Supporting Information

Zinc and trimethylsilyl chloride mediated synthesis of 2,3,5-tri-substituted pyrrole diesters from nitriles and ethyl bromoacetate

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**General experimental methods**

Progression of all the reactions was monitored by TLC using hexanes (60-80 °C boiling mixture) / ethyl acetate mixture as eluent. Column chromatography was performed on silica gel (100-200 mesh SRL Chemicals) using increasing percentage of ethyl acetate in hexanes. \(^1\)H-NMR spectra (400 MHz), \(^1\)C NMR (100MHz) and DEPT-135 spectra were recorded for (CDCl\(_3\) and CDCl\(_3\) + CCl\(_4\)) solutions on a BrukerAvance - 400 spectrometer with TMS as internal standard. Coupling constants \(J\) are given in Hz. IR spectra were recorded as KBr pellets on a Nicolet-6700 FT-IR spectrometer. Melting points were recorded using open-ended capillary tubes on VEEGO VMP-DS instrument and are uncorrected. High resolution mass spectra were recorded on Micromass Q-TOF micro mass spectrometer using electron spray ionization mode. The X- ray diffraction measurements were carried out at 298 K on Oxford CrysAlis CCD area detector system equipped with a graphite monochromator and a Mo-K\(\alpha\) fine-focus sealed tube (\(\lambda\) = 0.71073 Å). Organic solvents were dried by standard methods. Commercially obtained reagents were used after purification. Nitriles were purchased from Sigma Aldrich and Avra chemical private limited

![Ethyl 2-(4-chlorophenyl)-5-(2-ethoxy-2-oxoethyl)-1H-pyrrole-3-carboxylate 2b:](image)

**Ethyl 2-(4-chlorophenyl)-5-(2-ethoxy-2-oxoethyl)-1H-pyrrole-3-carboxylate 2b:**

Following the general procedure reaction of 4-chlorobenzonitrile \(1b\) (508 mg, 3.70 mmol) with ethyl bromoacetate (1.85 g, 11.12 mmol), zinc (481m g, 7.4 mmol) and catalytic amounts of TMSCl (50 mol%) afforded ethyl 2-(4-chlorophenyl)-5-(2-ethoxy-2-oxoethyl)-1H-pyrrole-3-carboxylate \(2b\) as light yellow viscous liquid (968 mg, 78% yield); IR (KBr, cm\(^{-1}\))
1642, 1607, 1467, 1401, 1369, 1209, 1168, 1065, 754, 698; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.26 (s, 1H), 7.51 (d, \(J = 2.1\) Hz, 1H), 7.49 (t, \(J = 2.2\) Hz, 1H), 7.34 (t, \(J = 2.2\) Hz, 1H), 7.32 (d, \(J = 2.1\) Hz, 1H), 6.54-6.48 (s, 1H), 4.18 (qd, \(J = 7.1, 5.7\) Hz, 4H), 3.65 (d, \(J = 0.6\) Hz, 2H), 1.28-1.23 (m, 6H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 171.0, 164.8, 135.7, 134.1, 130.5, 130.3, 128.3, 123.3, 112.4, 111.2, 61.5, 59.8, 32.7, 14.4, 14.2; HRMS (ESI) calcd for C\(_{17}\)H\(_{18}\)ClNO\(_4\)Na [M + Na] 358.0822, found 358.0818.

![Chemical structure](image)

**Ethyl 2-(4-bromophenyl)-5-(2-ethoxy-2-oxoethyl)-1H-pyrrole-3-carboxylate 2c:**

Following the general procedure reaction of 4-bromobenzonitrile 1c (506 mg, 2.79 mmol) with ethyl bromoacetate (1.39 g, 8.36 mmol), zinc (362 mg, 5.6 mmol) and catalytic amounts of TMSCl (50 mol%) afforded ethyl 2-(4-bromophenyl)-5-(2-ethoxy-2-oxoethyl)-1H-pyrrole-3-carboxylate 2c as light yellow viscous liquid (792 mg, 75% yield); IR (KBr, cm\(^{-1}\)) 3323, 2980, 2934, 1733, 1704, 1265, 780; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.39 (s, 1H), 7.42 (td, \(J = 8.4, 4.4\) Hz, 4H), 6.48 (d, \(J = 2.1\) Hz, 1H), 4.21-4.11 (m, 4H), 3.61 (s, 2H), 1.29-1.23 (m, 6H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 171.1, 164.7, 135.7, 131.2, 131.1, 130.6, 123.8, 122.3, 112.5, 11.4, 31.5, 59.7, 32.8, 14.4, 14.2; HRMS (ESI) calcd for C\(_{17}\)H\(_{18}\)BrNO\(_4\)Na [M + Na] 402.0317, found 402.0317.

![Chemical structure](image)

**Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-fluorophenyl)-1H-pyrrole-3-carboxylate 2d:**
Following the general procedure reaction of 4-fluorobenzonitrile 1d (502 mg, 4.14 mmol) with ethyl bromoacetate (2.05 g, 12.44 mmol), zinc (536 mg, 8.26 mmol) and catalytic amounts of TMSCl (50 mol%) afforded ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-fluorophenyl)-1H-pyrrole-3-carboxylate 2d as light yellow viscous liquid (1.08 g, 82% yield); IR (KBr, cm⁻¹) 3313, 2983, 1733, 1708, 1675, 1230, 780; ¹H NMR (400 MHz, CDCl₃) δ 9.38 (s, 1H), 7.49 (dd, J = 8.6, 5.5 Hz, 2H), 7.01 (t, J = 8.7 Hz, 2H), 6.47 (d, J = 2.7 Hz, 1H), 4.19-4.10 (m, 4H), 3.60 (s, 2H), 1.25 (dt, J = 14.0, 7.1 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 171.0, 164.8, 136.1, 130.9, 128.2, 123.4, 115.1, 112.1, 111.1, 61.4, 59.6, 32.8, 14.4, 14.2; HRMS (ESI) calcd for C₁₇H₁₈FNO₄Na [M + Na] 342.1118, found 342.1116.

![Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-(trifluoromethyl)phenyl)-1H-pyrrole-3-carboxylate 2e](image)

**Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-(trifluoromethyl)phenyl)-1H-pyrrole-3-carboxylate 2e:**

Following the general procedure reaction of 4-trifluoromethylbenzonitrile 1e (511 mg, 4.36 mmol) with ethyl bromoacetate (2.18 g, 13.10 mmol), zinc (567 mg, 8.72 mmol) and catalytic amounts of TMSCl (50 mol%) afforded ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-(trifluoromethyl)phenyl)-1H-pyrrole-3-carboxylate 4e as light yellow viscous liquid (1.01 g, 71% yield); IR (KBr, cm⁻¹) 1642, 1607, 1467, 1401, 1369, 1209, 1168, 1065, 754, 698; ¹H NMR (400 MHz, CDCl₃) δ 9.49 (s, 1H), 7.65 (d, J = 8 Hz, 2H), 7.58 (d, J = 8.4 Hz, 2H), 6.51 (d, J = 2.8 Hz, 1H), 4.19-4.14 (m, 4H), 3.65 (s, 2H), 1.31-1.24 (m, 6H); ¹³C NMR (100 MHz, CDCl₃) δ δ 171.1, 164.7, 135.6, 135.2, 129.2, 124.9, 124.3, 113.2, 111.7, 61.5, 59.8, 32.7, 14.3, 14.2.; HRMS (ESI) calcd for C₁₈H₁₈F₃NO₄Na [M + Na] 392.1086, found 392.1083.
**Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-methoxyphenyl)-1H-pyrrole-3-carboxylate 2f.**

Following the general procedure reaction of 4-methoxybenzonitrile 1f (510 mg, 3.83 mmol) with ethyl bromoacetate (1.92 g, 11.50 mmol), zinc (497 mg, 7.66 mmol) and catalytic amounts of TMSCl (50 mol%) afforded ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-methoxyphenyl)-1H-pyrrole-3-carboxylate 2f as light yellow viscous liquid (825 mg, 65% yield); IR (KBr, cm⁻¹) 1642, 1607, 1467, 1401, 1369, 1209, 1168, 1065, 754, 698; ¹H NMR (400 MHz, CDCl₃) δ 9.31 (s, 1H), 7.45 (d, J = 8.6 Hz, 2H), 6.85 (d, J = 8.6 Hz, 2H), 6.46 (s, 1H), 4.14 (s, 4H), 3.79 (s, 3H), 3.60 (s, 2H), 1.28-1.21 (m, 6H); ¹C NMR (100 MHz, CDCl₃) δ 159.5, 147.6, 143.7, 129.7, 128.5, 128.2, 127.7, 126.9, 125.9, 125.0, 116.1, 109.0, 41.8, 27.9; HRMS (ESI) calcd for C₁₈H₁₄N₂O₅Na [M + Na] 305.0902, found 305.0900.

**Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(furan-2-yl)-1H-pyrrole-3-carboxylate 2g.**

Following the general procedure reaction of 2-furanitrile 1g (502 mg, 5.39 mmol) with ethyl bromoacetate (2.70 g, 16.19 mmol), zinc (702 mg, 10.78 mmol) and catalytic amounts of TMSCl (50 mol%) afforded ethyl 5-(2-ethoxy-2-oxoethyl)-2-(furan-2-yl)-1H-pyrrole-3-carboxylate 2g as light blue crystals (1.27 g, 80% yield) mp: 108 °C; IR (KBr, cm⁻¹) 1642, 1607, 1467, 1401, 1369, 1209, 1168, 1065, 754, 698; ¹H NMR (400 MHz, CDCl₃) δ 9.46 (s, 1H), 7.45 (d, J = 3.6 Hz, 1H), 7.39 (s, 1H), 6.48-6.44 (m, 2H), 4.29 (q, J = 7.2 Hz, 2H), 4.21 (q, J = 7.2 Hz, 2H), 3.64 (s, 2H), 1.36 (t, J = 7.2 Hz, 3H), 1.31 (t, J = 7.2 Hz, 3H); ¹C NMR (100 MHz, CDCl₃)
δ 170.5, 164.3, 146.2, 141.2, 127.8, 123.2, 112.3, 111.2, 111.1, 110.4, 61.5, 59.7, 32.9, 14.7, 14.3.; HRMS (ESI) calcd for C_{13}H_{17}NO_3Na [M + Na] 314.1004, found 314.1000.

**Figure 1.** ORTEP diagram of ethyl 5-(2-ethoxy-2-oxoethyl)-2-(furan-2-yl)-1H-pyrrole-3-carboxylate 2g.

**Crystal data for ethyl 5-(2-ethoxy-2-oxoethyl)-2-(furan-2-yl)-1H-pyrrole-3-carboxylate 2g.**

Empirical formula, C_{13}H_{17}NO_3; formula weight, 291; crystal colour, yellowish colour: crystal dimensions a = 11.5324(9) Å, b = 8.9339(5) Å, c = 14.7077(9) Å; α = 90, β = 103.983, γ = 90; crystal system, monoclinic; V = 1470.43(17); space group P 1 21/n 1; Z = 4; D_{calc} = 1.3158 g/cm³; F_{(000)} = 616.3810; R (I≥2σ) = 0.0247, wR² = 0.0962. Detailed X-ray crystallographic data was available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (for compound 2g CCDC 1038598).

![Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(thiophen-2-yl)-1H-pyrrole-3-carboxylate 2h](image)

**Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(thiophen-2-yl)-1H-pyrrole-3-carboxylate 2h:**
Following the general procedure reaction of 2-thiophenenitrile 1h (504 mg, 4.58 mmol) with ethyl bromoacetate (2.29 g, 13.74 mmol), zinc (595 mg, 9.2 mmol) and catalytic amounts of TMSCl (50 mol%) afforded ethyl 5-(2-ethoxy-2-oxoethyl)-2-(thiophen-2-yl)-1H-pyrrole-3-carboxylate 2h as red viscous liquid (1.09 g, 78% yield); IR (KBr, cm⁻¹) 1642, 1607, 1467, 1401, 1369, 1209, 1168, 1065, 754, 698; ¹H NMR (400 MHz, CDCl₃) δ 9.27 (s, 1H), 7.50-7.49 (m, 1H), 7.28-7.27 (m, 1H), 7.04-7.02 (m, 1H), 6.46 (d, J = 1.4 Hz, 1H), 4.25-4.18 (m, 4H), 3.62 (s, 2H), 1.33-1.28 (m, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 170.7, 164.6, 133.2, 130.2, 127.1, 126.9, 125.6, 123.7, 112.3, 111.3, 61.3, 59.6, 32.7, 14.4, 14.1.; HRMS (ESI) calcd for C₁₅H₁₇NO₄Na [M + Na] 330.0776, found 330.0774.

![Diagram](image)

**Ethyl 2-(3a,7a-dihydro-1H-indol-3-yl)-5-(2-ethoxy-2-oxoethyl)-1H-pyrrole-3-carboxylate 2i:**

Following the general procedure reaction of tert-butyl 3-cyano-1H-indole 1i (512 mg, 2.11 mmol) with ethyl bromoacetate (1.05 g, 6.34 mmol), zinc (274 mg, 4.2 mmol) and catalytic amounts of TMSCl (50 mol%) afforded ethyl -(3a,7a-dihydro-1H-indol-3-yl)-5-(2-ethoxy-2-oxoethyl)-1H-pyrrole-3-carboxylate 2i as light red solid (586 mg, 81% yield) mp: 87 °C; IR (KBr, cm⁻¹) 1642, 1607, 1467, 1401, 1369, 1209, 1168, 1065, 754, 698; ¹H NMR (400 MHz, CDCl₃) δ 9.32 (s, 1H), 9.01 (s, 1H), 7.71 (dd, J = 14.9, 8.5 Hz, 2H), 7.33-7.23 (m, 1H), 7.19-7.09 (m, 2H), 6.53 (d, J = 2.7 Hz, 1H), 4.22 (dq, J = 14.3, 7.1 Hz, 4H), 3.66 (s, 2H), 1.31-1.26 (m, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 159.5, 147.6, 143.7, 129.7, 128.5, 128.2, 127.7, 126.9, 125.9, 125.0, 116.1, 109.0, 41.8, 27.9; HRMS (ESI) calcd for C₁₉H₂₉N₂O₄Na [M + Na] 363.1321, found 363.1322.
**Ethyl 2-benzyl-5-(2-ethoxy-2-oxoethyl)-1H-pyrrole-3-carboxylate 2j:**

Following the general procedure reaction of benzylacetonitrile 1j (512 mg, 4.37 mmol) with ethyl bromoacetate (2.18 g, 13.11 mmol), zinc (568 mg, 8.75 mmol) and catalytic amounts of TMSCl (50 mol%) afforded ethyl 2-benzyl-5-(2-ethoxy-2-oxoethyl)-1H-pyrrole-3-carboxylate 2j as light yellow viscous liquid (1.18 g, 86% yield); IR (KBr, cm\(^{-1}\)) 3334, 2981, 1734, 1697, 1675, 1299, 779; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.86 (s, 1H), 7.31-7.07 (m, 5H), 6.38 (d, \(J = 2.5\) Hz, 1H), 4.29 (s, 2H), 4.22 (q, \(J = 7.1\) Hz, 2H), 4.06 (q, \(J = 7.1\) Hz, 2H), 3.49 (s, 2H), 1.29 (t, \(J = 7.1\) Hz, 3H), 1.18 (t, \(J = 7.1\) Hz, 3H); \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 170.7, 165.4, 138.6, 13.5, 128.7, 128.6, 126.5, 122.3, 111.7, 109.3, 61.1, 59.3, 33.1, 32.9, 14.4, 14.1; HRMS (ESI) calcd for C\(_{18}\)H\(_{21}\)NO\(_3\)Na [M + Na] 338.1368, found 338.1368.

**Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-1-ylmethyl)-1H-pyrrole-3-carboxylate 2k:**

Following the general procedure reaction of 1-naphthylacetonitrile 1k (183 mg, 1.06 mmol) with ethyl bromoacetate (502 mg, 3.18 mmol), zinc (139 mg, 2.12 mmol) and catalytic amounts of TMSCl (50 mol%) afforded ethyl 5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-1-ylmethyl)-1H-pyrrole-3-carboxylate 2k as yellow viscous liquid (342 mg, 86% yield); IR (KBr, cm\(^{-1}\)) 1642, 1607, 1467, 1401, 1369, 1209, 1168, 1065, 754, 698; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 109.01 (s, 1H), 7.75 (dd, \(J = 17.4, 8.1\) Hz, 3H), 7.62 (s, 1H), 7.42 (dd, \(J = 9.1, 5.2\) Hz, 2H), 7.33
(d, J = 8.4 Hz, 1H), 6.44 (s, 1H), 4.45 (s, 2H), 4.26 (q, J = 7.0 Hz, 2H), 4.01 (q, J = 7.2 Hz, 2H), 3.47 (s, 3H), 1.30 (dd, J = 14.7, 7.4 Hz, 4H), 1.12 (t, J = 7.1 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 159.5, 147.6, 143.7, 129.7, 128.5, 128.2, 127.7, 126.9, 125.9, 125.0, 116.1, 109.0, 41.8, 27.9; HRMS (ESI) calcd for C$_{25}$H$_{23}$NO$_4$Na [M + Na] 388.1525, found 388.1524.

![Chemical structure of compound 21](image)

**Ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-fluorobenzyl)-1H-pyrrole-3-carboxylate 21**.

Following the general procedure reaction of 4-fluorobenzylacetetonitrile 11 (508 mg, 4.19 mmol) with ethyl bromoacetate (2.10 g, 12.59 mmol), zinc (536 mg, 8.26 mmol) and catalytic amounts of TMSCl (50 mol%) afforded ethyl 2 5-(2-ethoxy-2-oxoethyl)-2-(4-fluorobenzyl)-1H-pyrrole-3-carboxylate 21 as light yellow viscous liquid (1.13 g, 82% yield); IR (KBr, cm$^{-1}$) 3267, 2983, 1734, 1699, 1673, 1510, 1225, 782; $^1$H NMR (400 MHz, CDCl$_3$) δ 8.83 (s, 1H), 7.20-7.09 (m, 2H), 6.94 (t, J = 8.4 Hz, 2H), 6.35 (s, 1H), 4.26-4.18 (m, 4H), 4.09 (q, J = 7.1 Hz, 2H), 3.51 (s, 2H), 1.30 (t, J = 7.1 Hz, 3H), 1.22 (t, J = 7.1 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 170.9, 165.3, 162.9, 160.5, 137.3, 134.4, 134.41, 130.3, 130.2, 122.3, 115.6, 115.4, 111.9, 109.5, 61.3, 59.5, 32.8, 32.4, 14.6, 14.2; HRMS (ESI) calcd for C$_{18}$H$_{20}$FNO$_4$Na [M + Na] 356.1274, found 356.1272.

![Chemical structure of compound 21](image)
**Ethyl 2-benzhydryl-5-(2-ethoxy-2-oxoethyl)-1H-pyrrole-3-carboxylate 2m:**

Following the general procedure reaction of diphenylacetonitrile \(1\text{m}\) (504 mg, 2.50 mmol) with ethyl bromoacetate (1.25 g, 7.5 mmol), zinc (325 mg, 5.0 mmol) and catalytic amounts of TMSCl (50 mol%) afforded ethyl 2-benzhydryl-5-(2-ethoxy-2-oxoethyl)-1H-pyrrole-3-carboxylate \(2\text{m}\) as light yellow solid (871 mg, 86% yield) mp: 92 °C; IR (KBr, cm\(^{-1}\)) 3324, 2981, 1736, 1699, 1211, 778; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.50 (s, 1H), 7.32-7.25 (m, 4H), 7.24-7.18 (m, 2H), 7.13-7.08 (m, 4H), 6.42 (d, \(J = 2.8\) Hz, 1H), 6.35 (s, 1H), 4.11 (ddd, \(J = 13.5, 10.7, 4.7\) Hz, 4H), 3.53 (s, 2H), 1.19 (td, \(J = 7.1, 2.7\) Hz, 6H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 170.4, 164.7, 142.4, 139.2, 128.9, 12.7, 126.8, 122.3, 114.2, 109.9, 61.1, 59.3, 48.6, 33.1, 14.4, 14.2; HRMS (ESI) calcd for C\(_{22}\)H\(_{24}\)NO\(_4\)Na [M + Na] 414.1681, found 414.1681.

![Chemical structure](image)

**Ethyl 5-(2-ethoxy-2-oxoethyl)-2-methyl-1H-pyrrole-3-carboxylate 2n:**

Following the general procedure reaction of acetonitrile \(1\text{n}\) (508 mg, 12.19 mmol) with ethyl bromoacetate (6.10 g, 36.58 mmol), zinc (1.58 g, 24.38 mmol) and catalytic amounts of TMSCl (50 mol%) afforded ethyl 5-(2-ethoxy-2-oxoethyl)-2-methyl-1H-pyrrole-3-carboxylate \(2\text{n}\) as light yellow viscous liquid (2.2 g, 78% yield); IR (KBr, cm\(^{-1}\)) 1642, 1607, 1467, 1401, 1369, 1209, 1168, 1065, 754, 698; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.18 (s, 1H), 6.34 (d, \(J = 2.7\) Hz, 1H), 4.24 (q, \(J = 6.9\) Hz, 2H), 4.16 (q, \(J = 7.2\) Hz, 2H), 3.57 (s, 1H), 2.45 (s, 3H), 1.32 (t, \(J = 7.2\) Hz, 3H), 1.26 (t, \(J = 7.2\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 159.5, 147.6, 143.7, 129.7, 128.5, 128.2, 127.7, 126.9, 125.9, 125.0, 116.1, 109.0, 41.8, 27.9; HRMS (ESI) calcd for C\(_{12}\)H\(_{17}\)NO\(_4\)Na [M + Na] 262.1055, found 262.1055.
Ethyl 5-(2-ethoxy-2-oxoethyl)-2-propyl-1H-pyrrole-3-carboxylate 2o:

Following the general procedure reaction of propanenitrile 1o (508 mg, 7.4 mmol) with ethyl bromoacetate (3.68 g, 22.08 mmol), zinc (956 mg, 14.72 mmol) and catalytic amounts of TMSCl (50 mol%) afforded ethyl 5-(2-ethoxy-2-oxoethyl)-2-propyl-1H-pyrrole-3-carboxylate 2o as light yellow viscous liquid (1.4 g, 74% yield); IR (KBr, cm\(^{-1}\)) 3334, 2930, 1738, 1702, 1675, 1223, 781; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 9.06 (s, 1H), 6.29 (s, 1H), 4.22-4.10 (m, 4H), 3.53 (s, 2H), 2.85-2.81 (m, 2H), 1.63-1.57 (m, 2H), 1.30-1.22 (m, 8H), 0.92-0.87 (m, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 171.1, 165.4, 140.0, 121.3, 111.2, 109.4, 61.2, 59.2, 32.9, 29.3, 22.8, 14.6, 14.2, 13.6 ppm; HRMS (ESI) calcd for C\(_{14}\)H\(_{21}\)NO\(_4\)Na [M + Na] 290.1368, found 290.1363.

Ethyl 5-(2-ethoxy-2-oxoethyl)-2-hexyl-1H-pyrrole-3-carboxylate 2p:

Following the general procedure reaction of hexynitrile 1b (504 mg, 4.50 mmol) with ethyl bromoacetate (2.27 g, 13.62 mmol), zinc (585 mg, 9.0 mmol) and catalytic amounts of TMSCl (50 mol%) afforded ethyl 5-(2-ethoxy-2-oxoethyl)-2-hexyl-1H-pyrrole-3-carboxylate 2p as light yellow viscous liquid (1.72 g, 75% yield); IR (KBr, cm\(^{-1}\)) 3334, 2930, 1738, 1702, 1675, 1223, 781; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.92 (s, 1H), 6.29 (s, 1H), 4.22-4.12 (m, 4H), 3.55 (s, 2H), 2.89-2.85 (m, 2H), 1.60-1.32 (m, 4H), 1.32-1.23 (m, 8H), 0.92-0.87 (m, 4H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 171.2, 165.3, 140.2, 121.2, 111.2, 109.4, 61.3, 59.2, 32.9, 31.7, 29.6, 29.2,
27.4, 22.7, 14.6, 14.2, 14.2.; HRMS (ESI) calcd for C$_{17}$H$_{27}$NO$_4$Na [M + Na] 332.1838, found 332.1838.

**Additional experiments to support suggested mechanism**

**Experiment 1: The Experiment suggested by the referee**

![Diagram](image)

The $^1$H NMR spectra were recorded after 30 min of the reaction, conducted according to the general procedure described in the manuscript. In the first batch, we evaporated THF at 30 °C in a rotator evaporator. To resulting solid, we added CDCl$_3$. But the CDCl$_3$ solution was turbid and the shim failed (paramagnetic impurities?). In the second batch we added CDCl$_3$ to THF solution of the reaction mixture and recorded spectra. Although the NMR spectrum had THF signals, it showed characteristic signals for enamine (singlet at $\delta$ 5.2 ppm) and pyrrole (singlet at $\delta$ 6.2 ppm). Integrations indicated that the enamine and pyrrole were present in the ratio of 10:1. To the third batch, we added 0.01 mL (1 drop) of 1 N aqueous HCl and recorded the spectrum in CDCl$_3$. The spectrum displayed signals for pyrrole 2a and enamine 3.

**Experiment 2: The Experiment without Zn**

![Diagram](image)

No change in the enamine 3
To evaluate if the reaction of enamine 3 could provide C-alkylated product 4 (See Scheme 2 in the manuscript) we treated it with ethyl bromoacetate (1 equiv) in presence of TMSCl (0.5 equiv) under THF reflux for 4 h. The TLC analysis indicated that enamine 3 remained intact in the reaction mixture. We deduce that Zn is crucial for transformation of 3 into pyrrole 2a.

**Experiment 3: The Experiment reduced amounts of Zn and ethyl bromoacetate**

To evaluate if reduced amounts of ethyl bromoacetate and Zn could provide 4 we treated enamine 3 with ethyl bromoacetate (1 equiv) in presence of TMSCl (0.5 equiv) and Zinc (1 equiv) under THF reflux for 5 h. The TLC showed presence of the pyrrole 2a in 18%. About 82% of enamine was not consumed and remained as such.

We deduce that the intermediates generated in the reaction react fast to generate stable aromatic pyrrole 2a

**Experiment 4: The Experiment with reverse addition to zinc enolate to enamine 3**

To evaluate if zinc enolate generated from ethyl bromoacetate and zinc is involved in the conversion of enamine 3 into pyrrole 2a, we conducted an experiment wherein the enamine 3 was treated with zinc enolate of ethyl bromoacetate in reverse addition manner under THF reflux for 6 h. The TLCs showed that the enamine remained intact and there was no change. This result
indicates that unless C-alkylation of 3 takes place to generate 4 further transformations into pyrrole does not take place.

**Figure 2.** $^1$H NMR (400 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 5-(2-ethoxy-2-oxoethyl)-2-phenyl-1H-pyrrole-3-carboxylate 2a.

**Figure 3.** $^{13}$C NMR (100 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 5-(2-ethoxy-2-oxoethyl)-2-phenyl-1H-pyrrole-3-carboxylate 2a.
Figure 4. $^1$H NMR (400 MHz, CDCl$_3$) spectrum of ethyl 2-(4-chlorophenyl)-5-(2-ethoxy-2-oxoethyl)-1H-pyrrole-3-carboxylate 2b.

Figure 5. $^{13}$C NMR (100 MHz, CDCl$_3$) spectrum of ethyl 2-(4-chlorophenyl)-5-(2-ethoxy-2-oxoethyl)-1H-pyrrole-3-carboxylate 2b.
Figure 6. $^1$H NMR (400 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 2-(4-bromophenyl)-5-(2-ethoxy-2-oxoethyl)-1$H$-pyrrole-3-carboxylate 2c.

Figure 7. $^{13}$C NMR (100 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 2-(4-bromophenyl)-5-(2-ethoxy-2-oxoethyl)-1$H$-pyrrole-3-carboxylate 2c.
**Figure 8.** $^1$H NMR (400 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-fluorophenyl)-1H-pyrrole-3-carboxylate 2d.

**Figure 9.** $^{13}$C NMR (100 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-fluorophenyl)-1H-pyrrole-3-carboxylate 2d.
Figure 10. $^1$H NMR (400 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-(trifluoromethyl)phenyl)-1$H$-pyrrole-3-carboxylate 2e.

Figure 11. $^{13}$C NMR (100 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-(trifluoromethyl)phenyl)-1$H$-pyrrole-3-carboxylate 2e.
Figure 12. $^1$H NMR (400 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-methoxyphenyl)-1H-pyrrole-3-carboxylate 2f.

Figure 13. $^{13}$C NMR (100 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-methoxyphenyl)-1H-pyrrole-3-carboxylate 2f.
Figure 14. $^1$H NMR (400 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 5-(2-ethoxy-2-oxoethyl)-2-(furan-2-yl)-1H-pyrrole-3-carboxylate 2g.

Figure 15. $^{13}$C NMR (100 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 5-(2-ethoxy-2-oxoethyl)-2-(furan-2-yl)-1H-pyrrole-3-carboxylate 2g.
Figure 16. $^1$H NMR (400 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 5-(2-ethoxy-2-oxoethyl)-2-(thiophen-2-yl)-1H-pyrrole-3-carboxylate 2h.

Figure 17. $^{13}$C NMR (100 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 5-(2-ethoxy-2-oxoethyl)-2-(thiophen-2-yl)-1H-pyrrole-3-carboxylate 2h.
Figure 18. $^1$H NMR (400 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 2-(3a,7a-dihydro-$1H$-indol-3-yl)-5-(2-ethoxy-2-oxoethyl)-$1H$-pyrrole-3-carboxylate 2i.

Figure 19. $^{13}$C NMR (100 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 2-(3a,7a-dihydro-$1H$-indol-3-yl)-5-(2-ethoxy-2-oxoethyl)-$1H$-pyrrole-3-carboxylate 2i.
**Figure 20.** $^1$H NMR (400 MHz, CDCl$_3$) spectrum of ethyl 2-benzyl-5-(2-ethoxy-2-oxoethyl)-1H-pyrrole-3-carboxylate 2j.

**Figure 21.** $^{13}$C NMR (100 MHz, CDCl$_3$) spectrum of ethyl 2-benzyl-5-(2-ethoxy-2-oxoethyl)-1H-pyrrole-3-carboxylate 2j.
Figure 22. $^1$H NMR (400 MHz, CDCl$_3$) spectrum of ethyl 5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-1-ylmethyl)-1H-pyrrole-3-carboxylate 2k.

Figure 23. $^{13}$C NMR (100 MHz, CDCl$_3$) spectrum of ethyl 5-(2-ethoxy-2-oxoethyl)-2-(naphthalen-1-ylmethyl)-1H-pyrrole-3-carboxylate 2k.
Figure 24. $^1$H NMR (400 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-fluorobenzyl)-1H-pyrrole-3-carboxylate 21.

Figure 25. $^{13}$C NMR (100 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 5-(2-ethoxy-2-oxoethyl)-2-(4-fluorobenzyl)-1H-pyrrole-3-carboxylate 21.
Figure 26. $^1$H NMR (400 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 2-benzhydryl-5-(2-ethoxy-2-oxoethyl)-1$H$-pyrrole-3-carboxylate 2m.

Figure 27. $^{13}$C NMR (100 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 2-benzhydryl-5-(2-ethoxy-2-oxoethyl)-1$H$-pyrrole-3-carboxylate 2m.
Figure 28. $^1$H NMR (400 MHz, CDCl$_3$) spectrum of ethyl 5-(2-ethoxy-2-oxoethyl)-2-methyl-$1H$-pyrrole-3-carboxylate 2n.

Figure 29. $^{13}$C NMR (100 MHz, CDCl$_3$) spectrum of ethyl 5-(2-ethoxy-2-oxoethyl)-2-methyl-$1H$-pyrrole-3-carboxylate 2n.
**Figure 30.** $^1$H NMR (400 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 5-(2-ethoxy-2-oxoethyl)-2-propyl-1H-pyrrole-3-carboxylate 2o.

**Figure 31.** $^{13}$C NMR (100 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 5-(2-ethoxy-2-oxoethyl)-2-propyl-1H-pyrrole-3-carboxylate 2o.
Figure 32. $^1$H NMR (400 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 5-(2-ethoxy-2-oxoethyl)-2-hexyl-$1H$-pyrrole-3-carboxylate $2p$.

Figure 33. $^{13}$C NMR (100 MHz, CCl$_4$ + CDCl$_3$; 1:1) spectrum of ethyl 5-(2-ethoxy-2-oxoethyl)-2-hexyl-$1H$-pyrrole-3-carboxylate $2p$. 