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Synthesis, characterization, *in silico* molecular docking study and biological evaluation of 5-(phenylthio) pyrazole based polyhydroquinoline core moiety

Nirav H. Sapariya[a], Beena K. Vaghasiya, Rahul P. Thummar, Ronak D. Kamani, Kirit H. Patel, Parth Thakor[b], Sampark S. Thakkar[c], Arabinda Ray[c] and Dipak K. Raval*

[a]*Department of Chemistry, Sardar Patel University, Vallabh Vidyanagar- 388 120, Gujarat, India*

[b]*B. R. Doshi School of Biosciences, Sardar Patel Maidan, Bakrol-Vadtal Road, Satellite Campus, Sardar Patel University, Vallabh Vidyanagar -388120, Gujarat,India*

[c]*Department of Advanced Organic Chemistry, P. D. Patel Institute of Applied Sciences (PDPIAS), Charotar University of Science & Technology (CHARUSAT), Changa-388421, Gujarat, India*

**Corresponding author. Tel.: +91-02692-226856 - Ext. - 211; Fax: +91-02692 236475.*

E-mail: nir.sapariya@gmail..com , dipanalka@yahoo.com

Supplementary Information

*6.1.1. General procedure for the synthesis of 3-methyl-5-substituted phenylthio-1-phenyl-1H-pyrazole-4-carbaldehydes (**3a-c**)*

5-Chloro-3-methyl-1-phenyl-1*H*-pyrazole-4-carbaldehyde 1 (1 mmol), substituted thiophenols **2a–c** (1 mmol) and anhydrous potassium carbonate (2.5 mmol) in dimethyl formamide (10 mL) were charged in a 100 mL round bottom flask equipped with a mechanical stirrer and a condenser. The reaction mixture was heated at 90 °C for 2 h and the progress of the reaction was monitored by TLC. After the completion of reaction as confirmed by the TLC, the reaction mixture was poured in to 100 mL ice water. The solid separated was filtered, washed thoroughly with water, dried and recrystallized from hot ethanol (10 mL) to obtain **3a-c**.

*6.1.1.1 5-((4-chlorophenyl)thio)-3-methyl-1-phenyl-1H-pyrazole-4-carbaldehyde (**3a**)*

Yield 83 %; m.p. 241-243 °C; ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 2.49 (s, 3H, CH_3 of pyrazole), 7.05-7.53 (m, 9H, Ar–H), 9.96 (s, 1H, -CHO) ; ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ: 13.8, 123.1, 126.3, 129.5, 129.6, 130.0, 130.3, 132.5, 133.0, 138.1, 138.3, 151.2, 186.2.

*6.1.1.2 3-methyl-1-phenyl-5-(p-tolylthio)-1H-pyrazole-4-carbaldehyde (**3b**)*

Yield 87 %; m.p. 225-227 °C; ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 2.34 (s, 3H, CH_3 of benzene ring), 2.47 (s, 3H, CH_3 of pyrazole), 7.07-7.62 (m, 9H, Ar–H), 9.73 (s, 1H, -CHO) ; ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ: 13.5, 21.3, 114.6, 119.9, 126.2, 128.6, 129.3, 137.9, 139.2, 141.8, 149.2, 191.0.

*6.1.1.3 5-((4-fluorophenyl)thio)-3-methyl-1-phenyl-1H-pyrazole-4-carbaldehyde (**3c**)*

Yield 79 %; m.p. 214-216 °C; ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 2.47 (s, 3H, CH_3 of pyrazole), 7.07-7.48 (m, 9H, Ar–H), 10.02 (s, 1H, -CHO) ; ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ: 13.8, 117.0, 117.2, 122.9, 126.4, 129.0, 129.6, 131.8, 131.9, 138.2, 139.5, 151.0, 160.7, 163.2, 186.3.

*6.1.2. General procedure for the synthesis of substituted 3-((substituted)amino)-5,5-dimethylcyclohex-2-enone (**6a-c**).*

1,3-Dimedone **4** (10 mmol), fluoro substituted amine **5a–c** (10 mmol) and methanol (10 mL) with catalytic amount of acetic acid were charged in a 100 mL round bottom flask equipped with a mechanical stirrer. The reaction mixture was stirred at room

temperature for 2 h. After the completion of reaction (checked by TLC), the separated substituted enhydrazinoketones **6a–c** were filtered and washed with methanol to obtain the pure solid product.

*6.1.3. General procedure for the synthesis of 2-amino-4-(5-((substituted phenyl)thio)-3-methyl-1-phenyl-1H-pyrazol-4-yl)-1-(phenylamino)-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carbonitrile (**8a-p**)*

A 50 mL round bottom flask, fitted with a reflux condenser, was charged with a mixture of 3-methyl-5-substituted phenylthio-1-phenyl-*1H*-pyrazole-4-carbaldehydes *(**3a-c**)* (1 mmol), malononitrile **7a** or ethylcynoacetate **7b** or cynoacetamide **7c** (1 mmol), substituted enaminones **6a-c** (1 mmol), and catalytic amount of piperidine (2-3 drops) in ethanol (10 mL). The mixture was heated under reflux for 1-3 h and the progress of the reaction was monitored by TLC. After the completion of reaction, the reaction mixture was cooled to room temperature and stirred magnetically for further 10 min. The solid mass separated was collected by filtration, washed well with ethanol (10 mL) and crystallized from hot chloroform. The physicochemical and spectroscopic characterization data of the synthesized compounds **8a-p** are given below.

*6.1.3.1. 2-amino-4-(5-((4-chlorophenyl)thio)-3-methyl-1-phenyl-1H-pyrazol-4-yl)-1-(4-fluorophenyl)-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carbonitrile (**8a**)*

Yield 81 %; m.p. 213-215 °C; IR (KBr, ν_{max}, cm^{-1}): 3472 & 3332 (asym. & sym. str. of $–NH_2$), 2180 (C≡N str.), 1652 (C=O str.), 1367 (–CH3 str.), 769 (C–S–C thioether str.);^{1}H NMR (400 MHz, DMSO-d_6): δ 0.73 (s, 3H, CH_3), 0.86 (s, 3H, CH_3), 1.04-1.92 (m, 4H, 2 × CH_2), 2.44 (s, 3H, CH_3 of pyrazole), 4.75 (s, 1H, CH),5.24 (bs, 2H, $-NH_2$), 6.89-7.45 (m, 13H, Ar–H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 12.22, 27.63, 27.88, 31.76, 40.81, 49.09, 58.24, 109.24, 116.99, 117.22, 121.66, 124.93, 126.66, 127.46, 127.66, 128.59, 128.88, 130.24, 131.54, 132.08, 132.11, 132.83, 134.73, 138.88, 147.79, 150.44, 151.00, 161.02, 163.48, 194.80; ESI-MS (m/z): 609.1 (M^+), 611.1 (M+2); Anal. Calcd (%) for $C_{34}H_{29}ClFN_5OS$: C, 66.93; H, 4.79; N, 11.48. Found: C, 66.89; H, 4.73; N, 11.42.

*6.1.3.2. Ethyl 2-amino-4-(5-((4-chlorophenyl)thio)-3-methyl-1-phenyl-1H-pyrazol-4-yl)-1-(4-fluorophenyl)-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**8b**)*

Yield 79 %; m.p. 224-226 °C; IR (KBr, ν_{max}, cm^{-1}): 3475 & 3342 (asym. & sym. str. of $–NH_2$), 2193 (C≡N str.), 1663 (C=O str.), 1373 ($–CH_3$ str.), 764 (C–S–C thioether str.);^{1}H NMR (400 MHz, DMSO-d_6): δ 0.70 (s, 3H, CH_3), 0.85 (s, 3H, CH_3), 1.09-1.36 (m, 4H, 2 × CH_2), 1.87 (m, 3H, CH_3), 2.55 (s, 3H, CH_3 of pyrazole), 4.01 (m, 2H, CH_2),4.93 (s, 1H, -CH), 6.56 (bs, 2H, NH_2), 6.68-7.30 (m, 13H, Ar–H) ; ^{13}C NMR (100 MHz, DMSO-d_6) δ: 12.45, 14.67, 25.88, 27.19, 28.26, 31.77, 40.81, 49.29, 58.31, 76.43, 111.95, 117.02, 117.25, 124.84, 125.39, 126.25, 127.41, 128.53, 128.73, 129.61, 132.26, 134.50, 135.65, 138.98, 148.98, 149.51, 152.59, 160.92, 163.37, 168.78, 194.81; ESI-MS (m/z): 656.2(M^+), 658.1 (M+2); Anal. Calcd (%) for $C_{36}H_{34}ClFN_4O_3S$: C, 65.79; H, 5.21; N, 8.53. Found: C, 65.74; H, 5.18; N, 8.49.

*6.1.3.3. 2-amino-4-(5-((4-chlorophenyl)thio)-3-methyl-1-phenyl-1H-pyrazol-4-yl)-1-(4-fluorophenyl)-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxamide (**8c**)*

Yield 73 %; m.p. 198-200 °C; IR (KBr, ν_{max}, cm^{-1}): 3440 & 3354 (asym. & sym. str. of $–NH_2$), 2213 (C≡N str.), 1664 (C=O str.), 1369 ($–CH_3$ str.), 776 (C–S–C thioether str.); 762 (C-Cl stretching);^{1}H NMR (400 MHz, DMSO-d_6): δ 0.71 (s, 3H, CH_3), 0.87 (s, 3H, CH_3), 1.39-2. 11 (m, 4H, 2 × CH_2), 2.51 (s, 3H, CH_3 of pyrazole), 4.91 (s, 1H, CH),6.00 (s, 2H, $-NH_2$), 6.79-7.41 (m, 15H, Ar–H and $CONH_2$); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 12.33, 27.64, 27.85, 31.55, 41.03, 49.17, 109.11, 116.93, 117.23, 121.56, 124.97, 126.76, 127.43, 127.69, 128.60, 128.83, 130.21, 131.57, 132.16, 132.20, 132.85, 134.75, 138.80, 147.82, 150.43, 151.03, 161.64, 163.86, 171.13, 194.73; ESI-MS (m/z): 627.1(M^+), 629.1 (M+2); Anal. Calcd (%) for $C_{34}H_{31}ClFN_5O_2S$: C, 65.01; H, 4.97; N, 11.15. Found: C, 65.06; H, 4.93; N, 11.11.

*6.1.3.4. 2-amino-1-(4-fluorophenyl)-7,7-dimethyl-4-(3-methyl-1-phenyl-5-(p-tolylthio)-1H-pyrazol-4-yl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carbonitrile (**8d**)*

Yield 84 %; m.p. 201-203 °C; IR (KBr, ν_{max}, cm^{-1}): 3433 & 3324 (asym. & sym. str. of $–NH_2$), 2190 (C≡N str.), 1658 (C=O str.), 1363 ($–CH_3$ str.), 761 (C–S–C thioether str.);^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 0.69 (s, 3H, CH_3), 0.85 (s, 3H, CH_3), 1.35-1.99 (m, 4H, 2 × CH_2), 2.15(s, 3H, CH_3 of benzene ring), 2.43 (s, 3H, CH_3 of pyrazole), 4.72 (s, 1H, CH), 5.23 (s, 2H, $-NH_2$), 6.75-7.40 (m, 13H, Ar–H); ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ: 12.36, 20.79, 27.56, 28.12, 28.56, 32.44, 41.45, 49.45, 58.19, 109.56, 117.12, 118.24, 125.61, 125.67, 127.57, 128.39, 129.84, 130.58, 131.94, 132.06, 135.23, 135.28, 139.05, 147.61, 150.28, 150.90, 161.15, 163.55, 193.88; ESI-MS (m/z): 589.2(M^+); Anal. Calcd (%) for $C_{35}H_{32}FN_5OS$: C, 71.28; H, 5.47; N, 11.88. Found: C, 71.32; H, 5.43; N, 11.84.

*6.1.3.5. Ethyl 2-amino-1-(4-fluorophenyl)-7,7-dimethyl-4-(3-methyl-1-phenyl-5-(p-tolylthio)-1H-pyrazol-4-yl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**8e**).*

Yield 76 %; m.p. 205-207 °C; IR (KBr, ν_{max}, cm^{-1}): 3453 & 3330(asym. & sym. str. of $–NH_2$), 2223 (C≡N str.), 1673(C=O str.), 1351($–CH_3$ str.), 771 (C–S–C thioether str.); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.79 (s, 3H, CH_3), 0.93 (s, 3H, CH_3), 1.25-1.47 (m, 4H, 2 × CH_2), 1.99 (s, 3H, CH_3 of benzene ring), 2.21(s, 3H, CH_3), 2.73 (s, 3H, CH_3 of pyrazole), 4.16 (m, 2H, CH_2), 5.14 (s, 1H, CH), 6.05 (bs, 2H, $-NH_2$), 6.61-7.55 (m, 13H, Ar–H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.66, 14.80, 20.78, 26.28, 28.14, 28.54, 32.43, 41.60, 50.02, 59.33, 113.42, 124.98, 125.34, 125.50, 127.21, 128.28, 128.32, 128.70, 128.96, 129.71, 132.23, 132.92, 133.60, 134.02, 134.91, 136.73, 149.21, 149.86, 151.68, 170.06, 196.02; ESI-MS (m/z): 636.2(M^+); Anal. Calcd (%) for $C_{37}H_{37}FN_4O_3S$: C, 69.79; H, 5.86; N, 8.80. Found: C, 69.75; H, 5.82; N, 8.84.

*6.1.3.6. 2-amino-7,7-dimethyl-4-(3-methyl-1-phenyl-5-(p-tolylthio)-1H-pyrazol-4-yl)-5-oxo-1-(4-(trifluoromethyl)phenyl)-1,4,5,6,7,8-hexahydroquinoline-3-carbonitrile (**8f**)*

Yield 72 %; m.p. 221-223 °C; IR (KBr, ν_{max}, cm^{-1}): 3471 & 3337 (asym. & sym. str. of $–NH_2$), 2197 (C≡N str.), 1654 (C=O str.), 1358 ($–CH_3$ str.), 781 (C–S–C thioether str.); ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 0.71 (s, 3H, CH_3), 0.84 (s, 3H, CH_3), 1.01-2.03 (m, 4H, 2 × CH_2), 2.13 (s, 3H, CH_3 of benzene), 2.51 (s, 3H, CH_3 of pyrazole), 4.63 (s, 1H, CH), 5.73 (s, 2H, $-NH_2$), 6.82-7.53 (m, 13H, Ar–H); ^{13}C NMR (100 MHz, DMSO-*d*$_6$) δ: 12.30, 20.79, 20.88, 27.58, 28.13, 28.60, 32.43, 41.50, 49.43, 58.10, 109.53, 117.13, 118.23,

125.57, 125.63, 127.59, 128.43, 129.83, 130.53, 131.92, 132.10, 135.20, 135.23, 139.01, 147.59, 150.27, 150.88, 161.13, 163.50, 193.94; ESI-MS (m/z): 639.2(M^+); Anal. Calcd (%) for $C_{37}H_{37}FN_4O_3S$: C, 67.59; H, 5.04; N, 10.95. Found: C, 67.55; H, 5.08; N, 10.99.

*6.1.3.7. Ethyl 2-amino-7,7-dimethyl-4-(3-methyl-1-phenyl-5-(p-tolylthio)-1H-pyrazol-4-yl)-5-oxo-1-(4-(trifluoromethyl)phenyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**8g**)*

Yield 80 %; m.p. 199-201 °C; IR (KBr, ν_{max}, cm^{-1}): 3462& 3329 (asym. & sym. str. of $–NH_2$), 2191 (C≡N str.), 1679 (C=O str.), 1359 ($–CH_3$ str.), 770 (C–S–C thioether str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.75(s, 3H, CH_3), 0.91 (s, 3H, CH_3), 1.21-1.43 (m, 4H, 2 × CH_2), 1.93 (s, 3H, CH_3 of benzene ring), 2.23(q, 3H, CH_3), 2.78 (s, 3H, CH_3 of pyrazole), 4.36 (m, 2H, CH_2), 5.43 (s, 1H, CH), 6.13 (bs, 2H, -NH_2), 6.63-7.57 (m, 13H, Ar–H) ; ^{13}C NMR (100 MHz, DMSO-d_6) δ: 12.43, 14.60, 20.67, 20.89, 25.89, 27.17, 28.30, 31.70, 40.82, 49.32, 58.32, 76.62, 111.98, 117.07, 117.29, 124.88, 125.39,126.23, 127.43, 128.57, 128.77, 129.60, 132.25, 134.52, 135.67, 138.95, 148.96, 149.53, 152.61, 160.93, 163.39, 168.75, 194.86; ESI-MS (m/z): 686.2(M^+); Anal. Calcd (%) for $C_{38}H_{37}F_3N_4O_3S$: C, 66.46; H, 5.43; N, 8.16. Found: C, 66.50; H, 5.47; N, 8.20.

*6.1.3.8. 2-amino-1-(2,4-difluorophenyl)-7,7-dimethyl-4-(3-methyl-1-phenyl-5-(p-tolylthio)-1H-pyrazol-4-yl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carbonitrile (**8h**)*

Yield 79 %; m.p. 217-219 °C; IR (KBr, ν_{max}, cm^{-1}): 3481 & 3343 (asym. & sym. str. of $–NH_2$), 2187 (C≡N str.), 1662 (C=O str.), 1372($–CH_3$ str.), 755 (C–S–C thioether str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.68 (s, 3H, CH_3), 0.81 (s, 3H, CH_3), 1.32-1.95 (m, 4H, 2 × CH_2), 2.17(s, 3H, CH_3 of benzene ring), 2.48 (s, 3H, CH_3 of pyrazole), 4.81 (s, 1H, CH), 5.38 (s, 2H, -NH_2), 6.71-7.53 (m, 12H, Ar–H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 12.35, 20.78, 27.55, 28.23, 28.63, 32.42, 41.53, 49.40, 58.12, 109.54, 117.17, 118.27, 125.56, 125.66, 127.58, 128.41, 129.85, 130.56, 131.96, 132.13, 132.38, 135.23, 135.28, 139.07, 147.63, 150.28, 150.89, 161.14, 163.53, 194.03; ESI-MS (m/z): 607.2(M^+); Anal. Calcd (%) for $C_{35}H_{31}F_2N_5OS$: C, 69.17; H, 5.14; N, 11.52. Found: C, 69.13; H, 5.10; N, 11.56.

*6.1.3.9. Ethyl 2-amino-1-(2,4-difluorophenyl)-7,7-dimethyl-4-(3-methyl-1-phenyl-5-(p-tolylthio)-1H-pyrazol-4-yl)-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**8i**)*

Yield 73 %; m.p. 216-218 °C; IR (KBr, ν_{max}, cm^{-1}): 3463 & 3342 (asym. & sym. str. of $–NH_2$), 2213 (C≡N str.), 1680 (C=O str.), 1367($–CH_3$ str.), 775 (C–S–C thioether str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.66 (s, 3H, CH_3), 0.74 (s, 3H, CH_3), 1.07-1.14 (m, 4H, 2 × CH_2), 1.82 (s, 3H, CH_3 of benzene ring), 2.13 (s, 3H, CH_3), 2.55 (s, 3H, CH_3 of pyrazole), 4.02 (m, 2H, CH_2),4.91 (s, 1H, -CH), 6.51 (s, 2H, NH_2), 6.57-7.59 (m, 12H, Ar–H) ; ^{13}C NMR (100 MHz, DMSO-d_6) δ: 12.67, 14.85, 20.81, 26.30, 28.17, 28.50, 32.42, 41.63, 50.07, 59.36, 109.10, 113.45, 125.01, 125.32, 125.53, 127.12, 128.17, 128.27, 128.73, 128.98, 129.77, 132.24, 132.95, 133.67, 134.05, 134.96, 136.75, 149.23, 149.82, 151.65, 170.02, 195.97; ESI-MS (m/z): 654.2(M^+), 658.1 (M+2); Anal. Calcd (%) for $C_{37}H_{36}F_2N_4O_3S$: C, 67.87; H, 5.54; N, 8.56. Found: C, 67.91; H, 5.50; N, 8.52.

*6.1.3.10. 2-amino-4-(5-((4-chlorophenyl)thio)-3-methyl-1-phenyl-1H-pyrazol-4-yl)-1-(2,4-difluorophenyl)-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carbonitrile (**8j**)*

Yield 75 %; m.p. 210-212 °C; IR (KBr, ν_{max}, cm^{-1}): 3481 & 3341 (asym. & sym. str. of $–NH_2$), 2191 (C≡N str.), 1660 (C=O str.), 1361 ($–CH_3$ str.), 766 (C–S–C thioether str.); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (s, 3H, CH_3), 0.98 (s, 3H, CH_3), 1.69-1.87 (m, 4H, 2 × CH_2), 2.65 (s, 3H, CH_3 of pyrazole), 3.60 (s, 2H, $-NH_2$), 4.95 (s, 1H, CH), 6.75-7.49 (m, 12H, Ar–H); ^{13}C NMR (100 MHz, $CDCl_3$) δ:12.40, 27.64, 27.95, 28.13, 28.45, 32.37, 40.54, 49.80, 58.87, 110.70, 112.13, 121.78, 127.33, 127.53, 127.62, 127.81, 127.96, 128.45, 128.51, 128.81, 129.18, 132.93, 133.33, 135.03, 137.02, 147.83, 150.97, 151.43, 162.12, 163.97, 195.59 ; ESI-MS (m/z): 627.1 (M^+), 629.1 (M+2); Anal. Calcd (%) for $C_{34}H_{28}ClF_2N_5OS$: C, 65.01; H, 4.49; 6.05; N, 11.15. Found: C, 65.05; H, 4.45; 6.05; N, 11.11

*6.1.3.11. Ethyl 2-amino-4-(5-((4-chlorophenyl)thio)-3-methyl-1-phenyl-1H-pyrazol-4-yl)-1-(2,4-difluorophenyl)-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**8k**)*

Yield 78 %; m.p. 213-215 °C; IR (KBr, ν_{max}, cm^{-1}): 3480 & 3347 (asym. & sym. str. of $–NH_2$), 2217 (C≡N str.), 1668 (C=O str.), 1365 ($–CH_3$ str.), 769 (C–S–C thioether str.); ^1H NMR (400 MHz, $CDCl_3$): δ 0.87 (s, 3H, CH_3), 0.95 (s, 3H, CH_3), 1.46-1.51 (m, 4H, 2 × CH_2), 1.55 (s, 3H, CH_3), 2.73 (s, 3H, CH_3 of pyrazole), 4.16 (m, 2H, CH_2), 5.15 (s, 1H, -CH), 5.92 (s, 2H, NH_2), 6.64-7.41 (m, 12H, Ar–H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.66, 14.78, 26.26, 28.14, 28.44, 32.36, 40.62, 50.03, 59.52, 110.23, 111.90, 117.68, 117.83, 125.19, 125.32, 126.27, 127.50, 128.37, 128.61, 129.07, 132.80, 134.00, 135.60, 138.13, 148.87, 149.67, 152.43, 161.11, 163.41, 168.71, 194.89; ESI-MS (m/z): 674.1(M^+), 676.1 (M+2); Anal. Calcd (%) for $C_{36}H_{33}ClF_2N_4O_3S$: C, 64.04; H, 4.93; N, 8.30. Found: C, 64.08; H, 4.97; N, 8.34.

*6.1.3.12. 2-amino-4-(5-((4-chlorophenyl)thio)-3-methyl-1-phenyl-1H-pyrazol-4-yl)-1-(2,4-difluorophenyl)-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxamide (**8l**)*

Yield 81 %; m.p. 201-203 °C; IR (KBr, ν_{max}, cm^{-1}): 3477 & 3342 (asym. & sym. str. of $–NH_2$), 2188 (C≡N str.), 1653 (C=O str.), 1366 ($–CH_3$ str.), 760 (C–S–C thioether str.); ^1H NMR (400 MHz, DMSO-d_6): δ 0.77(s, 3H, CH_3), 0.91 (s, 3H, CH_3), 1.33-2.23 (m, 4H, 2 × CH_2), 2.53 (s, 3H, CH_3 of pyrazole), 5.02 (s, 1H, CH), 6.11 (s, 2H, -NH_2), 6.73-7.51 (m, 14H, Ar–H and $CONH_2$); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 12.34, 27.64, 27.80, 31.57, 41.07, 49.19, 109.12, 111.03, 116.95, 117.27, 121.63, 125.01, 125.24, 126.79, 127.54, 127.75, 128.61, 128.86, 130.22, 131.59, 132.23, 132.35, 132.88, 134.73, 138.89, 147.85, 150.40, 151.09, 161.67, 163.89, 171.17, 194.87; ESI-MS (m/z): 645.1(M^+), 647.1 (M+2); Anal. Calcd (%) for $C_{34}H_{30}ClF_2N_5O_2S$: C, 63.20; H, 4.68; N, 10.84. Found: C, 63.24; H, 4.64; N, 10.83.

*6.1.3.13. 2-amino-1-(4-fluorophenyl)-4-(5-((4-fluorophenyl)thio)-3-methyl-1-phenyl-1H-pyrazol-4-yl)-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carbonitrile (**8m**)*

Yield 83 %; m.p. 227-228 °C; IR (KBr, ν_{max}, cm^{-1}): 3472 & 3342 (asym. & sym. str. of $–NH_2$), 2190 (C≡N str.), 1662 (C=O str.), 1368 ($–CH_3$ str.), 756 (C–S–C thioether str.); ^1H NMR (400 MHz, $CDCl_3$): δ 0.84 (s, 3H, CH_3), 0.86 (s, 3H, CH_3), 1.63-1.88 (m, 4H, 2 × CH_2), 2.59 (s, 3H, CH_3 of pyrazole), 3.77 (s, 2H, -NH_2), 4.99 (s, 1H, CH), 6.82-7.46 (m, 13H, Ar–H); ^{13}C NMR (100 MHz, $CDCl_3$)

δ: 12.46, 27.60, 28.15, 28.55, 32.41, 41.68, 49.84, 109.17, 115.99, 116.21, 117.63, 117.85, 125.69, 127.70, 128.44, 128.53, 131.50, 132.14, 132.23, 132.80, 134.67, 138.85, 147.64, 149.73, 149.98, 160.95, 163.40, 194.87; ESI-MS (m/z): 593.2 (M^+); Anal. Calcd (%) for $C_{34}H_{29}F_2N_5OS$: C, 68.78; H, 4.92; N, 11.80. Found: C, 68.74; H, 4.88; N, 11.84.

*6.1.3.14. Ethyl 2-amino-1-(4-fluorophenyl)-4-(5-((4-fluorophenyl)thio)-3-methyl-1-phenyl-1H-pyrazol-4-yl)-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**8n**)*

Yield 71 %; m.p. 231-233 °C; IR (KBr, ν_{max}, cm^{-1}): 3418 & 3362 (asym. & sym. str. of $–NH_2$), 2203 (C≡N str.), 1667 (C=O str.), 1372 ($–CH_3$ str.), 763 (C–S–C thioether str.); ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.83 (s, 3H, CH_3), 0.92 (s, 3H, CH_3), 1.15-1.31 (m, 4H, 2 × CH_2), 1.62 (t, 3H, CH_3), 2.75 (s, 3H, CH_3 of pyrazole), 4.17 (m, 2H, CH_2), 5.17 (s, 1H, -CH), , 6.69-7.35 (m, 15H, Ar–H and $–NH_2$) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.68, 14.81, 28.12, 28.57, 32.43, 41.86, 50.07, 59.63, 113.60, 117.52, 117.63, 125.88, 127.97, 128.13, 128.89, 129.06, 132.07, 133.23, 139.35, 149.67, 150.03, 151.73, 153.46, 158.93, 161.26, 162.07, 164.87, 170.03, 195.93; ESI-MS (m/z): 640.2(M^+); Anal. Calcd (%) for $C_{36}H_{34}F_2N_4O_3S$: C, 67.48; H, 5.35; N, 8.74. Found: C, 67.44; H, 5.39; N, 8.78.

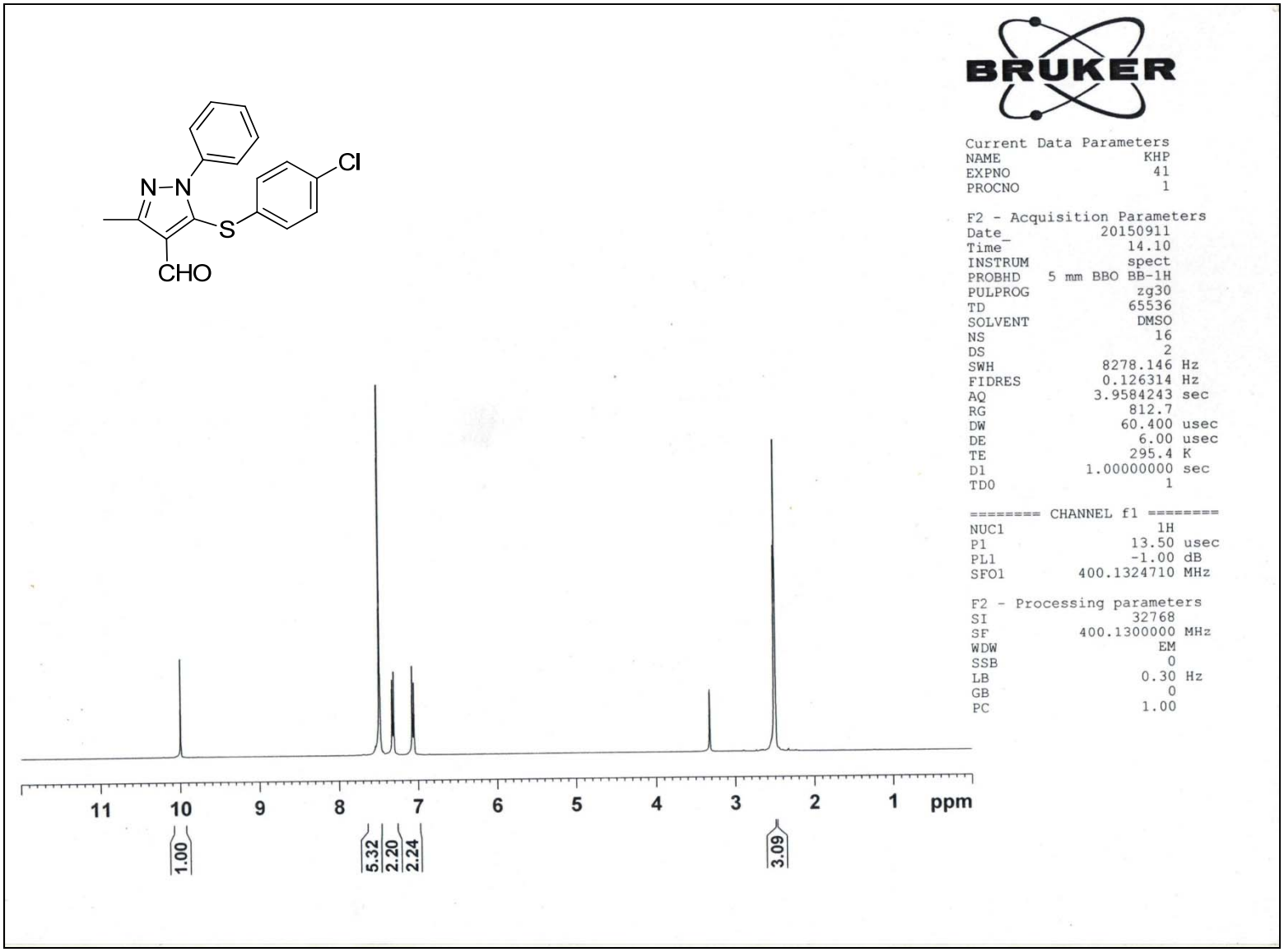
*6.1.3.15. 2-amino-1-(4-fluorophenyl)-4-(5-((4-fluorophenyl)thio)-3-methyl-1-phenyl-1H-pyrazol-4-yl)-7,7-dimethyl-5-oxo-1,4,5,6,7,8-hexahydroquinoline-3-carbonitrile (**8o**)*

Yield 72 %; m.p. 209-211 °C; IR (KBr, ν_{max}, cm^{-1}): 3414 & 3381 (asym. & sym. str. of $–NH_2$), 2192 (C≡N str.), 1670 (C=O str.), 1367 ($–CH_3$ str.), 764 (C–S–C thioether str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.72 (s, 3H, CH_3), 0.81 (s, 3H, CH_3), 1.01-1.89 (m, 4H, 2 × CH_2), 2.51 (s, 3H, CH_3 of pyrazole), 4.69 (s, 1H, CH), 5.36 (bs, 2H, $-NH_2$), 6.83-7.79 (m, 13H, Ar–H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 12.31, 20.89, 27.60, 28.17, 28.63, 32.45, 41.53, 49.44, 58.13, 109.56, 117.20, 118.25, 125.61, 125.68, 127.63, 128.50, 129.84, 130.53, 131.95, 132.23, 135.21, 135.29, 139.13, 147.60, 150.28, 150.90, 161.15, 163.48, 193.91; ESI-MS (m/z): 593.2 (M^+); Anal. Calcd (%) for $C_{34}H_{29}F_2N_5OS$: C, 68.78; H, 4.92; N, 11.80 Found: C, 68.74; H, 4.96; N, 11.84.

*6.1.3.16. Ethyl 2-amino-4-(5-((4-fluorophenyl)thio)-3-methyl-1-phenyl-1H-pyrazol-4-yl)-7,7-dimethyl-5-oxo-1-(4-(trifluoromethyl)phenyl)-1,4,5,6,7,8-hexahydroquinoline-3-carboxylate (**8p**)*

Yield 79 %; m.p. 229-231 °C; IR (KBr, ν_{max}, cm^{-1}): 3483 & 3339 (asym. & sym. str. of $–NH_2$), 2217 (C≡N str.), 1673 (C=O str.), 1363 ($–CH_3$ str.), 760 (C–S–C thioether str.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.74 (s, 3H, CH_3), 0.93 (s, 3H, CH_3), 1.13-1.37 (m, 4H, 2 × CH_2), 1.59 (t, 3H, CH_3), 2.73 (s, 3H, CH_3 of pyrazole), 4.19 (m, 2H, CH_2), 5.33 (s, 1H, -CH), , 6.63-7.47 (m, 15H, Ar–H and $–NH_2$) ; ^{13}C NMR (100 MHz, DMSO-d_6) δ: 12.65, 14.85, 20.86, 28.15, 28.60, 32.47, 41.85, 50.11, 59.67, 113.61, 118.55, 117.68, 125.94, 127.99, 128.15, 128.91, 129.06, 132.10, 133.19, 139.33, 149.69, 150.11, 151.65, 153.49, 159.03, 161.21, 162.13, 164.80, 169.97, 195.78; ESI-MS (m/z): 690.2(M^+); Anal. Calcd (%) for $C_{37}H_{34}F_4N_4O_3S$: C, 64.34; H, 4.96; N, 8.11. Found: C, 64.38; H, 4.92; N, 8.15.

^{1}H NMR spectra of compound **3a**



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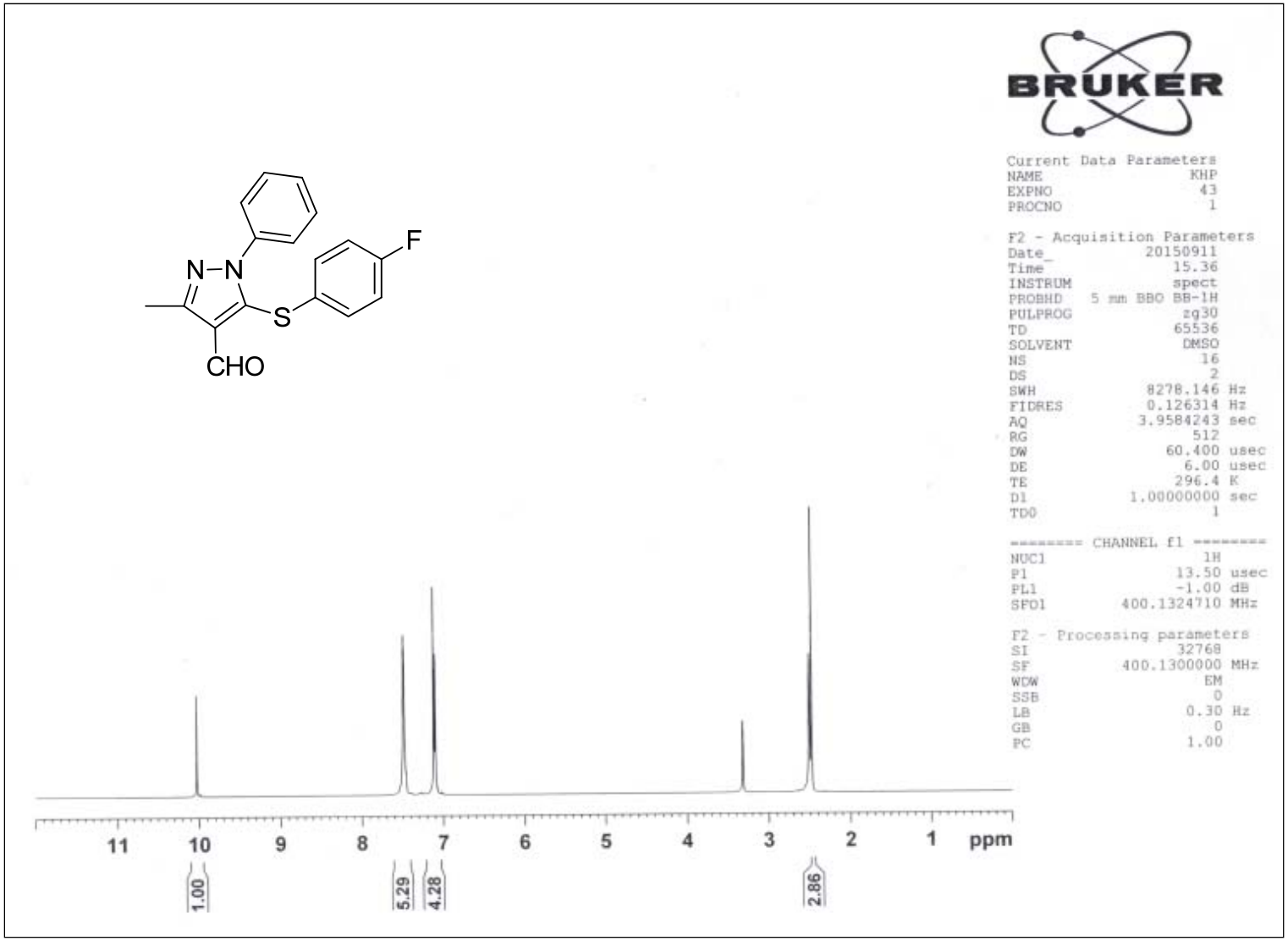
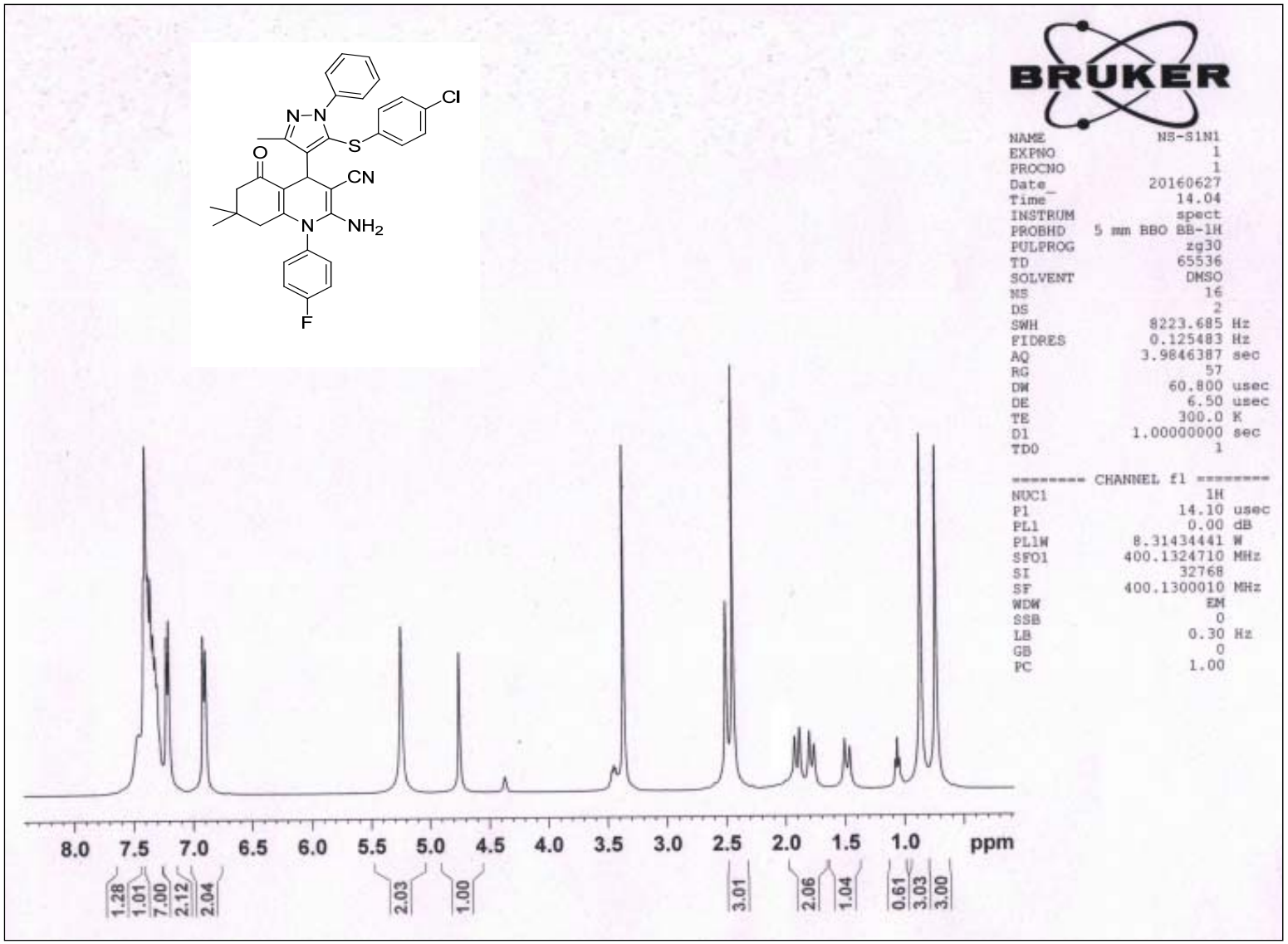
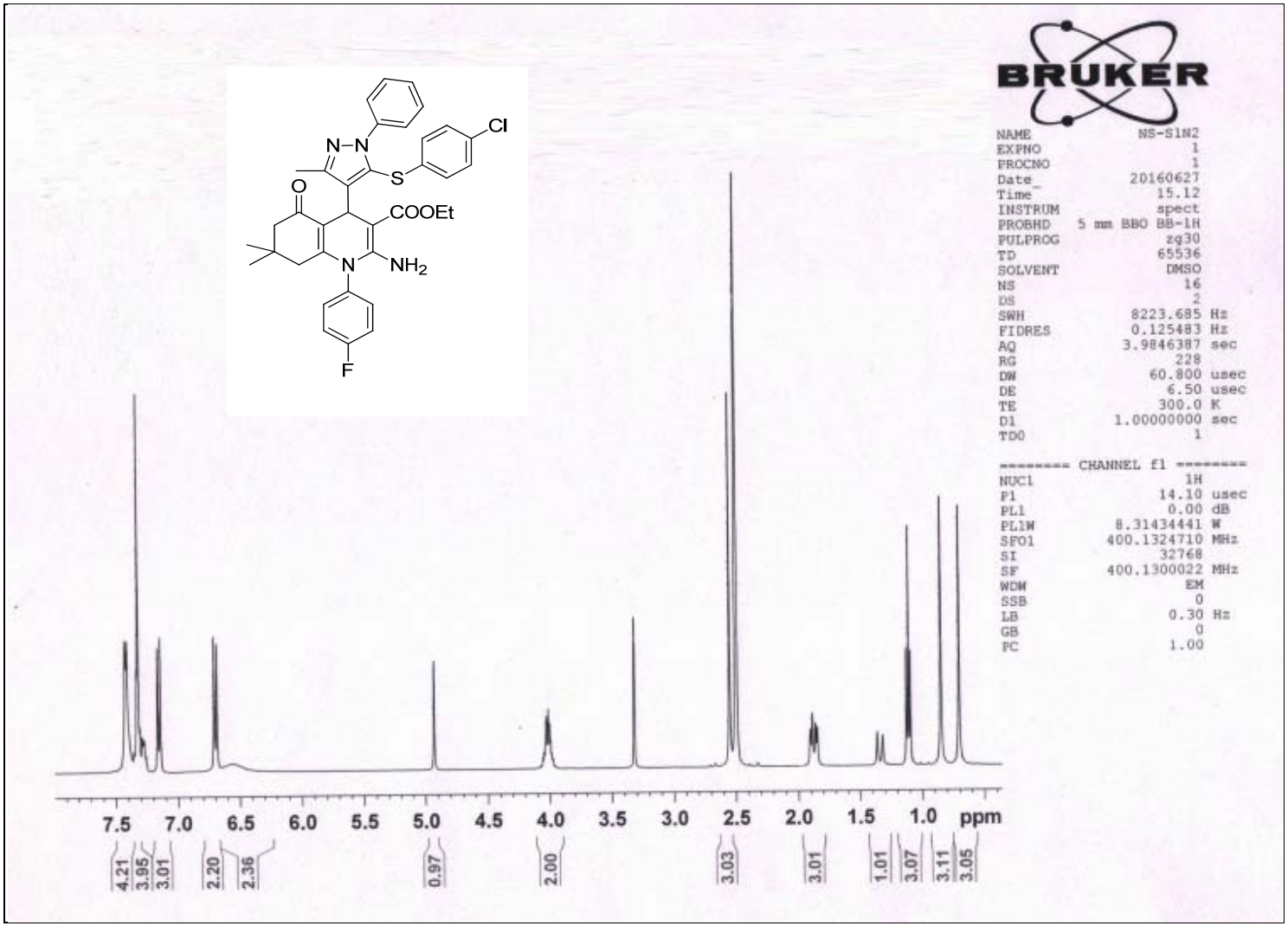
^{1}H NMR spectra of compound **3c**



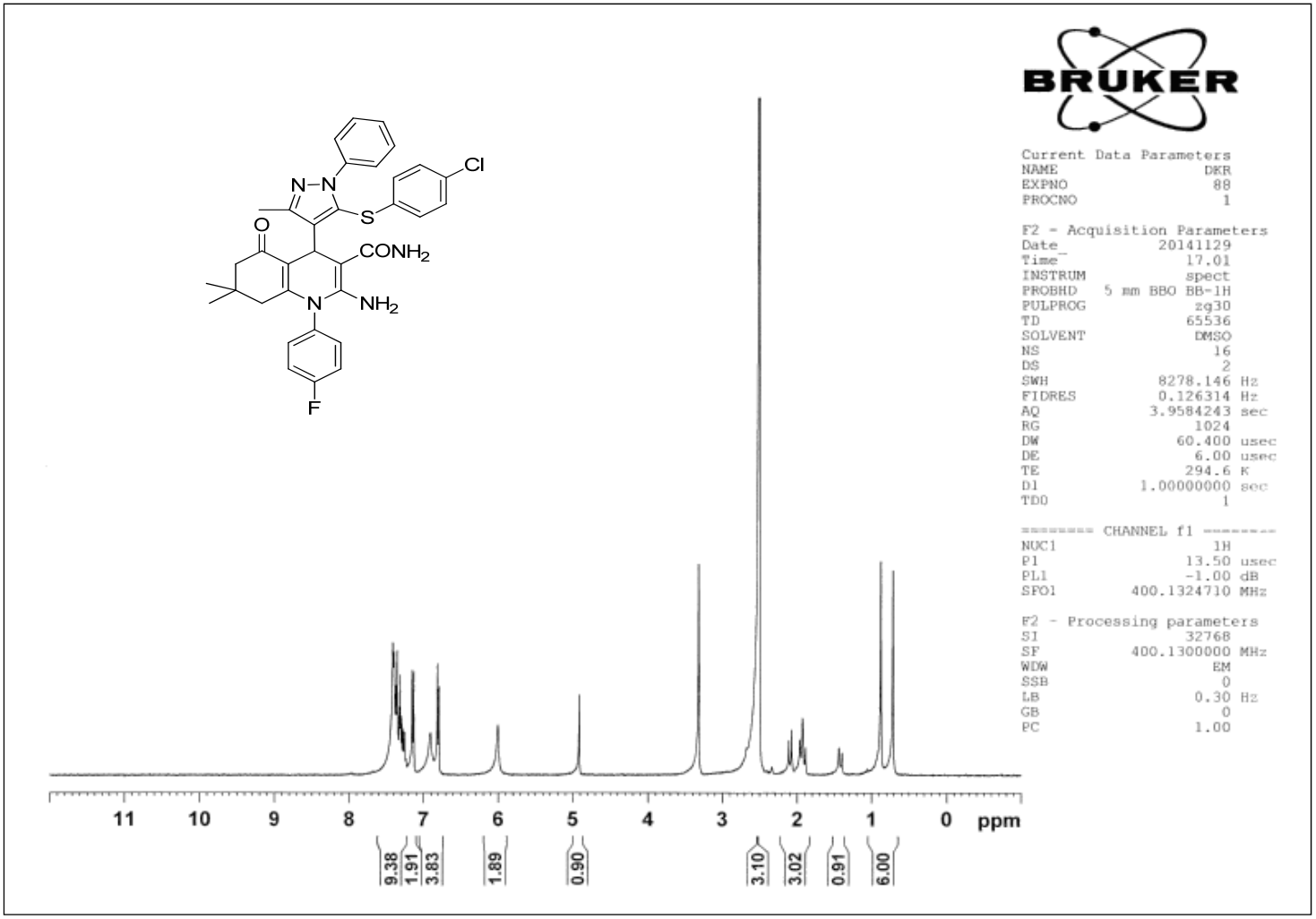
^{1}H NMR spectra of compound **8a**



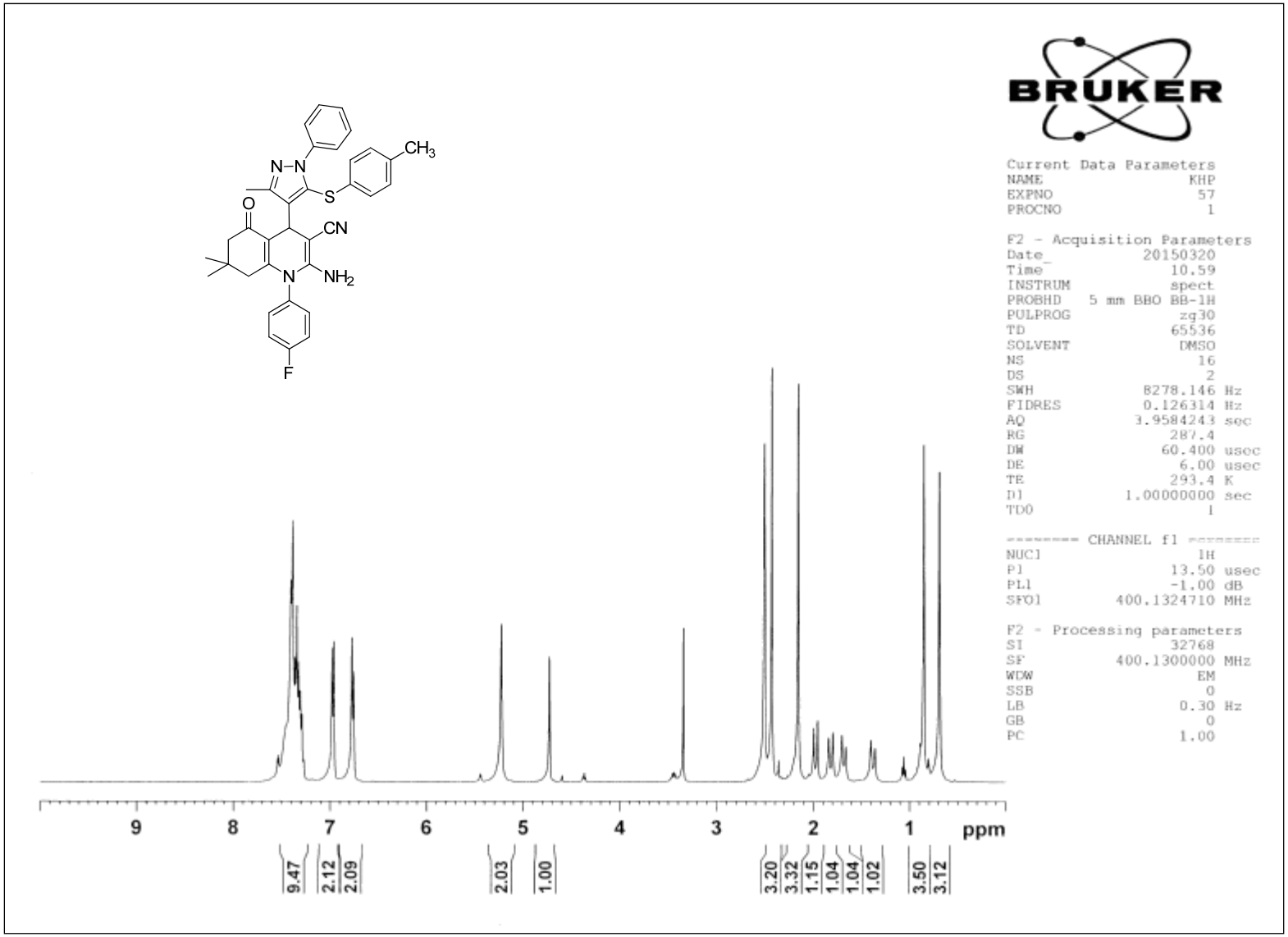
^{1}H NMR spectra of compound **8b**



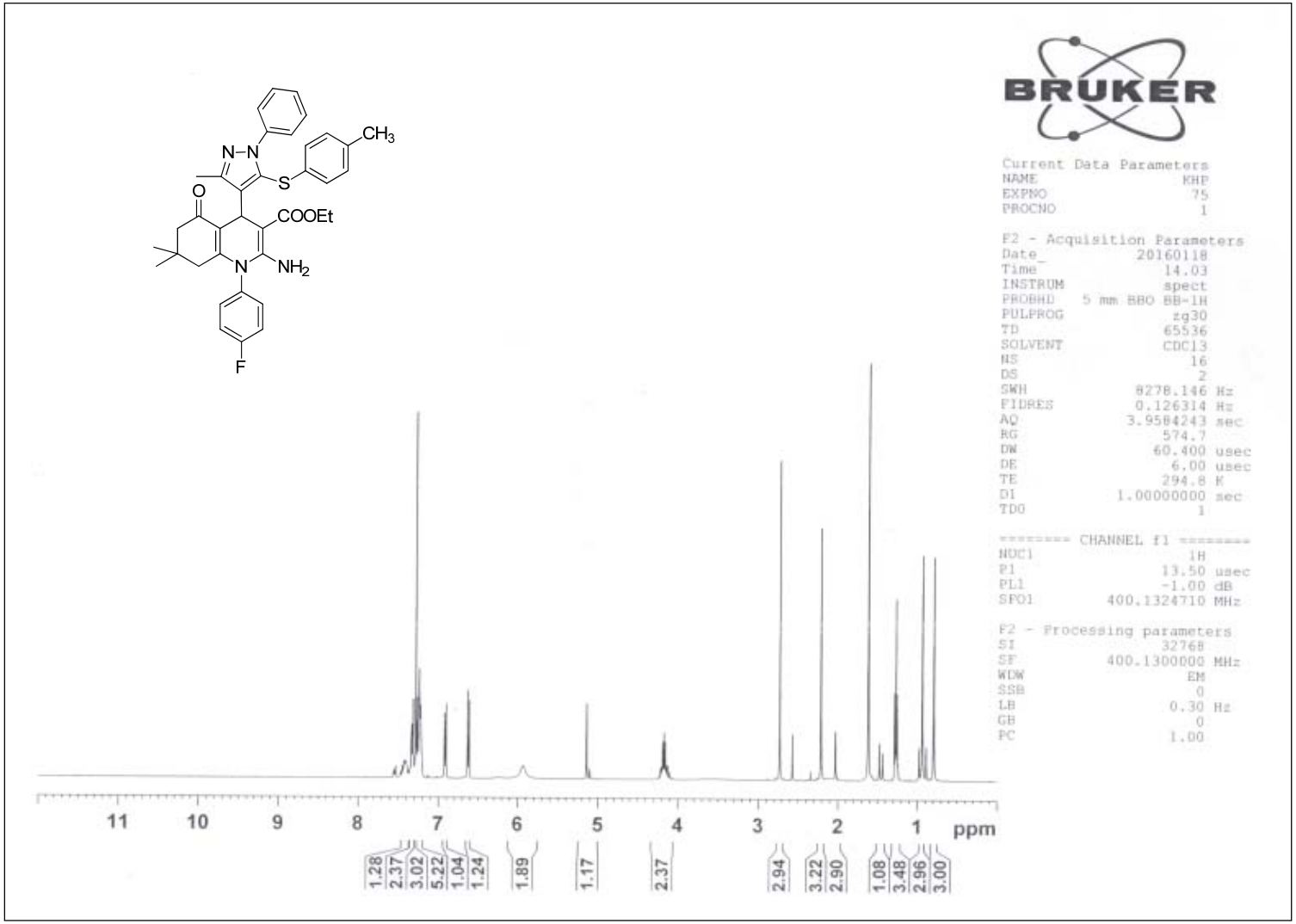
^{1}H NMR spectra of compound **8c**



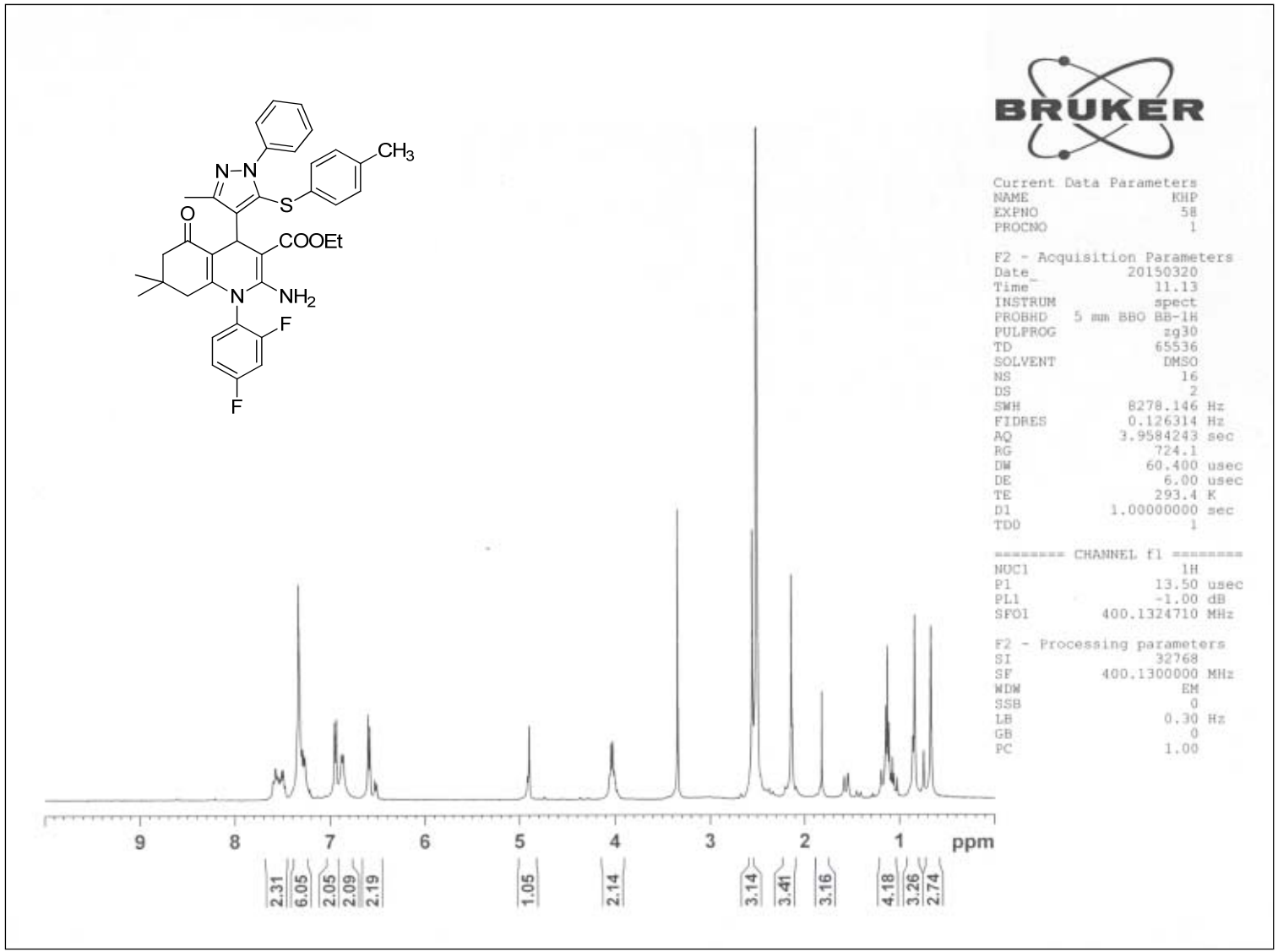
^{1}H NMR spectra of compound **8d**



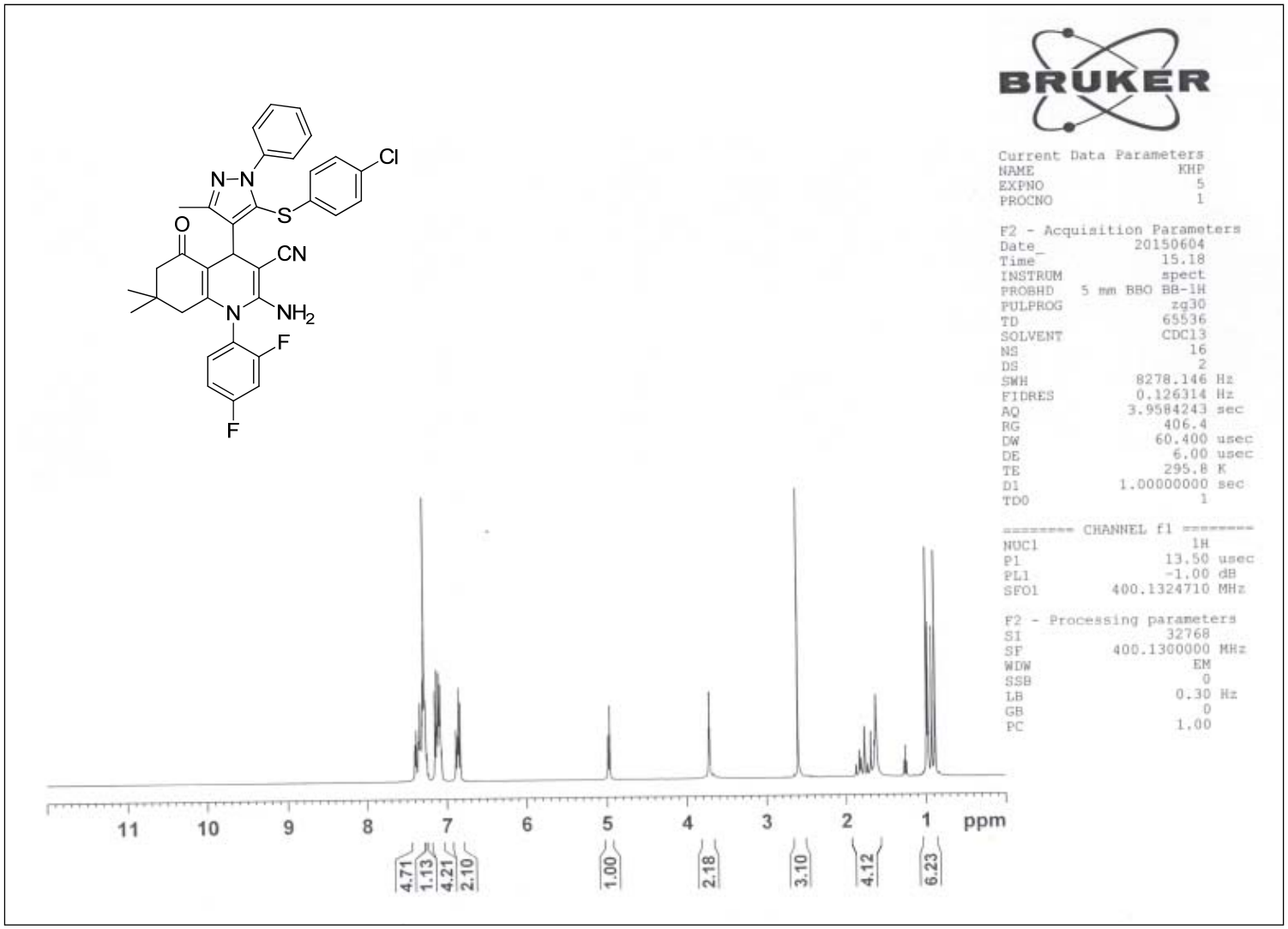
^{1}H NMR spectra of compound **8e**



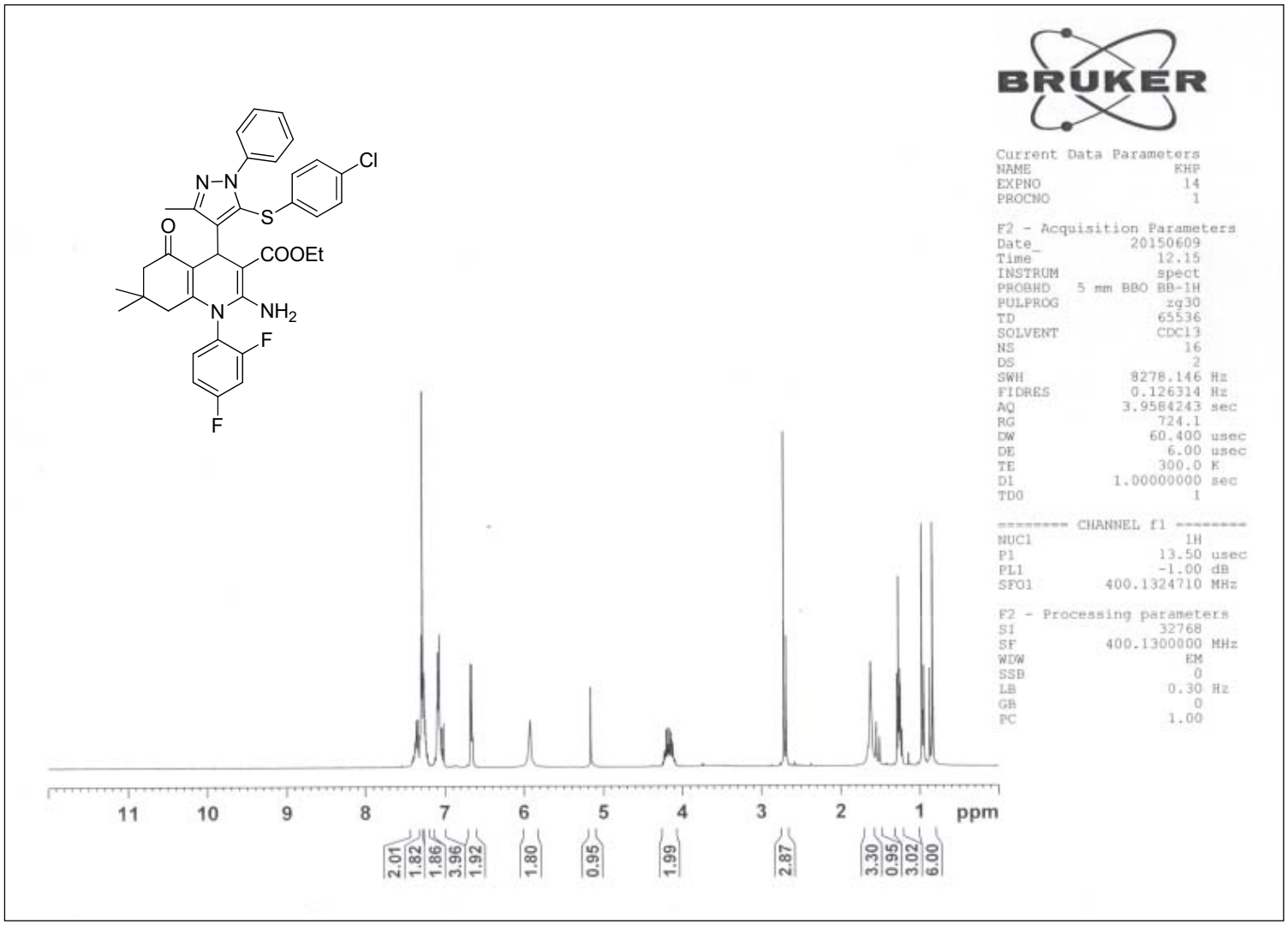
^{1}H NMR spectra of compound **8i**



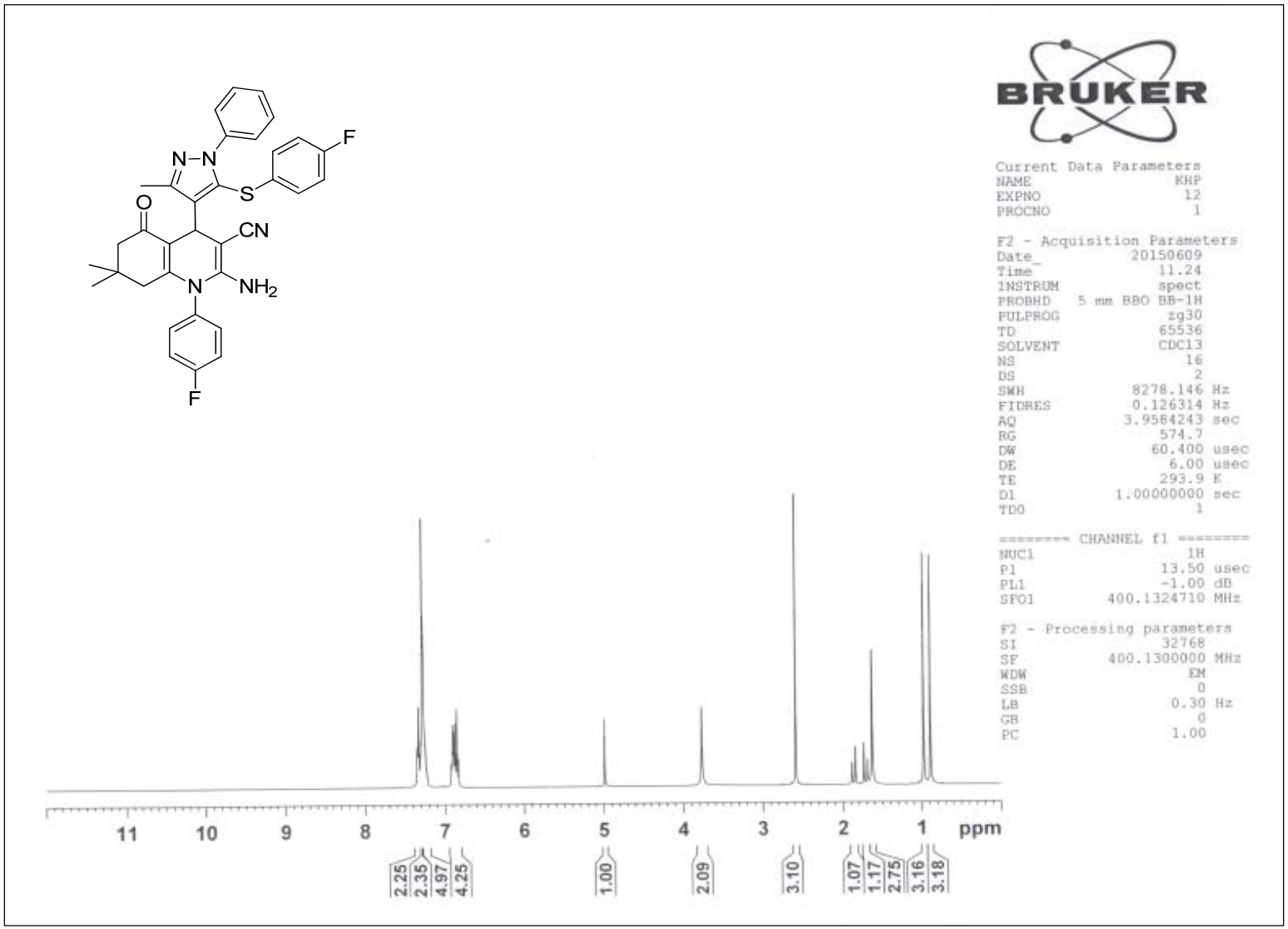
^{1}H NMR spectra of compound **8j**



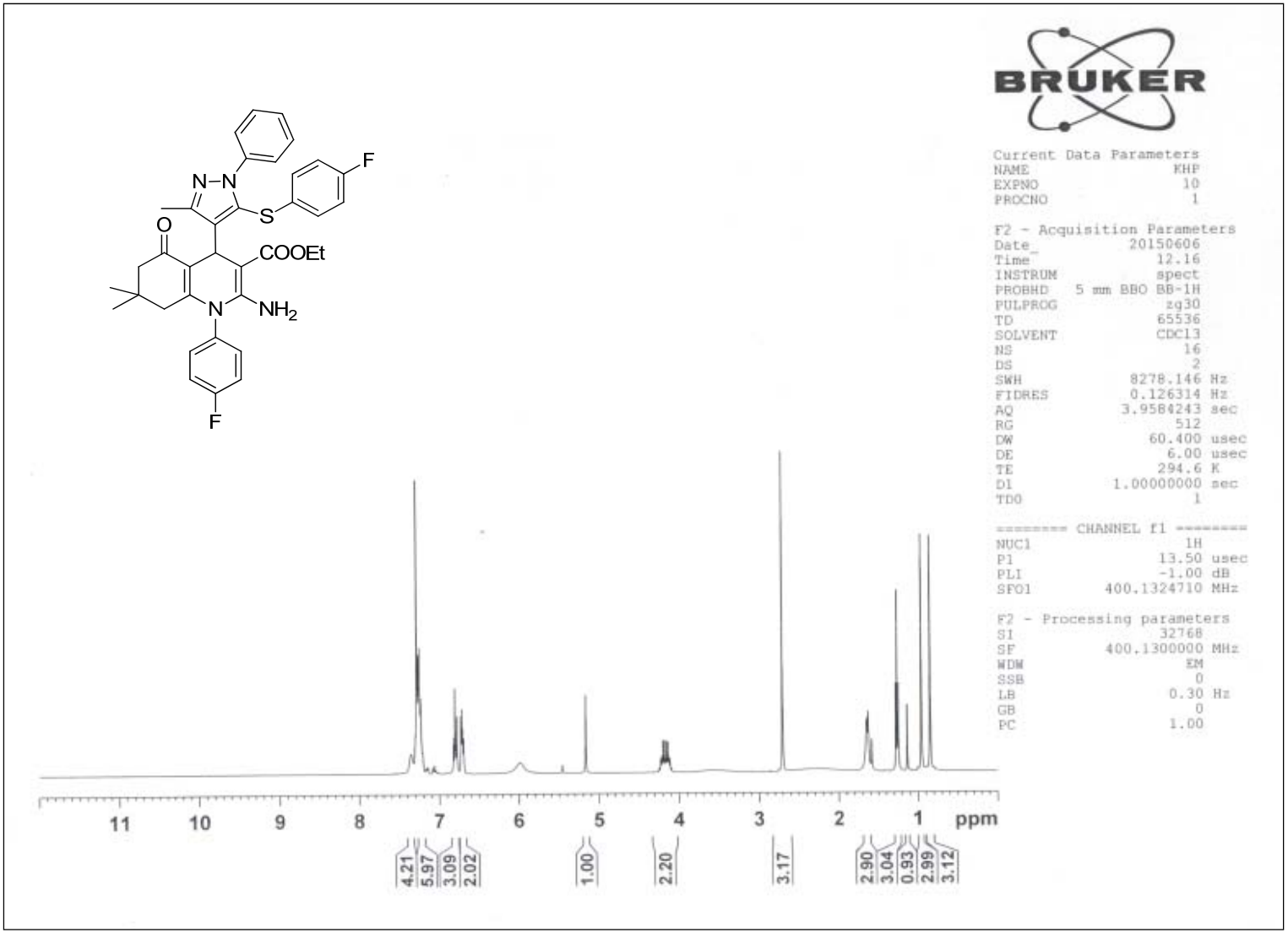
^{1}H NMR spectra of compound **8k**



^{1}H NMR spectra of compound **8m**



^{1}H NMR spectra of compound **8n**



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PROCNO                  1

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D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
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SFO1         400.1324710 MHz

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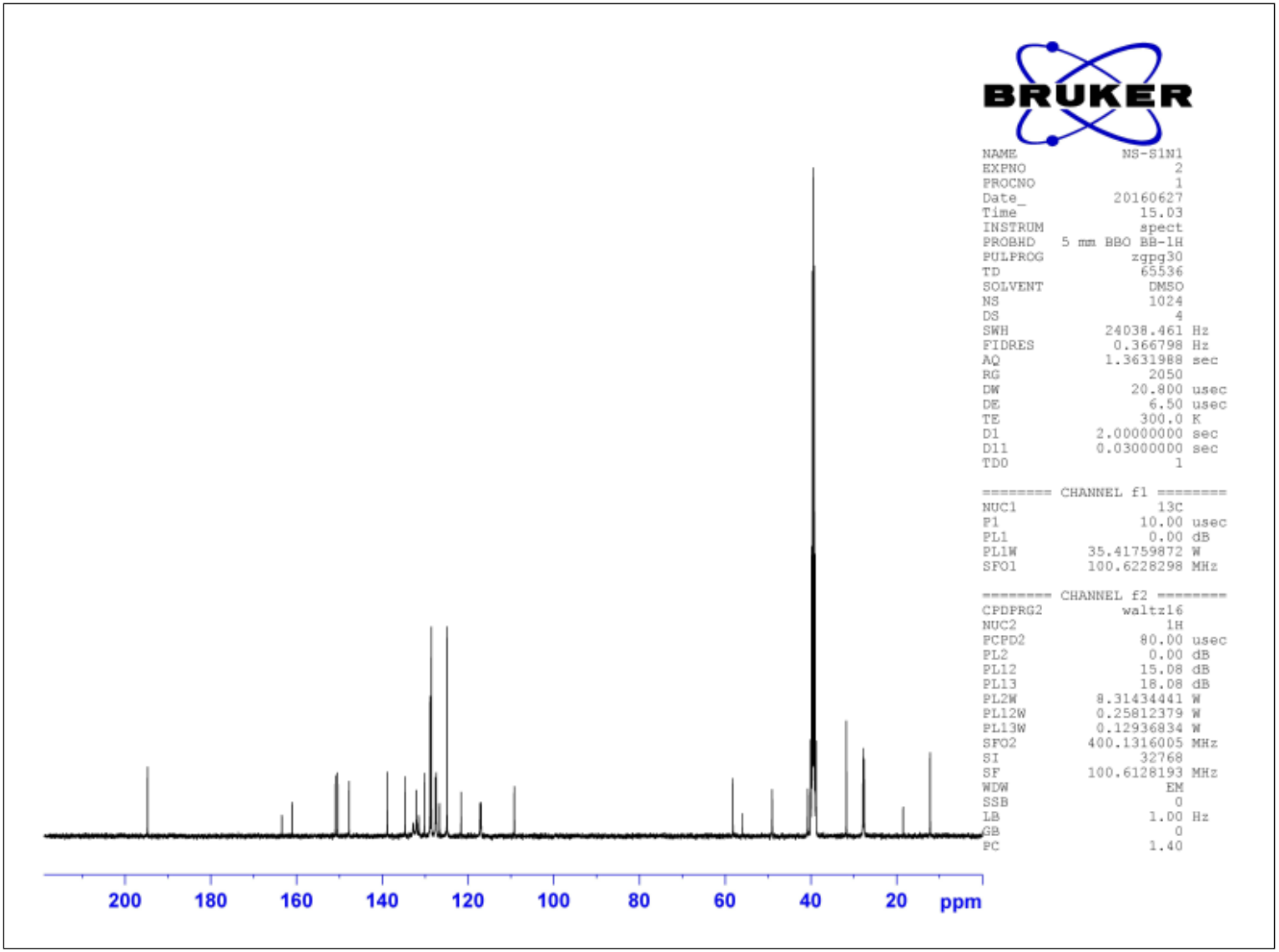
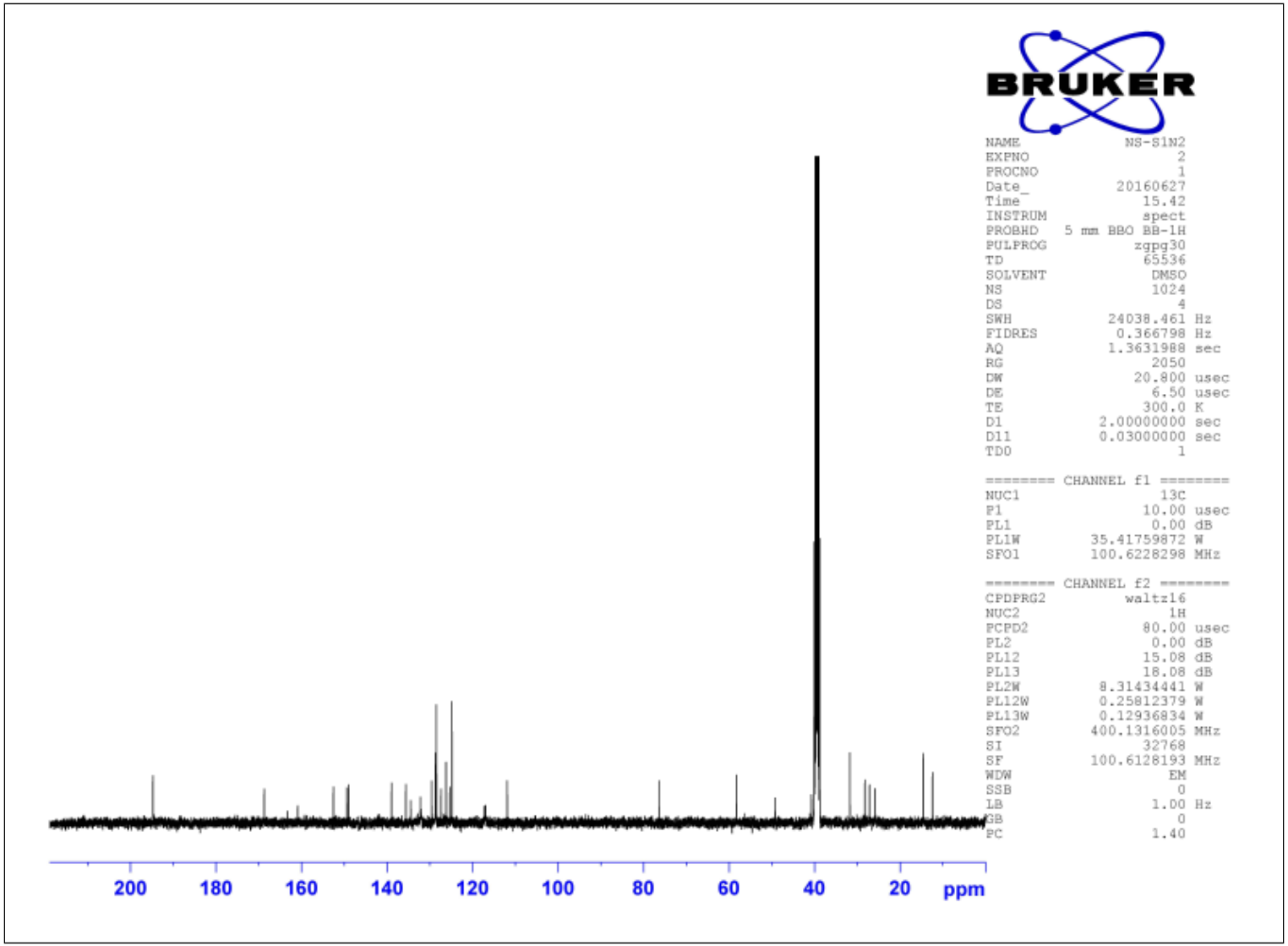
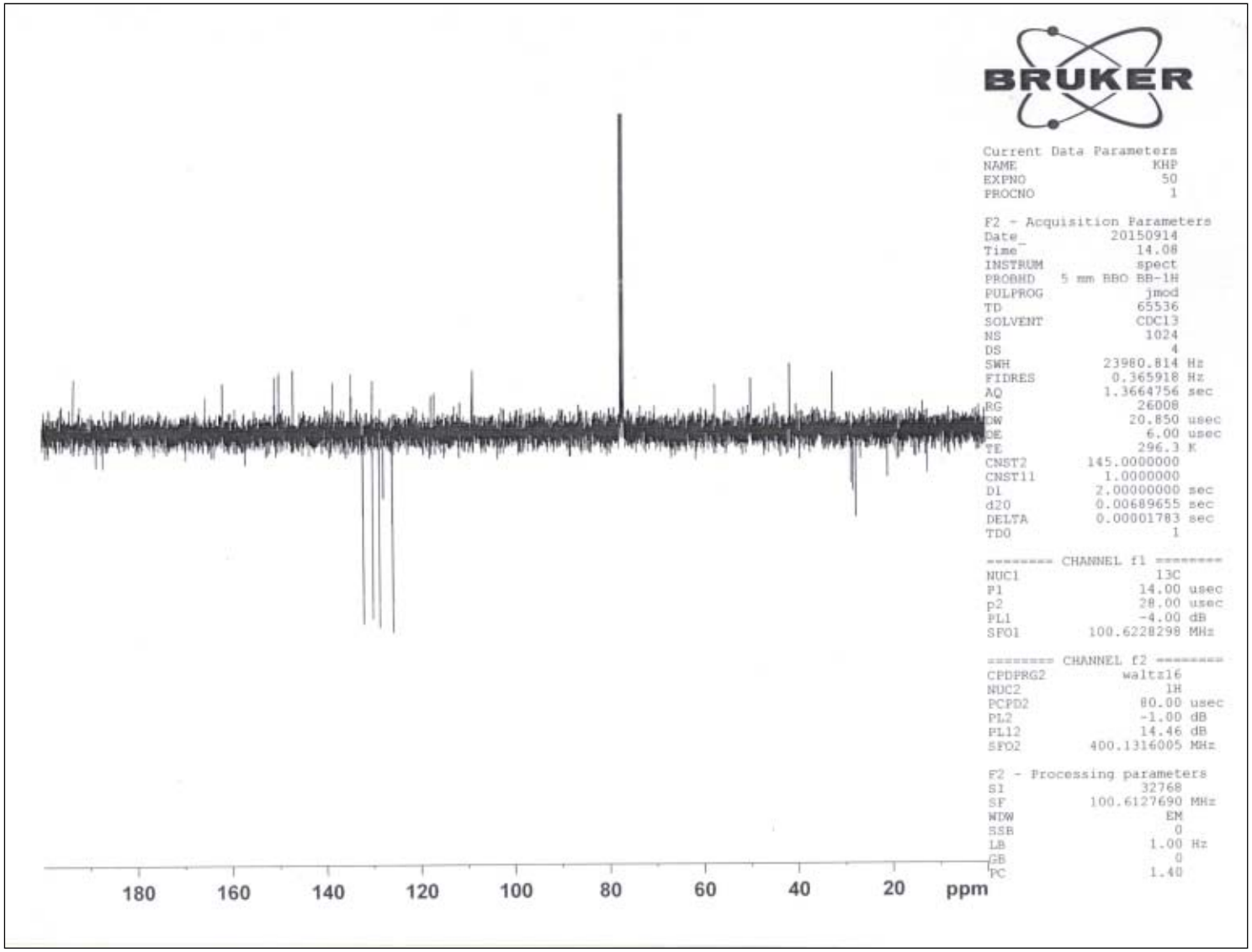
^{13}C NMR spectra of compound **8a**



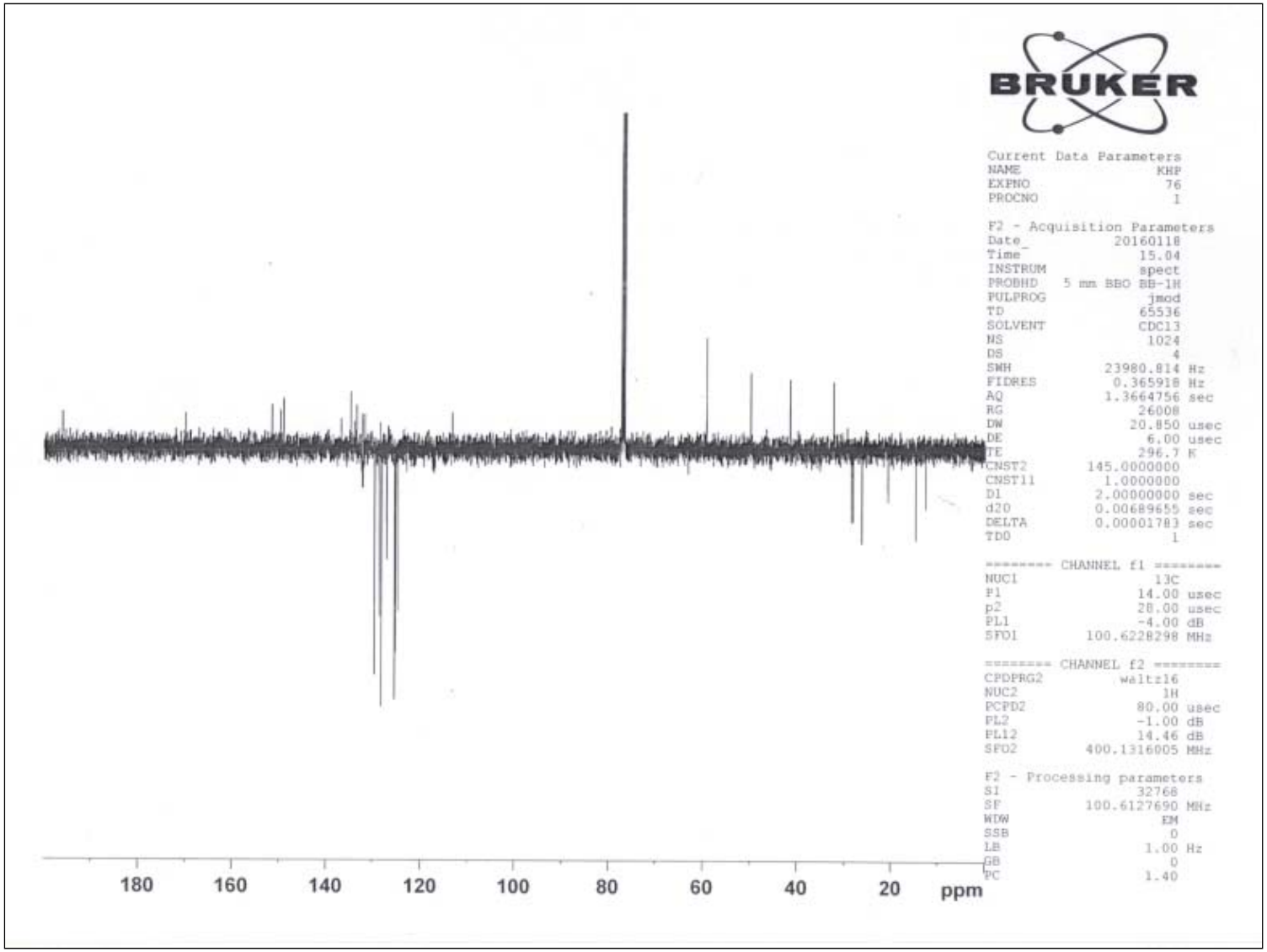
^{13}C NMR spectra of compound **8b**



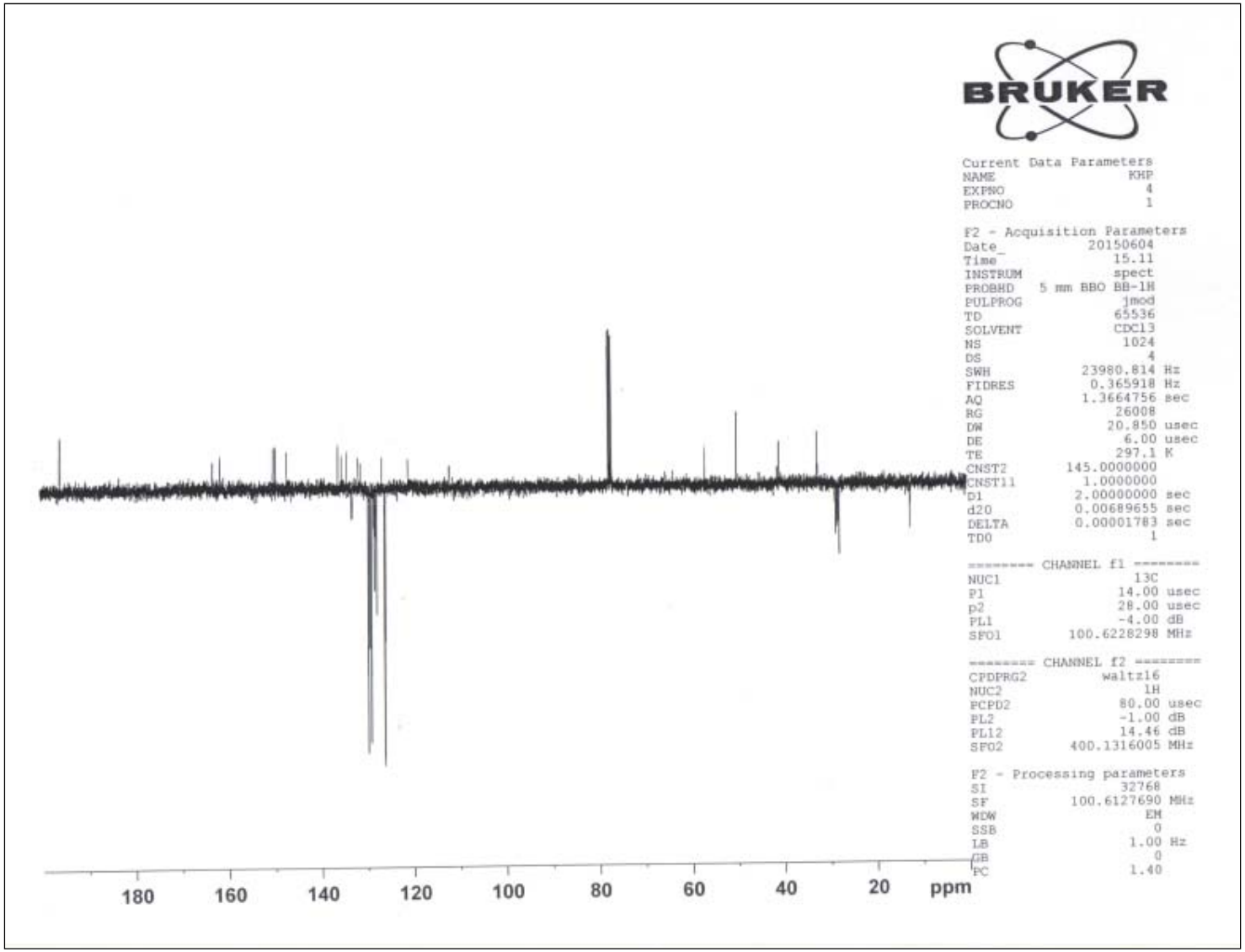
^{13}C NMR spectra of compound **8d**



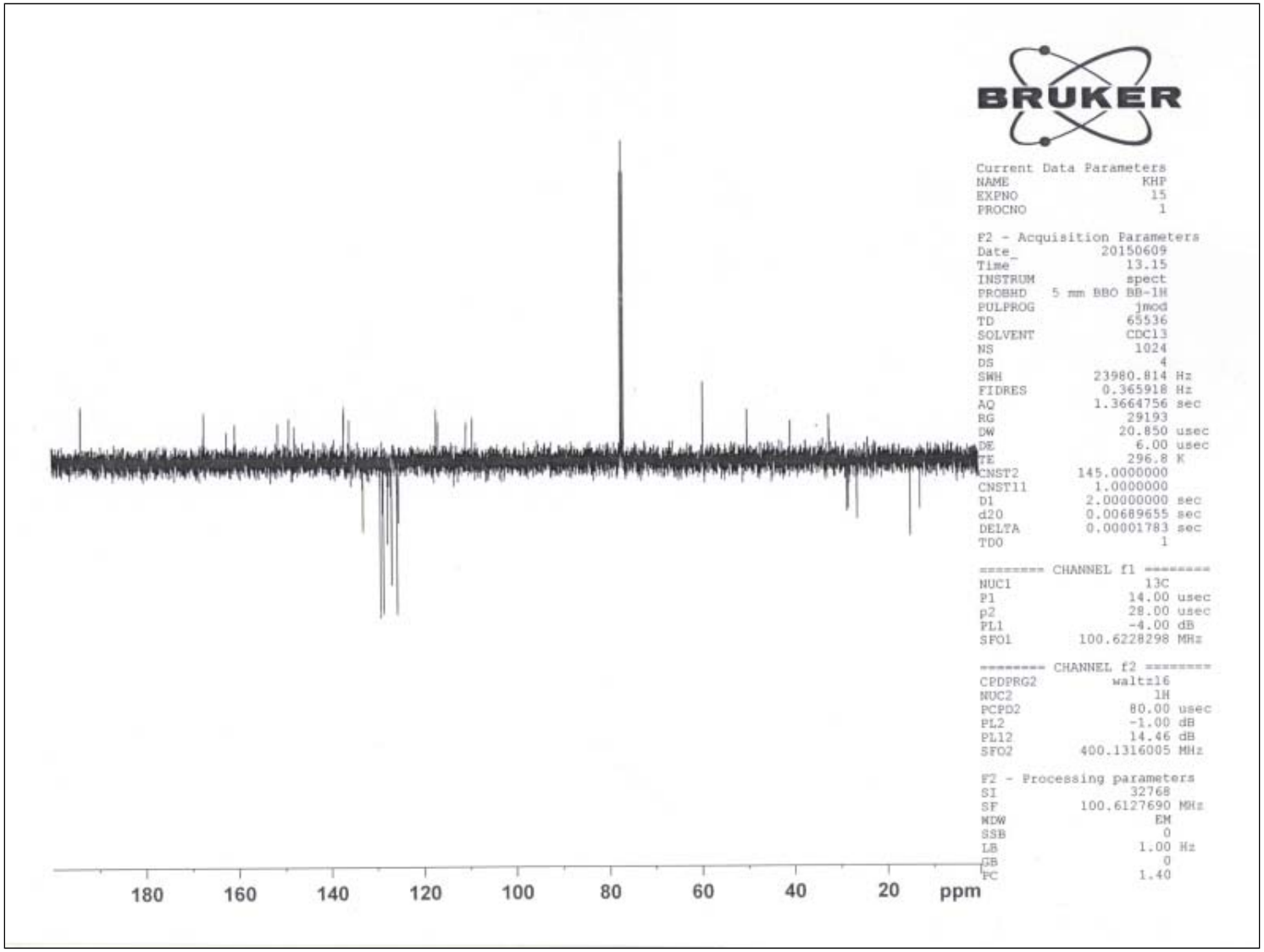
^{13}C NMR spectra of compound **8e**



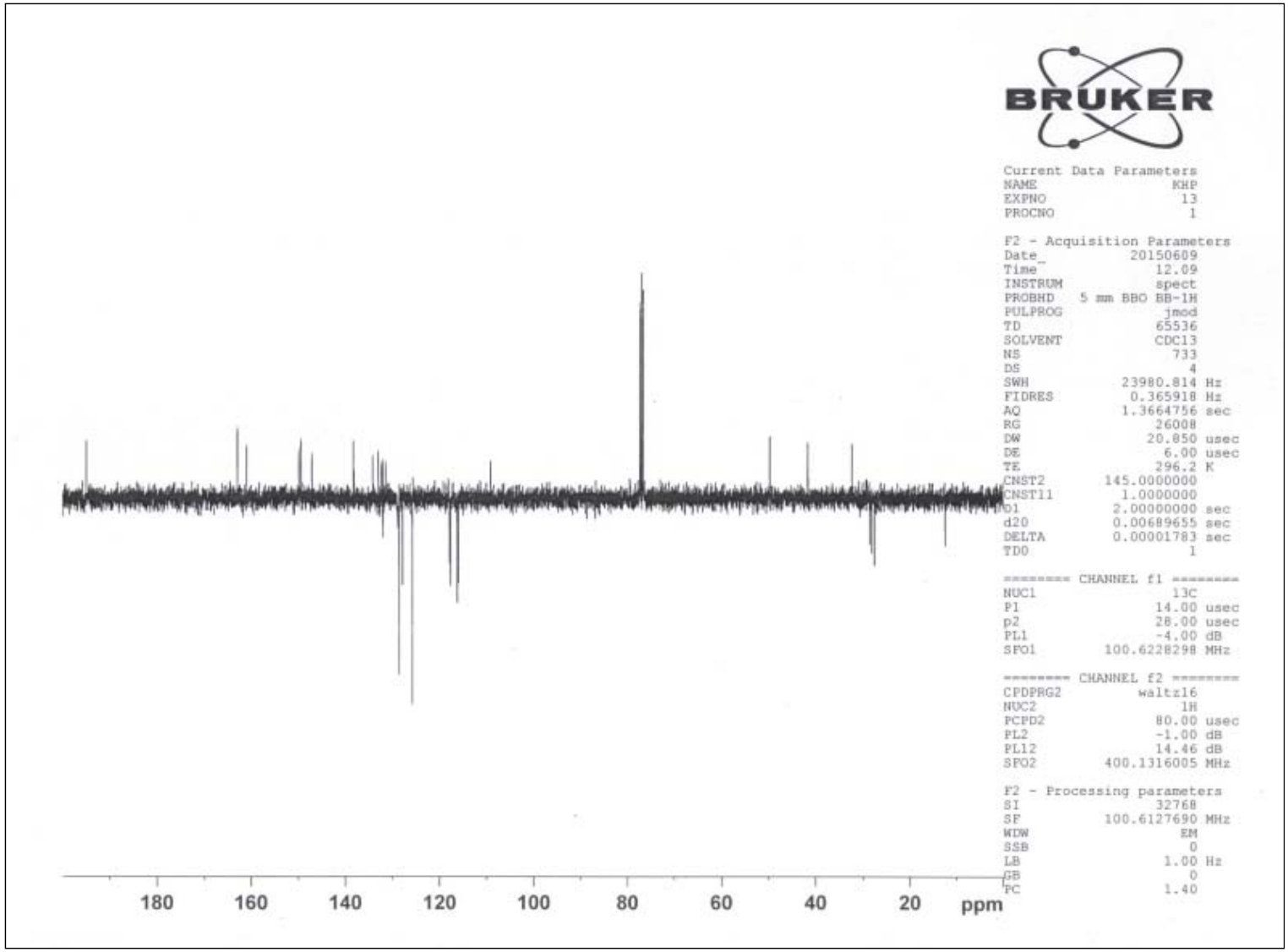
^{13}C NMR spectra of compound **8j**



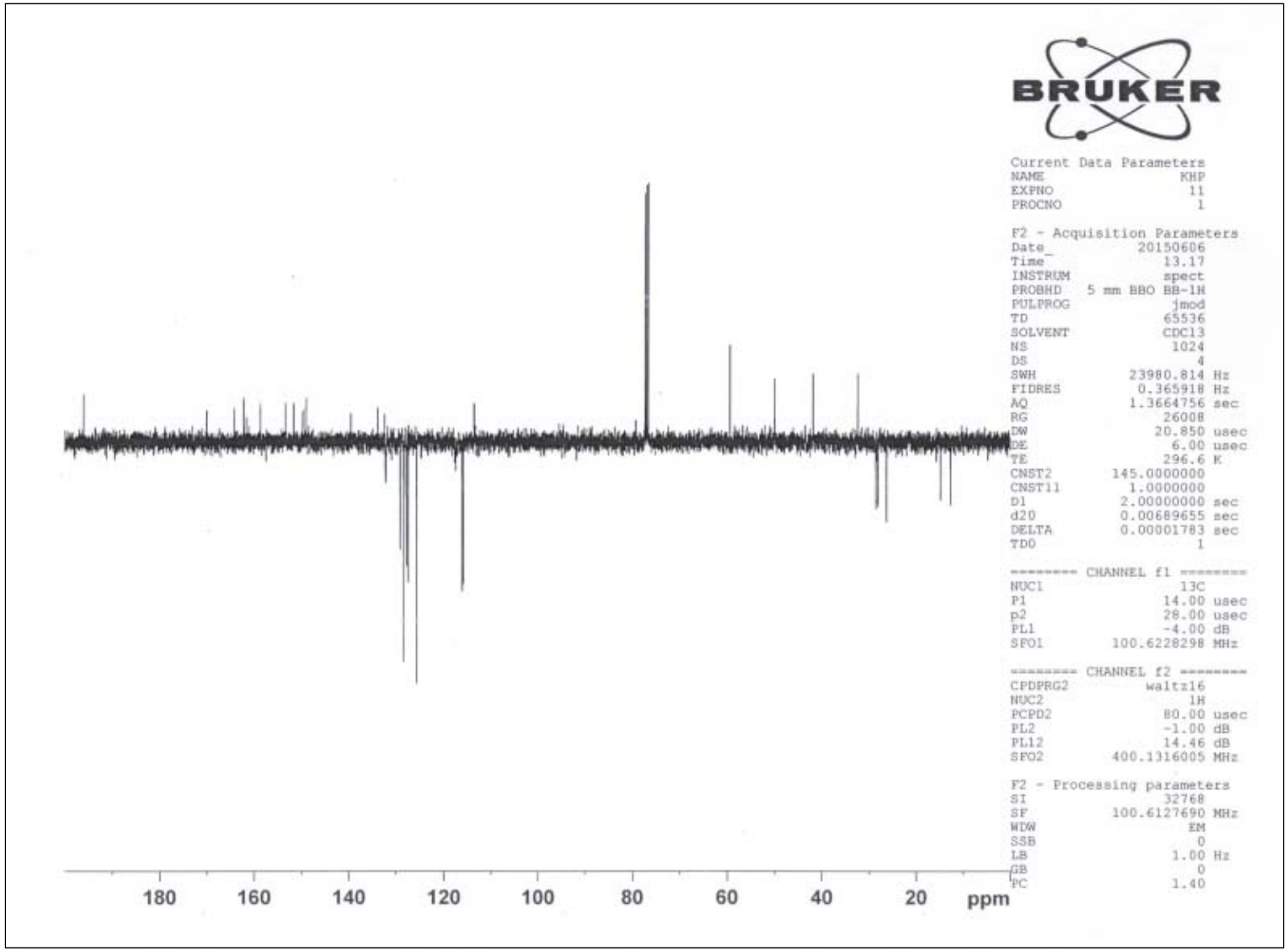
^{13}C NMR spectra of compound **8k**



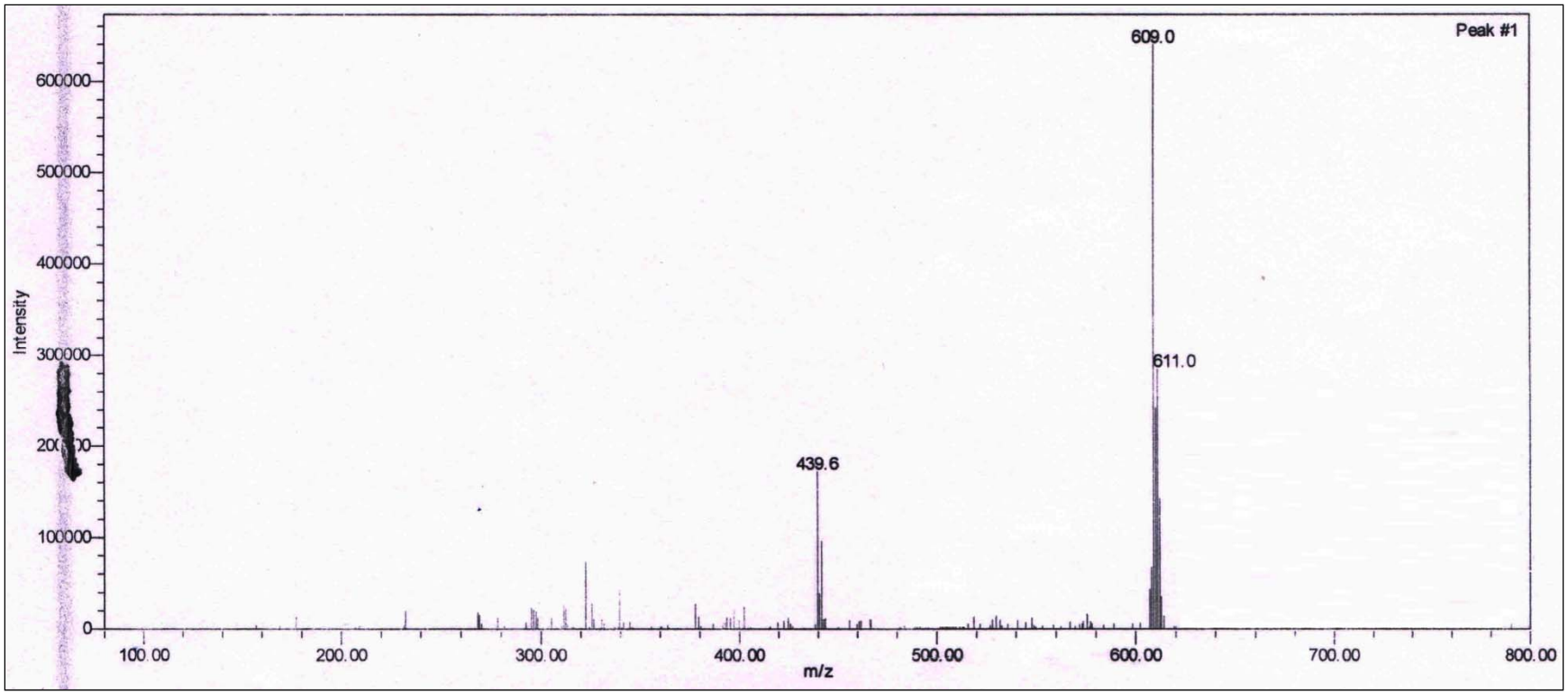
^{13}C NMR spectra of compound **8m**



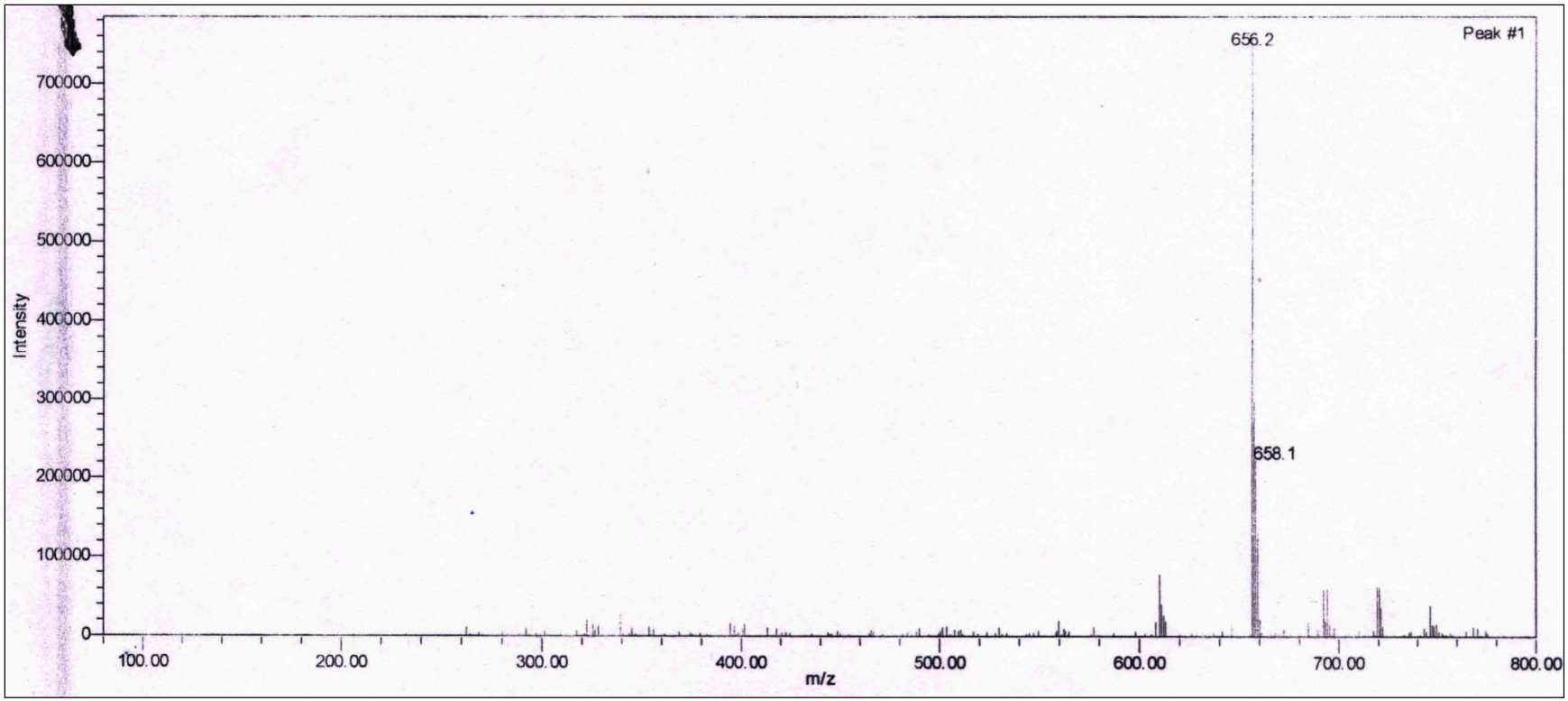
^{13}C NMR spectra of compound **8n**



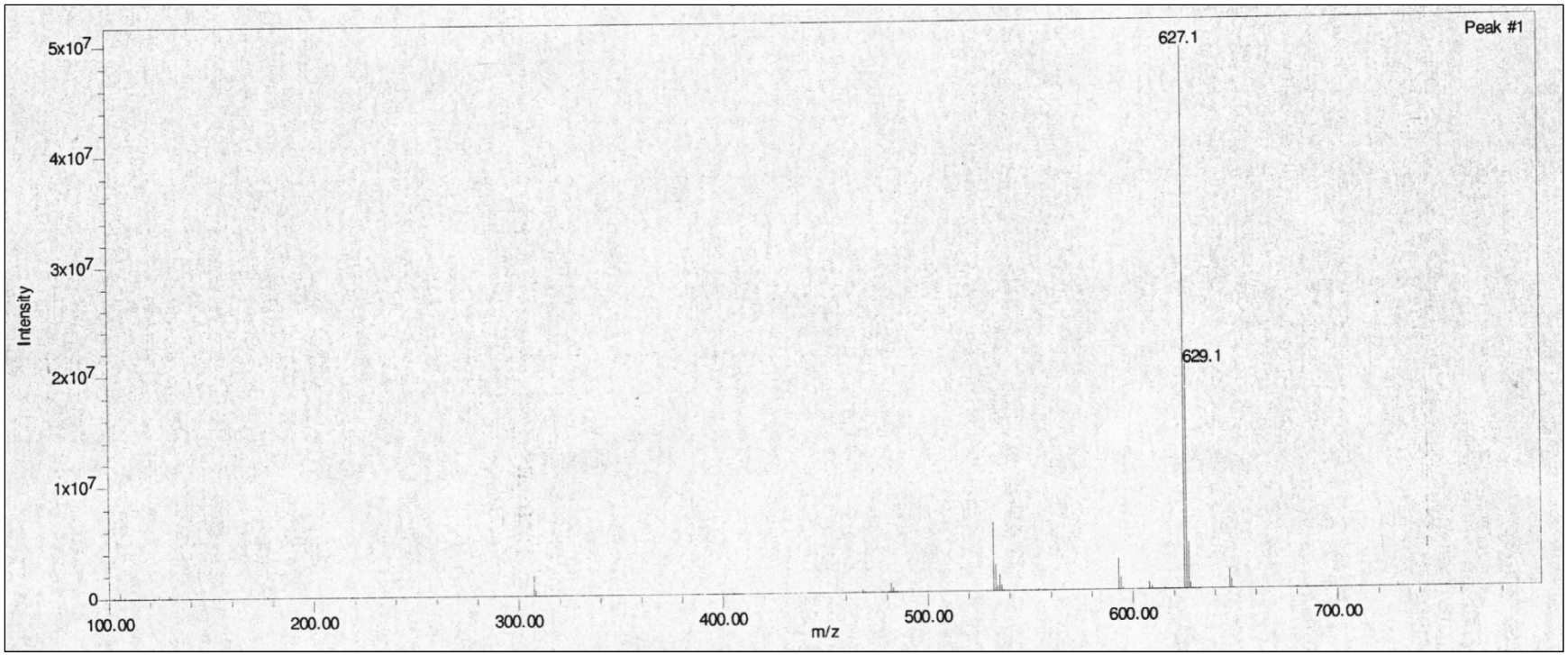
Mass spectrum of compound **8a**



Mass spectrum of compound **8b**



Mass spectrum of compound **8c**



Mass spectrum of compound **8d**