SYNTHESIS, BIOLOGICAL ACTIVITIES AND CHARACTERIZATION OF SOME SUBSTITUTED OXIME IMIDAZOLES

[1]KEYUR D. MARKANA, [2] Dr. RAVI B. PATEL
[1] M.Phil. , [2] Professor
[1,2]P.M. Patel College, Department of chemistry, Anand, Gujarat
[1,2]S.P. University, Vidhyanagar, Anand, Gujarat, India

***Abstract*:** There are series of new imidazole derivative. These are synthesise from 1- (2.4-dichlorophenyl)-2-(1H-imidazol-1yl) ethanone oxime condensation with different type halogenated compounds. These are all new compound characterized by NMR, Mass and IR spectra**.**

Keywords: Imidazole derivative, Schiff base, antifungal activity, condensation

I. INTRODUCTION:

Imidazole is a heterocyclic ring containing basically 3C and 2N atom present in 1st and 3rd positions [1]. Imidazole is a colourless organic compound having melting point 89-91 °C and boiling point is 256 °C. It has high boiling point as compared all other five member heterocyclic compounds. In marked contrast to imidazole, the boiling point of 1- methylimidazole is comparatively low. It demonstrates that hydrogen bonding exists in imidazole ring and may consist up to 20 molecules. Imidazole is more basic having pay value is about 7.2. It contains pyrrole type amino nitrogen in the ring and forms metallic salts with NaNH2 and RMgX which are extensively hydrolyzed by water. The introduction of alkyl groups into the ring increases the basicity. Imidazole is an aromatic compound and possesses resonance energy of 14.2Kcal/mole. The dipole moment of imidazole has been measured in several solvents [2]. Imidazoles are common scaffolds in highly significant biomolecules including the essential amino acid histidine, histamine, pilocarpine alkaloids [3,4], and other alkaloids, which have been shown to exhibit interesting biological activities such as antimicrobial, anti-inflammatory [5,6], histamine H3 antagonist [5,7], antioxidant [5,8], farnesyltransferase and geranyl transferase-I inhibitor [5,9], antitumor [10], ant parasitic [11], antiprotozoal [12,13], and ant diabetic activities [14]. Based on above observation it is synthesizing novel imidazole derivatives (D1-4) to elute possible pharmacological activities like antifungal.

II. MATERIALS AND METHODS:

Its synthesised by condensation reaction .In this synthesis used Schiff base. It is basic molecule of these new series and other compounds are halogenated. Halogenated compound used from AR grade and LR grade which companies are Merck, sigma, renkem etc. Product yield depends on conversion of reaction and purification. In during reaction, completion of the reaction is decided by the thin layer chromatography (TLC) with UV chambers. In this reaction raw material and product have different RF value and use different solvent system gives different RF value. Physical parameters data of compounds are recorded in Table 2.1 and spectral data recorded in Table 2.2.

Table 2.1: Physical parameters of compounds

Compound	Molecular Formula	Molecular Weight	%Yield
D1	C17H14Cl2N4O	361.23	60%
D2	C17H13Cl3N4O	395.67	59%
D3	C18H15Cl2N3O2	376.24	51%
D4	C18H13Cl2N3O2	374.22	60%

Table 2.2: Spectral analysis of synthesized compounds

Compound	IR	1HNMR	MASS
D1	736 (1,2 position), 920 (1,2,4 position), 1670 (- C=N), 1346-1548 (-N-O), 1286 (Aromatic amine), 820 (-C-Cl), 821 (-C-Cl)	5.759 (2H of –CH2), 6.955 (2H of –NH2), 7.306 – 8.037 (10H of phenyl)	m/z- 138 (M+2), 204 (M+2), 216 (M+2), 266 (M-1)
D2	736 (1,2,3 position), 920 (1,2,4 position), 1674 (- C=N), 1348-1550 (-N-O), 1288 (Aromatic amine), 856 (-C-Cl), 813 (-C-Cl), 661 (- C-Cl)	5.767 (2H of –CH2), 6.595 (2H of –NH2), 7.314 – 8.034 (9H of phenyl)	m/z- 171 (M-3), 204 (M+2), 216 (M), 232 (M+1)
D3	927 (1,2,4 position), 821 (1,4 position), 1238 (Alkyl aryl ether), 1629 (-C=N), 1301-1560 (-N-O), 734 (-C- Cl), 653 (-C-Cl)	3.478 (3H of –OCH3), 5.575 (2H of –CH2), 7.302-8.036 (10H of phenyl)	m/z- 108 (M), 136 (M-1), 165 (M+1), 231 (M+2)
D4	922 (1,2,4 position), 810 (1,4 position), 1701 (-CHO), 1629 (-C=N), 1346-1543 (- N-O), 732 (-C-Cl), 705 (-C- Cl)	5.575 (2H of –CH2), 7.302-8.036 (10H of phenyl), 9.287 (1H of –CHO)	m/z- 106 (M+1), 136 (M-1), 165 (M+1), 231 (M+2)

III. Synthesis of Compounds (D1 to D4)

Take a 1.00 gm. of 1-(2, 4-dichlorophenyl)-2-(1H-imidazol-1-yl) ethanone oxime in 25 ml RBF with condenser, thermometer pocket, magnetic stirrer on oil bath. Charge Dimethylsulfoxide (DMSO) and sodiumhydroxide flakes. Stir the reaction up to clear solution observe at 30±5ºC. Then add halogenated compound (-RX) at 30±5ºC. After completion of addition heat the reaction mass at 95±5ºC.Reaction monitoring by TLC. After completion of reaction cool the reaction mass at 30±5ºC and then charge Purified water and Ethyl acetate. Stir it for 10 to 15 minute and then separate the layer. Take Ethyl acetate layer and distil out below 60ºC under vacuumed. Solid mass observe. Recrystallized by acid–base purification. Scheme was illustrated in Figure 1 and physical data were given in the Table 3.1.

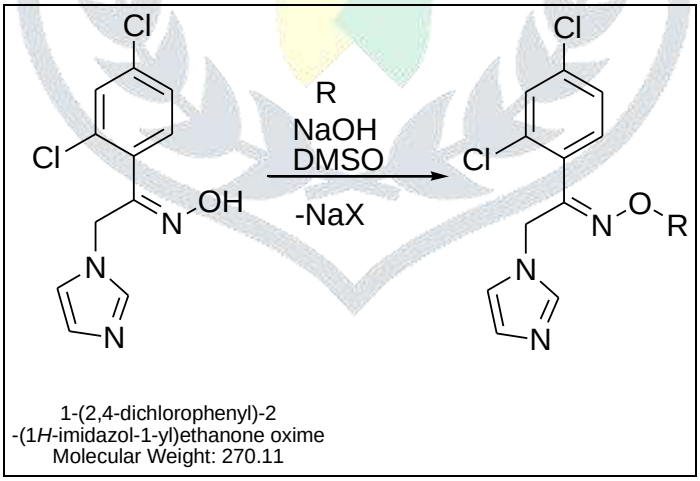
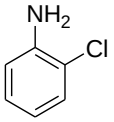
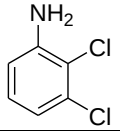
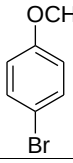
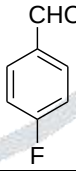


Fig 1: Scheme for the synthesis of compound

Table 3.1: Physical data of compounds

Sr. NO.	Compound Code	-R	Name of –R
1	D 1		2-Chloroaniline
2	D 2		2,3-Dichloroaniline
3	D 3		1-Bromo 4-methoxy benzene
4	D 4		4-Flourobenzaldehyde

IV. Antifungal activity

The compounds were tested in-vitro for their antifungal activity against Aspergillus Niger using Cup-plate agar diffusion method.

V. Results and discussion

All the synthesized compounds were characterized and identified by using TLC, IR, 1HNMR, and mass. The substituted imidazoles have been reported for number of pharmacology activities. The prepared compounds have antifungal activity by using cup-plate agar diffusion method against various gram positive, gram negative and fungal strain.

VI. Conclusion

The synthesized of derivatives of imidazoles compounds A1, A2, A3, and A4 are novel. In this view, we have derivatives for their medicinal values with the help text books. Compounds A1, A2, A3, and A4 have shown antifungal activity. These compounds with suitable modification can be explored better for their therapeutic activities in future.

VII. Acknowledgement

Greatly acknowledge to P.M. Patel College, Department of chemistry, Anand, Gujarat, India, for allowing to study of novel compound. I am also thankful to my guide Dr. Ravi B. Patel for support me to this work.

REFERENCES:

[1] McDonnell, M. Fungal infections in the newborn. Semin Neonatal, 1996, 1, 141-145.

[2] R. J. Bansal; Heterocyclic Chemistry, New Age Publishers, 2006.

[3] Bellina, F.; Cauteruccio, S.; Rossi, R. Synthesis and biological activity of vicinal diaryl- substituted 1H-imidazoles. Tetrahedron, 2007, 63, 4571-4624.

[4] Grimmett, M.R. Comprehensive Heterocyclic Chemistry II; Katritsky, A.R., Scriven, E.F.V., Eds.; Pergamon: Oxford, 1996, 3, 77-220.

[5] Boiani, M.; González, M. Imidazole and benzimidazole derivatives as chemotherapeutic agents. Mini-Reviews Med. Chem., 2005, 5, 409-424.

[6] Wright, S.W.; Harris, R.R.; Collins, R.J.; Corbett, R.L.; Green, A.M.; Wadman, E.A.; and Batt, D.G. Novel l-(Pyridylphenyl)-lphenyl- 2-imidazolyl ethanols with topical anti-inflammatory activity. J. Med. Chem., 1992, 35, 3148-3155.

[7] Gramann, S.; Sadek, B.; Ligneau, X.; Elz, S.; Ganellin, C.R.; Arrang, J.M.; Schwartz, J.C.; Stark H.; Schunack, W. Progress in the proxifan class: Heterocyclic congeners as novel potent and selective histamine H3-receptor antagonists. Eur. J. Pharm. Sci., 2002, 15, 367-378.

[8] Soujanya, Y.; Sastry, G.N. Theoretical elucidation of the antioxidant mechanism of 1,3- dihydro-1-methyl-2H-imidazole-2-selenol (MSeI). Tetrahedron Letters, 2007, 48, 2109-2112.

[9] Nguyen, D.N.; Stump, C.A.; Walsh, E.S.; Fernandes, C.; Davide, J.P.; Ellis-Hutchings, M.; Robinson, R.G.; Williams, T.M.; Lobell, R.B.; Huber H.E.; Buser, C.A. Potentinhibitors of farnesyltransferase and geranylgeranyltransferase-I. Bioorg. Med. Chem. Lett., 2002, 12, 1269-1273.

[10] Chen, J.; Wang, Z.; Lu, Y.; Dalton, J.T.; Millera, D.D.; Li, W. Synthesis and antiproliferative activity of imidazole and imidazoline analogues for melanoma. Bioorg. Med. Chem. Lett., 2008, 18, 3183-3187.

[11] Das, P.; Himaja, M. Design and synthesis of 4-[2-(5- Nitro)]imidazolylbenzoyl(N- methyl) aminoacids and peptides. Int. J. Drug Develop. Res., 2010, 2(2), 364-370.

[12] Ferreira, S.B.; Costa, M.S.; Boechat, N.; Bezerra, R.J.S.; Genestra, M.S.; Canto- Cavalheiro, M.M.; Kover, W.B.; Ferreira, V.F. Synthesis and evaluation of new difluoromethyl azoles as antileishmanial agents. Eur. J. Med. Chem., 2007, 42, 1388-1395.

[13] Valdez, C.A.; Tripp, J.C.; Miyamoto, Y.; Kalisiak, J.; Hruz, P.; Andersen, Y.S.; Brown, S .E.; Kangas, K.; Arzu, L. V.; Davds, B.J.; Gillin, F.D.; Upcroft, J.A.; Upcroft, P.; Fokin, V.V.; Smith, D.K.; Sharpless, K.B.; Eckmann, L. Synthesis and electrochemistry of 2-ethenyl and 2-ethanyl derivatives of 5-Nitroimidazole and antimicrobial activity against Giardia lamblia. J. Med. Chem., 2009, 52, 4038-4053.

[14] Dominianni, S.J.; Yen, T.T. Oral hypoglycemic agents. Discovery and structure-activity relationships of phenacylimidazolium halides. J. Med. Chem., 1989, 32, 2301-2306

[15] Bo¨hm, V. P. W.; Herrmann, W. A. Eur. J. Org. Chem. 2000, 3679–3681.

[16] Pd(PhCN)2Cl2/PBut 3 and CuI have been used for the coupling of aryl bromides at room temperature. See: Hundertmark, T.; Littke, A. F.; Buchwald, S. L.; Fu, G. C. Org. Lett. 2000, 2, 1729–1731.

[17] Mori, A.; Kawashima, J.; Shimada, T.; Suguro, M.; Hirabayashi, K.; Nishihara, Y. Org. Lett. 2000, 2, 2935– 2937.

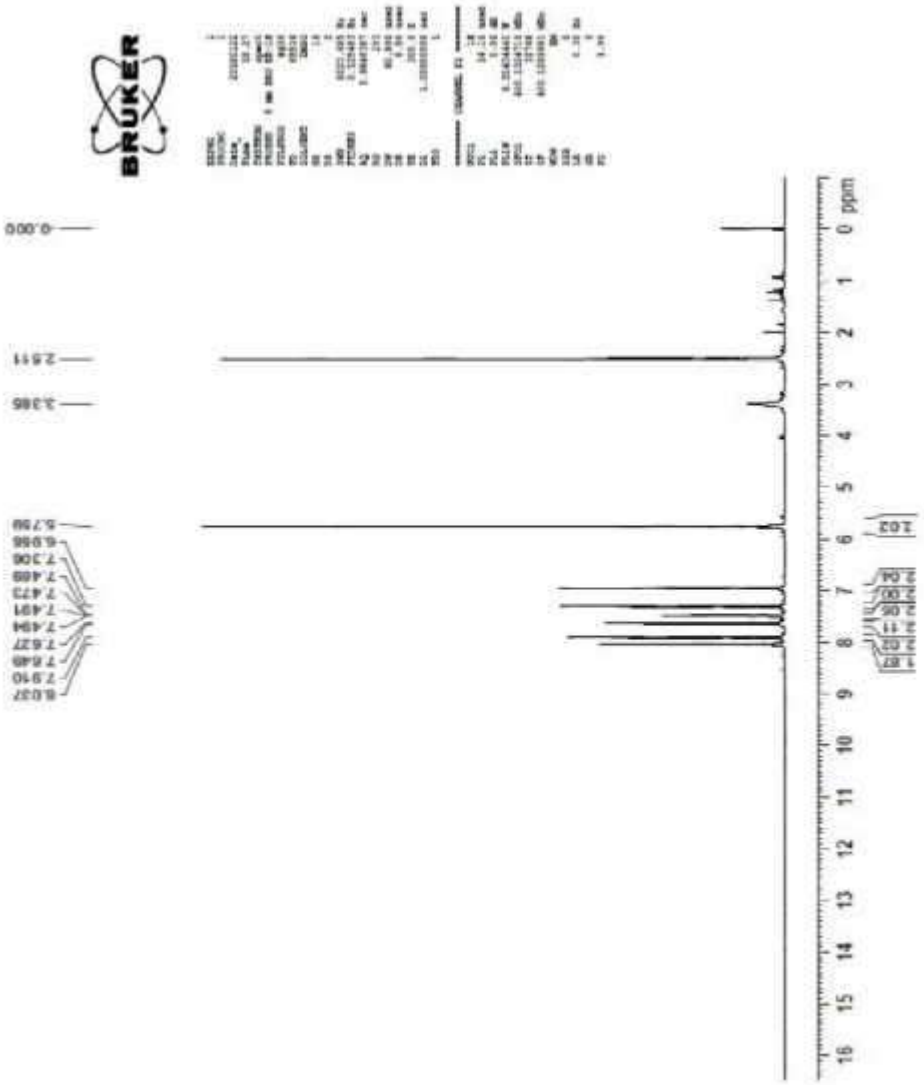
[18] In the case of using TBAF or TBAOH as activators, the reaction coupling is rather sluggish and copper iodide has to be added in a further improved procedure. See: Mori, A.; Shimada, T.; Kondo, T.; Sekiguchi, A. Synlett 2001, 649–651. 9368 D. A. Alonso et al. / Tetrahedron Letters 43 (2002) 9365–9368

[19] Eberhard, M. R.; Wang, Z.; Jensen, C. M. Chem. Commun. 2002, 818–819.

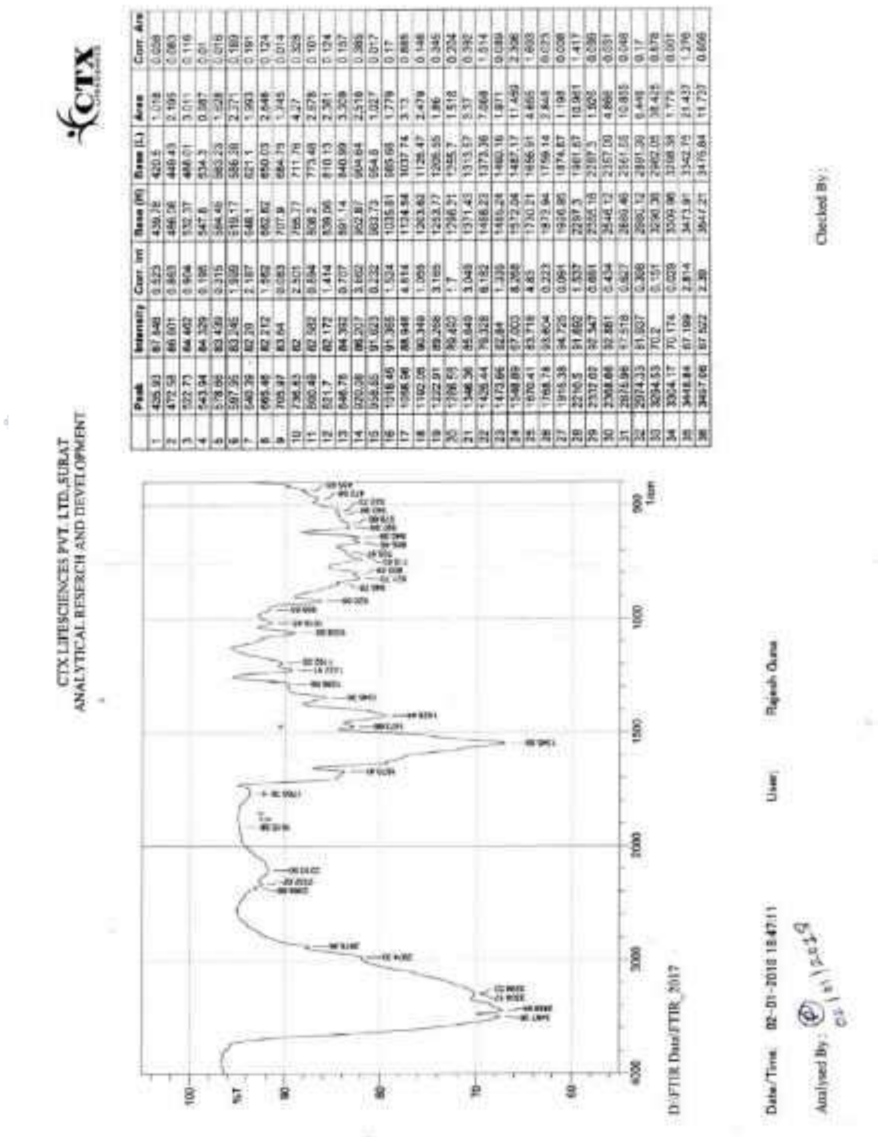
[20] Dang, H.; Garcia-Garibay, M. A. J. Am. Chem. Soc. 2001, 123, 355–356;

[21] Dang, H.; Levitus, M.; Garcia- Garibay, M. A. J. Am. Chem. Soc. 2002, 124, 136–143; [22] Godinez, C. E.; Zepeda, G.; Garcia-Garibay, M. A. J. Am. Chem. Soc. 2002, 124, 4701–4707

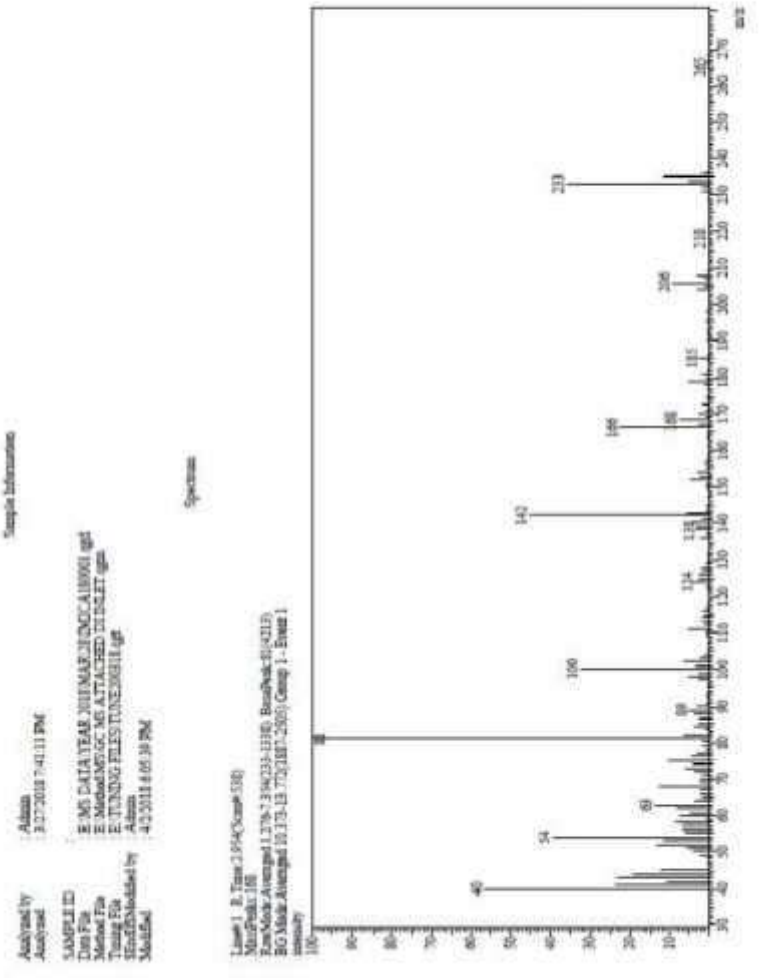
NMR of D_1


BRUKER
0.000
2.511
3.386
5.759
6.027
7.910
7.648
7.627
7.494
7.491
7.473
7.469
7.306
6.956
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16

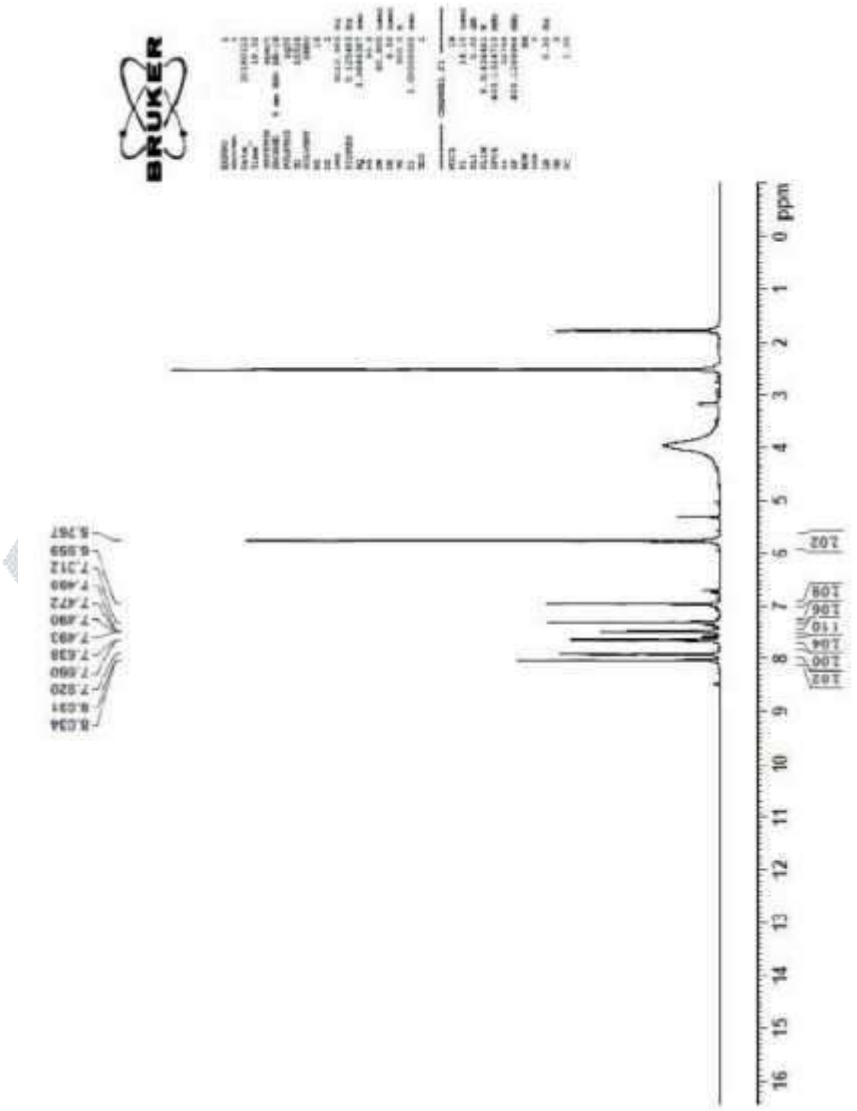
IR of D_1


CTX LIFESCIENCES PVT. LTD., SURAT
ANALYTICAL RESEARCH AND DEVELOPMENT
CTX

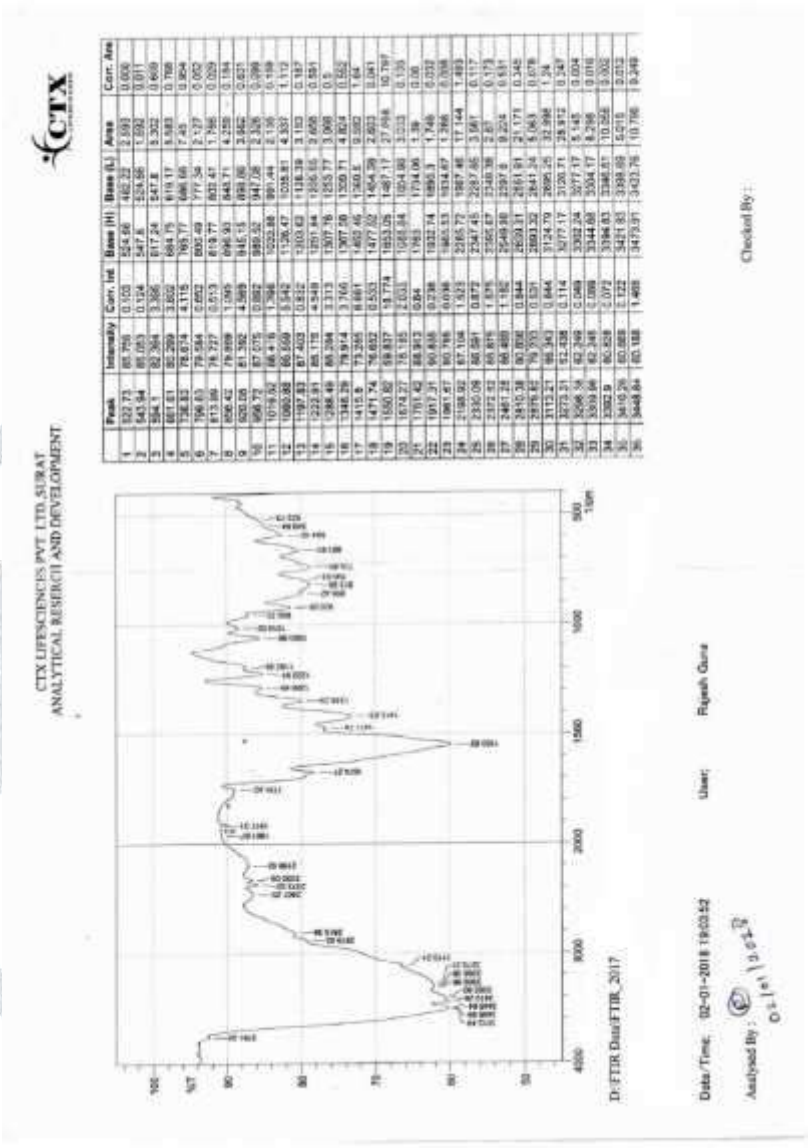
Mass of D_1



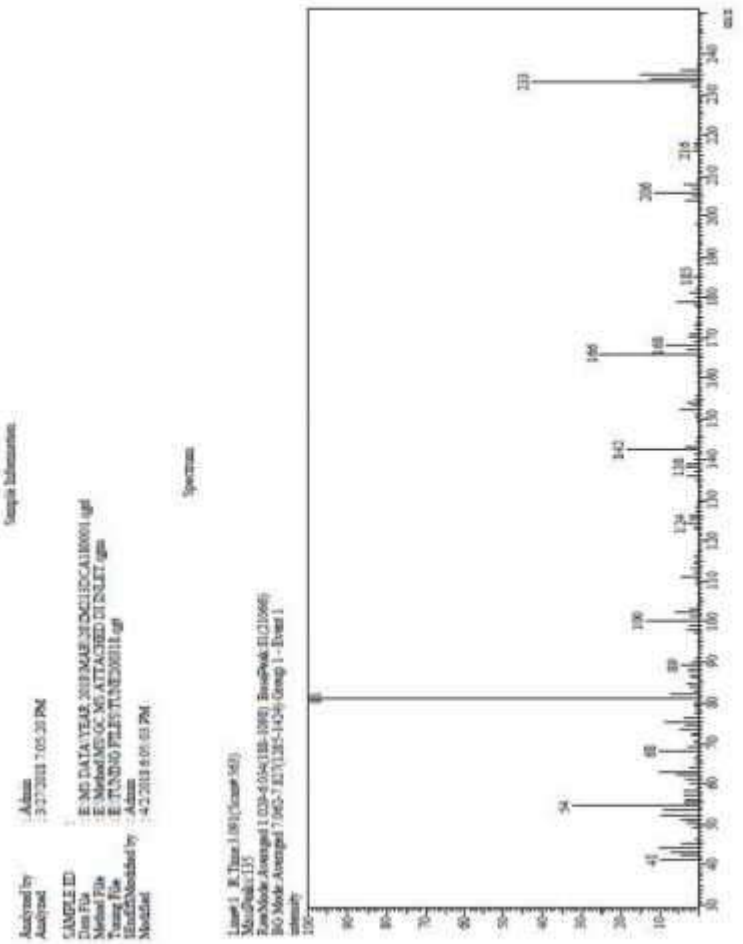
NNR of D_2


BRUKER
ppm
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
8.034
8.031
7.820
7.660
7.638
7.493
7.490
7.472
7.469
7.312
6.959
6.957
2.02
1.09
1.06
1.10
1.04
2.00
1.02

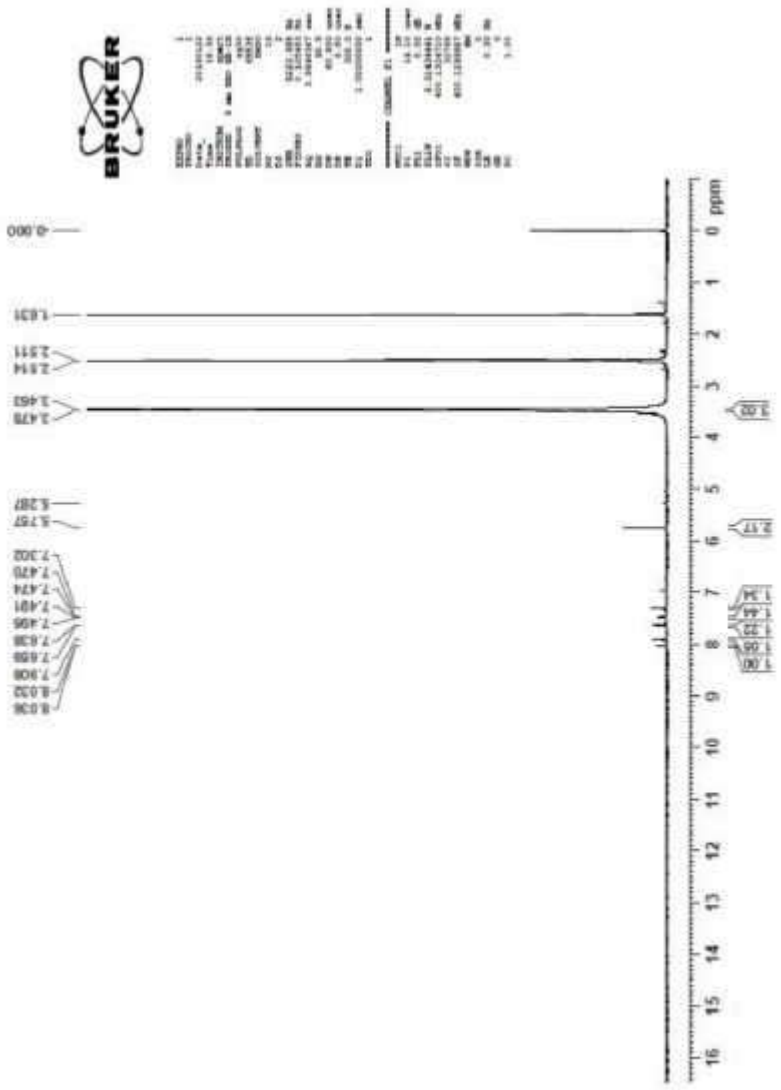
IR of D_2


CTX LIFESCIENCES PVT. LTD.,SURAT
ANALYTICAL RESEARCH AND DEVELOPMENT
D:\FTIR Data\FTIR_2017
Data/Time: 02-01-2018 19:03:52
User: Rajesh Guna
Checked By :

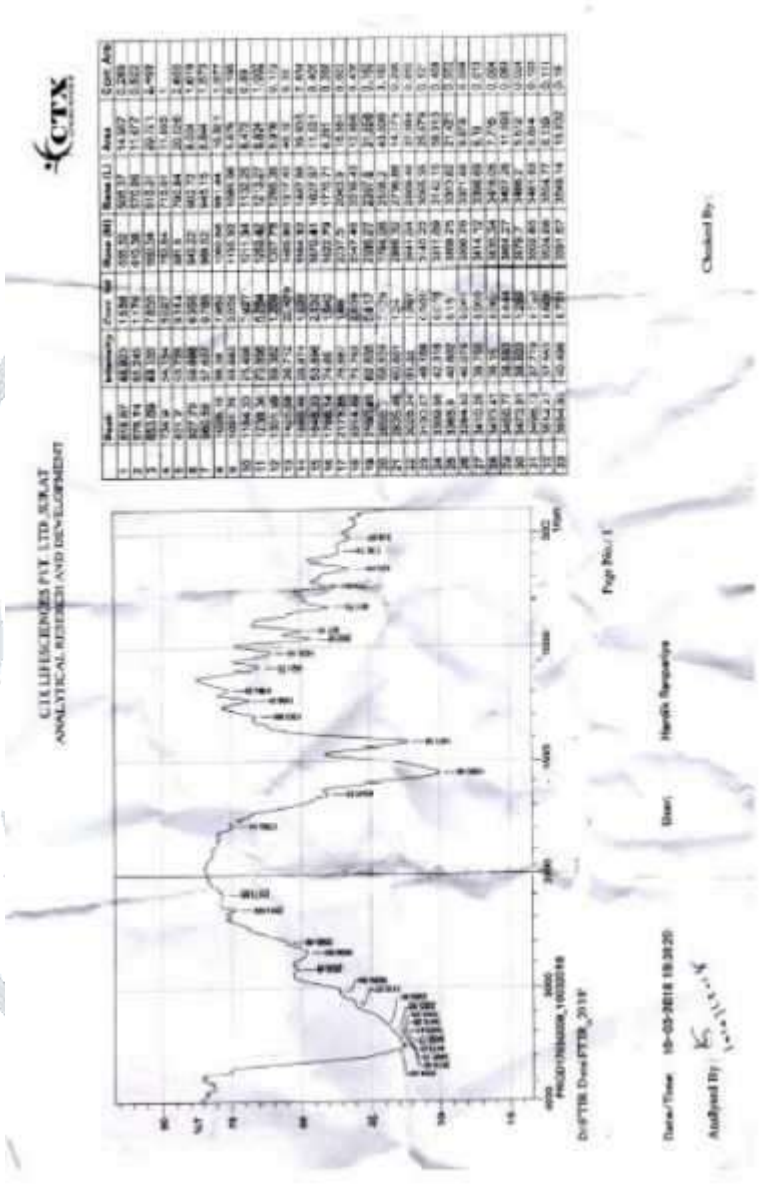
Mass of D_2



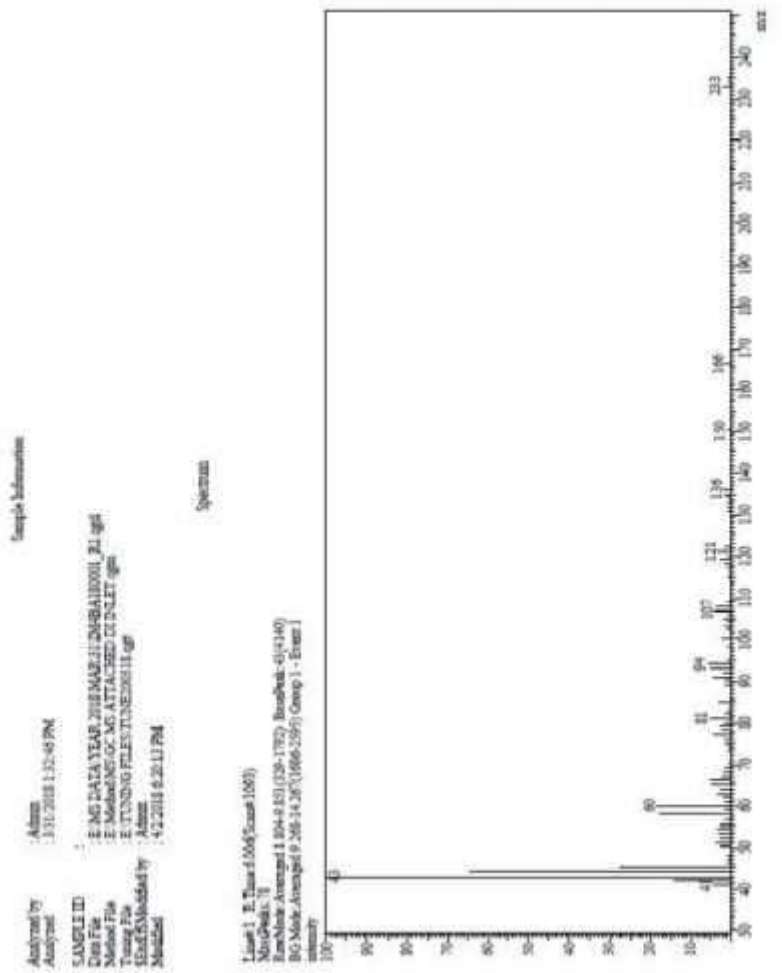
NMR of D_3


BRUKER
0.000
1.631
2.311
2.314
3.452
3.478
5.287
5.757
7.302
7.420
7.474
7.491
7.496
7.638
7.659
7.908
8.032
8.036
3.00
2.17
1.34
1.44
1.25
1.05
1.00
ppm

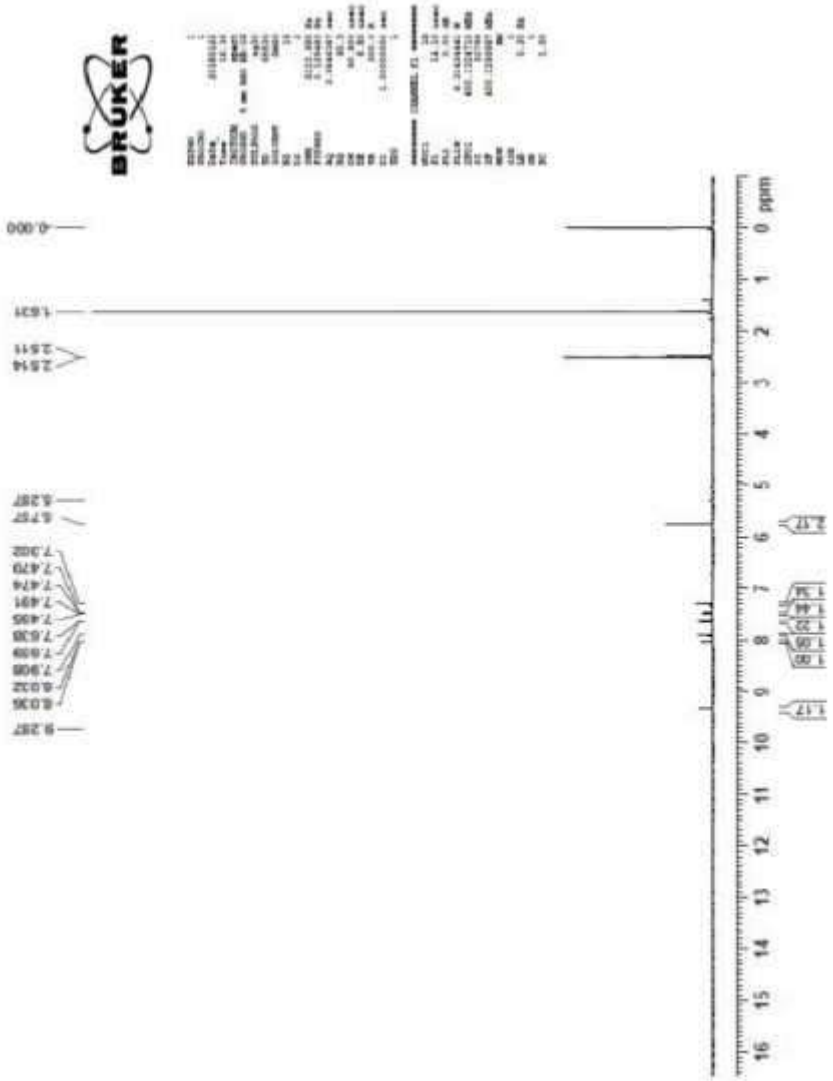
IR of D_3



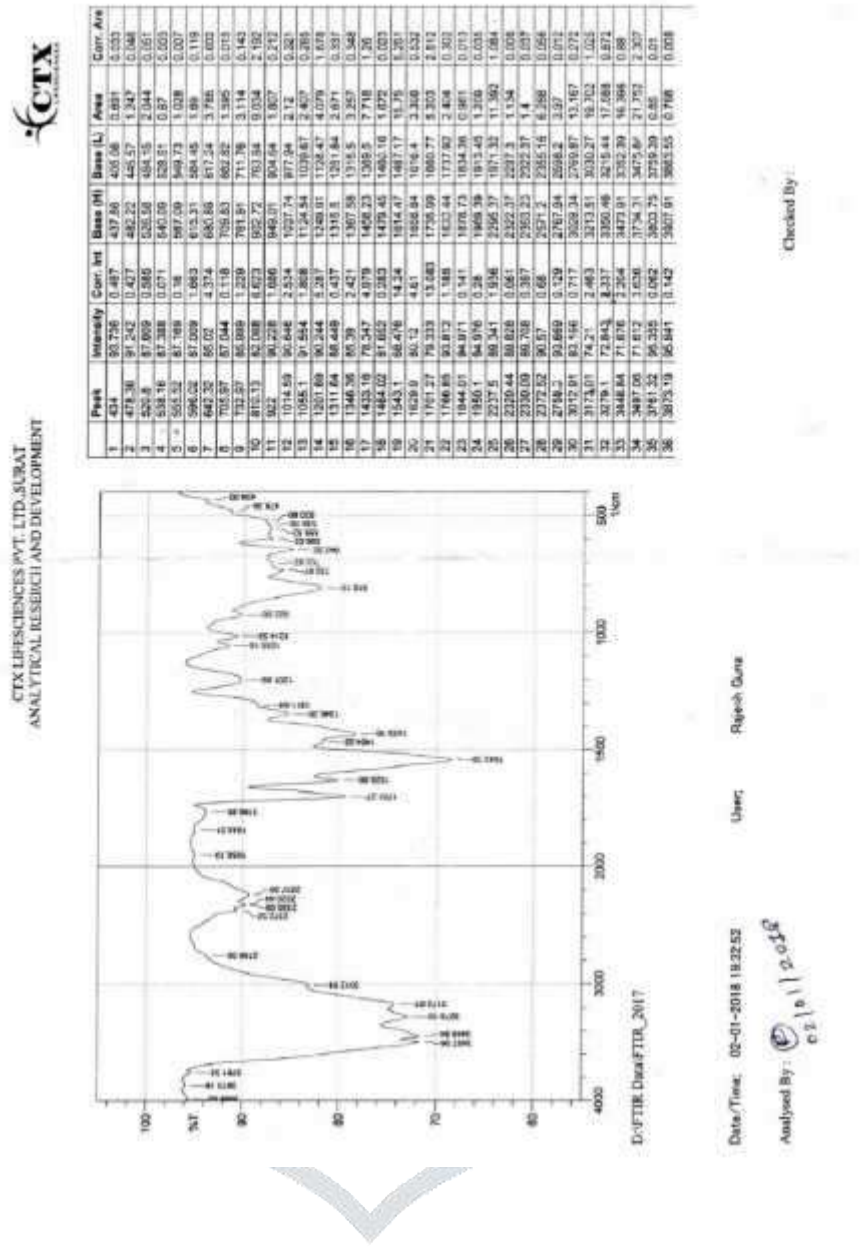
Mass of D_3



NMR of D_4



IR of D_4



	Peak	Intensity	Corr. Int.	Base (H)	Base (L)	Area	Corr. Area
1	434	93.726	0.487	437.86	406.98	0.691	0.033
2	478.36	91.242	0.427	482.22	445.57	1.347	0.068
3	524.8	87.909	0.386	528.58	484.15	2.044	0.161
4	538.16	87.388	0.071	640.06	528.51	0.87	0.003
5	555.52	87.189	0.18	597.09	549.73	1.028	0.007
6	596.02	87.009	1.663	615.31	564.45	1.99	0.119
7	642.32	86.02	4.374	680.86	617.24	3.788	0.603
8	705.97	87.044	0.118	709.83	682.82	1.395	0.013
9	732.87	86.089	1.229	791.91	711.76	3.114	0.143
10	815.13	82.088	6.623	952.72	763.84	9.034	2.192
11	922	91.428	1.086	948.01	904.14	1.807	0.242
12	1014.59	90.646	2.534	1037.74	977.94	2.12	0.321
13	1066.1	91.564	1.868	1124.54	1039.87	2.407	0.285
14	1201.89	90.244	5.287	1249.01	1128.47	4.079	1.678
15	1311.64	88.449	0.437	1316.1	1291.84	2.071	0.337
16	1346.36	89.39	2.421	1367.58	1316.5	3.267	0.548
17	1433.19	79.347	4.079	1458.23	1369.5	7.718	1.26
18	1464.02	81.662	0.363	1479.45	1460.16	1.072	0.103
19	1543.1	88.476	14.34	1614.47	1481.17	15.75	8.261
20	1629.9	90.12	4.61	1656.84	1616.4	3.368	0.532
21	1761.27	79.333	13.083	1795.99	1660.77	5.303	2.812
22	1796.85	93.872	1.188	1832.44	1737.82	2.404	0.303
23	1944.01	94.971	0.141	1978.73	1834.36	0.981	0.013
24	1960.1	94.976	0.26	1969.39	1913.45	1.376	0.035
25	2237.5	89.341	1.936	2295.37	1971.33	11.992	1.084
26	2320.44	89.828	0.061	2342.37	2297.3	1.134	0.008
27	2350.09	89.768	0.387	2363.23	2342.37	1.4	0.059
28	2372.02	90.57	0.68	2391.2	2365.16	6.398	0.056
29	2798.2	93.869	0.129	2807.84	2698.2	3.97	0.012
30	3012.91	83.166	0.717	3028.34	2799.87	13.167	0.272
31	3174.01	74.21	2.463	3213.51	3030.27	19.702	1.025
32	3279.1	72.843	4.237	3350.49	3215.44	17.688	0.872
33	3448.84	71.676	2.264	3473.91	3352.39	16.366	0.88
34	3497.06	71.612	1.636	3734.71	3475.89	21.752	2.357
35	3761.32	96.335	0.062	3803.75	3759.59	0.46	0.01
36	3875.19	95.841	0.142	3927.91	3865.55	0.766	0.008

Mass of D_4