Supplementary information

A simple and straightforward synthesis of substituted 2-arylbenzimidazoles over silica gel

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EXPERIMENTAL

1. General

Melting points were determined on E-Z Melt automated melting point apparatus, Stanford Research System, USA and were uncorrected. Merck aluminium thin layer chromatography (TLC, UV_{254nm}) plates were used to monitor the reactions and developed by spraying with a solution of 2% ceric sulphate in 10% aqueous sulphuric acid and charring at 100^{o}C. Column chromatography was carried out on silica gel (100-200 mesh, Thomas Baker). NMR spectra were obtained on Bruker Avance-300MHz instrument with tetramethylsilane (TMS, chemical shifts in δ ppm) as an internal standard. ESI mass spectra were recorded on API3000 LC-MS-MS system (Applied Biosystem) after dissolving the compounds in methanol. FT-IR spectra were recorded on Perkin-Elmer SpectrumBX after making palates with KBr. Scanning Electron Microscope (SEM) experiments were done on Zeiss Leica model SEMLEO430, UK after coating the sample with Polakon Sputter coater with gold-palladium target at Birbal Sahni Institute of Paleobotany (BSIP), Lucknow, India. Inductively Coupled Plasma atomic emission spectroscopy was done on Perkin Elmer OPTIMA 5300V at CSIR-CIMAP, Lucknow, India.

2. Spectral data[1a-h]

2-(2'-Methoxyphenyl)-1H-benzimidazole (**4a**). Mp=128-30°C; ^{1}HNMR ($CDCl_3$, 300 MHz): δ 4.03 (s, 3H, OCH_3), 6.99-8.60 (m, 8H, CH, aromatic); ESI MS (MeOH): 225.2 $[M+H]^+$; IR (KBr, cm^{-1}): 3425, 3167, 2964,1604, 1473,1243.

2-(3', 4'-Dimethoxyphenyl)-1H-benzimidazole (4b). oil; ^{1}HNMR ($CDCl_3$, 300 MHz) δ3.77 (s, 3H, OCH_3), 3.91(s, 3H, OCH_3), 6.90-7.73 (m, 7H, CH aromatic); ESI MS (MeOH): 255.2 $[M+H]^+$, 277.2 $[M+Na]^+$; IR (CCl_4, cm^{-1}): 3446, 2924, 1458, 1262.

1-(3', 4'-Dimethoxybenzyl)-2-(3", 4"-dimethoxyphenyl)-benzimidazole (5b). Mp=173-75°C; ^{1}HNMR ($CDCl_3$, 300 MHz) δ3.76 (s, 6H, 2x OCH_3), 3.84 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 5.39 (s, 2H, N-CH_2, benzylic), 6.61 (bs, 2H, 2xCH, aromatic), 6.79 (d, 1H, CH, aromatic), 6.91(d, 1H, CH, aromatic), 7.21-7.31(bs, 5H, 5xCH, aromatic), 7.85 (d, 1H, CH, aromatic); ^{13}C NMR ($CDCl_3$, 75 MHz) δ48.55, 56.24, 56.30, 56.34, 109.42, 110.67, 111.39, 111.92, 112.74, 118.50, 120.11, 122.25, 122.90, 123.07, 123.32, 129.46, 136.67, 143.36, 148.96, 149.49, 149.90, 150.89, 154.50; ESI MS (MeOH): 405.3 $[M+H]^+$, 427.2 $[M+Na]^+$, 443.3 $[M+K]^+$; HRMS (ESI) Calcd for $C_{24}H_{25}N_2O_4$ 405.1814; Found 405.1858; IR (KBr, cm^{-1}): 2922, 1608, 1591, 1515, 1485, 1256, 1022.

2-(3',4',5'-Trimethoxyphenyl)-1H-benzimidazole(4c). Mp=260-62°C; ^{1}HNMR ($CDCl_3$, 300 MHz) δ3.56 (s, 6H, 2xOCH_3), 3.83 (s, 3H, OCH_3), 7.13 (m, 2H, 2xCH, aromatic), 7.41 (s, 2H,2' & 6'-CH of 2-phenyl), 7.64 (m, 2H, 2xCH, aromatic); ESI MS (MeOH): 285.2 $[M+H]^+$; IR (KBr, cm^{-1}): 3448, 2930, 1588, 1498, 1428, 1129.

1-(3',4',5'-Trimethoxybenzyl)-2-(3',4',5'-trimethoxy phenyl)-benzimidazole (5c). Mp=140-42°C; ^{1}HNMR ($CDCl_3$, 300 MHz) δ3.69 (s, 12H, 4xOCH_3), 3.79 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 5.37 (s, 2H, CH_2, benzylic), 6.33 (s, 2H, 2'-CH & 6'-CH aromatic), 6.89 (s, 2H, 2'-CH &6'-CH aromatic), 7.33 (m, 3H, CH-aromatic benzimidazole ring), 7.88 (m, 1H, CH-aromatic benzimidazole ring); ^{13}C NMR ($CDCl_3$, 75 MHz) δ48.94, 56.33, 56.33, 56.59, 56.59, 61.28, 61.34, 103.12, 103.12, 106.78, 106.78, 110.47, 120.32, 123.33, 123.72, 125.42, 132.97, 136.85, 137.79, 139.88, 143.18, 153.76, 153.76, 154.30, 154.30, 154.54, 154.54; ESI MS (MeOH): 465.3 $[M+H]^+$, 487.2 $[M+Na]^+$, 503.3 $[M+K]^+$; HRMS (ESI) Calcd for $C_{26}H_{29}N_2O_6$ 465.2026; Found 465.2068; IR (KBr, cm^{-1}): 3049, 2934, 1585, 1508, 1412, 1237, 1121, 1005.

2-(3'-Hydroxy, 4'-methoxyphenyl)-1H-benzimidazole (4d). Mp=195-200°C; ^{1}HNMR ($CDCl_3$, 300 MHz) δ 3.96 (s, 3H, OCH_3), 6.81-7.80 (m, 7H, CH, aromatic); ESI MS (MeOH): 241.1 $[M+H]^+$, 263.2 $[M+Na]^+$; IR (KBr, cm^{-1}): 3419, 1616, 1560, 1260, 1122.

1-(3'-Hydroxy,4'-methoxybenzyl)-2-(3"-hydroxy, 4"-methoxyphenyl)-benzimidazole (5d). Mp=161-64°C; ^{1}HNMR ($CDCl_3$, 300 MHz) δ 3.86 (s, 3H, OCH_3), 3.94 (s, 3H, OCH_3), 5.36 (s, 2H, CH_2 benzylic), 6.53-7.83 (m, 10H, CH, aromatic) ; ESI MS (MeOH): 377.2 $[M+H]^+$, 399.3$[M+Na]^+$; IR (KBr, cm^{-1}): 3367, 2919, 1654, 1560, 1458, 1260, 1128.

2-(4'-Hydroxyphenyl)-1H-benzimidazole (4e). Mp=135-38°C; ^{1}HNMR ($CDCl_3$, 300 MHz) δ 6.78-7.71 (m, 8H, CH, aromatic); ESI MS (MeOH): 211.2 $[M+H]^+$; IR (KBr, cm^{-1}): 3336, 2923, 1654, 1560, 1260.

1-(3', 4'-Methylenedioxybenzyl)-2 -(3", 4"-Methylenedioxyphenyl)-benzimidazole (5f). Mp=170-72°C; ^{1}HNMR ($CDCl_3$, 300 MHz) δ5.34 (s, 2H, CH_2 benzylic), 5.94 (s, 2H, *O*-CH_2-*O*), 6.03 (s, 2H, *O*-CH_2-*O*), 6.55-7.90 (m, 10H, CH, aromatic); ^{13}C NMR ($CDCl_3$, 75 MHz) δ48.58, 101.69, 101.99, 106.91, 109.03, 109.09, 110.02, 110.89, 119.65, 120.10, 123.22, 123.48, 123.82, 124.05, 130.42, 136.26, 143.02, 147.66, 148.45, 148.80, 149.62, 154.04; ESI MS (MeOH): 373.2 $[M+H]^+$, 395.2 $[M+Na]^+$; HRMS (ESI) Calcd for $C_{22}H_{17}N_2O_4$ 373.1188; Found 373.1220; IR (KBr, cm^{-1}): 2920, 1500, 1498, 1448, 1247, 1037.

2-(4'-Fluorophenyl)-1H-benzimidazole (4g). Mp=233-35°C; ^{1}HNMR ($CDCl_3$, 300 MHz) δ 6.75-8.06 (m, 8H, CH, aromatic); ESI MS (MeOH): 213.2 $[M+H]^+$, 251.4 $[M+K]^+$; IR (KBr, cm^{-1}): 3432, 2921, 1603, 1498, 1451, 1228.

1-(4'-Fluorobenzyl)-2-(4"-fluorophenyl)-benzimidazole (5g). Mp=88-90°C; ^{1}HNMR ($CDCl_3$, 300 MHz) δ 5.34 (s, 2H, CH_2 benzylic), 6.76-7.86 (m, 12H, 12xCH, aromatic); ESI MS (MeOH): 321.2 $[M+H]^+$, 343.1 $[M+Na]^+$; IR (KBr, cm^{-1}): 2923, 1607, 1510, 1482, 1222, 1158.

2-(4'-Nitrophenyl)-1H-benzimidazole (4h). Mp=250-52°C; ^{1}HNMR ($CDCl_3$, 300 MHz) δ7.27 (m, 2H, CH aromatic benzimidazole ring), 7.68 (bs, 2H, CH aromatic benzimidazole ring), 8.41 (d, 2H, 2' & 6'-CH of 2-phenyl ring), 8.51 (d, 2H, 3' & 5'-CH of 2-phenyl ring); ESI MS (MeOH): 240.1$[M+H]^+$; IR (KBr, cm^{-1}): 3433, 2919, 1604, 1515, 1340, 1101.

2-(4'-Quinolinyl)-1H-benzimidazole (4i). Mp=140-42°C; ^{1}HNMR ($CDCl_3$, 300 MHz) δ 7.38-9.10 (m, 10H, CH, aromatic) ; ESI MS (MeOH): 246.1$[M+H]^+$; IR (KBr, cm^{-1}): 3419, 1617, 1570, 1120. ^{1}HNMR (CDCl3), 300 MHz) δ; ESI MS (MeOH): 246.1$[M+H]^+$.

5-Methoxy, 1-(2',4',5'-trimethoxybenzyl)-2-(2",4",5"-trimethoxyphenyl)-benzimidazole (5j). oil; ^{1}HNMR ($CDCl_3$, 300 MHz) δ 3.53 (s, 3H, OCH_3), 3.65 (s, 3H, OCH_3), 3.77 (s, 6H, 2xOCH_3), 3.79 (s, 6H, 2xOCH_3), 3.84 (s, 3H, OCH_3), 5.16 (s, 2H, N-CH_2, benzylic), 6.26- 7.31 (m, 7H, CH, aromatic); ESI MS (MeOH): 495.3 $[M+H]^+$, 517.3 $[M+Na]^+$, 533.4$[M+K]^+$.

5-Methoxy-2-(3', 4'-dimethoxyphenyl)-1H-benzimidazole (4k). Oil; ^{1}HNMR ($CDCl_3$, 300 MHz) δ 3.76 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.96 (s, 3H, OCH_3); ESI MS (MeOH): 285.2$[M+H]^+$; IR (CCl_4, cm^{-1}): 2924, 1591, 1458, 1262.

2.2.16 5-Methoxy-1-(3',4'-dimethoxybenzyl)-2-(3",4"-dimethoxyphenyl)-benzimidazole (5k). Mp=180-85°C; ^{1}HNMR ($CDCl_3$, 300 MHz) δ 3.81 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 3.95(s, 3H, OCH_3), 4.03 (s, 3H, OCH_3), 5.47 (s, 2H, CH_2, benzylic), 6.75-7.90 (m, 9H, 9xCH, aromatic); ESI MS (MeOH): 435.3$[M+H]^+$, 4.57.2 $[M+Na]^+$; HRMS (ESI) Calcd for $C_{25}H_{27}N_2O_5$ 435.19; Found 435.1957; IR (KBr, cm^{-1}): 2923, 1590, 1513, 1254, 1134.

5-Methoxy, 2-(3',4'-methylenedioxyphenyl)-1H-benzimidazole (4l). Mp=270-72°C; ^{1}HNMR ($CDCl_3$, 300 MHz) δ3.95 (s, 3H, OCH_3), 6.00 (s, 2H, -*O*-CH_2-*O*-), 6.69-7.83 (m, 6H, CH, aromatic); ESI MS (MeOH): 269 $[M+H]^+$; IR (KBr, cm^{-1}): 3448, 1654, 1610, 1025.

5-Methoxy,1-(3',4'-methylenedioxybenzyl)-2-(3",4"-methylenedioxyphenyl)-benzimidazole (5l). Mp=182-85°C; ^{1}HNMR ($CDCl_3$, 300 MHz) δ3.76 (s, 3H, OCH_3), 5.29 (s, 2H, CH_2, benzylic), 5.88 (s, 2H, -*O*-CH_2-*O*-), 5.95 (s, 2H, -*O*-CH_2-*O*-), 6.55-7.72 (m, 9H, 9xCH, aromatic); ESI MS (MeOH): 403.3 $[M+H]^+$, 425.1 $[M+Na]^+$, 441.5 $[M+K]^+$ HRMS (ESI) Calcd for $C_{23}H_{19}N_2O_5$ 403.1294; Found 403.1334; IR (KBr, cm^{-1}): 2922, 1619, 1502, 1468, 1250, 1036.

5-Methoxy-2-(4'-fluorophenyl)-1H-benzimidazole (4m). Oil; ^{1}HNMR ($CDCl_3$, 300 MHz) δ 3.88 (s, 3H, OCH_3), 6.88-8.39 (m, 7H, 7xCH, aromatic); ESI MS (MeOH): 243.1$[M+H]^+$; IR (CCl_4, cm^{-1}): 3401, 2928, 1603, 1508, 1389, 1228.

5-Methoxy-1-(4'-fluorobenzyl)-2-(4"-fluorophenyl)-benzimidazole (5m). Oil; ^{1}HNMR ($CDCl_3$, 300 MHz) δ 3.75(s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 5.32 (s, 2H, OCH_2), 6.62-7.73 (m, 11H, CH, aromatic); ^{13}C NMR ($CDCl_3$, 75 MHz) δ47.55, 55.57, 55.62, 93.94, 101.92, 110.59, 111.64, 113.10, 115.59, 115.63, 115.77, 115.88, 115.92, 116.03, 120.31, 126.03, 126.10, 126.14, 127.40, 127.51, 130.26, 130.79, 130.85, 130.90, 130.97, 131.70, 131.75, 131.81, 131.85, 136.44, 137.37, 143.64, 152.12, 153.02, 156.49, 156.80, 160.43, 161.74, 163.70, 165.06, 165.15; ESI MS (MeOH):351.2 $[M+H]^+$, 389.0 $[M+K]^+$; IR (CCl_4, cm^{-1}): 2927, 1606, 1509, 1478, 1223.

5-Methoxy-2-(4'-nitrophenyl)-1H-benzimidazole (4n). Oil; ^{1}HNMR ($CDCl_3$, 300 MHz) δ3.81(s, 3H, OCH_3), 6.85 (m,2H, 6 & 7-CH aromatic), 7.00 (s, 1H, 4-CH, aromatic), 7.34 (d, 2H, 2' & 6'-CH of 2-phenyl ring),

7.61 (d, 2H, 3' & 5'-CH of 2-phenyl ring); ESI MS (MeOH): 270.1$[M+H]^+$, 561.3$[2M+Na]^+$,577.6 $[2M+K]^+$; IR (CCl_4, cm^{-1}): 3398, 2925, 1601, 1519, 1346,1275.

3. Silica gel degradation analysis by inductively coupled plasma atomic emission spectrometry

The silica gel used in the reaction was washed with chloroform (3x20mL) and solvent was evaporated to dryness. The residue was dissolved in the 5ml Di-acid (3:1 nitric and perchloric acid) and heated at temperature 200°C for 2hr. Final volume was made-up with deionised water and it was processed for analysis.

Operating condition: outer gas flow/l min 15, Intermediate gas flow/l min 1.0; Pf power/kW 1.3, Plasma viewing mode Axial, Element wavelength Si: 251.611. [2]

References

1. (a) L. H. Du and X. P. Luo. Synth. Commun., 2010, 40, 2880-86; (b) T. K. Govindan, Proceedings-Ind. Acad. Sciences, 1956, 44A, 123-25; (c) V. D. Patil, J. Patil, P. Rege and G. Dere. Synth. Commun., 2011, 41, 58-62; (d) D. Sharma, B. Narasimhan, P. Kumar and A. Jalbout. Eur. J. Med. Chem., 2009, 44, 1119-1127; (e) S. Sntra, A. Majee and A. Hajra. Tet. Lett., 2012, 53,1974-77; (f) V. Narsaiah, A.R. Reddy and J. S. Yadav. Synth. Commun., 2011, 41, 262-67; (g) M. Shen and T. G. Driver. Org. Lett., 2008, 10, 3367-70; (h) T. Hisano, M. Ichikawa, K. Tsumoto and M. Tasaki. Chem. Pharm. Bull., 1982, 30, 2996-3004.

2. R. Sanchez, J. L. Todoli, C. P. Lienemann and J. M. Mermet. J. Anal. At. Spectrom., 2009, 24, 391-401.

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