

Enantioselective Strecker reaction of aldimines using potassium cyanide catalyzed by recyclable macrocyclic V(V) salen complex

S. Saravanan,^{a, b} Noor-ul H. Khan,*^{a, b} Ajay Jakhar,^{a, b} Amamudin Ansari,^{a, b} Rukhsana I. Kureshy,^{a, b} Sayed H. R. Abdi,^{a, b} Gaurav Kumar^{a, b}

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Experimental section

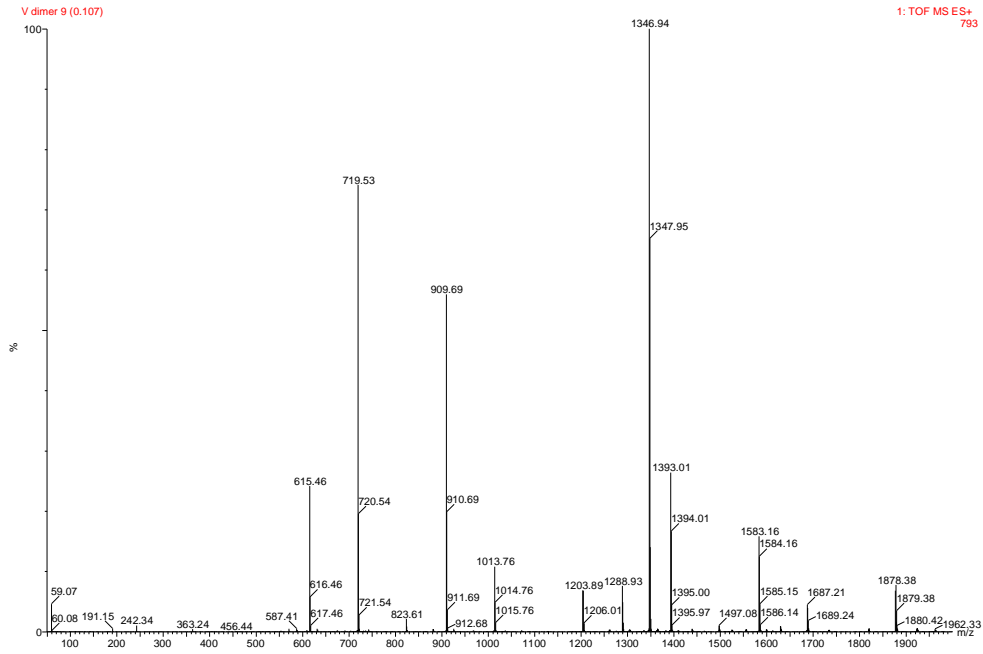
NMR spectra were obtained with a Bruker F113V spectrometer (500 MHz) and are referenced internally with TMS. Enantiomeric excess (*ee*) were determined by HPLC (Shimadzu SCL-10AVP) using Daicel Chiralpak AD-H, OD-H and OD chiral columns with 2-propanol/hexane as eluent. For the product purification flash chromatography was performed using silica gel 100-200 mesh. Manganese acetate (SD Fine Chem. Ltd.) Mumbai (India). (1*R*,2*R*)-(+)/(1*S*,2*S*)-(-)-1,2-diphenylethylenediamine and (1*R*,2*R*)-(-) / (1*S*,2*S*)-(+)-1,2 -diaminocyclohexane, TMSCN, benzaldehyde, 2-methoxy benzaldehyde, 4-methoxy benzaldehyde, 4-bromo benzaldehyde, 4-chlorobenzaldehyde, trimethylacetaldehyde, 2-naphthaldehyde, α -amino-diphenylmethane (Sigma Aldrich) and 2-methyl benzaldehyde, 3-methyl benzaldehyde, 4-methyl benzaldehyde, benzylamine (Merck Chemicals) were used as received. 3-*t*-Bu-5-chloromethyl-2-hydroxybenzaldehyde and trigol bis-aldehyde was synthesized by our previous reported procedure.¹ Chiral macrocyclic ligands and complexes **2-5** were prepared by the reported method.^{1,2} All the solvents were dried using standard procedures,³ distilled and stored under nitrogen.

Typical experimental procedure for addition of cyanide to aldimines

The chiral V(V) dinuclear salen complex (5 mol%) was dissolved in toluene (1 ml) and the solution was cooled to -20 °C under N₂ atmosphere. To the cooled solution *N*-benzylimine (0.09 mmol) was added which was followed by the addition of KCN (1.5 equiv) slowly over 30 min with stirring. To this stirred solution, H₂O (20 μl) was added and an over a period of 10 min. The reaction was monitored on TLC using hexane/ethyl acetate (90/10) as eluent. Then saturated NH₄Cl aqueous solution was added and the mixture was extracted with dichloromethane. The extracts were combined, dried over anhydrous Na₂SO₄ and the solvent was removed under reduced pressure. The product was purified by flash column chromatography on silica gel (eluted with hexane/ethyl acetate = 90:10). The purified products were characterized by ¹H NMR and were in agreement with the reported values.⁴

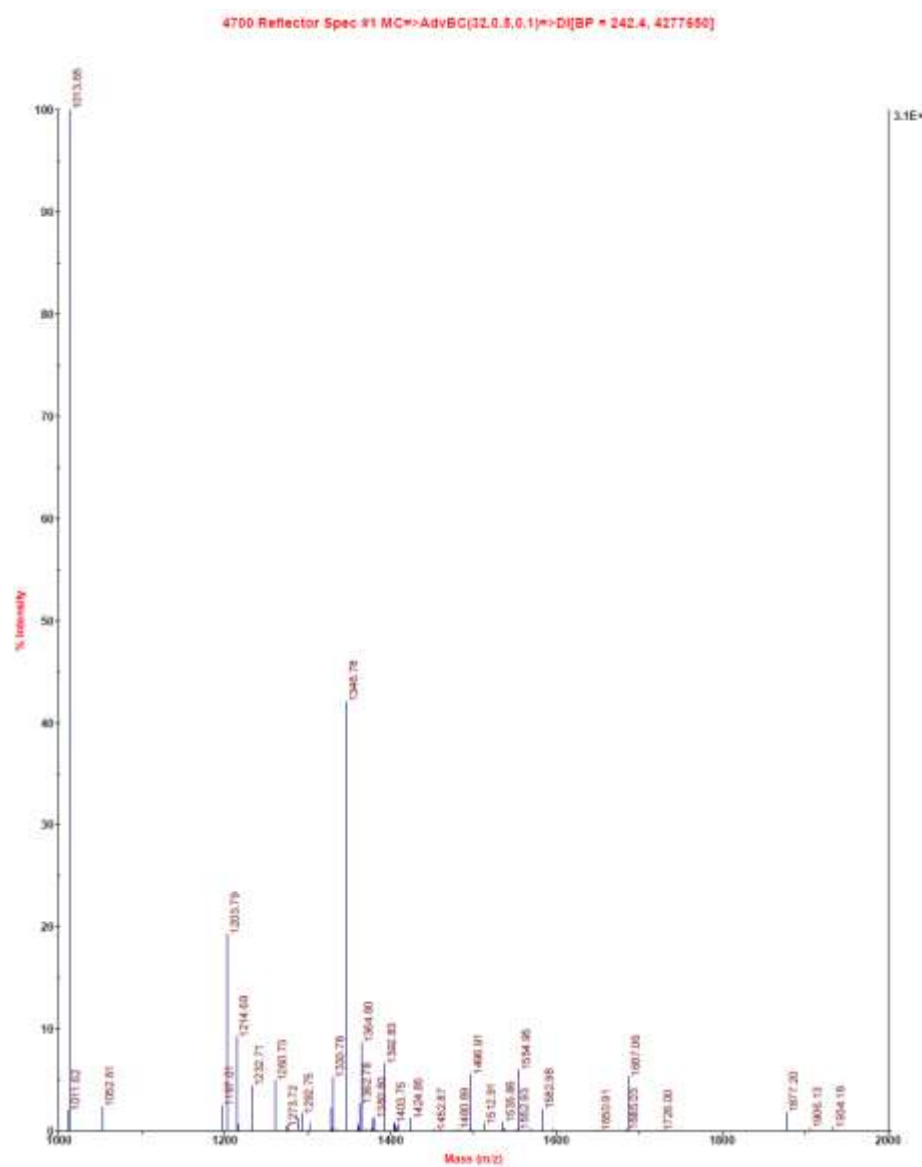
LC-MS of catalyst 4

MS (ESI): m/z found 1346.94 [C₇₂H₁₀₀N₄O₁₄V₂]



MALDI-TOF spectrum of catalyst 4

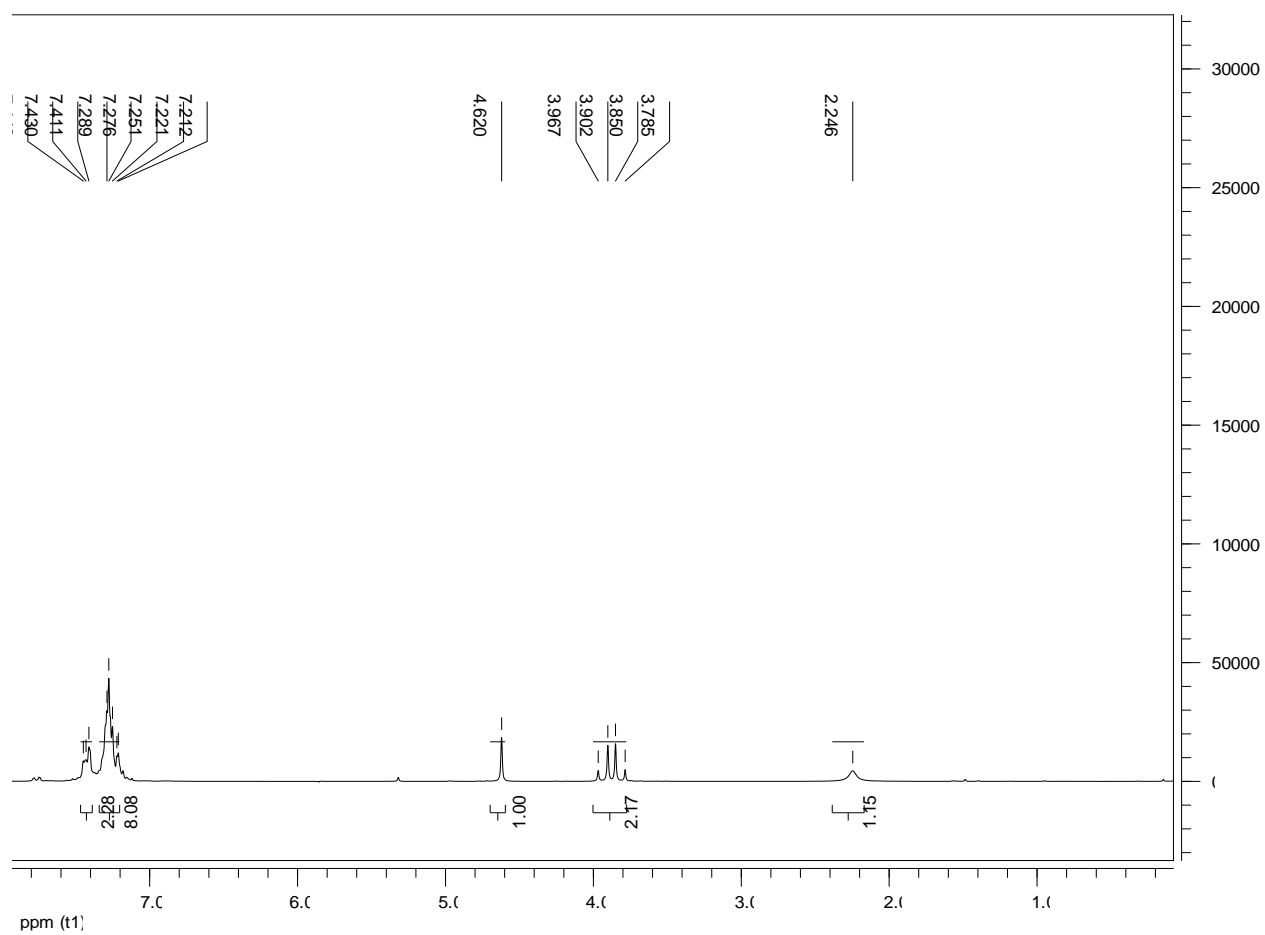
MALDI-TOF: m/z found 1346.78 [C₇₂H₁₀₀N₄O₁₄V₂]



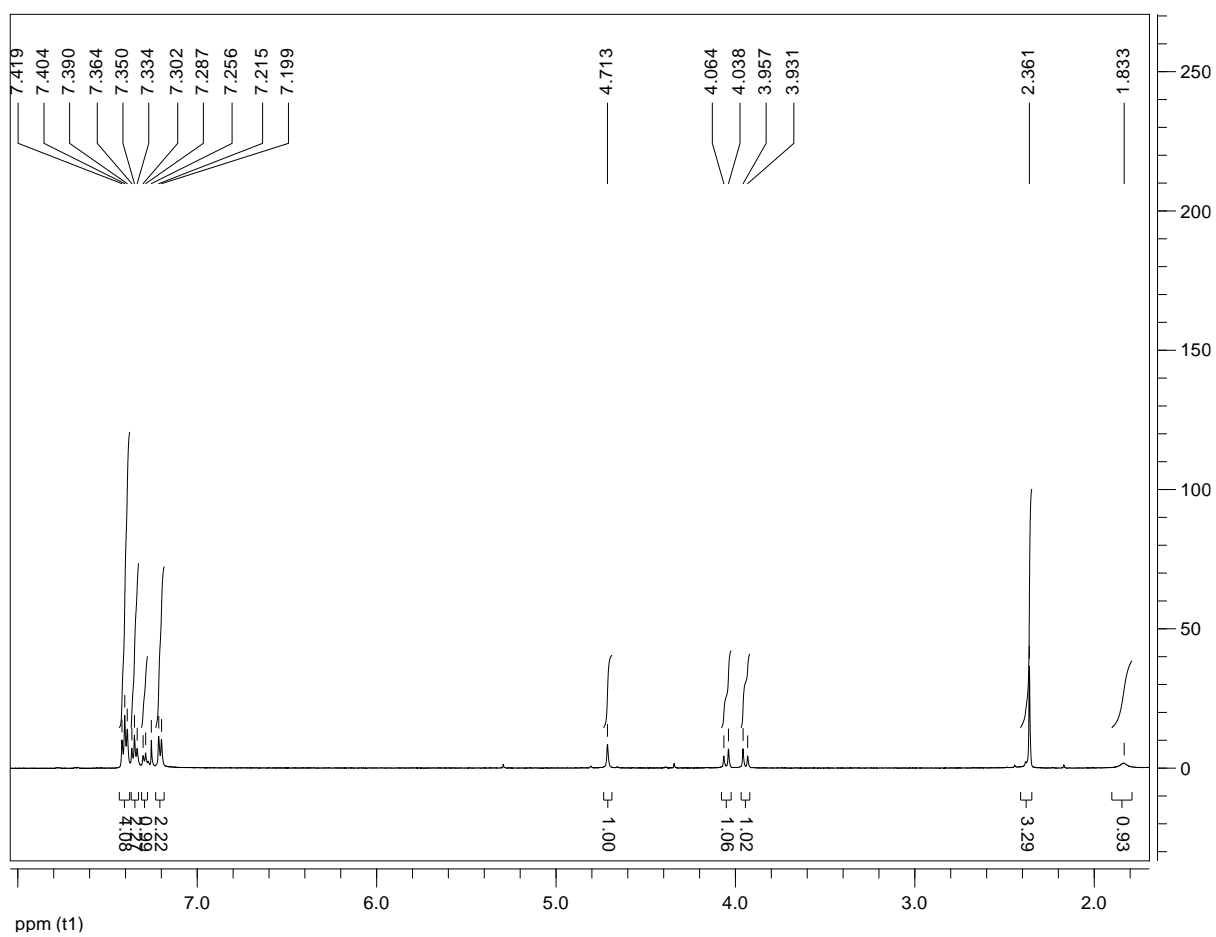
NMR Spectra of the products⁵

N-Benzyl-2-amino-phenylacetonitrile (Table 2, entry 1)

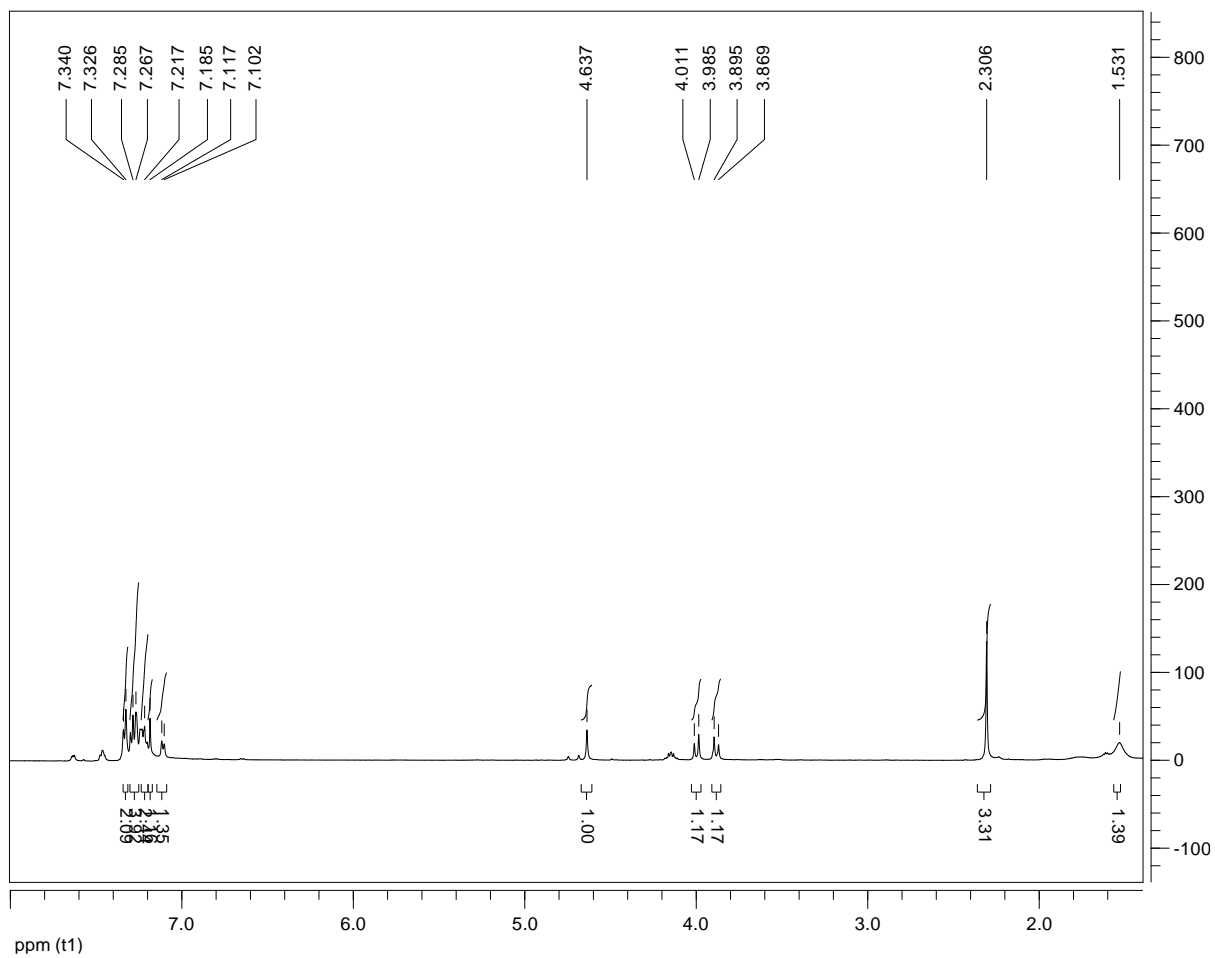
¹H NMR



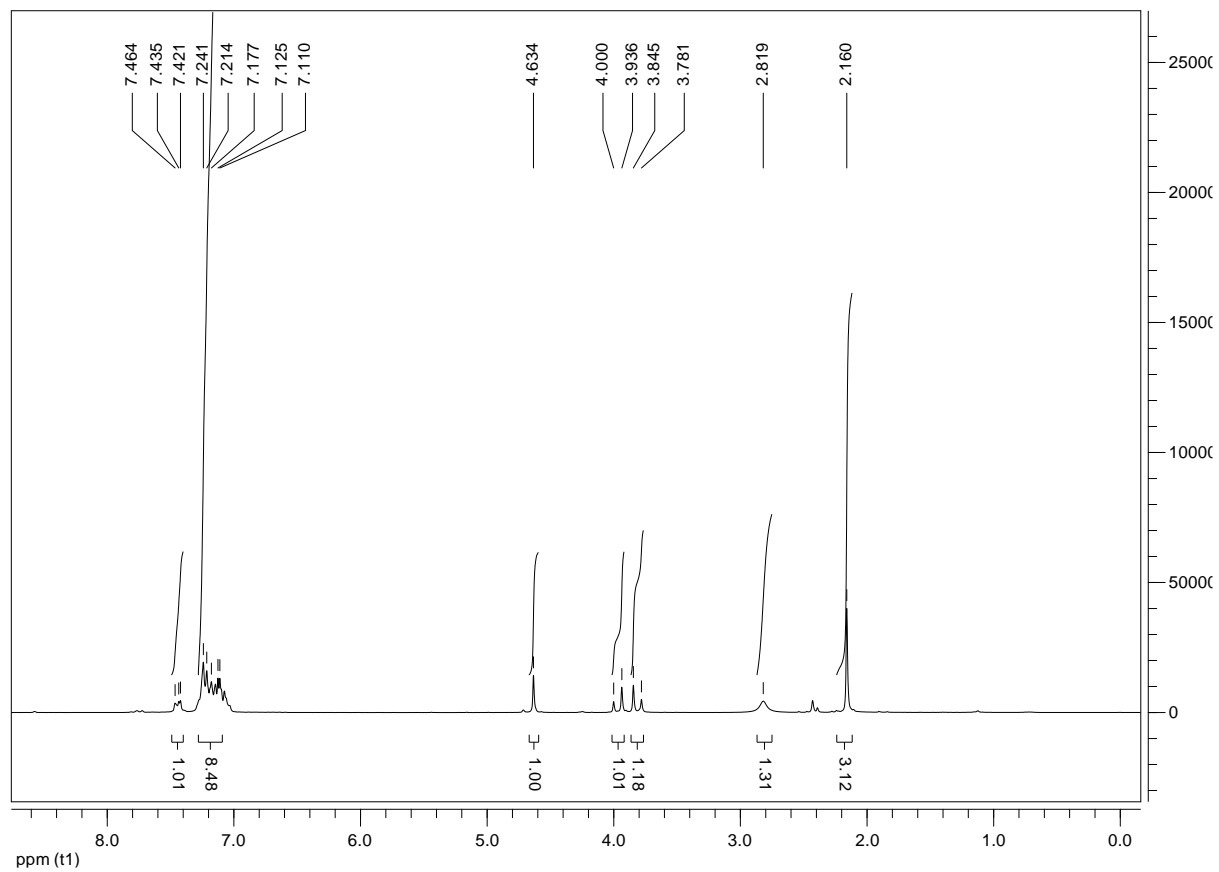
***N*-Benzyl-2-amino-(4-methylphenyl)acetonitrile (Table 2, entry 2)**



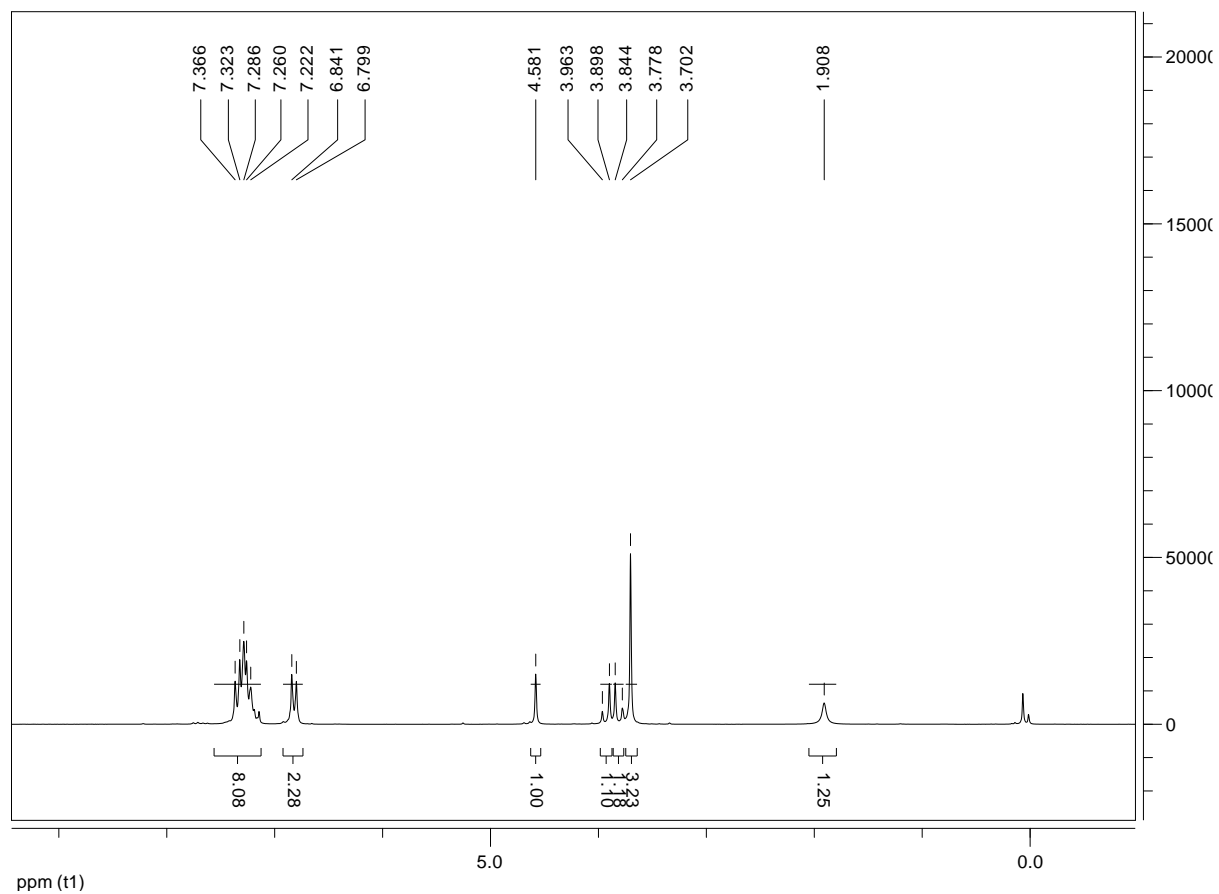
***N*-Benzyl-2-amino-(3-methylphenyl)acetonitrile (Table 2, entry 3)**



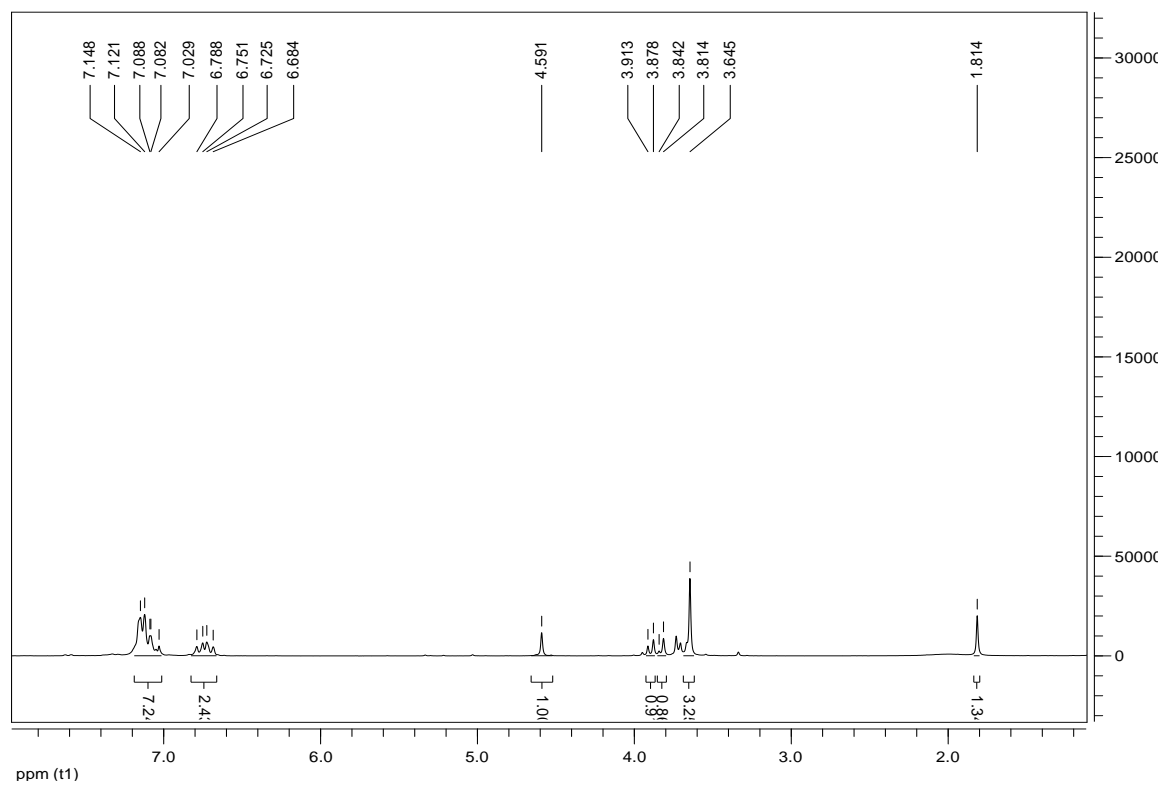
***N*-Benzyl-2-amino-(2-methylphenyl)acetonitrile (Table 2, entry 4)**



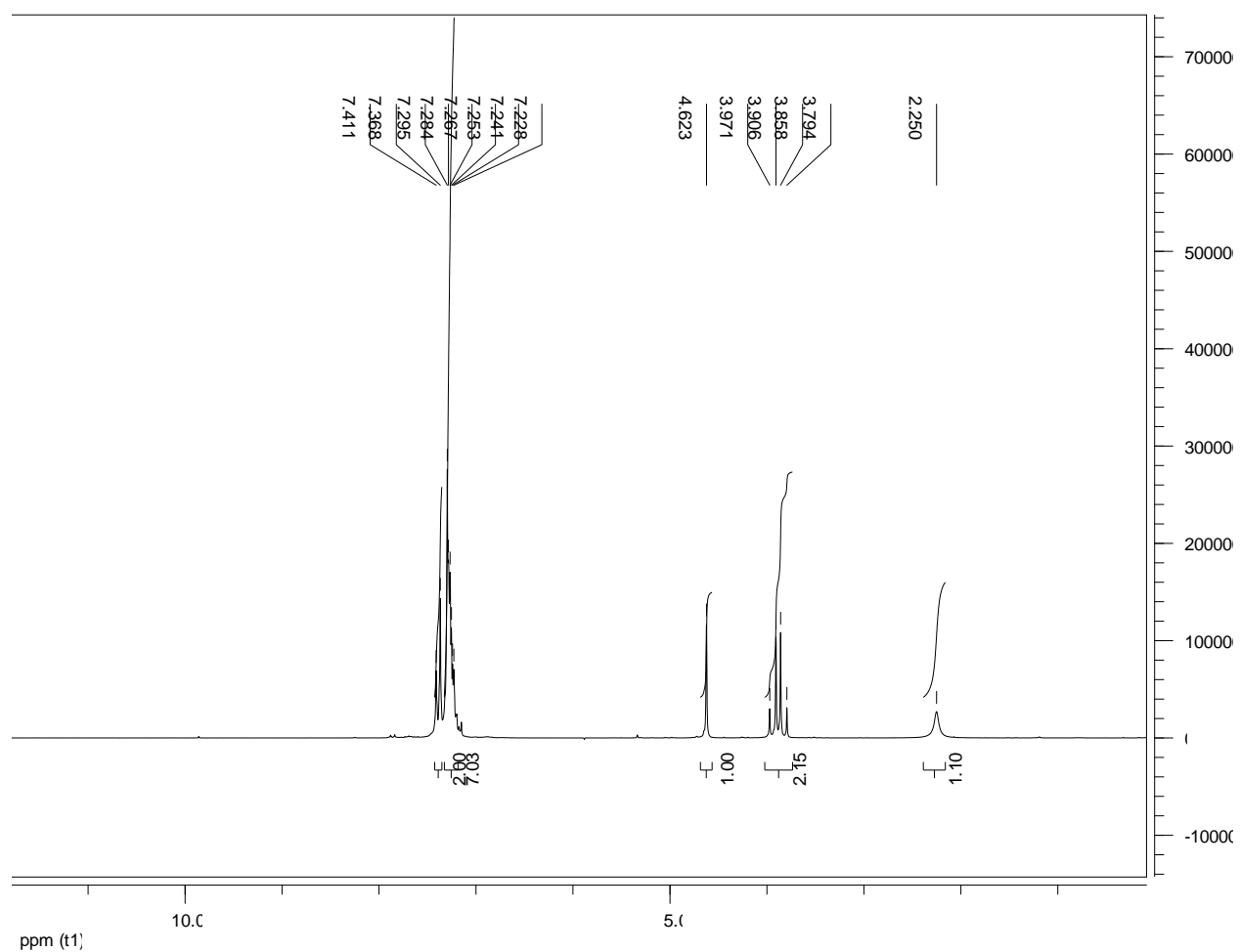
***N*-Benzyl-2-amino-(4-methoxyphenyl)acetonitrile (Table 2, entry 5)**



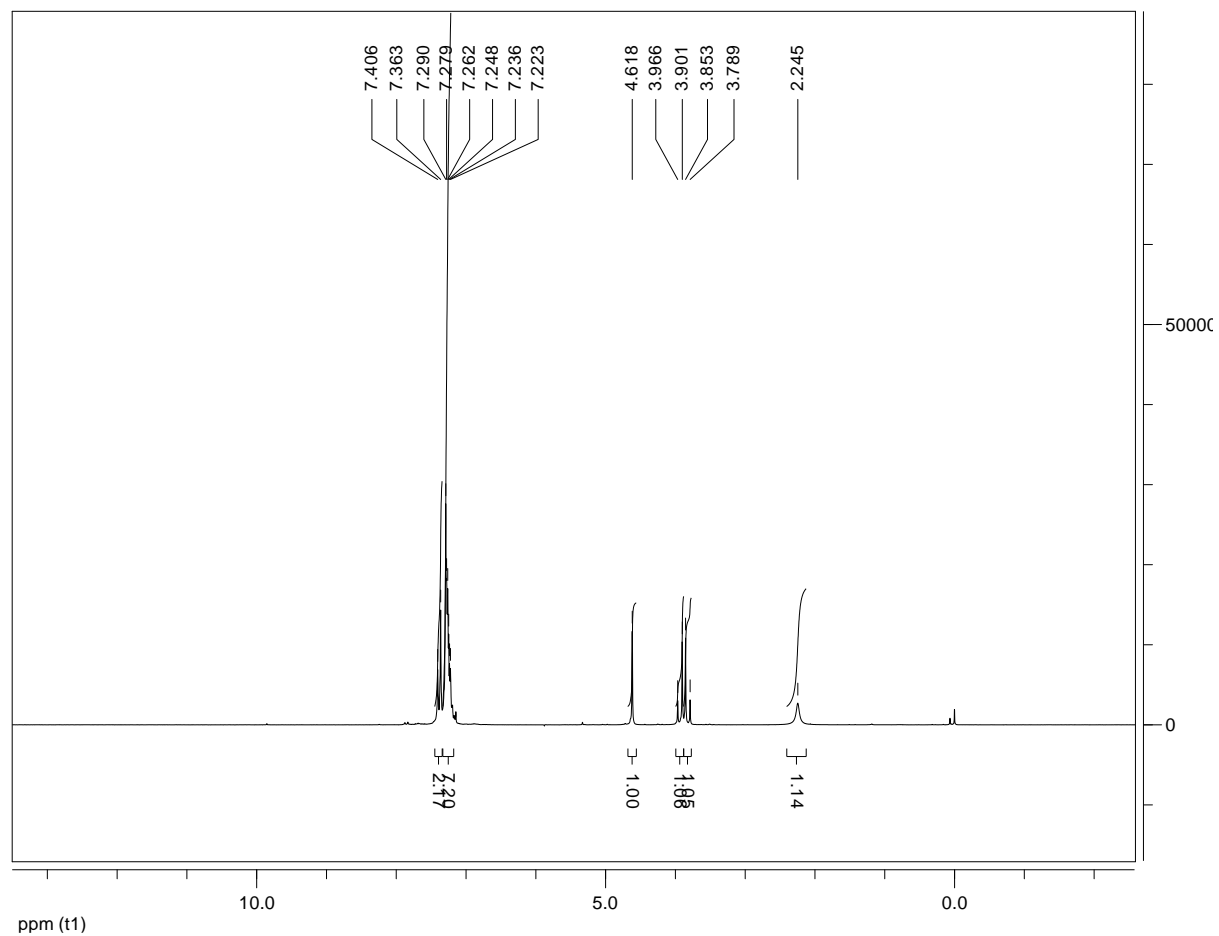
***N*-Benzyl-2-amino-(2-methoxyphenyl)acetonitrile (Table 2, entry 7)**



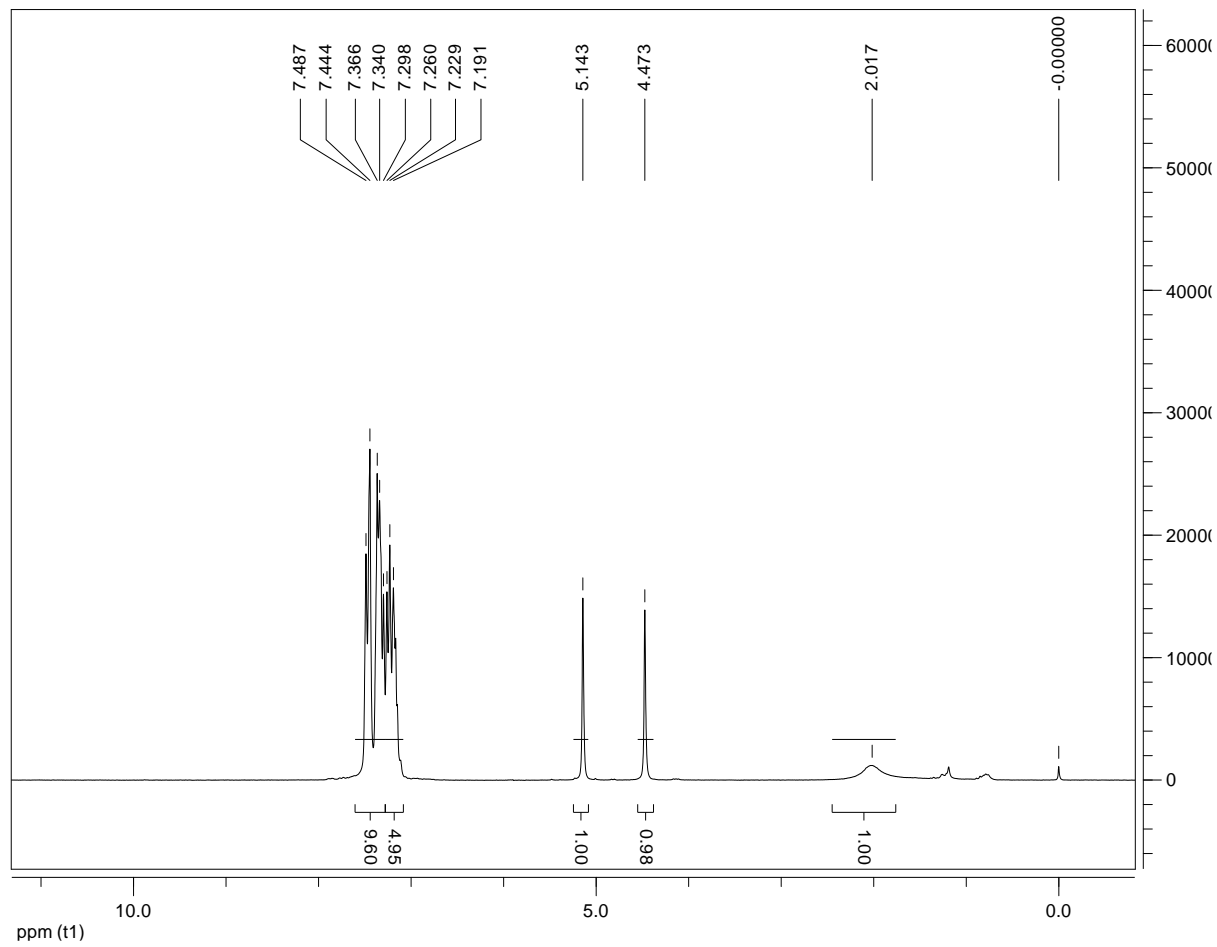
***N*-Benzyl-2-amino-(4-fluorophenyl)acetonitrile (Table 2, entry 8)**



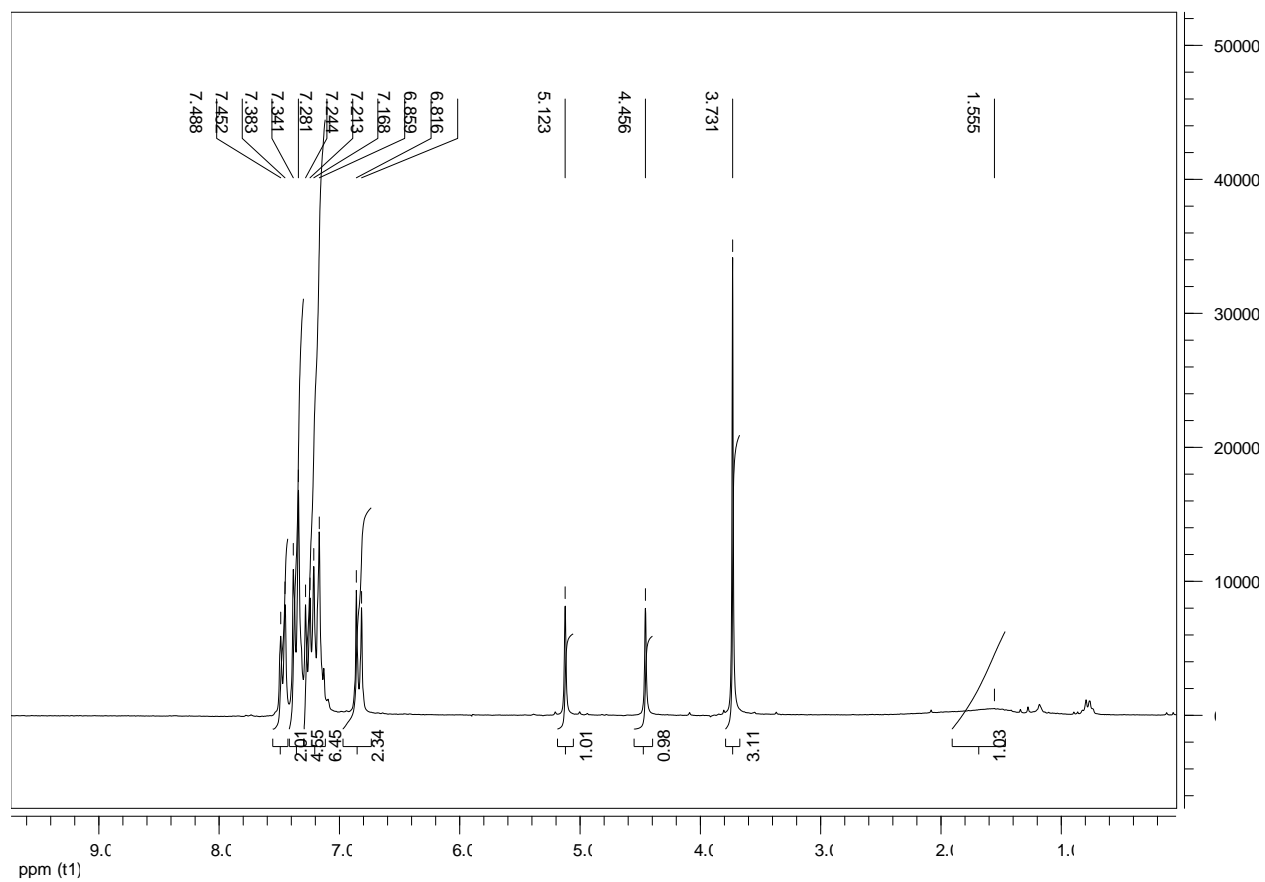
***N*-Benzyl-2-amino-(4-chlorophenyl)acetonitrile (Table 2, entry 9)**



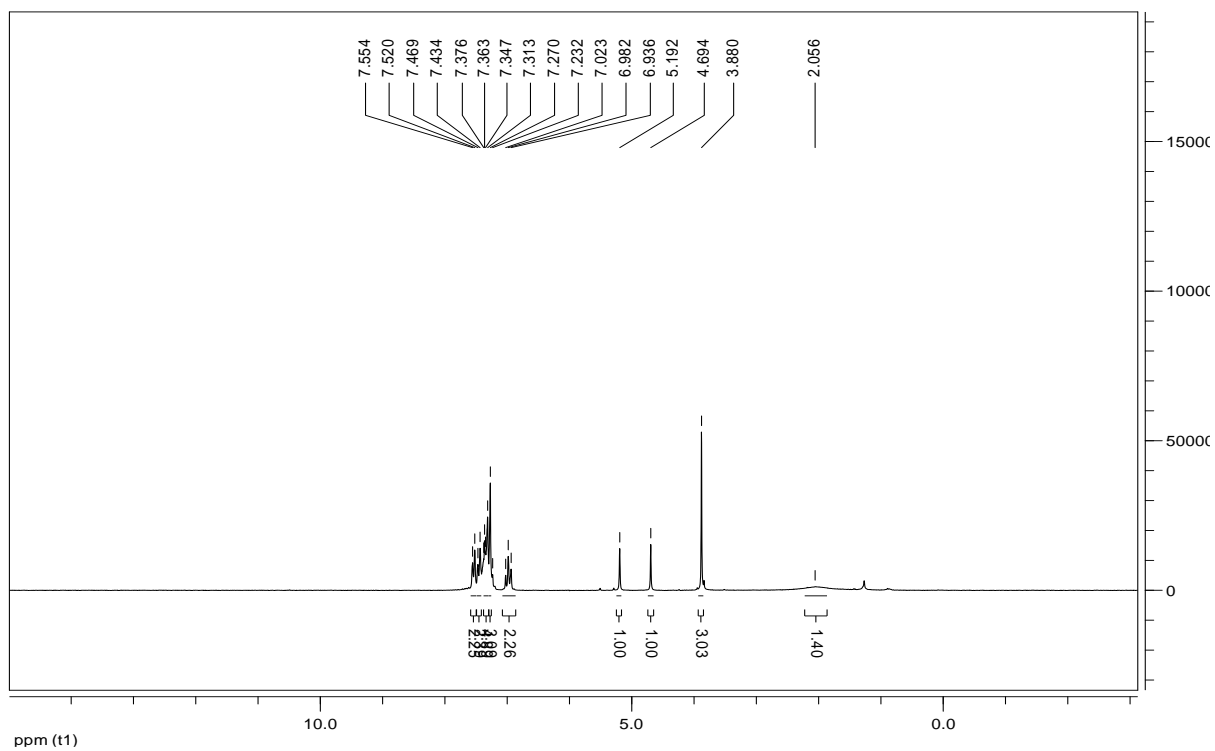
2-(Benzhydrylamino)-2-phenylacetonitrile (Table 2, entry 10)



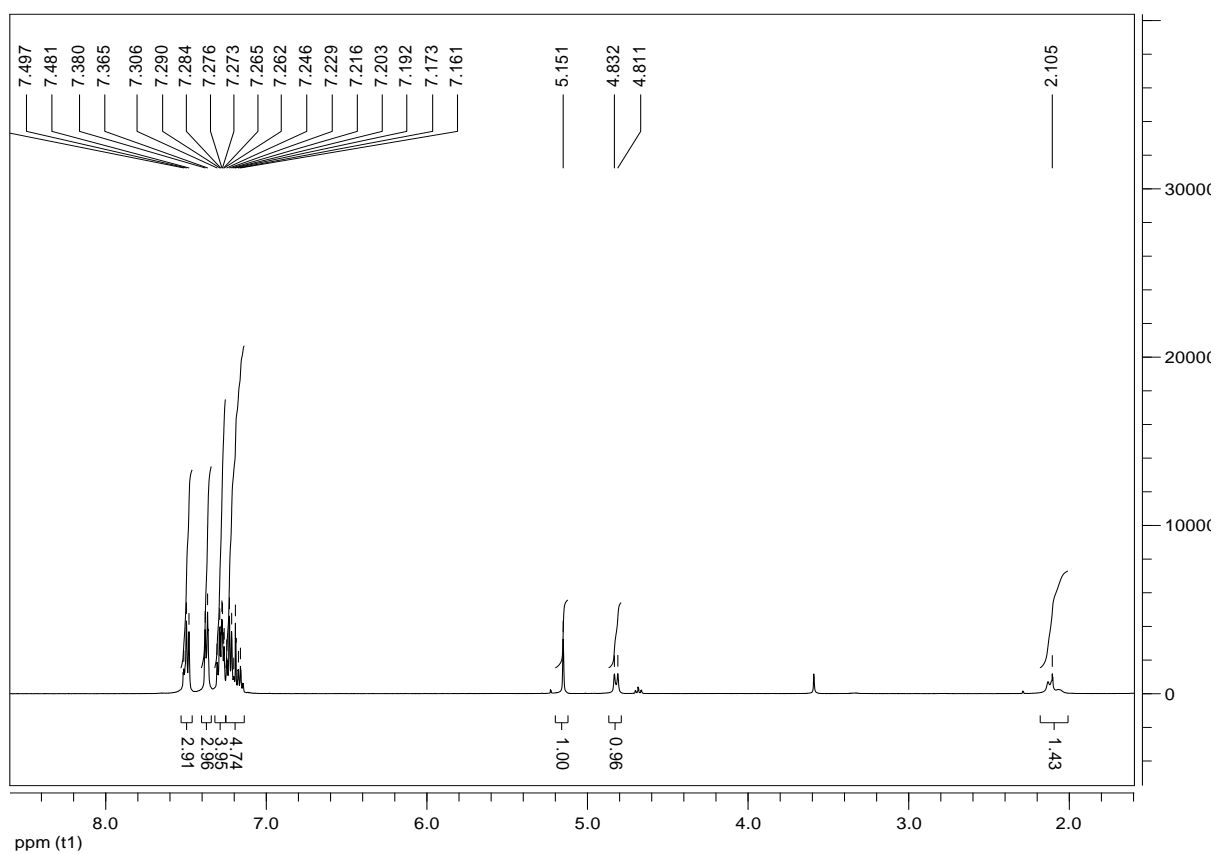
2-(Benzhydrylamino)-2-(4-methoxyphenyl)acetonitrile (Table 2, entry 11)



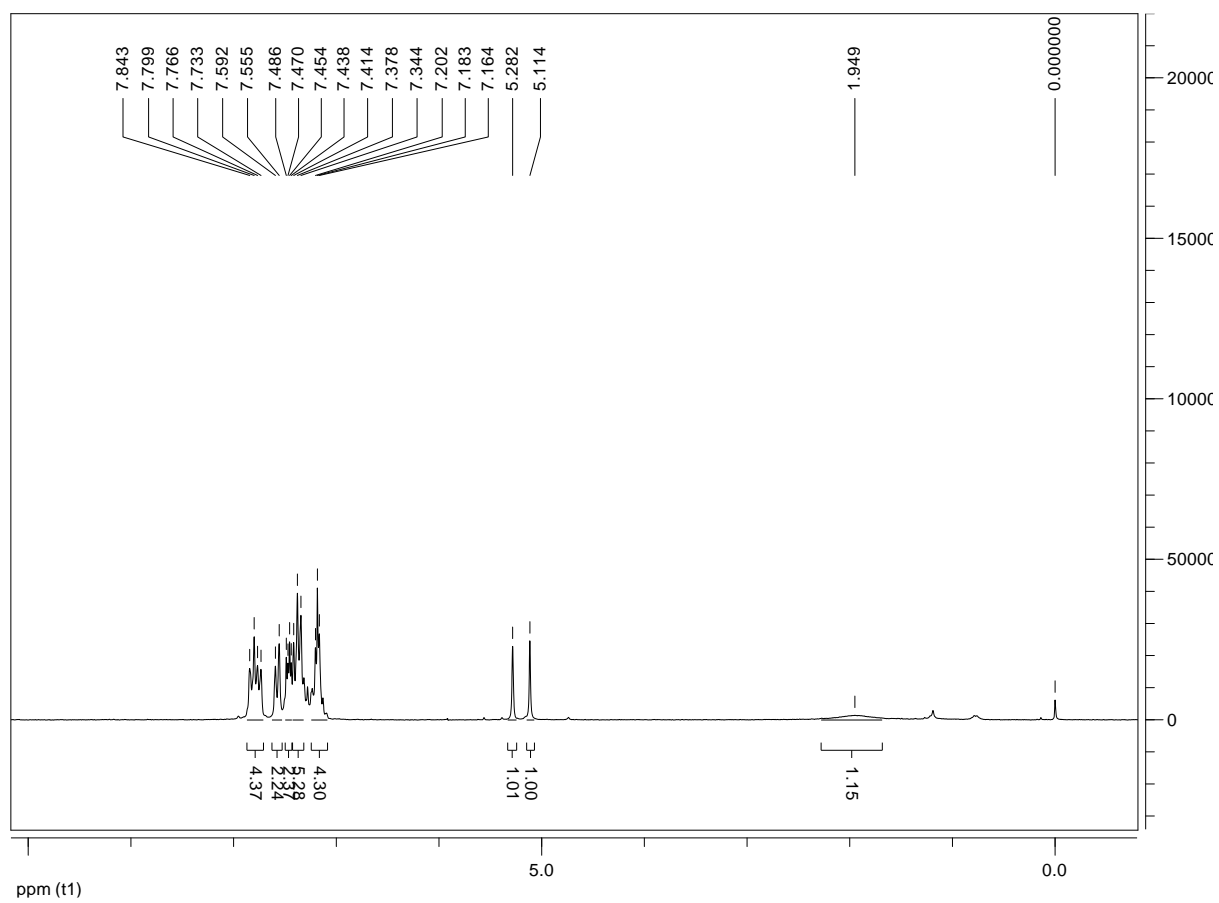
2-(Benzhydrylamino)-2-(2-methoxyphenyl)acetonitrile (Table 2, entry 12)



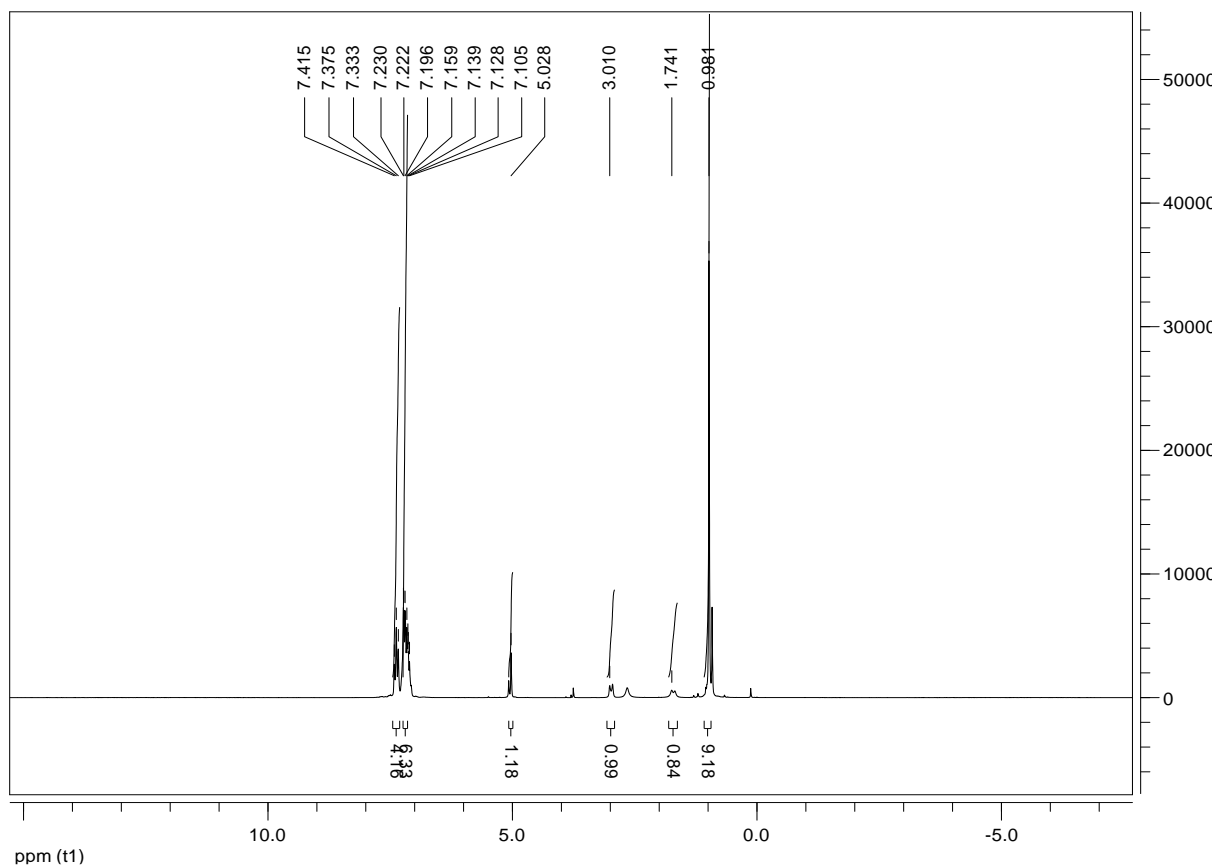
2-(Benzhydrylamino)-2-(4-bromophenyl)acetonitrile (Table 2, entry 13)



2-(Benzhydrylamino)-2-(naphthalen-2-yl)acetonitrile (Table 2, entry 14)



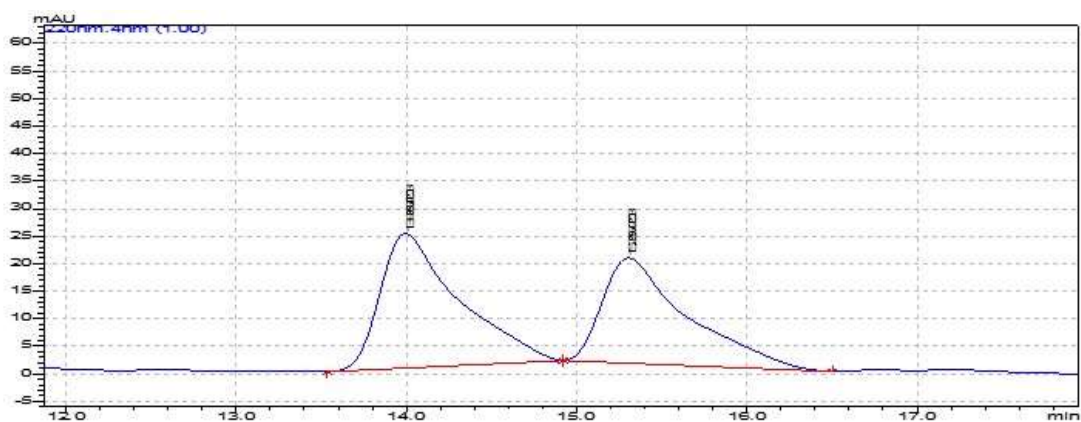
2-(benzhydrylamino)-3,3-dimethylbutanenitrile (Table 2, entry 15)

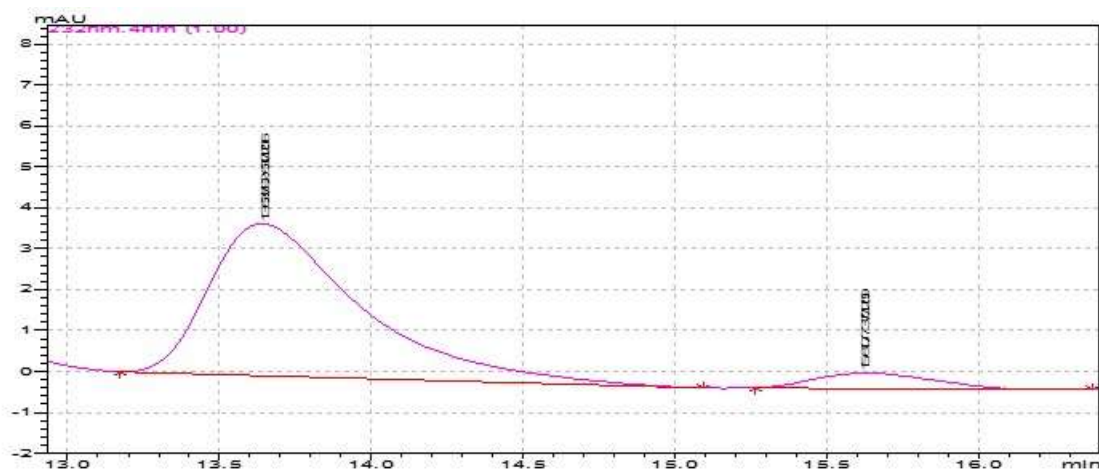


Characterization data of the products⁵

N-Benzyl-2-amino-phenylacetonitrile (Table 2, entry 1)

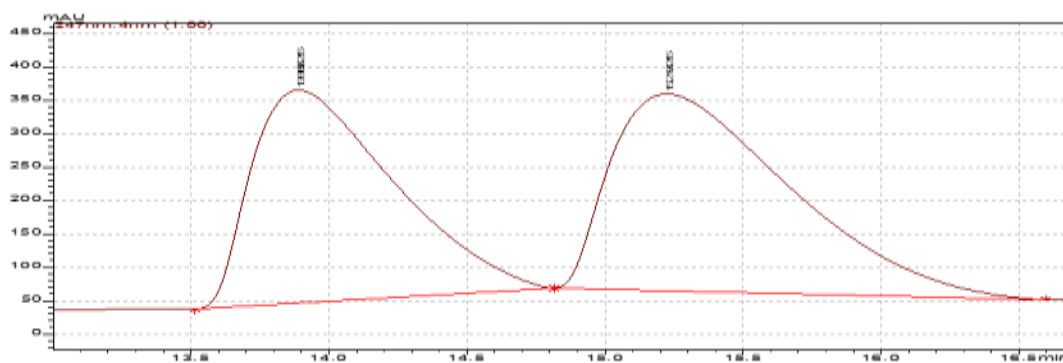
The title compound was isolated by column chromatography (Hexane / Ethylacetate 90/10) as yellow oil; ¹H NMR (500 MHz, CDCl₃) δ = 2.24 (br s, 1H), 3.78 (d, *J* = 13.0 Hz, 1H), 3.90 (d, *J* = 13.0 Hz, 1H), 4.6 (s, 1H), 7.28 - 7.41 (m, 10H); HPLC analysis: CHIRALCEL ODH column, hexane/2-propanol = 95:5, flow rate 0.8 ml/min, *t*_{r1} (major) = 13.65 min, *t*_{r2} (minor) = 15.8 min.

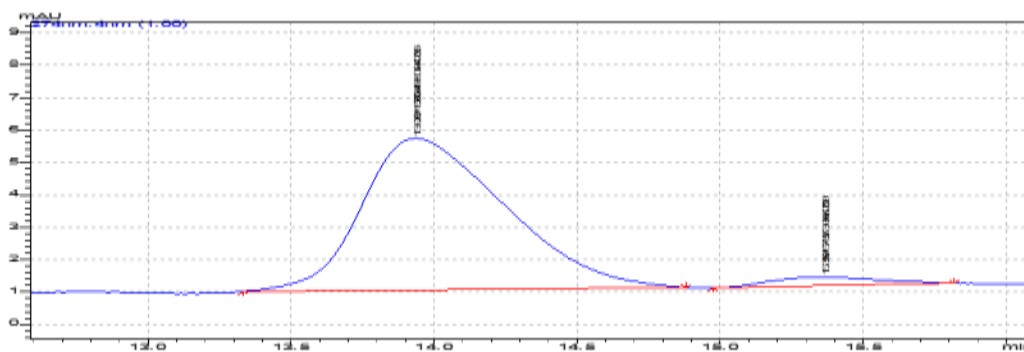




***N*-Benzyl-2-amino-(4-methylphenyl)acetonitrile (Table 2, entry 2)**

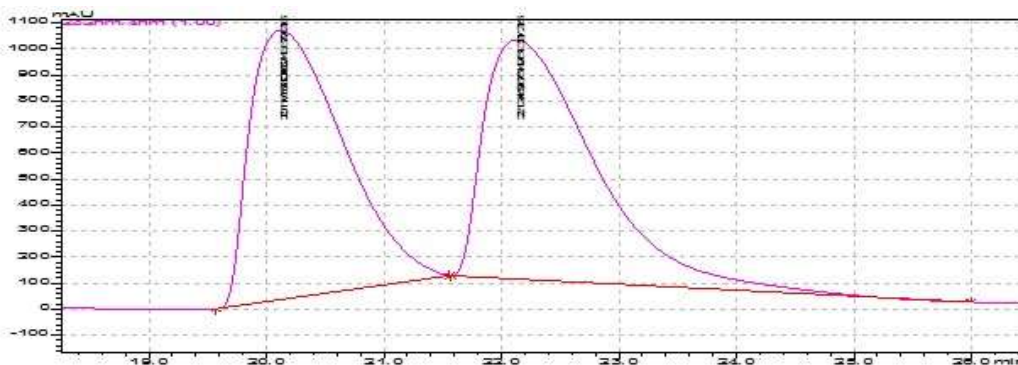
The title compound was isolated by column chromatography (Hexane / Ethylacetate 90/10) as yellow oil; ^1H NMR (500 MHz, CDCl_3) δ = 1.8 (1H, br s), 2.36 (3H, s), 3.93 (d, J = 13.0 Hz, 1H), 4.03 (d, J = 13.0 Hz, 1H), 4.71 (s, 1H), 7.19 - 7.42 (m, 9H); CHIRALCEL ODH column, hexane/2-propanol = 95:5, flow rate 0.8 ml/min, t_{r1} (major) = 13.9 min, t_{r2} (minor) = 15.4 min.





***N*-Benzyl-2-amino-(3-methylphenyl)acetonitrile (Table 2, entry 3)**

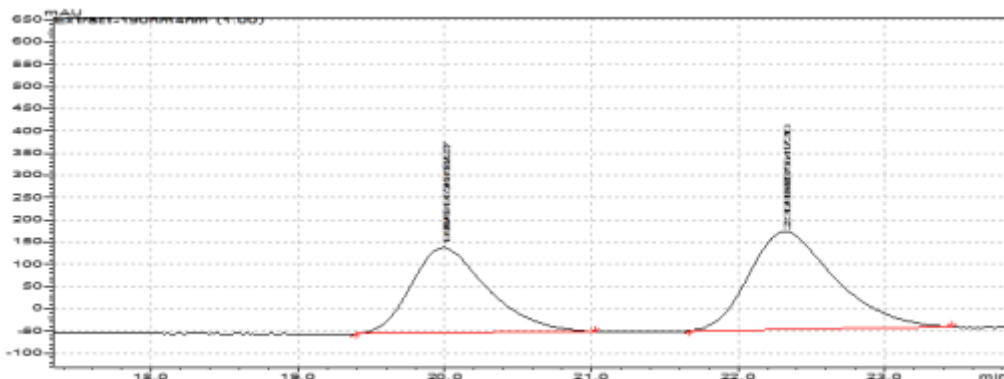
The title compound was isolated by column chromatography (Hexane / Ethylacetate 90/10) as yellow oil; ^1H NMR (500 MHz, CDCl_3) δ = 1.53 (br s, 1H), 2.30 (s, 3H), 3.86 (d, J = 13.0 Hz, 1H), 3.98 (d, J = 13.0 Hz, 1H), 4.63 (s, 1H), 7.1 - 7.4 (m, 9H); CHIRALCEL ODH column, hexane/2-propanol = 95:5, flow rate 0.8 ml/min, t_{r1} (minor) = 20.3 min, t_{r2} (major) = 21.9 min.

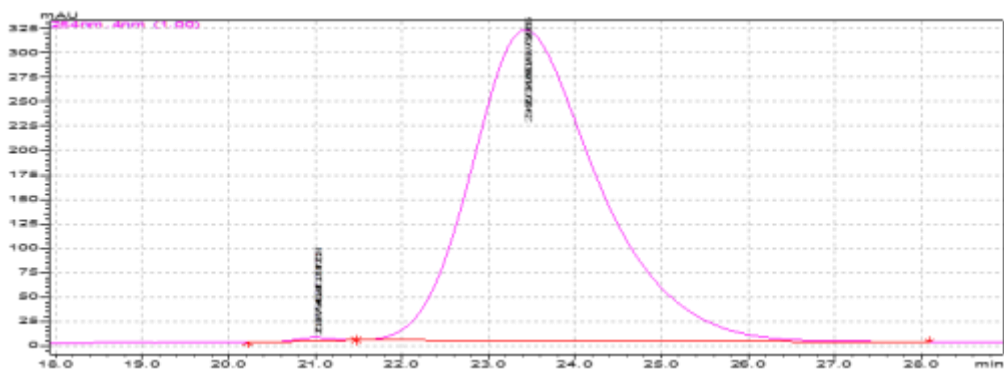




***N*-Benzyl-2-amino-(4-methoxyphenyl)acetonitrile (Table 2, entry 5)**

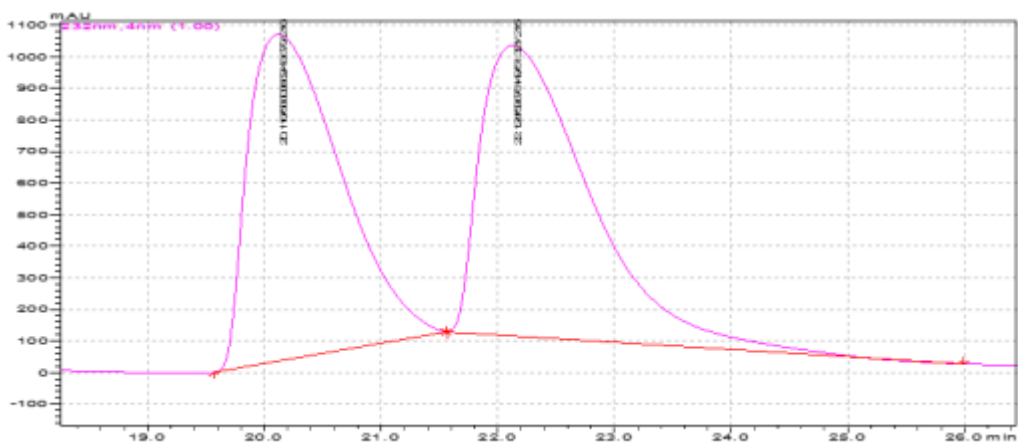
The title compound was isolated by column chromatography (Hexane / Ethylacetate 90/10) as yellow oil; ¹HNMR (500 MHz, CDCl₃) δ = 1.9 (br s, 1H), 3.7 (s, 3H), 3.77 (d, *J* = 13.0 Hz, 1H), 3.89 (d, *J* = 13.0 Hz, 1H), 4.58 (s, 1H), 6.79(d, *J* = 8.5 Hz, 2H), 7.2 - 7.4 (m, 7H); CHIRALCEL ODH column, hexane/2-propanol = 95:5, flow rate 0.8 ml/min, *t*₁ (minor) = 21.0 min, *t*₂ (major) = 23.4 min.

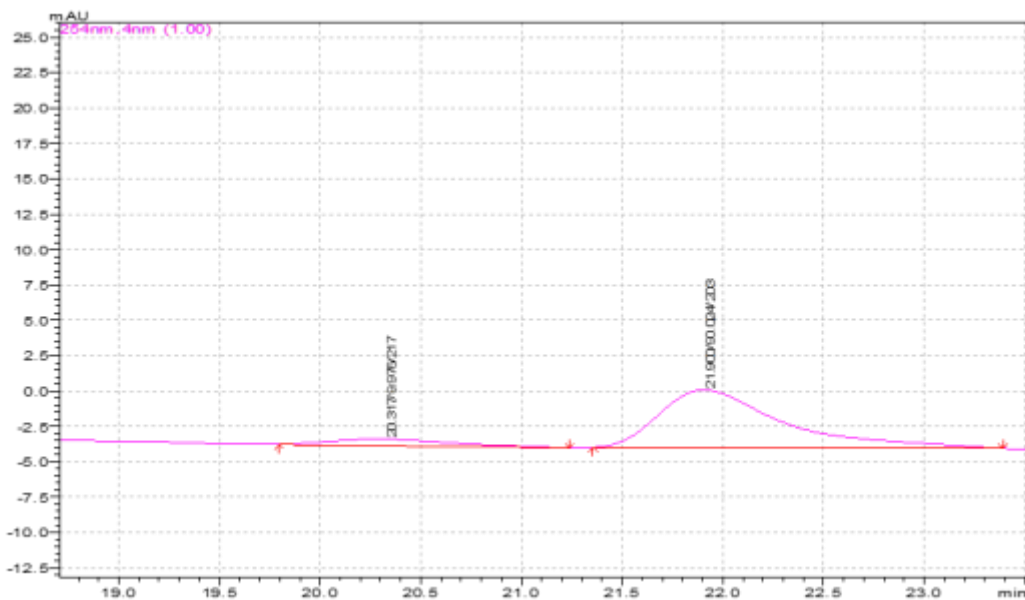




***N*-Benzyl-2-amino-(3-methoxyphenyl)acetonitrile (Table 2, entry 6)**

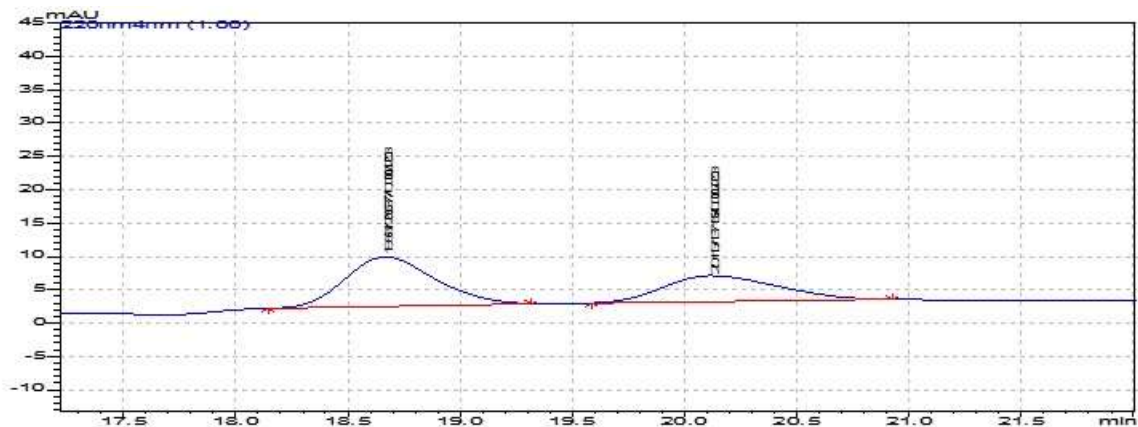
The title compound was isolated by column chromatography (Hexane / Ethylacetate 90/10) as yellow oil; ¹H NMR (500 MHz, CDCl₃) δ = 1.7 (br s, 1H), 3.79 (s, 3H), 3.92 (d, *J* = 13.0 Hz, 1H), 4.04 (d, *J* = 13.0 Hz, 1H), 4.6 (s, 1H), 6.92 (d, *J* = 8.5 Hz, 2H), 7.2 - 7.6 (m, 7H); CHIRALCEL OD column, hexane/2-propanol = 95:5, flow rate 0.8 ml/min, *t*_{r1} (minor) = 20.3 min, *t*_{r2} (major) = 21.9 min.

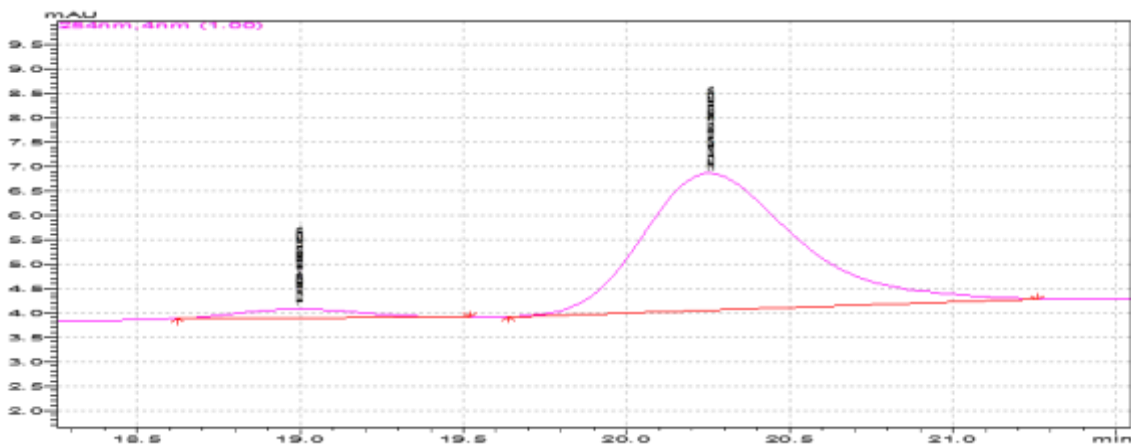




***N*-Benzyl-2-amino-(2-methoxyphenyl)acetonitrile (Table 2, entry 7)**

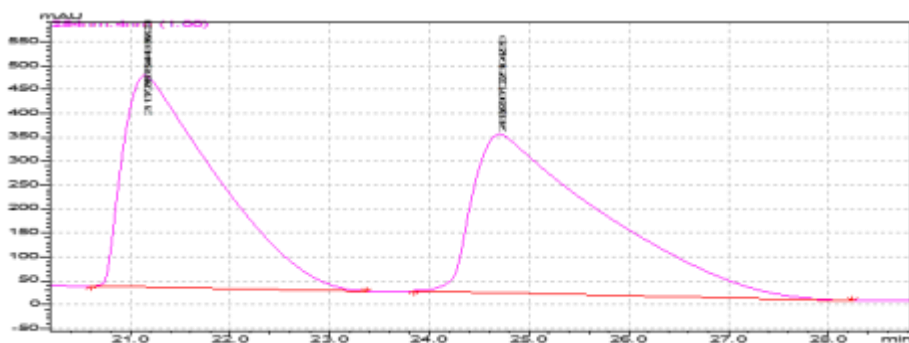
The title compound was isolated by column chromatography (Hexane / Ethylacetate 90/10) as yellow oil; ^1H NMR (500 MHz, CDCl_3) δ = 1.81 (br s, 1H), 3.64 (s, 3H), 3.81 (d, J = 13.0 Hz, 1H), 3.87 (d, J = 13.0 Hz, 1H), 4.59 (s, 1H), 6.68 (d, J = 8.5 Hz, 2H), 7.02 - 7.2 (m, 7H); CHIRALCEL OD column, hexane/2-propanol = 95:5, flow rate 0.8 ml/min, t_{r1} (minor) = 18.9 min, t_{r2} (major) = 20.2 min.

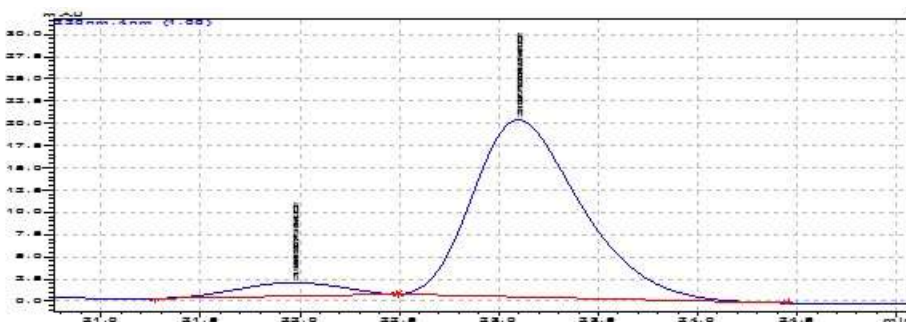




***N*-Benzyl-2-amino-(4-chlorophenyl)acetonitrile (Table 2, entry 9)**

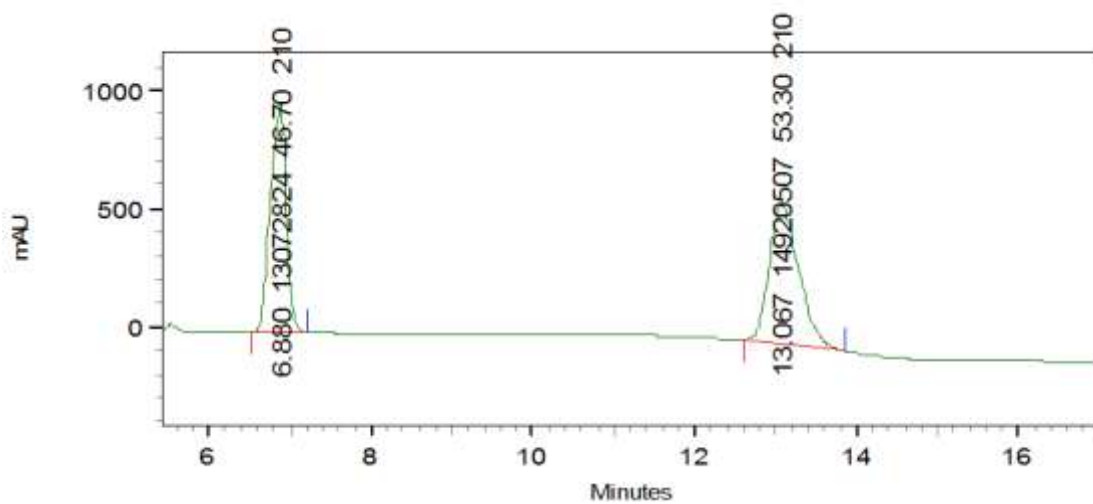
The title compound was isolated by column chromatography (Hexane / Ethylacetate 90/10) as yellow oil; ¹HNMR (500 MHz, CDCl₃) δ = 2.24 (br s, 1H), 3.78 (d, *J* = 13.0 Hz, 1H), 3.90 (d, *J* = 13.0 Hz, 1H), 4.62 (s, 1H), 7.2 - 7.4 (m, 9H); CHIRALCEL AD column, hexane/2-propanol = 95:5, flow rate 0.8 ml/min, *t*_{r1} (minor) = 21.9 min, *t*_{r2} (major) = 23.0 min.

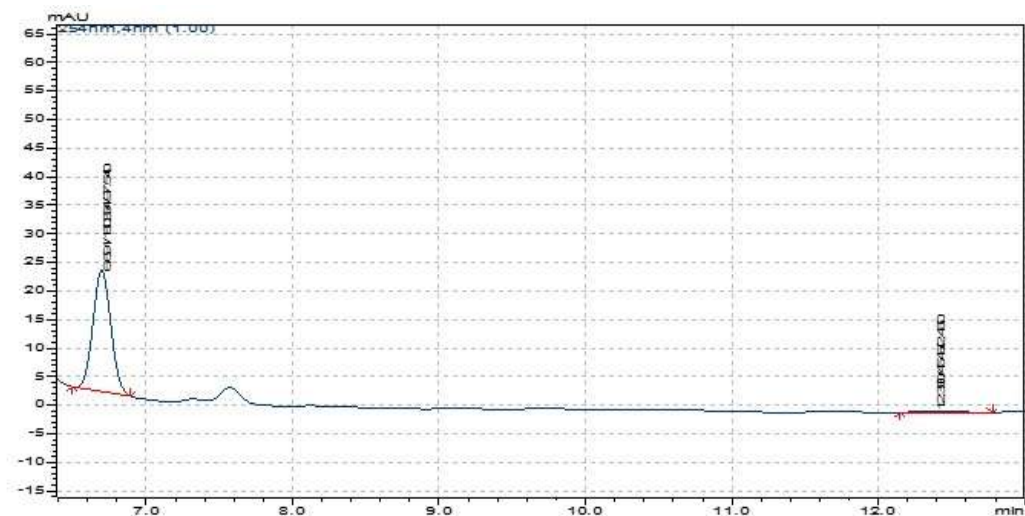




2-(Benzhydrylamino)-2-phenylacetonitrile (Table 2, entry 10)

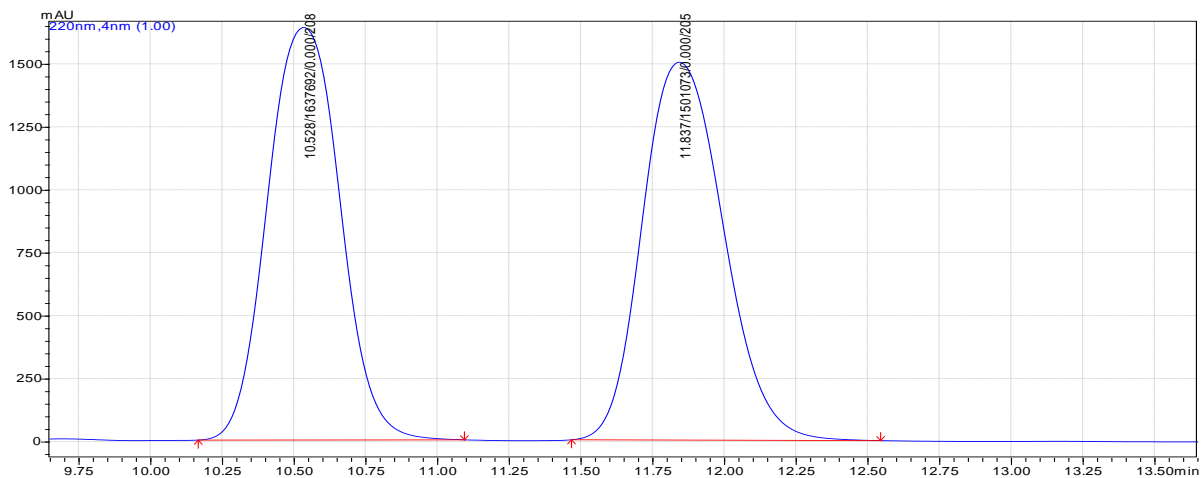
The title compound was isolated by column chromatography (Hexane / Diethylether 20/80) as white solid; ^1H NMR (500 MHz, CDCl_3) δ = 2.01 (d, J = 12.5 Hz, 1H), 4.47 (d, J = 12.5 Hz, 1H), 5.14 (s, 1H), 7.19 - 7.48 (m, 5H), 7.44 - 7.76 (m, 10H); CHIRALCEL ADH column, hexane/2-propanol = 80:20, flow rate 1 ml/min, t_{r1} (major) = 6.8 min, t_{r2} (minor) = 13.06 min.

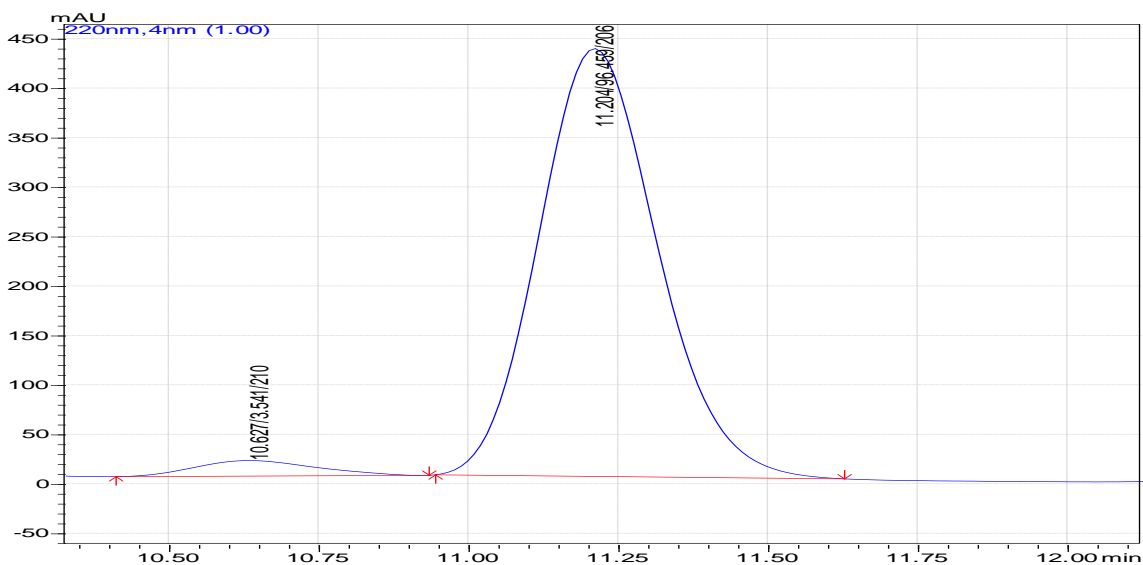




2-(Benzhydrylamino)-2-(4-methylphenyl) acetonitrile (Table 2, entry 11)

The title compound was isolated by column chromatography (Hexane / Diethylether 20/80) as white solid; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ = 2.11 (d, J = 12.5 Hz, 1H), 2.34 (s, 3H), 4.56 (d, J = 12.5 Hz, 1H), 5.21 (s, 1H), 7.20 - 7.54 (m, 14H); CHIRALCEL ADH column, hexane/2-propanol = 80:20, flow rate 1 ml/min, t_{r1} (minor) = 10.6 min, t_{r2} (major) = 11.2 min.

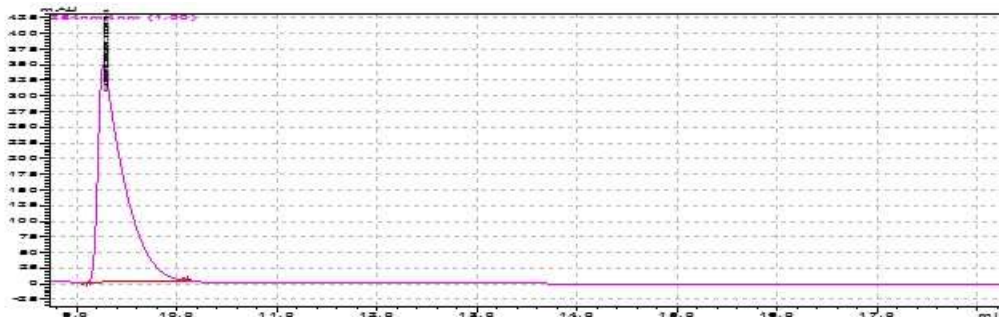




2-(Benzhydrylamino)-2-(2-methoxyphenyl) acetonitrile (Table 2, entry 12)

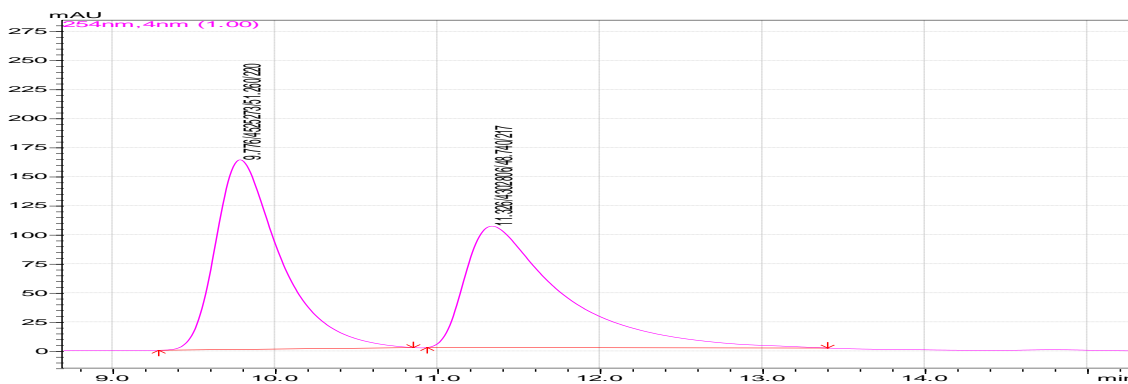
The title compound was isolated by column chromatography (Hexane / Diethylether 10/90) as a liquid; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ = 2.05 (d, J = 12.5 Hz, 1H), 3.88 (s, 3H), 4.69 (d, J = 12.5 Hz, 1H), 5.19 (s, 1H), 6.93-7.02 (m, 2H), 7.20 - 7.55 (m, 12H); CHIRALCEL ODH column, hexane/2-propanol = 80:20, flow rate 1 ml/min, t_{r1} (major) = 9.2 min.

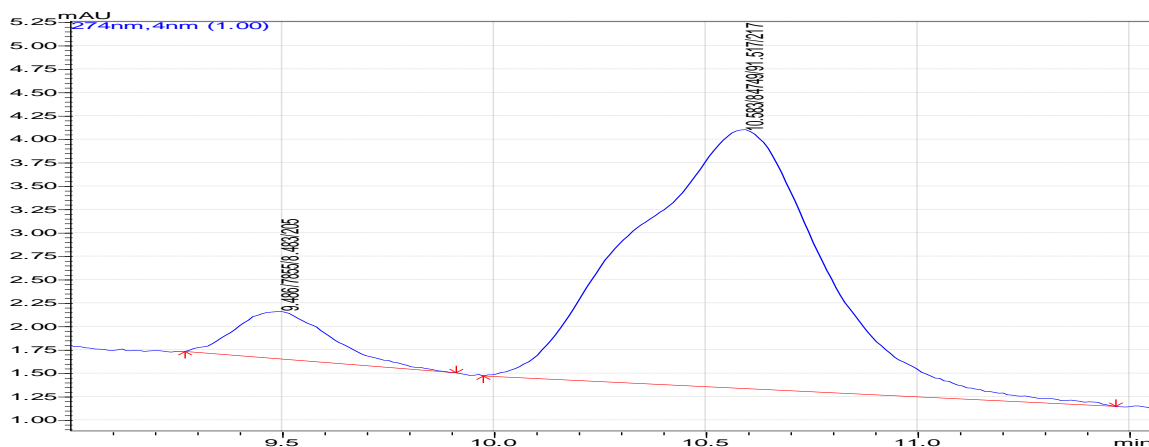




2-(Benzhydrylamino)-2-(4-bromophenyl) acetonitrile (Table 2, entry 13)

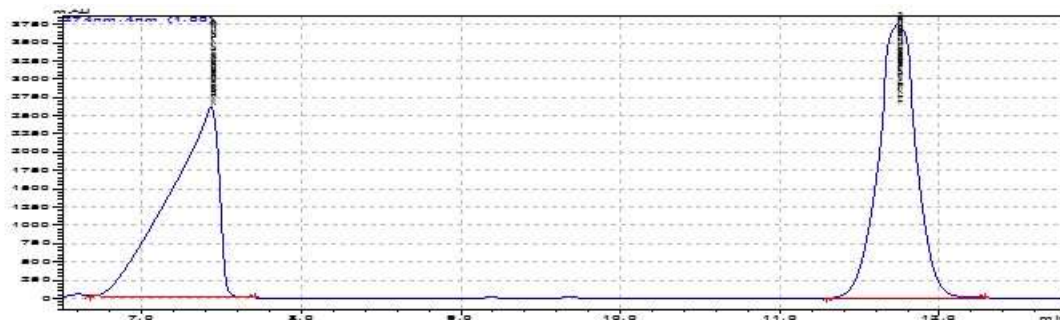
The title compound was isolated by column chromatography (Hexane/ethylacetate95/5) as a white solid; ^1H NMR (500 MHz, CDCl_3) δ = 2.10 (d, J = 12.5 Hz, 1H), 4.81 (d, J = 12.5 Hz, 1H), 5.15 (s, 1H), 7.16-7.22 (m, 4H), 7.24 - 7.30 (m, 4H), 7.36 - 7.56 (m, 6H); CHIRALCEL AD-H column, hexane/2-propanol = 80:20, flow rate 1 ml/min, t_{r1} (minor) = 9.4 min, t_{r2} (major) = 10.6min.





2-(Benzhydrylamino)-2-(naphthalen-2-yl)acetonitrile (Table 2, entry 14)

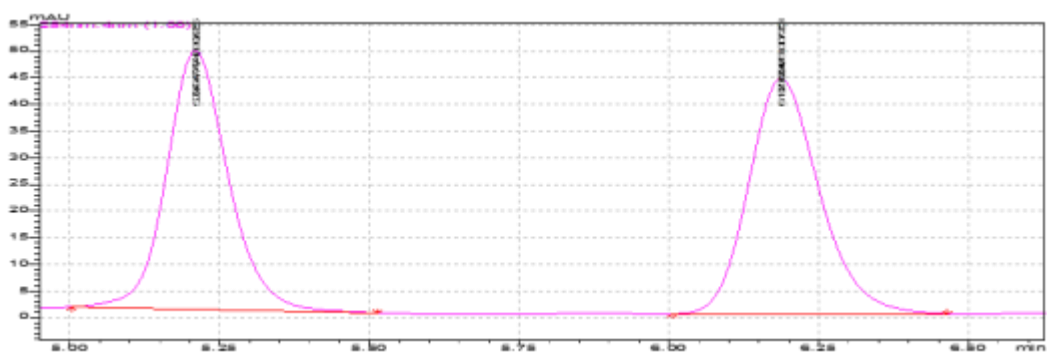
The title compound was isolated by column chromatography (Hexane / Diethylether 10/90) as a white solid; ^1H NMR (500 MHz, CDCl_3) δ = 1.94 (d, J = 12.5 Hz, 1H), 5.11 (d, J = 12.5 Hz, 1H), 5.28 (s, 1H), 7.16-7.59 (m, 13H), 7.73 - 7.78 (m, 4H); CHIRALCEL ODH column, hexane/2-propanol = 80:20, flow rate 1 ml/min, t_{r1} (minor) = 7.52 min, t_{r2} (major) = 11.7 min.

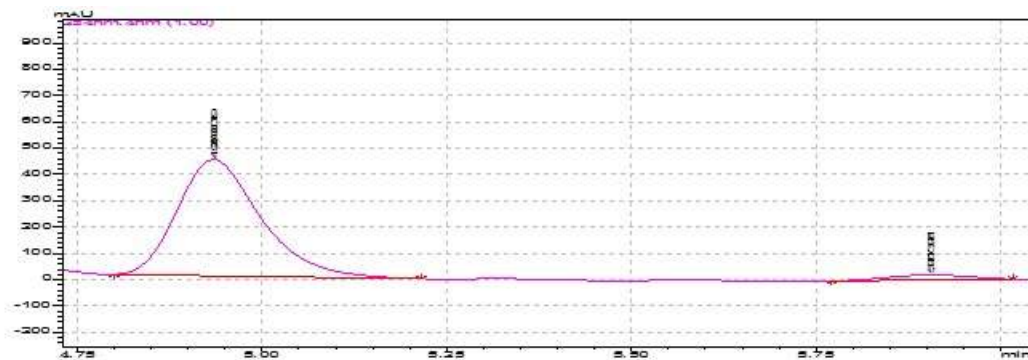




2-(benzhydrylamino)-3,3-dimethylbutanenitrile (Table 2, entry 15)

The title compound was isolated by column chromatography (Hexane / Diethylether 10/90) as a white solid; ^1H NMR (500 MHz, CDCl_3) δ = 0.98 (s, 9H), 1.74 (d, J = 12.5 Hz, 1H), 3.01 (d, J = 12.5 Hz, 1H), 5.02 (s, 1H), 7.1-7.51 (m, 10H); CHIRALCEL ADH column, hexane/2-propanol = 80:20, flow rate 1 ml/min, t_{r1} (minor) = 4.9 min, t_{r2} (major) = 5.9 min.





References:

1. N. H. Khan, A. Sadhukhan, N. C. Maity, R. I. Kureshy, S. H. R. Abdi, S. Saravanan, H. C. Bajaj, *Tetrahedron* 2011, **67**, 7073.
2. R. I. Kureshy, T. Roy, N. H. Khan, S. H. R. Abdi, A. Sadhukhan, H. C. Bajaj, *J. Catal.*, 2012, **286**, 41.
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4. Y. H. Wen, Y. Xiong, L. Chang, J. L. Huang, X. H. Liu, X. M. Feng. *J. Org. Chem.* 2007, **72**, 7715.
5. (a) A. M. Seayad, B. Ramalingam, K. Yoshinaga, T. Nagata, C. L. L. Chai, *Org. Lett.* 2010, **12**, 264; (b) S. Saravanan, N. H. Khan, R. I. Kureshy, S. H. R. Abdi, H. C. Bajaj, *ACS Catal.*, 2013, **3** (12), 2873.