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Sodium dithionite initiated reactions of Halothane® with enol ethers Facile synthesis of 3-trifluoromethyl substituted vinyl carbonyl compounds

Halina Plenkiewicz, Wojciech Dmowski*, Miroslaw Lipínski[1]

Institute of Organic Chemistry, Polish Academy of Sciences, 01-224 Warsaw, Poland

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Abstract

A convenient and simple method has been found for the preparation of 5,5,5-trifluoro-3-penten-2-one (**3**) and 4,4,4-trifluorocrotonaldehyde (**9**) by a sodium dithionite initiated addition of 1-bromo-1-chloro-2,2,2-trifluoroethane to 2-methoxypropene and ethyl vinyl ether, respectively. Reduction of **3** with aluminium isopropoxide afforded allyl alcohol, 5,5,5-trifluoro-3-penten-2-ol (**5**) and oxidation of **9** gave 4,4,4-trifluorocrotonic acid (**11**). © 2001 Elsevier Science B.V. All rights reserved.

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1. Introduction

The α,β-unsaturated carbonyl compounds containing trifluoromethyl groups as well as allylic alcohols are of considerable interest as building blocks for trifluoromethyl analogs of natural and bioactive molecules. A number of trifluoromethylated amino acids have been prepared *via* 4,4,4-trifluorocrotonic acid, 3-(trifluoromethyl)crotonates and 4,4,4-trifluoro-3-(trifluoromethyl)crotonates [1]. Vinyl ketones and unsaturated esters containing trifluoromethyl groups are valuable intermediates to trifluoromethyl substituted carbocycles [2,3], heterocycles [4–8] and aromatics [9]. Allylic alcohols, 3-trifluoromethyl-2-propanols, were reported to be useful precursors of trifluoromethyl substituted cyclopropane lactones, which in turn, are potential intermediates to trifluoromethyl-containing pyrethroids [10,11].

The most general method of synthesis of 3-trifluoromethyl substituted α,β-unsaturated carbonyl compounds consists of the Wittig-type condensation of phosphorus yields with trifluoromethyl aldehydes and ketones. A number of trifluoromethyl vinyl ketones and esters were obtained from reactions of 1,1,1-trifluoroacetone and 2,2,2-trifluoroacetophenone with alkylidene phosphoranes (prepared from α-haloketones or haloacetates and triphenylphosphine) [12,13]. This methodology was successfuly applied for the synthesis of bis(trifluoromethyl) ketones and esters from hexafluoroacetone [14,15]. A modification of the Wittig reaction, using antimony or arsenium yields has also been reported [3]. Numerous perfluoroalkyl substituted unsaturated esters, including CF_3-substituted, were prepared from chlorides or esters of perfluoroalkyl carboxylic acids and alkylidene phosphoranes in Horner–Wadsworth–Emmons reactions [16,17]. Highly stereoselective synthesis of either Z or E isomers were achieved by this method using, respectively, phosphonium salts or phosphonates [18,19]. A Knoevenagel condensation of trifluoromethyl ketones and aldehydes with malonic acid or acetylacetone, followed by dehydration [20,21], and an ultrasound promoted Reformatsky-type reaction between trifluoroacetaldehyde and ethyl bromoacetate [22] were also used for the synthesis of CF_3-substituted α,β-unsaturated carbonyl compounds.

The reduction of 3-trifluoromethyl vinyl aldehydes and esters with $LiAlH_4$ [23], $LiAlH_4/AlCl_3$ [22] or $NaBH_4$ [24] provided the corresponding allylic alcohols. Enzymatic reduction led to chiral trifluoromethyl allylic alcohols [25]. W.Y. Huang and co-workers have developed a new method of the synthesis of 3-perfluoroalkyl vinyl aldehydes and ketones. This method is based on a general procedure, named sulphinatodehalogenation, in which perfluoroalkyl radicals are generated from perfluoroalkyl iodides or bromides in a

* Corresponding author. Fax: +48-22-632-66-81.
E-mail address: dmowski@icho.edu.pl (W. Dmowski).

[1] A part of work for B.Sc. diploma of Akademia Podlaska, Siedlce, Poland.

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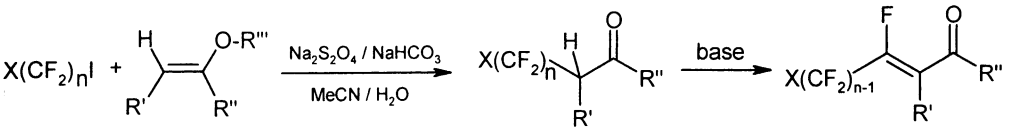
series of SET processes initiated by sodium dithionite and related reagents [26–28]. Addition of these radicals to alkyl vinyl ethers gives 3-perfluoroalkyl aldehydes or ketones [29,30] which on dehydrofluorination afford 3-fluoro-3-(perfluoroalkyl)-α,β-unsaturated carbonyl compounds according to the general scheme [31,32]:



X = Cl , F ; n = 2 - 8 ; R' = H, Me ; R'' = Me, Et, t-Bu ; R''' = Me, Et, $SiMe_3$

Reduction of perfluoroalkyl vinyl aldehydes and ketones allowed preparation of the corresponding allylic alcohols [32]. The Huang procedure has a number of advantages: simplicity, aqueous reaction medium, very mild reaction conditions and usually excellent yields. Furthermore, in this procedure there is no need to use highly toxic phosphorus compounds or drastic reaction conditions which are usually necessary to generate free radicals.

The Huang procedure was successfully applied for the synthesis of vinyl carbonyl compounds substituted with rather long perfluoroalkyl chains (C_4–C_8) but no trifluoromethylation has been reported till now. In the present paper we report an application of sulphinatodehalogenation methodology to the synthesis of 3-trifluoromethyl substituted α,β-unsaturated carbonyl compounds, namely, 5,5,5-trifluoro-3-penten-2-one (**3**) and 4,4,4-trifluoro-2-butenal (**9**), from commercially available and inexpensive reagents: 1-bromo-1-chloro-2,2,2-trifluoroethane (Halothane®), 2-methoxypropene and ethyl vinyl ether. Reductions of compound **3** to the corresponding allyl alcohol **5** and homoallyl alcohol **6** and oxidation of **9** to 4,4,4-trifluorocrotonic acid **11** are also reported.

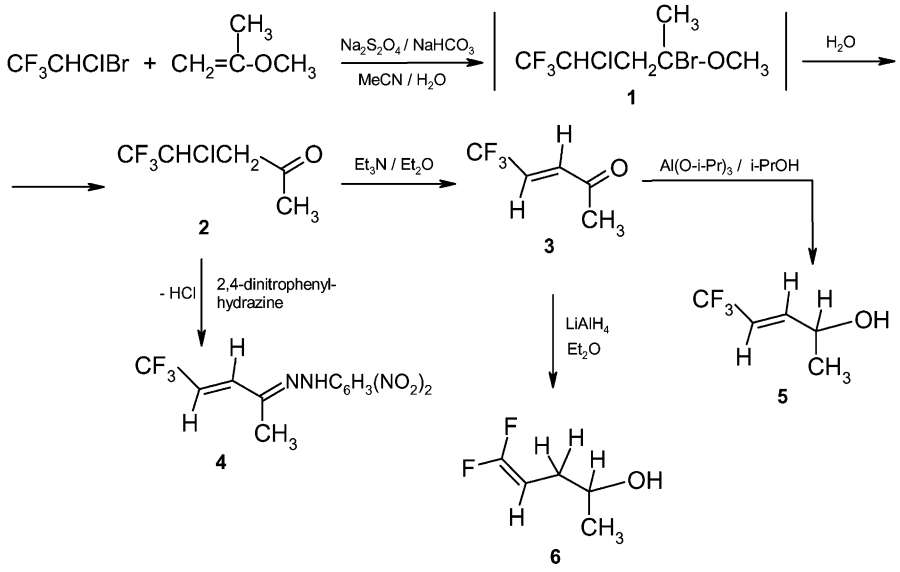
2. Results and discussion

Sodium dithionite was used as an initiator of an electron transfer processes together with sodium hydrogen carbonate as a base (neutralisation of evolved HBr). In primary trials, the reaction of $CF_3CHClBr$ with 2-methoxypropene was investigated on a 20 mmol scale under a variety of conditions, solvents compositions and reactant ratios. The best results were obtained when approximately equimolar amounts of $Na_2S_2O_4$ and $NaHCO_3$ suspended in an acetonitrile:water mixture (1:1 by volume) were used and the organic reagents were added to this mixture pre-cooled to 10°C and then allowed to warm up slowly, while stirring, to ambient temperature when a noticeable exothermic effect occurred. This procedure was then applied to preparative scale experiments. When the reaction was quenched after 2 h (by dilution with water), GC–MS investigations revealed the presence of 4-chloro-5,5,5-trifluoro-2-pentanone (**2**) as the main product together with small amount of unsaturated ketone, 5,5,5-trifluoro-3-penten-2-one (**3**). In some experiments, the presence of trace amounts of the primary adduct (component of longest retention time), 2-bromo-2-ethoxy-4-chloro-5,5,5-trifluoropentane (**1**) was also found (Scheme 1).

A composition of a mixture of the reaction products, even when separated from alkaline reaction medium, changed in time in favour of ketone **3** and at the expense of ketone **2**; after 1 day the contents of **3** increases from the initial 2–3 to 10–15% with the corresponding drop of the amount of saturated ketone **2**. This indicates the instability of **2** which easily undergoes dehydrochlorination.

The attempted isolation of **2** by distillation failed; 3:1 to 1:1 mixtures of **2** and **3** were obtained. Agitating this distillate with concentrated hydrochloric acid gave almost pure compound **2** (98%), a sample of which was separated and identified by elemental analysis and spectral data. With the aim to determine a yield of the addition product **2**, freshly prepared mixture of products, containing ca. 98% of **2**, was treated with 2,4-dinitrophenylhydrazine. Elemental analysis of the resulting hydrazone, after recrystallisation and drying over P_4O_{10} under reduced pressure for a few days, showed the absence of chlorine thus showing total dehydrochlorination; the analytical data were fully consistent with those calculated for unsaturated hydrazone **4**. The hydrazone **4** was obtained with over 70% yield (after recrystallisation) which gives evidence for high efficiency of the reaction of $CF_3CHClBr$ with 2-methoxypropene.

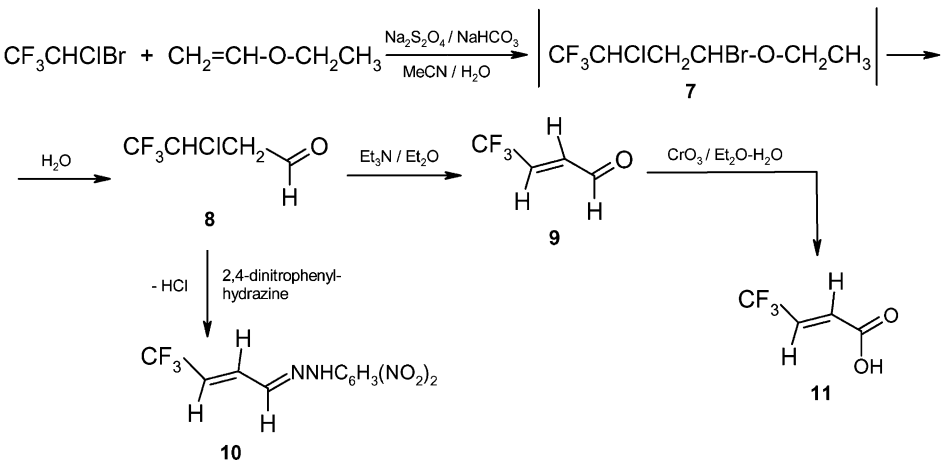
Treatment of an ether solution of a crude mixture of products with triethylamine gave unsaturated ketone **3** as practically the only product which was isolated by fractional distillation. The volatility of **3** makes its separation from ether rather difficult and because of that not a very high yield of pure product was obtained. The dehydrochlorination of **2** proceeded with full stereoselectivity. Ketone **3** was formed exclusively as *trans*-isomer, as shown by the high value of the coupling constant of vinylic protons across the double bond in its ^1H NMR spectrum. This is contrary to the reported dehydrofluorinations of 3-perfluoroalkyl substituted ketones which usually resulted in mixtures of *trans*- and *cis*-isomers [31,32]. Semiempirical structure modeling (PC Model 3.0) have shown that a conformation of **2** which by *trans*-elimination of HCl should give *trans*-**3** is by ca. 3 Kcal/mol more favourable then a conformation leading to the *cis*-isomer. Also, a very high rotational barrier (ca. 12 Kcal/mol) was found for compound **2**.



Scheme 1.

Selective reduction of pentenone **3** to allyl alcohol, *trans*-5,5,5-trifluoro-3-penten-2-ol (**5**), was successfully carried out with aluminium isopropoxide by classical Meerwein–Ponndorf–Verley methodology [33,34]. Alcohol **5** was obtained in good yield and purity. Reduction of **3** with $LiAlH_4$ proceeded in a rather unexpected way. After 2 h at room temperature almost equimolar amounts of **5** and the homoallylic alcohol, 5,5,-difluoro-4-penten-2-ol (**6**), were formed and after a prolonged reaction time compound **6** was the only product. The attempted isolation of pure **6**, free of ether, failed; the best fraction obtained by careful distillation afforded a sample containing 81% of **6**, nevertheless, spectroscopic investigations gave unequivocal evidence for its structure. A reaction pathway leading to **6** must involve attack of hydride ion on carbon atom C-3 in **5** followed by elimination of fluoride ion from the CF_3 group. Similar behaviour was previously reported for $LiAlH_4$ reduction of 3-(trifluoromethyl)crotonate [24].

Reactions of $CF_3CHClBr$ with ethyl vinyl ether were conducted and proceeded the same way as those with 2-methoxypropene. The 3-chloro-4,4,4-trifluorobutyraldehyde (**8**) was the main product together with a small amount of dehydrochlorinated product, 4,4,4-trifluorocrotonaldehyde (**9**), and a trace amount of primary adduct, 1-bromo-1-ethoxy-3-chloro-4,4,4-trifluorobutane (**7**) (Scheme 2). Instability of **8**, similarly to **2**, prevents its direct isolation. Treatment of the crude mixture of products with triethylamine or pyridine resulted in total conversion of **8** into trifluorocrotonaldehyde (**9**) but, unfortunately, high volatility did not allowed isolation of this compound in a pure state; fractional distillation gave only fractions of variable concentration of **9** in diethyl ether. ^1H NMR spectrum



Scheme 2.

showed the *trans*-conformation of aldehyde **9**. The 2,4-dinitrohydrazone prepared from **8**, similarly to that from **2**, dehydrochlorinated during the drying procedure to give unsaturated hydrazone **10** in over 63% yield.

The attempted reduction of ether solutions of **9**, either with aluminium isopropoxide or sodium borohydride, failed. Only trace amounts of the expected 4,4,4-trifluoro-2-buten-1-ol were detected by GC–MS analysis but a viscous unidentified oil remained after removal of the solvents. However, aldehyde **9** was, successfully oxidised with chromium(VI) oxide by following the procedure used by Huang and Lü [30]; high purity, crystalline *trans*-4,4,4-trifluorocrotonic acid (**11**) was obtained albeit in only moderate yield (ca. 22%). The yield of acid **11** was undoubtedly lowered by its inefficient extraction from aqueous solution with trichlorofluoromethane. This solvent was used instead of diethyl ether because acid **11** strongly binds diethyl ether so that it was not possible to remove the latter by distillation. On the other hand, the partition coefficient of **11** between water and CCl_3F is probably not satisfactory for efficient extraction.

In conclusion, sodium dithionite initiated reactions of $CF_3CHClBr$ with 2-methoxypropane and ethyl vinyl ether in a water–acetonitrile solutions provide an easy and environmentally friendly way to valuable, trifluoromethyl substituted α,β-unsaturated carbonyl compounds, ketone **3** and aldehyde **9**, and further, to the corresponding allylic alcohol **5** and acid **11**.

3. Experimental

Melting points were determined in capillaries and boiling points were measured during distillation; both are uncorrected. ^{1}H NMR spectra were recorded with a Brucker 500 instrument and ^{19}F NMR spectra with a Varian Gemini 200 spectrometer (at 188 MHz), both in $CDCl_3$ solutions. Chemical shifts are quoted in ppm from internal TMS for ^{1}H (positive downfield) and from internal $CFCl_3$ (positive upfield) for ^{19}F nuclei. Crude mixtures of products were analysed with a Shimadzu GC-14A chromatograph using a 3.5 m × 2 mm column packed with 5% silicone oil SE-52 on chromosorb G or a 30 m capillary column coated with a BPX-5 oil. GC–MS analyses were performed with a Hewlett-Packard 5890 apparatus (30 m capillary column, HP-5 oil). Mass spectra of pure compounds were obtained with an AMD-604 spectrometer and IR spectra with a Perkin-Elmer Spectrum 2000 instrument. The 1-bromo-1-chloro-2,2,2-trifluoroethane, 2-methoxypropene and ethyl vinyl ether were commercial reagents.

3.1. General procedure for the reactions of $CF_3CHClBr$ with enol ethers

Sodium dithionite (16.0 g (85%), 80 mmol) and sodium hydrogen carbonate (6.0 g, 72 mmol) were suspended in aqueous acetonitrile (1:1, 120 ml). The suspension was vigorously stirred and cooled to 10°C, then 2-methoxypropene or ethyl vinyl ether (6.92 g, 96 mmol) and $CF_3CHClBr$ (15.8 g, 80 mmol) were added one by one. The cooling bath was removed and the reaction mixture, while stirring, was allowed to warm up slowly. At about 20°C a noticeable exothermic effect occurred, the temperature reached 28–30°C and most inorganic salts dissolved. Stirring was continued for 1 h (altogether about 2 h from the beginning of the reaction) during which time the temperature of the reaction mixture returned to ambient. Water (120 ml) was added and the reaction mixture was extracted with diethyl ether (120 ml), the organic layer was separated and washed with water (4 × 60 ml, removal of CH_3CN) and dried over $MgSO_4$. GLC and GC–MS analyses of the extract revealed the presence of compounds **2** and **3** (from 2-methoxypropene) or **8** and **9** (from ethyl vinyl ether) in a ratio varying from 40:1 to 10:1; this ratio changed in favour of **3** or **9** on standing for several hours. Trace amounts of primary adducts **1** or **7** were also detected by GC–MS.

3.1.1. 2-Bromo-2-methoxy-4-chloro-5,5,5-trifluoropentane (*1*)

GC–MS: *m/z* (rel. int., ion): 177, 175 [4, 12 ($M - CH_2Br)^+$]; 139 [10, ($M - CH_2Br$–HCl)$^+$]; 77 (10, $C_3H_3F_2^+$); 69 (20, CF_3^+); 59 (100, $C_3H_7O^+$).

3.1.2. 4-Chloro-5,5,5-trifluoro-2-pentanone (*2*)

Distillation of a solution of compounds **2** and **3** prepared as above resulted in increased dehydrochlorination. A sample of the distillate (bp 126–128°C) containing roughly 70% of **2** and 30% of **3** was stirred overnight with concentrated hydrochloric acid, separated and dried over $CaCl_2$. GLC analysis shown only **2**. Analysis, found: C, 34.2; H, 3.5; Cl, 20.6; F, 32.6%. Calculated for C_5H_6ClFO (174.55): C, 34.4; H, 3.5; Cl, 20.3; F, 32.7%. ^{1}H NMR δ: 2.25 (s, CH_3); 3.05 (centre of narrow AB system, $J_{AB} = 17.9$ Hz, CH_2); 4.68 (dqd, $^3J_{HH} = 7.8$ Hz, $^3J_{HF} = 6.9$ Hz, $^3J_{HH} = 4.9$ Hz, CHCl) ppm. ^{19}F NMR δ: 75.4 (d, $^3J_{HF} = 6.9$ Hz) ppm. GC–MS: *m/z* (rel. int., ion): 176, 174 (8, 24, M^+); 161, 159 [8, 24, ($M - CH_3)^+$]; 133, 131 [30, 90, ($M - CH_3CO)^+$]; 123 [20, ($M - CH_3$–HCl)$^+$]; 95 [30, ($M - CH_3O$–HCl)$^+$]; 69 [100, CF_3^+ and ($M - CF_3$–HCl)$^+$].

3.1.3. Trans-5,5,5-trifluoro-3-penten-2-one (*3*)

Triethylamine (12 ml, 8.7 g, 86 mmol) was added to a solution of compounds **2** and **3** in diethyl ether, prepared as in Section 3.1. A precipitate of $Et_3N{\cdot}HCl$ began to form almost immediately. The reaction mixture was left overnight then washed water (100 ml) then with dilute hydrochloric acid (ca. 1%, 100 ml) followed by water until a neutral, organic layer was separated and dried over anhydrous $MgSO_4$. Careful distillation through a 10 cm Vigreux column gave compound **3** as colourless liquid possessing a strong irritating smell. GLC purity: ca. 98%. Yield: 5.3 g (38.4 mmol, 48% related to $CF_3CHClBr$). The bp 102–104°C (in agreement with [21]). Analysis, found: F,

41.5% (no C and H were determined due to a high volatility of **3**). Calculated for $C_5H_5F_3O$ (138.3): F, 41.3%. ^{1}H NMR δ: 2.37 (s, CH_3); 6.58 (dq, $^3J_{HH} = 16.1$ Hz, $^3J_{HF} = 6.3$ Hz, 1H); 6.69 (dq, $^3J_{HH} = 16.1$ Hz, $^4J_{HF} = 1.8$ Hz, 1H) ppm. ^{19}F NMR δ: 65.3 (d, broaden, $^3J_{HF}$ = ca. 6 Hz, CF_3) ppm. MS (EI, 70 eV): *m/z* (rel. int., ion): 138 (34, M^+); 123 [100, $(M - CH_3)^+$]; 95 [44, $(M - CH_3CO)]^+$; 69 [40, CF_3^+ and $(M - CF_3)^+$]; 43 (68, CH_3CO^+). IR (neat): ν (cm^{-1}): 1715.4 and 1698.3 (vs, C=O); 1665.8 (m, C=C). HRMS: M^+ 138.02885. Calculated for $C_5H_5F_3O$: 138.02925.

3.1.4. 2,4-Dinitrophenylhydrazone **4**

A freshly prepared ether solution of pentanone **2** (contaminated with ca. 2% of **3**), prepared from a quarter amount of reagents used in Section 3.1., was added to a reagent prepared by dissolution of 2,4-dinitrophenylhydrazine (4 g, 20 mmol) in warm 85% phosphoric acid (48 ml) and diluted (after cooling to ambient temperature) with 96% ethyl alcohol (32 ml). A yellow-orange precipitate was immediately formed. After 1 h the precipitate was filtered off, washed with ethanolic solution of 85% phosphoric acid (2:3) then with water until neutral. Removal of ether from the eluent on a rotary evaporator gave an additional amount of the precipitate which was worked up as above. The combined precipitates (6.4 g) were recrystallised from ethanol and dried over P_4O_{10} under reduced pressure. Yield: 4.54 g (14.3 mmol, 71.4% related to $CF_3CHClBr$). The mp 179–180°C. Analysis, found: C, 41.4; H, 2.7; N, 17.6; F, 17.9%; no Cl found. Calculated for $C_{11}H_9F_3N_4O_4$ (318.21): C, 41.5; H, 2.9; N, 17.6; F, 17.9%.

3.1.5. Trans-5,5,5-trifluoro-3-penten-2-ol (**5**)

A solution of pentenone **3** in Et_2O, prepared as in Section 3.1.3., dry isopropyl alcohol (120 ml) and aluminium isopropoxide (16.5 g, 81 mmol) were placed in a distillation apparatus fitted with a magnetic stirring bar and a short Vigreux column. The reaction mixture was slowly warmed up while stirring. Ether together with acetone formed in the reaction, were distilled off to ca. 60°C followed by isopropanol (60 ml, bp 81°C). Hydrochloric acid (10%) was added until dissolution of a suspension of inorganic solids. The reaction mixture was then extracted with ether (2 × 40 ml), the extract was washed with water (5 × 30 ml, removal of isopropanol) and dried over $MgSO_4$. Distillation gave compound **5** as a liquid possessing a strong, geranium-like smell. The GLC purity: 98%, yield: 4.7 g (33.5 mmol, 42% related to $CF_3CHClBr$), bp 130–132°C (Lit.: 130–133°C [25]). Analysis, found: C, 42.9; H, 5.2; F, 40.6%, calculated for $C_5H_7F_3O$ (140.11): C, 42.9; H, 5.0; F, 40.7%. ^{1}H NMR δ: 1.33 (d, $^3J_{HH} = 6.6$ Hz, CH_3); 1.91 (s br, OH); 4.45 (m, 1H); 5.88 (dqd, $^3J_{HH} = 15.7$ Hz, $^3J_{HF} = 6.5$ Hz, $^4J_{HH} = 1.8$ Hz, 1H); 6.42 (ddq, $^3J_{HH} = 15.7$ Hz, $^3J_{HH} = 4.4$ Hz, $^4J_{HF} = 2.2$ Hz, 1H) ppm. ^{19}F NMR δ: 64.6 (dt, $^3J_{HF} = 6.5$ Hz, $^4J_{HF}$ and $^5J_{HF}$ = ca. 2 Hz, CF_3) ppm. MS (EI, 70 eV)): *m/z* (rel. int., ion): 139 [2, $(M - H)^+$]; 125 [78, $(M - CH_3)^+$]; 120 [5, $(M - HF)^+$]; 105 [10, $(M - CH_3–HF)^+$]; 91 (12); 77 (33, $C_3H_3F_2^+$); 69 (9, CF_3^+); 45 (34, $C_2H_5O^+$); 43 (100, CH_3CO^+). IR (neat): ν (cm^{-1}): 3551 (br, OH); 1685.7 (m, C=C).

3.1.6. 5,5,-Difluoro-4-penten-2-ol (**6**)

Lithium aluminium hydride (0.76 g, 20 mmol) was added portionwise to a stirred solution of pentenone **3** in Et_2O, prepared as in Section 3.1.3. from a half amount of reagents used in Section 3.1. After 2 h GLC analysis revealed the presence of compound **5** and a shorter retention time component in ca. 1:1 ratio. The stirring was continued overnight after which time compound **5** disappeared and only a new compound remained. Inorganic solids were dissolved by stirring overnight with ca. 12% sulphuric acid, the organic layer was separated washed with water until neutral and dried over $MgSO_4$. Distillation gave a number of fraction; a small fraction (bp 116–118°C) contained 81% of a compound which was identified by spectral means as alcohol **6**. ^{1}H NMR δ: 1.19 (d, $^3J_{HH} = 6.2$ Hz, CH_3); 2.12 (centre of AB system, J_{AB} = ca. 8 Hz, CH_2); 3.1 (s, OH); 3.81 (sxt, $^3J_{HH} = 6.2$ Hz, 1H); 4.23 (dtd, $^3J_{HF\,trans} = 25.4$ Hz, $^3J_{HH} = 8.0$ Hz, $^3J_{HF\,cis} = 2.5$ Hz, 1H) ppm. ^{19}F NMR δ: 88.4 (d, $^2J_{FF} = 45.5$ Hz, 1F); 91.4 (dd, $^2J_{FF} = 45.5$ Hz, $^3J_{HF\,trans} = 25.4$ Hz, 1F) ppm. MS (EI, 70 eV): *m/z* (rel. int., ion): 107 [4, $(M - CH_3)^+$]; 77 (22, $C_3H_3F_2^+$); 69 (2, CF_3^+); 59 (15, $C_3H_7O^+$); 51 (9, CF_2H^+); 45 (100, $C_2H_5O^+$). IR (neat): ν (cm^{-1}): 3353 (br, OH); 1750.6 (s, C=C) (1730 cm^{-1} was reported for CH_2=CF_2 [35]. HRMS: $(M - CH_3)^+$: 107.02996. Calculated for $C_4H_5F_2O^+$: 107.03085.

3.1.7. 1-Bromo-1-ethoxy-3-chloro-4,4,4-trifluorobutane (**7**)

GC–MS: *m/z* (rel. int., ion): 191, 189 [30, 90, $(M - Br)^+$]; 163, 161 [33, 100 $(M - C_2H_4Br)^+$]; 143, 141 [15, 45, $(M - C_2H_4Br–HF)^+$]; 103 (50), 77 (30, $C_3H_3F_2^+$); 69 (15, CF_3^+).

3.1.8. 3-Chloro-4,4,4-trifluorobutyraldehyde (**8**)

GC–MS: *m/z* (rel. int., ion):160, 162 (2, 6, M^+); 142, 140 [3, 9, $(M - HF)^+$]; 114, 112 [5, 15, $(M - HF–CO)^+$]; 96 [100, $(M - HCl–CO)^+$]; 95 [100, $(M - HCl–CHO)^+$]; 77 (100, $C_3H_3F_2^+$); 69 (80, CF_3^+).

3.1.9. Trans-4,4,4-trifluorocrotonaldehyde (**9**)

A solution of compounds **8** and **9** in diethyl ether, prepared from ethyl vinyl ether as in Section 3.1., was treated with pyridine and worked up as described in Section 3.1.3. GLC analysis of an ether layer showed total conversion of **8** into **9** (GLC peak overlaps with Et_2O). Distillation gave a number of fractions; a small fraction (bp 62–64°C) containing 60% of aldehyde **9** (the richest one) was subjected to spectral investigations. ^{1}H NMR δ: 6.65 (centre of AB system, $J_{AB} = 16.0$ Hz, 2H); 9.72 (complex m, CHO) ppm. ^{19}F NMR δ: 66.3 (narrow m) ppm. MS (EI, 70 eV) *m/z* (rel. int., ion): 125 [37, $(M + H)^+$]; 124 (100, M^+); 123 [77, $(M - H)^+$]; 96 [56, $(M - CO)^+$]; 95 [83, $(M - CHO)^+$]; 77

(43, $C_3H_3F_2^+$); 69 (81, CF_3^+). IR (neat): ν (cm^{-1}): 1710.5 (vs, C=O); 1667.4 (m, C=C). HRMS: M^+ 124.01411, Calculated for $C_4H_3F_3O$: 124.01356.

3.1.10. 2,4-Dinitrophenylhydrazone (**10**)

The hydrazone was prepared as described in Section 3.1.4. from an ether solution of aldehyde **8**, yield: 3.95 g (13 mmol, 65%). The mp 208–210°C. Analysis, found: C, 39.2; H, 2.3; N, 18.4; F, 18.6; no Cl found. Calculated for $C_{10}H_7F_3N_4O_4$ (304.19): C, 39.5; H, 2.3; N, 18.4; F, 18.7%.

3.1.11. Trans-4,4,4-trifluorocrotonic acid (**11**)

A solution of aldehyde **9** in diethyl ether, prepared as in Section 3.1.9. was added portionwise to a pre-cooled to 5°C and stirred solution composed of acetone (100 ml), water (60 ml), concentrated sulphuric acid (16 ml) and chromium trioxide (14.5 g, 0.145 mol). An exothermic reaction occured and a gel-suspension of chromium salts began to form. The reaction mixture was stirred overnight at ambient temperature. The upper organic layer was separated, the bottom layer was extracted with ether (20 ml). The combined ether solutions were vigorously shaken with 20% aqueous NaOH (2×40 ml) and separated. The alkaline water solution, after removal of residual solvents on a rotary evaporator, was cooled to 5°C and strongly acidified with concentrated sulphuric acid and extracted with CCl_3F (5×30 ml). The extract was dried over $MgSO_4$ and the solvent was distilled off. Vacuum distillation of the residue gave acid **11** as a white crystalline substance (crystallised in the condenser) possessing a strong irritating smell. Yield: 2.5 g (18 mmol, 22.5% related to $CF_3CHClBr$). The mp 40°C, bp 78–80°C/37 Torr (Lit.: 68–69°C/20 Torr [36]. Analysis, found: C, 34.3; H, 2.3; F, 40.7%, Calculated for $C_4H_3F_3O_2$ (140.06): C, 34.3; H, 2.2; F, 40.7%. ^{1}H NMR δ: 6.50 (dq, $^3J_{HH} = 15.8$ Hz, $^4J_{HF} = 1.9$ Hz, 1H); 6.86 (dq, $^3J_{HH} = 15.8$ Hz, $^3J_{HF} = 6.4$ Hz, 1H); 10.72 (s, COOH) ppm. ^{19}F NMR δ: 66.4 (dd, $^3J_{HF} = 6.4$ Hz, $^4J_{HF} = 1.9$ Hz, CF_3) ppm. MS (EI, 70 eV): *m/z* (rel. int., ion): 140 [35, M^+]; 123 [60, $(M - OH)^+$]; 120 [15, $(M - HF)^+$]; 95 (40, $C_3H_2F_3^+$); 77 (40, $C_3H_3F_2^+$); 76 (50, $C_3H_2F_2^+$); 69 (100, CF_3^+); 45 (85, CO_2H^+). IR (neat); ν (cm^{-1}): ca. 3000 (vs, br, OH); 1717.0 (vs, C=O).

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