

SUPPORTING INFORMATION

Nucleophile–nucleofuge duality of azide and arylthiolate groups in the synthesis of quinazoline and tetrazoloquinazoline derivatives

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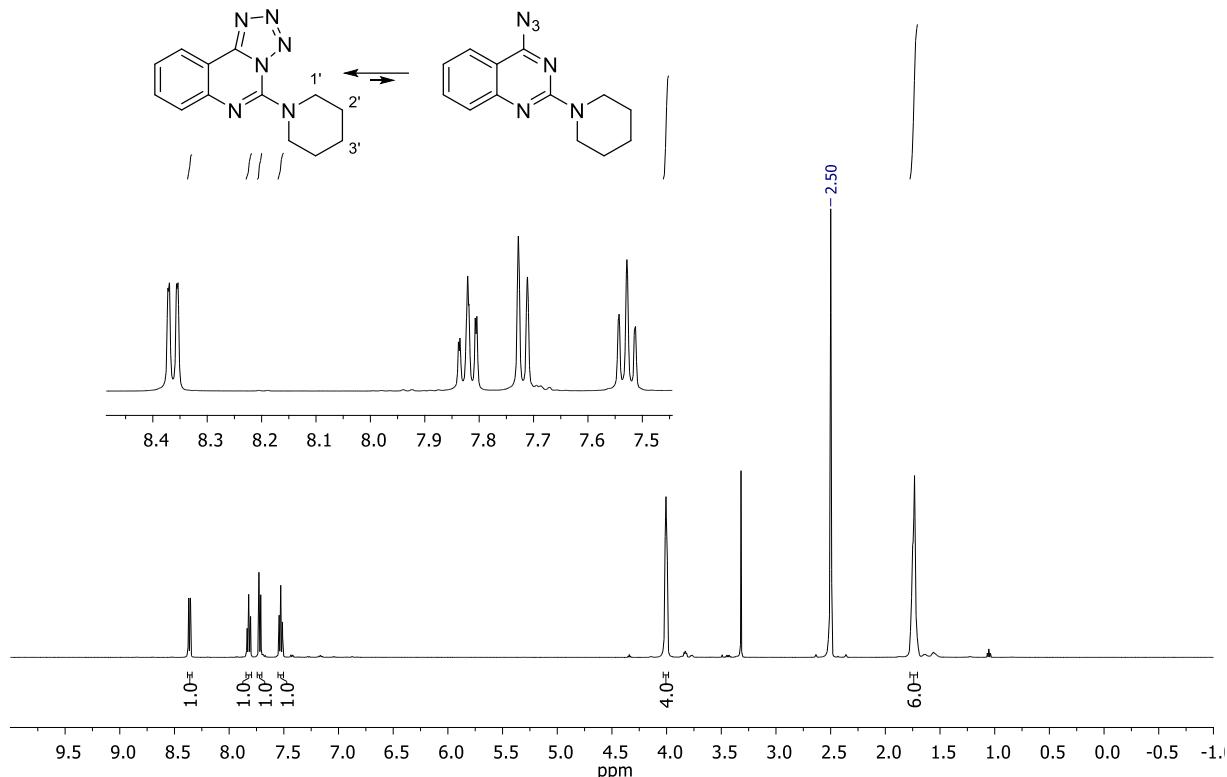
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NMR spectra

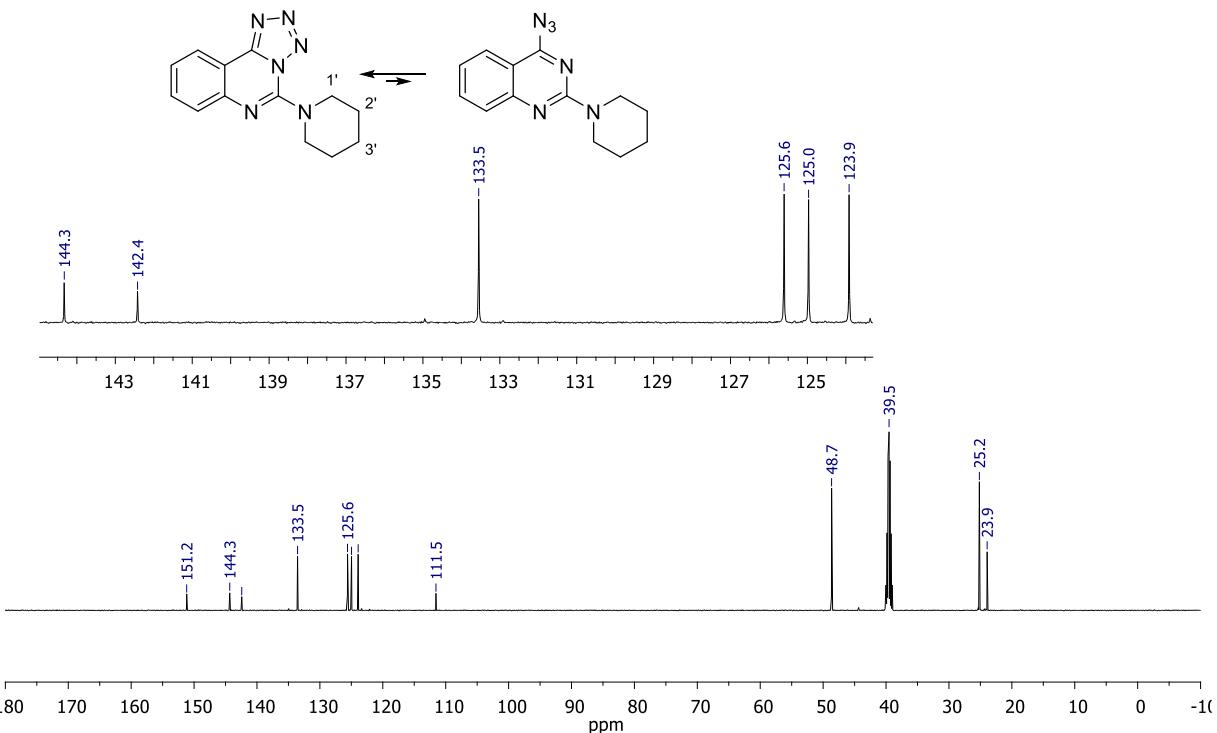
5-(Alkylamino)tetrazolo[1,5-c]quinazolines

Tautomeric mixture of 5-(piperidin-1-yl)tetrazolo[1,5-c]quinazoline (**4a-T**) and 4-azido-2-(piperidin-1-yl)quinazoline (**4a-A**)

¹H-NMR (500 MHz, DMSO-d₆) spectrum of compound **4a**:

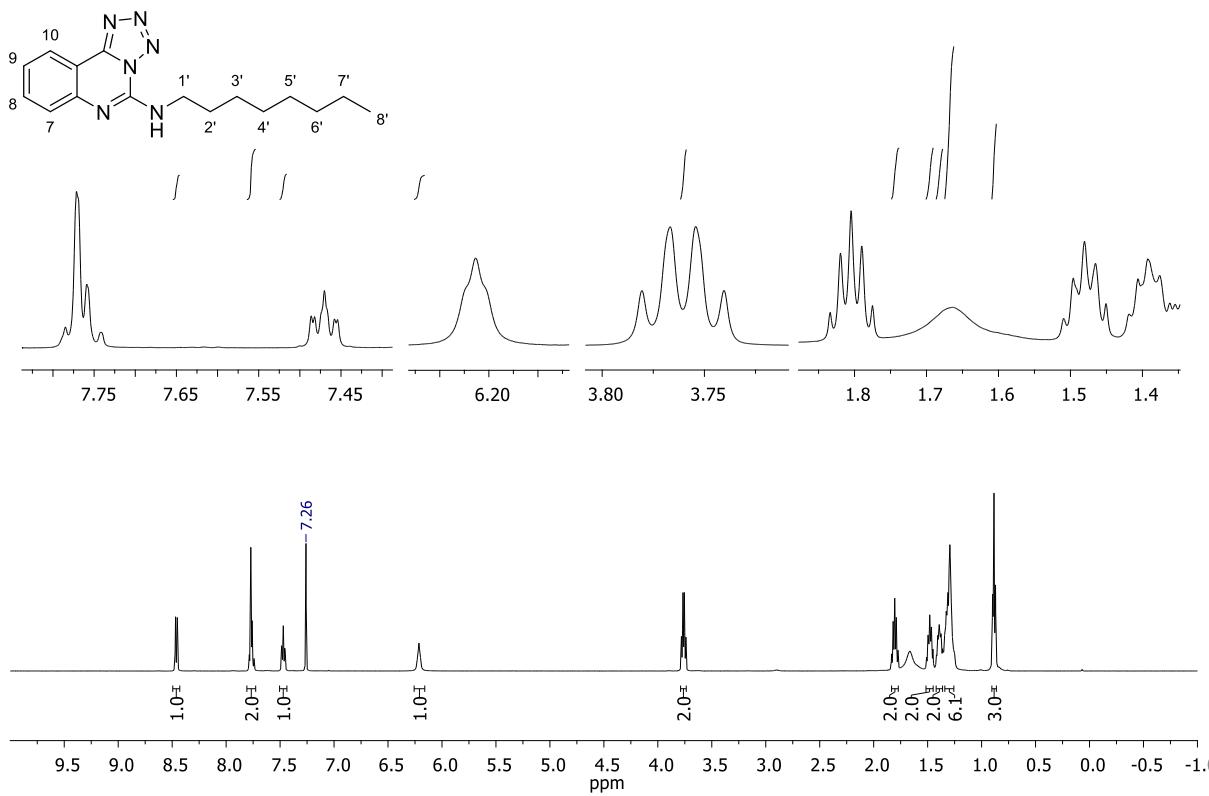


¹³C-NMR (125.7 MHz, DMSO-d₆) spectrum of compound 4a:

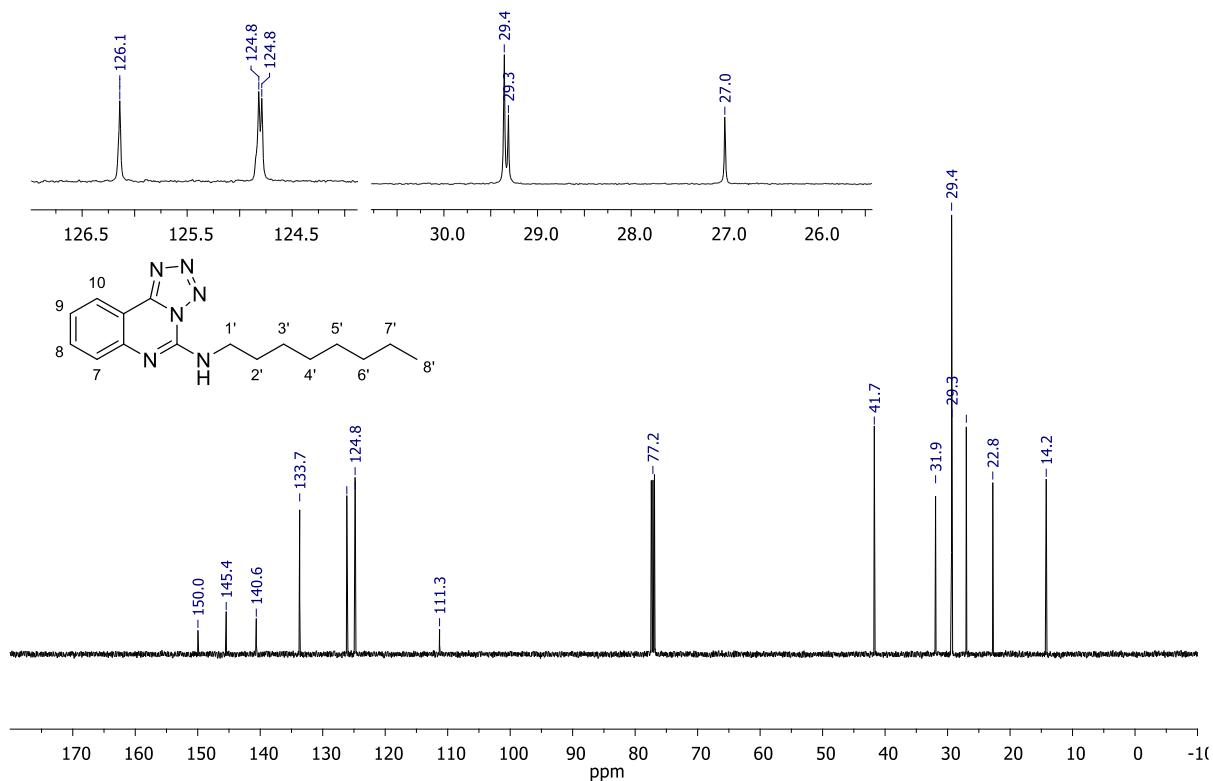


5-(Octylamino)tetrazolo[1,5-c]quinazoline (4b)

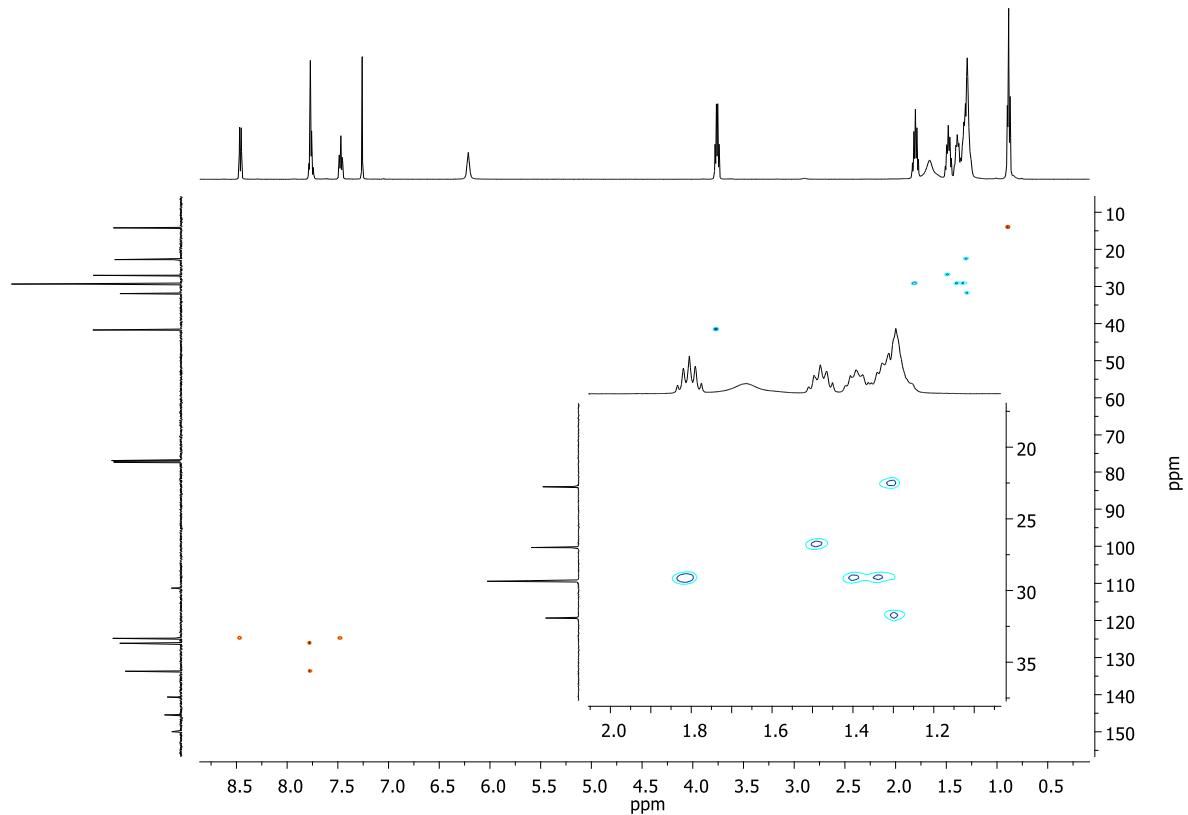
¹H-NMR (500 MHz, CDCl₃) spectrum of compound 4b:



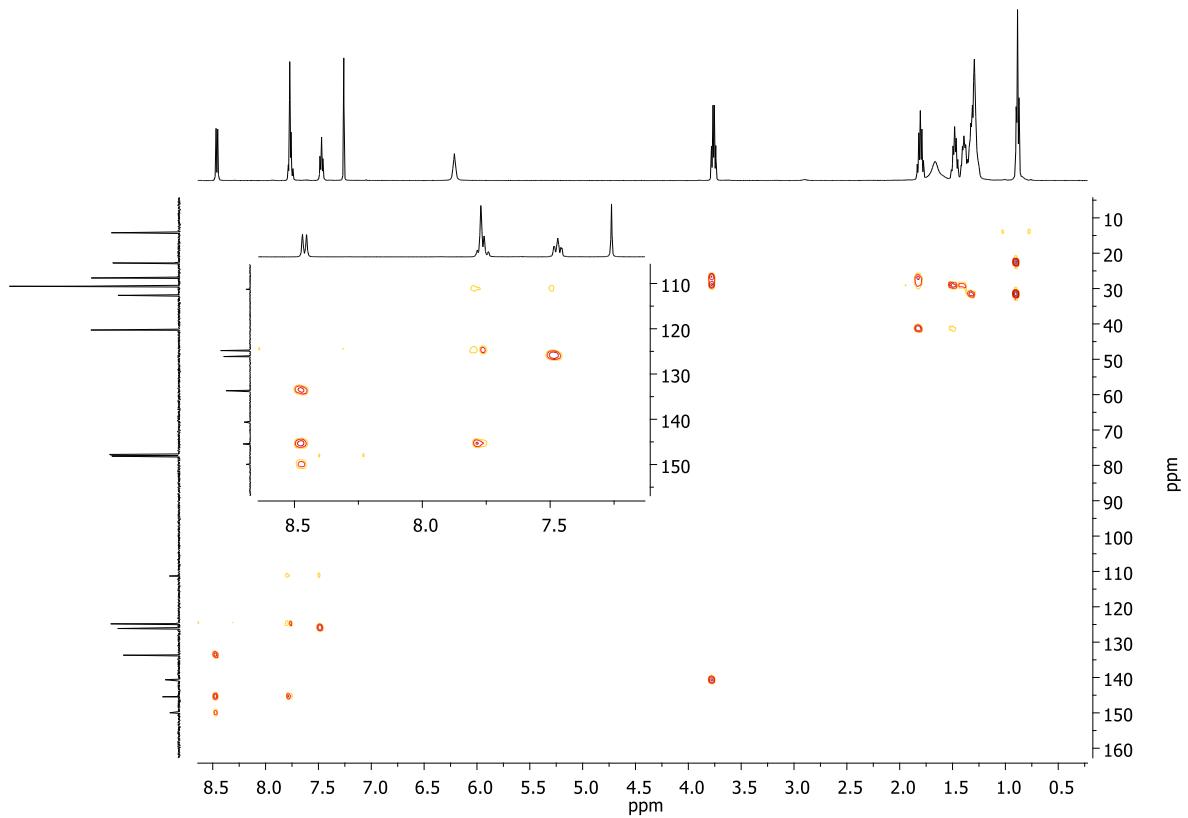
¹³C-NMR (125.7 MHz, CDCl₃) spectrum of compound 4b:



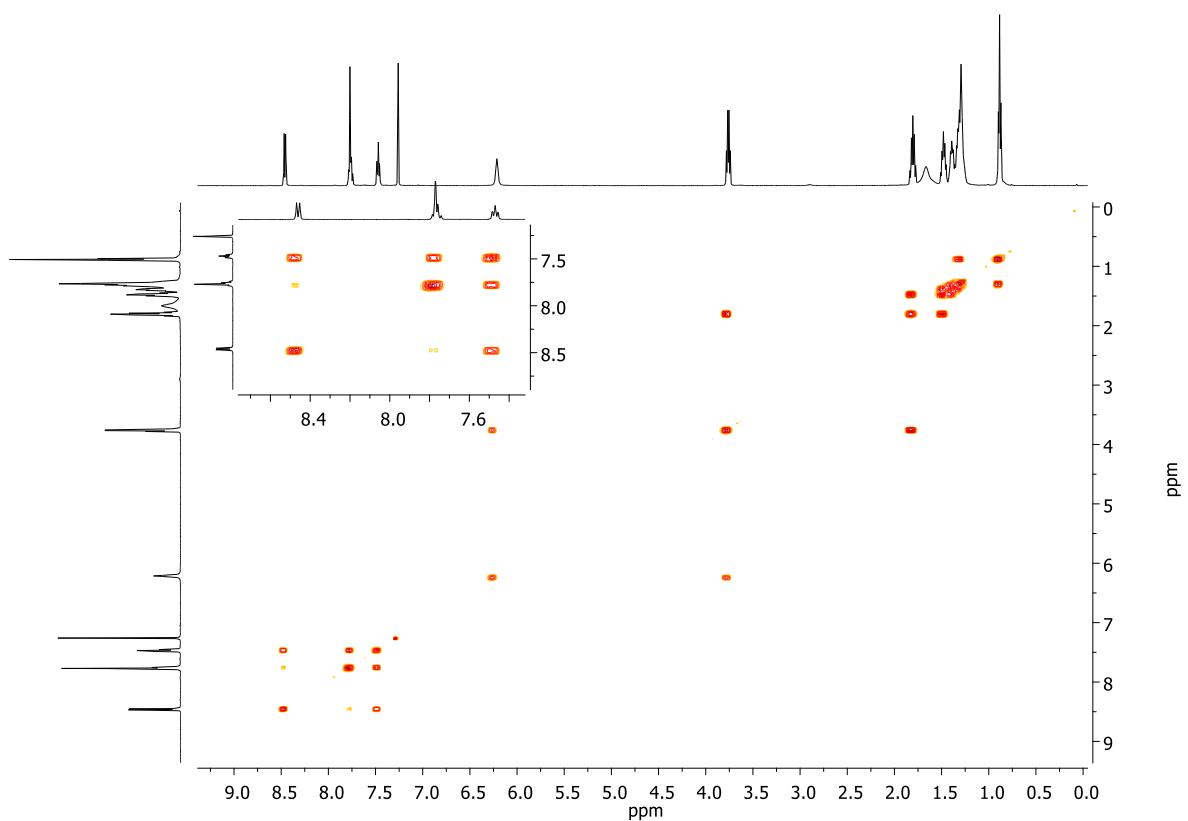
HSQC spectrum of compound 4b:



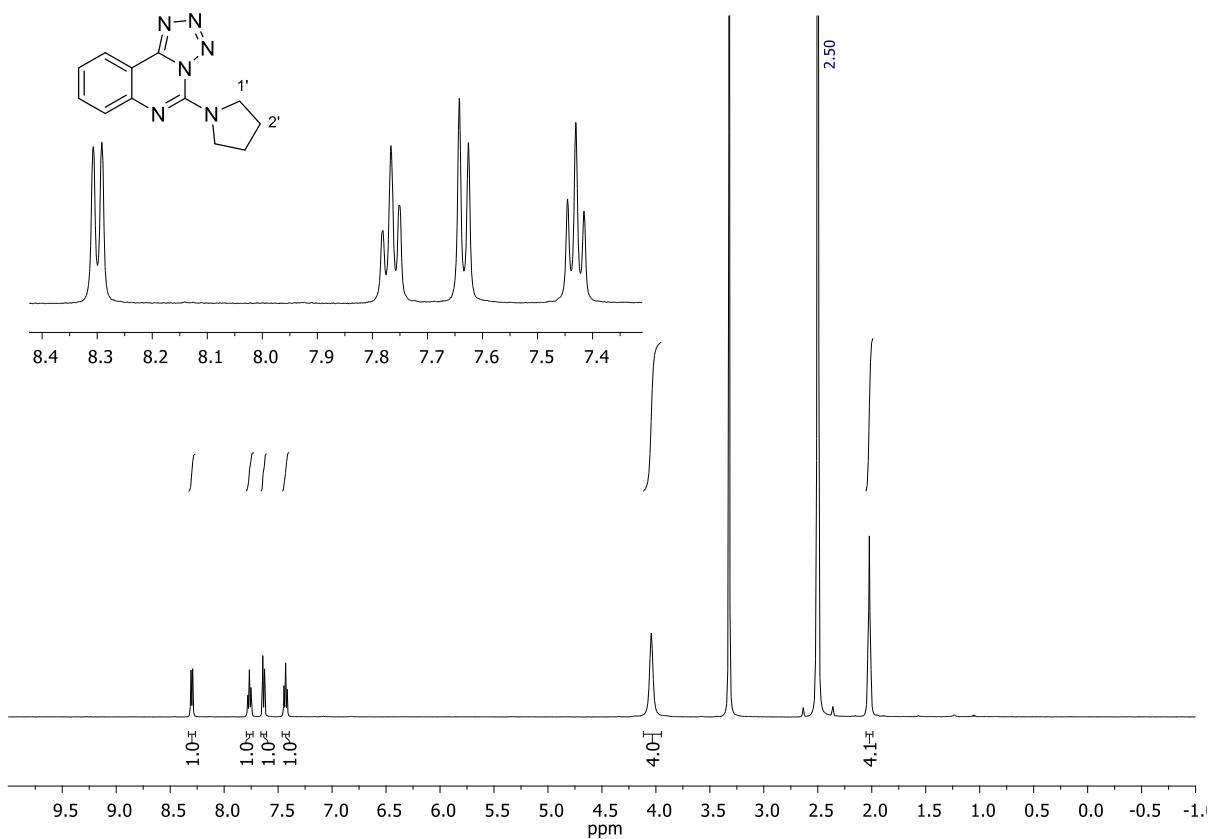
HMBC spectrum of compound 4b:



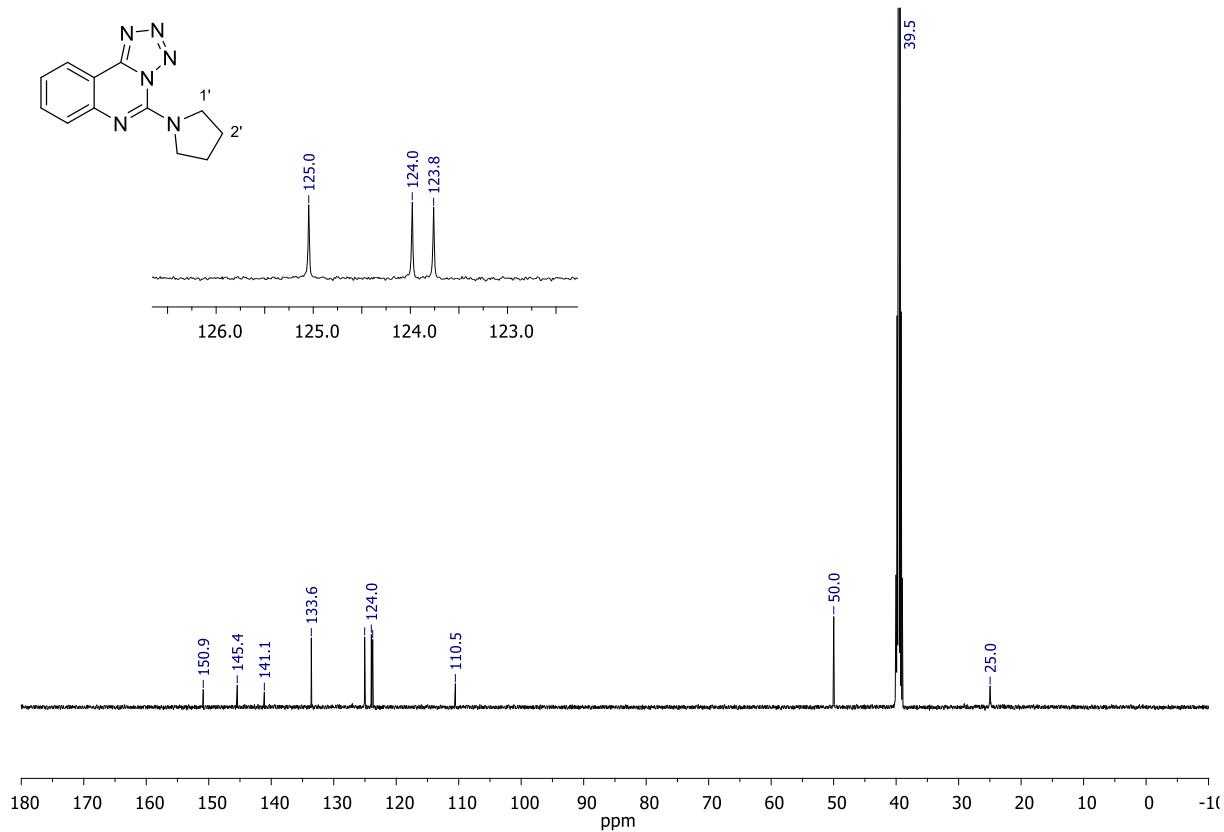
COSY spectrum of compound 4b:



5-(Pyrrolidin-1-yl)tetrazolo[1,5-*c*]quinazoline (4c)
¹H-NMR (500 MHz, DMSO-d₆) spectrum of compound 4c:

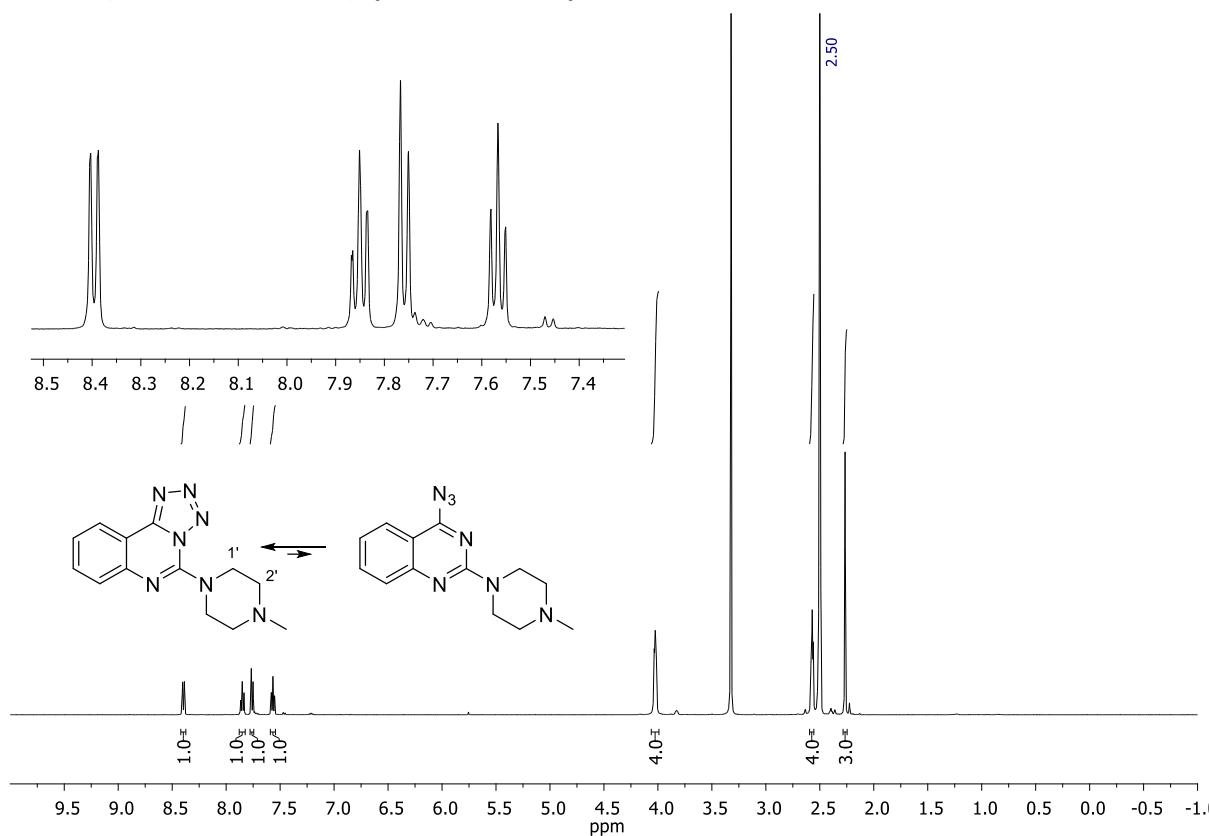


¹³C-NMR (125.7 MHz, DMSO-d₆) spectrum of compound 4c:

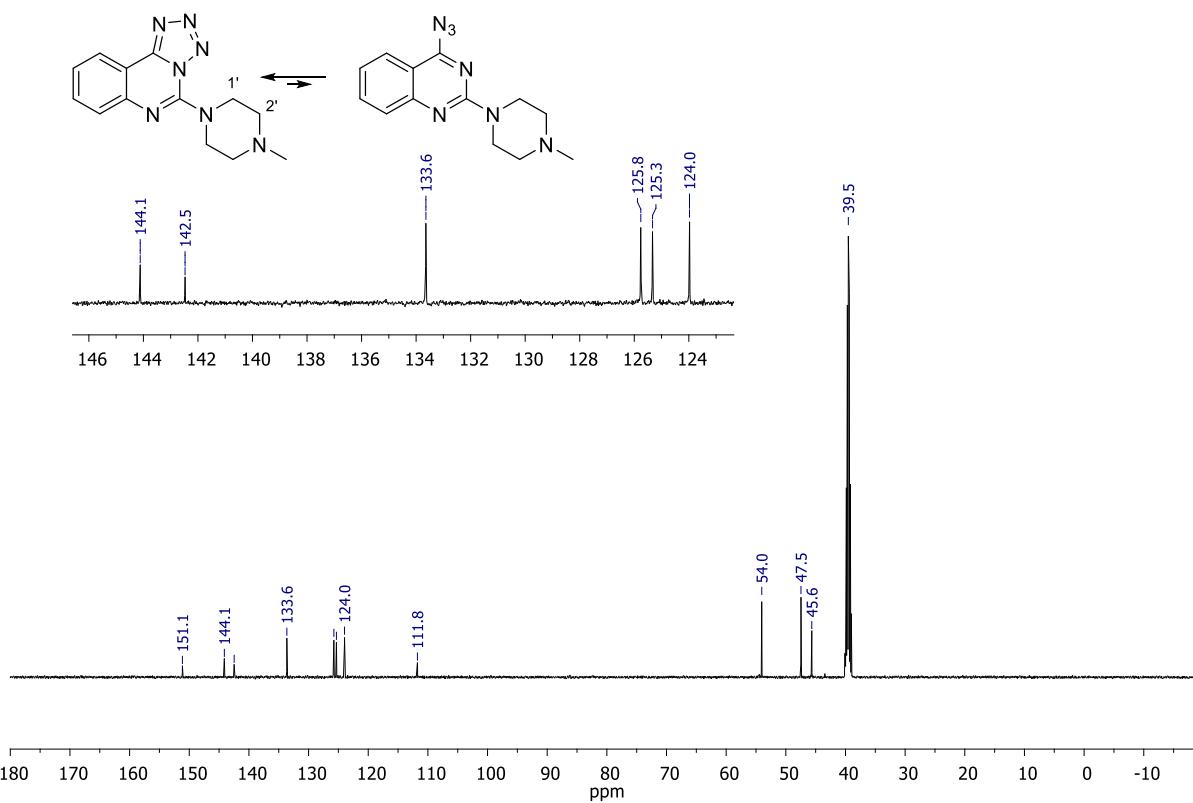


Tautomeric mixture of 5-(4-methylpiperazin-1-yl)tetrazolo[1,5-*c*]quinazoline (4d-T**) and 4-azido-2-(4-methylpiperazin-1-yl)quinazoline (**4d-A**)**

¹H-NMR (500 MHz, DMSO-d₆) spectrum of compound **4d:**

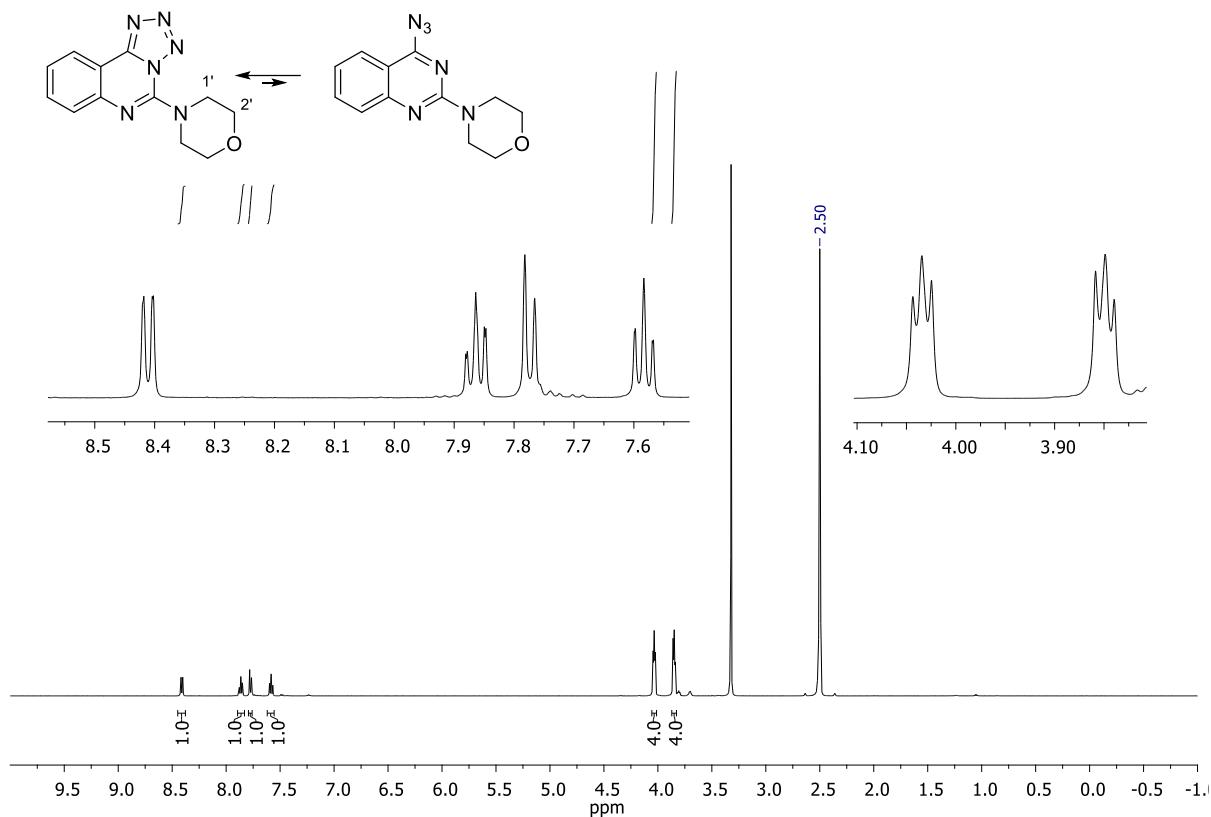


¹³C-NMR (125.7 MHz, DMSO-d₆) spectrum of compound **4d:**

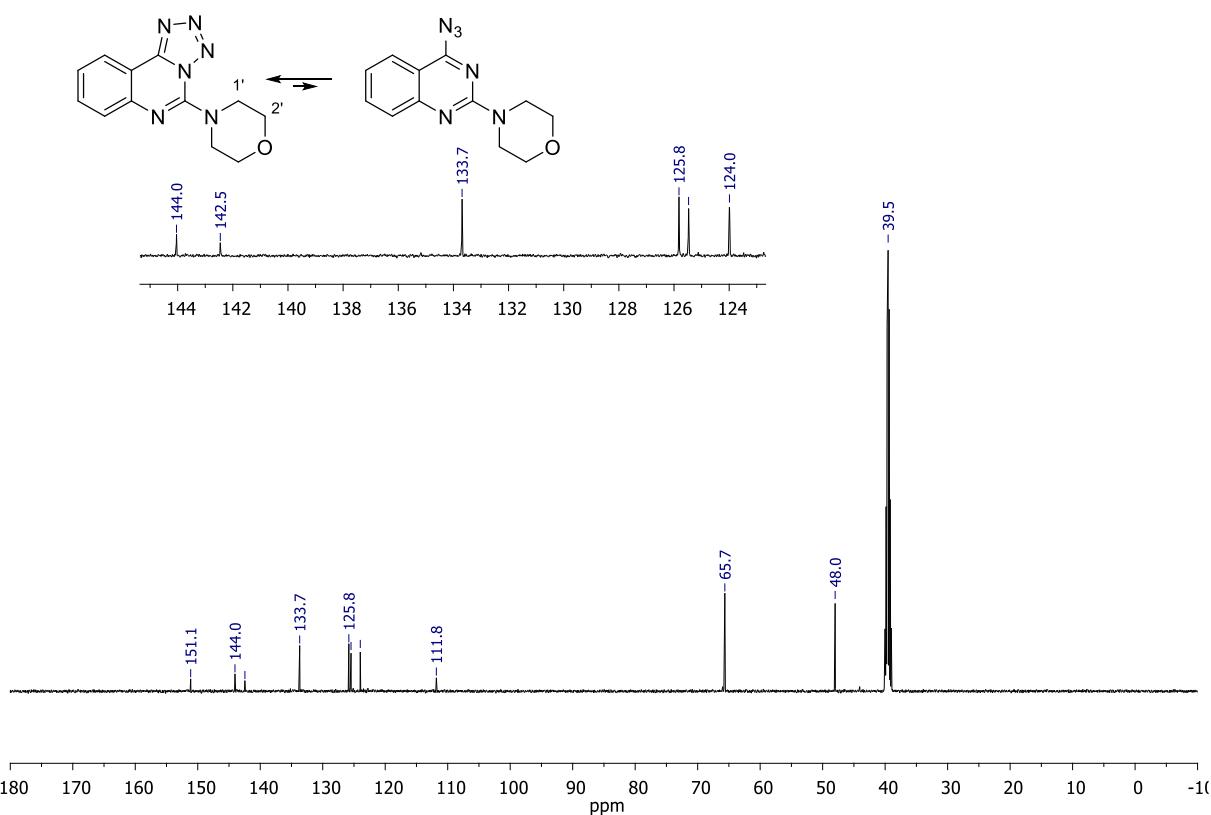


Tautomeric mixture of 5-(morpholin-4-yl)tetrazolo[1,5-c]quinazoline (4e-T) and 4-azido-2-(morpholin-4-yl)quinazoline (4e-A)

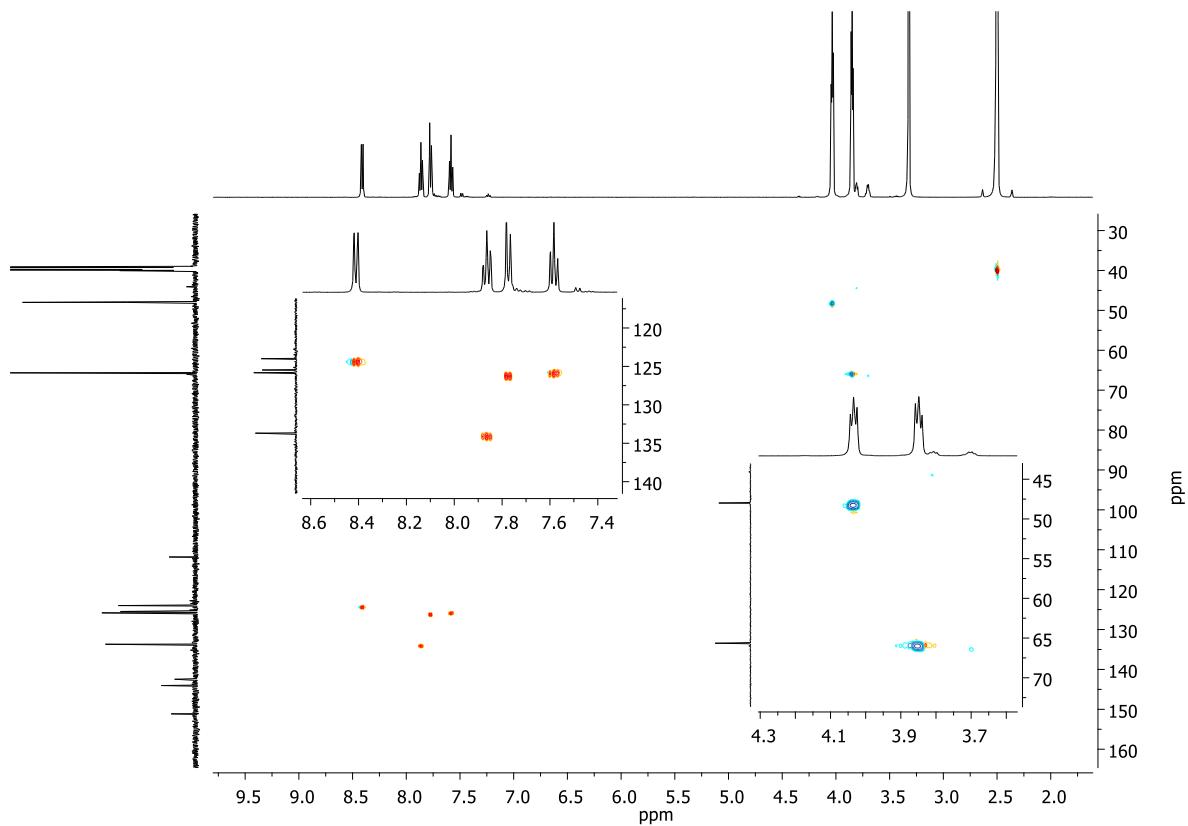
^1H -NMR (500 MHz, DMSO- d_6) spectrum of compound 4e:



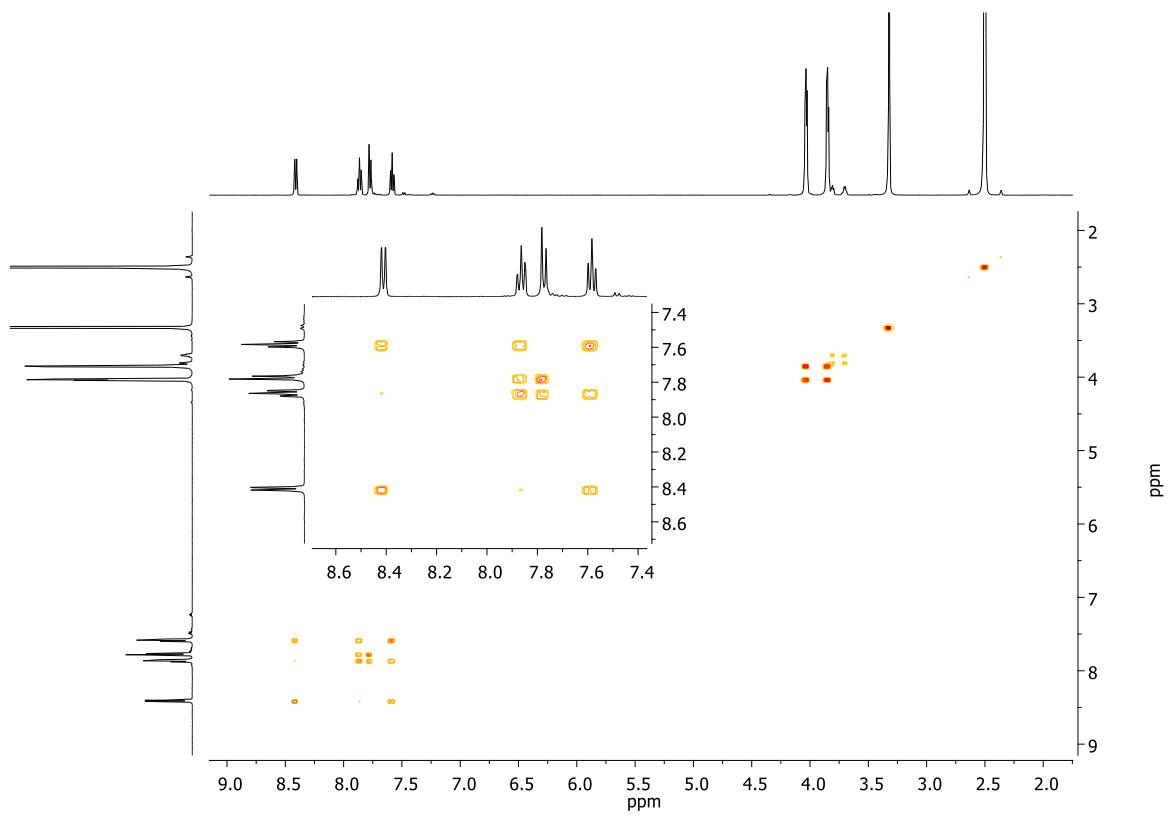
^{13}C -NMR (125.7 MHz, DMSO- d_6) spectrum of compound 4e:



HSQC spectrum of compound 4e:

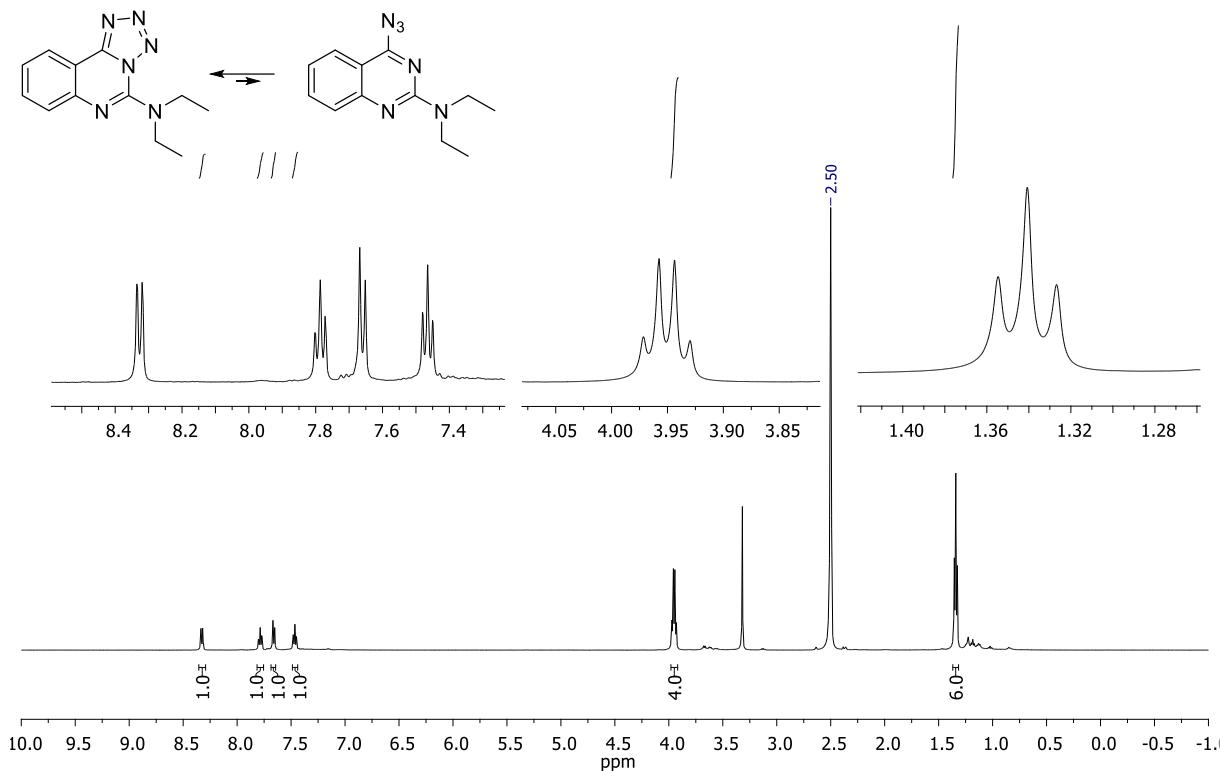


COSY spectrum of compound 4e:

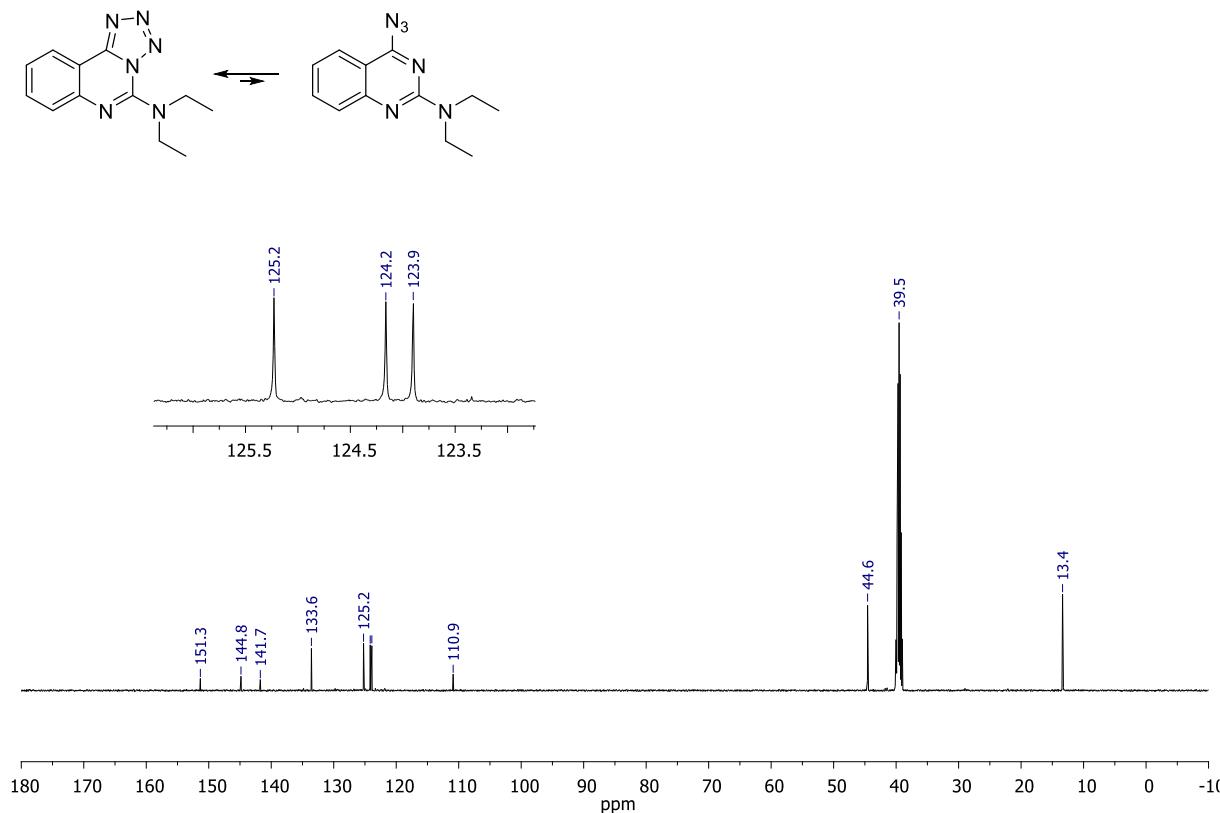


Tautomeric mixture of 5-(diethylamino)tetrazolo[1,5-*c*]quinazoline (4f-T) and 4-azido-2-(diethylamino)quinazoline (4f-A)

¹H-NMR (500 MHz, DMSO-d₆) spectrum of compound 4f:

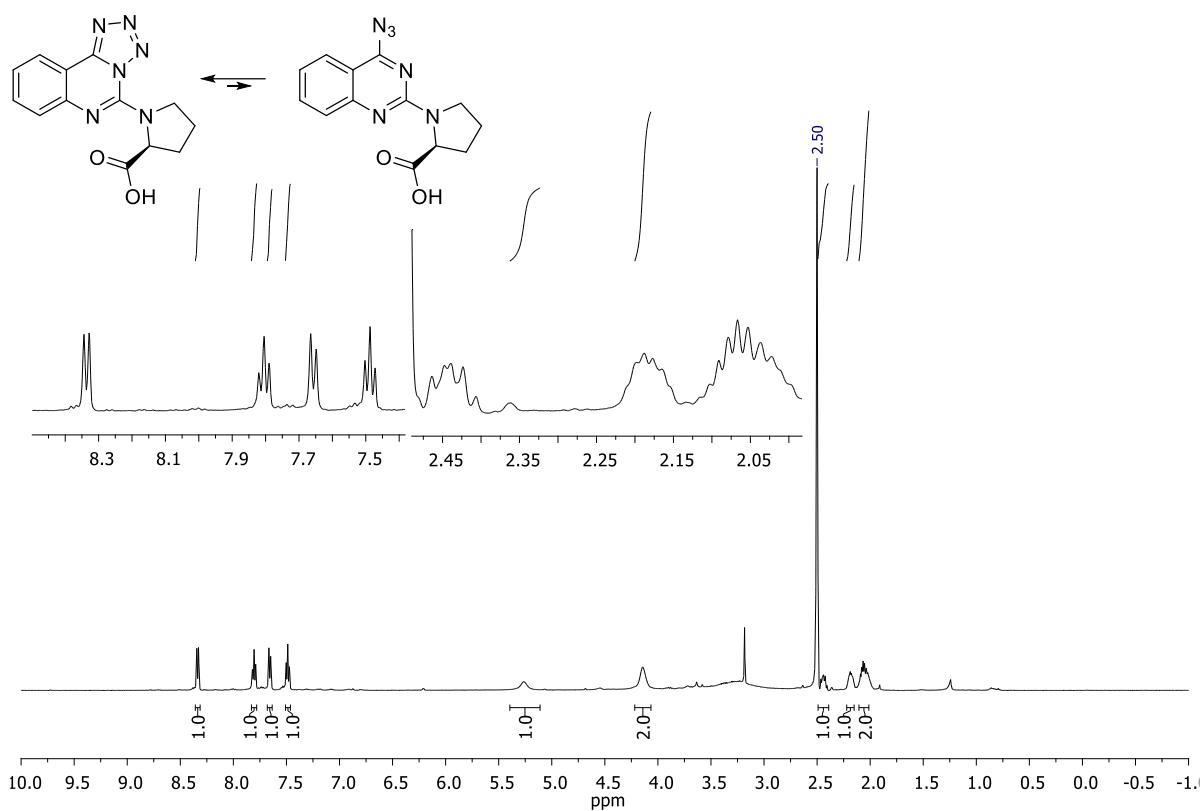


¹³C-NMR (125.7 MHz, DMSO-d₆) spectrum of compound 4f:

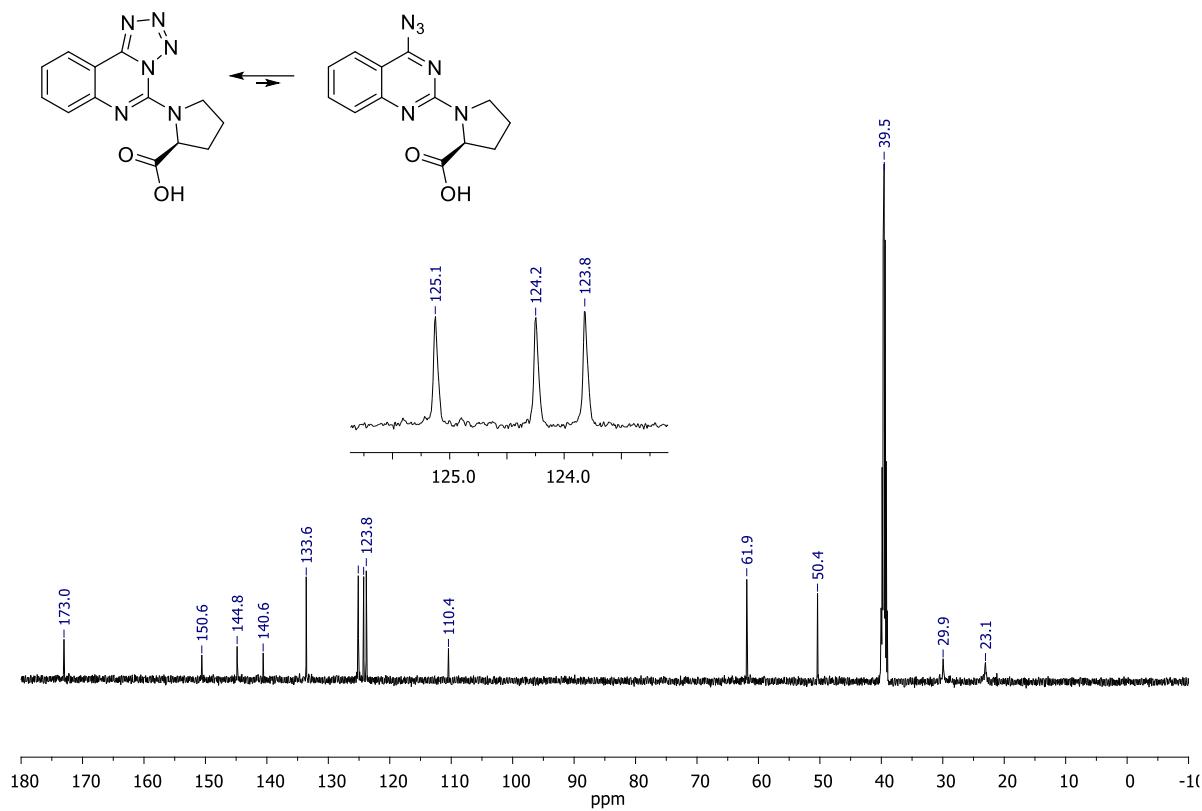


Tautomeric mixture of tetrazolo[1,5-c]quinazolin-5-yl-L-proline (4g-T) and (4-azidoquinazolin-2-yl)-L-proline (4g-A)

$^1\text{H-NMR}$ (500 MHz, DMSO-d₆, 50 °C) spectrum of compound 4g:



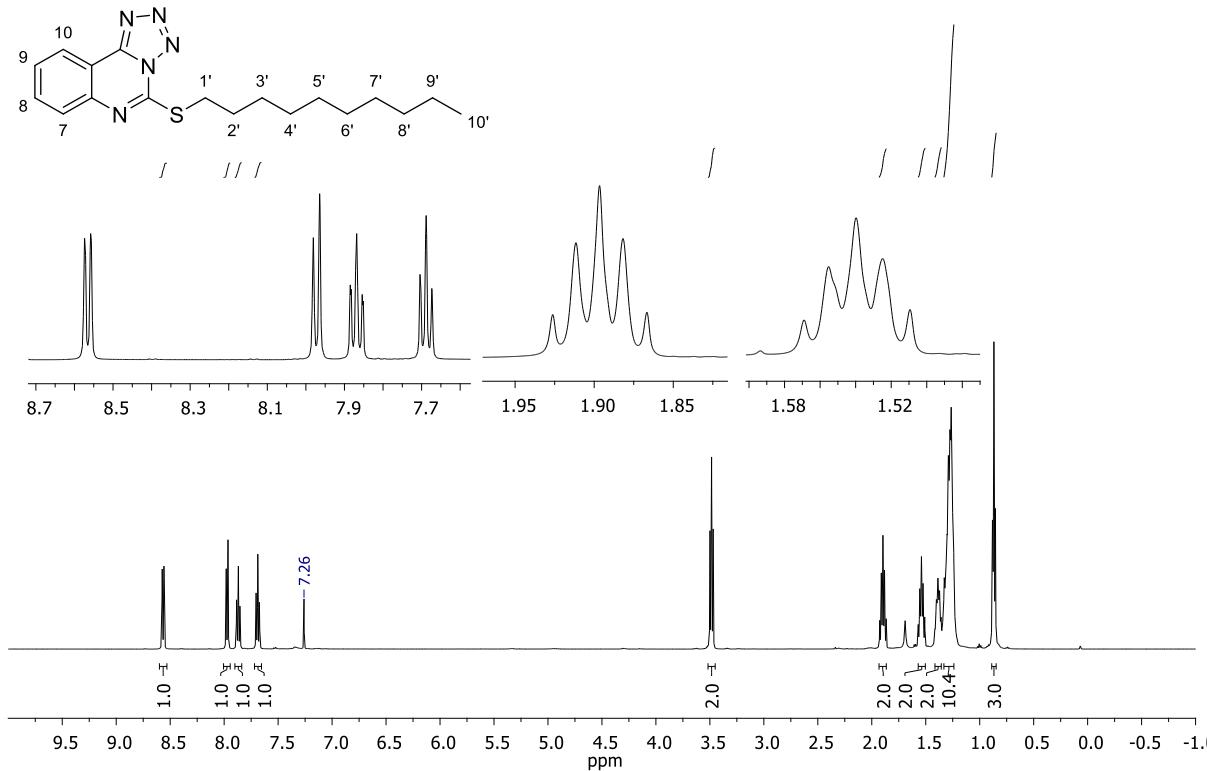
$^{13}\text{C-NMR}$ (125.7 MHz, DMSO-d₆, 50 °C) spectrum of compound 4g:



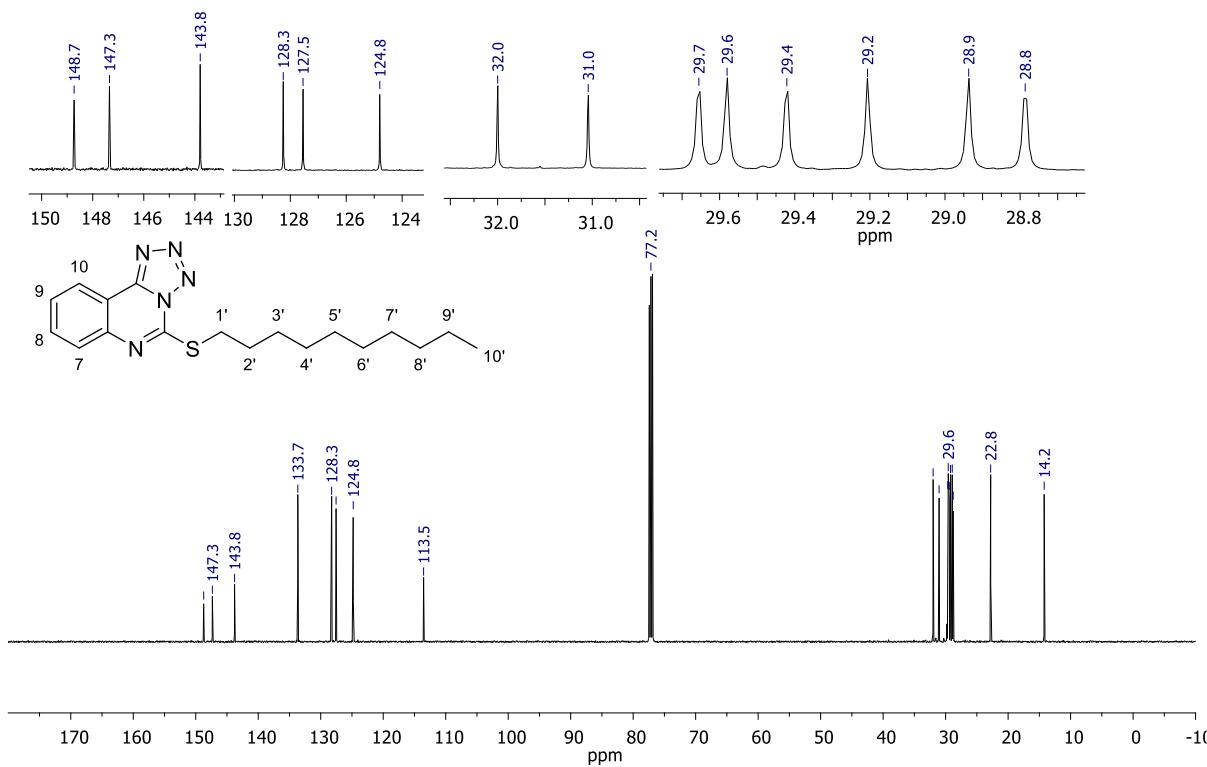
5-(Alkylthio)tetrazolo[1,5-c]quinazolines

5-(Decylthio)tetrazolo[1,5-c]quinazoline (6a)

¹H-NMR (500 MHz, CDCl₃) spectrum of compound 6a:

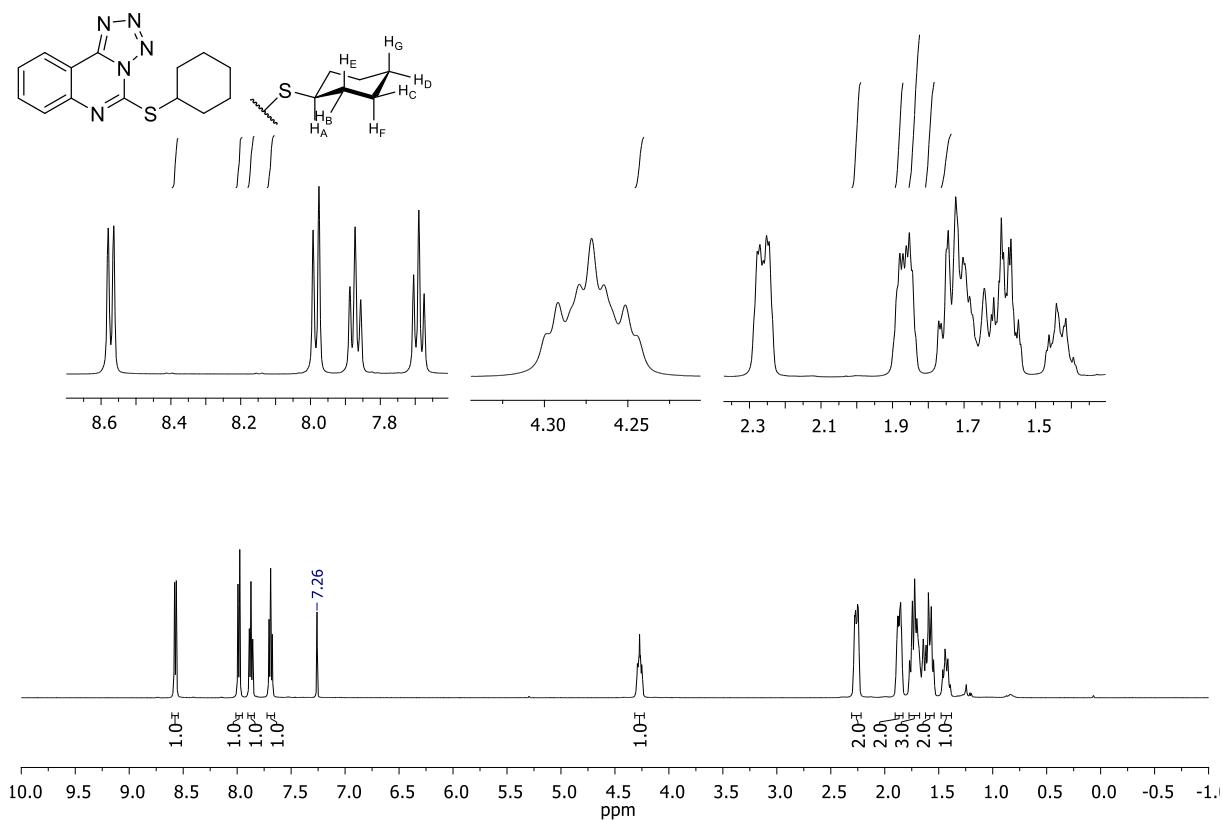


¹³C-NMR (125.7 MHz, CDCl₃) spectrum of compound 6a:

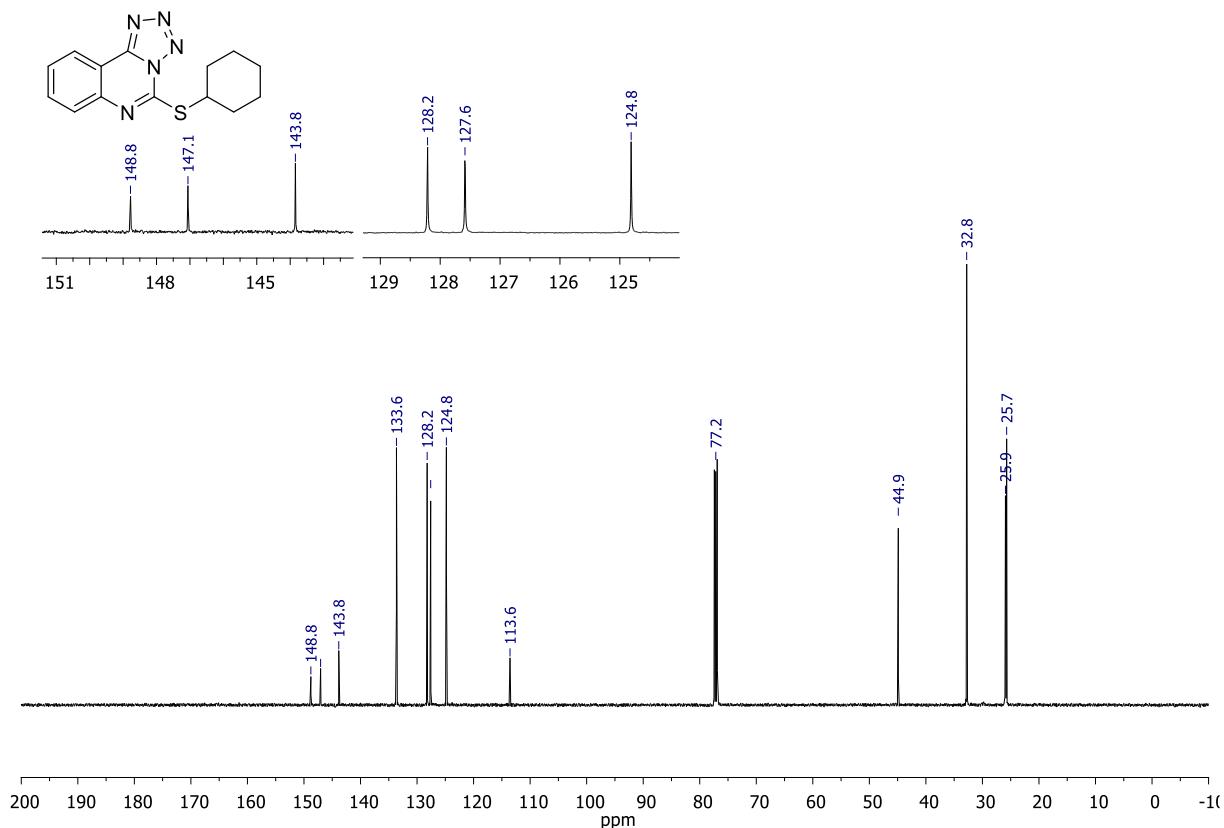


5-(Cyclohexylthio)tetrazolo[1,5-c]quinazoline(6b)

$^1\text{H-NMR}$ (500 MHz, CDCl_3) spectrum of compound 6b:

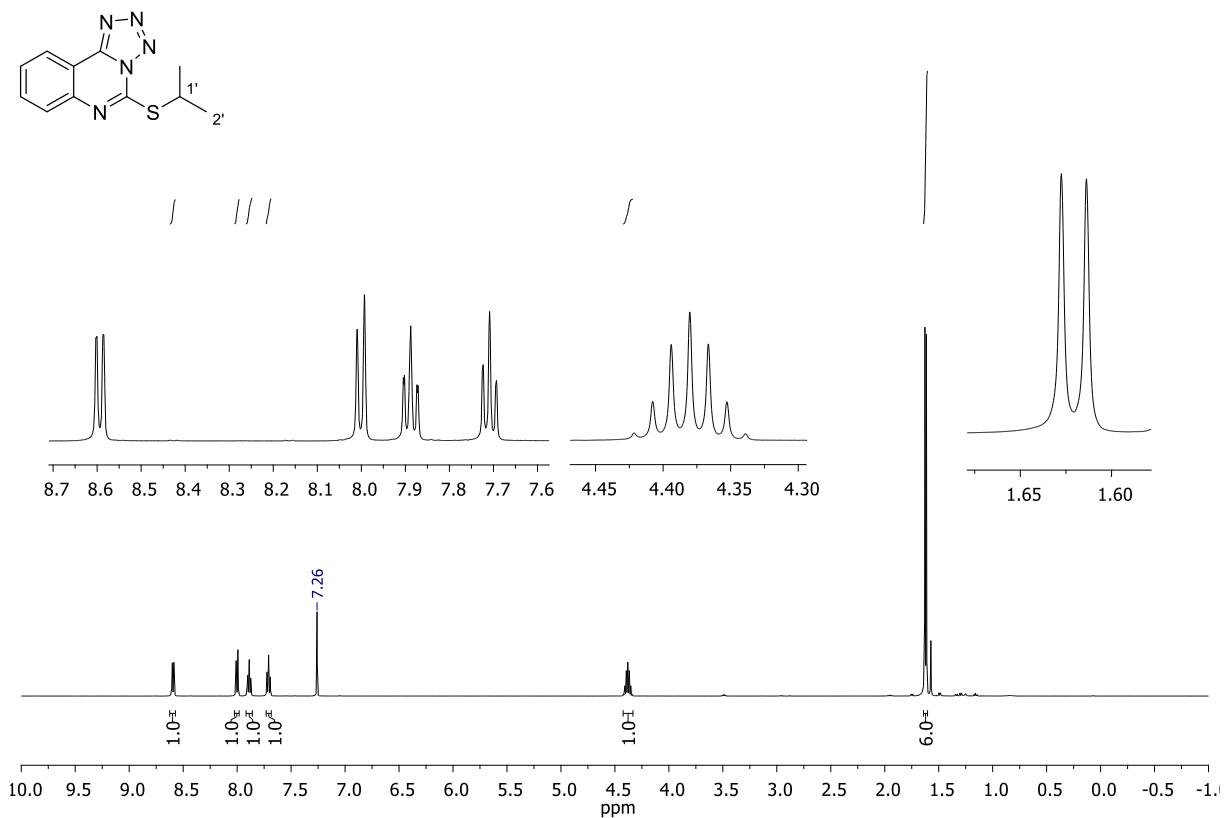


$^{13}\text{C-NMR}$ (125.7 MHz, CDCl_3) spectrum of compound 6b:

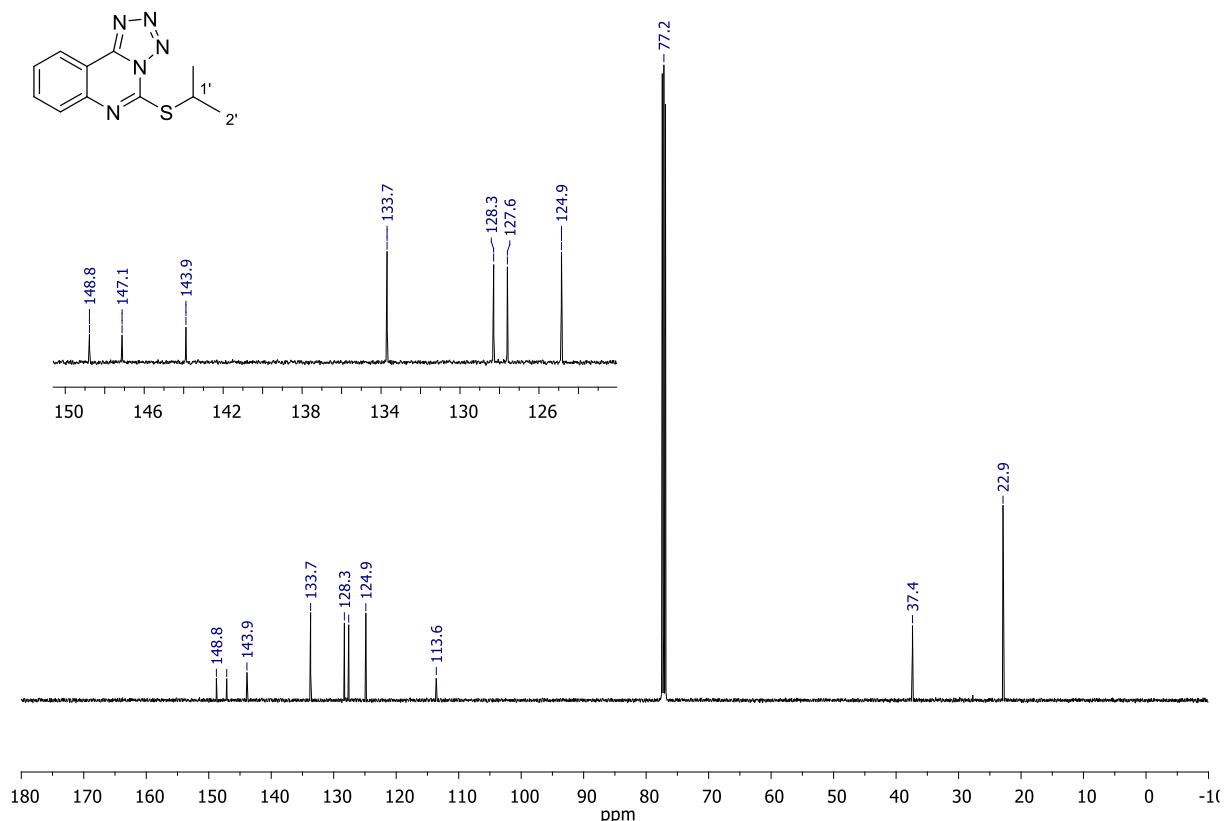


5-(Isopropylthio)tetrazolo[1,5-*c*]quinazoline (6c)

^1H -NMR (500 MHz, CDCl_3) spectrum of compound 6c:

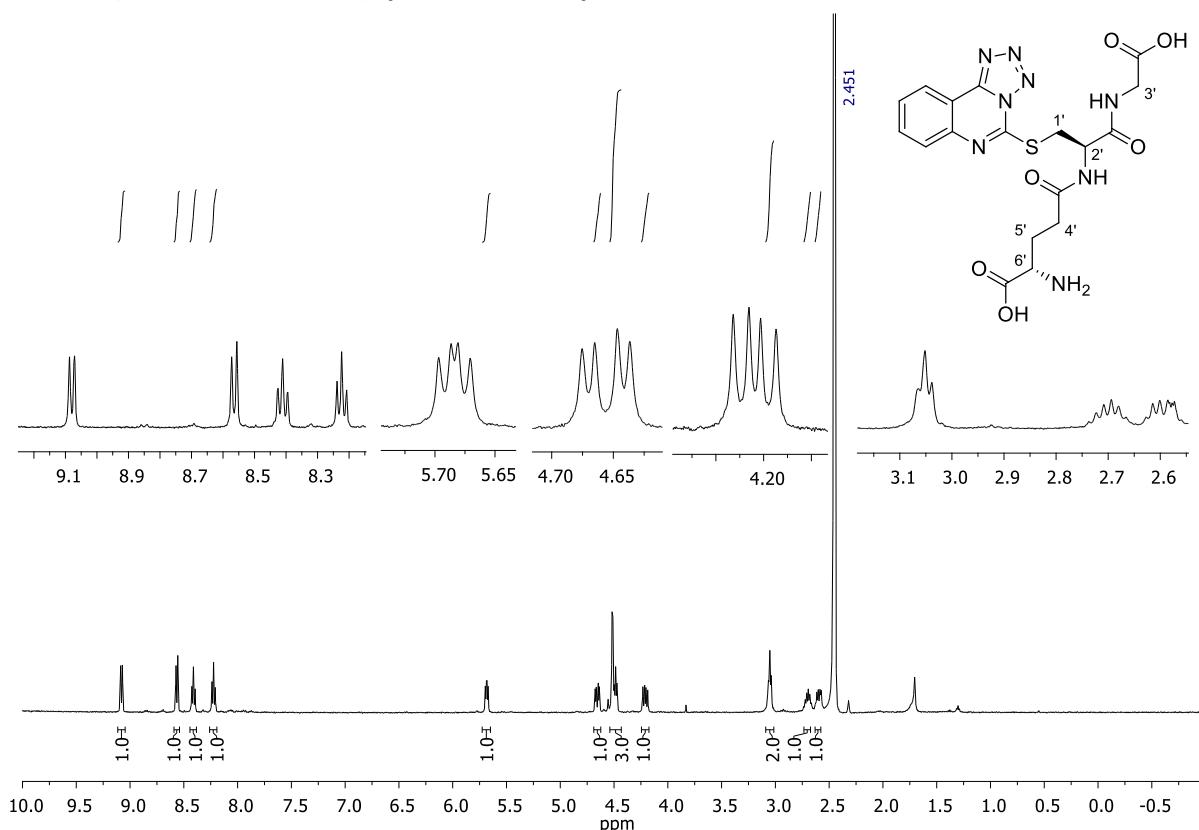


^{13}C -NMR (125.7 MHz, CDCl_3) spectrum of compound 6c:

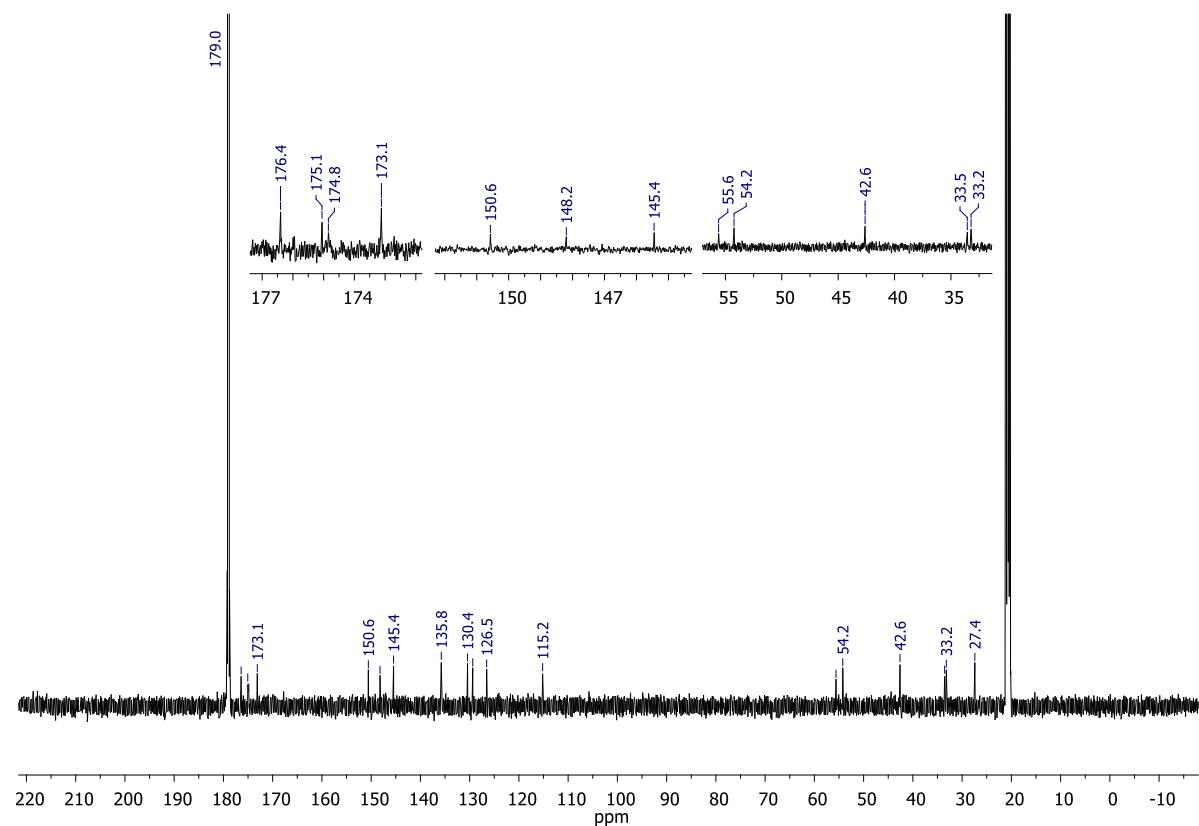


Glutathione–tetrazolo[1,5-c]quinazoline conjugate 6d

¹H-NMR (500 MHz, CD₃COOD) spectrum of compound 6d:

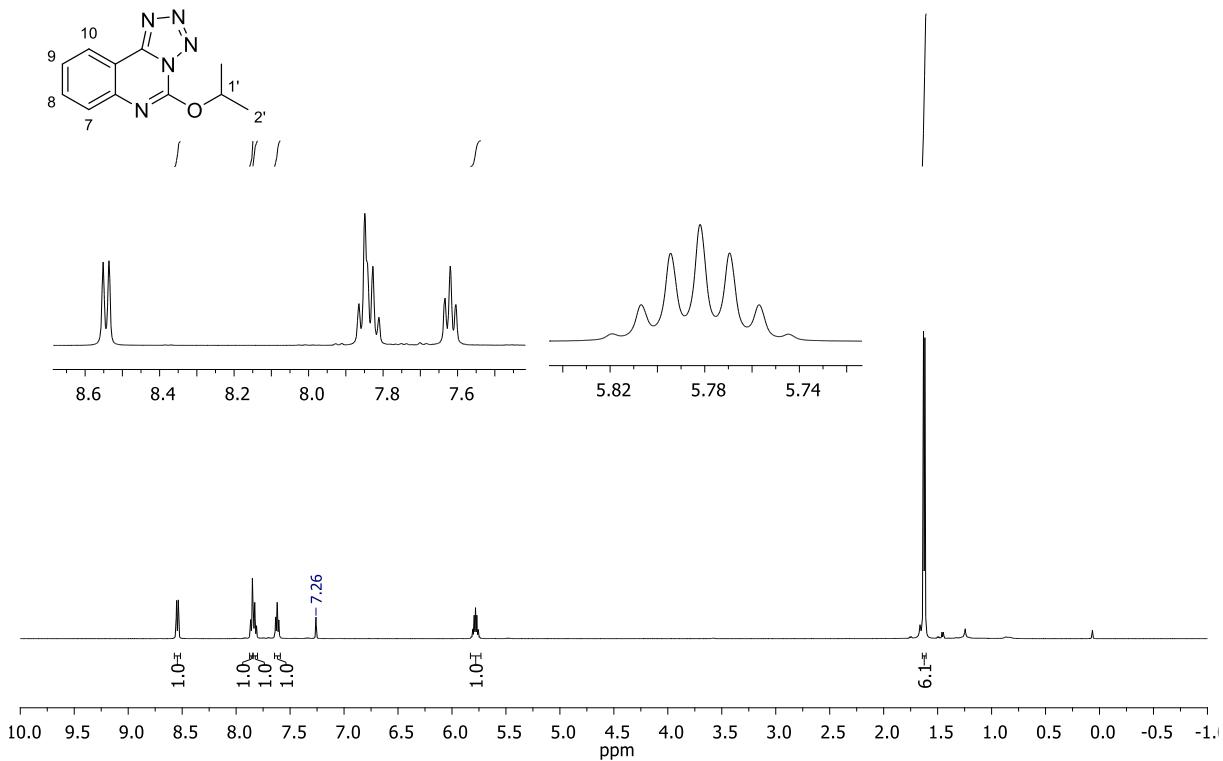


¹³C-NMR (125.7 MHz, CD₃COOD) spectrum of compound 6d:

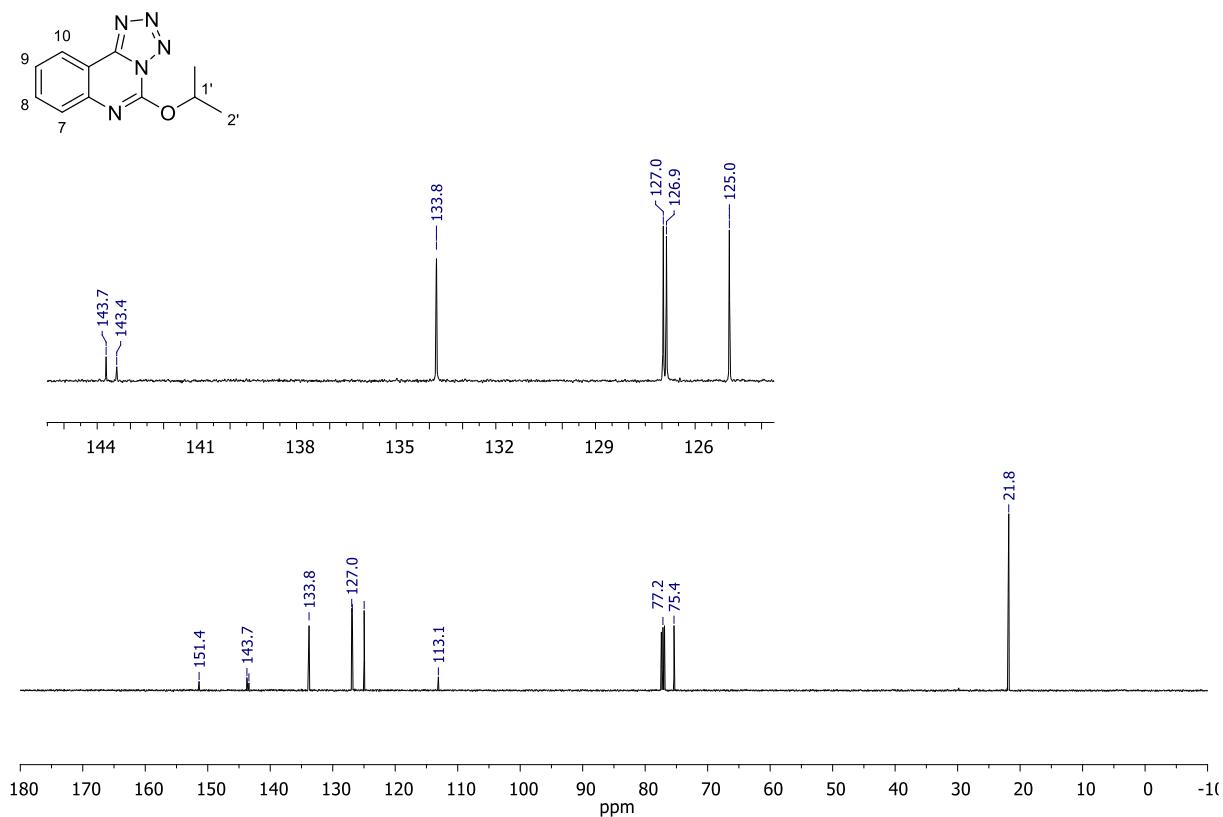


5-(Alkyloxy)tetrazolo[1,5-c]quinazolines

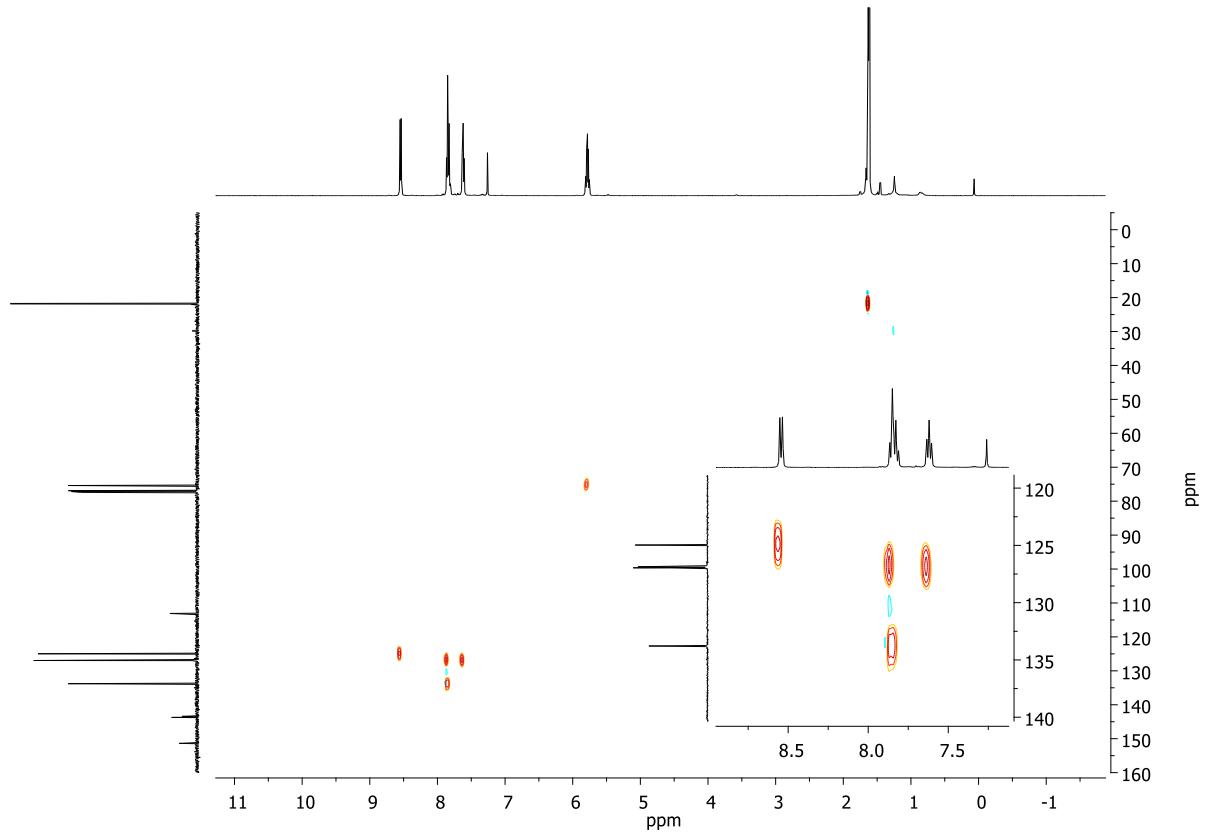
5-(Isopropoxy)tetrazolo[1,5-c]quinazoline (7a)
 $^1\text{H-NMR}$ (500 MHz, CDCl_3) spectrum of compound 7a:



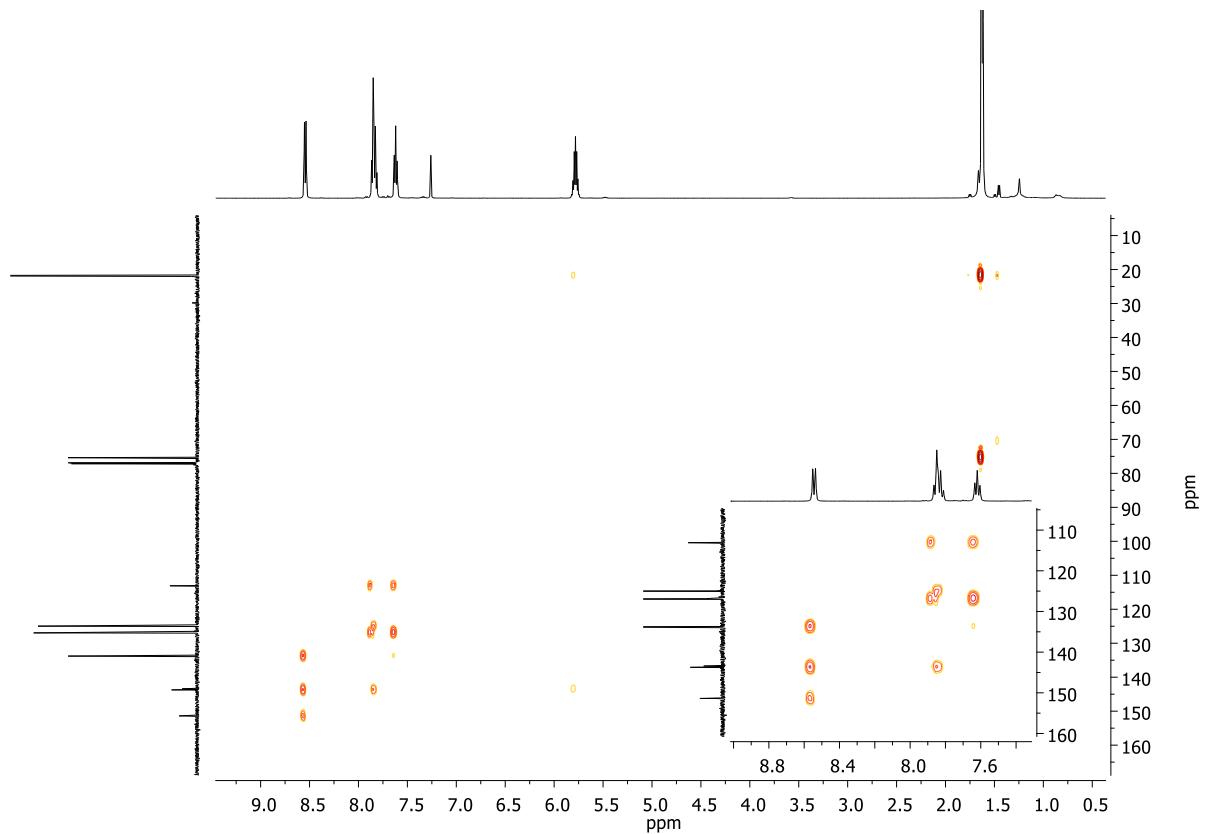
$^{13}\text{C-NMR}$ (125.7 MHz, CDCl_3) spectrum of compound 7a:



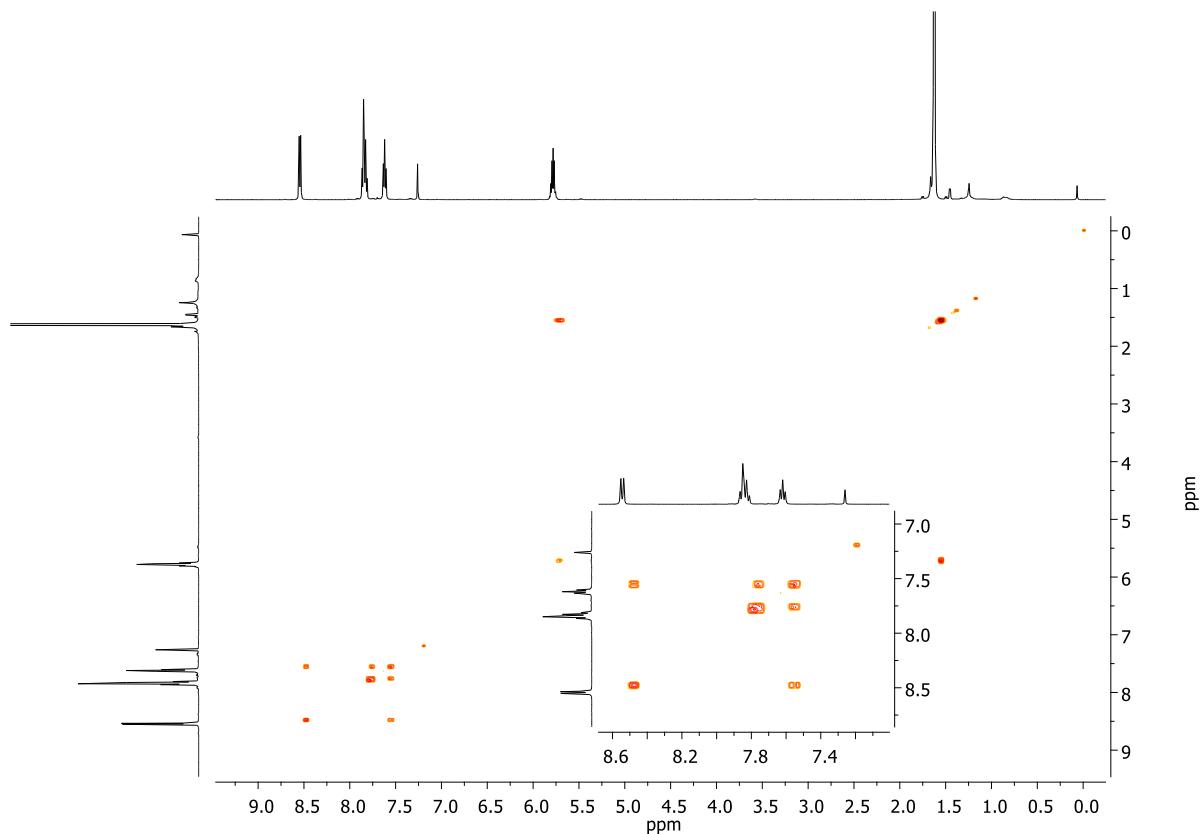
HSQC spectrum of compound 7a:



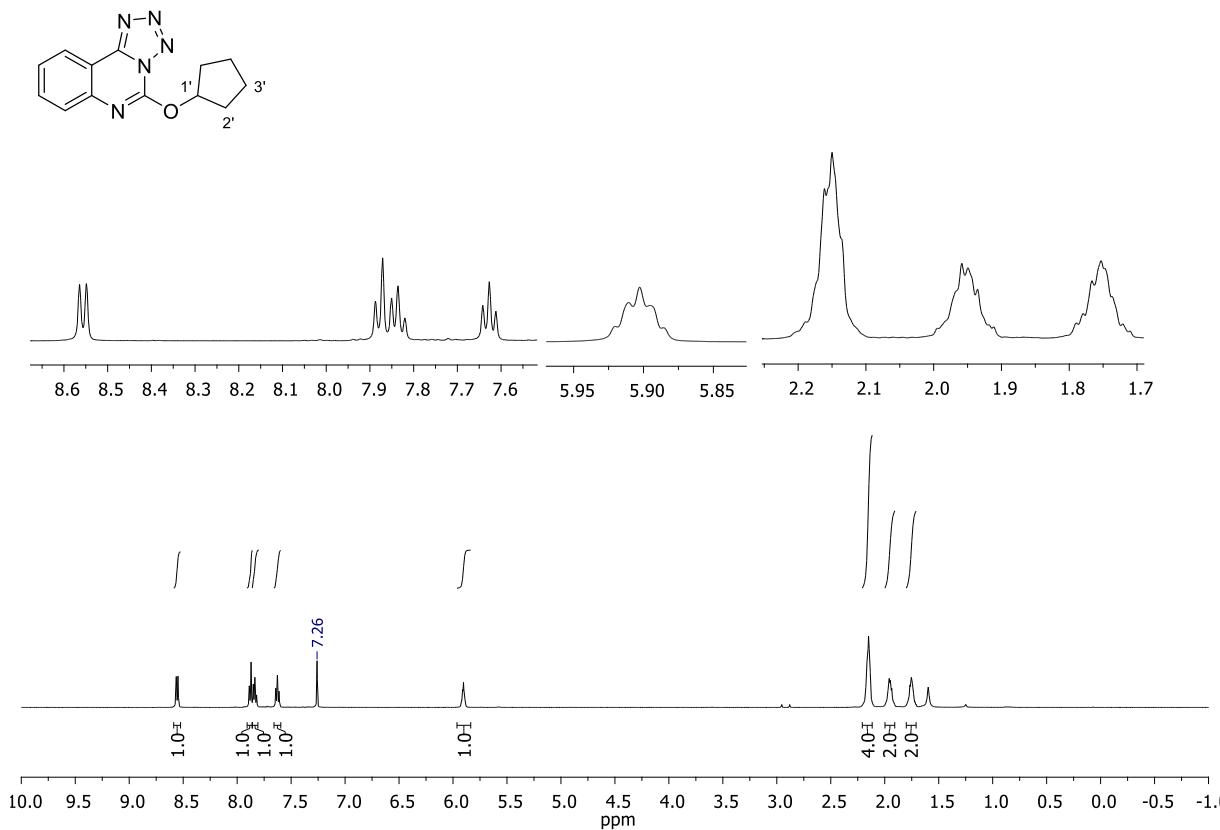
HMBC spectrum of compound 7a:



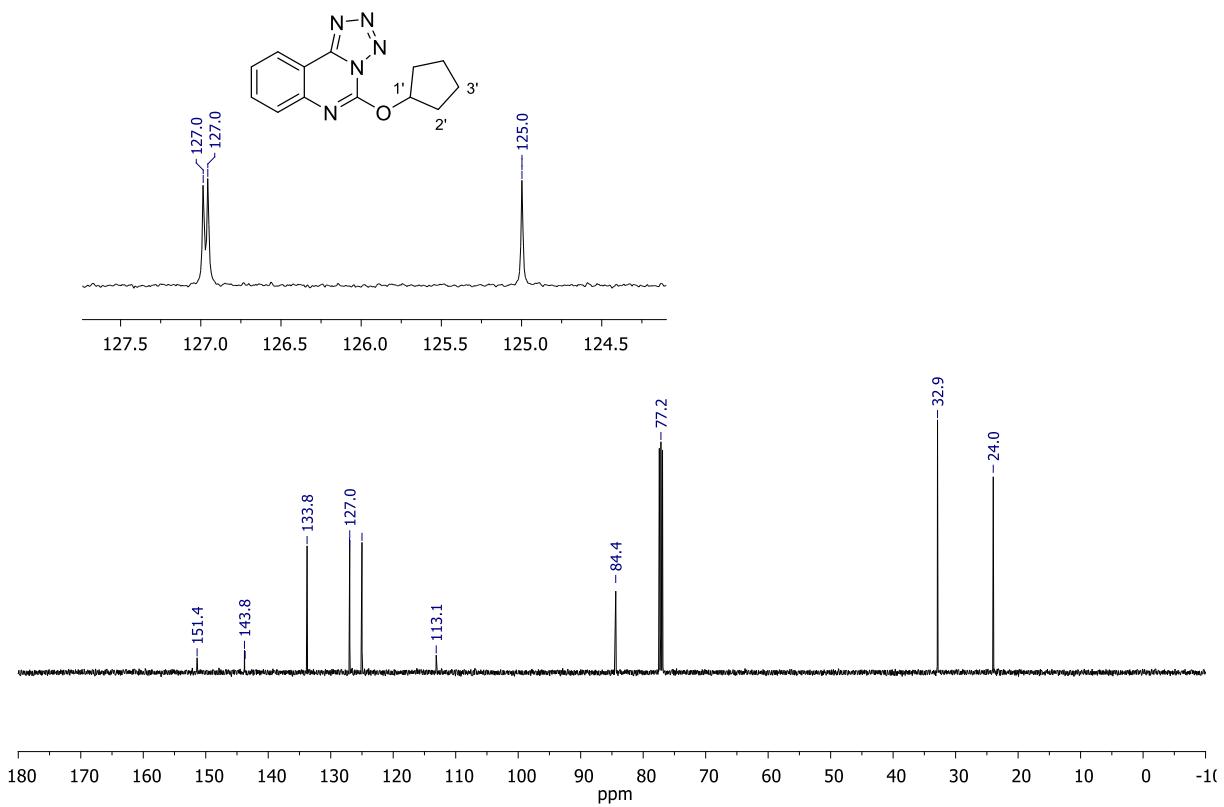
COSY spectrum of compound 7a:



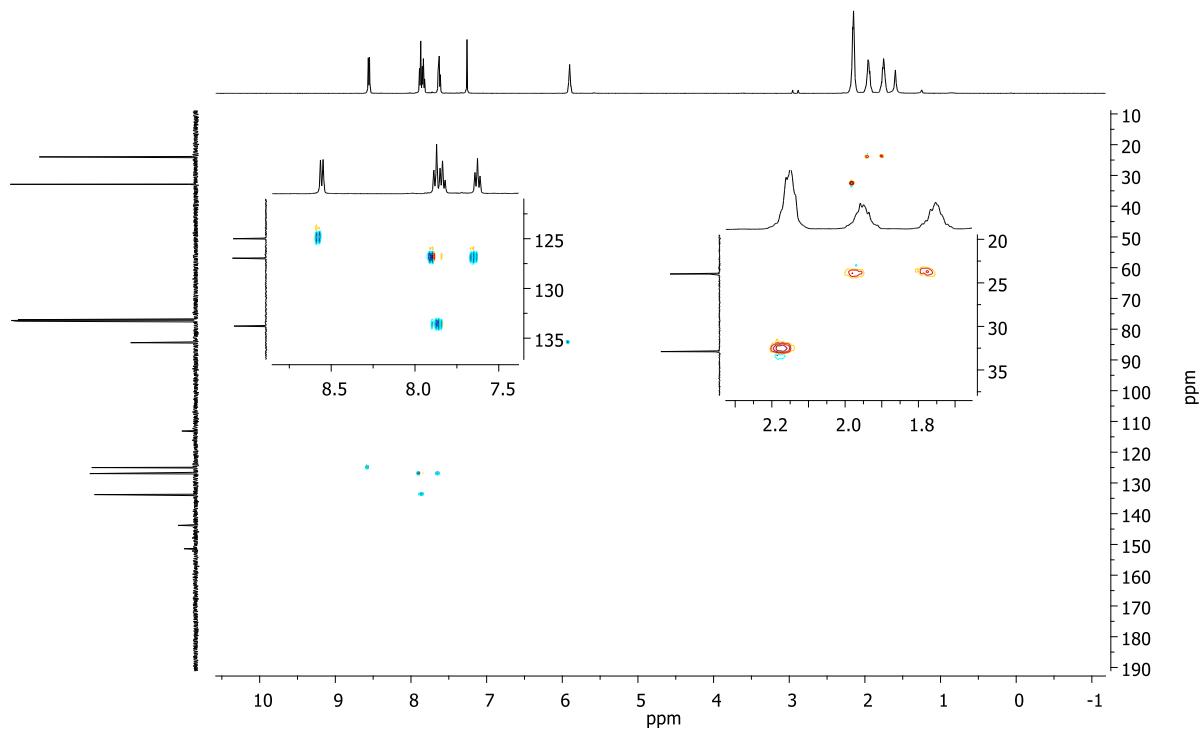
5-(Cyclopentyloxy)tetrazolo[1,5-c]quinazoline (7b)



¹³C-NMR (125.7 MHz, CDCl₃) spectrum of compound 7b:

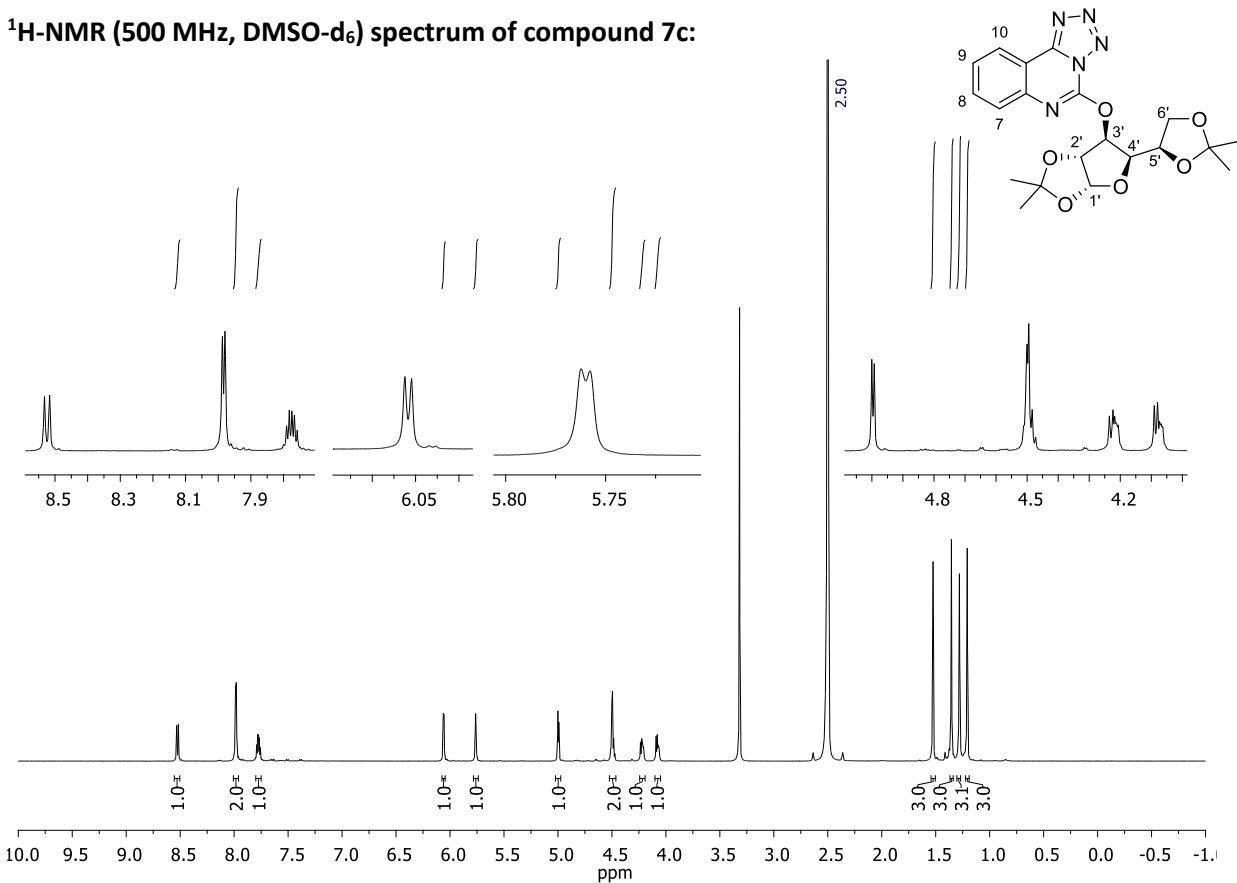


HSQC spectrum of compound 7b:

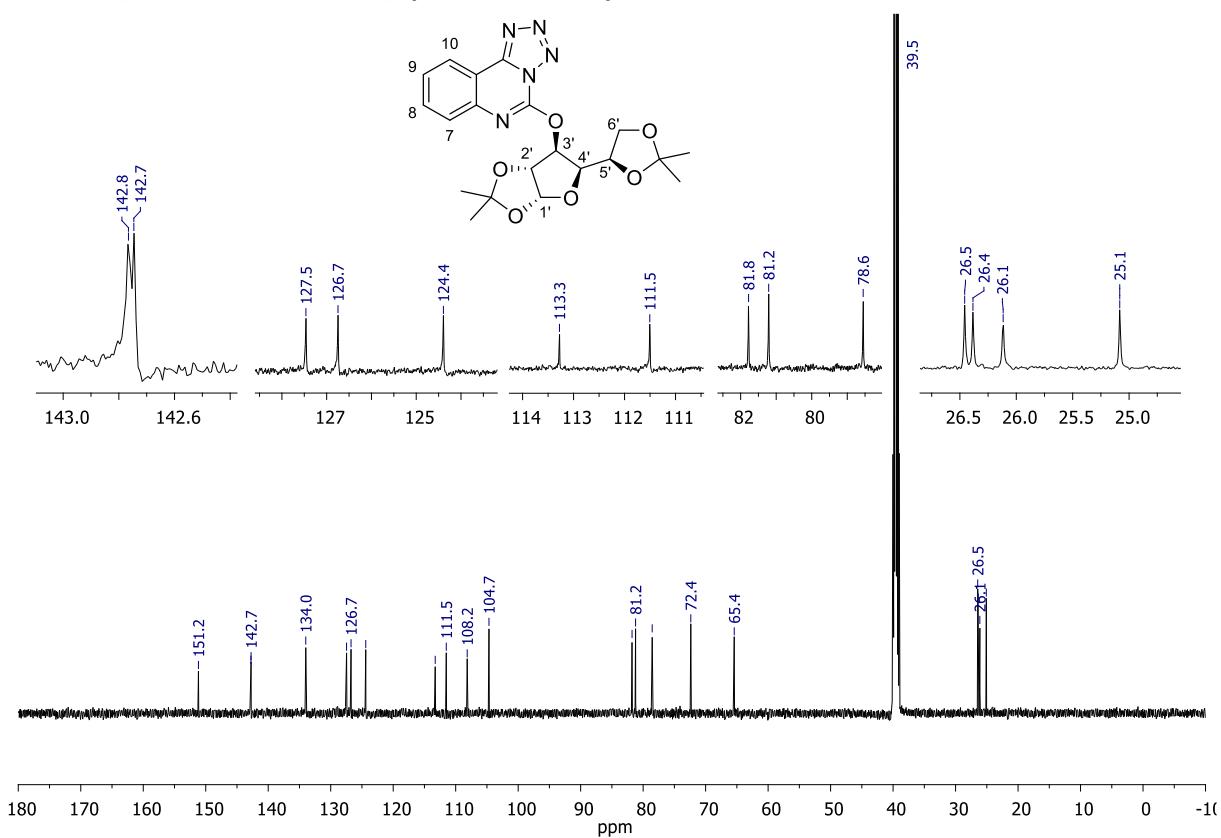


Diacetone glucose–quinazoline conjugate 7c

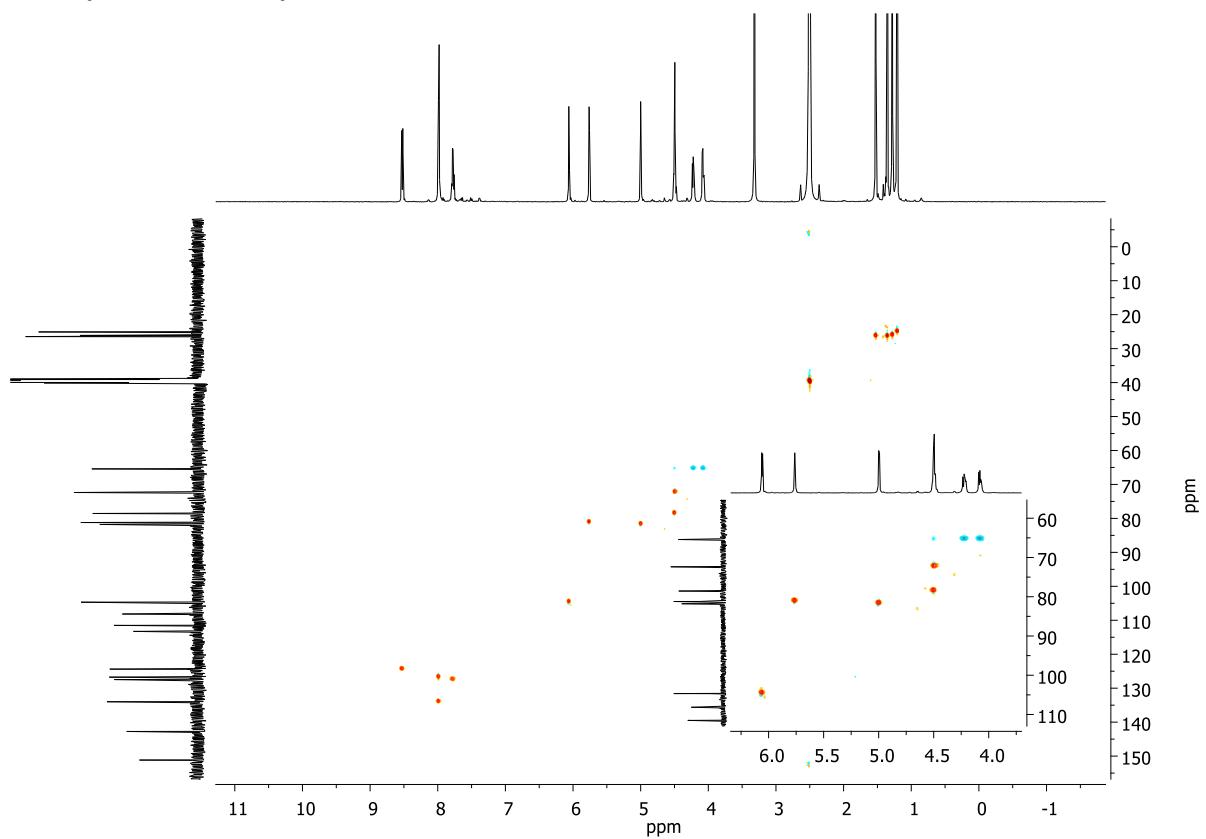
^1H -NMR (500 MHz, DMSO- d_6) spectrum of compound 7c:



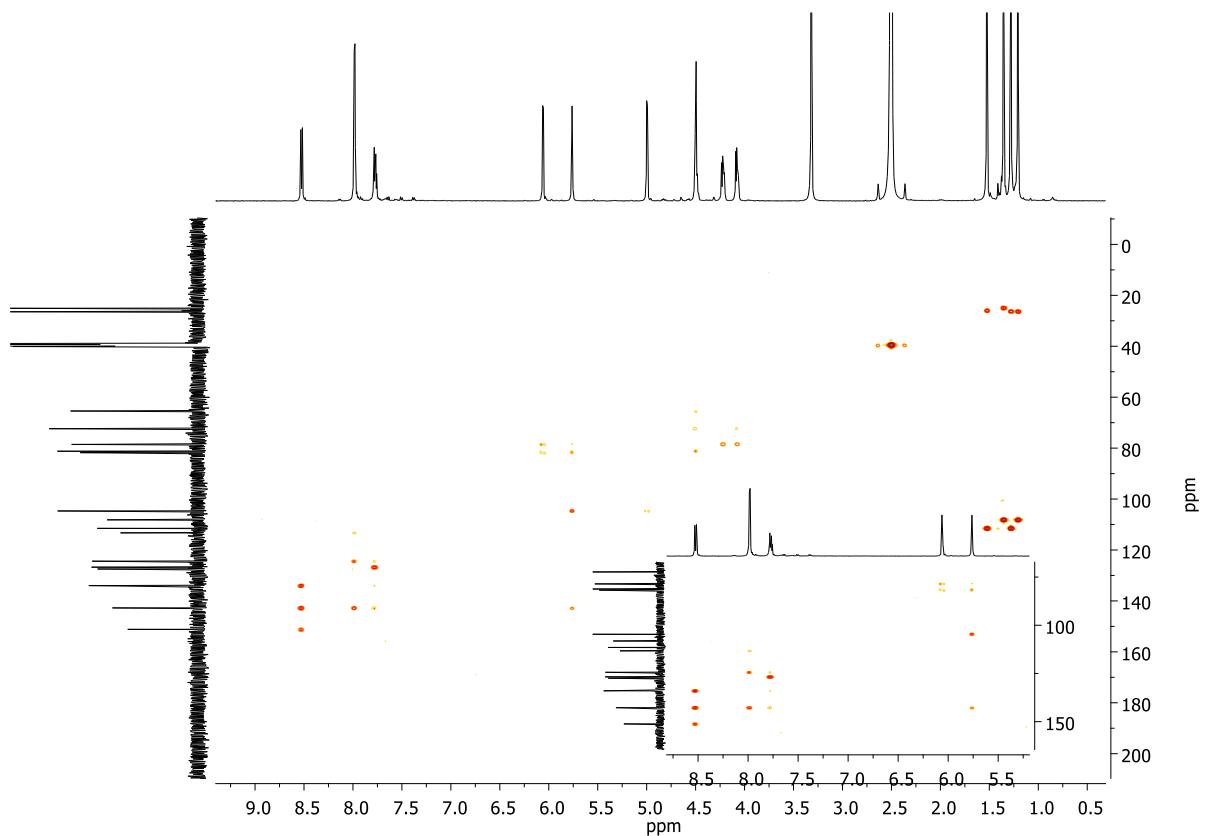
^{13}C -NMR (125.7 MHz, DMSO- d_6) spectrum of compound 7c:



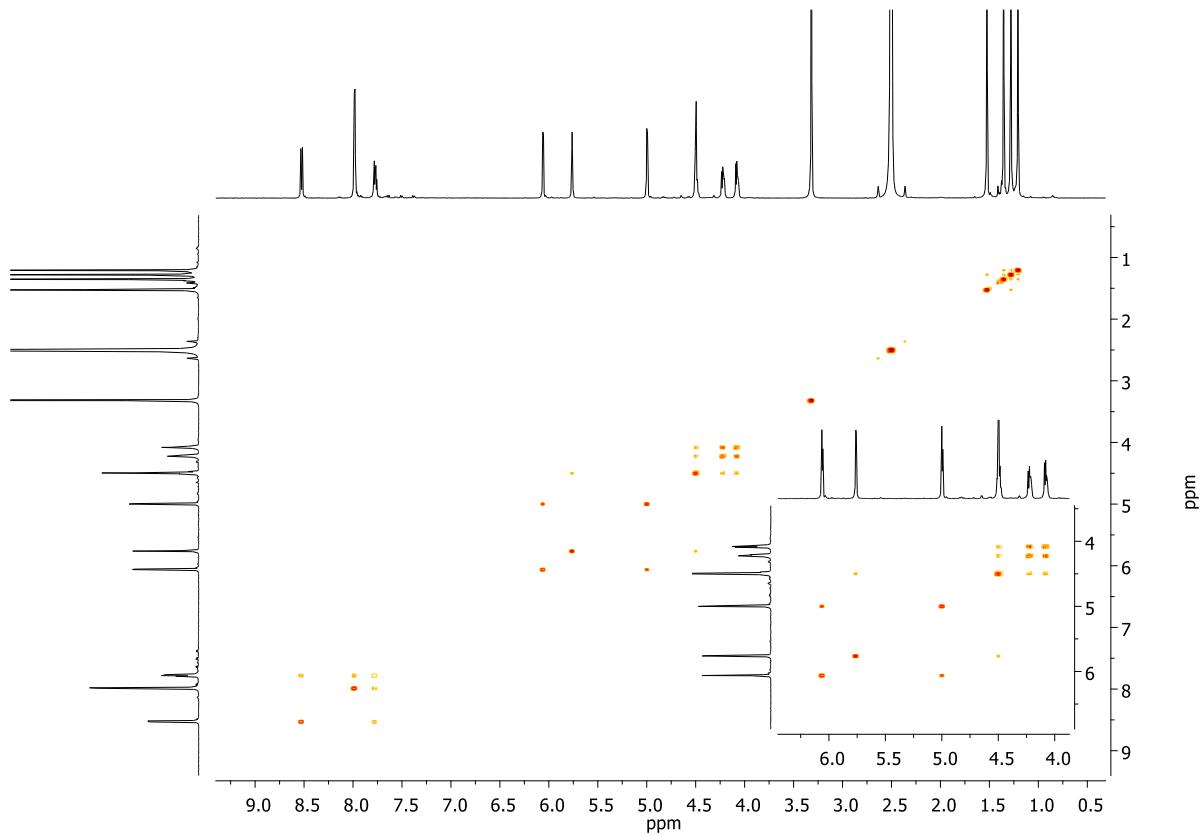
HSQC spectrum of compound 7c:



HMBC spectrum of compound 7c:



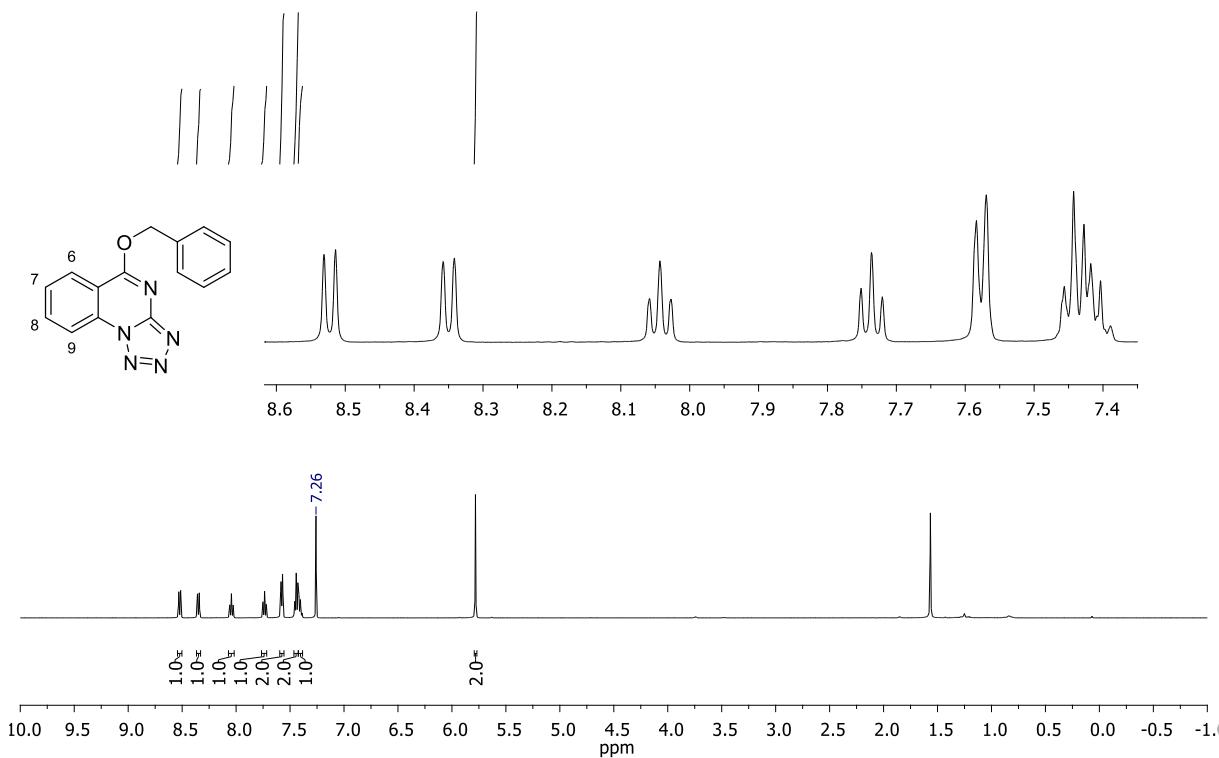
COSY spectrum of compound 7c:



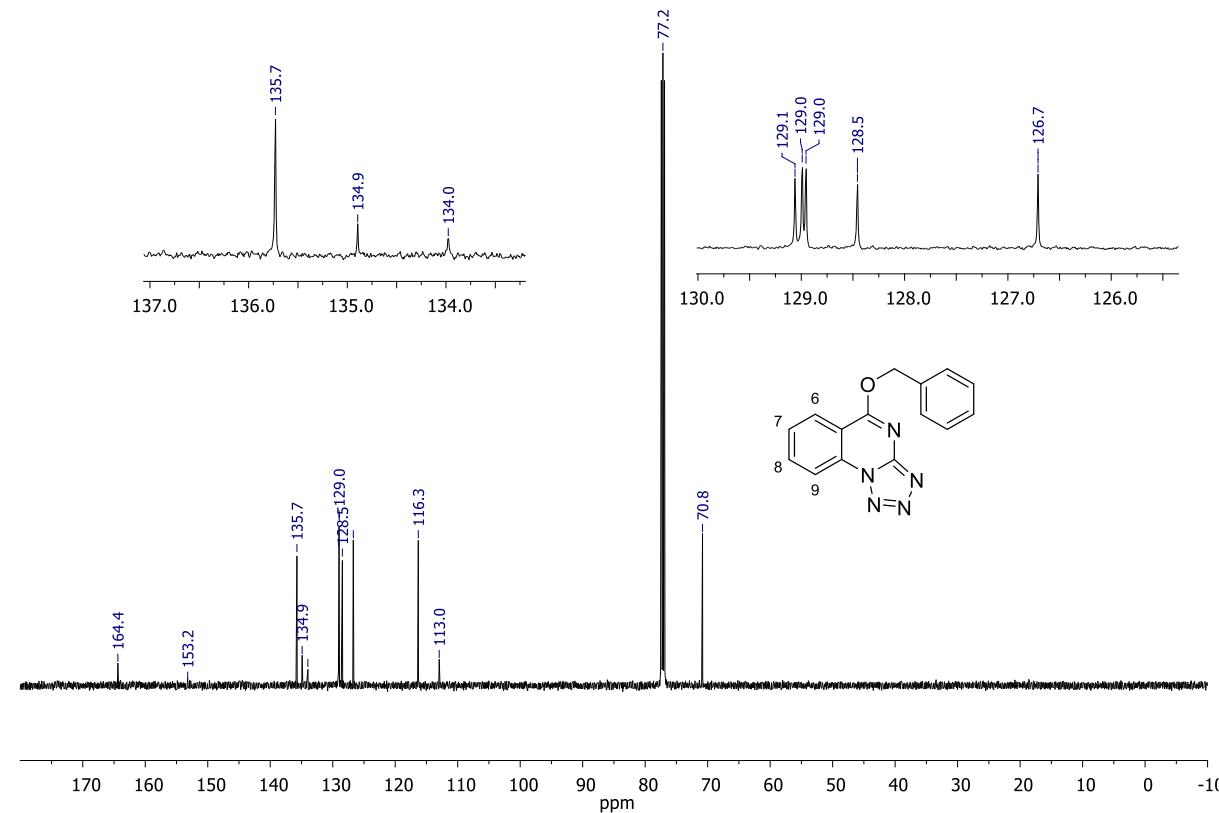
5-(Alkyloxy)tetrazolo[1,5- α]quinazolines

5-(BenzylOxy)tetrazolo[1,5- α]quinazoline (9a)

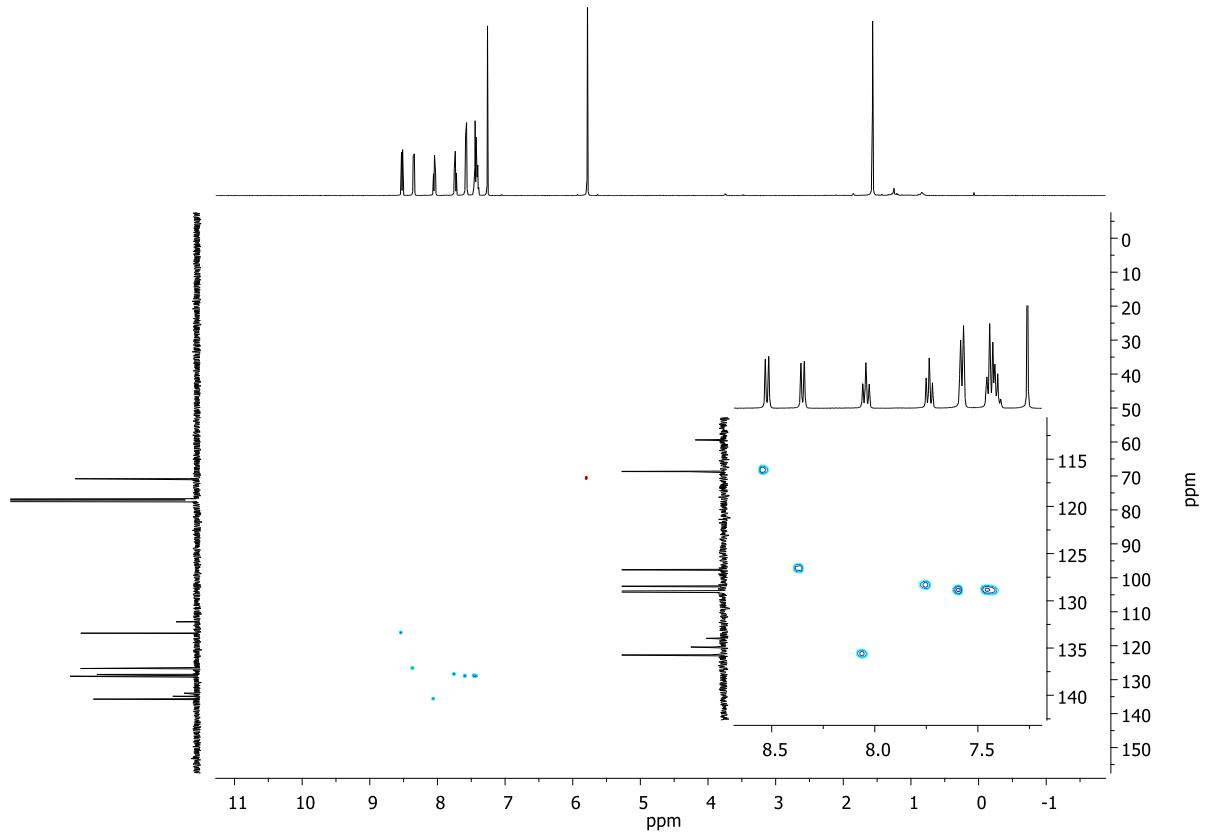
¹H-NMR (500 MHz, CDCl₃) spectrum of compound 9a:



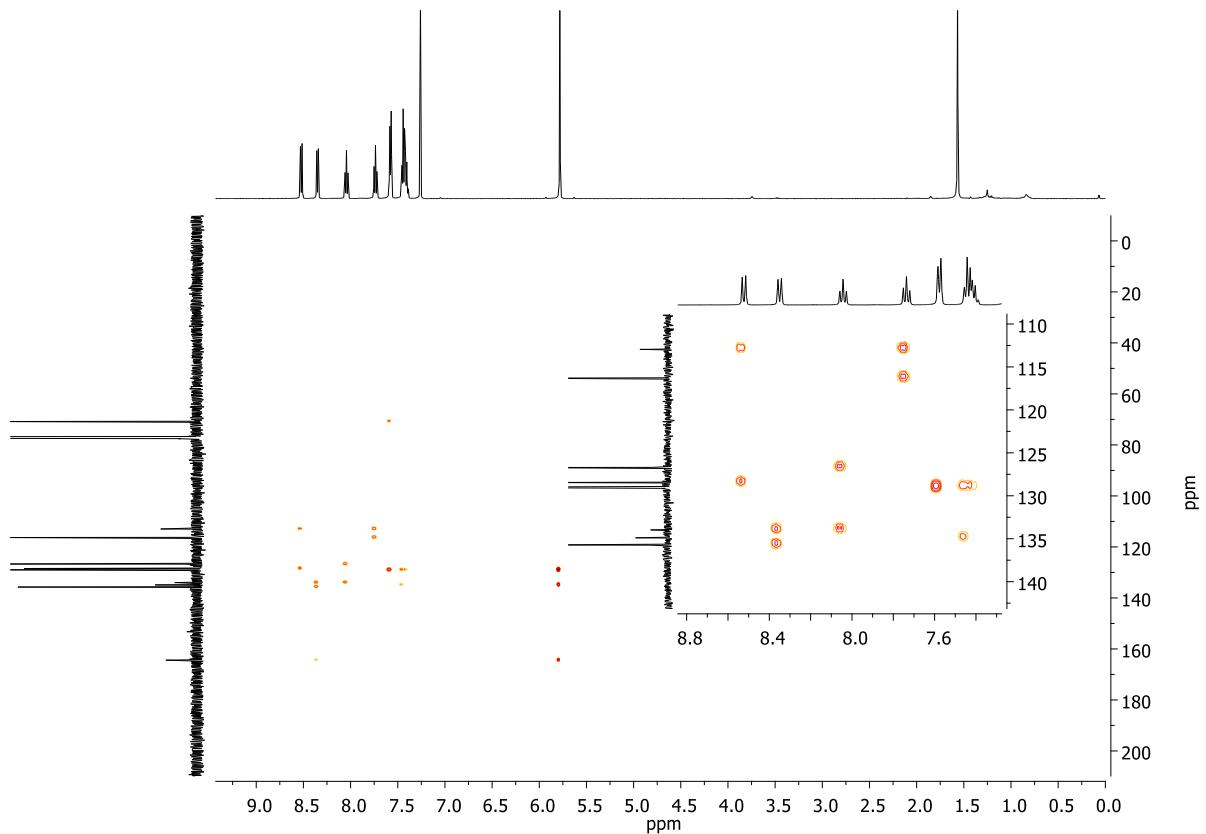
¹³C-NMR (125.7 MHz, CDCl₃) spectrum of compound 9a:



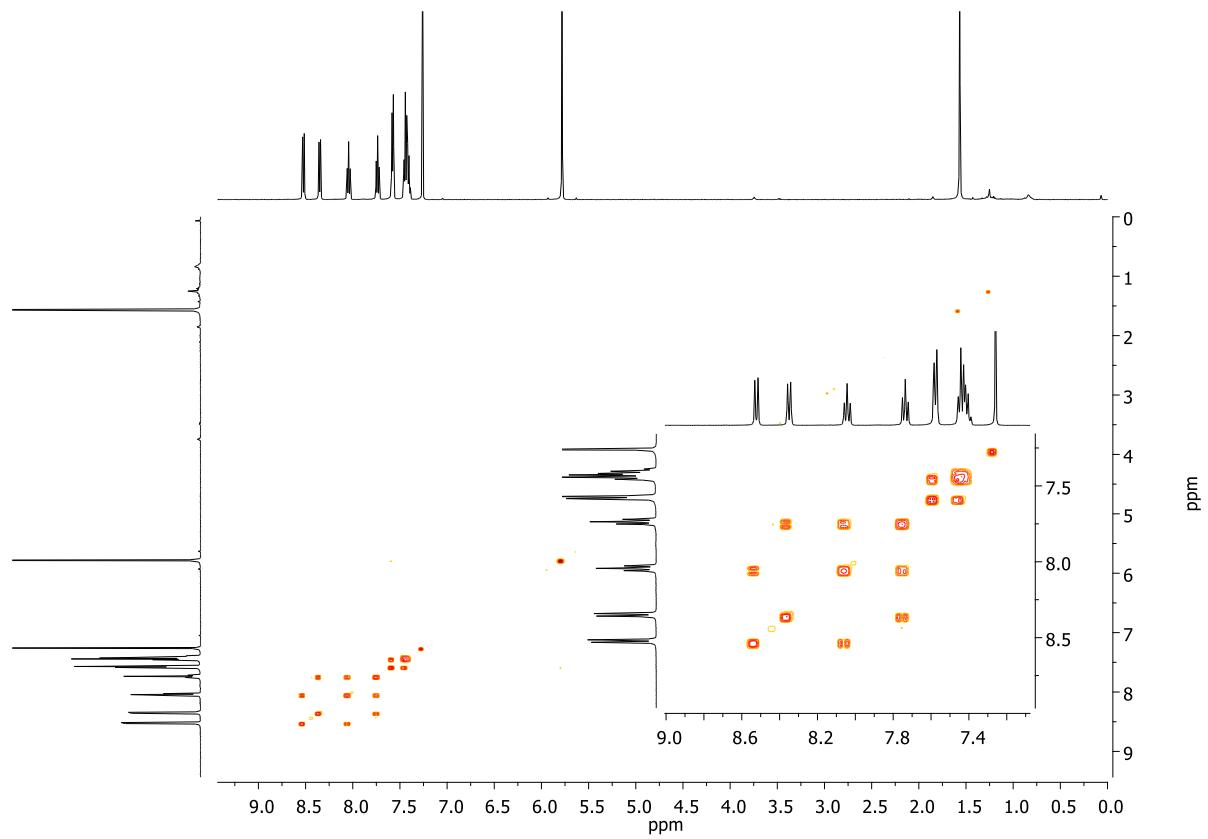
HSQC spectrum of compound 9a:



HMBC spectrum of compound 9a:



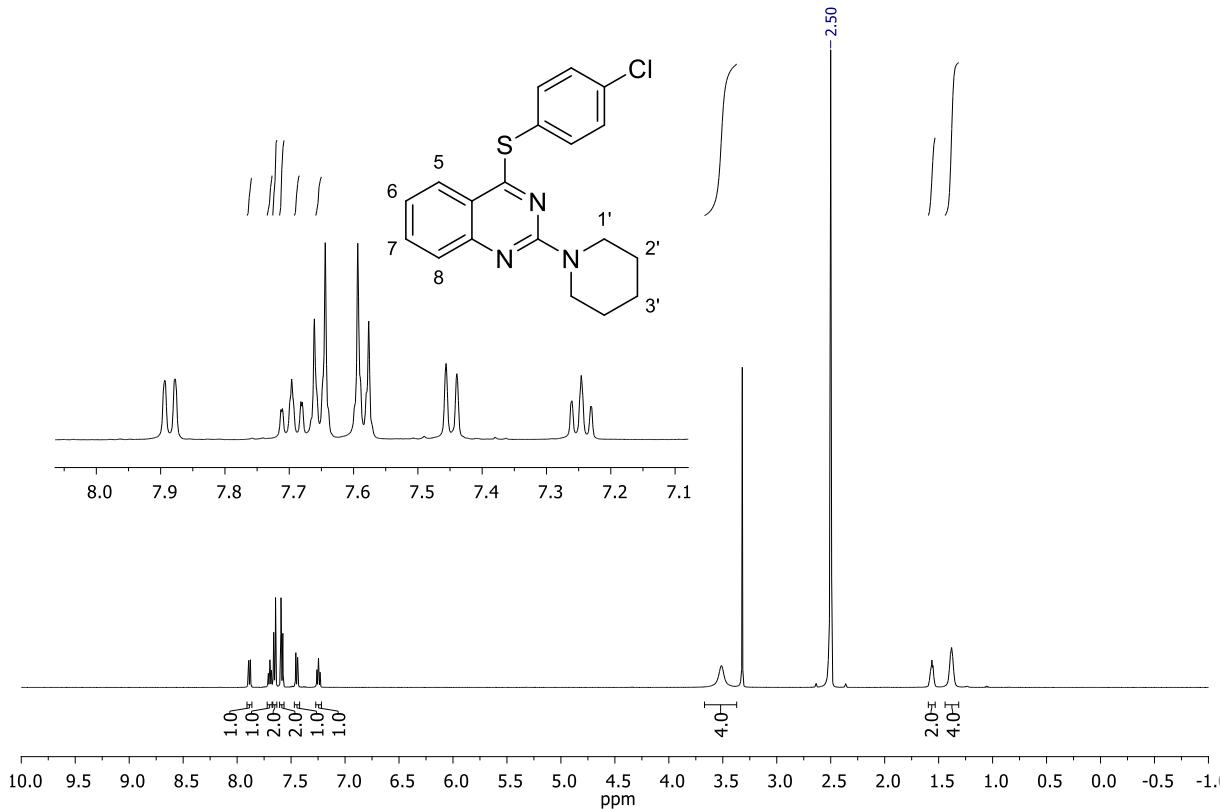
COSY spectrum of compound 9a:



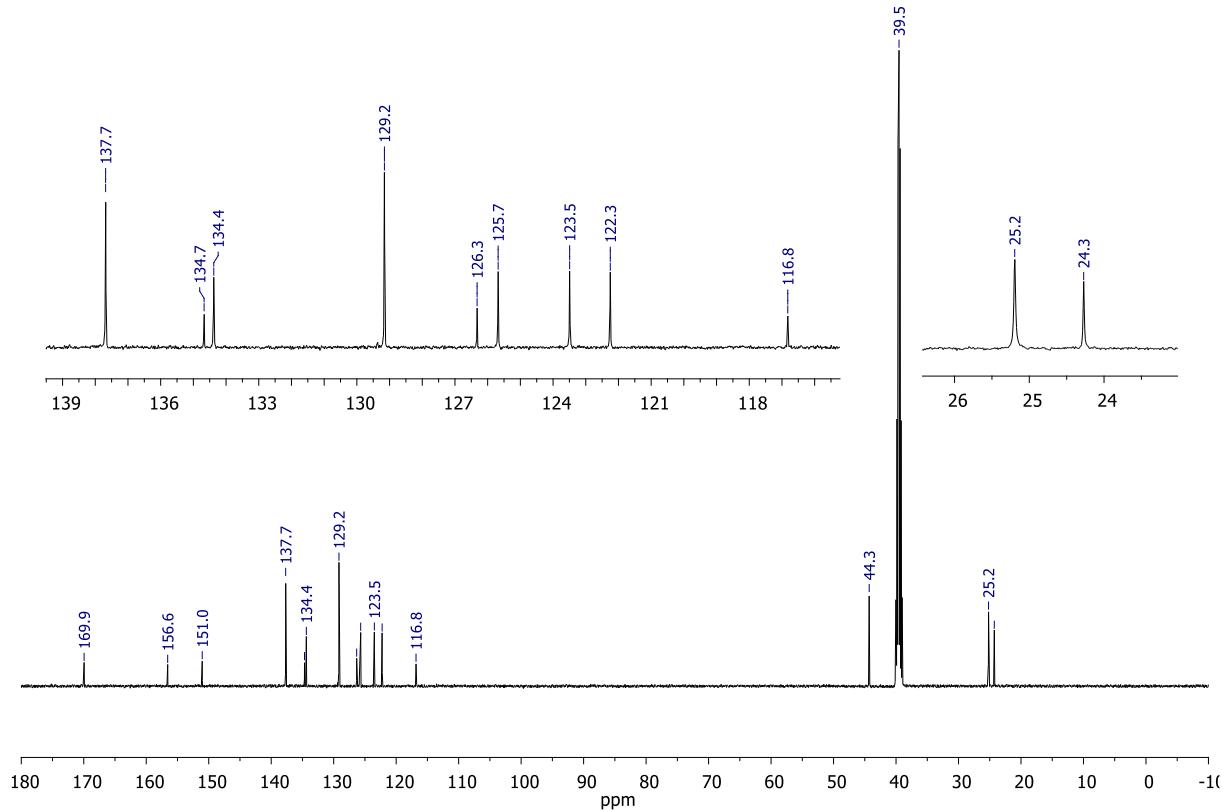
4-(Arylthio)-2-(piperidin-1-yl)quinazolines

4-[(4-Chlorophenyl)thio]-2-(piperidin-1-yl)quinazoline (5a)

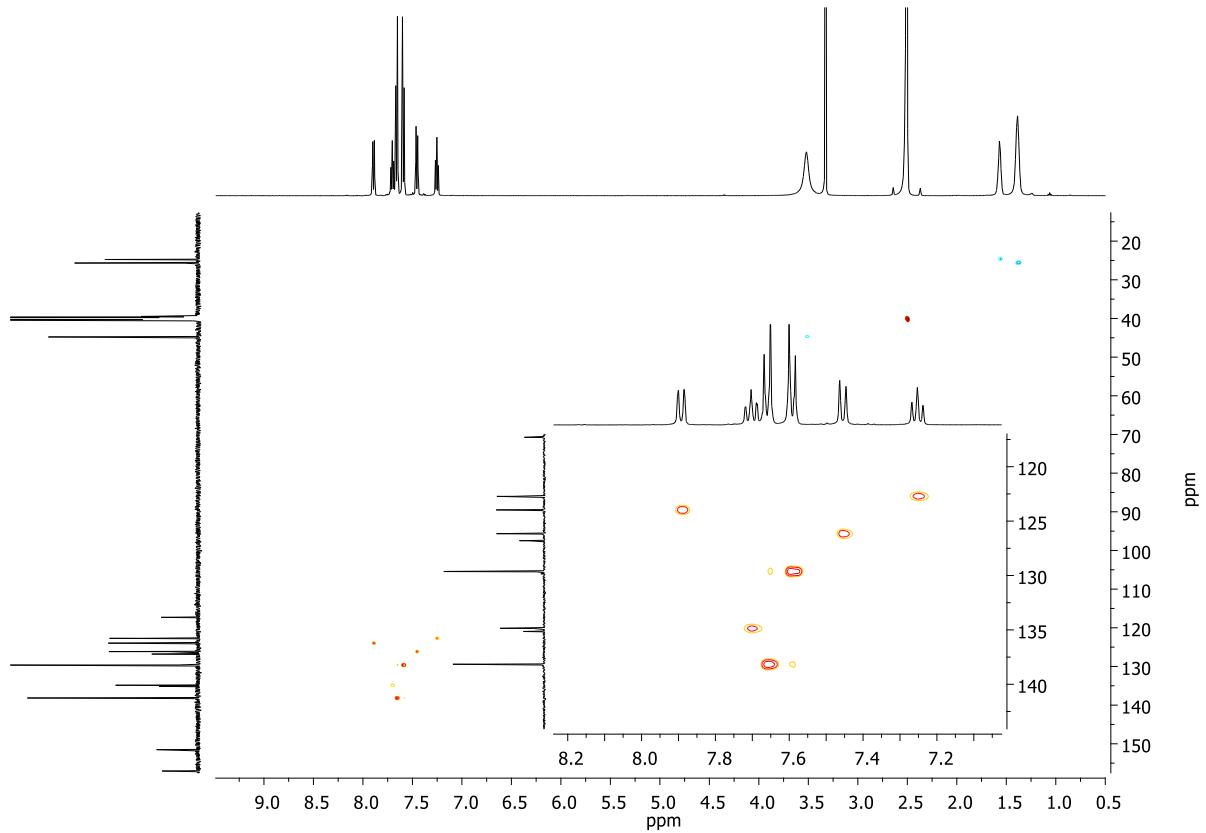
¹H-NMR (500 MHz, DMSO-d₆) spectrum of compound 5a:



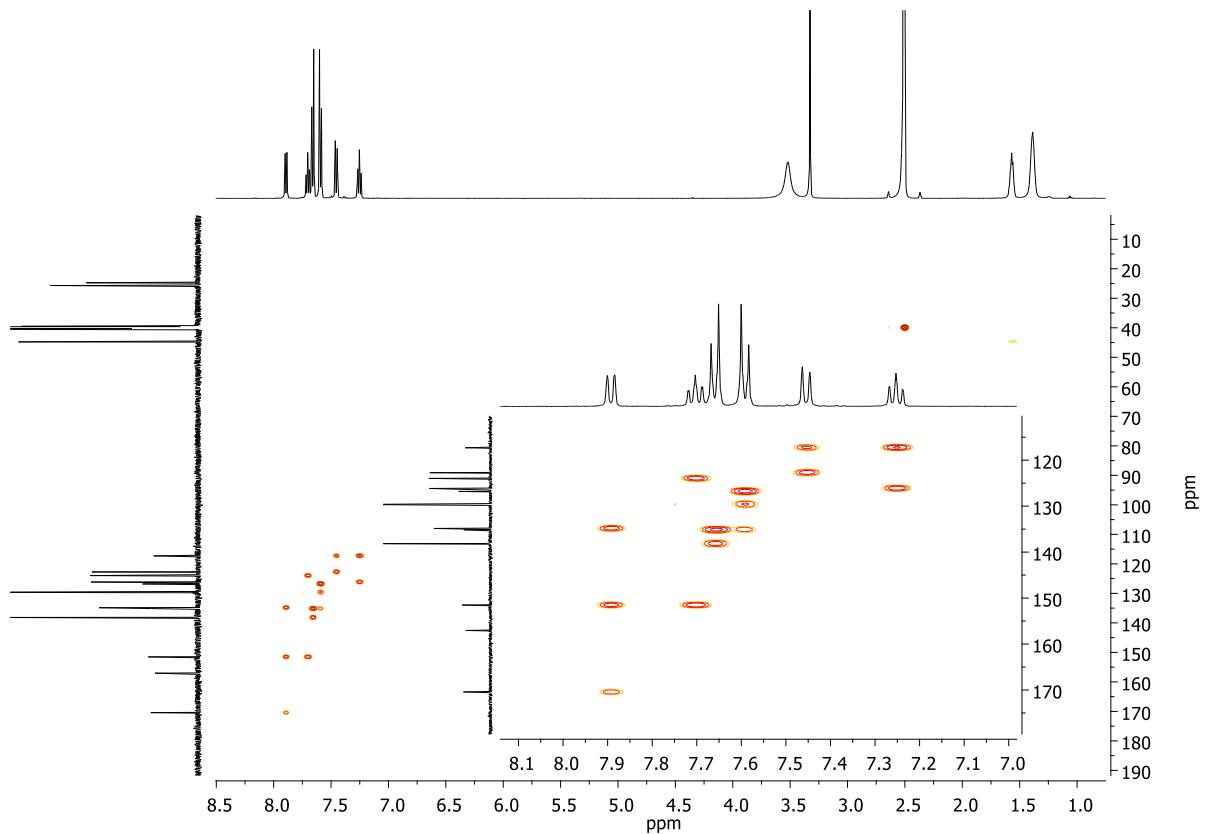
¹³C-NMR (125.7 MHz, DMSO-d₆) spectrum of compound 5a:



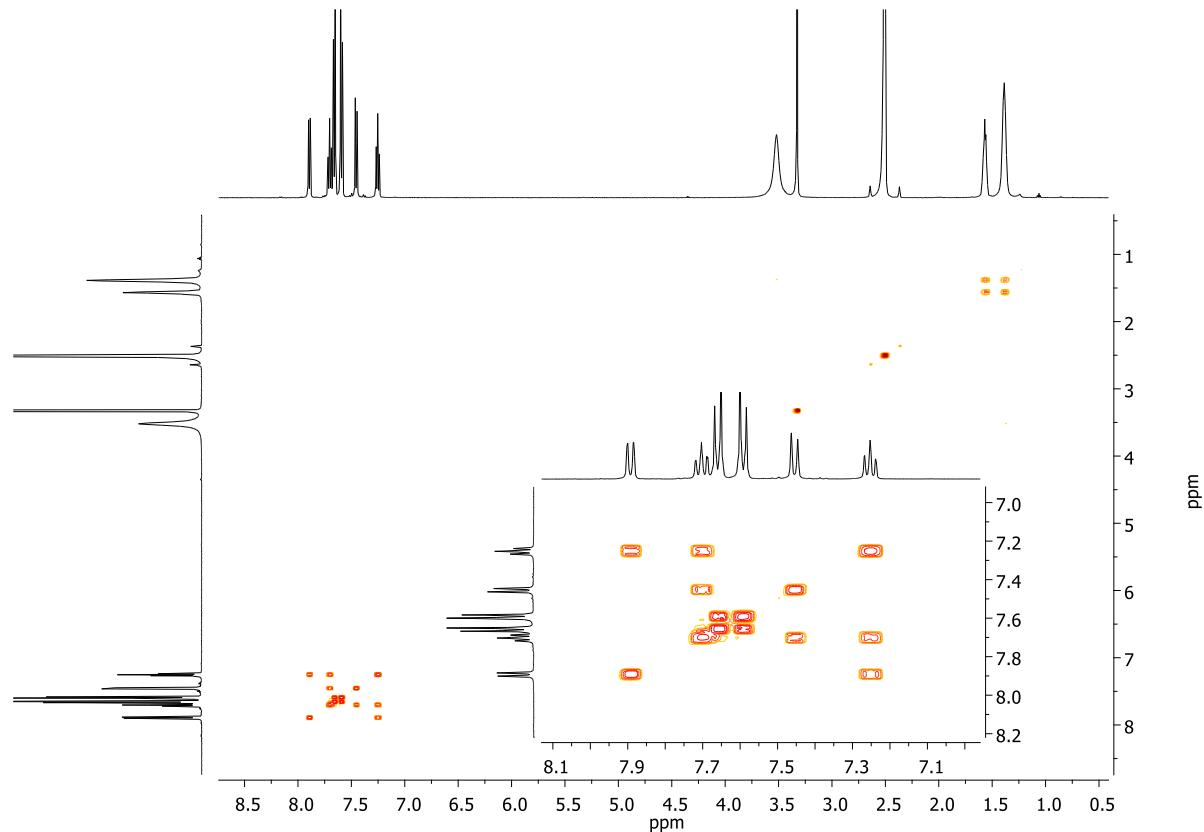
HSQC spectrum of compound 5a:



HMBC spectrum of compound 5a:

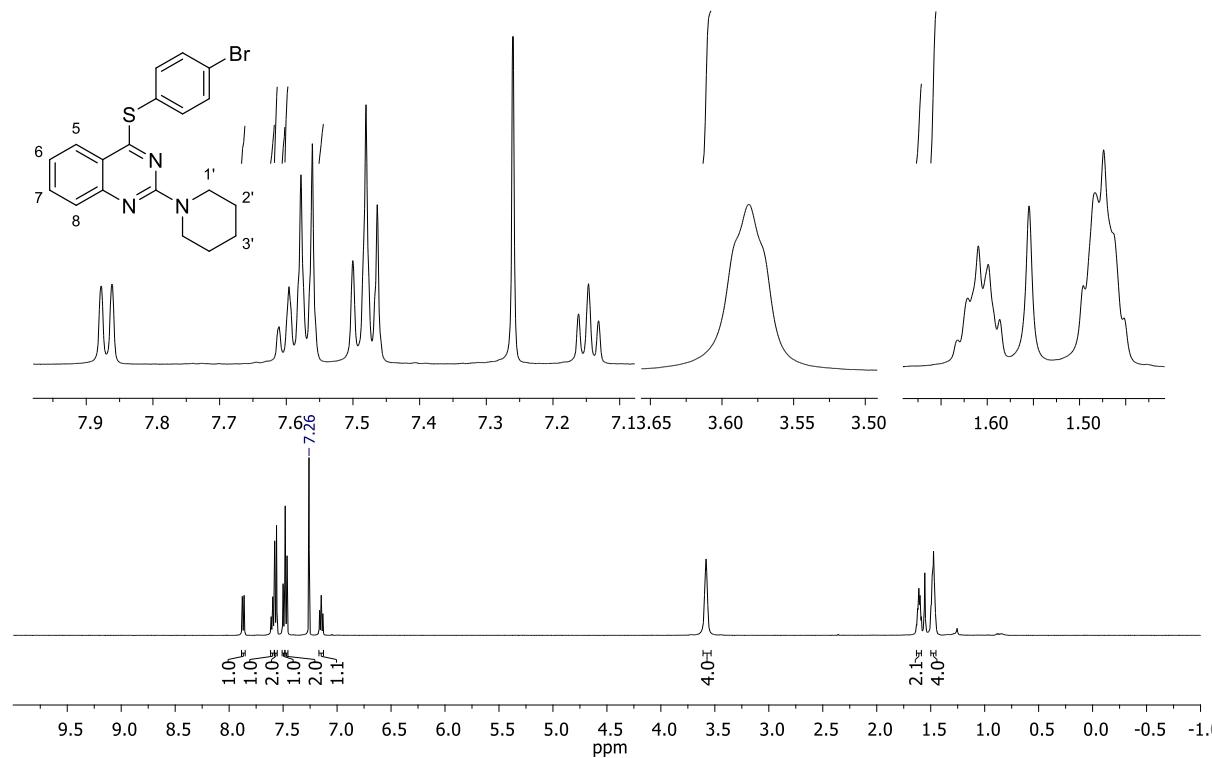


COSY spectrum of compound 5a:

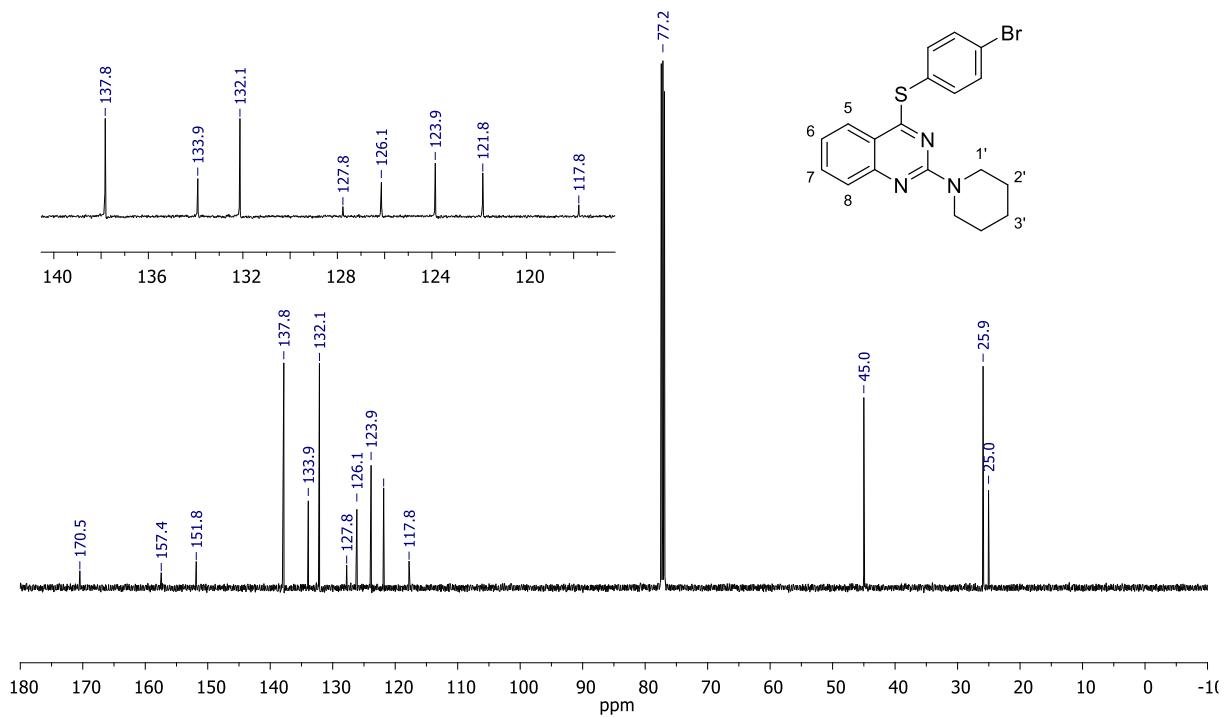


4-[(4-Bromophenyl)thio]-2-(piperidin-1-yl)quinazoline (5b)

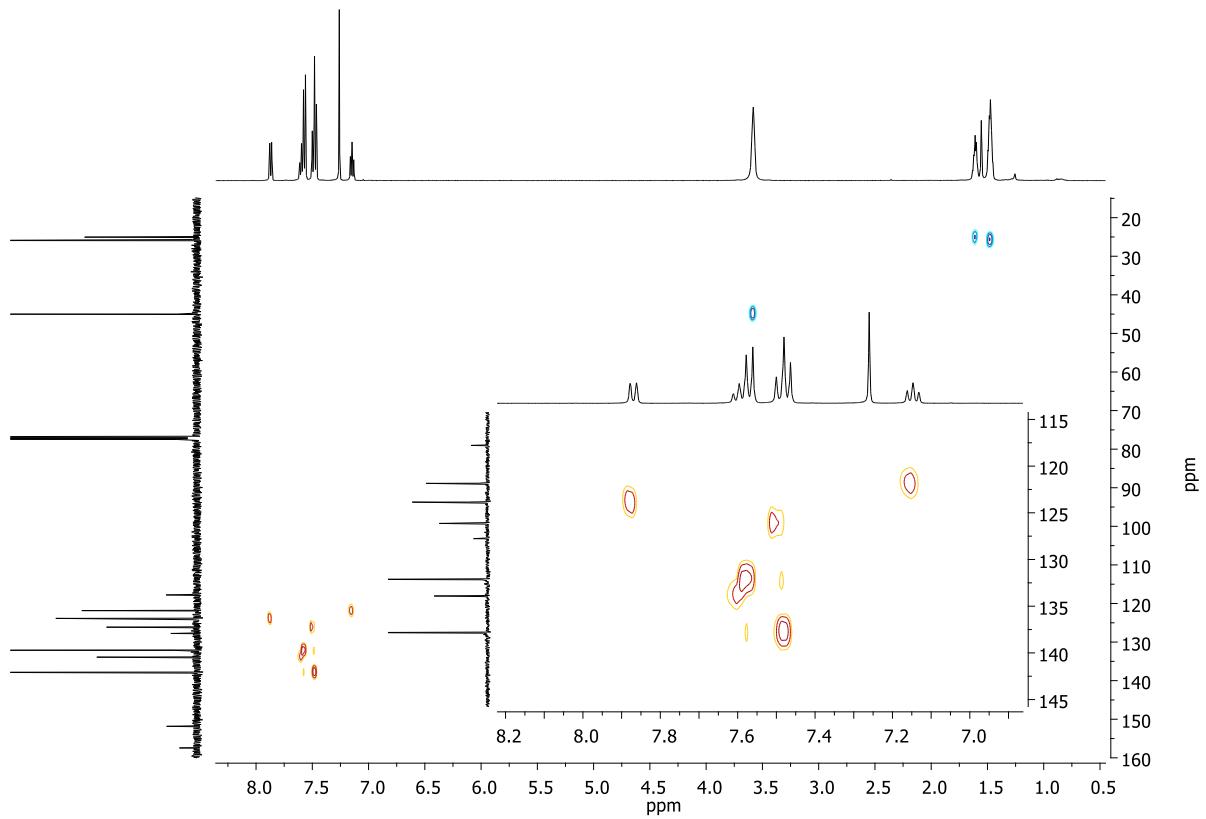
^1H -NMR (500 MHz, CDCl_3) spectrum of compound 5b:



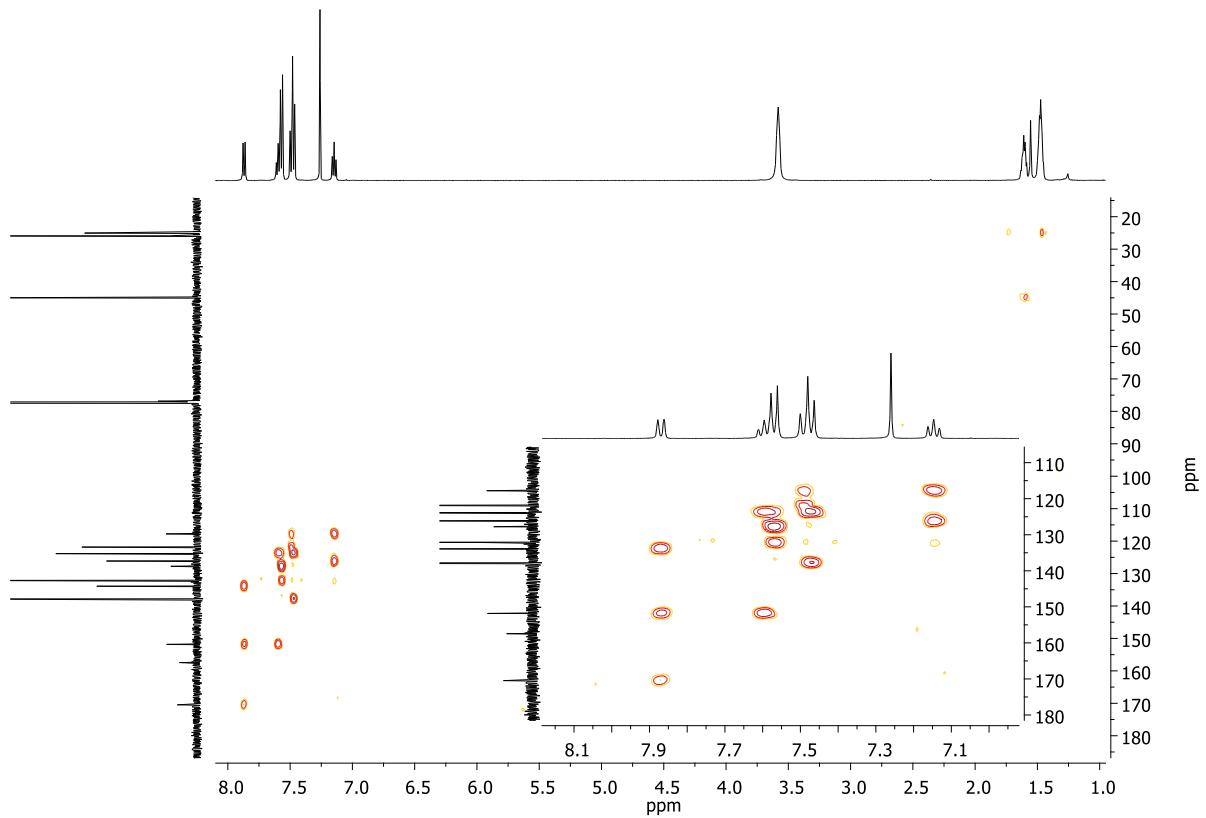
¹³C-NMR (125.7 MHz, CDCl₃) spectrum of compound 5b:



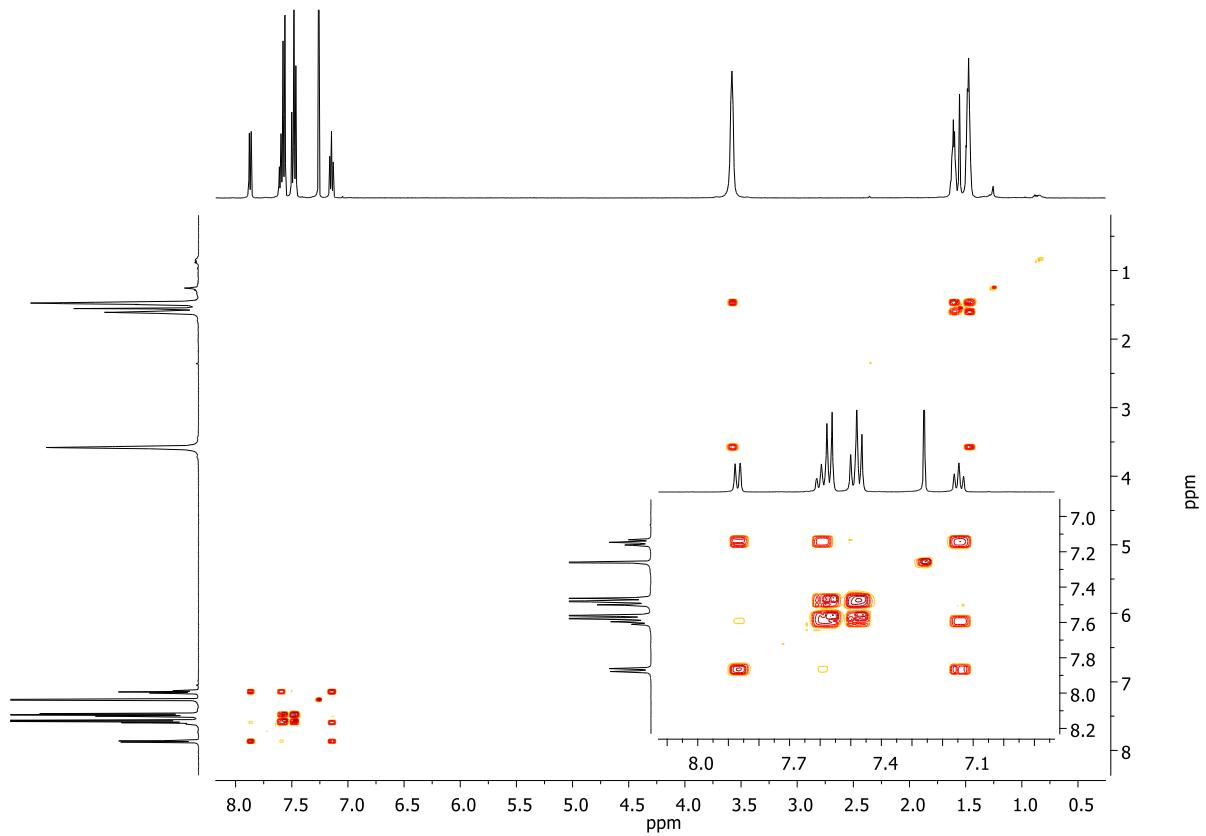
HSQC spectrum of compound 5b:



HMBC spectrum of compound 5b:



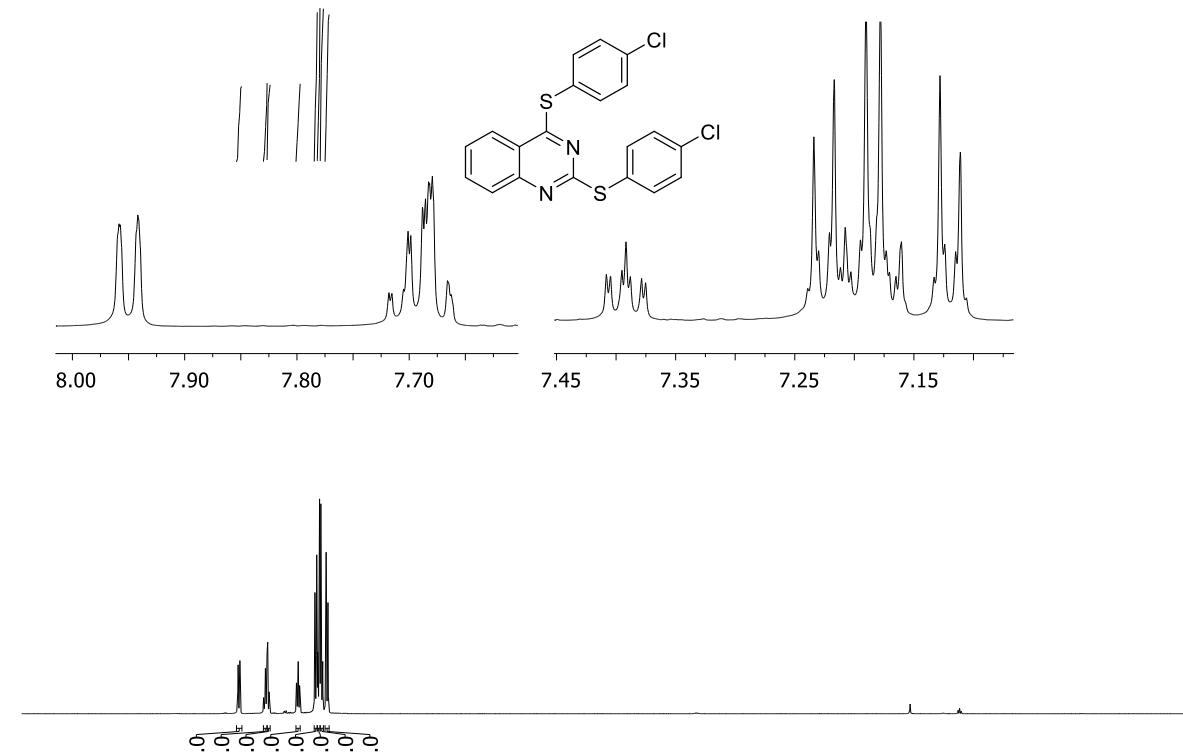
COSY spectrum of compound 5b:



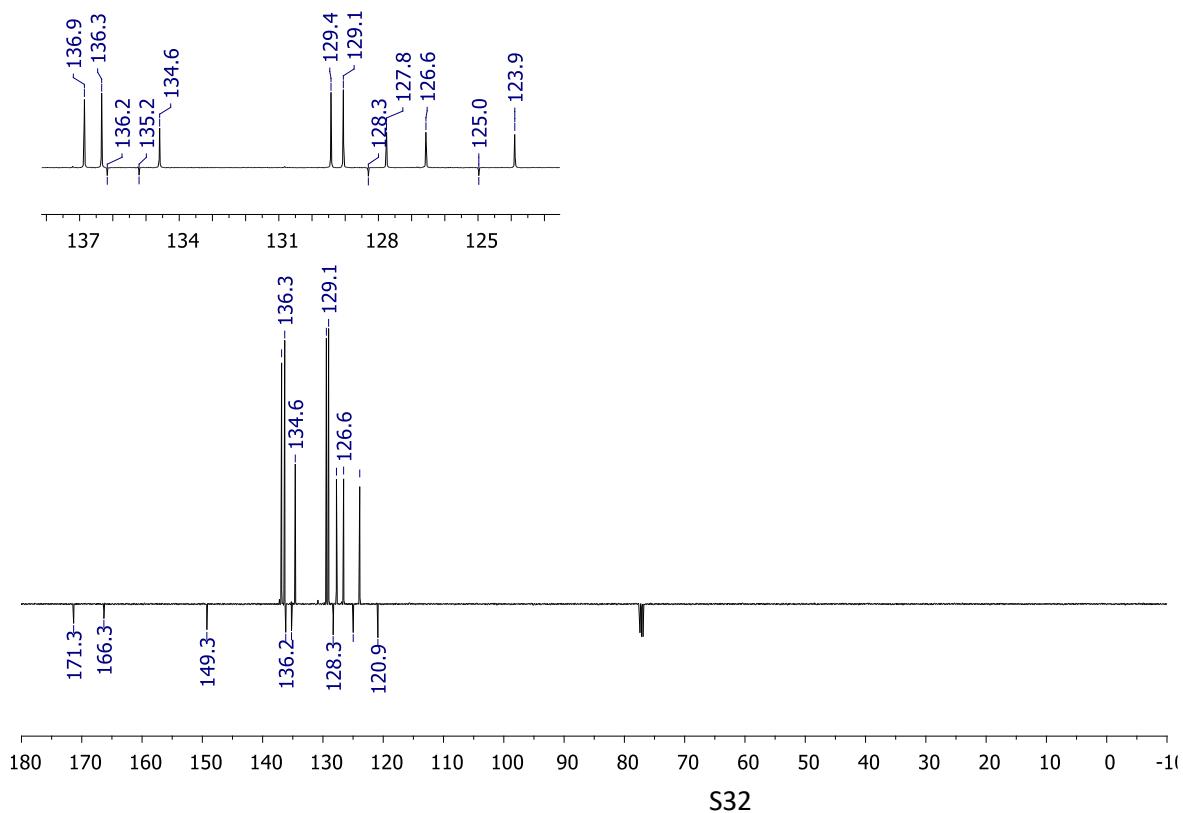
2,4-Bis-(arylthio)quinazolines

2,4-Bis-[4-chlorophenyl]thio]quinazoline (12a)

¹H NMR (500 MHz, CDCl₃) spectrum of compound 12a:

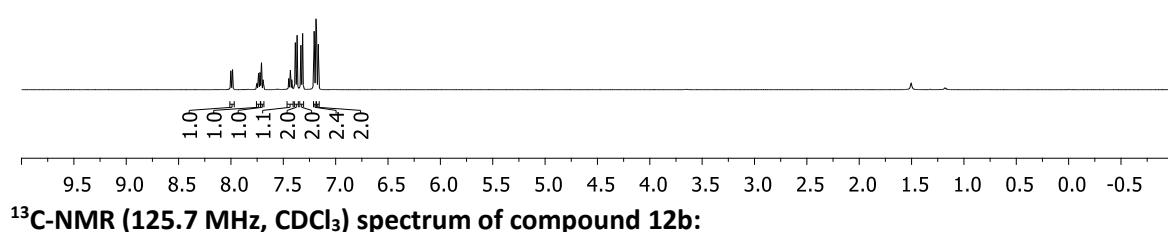
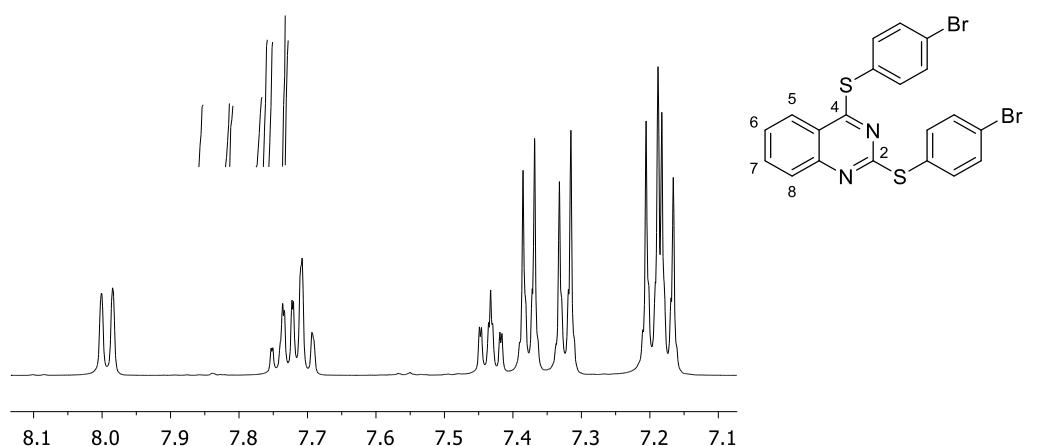


¹³C-NMR (125.7 MHz, CDCl₃) spectrum of compound 12a:

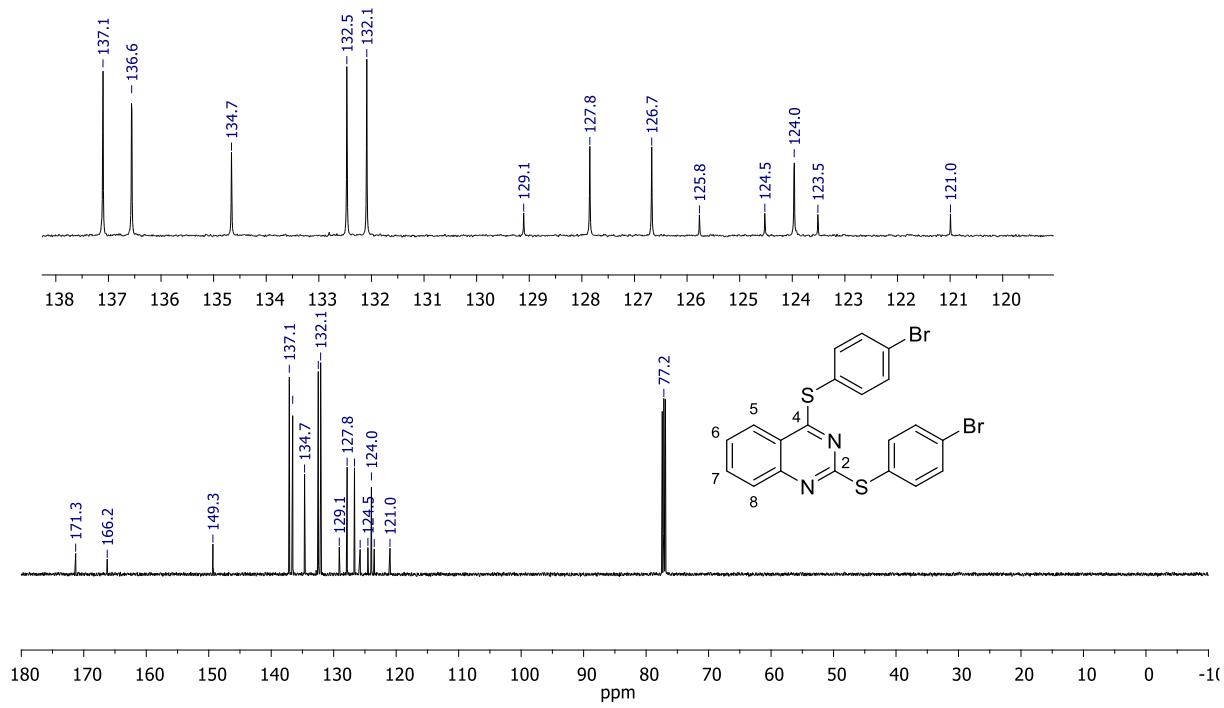


2,4-Bis-[(4-bromophenyl)thio]quinazoline (12b)

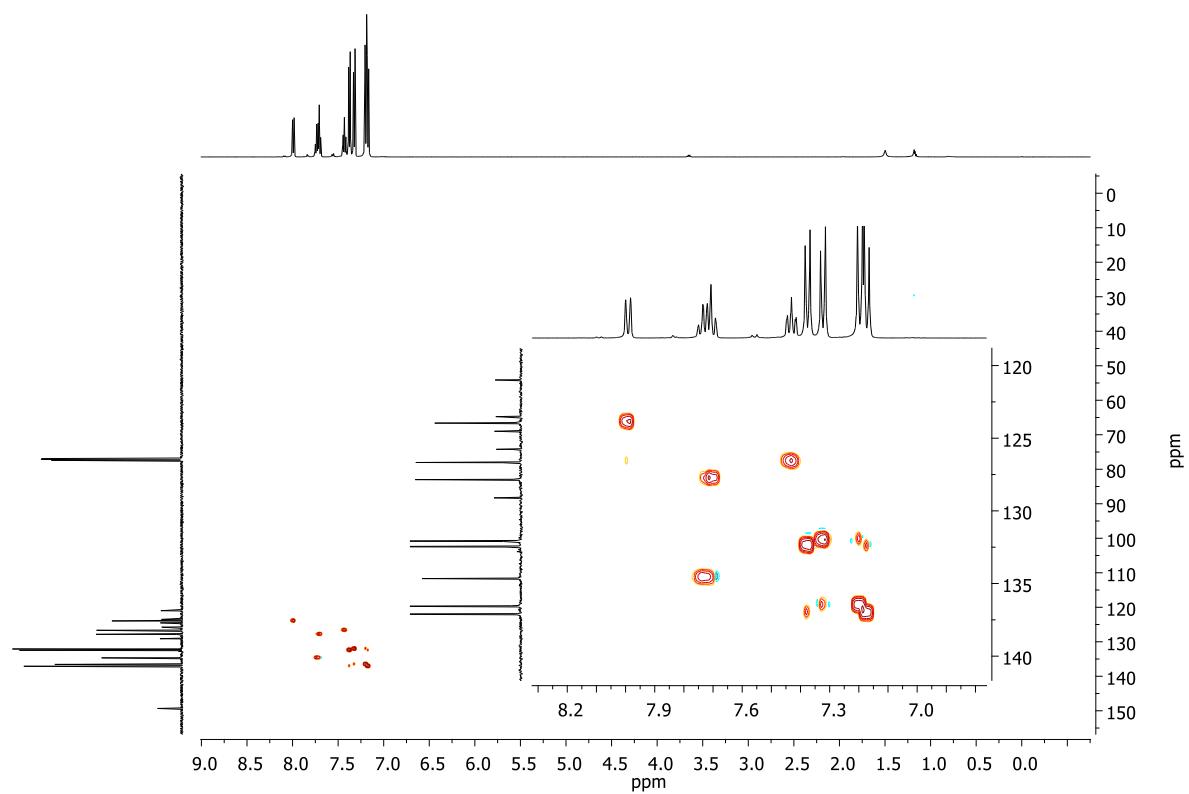
^1H NMR (500 MHz, CDCl_3) spectrum of compound 12b:



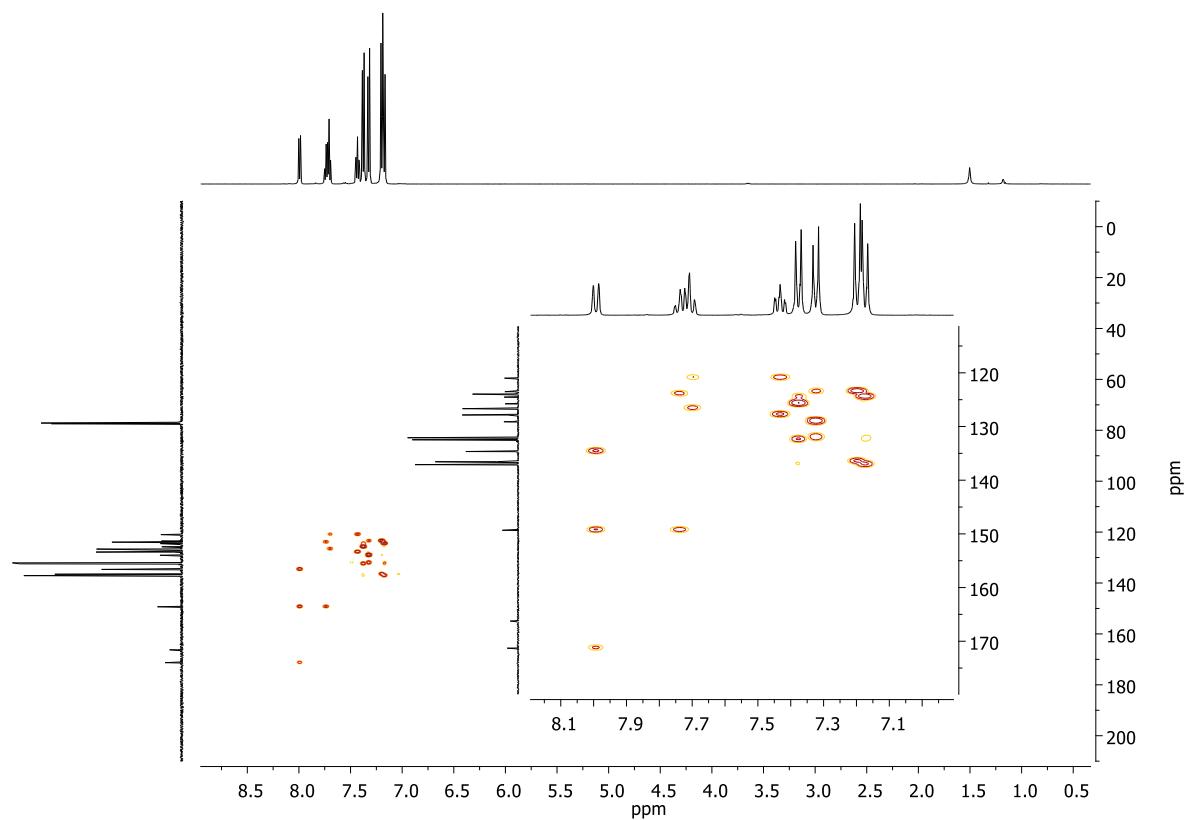
^{13}C -NMR (125.7 MHz, CDCl_3) spectrum of compound 12b:



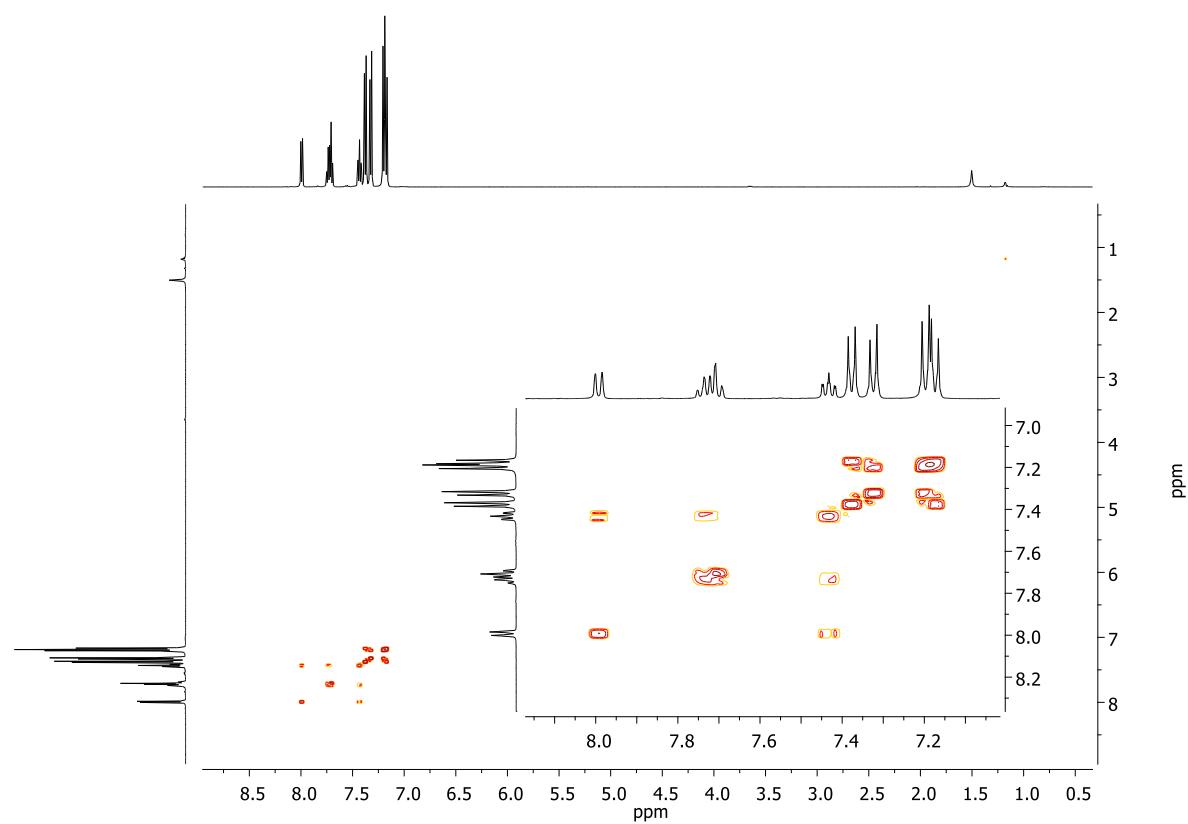
HSQC spectrum of compound 12b:



HMBC spectrum of compound 12b:



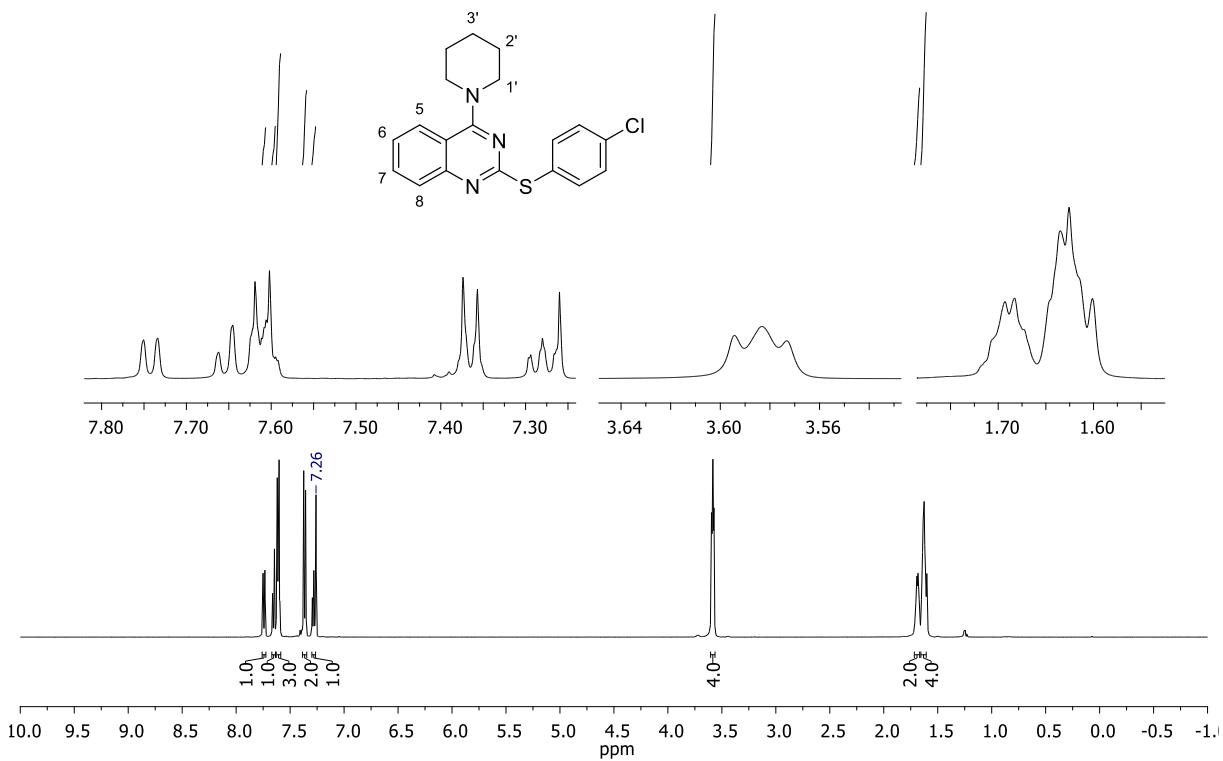
COSY spectrum of compound 12b:



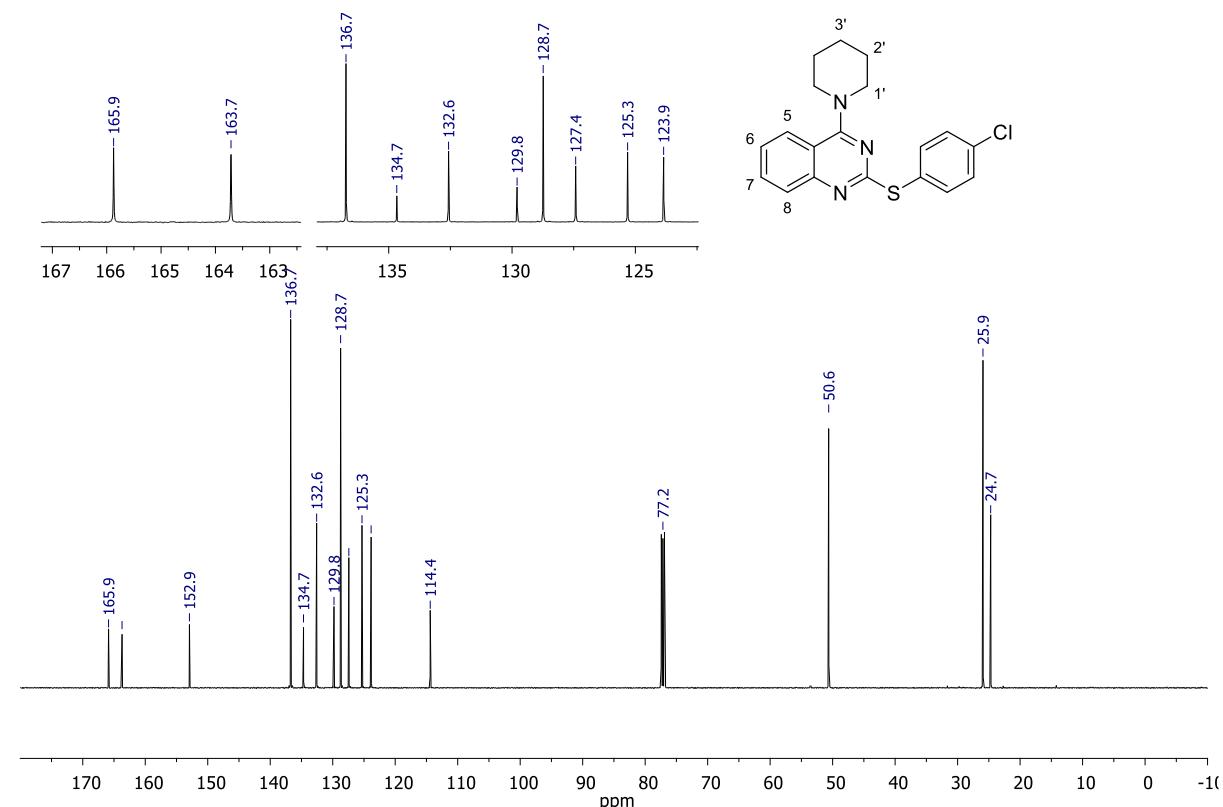
2-(Arylthio)-4-(piperidin-1-yl)quinazolines

2-[(4-Chlorophenyl)thio]-4-(piperidin-1-yl)quinazoline (13a)

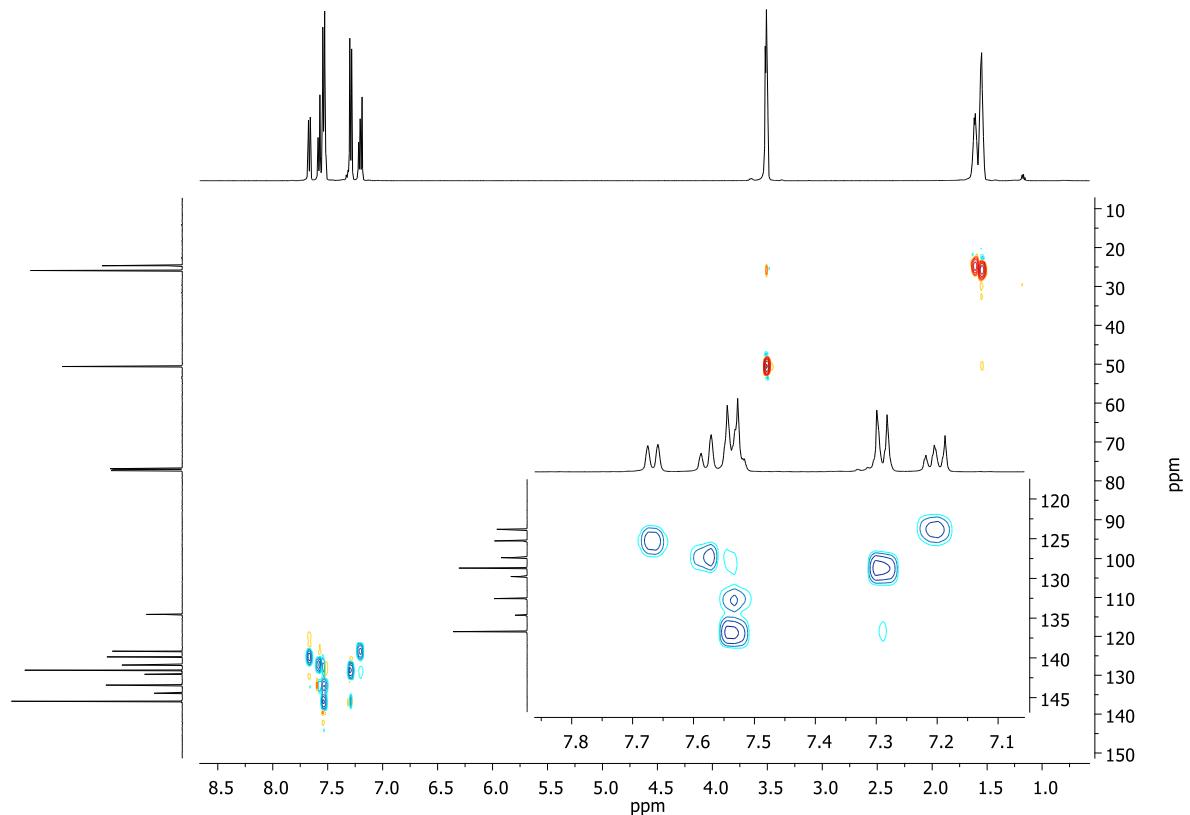
¹H-NMR (500 MHz, CDCl₃) spectrum of compound 13a:



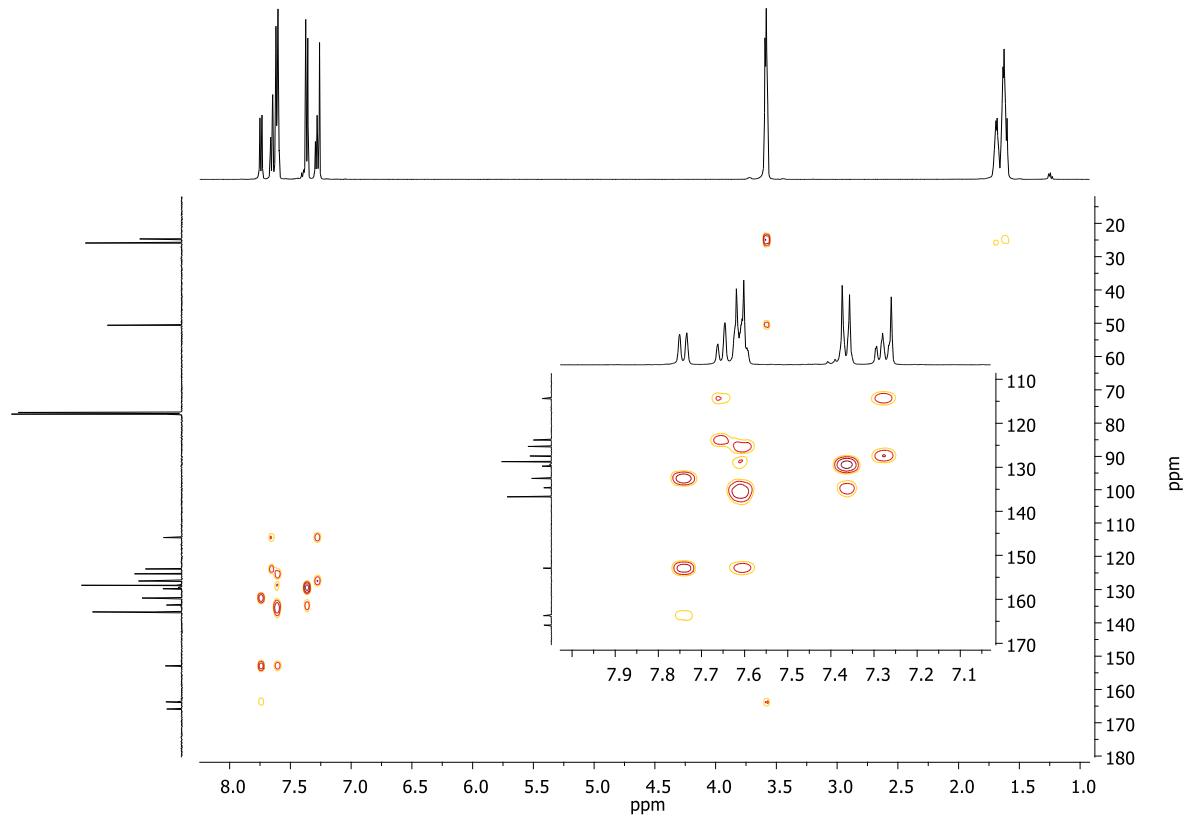
¹³C-NMR (125.7 MHz, CDCl₃) spectrum of compound 13a:



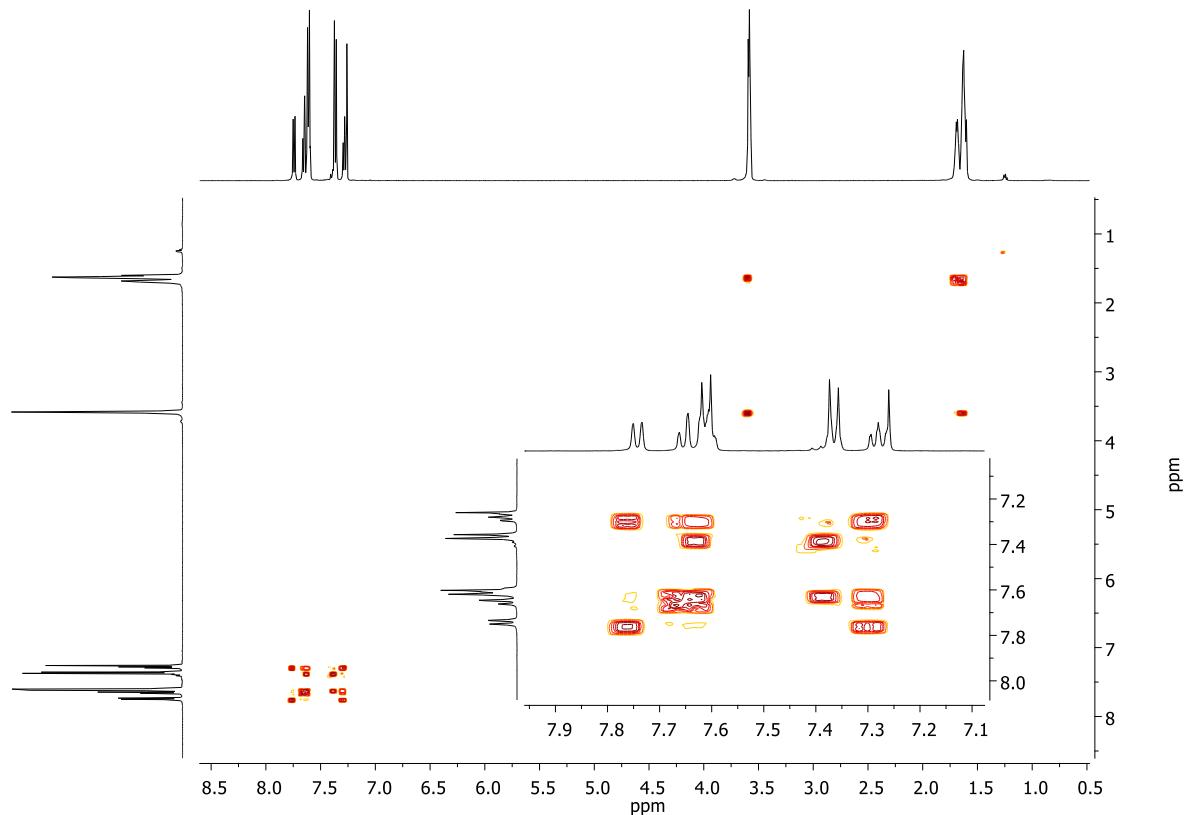
HSQC spectrum of compound 13a:



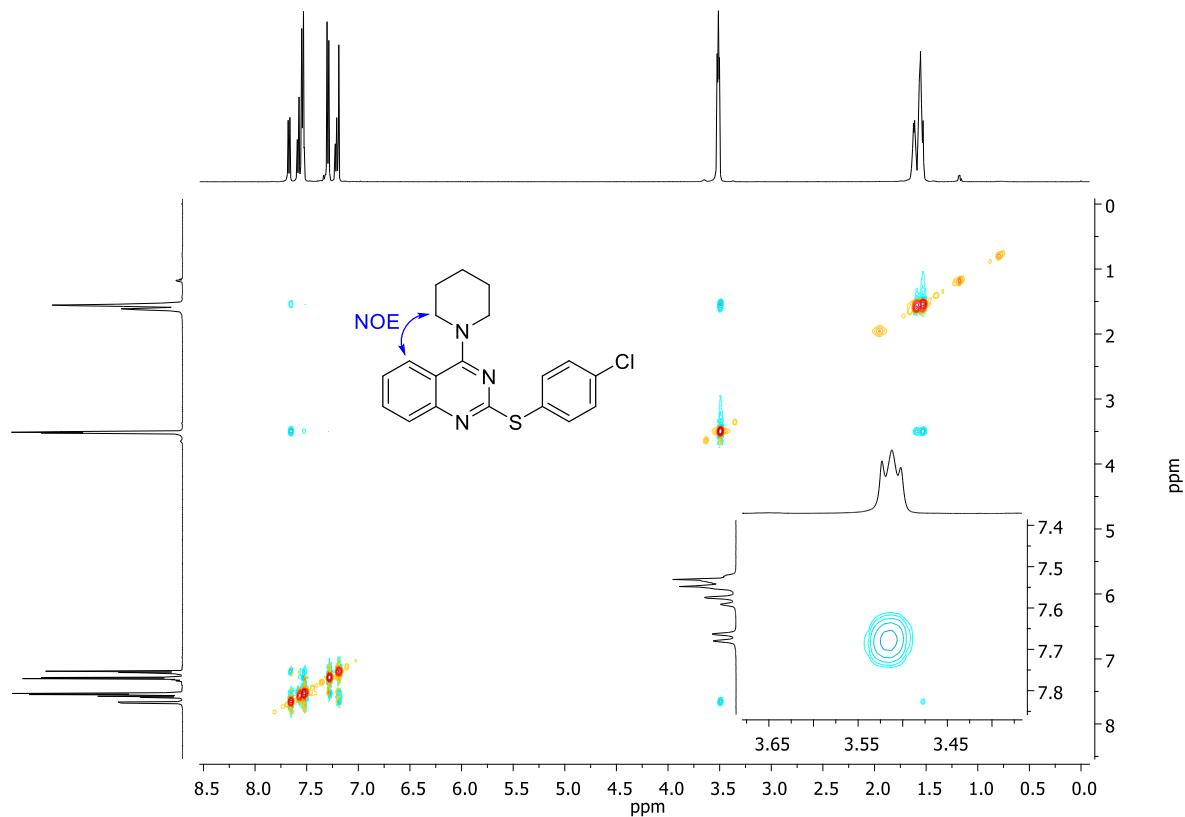
HMBC spectrum of compound 13a:



COSY spectrum of compound 13a:

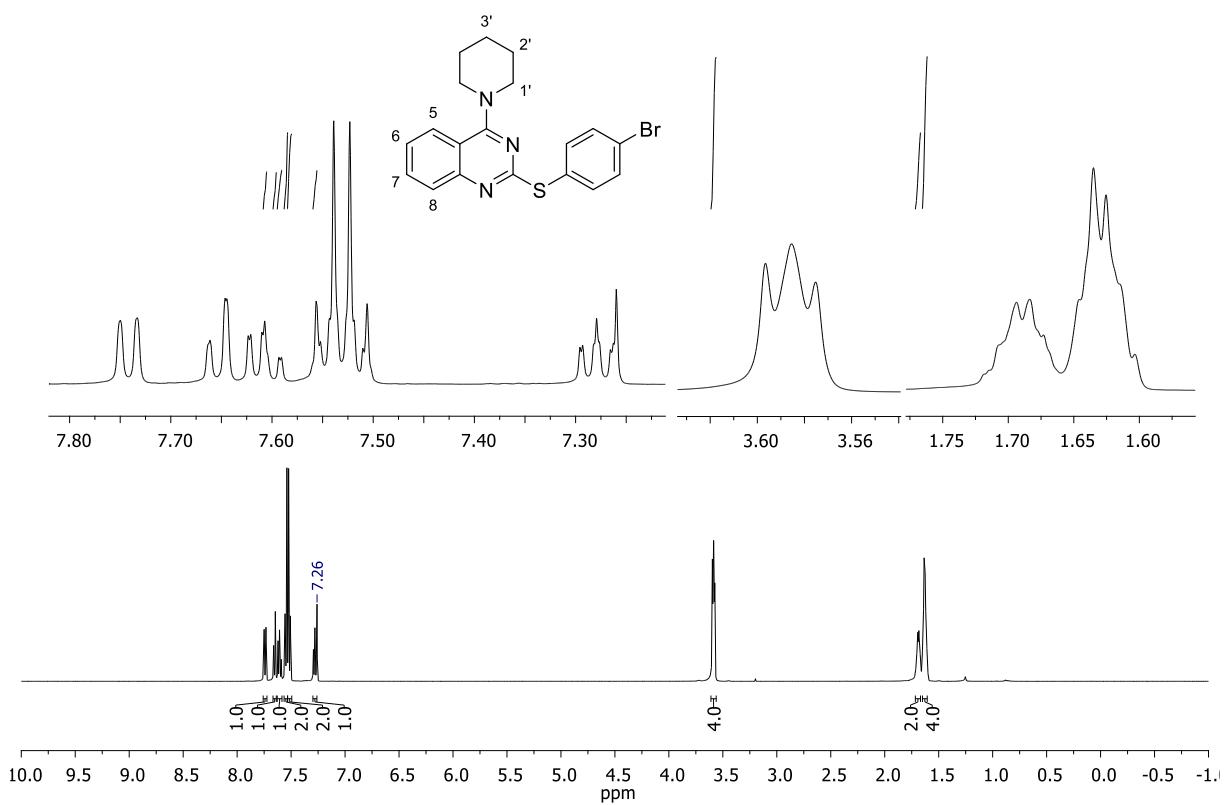


NOESY spectrum of compound 13a:

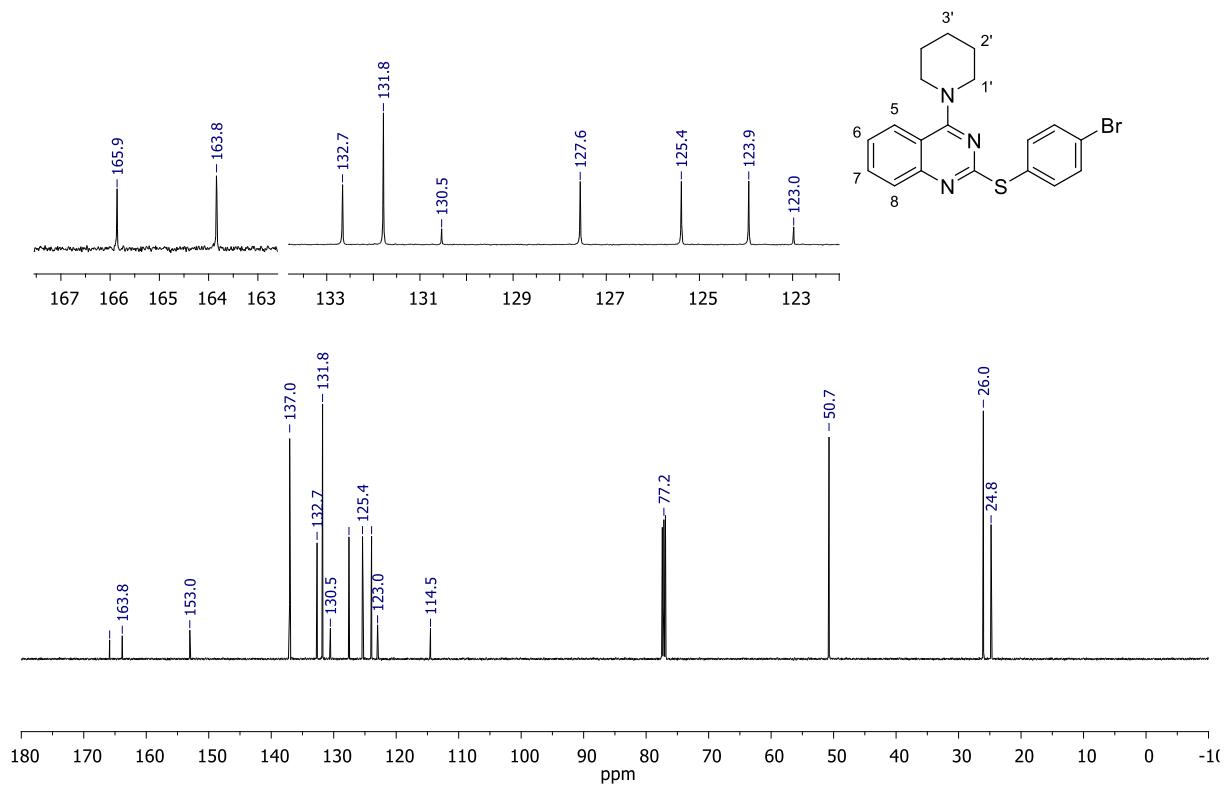


2-[(4-Bromophenyl)thio]-4-(piperidin-1-yl)quinazoline (13b)

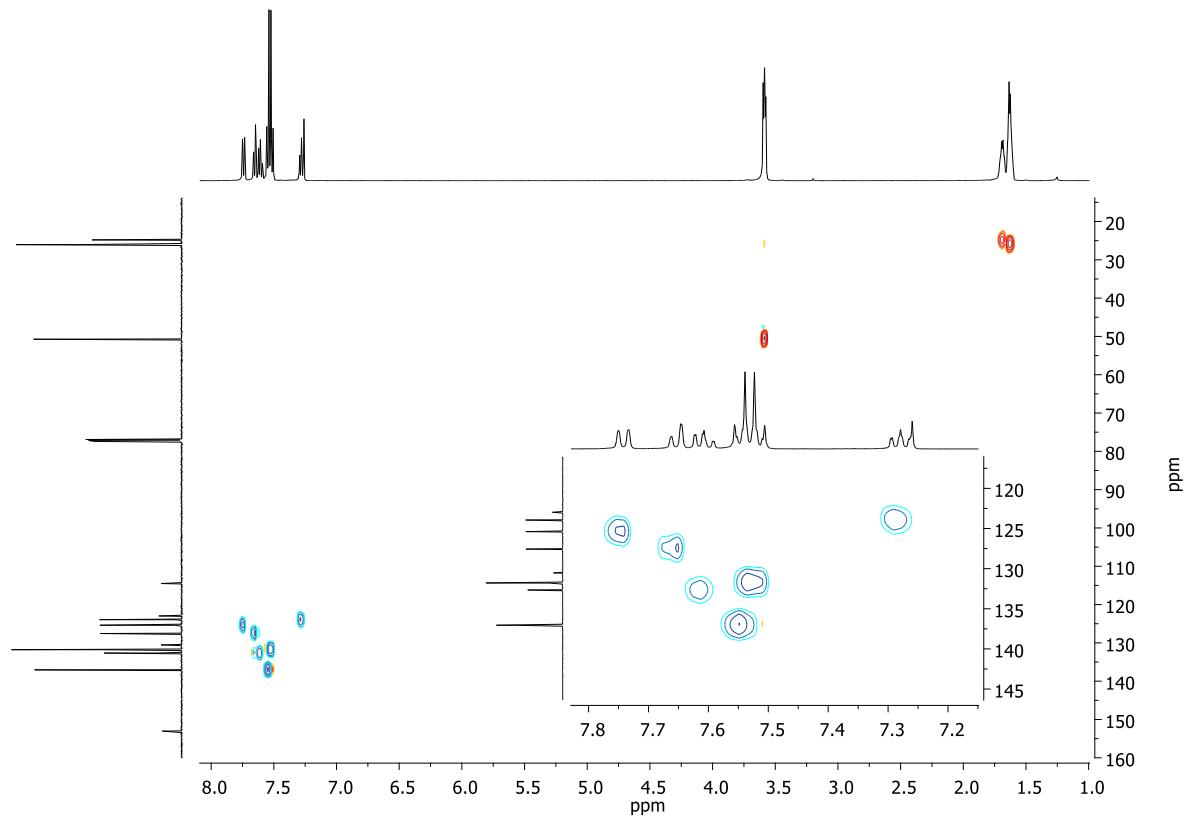
$^1\text{H-NMR}$ (500 MHz, CDCl_3) spectrum of compound 13b:



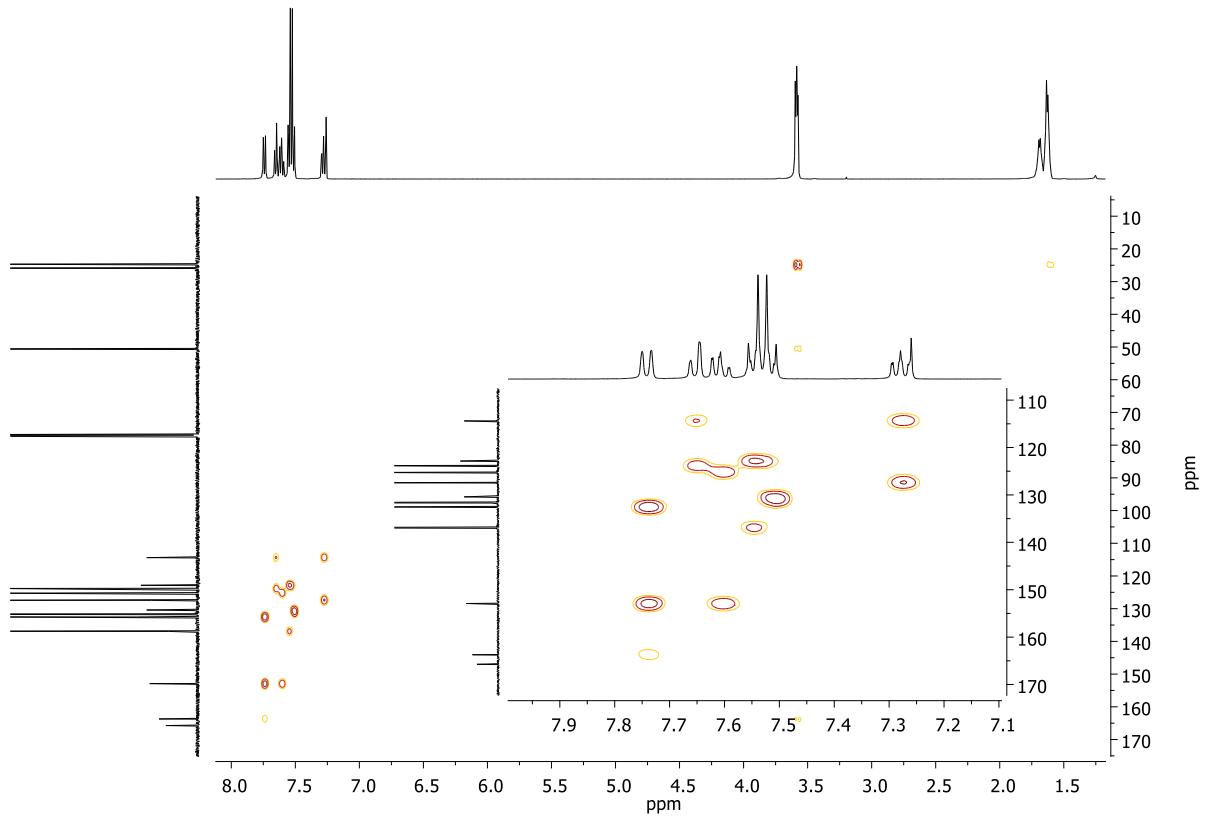
$^{13}\text{C-NMR}$ (125.7 MHz, CDCl_3) spectrum of compound 13b:



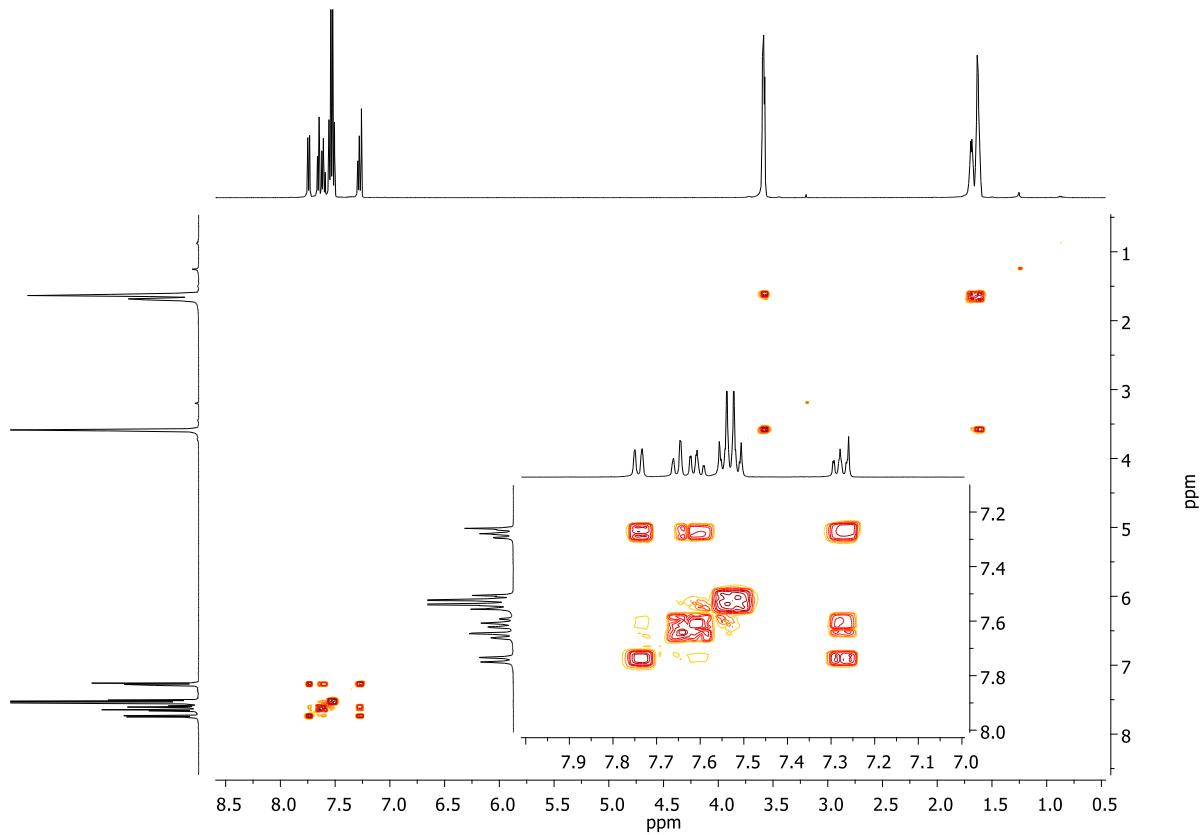
HSQC spectrum of compound 13b:



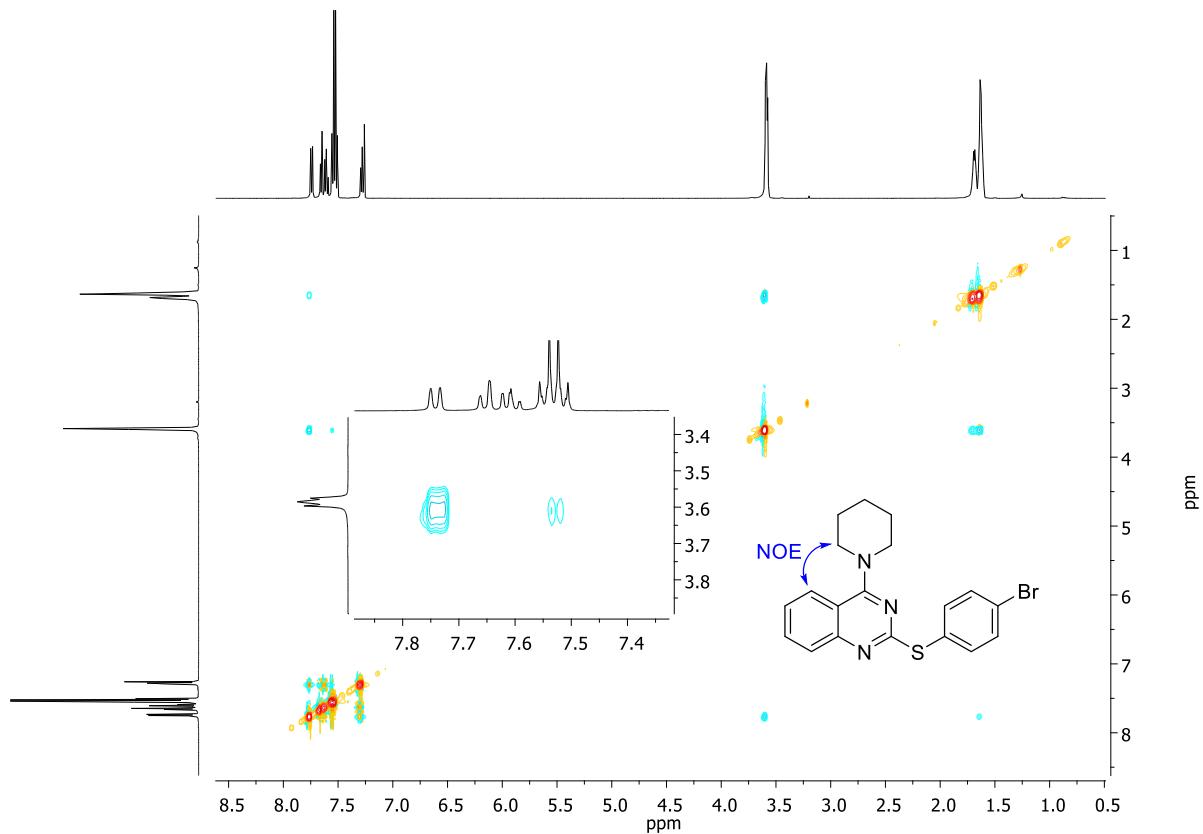
HMBC spectrum of compound 13b:



COSY spectrum of compound 13b:



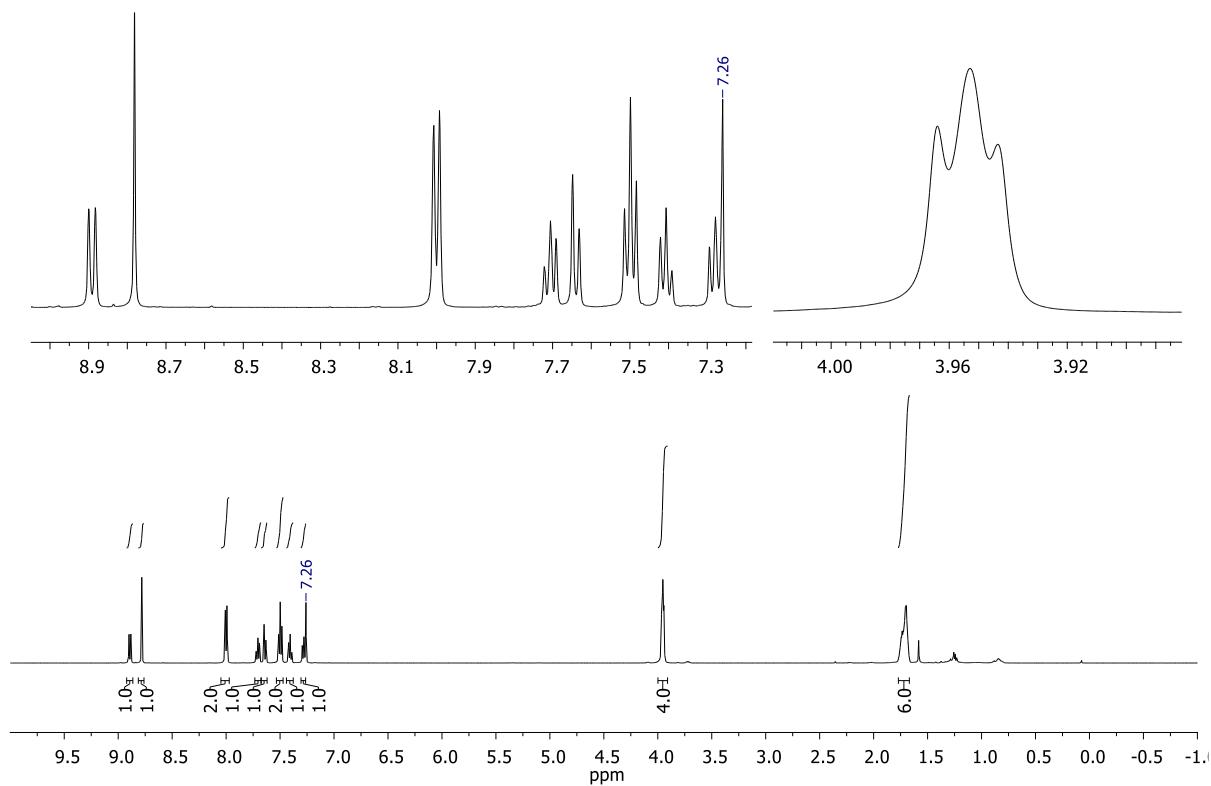
NOESY spectrum of compound 13b:



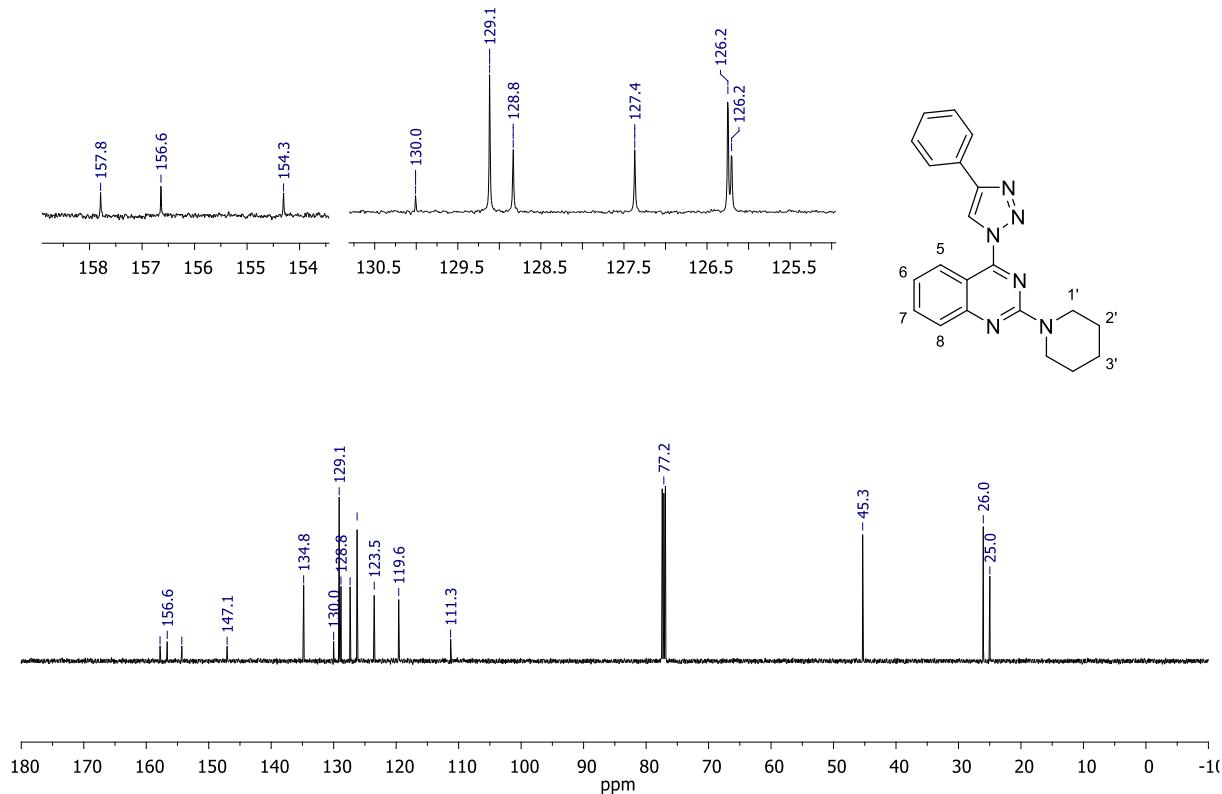
2-Amino-4-(1*H*-1,2,3-triazol-1-yl)quinazolines

4-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)-2-(piperidin-1-yl)quinazoline (14a)

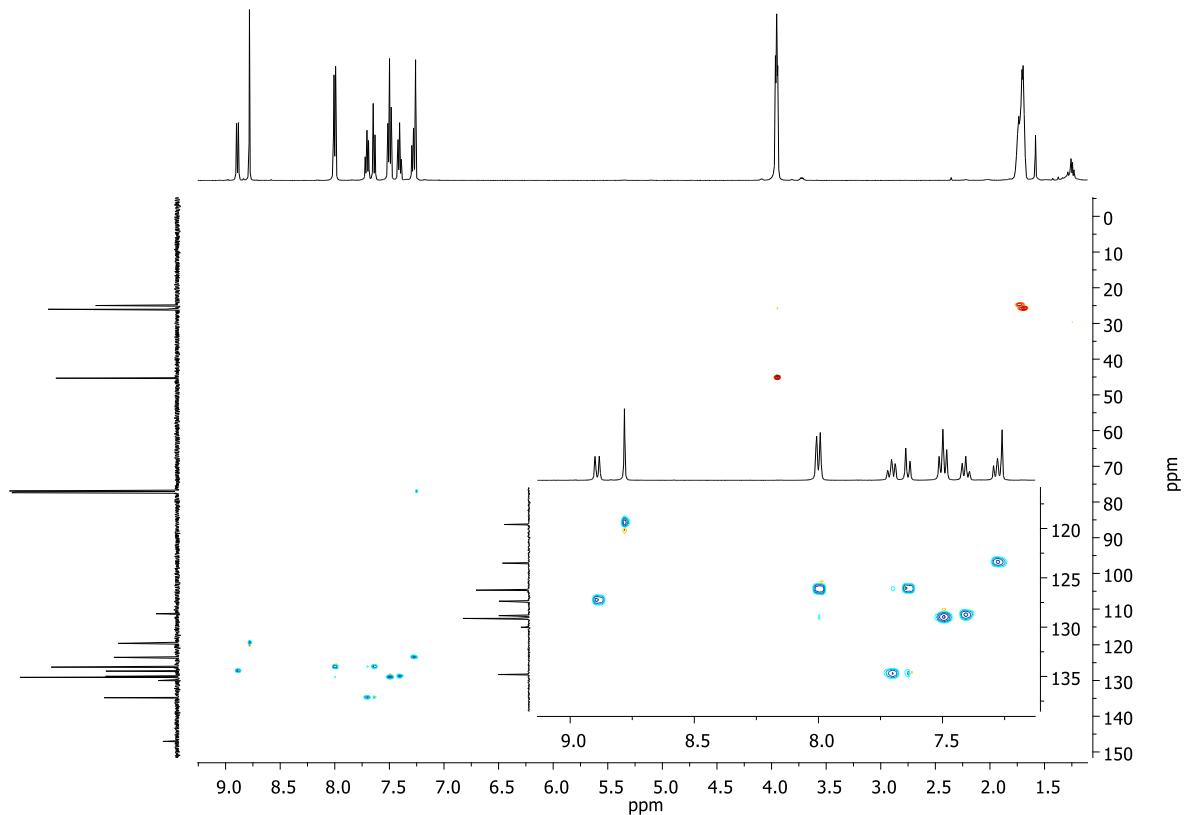
¹H-NMR (500 MHz, CDCl₃) spectrum of compound 14a:



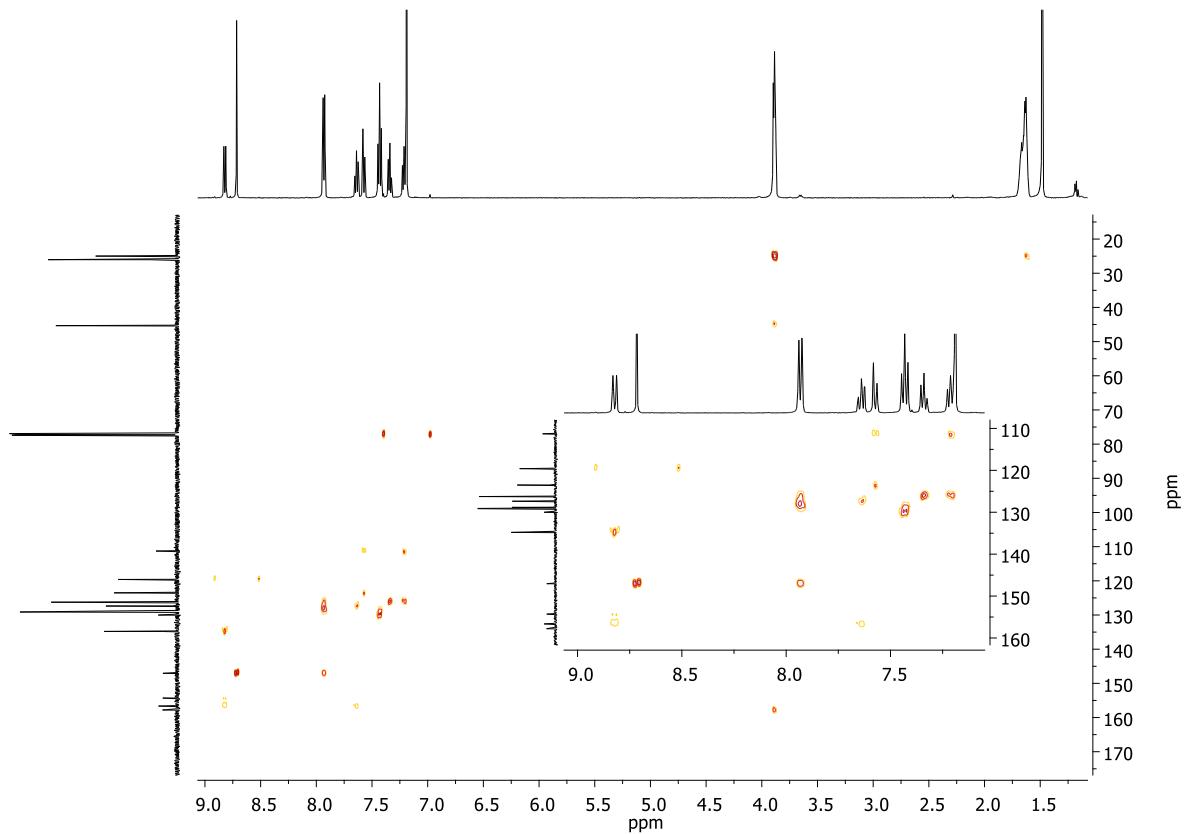
¹³C-NMR (125.7 MHz, CDCl₃) spectrum of compound 14a:



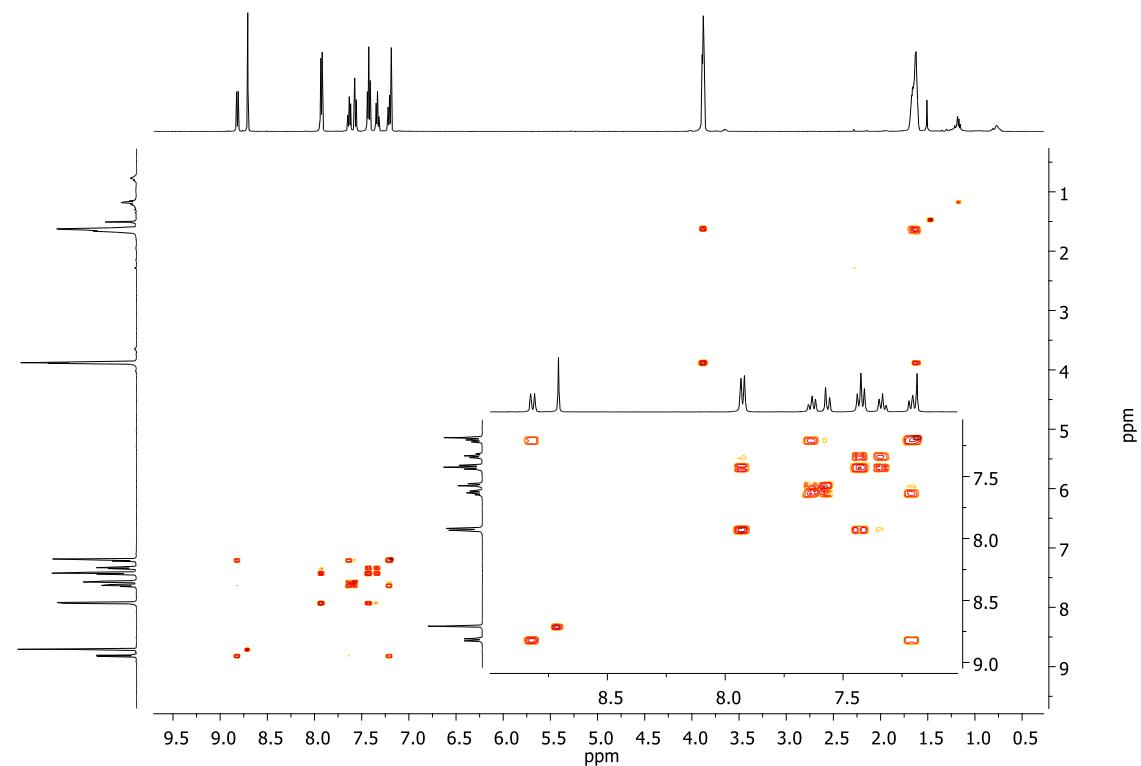
HSQC spectrum of compound 14a:



HMBC spectrum of compound 14a:

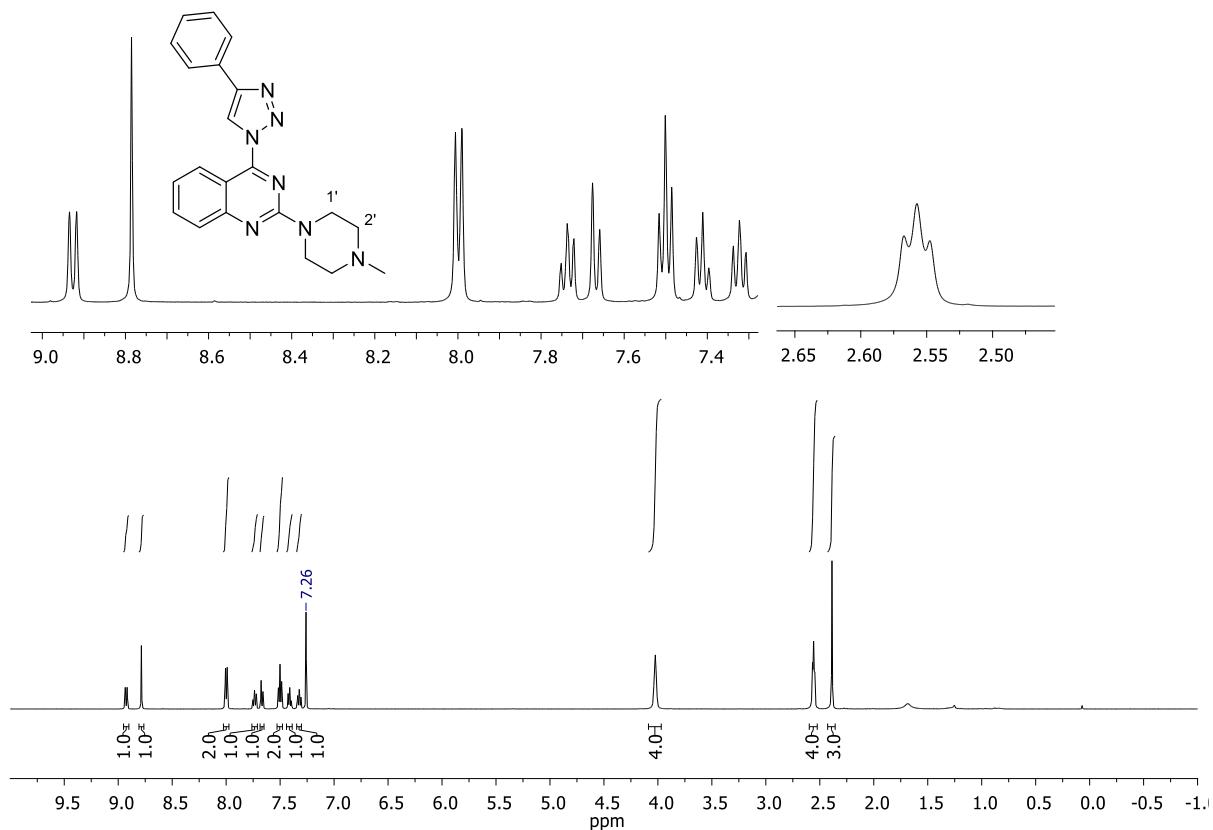


COSY spectrum of compound 14a:

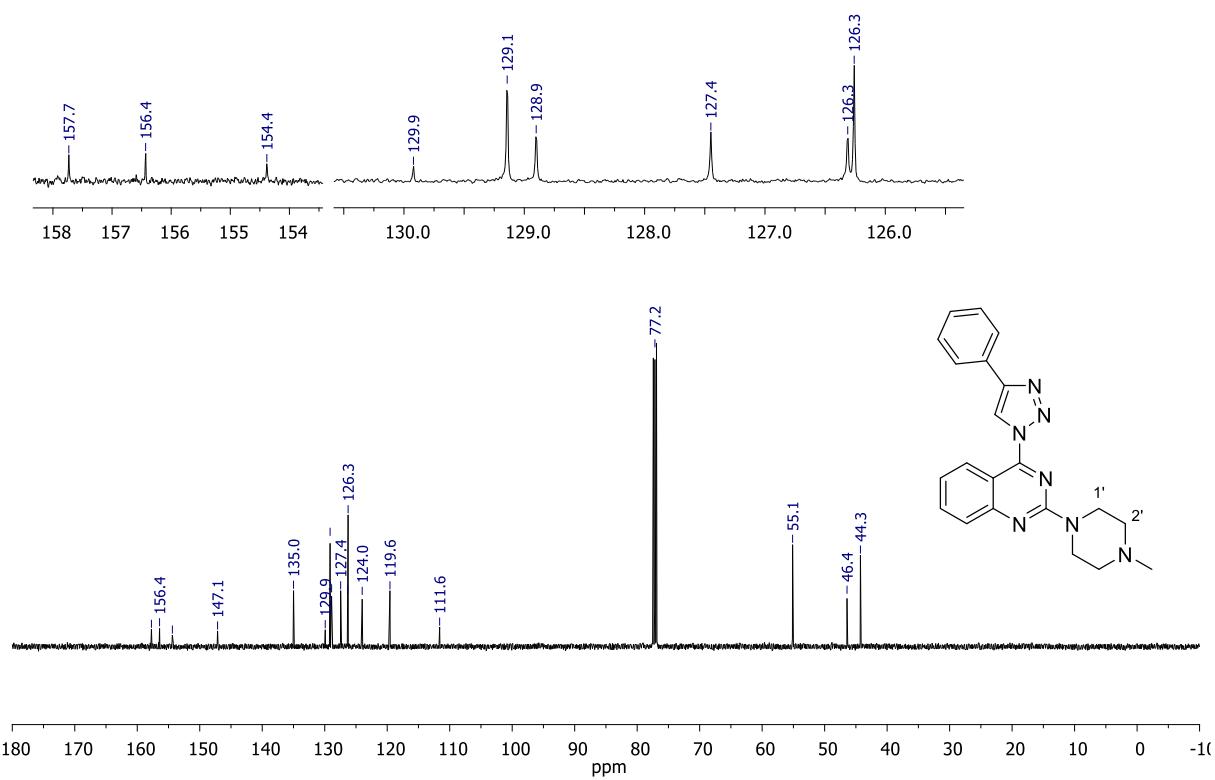


4-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)-2-(4-methylpiperazin-1-yl)quinazoline (14b)

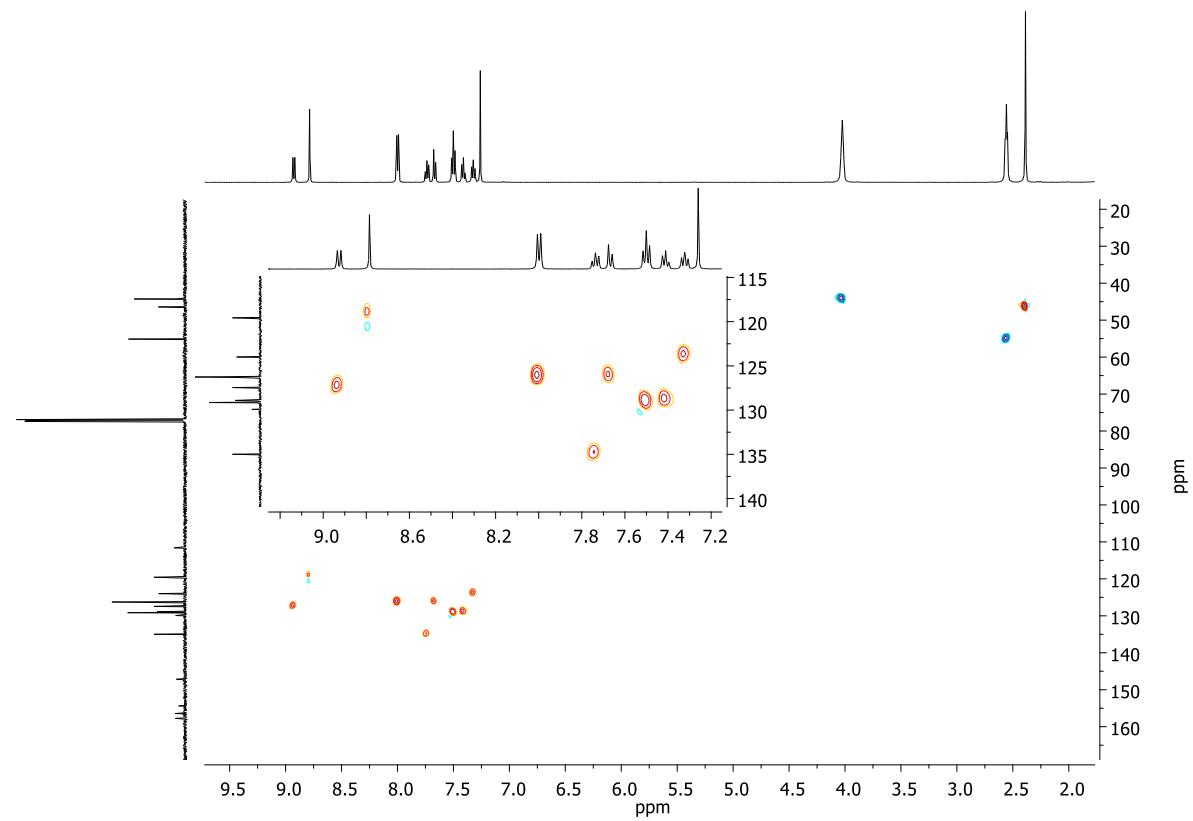
^1H -NMR (500 MHz, CDCl_3) spectrum of compound 14b:



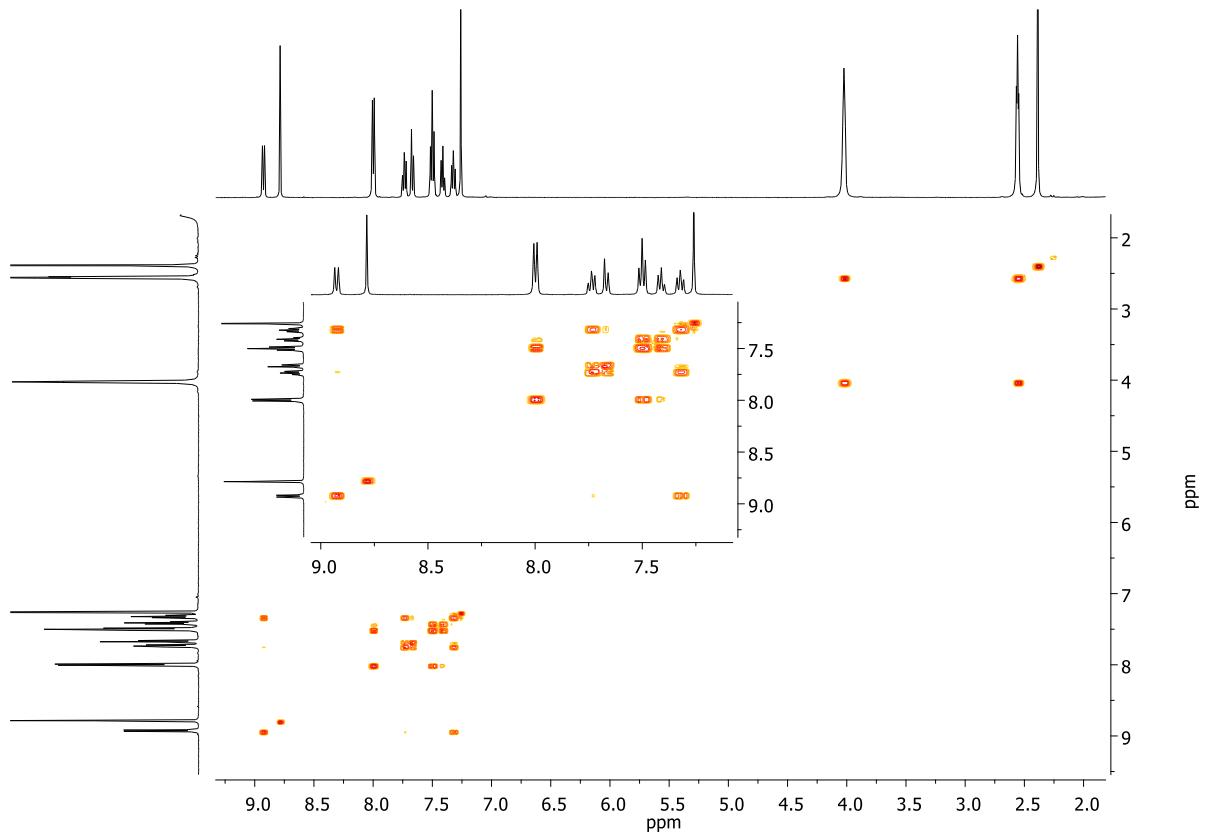
¹³C-NMR (125.7 MHz, CDCl₃) spectrum of compound 14b:



HSQC spectrum of compound 14b:

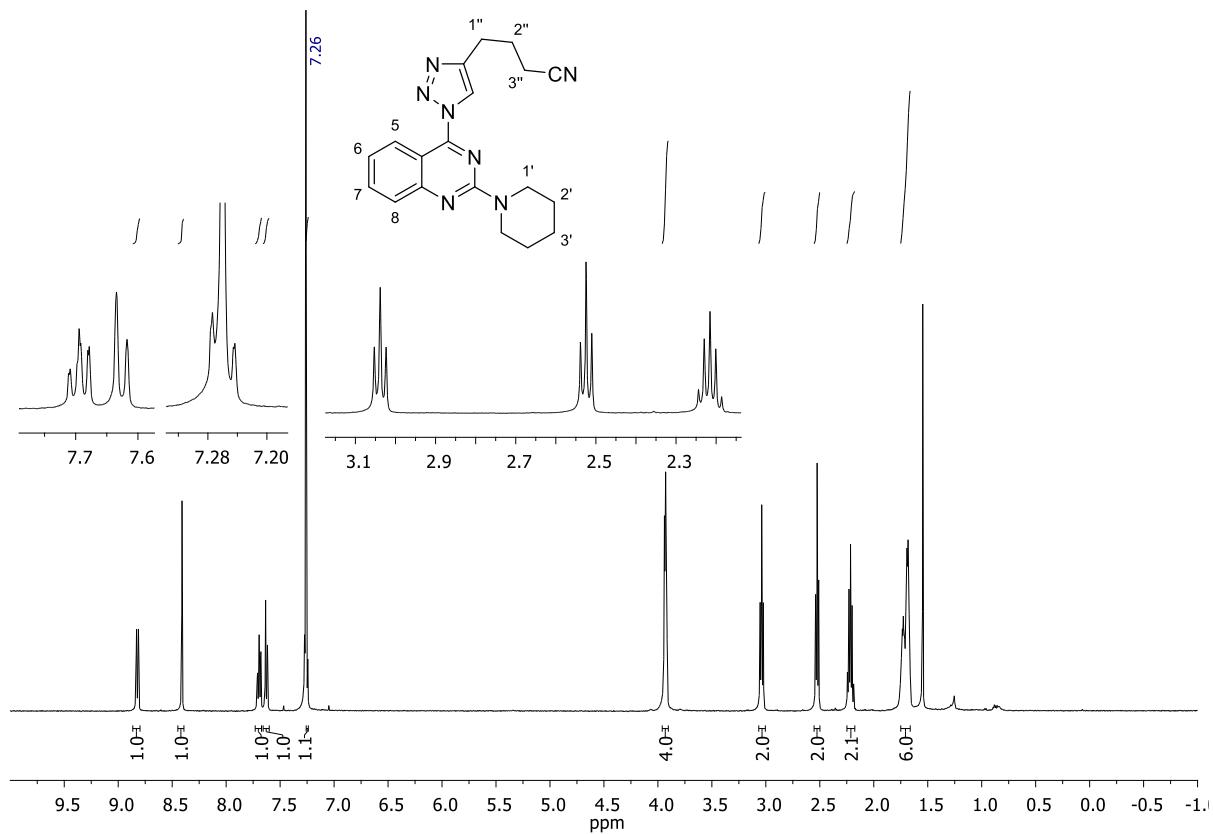


COSY spectrum of compound 14b:

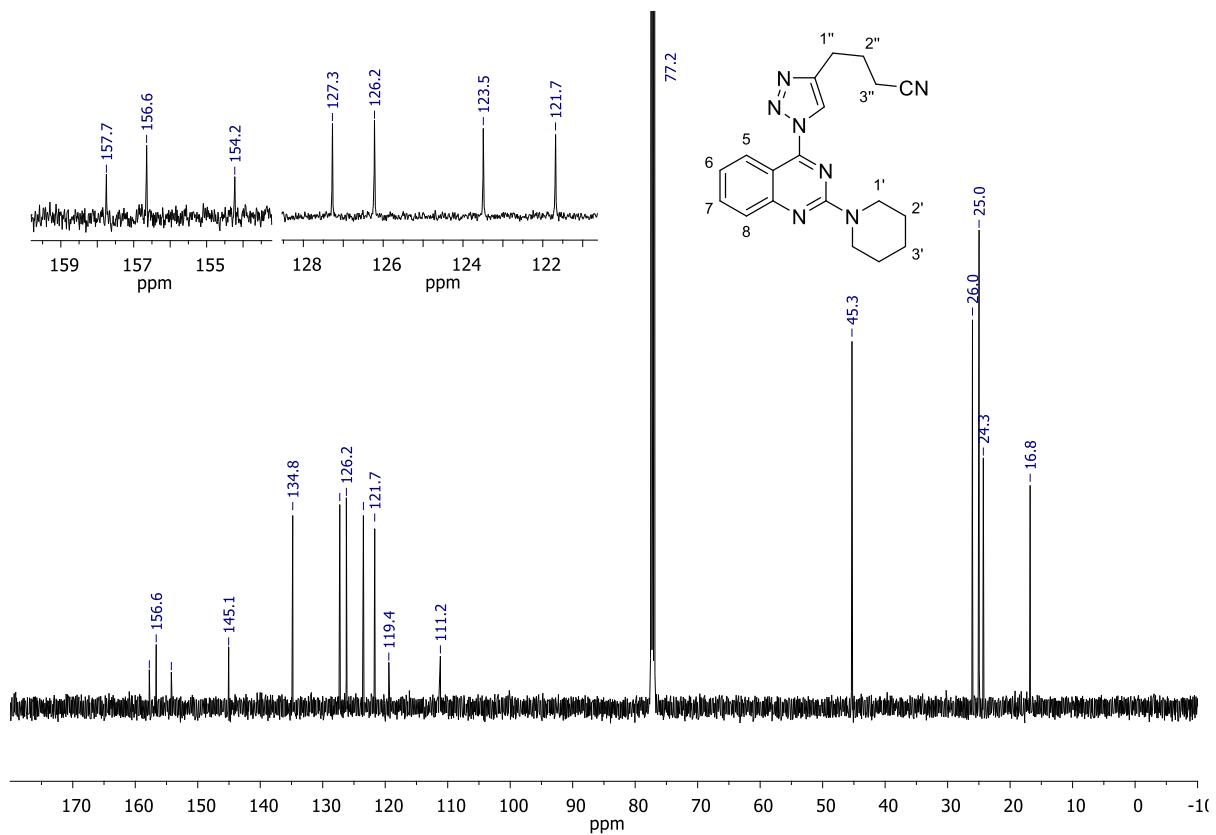


4-[4-(3-Cyanoprop-1-yl)-1*H*-1,2,3-triazol-1-yl]-2-(piperidin-1-yl)quinazoline (14c)

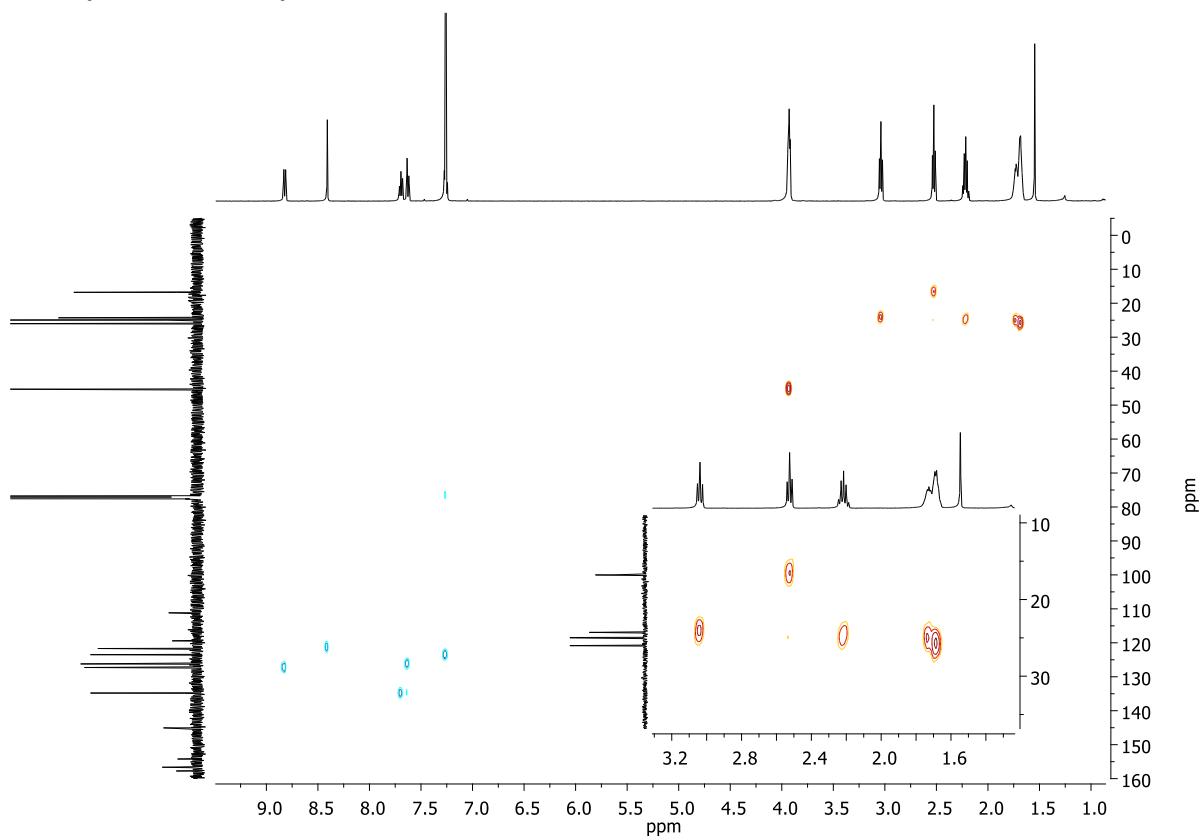
^1H -NMR (500 MHz, CDCl_3) spectrum of compound 14c:



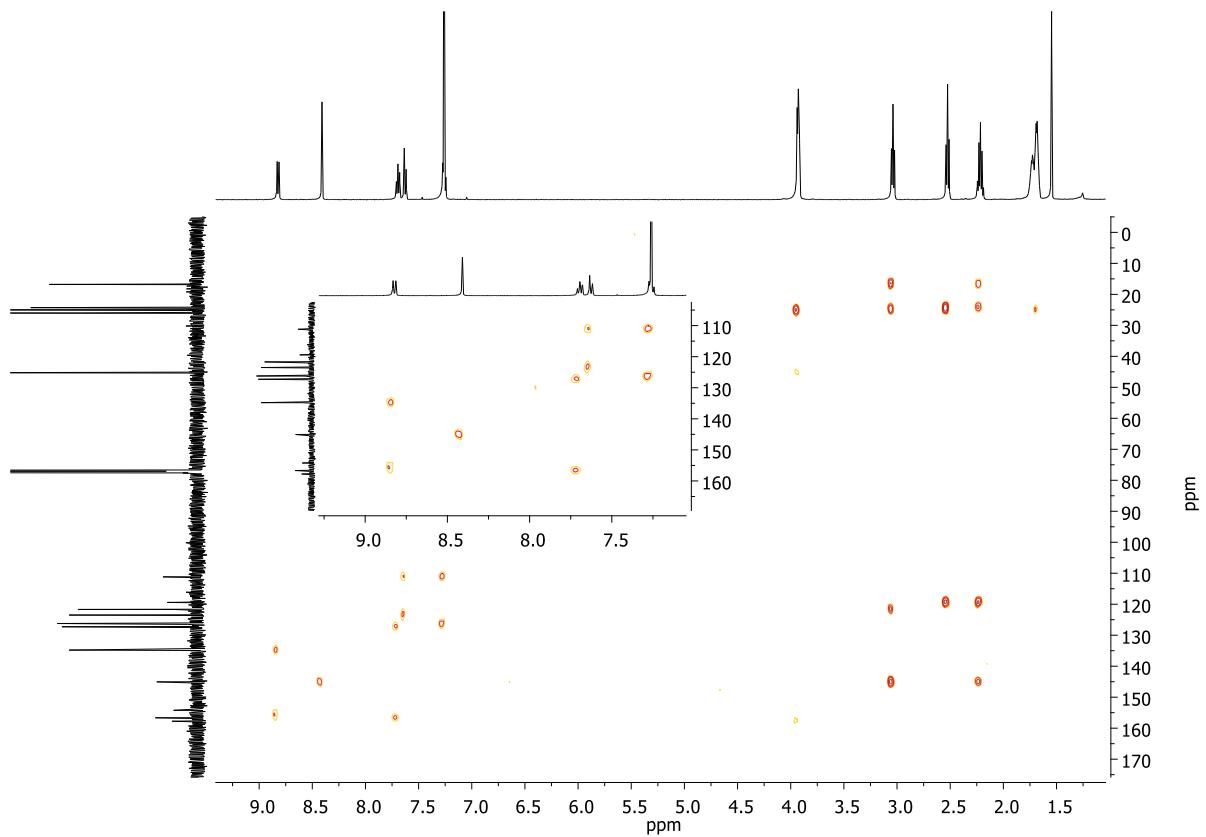
¹³C-NMR (125.7 MHz, CDCl₃) spectrum of compound 14c:



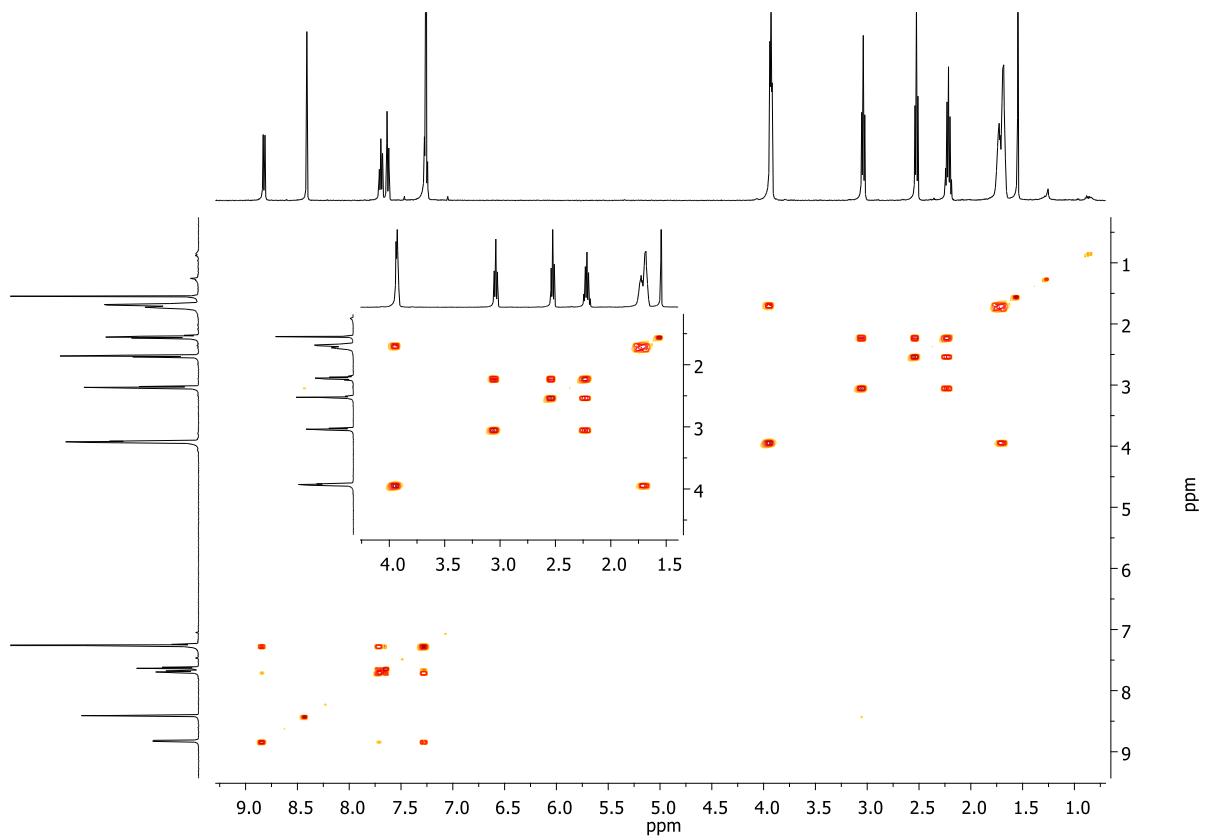
HSQC spectrum of compound 14c:



HMBC spectrum of compound 14c:

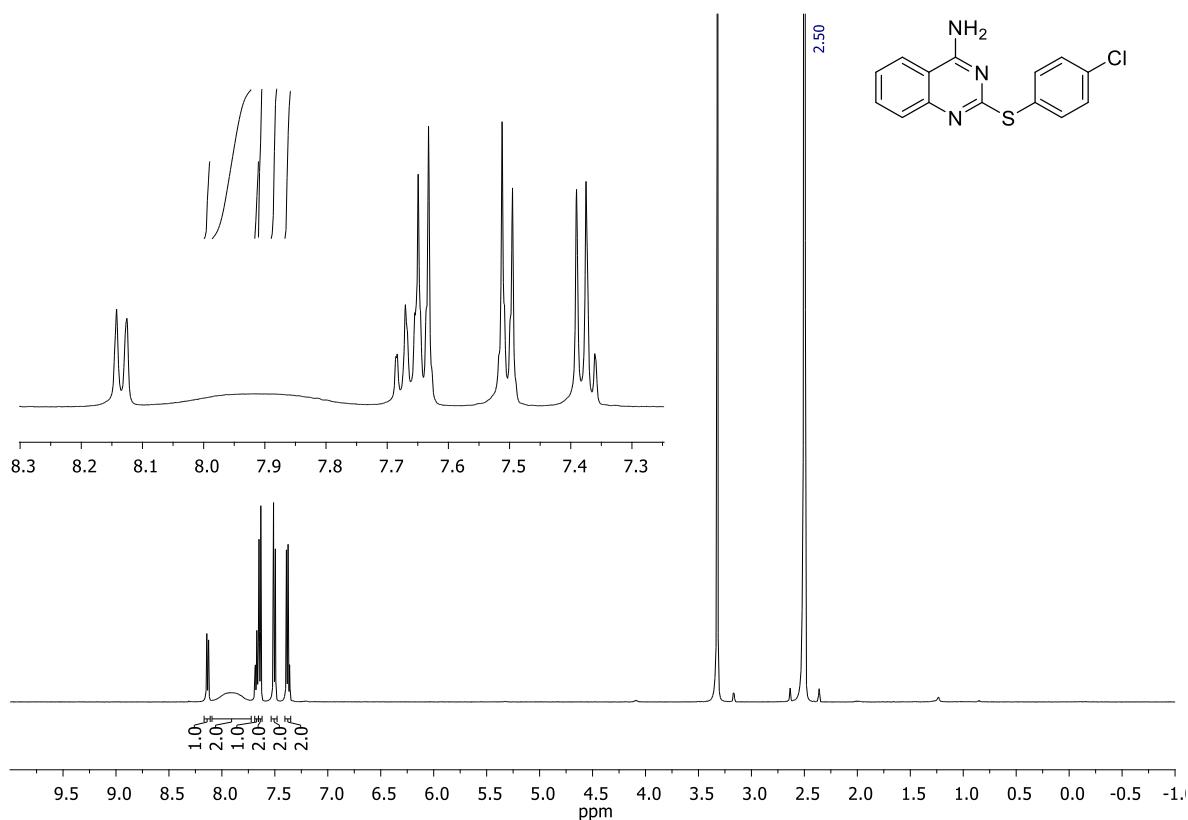


COSY spectrum of compound 14c:

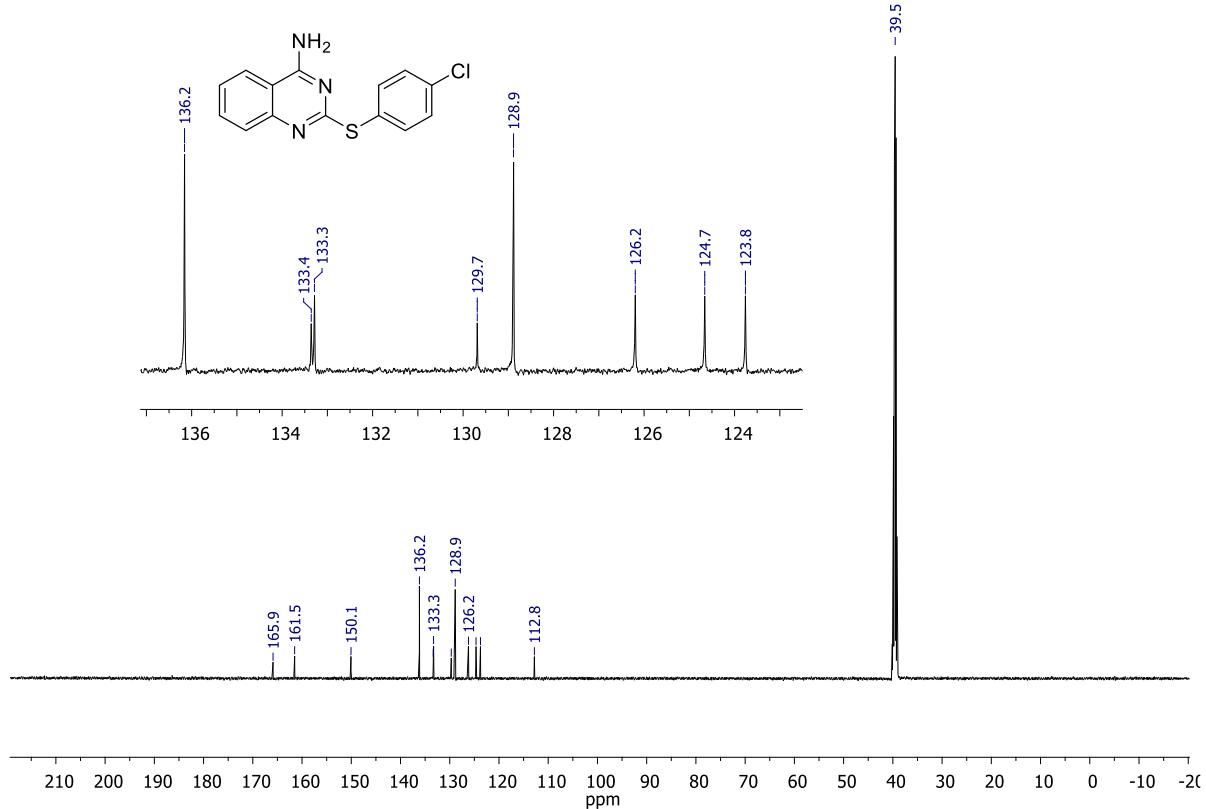


4-Amino-2-[(4-chlorophenyl)thio]quinazoline (15)

^1H -NMR (500 MHz, DMSO-d₆) spectrum of compound 15:



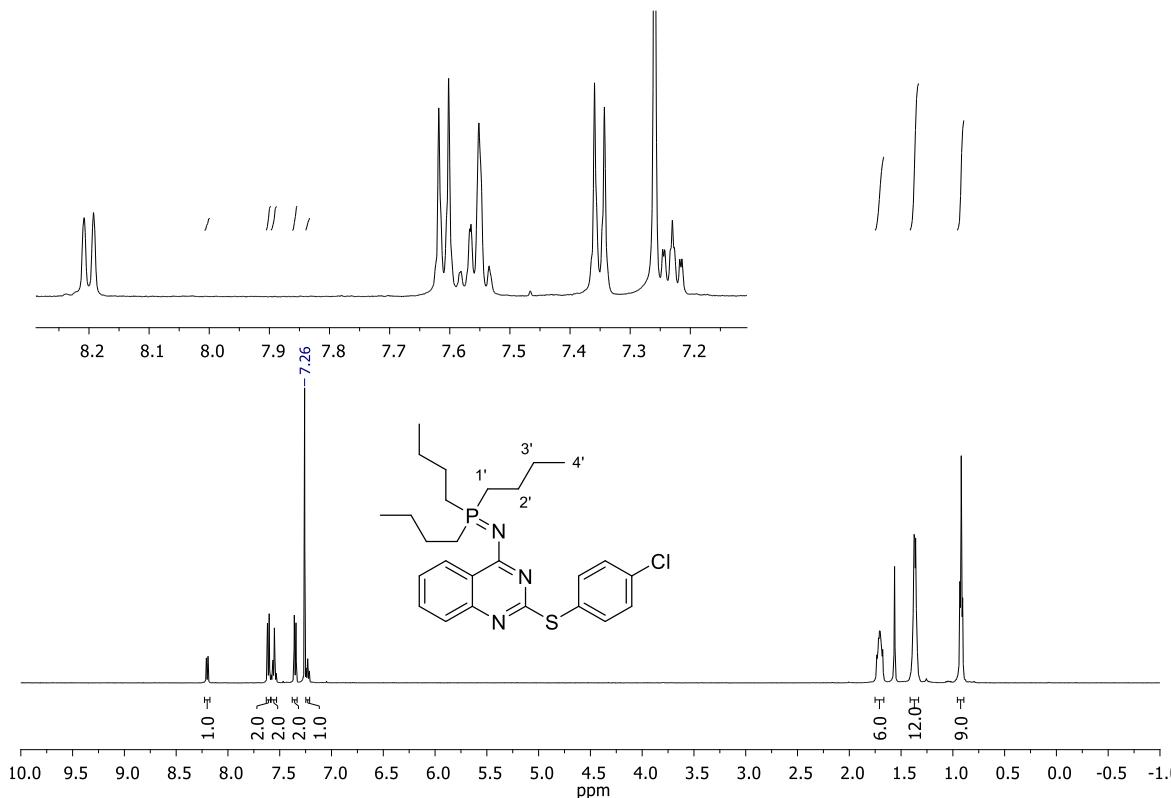
^{13}C -NMR (125.7 MHz, DMSO-d₆) spectrum of compound 15:



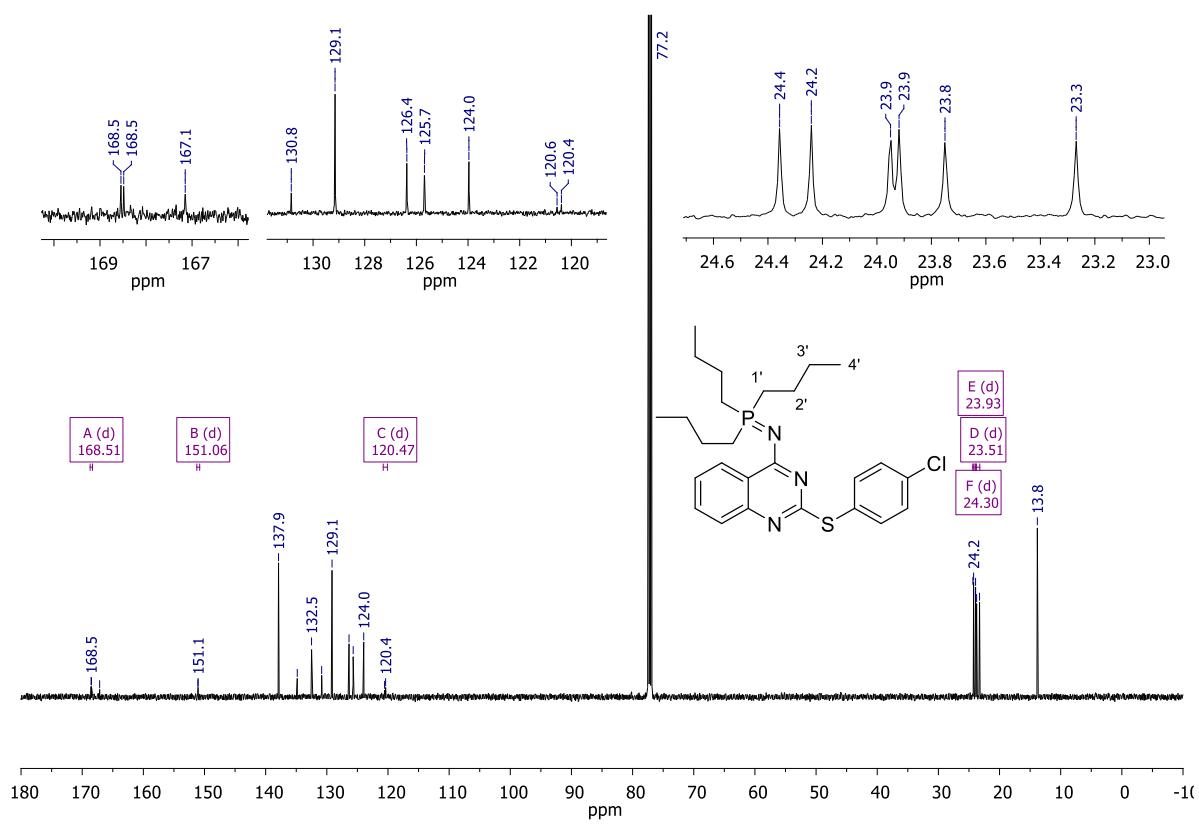
Quinazoline iminophosphoranes

2-[(4-Chlorophenyl)thio]-4-[(tributylphosphoronylidene)amino]quinazoline (16a)

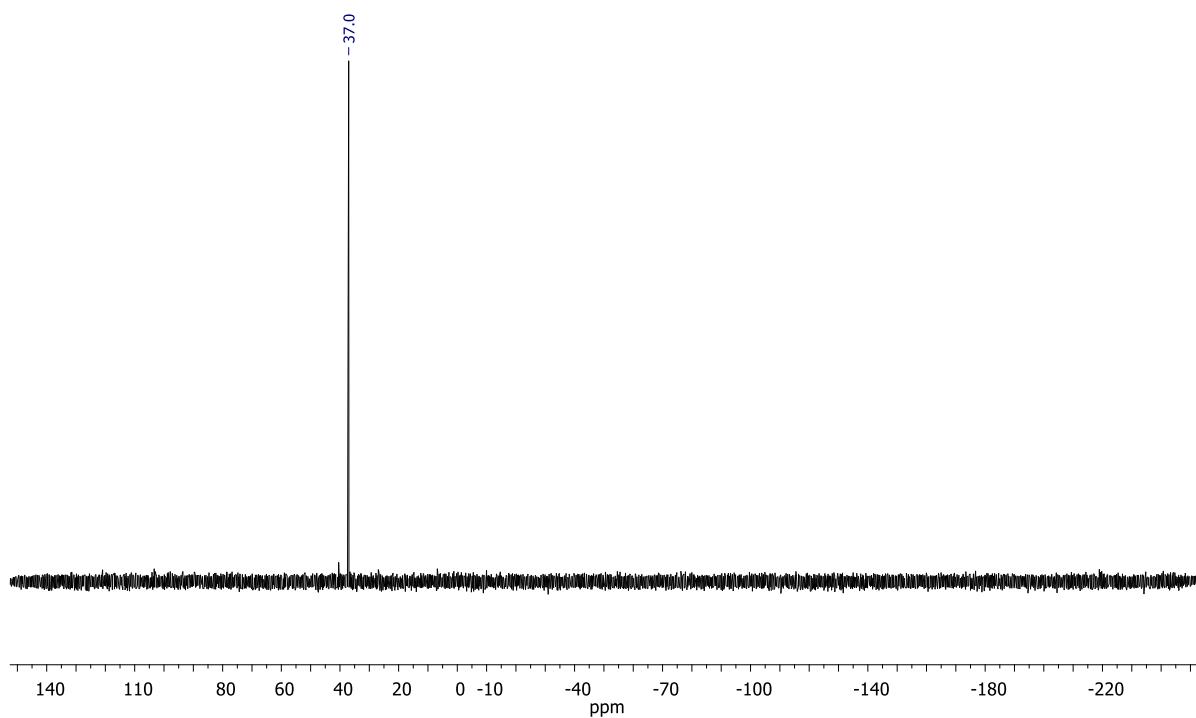
$^1\text{H-NMR}$ (500 MHz, CDCl_3) spectrum of compound 16a:



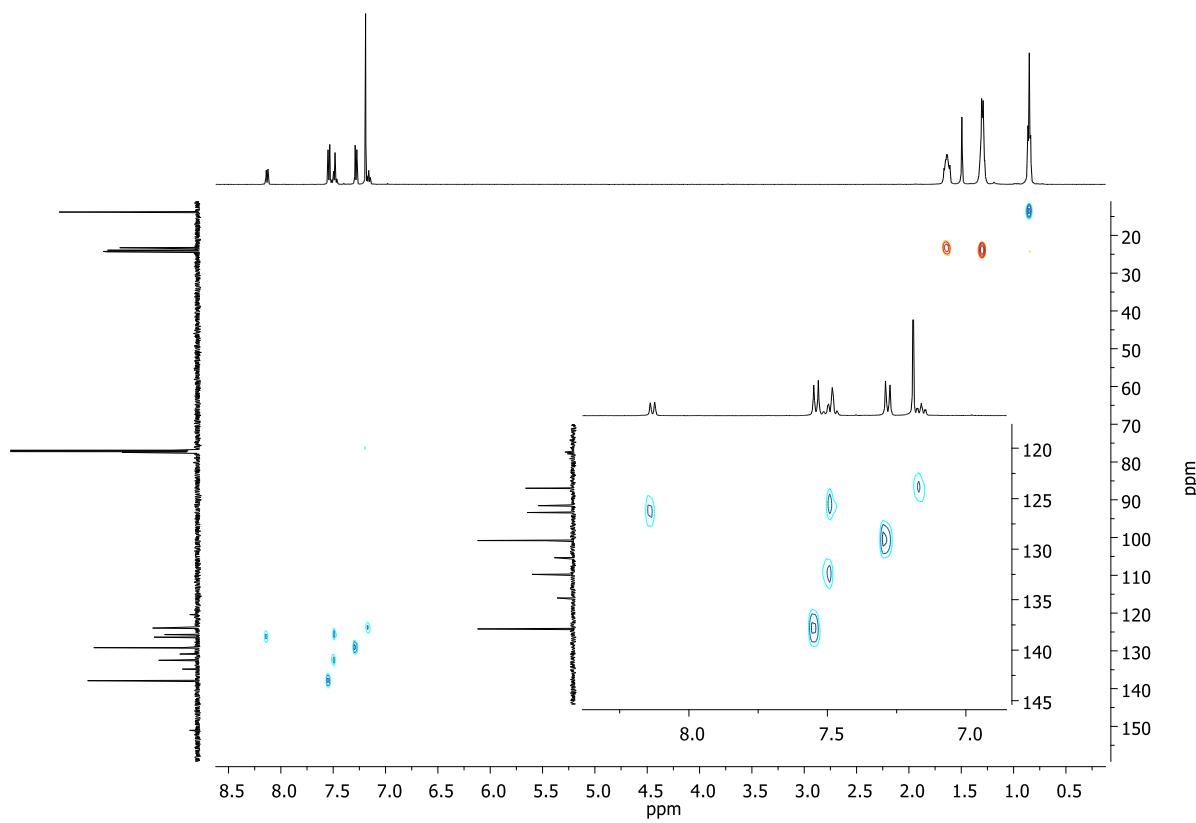
$^{13}\text{C-NMR}$ (125.7 MHz, CDCl_3) spectrum of compound 16a:



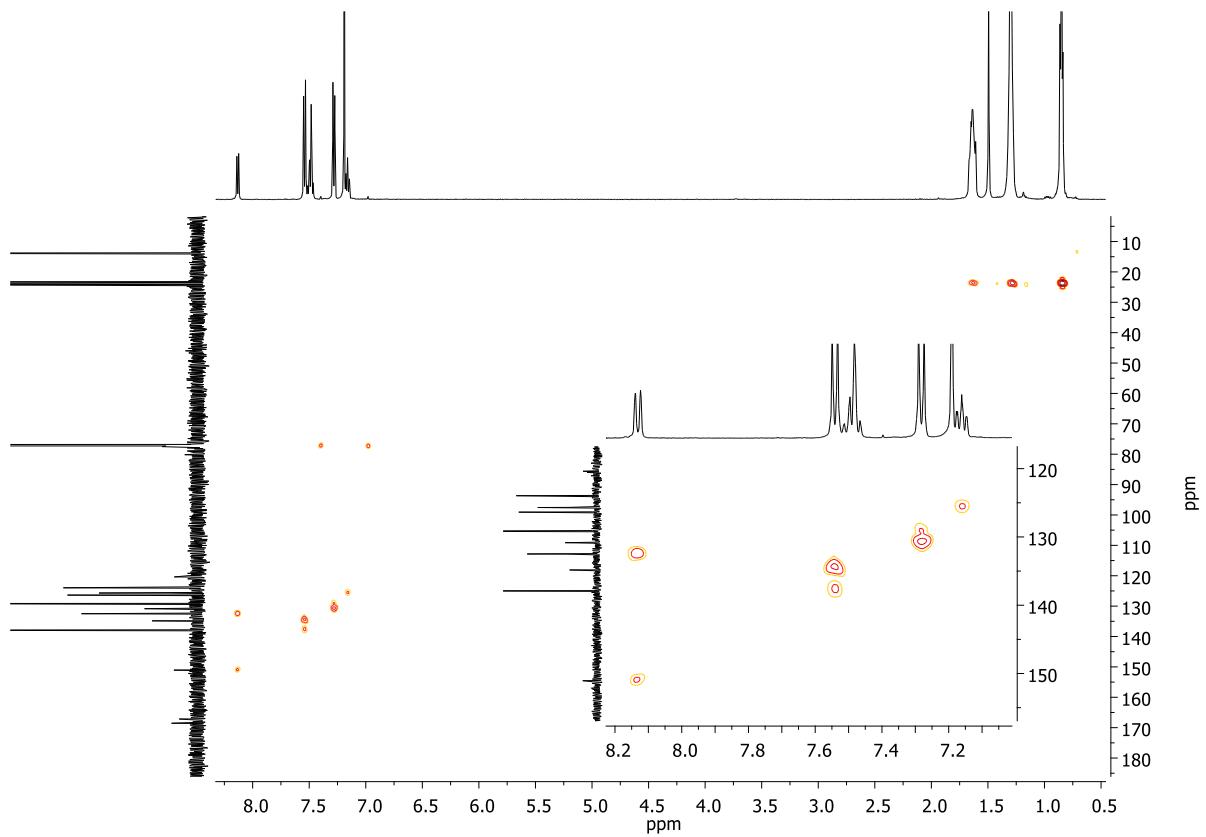
^{31}P -NMR (202 MHz, CDCl_3) spectrum of compound 16a:



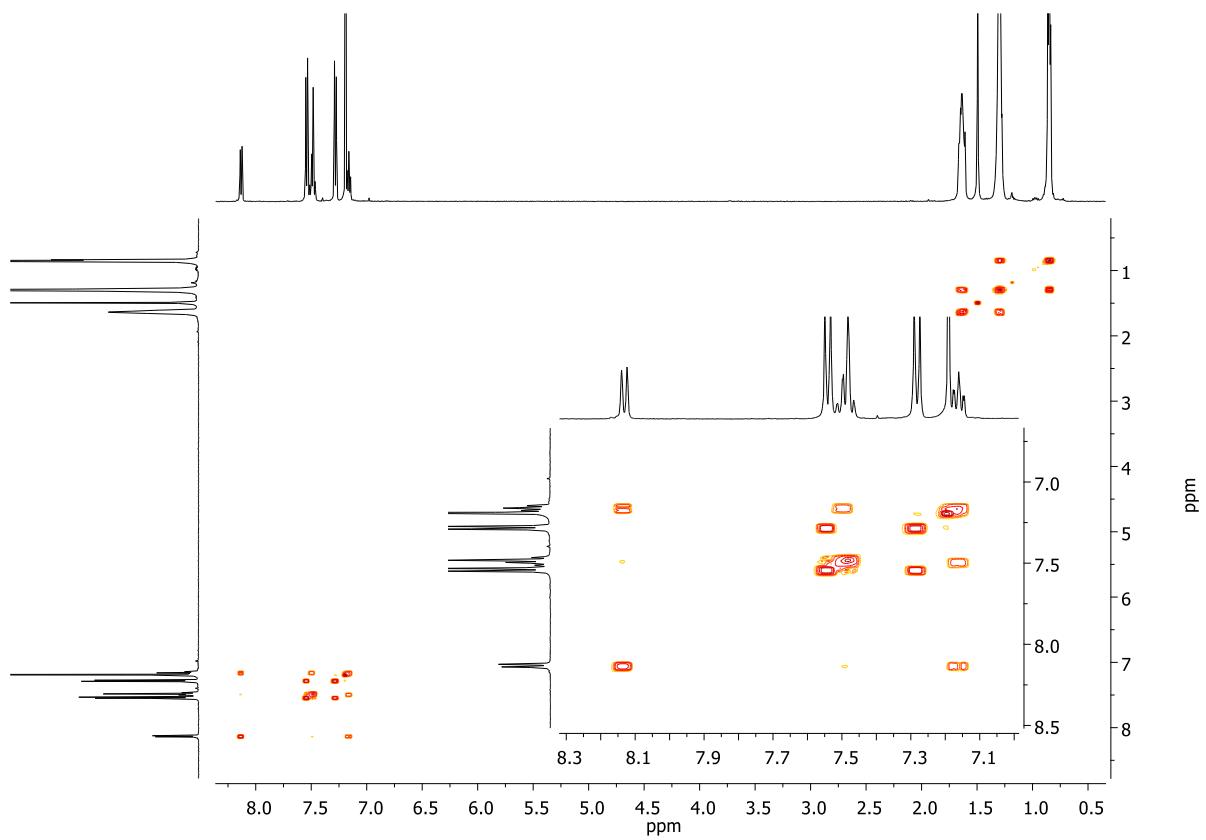
HSQC spectrum of compound 16a:



HMBC spectrum of compound 16a:

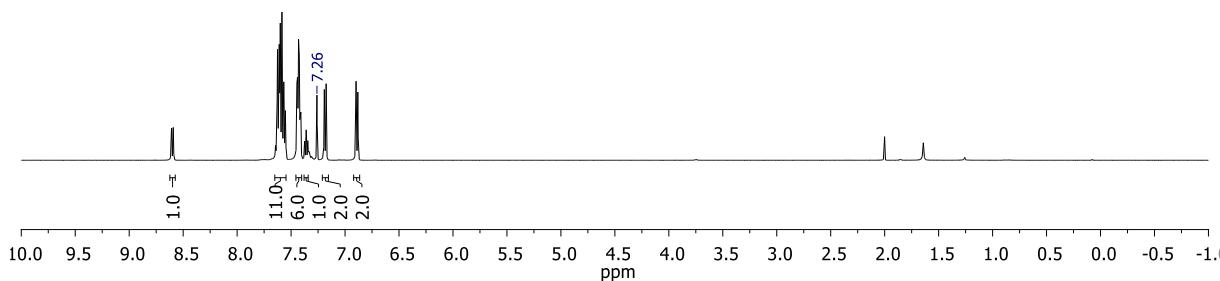
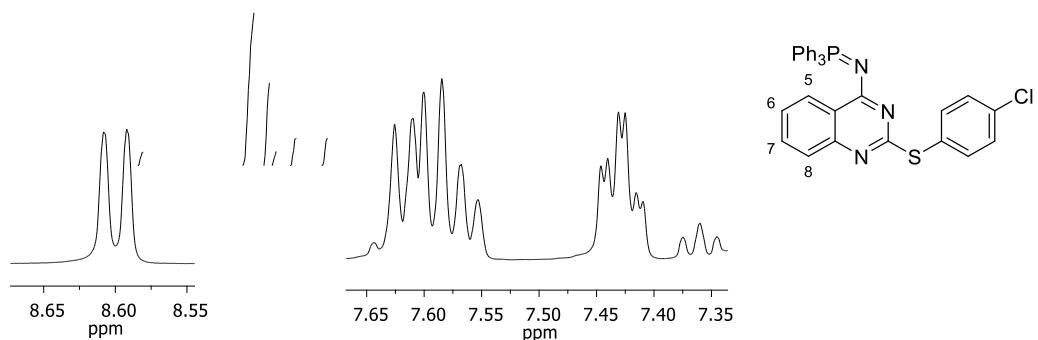


COSY spectrum of compound 16a:

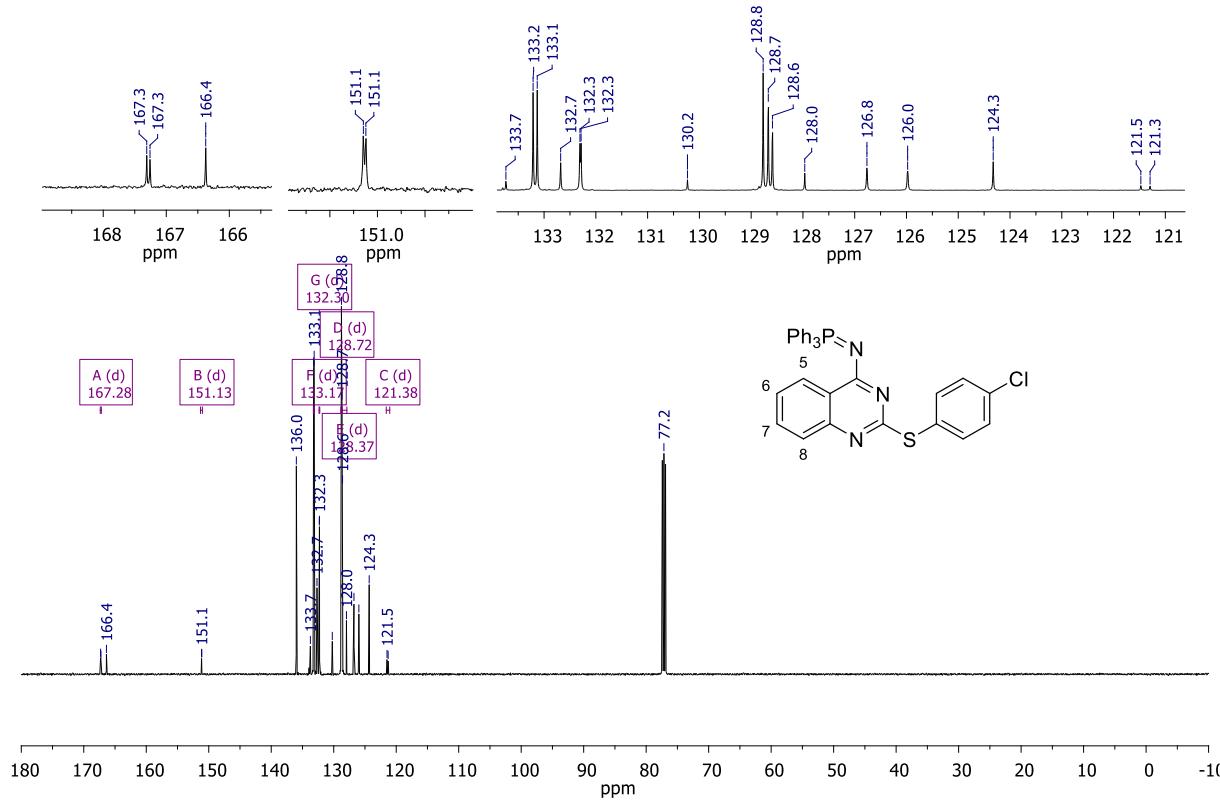


2-[(4-Chlorophenylthio)-4-[(triphenylphosphoronylidene)amino]quinazoline (16b)

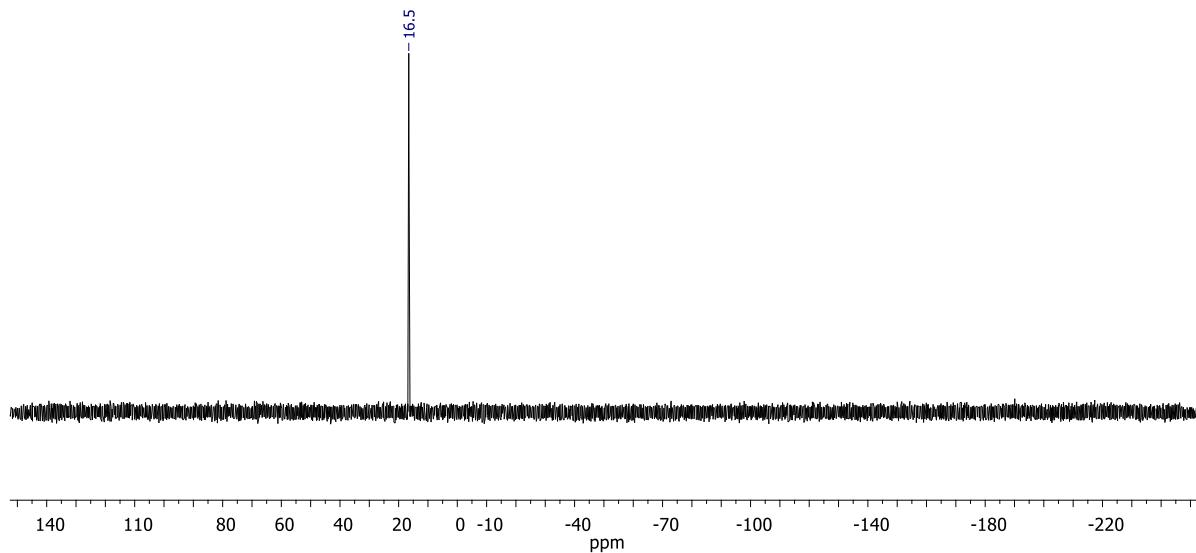
$^1\text{H-NMR}$ (500 MHz, CDCl_3) spectrum of compound 16b:



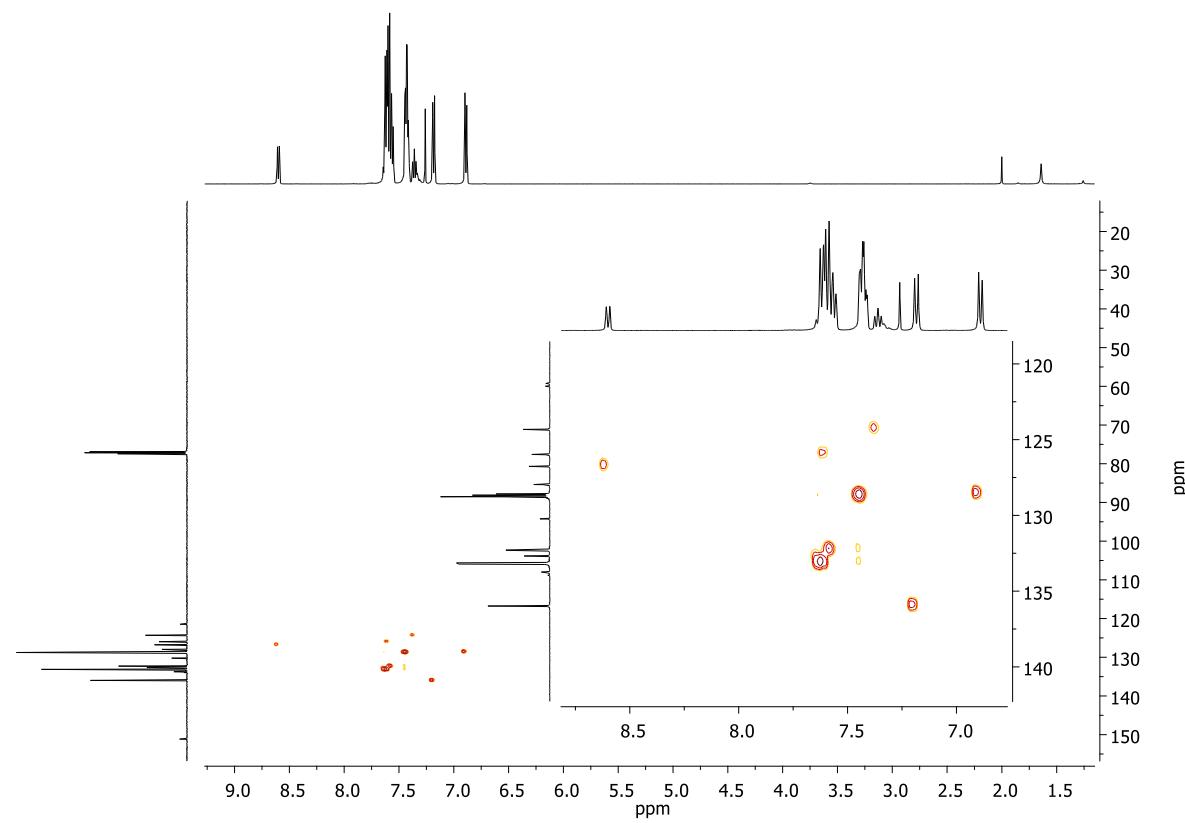
$^{13}\text{C-NMR}$ (125.7 MHz, CDCl_3) spectrum of compound 16b:



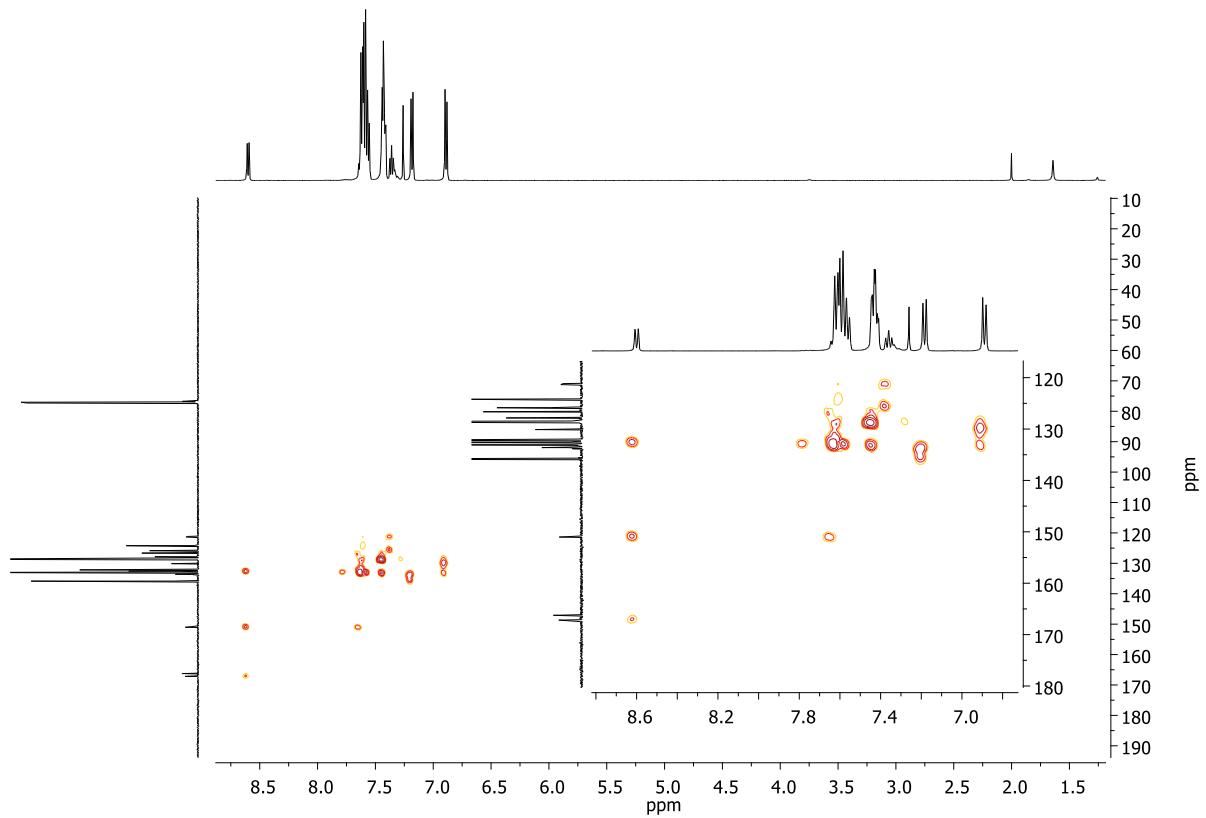
^{31}P -NMR (202 MHz, CDCl_3) spectrum of compound 16b:



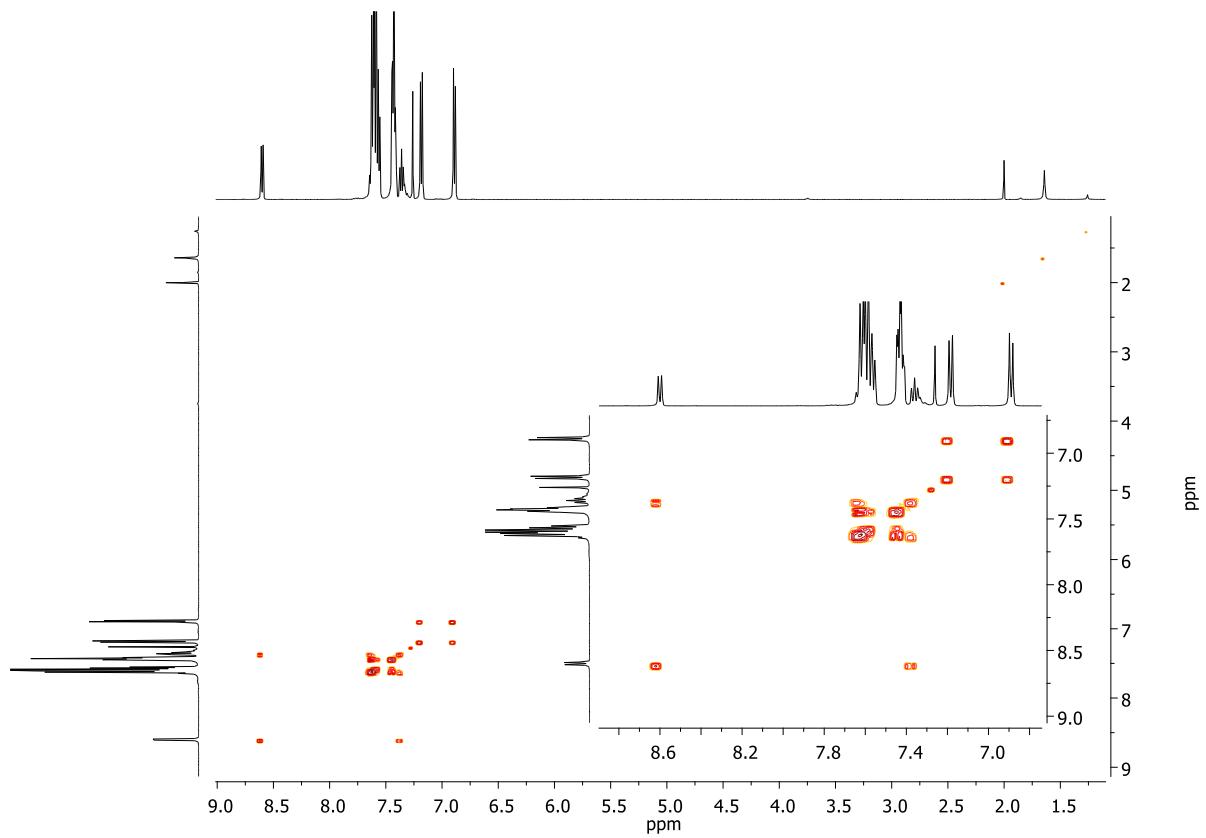
HSQC spectrum of compound 16b:



HMBC spectrum of compound 16b:



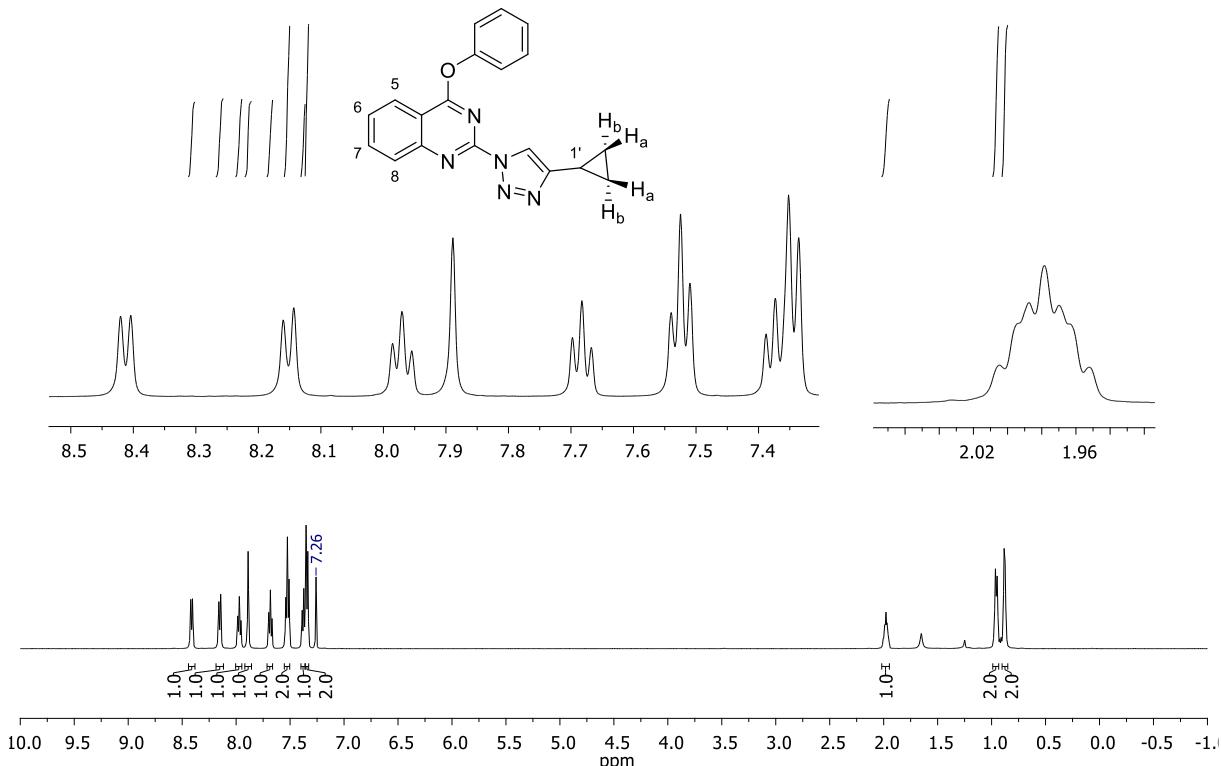
COSY spectrum of compound 16b:



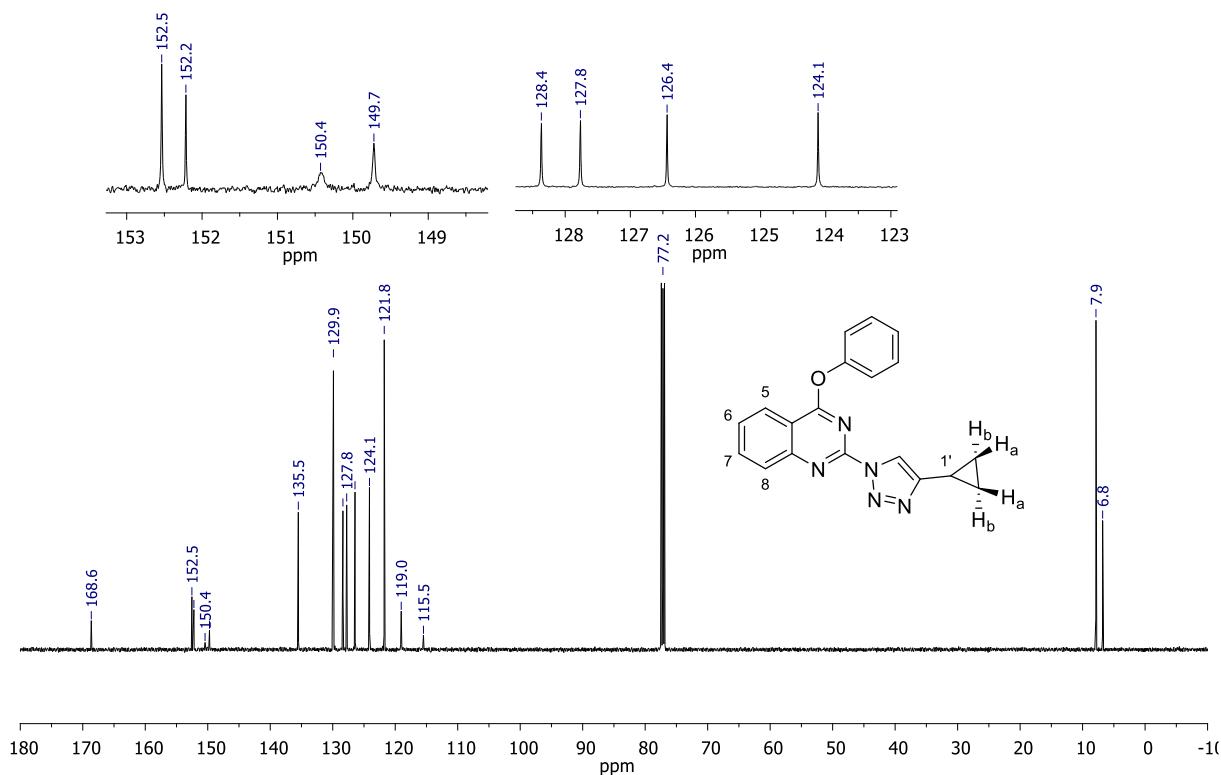
4-(Alkyl/Aryloxy)-2-(1*H*-1,2,3-triazol-1-yl)quinazolines

2-(4-Cyclopropyl-1*H*-1,2,3-triazol-1-yl)-4-(phenyloxy)quinazoline (17a)

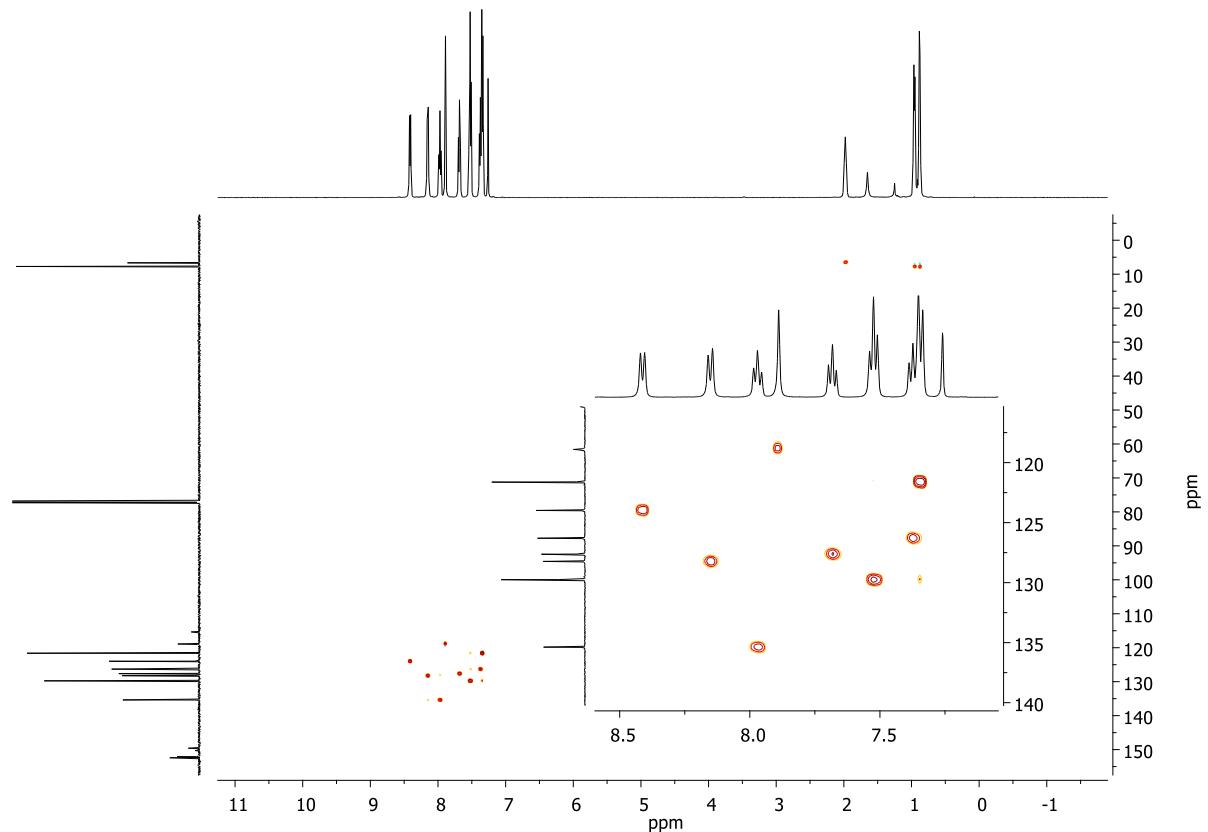
¹H-NMR (500 MHz, CDCl₃) spectrum of compound 17a:



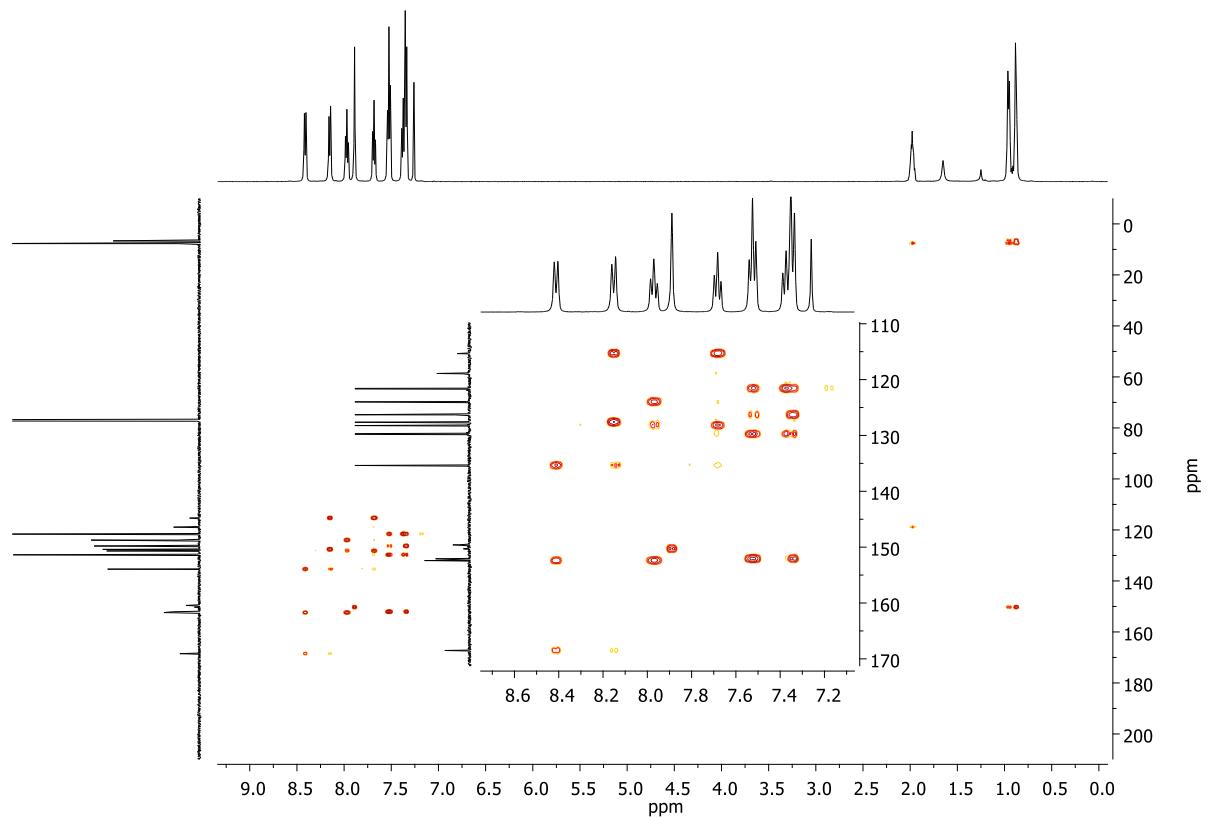
¹³C-NMR (125.7 MHz, CDCl₃) spectrum of compound 17a:



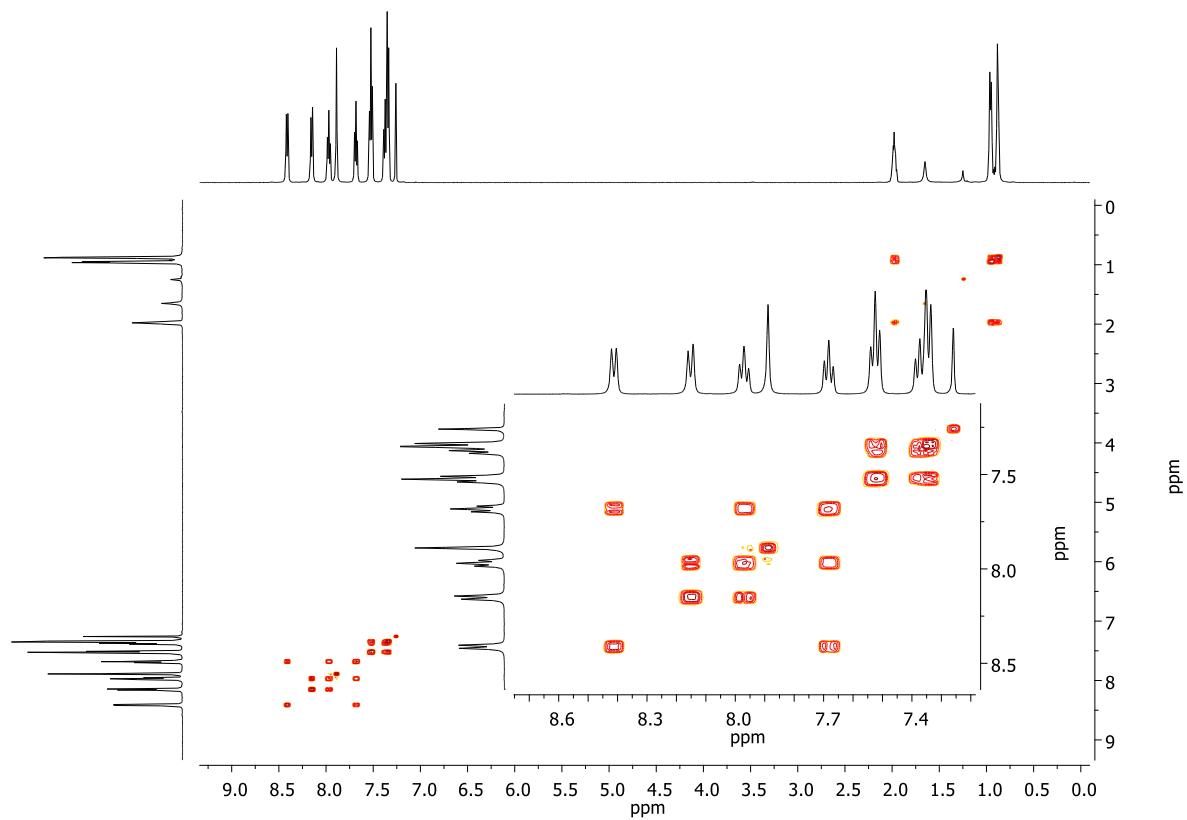
HSQC spectrum of compound 17a:



HMBC spectrum of compound 17a:

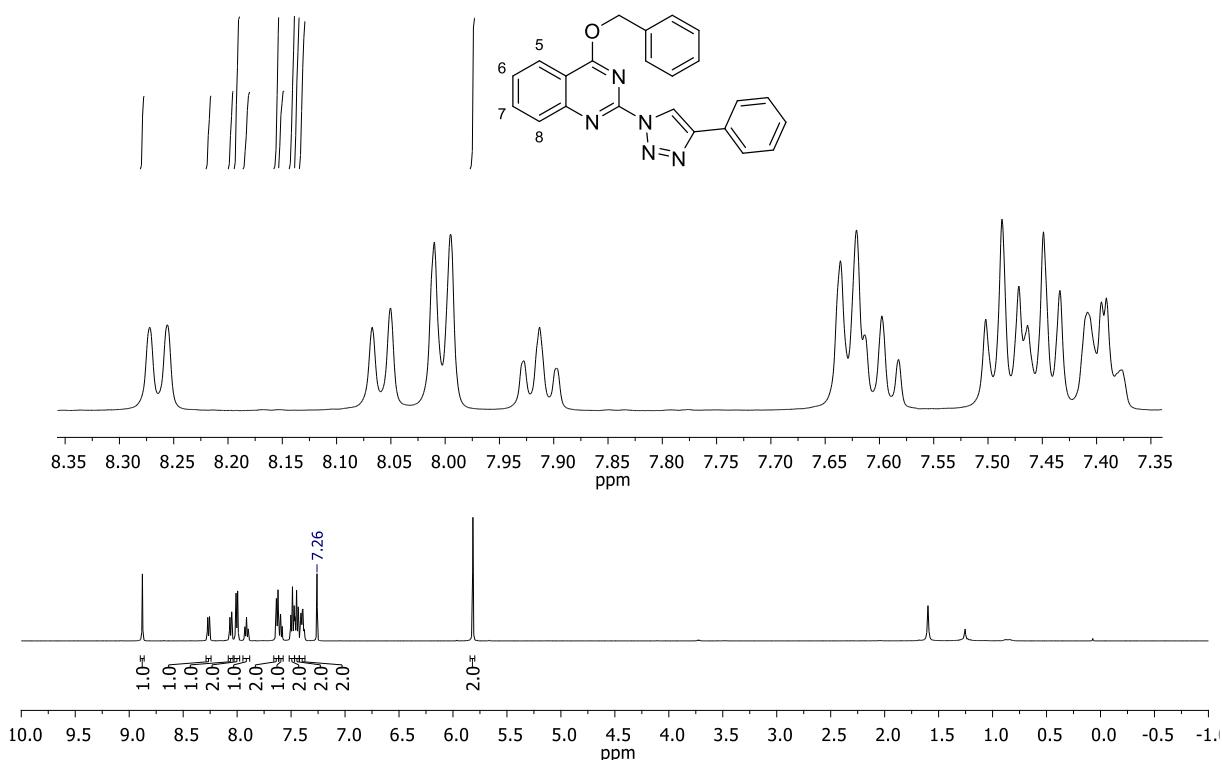


COSY spectrum of compound 17a:

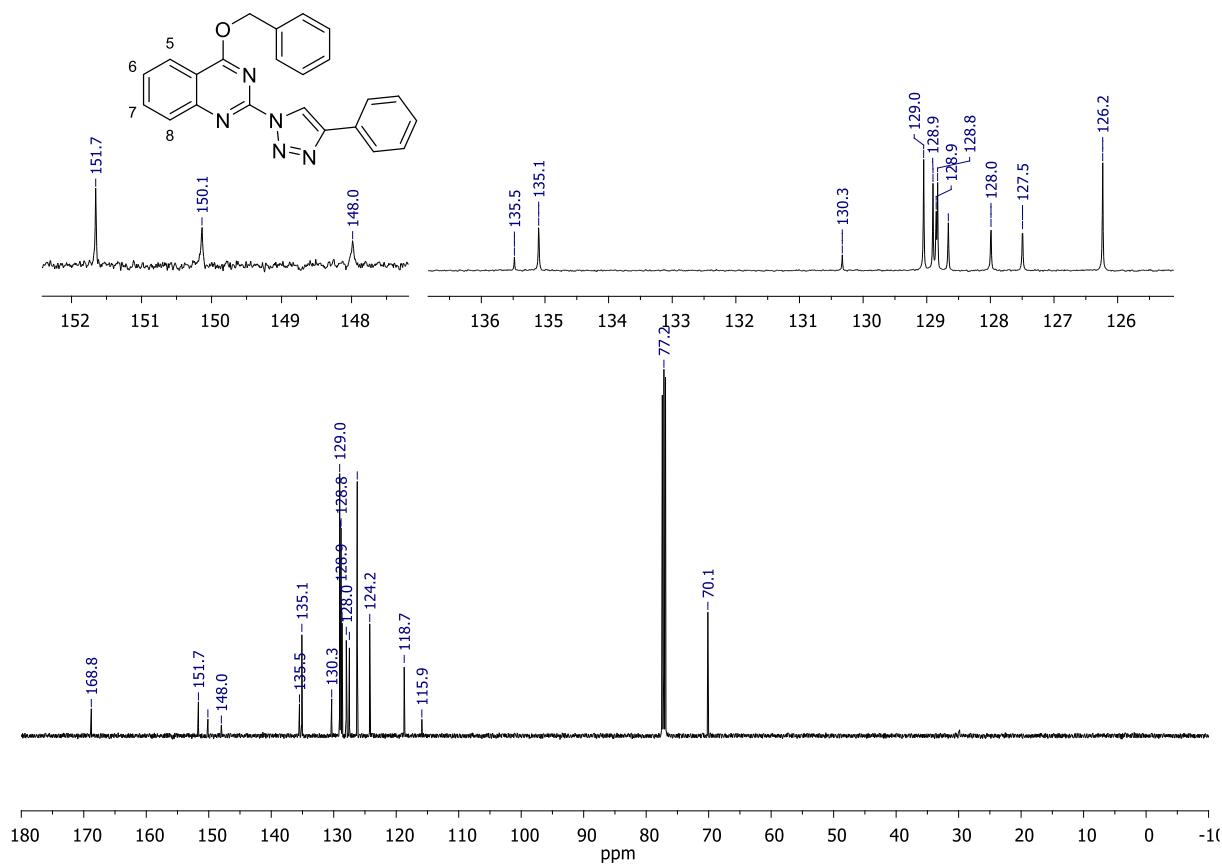


4-(BenzylOxy)-2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)quinazoline (17b)

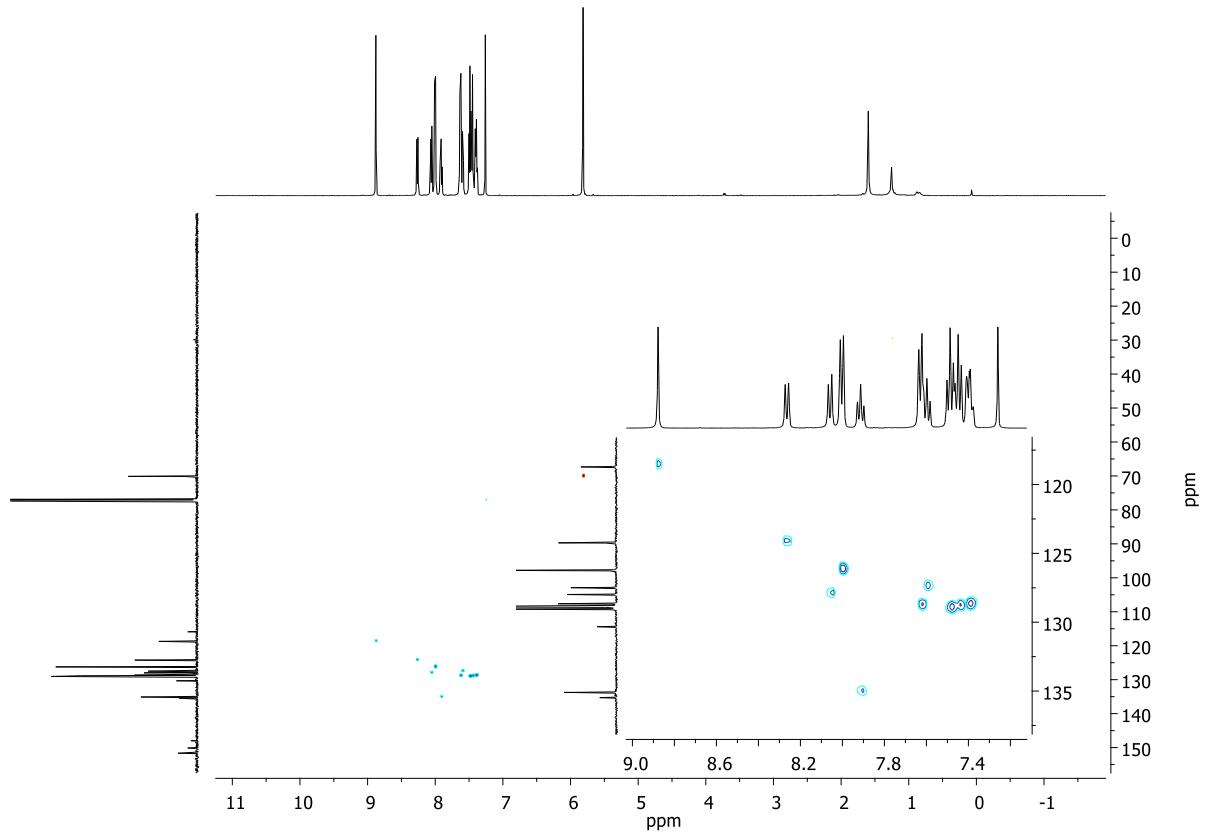
$^1\text{H-NMR}$ (500 MHz, CDCl_3) spectrum of compound 17b:



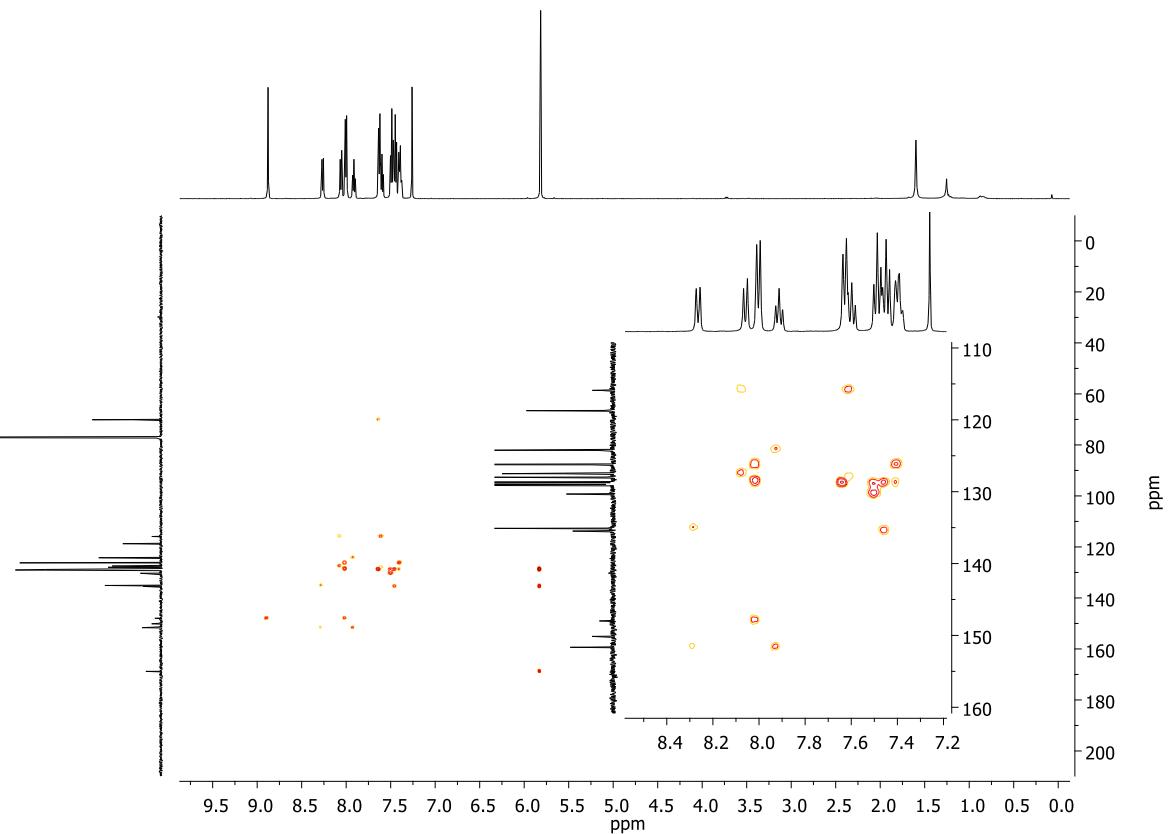
$^{13}\text{C-NMR}$ (125.7 MHz, CDCl_3) spectrum of compound 17b:



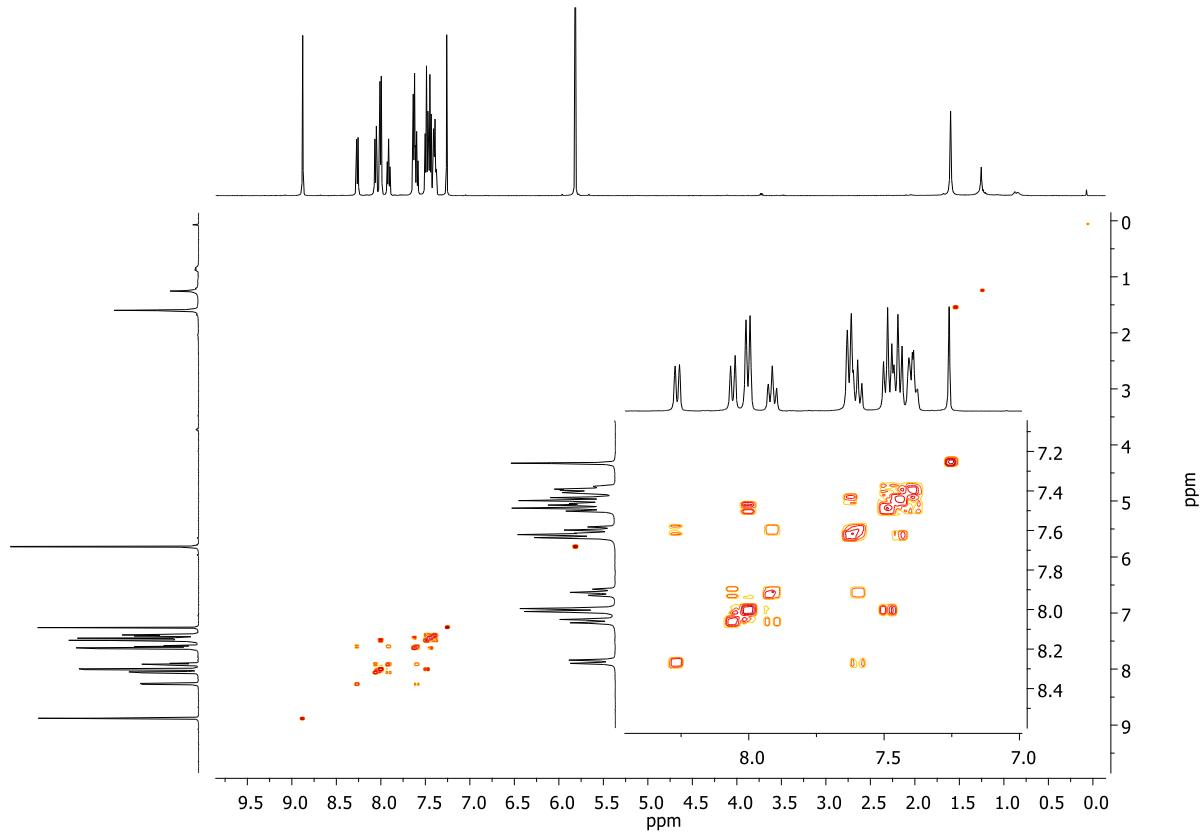
HSQC spectrum of compound 17b:



HMBC spectrum of compound 17b:



COSY spectrum of compound 17b:



Azide-tetrazole equilibrium studies

Table 1. Amount of azide (A) and tetrazole (T) forms (%) of compound 4d in different solvents and temperatures (300 MHz, 3 sets of measurements with standard deviation Δs).

	Solvent		CDCl ₃	DMSO-d ₆	Acetic acid-d ₄	Acetone-d ₆	CD ₃ CN	THF-d ₈
	Dielectric constant ϵ^1		4.8	46.7	6.1	20.7	37.5	7.6
	lg ϵ		0.68	1.67	0.79	1.32	1.57	0.88
T, °C	22	1	T, %	72	94	51	86	91
			A, %	28	6	49	14	9
		2	T, %	75	94	50	84	90
			A, %	25	6	50	16	10
		3	T, %	75	94	51	83	90
			A, %	25	6	49	17	10
	Average	T, %	74.0	94.0	50.7	84.3	90.3	76.3
		A, %	26.0	6.0	49.3	15.7	9.7	23.7
	Δs , %		1.73	0.00	0.58	1.53	0.58	1.15
	30	1	T, %	69	93	49	84	89
			A, %	31	7	51	16	11
		2	T, %	72	93	50	82	89
			A, %	28	7	50	18	11
		3	T, %	71	93	50	80	89
			A, %	29	7	50	20	11
	Average	T, %	70.7	93.0	49.7	82.0	89.0	73.3
		A, %	29.3	7.0	50.3	18.0	11.0	26.7
	Δs , %		1.53	0.00	0.58	2.00	0.00	1.15
40	40	1	T, %	65	92	47	80	87
			A, %	35	8	53	20	13
		2	T, %	66	91	47	79	87
			A, %	34	9	53	21	13
		3	T, %	69	91	48	77	87
			A, %	31	9	52	23	13
	Average	T, %	66.7	91.3	47.3	78.7	87.0	69.0
		A, %	33.3	8.7	52.7	21.3	13.0	31.0
	Δs , %		2.08	0.58	0.58	1.53	0.00	1.00

¹ O'Neil, M. J.; Heckelman, P. E.; Ko. The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals, 14th Edition. *J. Am. Chem. Soc.* **2007**, 129 (7), 2197–2197.

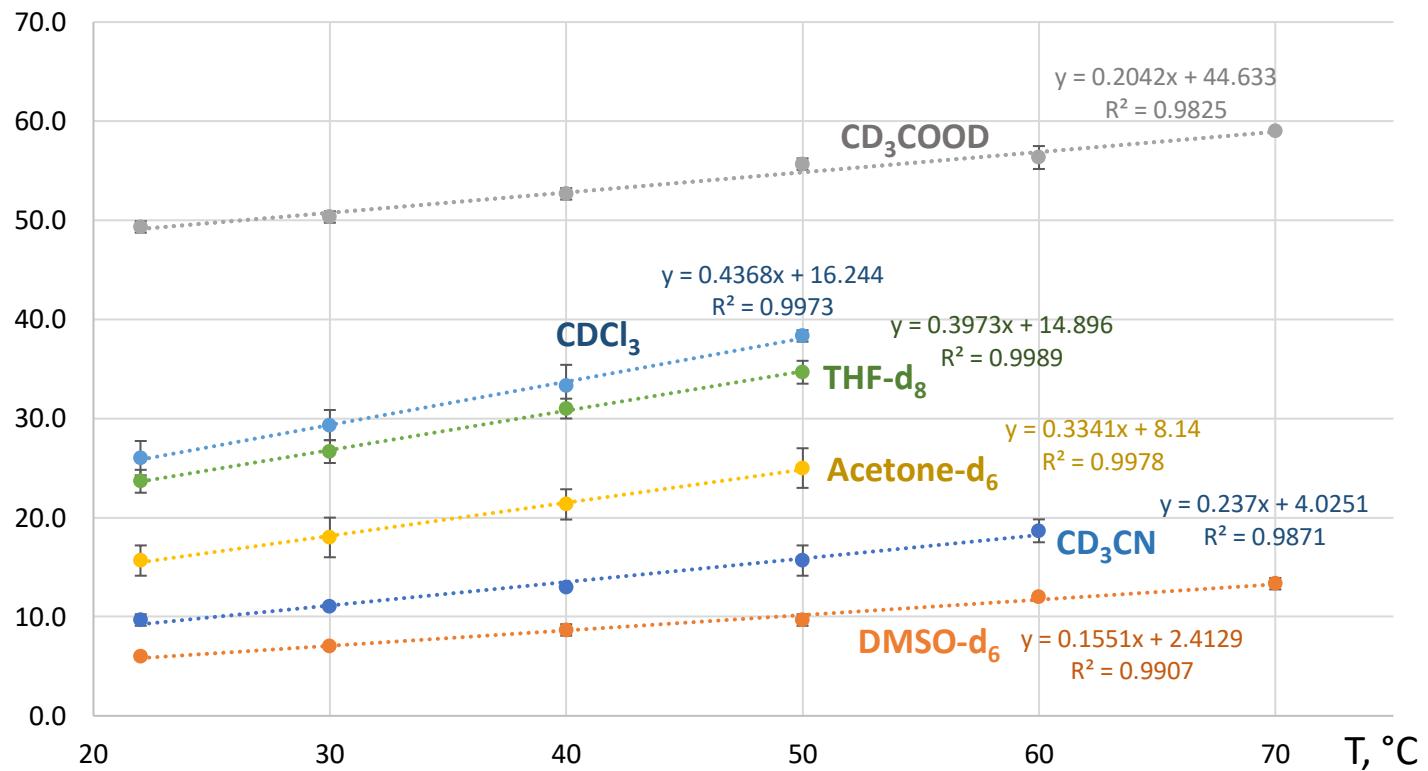
Table 1 (continued).

	Solvent		CDCl_3	DMSO-d_6	Acetic acid- d_4	Acetone- d_6	CD_3CN	THF-d_8
	Dielectric constant ϵ^1		4.8	46.7	6.1	20.7	37.5	7.6
	$\lg \epsilon$		0.68	1.67	0.79	1.32	1.57	0.88
T, °C	50	1	T, %	61	90	44	77	84
			A, %	39	10	56	23	16
	2		T, %	62	91	45	75	86
			A, %	38	9	55	25	14
	3		T, %	62	90	44	73	83
			A, %	38	10	56	27	17
	Average		T, %	61.7	90.3	44.3	75.0	84.3
			A, %	38.3	9.7	55.7	25.0	15.7
	Δs , %		0.58	0.58	0.58	2.00	1.53	1.15
	60	1	T, %		88	43		82
			A, %		12	57		18
		2	T, %		88	43		80
			A, %		12	57		20
		3	T, %		88	45		82
			A, %		12	55		18
		Average	T, %		88	43.67		81.33
			A, %		12	56.33		18.67
		Δs , %			0	1.154701		1.154701
		70	1	T, %	86	41		
				A, %	14	59		
			2	T, %	87	41		
				A, %	13	59		
			3	T, %	87	41		
				A, %	13	59		
			Average	T, %	86.67	41.00		
				A, %	13.33	59.00		
		Δs			0.57735	0.00		

¹ O'Neil, M. J.; Heckelman, P. E.; Ko. The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals, 14th Edition. *J. Am. Chem. Soc.* **2007**, 129 (7), 2197–2197.

Azide form tautomeric ratio (%) of compound 4d depending on temperature in different solvents (Table 1)

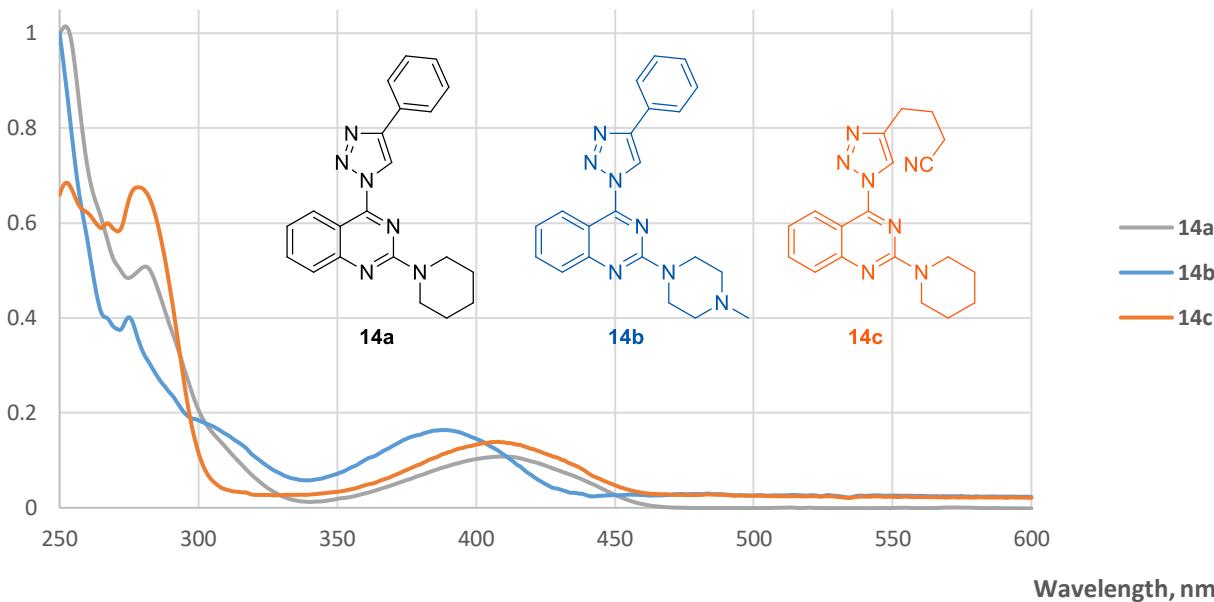
4d-A, %



UV/Vis absorption and emission spectra

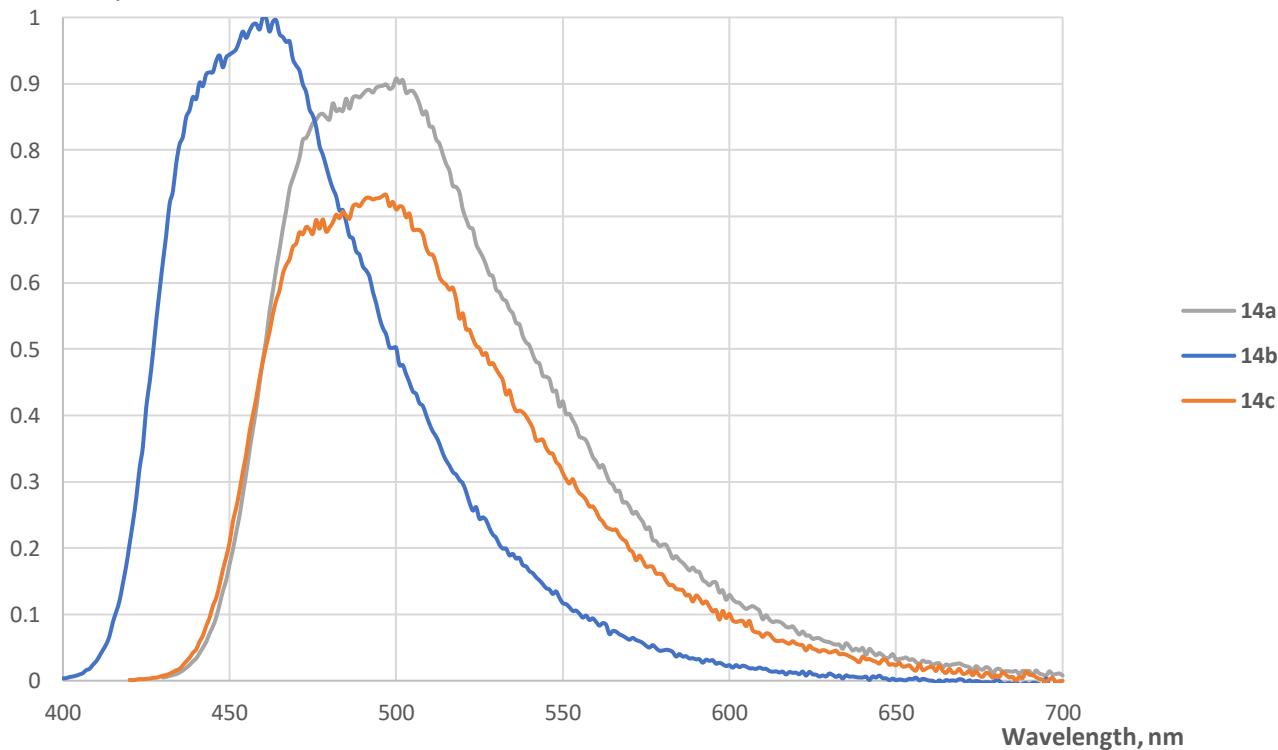
Absorbtion spectra of 4-triazolylquinazoline derivatives **14** ($c = 10^{-5}$ M; solvent – DCM):

Absorbtion, A

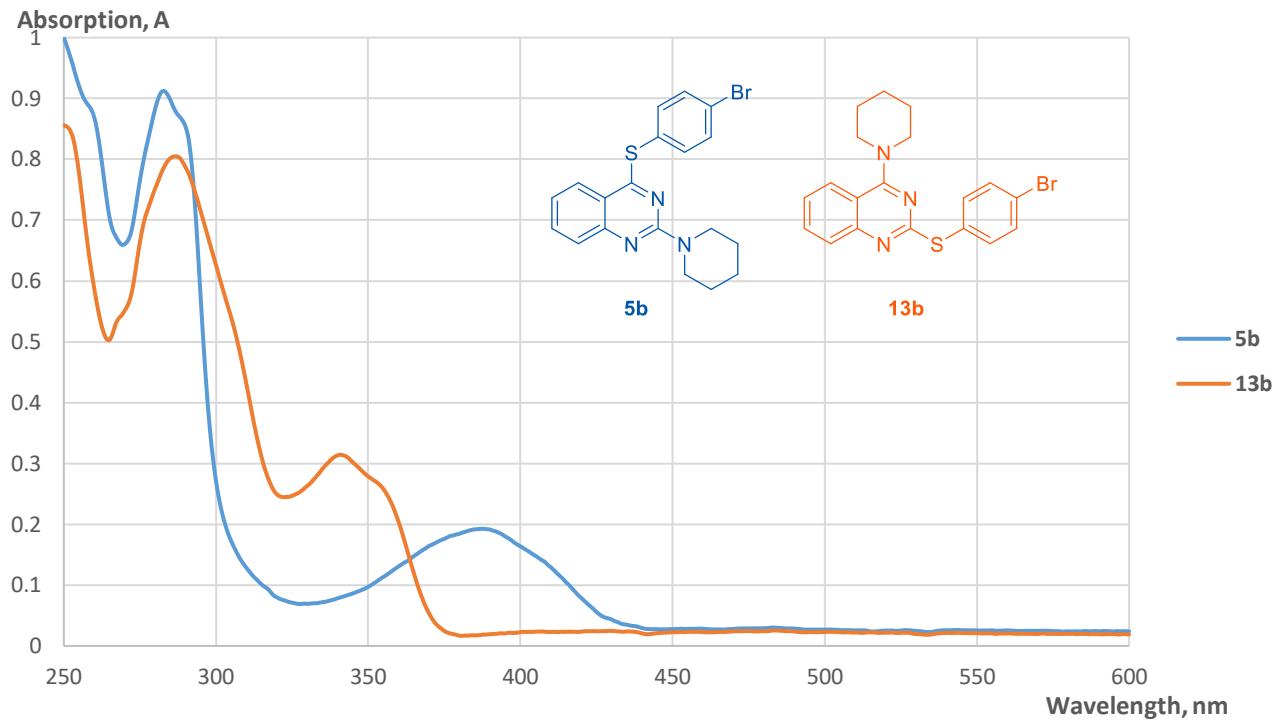


Emission spectra of 4-triazolylquinazoline derivatives **14a** ($\lambda_{\text{exc}} = 405$ nm), **14b** ($\lambda_{\text{exc}} = 380$ nm) and **14c** ($\lambda_{\text{exc}} = 400$ nm) ($c = 10^{-5}$ M; solvent – DCM):

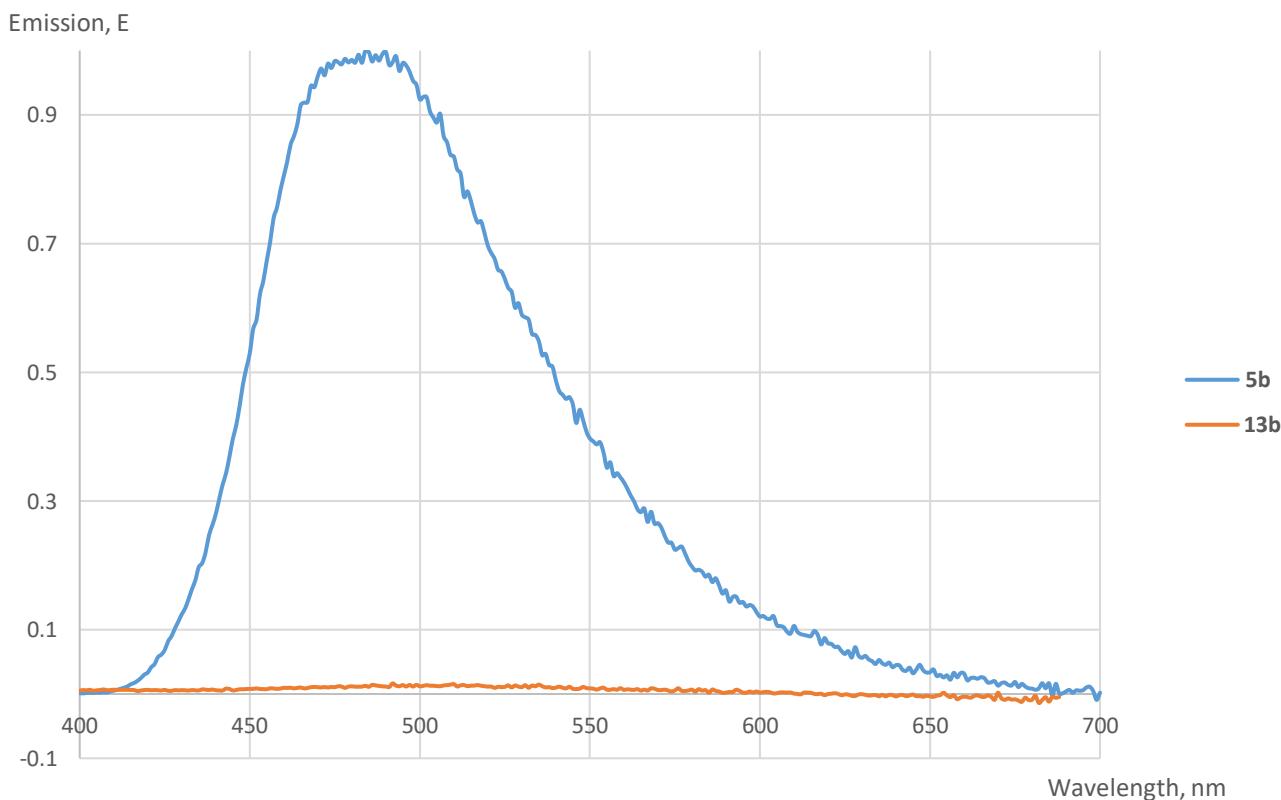
Emission, E



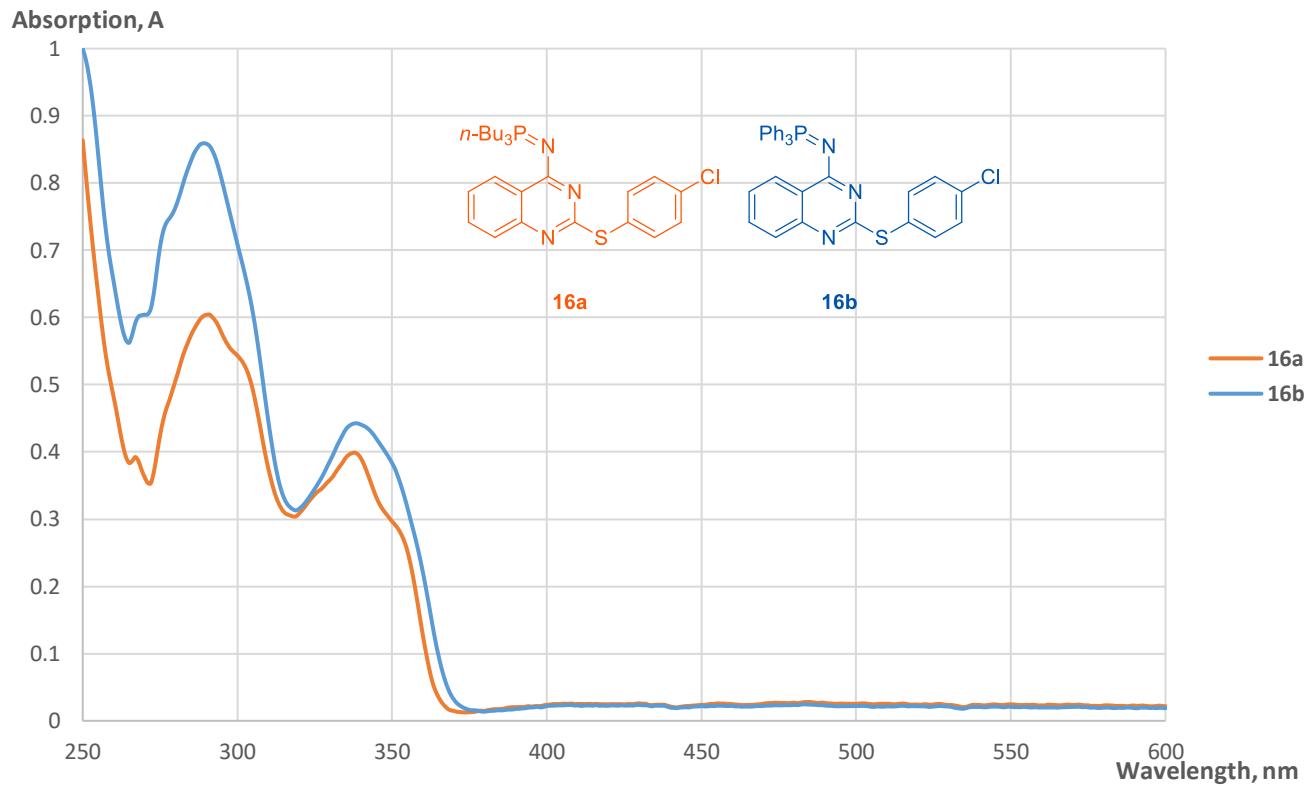
Absorbtion spectra of amino-arylthioquinazoline regioisomers 5b and 13b ($c = 8 \times 10^{-6}$ M; solvent – DCM):



Emission spectra of amino-arylthioquinazoline regioisomers 5b ($\lambda_{\text{exc}} = 380$ nm) and 13b ($\lambda_{\text{exc}} = 320$ nm) ($c = 8 \times 10^{-6}$ M; solvent – DCM):



Absorbtion spectra of quinazoline iminophosphoranes 16a and 16b ($c = 9 \times 10^{-6}$ M; solvent – DCM):



Emission spectra of quinazoline iminophosphoranes 16a and 16b ($\lambda_{exc} = 320$ nm) ($c = 9 \times 10^{-6}$ M; solvent – DCM):

