Electronic supplementary materials *Mendeleev Commun.*, 2020, **30**, 183–184

Synthesis of pyrano[3,4-*c*]thieno[3,2-*e*][1,2,4]triazolo[4,3-*a*]pyridines, representatives of a new fused heterocyclic system

Ervand G. Paronikyan, Shushanik Sh. Dashyan and Suren S. Mamyan

^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$, DMSO-d_6, DMSO-d_6/CCl_4 (1:3) solutions on a Varian Mercury 300VX 300 MHz spectrometer. Chemical shifts are reported as δ in ppm relative to TMS as the internal standard. IR spectra were recorded on Nicolet Avatar 330-FT-IR spectrophotometer and the reported wave numbers are given in cm^{-1}. All melting points were determined in an open capillary and are uncorrected. Elemental analyses were performed on a Carlo Erba 1108 machine. Quoted values are in the range ±0.4% of the theoretical ones.

*Synthesis of 8-hydrazino-3,3-dimethyl-6-thioxo-3,4,6,7-tetrahydro-1H-pyrano[3,4-c]pyridine-5-carbonitrile **3**.* Compound **1** (3.05 g, 10 mmol) and hydrazine hydrate (4 ml, 80 mmol) were heated together for 1 h. Ethanol (15 ml) was then added, and refluxing was continued for additional 1 h. The precipitate formed was filtered off and recrystallized from dioxane to afford a yellow solid; yield 83%; mp 278–279 ºC; IR *ν*/cm^{-1}: 3212-3259 (NH, NH_2), 2202 (CN), 1270 (C=S). ^{1}H NMR (300 MHz, DMSO-d_6/CCl_4, 1/3) δ 1.20 (s, 6H, $C(CH_3)_2$), 2.50 (s, 2H, CH_2), 4.25 (s, 2H, CH_2), 6.96 (br.s, 3H, $NHNH_2$), 9.49 (br.s, 1H, NH). ^{13}C NMR (300 MHz, DMSO-d_6/CCl_4, 1:3) δ 25.8, 37.6, 57.1, 69.5, 98.6, 102.3, 117.6, 148.4, 149.4, 171.7. Anal. Calcd for $C_{11}H_{14}N_4OS$: C 52.78; H 5.64; N 22.38; S 12.81 %. Found: C 52.93; H 5.47; N 22.56; S 12.94%.

*Compounds **4a-c** (general procedure).* Compound **3** (5.0 g, 20 mmol) was added to a solution of sodium carbonate (2.12 g, 20 mmol) in a mixture of water (5 ml) and ethanol (50 ml). After complete dissolution, the appropriate alkyl halide (20 mmol) was added with cooling, and the mixture was stirred at room temperature for 10 h. The obtained crystals were filtered off, washed with water, dried, and recrystallized from a mixture of ethanol–dioxane 1:2.

8-Hydrazino-3,3-dimethyl-6-methylthio-3,4-dihydro-1H-pyrano[3,4-c]pyridine-5-carbonitrile ***4a***. A white solid; yield 91%; mp 226–227 °C; IR *ν*/cm^{-1}: 3211-3289 (NH, NH_2), 2203 (CN). ^{1}H NMR (300 MHz, DMSO-d_6/CCl_4, 1:3) δ 1.24 (s, 6H, $C(CH_3)_2$), 2.54 (s, 2H, CH_2), 2.60 (s, 3H, SCH_3), 4.27 (br.s, 2H, NH_2), 4.32 (s, 2H, CH_2), 8.07 (br.s, 1H, NH). ^{13}C NMR (300 MHz, DMSO-d_6/CCl_4, 1:3) δ 12.2, 25.7, 37.0, 57.6, 68.9, 93.1, 107.9, 115.4, 143.0, 154.8, 159.7. Anal. Calcd for $C_{12}H_{16}N_4OS$: C 54.52; H 6.10; N 21.19; S 12.13%. Found: C 54.41; H 6.27; N 21.03; S 12.25%

8-Hydrazino-3,3-dimethyl-6-(prop-2-yn-1-ylthio)-3,4-dihydro-1H-pyrano[3,4-c]pyridine-5-carbonitrile ***4b***. A white solid; yield 95%; mp 189–190 °C; IR *ν*/cm^{-1}: 3211-3347 (C≡CH, NH, NH_2), 2205 (CN). ^{1}H NMR (300 MHz, DMSO-d_6/CCl_4, 1:3) δ 1.25 (s, 6H, $C(CH_3)_2$), 2.55 (s, 2H, CH_2), 2.57 (t, *J*= 2.6 Hz, 1H, CH), 4.02 (d, *J*= 2.6 Hz, 2H, SCH_2), 4.29 (br.s, 2H, NH_2), 4.33 (s, 2H, CH_2), 8.18 (s, 1H, NH). ^{13}C NMR (300 MHz, DMSO-d_6) δ 17.7, 25.7, 37.0, 57.6, 68.9, 71.6, 79.6, 92.8, 108.6, 115.1, 143.1, 154.8, 157.6. Anal. Calcd for $C_{14}H_{16}N_4OS$: C 58.31; H 5.59; N 19.43; S 11.12%. Found: C 58.46; H 5.72; N 19.27; S 11.29%

Ethyl [(5-cyano-8-hydrazino-3,3-dimethyl-3,4-dihydro-1H-pyrano[3,4-c]pyridin-6-yl)thio]-acetate ***4c***. A white solid; yield 89 %; mp 179–180 °C; IR *ν*/cm^{-1}: 3211-3320 (NH, NH_2), 2204 (CN), 1710 (C=O). ^{1}H NMR (300 MHz, DMSO-d_6/CCl_4, 1:3) δ 1.25 (s, 6H, $C(CH_3)_2$), 1.26 (t, *J*=7.1 Hz, 3H, $OCH_2\underline{CH_3}$), 2.55 (s, 2H, CH_2), 3.93 (s, 2H, SCH_2), 4.15 (t, *J*=7.1 Hz, 2H, $O\underline{CH_2}CH_3$), 4.27 (br.s, 2H, NH_2), 4.31 (s, 2H, CH_2), 8.20 (s, 1H, NH). ^{13}C NMR (300 MHz, DMSO-d_6/CCl_4, 1:3) δ 13.7, 25.7, 31.8, 37.0, 57.6, 60.5, 68.9, 92.4, 108.5, 115.1, 143.1, 154.6, 158.0, 168.6. Anal. Calcd for $C_{15}H_{20}N_4O_3S$: C 53.55; H 5.99; N 16.65; S 9.53%. Found: C 53.68; H 5.95; N 16.67; S 9.38%

Synthesis of 8,8-dimethyl-5-thioxo-1,7,8,10-tetrahydro-5H-pyrano[3,4-c][1,2,4]triazolo-[4,3-a]pyridine-6-carbonitrile ***5***. A mixture of compound **3** (6.3 g, 25 mmol) and formic acid (60 ml) was refluxed for 0.5 h. The solid formed was filtered off, washed with water, dried, and recrystallized from a 2:1 chloroform–ethanol mixture. A yellow solid; yield 86%; mp 274–275 °C; IR *ν*/cm^{-1}: 3113 (NH), 2221 (CN), 1257 (C=S). ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.29 (s, 6H, $C(CH_3)_2$), 2.69 (s, 2H, CH_2), 4.70 (s, 2H, CH_2), 9.56 (s, 1H, CH), 11.73 (br.s, 1H, NH). ^{13}C NMR (300 MHz, DMSO-d_6) δ 25.9, 37.2, 57.3, 70.4, 102.5, 103.0, 117.4, 137.3, 141.3, 142.1, 163.6. Anal. Calcd for $C_{12}H_{12}N_4OS$: C 55.37; H 4.65; N 21.52; S 12.32%. Found: C 55.25; H 4.78; N 21.39; S 12.18%.

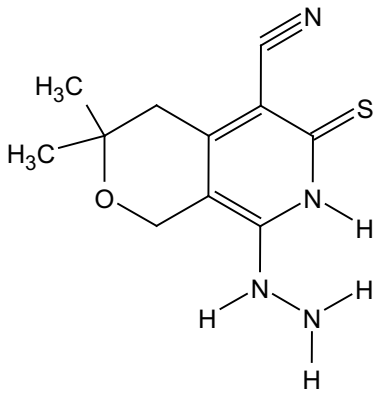
*Compounds **6a-c** (General procedure).* A mixture of compound **5** (0.52 g, 2 mmol), the appropriate chloroacetic acid derivative (2 mmol) in the presence of anhydrous sodium acetate (0.66 g, 8 mmol) was refluxed in ethanol (15 ml) for 4 h. The precipitate formed was filtered off, washed with water, dried, and recrystallized from a mixture of ethanol–chloroform, 1:3.

*Ethyl 7-amino-9,9-dimethyl-8,11-dihydro-9H-pyrano[3,4-c]thieno[3,2-e][1,2,4]triazolo-[4,3-a]pyridine-6-carboxylate **6a**.* A white solid; yield 91 %; mp 299–300 °C; IR ν/cm^{-1}: 3325, 3431 (NH_2), 1664 (C=O). ^{1}H NMR (300 MHz, DMSO-d_6/CCl_4, 1:3) δ 1.35 (s, 6H, $C(CH_3)_2$), 1.38 (t, J= 7.1 Hz, 3H, $OCH_2\underline{CH_3}$), 3.09 (s, 2H, CH_2), 4.30 (q, J= 7.1 Hz, 2H, $O\underline{CH_2}CH_3$), 4.95 (s, 2H, CH_2), 6.72 (s, 2H, NH_2), 9.24 (s, 1H, CH). ^{13}C NMR (300 MHz, DMSO-d_6/CCl_4, 1:3) δ 14.1, 26.0, 35.4, 58.3, 59.5, 69.3, 92.0, 115.9, 117.7, 129.2, 134.3, 145.4, 151.0, 163.6. Anal. Calcd for $C_{16}H_{18}N_4O_3S$: C 55.48; H 5.24; N 16.17; S 9.26%. Found: C 55.34; H 5.36; N 16.02; S 9.13%.

7-Amino-9,9-dimethyl-8,11-dihydro-9H-pyrano[3,4-c]thieno[3,2-e][1,2,4]triazolo[4,3-a]-pyridine-6-carboxamide **6b**. A white solid; yield 81%; mp >360 °C; IR ν/cm^{-1}: 3172-3307 (NH_2), 1654 (C=O). ^{1}H NMR (300 MHz, DMSO-d_6/CCl_4, 1/3) δ 1.31 (s, 6H, $C(CH_3)_2$), 3.13 (s, 2H, CH_2), 4.94 (s, 2H, CH_2), 6.88 (s, 2H, NH_2), 7.24 (s, 2H, NH_2), 9.49 (s, 1H, CH). ^{13}C NMR (300 MHz, DMSO-d_6/CCl_4, 1:3) δ 26.2, 35.5, 58.5, 69.8, 115.6, 118.7, 129.7, 132.0, 135.1, 135.2, 145.7, 149.5, 166.5. Anal. Calcd for $C_{14}H_{15}N_5O_2S$: C 52.98; H 4.76; N 22.07; S 10.10%. Found: C 53.14; H 4.61; N 22.19; S 9.94%.

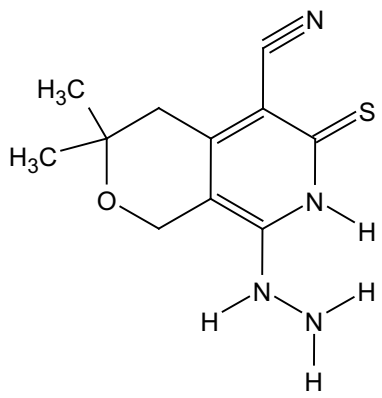
7-Amino-9,9-dimethyl-8,11-dihydro-9H-pyrano[3,4-c]thieno[3,2-e][1,2,4]triazolo[4,3-a]-pyridine-6-carbonitrile **6c**. A white solid; yield 87 %; mp >360 °C; IR ν/cm^{-1}: 3249, 3353 (NH_2), 2197 (CN). ^{1}H NMR (300 MHz, DMSO-d_6/CCl_4, 1:3) δ 1.29 (s, 6H, $C(CH_3)_2$), 3.09 (s, 2H, CH_2), 4.92 (s, 2H, CH_2), 6.59 (s, 2H, NH_2), 9.63 (s, 1H, CH). ^{13}C NMR (300 MHz, DMSO-d_6/CCl_4, 1:3) δ 26.1, 35.3, 58.4, 69.8, 71.6, 115.0, 116.4, 116.9, 129.4, 134.5, 135.7, 145.5, 153.3. Anal. Calcd for $C_{14}H_{13}N_5OS$: C 56.17; H 4.38; N 23.40; S 10.71%. Found: C 56.26; H 4.21; N 23.54; S 10.63%.

comp.3


N
H3C
S
H3C
O
N
H
N
H
H
N
H

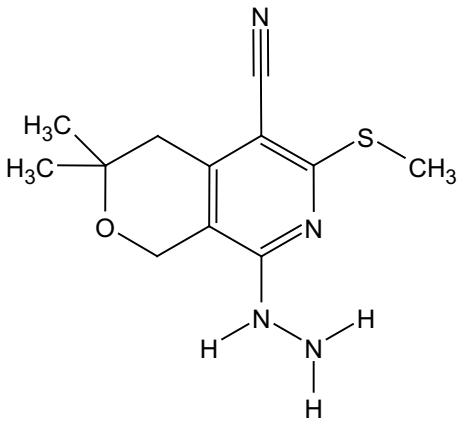
40.34
40.06
39.78
39.50
39.50
39.22
38.94
38.67
37.60
25.78
69.55
57.14
171.71
149.44
148.36
117.57
102.26
98.60
165
155
145
135
125
115
105
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
f1 (ppm)

comp.3


N
H3C
S
H3C
O
N
H
N
H
H
N
H

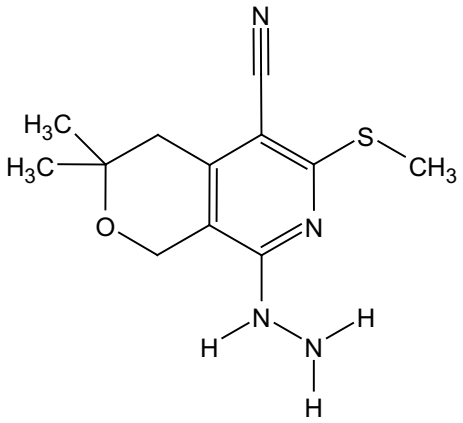
1.0
2.8
2.0
3.2
6.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

comp.4a


N
H3C
H3C
O
S
CH3
N
N
H
H
N
H

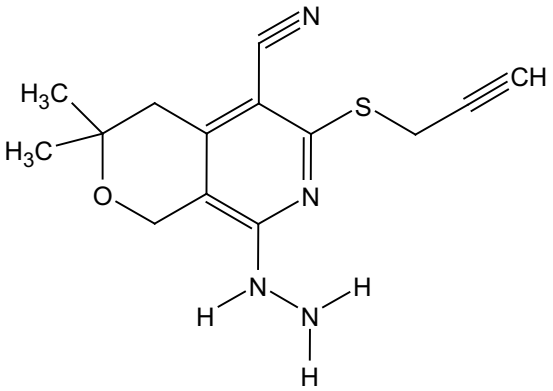
159.71
154.79
143.00
115.37
107.94
93.11
68.84
57.62
40.06
39.78
39.50
39.50
39.22
38.94
37.03
25.73
12.25
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

comp.4a


N
H3C
H3C
O
S
CH3
N
N
H
H
N
H

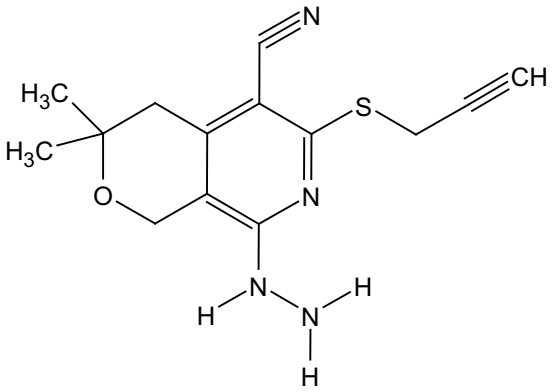
1.0
4.0
5.7
6.2
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

comp.4b


N
CH
S
H_3C
H_3C
O
N
N
H
H
N
H

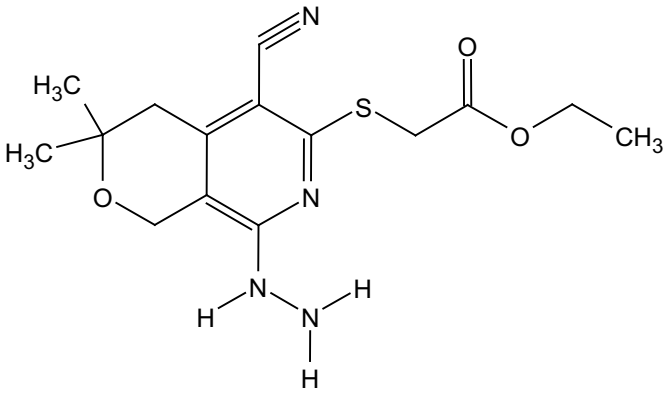
157.55
154.79
143.10
115.05
108.60
92.80
79.62
71.63
68.85
57.61
40.06
39.78
39.50
39.50
39.22
38.94
37.03
25.73
17.74
160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15
f1 (ppm)

comp.4b


N
CH
S
H_3C
H_3C
O
N
N
H
H
N
H

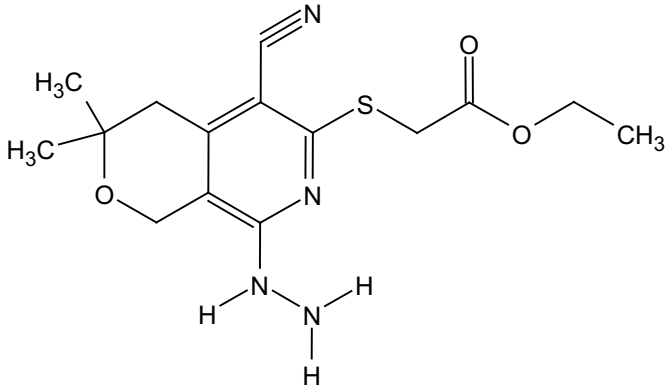
1.0
3.8
2.0
2.8
6.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

comp.4c


N
O
H3C
S
H3C
O
CH3
O
N
N
H
H
N
H

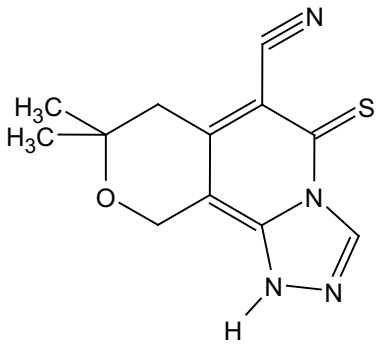
168.55
158.03
154.61
143.05
115.13
108.48
92.34
68.86
60.53
57.61
40.05
39.77
39.50
39.50
39.22
38.94
37.01
31.79
25.73
13.66
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

comp.4c


N
O
H3C
S
H3C
O
CH3
O
N
N
H
H
N
H

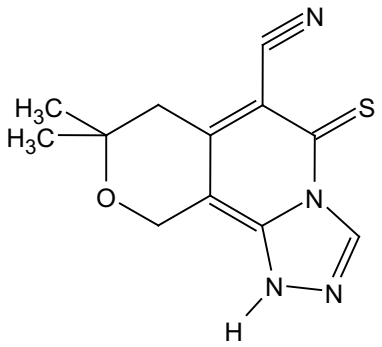
1.2
3.9
2.2
2.0
2.0
9.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

comp.5


N
H3C
H3C
S
O
N
N
N
H

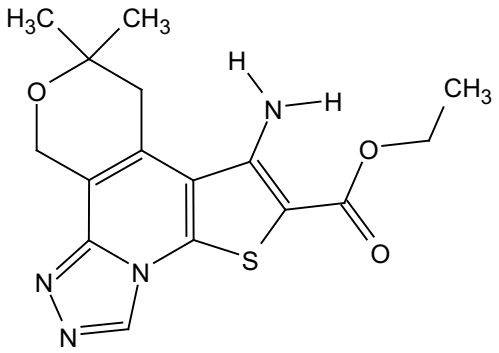
40.34
40.06
39.78
39.50
39.50
39.22
38.94
38.66
37.24
25.87
70.37
57.30
102.96
102.53
142.12
141.31
137.32
117.35
163.59
165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25
f1 (ppm)

comp.5


N
S
H_3C
H_3C
O
N
N
N
H

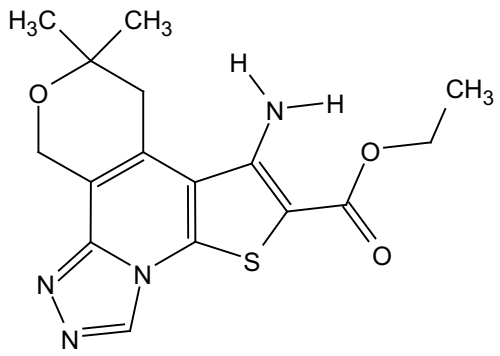
0.9
1.0
2.0
2.1
6.1
14.5
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

comp.6a


H3C
CH3
O
H
N
H
CH3
O
O
N
N
N
S

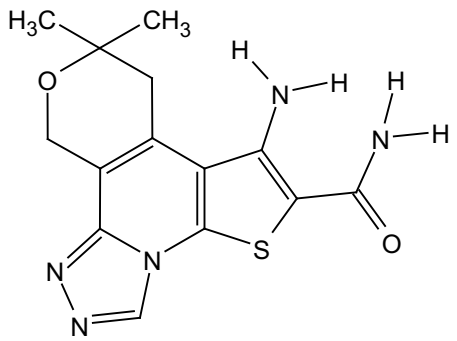
163.57
150.96
145.36
134.33
129.23
117.69
115.85
92.00
69.35
59.49
58.34
40.33
40.06
39.78
39.50
39.50
39.22
38.95
35.38
26.04
14.06
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

comp.6a


H3C
CH3
O
H
N
H
CH3
O
O
S
N
N
N

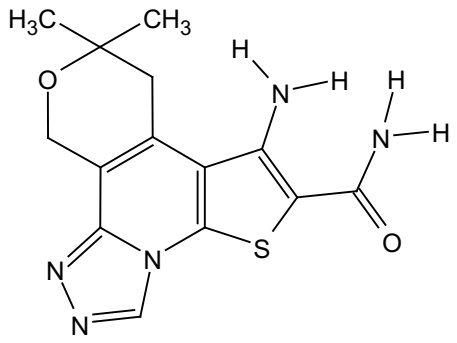
1.0
1.9
2.0
2.0
2.0
9.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

comp.6b


H3C
CH3
O
H
N
H
H
N
H
O
S
N
N
N

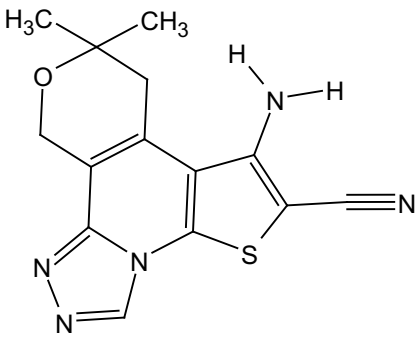
40.33
40.05
39.78
39.50
39.50
39.22
38.94
38.67
35.49
26.17
166.48
149.50
145.67
135.21
131.95
129.69
118.70
115.62
95.48
69.76
58.45
165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25
f1 (ppm)

comp.6b


H3C
CH3
O
H
N
H
H
N
H
O
N
N
N
S

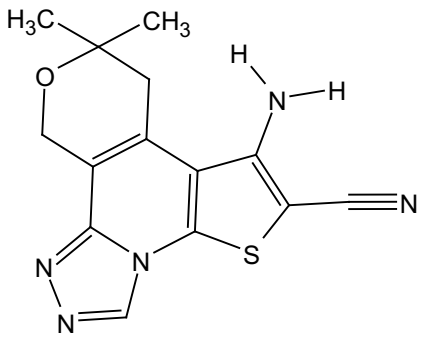
0.9
1.9
1.9
2.0
2.0
6.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

comp.6c


H3C
CH3
O
H
N
H
N
N
N
S
N

40.33
40.06
39.78
39.50
39.50
39.22
38.94
38.67
153.25
145.46
135.64
134.44
129.38
116.87
116.37
115.03
71.63
69.81
58.37
35.30
26.12
155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25
f1 (ppm)

comp.6c


H3C
CH3
O
H
N
H
N
N
N
S
N

1.0
2.0
2.1
2.1
6.1
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)