SUPPORTING INFORMATION

Ring Closing Alkyne Metathesis. Comparative Investigation of Two Different Catalyst Systems and Application to the Stereoselective Synthesis of Olfactory Lactones, Azamacrolides and the Macrocyclic Perimeter of the Marine Alkaloid Nakadomarin A

Alois Fürstner*, Oliver Guth, Antonio Rumbo and Günter Seidel

Max-Planck-Institut für Kohlenforschung, D-45470 Mülheim/Ruhr, Germany

e-mail: fuerstner@mpi-muelheim.mpg.de

General. All reactions were carried out under Ar in pre-dried glassware using Schlenk techniques. The solvents were dried by distillation over the drying agents indicated and were stored and transferred under Ar: CH_2Cl_2, chlorobenzene, 1,2,4-trichlorobenzene (P_4O_{10}), toluene (Na/K), THF (magnesium/anthracene), DMF (Desmodur®, Bayer AG; dibutyltin dilaurate), Et_3N (CaH_2), pyridine (KOH), EtOH (Mg), MeOH (Mg). Flash chromatography: Merck silica gel (230-400 mesh) or activated aluminum oxide (Aldrich, neutral, Brockmann I, STD grade, ≈ 150 mesh) using hexane/ethyl acetate in various proportions as eluent. NMR: Spectra were recorded on a Bruker AC 200, DPX 300, AMX 400 or DMX 600 spectrometer in $CDCl_3$ unless stated otherwise. Chemical shifts (δ) are given in ppm relative to TMS, coupling constants (*J*) in Hz. The multiplicity in the ^{13}C NMR spectra refers to the geminal protons (DEPT). IR: Nicolet FT-7199, wavenumbers in cm^{-1}. MS: Varian CH-5 (70 eV); HR-

MS: Finnigan MAT SSQ 7000 (70 eV). Specific optical rotations: Perkin Elmer 241. Elemental analyses: Dornis & Kolbe, Mülheim. 6-Octynol,[1] 7-nonynol[2] and 5-heptynoic acid[3] were prepared according to literature procedure. Commercially available reagents (Aldrich, Fluka) were used as received.

Model Studies (Table 1)

General Procedures for Ring Closing Alkyne Metathesis. Method A. A solution of the diyne substrate (0.5 mmol) and the tungsten alkylidyne catalyst $(tBuO)_3W{\equiv}CCMe_3$ (**1a**) (5 mol%) in chlorobenzene or toluene (20 mL) is heated to 80°C for 0.5-3 h under Ar. Evaporation of the solvent and purification of the residue via flash chromatography using hexane/ethyl acetate in different proportions as the eluent affords the corresponding cycloalkyne in analytically pure form. For the yields obtained see Table 1.

Method B. A solution of the diyne substrate (0.5 mmol), *p*-chlorophenol (0.5 mmol) and $Mo(CO)_6$ (0.025 mmol) in chlorobenzene (100 mL) is refluxed until TLC shows complete conversion of the starting material (usually 3-14 h). During this period, a gentle stream of Ar is bubbled through the reaction mixture. Evaporation of the solvent and purification of the crude product by flash chromatography with hexane/ethyl acetate in different proportions as the eluent affords the cycloalkyne products in the yields indicated in Table 1. The products thus obtained exhibit the following analytical and spectral data:

1,6-Dioxa-2,5-dioxocyclododec-9-yne (3). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.27 (t, 4H, J = 5.8), 2.70 (s, 4H), 2.47 (t, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.6, 78.7, 61.3, 29.9, 19.6. MS: *m/z* (rel intensity): 196 ([M^+], < 1), 166 (1), 101 (13), 78 (100), 66 (58), 55 (6), 40 (10), 28 (8).

---

[1] De Medeiros, E. F.; Herbert, J. M.; Taylor, R. J. K. *J. Chem. Soc. Perkin Trans. 1*, **1991**, 2725.

[2] Rossi, R.; Carpita, A.; Gaudenzi, L.; Quirici, M. G. *Gazz. Chim. Ital.* **1980**, *110*, 237.

[3] Flohr, H.; Pannhorst, W.; Retey, J. *Helv. Chim. Acta* **1978**, *61*, 1565.

Benzo-[c]-1,6-dioxa-2,5-dioxocyclododec-9-yne (4). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.69 (dd, 2H, *J* = 5.7 and 3.3 Hz), 7.53 (dd, 2H, *J* = 5.7 and 3.3 Hz), 4.45 (t, 4H, *J* = 5.5 Hz), 2.54 (quint., 4H, *J* = 5.5 and 1.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.7 (s), 133.1 (s), 130.9 (d), 128.4 (d), 78.9 (s), 62.7 (t), 19.2 (t); IR (KBr) υ = 3459, 3411, 3104, 3076, 3042, 2971, 2953, 2938, 2915, 1739, 1716, 1598, 1578, 1486, 1456, 1281, 1264, 746; MS *m/z* (rel. intensity): 244 ([M^+], 1), 149 (28), 78 (100).

2,4-Dioxo-cyclodedec-3-(*E*)-en-9-yn-1,6-dione (5). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.28 (s, 2H), 4.32 (t, 4H, *J* = 7.6 Hz), 2.49 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 165.0 (s), 129.6 (d), 79.4 (s), 62.4 (t), 19.4 (t); IR (KBr) ν = 3071, 2987, 2961, 2921, 1737, 1722, 1683, 1627, 1275; MS *m/z* (rel. intensity): 194 ([M^+], <1), 99 (12), 82 (6), 79 (7), 78 (100), 66 (53), 65 (20), 54 (11), 40 (19), 39 (15).

1-Oxa-2-oxocyclotetradec-11-yne (6). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.14 (t, 2H, *J* = 5.4), 2.53 (m, 2H), 2.39 (m, 2H), 2.17 (m, 2H), 1.65 (m, 2H), 1.56-1.28 (m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.8, 81.5, 77.4, 63.3, 26.8, 26.4, 25.9, 25.3, 24.7, 24.2, 19.1, 18.0. MS: *m/z* (rel intensity): 208 ([M^+], 5), 180 (20), 179 (20), 121 (14), 107 (32), 93 (41), 80 (100), 67 (34), 55 (32), 41 (39), 29 (14). Anal. *Calcd.* for $C_{13}H_{20}O_2$ (208.3): C, 74.94; H, 9.70; *Found*: C, 74.99; H, 9.41.

1,8-Dioxa-2,7-dioxocyclotetradec-11-yne (7). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.14 (t, 4H, *J* = 5.5), 2.53 (t, 4H, *J* = 5.6), 2.40 (m, 4H), 1.76 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.0, 77.8, 62.4, 34.8, 24.9, 19.0. MS: *m/z* (rel intensity): 224 ([M^+], < 1), 78 (100), 66 (21), 55 (10). Anal. *Calcd.* for $C_{12}H_{16}O_4$ (224.26): C, 64.24; H, 7.18; *Found*: C, 64.14; H, 7.15.

1-Azacyclopentandec-6-yn-2-one (8a). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.52 (bs, 1H), 3.28 (q, 2H, *J* = 5 Hz), 2.38 (t, 2H, *J* = 5 Hz), 2.29 (t, 2H, *J* = 6 Hz), 1.78 (m, 2H), 1.57-1.23 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 72.4 (s), 82.0 (s), 79.4 (s), 38.6 (t), 34.1 (t), 27.4 (t), 27.0 (t), 25.8 (t), 25.6 (t), 23.2 (t), 18.6 (t), 17.1 (t); IR (KBr) υ = 3311, 2933, 2859, 1649, 1550; MS *m/z* (rel. intensity): 222 (9), 221 ([M^+], 49), 220 (10), 193 (13), 192 (14), 178 (26), 165 (11), 164 (26), 138 (12), 137 (28), 136 (13), 133 (11), 124 (20), 123 (13), 122 (14), 121 (13), 112 (13), 111 (13), 110 (19), 109 (14), 108 (15), 97 (25), 96 (26), 95 (37), 94 (16), 83 (27), 82 (75), 81 (51), 79 (79), 67 (61), 56 (43), 55 (78).

1-Methyl-1-azacyclopentadec-6-yn-2-one (8b). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.20 (2H, t, *J* = 7.9 Hz), 2.90 (3H, s), 2.52 (2H, t, *J* = 7.7 Hz), 2.29-2.20 (4H, m), 1.78 (2H, m), 1.57 (2H, m), 1.45-1.23 (10H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.1 (s), 80.7 (s) , 79.9 (s), 49.8 (t), 33.5 (q), 31.3 (t), 27.4 (t), 26.3 (t), 26.0 (t), 25.9 (t), 25.6 (t), 23.9 (t), 23.6 (t), 17.9 (t), 17.8 (t); IR (KBr) υ = 2931, 2854, 1633, 1491, 1438, 1398, 1158; MS *m/z* (rel. intensity): 235 ([M^+], 32), 164 (12), 114 (12), 99 (13), 98 (11), 96 (44), 87 (16), 86 (13), 79 (24), 55 (40), 44 (100).

N-(9-Fluorenylmethyloxycarbonyl)-1-azacyclopentadec-6-yne (9). ^{1}H NMR (300 MHz, $CDCl_3$) (rotamers): δ = 7.75 (d, 2H, *J* = 7.2 Hz), 7.58 (d, 2H, *J* = 7.2 Hz), 7.41 (m, 4H), 4.56 (d, 1H, *J* = 5.5 Hz), 4.49 (d, 1H, *J* = 5.9 Hz), 4.22 (d, 1H, *J* = 2.4 Hz), 3.28 (d, 1H, *J* = 6.4 Hz), 3.20 (t, 1H, *J* = 8 Hz), 3.12 (t, 1H, *J* = 6.9 Hz), 2.91 (m, 3H), 2.20 (m, 3H), 2.12 (t, 1H, *J* = 6.4 Hz), 1.75 (m, 1H), 1.49-1.20 (m, 13H), 1.15 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) (rotamers): δ = 156.3 (s), 156.2 (s), 144.2 (s), 141.4 (d), 127.5 (d), 126.9 (d), 124.8 (d), 124.7 (t), 119.8 (d), 81.0 (s), 80.8 (s), 79.9 (s), 79.8 (s), 66.5 (t), 66.2 (t), 49.8 (t), 49.3 (t), 49.3 (t), 48.6 (t), 47.5 (d), 28.6 (t), 28.1 (t), 28.0 (t), 28.0 (t), 27.6 (t), 27.4 (t), 27.3 (t), 27.0 (t), 26.4 (t), 26.2 (t), 25.6 (t), 24.5 (t), 24.4 (t), 18.3 (t), 18.2 (t), 18.0 (t); IR (neat) υ = 3065, 3041, 3015, 2926, 2854, 1701, 1609, 1582, 1525, 1474, 1454, 1423, 1259, 1179, 739; MS *m/z* (rel. intensity): 429 ([M^+], 0.2), 179 (24), 178 (100).

1-Tosyl-1-aza-heptadec-9-yne (10). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.59 (d, 2H, *J* = 8.4), 7.22 (d, 2H), 2.95 (t, 4H, *J* = 7.2), 2.34 (s, 3H), 2.12 (m, 4H), 1.56 (m, 4H), 1.45 – 1.2 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.8, 136.1, 129.5, 127.1, 80.3, 50.3, 28.9, 28.4, 28.2, 27.5, 26.3, 21.4, 18.6. MS: *m/z* (rel intensity): 389 ([M^+], 9), 234 (100), 155 (12), 91 (38), 67 (10), 44 (14). Anal. *Calcd.* for $C_{23}H_{35}NO_2S$ (389.6): C, 70.91; H, 9.06; *Found*: C, 70.83; H, 9.23.

Cycloalkyne 11. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.21 (dd, 1H, *J* = 7.9), 7.03 (t, 1H, *J* = 1.9), 6.80 (ddd, 1H, *J* = 8.3, 2.5, 1), 6.75 (d, 1H, *J* = 7.9), 6.43 (d, 1H, *J* = 11.6), 5.72 (dt, 1H, *J* = 11.6, 7.7), 2.4 (m, 4H), 2.21 (m, 2H), 1.97 (m, 2H), 1.6 - 1.3 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.8, 139.0, 133.1, 129.2, 128.9, 121.6, 115.5, 111.4, 81.0, 79.4, 66.7, 30.0, 28.8, 28.7, 28.1, 28.0, 27.6, 18.3, 15.4. MS: *m/z* (rel intensity) 268 ([M^+], 100), 211

(23), 197 (15), 185 (17), 183 (13), 171 (17), 145 (18), 133 (23), 115 (21), 105 (23), 91 (31), 79 (35), 67 (20), 55 (16), 41 (25). Anal. *Calcd.* for $C_{19}H_{24}O$ (268.40): C, 85.02; H, 9.02. *Found*: C, 84.59; H, 8.95.

1-Oxa-cyclononadec-10-yn-2-one (12). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.13 (t, 2H, *J* = 5.5), 2.33 (t, 2H, *J* = 6.7), 2.17 (m, 4H), 1.65 (m, 4H), 1.55-1.25 (m, 18H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.0, 80.4, 80.3, 64.3, 34.9, 29.5, 29.4, 29.1, 29.0, 28.8, 28.7, 28.6, 28.3, 28.0, 26.2, 25.3, 18.6, 18.4. MS: *m/z* (rel intensity): 278 ([M^+], 33), 178 (15), 164 (49), 150 (37), 135 (47), 121 (72), 107 (46), 93 (71), 81 (88), 79 (81), 67 (96), 55 (100), 41 (92). Anal. *Calcd.* for $C_{18}H_{30}O_2$ (278.44): C, 77.66; H, 10.85; *Found*: C, 77.33; H, 11.01.

1-Phenylsulfonyl-cycloheneicos-11-yne (13). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.88 (m, 2H), 7.65 (m, 1H), 7.56 (m, 2H), 2.92 (m, 1H), 2.16 (m, 4H), 1.90 – 1.80 (m, 2H), 1.66 – 1.50 (m, 2H), 1.40 (m, 10H), 1.30 (m, 18H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.0, 133.4, 129.0, 128.7, 80.3, 63.9, 29.2, 28.9, 28.8, 28.54, 28.52, 28.4, 27.4, 25.8, 18.6. MS: *m/z* (rel intensity): 430 (20, [M^+]), 289 (51), 143 (59), 137 (17), 135 (19), 123 (31), 109 (55), 95 (96), 81 (100), 67 (84), 55 (77), 41 (53). Anal. *Calcd.* for $C_{27}H_{42}O_2S$ (430.68): C, 75.3; H 9.8; S 7.4; *Found*: C, 75.46, H 9.55, S 7.20.

1-Oxacyclotricos-12-yn-2-one (14). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.11 (t, 2H, *J* = 5.6 Hz), 2.30 (t, 2H, *J* = 7 Hz), 2.10 (m, 4H), 1.62 (m, 4H), 1.49-1.20 (m, 26H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.0 (s), 80.5 (s), 80.4(s), 64.2 (t), 34.8 (t), 29.6 (t), 29.5 (t), 29.4 (t), 29.3 (t), 29.2 (t), 29.0 (t), 28.7 (t), 28.6 (t), 28.5 (t), 28.4 (t), 28.2 (t), 26.2 (t), 25.3 (t), 18.5 (t), 18.4 (t); MS *m/z* (rel. intensity): 334 ([M^+], 30), 206 (13), 192 (21), 178 (28.3), 150 (14), 149 (29), 121 (51), 110 (23), 109 (31), 108 (33), 107 (33), 97 (15), 96 (44), 95 (66), 94 (51), 93 (53), 91 (20), 83 (25), 81 (90), 80 (57), 79 (62), 69 (56), 68 (39), 67 (90), 66 (10), 57 (15), 56 (11), 55 (100).

1-Sila-cyclotricos-12-yn-2,23-dione (15). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.65 (m, 4H), 7.38 (m, 6H), 3.78 (t, 4H, *J* = 6.3), 2.17 (m, 4H), 1.60 (m, 4H), 1.50 – 1.25 (m, 20H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 134.9, 133.3, 130.1, 127.8, 80.6, 63.7, 32.5, 29.8, 29.4, 29.2, 28.6, 28.4, 26.1, 18.5. MS: *m/z* (rel. intensity): 490 ([M^+], 25), 412 (80), 369 (14), 334 (29), 265 (9), 199 (98), 183 (31), 162 (19), 139 (100), 123 (42), 107 (16), 95 (26), 81 (35), 67 (41),

55 (35), 41 (26). Anal. *Calcd.* for $C_{32}H_{46}O_2Si$ (490.80): C, 78.3; H 9.4; *Found*: C, 78.18, H 9.29.

1,6-Dioxocyclotetracos-3-en-15-yn-2,5-dione (16). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.22 (s, 2H), 4.16 (t, 4H, *J* = 7.1 Hz), 2.10 (m, 4H), 1.66 (m, 4H), 1.45-1.30 (m, 20H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.3 (s), 129.5 (d), 80.6 (s), 65.4 (t), 28.9 (t), 28.5 (t), 28.4 (t), 28.3 (t), 25.6 (t), 18.5 (t); MS *m/z* (rel.intensity) 362 ([M^+], 11), 334 (17), 220 (12), 164 (20), 150 (37), 149 (14), 147 (10), 135 (37), 133 (14), 122 (18), 121 (56), 109 (17), 108 (25), 107 (36), 105 (16), 100 (11), 99 (35), 95 (45), 94 (43), 93 (57), 83 (19), 82 (31), 81 (68), 80 (54), 79 (73), 69 (27), 68 (30), 67 (81), 55 (100).

1,4-Dioxa-tetracos-14-yn-5,24-dione (17a). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.30 (s, 4H), 2.32 (t, 4H, *J* = 7.6), 2.17 (m, 4H), 1.64 (m, 4H), 1.42 (m, 8H), 1.31 (12H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.5, 80.6, 61.8, 34.5, 29.3, 29.0, 28.9, 28.5, 28.3, 25.3, 18.6. MS: *m/z* (rel intensity): 364 ([M^+], 21), 346 (15), 336 (4), 321 (5), 302 (4), 281 (6), 236 (14), 222 (14), 192 (72), 178 (100), 169 (82), 155 (72), 99 (83), 81 (57), 79 (54), 67 (65), 55 (86), 41 (62). Anal. *Calcd.* for $C_{22}H_{36}O_4$ (364.53): C, 72.48; H, 9.96; *Found*: C, 72.57; H, 9.88.

1,4-Diaza-5,24-dioxo-tetracos-14-yne (17b). MS: *m/z* (rel intensity): 362 ([M^+], 18), 334 (17), 237 (16), 221 (22), 206 (14), 178 (12), 168 (13), 154 (10), 135 (14), 126 (10), 95 (40), 81 (51), 67 (67), 55 (91), 44 (79), 30 (100).

1,8-Dioxa-cyclotriacont-4-(*E*)-en-19-yn-2,7-dione (18). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.68 (m, 2H), 4.07 (t, 4H, *J* = 6.5 Hz), 3.05 (dd, 4H, *J* = 4.0 and 1.6 Hz), 2.14 (m, 4H), 1.60 (t, 4H, *J* = 6.7 Hz), 1.43-1.28 (m, 28H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.3 (s), 125.9 (d), 80.4 (s), 64.7 (t), 38.2 (t), 29.3 (t), 29.2 (t), 29.1 (t), 28.9 (t), 28.7 (t), 28.5 (t), 28.3 (t), 25.8 (t), 18.57 (t); IR (KBr) υ = 3037, 2937, 2930, 2916, 2851, 1730, 1274, 961; MS *m/z* (rel. intensity): 446 ([M^+], 12), 192 (31), 178 (44), 149 (16), 136 (12), 135 (25), 127 (41), 122(15), 121 (34), 67 (73), 55 (100).

Syntheses of Ambrettolide (23) and Yuzu Lactone (24) (Scheme 2)

7-Nonynoic Acid. PDC (20.1 g, 53 mmol) was added to a solution of 7-nonyn-1-ol (3.0 g, 21.4 mmol) in DMF (80 mL). After stirring overnight, the reaction was quenched with brine (1 L), the aqueous layer was extracted with *tert*-butylmethyl ether (6x100 mL), the combined organic phases were washed with 10% HCl, brine (2x100 mL each), dried (Na_2SO_4), filtrated and evaporated. The residue was purified by flash chromatography (hexane/EtOAc, 4:1) to afford 7-nonynoic acid (2.6 g, 79 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 11.5 (bs, 1H), 2.36 (t, 2H, J = 7.4 Hz), 2.12 (m, 2H), 1.76 (t, 3H, J = 2.4 Hz), 1.69-1.40 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 180.4, 78.8, 75.6, 33.9, 28.6, 28.2, 24.1; IR (KBr) υ = 3039, 2935, 2859, 2688, 1690, 918; MS *m/z* (rel intensity): 154 ([M^+], 0.5), 95 (21), 94 (99), 93 (15), 83 (11), 81 (29), 79 (74), 77 (13), 73 (5), 69 (7), 68 (100).

9-Undecynyl 7-Nonynoate (26). DCC (1.47 g, 7.1 mmol) and DMAP (100 mg) were added to a solution of 7-nonynoic acid (1.0 g, 6.49 mmol) and 9-undecynol (1.1 g, 6.49 mmol) in CH_2Cl_2 (30 mL) and the resulting mixture was stirred overnight. A standard work-up followed by flash chromatography of the residue (hexane/Et_2O, 10:1) gave ester **26** as a colorless liquid (1.79 g, 98%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.04 (t, 2H, J = 6.7 Hz), 2.27 (t, 2H, J = 7.4 Hz), 2.11 (m, 4H), 1.76 (t, 6H, J = 2.2 Hz), 1.63-1.30 (m, 18H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.9 (s), 79.2 (s), 79.0 (s), 75.4 (s), 75.3 (s), 64.3 (t), 34.3 (t), 28.9 (t), 28.9 (t), 28.6 (t), 28.7 (t), 28.6 (t), 28.5 (t), 28.4 (t), 25.4 (t), 24.9 (t), 29.8 (t), 18.6 (t), 18.5 (t), 3.4 (q); MS *m/z* (rel. intensity): 289 ([M^+], 1.7), 161 (12), 147 (16), 133 (18), 123 (16), 122 (22), 121 (30), 120 (13), 119 (27), 109 (12), 108 (20), 107 (46), 105 (19), 95 (33), 94 (22), 93 (46), 91 (17), 82 (10), 81 (100).

1-Oxacycloheptadec-8-yn-2-one (27). A solution of diyne **26** (600 mg, 1.81 mmol), *p*-chlorophenol (231 mg, 1.81 mmol) and $Mo(CO)_6$ (24 mg, 0.09 mmol) in chlorobenzene was refluxed overnight. The reaction mixture was purged by a gentle stream of Ar. The solvent was evaporated and the residue was chromatographed (hexane/Et_2O, 30:1→20:1) to give cycloalkyne **27** (340 mg, 69%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.16 (t, 2H, J = 5.5 Hz), 2.34 (t, 2H, J = 6.2 Hz), 2.19 (d, 4H), 1.65 (m, 4H), 1.59-1.36 (m, 14 H); ^{13}C NMR (75 MHz,

$CDCl_3$): δ = 173.9 (s), 80.3 (s), 80.2 (s), 63.9 (t), 34.6 (t), 28.6 (t), 28.4 (t), 28.3 (t), 28.1 (t), 28.0 (t), 27.0 (t), 24.9 (t), 18.7 (t), 18.4 (t); IR (neat) υ = 2930, 2858, 2213,1735, 1184; MS *m/z* (rel. intensity): 250 ([M^+], 12), 136 (27), 135 (23), 122 (13), 121 (30), 119 (13), 109 (12), 108 (26), 107 (38), 106 (11), 105 (18), 97 (15), 96 (16), 95 (42), 94 (99), 93 (84), 92 (21), 91 (41), 82 (26), 81 (62), 80 (50), 79 (90), 78 (12), 77 (30), 67 (80), 55 (100).

Ambrettolide (23). To a solution of cycloalkyne **27** (125 mg, 0.5 mmol) in hexane was added 2 mL of a solution of quinoline (100 μL in 10 mL hexane) and Lindlar catalyst (20 mg). The mixture was cooled to -78°C, the flask was evacuated and purged with H_2 (1 atm). The reaction was stirred for 90 min and filtrated through celite. The solid residues were thoroughly washed with *tert*-butylmethyl ether (3x20 mL), the combined organic layers were washed with 10% aq. HCl (3x10 mL), dried (Na_2SO_4) and evaporated. Flash chromatography of the residue (hexane/Et_2O, 20:1) afforded ambrettolide **23** (123 mg, 98%). ^1H NMR (300 MHz, $CDCl_3$): δ = 5.30 (m, 2H), 4.12 (t, 2H, *J* = 5.3 Hz), 2.31 (t, 2H, *J* = 6.5 Hz), 2.03 (m. 4H), 1.60 (m, 4H), 1.43-1.17 (m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.9 (s), 130.1 (d), 13.0 (d), 63.7 (t), 34.5 (t), 29.4 (t), 28.7 (t), 28.6 (t), 28.4 (t), 28.4 (t), 28.31 (t), 27.6 (t), 26.9 (t), 26.7 (t), 25.3 (t), 25.2 (t).

9-Undecynoic acid. PDC (22.38 g, 59.5 mmol) was added to a solution of 9-undecinol (4.0 g, 23.8 mmol) in DMF (100 mL). After stirring overnight, the reaction was quenched with brine (1 L), the aqueous layer was extracted with *tert*-butylmethyl ether (6x100 mL), the combined organic phases were washed with 10% HCl and brine (2x100 mL each), dried (Na_2SO_4), filtrated and evaporated. Flash chromatography of the residue (hexane/EtOAc, 4:1) affords 9-undecynoic acid (3.29 g, 76%). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.32 (t, 2H, *J* = 6.4 Hz), 2.09 (m, 2H), 1.75 (t, 3H, *J* = 2.6 Hz), 1.61 (m, 2H), 1.44-1.31 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 180.4 (s), 79.2 (s), 75.3 (s), 34.0 (t), 28.9 (t), 28.9 (t), 28.7 (t), 28.6 (t), 28.5 (t), 24.6 (t), 18.6 (t), 3.4 (q); IR (KBr) υ = 3037, 2927, 2854, 2694, 1686, 1336, 1297, 1272, 917; MS *m/z* (rel.intensity): 182 ([M^+], 0.2), 95 (20), 93 (11), 81 (27), 79 (12), 69 (19), 68 (100).

3-Pentynyl 9-undecynoate (28). DCC (1.22 g, 6 mmol) and DMAP (100 mg) were added to a solution of 9-undecynoic acid (1.0 g, 5.4 mmol) and 3-pentynol (534 μL, 5.8 mmol) in CH_2Cl_2. The reaction was stirred overnight. For work-up, the white precipitate was filtered

off and the filtrate was processed as usual affording compound **28** as a colorless syrup after flash chromatography (hexane/EtOAc, 20:1) (1.33 g, 98%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.1 (t, 2H, *J* = 7 Hz), 2.44 (m, 2H), 2.29 (t, 2H, *J* = 7.5 Hz), 2.08 (m, 2H), 1.76 (t, 6H, *J* = 2.5 Hz), 1.61 (m, 2H), 1.44-1.28 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.5 (s), 79.2 (s), 77.1 (s), 75.3 (s), 74.7 (s), 62.6 (t), 34.1 (t), 28.7 (t), 28.6 (t), 24.8 (t), 19.2 (t), 18.6(t), 3.4 (q); IR (neat) υ = 2932, 2857, 2237, 1739, 1171; MS *m/z* (rel.intensity): 280 ([M^+], 0.2), 121 (11), 120 (13), 119 (31), 105 (22), 95 (18), 93 (14), 91 (11), 69 (12), 68 (34), 67 (100).

1-Oxacyclotridec-10-yn-2-one (29). A solution of the diyne **28** (600 mg, 2.42 mmol), *p*-chlorophenol (300 mg, 2.42 mmol) and $Mo(CO)_6$ (32 mg, 0.121 mmol) in chlorobenzene (500 mL) was refluxed overnight while a gentle stream of Ar was bubbled through the reaction mixture. The solvent was evaporated and the residue was chromatographed (hexane/Et_2O, 20:1→10:1) to give analytically pure cycloalkyne **29** (146 mg, 62%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.15 (t, 2H, *J* = 5.5 Hz), 2.48 (m, 2H), 2.35 (t, *J* = 6 Hz), 1.71 (m, 2H), 1.45-1.33 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.8 (s), 82.6 (d), 62.5 (t), 34.4 (t), 27.5 (t), 27.0 (t), 26.9 (t), 26.6 (t), 24.5 (t), 19.2 (t), 18.6 (t); IR (neat) υ = 2932, 2859, 2219, 1734, 1668, 1248; MS *m/z* (rel. intensity): 194 ([M^+], 0.5), 107 (21), 94 (15), 93 (39), 91 (21), 81 (22), 80 (100).

Yuzu Lactone (24). To a solution of cycloalkyne **29** (100 mg, 0.51 mmol) in hexane was added 2 mL of a solution of quinoline (100 μL in 10 mL hexane) and Lindlar catalyst (20 mg). The flask was filled with H_2 (1 atm) after freeze/thaw cycles and the mixture was stirred for 90 min at r.t. Standard work-up followed by flash chromatography (hexane/Et_2O, 20:1) gave analytically pure Yuzu Lactone **24** (99 mg, 98%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.39 (m, 2H), 4.23 (dd, 2H, *J* = 6.4 and 5.3 Hz), 2.38 (m, 2H), 2.28 (dd, 2H, *J* = 6.8 and 3.1 Hz), 2.09 (dd, 2H, *J* = 12.4 and 5.4 Hz), 1.71-1.13 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.7 (s), 132.2 (d), 127.1 (d), 64.1 (t), 35.3 (t), 29.7 (t), 27.5 (t), 27.2 (t), 25.9 (t), 25.8 (t), 24.6 (t), 23.5 (t).

Synthesis of Epilachnene (31) (Scheme 4)

Undec-2-yn-8-ol (39). PDC (17 g, 45.0 mmol) was added to a stirred solution of 6-octyn-1-ol (4.0 g, 31.7 mmol) in CH_2Cl_2 (250 mL) and the resulting suspension was stirred overnight. The reaction was quenched with brine (700 mL), the aqueous layer was extracted with CH_2Cl_2 (4x80 mL), the combined organic phases were successively washed with brine and H_2O (100 mL each), dried (Na_2SO_4) and evaporated. The residue was distilled in vacuo, thus providing 6-octynal as a colorless liquid (3.27 g, 76%). b.p. = 56°C (37.5 torr). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.77 (t, 1H, J = 1.8 Hz), 2.44 (dt, 2H, J = 7.2 and 1.8 Hz), 2.14 (2H, m), 1.76 (t, 2H, J = 2.6 Hz), 1.70 (2H, m), 1.51 (q, 2H, J = 7.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.4 (d) , 78.4 (s), 75.9 (s), 43.4 (t), 28.3 (t), 21.2 (t), 3.4 (q). This compound was used directly in the next reaction: A solution of n-propylmagnesium bromide (11 mL, 22 mmol, 2 M in Et_2O) was added to a solution of 6-octynal (3.0 g, 22.0 mmol) in THF (80 mL) at 0°C. After 1 h, the reaction was quenched with H_2O (30 mL) and the aqueous layer was extracted with *tert*-butylmethyl ether (3x80 mL). The residue was chromatographed (hexane/EtOAc 10:1) providing alcohol **39** as a colorless liquid (3.77 g, 94%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.58 (q, 1H, J = 6.2 Hz), 2.10 (m, 2H), 1.74 (t, 3H, J = 2.5 Hz), 1.62 (m, 1H), 1.48-1.28 (m, 9H), 0.90 (t, 3H, J = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 79.0 (s), 75.5 (s), 71.5 (d), 39.5 (t), 36.9 (t), 26.8 (t), 24.8 (q), 18.7 (q), 18.6 (t), 14.0 (t), 3.3 (t) IR (neat) υ = 3384, 2933, 2863, 1709, 1461, 1127; MS *m/z* 166 ([M^+], 0.1), 121 (17), 107 (20), 95 (11), 93 (23), 81 (49), 79 (40), 67 (56), 55 (100).

8-(Methanesulfonyloxy)-undec-2-yne (40). Mesyl chloride (1.53 mL, 19.8 mmol) was slowly added to a solution of alcohol **39** (3.0 g, 18.0 mmol) and Et_3N (2.76 mL, 19.8 mmol) in CH_2Cl_2 (25 mL) at 0°C. After 30 min, the reaction was quenched with H_2O (40 mL), the aqueous layer was extracted with CH_2Cl_2 (2 x 30 mL), the combined organic layers were successively washed with 10% HCl, aq. sat. $NaHCO_3$ and brine (30 mL each), dried (Na_2SO_4) and evaporated. Flash chromatography (hexane/EtOAc 10:1) afforded compound **40** as a colorless liquid (4.35 g, 98%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.69 (quint., 1H, J = 6Hz), 2.98 (s, 3H), 2.10 (m, 2H), 1.74 (t, 3H, J = 2.5 Hz), 1.65 (m, 4H), 1.40 (m, 6H), 0.9 (t,

3H, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 83.8 (d), 78.6 (s), 75.7 (s), 38.5 (t), 36.5 (t), 33.9 (t), 28.5 (t), 24.0 (t), 18.4 (t), 18.2 (t), 13.7 (q), 3.3 (q); IR (neat) υ = 3026, 2939, 2878, 1462, 1337, 1175, 910; MS *m/z* 246 ([M^+], 0.1), 162 (10), 150 (23), 135 (30), 122 (10), 121 (61), 109 (22), 108 (44), 107 (58), 96 (14), 94 (50), 93 (80), 91 (20), 81 (12), 81 (42), 79 (95), 66 (100).

2-(1-Propyloct-6-ynylamino)ethanol (41). A solution of mesylate **40** (2 g, 8.13 mmol) in 2-aminoethanol (10 mL) was refluxed for 6 h. After cooling, the reaction was quenched with sat. aq. $NaHCO_3$, the aqueous layer was extracted with *tert*-butylmethyl ether (5x30 mL), the combined organic layers were dried (Na_2SO_4) and the solvent evaporated. Flash chromatography (hexane/EtOAc, 10:1 → 0/1) furnished aminoalcohol **41** as a colorless syrup (1.44 g, 84%). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 3.60 (t, 2H, J = 5.3 Hz), 3.2 (bs, 2H), 2.74 (t, 2H, J = 5.5 Hz), 2.51 (quint, 1H, J = 5.2 Hz), 2.18-1.92 (m, 2H), 1.75 (t, 3H, J = 2.6 Hz), 1.53-1.23 (m, 8Hz), 0.89 (t, 3H, J = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 78.9 (s), 75.5 (s), 60.8 (t), 56.9 (d), 47.9 (t), 36.0 8t), 33.2 (t), 29.1 (t), 24.8 (t), 18.8 (t), 14.2 (q), 3.4 (q). IR (neat) ν = 3310, 2931, 2859, 1459, 1408, 1063; MS *m/z* (rel. intensity): 225 ([M^+], <2), 195 (1), 194 (9), 183 (6), 182 (56), 117 (7), 116 (100).

2-(1-Propyloct-6-ynylamino)ethyl hept-5-ynoate (42). A mixture of hept-5-ynoic acid (656 mg, 5.2 mmol), aminoalcohol **41** (1.0 g, 4.8 mmol) and *p*-TsOH·H_2O (990 mg, 5.2 mmol) in toluene (50 mL) was refluxed in a Dean-Stark apparatus for 5 h. The solvent was removed in vacuo, the residue was stirred with sat. aq. $NaHCO_3$ (50 mL) for 10 min, the aq. layer was extracted with *tert*-butylmethyl ether (2x30 mL), the combined organic phases were dried (Na_2SO_4) and evaporated. Flash chromatography (Alox, hexane/EtOAc 10:1) afforded amine **42** as a colorless syrup (1.11 g, 74%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.1 (t, 2H, J = 5.5 Hz), 2.81 (t, 2H, J = 5.5 Hz), 2.49 (m, 1H), 2.20-2.09 (m, 4H), 1.77 (m, 2H), 1.75 (t, 6H, J = 2.5 Hz), 1.48-1.29 (m, 11H), 0.89 (t, 3H, J = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.2 (s), 79.0 (s), 77.8 (s), 76.4 (s), 75.5 (s), 64.3 (t), 56.7 (t), 45.2 (t), 36.2 (t), 33.5 (t), 33.0 (t), 29.2 (t), 24.8 (t), 24.1 (t), 18.8 (q), 18.6 (q), 18.1 (q), 14.3 (q), 3.4 (q), 3.4 (q); IR (neat) υ = 3455, 3343, 2922, 2860, 1737, 1646, 1457, 1438, 1376, 1241, 1227, 1205, 1157; MS *m/z* 319 ([M^+], 5), 277 (12), 276 (60), 225 (15), 224 (100).

N-(9-Fluorenylmethoxycarbonyl)-2-(1-propyloct-6-ynylamino)ethyl Hept-6-ynoate (43). 9-Fluorenylmethyl chloroformate (774 mg, 3.0 mmol) in THF (10 mL) was added dropwise at 0°C to a slurry of amine **42** (800 mg, 2.5 mmol) in THF (20 mL) and aq. $NaHCO_3$ (10% w/w, 10mL). After stirring for 5 h, the reaction was extracted with *tert*-butylmethyl ether (3x80 mL), the organic layers were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue (hexane/EtOAc, 10:1) delivered compound **43** as a colorless syrup (1.15 g, 84%). ^1H NMR (300 MHz, $CDCl_3$) (rotamers): δ = 7.75 (2H, d, *J* = 7.3 Hz), 7.57 (2H, d, *J* = 7.3 Hz), 7.31 (2H, td, *J* = 7.3 and 1.1 Hz), 4.58 (2H, d, *J* = 5.3 Hz), 4.17 (1H, q, *J* = 6.7 Hz), 3.95 (0.5H, t, *J* = 6.4 Hz), 3.78 (1H, t, *J* = 6.9 Hz), 3.54 (0.5H, bs), 3.24 (1H, t, *J* = 6.5 Hz), 3.01 (1H, t, *J* = 6.9 Hz), 2.38, (2H, td, *J* = 7.5 and 1.7 Hz), 2.19 (2H, m), 2.05 (2H, m), 1.76 (6H, t, *J* = 2.4 Hz), 1.58-1.03 (10H, m), 0.86 (1.5H, t, *J* = 7.2 Hz), 0.72 (1.5H, t, *J* = 7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) (rotamers): δ = 172.8 (s), 156.8 (s), 156.5 (s), 143.8 (s), 141.4 (s), 127.6 (d), 127.0 (d), 124.6 (d), 119.9 (t), 78.9 (s), 77.9 (s), 66.5 (s), 62.4 (s), 62.1 (t), 56.4 (t), 47.6 (d), 47.3 (d), 35.5 (t), 35.4 (t), 32.9 (t), 32.7 (t), 28.8 (t), 28.6 (t), 25.5 (t), 24.9 (t), 19.6 (t), 18.6 (t), 18.2 (t), 13.9 (q), 13.8 (q), 3.4 (q); IR (neat) υ = 3073, 3041, 2955, 2861, 1736, 1696, 1451, 1416, 1342, 1230, 1160, 741; MS *m/z* 541 ([M^+], 0.2), 179 (36), 178 (100).

N-(9-Fluorenylmethoxycarbonyl)-5-propyl-1-oxa-4-azacyclopentadec-10-yn-15-one (44). **Method A**: A solution of the tungsten alkylidyne complex **1a** (27 mg, 0.055 mmol) in chlorobenzene (5 mL) was added to a solution of diyne **43** (600 mg, 1.1 mmol) in chlorobenzene (500 mL). The resulting brown mixture was kept at 80°C for 1 h. The solvent was evaporated and the residue was chromatographed (hexane/EtOAc, 15:1→10:1) to afford cycloalkyne **44** as a colorless oil (383 mg, 71%). **Method B**: A solution of diyne **43** (150 mg, 0.27 mmol), *p*-chlorophenol (35 mg, 0.27 mmol) and $Mo(CO)_6$ (4 mg, 0.014 mmol) in chlorobenzene (50 mL) was refluxed for 26 h while a gentle stream of Ar was bubbled through the reaction mixture. For work-up, the solvent was evaporated and the residue was chromatographed (hexane/EtOAc, 20:1→15:1) to give compound **44** (90 mg, 67%) showing the following analytical data: ^1H NMR (300 MHz, $CDCl_3$) (rotamers): δ = 7.74 (d, 2H, *J* = 6.9 Hz), 7.57 (d, 2H, *J* = 7.1 Hz), 7.39-7.27 (m, 4H), 4.66 (q, 1H, *J* = 5.5 Hz), 4.52 (q, 1H, *J* = 5.5 Hz), 4.23 (bs, 1H), 4.08-3.89 (1H), 3.07 (bs, 1H), 2.50 (m, 2H), 2.23-0.68 (m, 21H);

^{13}C NMR (75 MHz, $CDCl_3$) (rotamers): δ = 173.2 (s), 144.2 (s), 144.0 (s), 143.9 (s), 141.4 (s), 141.3 (s), 127.6 (d), 127.5 (d), 126.9 (d), 124.6 (d), 119.8 (d), 82.9 (s), 79.0 (s), 78.8 (s), 66.3 (t), 63.8 (t), 63.3 (t), 47.6 (s), 47.2 (s), 35.3 (t), 33.9 (t), 31.5 (t), 28.9 (t), 26.1 (t), 25.0 (t), 22.6 (t), 22.5 (t), 19.6 (t), 18.6 (t), 17.0 (t), 14.0 (q), 13.8 (q); IR (neat) υ = 3064, 3040, 2956, 2933, 2870, 1726, 1684, 1236, 747; MS *m/z* (rel. intensity): 487 ([M^+], 0.2), 179 (35), 178 (100).

Epilachnene (31). To a solution of compound **44** (200 mg, 0.41 mmol) and quinoline (40 μL, 0.003 mmol) in MeOH (40 mL) was added Lindlar catalyst (40 mg). The flask was flushed with H_2 (two freeze/thaw cycles) and the reaction was stirred 1 h under H_2 (1 atm) at ambient temperature. For work-up, the mixture was filtrated through celite, the celite was carefully washed with MeOH (4x30 mL), the combined filtrates were evaporated and the residue was chromatographed (hexane/EtOAc, 15:1) to give N-(9-fluorenylmethoxycarbonyl)-5-propyl-1-oxa-4-azacyclopentadec-10-(*Z*)-en-15-one (*Z*)-**37** as a colorless syrup (188 mg, 94%). ^{1}H NMR (300 MHz, $CDCl_3$) (rotamers): δ = 7.76 (t, 2H, *J* = 7.1 H), 7.57 (t, 2H, *J* = 7.5 Hz), 7.41-7.28 (m, 4H), 5.37-5.15 (m, 2H), 4.71-4.49 (m, 2H), 4.23-4.09 (m, 2H), 3.82 (t, 1H, *J* = 4.0 Hz), 3.35 (m, 1H), 2.93 (dt, 1H, *J* = 14.9 and 4.6, Hz), 2.10-1.70 (m, 7H), 1.56-0.67 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) (rotamers): δ = 173.55 (s), 173.5 (s), 157.0 (s), 144.3 (s), 144.1 (s), 144.0 (s), 141.5 (s), 141.4 (s), 131.7 (d), 131.5 (d), 129.1 (d), 129.0 (d), 127.6 (d), 127.5 (d), 126.9 (d), 124.6 (d), 124.3 (d), 119.9 (d), 119.8 (d), 66.2 (t), 66.1 (t), 64.5 (t), 64.1 (t), 47.6 (d), 47.3 (d), 35.3 (t), 35.2 (t), 33.1 (t), 33.0 (t), 31.6 (t), 29.4 (t), 28.9 (t), 26.7 (t), 25.6 (t), 25.5 (t), 25.2 (t), 19.7 (t), 19.6 (t), 14.1 (q), 13.8 (q); IR (neat) υ = 3066, 2955, 2929, 2859, 1734, 1695, 1451, 1207, 1156, 740; MS *m/z* (rel. intensity): 489 ([M^+], 0.2), 179 (35), 178 (100). Deprotection of this compound with TBAF·3H_2O was performed as previously described[25] thus affording epilachnene (**31**) in analytically pure form (62%). Its spectroscopic and analytical data match those reported in the literature.[23-25]

Synthesis of Homoepilachnene (33) (Scheme 5)

Dodec-2-yn-9-ol (46). PDC (16.1 g, 42.8 mmol) was added to a solution of **45** (4.0 g, 28.5 mmol) in CH_2Cl_2 (250 mL) and the resulting dark suspension was stirred overnight. The reaction was quenched with brine (700 mL), the aqueous layer was extracted with CH_2Cl_2 (4x80 mL), the combined organic phases were successively washed with brine and H_2O (100 mL each), dried (Na_2SO_4) and evaporated. The residue was distillated in vacuo to give 7-nonynal as a colorless liquid (3.31 g, 84%). This compound is rather unstable and was directly used in the next reaction: A solution of n-propylmagnesium bromide (11 mL, 22 mmol, 2M in Et_2O) was added to a solution of 7-nonynal (3.0 g, 21.7 mmol) in THF at 0°C. Standard extractive work-up after 40 min reaction time followed by flash chromatography afforded alcohol **46** as a colorless liquid (3.72 g, 94%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.59 (m, 1H), 2.16 (s, 1H), 2.11 (m, 2H), 1.77 (t, 3H, *J* = 2.5 Hz), 1.52-1.29 (m, 12H), 0.92 (t, 3H, *J* = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 79.2 (s), 75.4 (s), 71.6 (d), 39.7 (t), 37.3 (t), 28.9 (t), 28.8 (t), 25.1 (t), 18.8 (t), 18.6 (t), 14.1 (q), 3.4 (q); IR (neat) υ = 3353, 2932, 2860, 1464, 1436; MS *m/z* (rel. intensity): 135 (17), 121 (18), 108 (10), 107 (10), 95 (42), 94 (17), 93 (31), 82 (10), 81 (37), 79 (34), 73 (18), 71 (11), 69 (28), 68 (39), 67 (40), 66 (11), 57 (17), 55 (100).

9-(4-Methanesulfonyloxy)dodec-2-yne (47). Prepared in analogy to the epilachnene series from mesyl chloride (1.4 mL, 18.1 mmol) and alcohol **46** (3.0 g, 16.4 mmol). Colorless syrup (4.2 g, 98%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.70 (q, 1H, *J* = 6.1 Hz), 2.98 (s, 3H), 2.10 (m, 2H), 1.76 (m, 3H), 1.66 (m, 4H), 1.49-1.33 (m, 8H), 0.93 (t, 3H, *J* = 7.3Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 83.9 (d), 78.9 (s), 75.6 (s), 38.6 (t), 36.5 (t), 34.4 (t), 28.7 (t), 28.5 (t), 24.5 (t), 18.6 (t), 18.3 (t), 13.8 (q), 3.4 (q); IR (neat) υ = 3024, 2936, 2862, 1465, 1353, 1333, 1174, 909; MS *m/z* (rel intensity) 260 ([M^+], 0.1), 164 (19), 149 (12), 135 (53), 122 (18), 121 (45), 109 (32), 108 (37), 107 (42), 96 (15), 95 (61), 94 (53), 93 (87), 91 (14), 82 (13), 81 (44), 80 (23), 79 (100).

2-(1-Propylnon-7-ynylamino)ethanol. Prepared in analogy to the epilachnene series from mesylate **47** (3.5 g, 13.4 mmol). Colorless syrup (2.27 g, 75%). ^{1}H NMR (300 MHz, $CDCl_3$)

δ = 3.59 (t, 2H, *J* = 5.2 Hz), 2.73-2.49 (m, 4H), 2.47 (quint, 1H, *J* = 5.5 Hz), 2.12-2.01 (m, 2H), 1.75 (t, 3H, *J* = 2.5 Hz), 1.47-1.28 (m, 10H), 0.88 (t, 3H, *J* = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 79.1 (s), 75.4 (s), 60.8 (t), 56.9 (d), 48.0 (t), 36.1 (t), 33.7 (t), 29.0 (t), 28.9 (t), 25.2 (t), 18.8 (t), 18.6 (t), 14.2 (q), 3.4 (q); IR (neat) ν = 3310, 2931, 2859, 1459, 1408, 1063; MS *m/z* (rel. intensity): 225 ([M^+], <2), 195 (1), 194 (9), 183 (6), 182 (56), 117 (7), 116 (100).

2-(1-Propylnon-7-ynylamino)ethyl Hept-5-ynoate (48). Prepared in analogy to the epilachnene series from hept-5-ynoic acid (1.0 g, 7.9 mmol), the aminoalcohol described above (1.5 g, 6.6 mmol) and *p*-TsOH·H_2O (1.5 g, 7.9 mmol) in benzene (50 mL). Colorless syrup (1.62 g, 73%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.15 (t, 2H, *J* = 5.5 Hz), 2.81 (t, 2H, *J* = 5.7 Hz), 2.45 (m, 1H), 2.43 (t, 2H, *J* = 7.4 Hz), 2.18 (m, 1H), 2.11 (m, 1H), 1.80 (m, 2H), 1.76 (t, 6H, *J* = 2.5 Hz), 1.38-1.30 (m, 15H), 0.90 (t, 3H, *J* = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.3 (s), 79.2 (s), 77.9 (s), 76.4 (s), 75.4 (s), 64.3 (t), 56.9 (t), 45.2 (t), 36.3 (t), 33.9 (t), 33.0 (t), 29.1 (t), 29.0 (t), 25.2 (t), 14.2 (t), 18.9 (t), 18.7 (t), 18.2 (t), 14.3 (t), 3.4 (q), 3.4 (q); IR (neat) υ = 2931, 2858, 1737, 1646, 1457, 1158; MS *m/z* (rel. intensity): 333 ([M^+], 4), 291 (13), 290 (66), 225 (15), 224 (100), 185 (22), 153 (21), 116 (32).

N-(9-Fluorenylmethoxycarbonyl)-2-(1-propylnon-7-ynylamino)ethyl Hept-6-ynoate (49). Prepared in analogy to the epilachnene series outlined above from 9-fluorenylmethyl chloroformate (930 mg, 3.6 mmol) and amine **48** (1.0 g, 3.0 mmol). Colorless syrup (1.36 g, 82%). ^{1}H NMR (300 MHz, $CDCl_3$) (rotamers): δ = 7.75 (d, 2H, *J* = 7.4 Hz), 7.57 (d, 2H, *J* = 7.4 Hz), 7.39 (m, 2H), 7.32 (m, 2H), 4.58 (d, 2H, *J* = 5.5 Hz), 4.23 (d, 1H, *J* = 4.4 Hz), 4.14 (t, 1H, *J* = 4.4 Hz) 3.94 (m, 0.5 H), 3.76 (t, 1H, *J* = 6.8 Hz), 3.24 (t, 1H, *J* = 6.5 Hz), 3.00 (t, 1H, *J* = 6,8 Hz), 2.42-2.39 (m, 2H), 2.19 (m, 2H), 2.08 (m, 2H), 1.81 (m, 2H), 1.77 (t, 6H, *J* = 2.3 Hz), 1.72-0.99 (m, 13H), 0.85 (t, 1.5H, *J* = 7.2Hz), 0.72 (t, 1.5H, *J* = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) (rotamers): δ = 173.0 (s), 172.9 (s), 156.8 (s), 144.0 (s), 141.4 (s), 127.6 (d), 127.9 (d), 126.9 (d), 124.6 (d), 124.5 (d), 119.9 (d), 119.8 (d), 79.2 (s), 77.8 (s), 75.4 (s), 66.5(t), 62.4 (t), 62.0 (t), 47.5 (d), 47.3 (d), 35.4 (t), 35.3 (t), 33.2 (t), 33.1 (t), 32.9 (t), 32.8 (t), 28.9 (t), 28.6 (t), 25.9 (t), 24.0 (t), 19.5 (t), 18.6 (t), 18.1 (t), 13.9 (q), 13.8 (q), 3.4 (q), 3.4

(q); IR (neat) υ = 3066, 3041, 2931, 2859, 2737, 1737, 1693, 1451, 1415, 741; MS *m/z* (rel. intensity): 555 ([M^+], 0.5), 280 (12), 224 (18), 179 (32), 178 (100).

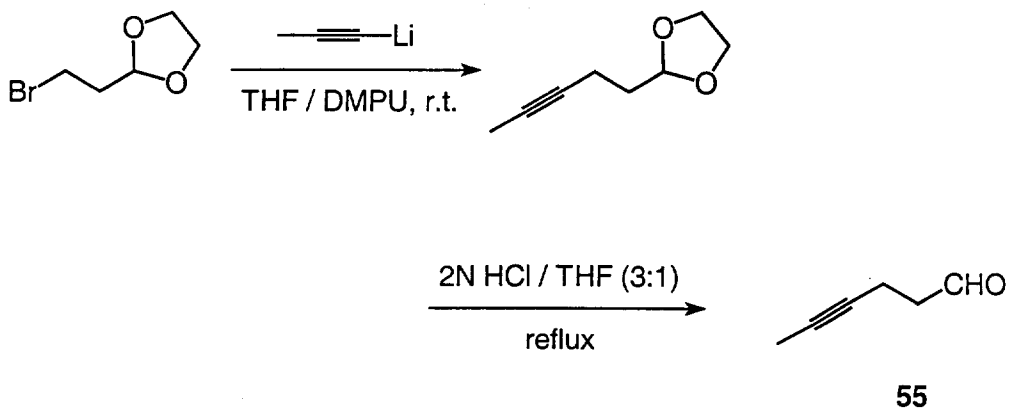
N-(9-Fluorenylmethoxycarbonyl)-5-propyl-1-oxa-4-azacyclohexadec-11-yn-16-one (50). **Method A**: A solution of the tungsten alkylidyne complex **1a** (17 mg, 0.036 mmol) in chlorobenzene (5 mL) was added to a solution of **49** (400 mg, 0.72 mmol) in chlorobenzene (300 mL). The resulting brown mixture was heated to 80°C for 1 h. The solvent was evaporated and the dark residue was chromatographed (hexane/EtOAc, 15:1→10:1) affording compound **50** as a colorless syrup (251 mg, 69%). **Method B**: A solution of diyne **49** (150 mg, 0.27 mmol), *p*-chlorophenol (35 mg, 0.27 mmol) and $Mo(CO)_6$ (4 mg, 0.014 mmol) in chlorobenzene (50 mL) was refluxed for 24 h while a gentle stream of argon was bubbled through the reaction mixture. Evaporation of the solvent and subsequent flash chromatography (hexane/EtOAc, 20:1→15:1) provided compound **50** as a colorless syrup (86 mg, 64%). ^{1}H NMR (300 MHz, $CDCl_3$) (rotamers): δ = 7.74 (d, 2H, *J* = 7.4 Hz), 7.56 (d, 2H, *J* = 7.9 Hz), 7.34 (m, 4H), 4.68 (dd, 1H, *J* = 107 and 5.2 Hz), 4.57 (dd, 1H, *J* = 10.7 and 5.1 Hz), 4.25 (m, 1H), 4.21 (d, 1H, *J* = 3.8 Hz), 3.83-3.67 (m, 2.5H), 3.37 (bs, 0.5H), 2.97 (m, 1H), 2.64-2.39 (m, 2H), 2.28-1.67 (m, 4H), 1.53-0.69 (m, 19H); ^{13}C NMR (75 MHz, $CDCl_3$) (rotamers): δ = 173.2 (s), 173.1 (s), 156.7 (s), 156.3 (s), 144.1 (s), 143.9 (s), 143.8 (s), 141.4 (s), 141.3 (s), 127.5 (d), 127.4 (d), 126.9 (d), 124.5 (d), 119.8 (d), 119.7 (d), 85.5 (s), 79.5 (s), 79.3 (s), 66.3 (t), 66.1 (t), 63.3 (t), 47.5 (d), 47.3 (d), 34.8 (t), 34.5 (t), 34.4 (t), 32.3 (t), 32.2 (t), 28.4 (t), 28.1 (t), 26.6 (t), 26.5 (t), 23.4 (t), 23.3 (t), 19.4 (t), 18.1 (t), 17.6 (t), 13.9 (q), 13.7 (q); IR (KBr) υ = 3066, 3041, 2933, 2859, 1954, 1907, 1736, 1694, 1451, 1223, 1158, 763, 741; MS *m/z* (rel. intensity): 501 ([M^+], 0.2), 179 (35), 178 (100).

Homoepilachnene (33). To a solution of cycloalkyne **50** (300 mg, 0.6 mmol) and quinoline (30 μL) in MeOH (40 mL) was added Lindlar catalyst (38 mg). The flask was flushed with H_2 (1 atm) (two freeze/thaw cycles) and the mixture was stirred for 50 min at ambient temperature. A standard work-up followed by flash chromatography (hexane/EtOAc, 15:1) afforded N-(9-fluorenylmethoxycarbonyl)-5-propyl-1-oxa-4-azacyclohexadec-11-(*Z*)-en-16-one as a colorless syrup (275 mg, 92%) which exhibits the following spectroscopic data: ^{1}H NMR (300 MHz, $CDCl_3$) (rotamers): δ = 7.75 (dd, 2H, *J* = 7.3 and 3.3 Hz), 7.57 (d, 2H, *J* =

7.2 Hz), 7.31 (m, 4H), 5.33 (m, 2H), 4.58 (m, 2H), 4.20 (m, 2H), 3.79 (t, 1H, J = 4.6 Hz), 3.63 (bs, 0.5 Hz), 3.03 (m, 1.5H), 2.26 (m, 2H), 2.06 (m, 3H), 1.96-0.68 (m, 19H); ^{13}C NMR (75 MHz, $CDCl_3$) (rotamers): δ = 173.4 (s), 173.3 (s), 156.8 (s), 144.2 (s), 144.2 (s), 144.0 (s), 141.5 (s), 141.4 (s), 131.7 (d), 131.6 (d), 128.7 (d), 127.6 (d), 127.5 (d), 126.9 (d), 124.6 (d), 124.4 (d), 119.9 (d), 119.8 (d), 66.3 (t), 66.2 (t), 64.1 (t), 63.9 (t), 47.6 (d), 47.3 (d), 34.9 (t), 33.8 (t), 33.6 (t), 32.9 (t), 28.1 (t), 27.9 (t), 27.5 (t), 27.2 (t), 26.3 (t), 25.5 (t), 25.4 (t), 24.4 (t), 24.3 (t), 19.6 (t), 14.0 (q), 13.8 (q); IR (neat) υ = 3067, 2929, 2859, 1735, 1693, 1450, 1414, 1225, 740; MS *m/z* (rel. intensity): 503 ([M^+], 0.2), 179 (43), 178 (100). This compound was deprotected as follows: TBAF·3H_2O (85 mg, 0.26 mmol) was added to a solution of this alkene (100 mg, 0.20 mmol) in THF (7 mL) and the resulting mixture was stirred for 1 h. The reaction was then quenched with H_2O (5 mL), the aqueous layer was extracted with *tert*-butylmethyl ether (4x10 mL), the combined organic phases were dried (Na_2SO_4) and concentrated, and the remaining residue was chromatographed (Alox, hexane/EtOAc, 15:1) to give homoepilachnene as a colorless syrup (35.7 mg, 64%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.32 (2H, m), 4.28 (m,1H), 4.12 (m,1H), 2.92-2.75 (m, 2H), 2.51 (bs, 1H), 2.34 (m,3H), 2.12-1.99 (m, 4H), 1.78-1.58 (m, 3H), 1.43-1.26 (m, 13H), 0.88 (t, 3H, J = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.5 (s), 130.9 (d), 128.8 (d), 64.0 (t), 56.0 (d), 45.1 (t), 36.7 (t), 33.7 (t), 32.6 (t), 27.6 (t), 25.1 (t), 25.0 (t), 23.5 (t), 19.1 (t), 14.3 (q).

Preparation of the Macrocyclic Perimeter (64) of Nakadomarin A

Substrates



55

4-Hexynal (55) was prepared by a slightly modified literature procedure as outlined below:[4]

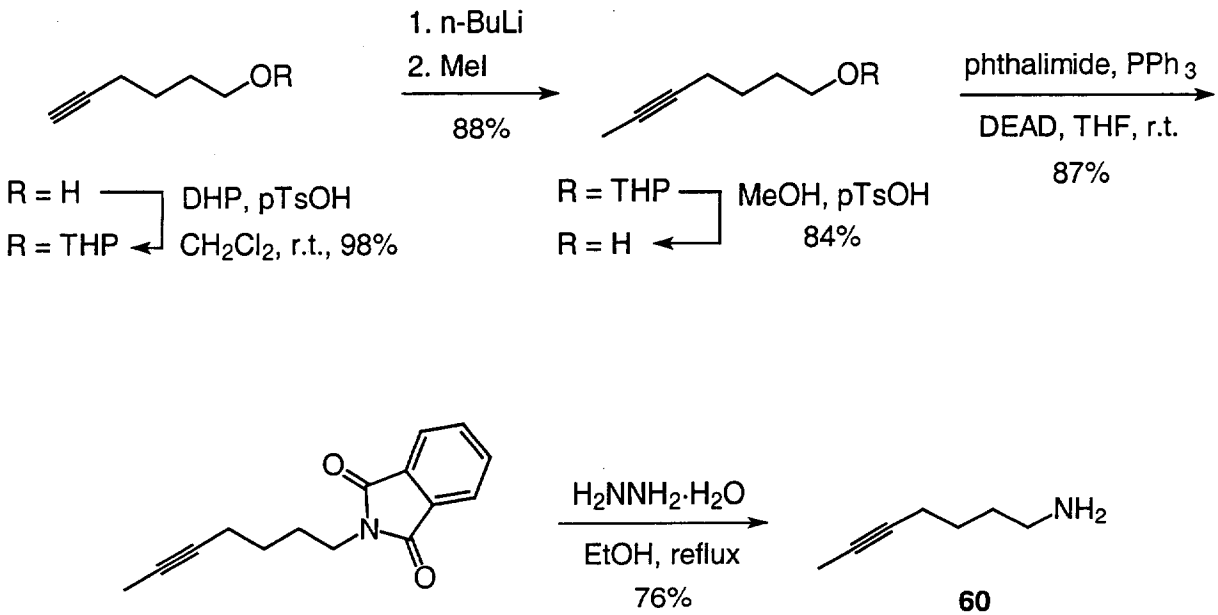
2-(3-Pentinyl)-1,3-dioxolane. 2-(2-Bromoethyl)-1,3-dioxolane (71.6 g, 0.395 mol) was added dropwise at 0 °C over a period of 60 min to a suspension of propinyllithium (24.0 g, 0.522 mol) in THF (500 mL) and DMPU (63.1 mL, 0.522 mol). The resulting yellow suspension was stirred at rt overnight and then poured into chilled saturated aqueous NH_4Cl (500 mL). The aqueous phase was extracted with ether, the combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated. Distillation of the residue gave the title compound (49.3 g, 89 %) as a colorless liquid (bp 38 °C / $2 \cdot 10^{-2}$ mbar). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.83 (dt, J = 4.7, 1.3, 1H), 3.86–3.68 (m, 4H), 2.17–2.07 (m, 2H), 1.73–1.62 (m, 5H) . ^{13}C NMR (75 MHz, $CDCl_3$): δ = 103.1, 77.9, 75.4, 64.7, 33.1, 13.4, 3.1. MS: *m/z* (rel. intensity): 140 ([M^+], 3), 73 (100), 67 (16), 53 (14), 45 (53), 41 (14), 39 (15), 29 (11), 27 (20). IR (neat): 2960, 2920, 2884, 1476, 1438, 1412, 1363, 1329, 1214, 1191, 1145, 1135,

---

[4] (a) Johnson, W. S.; Fletcher, V. R.; Chenera, B.; Bartlett, W. R.; Tham, F. S.; Kullnig, R. K. *J. Am. Chem. Soc.* **1993**, *115*, 497. (b) Nugent, W. A.; Thorn, D. L.; Harlow, R. L. *J. Am. Chem. Soc.* **1987**, *109*, 2788.

1071, 1041, 944, 896 cm^{-1}. Anal. *Calcd.* for $C_8H_{12}O_2$: C, 68.55; H, 8.63. *Found*: C, 68.34; H, 8.54.

4-Hexynal (55). A solution of 2-(3-pentinyl)-1,3-dioxolane (28.0 g, 0.200 mol) in THF (150 mL) was added to 2.4 M HCl (400 mL) and the resulting mixture was stirred overnight at rt. The reaction mixture was extracted with ether, the combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine and dried over Na_2SO_4. After evaporation of the solvent, the residue was distilled under vacuum through a Vigreux column to afford 4-hexynal (12.5 g, 65 %) as a colorless liquid. ^1H NMR (300 MHz, $CDCl_3$): δ = 9.71 (s, 1H), 2.55 (t, J = 6.9 Hz, 2H), 2.41–2.35 (m, 2H), 1.68 (t, J = 2.5, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 201.0, 76.8, 76.6, 42.8, 11.9, 3.3. MS: *m/z* (rel. intensity): 96 ([M^+], 3), 95 (22), 81 (100), 68 (32), 67 842), 65 (18), 53 (49), 51 (14), 41 (61), 40 (16), 39 (47), 27 (20). IR (neat): 2921, 2852, 2833, 2734, 2236, 1728, 1439, 1411, 1390, 1359, 1333, 1057, 851, 636 cm^{-1}.



2-(5-Hexynyl-1-oxy)-2*H*-pyran. *p*-Toluenesulfonic acid (156 mg, 0.766 mmol) was added at 0°C to solution of 5-hexyn-1-ol (7.52 g, 76.6 mmol) and 3,4-dihydro-2*H*-pyran (9.67 g, 115 mmol) in CH_2Cl_2 (100 mL), and the mixture was stirred overnight at rt. After extraction with

H_2O/CH_2Cl_2, the organic layer was washed with brine, dried over Na_2SO_4 and evaporated. The residue was purified by flash chromatography (SiO_2, hexane/ethyl acetate = 20/1) affording the title compound (13.7 g, 98 %) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.53 (t, J = 3.5 Hz, 1H), 3.83–3.67 (m, 2H), 3.48–3.32 (m, 2H), 2.18 (dt, J = 9.7, 6.0, 2H), 1.89 (t, J = 6.9, 1H), 1.81–1.44 (m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 99.7, 84.3, 68.3, 66.8, 62.1, 30.6, 28.7, 25.4, 25.3, 19.5, 18.2. MS: *m/z* (rel. intensity): 182 ([M^+], <1), 101 (21), 85 (100), 81 (25), 79 (22), 67 (17), 56 (21), 55 (12), 53 (13), 43 (14), 41 (32), 39 (11), 29 (14). IR (neat): 3297, 2943, 2870, 2117, 1454, 1441, 1353, 1201, 1137, 1121, 1076, 1035, 1022, 989, 905, 869, 815, 632 cm^{-1}. Anal. *Calcd.* for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. *Found*: C, 72.57; H, 9.93.

2-(5-Heptynyl-1-oxy)-2*H*-pyran. *n*-BuLi (43.3 mL, 69.2 mmol, 1.60 M in hexane) was added dropwise to a solution of 2-(5-hexynyl-1-oxy)-2*H*-pyran (9.00 g, 49.4 mmol) in THF (300 mL) at –78 °C. The resulting solution was stirred at 0 °C for 2 h, cooled to –78 °C, and MeI (11.2 g, 79.0 mmol) was introduced over a period of 60 min. The reaction mixture was allowed to warm to rt overnight. Saturated aqueous NH_4Cl (100 mL) was added for work-up and the aqueous phase was extracted with ether. The combined organic phases were washed with brine, dried over Na_2SO_4 and evaporated. Flash chromatography (SiO_2, hexane/ethyl acetate = 20/1) of the residue provided the title compound (8.52 g, 88 %) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$): δ = 4.51 (d, J = 3.9, 1H), 3.83–3.65 (m, 2H), 3.47–3.28 (m, 2H), 2.13–2.06 (m, 2H), 1.85–1.40 (m, 10H), 1.71 (t, J = 2.1, 3H) . ^{13}C NMR (75 MHz, $CDCl_3$): δ = 98.7, 78.9, 75.5, 67.0, 62.1, 30.6, 28.9, 25.8, 25.4, 19.5, 18.5, 3.3. MS: *m/z* (rel. intensity): 95 (21), 85 (100), 79 (14), 67 (50), 57 (13), 56 (10), 55 (29), 53 (20), 43 (14), 41 (33), 39 (13), 29 (17), 27 (14). IR (neat): 2942, 2868, 1453, 1440, 1352, 1201, 1137, 1120, 1076, 1034, 1022, 983, 906, 869, 815 cm^{-1}. Anal. *Calcd.* for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. *Found*: C, 72.52; H, 10.36.

5-Heptyn-1-ol. A solution of 2-(5-heptynyl-1-oxy)-2*H*-pyran (7.97 g, 40.6 mmol) and pyridinium *p*-toluenesulfonate (102 mg, 0.406 mmol) in MeOH (150 mL) was stirred at rt overnight. For workup, the mixture was extracted with H_2O/ether, the organic layer was washed with brine, dried over Na_2SO_4 and evaporated. The residue was purified by flash

chromatography (SiO_2, hexane/ethyl acetate = 4/1) affording 5-heptyn-1-ol (3.82 g, 84 %) as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$): δ = 3.62 (t, J = 6.3, 2H), 2.17–2.08 (m, 2H), 1.73 (t, J = 2.5, 3H), 1.69–1.46 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 78.8, 75.7, 62.2, 31.7, 25.2, 18.4, 3.3. MS: *m/z* (rel. intensity): 112 ([M^+], <1), 97 (20), 91 (10), 84 (47), 83 (12), 79 (40), 77 (31), 68 (100), 67 (23), 66 (46), 65 (14), 57 (17), 55 (19), 54 (12), 53 (42), 51 (11), 41 (39), 39 (32), 31 (27), 29 (13)27 (23). IR (neat): 3346, 2940, 2920, 2864, 1454, 1436, 1377, 1333, 1060, 1030, 981, 932, 908, 658 cm^{-1}. Anal. *Calcd.* for $C_7H_{12}O$: C, 74.95; H, 10.78. *Found*: C, 74.82; H, 10.71.

***N*-(5-Heptynyl)-phthalimide.** A solution of diethyl azodicarboxylate (11.8 g, 68.0 mmol) in THF (25 mL) is added dropwise to a solution of 5-heptyn-1-ol (6.36 g, 56.7 mmol), phthalimide (10.0 g, 68.0 mmol) and triphenylphosphine (17.8 g, 68.0 mmol) in THF (150 mL) at 0°C. After 15 min, the reaction mixture was allowed to warm to ambient temperature and stirred overnight. After evaporation of the solvent, ether was added to the residue in order to precipitate triphenylphosphine oxide and diethyl hydrazinedicarboxylate, which were filtered off. The filtrate was evaporated and the residue was purified by flash chromatography (SiO_2, toluene) providing the title compound (12.0 g, 88 %) as colorless needles. mp = 81-82°C. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.81 (dd, J = 5.4, 3.0, 2H), 7.68 (dd, J = 5.4, 3.0, 2H), 3.67 (t, J = 7.1, 2H), 2.18–2.12 (m, 2H), 1.82–1.70 (m, 5H), 1.54–1.43 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.4, 133.8, 132.1, 123.1, 78.4, 76.0, 37.6, 27.8, 26.2, 18.3, 3.4. MS: *m/z* (rel. intensity): 241 ([M^+], 13), 186 (15), 185 (11), 174 (22), 173 (12), 161 (19), 160 (100), 149 (19), 148 (18), 133 (14), 130 (25), 105 (20), 104 (22), 94 (77), 79 (37), 77 (38), 76 (27), 68 (15), 53 (11), 51 (11), 50 (12), 41 (15), 39 (11), 27 (12). IR (neat): 3062, 2935, 2865, 1773, 1727, 1609, 1463, 1438, 1398, 1367, 1331, 1284, 1232, 1188, 1115, 1034, 951, 892, 861, 795, 723, 712, 622, 530 cm^{-1}. Anal. *Calcd.* for $C_{15}H_{15}N_1O_2$: C, 74.67; H, 6.27; N, 5.81. *Found*: C, 74.75; H, 6.07; N, 5.77.

1-Amino-5-heptyne (60). *N*-(5-Heptynyl)-phthalimide (12.0 g, 49.7 mmol) is refluxed overnight in the presence of hydrazine hydrate (2.99 g, 59.7 mmol) in ethanol (150 mL). The resulting white suspension was cooled to rt, treated with concentrated hydrochloric acid (10 mL) and the precipitate was filtered off. After evaporation of the filtrate, the residue was

dissolved in H_2O/ethyl acetate, treated with sodium hydroxide (1M) and continuously extracted for 48 h. After drying over Na_2SO_4 and evaporation of all volatiles, the residue was distilled *in vacuo* to afford amine **60** (4.20 g, 76 %) as a colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.63 (t, *J* = 6.6, 2H), 2.11–2.06 (m, 2H), 1.71 (t, *J* = 2.5, 3H), 1.52–1.37 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 78.9, 75.6, 41.7, 32.9, 26.3, 18.5, 3.4. MS: *m/z* (rel. intensity): 241 ([M^+], 13), 186 (15), 185 (11), 174 (22), 173 (12), 161 (19), 160 (100), 149 (19), 148 (18), 133 (14), 130 (25), 105 (20), 104 (22), 94 (77), 79 (37), 77 (38), 76 (27), 68 (15), 53 (11), 51 (11), 50 (12), 41 (15), 39 (11), 27 (12). IR (neat): 3366, 3296, 2933, 2859, 2742, 1587, 1455, 1437, 1388, 1331, 1095, 1071, 845, 822, 754, 734 cm^{-1}. Anal. *Calcd.* for $C_7H_{13}N_1$: C, 75.62; H, 11.79. *Found*: C, 75.72; H, 11.71.

Compounds in Scheme 7

2-(3-Pentynyl)-3-[3-(*tert*-butyldimethylsilyoxy)-propen-2-yl]-oxiran (56). To a solution of the sulfonium salt **54** (2.20 g, 6.11 mmol) in THF (100 mL) was added *t*-BuLi (4.89 mL, 7.33 mmol, 1.50 M in hexane) via syringe at –78 °C. After stirring for 30 min, 5-hexynal **55** (822 mg, 8.55 mmol) was added, the mixture was stirred for an additional 30 min at that temperature and then slowly warmed to rt. The reaction mixture was extracted with H_2O/ethyl acetate, the organic layer was dried over Na_2SO_4 and evaporated. Purification of the crude product by flash chromatography (SiO_2, hexane/ethyl acetate = 50/1) afforded vinyl oxirane **56** (1.22 g, 71 %, mixture of diastereoisomers, ratio ≈ 60:40) as a colorless syrup. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.18–5.13 (m), 4.96 (t, *J* = 1.4) [2H], 4.13 (s), 4.08–4.05 (m) [2H], 3.43 (d, *J* = 4.1), 3.20–3.13 (m), 2.95 (ddd, *J* = 7.2, 5.2, 2.2) [2H], 2.28–2.15 (m, 2H), 1.70 (t, *J* = 2.6, 3H), 1.68–1.50 (m, 2H), 0.864 (s), 0.860 (s) [6H], 0.04 (s), 0.03 (s) [9H]. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.6, 142.0, 112.0, 111.4, 78.0, 77.8, 76.0, 64.4, 62.6, 59.0, 58.4, 57.7, 56.3, 31.8, 26.3, 25.8, 18.3, 18.2, 15.7, 15.4, 3.3, –5.4, –5.5. MS: *m/z* (rel. intensity): 143 (11), 131 (33), 105 (14), 91 (17), 75 (100), 59 (11), 53 (10), 41 (10). IR (neat): 2956, 2930, 2857, 1740, 1657, 1472, 1463, 1390, 1362, 1256, 1086, 1006, 939, 912, 838, 777, 671

cm^{-1}. HRMS ($C_{16}H_{28}O_2Si_1$+Na): *calcd.* 303.17563; *found* 303.17534. Anal. *Calcd.* for $C_{16}H_{28}O_2Si_1$: C, 68.52; H, 10.06. *Found*: C, 68.34; H, 10.01.

6-Hydroxy-2-(phenylsulfonyl)-4-(*tert*-butyldimethylsilyloxymethyl)-undec-4-en-9-ynoic Acid Methyl Ester (57). Epoxide **56** (4.93 g, 17.6 mmol) was added to a solution of $Pd(PPh_3)_4$ (203 mg, 0.176 mmol) and methyl phenylsulfonylacetate (3.77 g, 17.6 mmol) in THF (150 mL), and the resulting yellow mixture was refluxed overnight. An extractive workup with H_2O/ethyl acetate, drying of the organic layer over Na_2SO_4, evaporation of the solvent and flash chromatography (SiO_2, hexane/ethyl acetate = 4/1→1/1) afforded product **57** (7.01 g, 81 %, mixture of diastereoisomers) as a pale yellow syrup. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.97–7.80 (m, 2H), 7.72–7.59 (m, 3H), 5.46 (dd, *J* = 8.9, 16.8), 5.26 (dd, *J* = 8.5, 4.1) [1H], 4.55–3.95 (m), 3.68 (s) [4H], 3.61 (s), 3.60 (s), 3.57 (s), 3.55 (s) [3H], 3.15–2.55 (m, 2H), 2.40–2.00 (m, 3H), 1.78–1.35 (m, 5H), 0.88 (s), 0.87 (s), 0.83 (s), 0.82 (s) [9H], 0.04 (s), 0.03 (s), 0.02 (s), –0.01 (s), –0.02 (s), –0.03 (s) [6H]. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.8, 166.2, 166.0, 156.9, 137.2, 137.0, 135.6, 135.4, 135.3, 134.5, 134.4, 134.3, 134.2, 133.2, 132.9, 132.7, 131.3, 129.3, 129.2, 129.1, 129.0, 128.4, 78.5, 78.3, 78.2, 78.0, 76.4, 76.2, 69.5, 69.4, 69.1, 67.0, 66.8, 66.6, 66.5, 66.57, 66.49, 66.2, 60.9, 60.8, 60.4, 53.1, 52.9, 52.8, 52.7, 36.1, 36.0, 35.7, 32.6, 32.2, 26.9, 25.8, 25.5, 25.5, 25.4, 18.19, 18.17, 18.13, 15.03, 14.96, 14.8, 14.7, 3.46, 3.45, 3.41, -5.51, -5.55, -5.60. MS: *m/z* (rel. intensity): 438 (20), 437 (66), 419 (28), 295 (13), 277 (12), 221 (39), 203 (35), 199 (64), 189 (17), 171 (21), 167 (11), 161 (36), 153 (11), 147 (11), 143 (24), 136 (13), 135 (96), 131 (11), 125 (20), 119 813), 105 (12), 95 (19), 91 (20), 89 (25), 79 (12), 77 (28), 75 (100), 73 (83), 67 (24), 59 (12), 55 (23), 53 (12), 43 (10), 41 (23). IR (neat): 3533, 3065, 2953, 2929, 2857, 1744, 1585, 1472, 1463, 1448, 1437, 1328, 1256, 1150, 1084, 838, 779, 723, 689, 592, 531 cm^{-1}. HRMS ($C_{25}H_{38}O_6S_1Si_1$+Na): *calcd.* 517.20561; *found* 517. 20556. Anal. *Calcd.* for $C_{25}H_{38}O_6S_1Si_1$: C, 60.69; H, 7.74. *Found*: C, 60.54; H, 7.81.

6-(Tetrahydropyran-2-yloxy)-2-(phenylsulfonyl)-4-(*tert*-butyldimethylsilyloxymethyl)-undec-4-en-9-ynoic Acid Methyl Ester (58). Pyridinium *p*-toluenesulfonate (53 mg, 0.210 mmol) was added to a solution of allylic alcohol **57** (2.10 g, 4.24 mmol) and 3,4-dihydro-2*H*-pyran (535 mg, 6.36 mmol) in CH_2Cl_2 (50 mL) and the resulting mixture was stirred

overnight at rt. After extraction with H_2O/CH_2Cl_2, the organic layer was dried over Na_2SO_4 and evaporated. The residue was purified by flash chromatography (SiO_2, hexane/ethyl acetate = 4/1) providing product **58** (2.18 g, 89 %, mixture of diastereoisomers) as a yellow syrup. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.81–7.76 (m, 2H), 7.60 (t, *J* =7.4, 1H), 7.48 (dd, *J* = 8.2, 7.4, 2H), 5.48 (t, *J* = 10.2), 5.24 (vquart, *J* = 11.2), 4.97 (dd, *J* = 9.4, 4.9) [1H], 4.62–4.03 (m, 3H), 3.90 (s), 3.88 (s), 3.85 (s) [2H], 3.82–3.60 (m, 1H), 3.54 (s), 3.52 (s), 3.50 (s) [3H], 3.48–3.23 (m, 1H), 2.88–2.43 (m, 2H), 2.24–1.95 (m, 2H), 1.80–1.34 (m, 11H), 0.780 (s), 0.776 (s), 0.766 (s), 0.751 (s), 0.746 (s) [9H], -0.0484 (s), -0.052 (s), -0.08 (s), -0.096 (s), -0.010 (s) [6H]. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.3, 166.1, 166.02. 165.96, 165.8, 137.35, 137.33. 137.29, 137.13, 137.10, 137.0, 136.95, 136.92, 134.09, 134.05, 133.93, 133.6, 132.9, 131.4, 130.5, 130.1, 129.1, 129.0, 128.88, 128.85, 128.81, 128.5, 99.3, 98.8, 98.6, 98.3, 97.8, 94.2, 94.0, 93.97, 93.4, 78.4, 78.2, 78.15, 78.07, 77.9, 77.2, 76.3, 76.1, 76.0, 75.74, 75, 70, 75.67, 75.54, 75.48, 73.0, 72.8, 72.5, 71.6, 71.2, 69.6, 69.45, 69.38, 69.3, 69.2, 68.9, 68.7, 68.5, 67.93, 67.86, 67.76, 67.73, 66.3, 66.0, 65.9, 62.3, 62.2, 62.1, 61.9, 61.7, 61.6, 61.4, 61.3, 60.5, 60.31, 60.26, 60.1, 52.73, 52.66, 52.64, 52.5, 52.4, 35.02, 34.97, 34.9, 34.61, 34.55, 34.4, 32.6, 32.5, 32.1, 31.7, 306, 30.51, 30.47, 30.4, 30.3, 26.8, 25.6, 25.35, 25.30, 25.25, 25.20, 19.52, 19.46, 19.3, 19.1, 19.0, 18.8, 18.03, 17.99, 17.9, 15.0, 14.7, 14.60, 14.59, 14.4, 14.3, 3.30, 3.27, 3.2, -5.6, -5.7, 5.8, -5.9. MS: *m/z* (rel. intensity): 522 (16), 521 (46), 476 (14), 437 (14), 421 (16), 420 (29), 419 (100), 278 (13), 277 (20), 221 (24), 203 (21), 199 (51), 171 (11), 161 (10), 159 (70), 153 (11), 143 (11), 135 (44), 89 (12), 85 (92), 75 (31), 73 (38), 67 (20), 55 (11), 43 (20), 41 (19), 29 (12). IR (neat): 3066, 2952, 2856, 1745, 1585, 1471, 1463, 1328, 1257, 1201, 1150, 1113, 1084, 1021, 989, 838, 779, 722, 689, 592, 532 cm^{-1}. HRMS ($C_{30}H_{46}O_7S_1Si_1$+Na): *calcd.* 579.28228; *found* 579.27980. Anal. *Calcd.* for $C_{30}H_{46}O_7S_1Si_1$: C, 62.25; H, 8.01. *Found*: C, 62.38; H, 7.94.

Lactone 59. To a solution of silyl ether **58** (5.89 g, 10.2 mmol) in THF (300 mL) was successively added NH_4F (1.73 g, 50.8 mmol) and TBAF (50.8 mL, 50.8 mmol, 1 M in THF). After stirring overnight at ambient temperature, the reaction mixture was extracted with saturated aqueous NaCl/ethyl acetate, the organic layer was dried over Na_2SO_4 and evaporated. Purification of the residue by flash chromatography (SiO_2, hexane/ethyl acetate =

2/1) afforded lactone **59** (2.18 g, 89 %, mixture of diastereoisomers) as a colorless syrup. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.95–7.83 (m, 2H), 7.63 (t, *J* = 7.4, 1H), 7.51 (vt, *J* = 7.6, 2H), 5.62–4.77 (m, 2H), 4.72–4.03 (m, 4H), 3.88–3.64 (m, 1H), 3.55–2.90 (m, 3H), 2.30–2.00 (m, 2H), 1.88–1.35 (m, 11H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.7, 163.5, 163.4, 163.3, 163.2, 163.10, 163.06, 163.04, 137.6, 137.5, 137.4, 137.27, 137.26, 137.20, 134.33, 134.29, 134.25, 132.4, 131.9, 131.0, 130.9, 130.29, 130.25, 129.7, 129.6, 129.4, 129.32, 129.28, 129.18, 129.13, 129.09, 129.06, 128.98, 128.93, 128.89, 126.6, 126.3, 125.99, 125.97, 125.6, 125.5, 99.4, 99.2, 99.1, 98.8, 94.9, 94.6, 94.2, 93.8, 78.07, 78.02, 77.97, 77.88, 77.85, 77.79, 77.2, 76.5, 76.4, 76.3, 76.22, 76.16, 76.12, 76.02, 75.98, 73.1, 72.9, 72.70, 72.66, 72.62, 72.44, 72.36, 72.0, 71.9, 68.62, 68.58, 68.46, 68.4, 68.3, 68.0, 67.8, 67.7, 66.8, 66.4, 64.6, 64.5, 64.4, 64.3, 64.1, 63.9, 63.7, 63.6, 62.9, 62.7, 62.6, 62.23, 62.17, 61.6, 61.2, 35.5, 35.2, 34.1, 34.0, 33.93, 33.85, 33.80, 30.56, 30.53, 30.46, 30.40, 30.2, 30.1, 29.4, 28.2, 27.9, 25.3, 25.2, 25.08, 25.06, 22.8, 22.7, 22.64, 22.59, 22.51, 19.6, 19.5, 19.3, 18.9, 18.6, 14.91, 14.86, 14.81, 14.7, 14.5, 14.4, 3.3. MS: *m/z* (rel. intensity): 189 (25), 85 (100), 77 (12), 67 (11). IR (neat): 3065, 2943, 2867, 1745, 1585, 1448, 1323, 1259, 1201, 1148, 1083, 1022, 988, 902, 869, 813, 757, 721, 688, 633, 611, 587 cm^{-1}. HRMS ($C_{23}H_{28}O_6S_1$+Na): *calcd.* 455.15043; *found* 455.15086.

***N*-(5-Heptynyl)-4-(hydroxymethyl)-2-(phenylsulfonyl)-6-(2-tetrahydropyranyloxy)-undec-4-en-9-ynoic Acid Amide (61).** Amine **60** (1.61 g, 14.5 mmol) was added at rt to a solution of lactone **59** (3.13 g, 7.24 mmol) and NaCN (709 mg, 14.5 mmol) in MeOH (100 mL) and the resulting mixture was stirred overnight at rt. For workup, the reaction mixture was extracted with saturated aqueous NaCl/ethyl acetate, the combined organic layers were dried over Na_2SO_4. Removal of the solvent *in vacuo* and purification of the crude product by flash chromatography (SiO_2, hexane/ethyl acetate = 1/1) afforded amide **61** (3.78 g, 96 %, mixture of diastereoisomers) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.75–7.88 (m, 2H), 7.61 (vt, *J* = 7.5 Hz, 1H), 7.50 (vt, *J* = 7.5 Hz, 2H), 6.45-6.95 (m, 1H), 5.00-5.52 (m, 1H), 4.30-4.72 (m, 3H), 1.97-2.25 (m, 8H), 1.30-1.85 (m, 20H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.9, 164.7, 164.3, 163.9, 163.8, 163.7, 139.6, 139.0, 138.9, 136.4, 136.3, 136.2, 136.1, 134.8, 134.2, 134.0, 133.5, 131.6, 131.2, 130.6, 129.5, 129.4, 129.24,

129.17, 129.1, 129.0, 128.9, 128.8, 128.74, 128.66, 127.9, 100.4, 99.4, 99.3, 93.6, 93.3, 92.0, 78.8, 78.5, 78.42, 78.40, 78.36, 78.0, 77.9, 77.2, 76.8, 76.7, 75.9, 75.8, 73.5, 73.3, 70.4, 70.3, 69.75, 69.71, 69.2, 69.1, 68.1, 68.0, 67.8, 67.4, 66.5, 66.1, 64.4, 61.4, 61.3, 60.4, 39.64, 39.57, 39.51, 39.42, 39.36, 39.30, 35.1, 34.8, 34.6, 34.5, 34.4, 34.1, 33.3, 31.5, 30.9, 30.7, 30.3, 30.1, 29.8, 29.5, 28.3, 28.14, 28.11, 26.8, 26.04, 25.99, 25.91, 25.8, 25.4, 25.2, 25.0, 24.8, 24.7, 20.9, 20.8, 20.0, 19.2, 18.8, 18.6, 18.2, 18.0, 17.9, 15.0, 14.8, 14.7, 14.6, 14.4, 14.0, 3.4, 3.3. MS: *m/z* (rel. intensity): 458 (23), 442 (26), 441 (18), 402 (24), 318 (33), 301 (18), 300 (79), 282 (11), 272 (11), 189 (20), 163 (14), 161 (19), 152 (18), 145 (22), 119 (11), 112 (26), 110 (13), 105 (11), 95 (45), 91 (18), 93 (15), 91 (18), 85 (100), 79 (17), 77 (22), 67 (45), 57 (25), 55 (31), 53 (16), 43 (33), 41 (31), 30 (15), 29 (15). IR (neat): 3364, 3067, 2942, 2862, 1673, 1584, 1542, 1447, 1309, 1261, 1201, 1149, 1083, 1020, 807, 689, 595, 535 cm^{-1}. HRMS ($C_{30}H_{41}N_1O_6S_1$+Na): *calcd.* 566.25523; *found* 566.25443. Anal. *Calcd.* for $C_{30}H_{41}N_1O_6S_1$: C, 66.27; H, 7.60. *Found*: C, 66.15; H, 7.49.

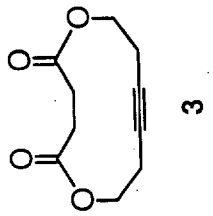
***N*-(5-Hepynyl)-3-[2-(3-pentynyl)-4-furyl]-2-phenylsulfonyl-propionic Acid Amide (62).** To a solution of compound **61** (3.52 g, 7.02 mmol) in CH_2Cl_2 (100 mL) was added MnO_2 (6.11 g, 70.2 mmol) at rt. After stirring for 4 h at rt, the resulting black suspension was filtered through a short pad of silica, the residues were washed with ethyl acetate, and the combined organic layers were evaporated. The residue was dissolved in ethyl acetate (100 mL), acidified with 10 % HCl (1.0 mL), and the reaction mixture was stirred for 3 h at rt. The resulting white suspension was extracted with H_2O/ethyl acetate, the combined organic layers were washed with brine and dried over Na_2SO_4. After evaporation of the solvent, the residue was purified by flash chromatography (SiO_2, hexane/ethyl acetate = 2/1) thus providing furan **62** (2.95 g, 96 %) as a white solid. mp = 140-141°C. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.88–7.82 (m, 2H), 7.67 (tt, *J* = 7.4, 2.0, 1H), 7.55 (vt, *J* = 7.6, 2H), 7.05 (s, 1H), 6.22 (bs, 1H), 5.87 (s, 1H), 3.84 (dd, *J* = 10.6, 3.5, 1H), 3.21 (quart, *J* = 6.5, 2H), 3.10-2.91 (m, 2H), 2.68 (t, *J* = 7.5, 2H), 2.40-2.30 (m, 2H), 2.05-2.15 (m, 2H), 1.76 (t, *J* = 2.5, 3H), 1.73 (t, *J* = 2.5, 3H), 1.54 (quin, *J* = 7.0, 2H), 1.41 (quin, *J* = 7.0, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.4, 155.3, 138.8, 136.3, 134.4, 129.3, 129.1, 119.8, 106.6, 78.5, 77.8, 76.2, 76.0, 72.0, 39.7, 28.3, 27.9, 26.0, 22.8, 18.3, 17.8, 3.4. MS: *m/z* (rel. intensity): 299 (21), 298 (100), 187

(32), 77 (12), 55 (16). IR (neat): 3335, 3091, 2964, 2926, 2859, 1657, 1527, 1448, 1366, 1311, 1146, 1084, 928, 858, 831, 764, 726, 687, 662, 619, 574, 539 cm^{-1}. HRMS ($C_{25}H_{29}N_1O_4S_1$+H): *calcd.* 440.18956; *found* 440.18996.

4-Oxo-3-phenylsulfonyl-5-aza-15-oxabicyclo[12.2.1]hepta-1,14-dien-10-yne (63). To a solution of diyne **62** (970 mg, 2.2.1 mmol) in chlorobenzene (350 mL) at 80 °C was added (*t*-BuO)$_3$W≡CCMe$_3$ **1a** (107 mg, 0.221 mmol), and the reaction mixture was stirred at that temperature for 2 h. After evaporation of the solvent, the residue was purified by flash chromatography (SiO_2, hexane/ethyl acetate = 2/1) affording macrocycle **63** (766 mg, 90 %) as a colorless solid. mp > 195°C (decomp.). ^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.30 (dd, *J* = 8.6, 3.3, 1H), 7.84–7.72 (m, 3H), 7.66 (t, *J* = 7.5, 2H), 7.36 (s, 1H), 5.89 (s, 1H), 4.17 (t, *J* = 7.7, 1H), 3.67–3.53 (m, 1H), 2.80 (d, *J* = 7.7, 2H), 2.60 (t, *J* = 5.8, 2H), 2.45–2.32 (m, 3H), 2.23–2.11 (m, 1H), 2.00–1.84 (m, 1H), 1.45–1.15 (m, 4H). ^{13}C NMR (75 MHz, DMSO-d_6): δ = 163.1, 154.5, 139.4, 137.1, 134.4, 129.3, 119.7, 107.6, 80.9, 79.7, 70.1, 38.3, 29.0, 27.3, 26.2, 22.3, 17.9, 16.7. MS: *m/z* (rel. intensity): 385 ([M^+], 2), 245 (17), 244 (100), 77 (18). IR (neat): 3335, 3102, 3066, 2965, 2937, 2910, 2848, 1658, 1610, 1583, 1537, 1448, 1441, 1371, 1305, 1145, 1080, 996, 988, 939, 926, 905, 852, 819, 728, 690, 609, 582, 558, 544, 523 cm^{-1}. HRMS ($C_{21}H_{23}N_1O_4S_1$+H): *calcd.* 386.14261; *found* 386.14248. Anal. *Calcd.* for $C_{21}H_{23}N_1O_4S_1$: C, 65.43; H, 3.53. *Found*: C, 65.52; H, 3.64.

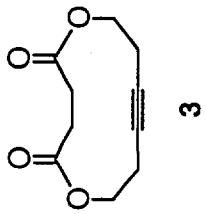
(10Z)-4-Oxo-3-phenylsulfonyl-5-aza-15-oxabicyclo[12.2.1]hepta-1,10,14-triene (64). A solution of quinoline in hexane (0.70 mL of a solution of 100 µL quinoline in 10 mL of hexane) was added to a solution of alkyne **63** (366 mg, 0.949 mmol) in CH_2Cl_2 (75 mL). Lindlar catalyst (175 mg) was added and the resulting suspension was exposed to hydrogen gas (1 atm). After stirring for 2 h at rt, the catalyst was filtered off, the solvent was evaporated, and the crude product was purified by flash chromatography (SiO_2, hexane/ethyl acetate = 2/1) affording (*Z*)-alkene **64** (357 mg, 97 %) as a colorless solid. mp > 195°C (decomp.). ^{1}H NMR (300 MHz, CD_2Cl_2/DMSO-d_6): δ = 7.88–7.82 (m, 2H), 7.71–7.60 (m, 2H), 7.55 (t, *J* = 7.5, 2H), 7.12 (s, 1H), 5.79 (s, 1H), 5.42–5.20 (m, 2H), 4.21 (dd, *J* = 10.8, 5.4, 1H), 3.48–3.34 (m, 1H), 2.90–2.80 (m, 2H), 2.75–2.54 (m, 3H), 2.28 (quin, *J* = 6.8, 2H), 1.72 (quart, *J* =7.8, 2H), 1.38–1.02 (m, 2H), 0.92–0.73 (m, 1H), 0.56–0-38 (m, 1H). ^{13}C

NMR (75 MHz, CD_2Cl_2/DMSO-d_6): δ = 163.6, 155.6, 139.0, 137.1, 133.8, 130.6, 129.5, 128.6, 128.0, 119.4, 107.1, 70.3, 39.0, 29.2, 27.5, 27.2, 26.8, 26.0, 23.1. MS: *m/z* (rel. intensity): 387 ([M^+], 4), 247 (16), 246 (100), 135 (22). IR (neat): 3296, 3121, 3096, 3074, 3004, 2943, 2855, 1658, 1628, 1609, 1548, 1446, 1439, 1307, 1261, 1143, 1083, 1026, 947, 916, 814, 756, 724, 690, 562, 529 cm^{-1}. HRMS ($C_{21}H_{25}N_1O_4S_1$+H): *calcd.* 388.15826; *found* 388.15778. Anal. *Calcd.* for $C_{21}H_{25}N_1O_4S_1$: C, 65.09; H, 6.50; N, 3.61. *Found*: C, 64.91; H, 6.57; N, 3.48.

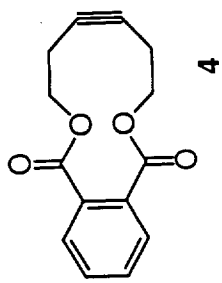


3

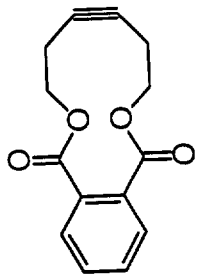
128.96
134.63
139.28
140.30
803.21
1267.58
1268.53
1273.15
1277.75
1278.76
2179.01
0
1
2
3
4
5
6
7
8
9



3

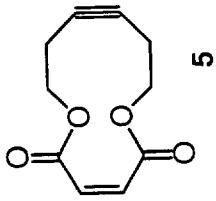


4



```
Current Data Parameters
NAME          my08-40
EXPNO              10
PROCNO              1
DU                  u
USER               au

F2 - Acquisition Parameters
Date_          980510
Time            15.33
INSTRUM        dpx300
PROBHD  5 mm QNP
PULPROG          zg30
TD              32768
SOLVENT         CDCl3
NS                 32
DS                  0
SWH          6172.839 Hz
FIDRES       0.188380 Hz
AQ           2.6542580 sec
RG               287.4
DW              81.000 usec
DE                4.50 usec
TE               300.0 K
D1           2.00000000 sec
P1              7.30 usec
SFO1         300.1318534 MHz
NUC1               1H
PL1              -6.00 dB

F2 - Processing parameters
SI              16384
SF         300.1300211 MHz
SR             21.15 Hz
WDW                EM
SSB                 0
LB              0.30 Hz
GB                  0
PC                2.00

1D NMR plot parameters
CX             22.00 cm
F1P             9.500 ppm
F1           2851.24 Hz
F2P            -0.500 ppm
F2           -150.07 Hz
PPMCM         0.45455 ppm/cm
HZCM        136.42276 Hz/cm
```

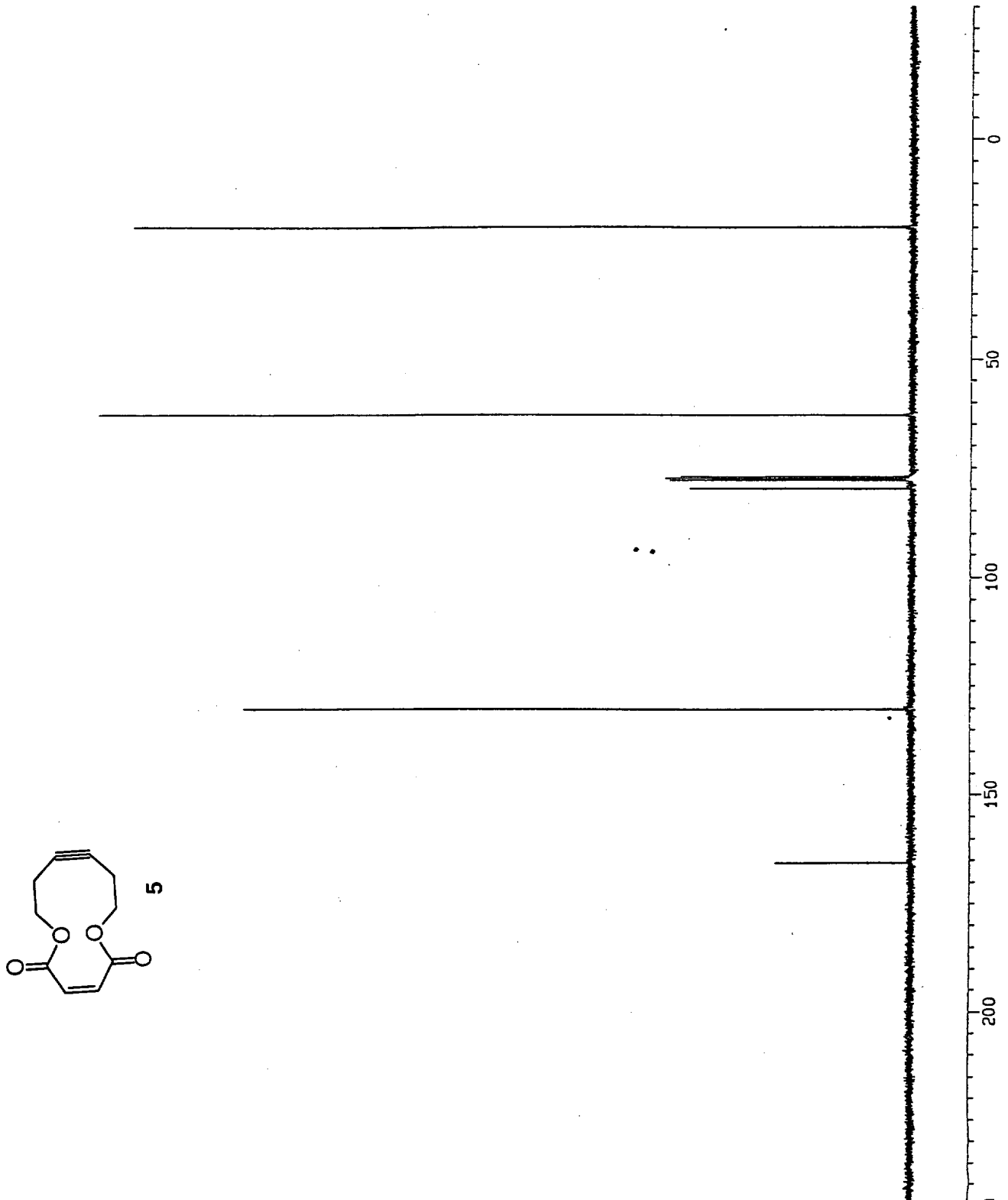
RUM-RA-073-01



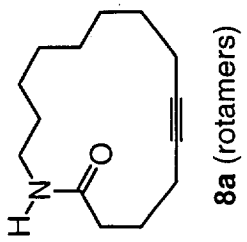
5

```
Current Data Parameters
NAME                  my08-40
EXPNO                      11
PROCNO                      1
DU                          u
USER                       au

F2 - Acquisition Parameters
Date_                  980510
Time                    16.06
INSTRUM                dpx300
PROBHD     5 mm QNP
PULPROG                zgdc30
TD                      65536
SOLVENT                 CDCl3
NS                       1200
DS                          2
SWH                 21231.422 Hz
FIDRES              0.323966 Hz
AQ                  1.5434228 sec
RG                      16384
DW                     23.550 usec
DE                      4.50 usec
TE                     300.0 K
D11                 0.03000000 sec
PL12                   16.20 dB
CPDPRG2                waltz16
PCPD2                  80.00 usec
SFO2                300.1312005 MHz
NUC2                        1H
PL2                    -6.00 dB
D1                  0.03000000 sec
P1                      6.60 usec
SFO1                75.4760670 MHz
NUC1                        13C
PL1                    -6.00 dB

F2 - Processing parameters
SI                         32768
SF                  75.4677190 MHz
SR                      0.00 Hz
WDW                         EM
SSB                          0
LB                      1.00 Hz
GB                           0
PC                      1.40

1D NMR plot parameters
CX                     22.00 cm
F1P                   250.000 ppm
F1                   18866.93 Hz
F2P                    -41.517 ppm
F2                   -3133.19 Hz
PPMCM               13.25077 ppm/cm
HZCM                1000.00562 Hz/cm
```

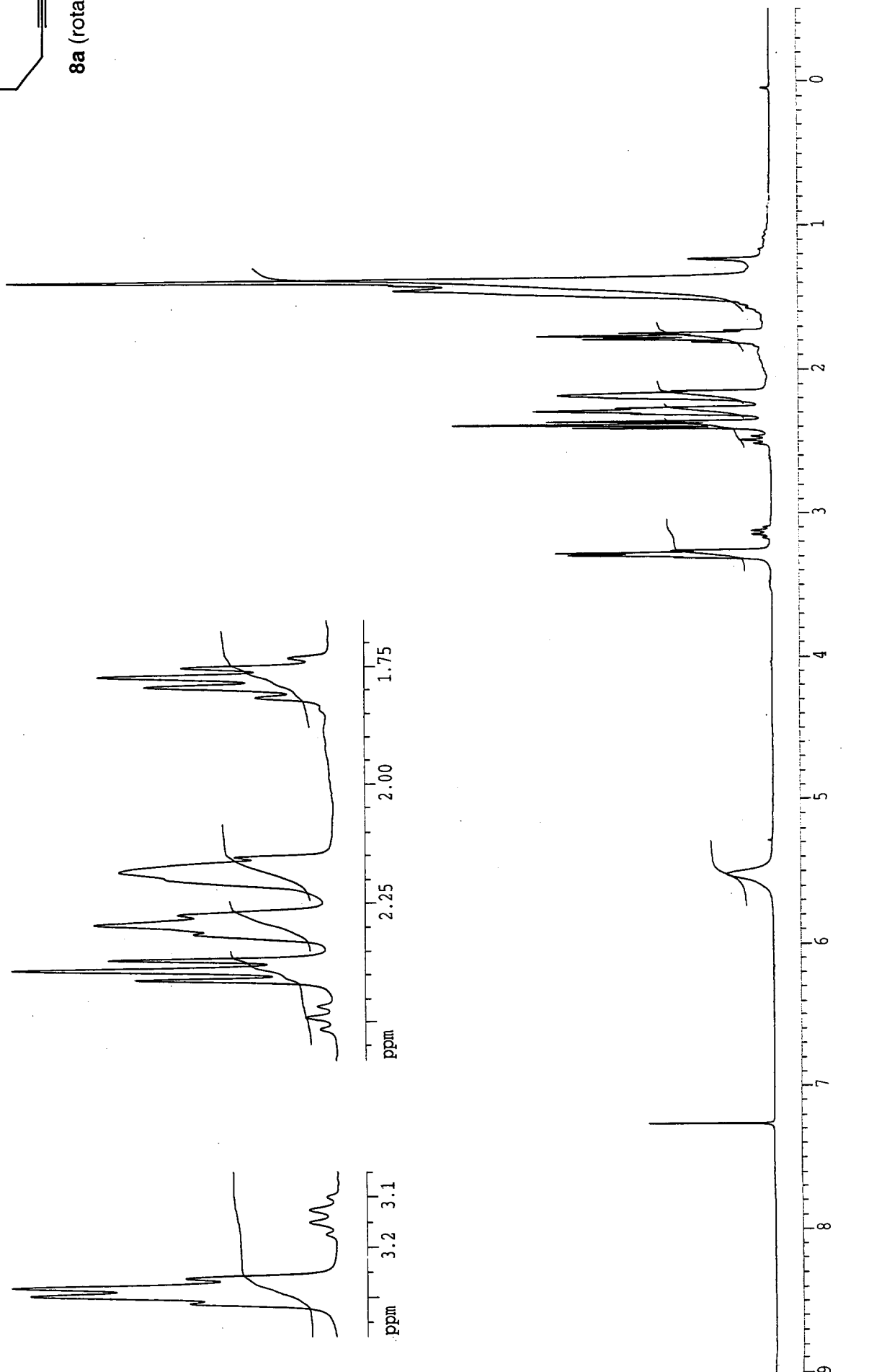
RUM-RA-073-01

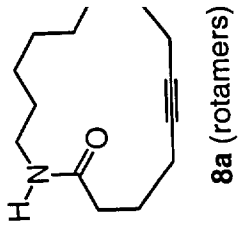


5

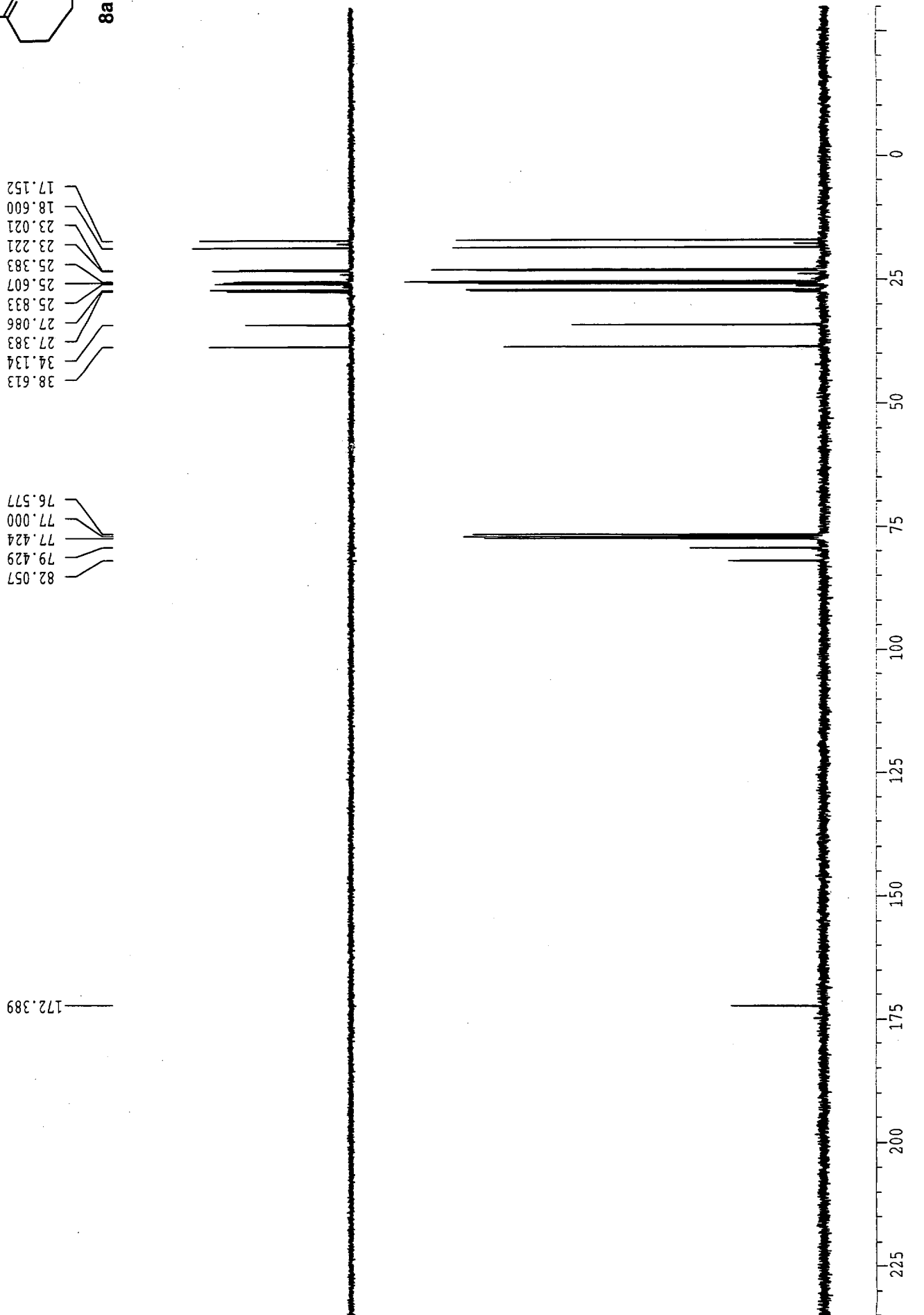


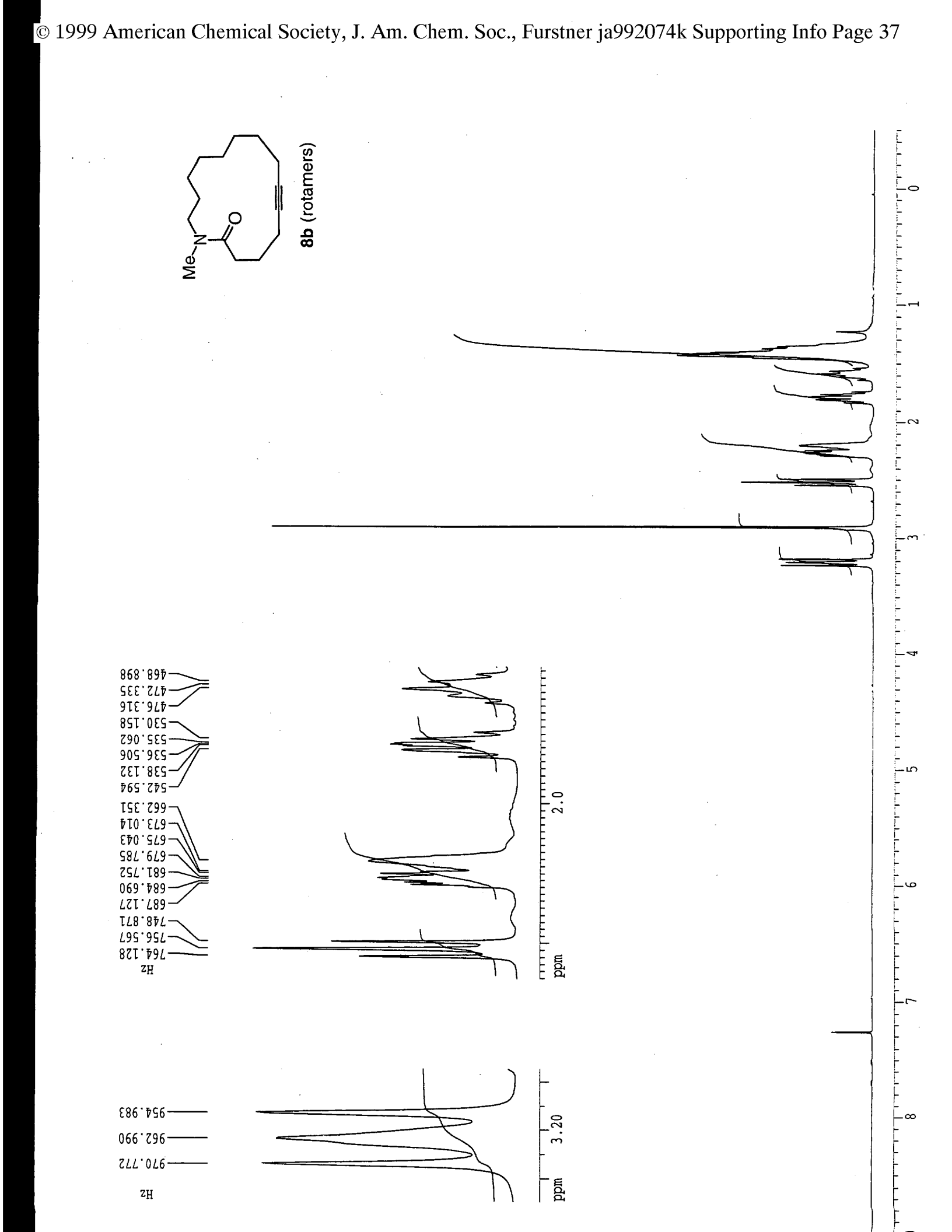
8a (rotamers)

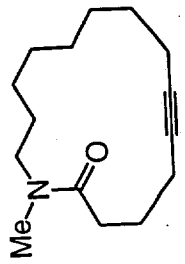




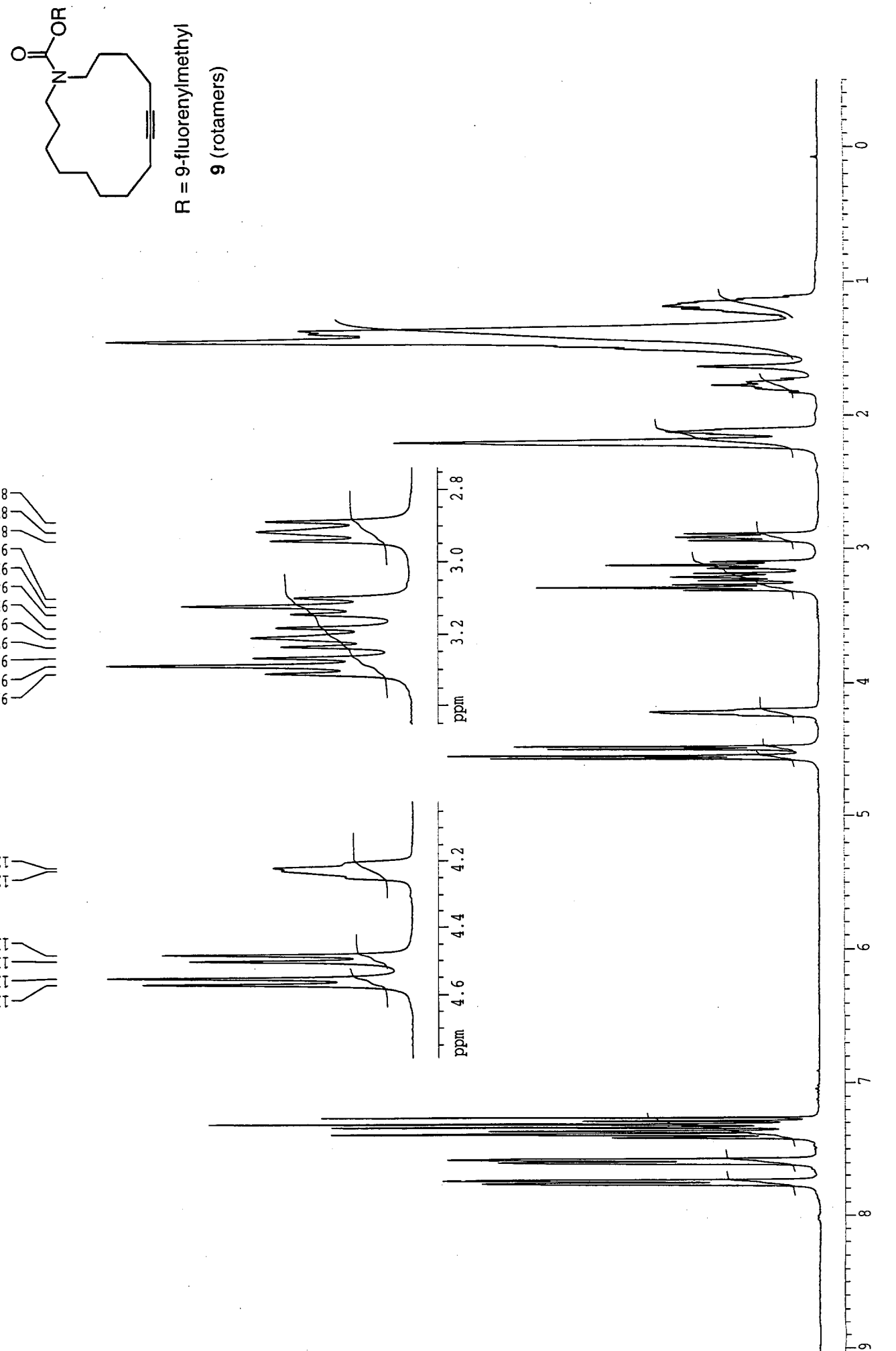
8a (rotamers)

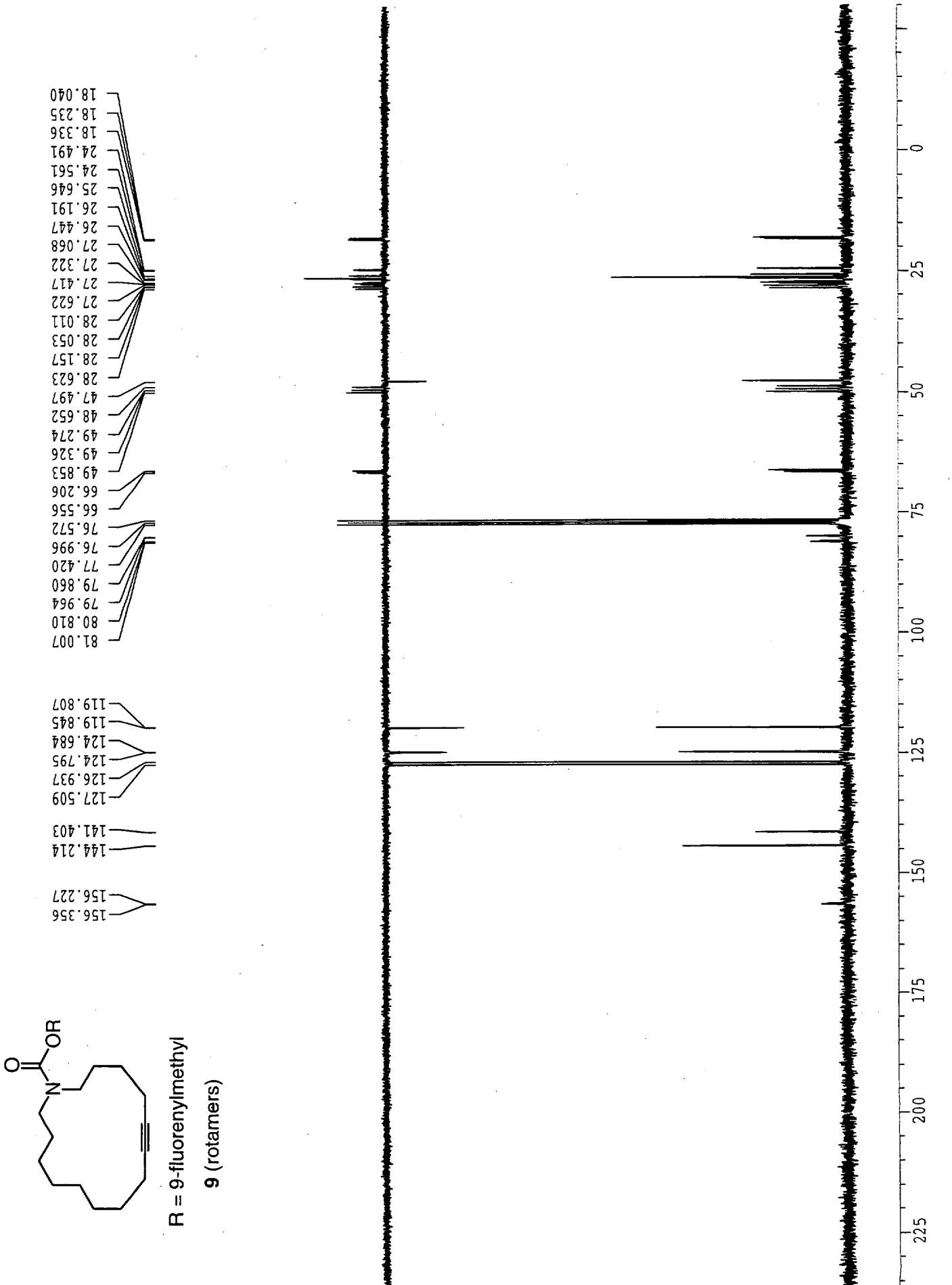






17.798
17.987
23.600
23.946
25.597
25.934
26.018
26.283
27.425
31.333
33.480
49.785
76.575
76.999
77.422
79.889
80.701
172.132
0
25
50
75
100
125
150
175
200
225




18.040
18.235
18.336
24.491
24.561
25.646
26.191
26.447
27.068
27.322
27.417
27.622
28.011
28.053
28.157
28.623
47.497
48.652
49.274
49.326
49.853
66.206
66.556
76.572
76.996
77.420
79.860
79.964
80.810
81.007
119.807
119.845
124.684
124.795
126.937
127.509
141.403
144.214
156.227
156.356
0
25
50
75
100
125
150
175
200
225
OR
O
N
R = 9-fluorenylmethyl
9 (rotamers)