Electronic Supplementary Material (ESI) for RSC Advances

Supplementary Information

Titania nanomaterials: efficient and recyclable heterogeneous catalysts for the solvent-free synthesis of poly-substituted quinolines *via* Friedlander hetero-annulation

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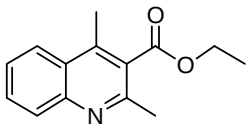
Contents:

General Experimental Information: All chemicals were purchased from Sigma-Aldrich, India and used without further purification. Solvents were distilled prior to use. Triple distilled water was used for the reaction. The reactions were performed in air atmosphere without any specific precautions. Reactions were carried out on controlled temperature oil bath in conventional heating method. Melting points were determined with open capillary tube on a Gallenkamp (variable heater) melting point apparatus and were uncorrected. FT-IR spectra were recorded as KBr pellets on a Bruker Tensor 27 spectrometer with Opus 5.5 software. The ^{1}H and ^{13}C NMR spectra of the synthesized compounds were recorded at 400 MHz and 100 MHz respectively using Bruker AVANCE 400 MHz NMR spectrometer in DMSO-d_6 and $CDCl_3$ solvent and the chemical shifts (δ) were expressed in ppm relative to TMS as internal standard and coupling constants (*J*) in Hz. Spin multiplicities are described as s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). Mass analysis was performed on quadruple-time of flight (Q-Tof) mass spectrometer (Micromass, USA) using electrospray ionization (ESI) in positive mode. TLC is performed using precoated aluminium sheets with silica gel 60 F_{254}. GC–MS system (5975C) of Agilent, USA make was used for characterization of reaction products.

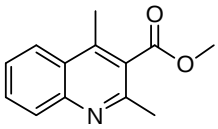
All the synthesized poly-substituted quinoline derivatives are fully characterized by four independent characterization techniques (Melting point, FT-IR, ^{1}H-NMR, ^{13}C NMR and ESI-MS) as follows:



3a

Ethyl 2,4-dimethylquinoline-3-carboxylate (3a)[1]

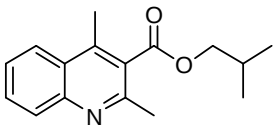
Viscous oil; Yield: 0.211 g, 92%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.44 (t, J = 7.1 Hz, 3H, CH_3), 2.66 (s, 3H, CH_3), 2.71 (s, 3H, CH_3), 4.49 (q, J = 7.1 Hz, 2H, OCH_2), 7.54-7.56 (m, 1H, Ar-H), 7.69-7.71 (m, 1H, Ar-H), 7.98-8.02 (m, 2H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.1, 15.5, 23.6, 61.2, 123.6, 125.7, 126.1, 127.8, 129.7, 141.1, 147.2, 154.2, 168.9. ESI-MS: *m/z* 230 $[M+H]^+$; Anal. Calcd. for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11%; Found: C, 73.24; H, 6.66; N, 5.99%.



3b

Methyl 2,4-dimethylquinoline-3-carboxylate (3b)

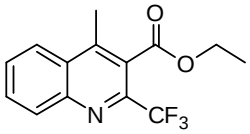
Viscous oil; Yield: 0.202 g, 94%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.65 (s, 3H, CH_3), 2.71 (s, 3H, CH_3), 3.82 (s, 3H, OCH_3), 7.53-7.55 (m, 1H, Ar-H), 7.71-7.73 (m, 1H, Ar-H), 7.99-8.03 (m, 2H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 15.8, 23.9, 52.5, 123.6, 125.8, 126.2, 127.7, 128.8, 129.6, 141.3, 147.0, 154.4, 168.5. ESI-MS: *m/z* 216 $[M+H]^+$. Anal. Calcd. for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51%; Found: C, 72.66; H, 6.12; N, 6.43%.



3c

Isobutyl 2,4-dimethylquinoline-3-carboxylate (3c)

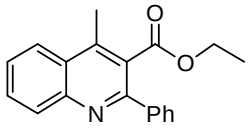
Viscous oil; Yield: 0.224 g, 87%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.03 (d, J = 5.6 Hz, 6H, CH_3), 2.07 (m, 1H, CH), 2.68 (s, 3H, CH_3), 2.74 (s, 3H, CH_3), 4.08 (d, J = 6.8 Hz, 2H, CH_2), 7.55-7.57 (m, 1H, Ar-H), 7.70-7.72 (m, 1H, Ar-H), 8.02-8.04 (m, 1H, Ar-H), 8.05-8.07 (m, 1H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 16.9, 22.5, 27.3 72.6, 125.6, 126.3, 127.9, 128.5, 129.4, 141.3, 147.0, 154.6, 166.8. ESI-MS: *m/z* 258 $[M+H]^+$. Anal. Calcd. for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44; N, 5.44%; Found: C, 74.61; H, 7.52; N, 5.39%.



3d

Ethyl 4-methyl-2-(trifluoromethyl)quinoline-3-carboxylate (3d)

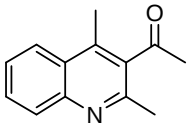
Viscous oil; Yield: 0.235 g, 83%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.36 (t, J = 7.2 Hz, 3H, CH_3), 2.63 (s, 3H, CH_3), 4.45 (q, J = 7.2 Hz, 2H, CH_2), 7.57-7.59 (m, 1H, Ar-H), 7.75-7.77 (m, 1H, Ar-H), 8.08-8.12 (m, 2H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.2, 15.7, 61.1, 119.6, 127.1, 128.5, 129.8, 130.7, 135.1, 141.1, 147.2, 149.8, 169.0. ESI-MS: *m/z* 284 $[M+H]^+$. Anal. Calcd. for $C_{14}H_{12}F_3NO_2$: C, 59.37; H, 4.27; N, 4.95%; Found: C, 59.46; H, 4.17; N, 5.03%.



3e

Ethyl 4-methyl-2-phenylquinoline-3-carboxylate (3e)

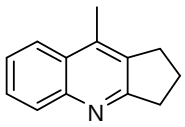
Solid; Yield: 0.236 g, 81%; m.p 97-98 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.47 (t, J = 7.2 Hz, 3H, CH_3), 2.71 (s, 3H, CH_3), 4.51 (q, J = 7.2 Hz, 2H, OCH_2), 6.77-6.79 (m, 1H, Ar-H), 7.56-7.60 (m, 2H, Ar-H), 7.70-7.72 (m, 1H, Ar-H), 7.96-7.98 (m, 1H, Ar-H), 7.99-8.03 (m, 2H, Ar-H), 8.05-8.07 (m, 2H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.4, 15.3, 61.2, 123.9, 126.7, 127.8, 128.5, 129.8, 130.4, 131.7, 135.3, 141.1, 148.5, 151.2, 168.9. ESI-MS: *m/z* 292 $[M+H]^+$. Anal. Calcd. for $C_{19}H_{17}NO_2$: C, 78.33; H, 5.88; N, 4.81%; Found: C, 78.24; H, 5.71; N, 4.94%.



3f

1-(2,4-Dimethylquinolin-3-yl)ethanone (3f)[1]

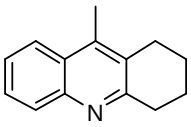
Viscous oil; Yield: 0.177 g, 89%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.54 (s, 3H, CH_3), 2.58 (s, 3H, CH_3), 2.62 (s, 3H, $COCH_3$), 7.49-7.51 (m, 1H, Ar-H), 7.64-7.66 (m, 1H, Ar-H), 7.93-7.95 (m, 1H, Ar-H), 7.99-8.01 (m, 1H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 15.9, 23.9, 32.6, 123.5, 126.2, 128.3, 129.8, 135.6, 138.4, 146.7, 153.6, 206.3. ESI-MS: *m/z* 200 $[M+H]^+$. Anal. Calcd. for $C_{13}H_{13}NO$: C, 78.36; H, 6.58; N, 7.03%; Found: C, 78.42; H, 6.39; N, 7.11%.



3g

9-Methyl-2,3-dihydro-1*H*-cyclopenta[*b*]quinoline (3g)[1]

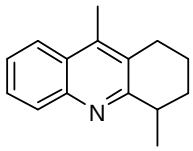
Solid; Yield: 0.161 g, 88%; m.p. 58-60 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.18 (quint., 2H, ring CH_2), 2.55 (s, 3H, CH_3), 3.05 (t, J = 7.4 Hz, 2H, ring CH_2), 3.15 (t, J = 7.7 Hz, 2H, ring CH_2), 7.44-7.48 (m, 1H, Ar-H), 7.58-7.62 (m, 1H, Ar-H), 7.90-7.92 (m, 1H, Ar-H), 7.99-8.01 (m, 1H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.7, 22.6, 29.8, 34.8, 123.1, 125.5, 126.9, 127.8, 128.9, 133.7, 137.8, 141.3, 147.5, 166.6. ESI-MS: *m/z* 184 $[M+H]^+$. Anal. Calcd. for $C_{13}H_{13}N$: C, 85.21; H, 7.15; N, 7.64%; Found: C, 85.32; H, 7.06; N, 7.55%.



3h

9-Methyl-1,2,3,4-tetrahydro-acridine (3h)[2]

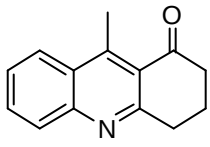
Solid; Yield: 0.167 g, 85%; m.p. 76-77 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.93 (quint., 4H, ring CH_2), 2.54 (s, 3H, CH_3), 2.90 (t, J = 5.9 Hz, 2H, ring CH_2), 3.11 (t, J = 6.4 Hz, 2H, ring CH_2), 7.45-7.47 (m, 1H, Ar-H), 7.57-7.60 (m, 1H, Ar-H), 7.95-7.97 (m, 2H, Ar-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 13.6, 22.9, 23.3, 27.1, 34.6, 123.4, 125.3, 127.0, 128.1, 128.7, 129.1, 141.3, 146.0, 158.6. ESI-MS: *m/z* 198 $[M+H]^+$. Anal. Calcd. for $C_{14}H_{15}N$: C, 85.24; H, 7.66; N, 7.10%; Found: C, 85.16; H, 7.76; N, 6.99%.



3i

4,9-Dimethyl-1,2,3,4-tetrahydroacridine (3i)

Solid; Yield: 0.179 g, 85%; m.p. 82-83 °C ; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.47 (d, J = 6.2 Hz, 3H, CH_3), 1.91 (quint., 2H, ring CH_2), 2.07 (q, J = 6.4 Hz, 2H, ring CH_2), 2.56 (s, 3H, CH_3), 2.90 (t, J = 6.2 Hz, 2H, ring CH_2), 3.13 (sext., J = 6.4 Hz, 1H, ring CH), 7.47-7.49 (m, 1H, Ar-H), 7.57-7.61 (m, 1H, Ar-H), 7.93-7.95 (m, 1H, Ar-H), 7.97-7.99 (m, 1H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 13.6, 22.8, 23.1, 27.5, 34.6, 38.4, 123.4, 125.3, 127.2, 128.2, 128.9, 129.1, 141.1, 146.5, 155.8. ESI-MS: *m/z* 212 $[M+H]^+$. Anal. Calcd. for $C_{15}H_{17}N$: C, 85.26; H, 8.11; N, 6.63%; Found: C, 85.19; H, 7.98; N, 6.56%.

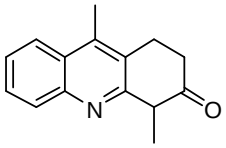


3j

9-Methyl-3,4-dihydroacridin-1(2*H*)-one (3j)[3]

Solid; Yield: 0.184 g, 87%; m.p. 64-66 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.87 (quint., 2H, ring CH_2), 2.51 (s, 3H, CH_3), 2.88 (t, J = 6.0 Hz, 2H, ring CH_2), 3.12 (t, J = 6.4 Hz, 2H, ring CH_2), 7.51-7.55 (m, 1H, Ar-H), 7.58-7.61 (m, 1H, Ar-H), 7.98-8.00 (m, 1H, Ar-H), 8.03-8.05 (m, 1H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 15.6, 20.8, 34.2, 40.4, 124.4, 125.3, 127.2, 129.2, 130.9, 147.9, 149.2, 160.1, 199.6.

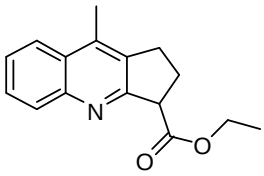
ESI-MS: *m/z* 212 $[M+H]^+$. Anal. Calcd. for $C_{14}H_{13}NO$: C, 79.59; H, 6.20; N, 6.63%; Found: C, 79.47; H, 6.33; N, 6.48%.



3k

4,9-Dimethyl-1,2-dihydroacridin-3(4*H*)-one (3k)

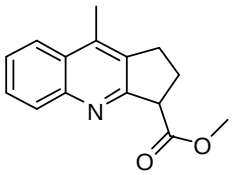
Solid; Yield: 0.189 g, 84%; m.p. 66-67 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.97 (d, J = 6.0 Hz, 3H, CH_3), 2.52 (s, 3H, CH_3), 2.84 (t, J = 6.0 Hz, 2H, ring CH_2), 3.09 (t, J = 6.2 Hz, 2H, ring CH_2), 3.53 (q, J = 6.8 Hz, 1H, ring CH), 7.50-7.54 (m, 1H, Ar-H), 7.59-7.63 (m, 1H, Ar-H), 7.95-7.97 (m, 1H, Ar-H), 7.99-8.01 (m, 1H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 15.5, 20.8, 23.1, 38.7, 43.4, 123.4, 125.2, 127.6, 129.3, 131.5, 143.2, 149.4, 160.9, 201.2. ESI-MS: *m/z* 226 $[M+H]^+$. Anal. Calcd. for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22%; Found: C, 79.78; H, 6.86; N, 6.11%.



3l

Ethyl 9-methyl-2,3-dihydro-1*H*-cyclopenta[*b*]quinoline-3-carboxylate (3l)

Viscous oil; Yield: 0.229 g, 90%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.43 (t, J = 7.2 Hz, 3H, CH_3), 2.23 (q, J = 7.4 Hz, 2H, ring CH_2), 2.55 (s, 3H, CH_3), 3.11 (t, J = 7.4 Hz, 2H, ring CH_2), 3.35 (t, J = 7.6 Hz, 1H, ring CH), 4.47 (q, J = 7.2 Hz, 2H, OCH_2), 7.45-7.49 (m, 1H, Ar-H), 7.60-7.64 (m, 1H, Ar-H), 7.93-7.95 (m, 1H, Ar-H), 8.00-8.02 (m, 1H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.3, 15.7, 24.4, 29.8, 54.8, 61.2, 123.3, 125.5, 126.0, 127.8, 129.1, 141.5, 146.1, 156.2, 168.7. ESI-MS: *m/z* 256 $[M+H]^+$. Anal. Calcd. for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49%; Found: C, 75.34; H, 6.83; N, 5.31%.

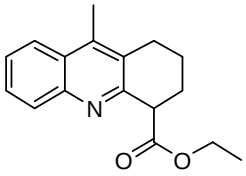


3m

Methyl 9-methyl-2,3-dihydro-1*H*-cyclopenta[*b*]quinoline-3-carboxylate (3m)

Viscous oil; Yield: 0.202 g, 84%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.29 (q, J = 7.4 Hz, 2H, ring CH_2), 2.59 (s, 3H, CH_3), 2.89 (s, 3H, CH_3), 3.19 (t, J = 7.4 Hz, 2H, ring CH_2), 3.35 (t, J = 7.6 Hz, 1H, ring CH), 7.46-7.50 (m, 1H, Ar-H), 7.60-7.64 (m, 1H, Ar-H), 7.95-7.97 (m, 1H, Ar-H), 8.01-8.03 (m, 1H, Ar-H). ^{13}C NMR (100 MHz,

$CDCl_3$): δ (ppm) 15.7, 24.2, 29.3, 53.8, 123.5, 125.8, 126.1, 127.8, 129.5, 141.3, 146.4, 156.2, 168.6. ESI-MS: *m/z* 242 $[M+H]^+$. Anal. Calcd. for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.81%; Found: C, 74.56; H, 6.38; N, 5.72%.



3n

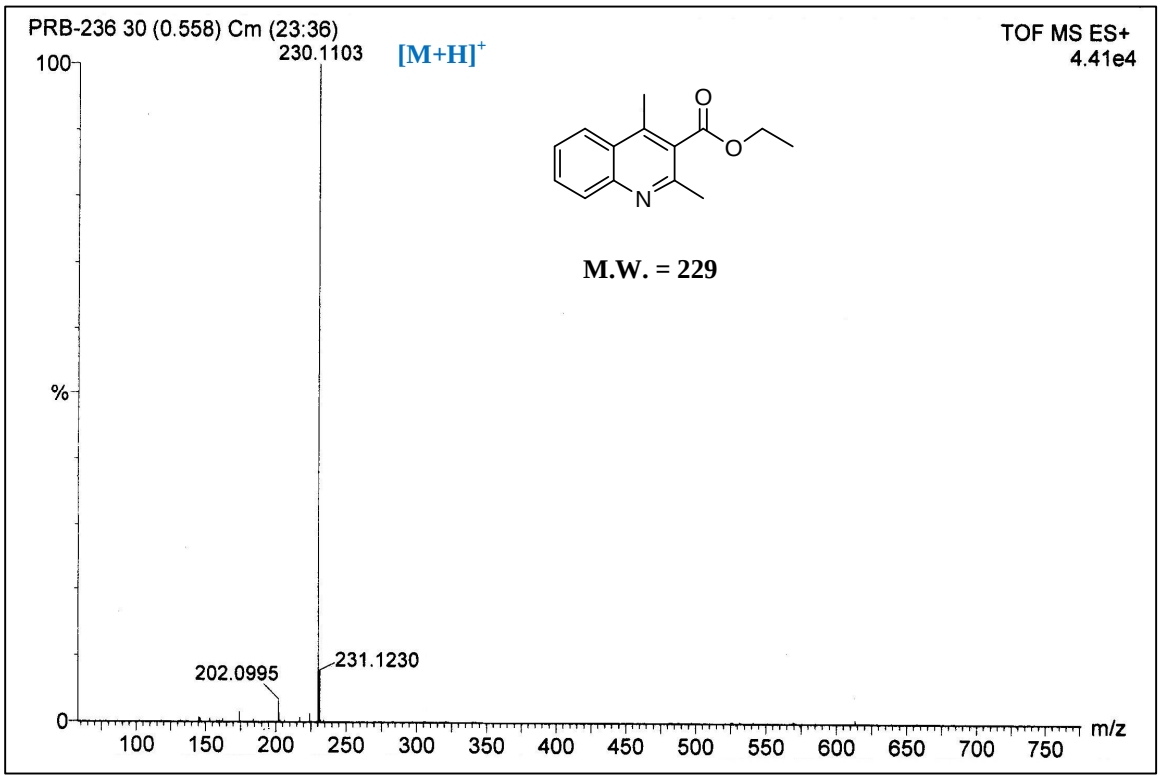
Ethyl 9-methyl-1,2,3,4-tetrahydroacridine-4-carboxylate (3n)

Viscous oil; Yield: 0.210 g, 78%; ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 1.42 (t, J = 7.2 Hz, 3H, CH_3), 1.89 (quint., 2H, ring CH_2), 2.12 (q, J = 6.0 Hz, 2H, ring CH_2), 2.56 (s, 3H, CH_3), 3.07 (t, J = 6.4 Hz, 2H, ring CH_2), 3.43 (t, J = 7.1 Hz, 1H, ring CH), 4.46 (q, J = 7.2 Hz, 2H, OCH_2), 7.47-7.49 (m, 1H, Ar-H), 7.56-7.60 (m, 1H, Ar-H), 7.97-7.99 (m, 1H, Ar-H), 8.01-8.03 (m, 1H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 14.5, 15.9, 23.4, 28.8, 54.8, 61.6, 123.4, 125.5, 126.6, 127.3, 129.1, 141.5, 146.4, 157.7, 168.9. ESI-MS: *m/z* 270 $[M+H]^+$. Anal. Calcd. for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20%; Found: C, 75.89; H, 7.07; N, 5.32%.

References

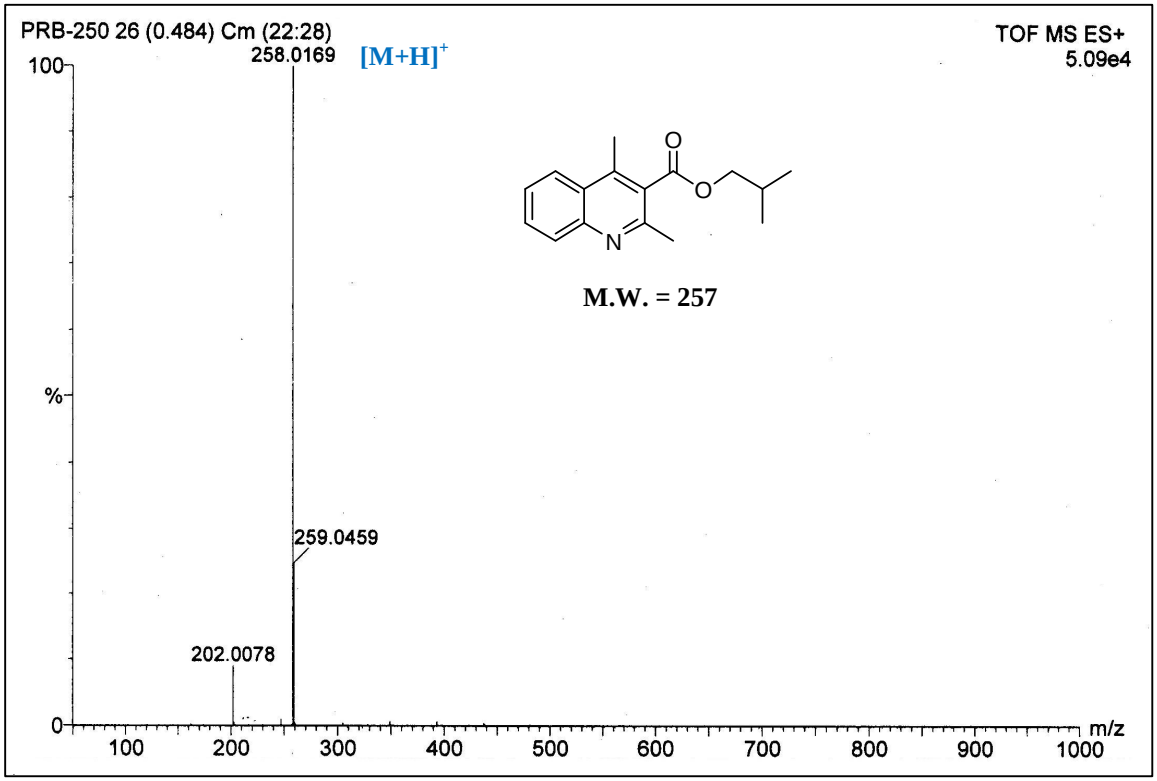
1. S. S. Palimkar, S. A. Siddiqui, T. Daniel, R. J. Lahoti and K. V. Srinivasan, *J. Org. Chem.*, 2003, **68**, 9371–9378.
2. L. Zhang and J. Wu, *Adv. Synth. Catal.*, 2007, **349**, 1047–1051.
3. C. S. Jia and G. W. Wang, *Lett. Org. Chem.*, 2006, **3**, 289–291.

ESI-MS spectrum of Ethyl 2,4-dimethylquinoline-3-carboxylate (3a)



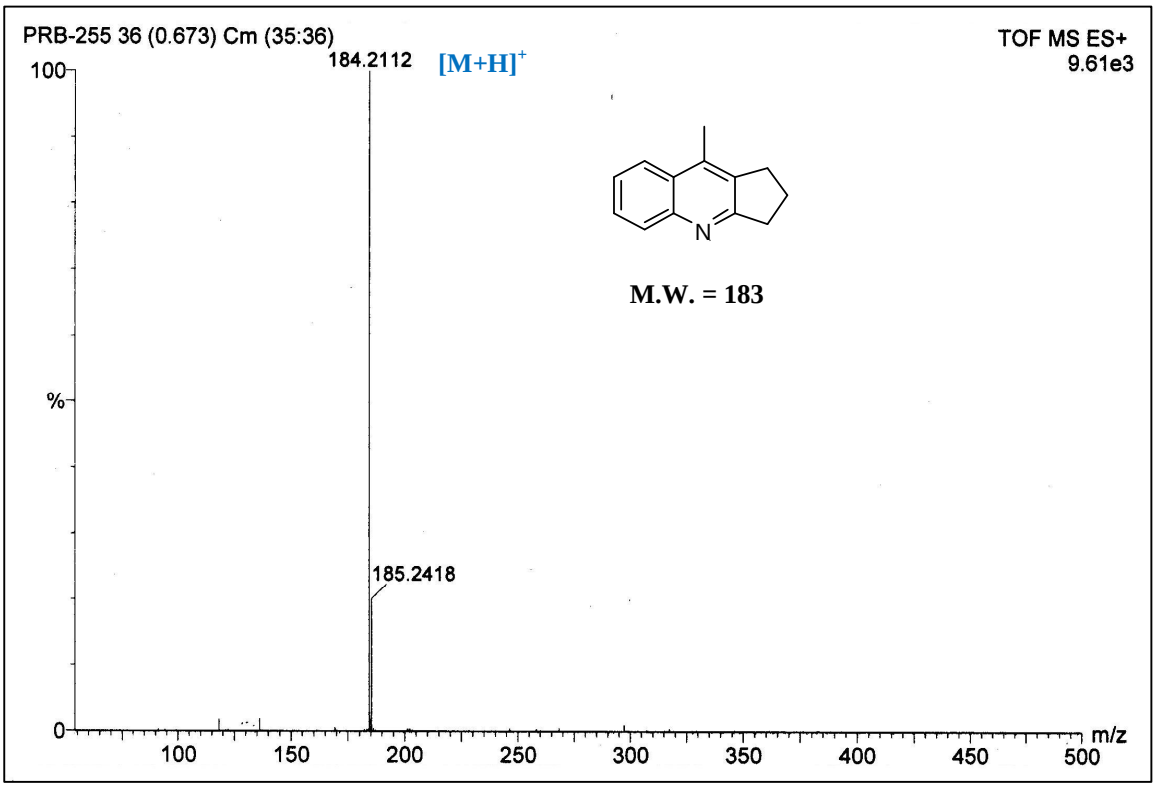
M.W. = 229

ESI-MS spectrum of Isobutyl 2,4-dimethylquinoline-3-carboxylate (3c)



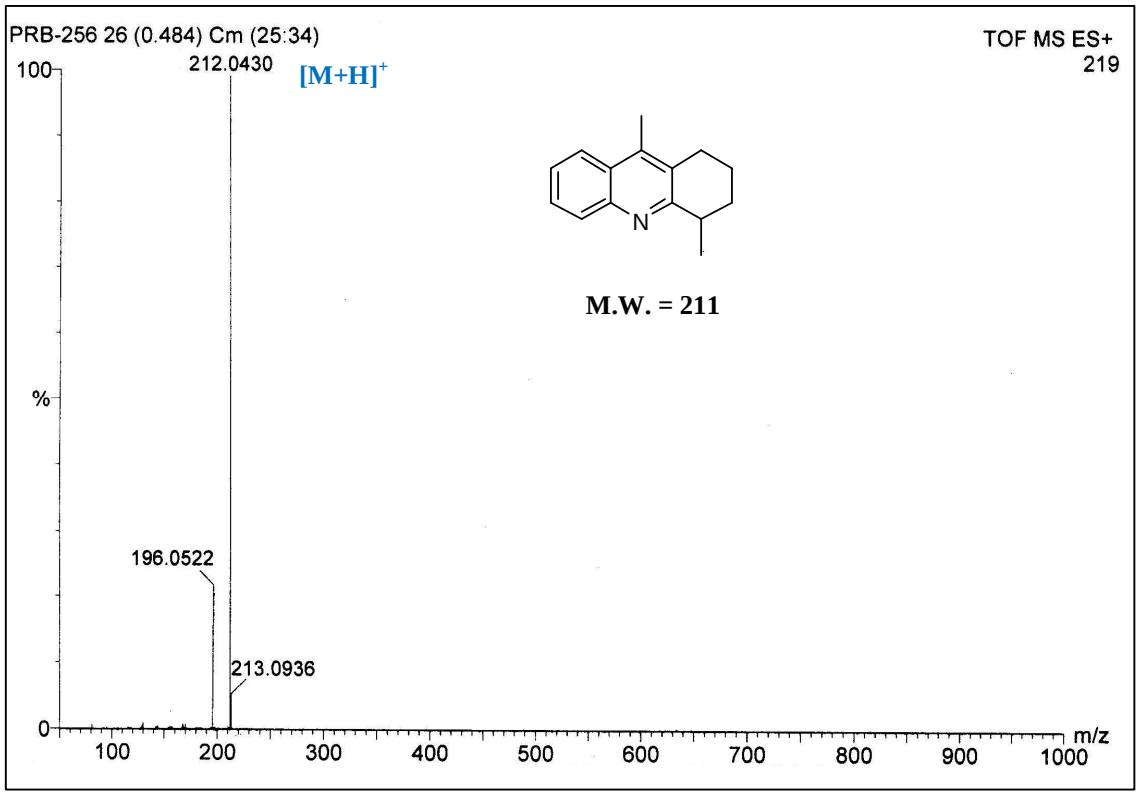
M.W. = 257

ESI-MS spectrum of 9-Methyl-2,3-dihydro-1*H*-cyclopenta[*b*]quinoline (3g)



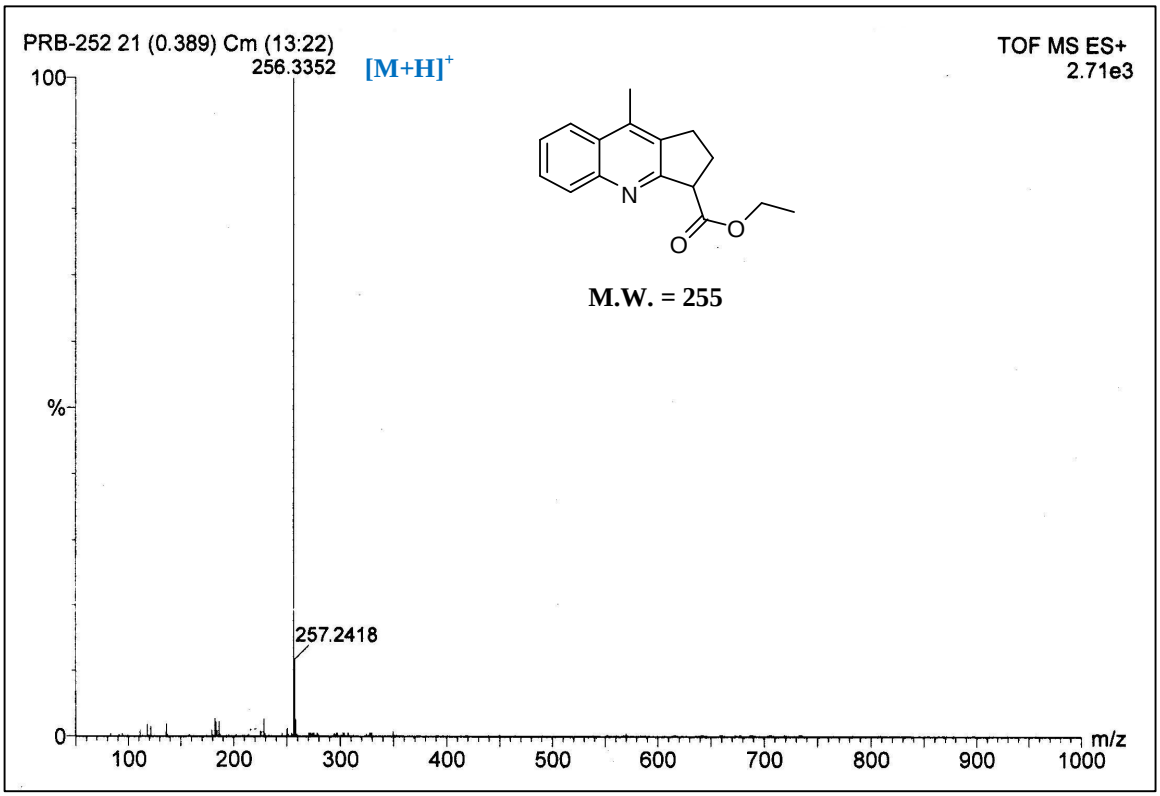
M.W. = 183

ESI-MS spectrum of 4,9-Dimethyl-1,2,3,4-tetrahydroacridine (3i)



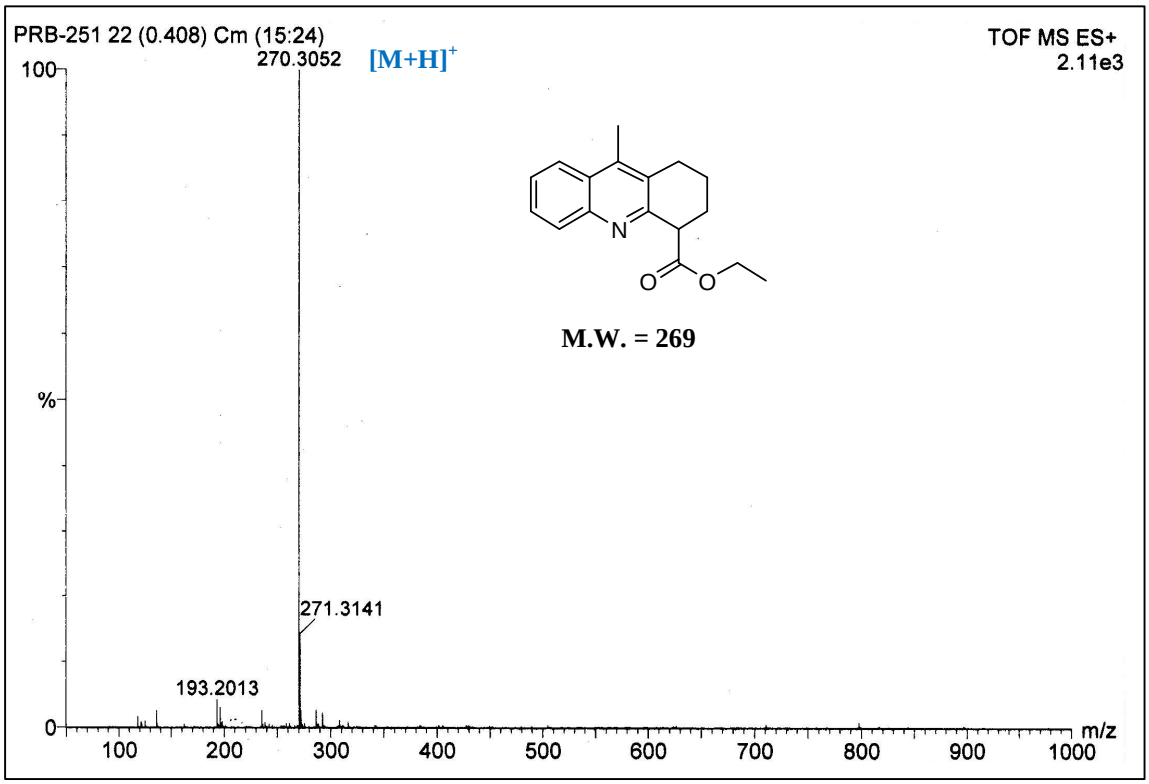
M.W. = 211

ESI-MS spectrum of Ethyl 9-methyl-2,3-dihydro-1*H*-cyclopenta[*b*]quinoline-3-carboxylate (3l)



M.W. = 255

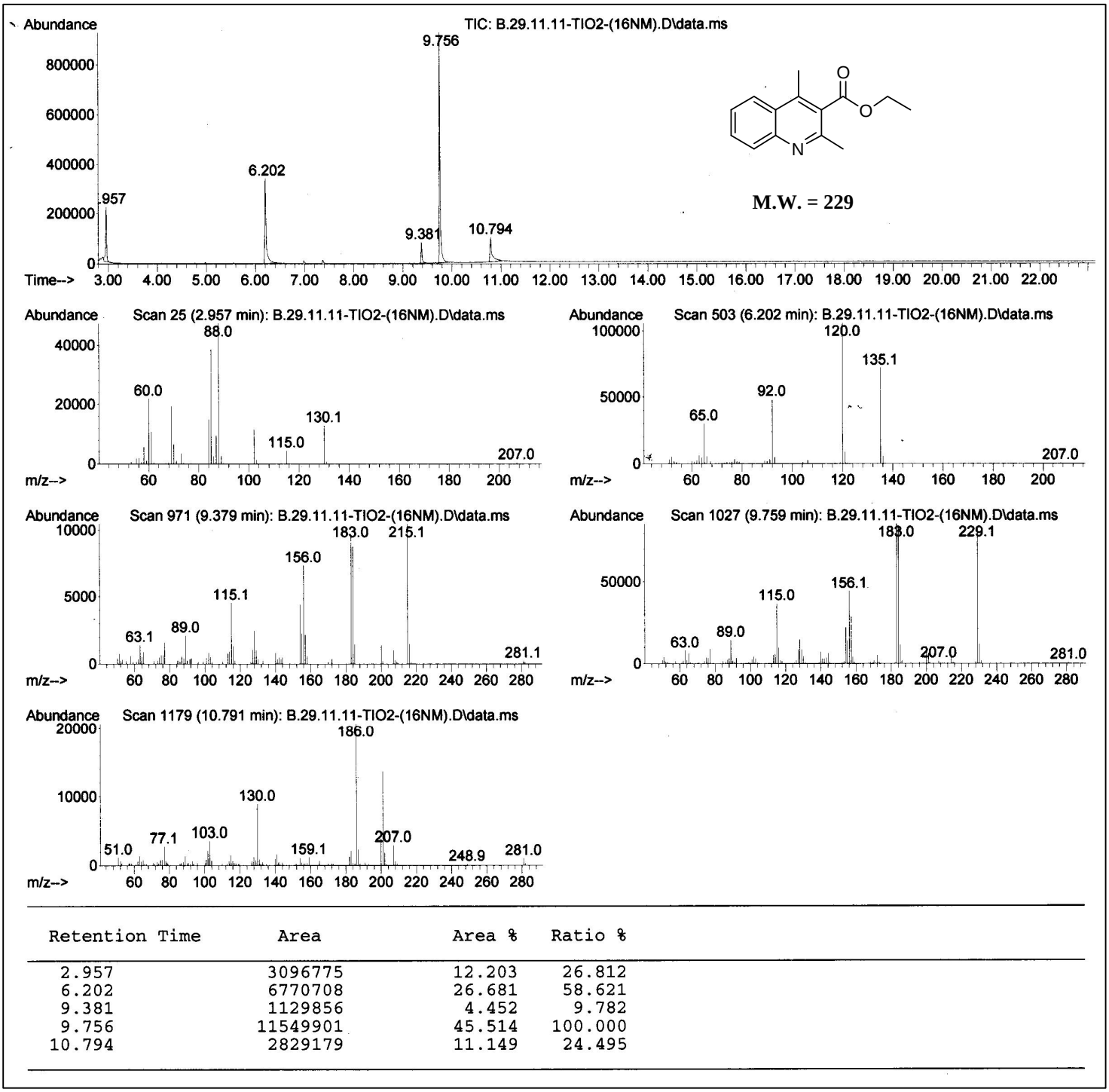
ESI-MS spectrum of Ethyl 9-methyl-1,2,3,4-tetrahydroacridine-4-carboxylate (3n)



M.W. = 269

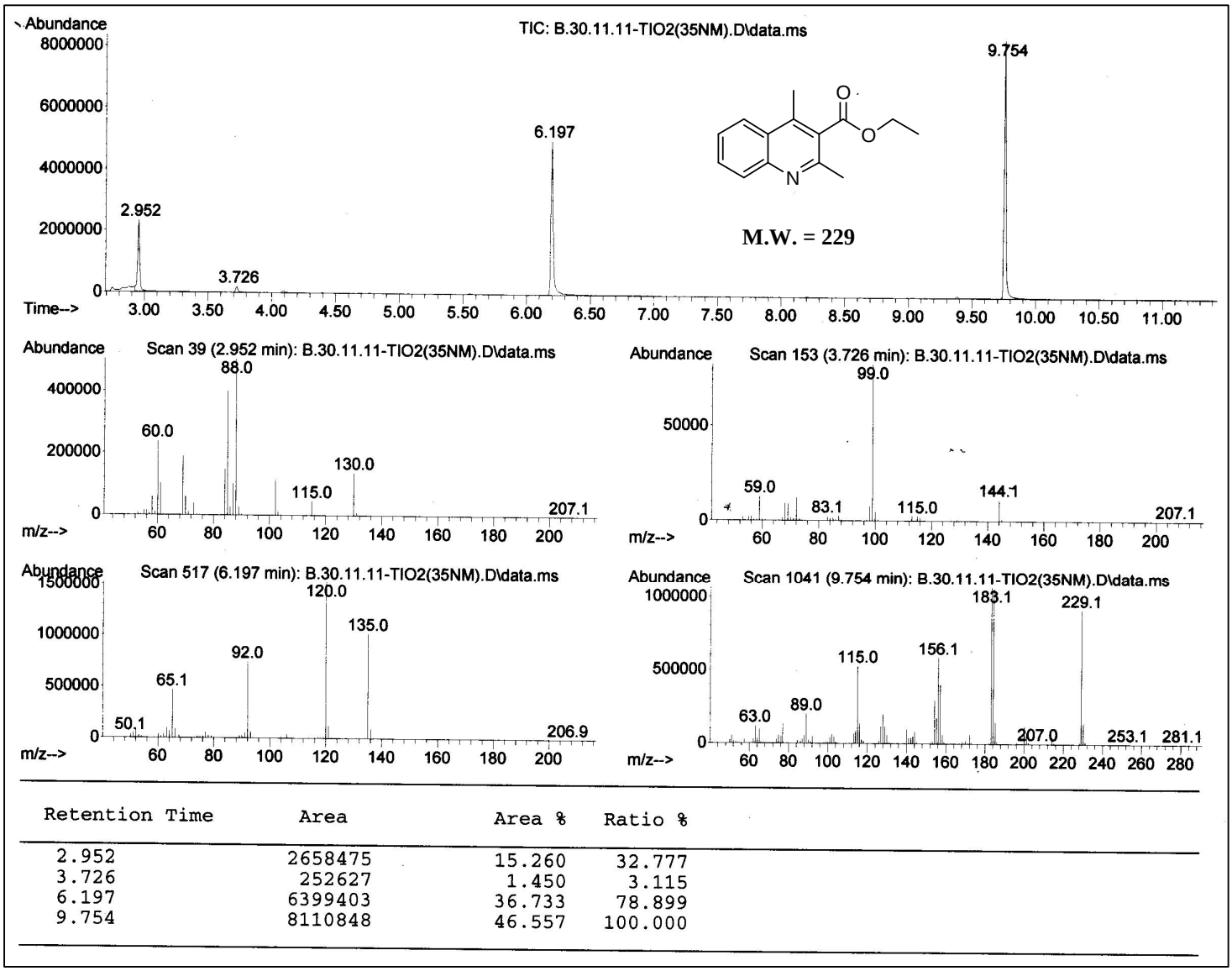
All the chromatograms were obtained under the same conditions and these results were obtained before the reaction was optimized.

Product (3a) formation monitored by GC-MS [TiO_2 nanoparticles (16 nm) as the catalyst]



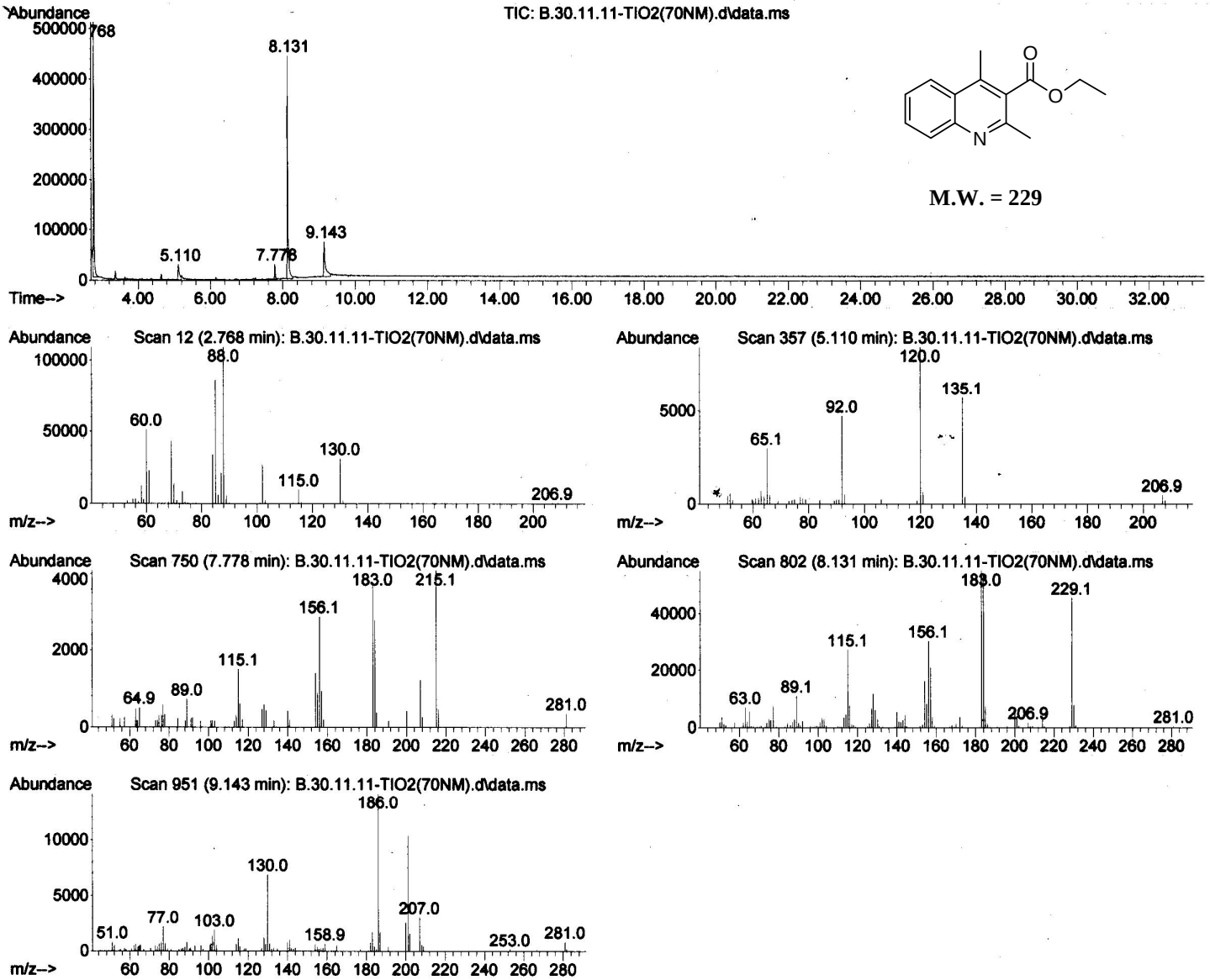
Retention Time	Area	Area %	Ratio %
2.957	3096775	12.203	26.812
6.202	6770708	26.681	58.621
9.381	1129856	4.452	9.782
9.756	11549901	45.514	100.000
10.794	2829179	11.149	24.495

Product (3a) formation monitored by GC-MS [TiO_2 nanoparticles (35 nm) as the catalyst]



Retention Time	Area	Area %	Ratio %
2.952	2658475	15.260	32.777
3.726	252627	1.450	3.115
6.197	6399403	36.733	78.899
9.754	8110848	46.557	100.000

Product (3a) formation monitored by GC-MS [TiO_2 nanoparticles (70 nm) as the catalyst]



Retention Time	Area	Area %	Ratio %
2.768	612401	38.750	98.180
5.110	83057	5.256	13.316
7.778	43032	2.723	6.899
8.131	623753	39.469	100.000
9.143	218133	13.803	34.971