A New Synthesis of 1,1-Bis(trifluoromethyl)-Substituted Alkenes

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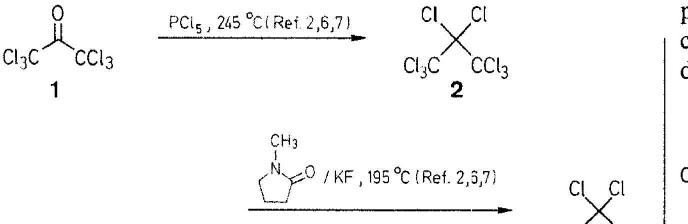
1,1-Bis(trifluoromethyl)-substituted alkenes **6** are obtained by the reaction of aldehydes **5** with triphenylphosphine **(4)** and 2,2-dichlorohexafluoropropane **(3)** in modest to good yields. The alkenes **6** are not easily accessible by other routes.

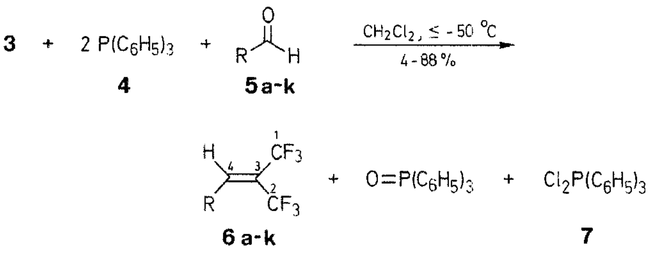
Bis(trifluoromethyl)alkenes **6** are an interesting class of compounds, which are, for instance, used as starting material for the synthesis of fluorinated pyrethroids.[1] Because of the inductive effect of the geminal trifluoromethylgroups, Michael-addition reactions can be performed quite easily with **6** giving rise to a number of useful compounds in high yields.[2] Until now, only a few 1,1-bis(trifluoromethyl)alkenes **6** have been prepared, mainly by the following methods:

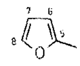
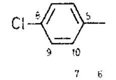
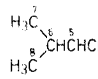
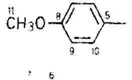
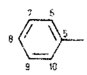
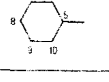
- by the reaction of hexafluoroacetone with a corresponding phosphorus-ylide in a Wittig-reaction;[3]
- by the reaction of hexafluoroacetone with phosphono-ylides[4] in a Horner-Emmons-reaction (particularly for the synthesis of unsaturated trifluoromethyl-aldehydes); and
- by the Wittig-reaction of hexafluoroisopropyliden-triphenylphosphorane with aldehydes.[5]

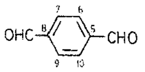
These methods, however, involve relatively high costs and are time-consuming. We have now looked into a new synthetic route, which dispenses with hexafluoroacetone and hexafluoropropene,[5] which are highly toxic, relatively expensive and not easily prepared in the laboratory. The synthesis described here starts from 2,2-dichlorohexafluoropropane (**3**), which is obtained in high yields from hexachloroacetone (**1**) *via* octachloropropane (**2**).[2,6,7]



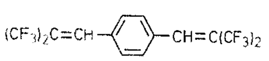
2,2-Dichlorohexafluoropropane (**3**) reacts in an aprotic solvent at −65 °C until −50 °C with triphenylphosphine (**4**) and an aldehyde **5** to give the corresponding bis(trifluoromethyl)alkenes **6** in modest to good yields, depending on the reactivity of the aldehyde (Table).



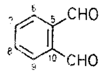
5,6	R	5,6	R
a	$\overset{6}{C}H_3\overset{5}{C}H_2$	f	
b	$\overset{7}{C}H_3\overset{6}{C}H_2\overset{5}{C}H_2$	i	$Cl_2\overset{6}{C}=\overset{5}{C}H$
c		j	
d		k	
e			



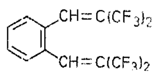
5g



6g



5h

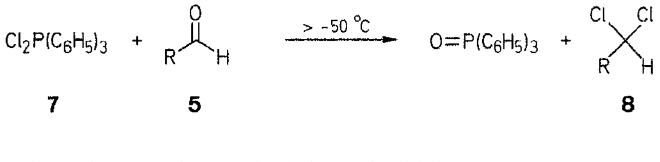


6h

It is necessary to work under anhydrous conditions during the reaction of **3** with **4** and **5**, because first a chlorine atom from 2,2-dichlorohexafluoropropane (**3**) is removed by triphenylphosphine (**4**) as a chlorocation. In the presence of water, the carbanion left behind is at once withdrawn from the reaction as 2-chloro-1,1,1,3,3,3-hexafluoropropane. The mechanism of further reaction-steps is still not clear. It is possible that the carbanion reacts directly with the aldehyde or a phosphorus-ylide is intermediately formed analogous to the reaction of triphenylphosphine (**4**) with tetrachloromethane.[8,9]

Later we shall report elsewhere on the experiments designed to clarify the mechanism of this reaction.

The olefination reaction described here can be applied generally, with a few exceptions. The following rule is valid: The higher the activity of the carbonyl group of the aldehyde, the easier is the formation of the corresponding 1,1-bis(trifluoromethyl)alkene **6**. During the olefination reaction, the carbonyl function of the aldehyde is partially chlorinated to **8** by the dichlorotriphenylphosphorane (**7**) formed during the reaction. This side reaction can be suppressed by using suitable reaction conditions (several days at −63 °C to −50 °C).



When a less reactive aldehyde is used, a higher reaction temperature must be used, and hence the chlorination of the aldehyde becomes the main reaction. Because of the lower reactivity of ketones, no reaction was observed, with the exception of α,α,α-trifluoroacetophenone. In this case, the yield was less than 2 %, although the ketone is activated by the three fluorine atoms.

2-Chloro-3-methylbutanal (**5j**) was prepared according to a literature procedure.[12] The reported procedure[10] for the preparation of 3,3-dichloro-2-propenal (**5i**) was improved with a yield of 72 % by varying the reaction conditions.

3,3-Dichloro-2-propenal (5i):[10]

A solution of 1,1,1,3-tetrachloro-3-ethoxypropane[11] (225.8 g, 1.0 mol) in acetone (400 mL) is added dropwise to a stirred mixture of acetone (400 mL) and water (600 mL). Acetone is then removed by distillation at 95 °C through a packed column (40 cm). The acetone fraction is redistilled and the residue is mixed with the residue obtained from the first destillation. After separation of the organic layer, the aqueous phase is extracted with ether (5 × 100 mL). The ether extract is combined with the organic layer and dried ($MgSO_4$). The solvent is removed, and the product is distilled to afford pure **5i** as a yellow oil; yield: 89.9 g (72 %); b.p. 124 °C/1 bar (Lit.[10] b.p. 124–125 °C/1 bar).

Bis(trifluoromethyl)alkenes 6; General Procedure:

Method A (for **6c, 6d, 6g–k**): To a soluton of triphenylphosphine (285.6 g, 1.09 mol) in dry CH_2Cl_2 (1450 mL) cooled to −63 °C (cryostat) a precooled (−63 °C) solution of the corresponding aldehyde (0.5 mol, 0.25 mol in the case of dialdehydes) in dry CH_2Cl_2 (200 mL) is added. 2,2-Dichlorohexafluoropropane (110.0 g, 0.5 mol) is added dropwise to the mixture from a dropping funnel that is cooled to 0 °C. After stirring for 72 h at −63 °C, the mixture is slowly warmed to room temperature. The solvent is then removed under reduced pressure using a distillation bridge, whereby the cooler and the receiver are cooled to −60 °C. The residue is dissolved in MeOH (120 mL) and then extracted with petroleum ether (30/50) (8 × 30 mL). The petroleum ether phase and the distilled CH_2Cl_2 are combined and the solvent is distilled through an efficient packed column (40 cm). The pure bis(trifluoromethyl)alkenes can be obtained by distillation.

Method B (for **6a**): instead of CH_2Cl_2, the higher boiling CH_2Br_2 is used. The desired alkene is distilled out of the reaction mixture over a slit tube column (reaction temperature: −50 °C).

Table. 1,1-Bis(trifluoromethyl)alkenes **6a**–**k** Prepared

Product	Yield[a] (%)	b.p. (°C/mbar)	Molecular Formula[b]	IR (film)[c] ν (cm^{-1})	^{1}H-NMR (CDCl$_3$)[d] δ, J(Hz)	^{13}C-NMR (CDCl$_3$)[e] δ, J(Hz)
6a	31	58/1013	$C_6H_6F_6$ (192.2)	1678, 1400, 1350–1100	1.2 (t, 3H, J = 7.9, H-3); 2.45 (dq, 2H, J = 7, 7.9, H-5); 6.7 (t, 1H, J = 7, H-4)	
6b	22	74/1013	$C_7H_8F_6$ (206.1)	1680, 1400, 1330–1120	0.96 (t, 3H, J = 7.3, H-7); 1.53 (tq, 2H, J = 7.3, H-6); 2.54–2.22 (m, 2H, H-5); 6.72 (t, 1H, J = 7.9, H-4)	13.2 (C-7 [q]); 21.6 (C-6 [t]); 30.0 (C-5 [t]); 121.4 (q, $^1J_{C-F}$ = 274, C-1 and 2); 122.3 (sept, $^2J_{C-F}$ = 32, C-3); 147.6 (C-4 [d])
6c	88	78/16	$C_{10}H_5ClF_6$ (274.6)	1665, 1400, 1350–1100	7.37 (s, 4H, H-6, 7, 9, and 10); 7.57 (s, 1H, H-4)	120.6 (sept, $^2J_{C-F}$ = 31, C-3); 121.1, 121.6 (2q, $^1J_{C-F}$ = 271, C-1 and 2); 129.0, 129.6, 130.7 (C-6, 7, 9 and 10, [2d], C-5); 137.1 (C-8); 142.1 (C-4, [d])
6d	27	101/16 67/1.7[5]	$C_{11}H_8F_6O$ (270.2)	1650, 1505, 1400, 1350–1100	3.84 (s, 3H, H-11); 6.92 (d, 2H, J = 9, H-7 and 9); 7.44 (d, 2H, J = 9, H-6 and 10); 7.49 (s, 1H, H-4)	54.8 (C-11 [q]); 114.1 (C-7 and 9 [d]); 117.0 (sept, $^2J_{C-F}$ = 31, C-3); 120.7, 121.7 (2q, $^1J_{C-F}$ = 274, C-1 and 2); 123.1 (C-5); 132.3 (C-6 and 10 [d]); 143.0 (C-4 [d]); 162.3 (C-8)
6e	4	76/100	$C_{10}H_{12}F_6$ (246.2)	2940, 2860, 1670, 1340–1140	0.93–2.04 (m, 10H, H-6 to 10); 2.48–2.79 (m, 1H, H-5; 6.49 (dsept, 1H, J = 11.10, $^4J_{H-F}$ = 1.24, H-4)	
6f	37	141/1013	$C_8H_4F_6O$ (230.1)	1660, 1390, 1380, 1310–1150	6.56 (dd, 1H, J = 3.6, 1.8, H-7); 6.99 (d, 1H, J = 3.6, H-6); 7.25 (s, 1H, H-4); 7.63 (d, 1H, J = 1.8 Hz, H-8)	113.1 (C-7 [d]); 120.6 (C-6 [d]); 121.3, 122.1 (2q, $^1J_{C-F}$ = 273, C-1 and 2); 128.0 (m, C-3)[f]; 128.1 (C-4 [d]); 146.2 (C-5); 147.4 (C-8 [d])
6g[g]	50	106/20 m.p. 51 °C	$C_{14}H_6F_{12}$ (402.2)	1660, 1395, 1320–1150 (KBr)	7.45 (s, 4H, H-6, 7, 9 and 10); 7.63 (s, 2H, 2 × H-4)	121.0, 121.4 (2q, $^1J_{C-F}$ = 274, 2 × (C-1 and 2); 122.3 (sept, $^2J_{C-F}$ = 32, 2 × C-3); 129.2 (C-6, 7, 9 and 10 [d]); 133.2 (C-5 and -8); 142.0 (2 × C-4 [d])
6h[g]	10	123/100	$C_{14}H_6F_{12}$ (402.2)	1670, 1400, 1310–1150	7.27–7.50 (m, 4H, H-6 to 9); 7.56 (s, 2H, 2 × H-4)	120.6, 121.1 (2q, $^1J_{C-F}$ = 274, 2 × (C-1 and 2)); 124.8 (sept, $^2J_{C-F}$ = 32.4, 2 × C-3); 128.2 (C-7 and 8 [d]); 129.9 (C-6 and 9 [d]); 130.2 (C-5 and 10); 140.5 (m, $^3J_{C-F}$ = 2.5, 2 × C-4 [d])
6i	83	126/1013	$C_6H_2Cl_2F_6$ (259.0)	1650, 1580, 1400, 1350–1100	6.93 (d, 1H, J = 12.0, H-5); 7.3 (d, 1H, J = 12.0, H-4)	121.38 (q, $^1J_{C-F}$ = 273, C-1 and 2); 121.4 (sept, $^2J_{C-F}$ = 33, C-3); 121.4 (C-5 [d]); 133.8 (C-4, [d]); 136.8 (C-6)
6j	62	73/133	$C_8H_9ClF_6$ (254.6)	1680, 1470, 1350–1100	1.00 and 1.08 (2d, 6H, J = 6.6, H-7 and 8); 2.00 (dsept, 1H, J = 6.6 Hz, H-6); 4.61 (dd, 1H, J = 11.4, 6.6, H-5); 6.68 (d, 1H, J = 11.4, H-4)	17.9, 18.8 (C-7 and 8, [2q]); 35.2 (C-6, [d]); 59.8 (C-5, [d]); 121.1 (q, $^1J_{C-F}$ = 275, C-1 and 2); 122.5 (sept, $^2J_{C-F}$ = 33, C-3); 144.0 (C-4, [d])
6k	54	74/52 52/13[5]	$C_{10}H_6F_6$ (240.2)	3060, 3040, 1660, 1400–1160, 980	7.43 (s, 5H, H-6 to 10); 7.66 (s, 1H, H-4)	120.7 (sept, $^2J_{C-F}$ = 32, C-3); 121.2, 121.9 [(q, $^1J_{C-F}$ = 275) and (q, $^1J_{C-F}$ = 273), C-1 and 2]; 128.7 (C-6 and 10 [d]); 129.3 (C-8 [d]); 130.6 (C-7 and 9 [d]); 131.3 (C-5); 143.4 (sept, $^3J_{C-F}$ = 2.5, C-4 [d])

[a] Yield of pure isolated product.

[b] Satisfactory microanalyses obtained: C ± 0.24, H ± 0.09, Cl ± 0.19, F ± 0.31. Exception: **6g** (C −0.60).

[c] Recorded on a Perkin Elmer 398 Infrared spectrophotometer.

[d] Recorded on Varian EM 360 (60 MHz), Bruker WH 90 (90 MHz) and Bruker HFX 90 (90 MHz) spectrometers.

[e] Recorded on a Bruker WH 90 (22.63 MHz) spectrometer; [ ] refers to the multiplicity of the signal in the off-resonance spectrum.

[f] Coupling constants are not clearly definable, because the expected septet signals superimpose with both the quartets of C-1 and C-2 and the singlet of C-4.

[g] The *p*- and the *o*-dialdehydes were converted to the corresponding dienes **6g** and **6h**, respectively.

Method C (for **6b** and **6e**): Method A is followed with the following changes. The reaction temperature is kept at −50 °C. At the end of the reaction, the CH_2Cl_2 is distilled unter reduced pressure and the pasty residue is ground fine with white sand and extracted with *n*-pentane for 6 h in a soxhlet extractor. After recombination of the CH_2Cl_2 and the *n*-pentane solution, the product is worked up further according to Method A.

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