Chitosan: A Highly Efficient Renewable and Recoverable Bio-Polymer Catalyst for Expeditious Synthesis of α-Amino nitriles and Imines under Mild Conditions

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Experimental

All chemicals were purchased from Merck or Aldrich and used as received except for benzaldehyde which a fresh distilled sample was used. Chitosan (MW= 600000-800000 Dalton) was purchased from Acros Organics company and used without any post-modification. Melting points were determined using an Electrothermal 9100 apparatus and are uncorrected. FT-IR spectra were recorded as KBr pellets on a Shimadzu FT IR-8400S spectrometer. ^{1}H NMR (500 MHz) spectra were obtained using a Bruker DRX-500 AVANCE spectrometer. Analytical TLC was carried out using Merck 0.2 mm silica gel 60 F-254 Al-plates.

General procedure for synthesis of α-amino nitriles 4 catalysed by chitosan (1a)

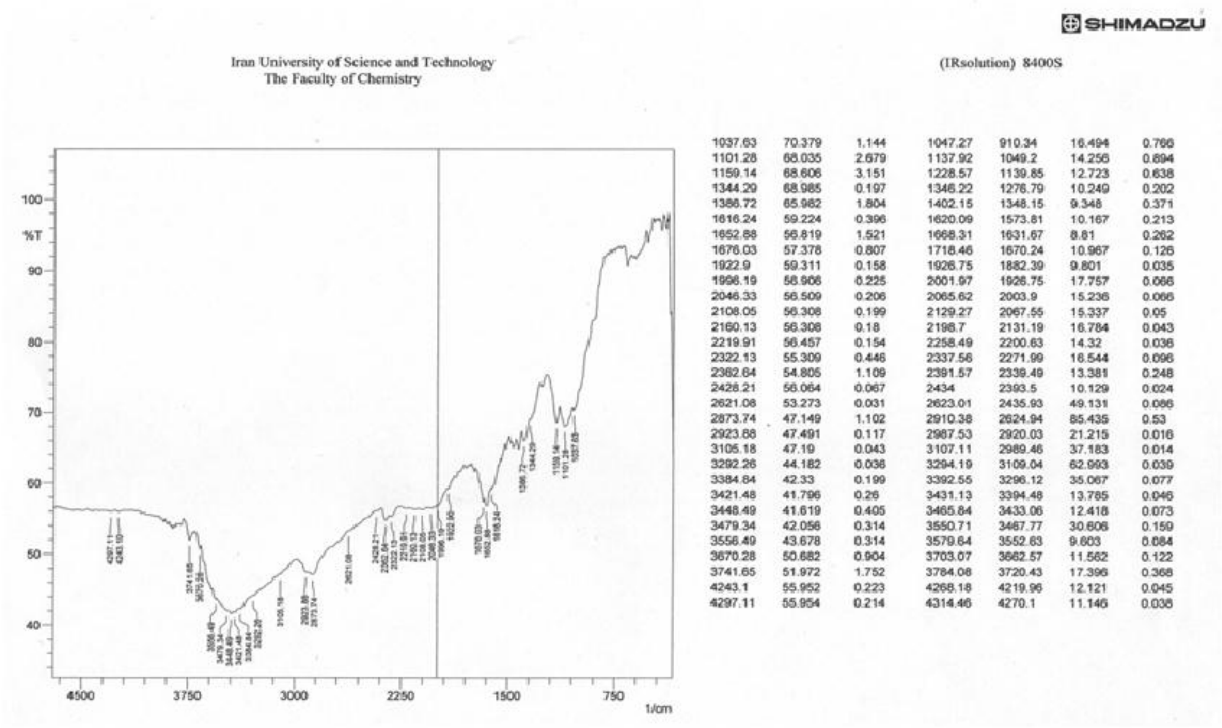
In a 5 mL round bottom flask equipped with a magnetic bar and condenser, a mixture of aldehyde **2** (1 mmol), amine **3** (1 mmol), and TMSCN (1.2 eq, 0.15 mL) and 6 mg chitosan (**1a**) was stirred under solvent-free conditions at room temperature. After completion of the reaction, as indicated by precipitation of solid products from liquid reaction mixture and TLC experiments using authentic samples,[8] the reaction mixture was crystalyzed from EtOH 96% (5 mL) to afford pure desired α-amino nitriles **4**.[8,10,26i,j,27a]

References: (a) M. G. Dekamin, Z. Mokhtari, *Tetrahedron*, 2012, **68**, 922-930; (b) M. G. Dekamin, J. Mokhtari, Z. Karimi, *Sci. Iran. Trans. C: Chem. Chem. Eng*., 2011**,** **18**, 1356-1364; (c) A. Shaabani and A. Maleki, *Appl. Catal.: A.*, 2007, **331**, 149-151; (d) L. X. Cheng, J. J. Tang, H. Luo, X. L. Jin, F. Dai, J. Yang, Y. P. Qian, X. Z. Li and B. Zhou, *Bioorg. Med. Chem. Lett.*, 2010, **20**, 2417-2420; (e) J. J. Eisch and T. Dluzniewski, *J. Org. Chem*., 1989, **54**, 1269-1274.

General procedure for synthesis of imines 5 catalysed by chitosan (1a)

In a 5 mL round bottom flask equipped with a magnetic bar and condenser, a mixture of aldehyde **2** (1 mmol), amine **3** (1 mmol) and 6 mg chitosan was added to 0.5 mL of EtOH 96%. The obtained mixture was stirred at room temperature for times indicated in Table 4. After completion of the reaction, as indicated by precipitation of solid products from liquid reaction mixture and TLC experiments using authentic samples,[8] the crude product was recrystalyzed from EtOH 96% mL) to afford pure desired imines **5**.[43-56]

References: (a) K. A. T. E. Saitou, *Bull. Chem. Soc. Jpn.*, 1969, **42**, 2693-2694; (b) J. S. Bennett, K. L. Charles, M. R. Miner, C. F. Heuberger, E. J. Spina, M. F. Bartels and T. Foreman, *Green Chem.*, 2009, **11**, 166-168; (c) Y. M. S. A. Al-Kahraman, H. M. F. Madkour, D. Ali and M. Yasinzai, *Molecules*, 2010, **15**, 660-671; (d) Z. Galewski, *Mol. Cryst. Liq. Cryst*., 1990, **191**, 211- 218; (e) M. Á. Vázquez, M. Landa, L. Reyes, R. Miranda, J. Tamariz and F. Delgado, *Synth. Commun.*, 2004, **34**, 2705-2718; (f) R. A. Champa, *Mol. Cryst. Liq. Cryst.*, 1973, **19**, 233-247; (g) A. S. Hirwe, R. L. Metcalf and I. P. Kapoor, *J. Agri. Food Chem.*, 1972, **20**, 818-824; (h) K. Tanaka, R. Shiraishi, *Green Chem*., 2000, **2**, 272-273; (i) I. Kraicheva, A. Bogomilova, I. Tsacheva, G. Momekov and K. Troev, *Eur. J. Med. Chem.*, 2009, **44**, 3363-3367; (j) J. Schmeyers, F. Toda, J. Boy and G. Kaupp, *J. Chem. Soc. Perkin Trans. 2*, 1998, 989-993; (k) H. R. Snyder and J. R. Demuth, *J. Am. Chem. Soc.*, 1956, **78**, 1981-1984; (l) C. G. Overberger, N. P. Marullo and R. G. Hiskey, *J. Am. Chem. Soc*., 1961, **83**, 1374-1378; (m) S. Inoue, *Chem. Pharm. Bull*. 1967, ***15***, 1540-1556; (n) V. Madan and L. B. Clapp, *J. Am. Chem. Soc.*, 1969, **91**, 6078-6083.



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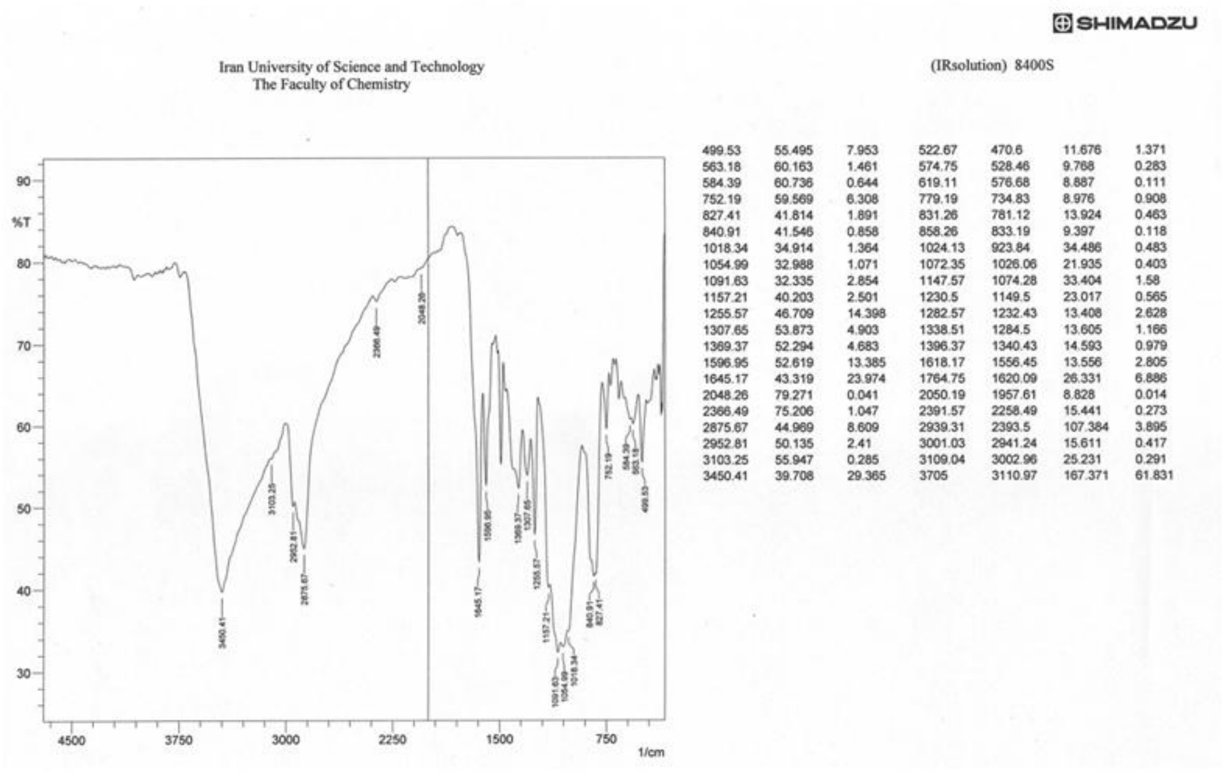
1037.63	70.379	1.144	1047.27	910.34	16.494	0.766
1101.28	68.035	2.679	1137.92	1049.2	14.256	0.694
1159.14	68.606	3.151	1228.57	1139.85	12.723	0.638
1344.29	68.985	0.197	1346.22	1276.79	10.249	0.202
1386.72	65.982	1.804	1402.15	1348.15	9.348	0.371
1616.24	59.224	0.396	1620.09	1573.81	10.167	0.213
1652.88	56.819	1.521	1668.31	1631.67	8.81	0.262
1676.03	57.378	0.807	1718.46	1670.24	10.967	0.126
1922.9	59.311	0.158	1926.75	1882.39	9.801	0.035
1996.19	58.906	0.225	2001.97	1926.75	17.757	0.066
2046.33	56.509	0.206	2065.62	2003.9	15.236	0.066
2108.05	56.308	0.199	2129.27	2067.55	15.337	0.05
2160.13	56.308	0.18	2198.7	2131.19	16.784	0.043
2219.91	56.457	0.154	2258.49	2200.63	14.32	0.036
2322.13	55.309	0.446	2337.56	2271.99	16.544	0.096
2382.64	54.805	1.109	2391.57	2339.49	13.381	0.248
2428.21	56.064	0.067	2434	2393.5	10.129	0.024
2621.08	53.273	0.031	2623.01	2435.93	49.131	0.086
2873.74	47.149	1.102	2910.38	2624.94	85.435	0.53
2923.88	47.491	0.117	2987.53	2920.03	21.215	0.016
3105.18	47.19	0.043	3107.11	2989.46	37.183	0.014
3292.26	44.182	0.036	3294.19	3109.04	62.993	0.039
3384.84	42.33	0.199	3392.55	3296.12	35.067	0.077
3421.48	41.796	0.26	3431.13	3394.48	13.785	0.046
3448.49	41.619	0.405	3465.84	3433.06	12.418	0.073
3479.34	42.056	0.314	3550.71	3467.77	30.606	0.159
3556.49	43.678	0.314	3579.64	3552.63	9.603	0.084
3670.28	50.682	0.904	3703.07	3662.57	11.562	0.122
3741.65	51.972	1.752	3784.08	3720.43	17.396	0.368
4243.1	55.952	0.223	4268.18	4219.96	12.121	0.045
4297.11	55.954	0.214	4314.46	4270.1	11.146	0.036

Fig.1 FT-IR spectrum of the commercial chitosan



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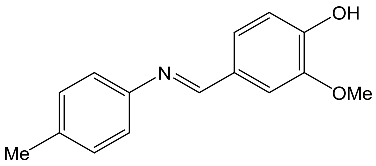
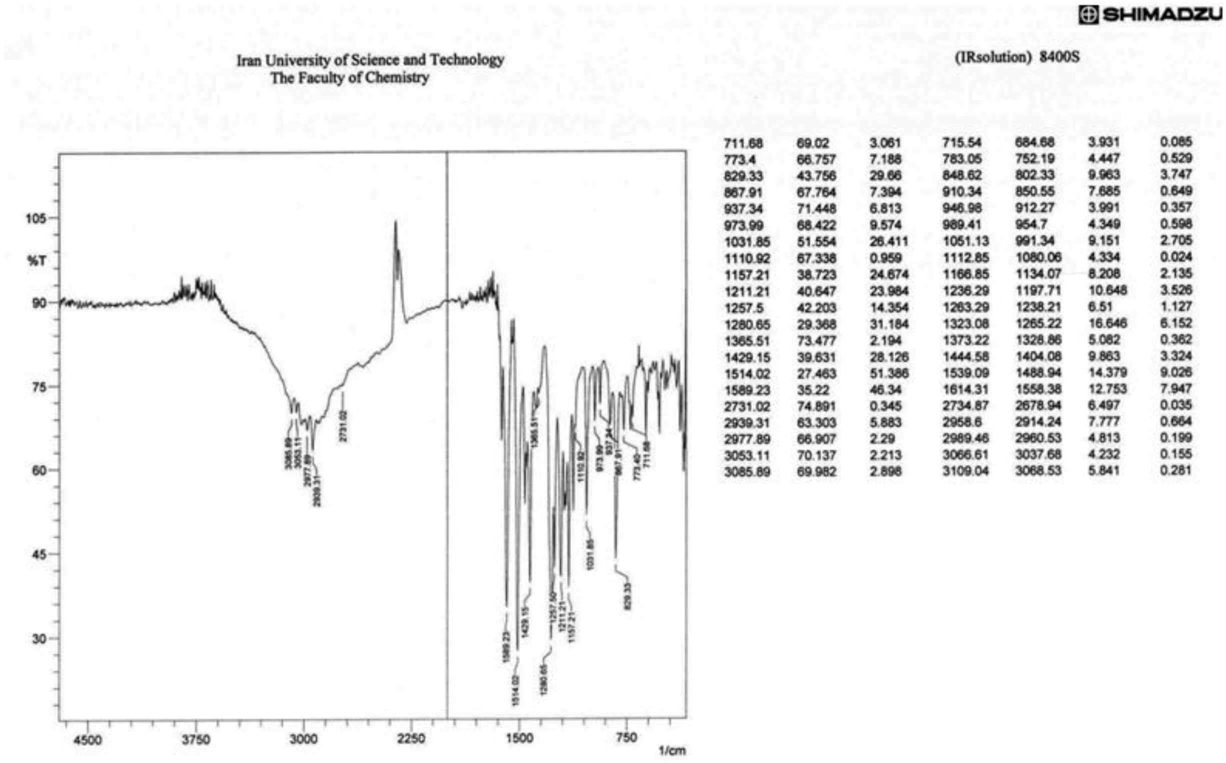
499.53	55.495	7.953	522.67	470.6	11.676	1.371
563.18	60.163	1.461	574.75	528.46	9.768	0.283
584.39	60.736	0.644	619.11	576.68	8.887	0.111
752.19	59.569	6.308	779.19	734.83	8.976	0.908
827.41	41.814	1.891	831.26	781.12	13.924	0.463
840.91	41.546	0.858	858.26	833.19	9.397	0.118
1018.34	34.914	1.364	1024.13	923.84	34.486	0.483
1054.99	32.988	1.071	1072.35	1026.06	21.935	0.403
1091.63	32.335	2.854	1147.57	1074.28	33.404	1.58
1157.21	40.203	2.501	1230.5	1149.5	23.017	0.565
1255.57	46.709	14.398	1282.57	1232.43	13.408	2.628
1307.65	53.873	4.903	1338.51	1284.5	13.605	1.166
1369.37	52.294	4.683	1396.37	1340.43	14.593	0.979
1596.95	52.619	13.385	1618.17	1556.45	13.556	2.805
1645.17	43.319	23.974	1764.75	1620.09	26.331	6.886
2048.26	79.271	0.041	2050.19	1957.61	8.828	0.014
2366.49	75.206	1.047	2391.57	2258.49	15.441	0.273
2875.67	44.969	8.609	2939.31	2393.5	107.384	3.895
2952.81	50.135	2.41	3001.03	2941.24	15.611	0.417
3103.25	55.947	0.285	3109.04	3002.96	25.231	0.291
3450.41	39.708	29.365	3705	3110.97	167.371	61.831

Fig.2 FT-IR spectrum of the chitosan after first run in the Strecker reaction





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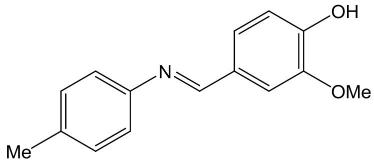
711.68	69.02	3.061	715.54	684.68	3.931	0.085
773.4	66.757	7.188	783.05	752.19	4.447	0.529
829.33	43.756	29.66	848.62	802.33	9.963	3.747
867.91	67.764	7.394	910.34	850.55	7.685	0.649
937.34	71.448	6.813	946.98	912.27	3.991	0.357
973.99	68.422	9.574	989.41	954.7	4.349	0.598
1031.85	51.554	26.411	1051.13	991.34	9.151	2.705
1110.92	67.338	0.959	1112.85	1080.06	4.334	0.024
1157.21	38.723	24.674	1166.85	1134.07	8.208	2.135
1211.21	40.647	23.984	1236.29	1197.71	10.648	3.526
1257.5	42.203	14.354	1263.29	1238.21	6.51	1.127
1280.65	29.368	31.184	1323.08	1265.22	16.646	6.152
1365.51	73.477	2.194	1373.22	1328.86	5.082	0.362
1429.15	39.631	28.126	1444.58	1404.08	9.863	3.324
1514.02	27.463	51.386	1539.09	1488.94	14.379	9.026
1589.23	35.22	46.34	1614.31	1558.38	12.753	7.947
2731.02	74.891	0.345	2734.87	2678.94	6.497	0.035
2939.31	63.303	5.883	2958.6	2914.24	7.777	0.664
2977.89	66.907	2.29	2989.46	2960.53	4.813	0.199
3053.11	70.137	2.213	3066.61	3037.68	4.232	0.155
3085.89	69.982	2.898	3109.04	3068.53	5.841	0.281

Fig. 3. FT-IR spectrum of (4-hydroxy-3-methoxy benzylidine)-*p*-tolyl amine



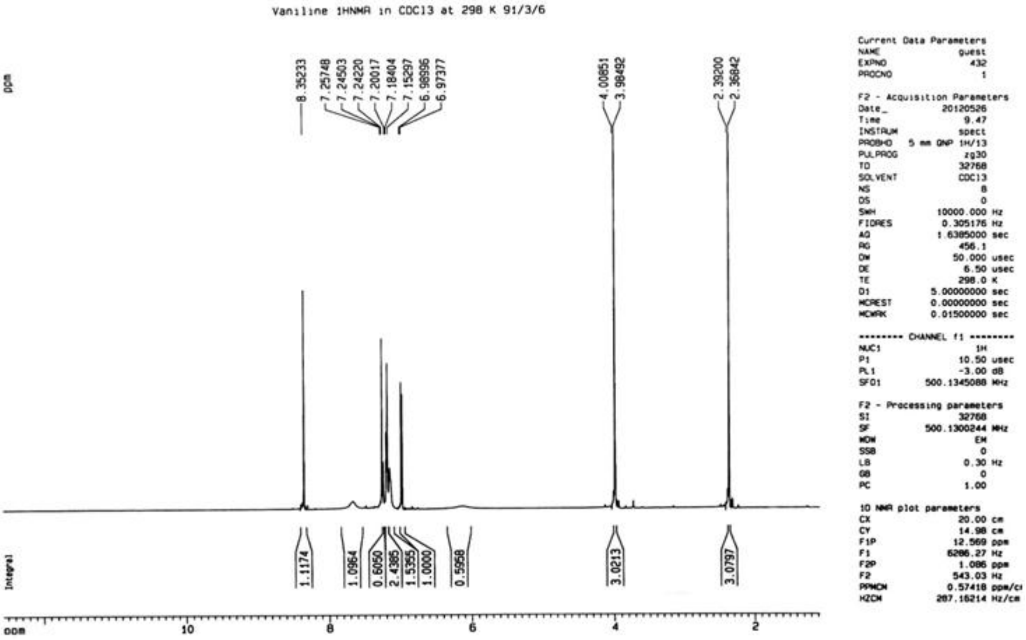


Fig. 4. ^{1}H NMR spectrum of (4-hydroxy-3-methoxy benzylidine)-*p*-Tolyl amine

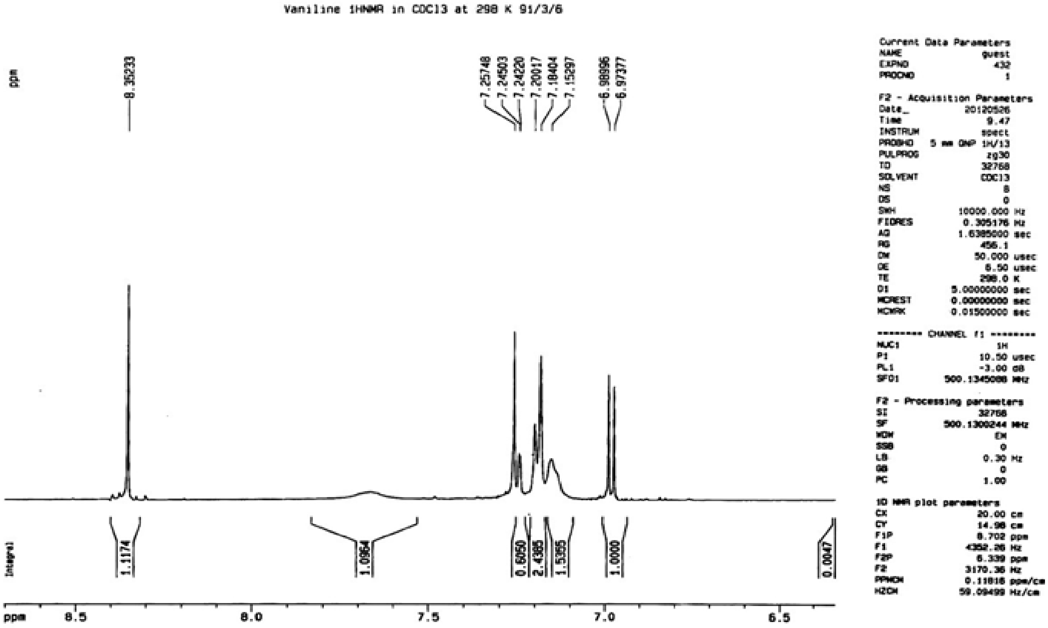
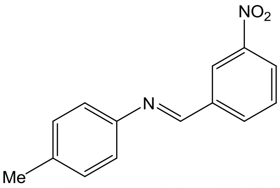
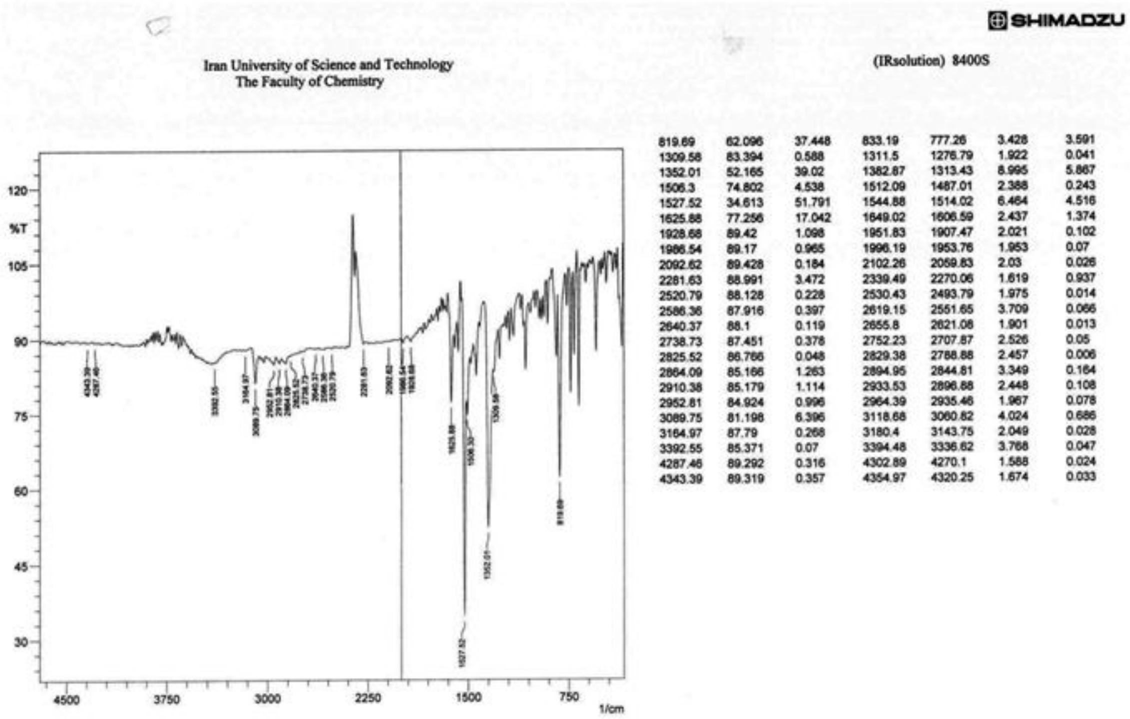


Fig. 5. ^{1}H NMR spectrum of (4-hydroxy-3-methoxy benzylidine)-*p*-tolyl amine (Expanded aromatic region)





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819.69	62.096	37.448	833.19	777.26	3.428	3.591
1309.58	83.394	0.588	1311.5	1276.79	1.922	0.041
1352.01	52.165	39.02	1382.87	1313.43	8.995	5.867
1506.3	74.802	4.538	1512.09	1487.01	2.388	0.243
1527.52	34.613	51.791	1544.88	1514.02	6.464	4.516
1625.88	77.256	17.042	1649.02	1606.59	2.437	1.374
1928.68	89.42	1.098	1951.83	1907.47	2.021	0.102
1986.54	89.17	0.965	1996.19	1953.76	1.953	0.07
2092.62	89.428	0.184	2102.26	2059.83	2.03	0.026
2281.63	88.991	3.472	2339.49	2270.06	1.619	0.937
2520.79	88.128	0.228	2530.43	2493.79	1.975	0.014
2586.36	87.916	0.397	2619.15	2551.65	3.709	0.066
2640.37	88.1	0.119	2655.8	2621.08	1.901	0.013
2738.73	87.451	0.378	2752.23	2707.87	2.526	0.05
2825.52	86.766	0.048	2829.38	2788.88	2.457	0.006
2864.09	85.166	1.263	2894.95	2844.81	3.349	0.164
2910.38	85.179	1.114	2933.53	2896.88	2.448	0.108
2952.81	84.924	0.996	2964.39	2935.46	1.967	0.078
3089.75	81.198	6.396	3118.68	3060.82	4.024	0.686
3164.97	87.79	0.268	3180.4	3143.75	2.049	0.028
3392.55	85.371	0.07	3394.48	3336.62	3.768	0.047
4287.46	89.292	0.316	4302.89	4270.1	1.588	0.024
4343.39	89.319	0.357	4354.97	4320.25	1.674	0.033

Fig. 6. FT-IR spectrum of (3-Nitro benzylidine)-*p*-tolyl amine

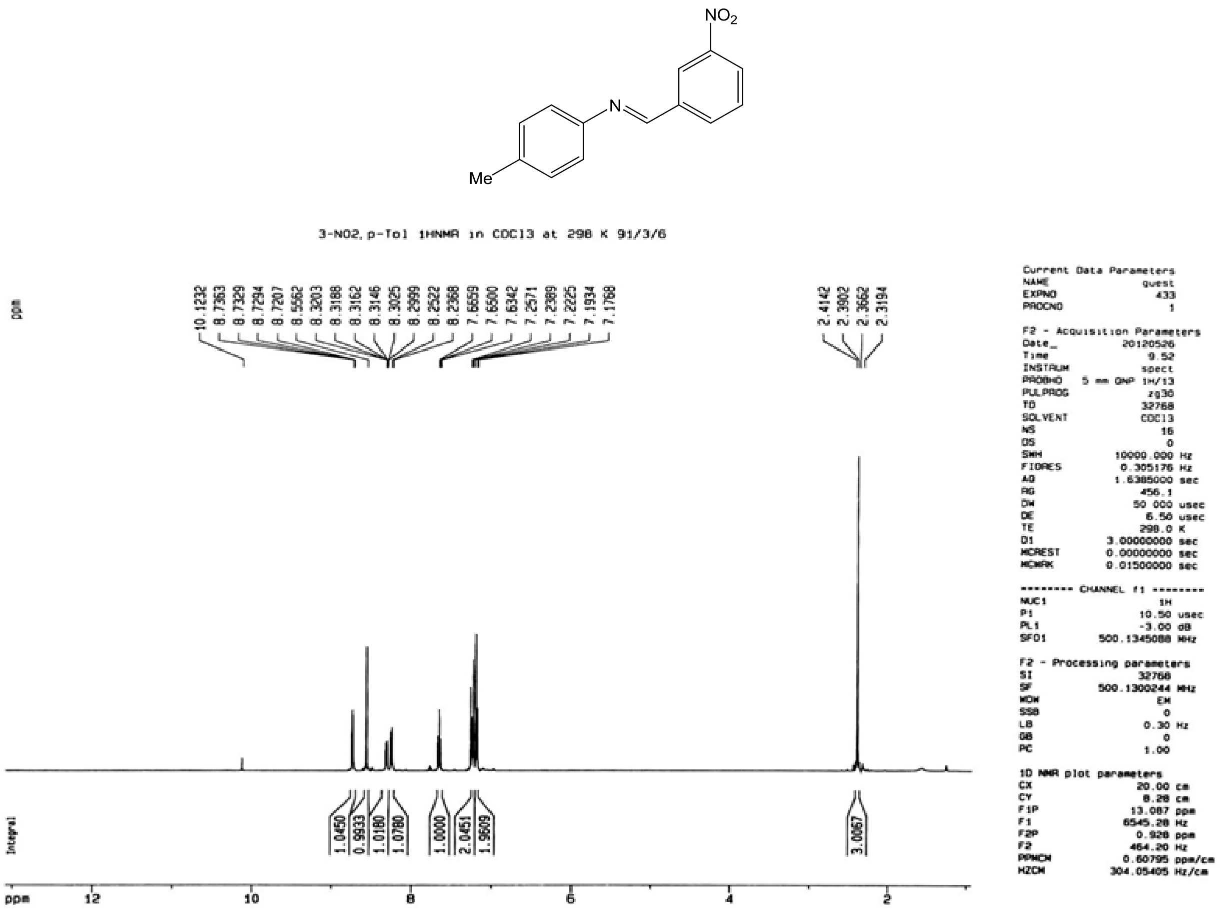

Fig. 7. ^{1}H NMR spectrum of (3-Nitro benzylidine)-*p*-tolyl amine

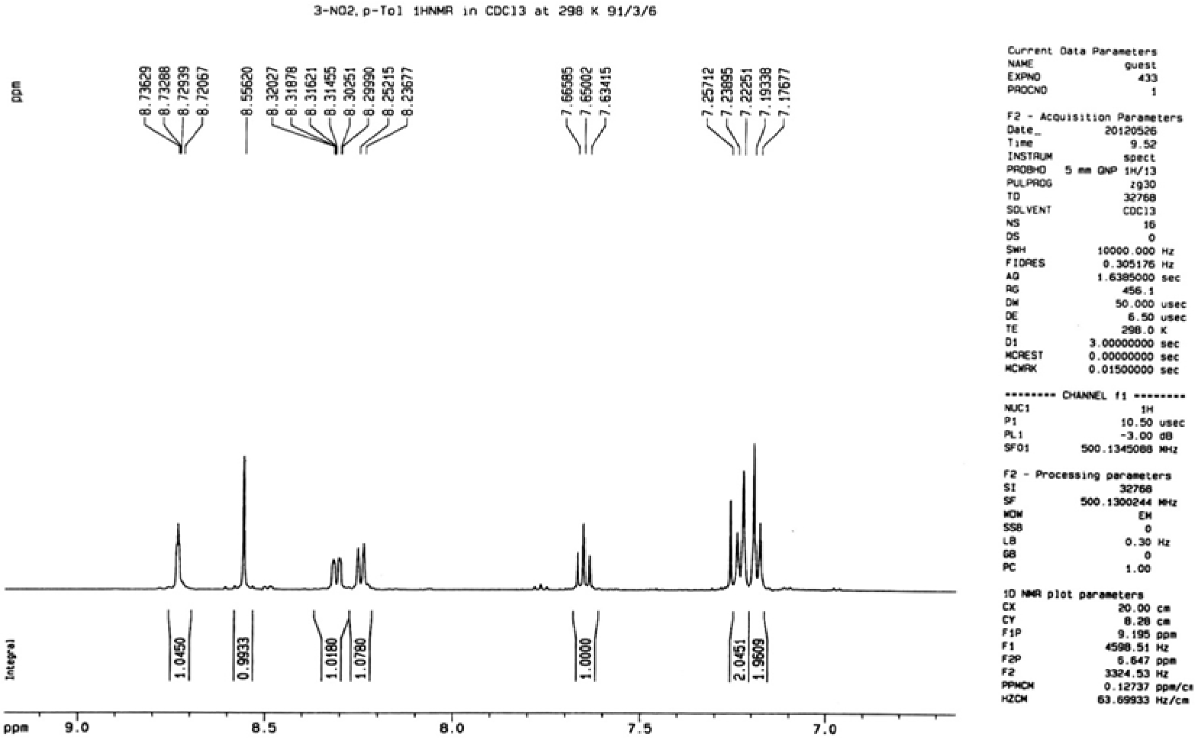

Fig. 8. ^{1}H NMR spectrum of (3-Nitro benzylidine)-*p*-tolyl amine (Expanded aromatic region)