

## Supplementary Information

### Synthesis and biological evaluation of 1,2,4-triazoloazines as potent anticancer agents.

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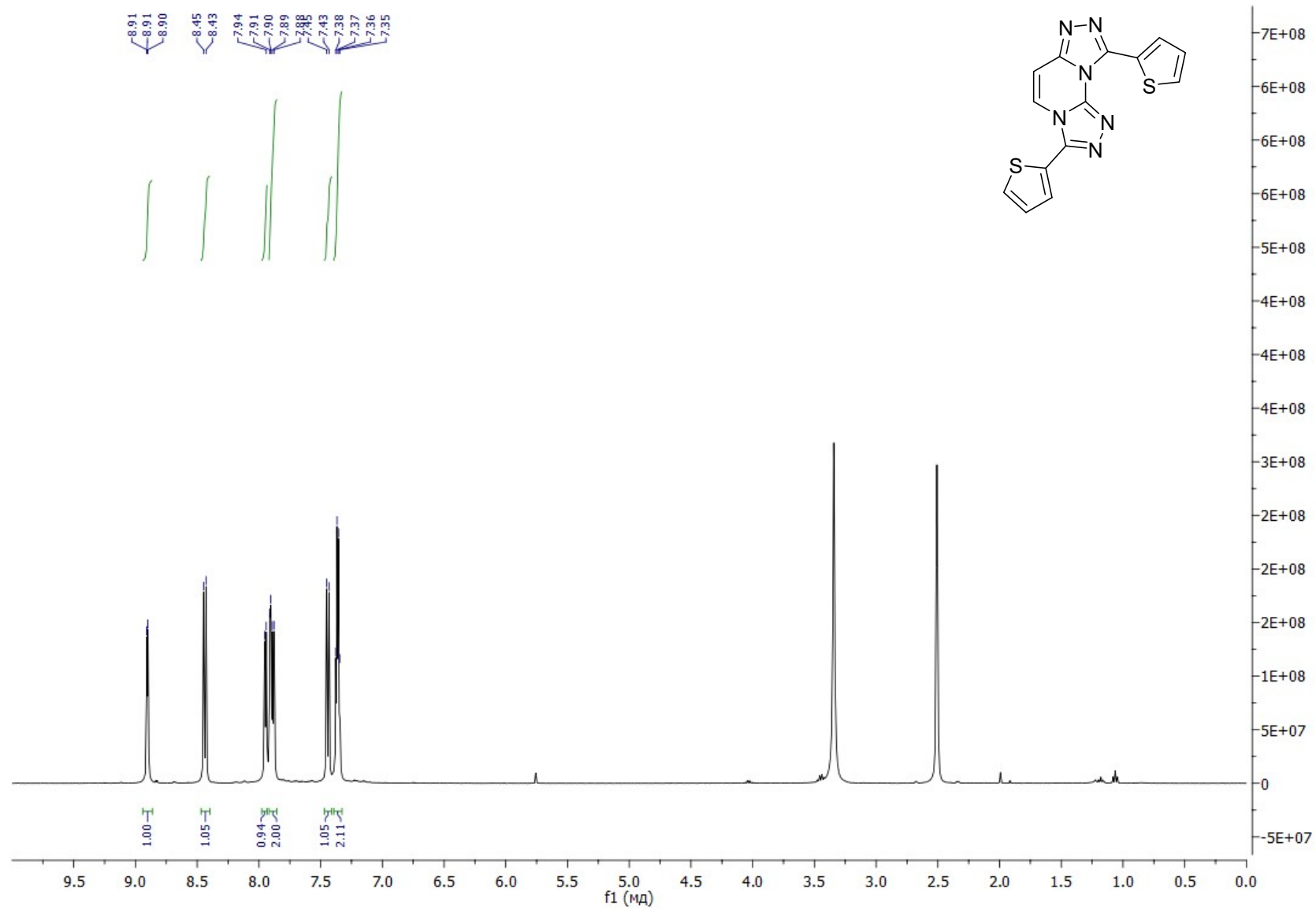
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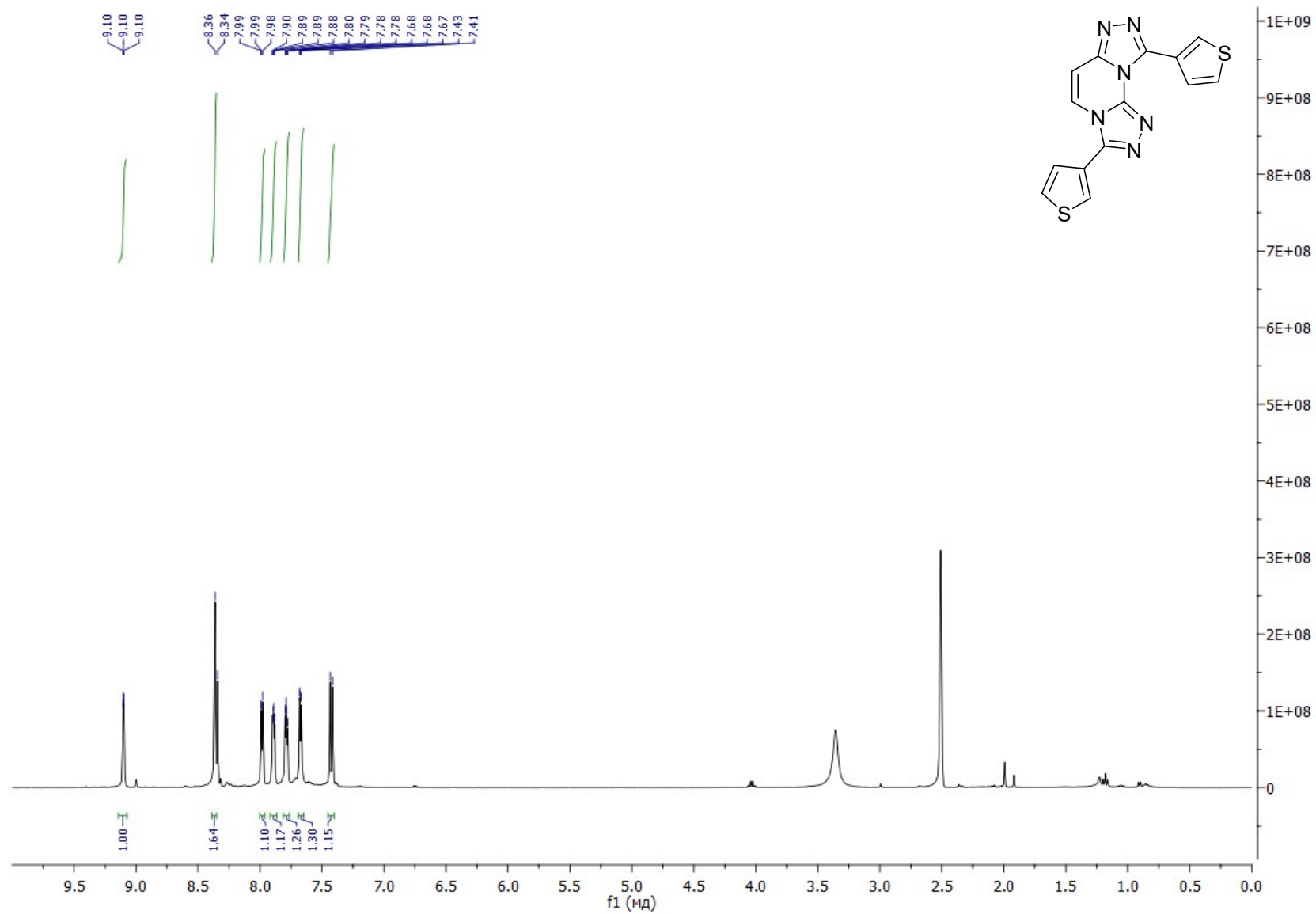
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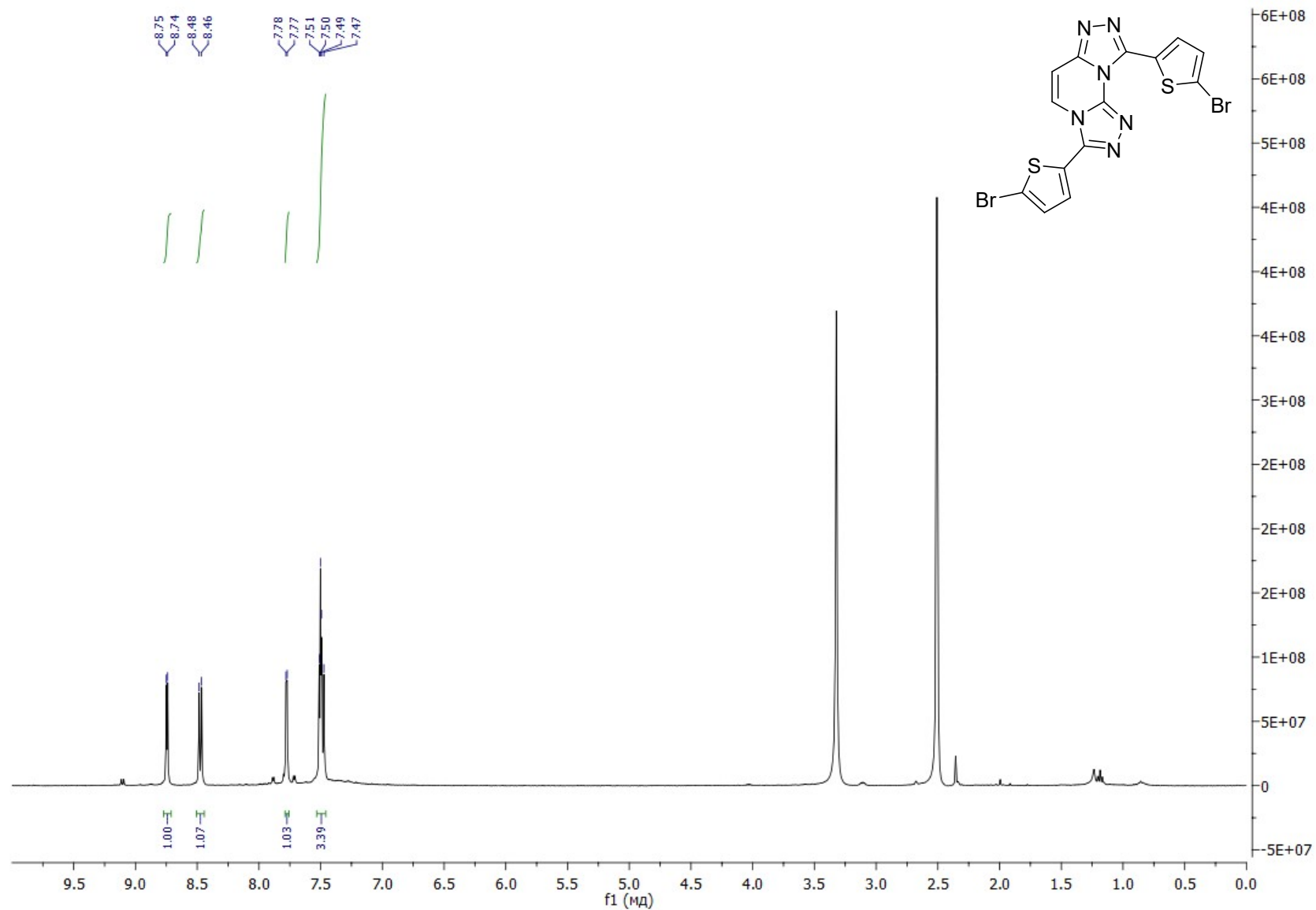
# NMR <sup>1</sup>H Spectra



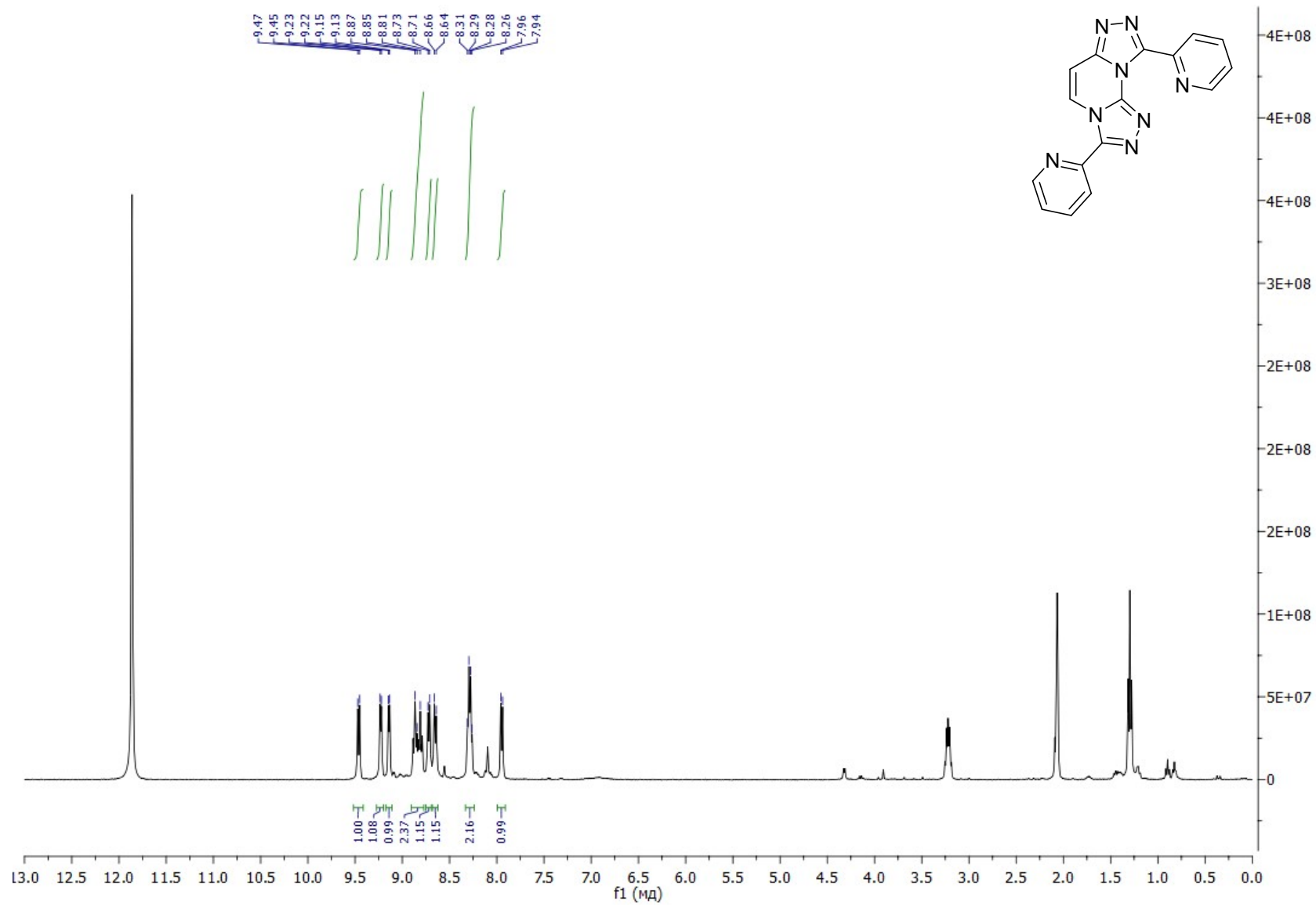
**Fig. 1** <sup>1</sup>H NMR spectrum for 3,9-di(thiophen-2-yl)bis([1,2,4]triazolo)[4,3-a:4',3'-c]pyrimidine (**8a**).



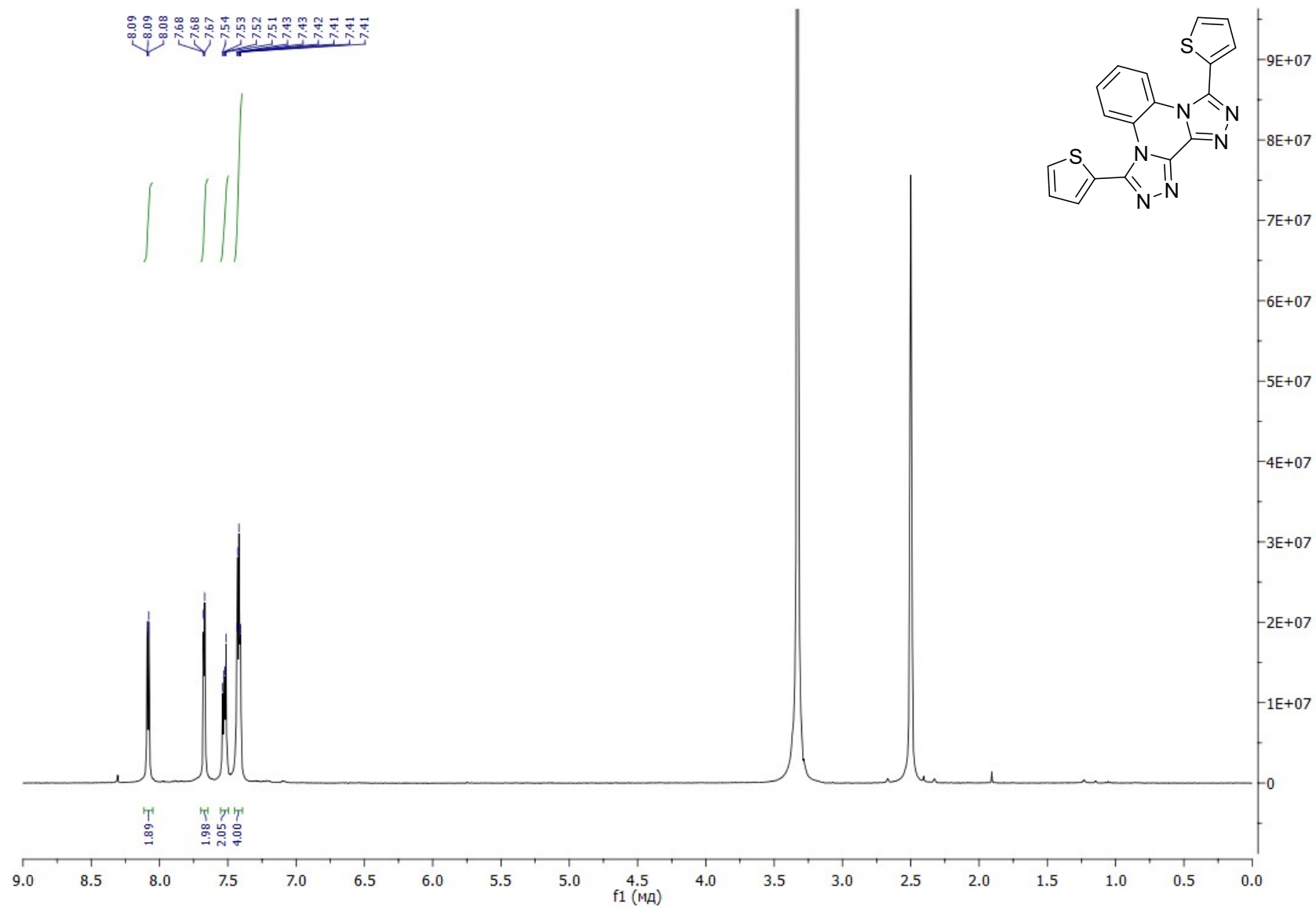
**Fig. 2** <sup>1</sup>H NMR spectrum for 3,9-di(thiophen-3-yl)bis([1,2,4]triazolo)[4,3-*a'*:3'-*c*]pyrimidine (**8b**).



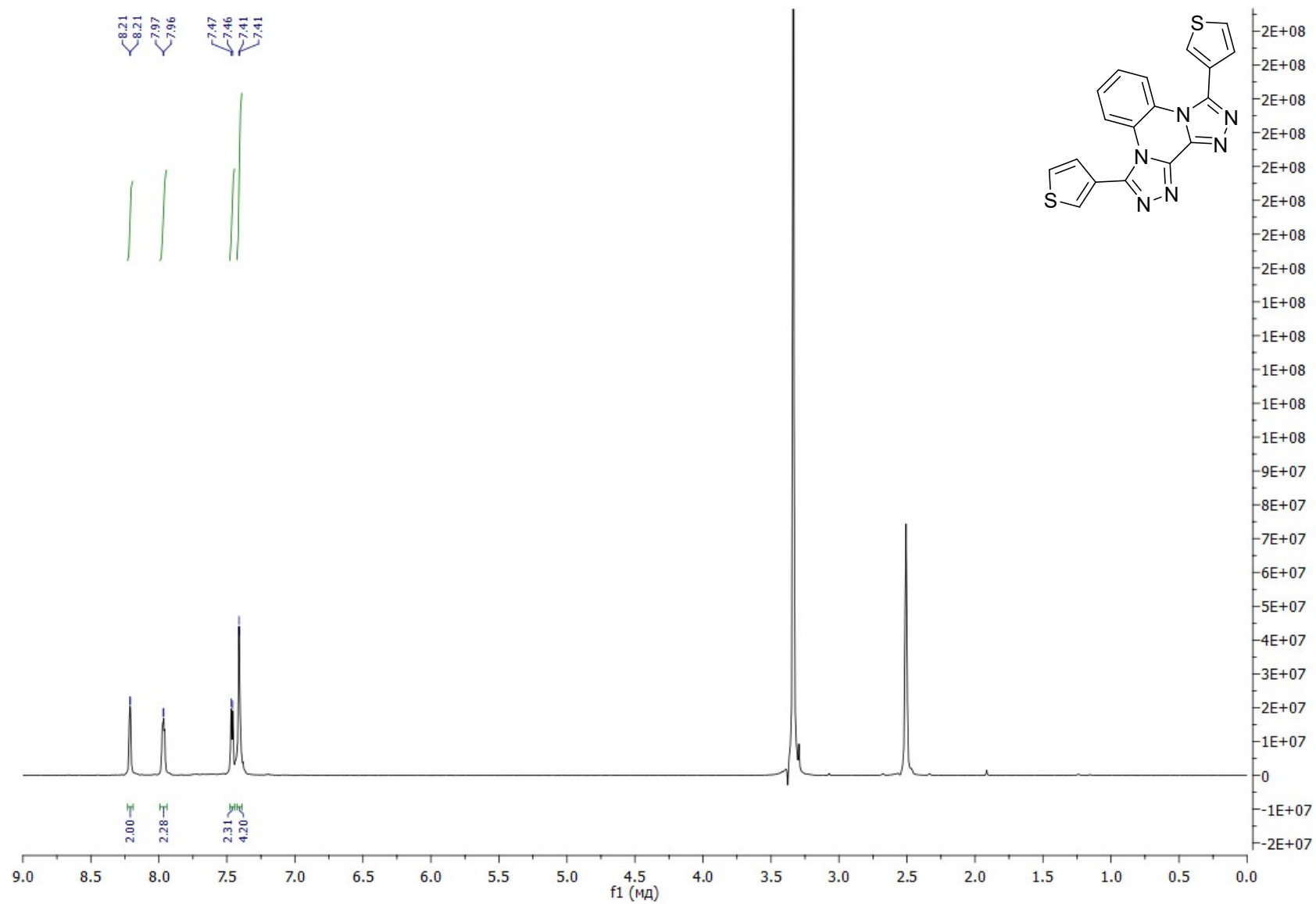
**Fig. 3** <sup>1</sup>H NMR spectrum for 3,9-bis(5-bromothiophen-2-yl)bis([1,2,4]triazolo)[4,3-*a*:4',3'-*c*]pyrimidine (**8c**).



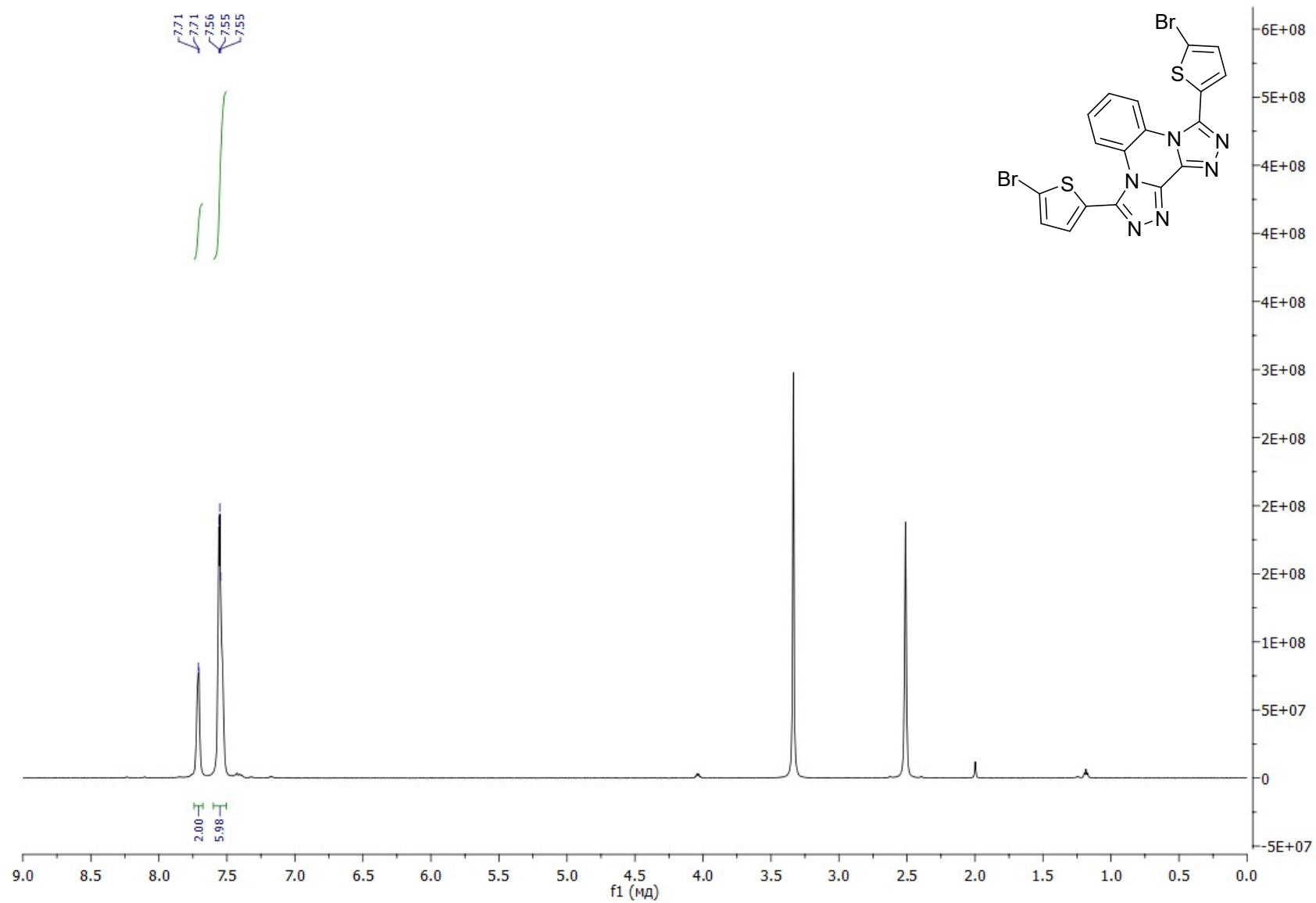
**Fig. 4** <sup>1</sup>H NMR spectrum for 3,9-di(pyridin-2-yl)bis([1,2,4]triazolo)[4,3-*a*:4',3'-*c*]pyrimidine (**8d**).



**Fig. 5** <sup>1</sup>H NMR spectrum for 3,10-di(thiophen-2-yl)bis([1,2,4]triazolo)[4,3-*a*:3',4'-*c*]quinoxaline (**8e**).

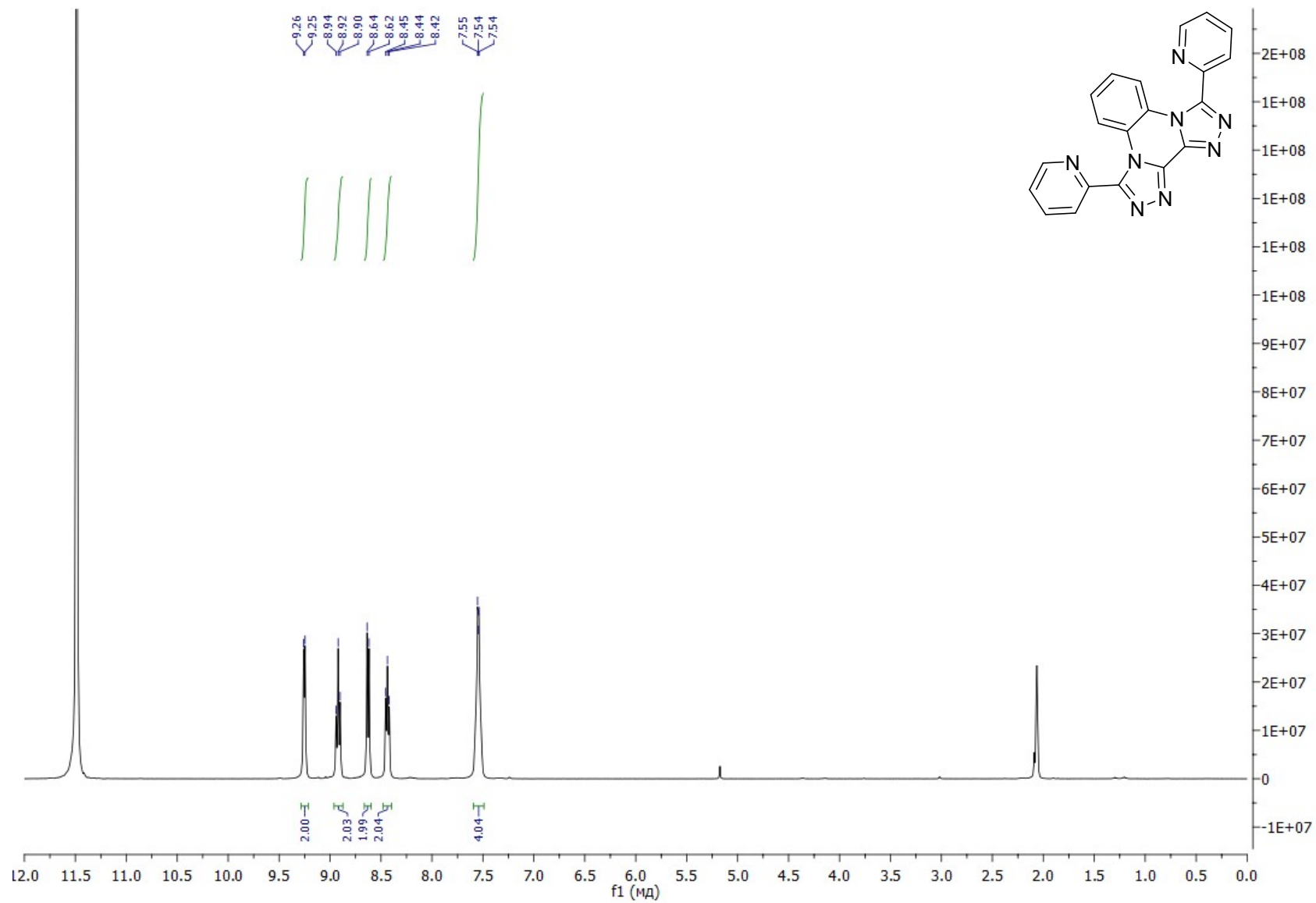


**Fig. 6** <sup>1</sup>H NMR spectrum for 3,10-di(thiophen-3-yl)bis([1,2,4]triazolo)[4,3-*a*:3',4'-*c*]quinoxaline (**8f**).

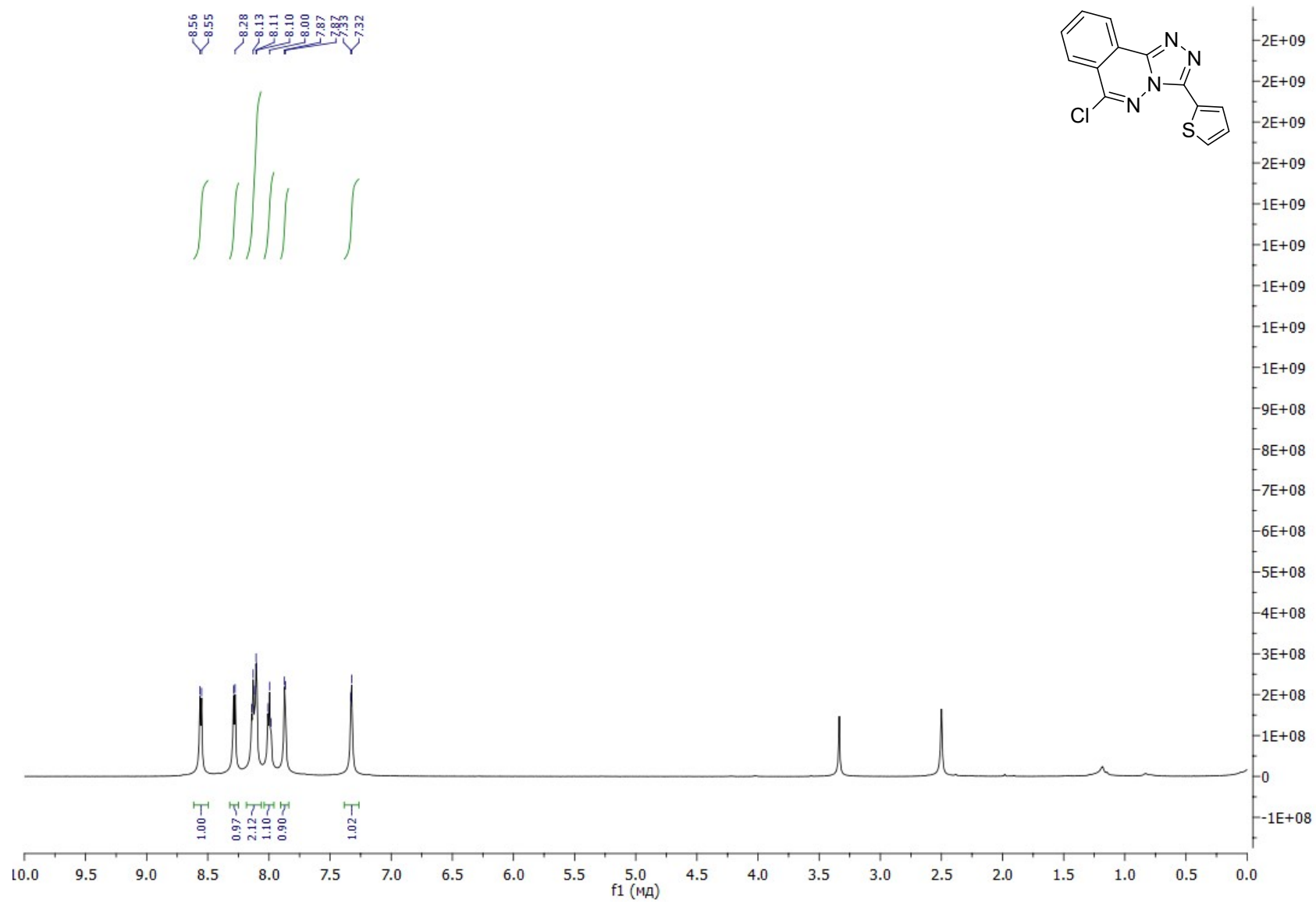


**Fig. 7** <sup>1</sup>H NMR spectrum for 3,10-bis(5-bromothiophen-2-yl)bis([1,2,4]triazolo)[4,3-*a*:3',4'-*c*]quinoxaline (**8g**).

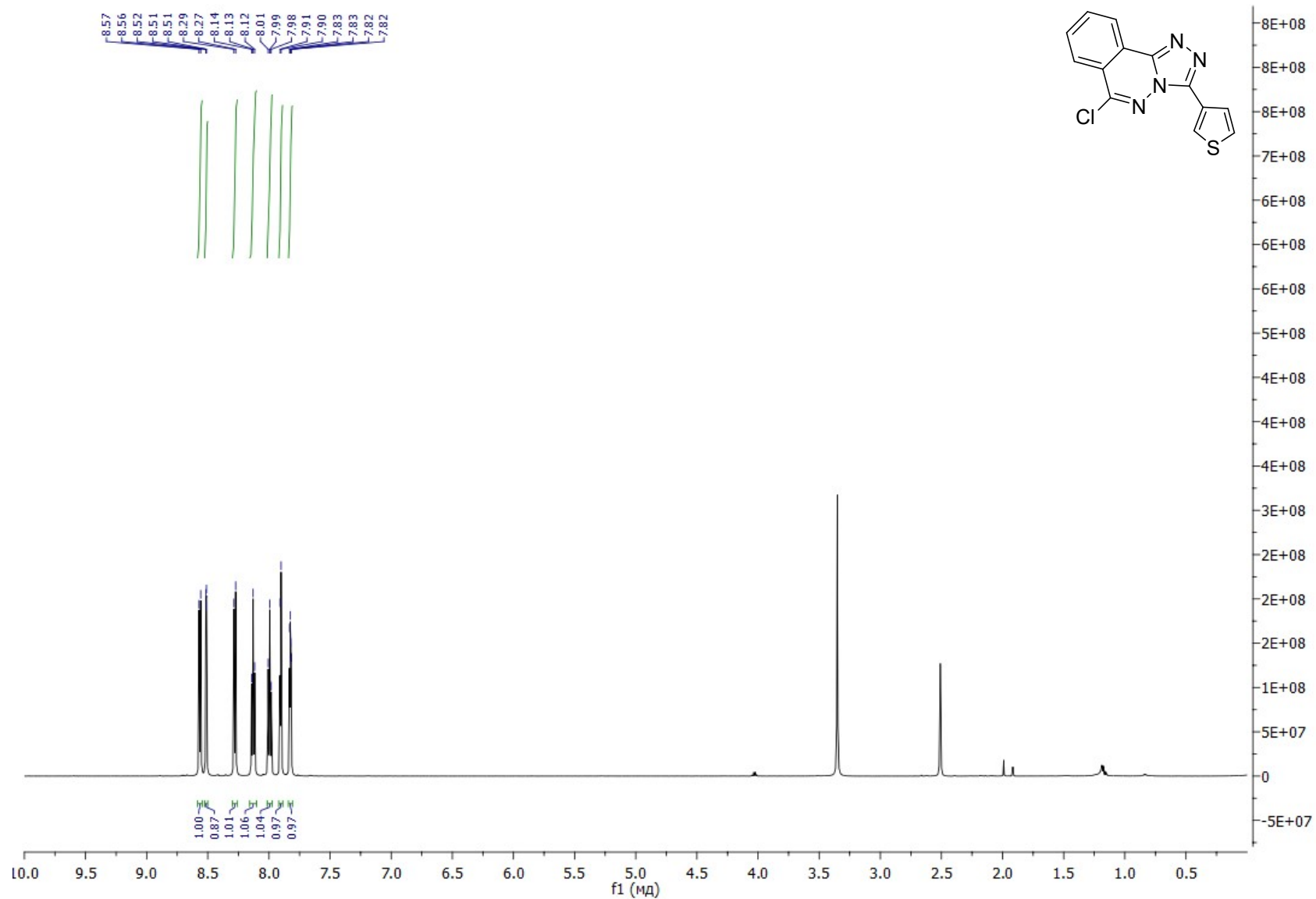




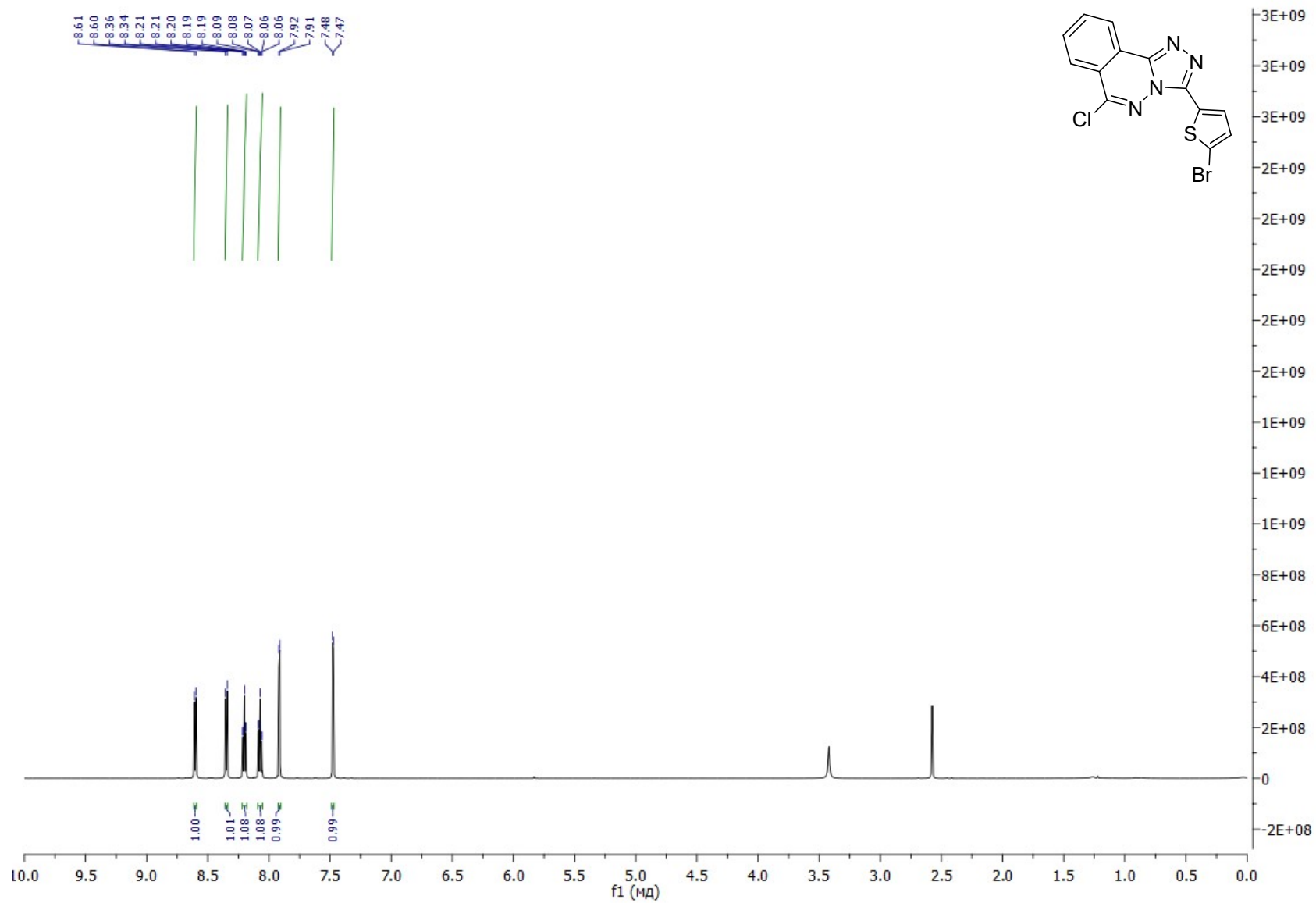
**Fig. 8** <sup>1</sup>H NMR spectrum for 3,10-di(pyridin-2-yl)bis([1,2,4]triazolo)[4,3-*a*:3',4'-*c*]quinoxaline (**8h**).



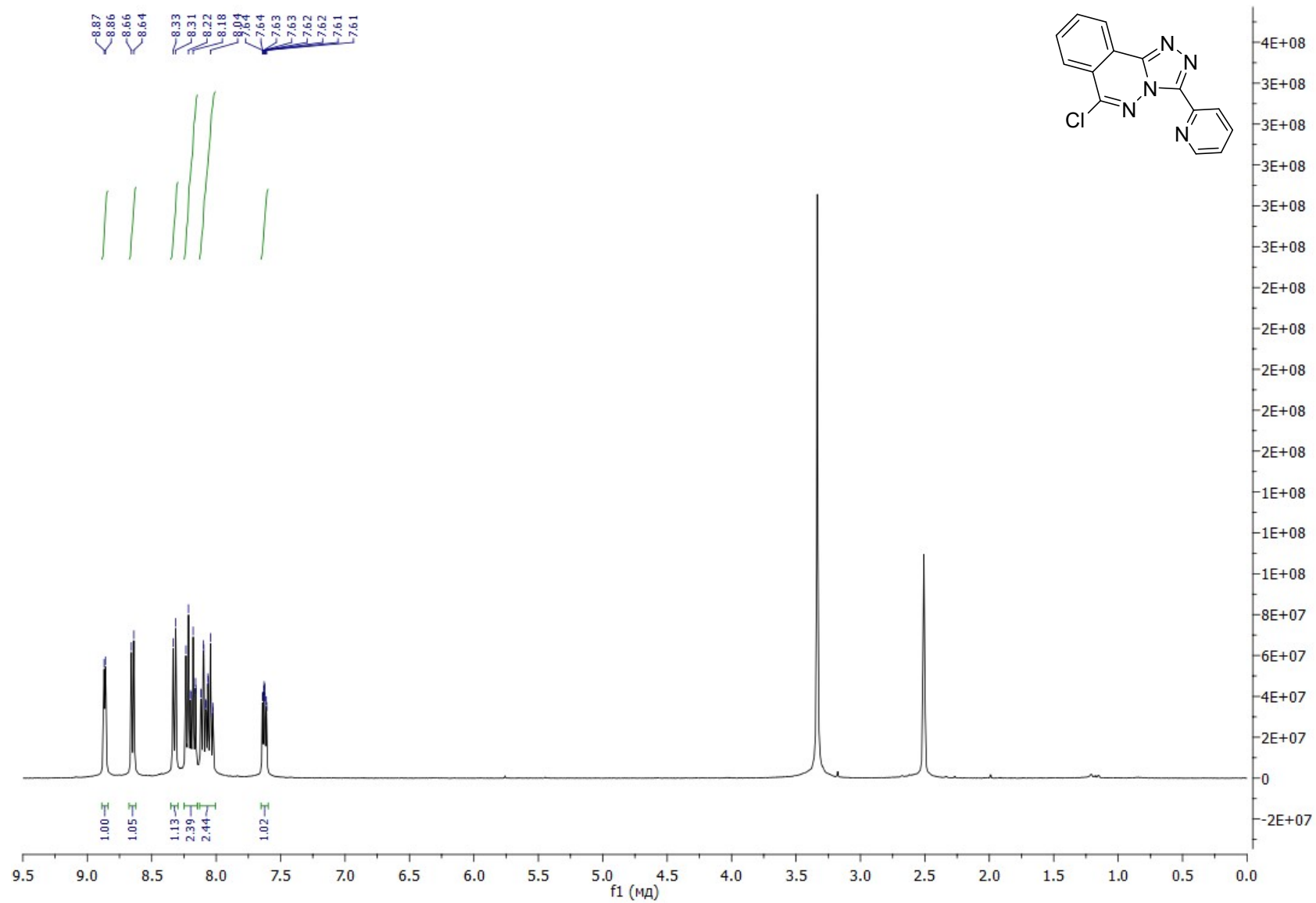
**Fig. 9**  $^1\text{H}$  NMR spectrum for 6-chloro-3-(thiophen-2-yl)-[1,2,4]triazolo[3,4-*a*]phthalazine (**12a**).



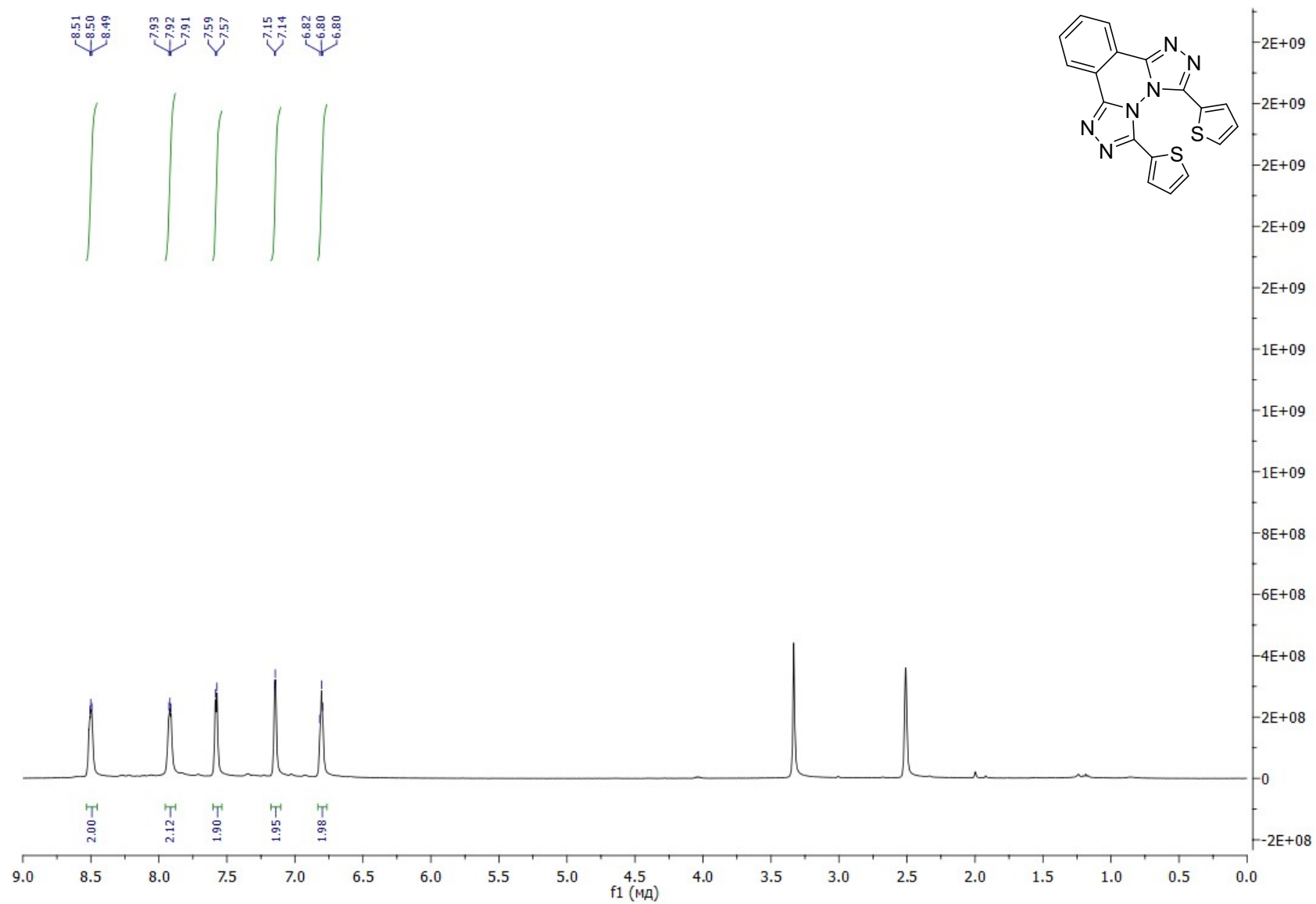
**Fig. 10** <sup>1</sup>H NMR spectrum for 6-chloro-3-(thiophen-3-yl)-[1,2,4]triazolo[3,4-*a*]phthalazine (**12b**).



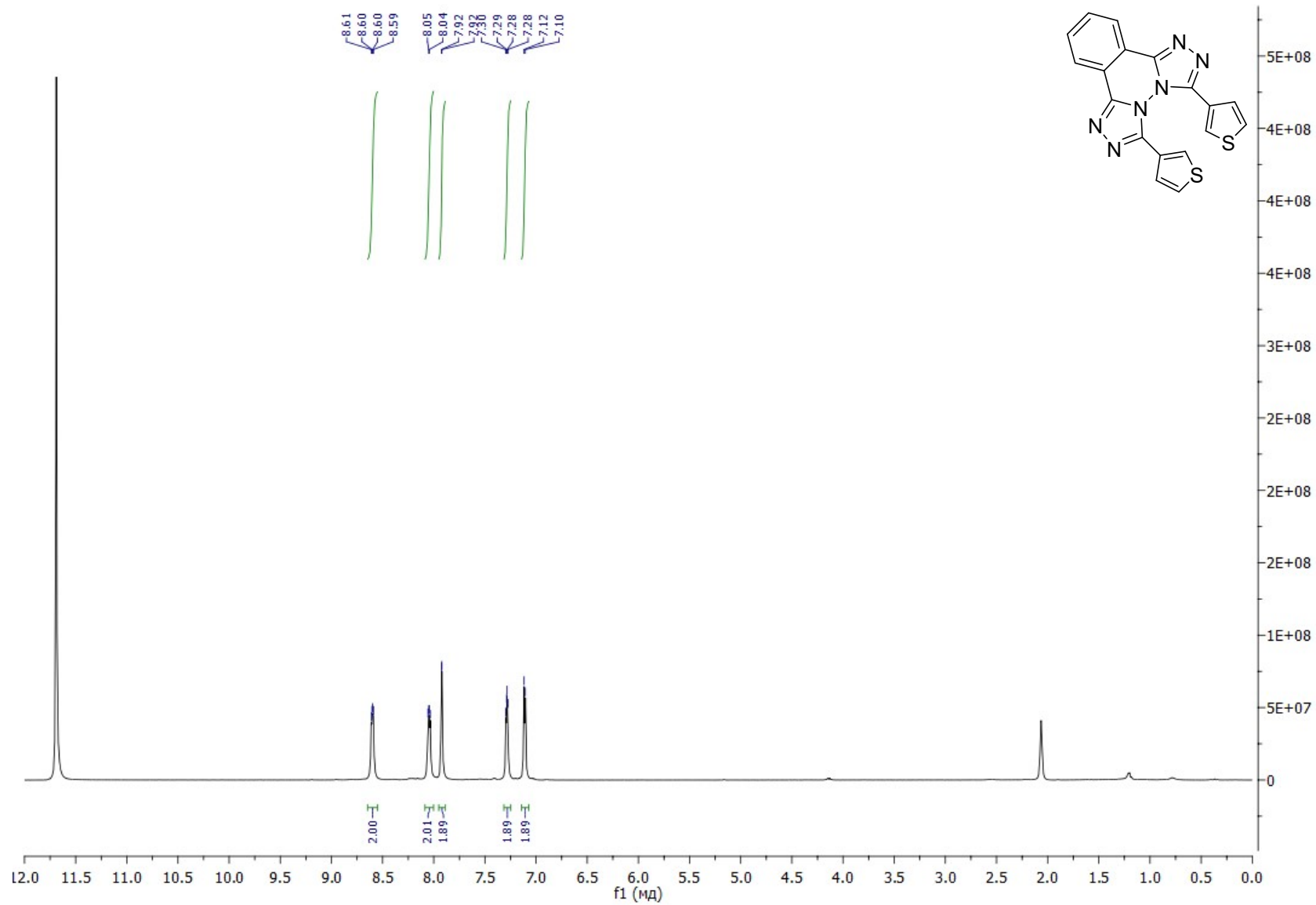
**Fig. 11** <sup>1</sup>H NMR spectrum for 3-(5-bromothiophen-2-yl)-6-chloro-[1,2,4]triazolo[3,4-*a*]phthalazine (**12c**).



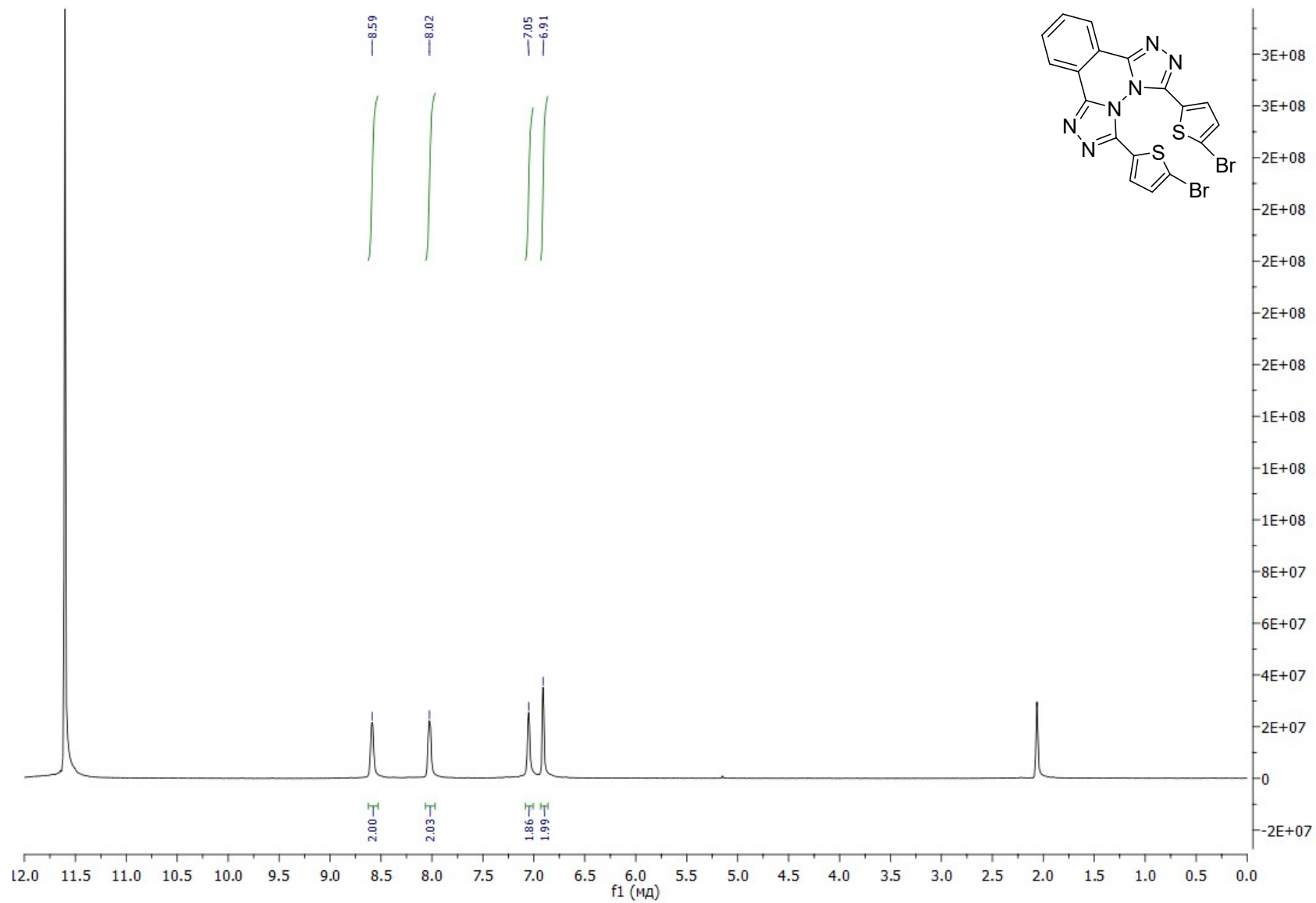
**Fig. 12**  $^1\text{H}$  NMR spectrum for 6-chloro-3-(pyridin-2-yl)-[1,2,4]triazolo[3,4-*a*]phthalazine (**12d**).



**Fig. 13** <sup>1</sup>H NMR spectrum for 3,6-di(thiophen-2-yl)bis([1,2,4]triazolo)[3,4-a:4',3'-c]phthalazine (**14a**).

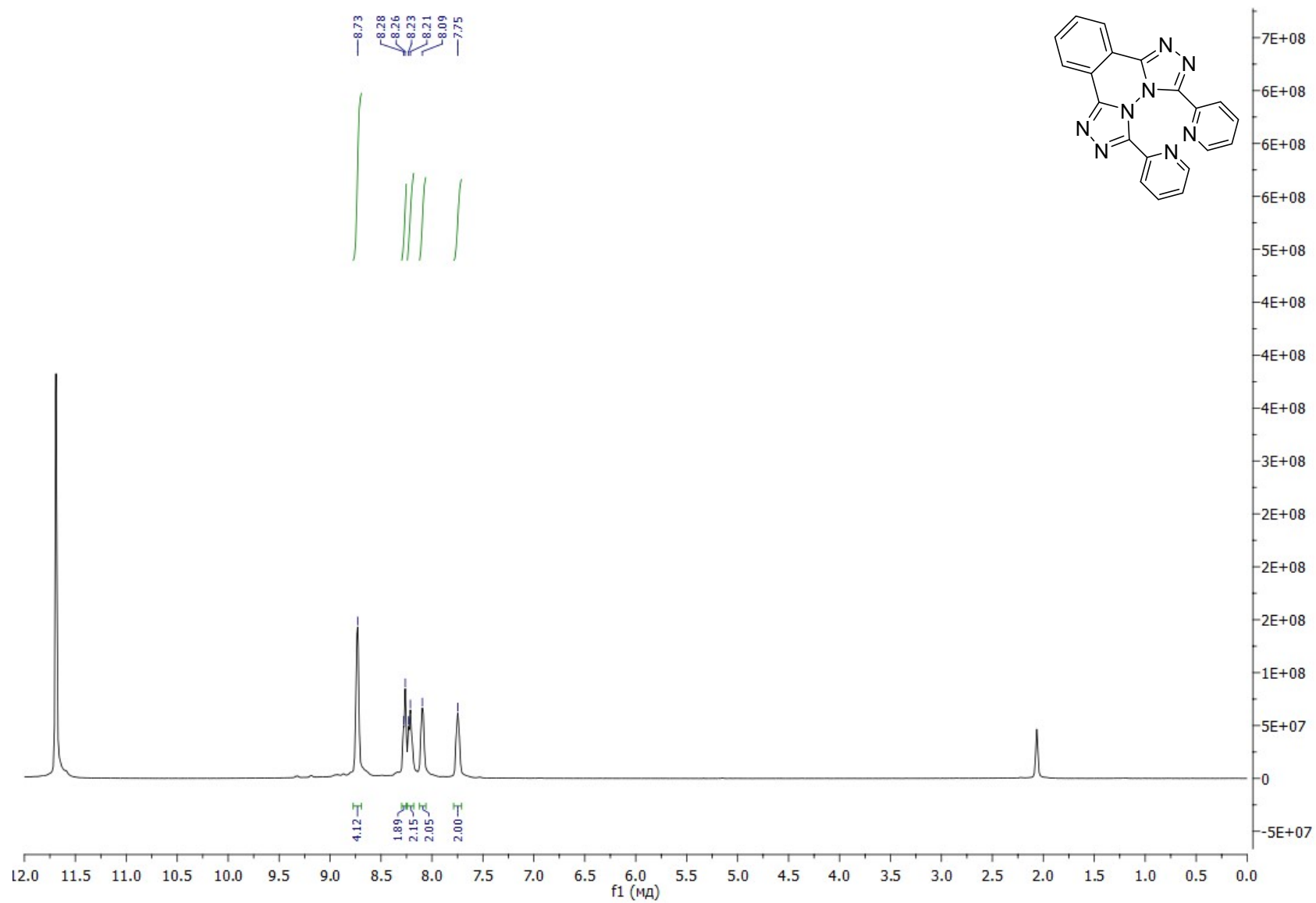


**Fig. 14**  $^1\text{H}$  NMR spectrum for 3,6-di(thiophen-3-yl)bis([1,2,4]triazolo)[3,4-a:4',3'-c]phthalazine (**14b**).



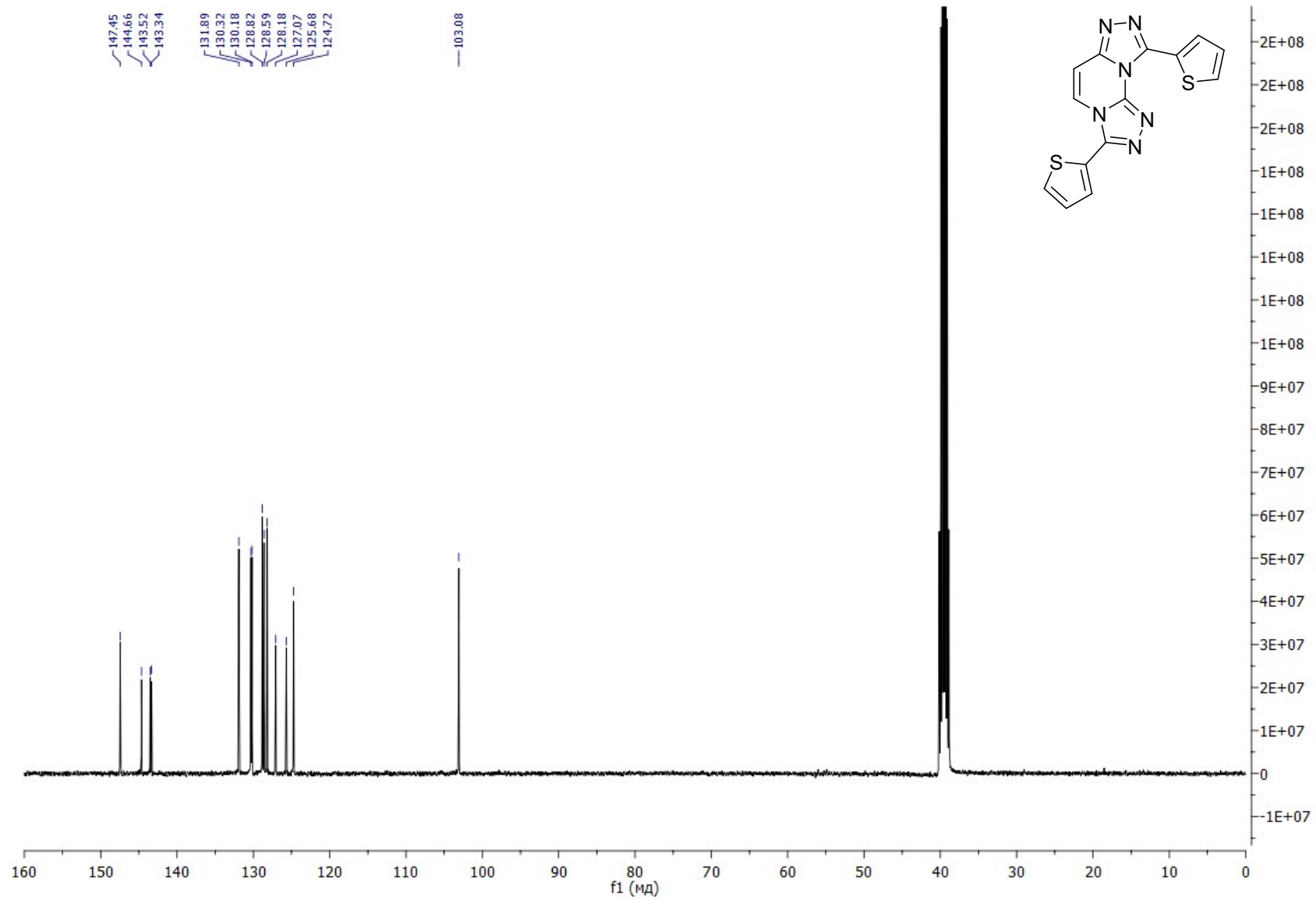
**Fig. 15** <sup>1</sup>H NMR spectrum for 3,6-bis(5-bromothiophen-2-yl)bis([1,2,4]triazolo)[3,4-*a*:4',3'-*c*]phthalazine (**14c**).





**Fig. 16** <sup>1</sup>H NMR spectrum for 3,6-di(pyridin-2-yl)bis([1,2,4]triazolo)[3,4-*a*:4',3'-*c*]phthalazine (**14d**).

# NMR <sup>13</sup>C Spectra



**Fig. 17** <sup>13</sup>C NMR spectrum for 3,9-di(thiophen-2-yl)bis([1,2,4]triazolo)[4,3-a:4',3'-c]pyrimidine (**8a**).

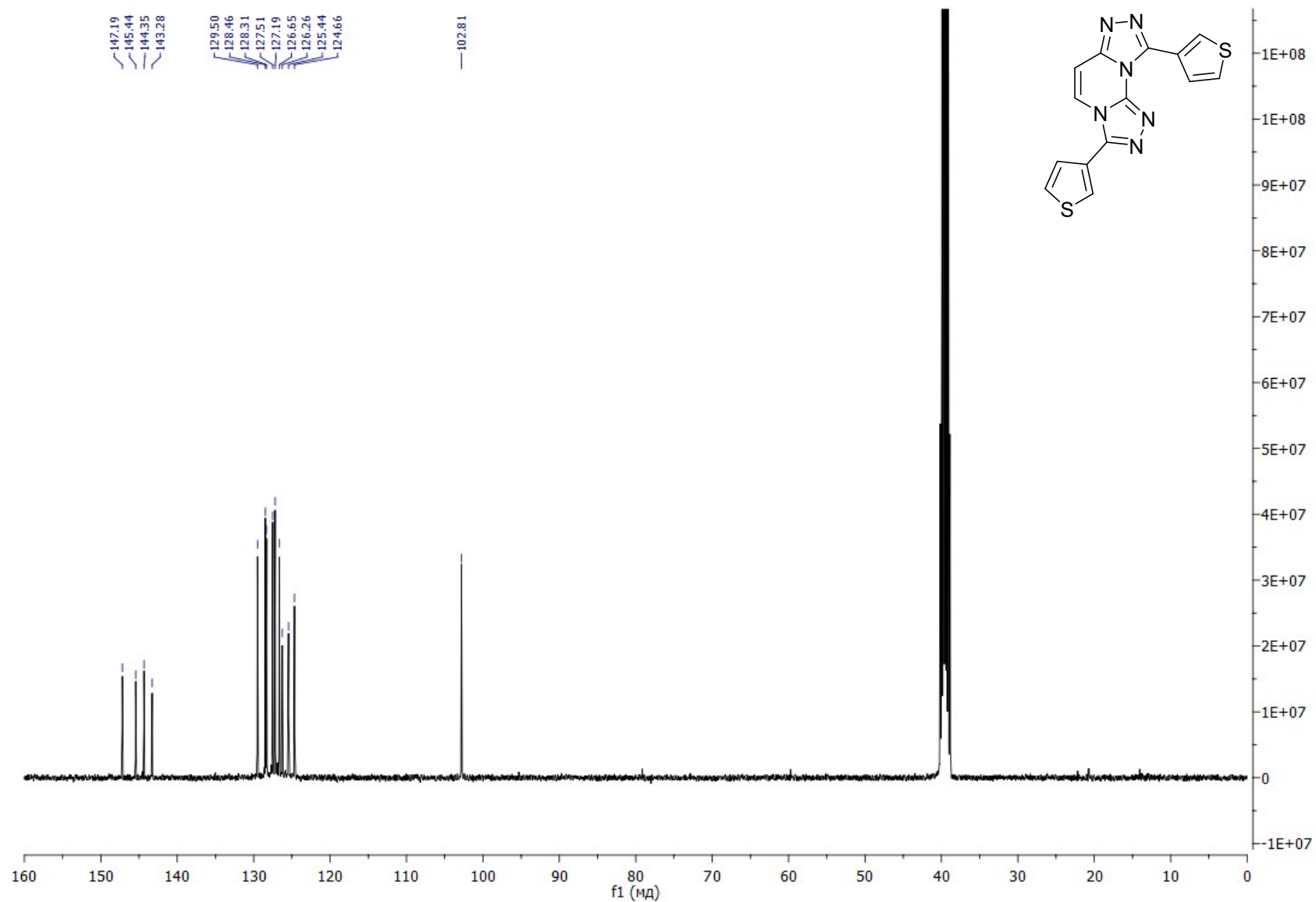
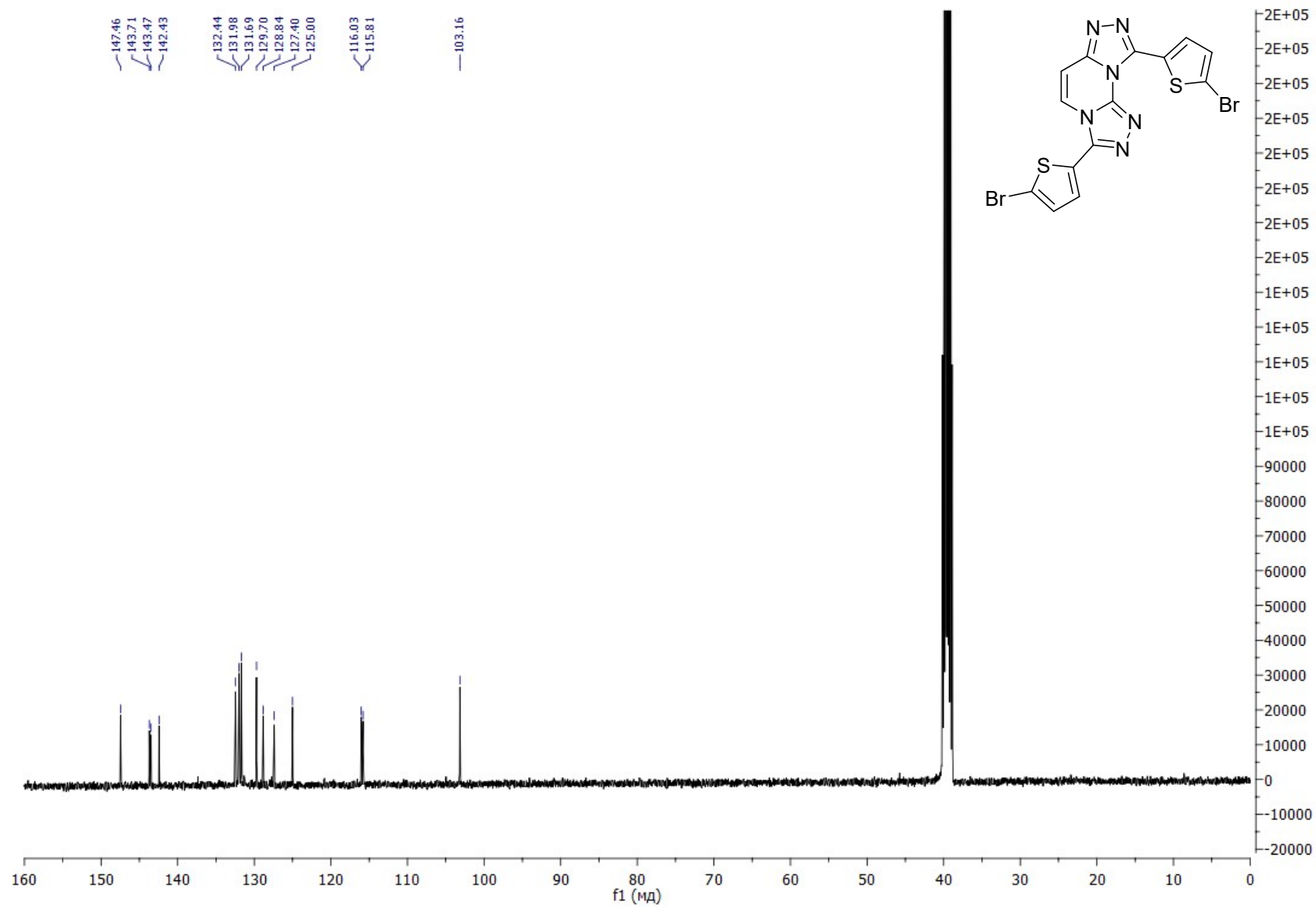
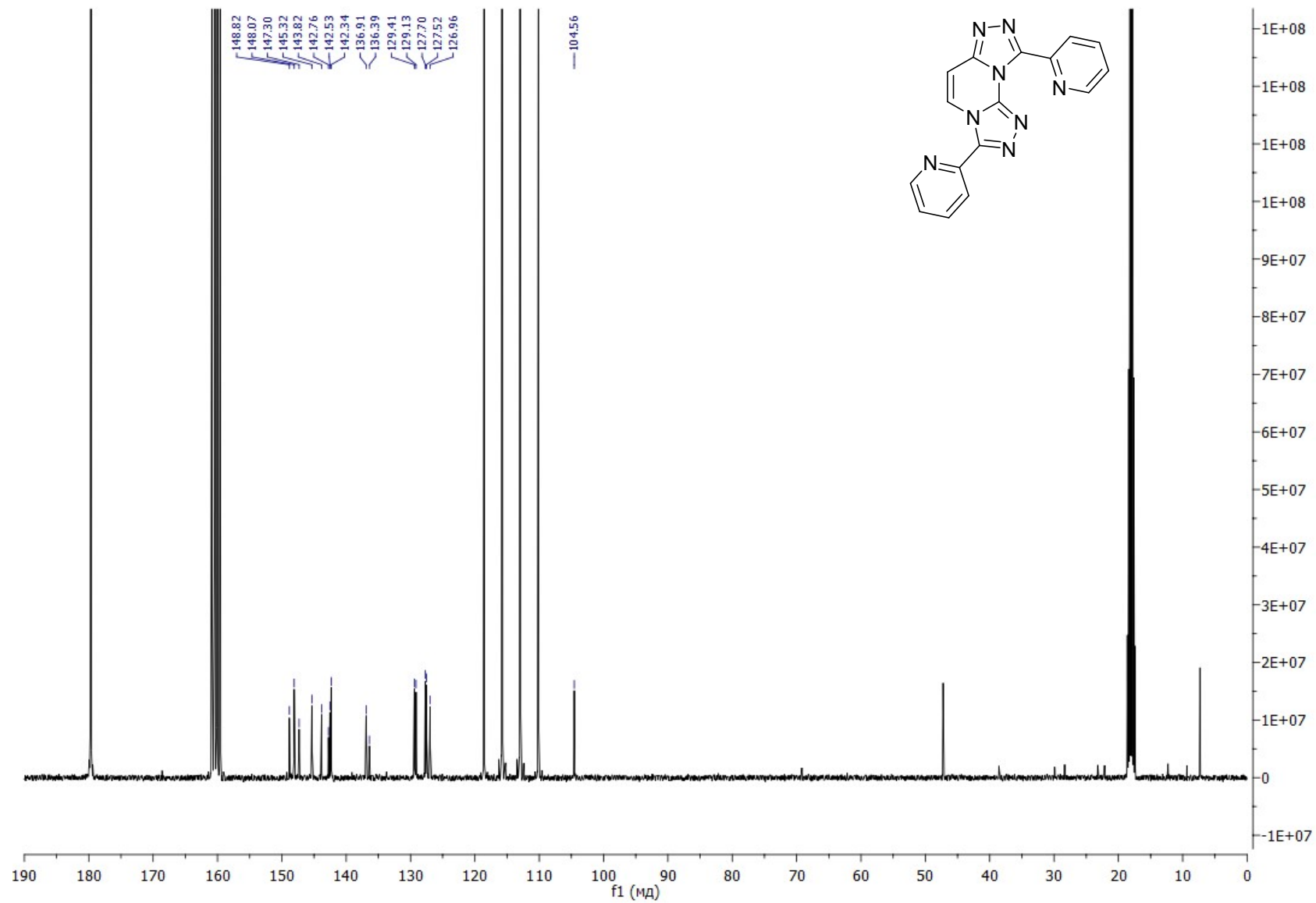


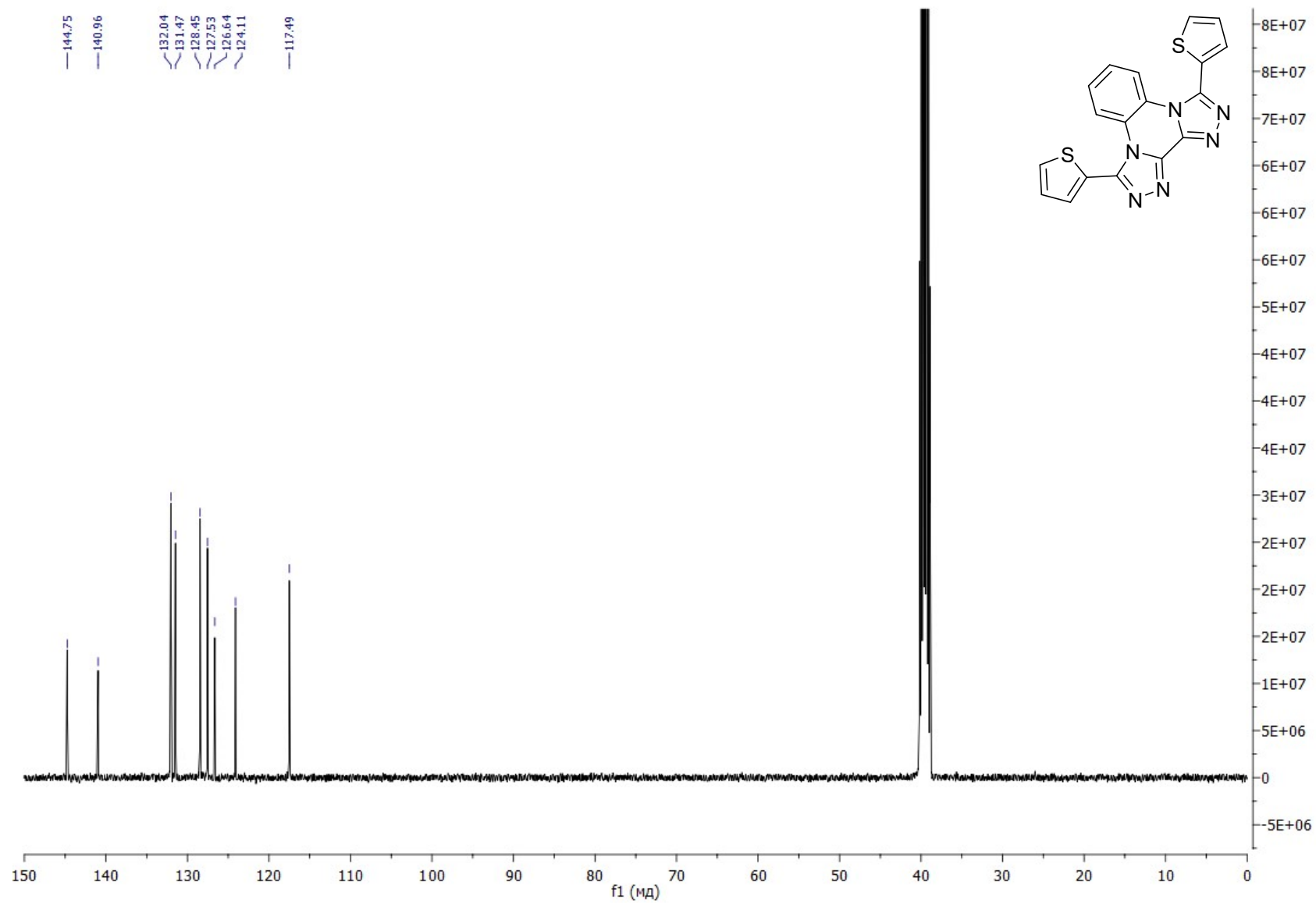
Fig. 18  $^{13}\text{C}$  NMR spectrum for 3,9-di(thiophen-3-yl)bis([1,2,4]triazolo)[4,3-*a*:4',3'-*c*]pyrimidine (**8b**).



**Fig. 19**  $^{13}\text{C}$  NMR spectrum for 3,9-bis(5-bromothiophen-2-yl)bis([1,2,4]triazolo)[4,3-*a*:4',3'-*c*]pyrimidine (**8c**).



**Fig. 12**  $^{13}\text{C}$  NMR spectrum for 3,9-di(pyridin-2-yl)bis([1,2,4]triazolo)[4,3-*a'*:3'-*c*]pyrimidine (**8d**).



**Fig. 21**  $^{13}\text{C}$  NMR spectrum for 3,10-di(thiophen-2-yl)bis([1,2,4]triazolo)[4,3-*a*:3',4'-*c*]quinoxaline (**8e**).

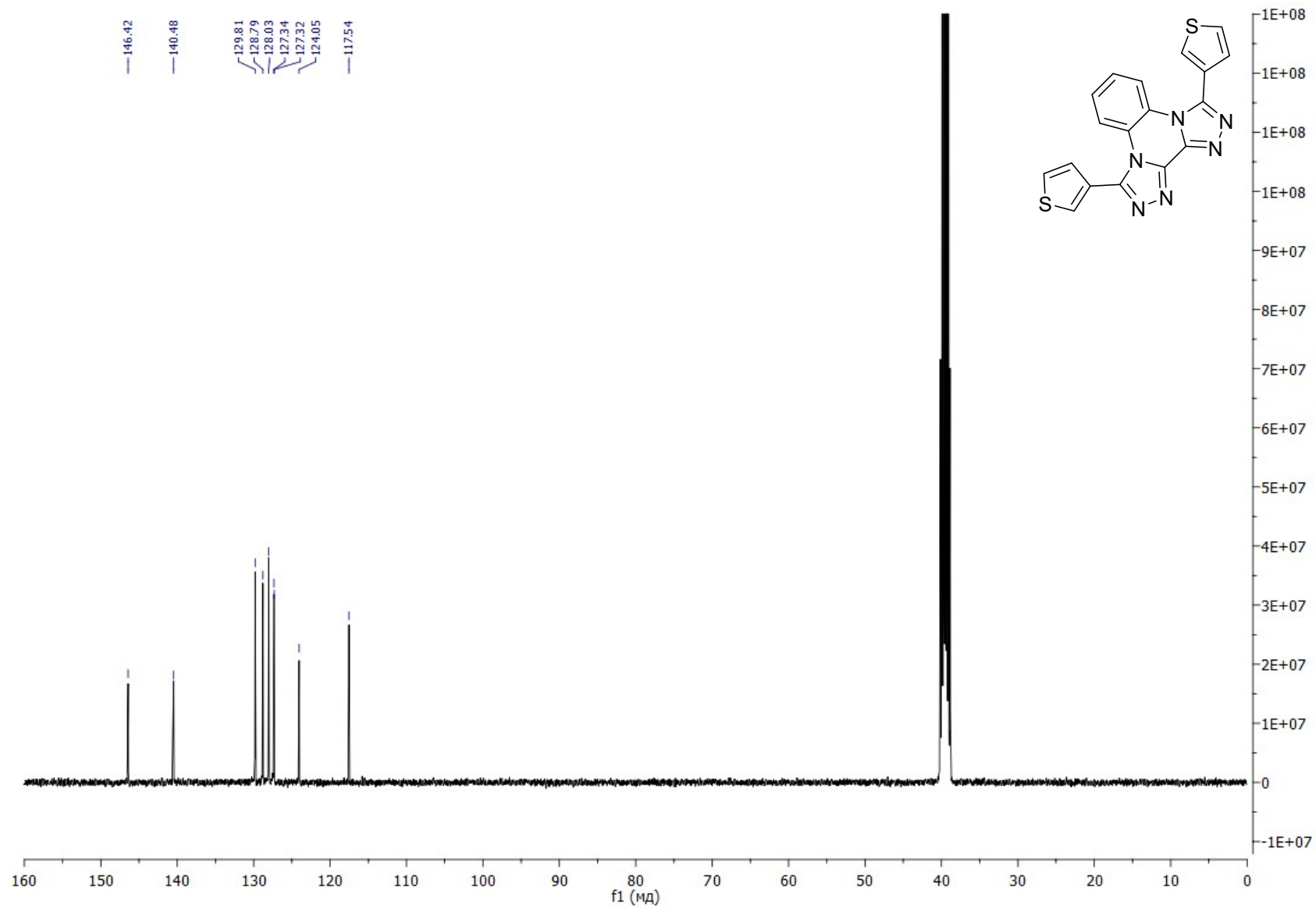
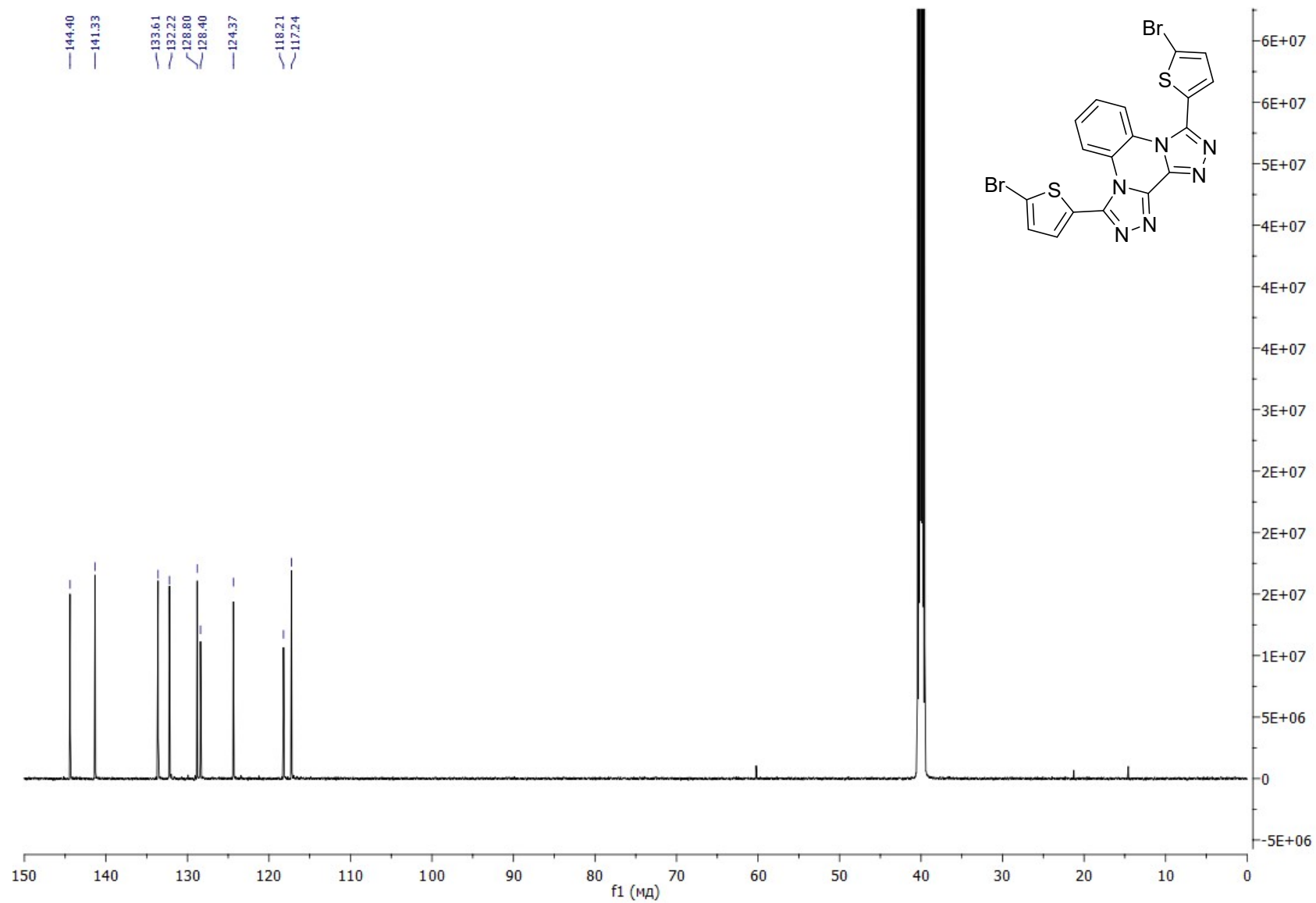
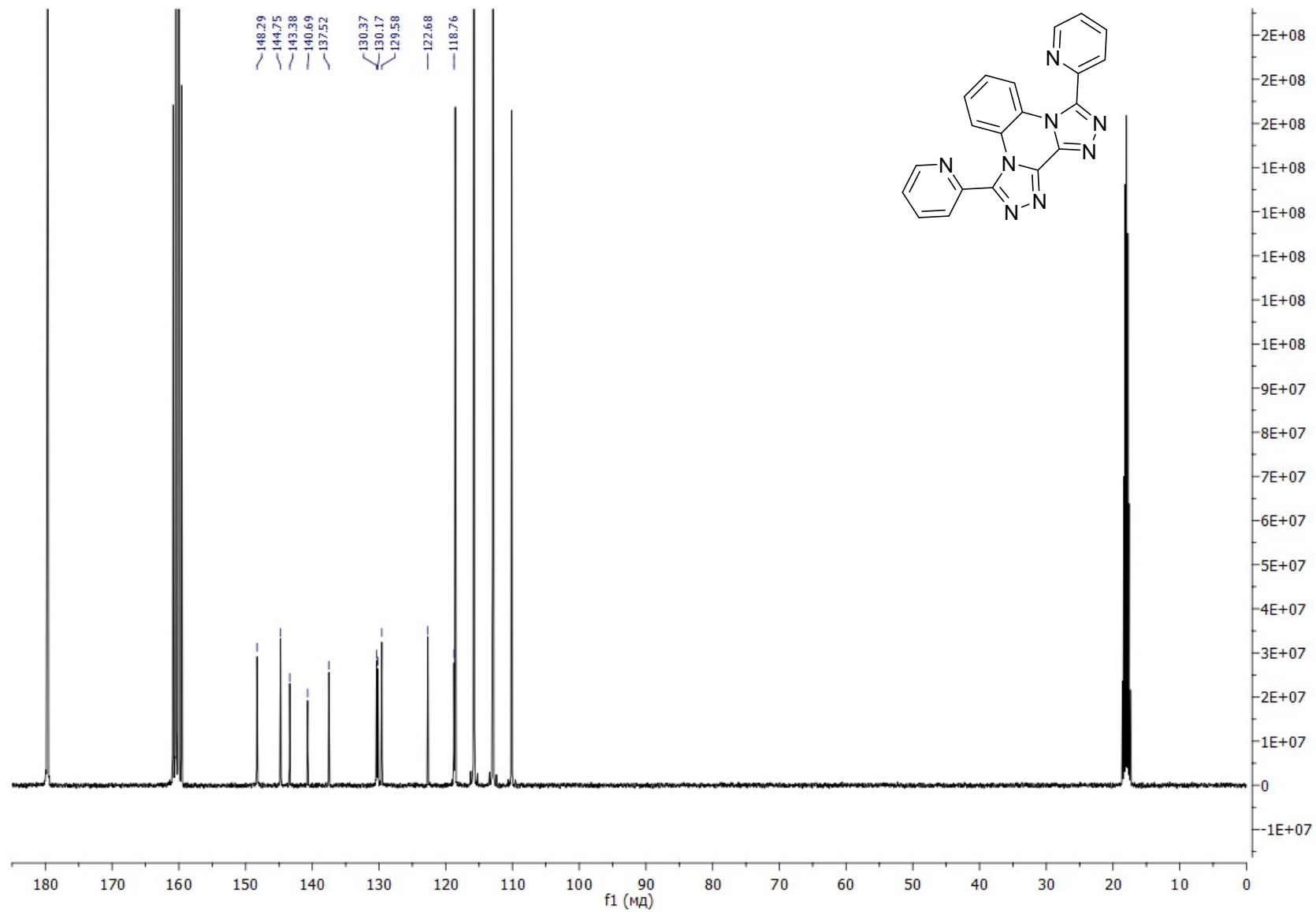


Fig. 22 <sup>13</sup>C NMR spectrum for 3,10-di(thiophen-3-yl)bis([1,2,4]triazolo)[4,3-*a*:3',4'-*c*]quinoxaline (**8f**).

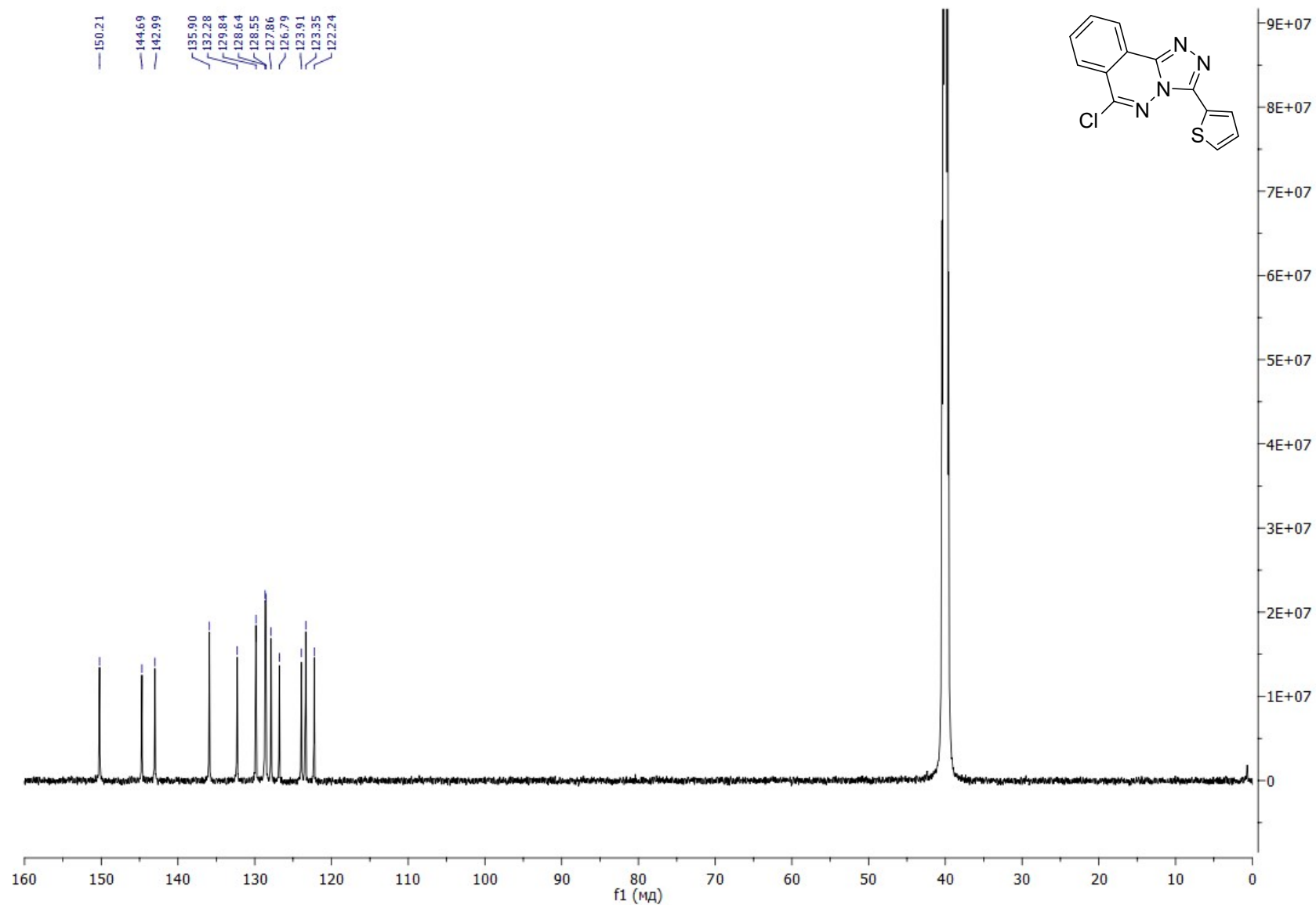


**Fig. 23**  $^{13}\text{C}$  NMR spectrum for 3,10-bis(5-bromothiophen-2-yl)bis([1,2,4]triazolo)[4,3-*a*:3',4'-*c*]quinoxaline (**8g**).

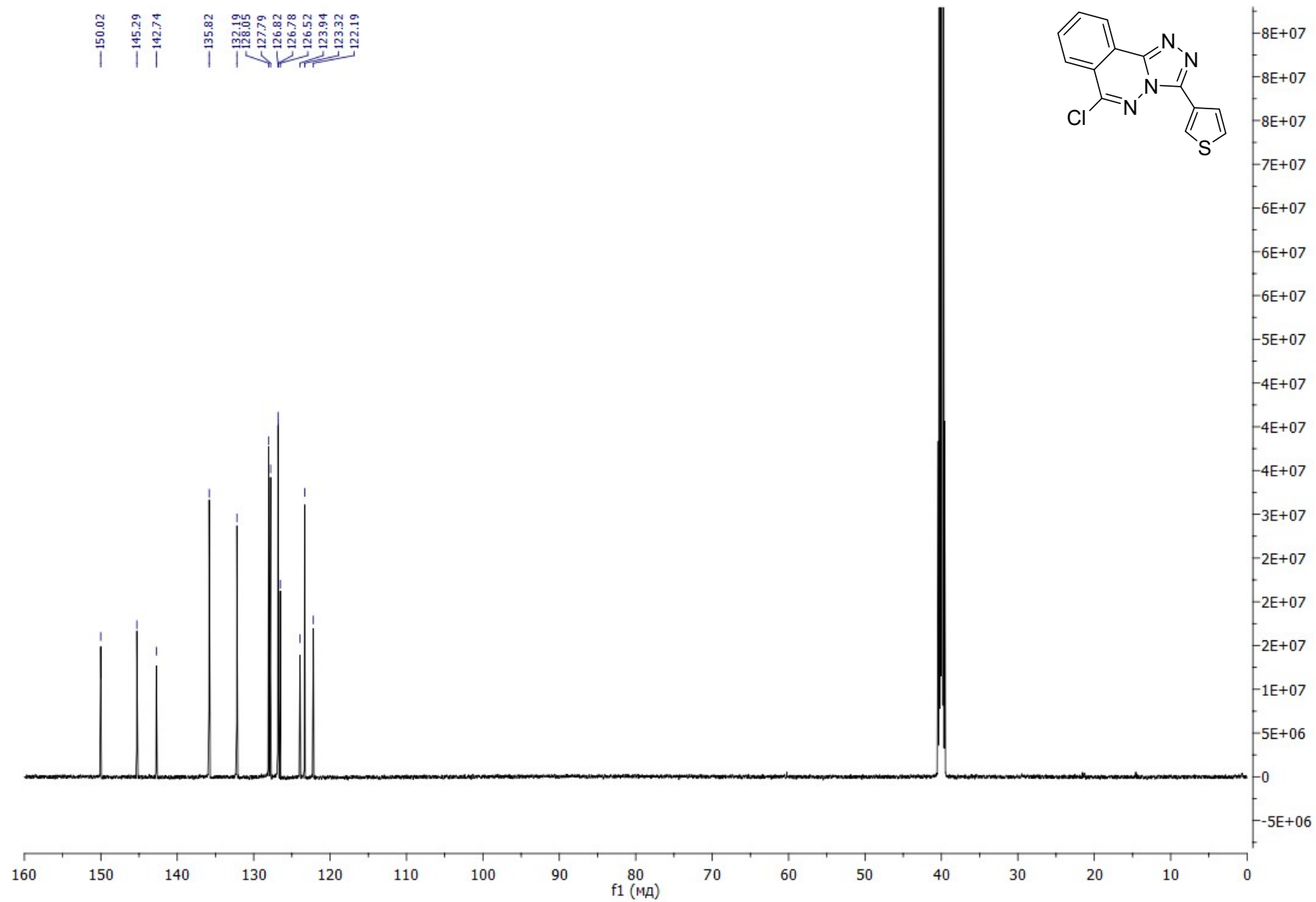




**Fig. 24**  $^{13}\text{C}$  NMR spectrum for 3,10-di(pyridin-2-yl)bis([1,2,4]triazolo)[4,3-*a*:3',4'-*c*]quinoxaline (**8h**).



**Fig. 25**  $^{13}\text{C}$  NMR spectrum for 6-chloro-3-(thiophen-2-yl)-[1,2,4]triazolo[3,4-*a*]phthalazine (**12a**).



**Fig. 26** <sup>13</sup>C NMR spectrum for 6-chloro-3-(thiophen-3-yl)-[1,2,4]triazolo[3,4-*a*]phthalazine (**12b**).

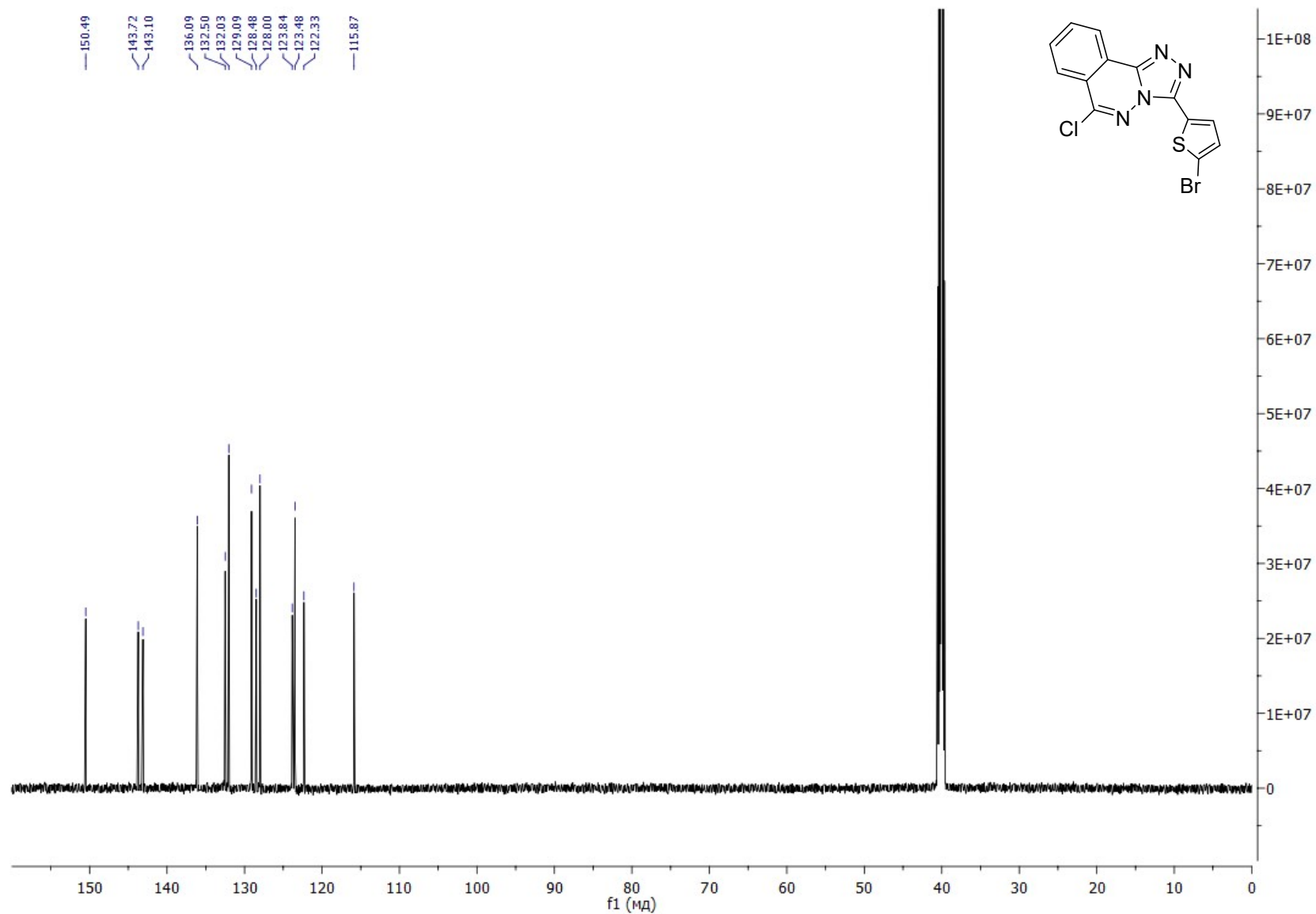
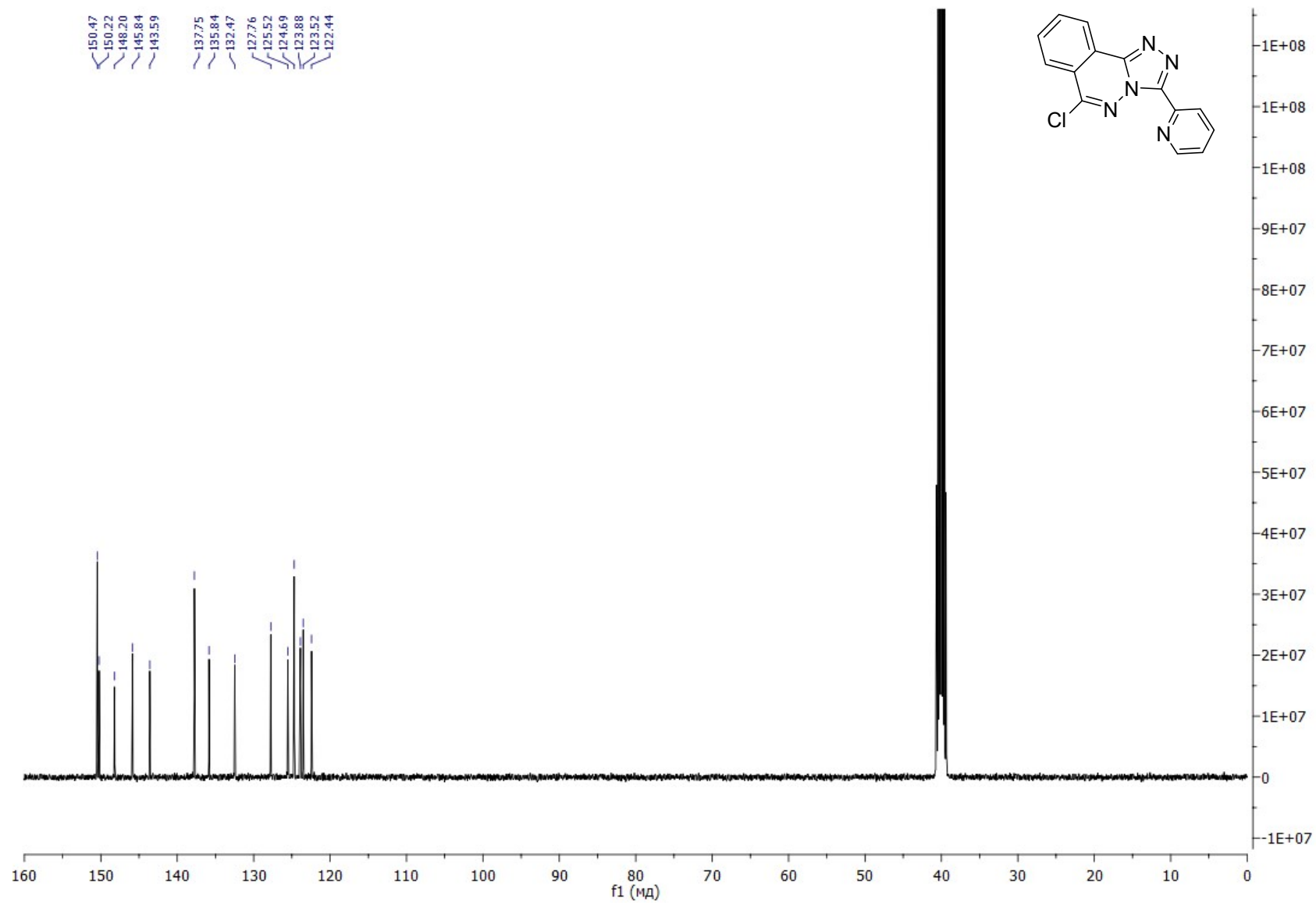
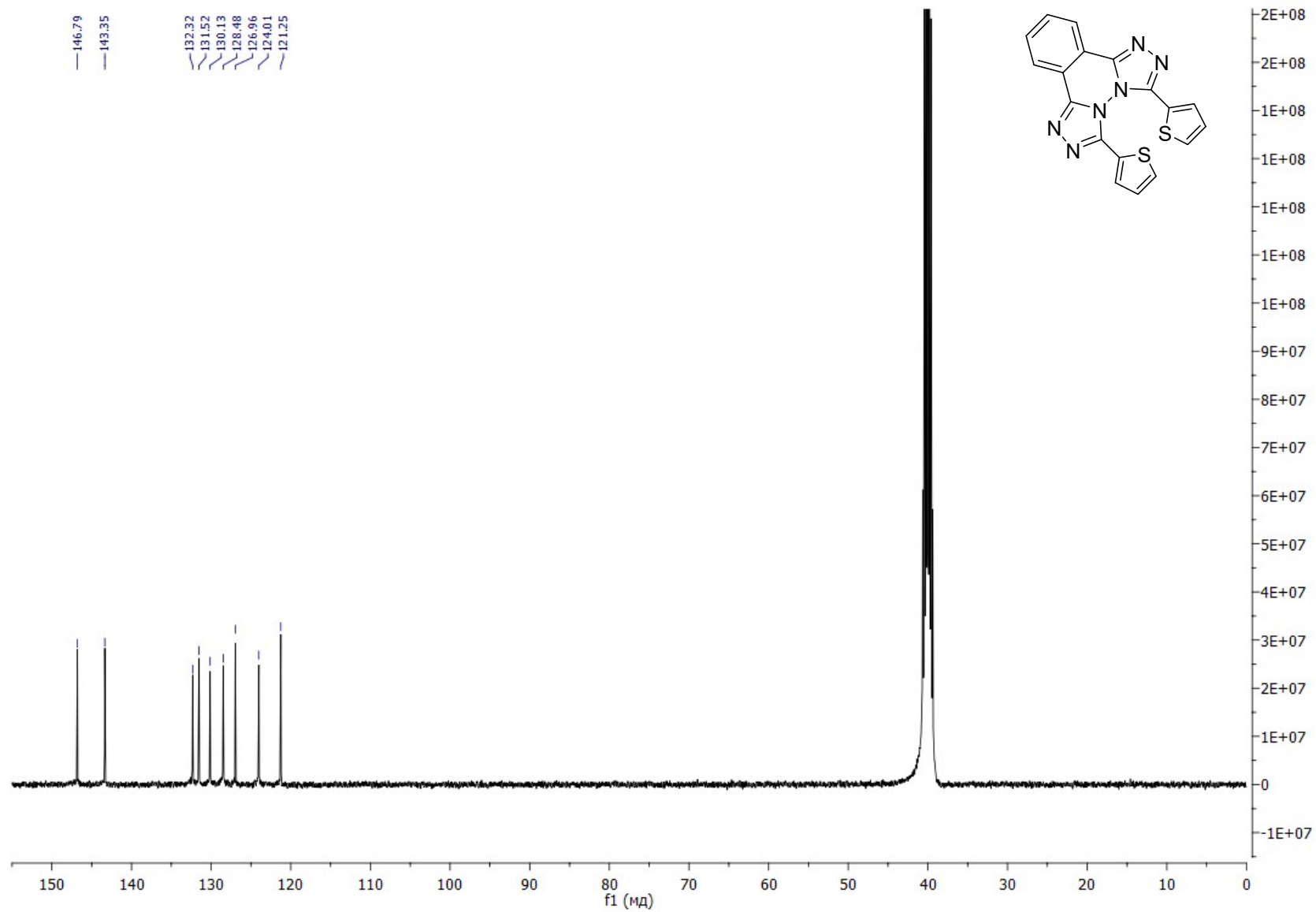


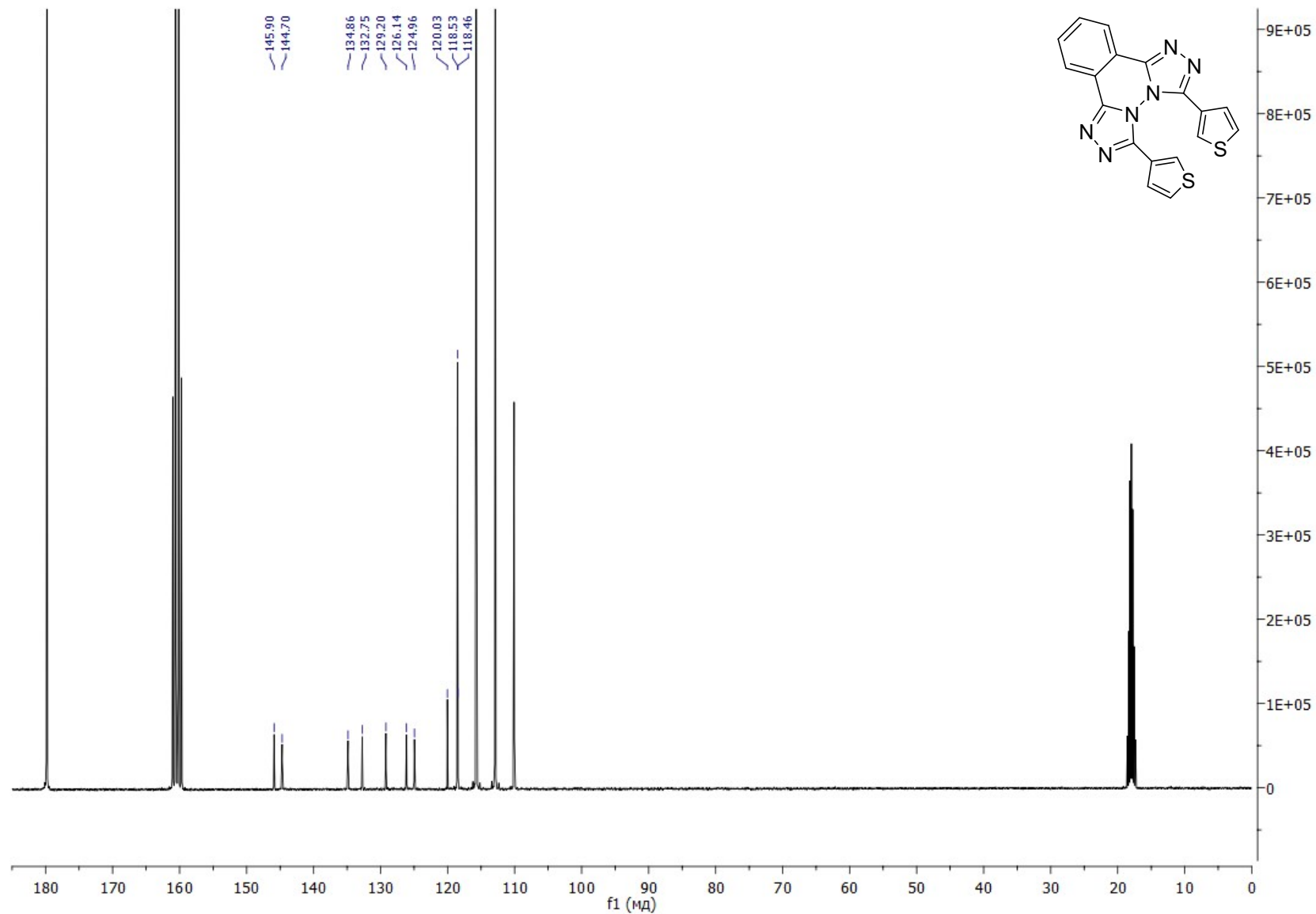
Fig. 27  $^{13}\text{C}$  NMR spectrum for 3-(5-bromothiophen-2-yl)-6-chloro-[1,2,4]triazolo[3,4-*a*]phthalazine (**12c**).



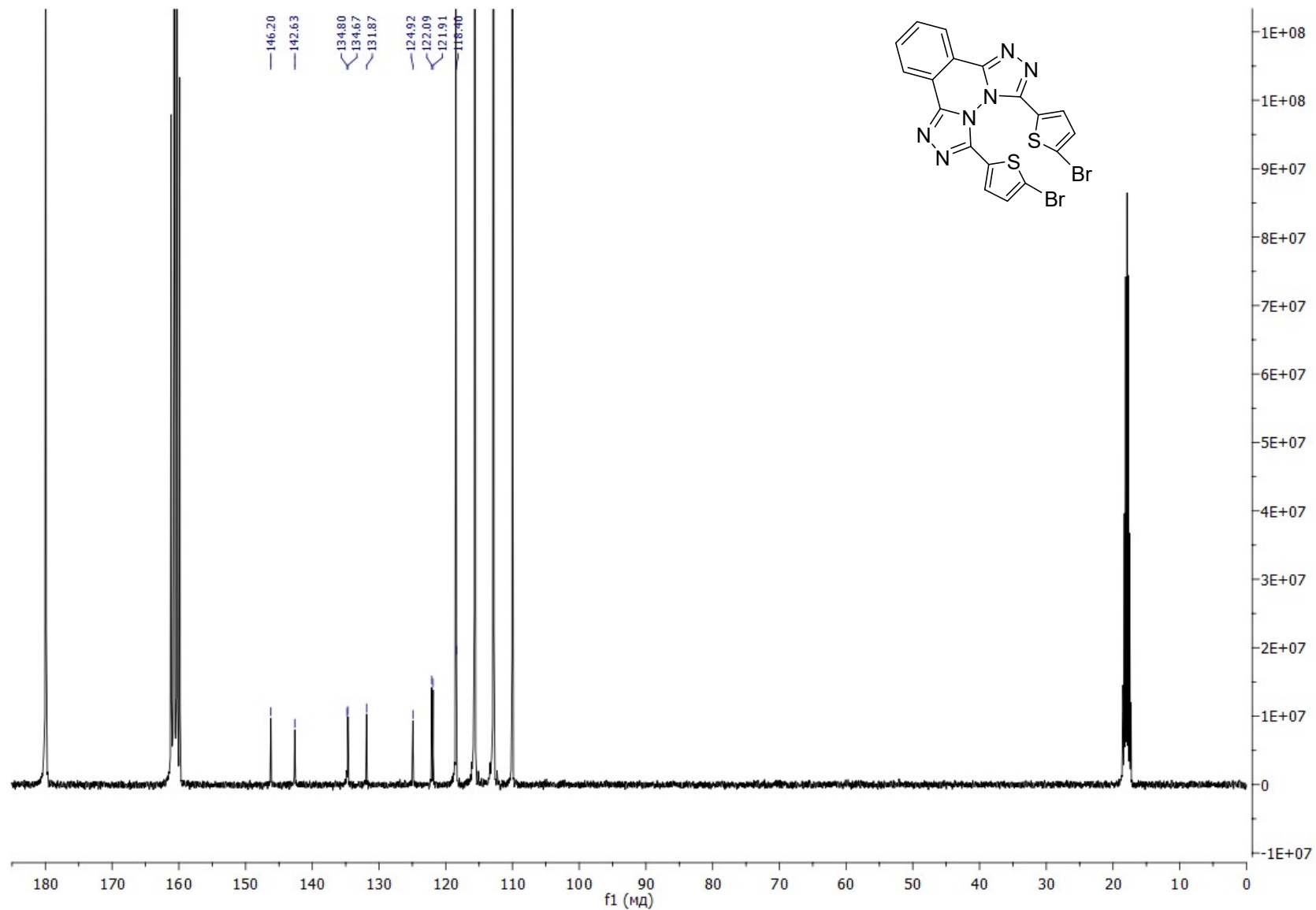
**Fig. 28** <sup>13</sup>C NMR spectrum for 6-chloro-3-(pyridin-2-yl)-[1,2,4]triazolo[3,4-*a*]phthalazine (**12d**).



**Fig. 29**  $^{13}\text{C}$  NMR spectrum for 3,6-di(thiophen-2-yl)bis([1,2,4]triazolo)[3,4-*a*:4',3'-*c*]phthalazine (**14a**).

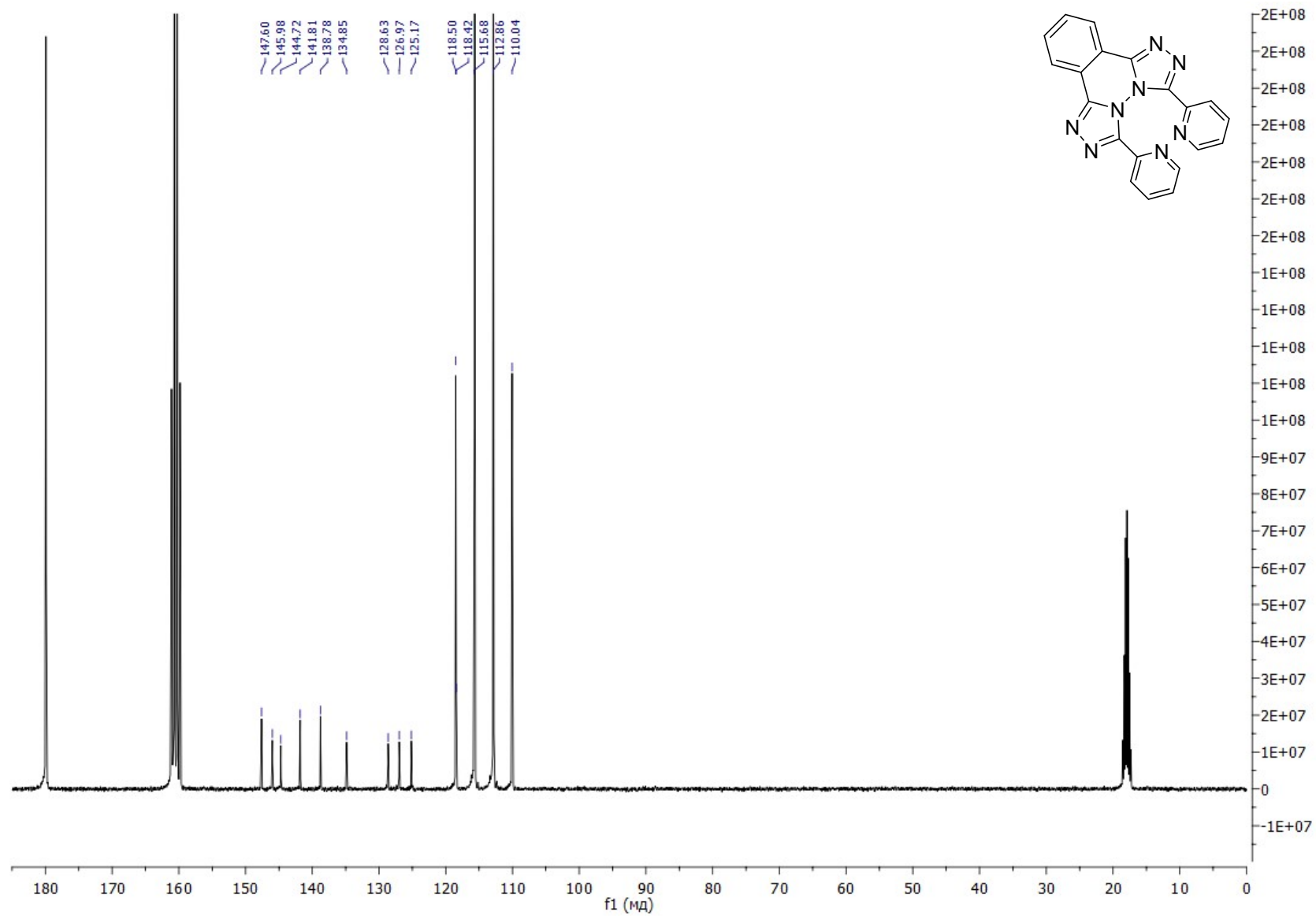


**Fig. 30**  $^{13}\text{C}$  NMR spectrum for 3,6-di(thiophen-3-yl)bis([1,2,4]triazolo)[3,4-*a'*:4',3'-*c*]phthalazine (**14b**).



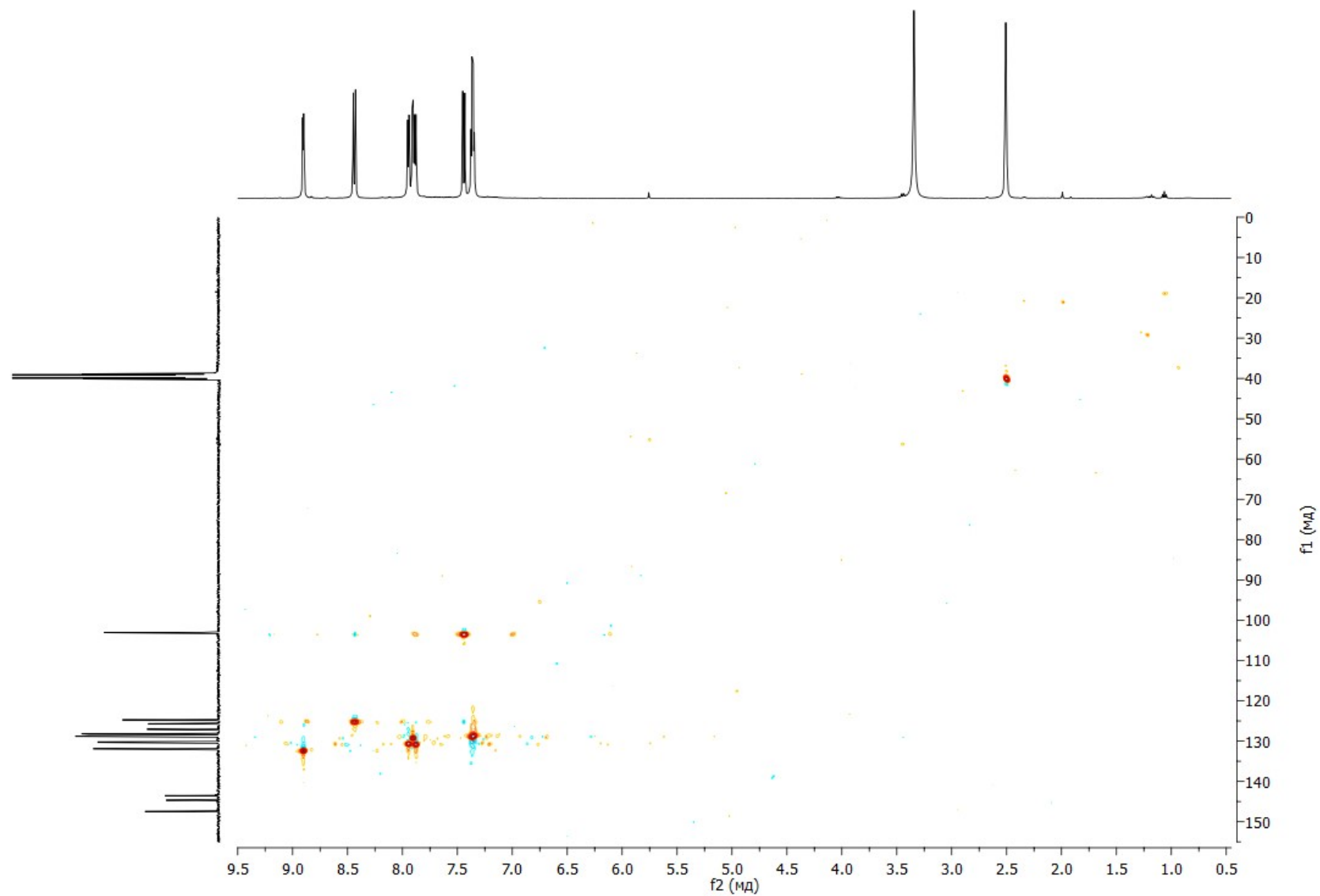
**Fig. 31**  $^{13}\text{C}$  NMR spectrum for 3,6-bis(5-bromothiophen-2-yl)bis([1,2,4]triazolo)[3,4-*a'*:3'-*c*]phthalazine (**14c**).



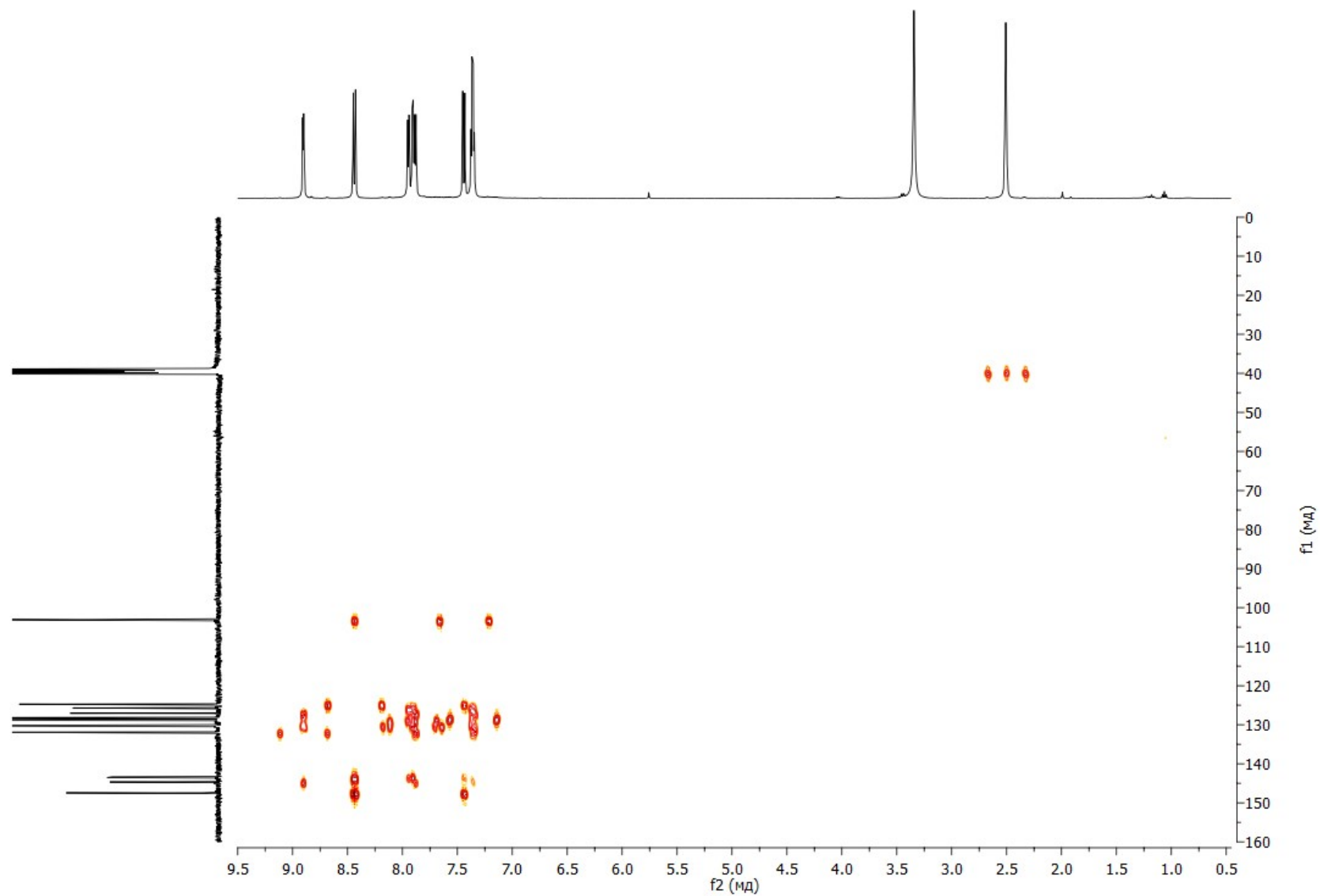


**Fig. 32**  $^{13}\text{C}$  NMR spectrum for 3,6-di(pyridin-2-yl)bis([1,2,4]triazolo)[3,4-*a*:4',3'-*c*]phthalazine (**14d**).

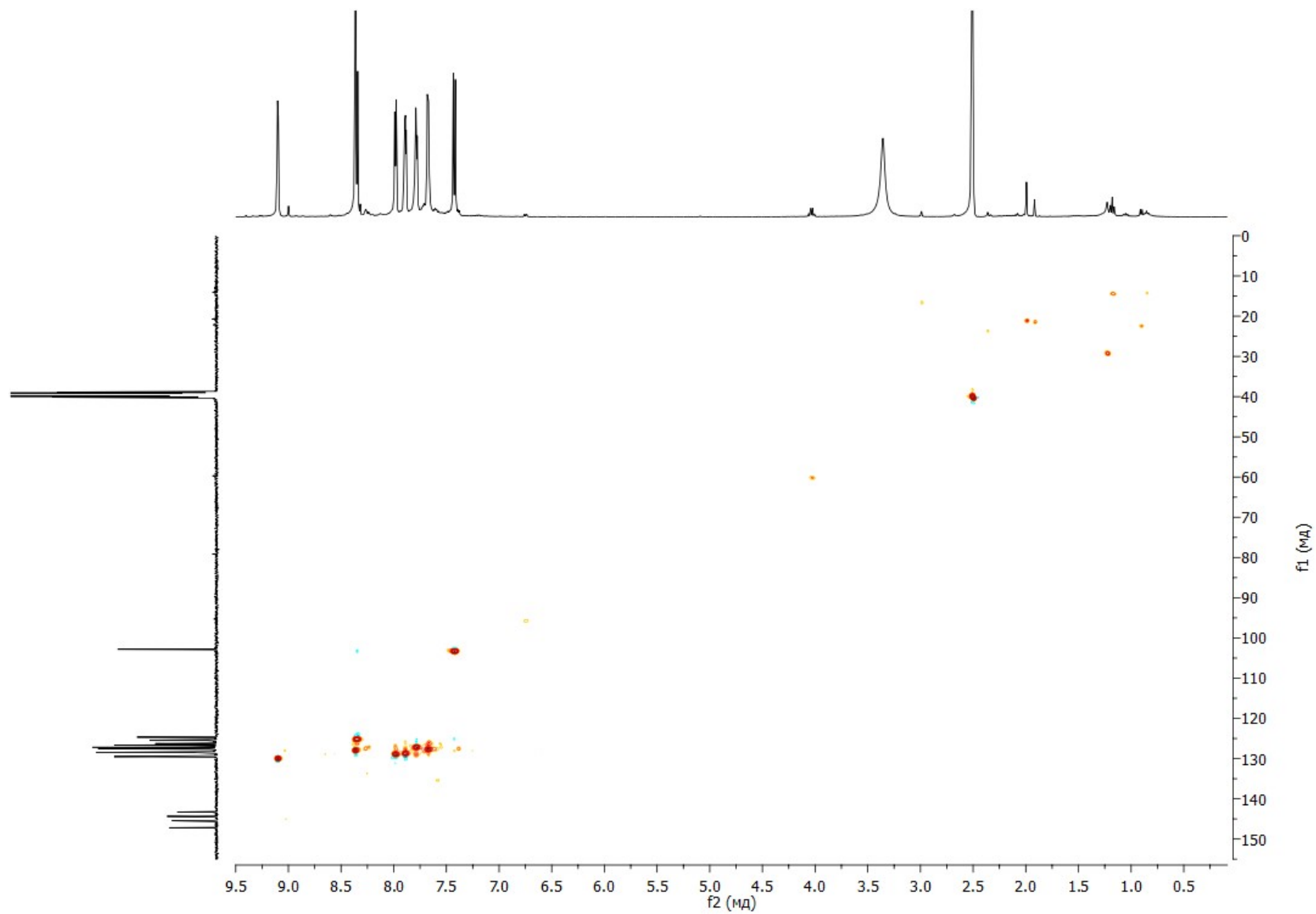
### HSQC and HMBC Spectra



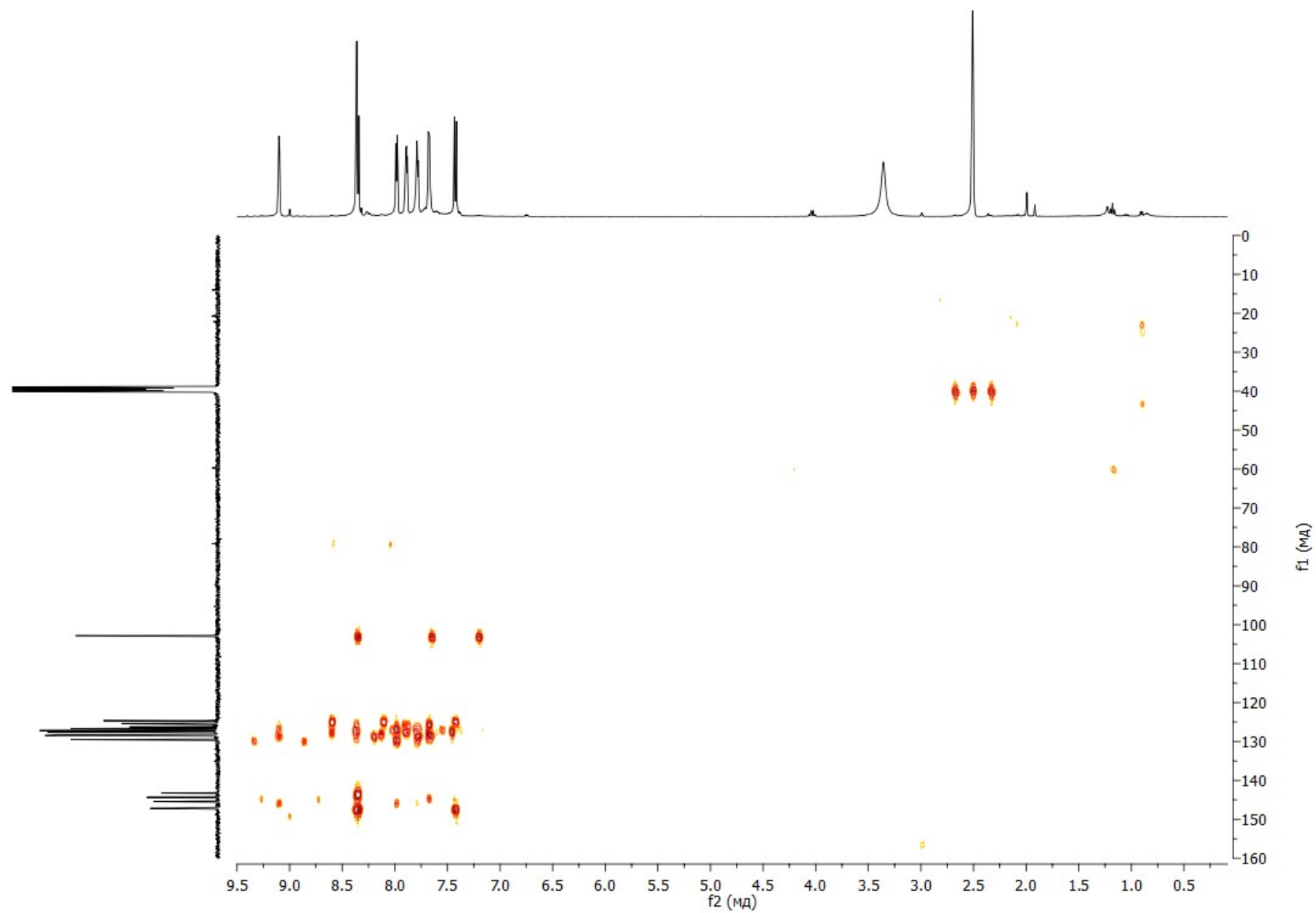
**Fig. 33** 2D  $^1\text{H}$ - $^{13}\text{C}$  HSQC spectrum for 3,9-di(thiophen-2-yl)bis([1,2,4]triazolo)[4,3-*a*:4',3'-*c*]pyrimidine (**8a**).



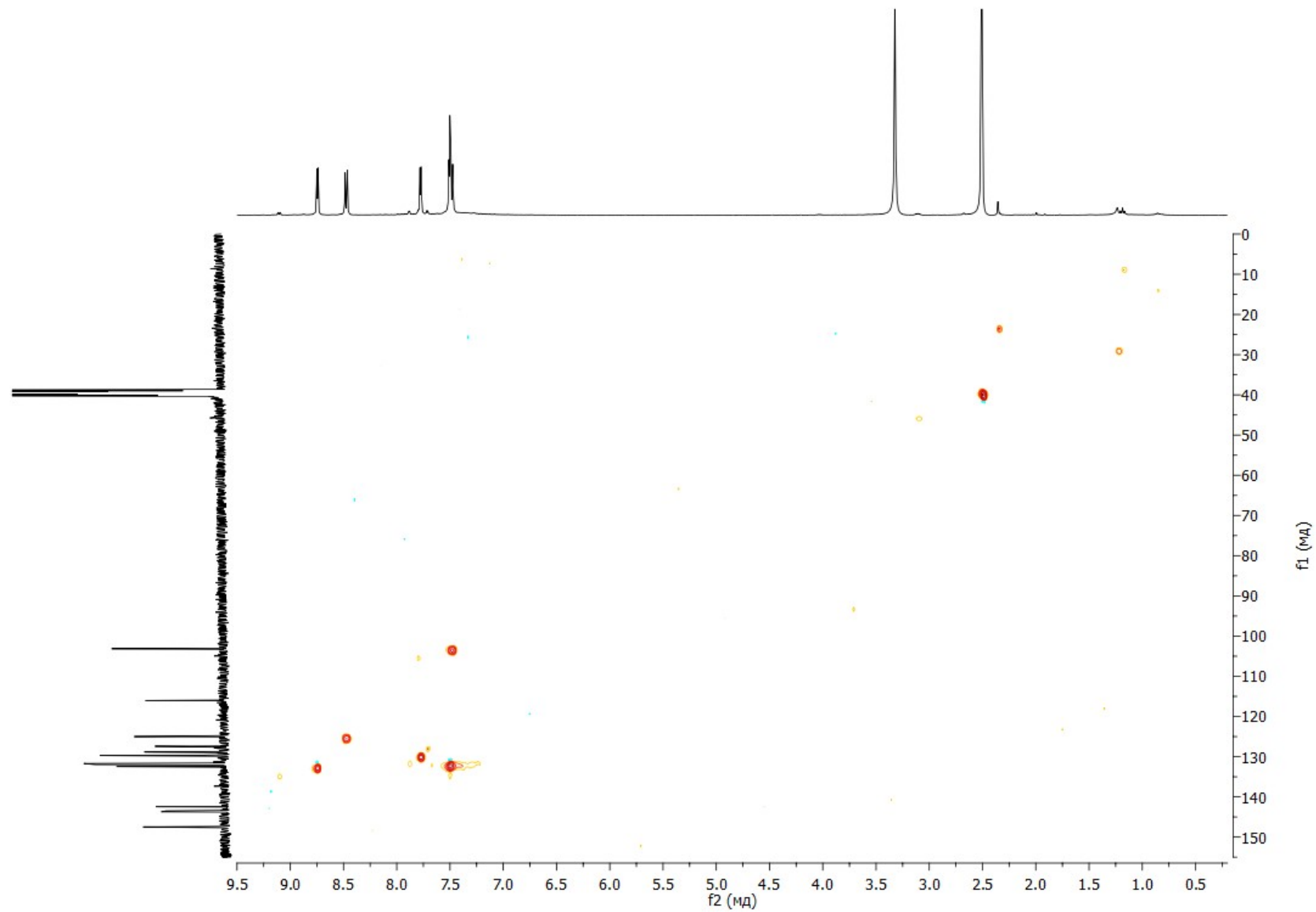
**Fig. 34** 2D  $^1\text{H}$ - $^{13}\text{C}$  HMBC spectrum for 3,9-di(thiophen-2-yl)bis([1,2,4]triazolo)[4,3-*a*:4',3'-*c*]pyrimidine (**8a**).



**Fig. 35** 2D  $^1\text{H}$ - $^{13}\text{C}$  HSQC spectrum for 3,9-di(thiophen-3-yl)bis([1,2,4]triazolo)[4,3-*a*:4',3'-*c*]pyrimidine (**8b**).



**Fig. 36** 2D  $^1\text{H}$ - $^{13}\text{C}$  HMBC spectrum for 3,9-di(thiophen-3-yl)bis([1,2,4]triazolo)[4,3-*a*:4',3'-*c*]pyrimidine (**8b**).



**Fig. 37** 2D  $^1\text{H}$ - $^{13}\text{C}$  HSQC spectrum for 3,9-bis(5-bromothiophen-2-yl)bis([1,2,4]triazolo)[4,3-*a*:4',3'-*c*]pyrimidine (**8c**).

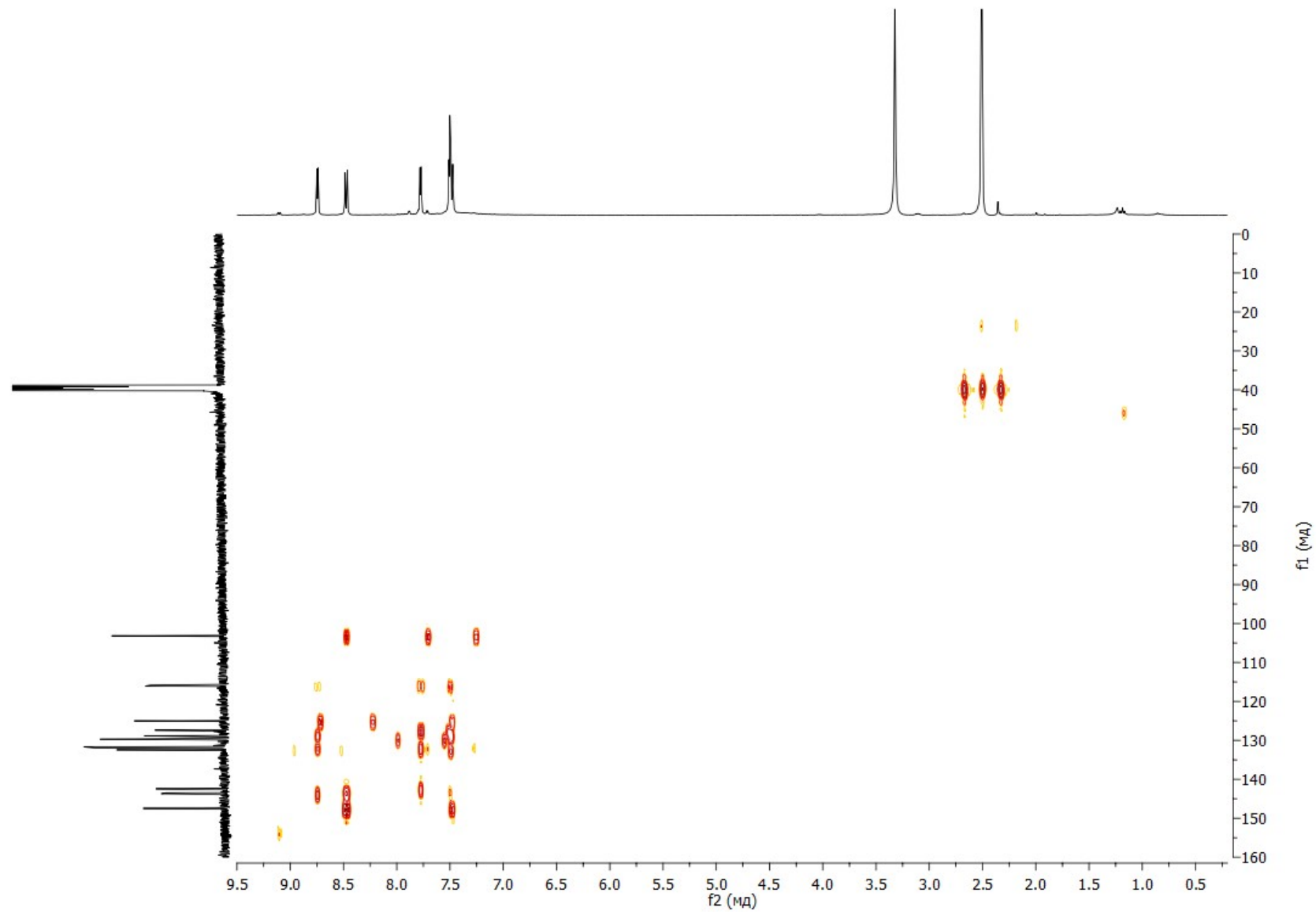
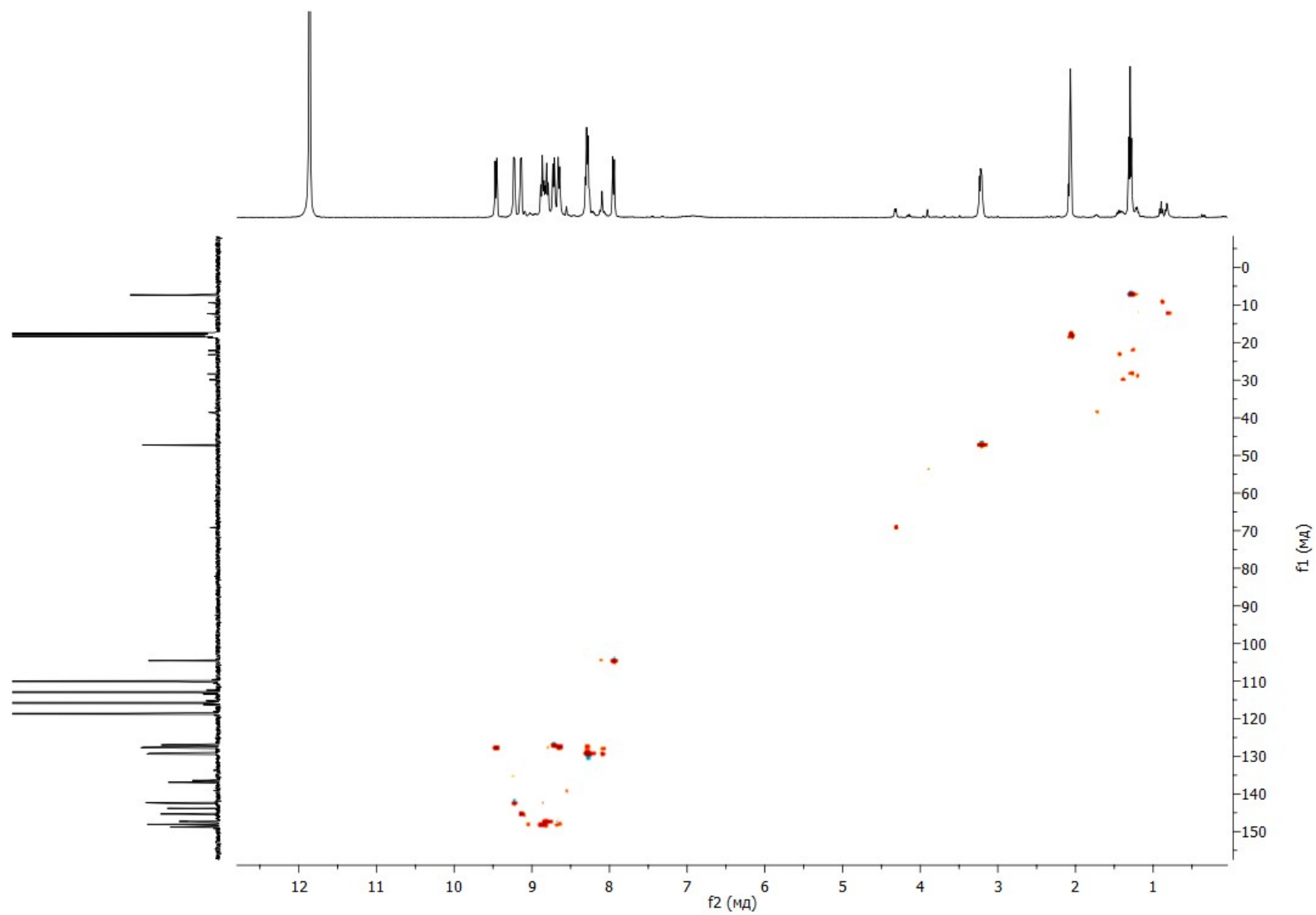
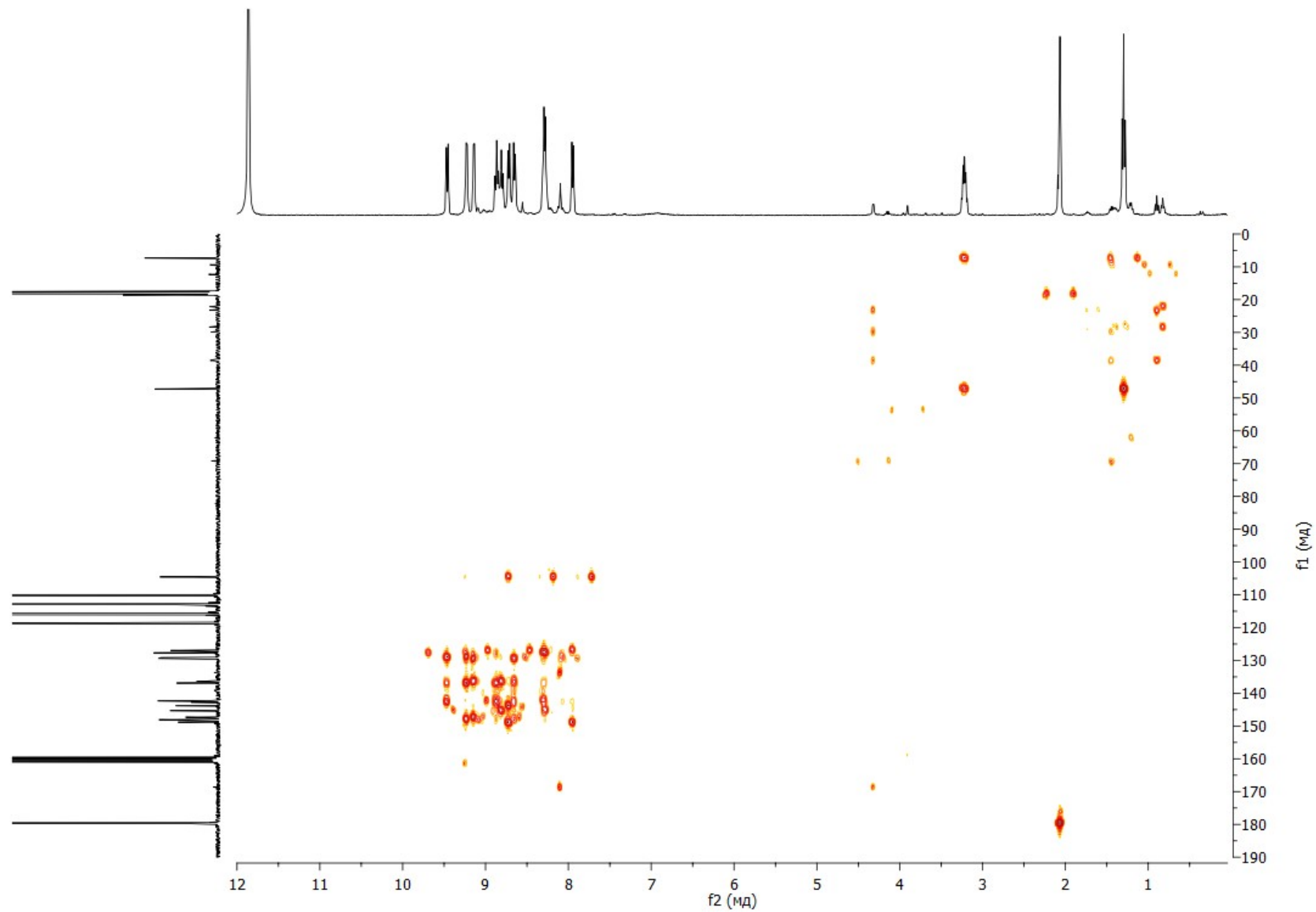


Fig. 38 2D  $^1\text{H}$ - $^{13}\text{C}$  HMBC spectrum for 3,9-bis(5-bromothiophen-2-yl)bis([1,2,4]triazolo)[4,3-*a*:4',3'-*c*]pyrimidine (**8c**).



**Fig. 39** 2D  $^1\text{H}$ - $^{13}\text{C}$  HSQC spectrum for 3,9-di(pyridin-2-yl)bis([1,2,4]triazolo)[4,3-*a*:4',3'-*c*]pyrimidine (**8d**).





**Fig. 40** 2D  $^1\text{H}$ - $^{13}\text{C}$  HMBC spectrum for 3,9-di(pyridin-2-yl)bis([1,2,4]triazolo)[4,3-*a*:4',3'-*c*]pyrimidine (**8d**).

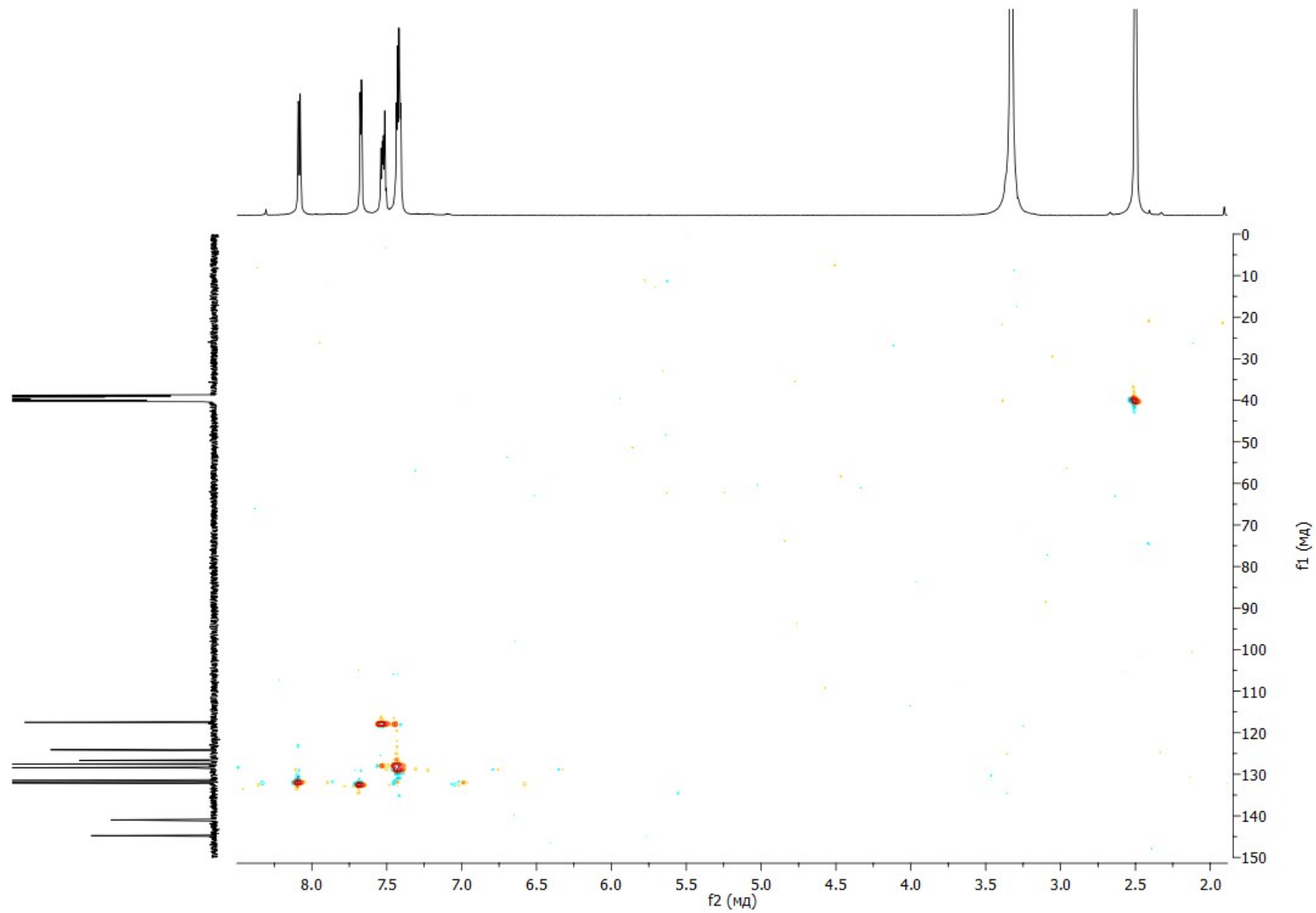
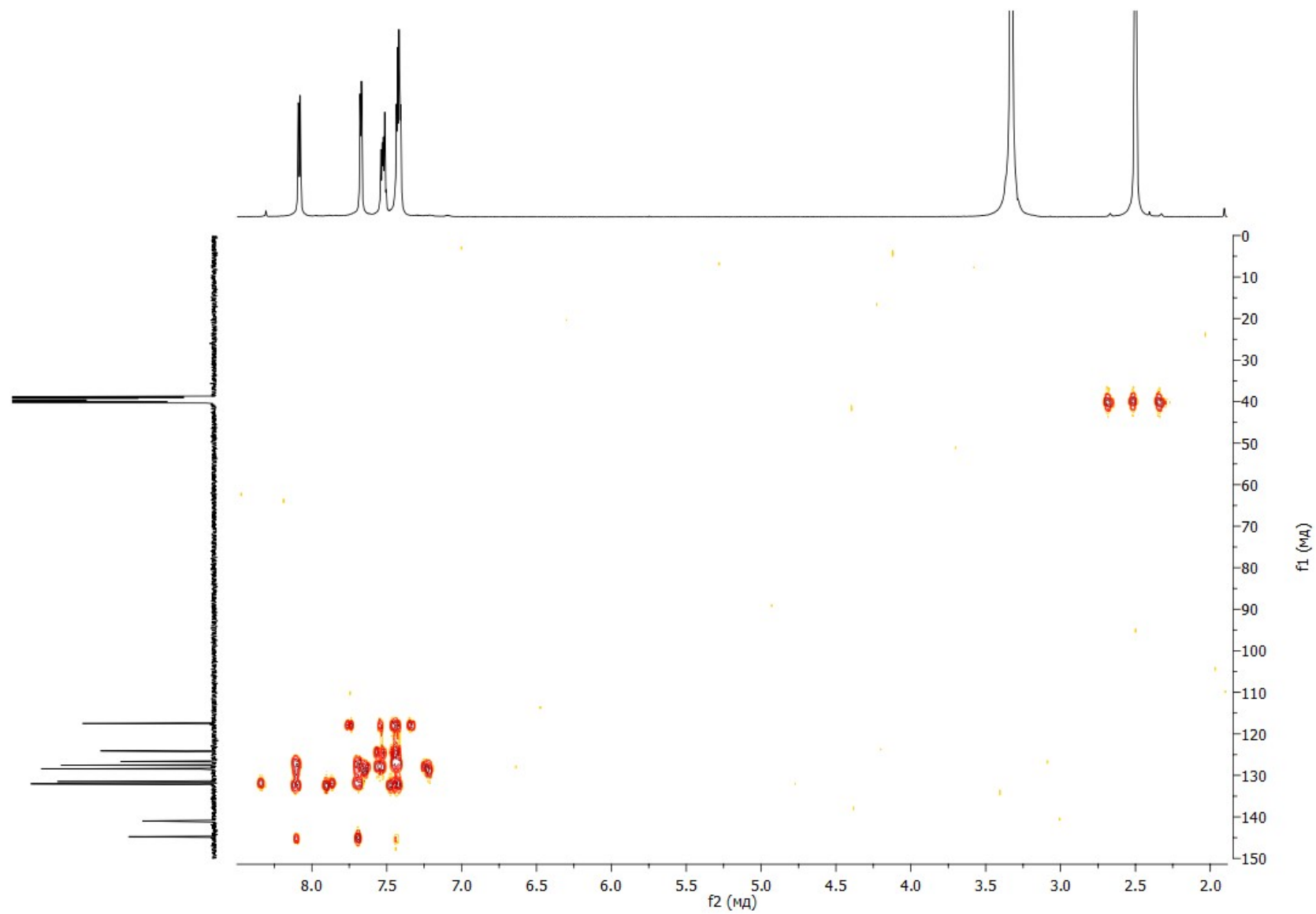


Fig. 41 2D  $^1\text{H}$ - $^{13}\text{C}$  HSQC spectrum for 3,10-di(thiophen-2-yl)bis([1,2,4]triazolo)[4,3-*a*:3',4'-*c*]quinoxaline (**8e**).



**Fig. 42** 2D  $^1\text{H}$ - $^{13}\text{C}$  HMBC spectrum for 3,10-di(thiophen-2-yl)bis([1,2,4]triazolo)[4,3-*a*:3',4'-*c*]quinoxaline (**8e**).

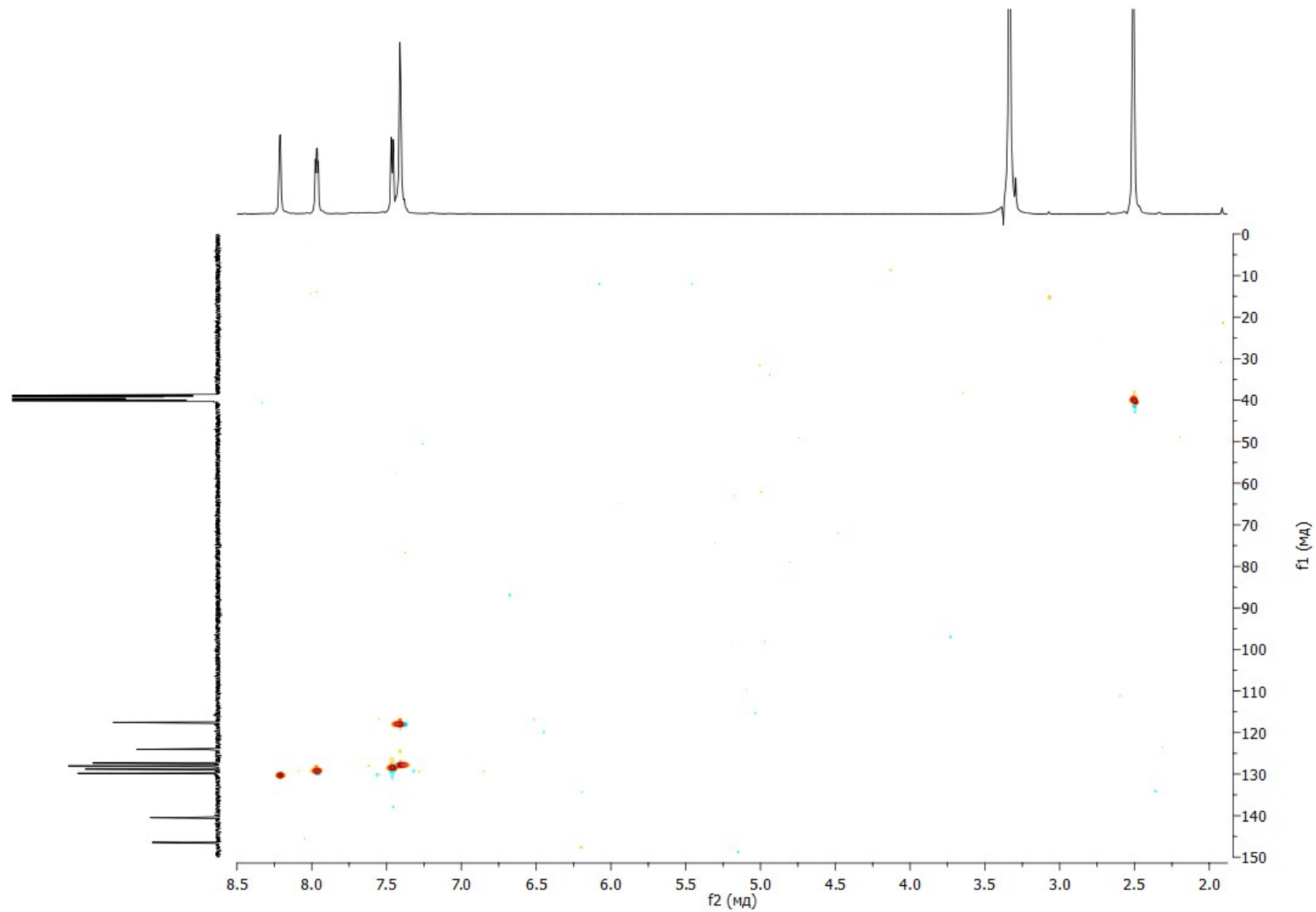
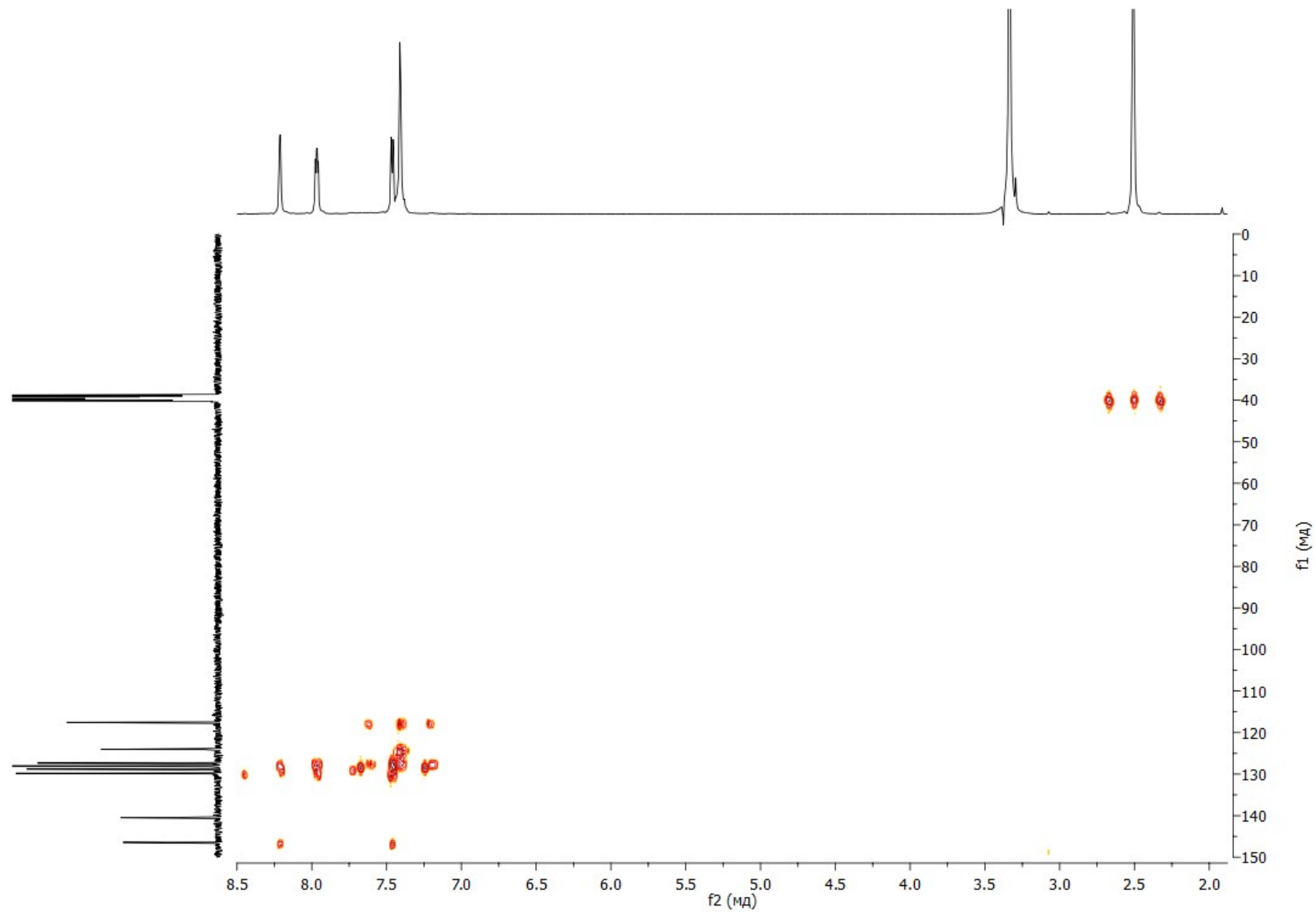
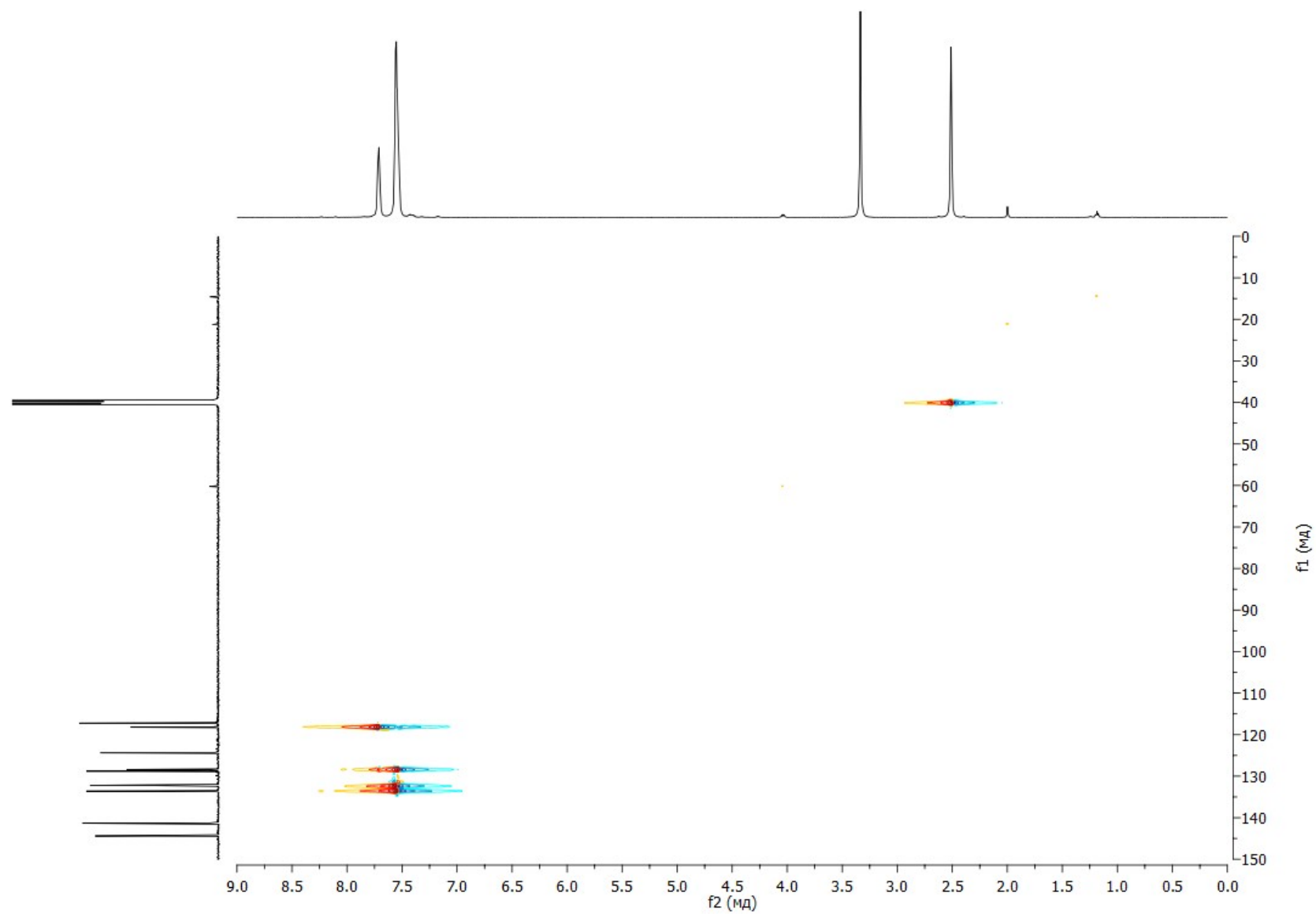


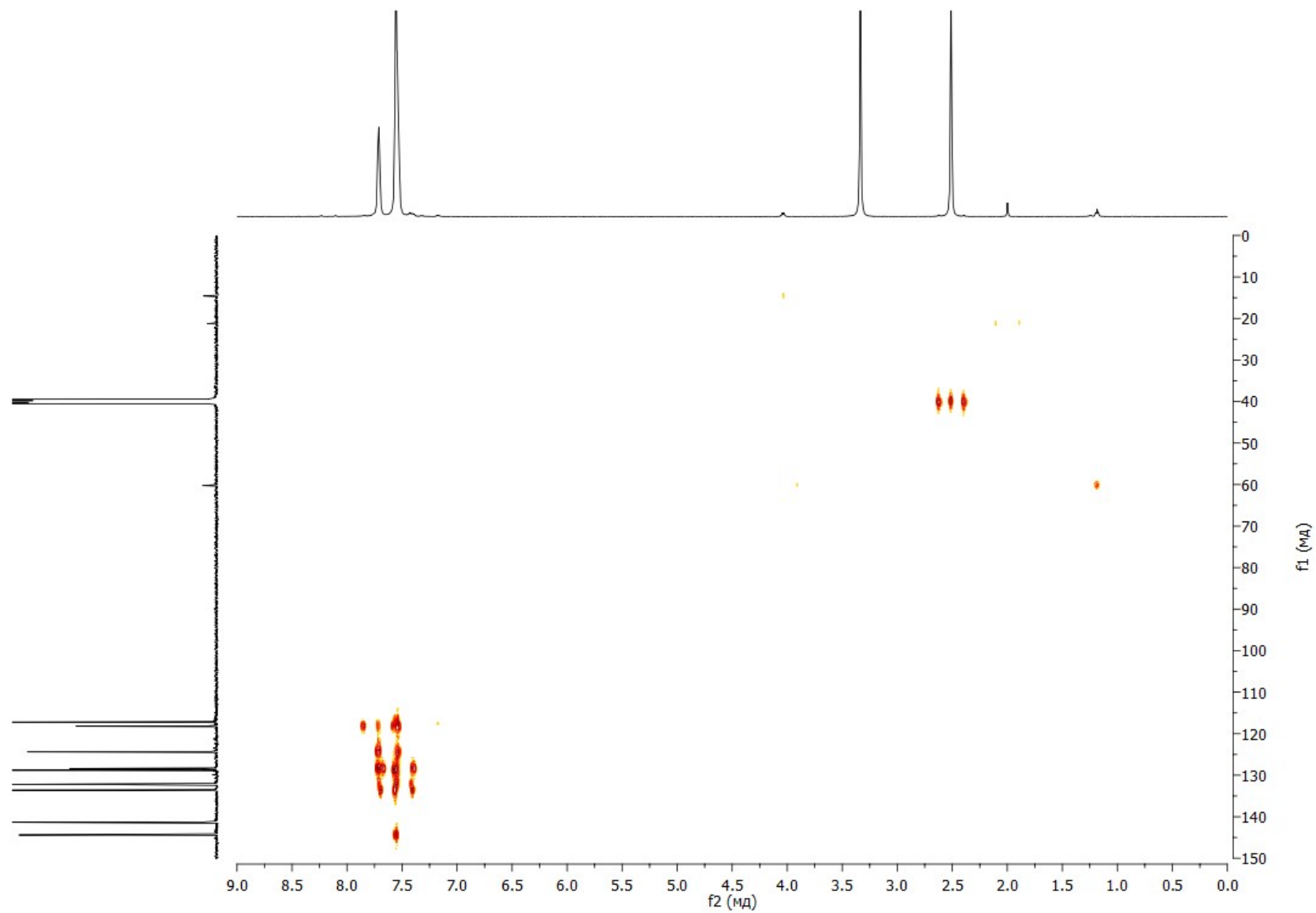
Fig. 43 2D  $^1\text{H}$ - $^{13}\text{C}$  HSQC spectrum for 3,10-di(thiophen-3-yl)bis([1,2,4]triazolo)[4,3-*a*:3',4'-*c*]quinoxaline (**8f**).



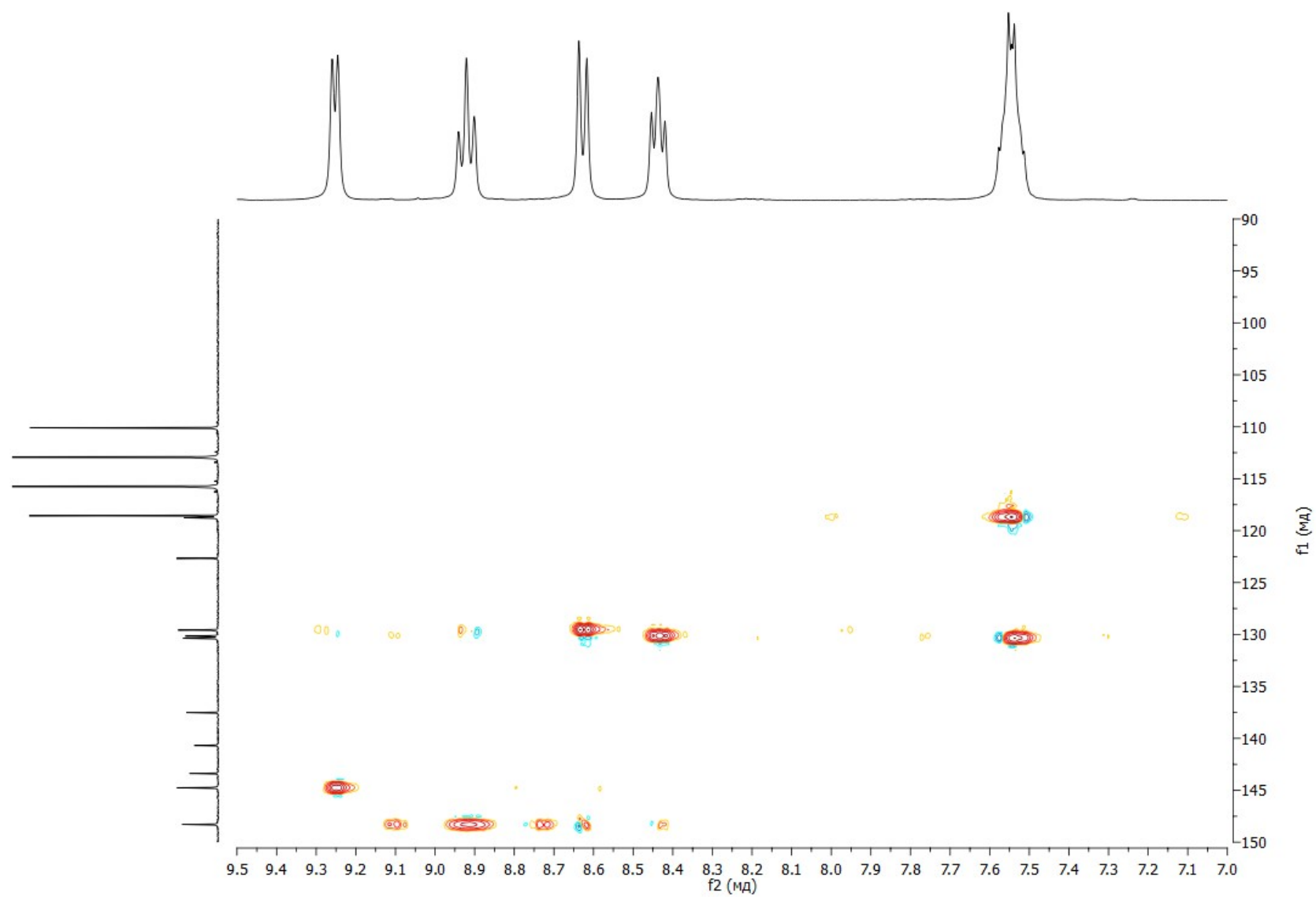
**Fig. 44** 2D  $^1\text{H}$ - $^{13}\text{C}$  HMBC spectrum for 3,10-di(thiophen-3-yl)bis([1,2,4]triazolo)[4,3-*a*:3',4'-*c*]quinoxaline (**8f**).



**Fig. 45** 2D  $^1\text{H}$ - $^{13}\text{C}$  HSQC spectrum for 3,10-bis(5-bromothiophen-2-yl)bis([1,2,4]triazolo)[4,3-*a*:3',4'-*c*]quinoxaline (**8g**).

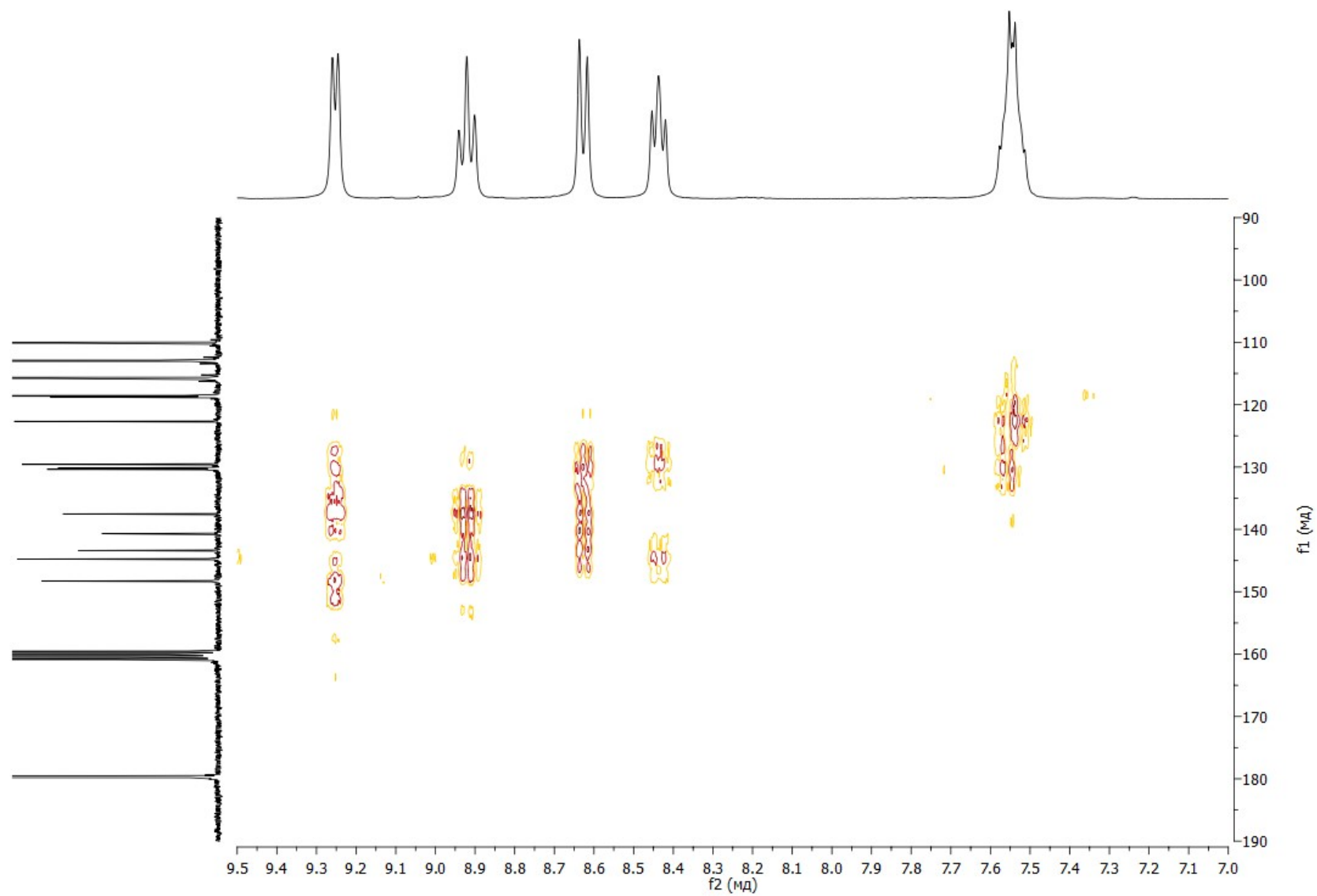


**Fig. 46** 2D  $^1\text{H}$ - $^{13}\text{C}$  HMBC spectrum for 3,10-bis(5-bromothiophen-2-yl)bis([1,2,4]triazolo)[4,3-*a*:3',4'-*c*]quinoxaline (**8g**).

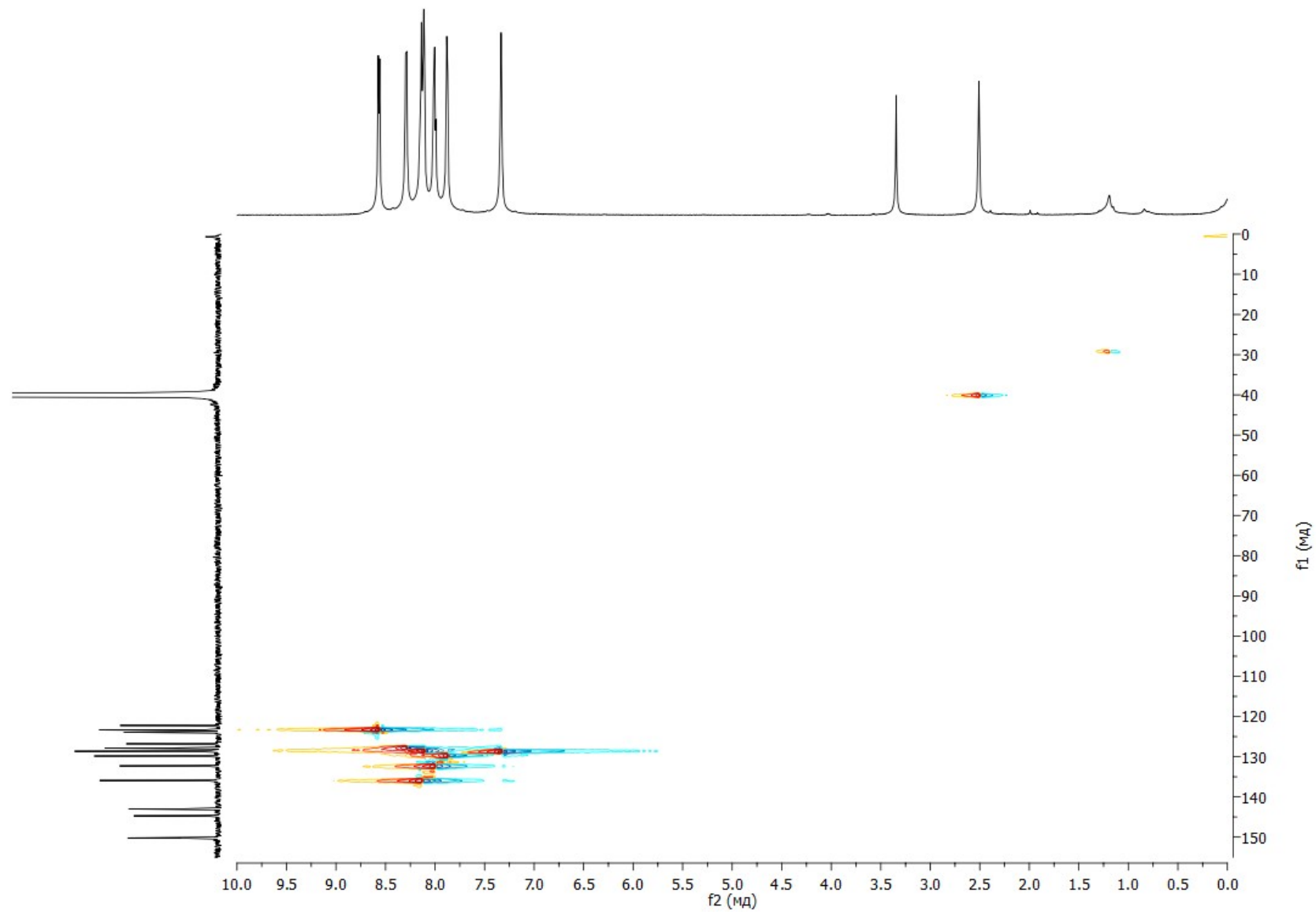


**Fig. 47** 2D  $^1\text{H}$ - $^{13}\text{C}$  HSQC spectrum for 3,10-di(pyridin-2-yl)bis([1,2,4]triazolo)[4,3-*a*:3',4'-*c*]quinoxaline (**8h**).

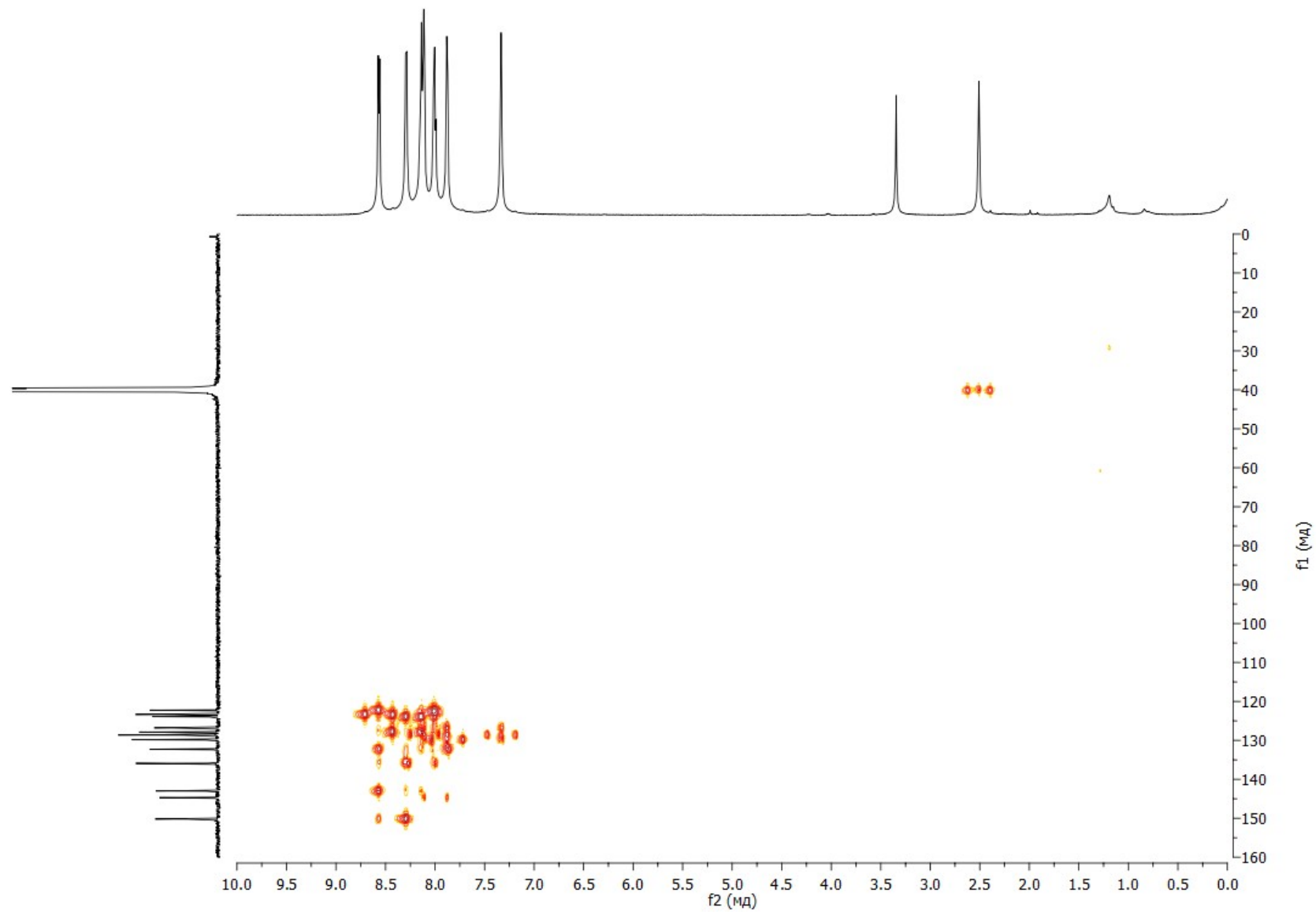




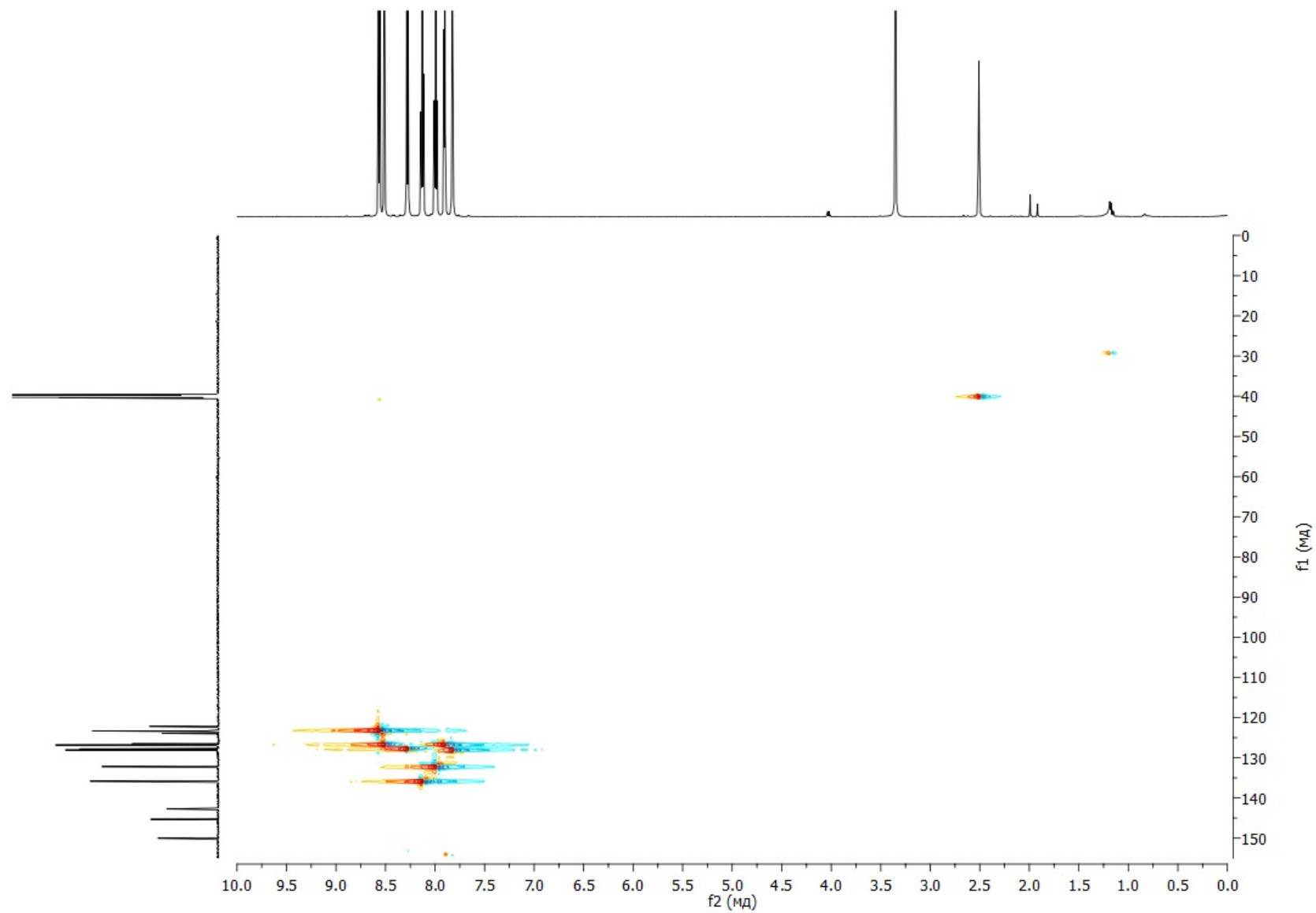
**Fig. 48** 2D  $^1\text{H}$ - $^{13}\text{C}$  HMBC spectrum for 3,10-di(pyridin-2-yl)bis([1,2,4]triazolo)[4,3-*a*:3',4'-*c*]quinoxaline (**8h**).



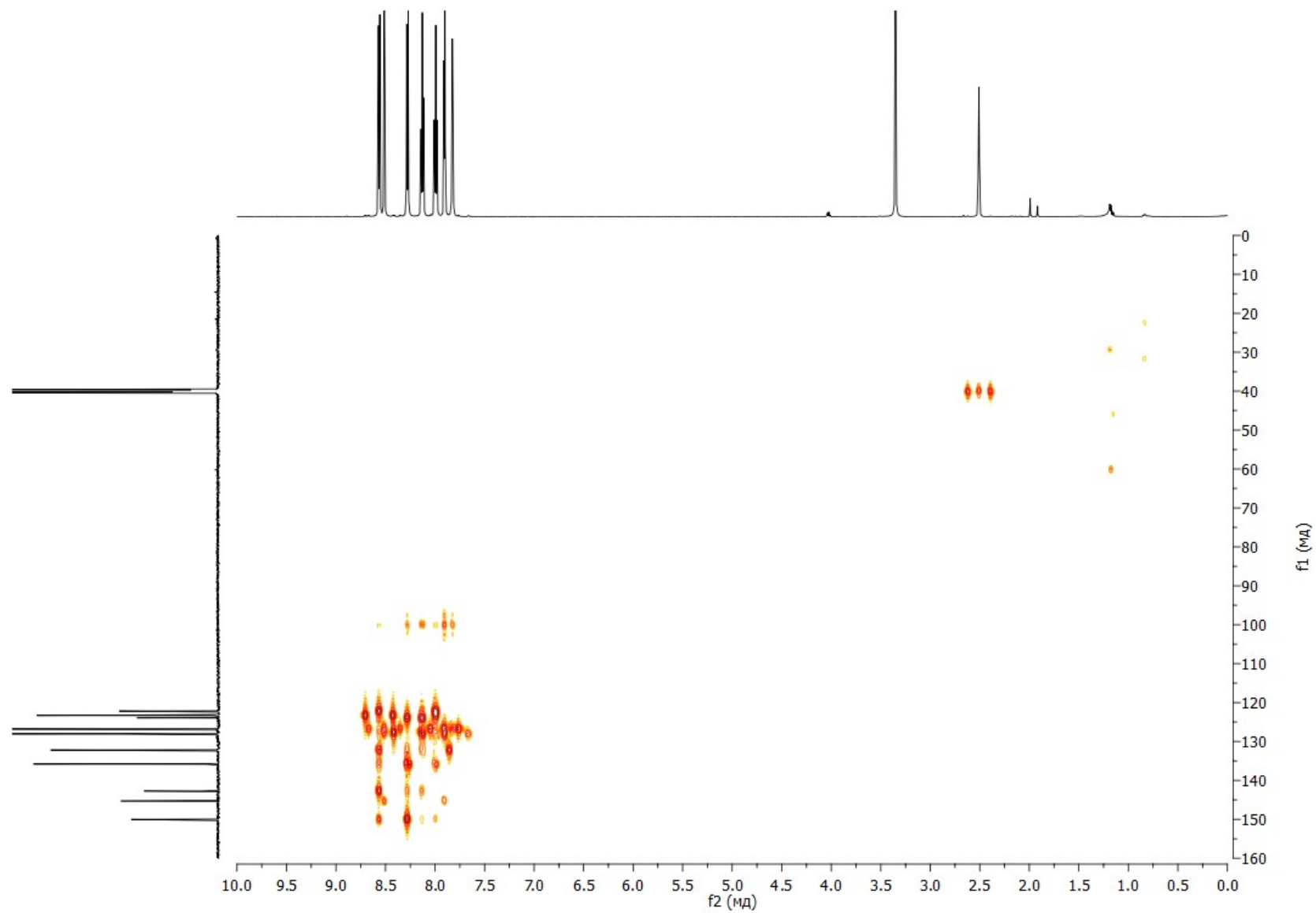
**Fig. 49** 2D  $^1\text{H}$ - $^{13}\text{C}$  HSQC spectrum for 6-chloro-3-(thiophen-2-yl)-[1,2,4]triazolo[3,4-*a*]phthalazine (**12a**).



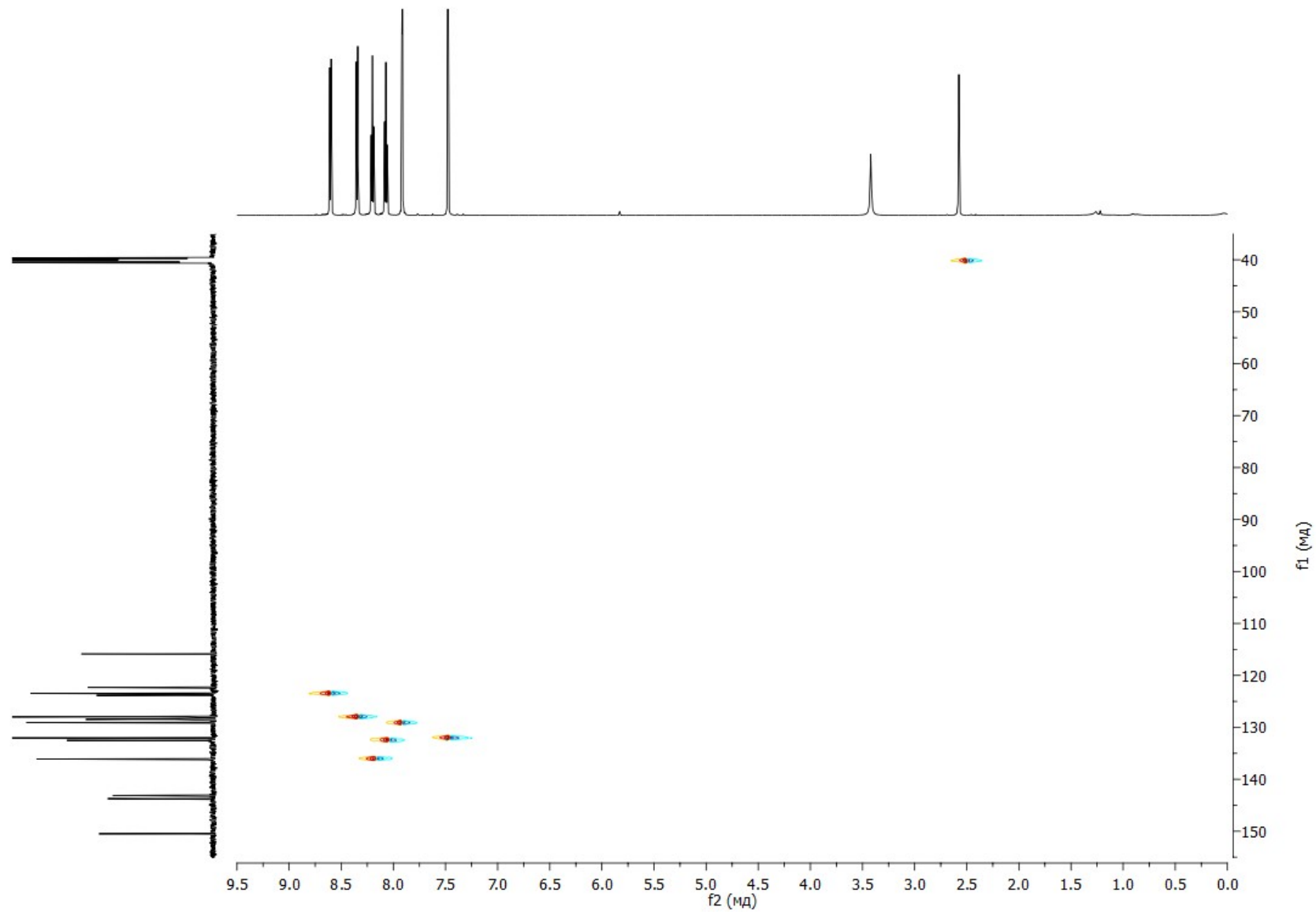
**Fig. 50** 2D  $^1\text{H}$ - $^{13}\text{C}$  HMBC spectrum for 6-chloro-3-(thiophen-2-yl)-[1,2,4]triazolo[3,4-*a*]phthalazine (**12a**).



**Fig. 51** 2D  $^1\text{H}$ - $^{13}\text{C}$  HSQC spectrum for 6-chloro-3-(thiophen-3-yl)-[1,2,4]triazolo[3,4-*a*]phthalazine (**12b**).



**Fig. 52** 2D  $^1\text{H}$ - $^{13}\text{C}$  HMBC spectrum for 6-chloro-3-(thiophen-3-yl)-[1,2,4]triazolo[3,4-*a*]phthalazine (**12b**).



**Fig. 53** 2D  $^1\text{H}$ - $^{13}\text{C}$  HSQC spectrum for 3-(5-bromothiophen-2-yl)-6-chloro-[1,2,4]triazolo[3,4-*a*]phthalazine (**12c**).

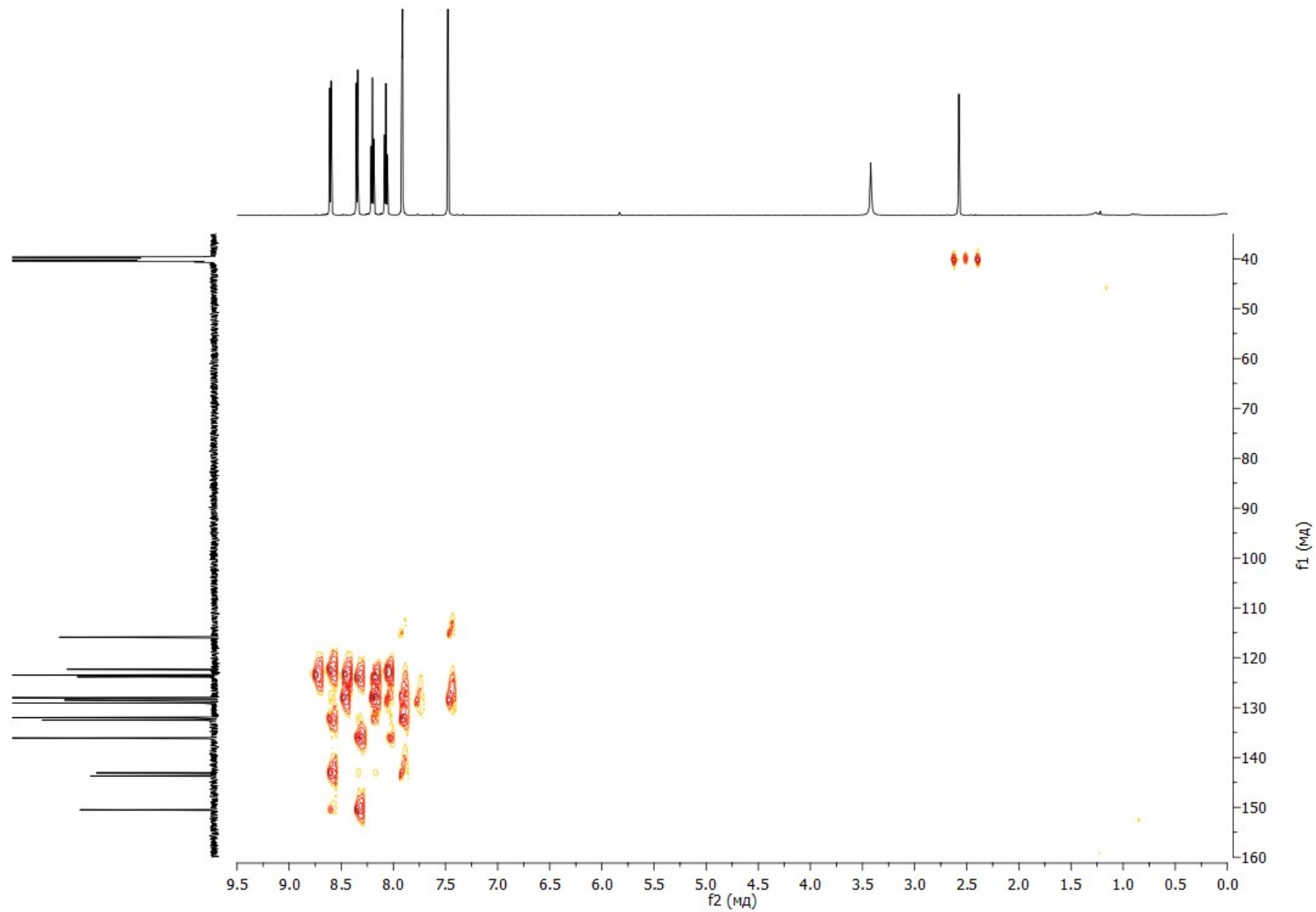


Fig. 54 2D  $^1\text{H}$ - $^{13}\text{C}$  HMBC spectrum for 3-(5-bromothiophen-2-yl)-6-chloro-[1,2,4]triazolo[3,4-*a*]phthalazine (**12c**).

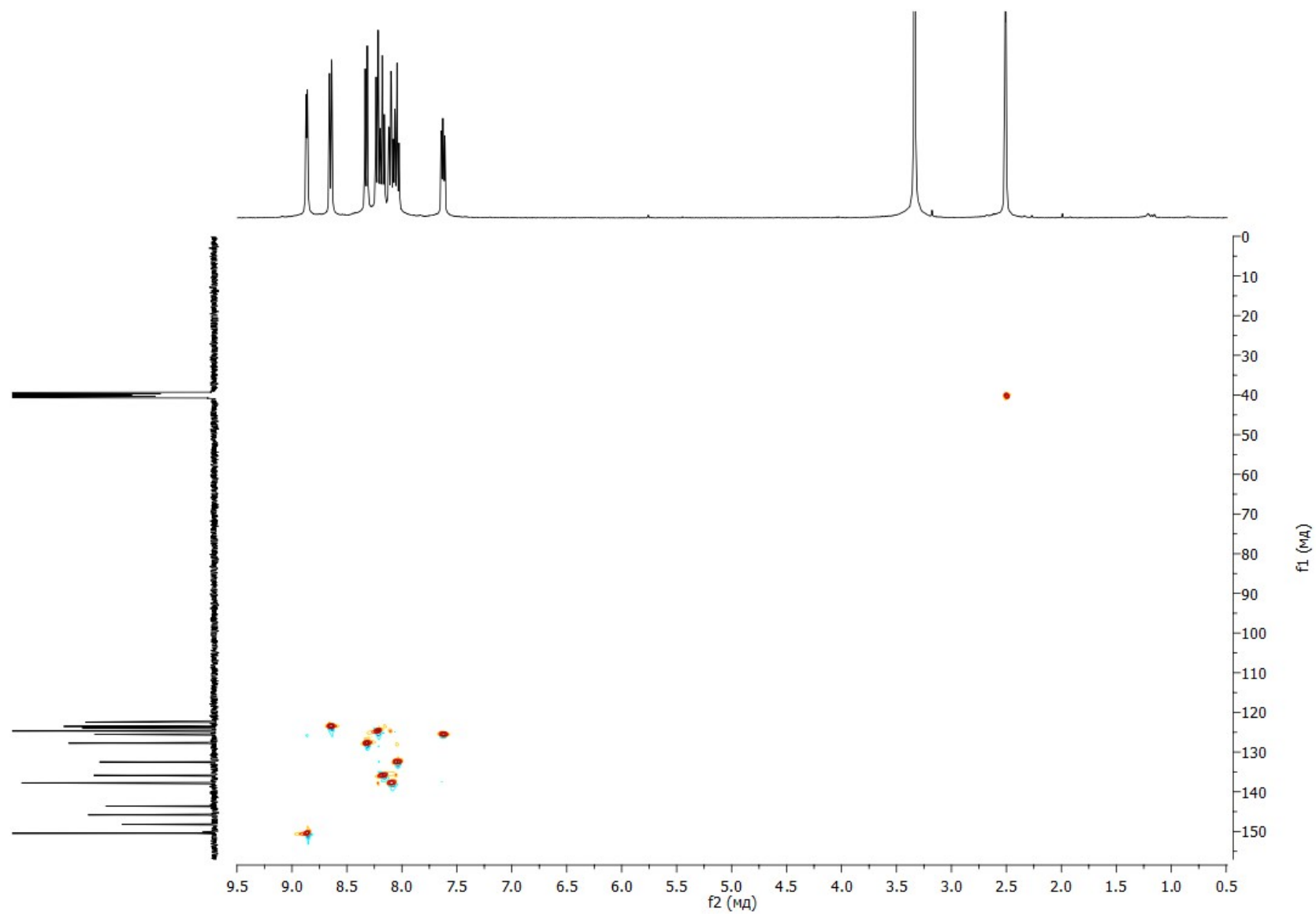


Fig. 55 2D  $^1\text{H}$ - $^{13}\text{C}$  HSQC spectrum for 6-chloro-3-(pyridin-2-yl)-[1,2,4]triazolo[3,4-*a*]phthalazine (**12d**).



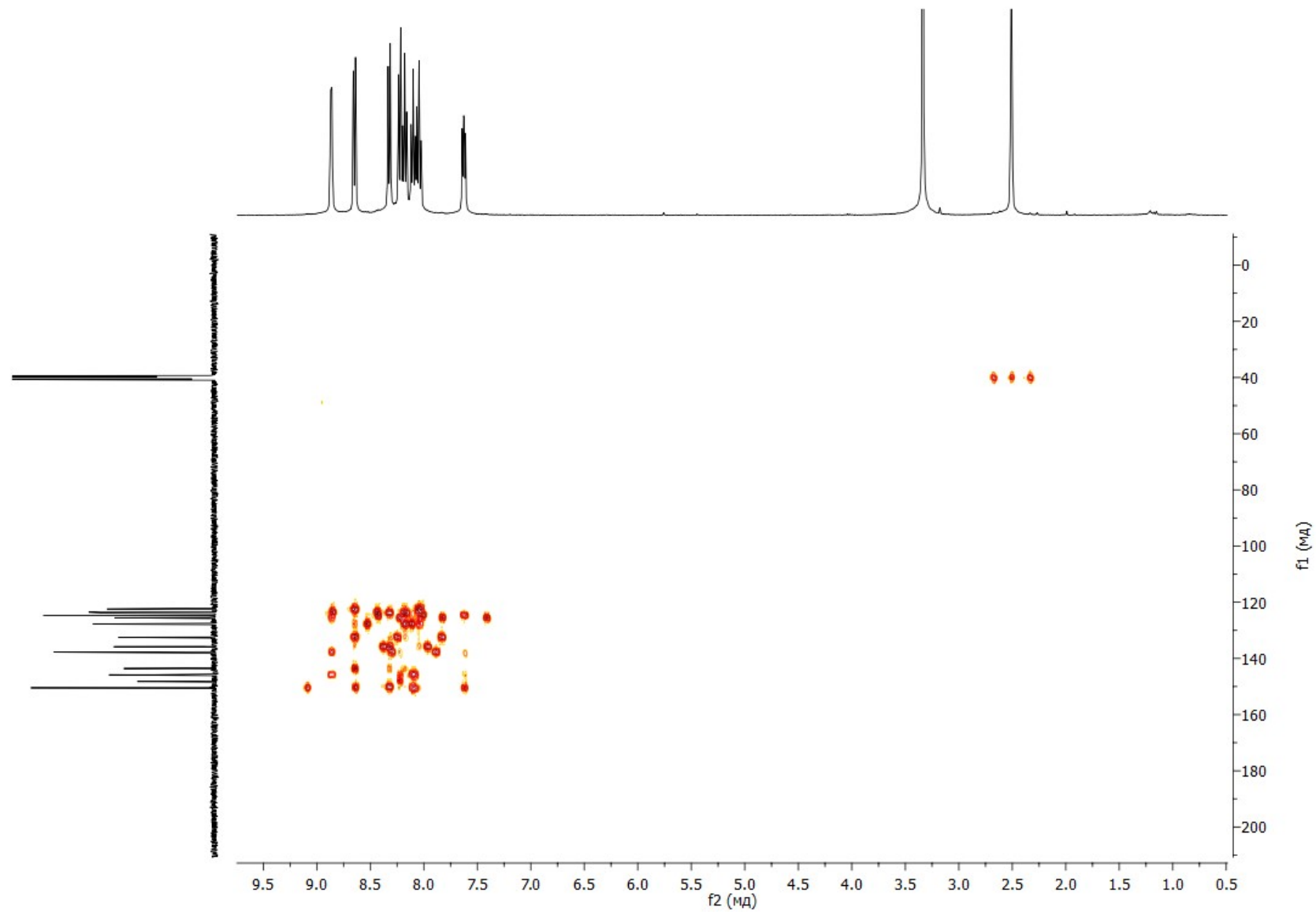
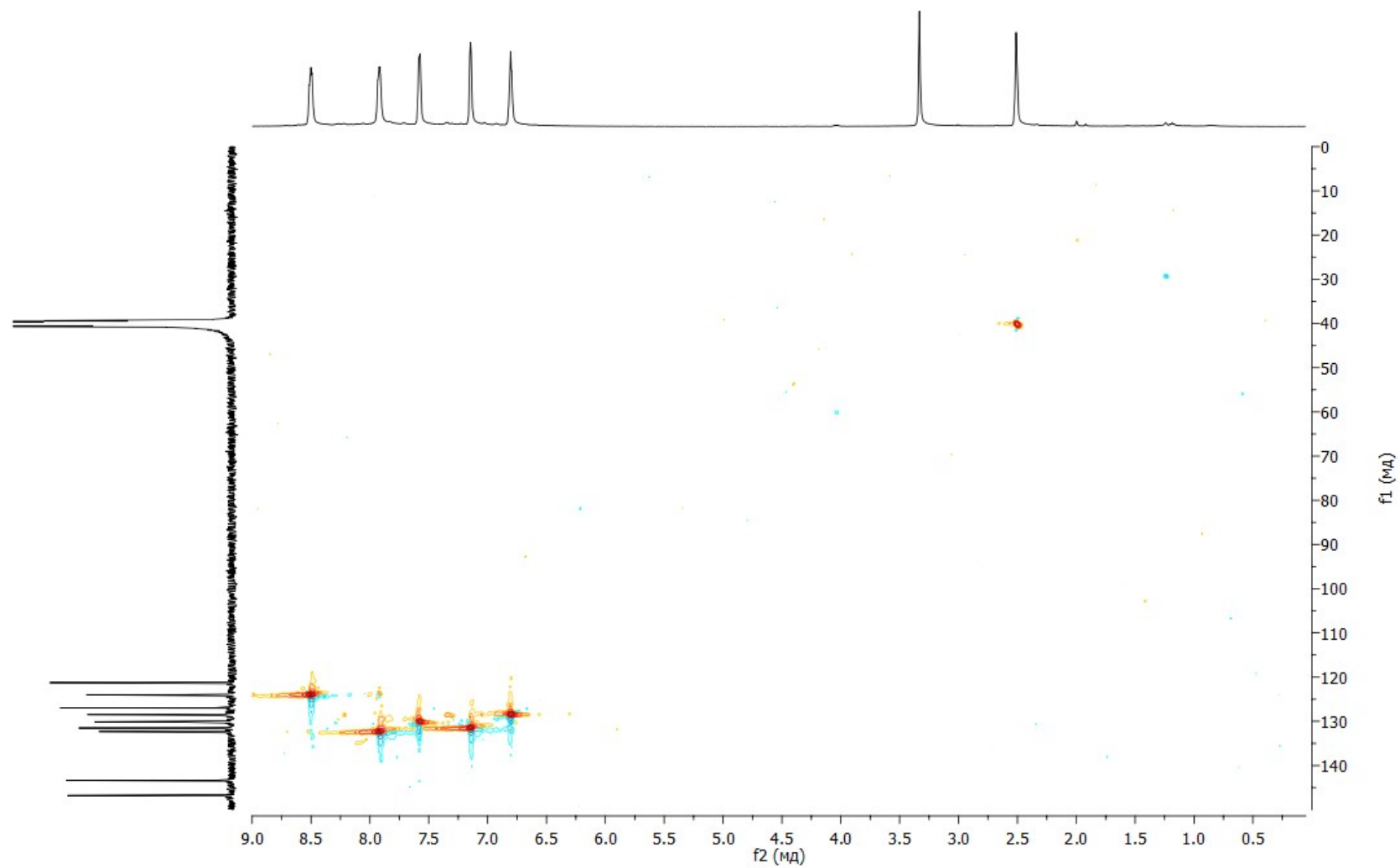


Fig. 56 2D  $^1\text{H}$ - $^{13}\text{C}$  HMBC spectrum for 6-chloro-3-(pyridin-2-yl)-[1,2,4]triazolo[3,4-*a*]phthalazine (**12d**).



**Fig. 57** 2D <sup>1</sup>H-<sup>13</sup>C HSQC spectrum for 3,6-di(thiophen-2-yl)bis([1,2,4]triazolo)[3,4-*a*:4',3'-*c*]phthalazine (**14a**).

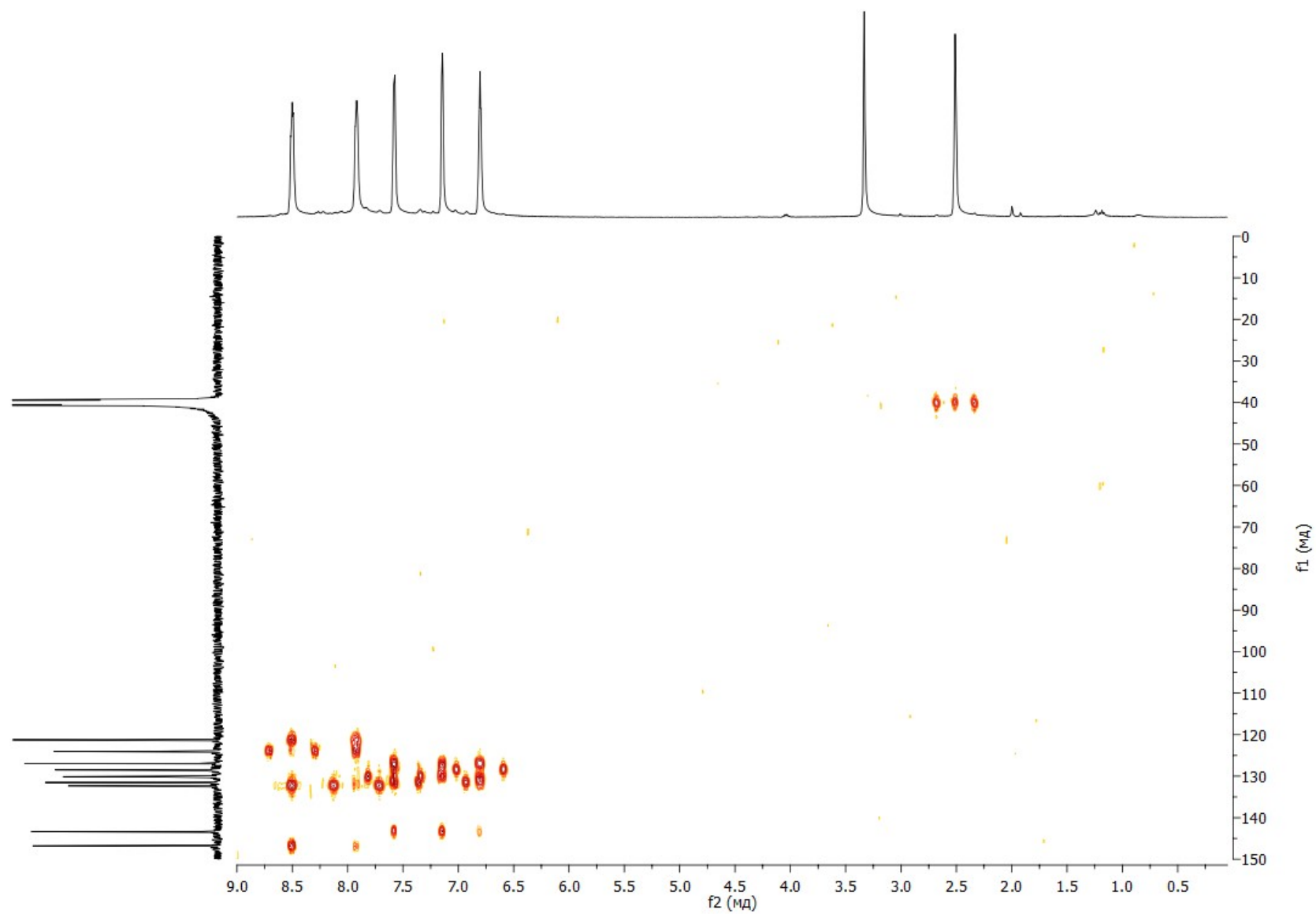
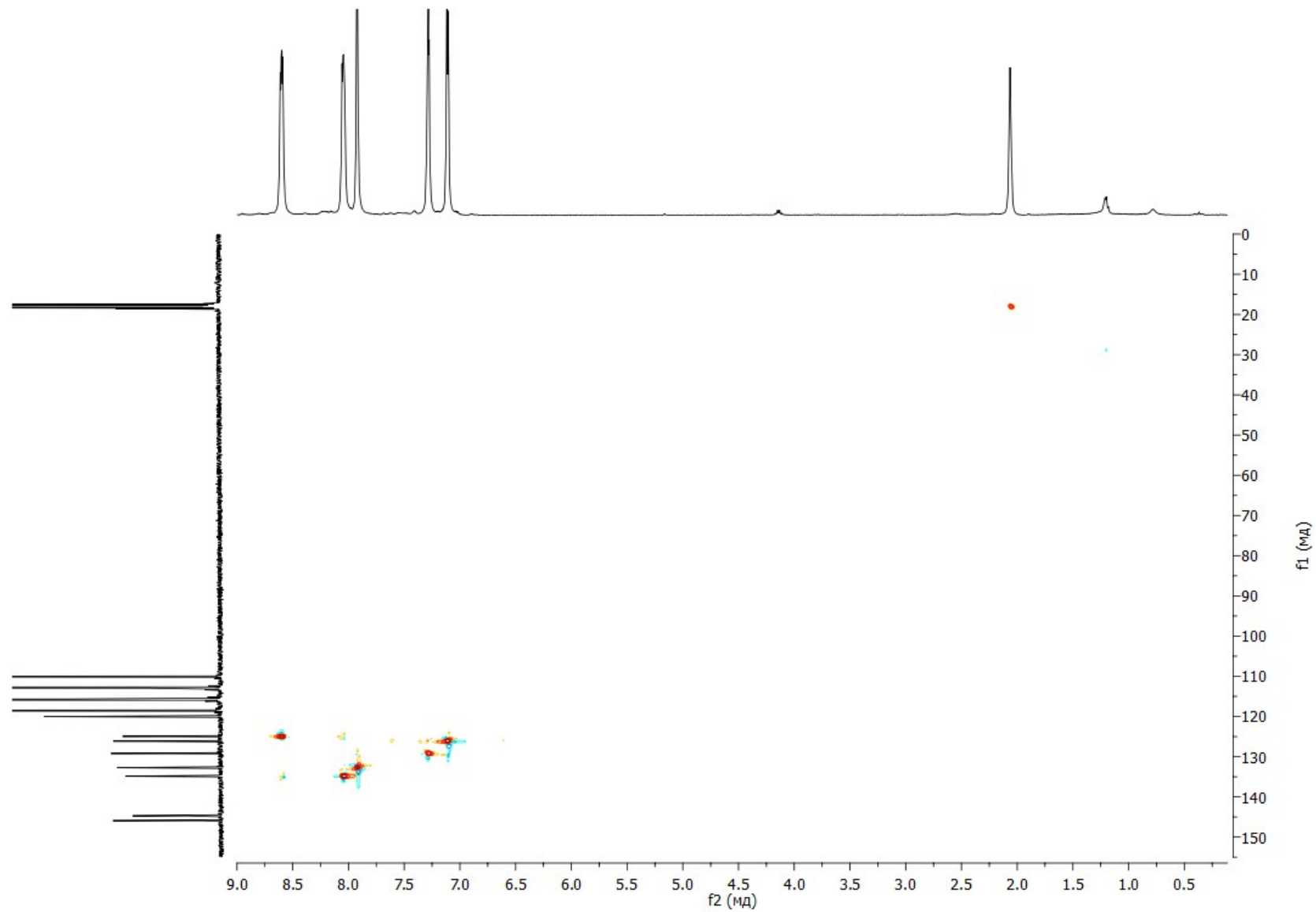


Fig. 58 2D  $^1\text{H}$ - $^{13}\text{C}$  HMBC spectrum for 3,6-di(thiophen-2-yl)bis([1,2,4]triazolo)[3,4-*a*:4',3'-*c*]phthalazine (**14a**).



**Fig. 59** 2D <sup>1</sup>H-<sup>13</sup>C HSQC spectrum for 3,6-di(thiophen-3-yl)bis([1,2,4]triazolo)[3,4-*a*:4',3'-*c*]phthalazine (**14b**).

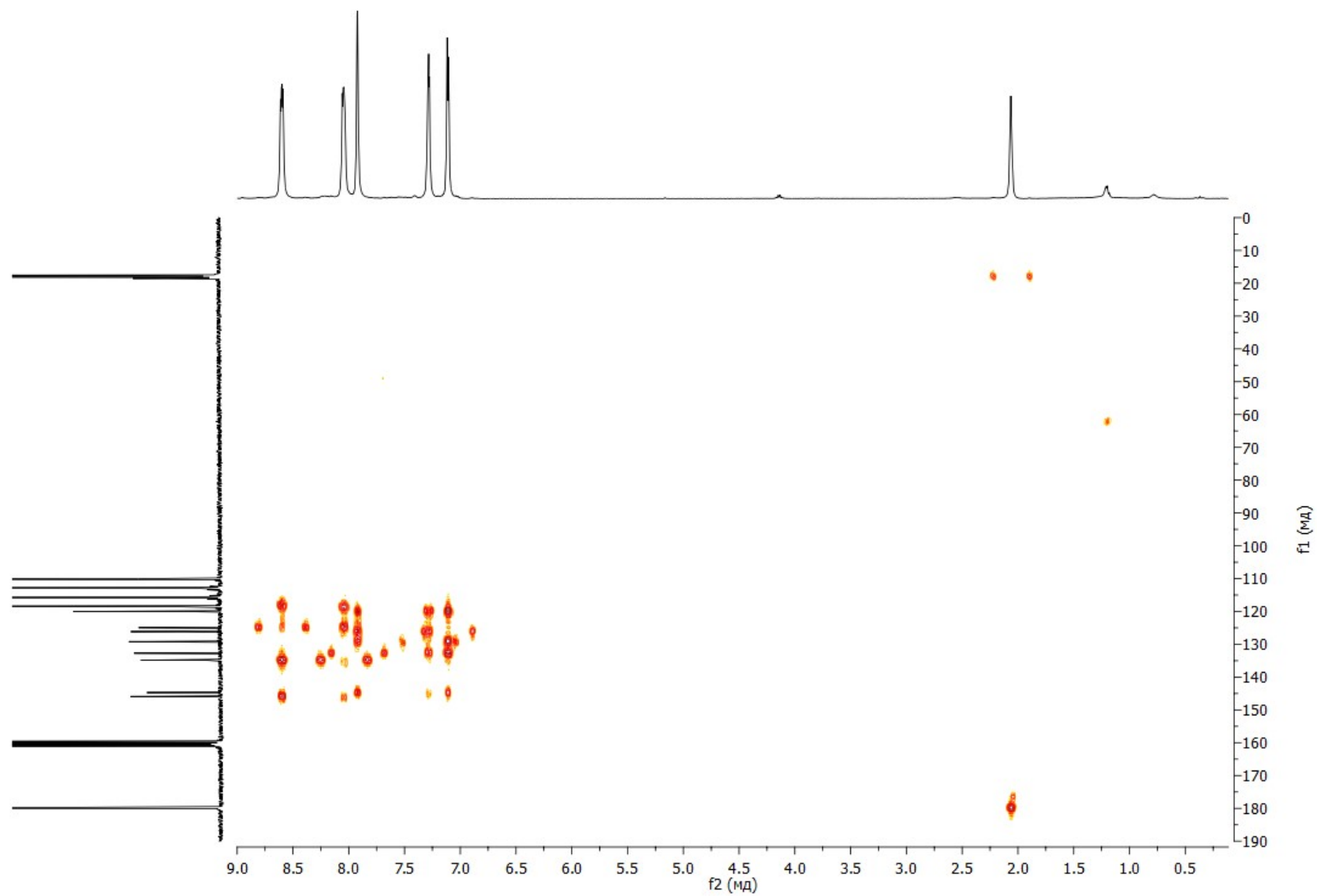
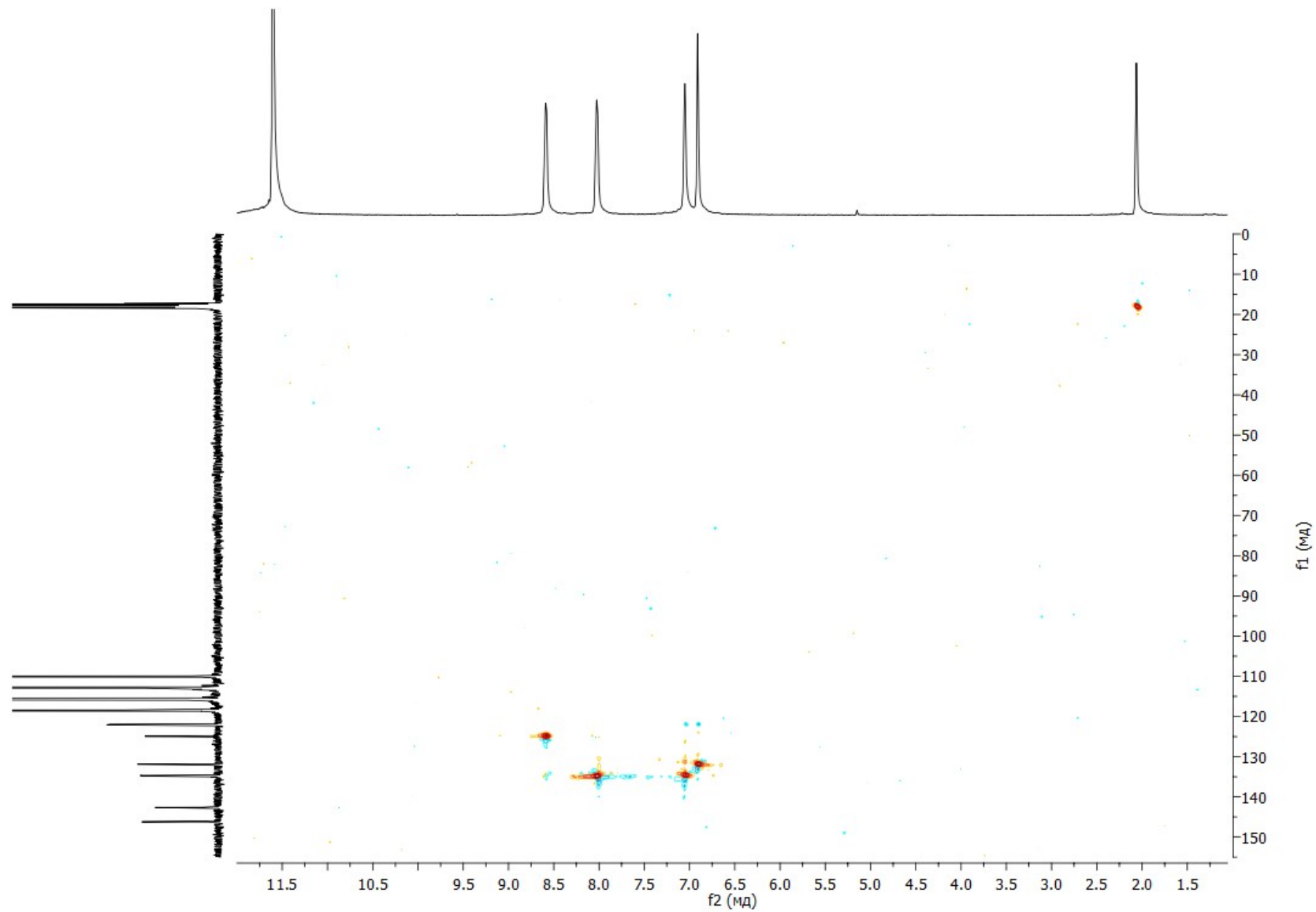


Fig. 60 2D  $^1\text{H}$ - $^{13}\text{C}$  HMBC spectrum for 3,6-di(thiophen-3-yl)bis([1,2,4]triazolo)[3,4-*a*:4',3'-*c*]phthalazine (**14b**).



**Fig. 61** 2D  $^1\text{H}$ - $^{13}\text{C}$  HSQC spectrum for 3,6-bis(5-bromothiophen-2-yl)bis([1,2,4]triazolo)[3,4-*a*:4',3'-*c*]phthalazine (**14c**).

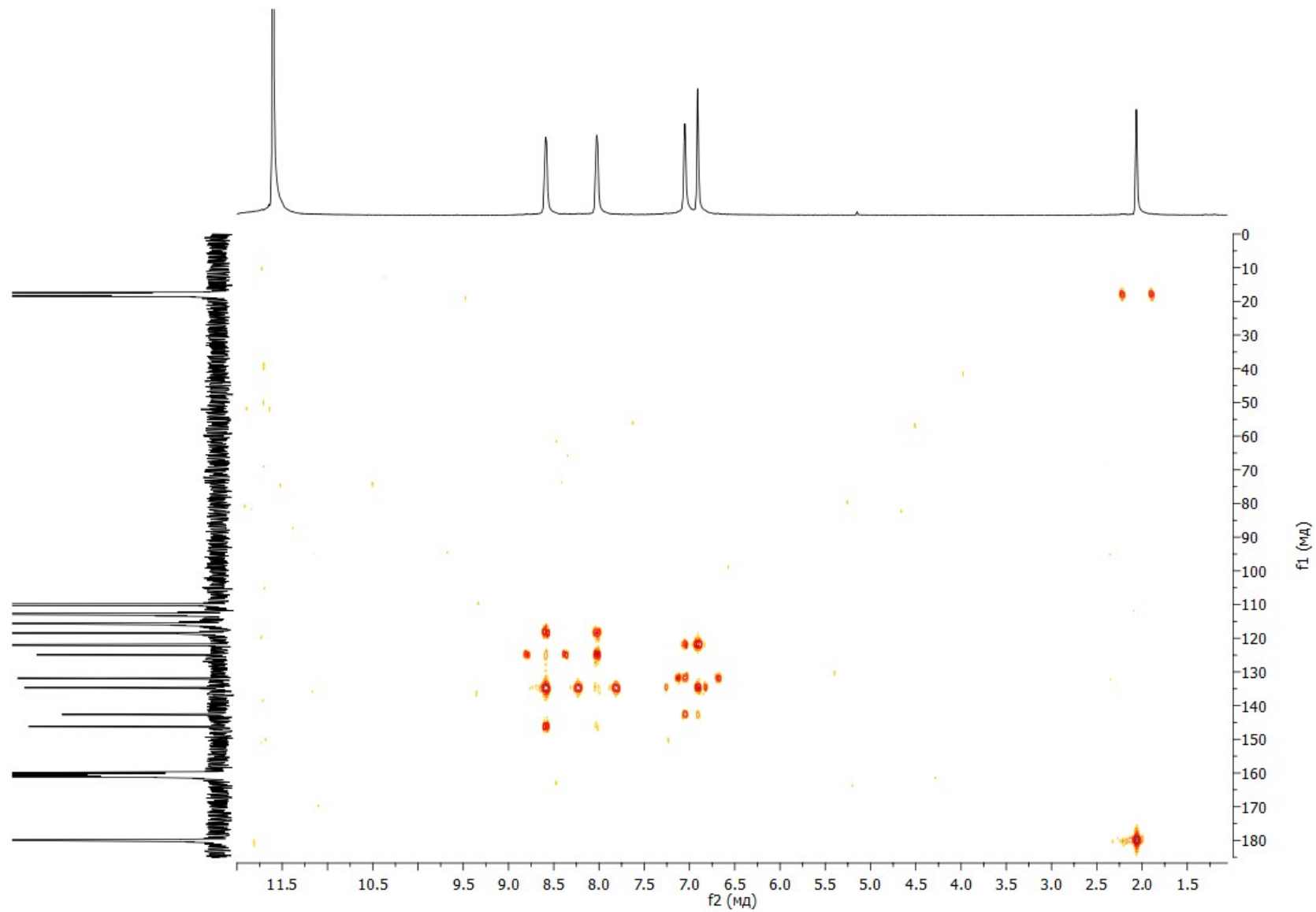


Fig. 62 2D  $^1\text{H}$ - $^{13}\text{C}$  HMBC spectrum for 3,6-bis(5-bromothiophen-2-yl)bis([1,2,4]triazolo)[3,4-*a*:4',3'-*c*]phthalazine (**14c**).

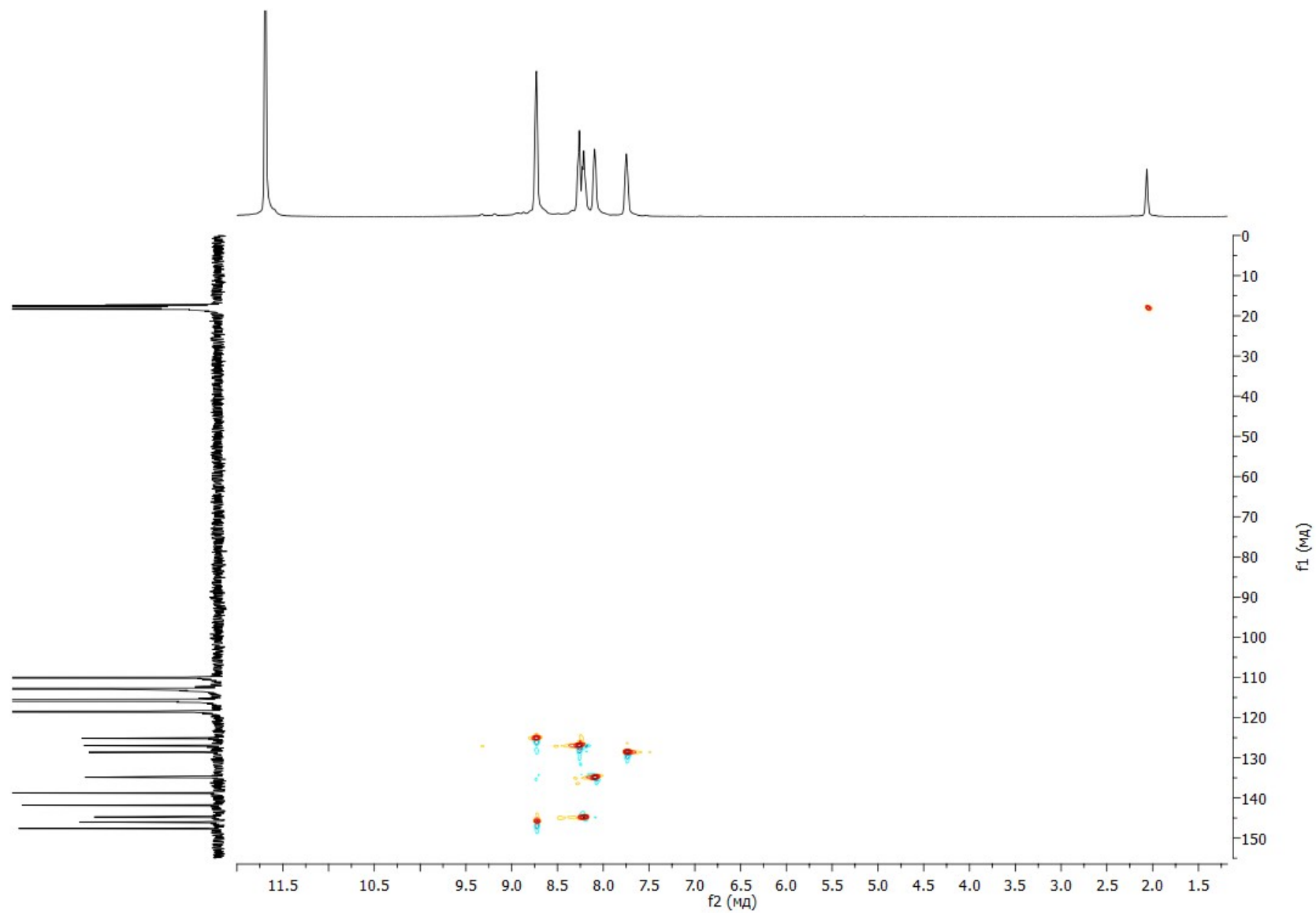
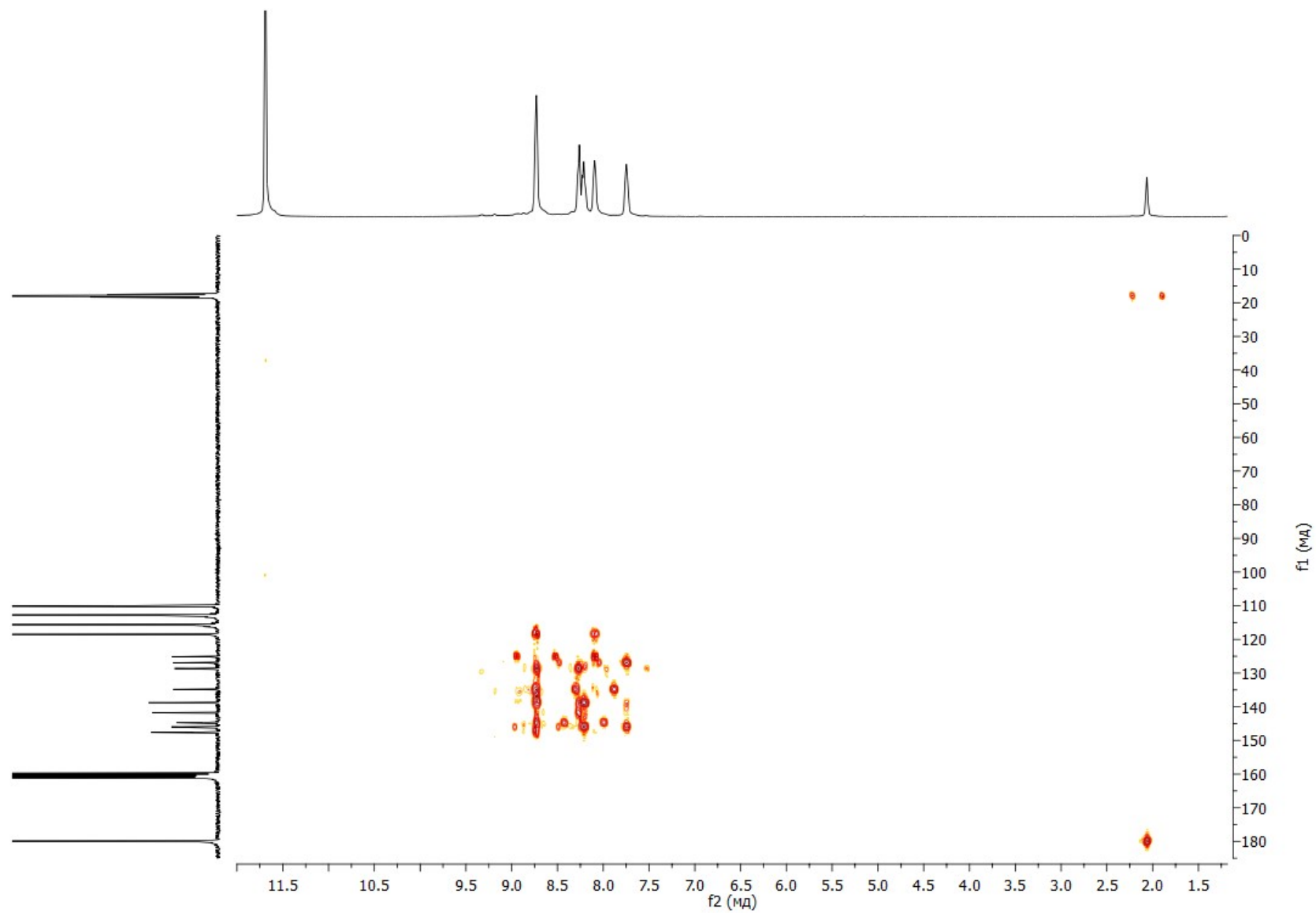


Fig. 63 2D  $^1\text{H}$ - $^{13}\text{C}$  HSQC spectrum for 3,6-di(pyridin-2-yl)bis([1,2,4]triazolo)[3,4-*a*:4',3'-*c*]phthalazine (**14d**).





**Fig. 64** 2D  $^1\text{H}$ - $^{13}\text{C}$  HMBC spectrum for 3,6-di(pyridin-2-yl)bis([1,2,4]triazolo)[3,4-*a*:4',3'-*c*]phthalazine (**14d**).