Supplementary information

STUDY OF THE DIVALENT CATION COMPLEXATION OF 2-HYDROXYISOQUINOLINE-1,3-DIONES, DISCOVERY OF A NOVEL SELECTIVE INHIBITOR OF THE HIV-1 REVERSE TRANSCRIPTASE RIBONUCLEASE H FUNCTION

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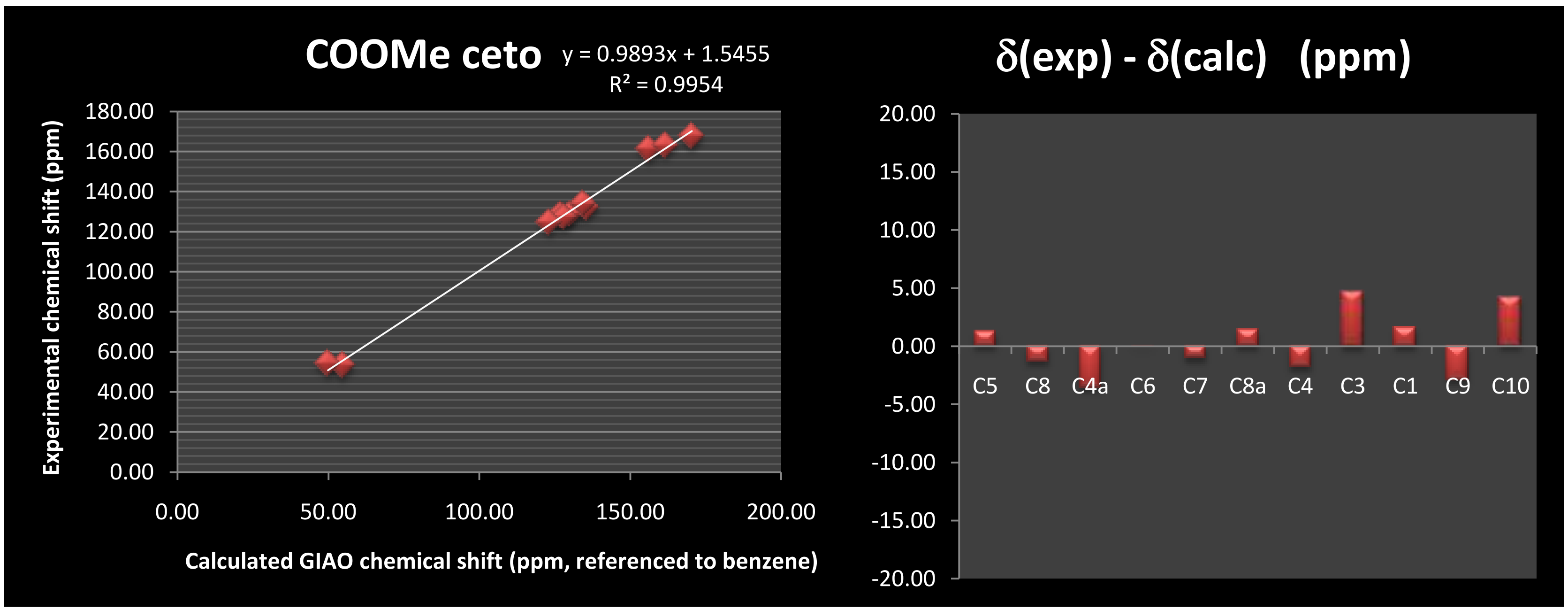
MMFF conformer // AM1 geometry // B3LYP/6-31G(d) geometry optimization // GIAO B3LYP/6-311+G(d,p)

Carbon number	C_5	C_8	C_{4a}	C_6	C_7	C_{8a}	C_4	C_3	C_1	C_9	C_{10}
gaussian carbon label	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**C11**	**C12**	**C17**	**C20**	**C23**
COOMe ceto GIAO shielding (ppm)	50.47	47.22	41.66	43.14	49.06	54.11	122.70	21.00	15.71	7.01	127.57
COOMe ceto GIAO chemical shift (ppm)	**126.94**	**130.19**	**135.74**	**134.27**	**128.35**	**123.30**	**54.71**	**156.40**	**161.70**	**170.40**	**49.83**
experimental chemical shift (ppm)	**128.20**	**128.90**	**132.20**	**134.20**	**127.30**	**124.70**	**52.90**	**161.00**	**163.30**	**167.50**	**54.00**
δ(exp) - δ(calc) (ppm)	1.26	-1.29	-3.54	-0.07	-1.05	1.40	-1.81	4.60	1.60	-2.90	4.17
| δ(exp) - δ(calc) | (ppm)	**1.26**	**1.29**	**3.54**	**0.07**	**1.05**	**1.40**	**1.81**	**4.60**	**1.60**	**2.90**	**4.17**
MEAN ABSOLUTE ERROR (ppm) 2.15											

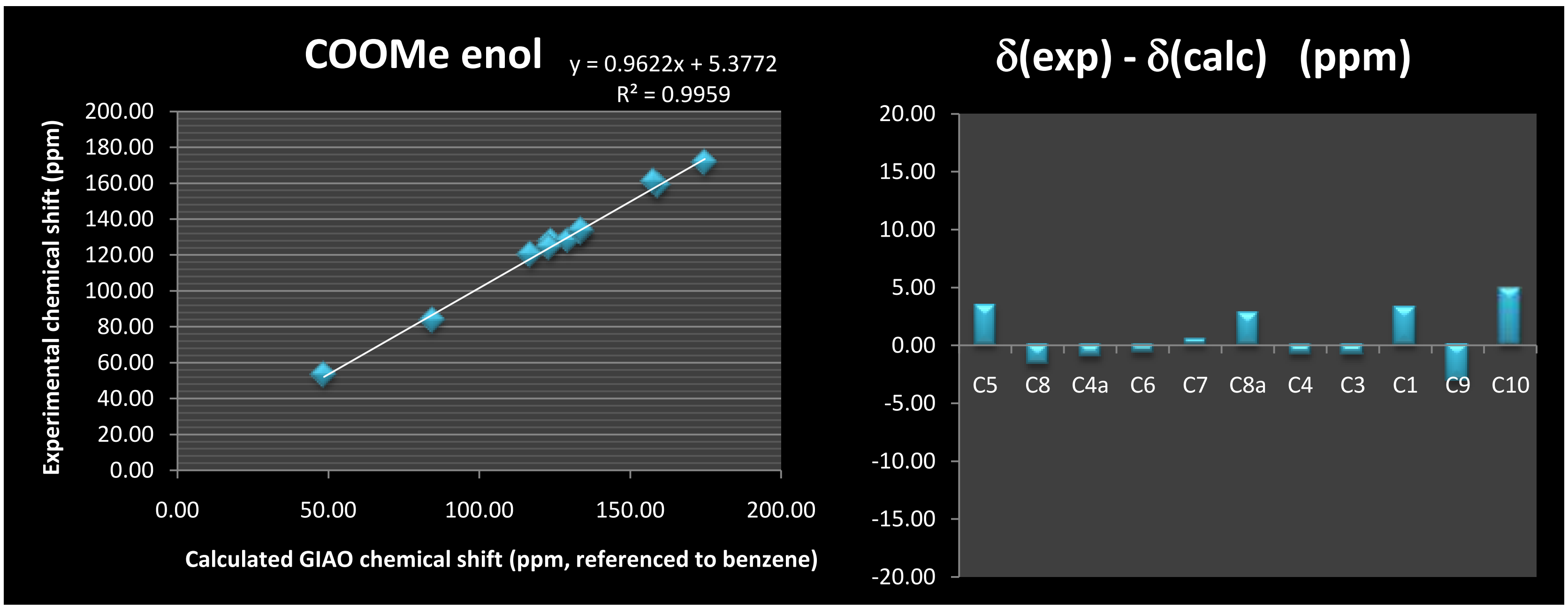


3b

MMFF conformer // AM1 geometry // B3LYP/6-31G(d) geometry optimization // GIAO B3LYP/6-311+G(d,p)

Carbon number	C_5	C_8	C_{4a}	C_6	C_7	C_{8a}	C_4	C_3	C_1	C_9	C_{10}
gaussian carbon label	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**C11**	**C12**	**C16**	**C20**	**C23**
COOMe enol GIAO shielding (ppm)	53.26	47.86	43.60	43.56	53.99	60.20	92.91	18.27	19.64	2.68	128.83
COOMe enol GIAO chemical shift (ppm)	**124.15**	**129.55**	**133.80**	**133.85**	**123.42**	**117.20**	**84.49**	**159.14**	**157.77**	**174.73**	**48.58**
experimental chemical shift (ppm)	**127.60**	**127.90**	**132.80**	**133.20**	**123.90**	**120.00**	**83.70**	**158.30**	**161.00**	**171.60**	**53.40**
δ(exp) - δ(calc) (ppm)	3.45	-1.65	-1.00	-0.65	0.48	2.80	-0.79	-0.84	3.23	-3.13	4.82
| δ(exp) - δ(calc) | (ppm)	**3.45**	**1.65**	**1.00**	**0.65**	**0.48**	**2.80**	**0.79**	**0.84**	**3.23**	**3.13**	**4.82**

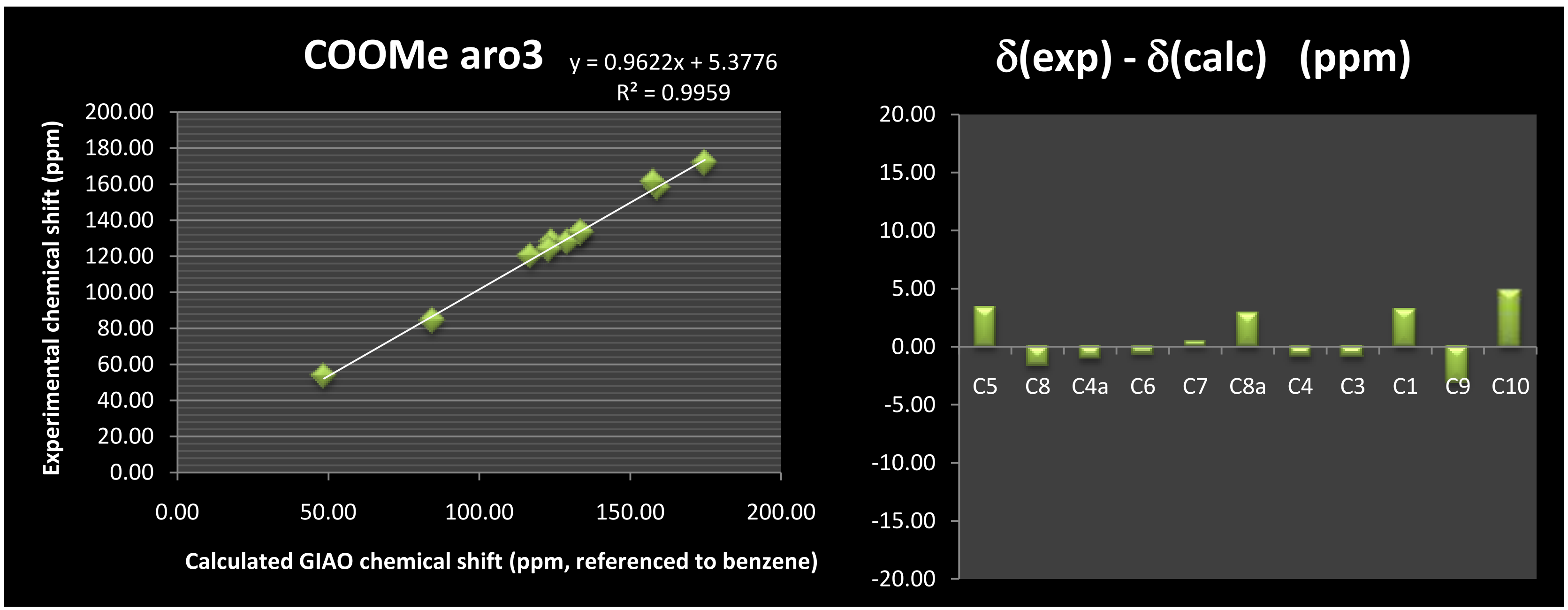
MEAN ABSOLUTE ERROR (ppm)
2.07



3c

MMFF conformer // AM1 geometry // B3LYP/6-31G(d) geometry optimization // GIAO B3LYP/6-311+G(d,p)

Carbon number	C_5	C_8	C_{4a}	C_6	C_7	C_{8a}	C_4	C_3	C_1	C_9	C_{10}
gaussian carbon label	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**C11**	**C12**	**C14**	**C18**	**C21**
COOMe aro3 GIAO shielding (ppm)	53.21	47.88	43.54	43.59	53.96	60.19	92.90	18.24	19.63	2.73	128.87
COOMe aro3 GIAO chemical shift (ppm)	**124.19**	**129.53**	**133.86**	**133.81**	**123.45**	**117.21**	**84.51**	**159.17**	**157.77**	**174.67**	**48.54**
experimental chemical shift (ppm)	**127.60**	**127.90**	**132.80**	**133.20**	**123.90**	**120.00**	**83.70**	**158.30**	**161.00**	**171.60**	**53.40**
δ(exp) - δ(calc) (ppm)	3.41	-1.63	-1.06	-0.61	0.45	2.79	-0.81	-0.87	3.23	-3.07	4.86
| δ(exp) - δ(calc) | (ppm)	**3.41**	**1.63**	**1.06**	**0.61**	**0.45**	**2.79**	**0.81**	**0.87**	**3.23**	**3.07**	**4.86**
MEAN ABSOLUTE ERROR (ppm)											
2.07											

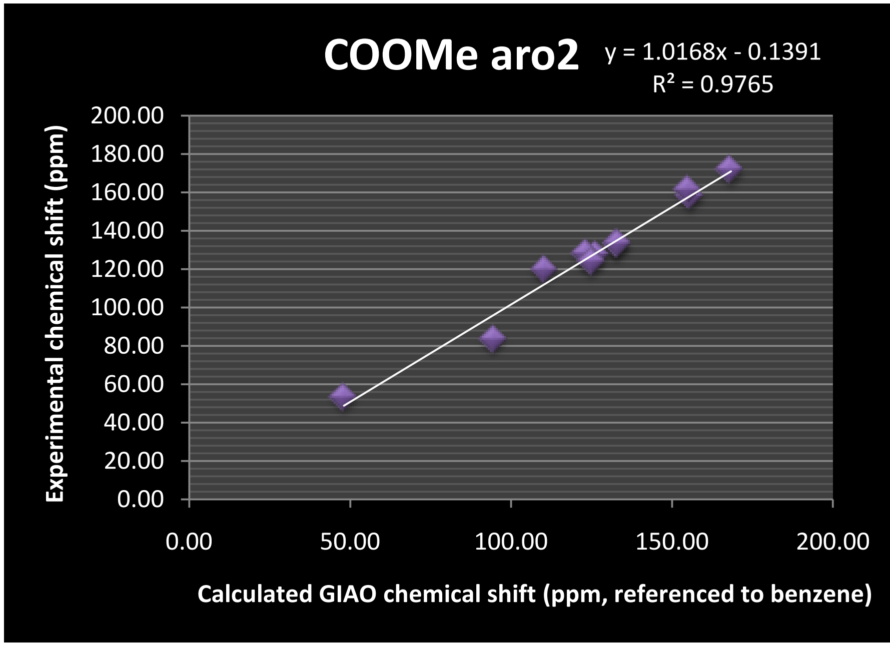


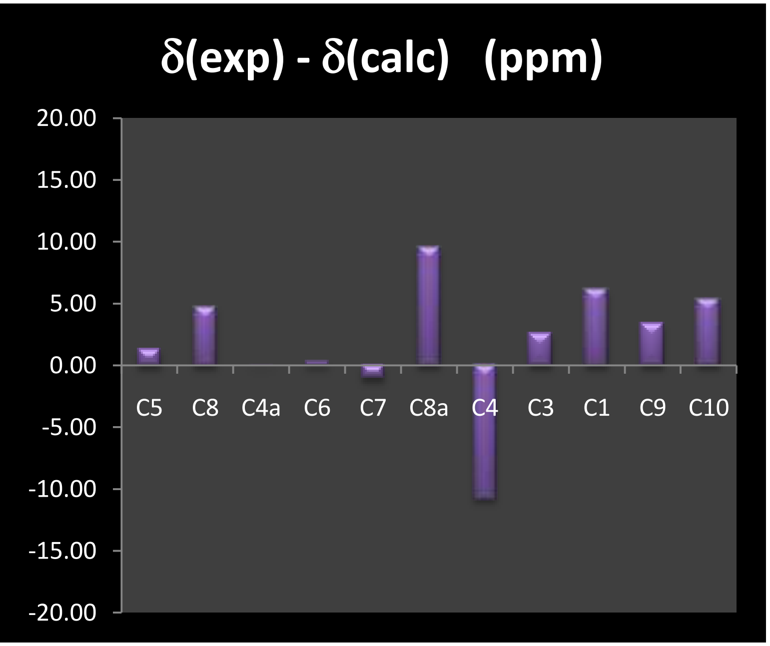
3d

MMFF conformer // AM1 geometry // B3LYP/6-31G(d) geometry optimization // GIAO B3LYP/6-311+G(d,p)

Carbon number	C_5	C_8	C_{4a}	C_6	C_7	C_{8a}	C_4	C_3	C_1	C_9	C_{10}
gaussian carbon label	C2	C3	C4	C5	C6	C7	C11	C12	C15	C20	C23
COOMe aro2 GIAO shielding (ppm)	51.15	54.26	44.58	44.48	52.47	66.96	82.94	21.68	22.52	9.13	129.38
COOMe aro2 GIAO chemical shift (ppm)	**126.25**	**123.15**	**132.82**	**132.93**	**124.93**	**110.45**	**94.47**	**155.73**	**154.88**	**168.28**	**48.03**
experimental chemical shift (ppm)	**127.60**	**127.90**	**132.80**	**133.20**	**123.90**	**120.00**	**83.70**	**158.30**	**161.00**	**171.60**	**53.40**
δ(exp) - δ(calc) (ppm)	1.35	4.75	-0.02	0.27	-1.03	9.55	-10.77	2.57	6.12	3.32	5.37
| δ(exp) - δ(calc) | (ppm)	**1.35**	**4.75**	**0.02**	**0.27**	**1.03**	**9.55**	**10.77**	**2.57**	**6.12**	**3.32**	**5.37**

MEAN ABSOLUTE ERROR (ppm)
4.10



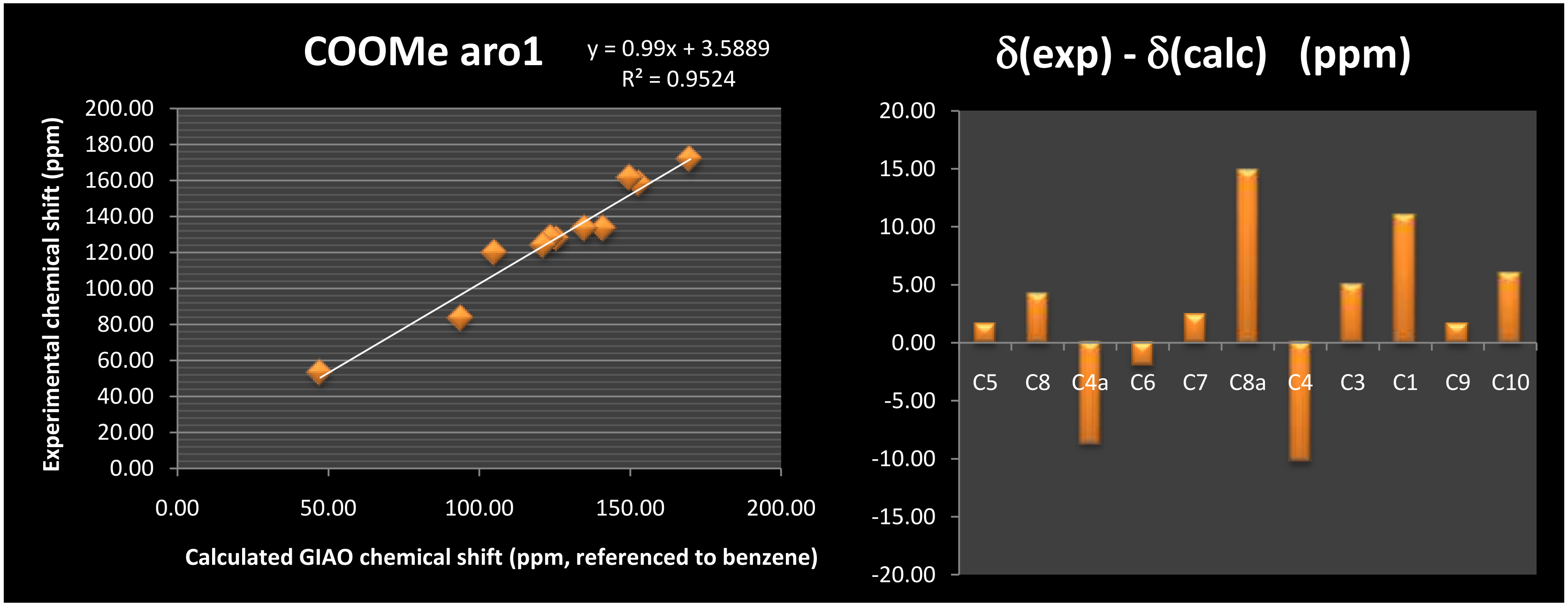


3e

MMFF conformer // AM1 geometry // B3LYP/6-31G(d) geometry optimization // GIAO B3LYP/6-311+G(d,p)

Carbon number	C_5	C_8	C_{4a}	C_6	C_7	C_{8a}	C_4	C_3	C_1	C_9	C_{10}
gaussian carbon label	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**C11**	**C12**	**C14**	**C18**	**C21**
COOMe aro1 GIAO shielding (ppm)	51.405	53.7459	35.9422	42.2634	55.8771	72.2202	83.5289	24.064	27.3574	7.4857	130.037
COOMe aro1 GIAO chemical shift (ppm)	**126.00**	**123.66**	**141.46**	**135.14**	**121.53**	**105.19**	**93.88**	**153.34**	**150.05**	**169.92**	**47.37**
experimental chemical shift (ppm)	**127.60**	**127.90**	**132.80**	**133.20**	**123.90**	**120.00**	**83.70**	**158.30**	**161.00**	**171.60**	**53.40**
δ(exp) - δ(calc) (ppm)	1.60	4.24	-8.66	-1.94	2.37	14.81	-10.18	4.96	10.95	1.68	6.03
| δ(exp) - δ(calc) | (ppm)	**1.60**	**4.24**	**8.66**	**1.94**	**2.37**	**14.81**	**10.18**	**4.96**	**10.95**	**1.68**	**6.03**

MEAN ABSOLUTE ERROR (ppm)
6.12

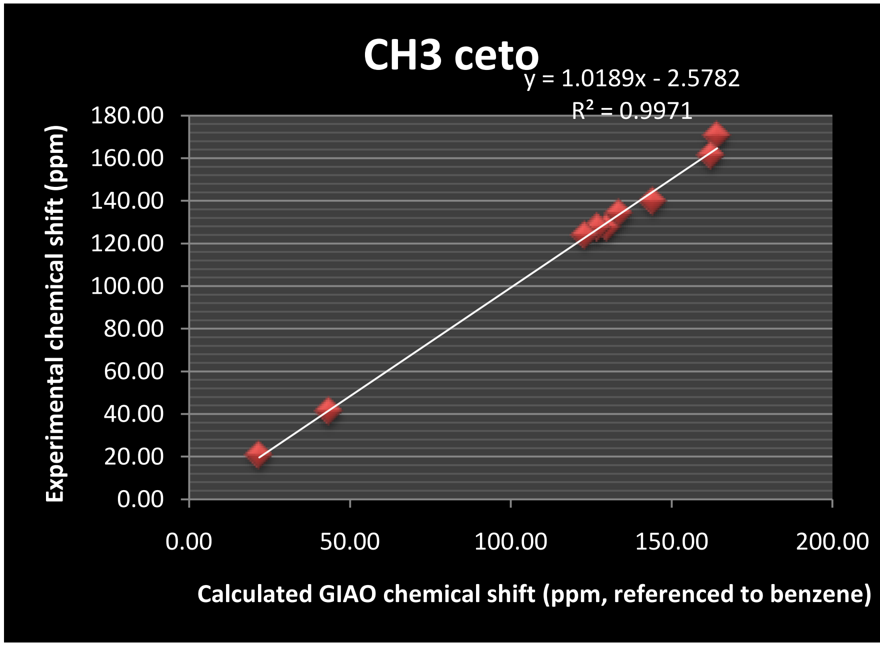


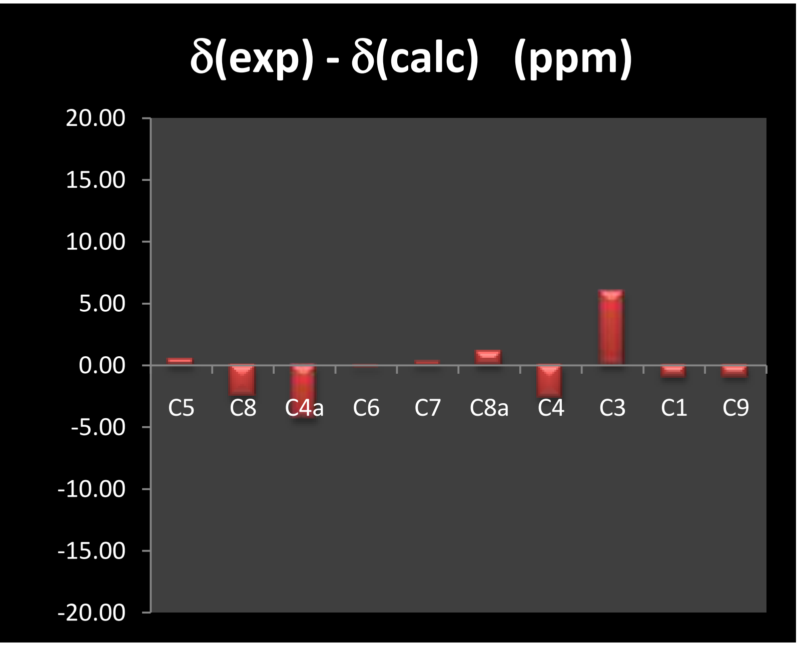
4a

MMFF conformer // AM1 geometry // B3LYP/6-31G(d) geometry optimization // GIAO B3LYP/6-311+G(d,p)

Carbon number	C_5	C_8	C_{4a}	C_6	C_7	C_{8a}	C_4	C_3	C_1	C_9
gaussian carbon label	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**C11**	**C12**	**C17**	**C19**
CH3 ceto GIAO shielding (ppm)	50.5872	47.2093	33.1608	43.5783	50.1568	54.4161	133.807	13.2645	15.1571	155.598
CH3 ceto GIAO chemical shift (ppm)	**126.82**	**130.20**	**144.25**	**133.83**	**127.25**	**122.99**	**43.60**	**164.14**	**162.25**	**21.81**
experimental chemical shift (ppm)	**127.30**	**127.70**	**140.00**	**133.70**	**127.50**	**124.10**	**41.00**	**170.10**	**161.30**	**20.90**
δ(exp) - δ(calc) (ppm)	0.48	-2.50	-4.25	-0.13	0.25	1.11	-2.60	5.96	-0.95	-0.91
| δ(exp) - δ(calc) | (ppm)	**0.48**	**2.50**	**4.25**	**0.13**	**0.25**	**1.11**	**2.60**	**5.96**	**0.95**	**0.91**

MEAN ABSOLUTE ERROR (ppm)
1.91



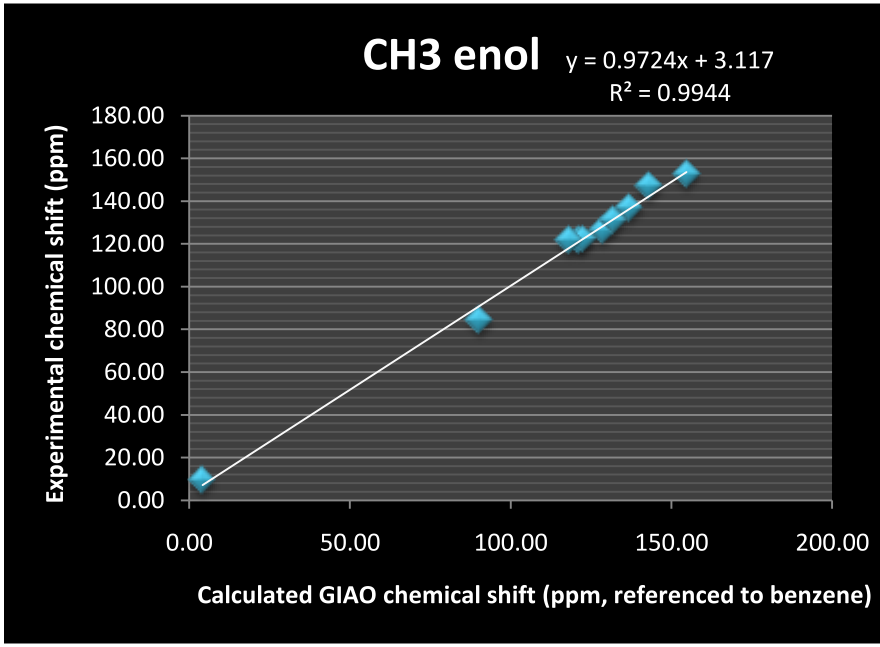


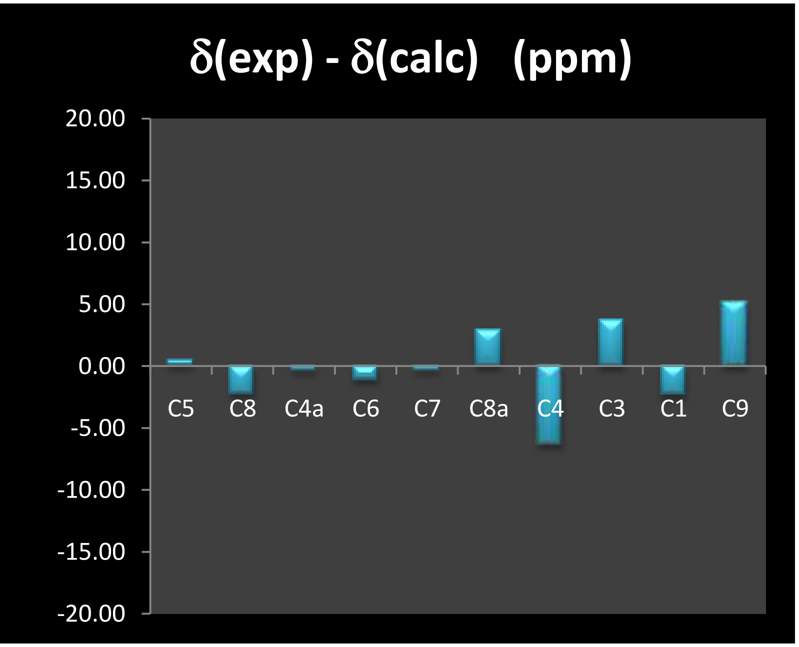
4b

MMFF conformer // AM1 geometry // B3LYP/6-31G(d) geometry optimization // GIAO B3LYP/6-311+G(d,p)

Carbon number	C_5	C_8	C_{4a}	C_6	C_7	C_{8a}	C_4	C_3	C_1	C_9
gaussian carbon label	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**C11**	**C12**	**C16**	**C18**
CH3 enol GIAO shielding (ppm)	56.0559	48.6781	40.1706	45.3227	54.9541	58.9598	87.0844	34.3345	22.6702	173.241
CH3 enol GIAO chemical shift (ppm)	**121.35**	**128.73**	**137.24**	**132.08**	**122.45**	**118.45**	**90.32**	**143.07**	**154.74**	**4.17**
experimental chemical shift (ppm)	**121.80**	**126.50**	**136.90**	**131.00**	**122.10**	**121.30**	**84.00**	**146.70**	**152.40**	**9.30**
δ(exp) - δ(calc) (ppm)	0.45	-2.23	-0.34	-1.08	-0.35	2.85	-6.32	3.63	-2.34	5.13
| δ(exp) - δ(calc) | (ppm)	**0.45**	**2.23**	**0.34**	**1.08**	**0.35**	**2.85**	**6.32**	**3.63**	**2.34**	**5.13**

MEAN ABSOLUTE ERROR (ppm)
2.47



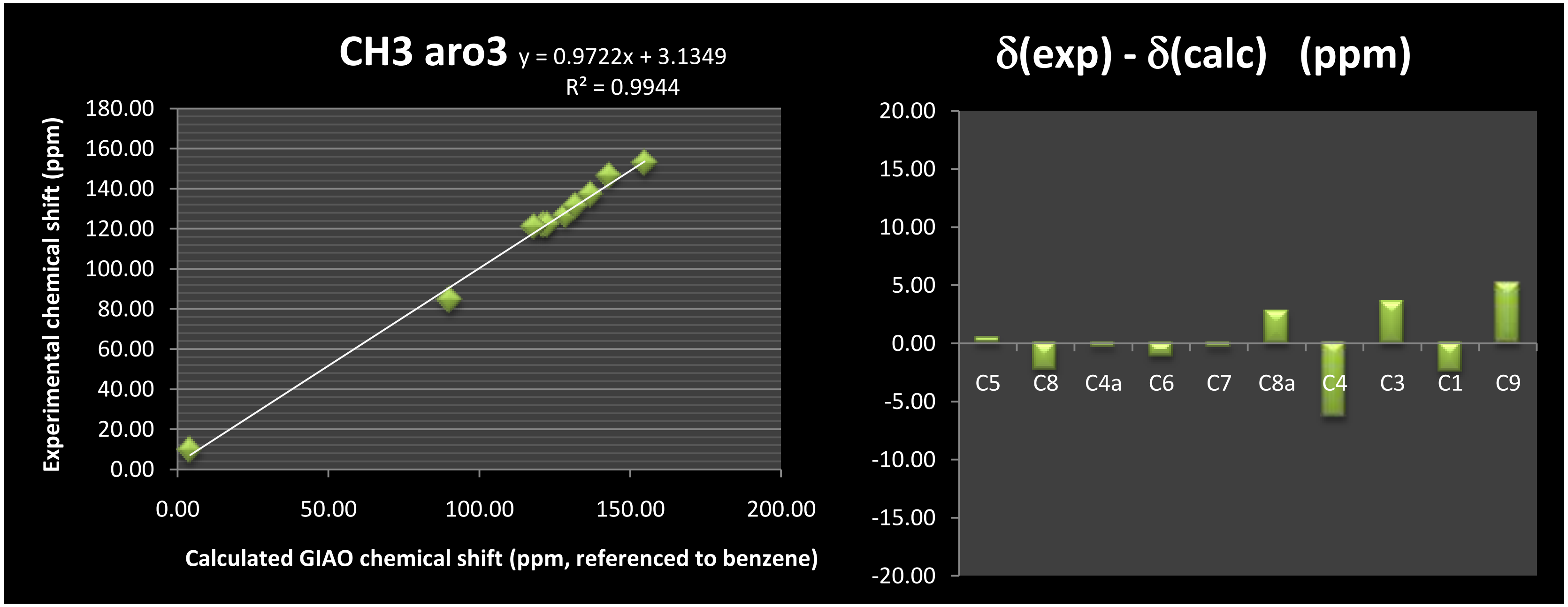


4c

MMFF conformer // AM1 geometry // B3LYP/6-31G(d) geometry optimization // GIAO B3LYP/6-311+G(d,p)

Carbon number	C_5	C_8	C_{4a}	C_6	C_7	C_{8a}	C_4	C_3	C_1	C_9
gaussian carbon label	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**C11**	**C12**	**C14**	**C15**
CH3 aro3 GIAO shielding (ppm)	56.0485	48.6668	40.1673	45.3118	54.9556	58.9366	87.0847	34.3303	22.6003	173.249
CH3 aro3 GIAO chemical shift (ppm)	**121.36**	**128.74**	**137.24**	**132.10**	**122.45**	**118.47**	**90.32**	**143.08**	**154.81**	**4.16**
experimental chemical shift (ppm)	**121.80**	**126.50**	**136.90**	**131.00**	**122.10**	**121.30**	**84.00**	**146.70**	**152.40**	**9.30**
δ(exp) - δ(calc) (ppm)	0.44	-2.24	-0.34	-1.10	-0.35	2.83	-6.32	3.62	-2.41	5.14
| δ(exp) - δ(calc) | (ppm)	**0.44**	**2.24**	**0.34**	**1.10**	**0.35**	**2.83**	**6.32**	**3.62**	**2.41**	**5.14**

MEAN ABSOLUTE ERROR (ppm)
2.47

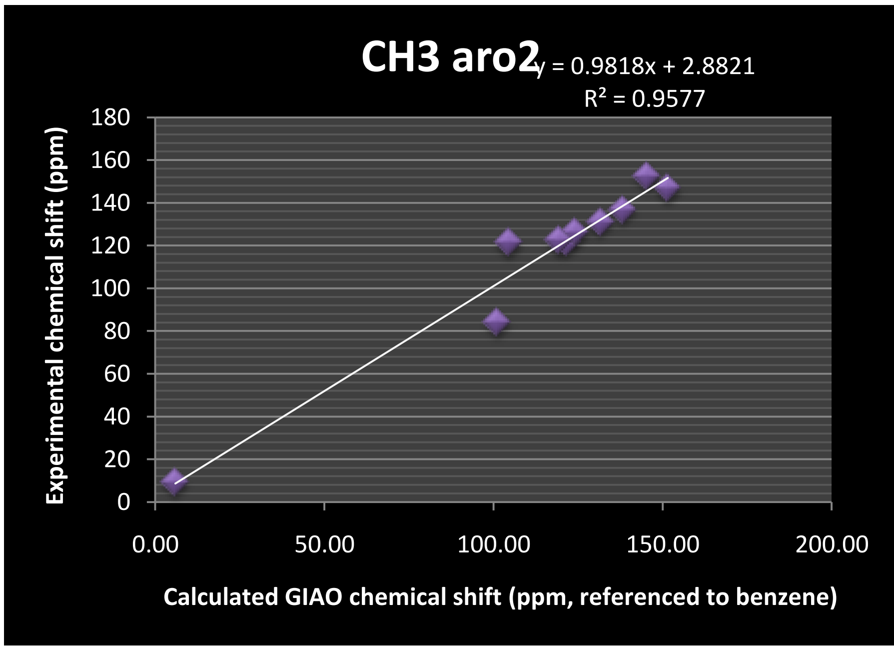


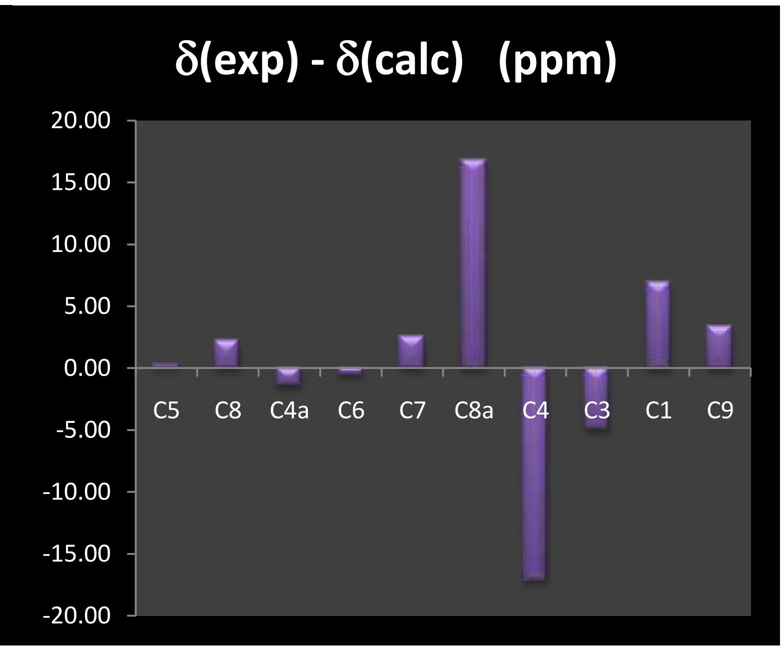
4d

MMFF conformer // AM1 geometry // B3LYP/6-31G(d) geometry optimization // GIAO B3LYP/6-311+G(d,p)

Carbon number	C_5	C_8	C_{4a}	C_6	C_7	C_{8a}	C_4	C_3	C_1	C_9
gaussian carbon label	C2	C3	C4	C5	C6	C7	C11	C12	C14	C15
CH3 aro2 GIAO shielding (ppm)	55.887	53.0938	39.1032	45.8544	57.8362	72.8063	76.269	25.8215	31.9243	171.526
CH3 aro2 GIAO chemical shift (ppm)	**121.52**	**124.31**	**138.30**	**131.55**	**119.57**	**104.60**	**101.14**	**151.59**	**145.48**	**5.88**
experimental chemical shift	**121.8**	**126.5**	**136.9**	**131**	**122.1**	**121.3**	**84**	**146.7**	**152.4**	**9.3**
δ(exp) - δ(calc) (ppm)	0.28	2.19	-1.40	-0.55	2.53	16.70	-17.14	-4.89	6.92	3.42
| δ(exp) - δ(calc) | (ppm)	**0.28**	**2.19**	**1.40**	**0.55**	**2.53**	**16.70**	**17.14**	**4.89**	**6.92**	**3.42**

MEAN ABSOLUTE ERROR (ppm)
5.60



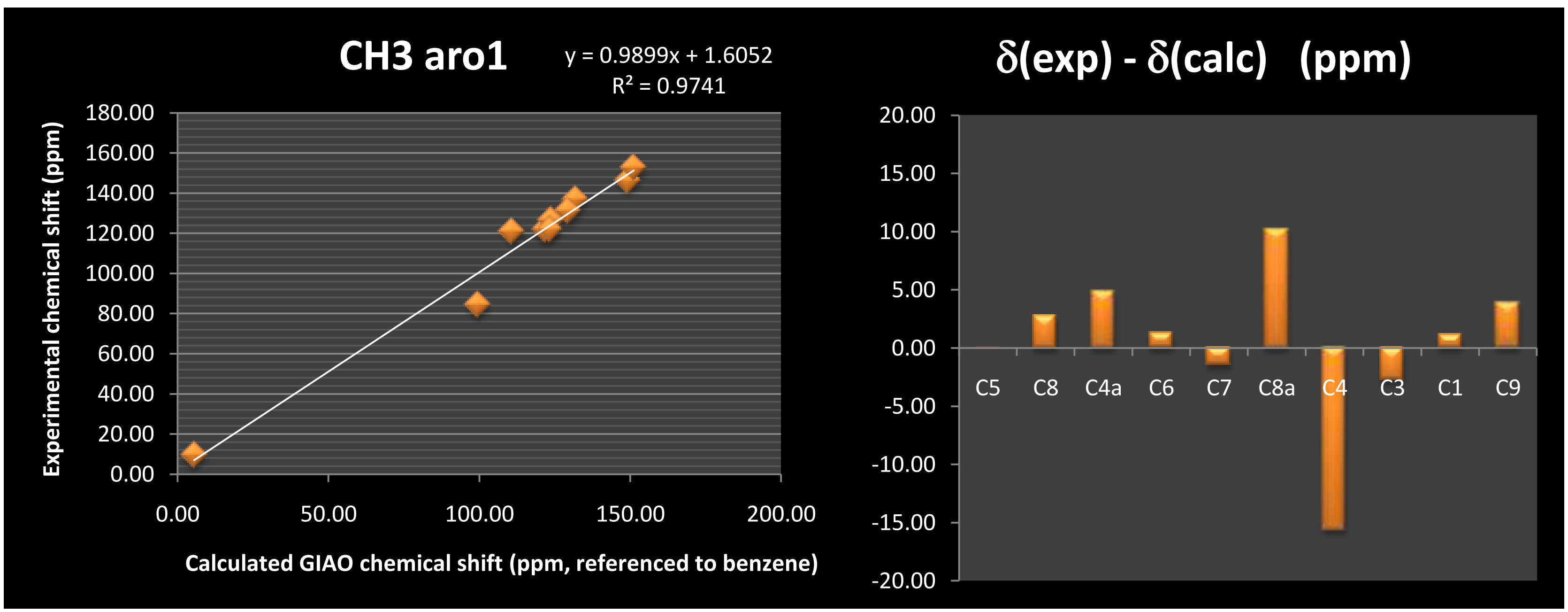


4e

MMFF conformer // AM1 geometry // B3LYP/6-31G(d) geometry optimization // GIAO B3LYP/6-311+G(d,p)

Carbon number	C_5	C_8	C_{4a}	C_6	C_7	C_{8a}	C_4	C_3	C_1	C_9
gaussian carbon label	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**C11**	**C12**	**C15**	**C16**
CH3 aro1 GIAO shielding (ppm)	55.5866	53.7329	45.4254	47.6505	53.8292	66.36	77.8392	28.0354	26.1694	171.943
CH3 aro1 GIAO chemical shift (ppm)	**121.82**	**123.67**	**131.98**	**129.76**	**123.58**	**111.05**	**99.57**	**149.37**	**151.24**	**5.46**
experimental chemical shift (ppm)	**121.80**	**126.50**	**136.90**	**131.00**	**122.10**	**121.30**	**84.00**	**146.70**	**152.40**	**9.30**
δ(exp) - δ(calc) (ppm)	-0.02	2.83	4.92	1.24	-1.48	10.25	-15.57	-2.67	1.16	3.84
| δ(exp) - δ(calc) | (ppm)	**0.02**	**2.83**	**4.92**	**1.24**	**1.48**	**10.25**	**15.57**	**2.67**	**1.16**	**3.84**

MEAN ABSOLUTE ERROR (ppm)
4.39



MMFF conformer // AM1 geometry // B3LYP/6-31G(d) geometry optimization // GIAO B3LYP/6-311+G(d,p)

	calculated energy		relative energy
	hartrees (a.u.)	kcal/mol	kcal/mol
COOMe ceto	-855.6846	-536950.2042	5.5649
COOMe enol	-855.6935	-536955.7593	0.0098
COOMe aro3	-855.6935	-536955.7691	0.0000
COOMe aro2	-855.6765	-536945.1033	10.6658
COOMe aro1	-855.6700	-536941.0557	14.7134
CH3 ceto	-667.0735	-418594.9676	0.0000
CH3 enol	-667.0676	-418591.2345	3.7331
CH3 aro3	-667.0676	-418591.2310	3.7366
CH3 aro2	-667.0584	-418585.4430	9.5246
CH3 aro1	-667.0670	-418590.8760	4.0916

GIAO Standard:	Benzene
shielding (ppm)	49.1069
experimental chemical shift in DMSO-d_6	128.3