.3)	3055–2856, 1588, 1487, 1439, 1414–1002	2.32–2.57 (m, 2H, CH_2); 3.76–4.08 (m, 2H, CH_2); 7.25–7.89 (m, 15H, H_{arom})	15.8 (d, $^1J_{C-P}$ = 58, CH_2P); 26.1 (q, $^2J_{C-F}$ = 32, CH_2CF_3); 115.3 (d, $^1J_{C-P}$ = 87, C-1_{arom}); 124.5 (dq, $^1J_{C-F}$ = 277, $^3J_{C-P}$ = 16, CF_3); 129.5 (d, $^3J_{C-P}$ = 12, C-3_{arom}); 132.3 (d, $^2J_{C-P}$ = 10, C-2_{arom}); 134.3 (d, $^4J_{C-P}$ = 2, C-4_{arom})
6a	40[c]	$C_8H_{13}F_3$ (166.2)		0.96, 0.99 (2t, 3H each, J = 7.5, CH_3); 2.04 (q, 2H each, J = 7.6, CH_2CH_3); 2.79 (dq, 2H, J = 11.0, J = 7.3, CH_2CF_3); 5.08 (t, 1H, J = 7.3, CH)	12.5, 12.8 (2s, CH_3); 23.4, 29.1 (2s, CH_2); 32.6 (q, $^2J_{C-F}$ = 29, CH_2CF_3); 109.9 (q, $^3J_{C-F}$ = 3, CH); 126.5 (q, $^1J_{C-F}$ = 276, CF_3); 149.7 (s, CH=C)
6b	50	$C_{12}H_{21}F_3$ (222.3)	2960–2863, 1667, 1468–1057	0.79–0.96 (m, 6H, CH_3); 1.11–1.46 (m, 8H, CH_2); 1.96–2.01 (m, 4H, CH_2); 2.79 (qd, 2H, J = 11.0, J = 7.3, CH_2CF_3); 5.12 (t, 1H, J = 7.2, CH)	13.9 (s, CH_3); 22.4, 22.8 (2s, CH_2CH_3); 30.1, 30.2, 30.4 (3s, CH_2), 32.8 (q, $^2J_{C-F}$ = 29, CH_2CF_3); 36.6 (s, CH_2); 111.6 (q, $^3J_{C-F}$ = 3, CH), 126.5 (q, $^1J_{C-F}$ = 276, CF_3); 146.9 (s, CH=C)
6c	73	$C_{16}H_{13}F_3$ (262.3)	3082–3030, 2925, 1601, 1577, 1497–1001	2.98 (qd, 2H, J = 10.7, J = 7.4, CH_2); 6.16 (t, 1H, J = 7.4, CH); 7.08–7.59 (m, 10H, H_{arom})	34.8 (q, $^2J_{C-F}$ = 30, CH_2); 116.0 (q, $^3J_{C-F}$ = 3, CH); 126.2 (q, $^1J_{C-F}$ = 277, CF_3); 127.4, 127.7, 127.9, 128.3, 128.5, 129.5 (6s, CH_{arom}); 138.8, 141.4, 147.8 (3s, C_{arom} and CH=C)
6d	40[d]	$C_6H_7Cl_2F_3$ (207.0)	2963, 1442, 1064	2.97 (qd, 2H, J = 10.4, J = 7.4, CH_2CF_3); 4.17, 4.20 (2s, 2H each, CH_2Cl); 5.76 (t, 1H, J = 7.4, CH)	32.9 (q, $^2J_{C-F}$ = 31, CH_2-CF_3); 38.1, 46.2 (2s, CH_2Cl); 122.4 (q, $^3J_{C-F}$ = 3, CH); 125.3 (q, $^1J_{C-F}$ = 277, CF_3), 138.7 (s, CH=C)
6e[d]	8	$C_6H_7BrClF_3$ (251.5)	2961–2859, 1726, 1441–1060	2.96 (qd, 2H, J = 10.4, J = 7.3, CH_2CF_3); 4.05, 4.21 (2s, 2H each, CH_2Br and CH_2Cl); 5.74 (t, 1H, J = 7.3, CH)	25.2 (s, CH_2Br); 33.0 (q, $^2J_{C-F}$ = 31, CH_2-CF_3); 46.4 (s, CH_2Cl); 122.3 (q, $^3J_{C-F}$ = 4, CH); 125.3 (q, $^1J_{C-F}$ = 277, CF_3); 138.9 (s, CH=C)
6f	69	$C_9H_{13}F_3$ (178.2)	2935, 2858, 1674, 1449–985	1.52–1.65 (m, 6H, CH_2); 2.11–2.17 (m, 4H, CH_2); 2.77 (qd, 2H, J = 11.0, J = 7.4, CH_2CF_3); 5.07 (tm, 1H, J = 7.4, J = 1.1, CH)	26.7, 27.6, 28.5, 29.0 (4s, CH_2); 32.1 (q, $^2J_{C-F}$ = 29, CH_2CF_3); 37.2 (s, CH_2); 108.6 (q, $^3J_{C-F}$ = 3, CH); 126.6 (q, $^1J_{C-F}$ = 276, CF_3); 146.9 (s, CH=C)
6g	74	$C_8H_{11}F_3O$ (180.2)	2962–2851, 1734, 1679, 1470–994	2.23 (t, 2H each, J = 5.4, CH_2); 2.78 (qd, 2H, J = 10.8, J = 7.5, CH_2CF_3); 3.63, 3.66 (2t, 2H each, J = 3.6, CH_2O); 5.18 (tm, 1H, J = 7.5, J = 1.1, CH)	29.8 (s, CH_2); 31.8 (q, $^2J_{C-F}$ = 30, CH_2-CF_3), 36.8 (s, CH_2); 68.3, 69.2 (2s, CH_2O); 110.4 (q, $^3J_{C-F}$ = 3, CH); 126.1 (q, $^1J_{C-F}$ = 277, CF_3); 141.7 (s, CH=C)
6h	76[e]	$C_{11}H_{18}NF_3$ (221.3)	2961–2876, 2804–2778, 1722, 1707, 1679, 1470–991	0.84 (t, 3H, J = 7.2, CH_3); 1.27–1.68 (m, 2H, CH_2CH_3); 2.12–2.48 (m, 10H, CH_2); 2.74 (qd, 2H, J = 10.9, J = 7.5, CH_2CF_3); 5.10 (t, 1H, J = 7.5, CH)	11.9 (s, CH_3); 20.2, 28.4 (2s, CH_2); 32.0 (q, $^2J_{C-F}$ = 30, CH_2CF_3); 35.9, 54.2, 54.9, 60.4 (4s, CH_2); 109.5 (s, CH); 126.2 (q, $^1J_{C-F}$ = 276, CF_3); 143.5 (s, CH=C)

[a] Satisfactory microanalyses obtained: C ± 0.37, H ± 0.29, N − 0.25, Cl + 0.26, Br + 0.20 and F ± 0.33, except F values for **6c**, **6d**, **6g** and **6h**: −0.69. For **6a** and **6e**, no elemental analyses were performed. All MS spectra of the alkenes **6** show a M^+ peak.

[b] **3**, (KBr).

[c] If the eluent is not evaporated very cautiously under slightly reduced pressure, major amounts of **6a** are lost.

[d] Some of the allylic chlorine atoms are substituted by bromide ions, derived from phosphonium salt **3** to give a mixture of *E*-,*Z*-**6e** (R^1 = CH_2Cl, R^2 = CH_2Br).

[e] The concentrated extracts of column chromatography are condensed in a trap to remove a white solid.

to the "salt-free" method. Sodium hydride is the only exception. It is able to produce **4**, but very slowly and in moderate amounts.

This new method of obtaining olefins **6** is not limited by the reactivity of ylid **4**, but by the lack of stereochemical control when aldehydes are used.

Mass spectra were obtained using a Varian MAT 711 spectrometer, EI, 70eV at 200°C. IR spectra were obtained using a Perkin-Elmer 398 (for **3**) and a Bruker IFS 48 spectrometer (for **6**). ^{1}H-NMR spectra were obtained using a Bruker WH 90 spectrometer (90 MHz). ^{13}C- and ^{19}F-NMR spectra were obtained using a Bruker WM 400 spectrometer (100 MHz and 376.91 MHz respectively). ^{31}P-NMR were obtained using a Bruker WP 80 spectrometer (32.39 MHz). The ^{31}P chemical shifts are reported in ppm downfield from 85% H_3PO_4, the ^{19}F chemical shifts upfield from CCl_3F. Melting points and boiling points are uncorrected.

1,1,1-Trifluoroisopropyl Bromide (1):
A solution of triphenylphosphine (29 g, 110.6 mmol) in toluene (80 mL) is added dropwise to a stirred solution of trifluoro-2-propanol (8 mL, 89.8 mmol) and CBr_4 (47 g, 141.7 mmol) in toluene (150 mL) under N_2. When the addition is completed, the reaction mixture is stirred for 1 h, and then distilled, to yield the product as a solution in toluene (92% conversion). The distillate is neutralized with $NaHCO_3$ and redistilled through a Spaltrohr column to give pure **1**; yield 13.5 g (85%); bp 48.4–49.0. Spectroscopic data are in agreement with those of an authentic sample.[9]

3,3,3-Trifluoropropyltriphenylphosphonium Bromide (3):
Triphenylphosphine (7 g, 26.7 mmol) and 1,1,1-trifluoroisopropyl bromide (**1**; 2.8 mL, 25.8 mmol), sealed in a heavy wall glass tube *in vacuo*, are heated at 200°C for 20 h. If the contents remain viscous, instead of solid, the glass tube is heated once more to 200°C for the same period. The white solid, pounded to powder, washed twice with toluene to dissolve unreacted triphenylphosphine, and then with Et_2O. The solid is dried *in vacuo* (0.1 mbar, 25°C) to give spectroscopically pure **3**; yield 8.8 g (78%); mp 178–182°C (dec.).

^{31}P-NMR ($CHCl_3$/85% H_3PO_{4ext}): δ = 25.2.

^{19}F-NMR ($CDCl_3$/CCl_3F): δ = −66.29 (t, $^3J_{F-H}$ = 10.0, CF_3).

Alkenes 6; General Procedure:
To a stirred suspension of fine pulverized 3,3,3-trifluoropropyltriphenylphosphonium bromide **(3)** (1 equiv) in Et_2O (7 mL/mmol) under N_2 is added dropwise BuLi (1 equiv, 1.6 M solution in *n*-hexane). The generation of the reddish-yellow ylid **4** is generally completed after 20–30 min.

^{31}P-NMR (C_7H_8/85% H_3PO_{4ext}): δ = 17.3.

^{19}F-NMR [$(C_2H_5)_2O$/C_6D_{6ext}/CCl_3F_{ext}]: δ = −68.38 (t, $^3J_{F-H}$ = 11.3, CF_3).

When the formation of **4** is completed, ketone **5** (1 equiv, **5c** and **5d** as a saturated solution in Et_2O) is added dropwise. The colour disappears immediately, and after 12 h stirring at room temperature water is added. The mixture is stirred for another 30 min, the layers are separated, the aqueous phase is extracted twice with Et_2O, and the combined ethereal solution is dried (molecular sieve 4 A) and concentrated at r.t. under aspirator pressure using a rotary evaporator. The crude product is purified by chromatography on silica gel eluting with: CCl_4 (for **6a–f**), $CHCl_3$ (for **6g**), or $CHCl_3$/acetone 1:1 (for **6h**).

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