Supporting Information

Novel Dolabellane-type Diterpene Alkaloids with Lipid Metabolism Promoting Activities from the Seeds of *Nigella sativa*

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General Experimental Procedures. The following instruments were used to obtain physical data: specific rotations, Horiba SEPA-300 digital polarimeter (*l*=5 cm); CD spectra, JASCO J-720WI spectrometer; UV spectra, Shimadzu UV-1600 spectrometer; IR spectra, Shimadzu FTIR-8100 spectrometer; ^{1}H NMR spectra, JEOL JNM LA-500 (500 MHz) spectrometer; ^{13}C NMR spectra, JEOL JNM LA-500 (125 MHz) spectrometer with tetramethylsilane as an internal standard; FABMS and HRFABMS, JEOL JMS-SX 102A mass spectrometer; EIMS, CIMS, HREIMS, and HRCIMS, JEOL JMS-GCMATE mass spectrometer; HPLC detector, Shimadzu RID-6A refractive index and SPD-10A*vp* UV-VIS detectors.

The following experimental conditions were used for chromatography: normal-phase silica gel column chromatography, Silica gel BW-200 (Fuji Silysia Chemical, 150–350 mesh); reversed-phase silica gel column chromatography, Chromatorex ODS DM1020T (Fuji Silysia Chemical, 100–200 mesh); HPLC column, YMC-Pack ODS-A (YMC, 250 × 20 mm i.d.); TLC, pre-coated TLC plates with Silica gel 60F_{254} (Merck, 0.25 mm) (normal-phase) and Silica gel RP-18 F_{254S} (Merck, 0.25 mm) (reversed-phase); reversed-phase HPTLC, pre-coated TLC plates with Silica gel RP-18 WF_{254S} (Merck, 0.25 mm); detection was achieved by spraying with 1% $Ce(SO_4)_2$–10% aqueous H_2SO_4 followed by heating.

Extraction and Isolation. The seeds of *N. sativa* (10.0 kg, collected in Egypt) were extracted with methanol 3 times under reflux for 3 h. Evaporation of the solvent under reduced pressure provided the methanolic extract (1740 g, 17.4% from this natural medicine). The methanolic extract (1245 g) was partitioned into an EtOAc and water mixture to give an EtOAc-soluble fraction (723 g, 10.1%) and an aqueous phase (522 g, 7.3%). The EtOAc-soluble fraction (285 g) was subjected to ordinary-phase silica gel column chromatography [3.0 kg, *n*-hexane–EtOAc (20:1–10:1–5:1–2:1–1:2)–$CHCl_3$–MeOH–H_2O (20:3:1, lower layer–6:4:1)–MeOH] to give 12 fractions [Fr. 1 (12.36 g), 2 (55.91 g), 3 (74.90 g), 4 (18.51 g), 5 (61.82 g), 6 (2.55 g), 7 (0.97 g), 8 (9.68 g), 9 (6.69 g), 10 (8.13 g), 11 (15.82 g), and 12 (16.57 g)]. Fraction 7 (0.97 g) was subjected to reversed-phase silica gel column chromatography [30 g, MeOH–H_2O (50:50–70:30–85:15, v/v)–MeOH] to give seven fractions [Fr. 7-1 (112 mg), 7-2 (105 mg), 7-3 (68 mg), 7-4 (315 mg), 7-5 (87 mg), 7-6 (152 mg), and 7-7 (120 mg)]. Fraction 7-4 (315 mg) was further separated by HPLC [YMC-Pack ODS-5-A, 250×20 mm i.d., MeOH–H_2O (85:15, v/v)] to give nigellamine A_1 (**1**, 271 mg, 0.0096% from the natural medicine). Fraction 7-6 (152 mg) was purified by HPLC [MeOH–H_2O (80:20, v/v)] to give nigellamine B_1 (**3**, 33 mg, 0.0012%). Fraction 9 (6.69 g) was subjected to reversed-phase silica gel column chromatography [200 g, MeOH–H_2O (40:60–60:40–80:20, v/v)–MeOH] to give ten fractions [Fr. 9-1 (1.150 g), 9-2 (943 mg), 9-3 (627 mg), 9-4 (1.312 g), 9-5 (142 mg), 9-6 (750 mg), 9-7 (150 mg), 9-8 (241 mg), 9-9 (805 mg), and 9-10 (428 mg)]. Fraction 9-6 (750 mg) was purified by HPLC [MeOH–H_2O (75:25, v/v)] to give nigellamine B_2 (**4**, 102 mg, 0.0036%). Fraction 9-9 (805 mg) was purified by HPLC [MeOH–H_2O (80:20, v/v)] to give nigellamine A_2 (**2**, 221 mg, 0.0078%).

Treatment of Nigellamine A_1 (1) with 0.1% NaOMe–MeOH. **A** solution of **1** (10.0 mg) in 0.1% NaOMe–MeOH (2.0 mL) was stirred at room temperature for 8 h. From the reaction mixture, methyl nicotinate (**i**) and methyl benzoate (**ii**) were identified by HPLC analyses [t_R (**i**): 5.58, (**ii**): 15.80 min, detection: UV (254 nm), column: YMC-Pack ODS-5-A, 250×4.6 mm i.d., mobile phase: MeOH–H_2O (60:40, v/v); flow rate 0.7 ml/min (standard samples were obtained by diazomethane methylation of commercial nicotinic acid and benzoic acid)].
Then the reaction mixture was neutralized with Dowex HCR-W2 (H^+ form) and the resin was removed by filtration. Evaporation of the solvent from the filtrate under reduced pressure furnished a residue, which was purified by HPLC [detection: RI, column: YMC-Pack ODS-5-A, 250×20 mm i.d., mobile phase: MeOH–H_2O (60:40, v/v)] to give **1a** (4.0 mg, 77%).
On the other hand, a solution of **1** (15.0 mg) in 0.1% NaOMe–MeOH (2.0 mL) was stirred at 0°C for 3.5 h. The reaction mixture was poured into ice-water and the whole was extracted with EtOAc. The EtOAc extract was successively washed with brine then dried over $MgSO_4$ powder and filtrated. Evaporation of the solvent from the filtrate under reduced pressure furnished a residue, which was purified by HPLC [detection: RI, column: YMC-Pack ODS-5-A, 250×20 mm i.d., mobile phase: MeOH–H_2O (80:20, v/v)] to give **1b** (4.1 mg, 40%) and 10-desacyl derivative (**1c**, 4.8 mg, 38%).

1a: A white powder, $[a]_D^{23}$ +33.9° (*c*=0.20, MeOH). IR (KBr): 3304, 3240, 1655, 1561, 1509, 1375, 1122, 1038, 1017, 953, 777, 718 cm^{-1}. ^{13}C NMR (CD_3OD): δ_C 59.5 (C-1), 71.9 (C-2), 129.4 (C-3), 136.5 (C-4), 38.8 (C-5), 23.9 (C-6), 67.4 (C-7), 60.9 (C-8), 46.5 (C-9), 74.4 (C-10), 49.8 (C-11), 141.5 (C-12), 28.7 (C-13), 29.4 (C-14), 62.7 (C-15), 16.4 (C-16), 18.8 (C-17), 124.5 (C-18), 22.3 (C-19), 22.4 (C-20).
1b: A white powder, $[a]_D^{24}$ +36.3° (*c*=0.40, $CHCl_3$). High resolution positive-ion FAB-MS: Calcd for $C_{27}H_{37}O_5$ $(M+H)^+$: 441.2641. Found: 441.2650. UV (MeOH, log ε): 230 (4.10), 273 (2.91) nm. IR (KBr): 3325, 1717, 1636, 1603, 1541, 1509, 1451, 1271, 1111, 1071, 1026, 953, 754, 714 cm^{-1}. ^{13}C NMR ($CDCl_3$): δ_C 57.6 (C-1), 73.7 (C-2), 123.3 (C-3), 139.1 (C-4), 37.9 (C-5), 22.8 (C-6), 65.9 (C-7), 59.4 (C-8), 44.8 (C-9), 73.6 (C-10), 48.4 (C-11), 138.4 (C-12), 28.3 (C-14), 27.5 (C-14), 61.5 (C-15), 16.2 (C-16), 18.5 (C-17), 124.9 (C-18), 21.9 (C-19), 22.3 (C-20), 130.2 (C-1'), 129.6 (C-2',6'), 128.5 (C-3',5'), 133.1 (C-4'), 165.9 (C-7'). Positive-ion FAB-MS: *m/z* 441 $(M+H)^+$.
1c: A white powder, $[a]_D^{24}$ +29.8° (*c*=0.50, $CHCl_3$). High resolution positive-ion FAB-MS: Calcd for $C_{34}H_{41}O_6$ $(M+H)^+$: 545.2903. Found: 545.2906. UV (MeOH, log ε): 228 (4.46), 274 (3.30) nm. IR (KBr): 3517, 1717, 1647, 1636, 1603, 1541, 1509, 1451, 1281, 1113, 1069, 1026, 953, 756, 712 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.40, 1.74, 1.79 (3H each, all s, H_3-17, 19, 20), 1.52 (1H, dd, *J* = 12.8, 13.5 Hz, Hβ-9), 1.66 (1H, m, Hα-6), 1.82 (3H, d, *J* = 0.9 Hz, H_3-16), 1.97 (1H, m, Hβ-6), 2.20 (2H, m, H_2-14), 2.31 (2H, m, H_2-13), 2.37 (1H, dd, *J* = 5.5, 13.5 Hz, Hα-9), 2.39 (1H, m, Hα-5), 2.43 (1H, ddd, *J* = 5.2, 12.8, 12.8 Hz, Hβ-5), 2.51 (1H, br s, H-11), 3.02 (1H, br d, *J* = *ca.* 9 Hz, H-7), 4.21 (1H, m, H-10), 4.76, 5.25 (1H each, both d, *J* = 11.0 Hz, H_2-15), 5.40 (1H, d, *J* = 10.1 Hz, H-2), 5.62 (1H, dd, *J* = 0.9, 10.1 Hz, H-3), 7.19 (2H, dd, *J* = 7.6, 8.3 Hz, H-3',5'), 7.42 (2H, dd, *J* = 7.6, 8.3 Hz, H-3''',5'''), 7.45 (1H, tt, *J* = 1.2, 7.6 Hz, H-4'), 7.58 (1H, tt, *J* = 1.2, 7.6 Hz, H-4'''), 7.87 (2H, dd, *J* = 1.2, 8.3 Hz, H-2',6'), 8.07 (2H, dd, *J* = 1.2, 8.3 Hz, H-2''',6'''). ^{13}C NMR ($CDCl_3$): δ_C 56.2 (C-1), 73.2 (C-2), 123.7

(C-3), 139.4 (C-4), 37.8 (C-5), 22.9 (C-6), 65.6 (C-7), 58.9 (C-8), 45.4 (C-9), 73.5 (C-10), 49.1 (C-11), 137.8 (C-12), 28.5 (C-13), 30.5 (C-14), 66.5 (C-15), 16.4 (C-16), 18.5 (C-17), 125.8 (C-18), 21.9 (C-19), 22.5 (C-20), 130.0 (C-1'), 129.6 (C-2',6'), 128.2 (C-3',5'), 132.8 (C-4'), 166.3 (C-7'), 130.3 (C-1'"), 129.8 (C-2'",6'"), 128.5 (C-3'",5'"), 133.1 (C-4'"), 166.3 (C-7'"). Positive-ion FAB-MS: *m/z* 545 $(M+H)^+$.

Treatment of Nigellamine A_2 (2) with 0.1% NaOMe–MeOH. A solution of **2** (10.0 mg) in 0.1% NaOMe–MeOH (2.0 mL) was stirred at room temperature for 8 h. From the reaction mixture, methyl nicotinate and methyl benzoate were identified by HPLC analyses and **1a** (3.8 mg, 74%) was purified by the similar procedure.

On the other hand, a solution of **2** (5.0 mg) in 0.1% NaOMe–MeOH (1.0 mL) was stirred at 0°C for 2 h. The reaction mixture was poured into ice-water and the whole was extracted with EtOAc. The EtOAc extract was successively washed with brine then dried over $MgSO_4$ powder and filtrated. Evaporation of the solvent from the filtrate under reduced pressure furnished a residue, which was purified by HPLC [detection: RI, column: YMC-Pack ODS-5-A, 250×20 mm i.d., mobile phase: MeOH–H_2O (80:20, v/v)] to give **2a** (0.1 mg, 3%), 10-desacyl derivative (**2b**, 1.8 mg, 43%), 2-desacyl derivative (**2c**, 1.0 mg, 24%), 2,15-desacyl derivative (**2d**, 0.2 mg, 6%), 2,10-desacyl derivative (**2e**, 0.4 mg, 12%), and **1a** (0.3 mg, 9%).

2a: A white powder.

2b: A white powder. High resolution EI-MS: Calcd for $C_{33}H_{39}NO_6$ (M^+): 545.2777. Found: 545.2781. ^{1}H NMR (CD_3OD): δ1.41, 1.76, 1.83 (3H each, all s, H_3-17, 19, 20), 1.45 (1H, dd, J = 12.5, 13.5 Hz, Hβ-9), 1.76 (1H, m, Hα-6), 1.79 (3H, d, J = 1.2 Hz, H_3-16), 1.92 (1H, m, Hβ-6), 2.24 (2H, m, H_2-14), 2.32 (2H, m, H_2-13), 2.39, 2.57 (1H each, both m, H_2-5), 2.45 (1H, br s, H-11), 2.48 (1H, dd, J = 5.8, 13.5 Hz, Hα-9), 3.09 (1H, d-like, H-7), 4.22 (1H, br dd, J = *ca.* 6, 13 Hz, H-10), 4.77, 5.33 (1H each, both d, J = 10.7 Hz, H_2-15), 5.49 (1H, d, J = 10.4 Hz, H-2), 5.77 (1H, d, J = *ca.* 10 Hz, H-3), 7.10 (1H, dd, J = 4.8, 7.9 Hz, H-5'), 7.42 (2H, dd, J = 7.7, 8.4 Hz, H-3'", 5'"), 7.61 (1H, br t, J = *ca.* 8 Hz, H-4'"), 7.97 (1H, ddd, J = 1.2, 2.1, 7.9 Hz, H-6'), 8.04 (2H, dd, J = 1.7, 8.4 Hz, H-2'", 6'"), 8.59 (1H, br s, H-4'), 8.92 (1H, br s, H-2'). EI-MS (%): *m/z* 545 (M^+, 2), 423 (3), 300 (72), 121 (59), 105 (100).

2c: A white powder. High resolution EI-MS: Calcd for $C_{33}H_{39}NO_6$ (M^+): 545.2777. Found: 545.2772. ^{1}H NMR (CD_3OD): δ1.50, 1.65 1.86 (3H each, all s, H_3-17, 19, 20), 1.62 (1H, dd, J = 12.2, 13.2 Hz, Hβ-9), 1.72 (3H, d, J = 1.2 Hz, H_3-16), 1.76, 1.91 (1H each, both m, H_2-6), 2.27, 2.48 (1H, each, both m, H_2-14), 2.32 (2H, m, H_2-13), 2.47 (1H, dd, J = 5.5, 13.2 Hz, Hα-9), 2.48, 2.53 (1H each, both m, H_2-5), 2.60 (1H, br s, H-11), 3.08 (1H, br d, J = *ca.* 9 Hz, H-7), 4.04 (1H, d, J = 10.7 Hz, H-2), 4.97, 5.02 (1H each, both d, J = 11.3 Hz, H_2-15), 5.68 (1H, dd, J = 5.5, 11.0 Hz, H-10), 5.69 (1H, br d, J = *ca.* 11 Hz, H-3), 7.37 (2H, dd, J = 7.8, 8.5 Hz, H-3'", 5'"), 7.53 (1H, m, H-5"), 7.53 (1H, tt, J = 1.2, 7.8 Hz, H-4'"), 8.08 (2H, dd, J = 1.2, 8.5 Hz, H-2'", 6'"), 8.38 (1H, ddd, J = 1.9, 2.2, 8.0 Hz, H-6"), 8.71 (1H, br s, H-4"), 9.11 (1H, br s, H-2"). EI-MS (%): *m/z* 545 (M^+, 2), 527 (M^+–H_2O, 1), 423 (29), 300 (45), 121 (100), 105 (95).

2d: A white powder. High resolution EI-MS: Calcd for $C_{26}H_{35}NO_5$ (M^+): 441.2515. Found: 441.2520. ^{1}H NMR (CD_3OD): δ1.42 (1H, dd, J = 13.1, 15.3 Hz, Hβ-9), 1.45, 1.63, 1.82 (3H

each, all s, H_3-17, 19, 20), 1.67 (3H, d, J = 1.2 Hz, H_3-16), 1.75, 1.88 (1H each, both m, H_2-6), 1.99, 2.23 (1H, each, both m, H_2-14), 2.34 (2H, m, H_2-13), 2.34, 2.63 (1H each, both m, H_2-5), 2.45 (1H, dd-like, Hα-9), 2.48 (1H, br s, H-11), 3.06 (1H, br d, J = *ca.* 9 Hz, H-7), 3.97, 4.06 (1H each, both d, J = 10.7 Hz, H_2-15), 4.49 (1H, d, J = 10.4 Hz, H-2), 5.58 (1H, dd, J = 5.8, 13.5 Hz, H-10), 5.67 (1H, br d, J = *ca.* 10 Hz, H-3), 7.60 (1H, m, H-5''), 8.38 (1H, br d, J = *ca.* 8 Hz, H-6''), 8.79 (1H, br s, H-4''), 9.13 (1H, br s, H-2''). EI-MS (%): *m/z* 441 (M^+, 1), 423 (M^+–H_2O, 6), 300 (25), 121 (100).

2e: A white powder. High resolution positive-ion FAB-MS: Calcd for $C_{27}H_{37}O_5$ $(M+H)^+$: 441.2641. Found: 441.2642. ^{1}H NMR (CD_3OD): δ 1.37, 1.73, 1.77 (3H each, all s, H_3-17, 19, 20), 1.66 (3H, d, J = 1.2 Hz, H_3-16), 2.52 (1H, br s, H-11), 3.03 (1H, br d, J = *ca.* 10 Hz, H-7), 3.98 (1H, d, J = 10.3 Hz, H-2), 4.14 (1H, m, H-10), 4.70, 4.98 (1H each, both d, J = 10.7 Hz, H_2-15), 5.59 (1H, br d, J = *ca.* 10 Hz, H-3), 7.46 (2H, dd, J = 7.8, 8.2 Hz, H-3''',5'''), 7.58 (1H, t-like, H-4'''), 8.07 (2H, dd, J = 1.2, 8.2 Hz, H-2''',6'''). Positive-ion FAB-MS: *m/z* 441 $(M+H)^+$.

Triphenylphosphine (PPh_3) Reduction of Nigellamines B_1 (3) and B_2 (4). A solution of **3** (20.0 mg) or **4** (15.0 mg) in CH_2Cl_2 (1.0 mL) was treated with PPh_3 (20.0 mg), and the mixture was stirred at 0 °C for 30 min. Removal of the solvent from the filtrate under reduced pressure furnished a residue, which was purified by HPLC [detection: RI, column: YMC-Pack ODS-5-A, 250×20 mm i.d., mobile phase: MeOH–H_2O (80:20 or 75:25, v/v)] to give **3a** (13.2 mg, 68% from **3**) or **4a** (9.4 mg, 64% from **4**), respectively.

3a: A white powder, $[\alpha]^{24}_D$ +22.8° (c=0.20, $CHCl_3$). High resolution EI-MS: Calcd for $C_{40}H_{43}NO_8$ (M^+): 665.2988. Found: 665.2995. CD (MeOH, $\Delta\varepsilon$): +8.01 (216 nm), –1.54 (236 nm). UV (MeOH, log ε): 226 (4.52), 264 (3.68) nm. IR (KBr): 3517, 1717, 1647, 1636, 1592, 1453, 1279, 1115, 1026, 941, 756, 712 cm^{-1}. ^{13}C NMR ($CDCl_3$): δ_C 54.6 (C-1), 73.3 (C-2), 122.6 (C-3), 141.1 (C-4), 38.1 (C-5), 23.0 (C-6), 66.8 (C-7), 59.0 (C-8), 41.4 (C-9), 73.9 (C-10), 52.0 (C-11), 149.0 (C-12), 125.2 (C-13), 38.2 (C-14), 66.2 (C-15), 17.4 (C-16), 17.1 (C-17), 71.5 (C-18), 32.1 (C-19), 32.5 (C-20), 129.8 (C-1'), 129.4 (C-2',6'), 127.9 (C-3',5'), 132.5 (C-4'), 166.2 (C-7'), 125.5 (C-1''), 150.7 (C-2''), 153.5 (C-4''), 123.3 (C-5''), 137.0 (C-6''), 164.9 (C-7''), 130.0 (C-1'''), 129.9 (C-2''',6'''), 128.2 (C-3''',5'''), 132.9 (C-4'''), 166.3 (C-7'''). EI-MS (%): *m/z* 665 (M^+, 13), 122 (100).

4a: A white powder, $[\alpha]^{26}_D$ +22.8° (c=0.40, $CHCl_3$). High resolution Positive-ion FAB-MS: Calcd for $C_{39}H_{43}N_2O_8$ $(M+H)^+$: 667.3019. Found: 667.3022. CD (MeOH, $\Delta\varepsilon$): +7.37 (221 nm), –0.41 (256 nm). UV (MeOH, log ε): 222 (4.58), 264 (3.94) nm. IR (KBr): 3415, 1717, 1647, 1636, 1592, 1456, 1283, 1113, 1026, 745, 714 cm^{-1}. ^{13}C NMR ($CDCl_3$): δ_C 54.8 (C-1), 74.1 (C-2), 122.4 (C-3), 141.9 (C-4), 38.2 (C-5), 23.0 (C-6), 66.9 (C-7), 59.1 (C-8), 41.5 (C-9), 74.0 (C-10), 52.1 (C-11), 149.5 (C-12), 125.2 (C-13), 38.3 (C-14), 66.2 (C-15), 17.4 (C-16), 17.1 (C-17), 71.6 (C-18), 32.2 (C-19), 32.7 (C-20), 126.0 (C-1'), 150.9 (C-2'), 153.2 (C-4'), 122.9 (C-5'), 136.9 (C-6'), 165.2 (C-7'), 125.6 (C-1''), 150.9 (C-2''), 153.6 (C-4''), 123.8 (C-5''), 137.3 (C-6''), 165.1 (C-7''), 130.1 (C-1'''), 129.9 (C-2''',6'''), 128.6 (C-3''',5'''), 133.3 (C-4'''). Positive-ion FAB-MS: *m/z* 667 $(M+H)^+$.

Treatment of 3a with 0.1% NaOMe–MeOH. A solution of **3a** (5.0 mg) in 0.1% NaOMe–MeOH (2.0 mL) was stirred at room temperature for 8 h. From the reaction mixture, methyl nicotinate and methyl benzoate were identified by HPLC analyses and **3b** (1.9 mg, 72%) was purified by the similar procedure.

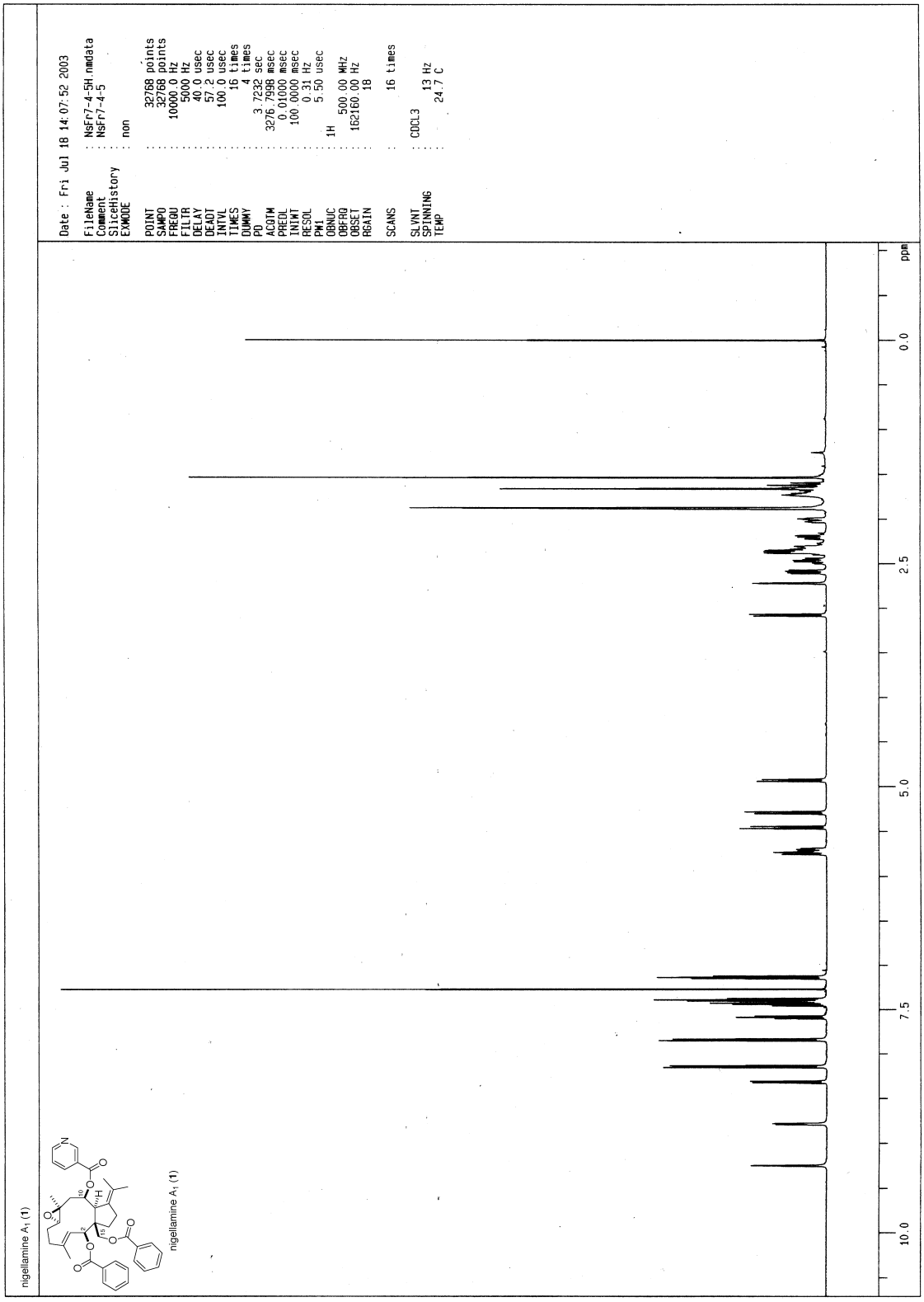
On the other hand, a solution of **3a** (8.0 mg) in 0.1% NaOMe–MeOH (2.0 mL) was stirred at 0°C for 3.5 h. The reaction mixture was poured into ice-water and the whole was extracted with EtOAc. The EtOAc extract was successively washed with brine then dried over $MgSO_4$ powder and filtrated. Evaporation of the solvent from the filtrate under reduced pressure furnished a residue, which was purified by HPLC [detection: RI, column: YMC-Pack ODS-5-A, 250×20 mm i.d., mobile phase: MeOH–H_2O (80:20, v/v)] to give **3c** (2.3 mg, 42%) and 10-desacyl derivative (**3d**, 2.5 mg, 37%).

3b: A white powder, $[\alpha]^{24}_D$ +35.6° (*c*=0.10, MeOH). High resolution EI-MS: Calcd for $C_{20}H_{30}O_4$ (M^+–H_2O): 334.2144. Found: 334.2140. IR (KBr): 3346, 1653, 1559, 1507, 1387, 1262, 1120, 1044, 938, 756, 718 cm^{-1}. ^{13}C NMR ($CDCl_3$): δ_C 56.3 (C-1), 72.3 (C-2), 127.6 (C-3), 137.3 (C-4), 38.1 (C-5), 23.0 (C-6), 66.6 (C-7), 59.5 (C-8), 43.3 (C-9), 70.1 (C-10), 52.4 (C-11), 149.1 (C-12), 126.2 (C-13), 36.4 (C-14), 63.6 (C-15), 16.8 (C-16), 17.5 (C-17), 71.6 (C-18), 33.0 (C-19), 33.2 (C-20). EI-MS (%): *m/z* 334 (M^+–H_2O, 1), 120 (100).

3c: A white powder, $[\alpha]^{24}_D$ +32.9° (*c*=0.20, $CHCl_3$). High resolution positive-ion CI-MS: Calcd for $C_{27}H_{37}O_6$ $(M+H)^+$: 457.2590. Found: 457.2587. UV (MeOH, log ε): 230 (3.93), 273 (2.84) nm. IR (KBr): 3368, 1717, 1636, 1601, 1584, 1453, 1279, 1098, 1026, 938, 756, 714 cm^{-1}. ^{13}C NMR ($CDCl_3$): δ_C 56.6 (C-1), 74.5 (C-2), 122.8 (C-3), 140.0 (C-4), 38.0 (C-5), 23.0 (C-6), 66.8 (C-7), 59.4 (C-8), 43.1 (C-9), 70.2 (C-10), 52.4 (C-11), 148.5 (C-12), 126.3 (C-13), 34.7 (C-14), 61.1 (C-15), 16.8 (C-16), 17.7 (C-17), 71.6 (C-18), 32.7 (C-19), 33.1 (C-20), 130.2 (C-1'), 129.6 (C-2',6'), 128.5 (C-3',5'), 133.1 (C-4'), 166.0 (C-7'). Positive-ion CI-MS: *m/z* 457 $(M+H)^+$.

3d: A white powder, $[\alpha]^{24}_D$ +18.2° (*c*=0.20, $CHCl_3$). High resolution positive-ion CI-MS: Calcd for $C_{34}H_{41}O_7$ $(M+H)^+$: 561.2852. Found: 561.2869. UV (MeOH, log ε): 228 (4.11), 274 (3.03) nm. IR (KBr): 3517, 1717, 1647, 1603, 1559, 1451, 1283, 1117, 1026, 941, 756, 712 cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.38, 1.54, 1.56 (3H each, all s, H_3-17, 19, 20), 1.62 (1H, m, Hβ-9), 1.66 (1H, m, Hα-6), 1.89 (3H, d, *J* = 0.9 Hz, H_3-16), 1.96 (1H, m, Hβ-6), 2.32 (1H, m, Hα-5), 2.41 (1H, dd, *J* = 5.5, 13.5 Hz, Hα-9), 2.44 (1H, ddd, *J* = 4.9, 12.5, 12.5 Hz, Hβ-5), 2.64 (1H, dd, *J* = 3.1, 17.7 Hz, Hα-14), 2.73 (1H, br d, *J* = *ca.* 18 Hz, Hβ-14), 2.75 (1H, br s, H-11), 2.95 (1H, br d, *J* = *ca.* 10 Hz, H-7), 4.62 (1H, br dd, *J* = *ca.* 6, 13 Hz, H-10), 4.87, 5.29 (1H each, both d, *J* = 11.0 Hz, H_2-15), 5.46 (1H, d, *J* = 10.4 Hz, H-2), 5.67 (1H, dd, *J* = 0.9, 10.4 Hz, H-3), 5.73 (1H, br s, H-13), 7.12 (2H, dd, *J* = 7.7, 8.3 Hz, H-3',5'), 7.42 (1H, tt, *J* = 1.3, 7.7 Hz, H-4'), 7.43 (2H, dd, *J* = 7.7, 8.3 Hz, H-3''',5'''), 7.58 (1H, tt, *J* = 1.3, 7.7 Hz, H-4'''), 7.82 (2H, dd, *J* = 1.3, 8.3 Hz, H-2',6'), 8.07 (2H, dd, *J* = 1.3, 8.3 Hz, H-2''',6'''). ^{13}C NMR ($CDCl_3$): δ_C 54.3 (C-1), 73.9 (C-2), 123.1 (C-3), 140.6 (C-4), 38.1 (C-5), 22.9 (C-6), 66.6 (C-7), 59.4 (C-8), 43.8 (C-9), 70.0 (C-10), 53.2 (C-11), 149.6 (C-12), 125.5 (C-13), 37.9 (C-14), 65.7 (C-15), 17.0 (C-16), 17.5 (C-17), 71.7 (C-18), 33.1 (C-19), 33.2 (C-20), 130.1 (C-1'), 129.6 (C-2',6'), 128.1 (C-3',5'), 132.8 (C-4'), 166.4 (C-7'), 130.4 (C-1'''), 129.8 (C-2''',6'''), 128.5 (C-3''',5'''), 133.0 (C-4'''), 166.4 (C-7'''). Positive-ion CI-MS: *m/z* 561 $(M+H)^+$.

Treatment of 4a with 0.1% NaOMe–MeOH. A solution of **4a** (6.0 mg) in 0.1% NaOMe–MeOH (2.0 mL) was stirred at room temperature for 8 h. From the reaction mixture, methyl nicotinate and methyl benzoate were identified by HPLC analyses and **3b** (2.1 mg, 66%) was purified by the similar procedure.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nigellamine A1 (1)
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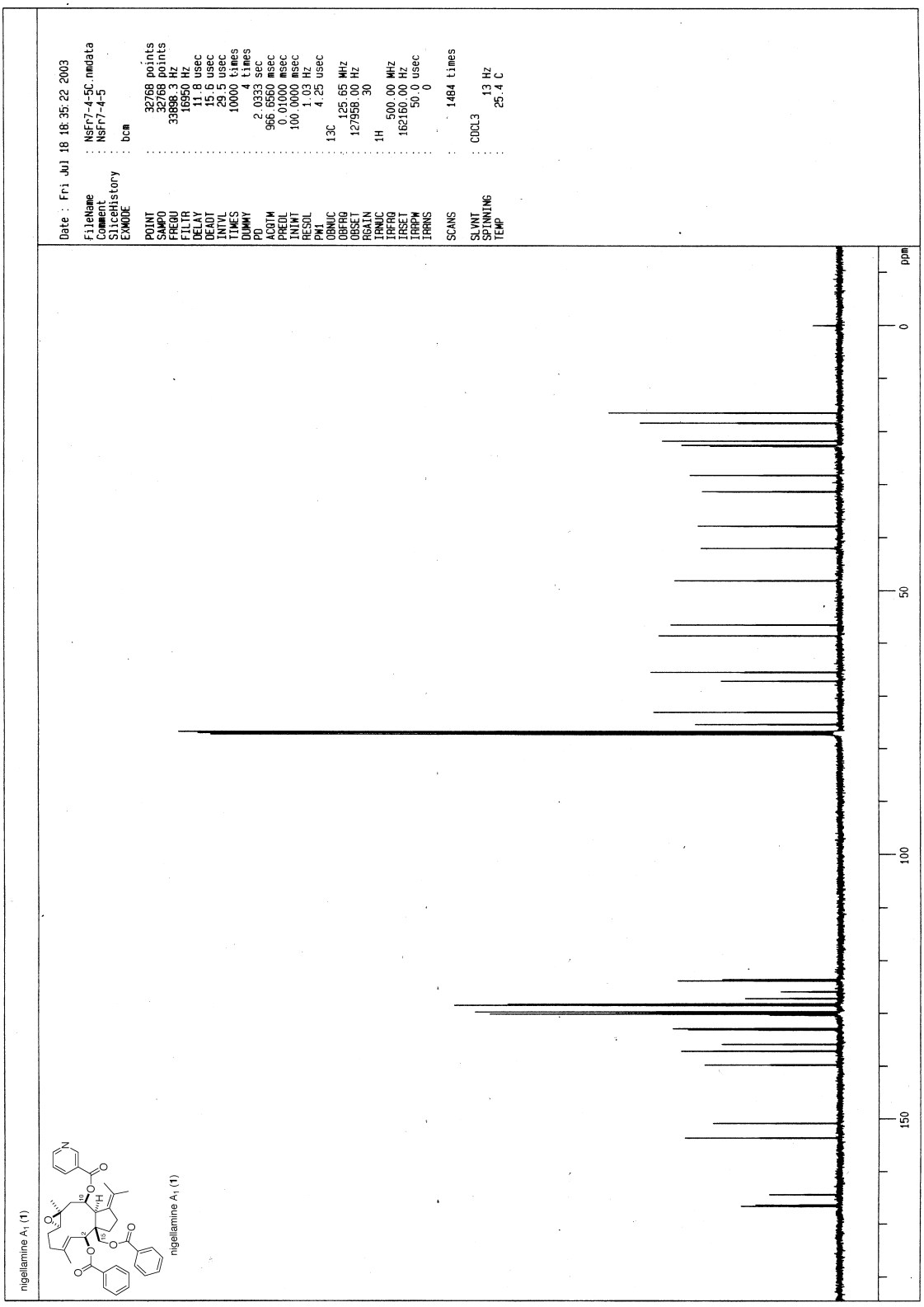
DEADT : 57.2 usec
INTVL : 100.0 usec
TIMES : 16 times
DUMMY : 4 times
PD : 3.7232 sec
ACQTM : 3276.7998 msec
PREDL : 0.01000 msec
INTWT : 100.0000 msec
RESOL : 0.31 Hz
PW1 : 5.50 usec
OBNUC : 1H
OBFRQ : 500.00 MHz
OBSET : 162160.00 Hz
RGAIN : 18
SCANS : 16 times
SLVNT : CDCL3
SPINNING : 13 Hz
TEMP : 24.7 C
10.0
7.5
5.0
2.5
0.0
ppm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SliceHistory :
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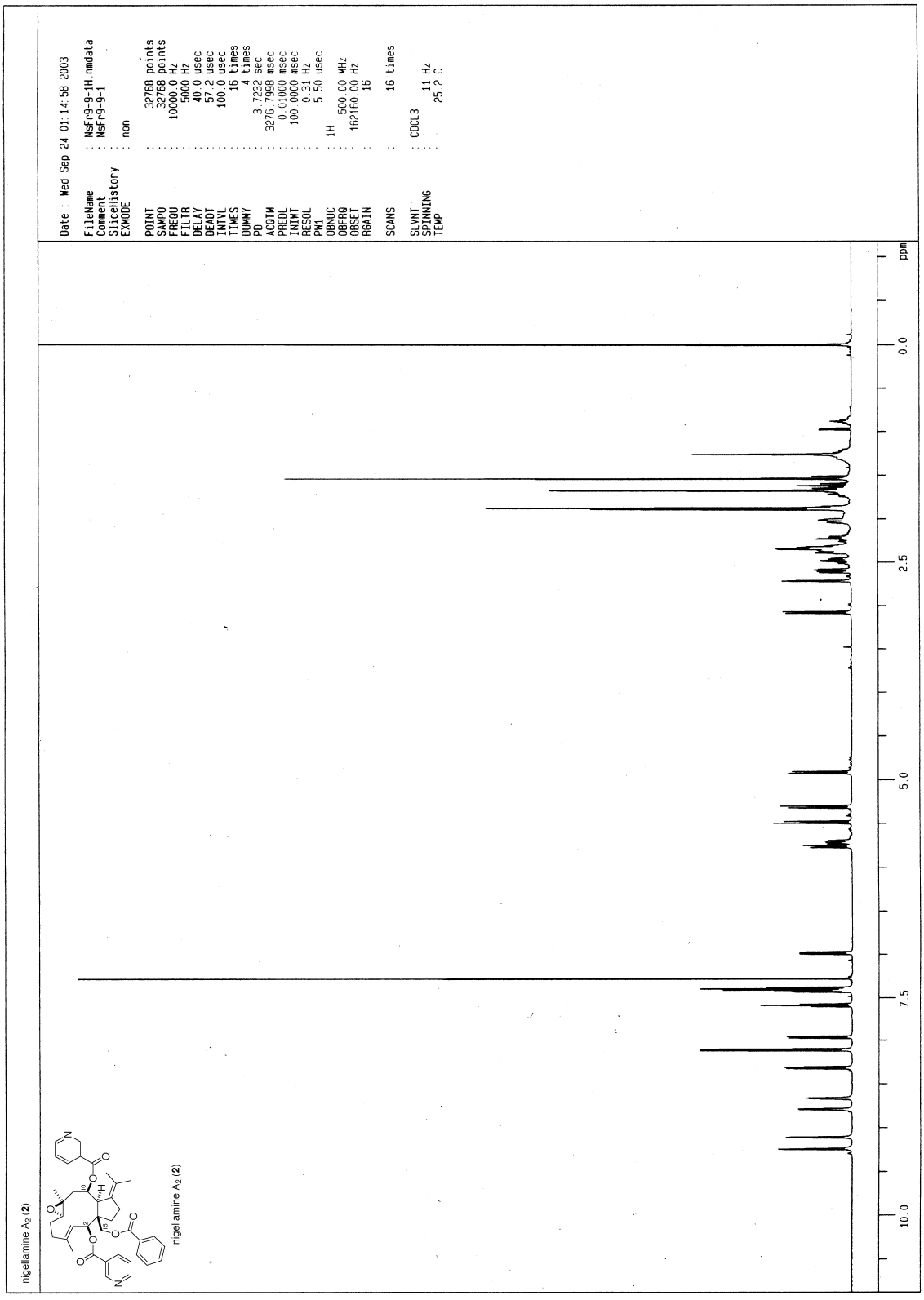
SAMPO : 32768 points
FREQU : 33898.3 Hz
FILTR : 16950 Hz
DELAY : 11.8 usec
DEADT : 15.6 usec
INTVL : 29.5 usec
TIMES : 10000 times
DUMMY : 4 times
PD : 2.0333 sec
ACQTM : 966.6560 msec
PREDL : 0.01000 msec
INIMT : 100.0000 msec
RESOL : 1.03 Hz
PW1 : 4.25 usec
OBNUC : 13C
OBFRQ : 125.65 MHz
OBSET : 127958.00 Hz
OBFIN : 30
IRNUC : 1H
IRFRQ : 500.00 MHz
IRSET : 162160.00 Hz
IRPPM : 50.0 usec
IRRNS : 0
SCANS : 1484 times
SLVNT : CDCL3
SPINNING : 13 Hz
TEMP : 25.4 C
nigellamine A1 (1)
150
100
50
0
ppm


nigellamine A2 (2)
Date : Wed Sep 24 01:14:58 2003
FileName : NsFr9-9-1H.nmdata
Comment : NsFr9-9-1
SliceHistory :
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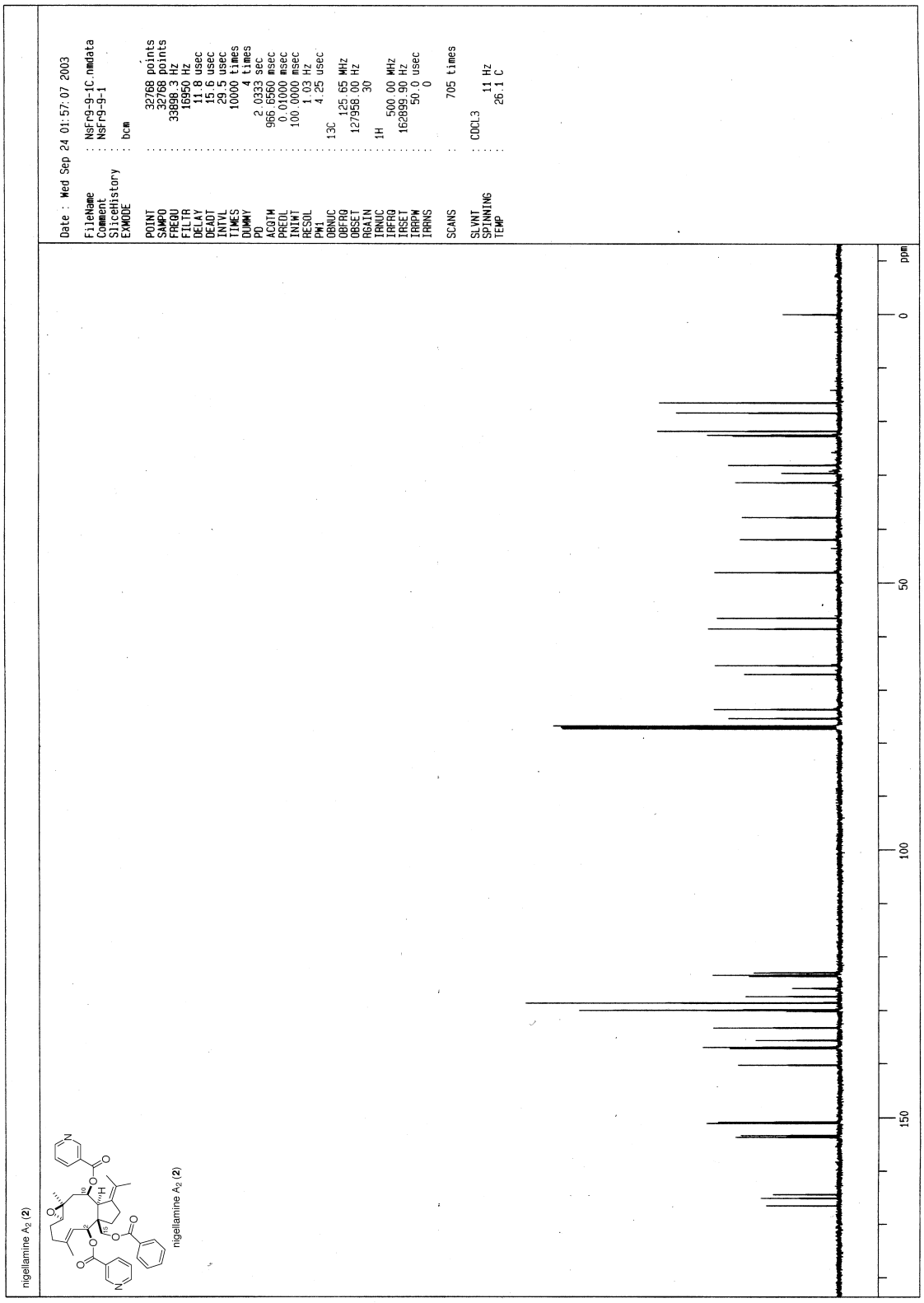
DEADT : 57.2 usec
INTVL : 100.0 usec
TIMES : 16 times
DUMMY : 4 times
PD : 3.7232 sec
ACQTM : 3276.7998 msec
PREDL : 0.01000 msec
ININT : 100.0000 msec
RESOL : 0.31 Hz
PW1 : 5.50 usec
OBNUC : 1H
OBFRQ : 500.00 MHz
OBSET : 16216.00 Hz
AGAIN : 16
SCANS : 16 times
SLVNT : CDCl3
SPINNING : 11 Hz
TEMP : 25.2 C
nigellamine A2 (2)
10.0
7.5
5.0
2.5
0.0
ppm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Comment : NsFr9-9-1
SliceHistory :
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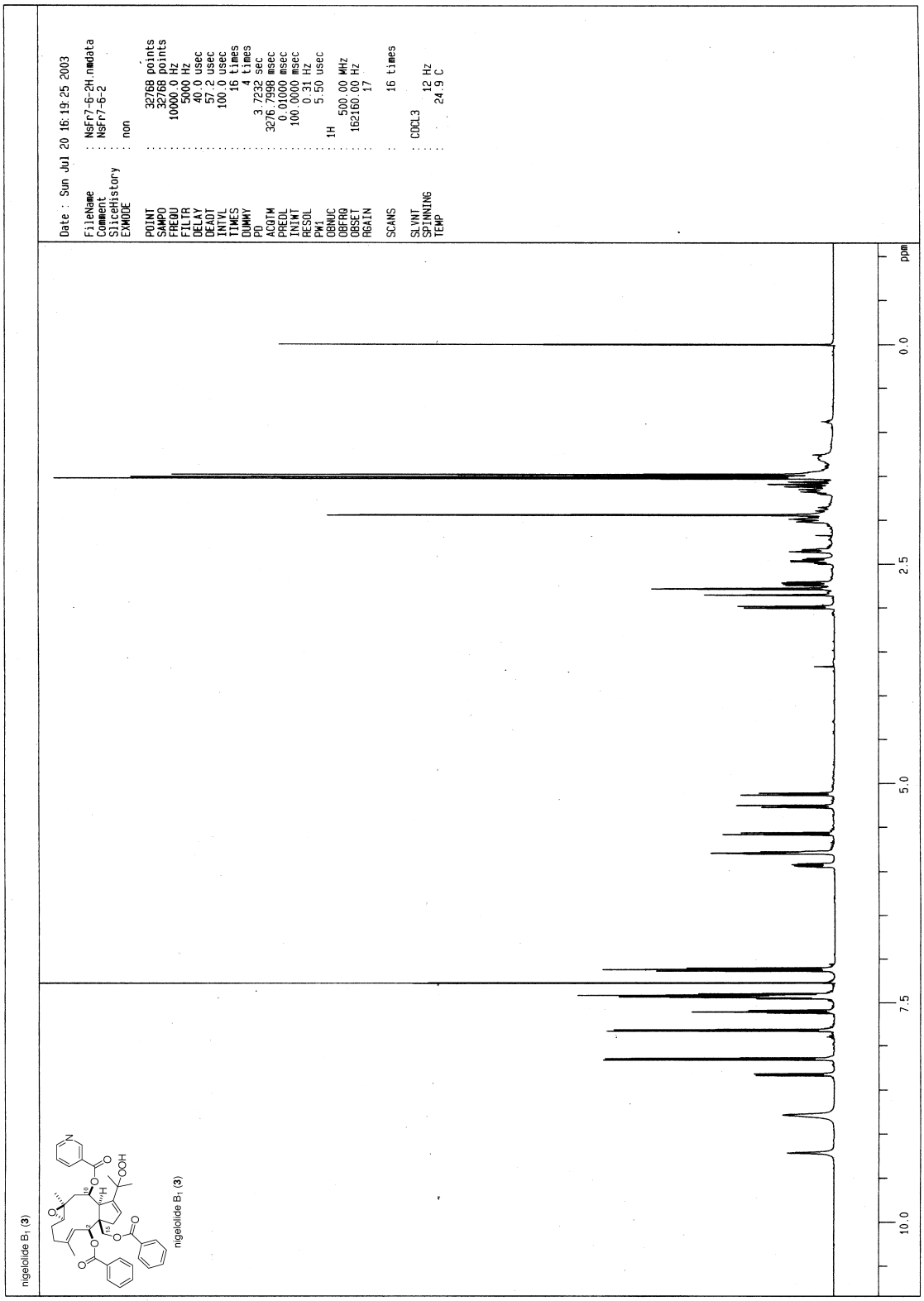
POINT : 32768 points
SAMPO : 32768 points
FREQU : 33898.3 Hz
FILTR : 16950 Hz
DELAY : 11.8 usec
DEADT : 15.6 usec
INTVL : 29.5 usec
TIMES : 10000 times
DUMMY : 4 times
PD : 2.0333 sec
ACQTM : 966.6560 msec
PREDL : 0.01000 msec
INIWT : 100.0000 msec
RESOL : 1.03 Hz
PW1 : 4.25 usec
OBNUC : 13C
OBFRQ : 125.65 MHz
OBSET : 127958.00 Hz
OBATN : 30
IRNUC : 1H
IRFRQ : 500.00 MHz
IRSET : 162899.90 Hz
IRPPW : 50.0 usec
IRPNS : 0
SCANS : 705 times
SLVNT : CDCL3
SPINNING : 11 Hz
TEMP : 26.1 C
150
100
50
0
ppm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FileName : NsFr7-6-2H.nmdata
Comment : NsFr7-6-2
SliceHistory : :
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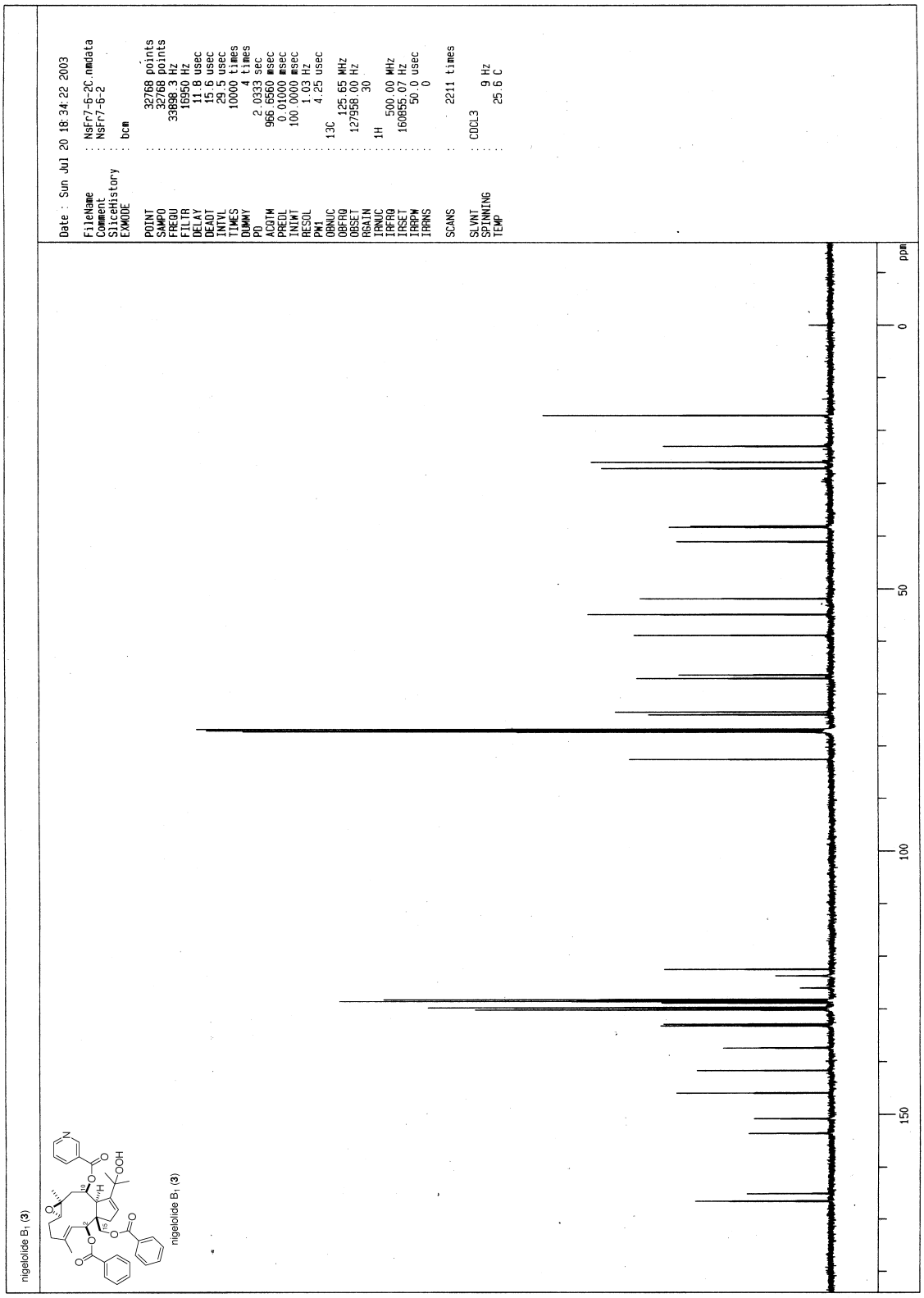
POINT : 32768 points
SAMPO : 32768 points
FREQU : 10000.0 Hz
FILTR : 5000 Hz
DELAY : 40.0 usec
DEADT : 57.2 usec
INTVL : 100.0 usec
TIMES : 16 times
DUMMY : 4 times
PD : 3.7232 sec
ACQTM : 3276.7998 msec
PREDL : 0.01000 msec
INIWT : 100.0000 msec
RESOL : 0.31 Hz
PW1 : 5.50 usec
OBNUC : 1H 500.00 MHz
OBFRQ : 162160.00 Hz
OBSET : 17
AGAIN :
SCANS : 16 times
SLVNT : CDCL3
SPINNING : 12 Hz
TEMP : 24.9 C
nigelolide B1 (3)
10.0
7.5
5.0
2.5
0.0
ppm


nigeloilde B1 (3)
nigeloilde B1 (3)
Date : Sun Jul 20 18:34:22 2003
FileName : NsFr7-6-2C.nmdata
Comment : NsFr7-6-2
SliceHistory :
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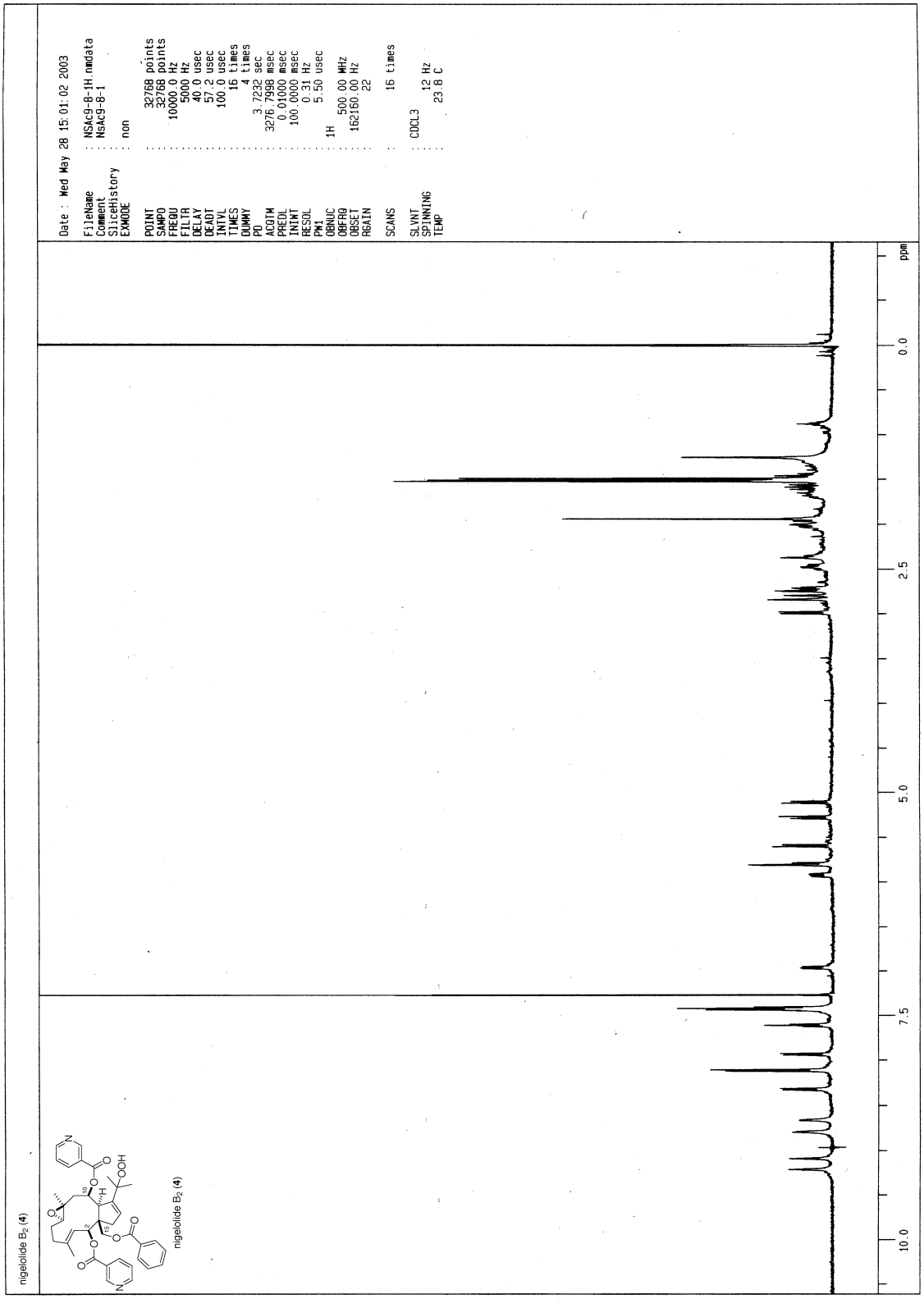
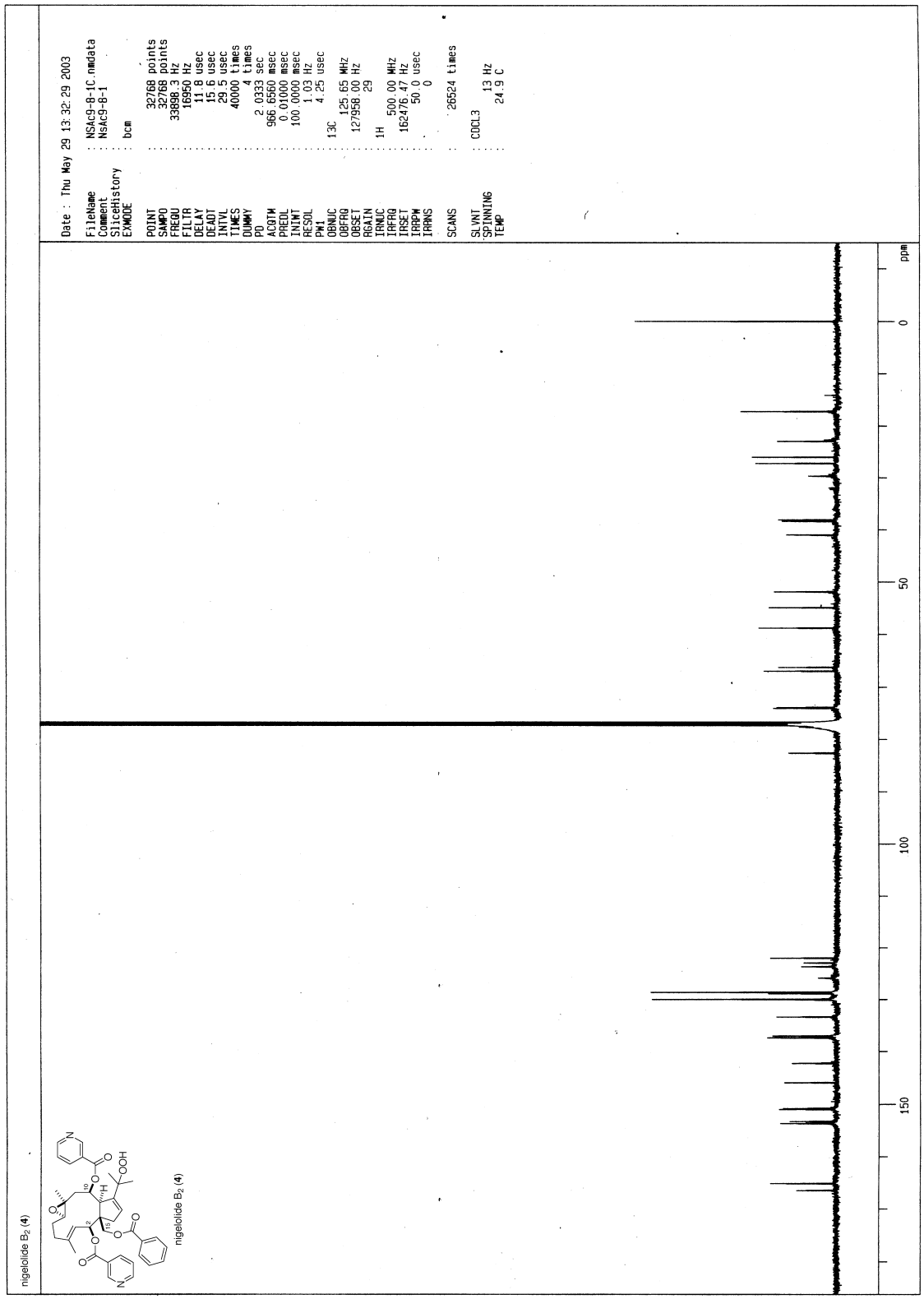
POINT 32768 points
SAMPO 32768 points
FREQU 33898.3 Hz
FILTR 16950 Hz
DELAY 11.8 usec
DEADT 15.6 usec
INTYL 29.5 usec
TIMES 10000 times
DUMMY 4 times
PD 2.0333 sec
ACQTM 966.6560 msec
PREDL 0.01000 msec
INIWT 100.0000 msec
RESOL 1.03 Hz
PW1 4.25 usec
OBNUC 13C
OBFRQ 125.65 MHz
OBSET 12795B.00 Hz
AGAIN 30
IRNUC 1H
IRFRQ 500.00 MHz
IRSET 160855.07 Hz
IRAPM 50.0 usec
IRANS 0
SCANS 2211 times
SLVNT CDCL3
SPINNING 9 Hz
TEMP 25.6 C
ppm
0
50
100
150


nigelolide B2 (4)
nigelolide B2 (4)
Date : Wed May 28 15:01:02 2003
FileName : NSAc9-B-1H.nmdata
Comment : NSAc9-B-1
SliceHistory :
EXMODE : non
POINT : 32768 points
SAMPO : 32768 points
FREQU : 10000.0 Hz
FILTR : 5000 Hz
DELAY : 40.0 usec
DEADT : 57.2 usec
INTVL : 100.0 usec
TIMES : 16 times
DUMMY : 4 times
PD : 3.7232 sec
ACQTM : 3276.7998 msec
PREDL : 0.01000 msec
INTWT : 100.0000 msec
RESOL : 0.31 Hz
PW1 : 5.50 usec
OBNUC : 1H 500.00 MHz
OBFRQ : 162160.00 Hz
OBSET : 22
AGAIN :
SCANS : 16 times
SLVNT : CDCL3
SPINNING : 12 Hz
TEMP : 23.8 C
10.0
7.5
5.0
2.5
0.0
ppm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Date : Thu May 29 13:32:29 2003
FileName : NSAc9-8-1C.nmdata
Comment : NSAc9-8-1
SiteHistory :
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SAMPO : 32768 points
FREQU : 33898.3 Hz
FILTR : 16950 Hz
DELAY : 11.8 usec
DEADT : 15.6 usec
INTVL : 29.5 usec
TIMES : 40000 times
DUMMY : 4 times
PD : 2.0333 sec
ACQTM : 966.6560 msec
PREDL : 0.01000 msec
INIMT : 100.0000 msec
RESOL : 1.03 Hz
PW1 : 4.25 usec
OBNUC : 13C
OBFRQ : 125.65 MHz
OBSET : 127958.00 Hz
AQAIN : 29
IRNUC : 1H
IRFRQ : 500.00 MHz
IRSET : 162476.47 Hz
IRPPM : 50.0 usec
IRPNS : 0
SCANS : 26524 times
SLVNT : CDCl3
SPINNING : 13 Hz
TEMP : 24.9 C
nigelolide B2 (4)
150
100
50
0
ppm