Electronic supplementary materials *Mendeleev Commun.*, 2018, **28**, 14–16

Synthesis and photophysical studies of novel 2-[5-(4-diethylaminophenyl)thiophen-2-yl]quinazoline derivatives

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General. Unless otherwise indicated, all common reagents and solvents were used from commercial suppliers without further purification. Melting points were measured on the instrument Boetius. ^{1}H and ^{13}C NMR spectra were acquired in DMSO-d_6 solutions on a Bruker Avance-400 spectrometer at 298 K, using TMS as internal reference. Mass spectra were recorded on the SHIMADZU GCMS-QP2010 Ultra instrument with electron ionization (EI) of the sample. Microanalyses (C, H, N) were performed using the Perkin–Elmer 2400 elemental analyzer. The absorption spectra were recorded in the interval 220–800 nm on a UV–2600 (Shimadzu, λ = 310 nm). The emission spectra were registered by means of a Varian Cary Eclipse fluorimeter (75 kW xenon lamp). The Raman spectra were obtained at room temperature on a module attachment RAMII compatible with an IR Fourier spectrometer Vertex 80 (λ = 1064 nm, Nd:YAG, P = 100 mW).

Starting 2-(thiophen-2-yl)-3*H*-quinazolin-4-one **2** was synthesized as described.[1]

4-Cyano-2-(thiophen-2-yl)quinazoline (3). Freshly prepared potassium cyanide (0.19 g, 2.9 mmol) and sodium *p*-toluenesulfonate (0.13 g, 0.7 mmol) were added to a solution of compound **2** (0.5 g, 2 mmol) in dry DMF (9.6 ml). The mixture was stirred at 95 ^{0}C for 3 h. After cooling the light-grey precipitate was filtered off, the filtrate was diluted with water (15 ml). The bright-yellow precipitate formed was filtered off, washed with diethyl ether (5 ml) and recrystallized from DMSO. Yield 0.28 g (66%), mp 179-181 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6): δ7.24 (m, 1H, H-4'), 7.73 (dd, 1H,H-5', J= 3.7, 1.5), 7.85 (m, 1H, arom.), 8.10-8.16 (m, 3H, arom.), 8.22 (d, 1H, H-8, J = 8.0 Hz).^{13}C NMR (100 MHz, DMSO-d_6): δ114.34, 122.28, 125.13, 128.27, 128.91, 129.77, 130.39, 132.22, 136.80, 141.45, 143.33, 150,85, 156.66.RS: 2240, 1613, 1563, 1538, 1486, 1424, 1393 cm^{-1}.MS(m/z, I_{rel} %): 237 $[M]^+$ (100), 211 (14), 141 (8), 140 (8), 118 (8), 109 (9), 102 (13), 76 (16), 75 (11), 50 (13), 45 (8), 39 (8).Calcd for $C_{13}H_7N_3S$: C 65.80; H 2.97; N 17.71. Found: C 68.78; H 2.85; N 17.79.

2-(5-Bromothiophen-2-yl)-4-cyanoquinazoline (4). A solution of *N*-bromosuccinimide (0.133 g, 0.7 mmol) in DMF (1.5 ml) was added portionwise to a solution of thienylquinazoline **3** (0.154 g, 0.5 mmol) in DMF (1.5 ml). The mixture was stirred at 80 ^{0}C for 6 h and then cooled. The light-yellow precipitate formed was filtered off and recrystallized from DMSO. Yield 0.158 g (63%), mp 162-164 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.30 (d, 1H, H-4', J = 3.9 Hz), 7.9 (m, 2H, arom.), 8.08 (m, 1H, arom.) 8.16 (m, 1H, arom.), 8.22 (dd, 1H, H-8, J = 7.9, 1.0).^{13}C NMR (100 MHz, DMSO-d_6): δ 114.24, 117.90,122.40, 125.26, 128.22, 130.08, 130.79, 132.44, 137.03, 142.75, 143,43, 150.67, 155.42.MS(m/z, I_{rel} %): 317 $[M+2]^+$ (76), 316 (12), 315 $[M]^+$ (71), 237 (18), 236 $[M-Br]^+$ (100), 184 (13), 140 (18), 118 (14), 102 (19), 76 (18), 75 (10), 50 (11).Calcd for $C_{13}H_6BrN_3S$ (315.18): C 49.38; H 1.91; N 13.29. Found: C 49.33; H 1.95; N 13.31.

4-Cyano-2-[5-(4-diethylaminophenyl)thiophen-2-yl]quinazoline (5). A suspension of quinazoline **4** (0.087 g, 0.28 mmol) in toluene (6.4 ml) was stirred at room temperature for 5 min, then 4-diethylaminophenylboronic acid (0.054 g, 0.28 mmol), $PdCl_2(PPh_3)_2$ (6.35 mg), PPh_3 (3.3 mg), solution of K_2CO_3 (0.287 g, 2.1 mmol) in water (2.4 ml) and ethanol (2.5 ml) were added. The mixture was stirred at 85 ^{0}C for 7 h in argon atmosphere. After cooling the organic layer was separated, washed with saturated K_2CO_3 solution (15 ml), then with saturated NH_4Cl solution (15 ml) and dried over Na_2SO_4. The solvent was removed under reduced pressure, and residue was washed with hexane (10 ml). The product was isolated by column chromatography on silica with chloroform as eluent to give red crystals of **5**. Yield 0.06 g (56%), mp 219-221 ^{0}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ1.23 (t, 6H, 2 CH_3, J = 6.8 Hz), 3.44 (q, 4H, 2 CH_2, J = 6.8 Hz), 6.72 (m, 2H, H-5'', H-3''), 7.25 (d, 1H, H-4', J 3.9), 7.61 (m, 2H, H-2'', H-6''), 7.69 (m, 1H, H-6), 7.98 (m, 1H, H-7), 8.07 (d, 1H, H-5, J = 7.8), 8.12 (d, 1H, H-3', J = 3.9), 8.19 (d, 1H, H-8, J = 8.0). ^{13}C NMR (100 MHz, DMSO-d_6): δ 12.43, 43.70, 111.70, 118.96, 121.79, 123.40, 126.26, 126.71, 129.22, 131.03, 131.90, 133.49, 137.66, 138.08, 143.44, 144.49, 149.75, 151.67, 156.42.RS: 2240, 1607, 1540, 1521, 1460, 1441, 1396, 1354, 1302, 1264, 1214, 1198, 1158 1080, 1040, 855, 737 cm^{-1}.MS (m/z, I_{rel} %): 384 $[M]^+$ (71), 371 (8), 370 (27), 369 $[M-CH_3]^+$ (100), 341 (18), 340 (41), 313 (8), 312 (13), 184 (8). Calcd for$C_{23}H_{20}N_4S$ (384.51): C 71.85; H 5.24; N 14.57. Found: C 71.72; H 5.20; N 14.59.

2-[(5-Bromothiophen-2-yl)methylideneamino]benzamide (8). 5-Bromothiophene-2-carboxaldehyde **7** (0.89 ml, 7.3 mmol) was added to a solution of 2-aminobenzamide **6** (1 g, 7.3 mmol) in ethanol (13 ml), and the mixture was refluxed for 3 h. After cooling the light-brown precipitate was filtered off and washed with hexane. Yield 1.65 g (77%), mp 175-178 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.91 (m, 1H, NH_2), 6.70 (m, 1H, Ar), 6.74 (d, 1H, Ar, J = 8.0), 6.92 (d, 1H, H-3', J =3.8), 6.96 (d, 1H, H-4', J = 3.8), 7.16 (s, 1H, NH_2), 7.23 (m, 1H, Ar), 7.62

(m, 1H, Ar), 8.36 (s, 1H, CH). Calcd for $C_{12}H_9BrN_2OS$ (309.19): C 46.62; H 2.93; N 9.06. Found: C 46.58; H 3.01; N 9.13.

2-(5-Bromothiophen-2-yl)quinazolin-4(3*H*)-one (9). Copper(II) chloride (1.24 g, 9.2 mmol) was added to a suspension of azomethine **8** (1.63 g, 5.56 mmol) in ethanol (28 ml), the mixture was refluxed for 5 h. After cooling, the colourless precipitate was filtered off and recrystallized from DMSO. Yield 0.8 g (52%), mp. 310-312 ^{0}C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.21 (d, 1H, H-4', J= 4.1), 7.45 (m, 1H, arom.), 7.60 (d, 1H, H-5, J 7.9), 7.75 (m, 1H, arom.), 8.01 (d, 1H, H-3', J 4.1), 8.11 (d, 1H, H-8, J = 7.5), 12.61 (s, 1H, NH).^{13}C NMR (100 MHz, DMSO-d_6): δ =117.92, 121.03, 125.97, 126.90, 129.96, 129.99, 131.74, 131.94, 139.07, 146.93, 148.32, 161.56. MS (m/z, I_{rel} %): 308 $[M]^+$ (60), 306 (60), 228 (16), 227 $[M-Br]^+$ (100), 109 (12), 92 (14), 90 (27), 82 (15), 76 (11), 64 (21), 63 (18), 50 (12), 39 (13). Calcd for$C_{12}H_7BrN_2OS$ (307.17): C 46.92; H 2.30; N 9.12. Found: C 46.70; H 2.35; N 9.19.

2-[5-(4-Diethylaminophenyl)thiophen-2-yl]quinazolin-4(3*H*)-one (10). 4-Diethyl-aminophenylboronic acid (0.21 g, 1.1 mmol), $Pd(PPh_3)_4$ (0.128 g) and solution of K_2CO_3 (0.46 g, 3.3 mmol) in water (8.9 ml) were added to a suspension of quinazolin-4(3*H*)-one **9** (0.3 g, 1.1 mmol) in THF (6.6 ml). The mixture was stirred at 85 ^{0}C for 12 h in argon atmosphere, then cooled and concentrated in vacuum. The residue was washed with hexane and purified by flash chromatography (ethyl acetate as eluent). Yield 0.21 g (50%), mp>300 ^{0}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ1.23 (t, 6H, 2 CH_3, J 7.1), 3.44 (q, 4H, 2 CH_2, J = 7.1), 6.72 (m, 2H, H-5'', H-3''), 7.25 (d, 1H, H-4', J = 3.9), 7.48 (m, 1H, arom), 7.58 (m, 2H, H-2'', H-6''), 7.78 (m, 2H, arom), 7.87 (d, 1H, H-3', J 3.9), 8.33 (d, 1H, H-8, J = 8.0), 10.64 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 12.43, 43.69, 111.61, 119.75, 120.69, 125.95, 126.66, 127.03, 128.63, 128.75, 131.40, 131.49, 132.83, 134.57, 147.84, 148.97, 150.48, 161.69. MS (m/z, I_{rel} %): 375 $[M]^+$ (81), 361 (26), 360 $[M-CH_3]^+$ (100), 332 (14), 331 $[M-C_3H_8]^+$ (33), 180 (14), 119 (17). Calcd for$C_{22}H_{21}N_3OS$ (375.50): C 70.37; H 5.64; N 11.19. Found: C 70.29; H 6.70; N 11.13.

References

1. R.J. Abdel-Jalil, W. Voelter and M. Saeed, *Tetrahedron Lett.*, 2004, **45**, 3475.

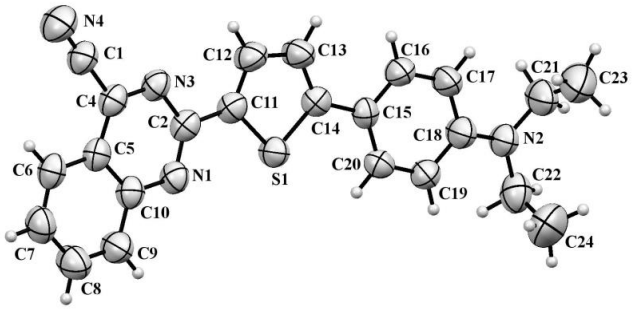


Figure S1 Molecular structure of quinazoline **5** in the thermal ellipsoids of 50 % probability. The disordered components are omitted for clarity.

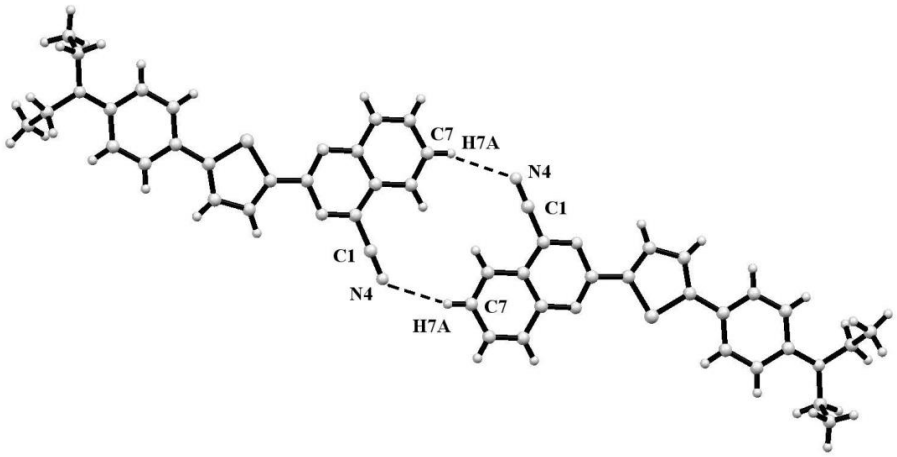
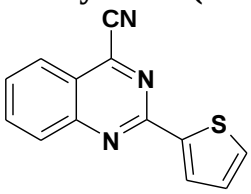


Figure S2 Dimers of the molecules **5**.

NMR and mass spectra of 4-cyano-2-(thiophen-2-yl)quinazoline 3



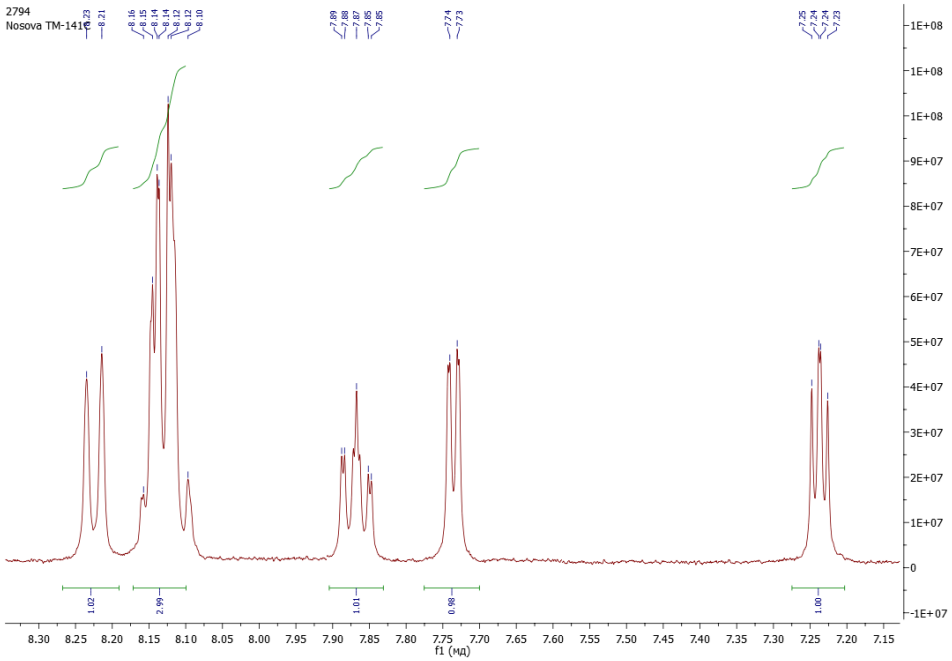


Figure S3 NMR ^{1}H spectrum of quinazoline **3** in DMSO-d$_6$.

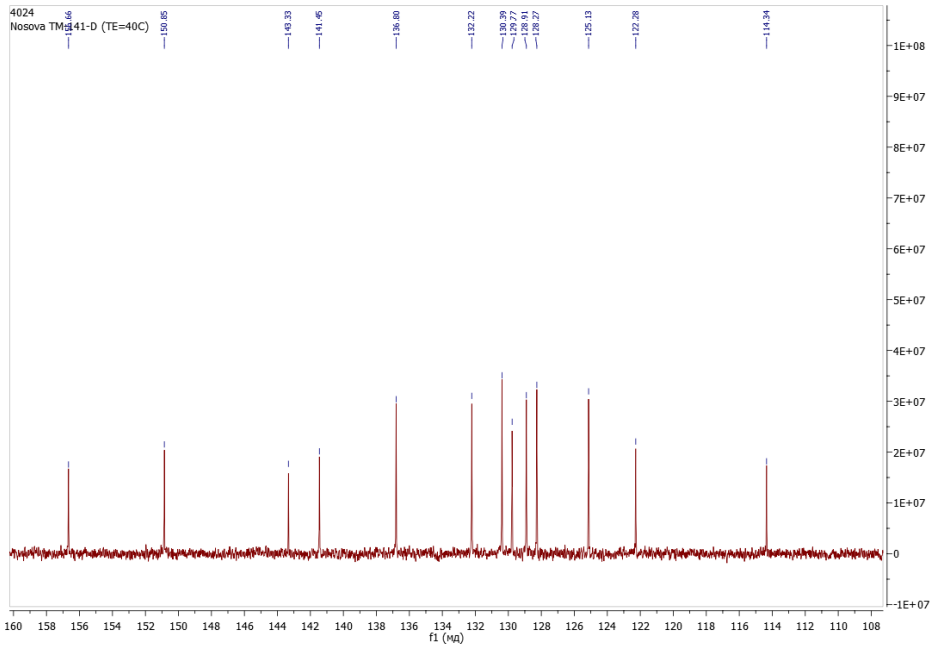


Figure S4 NMR ^{13}C spectrum of quinazoline **3** in DMSO-d$_6$.

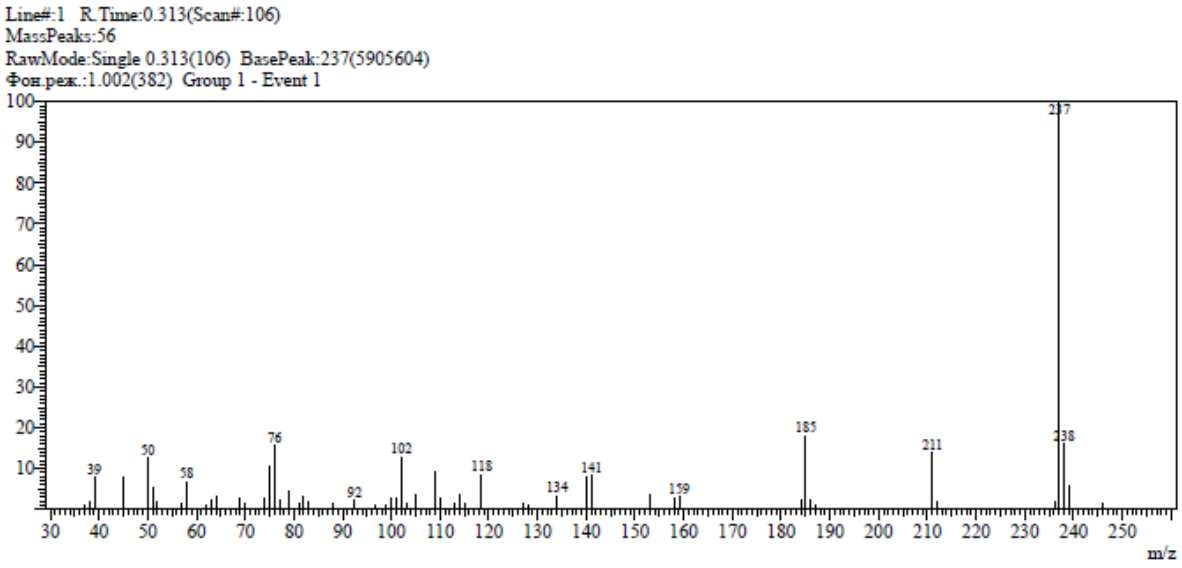
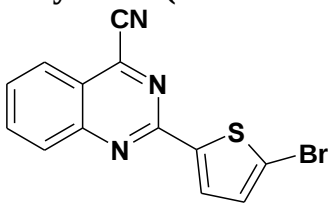


Figure S5 Mass spectrum (EI) of quinazoline **3.**

NMR and mass spectra of 4-cyano-2-(5-bromothiophen-2-yl)quinazoline 4



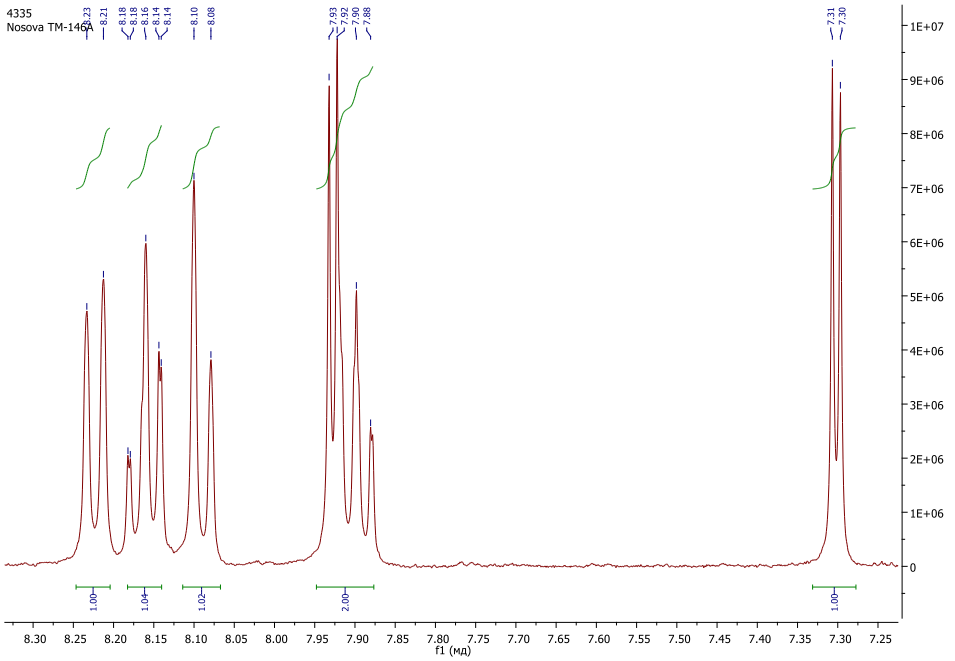


Figure S6 NMR ^{1}H spectrum of quinazoline**4** in DMSO-d$_6$.

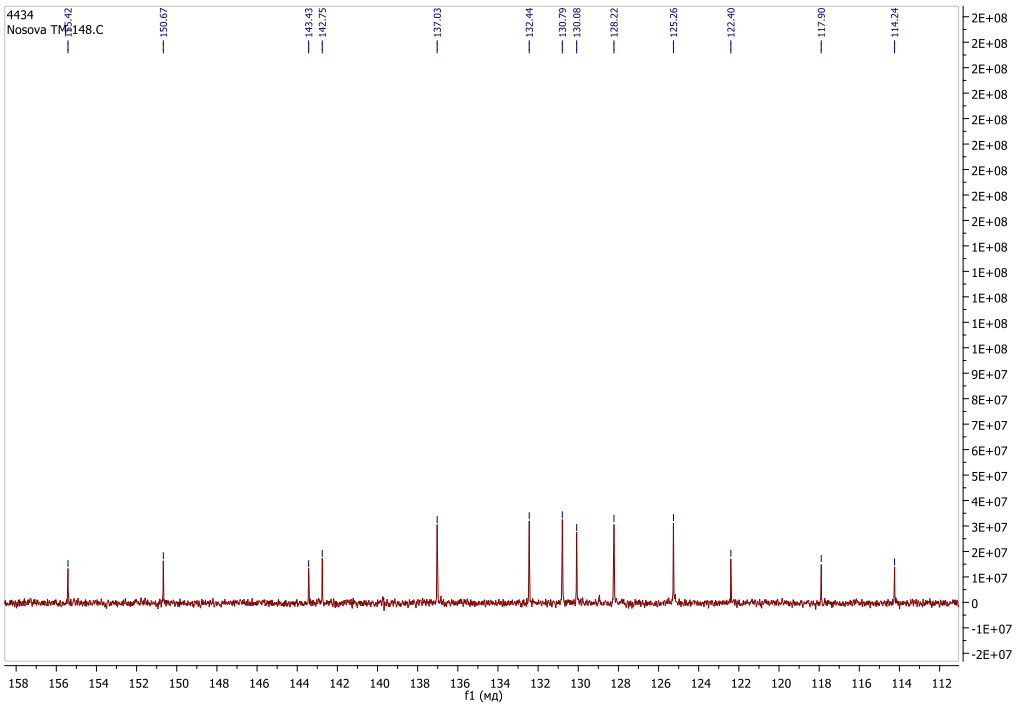


Figure S7 NMR ^{13}C spectrum of quinazoline **4** in DMSO-d_6.

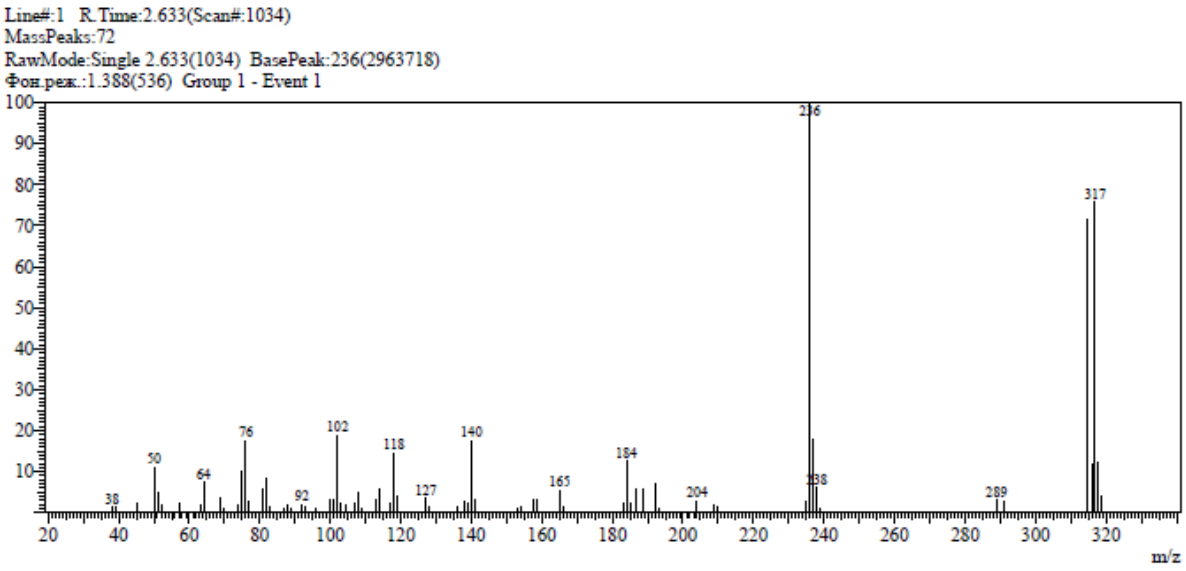


Figure S8 Mass spectrum (EI) of quinazoline **4.**

NMR, RS and mass spectra of 4-cyano-2-[5-(4-diethylaminophenyl)-thiophen-2-yl]quinazoline 5

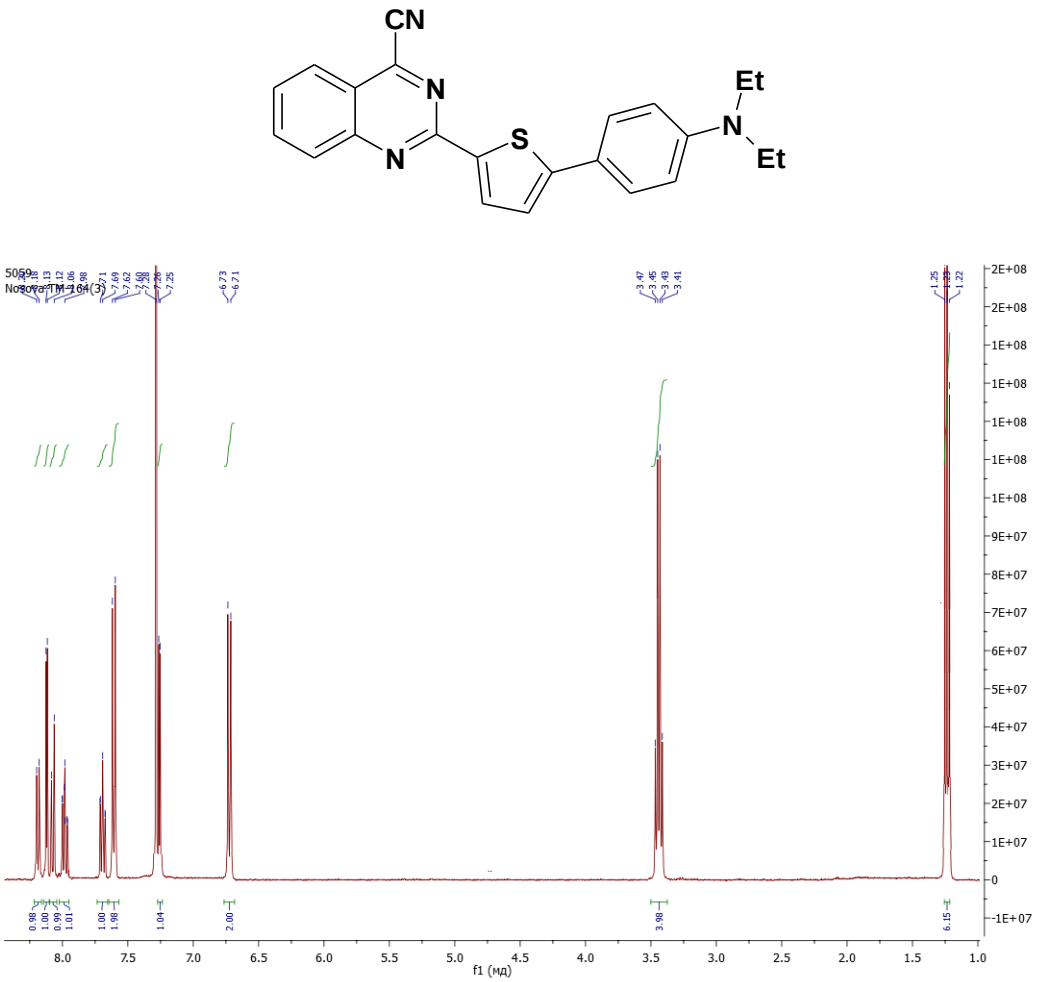


Figure S9 NMR ^{1}H spectrum of quinazoline **5** in $CDCl_3$.

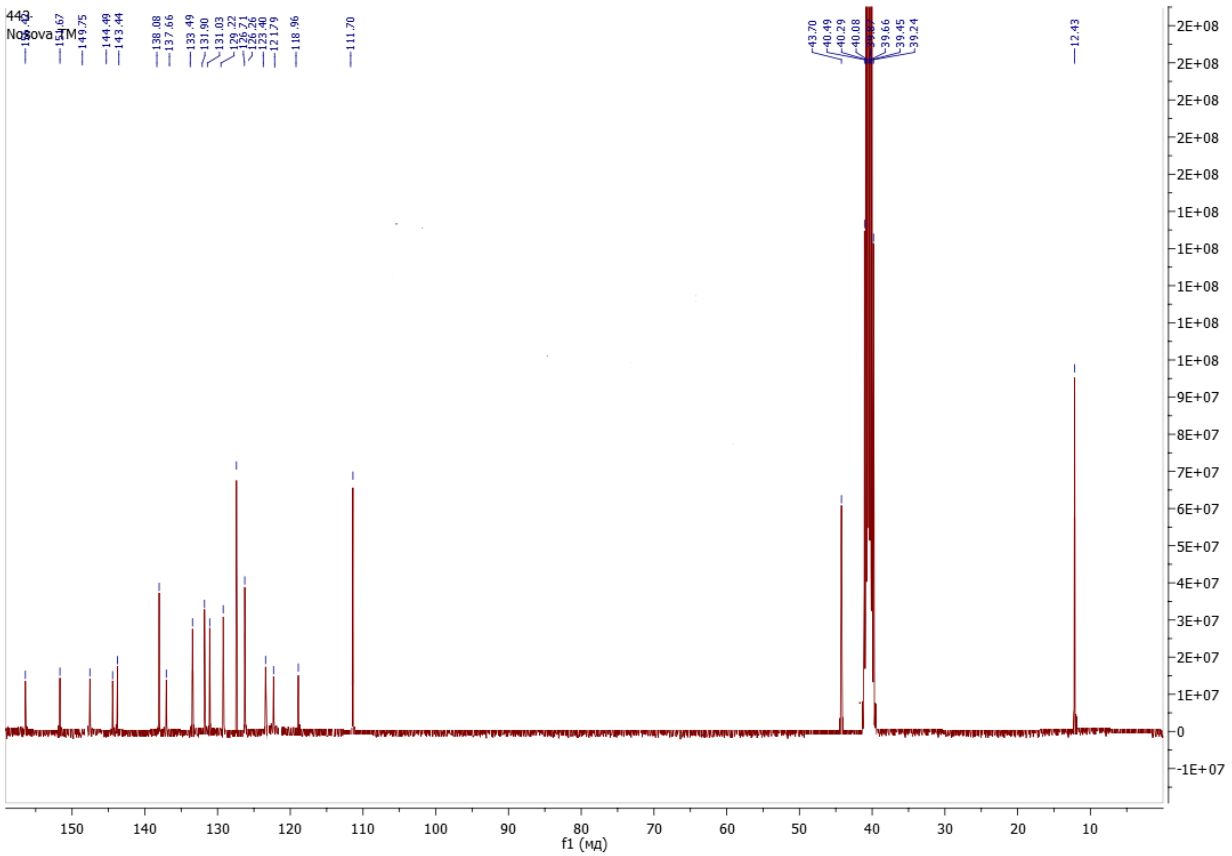


Figure S10 NMR ^{13}C spectrum of quinazoline **5** in DMSO-d_6.

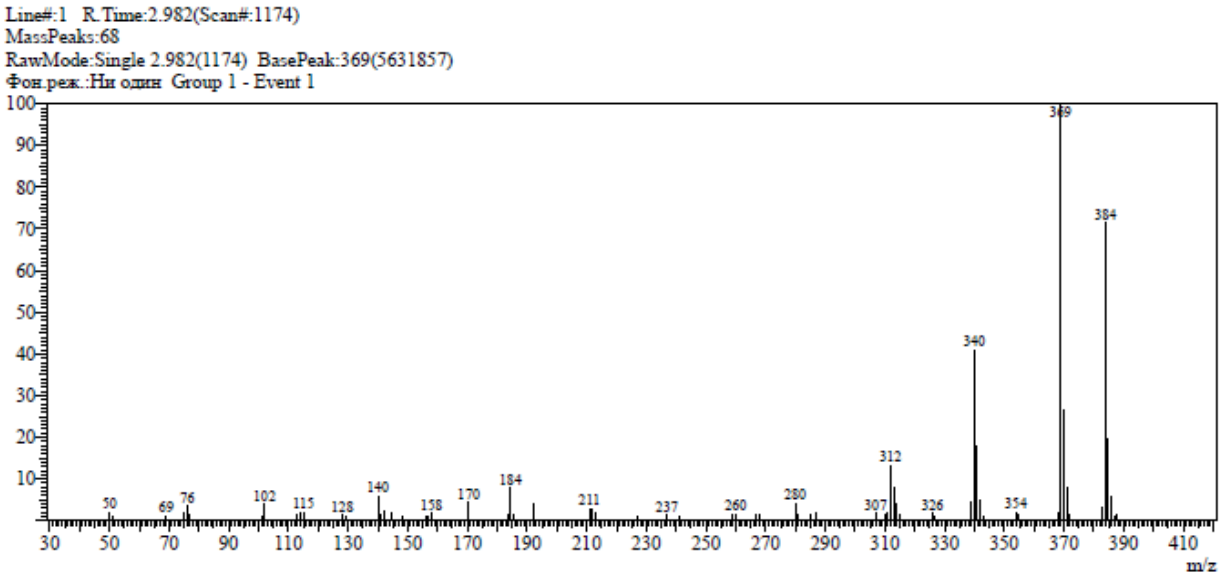


Figure S11 Mass spectrum (EI) of quinazoline **5.**

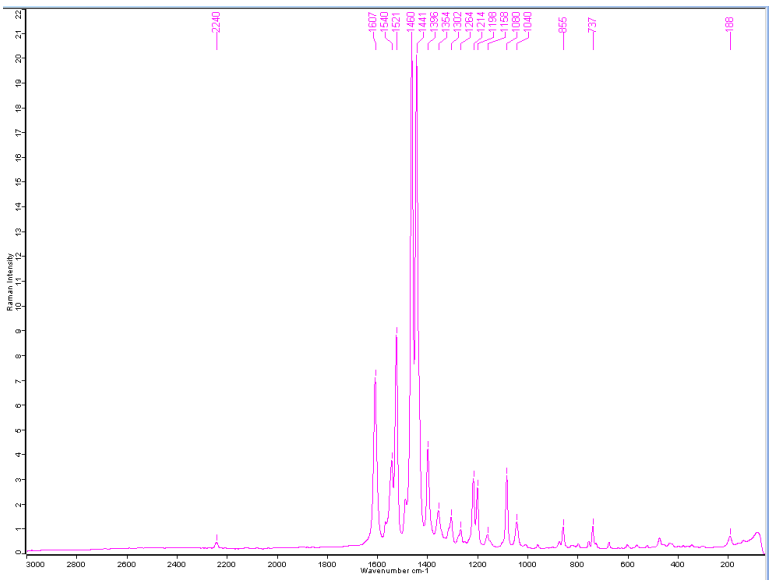
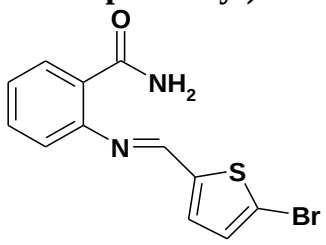


Figure S12 Raman spectrum of quinazoline **5.**

NMR spectrum of 2-[(5-bromothiophen-2-yl)methylideneamino]benzamide 8



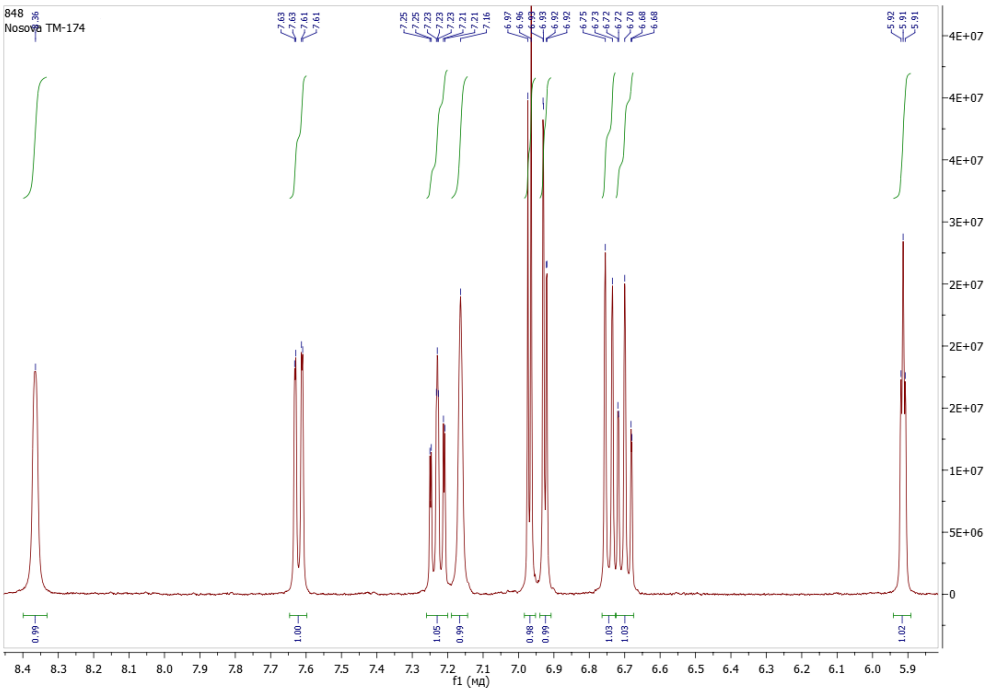
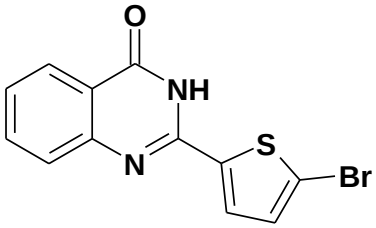


Figure S13 NMR ^{1}H spectrum of benzamide **8** in DMSO-d$_6$.

NMR and mass spectra of 2-(5-bromothiophen-2-yl)quinazolin-4(3*H*)-one 9



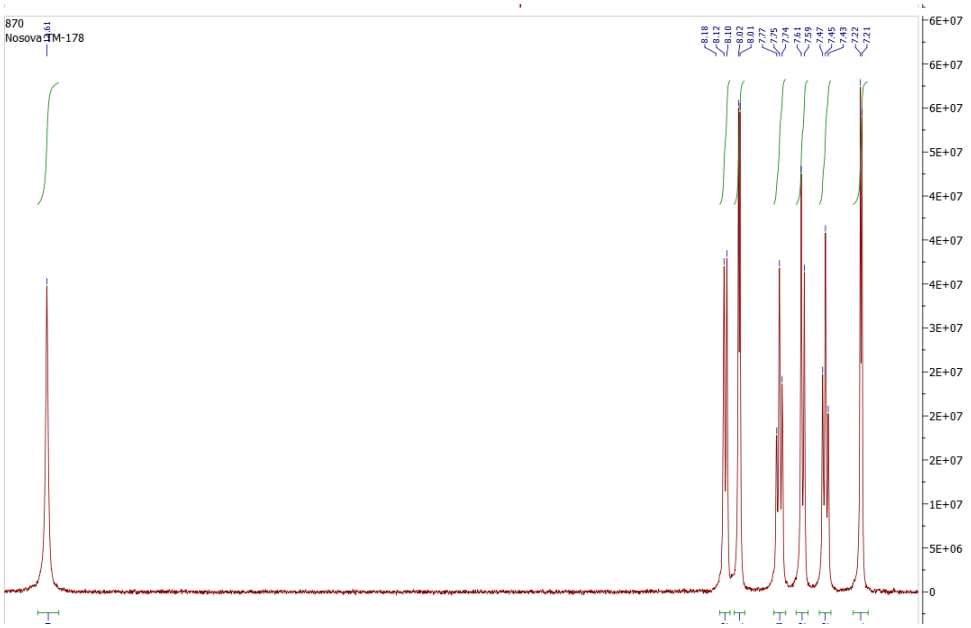


Figure S14 NMR ^{1}H spectrum of quinazolinone **9** in DMSO-d$_6$.

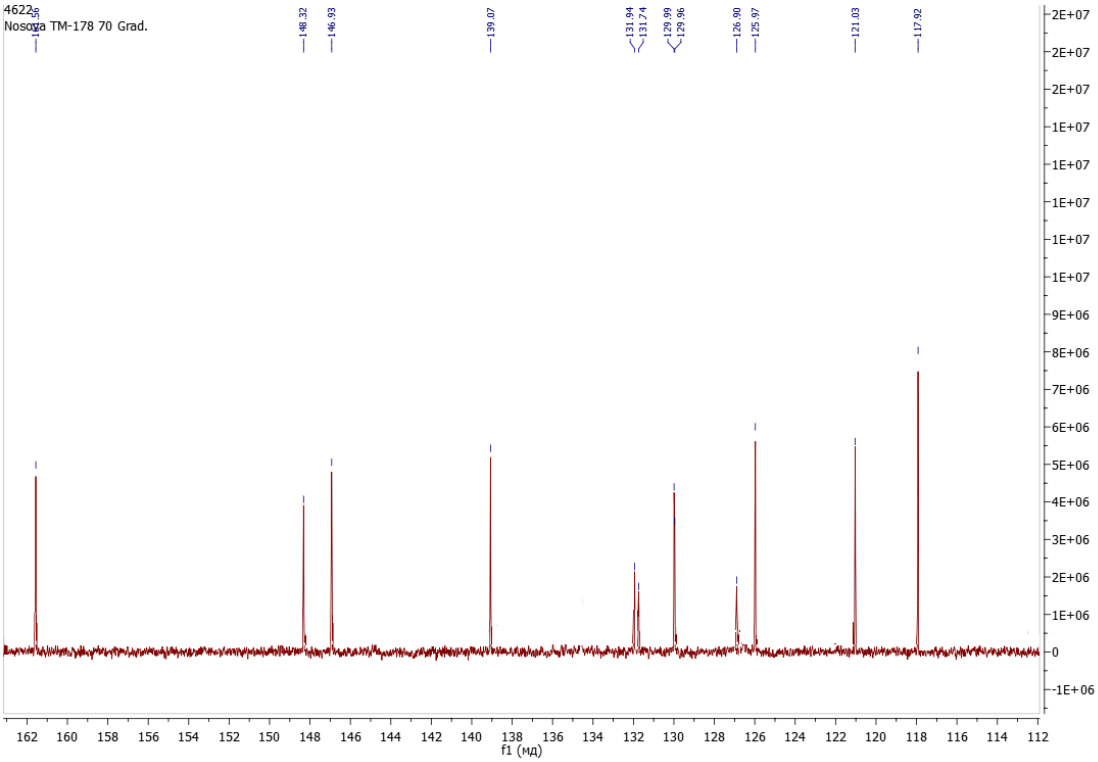


Figure S15 NMR ^{13}C spectrum of quinazolinone **9** in DMSO-d$_6$.

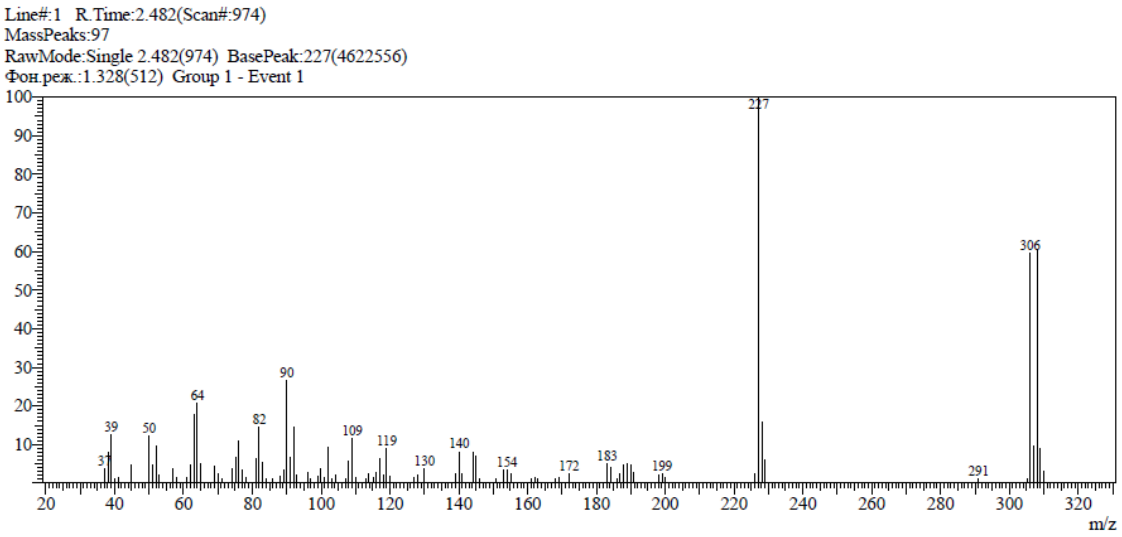
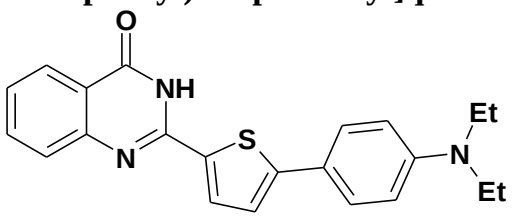


Figure S16 Mass spectrum (EI) of quinazolinone **9.**

NMR and mass spectra of 2-[5-(4-diethylaminophenyl)thiophen-2-yl]quinazolin-4(3*H*)-one 10



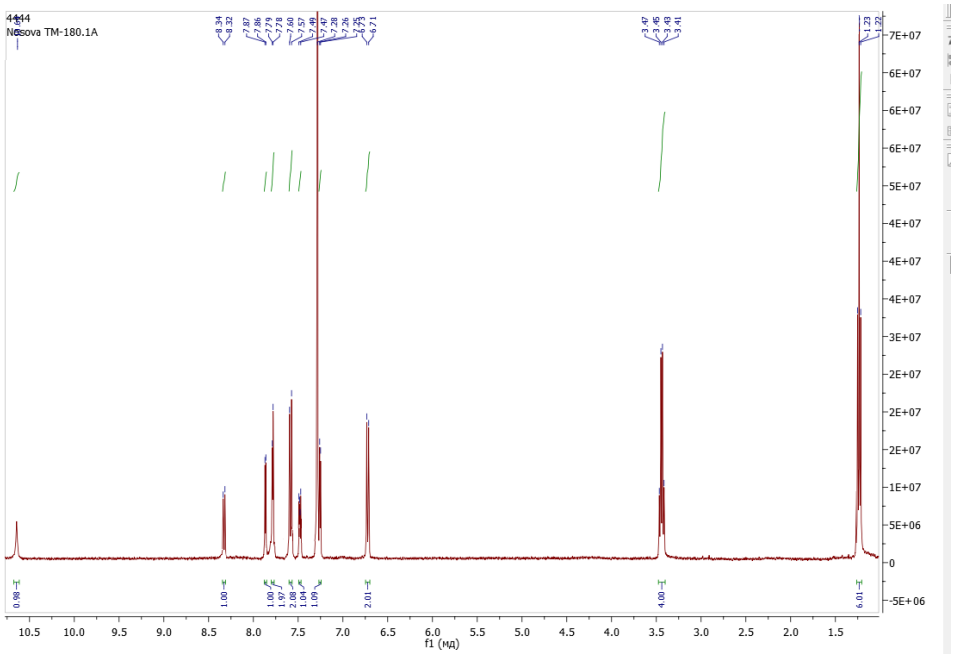


Figure S17 NMR ^{1}H spectrum of quinazolinone **10** in $CDCl_3$.

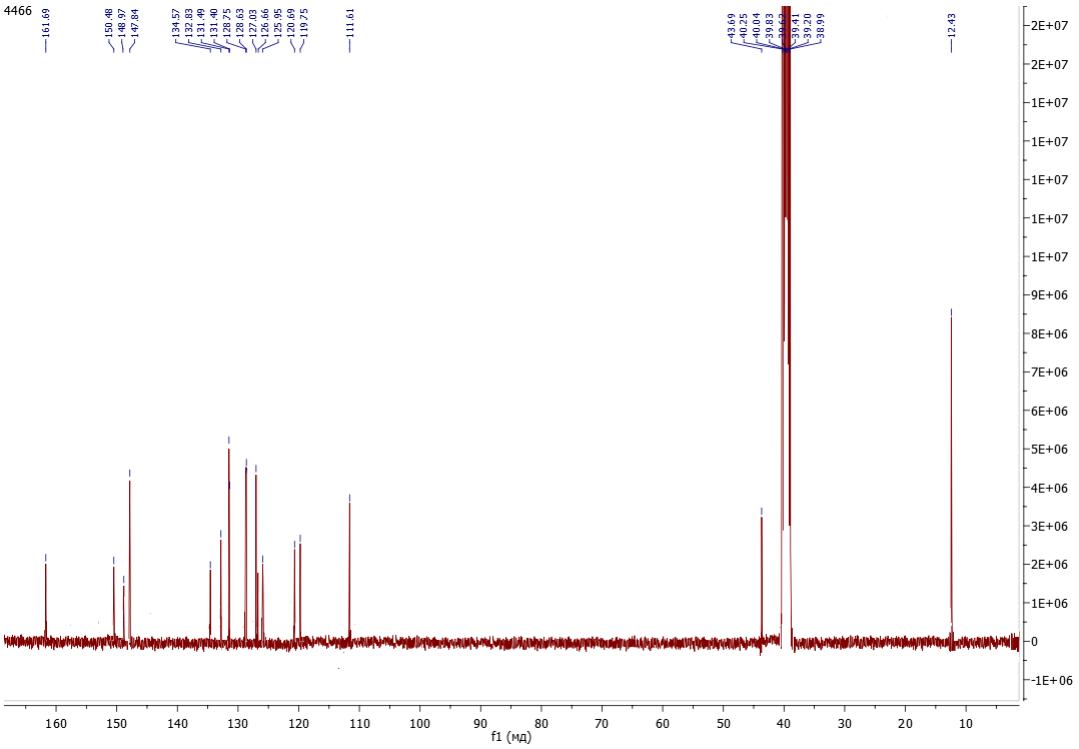


Figure S18 NMR ^{13}C spectrum of quinazolinone **10** in DMSO-d_6.

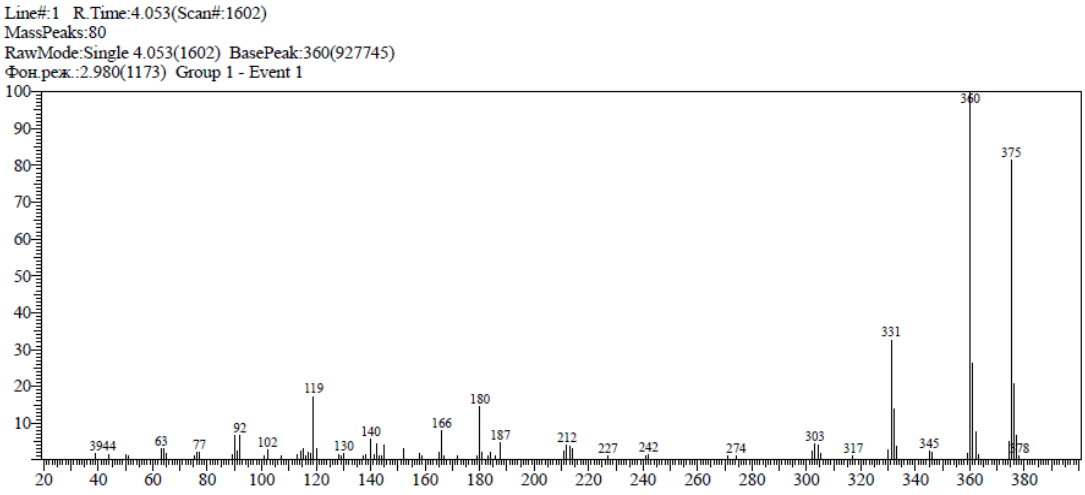
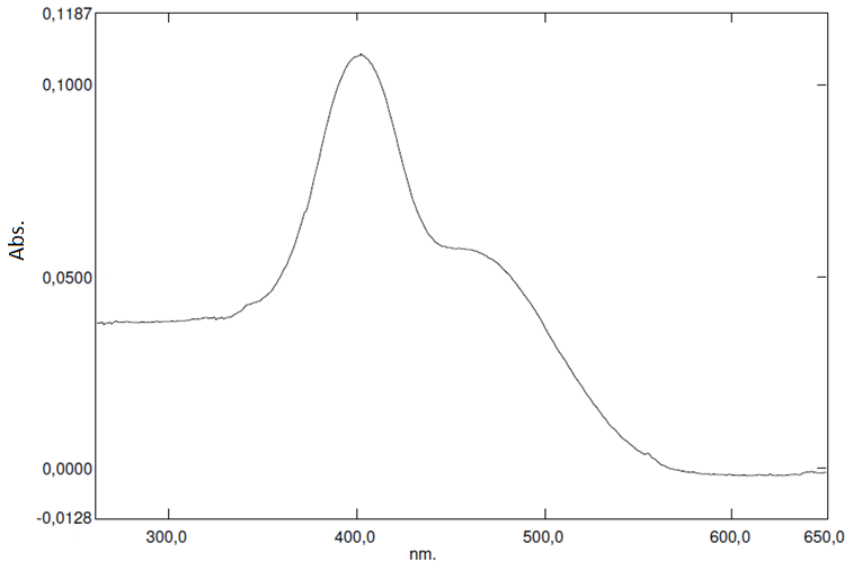


Figure S19 Mass spectrum (EI) of quinazolinone **10.**

Absorption and emission spectra of 4-cyano-2-[5-(4-diethylaminophenyl)thiophen-2-yl]quinazoline 5



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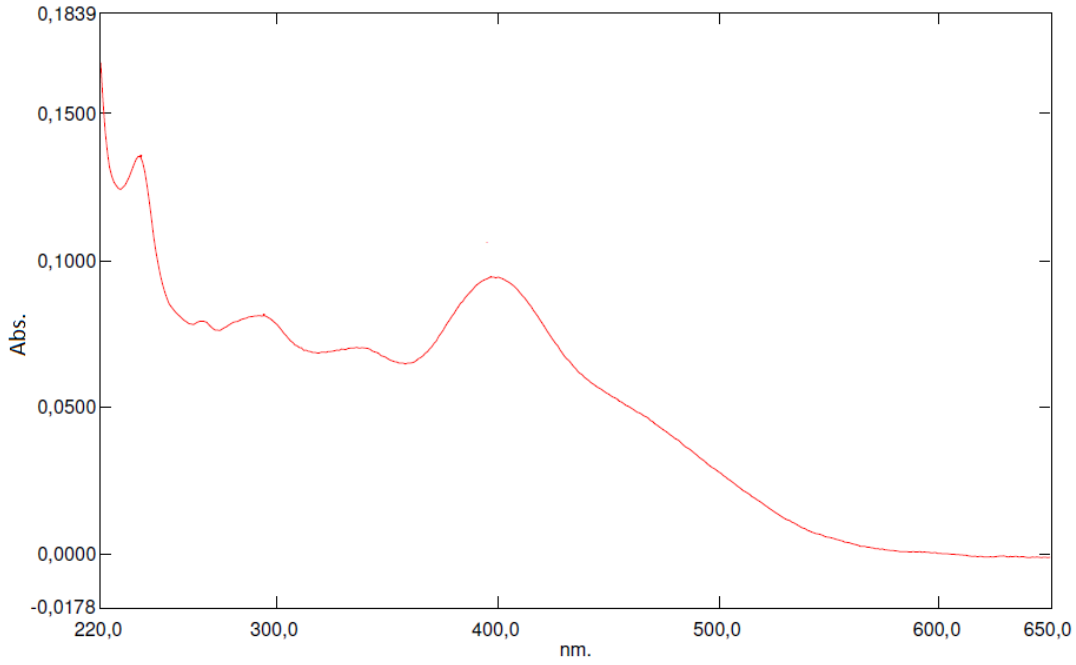
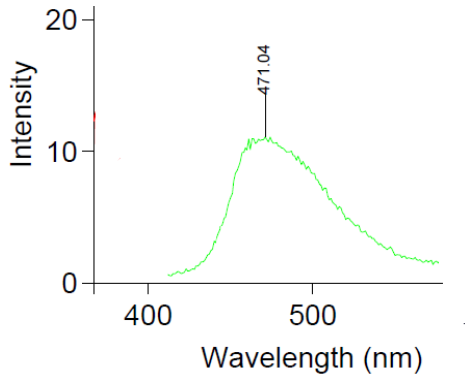


B

Figure S20 Absorption spectra of quinazolinone **5** in toluene (a); in acetonitrile (b).



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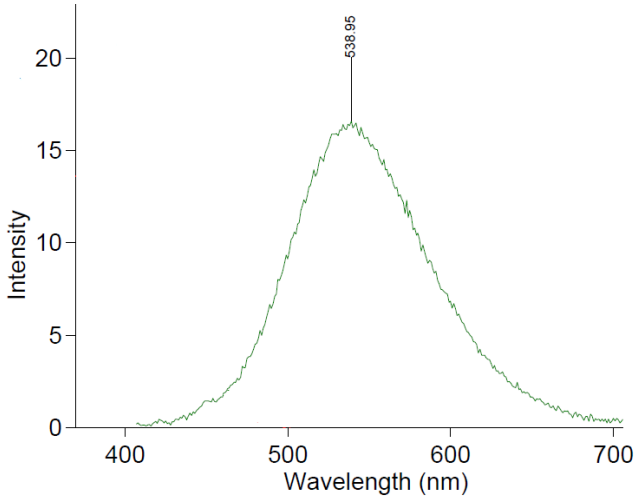
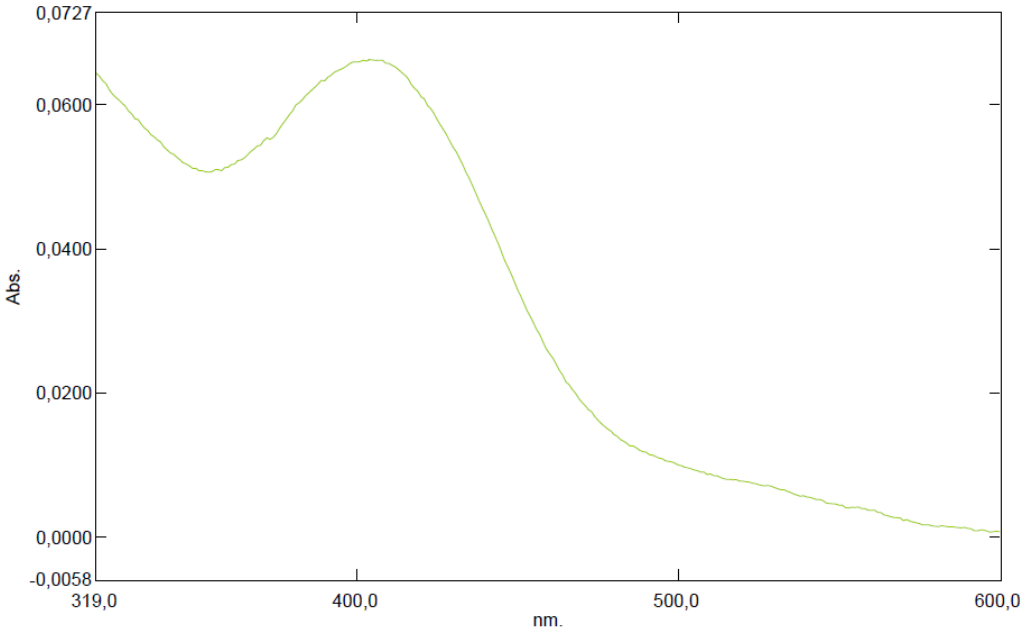


b

Figure S21 Emission spectra of quinazolinone **5** in toluene (excitation at 410 nm) (a); in acetonitrile (excitation at 400 nm) (b).

Absorption and emission spectra of
2-[5-(4-diethylaminophenyl)thiophen-2-yl]quinazolin-4(3*H*)-one 10



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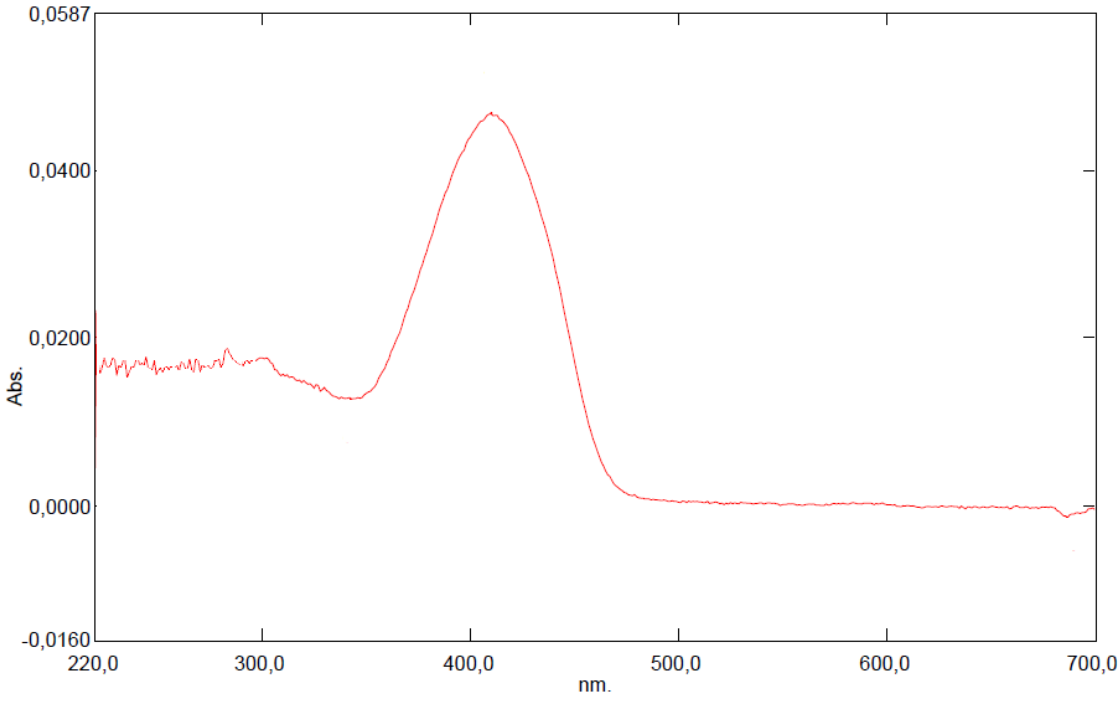
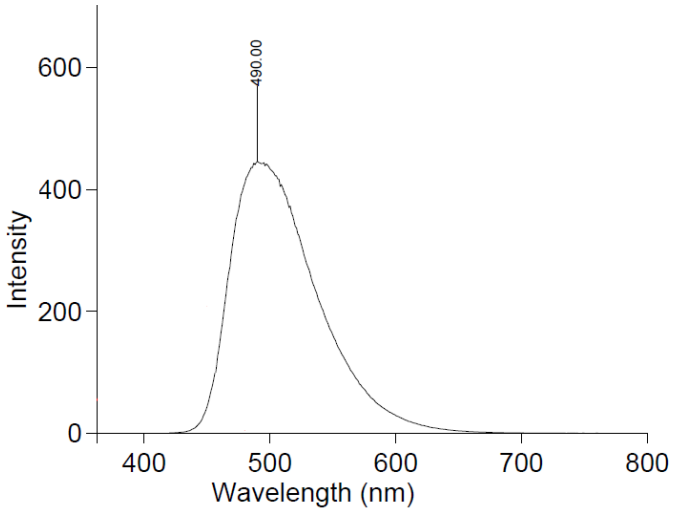
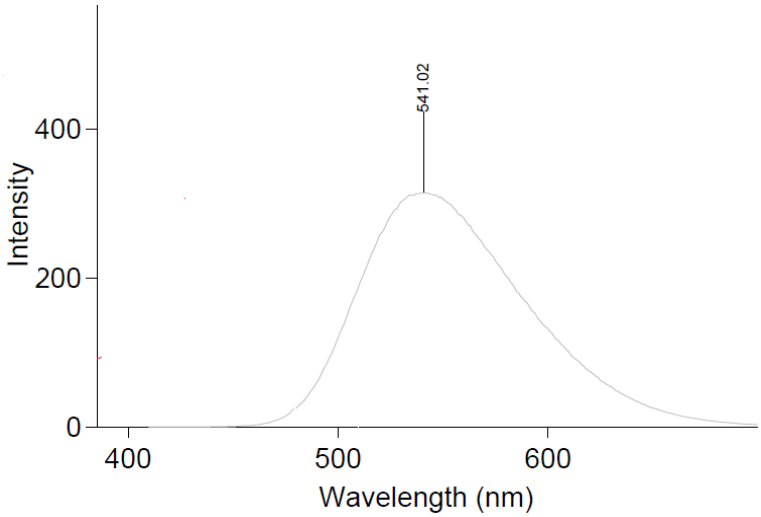


b

Figure S22 Absorption spectra of quinazolinone **10** in toluene (a);
in acetonitrile (b).



a



b

Figure S23 Emission spectra of quinazolinone **10** in toluene (excitation at 410 nm) (a); in acetonitrile (excitation at 400 nm) (b).

Table S1 Selected bond lengths of quinazoline **5**.

Bond	Bond length (Å)	Bond	Bond length (Å)
S(1)-C(11)	1.718(3)	C(8)-C(9)	1.349(5)
S(1)-C(14)	1.715(3)	C(9)-C(10)	1.404(4)
N(1)-C(2)	1.320(3)	C(12)-C(13)	1.388(4)
N(1)-C(10)	1.358(3)	C(13)-C(14)	1.345(4)
C(1)-C(4)	1.445(4)	C(14)-C(15)	1.468(4)
C(1)-N(4)	1.135(4)	C(15)-C(16)	1.378(4)
C(2)-N(3)	1.368(3)	C(15)-C(20)	1.373(4)
C(2)-C(11)	1.438(4)	C(16)-C(17)	1.377(5)
N(3)-C(4)	1.306(3)	C(17)-C(18)	1.387(5)
C(4)-C(5)	1.416(4)	C(18)-C(19)	1.403(5)
C(5)-C(6)	1.398(4)	C(18)-N(2)	1.395(6)
C(5)-C(10)	1.403(4)	C(19)-C(20)	1.367(4)
C(6)-C(7)	1.362(5)	N(2)-C(21)	1.441(8)
C(7)-C(8)	1.388(5)	N(2)-(22)	1.442(8)

Table S2 Selected bond angles of quinazoline **5**.

Angle	(°)	Angle	(°)
C(11)-S(1)-C(14)	92.2(1)	S(1)-C(11)-C(2)	121.6(2)
C(2)-N(1)-C(10)	117.0(2)	S(1)-C(11)-C(12)	110.1(2)
C(4)-C(1)-N(4)	178.8(3)	C(2)-C(11)-C(12)	128.3(3)
N(1)-C(2)-N(3)	126.0(2)	C(11)-C(12)-C(13)	113.4(3)
N(1)-C(2)-C(11)	119.4(2)	C(12)-C(13)-C(14)	114.0(3)
N(3)-C(2)-C(11)	114.6(2)	S(1)-C(14)-C(13)	110.2(2)
C(2)-N(3)-C(4)	116.0(2)	S(1)-C(14)-C(15)	121.4(2)
C(1)-C(4)-N(3)	115.9(2)	C(13)-C(14)-C(15)	128.4(3)
C(1)-C(4)-C(5)	119.9(2)	C(14)-C(15)-C(16)	119.7(2)
C(8)-C(9)-C(10)	119.9(3)	C(14)-C(15)-C(20)	122.9(2)
N(1)-C(10)-C(5)	121.9(2)	C(16)-C(15)-C(20)	117.4(2)
N(1)-C(10)-C(9)	119.7(3)	C(15)-C(16)-C(17)	121.4(3)
C(5)-C(10)-C(9)	118.4(3)		