Supplementary Material

Synthesis of nucleoside-like molecules from a pyrolysis product of cellulose and their computational prediction as SARS-CoV-2 RNA-dependent RNA polymerase inhibitors

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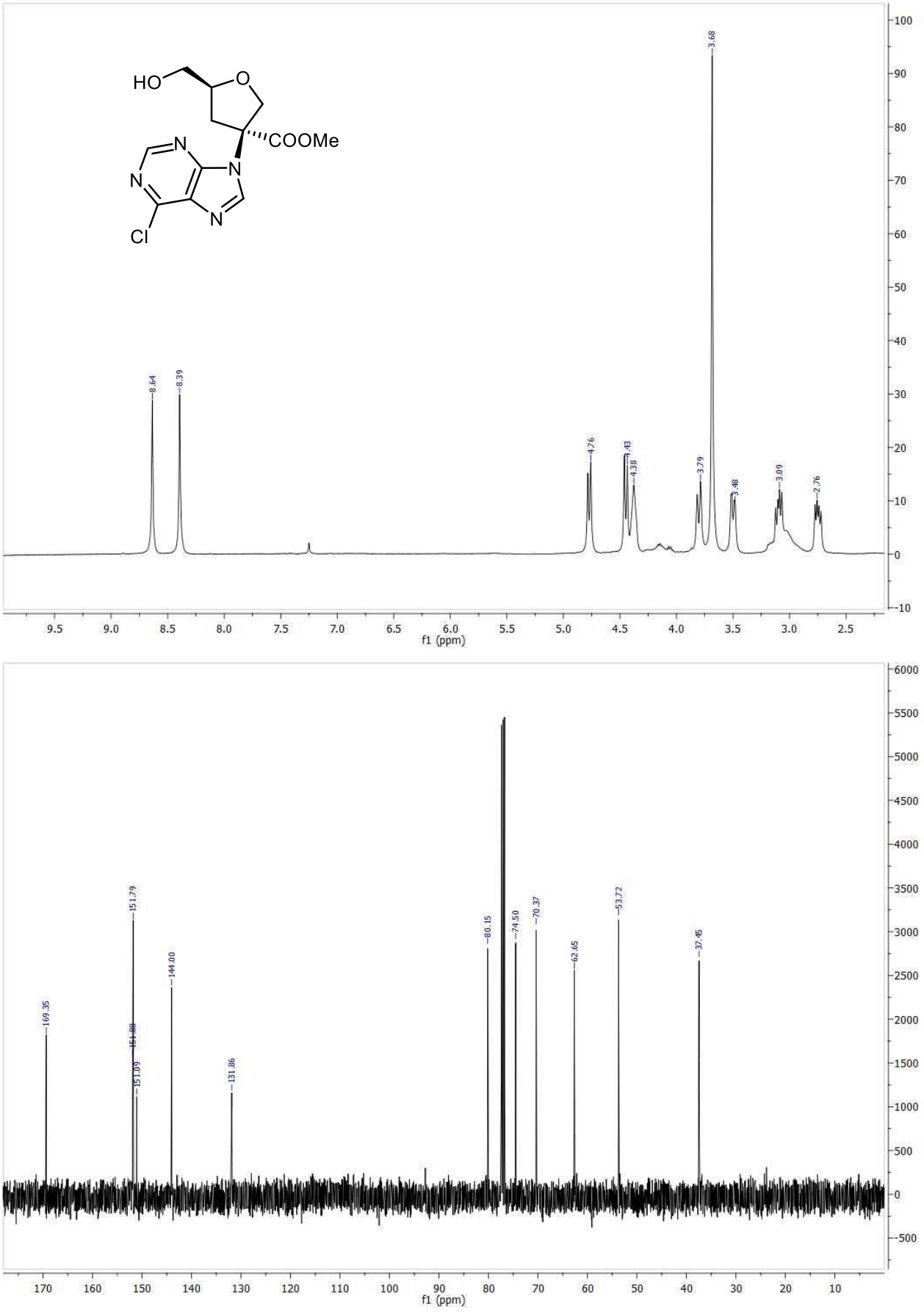

Figure S1. [1]HNMR (400MHz) and [13]CNMR (100MHz) spectra of compound **5** in $CDCl_3$.

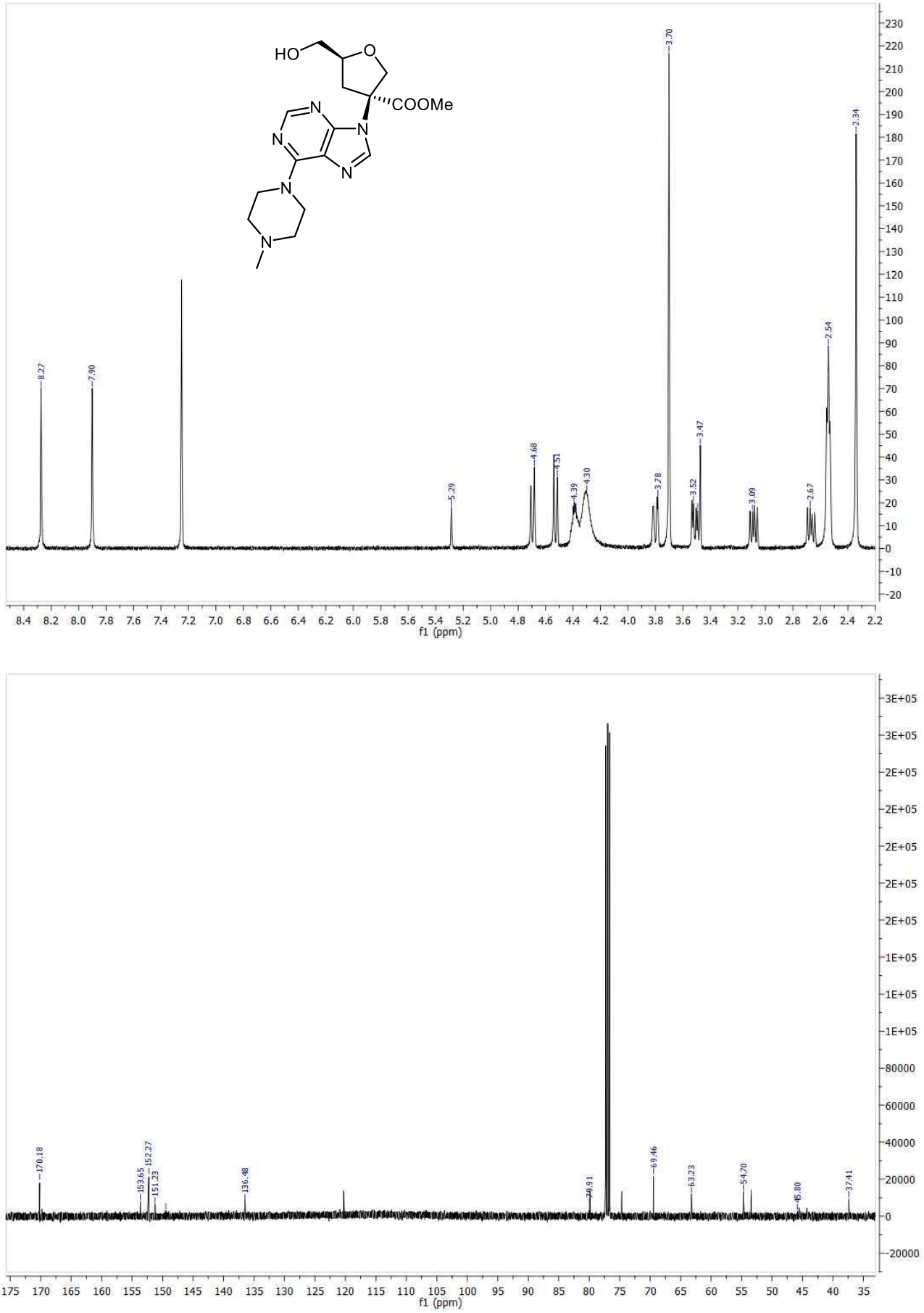

Figure S2. [1]HNMR (400MHz) and [13]CNMR (100MHz) spectra of compound **6** in $CDCl_3$.

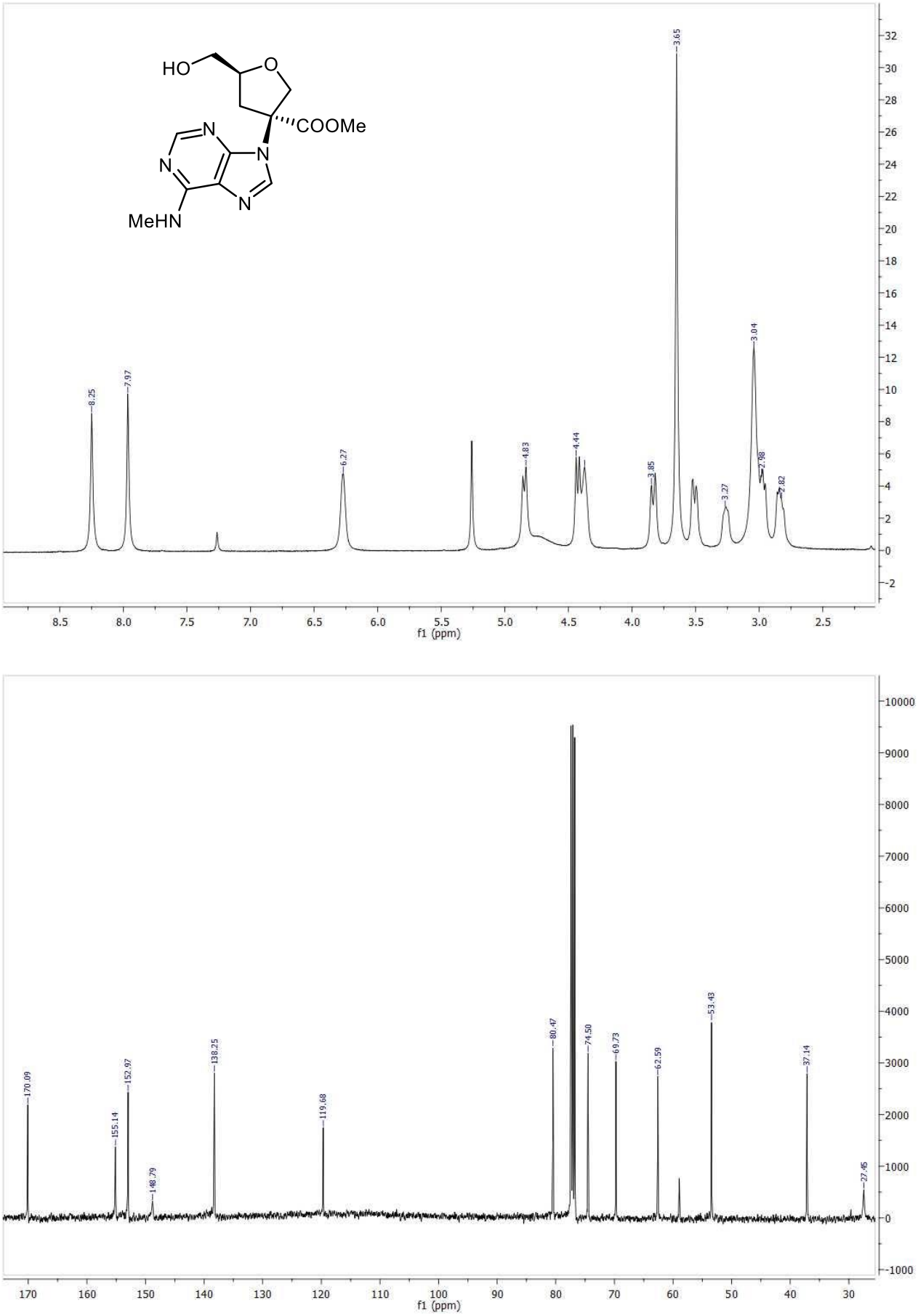

Figure S3. [1]HNMR (400MHz) and [13]CNMR (100MHz) spectra of compound **7** in $CDCl_3$.

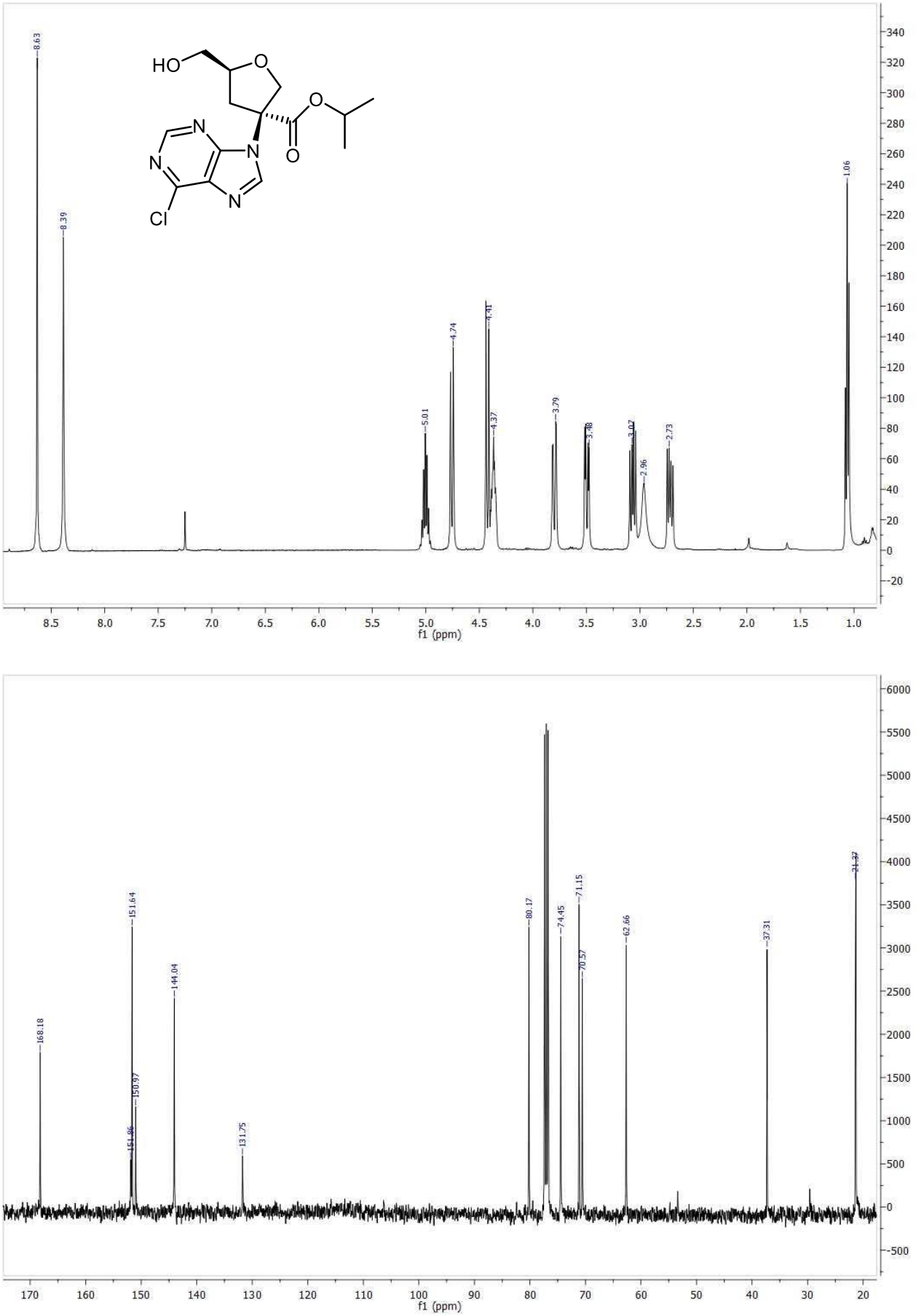

Figure S4. [1]HNMR (400MHz) and [13]CNMR (100MHz) spectra of compound **8** in $CDCl_3$.

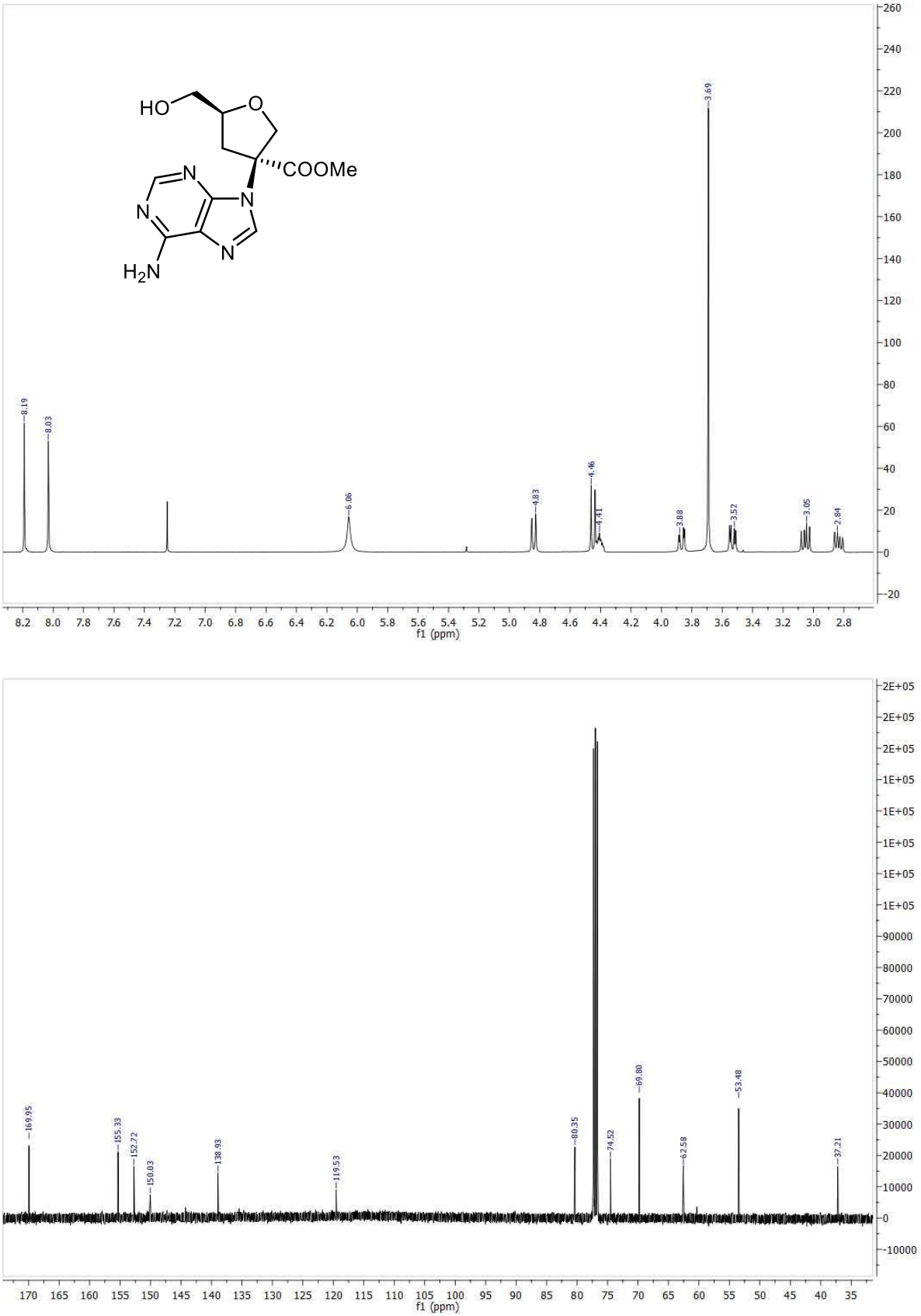

Figure S5. [1]HNMR (400MHz) and [13]CNMR (100MHz) spectra of compound **9** in $CDCl_3$.

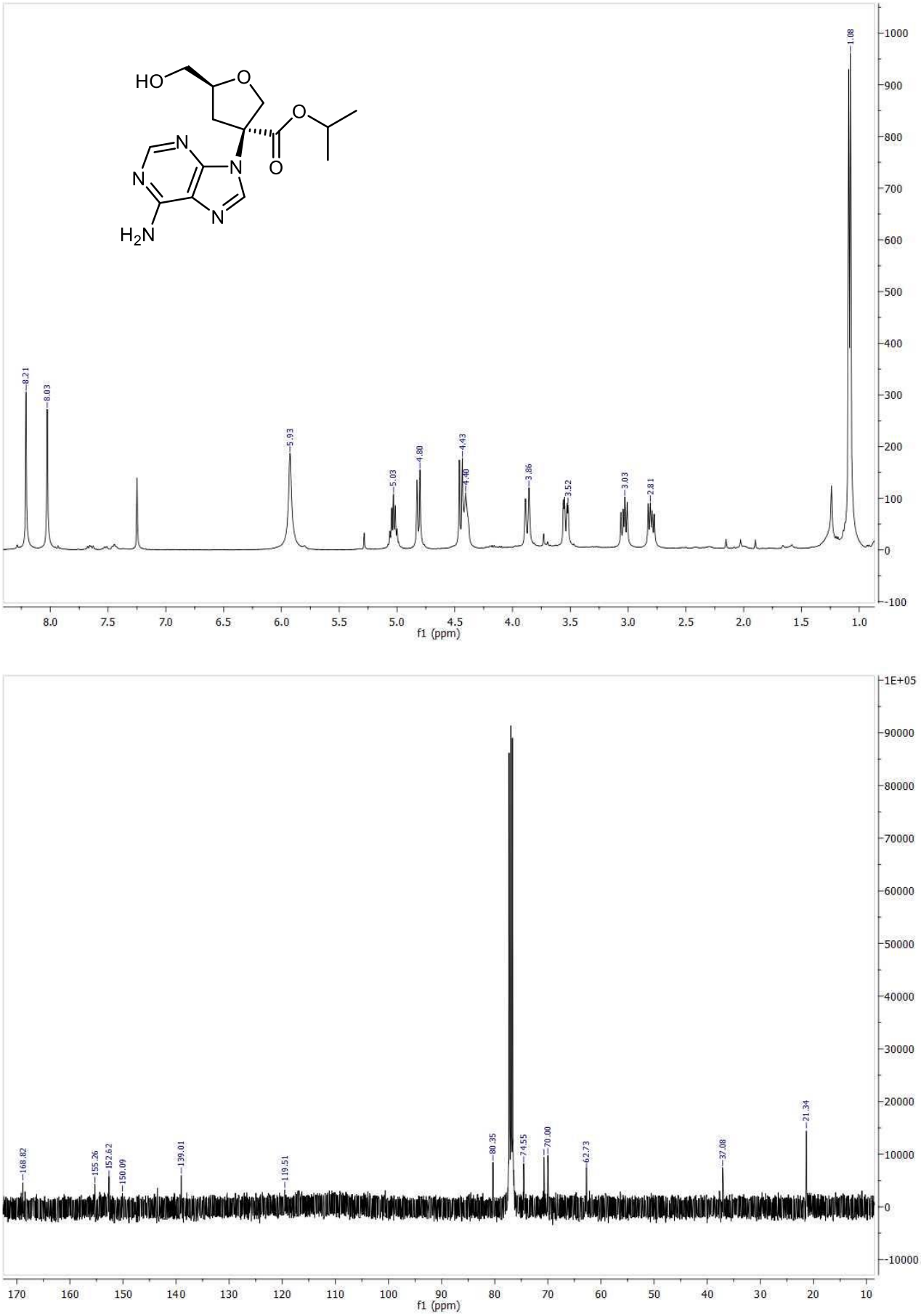

Figure S6. [1]HNMR (400MHz) and [13]CNMR (100MHz) spectra of compound **10** in $CDCl_3$

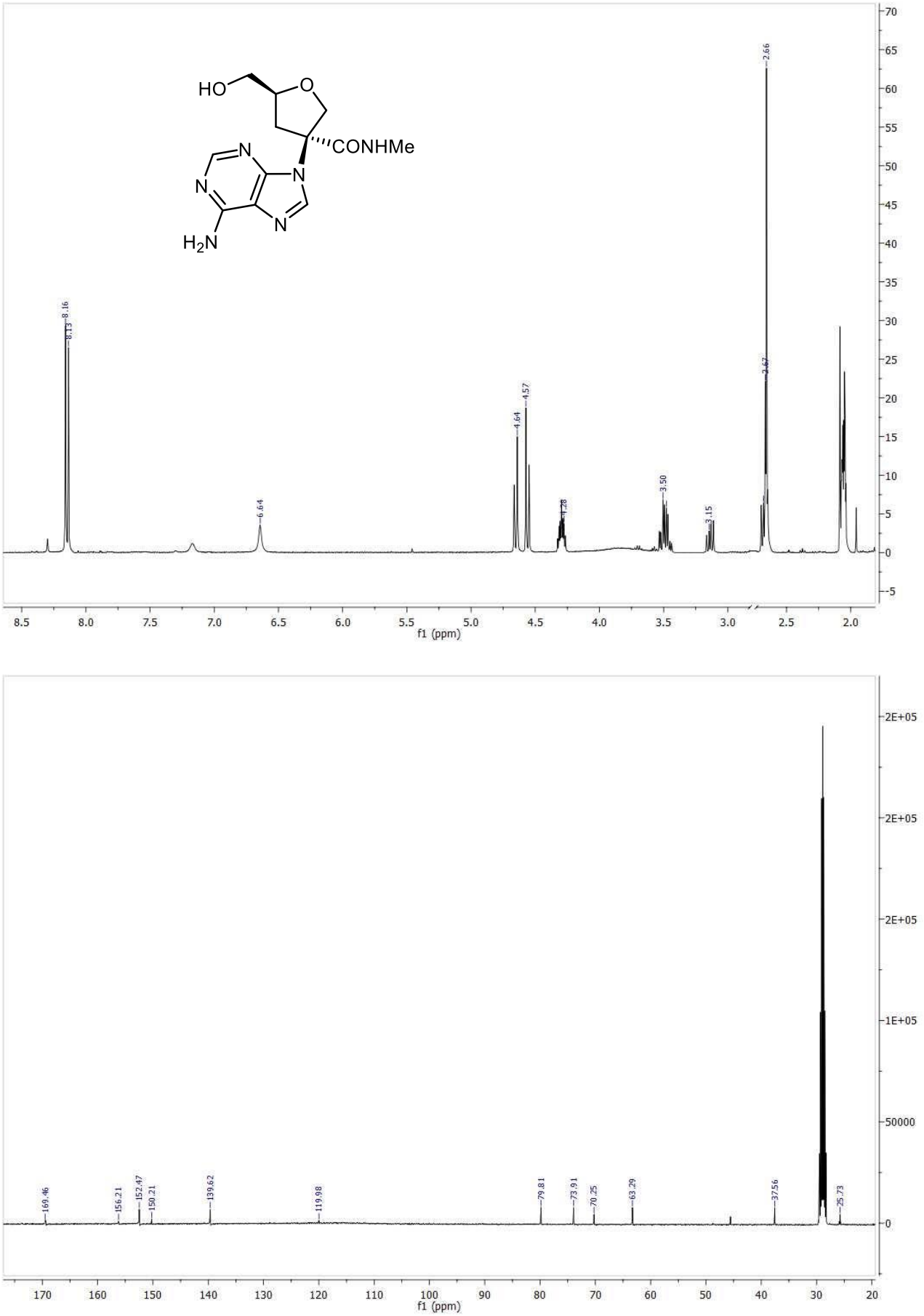

Figure S7. [1]HNMR (400MHz) and [13]CNMR (100MHz) spectra of compound **11** in acetone-d_6

Figure S8. Chemical structure and bioavailability radar for compounds **5**-**11**, remdesivir and GS-441524 evaluated by Swiss-ADME.

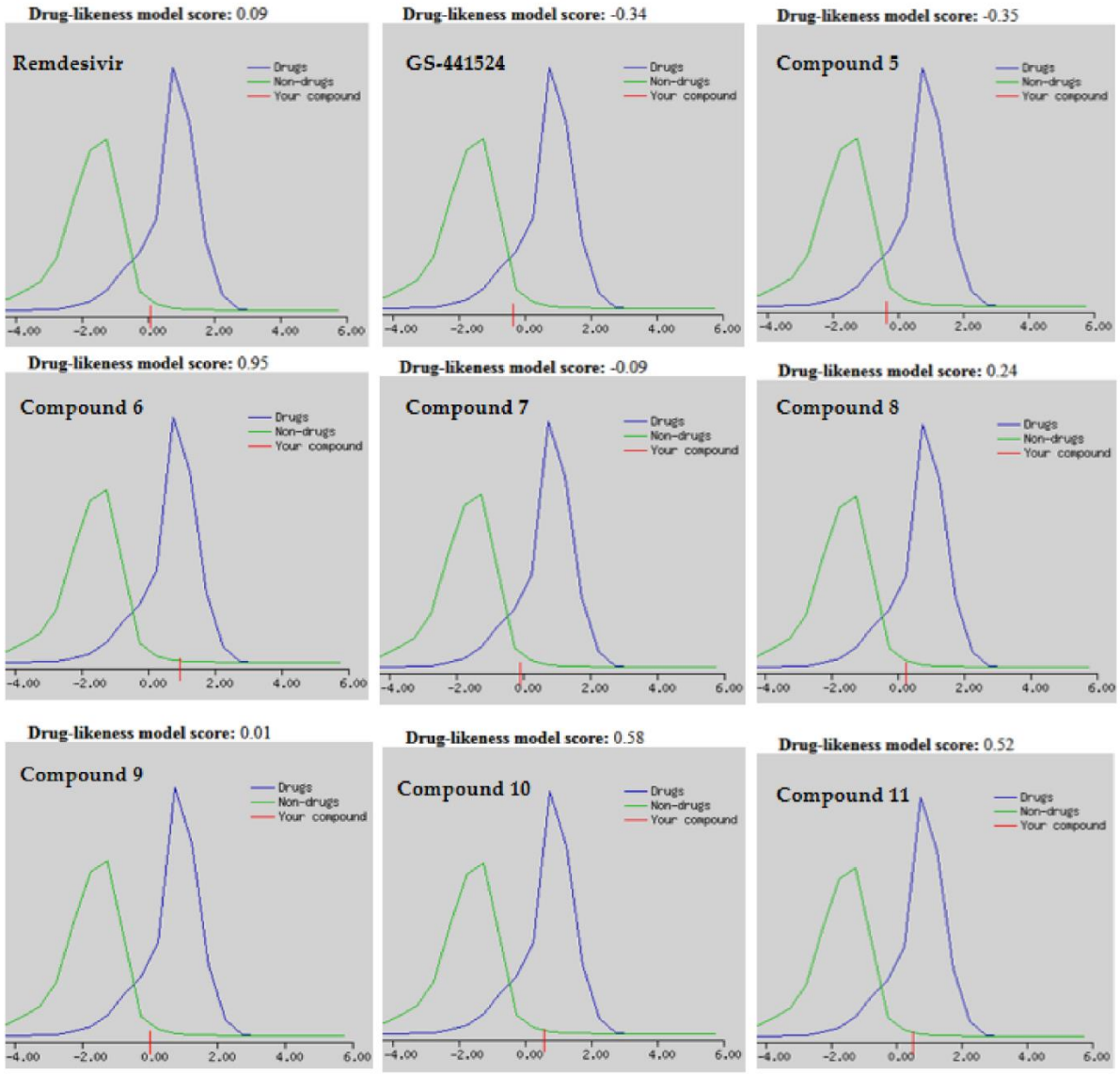

Figure S9. Drug-likeness prediction for compounds **5-11**, remdesivir and GS-441524 by Molsoft server (https://molsoft.com/mprop/)

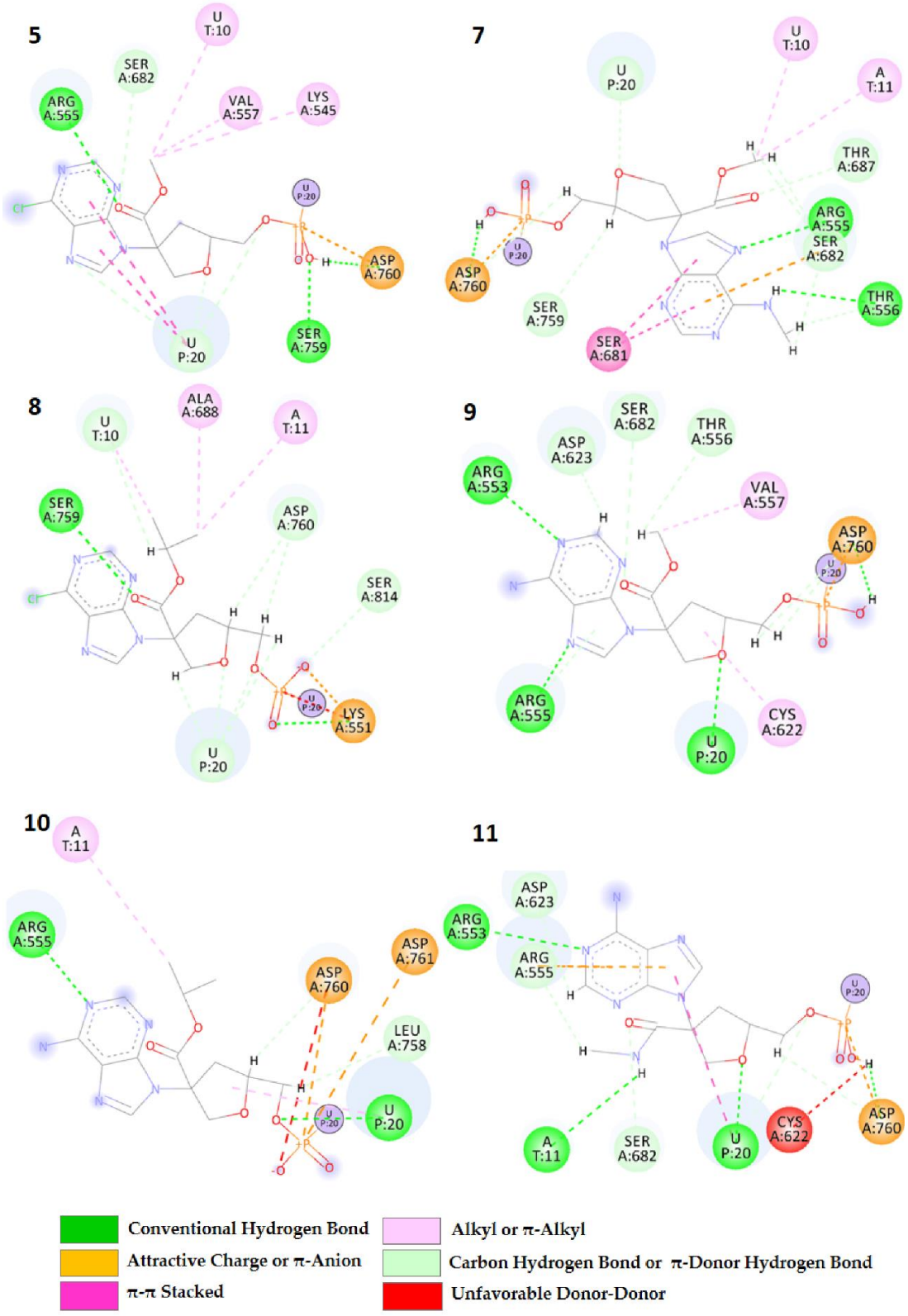

Figure S10. Two-dimensional representations for the interactions of compounds **5** and **7-11** linked to RNA in the receptor pocket of free RdRp (7BV2), as deduced by docking calculation.

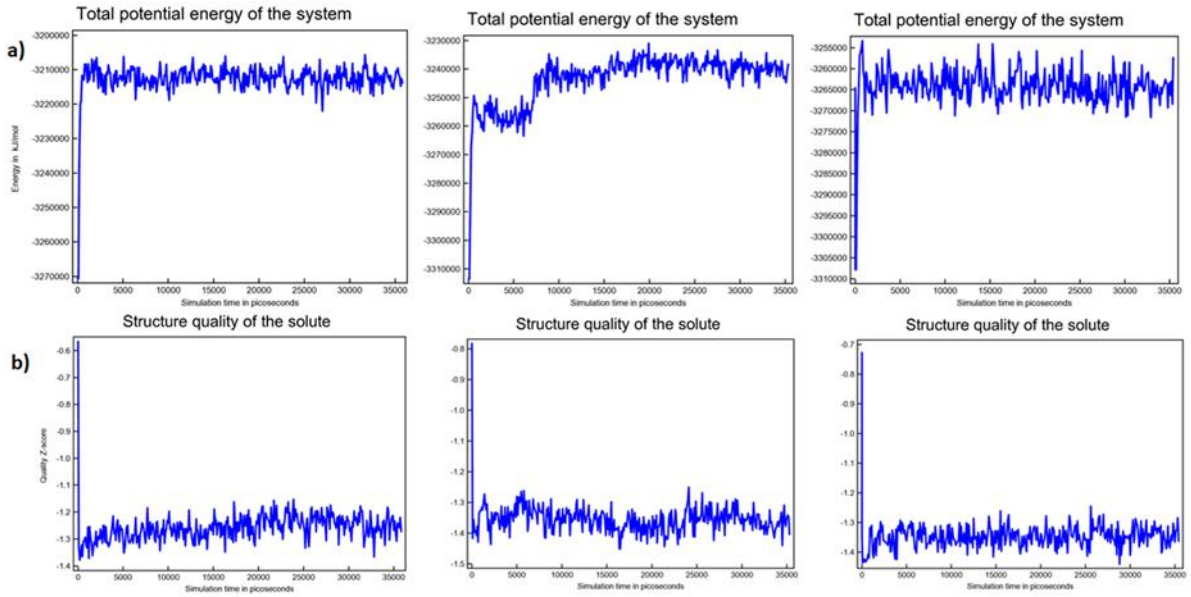

Figure S11. Data from MD simulation: (a) total potential energy of the system during all simulation time and (b) quality Z-score of structure for free RdRp on the left, compound **6** at the center and GS-441524 on the right.

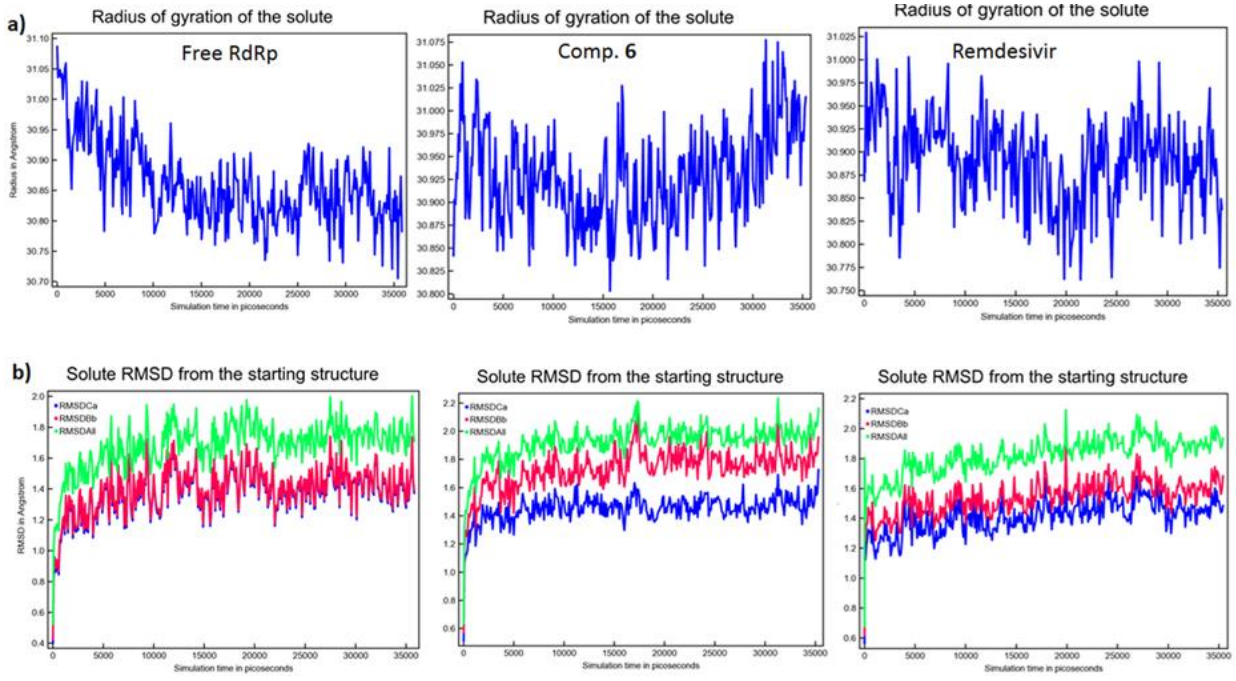

Figure S12. Data from MD simulatio: (a) radius of gyration (in Å) during all simulation time and (b) RMSD (in Å) from the starting structure (Cα in blu, backbone in red and all heavy atoms in green) for free RdRp on the left, compound **6** at the center and GS-441524 on the right.

Table S1. ADME Prediction of compounds **5-11** and reference compounds remdesivir and GS-441524 evaluated by on-line Server Swiss-ADME (http://www.swissadme.ch/)

Molecule	Remdesivir	GS-441524	5	6	7	8	9	10	11
Formula	$C_{24}H_{29}N_6O_8P$	$C_{12}H_{13}N_5O_4$	$C_{12}H_{13}ClN_4O_4$	$C_{17}H_{24}N_6O_4$	$C_{13}H_{17}N_5O_4$	$C_{14}H_{17}ClN_4O_4$	$C_{12}H_{15}N_5O_4$	$C_{14}H_{19}N_5O_4$	$C_{12}H_{16}N_6O_3$
MW	560.50	291.26	312.71	376.41	307.31	340.76	293.28	321.33	292.29
#Heavy atoms	39	21	21	27	22	23	21	23	21
#Aromatic heavy	15	9	9	9	9	9	9	9	9
Fraction Csp3	0.42	0.42	0.50	0.65	0.54	0.57	0.50	0.57	0.50
#Rotatable bonds	12	2	4	5	5	5	4	5	4
#H-bond acceptors	12	7	7	8	7	7	7	7	6
#H-bond donors	4	4	1	1	2	1	2	2	3
MR	136.01	68.48	71.74	102.99	76.03	81.35	71.13	80.75	72.85
TPSA	213.36	149.92	99.36	105.84	111.39	99.36	125.38	125.38	128.18
iLOGP	3.20	0.55	2.09	2.79	2.02	2.53	1.57	2.00	1.46
XLOGP3	0.76	-1.41	0.26	-0.43	-0.38	1.06	-1.05	-0.25	-1.63
WLOGP	1.19	-1.96	0.13	-1.53	-0.67	0.91	-0.93	-0.16	-1.36
MLOGP	-0.43	-1.83	-0.78	-0.91	-1.15	-0.26	-1.42	-0.88	-1.83
Silicos-IT Log P	-1.10	-1.93	0.65	-0.49	-0.28	1.21	-0.71	-0.15	-1.03
Consensus Log P	0.72	-1.32	0.47	-0.11	-0.09	1.09	-0.51	0.11	-0.88
ESOL Log S	-3.29	-0.94	-2.00	-1.82	-1.48	-2.58	-1.05	-1.63	-0.68
ESOL Solubility	2.90e-01	3.32e+01	3.16e+00	5.70e+00	1.02e+01	8.96e-01	2.61e+01	7.46e+00	6.13e+01
ESOL Solubility	5.17e-04	1.14e-01	1.01e-02	1.52e-02	3.32e-02	2.63e-03	8.91e-02	2.32e-02	2.10e-01
ESOL Class	Soluble	Very sol.	Very sol.	Very sol.	Very sol.	Soluble	Very sol.	Very sol.	Very sol.
Ali Log S	-4.82	-1.24	-1.91	-1.33	-1.50	-2.74	-1.09	-1.92	-0.55
Ali Solubility	8.48e-03	1.69e+01	3.87e+00	1.77e+01	9.81e+00	6.23e-01	2.36e+01	3.82e+00	8.21e+01
Ali Solubility (mol/l)	1.51e-05	5.80e-02	1.24e-02	4.70e-02	3.19e-02	1.83e-03	8.04e-02	1.19e-02	2.81e-01
Ali Class	Moderately	Very sol.	Very sol.	Very sol.	Very sol.	Soluble	Very sol.	Very sol.	Very sol.
Silicos-IT LogSw	-3.98	-0.26	-2.45	-1.97	-2.28	-2.87	-1.49	-1.91	-1.80
Silicos-IT Solubility	5.86e-02	1.60e+02	1.10e+00	4.08e+00	1.61e+00	4.57e-01	9.53e+00	3.95e+00	4.63e+00
Silicos-IT Solubility	1.04e-04	5.48e-01	3.52e-03	1.08e-02	5.25e-03	1.34e-03	3.25e-02	1.23e-02	1.58e-02
Silicos-IT class	Soluble	Soluble	Soluble	Soluble	Soluble	Soluble	Soluble	Soluble	Soluble
GI absorption	Low	Low	High	High	High	High	High	High	Low
BBB permeant	No	No	No	No	No	No	No	No	No
Pgp substrate	Yes	No	No	Yes	No	No	No	Yes	No

Molecule	Remdesivir	GS-441524	5	6	7	8	9	10	11
CYP1A2 inhibitor	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes
CYP2C19 inhibitor	No	No	No	No	No	No	No	No	No
CYP2C9 inhibitor	No	No	No	No	No	No	No	No	No
CYP2D6 inhibitor	No	No	No	No	No	No	No	No	No
CYP3A4 inhibitor	Yes	No	No	No	No	No	No	No	No
log Kp (cm/s)	-9.18	-9.08	-8.02	-8.90	-8.44	-7.63	-8.83	-8.44	-9.24
Lipinski #violations	2	0	0	0	0	0	0	0	0
Ghose #violations	2	1	0	1	1	0	1	0	1
Veber #violations	2	1	0	0	0	0	0	0	0
Egan #violations	1	1	0	0	0	0	0	0	0
Muegge #violations	2	0	0	0	0	0	0	0	0
Bioavailability Score	0.17	0.55	0.55	0.55	0.55	0.55	0.55	0.55	0.55
Synthetic	5.96	3.89	3.44	4.17	3.73	3.67	3.57	3.80	3.48