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ORIGINAL PAPER

Syntheses and Crystal Structures of Benzyl Substituted Thiazolidin-2-cyanamide Derivatives

Jun-Ling Wang[1] · Sen Ma[1] · Ai-Quan Jia[1] · Qian-Feng Zhang[1]

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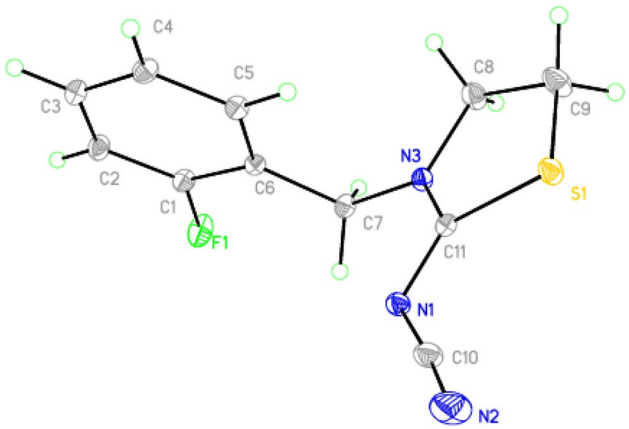
Abstract

Reaction of thiazolidin-2-cyanamide and substituted benzyl bromide compounds in acetonitrile at room temperature afforded the 3-(2′-substituted benzyl)thiazolidin-2-cyanamide derivatives **1–13** in good yields. Compounds **1–13** were characterized by proton nuclear magnetic resonance (^{1}H NMR) and infrared spectroscopies, of which the structures of the isomeric *o*-, *m*-, and *p*-fluoro derivatives **4–6** were established by single crystal X-ray crystallography. Compound **4** crystallizes in the monoclinic space group $P2_1/n$, with $a = 9.177(19)$, $b = 8.551(18)$, $c = 14.090(3)$ Å, $\beta = 98.243(3)°$, and $Z = 4$. The unit cell of **5** has a monoclinic $P2_1/c$ symmetry with the cell parameters $a = 9.289(2)$, $b = 14.057(4)$, $c = 8.574(2)$ Å, $\beta = 100.350(3)°$, and $Z = 4$. The unit cell of **6** also has a monoclinic $P2_1/c$ symmetry with the cell parameters $a = 9.333(4)$, $b = 14.034(5)$, $c = 8.508(3)$ Å, $\beta = 99.15(5)°$, and $Z = 4$.

Graphic Abstract

A series of 3-(2′-substituted benzyl)thiazolidin-2-cyanamide derivatives were efficiently synthesized via the reaction of benzyl bromide compounds with thiazolidin-2-cyanamide, of which the structures of the isomeric o-, m-, and p-fluoro derivatives were characterized by X-ray crystallography.



Keywords Thiazolidin-2-cyanamide · Synthesis · Crystal structure · Hydrogen bond

Introduction

As known, thiacloprid (3-(6-chloropyridin-3-ylmethyl)-thiazolidin-2-ylidene cyanamide) is a novel chlorinated broad-spectrum nicotinic insecticide agent with high efficiency and low toxicity, developed in the 1990s by Bayer Agrochemical Company of Germany and Bayer Agrochemical Company

✉ Qian-Feng Zhang
zhangqf@ahut.edu.cn

[1] Institute of Molecular Engineering and Applied Chemistry, Anhui University of Technology, Ma'anshan 243002, Anhui, People's Republic of China

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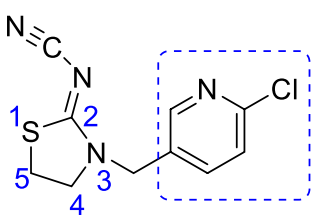
of Japan as a new type of bio-pesticide [1]. Therefore, how to develop thiacloprid at a lower cost and how to modify its structure to achieve drug improvement has become a research hotspot at present [2, 3]. It is well known that thiazolidin-2-cyanamide is an important substrate in the syntheses of thiacloprid and its derivatives [4]. For examples, the compounds synthesized by the reaction of thiazolidin-2-cyanamide and acid chloride have good antifungal activity [5]. A related phenyl oxazol-based neonicotinoid derivative with thiazolidin-2-ylidene-cyanamide moiety is reported to have moderate insecticidal activity against pea aphids, and favorable fungicidal activities and anti-tumor activities [6]. Moreover, the phenyl furyl-based thiazolidin-2-cyanamide derivatives showed bioactivity against type III secretion system of *Xanthomonas oryzae* on rice [7]. Syntheses and structures of *N*-[(*Z*)-3-(4-chlorobenzoyl)-1,3-thiazolidin-2- ylidene] cyanamide and (*Z*)-*N*-[3-(4-bromobenzoyl)-1,3-thiazolidin-2-ylidene]- cyanamide were also reported, showing that the typical dihedral angle between the benzene and thiazolidine rings is about 63.0° [8, 9]. Herein, we report the syntheses of thiacloprid analogues by using various substituted benzyl bromide compounds instead of chloromethylpyridine to react with thiazolidin-2-cyanamide (see Scheme 1).

Experimental

General Procedure

All solvents were purified by routine procedures and distilled under an atmosphere of dry nitrogen before use. 2-Methylbenzyl bromide, 3-methylbenzyl bromide, 4-methylbenzyl bromide, 2-cyanobenzyl bromide, 3-cyanobenzyl bromide, 4-cyanobenzyl bromide, 2-fluorobenzyl bromide, 3-fluorobenzyl bromide, 4-fluorobenzyl bromide, 2-bromobenzyl bromide, benzylbromide and 4-chlorobenzyl bromide were purchased from Alfa Aesar Ltd. and used without further purification. Thiazolidin-2-ylidene-cyanamide was synthesized according to literature methods [10, 11]. The infrared spectra were recorded on a Digilab FTS-40 spectrophotometer with use of pressed KBr pellets. For IRs, labels with s (strong), m(medium), w (weak), sh (shoulder), br (broad) are reported for each band. ^{1}H-NMR spectra were recorded on a Bruker AV400-MHz Advance NMR spectrometer at 400 MHz.



Scheme 1 Structure of thiacloprid

General Synthetic Route for Substituted Thiacloprid Derivatives

Thiazolidin-2-ylidene-cyanamide (0.317 g, 2.50 mmol) in acetonitrile (20 mL) was dropwise added to a stirred solution of substituted benzyl bromide (2.5 mmol) and 14 mL NaOH aqueous solution (1 M). The mixture is stirred at room temperature for 8–10 h. The soild was collected by filtration, washed with *n*-hexane and dried *in vacuo*.

3-(2-methylbenzyl)thiazolidin-2-ylidene-cyanamide (1) white solid, yield: 0.494 g (85.4%), m.p.: 115–16 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.34 (s, 3H, CH_3), 3.32 (t, $J=7.6$ Hz, 2H, NCH_2), 3.74 (t, 2H, $J=7.6$ Hz, SCH_2), 4.57 (s, 2H, CH_2), 7.14–7.19 (m, 2H, *Ph*). IR (KBr disc, cm^{-1}): 2918, w, ν(CH); 2182, s, 2160 sh, v(C≡N); 1573, s, v(C=N).

3-(3-methylbenzyl)thiazolidin-2-ylidene-cyanamide (2) white solid, yield: 0.664 g (89.7%), m.p.: 126–128 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.37 (t, $J=7.6$ Hz, 2H, NCH_2), 3.82 (t, $J=7.6$ Hz, 2H, SCH_2), 4.76 (s, 2H, CH_2), 7.19–7.24 (m, 1H, *Ph*), 7.32–7.36 (m, 2H, *Ph*), 7.59–7.60 (m, 1H, *Ph*). IR (KBr disc, cm^{-1}): 3012, w, ν(CH); 2181, s, 2152 sh, v(C≡N); 1573, s, v(C=N).

3-(4-methylbenzyl)thiazolidin-2-ylidene-cyanamide (3) white solid, yield: 0.529 g (87.4%), m.p.: 120–121 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.41 (t, $J=7.6$ Hz, 2H, NCH_2), 3.80 (t, $J=7.6$ Hz, 2H, SCH_2), 4.65 (s, 2H, CH_2), 7.52–7.49 (m, 1H, *Ph*), 7.55 (dd, $J=5.7$, 4.1 Hz, 2H, *Ph*), 7.65 (dt, $J=7.3$, 1.6 Hz, 1H, *Ph*). IR (KBr disc, cm^{-1}): 2916, w, ν(CH); 2182, s, 2146 sh, v(C≡N); 1570, s, v(C=N).

3-(2-fluorobenzyl)thiazolidin-2-ylidene-cyanamide (4) white solid, yield: 0.492 g (83.6%), m.p.: 105–106 °C. ^{1}HNMR (400 MHz, $CDCl_3$): δ (ppm) 3.36–3.39 (t, $J=7.6$ Hz, 2H, NCH_2), 3.78 (t, $J=7.6$ Hz, 2H, SCH_2), 4.61 (s, 2H, CH_2), 6.96–7.06 (m, 3H, *Ph*), 7.26–7.37 (m, 1H, *Ph*). IR (KBr disc, cm^{-1}): 3056, w, ν(CH); 2182, s, 2151 sh v(C≡N); 1568, s, v(C=N).

3-(3-fluorobenzyl)thiazolidin-2-ylidene-cyanamide (5) yellow solid, yield: 0.494 g (84.9%), m.p.: 101–102 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.35 (t, $J=7.6$ Hz, 2H, NCH_2), 3.75 (t, $J=7.6$ Hz, 2H, SCH_2), 4.58 (s, 2H, CH_2), 7.05 (m, 2H, *Ph*), 7.22–7.29 (m, 1H, *Ph*), 7.29–7.24 (m, 1H, *Ph*). IR (KBr disc, cm^{-1}): 2987, w, ν(CH); 2178, s, 2149 sh v(C≡N); 1571, s, v(C=N).

3-(4-fluorobenzyl)thiazolidin-2-ylidene-cyanamide (6) yellow solid, yield: 0.528 g (87.2%), m.p.: 109–110 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.35 (t, $J=7.6$ Hz, 2H, NCH_2), 3.75 (t, $J=7.6$ Hz, 2H, SCH_2), 4.68 (s, 2H, CH_2), 7.01–7.09 (m, 2H, *Ph*), 7.28–7.24 (m, 2H, *Ph*). IR (KBr disc,

Table 1 Crystallographic data and details for compounds **4**, **5** and **6** with estimated standard deviations in parentheses

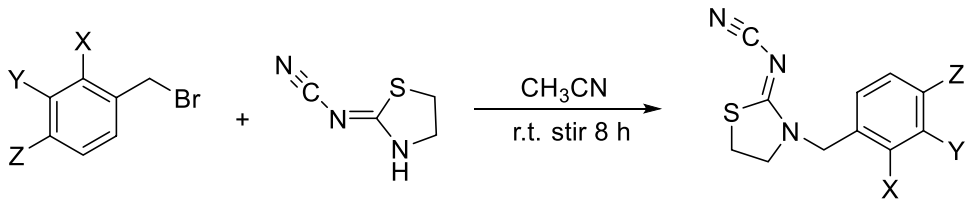
Compound	**4**	**5**	**6**
Empirical formula	$C_{11}H_{10}N_3FS$	$C_{11}H_{10}N_3FS$	$C_{11}H_{10}N_3FS$
Formula weight	235.28	235.28	235.28
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_1/n$	$P2_1/c$	$P2_1/c$
a (Å)	9.177 (19)	9.289 (2)	9.333 (4)
b (Å)	8.551 (18)	14.057 (4)	14.034 (5)
c (Å)	14.090 (3)	8.574 (2)	8.508 (3)
β (°)	98.243 (3)	100.350 (3)	99.15 (5)
V(Å^3)	1094.3 (4)	1101.4 (5)	1100.2 (7)
Z	4	4	4
D_{calc} (Mg m^{-3})	1.428	1.419	1.420
Crystal size (mm^3)	0.11×0.14×0.16	0.10×0.13×0.18	0.12×0.14×0.19
Temperature (K)	296 (2)	296 (2)	296 (2)
F(000)	488	488	488
μ(Mo-Kα) (mm^{-1})	0.283	0.281	0.282
Total refln	6504	6577	6704
Independent refln, I > 2σ	2470, 1868	2481, 1632	2503, 1596
R_{int}	0.0250	0.0307	0.0352
Parameters	145	145	145
$R1$[a], $wR2$[b] ($I > 2\sigma(I)$)	0.0419, 0.1122	0.0426, 0.0941	0.0433, 0.1029
$R1$, $wR2$ (all data)	0.0558, 0.1213	0.0731, 0.1082	0.0754, 0.1187
GoF[c]	1.055	1.008	1.045

[a] $R1 = \| |F_o| - |F_c| \| / |F_o|$

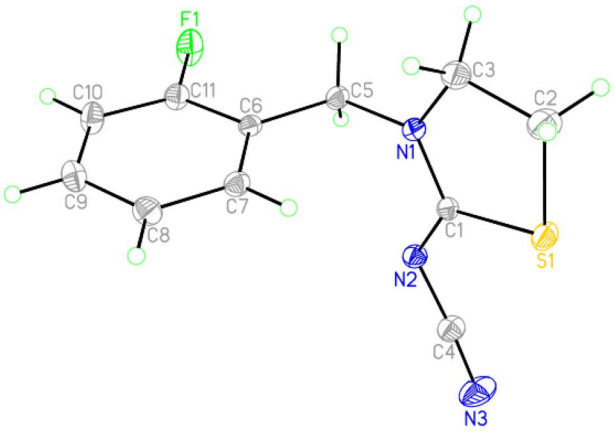
[b] $wR2 = [w(|F_o^2| - |F_c^2|)^2 / w|F_o^2|^2]^{1/2}$

cGoF = $[w(|F_o| - |F_c|)2/(N_{obs} - N_{param})]1/2$

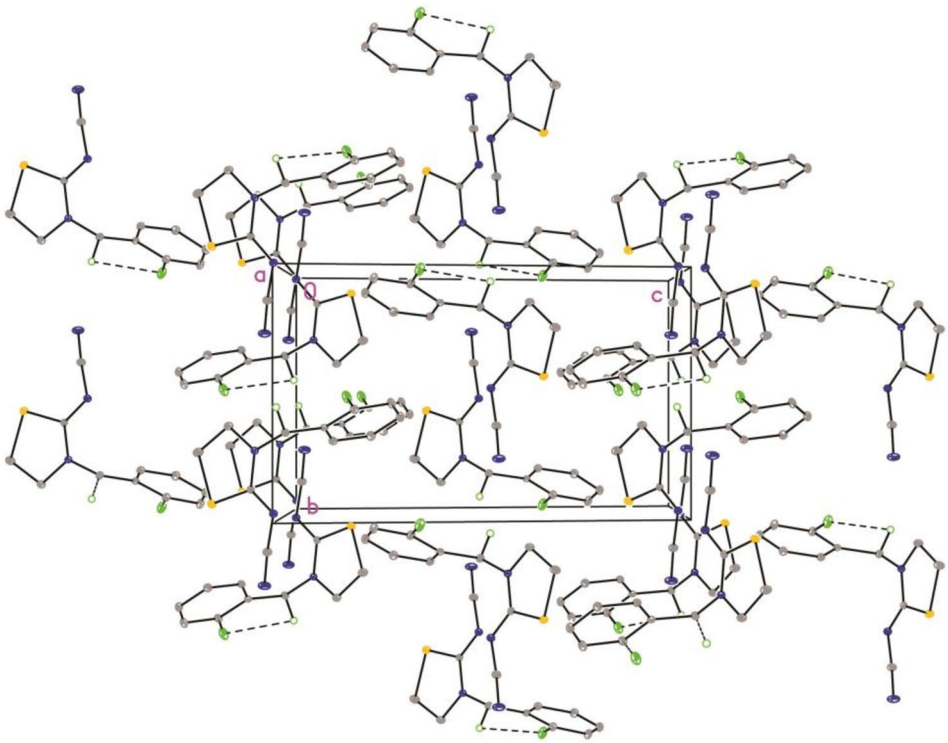
Scheme 2 Synthesis of 3-(2′-substituted benzyl)thiazolidin-2-cyanamide derivatives



	X	Y	Z
1	Me	H	H
2	H	Me	H
3	H	H	Me
4	F	H	H
5	H	F	H
6	H	H	F
7	CN	H	H
8	H	CN	H
9	H	H	CN
10	Br	H	H
11	H	H	Cl
12	H	H	H
13	H	H	^{t}Bu



(a)



(b)

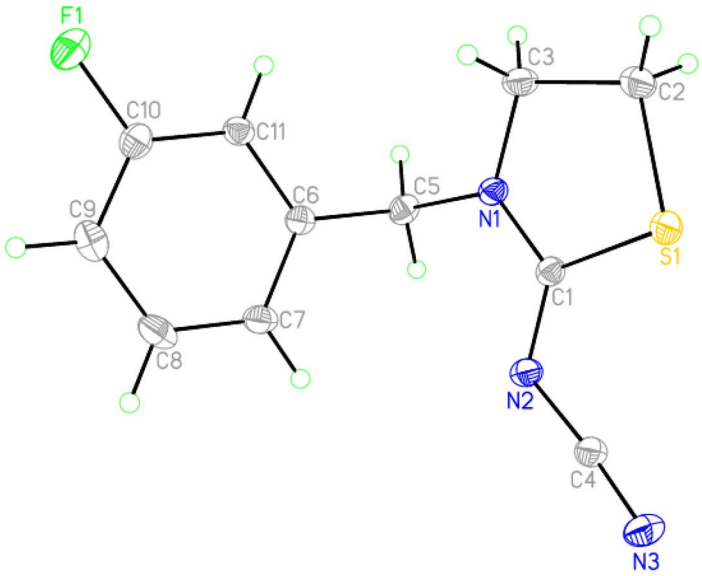
Fig. 1 **a** Structure of **4**, showing the atom-labelling scheme of one molecule in the asymmetric unit. Displacement ellipsoids are drawn at 30% probability level and H atoms are shown as small spheres of arbitrary radii. The crystal structure of (**b**), viewed along the *a* axis. Dashed lines indicate C–H···F hydrogen bonds

cm^{-1}): 2963, w, ν(CH); 2180, s, 2143 sh v(C≡N); 1580, s, v(C=N).

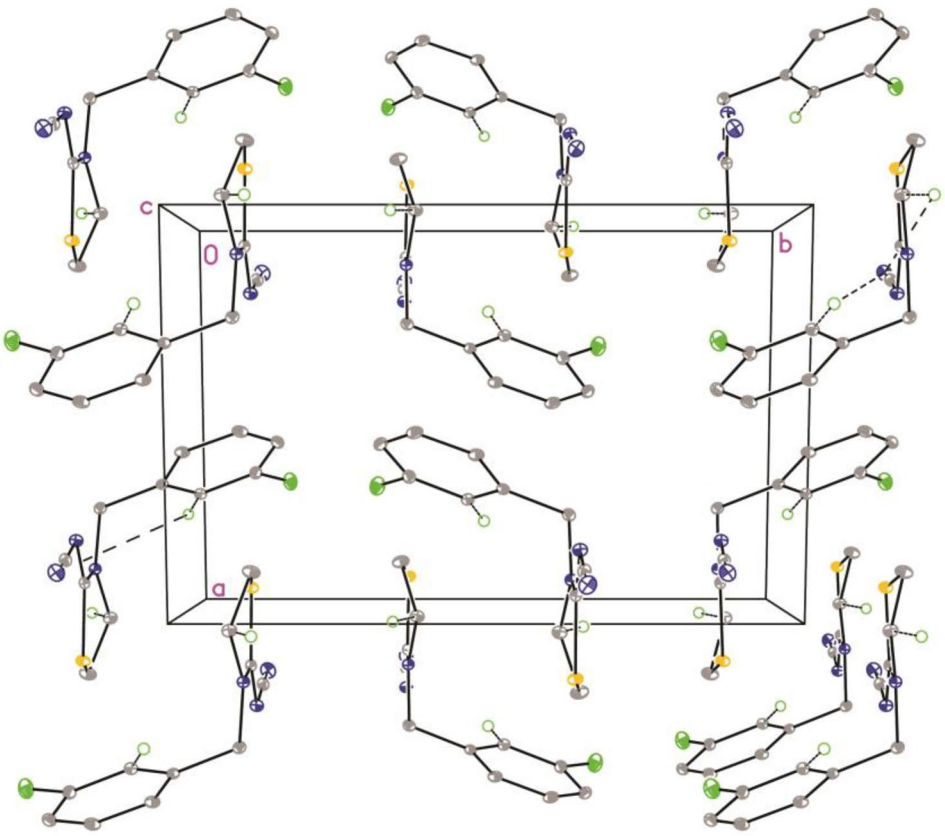
3-(2-cyanobenzyl)thiazolidin-2-ylidene-cyanamide (7) white solid, yield: 0.496 g (85.7%), m.p.: 132–133 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.30 (s, 3H, CH_3), 3.33 (t, J = 7.6 Hz, 2H, NCH_2), 3.67 (t, J = 7.6 Hz, 2H, SCH_2), 4.62 (s, 2H, CH_2), 7.14–7.28 (m, 4H, *Ph*). IR (KBr disc, cm^{-1}): 2918, w, ν(CH); 2180, s, 2143 sh v(C≡N); 1591, s, v(C=N).

3-(3-cyanobenzyl)thiazolidin-2-ylidene-cyanamide (8) white solid, yield: 0.498 g (86.1%), 128–129 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.35 (s, 3H, CH_3), 3.34 (t, J = 7.6 Hz, 2H, NCH_2), 3.73–3.77 (t, J = 7.6 Hz, 2H, SCH_2), 4.56 (s, 2H, CH_2), 7.03–7.27 (m, 4H, *Ph*). IR (KBr disc, cm^{-1}): 2917 w, ν(CH); 2180, s, 2147 sh v(C≡N); 1590, s, v(C=N).

3-(4-cyanobenzyl)thiazolidin-2-ylidene-cyanamide (9) white solid, yield: 0.514 g (87.3%), 138–139 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.36 (t, J = 7.5 Hz, 2H, NCH_2),



(a)

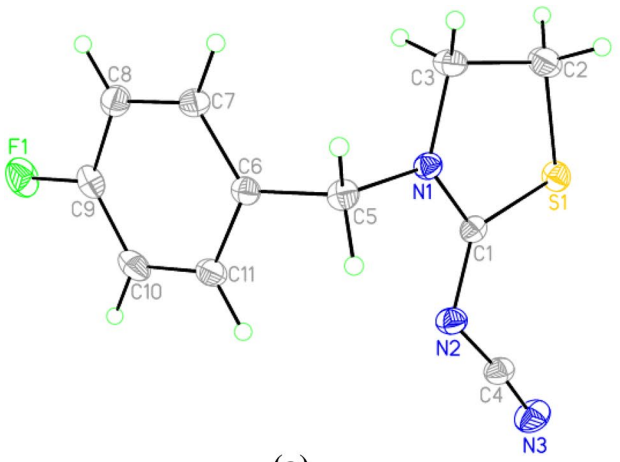


(b)

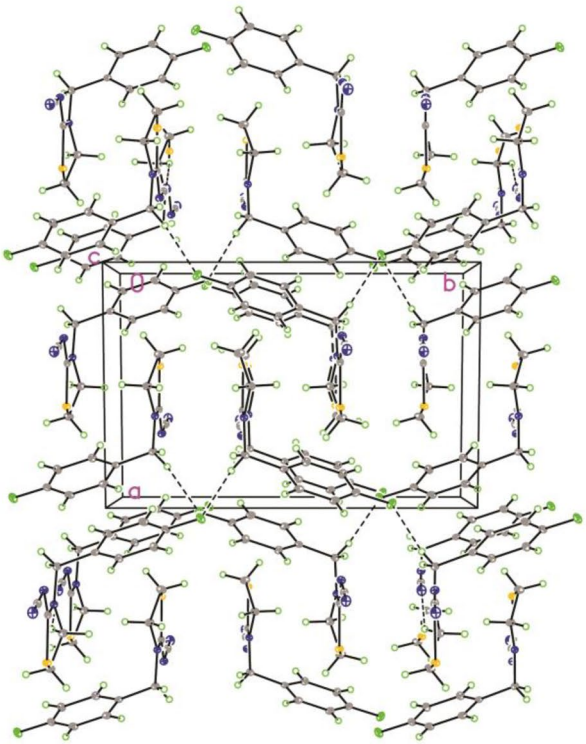
Fig. 2 **a** Structure of **5**, showing the atom-labelling scheme of one molecule in the asymmetric unit. Displacement ellipsoids are drawn at 30% probability level and H atoms are shown as small spheres of arbitrary radii. The crystal structure of (**b**), viewed along the *c* axis. Dashed lines indicate C–H···N hydrogen bonds

3.83–3.87 (t, $J = 7.5$ Hz, 2H, SCH_2), 4.67 (s, 2H, CH_2), 7.04–7.20 (m, 2H, *Ph*), 7.29–7.42 (m, 2H, *Ph*). IR (KBr disc, cm^{-1}): 2944, w, ν(CH); 2181, s, 2150 sh ν(C≡N); 1590, s, ν(C=N).

3-(2-bromobenzyl)thiazolidin-2-ylidene-cyanamide (10) white solid, yield: 0.511 g (84.3%), 122–123 °C. 1H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.42 (t, $J = 7.5$ Hz, 2H, NCH_2), 3.94 (t, $J = 7.5$ Hz, 2H, SCH_2), 4.83 (s, 2H, CH_2), 7.38–7.78



(a)



(b)

Fig. 3 **a** Structure of **6**, showing the atom-labelling scheme of one molecule in the asymmetric unit. Displacement ellipsoids are drawn at 30% probability level and H atoms are shown as small spheres of arbitrary radii. The crystal structure of (**b**), viewed along the *c* axis. Dashed lines indicate C–H···N and C–H···F hydrogen bonds

(m, 4H, Ph).IR (KBr disc, cm − 1): 2940, w, ν(CH); 2182, s, 2149 sh v(C≡N); 1582, s, v(C=N).

3-(4-chlorobenzyl)thiazolidin-2-ylidene-cyanamide (11) white solid, yield: 0.548 g (80.2%), 112–113 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.01–2.08 (s, 9H, $(CH_3)_3$), 3.34 (t, $J = 7.6$ Hz, 2H, NCH_2), 3.76 (t, $J = 7.6$ Hz, 2H, SCH_2), 4.57(s, 2H, CH_2), 7.19 (d, $J = 8.4$ Hz, 2H, *Ph*), 7.34–7.40 (m, 2H, *Ph*). IR (KBr disc, cm^{-1}): 2950, w, ν(CH); 2181, s, 2140 sh v(C≡N); 1583, s, v(C=N).

3-benzylthiazolidin-2-ylidene-cyanamide (12) white solid, yield: 0.580 g (78.2%), 110–111 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.28 (t, $J = 7.6$ Hz, 2H, NCH_2), 3.69 (t, $J = 7.6$ Hz, 2H, SCH_2), 4.54 (s, 2H, CH_2), 7.18–7.44 (m, 5H, *Ph*). IR (KBr disc, cm^{-1}): 2878, w, ν(CH); 2178, s, 2142, sh v(C≡N); 1583, s, v(C=N).

Table 2 Selected bond lengths (Å) and angles (°) for compound **4** with estimated standard deviations in parentheses

S(1)–C(1)	1.743(17)	S(1)–C(2)	1.798(2)
F(1)–C(11)	1.358(2)	N(1)–C(1)	1.331(2)
N(1)–C(3)	1.457(2)	N(1)–C(5)	1.458(2)
N(2)–C(1)	1.307(2)	N(2)–C(4)	1.320(3)
N(3)–C(4)	1.146(3)		
C(1)–S(1)–C(2)	92.35(9)	C(1)–N(1)–C(3)	116.55(16)
C(1)–N(1)–C(5)	122.74(15)	C(3)–N(1)–C(5)	120.43(16)
C(1)–N(2)–C(4)	111.77(16)	N(2)–C(1)–N(1)	121.74(16)
N(2)–C(1)–S(1)	125.55(14)	N(1)–C(1)–S(1)	112.71(13)
N(3)–C(4)–N(2)	175.0(2)		

Table 3 Selected bond lengths (Å) and angles (°) for compound **5** with estimated standard deviations in parentheses

S(1)–C(1)	1.739(2)	S(1)–C(2)	1.808(2)
F(1)–C(10)	1.349(3)	N(1)–C(1)	1.323(2)
N(1)–C(3)	1.461(2)	N(1)–C(5)	1.463(3)
N(2)–C(1)	1.323(2)	N(2)–C(4)	1.323(2)
N(3)–C(4)	1.148(3)		
C(1)–S(1)–C(2)	91.14(10)	C(1)–N(1)–C(3)	115.49(16)
C(1)–N(1)–C(5)	122.78(16)	C(3)–N(1)–C(5)	121.11(16)
C(1)–N(2)–C(4)	116.78(17)	N(2)–C(1)–N(1)	122.10(18)
N(2)–C(1)–S(1)	124.64(15)	N(1)–C(1)–S(1)	113.26(14)
N(3)–C(4)–N(2)	174.8(2)		

Table 4 Selected bond lengths (Å) and angles (°) for compound **6** with estimated standard deviations in parentheses

S(1)–C(1)	1.746(2)	S(1)–C(2)	1.804(3)
F(1)–C(9)	1.362(3)	N(1)–C(1)	1.324(2)
N(1)–C(3)	1.454(2)	N(1)–C(5)	1.470(2)
N(2)–C(1)	1.315(3)	N(2)–C(4)	1.329(3)
N(3)–C(4)	1.144(3)		
C(1)–S(1)–C(2)	91.04(10)	C(1)–N(1)–C(3)	115.72(17)
C(1)–N(1)–C(5)	122.86(17)	C(3)–N(1)–C(5)	120.74(17)
C(1)–N(2)–C(4)	117.19(19)	N(2)–C(1)–N(1)	122.08(19)
N(2)–C(1)–S(1)	124.85(16)	N(1)–C(1)–S(1)	113.05(15)
N(3)–C(4)–N(2)	174.6(3)		

Table 5 Hydrogen-bonding system for compounds **4**, **5** and **6** with estimated standard deviations in parentheses

Compound	D–H···A	d(D–H) (Å)	d(H···A) (Å)	d(D···A) (Å)	∠(DHA) (deg)
4	C(5)–H(5B)···F(1)^{i}	0.97	2.56	3.277(2)	130.5
5	C(3)–H(3B)···N(3)^{ii}	0.97	2.66	3.434(3)	137.4
	C(11)–H(11)···N(3)^{ii}	0.93	2.69	3.546(3)	153.7
6	C(3)–H(3A)···N(3)^{iii}	0.97	2.58	3.383(3)	140.5
	C(5)–H(5B)···F(1)^{iv}	0.97	2.48	3.440(3)	170.3

Symmetry codes: $^{(i)}$ $-x+1, -y+1, -z+2$; $^{(ii)}$ $x, y, z-1$; $^{(iii)}$ $x, y, z-1$; $^{(iv)}$ $-x, y+½, -z+3/2$

3-(4-tert-butylbenzyl)thiazolidin-2-ylidene-cyanamide (13) white solid, yield: 0.533 (84.7%), 124–125 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.29 (t, $J=7.6$ Hz, 2H, NCH_2), 3.68 (t, $J=7.6$ Hz, 2H, SCH_2), 4.51 (s, 2H, CH_2), 7.11–7.22 (m, 2H, *Ph*), 7.23–7.44 (m, 2H, *Ph*). IR (KBr disc, cm^{-1}): 2987, w, ν(CH); 2178, s, 2149 sh ν(C≡N); 1585, s, ν(C=N).

X-Ray Crystallography

A summary of crystallographic data and experimental details for 3-(2-fluorobenzyl)thiazolidin-2-ylidene cyanamide (**4**), 3-(3-fluorobenzyl)- thiazolidin-2-ylidene cyanamide (**5**) and 3-(4-fluorobenzyl)thiazolidin-2-ylidene cyanamide (**6**) are summarized in Table 1. Intensity data were collected on a Bruker SMART APEX 2000 CCD diffractometer using graphite-monochromated Mo-Kα radiation ($\lambda=0.71073$ Å) at 296(2) K. The collected frames were processed with the software SAINT [12]. The data was corrected for absorption using the program SADABS [13]. Structures were solved by the direct methods and refined by full-matrix least-squares on F^2 using the SHELXTL software package [14, 15]. All non-hydrogen atoms were refined anisotropically. The positions of all hydrogen atoms were generated geometrically (C_{sp3}–H = 0.96 Å) and C_{sp2}–H = 0.93 Å), assigned isotropic thermal parameters, and allowed to ride on their respective parent carbon atoms before the final cycle of least-squares refinement.

Results and Discussion

As shown in Scheme 2, the target compounds **1–13** were conveniently synthesized by treatment of substituted benzyl bromide compound with thiazolidin-2-ylidene-cyanamide in acetonitrile at room temperature in good yields (80–90%). In the 1H NMR spectra of compounds **1–13**, the peaks in the range of 6.96–7.78 ppm are attributed to the protons of the aryl moiety. The triplet in the range of 3.20–3.50 ppm may be attributed to the NCH_2 proton and the signal in the range of 3.65–3.98 ppm may be assigned to the proton of SCH_2 with coupling constant being about 7.6 Hz, which agree well to those in the known compounds [16, 17]. Chemical shift of the typical NCH_2Ar protons appeared as singlet in the range of 4.57–4.83 ppm. In the IR spectra of compounds **1–13**, the two peaks (a shoulder peak on the main peak) around 2190–2140 cm^{-1} could be assigned to the C≡N stretching vibration due to the possible *syn-anti* isomerism about the C=N bond [18]. While the characteristic C=N stretching vibrations are shown as strong absorptions at around 1580 cm^{-1}.

Molecular structures of compounds **4**, **5** and **6** were further confirmed by single crystal X-ray crystallography, as shown in Figs. 1a, 2a, and 3a, respectively. Selected bond lengths and angles are accordingly given in Tables 2, 3, 4. The crystals of **5** and **6** are isomorphous. In the structures of compounds **4**–**6**, the C(4)– N(3) bond lengths are 1.146(3), 1.148(3) and 1.144(3) Å, respectively, which indicate their predominantly triple-bond character. The C(4)–N(2), C(1)–N(2) and C(1)–N(1) bond lengths being of 1.320(3), 1.307(2), and 1.331(2) Å, respectively in **4**, 1.323(2) Å in **5**, and according 1.329(3), 1.315(3), and 1.324(2) Å in **6**, infer their partial double bonds. Moreover, the N(3)–C(4)–N(2) bond angles are 175.0(2)° for **4**, 174.8(2)° for **5** and 174.6(3)° for **6**, indicatives of the typical N≡C–N=C(SCH_2CH_2)–N group of thiazolidin-2-cyanamide compounds. The solid states of compounds **4**–**6** all adopt *syn*-isomerism about the C=N bond, which are also observed in related thiazolidin-2-cyanamide compounds [6, 8, 9, 19]. The dihedral angles between the benzene and thiazolidine rings of compounds **4**–**6** are 86.7(2)°, 75.5(2)°, and 77.1(2)°, respectively, which are larger than those in benzoyl substituted related compounds (*ca.* 63.0°) [8, 9]. The packing views of compounds **4**–**6** are shown in Figs. 1b, 2b, 3b, respectively. Crystal packing in molecules **4**–**6** are governed by the weak intermolecular C–H···N and C–H···F hydrogen-bonding interactions (see Table 5). The separations of C···N/F in molecules **4**–**6** are in the range of 3.277(2)–3.546(3) Å, similar to the C···N distance in (*Z*)-*N*-[3-(4-bromobenzoyl)-1,3-thiazolidin- 2-ylidene]cyanamide (3.281(5) Å) [9]. The bond angles of C–H···N in molecules **2** and **3** are ranging from 137.4(1)° to 153.7(2)°, while C–H···F bond angles are 130.5(1)° in compound **4** and 170.3(2)° in compound **6**. Moreover, H-pi interactions (3.06 Å) of the phenyl groups exist in compound **4**, and pi-pi interactions (3.79 Å) of the phenyl groups was observed in compound **5**.

In summary, a new series of thiazolidin-2-cyanamide derivatives containing various substituted benzyl moieties were synthesized in good yields by an efficient method, of which three compounds were further characterized by single crystal X-ray crystallography, displaying the solid states being of *syn*-isomerism characteristic of the C=N bonds. There are weak C−H···N and C–H···F hydrogen bonds in the crystal packing of compounds **4**−**6** with the separation of H···N/F being about 2.48−2.69 Å (see Figs. 1b, 2b and 3b).

Supplementary Material

Crystallographic data for A summary of crystallographic data and experimental details for 3-(2-fluorobenzyl)thiazolidin-2-ylidene cyanamide (**4**), 3-(3-fluorobenzyl)thiazolidin-2-ylidene cyanamide (**5**) and 3-(4-fluorobenzyl) thiazolidin-2-ylidene cyanamide (**6**) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 1963653, 1963654, and 1963655, respectively. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: (+44)1233–336-033; e-mail: deposit@ccdc.cam.ac.uk].

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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