Journal of the Serbian Chemical Society
JSCS@tmf.bg.ac.rs • www.shd.org.rs/JSCS
J. Serb. Chem. Soc. 84 (1) S1–S11 (2019) *Supplementary material*

SUPPLEMENTARY MATERIAL TO

Synthesis and antimicrobial screening of novel 1,3-dioxolanes linked to N-5 of 5*H*-1,2,4-triazino[5,6-*b*]indole-3-thiol

EL SAYED RAMADAN*, HANAA A. RASHEED and EL SAYED H. EL ASHRY

Department of Chemistry, Faculty of Science, Alexandria University, Alexandria 21524, Egypt

J. Serb. Chem. Soc. 84 (1) (2019) 1–10

ANALYTICAL AND SPECTRAL DATA FOR THE SYNTHESIZED COMPOUNDS

*1-[(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl]-1*H*-indole-2,3-dione (**10**).* Yield: 69 %; red syrup; Anal. Calcd for $C_{14}H_{15}NO_4$ (*FW*: 262.27): C, 64.36; H, 5.79; N, 5.36 %. Found: C, 64.25; H, 5.59; N, 5.33 %; IR (KBr, cm^{-1}): 2996.67, 1760.87, 1710.99, 1614.64, 1467.38, 1446.22, 1384.49, 1270.17, 1208.96, 1052.74; ^{1}H-NMR (200 MHz, $CDCl_3$, δ / ppm): 1.26, 1.31 (6H, 2*s*, 2 × CH_3), 3.74–3.85 (3H, *m*, N–CH_2 & H-3′a), 4.04 (1H, *dd*, J_1 = 6.4 Hz, J_2 = 8.8 Hz, H-3′b), 4.36–4.42 (1H, *m*, H-2′), 7.03–7.10 (2H, *m*, Ar-H), 7.51–7.59 (2H, *m*, Ar-H).

*2-[1,2-Dihydro-{(2,2-dimethyl-1,3-dioxolan-4-yl)methyl}-2-oxo-3*H*-indol-3--ylidene]hydrazinecarbothioamide (**17**).* Yield: 84 %; orange crystals; m.p.: 168–170 °C; IR (KBr, cm^{-1}): 3359.77, 3245.97, 3151.47, 2968.24, 1691.46, 1610.45, 1473.51, 1361.65, 1228.57, 1066.56; ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 1.21 & 1.27 (6H, 2*s*, 2 × CH_3), 3.74 (1H, *dd*, J_1 = 5.6 Hz, J_2 = 8.5 Hz, H-3′a), 3.87 (2H, *d*, *J* = 5.5 Hz, N–CH_2), 4.04 (1H, *dd*, J_1 = 6.4 Hz, J_2 = 8.5 Hz, H-3′b), 4.33–4.39 (1H, *m*, H-2′), 7.14 (1H, *t*, *J* = 7.5 Hz, Ar-H), 7.24 (1H, *d*, *J* = 7.9 Hz, Ar-H), 7.41 (1H, *t*, *J* = 7.6 Hz, Ar-H), 7.70 (1H, *d*, *J* = 7.6 Hz, Ar-H), 8.73 (1H, *s*, D_2O-exchangeable, NH_c), 9.08 (1H, *s*, D_2O-exchangeable, NH_b), 12.35 (1H, *s*, D_2O-exchangeable, NH_a); ^{13}C-NMR (125 MHz, DMSO-d_6, δ / ppm): 25.21 (CH_3), 26.52 (CH_3), 42.31 (N–CH_2), 66.46 (CH_2–O), 72.93 (CH–O), 108.92, 110.76, 119.25, 120.60, 122.91, 130.89, 131.00, 143.18 (**C**Me_2 & Ar-C), 161.06 (C=O), 178.66 (C=S); MS (70 eV, *m/z* (%)): 334.1 (M^+, 16.83), 221.0 (37.84), 205.0 (53.62), 188.0 (42.23), 145.0 (15.67), 144.0 (22.40), 131.1 (28.37), 130.0 (28.33), 118.0 (16.80), 117.0 (46.27), 116.0 (26.50), 101.0 (42.68), 89.0 (24.34), 77.1 (21.28), 76.1 (21.04), 60.0 (100.00); FABMS (*m/z*): Calcd. for $[C_{15}H_{18}N_4O_3S]^+$: 334.1100. Found: 334.1041.

* Corresponding author. E-mail: elsayedramadan2008@yahoo.com

*5-[(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl]-5*H-*1,2,4-triazino[5,6-*b*]indole--3-thiol* (***19***). Yield: 75 % (method a), 82 % (method b); yellow needles; m.p.: 286–290 °C; IR (KBr, cm^{-1}): 3078.18, 2981.74, 2867.95, 1573.81, 1460.01, 1348.15, 1151.42, 1051.13; ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 1.19 & 1.26 (6H, 2*s*, 2 × CH_3), 3.84 (1H, *dd*, J_1 = 5.3 Hz, J_2 = 8.6 Hz, H-3′a), 4.07 (1H, *dd*, J_1 = 6.5 Hz, J_2 = 8.7 Hz, H-3′b), 4.32 (2H, *d*, *J* = 6.6 Hz, N–CH_2), 4.50–4.53 (1H, *m*, H-2′), 7.38 (1H, *t*, *J* = 7.1 Hz, Ar-H), 7.68–7.74 (2H, *m*, Ar-H), 8.03 (1H, *d*, *J* = 7.6 Hz, Ar-H), 14.62 (1H, *s*, D_2O-exchangeable, SH); ^{13}C-NMR (125 MHz, DMSO-d_6, δ / ppm): 25.09 (CH_3), 26.47 (CH_3), 44.00 (N–CH_2), 66.45 (CH_2–O), 73.03 (CH–O), 109.10, 112.53, 117.33, 121.59, 123.51, 131.61, 135.21, 143.98, 148.43, 179.08 (CMe_2 & Ar-C); MS (70 eV, *m/z* (%)): 316.1 (M^+, 46.59), 301.1 (14.17), 258.0 (17.87), 245.0 (16.38), 216.0 (73.44), 202.0 (100.00), 187.0 (20.34), 143.0 (35.08), 128.1 (27.19), 114.9 (20.11), 101.0 (49.02), 88.0 (12.11), 77.1 (14.72), 59.0 (43.14); FABMS (*m/z*): Calcd. for $[C_{15}H_{16}N_4O_2S]^+$: 316.0994. Found: 316.0996.

*3-(Allylthio)-5*H-*1,2,4-triazino[5,6-*b*]indole* (***23***). Yield: 80 %; yellow crystals; m.p.: 246–248 °C, Lit.[1] m.p.: 250 °C; IR (KBr, cm^{-1}): 3456.20, 3058.89, 2947.03, 2781.16, 2673.15, 1600.81, 1421.44, 1321.44, 1188.07; ^{1}H--NMR (300 MHz, DMSO-d_6, δ / ppm): 3.96 (2H, *d*, *J* = 6.8 Hz, S–CH_2), 5.16 (1H, *d*, J_{cis} = 10.0 Hz, =CH_2), 5.41 (1H, *d*, J_{trans} = 17.0 Hz, =CH_2), 5.96–6.10 (1H, *m*, =CH), 7.42 (1H, *t*, *J* = 7.6 Hz, Ar-H), 7.57 (1H, *d*, *J* = 8.1 Hz, Ar-H), 7.68 (1H, *t*, *J* = 7.6 Hz, Ar-H), 8.30 (1H, *d*, *J* = 7.7 Hz, Ar-H), 12.62 (1H, *bs*, D_2O-exchangeable, NH); ^{13}C-NMR (125 MHz, DMSO-d_6, δ / ppm): 32.68 (S–CH_2), 112.64, 117.60, 118.21, 121.44, 122.43, 130.82, 133.57, 140.24, 140.98, 146.59, 166.54 (Ar-C & CH=CH_2); MS (70 eV, *m/z* (%)): 242.0 (M^+, 13.40), 227.0 (59.01), 209.1 (20.72), 173.0 (43.99), 146.0 (100.00), 102.1 (30.45), 88.1 (15.50), 76.1 (10.32); FABMS (*m/z*): Calcd. for $[C_{12}H_{10}N_4S]^+$: 242.0626. Found: 242.0600.

*3-(Benzylthio)-5*H-*1,2,4-triazino[5,6-*b*]indole* (***24***). Yield: 85 %; yellow crystals; m.p.: 288–292 °C, Lit.[2] m.p.: 290–292 °C.

*3-(Allylthio)-5-[(2,2-dimethyl-1,3-dioxolan-4-yl)methyl]-5*H-*1,2,4-triazino--[5,6-*b*]indole* (***20***). Yield 81 % (method a), 72 % (method b); yellow needles; m.p.: 118–120 °C; IR (KBr, cm^{-1}): 2923.88, 1569.95, 1450.37, 1350.08, 1170.71, 1068.49; ^{1}H-NMR (200 MHz, $CDCl_3$, δ / ppm): 1.29 & 1.32 (6H, 2*s*, 2 × CH_3), 3.85 (1H, *dd*, J_1 = 5.6 Hz, J_2 = 8.6 Hz, H-3′a), 4.02 (2H, *d*, *J* = 6.8 Hz, S–CH_2), 4.10 (1H, *dd*, J_1 = 6.4 Hz, J_2 = 8.6 Hz, H-3′b), 4.42 (2H, *dd*, J_1 = 2.8 Hz, J_2 = 4.6 Hz, N–CH_2), 4.57–4.62 (1H, *m*, H-2′), 5.15 (1H, *dd*, J_{gem} = 1.4 Hz, J_{cis} = 10.1 Hz, =CH_2), 5.36 (1H, *dd*, J_{gem} = 1.4 Hz, J_{trans} = 15.6 Hz, =CH_2), 6.01–6.14 (1H, *m*, =CH), 7.38–7.46 (1H, *m*, Ar-H), 7.59–7.65 (2H, *m*, Ar-H), 8.38 (1H, *d*, *J* = 7.8 Hz, Ar-H).

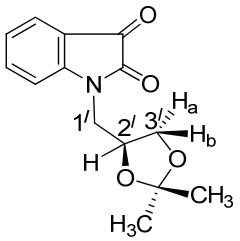
Compound **20** was isomerized to a mixture of (*E*/*Z*)-5-[(2,2-dimethyl-1,3--dioxolan-4-yl)methyl]-3-(prop-1-en-1-ylthio)-5*H*-1,2,4-triazino[5,6-*b*]indoles **25** and **26** on performing ^{1}H-NMR and ^{13}C-NMR measurements in deuterodimethyl sulfoxide. ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 1.16 & 1.22 (6H, 2*s*, 2×CH_3), 1.80 & 1.88 (3H, 2×*d*, J = 6.8 Hz & 6.7 Hz, CH_3), 3.85 (1H, *dd*, J_1 = 4.3 Hz, J_2 = 8.50 Hz, H-3′a), 4.07 (1H, *dd*, J_1 = 6.1 Hz, J_2 = 8.5 Hz, H-3′b), 4.47 (2H, *d*, J = 7.4 Hz, N–CH_2), 4.56–4.60 (1H, *m*, H-2′), 5.94–6.14 (1H, *m*, =CH), 6.84 (0.4H, *d*, J = 15.0 Hz, =CH, *E*-isomer), 7.08 (0.6H, *d*, J = 9.6 Hz, =CH, *Z*-isomer), 7.46 (1H, *t*, J = 7.5 Hz, Ar-H), 7.74 (1H, *t*, J = 7.4 Hz, Ar-H), 7.87 (1H, *d*, J = 8.3 Hz, Ar-H), 8.33 (1H, *dd*, J_1 = 3.2 Hz, J_2 = 7.8 Hz, Ar-H); ^{13}C-NMR (125 MHz, DMSO-d_6, δ / ppm): 15.09 (CH_3, *Z*-isomer), 18.59 (CH_3, *E*-isomer), 25.09 (CH_3), 25.16 (CH_3), 26.47 (CH_3), 26.49 (CH_3), 44.27 (N–CH_2), 44.31 (N–CH_2), 66.45 (CH_2–O), 73.14 (CH–O), 109.10, 112.03, 112.10, 117.32, 117.34, 117.83, 118.75, 121.41, 121.46, 123.00, 123.04, 126.72, 130.91, 130.95, 131.07, 141.07, 141.18, 141.25, 141.36, 146.38, 165.01, 166.19 (CMe_2, CH=CH & Ar-C); MS (70 eV, *m*/*z* (%)): 356.1 (M^+, 12.54), 342.1 (20.32), 341.1 (100.00), 227.0 (10.47), 101.1 (14.33), 83.1 (12.50), 71.1 (14.32), 59.1 (13.90), 57.1 (31.49), 55.1 (19.03); FABMS (*m*/*z*): Calcd. for $[C_{18}H_{20}N_4O_2S]^+$: 356.1307. Found: 356.1288.

*3-(Benzylthio)-5-[(2,2-dimethyl-1,3-dioxolan-4-yl)methyl]-5*H*-[1,2,4]triazino[5,6-*b*]indole (**21**).* Yield 86 % (method a), 74 % (method b); yellow needles; m.p.: 140–141 °C. IR (KBr, cm^{-1}): 3049.25, 2950.89, 1554.52, 1442.66, 1342.36, 1234.36, 1155.28, 1062.70. ^{1}H-NMR (300 MHz, DMSO-d_6, δ / ppm): 1.16, 1.21 (6H, 2*s*, 2×CH_3), 3.82 (1H, *dd*, J_1 = 4.9 Hz, J_2 = 8.7 Hz, H-3'a), 4.06 (1H, *dd*, J_1 = 6.2 Hz, J_2 = 8.6 Hz, H-3'b), 4.47–4.54 (3H, *m*, N–CH_2, H-2'), 4.57 (2H, *s*, S–CH_2), 7.22–7.34 (3H, *m*, Ar-H), 7.39–7.58 (3H, *m*, Ar-H), 7.74 (1H, *t*, J = 8.2 Hz, Ar-H), 7.86 (1H, *d*, J = 8.2 Hz, Ar-H), 8.33 (1H, *d*, J = 7.8 Hz, Ar-H); ^{13}C-NMR (125 MHz, DMSO-d_6, δ / ppm): 25.08 (CH_3), 26.45 (CH_3), 34.10 (S–CH_2), 44.16 (N–CH_2), 66.46 (CH_2–O), 73.25 (CH–O), 109.06, 112.10, 117.37, 117.83, 121.33, 122.95, 127.20, 128.45, 129.02, 130.79, 137.68, 140.83, 141.30, 146.33, 166.89 (CMe_2, Ar-C). MS (70 eV, *m*/*z* (%)): 406.0 (M^+, 15.03), 142.1 (11.85), 102.1 (10.94), 101.1 (24.54), 91.1 (100.00), 65.1 (21.13), 59.0 (19.07); FABMS (*m*/*z*). Calcd. $[C_{22}H_{22}N_4O_2S]^+$: 406.1463, found: 406.1384.

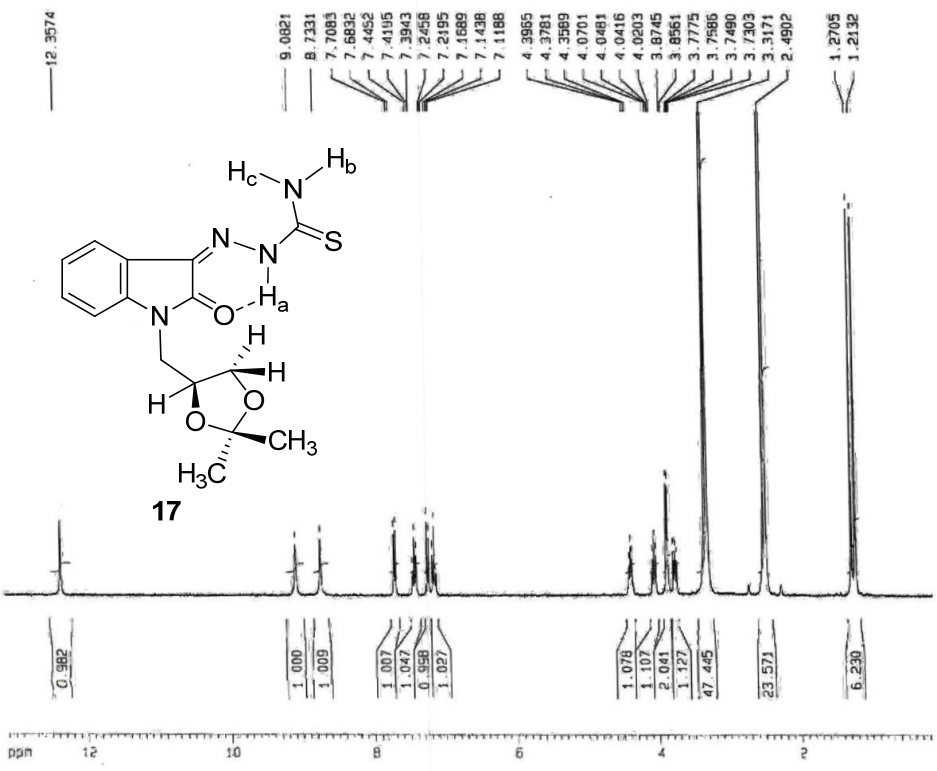
REFERENCES

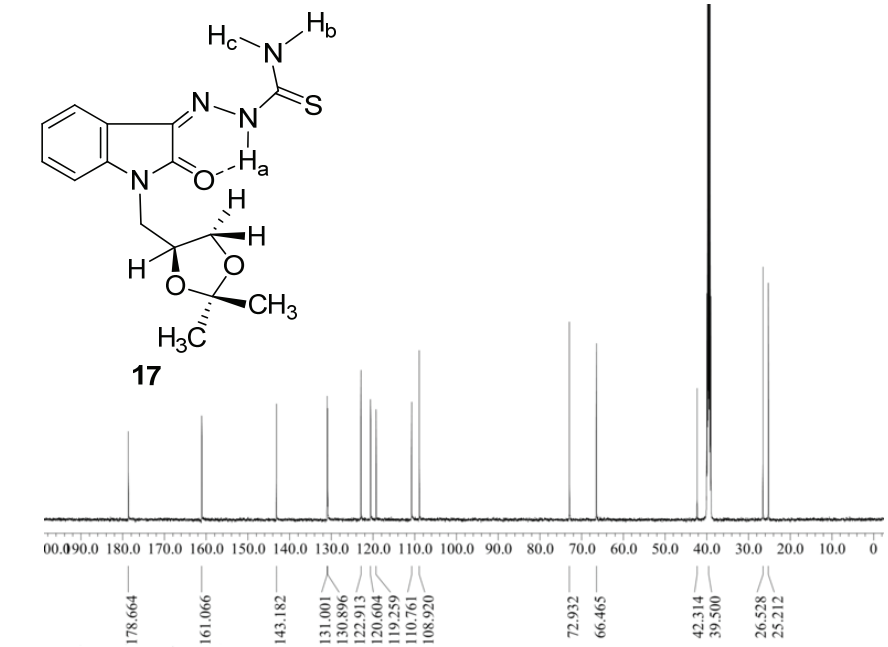
1. D. G. Kim, A. V. Zhuravlyova, *Chem. Heterocycl. Comp*. **46** (2010) 896
2. M. Gianella-Borradori, I. Christou, C. J. R. Bataille, R. L. Cross, G. M. Wynne, D. R. Greaves, A. J. Russell, *Bioorg. Med. Chem*. **23** (2015) 241.

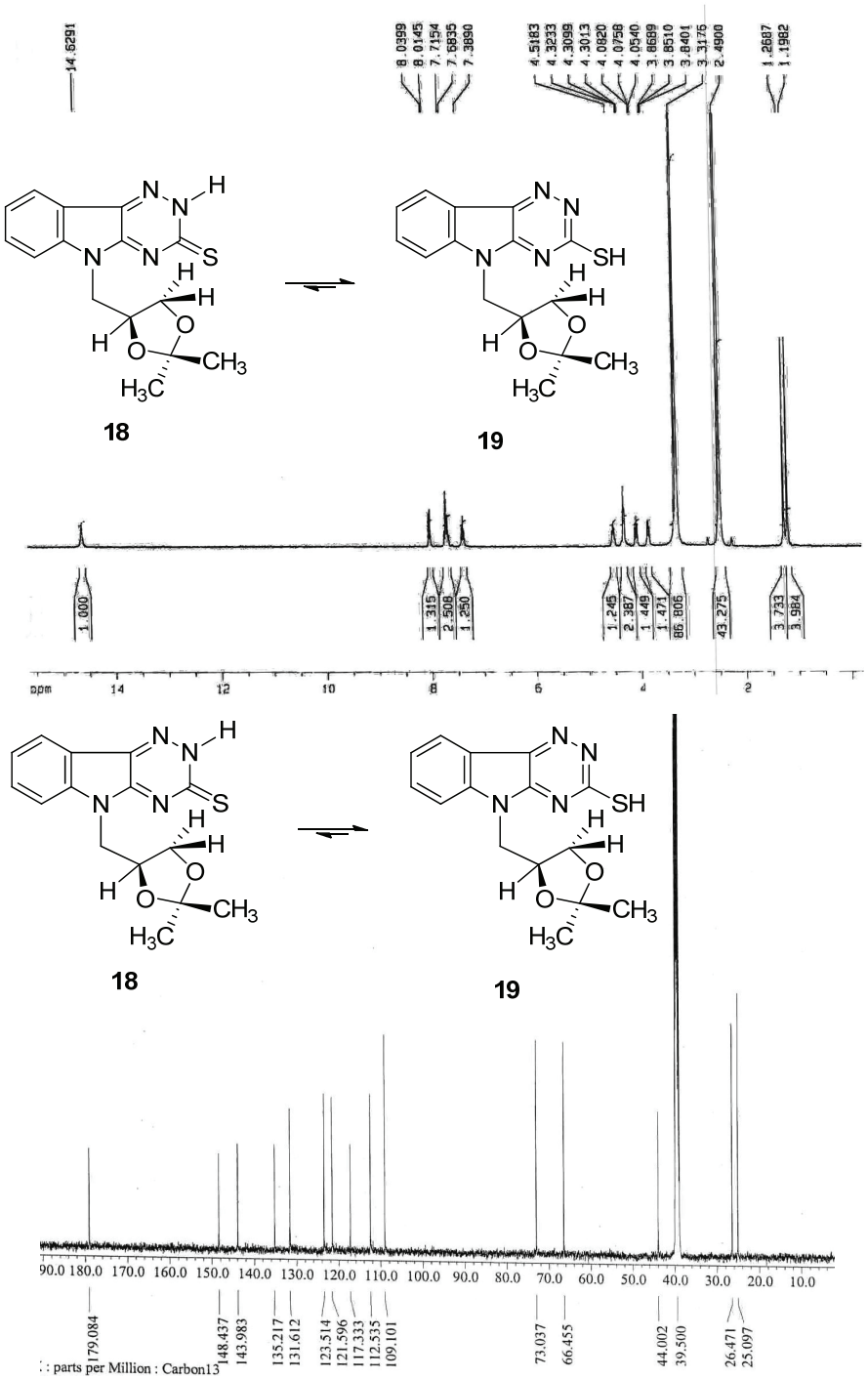
COPIES OF THE ^{1}H-NMR AND ^{13}C-NMR SPECTRA OF THE SYNTHESIZED COMPOUNDS

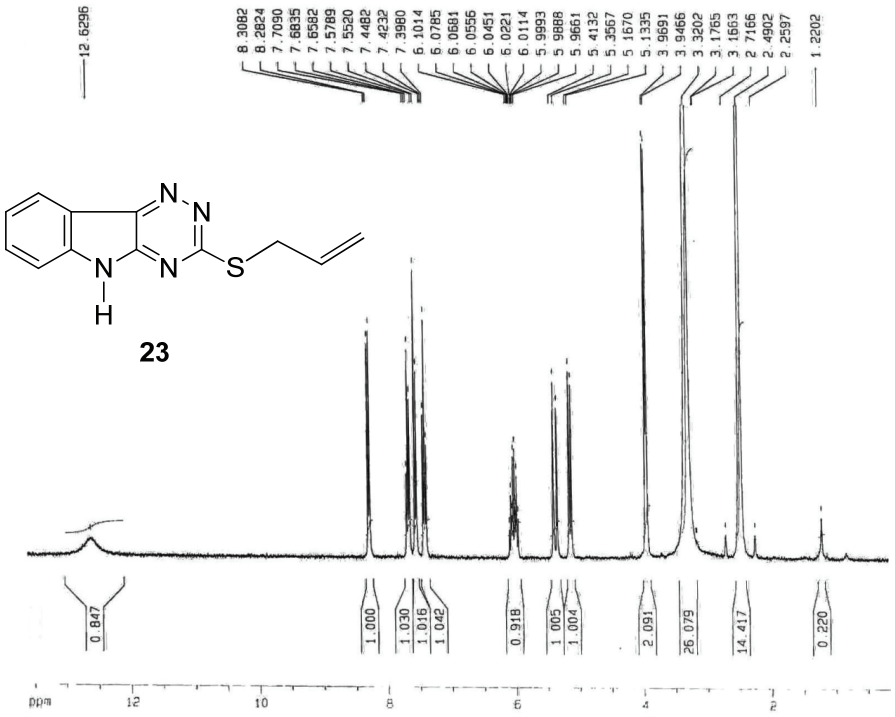


10

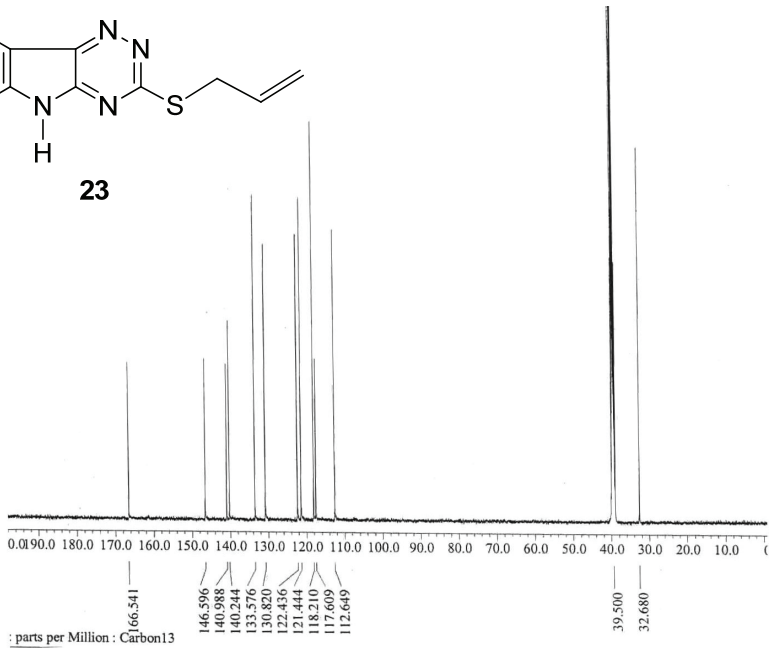

12.3574
9.0821
8.7331
7.7083
7.6832
7.4452
7.4195
7.3943
7.2456
7.2195
7.1689
7.1438
7.1188
4.3965
4.3781
4.3589
4.0701
4.0481
4.0416
4.0203
3.8745
3.8561
3.7775
3.7586
3.7490
3.7303
3.3171
2.4902
1.2705
1.2132
0.982
1.000
1.009
1.007
1.047
0.958
1.027
1.078
1.107
2.041
1.127
47.445
23.571
6.230
ppm
12
10
8
6
4
2
17


17
178.664
161.066
143.182
131.001
130.896
122.913
120.604
119.259
110.761
108.920
72.932
66.465
42.314
39.500
26.528
25.212

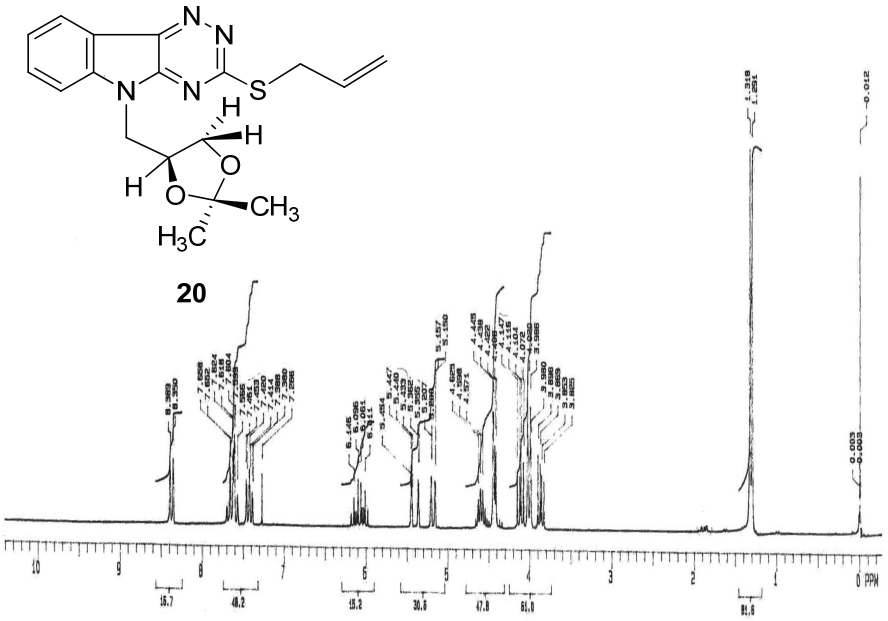

14.6291
8.0399
8.0145
7.7154
7.6835
7.3890
4.5183
4.3233
4.3099
4.3013
4.0820
4.0758
4.0540
3.8689
3.8510
3.8401
3.3176
2.4900
1.2687
1.1982
18
19
1.000
1.315
2.508
1.250
1.245
2.387
1.449
1.471
86.806
43.275
3.733
3.984
ppm
14
12
10
8
6
4
2
18
19
90.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0
179.084
148.437
143.983
135.217
131.612
123.514
121.596
117.333
112.535
109.101
73.037
66.455
44.002
39.500
26.471
25.097
: parts per Million : Carbon13



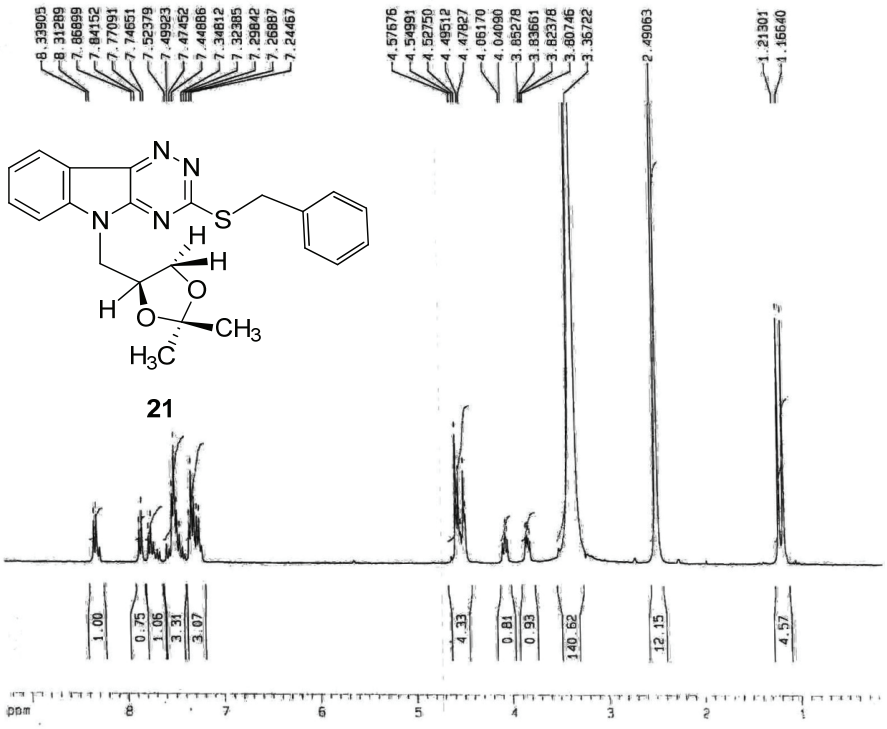
23



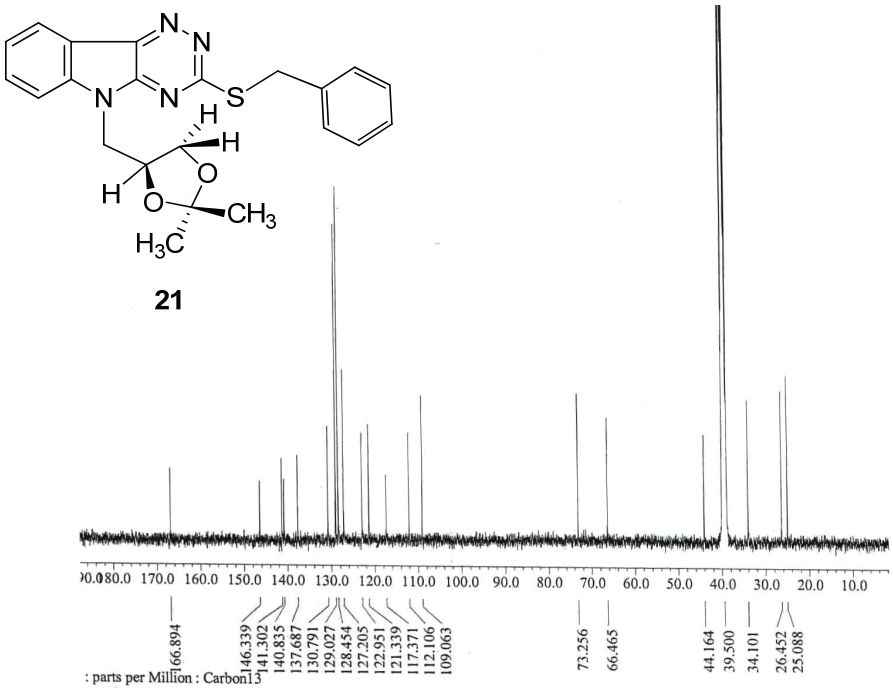
23



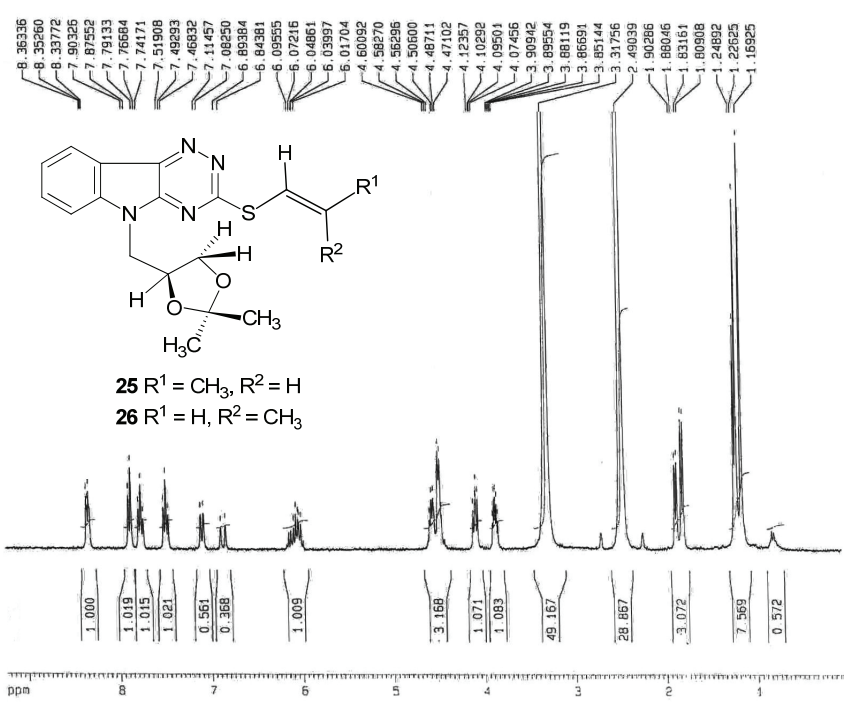
20



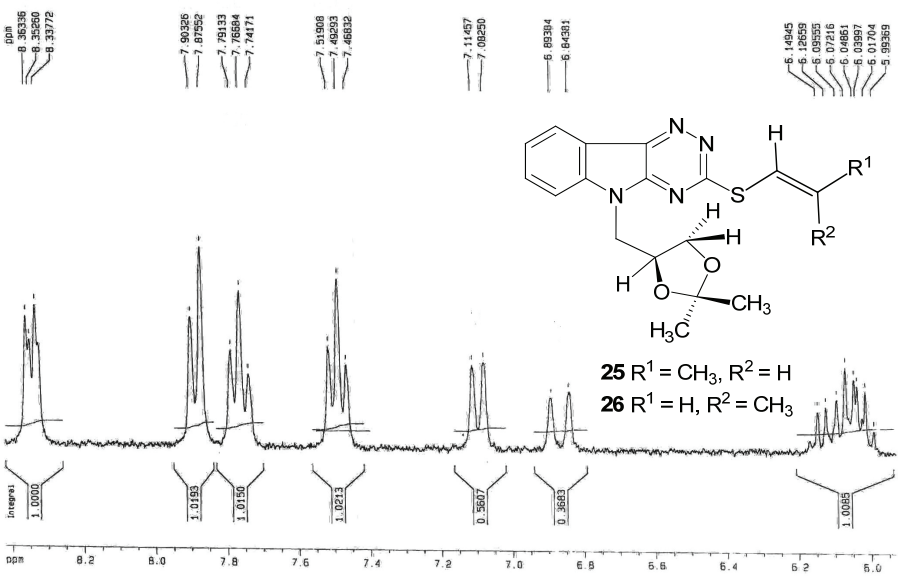
21

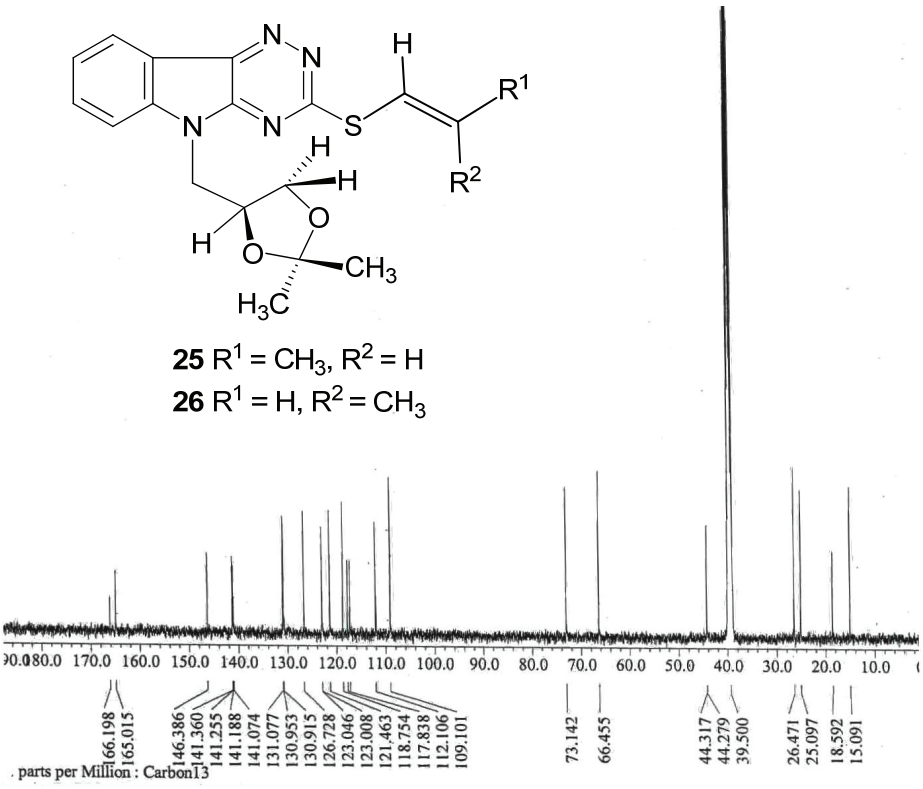


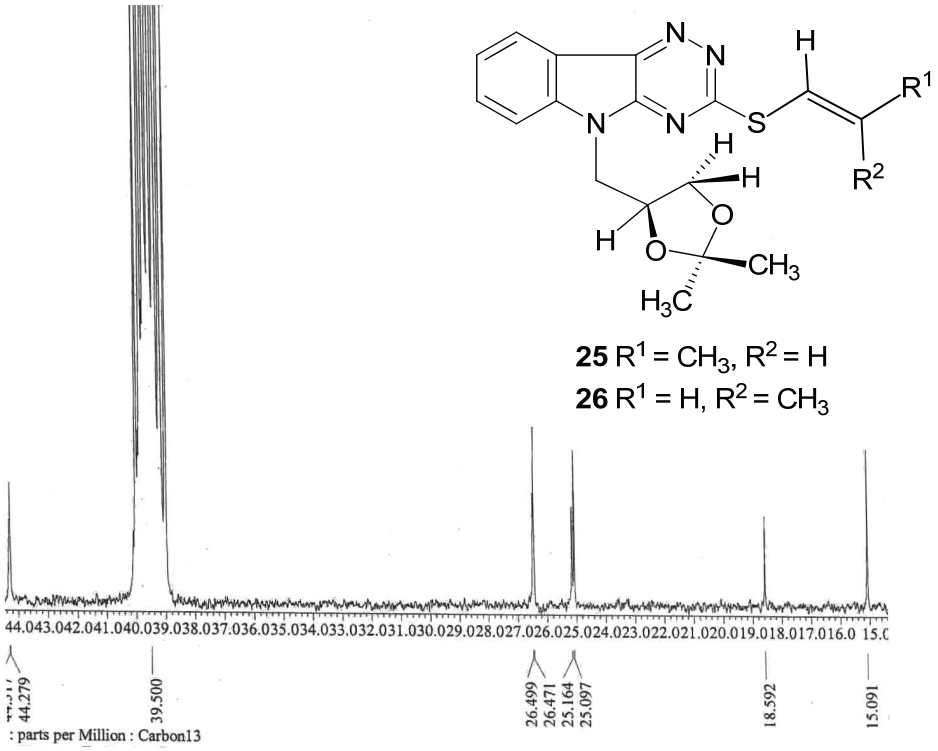
21

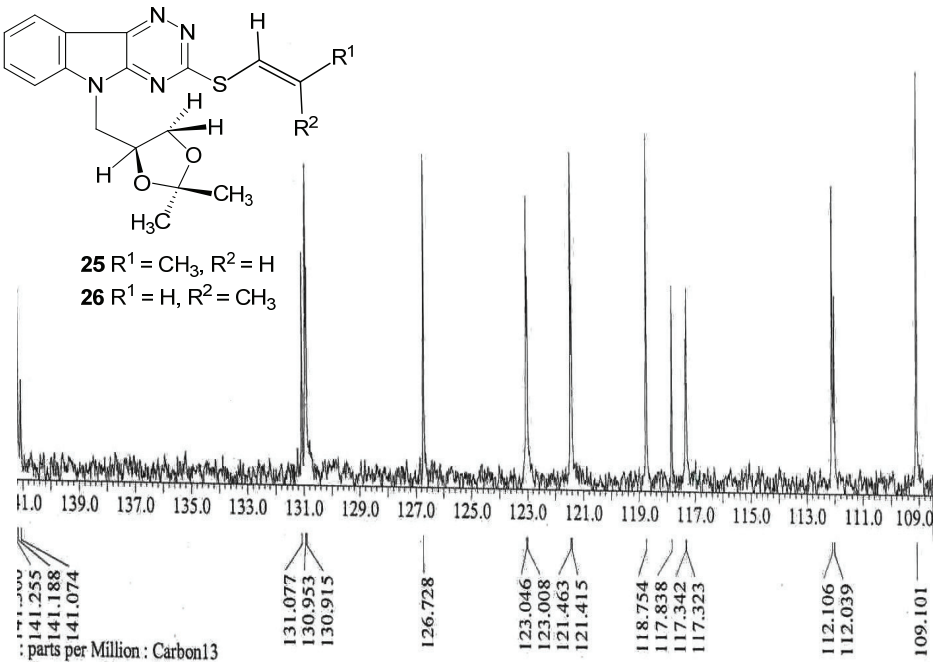


25 $R^1 = CH_3$, $R^2 = H$
26 $R^1 = H$, $R^2 = CH_3$


ppm
8.36336
8.35260
8.33772
7.90326
7.87552
7.79133
7.76684
7.74171
7.51908
7.49293
7.46832
7.11457
7.09250
6.89384
6.84381
6.14945
6.12659
6.09555
6.07216
6.04861
6.03997
6.01704
5.99369
integral
1.0000
1.0193
1.0150
1.0213
0.5607
0.3683
1.0085
ppm
8.2
8.0
7.8
7.6
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
25 R1 = CH3, R2 = H
26 R1 = H, R2 = CH3


25 R1 = CH3, R2 = H
26 R1 = H, R2 = CH3
90.0
80.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
166.198
165.015
146.386
141.360
141.255
141.188
141.074
131.077
130.953
130.915
126.728
123.046
123.008
121.463
118.754
117.838
112.106
109.101
73.142
66.455
44.317
44.279
39.500
26.471
25.097
18.592
15.091
. parts per Million : Carbon13


25 R1 = CH3, R2 = H
26 R1 = H, R2 = CH3
44.043.042.041.040.039.038.037.036.035.034.033.032.031.030.029.028.027.026.025.024.023.022.021.020.019.018.017.016.0 15.0
44.279
39.500
26.499
26.471
25.164
25.097
18.592
15.091
: parts per Million : Carbon13


25 R1 = CH3, R2 = H
26 R1 = H, R2 = CH3
141.255
141.188
141.074
131.077
130.953
130.915
126.728
123.046
123.008
121.463
121.415
118.754
117.838
117.342
117.323
112.106
112.039
109.101
: parts per Million : Carbon13