S1

Contents:

Experimental section

General methods. Diethyl acetylsuccinate (**2a**), dimethyl acetylsuccinate (**2b**), diethyl 2-acetylglutarate (**2c**), methyl 2-(1,3-dioxo-2-cyclotetradecyl)acetate (**2d**), ethyl 4-acetyl-5-oxo-hexanoate (**2e**), methyl 4-acetyl-5-oxo-hexanoate (**2f**) and ethyl 2-methylacetoacetate (**13a**) were commercial materials and were used without further purification. Solvents and reagents were purchased and were used without further purification with the exception of THF, which was distilled from sodium hydroxide. Light petroleum ether refers to the fraction with bp 40-60 °C. 1,2-Diaza-1,3-butadienes **1a-l** were synthesized as a mixture of *E/Z* isomers as previously reported procedure.[10,11] Melting points were determined in open capillary tubes and are uncorrected. IR-FT spectra were obtained as Nujol mulls. Mass spectra were made at an ionizing voltage of 70 eV. All ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 MHz and at 100.65 MHz, respectively, in $CDCl_3$ solutions unless specified otherwise. Chemical shifts (δ_H) are reported relative to TMS as internal standard. All coupling constants (*J*) values are given in Hz. Chemical shifts (δ_C) are reported relative to $CDCl_3$ as internal standard, unless otherwise stated, in a broad band decoupled mode; the multiplicities were obtained using 135 and 90° DEPT experiments to aid in assignment (q = methyl, t = methylene, d = methine, s = quaternary). The abbreviations used are as follows: s, singlet; d, doublet; t, triplet; q, quartet, m, multiplet; br, broad. All the NH and NH_2 exchanged with D_2O. Precoated silica gel plates 0.25 mm were employed for analytical thin-layer chromatography and silica gel 60 Å (35-70 μ) for column chromatography. All new compounds showed satisfactory elemental analysis (C ± 0.35; H ± 0.30; N ± 0.30). The nomenclature was generated using ADC/IUPAC Name (version 3.50, 5 Apr 1998), Advanced Chemistry Development Inc., Toronto, ON (Canada).

General procedure for the synthesis of 3-ethyl 4-methyl 1-[(anilinocarbonyl)amino]-3-(2-ethoxy-2-oxoethyl)-5-methyl-2-hydroxy-2,3-dihydro-pyrrole-3,4-dicarboxylate 4a and of 6-amino-5,6a-dimethyl-2-oxo-2,3,6,6a-tetrahydro-3a-*H*-furo[2,3-*b*]pyrrole-3a,4-dicarboxylates 5a-m. To a magnetically stirred solution of 1,2-diaza-1,3-butadienes **1a-l** (1.0 mmol), prepared as a mixture of *E/Z*

isomers, as reported elsewhere,[10,11] and diethyl or dimethyl acetylsuccinate **2a,b** (1.0 mmol) in THF (25 mL) was added potassium carbonate (5.0 equiv.). The mixture was allowed to stand at room temperature until the disappearance of the reagents (0.5–2.0 h) and the formation of two spots as major components (**4** and **5**) was detected by TLC. Potassium carbonate was removed by filtration, and the reaction solvent was evaporated under reduced pressure. Products **5a-m** were crystallized by adding to the crude the appropriate solvents, for **5a,c,e,f,h-j,** ethyl acetate–light petroleum ether (at 40–60°C) and, for **5b,d,g,k-m,** ethyl acetate-cyclohexane were added. In the case of the reaction between **1a** and **2a**, along with **5a**, product **4a** was isolated as a colorless oil by flash chromatography on silica gel and was immediately subjected to ^{1}H NMR analysis because of its poor stability.

3-Ethyl 4-methyl 1-[(anilinocarbonyl)amino]-3-(2-ethoxy-2-oxoethyl)-5-methyl-2-hydroxy-2,3-dihydropyrrole-3,4-dicarboxylate (4a): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.13-1.25 (m, 6 H), 1.60 and 1.74 (2 s, 3 H), 2.13 and 2.19 (2 s, 3 H), 3.17 and 3.31 (AB-system, 2 H, *J* = 15.6), 3.62 and 3.65 (2 s, 3 H), 3.97 and 4.25 (m, 4 H), 5.42 and 5.78 (2 brs, 1 H), 7.20 and 7.70 (m, 6 H), 8.06 and 8.13 (2 brs, 1 H).

3a-Ethyl 4-methyl 6-[(anilinocarbonyl)amino]-5,6a-dimethyl-2-oxo-2,3,6,6a-tetrahydro-3a*H*-furo[2,3-*b*]pyrrole-3a,4-dicarboxylate (5a): mp 134-136 °C; IR (nujol) ν_{max} 3307, 3299, 1798, 1742, 1697, 1665 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.16 (t, 3 H, *J* = 7.0), 1.47 and 1.48 (2 s, 3 H), 2.17 and 2.18 (2 s, 3 H), 2.91 and 3.69 (AB-system, 2 H, *J* = 18.0), 3.59 (s, 3 H), 4.04-4.23 (m, 2 H), 6.97 (t, 1 H, *J* = 8.4), 7.26 (t, 2 H, *J* = 8.4), 7.42 (d, 2 H, *J* = 8.4), 8.71-8.95 (m, 2 H); ^{13}C NMR (100.65 MHz, DMSO-d_6) δ 12.6 (q), 12.8 (q), 13.7 (q), 14.8 (q), 18.8 (q), 19.6 (q), 38.4 (s), 39.1 (s), 51.5 (q), 60.1 (t), 62.5 (t), 100.2 (s), 104.2 (s), 119.2 (d), 119.8 (d), 122.9 (d), 123.0 (d), 139.7 (s), 155.2 (s), 155.4 (s), 161.8 (s), 164.6 (s), 164.8 (s), 169.4 (s), 170.3 (s), 173.3 (s), 173.8 (s); EIMS *m/z* 418 (8) [M^++1], 417 (34) [M^+], 386 (5), 344 (19), 299 (15), 298 (100). Anal. Calcd for $C_{20}H_{23}N_3O_7$: C, 57.55; H, 5.55; N, 10.07. Found: C, 57.43; H, 5.41; N, 10.29.

3a-Ethyl 4-(2-methoxyethyl) 6-[(anilinocarbonyl)amino]-5,6a-dimethyl-2-oxo-2,3,6,6a-tetrahydro-3a*H*-furo[2,3-*b*]pyrrole-3a,4-dicarboxylate (5b): mp 118-120 °C; IR (nujol) ν_{max} 3305, 3229, 1797, 1749, 1721, 1669, 1631 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.20-1.33 (m, 3 H), 1.63 (s, 3 H), 2.35 (s, 3 H), 3.16 and 3.59 (AB-system, 2 H, *J* = 18.4), 3.36 (s, 3 H), 3.50-3.54 (m, 2 H), 4.20-4.33 (m, 4 H), 7.02-7.70 (m, 7 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 12.5 (q), 14.5 (q), 18.3 (q), 18.6 (q), 37.0 (s), 59.1 (q), 60.1 (t), 63.0 (t), 63.8 (t), 70.6 (t), 103.2 (s), 103.8 (s), 104.6 (s), 119.8 (d), 120.1 (d), 124.3 (d), 124.5 (d), 129.4 (d), 137.5 (s), 154.9 (s), 161.1 (s), 163.9 (s), 169.2 (s), 172.3 (s), 172.9 (s); EIMS *m/z* 462 (8) $[M^+ +1]$, 461 (31) $[M^+]$, 388 (19), 343 (18), 342 (100). Anal. Calcd for $C_{22}H_{27}N_3O_8$: C, 57.26; H, 5.90; N, 9.11. Found: C, 57.12; H, 6.02; N, 9.43.

Diethyl 6-{[(3-fluoro)anilinocarbonyl]amino}-5,6a-dimethyl-2-oxo-2,3,6,6a-tetrahydro-3a*H*-furo[2,3-*b*]pyrrole-3a,4-dicarboxylate (5c): mp 105-108 °C; IR (nujol) ν_{max} 3356, 3297, 1794, 1765, 1748, 1734 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.16-1.36 (m, 6 H), 1.60 (s, 3 H), 2.31 (s, 3 H), 3.02-3.15 and 3.57-3.83 (m, 2 H), 4.06-4.35 (m, 4 H), 6.75-7.79 (m, 6 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 12.1 (q), 12.3 (q), 14.3 (q), 14.5 (q), 18.3 (s), 18.5 (q), 37.2 (s), 60.2 (t), 60.5 (t), 61.1 (t), 63.0 (t), 103.0 (s), 103.6 (s), 104.8 (s), 107.4 (d, $^2J_{CF}$ = 27.5), 111.1 (d, $^2J_{CF}$ = 21.2), 114.9 (d), 130.4 (d, $^3J_{CF}$ = 9.1), 139.3 (s, $^3J_{CF}$ = 11.4), 154.9 (s), 156.1 (s), 159.6 (s, $^1J_{CF}$ = 213.8), 162.1 (s), 164.2 (s), 164.5 (s), 169.3 (s), 169.4 (s), 173.1 (s); EIMS *m/z* 450 (9) $[M^+ +1]$, 449 (37) $[M^+]$, 376 (25), 332 (25), 313 (16), 312 (100). Anal. Calcd for $C_{21}H_{24}N_3O_7F$: C, 56.12; H, 5.38; N, 9.35. Found: C, 56.22; H, 5.09; N, 9.44.

3a-Ethyl 4-methyl 6-[(aminocarbonyl)amino)-5,6a-dimethyl-2-oxo-2,3,6,6a-tetrahydro-3a*H*-furo[2,3-*b*]pyrrole-3a,4-dicarboxylate (5d): mp 158-161 °C; IR (nujol) ν_{max} 3413, 3296, 3180, 1784, 1743, 1717, 1654 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 0.96-1.18 (m, 3 H), 1.39 and 1.46 (2 s, 3 H), 2.09 and 2.13 (2 s, 3 H), 2.88 and 3.64 (AB-system, 2 H, *J* = 18.0), 3.56 and 3.57 (2 s, 3 H), 4.06-4.22 (m, 2 H), 6.01 and 6.27 (2 brs, 2 H), 8.40 and 8.56 (2 brs, 1 H); ^{13}C NMR (100.65 MHz, DMSO-d_6) δ 12.5 (q), 14.7 (q), 18.6 (q), 19.5 (q), 38.2 (s), 39.2 (s), 51.4 (q), 51.5 (q), 60.0 (t), 60.1 (t), 62.5 (t), 100.3 (s), 104.1 (s), 104.7 (s), 158.5 (s), 158.9 (s), 160.6 (s), 161.8 (s), 164.6 (s), 164.8 (s), 169.4 (s),

170.4 (s), 173.1 (s), 173.9 (s); EIMS *m/z* 342 (7) [M^++1], 341 (43) [M^+], 298 (45), 255 (53), 224 (77), 196 (18), 195 (100). Anal. Calcd for $C_{14}H_{19}N_3O_7$: C, 49.27; H, 5.61; N, 12.31. Found: C, 49.11; H, 5.48; N, 12.09.

Diethyl 6-({[(4-methoxybenzyl)oxy]carbonyl}amino)-5,6a-dimethyl-2-oxo-2,3,6,6a-tetrahydro-3a*H*-furo[2,3-*b*]pyrrole-3a,4-dicarboxylate (5e): mp 121-123 °C; IR (nujol) ν_{max} 3258, 1770, 1753, 1670, 1632 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.03-1.26 (m, 6 H), 1.38 and 1.50 (2 s, 3 H), 2.14 and 2.18 (2 s, 3 H), 2.98 and 3.69 (AB-system, 2 H, *J* = 18.4), 3.77 (s, 3 H), 3.96-4.27 (m, 4 H), 5.09 (s, 2 H), 6.85 (d, 2 H, *J* = 8.4), 7.01 and 7.17-7.31 (s and m, 3 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 11.6 (q), 13.9 (q), 14.2 (q), 18.4 (q), 37.9 (s), 55.1 (q), 59.7 (t), 62.1 (t), 62.2 (t), 67.6 (t), 67.7 (t), 101.0 (s), 101.3 (s), 103.4 (s), 103.4 (s), 113.8 (d), 127.3 (s), 130.0 (d), 130.2 (s), 155.8 (s), 159.6 (s), 160.3 (s), 164.0 (s), 168.9 (s), 173.2 (s); MS *m/z* 476 (7) [M^+], 432 (66), 311 (90), 223 (100). Anal. Calcd for $C_{23}H_{28}N_2O_9$: C, 57.98; H, 5.92; N, 5.88. Found: C, 57.69; H, 5.78; N, 5.73.

3a-Ethyl 4-methyl 6-[(benzyloxycarbonyl)amino]-5,6a-dimethyl-2-oxo-2,3,6,6a-tetrahydro-3a*H*-furo[2,3-*b*]pyrrole-3a,4-dicarboxylate (5f): mp 110-112 °C; IR (nujol) ν_{max} 3276, 1769, 1731, 1729, 1685, 1637 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.22 (m, 3 H), 1.50 and 1.52 (2 s, 3 H), 2.14 and 2.20 (2 s, 3 H), 3.00 and 3.64 (AB-system, 2 H, *J* = 18.4), 3.66 (s, 3 H), 4.00-4.18 (m, 2 H), 6.95 and 7.08 (2 brs, 1 H), 7.14-7.27 (m, 5 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 12.0 (q), 14.3 (q), 18.7 (q), 18.7 (q), 38.1 (s), 38.2 (s), 51.3 (q), 60.0 (t), 62.6 (t), 68.2 (t), 68.2 (t), 101.7 (s), 102.6 (s), 103.8 (s), 128.3 (d), 128.8 (d), 128.9 (d), 135.6 (s), 156.0 (s), 160.7 (s), 164.8 (s), 169.2 (s), 173.0 (s), 173.4 (s); EIMS *m/z* 433 (2) [M^++1], 432 (11) [M^+], 401 (3), 387 (2), 359 (4), 345 (2), 315 (5), 298 (15), 297 (100). Anal. Calcd for $C_{21}H_{24}N_2O_8$: C, 58.33; H, 5.59; N, 6.48. Found: C, 58.05; H, 5.43; N, 6.57.

3a-Ethyl 4-methyl 6-[(*tert*-butoxycarbonyl)amino]-5,6a-dimethyl-2-oxo-2,3,6,6a-tetrahydro-3a*H*-furo[2,3-*b*]pyrrole-3a,4-dicarboxylate (5g): mp 133-135 °C; IR (nujol) ν_{max} 3355, 1794, 1757, 1733, 1702, 1640 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.21 and 1.22 (2 t, 3 H, *J* = 7.0), 1.44 and 1.46 (2 s, 9 H), 1.52 and 1.54 (2 s, 3 H), 2.23 (s, 3 H), 3.00 and 3.72 (AB-system, 2 H, *J* = 18.8), 3.66 (s, 3

H), 4.16 and 4.25 (2 q, 2 H, *J* = 7.0), 6.58 and 6.72 (2 brs, 1 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 11.7 (q), 14.0 (q), 18.4 (q), 28.0 (q), 38.1 (s), 38.3 (s), 50.9 (q), 59.7 (t), 62.2 (t), 81.9 (s), 101.1 (s), 103.6 (s), 154.6 (s), 160.1 (s), 160.7 (s), 164.5 (s), 169.0 (s), 173.2 (s); EIMS *m/z* 399 (3) [M^++1], 398 (16) [M^+], 367 (8), 342 (27), 325 (26), 311 (14), 299 (20), 298 (100). Anal. Calcd for $C_{18}H_{26}N_2O_8$: C, 54.26; H, 6.58; N, 7.03. Found: C, 54.38; H, 6.44; N, 6.99.

4-Ethyl 3a-methyl 6-[(anilinocarbonyl)amino]-5,6a-dimethyl-2-oxo-2,3,6,6a-tetrahydro-3a*H*-furo[2,3-*b*]pyrrole-3a,4-dicarboxylate (5h): mp 170-172 °C; IR (nujol) ν_{max} 3310, 3300, 1796, 1740, 1698, 1667 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.14 (t, 3 H, *J* = 7.2), 1.46 (s, 3 H), 2.18 (s, 3 H), 2.90 and 3.71 (AB-system, 2 H, *J* = 18.4), 3.69 (s, 3 H), 4.05 (q, 2 H, *J* = 7.2), 6.97 (t, 1 H, *J* = 7.6), 7.28 (m, 2 H), 7.42 (d, 2 H, *J* = 8.4), 8.47 and 8.81 (2 brs, 2 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 12.4 (q), 14.9 (q), 18.8 (q), 38.5 (s), 53.6 (q), 60.0 (t), 100.9 (s), 104.1 (s), 119.4 (d), 122.7 (d), 129.6 (d), 139.8 (d), 155.4 (s), 161.9 (s), 164.3 (s), 170.4 (s), 173.4 (s); EIMS *m/z* 418 (7) [M^++1], 417 (27) [M^+], 344 (13), 299 (16), 298 (100). Anal. Calcd for $C_{20}H_{23}N_3O_7$: C, 57.55; H, 5.55; N, 10.07. Found: C, 57.48; H, 5.61; N, 10.31.

Dimethyl 6-[(aminocarbonyl)amino)-5,6a-dimethyl-2-oxo-2,3,6,6a-tetrahydro-3a*H*-furo[2,3-*b*]pyrrole-3a,4-dicarboxylate (5i): mp 159-160 °C; IR (nujol) ν_{max} 3410, 3298, 3178, 1786, 1740, 1720, 1658 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.44 (s, 3 H), 2.12 (s, 3 H), 2.88 and 3.63 (AB-system, 2 H, *J* = 18.4), 3.58 (s, 3 H), 3.66 (s, 3 H), 6.04 and 6.27 (2 brs, 2 H), 8.53 (s, 1 H); ^{13}C NMR (100.65 MHz, DMSO-d_6) δ 12.4 (q), 18.6 (q), 38.2 (s), 51.6 (q), 53.7 (q), 59.9 (t), 102.3 (s), 104.2 (s), 158.7 (s), 162.1 (s), 164.8 (s), 170.3 (s), 173.3 (s); EIMS *m/z* 328 (3) [M^++1], 327 (26) [M^+], 296 (36), 268 (71), 237 (36), 209 (100). Anal. Calcd for $C_{13}H_{17}N_3O_7$: C, 47.71; H, 5.24; N, 12.84. Found: C, 47.81; H, 5.18; N, 12.79.

4-Ethyl 3a-methyl 6-[(aminocarbonyl)amino)-5,6a-dimethyl-2-oxo-2,3,6,6a-tetrahydro-3a*H*-furo[2,3-*b*]pyrrole-3a,4-dicarboxylate (5j): mp 122-125 °C; IR (nujol) ν_{max} 3410, 3298, 3182, 1790, 1741, 1718, 1650 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.15 (t, 3 H, *J* = 7.2), 1.43 (s, 3 H), 2.12 (s, 3

H), 2.86 and 3.63 (AB-system, 2 H, *J* = 19.2), 3.65 (s, 3 H), 4.01 (q, 2 H, *J* = 7.2), 5.95 and 6.23 (2 brs, 2 H), 8.38 and 8.49 (2 brs, 1 H); ^{13}C NMR (100.65 MHz, DMSO-d_6) δ 11.8 (q), 17.4 (q), 18.9 (q), 39.0 (s), 39.2 (s), 51.1 (q), 59.7 (t), 59.8 (t), 62.1 (t), 101.1 (s), 104.8 (s), 157.6 (s), 157.9 (s), 157.9 (s), 161.1 (s), 161.3 (s), 164.2 (s), 169.7 (s), 170.1 (s), 173.1 (s), 174.2 (s); EIMS *m/z* 342 (5) [M^++1], 341 (37) [M^+], 298 (51), 255 (61), 224 (72), 196 (16), 195 (100). Anal. Calcd for $C_{14}H_{19}N_3O_7$: C, 49.27; H, 5.61; N, 12.31. Found: C, 49.21; H, 5.56; N, 12.23.

4-Ethyl 3a-methyl 6-[(benzyloxycarbonyl)amino]-5,6a-dimethyl-2-oxo-2,3,6,6a-tetrahydro-3a*H*-furo[2,3-*b*]pyrrole-3a,4-dicarboxylate (5k): mp 99-101 °C; IR (nujol) ν_{max} 3310, 3298, 1796, 1740, 1695, 1660 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (t, 3 H, *J* = 7.2), 1.53 (s, 3 H), 2.22 (s, 3 H), 3.05 and 3.68 (AB-system, 2 H, *J* = 18.4), 3.75 (s, 3 H), 4.18 (q, 2 H, *J* = 7.2), 5.22 (s, 2 H), 6.78 and 6.97 (2 brs, 1 H), 7.36 (s, 5 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 12.1 (q), 14.6 (q), 18.8 (q), 38.4 (s), 53.5 (q), 60.1 (t), 68.3 (t), 102.7 (s), 103.6 (s), 128.4 (d), 128.9 (d), 128.9 (d), 135.5 (s), 156.0 (s), 160.4 (s), 164.2 (s), 169.9 (s), 173.2 (s); EIMS *m/z* 433 (4) [M^++1], 432 (37) [M^+], 341 (64), 325 (19), 297 (100). Anal. Calcd for $C_{21}H_{24}N_2O_8$: C, 58.33; H, 5.59; N, 6.48. Found: C, 58.41; H, 5.48; N, 6.39.

4-Ethyl 3a-methyl 6-[(*tert*-butoxycarbonyl)amino]-5,6a-dimethyl-2-oxo-2,3,6,6a-tetrahydro-3a*H*-furo[2,3-*b*]pyrrole-3a,4-dicarboxylate (5l): mp 109-112 °C; IR (nujol) ν_{max} 3350, 1790, 1760, 1731, 1700, 1640 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.14 (t, 3 H, *J* = 7.1), 1.21-1.55 (m, 12 H), 2.10 (s, 3 H), 2.87 and 3.61 (AB-system, 2 H, *J* = 18.4), 3.65 (s, 3 H), 4.00 (q, 2 H, *J* = 7.1), 9.21 and 9.57 (2 brs, 1 H); ^{13}C NMR (100.65 MHz, DMSO-d_6) δ 12.1 (q), 14.9 (q), 18.7 (q), 28.5 (q), 38.4 (s), 53.6 (q), 59.7 (t), 60.0 (t), 80.9 (s), 100.1 (s), 104.0 (s), 155.9 (s), 161.0 (s), 164.2 (s), 170.3 (s), 173.3 (s); EIMS *m/z* 399 (2) [M^++1], 398 (14) [M^+], 367 (8), 342 (28), 325 (11), 311 (8), 299 (27), 298 (100). Anal. Calcd for $C_{18}H_{26}N_2O_8$: C, 54.26; H, 6.58; N, 7.03. Found: C, 54.31; H, 6.51; N, 6.49.

Dimethyl 6-[(methoxycarbonyl)amino]-5,6a-dimethyl-2-oxo-2,3,6,6a-tetrahydro-3a*H*-furo[2,3-*b*]pyrrole-3a,4-dicarboxylate (5m): mp 163-165 °C; IR (nujol) ν_{max} 3358, 1798, 1760, 1730, 1710, 1638 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.42 (s, 3 H), 2.12 (s, 3 H), 2.90 and 3.69 (AB-system, 2

H, J = 18.4), 3.58 (s, 3 H), 3.64 (s, 3 H), 3.67 (s, 3 H), 9.85 (brs, 1 H); ^{13}C NMR (100.65 MHz, DMSO-d_6) δ 12.2 (q), 18.6 (q), 38.0 (s), 51.5 (q), 53.2 (q), 53.8 (q), 60.0 (t), 100.2 (s), 103.9 (s), 157.4 (s), 161.0 (s), 164.8 (s), 170.1 (s), 173.2 (s); EIMS *m/z* 343 (2) [M^++1], 342 (23) [M^+], 311 (37), 283 (56), 236 (72), 208 (100). Anal. Calcd for $C_{14}H_{18}N_2O_8$: C, 49.12; H, 5.30; N, 8.18. Found: C, 49.28; H, 5.50; N, 8.24.

General procedure for the synthesis of 3-(2-ethoxy-2-oxoethyl)-5-methyl-2-methylene-2,3-dihydro-1-aminopyrroles 6a-g. The crude product, which was obtained after the filtration of compounds **5a-d,h-j** and the evaporation of the crystallization solvents, as well as pure **4a,** were refluxed in THF after the addition of a drop of acetic acid. The conversion into pertinent 2-methylene pyrroles **6a-g** occurred in 2–12 h (as tested by TLC). Products **6a-g** were purified by flash chromatography on a silica gel column and crystallized from diethyl ether–light petroleum ether (at 40–60°C).

3-Ethyl 4-methyl 1-[(anilinocarbonyl)amino]-3-(2-ethoxy-2-oxoethyl)-5-methyl-2-methylene-2,3-dihydropyrrole-3,4-dicarboxylate (6a): mp 148-150 °C; IR (nujol) ν_{max} 3324, 3201, 3121, 1749, 1722, 1690, 1669 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.14-1.27 (m, 6 H), 2.39 (s, 3 H), 3.14 and 3.53 (AB-system, 2 H, J = 17.2), 3.70 (s, 3 H), 4.01-4.17 (m, 4 H), 4.35 and 4.50 (AB-system, 2 H, J = 2.8), 7.04 (t, 1 H, J = 7.2), 7.28 (t, 2 H, J = 7.2), 7.39 (s, 1 H), 7.63 (d, 2 H, J = 7.2), 8.62 (s, 1 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 11.8 (q), 14.2 (q), 14.3 (q), 41.6 (t), 51.1 (q), 54.5 (s), 61.3 (t), 62.1 (t), 84.4 (t), 102.2 (s), 120.0 (d), 123.7 (d), 128.9 (d), 138.6 (s), 150.9 (s), 155.6 (s), 158.8 (s), 164.8 (s), 170.7 (s), 172.1 (s); EIMS *m/z* 446 (5) [M^++1], 445 (23) [M^+], 372 (83), 340 (36), 313 (24), 312 (100). Anal. Calcd for $C_{22}H_{27}N_3O_7$: C, 59.32; H, 6.11; N, 9.43. Found: C, 59.14; H, 5.98; N, 9.61.

3-Ethyl 4-(2-methoxyethyl) 1-[(anilinocarbonyl)amino]-3-(2-ethoxy-2-oxoethyl)-5-methyl-2-methylene-2,3-dihydropyrrole-3,4-dicarboxylate (6b): mp 154-157 °C; IR (nujol) ν_{max} 3321, 3198, 3118, 1752, 1721, 1688, 1671 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16-1.33 (m, 6 H), 2.37 (s, 3 H), 3.15 and 3.57 (AB-system, 2 H, J = 17.2), 3.34 (s, 3 H), 3.30-3.49 (m, 2 H), 4.07-4.29 (m, 6 H), 7.02

(t, 1 H, J = 7.3), 7.24 (t, 2 H, J = 7.3), 7.39-7.57 (m, 3 H), 8.76 (s, 1 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 11.8 (q), 14.3 (q), 14.6 (q), 41.6 (t), 54.6 (s), 59.1 (q), 61.3 (t), 63.0 (t), 63.1 (t), 70.4 (t), 83.4 (t), 103.8 (s), 120.6 (d), 122.9 (d), 129.9 (d), 136.0 (s), 151.0 (s), 155.0 (s), 158.7 (s), 164.2 (s), 170.7 (s), 172.9 (s); EIMS *m/z* 490 (2) [M^++1], 489 (12) [M^+], 414 (23), 369 (16), 340 (73), 313 (24), 312 (100). Anal. Calcd for $C_{24}H_{31}N_3O_8$: C, 58.89; H, 6.38; N, 8.58. Found: C, 58.72; H, 6.48; N, 8.63.

Diethyl 1-{[(3-fluoro)anilinocarbonyl]amino}-3-(2-ethoxy-2-oxoethyl)-5-methyl-2-methylene-2,3-dihydropyrrole-3,4-dicarboxylate (6c): mp 159-161 °C; IR (nujol) ν_{max} 3319, 3205, 1753, 1718, 1695, 1670 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.13-1.29 (m, 9 H), 2.38 (s, 3 H), 3.13 and 3.54 (AB-system, 2 H, J = 17.2), 4.10-4.20 (m, 6 H), 4.36 and 4.48 (AB-system, 2 H, J = 2.8), 6.63 (s, 1 H), 6.70-6.85 (m, 1 H), 7.13-7.26 (m, 2 H), 7.40-7.49 (m, 2 H), 8.73 (s, 1 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 11.7 (q), 14.2 (q), 14.2 (q), 14.6 (q), 41.7 (t), 54.6 (s), 59.9 (t), 61.4 (t), 62.2 (t), 83.4 (t), 102.7 (s), 107.2 (d, $^2J_{CF}$ = 26.6), 110.3 (d, $^2J_{CF}$ = 20.4), 115.1 (d), 130.0 (d, $^3J_{CF}$ = 9.8), 140.3 (s, $^3J_{CF}$ = 10.6), 150.9 (s), 155.0 (s), 158.2 (s), 163.1 (s, $^1J_{CF}$ = 228.0), 164.4 (s), 170.6 (s), 172.3 (s); MS *m/z* 478 (6) [M^++1], 477 (29) [M^+], 432 (12), 405 (27), 404 (100). Anal. Calcd for $C_{23}H_{28}N_3O_7F$: C, 57.85; H, 5.91; N, 8.80. Found: C, 57.72; H, 5.98; N, 8.73.

Ethyl 4-methyl 1-[(aminocarbonyl)amino]-3-(2-ethoxy-2-oxoethyl)-5-methyl-2-methylene-2,3-dihydropyrrole-3,4-dicarboxylate (6d): mp 173-175 °C; IR (nujol) ν_{max} 3377, 3274, 3169, 1750, 1721, 1698, 1672 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.15-1.28 (m, 6 H), 2.34 (s, 3 H), 3.14 and 3.54 (AB-system, 2 H, J = 17.2), 3.72 (s, 3 H), 4.03-4.18 (m, 4 H), 4.36 and 4.49 (AB-system, 2 H, J = 2.8), 6.03 and 6.34 (2 brs, 2 H), 8.59 (s, 1 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 11.6 (q), 14.3 (q), 14.3 (q), 41.6 (t), 52.0 (q), 54.6 (s), 61.6 (t), 62.3 (t), 83.4 (t), 102.5 (s), 151.1 (s), 155.7 (s), 158.9 (s), 164.4 (s), 170.7 (s), 172.3 (s); EIMS *m/z* 370 (3) [M^++1], 369 (16) [M^+], 324 (78), 293 (21), 250 (26), 249 (100). Anal. Calcd for $C_{16}H_{23}N_3O_7$: C, 52.03; H, 6.28; N, 11.38. Found: C, 51.97; H, 6.38; N, 11.12.

3-Ethyl 4-methyl 1-[(anilinocarbonyl)amino]-3-(2-methoxy-2-oxoethyl)-5-methyl-2-methylene-2,3-dihydropyrrole-3,4-dicarboxylate (6e): mp 149-152 °C; IR (nujol) ν_{max} 3322, 3200, 3120, 1750,

1721, 1690, 1670 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.22 (t, 3 H, *J* = 7.2), 2.38 (s, 3 H), 3.15 and 3.54 (AB-system, 2 H, *J* = 17.6), 3.65 (s, 3 H), 4.16 (q, 2 H, *J* = 7.2), 4.32 and 4.49 (AB-system, 2 H, *J* = 2.8), 7.02 (t, 1 H, *J* = 7.6), 7.20-7.28 (m, 2 H), 7.43 (s, 1 H), 7.60 (d, 2 H, *J* = 7.6), 8.59 (s, 1 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 11.8 (q), 14.5 (q), 41.2 (t), 52.2 (q), 53.3 (s), 54.4 (q), 59.8 (t), 83.5 (t), 102.2 (s), 120.0 (d), 123.7 (d), 128.9 (d), 138.5 (s), 150.8 (s), 155.7 (s), 158.8 (s), 164.3 (s), 171.4 (s), 172.4 (s); EIMS *m/z* 432 (3) [M^++1], 431 (27) [M^+], 400 (16), 386 (33), 372 (71), 358 (60), 327 (100). Anal. Calcd for $C_{21}H_{25}N_3O_7$: C, 58.46; H, 5.84; N, 9.74. Found: C, 58.34; H, 5.99; N, 9.61.

Dimethyl 1-[(aminocarbonyl)amino]-3-(2-ethoxy-2-oxoethyl)-5-methyl-2-methylene-2,3-dihydro-pyrrole-3,4-dicarboxylate (6f): mp 171-173 °C; IR (nujol) ν_{max} 3375, 3278, 3170, 1752, 1720, 1695, 1670 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.34 (s, 3 H), 3.07 and 3.50 (AB-system, 2 H, *J* = 17.2), 3.57 (s, 3 H), 3.68 (s, 3 H), 3.69 (s, 3 H), 4.24 and 4.29 (AB-system, 2 H, *J* = 2.8), 6.01 and 6.32 (2 brs, 2 H), 6.82 and 7.26 (2 brs, 1 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 14.6 (q), 41.3 (t), 51.9 (q), 52.4 (s), 54.4 (q), 51.3 (q), 83.3 (t), 101.8 (s), 103.4 (s), 150.4 (s), 159.4 (s), 164.3 (s), 171.4 (s), 172.1 (s); EIMS *m/z* 342 (2) [M^++1], 441 (16) [M^+], 310 (67), 282 (100). Anal. Calcd for $C_{14}H_{19}N_3O_7$: C, 49.27; H, 5.61; N, 12.31. Found: C, 49.14; H, 5.78; N, 12.48.

4-Ethyl 3-methyl 1-[(anilinocarbonyl)amino]-3-(2-methoxy-2-oxoethyl)-5-methyl-2-methylene-2,3-dihydropyrrole-3,4-dicarboxylate (6g): mp 169-171 °C; IR (nujol) ν_{max} 3374, 3274, 3172, 1750, 1720, 1698, 1671 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.19 (t, 3 H, *J* = 7.2), 2.32 (s, 3 H), 3.06 and 3.48 (AB-system, 2 H, *J* = 17.2), 3.55 (s, 3 H), 3.62 (s, 3 H), 4.11 (q, 2 H, *J* = 7.2), 4.26 and 4.42 (AB-system, 2 H, *J* = 2.8), 6.61 and 6.80 (2 brs, 2 H), 7.67 (brs, 1 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 11.6 (q), 14.5 (q), 41.2 (t), 52.0 (q), 53.2 (s), 54.3 (q), 59.7 (t), 83.0 (t), 101.7 (s), 108.1 (s), 150.3 (s), 158.7 (s), 164.3 (s), 171.4 (s), 172.1 (s); EIMS *m/z* 355 (13) [M^++1], 324 (51) [M^+], 310 (57), 296 (100). Anal. Calcd for $C_{15}H_{21}N_3O_7$: C, 50.70; H, 5.96; N, 11.82. Found: C, 50.74; H, 5.77; N, 11.88.

General procedure for the synthesis of 3-ethyl 4-methyl 1-[(anilinocarbonyl)amino]-3-(3-ethoxy-3-oxopropyl)-5-methyl-2-hydroxy-2,3-dihydro-pyrrole-3,4-dicarboxylate 4b and 2-

methylenepyrroles 6h-l. To a magnetically stirred solution of 1,2-diaza-1,3-butadienes **1a,d,g,i,j** (1.0 mmol), prepared as a mixture of *E/Z* isomers as reported elsewhere,[10,11] and 2-acetylglutarate **2c** (1.0 mmol) in THF (25 mL) was added potassium carbonate (5.0 equiv.). The mixture was allowed to stand at room temperature until the disappearance of the reagents (0.5 h, monitored by TLC). Then, potassium carbonate was removed by filtration. In the case of the reaction between **1a** and **2c**, product **4b** was purified by flash chromatography on a silica gel column and immediately subjected to ^{1}H NMR analysis because of its poor stability. In all the other cases, the isolation of pure **4** was not possible and the crude product, which was obtained after the filtration of potassium carbonate, as well as pure **4b,** were refluxed in THF after the addition of a drop of acetic acid. The conversion into pertinent 2-methylenepyrroles **6h-l** occurred in 4–12 h (as tested by TLC). Products **6h-l** were purified by flash chromatography on silica gel and then crystallized from diethyl ether–light petroleum ether (at 40–60°C).

3-Ethyl 4-methyl 1-[(anilinocarbonyl)amino]-3-(2-ethoxy-3-oxopropyl)-5-methyl-2-hydroxy-2,3-dihydropyrrole-3,4-dicarboxylate (4b): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07-1.21 (m, 6 H), 1.40 (2 s, 3 H), 1.42-1.68 and 2.05-2.97 (2 m, 4 H), 2.01 and 2.04 (2 s, 3 H), 3.50 and 3.54 (2 s, 3 H), 3.94-4.14 (m, 4 H), 6.14 and 6.39 (2 brs, 1 H), 8.23, 8.58, 8.66 and 9.02 (4 brs, 2 H).

3-Ethyl 4-methyl 1-[(anilinocarbonyl)amino]-3-(3-ethoxy-3-oxopropyl)-5-methyl-2-methylene-2,3-dihydropyrrole-3,4-dicarboxylate (6h): mp 99-102 °C; IR (nujol) ν_{max} 3433, 3286, 1761, 1679, 1613 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06-1.40 (m, 6 H), 1.50-2.80 (m, 4 H), 2.32 and 2.35 (2 s, 3 H), 3.69 (s, 3 H), 4.00-4.60 (m, 6 H), 7.04 (t, 1 H, *J* = 7.2), 7.26 (t, 2 H, *J* = 7.2), 7.40 and 7.42 (2 s, 1 H), 7.57 (d, 2 H, *J* = 7.2), 7.80 and 8.76 (2 brs, 1 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 11.4 (q), 13.8 (q), 13.9 (q), 13.9 (q), 14.0 (q), 29.6 (t), 29.9 (t), 30.0 (t), 31.0 (t), 50.6 (q), 50.8 (s), 56.8 (s), 57.3 (s), 60.5 (t), 61.2 (t), 61.5 (t), 62.0 (t), 84.5 (t), 103.2 (s), 103.8 (s), 119.9 (d), 120.0 (d), 123.6 (d), 123.9 (d), 128.7 (d), 128.8 (d), 137.4 (s), 138.1 (s), 150.2 (s), 150.8 (s), 159.5 (s), 164.2 (s), 164.3 (s), 171.2

(s), 172.7 (s), 173.2 (s), 174.9 (s); EIMS *m/z* 460 (6) [M^++1], 459 (31) [M^+], 414 (13), 387 (21), 386 (100). Anal. Calcd for $C_{23}H_{29}N_3O_7$: C, 60.12; H, 6.36; N, 9.14. Found: C, 60.21; H, 6.48; N, 9.02.

3-Ethyl 4-methyl 1-[(aminocarbonyl)amino]-3-(3-ethoxy-3-oxopropyl)-5-methyl-2-methylene-2,3-dihydropyrrole-3,4-dicarboxylate (6i): mp 98-101 °C; IR (nujol) ν_{max} 3453, 3268, 3212, 1737, 1688, 1674, 1620 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.15-1.28 (m, 6 H), 2.00-2.46 and 2.35-2.74 (2 m, 4 H), 2.27 and 2.31 (2 s, 3 H), 3.66 (s, 3 H), 4.00-4.24 (m, 4 H), 4.25, 4.51 and 4.31, 4.52 (AB-system, 2 H, *J* = 3.2), 5.39 (brs, 2 H), 6.94 and 7.70 (2 brs, 1 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 11.5 (q), 11.6 (q), 14.1 (q), 14.2 (q), 14.3 (q), 14.4 (q), 29.9 (t), 30.0 (t), 30.9 (t), 31.3 (t), 50.9 (q), 51.1 (q), 57.0 (s), 57.2 (s), 60.6 (t), 60.8 (t), 61.7 (t), 62.0 (t), 84.4 (t), 102.5 (s), 150.1 (s), 150.6 (s), 159.4 (s), 159.5 (s), 164.6 (s), 164.7 (s), 171.6 (s), 172.0 (s), 173.5 (s), 175.1 (s); EIMS *m/z* 384 (4) [M^++1], 383 (21) [M^+], 338 (3), 311 (21), 310 (100). Anal. Calcd for $C_{17}H_{25}N_3O_7$: C, 53.26; H, 6.57; N, 10.96. Found: C, 53.37; H, 6.48; N, 11.02.

3-Ethyl 4-methyl 1-[(*tert*-butoxycarbonyl)amino]-3-(3-ethoxy-3-oxopropyl)-5-methyl-2-methylene-2,3-dihydropyrrole-3,4-dicarboxylate (6j): mp 97-99 °C; IR (nujol) ν_{max} 3430, 1756, 1671, 1630, 1601 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.12-1.25 (m, 6 H), 1.39 and 1.44 (2 s, 9 H), 1.49-1.76 and 2.04-2.77 (2 m, 4 H), 2.16 and 2.26 (2 s, 3 H), 3.62 (s, 3 H), 4.00-4.40 (m, 6 H), 6.60 and 6.93 (2 brs, 1 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 11.2 (q), 13.9 (q), 14.0 (q), 14.1 (q), 28.0 (q), 29.3 (q), 30.0 (t), 30.2 (t), 31.0 (t), 31.7 (t), 50.5 (q), 50.6 (q), 56.6 (s), 60.1 (t), 60.3 (t), 61.2 (t), 82.1 (s), 82.3 (s), 83.2 (t), 100.9 (s), 101.1 (s), 150.7 (s), 153.4 (s), 157.6 (s), 158.2 (s), 164.7 (s), 171.3 (s), 172.6 (s), 173.2 (s), 173.8 (s); EIMS *m/z* 441 (2) [M^++1], 440 (11) [M^+], 395 (3), 367 (50), 339 (14), 312 (21), 311 (100). Anal. Calcd for $C_{21}H_{32}N_2O_8$: C, 57.26; H, 7.32; N, 6.36. Found: C, 57.47; H, 7.45; N, 6.32.

Diethyl 1-[(aminocarbonyl)amino]-3-(3-ethoxy-3-oxopropyl)-5-methyl-2-methylene-2,3-dihydropyrrole-3,4-dicarboxylate (6k): mp 100-102 °C; IR (nujol) ν_{max} 3461, 3260, 1745, 1671, 1660, 1617 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.06-1.18 (m, 9 H), 1.84-3.96 (m, 4 H), 2.18 and 2.22

(2 s, 3 H), 3.91-4.45 (m, 8 H), 5.83 (brs, 2 H), 7.50 and 8.10 (2 brs, 1 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 11.0 (q), 11.1 (q), 13.7 (q), 13.7 (q), 13.8 (q), 13.9 (q), 14.0 (q), 29.4 (t), 29.6 (t), 30.3 (t), 30.9 (t), 56.6 (s), 56.9 (s), 59.1 (t), 59.3 (t), 60.4 (t), 60.8 (t), 61.1 (t), 61.5 (t), 83.8 (t), 102.1 (s), 149.8 (s), 150.4 (s), 159.0 (s), 159.1 (s), 163.8 (s), 171.4 (s), 171.6 (s), 173.1 (s), 173.4 (s), 174.5 (s); EIMS *m/z* 398 (2) [M^++1], 397 (12) [M^+], 352 (4), 324 (86), 296 (8), 279 (17), 278 (100). Anal. Calcd for $C_{18}H_{27}N_3O_7$: C, 54.40; H, 6.85; N, 10.57. Found: C, 54.31; H, 6.98; N, 10.72.

Diethyl 1-[(benzyloxycarbonyl)amino]-3-(3-ethoxy-3-oxopropyl)-5-methyl-2-methylene-2,3-dihydropyrrole-3,4-dicarboxylate (6l): mp 81-84 °C; IR (nujol) ν_{max} 3501, 1741, 1690, 1661, 1608 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12-1.27 (m, 9 H), 1.40-2.77 (m, 4 H), 2.25 and 2.27 (2 s, 3 H), 3.70-4.20 (m, 8 H), 5.17 and 5.20 (2 s, 2 H), 6.63 and 6.85 (2 brs, 1 H), 7.20-7.40 (m, 5 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 11.2 (q), 13.9 (q), 14.0 (q), 14.1 (q), 14.2 (q), 14.3 (q), 29.2 (t), 29.7 (t), 31.6 (t), 31.8 (t), 56.9 (s), 59.4 (t), 60.2 (t), 60.4 (t), 61.1 (t), 61.4 (t), 66.9 (t), 68.2 (t), 82.6 (t), 82.8 (t), 101.8 (s), 128.1 (d), 128.3 (d), 128.5 (d), 128.7 (t), 135.1 (s), 135.3 (s), 150.6 (s), 154.5 (s), 155.4 (s), 157.5 (s), 164.2 (s), 171.0 (s), 171.7 (s), 172.5 (s), 173.7 (s); EIMS *m/z* 489 (6) [M^++1], 488 (32) [M^+], 399 (11), 383 (37), 339 (23), 338 (100). Anal. Calcd for $C_{25}H_{32}N_2O_8$: C, 61.46; H, 6.60; N, 5.73. Found: C, 61.57; H, 6.48; N, 5.82.

General procedure for the synthesis of 19-methyl-15-oxa-20azatriciclo[12.3.3.0^{1,14}]icos-18-en-18-carboxylates 8a-d. To a magnetically stirred solution of 1,2-diaza-1,3-butadienes **1g,i,j,k** (1.0 mmol), prepared as a mixture of *E/Z* isomers, as reported elsewhere,[10,11] and methyl 2-(1,3-dioxo-2-cyclotetradecyl)acetate **2d** (1.0 mmol) in THF (25 mL) was added potassium carbonate (5.0 equiv.). The mixture was allowed to stand at room temperature until the disappearance of the reagents (1.5–3.0 h, as monitored by TLC), and then potassium carbonate was removed by filtration The reaction solvent was evaporated under reduced pressure; products **8a-d** were purified by flash chromatography on a silica gel column and crystallized from diethyl ether–light petroleum ether (at 40–60°C).

Methyl 20-[(*tert*-butoxycarbonyl)amino]-19-Methyl-15-oxa-20azatriciclo[12.3.3.0^{1,14}]icos-18-en-18-carboxylate (8a): mp 97-99°C; IR (nujol) ν_{max} 3320, 3212, 1760, 1698, 1672 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10-1.39 (m, 20 H), 1.48 (s, 9 H), 1.71-1.84 (m, 2 H), 2.28 (s, 3 H), 2.89 and 3.73 (AB-system, 2 H, *J* = 18.4), 3.66 (s, 3 H), 6.76 and 6.98 (2 s, 1 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 12.2 (q), 19.1 (t), 21.6 (t), 23.8 (t), 25.0 (t), 25.4 (t), 25.7 (t), 26.6 (t), 27.1 (t), 28.3 (q), 30.5 (t), 32.5 (t), 36.1 (t), 38.1 (t), 51.5 (q), 65.4 (s), 82.4 (s), 102.3 (s), 105.4 (s), 154.9 (s), 162.5 (s), 164.8 (s), 174.0 (s), 204.6 (s); EIMS *m/z* 493 (6) [M$^+$+1], 492 (19) [M$^+$], 436 (34), 420 (5), 392 (100). Anal. Calcd for $C_{26}H_{40}N_2O_7$: C, 63.39; H, 8.18; N, 5.69. Found: C, 63.49; H, 8.25; N, 5.73.

Ethyl 20-[(aminocarbonyl)amino]-19-methyl-15-oxa-20-azatriciclo[12.3.3.0^{1,14}]icos-18-en-18-carboxylate (8b): mp 178-180 °C; IR (nujol) ν_{max} 3410, 3330, 3178, 1780, 1741, 1721, 1657 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.03-1.48 (m, 23 H), 1.60-1.81 (m, 2 H), 2.28 (s, 3 H), 2.92 and 3.54 (AB-system, 2 H, *J* = 18.2), 4.14 (q, 2 H, *J* = 7.2), 5.56 (brs, 2 H), 6.97 (brs, 1 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 12.6 (q), 14.5 (q), 20.2 (t), 21.5 (t), 23.3 (t), 24.9 (t), 25.9 (t), 26.6 (t), 27.1 (t), 29.9 (t), 30.4 (t), 31.8 (t), 36.9 (t), 39.1 (t), 60.6 (t), 64.2 (s), 106.1 (s), 107.0 (s), 159.0 (s), 160.6 (s), 164.3 (s), 172.5 (s), 207.7 (s); EIMS *m/z* 450 (2) [M$^+$+1], 449 (11) [M$^+$], 405 (17), 360 (36), 332 (100). Anal. Calcd for $C_{23}H_{35}N_3O_6$: C, 61.45; H, 7.85 N, 9.35. Found: C, 61.49; H, 7.93; N, 5.62.

Ethyl 20-[(benzyloxycarbonyl)amino]-19-methyl-15-oxa-20-azatriciclo[12.3.3.0^{1,14}]icos-18-en-18-carboxylate (8c): mp 103-105 °C; IR (nujol) ν_{max} 3318, 3210, 1762, 1670, 1668 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.11-1.43 (m, 23 H), 1.59-1.86 (m, 2 H), 2.28 (s, 3 H), 2.84 and 3.71 (AB-system, 2 H, *J* = 18.4), 4.15 (q, 2 H, *J* = 7.2), 5.21 (s, 2 H), 6.98 (brs, 1 H), 7.36 (s, 5 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 12.2 (q), 14.5 (q), 21.3 (t), 24.8 (t), 25.2 (t), 25.6 (t), 25.8 (t), 26.5 (t), 28.2 (t), 29.9 (t), 32.5 (t), 36.4 (t), 38.2 (t), 40.7 (t), 60.4 (t), 65.3 (s), 68.3 (t), 103.8 (s), 105.4 (s), 128.4 (d), 128.9 (d), 129.7 (d), 135.6 (s), 155.9 (s), 161.8 (s), 164.2 (s), 172.1 (s), 204.9 (s); EIMS *m/z* 541 (5) [M$^+$+1], 540 (19) [M$^+$], 495 (7), 449 (31), 433 (100). Anal. Calcd for $C_{30}H_{40}N_2O_7$: C, 66.65; H, 7.46 N, 5.18. Found: C, 66.45; H, 7.38; N, 5.33.

Ethyl 20-[(*tert*-butoxycarbonyl)amino]-19-methyl-15-oxa-20-azatriciclo[12.3.3.0^{1,14}]icos-18-en-18-carboxylate (8d): mp 102-104 °C; IR (nujol) ν_{max} 3318, 3212, 1762, 1700, 1674 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08-1.37 (m, 23 H), 1.50 (s, 9 H), 1.68-1.93 (m, 2 H), 2.30 (s, 3 H), 2.81 and 3.74 (AB-system, 2 H, *J* = 18.4), 4.15 (q, 2 H, *J* = 7.2), 6.37 and 6.65 (2 brs, 1 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 12.0 (q), 14.2 (q), 18.9 (t), 21.4 (t), 23.5 (t), 24.7 (t), 25.1 (t), 26.3 (t), 26.8 (t), 27.0 (t), 28.1 (q), 30.1 (t), 32.2 (t), 36.0 (t), 37.8 (t), 60.0 (t), 65.1 (s), 82.1 (s), 102.3 (s), 105.7 (s), 154.6 (s), 162.0 (s), 164.1 (s), 173.8 (s), 204.3 (s); EIMS *m/z* 507 (4) [M$^+$+1], 506 (18) [M$^+$], 450 (27), 434 (3), 406 (100). Anal. Calcd for $C_{27}H_{42}N_2O_7$: C, 64.01; H, 8.36; N, 5.53. Found: C, 63.98; H, 8.21; N, 5.62.

General procedure for the synthesis of 4-(3-oxopropyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylates 12a-e. To a magnetically stirred solution of 1,2-diaza-1,3-butadienes **1g,i,k** (1.0 mmol), prepared as a mixture of *E/Z* isomers, as reported elsewhere,[10,11] and ethyl or methyl 4-acetyl-5-oxo-hexanoate **2e,f** (1.0 mmol) in THF (25 mL) was added potassium carbonate (5.0 equiv.). The mixture was allowed to stand at room temperature until the disappearance of the reagents (3.0-4.5 h, as monitored by TLC) and then refluxed in THF. The formation of 4-(3-oxopropyl)-2,5-dimethyl-1*H*-pyrrole-3-carboxylates **12a-e** occurred in 4–12 h (as tested by TLC). Potassium carbonate was removed by filtration, and products **12a-e** were purified by flash chromatography on silica gel and crystallized from ethyl acetate–light petroleum ether (at 40–60°C).

Methyl 4-(3-ethoxy-3-oxopropyl)-1-[(*tert*-butoxycarbonyl)amino]-2,5-dimethyl-1*H*-pyrrole-3-carboxylate (12a): oil; IR (nujol) ν_{max} 3428, 1760, 1672, 1628, 1610 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.11 (t, 3 H, *J* = 7.2), 1.38 (s, 9 H), 1.90 (s, 3 H), 2.20 (s, 3 H), 2.29-2.40 (m, 2 H), 2.61-2.83 (m, 2 H), 3.62 (s, 3 H), 3.94 (q, 2 H, *J* = 7.2), 8.18 (brs, 1 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 8.5 (q), 10.9 (q), 14.3 (q), 21.3 (t), 28.1 (q), 35.6 (t), 50.5 (q), 60.2 (t), 82.0 (s), 107.9 (s), 116.8 (s), 126.1 (s), 136.7 (s), 154.5 (s), 166.4 (s), 174.0 (s); EIMS *m/z* 369 (6) [M$^+$+1], 368 (38) [M$^+$], 295 (76), 267 (100). Anal. Calcd for $C_{18}H_{28}N_2O_6$: C, 58.68; H, 7.66; N, 7.60. Found: C, 58.47; H, 7.55; N, 7.82.

Ethyl 4-(3-ethoxy-3-oxopropyl)-1-[aminocarbonyl)amino]-2,5-dimethyl-1*H*-pyrrole-3-carboxylate (12b): oil; IR (nujol) ν_{max} 3448, 3268, 3210, 1738, 1690, 1671, 1620 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.16 (t, 3 H, *J* = 7.2), 1.25 (t, 3 H, *J* = 7.2), 1.96 (s, 3 H), 2.27 (s, 3 H), 2.37-2.45 (m, 2 H), 2.63-2.89 (m, 2 H), 4.03 (q, 2 H, *J* = 7.2), 4.14 (q, 2 H, *J* = 7.2), 6.18 (brs, 2 H), 9.06 (s, 1 H); ^{13}C NMR (100.65 MHz, DMSO-d_6) δ 9.0 (q), 11.5 (q), 14.8 (q), 14.9 (q), 21.6 (t), 35.9 (t), 59.3 (t), 60.3 (t), 107.6 (s), 116.1 (s), 126.9 (s), 136.7 (s), 158.0 (s), 165.5 (s), 173.3 (s); EIMS *m/z* 328 (6) [M^++1], 327 (100) [M^+]). Anal. Calcd for $C_{15}H_{23}N_3O_5$: C, 55.37; H, 7.13; N, 12.91. Found: C, 55.45; H, 7.15; N, 13.01.

Methyl 4-(3-methoxy-3-oxopropyl)-1-[(*tert*-butoxycarbonyl)amino]-2,5-dimethyl-1*H*-pyrrole-3-carboxylate (12c): oil; IR (nujol) ν_{max} 3425, 1762, 1670, 1630, 1618 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.45 (s, 9 H), 1.99 (s, 3 H), 2.30 (s, 3 H), 2.38-2.49 (m, 2 H), 2.80-2.88 (m, 2 H), 3.58 (s, 3 H), 3.70 (s, 3 H), 7.63 (brs, 1 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 8.6 (q), 11.0 (q), 21.4 (t), 28.2 (q), 35.5 (t), 50.7 (q), 51.6 (q), 82.4 (s), 108.2 (s), 117.0 (s), 126.3 (s), 136.7 (s), 154.3 (s), 166.4 (s), 174.5 (s); EIMS *m/z* 355 (8) [M^++1], 354 (49) [M^+], 281 (76), 253 (100). Anal. Calcd for $C_{17}H_{26}N_2O_6$: C, 57.61; H, 7.39; N, 7.90. Found: C, 57.48; H, 7.45; N, 7.92.

Ethyl 4-(3-methoxy-3-oxopropyl)-1-[(aminocarbonyl)amino]-2,5-dimethyl-1*H*-pyrrole-3-carboxylate (12d): mp 157-159 °C; IR (nujol) ν_{max} 3450, 3270, 3212, 1740, 1685, 1672, 1623 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.32 (t, 3 H, *J* = 6.8), 1.94 (s, 3 H), 2.25 (s, 3 H), 2.21-2.42 (m, 2 H), 2.73-2.85 (m, 2 H), 3.54 (s, 3 H), 4.13 (q, 2 H, *J* = 7.2), 6.15 (brs, 2 H), 9.04 (s, 1 H); ^{13}C NMR (100.65 MHz, DMSO-d_6) δ 8.3 (q), 10.7 (q), 14.2 (q), 20.9 (t), 35.0 (t), 51.0 (q), 58.6 (t), 106.9 (s), 115.4 (s), 126.2 (s), 135.9 (s), 157.2 (s), 164.7 (s), 173.0 (s); EIMS *m/z* 312 (1) [M^++1], 311 (100) [M^+]. Anal. Calcd for $C_{14}H_{21}N_3O_5$: C, 54.01; H, 6.80; N, 13.50. Found: C, 54.15; H, 6.75; N, 13.31.

Ethyl 4-(3-methoxy-3-oxopropyl)-1-[(*tert*-butoxycarbonyl)amino]-2,5-dimethyl-1*H*-pyrrole-3-carboxylate (12e): oil; IR (nujol) ν_{max} 3430, 1762, 1671, 1630, 1612 cm^{-1}; ^1H NMR (400 MHz,

$CDCl_3$) δ 1.22 (t, 3 H, *J* = 7.2), 1.33 (s, 9 H), 1.94 (s, 3 H), 2.25 (s, 3 H), 2.37-2.49 (m, 2 H), 2.68-2.96 (m, 2 H), 3.53 (s, 3 H), 4.13 (q, 2 H, *J* = 7.2), 7.97 (s, 1 H); ^{13}C NMR (100.65 MHz, $CDCl_3$) δ 8.5 (q), 11.3 (q), 14.4 (q), 21.5 (t), 28.2 (q), 35.7 (t), 51.4 (q), 59.4 (t), 82.1 (s), 108.2 (s), 116.7 (s), 126.2 (s), 136.7 (s), 154.5 (s), 166.0 (s), 174.4 (s); MS *m/z* 369 (7) [M^++1], 368 (41) [M^+], 295 (65), 267 (100). Anal. Calcd for $C_{18}H_{28}N_2O_6$: C, 58.68; H, 7.66; N, 7.60. Found: C, 58.57; H, 7.55; N, 7.52.

13.31.

General procedure for the synthesis of 1-ethyl 4-methyl 2-acetyl-3-{1-[2-(aminocarbonyl)hydrazono]ethyl}-2-methylsuccinate 14a. To a magnetically stirred solution of 1,2-diaza-1,3-butadiene **1d** (1.0 mmol), prepared as a mixture of *E/Z* isomers, as reported elsewhere,[10,11] and ethyl 2-methylacetoacetate **13a** (1.0 mmol) in THF (25 mL) was added sodium methoxide (0.1 equiv.). The mixture was allowed to stand at room temperature until the disappearance of the reagents (1.5 h, as monitored by TLC). The reaction solvent was evaporated under reduced pressure, and product **14a** was purified by chromatography on a silica gel column and then crystallized from ethyl acetate–light petroleum ether (at 40–60°C).

1-Ethyl 4-methyl 2-acetyl-3-{1-[2-(aminocarbonyl)hydrazono]ethyl}-2-methylsuccinate (14a): mp 100-102 °C; IR (nujol) ν_{max} 3471, 1775, 1723, 1690, 1683 cm^{-1}; ^{1}H NMR (400MHz, DMSO-d_6) δ 1.08-1.28 (m, 6 H), 1.82 and 1.85 (2 s, 3 H), 2.07 and 2.21 (2 s, 3 H), 3.53 and 3.58 (2 s, 3 H), 3.98-4.17 (m, 2 H), 4.25 (s, 1 H), 6.02 (brs, 2 H), 9.30 (s, 1 H); ^{13}C NMR (100.65MHz, DMSOd_6) δ 12.7 (q), 14.2 (q), 14.6 (q), 18.0 (q), 19.2 (q), 26.4 (q), 50.8 (d), 52.7 (q), 57.1 (s), 58.1 (s), 61.6 (t), 62.0 (t), 142.7 (s), 157.9 (s), 166.1 (s), 171.1 (s), 172.3 (s), 205.0 (s); EIMS *m/z* 315 (6) [M^+], 297 (11), 272 (19), 254 (9), 224 (100). Anal. Calcd for $C_{13}H_{21}N_3O_6$: C, 49.52; H, 6.71; N, 13.33. Found: C, 49.41; H, 6.78; N, 13.46.

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