Ring-Opening Cyclization of Alkylidenecyclopropyl Ketones with Amines. An Efficient Synthesis of 2,3,4-Trisubstituted Pyrroles

Shengming Ma^{a,b}, Lianghua Lu^a and Guofei Chen^b

^a*State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, P. R. China.*

^b*Laboratory of Molecular Recognition and Synthesis, Department of Chemistry, Zhejiang Univ., Hangzhou 310027, P. R. China*

masm@mail.sioc.ac.cn

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Typical Procedure for Intermolecular Cyclization of Alkylidenecyclopropyl

Ketones 1 with Amines 2. Preparation of Compounds 3: A solution of **1a** (67 mg, 0.25 mmol), amine **2a** (108 mg, 1 mmol), and anhydrous MgSO₄ (15 mg, 0.125 mmol) in 1 mL of MeCN was stirred for 22 h at 80°C. After evaporation, the residue was purified by column chromatography (eluent: petroleum ether:CH₂Cl₂ = 2:1) on silica gel to afford 70 mg (78 %) of **3aa**.

(1) **1-Benzyl-2-methyl-3-(ethoxycarbonyl)-4-octyl-1H-pyrrole** (3aa)

3aa: liquid; ¹H NMR (300 MHz, CDCl₃) δ 7.37-7.23 (m, 3 H), 7.00 (d, *J* = 6.9 Hz, 2 H), 6.37 (s, 1 H), 5.00 (s, 2 H), 4.29 (q, *J* = 7.2 Hz, 2 H), 2.68 (t, *J* = 7.8 Hz, 2 H), 2.43 (s, 3 H), 1.63-1.50 (m, 2 H), 1.36 (t, *J* = 7.2 Hz, 3 H), 1.42-1.20 (m, 10 H), 0.90 (t, *J* = 6.6 Hz, 3 H); ¹³C NMR (75 MHz, CDCl₃) δ 166.2, 137.2, 136.3, 128.8, 127.5, 126.2, 126.0, 119.0, 110.9, 59.0, 50.1, 31.9, 30.6, 29.7, 29.6, 29.4, 27.0, 22.7, 14.4, 14.1, 11.5; MS (EI) *m/z* (%): 355 (M⁺, 32.53), 257 (100); IR (neat) *v* (cm⁻¹): 1697, 1565, 1521, 1454, 1426, 1129, 1082; HRMS calcd for C₂₃H₃₄NO₂⁺ (MH⁺): 356.2584. Found: 356.2584.

(2) **1-Benzyl-2-methyl-3-(ethoxycarbonyl)-4-pentyl-1H-pyrrole** (3ba)

The reaction of **1b** (56 mg, 0.25 mmol), amine **2a** (109 mg, 1 mmol), and anhydrous MgSO_4 (16 mg, 0.13 mmol) in 1 mL of CH_3CN afforded 61 mg (78 %) of **3ba**: liquid; ^1H NMR (300 MHz, CDCl_3) δ 7.32-7.15 (m, 3 H), 6.92 (d, $J = 6.9$ Hz, 2 H), 6.29 (s, 1 H), 4.92 (s, 2 H), 4.20 (q, $J = 7.2$ Hz, 2 H), 2.60 (t, $J = 7.7$ Hz, 2 H), 2.34 (s, 3 H), 1.58-1.42 (m, 2 H), 1.27 (t, $J = 7.2$ Hz, 3 H), 1.38-1.15 (m, 4 H), 0.82 (t, $J = 6.9$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 166.2, 137.2, 136.3, 128.8, 127.5, 126.2, 126.0, 119.0, 110.9, 59.0, 50.1, 31.9, 30.3, 27.0, 22.6, 14.4, 14.1, 11.5; MS (EI) m/z (%): 313 (M^+ , 16.16), 91 (100); IR (neat) ν (cm^{-1}): 1692, 1564, 1520, 1454, 1427, 1278, 1257, 1129, 1081; HRMS calcd for $\text{C}_{20}\text{H}_{28}\text{NO}_2^+$ (MH^+): 314.2115. Found: 314.2107.

(3) **1-Benzyl-2-methyl-3-(ethoxycarbonyl)-4-(2'-phenylethyl)-1H-pyrrole (3ca)**

The reaction of **1c** (65 mg, 0.25 mmol), amine **2a** (109 mg, 1 mmol), and anhydrous MgSO_4 (16 mg, 0.13 mmol) in 1 mL of CH_3CN afforded 66 mg (75 %) of **3ca**: liquid; ^1H NMR (300 MHz, CDCl_3) δ 7.40-7.18 (m, 8 H), 6.98 (d, $J = 7.2$ Hz, 2 H), 6.31 (s, 1 H), 4.98 (s, 2 H), 4.34 (q, $J = 7.2$ Hz, 2 H), 3.07-3.00 (m, 2 H), 2.96-2.87 (m, 2 H), 2.45 (s, 3 H), 1.39 (t, $J = 7.2$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 166.0, 142.6,

137.1, 136.4, 128.7, 128.5, 128.0, 127.5, 126.2, 125.5, 124.7, 119.5, 110.9, 59.1, 50.1, 37.0, 28.9, 14.5, 11.5; MS (EI) m/z (%): 347 (M^+ , 29.02), 256 (100), 91 (94.33); IR (neat) ν (cm^{-1}): 1692, 1564, 1520, 1496, 1453, 1428, 1271, 1128, 1084; HRMS calcd for $\text{C}_{23}\text{H}_{26}\text{NO}_2^+$ (MH^+): 348.1958. Found: 348.1961.

(4) **1-Benzyl-2-methyl-3-(ethoxycarbonyl)-4-(4'-*tert*-butyldimethylsilyloxybutyl)-1*H*-pyrrole (3da)**

The reaction of **1d** (87 mg, 0.26 mmol), amine **2a** (109 mg, 1 mmol), and anhydrous MgSO_4 (16 mg, 0.13 mmol) in 1 mL of CH_3CN afforded 85 mg (77 %) of **3da**: liquid; ^1H NMR (300 MHz, CDCl_3); δ 7.29-7.15 (m, 3 H), 6.92 (d, $J = 6.9$ Hz, 2 H), 6.29 (s, 1 H), 4.91 (s, 2 H), 4.19 (q, $J = 7.1$ Hz, 2 H), 3.56 (t, $J = 6.2$ Hz, 2 H), 2.62 (t, $J = 7.1$ Hz, 2 H), 2.34 (s, 3 H), 1.58-1.49 (m, 4 H), 1.27 (t, $J = 7.1$ Hz, 3 H), 0.82 (s, 9 H), -0.03 (s, 6 H), ^{13}C NMR (75 MHz, CDCl_3) δ 166.1, 137.2, 136.4, 128.7, 127.5, 126.2, 125.6, 119.1, 110.9, 63.3, 59.0, 50.1, 32.9, 26.8, 26.6, 25.9, 18.3, 14.4, 11.5, -5.3; MS (EI) m/z (%): 430 ($M^+ + 1$, 5.47), 429 (M^+ , 0.77), 372 (100); IR (neat) ν (cm^{-1}): 1701, 1691, 1565, 1521, 1471, 1429, 1255, 1087; HRMS calcd for $\text{C}_{25}\text{H}_{39}\text{NO}_3\text{SiNa}^+$ ($M\text{Na}^+$): 452.2591. Found: 452.2574.

(5) **1-Benzyl-2-methyl-3-(ethoxycarbonyl)-4-(2'-butyl)-1*H*-pyrrole (3ea)**

The reaction of **1e** (115 mg, 0.55 mmol), amine **2a** (219 mg, 2 mmol), and anhydrous MgSO_4 (30 mg, 0.25 mmol) in 2 mL of CH_3CN afforded 94 mg (57 %) of **3ea**: liquid; ^1H NMR (300 MHz, CDCl_3) δ 7.32-7.18 (m, 3 H), 6.93 (d, $J = 6.6$ Hz, 2 H), 6.32 (s, 1 H), 4.95 (s, 2 H), 4.23 (q, $J = 7.2$ Hz, 2 H), 3.25-3.10 (m, 1 H), 2.36 (s, 3 H), 1.71-1.58 (m, 1 H), 1.45-1.30 (m, 1 H), 1.30 (t, $J = 7.2$ Hz, 3 H), 1.14 (d, $J = 7.2$ Hz, 3 H), 0.88 (t, $J = 7.5$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 166.1, 137.2, 136.0, 131.7, 128.7, 127.4, 126.1, 117.6, 110.7, 59.0, 50.2, 32.0, 30.6, 20.6, 14.3, 11.9, 11.6; MS (EI) m/z (%): 299 (M^+ , 30.89), 91 (100); IR (neat) ν (cm^{-1}): 1693, 1516, 1454, 1240; HRMS calcd for $\text{C}_{19}\text{H}_{26}\text{NO}_2^+$ (MH^+): 300.1958. Found: 300.1957.

(6) 1-Benzyl-2-methyl-3-acetyl-4-octyl-1H-pyrrole (3fa)

The reaction of **1f** (59 mg, 0.25 mmol), amine **2a** (109 mg, 1 mmol), and anhydrous MgSO_4 (15 mg, 0.125 mmol) in 1 mL of CH_3CN afforded 52 mg (64 %) of **3fa**: liquid; ^1H NMR (300 MHz, CDCl_3) δ 7.25-7.14 (m, 3 H), 6.90 (d, $J = 6.6$ Hz, 2 H), 6.26 (s, 1 H), 4.90 (s, 2 H), 2.57 (t, $J = 7.8$ Hz, 2 H), 2.34 (s, 3 H), 2.29 (s, 3 H), 1.54-1.38 (m, 2 H), 1.33-1.10 (m, 10 H), 0.78 (t, $J = 6.9$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ

195.7, 137.0, 135.6, 128.8, 127.6, 126.2, 124.9, 121.6, 119.3, 50.1, 31.8, 31.1, 30.3, 29.7, 29.5, 29.3, 27.6, 22.6, 14.1, 12.3; MS (EI) m/z (%): 325 (M^+ , 22.94), 91 (100); IR (neat) ν (cm^{-1}): 1645, 1504, 1499, 1454, 1418; HRMS calcd for $\text{C}_{22}\text{H}_{32}\text{NO}^+$ (MH^+): 326.2478. Found: 326.2469.

(7) **1-Benzyl-2-methyl-3-(benzenesulfonyl)-4-octyl-1H-pyrrole** (**3ga**)

3ga

The reaction of **1g** (84 mg, 0.25 mmol), amine **2a** (111 mg, 1 mmol), and anhydrous MgSO_4 (16 mg, 0.13 mmol) in 1 mL of CH_3CN afforded 80 mg (75 %) of **3ga**: liquid; ^1H NMR (300 MHz, CDCl_3) δ 7.91-7.82 (m, 2 H), 7.55-7.42 (m, 3 H), 7.37-7.25 (m, 3 H), 6.96 (d, J = 6.6 Hz, 2 H), 6.38 (s, 1 H), 4.98 (s, 2 H), 2.61 (t, J = 7.7 Hz, 2 H), 2.46 (s, 3 H), 1.52-1.40 (m, 2 H), 1.38-1.17 (m, 10 H), 0.88 (t, J = 6.8 Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 144.6, 136.3, 134.2, 131.9, 128.9, 128.7, 127.7, 126.2, 126.1, 124.5, 119.6, 117.1, 50.5, 31.8, 29.7, 29.5, 29.4, 29.2, 25.4, 22.6, 14.1, 10.8; MS (EI) m/z (%): 424 ($M^+ + 1$, 14.95), 423 (M^+ , 1.03), 91 (100); IR (neat) ν (cm^{-1}): 1498, 1454, 1446, 1414, 1302, 1166, 1133; HRMS calcd for $\text{C}_{26}\text{H}_{33}\text{NO}_2\text{SNa}^+$ ($M\text{Na}^+$): 446.2124. Found: 446.2114.

(8) **1-Benzyl-2-methyl-3-(benzenesulfonyl)-4-pentyl-1H-pyrrole** (**3ha**)

The reaction of **1h** (77 mg, 0.26 mmol), amine **2a** (111 mg, 1 mmol), and anhydrous MgSO_4 (16 mg, 0.13 mmol) in 1 mL of CH_3CN afforded 82 mg (82 %) of **3ha**: solid, mp: 81-82 °C, (petroleum ether/ethyl acetate). ^1H NMR (300 MHz, CDCl_3) δ 7.80-7.73 (m, 2 H), 7.43-7.30 (m, 3 H), 7.26-7.15 (m, 3 H), 6.88-6.83 (m, 2 H), 6.29 (s, 1 H), 4.88 (s, 2 H), 2.51 (t, $J = 7.5$ Hz, 2 H), 2.35 (s, 3 H), 1.45-1.30 (m, 2 H), 1.23-1.10 (m, 4 H), 0.76 (t, $J = 7.2$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 144.6, 136.3, 134.2, 131.9, 128.8, 128.7, 127.7, 126.2, 126.0, 124.4, 119.6, 117.1, 50.4, 31.6, 29.3, 25.3, 22.4, 14.0, 10.7; MS (EI) m/z (%): 381 (M^+ , 14.93), 91 (100); IR (neat) ν (cm^{-1}): 1498, 1453, 1445, 1417, 1310, 1300, 1167, 1136; Anal. Calcd for $\text{C}_{23}\text{H}_{27}\text{NO}_2\text{S}$: C 72.40, H 7.13, N 3.67. Found: C 72.12, H 7.02, N 3.53.

(9) 1-Benzyl-2-(trifluoromethyl)-3-(ethoxycarbonyl)-4-octyl-1H-pyrrole (3ia)

The reaction of **1i** (80 mg, 0.25 mmol), amine **2a** (110 mg, 1 mmol), and anhydrous MgSO_4 (15 mg, 0.125 mmol) in 1 mL of CH_3CN afforded 41 mg (40 %) of **3ia**: liquid; ^1H NMR (300 MHz, CDCl_3) δ 7.30-7.18 (m, 3 H), 7.05-6.95 (m, 2 H), 6.41 (s, 1 H), 5.10 (s, 2 H), 4.24 (q, $J = 7.2$ Hz, 2 H), 2.49 (t, $J = 7.5$ Hz, 2 H), 1.50-1.37 (m, 2 H),

1.27 (t, $J = 7.2$ Hz, 3 H), 1.30-1.08 (m, 10 H), 0.80 (t, $J = 6.9$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 164.4, 136.4, 128.7, 127.9, 126.6, 126.0, 123.6 (q, $^4J_{\text{C-F}} = 1.7$ Hz), 120.9 (q, $^1J_{\text{C-F}} = 267.4$ Hz), 120.6 (q, $^2J_{\text{C-F}} = 38.0$ Hz), 117.8 (q, $^3J_{\text{C-F}} = 2.3$ Hz), 60.7, 52.5 (q, $^4J_{\text{C-F}} = 3.3$ Hz), 31.8, 30.4, 29.41, 29.38, 29.2, 25.6, 22.6, 14.1, 14.0; ^{19}F NMR (91 MHz, CDCl_3) δ -55.1; MS (EI) m/z (%): 409 (M^+ , 0.57), 91 (100); MS (MALDI): 432.2 ($\text{M}^+ + \text{Na}$), 410.2 ($\text{M}^+ + 1$); IR (neat) ν (cm^{-1}): 1720, 1512, 1457, 1463, 1435, 1236, 1157, 1110; HRMS calcd for $\text{C}_{23}\text{H}_{31}\text{NO}_2\text{F}_3^+$ (MH^+): 410.2301. Found: 410.2303.

(10) 1-(4'-Methoxybenzyl)-2-phenyl-3-(ethoxycarbonyl)-4-octyl-1H-pyrrole (3jb)

The reaction of **1j** (83 mg, 0.25 mmol), amine **2b** (140 mg, 1 mmol), and anhydrous MgSO_4 (15 mg, 0.125 mmol) in 1 mL of CH_3CN afforded 76 mg (67 %) of **3jb**: liquid; ^1H NMR (300 MHz, CDCl_3) δ 7.40-7.33 (m, 3 H), 7.29-7.22 (m, 2 H), 6.87 (d, $J = 8.8$ Hz, 2 H), 6.79 (d, $J = 8.8$ Hz, 2 H), 6.46 (s, 1 H), 4.77 (s, 2 H), 4.04 (q, $J = 7.2$ Hz, 2 H), 3.78 (s, 3 H), 2.73 (t, $J = 7.8$ Hz, 2 H), 1.67-1.55 (m, 2 H), 1.43-1.20 (m, 10 H), 1.01 (t, $J = 7.2$ Hz, 3 H), 0.89 (t, $J = 6.8$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 165.4, 158.9, 139.1, 132.7, 130.6, 129.7, 128.1, 128.0, 127.7, 126.7, 119.3, 113.9, 111.9, 58.9, 55.2, 49.9, 31.9, 30.4, 29.8, 29.5, 29.4, 26.8, 22.7, 14.1, 13.8; MS (EI) m/z (%): 448 ($\text{M}^+ + 1$, 10.65), 121 (100); IR (neat) ν (cm^{-1}): 1700, 1613, 1514, 1481,

1249, 1175, 1082; HRMS calcd for $C_{29}H_{38}NO_3^+$ (MH^+): 448.2846. Found: 448.2832.

(11) **1-(4'-Methoxybenzyl)-2-phenyl-4-methyl-1*H*-pyrrole (3kb)**

The reaction of **1k** (40 mg, 0.25 mmol), amine **2b** (140 mg, 1 mmol), and anhydrous $MgSO_4$ (15 mg, 0.125 mmol) in 1 mL of CH_3CN afforded 25 mg (36%) of **3kb**. **1k** (20 mg, 50%) was recovered. **3kb**: liquid; 1H NMR (300 MHz, $CDCl_3$) δ 7.42-7.23 (m, 5 H), 7.00 (d, $J = 8.8$ Hz, 2 H), 6.86 (d, $J = 8.8$ Hz, 2 H), 6.55-6.50 (m, 1 H), 6.17-6.13 (m, 1H), 5.04 (s, 2 H), 3.81 (s, 3 H), 2.17 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.7, 134.7, 133.4, 130.9, 128.7, 128.3, 127.8, 126.7, 120.7, 118.9, 113.9, 110.1, 55.2, 49.8, 11.9; MS (EI) m/z (%): 277 (M^+ , 19.98), 121 (100); IR (neat) ν (cm^{-1}): 1699, 1613, 1586, 1513, 1464, 1443, 1249, 1175, 1035; HRMS calcd for $C_{19}H_{20}NO^+$ (MH^+): 278.1539. Found: 278.1536.

(12) **1-(4'-Methoxybenzyl)-2-methyl-3-(ethoxycarbonyl)-4-octyl-1*H*-pyrrole (3ab)**

The reaction of **1a** (67 mg, 0.25 mmol), amine **2b** (135 mg, 1 mmol), and anhydrous

MgSO₄ (15 mg, 0.125 mmol) in 1 mL of CH₃CN afforded 83 mg (86 %) of **3ab**: solid, mp 48-50 °C (petroleum ether/Et₂O). ¹H NMR (300 MHz, CDCl₃) δ 6.93 (d, *J* = 8.5 Hz, 2 H), 6.83 (d, *J* = 8.5 Hz, 2 H), 6.32 (s, 1 H), 4.91 (s, 2 H), 4.26 (q, *J* = 7.0 Hz, 2 H), 3.78 (s, 3 H), 2.64 (t, *J* = 7.8 Hz, 2 H), 2.42 (s, 3 H), 1.60-1.45 (m, 2 H), 1.34 (t, *J* = 7.0 Hz, 3 H), 1.36-1.20 (m, 10 H), 0.87 (t, *J* = 6.8 Hz, 3 H); ¹³C NMR (75 MHz, CDCl₃) δ 166.2, 158.9, 136.1, 129.1, 127.6, 125.8, 118.8, 114.1, 110.8, 58.9, 55.2, 49.6, 31.8, 30.6, 29.7, 29.5, 29.3, 27.0, 22.6, 14.4, 14.1, 11.5; MS (EI) *m/z* (%): 385 (*M*⁺, 10.44), 121 (100); IR (neat) *ν* (cm⁻¹): 1675, 1515, 1467, 1277, 1135; Anal. Calcd for C₂₄H₃₅NO₃: C 74.77, H 9.15, N 3.63. Found: C 74.62, H 9.15, N 3.29.

(13) **1-(4'-Methoxybenzyl)-2-methyl-3-(ethoxycarbonyl)-4-(2'-phenylethyl)-1*H*-pyrrole (3cb)**

The reaction of **1c** (67 mg, 0.26 mmol), amine **2b** (133 mg, 1 mmol), and anhydrous MgSO₄ (15 mg, 0.125 mmol) in 1 mL of CH₃CN afforded 75 mg (77 %) of **3cb**: liquid; ¹H NMR (300 MHz, CDCl₃) δ 7.34-7.15 (m, 5 H), 6.92 (d, *J* = 8.7 Hz, 2 H), 6.85 (d, *J* = 8.7 Hz, 2 H), 6.29 (s, 1 H), 4.91 (s, 2 H), 4.33 (t, *J* = 7.2 Hz, 2 H), 3.81 (s, 3 H), 3.05-2.98 (m, 2 H), 2.95-2.87 (m, 2 H), 2.46 (s, 3 H), 1.38 (t, *J* = 7.2 Hz, 3 H); ¹³C NMR (75 MHz, CDCl₃) δ 166.1, 158.9, 142.7, 136.3, 129.0, 128.5, 128.1, 127.7, 125.5, 124.6, 119.3, 114.1, 110.8, 59.0, 55.2, 49.7, 37.1, 28.9, 14.5, 11.6; MS (EI) *m/z*

(%): 377 (M^+ , 11.65), 121 (100); IR (neat) ν (cm^{-1}): 1690, 1613, 1514, 1454, 1428, 1249, 1082; HRMS calcd for $\text{C}_{24}\text{H}_{28}\text{NO}_3^+$ (MH^+): 378.2064. Found: 378.2070.

(14) **1-(*n*-Butyl)-2-methyl-3-(ethoxycarbonyl)-4-octyl-1*H*-pyrrole (3ac)**

The reaction of **1a** (68 mg, 0.26 mmol), amine **2c** (72 mg, 1 mmol), and anhydrous MgSO_4 (15 mg, 0.125 mmol) in 1 mL of CH_3CN afforded 41 mg (50 %) of **3ac**: liquid; ^1H NMR (300 MHz, CDCl_3) δ 6.28 (s, 1 H), 4.25 (q, $J = 7.2$ Hz, 2 H), 3.74 (t, $J = 7.4$ Hz, 2 H), 2.63 (t, $J = 7.4$ Hz, 2 H), 2.47 (s, 3 H), 1.70-1.58 (m, 2 H), 1.58-1.40 (m, 2 H), 1.36 (t, $J = 7.2$ Hz, 3 H), 1.40-1.10 (m, 12 H), 0.93 (t, $J = 7.4$ Hz, 3 H), 0.88 (t, $J = 7.2$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 166.2, 135.7, 125.5, 118.1, 110.2, 58.9, 46.2, 32.9, 31.9, 30.7, 29.7, 29.6, 29.3, 27.0, 22.6, 19.9, 14.4, 14.1, 13.6, 11.4; MS (EI) m/z (%): 321 (M^+ , 24.34), 223 (100); IR (neat) ν (cm^{-1}): 1694, 1519, 1465, 1429, 1259, 1097; HRMS calcd for $\text{C}_{20}\text{H}_{36}\text{NO}_2^+$ (MH^+): 322.2741. Found: 322.2728.

(15) **1-(*t*-Butyl)-2-methyl-3-(ethoxycarbonyl)-4-octyl-1*H*-pyrrole (3ad)**

The reaction of **1a** (68 mg, 0.25 mmol), amine **2d** (78 mg, 1.1 mmol), and anhydrous

MgSO₄ (16 mg, 0.13 mmol) in 1 mL of CH₃CN afforded 41 mg (50 %) of **3ad**: liquid; ¹H NMR (300 MHz, CDCl₃) δ 6.49 (s, 1 H), 4.25 (q, *J* = 7.2 Hz, 2 H), 2.70 (s, 3 H), 2.59 (t, *J* = 7.8 Hz, 2 H), 1.59 (s, 9 H), 1.60-1.45 (m, 2 H), 1.33 (t, *J* = 7.2 Hz, 3 H), 1.38-1.20 (m, 10 H), 0.87 (t, *J* = 6.6 Hz, 3 H); ¹³C NMR (75 MHz, CDCl₃) δ 166.6, 136.3, 123.7, 115.9, 112.3, 58.9, 56.4, 31.9, 30.9, 30.6, 29.8, 29.6, 29.3, 27.4, 22.7, 14.8, 14.4, 14.1; MS (EI) *m/z* (%): 321 (*M*⁺, 22.58), 167 (100); IR (neat) *v* (cm⁻¹): 1694, 1563, 1512, 1254, 1215, 1101; HRMS calcd for C₂₀H₃₆NO₂⁺ (*MH*⁺): 322.2741. Found: 322.2741.

(16) **1-(1'-(Methoxycarbonyl)-2'-phenylethyl)-2-methyl-3-(ethoxycarbonyl)-4-octyl-1*H*-pyrrole (3ae)**

The reaction of **1a** (65 mg, 0.24 mmol), amine **2e** (179 mg, 1.0 mmol), and anhydrous MgSO₄ (15 mg, 0.125 mmol) in 1 mL of CH₃CN afforded 61 mg (60 %) of **3ae**. The reaction of **1a** (134 mg, 0.5 mmol), amine (*S*)-**2e** (359 mg, 2.0 mmol), and anhydrous MgSO₄ (30 mg, 0.25 mmol) in 2 mL of CH₃CN afforded 158 mg (74 %) of (*S*)-**3ae** with 96 ee% as determined by HPLC analysis (Chiralpak AD-H, hexane: *i*-PrOH = 90:10, 230 nm), *t_r* = 4.3 (minor), 4.7 (major), [*α*]_D²⁰ -92.6° (*c* 1.3, CHCl₃); oil, ¹H NMR (300 MHz, CDCl₃) δ 7.27-7.15 (m, 3 H), 7.03-6.93 (m, 2 H), 6.55 (s, 1 H), 4.81 (dd, *J* = 9.6, 5.7 Hz, 1 H), 4.23 (q, *J* = 7.2 Hz, 2 H), 3.71 (s, 3 H), 3.42 (dd, *J* = 13.8,

5.7 Hz, 1 H), 3.18 (dd, $J = 13.8, 9.6$ Hz, 1 H), 2.80-2.50 (m, 2 H), 2.19 (s, 3 H), 1.62-1.50 (m, 2 H), 1.42-1.19 (m, 10 H), 1.32 (t, $J = 6.9$ Hz, 3 H), 0.89 (t, $J = 7.2$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 170.1, 166.0, 136.6, 136.0, 128.8, 128.5, 127.1, 126.5, 115.5, 110.5, 59.2, 58.9, 52.6, 38.7, 31.8, 30.4, 29.6, 29.5, 29.3, 27.1, 22.6, 14.3, 14.0, 10.9; MS (ESI) m/z : 428 [$\text{M}^+ + 1$]; IR (neat) ν (cm^{-1}): 1748, 1695, 1521, 1426, 1256, 1087; HRMS calcd for $\text{C}_{26}\text{H}_{38}\text{NO}_4^+$ (MH^+): 428.2795. Found: 428.2782.

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Pulse Sequence: s2pu1

cgf-1-33c
 Archive directory: /export/home/wasm/vnmr/sys/data
 Sample directory:
 File: CARBON

Pulse Sequence: zgpg30

```
cgf-1-36c
Archive directory: /export/home/masa/vmarsys/data
Sample directory:
File: CARBON
Pulse Sequence: s2pul
```

Cgf-1-25-c
 Archive directory: /export/home/masm/vnmrsys/data
 Sample directory:
 File: CARBON
 Pulse Sequence: s2pul

cgf-1-34-1c
 Archive directory: /export/home/masam/vnmr/sys/data
 Sample directory:
 File: CARBON
 Pulse Sequence: s2pu1

Cgf-1-15-2c

Archive directory: /export/home/masm/vnmr/sys/data
Sample directory:
File: CARBON

Pulse Sequence: c2pul

cpf-1-27c
 Archive directory: /export/home/masm/vnmrsys/data
 Sample directory:
 File: CARBON
 Pulse Sequence: s2pul

11h-7-155-1c
Pulse Sequence: s2pu1