Content:

1. ¹H NMR spectra of new compounds (pages S2-S6)
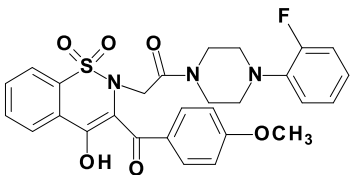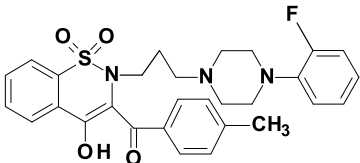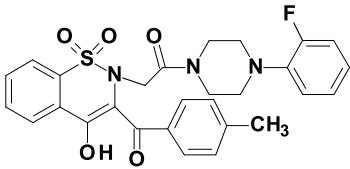
2. Computational studies:

¹H NMR spectra of new compounds

compound	structure	page
PR23		S2
PR24		S3
PR25		S4
PR49		S5
PR50		S6

Figure S1. ^{1}H NMR spectra of **PR23** (full range at the top, aromatic range at the bottom).

Figure S2. ¹H NMR spectra of **PR24** (full range at the top, aromatic range at the bottom).

Figure S3. ¹H NMR spectra of **PR25** (full range at the top, aromatic range at the bottom).

Figure S4. ^{1}H NMR spectra of **PR49** (full range at the top, aromatic range at the bottom).

Current Data Parameters
NAME   Siega B
EXPNO   11
PROCNO   6407

F2 - Acquisition Parameters
Date_   20120120
Time   10.44
INSTRUM   spect
PROBHD   5 mm DUL 13C-1
PULPROG   zg30
TD   65536
SOLVENT   CDCl3
NS   16
DS   0
SWH   6172.839 Hz
FIDRES   0.094190 Hz
AQ   5.3084660 sec
RG   80.6
DW   81.000 usec
DE   8.00 usec
TE   294.4 K
D1   1.00000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   1H
P1   10.40 usec
PL1   2.00 dB
SFO1   300.1518535 MHz

F2 - Processing parameters
SI   32768
SF   300.1500045 MHz
WDW   EM
SSB   0
LB   0.30 Hz
GB   0
PC   20.00

Current Data Parameters
NAME   Siega B
EXPNO   11
PROCNO   6407

F2 - Acquisition Parameters
Date_   20120120
Time   10.44
INSTRUM   spect
PROBHD   5 mm DUL 13C-1
PULPROG   zg30
TD   65536
SOLVENT   CDCl3
NS   16
DS   0
SWH   6172.839 Hz
FIDRES   0.094190 Hz
AQ   5.3084660 sec
RG   80.6
DW   81.000 usec
DE   8.00 usec
TE   294.4 K
D1   1.00000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   1H
P1   10.40 usec
PL1   2.00 dB
SFO1   300.1518535 MHz

F2 - Processing parameters
SI   32768
SF   300.1500045 MHz
WDW   EM
SSB   0
LB   0.30 Hz
GB   0
PC   20.00

Figure S5. ^{1}H NMR spectra of **PR50** (full range at the top, aromatic range at the bottom).
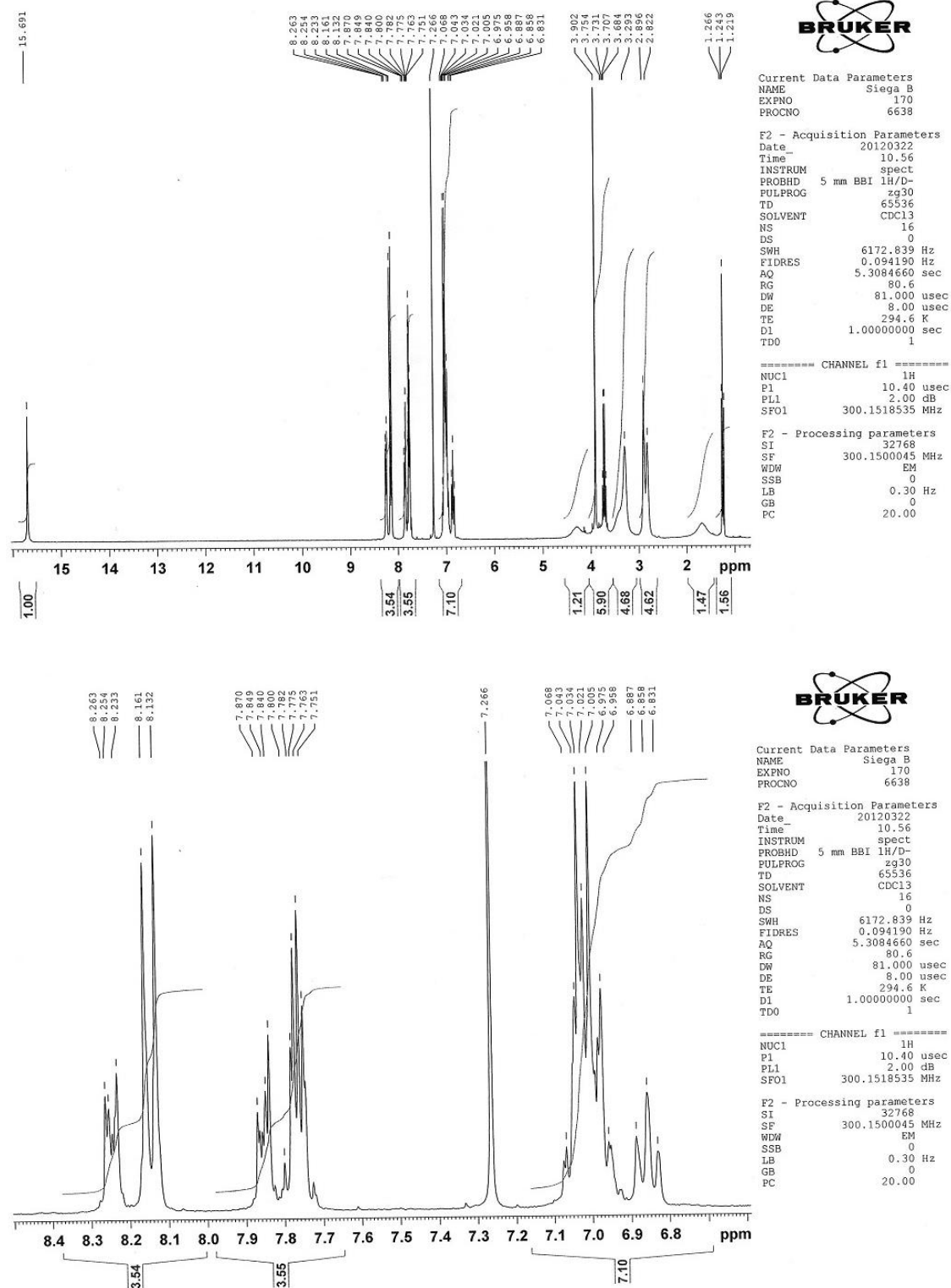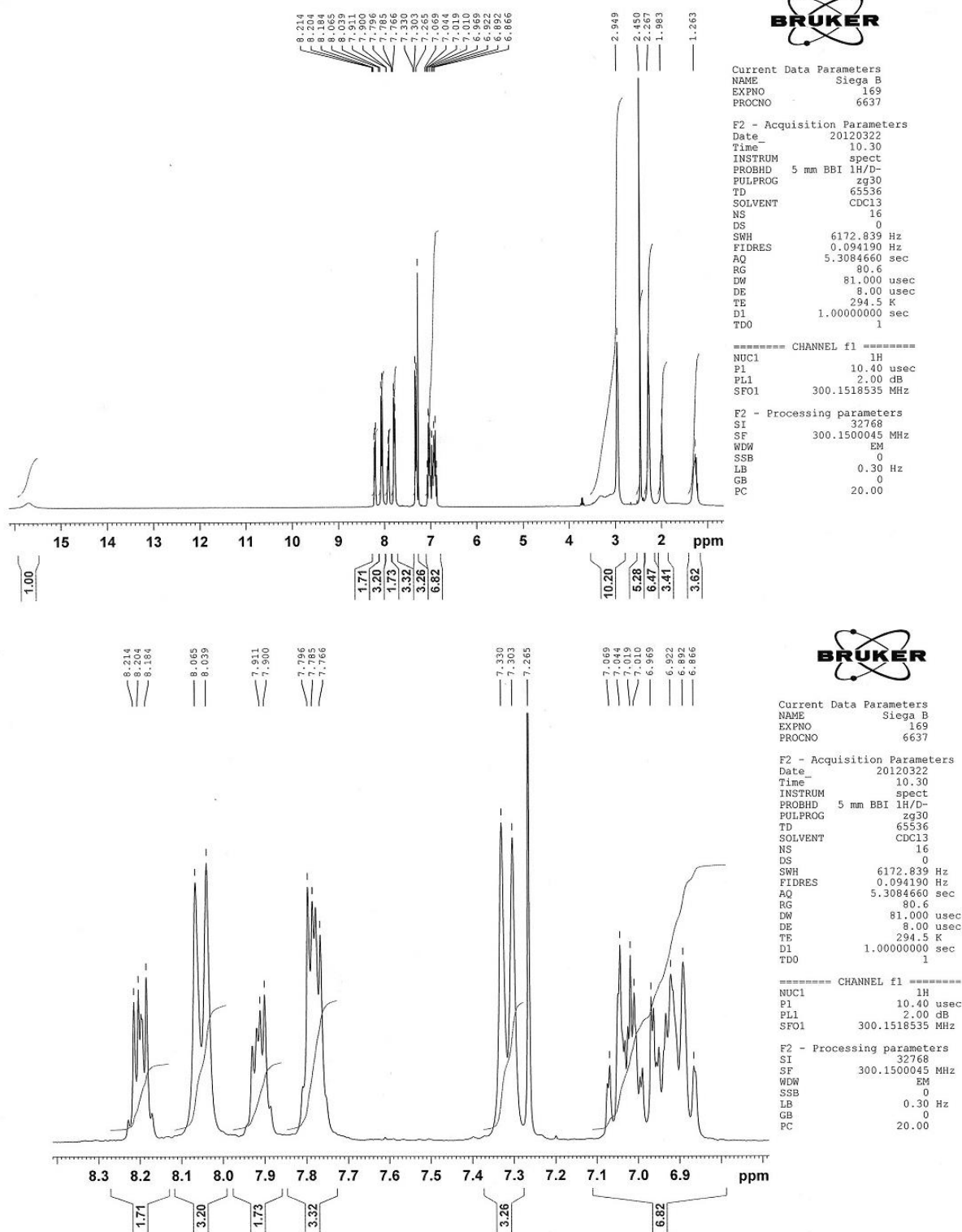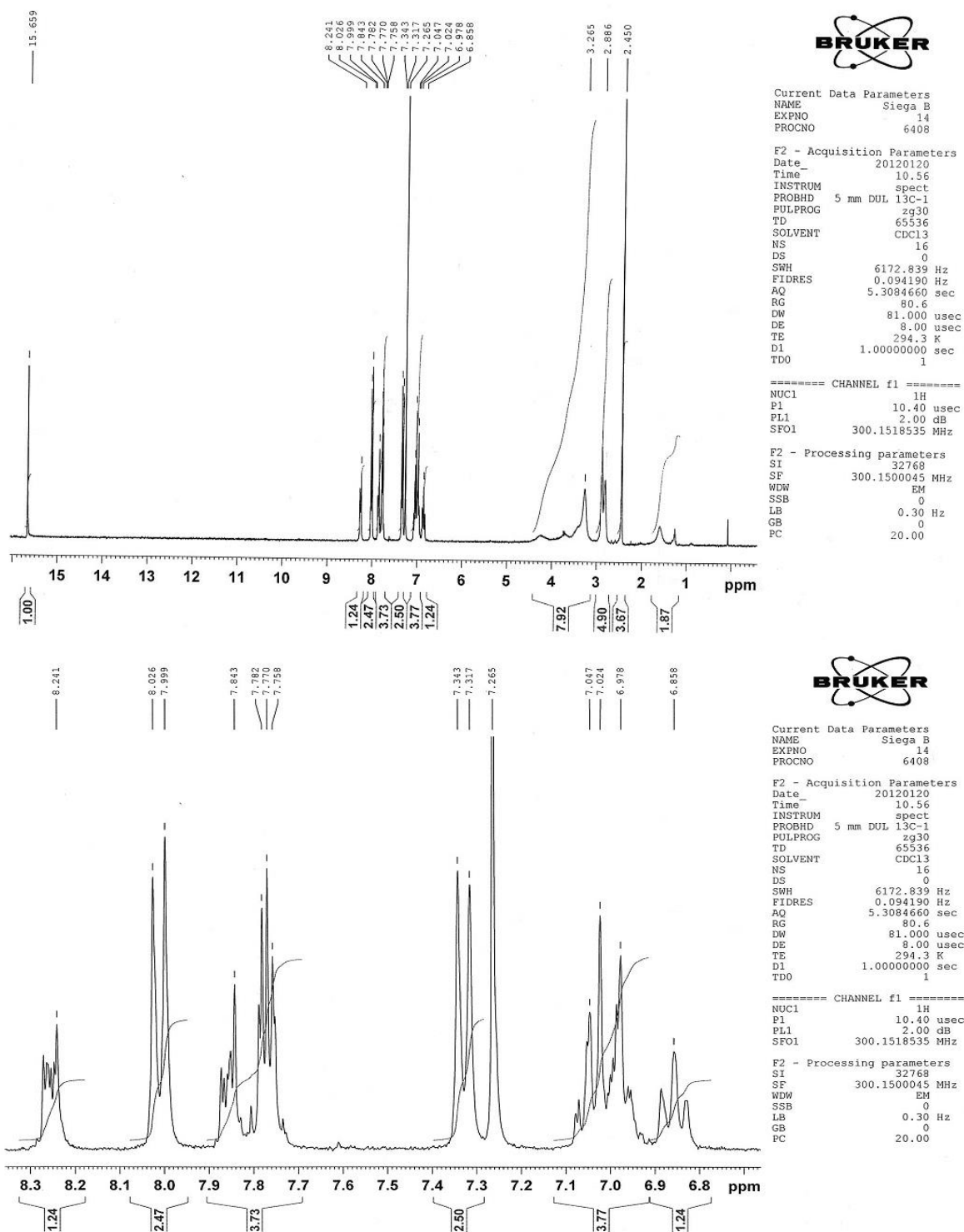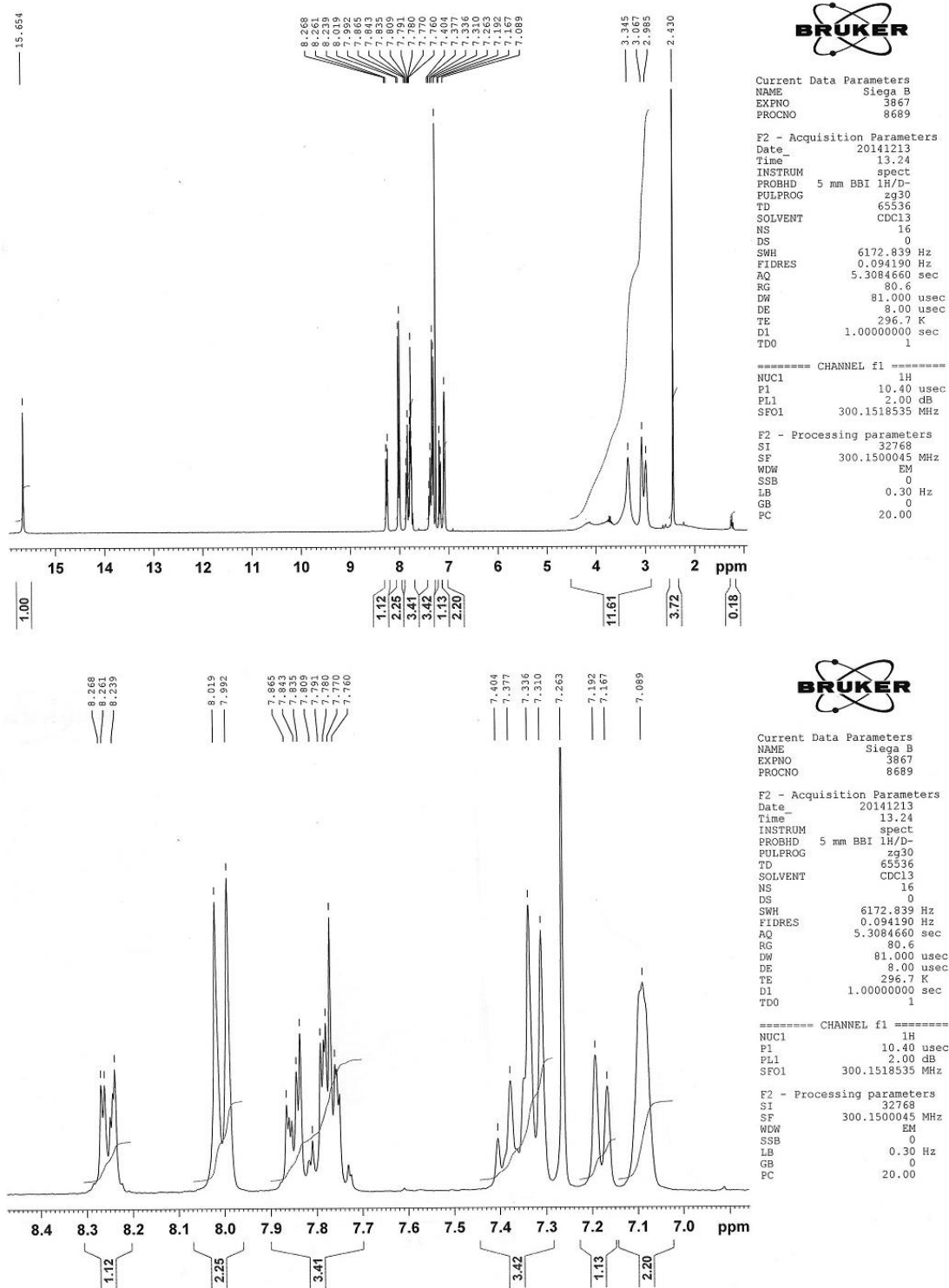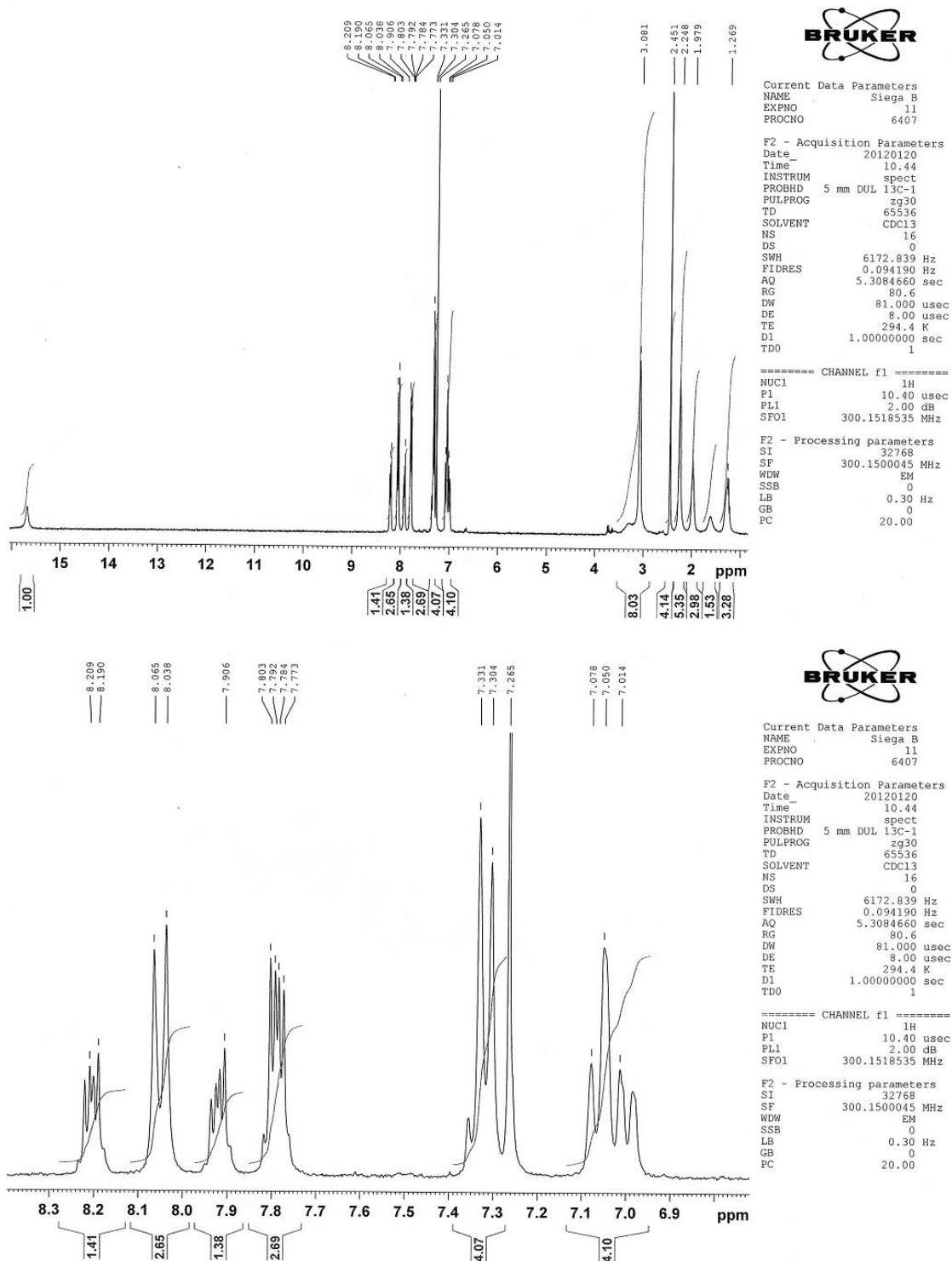
Table S1. Absorption and distribution of studied compounds and meloxicam (MLX).

Parameter	Compound					
	PR23	PR24	PR25	PR49	PR50	MLX
HIA (Human Intestinal Absorption); Category 1: HIA+(HIA < 30%); Category 0: HIA-(HIA < 30%); The output value is the probability of being HIA+)	0.01	0.004	0.005	0.009	0.005	0.004
Caco-2 Permeability; optimal higher than −5.15 log cm/s	−5.5	−5.6	−5.6	−5.584	−5.7	−4.71
MDCK Permeability; high passive permeability: >20·10^{-6}	3.2·10^{-5}	2.9·10^{-5}	2.7·10^{-5}	2.3·10^{-5}	1.9·10^{-5}	1.8·10^{-5}
Pgp-inhibitor	+	+	+	+	+	-
Pgp-substrate	-	-	-	-	-	-
PPB (Plasma Protein Binding; optimal < 90%. Drugs with high protein-bound may have a low therapeutic index)	98%	98%	99%	99%	98%	99%
VD (Volume Distribution; optimal 0.04–20 L/kg)	0.4	1.7	0.4	0.5	2.0	0.4
BBB Penetration (Blood-Brain Barrier Penetration Category; 1: BBB+; Category 0: BBB−; The output value is the probability of being BBB+)	0.1	0.4	0.1	0.1	0.5	0.1

Table S2. Metabolism and excretion of studied compounds and meloxicam (MLX).

Parameter	Compound					
	PR23	PR24	PR25	PR49	PR50	MLX
CYP1A2 inhibitor	no	no	no	no	no	no
CYP2C19 inhibitor	yes	yes	yes	yes	yes	no
CYP2C9 inhibitor	yes	yes	yes	yes	yes	yes
CYP2D6 inhibitor	no	yes	no	no	yes	no
CYP3A4 inhibitor	yes	yes	yes	yes	yes	no
CL—Clearance (high: > 15 mL/min/kg; moderate: 5–15 mL/min/kg; low < 5 mL/min/kg)	5.3	5.1	3.8	2.9	4.2	3.867
T ½ (category 1: long half-life > 3h; category 0: short half-life < 3h)	0.08	0.01	0.06	0.05	0.01	0.427

Table S3. Toxicity of studied compounds and meloxicam (MLX).

Parameter	Compound					
	PR23	PR24	PR25	PR49	PR50	MLX
hERG Blockers (heart rhythm disturbances) 1: active; 0: inactive	0.2	0.8	0.1	0.2	0.8	0.9
H-HT—Human Hepatotoxicity 1: positive(+); 0: negative(−)	1.0	1.0	0.9	1.0	0.9	0.9
DILI—Drug Induced Liver Injury 1: drugs with a high risk; 0: drugs with no risk.	1.0	1.0	1.0	1.0	1.0	1.0
AMES Toxicity 1: Ames positive(+); 0: Ames negative(−)	0.06	0.3	0.05	0.2	0.3	0.03
Rat Oral Acute Toxicity 0: low toxicity; 1: high toxicity	0.6	0.2	0.1	0.8	0.4	0.3
Skin Sensitization 1: sensitizer; 0: non-sensitizer	0.04	0.03	0.04	0.04	0.02	0.07
Carcinogen 1: carcinogens; 0: non-carcinogens	0.5	0.1	0.5	0.1	0.1	0.7
Eye Irritation 1: irritants; 0: non-irritants	0.006	0.006	0.006	0.003	0.006	0.011
Respiratory Toxicity 1: toxicants; 0: non-toxicants	0.07	0.13	0.1	0.3	0.4	0.7