Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting information

for

Experimental and computational study of BF_3-catalyzed transformations of *ortho*-(pivaloylaminomethyl)benzaldehydes: an unexpected difference from TFA catalysis

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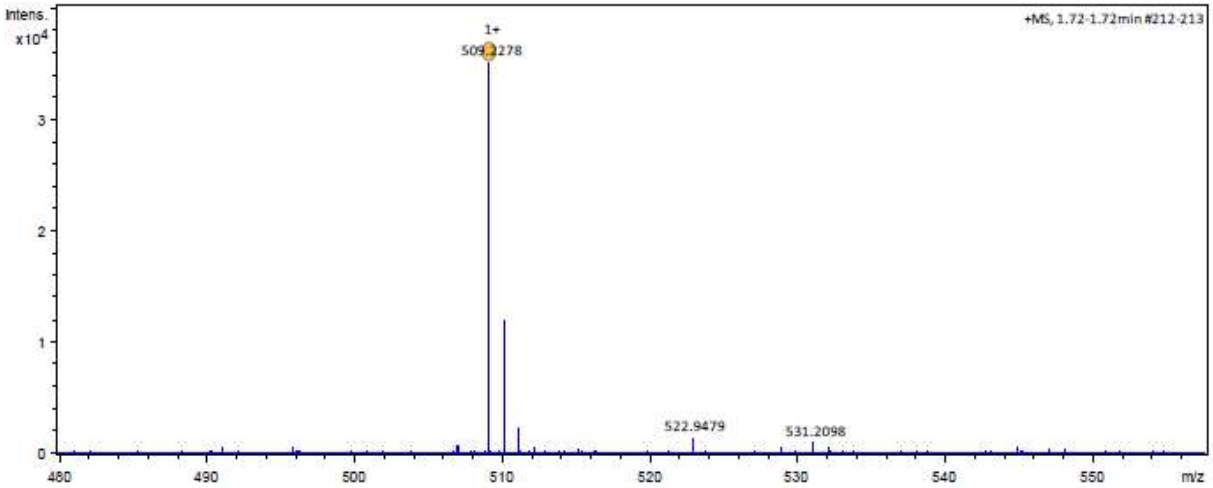
S4. Compound **13**, description of structure determination

The molecular formula of compound **10** was established as $C_{28}H_{32}N_2O_7$ by means of HRMS (page S5), indicating the presence of 14 double bond equivalents. Based on ^1H and ^{13}C NMR data (see pages S6–S14), this compound therefore contains 5 rings and 9 double bonds, which corresponds to two phenyl groups, two pivaloyl amide moieties N-C=O (δ177.73 and δ176.86 ppm) and one conjugated C=O group (δ198.63 ppm). The ^1H,^1H-COSY experiment (page S7) revealed the connectivity of the ^1H signals. To achieve an unambiguous assignment of the overlapping aromatic ^1H signals, selective one-dimensional TOCSY experiment on δ7.78d signal (page S7) was also performed. Steric hydrogen-hydrogen proximities detected by two-dimensional NOESY (page S8) supported the differentiation of the two pivaloyl groups. However, due to the much higher resolution of the selective one-dimensional NOE experiments on the δ5.19, 5.06 and 6.51 signals, even the selective detections of the interacting ^1H signals (page S9) were achieved. The edited HSQC spectrum (page S11) served as the unambiguous $^1H/^{13}C$ signal assignment even in case of the very close δMe_3 (27.40 and 27.16 ppm) signals. Quaternary carbon signals and also the connectivity of the various structural units of the molecule were identified on the basis of the HMBC spectrum (page S12). Out of the four aromatic =CH signals, only δ7.78d gave a HMBC cross-peak with the ketone C=O (δ198.63 ppm), its connection to this aromatic ring is thus straightforward. In order to achieve the required extremely high ^{13}C chemical shift resolution in cases of close ^{13}C signals, the band-selective HMBC experiment (pages S13–14) proved to be the method of choice. Finally, structure of compound **10** was also confirmed by single-crystal X-ray measurement.

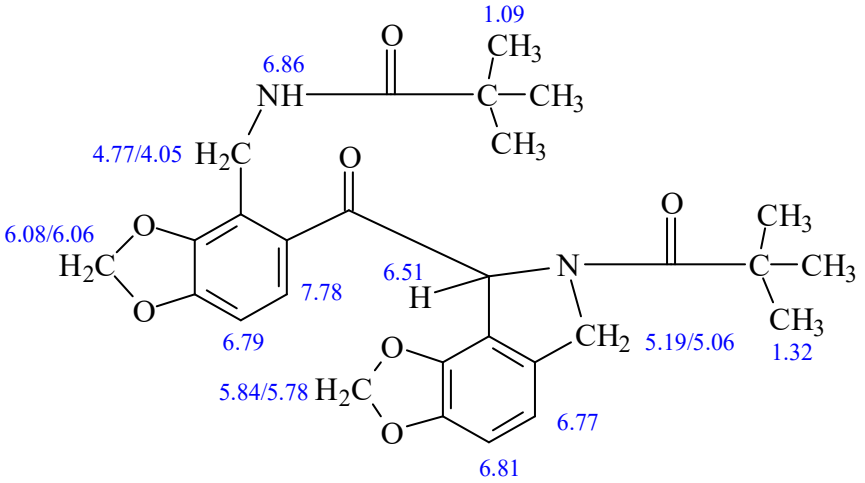
S5. Compound **13**, HRMS

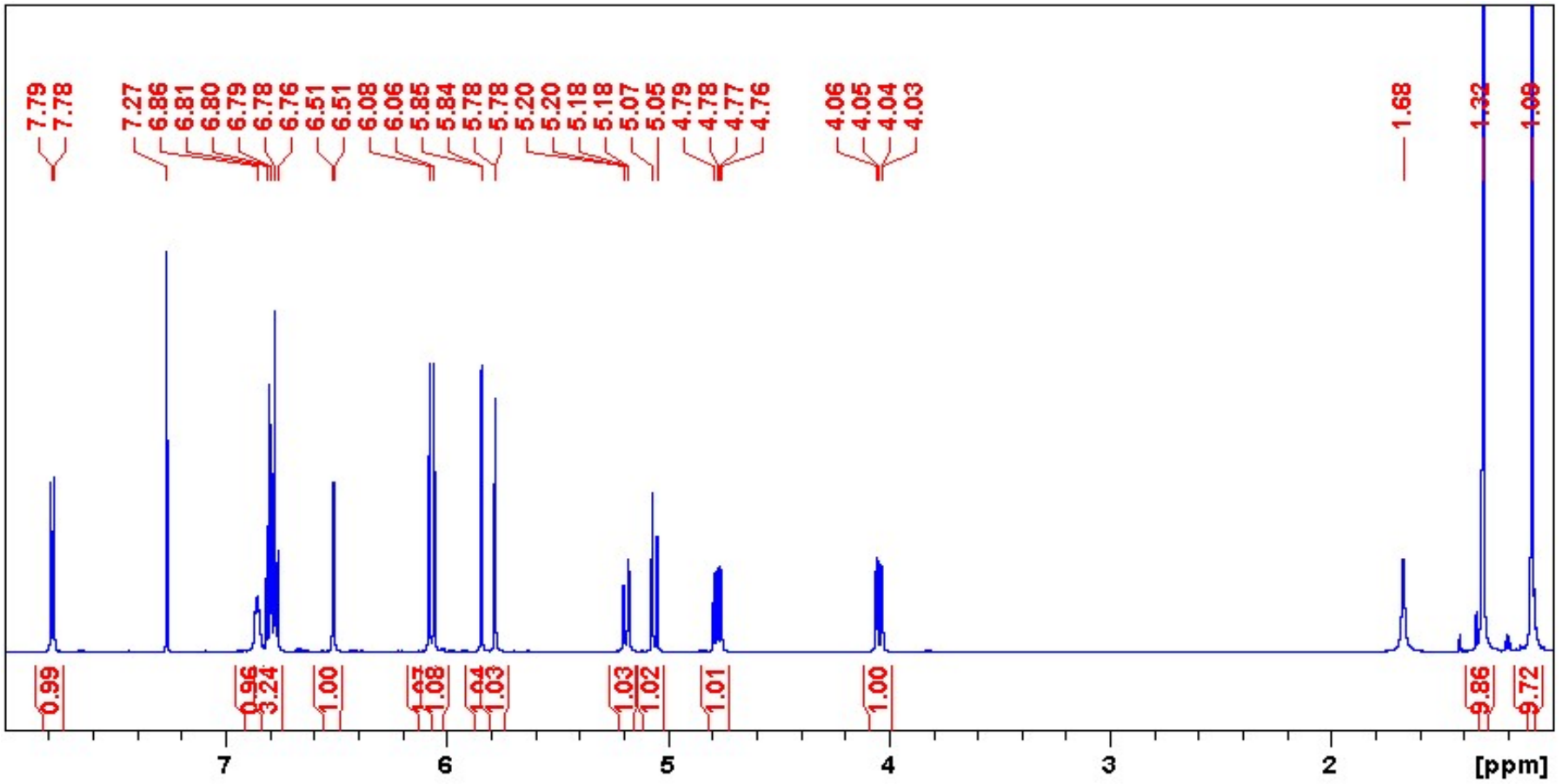
MH+:509.2288
C28H33N2O7



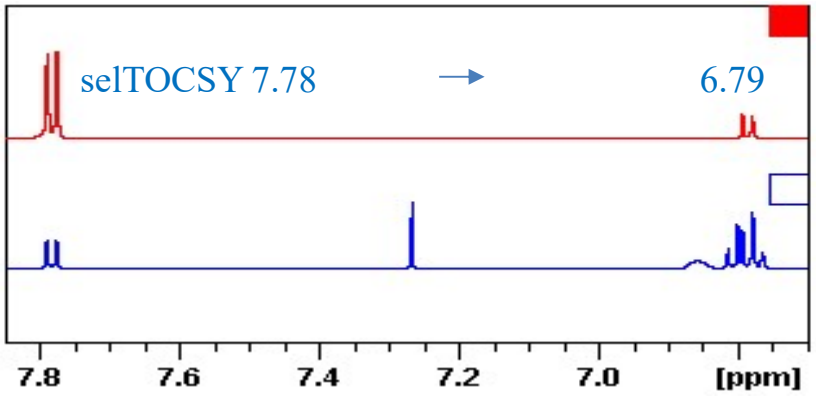
Meas. m/z	Ion Formula	m/z	|err| [ppm]
509.2278	C28H33N2O7	509.2282	0.9

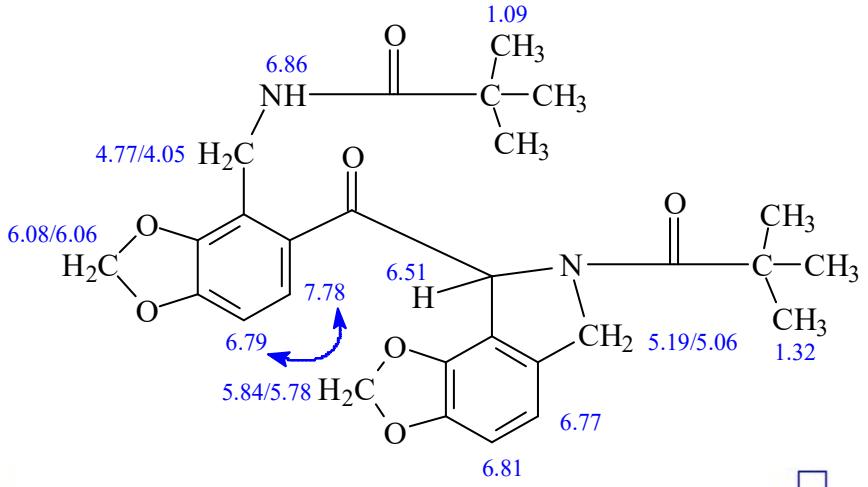
S6. Compound **13**, ^{1}H (600 MHz, $CDCl_3$)

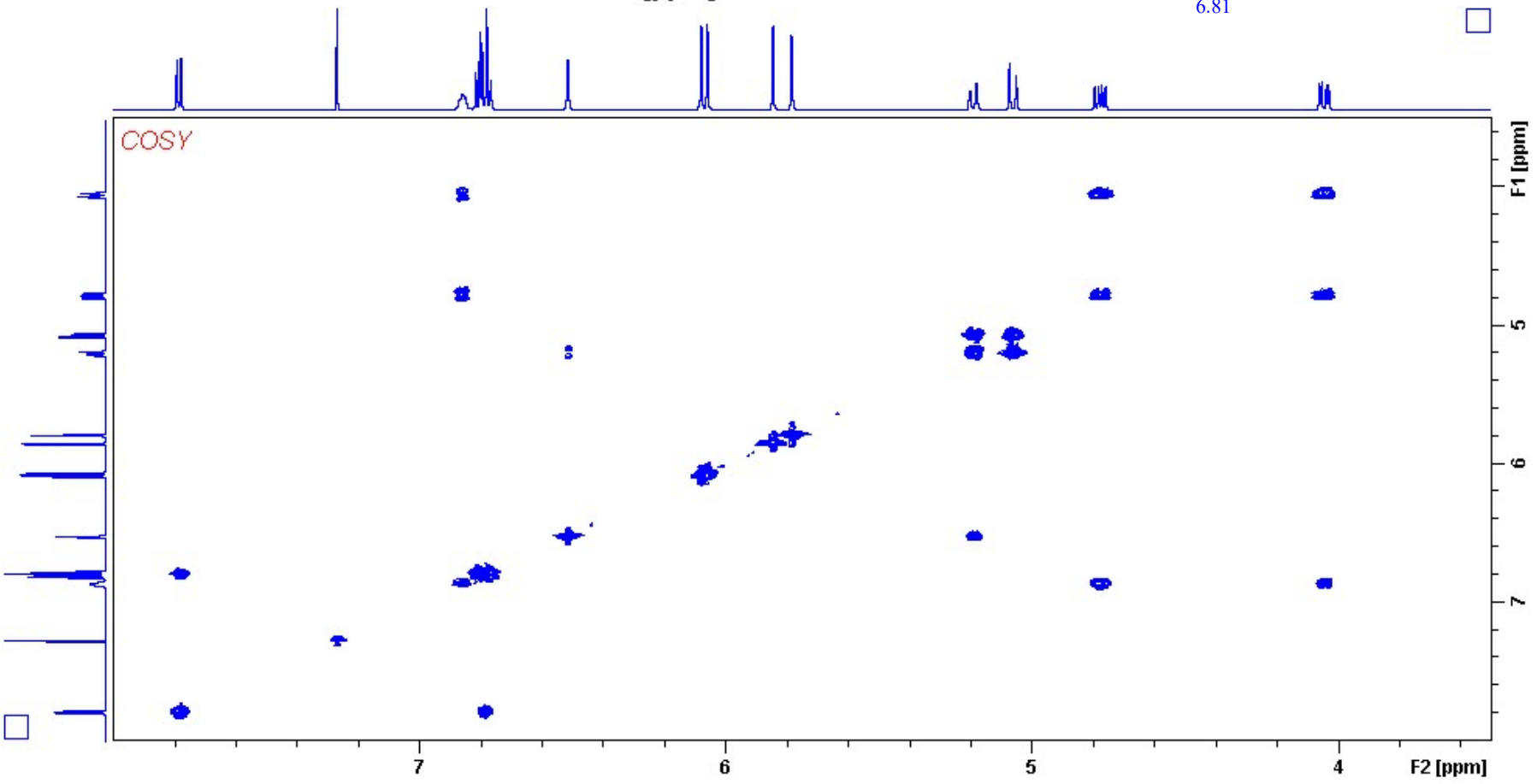




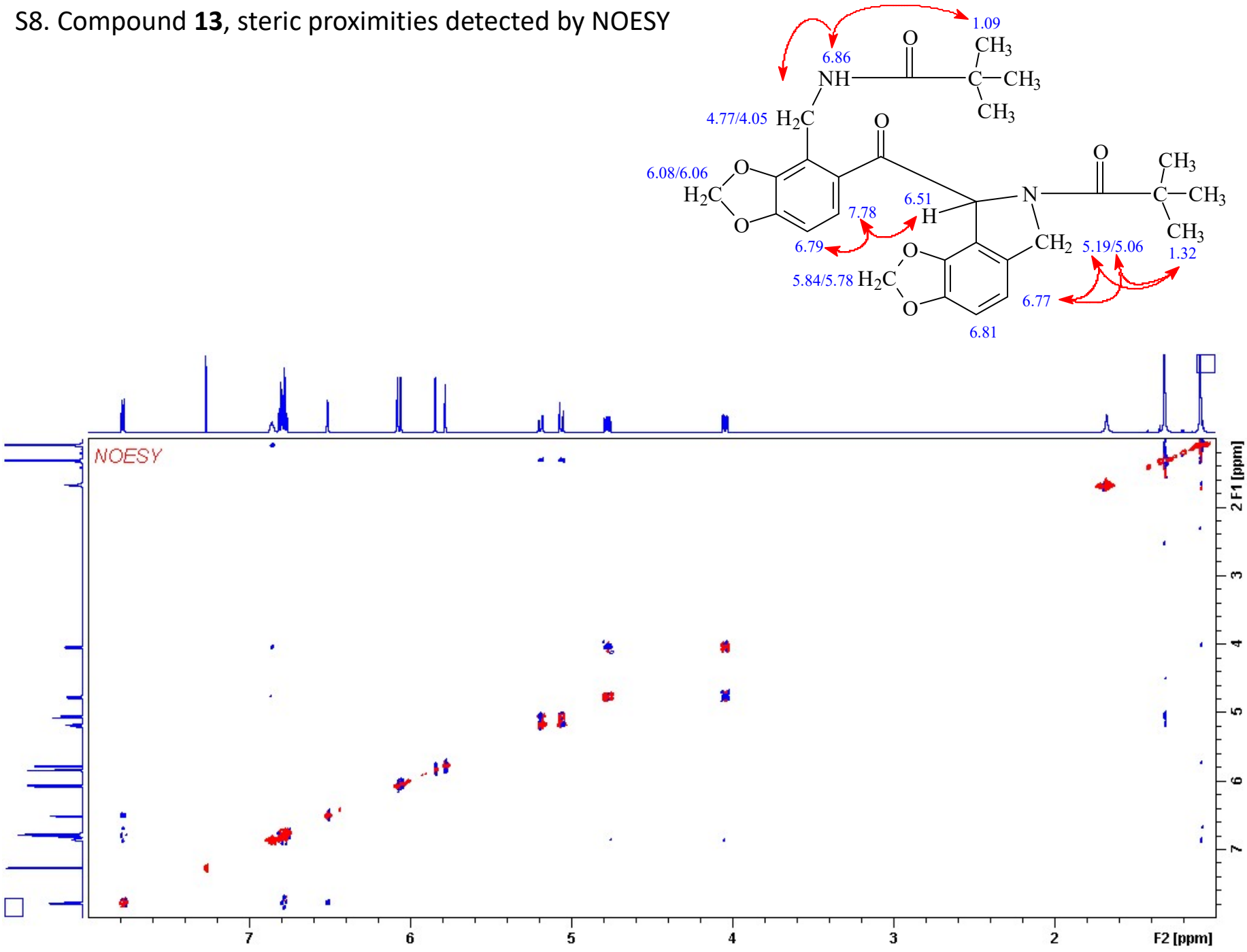
S7. Compound **13**, ^{1}H,^{1}H-COSY and selTOCSY



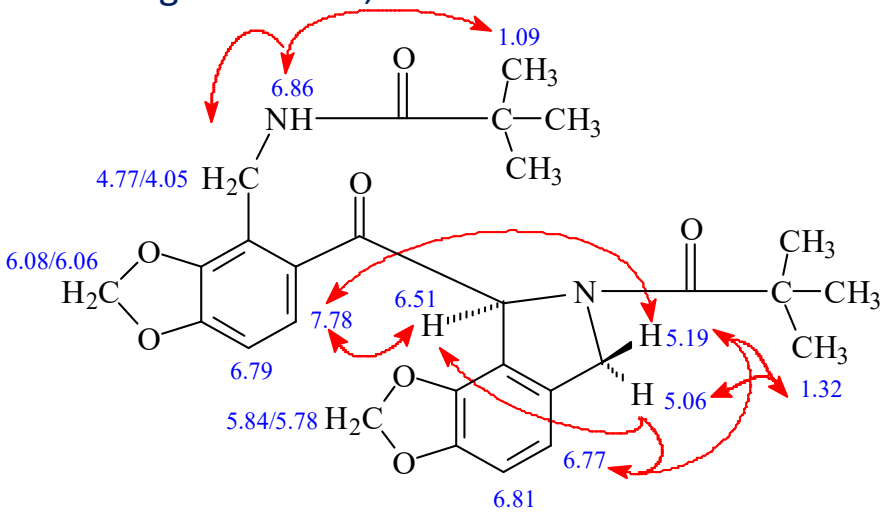


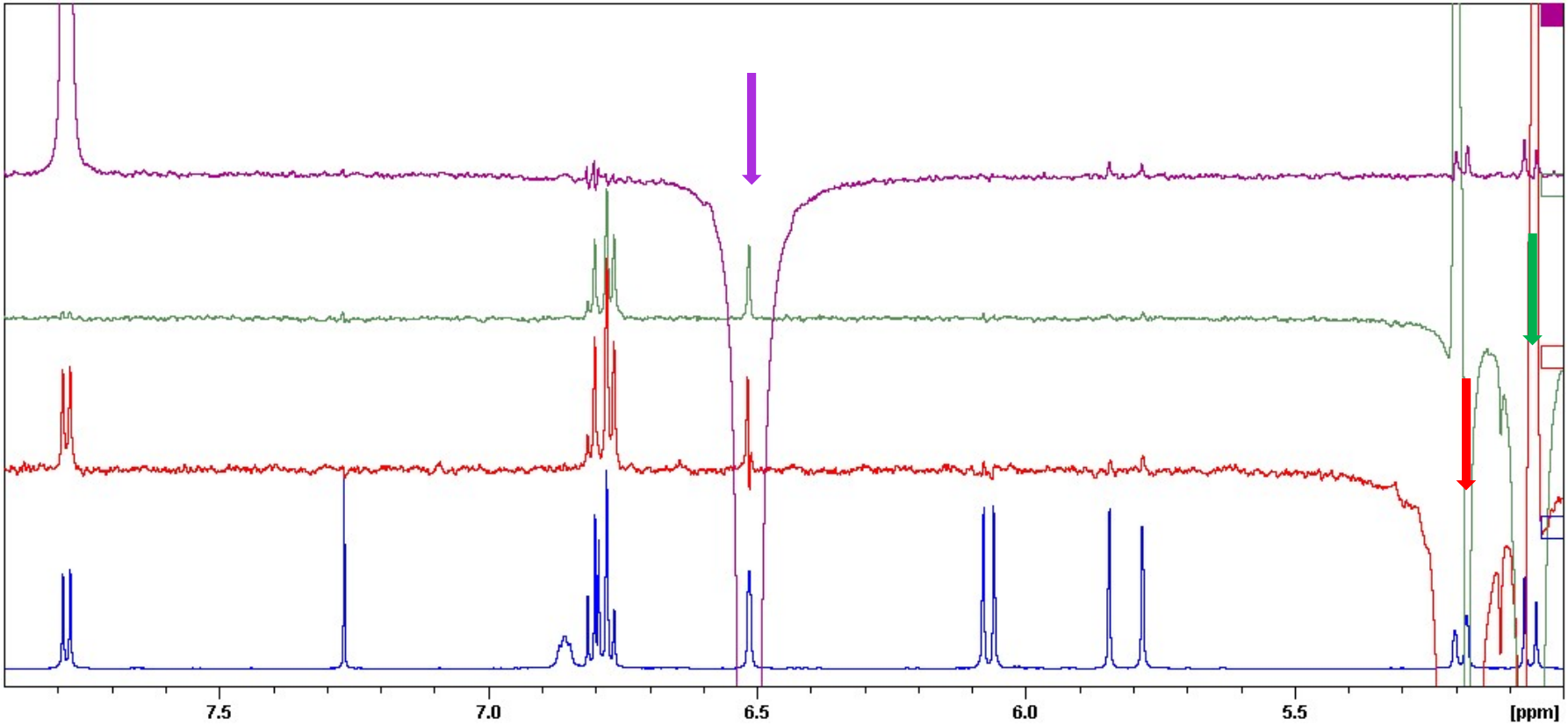


S8. Compound **13**, steric proximities detected by NOESY

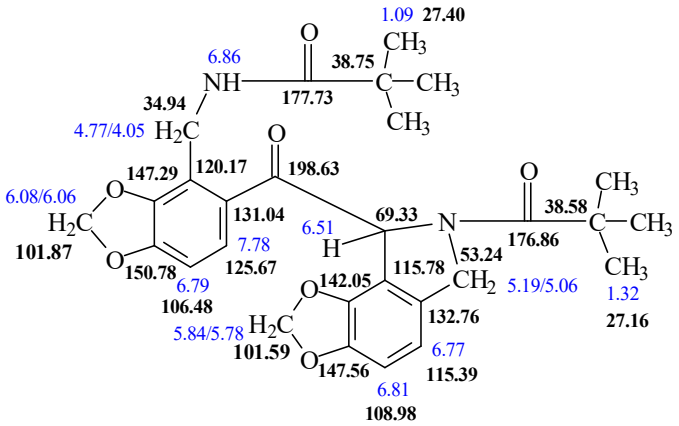


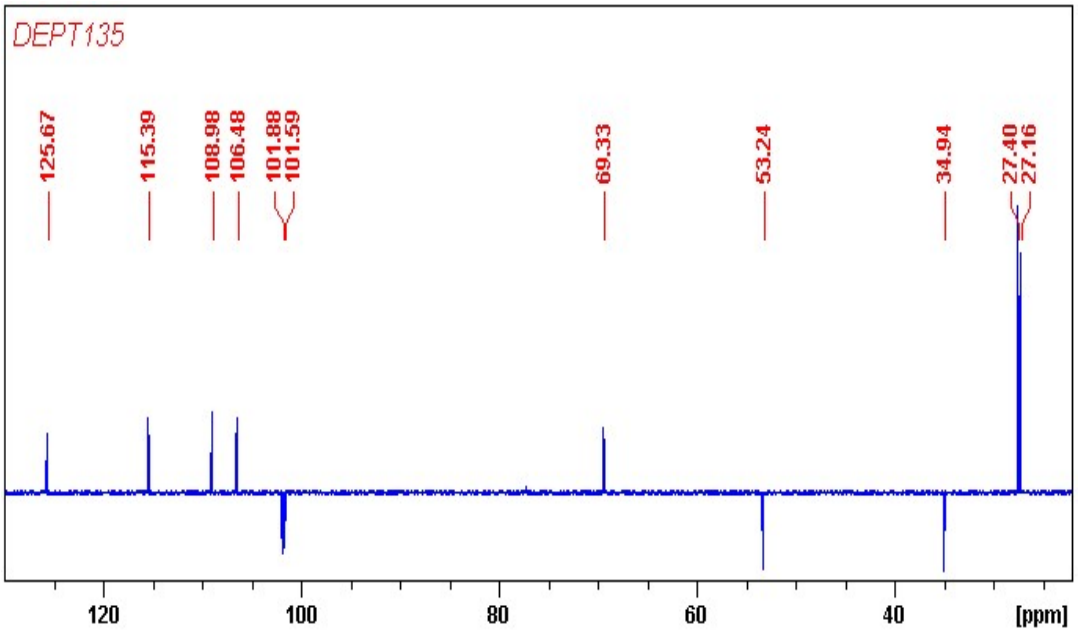
S9. Compound **13**, steric proximities detected by selNOE on signals δ 5.19, 5.06 and 6.51

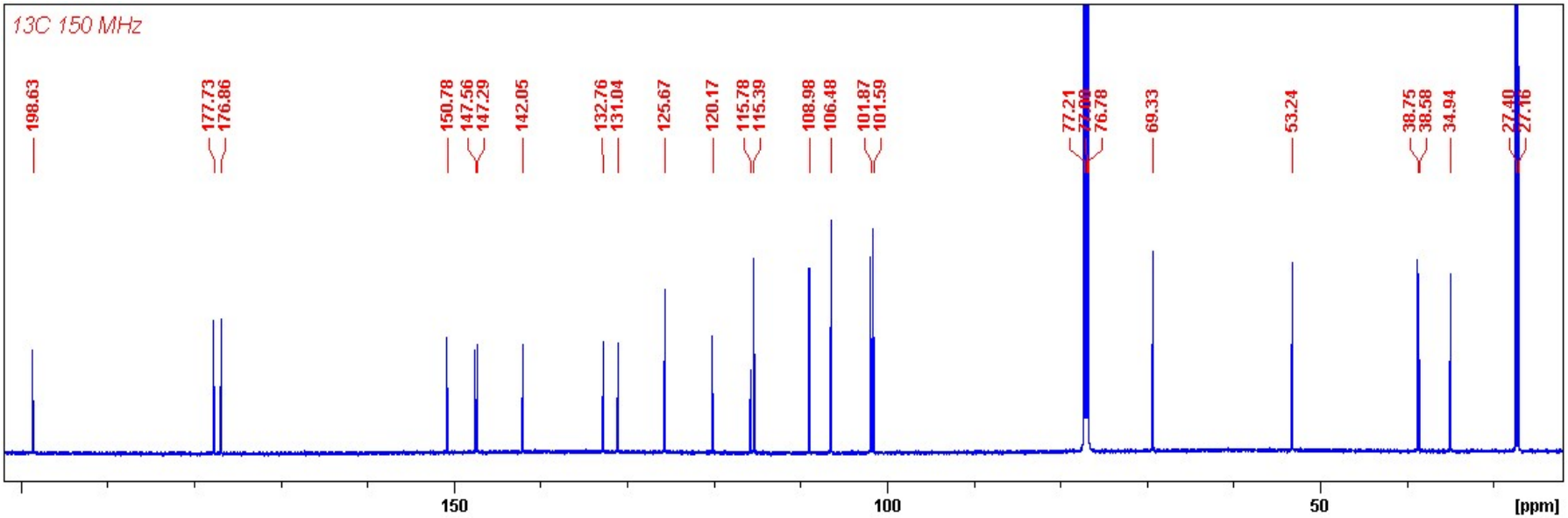




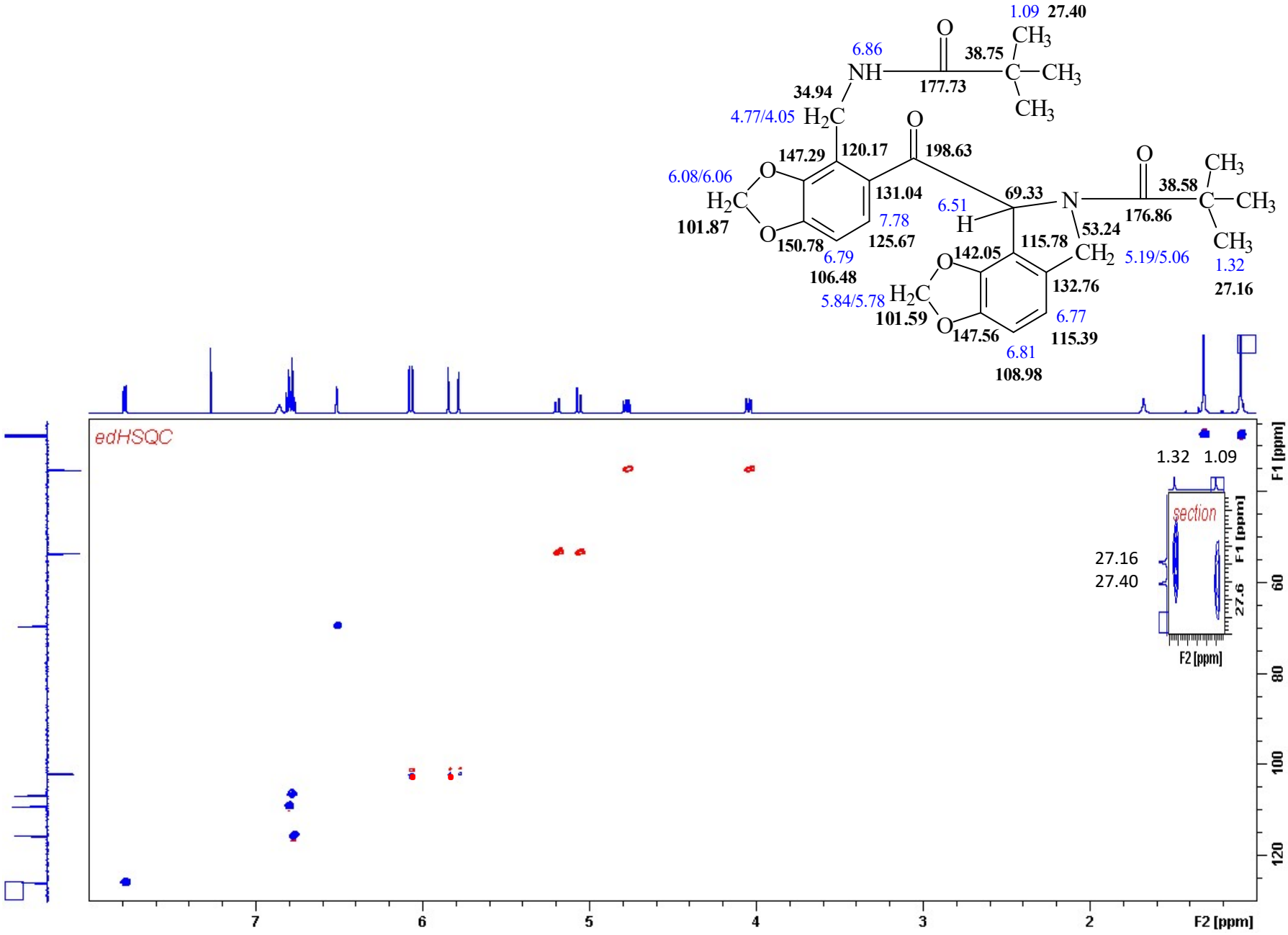
S10. Compound **13**, ^{13}C and DEPT-135 (150 MHz, $CDCl_3$)



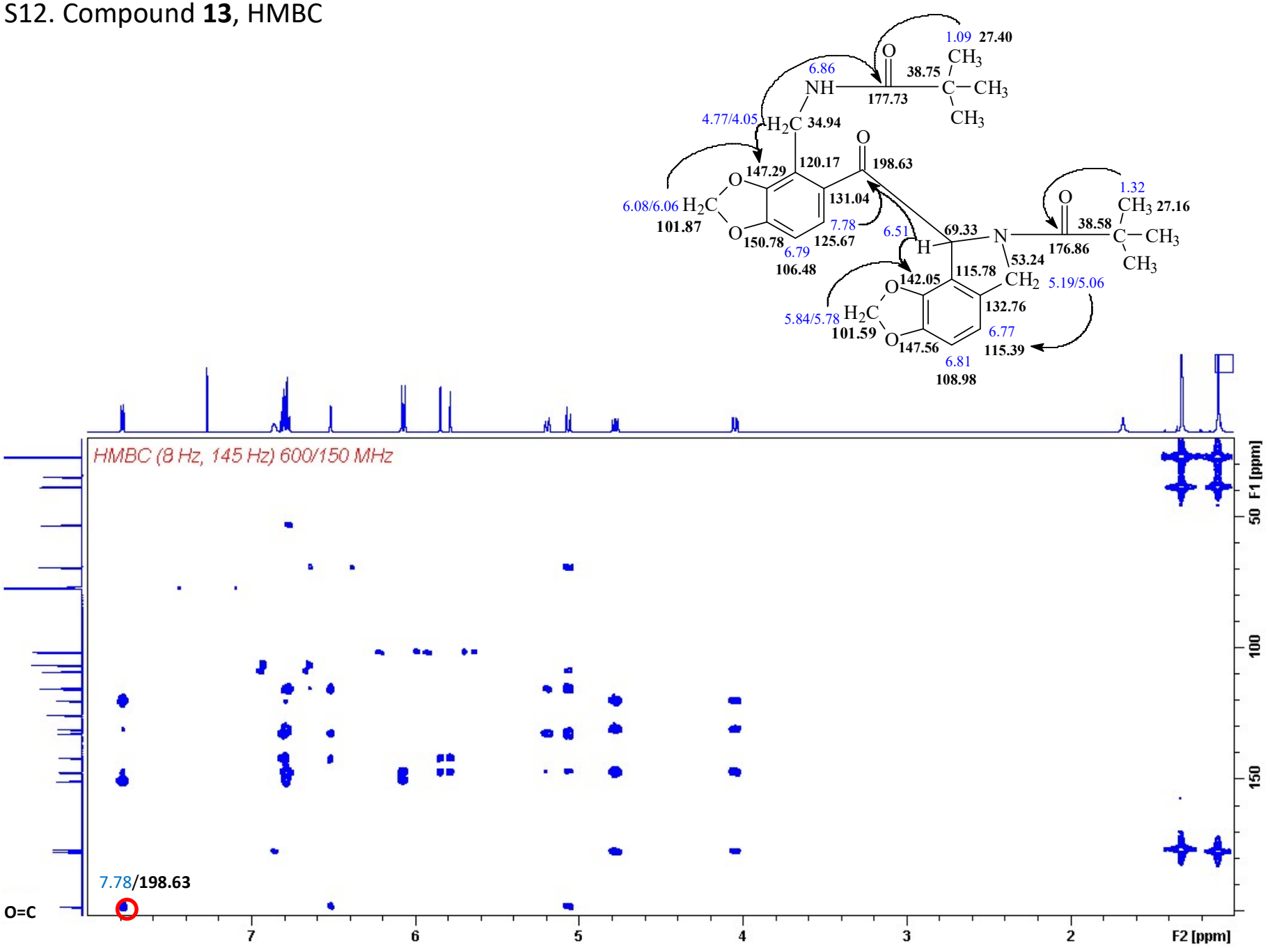




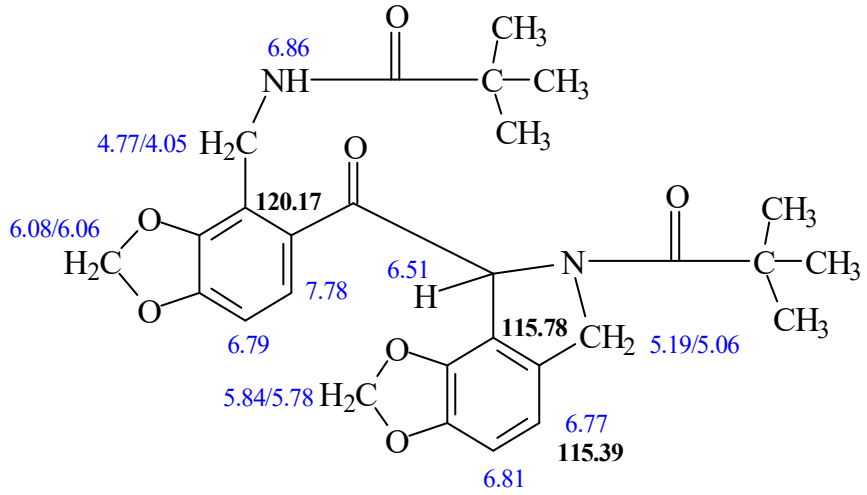
S11. Compound **13**, edHSQC and CH_3 section

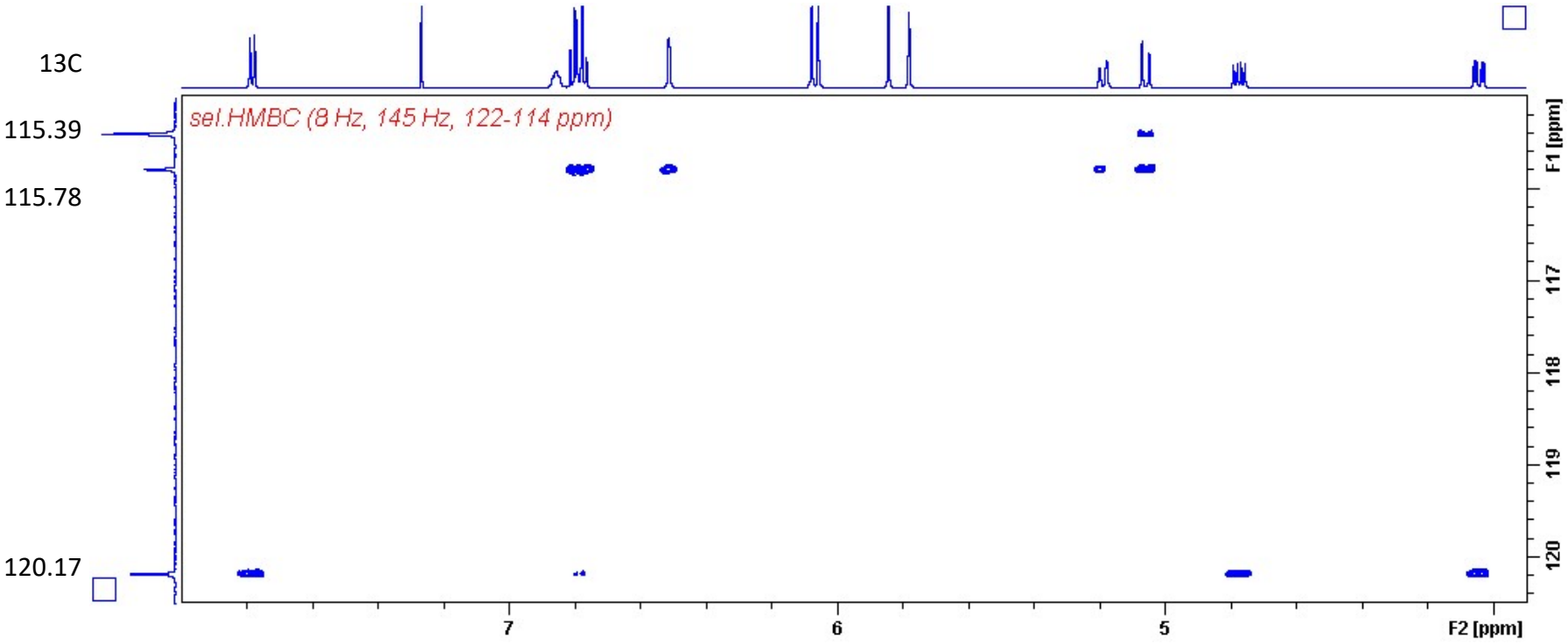


S12. Compound **13**, HMBC

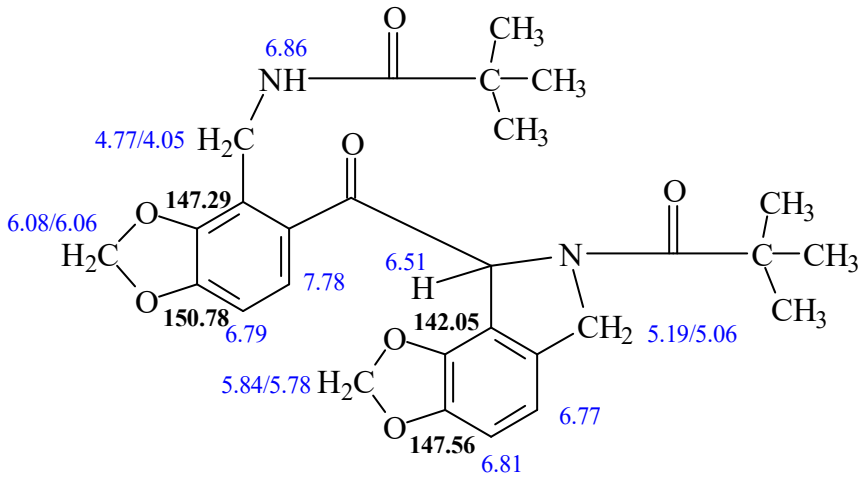


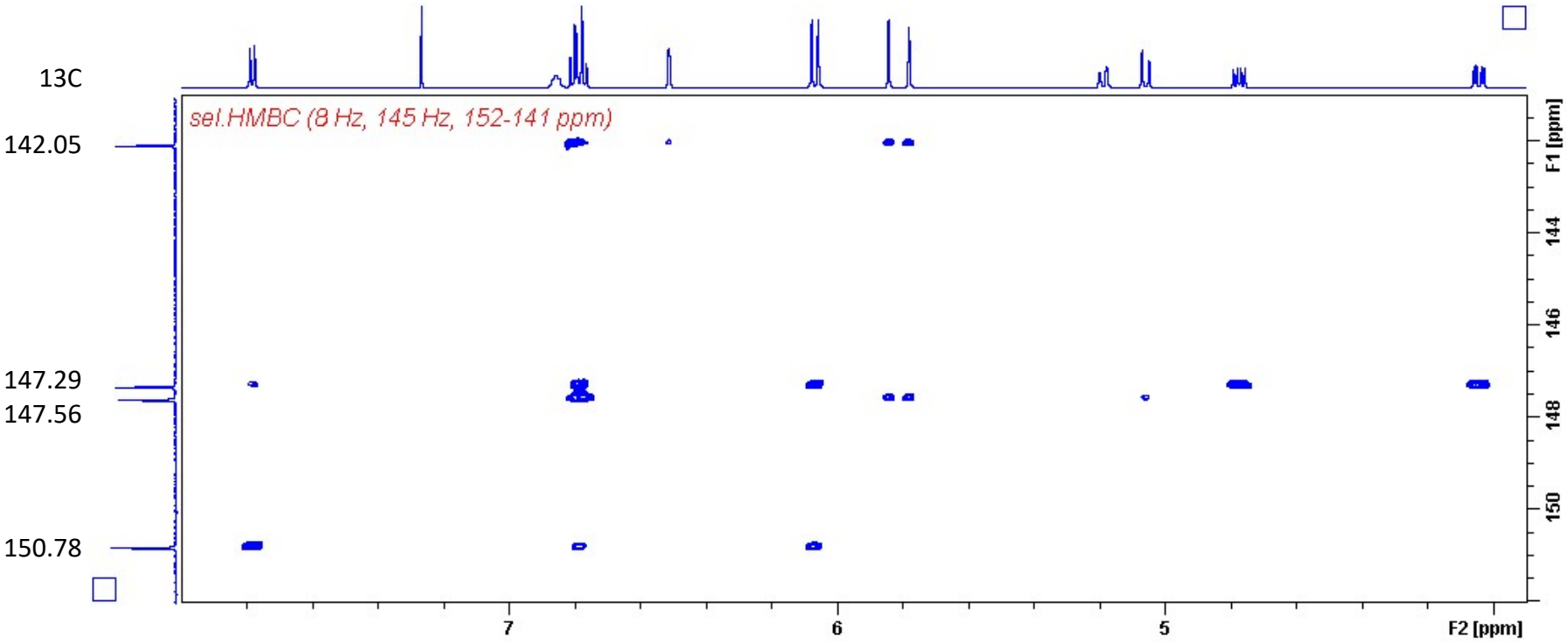
S13. Compound **13**, selective HMBC (122–114 ppm)





S14. Compound **13**, selective HMBC (152–141 ppm)

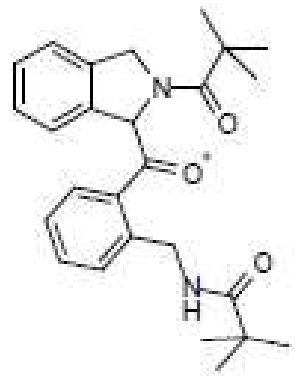




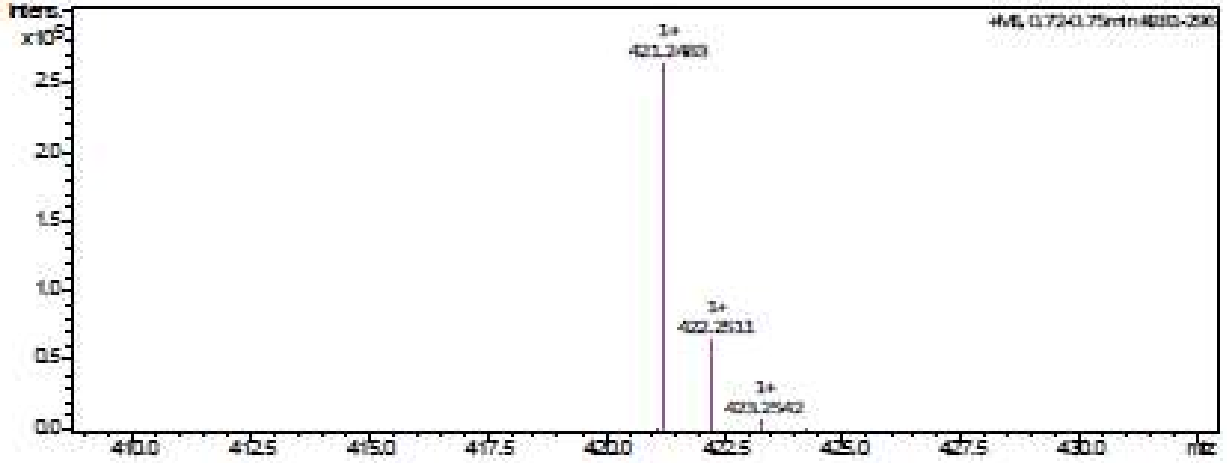
S15. Compound **14**, description of structure determination

The molecular formula of compound **11** was established as $C_{26}H_{32}N_2O_3$ by means of HRMS (page S16), indicating the presence of 12 double bond equivalents, meaning in this case, according to ^{1}H and ^{13}C NMR data (pages S17–S21), 3 rings and 9 double bonds. This corresponds to two phenyl groups, two pivaloyl amide moieties N-C=O (δ177.61 and δ175.88 ppm) and one conjugated C=O group (δ200.34 ppm), see DEPTQ spectrum on page S16. For the aromatic =CH signals, the ^{1}H NMR spectrum (page S17) exhibited two different four-spin systems with d; t; t; d multiplicities. The $^{1}H,^{1}H$-COSY experiment (page S18) revealed the connectivity of the ^{1}H atoms for both sets of signals. The edited HSQC spectrum (page S20) gave the unambiguous $^{1}H/^{13}C$ signal assignment. Quaternary carbon signals and also the connectivity of the various structural units of the molecule were identified on the basis of the HMBC spectrum (page S21). Similarly to compound **10**, only one aromatic =CH atom (δ7.71d) gave a HMBC cross-peak with the ketone C=O (δ200.34 ppm), therefore its connection to this aromatic ring is identified, leading to a complete NMR assignment. Structure of compound **11** was also justified by single-crystal X-ray measurement.

S16. Compound **14**, HRMS

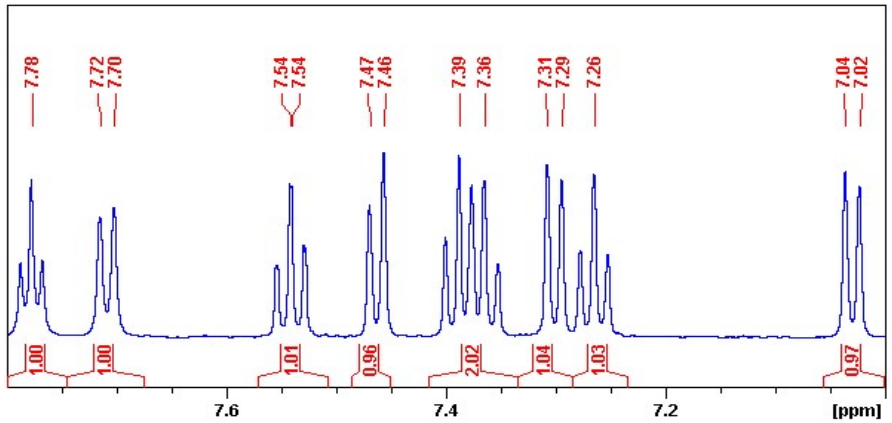


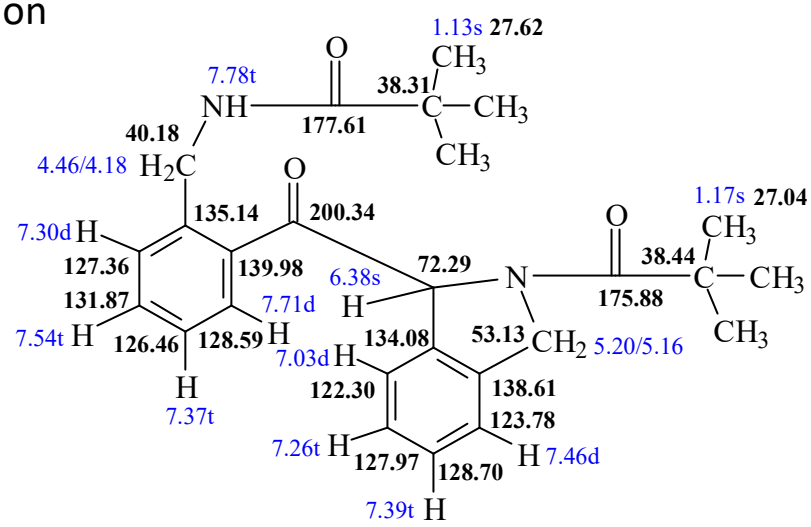
Exact Mass =421.249118
Molecular Formula =C26H33N2O3
HCS0484_1E

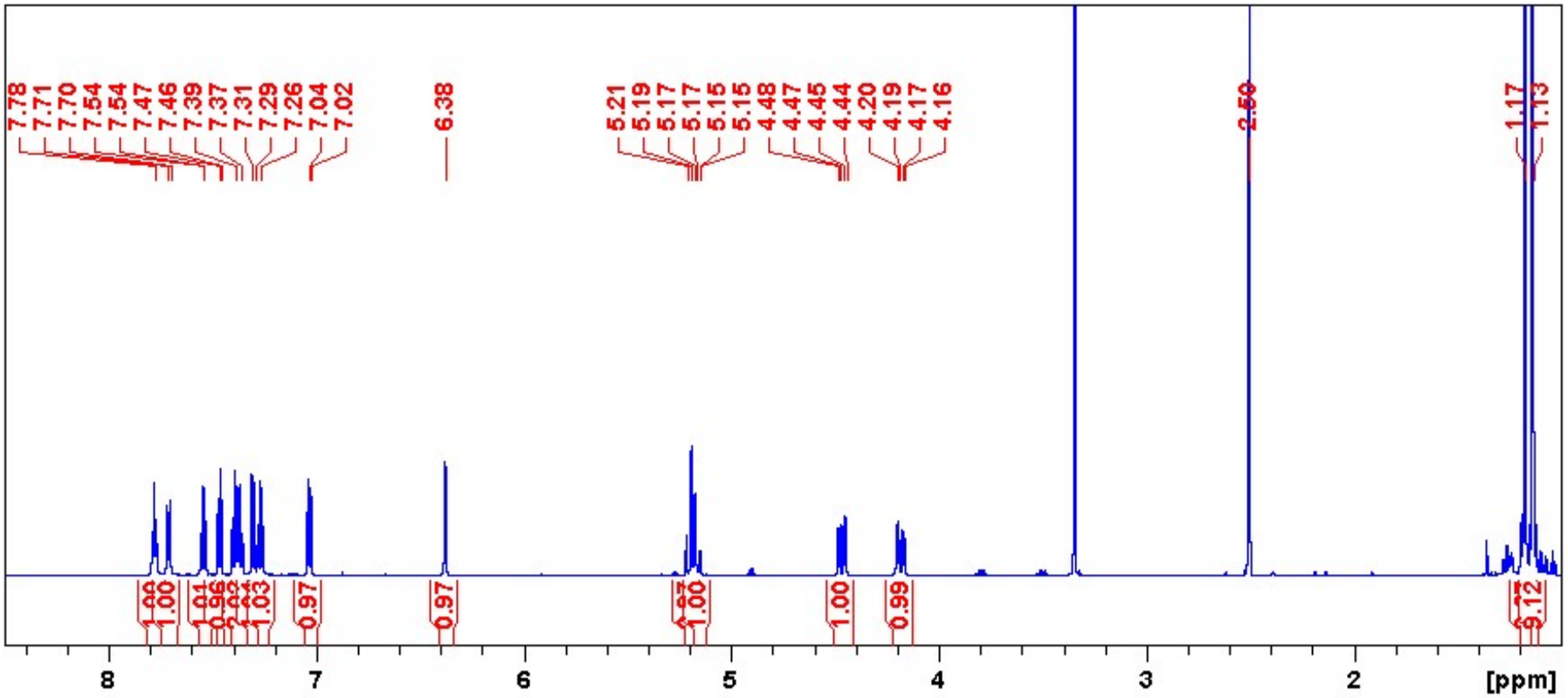


Meas. m/z	Ion Formula	Score	m/z	err [ppm]
421.2483	C26H33N2O3	100.00	421.2486	0.6

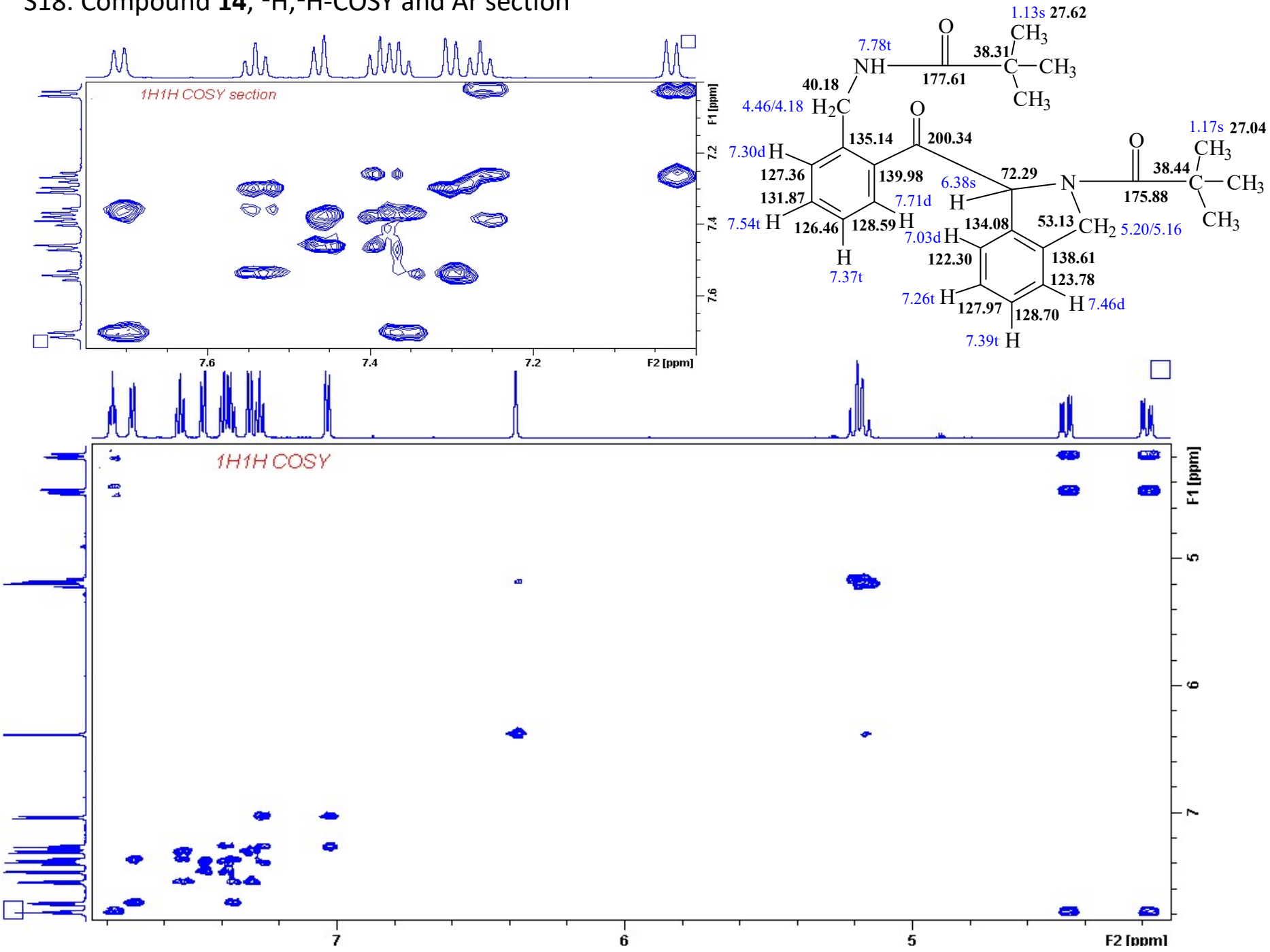
S17. Compound **14**, ^{1}H NMR (600 MHz, DMSO) and Ar section



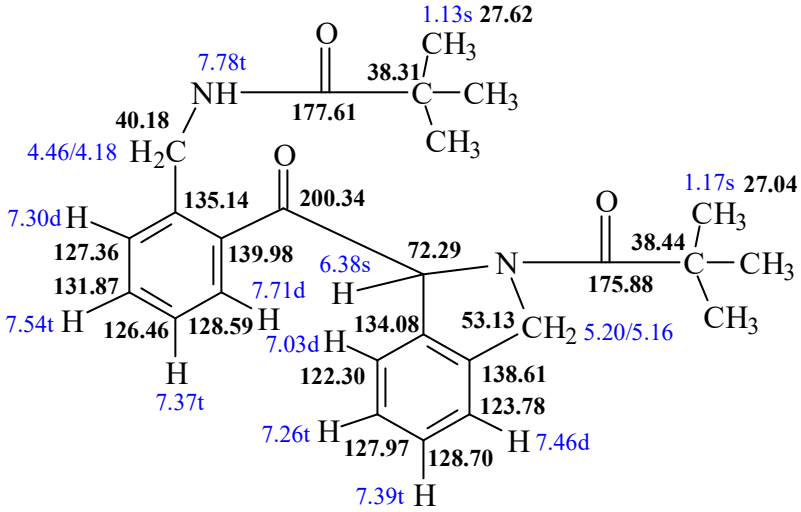


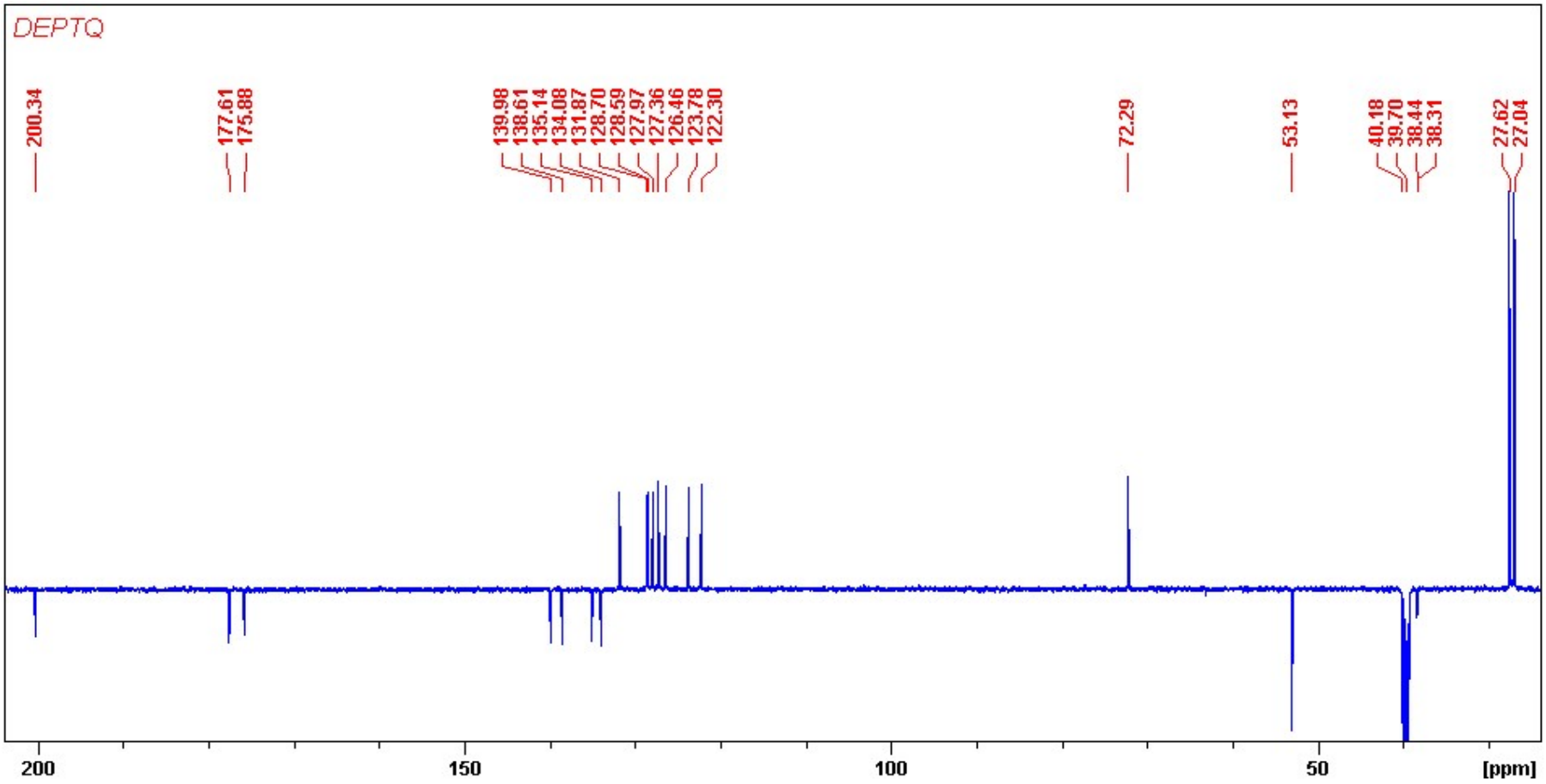


S18. Compound **14**, ^{1}H,^{1}H-COSY and Ar section

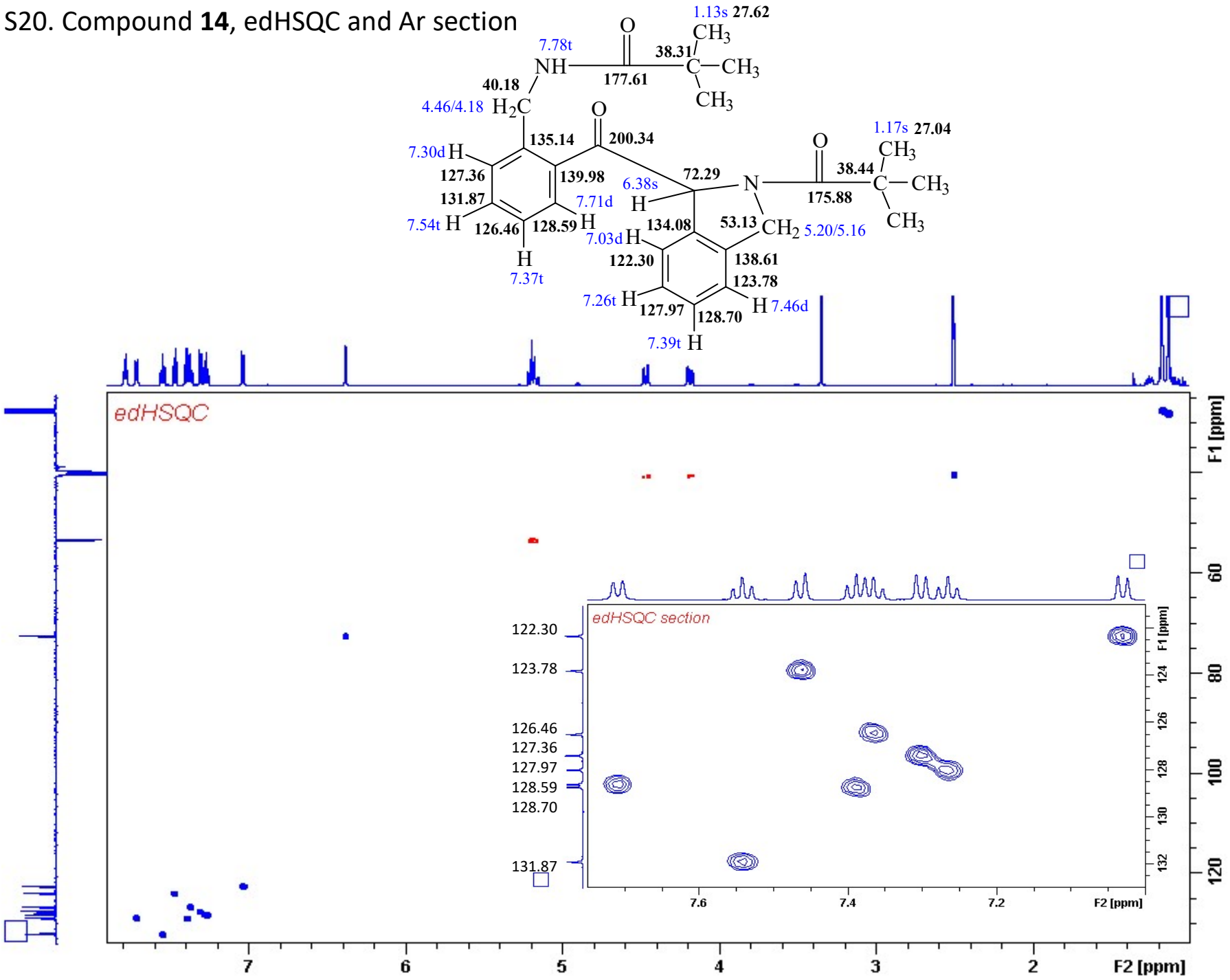


S19. Compound **14**, DEPTQ (^{13}C 150 MHz)

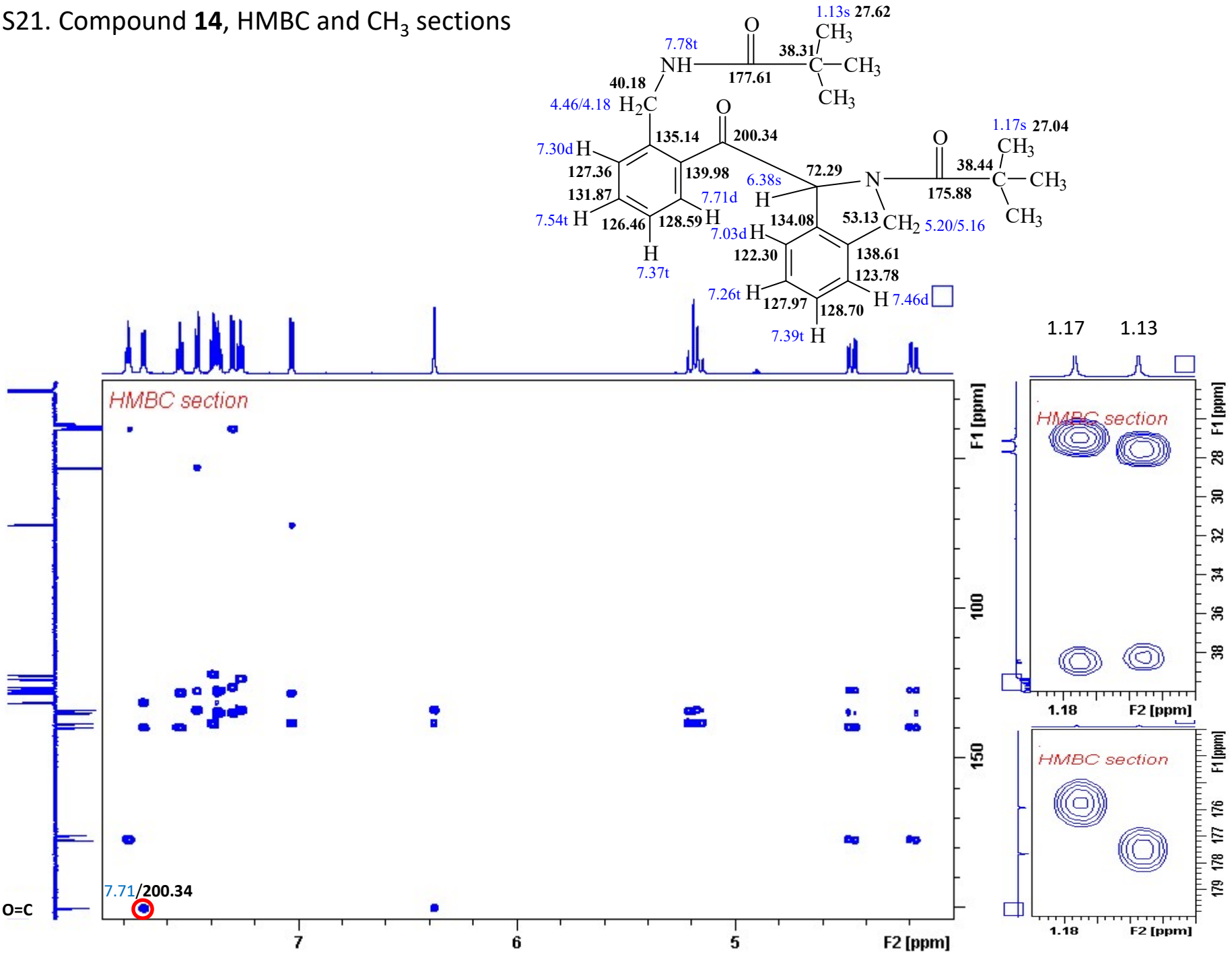




S20. Compound **14**, edHSQC and Ar section



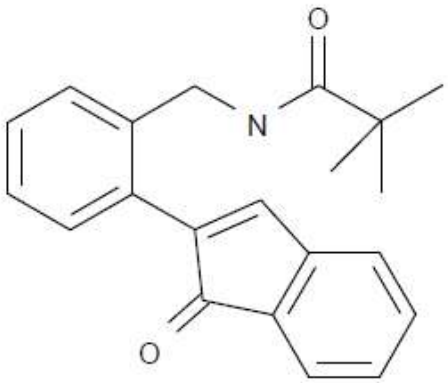
S21. Compound **14**, HMBC and CH_3 sections



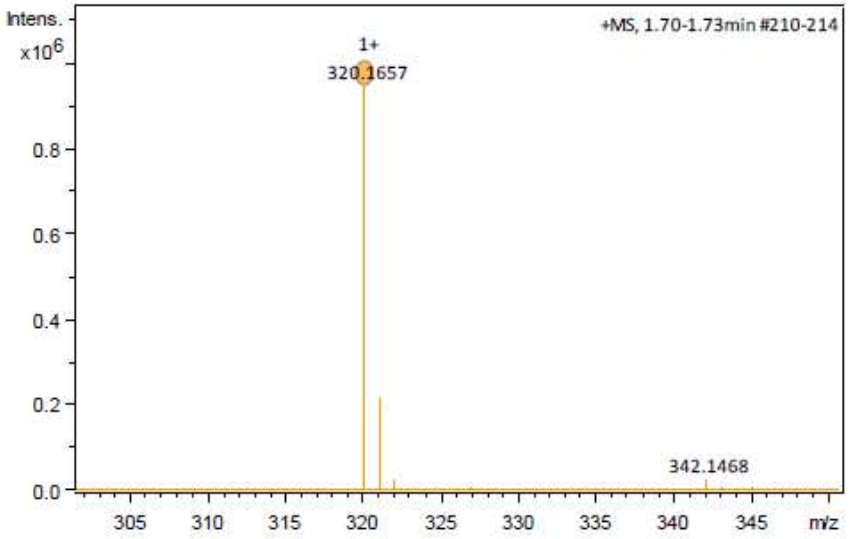
S22. Compound **15**, description of structure determination

The structural formula of compound **12** was established as $C_{21}H_{21}NO_2$ by means of HRMS (page S23), i.e. this compound contains 12 double bond equivalents. Taking into consideration the ^{1}H and ^{13}C NMR data (page S24), this compound contains 3 rings and 9 double bonds. This corresponds to two phenyl groups, one pivaloyl amide unit N-C=O (δ177.42 ppm), one cross-conjugated C=O group (δ196.58 ppm) and one conjugated C=CH moiety (δ136.81 and δ147.02 ppm), see page S24 (^{13}C spectrum). The character of the third ring was determined by HMBC (see below). The selTOCSY experiment (page S25) on =CH δ7.49t (7.4 Hz) revealed the four-spin system 7.27d; 7.49t; 7.31t and 7.44d, i.e. the signals of the condensed phenyl ring. SelTOCSY (page S25) on =CH δ7.36t (7.4 Hz) showed a second four-spin system 7.30d; 7.36t; 7.30t and 7.26d for the *ortho*-disubstituted phenyl group. Unambiguous identification of the aromatic rings was based on the ROESY experiment (page S26). The δNCH_2 (4.29d ppm) signal showed a steric proximity to =CH δ7.30d, marking this spin system as a sterically close one, and also to the single =CH (δ7.81s ppm) hydrogen atom. Furthermore, the signal δ7.81s resulted in a NOE response on δ7.27d and thereby revealed the location of the other four-spin system (7.27d; 7.49t; 7.31t and 7.44d) in the condensed 1-oxo-1*H*-indene moiety. The HSQC experiment (page S27) served as the unambiguous $^{1}H/^{13}C$ signal assignment in case of very close, even partly overlapping =CH signals. To facilitate the evaluation of the HSQC, we have inserted into this spectrum the one-dimensional selTOCSY spectrum with irradiation on δ7.36t (page S27). The TOCSY signals exactly picked out the corresponding C-H cross-peaks. The assignment of quaternary carbon atoms and the connectivity of the structural elements of the molecule were supported by HMBC measurements (page S28). Cross-peaks of the C=O signal (196.58 ppm) with the δ7.81s and δ7.44d hydrogens disclosed its position. The occasionally appearing doublet at δ147.02 ppm gave a coupling of $^{1}J(CH)$=173 Hz. The CH_2 hydrogens (δ4.29d) resulted in HMBC responses on the aromatic carbon atoms at 127.48, 130.27 and 138.81 ppm, and provided an independent evidence for the differentiation and assignment of the disubstituted aromatic rings. By taking advantage of the extremely high ^{13}C chemical shift resolution of the band-selective version of HMBC (page S29), a complete NMR assignment was finally achieved.

S23. Compound **15**, HRMS

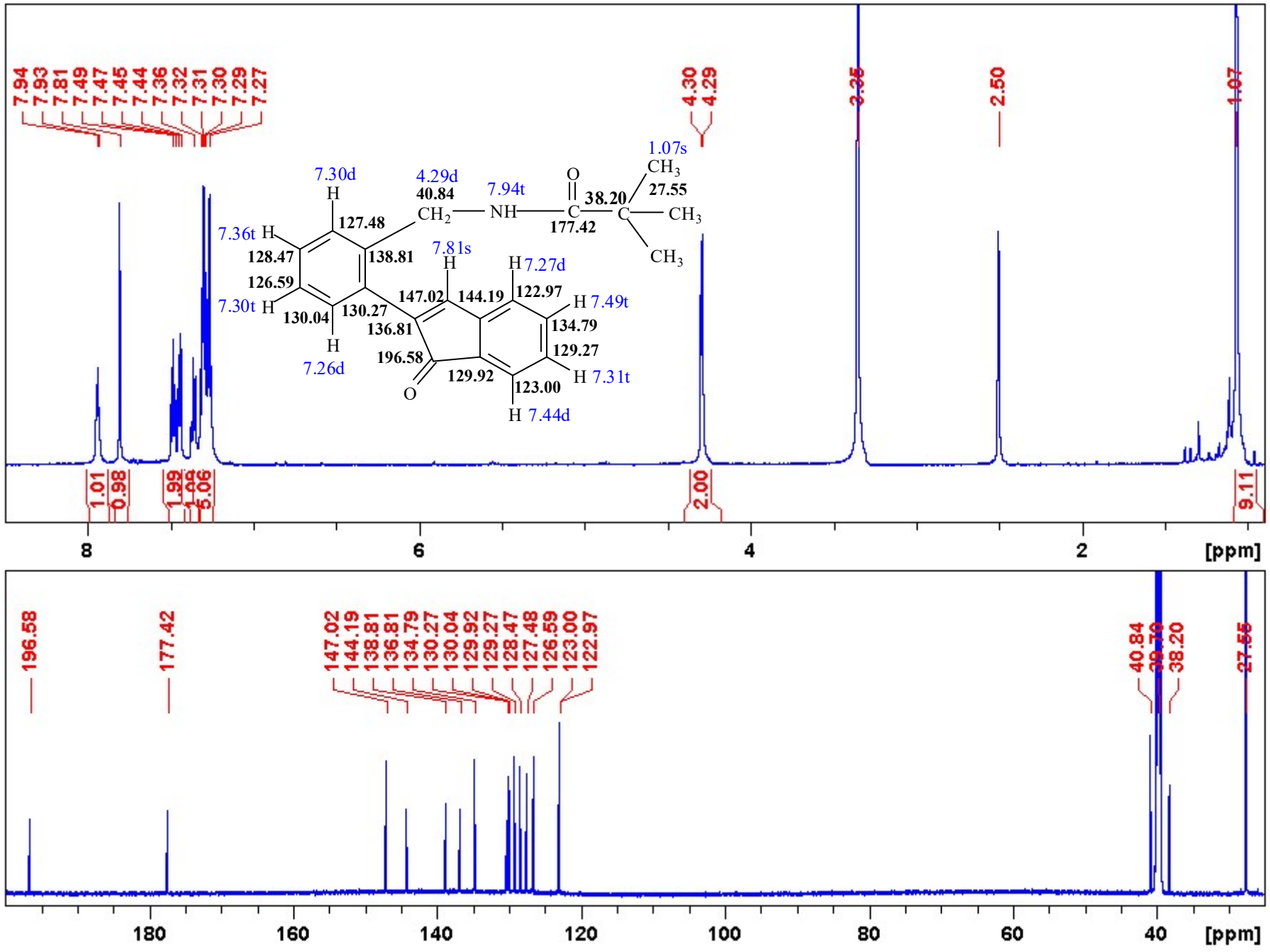


MH+:320.1651
C21H22NO2

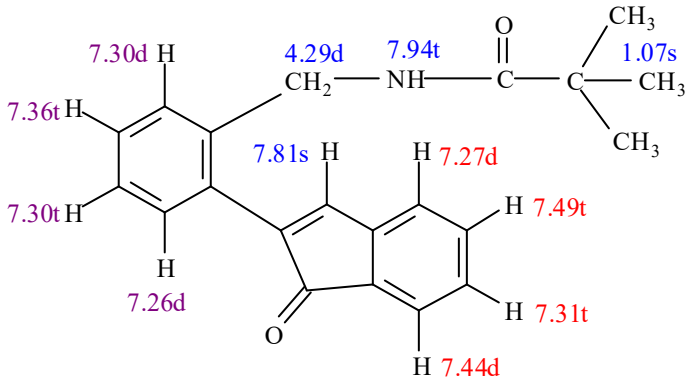


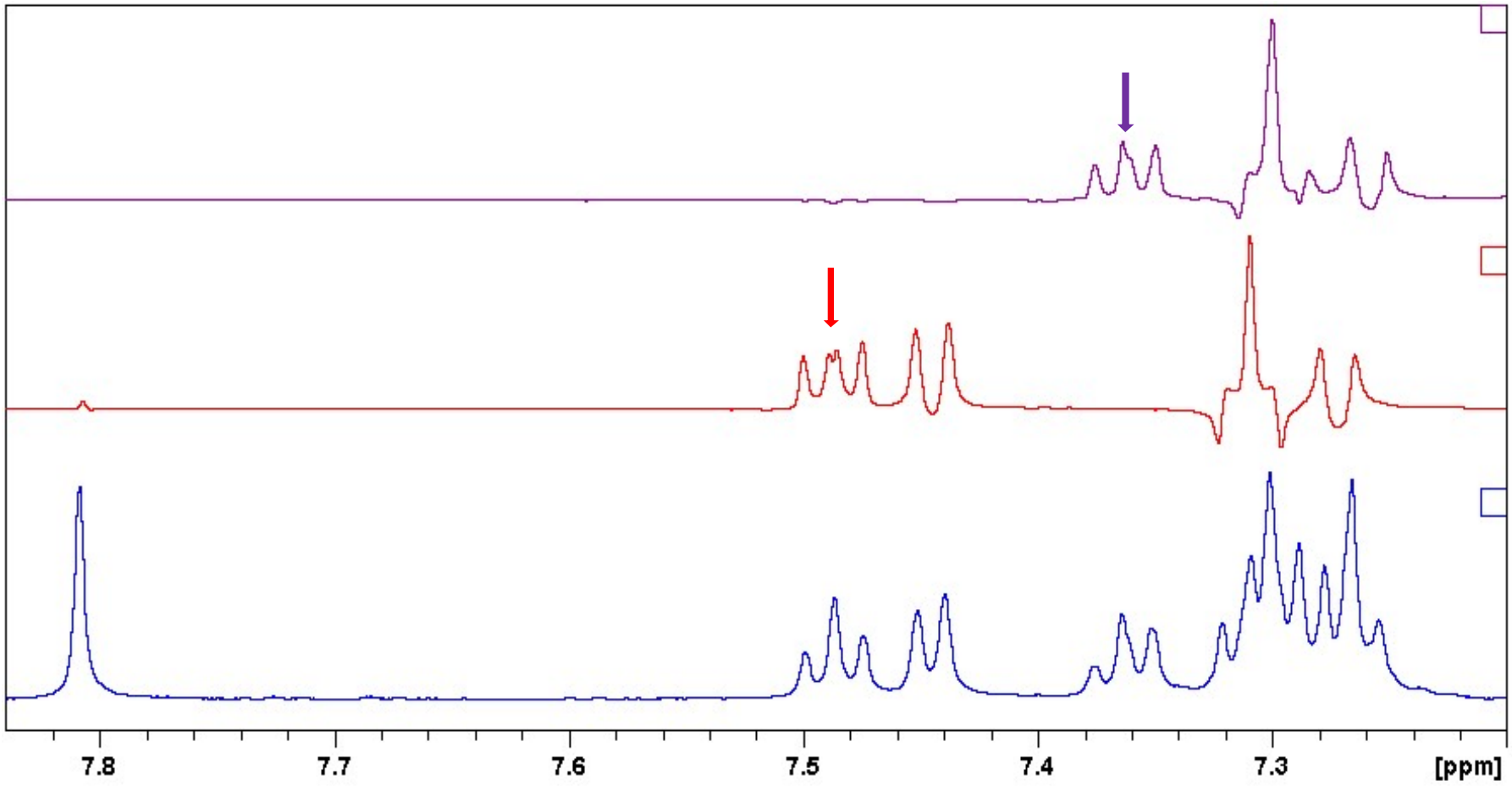
Meas. m/z	Ion Formula	m/z	err [ppm]
320.1657	C21H22NO2	320.1645	-3.8

S24. Compound **15**, ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) in DMSO-d_6

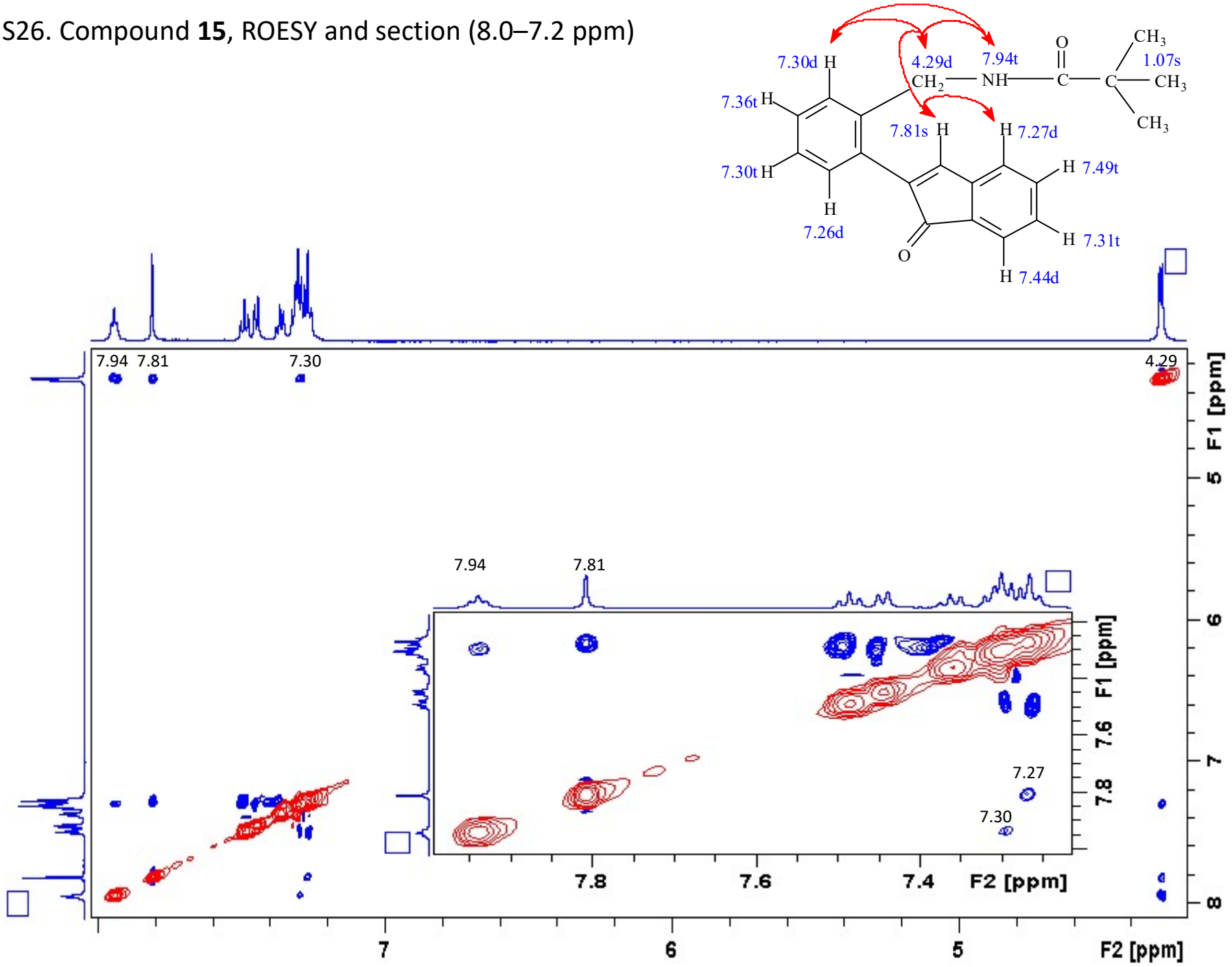


S25. Compound **15**, ^{1}H NMR and sel-Tocsy on δ 7.49t and δ 7.36t signals

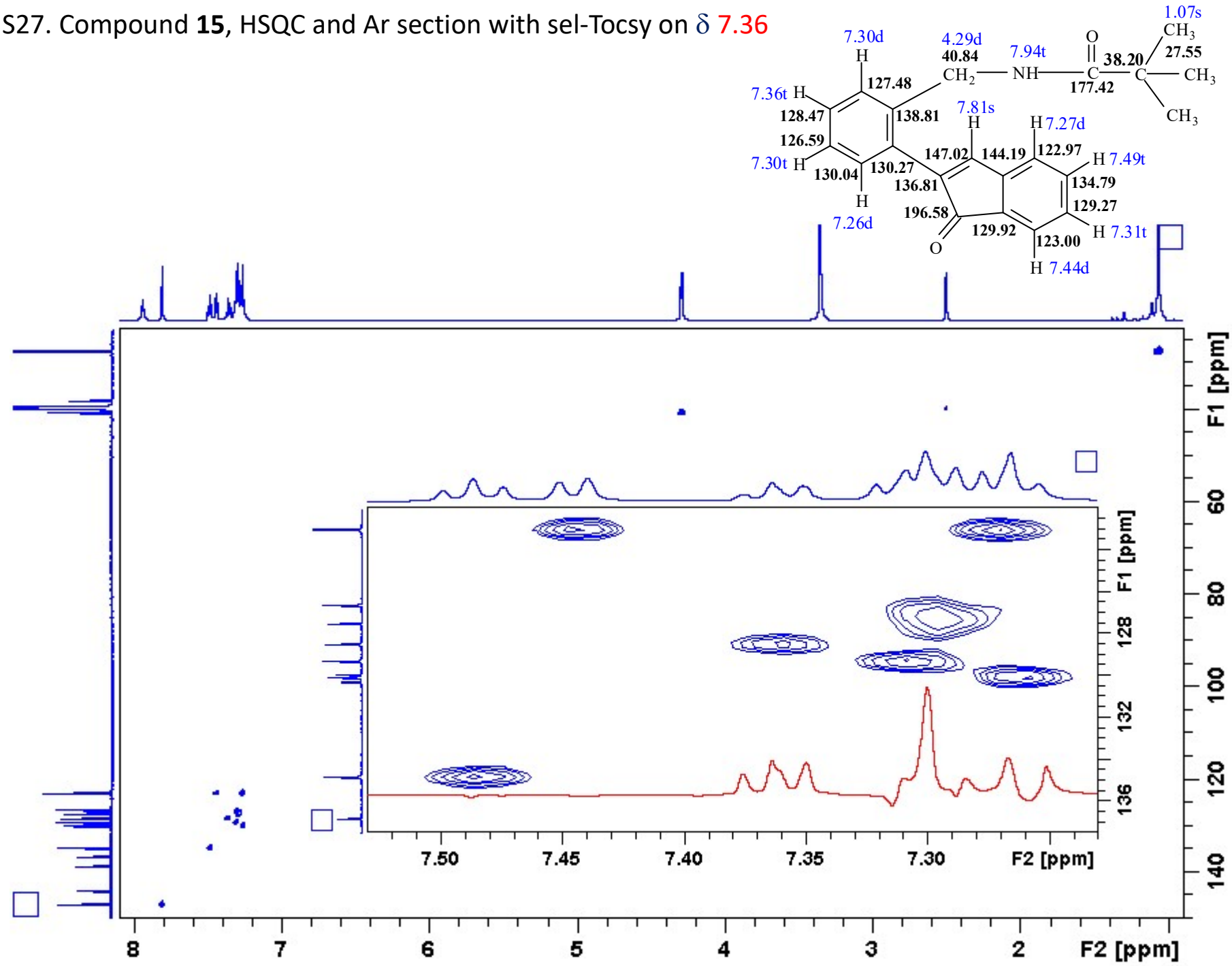




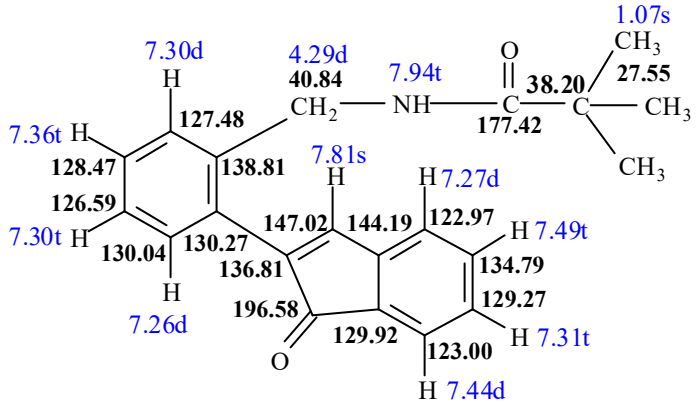
S26. Compound **15**, ROESY and section (8.0–7.2 ppm)

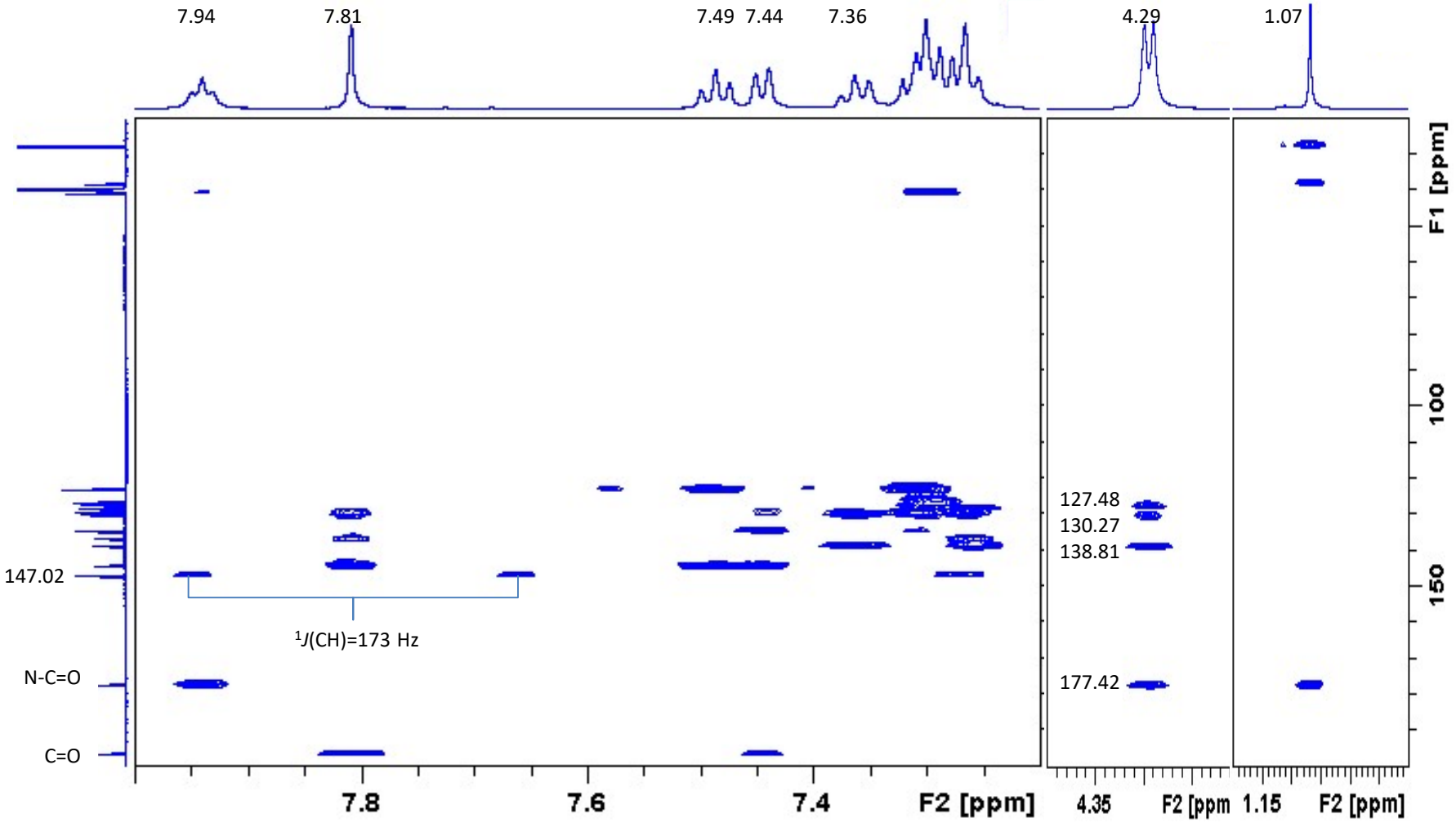


S27. Compound **15**, HSQC and Ar section with sel-Tocsy on δ 7.36

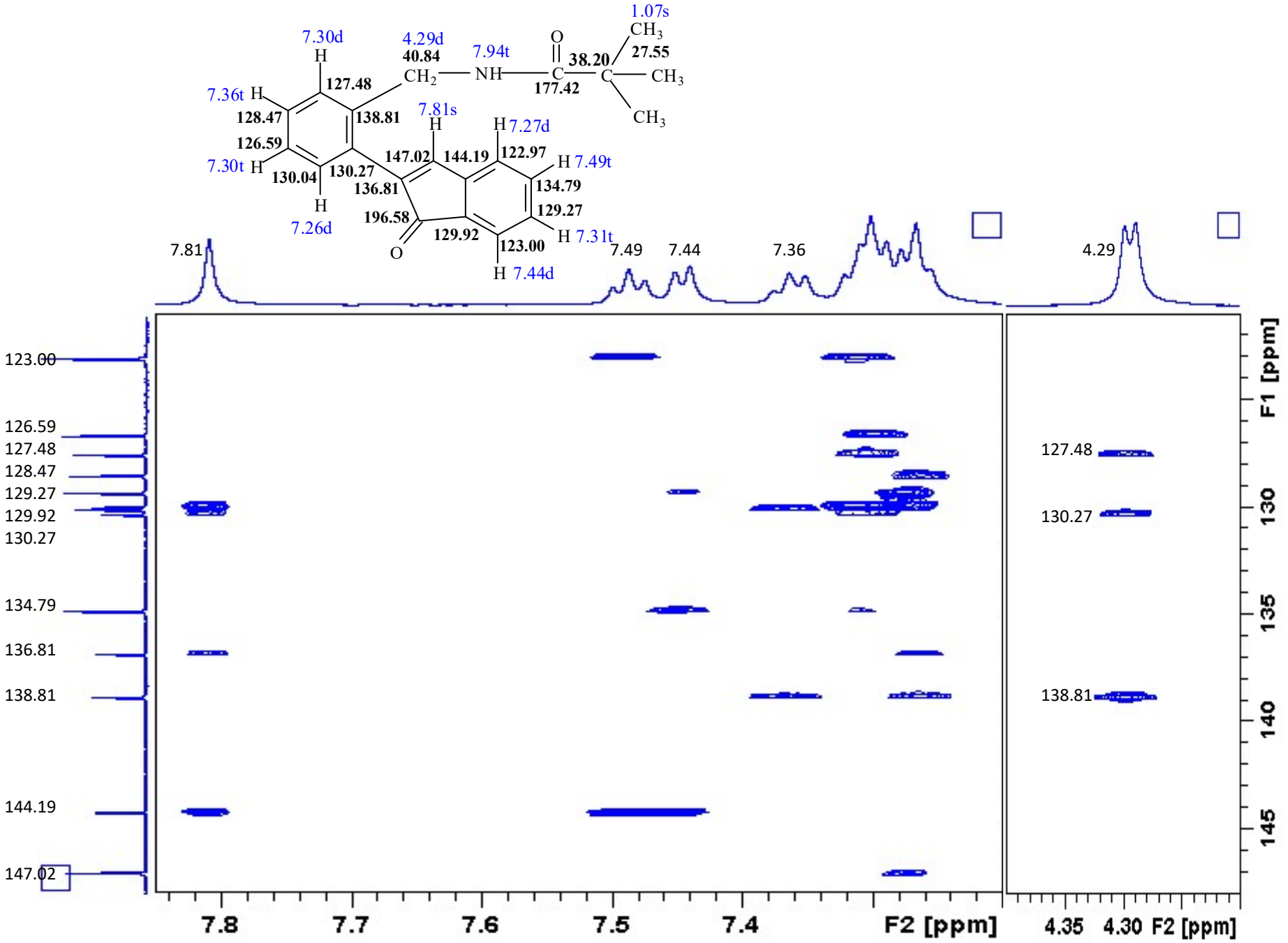


S28. Compound **15**, HMBC





S29. Compound **15**, selective HMBC (148–121 ppm)



S30. Monitoring of the composition of the reaction mixture by LC-MS during the $BF_3 \cdot H_2O$-catalyzed transformation of **5** (Scheme 4)

Reaction time [h]	**5** [%] R_t=2.99 min	**15** [%] R_t=3.94 min	M=520 g/mol (unidentified structure) R_t=4.05 min	**14** [%] "BF_3-dimer" R_t=4.17 min	**6a** [%] "TFA dimer" R_t=4.23 min	M=520 g/mol (unidentified structure) R_t=4.47 min	M=622 g/mol (unidentified structure) R_t=4.94 min
3.5	9.0	<0.3	10.0	11.0	37.0	14.0	1.0
6.5	4.0	5.0	10.0	22.0	24.0	15.0	1.0
23.5	<0.3	40.0	6.0	30.0	<0.3	11.0	1.0
25.0	<0.3	44.0	<0.3	32.0	<0.3	11.0	1.0

S31. Monitoring of the composition of the reaction mixture by LC-MS during the $BF_3 \cdot H_2O$-catalyzed transformation of **6a** (Scheme 9)

Reaction time [h]	**5** [%] R_t=2.98 min	**15** [%] R_t=3.94 min	M=520 g/mol (unidentified structure) R_t=4.05 min	**14** [%] "BF_3-dimer" R_t=4.16 min	**6a** [%] "TFA-dimer" R_t=4.23 min	M=520 g/mol (unidentified structure) R_t=4.46 min	M=720 g/mol (unidentified structure) R_t=5.04 min
3.5	2.0	<0.3	5.0	11.0	53.0	7.0	2.0
6.5	2.0	<0.3	5.0	15.0	45.0	3.0	3.0
23.5	2.0	2.6	5.0	35.0	22.0	1.0	4.0
27.5	2.0	9.0	6.0	41.0	13.0	11.0	3.0
32.0	1.0	9.0	4.5	44.0	7.0	10.0	4.0
47.0	<0.3	17.0	5.0	46.0	2.0	9.0	1.0

S33. Energy values obtained for the computation of the **11**→**18** transformation. The E, ZPE, U, H and G values were computed using the M062X/6-31+G (d,2p) method.

ID	E	ZPE	U	H	G	S	Imaginary frequencies
11A	-1795.04	-1794.49	-1794.45	-1794.45	-1794.55	221.704	
TS1A	-1795.00	-1794.45	-1794.42	-1794.42	-1794.52	214.197	-1227.23
16+TFA	-1795.05	-1794.50	-1794.46	-1794.46	-1794.56	213.770	
TS2A	-1795.01	-1794.47	-1794.43	-1794.43	-1794.53	205.529	-1372.28
17A	-1795.03	-1794.48	-1794.44	-1794.44	-1794.54	220.323	
17A--H_2O	-1871.44	-1870.87	-1870.83	-1870.83	-1870.94	231.422	
TS3A	-1871.44	-1870.86	-1870.82	-1870.82	-1870.93	221.810	-196.35
18+TFA	-1871.48	-1870.90	-1870.86	-1870.86	-1870.97	219.313	
11B	-1669.31	-1668.76	-1668.73	-1668.73	-1668.83	208.850	
TS1B	-1669.30	-1668.75	-1668.72	-1668.72	-1668.81	196.250	-1274.25
16+BF_3·H_2O	-1669.32	-1668.77	-1668.74	-1668.74	-1668.83	206.840	
TS2B	-1669.28	-1668.74	-1668.71	-1668.71	-1668.81	209.162	-1157.79
17B	-1669.30	-1668.75	-1668.71	-1668.71	-1668.82	222.012	
17B--H_2O	-1745.73	-1745.15	-1745.11	-1745.11	-1745.22	220.838	
TS3B	-1745.72	-1745.14	-1745.11	-1745.10	-1745.21	215.080	-209.32
18+BF_3·H_2O	-1745.76	-1745.18	-1745.14	-1745.14	-1745.24	217.278	
H_2O	-76.4053	-76.3840	-76.3812	-76.3802	-76.4017	45.111	