JOURNAL OF PHYSICAL ORGANIC CHEMISTRY
*J. Phys. Org. Chem.* 2004; **17:** 332–342
Published online in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/poc.733

# Synthesis of new heterocyclic compounds: 4-(3,3,3-trifluoro-2-trifluoromethyl-1-propenyl)-1, 3-thiazoles: structural and conformational study of 2-phenyl-4-(3,3,3-trifluoro-2-trifluoromethyl-1-propenyl)-1,3-thiazole†

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*Received 30 July 2003; revised 8 November 2003; accepted 13 November 2003*

**epoc** ABSTRACT: The synthesis of 4-(3,3,3-trifluoro-2-trifluoromethyl-1-propenyl)-1,3-thiazole derivatives from 5,5,5-trifluoro-4-(trifluoromethy)-3-penten-2-one is described. Attention is mainly focused on 2-*N*-phenylamino-4-(3,3,3-trifluoro-2-trifluoromethyl-1-propenyl)-1,3-thiazole. Structural and conformational studies using several spectroscopic methods (FT-IR, NMR, Raman, x-ray, MS) were performed. Geometry optimization and prediction of vibrational and magnetic properties were carried out using *ab initio* Hartree–Fock (HF) and density functional theory (DFT) calculations to assist the spectroscopic analysis. Copyright © 2004 John Wiley & Sons, Ltd.
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KEYWORDS: 4-(3,3,3-trifluoro-2-trifluoromethyl-1-propenyl)-1,3-thiazoles; structure; conformation; x-ray; NMR

## INTRODUCTION

The synthesis of heterocyclic rings containing sulphur and nitrogen atoms has been particularly attractive because of its application in the pharmacological field.[1,2] It is already known that the introduction of fluorine in organic compounds often modifies their chemical and biochemical properties.[3] General routes for the preparation of fluorinated heterocyclic compounds involve both direct fluorination of an already existing heterocyclic ring or ring construction using, for example, cycloaddition reactions with fluorinated synthons such as trifluoromethyl unsaturated ketones.[4] Electron-deficient compounds such as *gem*-bis(trifluoromethyl-$\alpha$,$\beta$-unsaturated ketones are precursors for a variety of heterocyclic compounds. Starting from 5,5,5-trifluoro-4-trifluoromethyl-3-penten-2-one (**1**), interesting trifluoromethyl heterocyclic compounds, such as thiazoles, tetrahydrofuranones and diazepines, have been obtained.[5–7] Current methods for thiazole preparation involve the use of substituted carbonyl compounds; the most common procedure is the reaction between thioamides and $\alpha$-halocarbonyl compounds.

We report the synthesis of 1-chloro-5,5,5-trifluoro-4-trifluoromethyl-3-penten-2-one (**2**) as starting material for reaction with thiobenzamide, *N*-phenyl- and *N*-allylthioureas and acetamide to obtain 2-phenyl-4-(3,3,3-trifluoro-2-trifluoromethyl-1-propenyl)-1,3-thiazole (**3**), 2-*N*-phenylamino-4-(3,3,3-trifluoro-2-trifluoromethyl-1-propenyl)-1,3-thiazole (**4**), 2-allylamino-4-(3,3,3-trifluoro-2-trifluoromethyl-1-propenyl)-1,3-thiazole (**5**) and the intermediate 4-hydroxy-2-methyl-4-(3,3,3-trifluoro-2-trifluoromethyl-1-propenyl)-1,3-thiazoline (**6**) (Scheme 1). Trifluoromethyl-containing alkenylthiazoles are useful in the construction of natural products such as terpenes, steroids and alkaloids.[8–10]

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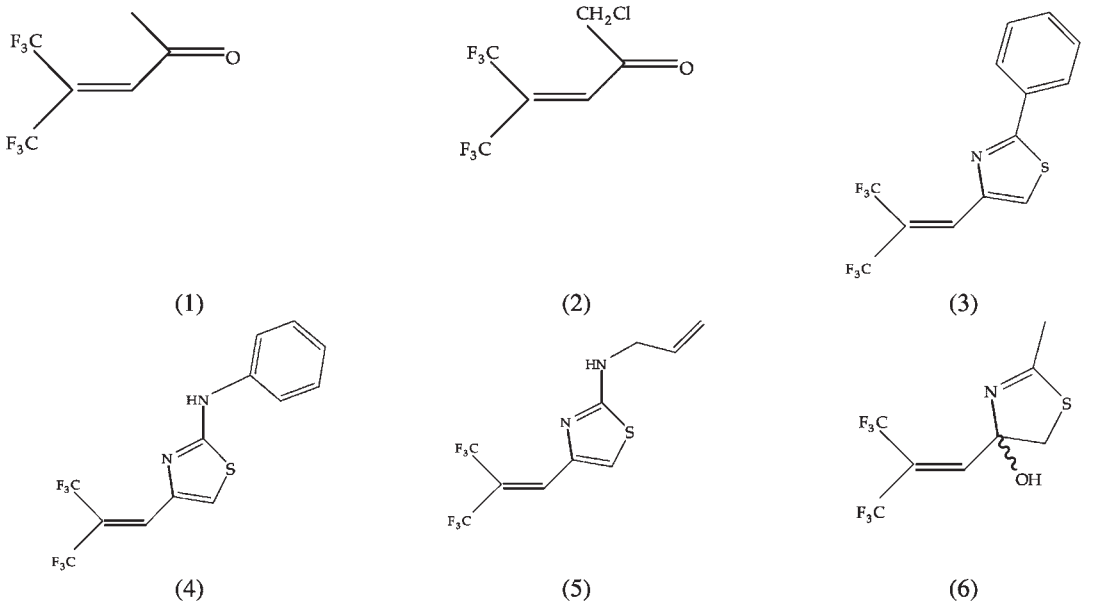
*Contract/grant sponsors:* Deutscher Akademischer Austauschdienst (DAAD); Ruhr-Universität Bochum; Comisión de Investigaciones Científicas de la Provincia de Buenos Aires (CICBA); Fundación Antorchas; Alexander von Humboldt Foundation; Agencia Nacional de Promoción Científica y Técnica (ANPCYT); Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET); British Council; Jesus College, Oxford; Facultad de Ciencias Exactas (UNLP); AvH–Fundación Antorchas; ANPCYT–DAAD.
†Dedicated to Professor Dr Pedro J. Aymonino on the occasion of his 75th birthday.
‡CODV is a member of the Carrera del Investigador Científico y Tecnológico del CONICET, Agrentina.




**Scheme 1**

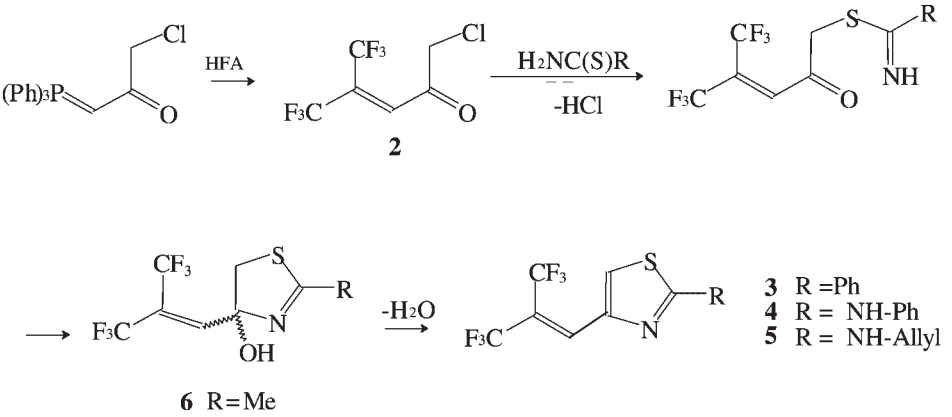
For one selected molecule, the 2-phenyl derivative (**3**), we were also interested in a more detailed structural study. This includes the analysis of the possible conformational relationship s-*cis*/s-*trans* using one-($^{1}$H, $^{19}$F and $^{13}$C) and two-dimensional heteronuclear correlation (HETCOR) and C,H correlation via long-range coupling (COLOC) NMR spectroscopy and x-ray analysis. In order to assist the analysis, geometry optimization and prediction of vibrational and magnetic properties were performed using *ab initio* Hartree–Fock (HF) and density functional theory (DFT) calculations.

## EXPERIMENTAL

Solvents were distilled before use. Volatile compounds were handled in a vacuum line. Microanalyses were performed with a Carlo Erba Model 1106 elemental analyser. For NMR analyses, dried solvents with actived molecular sieves (4 Å) were used for $^{13}$C and $^{1}$H and $CFCl_3$ for $^{19}$F NMR, respectively. A Bruker WP-80 instrument was used for **6**, an AC- 250 for **3** and an AM-400 for **4** and **5**. FT-IR spectra were measured with a Bruker IFS 85 FTIR instrument (4000–400 $cm^{-1}$) in KBr pellets. Raman spectra were obtained with the Raman accessory of a Bruker IFS 66 spectrometer equipped with an Nd:YAG laser (3500–100 $cm^{-1}$). Theoretical calculations were performed using the Gaussian 98 program.[11] For GC–MS, a Hewlett-Packard Model 5989 TO and a Hewlett-Packard Model 5890 instruments (12.5 m capillary column coated with OV-1), 70 eV, were used. Crystallographic analysis was carried out using single crystals formed from hexane solutions by slow solvent evaporation at room temperature The determination of the crystalline structure was carried out using a Siemens Model P4 four-circle automatic diffractometer, using Mo K$\alpha$ radiation ($\lambda_{\text{Mo K}\alpha} = 0.71073$ Å) monochromated with graphite. Computations were made with SHELXL-93.[12] Crystal data and structure refinement of **3** are summarized in Table 1. The starting materials thiobenzamide, *N*-allylthiourea and *N*-phenylthiourea were

**Table 1.** Crystal data and structure refinement for $C_{13}H_7N F_6S$ (**3**)

| Empirical formula | $C_{13}H_7N F_6S$ |
|---|---|
| Formula weight | 323.26 |
| Temperature | 293(2) K |
| Wavelength | 0.71073 Å |
| Crystal system | Orthorhombic |
| Space group | *Pbca* |
| Unit cell dimensions | |
| $a$ | 10.930(5) Å |
| $b$ | 10.617(3) Å |
| $c$ | 23.201(7) Å |
| $\alpha$ | 90° |
| $\beta$ | 90° |
| $\gamma$ | 90° |
| Volume | 2692(2) Å$^3$ |
| $Z$ | 8 |
| Density (calculated) | 1.595 mg m$^{-3}$ |
| Absorption coefficient | 0.301 mm$^{-1}$ |
| $F$(000) | 1296 |
| Crystal size | 0.68 × 0.60 × 0.38 mm |
| Theta range for data collection | 2.56–27.52° |
| Index ranges | $0 \le h \le 14$, $0 \le k \le 13$, $-30 \le l \le 0$ |
| Reflections collected | 3061 |
| Independent reflections | 3061 [$R$(int) = 0.0000] |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data/restraints/parameters | 3061/0/190 |
| Goodness-of-fit on $F^2$ | 1.033 |
| Final $R$ indices [$I > 2\sigma(I)$] | $R1 = 0.0486$, $wR2 = 0.1129$ |
| $R$ indices (all data) | $R1 = 0.0843$, $wR2 = 0.1350$ |
| Largest diff. peak and hole | 0.262 and −0.239 e Å$^{-3}$ |




**Scheme 2**

commercially available and were used without further purification. 1-Triphenylphosphoraniliden-3-chloropropanone was obtained by the published method.[13] Crystal structure data have been deposited of the Cambridge Crystallographic Data Centre (CCDC) under the reference number 2 15 128.

## Syntheses

The Hantzsch reaction is a well-known method for the synthesis of thiazoles by cyclization of $\alpha$-halocarbonyl compounds and a great variety of reactants bearing the N—C—S fragment in the ring have been reported.[14]

The $\alpha$-halocarbonyl derivative **2** was synthesized by the Wittig reaction between hexafluoroacetone (HFA) and a chloro-containing phosphorane (Scheme 2) in order to avoid secondary products of enone **1** caused by direct halogenation.[10] The separation of the product from the reaction mixture had to be carried out under vacuum to avoid polymerization when excessive heating is applied.

*1-Chloro-5,5,5-trifluoro-4-trifluoromethyl-3-penten-2-one (**2**).* A 16.0 g (45.4 mmol) amount of dry 1-triphenylphosphoraniliden-3-chloropropanone, previously blended in a mortar with 0.8 g of hydroquinone, was placed in a 200 ml Carius tube with a Young valve, then 7.5 g (45 mmol) of hexafluoroacetone were condensed on the mixture *in vacuo*. The closed tube with the solid mixture was shaken vigorously until heat evolution and then allowed to stand until it reached room temperature. The product was separated for condensation under static vacuum The liquid obtained, 6.2 g (25.7 mmol), was examined by GC–MS and used without further purification. The yield was 57%.

**General Procedure for the synthesis of thiazoles *3–5*.** To a stirred solution of thiobenzamide, 0.55 g (4 mmol), in methanol (20 ml), a methanolic solution of 1-chloro-5,5,5-trifluoro-4-trifluoromethyl-3-penten-2-one (**2**), 0.96 g (4 mmol), in 5 ml of the same solvent was slowly added. After 15 min the reaction mixture turned green–yellow. The solution was then refluxed with stirring for another 2 h. The solvent was evaporated and the residual solid was dissolved in benzene and washed with $NaHCO_3$ and water. After drying over $MgSO_4$, the benzene was evaporated. The solid obtained was separated by column chromatography [silica gel, hexane–ethyl acetate (4:1)]. The products obtained were recrystalized from hexane (**3**, **4**, **5**) and benzene–pentane (**6**) in 83, 77, 87 and 96% yield, respectively (Scheme 2)

*2-Phenyl-4-(3,3,3-trifluoro-2-trifluoromethyl-1-propenyl)-1,3-thiazole (**3**).* This compound (for numbering of the compound, see Fig. 1) was obtained as a white solid (hexane), m.p. 63–64°C. $^1$H NMR (250 MHz, $CDCl_3$), $\delta$ 7.42–7.50 (m, 3H, 8-CH, 9-CH and 10-CH), 7.63 (broad, 1H, 12-CH), 7.75 (s, 1H, 5-CH), 7.93–7.97 (m, 2H, 7-CH and 11-CH); $^{19}$F NMR (75.26 MHz, $CDCl_3/CFCl_3$), $\delta$ −59.20 (q, 13-$CF_3$, $^4J_{FF} = 7.9$ Hz), −64.43 (dq, 12-$CF_3$, $^4J_{FF} = 7.9$ Hz, $^4J_{FH} = 1.6$ Hz); $^{13}$C NMR (62.90 MHz, $CDCl_3$), $\delta$ 120.91 (q, 15-$CF_3$, $^1J_{CF} = 275.0$), 121.71 (qq, 14-$CF_3$, $^1J_{CF} = 273.1$ Hz, $^3J_{CF} = 2.9$ Hz), 125.45 (dq, 5-CH, $^2J_{CH} = 186.9$ Hz, $^5J_{CF} = 3.9$ Hz), 125.73 (7-CHand 11-CH), 128.12 (8-CH and 10-CH), 129.83 (9-CH), 131.61 (s, 6-CH), 134.72 (dqq, 12-CH, $^1J_{CH} = 156.4$ Hz, $^3J_{CF} = 2.9$ Hz, $^3J_{CF} = 2.9$ Hz), 146.80 (d, 4-CH, $^2J_{CH} = 3.8$ Hz), 168.30 (d, 2-CH, $^3J_{CH} = 3.8$ Hz), 13-CH not observed; GC–MS, *m/z* 323 (75)/$M^+$; 304 (15/$[M - F]^+$); 254 (100/$[M - CF_3]^+$); 220 (2/$[M - RCN]^{+\cdot}$);

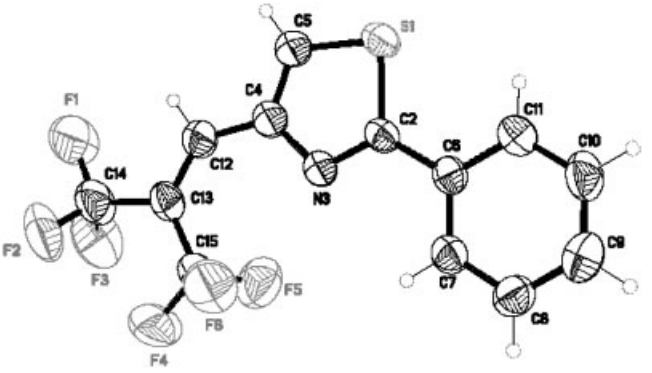



**Figure 1.** A perspective drawing of **3** with 50% probability thermal ellipsoids

219 (2); 201 (7/$[220-F]^+$); 199 (2); 170 (16); 151 (22/$[220-CF_3]^+$); 131 (8/$[CF_3CCF_2]^+$); 106 (5); 104 (11/$[C_6H_5CNH]^+$); 77 (36/$[C_6H_5]^+$); 69 (20/$[CF_3]^+$); 51 (10/$[CF_2H]^+$).

Anal. Calcd For $C_{13}H_7F_6N_nS_n$: C, 48.3; H, 2.2; N, 4.3; S, 9.9. Found: C, 48.4; H, 2.0; N, 4.2; S, 10.1%.

*2-N-Phenylamino-4-(3,3,3-trifluoro-2-trifluoromethyl-1-propenyl)-1,3-thiazole (**4**).* This compound was obtained as white needles, m.p. 90–92°C (hexane). $^1$H NMR (400.13 MHz, $CDCl_3$): $\delta$ 7.10 (broad s, 1H, 10-CH), 7.10 (t, 1H, 9-CH, $^3J_{HH}=7.5$ Hz), 7.32 (broad s, 1H, 5-CH), 7.33–7.42 (m, 4 H, 7-CH and 8-CH), NH not observed; $^{19}$F NMR (235.35 MHz, $CDCl_3/CFCl_3$), $\delta$ −58.43 (c, 13-$CF_3$, $^4J_{FF}=7.6$ Hz), −63.86 (mc, 12-$CF_3$, $^4J_{FF}=7.6$ Hz); $^{13}$C NMR (100.61 MHz, $CDCl_3$), $\delta$ 116.83 (dc, 5-CH, $^1J_{CH}=191.2$ Hz, $^5J_{CF}=3.7$ Hz), 118.74 (ddd, 9-CH, $^1J_{CH}=159.9$ Hz, $^2J_{CH}=7.4$ Hz, $^2J_{CH}=5.5$ Hz), 120.89 (c, 12-$CF_3$, $^1J_{CF}=273.9$ Hz), 121.85 (c, 13-$CF_3$, $^1J_{CF}=272.1$ Hz), 123.83 (dt, 8-CH, $^1J_{CH}=161.8$ Hz, $^2J_{CH}=7.4$ Hz), 129.53 (ddd, 7-CH, $^1J_{CH}=159.9$ Hz, $^2J_{CH}=7.4$ Hz, $^3J_{CH}=3.7$ Hz), 134.56 (dcc, 10-CH, $^1J_{CH}=161.8$ Hz, $^3J_{CF}=3.7$ Hz, $^3J_{CF}=3.7$ Hz), 139.26 (t, 6-C, $^3J_{CH}=7.4$ Hz), 142.93 (d, 4-C, $^2J_{CH}=3.7$ Hz), 164.31 (d, 2-C, $^3J_{CH}=9.2$ Hz), 11-C not observed; GC–MS, *m/z* 338 (100)/$M^+$), 318 (28/$[M-FH]^{+\cdot}$), 298 (10/$[M-FH-FH]^{+\cdot}$), 279 (6/$[M-FH-FH-F]^+$), 269 (6/$[M-CF_3]^+$), 249 (4/$[M-CF_3-FH]^+$), 201 (7/$[M-RCN-F]^+$), 150 (13/$[C_6H_5NHCSN]^{+\cdot}$), 149 (17/$[C_6H_5NCSN]^+$), 131 (4/$[CF_3CCF_2]^+$), 118 (6), 104(18/$[C_6H_5NCH]^+$), 92(7), 91(5), 77 (21/$[C_6H_5]^+$), 69 (6/$[CF_3]^+$), 51 (11/$[CF_2H]^+$).

Anal. Calcd for $C_{13}H_8F_6N_2S$: C, 46.3; H, 2.4; N, 8.3; S, 9.5. Found: C, 46.3; H, 2.3; N, 8.2; S, 9.5%.

*2-Allylamino-4-(3,3,3-trifluoro-2-trifluoromethyl-1-propenyl)-1,3-thiazole (**5**).* This compound was obtained as yellow crystals, m.p. 120–122°C (hexane). $^1$H NMR (400.13 MHz, $CDCl_3$), $\delta$ 3.89 (broad, 2H, 6-$CH_2$), 5.16 (dc, 1H, 8-CHb, $^3J_{HbH}=17.1$ Hz, $^2J_{HbHa}=1.5$ Hz), 5.26 (dc, 1H, 8-CHa, $^3J_{HaH}=10.5$ Hz, $^2J_{HaHb}=1.5$ Hz), 5.46 (broad, 1H, NH), 5.87 (ddt, 1H, 7-CH, $^3J_{HHb}=17.1$ Hz, $^3J_{HHa}=10.5$ Hz, $^3J_{HH}=5.5$ Hz), 7.01 (s, 1H, 9-CH), 7.60 (s, 1H, 5-CH); $^{19}$F NMR (62.90 MHz, $CDCl_3/CFCl_3$), $\delta$ −59.78 (c, 12-$CF_3$, $^4J_{FF}=7.9$ Hz), −64.60 (c, 11-$CF_3$, $^4J_{FF}=7.9$ Hz); $^{13}$C NMR (100.61 MHz, $CDCl_3$), $\delta$ 48.04 (tdd, 6-$CH_2$, $^1J_{CH}=146.9$ Hz, $J_{CH}=8.2$ Hz, $J_{CH}=8.5$ Hz), 116.08 (dc, 5-CH, $^1J_{CH}=191.1$ Hz, $^5J_{CF}=3.7$ Hz), 117.61 (dd, 8-CHaHb, $^1J_{CH}=159.8$ Hz, $^1J_{CH}=154.6$ Hz), 120.89 (c, 12-$CF_3$, $^1J_{CF}=273.9$ Hz), 121.88 (c, 11-$CF_3$, $^1J_{CF}=270.2$ Hz), 133.15 (dm, 7-*C*H, $^1J_{CH}=142.9$ Hz), 134.83 (dcc, 9-*C*H, $^1J_{CH}=143.3$ Hz, $^3J_{CF}=3.7$ Hz, $^3J_{CF}=3.7$ Hz), 142.74 (d, 4-*C*, $^2J_{CH}=3.8$ Hz), 168.37 (m, 2-*C*), (10-C not observed); GC–MS, *m/z* 302 (18/$M^+$), 287 (16/$[M-CH_3]^+$), 283 (4/$[M-F]^+$), 281 (3), 262 (4/$[M-CH_2CHCH_2]^+$), 261 (3), 255 (8), 245 (13), 243 (4), 242 (5), 241 (4), 233 (100/$[M-CF_3]^+$), 205 (7), 201 (11), 192 (55/$[M-CF_3-CH_2CHCH_2]^+$), 191 (15), 170 (12), 165 (12), 151 (14/$[M-RCN-CF_3]^+$), 145 (7), 131 (9/$[CF_3CCF_2]^+$), 120 (4), 107 (8), 99 (7), 81 (12), 75 (15), 69 (56/$[CF_3]^+$), 63 (11), 59 (27), 56 (25/$[NHCH_2CHCH_2]^+$).

Anal. Calcd for $C_{10}H_8F_6N_2S$: C, 39.7; H, 2.6; N, 9.3; S, 10.6. Found: C, 39.5; H, 2.6; N, 9.2; S, 10.6%.

**Reaction with thioacetamide: preparation of 4-hydroxy-2-methyl-4-(3,3,3-trifluoro-2-trifluromethyl-1-propenyl)-1,3-thiazoline (*6*).** The 2-methyl-trifluoromethyl-containing thiazole, resulting from **2** and thioacetamide, could not be obtained by this method. However, the presence of the hydroxythiazoline intermediate 4-hydroxy-2-methyl-4-[3,3,3-trifluoro-2-(trifluoromethyl)-1-propenyl]-1,3-thiazoline **6** (*m/z* 279) was observed by mass spectrometry, $^1$H NMR, $^{19}$F NMR and IR, which shows a band at 3446 $cm^{-1}$ assigned to $\nu$OH, with no sign of carbonylic stretching $\nu$C=O. The hydroxythiazoline **6** underwent decomposition with any attempt at dehydration. A similar situation has been reported for other 2-methylthiazoles, the acidity of the methyl hydrogens being responsible for the high reactivity of the product, owing to the anion stabilization caused by the ring nitrogen atom.[15]

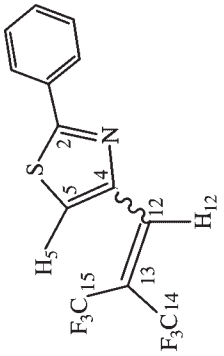
*4-Hydroxy-2-Methyl-4-(3,3,3-trifluoro-2-trifluoromethyl-1-propenyl)-1,3-thiazoline (**6**).* This compound was obtained as a white solid, m.p. 112–113°C (benzene–pentane). $^1$H NMR (80 Mhz, $CDCl_3$), $\delta$ 2.3 (s, 3H, 2-$CH_3$), 3.7 (m, 2H, 5-$CH_2$), 6 (broad s, 1H, OH), 7.1 (broad s, 1H, 7-CH); $^{19}$F NMR (62.90 MHz, $CDCl_3/CFCl_3$), $\delta$ −57.67 (c, 10-$CF_3$, $^4J_{FF}=7.9$ Hz), −64.80 (dc, 9-$CF_3$, $^4J_{FF}=7.9$ Hz, $^4J_{FH}=2.0$ Hz); GC–MS, *m/z* 279 (2/$M^{+\cdot}$), 261 (42/$[M-H_2O]^{+\cdot}$), 242 (13/$[M-H_2O-F]^+$), 238 (35/$[M-CH_3CN]^{+\cdot}$), 201 (12/$[238-H_2O-F]^+$), 192 (67/$[238-SCH_2]^{+\cdot}$), 172 (16/$[192-FH]^+$), 170 (21/$[238-H_2O-CF_2]^+$), 163 (10/$[(CF_3)_2CCH]^+$), 151 (27/$[238-H_2O-CF_3]^+$), 131 (7/$[CF_3CCF_2]^+$), 107 (6), 106 (6), 100 (5), 99 (3), 88 (14), 75 (30/$[CF_2CCH]^+$), 69 (42/$[CF_3]^+$), 63 (9), 58 (14), 57 (12), 51 (7/$[CF_2H]^+$), 47 (100/$[CH_2SH]^+$); IR (KBr), 3446(m), 1717(w), 1669(w), 1684(w), 1668(w), 1652 (w), 1646(w), 1634(w), 1622(w), 1616(d), 1558(w), 1539(w), 1521(w), 1506(m), 1472(w), 1456(w), 1390 (w), 1297(d), 1261(w), 1229(d), 1177(m), 1075(w), 956(w), 801(w), 686(w), 649(w), 475 $cm^{-1}$(w).

## RESULTS AND DISCUSSION

### Nuclear magnetic resonance

Notable characteristics of the $^1$H, $^{13}$C and $^{19}$F NMR spectra corresponding to compound **3** are given in Table 2 and also the assignment of the signals.

**Table 2.** $^{13}C-^{1}H-^{19}F$ NMR chemical shifts [$\delta$ (ppm)] and coupling constants [$J$ ($H_2$)] for 4-(3,3,3-trifluoro-2-trifluoromethyl-1-propenyl)-1,3-thiazoles




| $C_{15}F_3$ | $C_{14}F_3$ | $(CF_3)_2C_{13}$ | $(CF_3)_2C{=}C_{12}H$ | $C_2$ | $C_4$ | $C_5$ | $H_{12}$ | $H_5$ | $CF_3$ $(E)$ | $CF_3$ $(Z)$ |
|---|---|---|---|---|---|---|---|---|---|---|
| 120.91 (q)<br>$^{1}J_{CF} = 275.0$ Hz | 121.71<br>(dq)<br>$^{1}J_{CF} = 273.1$ Hz<br>$^{3}J_{CF} = 2.9$ Hz | [a] | 134.72<br>(dqq)<br>$^{1}J_{CH} = 156.4$ Hz<br>$^{3}J_{CF} = 2.9$ Hz<br>$^{3}J_{CF} = 2.9$ Hz | 168.30<br>(d)<br>$^{3}J_{CH} = 3.8$ Hz | 146.80<br>(d)<br>$^{2}J_{CH} = 3.8$ Hz | 125.45<br>(dq)<br>$^{1}J_{CH} = 186.9$ Hz<br>$^{5}J_{CF} = 3.9$ Hz | 7.63<br>(s broad) | 7.75<br>(s) | −59.20<br>$^{4}J_{FF} = 7.9$ Hz | −64.43<br>$^{4}J_{FF} = 7.9$ Hz<br>$^{4}J_{FH} = 1.6$ Hz |

[a] $(CF_3)_2C_{13}$ signals were not detected in their respective spectra.

In the $^{1}H$ NMR spectrum of **3**, the hexafluoroisobutenylidene hydrogen H(12) is observed as a broad singlet at $\delta$ 7.3 ± 0.4 ppm, due to an unsolved coupling with the $CF_3$ groups. The thiazole ring hydrogen H(5) is observed as a slightly broad singlet. In some 5-alkenyl-2,4-disubstituted-1,3-thiazoles the corresponding hydrogen (observed in the region of 6.8 and 7.3 ppm) was used by Williams *et al.* to determine *E/Z* relationships in mixtures of raw products.[16] However, in the present work only one signal assignable to this hydrogen was observed.

In the $^{19}F$ NMR spectra of $(CF_3)_2C{=}CHR$ compounds, fluorine signals are observed between −58 and 65 ppm. The $CF_3$ groups show a different chemical shift due to the asymmetric substitution on the double bond, resulting in quartets ($^{4}J_{FF} = 7$–$8$ Hz). In addition, that one of the $CF_3$ groups is spitted into a double quartet by a four-bond interaction with the vinyl proton H(12), probably in a *trans* spatial relationship. Since the coupling constant $^{4}J_{FH}$ was reported to be between 1 and 2 Hz and 0 and 1 Hz[17] for *trans* and *cis* configurations, respectively, $^{4}J_{FH}$ (*cis*) might be too small to be detectable in this case.

With respect to $^{13}C$ NMR, we can see that signals corresponding to the trifluoromethyl groups appear as quartets showing $^{1}J_{CF}$ between 270 and 275 Hz. One of the $CF_3$ groups of this compound is a quartet of quartets due to interaction with the other $CF_3$ group ($^{3}J_{CF} = 3$ Hz). Although we did not identify $\delta(CF_3)_2C$ in the spectra of **3**, probably owing to the lack of NOE, the corresponding signal was reported in other related compounds as a double quartet (dq) at about 125 ppm.[10,18] Signals originated by the group $(CF_3)_2C{=}CH$— are observed between 134 and 135 ppm as a double quartet of quartets (dqq) or as a double multiplet, with $^{3}J_{CF} = 3$–$4$ Hz.

The C(2) thiazole ring [$\delta_{C(2)} \approx 168$ ppm] is observed as a doublet owing to a long-range coupling across the thiazole S heteroatom with H(5). This was also observed in other related structures such as thiadiazoles.[19] C(4) is also a doublet, with a two-bond coupling either with H(5) or with H(12) ($^{2}J_{CH} = 3.7$–$3.8$ Hz).

Two-dimensional CH correlations were measured in order to assign unequivocally the C(5) signal to H(5). HETCOR and COLOC experiments were performed in $CDCl_3$ and the results are deposited as supplementary information [supplementary Fig. 1 (a) and (b)] in Wiley Interscience. It was also observed that $\delta$C(5) in **3** is affected by the change of the solvent, being shifted downfields to 130.8 ppm (ACN-$d_3$), and to 132.4 ppm (DMSO-$d_6$) (Table 3).The coupling constant $^{1}J_{C(5)H(5)}$, for **3** of ∼187 Hz is higher than that in benzene (∼159 Hz) and is consistent with those observed in other related heterocycles, such as thiazole and 1,2,3-thiadiazoles (∼189 Hz).[19–22] Long-range CF interaction (3.7–3.9 Hz) is observed through the C(5) splitting of the signal into quartets. This CF coupling might be (a) a five-bond coupling along the conjugated system favored in a planar conformation (s-*cis* or s-*trans*) or (b) an F—HC short contact coupling in an s-*cis* conformation.

**Table 3.** $^{13}C$ chemical shifts [$\delta$ (ppm)] for **3** in different solvents

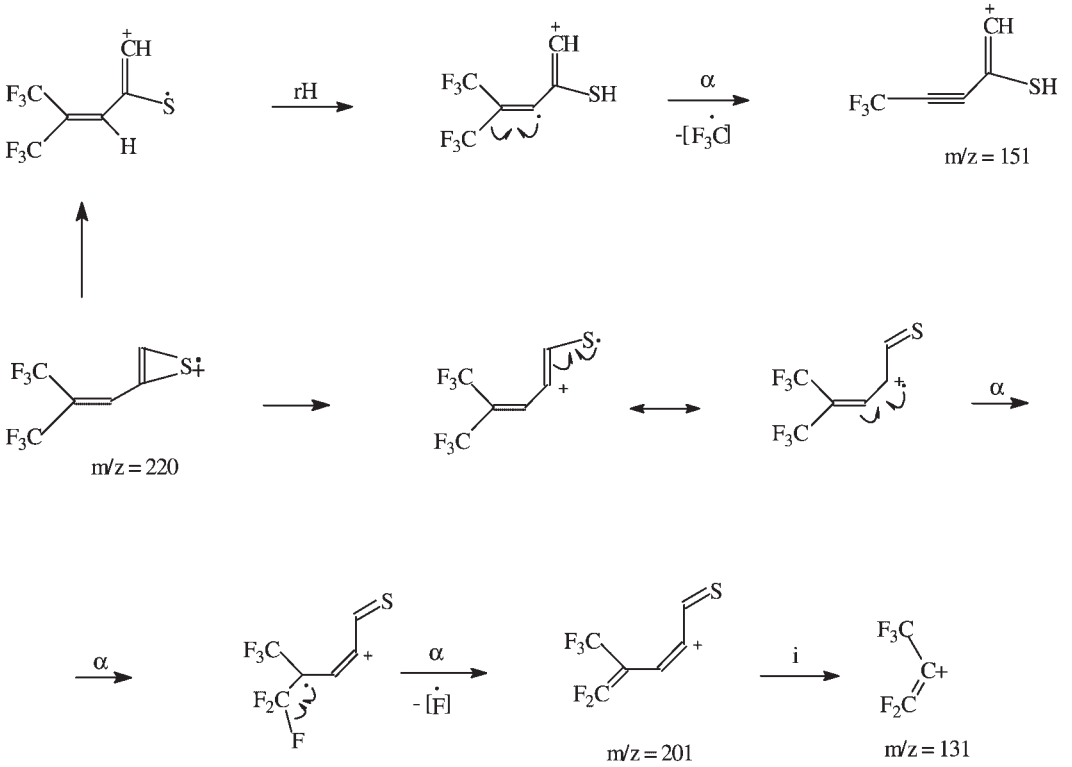
| | $DCCl_3$ | | ACN-$d_3$ | | DMSO-$d_6$ | | Average | SD |
|---|---|---|---|---|---|---|---|---|
| C(2) | 169.0 | +0.2 | 169.4 | +0.6 | 167.9 | −0.9 | 168.8 ± 0.9 | 0.8 |
| C(4) | 147.5 | +0.3 | 147.8 | +0.6 | 146.4 | −0.8 | 147.2 ± 0.9 | 0.7 |
| C(5) | 125.4 | −4.1 | 130.8 | +1.3 | 132.4 | +2.9 | 129.5 ± 4.2 | 3.7[a] |
| C(6) | 133.0 | +0.1 | 133.6 | +0.7 | 132.1 | −0.8 | 132.9 ± 0.8 | 0.8 |
| C(7) | 127.5 | +0.4 | 127.4 | +0.3 | 126.3 | −0.8 | 127.1 ± 0.8 | 0.7 |
| C(8) | 129.8 | 0.0 | 130.2 | +0.4 | 129.3 | −0.5 | 129.8 ± 0.5 | 0.5 |
| C(9) | 131.5 | +0.4 | 131.8 | +0.7 | 130.1 | −1.0 | 131.1 ± 1.1 | 0.9 |
| C(10) | 129.8 | 0.0 | 130.2 | +0.4 | 129.3 | −0.5 | 129.8 ± 0.5 | 0.5 |
| C(11) | 127.5 | +0.4 | 127.4 | +0.3 | 126.3 | −0.8 | 127.1 ± 0.8 | 0.7 |
| C(12) | 134.7 | −1.0 | 136.4 | +0.7 | 136.0 | +0.3 | 135.7 ± 1.0 | 0.9 |
| C(14) | 121.0 | −0.3 | 122.1 | +0.8 | 120.8 | −0.5 | 121.3 ± 0.8 | 0.7 |
| C(15) | 122.0 | −0.4 | 123.1 | +0.7 | 122.0 | −0.4 | 122.4 ± 0.8 | 0.6 |

[a] The most affected value.

Taking into account that one-, two-, three- and four-bond CF couplings were reported for trifluorobenzene of 271.7, 32.3, 3.9 and 1.3 Hz, respectively,[23] we can assume that the splitting of the C(5) signal is produced by the second explanation. That means that the preferred conformation in solution is s-*syn*. This possibility will be explored again in the discussion of the theoretical calculations results.

## Mass spectrometry

The mass spectrum of **3** is characterized by fragments $[M-(F)]^+$, $[M-(FH)]^{+\cdot}$, $[M-(CF_3)]^+$ and $[M-(FH)-(CF_3)]^+$. On electron ionization, fragmentation occurs according to two main routes: the rupture of connections 1–2 and 3–4 and the less common one generated by the cleavage of connections 2–3 and 5–1. The first is the most frequently observed, and has been reported for thiazole and isothiazole[24] and many thiazole derivatives with R substituted in position 2.[25] This route, with RCN loss and retention of the positive charge by the sulphur-containing fragment, generates a thiirenium radical ion. Fragments at *m/z* 220, 201, 170, 151 and 131 can be explained according to Scheme 3, where *m/z* 220 corresponds to the above-mentioned radical ion. The compound also shows, as expected, the fragments $[C_6H_5CNH]^+$ and $[C_6H_5]^+$.




**Scheme 3**

## Crystal structure

The molecular skeleton [C(14)—C(13)—C(12)—thiazole ring—phenyl ring] lies in approximately one plane, which indicates that the conjugation is extended over the whole structure (Fig. 1). One fluorine atom of each $CF_3$ group is coplanar with the lateral chain [F(1) and F(4)]. The distance between the hydrogen H(12) and the closest fluorine atom in the *trans* $CF_3$ group is 2.21 Å, C(12)H(12)—F(1), smaller than the sum of their van der Waals radii.[26] This could be due to the high steric congestion caused by the voluminous $CF_3$ groups.

Both rings are almost coplanar, with a deviation from planarity of 4.8(4)°. The dihedral angle between the thiazole ring and the plane containing the conjugated hexafluoroisobutenyl double bond is 2.7(5)°. The double bond maintains a *trans* conformational relationship towards the C(4)═C(5) endocyclic double bond. Molecules in the unit cell are disposed in layers in an antiparallel arrangement (see supplementary material Fig. 2).

## Theoretical calculations

In order to assist the conformational analysis for 3, theoretical studies, involving geometry optimization and determination of relative stabilities, and also prediction of the vibrational and magnetic properties of the most stable forms, were made and compared with the experimental data.

The geometry optimizations and the calculation of the vibrational frequencies for the s-*cis* and s-*trans* conformers of **3** were performed at the HF/6–31G** and B3LYP/6–31G** levels of theory. Energy minima with respect to the nuclear coordinates were obtained by simultaneous relaxation of all geometric parameters leading to structures for which no imaginary frequencies occur. Some selected calculated geometric parameters for the main conformers and crystallographic data for **3** are listed in Tables 4 and 5.

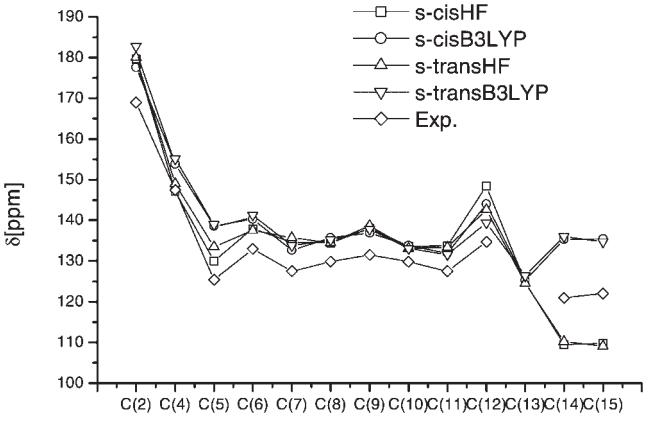



**Figure 2.** Comparison of experimental and theoretical $^{13}C$ chemical shifts of **3** as calculated at the HF/6–311 + G(2d,p) and B3LYP/6–311 + G(2d,p) levels of theory

**Table 4.** Selected calculated (6–31G**) and experimental bond lengths (Å) for **3**

| | s-*cis* | | s-*trans* | | |
|---|---|---|---|---|---|
| Bond | HF | B3LYP | HF | B3LYP | Exp. |
| C(2)—S(1) | 1.744 | 1.827 | 1.750 | 1.782 | 1.733(2) |
| C(2)—N(3) | 1.280 | 1.271 | 1.277 | 1.301 | 1.299(3) |
| S(1)—C(5) | 1.716 | 1.776 | 1.715 | 1.718 | 1.693(3) |
| N(3)—C(4) | 1.379 | 1.404 | 1.372 | 1.376 | 1.375(3) |
| C(5)—C(4) | 1.348 | 1.340 | 1.351 | 1.382 | 1.362(4) |
| C(5)—H(5) | 1.070 | 1.060 | 1.070 | 1.080 | 0.930 |
| C(4)—C(12) | 1.472 | 1.454 | 1.465 | 1.453 | 1.450(4) |
| C(12)—C(13) | 1.326 | 1.320 | 1.328 | 1.350 | 1.330(4) |
| C(12)—H(12) | 1.070 | 1.07 | 1.07 | 1.08 | 0.930 |
| C(13)—C(15) | 1.511 | 1.489 | 1.518 | 1.518 | 1.495(4) |
| C(13)—C(14) | 1.513 | 1.485 | 1.513 | 1.514 | 1.501(4) |
| C(15)—F(4) | 1.324 | 1.349 | 1.325 | 1.355 | 1.334(3) |
| C(15)—F(6) | 1.324 | 1.349 | 1.320 | 1.353 | 1.311(4) |
| C(15)—F(5) | 1.321 | 1.351 | 1.320 | 1.353 | 1.318(4) |
| C(14)—F(3) | 1.318 | 1.344 | 1.323 | 1.355 | 1.336(4) |
| C(14)—F(2) | 1.329 | 1.360 | 1.323 | 1.355 | 1.321(4) |
| C(14)—F(1) | 1.321 | 1.352 | 1.324 | 1.357 | 1.303(4) |

The geometry optimization for the s-*cis* conformer was conducted to a calculated absolute structural minimum with a dihedral angle around C(4)—C(12) of 31.3° with the HF method, corresponding to the s-*syn* isomer. This dihedral angle was calculated to be 13.0° with B3LYP/6–31G**. The approximation HF/6–31G** geometry optimization also predicts for the s-*cis* conformer a short contact between F(2) and H(5); this contact of 2.394 Å is shorter than the sum of their respective van der Waals radii. Both methods calculate the s-*syn* form to be slightly more stable: $0.42\,kcal\,mol^{-1}$ (HF/6–31G**) and $0.59\,kcal\,mol^{-1}$ (B3LYP/6–31G**) (1 kcal = 4.184 kJ), resulting in the prediction of co-existence of the molecule forms in a relation 2:1 *syn*:*trans* at room temperature. These results are in accordance with the analysis of the $^{13}C$ NMR spectra that provide experimental evidence of the short contact between F(2) and C(5).

In order to compensate for systematic errors of the quantum chemical force field calculation, calculated vibrational frequencies for s-*cis* and s-*trans* forms (HF/6–31G**) frequencies were scaled uniformly by a factor of 0.9. The scaling results in reasonable agreement with the experimentally determined frequencies, especially those for the s-*trans* forms, as shown in Table 6. Whereas calculations were made for the free molecules, the IR and the Raman spectra were recorded in the solid state (see supplementary material Fig. 3).

In addition, chemical shifts were calculated with the use of the GIAO method (implemented in the Gaussian 98 program)[11] on the basis of the calculated absolute structural minima, at the HF/6–311 + G(2d,p) and B3LYP/6–311 + G(2d,p) levels, as the difference in the chemical shifts of the hydrogen, carbon and fluorine

**Table 5.** Selected calculated and experimental bond angles and torsions (°) for **3**

| | s-*cis* | | s-*trans* | | |
|---|---|---|---|---|---|
| Bond | HF | B3LYP | HF | B3LYP | Exp. |
| C(2)—S(1)—C(5) | 89.4 | 87.4 | 89.0 | 88.9 | 89.2(12) |
| C(2)—N(3)—C(4) | 112.2 | 114.3 | 112.4 | 112.5 | 111.0(2) |
| S(1)—C(5)—C(4) | 109.9 | 111.0 | 110.1 | 110.7 | 110.9(2) |
| C(4)—C(5)—H(5) | 128.8 | 127.7 | 128.0 | 127.9 | 124.5(2) |
| N(3)—C(4)—C(12) | 115.4 | 114.9 | 123.6 | 124.2 | 124.0(2) |
| C(5)—C(4)—C(12) | 129.5 | 130.2 | 121.5 | 121.1 | 121.5(2) |
| C(4)—C(12)—H(12) | 112.0 | 111.7 | 112. 5 | 112.8 | 113.7(2) |
| C(13)—C(12)—H(12) | 116.7 | 117.1 | 115.7 | 115.3 | 113.7(2) |
| C(11)—C(6)—C(2)—S(1) | 14.0 | 0.3 | 1.1 | 0.0 | 4.9(3) |
| S(1)—C(2)—N(3)—C(4) | 0.6 | 0.5 | 0.0 | 0.0 | 0.7(3) |
| C(2)—N(3)—C(4)—C(12) | −177.7 | −179.3 | −179.0 | 180.0 | 179.8(3) |
| S(1)—C(5)—C(4)—N(3) | 1.2 | 0.4 | 0.0 | 0.0 | 0.4(3) |
| N(3)—C(4)—C(12)—C(13) | −152.9 | −168.4 | −0.5 | 0.0 | −2.7(5) |
| C(5)—C(4)—C(12)—C(13) | 31.3 | 13.0 | 179.6 | −179.0 | 177.8(3) |
| C(12)—C(13)—C(15)—F(4) | −114.4 | −118.0 | −179.6 | 180.0 | −176.9(3) |
| C(12)—C(13)—C(15)—F(6) | 125.5 | 121.8 | 61.4 | 60.6 | 62.5(4) |
| C(12)—C(13)—C(15)—F(5) | 5.7 | 1.9 | −60.6 | −60.7 | −57.8(4) |
| C(12)—C(13)—C(14)—F(3) | 166.6 | 175.6 | 119.5 | 119.7 | 122.0(3) |
| C(12)—C(13)—C(14)—F(2) | −73.7 | −64.1 | −119.8 | −119.7 | −119.1(3) |
| C(12)—C(13)—C(14)—F(1) | 46.2 | 54.6 | 0.0 | 0.0 | 1.7(5) |

**Table 6.** Calculated and experimental vibrational frequencies for **3**

| | s-*cis* | | s-*trans* | | Exp. | |
|---|---|---|---|---|---|---|
| | HF/6–31 + G** | B3LYP/6–31 + G** | HF/6–31 + G** | B3LYP/6–31 + G** | FT-IR | Raman |
| 1 | 3118 | 3303 | 3089 | 3265 | 3097 | 3097 |
| 2 | 3056 | 3225 | 3060 | 3227 | 3023 | |
| 3 | 3051 | 3213 | 3049 | 3210 | | |
| 4 | 3039 | 3210 | 3039 | 3204 | | |
| 5 | 3029 | 3199 | 3030 | 3200 | | |
| 6 | 3020 | 3189 | 3019 | 3189 | | |
| 7 | 3012 | 3181 | 3012 | 3181 | | |
| | | | | | 1865 | |
| 8 | 1695 | 1699 | 1693 | 1699 | 1658 | 1657 |
| 9 | 1618 | 1649 | 1618 | 1649 | 1632 | |
| 10 | 1596 | 1627 | 1597 | 1627 | | 1599 |
| 11 | 1555 | 1553 | 1551 | 1560 | 1564 | |
| 12 | 1522 | 1524 | 1507 | 1523 | 1508 | |
| 13 | 1487 | 1518 | 1487 | 1503 | 1477 | 1467 |
| 14 | 1440 | 1480 | 1441 | 1480 | 1443 | 1442 |
| 15 | 1405 | 1422 | 1405 | 1421 | | |
| 16 | 1329 | 1365 | 1363 | 1390 | 1397 | 1395 |
| 17 | 1322 | 1347 | 1324 | 1365 | 1362 | 1362 |
| 18 | 1265 | 1330 | 1289 | 1340 | 1289 | 1281 |
| 19 | 1255 | 1274 | 1243 | 1287 | | |
| 20 | 1235 | 1260 | 1234 | 1263 | | 1249 |
| 21 | 1223 | 1244 | 1224 | 1227 | 1227 | |
| 22 | 1208 | 1208 | 1224 | 1208 | 1205 | |
| 23 | 1204 | 1196 | 1205 | 1191 | | 1183 |
| 24 | 1189 | 1187 | 1191 | 1187 | | |
| 25 | 1175 | 1181 | 1174 | 1167 | | |
| 26 | 1168 | 1144 | 1169 | 1161 | 1148 | 1147 |
| 27 | 1155 | 1134 | 1143 | 1126 | | |
| 28 | 1098 | 1111 | 1099 | 1119 | | |
| 29 | 1065 | 1106 | 1066 | 1111 | 1075 | |
| 30 | 1019 | 1053 | 1019 | 1053 | | |
| 31 | 1016 | 1021 | 1017 | 1019 | 1009 | |
| 32 | 1003 | 1013 | 1001 | 1013 | | |
| 33 | 1000 | 1009 | 999 | 1011 | 1000 | 1000 |
| 34 | 980 | 989 | 979 | 990 | | |

*Continues*

**Table 6.** Continued

| | | | | | | |
|---|---|---|---|---|---|---|
| 35 | 974 | 976 | 970 | 970 | 971 | |
| 36 | 967 | 972 | 962 | 958 | | |
| 37 | 946 | 945 | 947 | 945 | 934 | |
| 38 | 916 | 937 | 913 | 939 | 923 | |
| 39 | 858 | 900 | 856 | 887 | | |
| 40 | 857 | 855 | 855 | 855 | 837 | |
| 41 | 814 | 784 | 794 | 777 | 783 | |
| 42 | 774 | 777 | 767 | 773 | 761 | 768 |
| 43 | 770 | 766 | 766 | 759 | | |
| 44 | 726 | 727 | 751 | 758 | | |
| 45 | 708 | 715 | 705 | 701 | 706 | 705 |
| 46 | 704 | 700 | 691 | 698 | 690 | |
| 47 | 685 | 694 | 683 | 693 | | |
| 48 | 676 | 681 | 676 | 688 | 675 | |
| 49 | 663 | 681 | 663 | 679 | | |
| 50 | 626 | 634 | 631 | 641 | 641 | |
| 51 | 606 | 625 | 608 | 629 | 617 | |
| 52 | 601 | 609 | 599 | 609 | 608 | |
| 53 | 582 | 567 | 583 | 585 | 598 | |
| 54 | 543 | 540 | 544 | 542 | 539 | |
| 55 | 530 | 529 | 528 | 526 | 522 | |
| 56 | 515 | 518 | 511 | 511 | | |
| 57 | 488 | 485 | 491 | 487 | | |
| 58 | 466 | 469 | 458 | 470 | 462 | |
| 59 | 417 | 425 | 403 | 412 | | |
| 60 | 403 | 411 | 394 | 406 | | |
| 61 | 370 | 375 | 370 | 381 | | |
| 62 | 335 | 341 | 338 | 342 | | |
| 63 | 317 | 328 | 314 | 321 | | 324 |
| 64 | 307 | 311 | 301 | 307 | | |
| 65 | 297 | 299 | 300 | 303 | | |
| 66 | 263 | 252 | 276 | 285 | | 267 |
| 67 | 223 | 243 | 252 | 255 | | |
| 68 | 205 | 220 | 181 | 187 | | |
| 69 | 187 | 177 | 181 | 183 | | |
| 70 | 156 | 164 | 168 | 172 | | |
| 71 | 127 | 117 | 122 | 124 | | |
| 72 | 96 | 104 | 112 | 112 | | |
| 73 | 77 | 78 | 79 | 79 | | 95 |
| 74 | 65 | 61 | 70 | 67 | | |
| 75 | 49 | 53 | 48 | 48 | | |
| 76 | 45 | 49 | 47 | 47 | | |
| 77 | 18 | 20 | 7 | 20 | | |
| 78 | 12 | 6 | 5 | 13 | | |

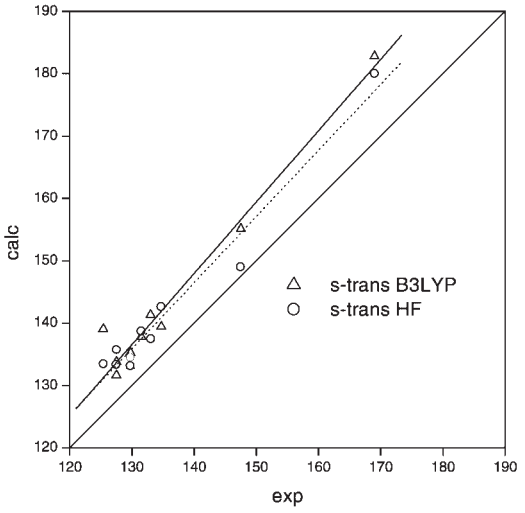



**Figure 3.** Correlation of experimental and theoretically calculated $^{13}C$ chemical shifts of **3** for the s-*cis* structure. (■) HF/6–311 + G(2d,p), $r = 0.96621$, SD = 3.97985, $N = 10$; (○) B3LYP/6–311 + G(2d,p), $r = 0.98014$, SD = 2.92961, $N = 10$

atoms in the molecule and the reference compounds (TMS for $^{1}H$ and $^{13}C$ and $CFCl_3$ for $^{19}F$) at the same level of theory in order to make the comparison valid.

Experimental and calculated $^{1}H$, $^{19}F$ and $^{13}C$ chemical shifts are listed in Table 7. Figure 2 shows a comparison of experimental and calculated $^{13}C$ chemical shifts. There is a fair coincidence of the methods employed in reproducing the $^{13}C$ spectrum, except in the case of the trifluoromethyl groups. The difference between theoretical and experimental data does not depend on the conformer taken into consideration but on the method used for the calculation. The $^{13}C$ chemical shifts are correlated with each other in Figs 3 and 4 (*cis* and *trans* forms, respectively) in which trifluoromethyl carbons were omitted. The correlation of the $^{13}C$ chemical shifts was satisfactory and for both methods the values deviate ~7 ppm to lower field from the line of correlation. Hence the methods used for the prediction of the magnetic properties of the molecule proved to be good enough;

**Table 7.** Data for calculated and experimental $^{13}C$, $^{1}H$ and $^{19}F$ chemical shifts [$\delta$ (ppm)], estimated at the B3LYP/6–31G**// B3LYP/6–311 + G(2d,p), for s-*trans*- and s-*cis*-2-phenyl-4-(3,3,3-trifluoro-2-trifluoromethyl-1-propenyl)-1,3-thiazole

| | | s-*cis* | | | | s-*trans* | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| $\delta$ | | HF | $\Delta^a$ | B3LYP | $\Delta^a$ | HF | $\Delta^a$ | B3LYP | $\Delta^a$ | Exp. ($CDCl_3$) |
| $^{13}C$ | C(2) | 179.6 | −10.6 | 177.6 | −8.6 | 180.0 | −11 | 182.8 | −13.8 | 168.30 |
| | C(4) | 147.1 | 0.4 | 153.8 | −6.3 | 149.0 | −1.5 | 155.1 | −7.6 | 146.80 |
| | C(5) | 130.0 | −4.6 | 138.6 | −13.2 | 133.5 | −8.1 | 139.0 | −13.6 | 125.45 |
| | C(6) | 138.0 | −5 | 140.3 | −7.3 | 137.5 | −4.5 | 141.3 | −8.3 | 131.61 |
| | C(7) | 134.6 | −7.1 | 132.6 | −5.1 | 135.7 | −8.2 | 133.8 | −6.3 | 125.73 |
| | C(8) | 134.4 | −4.6 | 135.7 | −5.9 | 134.5 | −4.7 | 135.2 | −5.4 | 128.12 |
| | C(9) | 138.1 | −6.6 | 136.9 | −5.4 | 138.7 | −7.2 | 137.8 | −6.3 | 129.83 |
| | C(10) | 133.6 | −3.8 | 133.8 | −4 | 133.1 | −3.3 | 133.1 | −3.3 | 128.12 |
| | C(11) | 133.7 | −6.2 | 131.9 | −4.4 | 133.4 | −5.9 | 131.6 | −4.1 | 125.73 |
| | C(12) | 148.4 | −13.7 | 144.0 | −9.3 | 142.6 | −7.9 | 139.4 | −4.7 | 134.72 |
| | C(13) | 124.8 | — | 125.3 | — | 124.5 | — | 126.4 | — | —[b] |
| | C(14) | 109.5 | 11.5 | 135.3 | −14.3 | 110.2 | 10.8 | 136.0 | −15 | 121.71 |
| | C(15) | 109.8 | 12.2 | 135.4 | −13.4 | 109.1 | 12.9 | 134.7 | −12.7 | 120.91 |
| $^{1}H$ | H(5) | 8.2 | −0.5 | 8.3 | −0.6 | 7.6 | 0.1 | 7.36 | 0.34 | 7.75 |
| | H(7) | 8.9 | −1.0 | 8.8 | −0.9 | 9.3 | −1.4 | 9.06 | −1.16 | 7.90 |
| | H(8) | 7.9 | −0.4 | 7.8 | −0.3 | 7.9 | −0.4 | 7.86 | −0.36 | 7.42 |
| | H(9) | 7.9 | −0.4 | 7.8 | −0.3 | 7.9 | −0.4 | 7.86 | −0.36 | 7.50 |
| | H(10) | 7.8 | −0.3 | 7.6 | −0.1 | 7.8 | −0.3 | 7.56 | −0.06 | 7.42 |
| | H(11) | 8.2 | −0.3 | 8.1 | −0.2 | 8.2 | −0.3 | 8.46 | −0.56 | 7.95 |
| | H(12) | 7.9 | −0.3 | 8.6 | −1.0 | 7.6 | 0.0 | 7.16 | 0.44 | 7.63 |
| $^{19}F$ | F(1) | −51.9 | −7.3 | −71.7 | 12.5 | −59.7 | 0.5 | –89.1 | 29.9 | −59.20 |
| | F(2) | −34.3 | −24.9 | −71.7 | 12.5 | −49.1 | −10.1 | –73.8 | 14.6 | −59.20 |
| | F(3) | −56.4 | −2.8 | −84.3 | 25.1 | −49.0 | −10.2 | −73.8 | 14.6 | −59.20 |
| | F(4) | −48 | −16.4 | −74.5 | 10.1 | −53.7 | −10.7 | −81.4 | 17.0 | −64.43 |
| | F(5) | −59.6 | −4.8 | −88.9 | 24.5 | −40.0 | −24.4 | –66.4 | 2.0 | −64.43 |
| | F(6) | −51.4 | −13.0 | −74.5 | 10.1 | −40.7 | −23.7 | −66.4 | 2.0 | −64.43 |

[a] Difference between the experimental and calculated data.
[b] Not observed in the corresponding spectra.

nevertheless, these results are not conclusive for determining the actual conformations in solution since the methods used do not predict the coupling pattern.

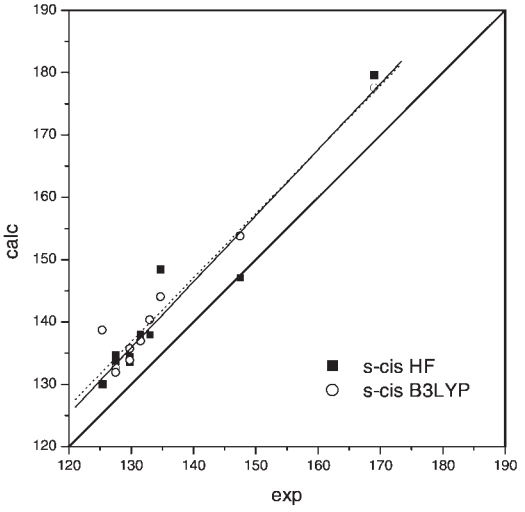



**Figure 4.** Correlation of experimental and theoretically calculated $^{13}C$ chemical shifts of **3** for the s-*trans* structure. (○) HF/6–311 + G(2d,p), $r = 0.982337$, SD = 2.83938, $N = 10$; (△) B3LYP/6–311 + G(2d,p), $r = 0.97929$, SD = 3.32909, $N = 10$

## CONCLUSIONS

Compound **3** was systematically analysed by both theoretical and experimental methods. The theoretical results agree with the observed behaviour of the compound in solution, which can be interpreted as a mixture of s-*cis* and s-*trans* conformations in a roughly 2:1 ratio.

The solid-state structure was interpreted in terms of an s-*trans* conformation. According to these results, packing effects should play a major role to apart the solid conformation from the most stable s-*cis* form of the free molecule.

Overall, the results coincide in that the energy difference of the two conformers is small depending the most stable form from relative interactions accounted in solution or in the solid state.

### Acknowledgements

The authors thank the Deutscher Akademischer Austauschdienst (DAAD), the Ruhr-Universität Bochum, Germany, and the Comisión de Investigaciones Científicas de la Provincia de Buenos Aires (CICBA), Argentina, for financial support and for a fellowship to E.M.C. The

authors also thank the Fundación Antorchas, Alexander von Humboldt Foundation, Agencia Nacional de Promoción Científica y Técnica (ANPCYT), Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), the British Council, Jesus College, Oxford, and the Facultad de Ciencias Exactas (UNLP) for financial support. They are indebted to the AvH–Fundación Antorchas and ANPCYT-DAAD for German–Argentinean Cooperation Awards.

## REFERENCES

1. Hudlický M, Pavlath A. *Chemistry of Organic Fluorine Compounds II—A Critical Review.* American Chemical Society: Washington, DC, 1995.
2. Welch JT. *Tetrahedron* 1987; **43**: 3123–3197.
3. Nenajdenko VG, Sanin AV, Balenkova ES. *Molecules* 1997; **2**: 186–232.
4. Bonnet-Delpon D, Bégué J-P, Leqeux T, Ourévitch M. *Tetrahedron* 1996; **52**: 59–70.
5. Coyanis EM. PhD Thesis, Universidad Nacional de La Plata, 1999.
6. Abele H, Haas A, Lieb M, Zwingenberger J. *Chem. Ber.* 1994; **127**: 145–149.
7. Haas A, Lieb M, Schelvis M. *J. Fluorine. Chem.* 1997; **83**: 133–143.
8. Bonnet-Delpon D, Bégué J-P, Leqeux T, Ourévitch M. *Tetrahedron* 1996; **52**: 59–70.
9. Wallmichrath T. *Dissertation*, Ruhr-Universität Bochum, 1997.
10. Schelvis M. *Dissertation*, Ruhr-Universität Bochum, 1996.
11. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Zakrzewski VG, Montgomery JA Jr, Stratmann RE, Burant JC, Dapprich S, Millam JM, Daniels AD, Kudin KN, Strain MC, Farkas O, Tomasi J, Barone V, Cossi M, Cammi R, Mennucci B, Pomelli C, Adamo C, Clifford S, Ochterski J, Petersson GA, Ayala PY, Cui Q, Morokuma K, Malick DK, Rabuck AD, Raghavachari K, Foresman JB, Cioslowski J, Ortiz JV, Baboul AG, Stefanov BB, Liu G, Liashenko A, Piskorz P, Komaromi I, Gomperts R, Martin RL, Fox DJ, Keith T, Al-Laham MA, Peng CY, Nanayakkara A, Gonzalez C, Challacombe M, Gill PMW, Johnson B, Chen W, Wong MW, Andres JL, Gonzalez C, Head-Gordon M, Replogle ES, Pople JA. *Gaussian 98, Revision A.7*. Gaussian: Pittsburgh PA, 1998.
12. Sheldrick GM. *SHELXS-93, Program for Crystal Structure Solution*. University of Göttingen: Göttingen, 1993.
13. Hudson RF, Chopard PA. *J. Org. Chem*. 1963; **28**: 2446–2447.
14. Metzger JV. In *The Chemistry of Heterocyclic Compounds*, vol. 6(4B), Katritzky AR, Rees CW (eds). Pergamon Press: Oxford, 1984; 235–246.
15. Stowell JC. *Carbanions in Organic Chemistry.* Wiley–Interscience: New York, 1979.
16. Williams DR, Brooks DA, Moore JL, Stewart AO. *Tetrahedron Lett.* 1996; **37**(7): 983–986, and references cited therein.
17. Jackman LM, Sternhell S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*. Pergamon Press: Oxford, 1969.
18. Hardt T. *Dissertation*, Ruhr-Universität Bochum, 1998.
19. Looker JH, Khatri NA, Patterson RB, Kingsbury CB. *J. Heterocycl Chem.* 1978; **15**: 1383–1385, and references cited therein.
20. Breitmaier E, Voelter W. *Carbon-13 NMR Spectroscopy* (3rd edn). VCH: Wienheim, 1990.
21. Breitmaier E. *Vom NMR-Spektrum zur Strukturformel Organischer Verbindungen*. Teubner: Stuttgart, 1992.
22. Pretsch E, Clerc T, Siebl J, Simon W. *Tables of Spectral Data for Structure Determination of Organic Compounds* (2nd edn). Springer: Berlin, 1989.
23. Salmona G, Vincent E-J. *Org. Mass Spectrom.* 1978; **13**(2): 119–120.
24. Clarke GM, Grigg R, Williams DH. *J. Chem. Soc. B* 1966; **4**: 339–343.
25. Bondi A. *J. Phys. Chem*. 1964; **68**: 441–451.