Supporting Information

Expedient entry to the piperazinohydroisoquinoline ring system using a sequential Ugi/Pictet-Spengler/reductive methylation reaction protocol.

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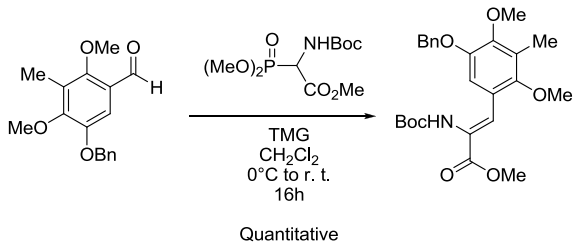
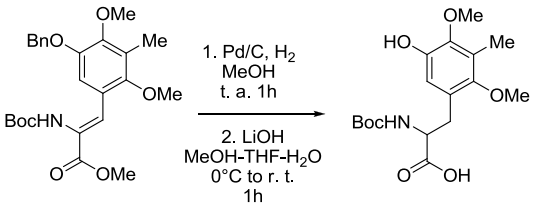
Experimental Methods

General. All reagents and solvents were obtained from Aldrich and Fluka. Methanol was distilled from magnesium/iodide, Melting points were determined on a Fisher apparatus and are uncorrected. Reaction progress was monitored by analytical thin layer chromatography using GF silica plates purchased from Merck. Visualization was achieved by short-wave UV light (254 nm). ^{1}H and ^{13}C NMR spectra were recorded on both a Varian Gemini-200 and JEOL Eclipse-300 model spectrometers using $CDCl_3$ as solvent. Chemical shifts are reported as parts per million downfield from an internal tetramethylsilane standard ($\delta = 0.0$ for ^{1}H) or from solvent references. NMR coupling constants are reported in hertz (Hz). IR spectra were obtained with a Nicolet Magna 750 FT-IR spectrometer. Low- and high-resolution electron impact mass spectra were obtained on JEOL JMS-AX505HA spectrometer.



Quantitative

Dehydroamino ester. To a mixture of aldehyde (82.3 mg, 0.2874 mmol, 1.0 equiv) and phosphonate (102.54 mg, 0.3450 mmol, 1.2 equiv) in CH_2Cl_2 anhydrous (1.4 mL) at 10ºC was added N, N, N', N'-tetramethylguanidine (0.054 mL, 0.4311 mmol, 1.5 equiv), and the mixture was allowed to warm to room temperature and stirred for 24 h. The reaction mixture was sequentially washer with 10% aqueous citric acid and saturated aqueous $NaHCO_3$, and the organic layer was dried over anhydrous $NaSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (10% EtOAc in n-hexane) to afford the dehydroamino ester (99%) as a white solid, Mp: 63-70°C.**^{1}HNMR** (300 MHz, $CDCl_3$) δ (ppm) 7.46-7.29 (m, 5H), 7.21 (s, 1H), 6.99 (s, 1H), 6.87 (bs, 1H), 5.04 (s, 2H), 3.86 (s, 3H), 3.85 (s, 3H), 3.65 (s, 3H), 2.23 (s, 3H), 1.42 (s, 9H). **^{13}CNMR** (75.4 MHz, $CDCl_3$) δ (ppm) 166.2, 152.9, 151.3, 149.4, 148.2, 136.8, 128.5, 127.9, 127.3, 126.1, 125.9, 122.8, 122.1, 111.9, 80.7, 70.9, 61.5, 60.3, 52.4, 28.1, 9.5. **IR** γ (cm^{-1}) 700, 737, 848, 1007, 1074, 1121, 1162, 1231, 1255, 1338, 1367, 1454, 1483, 1591, 1640, 1720, 2936, 2978, 3321. **HRMS (IE, M+)** calcd for **$C_{25}H_{31}NO_7$**: 457.2101, found: 457.2101.



82% (two steps)

Aminoacid 10b. To a solution of dehydroamino ester (37 mg, 0.0809 mmol, 1equiv) in MeOH (0.5 mL) was added Pd on carbon (5% w/w, 51.68 mg) at room temperature. The resulting mixture was stirred under a hydrogen atmosphere for one hour. After stirring one hour, the resulting mixture was filtered through a pad of celite and washed with AcOEt. Then the filtrate was concentrated under vacuum to give the ester. The crude product obtained was used without further purification. To a solution of ester in a mixture of MeOH (0.6 mL), H_2O (0.1 mL), THF (0.1 mL) at 0°C was added lithium hydroxide (5.8 mg, 0.2427 mmol, 3 equiv), and the mixture was allowed to warm to room temperature. The reaction mixture was concentrated under reduced pressure, and to the resulting residue was added 10% aqueous citric acid, and the resulting suspension was extracted with AcOEt. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous $NaSO_4$, and concentrated under reduced pressure to afford the amino acid **10b** (82%, two steps) as a pale yellow solid, Mp: 57-60°C.**^{1}HNMR** (200 MHz, $CDCl_3$) δ (ppm) 6.63 (s, 1H), 5.57 (bd, J= 5.8 Hz, 1H), 4.41 (dd, J=6.4 Hz, J= 8.0 Hz, J= 12.8 Hz 1H), 3.78 (s, 3H), 3.68 (s, 3H), 3.15-2.98 (m, 2H), 2.22 (s, 3H), 1.39 (s, 9H). **^{13}CNMR** (50.2 MHz, $CDCl_3$) δ (ppm) 176.1, 156.1, 150.3, 145.4, 145.1, 125.1, 124.6, 114.4, 80.3, 60.7, 60.5, 54.9, 31.8, 28.2, 9.9. **IR** γ (cm^{-1}) 756, 839, 1009, 1051, 1111, 1168, 1249, 1367, 1418, 1454, 1485, 1506, 1593, 1693, 2935, 2977, 3359. **HRMS (IE, M+)** calcd for **$C_{17}H_{25}NO_7$**: 355.1631, found: 355.1636.

*General procedure for the synthesis of Ugi adducts **15a-g***. To a mixture of aminoacetaldehyde dimethylacetal **9** (41.73 mg, 0.3969 mmol, 1.2 equiv), (-)-(S)-N-Boc phenyl glycine **10** (129.15 mg, 0.3969 mmol, 1.2 equiv), and *t*-butyl isocyanide **11** (0.037 mL, 0.3308 mmol, 1 equiv) in MeOH anhydrous (1.1 mL) at room temperature was added the aldehyde **8** (1 equiv), and the resulting solution was heated at 50°C for 1-2 h using microwave irradiation. The reaction mixture was concentrated under reduced pressure, and the resulting syrup was purified by flash column chromatography.

N-(*tert*-butoxycarbonyl)-3-methoxy-O-methyltyrosyl-N^1-(*tert*-butyl)-N^2-(2, 2-dimethoxyethyl)glycinamide 15a. This residue was purified by flash chromatography

(6:4 hexane/EtOAc) to give **15a (51%)** as a white solid, Mp: 66-68°C.**^{1}HNMR** (300 MHz, $CDCl_3$) δ (ppm) 6.81-6.72 (m, 6H), 6.50 (bs, 1H), 6.20 (bs, 1H), 5.09 (bs, 1H), 5.11 (bs, 1H), 4.81 (dd, J=7.2 Hz, J= 15 Hz, 1H), 4.53 (dd, J=7.2 Hz, J= 15 Hz, 1H), 4.50 (dd, J= 5.1 Hz, J= 10.2 Hz, 1H), 4.25 (dd, J= 4.5 Hz, J= 9 Hz, 1H), 3.86 (s, 6H), 3.85 (s, 6H), 3.81-3.75 (m, 4H), 3.62-3.44 (m, 4H), 3.38 (s, 3H), 3.36 (s, 3H), 3.34 (s, 3H), 3.33 (s, 3H), 3.06-2.79 (m, 4H), 1.39 (s, 18H), 1.34 (s, 9H), 1.32 (s, 9H). **^{13}CNMR** (75.4 MHz, $CDCl_3$) δ (ppm) 173.6, 173.4, 167.6, 167.1, 155.1, 148.9, 148.1, 148.0, 129.0, 128.4, 121.4, 112.5, 111.3, 103.0, 102.4, 79.8, 55.8, 55.1, 54.7, 54.6, 54.2, 53.4, 53.0, 52.0, 51.6, 51.0, 49.5, 38.7, 38.5, 28.6, 28.5, 28.2. **IR** γ (cm^{-1}) 549, 761, 1028, 1066, 1129, 1165, 1237, 1264, 1365, 1458, 1517, 1656, 1698, 2836, 2936, 2970, 3339. **HRMS (FAB+, M+)** calcd for $C_{26}H_{43}N_3O_8$: [M+1] 525.3050, found: 525.3052.

N-(*tert*-butoxycarbonyl)-N-{1-[(*tert*-butylamino)carbonyl]propyl}-N-(2,2-dimethoxyethyl)-3-methoxy-O-methyltyrosinamide 15b. This residue was purified by flash chromatography (6:4 hexane/EtOAc) to give **15b (93%)** as a yellow oil.**^{1}HNMR** (300 MHz, $CDCl_3$) δ (ppm) 6.79-6.73 (m, 6H), 6.47 (bs, 1H), 6.45 (bs, 1H), 5.09-4.88 (m, 4H), 4.75-4.66 (m, 1H), 4.53 (dd, J=3.6 Hz, J= 6.6 Hz, 2H), 4.44-4.37 (m, 1H), 4.39 (t, J= 5.1 Hz, 1H), 4.13-4.08 (m, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.86 (s, 3H), 3.84 (s, 3H), 3.59 (dd, J=5.6 Hz, J= 6.6 Hz, 3H), 3.41 (s, 3H), 3.38 (s, 3H), 3.37 (s, 3H), 3.35 (s, 3H), 3.22 (dd, J=5.4 Hz, J= 15.9 Hz, 1H), 3.07-2.93 (m, 2H), 1.70 (m, 2H), 1.50 (m, 2H), 1.30 (s, 18H), 1.25 (s, 18H), 0.83 (t, J= 7.2 Hz, 3H), 0.77 (t, J= 7.2 Hz, 3H). **^{13}CNMR** (75.4 MHz, $CDCl_3$) δ (ppm) 174.9, 174.0, 169.5, 169.4, 154.9, 148.9, 147.9, 129.3, 129.2, 121.3, 112.6, 112.4, 111.4, 111.3, 103.2, 80.2, 79.5, 63.3, 61.6, 55.9, 55.8, 55.2, 54.9, 54.8, 52.0, 51.8, 50.9, 50.7, 48.7, 47.7, 38.9, 38.7, 28.6, 28.2, 21.3, 21.2, 10.8, 10.6. **IR** γ (cm^{-1}) 1029, 1069, 1127, 1165, 1240, 1263, 1365, 1456, 1516, 1640, 1680, 2835, 2935, 2970, 3332. **HRMS (FAB+, M+)** calcd for $C_{28}H_{47}N_3O_8$: [M+1] 554.3441, found: 554.34

N-(*tert*-butoxycarbonyl)-N-[2-(*tert*-butylamino)-2-oxo-1-phenylethyl]-N-(2,2-dimethoxyethyl)-3-methoxy-O-methyltyrosinamide 15c. This residue was purified by flash chromatography (7:3 hexane/EtOAc) to give **15c (82%)** as a white solid.**^{1}HNMR** (300 MHz, $CDCl_3$) δ (ppm) 7.35-7.28 (m, 10H), 6.81-6.69 (m, 6H), 6.14 (bs, 1H), 5.89 (bs, 1H), 5.65 (s, 1H), 5.62 (s, 1H), 5.17 (d, J= 9 Hz, 1H), 5.08 (d, J= 8.4 Hz, 1H), 4.99 (dd, J=7.5 Hz, J= 14.1 Hz, 2H), 3.95 (m, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.83 (s, 3H), 3.83 (s, 3H), 3.87-3.78 (m, 1H), 3.59 (dd, J=4.8 Hz, J= 15.9 Hz, 2H), 3.36 (d, J= 6 Hz, 1H), 3.29 (d, J= 7.2 Hz, 1H), 3.22 (s, 6H), 3.18 (s, 6H), 3.08-2.97 (m, 2H), 2.88-2.77

(m, 2H), 1.39 (s, 18H), 1.35 (s, 18H). **^{13}CNMR** (75.4 MHz, $CDCl_3$) δ (ppm) 174.4, 173.9, 168.2, 168.1, 155.2, 154.8, 148.9, 148.7, 147.9, 147.7, 135.4, 135.3, 129.6, 129.5, 129.2, 129.0, 128.6, 128.3, 128.2, 121.7, 121.4, 112.8, 112.5, 111.3, 111.2, 103.3, 79.5, 79.3, 64.7, 64.4, 58.8, 55.3, 55.1, 54.8, 54.7, 52.1, 51.9 51.4, 48.6, 38.7, 38.6, 28.6, 28.2. **IR** γ (cm^{-1}) 630, 810, 1029, 1074, 1128, 1166, 1261, 1366, 1454, 1516, 1641, 1686, 2836, 2935, 2971, 3350, 3427. **HRMS (FAB+, M+)** calcd for $C_{32}H_{47}N_3O_8$: [M+1] 602.3441, found: 602.3448.

N-(*tert*-butoxycarbonyl)-N-[2-(*tert*-butylamino)-1-(4-methoxyphenyl)-2-oxoethyl]-N-(2,2-dimethoxyethyl)-3-methoxy-O-methyltyrosinamide 15d. This residue was purified by flash chromatography (6:4 hexane/EtOAc) to give **15d (94%)** as a pale yellow solid.**^{1}HNMR** (300 MHz, $CDCl_3$) δ (ppm) 7.29 (d, J= 8.7 Hz, 2H), 7.19 (d, J= 8.4 Hz, 2H), 6.89-6.66 (m, 10H), 6.08 (bs, 1H), 5.82 (bs, 1H), 5.06 (s, 2H), 5.19 (d, J= 8.7 Hz, 1H), 5.09 (d, J= 8.1 Hz, 1H), 4.99 (dd, J=8.1 Hz, J= 14.4 Hz, 2H), 3.86 (s, 3H), 3.85 (s, 3H), 3.84 (s, 3H), 3.83 (s, 3H), 3.81 (s, 3H), 3.80 (s, 3H), 3.86-3.80 (m, 2H), 3.61-3.52 (m, 2H), 3.36 (d, J= 5.4 Hz, 1H), 3.31 (d, J= 3 Hz, 1H), 3.24 (s, 6H), 3.23 (s, 3H), 3.20 (s, 3H), 3.06-2.97 (m, 2H), 2.89-277 (m, 2H), 1.39 (s, 18H), 1.34 (s, 18H). **^{13}CNMR** (75.4 MHz, $CDCl_3$) δ (ppm) 174.3, 173.7, 168.5, 168.4, 159.6, 159.5, 155.3, 155.1, 148.8, 148.6, 147.8, 147.7, 131.1, 130.9, 129.4, 129.2, 127.2, 127.1, 121.6, 121.4, 114.0, 112.7, 112.4, 111.2, 103.2, 79.4, 79.2, 63.9, 63.6, 55.8, 55.2, 54.7, 54.6, 52.1, 51.9, 51.3, 48.3, 48.1, 38.8, 38.7, 28.6, 28.2. **IR** γ (cm^{-1}) 757, 809, 975, 1031, 1175, 1255, 1366, 1457, 1514, 1637, 1684, 2837, 2934, 2967, 3344. **HRMS (FAB+, M+)** calcd for $C_{33}H_{49}N_3O_9$: [M+1] 632.3547, found: 632.3535.

N-(*tert*-butoxycarbonyl)-N-[2-(*tert*-butylamino)-1-(4-chlorophenyl)-2-oxoethyl]-N-(2,2-dimethoxyethyl)-3-methoxy-O-methyltyrosinamide 15e. This residue was purified by flash chromatography (7:3 hexane/EtOAc) to give **15e (82%)** as a white solid.**^{1}HNMR** (300 MHz, $CDCl_3$) δ (ppm) 7.29-7.19 (m, 8H), 6.80-6.61 (m, 6H), 6.25 (bs, 1H), 6.09 (bs, 1H), 5.52 (s, 1H), 5.35 (s, 1H), 5.12 (d, J= 8.7 Hz, 1H), 5.05 (d, J= 9 Hz, 1H), 4.97 (dd, J=6.9 Hz, J= 14.1 Hz, 2H), 4.23 (m, 1H), 4.01 (dd, J= 5.1 Hz, J= 10.2 Hz 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.83 (s, 3H), 3.82 (s, 3H), 3.66 (dd, J=6.3 Hz, J= 15.6 Hz, 1H), 3.66 (dd, J=5.4 Hz, J= 15.6 Hz, 1H), 3.32-3.24 (m, 2H), 3.32 (s, 3H), 3.29 (s, 3H), 3.28 (s, 3H), 3.24 (s, 3H), 2.99 (dd, J=6.6 Hz, J= 14.1 Hz, 2H), 2.84 (dd, J=7.8 Hz, J= 13.5 Hz, 2H), 1.39 (s, 18H), 1.35 (s, 18H). **^{13}CNMR** (75.4 MHz, $CDCl_3$) δ (ppm) 174.4, 173.7, 167.7, 155.2, 154.9, 149.0, 148.8, 148.0, 147.9, 134.1, 133.9, 130.9, 130.7, 129.2, 128.9, 128.6, 121.6, 121.4, 112.5, 111.3, 111.2, 103.4, 103.3, 79.6,

65.1, 64.7, 55.9, 55.3, 55.1, 55.1, 54.9, 52.9, 51.9, 51.4, 49.1, 38.7, 28.6, 28.2. **IR** γ (cm^{-1}) 757, 809, 1027, 1082, 1166, 1260, 1365, 1455, 1516, 1646, 1688, 2837, 2933, 2970, 3333. **HRMS (FAB+, M+)** calcd for $C_{32}H_{46}ClN_3O_8$: [M+1] 635.2973, found: 635.2983.

N-(*tert*-butoxycarbonyl)-N-[2-(*tert*-butylamino)-1-(2-nitrophenyl)-2-oxoethyl]-N-(2,2-dimethoxyethyl)-3-methoxy-O-methyltyrosinamide 15f. This residue was purified by flash chromatography (6:4 hexane/EtOAc) to give **15f (82%)** as a pale yellow solid.**^{1}HNMR** (300 MHz, $CDCl_3$) δ (ppm) 7.98 (dd, J=1.5 Hz, J= 7.6 Hz, 1H), 7.96 (dd, J=2.1 Hz, J= 8.5 Hz, 1H), 7.51-7.30 (m, 4H), 7.31 (d, J= 7.8 Hz, 1H), 7.01 (d, J= 7.8 Hz, 1H), 6.81 (d, J= 4.8 Hz, 6H), 6.25 (bs, 1H), 6.20 (bs, 1H), 6.11 (s, 1H), 6.06 (s, 1H), 5.08-4.91 (m, 4H), 4.59 (m, 1H), 4.33 (m, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.42 (s, 12H), 3.46-3.29 (m, 4H), 3.07 (dd, J=4.5 Hz, J= 14.4 Hz, 1H), 2.91 (dd, J=6.9 Hz, J= 14.4 Hz, 2H), 2.78 (dd, J=8.7 Hz, J= 14.1 Hz, 1H), 1.42 (s, 9H), 1.41 (s, 9H), 1.33 (s, 9H), 1.31 (s, 9H). **^{13}CNMR** (75.4 MHz, $CDCl_3$) δ (ppm) 174.4, 173.5, 166.0, 165.8, 155.8, 155.0, 150.1, 149.9, 149.0, 148.0, 148.0, 132.7, 132.6, 129.6, 129.3, 129.0, 128.4, 124.8, 121.4, 121.2, 112.9, 112.5, 111.9, 111.4, 111.3, 110.9, 103.8, 103.1, 80.5, 79.8, 63.7, 63.3, 55.9, 55.8, 55.7, 55.3, 55.1, 55.1, 51.7, 51.4, 51.3, 50.0, 49.5, 38.8, 37.7, 28.6, 28.5, 28.2. **IR** γ (cm^{-1}) 548, 632, 855, 1027, 1067, 1164, 1260, 1361, 1456, 1526, 1697, 2838, 2935, 2971, 3350. **HRMS (FAB+, M+)** calcd for $C_{32}H_{46}N_4O_{10}$: [M+1] 647.3292, found: 647.3286.

N-(*tert*-butoxycarbonyl)-N-[2-(*tert*-butylamino)-1-(4-fluoro-3-nitrophenyl)-2-oxoethyl]-N-(2,2-dimethoxyethyl)-3-methoxy-O-methyltyrosinamide 15g. This residue was purified by flash chromatography (6:4 hexane/EtOAc) to give **15g (65%)** as a yellow solid.**^{1}HNMR** (300 MHz, $CDCl_3$) δ (ppm) 8.06-8.02 (m, 2H), 7.68 (ddd, J=2.4 Hz, J= 4.2 Hz, J= 8.8 Hz, 1H), 7.61-7.17 (m, 1H), 6.81-6.39 (m, 6H), 5.35 (s, 1H), 5.09 (s, 1H), 5.11 (d, J= 10.5 Hz, 1H), 5.01 (d, J= 8.1 Hz, 1H), 4.88 (dd, J=7.2 Hz, J= 14.1 Hz, 1H), 4.81 (dd, J=7.8 Hz, J= 15.3 Hz, 1H), 4.47 (bs, 1H), 4.28 (dd, J= 4.2 Hz, J= 8.4 Hz 1H), 3.89-3.74 (m, 2H), 3.87 (s, 3H), 3.85 (s, 3H), 3.82 (s, 3H), 3.81 (s, 3H), 3.47 (s, 3H), 3.45 (s, 3H), 3.41 (s, 3H), 3.41-3.31 (m, 2H), 3.38 (s, 3H), 3.02 (dd, J=6 Hz, J= 13.8 Hz, 2H), 2.92 (dd, J=7.5 Hz, J= 13.8 Hz, 1H), 2.83 (dd, J=7.8 Hz, J= 14.1 Hz, 1H), 1.38 (s, 18H), 1.35 (s, 18H). **^{13}CNMR** (75.4 MHz, $CDCl_3$) δ (ppm) 174.2, 173.6, 166.8, 166.6, 155.4, 155.0, 153.1, 149.1, 148.1, 137.0, 136.2, 136.1, 132.9, 132.5, 128.9, 128.4, 127.1, 126.7, 121.3, 121.2, 117.8, 112.5, 111.4, 89.1, 79.9, 66.3, 65.6, 55.9, 55.8, 55.5, 55.4, 51.9, 51.4, 50.1, 38.9, 38.3, 28.6, 28.3, 28.2. **IR** γ (cm^{-1}) 550, 812, 1027, 1069, 1165, 1260, 1357, 1456, 1516, 1539, 1692, 2838, 2936, 2972,

3064, 3346. **HRMS (FAB+, M+)** calcd for $C_{32}H_{45}FN_4O_{10}$: [M+1] 664.3120, found: 664.3113.

*General procedure for the synthesis of the products **12a-g***. A solution of the corresponding Ugi adduct (0.1412 mmol, 1 equiv) in formic acid (0.5 mL) was stirred at room temperature for 2 h. Then formaldehyde (37%, 2.4018 mmol, 17 equiv) was added to the solution and the resulting solution was heated at 60°C for 1 h. The reaction mixture was washed with water (2x5mL), and saturated aqueous $NaHCO_3$, and the organic layer was dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography.

General procedure to one-pot reaction. To a solution of the corresponding Ugi adduct (0.1412 mmol, 1 equiv) in formic acid (0.5 mL) at room temperature was added formaldehyde (37%, 2.4018 mmol, 17 equiv), and the mixtures was stirred for 1 h at 60°C. The reaction mixture was washed with water (2x5mL), and saturated aqueous $NaHCO_3$, and the organic layer was dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The resulting residue was purified by flash chromatography.

N-(*tert*-butyl)-2-(8,9-dimethoxy-11-methyl-4-oxo-1,4,5,6-tetrahydro-1,5-epimino-3-benzazocin-3(2H)-yl)acetamide 12a. This residue was purified by flash chromatography (95:5 methanol/EtOAc) to give **12a (66%)** as a white solid.**^{1}HNMR** (300 MHz, $CDCl_3$) δ (ppm) 6.58 (s, 2H), 5.51 (bs, 1H), 4.37 (d, J=15.3 Hz, 1H), 4.04 (dd, J=4.5 Hz, J= 11.4 Hz, 1H), 3.88 (d, J=4.2 Hz, 1H), 3.84 (s, 3H), 3.83 (s, 3H), 3.71 (d, J=6.3 Hz, 1H), 3.34 (d, J=15.3 Hz, 1H), 3.25 (dd, J=6 Hz, J= 16.8 Hz, 1H), 3.20 (dd, J=0.9 Hz, J= 11.4 Hz, 1H), 2.83 (d, J=16.8 Hz, 1H), 2.53 (s, 3H), 1.03 (s, 9H). **^{13}CNMR** (75.4 MHz, $CDCl_3$) δ (ppm) 171.1, 167.2, 148.9, 148.3, 126.1, 124.3, 111.2, 110.0, 59.5, 56.0, 55.9, 53.8, 51.4, 50.8, 39.9, 28.2, 28.1. **IR** γ (cm^{-1}) 732, 767, 1017, 1114, 1133, 1221, 1257, 1364, 1453, 1516, 1643, 1667, 2935, 2967, 3071, 3352, 3399. **HRMS (IE ,M+)** calcd for **$C_{20}H_{29}N_3O_4$**: [M+1] 376.2236, found: 376.2243.

N-(*tert*-butyl)-2-(8,9-dimethoxy-11-methyl-4-oxo-1,4,5,6-tetrahydro-1,5-epimino-3-benzazocin-3(2H)-yl)butanamide 12b. This residue was purified by flash chromatography (95:5 methanol/EtOAc) to give **12b (70%)** as a white solid.**^{1}HNMR** (300 MHz, $CDCl_3$) δ (ppm) 6.57 (s, 3H), 6.55 (s, 1H), 5.97 (bs, 1H), 5.51 (bs, 1H), 4.92 (dd, J=6.3 Hz, J= 9.3 Hz, 1H), 4.70 (dd, J=6.6 Hz, J= 9 Hz, 1H), 3.85 (s, 3H), 3.84 (s, 3H), 3.82 (s, 3H), 3.81 (s, 3H), 3.88-3.76 (m, 4H), 3.69 (dd, J=6 Hz, J= 14.1 Hz, 2H), 3.23 (dd, J=6.3 Hz, J= 16.8 Hz, 2H), 3.12 (dd, J=1.2 Hz, J= 12 Hz, 1H), 3.07 (d, J=10.8

Hz, 1H), 2.86 (d, J=16.2 Hz, 1H), 2.79 (d, J=16.5 Hz, 1H), 2.51 (s, 3H), 2.51 (s, 3H), 1.92 (q, J=7.5 Hz, 1H), 1.64 (q, J=7.5 Hz, 1H), 1.60 (q, J=7.2 Hz, 1H), 1.34-1.31 (m, 1H), 1.31 (s, 9H), 0.91 (t, J=7.5 Hz, 3H), 0.88 (s, 9H), 0.35 (t, J=7.5 Hz, 3H). **^{13}CNMR** (75.4 MHz, $CDCl_3$) δ (ppm) 171.6, 171.4, 168.9, 168.6, 148.3, 148.1, 147.8, 126.5, 126.2, 124.6, 124.4, 110.9, 110.0, 109.5, 60.0, 59.6, 57.4, 57.1, 55.9, 55.8, 55.7, 51.1, 50.4, 47.9, 47.0, 40.1, 39.9, 28.9, 28.4, 28.6, 27.9, 19.7, 19.2, 10.4, 9.0. **IR** γ (cm^{-1}) 756, 1113, 1134, 1222, 1255, 1332, 1365, 1517, 1632, 1680, 2936, 2967, 3325, 3408. **HRMS (IE, M+)** calcd for **$C_{22}H_{33}N_3O_4$**: [M+1] 404.2549, found: 404.2547.

N-(*tert*-butyl)-2-(8,9-dimethoxy-11-methyl-4-oxo-1,4,5,6-tetrahydro-1,5-epimino-3-benzazocin-3(2H)-yl)-2-phenylacetamide 12c. This residue was purified by flash chromatography (95:5 methanol/EtOAc) to give **12c (88%)** as a white solid.**^{1}HNMR** (300 MHz, $CDCl_3$) δ (ppm) 7.37-7.29 (m, 5H), 7.17-7.11 (m, 1H), 7.05 (t, J=7.5 Hz, 2H), 6.65 (d, J=7.8 Hz, 2H), 6.60 (s, 1H), 6.59 (s, 1H), 6.57 (s, 1H), 6.24 (s, 1H), 6.19 (s, 1H), 6.09 (s, 1H), 5.80 (bs, 1H), 5.36 (bs, 1H), 4.14 (dd, J=3.9 Hz, J= 12 Hz, 1H), 3.87 (s, 3H), 3.84 (s, 3H), 3.83 (s, 3H), 3.80-3.69 (m, 4H), 3.64 (s, 3H), 3.51 (dd, J=4.5 Hz, J= 11.7 Hz, 1H), 3.29 (dd, J=5.7 Hz, J= 11.1 Hz, 1H), 3.23 (dd, J=5.7 Hz, J= 11.7 Hz, 1H), 3.16 (dd, J=1.2 Hz, J= 11.7 Hz, 1H), 2.90 (d, J=12.6 Hz, 1H), 2.84 (d, J=11.7 Hz, 1H), 2.83 (dd, J=1.5 Hz, J= 12.3 Hz, 1H), 2.57 (s, 3H), 2.40 (s, 3H), 1.38 (s, 9H), 1.00 (s, 9H). **^{13}CNMR** (75.4 MHz, $CDCl_3$) δ (ppm) 171.1, 171.0, 167.9, 167.1, 148.9, 148.3, 147.8, 134.6, 134.0, 129.8, 128.3, 128.0, 128.2, 128.0, 127.5, 126.6, 126.2, 124.8, 124.5, 111.2, 111.0, 110.1, 109.6, 60.1, 59.9, 59.4, 56.2, 55.9, 55.9, 55.7, 51.7, 50.9, 49.7, 48.1, 40.3, 39.8, 29.8, 28.6, 28.3, 28.1. **IR** γ (cm^{-1}) 521, 701, 820, 1031, 1111, 1135, 1221, 1253, 1332, 1363, 1456, 1515, 1637, 1681, 2863, 2934, 2965, 3064, 3333, 3402. **HRMS (IE, M+)** calcd for **$C_{26}H_{33}N_3O_4$**: [M+1] 451.2471, found: 451.2473.

N-(*tert*-butyl)-2-(8,9-dimethoxy-11-methyl-4-oxo-1,4,5,6-tetrahydro-1,5-epimino-3-benzazocin-3(2H)-yl)-2-(4-methoxyphenyl)acetamide 12d. This residue was purified by flash chromatography (95:5 methanol/EtOAc) to give **12f (81%)** as a pale yellow solid.**^{1}HNMR** (300 MHz, $CDCl_3$) δ (ppm) 7.30 (d, J=8.4 Hz, 2H), 6.86 (d, J=9 Hz, 2H), 6.58 (d, J=8.7 Hz, 4H), 6.62 (s, 1H), 6.61 (s, 1H), 6.58 (s, 1H), 6.19 (s, 1H), 6.18 (s, 1H), 6.02 (s, 1H), 5.69 (bs, 1H), 5.36 (bs, 1H), 4.13 (dd, J=3.9 Hz, J= 12.3 Hz, 1H), 3.87 (s, 3H), 3.84 (s, 3H), 3.83 (s, 3H), 3.79 (s, 3H), 3.79-3.73 (m, 4H), 3.73 (s, 3H), 3.65 (s, 3H), 3.52 (dd, J=4.5 Hz, J= 11.7 Hz, 1H), 3.30 (dd, J=6 Hz, J= 15 Hz, 1H), 3.25 (dd, J=6.3 Hz, J= 16.3 Hz, 1H), 2.91 (d, J=6 Hz, 1H), 2.86 (d, J=5.4 Hz, 1H), 2.82 (dd,

J=1.2 Hz, J= 12.3 Hz, 1H), 2.63 (s, 3H), 2.40 (s, 3H), 1.37 (s, 9H), 0.99 (s, 9H). **^{13}CNMR** (75.4 MHz, $CDCl_3$) δ (ppm) 171.0, 170.9, 168.2, 167.4, 159.3, 159.1, 148.9, 148.4, 148.3, 147.8, 131.2, 129.6, 126.1, 124.4, 124.6, 113.8, 113.7, 111.2, 111.0, 110.1, 109.5, 60.1, 59.9, 59.2, 59.2, 56.0, 55.9, 55.7, 55.2, 55.1, 50.8, 51.7, 49.5, 47.7, 40.4, 39.8, 29.9, 28.6, 28.4, 28.1. **IR** γ (cm^{-1}) 465, 535, 581, 834, 1032, 1111, 1176, 1250, 1363, 1460, 1513, 1636, 1680, 2839, 2935, 2963, 3325, 3402. **HRMS (IE, M+)** calcd for **$C_{27}H_{35}N_3O_5$**: [M+1] 482.2655, found: 482.2656.

N-(*tert*-butyl)-2-(4-chlorophenyl)-2-(8,9-dimethoxy-11-methyl-4-oxo-1,4,5,6-tetrahydro-1,5-epimino-3-benzazocin-3(2H)-yl)acetamide 12e. Diastereoisomer 1. This residue was purified by flash chromatography (95:5 methanol/EtOAc) to give **12e (91%)** as a pale yellow solid, Mp: 77-85°C.**^{1}HNMR** (300 MHz, $CDCl_3$) δ (ppm) 7.32 (d, J=2.1 Hz, 4H), 6.61 (s, 1H), 6.58 (s, 1H), 6.26 (s, 1H), 5.36 (bs, 1H), 3.85 (s, 3H), 3.84 (s, 3H), 3.80 (d, J=4.2 Hz, 1H), 3.74 (d, J=6.3 Hz, 1H), 3.51 (dd, J=4.5 Hz, J= 11.4 Hz, 1H), 3.25 (dd, J=6.3 Hz, J= 16.8 Hz, 1H), 3.13 (d, J=11.4 Hz, 1H), 2.88 (d, J=17.1 Hz, 1H), 2.40 (s, 3H), 0.99 (s, 9H). **^{13}CNMR** (75.4 MHz, $CDCl_3$) δ (ppm) 171.2, 167.5, 148.4, 148.0, 133.6, 133.1, 129.4, 128.4, 126.5, 124.8, 111.1, 109.7, 60.2, 58.8, 56.3, 48.5, 40.3, 28.6. **IR** γ (cm^{-1}) 928, 1016, 1113, 1134, 1206, 1234, 1253, 1365, 1465, 1493, 1516, 1642, 1679, 2938, 2972, 3011, 3405. **HRMS (IE, M+)** calcd for **$C_{26}H_{32}ClN_3O_4$**: [M+1] 485.2081, found: 485.2090.

N-(*tert*-butyl)-2-(4-chlorophenyl)-2-(8,9-dimethoxy-11-methyl-4-oxo-1,4,5,6-tetrahydro-1,5-epimino-3-benzazocin-3(2H)-yl)acetamide 12e. Diastereoisomer 2. This residue was purified by flash chromatography **(95:5 methanol/EtOAc)** to give **12e** as a white solid, Mp: 70-75°C.**^{1}HNMR** (300 MHz, $CDCl_3$) δ (ppm) 7.02 (d, J=8.7 Hz, 2H), 6.59 (s, 1H), 6.55 (d, J=9.0 Hz, 2H), 6.24 (s, 1H), 6.03 (s, 1H), 5.88 (bs, 1H), 4.09 (dd, J=3.9 Hz, J= 12.3 Hz, 1H), 3.88 (s, 3H), 3.77 (d, J= 3.6 Hz, 1H), 3.72 (d, J=6.0 Hz, 1H), 3.69 (s, 3H), 3.27 (dd, J=6.0 Hz, J= 16.8 Hz, 1H), 2.83 (d, J=12.3 Hz, 1H), 2.80 (d, J=6.3 Hz, 1H), 2.56 (s, 3H), 1.38 (s, 9H). **^{13}CNMR** (75.4 MHz, $CDCl_3$) δ (ppm) 171.0, 167.5, 148.5, 148.0, 133.6, 133.0, 129.3, 128.4, 126.3, 124.7, 111.1, 109.6, 60.2, 58.8, 56.3, 55.9, 55.8, 51.8, 40.3, 29.4, 28.6. **IR** γ (cm^{-1}) 541, 830, 1015, 1111, 1222, 1254, 1331, 1363, 1457, 1515, 1633, 1679, 2935, 2966, 3323, 3450. **HRMS (IE, M+)** calcd for **$C_{26}H_{32}ClN_3O_4$**: [M+1] 486.2160, found: 486.2154.

N-(*tert*-butyl)-2-(8,9-dimethoxy-11-methyl-4-oxo-1,4,5,6-tetrahydro-1,5-epimino-3-benzazocin-3(2H)-yl)-2-(2-nitrophenyl)acetamide 12f. Diastereoisomer 1. This residue was purified by flash chromatography (EtOAc) to give **12f (69%)** as a yellow

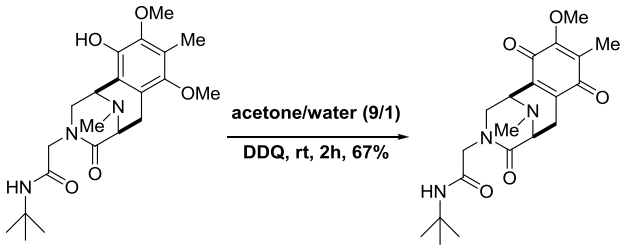
solid, Mp: 115-117°C.**^{1}HNMR** (300 MHz, $CDCl_3$) δ (ppm) 7.93 (dd, J=1.2 Hz, J= 8.1 Hz, 1H), 7.24 (tt, J=7.5 Hz, J= 0.6 Hz, 1H), 6.87 (td, J=7.5 Hz, J= 1.2 Hz, 1H), 6.69 (s, 1H), 6.67 (s, 1H), 6.58 (s, 1H), 5.92 (bs, 1H), 5.77 (d, J=7.8 Hz, 1H), 3.91 (s, 3H), 3.80 (s, 3H), 3.84 (dd, J=5.7 Hz, J= 11.1 Hz, 1H), 3.33 (dd, J=6 Hz, J= 16.8 Hz, 1H), 3.95-3.80 (m, 2H), 3.18 (d, J=11.7 Hz, 1H), 2.86 (d, J=16.5 Hz, 1H), 2.60 (s, 3H), 1.37 (s, 9H). **^{13}CNMR** (75.4 MHz, $CDCl_3$) δ (ppm) 171.1, 166.1, 149.2, 148.8, 148.5, 132.8, 130.1, 128.1, 127.0, 126.0, 125.2, 125.1, 111.4, 110.1, 60.3, 58.7, 56.0, 56.0, 53.8, 49.5, 40.0, 28.6. **IR** γ (cm^{-1}) 465, 672, 726, 782, 859, 1028, 1111, 1137, 1217, 1254, 1281, 1345, 1521, 1647, 2857, 2933, 3070, 3444. **HRMS (IE, M+)** calcd for **$C_{26}H_{32}N_4O_6$**: [M+1] 497.2400, found: 497.2401.

N-(*tert*-butyl)-2-(8,9-dimethoxy-11-methyl-4-oxo-1,4,5,6-tetrahydro-1,5-epimino-3-benzazocin-3(2H)-yl)-2-(2-nitrophenyl)acetamide 12f. Diastereoisomer 2. This residue was purified by flash chromatography (EtOAc) to give **12f** as a pale yellow solid, Mp: 198-199°C.**^{1}HNMR** (300 MHz, $CDCl_3$) δ (ppm) 7.99 (dd, J=8.1 Hz, J= 1.2 Hz, 1H), 7.58 (td, J=7.5 Hz, J= 1.5 Hz, 1H), 7.45 (tt, J=7.2 Hz, J= 0.6 Hz, 1H), 7.38 (d, J=7.8 Hz, 1H), 6.68 (s, 1H), 6.61 (s, 1H), 6.56 (s, 1H), 5.19 (bs, 1H), 3.87 (m, 3H), 3.85 (s, 3H), 3.82 (s, 3H), 3.28 (dd, J=6.3 Hz, J= 16.8 Hz, 1H), 3.18 (d, J=10.5 Hz, 1H), 2.91 (d, J=17.1 Hz, 1H), 2.53 (s, 3H), 1.02 (s, 9H). **^{13}CNMR** (75.4 MHz, $CDCl_3$) δ (ppm) 171.3, 165.2, 150.0, 148.9, 148.3, 132.8, 129.4, 129.3, 128.6, 125.5, 125.1, 124.3, 111.2, 110.2, 59.8, 58.7, 56.1, 55.9, 55.8, 51.5, 51.0, 39.8, 28.1, 27.2. **IR** γ (cm^{-1}) 503, 580, 731, 828, 867, 1013, 1113, 1136, 1220, 1252, 1361, 1459, 1526, 1640, 1687, 2938, 2967, 3322, 3409. **HRMS (IE, M+)** calcd for **$C_{26}H_{32}N_4O_6$**: [M+1] 497.2400, found: 497.2397.

N-(*tert*-butyl)-2-(8,9-dimethoxy-11-methyl-4-oxo-1,4,5,6-tetrahydro-1,5-epimino-3-benzazocin-3(2H)-yl)-2-(4-fluoro-3-nitrophenyl)acetamide 12g. This residue was purified by flash chromatography (95:5 methanol/EtOAc) to give **12g (95%)** as a yellow solid.**^{1}HNMR** (300 MHz, $CDCl_3$) δ (ppm) 8.18 (ddd, J=2.4 Hz, J= 3.5 Hz, J= 8.9 Hz, 1H), 7.69 (ddd, J=2.1 Hz, J= 3.7 Hz, J= 9 Hz, 1H), 7.58 (dd, J=0.9 Hz, J= 2.4 Hz, J= 7 Hz, 1H), 7.27 (dd, J=7.8 Hz, J= 11.4 Hz, 1H), 6.87 (dd, J=8.7 Hz, J= 10.5 Hz, 1H), 6.64 (dddd, J=0.9 Hz, J=2.4 Hz, J= 4.1 Hz, J= 8.7 Hz, 1H), 6.61 (s, 2H), 6.60 (s, 1H), 6.35 (s, 1H), 6.31 (s, 1H), 6.16 (bs, 1H), 6.09 (s, 1H), 5.42 (bs, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 3.85 (s, 3H), 3.83-3.76 (m, 2H), 3.71 (s, 3H), 3.57 (dd, J=4.5 Hz, J= 11.1 Hz, 1H), 3.31 (dd, J=3 Hz, J= 6.6 Hz, 1H), 3.25 (dd, J=3.6 Hz, J= 5.7 Hz, 1H), 3.17 (dd, J=1.2 Hz, J= 11.1 Hz, 1H), 2.59 (dd, J=1.5 Hz, J= 12 Hz, 1H), 2.87 (d, J=15.6 Hz, 1H),

2.82 (d, J=15.6 Hz, 1H), 2.54 (s, 3H), 2.41 (s, 3H), 1.39 (s, 9H), 0.99 (s, 9H). **^{13}CNMR** (75.4 MHz, $CDCl_3$) δ (ppm) 171.4, 166.2, 165.9, 156.7, 153. 2, 152.6, 148.9, 148.6, 148.4, 148.1, 137.3, 137.2, 137.1, 134.4, 134.3, 131.8, 131.0, 127.5, 125.6, 125.4, 125.3, 124.4, 124.1, 118.4, 118.2, 117.9, 117.7, 111.0, 110.9, 109.9, 109.4, 60.0, 59.7, 57.9, 57.8, 55.9, 55.9, 55.8, 55.6, 52.1, 51.2, 50.1, 49.5, 40.0, 39.3, 28.5, 27.9, 27.4. **IR** γ (cm^{-1}) 540, 825, 1029, 1114, 1134, 1255, 1354, 1460, 1515, 1539, 1637, 1682, 2936, 2968, 3066, 3339, 3400. **HRMS (FAB+)** calcd for **$C_{26}H_{31}FN_4O_6$**: [M+1] 515.2306, found: 515.2310.

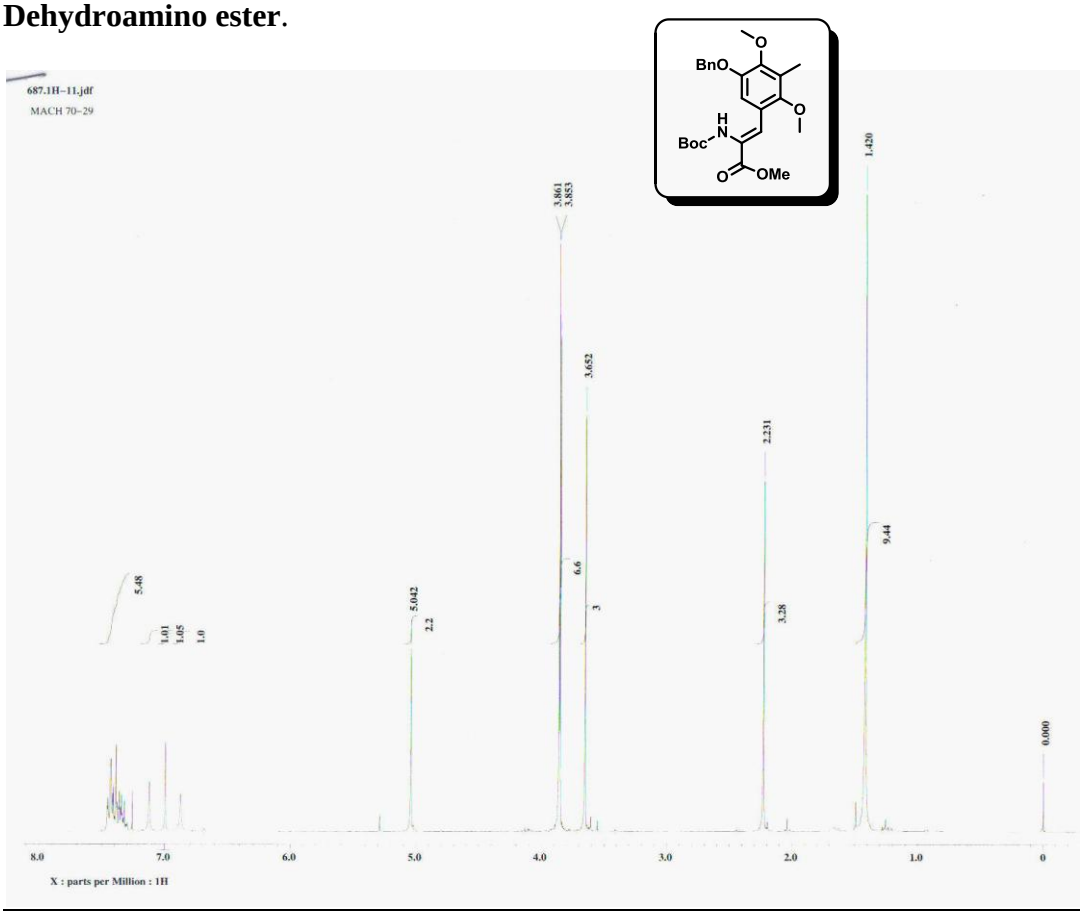
N-(*tert*-butyl)-2-(10-hydroxy-7,9-dimethoxy-8,11-dimethyl-4-oxo-1,4,5,6-tetrahydro-1,5-epimino-3-benzazocin-3(2H)-yl)acetamide 12h. This residue was purified by flash chromatography **(95:5 methanol/EtOAc)** to give **12h** as a pale yellow solid, Mp: 73-77°C.**^{1}HNMR** (300 MHz, $CDCl_3$) δ (ppm) 5.64 (bs, 1H), 4.40 (d, J=15.3 Hz, 1H), 4.22 (d, J=4.5 Hz, 1H), 3.96 (dd, J=4.5 Hz, J= 12 Hz, 1H), 3.75 (s, 3H), 3.78-3.65 (m, 1H), 3.66 (s, 3H), 3.32 (d, J=11.7 Hz, 1H), 3.31 (d, J=15.3 Hz, 1H), 3.09 (dd, J=6.3 Hz, J= 18 Hz, 1H), 2.98 (dd, J=1.2 Hz, J= 17.4 Hz, 1H), 2.53 (s, 3H), 2.19 (s, 3H), 1.01 (s, 9H). **^{13}CNMR** (75.4 MHz, $CDCl_3$) δ (ppm) 171.2, 167.6, 149.3, 143.9, 142.2, 123.1, 122.0, 119.1, 60.8, 60.0, 58.9, 51.5, 51.4, 50.8, 50.6, 40.0, 28.1, 23.8, 9.4. **IR** γ (cm^{-1}) 928, 1007, 1050, 1108, 1202, 1231, 1255, 1310, 1366, 1414, 1469, 1523, 1672, 2858, 2937, 2968, 3014, 3406, 3535. **HRMS (IE, M+)** calcd for **$C_{21}H_{32}N_3O_5$**: 406.2342, found: 406.2343.

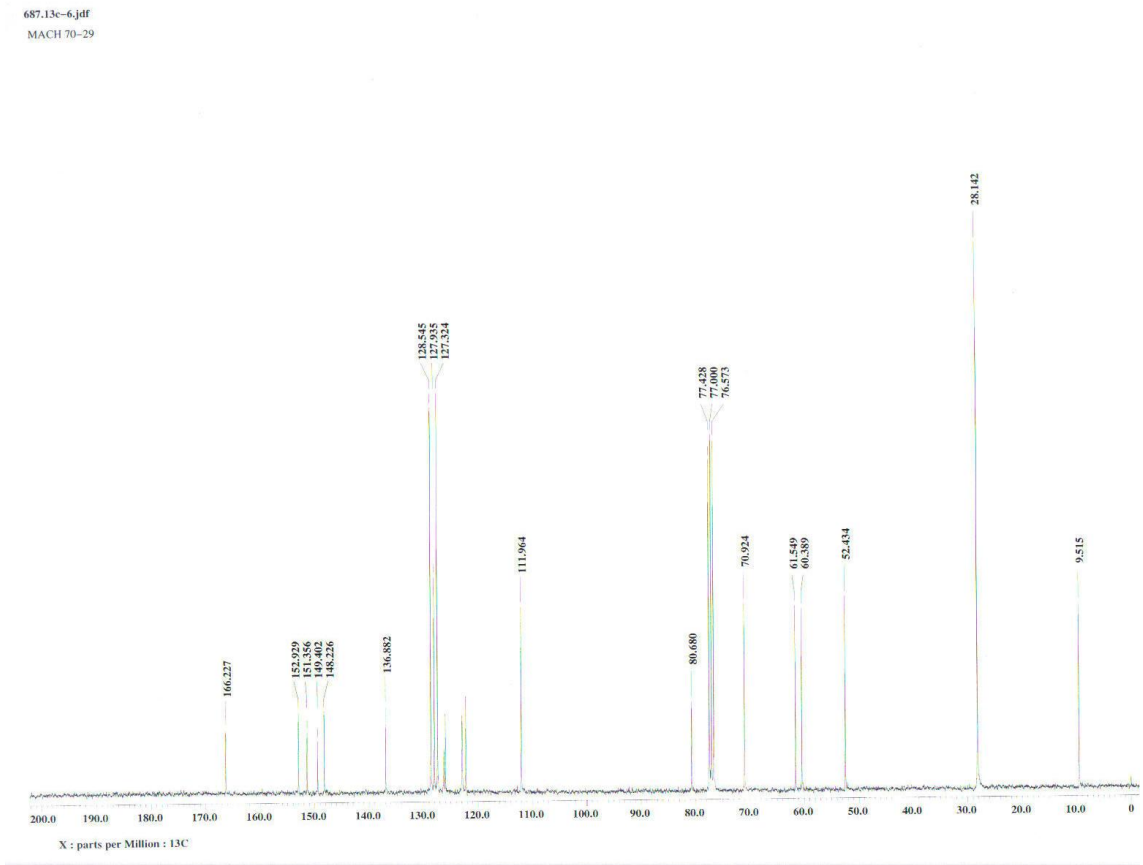


Quinone 16. To a solution of alcohol **12h** (28.7 mg, 0.0708 mmol, 1equiv) in 7 mL of acetone/H_2O mixture (v/v, 9:1), 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ, 32.15 mg, 0.1416 mmol) was added at room temperature. The resulting mixture was stirred at room temperature for 2 h, quenched with saturated aqueous sodium bicarbonate ($NaHCO_3$, 5 mL), and added with ethyl acetate (7 mL). The two layers were separated, and the aqueous layer was extracted with ethyl acetate (5 mL x 3) and the organic layer was dried over anhydrous $NaSO_4$, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (EtOAc) to afford the

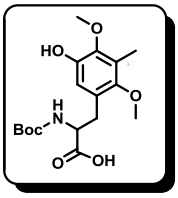
quinone (67%) as a orange solid, Mp: 160-168°C. **^{1}HNMR** (300 MHz, $CDCl_3$) δ (ppm) 5.87 (bs, 1H), 4.03 (d, J=12 Hz, 1H), 3.99 (s, 4H), 3.97 (d, J=15 Hz, 1H), 3.64 (ddd, J=1.2 Hz, J= 5.4 Hz, 1H), 3.65 (d, J=14.4 Hz, 1H), 3.18 (d, J=11.4 Hz, 1H), 2.82 (dd, J= 5.7 Hz, J= 20.1 Hz, 1H), 2.73 (dd, J= 1.5 Hz, J= 19.8 Hz, 1H), 2.50 (s, 3H), 1.94 (s, 3H), 1.21 (s, 9H). **^{13}CNMR** (75.4 MHz, $CDCl_3$) δ (ppm) 186.70, 181.83, 170.18, 167.05, 155.58, 140.38, 137.67, 129.15, 60.98, 58.15, 51.52, 51.12, 50.10, 49.74, 39.94, 28.52, 24.77, 8.63. **IR** γ (cm^{-1}) 999, 1042, 1069, 1148, 1231, 1264, 1308, 1364, 1452, 1548, 1655, 2934, 2967, 3316. **HRMS (IE, M+)** calcd for **$C_{20}H_{27}N_3O_5$**: 389.1951, found: 389.195

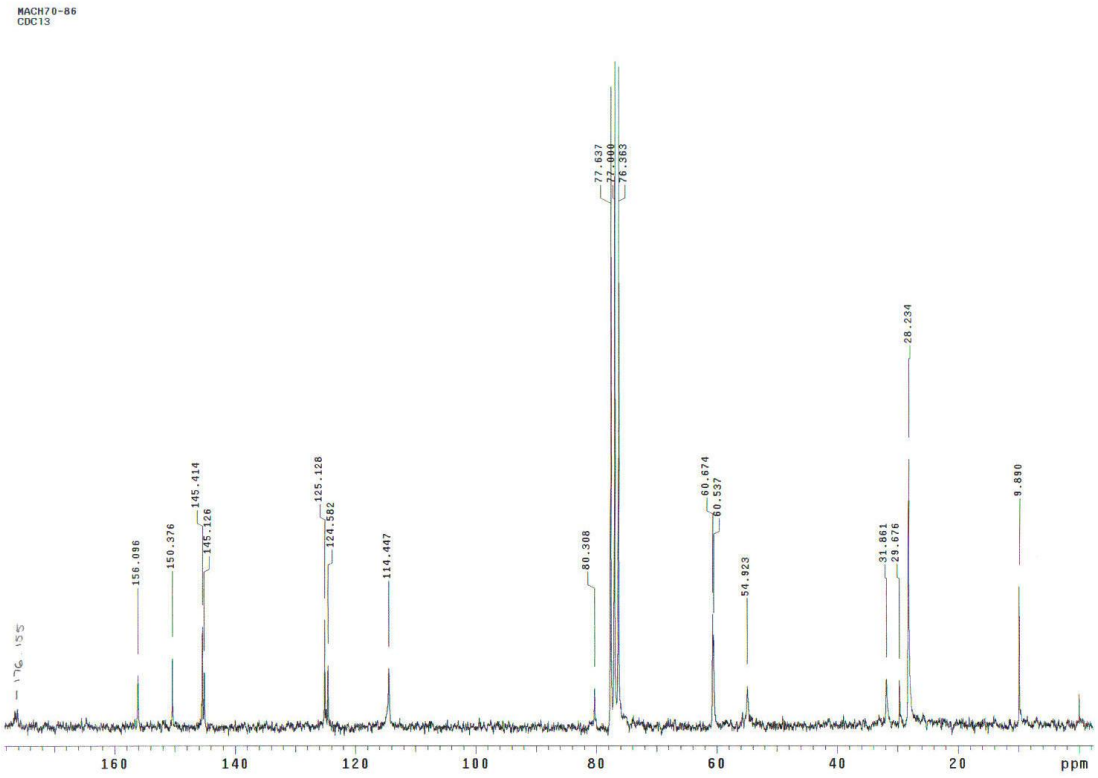
Dehydroamino ester.



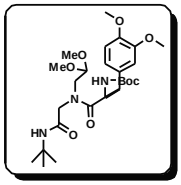


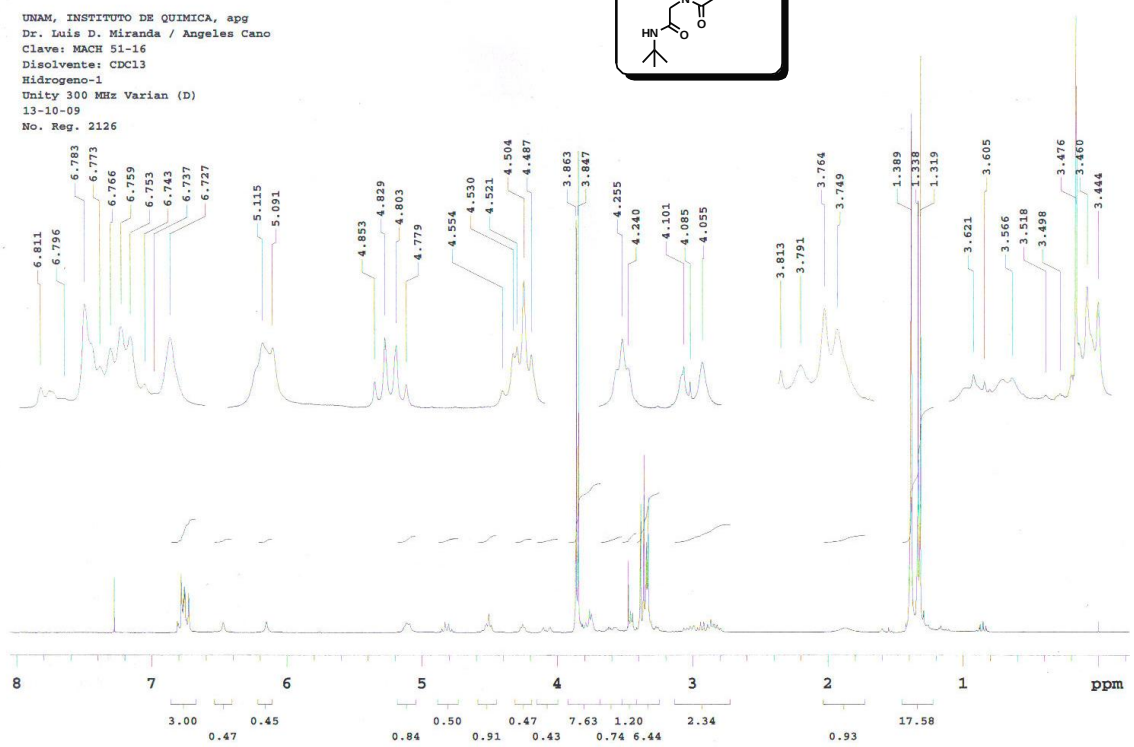
Aminoacid 10b

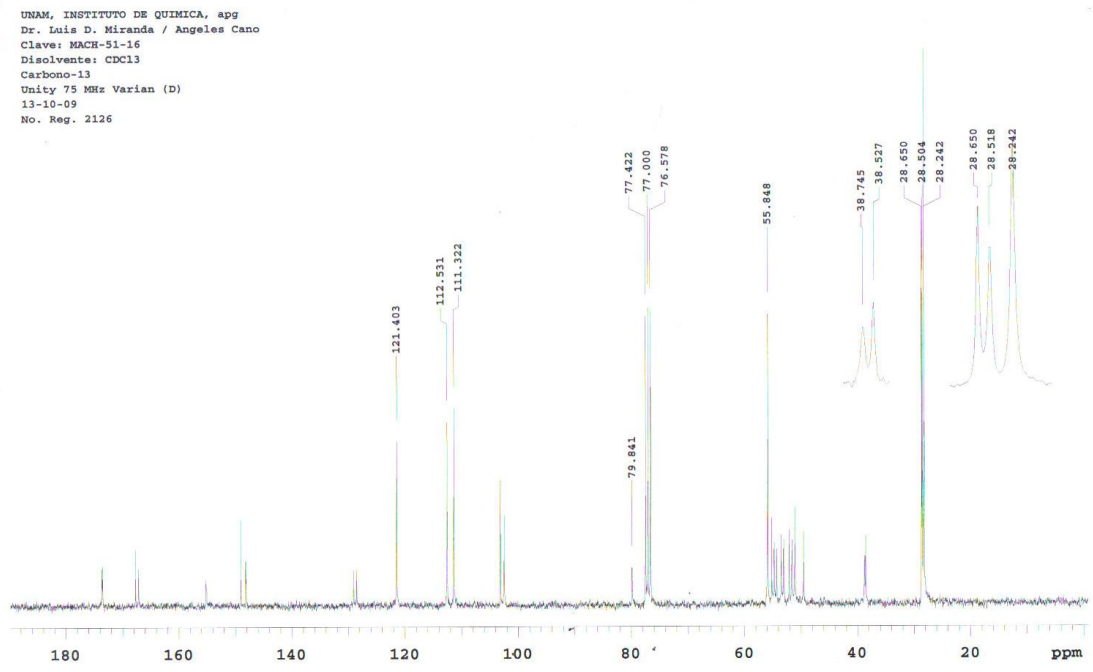




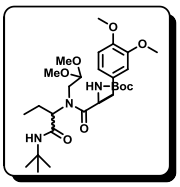
N-(*tert*-butoxycarbonyl)-3-methoxy-O-methyltyrosyl-N^1-(*tert*-butyl)-N^2-(2, 2-dimethoxyethyl)glycinamide 15a

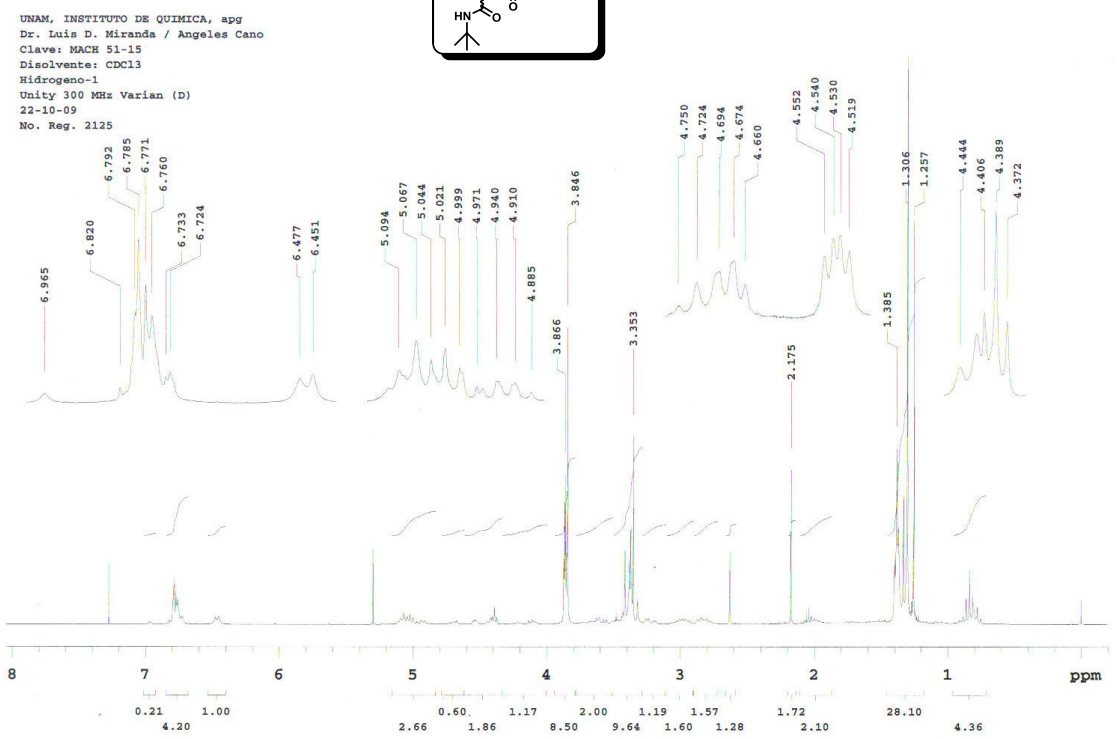


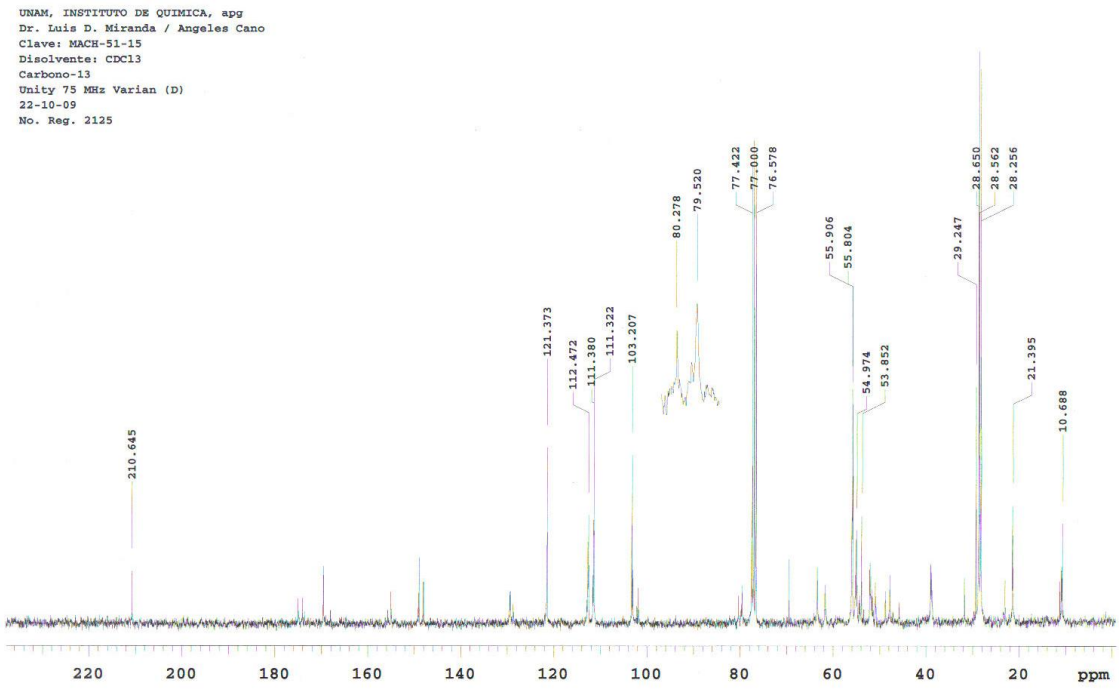




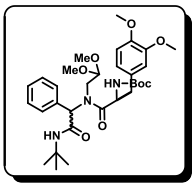
N-(*tert*-butoxycarbonyl)-N-{1-[(*tert*-butylamino)carbonyl]propyl}-N-(2,2-dimethoxyethyl)-3-methoxy-O-methyltyrosinamide 15b

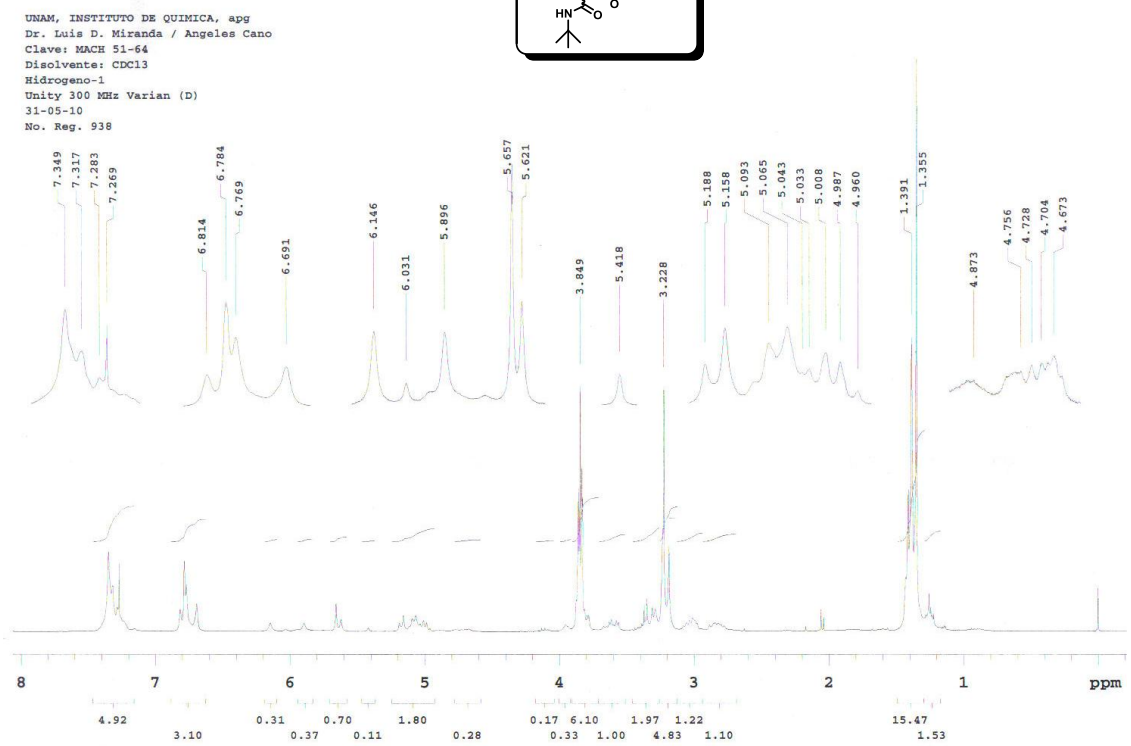


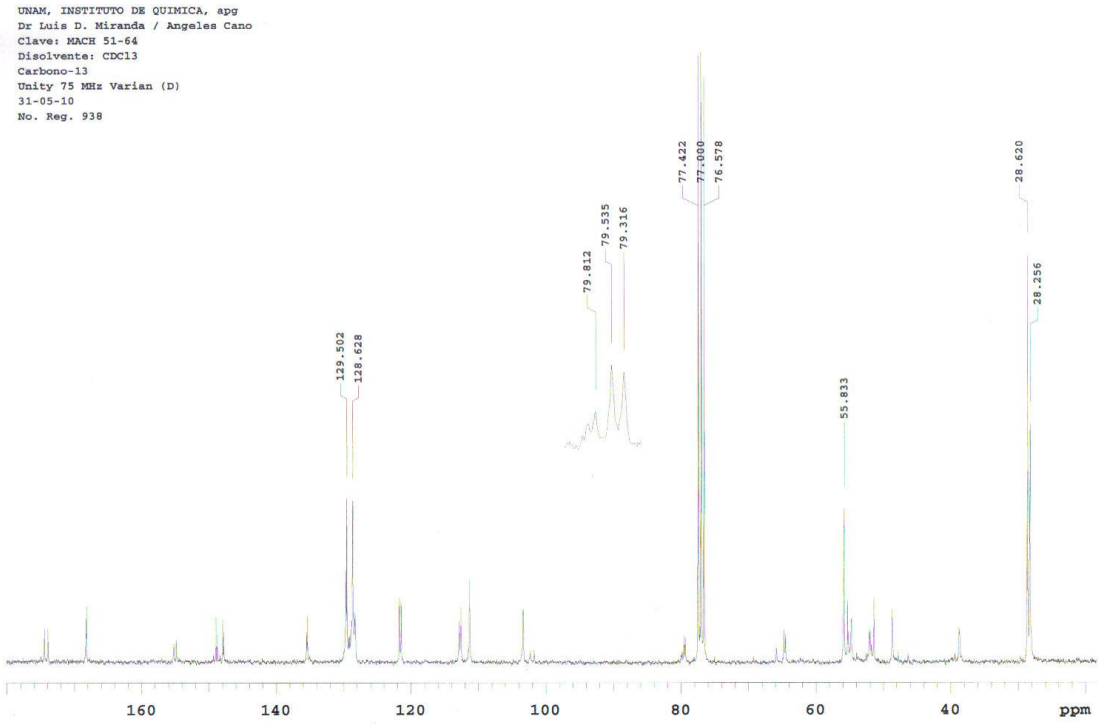




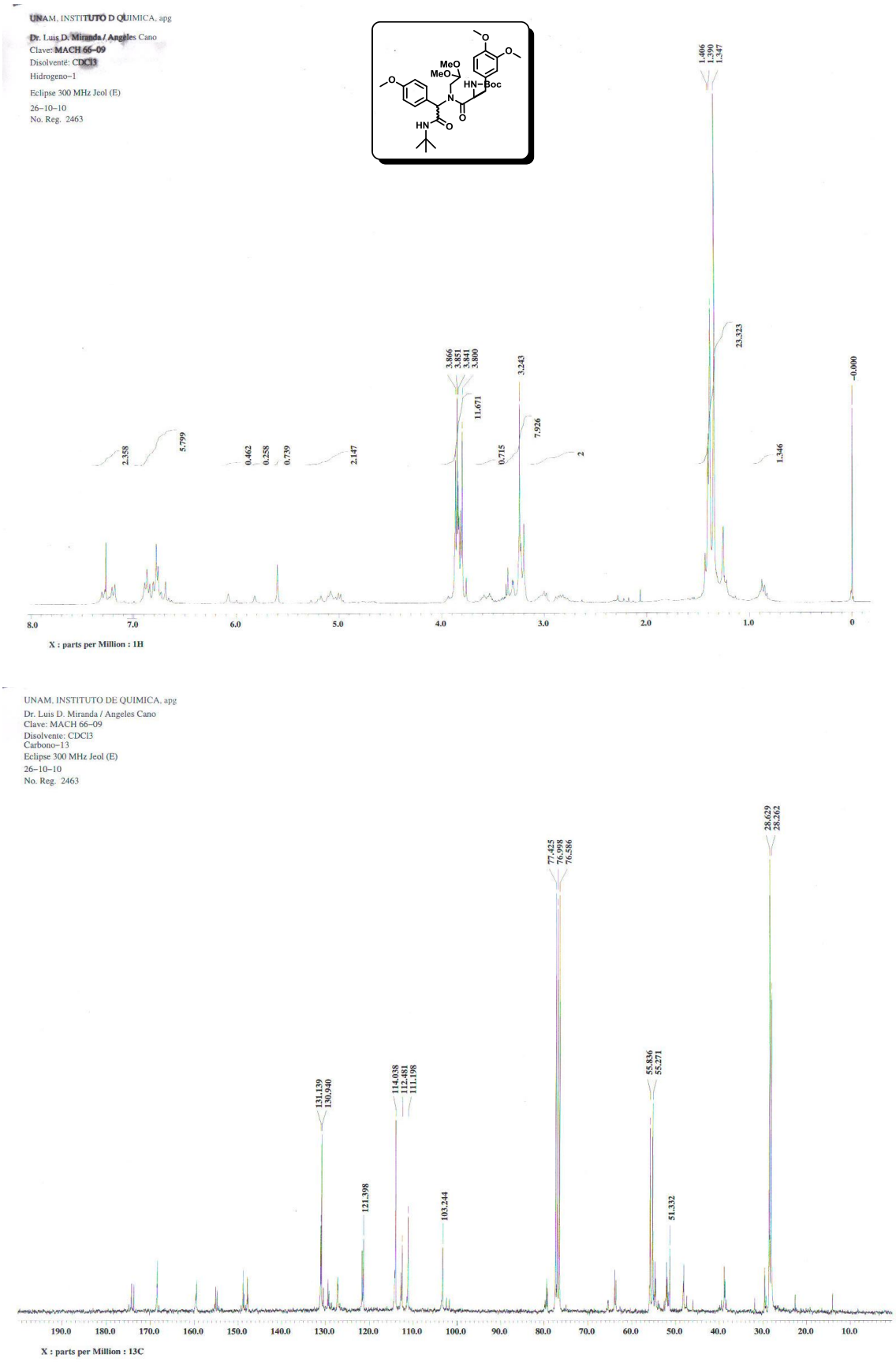
N-(*tert*-butoxycarbonyl)-N-[2-(*tert*-butylamino)-2-oxo-1-phenylethyl]-N-(2,2-dimethoxyethyl)-3-methoxy-O-methyltyrosinamide 15c







N-(*tert*-butoxycarbonyl)-N-[2-(*tert*-butylamino)-1-(4-methoxyphenyl)-2-oxoethyl]-N-(2,2-dimethoxyethyl)-3-methoxy-O-methyltyrosinamide 15d



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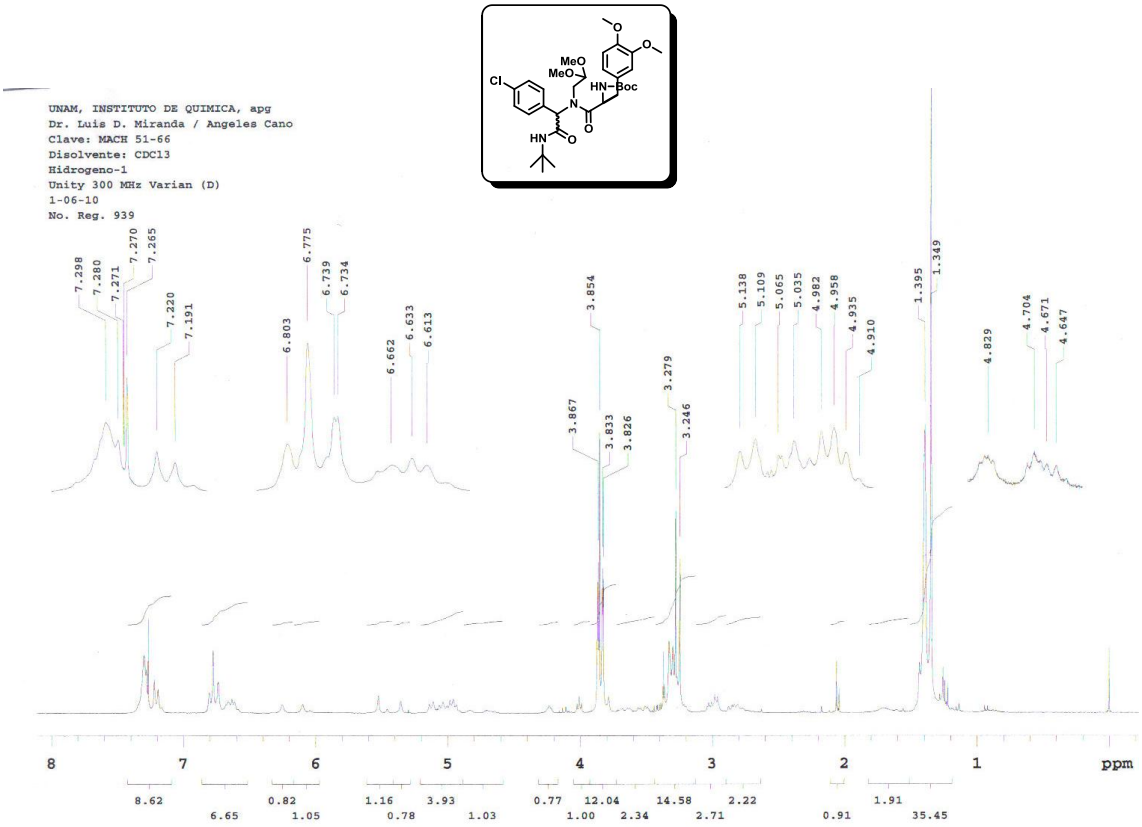
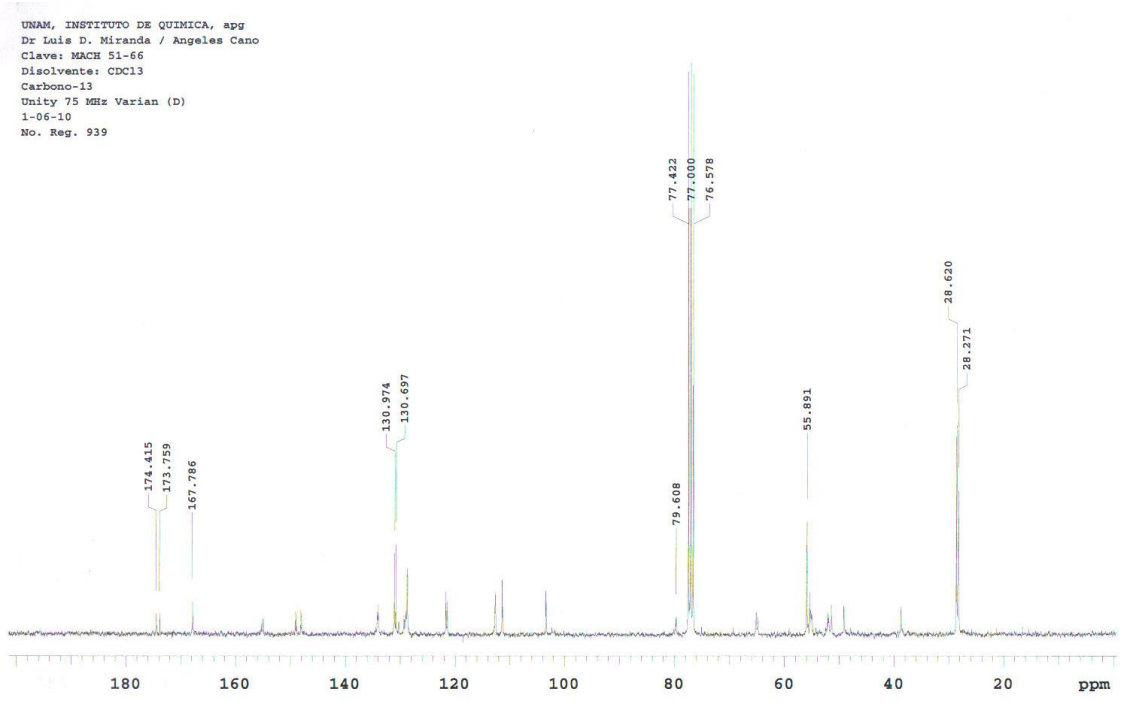
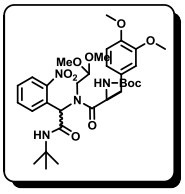
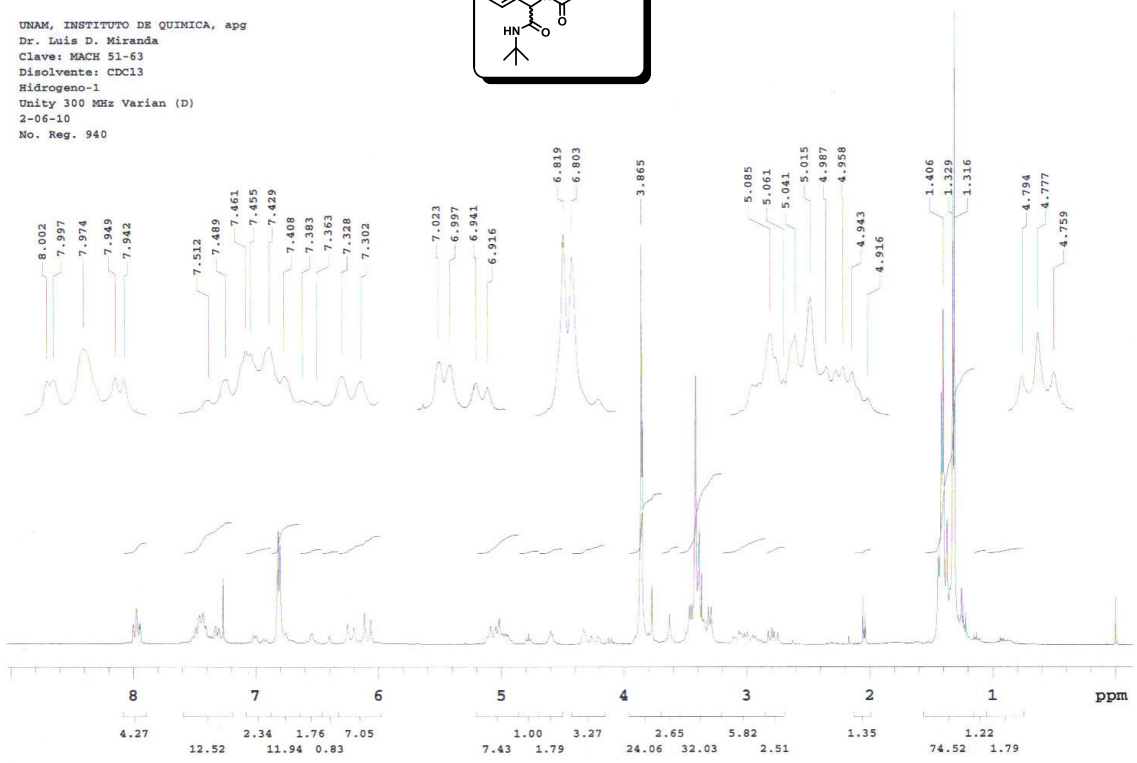
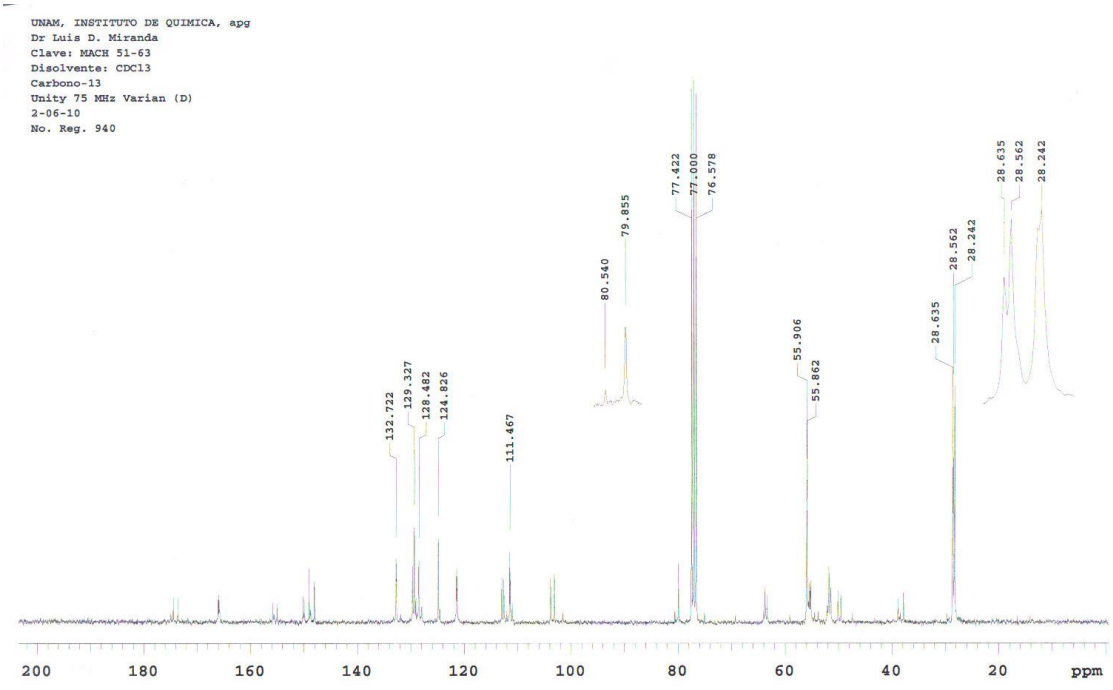




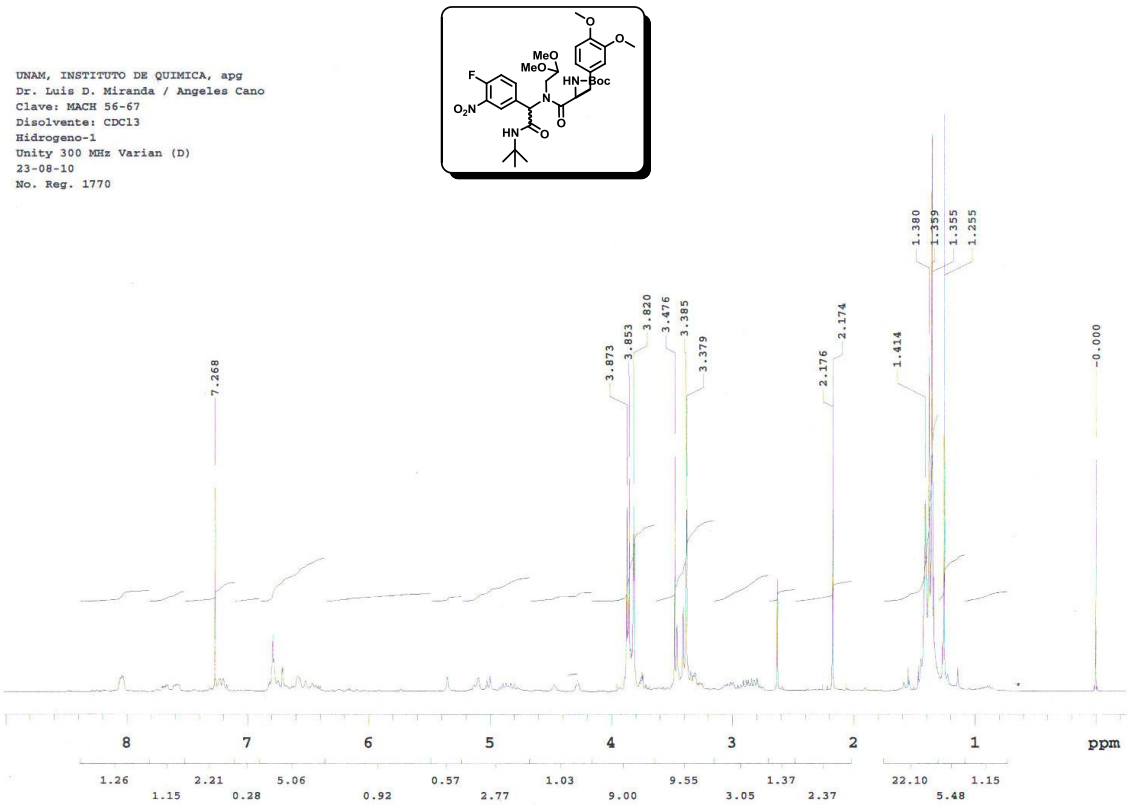
N-(*tert*-butoxycarbonyl)-N-[2-(*tert*-butylamino)-1-(2-nitrophenyl)-2-oxoethyl]-N-(2,2-dimethoxyethyl)-3-methoxy-O-methyltyrosinamide 15f

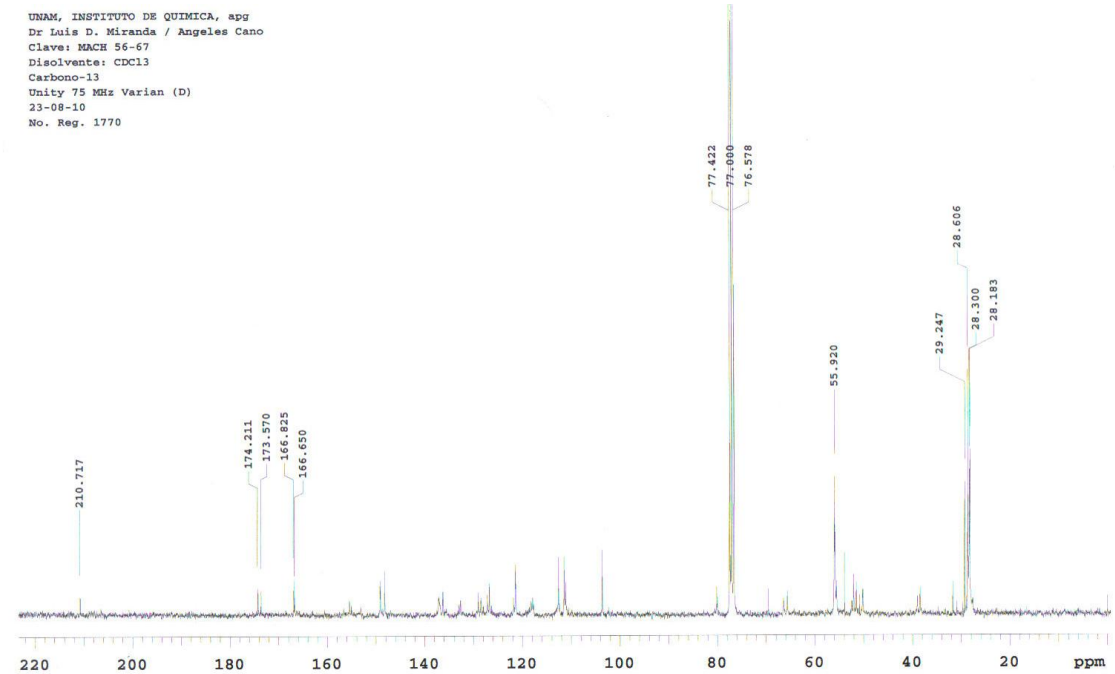




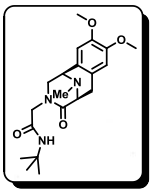


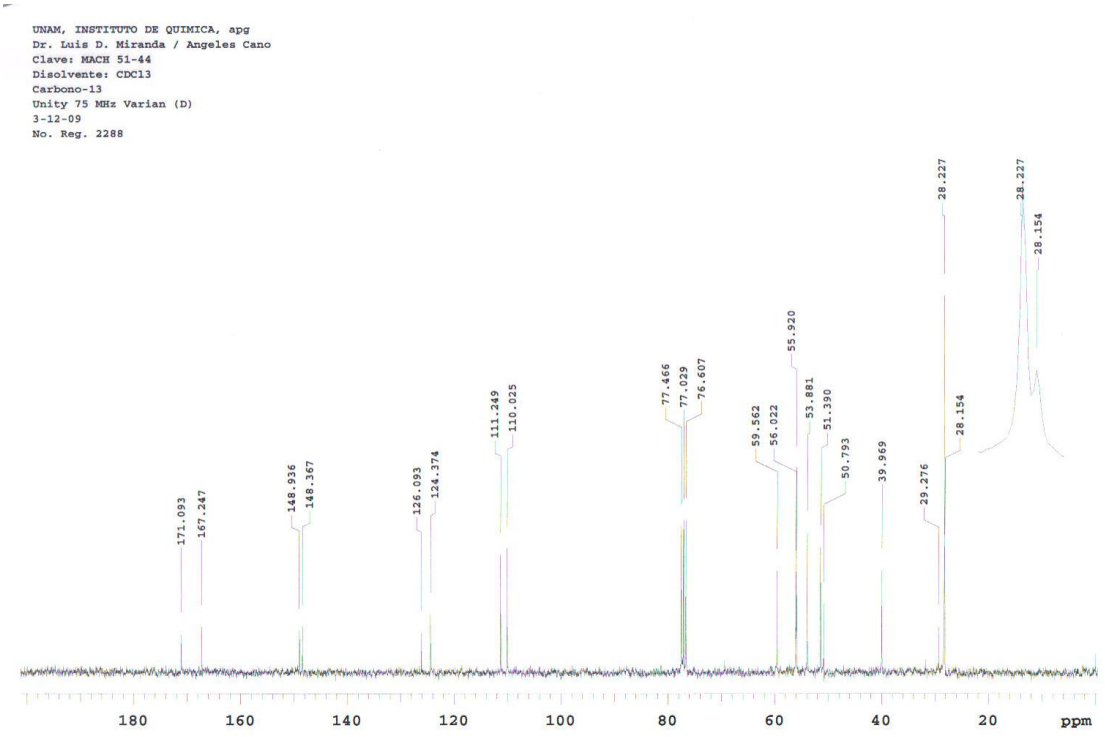
N-(*tert*-butoxycarbonyl)-N-[2-(*tert*-butylamino)-1-(4-fluoro-3-nitrophenyl)-2-oxoethyl]-N-(2,2-dimethoxyethyl)-3-methoxy-O-methyltyrosinamide 15g



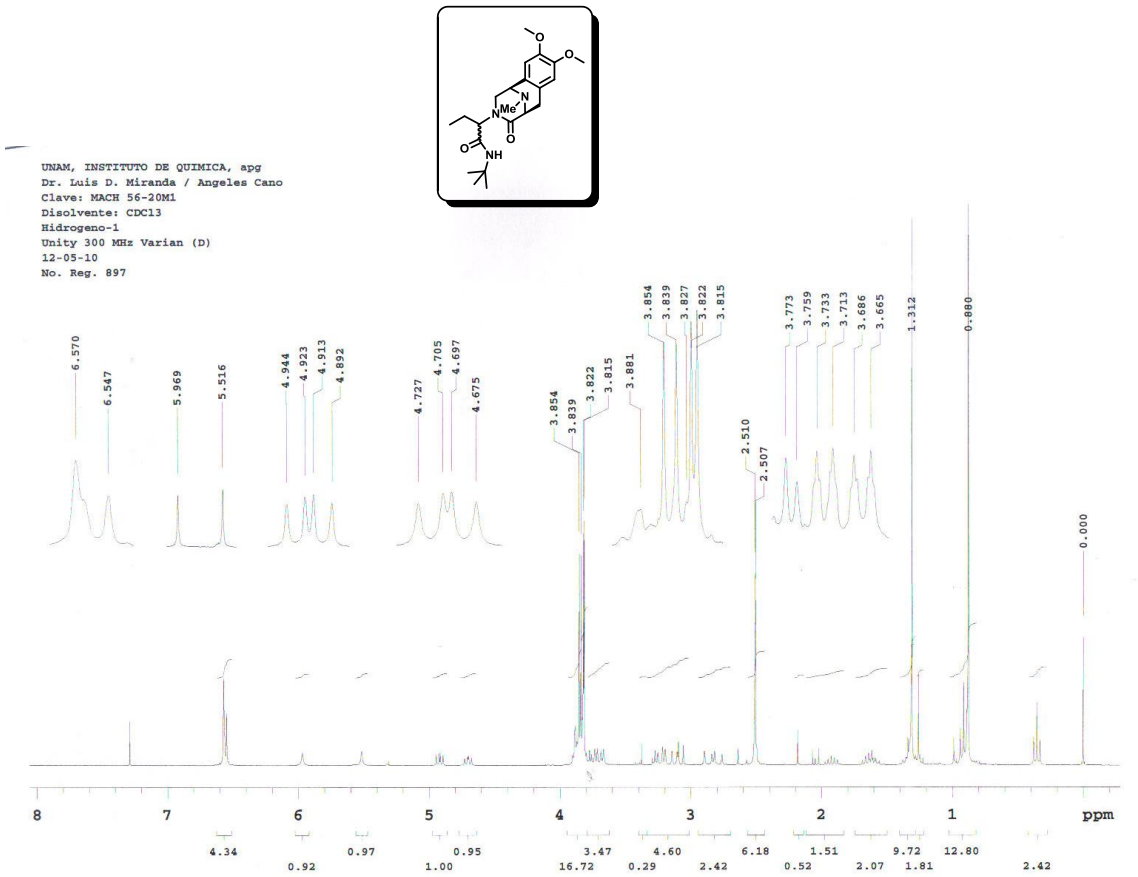


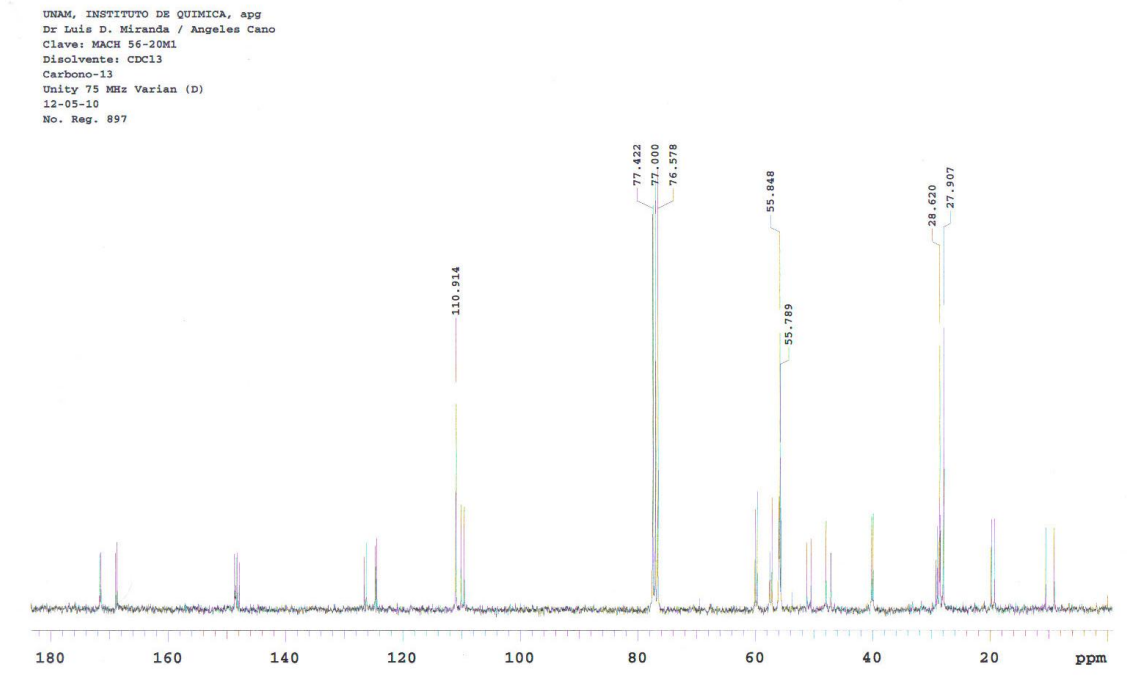
N-(*tert*-butyl)-2-(8,9-dimethoxy-11-methyl-4-oxo-1,4,5,6-tetrahydro-1,5-epimino-3-benzazocin-3(2H)-yl)acetamide 12a



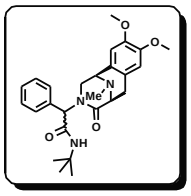


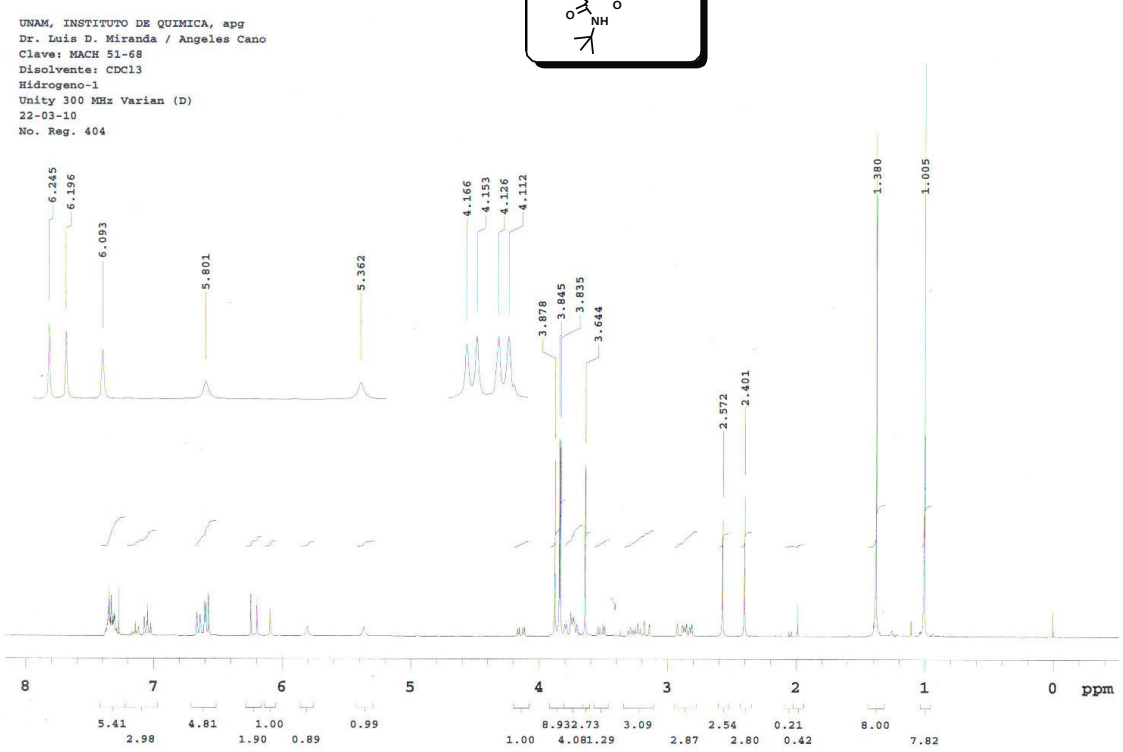
N-(*tert*-butyl)-2-(8,9-dimethoxy-11-methyl-4-oxo-1,4,5,6-tetrahydro-1,5-epimino-3-benzazocin-3(2H)-yl)butanamide 12b

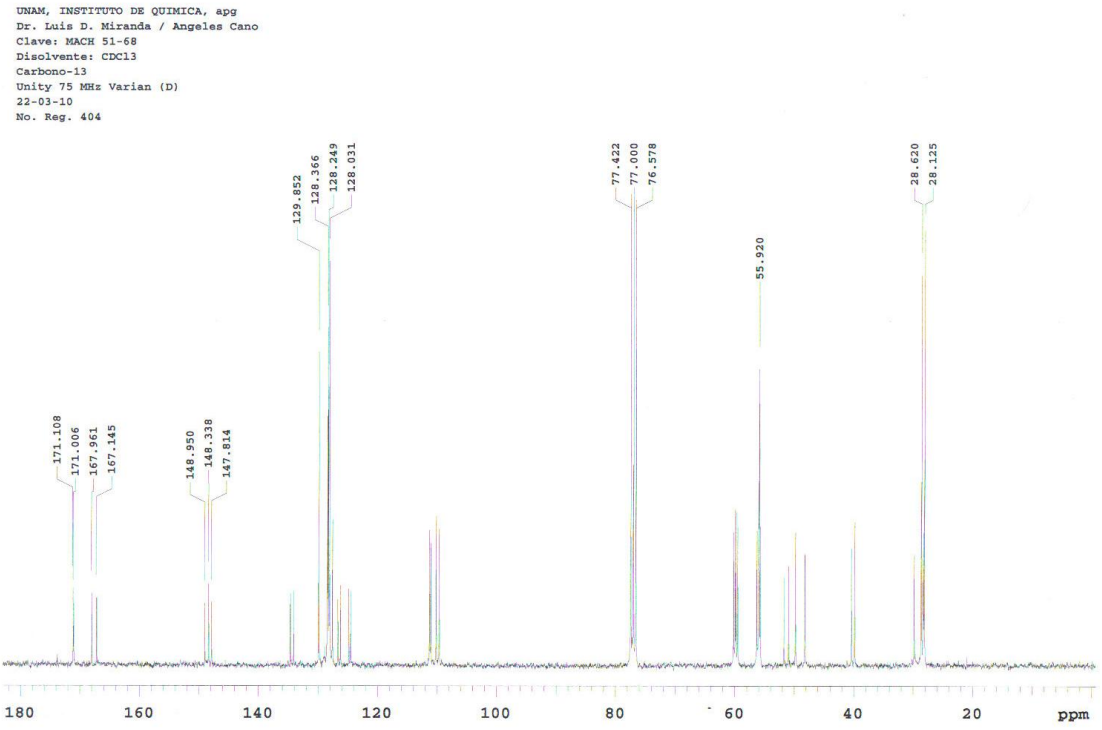




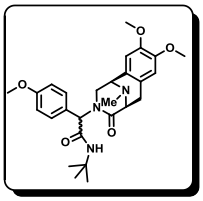
N-(*tert*-butyl)-2-(8,9-dimethoxy-11-methyl-4-oxo-1,4,5,6-tetrahydro-1,5-epimino-3-benzazocin-3(2H)-yl)-2-phenylacetamide 12c

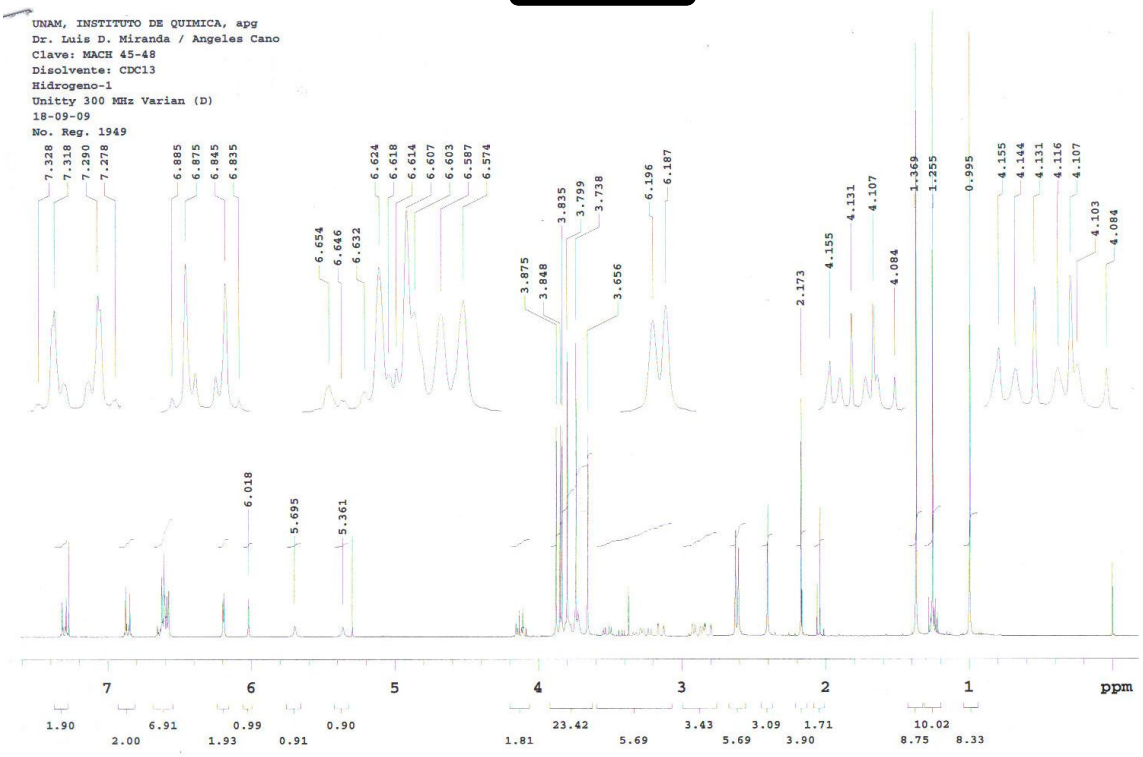


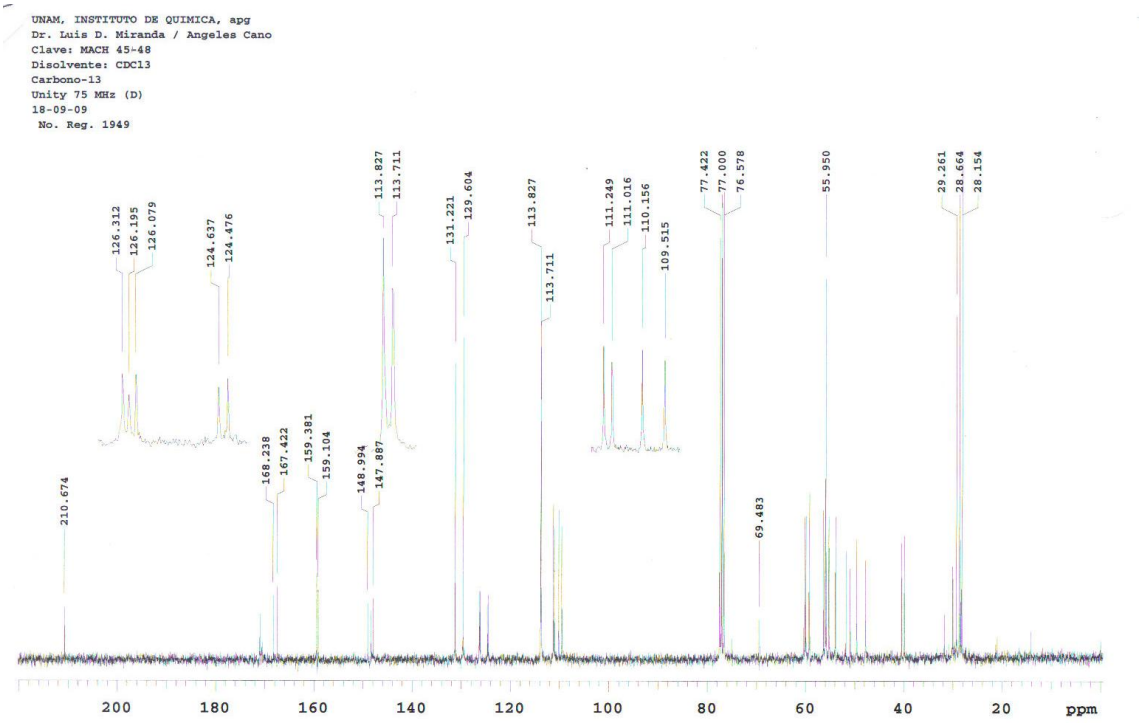




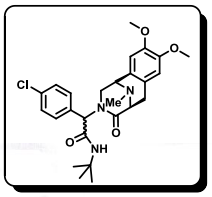
N-(*tert*-butyl)-2-(8,9-dimethoxy-11-methyl-4-oxo-1,4,5,6-tetrahydro-1,5-epimino-3-benzazocin-3(2H)-yl)-2-(4-methoxyphenyl)acetamide 12d

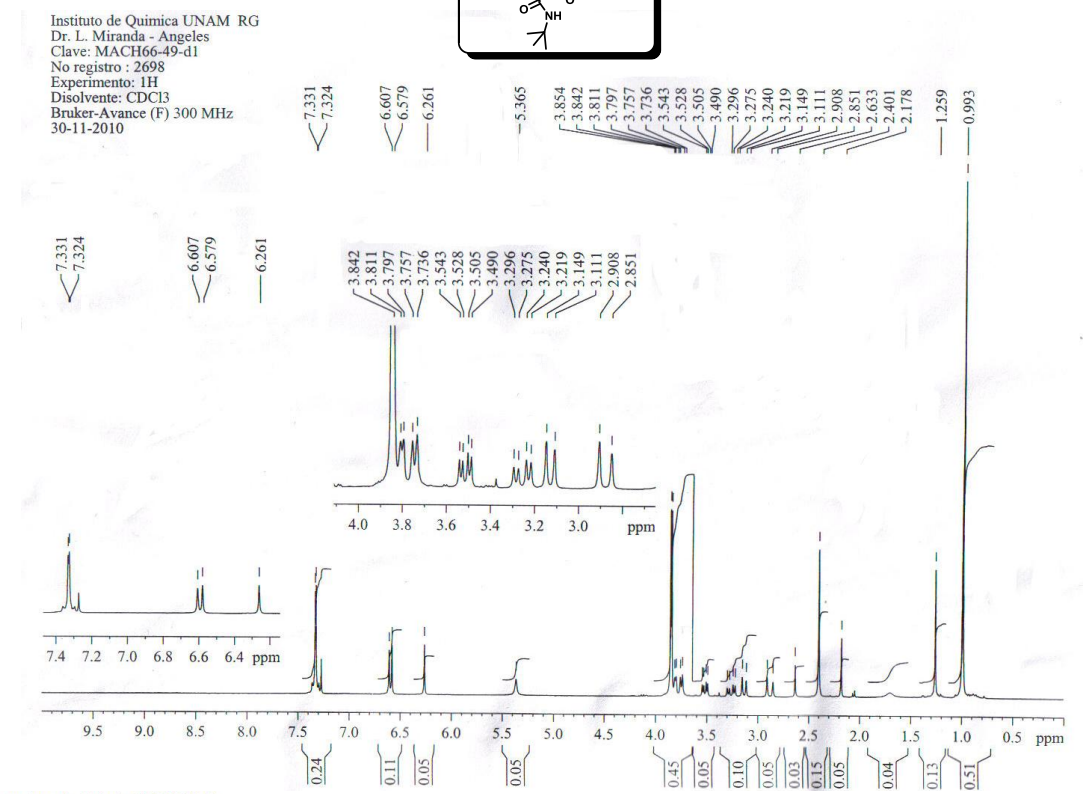


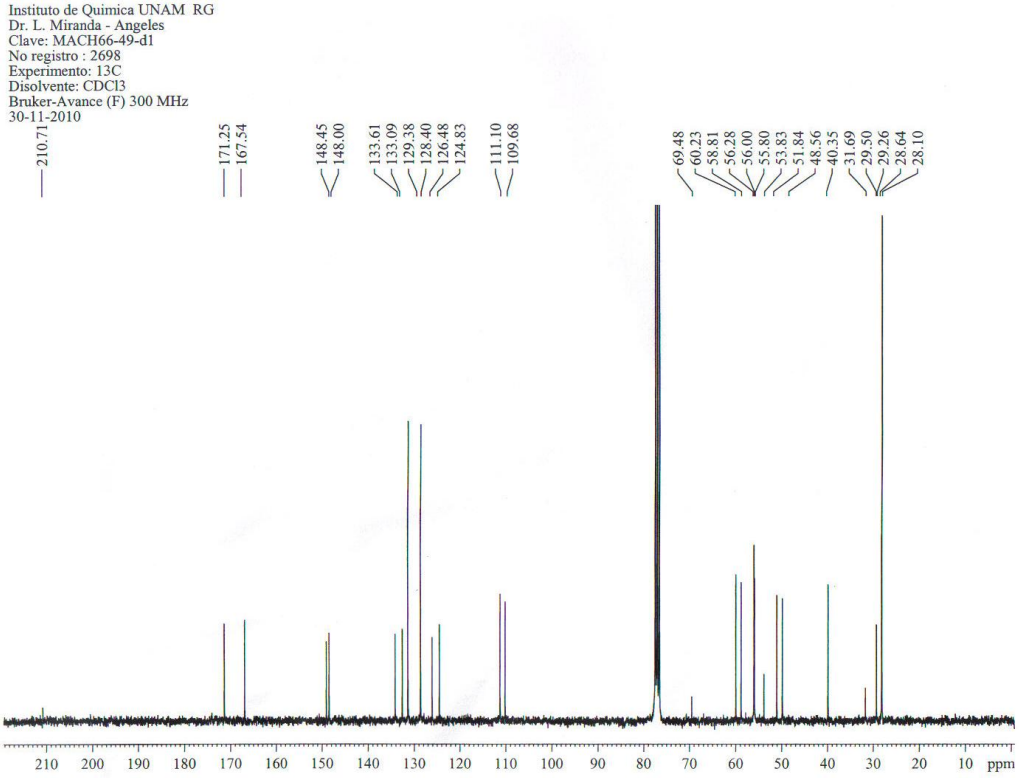




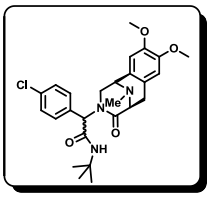
N-(*tert*-butyl)-2-(4-chlorophenyl)-2-(8,9-dimethoxy-11-methyl-4-oxo-1,4,5,6-tetrahydro-1,5-epimino-3-benzazocin-3(2H)-yl)acetamide 12e. Diastereoisomer 1

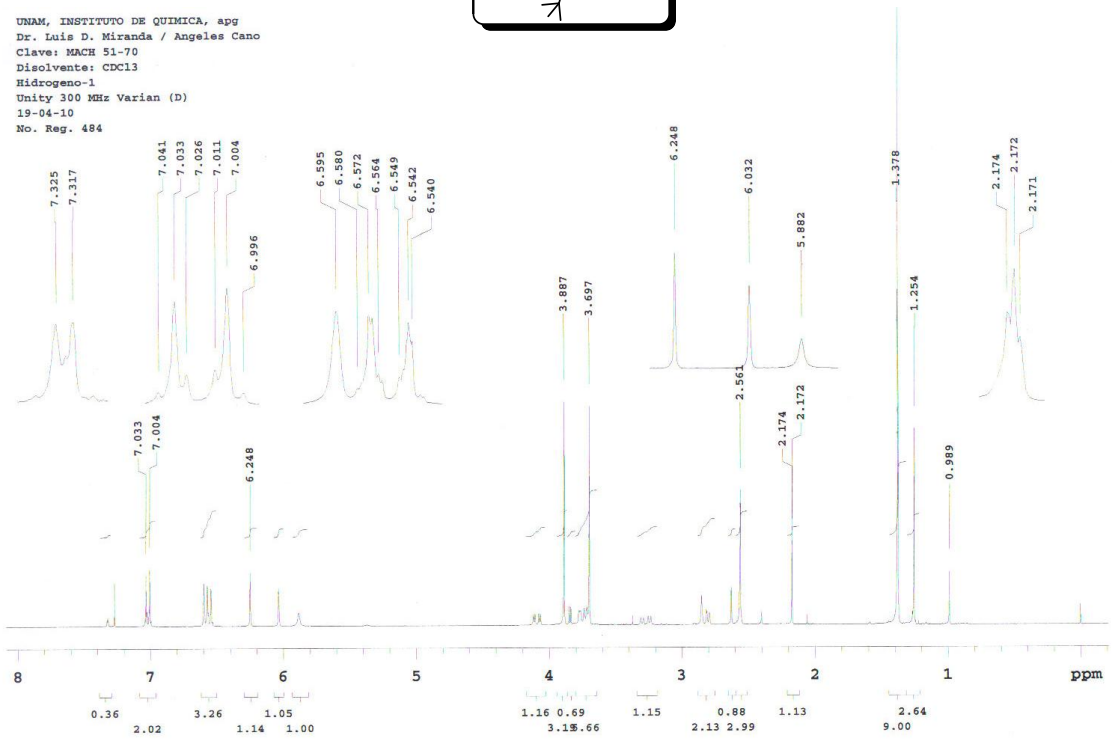


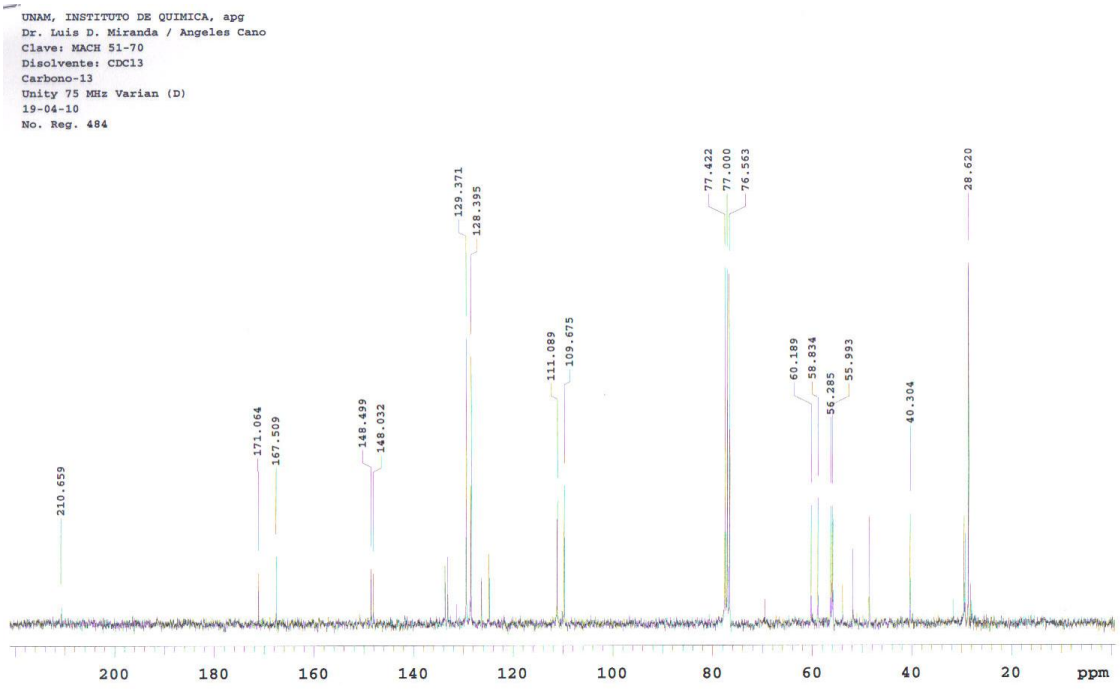




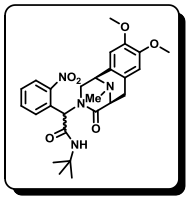
N-(*tert*-butyl)-2-(4-chlorophenyl)-2-(8,9-dimethoxy-11-methyl-4-oxo-1,4,5,6-tetrahydro-1,5-epimino-3-benzazocin-3(2H)-yl)acetamide 12e. Diastereoisomer 2

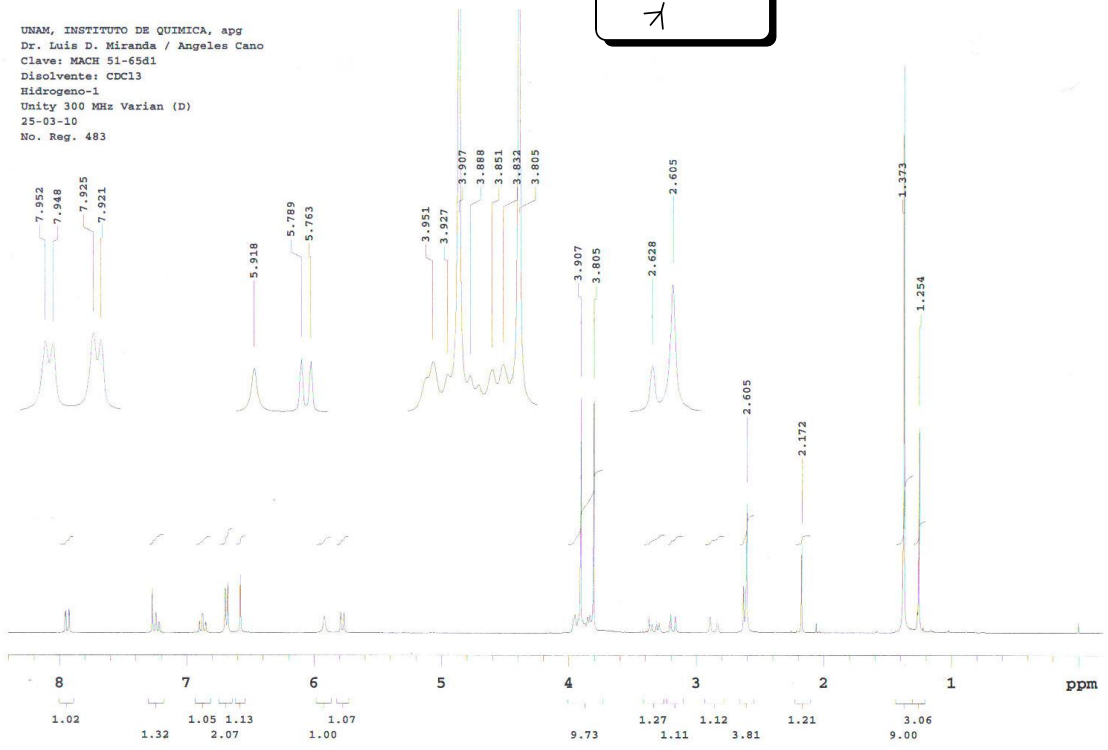


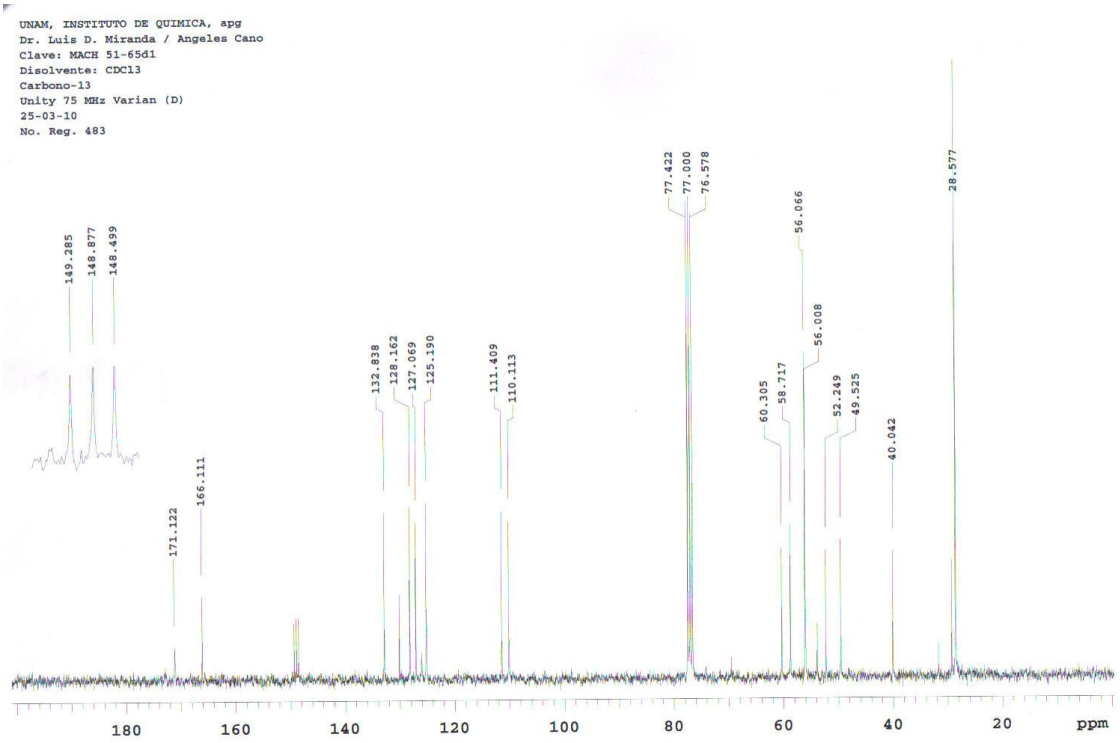




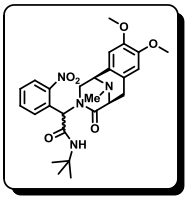
N-(*tert*-butyl)-2-(8,9-dimethoxy-11-methyl-4-oxo-1,4,5,6-tetrahydro-1,5-epimino-3-benzazocin-3(2H)-yl)-2-(2-nitrophenyl)acetamide 12f. Diastereoisomer 1

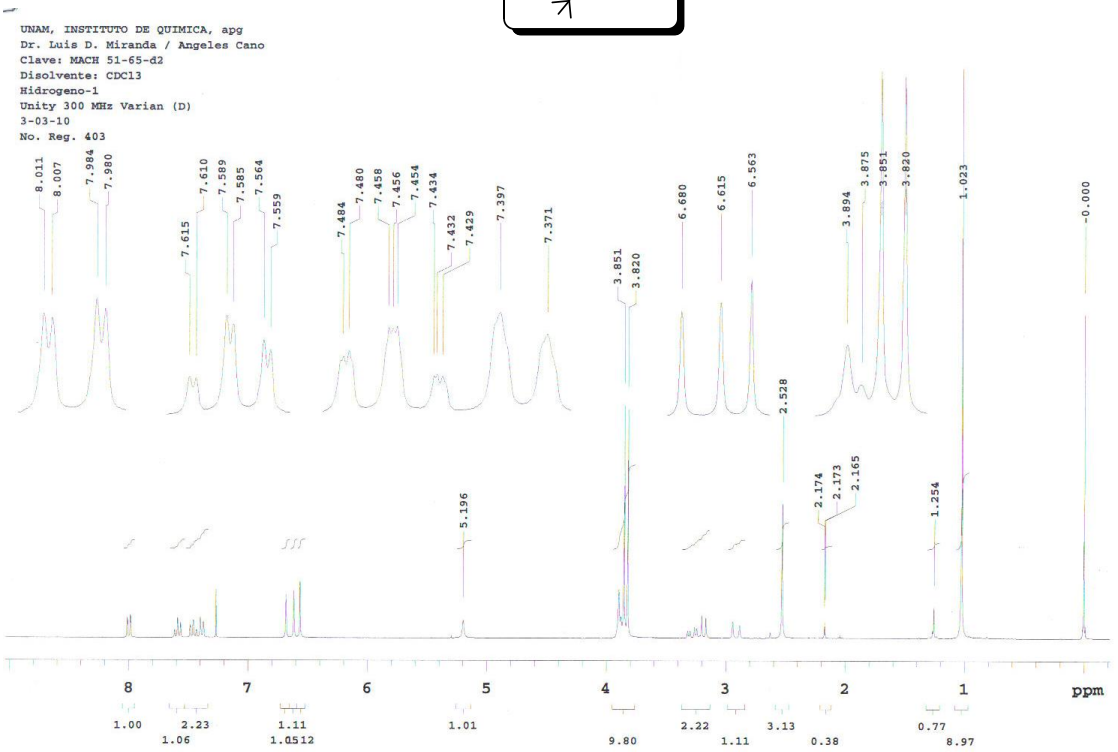


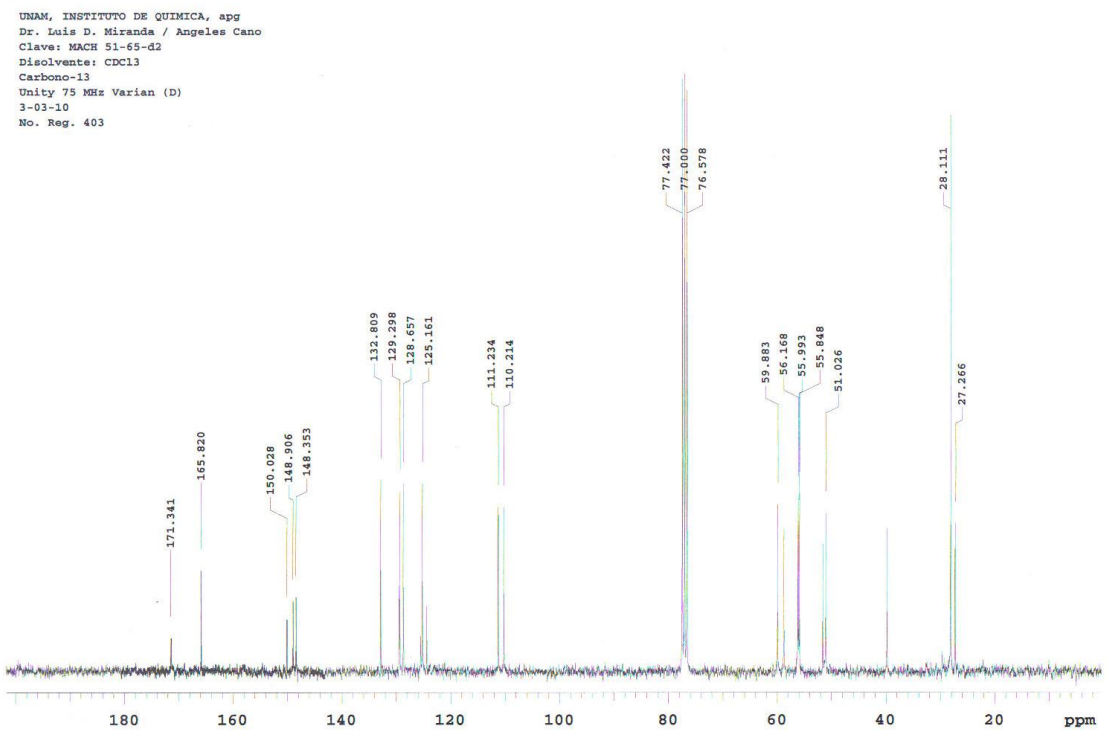




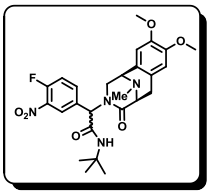
N-(*tert*-butyl)-2-(8,9-dimethoxy-11-methyl-4-oxo-1,4,5,6-tetrahydro-1,5-epimino-3-benzazocin-3(2H)-yl)-2-(2-nitrophenyl)acetamide 12f. Diastereoisomer 2

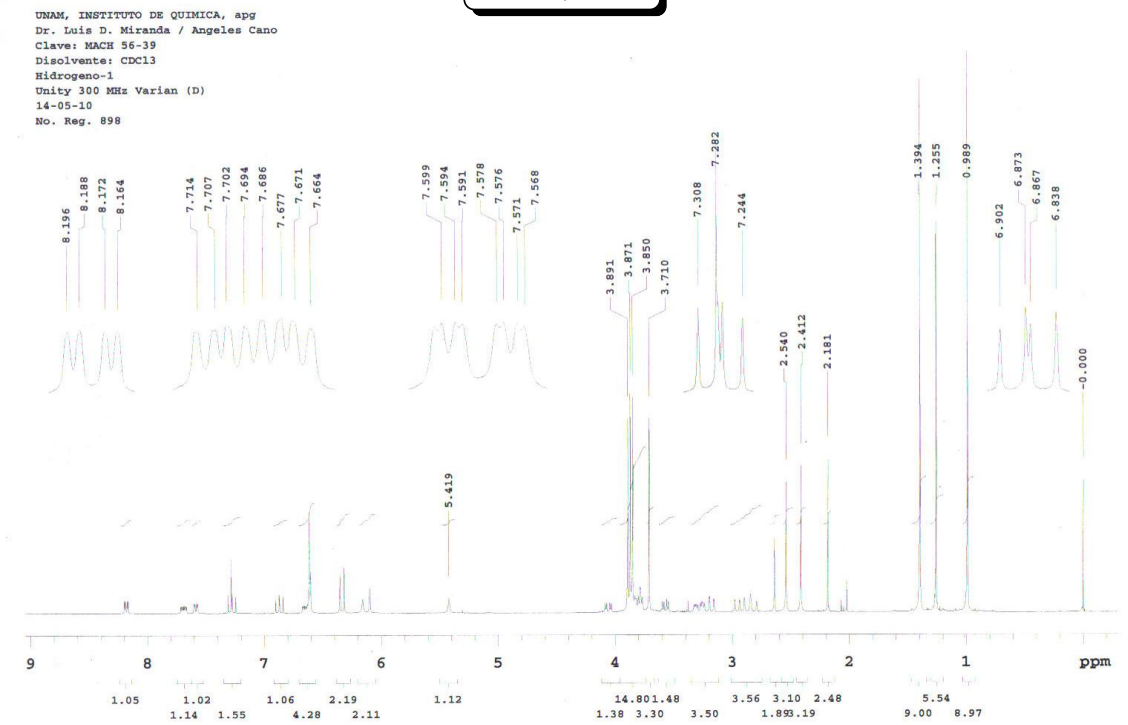


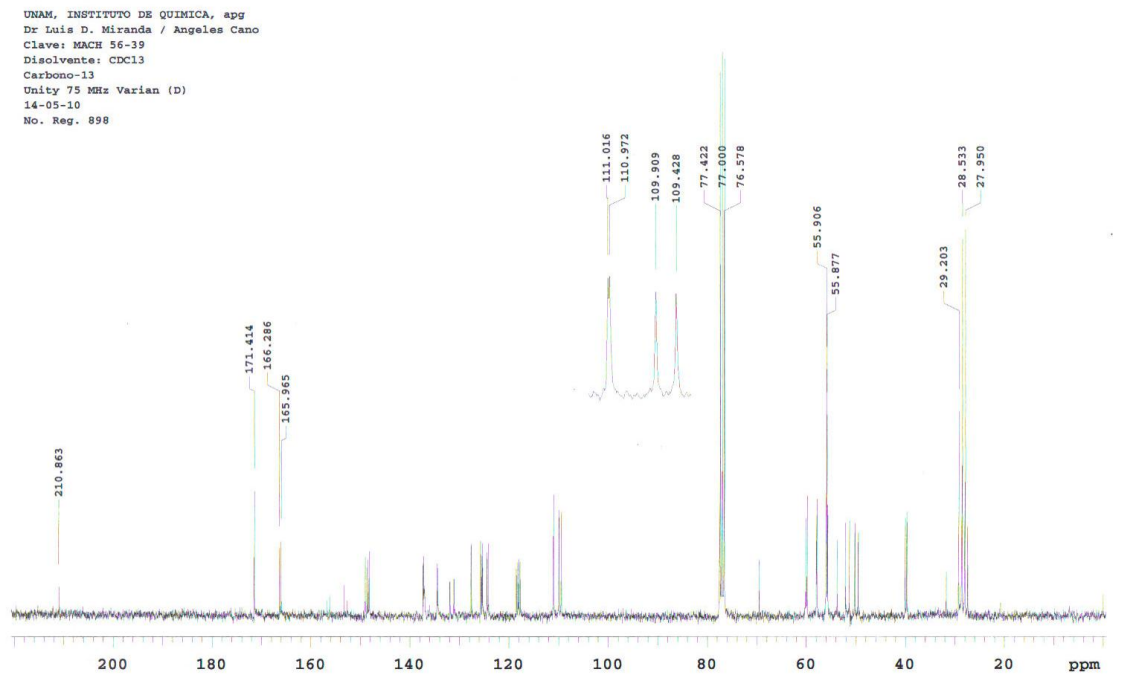




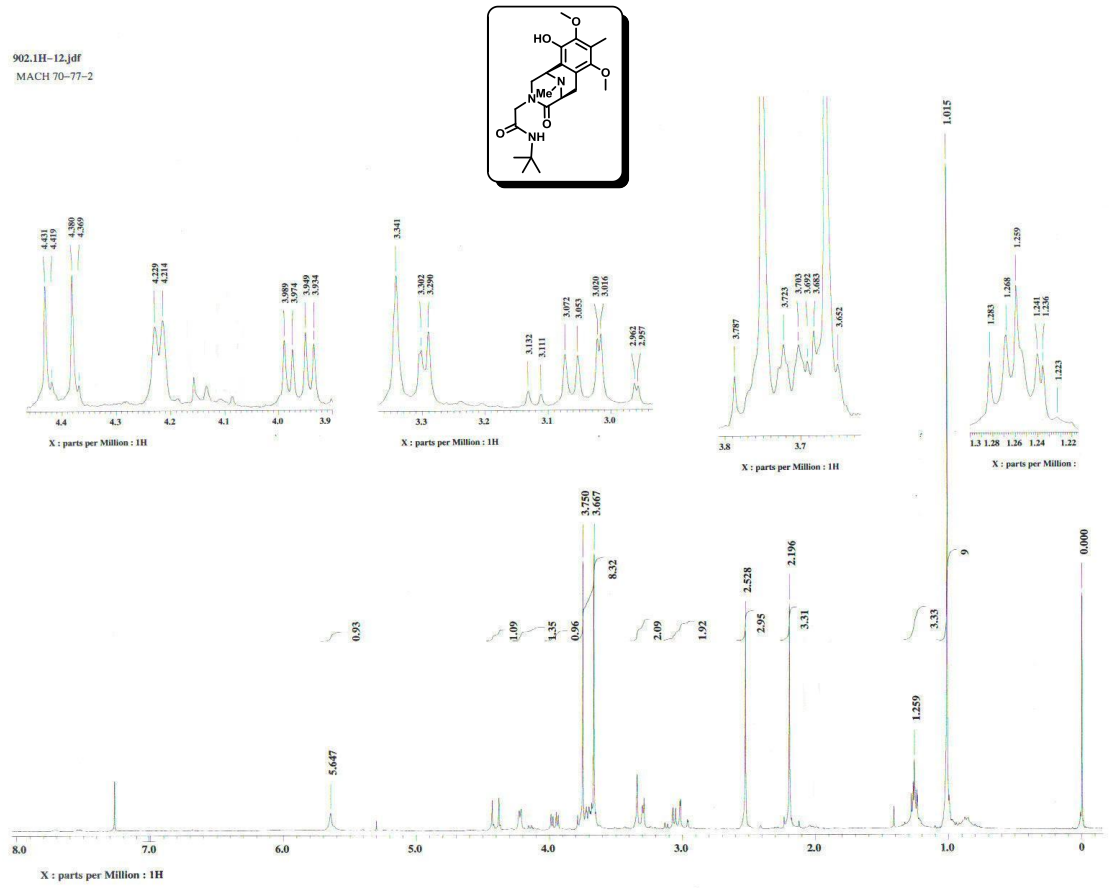
N-(*tert*-butyl)-2-(8,9-dimethoxy-11-methyl-4-oxo-1,4,5,6-tetrahydro-1,5-epimino-3-benzazocin-3(2H)-yl)-2-(4-fluoro-3-nitrophenyl)acetamide 12g

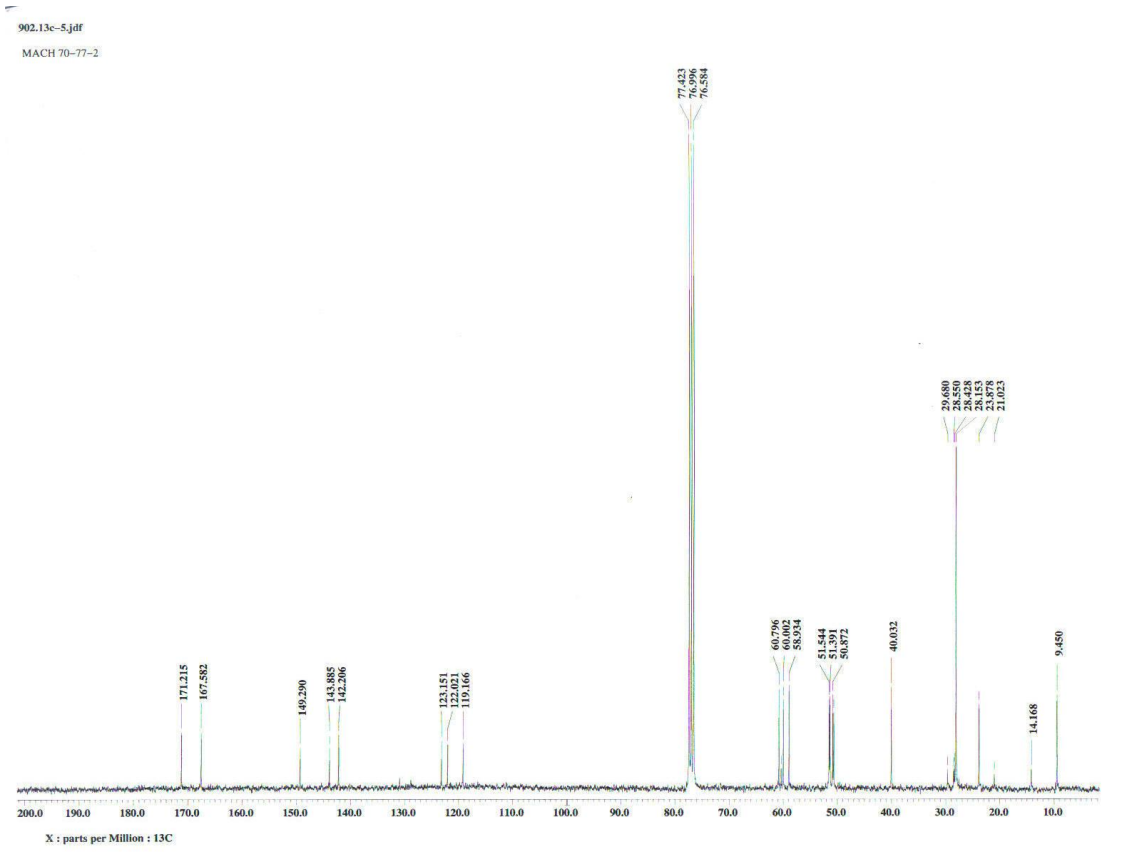




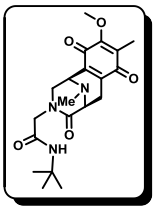


N-(*tert*-butyl)-2-(10-hydroxy-7,9-dimethoxy-8,11-dimethyl-4-oxo-1,4,5,6-tetrahydro-1,5-epimino-3-benzazocin-3(2H)-yl)acetamide 12h





Quinone 16



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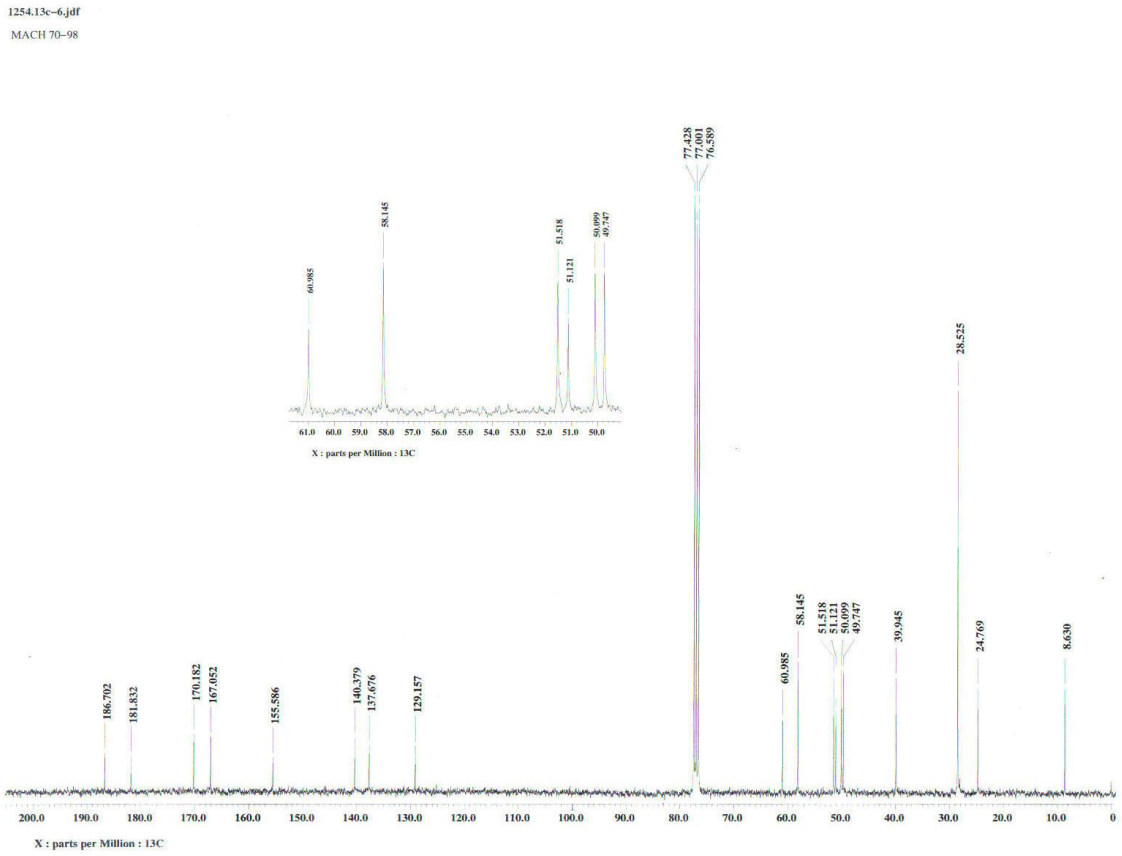
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