RSC Advances

Electronic Supplementary Information

Vanillic Mannich Bases: Synthesis and Screening of Biological Activity. Mechanistic Insight into the Reaction with 4-Chloroaniline

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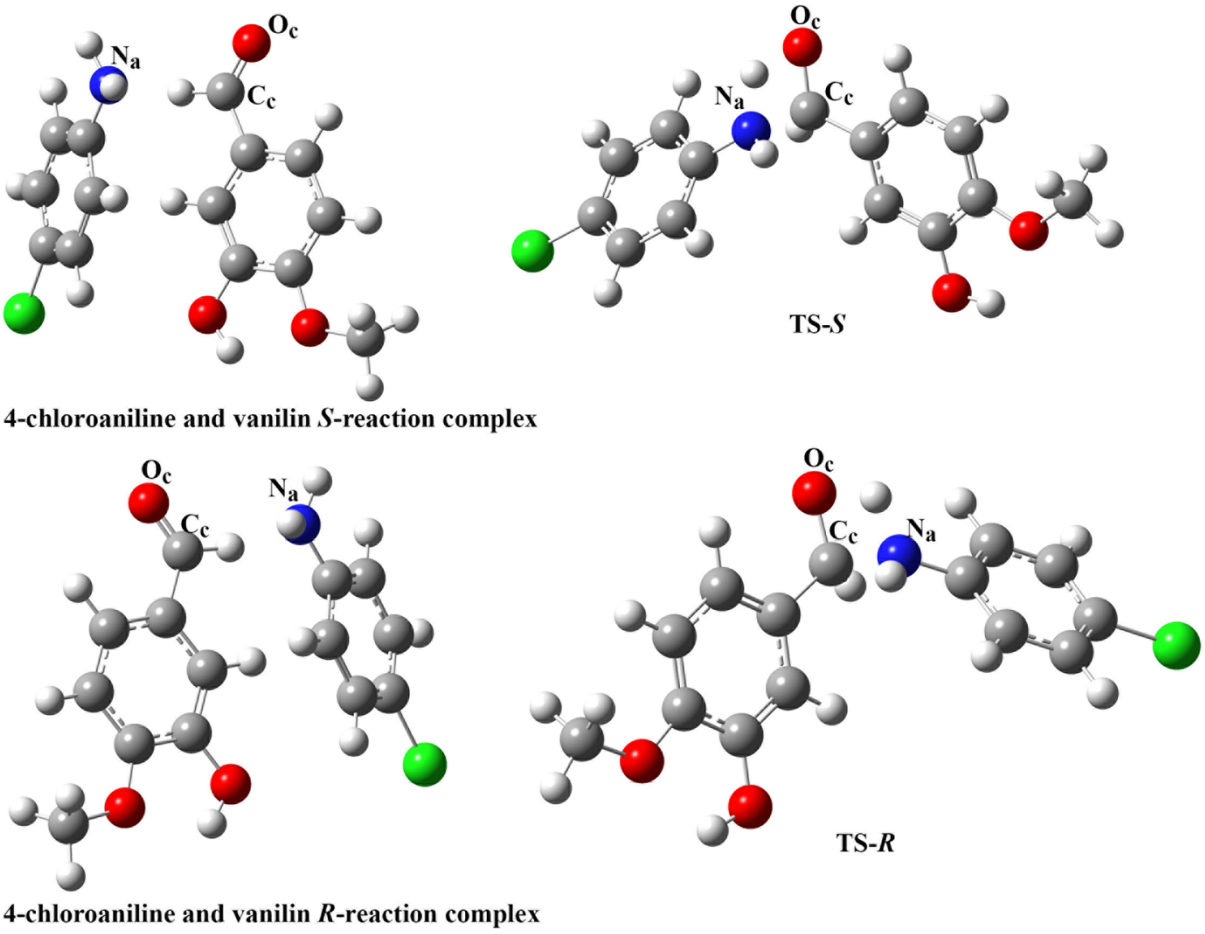


Figure S1. Nucleophilic attack of the 4-chloroaniline nitrogen at the carbonyl group of vanilin.

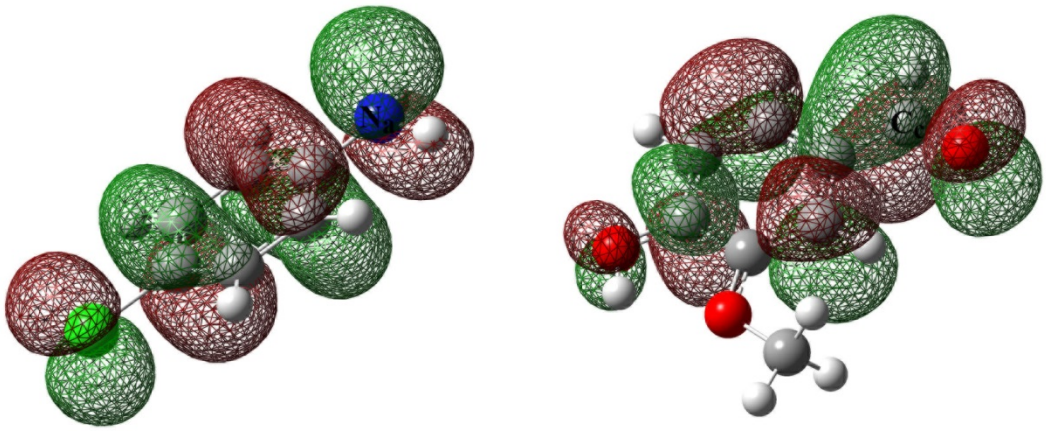


Figure S2. HOMO of 4-chloroaniline and LUMO of vanilin.

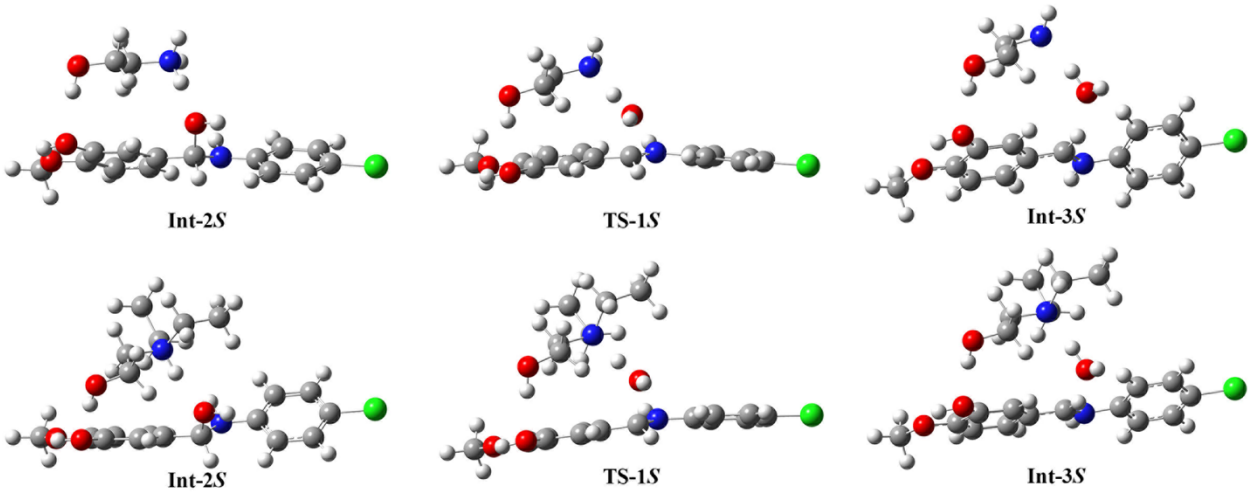


Figure S3. Intermediates and transition states in the transformation of **Int-2S** catalyzed with [HMEA][ClAc] and [HDEAE][ClAc].

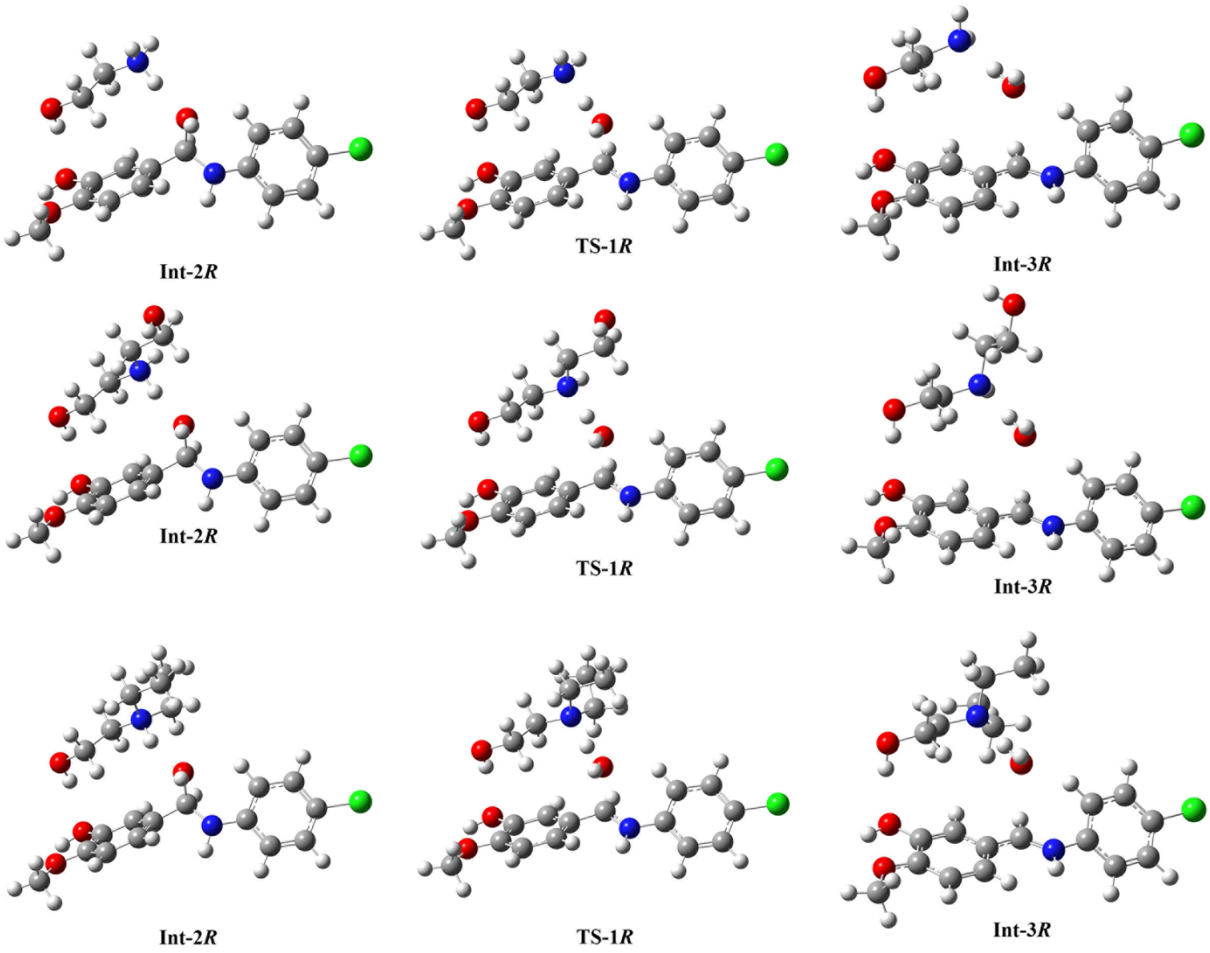


Figure S4. Intermediates and transition states in the transformation of **Int-2*R*** catalyzed with [HDEA][ClAc], [HMEA][ClAc] and [HDEAE][ClAc].

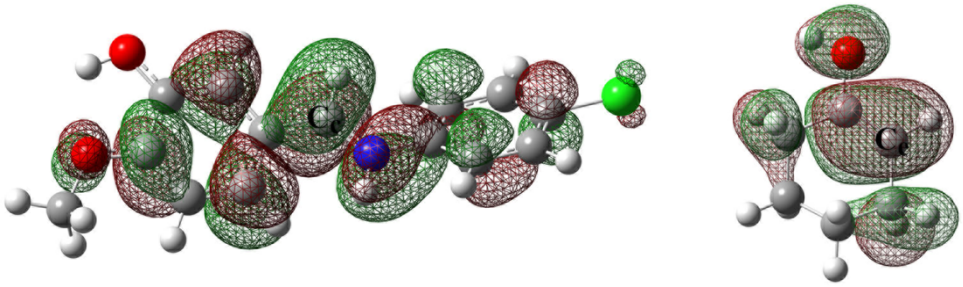


Figure S5. LUMO of the imminium ion and HOMO of the enol.

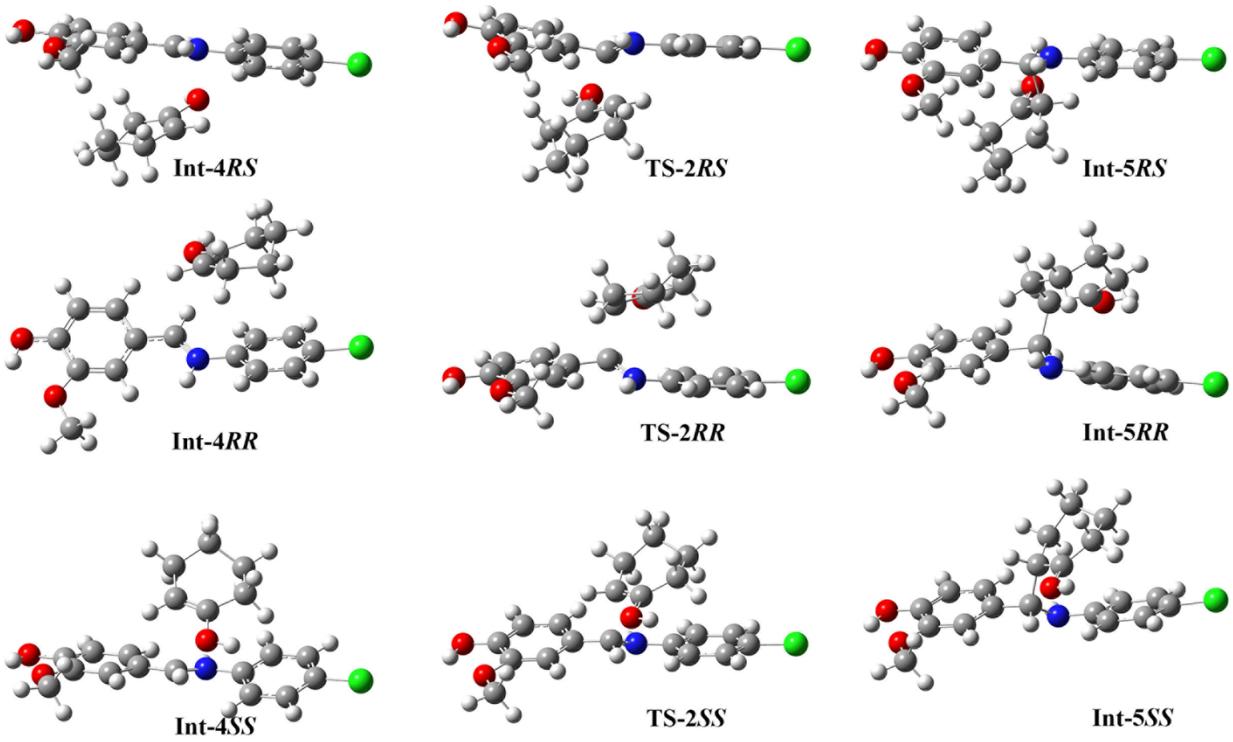


Figure S6. Reactant complexes **Int-4*RS***, **Int-4*SS***, and **Int-4*RR***, and transition states **TS-2*RS***, **TS-2*SS***, and **TS-2*RR***.

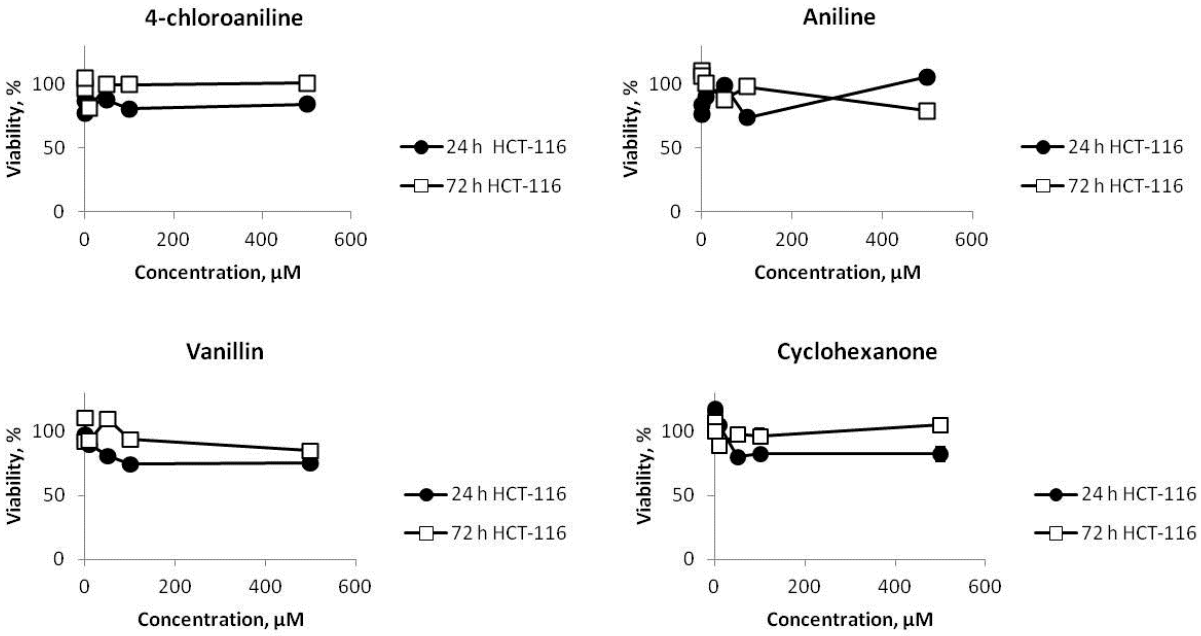


Figure S7. Growth inhibitory effects of the starting compounds on HCT-116 cell line.

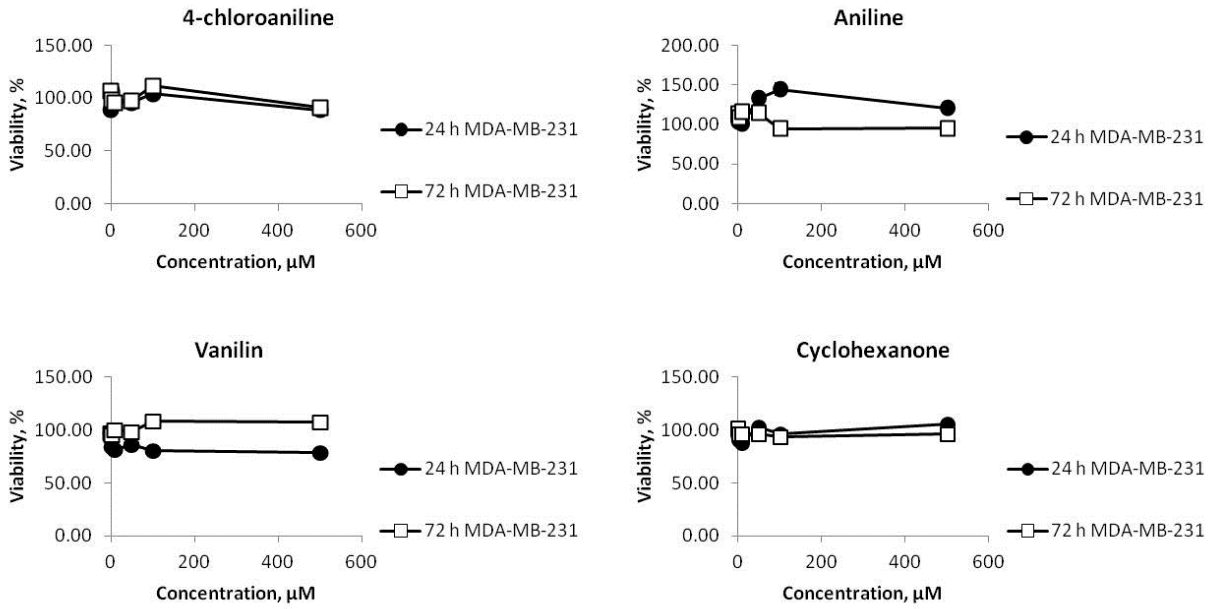


Figure S8. Growth inhibitory effects of the starting compounds on MDA-MB-231 cell line.

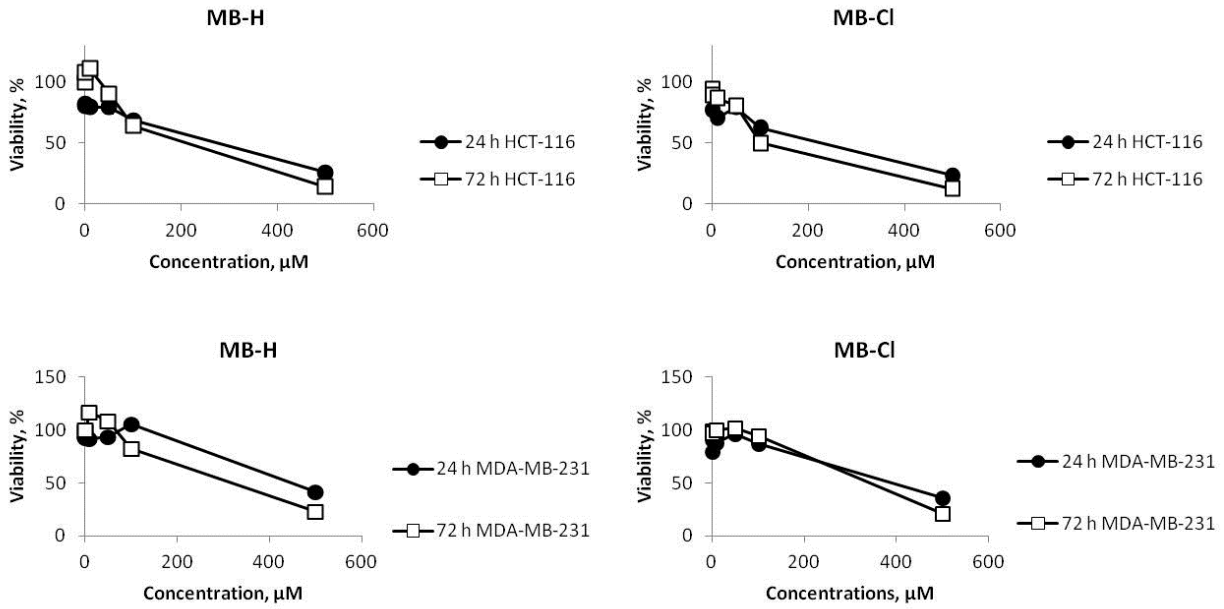
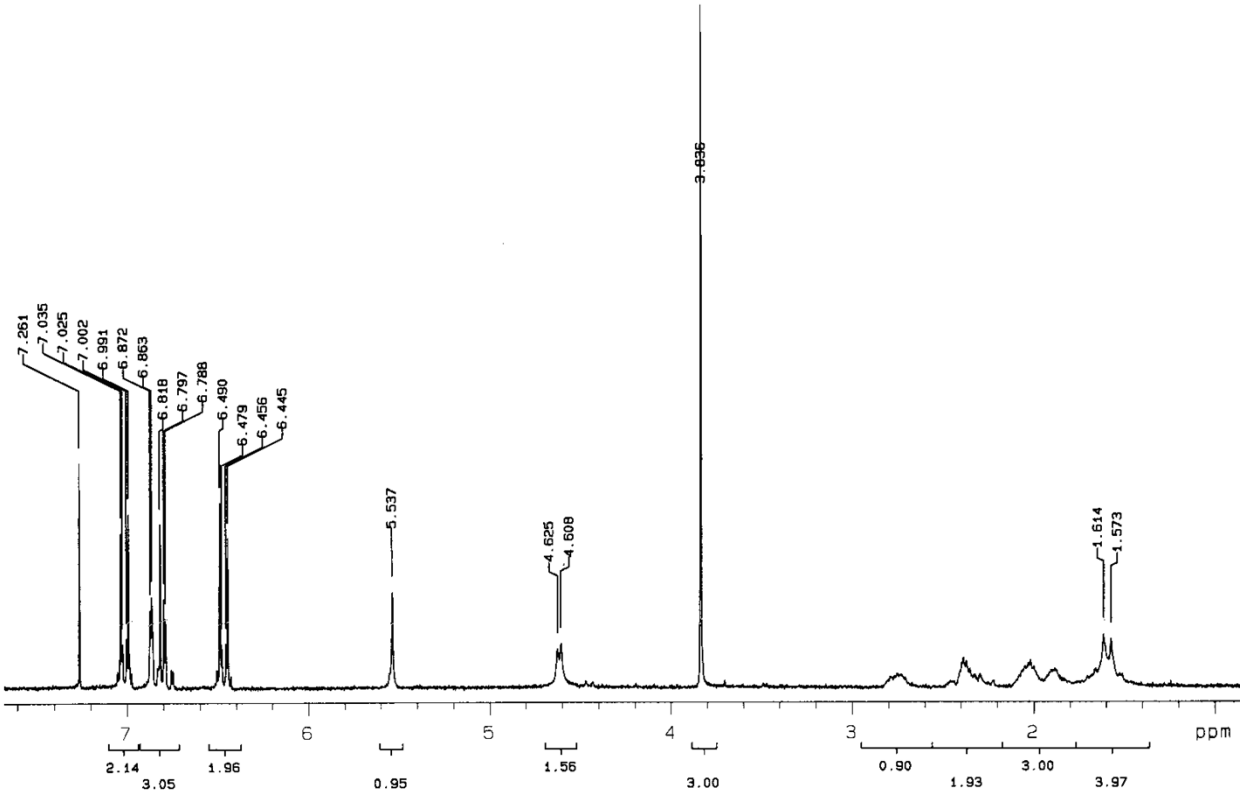


Figure S9. Growth inhibitory effects of MB-H and MB-Cl on HCT-116 and MDA-MB-231 cell lines

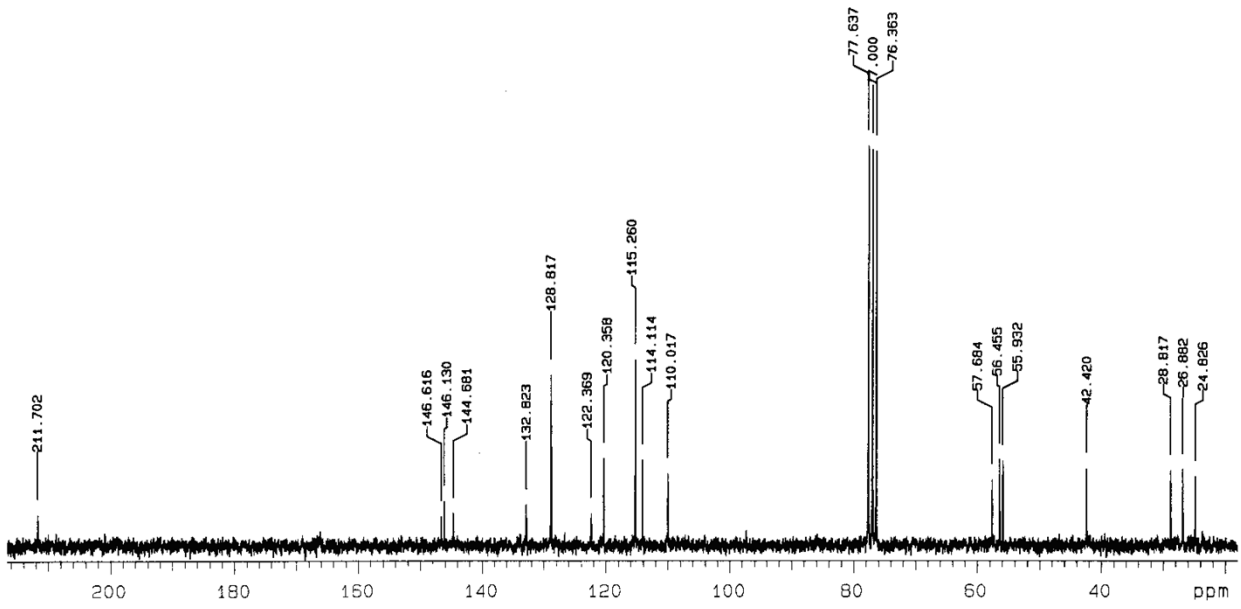
Table S1. Energy profiles for the ILs catalyzed transformation of **Int-1** (*R* isomer). The free energy values (kJ/mol) were calculated relative to **Int-2**.

Catalyst	**Int-2**	**TS-1**	**Int-3**
[HDEA][ClAc]	0.0	55.7	33.3
[HMEA][ClAc]	0.0	58.7	14.3
[HDEAE][ClAc]	0.0	76.9	43.7

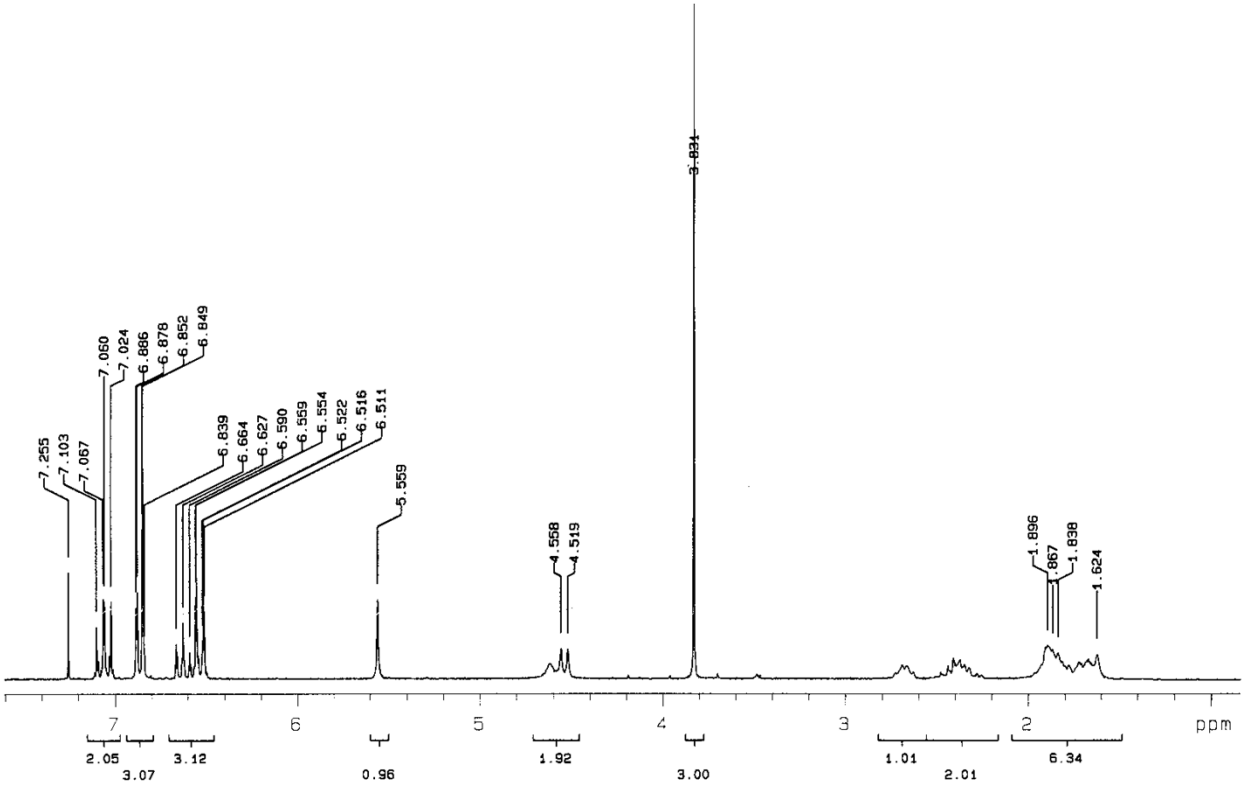
MB-Cl ^{1}H NMR


7.261
7.035
7.025
7.002
6.991
6.872
6.863
6.818
6.797
6.788
6.490
6.479
6.456
6.445
5.537
4.625
4.608
3.836
1.614
1.573
7
6
5
4
3
2
ppm
2.14
3.05
1.96
0.95
1.56
3.00
0.90
1.93
3.00
3.97

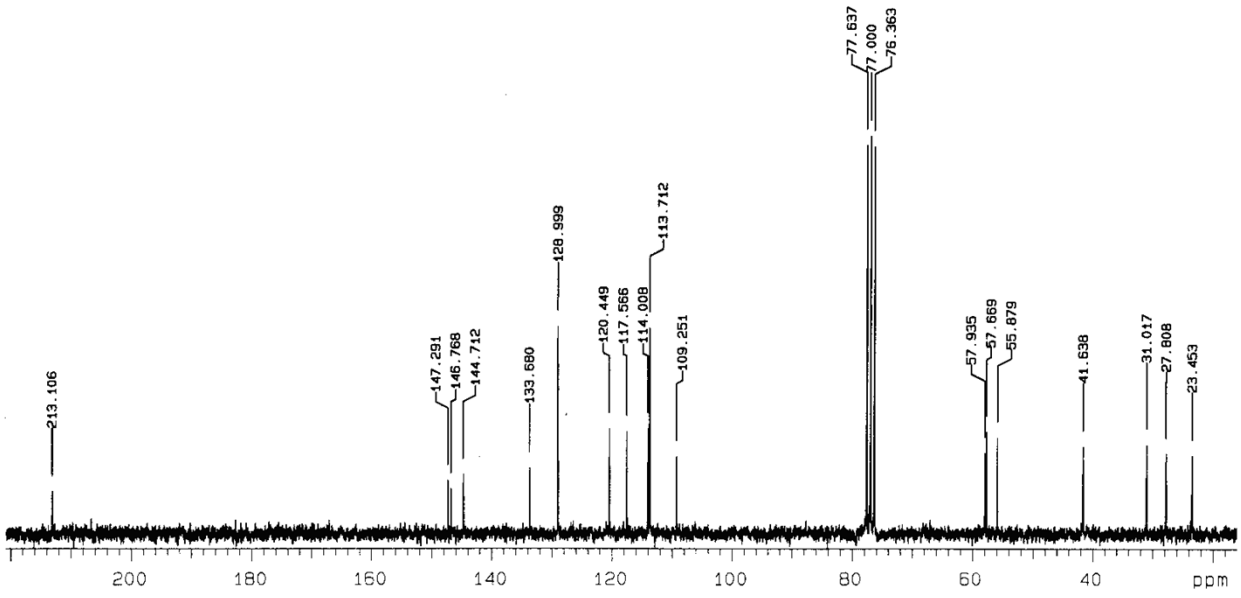
MB-Cl ^{13}C NMR


211.702
146.616
146.130
144.681
132.823
128.817
122.369
120.358
115.260
114.114
110.017
77.637
77.000
76.363
57.684
56.455
55.932
42.420
28.817
26.882
24.626
200
180
160
140
120
100
80
60
40
ppm

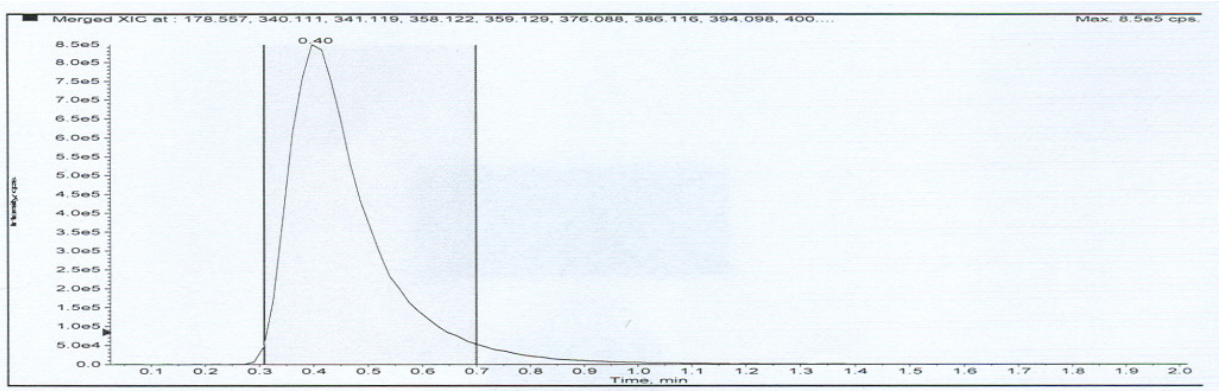
MB-H ^{1}H NMR


7.255
7.103
7.067
7.050
7.024
6.886
6.878
6.852
6.849
6.839
6.664
6.627
6.590
6.559
6.554
6.522
6.516
6.511
5.559
4.558
4.519
3.831
1.896
1.867
1.838
1.624
7
6
5
4
3
2
ppm
2.05
3.07
3.12
0.96
1.92
3.00
1.01
2.01
6.34

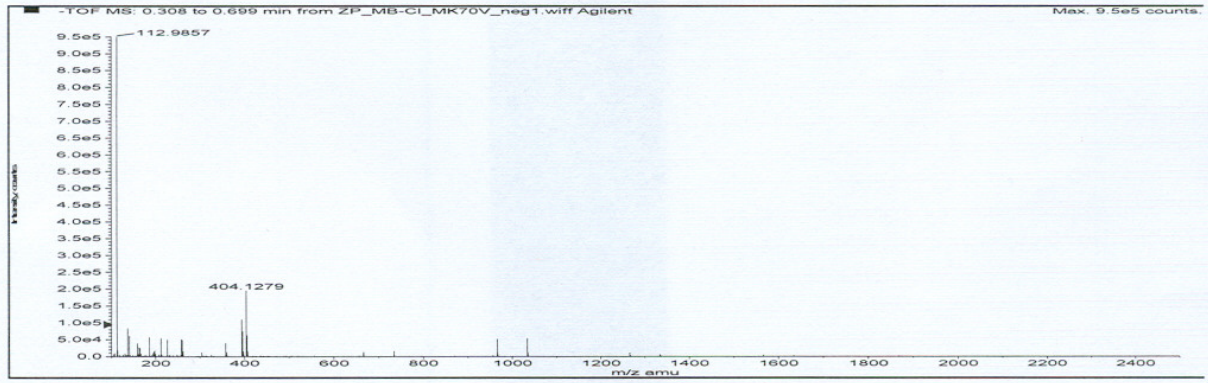
MB-H ^{13}C NMR

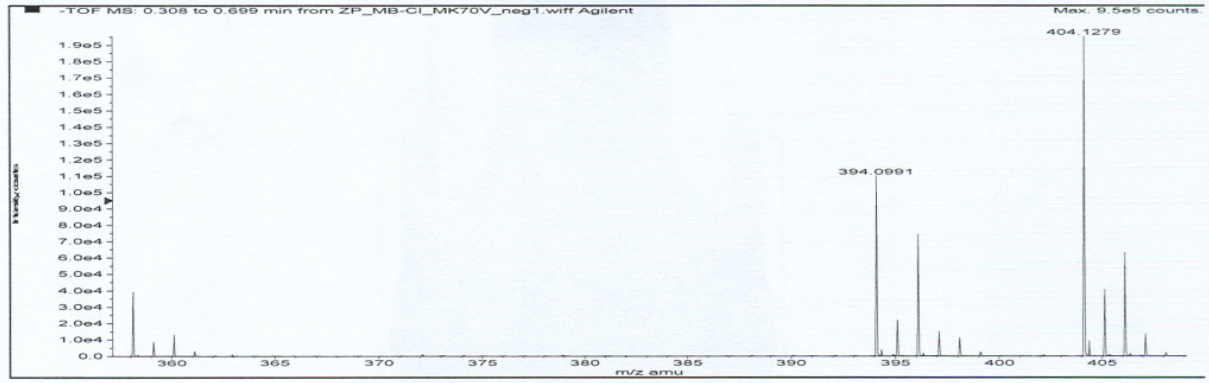

213.106
147.291
146.768
144.712
133.680
128.999
120.449
117.566
114.008
113.712
109.251
77.637
77.000
76.363
57.935
57.669
55.879
41.638
31.017
27.808
23.453
200
180
160
140
120
100
80
60
40
ppm

ESI-MS **MB-Cl**



Merged XIC, Period# : 1 Experiment# : 1

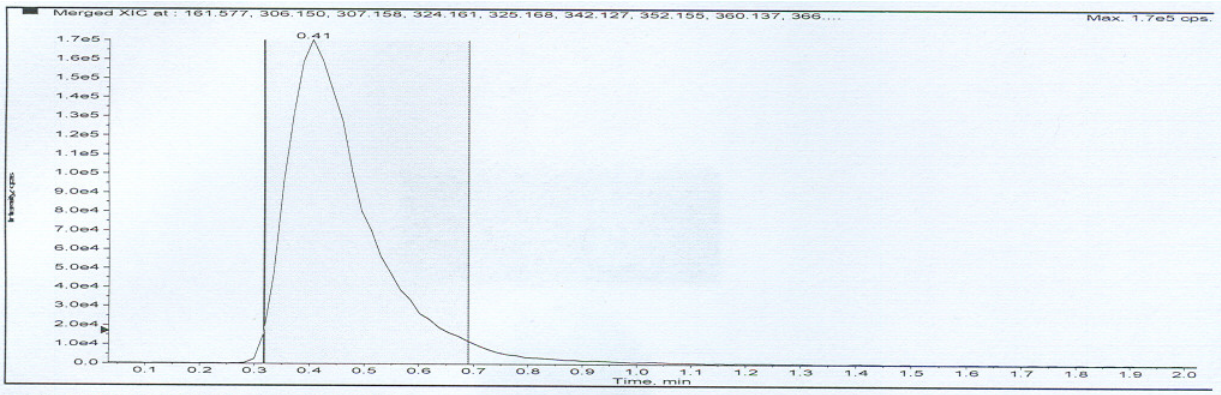




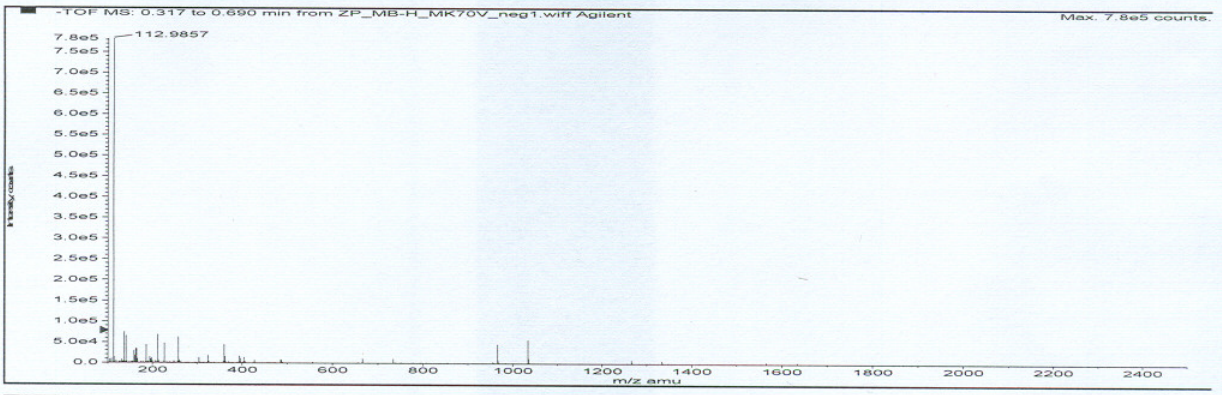
Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C20H22NO3Cl	--	359.12882	0.40	8.67711 E6	--

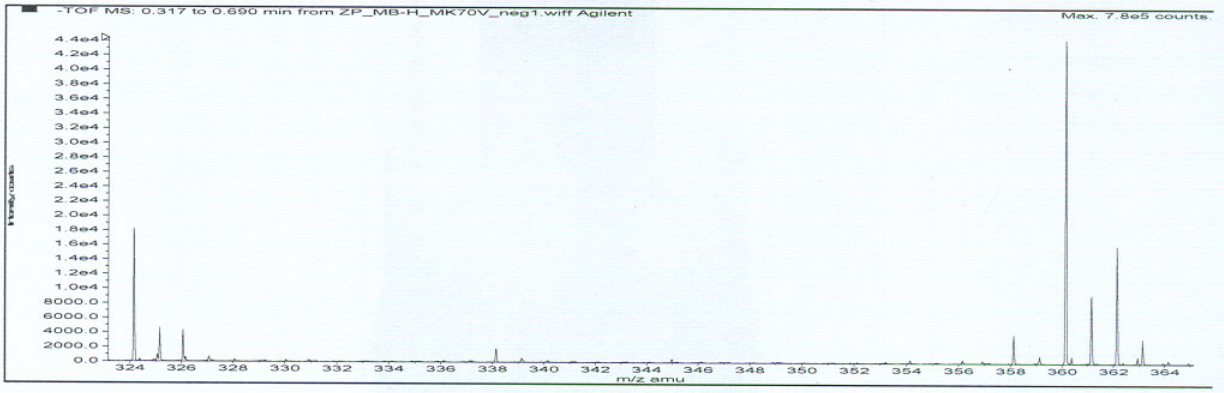
Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	39562.57	358.12154	358.12247	0.92653	2.59	--
[M+Cl]-	113751.31	394.09822	394.09906	0.83606	2.12	--
[M+HCOO]-	197614.69	404.12702	404.12791	0.88716	2.20	--

ESI-MS **MB-H**



Merged XIC, Period# : 1 Experiment# : 1





Formula	Compound name	Mass	Peak RT (min)	Peak area	Description
C20H23NO3	--	325.16779	0.41	1.71673 E6	--

Species	Abundance (counts)	Ion Mass	Measured Mass	Error (mDa)	Error (ppm)	Ret. Time Error (min)
[M-H]-	19551.22	324.16052	324.16117	0.65461	2.02	--
[M+Cl]-	47840.74	360.13719	360.13748	0.28213	0.78	--