**Supporting Information**

# Two-Stage Synthesis and Antibacterial Profiling of Novel Symmetric and Unsymmetrical 1,2-Dialkylpyrazolium Salts

**Nazym A. Alzhapparova [1], Svetlana Yu. Panshina [1]*, Oxana V. Ponomarenko [2], Marat K. Ibrayev [1], Zhanerke T. Amirkhanova [3], Saule B. Akhmetova [3], Eugene V. Babaev [4], Tulegen M. Seilkhanov [2]**

[1]*Chemistry Department, Karaganda National Research University named after Academician E.A. Buketov, Karaganda, 100024, Kazakhstan*
*e-mail: nazym285@mail.ru, janim_svetatusik@mail.ru*, mkibr@mail.ru*

[2]*Chemistry and Biotechnology Department, Sh. Ualikhanov Kokshetau State University, Kokshetau, 020000, Kazakhstan*
*e-mail:* amirhanova@qmu.kz, S.Ahmetova@qmu.kz

[3]*Department of Molecular Biology, Biochemistry and Microbiology, Karaganda Medical University, Karaganda, 100012, Kazakhstan*
*e-mail:* oksana.ponomarenko.88@mail.ru, tseilkhanov@mail.ru

[4]*Chemistry Department, Lomonosov Moscow State University, Moscow, 119899, Russia*
*e-mail:* babaev@org.chem.msu.ru

**Table of content**


Spectra of N-acylalkylpyrazoles 3d, 8a-c ..... 3
Spectra of 1-(4-fluorophenyl)-2-(1H-pyrazol-1-yl)ethan-1-one (3d) ..... 3
Spectra of 1-(*tert*-butyl)-2-(3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl)ethan-1-one (8a) ..... 7
Spectra of 1-phenyl-2-(3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl)ethan-1-one (8b) ..... 11
Spectra of symmetrical salts of N-acylalkylpyrazole bromide 5a–i, 6a–d ..... 15
Spectra of 1,2-bis(3,3-dimethyl-2-oxobutyl)-1*H*-pyrazol-1-ium bromide (5a) ..... 15
Spectra of 1,2-bis(2-phenyl-2-oxoethyl)-1H-pyrazol-1-ium bromide (5b) ..... 18
Spectra of 1,2-bis(2-(4-bromophenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (5c) ..... 21
Spectra of 1,2-bis(2-(4-nitrophenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (5d) ..... 26
Spectra of 1-(3,3-dimethyl-2-oxobutyl)-2-(2-(4-(trifluoromethoxy)phenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (5e) ..... 28
Spectra of 1-(3,3-dimethyl-2-oxobutyl)-2-(2-(4-fluorophenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (5f) ..... 31
Spectra of 1-(2-(4-fluorophenyl)-2-oxoethyl)-2-(2-phenyl-2-oxoethyl)-1H-pyrazol-1-ium bromide (5g) ..... 37
Spectra of 1-(2-(4-bromophenyl)-2-oxoethyl)-2-(2-phenyl-2-oxoethyl)-1H-pyrazol-1-ium bromide (5h) ..... 41
Spectra of 1,2-bis(2-phenyl-2-oxoethyl)-3,5-dimethyl-1H-pyrazol-1-ium bromide (6b) ..... 43
Spectra of 1,2-bis(2-(4-bromophenyl)-2-oxoethyl)-3,5-dimethyl-1H-pyrazol-1-ium bromide (6c) ..... 46
Spectra of 2-(2-(4-bromophenyl)-2-oxoethyl)-1-(2-oxo-2-phenylethyl)-3,5-dimethyl-1H-pyrazol-1-ium bromide (6d) ..... 49
In vitro antimicrobial and antifungal activity ..... 52

## Spectra of N-acylalkylpyrazoles 3d, 8a-c

### Spectra of 1-(4-fluorophenyl)-2-(1H-pyrazol-1-yl)ethan-1-one (3d)

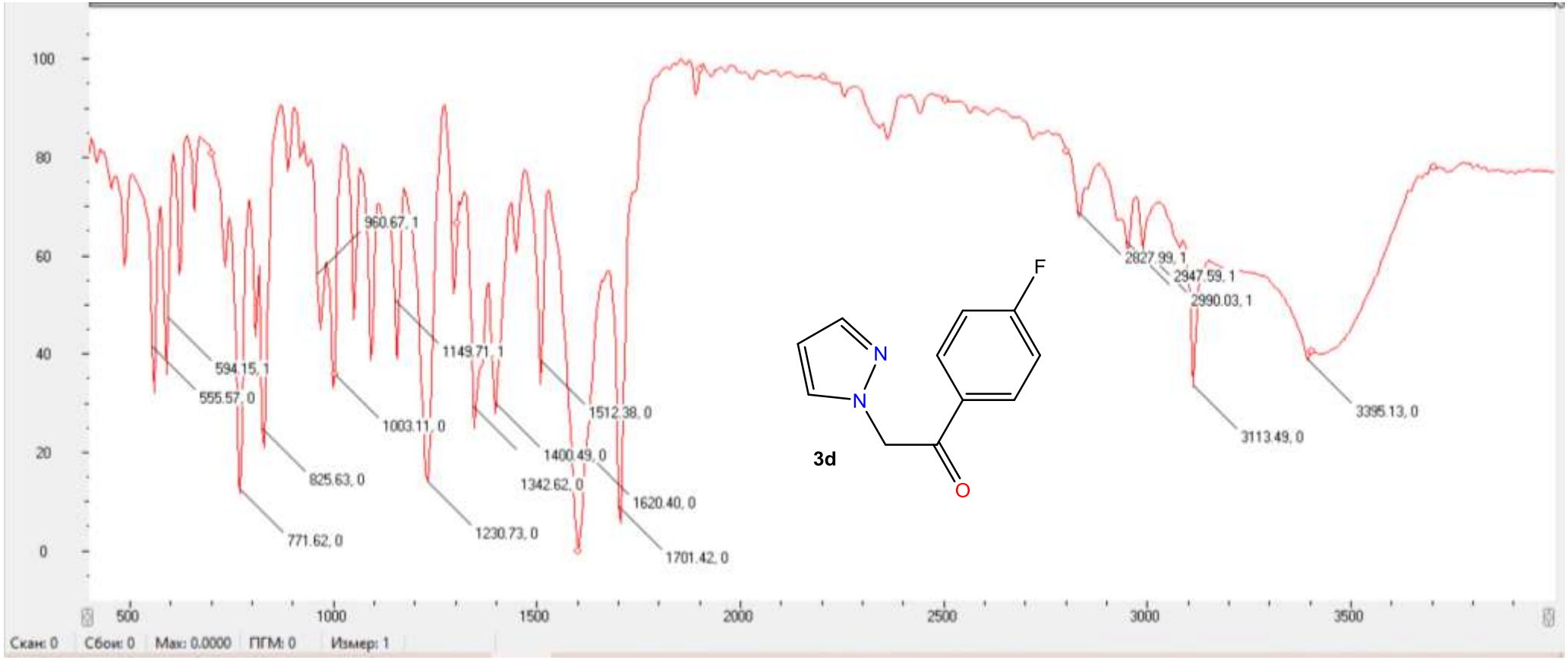



Figure S1. IR spectrum of 1-(4-fluorophenyl)-2-(1H-pyrazol-1-yl)ethan-1-one (**3d**)

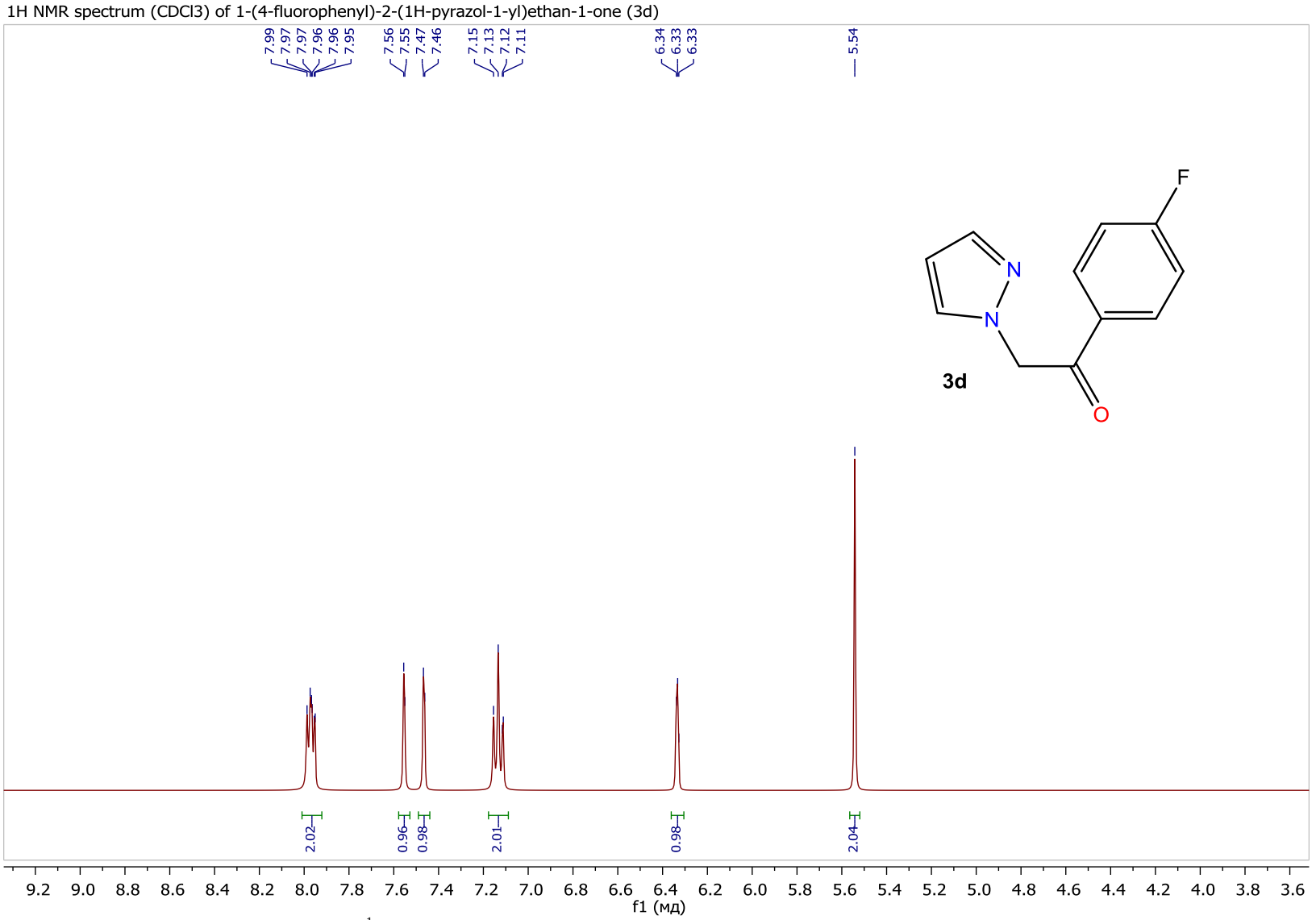



Figure S2. $^{1}$H NMR spectrum of 1-(4-fluorophenyl)-2-(1H-pyrazol-1-yl)ethan-1-one (**3d**)

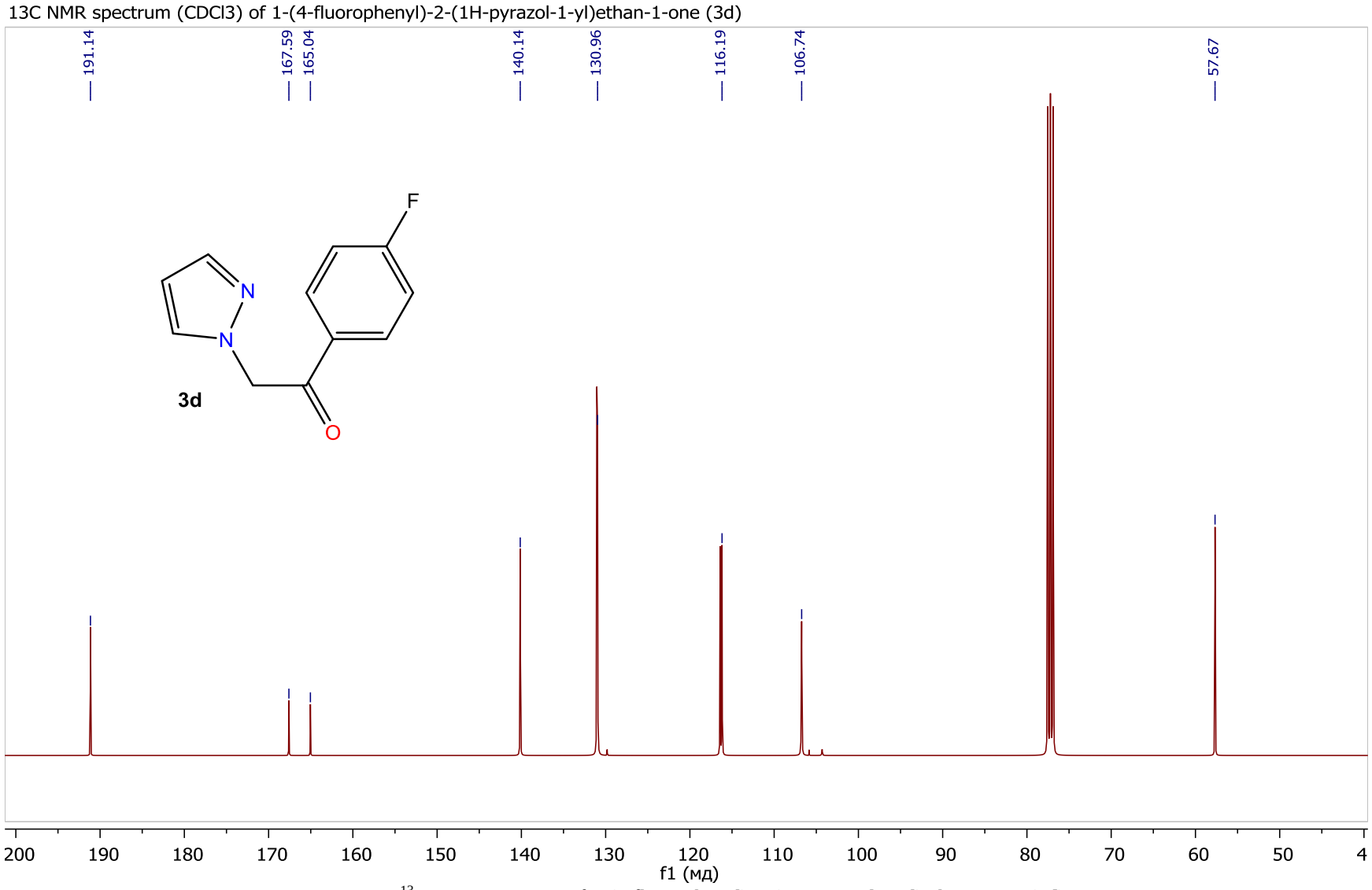



Figure S3. $^{13}$C NMR spectrum of 1-(4-fluorophenyl)-2-(1H-pyrazol-1-yl)ethan-1-one (**3d**)

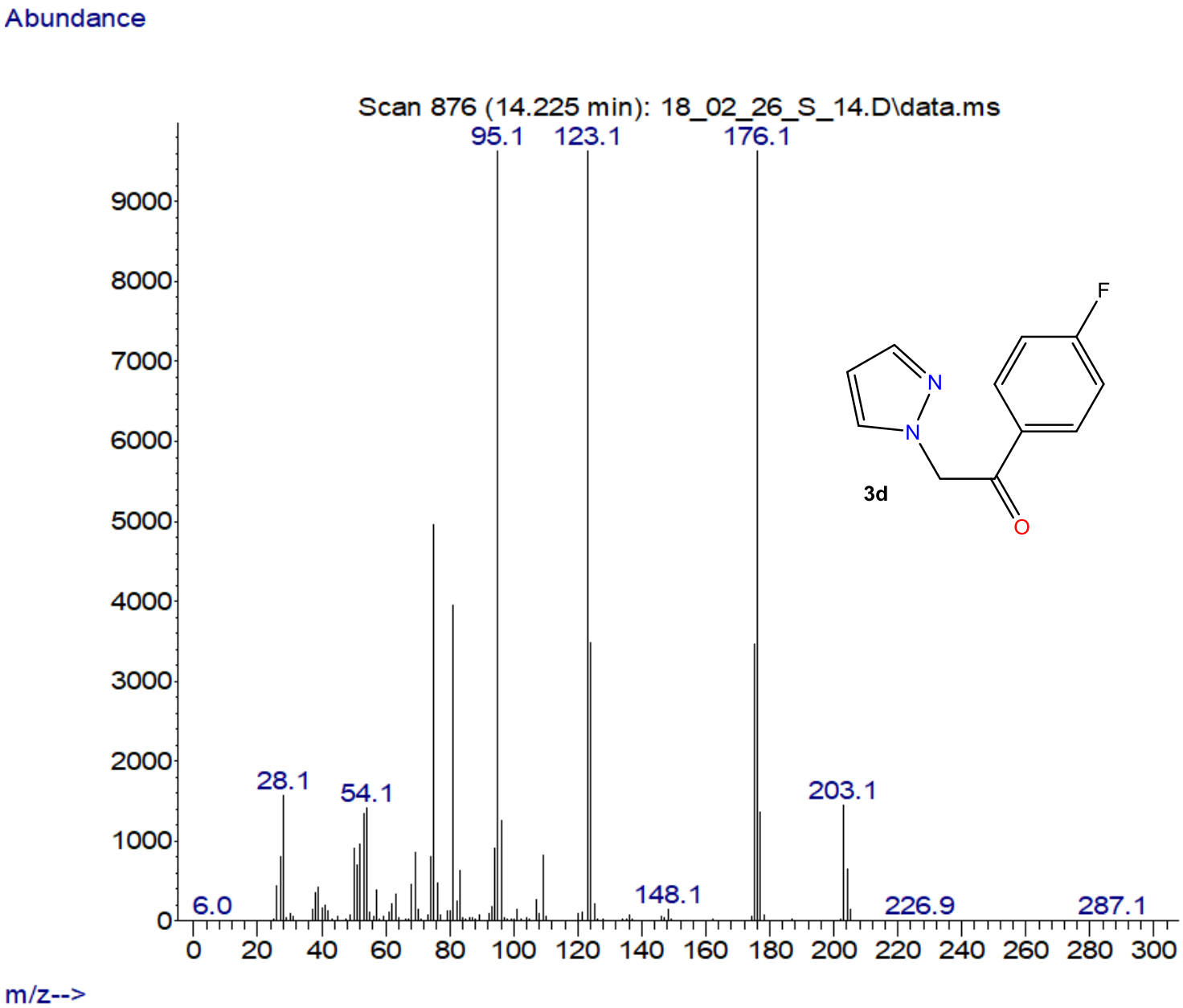



Figure S4. Mass spectrum of 1-(4-fluorophenyl)-2-(1H-pyrazol-1-yl)ethan-1-one (**3d**)

**Spectra of 1-(*tert*-butyl)-2-(3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl)ethan-1-one (8a)**

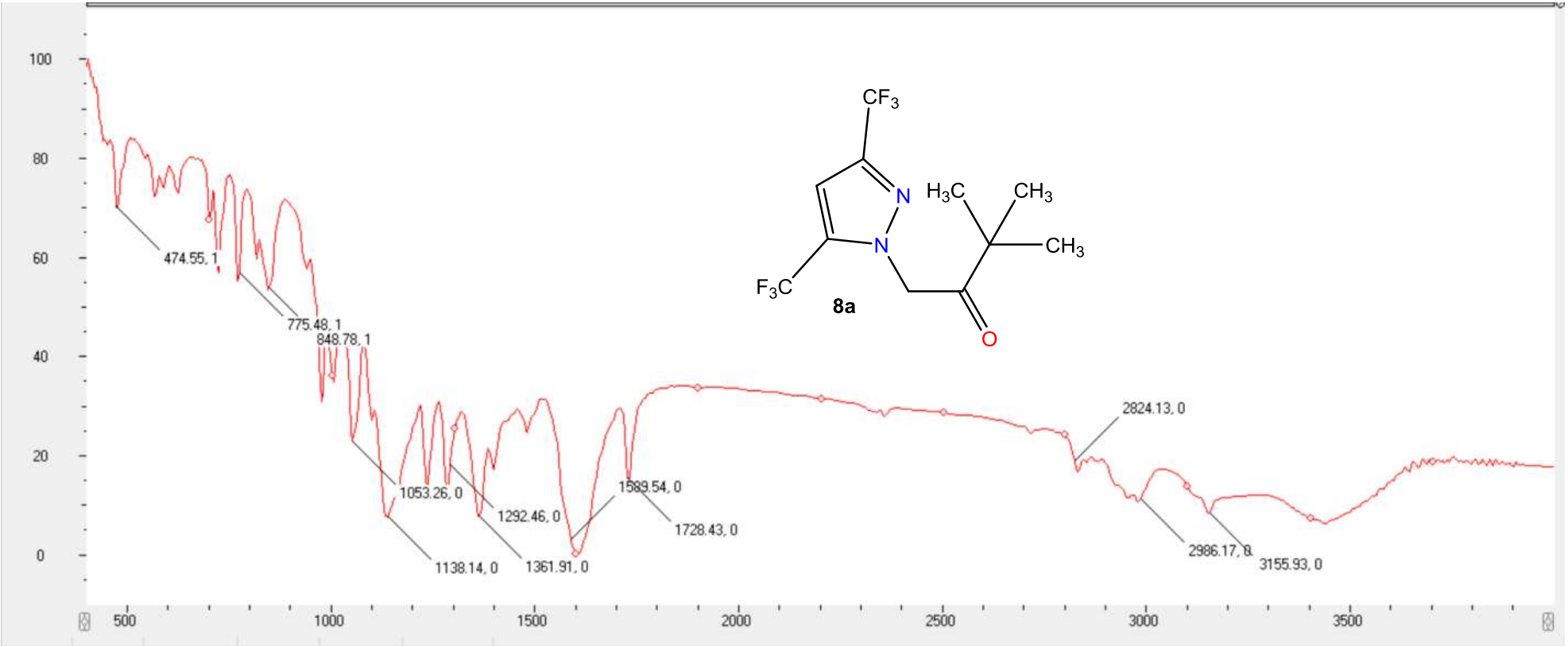



Figure S5. IR spectrum of 1-(tert-butyl)-2-(3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl)ethan-1-one (**8a**)

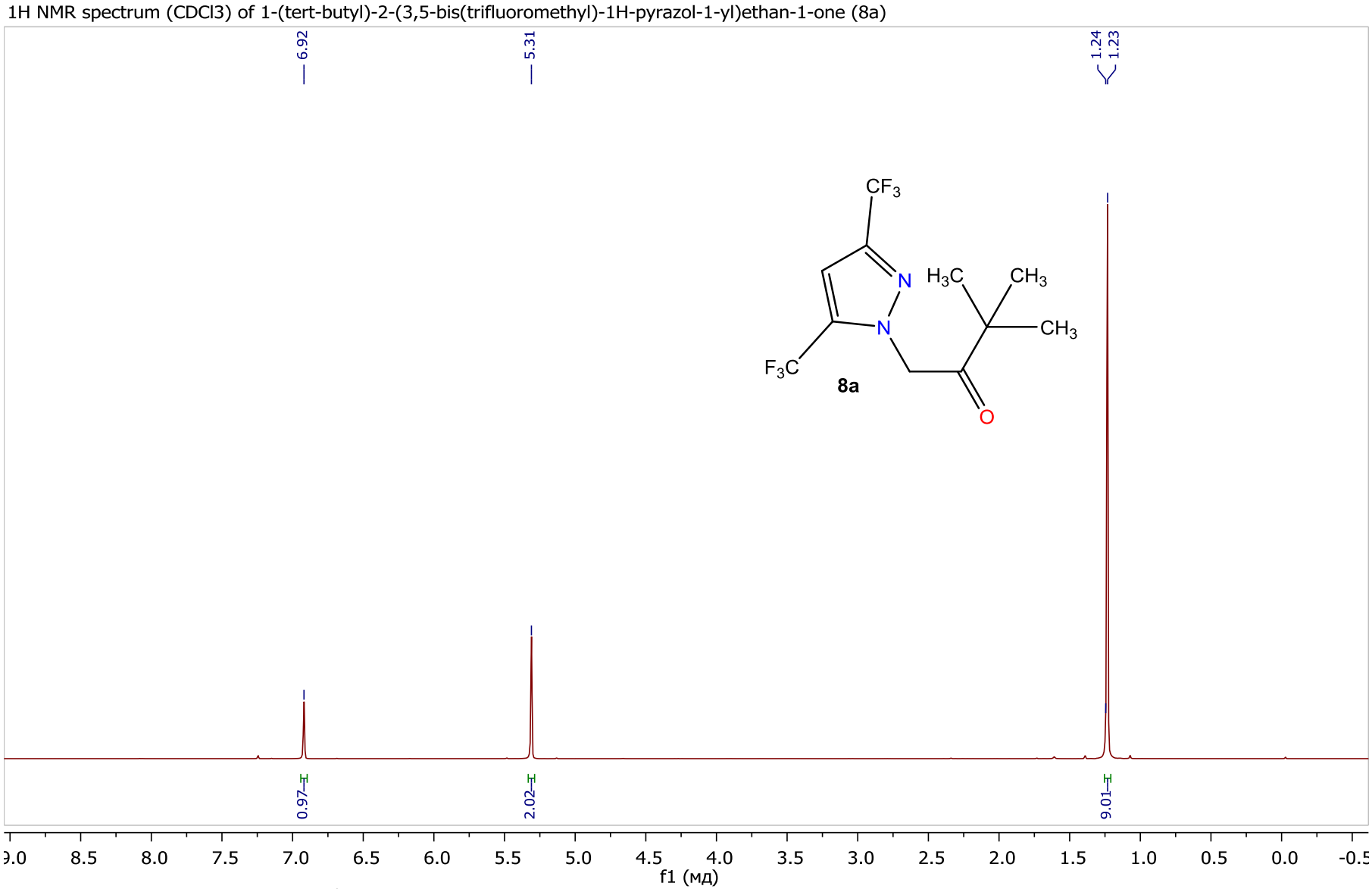



Figure S6. $^{1}$H NMR spectrum of 1-(*tert*-butyl)-2-(3,5-bis(trifluoromethyl))-1H-pyrazol-1-yl)ethan-1-one (**8a**)

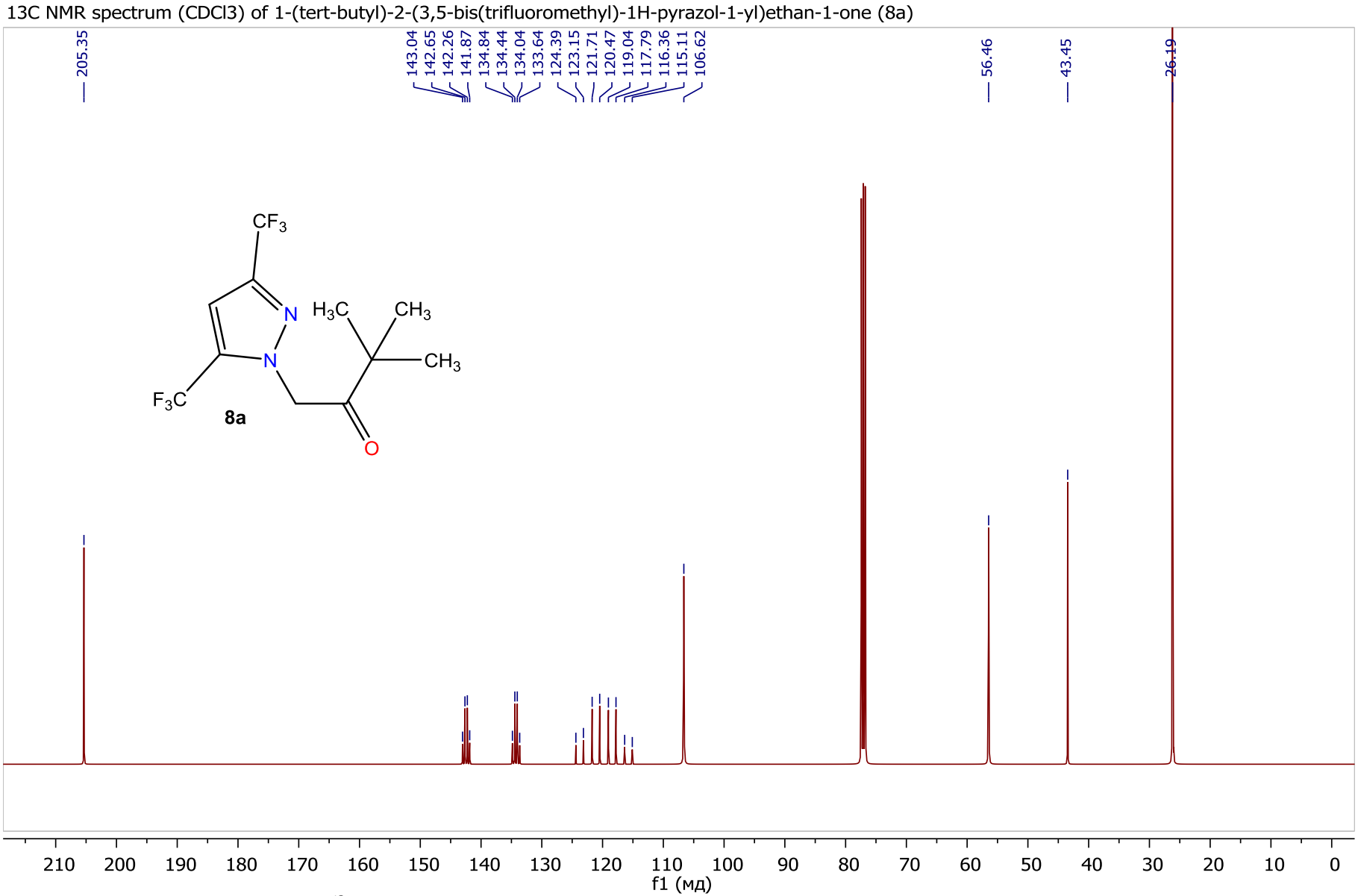



Figure S7. $^{13}$C NMR spectrum of 1-(*tert*-butyl)-2-(3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl)ethan-1-one (**8a**)

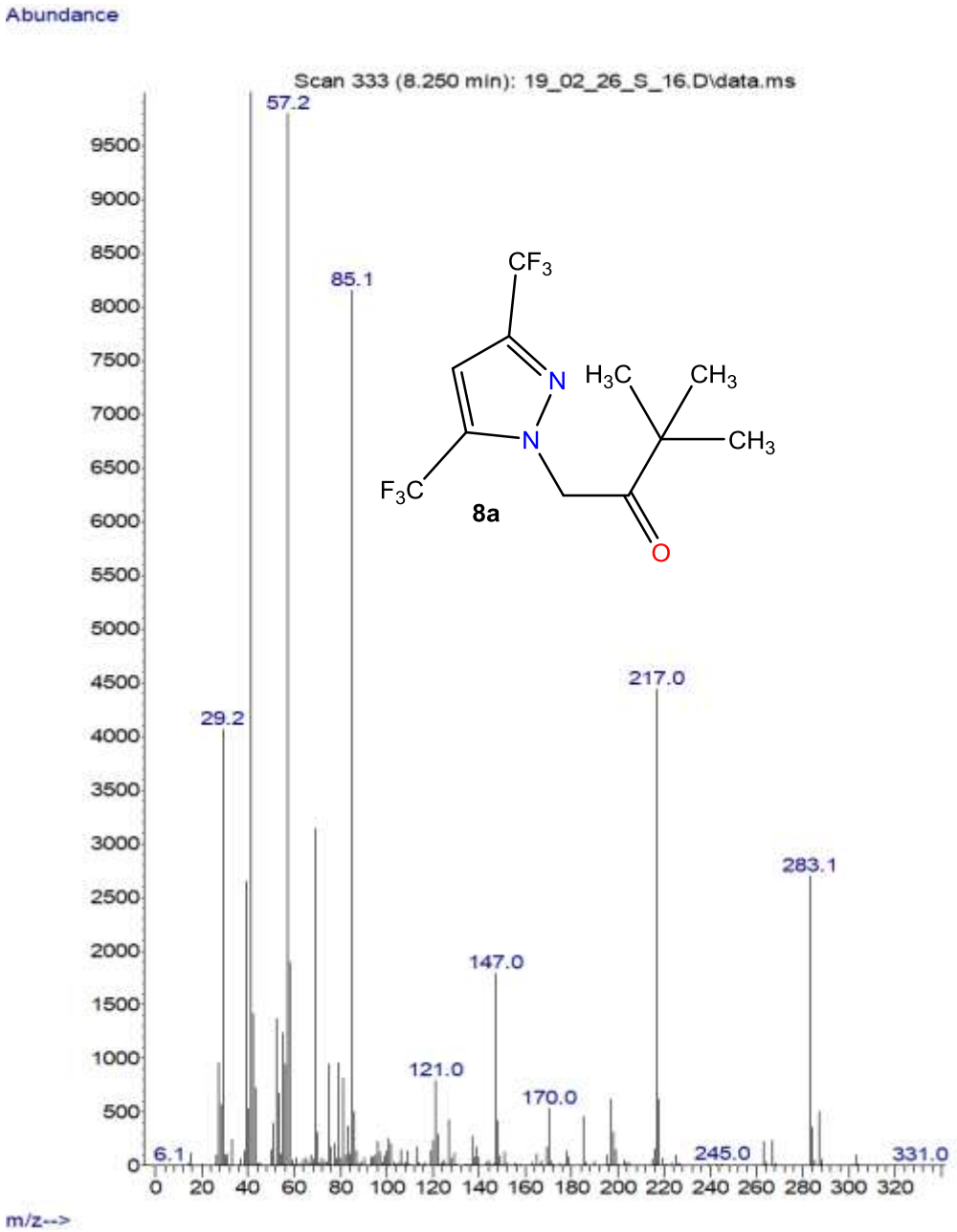



Figure S8. Mass spectrum of 1-(tert-butyl)-2-(3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl)ethan-1-one (**8a**)

**Spectra of 1-phenyl-2-(3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl)ethan-1-one (8b)**

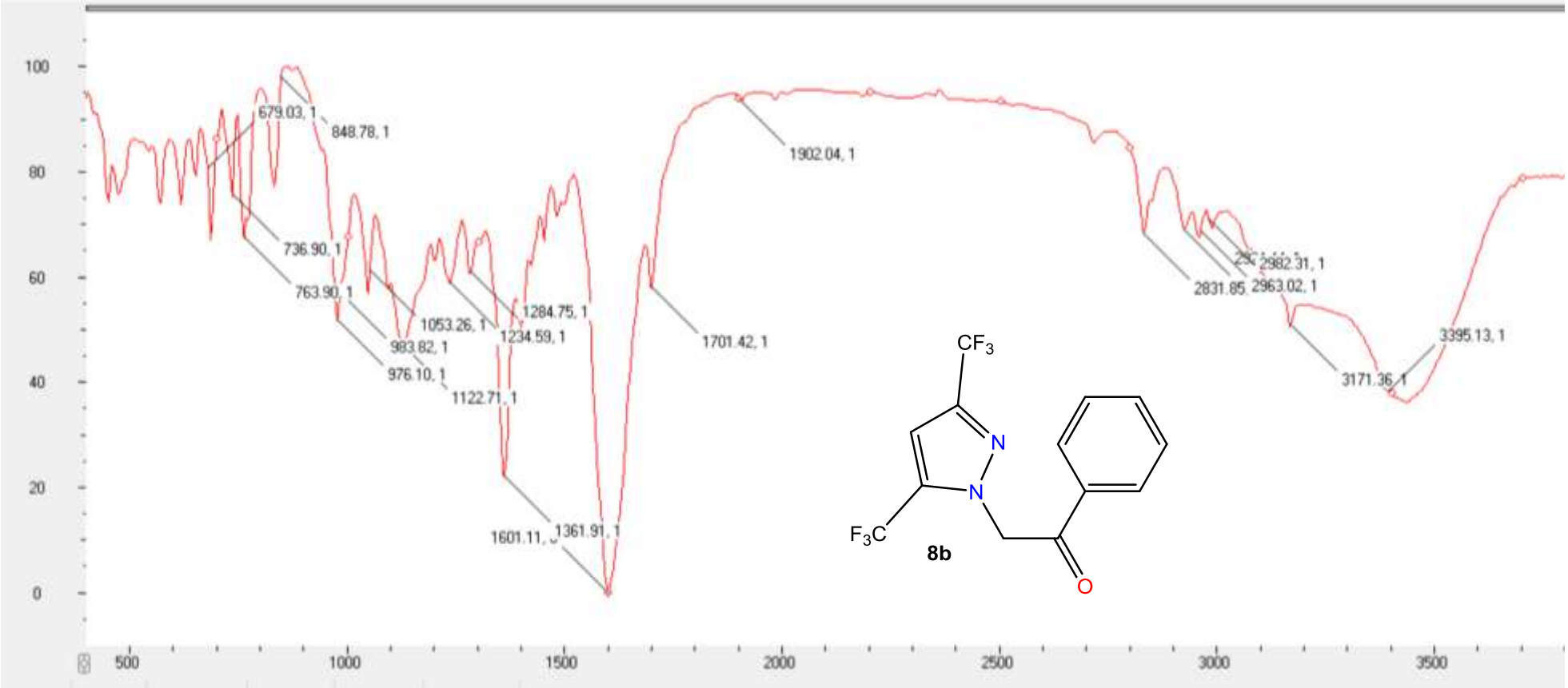



Figure S9. IR spectrum of 1-phenyl-2-(3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl)ethan-1-one (**8b**)

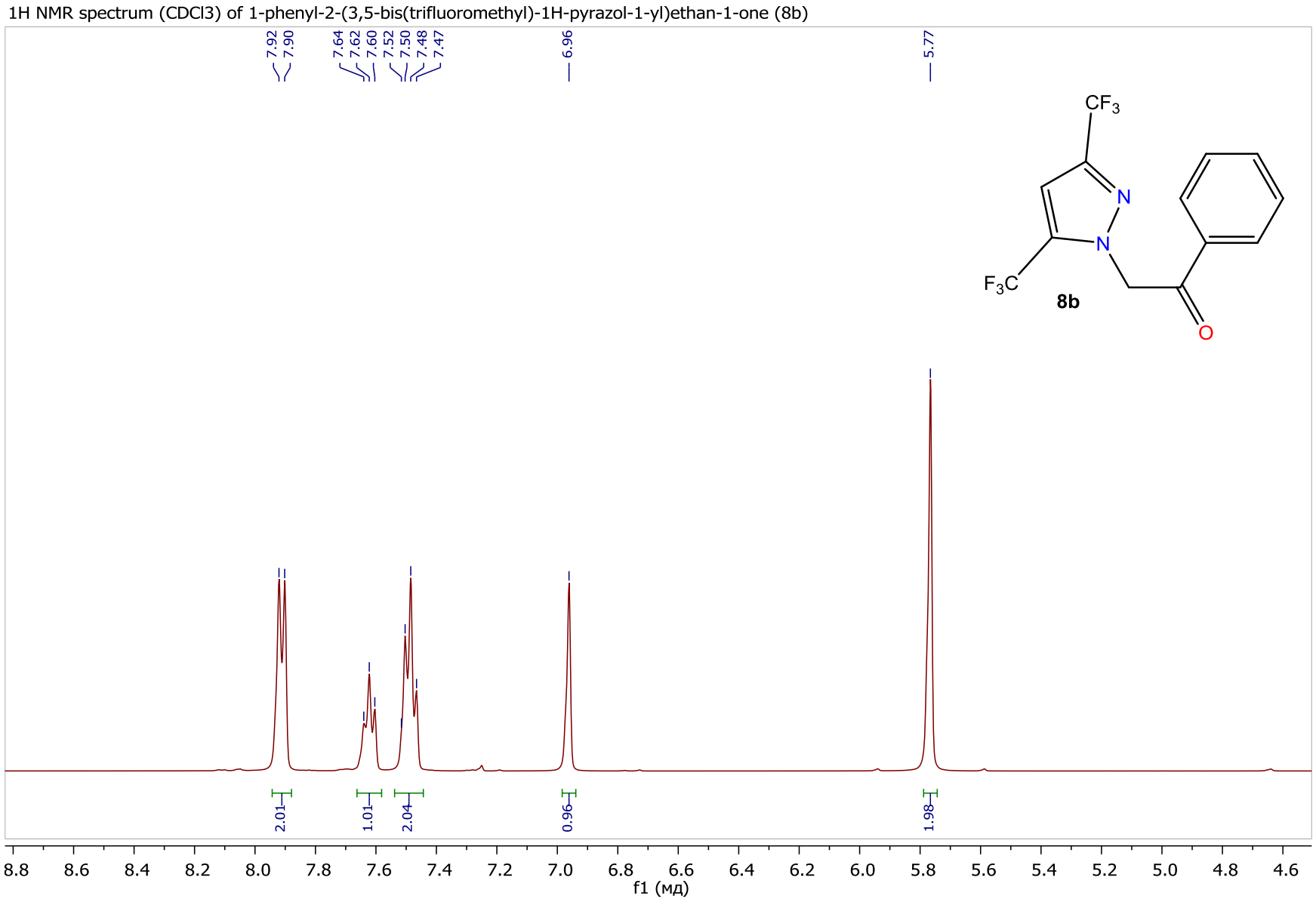



Figure S10. $^{1}$H NMR spectrum of 1-phenyl-2-(3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl)ethan-1-one (**8b**)

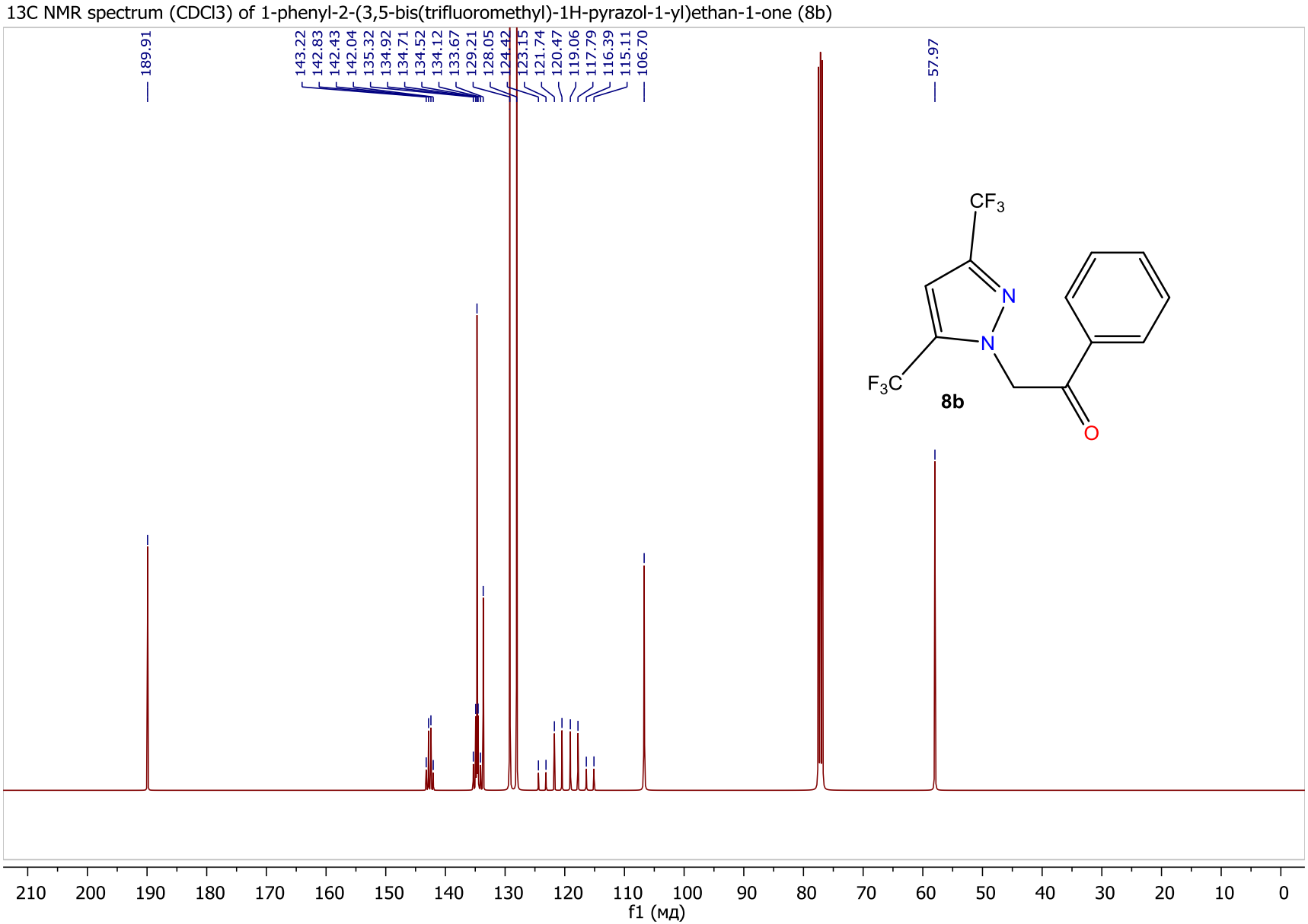



Figure S11. $^{1}$H NMR spectrum of 1-phenyl-2-(3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl)ethan-1-one (**8b**)

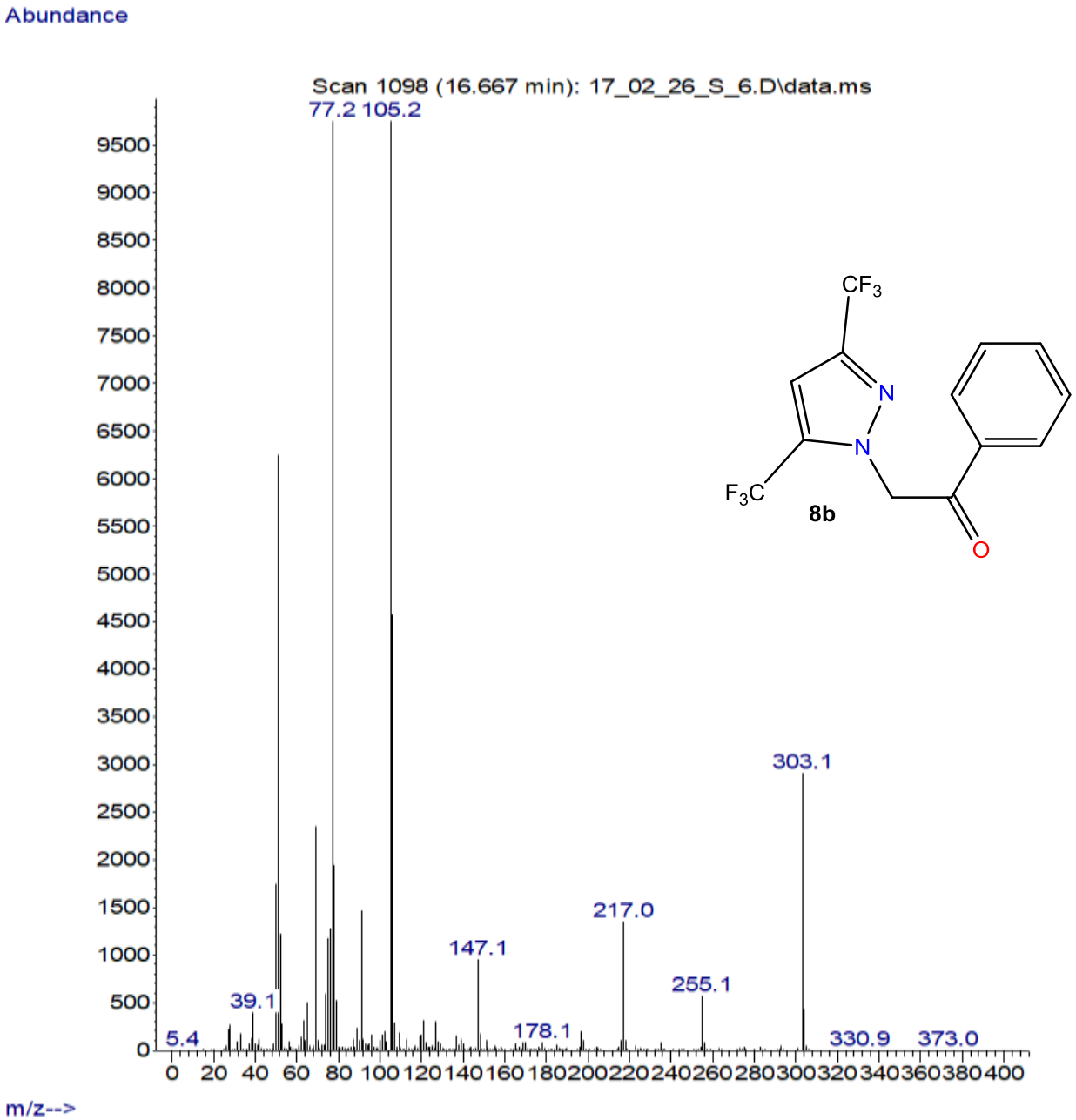



Figure S12. Mass spectrum of 1-phenyl-2-(3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl)ethan-1-one (**8b**)

**Spectra of symmetrical salts of N-acylalkylpyrazole bromide 5a–i, 6a–d**

**Spectra of 1,2-bis(3,3-dimethyl-2-oxobutyl)-1*H*-pyrazol-1-ium bromide (5a)**

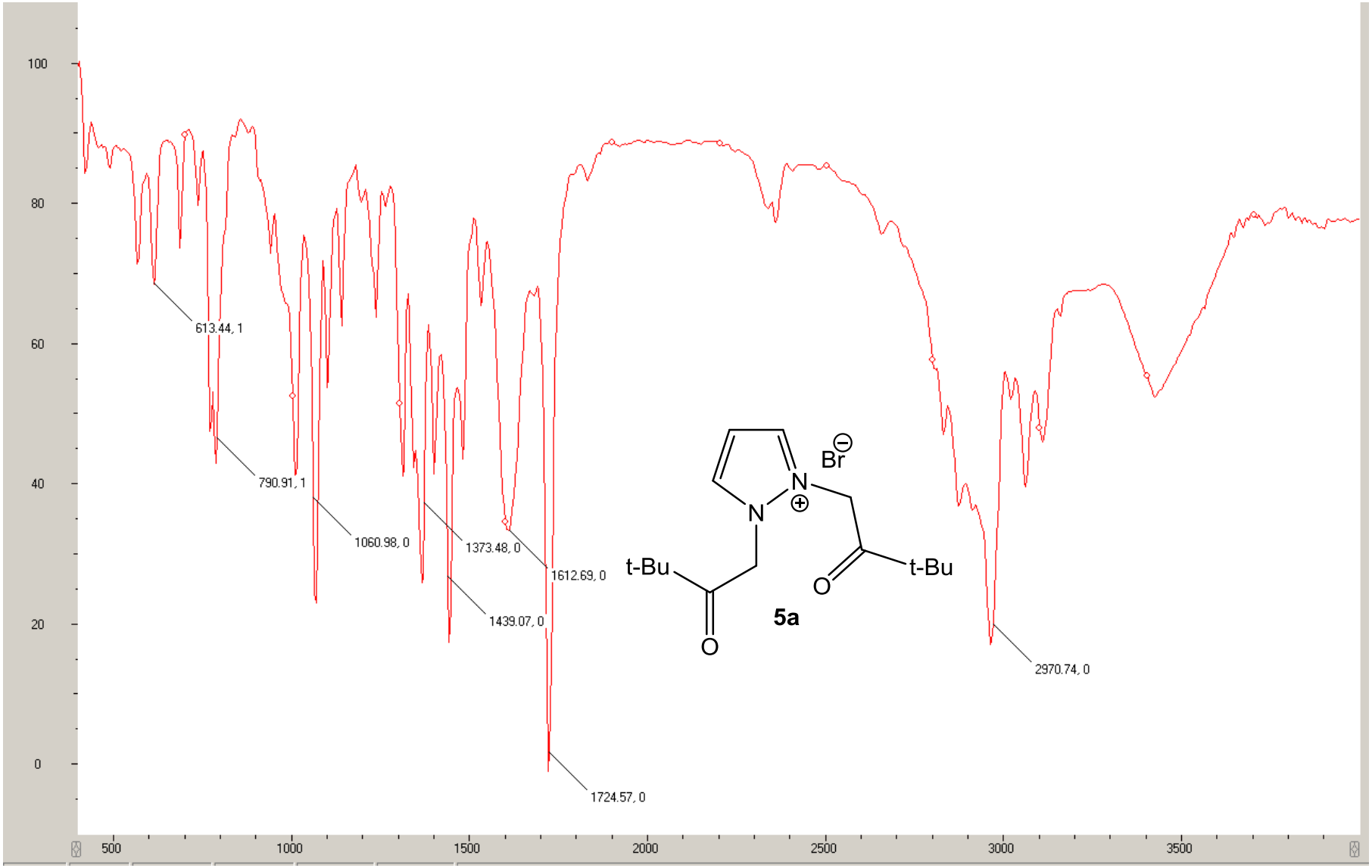



Figure S13. IR spectrum of 1,2-bis(3,3-dimethyl-2-oxobutyl)-1H-pyrazol-1-ium bromide (**5a**)

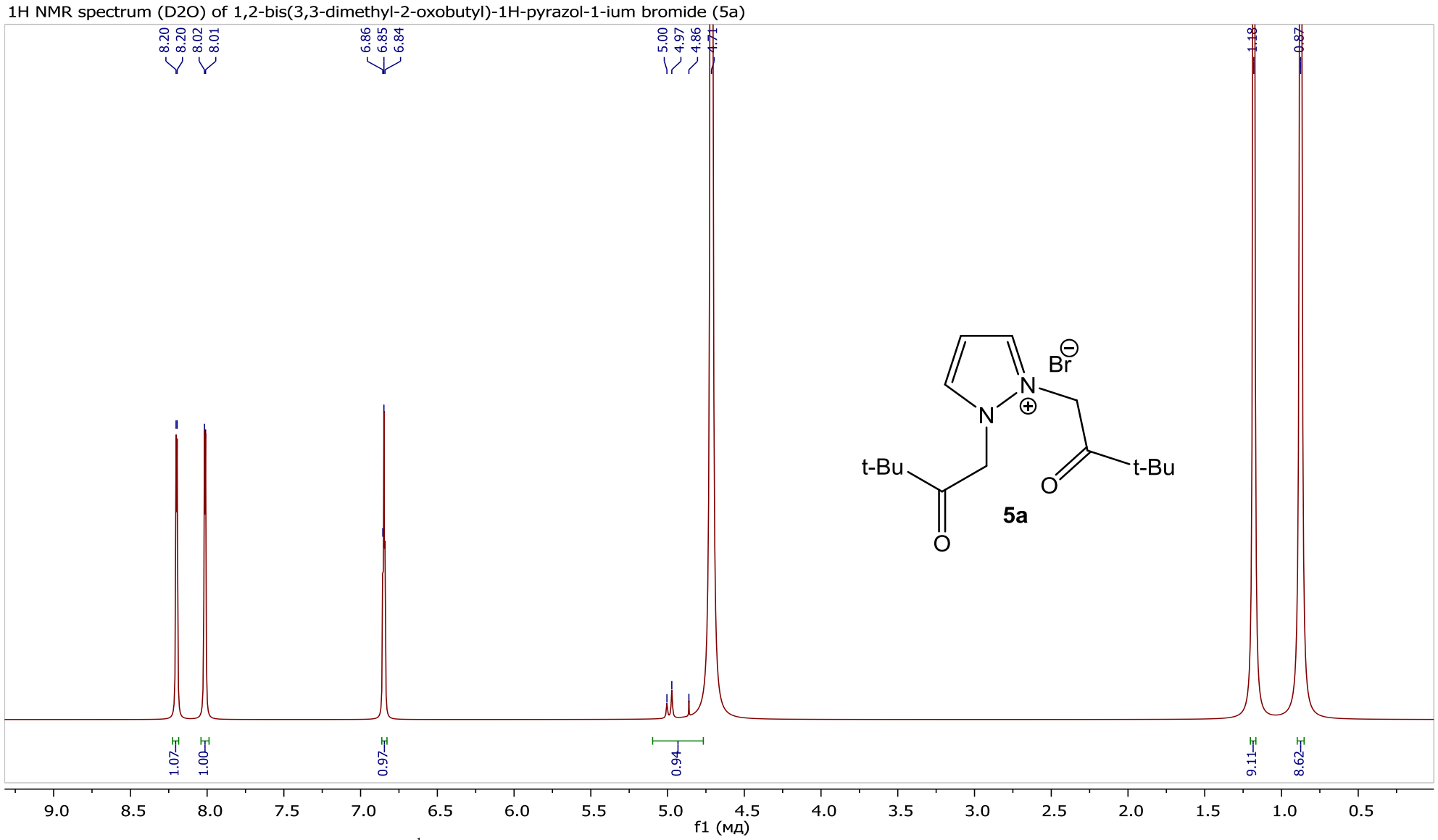



Figure S14. $^{1}$H NMR spectrum of 1,2-bis(3,3-dimethyl-2-oxobutyl)-1*H*-pyrazol-1-ium bromide (**5a**)

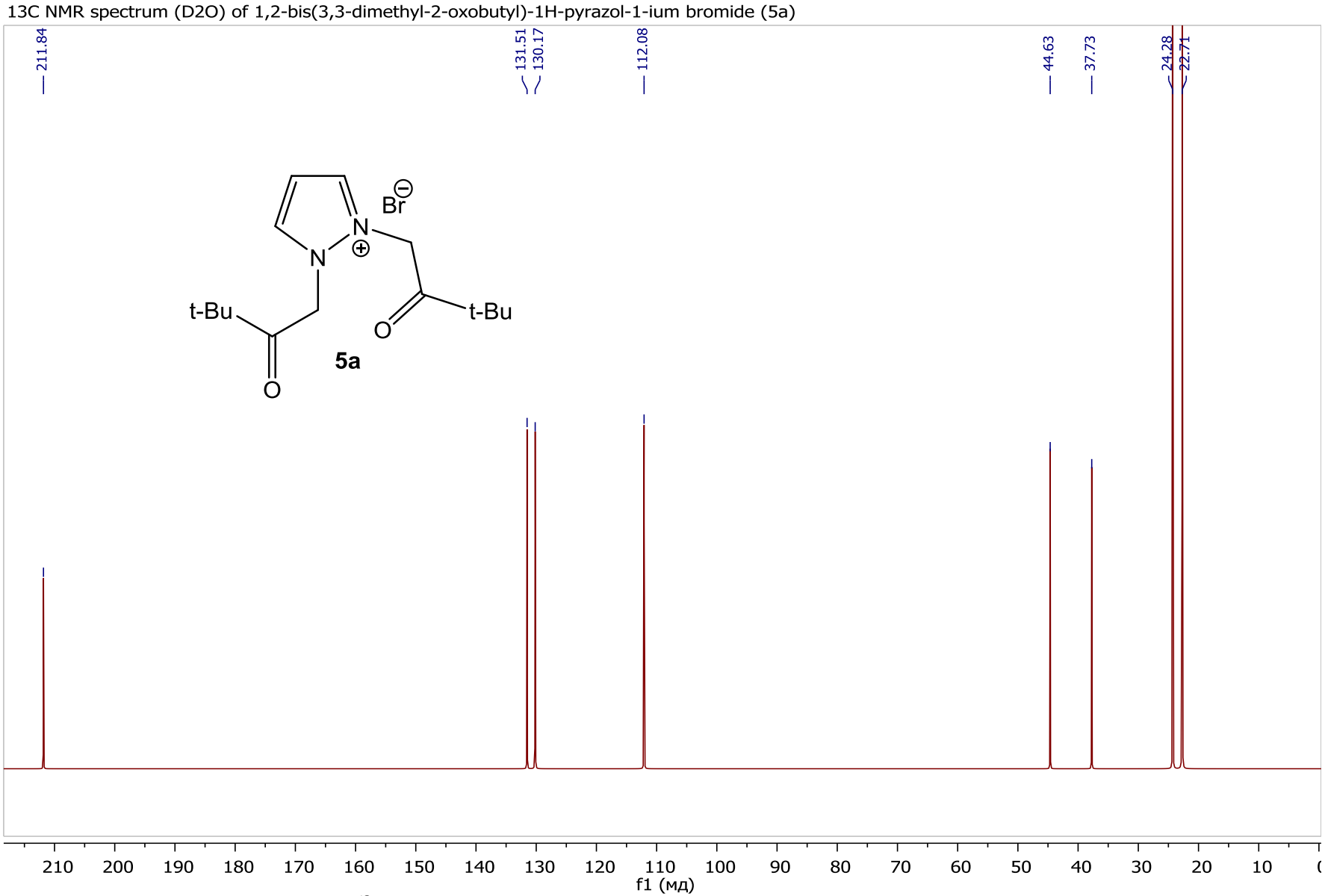



Figure S15. $^{13}$C NMR spectrum of 1,2-bis(3,3-dimethyl-2-oxobutyl)-1H-pyrazol-1-ium bromide (**5a**)

**Spectra of 1,2-bis(2-phenyl-2-oxoethyl)-1H-pyrazol-1-ium bromide (5b)**

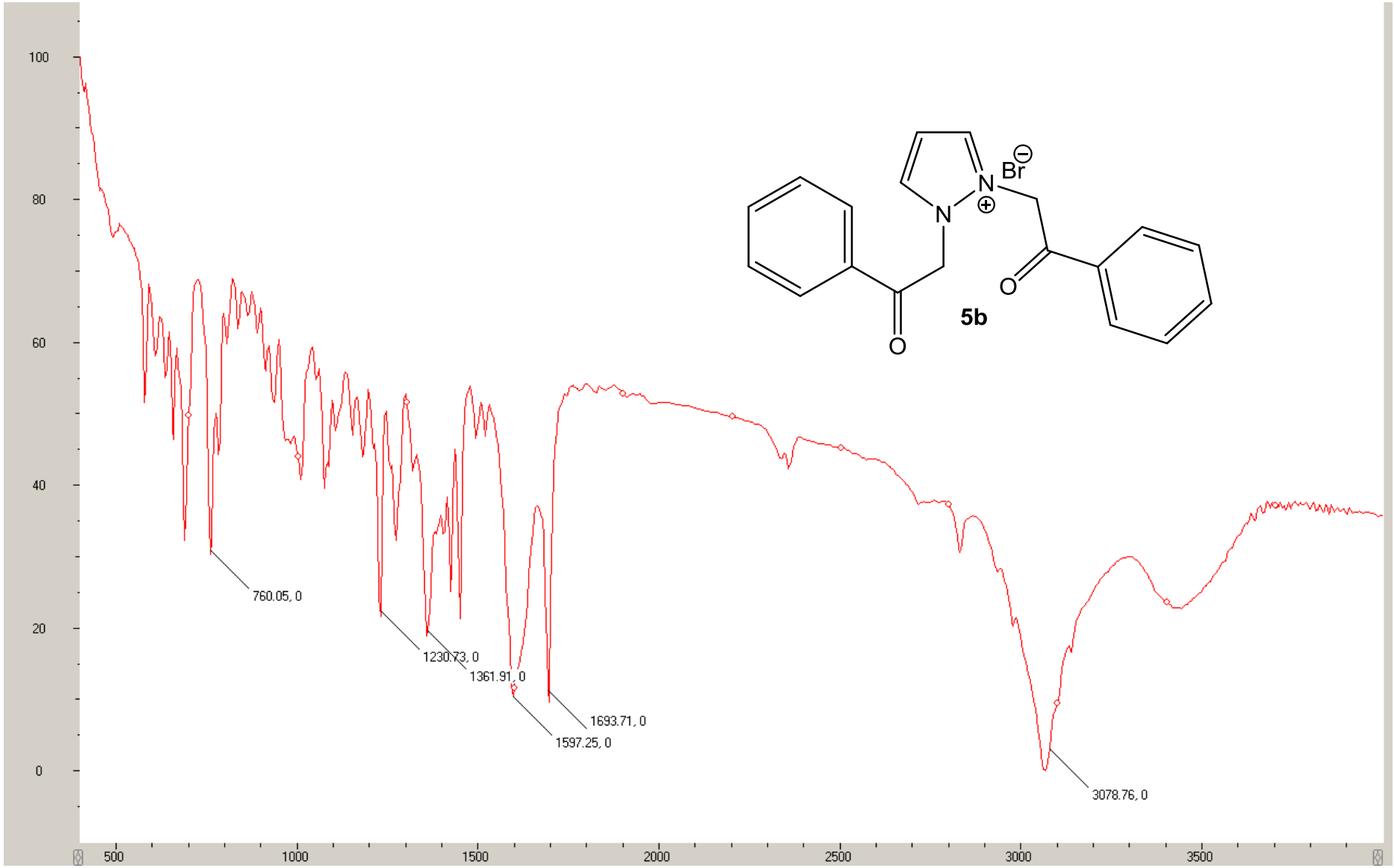



Figure S16. IR spectrum of 1,2-bis(2-phenyl-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5b**)

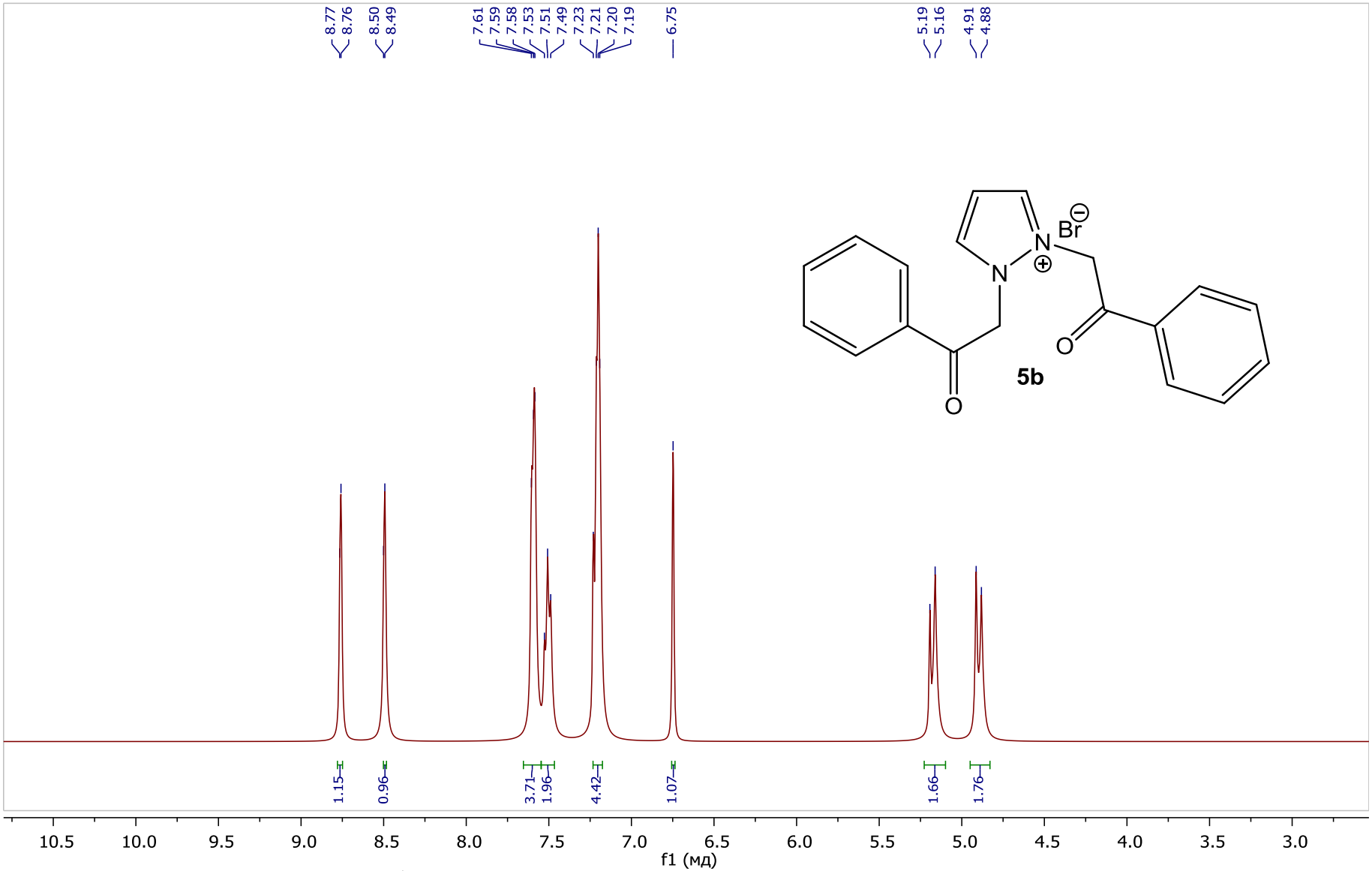



Figure S17. $^{1}$H NMR spectrum of 1,2-bis(2-phenyl-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5b**)

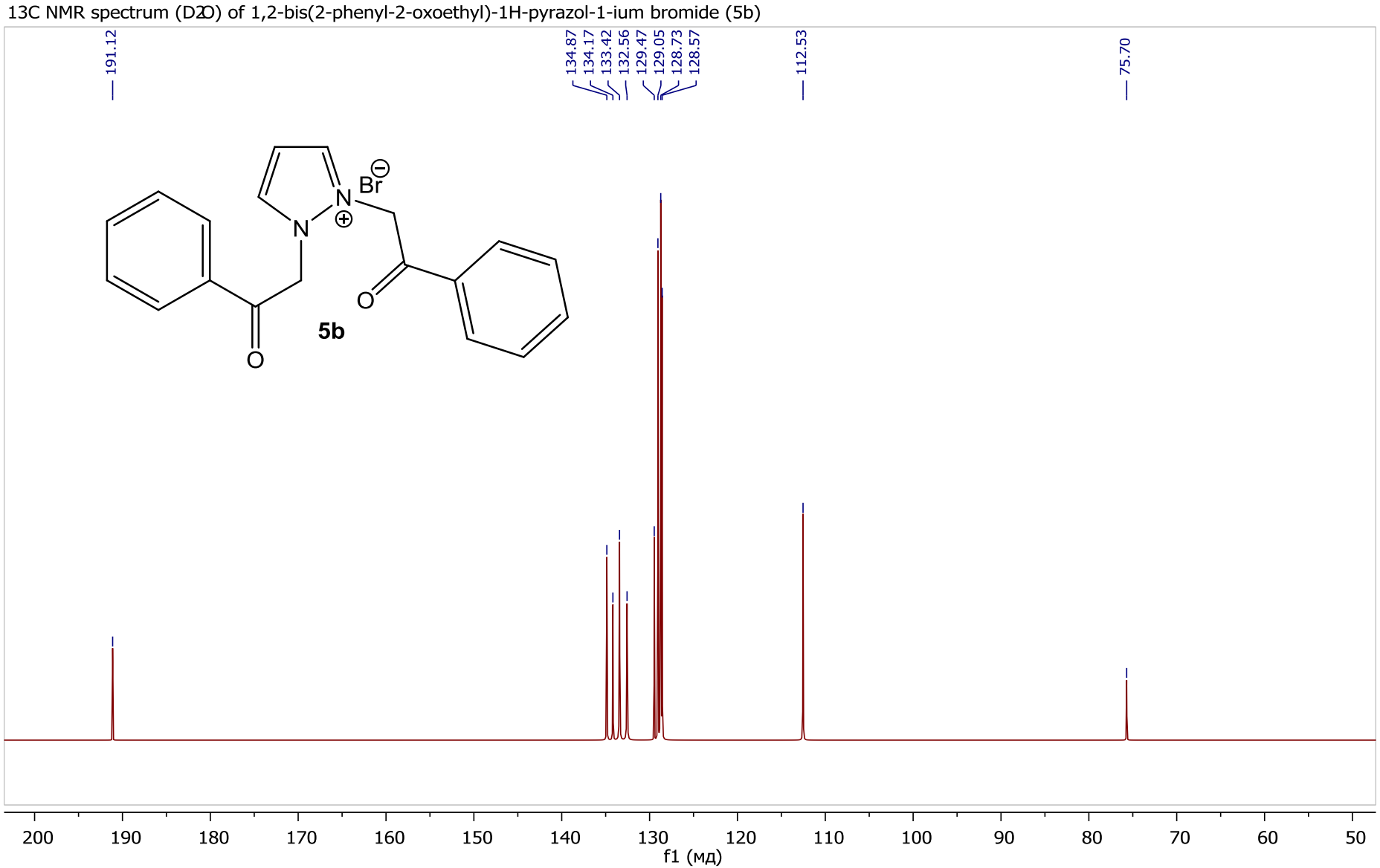



Figure S18. $^{13}$C NMR spectrum of 1,2-bis(2-phenyl-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5b**)

**Spectra of 1,2-bis(2-(4-bromophenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (5c)**

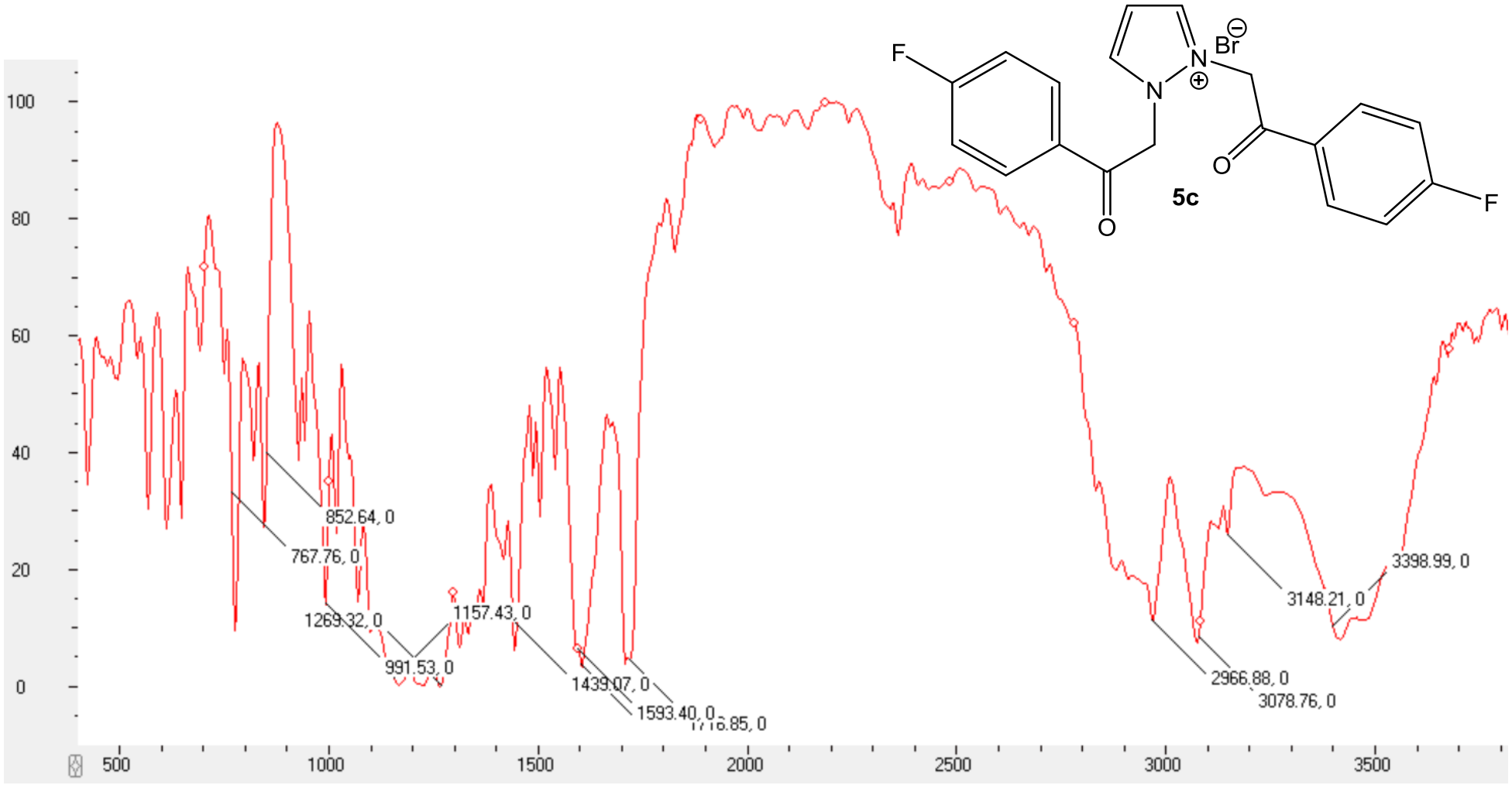



Figure S19. IR spectrum of 1,2-bis(2-(4-bromophenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5c**)

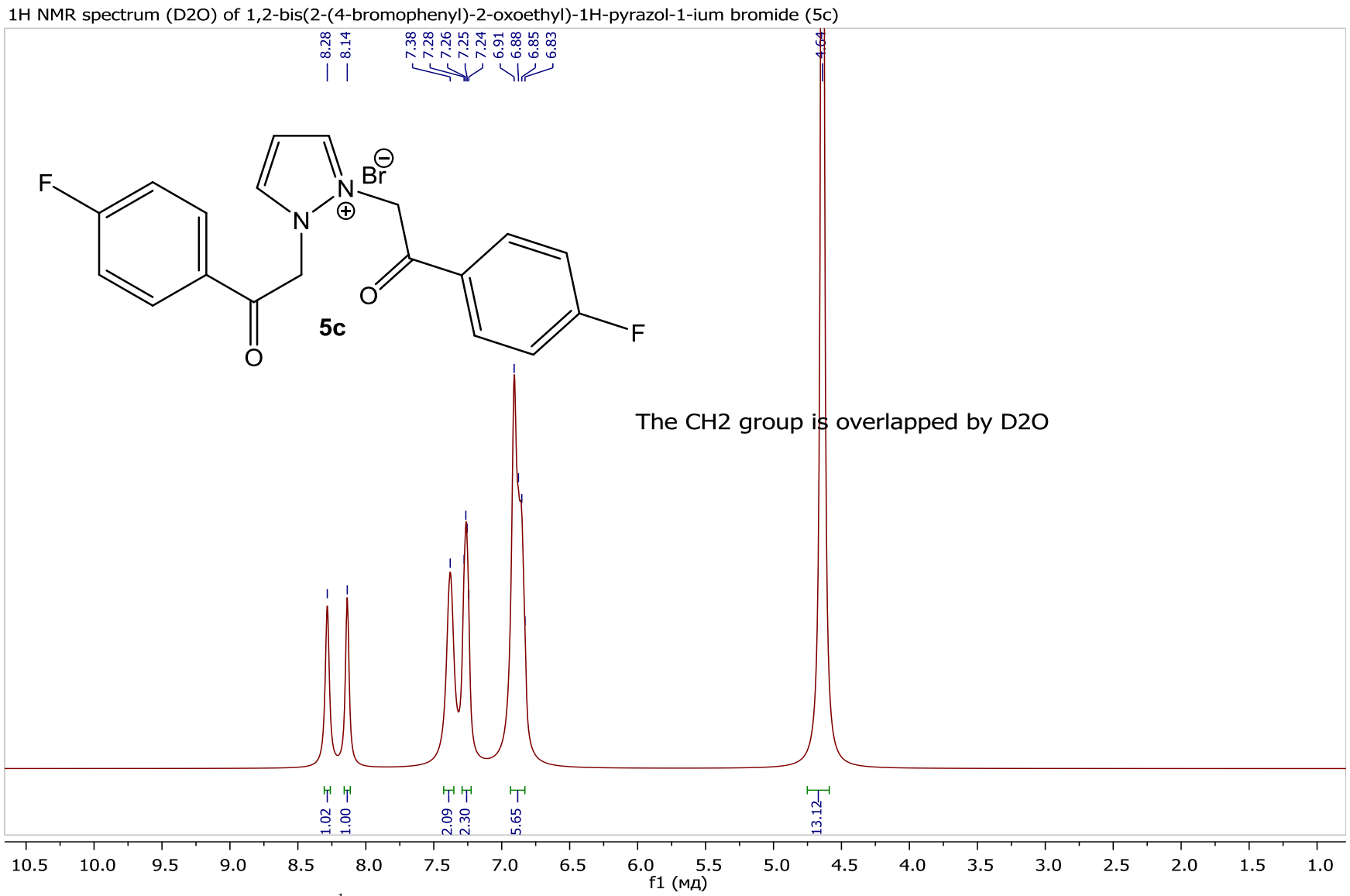



Figure S20. $^{1}$H NMR spectrum of 1,2-bis(2-(4-bromophenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5c**)

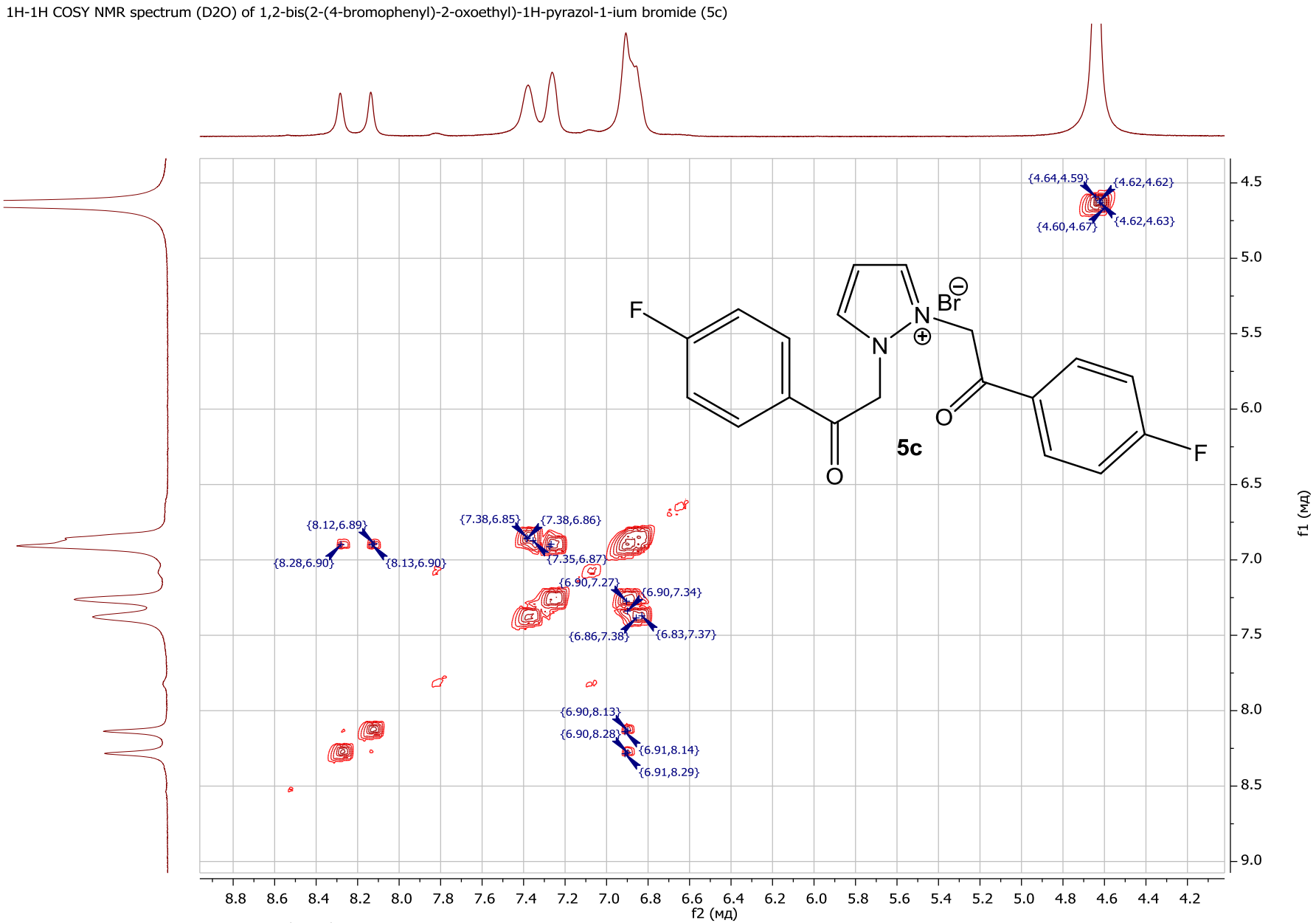



Figure S21. $^{1}$H – $^{1}$H COSY NMR spectrum of 1,2-bis(2-(4-bromophenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5c**)

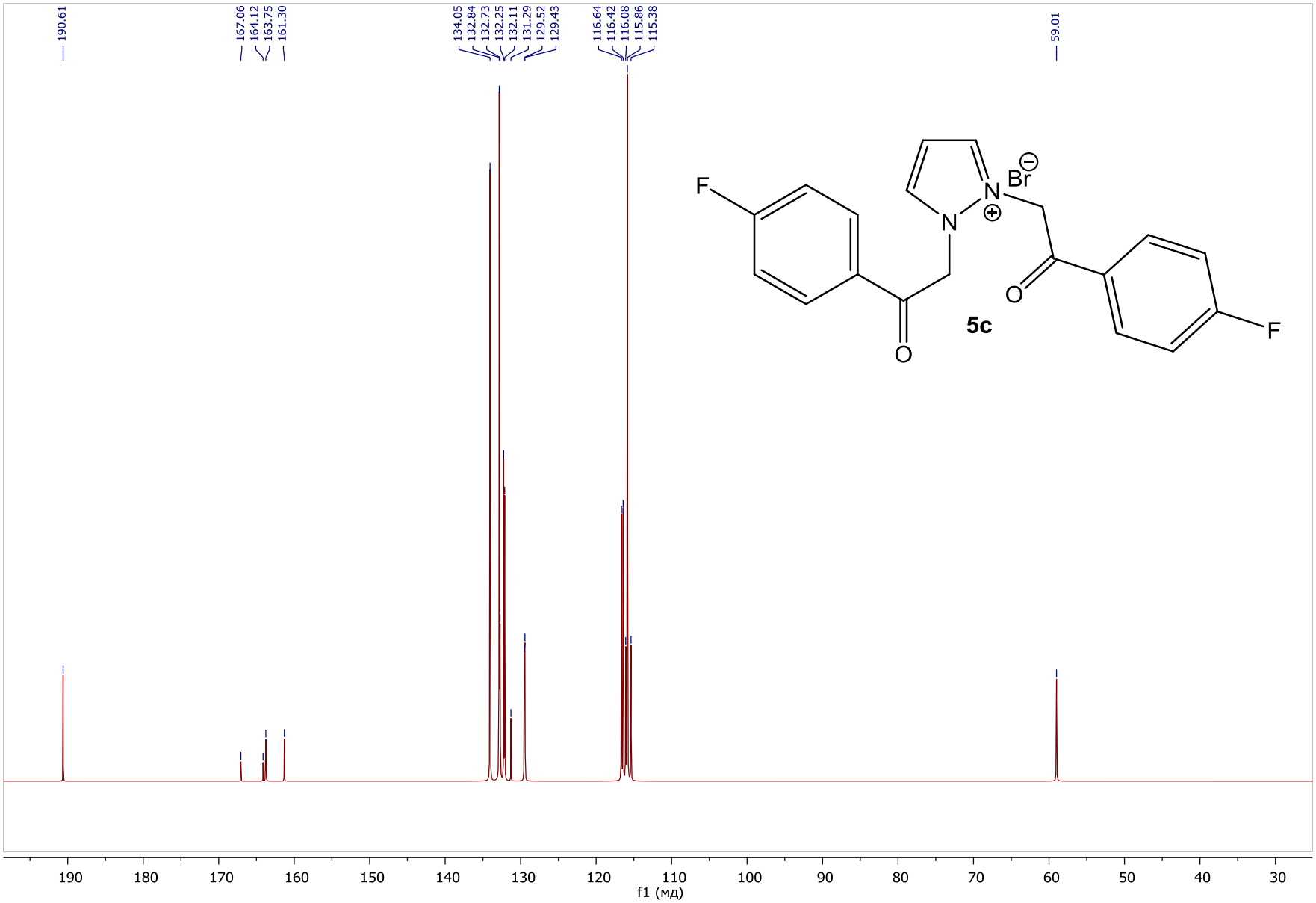



Figure S22. $^{13}$C NMR spectrum of 1,2-bis(2-(4-bromophenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5c**)

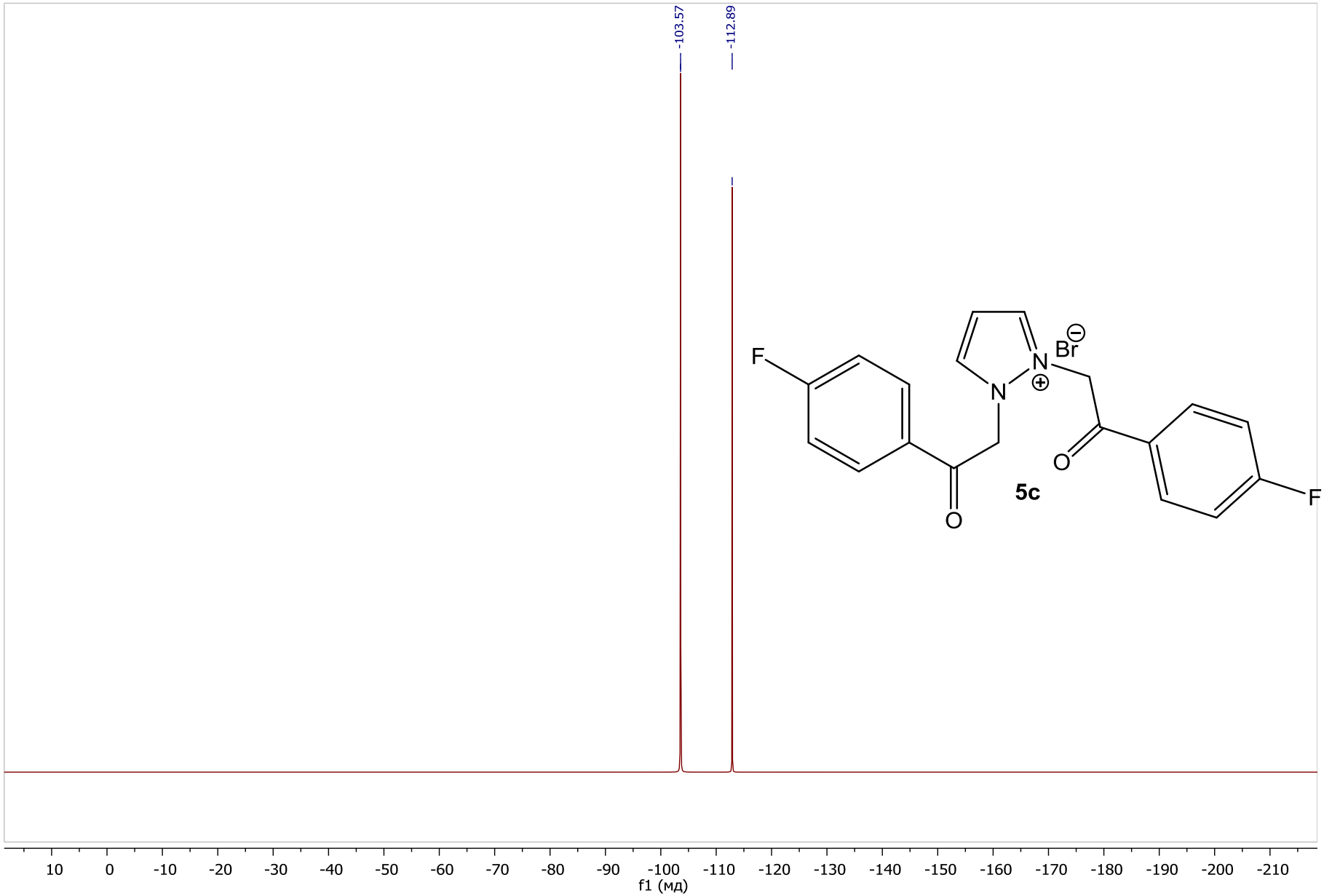



Figure S23. $^{19}$F NMR spectrum of 1,2-bis(2-(4-bromophenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5c**)

**Spectra of 1,2-bis(2-(4-nitrophenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (5d)**

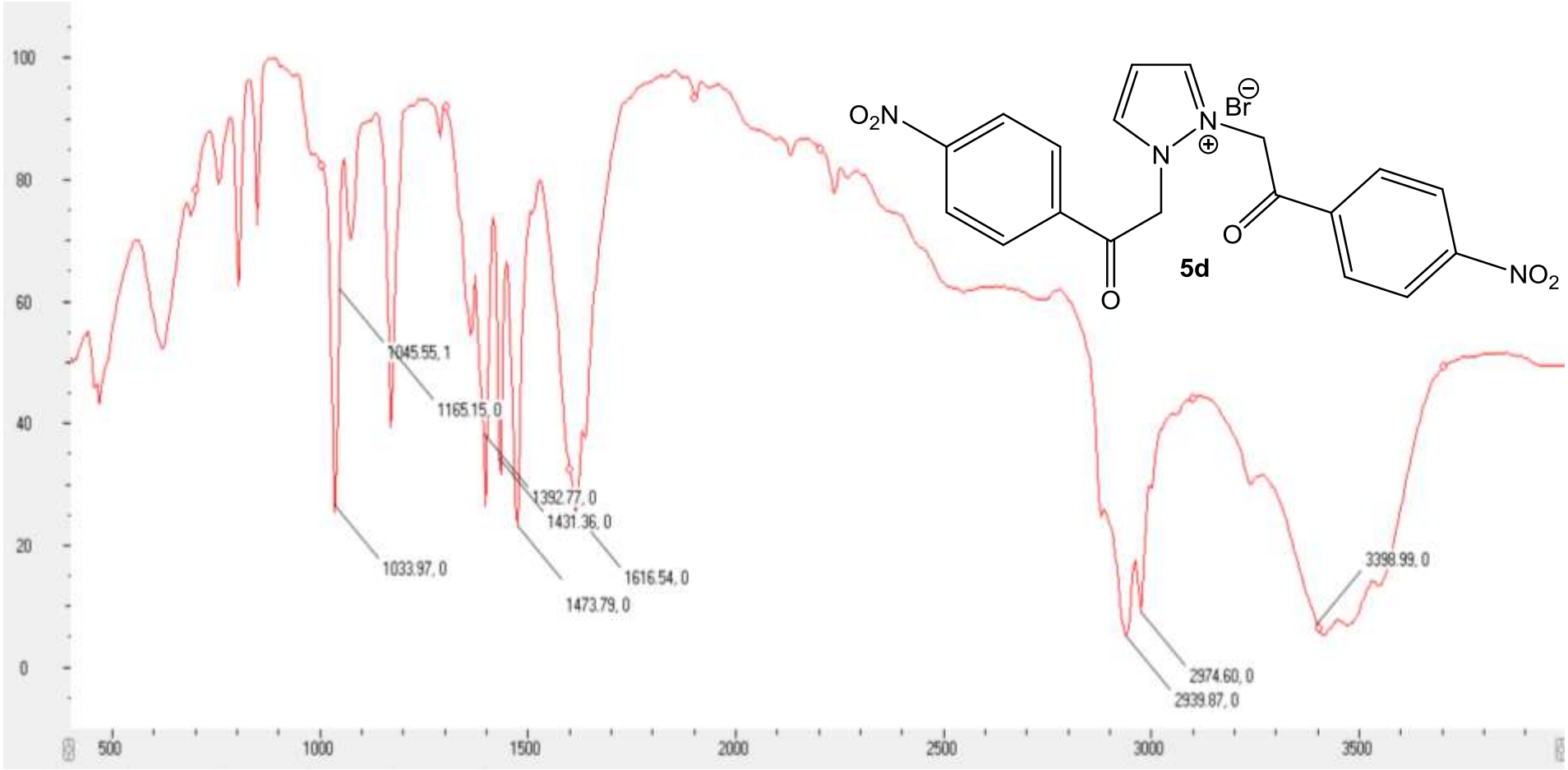



Figure S24. IR spectrum of 1,2-bis(2-(4-nitrophenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5d**)

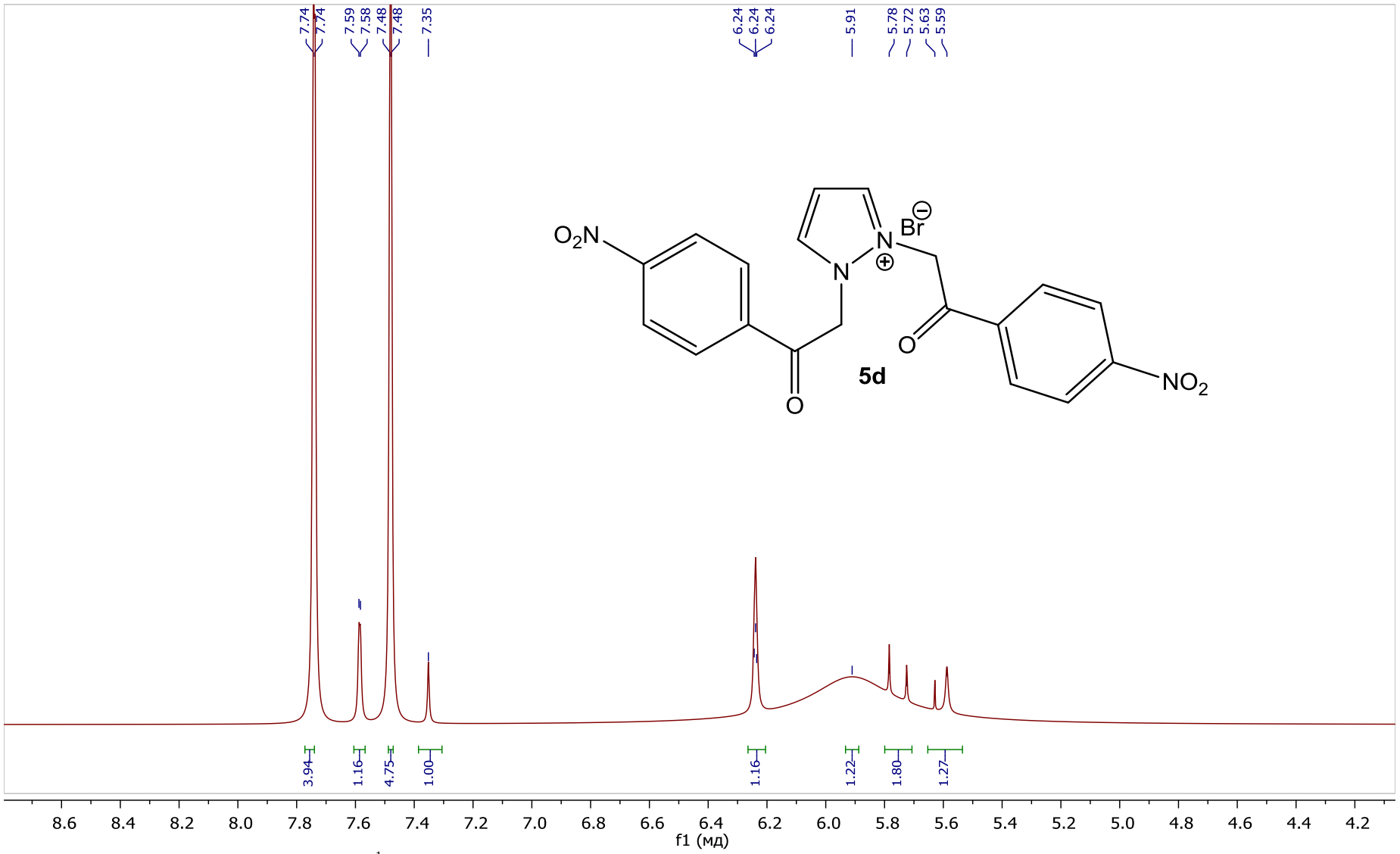



Figure S25. $^{1}$H NMR spectrum of 1,2-bis(2-(4-nitrophenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5d**)

**Spectra of 1-(3,3-dimethyl-2-oxobutyl)-2-(2-(4-(trifluoromethoxy)phenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (5e)**

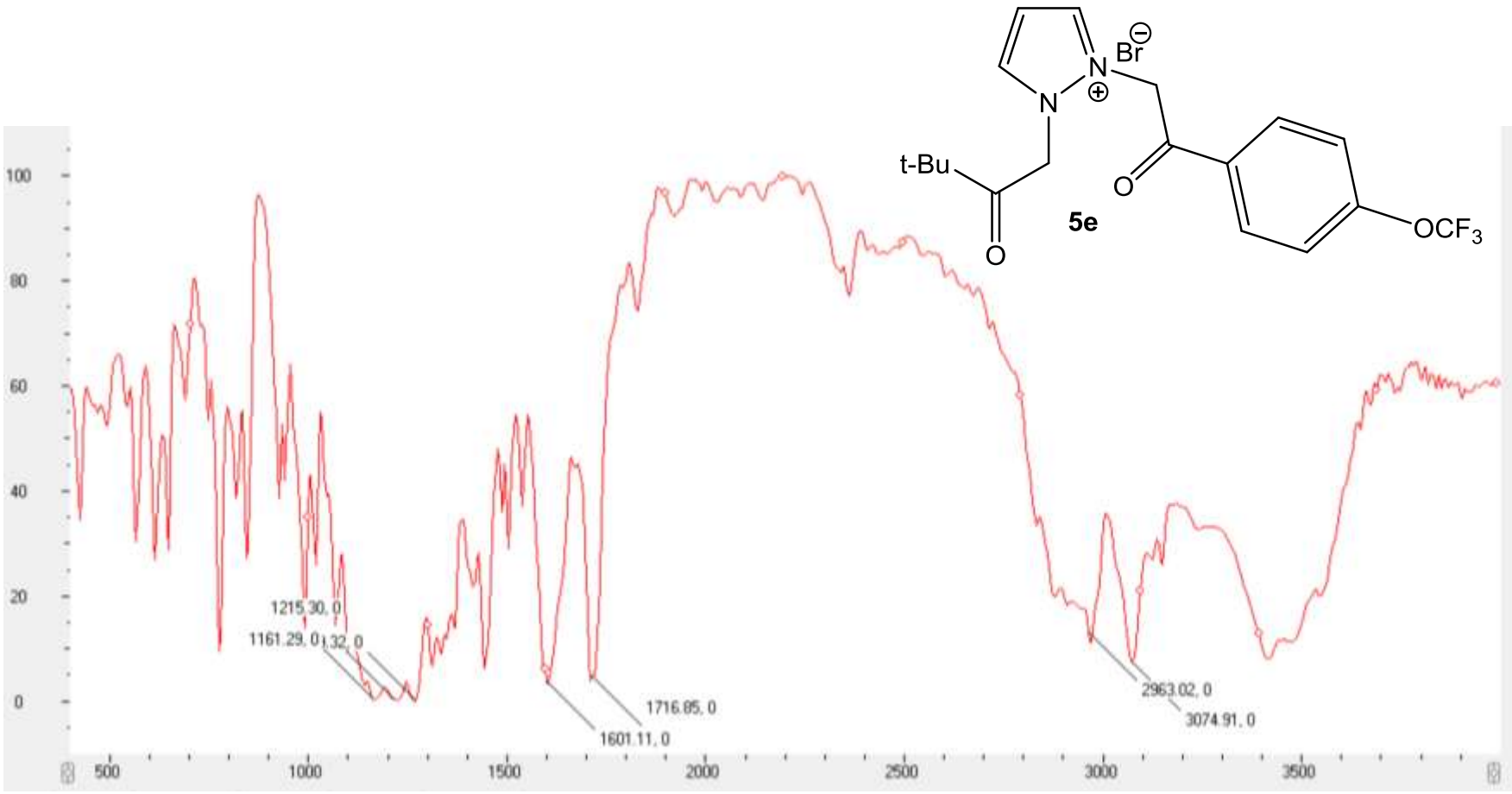



Figure S26. IR spectrum of 1-(3,3-dimethyl-2-oxobutyl)-2-(2-(4-(trifluoromethoxy)phenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5e**)

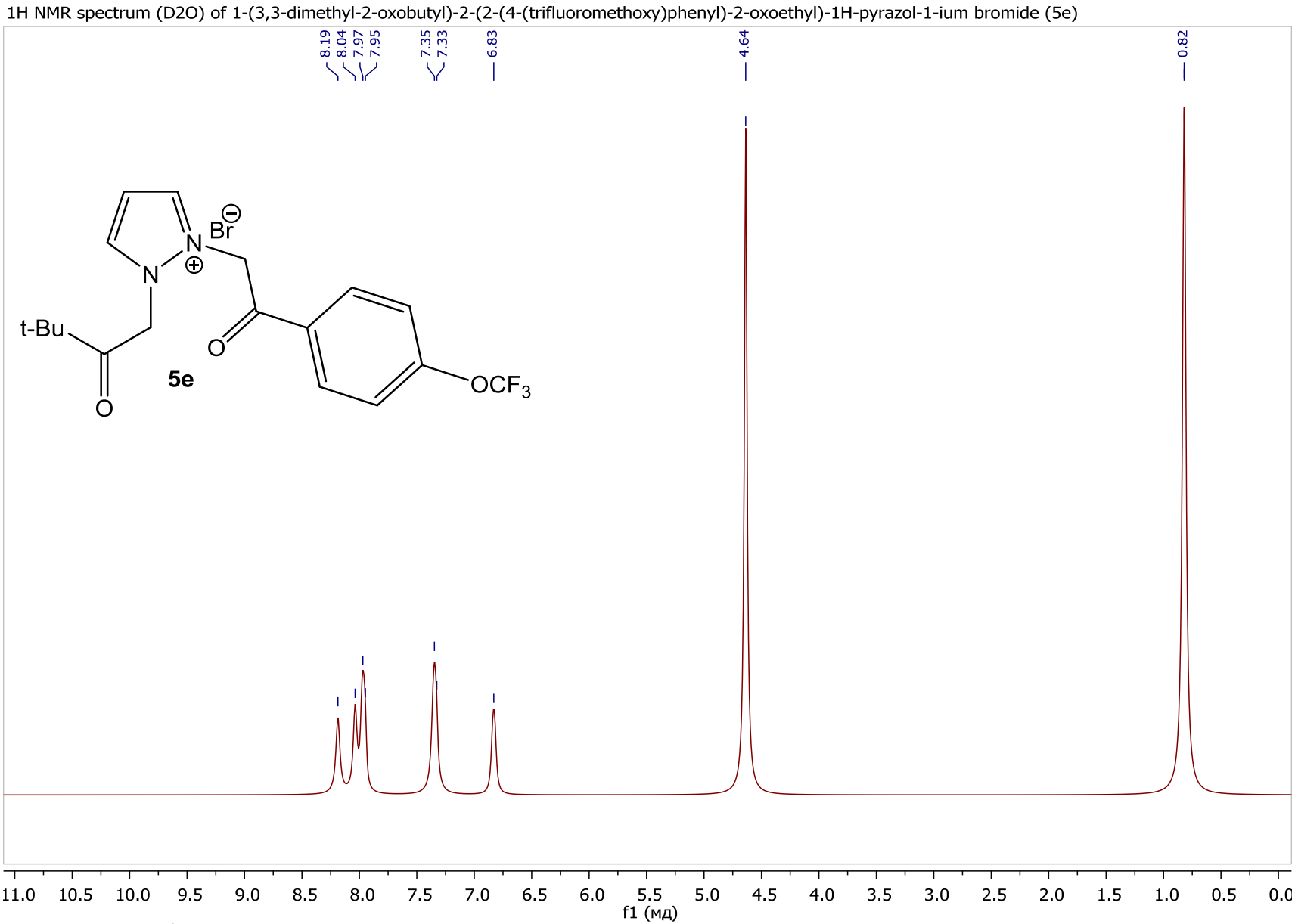



Figure S27. $^{1}$H NMR spectrum of 1-(3,3-dimethyl-2-oxobutyl)-2-(2-(4-(trifluoromethoxy)phenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5e**)

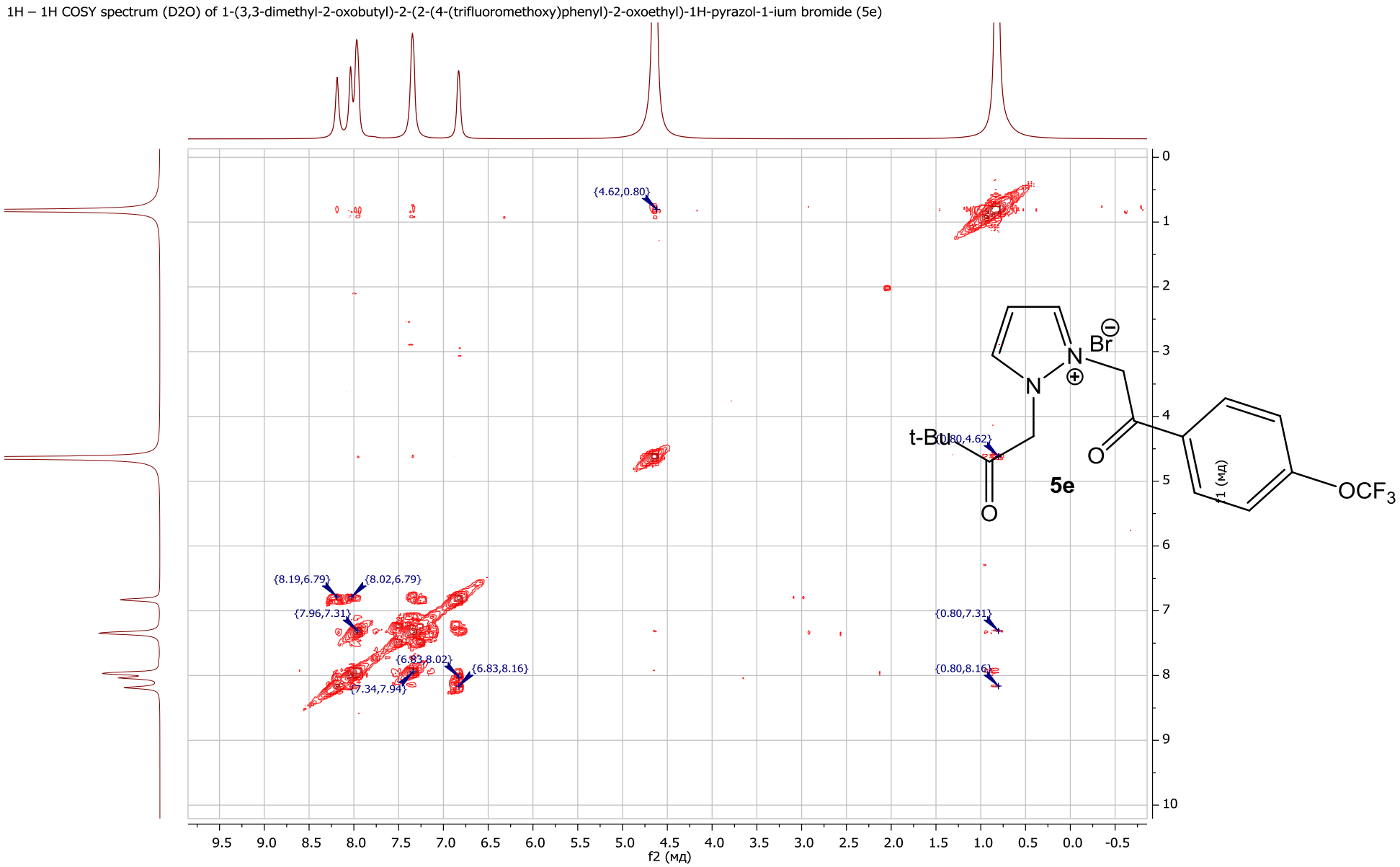



Figure S28. $^{1}$H – $^{1}$H COSY spectrum of 1-(3,3-dimethyl-2-oxobutyl)-2-(2-(4-(trifluoromethoxy)phenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5e**)

**Spectra of 1-(3,3-dimethyl-2-oxobutyl)-2-(2-(4-fluorophenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (5f)**

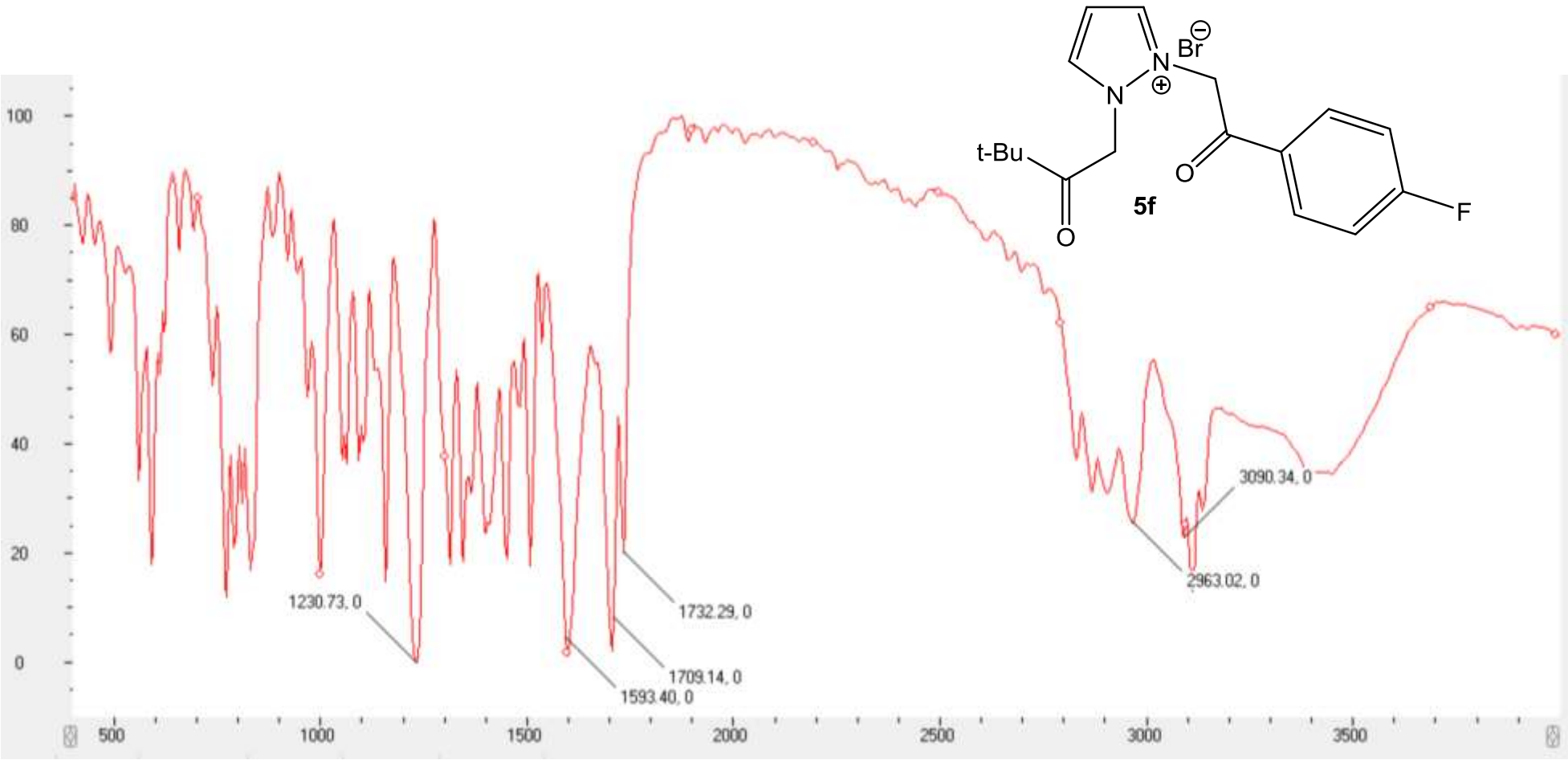



Figure S29. IR spectrum of 1-(3,3-dimethyl-2-oxobutyl)-2-(2-(4-fluorophenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5f**)

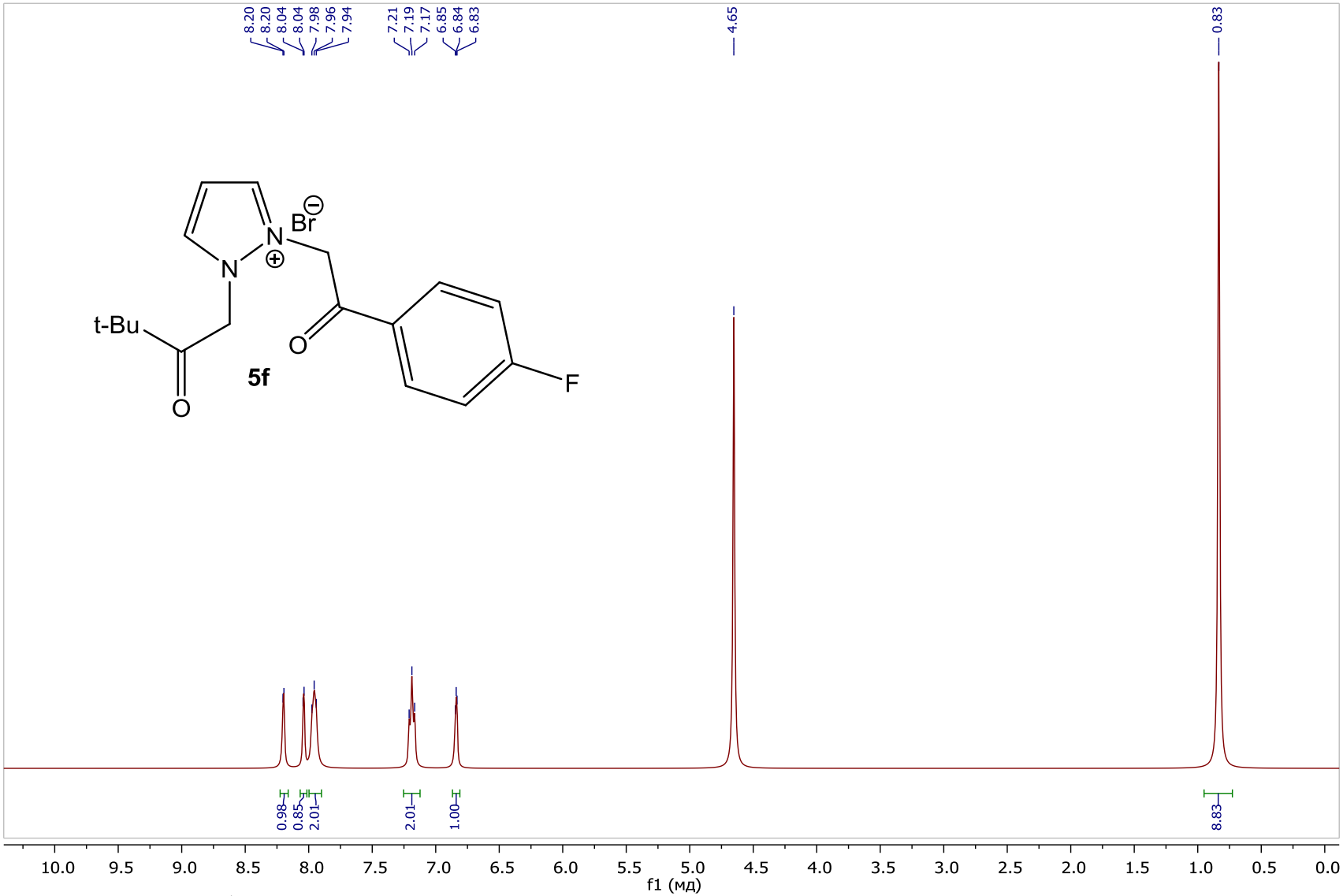



Figure S30. $^{1}$H NMR spectrum of 1-(3,3-dimethyl-2-oxobutyl)-2-(2-(4-fluorophenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5f**)

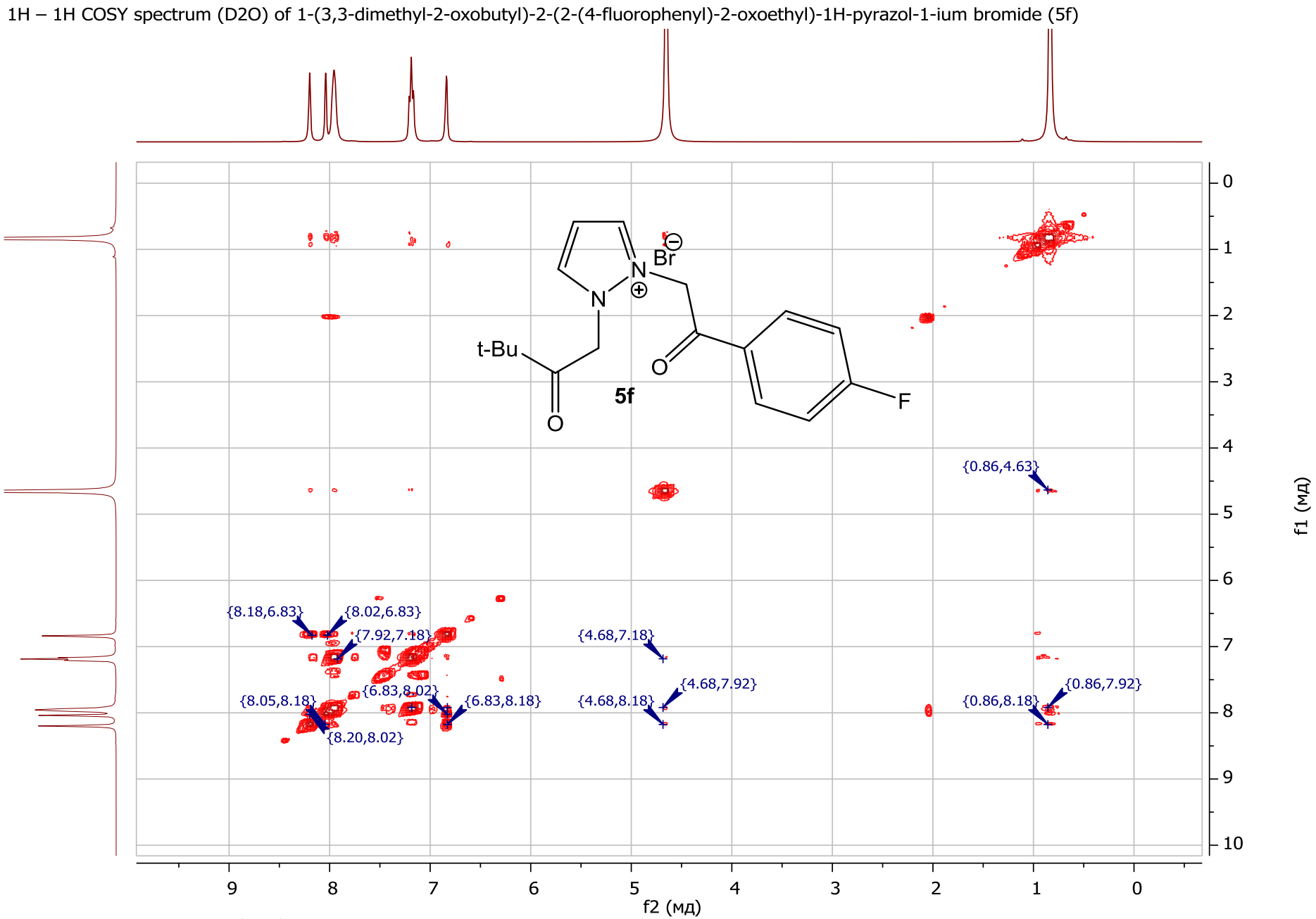



Figure S31. $^{1}$H – $^{1}$H COSY spectrum of 1-(3,3-dimethyl-2-oxobutyl)-2-(2-(4-fluorophenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5f**)

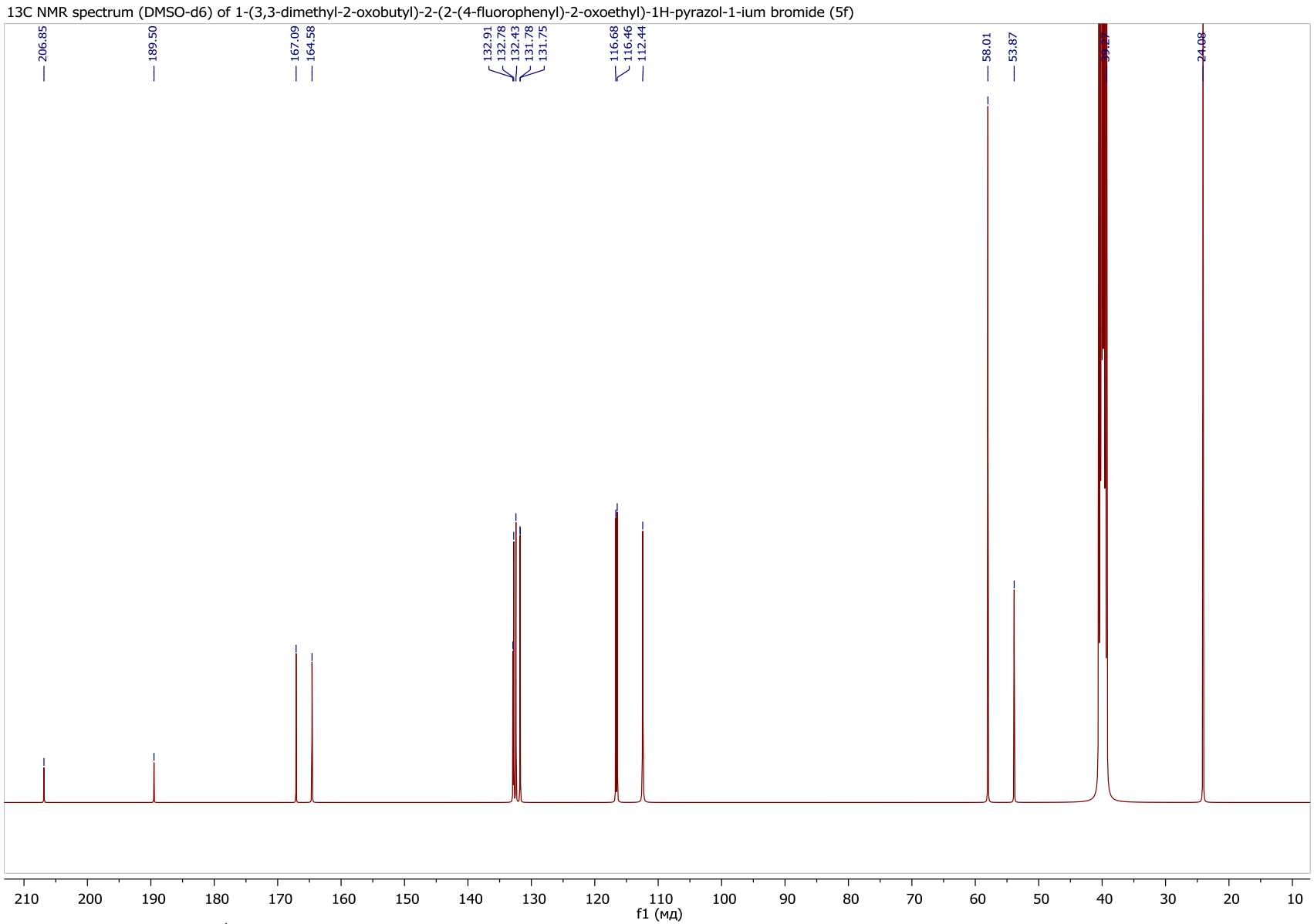



Figure S32. $^{1}$H NMR spectrum of 1-(3,3-dimethyl-2-oxobutyl)-2-(2-(4-fluorophenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5f**)

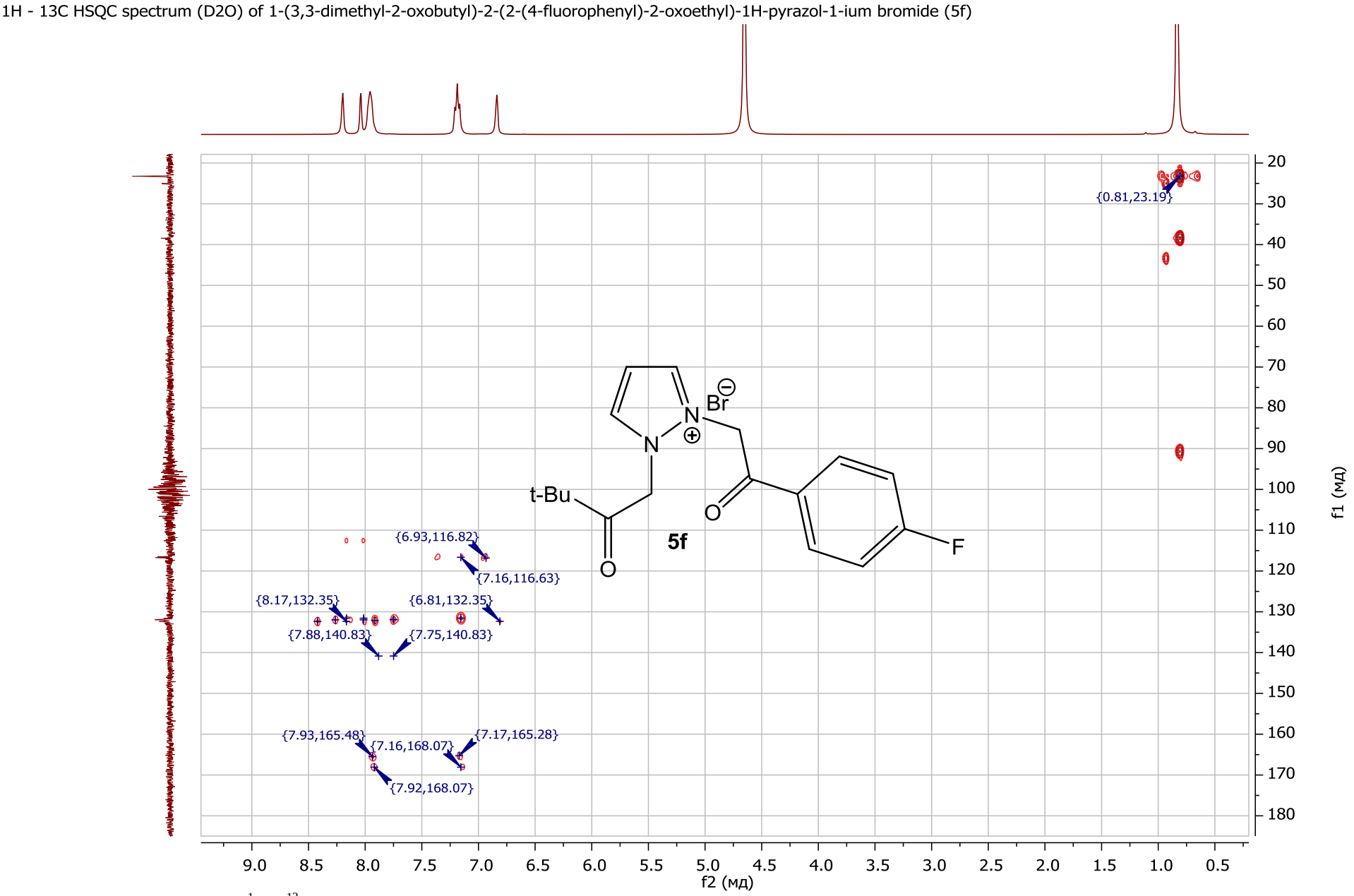



Figure S33. $^{1}H$ – $^{13}C$ HMBC spectrum of 1-(3,3-dimethyl-2-oxobutyl)-2-(2-(4-fluorophenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5f**)

19F NMR spectrum (DMSO-d6) of 1-(3,3-dimethyl-2-oxobutyl)-2-(2-(4-fluorophenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (5f)

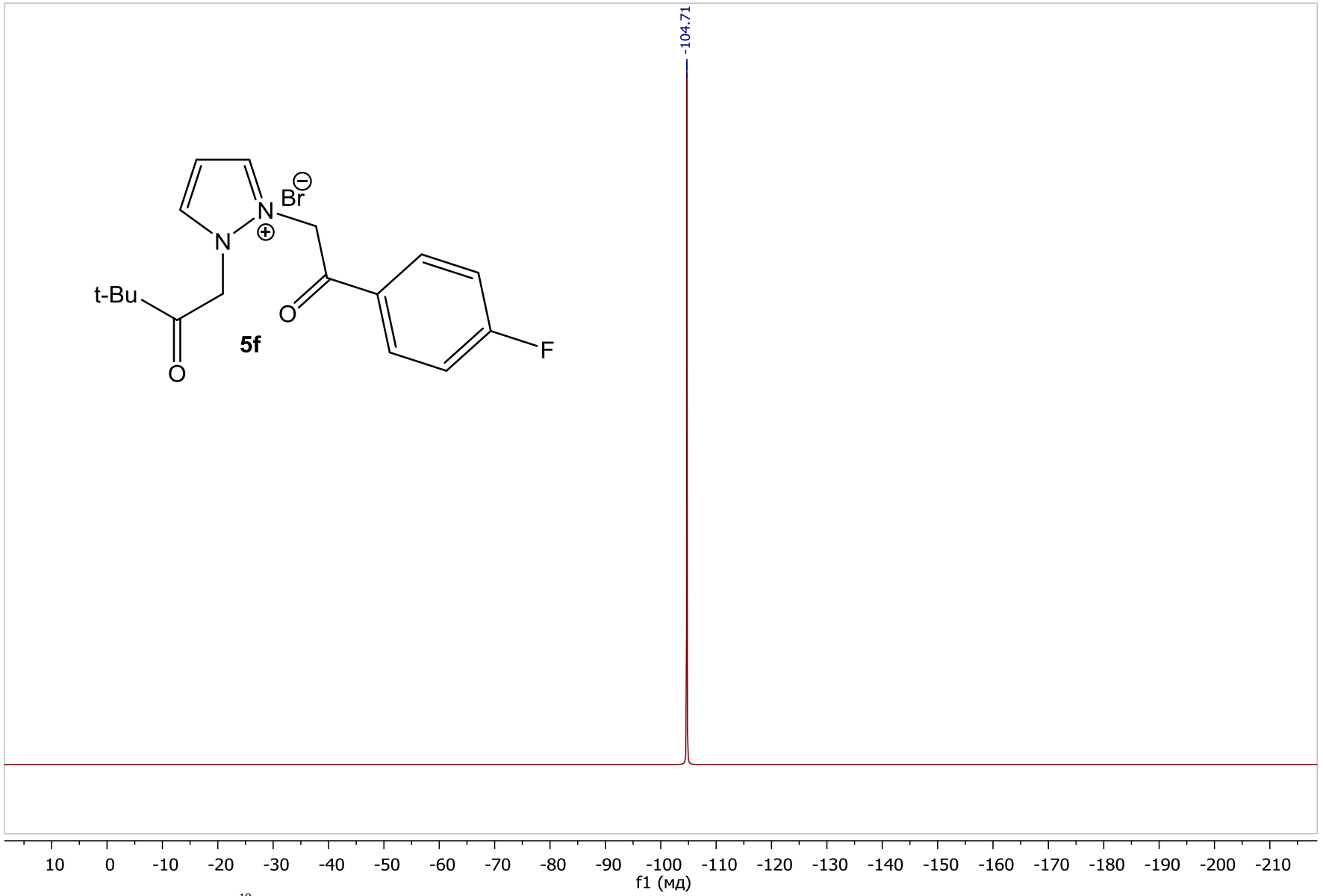



Figure S34. $^{19}$F NMR spectrum of 1-(3,3-dimethyl-2-oxobutyl)-2-(2-(4-fluorophenyl)-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5f**)

**Spectra of 1-(2-(4-fluorophenyl)-2-oxoethyl)-2-(2-phenyl-2-oxoethyl)-1H-pyrazol-1-ium bromide (5g)**

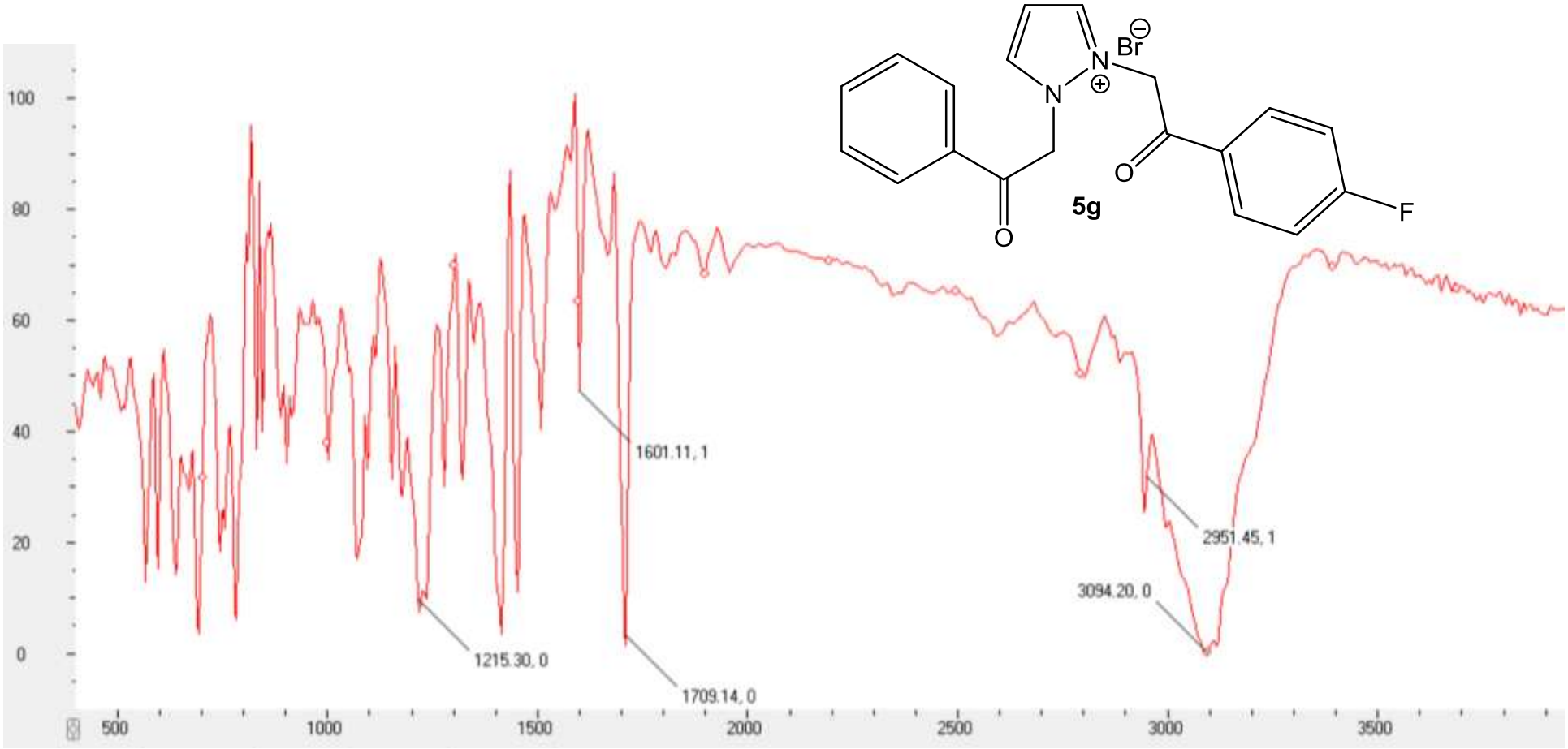



Figure S35. IR spectrum of 1-(2-(4-fluorophenyl)-2-oxoethyl)-2-(2-phenyl-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5g**)

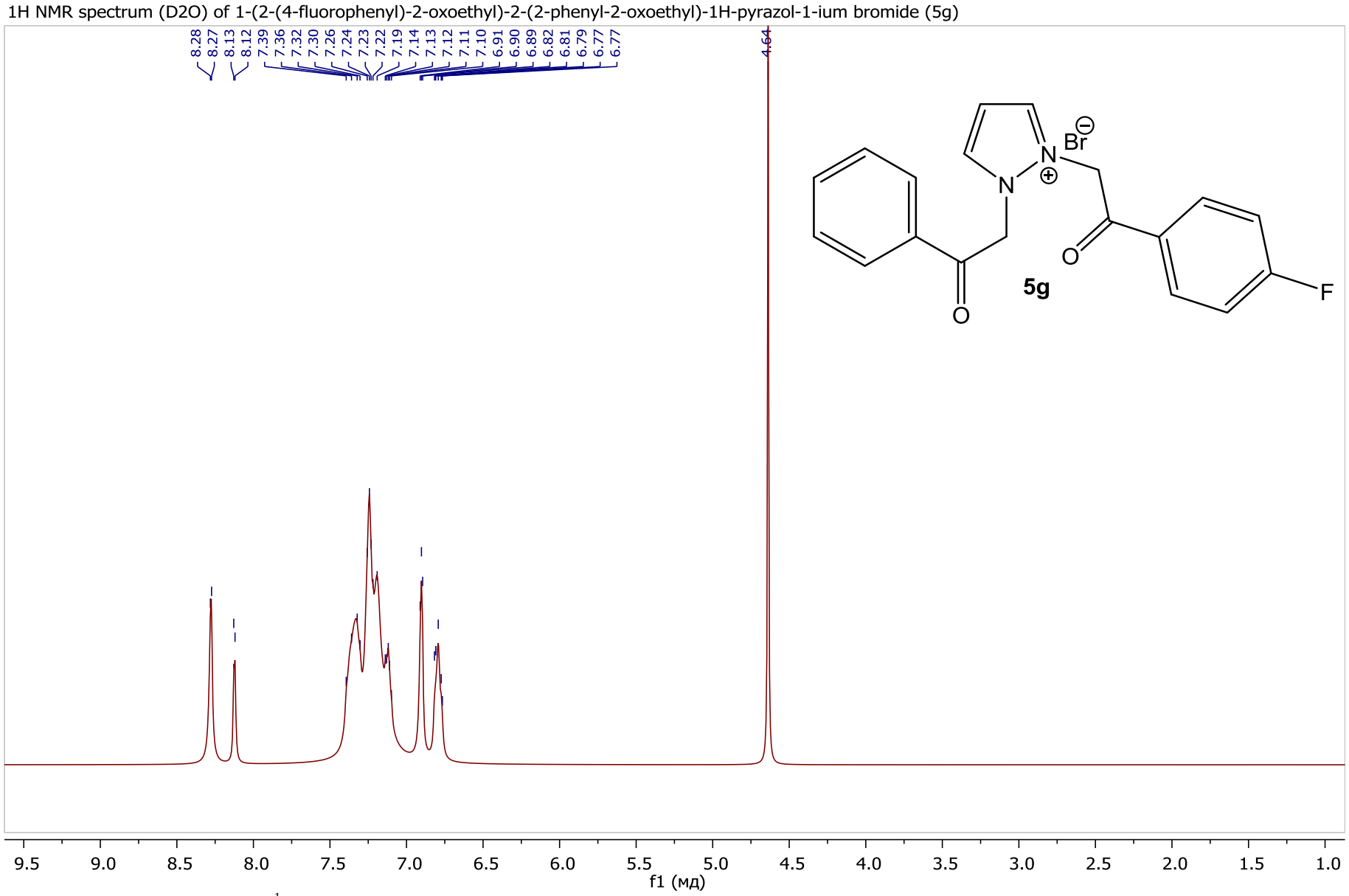



Figure S36. $^{1}$H NMR spectrum of 1-(2-(4-fluorophenyl)-2-oxoethyl)-2-(2-phenyl-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5g**)

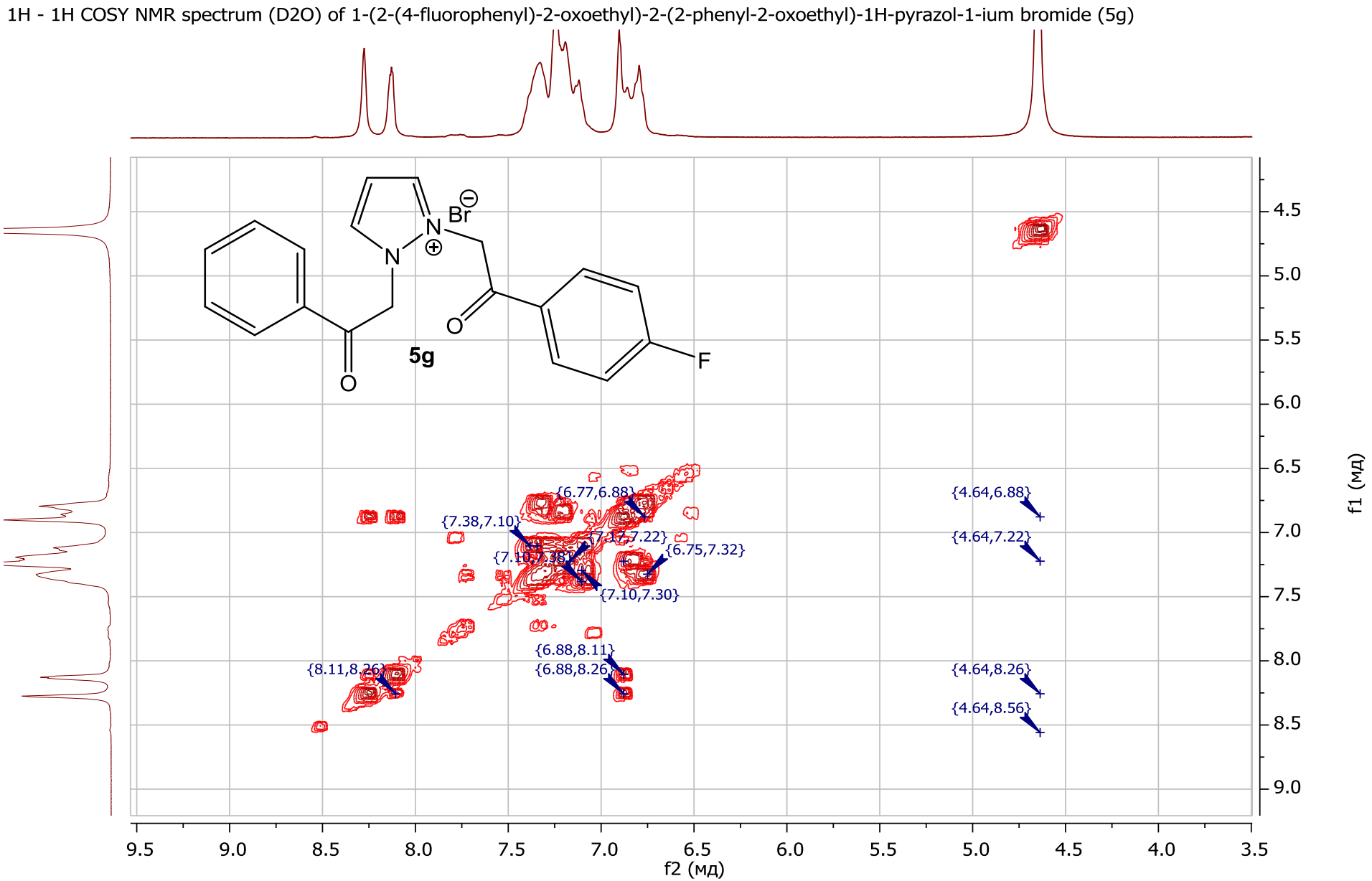



Figure S37. $^{1}H$ – $^{1}H$ COSY NMR spectrum of 1-(2-(4-fluorophenyl)-2-oxoethyl)-2-(2-phenyl-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5g**)

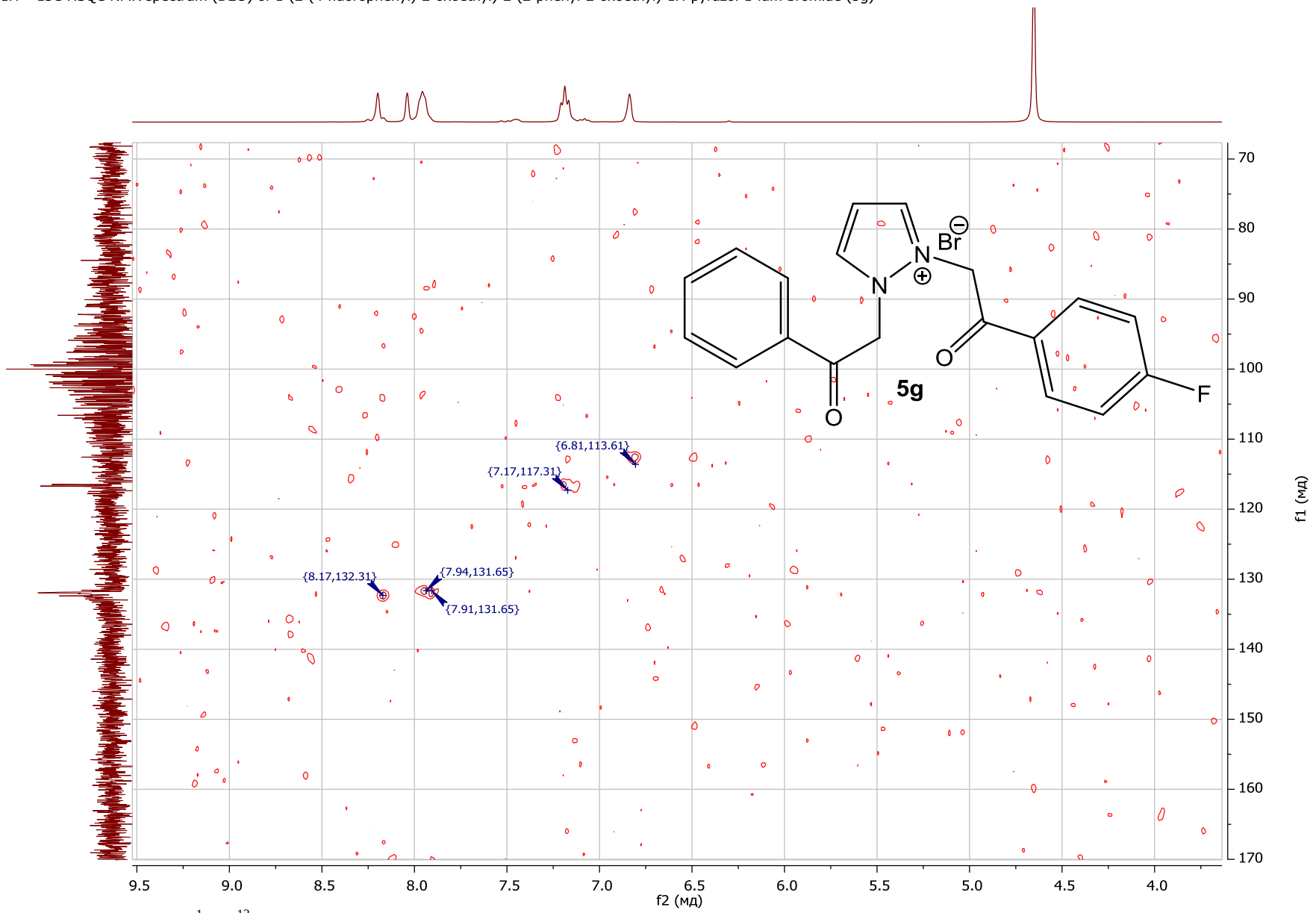



Figure S38. $^{1}H$ – $^{13}C$ HSQC NMR spectrum of 1-(2-(4-fluorophenyl)-2-oxoethyl)-2-(2-phenyl-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5g**)

**Spectra of 1-(2-(4-bromophenyl)-2-oxoethyl)-2-(2-phenyl-2-oxoethyl)-1H-pyrazol-1-ium bromide (5h)**

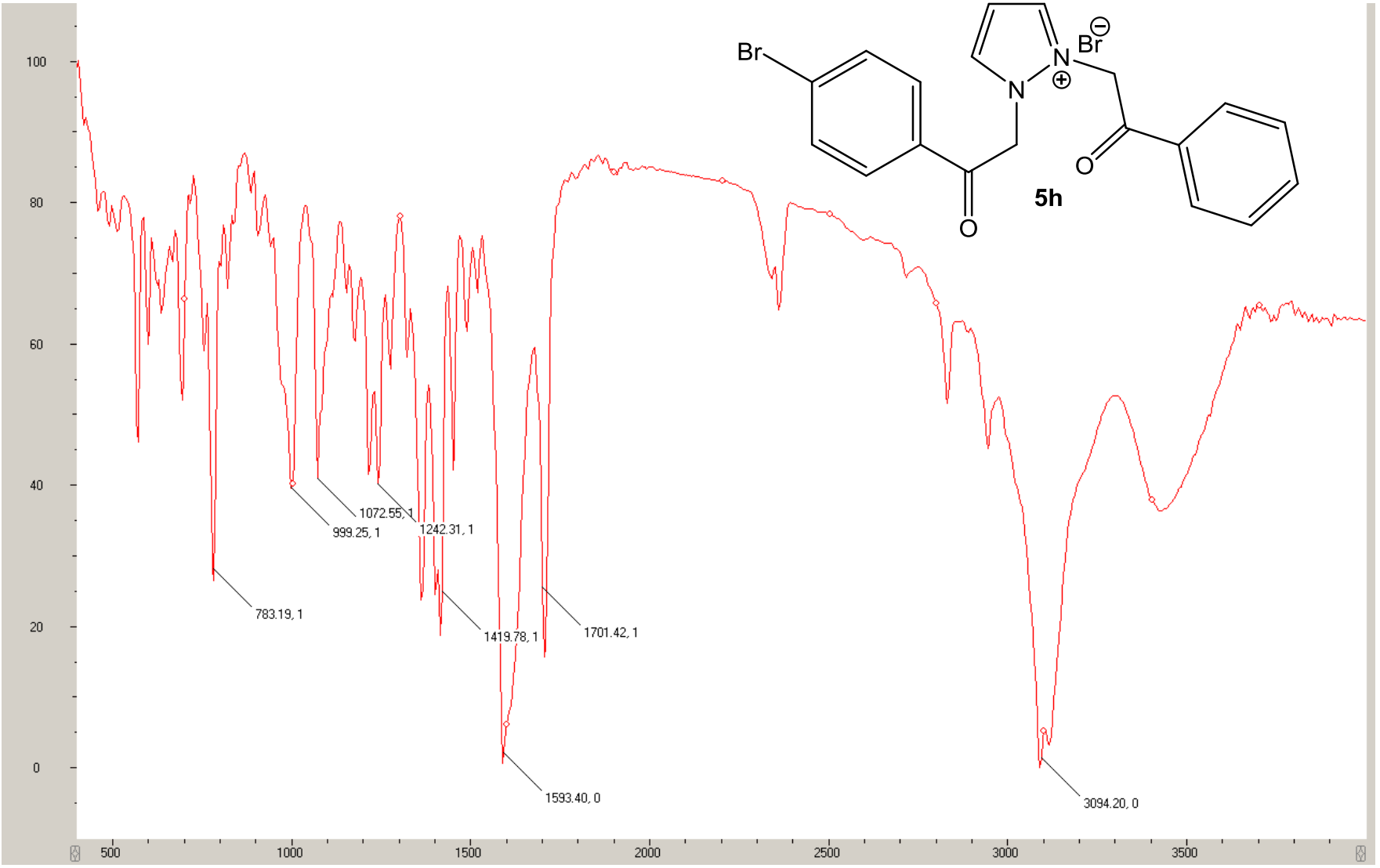



Figure S39. IR spectrum of 1-(2-(4-bromophenyl)-2-oxoethyl)-2-(2-phenyl-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5h**)

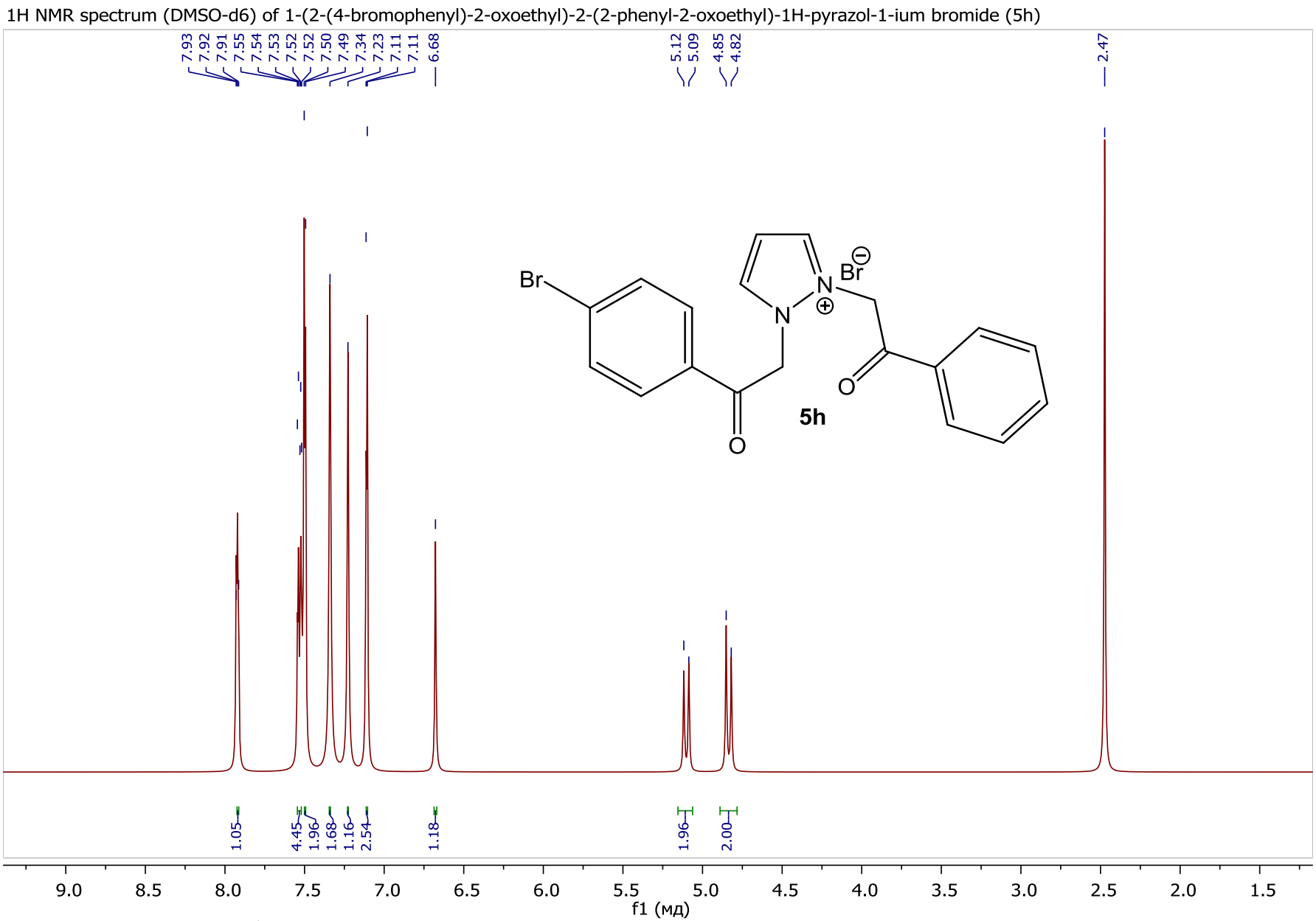



Figure S40. $^{1}$H NMR spectrum of 1-(2-(4-bromophenyl)-2-oxoethyl)-2-(2-phenyl-2-oxoethyl)-1H-pyrazol-1-ium bromide (**5h**)

**Spectra of 1,2-bis(2-phenyl-2-oxoethyl)-3,5-dimethyl-1H-pyrazol-1-ium bromide (6b)**

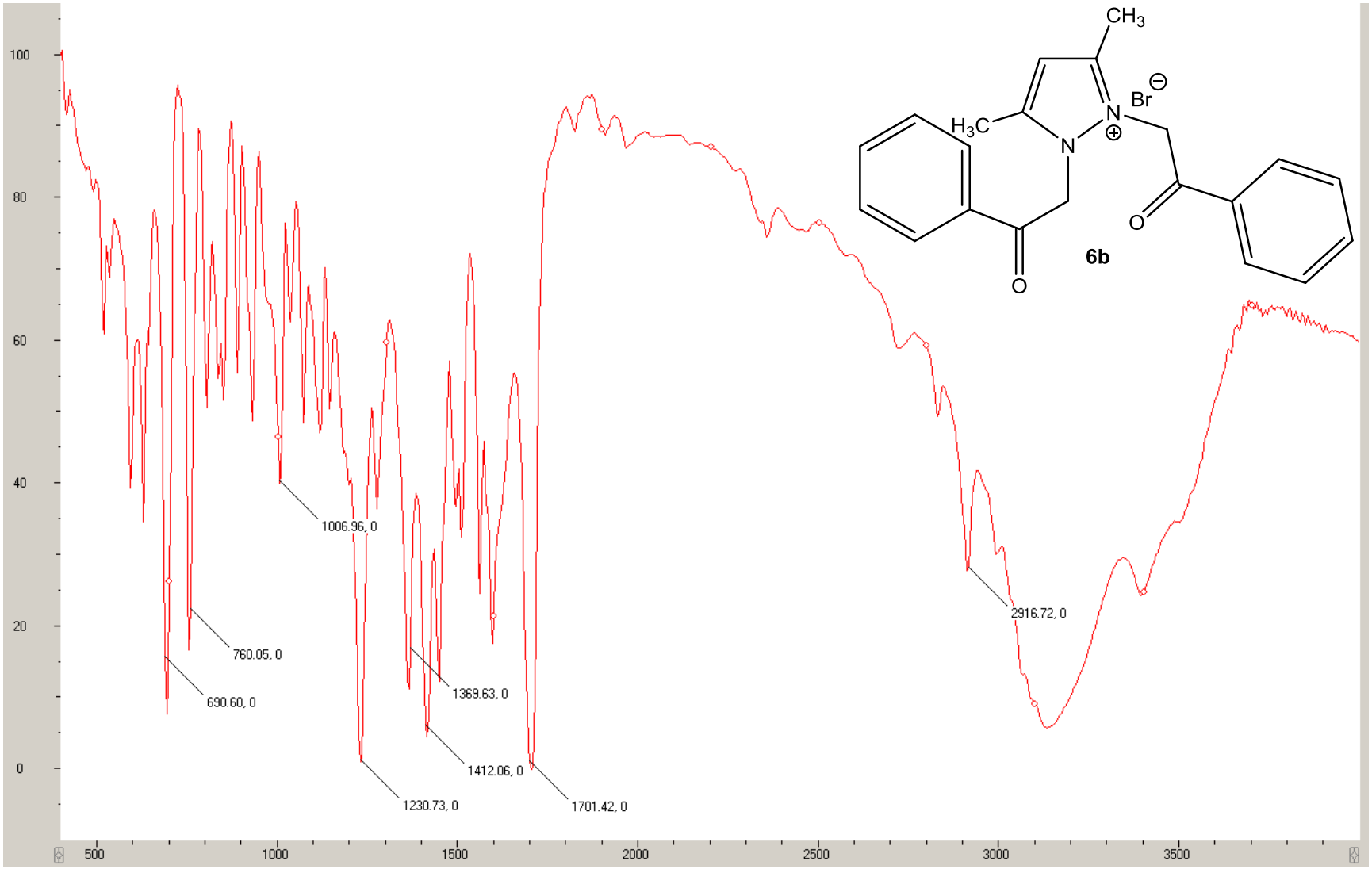



Figure S41. IR spectrum of 1,2-bis(2-phenyl-2-oxoethyl)-3,5-dimethyl-1H-pyrazol-1-ium bromide (**6b**)

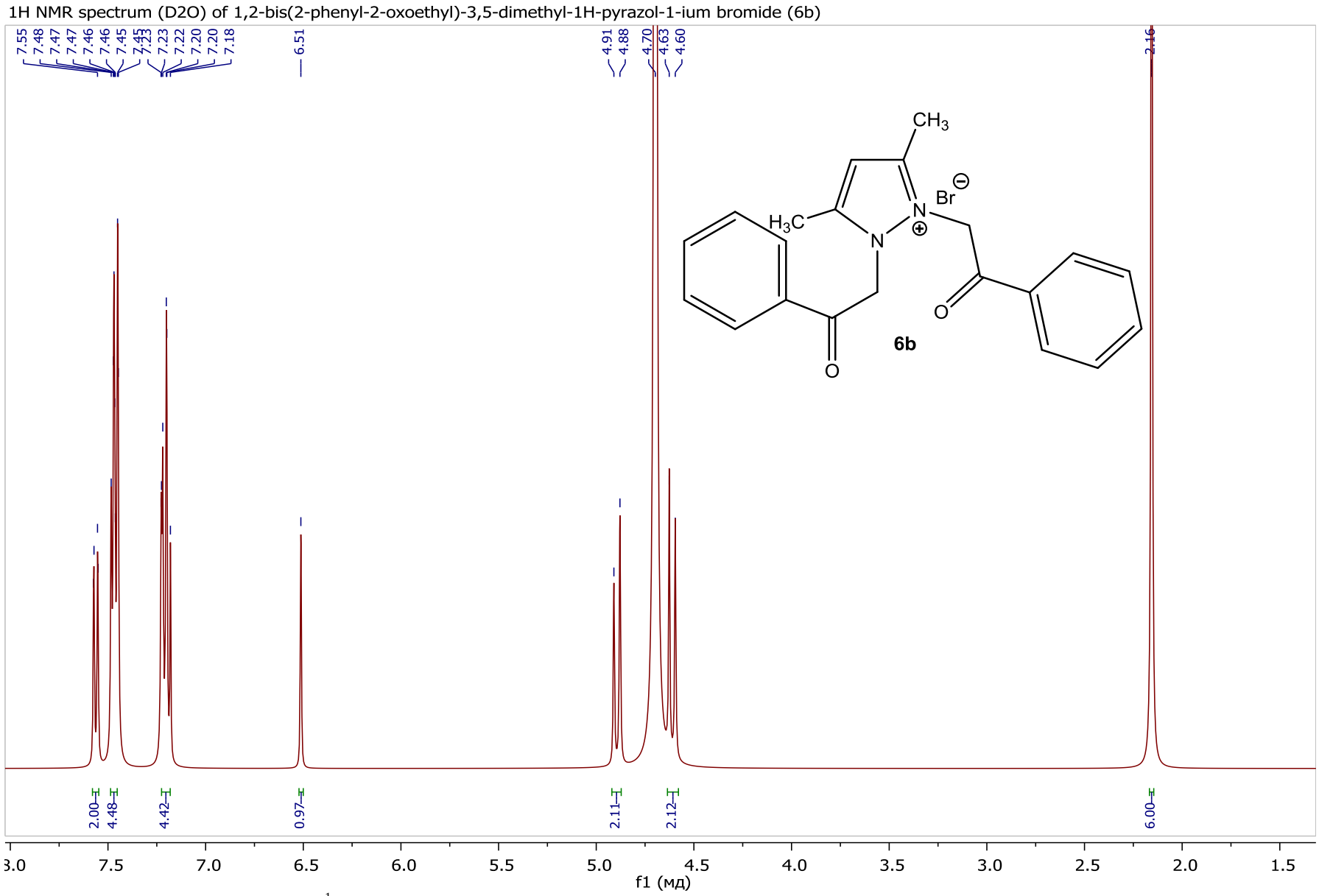



Figure S42. $^{1}$H NMR spectrum of 1,2-bis(2-phenyl-2-oxoethyl)-3,5-dimethyl-1H-pyrazol-1-ium bromide (**6b**)

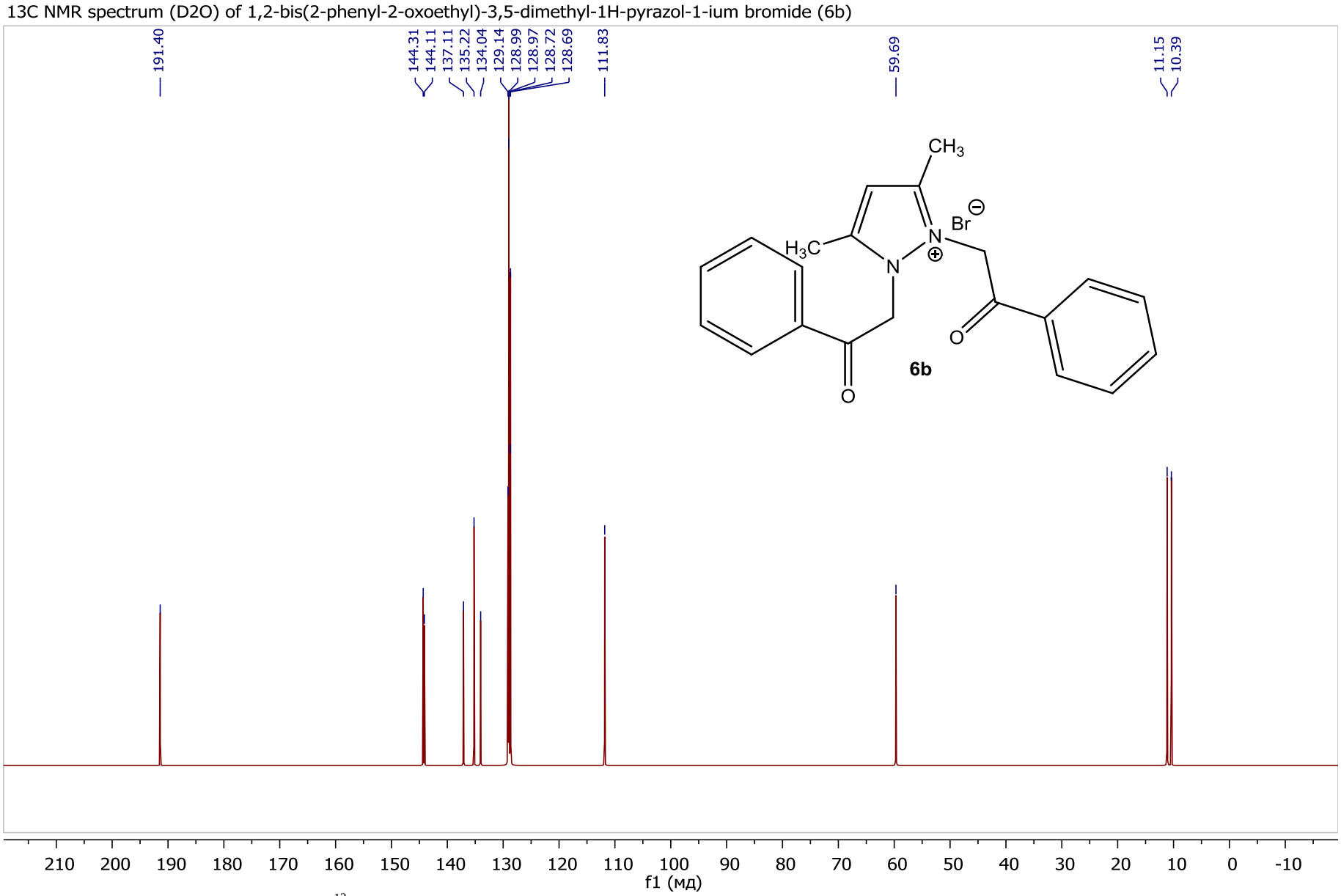



Figure S43. $^{13}$C NMR spectrum of 1,2-bis(2-phenyl-2-oxoethyl)-3,5-dimethyl-1H-pyrazol-1-ium bromide (**6b**)

**Spectra of 1,2-bis(2-(4-bromophenyl)-2-oxoethyl)-3,5-dimethyl-1H-pyrazol-1-ium bromide (6c)**

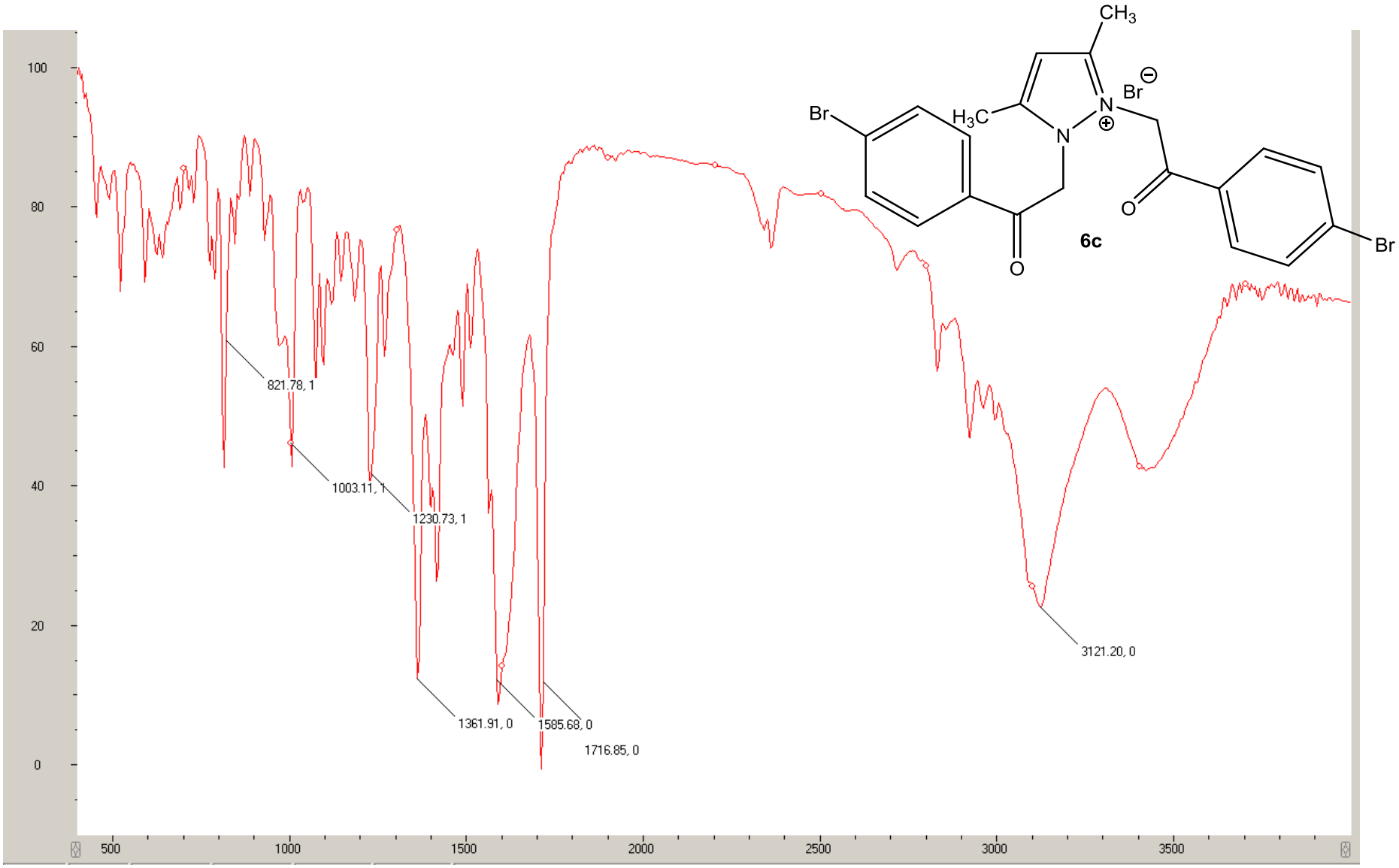



Figure S44. IR spectrum of 1,2-bis(2-(4-bromophenyl)-2-oxoethyl)-3,5-dimethyl-1H-pyrazol-1-ium bromide (**6c)**

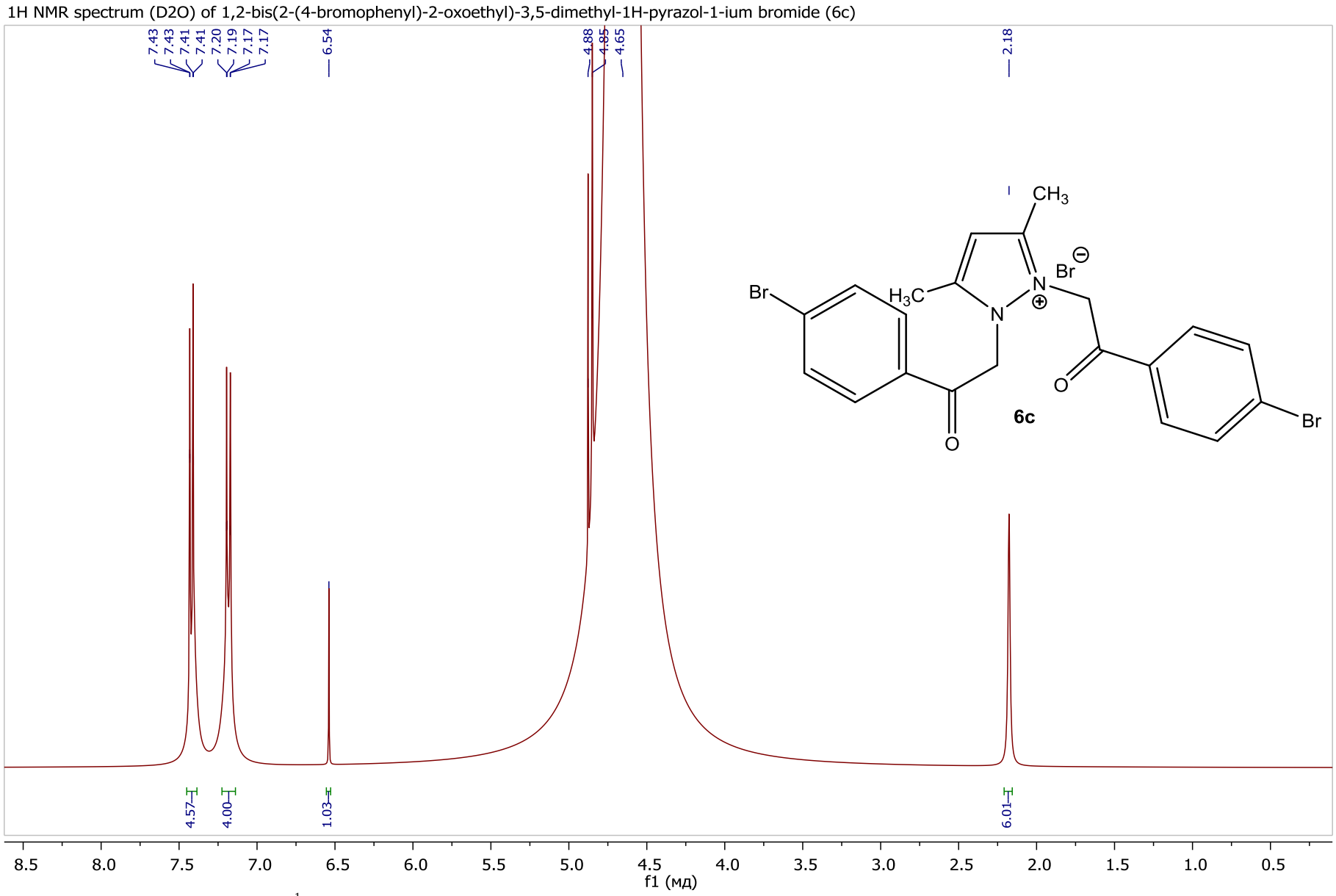



Figure S45. $^{1}$H NMR spectrum of 1,2-bis(2-(4-bromophenyl)-2-oxoethyl)-3,5-dimethyl-1H-pyrazol-1-ium bromide (**6c)**

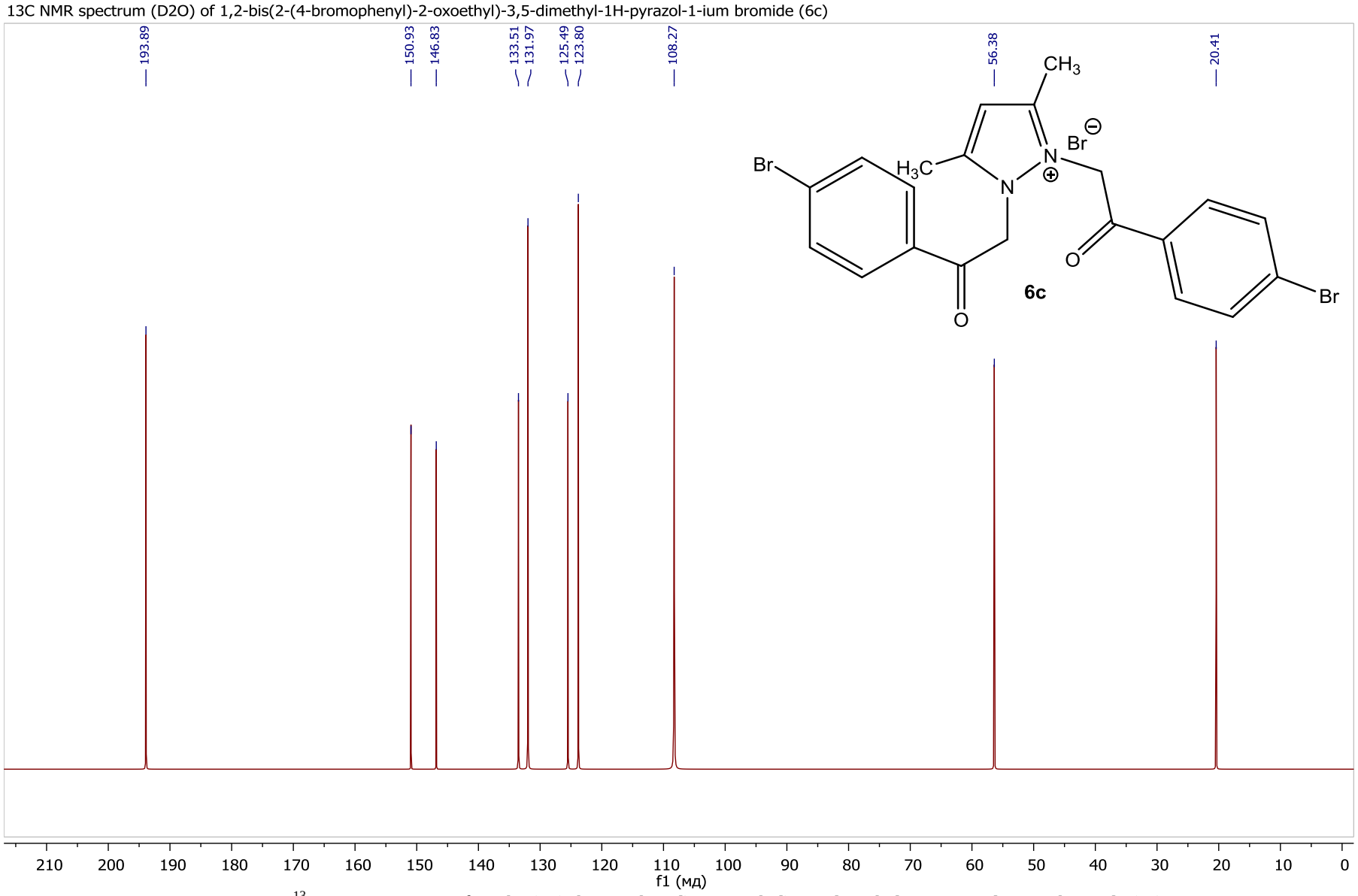



Figure S46. $^{13}$C NMR spectrum of 1,2-bis(2-(4-bromophenyl)-2-oxoethyl)-3,5-dimethyl-1H-pyrazol-1-ium bromide (**6c**)

**Spectra of 2-(2-(4-bromophenyl)-2-oxoethyl)-1-(2-oxo-2-phenylethyl)-3,5-dimethyl-1H-pyrazol-1-ium bromide (6d)**

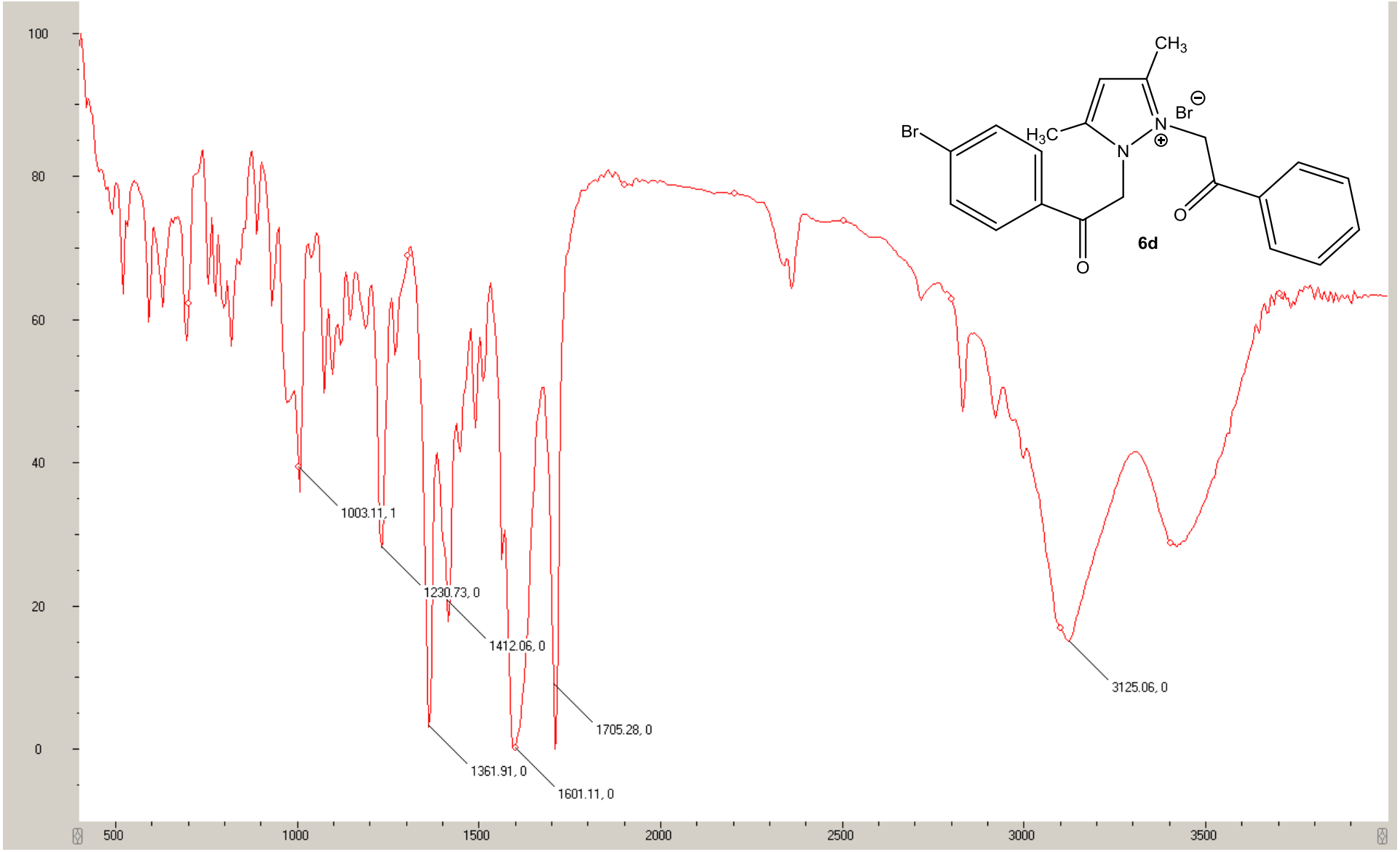



Figure S47. IR spectrum of 2-(2-(4-bromophenyl)-2-oxoethyl)-1-(2-oxo-2-phenylethyl)-3,5-dimethyl-1H-pyrazol-1-ium bromide (**6d**)

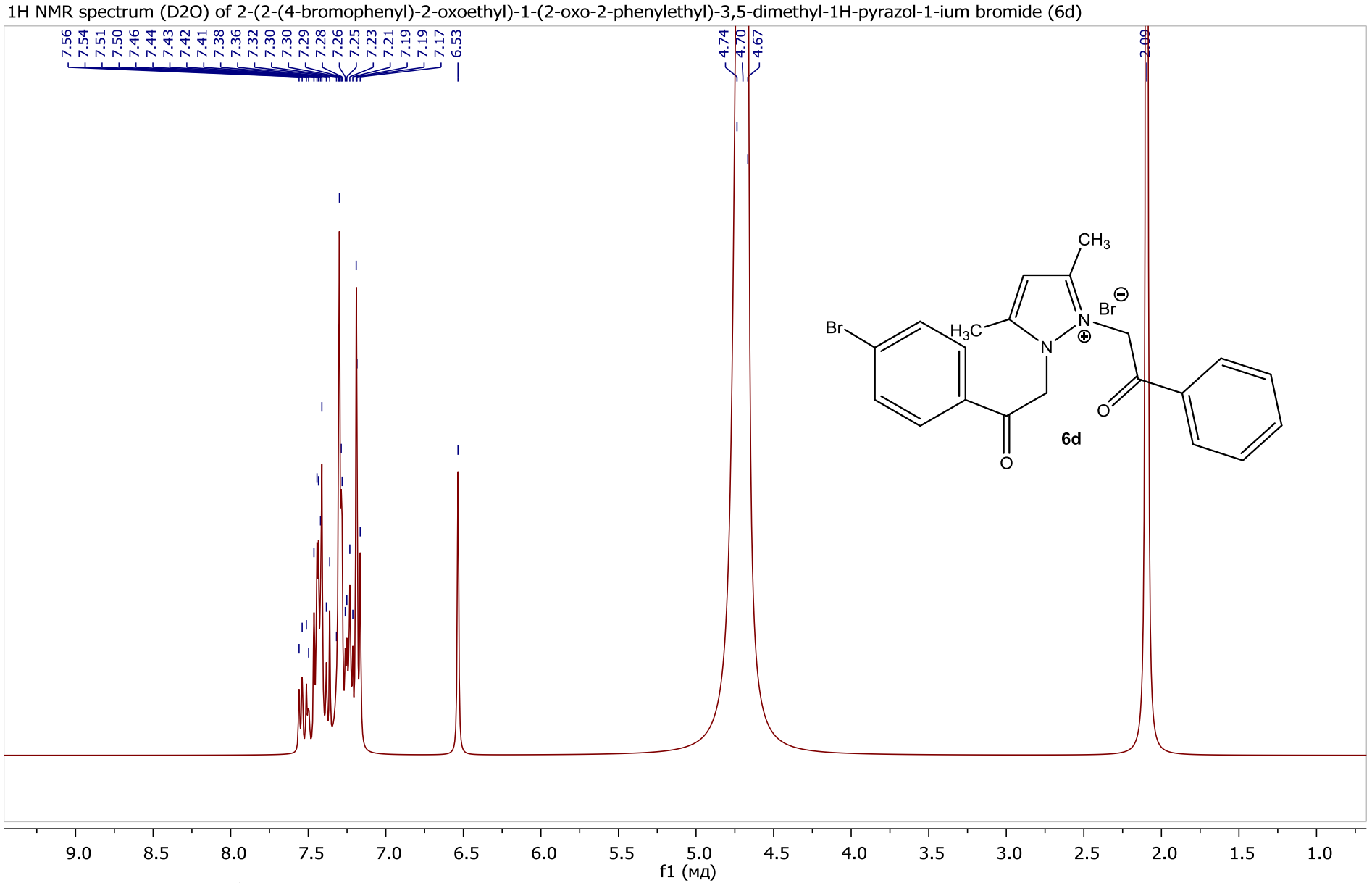



Figure S48. $^{1}$H NMR spectrum of 2-(2-(4-bromophenyl)-2-oxoethyl)-1-(2-oxo-2-phenylethyl)-3,5-dimethyl-1H-pyrazol-1-ium bromide (**6d**)

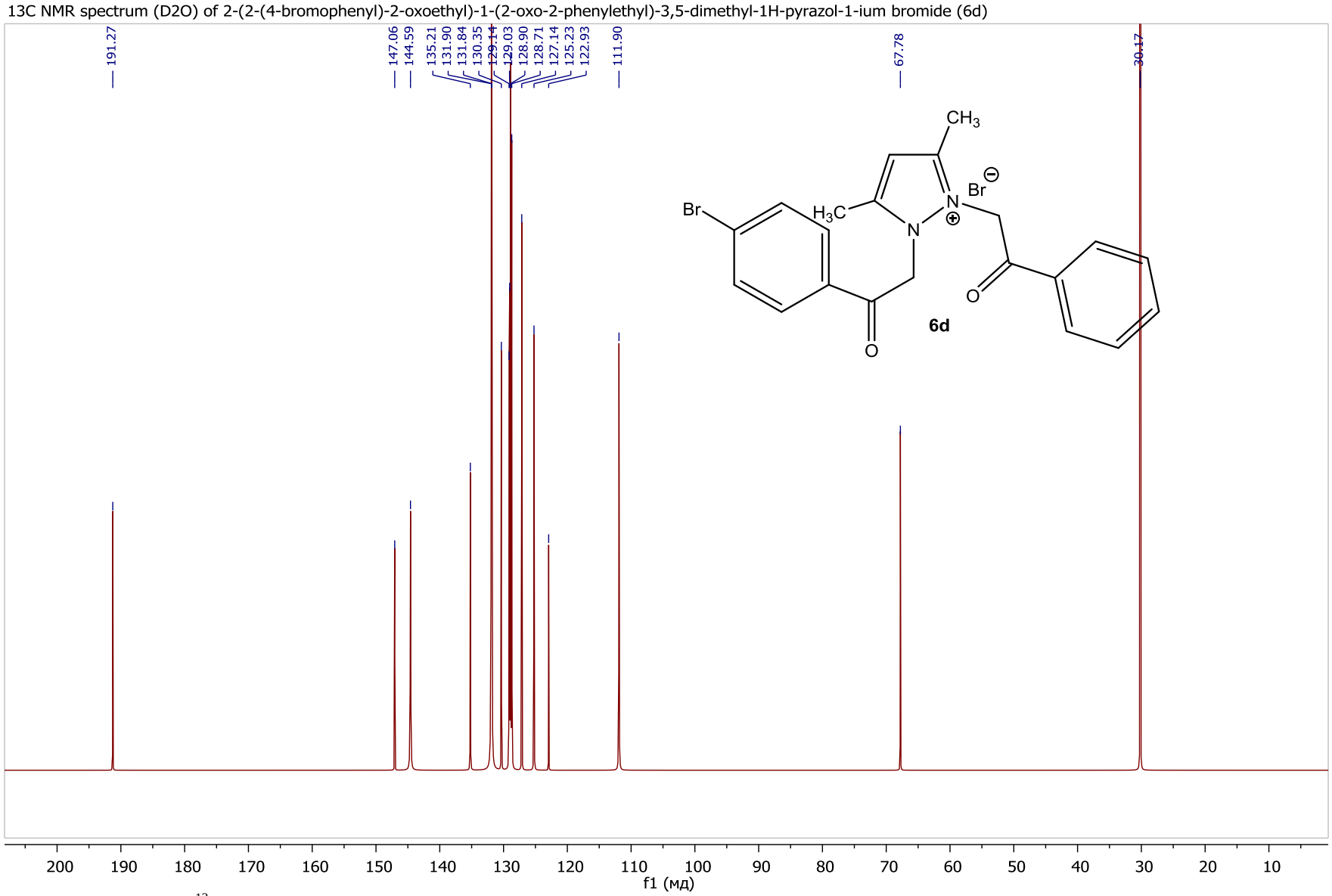



Figure S49. $^{13}$C NMR spectrum of 2-(2-(4-bromophenyl)-2-oxoethyl)-1-(2-oxo-2-phenylethyl)-3,5-dimethyl-1H-pyrazol-1-ium bromide (**6d**)

**In vitro antimicrobial and antifungal activity**

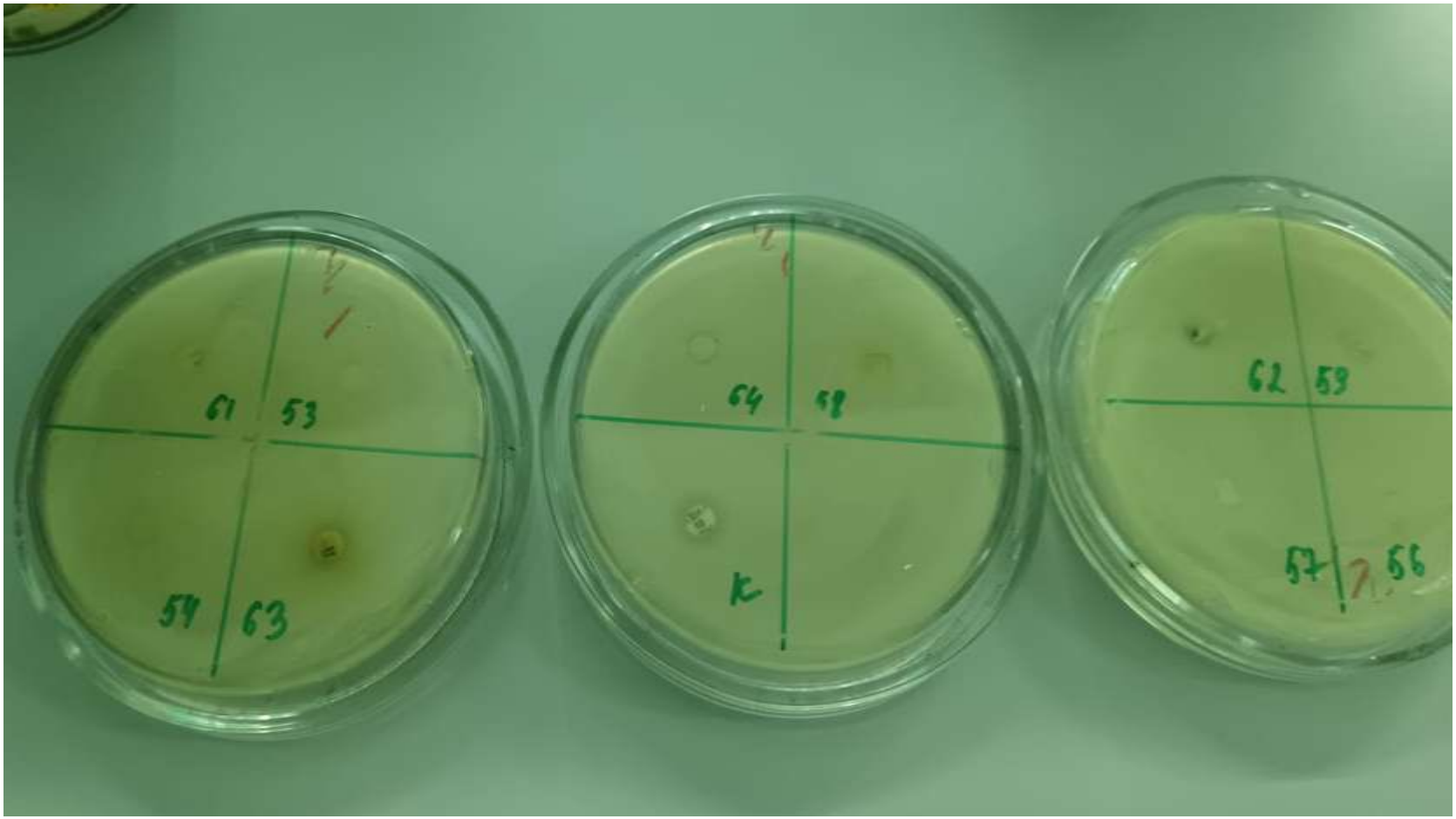



Figure S50. Antimicrobial activity of samples: **5a** (No. 53), **5b** (No. 54), **5c** (No. 61), **5e** (No. 64), **5f** (No. 62), **5g** (No. 63), **5h** (No. 58), **6b** (No. 57), **6c** (No. 56), **6d** (No. 59) against *Staphylococcus aureus* (ATCC 6538) on egg-yolk salt agar

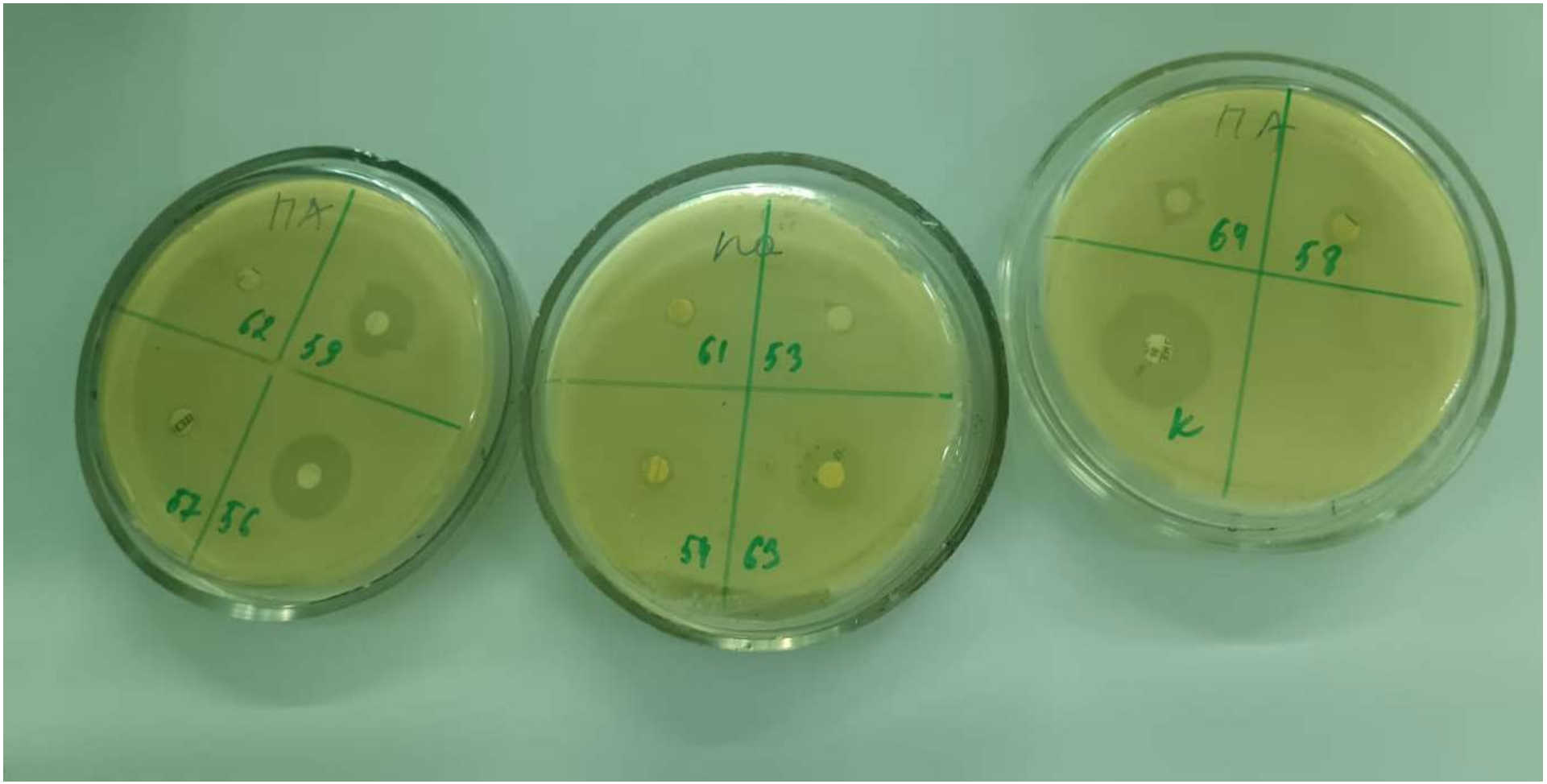



Figure S51. **Antimicrobial activity of samples: 5a** (No. 53), **5b** (No. 54), **5c** (No. 61), **5e** (No. 64), **5f** (No. 62), **5g** (No. 63), **5h** (No. 58), **6b** (No. 57), **6c** (No. 56), **6d** (No. 59) against *Bacillus subtilis (ATCC 6633)* on meat-peptone agar.

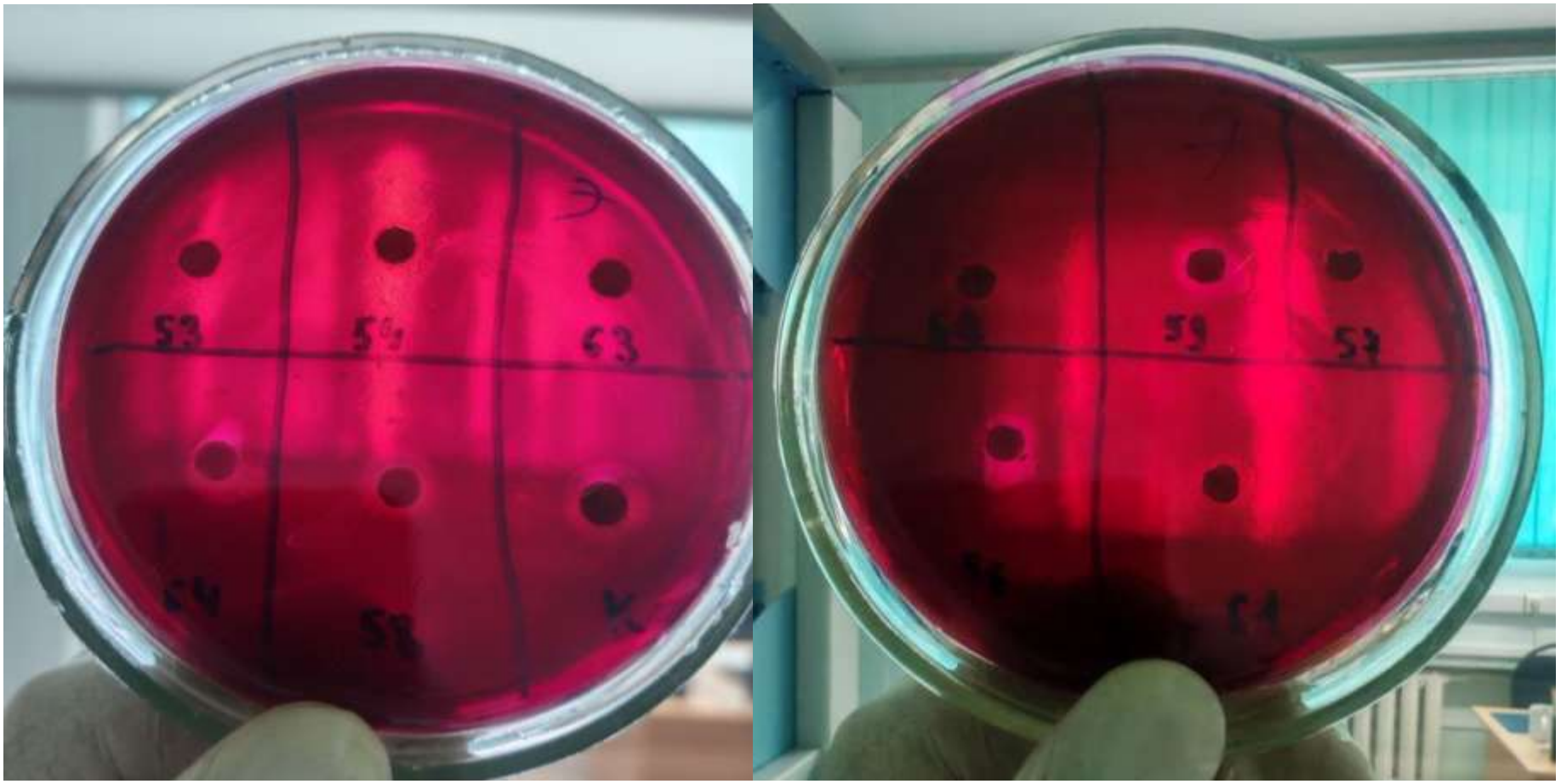


Figure S52. Antimicrobial activity of samples: **5a** (No. 53), **5b** (No. 54), **5c** (No. 61), **5e** (No. 64), **5f** (No. 62), **5g** (No. 63), **5h** (No. 58), **6b** (No. 57), **6c** (No. 56), **6d** (No. 59) against *Escherichia coli* (ATCC 25922) on Endo agar.

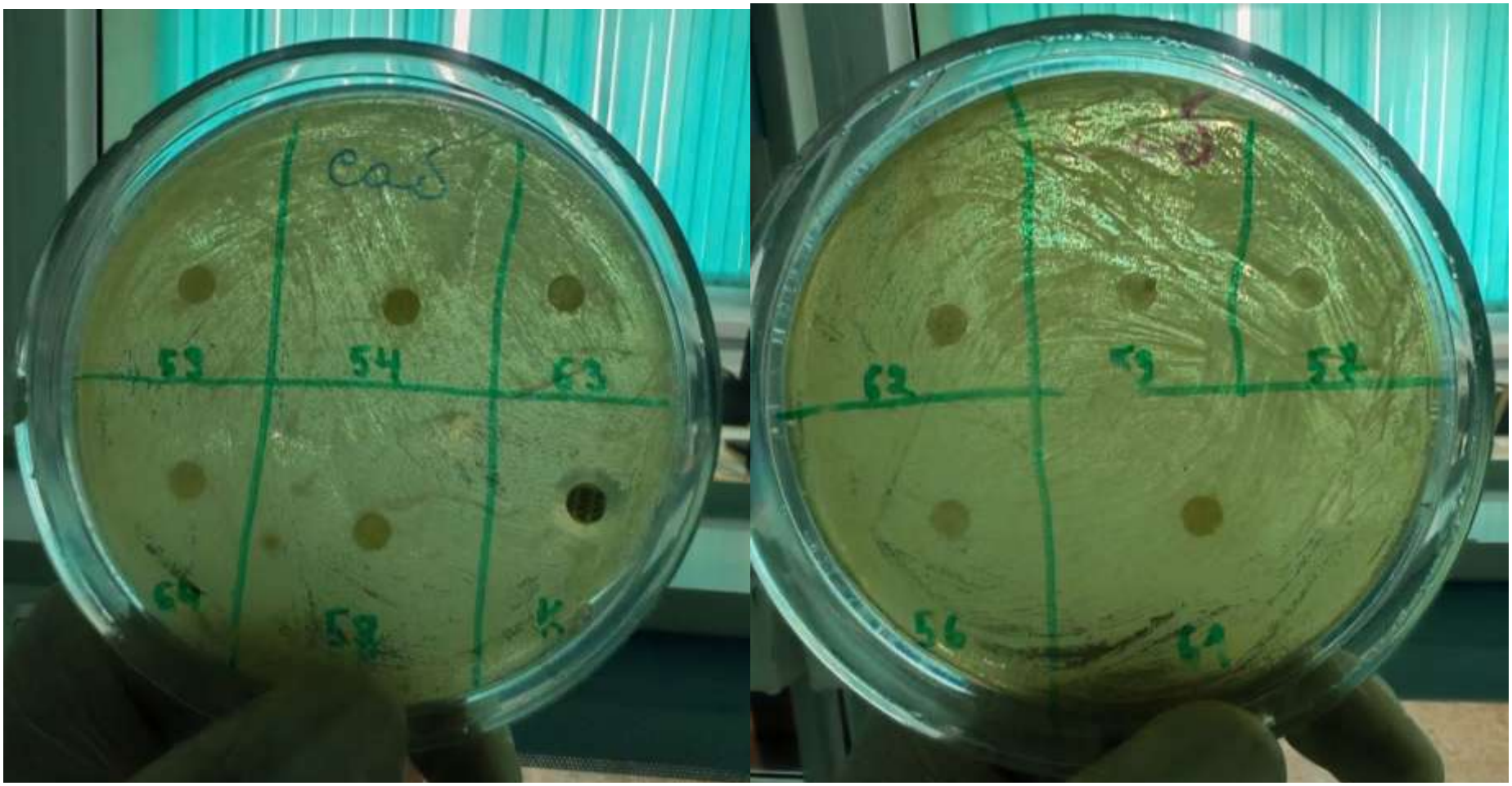


Figure S53. Antifungal activity of samples: **5a** (No. 53), **5b** (No. 54), **5c** (No. 61), **5e** (No. 64), **5f** (No. 62), **5g** (No. 63), **5h** (No. 58), **6b** (No. 57), **6c** (No. 56), **6d** (No. 59) against *Candida albicans* (ATCC 10231) on Sabouraud agar.

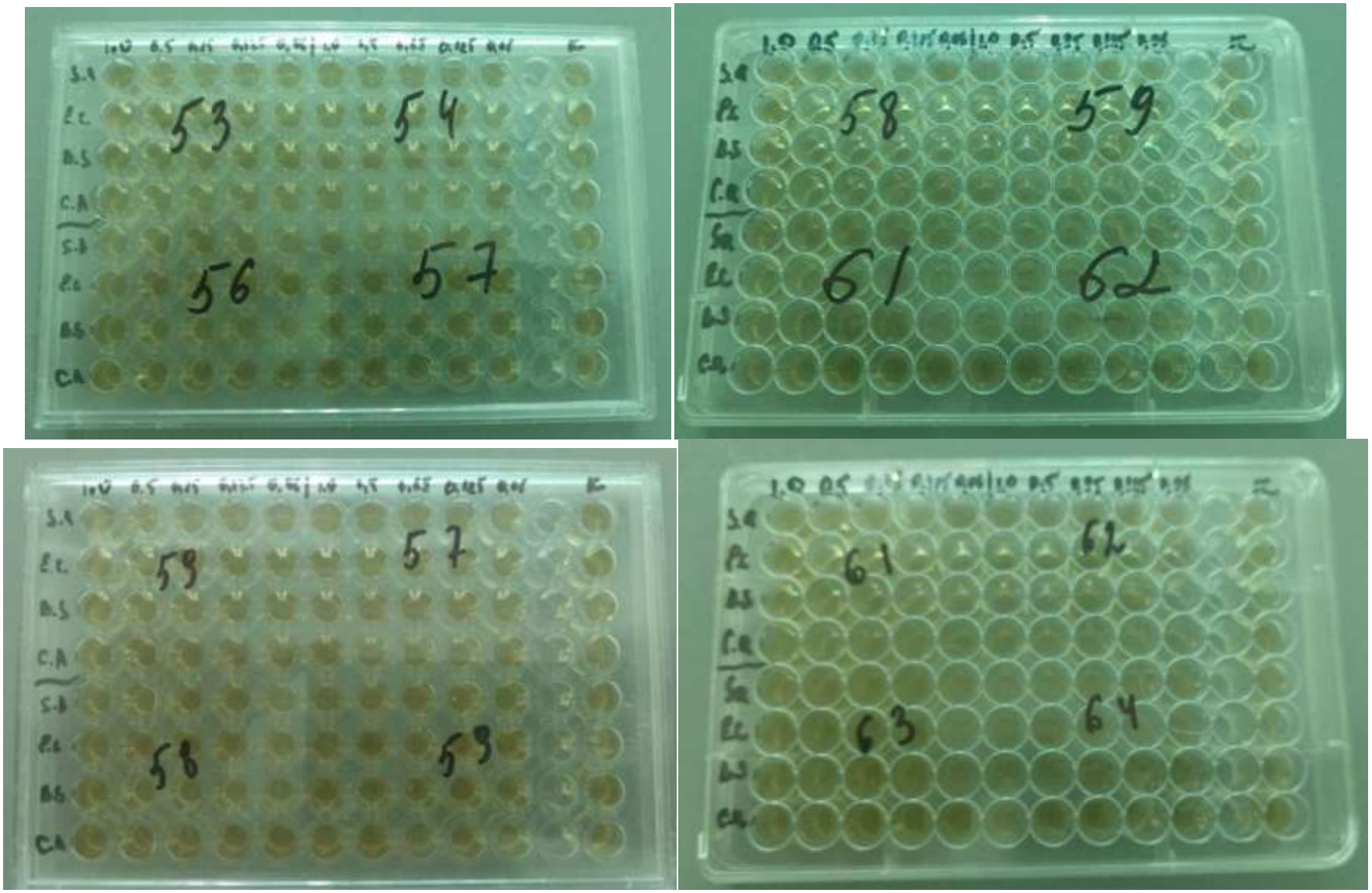



Figure S54. Representative images showing the determination of the minimum inhibitory concentration (MIC) of the studied samples **5a** (No. 53), **5b** (No. 54), **5c** (No. 61), **5e** (No. 64), **5f** (No. 62), **5g** (No. 63), **5h** (No. 58), **6b** (No. 57), **6c** (No. 56), and **6d** (No. 59) against *S. aureus* (ATCC 6538), *E. coli* (ATCC 25922), *B. subtilis* (ATCC 6633), and *C. albicans* (ATCC 10231) test strains (n = 3).

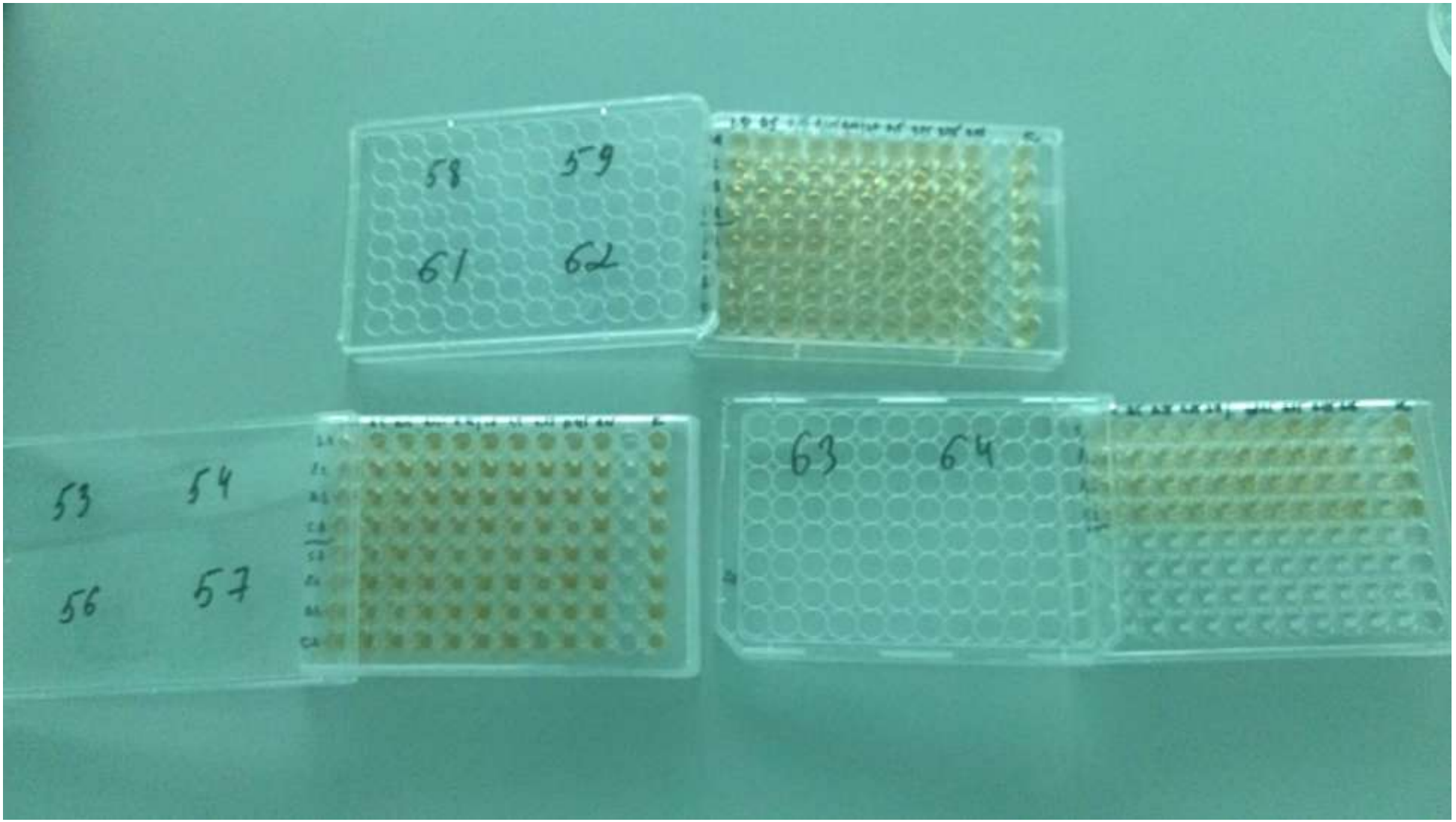



Figure S55. Representative images showing the determination of the minimum inhibitory concentration (MIC) of the studied samples **5a** (No. 53), **5b** (No. 54), **5c** (No. 61), **5e** (No. 64), **5f** (No. 62), **5g** (No. 63), **5h** (No. 58), **6b** (No. 57), **6c** (No. 56), and **6d** (No. 59) against *S. aureus* (ATCC 6538), *E. coli* (ATCC 25922), *B. subtilis* (ATCC 6633), and *C. albicans* (ATCC 10231) test strains (n = 3).