Electronic supplementary materials *Mendeleev Commun.*, 2021, **31**, 248–250

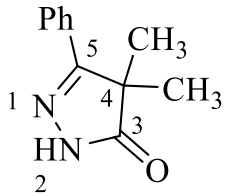
Reaction of Reformatsky reagents with 2,5-diphenyl-1,3,4-oxadiazole

Elena A. Nikiforova, Nikolay F. Kirillov, Daniil V. Baibarodskikh, Sergey N. Shurov,

Maksim V. Dmitriev and Dmitriy P. Zverev

The IR spectra of compounds **3a-d**, **4** and **6a–c** from mulls in mineral oil were measured on a Spectrum Two PerkinElmer Fourier spectrometer. The ^{1}H NMR (400 MHz) and ^{13}C (100 MHz) spectra of compounds **3**, **4** were recorded on a Bruker Avance III HD 400 instrument in $CDC1_3$ with HMDS as an internal standard. The ^{1}H NMR spectra of compounds **6** were recorded on a Varian Mercury Plus-300 spectrometer (300 MHz) in $CDC1_3$ with TMS as internal standard. Elemental analyses were performed on vario MICRO cube elemental analyzer. Melting points were measured with a MP-70 Mettler Toledo.

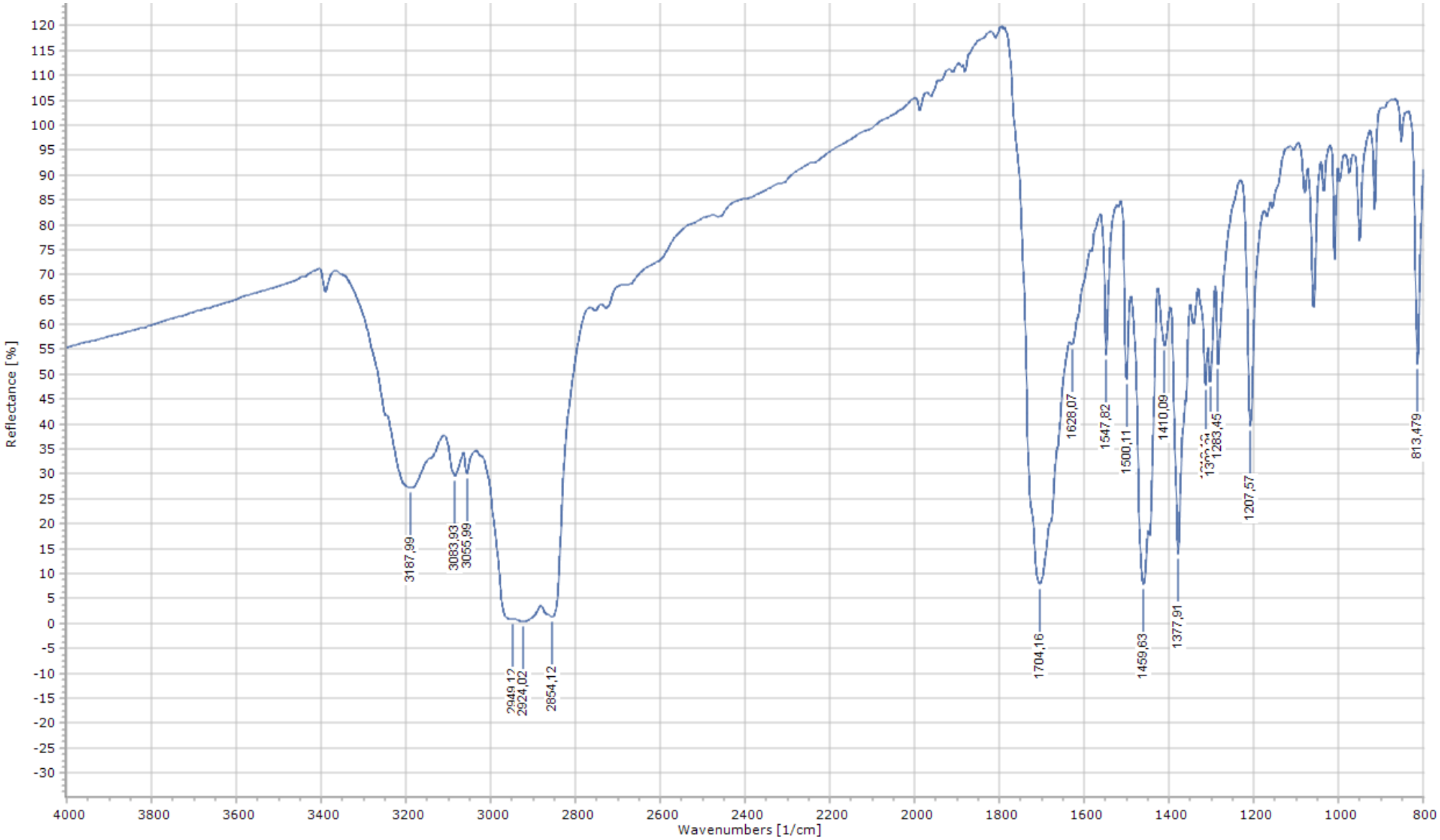
Yields, melting points, spectral and elemental analysis data for compounds 3, 4, 6 and quantum-chemical calculations of proposed mechanism of formation of compound 3a:



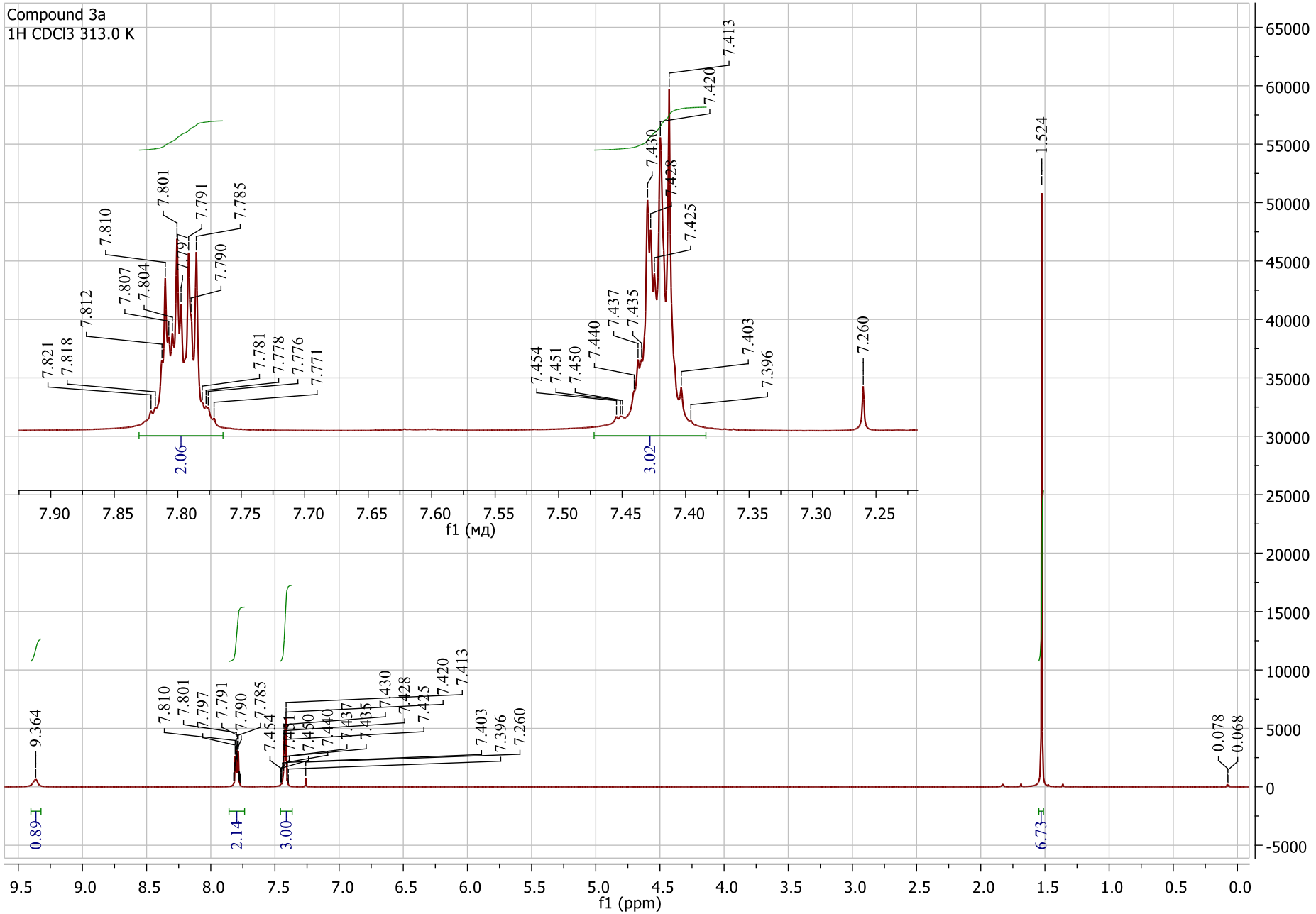
4,4-Dimethyl-5-phenyl-2,4-dihydro-3H-pyrazol-3-one 3a

Yield 36%, mp 116 – 117°C (Lit. mp 117 – 118°C[S1]). IR (ν, cm^{-1}): 3188 (NH), 1704 (C=O). ^{1}H NMR (δ, ppm): 1.52 s (6H, 2 Me), 7.40 – 7.45 m ($3H^{Ar}$), 7.77 – 7.82 m ($2H^{Ar}$), 9.36 s (1H, NH). ^{13}C NMR (δ, ppm): 22.57 (Me), 126.39, 128.93, 130.15, 131.29 (Ph), 163.60 (C=N), 181.71 (C=O). Found (%): C 70.32; H 6.49; N 15.03. Calc. for $C_{11}H_{12}N_2O$ (%): C 70.19; H 6.43; N 14.88.

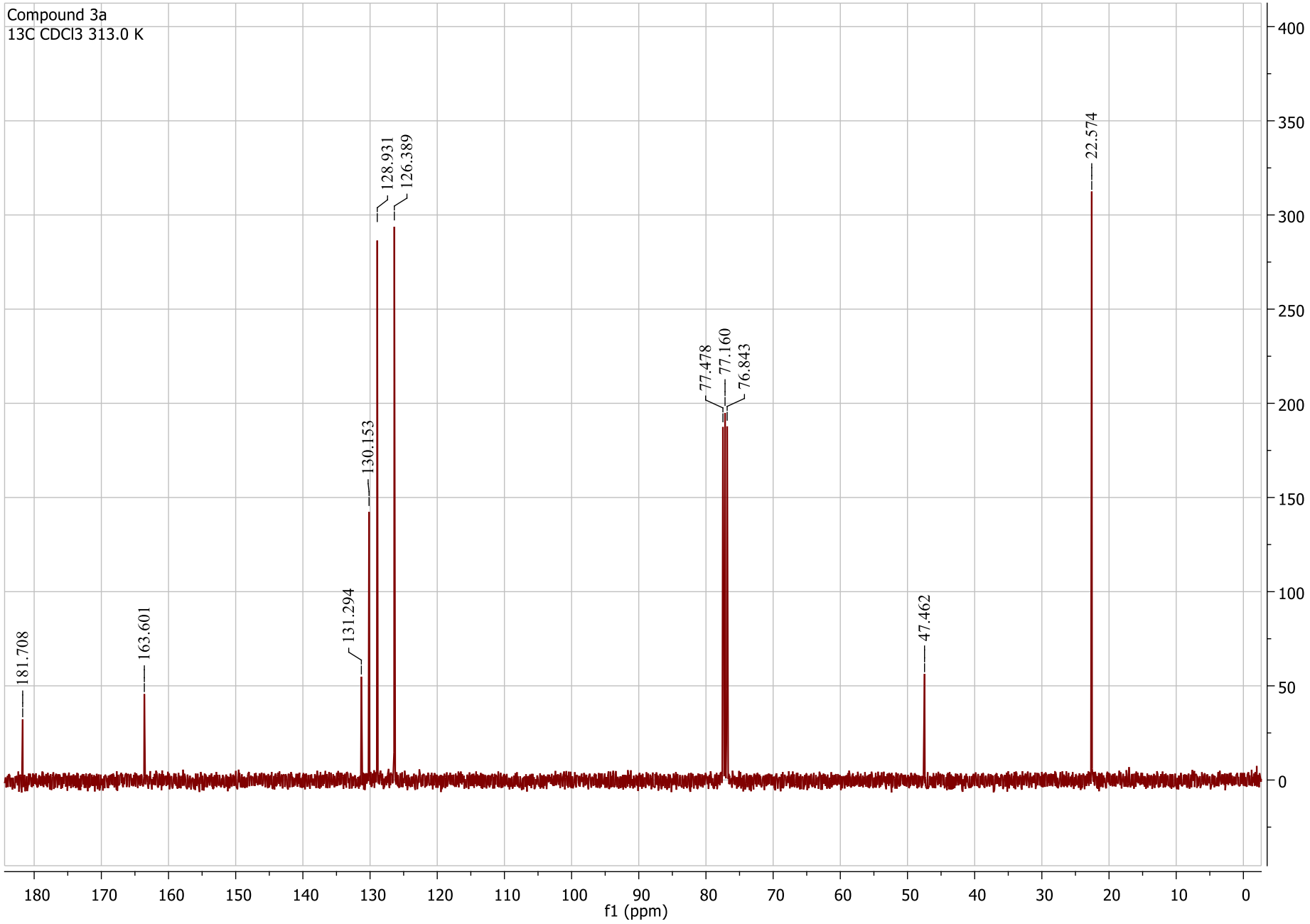
[S1] D.J. Dagli, R.A. Gorski, J.Wemple, *J. Org. Chem.*, 1975, **40**, 1741.



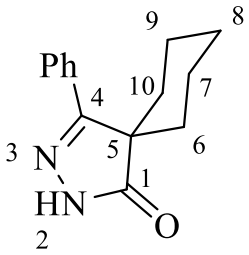
IR spectrum of compound **3a**



NMR ^{1}H spectrum of compound **3a**

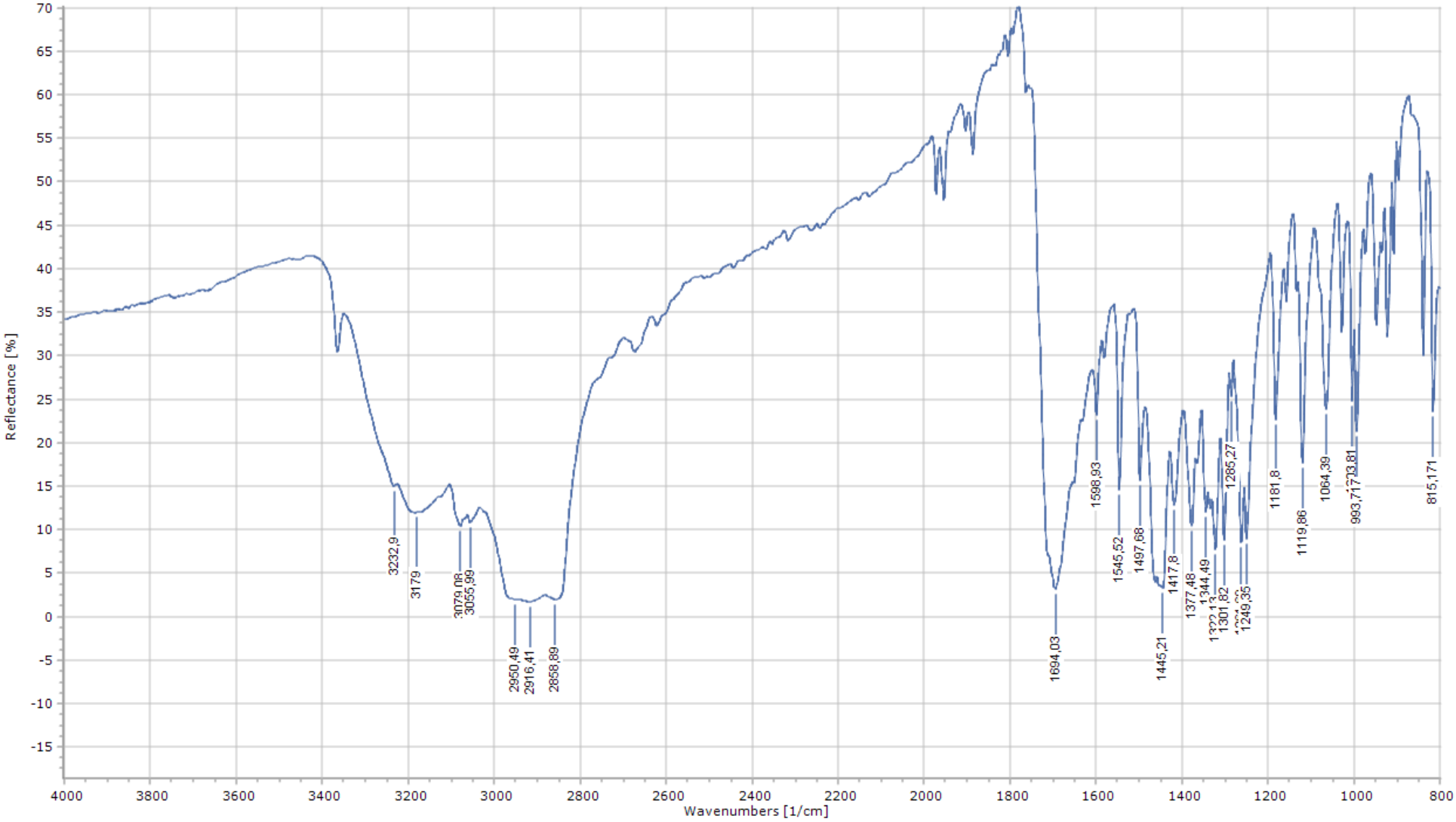


NMR ^{13}C spectrum of compound **3a**

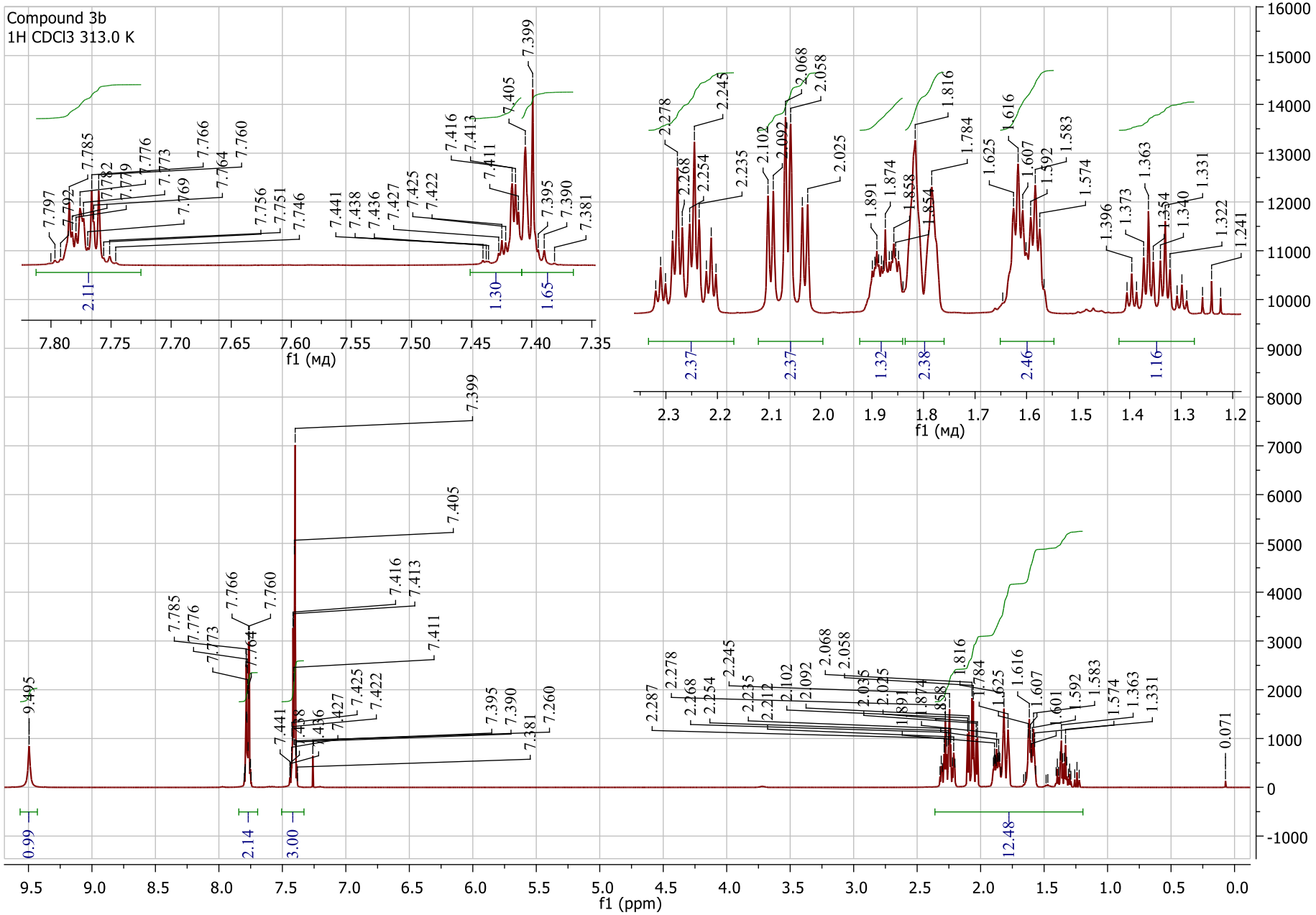


4-Phenyl-2,3-diazaspiro[4.5]dec-3-en-1-one 3b

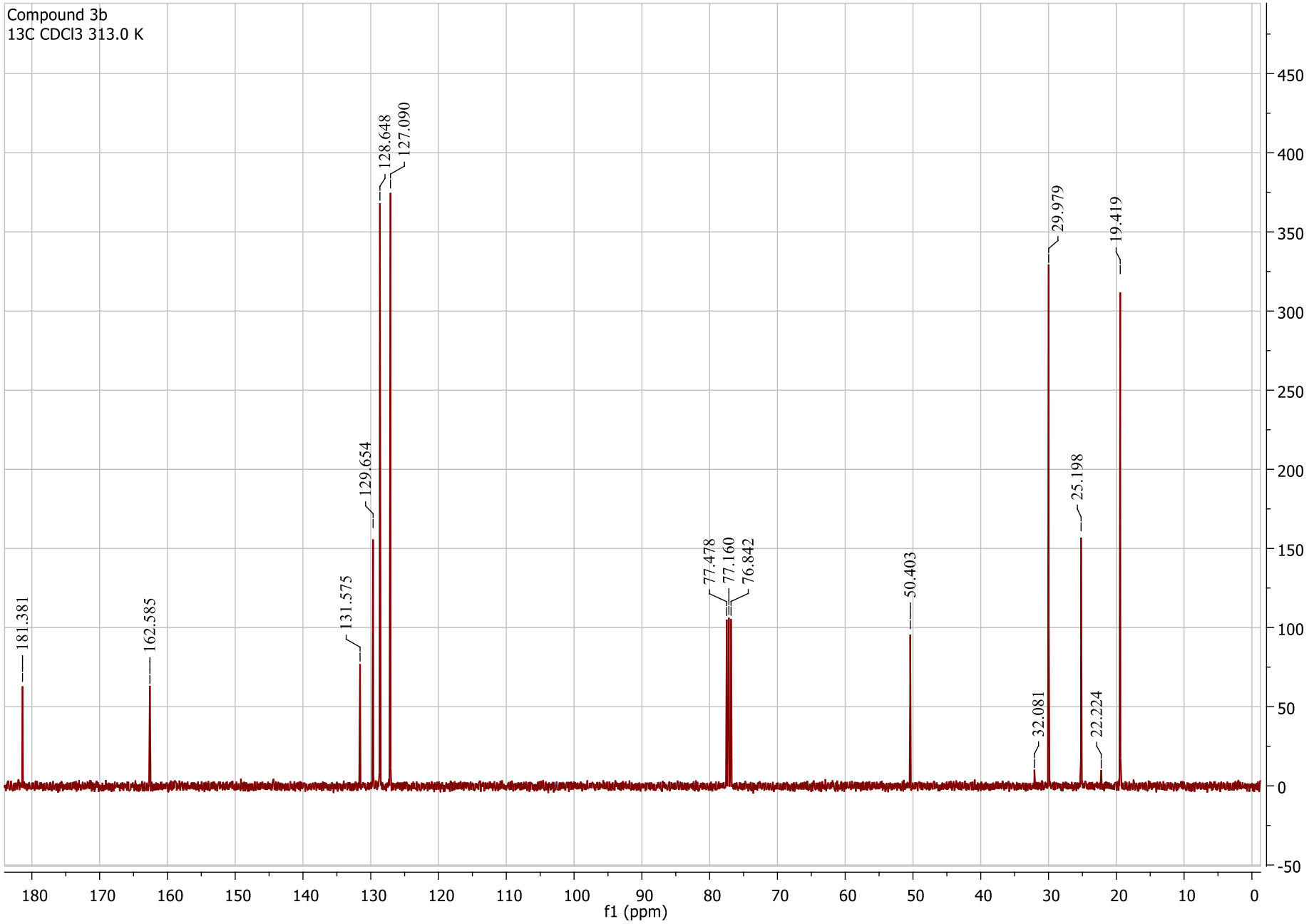
Yield 42 %, mp 155 – 156°C. IR (ν, cm^{-1}): 3179 (NH), 1694 (C=O). ^{1}H NMR (δ, ppm): 1.25 – 2.32 m [10H, $(CH_2)_5$], 7.38 – 7.44 m ($3H^{Ar}$), 7.75 – 7.80 m ($2H^{Ar}$), 9.50 s (1H, NH). ^{13}C NMR (δ, ppm): 19.42, 25.20, 29.98, 50.40 ($C^{cyclohexane}$), 127.09, 128.65, 129.65, 131.58 (Ph), 162.59 (C=N), 181.38 (C=O). Found (%): C 73.78; H 6.93; N 12.49. Calc. for $C_{14}H_{16}N_2O$ (%): C 73.66; H 7.06; N 12.27.



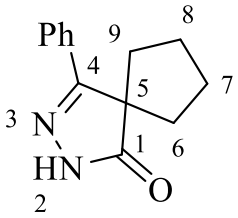
IR spectrum of compound **3b**



NMR ^{1}H spectrum of compound **3b**

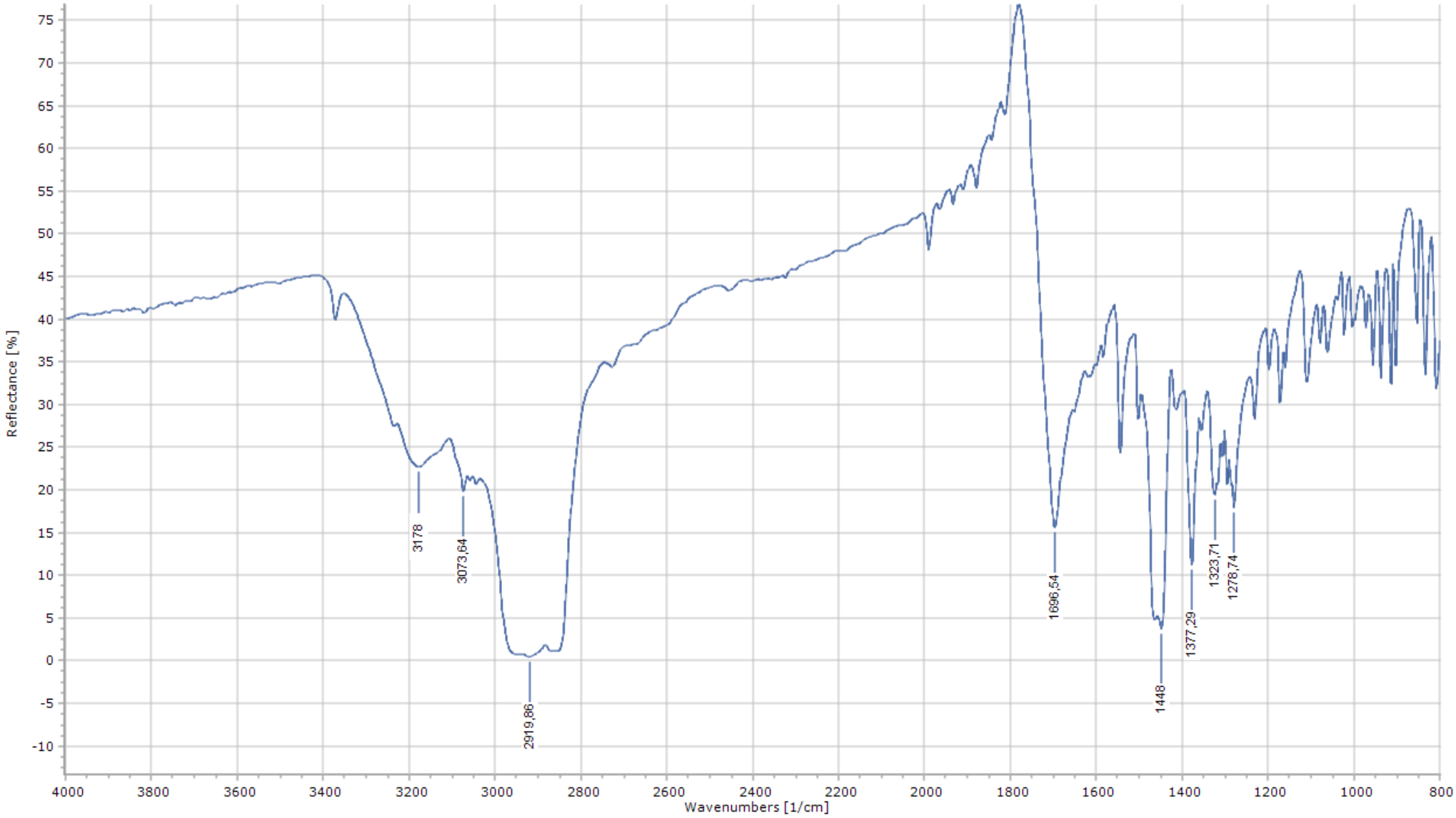


NMR ^{13}C spectrum of compound **3b**

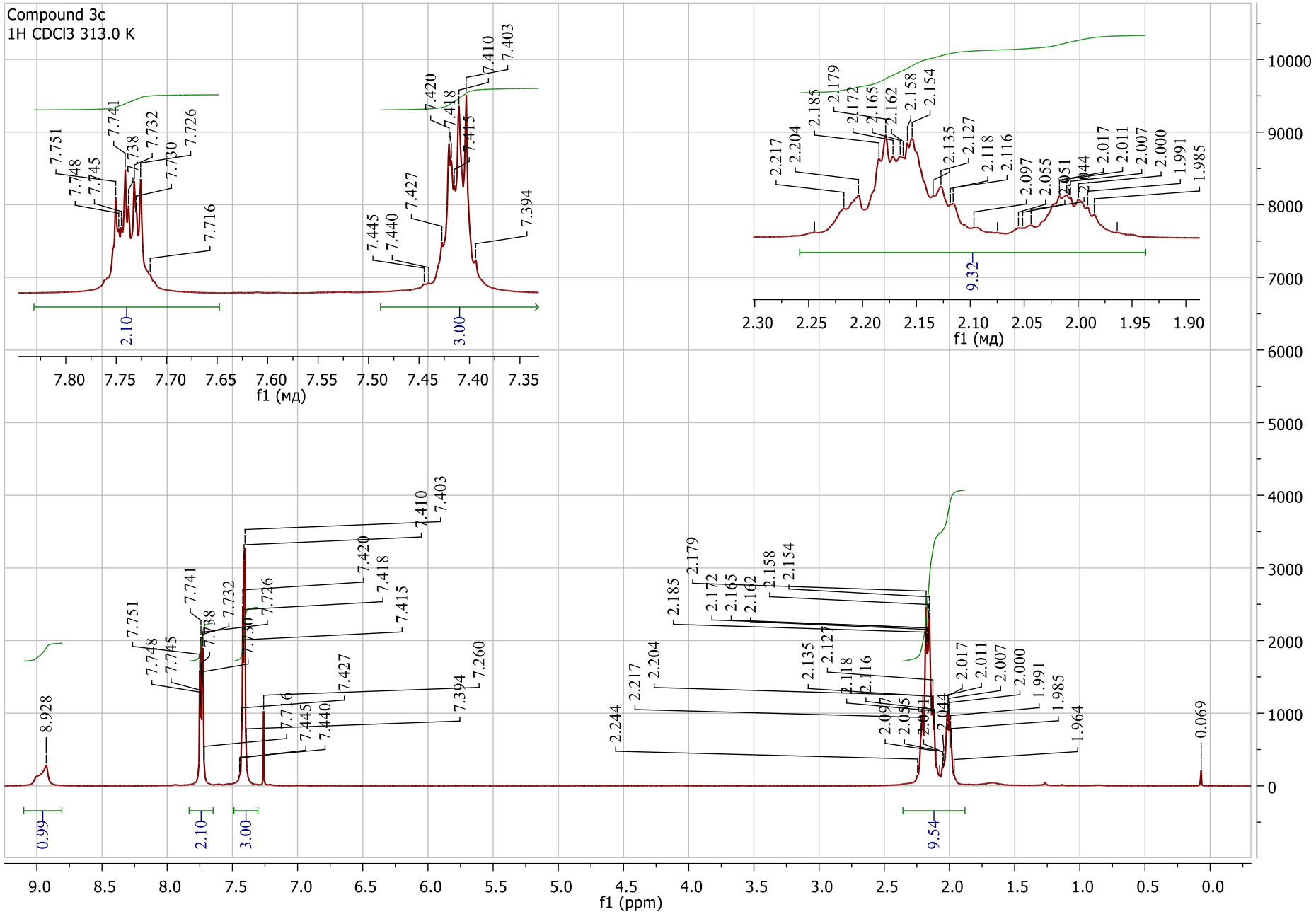


4-Phenyl-2,3-diazaspiro[4.4]non-3-en-1-one 3c

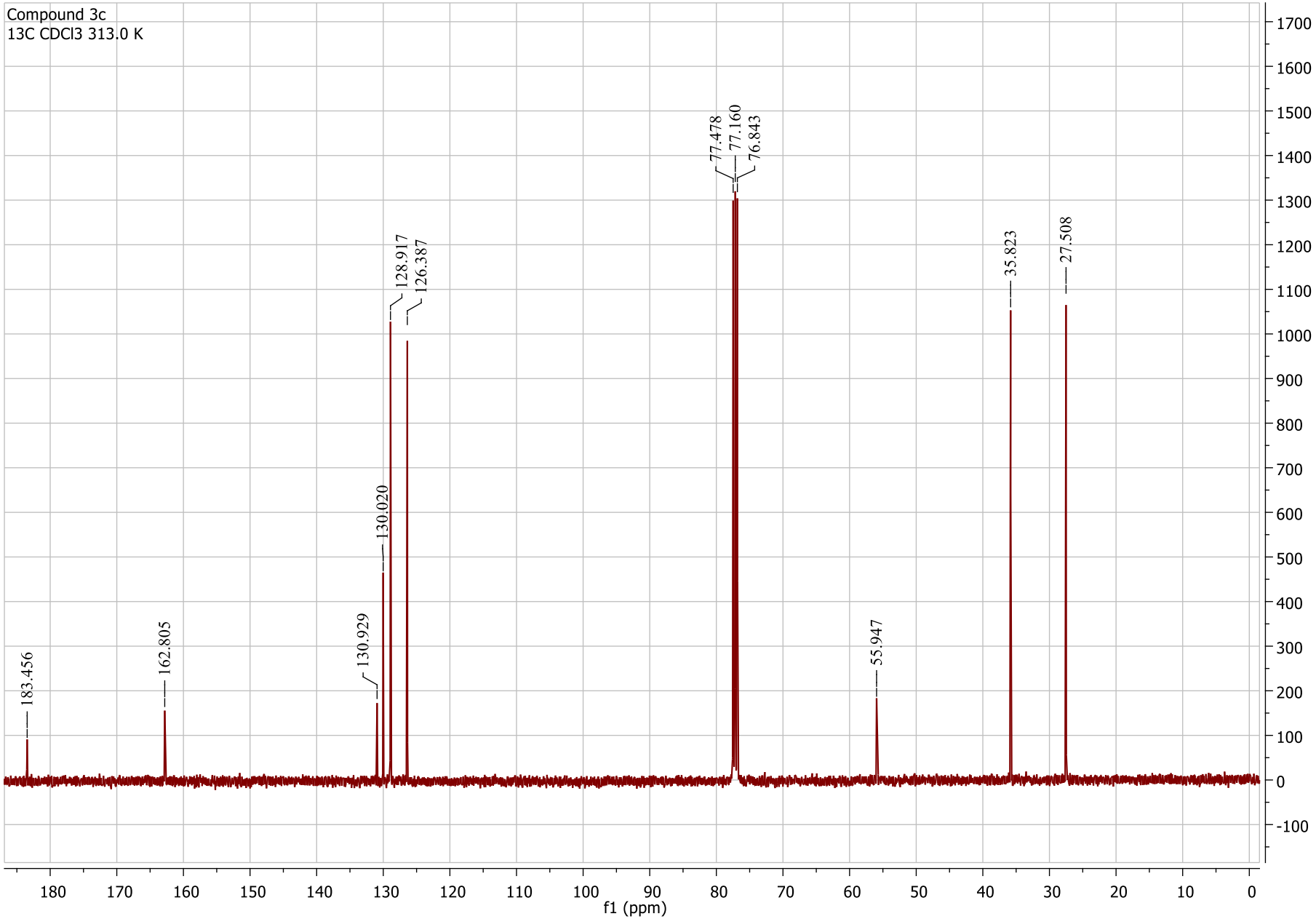
Yield 38 %, mp 182 – 183°C. IR (ν, cm^{-1}): 3178 (NH), 1697 (C=O). ^{1}H NMR (δ, ppm): 1.99 – 2.44 m [8H, $(CH_2)_4$], 7.37 – 7.44 m ($3H^{Ar}$), 7.70 – 7.76 m ($2H^{Ar}$), 8.93 s (1H, NH). ^{13}C NMR (δ, ppm): 27.51, 35.82, 55.95 ($C^{cyclopentane}$), 126.39, 128.92, 130.02, 130.93 (Ph), 162.81 (C=N), 183.46 (C=O). Found (%): C 73.02; H 6.47; N 13.25. Calc. for $C_{13}H_{14}N_2O$ (%): C 72.87; H 6.59; N 13.07.



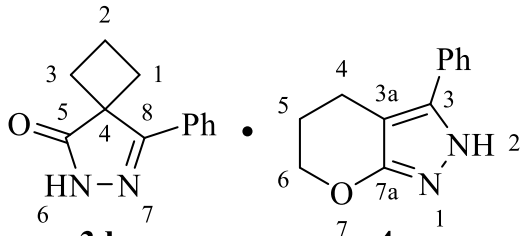
IR spectrum of compound **3c**



NMR ^{1}H spectrum of compound **3c**



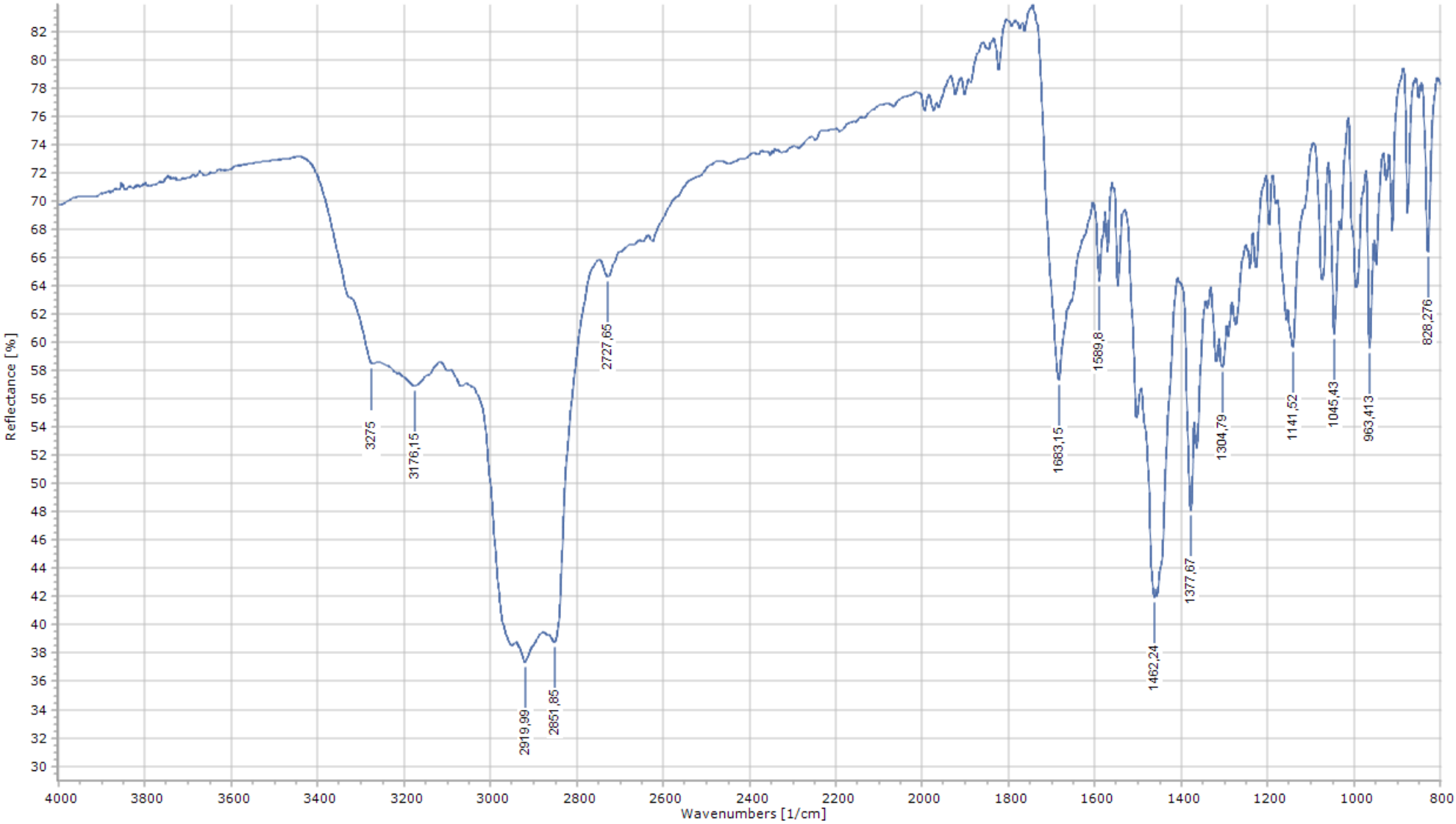
NMR ^{13}C spectrum of compound **3c**



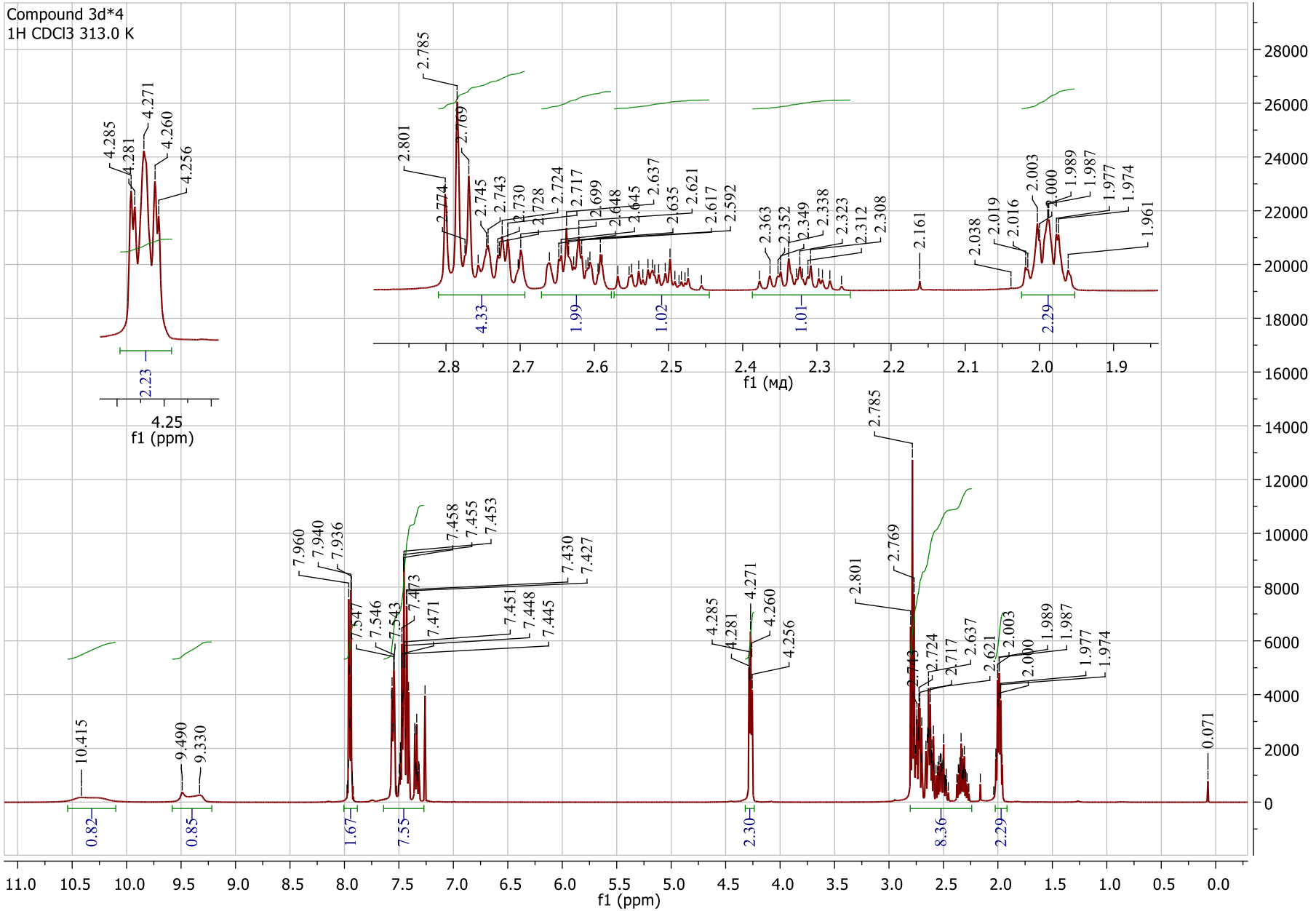
3d • **4**

8-Phenyl-6,7-diazaspiro[3.4]oct-7-en-5-one 3d + 3-phenyl-2,4,5,6-tetrahydropyrano[2,3-*c*]pyrazole 4

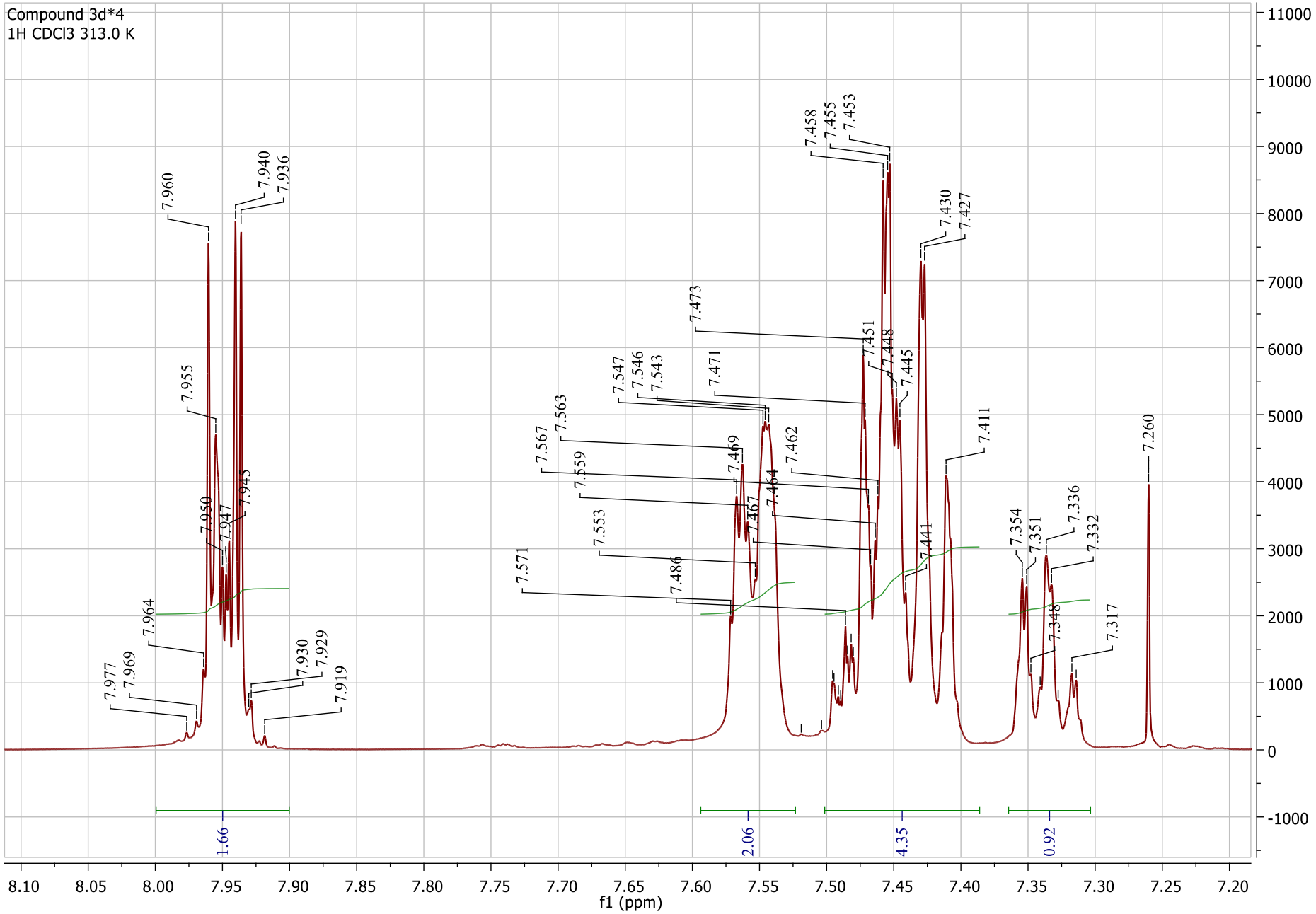
Total yield of co-cristallizate 36% (ratio of spiro compound **3d** and rearrangement product **4** is 1:1), mp 219 – 220°C. IR (ν, cm^{-1}): 3275, 3176 (NH), 1685 (C=O). ^{1}H NMR (δ, ppm): 1.95–2.02 m (2H, $C^{5}H_2$), 2.26–2.76 m [6H, cyclobutane], 2.79 t (2H, $C^{4}H_2$, *J* 6.4 Hz), 4.27 t (2H, $C^{6}H_2$, *J* 5.6 Hz), 7.31-7.57 m, 7.92-7.97 m (10H, 2 Ph), 9.41 br. s (1H, NH), 10.34 br. s (1H, NH). ^{13}C NMR (δ, ppm): 15.93, 19.46, 23.05, 28.44, 49.97, 67.99, 97.22, 125.93, 126.22, 128.17, 128.23, 129.06, 129.09, 130.10, 130.61, 131.64, 160.55, 181.53. Found (%): C 72.11; H 6.12; N 14.18. Calc. for $C_{12}H_{12}N_2O$ (%): C 71.98; H 6.04; N 13.99.



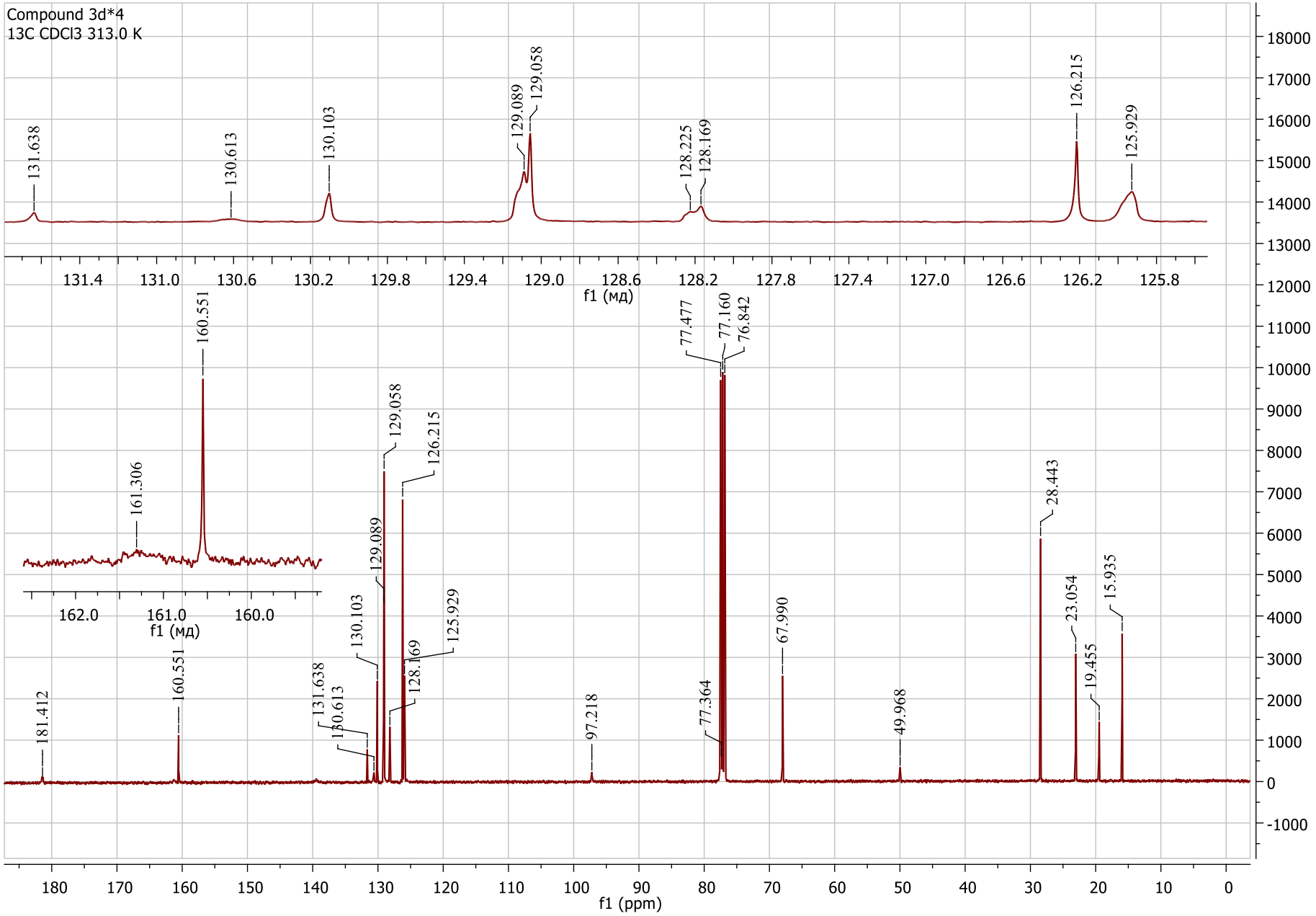
IR spectrum of cocrystallizate **3d** and **4**



NMR ^{1}H spectrum of cocrystallizate **3d** and **4**

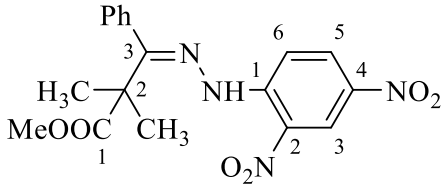


Part of the NMR ^{1}H spectrum of cocrystallizate **3d** and **4**



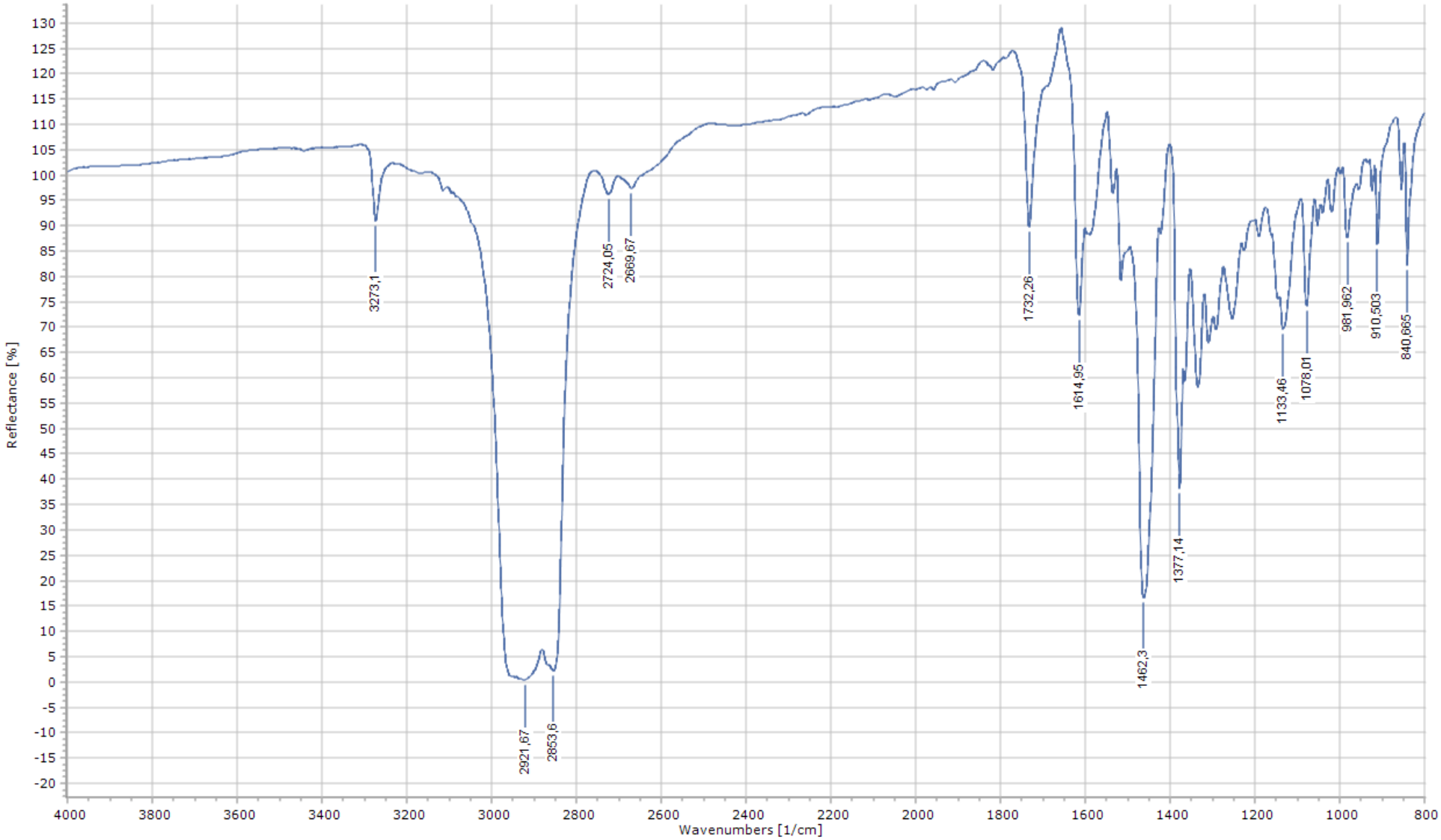
NMR ^{13}C spectrum of cocrystallizate **3d** and **4**

¶ *Oxo ester 2,4-dinitrophenylhydrazones* **6a-c** *(general procedure).* Ethanol solution after separating of the solid products **3a-c** (1 ml) was added to a mixture of 2,4-dinitrophenylhydrazine (0.5 g), concentrated sulfuric acid (1 ml) and anhydrous ethanol (10 ml). After 24 h of storage at ambient temperature, oxo ester 2,4-dinitrophenylhydrazones **6a-c** were filtered off, washed with anhydrous ethanol (5 ml) and recrystallized from ethanol.

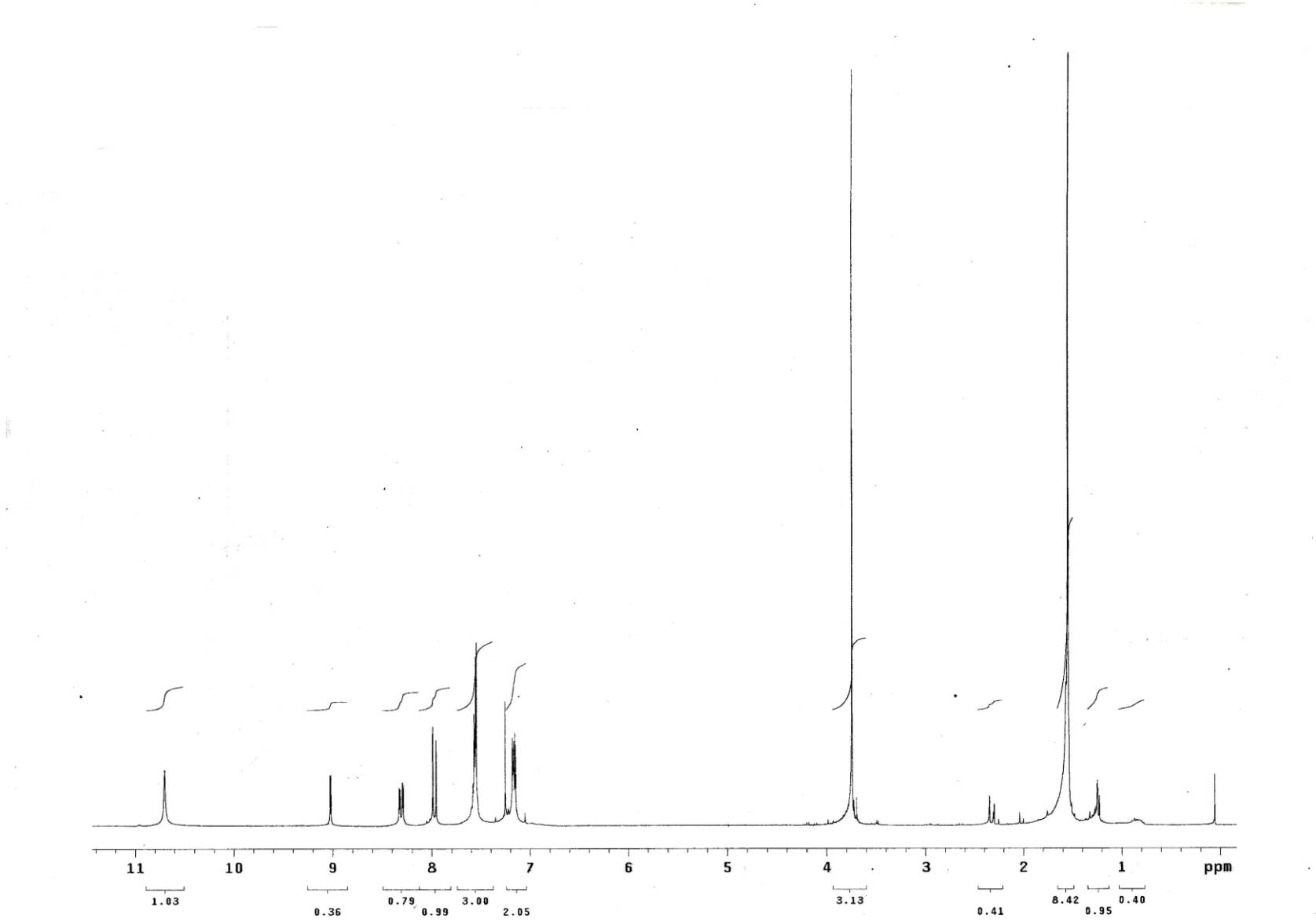


Methyl 3-(2-(2,4-dinitrophenyl)hydrazinylidene)-2,2-dimethyl-3-phenylpropanoate 6a

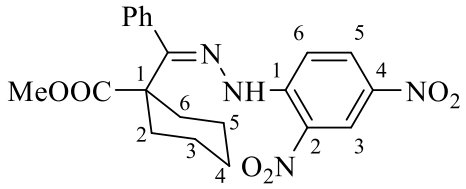
mp 135 – 136°C. IR (ν, cm^{-1}): 3273 (NH), 1732 (C=O). ^{1}H NMR (δ, ppm): 1,54 c (6H, 2 Me), 3.74 s (3H, MeO), 7.14 – 7.20 m ($3H^{Ar}$), 7.53 – 7.60 m ($2H^{Ar}$), 7.97 d ($1H^{Ar}$, *J* 9.6 Hz), 8.31 dd ($1H^{Ar}$, *J* 9.6 Hz, *J* 2.4 Hz), 9.02 d ($1H^{Ar}$, *J* 2.4 Hz), 10.70 s (1H, NH). Found (%): C 56.18; H 4.57; N 14.31. Calc. for $C_{18}H_{18}N_4O_6$ (%): C 55.96; H 4.70; N 14.50.



IR spectrum of compound **6a**

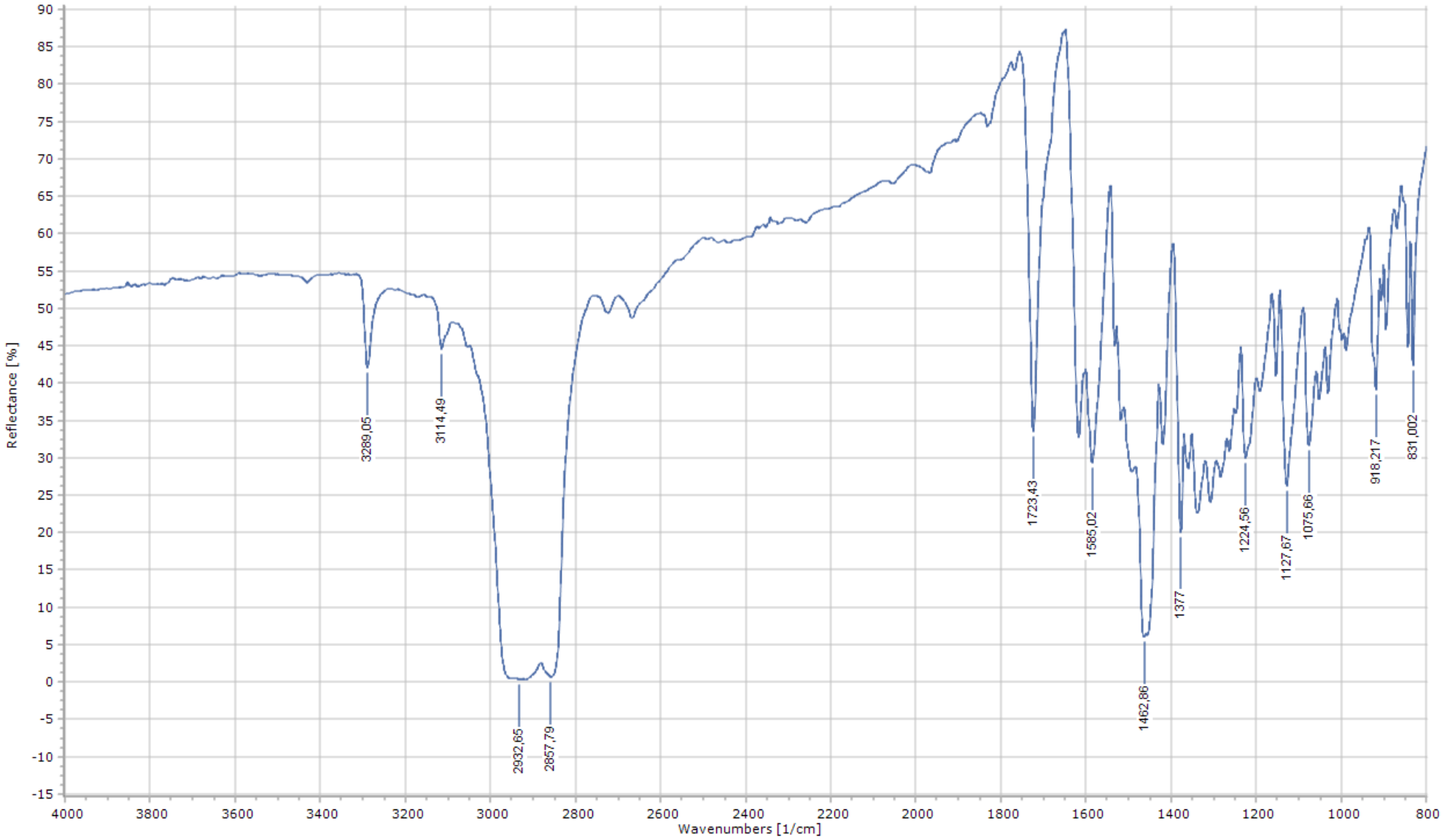


NMR ^{1}H spectrum of compound **6a**

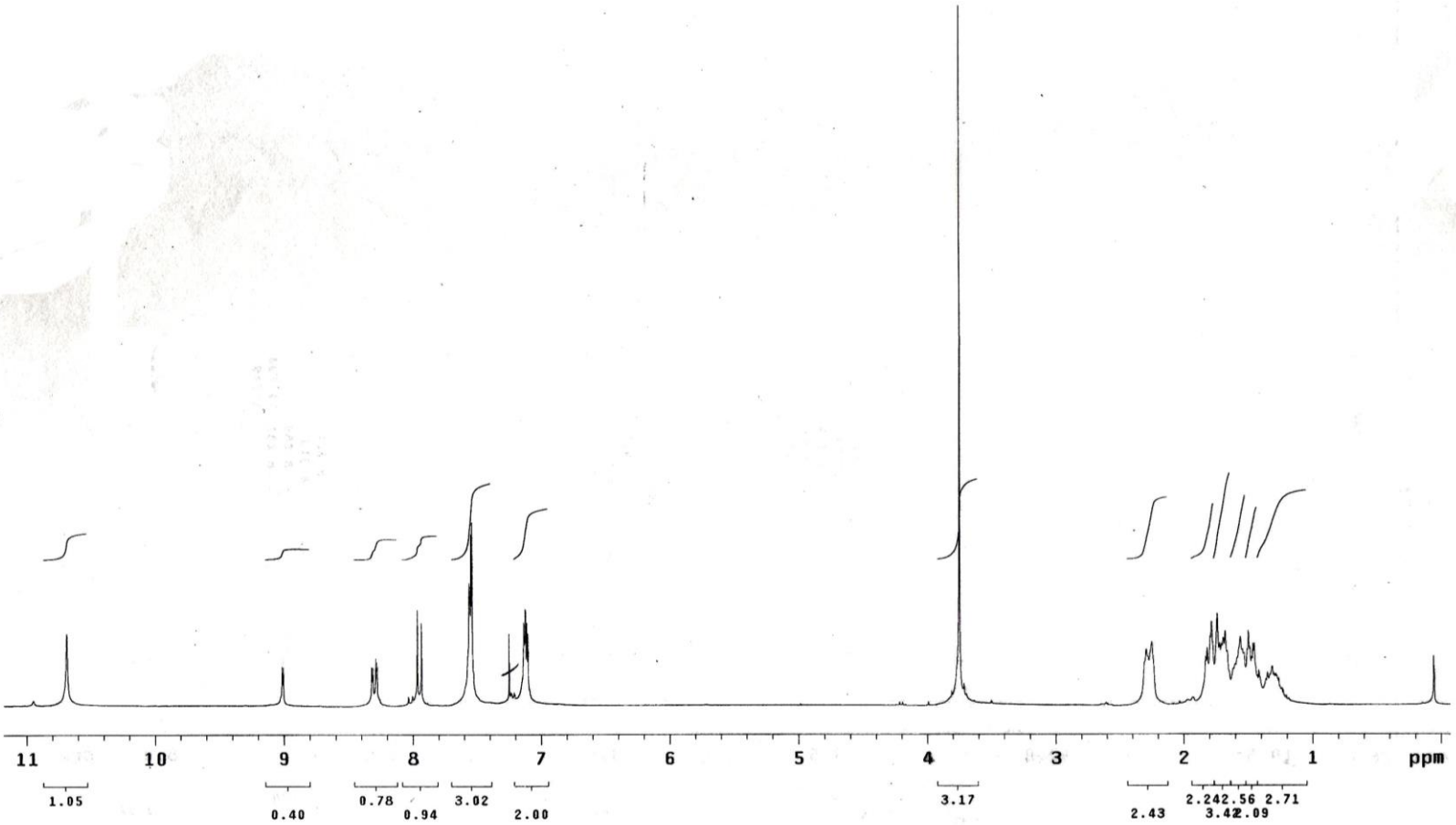


Methyl 1-((2-(2,4-dinitrophenyl)hydrazinylidene)(phenyl)methyl)cyclohexane-1-carboxylate 6b

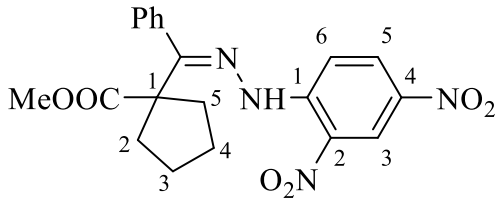
mp 133 – 135°C. IR (ν, cm^{-1}): 3289 (NH), 1723 (C=O). ^{1}H NMR (δ, ppm): 1.22 – 2.32 m [10H, $(CH_2)_5$], 3.75 s (3H, MeO), 7.10 – 7.14 m ($3H^{Ar}$), 7.53 – 7.57 m ($2H^{Ar}$), 7.95 d (1H, $2H^{Ar}$, *J* 9.6 Hz), 8.30 dd (1H, H^{Ar}, *J* 9.6 Hz, *J* 2.4 Hz), 9.01 d (1H, H^{Ar}, *J* 2.4 Hz), 10.69 s (1H, NH). Found (%): C 58.96; H 5.31; N 13.27. Calc. for $C_{21}H_{22}N_4O_6$ (%): C 59.15; H 5.20; N 13.14.



IR spectrum of compound **6b**

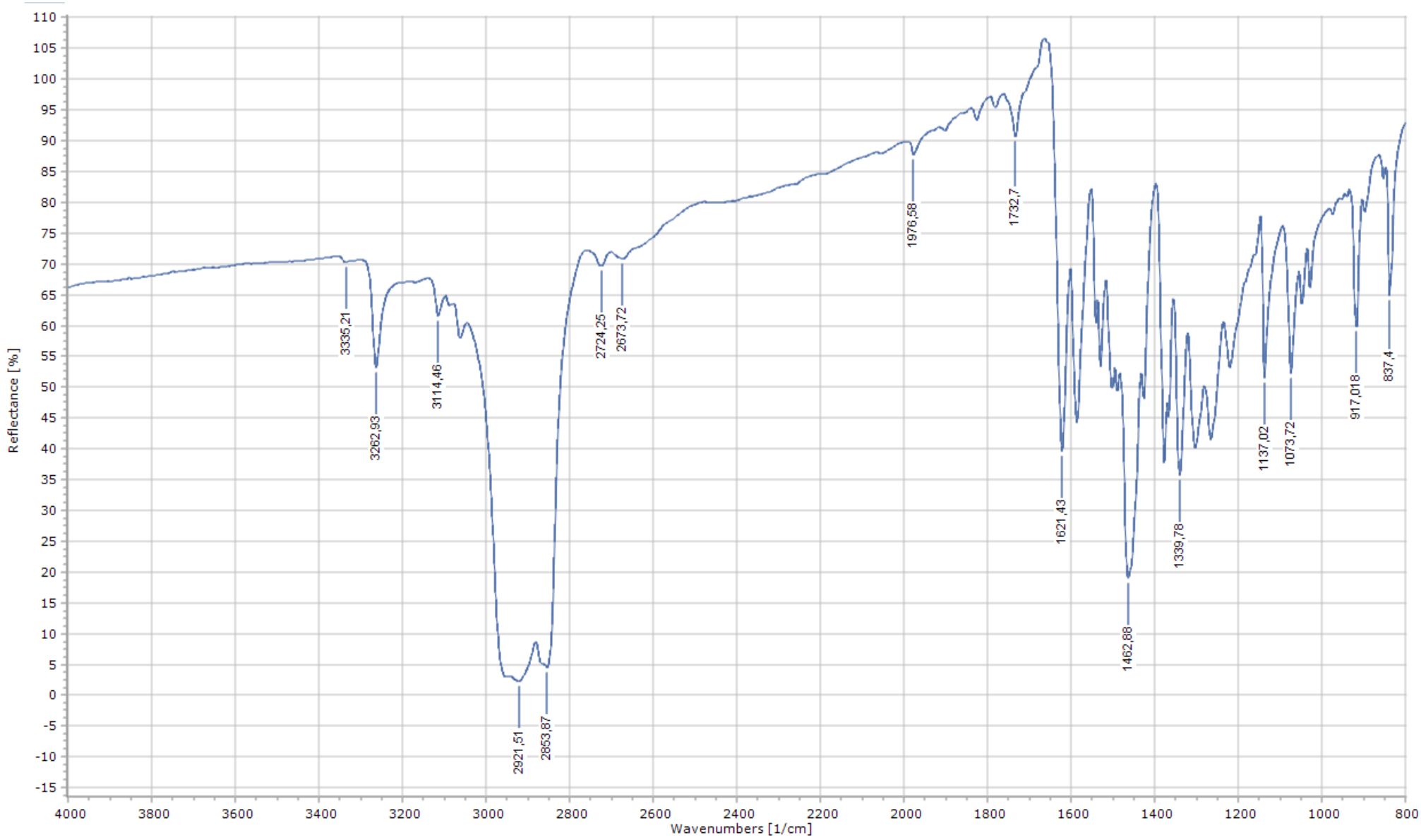


NMR ^{1}H spectrum of compound **6b**

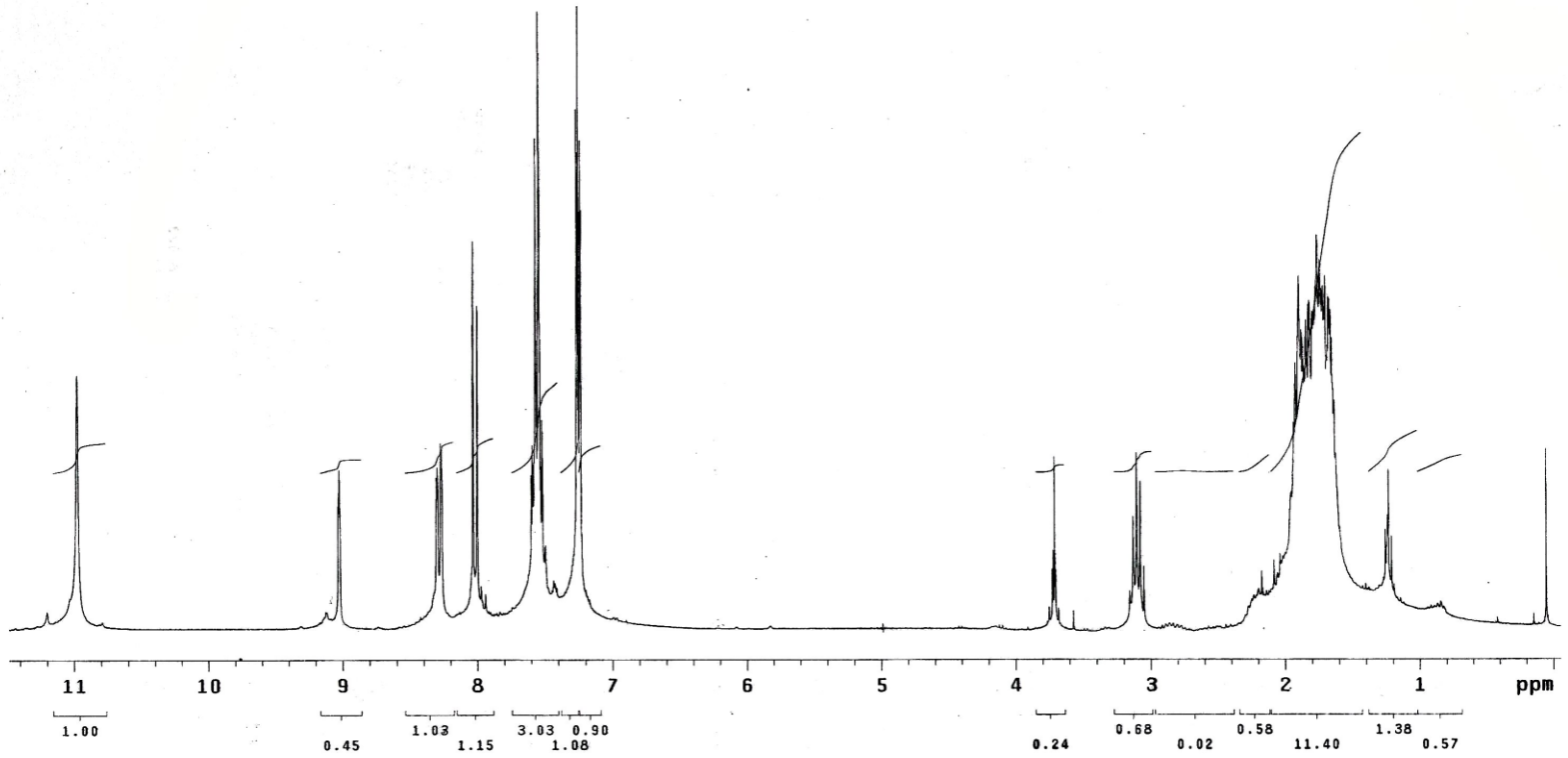


Methyl 1-((2-(2,4-dinitrophenyl)hydrazinylidene)(phenyl)methyl)cyclopentane-1-carboxylate 6c

mp 129 – 131°C. IR (ν, cm^{-1}): 3262 (NH), 1733 (C=O). ^{1}H NMR (δ, ppm): 1.38 – 2.32 m [8H, $(CH_2)_4$], 3.70 s (3H, MeO), 7.14 – 7.23 m ($3H^{Ar}$), 7.52 – 7.57 m ($2H^{Ar}$), 7.84 d ($1H^{Ar}$, *J* 9.6 Hz), 8.29 dd ($1H^{Ar}$, *J* 9.6 Hz, *J* 2.1 Hz), 9.09 d ($1H^{Ar}$, *J* 2.1 Hz), 9.42 br. s (1H, NH). Found (%): C 58.09; H 4.97; N 13.76. Calc. for $C_{20}H_{20}N_4O_6$ (%): C 58.25; H 4.89; N 13.59.



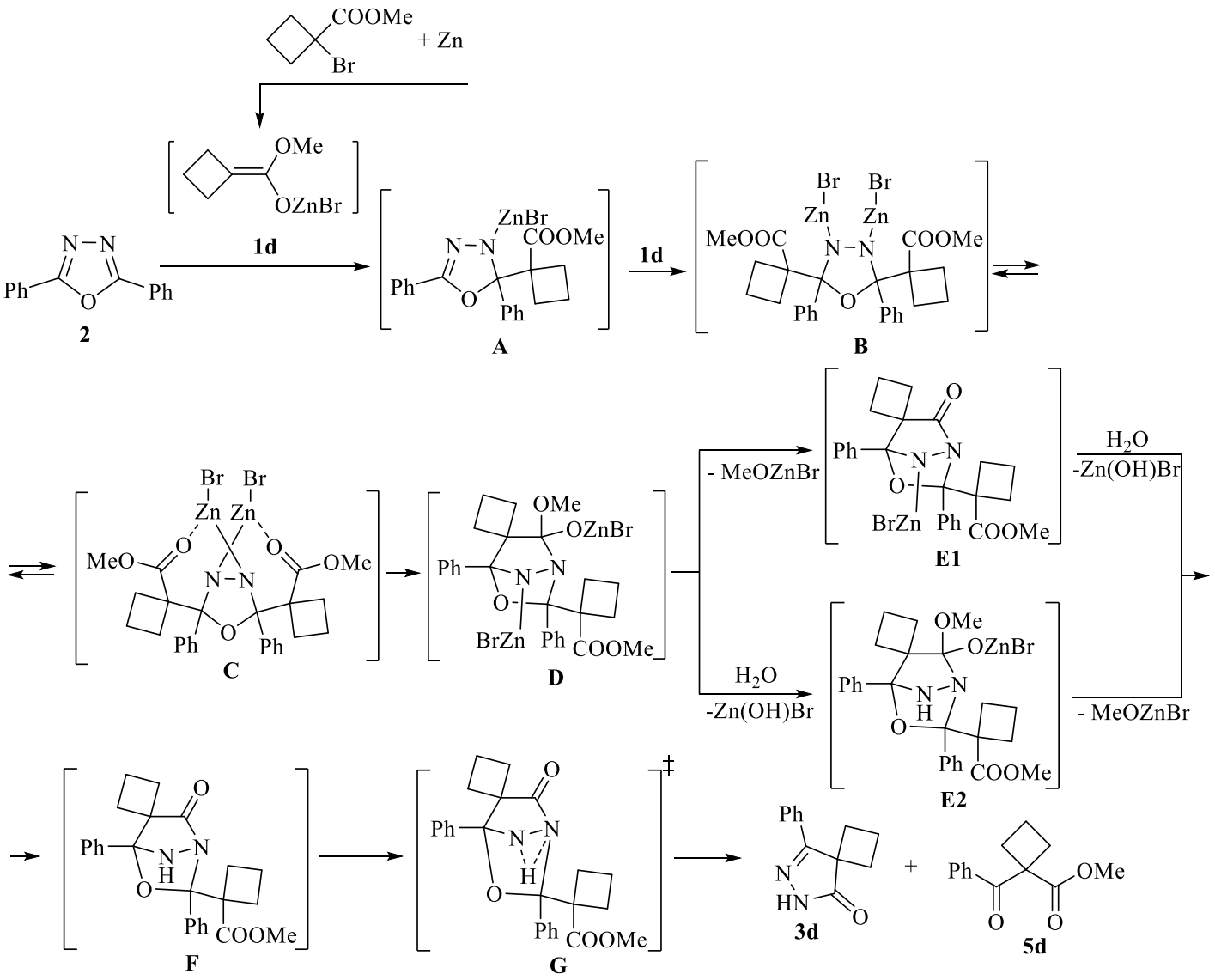
IR spectrum of compound **6c**



NMR ^{1}H spectrum of compound **6c** (solvate with EtOH)

Quantum-chemical calculations of energy, electronic and geometric characteristics of probable intermediates using the using the B3LYP density functional and the 6-311G(d) basis set for reaction of oxadiazole 2 with Reformatsky reagent 1d

Apparently, Reformatsky's reagent **1d** reacts with oxadiazole **2** in cyclobutylidene form ($E_{tot.}$ = -4737.9041 hartree). This form is characterized not only by the C=C–O–Zn covalent bond (its length is 1.854 Å), but also by the MeO···Zn coordination bond (2.134 Å). The nucleophilic center of molecule **1d** is the C^1 carbon atom of the cycle (charge -0.044 a.u.). According to calculations the molecule of oxadiazole **2** ($E_{tot.}$ = -724.4029 hartree) is planar, which favors the attachment of the Reformatsky reagent **1d** to the C^2=N^3 bond (the



charges of these atoms are +0.347 and -0.234 a.u., respectively). The formation of the intermediate **A** ($E_{tot.}$ = -5462.3670 hartree) is energetically favorable, since the value of its $E_{tot.}$ is 0.058 hartree less than the total energy of compounds **1d** and **2**. In the intermediate **A**, along with the C^2–C (1.562 Å) and N^3–Zn (1.852 Å) bonds, there is an additional coordination bond of the zinc atom and the oxygen atom Zn···O=C-OMe (2.083 Å). In the intermediate **A**, the charges of the reaction centers are C^5 +0.350 and N^4 -0.177 a.u., which does not prevent the addition of the second molecule of the Reformatsky reagent **1d** and the formation of the intermediate **B** ($E_{tot.}$ = -10200.3425 hartree). In this intermediate, both N–Zn bonds are equal (it's length is 1.850 Å). The MeO–C=O···Zn interatomic distances are also the same and value to 2.152 Å. The formation of the intermediate **B** can also be considered energetically favorable, since its total energy is 0.070 hartree less than the sum of the total energies of the intermediate **A** and the Reformatsky reagent **1d**. Further, from our point of view, the intermediate **B** is isomerized into the intermediate **C** ($E_{tot.}$ = -10200.3381 hartree), which differs in a coordination of the zinc and oxygen atoms of the ester groups. Due to the deformation of the oxadiazolidine ring, the N–Zn bonds lose their equivalence and slightly elongate to 1.875 and 1.897 Å. The MeO–C=O···Zn interatomic distances become shorter (2.065 and 2.046 Å). Despite the fact that the intermediate **C** is characterized by a calculated total energy by 0.0044 hartree higher than the intermediate **B**, its formation is postulated by us, since it explains the further course of the reaction. In the intermediate **C**, it becomes possible to transfer the ZnBr group bonded to the nitrogen atom N^4 to the oxygen atom of the fragment bonded to C^2, which leads to the intermediate **D** ($E_{tot.}$ = -10200.3097 hartree). Under the experimental conditions, the intermediate **D** cleaves the methoxyzinc bromide molecule ($E_{tot.}$ = -4468.4908 hartree) and converts into the intermediate **E1** ($E_{tot.}$ = -5731.7717 hartree) or hydrolyzes to the intermediate **E2** ($E_{tot.}$ = -5847.5336 hartree). The

total energy of methoxyzinc bromide and intermediate **E1** is 0.0472 hartree higher than the energy of intermediate **D**, while the total energy of intermediate **E2** and zinc bromide hydroxide is 0.0290 hartree higher than the total energy of intermediate **D** and water ($E_{tot.}$= -76.4339 hartree). Based on these data, it can be assumed that the hydrolysis of the **D** intermediate is preferable. Each of these intermediates under the conditions of further hydrolysis is converted into intermediate **F** ($E_{tot.}$ = -1378.9959 hartree). In this intermediate, the N^7–H bond length is 1.017 Å, N^1···H = 2.028 Å, N^1–N^7 is 1.460 Å. Proton migration from the "bridge" nitrogen atom N^7 to the N^1 atom through the activated complex **G** ($E_{tot.}$ = -1378.8747 hartree) gives product **3d** and ester **5d**. In **G**, the N^7···H and N^1···H interatomic distances become equal to 1.287 and 1.182 Å, respectively, and the N^1···N^7 interatomic distance increases to 1.616 Å. Based on quantum-chemical calculations, the interaction scheme can be represented as follows:

1d + **2** → **A** → **B** → **C** → **D** → **E2** → **F** → **G** → **3d** + **5d**