Cooperative Assistance of a Sulfonamide in the Proline-mediated Direct Asymmetric Aldol Addition

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SUPPORTING INFORMATION

Contents

General

- Chiral HPLC studies were carried out on a Shimadzu LC-2010CHT HPLC system.

- ^{1}H and ^{13}C NMR spectra were recorded on a Brucker Avance 500 MHz NMR Spectrometer.

- Mass spectra were obtained using a HRMS-ESI-Q-Time of Flight LC-MS (Synapt G2, Waters).

- Diastereomeric ratios were calculated from the ^{1}H NMR of the crude reaction mixtures.

- All the aldol products were isolated as a mixture of *syn* and *anti*-diastereomers, all the ^{1}H and ^{13}C NMR spectra provided here are of the respective isolated diastereomeric mixture.

- The enantiomeric excess was determined by HPLC analysis of the purified products on a chiral stationary phase (details provided below).

Computational studies on the proposed transition states

For the computational study, all the stationary and saddle point optimizations were carried out at the density functional theory level, employing the B3LYP hybrid functional[1] and 6-31G (d, p)[2] basis set in the gaseous phase. All the computations were performed using Gaussian 09 program package.[3] Computational studies were conducted in order to rationalize the role of the proline-based sulphonamide catalyst in the asymmetric aldol reaction mechanistically and to corroborate the experimental results. First, we carried out the energy calculations for both the catalysts **1a** and **1b**, where the *"cis"* sulfonamide-tagged proline **1a** was more stabilized than the *"trans"* sulfonamide-tagged proline **1b** by an energy difference of 2.31 kcal/mol, conducive to the presence of intramolecular hydrogen bonding interaction between the sulfonamide and carboxylic acid in **1a** (**Figure S1**). The optimized geometries of the species participating in the aldol reaction are shown in **Figures S2-S4**; the lowest vibrational frequencies (v_1) are also provided.

(a) **1a**

E = -1275.46992559 au

$v_1 = 13.42$ cm^{-1}

(b) **1b**

E = -1275.4662439 au

$v_1 = 23.05$ cm^{-1}
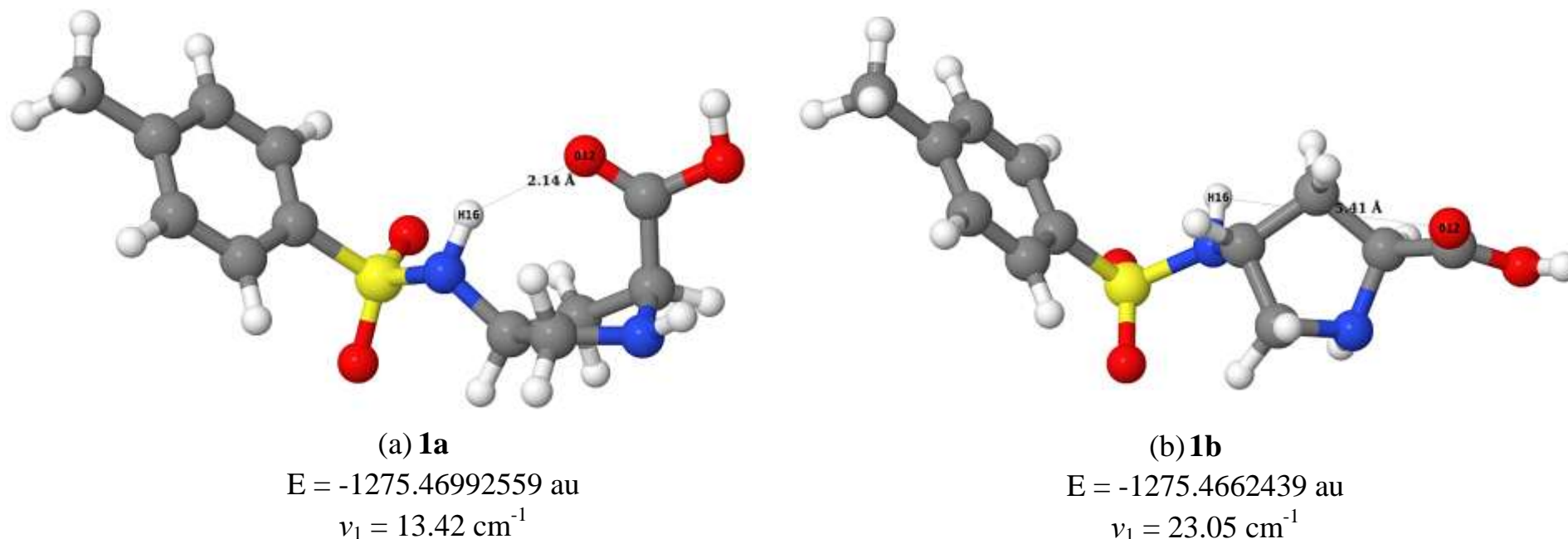
Figure S1: The ball-stick representation of the "*cis*" (**1a**) and "*trans*" (**1b**) catalysts along with the energies and the lowest vibrational frequencies (v_1). The dashed line shows the distance between O12 and H16.

(a) $\mathbf{I_{1a}}$

E = -2059.02276227 au

v_1 = 14.22 cm^{-1}

(b) $\mathbf{TS_{1a}}$

E = -2059.00632853 au

v_1 = -336.08 cm^{-1}

(c) $\mathbf{II_{1a}}$

E = -2059.02170656 au

v_1 = 16.01 cm^{-1}
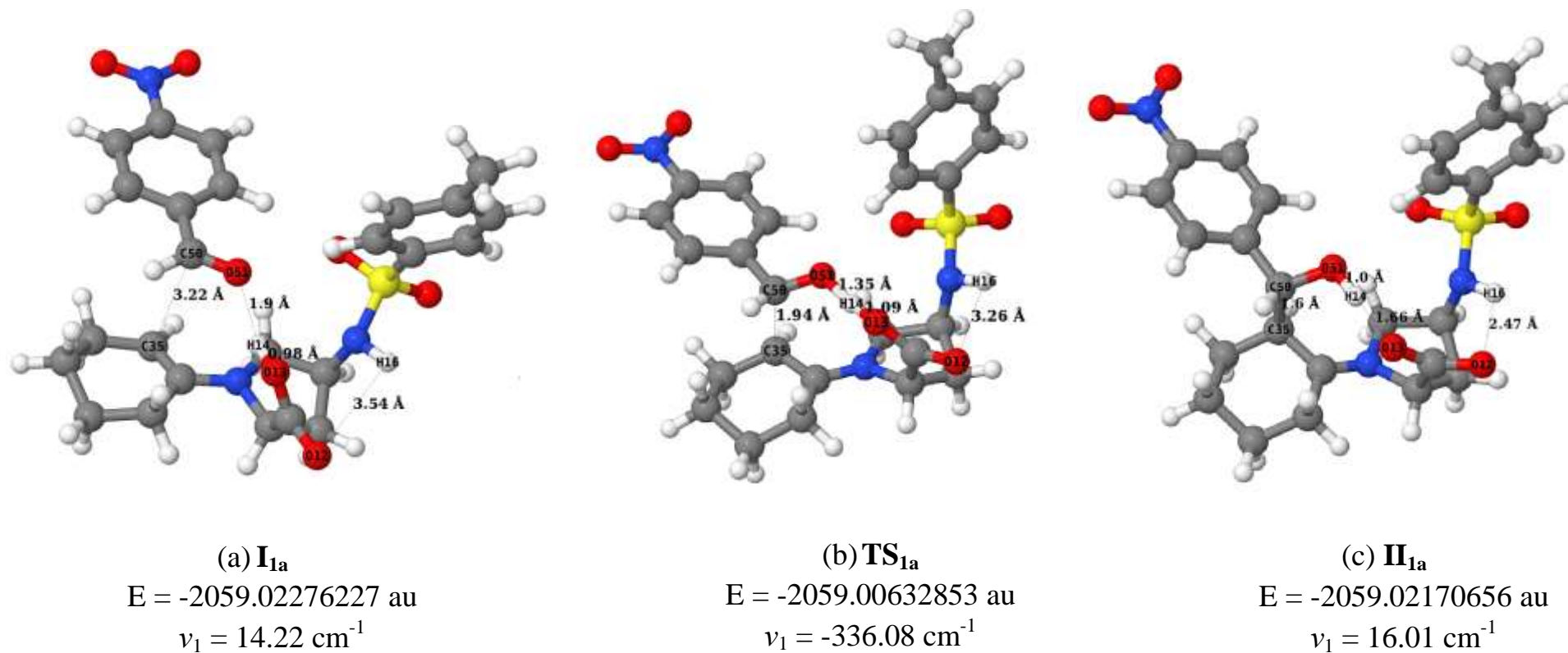
Figure S2: The ball and stick representation of the main constituents of **1a** catalysed aldol reaction along with their energies and lowest negative frequencies
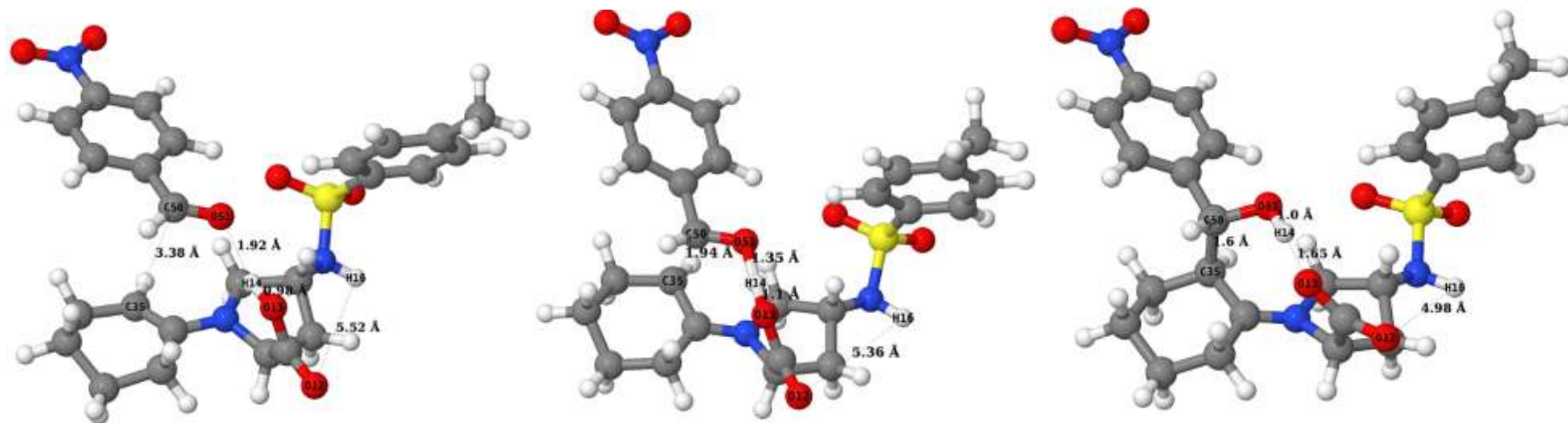
(a) **I$_{1b}$**

E = -2059.02199704 au

v_1 = 13.21 cm^{-1}

(b) **TS$_{1b}$**

E = -2059.00473652 au

v_1 = -353.57 cm^{-1}

(c) **II$_{1b}$**

E = -2059.01844174 au

v_1 = 8.61 cm^{-1}

Figure S3: The ball and stick representation of the main constituents of **1b** catalysed aldol reaction along with their energies and lowest negative frequencies
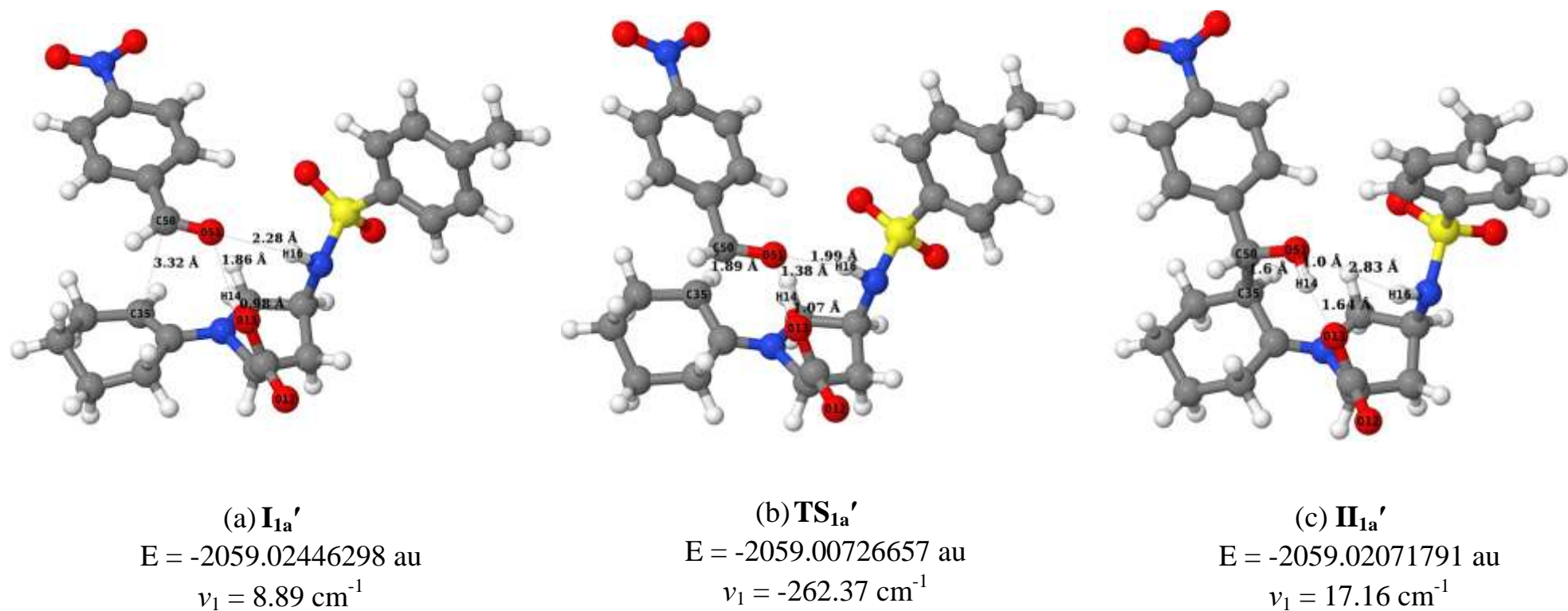
(a) $\mathbf{I_{1a}}'$
E = -2059.02446298 au
$v_1 = 8.89$ cm^{-1}

(b) $\mathbf{TS_{1a}}'$
E = -2059.00726657 au
$v_1 = -262.37$ cm^{-1}

(c) $\mathbf{II_{1a}}'$
E = -2059.02071791 au
$v_1 = 17.16$ cm^{-1}

Figure S4: The ball and stick representation of the main constituents involving a second transition state $\mathbf{TS_{1a}}'$ for the reaction with the catalyst **1a** catalysed aldol reaction along with their energies and lowest negative frequencies

Optimized cartesian coordinates (in angstrom units):

1a

Energy = -1275.46992559 au

C	3.91170	0.00983	-0.01174
C	2.49028	-0.43427	1.83709
C	1.80474	-1.08225	0.60280
C	2.86678	-0.98660	-0.53412
H	4.91447	-0.15917	-0.41392
H	2.42848	-1.07010	2.72591
H	1.98281	0.51369	2.06823
H	1.54669	-2.12377	0.79541
H	3.35473	-1.95506	-0.66900
H	2.41893	-0.69465	-1.48554
C	3.51456	1.45948	-0.28336
O	4.59003	2.26772	-0.40809
O	2.37705	1.89691	-0.30441
H	4.24657	3.17239	-0.51263
N	0.53512	-0.37904	0.33929
H	0.72548	0.56707	-0.00305
N	3.89265	-0.27525	1.43095
S	-0.54352	-1.15345	-0.71361
C	-2.08086	-0.34905	-0.26892
C	-2.65487	0.56617	-1.14823
C	-2.70020	-0.67268	0.94124
C	-3.86167	1.17438	-0.80049
H	-2.16209	0.78761	-2.08831
C	-3.90283	-0.05788	1.27038
H	-2.24360	-1.39768	1.60604
C	-4.50277	0.87375	0.40695
H	-4.31273	1.89077	-1.48169
H	-4.38860	-0.30472	2.21076
O	-0.26060	-0.81778	-2.11930
O	-0.58988	-2.55885	-0.29024
C	-5.82228	1.51207	0.76748
H	-6.01709	2.40013	0.16061
H	-6.65248	0.81358	0.60682
H	-5.84869	1.80673	1.82133
H	4.40073	0.40670	1.98675

1b

Energy = -1275.46624391 au

C	1.91020	-0.09975	1.26680
C	3.42737	0.10929	-0.52545
C	2.11164	0.84636	-0.90708
C	1.04915	0.25717	0.03816
H	1.43390	-0.81657	1.93535
H	2.11877	0.82085	1.82542
H	3.77090	-0.57708	-1.30303
H	2.22073	1.91399	-0.70131
H	1.85768	0.73248	-1.96581

H	0.26240	0.98778	0.26833
C	4.55761	1.09214	-0.22702
O	4.41714	2.22006	0.19553
O	5.76948	0.53885	-0.44757
H	6.42631	1.19759	-0.16410
N	3.16331	-0.64146	0.72686
H	3.01275	-1.61709	0.48747
N	0.48845	-0.96332	-0.58380
H	0.37736	-0.90155	-1.59234
S	-0.88010	-1.71860	0.05340
O	-1.20787	-2.76381	-0.91840
O	-0.59173	-2.01474	1.45865
C	-2.21142	-0.51267	0.02849
C	-2.98187	-0.36579	-1.12795
C	-2.45401	0.27808	1.15336
C	-3.99371	0.58989	-1.15373
H	-2.80119	-1.00870	-1.98286
C	-3.47036	1.23131	1.10851
H	-1.86816	0.12857	2.05345
C	-4.25373	1.40355	-0.04044
H	-4.59765	0.70223	-2.05015
H	-3.66158	1.84666	1.98346
C	-5.37481	2.41351	-0.06897
H	-6.32369	1.95180	0.23043
H	-5.18490	3.24282	0.61798
H	-5.51686	2.82587	-1.07205

I$_{1a}$ (Enamine with *cis*-catalyst **1a**)

Energy = -2059.02276227 au

C	-1.16117	3.44347	-0.54806
C	-0.06362	1.64832	-1.74551
C	-1.55297	1.62914	-2.11057
C	-1.97266	3.07402	-1.80760
H	-0.93572	4.51356	-0.56455
H	0.52174	1.98321	-2.61624
H	0.29723	0.66426	-1.44823
H	-1.70127	1.37604	-3.16660
H	-1.66446	3.70895	-2.64348
H	-3.04571	3.21510	-1.65785
C	-1.99775	3.23187	0.73573
O	-3.00339	3.88431	0.91291
O	-1.56275	2.33966	1.62794
H	-0.81995	1.80154	1.27573
N	-2.31824	0.71554	-1.22357
H	-3.28843	1.01967	-1.14049
N	0.04501	2.61559	-0.64391
S	-2.36060	-0.92201	-1.70301
C	-3.21693	-1.63291	-0.30639
C	-2.66811	-1.52128	0.97535
C	-4.40240	-2.33054	-0.53262

C	-3.33739	-2.11395	2.04037
H	-1.74410	-0.97530	1.13139
C	-5.05279	-2.92151	0.55021
H	-4.79954	-2.40409	-1.53879
C	-4.53615	-2.82049	1.84770
H	-2.92367	-2.02691	3.04136
H	-5.97620	-3.46865	0.38263
O	-3.19430	-1.10257	-2.90074
O	-0.96183	-1.37644	-1.74434
C	-5.25532	-3.43851	3.02158
H	-4.56314	-3.98777	3.66781
H	-5.72958	-2.66687	3.63957
H	-6.03703	-4.12918	2.69540
C	2.44809	2.42357	-0.62488
C	1.30851	3.02310	-0.19969
C	1.33864	4.10677	0.86503
C	2.74457	4.67834	1.09812
C	3.79116	3.56642	1.19179
C	3.82724	2.76674	-0.11568
H	0.93100	3.69828	1.80080
H	2.40044	1.66447	-1.39853
H	3.00614	5.34531	0.26641
H	2.73944	5.29285	2.00496
H	4.78041	3.98199	1.41370
H	3.53437	2.90126	2.02835
H	4.37686	3.34097	-0.87844
H	4.40834	1.84431	0.02202
H	0.66857	4.92909	0.59282
C	1.50524	0.17835	1.48016
O	0.30023	0.26476	1.28444
H	2.02490	0.91087	2.12535
C	2.35923	-0.90067	0.93893
C	1.83547	-1.85351	0.04815
C	3.70206	-0.97045	1.34109
C	2.65368	-2.86677	-0.43701
H	0.80100	-1.78096	-0.27218
C	4.52753	-1.98383	0.86575
H	4.09725	-0.23025	2.03136
C	3.98381	-2.91499	-0.01680
H	2.28538	-3.61207	-1.13041
H	5.56612	-2.06762	1.15845
N	4.85358	-3.99333	-0.52769
O	6.02262	-4.01032	-0.14452
O	4.35555	-4.80675	-1.30304

TS$_{1a}$ (TS with the *cis*-catalyst **1a**)

Energy = -2059.00632853 au

C	1.57705	-3.36259	-0.17221
C	0.55218	-1.82045	-1.75950
C	2.08098	-1.75141	-1.89986

C	2.53723	-3.10634	-1.33936
H	1.45718	-4.43405	0.00074
H	0.09983	-2.23866	-2.66655
H	0.13281	-0.84355	-1.55354
H	2.36780	-1.63002	-2.95068
H	2.41200	-3.87159	-2.11196
H	3.57403	-3.13033	-0.99970
C	2.12165	-2.79178	1.18134
O	3.23004	-3.17768	1.50726
O	1.34590	-2.02982	1.90419
H	0.60658	-1.40559	1.40157
N	2.63302	-0.67384	-1.04854
H	3.59291	-0.86991	-0.76740
N	0.30938	-2.76552	-0.63175
S	2.59576	0.89905	-1.71429
C	2.94285	1.88192	-0.26643
C	2.09012	1.81833	0.84067
C	4.04196	2.74018	-0.29511
C	2.36843	2.62882	1.93659
H	1.23697	1.14602	0.84939
C	4.29558	3.54541	0.81398
H	4.67871	2.77097	-1.17200
C	3.46940	3.50029	1.94408
H	1.71693	2.58358	2.80498
H	5.14837	4.21838	0.79936
O	3.69357	1.08237	-2.67460
O	1.21212	1.10073	-2.17270
C	3.76529	4.34995	3.15552
H	2.84760	4.75739	3.59049
H	4.25779	3.75742	3.93610
H	4.42648	5.18476	2.90880
C	-1.99000	-2.14772	-0.38030
C	-0.89112	-3.02823	-0.12774
C	-1.03605	-4.11639	0.91286
C	-2.45354	-4.70952	0.97066
C	-3.52097	-3.61622	1.04596
C	-3.40489	-2.67432	-0.15798
H	-0.76036	-3.68193	1.88433
H	-1.90182	-1.56236	-1.29197
H	-2.62479	-5.32339	0.07679
H	-2.51841	-5.38382	1.83084
H	-4.52113	-4.06180	1.07459
H	-3.40307	-3.05561	1.98222
H	-3.73032	-3.20875	-1.06185
H	-4.09073	-1.82815	-0.05252
H	-0.31201	-4.91476	0.73097
C	-1.53342	-0.76673	0.90475
O	-0.25646	-0.51834	0.85304
H	-1.91319	-1.28196	1.80384

C	-2.44261	0.36311	0.49245
C	-2.00944	1.31146	-0.44876
C	-3.70883	0.50790	1.07838
C	-2.83498	2.36803	-0.81554
H	-1.01647	1.22789	-0.87865
C	-4.54595	1.56221	0.72312
H	-4.03531	-0.19833	1.83654
C	-4.09577	2.47551	-0.22667
H	-2.52067	3.10892	-1.53984
H	-5.52419	1.69282	1.16800
N	-4.97312	3.59127	-0.61067
O	-6.07988	3.66043	-0.07415
O	-4.55172	4.38978	-1.44714

II$_{1a}$ (Intermediate with *cis*-catalyst **1a**)

Energy = -2059.02170656 au

C	-1.80590	3.32748	-0.04614
C	-0.77418	1.86514	-1.68732
C	-2.30440	1.75100	-1.77783
C	-2.78503	3.08454	-1.18691
H	-1.72853	4.37796	0.23762
H	-0.35113	2.30799	-2.59487
H	-0.32683	0.89667	-1.49302
H	-2.61930	1.63084	-2.81969
H	-2.71959	3.86506	-1.95274
H	-3.80349	3.05160	-0.79902
C	-2.20658	2.50822	1.29830
O	-3.42408	2.44362	1.48196
O	-1.22916	2.09376	1.97695
H	-0.20420	0.94771	1.34434
N	-2.76201	0.62780	-0.93743
H	-3.59224	0.82606	-0.38096
N	-0.52293	2.81408	-0.55244
S	-2.82121	-0.88363	-1.69286
C	-3.02152	-1.96110	-0.28393
C	-2.03398	-2.01012	0.70546
C	-4.14886	-2.77984	-0.22777
C	-2.20109	-2.89059	1.76893
H	-1.15917	-1.37058	0.65238
C	-4.29228	-3.65711	0.84612
H	-4.89213	-2.72521	-1.01501
C	-3.32773	-3.72390	1.85905
H	-1.44226	-2.93111	2.54552
H	-5.16758	-4.29875	0.89627
O	-4.00686	-1.02209	-2.55100
O	-1.48958	-1.04712	-2.30230
C	-3.49970	-4.65289	3.03569
H	-2.55932	-5.15140	3.29070
H	-3.82344	-4.09939	3.92539
H	-4.24986	-5.42187	2.83382

C	1.78059	2.05731	-0.26312
C	0.62731	2.97738	0.03927
C	0.83331	4.02152	1.10636
C	2.18062	4.75474	0.95393
C	3.34690	3.76828	0.86532
C	3.13574	2.79939	-0.30335
H	0.78631	3.50627	2.07271
H	1.63082	1.57276	-1.22906
H	2.16063	5.38105	0.05219
H	2.30316	5.43365	1.80397
H	4.29156	4.30581	0.72979
H	3.43528	3.21907	1.81154
H	3.18428	3.36662	-1.24185
H	3.94093	2.06089	-0.35231
H	0.00875	4.73484	1.11807
C	1.70843	0.87510	0.81656
O	0.42010	0.32845	0.87167
H	2.00790	1.29256	1.78896
C	2.68276	-0.22636	0.43961
C	2.31297	-1.19592	-0.50552
C	3.95475	-0.29022	1.02320
C	3.20219	-2.20092	-0.87225
H	1.31752	-1.17597	-0.93656
C	4.85755	-1.28850	0.66548
H	4.24003	0.43848	1.77670
C	4.46580	-2.22847	-0.28349
H	2.93468	-2.95951	-1.59692
H	5.84300	-1.35547	1.10846
N	5.41299	-3.28690	-0.66912
O	6.52212	-3.28364	-0.13436
O	5.04136	-4.11026	-1.50439

I_{1b} (Enamine with *trans*-catalyst **1b**)

Energy = -2059.02199704 au

C	-0.96085	3.38914	-0.56430
C	-0.15640	1.27988	-1.42827
C	-1.66774	1.17889	-1.20684
C	-2.09279	2.64716	-1.32166
H	-0.78071	4.36422	-1.02730
H	0.05599	1.38659	-2.50362
H	0.37962	0.40823	-1.05835
H	-1.85569	0.84204	-0.17922
H	-2.09000	2.94614	-2.37582
H	-3.07753	2.86508	-0.90153
C	-1.40140	3.69068	0.88523
O	-2.11939	4.63344	1.12821
O	-0.99379	2.84269	1.83979
H	-0.42835	2.12478	1.47827
N	-2.33837	0.30905	-2.17676
H	-3.24109	0.63820	-2.50753

N	0.18847	2.47925	-0.66550
S	-2.40559	-1.34870	-1.86624
C	-3.44311	-1.58080	-0.42025
C	-2.89764	-1.46313	0.86221
C	-4.80153	-1.85232	-0.59829
C	-3.73248	-1.60691	1.96819
H	-1.83899	-1.26862	0.99502
C	-5.61738	-1.99941	0.52096
H	-5.20171	-1.96452	-1.60007
C	-5.10017	-1.87745	1.81849
H	-3.31202	-1.50957	2.96529
H	-6.67327	-2.21641	0.38444
O	-3.10134	-1.92762	-3.01470
O	-1.04131	-1.74094	-1.49342
C	-5.98531	-2.06300	3.02646
H	-5.68089	-1.40876	3.84847
H	-7.03238	-1.85321	2.79209
H	-5.93187	-3.09484	3.39474
C	2.55102	2.16370	-1.02613
C	1.51998	2.89413	-0.53904
C	1.75438	4.16247	0.26284
C	3.19183	4.68633	0.13706
C	4.20741	3.55199	0.29174
C	4.00481	2.50818	-0.81325
H	1.51316	3.97019	1.31789
H	2.34965	1.28549	-1.63116
H	3.32349	5.15395	-0.84733
H	3.35872	5.47014	0.88377
H	5.23156	3.94050	0.26720
H	4.07199	3.08068	1.27557
H	4.44214	2.88035	-1.75328
H	4.56865	1.59496	-0.57672
H	1.05959	4.94750	-0.05579
C	1.64105	0.26123	1.61999
O	0.43102	0.40294	1.49519
H	2.24572	1.03170	2.13459
C	2.39673	-0.91937	1.15176
C	1.76964	-1.93537	0.40953
C	3.75955	-1.01874	1.47313
C	2.50200	-3.04069	-0.00629
H	0.72227	-1.84671	0.14171
C	4.50018	-2.12374	1.06776
H	4.23734	-0.22856	2.04570
C	3.85313	-3.11636	0.33476
H	2.05073	-3.83507	-0.58691
H	5.55116	-2.23189	1.30255
N	4.63253	-4.29358	-0.09952
O	5.82415	-4.32880	0.20396
O	4.04116	-5.16364	-0.73465

TS_{1b} (TS with *trans*-catalyst **1b**)

Energy = -2059.00473652 au

C	-1.17844	3.44709	-0.18485
C	-0.57768	1.50332	-1.52742
C	-2.02147	1.37691	-1.03299
C	-2.42533	2.84468	-0.86338
H	-1.05939	4.50037	-0.44402
H	-0.57086	1.77434	-2.59038
H	-0.00904	0.59847	-1.37218
H	-2.00839	0.90446	-0.04262
H	-2.59227	3.29931	-1.84643
H	-3.31322	3.00117	-0.24791
C	-1.32501	3.40279	1.37216
O	-2.06628	4.23810	1.85641
O	-0.67722	2.49243	2.05142
H	-0.16240	1.66998	1.53993
N	-2.86952	0.64501	-1.97371
H	-3.84994	0.91488	-1.95221
N	-0.05714	2.63558	-0.72259
S	-2.75039	-1.05049	-1.99339
C	-3.30611	-1.64272	-0.39436
C	-2.43772	-1.63180	0.70351
C	-4.62200	-2.09263	-0.26529
C	-2.91127	-2.06517	1.93964
H	-1.41209	-1.29173	0.60518
C	-5.07066	-2.53028	0.97874
H	-5.27148	-2.11359	-1.13349
C	-4.22767	-2.52198	2.09874
H	-2.24169	-2.04920	2.79500
H	-6.09182	-2.88727	1.08016
O	-3.71740	-1.48375	-3.00073
O	-1.31634	-1.33929	-2.10477
C	-4.71184	-3.01828	3.43890
H	-4.31097	-2.41208	4.25661
H	-5.80300	-3.00103	3.50301
H	-4.38776	-4.05167	3.61207
C	2.19551	1.81855	-0.65148
C	1.22463	2.85117	-0.45009
C	1.60653	4.09917	0.31382
C	3.06416	4.52531	0.07989
C	4.02335	3.35091	0.28108
C	3.67165	2.20750	-0.67763
H	1.44333	3.89307	1.38130
H	1.94771	1.11082	-1.43747
H	3.17144	4.91507	-0.94068
H	3.30285	5.35072	0.75827
H	5.05817	3.66887	0.11519
H	3.96537	3.00774	1.32233
H	3.93636	2.50716	-1.70149

H	4.28061	1.32356	-0.46331
H	0.93029	4.92010	0.06134
C	1.75985	0.72183	0.88262
O	0.46509	0.60453	1.00838
H	2.28074	1.32414	1.64617
C	2.51380	-0.54898	0.58084
C	1.93011	-1.56233	-0.19702
C	3.79549	-0.75003	1.11348
C	2.61840	-2.74241	-0.45320
H	0.93039	-1.43108	-0.59760
C	4.49672	-1.92803	0.86957
H	4.24187	0.01414	1.74338
C	3.89592	-2.90751	0.08360
H	2.18576	-3.53282	-1.05347
H	5.48417	-2.10260	1.27754
N	4.62852	-4.15485	-0.18132
O	5.75556	-4.27028	0.30195
O	4.07322	-5.00926	-0.87141

II₁b (Intermediate with *trans*-catalyst **1b**)

Energy = -2059.01844174 au

C	-1.51386	3.33437	-0.01255
C	-0.85490	1.40220	-1.32577
C	-2.32824	1.30034	-0.90802
C	-2.73052	2.76974	-0.74559
H	-1.40621	4.41248	-0.13318
H	-0.78491	1.58703	-2.40236
H	-0.28489	0.52422	-1.05574
H	-2.38388	0.81886	0.07808
H	-2.87517	3.23105	-1.72980
H	-3.62028	2.92132	-0.13270
C	-1.60534	3.04080	1.58001
O	-2.64852	3.47109	2.06787
O	-0.61507	2.45072	2.09673
H	0.17820	1.11472	1.53785
N	-3.12552	0.58566	-1.90587
H	-4.11764	0.80874	-1.87145
N	-0.36513	2.60812	-0.59571
S	-2.93352	-1.09971	-2.02684
C	-3.42504	-1.80563	-0.45399
C	-2.51225	-1.86655	0.60522
C	-4.73584	-2.26103	-0.29887
C	-2.93388	-2.37639	1.83036
H	-1.48895	-1.52993	0.47794
C	-5.13403	-2.77518	0.93323
H	-5.42135	-2.22715	-1.13860
C	-4.24570	-2.83757	2.01556
H	-2.22905	-2.41703	2.65604
H	-6.15151	-3.13593	1.05515
O	-3.90328	-1.51575	-3.03903

O	-1.49097	-1.31838	-2.18187
C	-4.67664	-3.40707	3.34467
H	-4.32532	-2.78634	4.17467
H	-5.76455	-3.48542	3.41389
H	-4.26138	-4.41108	3.49304
C	1.93504	1.78669	-0.52896
C	0.87964	2.83123	-0.27821
C	1.28264	4.08651	0.45164
C	2.63513	4.65069	-0.02070
C	3.72204	3.57488	-0.01376
C	3.30456	2.39872	-0.90224
H	1.32931	3.81974	1.51525
H	1.62729	1.13306	-1.34693
H	2.53150	5.05971	-1.03436
H	2.90565	5.48914	0.62902
H	4.67009	3.98836	-0.37404
H	3.90077	3.23828	1.01561
H	3.25034	2.74695	-1.94170
H	4.05839	1.60670	-0.88551
H	0.50440	4.84697	0.37411
C	1.97489	0.85074	0.77363
O	0.69569	0.37896	1.10075
H	2.39839	1.44585	1.59531
C	2.88162	-0.34130	0.52321
C	2.42451	-1.42659	-0.24026
C	4.17816	-0.37800	1.05198
C	3.24798	-2.52109	-0.48129
H	1.41363	-1.42332	-0.63402
C	5.01689	-1.46549	0.81978
H	4.53450	0.44635	1.66312
C	4.53658	-2.52180	0.05139
H	2.91247	-3.36791	-1.06652
H	6.02002	-1.51185	1.22408
N	5.41481	-3.67572	-0.20076
O	6.54797	-3.64685	0.27966
O	4.96500	-4.59903	-0.87825

I$_{1a}'$

Energy = -2059.02446298 au

C	-0.57226	-3.50532	0.55612
C	0.23542	-1.55389	1.74784
C	-1.29599	-1.53491	1.83278
C	-1.65656	-3.00270	1.54624
H	-0.26809	-4.51872	0.83775
H	0.67591	-1.86698	2.70843
H	0.64398	-0.57221	1.49621
H	-1.64473	-1.22711	2.81903
H	-1.58321	-3.57336	2.47681
H	-2.66754	-3.12183	1.15542
C	-1.14794	-3.64627	-0.86842

O	-1.87104	-4.57640	-1.14163
O	-0.84334	-2.69962	-1.76758
H	-0.25337	-2.00573	-1.39832
N	-1.93032	-0.62535	0.85468
H	-1.40923	-0.54013	-0.01816
N	0.52268	-2.53132	0.69037
S	-2.35021	0.92633	1.38956
C	-3.74943	1.29645	0.33930
C	-3.63710	2.29094	-0.62915
C	-4.94998	0.60583	0.52977
C	-4.74326	2.58687	-1.42677
H	-2.70081	2.82422	-0.74612
C	-6.04056	0.91484	-0.27368
H	-5.02452	-0.15560	1.29831
C	-5.95514	1.90598	-1.26629
H	-4.66118	3.36207	-2.18339
H	-6.97643	0.38177	-0.12960
O	-2.80045	0.77372	2.77758
O	-1.29182	1.90232	1.06902
C	-7.14503	2.21418	-2.14171
H	-6.98341	3.11793	-2.73451
H	-7.34376	1.39032	-2.83731
H	-8.05157	2.35675	-1.54449
C	2.89495	-2.12076	0.86013
C	1.85372	-2.83598	0.36968
C	2.07191	-3.95575	-0.63402
C	3.53571	-4.41190	-0.70622
C	4.48527	-3.21453	-0.78192
C	4.33630	-2.34405	0.47181
H	1.73035	-3.62594	-1.62507
H	2.71829	-1.35024	1.60299
H	3.77611	-5.00493	0.18571
H	3.66640	-5.07348	-1.56930
H	5.52315	-3.54651	-0.89500
H	4.24506	-2.62243	-1.67642
H	4.87784	-2.81228	1.30888
H	4.82939	-1.37381	0.31911
H	1.44373	-4.81739	-0.38408
C	1.67634	-0.07972	-1.45988
O	0.48758	-0.30722	-1.26198
H	2.28947	-0.78875	-2.04516
C	2.38213	1.13090	-0.99764
C	1.71307	2.11402	-0.24794
C	3.73479	1.29578	-1.33631
C	2.39788	3.25173	0.16252
H	0.66847	1.97869	0.01478
C	4.42754	2.43124	-0.93129
H	4.24233	0.53212	-1.91915
C	3.74171	3.38969	-0.18762

H	1.91456	4.02601	0.74459
H	5.47004	2.58930	-1.17536
N	4.47005	4.59966	0.24535
O	5.65579	4.69169	-0.06902
O	3.84556	5.43801	0.89156

TS_{1a}′

Energy= -2059.00726657 au

C	0.30098	3.75948	0.28054
C	-0.14923	1.94613	1.86920
C	1.37164	2.08943	1.73190
C	1.53086	3.51877	1.18441
H	-0.07906	4.77420	0.41558
H	-0.50201	2.37477	2.81552
H	-0.46083	0.90925	1.80440
H	1.86740	1.99332	2.69940
H	1.51900	4.22452	2.02098
H	2.46394	3.65652	0.63864
C	0.67465	3.67472	-1.23362
O	1.27430	4.63346	-1.67927
O	0.33729	2.61859	-1.93292
H	-0.03783	1.75371	-1.41769
N	1.96169	1.07791	0.83343
H	1.29234	0.77276	0.11672
N	-0.70210	2.77031	0.75866
S	2.53723	-0.31127	1.62975
C	3.55217	-1.03552	0.35232
C	3.14298	-2.22027	-0.25646
C	4.76048	-0.42282	0.00858
C	3.95627	-2.79147	-1.23479
H	2.20871	-2.68321	0.03913
C	5.55641	-1.00745	-0.96950
H	5.06885	0.49064	0.50481
C	5.16712	-2.19628	-1.60858
H	3.64461	-3.71617	-1.71210
H	6.49769	-0.53798	-1.24174
O	3.37745	0.17070	2.73286
O	1.43488	-1.24796	1.92555
C	6.02987	-2.80341	-2.68752
H	5.78030	-3.85411	-2.85653
H	5.89445	-2.27446	-3.63873
H	7.09197	-2.74110	-2.43159
C	-2.66263	1.42879	0.43737
C	-1.92850	2.65191	0.26711
C	-2.43753	3.69315	-0.70371
C	-3.97210	3.78520	-0.72825
C	-4.60522	2.40571	-0.91810
C	-4.17372	1.46283	0.21094
H	-2.06379	3.42956	-1.70307
H	-2.40736	0.86882	1.33292

H	-4.32824	4.22656	0.21161
H	-4.26964	4.46931	-1.52935
H	-5.69739	2.48490	-0.93730
H	-4.30447	1.99883	-1.89217
H	-4.65814	1.78102	1.14465
H	-4.53153	0.44571	0.02483
H	-2.00416	4.66960	-0.47125
C	-1.76015	0.38422	-0.85908
O	-0.46463	0.58906	-0.80676
H	-2.27204	0.76844	-1.75789
C	-2.22191	-1.01875	-0.54162
C	-1.50468	-1.81697	0.36326
C	-3.34974	-1.55372	-1.18160
C	-1.92225	-3.11315	0.64464
H	-0.60469	-1.43280	0.83175
C	-3.77839	-2.85086	-0.91280
H	-3.88672	-0.95839	-1.91464
C	-3.05836	-3.61070	0.00540
H	-1.38342	-3.74220	1.34209
H	-4.64353	-3.28135	-1.40079
N	-3.50434	-4.98087	0.29876
O	-4.51326	-5.39032	-0.27721
O	-2.84491	-5.63799	1.10394

II₁ₐ′

Energy= -2059.02071791 au

C	-1.78926	-3.41921	0.27695
C	-0.70930	-1.88338	1.85478
C	-2.23313	-1.65030	1.87708
C	-2.78340	-2.99180	1.36599
H	-1.70221	-4.50255	0.19789
H	-0.37477	-2.38855	2.76776
H	-0.16634	-0.95397	1.71745
H	-2.57418	-1.43022	2.89101
H	-2.79859	-3.71350	2.19023
H	-3.79200	-2.90934	0.96012
C	-2.22093	-2.86272	-1.16090
O	-3.13330	-3.50959	-1.66490
O	-1.60777	-1.82869	-1.57586
H	-0.31801	-0.91635	-1.13764
N	-2.67504	-0.54027	1.02014
H	-2.32540	-0.62066	0.05842
N	-0.49422	-2.82409	0.71304
S	-2.37812	1.00917	1.65857
C	-2.95274	2.02777	0.31258
C	-2.12314	2.23956	-0.79214
C	-4.21584	2.61167	0.40113
C	-2.58935	3.04247	-1.82945
H	-1.13914	1.78314	-0.84011
C	-4.65635	3.41914	-0.64489

H	-4.82820	2.43939	1.27918
C	-3.85695	3.64155	-1.77461
H	-1.95541	3.21169	-2.69539
H	-5.63588	3.88499	-0.58261
O	-3.25714	1.15259	2.82453
O	-0.93158	1.24390	1.84763
C	-4.35612	4.48781	-2.92002
H	-3.54361	5.05777	-3.38004
H	-4.79712	3.86002	-3.70397
H	-5.12569	5.19217	-2.59276
C	1.78520	-2.03262	0.27086
C	0.61135	-2.94238	0.03624
C	0.72343	-3.91999	-1.10359
C	2.06673	-4.67864	-1.08838
C	3.25571	-3.71769	-1.01436
C	3.12844	-2.79595	0.20436
H	0.63575	-3.33429	-2.02898
H	1.70957	-1.55850	1.25011
H	2.08878	-5.35972	-0.22775
H	2.12070	-5.30449	-1.98459
H	4.19349	-4.28002	-0.95223
H	3.30837	-3.12881	-1.93879
H	3.22190	-3.40018	1.11595
H	3.94527	-2.06954	0.23497
H	-0.11197	-4.61906	-1.11662
C	1.65007	-0.84107	-0.79496
O	0.36509	-0.29071	-0.76437
H	1.88941	-1.25589	-1.78584
C	2.65155	0.25419	-0.47644
C	2.32324	1.25276	0.45390
C	3.90330	0.28483	-1.10562
C	3.23925	2.25442	0.76147
H	1.34032	1.25863	0.91422
C	4.83033	1.27952	-0.80592
H	4.15301	-0.46451	-1.85162
C	4.48246	2.24929	0.13041
H	3.00539	3.03643	1.47282
H	5.80023	1.32253	-1.28469
N	5.45551	3.30542	0.45337
O	6.54483	3.27355	-0.12012
O	5.12429	4.15568	1.27856

Transition state for the Desymmetrisation:
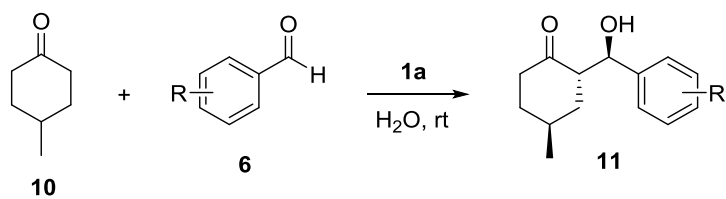
The absolute configuration of the desymmetrised adduct was confirmed based on comparison with the literature reports. The reaction may be expected to proceed via a transition state similar to the standard aldol addition, which is in accordance with the observed stereoselectivity (illustrated below).
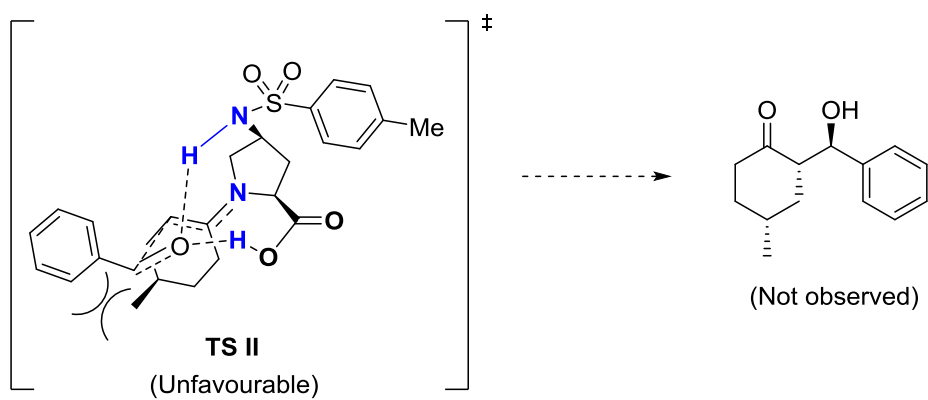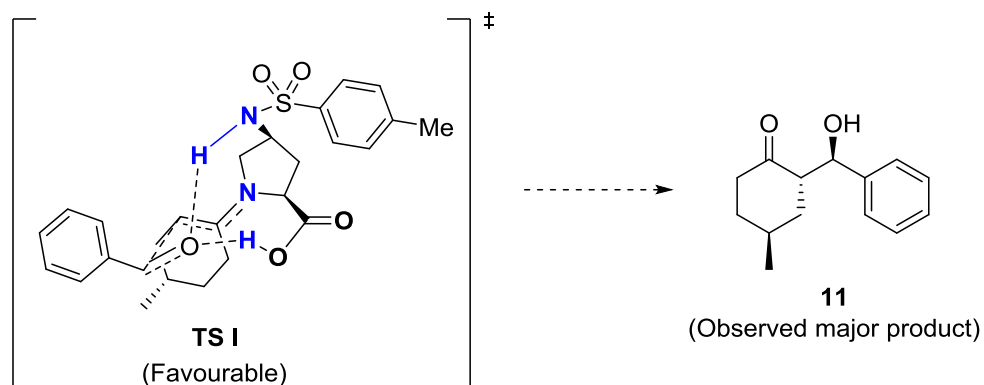
Specific rotation of the aldol adducts:

      The optical rotation was measured for a few purified aldol adducts and the corresponding specific rotation values are given below. It may be noted that the optical purity of the adducts, however, was determined by HPLC analysis on a chiral stationary phase, which follows further below:

(S)-2-((R)-hydroxy(4-nitrophenyl)methyl)cyclohexan-1-one (**7a**)

$[\alpha]_D^{23}$ +13.6 (*c* 1.0, CHCl$_3$) {Lit.[4] $[\alpha]_D^{25}$ +12.8 (*c* 1.85, CHCl$_3$)}

4-((R)-hydroxy((S)-2-oxocyclohexyl)methyl)benzonitrile (**7b**)

$[\alpha]_D^{23}$ +26.0 (*c* 1.0, CHCl$_3$) {Lit.[5] $[\alpha]_D^{20}$ +24.4 (*c* 0.50, CHCl$_3$)}

(S)-2-((R)-hydroxy(4-(trifluoromethyl)phenyl)methyl)cyclohexan-1-one (**7c**)

$[\alpha]_D^{23}$ +14.2 (*c* 1.0, CHCl$_3$) {Lit.[5] $[\alpha]_D^{20}$ +16.3 (*c* 0.5, CHCl$_3$)}

(S)-2-((R)-(4-bromophenyl)(hydroxy)methyl)cyclohexan-1-one (**7d**)

$[\alpha]_D^{23}$ +21.0 (*c* 1.0, CHCl$_3$) {Lit.[6] $[\alpha]_D^{25}$ +24.0 (*c* 1.0, CHCl$_3$)}

methyl 4-((R)-hydroxy((S)-2-oxocyclohexyl)methyl)benzoate (**7f**)

$[\alpha]_D^{23}$ +25.0 (*c* 1.0, CHCl$_3$) {Lit.[7] $[\alpha]_D^{20}$ +23.8 (*c* 1.0, CHCl$_3$)}

(S)-2-((R)-hydroxy(pyridin-4-yl)methyl)cyclohexan-1-one (**7h**)

$[\alpha]_D^{23}$ +26.0 (*c* 1.0, CHCl$_3$) {Lit.[8] $[\alpha]_D^{23}$ +30.2 (*c* 0.96, CHCl$_3$)}

(S)-2-((R)-hydroxy(perfluorophenyl)methyl)cyclohexan-1-one (**7i**)

$[\alpha]_D^{23}$ -17.0 (*c* 1.0, CHCl$_3$) {Lit.[8] $[\alpha]_D^{23}$ -17.0 (*c* 1.4, CHCl$_3$)}

(S)-2-((R)-(2-chlorophenyl)(hydroxy)methyl)cyclohexan-1-one (**7k**)

$[\alpha]_D^{23}$ +23.0 (*c* 1.0, CHCl$_3$) {Lit.[8] $[\alpha]_D^{23}$ +21.2 (*c* 0.9, CHCl$_3$)}

(S)-2-((R)-hydroxy(3-nitrophenyl)methyl)cyclohexan-1-one (**7l**)

$[\alpha]_D^{23}$ +25.0 (*c* 1.0, CHCl$_3$) {Lit.[6] $[\alpha]_D^{25}$ +26.0 (*c* 1.0, CHCl$_3$)}

(S)-2-((R)-hydroxy(3-phenoxyphenyl)methyl)cyclohexan-1-one (**7n**)

$[\alpha]_D^{23}$ -59.3 (*c* 1.0, CHCl$_3$)

(S)-2-((R)-(4-chloro-3-nitrophenyl)(hydroxy)methyl)cyclohexan-1-one (**7o**)

$[\alpha]_D^{23}$ +51.0 (*c* 1.0, CHCl$_3$)

(S)-2-((R)-hydroxy(naphthalen-2-yl)methyl)cyclohexan-1-one (**7q**)

$[\alpha]_D^{23}$ +13.0 (*c* 1.0, CHCl$_3$) {Lit.[8] $[\alpha]_D^{23}$ +17.3 (*c* 0.8, CHCl$_3$)}

(S)-2-((R)-hydroxy(4-nitrophenyl)methyl)cyclopentan-1-one (**9a**)

$[\alpha]_D^{23}$ -25.6 (*c* 1.0, CHCl$_3$) {Lit.[6] $[\alpha]_D^{25}$ -25.0 (*c* 0.5, CHCl$_3$)}

(R)-4-hydroxy-4-(4-nitrophenyl)butan-2-one (**9b**)

$[\alpha]_D^{23}$ +52.0 (*c* 1.0, CHCl$_3$) {Lit.[8] $[\alpha]_D^{23}$ +54.0 (*c* 0.55, CHCl$_3$)}

2-(Hydroxy(4-nitrophenyl)methyl)-4-methylcyclohexan-1-one (**11a**)

$[\alpha]_D^{23}$ -47.0 (*c* 1.0, CHCl$_3$) {Lit.[8] $[\alpha]_D^{23}$ -48.0 (*c* 0.55, CHCl$_3$)}

4-((R)-hydroxy((1S,5S)-5-methyl-2-oxocyclohexyl)methyl)benzonitrile (**11b**)

$[\alpha]_D^{23}$ +22.0 (*c* 1.0, CHCl$_3$)

References:

1. (a) A. D. Becke, Density-Functional Thermochemistry. III. The Role of Exact Exchange, *J. Chem. Phys.*, 1993, **98**, 5648-5652; (b) A. D. Becke, Density-Functional Exchange-Energy Approximation with Correct Asymptotic Behavior, *Phys. Rev. A*, 1988, **38**, 3098-3100; (c) C. Lee, W. Yang and R. G. Parr, Development of the Colle-Salvetti Correlation-Energy Formula into a Functional of the Electron Density, *Phys. Rev. B*, 1988, **37**, 785-789; (d) S. H. Vosko, L. Wilk and M. Nusair, Accurate Spin-Dependent Electron Liquid Correlation Energies for Local Spin Density Calculations: A Critical Analysis, *Can. J. Phys.*, 1980, **58**, 1200-1211.

2. (a) V. A. Rassolov, M. A. Ratner, J. A. Pople, P. C. Redfern and L. A. Curtiss, 6-31G* Basis Set for Third-Row Atoms, *J. Comput. Chem.*, 2001, **22**, 976-984; (b) V. A. Rassolov, J. A. Pople, M. A. Ratner and T. L. Windus, 6-31G* Basis Set for Atoms K through Zn, *J. Chem. Phys.*, 1998, **109**, 1223-1229; (c) R. Ditchfield, W. J. Hehre and J. A. Pople, Self- Consistent Molecular- Orbital Methods. IX. An Extended Gaussian- Type Basis for Molecular- Orbital Studies of Organic Molecules, *J. Chem. Phys.*, 1971, **54**, 720-723.

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HPLC Data of the Purified Aldol Adducts

Table 1, Entry 7

Daicel CHIRALPAK AD-H, hexane/2-propanol = 87.5:12.5, flow rate: 0.8 mL min^{-1}, λ = 254 nm

PDA Ch1 254nm 4nm
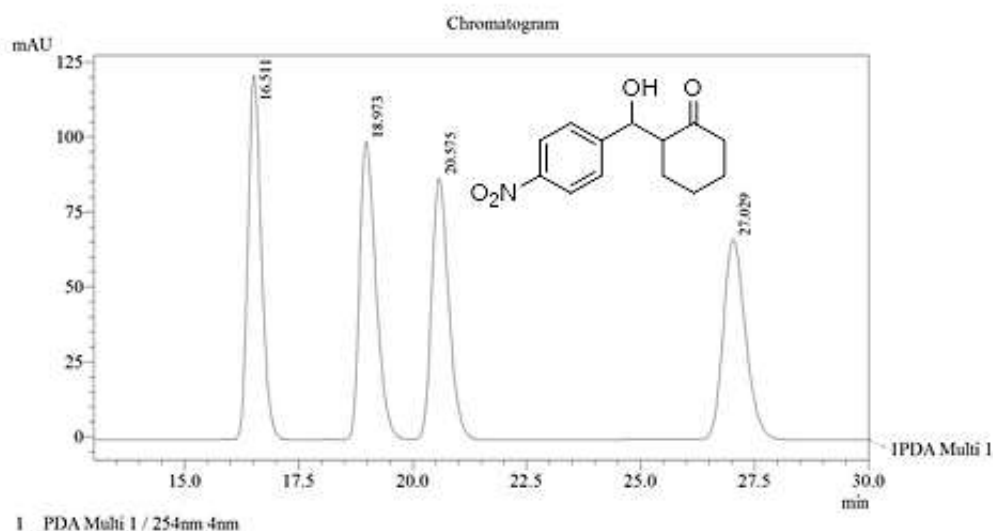
Peak#	Ret. Time	Area	Area Percent	Width
1	16.511	2463924	26.173	0.539
2	18.973	2474027	26.280	0.659
3	20.575	2233850	23.729	0.684
4	27.029	2242264	23.818	0.893
Total		9414064	100.000	

PDA Ch1 254nm 4nm
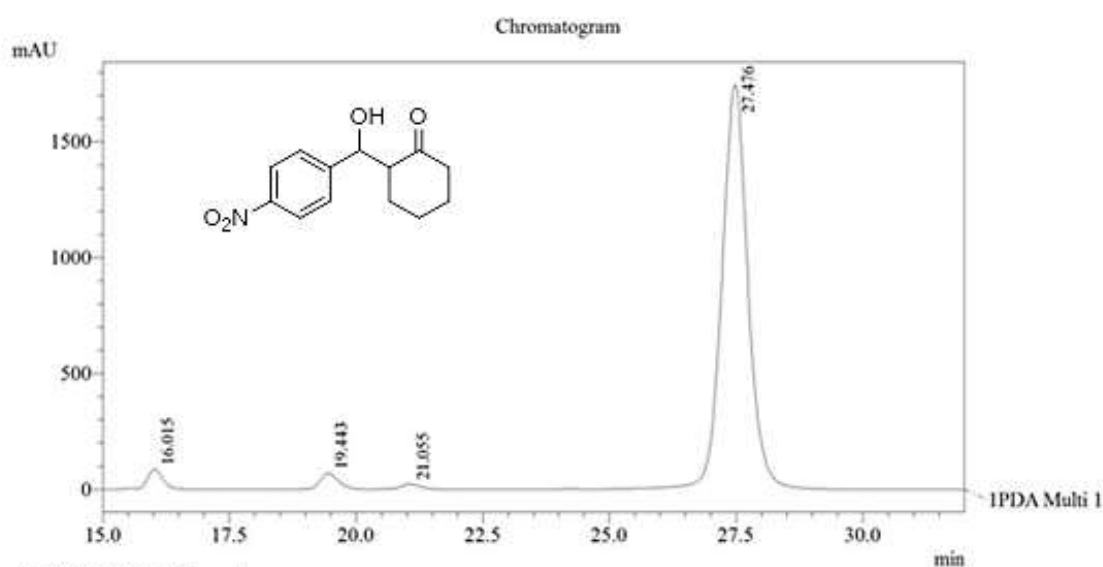
Peak#	Ret. Time	Area	Area Percent	Width
1	16.015	1670575	2.519	0.524
2	19.443	1678559	2.531	0.655
3	21.055	590343	0.890	0.691
4	27.476	62374302	94.059	0.915
Total		66313779	100.000	

Table 2, Entry 1

Daicel CHIRALPAK AD-H, hexane/2-propanol = 90:10, flow rate: 0.5 mL min^{-1}, λ = 254 nm

1 PDA Multi 2 / 230nm 4nm

PeakTable

PDA Ch2 230nm 4nm
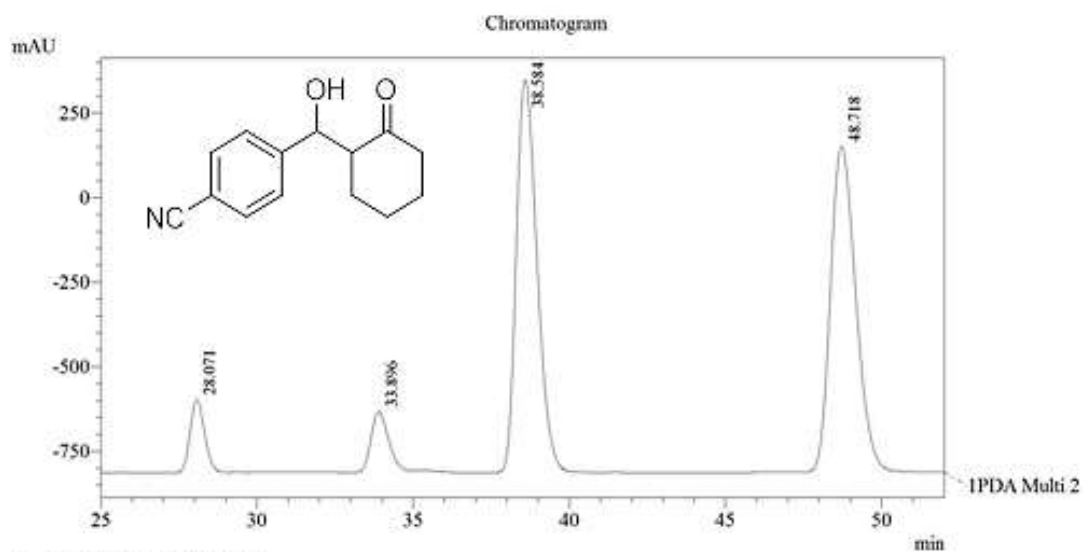
Peak#	Ret. Time	Area	Area Percent	Width
1	28.071	6832745	5.664	0.848
2	33.896	6676405	5.534	1.016
3	38.584	53238966	44.130	1.208
4	48.718	53893911	44.673	1.478
Total		120642027	100.000	

1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm
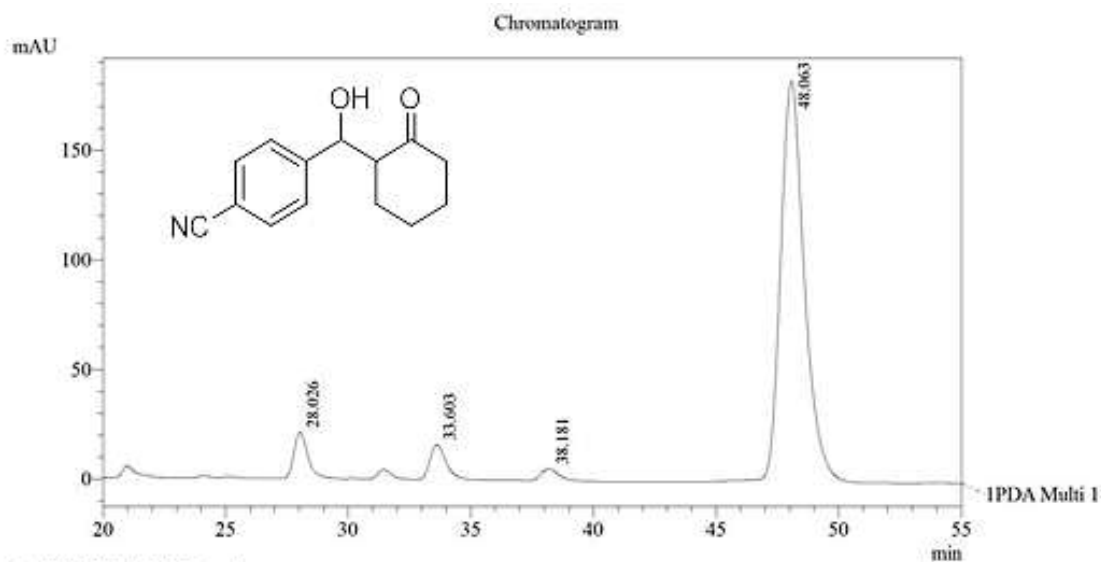
Peak#	Ret. Time	Area	Area Percent	Width
1	28.026	831930	5.872	0.998
2	33.603	711812	5.024	1.161
3	38.181	280854	1.982	1.289
4	48.063	12342286	87.121	1.735
Total		14166881	100.000	

Table 2, Entry 2

Daicel CHIRALCEL OD-H, hexane/2-propanol = 95:5, flow rate: 0.5 mL min^{-1}, λ = 217 nm

1   PDA Multi 1 / 217nm 4nm
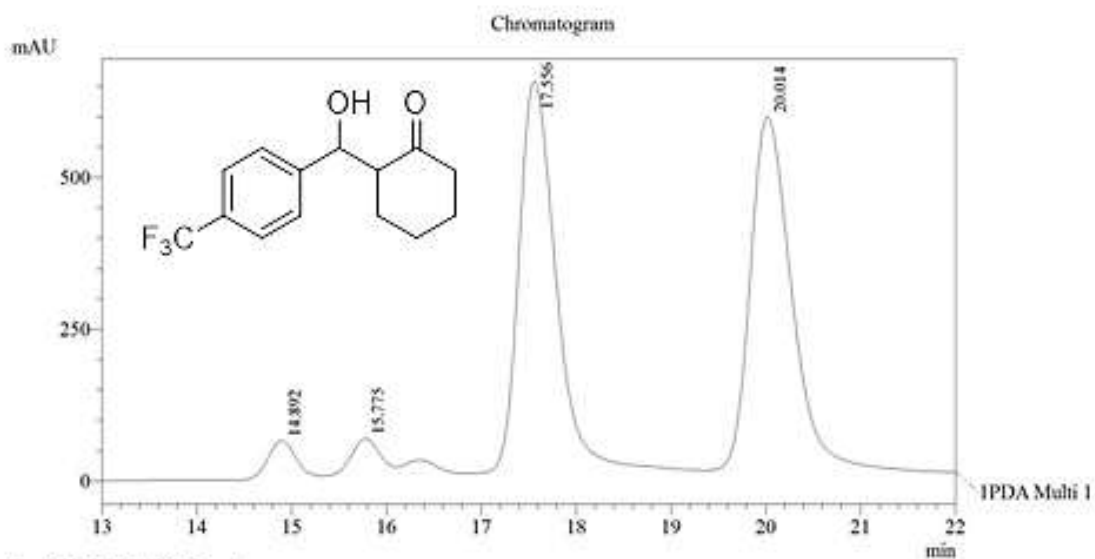
PeakTable

PDA Ch1 217nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	14.892	1156099	3.186	0.521
2	15.775	998246	2.751	0.513
3	17.556	16887162	46.534	0.683
4	20.014	17248144	47.529	0.772
Total		36289652	100.000	

1   PDA Multi 2 / 217nm 4nm
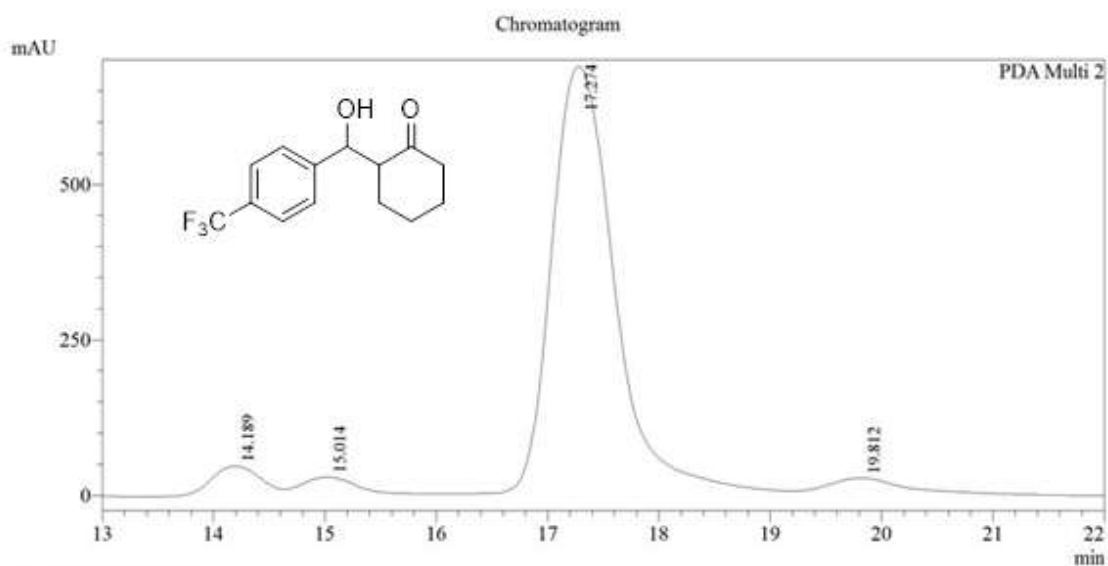
PeakTable

PDA Ch2 217nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	14.189	1153847	3.953	0.728
2	15.014	577608	1.979	0.723
3	17.274	26571846	91.030	0.952
4	19.812	886843	3.038	0.995
Total		29190144	100.000	

Table 2, Entry 3

Daicel CHIRALPAK AD-H, hexane/2-propanol = 90:10, flow rate: 0.5 mL min^{-1}, λ = 254 nm

Chromatogram

1 PDA Multi 1 / 220nm 4nm

PeakTable

PDA Ch1 220nm 4nm
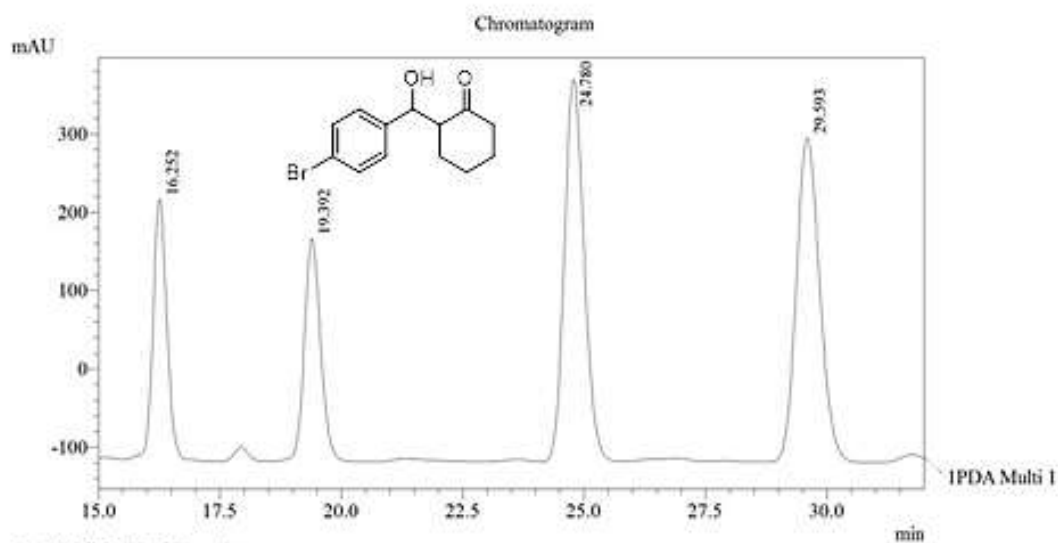
Peak#	Ret. Time	Area	Area Percent	Width
1	16.252	6504825	16.168	0.519
2	19.392	6502949	16.163	0.610
3	24.780	13436894	33.397	0.745
4	29.593	13789067	34.272	0.887
Total		40233735	100.000	

Chromatogram

1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm
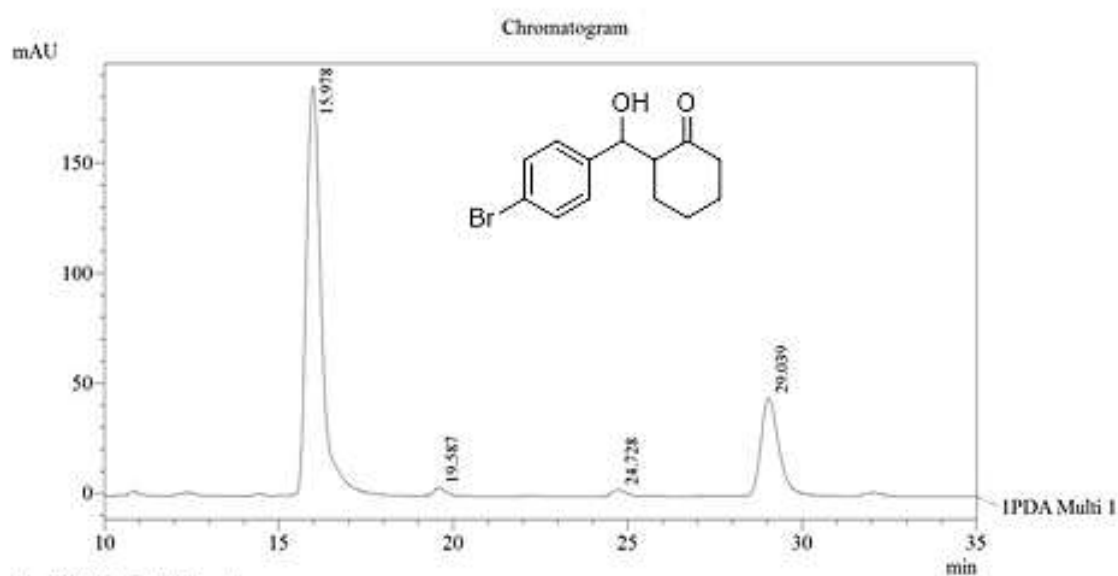
Peak#	Ret. Time	Area	Area Percent	Width
1	15.978	5611979	75.815	0.728
2	19.587	95707	1.293	0.635
3	24.728	85622	1.157	0.744
4	29.039	1608861	21.735	0.919
Total		7402169	100.000	

Table 2, Entry 4

Daicel CHIRALPAK AD-H, hexane/2-propanol = 90:10, flow rate: 0.5 mL min^{-1}, λ = 254 nm

Chromatogram
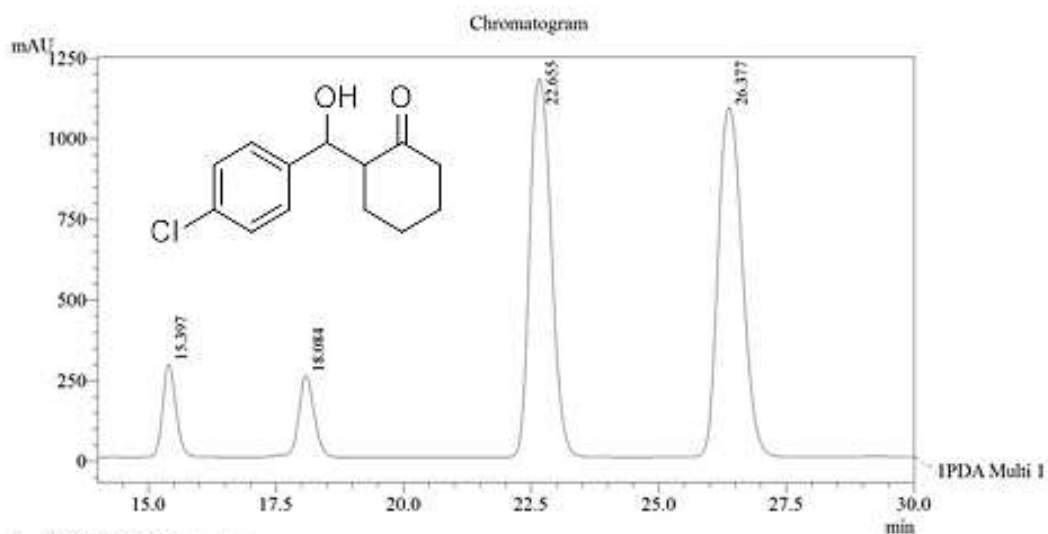
1 PDA Multi 1 / 220nm 4nm

PeakTable

PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	15.397	5173393	6.489	0.486
2	18.084	5068146	6.357	0.553
3	22.655	33901442	42.522	0.744
4	26.377	35584221	44.632	0.849
Total		79727201	100.000	

Chromatogram
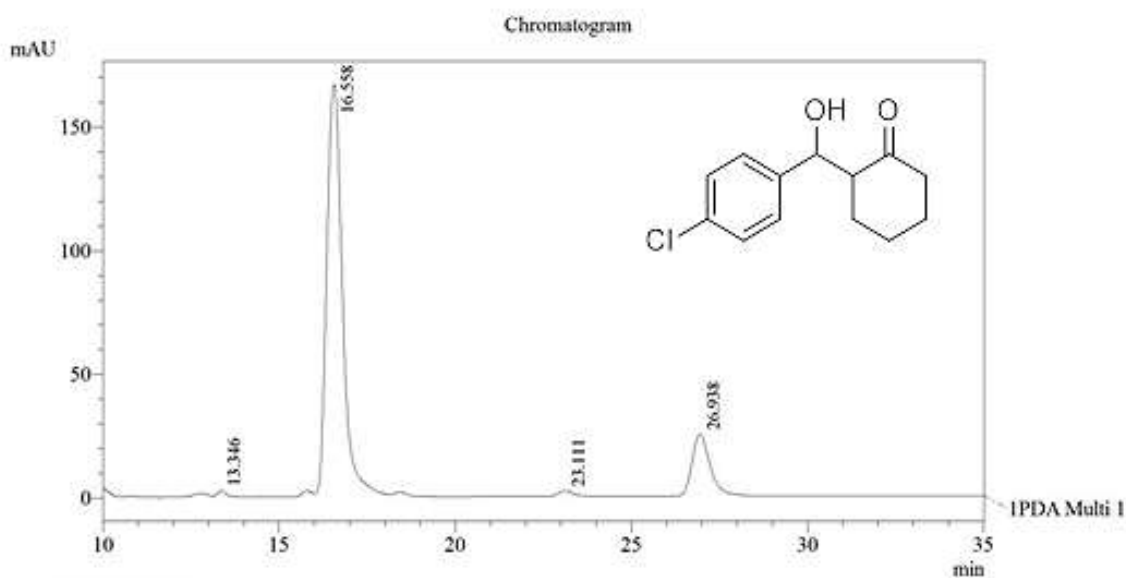
1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	13.346	88877	1.397	0.440
2	16.558	5310723	83.505	0.770
3	23.111	65722	1.033	0.751
4	26.938	894437	14.064	0.907
Total		6359758	100.000	

Table 2, Entry 5

Daicel CHIRALPAK AS-H, hexane/2-propanol = 80:20, flow rate: 0.5 mL min^{-1}, λ = 254 nm

Chromatogram
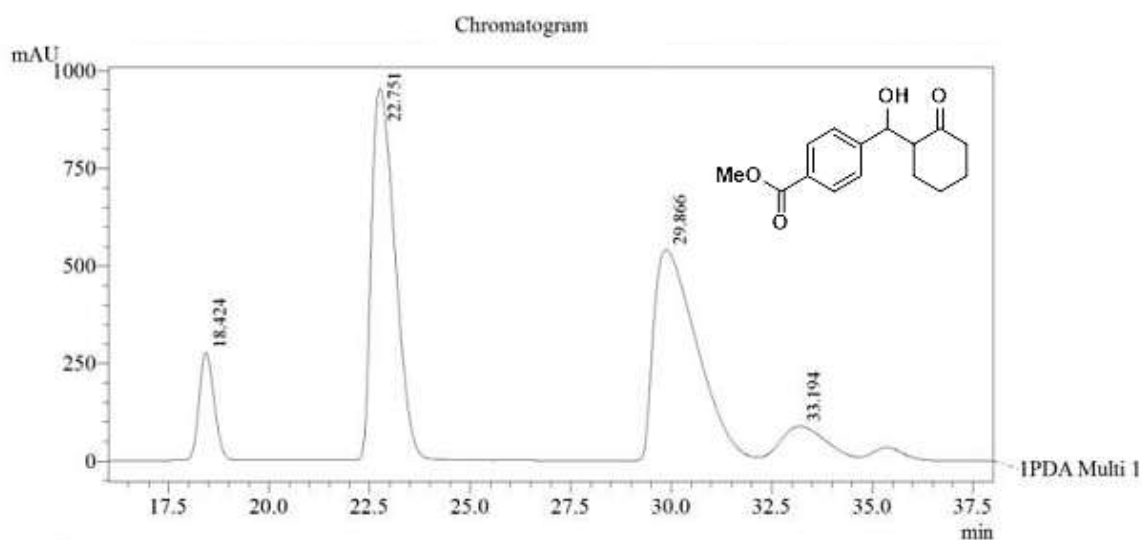
1　PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	18.424	7048568	7.764	0.691
2	22.751	38530859	42.439	1.086
3	29.866	39612511	43.631	2.017
4	33.194	5598374	6.166	1.947
Total		90790312	100.000	

Chromatogram
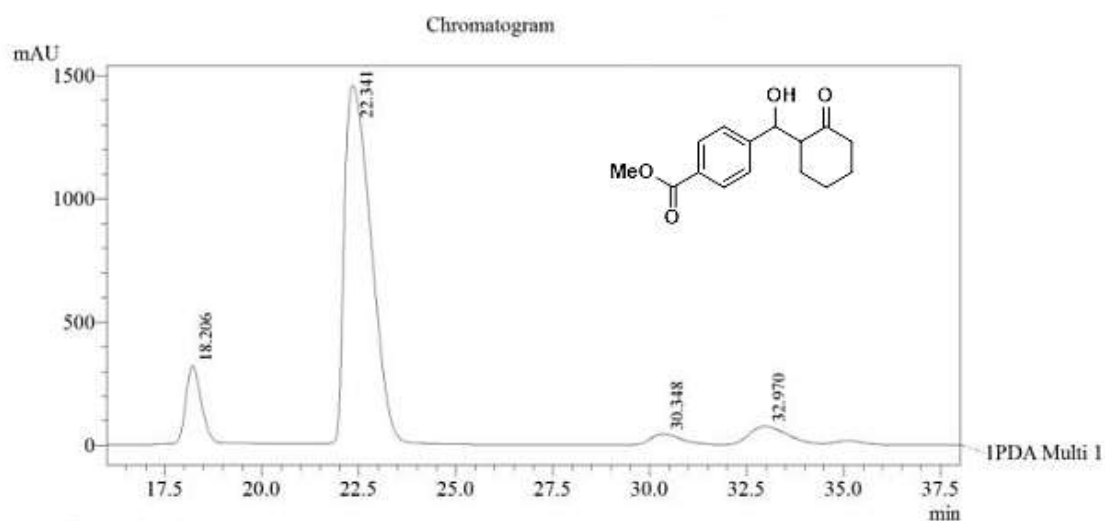
1　PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	18.206	8564866	10.189	0.731
2	22.341	68657770	81.675	1.263
3	30.348	2145331	2.552	1.342
4	32.970	4694471	5.585	1.772
Total		84062437	100.000	

Table 2, Entry 6

Daicel CHIRALPAK AD-H, hexane/2-propanol = 92:8, flow rate: 0.8 mL min^{-1}, λ = 254 nm

Chromatogram
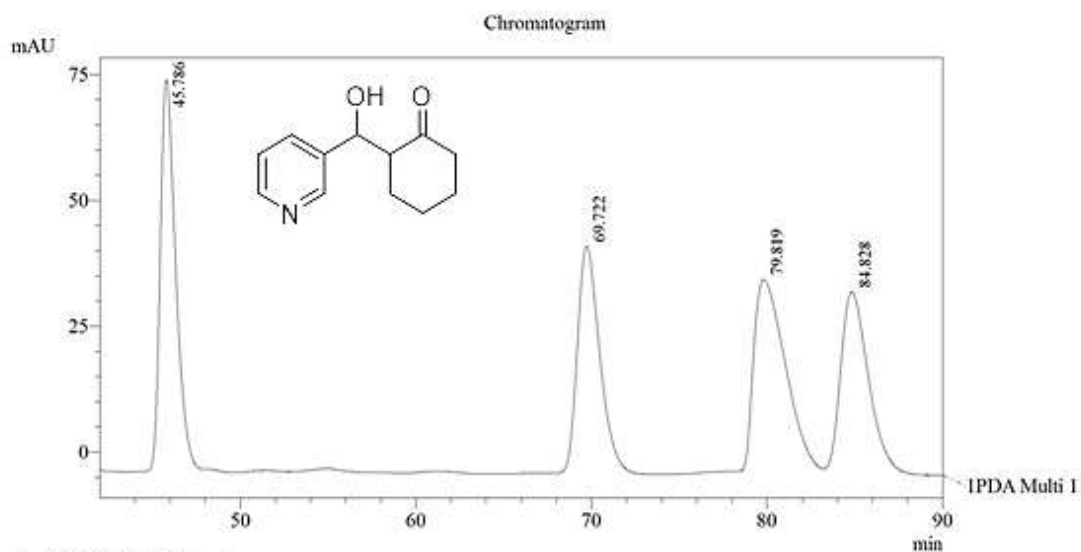
1   PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	45.786	4746087	27.920	1.596
2	69.722	4006024	23.567	2.333
3	79.819	4529064	26.644	3.329
4	84.828	3717425	21.869	2.826
Total		16998600	100.000	

Chromatogram
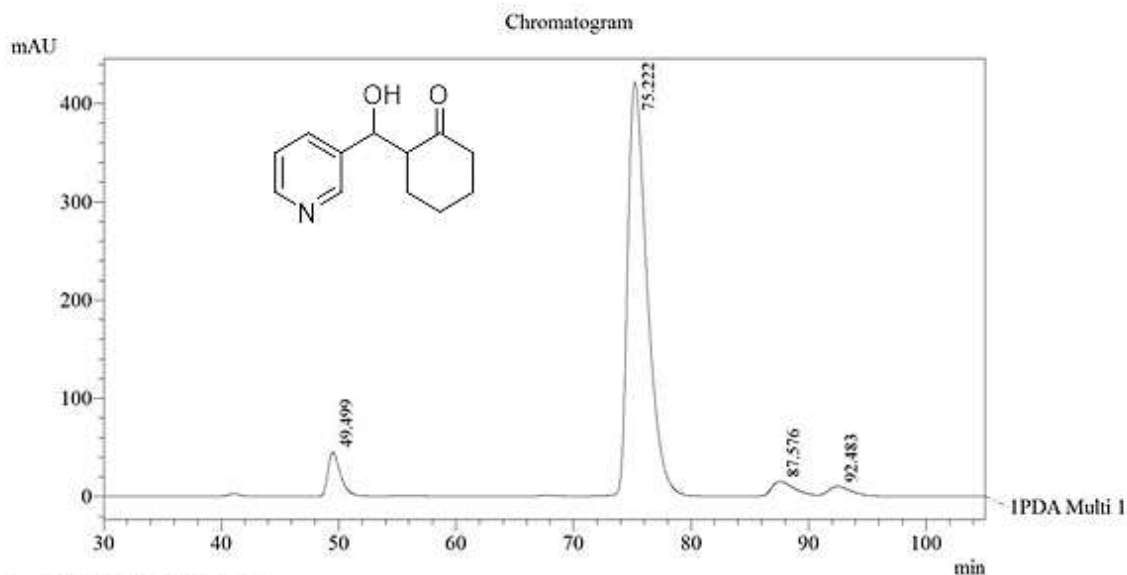
1   PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	49.499	3275727	6.063	1.892
2	75.222	47923833	88.696	2.930
3	87.576	1819860	3.368	3.393
4	92.483	1012254	1.873	3.152
Total		54031674	100.000	

Table 2, Entry 7

Daicel CHIRALPAK AD-H, hexane/2-propanol = 90:10, flow rate: 1.0 mL min^{-1}, λ = 254 nm

Chromatogram
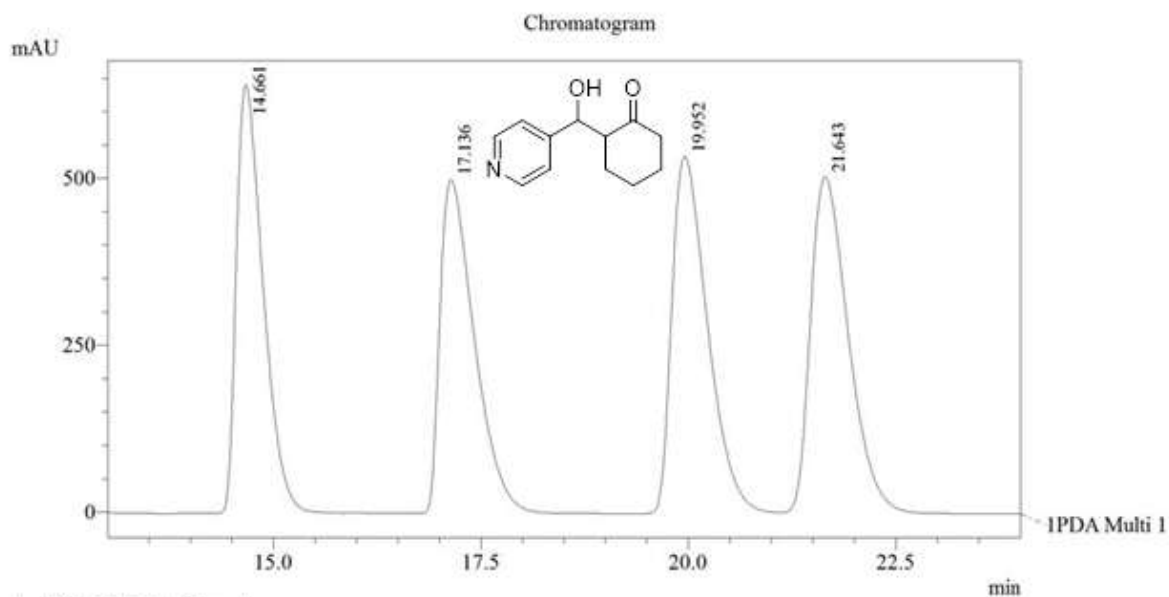
1   PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	14.661	14232997	23.761	0.597
2	17.136	14264060	23.813	0.759
3	19.952	15526861	25.921	0.782
4	21.643	15877047	26.505	0.832
Total		59900965	100.000	

Chromatogram
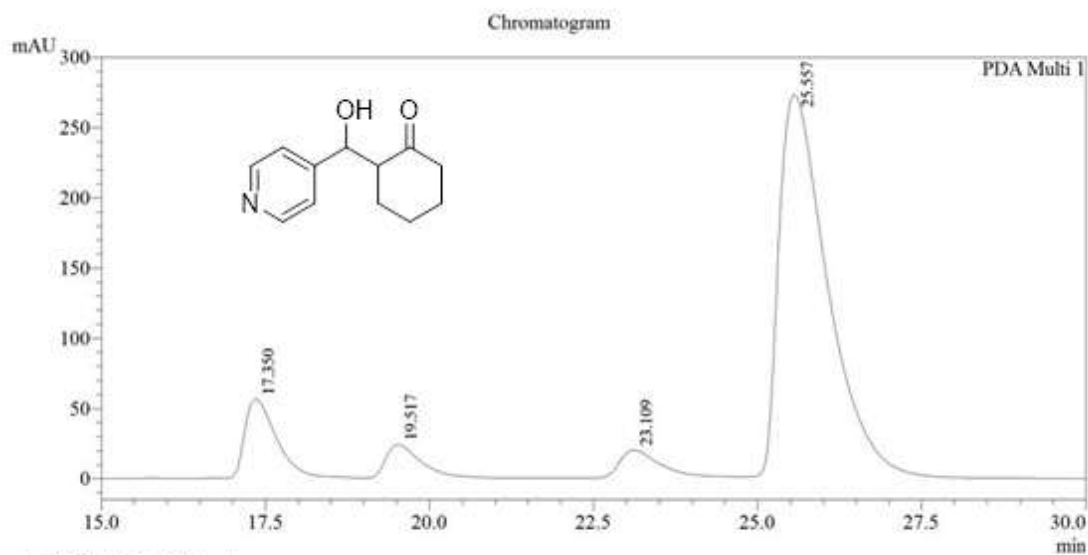
1   PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	17.350	1852211	10.569	0.857
2	19.517	861758	4.918	0.936
3	23.109	780524	4.454	1.051
4	25.557	14029666	80.059	1.312
Total		17524160	100.000	

Table 2, Entry 8

Daicel CHIRALPAK AD-H, hexane/2-propanol = 91.5:9.5, flow rate: 0.5 mL min^{-1}, λ = 254

Chromatogram
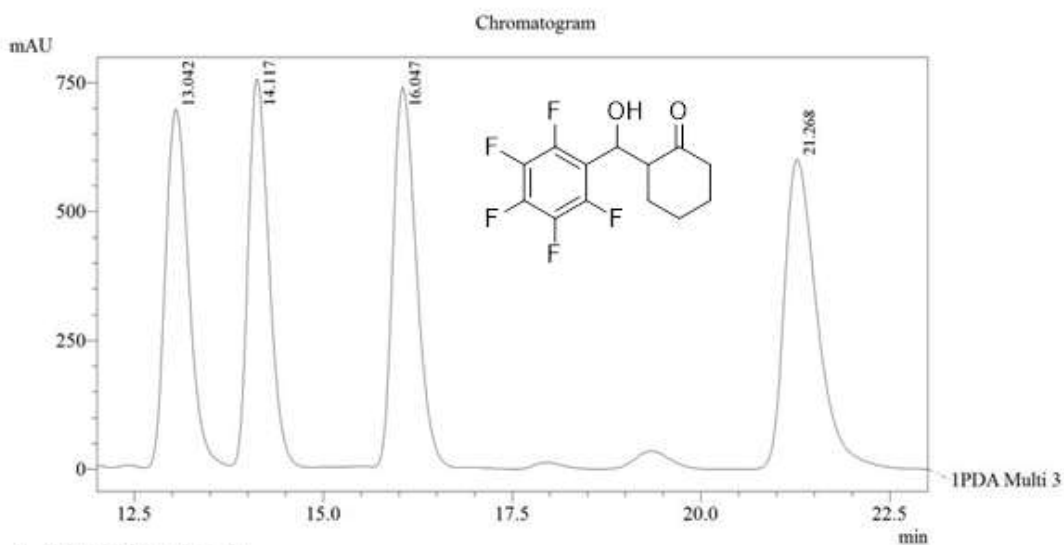
1   PDA Multi 3 / 220nm 4nm

PeakTable

PDA Ch3 220nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	13.042	14774896	23.479	0.558
2	14.117	14272469	22.680	0.507
3	16.047	15805005	25.116	0.569
4	21.268	18076518	28.725	0.768
Total		62928888	100.000	
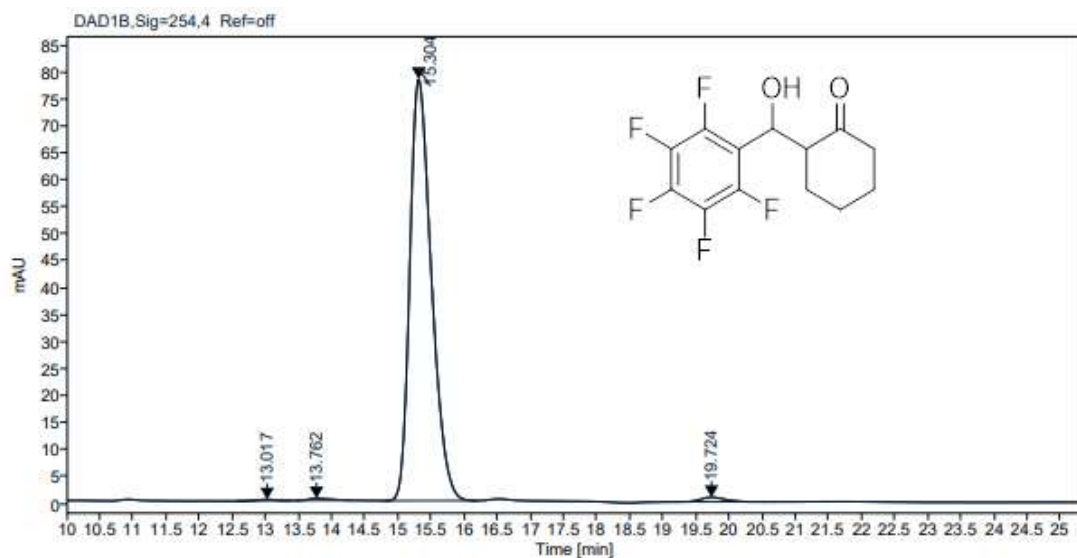
Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%
13.017	MM m	0.2442	4.6812	0.2312	0.2600
13.762	MM m	0.2962	8.2243	0.3499	0.4568
15.304	BB	1.3967	1766.8792	78.1140	98.1349
19.724	MM m	0.3347	20.6748	0.8356	1.1483
		Sum	1800.4596		

Table 2, Entry 9

Daicel CHIRALPAK AD-H, hexane/2-propanol = 95:5, flow rate: 0.5 mL min^{-1}, λ = 254 nm
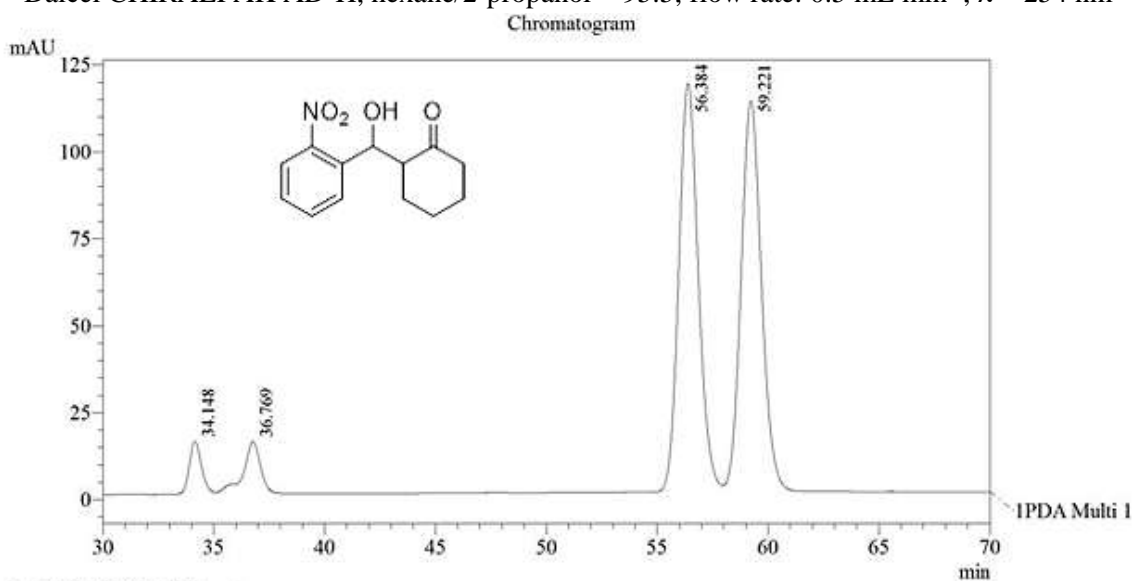
1   PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	34.148	609549	3.875	1.009
2	36.769	782747	4.976	1.229
3	56.384	7169349	45.574	1.608
4	59.221	7169422	45.575	1.680
Total		15731067	100.000	
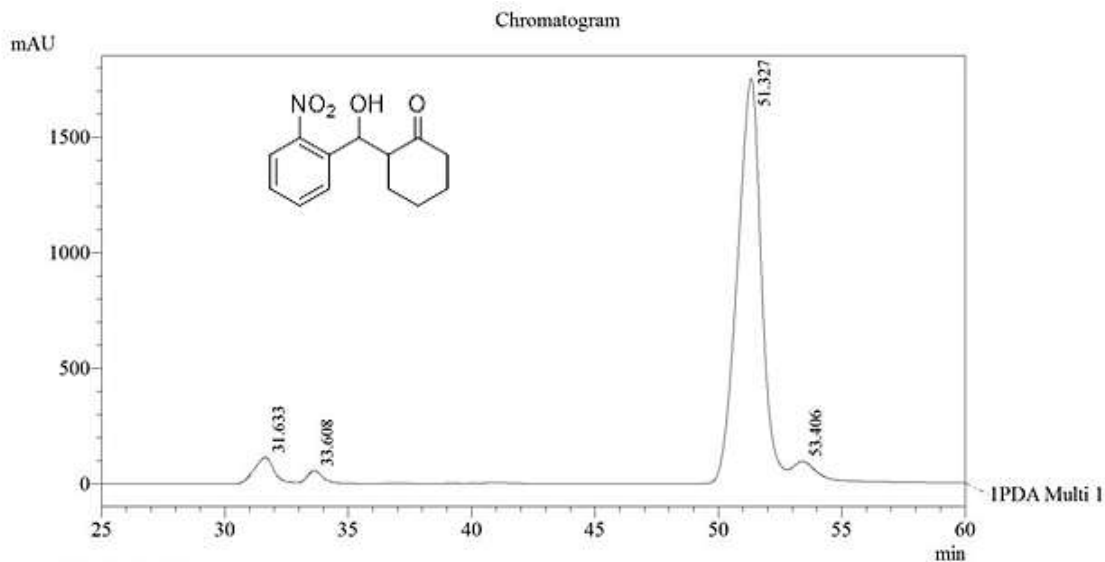
1   PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	31.633	5820763	4.816	1.441
2	33.608	2165859	1.792	1.078
3	51.327	111112091	91.929	1.762
4	53.406	1768807	1.463	1.264
Total		120867520	100.000	

Table 2, Entry 10

Daicel CHIRALCEL OD-H, hexane/2-propanol = 95:5, flow rate: 1 mL min^{-1}, λ = 220 nm
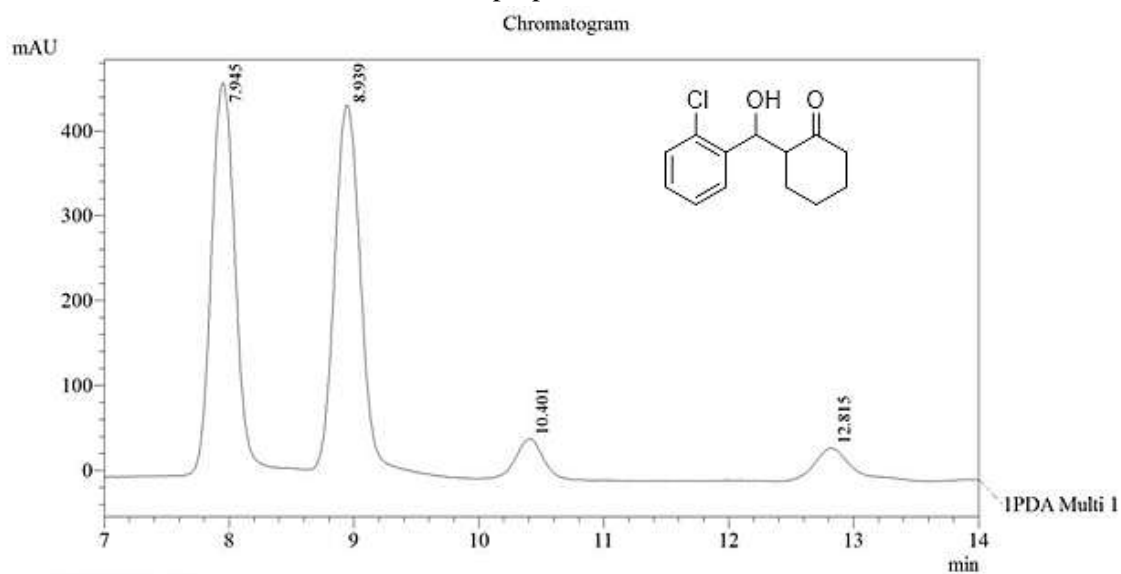
1   PDA Multi 1 / 190nm 4nm

PeakTable

PDA Ch1 190nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	7.945	5899685	44.060	0.344
2	8.939	6187375	46.209	0.377
3	10.401	662743	4.950	0.396
4	12.815	640176	4.781	0.480
Total		13389978	100.000	
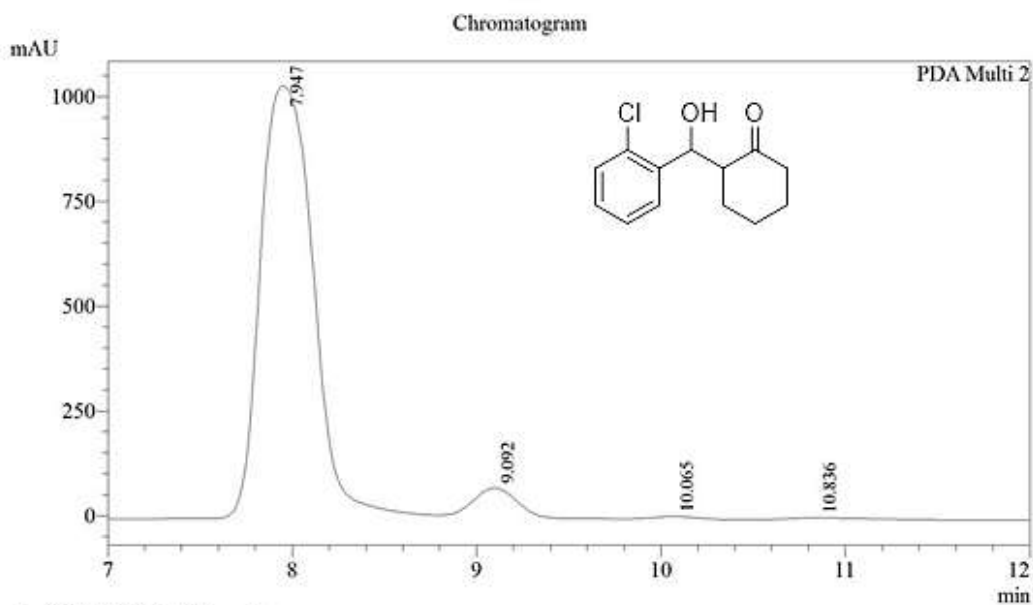
1   PDA Multi 2 / 220nm 4nm

PeakTable

PDA Ch2 220nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	7.947	20292277	94.025	0.480
2	9.092	1041927	4.828	0.429
3	10.065	96879	0.449	0.450
4	10.836	150650	0.698	0.872
Total		21581732	100.000	

Table 2, Entry 11

Daicel CHIRALPAK AD-H, hexane/2-propanol = 90:10, flow rate: 1 mLmin^{-1}, λ = 254 nm

Chromatogram
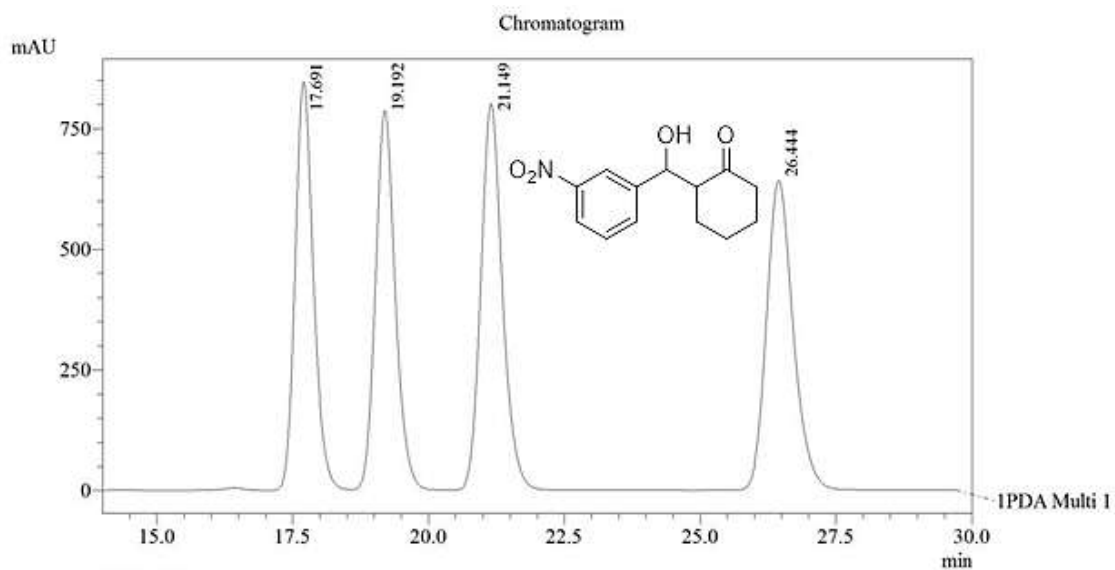
1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	17.691	19758413	23.813	0.616
2	19.192	19614529	23.640	0.661
3	21.149	21868775	26.357	0.718
4	26.444	21731034	26.191	0.889
Total		82972752	100.000	

DAD1B,Sig=254,4 Ref=off
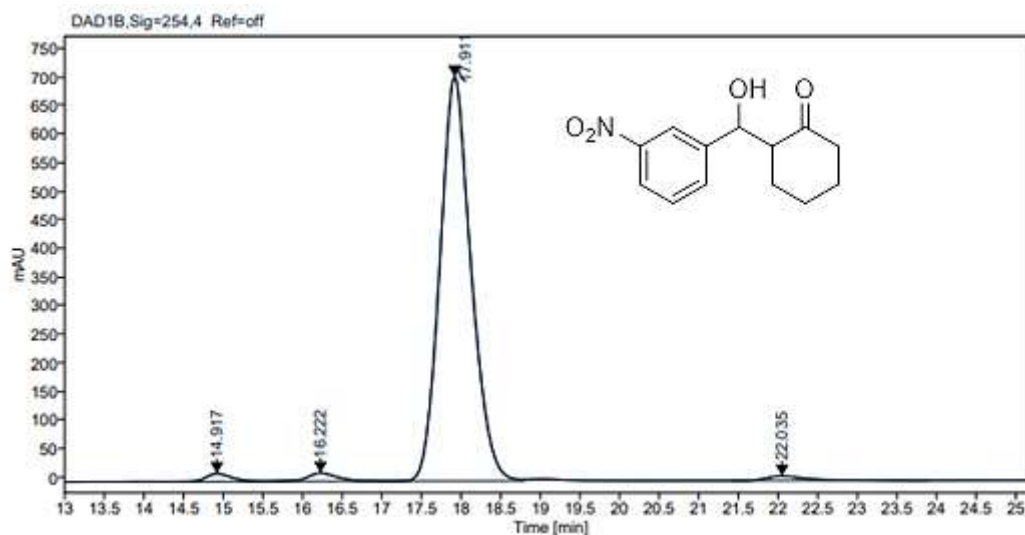
Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%
14.917	BV	1.0433	301.2994	13.8304	1.4876
16.222	VB	1.4683	371.6205	14.3989	1.8347
17.911	BV	1.8003	19290.1303	706.3337	95.2378
22.035	BB	2.4733	291.6395	7.9135	1.4399
	Sum		20254.6898		

Table 2, Entry 12

Daicel CHIRALCEL OD-H, hexane/2-propanol = 97:3, flow rate: 0.8 mL min^{-1}, λ = 254 nm

Chromatogram

1 PDA Multi 1 / 210nm 4nm
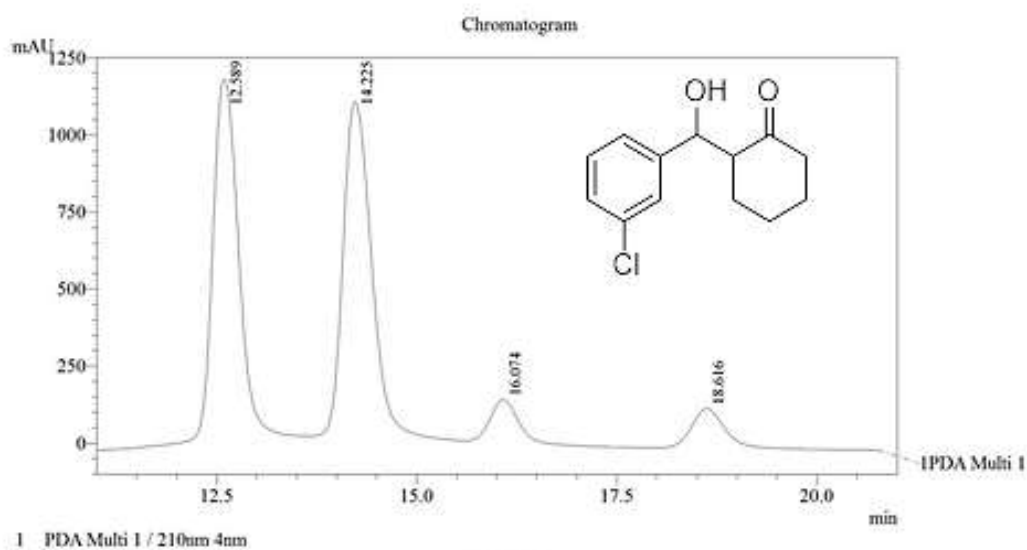
PeakTable

PDA Ch1 210nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	12.589	25486034	43.608	0.562
2	14.225	26192340	44.817	0.628
3	16.074	3261713	5.581	0.633
4	18.616	3503287	5.994	0.731
Total		58443374	100.000	

Chromatogram

1 PDA Multi 1 / 254nm 4nm
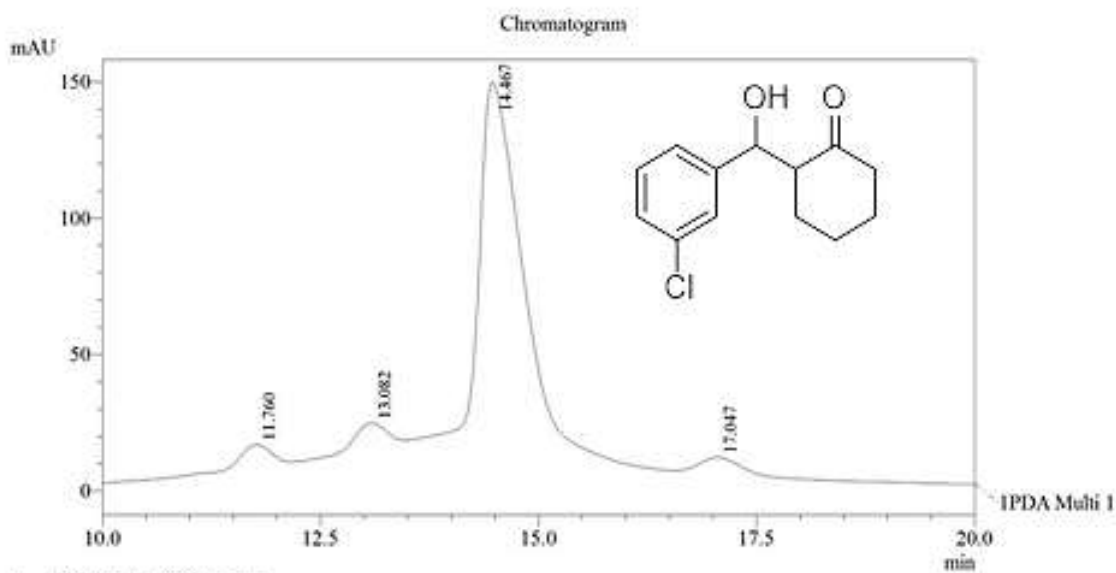
PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	11.760	192030	4.012	0.631
2	13.082	224280	4.686	0.647
3	14.467	4192285	87.586	0.857
4	17.047	177909	3.717	0.836
Total		4786505	100.000	

Table 2, Entry 13

Daicel CHIRALPAK AD-H, hexane/2-propanol = 75:25, flow rate: 1.0 mLmin^{-1}, λ = 254 nm
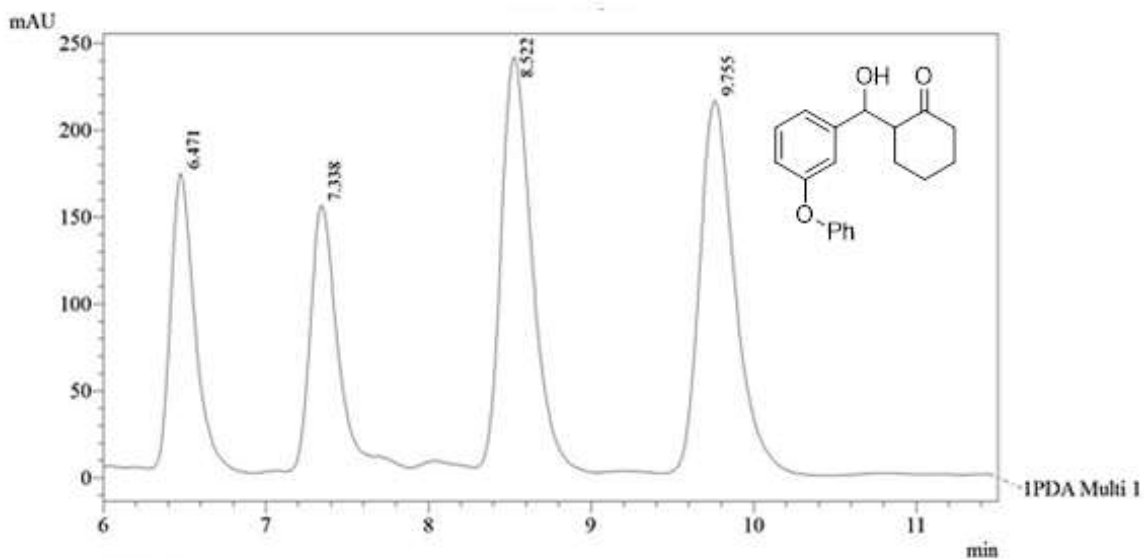
1   PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	6.471	1744562	17.830	0.276
2	7.338	1751891	17.905	0.300
3	8.522	3085913	31.540	0.350
4	9.755	3201843	32.725	0.394
Total		9784209	100.000	
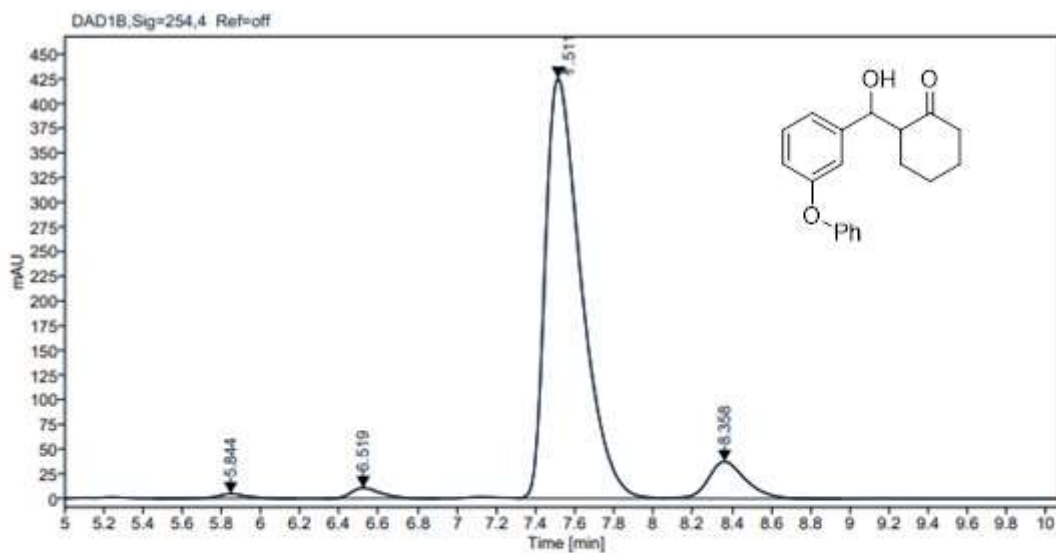
Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%
5.844	BB	0.7256	50.5646	4.6855	0.8381
6.519	BB	0.5900	112.4000	10.6396	1.8631
7.511	VV	0.7503	5375.1864	425.3457	89.0953
8.358	VB	0.9056	494.9254	37.3652	8.2035
		Sum	6033.0764		

Table 2, Entry 14

Daicel CHIRALPAK IC, hexane/2-propanol = 90:10, flow rate: 1.5 mL min^{-1}, λ = 254 nm

Chromatogram

1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm
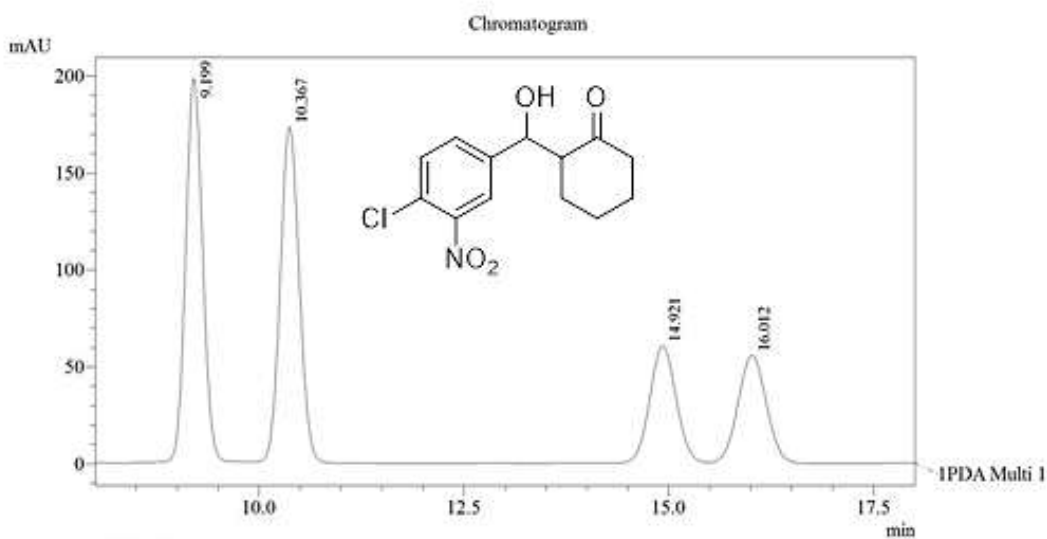
Peak#	Ret. Time	Area	Area Percent	Width
1	9.199	2798855	34.106	0.388
2	10.367	2771923	33.778	0.434
3	14.921	1323471	16.128	0.596
4	16.012	1312019	15.988	0.641
Total		8206268	100.000	

Chromatogram

1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm
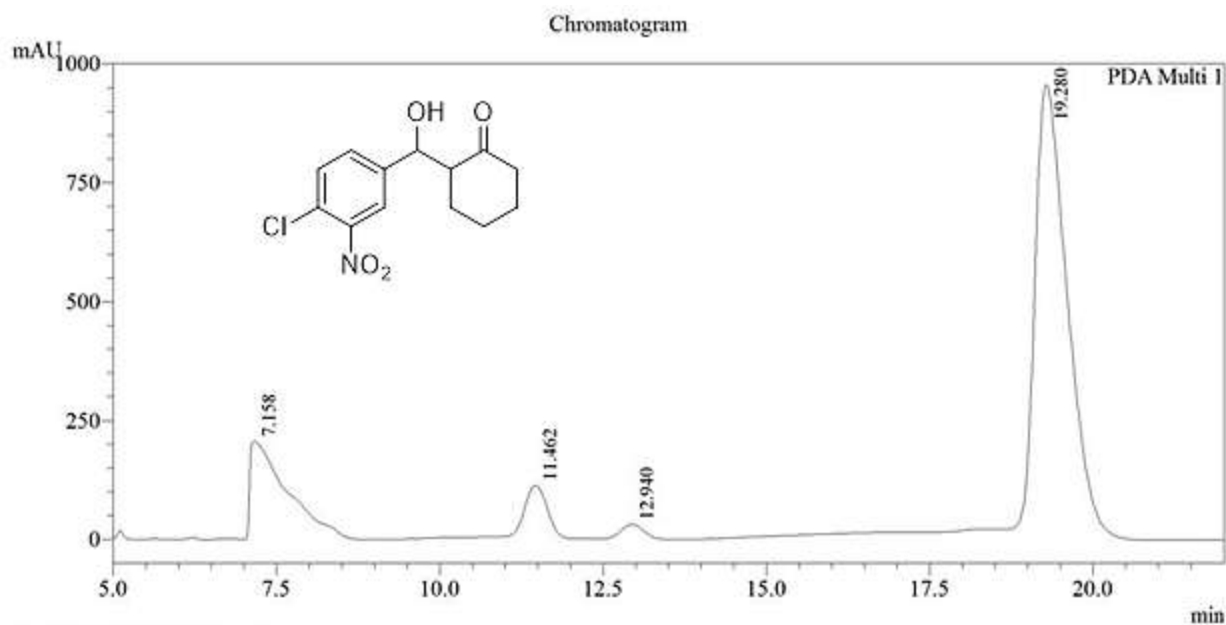
Peak#	Ret. Time	Area	Area Percent	Width
1	7.158	8084521	18.609	0.913
2	11.462	2582655	5.945	0.632
3	12.940	723696	1.666	0.642
4	19.280	32054124	73.781	0.914
Total		43444997	100.000	

Table 2, Entry 15

Daicel CHIRALCEL OD-H, hexane/2-propanol = 90:10 flow rate: 0.5 mL min^{-1}, λ = 254 nm

I   PDA Multi 2 / 254nm 4nm

PeakTable

PDA Ch2 254nm 4nm
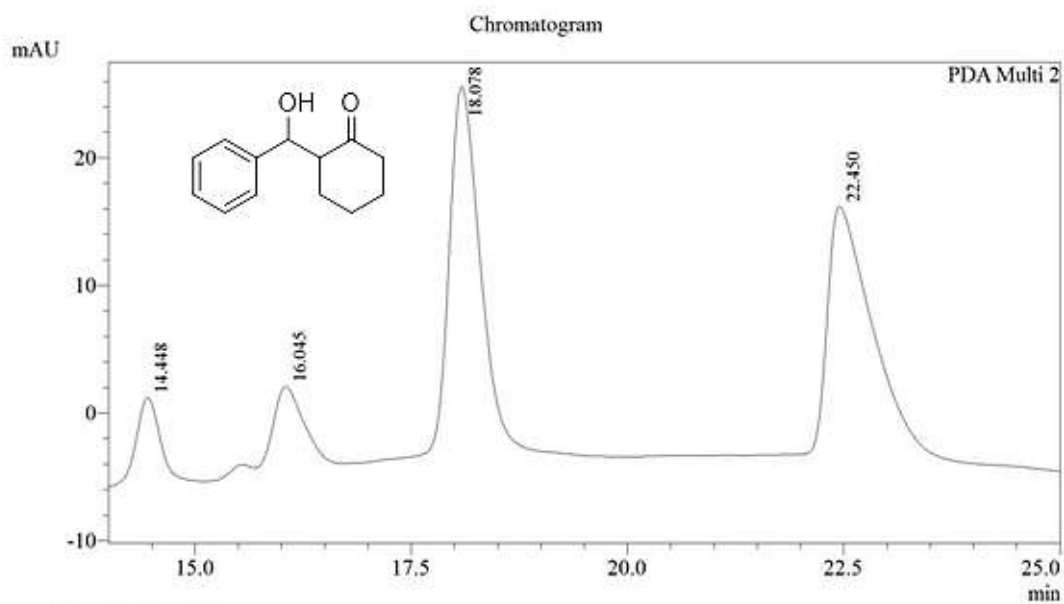
Peak#	Ret. Time	Area	Area Percent	Width
1	14.448	126256	7.544	0.492
2	16.045	148173	8.854	0.655
3	18.078	705692	42.168	0.650
4	22.450	693391	41.433	0.972
Total		1673512	100.000	

I   PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm
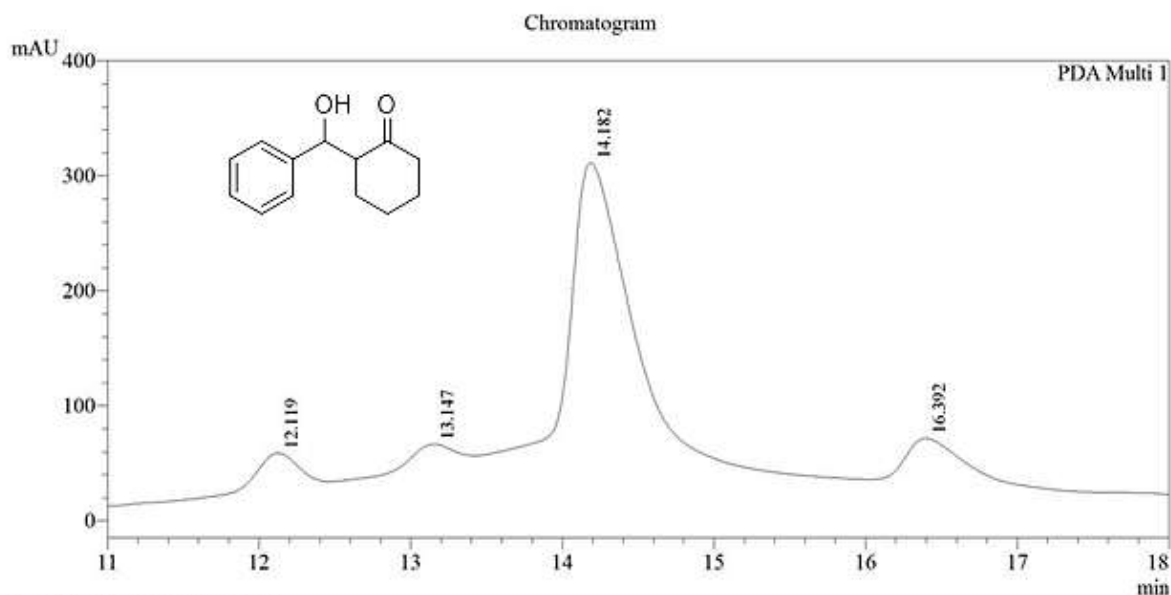
Peak#	Ret. Time	Area	Area Percent	Width
1	12.119	517570	6.346	0.480
2	13.147	305987	3.752	0.476
3	14.182	6319117	77.483	0.665
4	16.392	1012783	12.418	0.707
Total		8155456	100.000	

Table 2, Entry 16

Daicel CHIRALPAK IC, hexane/2-propanol = 90:10, flow rate: 1.5 mL min^{-1}, λ = 210 nm

Chromatogram

1   PDA Multi 1 / 210nm 4nm

PeakTable

PDA Ch1 210nm 4nm
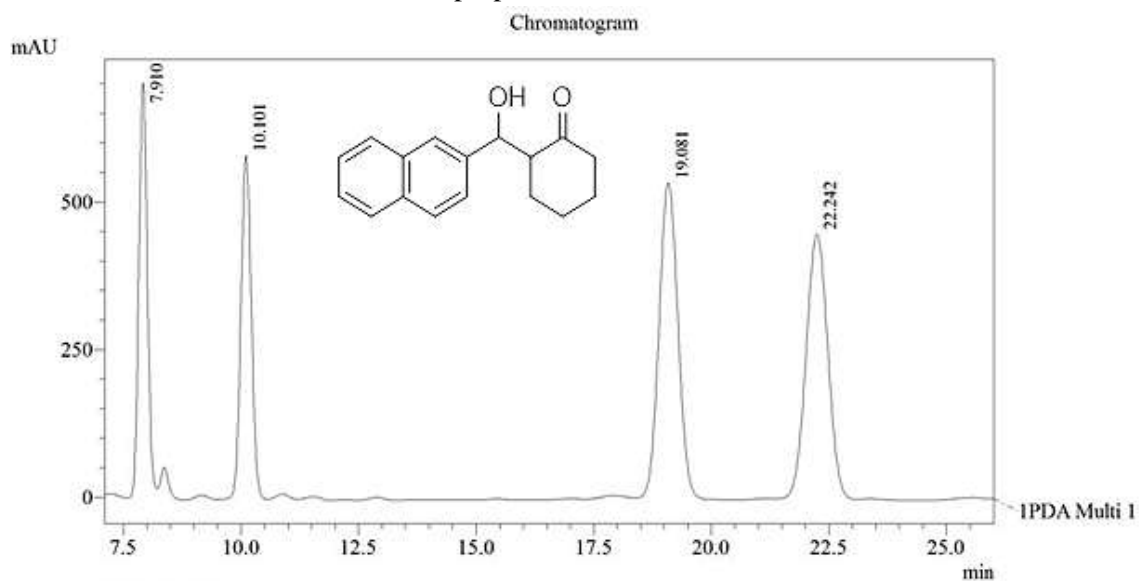
Peak#	Ret. Time	Area	Area Percent	Width
1	7.910	8451452	18.114	0.338
2	10.101	8936311	19.154	0.417
3	19.081	14914742	31.967	0.747
4	22.242	14353629	30.765	0.860
Total		46656133	100.000	

Chromatogram
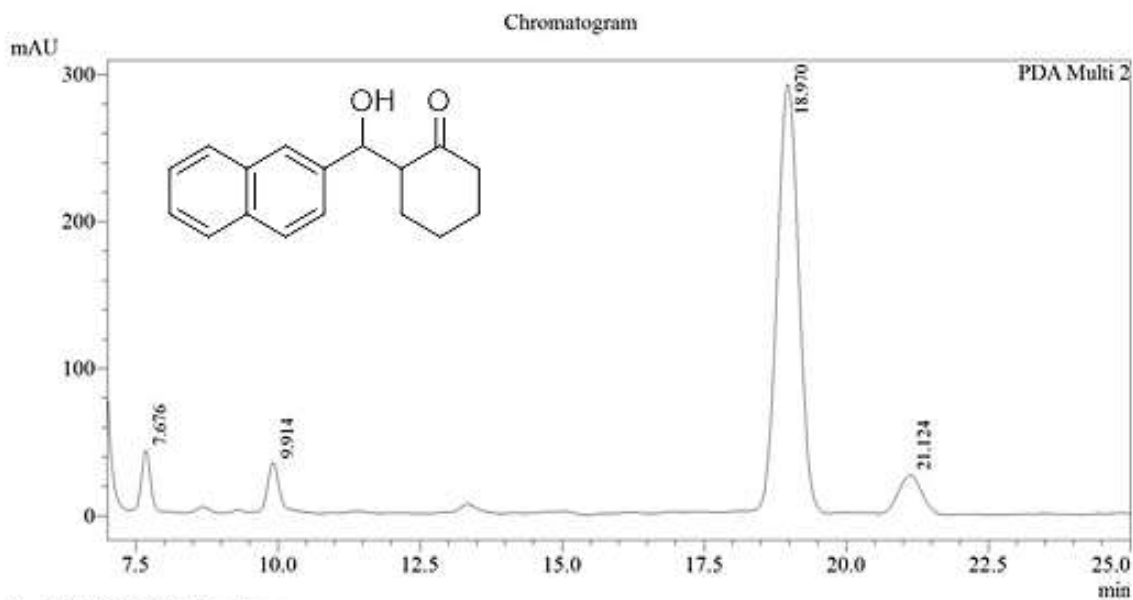
1   PDA Multi 2 / 210nm 4nm

PeakTable

PDA Ch2 210nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	7.676	424441	4.632	0.288
2	9.914	445863	4.865	0.360
3	18.970	7565160	82.554	0.696
4	21.124	728383	7.948	0.752
Total		9163846	100.000	

Table 2, Entry 17

Daicel CHIRALPAK AD-H, hexane/2-propanol = 95:5, flow rate: 1.0 mLmin^{-1}, λ = 254 nm

Chromatogram
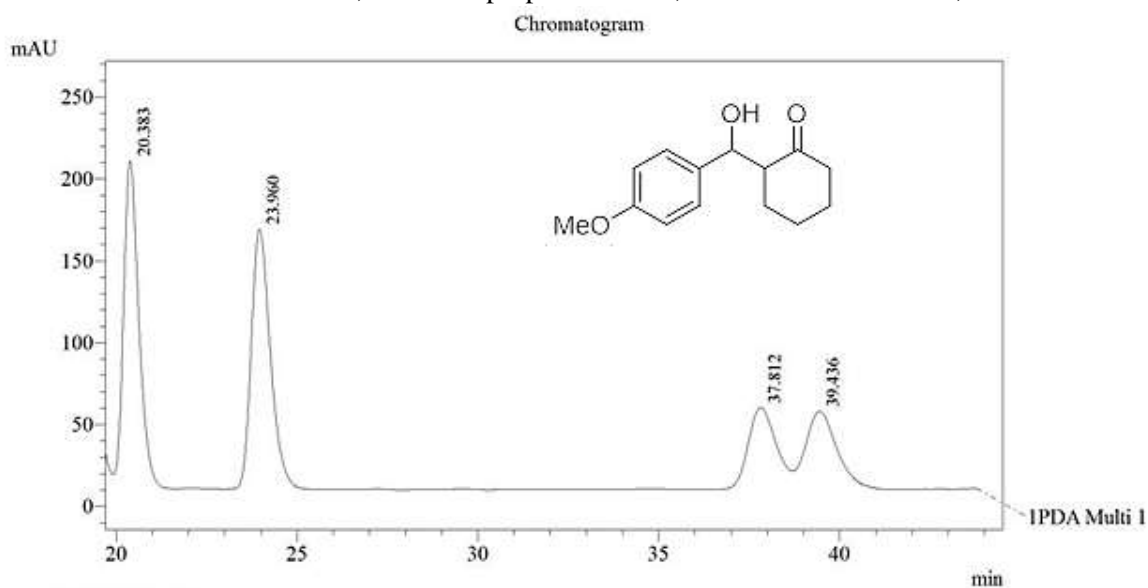
1 PDA Multi 1 / 220nm 4nm

PeakTable

PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	20.383	5501233	32.843	0.750
2	23.960	5713379	34.109	0.952
3	37.812	2685768	16.034	1.451
4	39.436	2849855	17.014	1.581
Total		16750236	100.000	

DAD1B,Sig=254,4 Ref=off
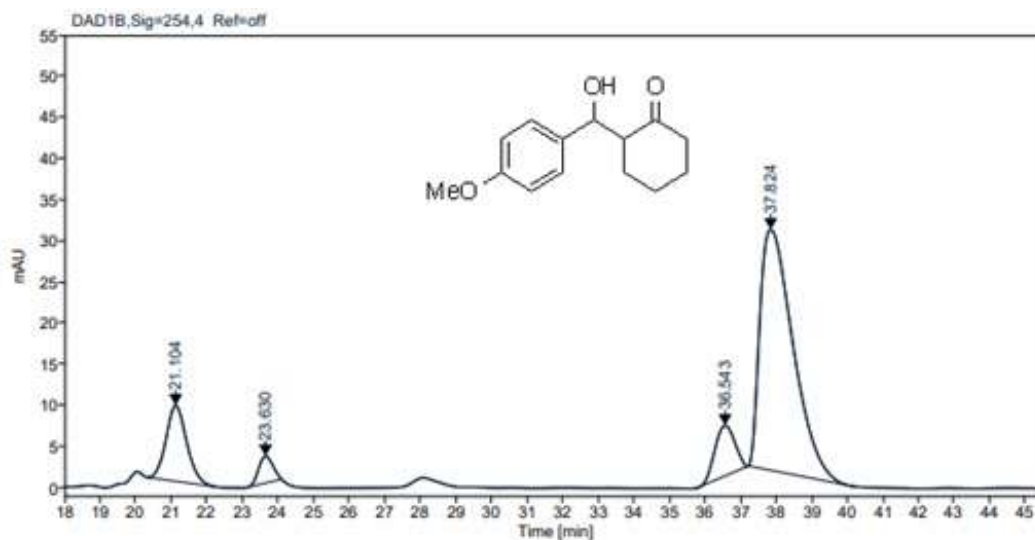
Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%
21.104	BB	1.9200	372.0884	9.2050	14.3374
23.630	MM m	0.4321	91.0437	3.2773	3.5081
36.543	MM m	0.6010	238.2309	6.1091	9.1796
37.824	MM m	0.9632	1893.8695	29.2584	72.9749
		Sum	2595.2326		

Table 3, Entry 1

Daicel CHIRALPAK AD-H, hexane/2-propanol = 95:5, flow rate: 0.5 mL min^{-1}, λ = 254 nm
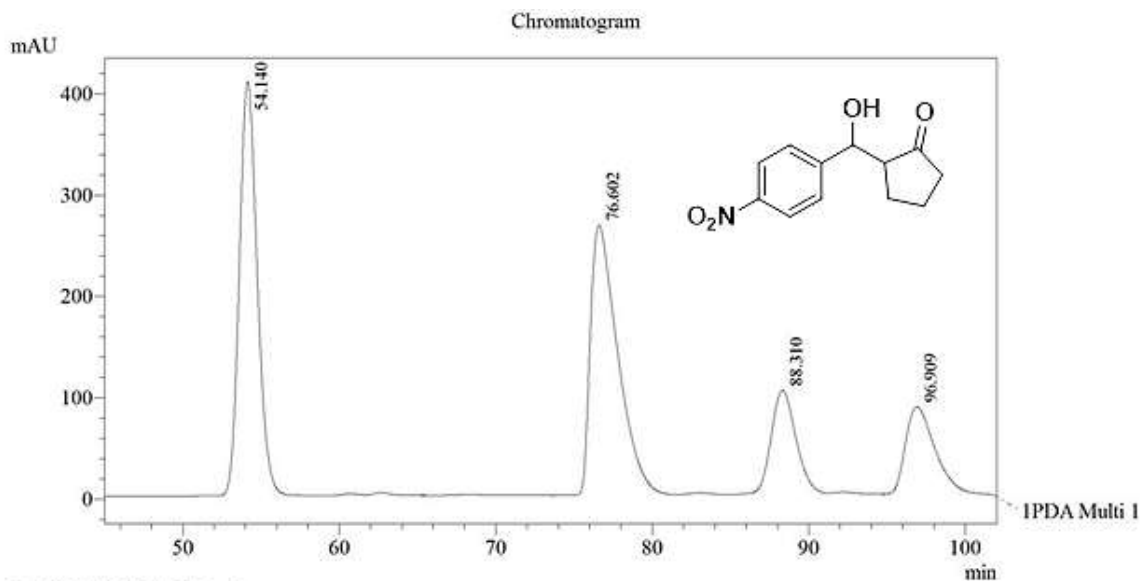
1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	54.140	32300458	37.372	2.088
2	76.602	32228981	37.289	3.288
3	88.310	10825106	12.525	2.870
4	96.909	11076105	12.815	3.404
Total		86430649	100.000	
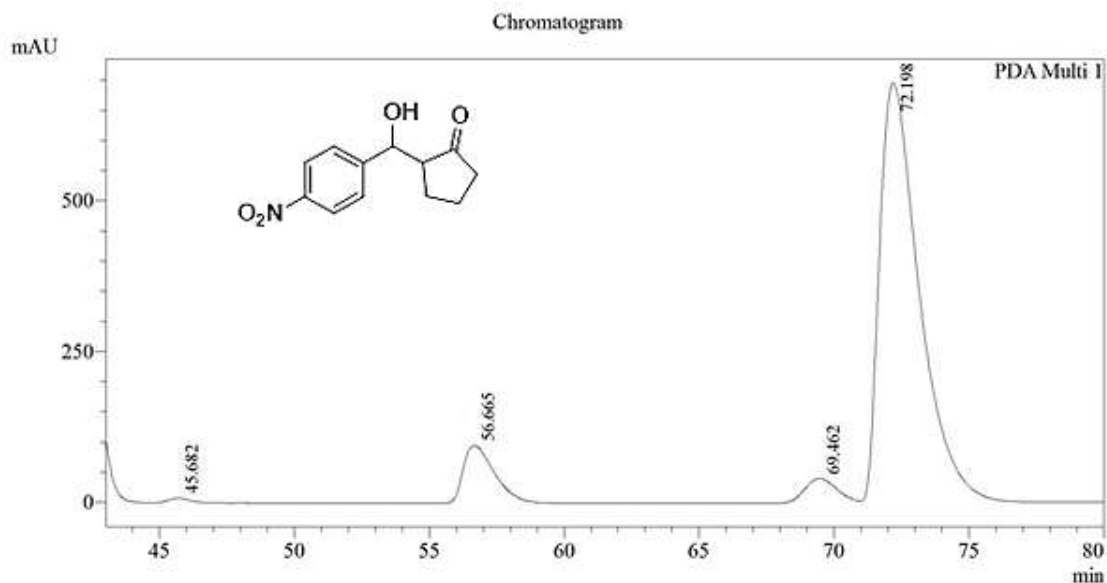
1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	45.682	412275	0.503	1.427
2	56.665	7643185	9.322	2.099
3	69.462	3104543	3.787	2.158
4	72.198	70829020	86.388	2.599
Total		81989022	100.000	

Table 3, Entry 2

Daicel CHIRALPAK IC, hexane/2-propanol = 92.5:7.5, flow rate: 0.8 mL min^{-1}, λ = 254 nm

Chromatogram

1 PDA Multi 1 / 254nm 4nm
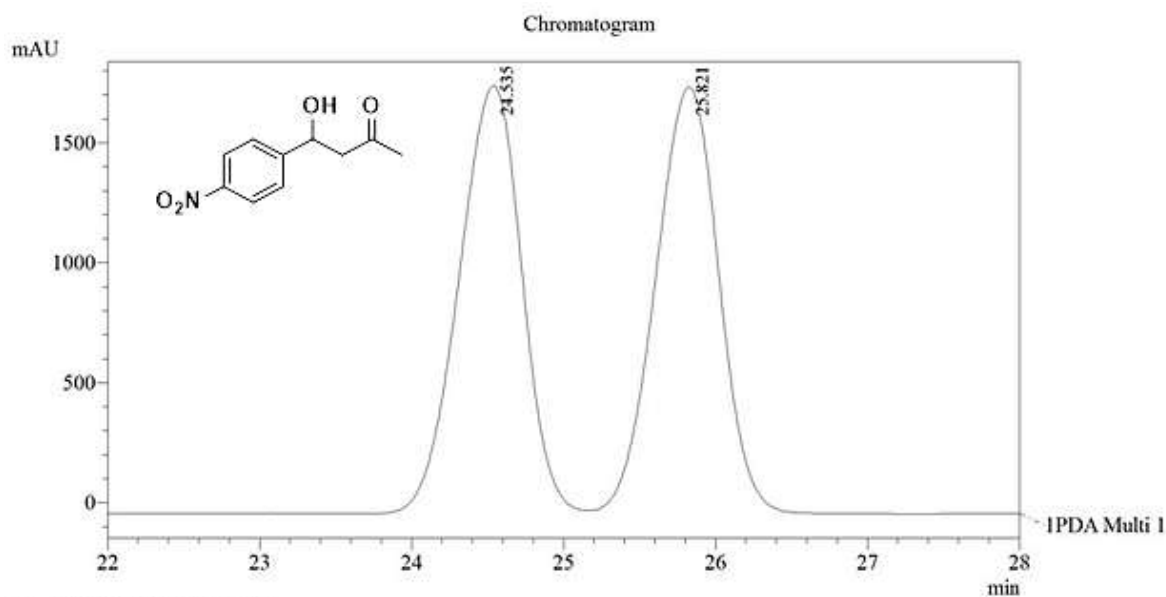
PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	24.535	50688232	49.993	0.766
2	25.821	50701588	50.007	0.767
Total		101389820	100.000	
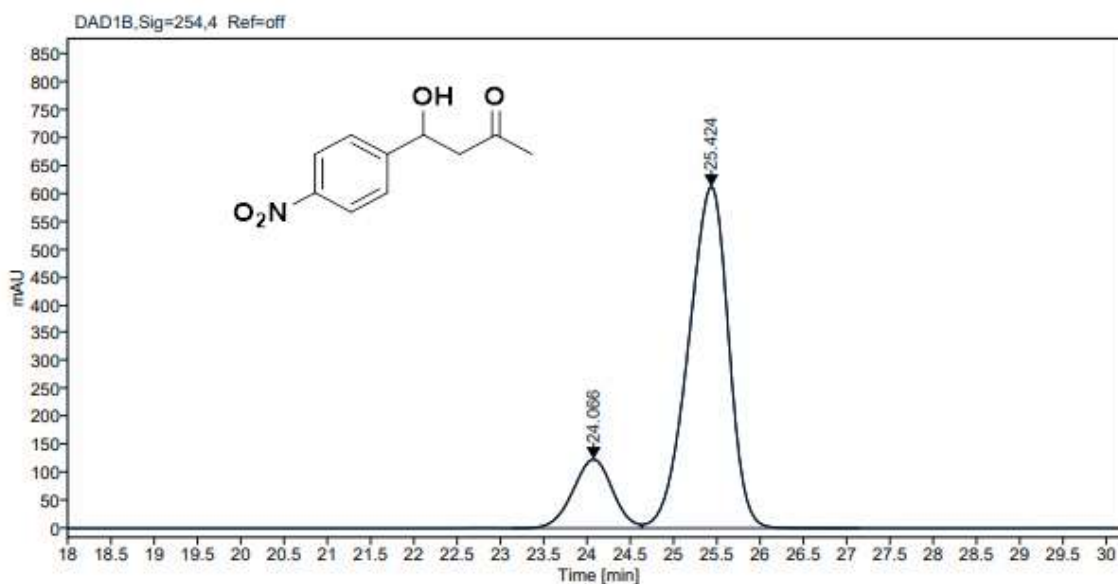
Signal: DAD1B,Sig=254,4 Ref=off

RT [min]	Type	Width [min]	Area	Height	Area%
24.066	BV	1.4951	3919.0046	123.4714	16.6043
25.424	VB	2.5049	19683.2861	613.4050	83.3957
	Sum		23602.2907		

Table 4, Entry 1

Daicel CHIRALPAK IC, hexane/2-propanol = 80:20, flow rate: 1.0 mL min^{-1}, λ = 254 nm

Chromatogram
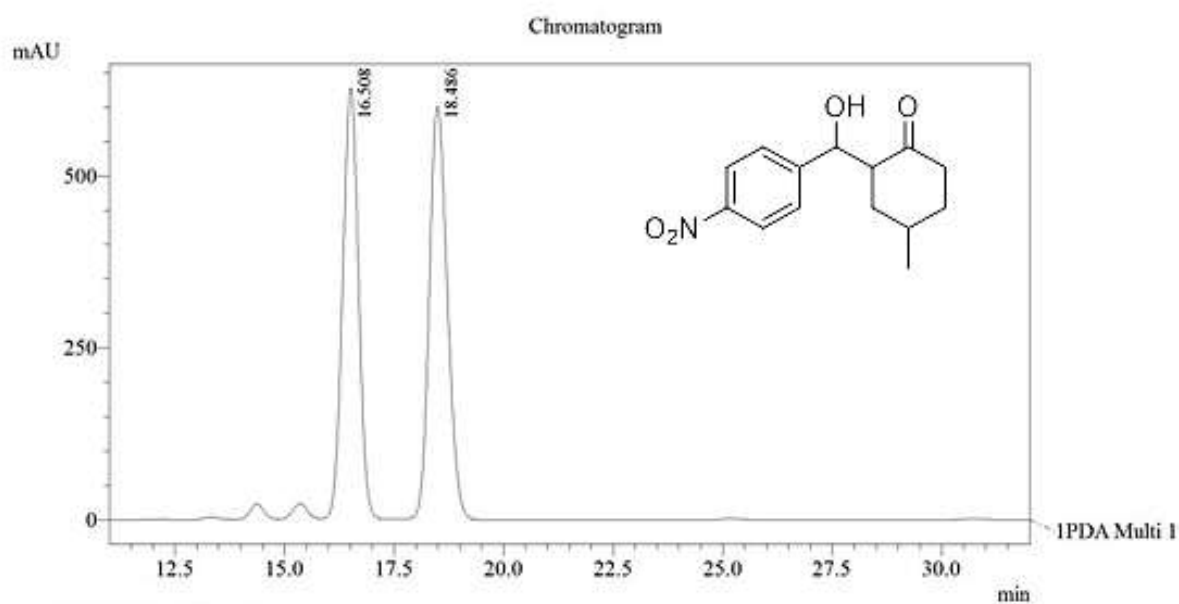
PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	16.508	15637465	47.728	0.670
2	18.486	17126070	52.272	0.764
Total		32763535	100.000	

Chromatogram
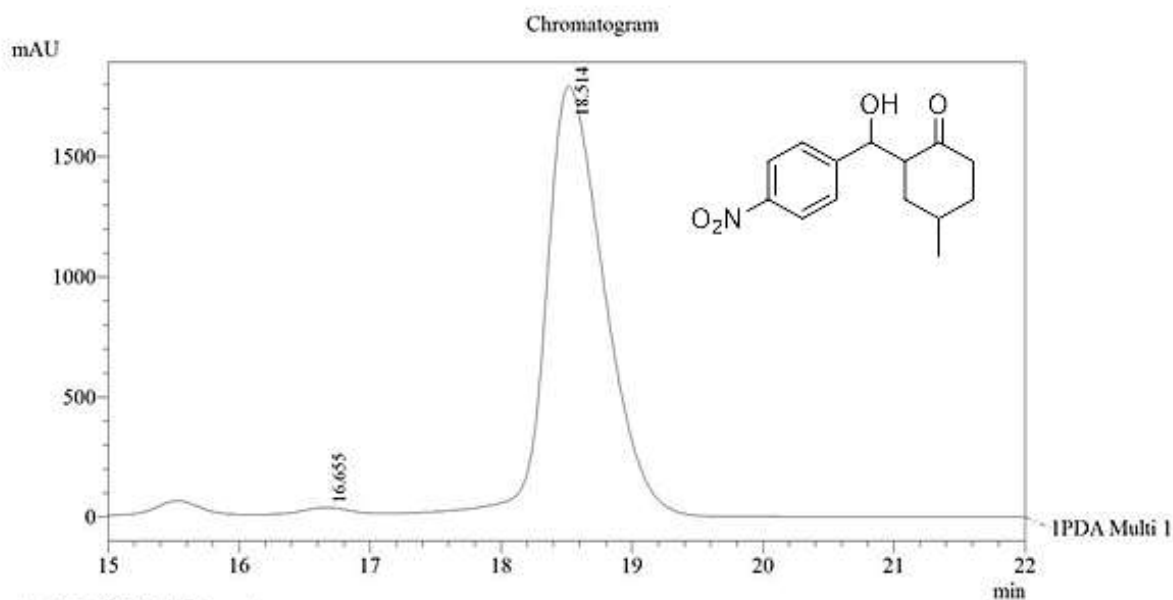
PeakTable

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	16.655	564069	1.034	0.606
2	18.514	53993716	98.966	0.797
Total		54557785	100.000	

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Table 4, Entry 2

Daicel CHIRALPAK IC, hexane/2-propanol = 80:20, flow rate: 1.0 mL min^{-1}, λ = 220 nm

Chromatogram
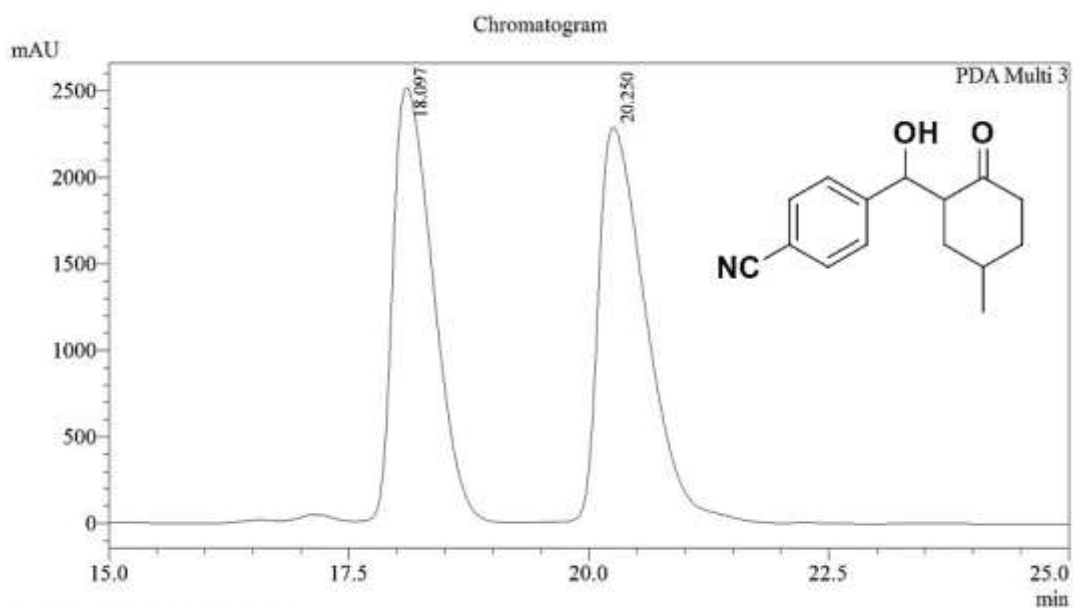
1   PDA Multi 3 / 220nm 4nm

PeakTable

PDA Ch3 220nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	18.097	72261841	48.429	0.769
2	20.250	76950809	51.571	0.894
Total		149212651	100.000	

Chromatogram
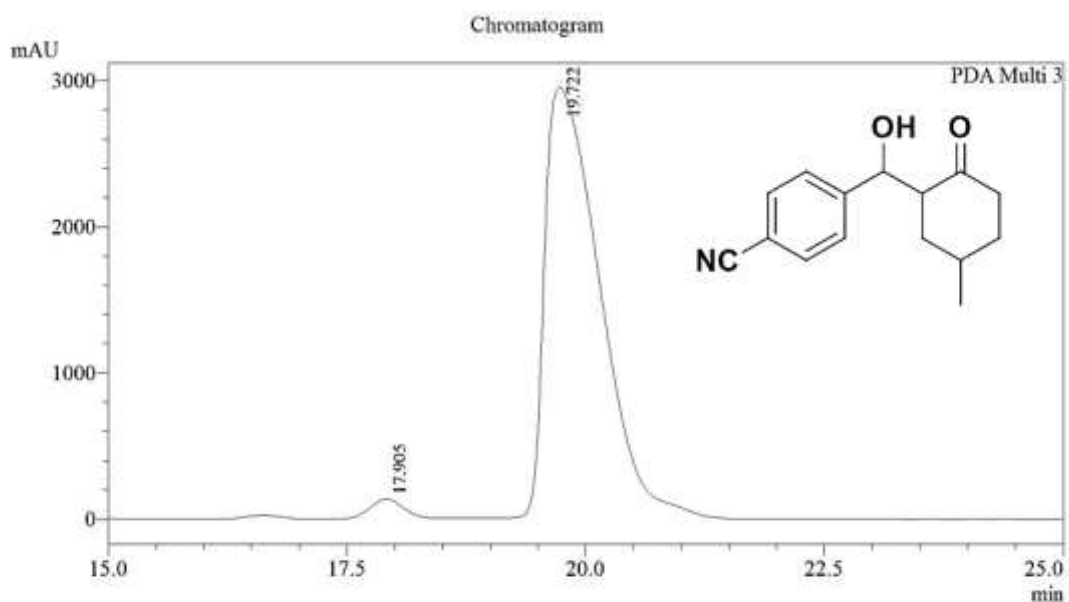
1   PDA Multi 3 / 220mm 4nm

PeakTable

PDA Ch3 220nm 4nm

Peak#	Ret. Time	Area	Area Percent	Width
1	17.905	3142169	2.606	0.636
2	19.722	117443105	97.394	1.030
Total		120585274	100.000	

Table 4, Entry 3

Daicel CHIRALPAK IC, hexane/2-propanol = 80:20, flow rate: 0.5 mL min^{-1}, λ = 254 nm

1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm
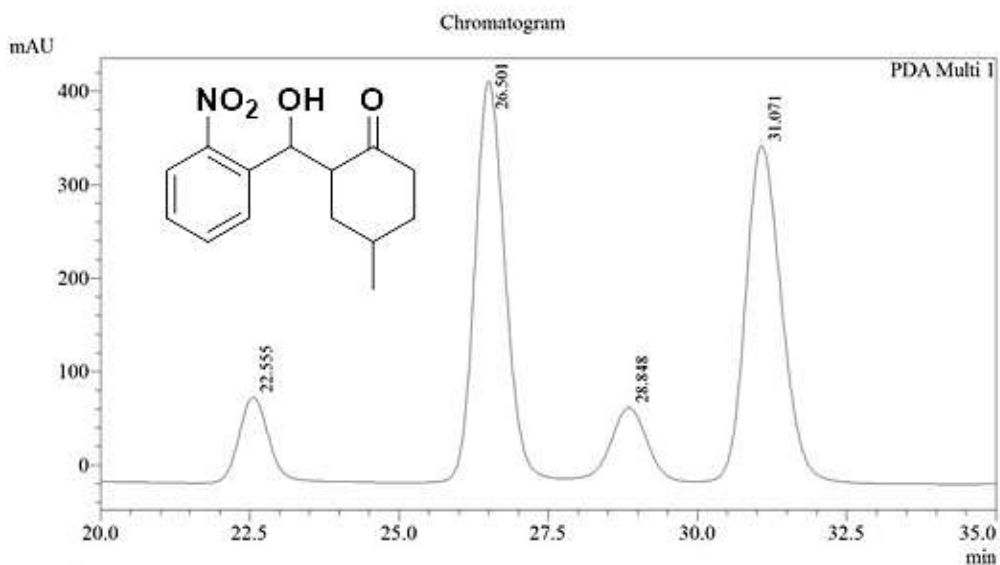
Peak#	Ret. Time	Area	Area Percent	Width
1	22.555	2972732	8.406	0.880
2	26.501	14657506	41.446	0.914
3	28.848	3075512	8.696	1.076
4	31.071	14659424	41.452	1.089
Total		35365174	100.000	

1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm
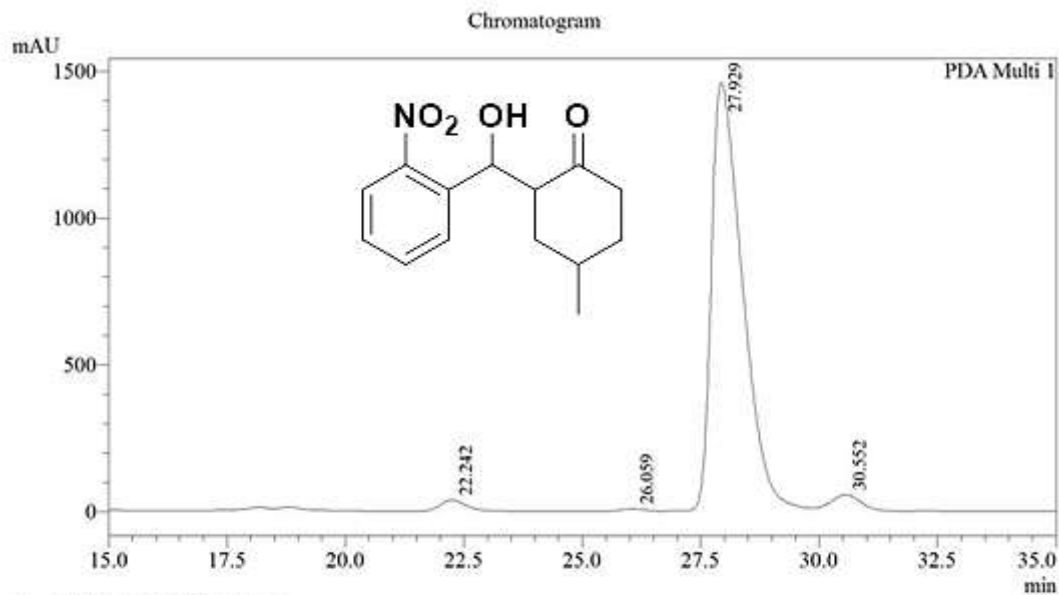
Peak#	Ret. Time	Area	Area Percent	Width
1	22.242	1345227	1.944	0.951
2	26.059	237373	0.343	0.839
3	27.929	65766784	95.048	1.217
4	30.552	1843920	2.665	1.051
Total		69193304	100.000	

¹H NMR spectra of the <u>crude reaction mixtures</u> (*for determination of the diastereomeric ratio*)

Table 1, Entry 7

ES-PTAP-CAT-9; 1H; CDCl3; 8 MAR 18
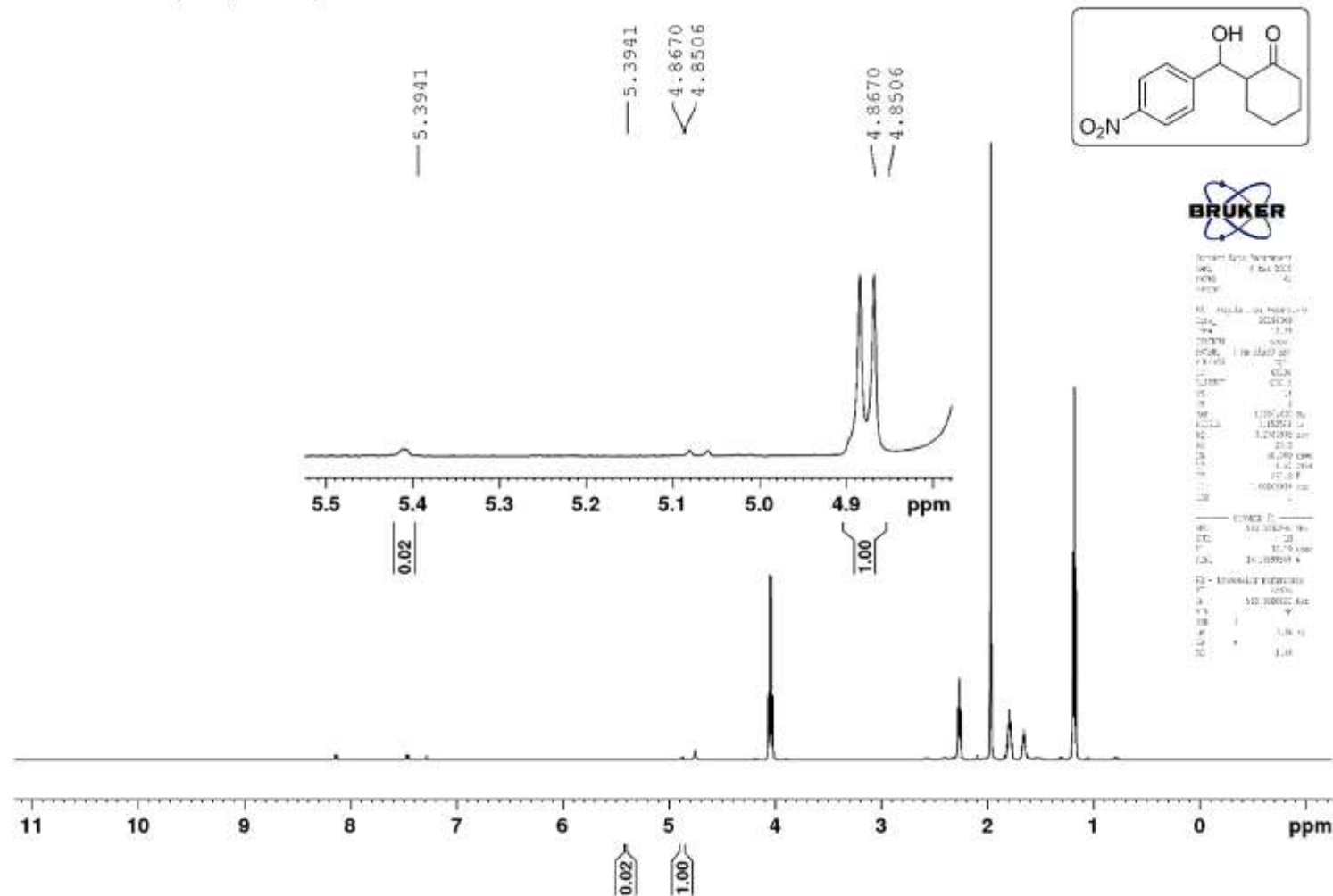
Table 2, Entry 1

ES-KK-PTAP-4CN; 1H; CDC13; 04/04/2018

Table 2, Entry 2

ES-KK-PTAP-PCF3-R; 12/04/2018

Table 2, Entry 3

ES-KK-PTAP-4Br;1H; CDCl3, 5/4/2018

Table 2, Entry 4

ES-KK-PTAP-4Cl; 1H; CDCl3; 29 MAR 18
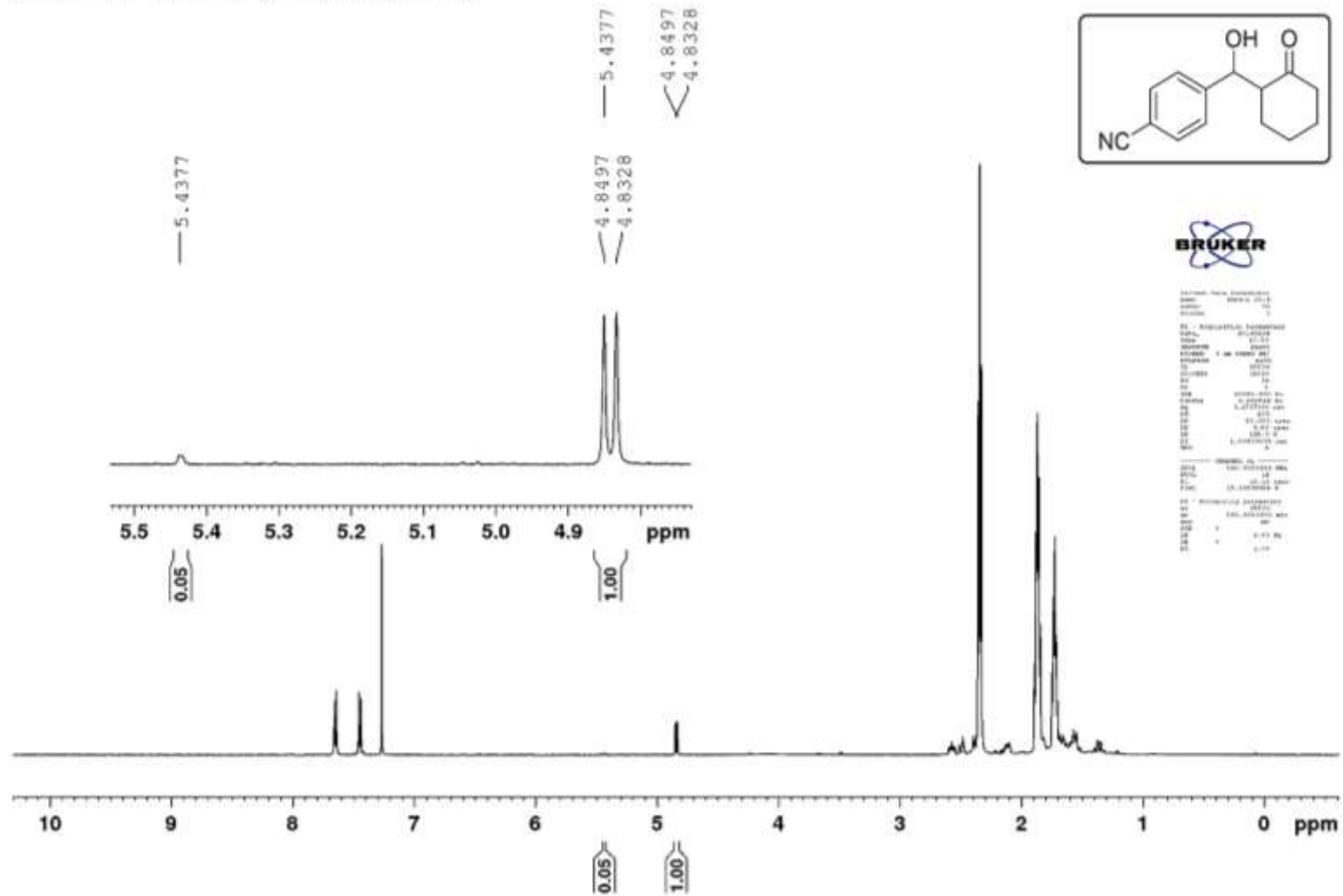
Table 2, Entry 5

ES-KK-PTAP-COOMe;1H;CDC13,10/04/18
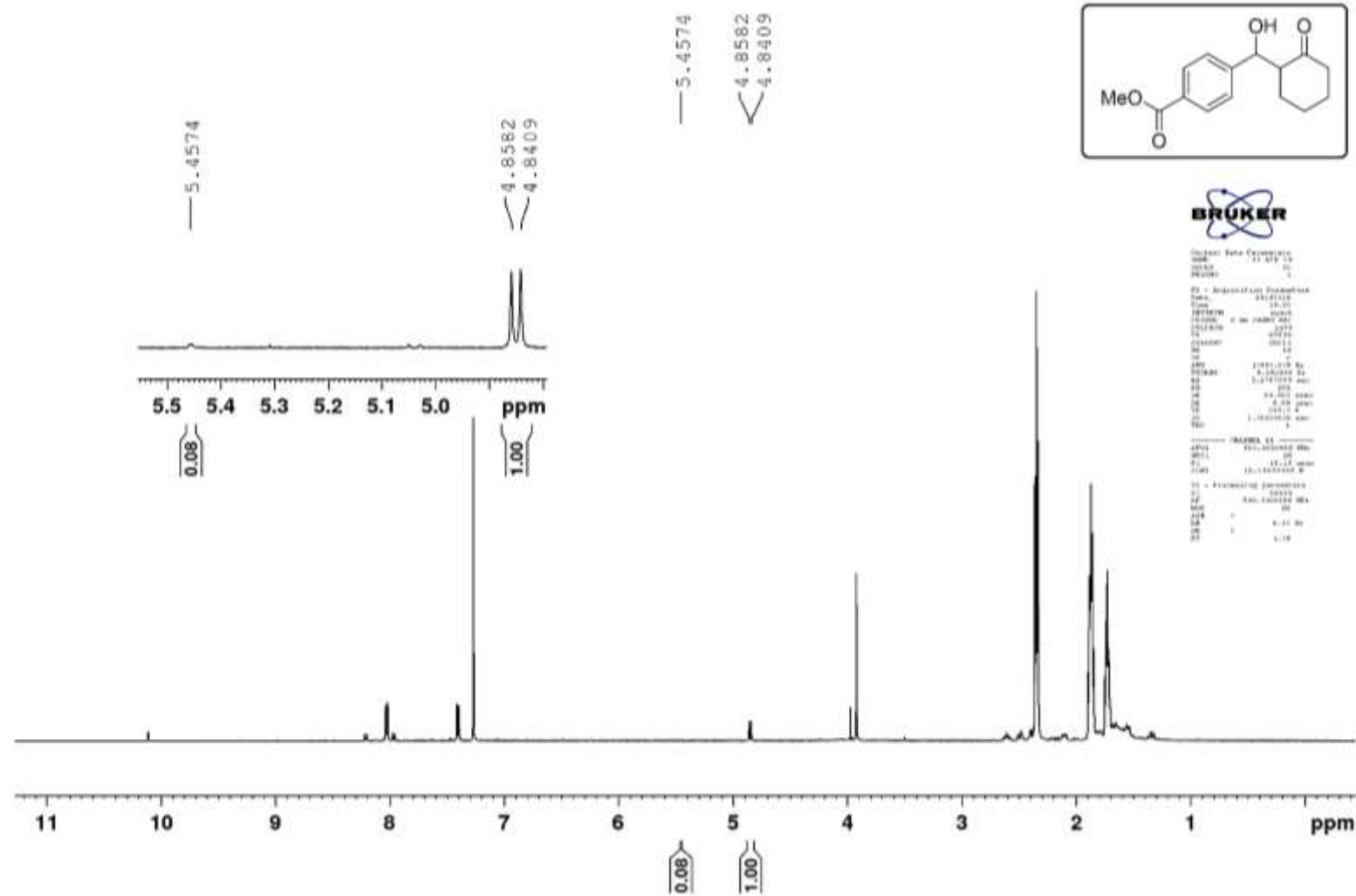
Table 2, Entry 6

ES-KK-PTAP-3PY; 27/03/2018
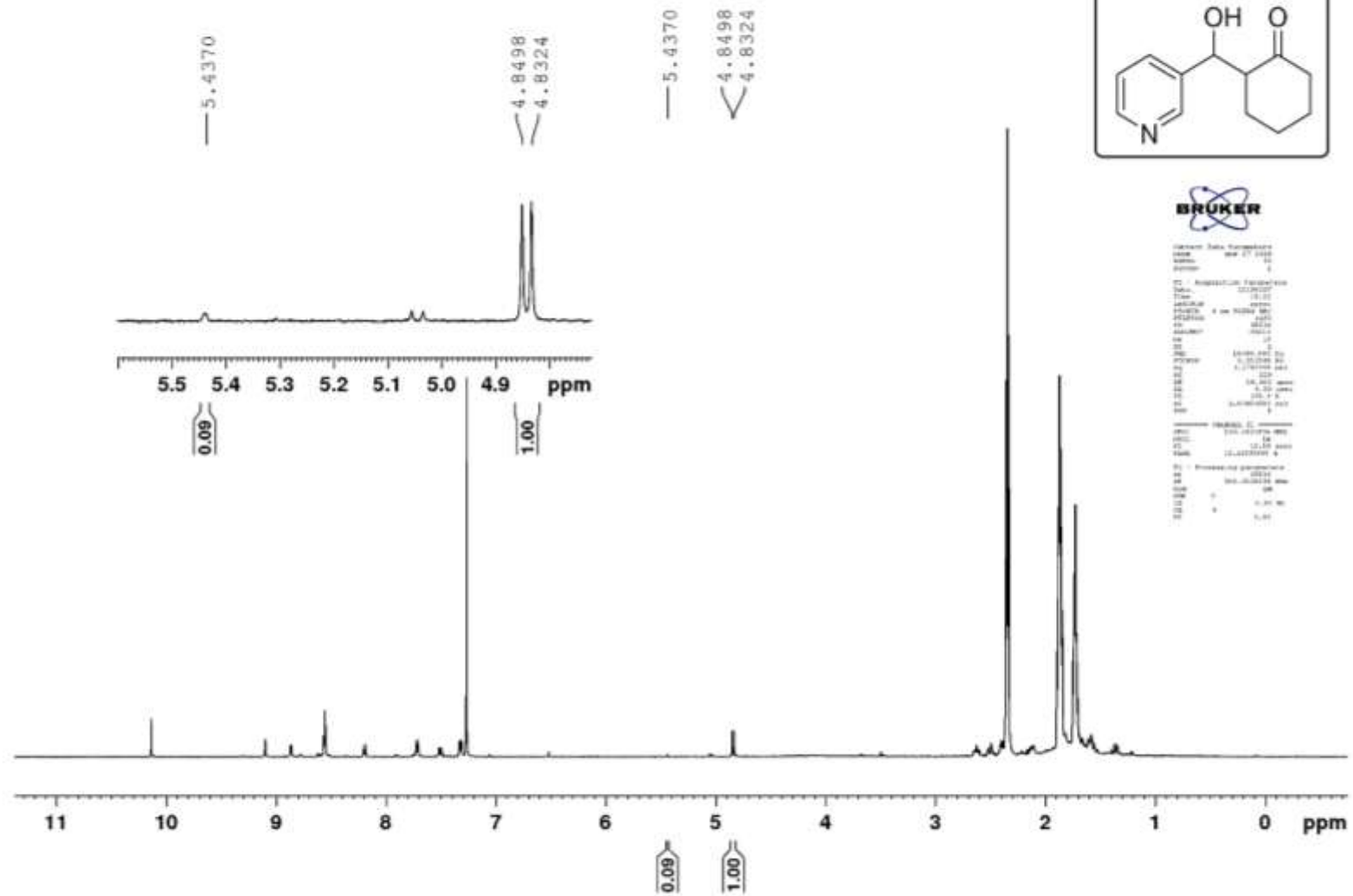
Table 2, Entry 7

ES-KK-PTAP-4PY; 1H; CRUDE; 31 MAR 18

Table 2, Entry 8

ES-KK-PTAP-C6F5; 1H; CRUDE; CDCl3; 26 MAR 18
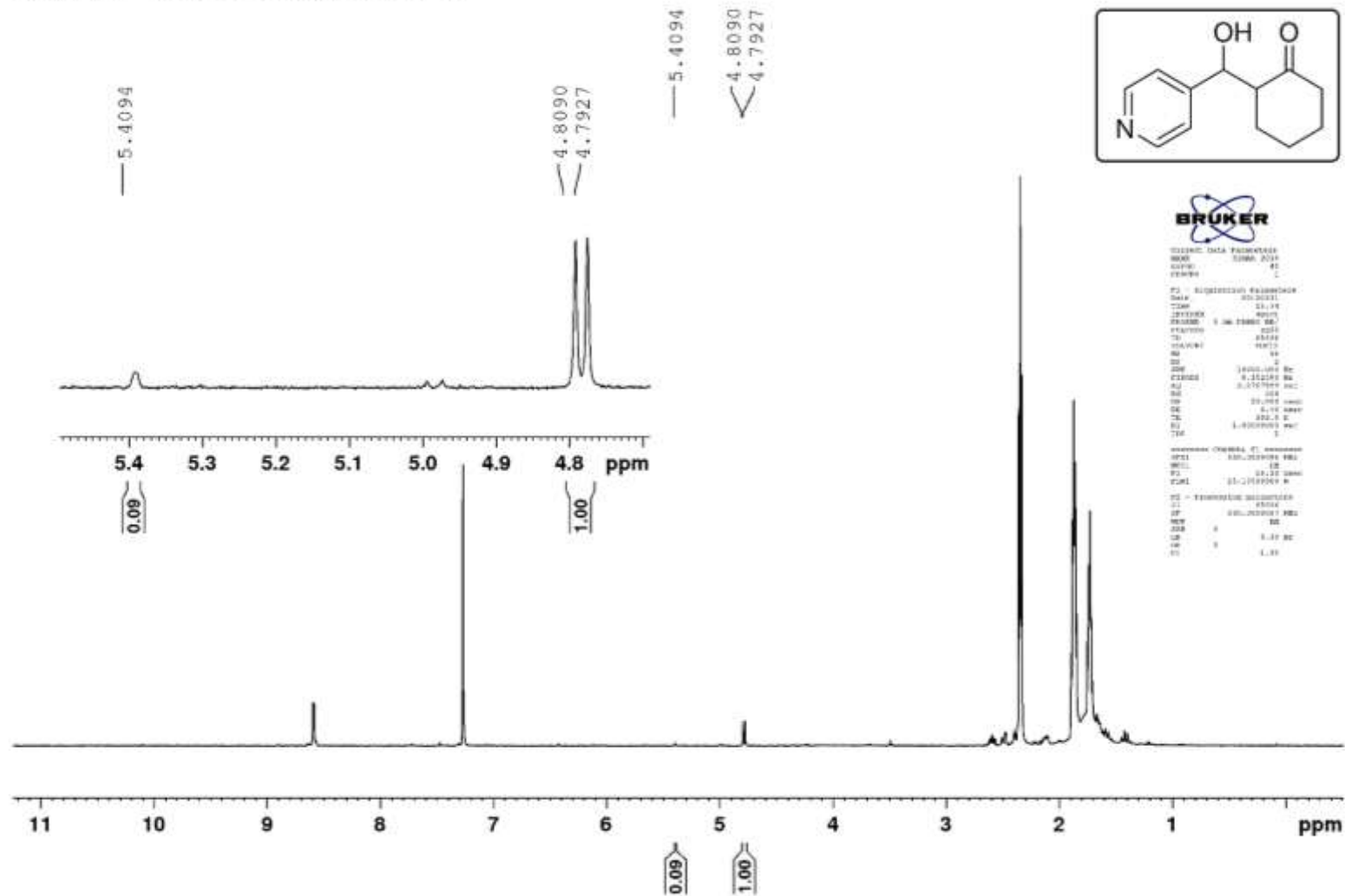
Table 2, Entry 9

ES-KK-PTAP-2NO2-1H; CRUDE; 2 April 2018
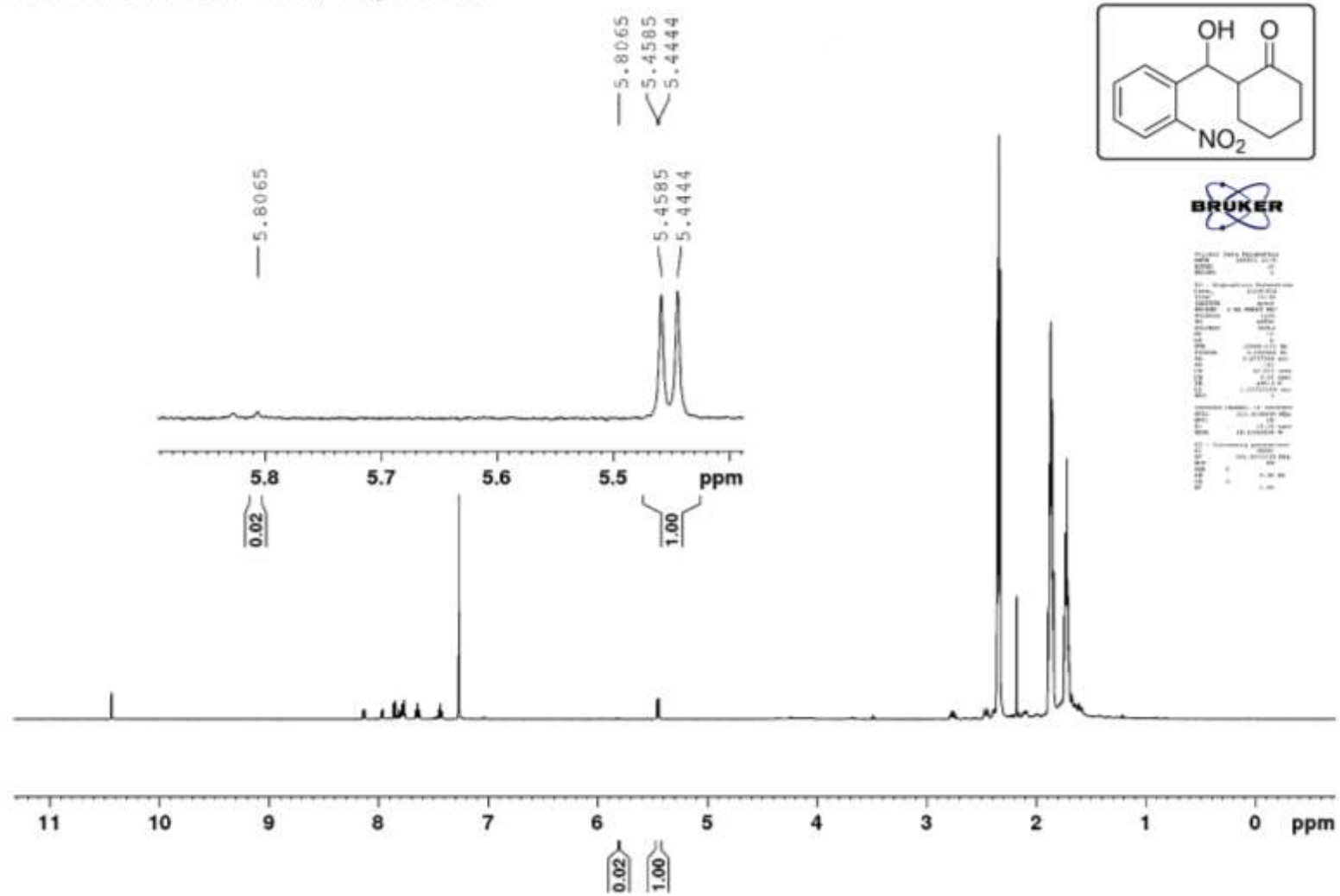
Table 2, Entry 10

ES-KK-PTAP-2Cl-(1H-CDCl3),
07-04-2018

5.7141

5.3620
5.3457

5.7141

5.3620
5.3457

BRUKER

5.7   5.6   5.5   5.4   ppm

0.06

1.00

11   10   9   8   7   6   5   4   3   2   1   0   ppm

0.06   1.00
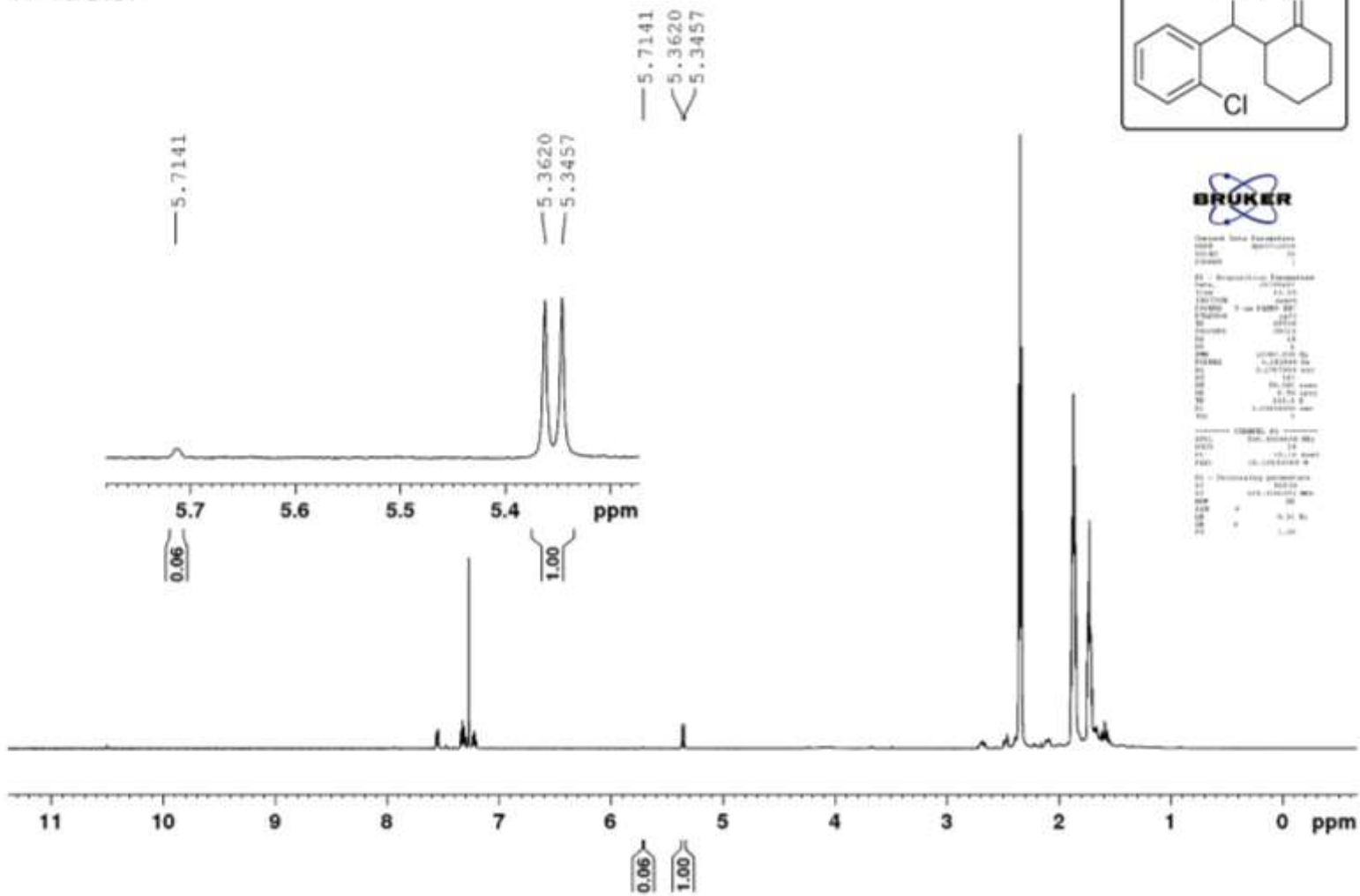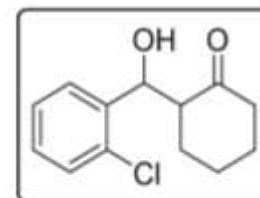
Table 2, Entry 11

ES-KK-3-NO2-crude

—5.463

—4.891
—4.869

5.5   5.4   5.3   5.2   5.1   5.0   4.9   4.8
f1 (ppm)

0.03

1.00

9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
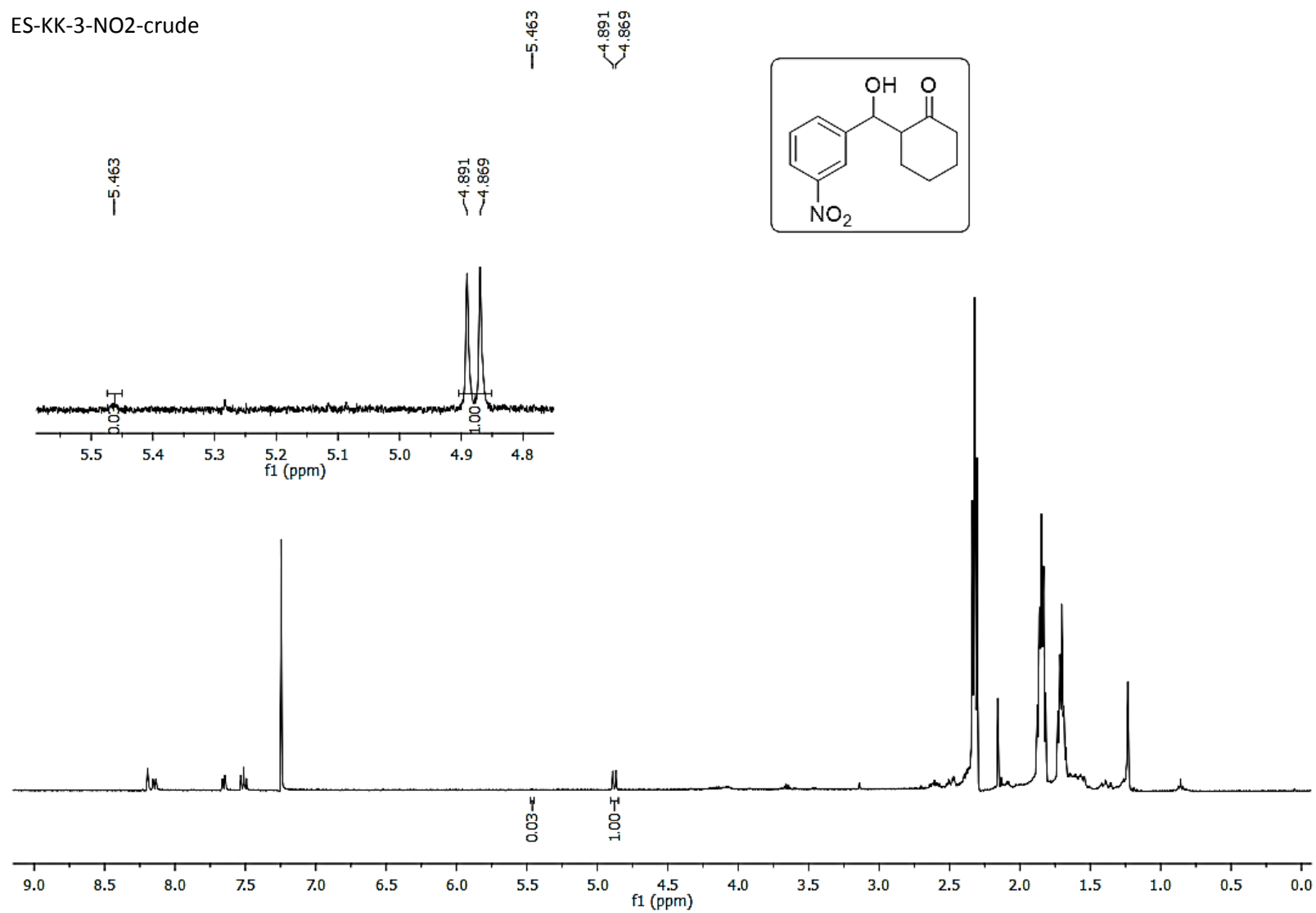
Table 2, Entry 12

ES-KK-PTAP-3CL
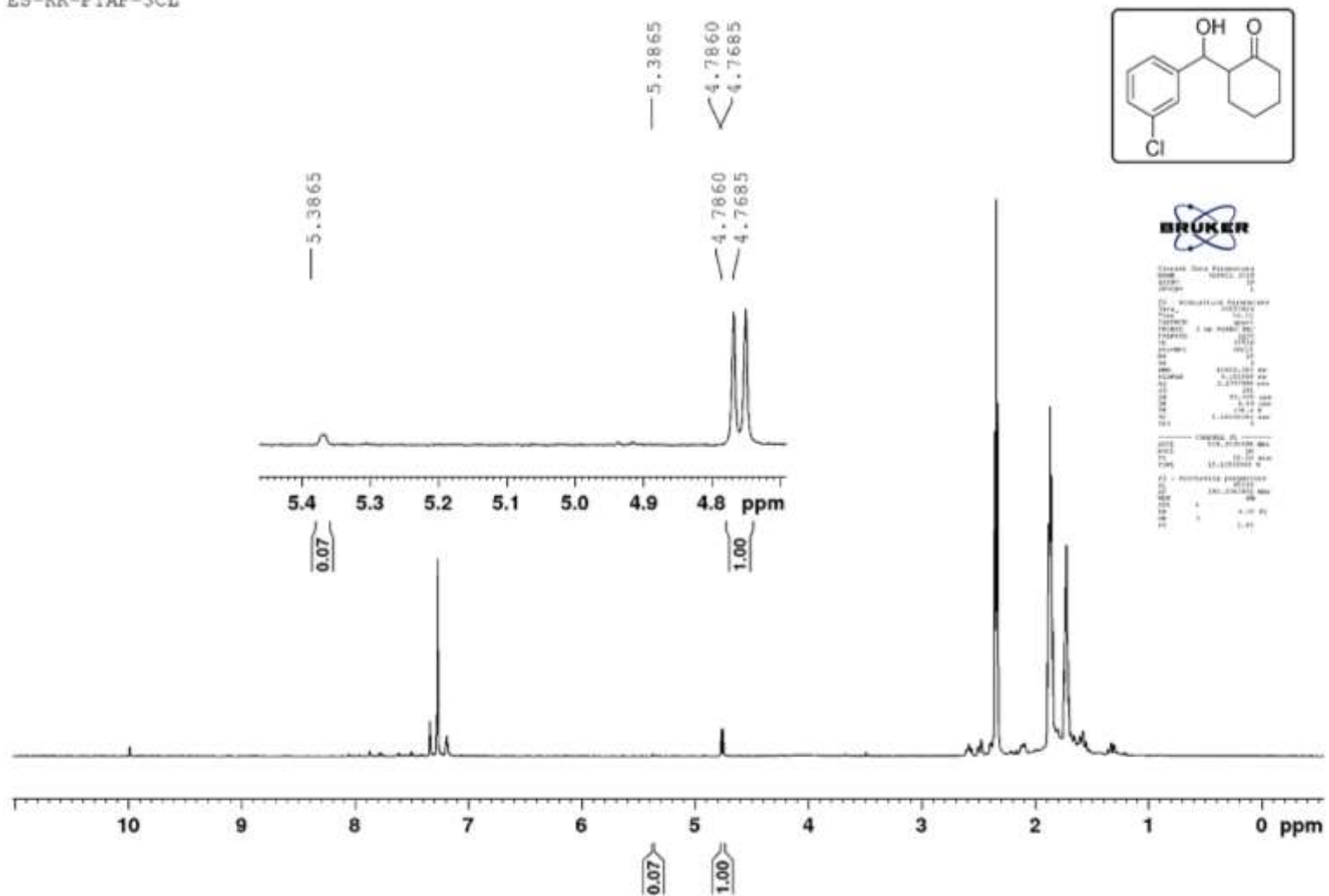
Table 2, Entry 13

ES-KK-3-OC6H5-crude
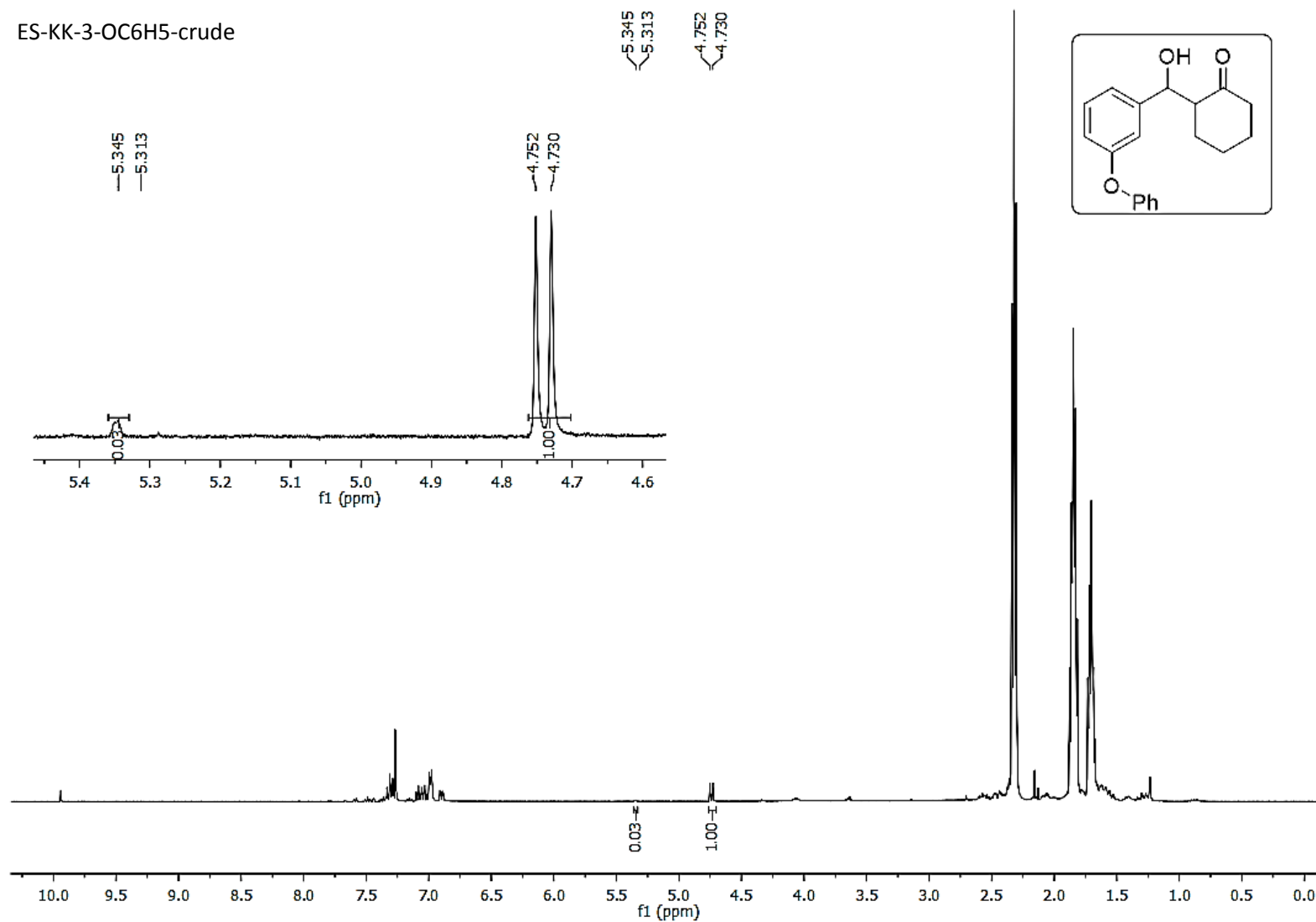
Table 2, Entry 14

ES-KK-PTAP-4Cl-3NO2;1H;CDC13,11/4/18
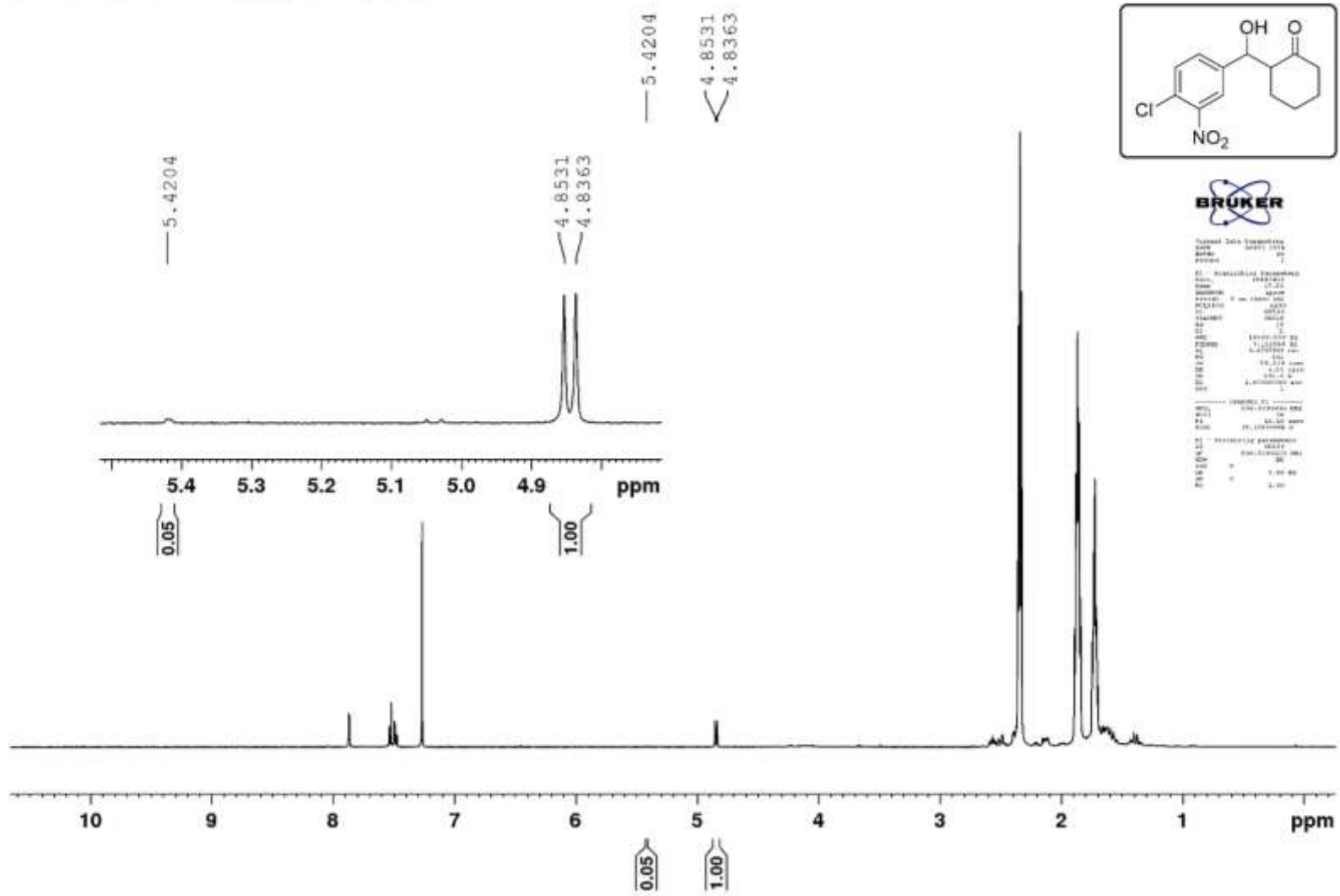
Table 2, Entry 15

ES-KK-PTAP-Ph-2; CDCl3; 18/04/2018
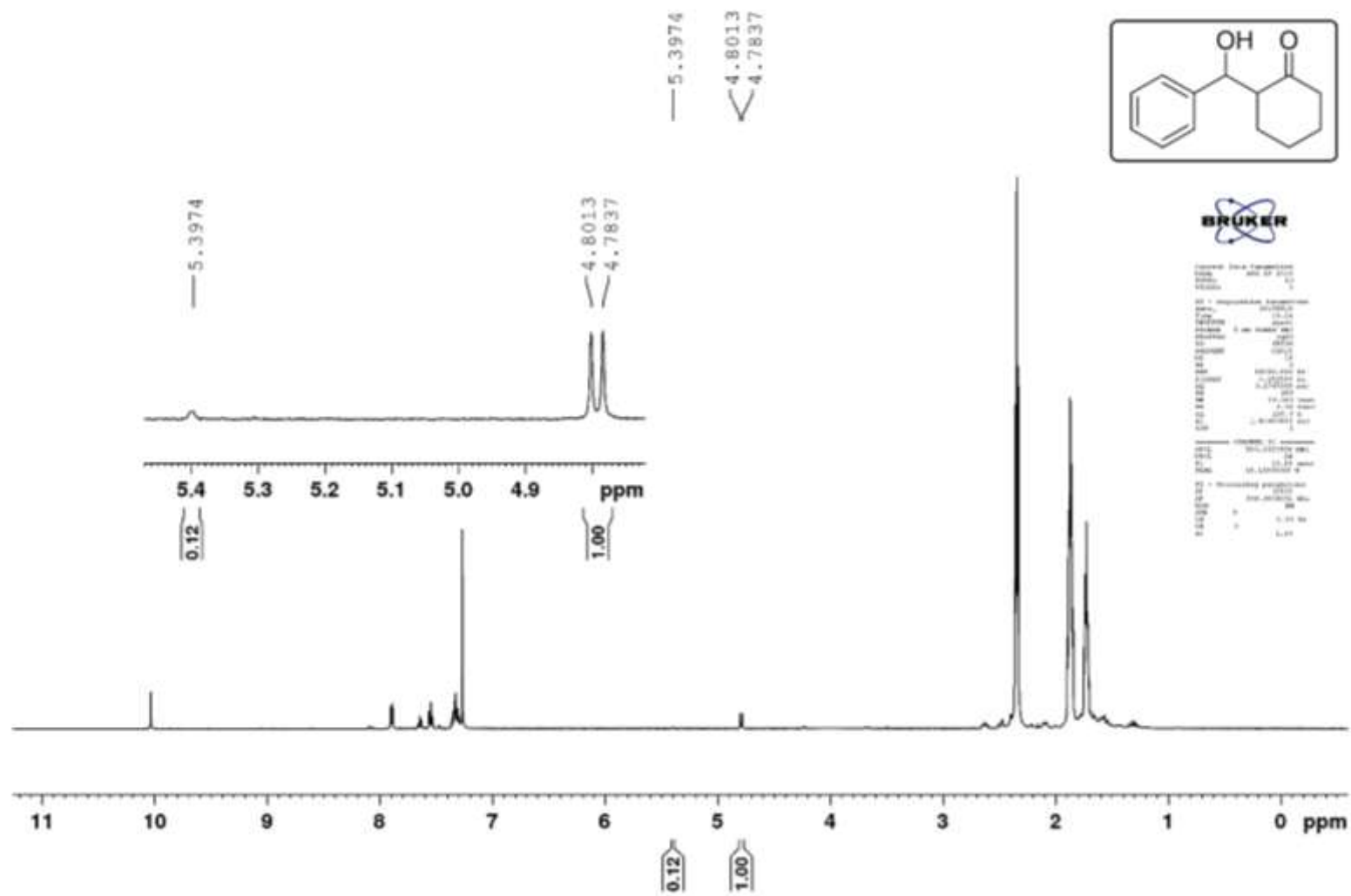
Table 2, Entry 16

ES-KK-PTAP-BNAPH

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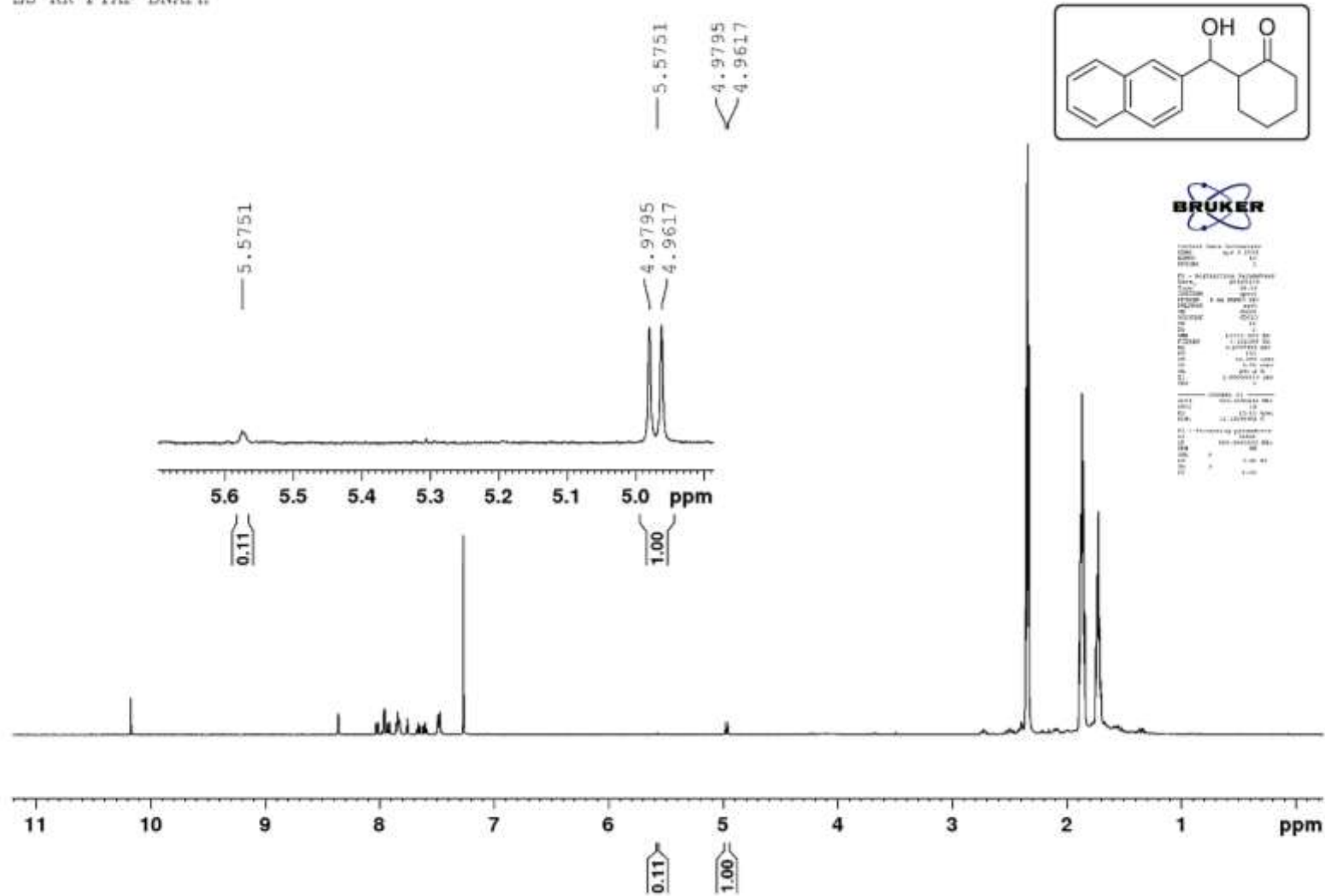
Table 2, Entry 17

ES-KK-4-OMe-crude

5.324

4.756
4.733

MeO

OH O

5.4 5.3 5.2 5.1 5.0 4.9 4.8 4.7 4.6
f1 (ppm)

0.07

1.00

10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

0.07 1.00
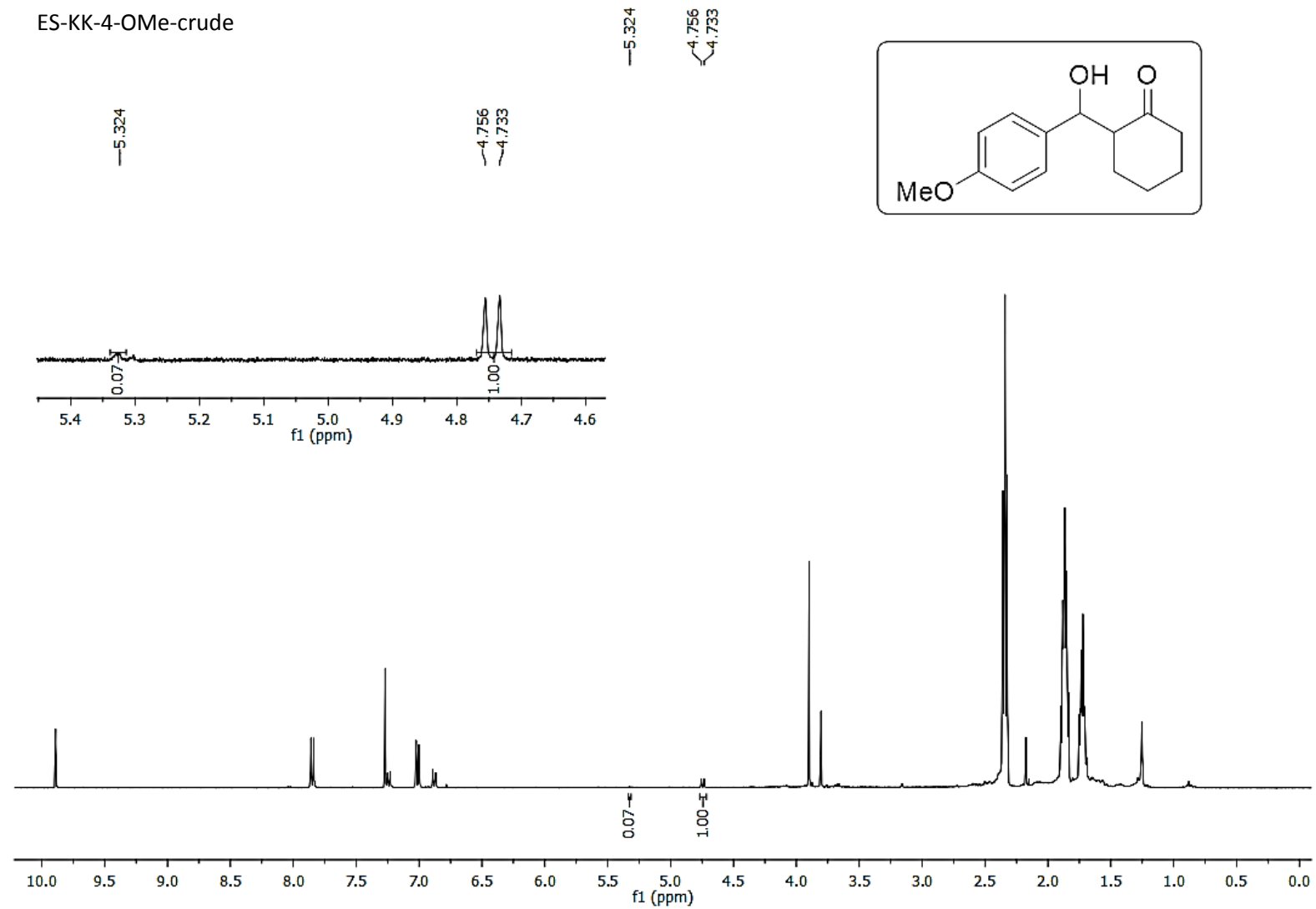
Table 3, Entry 1
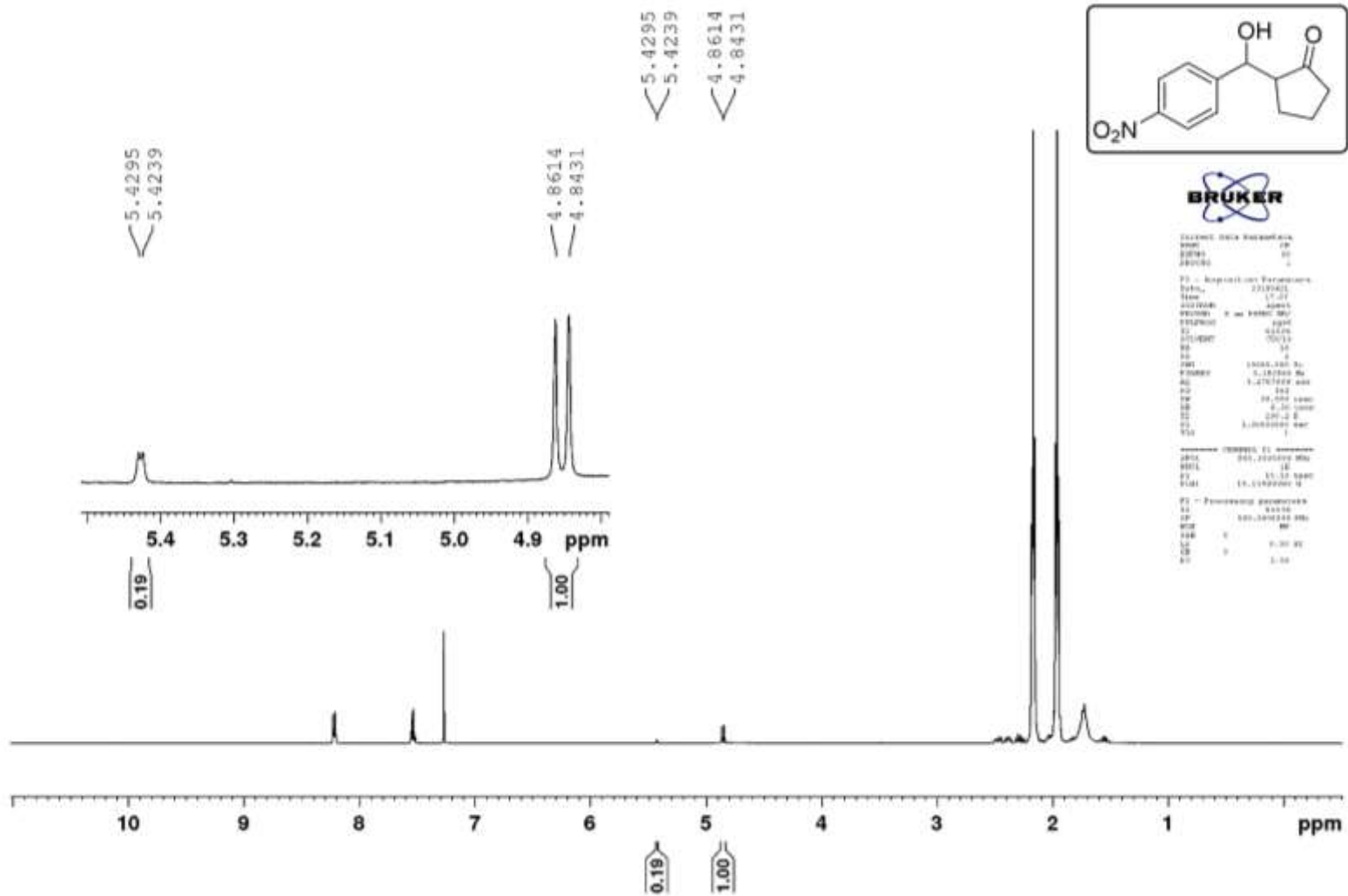
Table 4, Entry 1

ES-KK-PTAP-4MECY1H;CDCL3;25/4/18;
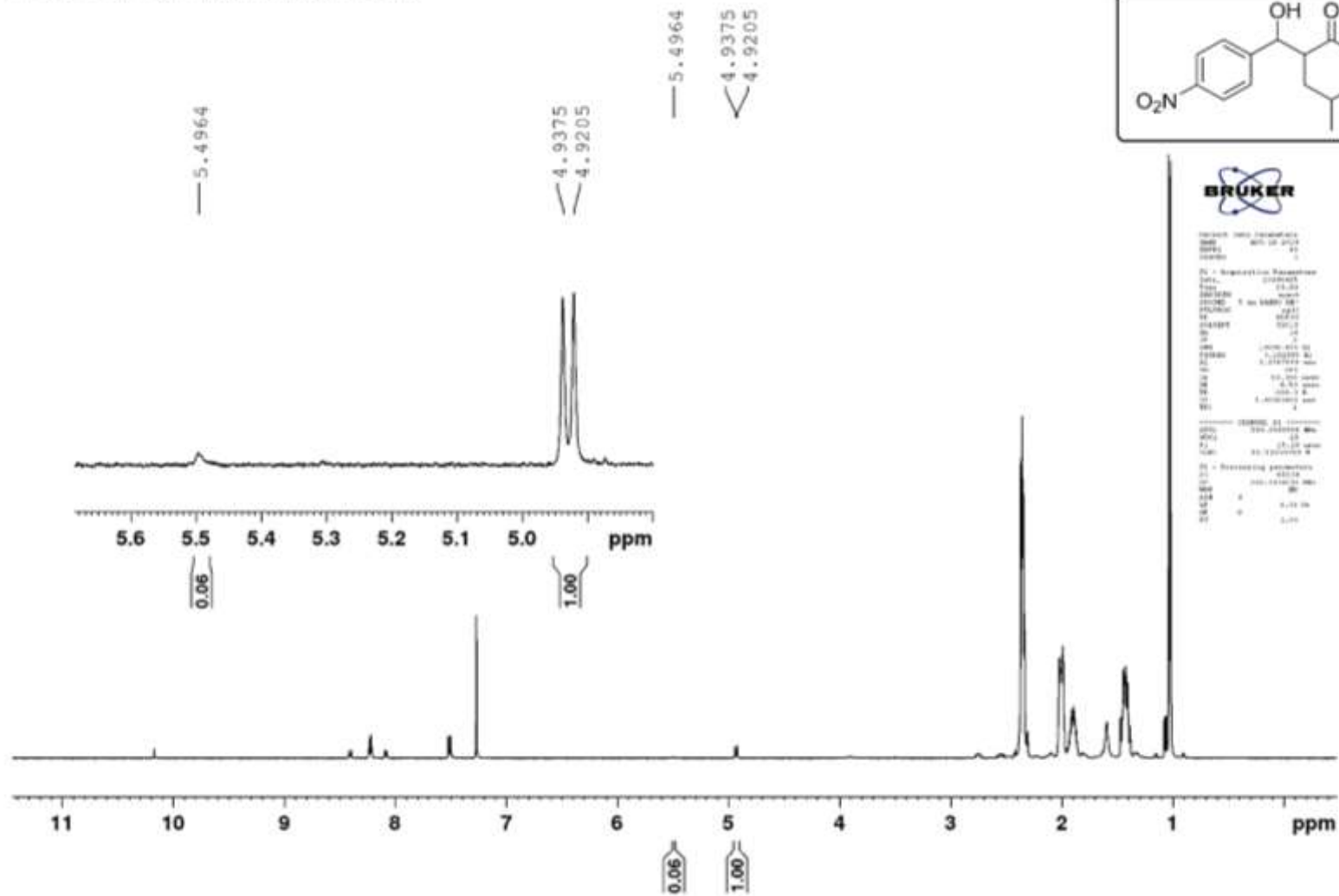
Table 4, Entry 2

ES-KK-EXP-167-CRUDE;1H;18/12/18
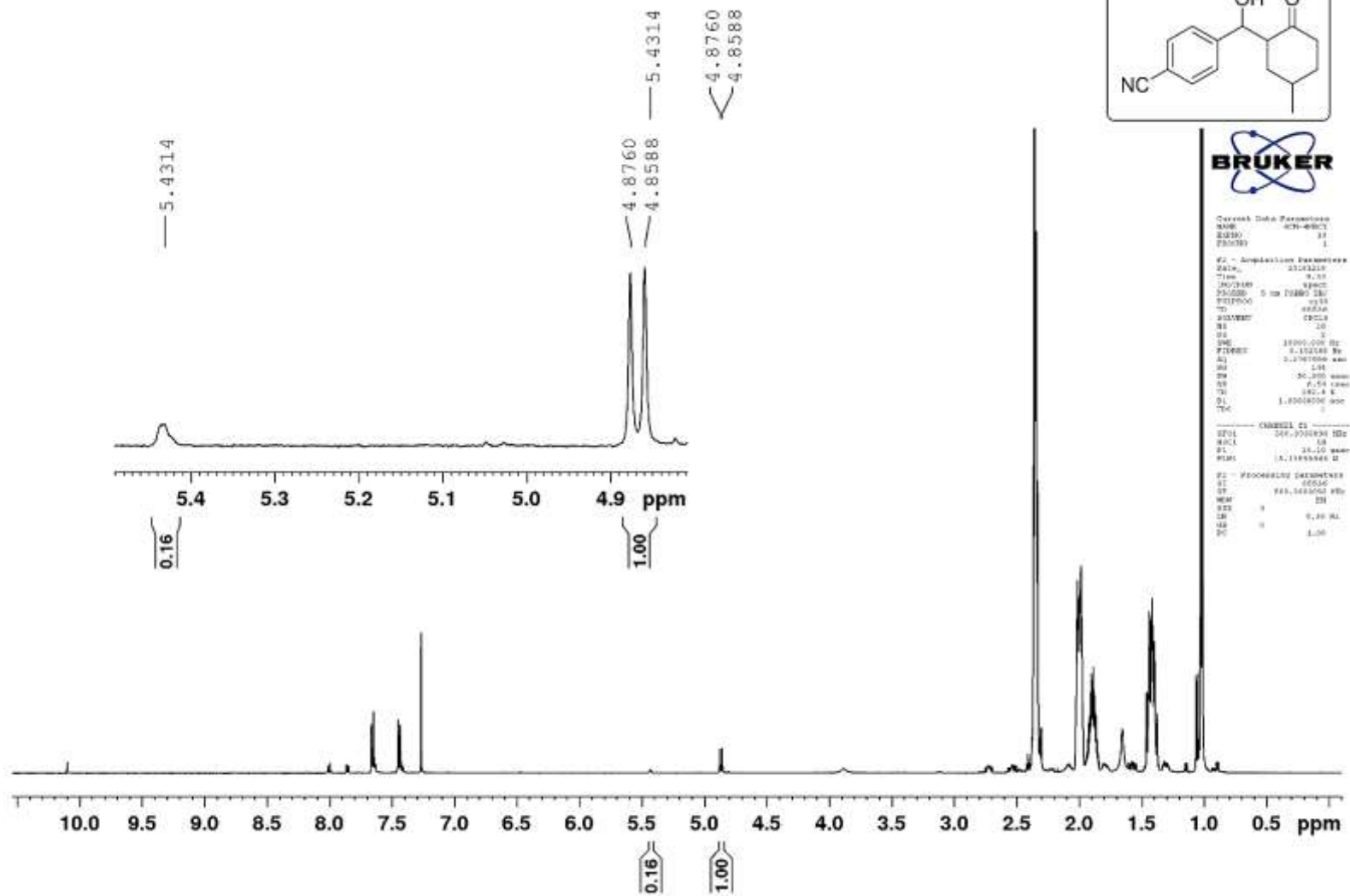
Table 4, Entry 3

ES-KK-EXP-183-CRUDE;1H;CDCl3;14/2/19
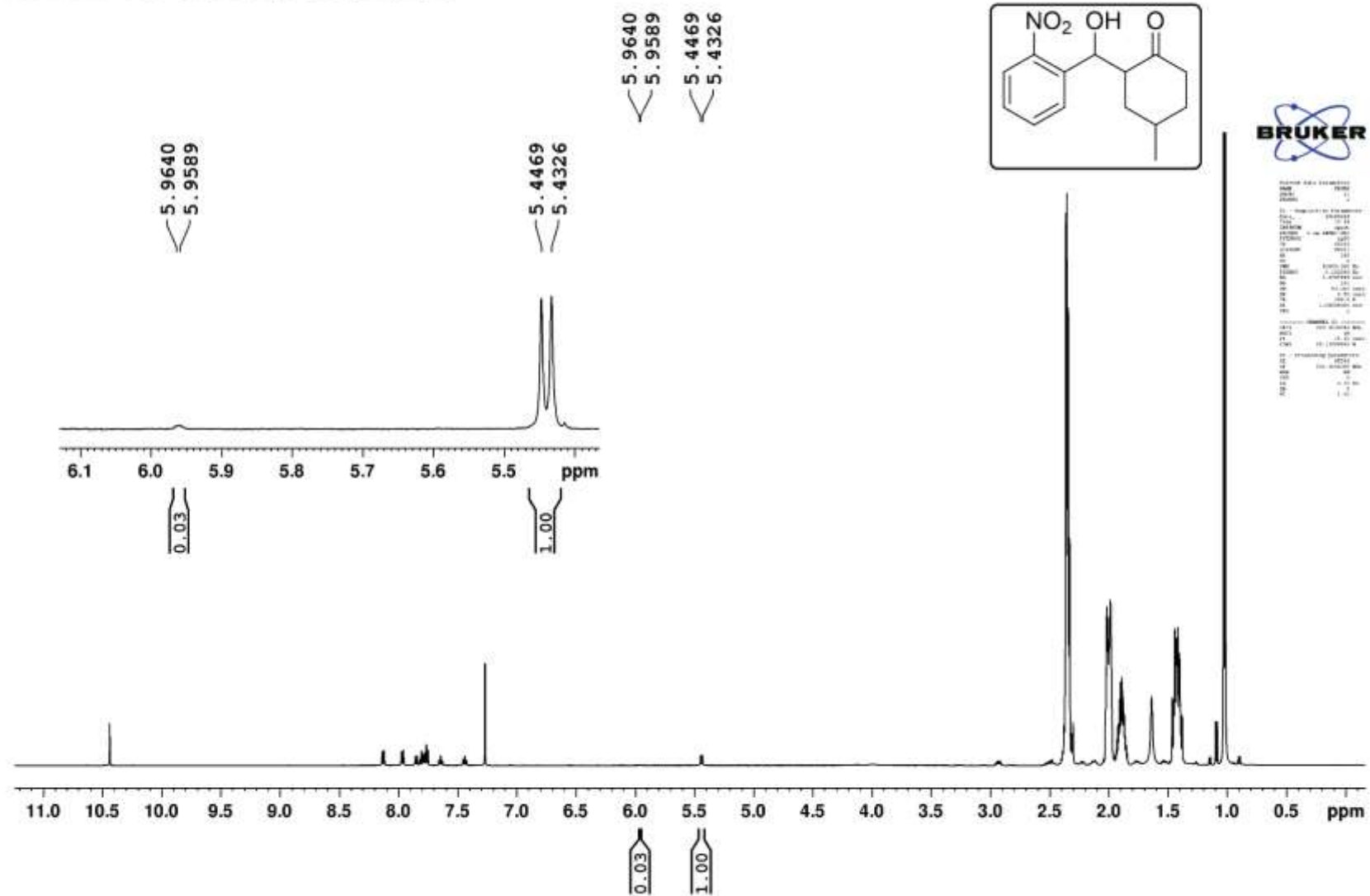
^{1}H and ^{13}C NMR spectra of the <u>purified aldol adducts</u> (*isolated as a mixture of syn and anti diastereomers*)

ES-KK-4-NO2-PDT; CDCl3; 01/05/18

BRUKER

BRUKER

214.7610

148.3522
147.5984

127.8829
126.6128
123.5874
123.4738

74.0353

57.2001

42.6874

30.7698
27.6477
24.6994

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm
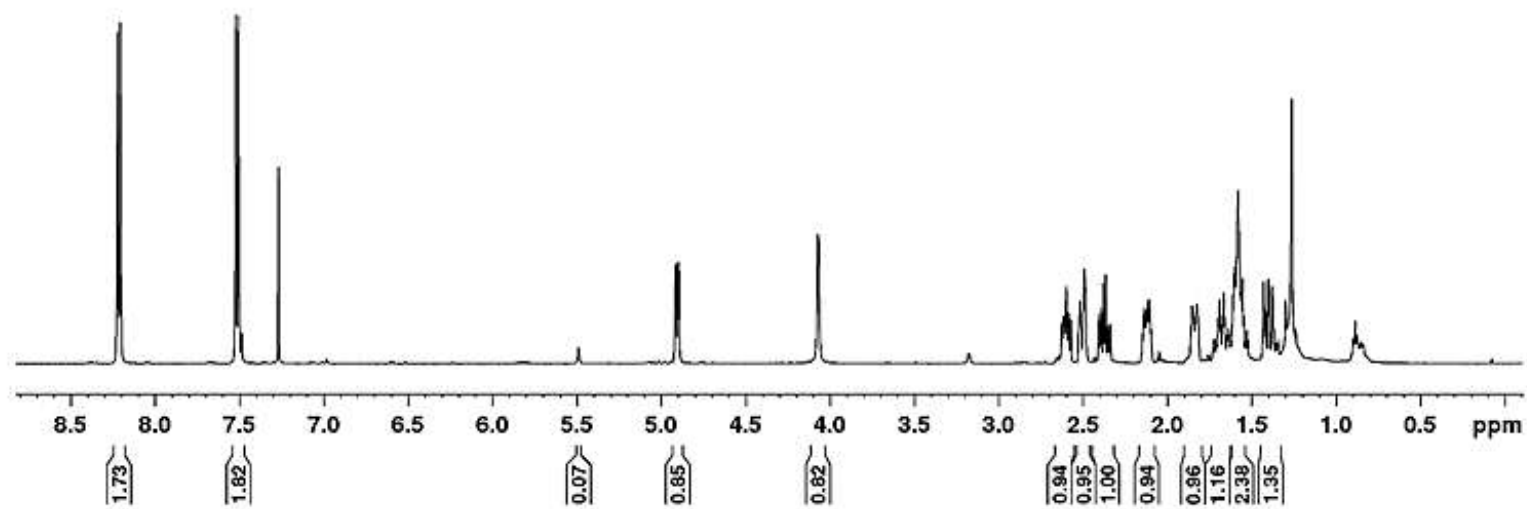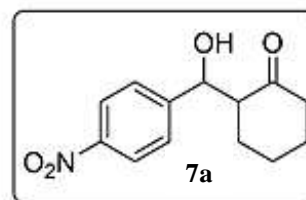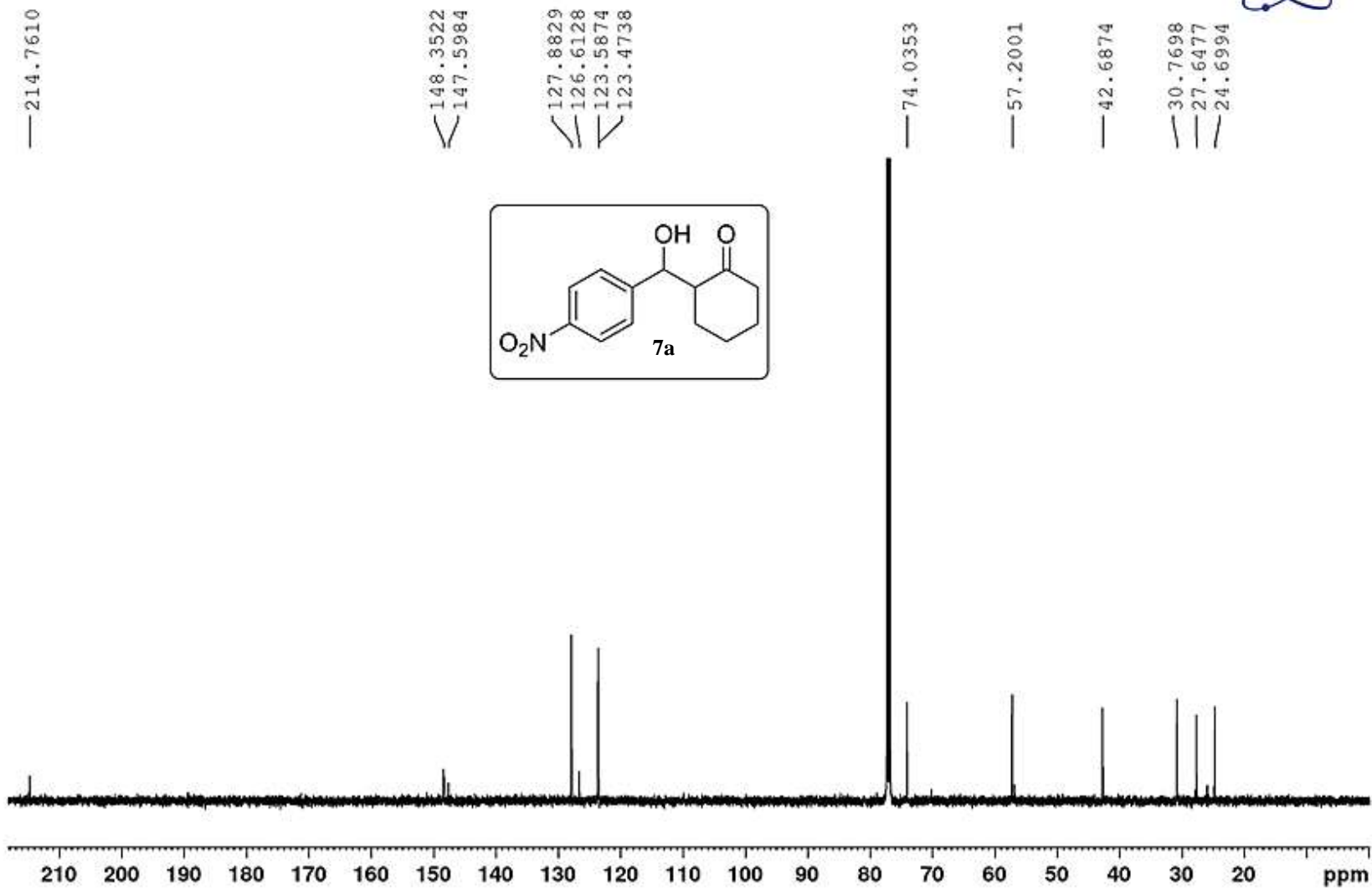
ES-KK-4-CN-PDT;CDCl3;13/11/18

BRUKER

7.6584
7.6421
7.4570
7.4406
7.2688

5.4339

4.8497
4.8329

4.0570
2.6008
2.5840
2.5747
2.5635
2.5481
2.5103
2.4829
2.3972
2.3855
2.3702
2.3580
2.3301
2.1289
2.1225
2.1087
2.1026
2.0968
1.8443
1.8167
1.7093
1.6829
1.6567
1.6306
1.5992
1.5742
1.5686
1.5539
1.5474
1.5212
1.3958
1.3757
1.3684

7b

8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

1.88 1.93   0.06   0.83   0.72   0.99 1.06 1.12 1.00 1.10 1.42 2.24 1.07
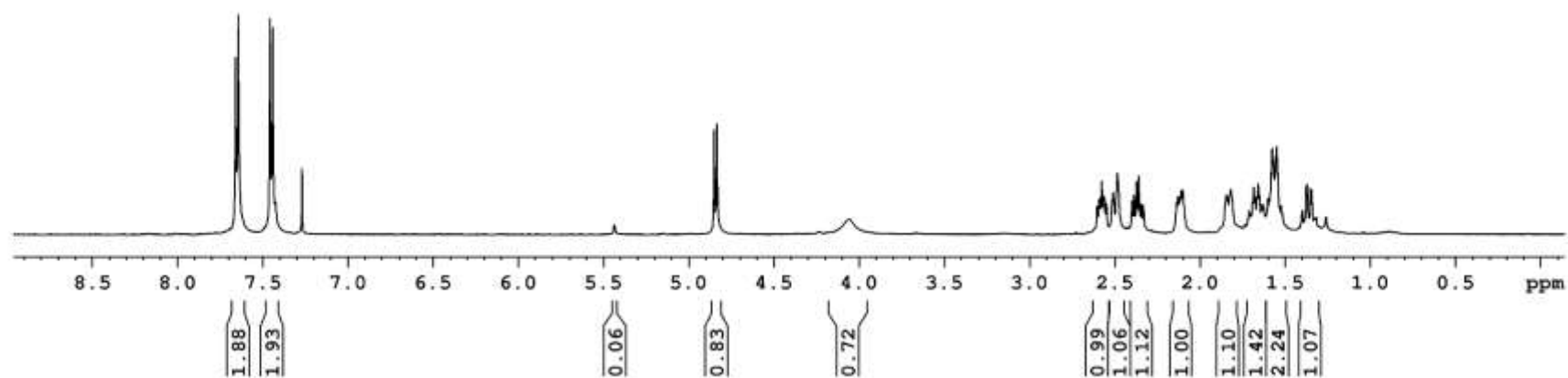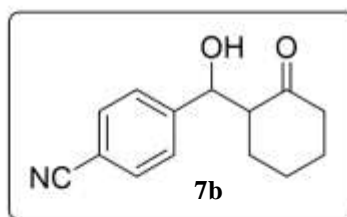
ES-KK-4-CN-PDT;CDC13;13/11/18

BRUKER

214.9006
146.3446
132.2136
127.7894
118.7423
111.7236
74.2607
57.1478
42.6923
30.7503
27.6635
24.7032

7b

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

ES-KK-4-CF3-PDT;CDCl3;08/09/18

7.6230
7.6069
7.4604
7.4442
7.2688

5.4525

4.8622
4.8450

4.0618
2.6289
2.6198
2.6029
2.5921
2.5749
2.5130
2.4857
2.4054
2.3933
2.3785
2.3662
2.3497
2.3372
2.1378
2.0875
1.8337
1.8304
1.6946
1.6869
1.6794
1.6684
1.6611
1.6532
1.5965
1.5898
1.5713
1.5516
1.5443

7c

1.80
1.82
0.03
0.89
0.80
0.95
0.97
1.08
1.00
1.19
1.41
2.20
0.87

9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

ES-KK-4-CF3-PDT; CDCl3;08/09/18

BRUKER

215.1279

144.9627

130.5462
127.3777
125.3425
125.3129

74.2959

57.2596

42.6739

30.7755
27.7091
24.7121

OH   O

F3C   **7c**

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

ES-KK-4Br-PDT;CDCl3;01/05/18

BRUKER

7.4890
7.4724
7.2689
7.2160
7.1994

5.3467
4.7701
4.7658
4.7528
4.7485
3.9734
3.9681
2.5870
2.5774
2.5696
2.5611
2.5507
2.5456
2.5341
2.5015
2.4742
2.3928
2.3808
2.3660
2.3537
2.3392
2.3266
2.1272
2.1211
2.1151
2.1086
2.1018
2.0947
2.0886
2.0826
2.0769
1.8226
1.7982
1.7127
1.7050
1.6865
1.6788
1.6711
1.6605
1.6527
1.6451
1.6342
1.6263
1.6168

7d

9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

1.89 1.95   0.09 0.92 0.85   1.00 1.06 1.06 1.04 1.04 1.15 0.98 1.48

ES-KK-4Br-PDT;CDCl3;23/05/2018

215.1995

140.0492
131.4969
128.7412
121.7235

74.2102

57.3464

42.6731

30.7672
27.7188
24.7314

7d

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

BRUKER

7.3188
7.2720
7.2552
4.7816
4.7768
4.7642
4.7594
3.9988
3.9934
2.5900
2.5813
2.5725
2.5642
2.5532
2.5489
2.5358
2.5067
2.5034
2.5004
2.4948
2.4846
2.4792
2.4760
2.4729
2.4675
2.3939
2.3835
2.3686
2.3564
2.3419
2.3294
2.1223
2.1163
2.1098
2.1031
2.0960
2.0899
2.0839
1.8233
1.8202
1.7966
1.7935
1.7039
1.6854
1.6778
1.6702
1.6595
1.6516
1.6442
1.5912
1.5811
1.5653
1.3402
1.3152
1.3085
1.2896
1.2816

7e

1.82
2.13
0.06
0.90
0.85
0.98
1.02
1.01
1.00
0.98
1.21
2.06
1.03

ES-KK-4-Cl-PDT;CDCl3;21/11/18

215.3713

139.4770
133.6010
128.5610
128.4021

74.1668

57.3808

42.6961

30.7719
27.7428
24.7325

BRUKER

7e

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

ES-KK-4COOMe-PDT;CDCl3;26/10/18

ES-KK-4-COOMe-PDT;CDCl3;31/10/18

215.2138
166.8976
146.0563
129.7027
127.0440
125.7377
74.4145
57.2993
52.1406
42.6958
30.7841
27.7362
24.7111

7f

210	200	190	180	170	160	150	140	130	120	110	100	90	80	70	60	50	40	30	20	ppm

BRUKER

8.5475
8.5447
8.5384
8.5354

7.7242
7.7119
7.7085
7.3264
7.3168
7.3108
7.3012
7.2689

5.4263

4.8480
4.8307

2.6468
2.6210
2.5930
2.4828
2.4796
2.3991
2.3871
2.3728
2.3601
2.3453
2.3329
2.1232
2.1172
2.1107
2.1037
2.0968
2.0907
2.0848
1.8319
1.8292
1.8053
1.8026
1.6870
1.6795
1.6720
1.6610
1.6533
1.6460
1.5958
1.5874
1.5701
1.5432
1.4199
1.3830

7g

8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

2.08

1.01

1.03

0.04

0.98

1.00
1.07
1.38

1.19

0.98
1.22

2.06

1.27

215.1002

149.0862
148.5522
136.6122
134.7937
123.6504

72.6057

57.1267

42.6579

30.6970
27.6945
24.6589

7g

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

ES-KK-4PY-PDT;CDCl3;03/01/19

8.5579
8.5486

7.2791
7.2686

5.3790

4.8074
4.7913
2.6138
2.6011
2.5877
2.5756
2.5615
2.4768
2.4500
2.3783
2.3665
2.3517
2.3397
2.3256
2.3129
2.0994
2.0930
2.0856
2.0793
2.0741
1.8341
1.8081
1.6611
1.6533
1.6421
1.6362
1.6229
1.6167
1.4123
1.4062
1.3866

7h

9.0   8.5   8.0   7.5   7.0   6.5   6.0   5.5   5.0   4.5   4.0   3.5   3.0   2.5   2.0   1.5   1.0   0.5   ppm

1.88   1.92   0.17   0.76   0.99 1.02 1.46   1.00   1.02 2.59   0.89

ES-KK-4PY-PDT;CDCl3;03/01/19

214.5284

149.3118
149.0515

122.2010

73.3737

56.8958

42.6512

30.6945
27.7048
24.6732

7h

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

ES-KK-C6F5-PDT;CDCl3;24/11/18

7.2688

5.3294
5.3106

3.9346
3.0341
3.0057
2.9789
2.5392
2.5369
2.5120
2.4219
2.4097
2.3970
2.3704
2.1428
2.1380
1.8716
1.8612
1.6713
1.6495
1.6210
1.5910
1.3631
1.3398
1.3180

7i

0.85   0.80   0.86   0.88   1.00   0.92   0.97   3.30   1.11
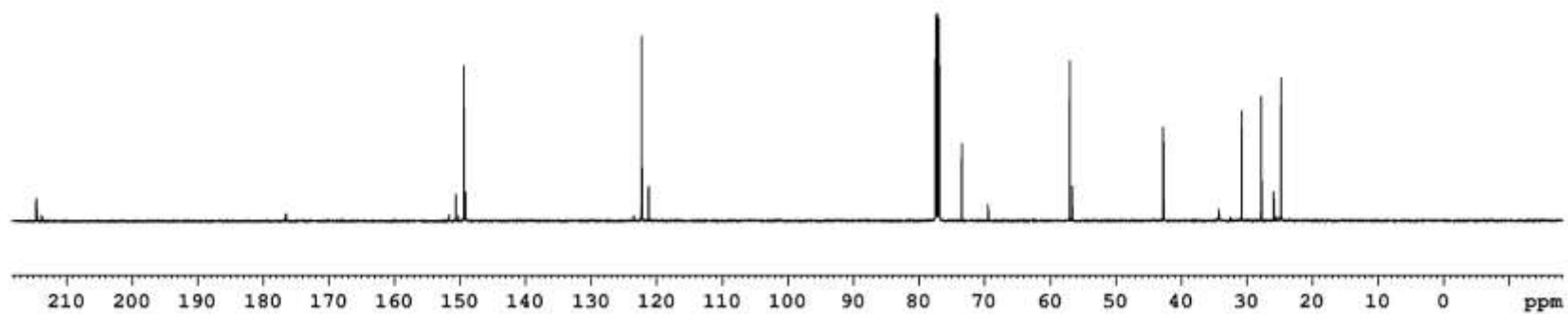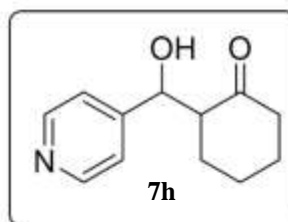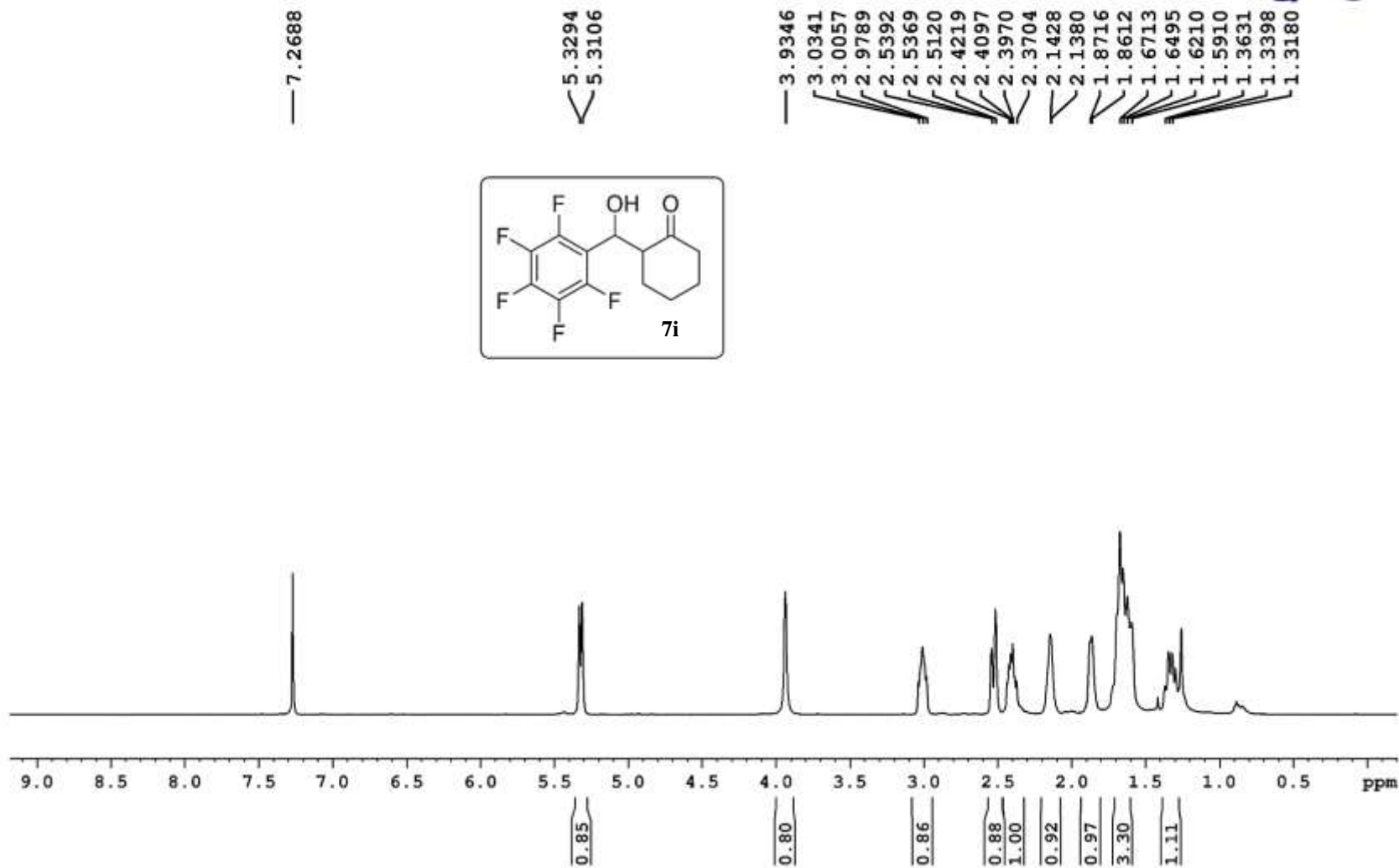
ES-KK-C6F5-PDT; CDCl3; 28/11/2018

214.0808

146.6936
144.6000
140.2732
138.5983
136.6442

113.8934

66.0609

54.2188

42.3709

30.1550
27.4686
24.5154

7i

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

ES-KK-2-NO2-PDT;CDC13;01/05/18

BRUKER
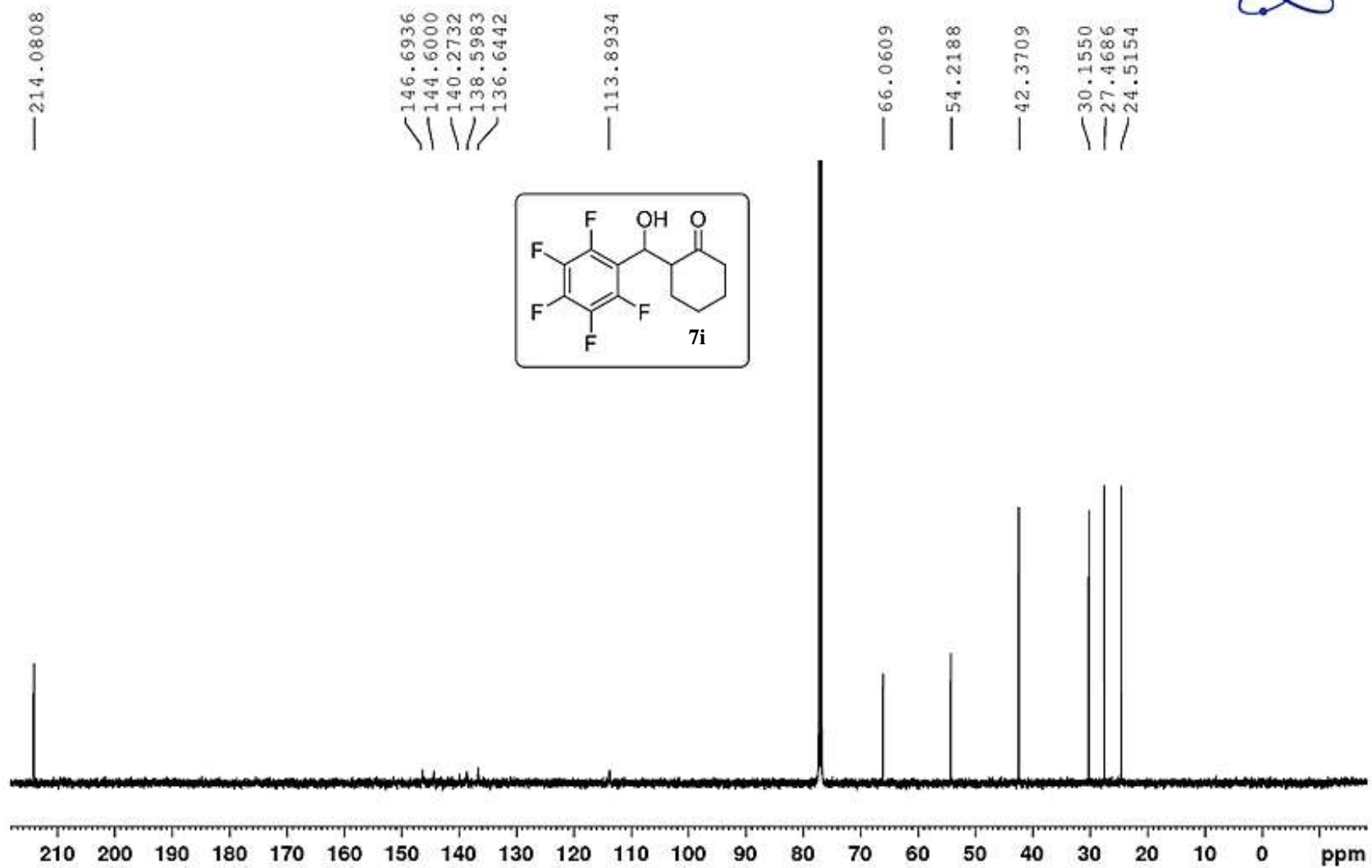
7.8503
7.8341
7.7752
7.7595
7.6477
7.6329
7.6178
7.4429
7.4271
7.4121
7.2690

5.9600

5.4538
5.4397

3.8628
2.7847
2.7720
2.7601
2.7474
2.7348
2.4651
2.4382
2.3722
2.3603
2.3456
2.3334
2.3190
2.3066
2.1129
2.1074
2.1012
2.0937
2.0874
2.0815
1.8616
1.8386
1.7743
1.7690
1.7621
1.7488
1.7436
1.7100
1.7031
1.6845

NO_2 OH O

7j

9.0   8.5   8.0   7.5   7.0   6.5   6.0   5.5   5.0   4.5   4.0   3.5   3.0   2.5   2.0   1.5   1.0   0.5   ppm

0.89 0.88 1.01 0.98   0.09   0.80   0.74   0.87 1.06 1.01 1.00 1.03 1.03 3.08

SI-86
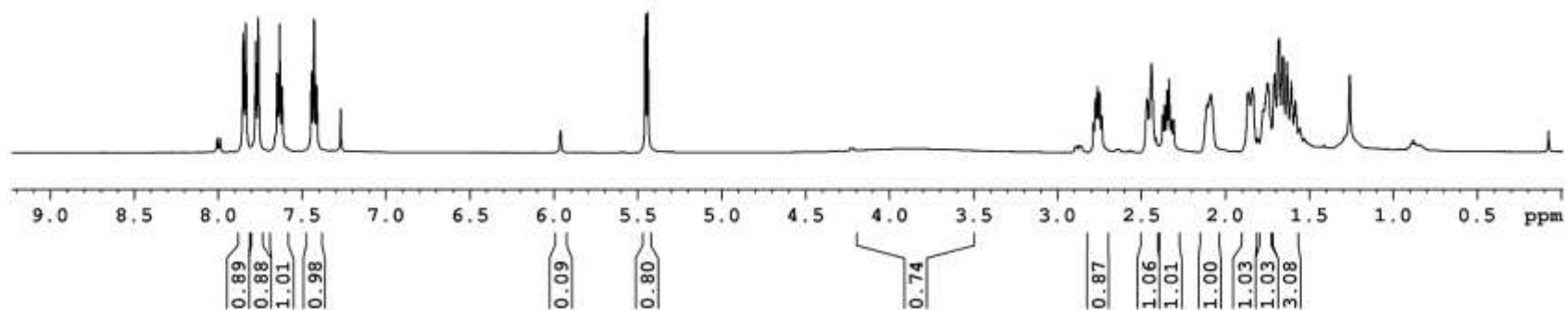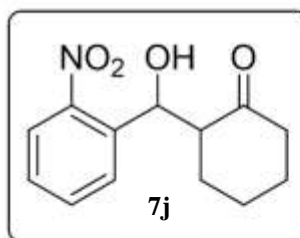
ES-KK-o-NO2-PDT;CDCl3;01/05/18

214.8735

148.7752

136.6175
133.0475
129.0289
128.3959
124.0661

69.7693

57.3194

42.8184

31.1115
27.7565
24.9785

BRUKER

7j

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

ES-KK-2-Cl-PDT;CDCl3;21/11/18

7.5575
7.5438
7.3387
7.3231
7.3095
7.2941
7.2689
7.2296
7.2144
7.1993

5.7138

5.3627
5.3465

4.0479
2.7070
2.6942
2.6815
2.6722
2.6560
2.4829
2.4559
2.3806
2.3686
2.3539
2.3417
2.3271
2.3148
2.1088
2.1037
2.0973
2.0907
2.0831
2.0778
1.8348
1.8195
1.8133
1.7340
1.7265
1.7078
1.7006
1.6822
1.6752
1.6659
1.6575
1.6332
1.6283
1.6084

7k

8.5   8.0   7.5   7.0   6.5   6.0   5.5   5.0   4.5   4.0   3.5   3.0   2.5   2.0   1.5   1.0   0.5   ppm

1.00
2.01
1.02

0.05
0.96

0.92

1.00
1.10
1.16
1.15
1.17
2.35
2.06

ES-KK-2-Cl-PDT;CDCl3;21/11/18

BRUKER

215.3474

139.0749
132.9869
129.2395
128.7699
128.2493
127.2697

70.4836

57.6105

42.7595

30.4125
27.8281
24.9409

7k

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

BRUKER

BRUKER

215.0058

148.2717
143.2175

133.2441
129.3523
122.9296
122.0492

74.0724

57.1432

42.6952

30.7616
27.6576
24.6744

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

BRUKER

7.3558
7.3407
7.2936
7.2836
7.2689
7.2144
7.2124
7.2059
7.1972
4.7835
4.7662
4.0142
2.6226
2.6127
2.6052
2.5966
2.5860
2.5810
2.5694
2.5158
2.4885
2.4092
2.3973
2.3827
2.3704
2.3559
2.3433
2.1369
2.1310
2.1245
2.1178
2.1108
2.1047
2.0989
2.0935
1.8408
1.8164
1.7347
1.7281
1.7197
1.7120
1.7018
1.6942
1.6868
1.6758
1.6682
1.6608
1.6494
1.6414
1.6347
1.6289
1.6236
1.6180
1.6111
1.5969
1.5922
1.5731
1.5662
1.5595
1.5474
1.5403
1.5336
1.3756
1.3696
1.3500
1.3435
1.3246
1.3173
1.2997

7m

0.94
1.93
0.97
0.08
0.88
0.72
0.99
1.02
1.03
1.00
1.00
3.38
1.02

ES-KK-3-Cl-PDT;CDCl3;30/11/18

215.1972

143.0792
134.3644
129.6057
128.0621
127.1605
125.3071

74.2953

57.2859

42.6824

30.7966
27.7306
24.7174

7m

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

ES-KK-3-OC6H5-PDT,CDCl3,18/7/19

BRUKER

7.3550 7.3527 7.3381 7.3231 7.3152 7.3069 7.2992 7.2911 7.2834 7.2689 7.1229 7.1162 7.1082 7.1016 7.0934 7.0809 7.0653 7.0583 7.0420 7.0245 7.0165 7.0027 6.9403 6.9367 6.9241 6.9205 5.3754 4.7738 4.7564 2.6089 2.6043 2.5940 2.5844 2.5795 2.4665 2.3777 2.3632 2.3504 2.1085 2.1021 2.0954 2.0886 2.0824 2.0766 1.8041 1.7640 1.7137 1.7065 1.6872 1.6801 1.6725 1.6528 1.6465 1.6403 1.6305 1.6257 1.6199 1.6137 1.6053 1.5871 1.5803 1.5738 1.5617 1.5546 1.5476 1.3287 1.3030 1.2961 1.2701

7n

3.06 2.05 3.01 0.98   0.35   0.58   0.50   0.99 1.04 1.06 1.00 2.01 4.17 1.20

ES-KK-3-OC6H5-PDT; CDCl3; 18/07/19

215.5793

157.3533
157.0306

143.0936

129.8530
123.3936
122.0104
118.9630
118.2759
117.6395

74.6303

57.3882

42.7629

30.9008
27.8592
24.8214

7n

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

BRUKER

7.8637 7.5321 7.5156 7.5070 7.4920 7.4883 7.4754 7.4716 4.8499 4.8333 2.5944 2.5836 2.5795 2.5686 2.5573 2.5538 2.5088 2.5055 2.4863 2.4817 2.4780 2.3957 2.3850 2.3695 2.3575 2.1397 2.1338 2.1272 2.1203 2.1136 2.1077 2.1019 1.8660 1.8630 1.8394 1.6872 1.6794 1.6723 1.6608 1.6527 1.6464 1.6410 1.6347 1.6264 1.6209 1.6151 1.6096 1.5990 1.5925 1.5736 1.5668 1.5597 1.4253 1.4001 1.3931 1.3745 1.3671

7o

ES-KK-4Cl-3NO2-PDT;CDCl3;01/11/18

214.6796

147.8090
141.7833
131.7212
131.6939
126.1771
124.0840

73.4307

57.0509

42.6567

30.6879
27.6009
24.6460

7o

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

BRUKER
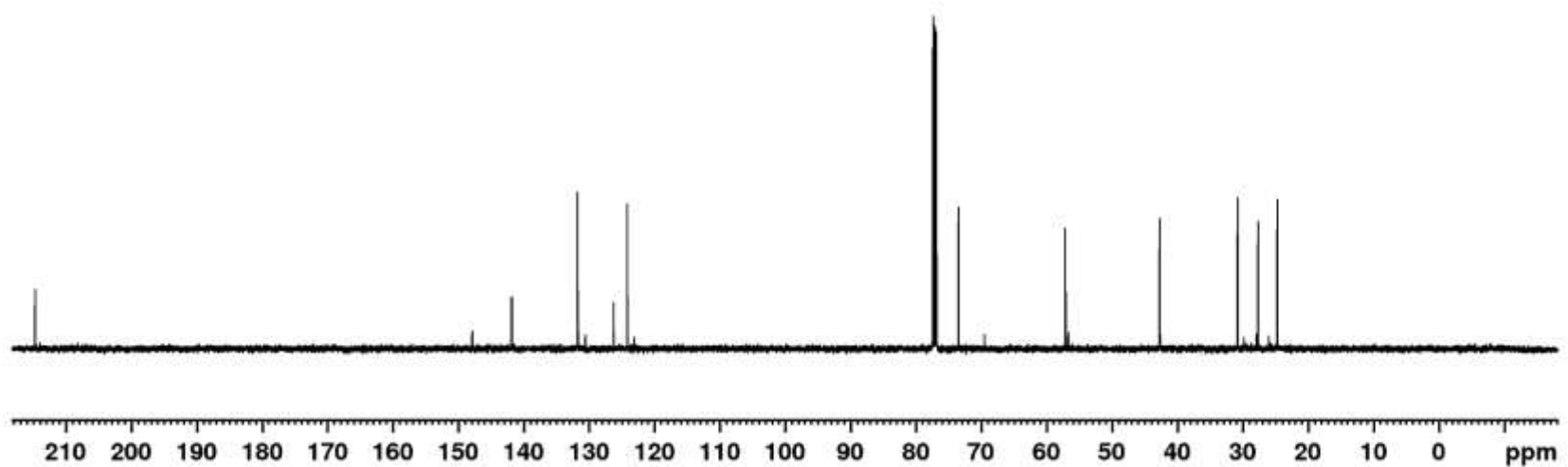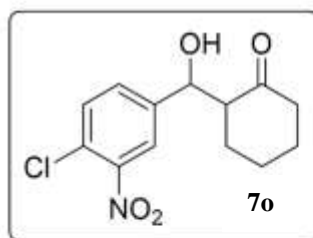
7.3407
7.3302
7.3155
7.2982
7.2687
4.8033
4.7856
2.6543
2.6453
2.6367
2.6284
2.6176
2.6131
2.6019
2.5038
2.4951
2.4853
2.4766
2.4679
2.4034
2.3894
2.3765
2.3627
2.3499
2.3374
2.3374
2.1128
2.1067
2.1003
2.0936
2.0865
2.0802
2.0742
1.8037
1.7797
1.7700
1.7184
1.6923
1.6847
1.6667
1.6586
1.6511
1.6324
1.6046
1.5986
1.5890
1.5816
1.5673
1.5629
1.5440
1.5368
1.3490
1.3233
1.3168
1.2981
1.2906
1.2728
1.2628

7p

4.99 0.12 0.85 0.67 1.00 1.02 1.13 1.06 1.17 1.39 2.10 1.27

8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

SI-98

215.5572

140.9563

128.3952
127.9168
127.0450

74.7860

57.4537

42.6954

30.8698
27.8223
24.7496

7p

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

BRUKER
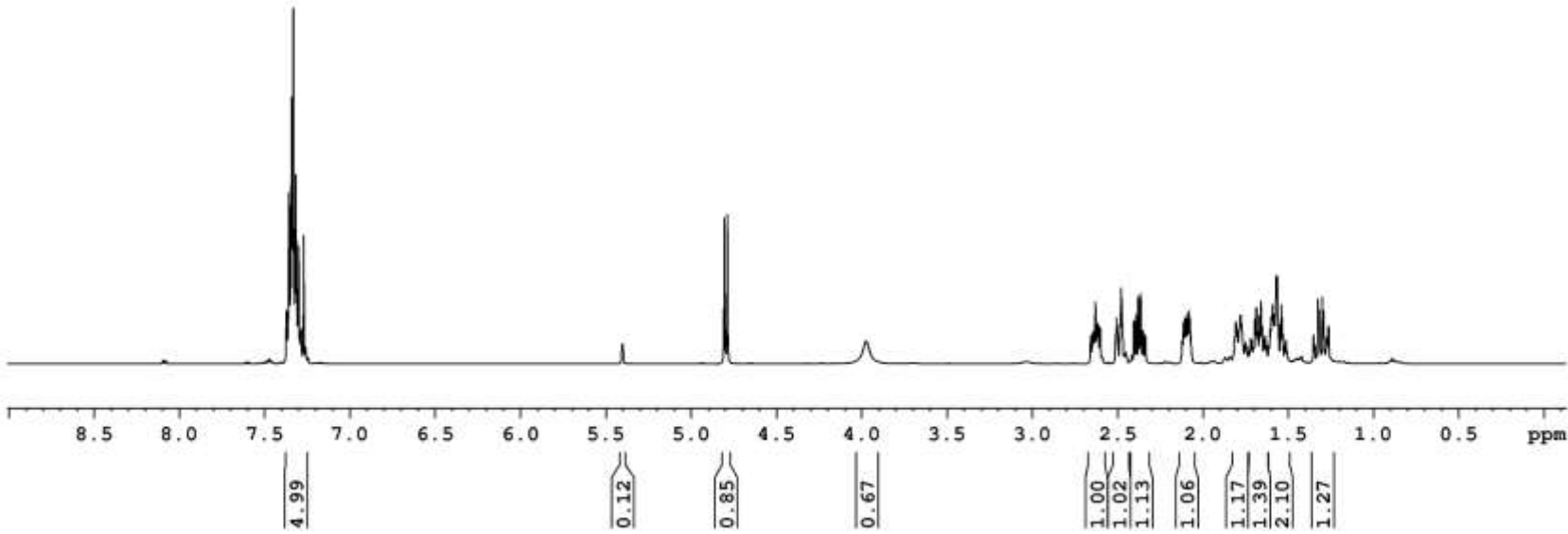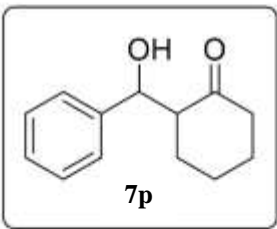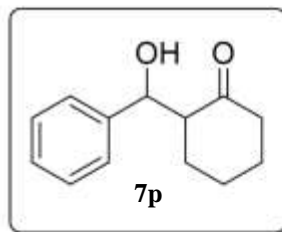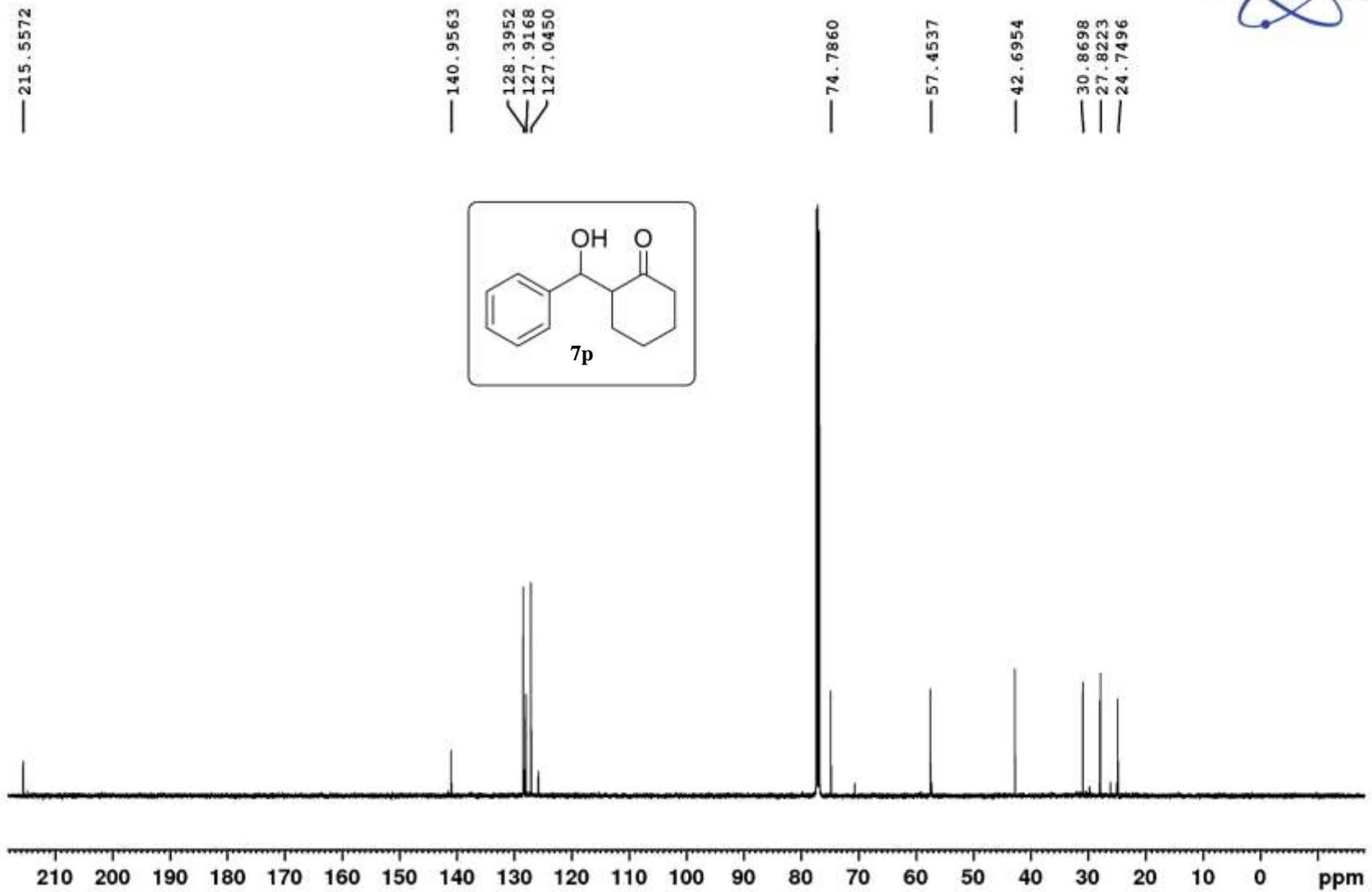
7.8617
7.8444
7.8379
7.8315
7.7652
7.5065
7.4974
7.4936
7.4856
7.4789
7.4649
7.2688
4.9862
4.9686
4.0665
2.7566
2.7464
2.7387
2.7304
2.7210
2.7149
2.7031
2.5286
2.5012
2.4250
2.4126
2.3980
2.3854
2.3712
2.3587
2.1210
2.1151
2.1091
2.1027
2.0958
2.0888
2.0826
2.0765
2.0706
1.7847
1.7819
1.7782
1.7552
1.7050
1.6972
1.6894
1.6793
1.6711
1.6635
1.6447
1.6060
1.6005
1.5946
1.5885
1.5753
1.5691
1.5630
1.5553
1.5481
1.5411
1.5296
1.5226
1.5157
1.3959
1.3704
1.3631
1.3449
1.3376
1.3128

7q

2.84 0.85 2.68 0.07 0.85 0.70 0.95 0.97 1.00 1.00 2.24 2.09 0.97

SI-100

ES-KK-2-Napth-PDT;CDCl3;30/11/18

7q
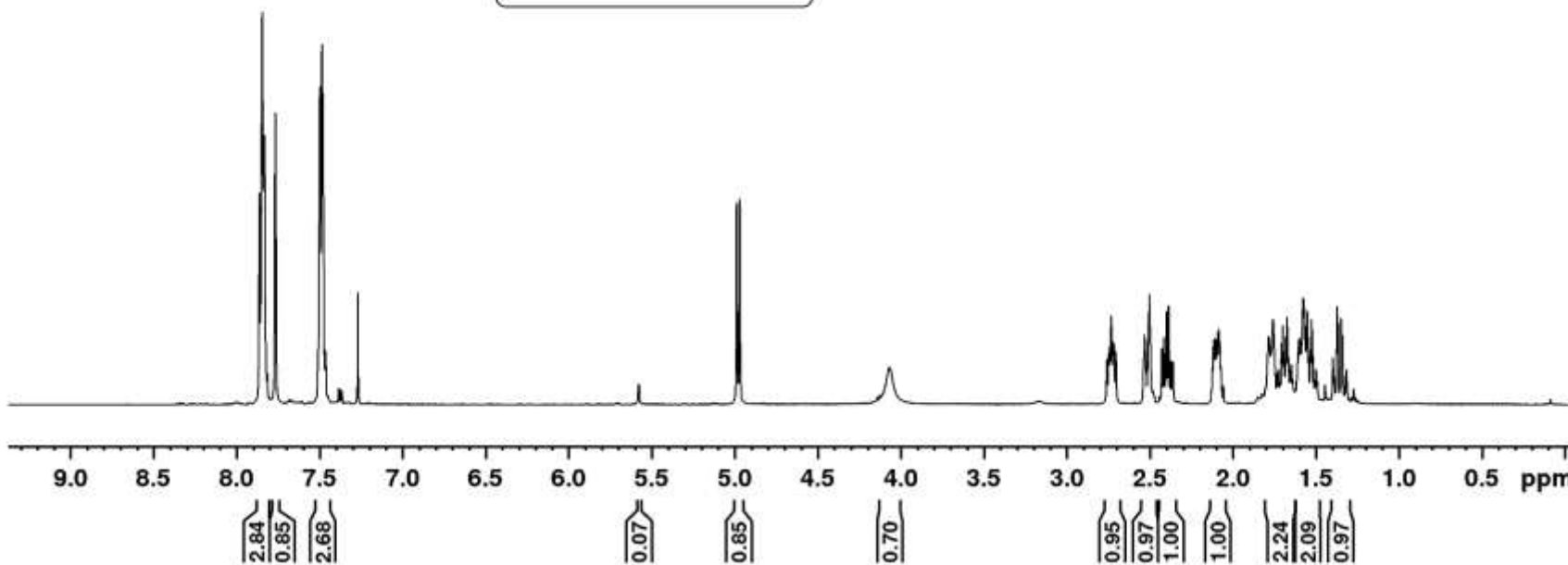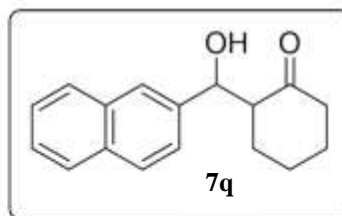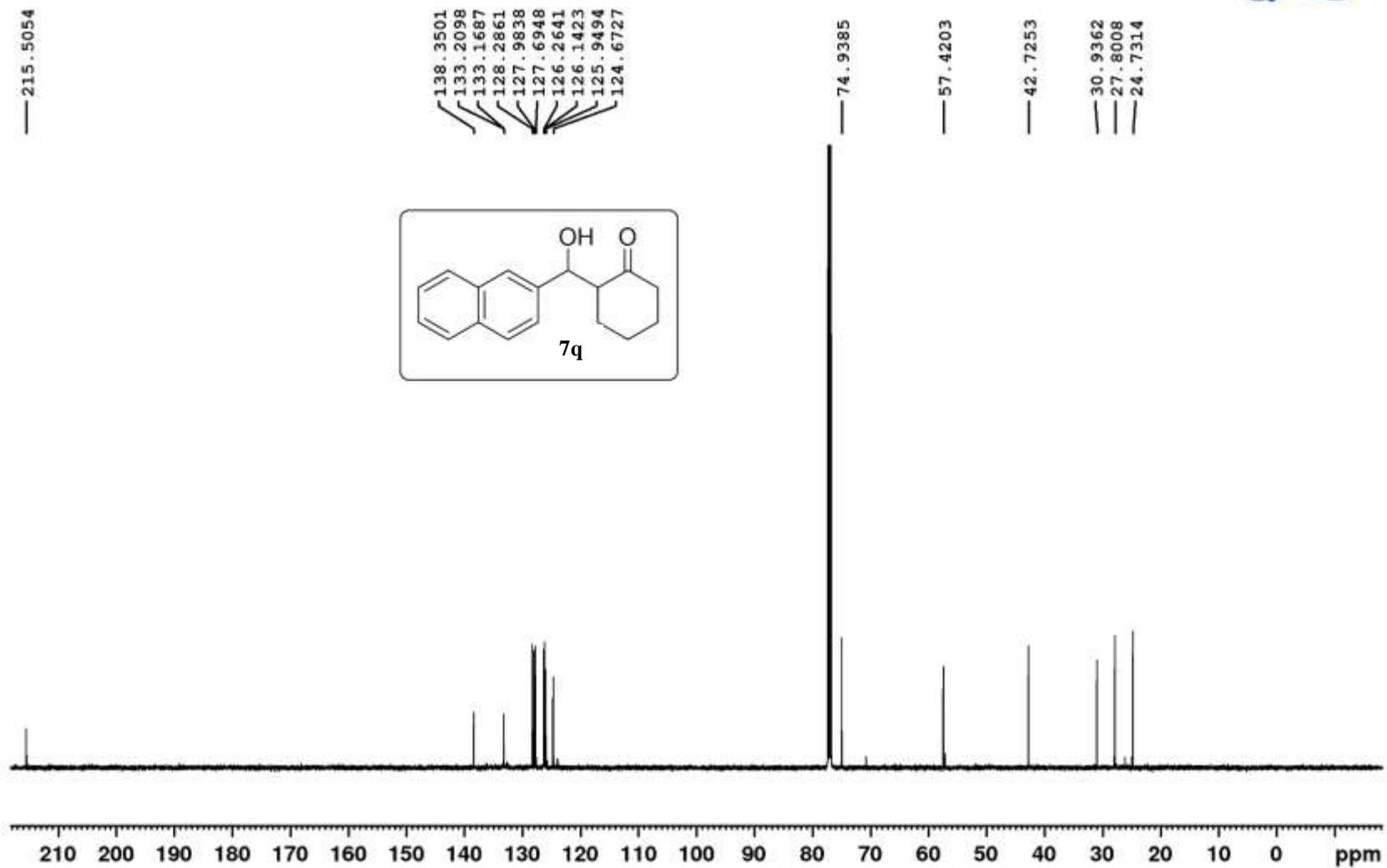
ES-KK-4-OMe-PDT;CDCl3;10/7/19

7r

ES-KK-4-OMe-PDT;CDCl3;10/07/19

214.8886

158.6393

133.6168
126.9282

113.5941

70.4254

57.2922
55.2652

42.7012

27.9900
26.2029
24.9031

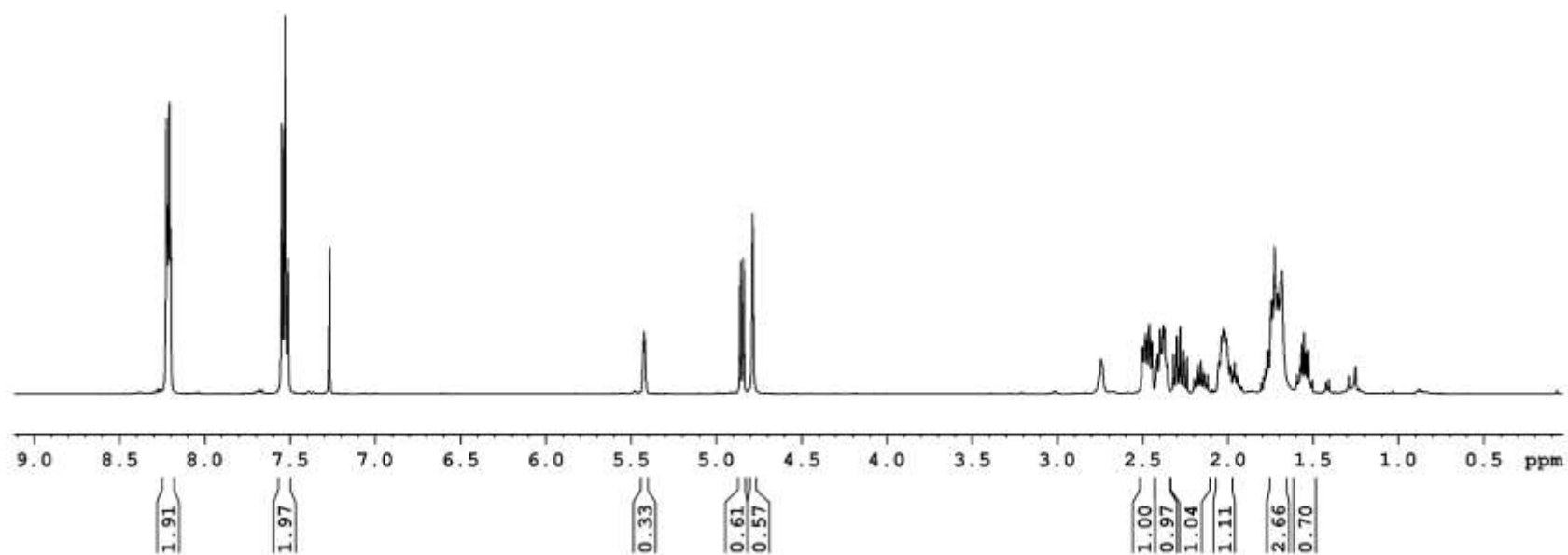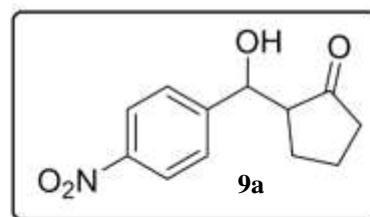210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
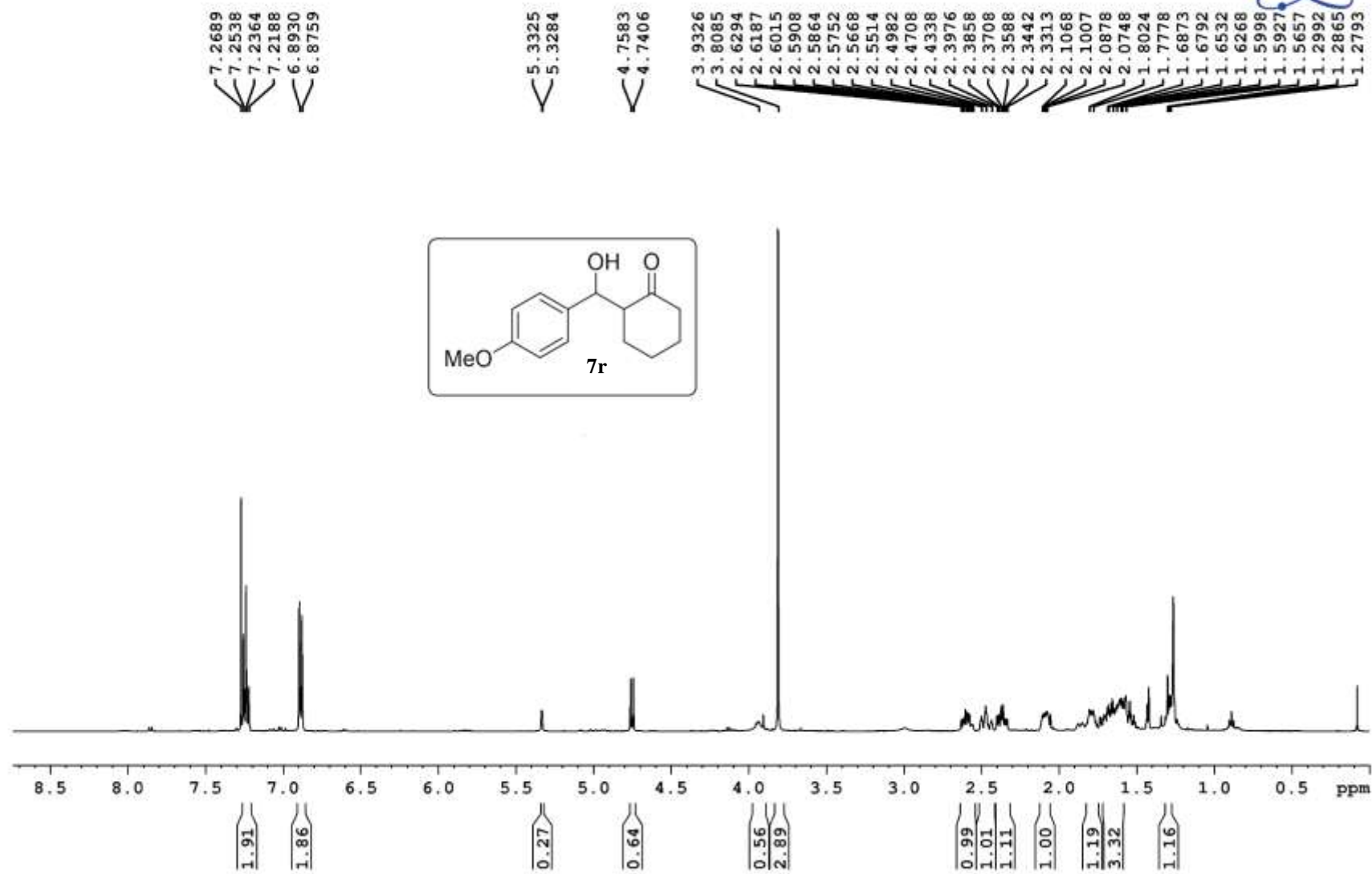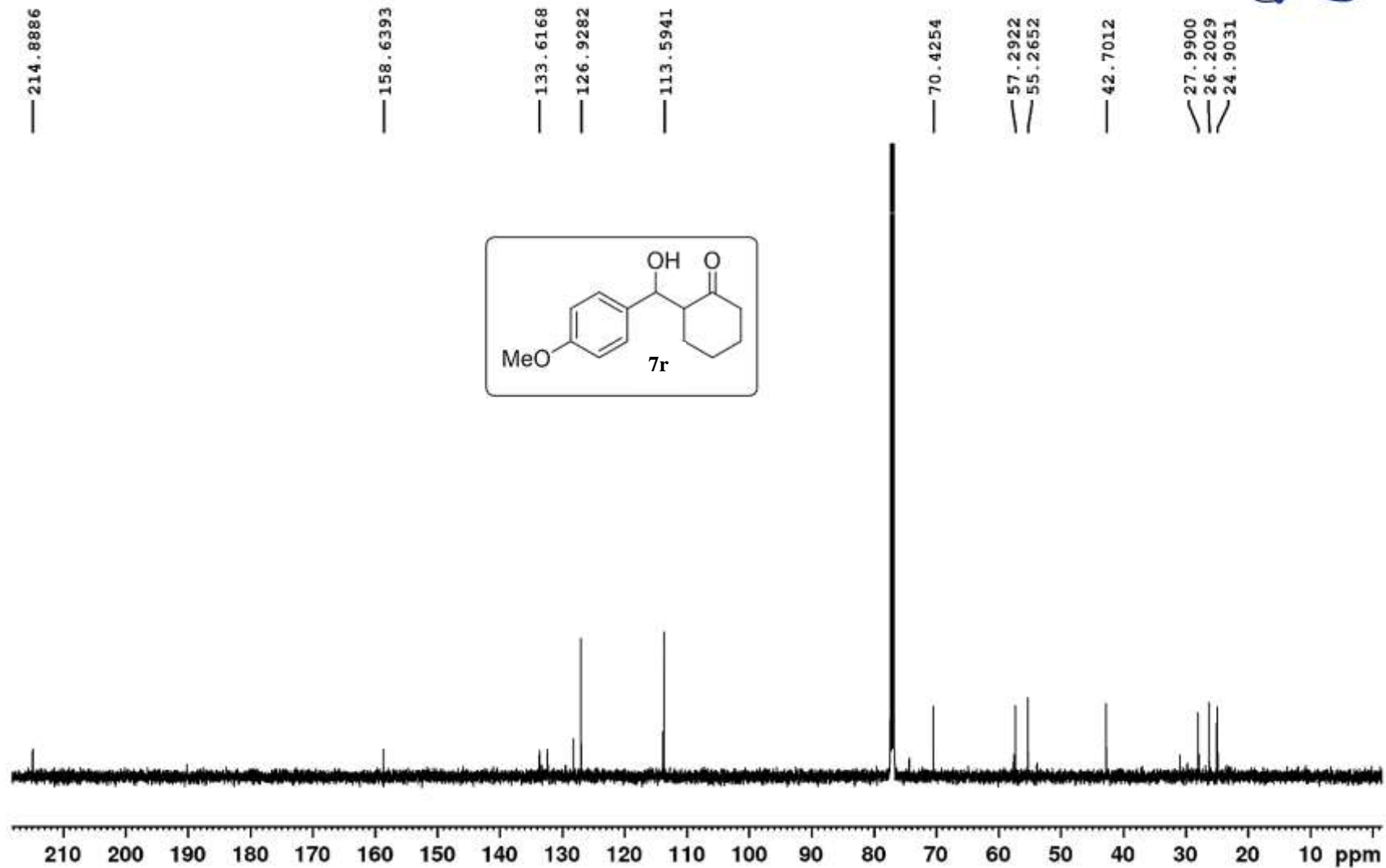
ES-KK-CYP-PDT;CDCl3;02/11/18

8.2242
8.2171
8.2070
8.1998
7.5470
7.5294
7.5115
7.2683
5.4225
4.8577
4.8394
4.7863
2.5011
2.4807
2.4593
2.4456
2.4138
2.3964
2.3784
2.3176
2.2999
2.2785
2.2612
2.2394
2.1769
2.1564
2.1397
2.1184
2.0350
2.0254
2.0054
1.9818
1.7444
1.7256
1.6845
1.5942
1.5659
1.5524

9a

ES-KK-CYP-PDT;CDCl3;02/11/18

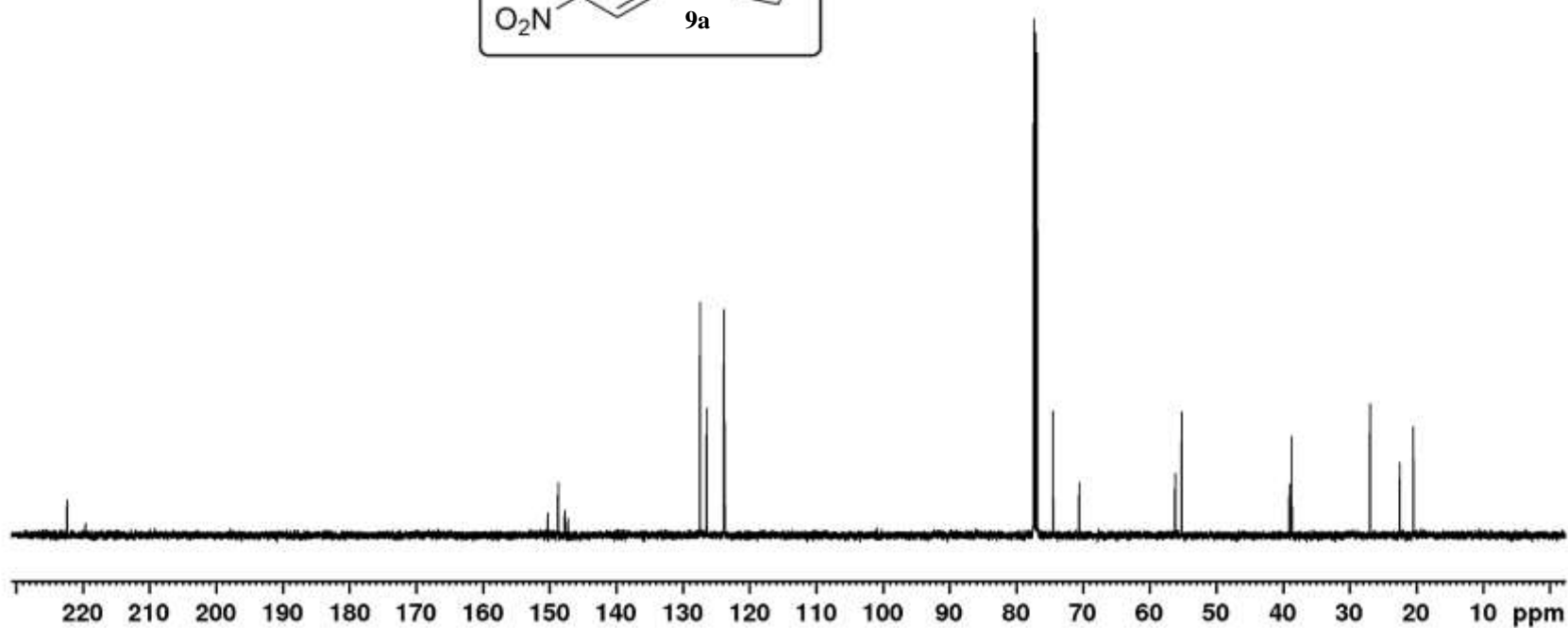222.3003
219.5245
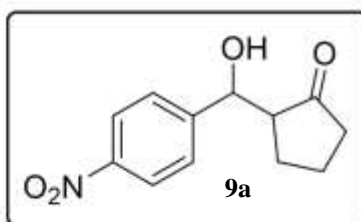
150.1702
148.6457
147.6537
147.1849
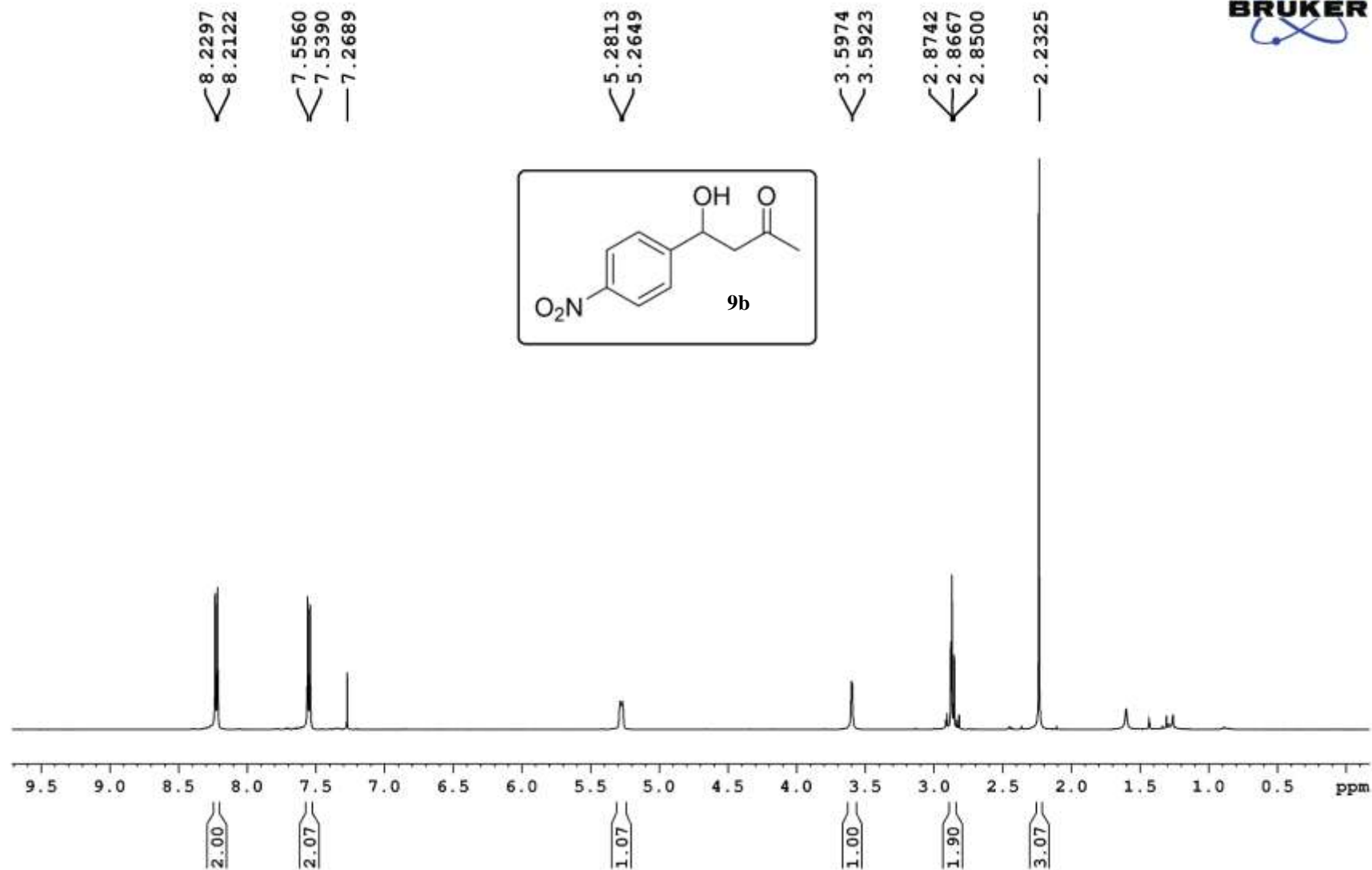
127.3707
126.3811
123.7549
123.6742

74.4482
70.4836

56.0949
55.1040

38.9505
38.6223

26.8641
22.4270
20.3867
20.3427

9a

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

8.2297
8.2122
7.5560
7.5390
7.2689
5.2813
5.2649
3.5974
3.5923
2.8742
2.8667
2.8500
2.2325

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OH   O

O₂N

9b

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

2.00 2.07 1.07 1.00 1.90 3.07

208.6147
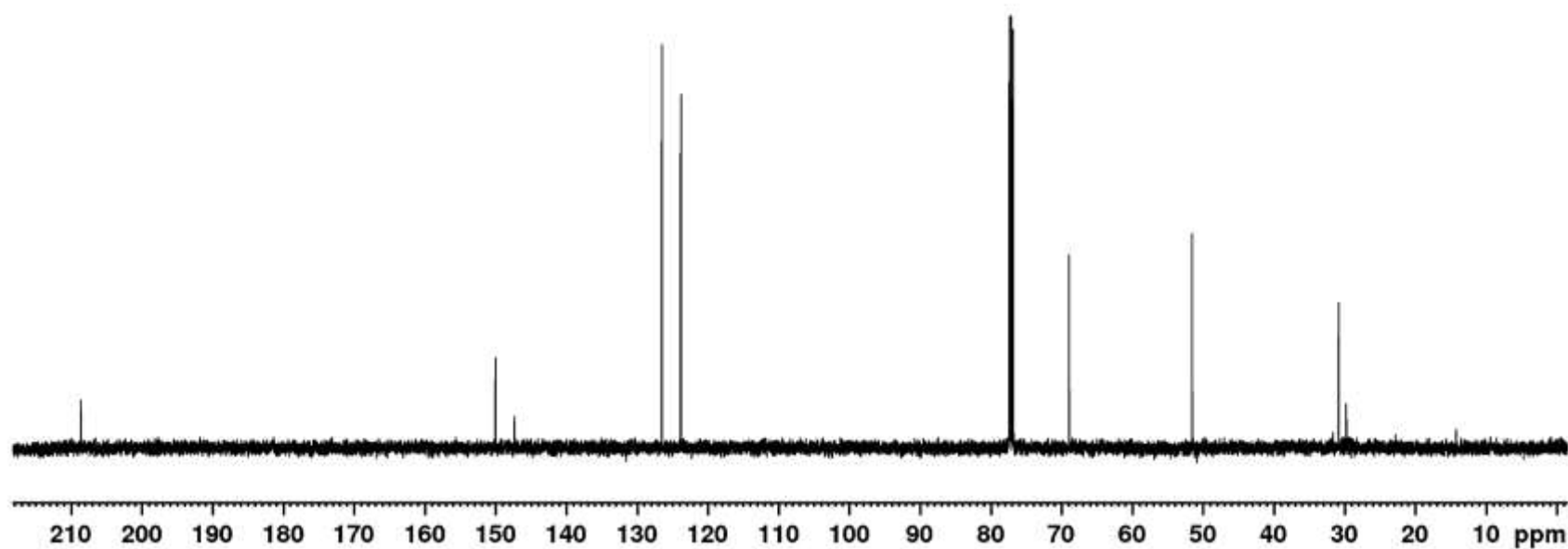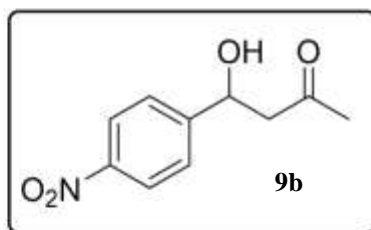
149.9894
147.3229
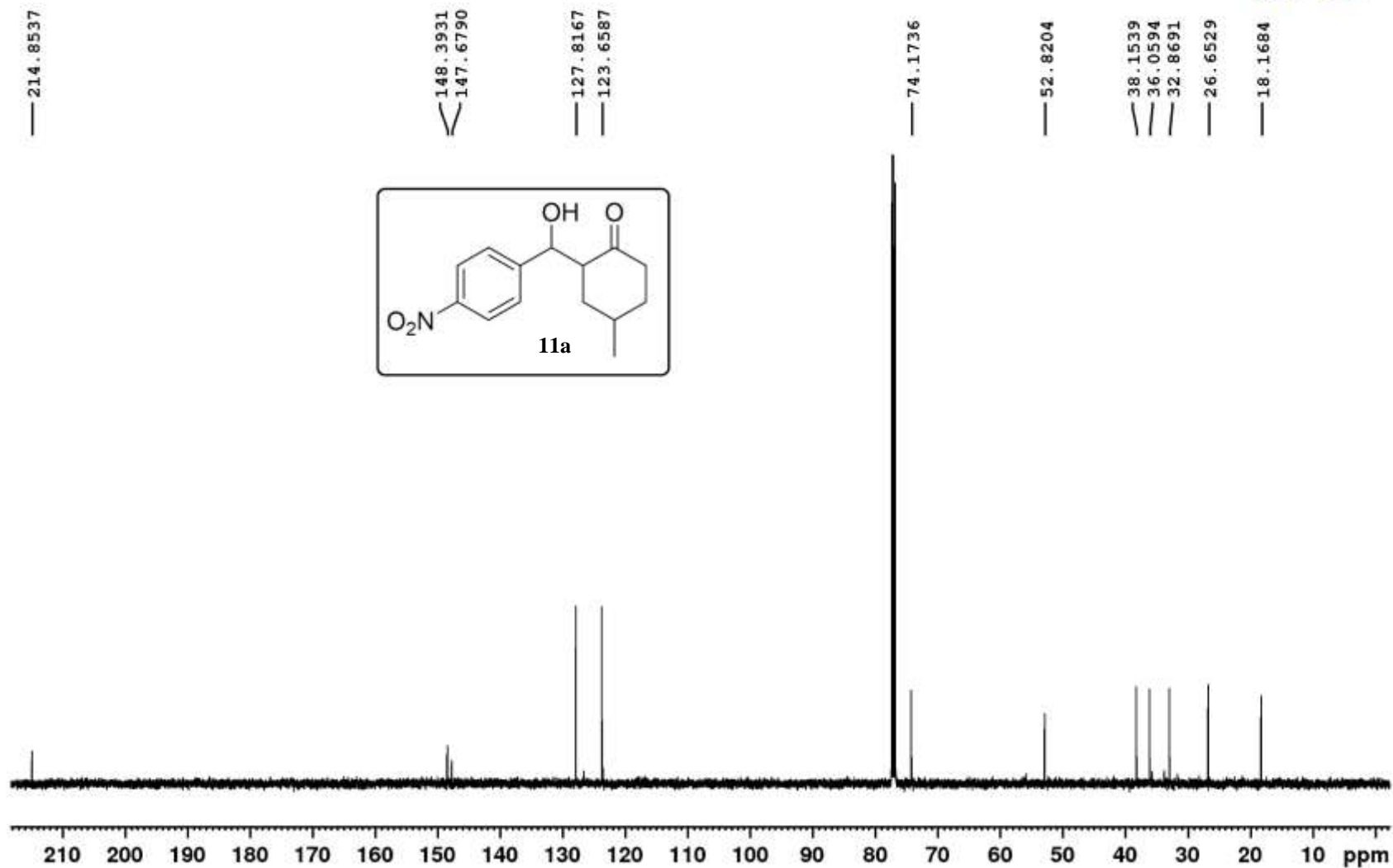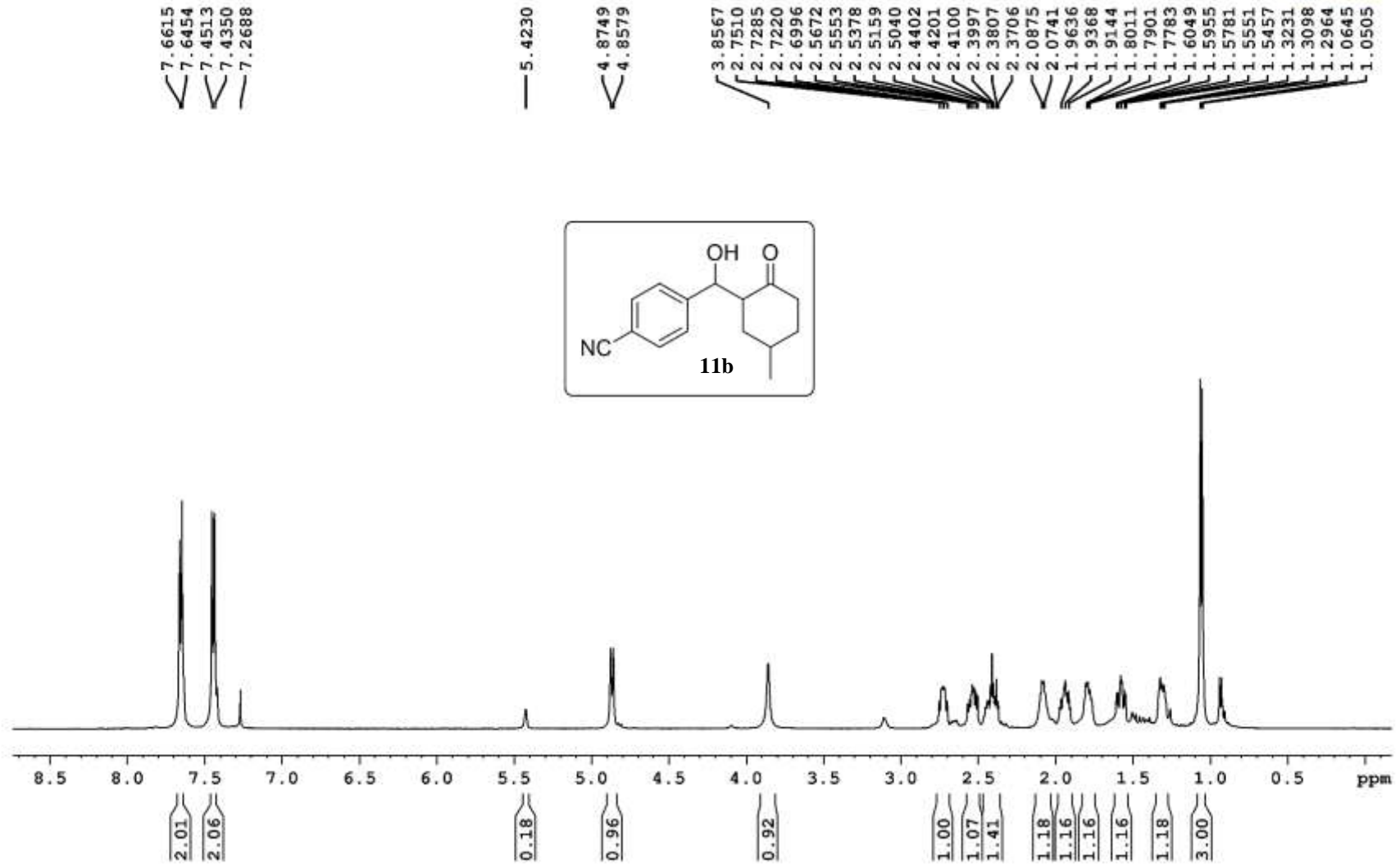
126.4448
123.8014

68.9108

51.5326

30.7519

9b
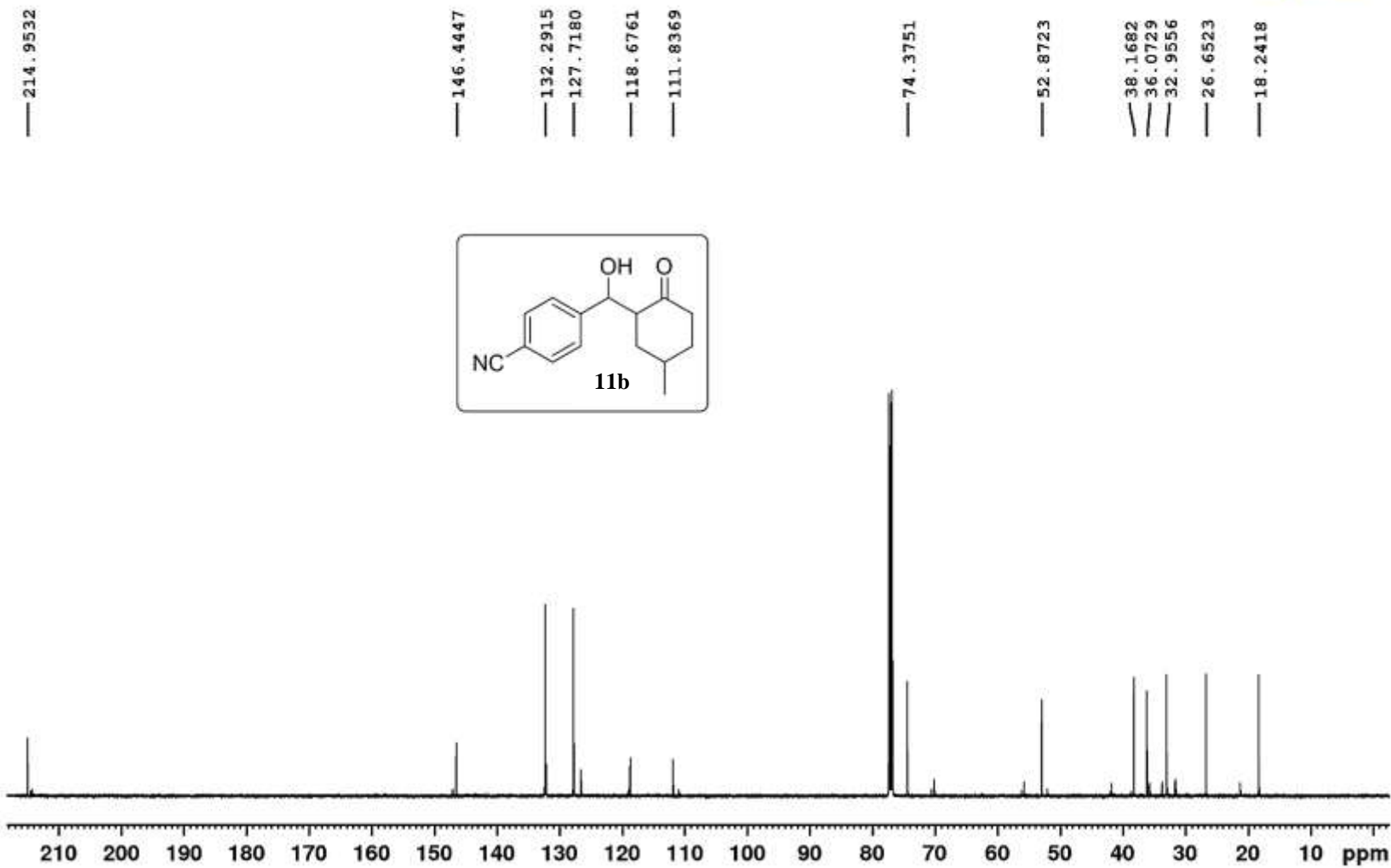
ES-KK-4NO2-4MC;CDC13;02/11/18

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8.2310
8.2138
7.5182
7.5010
7.2683
5.4936
5.4800
4.9367
4.9200
3.8930
2.7773
2.7643
2.7538
2.7416
2.7253
2.5817
2.5697
2.5522
2.5406
2.5298
2.5178
2.4258
2.4158
2.4058
2.3966
2.3865
2.3765
2.0983
2.0846
1.9815
1.9721
1.9452
1.9225
1.9130
1.8182
1.8070
1.7950
1.7826
1.6378
1.6283
1.6112
1.6040
1.5779
1.3419

11a

8.5   8.0   7.5   7.0   6.5   6.0   5.5   5.0   4.5   4.0   3.5   3.0   2.5   2.0   1.5   1.0   0.5   ppm

2.06   2.03   0.13   0.94   0.89   0.93 1.00 1.01   1.06 1.01 1.09   1.38   1.09   3.00

ES-KK-4NO2-4MC-PDT;CDCl3;24/11/18

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214.8537

148.3931
147.6790

127.8167
123.6587

74.1736

52.8204

38.1539
36.0594
32.8691

26.6529

18.1684

11a

ES-KK-4CN-4MC-PDT;CDCl3;27/12/18

ES-KK-4CN-4MeCY;CDCl3;30/01/2019

214.9532

146.4447

132.2915
127.7180

118.6761

111.8369

74.3751

52.8723

38.1682
36.0729
32.9556

26.6523

18.2418

11b

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

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7.8366
7.8203
7.7417
7.7274
7.6399
7.6245
7.6095
7.4399
7.4235
7.4090
7.2687
5.4383
5.4238
2.9373
2.9243
2.9137
2.9025
2.8895
2.5225
2.5109
2.4928
2.4723
2.4607
2.3954
2.3846
2.3739
2.3558
2.3451
2.3241
2.1261
2.1166
2.1031
2.0933
1.9777
1.9681
1.9573
1.9412
1.9305
1.9197
1.9102
1.8701
1.8609
1.8483
1.8429
1.8342
1.8213
1.8120
1.7486
1.7375
1.7257
1.7104
1.5181
1.5108
1.4960
1.4839
1.4738
1.0750
1.0610

11c

9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

0.94 0.94 0.95 0.98   0.05   0.91   0.89   0.91   0.96 1.48   0.94 1.01 1.30 1.16 1.06   2.87

ES-KK-2NO2-4MC-PDT;CDCl3;20/12/18

215.2640
148.9670
136.8128
133.2789
128.9629
128.6023
124.2150
69.9700
52.9213
38.5866
36.7465
33.2632
26.9352
18.2518

11c

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
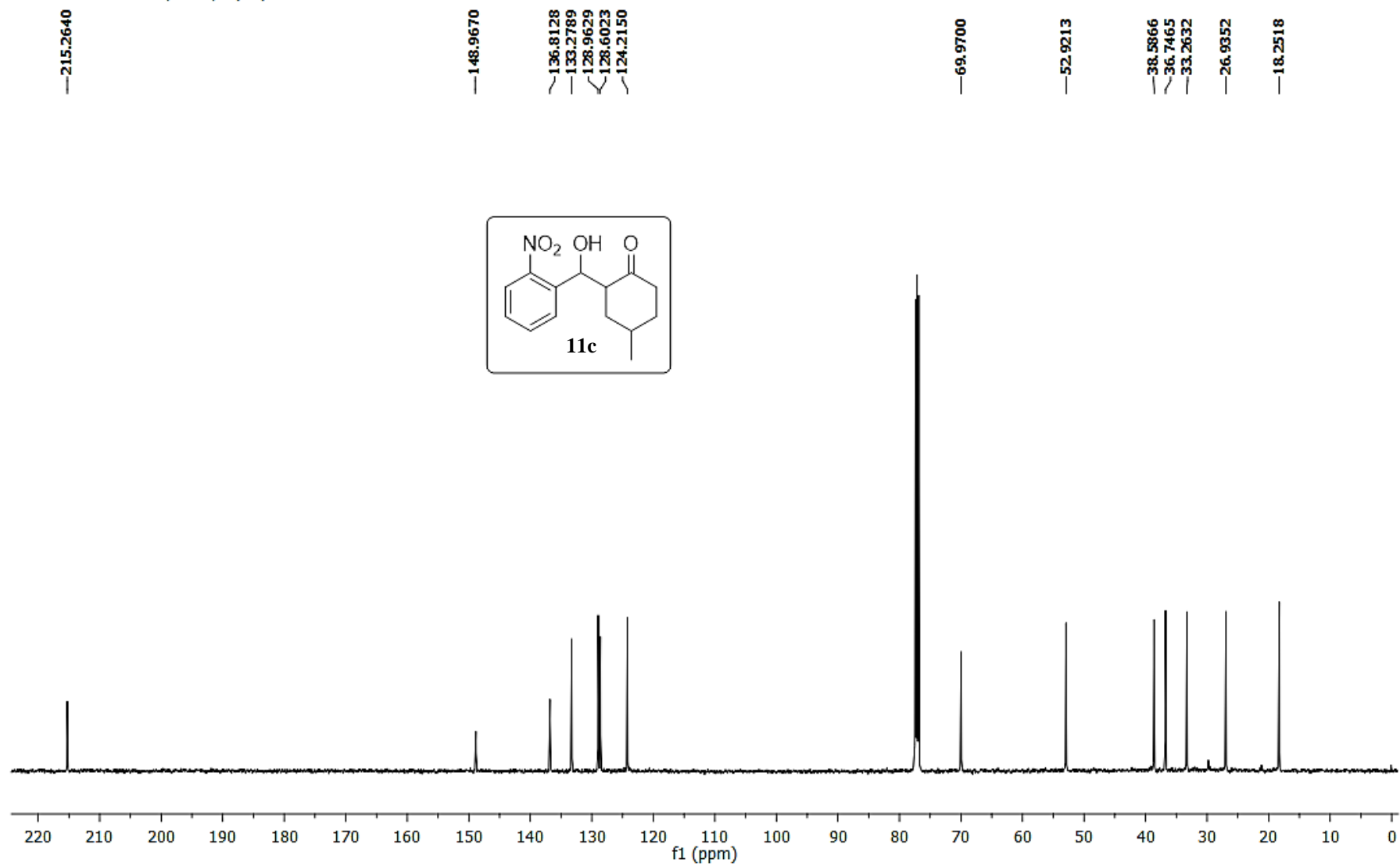
^{1}H, ^{13}C NMR spectra and HRMS analysis reports of the catalysts 1a & 1b and the catalyst precursors 4 & 4′

ES-KK-C-NHTs-CAT;1H;D2O;05/05/18

7.8776
7.8611
7.5810
7.5649

4.7899
4.1680
4.1512
4.1343
4.0641
4.0507
4.0373
4.0239
4.0104
3.5489
3.5354
3.5244
3.5109
3.4317
3.4218
3.4092
3.3973
3.3846
2.5853
2.5707
2.5572
2.5294
2.0415
2.0266
2.0129
1.9992
1.9840

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1a

9.0   8.5   8.0   7.5   7.0   6.5   6.0   5.5   5.0   4.5   4.0   3.5   3.0   2.5   2.0   1.5   1.0   0.5   ppm

2.10
2.12

0.96
0.98
1.00
1.14
0.98
3.23
1.06
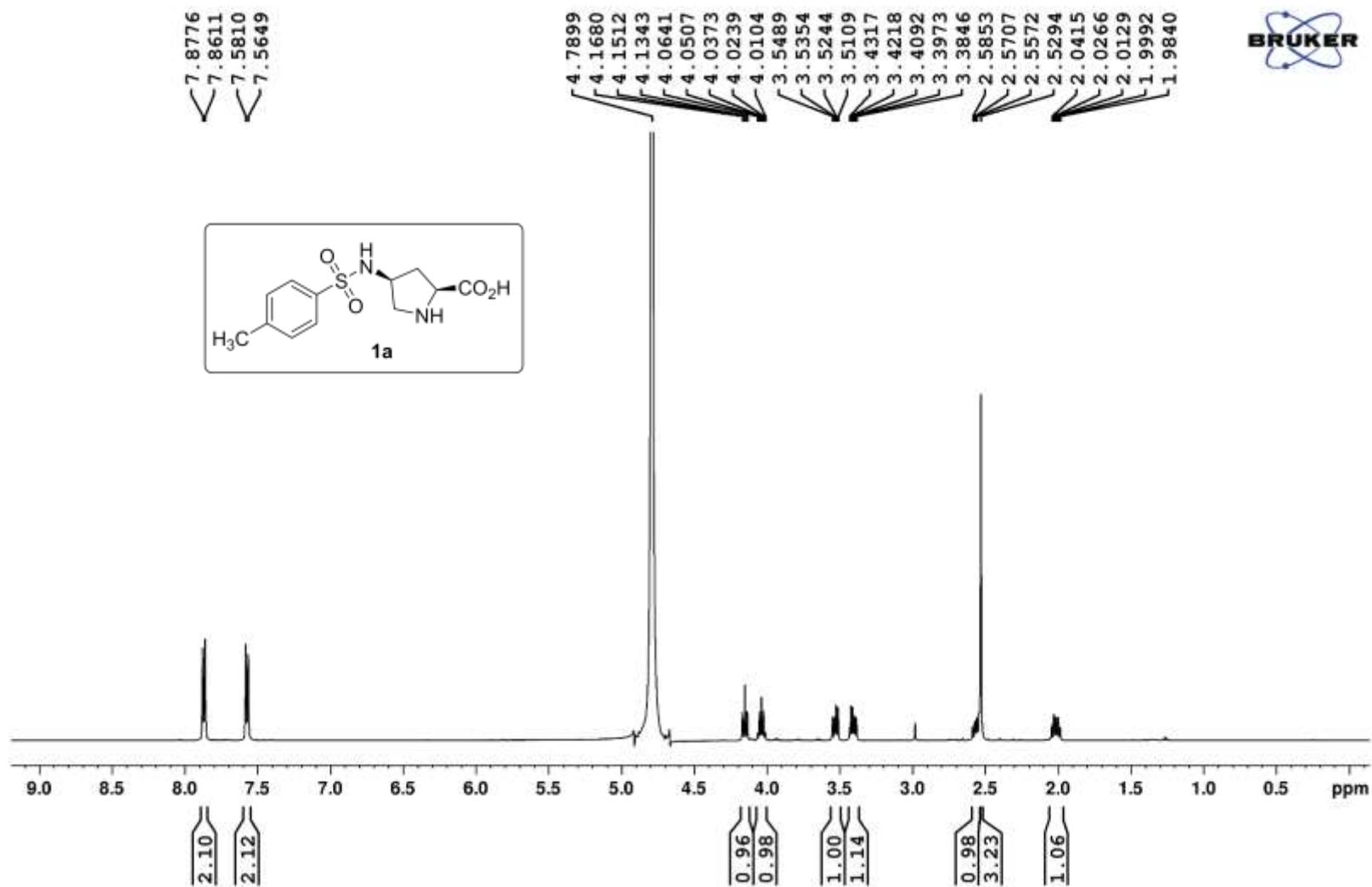
ES-KK-C-NHTs-CAT;13C;D2O;08/05/18

173.4311
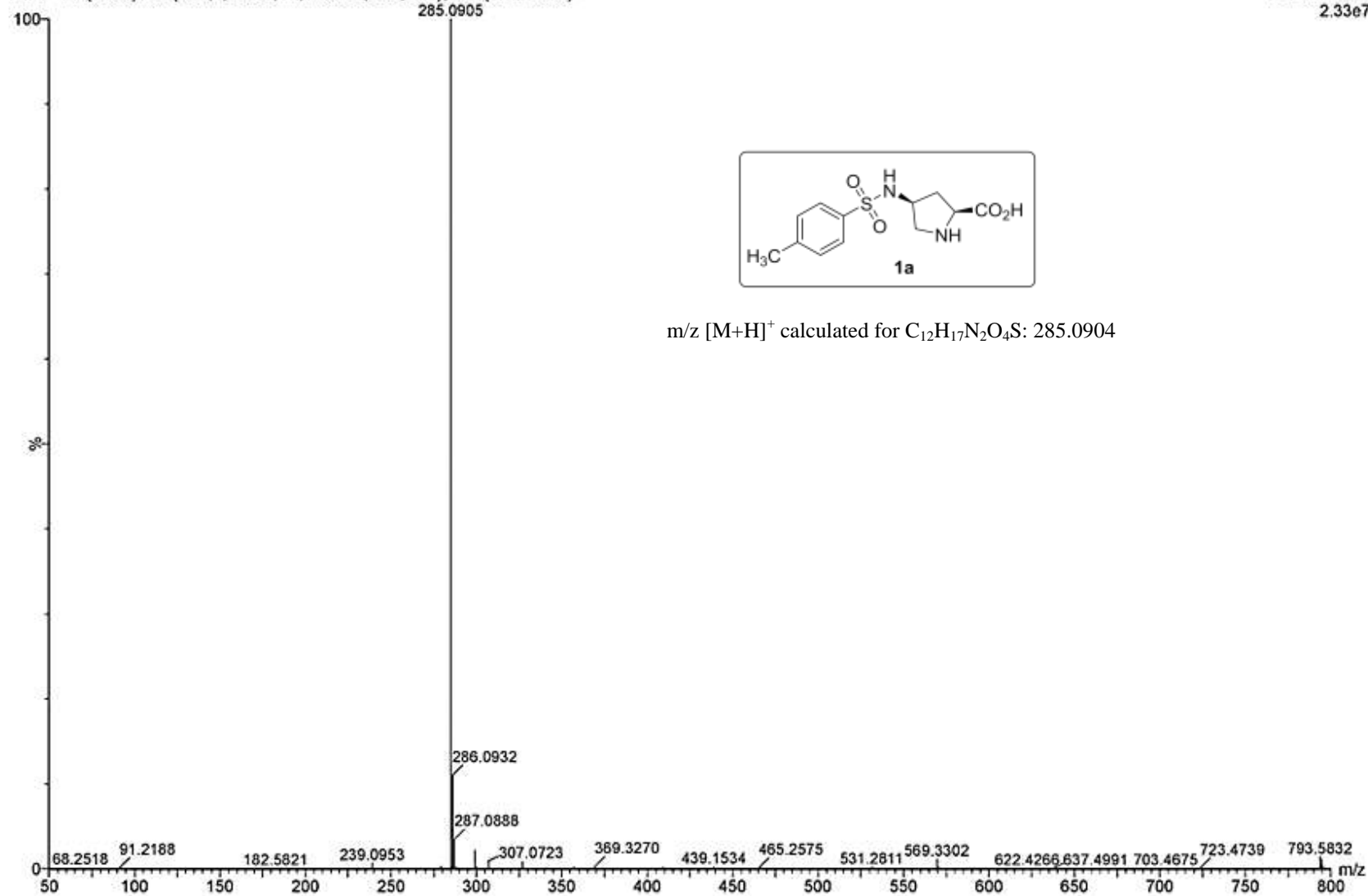145.6692
134.8340
130.3507
126.9679
59.8359
51.7571
49.8294
34.3173
20.7769

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1a

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
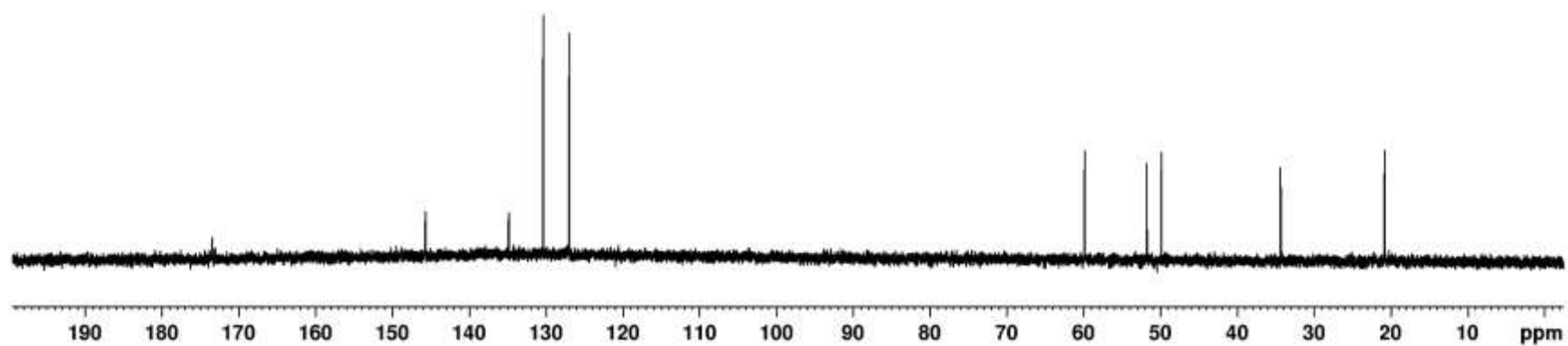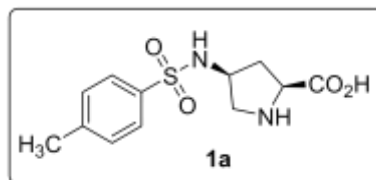
TOF MS ES+
2.33e7

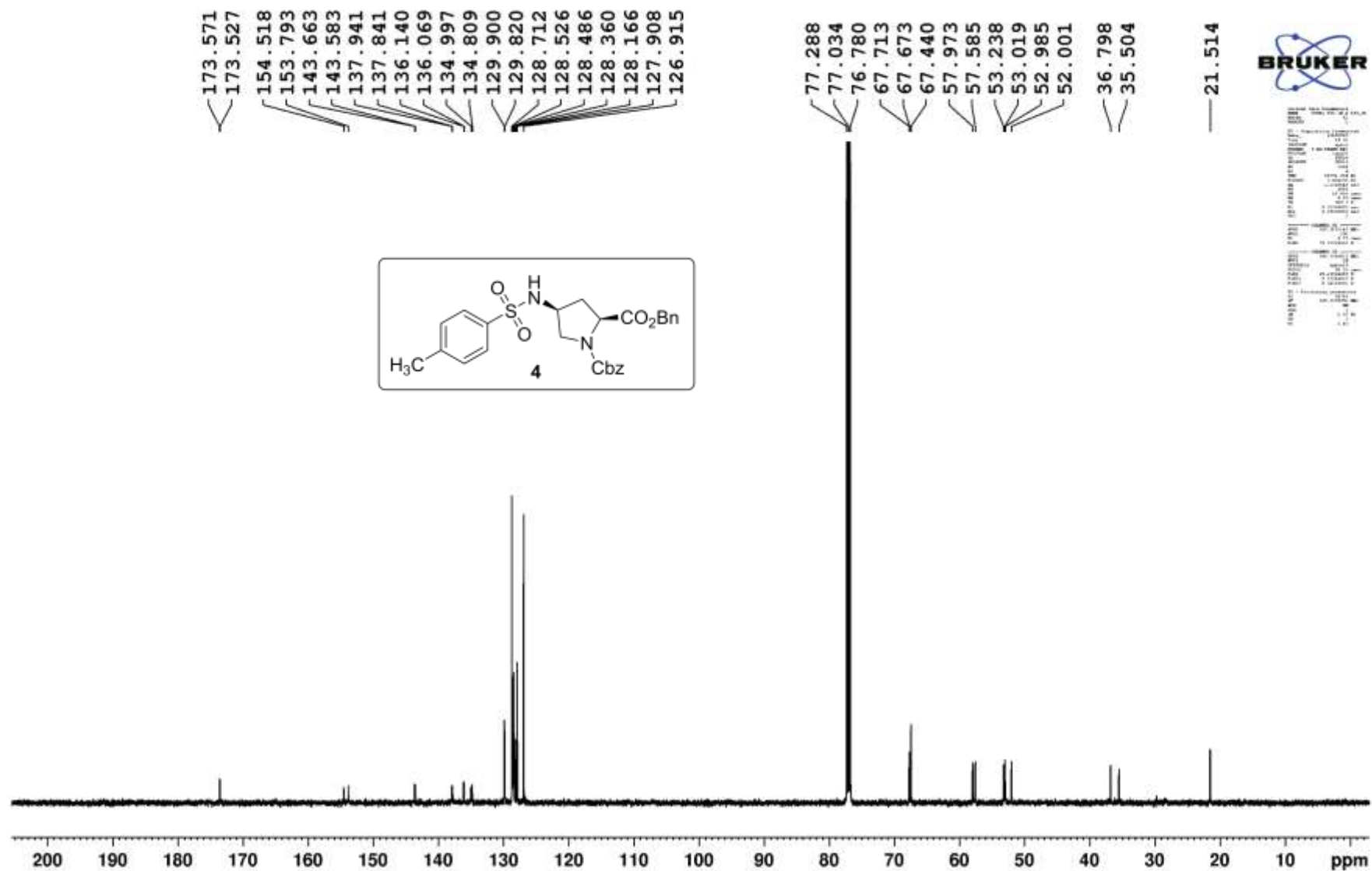m/z [M+H]$^+$ calculated for C$_{12}$H$_{17}$N$_2$O$_4$S: 285.0904

BRUKER
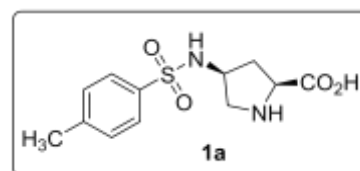
7.7072
7.6911
7.6749
7.3730
7.3500
7.3012
7.2689
7.2452
7.2325
5.7562
5.7367
5.6799
5.6604
5.2508
5.2264
5.1904
5.1659
5.1518
5.1271
5.0967
5.0717
5.0302
4.3726
4.3552
4.3301
4.3114
4.0487
4.0367
4.0309
4.0241
4.0179
4.0055
3.5782
3.5673
3.5556
3.5441
3.5342
3.4704
3.4470
3.4321
3.4087
2.4212
2.3857
2.3483
2.3211
2.3079
2.2920
2.2807
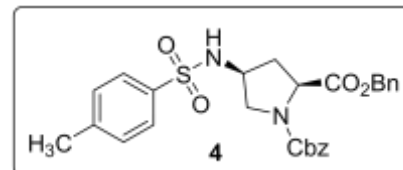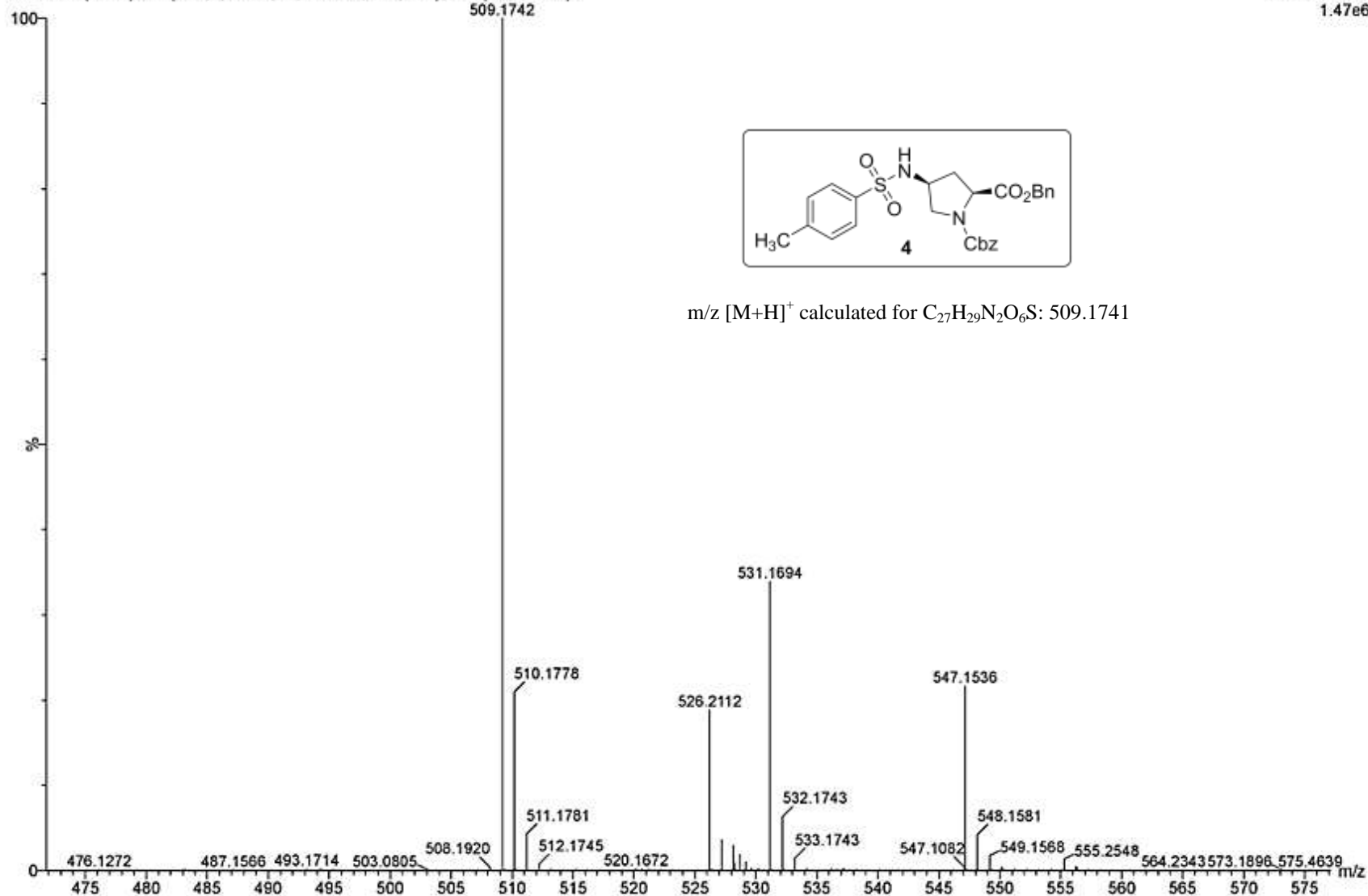2.2615
1.9660
1.9384
1.8388
1.8110

9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

1.95   11.92   0.98   1.84 2.25   1.00   1.01   1.04 1.04   3.46 0.57   1.06

SI-117
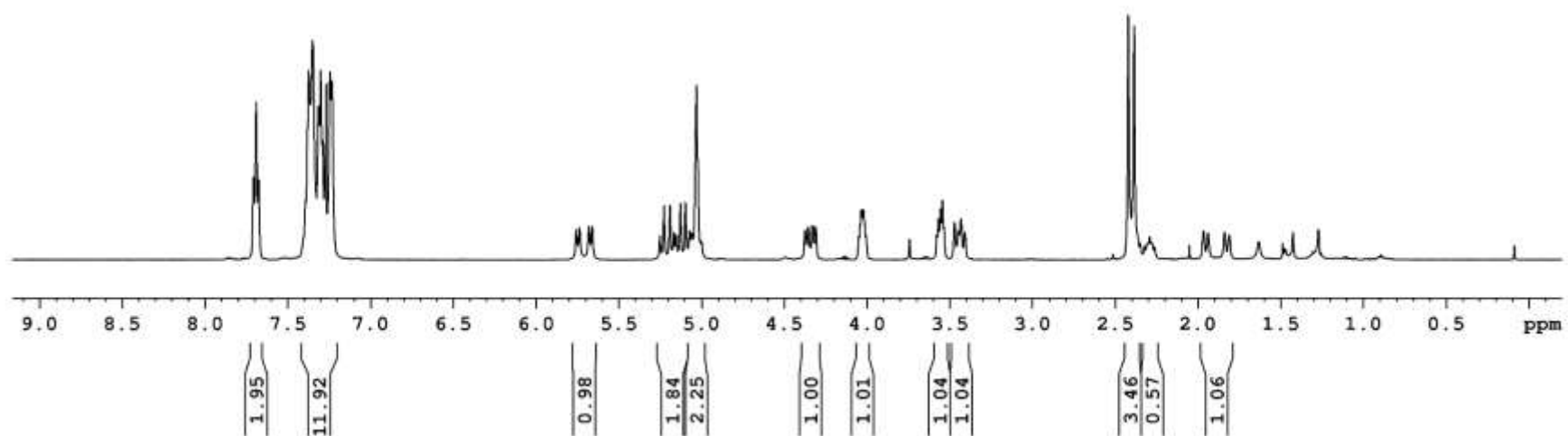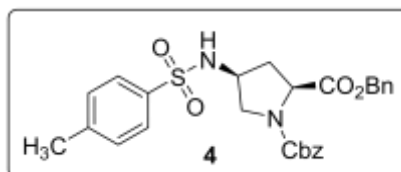
ES-KK-PRE-PTAP;13C;CDC13;23/05/2018

173.571
173.527
154.518
153.793
143.663
143.583
137.941
137.841
136.140
136.069
134.997
134.809
129.900
129.820
128.712
128.526
128.486
128.360
128.166
127.908
126.915

77.288
77.034
76.780
67.713
67.673
67.440
57.973
57.585
53.238
53.019
52.985
52.001

36.798
35.504

21.514

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4

TOF MS ES+
1.47e6

m/z [M+H]$^+$ calculated for C$_{27}$H$_{29}$N$_2$O$_6$S: 509.1741

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7.7896
7.7729
7.4913
7.4753

4.2629
4.2465
4.2300
3.9193
3.9088
3.8978
3.8865
3.8763
3.5427
3.5311
3.5179
3.5063
3.3945
3.3930
3.3854
3.3840
3.3698
3.3682
3.3607
3.3592
2.4414
2.2936
2.2781
2.2765
2.2685
2.2669
2.2611
2.2595
2.2499
2.2405
2.2389
2.2315
2.2250
2.1874
2.1743
2.1717
2.1589
2.1463
2.1436

1b

8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

1.98   1.99   0.89   0.96   0.94 0.96   3.00 1.20 0.97

BRUKER
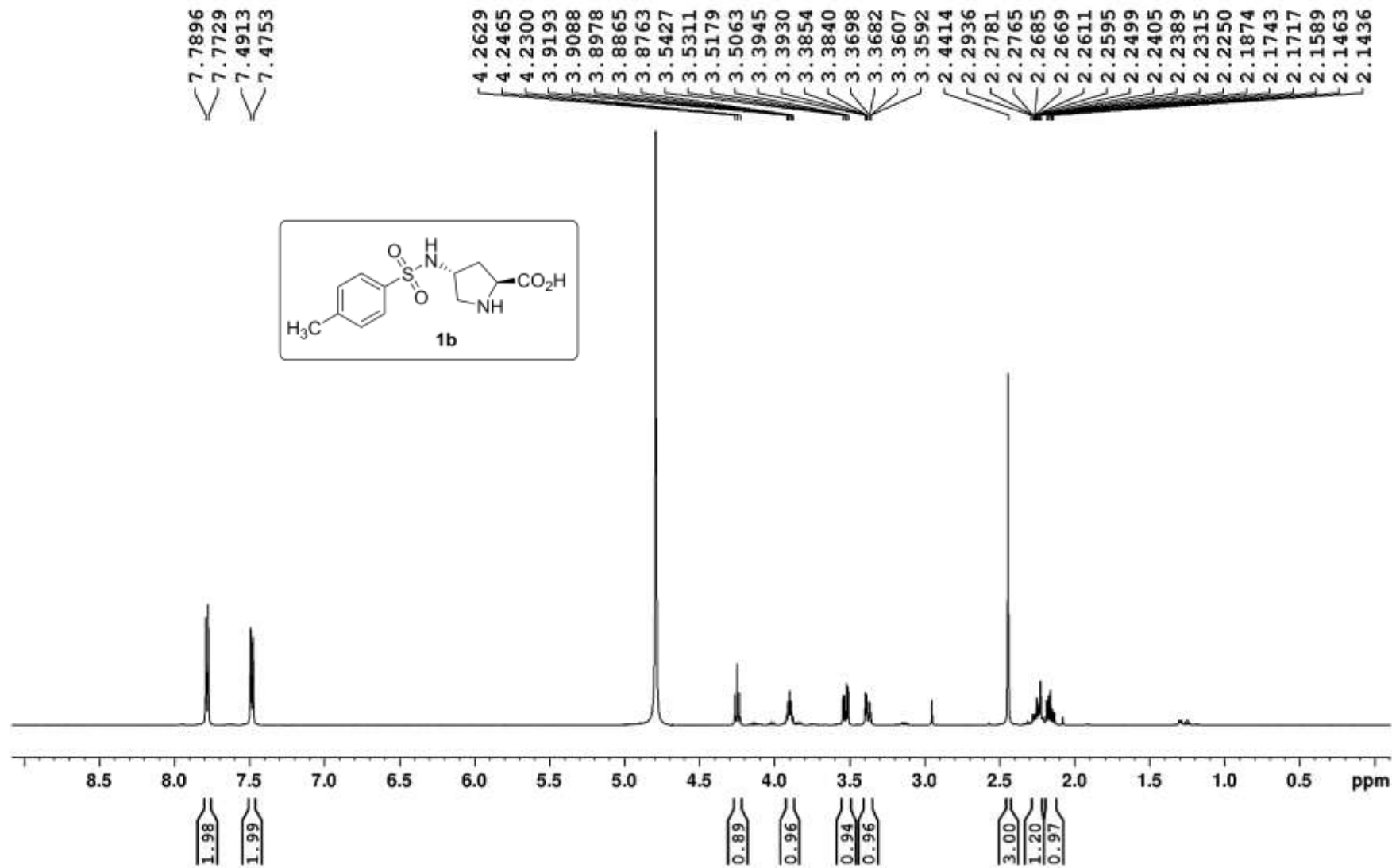
173.2935

145.5605

134.3709
130.2497
126.8925

59.7108

52.0086
50.5353

34.4308

20.6805

1b

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
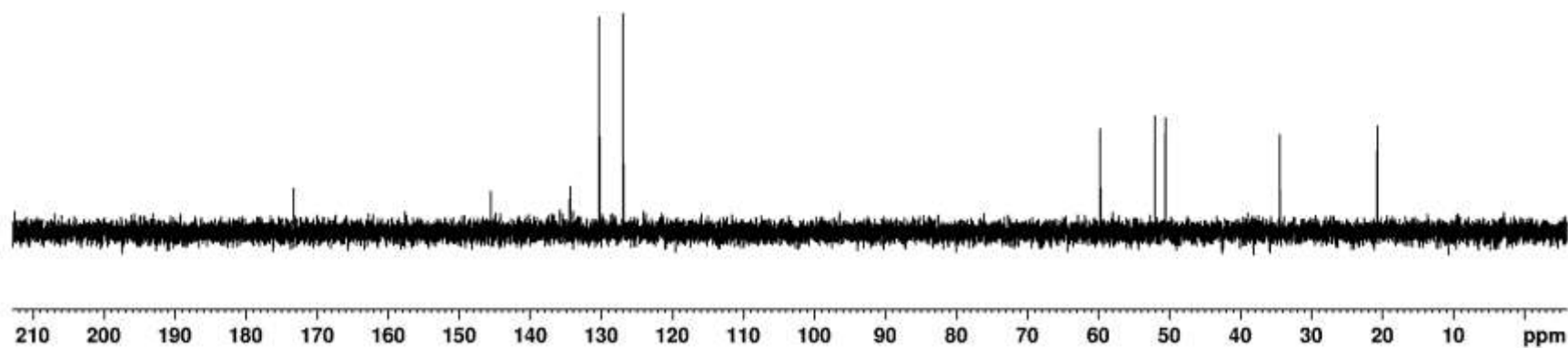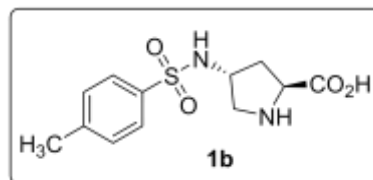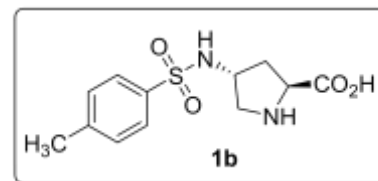
TOF MS ES+
4.38e7

m/z [M+H]$^+$ calculated for C$_{12}$H$_{17}$N$_2$O$_4$S: 285.0904

ES-KK-PRE-T-NHTS;1H;CDC13;30/6/19

7.7128
7.6973
7.6851
7.3622
7.3482
7.3321
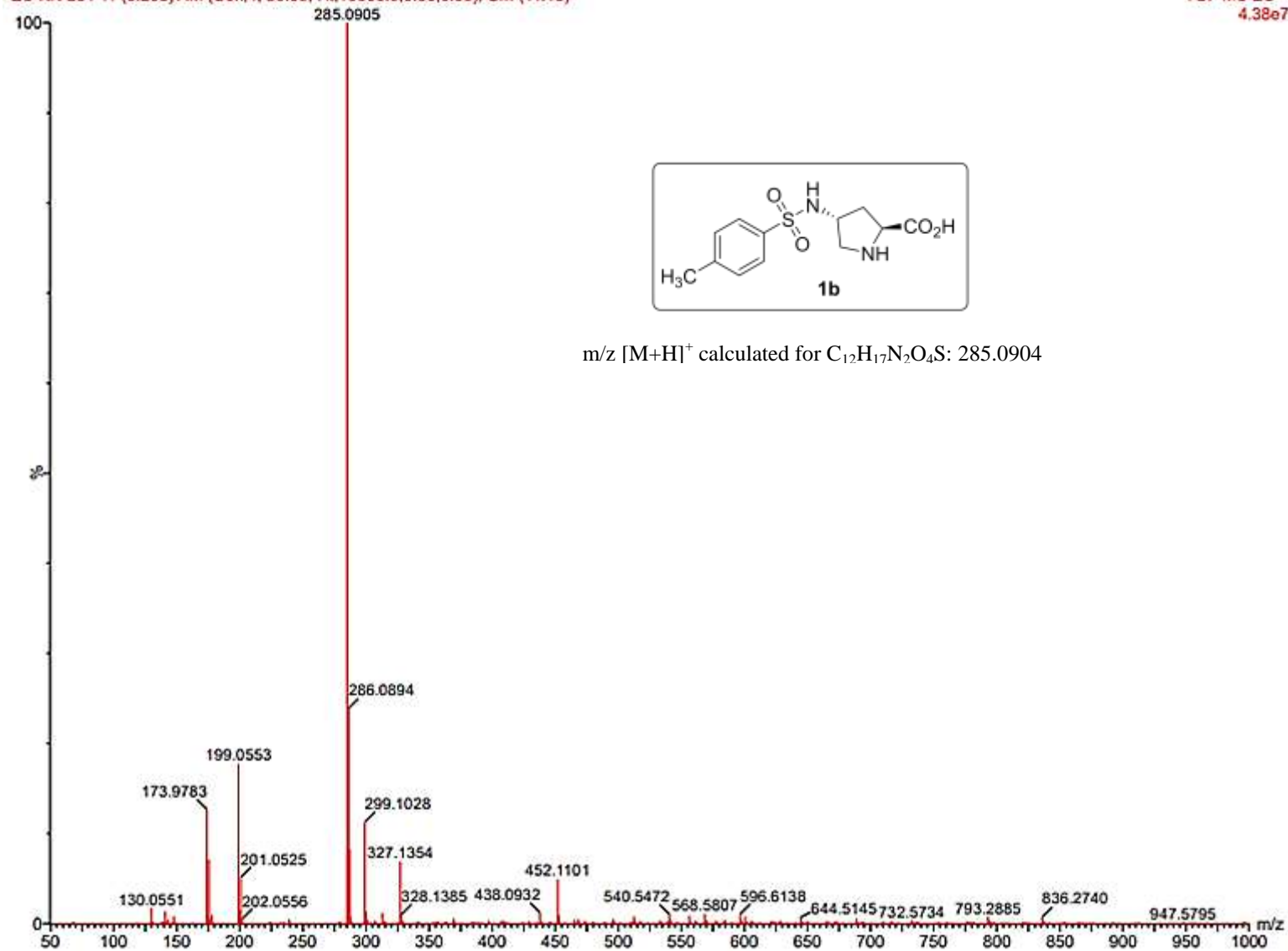7.3190
7.3095
7.2903
7.2688
7.2502
7.2323
7.2155
5.1858
5.1612
5.1392
5.1143
5.0936
5.0314
5.0014
4.9878
4.9633
4.4647
4.4512
4.4384
4.4108
4.4010
4.3942
4.3843
3.9385
3.9263
3.9139
3.7089
3.6956
3.6868
3.6687
3.6551
3.6458
3.6328
3.2792
3.2683
3.2569
3.2460
2.4245
2.4012
2.2756
2.2600
2.2485
2.2341
2.2188
2.1763
2.1655
2.1542
2.1388
2.1282
2.1011
2.0878
2.0750

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4'

2.00 9.96 2.07 5.33 1.02 1.05 1.05 1.04 3.08 0.58 0.59 0.90

8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

ES-KK-PRE-T-NHTS;13C;CDC13;30/6/19

171.7357
171.5417
154.6162
154.0031
143.9618
137.0073
136.9386
136.1548
136.0624
135.3492
135.1745
129.9921
129.9391
128.6313
128.5213
128.4685
128.4025
128.2056
128.1264
127.8816
127.8387
126.9985

77.2913
77.0374
76.7829
67.4065
67.3705
67.1760
67.0821
57.6528
57.4137
51.9564
51.7531
51.0973

37.2535
36.0250

21.5620

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200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

m/z $[M+H]^+$ calculated for $C_{27}H_{29}N_2O_6S$: 509.1741