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Sodium dithionite initiated addition of 1-bromo-1-chloro-2,2,2-trifluoroethane to β-pinene Synthesis of CF_3-substituted terpenoids

Wojciech Dmowski[*], Jolanta Ignatowska, Krystyna Piasecka-Maciejewska

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

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Abstract

Sodium dithionite effectively promotes the addition of 1-bromo-1-chloro-2,2,2-trifluoroethane to the exocyclic double bond of β-pinene. The reaction proceeded in an $MeCN/H_2O$ system to give almost quantitatively a 1:1 mixture of diastereoisomers of 4-(2-bromoisopropyl)-1-(2-chloro-3,3,3-trifluoropropyl)-cyclohexene (**1**). Dehydrobromination of **1** with pyridine gave a mixture of regioisomeric dienes **2** and **3**, while treatment with DBU at elevated temperature resulted in total dehydrohalogenation to give trienes **4** and **5**. Reduction of **1** with Bu_3SnH gave 1-(2-chloro-3,3,3-trifluoropropyl)-4-(isopropyl)cyclohexene (**6**) which on dehydrochlorination with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) afforded conjugated diene, 4-isopropyl-1-(*trans*-3,3,3-trifluoropropenyl)-cyclohexene (**7**), with 50% overall yield. All the transformations proceeded with the retention of configuration at the carbon atom C-4 and the final compound **7** exhibited high optical activity.

Keywords: 1-Bromo-1-chloro-2,2,2-trifluoroethane; Sodium dithionite; Pinene; Trifluoromethyl terpenoids

1. Introduction

The reaction of perfluoroalkyl halides (R_FI, R_FBr) with sodium dithionite in aqueous medium, known as "sulfinatodehalogenation", provides an easy way of generating perfluoroalkyl radicals [1,2]. These electron-deficient radicals could be effectively trapped by electron-rich substrates like alkenes, alkynes and arenes to give addition or substitution products. The addition of perfluoroalkyl iodides to α-pinene was reported to proceed with ring opening to give unstable (not isolated) adducts, 4-(2-iodoisopropyl)-1-methyl-6-perfluoroalkylcyclohexenes, which after in situ reduction of the iodine afforded 4-(isopropyl)-1-methyl-6-perfluoroalkylcyclohexenes in reasonable yields [3,4]. A similar reaction of 1,1,1-tribromo-2,2,2-trifluoroethane with β-pinene gave stable adduct, 4-(2-bromoisopropyl)-1-(1,1-dibromo-3,3,3-trifluoroethyl)cyclohexene in a 57% yield [5].

In the preceding papers [6–8], we reported that sulfinatodehalogenation procedure could be applied to 1-bromo-1-chloro-2,2,2-trifluoroethane, commercially available as Halothane® (inhalation anaesthetic), to generate $CF_3CHCl^{\cdot}$ radicals which readily reacted with vinyl ethers [6,7] and with pyrroles [8].

Presently, we report successful addition of 1-bromo-1-chloro-trifluoroethane, to (1*S*,5*S*)-(−)-β-pinene and transformations of the adduct **1** to new trifluoromethyl-substituted terpenoids **2–7**. The aim of this work was to verify applicability of the $CF_3CHClBr/Na_2S_2O_4$ system for introduction of the CF_3 group into more complex molecules, e.g. terpenes.

2. Results and discussion

1-Bromo-1-chloro-2,2,2-trifluoroethane reacted spontaneously with β-pinene under typical sulfinatodehalogenation conditions ($Na_2S_2O_4/NaHCO_3/MeCN/H_2O$) to give 4-(2-bromoisopropyl)-1-(2-chloro-3,3,3-trifluoropropyl)-cyclohexane (**1**) almost quantitatively (Scheme 1). Since the reaction mixture formed a three-phase system (organic phase, water phase saturated with inorganic salts and solid phase of insoluble salts), vigorous agitation was essential for the reaction to proceed and to give satisfactory yields. The reaction started at 18–20 °C, as evidenced by evolution of gaseous CO_2 (formed by the reaction of SO_2 with $NaHCO_3$)

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[*] Corresponding author. Tel.: +48-22-632-32-21; fax: +48-22-632-66-81.
E-mail address: dmowski@icho.edu.pl (W. Dmowski).

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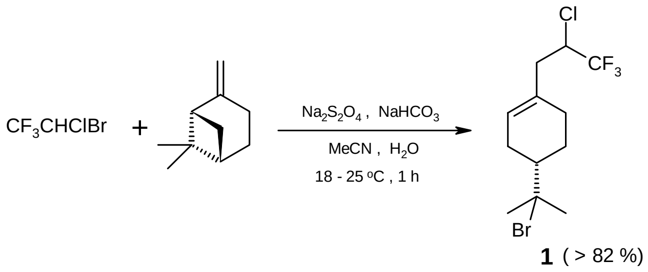


Scheme 1.

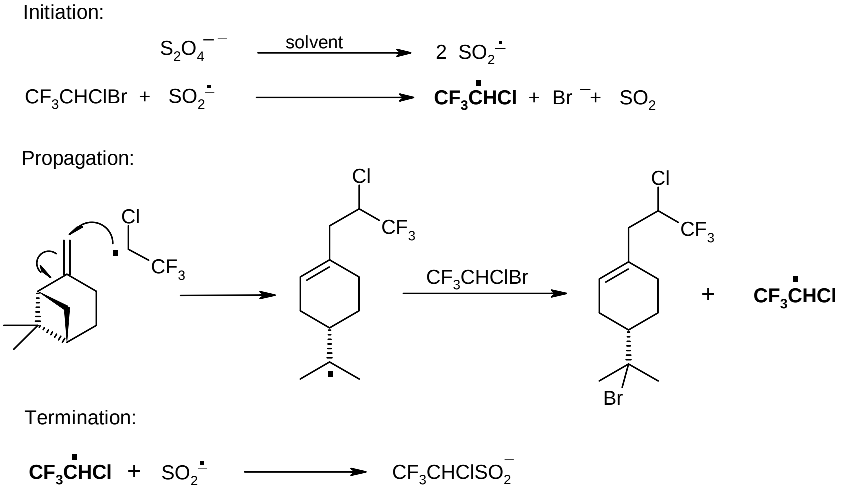
and a considerable exothermic effect (temperature rise to 30–32 °C), and was completed within about 15 min. Elemental analysis of the crude product gave almost theoretical values for all the elements indicating that it consisted essentially of compound **1**. The crude product crystallised soon after removal of a solvent, which phenomenon also confirmed high contents of **1**. The ^{1}H and ^{19}F NMR spectra disclosed, however, the presence of ca. 6–8% of dehydrobrominated compound **2**. Better results were obtained when the reaction temperature was kept at 25 °C; the reaction time was increased to about 1 h but the contents of **2** was reduced to 2–3%. Pure compound **1** (ca. 99%) was obtained by pressing out a liquid fraction from the crystalline row product at room temperature under reduced pressure. As evidenced by spectral data, compound **1** was always formed as a 1:1 mixture of two diastereoisomers (two signals for the CF_3 and CHCl groups) but their attempted separation by crystallisation failed; the isomer ratios in the crystals and in the liquid phases were almost the same. We were also unable to separate the isomers by TLC and GLC techniques. Compound **1** is stable at ambient temperature but the attempted distillation, even under low pressure (3.3 N/m^2), resulted in evolution of copious amounts of HBr and tar formation.

In most of the published works, including our earlier studies of the reactions of $CF_3CHClBr$ with enol ethers [6,7], equimolar amounts of the initiator and a perhaloalkane were reported to be necessary to achieve good yields. However, in the present case, as little as 0.25 equivalent of $Na_2S_2O_4$ was found to be satisfactory. The reactions proceeded at similar rates affording similar, high yields of products as with an equivalent amount of the initiator. There are only two papers [8,9] prior to the present work, reporting the use of a low ratio of the initiator to a perhaloalkane. Low ratio of the initiator to $CF_3CHClBr$ suggests a free radical chain mechanism, possibly as depicted in Scheme 2. High yields of **1** indicate that the attack of the CF_3CHCl radicals on the double bond of β-pinene and the bromine transfer, are much faster processes than the termination reaction with the SO_2 radical-anion leading to the sulfinate.

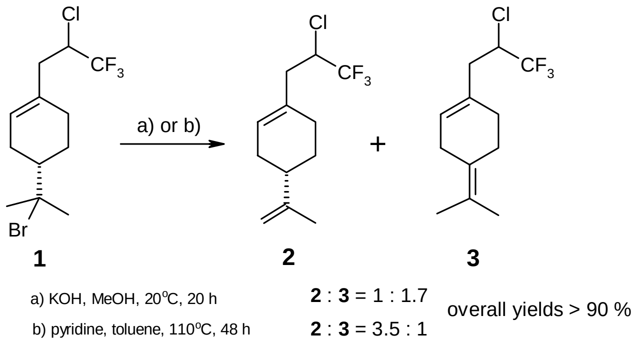
In spite of the thermal instability of **1**, this compound was found to be reasonably stable in alkaline media; no dehydrobromination occurred by stirring with 10% aqueous KOH for 24 h at room temperature. However, treatment of **1** with methanolic solution of KOH at ambient temperature resulted in dehydrobromination to give a mixture of regioisomeric dienes, 1-(2-chloro-3,3,3-trifluoropropyl)-4-(isopropenyl)cyclohexene (**2**) and 1-(2-chloro-3,3,3-trifluoro-propyl)-4-(isopropylidene)cyclohexene (**3**), in a 1:1.7 ratio. Compound **1** was also successfully dehydrobrominated with pyridine in refluxing toluene but in this case a limonene-like diene **2** was the major product (**2**:**3** = 3.5:1). In both cases, the reactions proceeded chemoselectively, i.e. no dehydrochlorinated products were found (Scheme 3).

Compounds **2** and **3** are difficult to separate from one another and therefore they were identified in their mixtures. These mixtures gave correct elemental analyses, identical GC–mass spectra for both components, structures of which were unambiguously determined by the ^{1}H and ^{19}F NMR spectra. Careful distillation allowed a fraction containing 90% of **2** to be obtained; this compound, as expected and confirmed by two NMR signals of the CF_3 and CHCl groups, always was a mixture of two diastereoisomers in a 1:1 ratio.

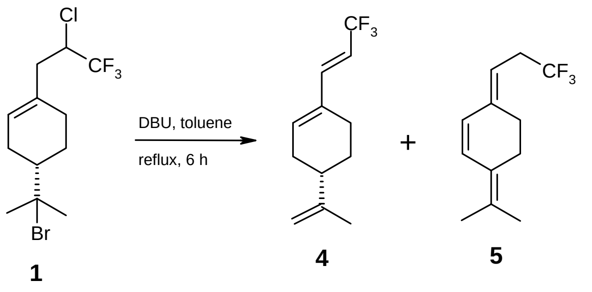
Total dehydrohalogenation of **1** was achieved by 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in refluxing toluene to give inseparable mixture of trienes, 4-isopropenyl-1-



Scheme 2.



Scheme 3.



Scheme 4.

(*trans*-3,3,3-trifluoropropenyl)cyclohexene (**4**) and 3-isopropylidene-6-(3,3,3-trifluoropropylidene)-cyclohexene (**5**) (Scheme 4) as the main components (total 68%) together with numerous unidentified compounds. ^{1}H and ^{19}F NMR spectra of this mixture were sufficiently clear to elucidate structures of both compounds; the presence of the CH_2CF_3 moiety in **5** was clearly evidenced by the CF_3 group signal which appeared as a triplet. Formation of **5** should be interpreted in terms of a base initiated proton abstraction from the most acidic position 3 in **4**, followed by π-electron shift. After 1 week at room temperature, this mixture polymerised to form a viscous resin.

The most successful transformation of **1** was reduction of the bromine atom with Bu_3SnH to give the menthene-like compound **6** which on dehydrochlorination afforded conjugated diene, 4-isopropyl-1-(*trans*-3,3,3-trifluoropropenyl)cyclohexene (**7**) (Scheme 5). The reduction proceeded cleanly to give, after double distillation, compound **6** of 95% purity and with over 75% isolated yield. Removal of the HCl molecule from **6** required prolonged treatment with DBU in refluxing toluene and gave a mixture containing ca. 82% of **7** together with 1–2% of unchanged **6**, 10–12% of **4** and **5** and some unidentified compounds. Careful distillation allowed diene **7** of 88% purity to be obtained. The presence of conjugated double bonds in **7** has been confirmed by strong IR absorption at 1656 cm^{-1} and the *trans* configuration of the exocyclic double bond by large coupling constant of the vinylic protons. No *cis* isomer was found.

Diene **7** exhibits high optical activity and the same sign of the optical rotation coefficient as the starting β-pinene; this suggests that all the transformations leading to **7** proceed with the retention of absolute configuration at carbon atom C-4. Compound **7** seems to be valuable intermediate to numerous CF_3-substituted bicyclic terpenenoids; its behaviour in the Diels–Alder cycloaddition reactions is under investigation.

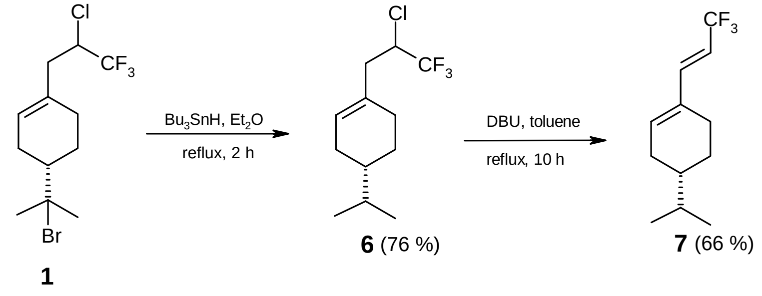
3. Experimental

Melting points were determined in capillaries and boiling points were measured during distillation; both are uncorrected. ^{1}H and ^{19}F NMR spectra were recorded with a Varian 400 spectrometer, both in $CDCl_3$ solutions. Chemical shifts are quoted in ppm from internal TMS for ^{1}H and from internal $CFCl_3$ for ^{19}F nuclei. GLC analyses were performed with a Shimadzu GC-14A chromatograph using a 3.5 m × 2 mm column packed with 5% silicone oil SE-52 on Chromosorb. 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.

1-Bromo-1-chloro-2,2,2-trifluoroethane and (1*S*,5*S*)-(−)-β-pinene [purity ≥ 99%, $\alpha_D^{20} = -21 \pm 1$ (neat)] were commercial reagents.

3.1. (4S)-4-(2-Bromoisopropyl)-1-(2-chloro-3,3,3-trifluoropropyl)cyclohexene (1) (two diastereo isomers in a 1:1 ratio)

Sodium dithionite (1.0 g [85%], 5 mmol) and sodium hydrogen carbonate (2.1 g, 25 mmol) were suspended in



Scheme 5.

an acetonitrile–water solution (2:1, 30 ml). The reaction mixture was vigorously stirred and cooled to 15 °C, then β-pinene (2.7 g, 20 mmol) and $CF_3CHClBr$ (4.15 g, 21 mmol) were added one by one. The cooling bath was removed and the reaction mixture was allowed to warm up. When the temperature reached 18–20 °C, gas evolution (CO_2) began and a noticeable exothermic effect occurred. When the temperature reached 25 °C, it was kept at this level, initially by cooling and then by warming with an external water bath. The reaction ceased after about 1 h (no more gas evolution) and most of inorganic salts dissolved. Stirring was continued for another 15 min, while keeping the temperature at 25 °C, then water (50 ml) was added. The reaction mixture was extracted with diethyl ether (30 + 2 × 20 ml), the combined extracts were washed with brine (3 × 30 ml) and dried over $MgSO_4$. Removal of the solvent on a rotary evaporator gave colourless oil, which soon solidified to form white, soft crystals (6.1 g, purity 92–94%). Pure compound **1** (ca. 99%) was obtained by putting the crude crystalline product on a Schott's funnel and sucking off an oily part under reduced pressure at room temperature. Yield: 5.5 g (82.5%). mp 30–32 °C. Analysis: Found: C, 43.3; H, 5.3; Br, 23.5; Cl, 10.7; F, 17.1%. Calculated for $C_{12}H_{17}BrClF_3$ (333.62): C, 43.2; H, 5.1; Br, 23.95; Cl, 10.6; F, 17.1%. ^{1}H NMR δ: ca. 1.45 (complex, ^{1}H); ca. 1.65 (complex, 1H); 1.75 (s, 3H, CH_3); 1.81 (d, $^4J_{HH} = 1.65$ Hz, 3H, CH_3); 1.9–2.2 (complex, 4H); 2.27 and 2.32 (m, 1H); 2.41 (ddd, $J_{AB} = 14.7$ Hz, $^3J_{HH} = 11.14$ and ca. 3.3 Hz, H_A, $-\underline{CH_2}-CHCl$); 2.68 (d of narrow m, $J_{AB} = 14.7$ Hz, H_B, $-\underline{CH_2}-CHCl$); ca. 4.18 (2× dqd, $^3J_{HH} =$ ca. 11 Hz, $^3J_{HF} =$ ca. 6.6 and 3.3 Hz, 1H, CHCl); 5.60 (narrow m, 1H, vinylic) ppm. ^{19}F NMR δ: 75.07 and 75.16 (d, $^3J_{HF} = 6.8$ Hz, CF_3, signal ratio = 1:1) ppm. MS (EI, 70 eV, 42 °C): m/z (rel. int., ion): 336, 334, 332 (1.5, M^+); 255, 253 [13, 39, $(M–Br)^+$]; 254, 252 [17, 36, $(M–HBr)^+$]; 239, 237 [7, 20, $(M–HBr–CH_3)^+$]; 213, 211 [7, 26, $(M–Br–C_3H_6)^+$]; 199, 197 [32, 100, $(M–Br–C_4H_8)^+$]; 173 (9); 135 (18); 121 (25); 109 (20); 93 (30); 91 (941); 79 (43); 77 (20); 69 (29, CF_3^+); 68 (42, $C_5H_8^+$); 67 (27, $C_5H_7^+$); 43 (37, $C_3H_7^+$); 41 (48, $C_3H_5^+$), 39 (20).

3.2. Dehydrohalogenation of *1*

3.2.1. With KOH in methanol

Compound **1** (6 g, 18 mmol), prepared as in Section 3.1, was added to a 1.5 M solution of KOH in methanol (50 ml) and stirred at ambient temperature overnight after which time a large amount of KBr precipitated. Methanol was removed on a rotary evaporator then water (80 ml) was added and excess KOH was neutralised with hydrochloric acid. The organic material was extracted with ether (30 + 2 × 20 ml) and the extract was dried over anhydrous $MgSO_4$. Evaporation of the solvent on a rotary evaporator gave 4.1 g (16.2 mmol, yield: 90%) of colourless liquid possessing a mild terpenic smell. Elemental analysis: Found: C, 56.85; H, 6.45; Cl, 14.2; F, 22.8%. Calculated for $C_{12}H_{16}ClF_3$ (252.70): C, 57.0; H, 6.4; Cl, 14.1; F, 22.55%. This liquid was shown by integrated ^{1}H and ^{19}F NMR spectra and the GLC analysis to contain ca. 34% of diene **2** and 58% of diene **3**.

3.2.2. With pyridine in refluxing toluene

Compound **1** (6 g, 18 mmol) and pyridine (4.3 g, 54 mmol) were refluxed in dry toluene (50 ml) for 48 h. The precipitate of pyridine hydrobromide was filtered off, the solution was washed with 3% hydrochloric acid (3 × 20 ml), followed with brine, until neutral, and dried over anhydrous $MgSO_4$. Evaporation of the solvent gave 4.3 g (17 mmol, yield: 95%) of colourless liquid composed of diene **2** (78%) and diene **3** (22%) (estimated from the integrated NMR spectra). Elemental analysis as above.

Careful distillation of the combined products of two experiments (8 g) through a 10 cm long Vigreux column gave a fraction containing 90% of **2** and 10% of **3** (3.2 g, bp 40–44 °C/13.3 N/m^2) and a fraction containing 85% of **2** and 15% of **3** (3.7 g, bp 44–46 °C/0.1 Torr). The residue contained mostly **3** (ca. 80%) and unknown impurities.

(4*S*)-1-(2-Chloro-3,3,3-trifluoropropyl)-4-(isopropenyl)-cyclohexene (**2**) (diastereoisomers ratio 1:1): ^{1}H NMR δ: ca. 1.45 (complex, 1H); ca. 1.65 (complex, 1H); 1.75 (s, 3H, CH_3) and 1.81 (d, $^4J_{HH} = 1.65$ Hz, 3H, CH_3); 1.9–2.2 (complex, 4H); 2.27 and 2.32 (m, 1H); 2.41 (ddd, $J_{AB} = 14.7$ Hz, $^3J_{HH} = 11.4$ and ca. 3.3 Hz, 1H, H_A, $\underline{CH_2}-CHCl$); 2.68 (d of narrow m, $J_{AB} = 14.7$ Hz, 1H, H_B, $-\underline{CH_2}-CHCl$); 4.18 (2× dqd, $^3J_{HH} =$ ca. 11 Hz, $^3J_{HF} =$ ca. 6.6 and 3.3 Hz, 1H, CHCl); 4.72 (narrow m, 1H, $CH_2=$); 4.73 (sext, $J =$ ca. 1.5 Hz, 1H, $CH_2=$); 5.60 (narrow m, 1H, vinylic) ppm. ^{19}F NMR δ: 75.07 (d, $^3J_{HF} = 6.8$ Hz) and 75.16 (d, $^3J_{HF} = 6.8$ Hz) ppm. MS (EI, 70 eV): m/z (rel. int., ion): 254, 252 (18, 47, M^+); 239, 237 [13, 34, $(M–CH_3)^+$]; 225, 223 [4, 12, $(M–C_2H_5)^+$]; 212, 210 [10, 42, $(M–C_3H_4)^+$]; 211, 209 [45, 84, $(M–C_3H_5)^+$]; 210, 208 [27, 34, $(M–C_3H_6)^+$]; 173 [36, $(M–HCl–C_3H_5)^+$]; 169 (20); 153 (28); 135 (19); 121 (49); 93 (55); 91 (59); 79 (48, $C_6H_5^+$); 68 (100, $C_5H_8^+$); 67 (34, $C_5H_7^+$). IR (neat): 1645 cm^{-1} (m, exocyclic C=C); 1676, 1717 cm^{-1} (vw, ring C=C).

1-(2-Chloro-3,3,3-trifluoropropyl)-4-(isopropylidene)cyclohexene (**3**): ^{1}H NMR δ: 1.66 (narrow m, $J =$ ca. 0.4 Hz, CH_3); 1.70 (narrow m, $J =$ ca. 0.4 Hz, CH_3); 1.8–2.4 (complex, 4H); 2.43 (dd, $^2J_{AB} = 14.7$ Hz, $^3J_{HH} = 10.8$ Hz, H_A, $\underline{CH_2}-CHCl$); 2.68 (dm, $^2J_{AB} = 14.7$ Hz, H_B, $\underline{CH_2}-CHCl$) 2.80 (narrow m, 2H); 4.19 (dqd, $^3J_{HH} = 10.8$ Hz; $^3J_{HF} = 6.7$ Hz; $^3J_{HH} = 3.3$ Hz, 1H, CHCl): 5.59 (narrow m, 1H, vinylic) ppm. ^{19}F NMR: 75.16 (d, $J_{HF} = 6.7$ Hz) ppm.

3.2.3. With 1,8-diazabicyclo[5.4.0]undec-7-ene in refluxing toluene

Crude **1** (10.5 g, 31.5 mmol) and DBU (13.7 g, 90 mmol) were refluxed in dry toluene (80 ml, distilled from sodium wire) for 6 h. The precipitate of DBU hydrohalides (11.5 g) was filtered off, washed with toluene, the combined solutions were washed with 3% hydrochloric acid (3 × 20 ml), followed with brine until neutral, and dried over anhydrous $MgSO_4$. Evaporation of the solvent under reduced pressure (660 N/m^2) gave 6.6 g (30.5 mmol, yield: 97%) of a brown liquid which was shown by integrated ^1H and ^{19}F NMR spectra to contain trienes **4** (30%) and **5** (38%), ca. 7% of dienes **2** and **3** and ca. 25% of numerous unidentified compounds containing the CF_3 group.

Alike treatment of a mixture of dienes **2** (85%) and **3** (15%) (5.8 g, 23 mmol) with DBU (5.3 g, 35 mmol) resulted in a mixture (4.9 g, 22.7 mmol, yield: 98%) containing 58% of **4**, 14% of **5**, 13% of unreacted **2** and **3** and ca. 15% of numerous minor components. Vacuum distillation (106.6 N/m^2) through a 10 cm long Vigreux column gave a colourless fraction (3.5 g, bp 58–60 °C/0.8 Torr) containing ca. 40% of **4**, 10% of **2** and **3**, 50% of numerous minor components, but not compound **5** was present.

(4*S*)-4-Isopropenyl-1-(*trans*-3,3,3-trifluoropropenyl)-cyclohexene (**4**): ^1H NMR δ: 1.75 (narrow q, $J =$ ca. 0.6 Hz, CH_3); 1.92 (dm, $J =$ ca. 12 Hz, 1H); 2.1–2.4 (6H); 4.73 (qn, $J =$ ca. 0.9 Hz, 1H, $=CH_2$); 4.76 (qn, $J =$ ca. 1.5 Hz, 1H, $=CH_2$); 5.54 (dq, $^3J_{HH} = 16.0\,Hz$, $^3J_{HF} = 6.8\,Hz$, 1H, $=CH–CF_3$); 6.07 (narrow m, 1H, =CH–); 6.75 (dq, $^3J_{HH} = 16.0\,Hz$, $^4J_{HF} = 2.0\,Hz$, exocyclic –CH=) ppm. ^{19}F NMR δ: 63.15 (broad d, $^3J_{HF} = 6.8\,Hz$) ppm.

3-Isopropylidene-6-(3,3,3-trifluoropropylidene)cyclohexene (**5**): ^1H NMR δ: 1.78 (s, CH_3); 1.82 (s, CH_3); 2.38 (broad s, 2H, H-4); 2.39 (broad s, 2H, H-5); 2.91 (qd, $^3J_{HF} = 10.9\,Hz$, $^3J_{HH} = 7.5\,Hz$, 2H, CH_2CF_3); 5.29 (br t, $^3J_{HH} = 7.5\,Hz$, 1H, H-7), 6.05 (d, $^3J_{HH} = 10.0\,Hz$, 1H, H-2); 6.49 (d, $^3J_{HH} = 10.0\,Hz$, 1H, H-1) ppm. ^{19}F NMR δ: 66.6 (t, $^3J_{HF} = 10.9\,Hz$, CF_3) ppm.

*3.3. (4S)-1-(2-Chloro-3,3,3-trifluoropropyl)-4-(isopropyl)cyclohexene (**6**)*

Compound **1** (12 g, 36 mmol, 99% purity) and $HSnBu_3$ (12 g, 41 mmol) were refluxed in dry ether (80 ml) under atmosphere of argon for 2 h then left overnight at ambient temperature while stirring. The reaction mixture was subjected to a vacuum distillation using a 5 cm long Vigreux column. A fraction collected at 50–58 °C/53.3 N/m^2 (9.6 g) was found by GLC to contain ca. 90% of **6** and some unidentified components. Re-distillation gave compound **6** of 95% purity (by integrated ^{19}F NMR contains ca. 3% of **2**) as colourless liquid with a mild terpenic smell. Yield: 7.0 g (76.4%). bp 54–56 °C/53.3 N/m^2. Analysis: Found: C, 56.4; H, 7.2; Cl, 13.7; F, 22.2%. Calculated for $C_{12}H_{18}ClF_3$ (254.72): C, 56.6; H, 7.1; Cl, 13.9; F, 22.4%. ^1H NMR δ: (400Mz, $CDCl_3$): 0.89 (d, $^3J_{HH} = 6.6\,Hz$, 3H, CH_3); 0.90 (d, $^3J_{HH} = 6.6\,Hz$, 3H, CH_3); 1.28 (m, 2H); 1.48 (oct d, $^3J = 6.8$ and ca. 1.1 Hz, 1H): ca. 1.8 (m, 2H); 1.9–2.1 (complex, 3H); 2.40 (dd, $^2J_{AB} = 14.6\,Hz$, $^3J_{HH} = 11.0\,Hz$, 1H, CH_2); 2.66 (dm, $^2J_{AB} = 14.6\,Hz$, 1H, CH_2); 4.18 (2× dqd, $^3J_{HH} = 11.0\,Hz$; $^3J_{HF} = 6.6\,Hz$; $^3J_{HH} =$ ca. 3.3 Hz, 1H, CHCl–); 5.59 (narrow m, 1H, H-2) ppm. ^{19}F NMR δ: (400Mz, $CDCl_3$): 70.20 (d, $^3J_{HF} = 6.7\,Hz$) and 70.28 (d, $^3J_{HF} = 6.5\,Hz$) ppm in a 1:1 ratio. MS (EI, 70 eV): *m/z* (rel. int., ion): 256, 254 (8, 26, M^+); 241, 239 [6, 18, $(M–CH_3)^+$]; 213, 211 [33, 100, $(M–C_3H_7)^+$]; 199, 197 [6, 18, $(M–C_4H_9)^+$]; 175 [10, $(M–C_3H_7–HCl)^+$]; 135 (14); 123 (17); 81 (34, $C_6H_9{}^+$); 79 (45, $C_6H_7{}^+$); 69 (30, $CF_3{}^+$); 67 (30, $C_5H_7{}^+$); 55 (29, $C_4H_7{}^+$); 43 (25, $C_3H_7{}^+$); 41 (38, $C_3H_5{}^+$). IR (neat): 1676 and 1726 cm^{-1} (vw, C=C).

*3.4. (4S)-(−)-4-Isopropyl-1-(trans-3,3,3-trifluoropropenyl)cyclohexene (**7**)*

Compound **6** (6.8 g, 26.7 mmol, purity 95%) and DBU (8.0 g, 53 mmol) were refluxed in dry toluene (60 ml) for 10 h and left overnight at ambient temperature. The precipitate of DBU hydrochloride was washed out with 3% hydrochloric acid (3 × 20 ml), followed by brine until neutral, and dried over anhydrous $MgSO_4$. The solvent was removed on a rotary evaporator and the residue was vacuum distilled using a 5 cm long Vigreux column. A fraction collected at 48–52 °C/0.4 Torr (4.7 g) was found by integrated ^{19}F NMR to contain ca. 82% of **7**, 3% of **4**, 8% of **5**, 1% of **6** and 6% of a unknown compound. Yield of **7**: 66%. Re-distillation of the combined fractions from three experiments (12.5 g) gave compound **7** of 88% purity (9.6 g); a colourless liquid possessing a weak irritating smell. bp 50–52 °C/0.4 mmHg. Analysis: Found: C, 65.5; H, 7.7; F, 25.9% and trace amount of Cl. Calculated for $C_{12}H_{17}F_3$ (218.16): C, 66.0; H, 7.85; F, 26.1%. ^1H NMR: 0.90 (d, $^3J_{HH} = 6.8\,Hz$, 3H, CH_3); 0.92 (d, $^3J_{HH} = 6.8\,Hz$, 3H, CH_3); 1.2–1.4 (m, 2H); 1.51 (oct, $^3J = 6.8\,Hz$, 1H): 1.8–1.9 (m, 2H); 2.08 (m, 1H); 2.20 (narrow m, 1H); 2.21 (narrow m, 1H): 5.52(dd, $^3J_{HH} = 15.8\,Hz$, $^3J_{HF} = 6.9\,Hz$, 1H, $=C\underline{H}-CF_3$); 6.05 (narrow m, 1H, H-2): 6.94 (dd, $^3J_{HH} = 15.8$ and 1.7 Hz, 1H, exocycle $-C\underline{H}=$) ppm. ^{19}F NMR: 63.1(d, $^3J_{HF} = 6.9\,Hz$) ppm. GC–MS: 218 (40, M^+); 203 [10, $(M–CH_3)^+$]; 189 [10, $(M–C_2H_5)^+$]; 175 [70, $(M–C_3H_7)^+$]; 161 [75, $(M–C_4H_9)^+$]; 127 (30); 91 (35, $C_7H_7{}^+$); 79 (85, $C_6H_7{}^+$); 77 (45, $C_6H_5{}^+$); 69 (50, $CF_3{}^+$); 55 (60, $C_4H_7{}^+$); 43 (60, $C_3H_7{}^+$); 41 (100, $C_3H_5{}^+$). HRMS: Found: 218.12747. Calculated for $C_{12}H_{17}F_3$: 218.12824. IR (film): 1656 cm^{-1} (s) (C=C–C=C). $\alpha_D^{30} = -89.7$ (5% w EtOH).

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