SUPPORTING INFORMATION FOR:

Design, Synthesis and Cyclization of 4-Aminobutyric Acid Derivatives: Potential Candidates as Self-Immolative Spacers

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Synthesis of phenyl ester 6b. The same procedure described above for the preparation of compound 6a was followed except that 5 was used as a starting material. The product was purified by column chromatography (9:1 cyclohexane:EtOAc) to provide 6b (0.128 g, 79%) as a clear, colorless oil. ν\text{max}/cm\textsuperscript{-1} 3103, 3074, 3045, 3014, 2979, 2937, 2873, 1762, 1697, 1596, 1494, 1477, 1396, 1366. \textsuperscript{1}H NMR (CDCl\textsubscript{3}): δ 7.42 – 7.36 (m, 2H), 7.26 – 7.21 (m, 2H), 7.12 – 7.07 (m, 1H), 3.35 (t, J = 6.6 Hz, 2H), 2.89 (s, 3H), 2.58 (t, J = 7.4 Hz, 2H), 1.97 (quint, J = 7.0 Hz, 2H), 1.48 (s, 9H). \textsuperscript{13}C NMR (CDCl\textsubscript{3}): δ 171.6, 155.7, 150.6, 129.3, 125.7, 121.4, 79.4, 48.0 & 47.4 (rotamers), 34.1, 31.3, 28.4, 23.0 & 22.8 (rotamers). HRMS: calc’d [M+H]\textsuperscript{+} (C\textsubscript{16}H\textsubscript{24}NO\textsubscript{4}): 294.1705. Found: (EI) 294.1711.

Synthesis of α-benzyl tert-butyl ester 8c. The same procedure described above for the preparation of compound 8a was followed except that benzyl bromide was used as the alkyl halide and only 1.2 equiv. of LHMDS was used. The product was purified by column chromatography (99:1 cyclohexane:EtOAc → 9:1 cyclohexane:EtOAc) to provide 8c (0.188 g, 70%) as a thick, colorless oil. ν\text{max}/cm\textsuperscript{-1} 3090, 3066, 3031, 3006, 2978, 2932, 2892, 1727, 1699, 1483, 1456, 1394, 1367. \textsuperscript{1}H NMR (CDCl\textsubscript{3}): δ 7.32 – 7.24 (m, 2H), 7.23 – 7.15 (m, 3H), 3.43 – 3.08 (m, 2H), 2.99 – 2.67 (m, 2H), 2.81 (s, 3H), 1.93 – 1.79 (m, 1H), 1.73 – 1.60 (m, 1H), 1.54 – 1.38 (m, 9H), 1.38 – 1.28 (m, 9H). \textsuperscript{13}C NMR (CDCl\textsubscript{3}): δ 171.6, 155.5, 139.1, 128.9, 128.2, 126.2, 80.3, 79.2, 47.2, 45.6, 38.5, 34.1, 29.9, 28.3, 27.9. HRMS: calc’d [M]\textsuperscript{+} (C\textsubscript{21}H\textsubscript{33}NO\textsubscript{4}): 363.2410. Found: (EI) 363.1924.

Synthesis of acid 9b. The same procedure described above for the preparation of compound 9a was followed except that 8b was used as a starting material. The product was purified by column
chromatography (5:1 cyclohexane:EtOAc) to provide 9b (0.122 g, 99%) as a thick, colorless oil. 
$\nu_{\text{max}}/\text{cm}^{-1}$ 3450, 2980, 2941, 1700, 1670, 1489, 1457, 1401, 1368. $^1$H NMR (CDCl$_3$): $\delta$ 10.77 (s, 1H), 5.80 – 5.67 (m, 1H), 5.14 – 5.10 (m, 2H), 3.40 – 3.16 (m, 2H), 2.81 (s, 3H), 2.46 – 2.35 (m, 2H), 2.33 – 2.22 (m, 1H), 1.90 – 1.78 (m, 1H), 1.75 – 1.64 (m, 1H), 1.43 (s, 9H). $^{13}$C NMR (CDCl$_3$): $\delta$ 180.2, 155.9, 134.7, 117.3, 80.0, 46.9 & 46.5 (rotamers), 42.2, 36.1, 34.1, 29.9, 28.3. HRMS: calc’d [M]$^+$ (C$_{13}$H$_{23}$NO$_4$): 257.1627. Found: (EI) 257.1634.

**Synthesis of acid 9c.** The same procedure described above for the preparation of compound 9a was followed except that 8c was used as a starting material. The product was purified by column chromatography (3:1 cyclohexane:EtOAc) to provide 9c (143 mg, 96%) as a thick, colorless oil. $\nu_{\text{max}}/\text{cm}^{-1}$ 3092, 3180, 3067, 3032, 2980, 2938, 1735, 1700, 1667, 1488, 1456, 1404, 1368. $^1$H NMR (CDCl$_3$): $\delta$ 10.90 (s, 1H), 7.34 – 7.15 (m, 5H), 3.45 – 3.19 (m, 2H), 3.14 – 3.00 (m, 1H), 2.84 – 2.73 (m, 1H), 2.77 (s, 3H), 2.73 – 2.64 (m, 1H), 1.94 – 1.82 (m, 1H), 1.78 – 1.67 (m, 1H), 1.54 – 1.34 (m, 9H). $^{13}$C NMR (CDCl$_3$): $\delta$ 180.2, 156.3, 138.6, 128.8, 128.4, 126.5, 80.5, 47.1 & 46.6 (rotamers), 44.4, 38.0, 34.1, 29.0, 28.2. HRMS: calc’d [M]$^+$ (C$_{17}$H$_{25}$NO$_4$): 307.1784. Found: (EI) 307.1783.

**Synthesis of phenyl ester 10b.** The same procedure described above for the preparation of compound 10a was followed except that 9b was used as a starting material. The product was purified by column chromatography (93:7 cyclohexane:EtOAc) to provide 10b (0.128 g, 86%) as a colorless oil. $\nu_{\text{max}}/\text{cm}^{-1}$ 3080, 3009, 2979, 2936, 2871, 1758, 1698, 1594, 1493, 1457, 1396, 1367. $^1$H NMR (CDCl$_3$): $\delta$ 7.37 (t, J = 7.4 Hz, 2H), 7.22 (t, J = 7.4 Hz, 1H), 7.08 (d, J = 7.8 Hz, 2H), 5.94 – 5.80 (m, 1H), 5.22 – 5.08 (m, 2H), 3.48 – 3.21 (m, 2H), 2.87 (s, 3H), 2.75 – 2.65 (m,
1H), 2.60 – 2.39 (m, 2H), 2.04 (sextet, J = 7.4 Hz, 1H), 1.80 (sextet, J = 7.4 Hz, 1H), 1.46 (s, 9H). $^1$C NMR (CDCl$_3$): δ 173.4, 155.6, 150.6, 134.7, 129.3, 125.7, 121.5, 117.5, 79.5, 47.0 & 46.4 (rotamers), 42.5, 36.5, 34.1, 29.4, 28.4. IR (cm$^{-1}$): HRMS: calc’d [M$^+$]$^+$ (C$_{19}$H$_{27}$NO$_4$): 333.1940. Found: (EI) 333.1932.

**Synthesis of phenyl ester 10c.** The same procedure described above for the preparation of compound 10a was followed except that 9c was used as a starting material. The product was purified by column chromatography (93:7 cyclohexane:EtOAc) to provide 10c (0.146 g, 82%) as a colorless oil. $\nu_{\text{max}}$/cm$^{-1}$ 3091, 3068, 3033, 2993, 2978, 2931, 2867, 1756, 1696, 1594, 1494, 1481, 1396, 1367. $^1$H NMR (CDCl$_3$): δ 7.33 – 7.26 (m, 4H), 7.25 – 7.19 (m, 3H), 7.15 (t, J = 7.4 Hz, 1H), 6.85 (d, J = 7.4 Hz, 2H), 3.52 – 3.18 (m, 2H), 3.13 – 2.84 (m, 3H), 2.81 (s, 3H), 2.04 (sextet, J = 7.8 Hz, 1H), 1.89 – 1.73 (m, 1H), 1.52 – 1.35 (m, 9H). $^1$C NMR (CDCl$_3$): δ 173.5, 155.6, 150.4, 138.5, 129.2, 129.0, 128.4, 126.6, 125.7, 121.4, 79.4, 47.1 & 46.3 (rotamers), 45.0, 38.5, 34.1, 29.8, 28.3. HRMS: calc’d [M+H]$^+$ (C$_{23}$H$_{30}$NO$_4$): 384.2169. Found: (EI) 384.2167.

**Synthesis of $\alpha$-dibenzyl tert-butyl ester 11c.** The same procedure described above for the preparation of compound 11b was followed except that benzyl bromide was used as the alkyl halide. The product was purified by column chromatography (93:7 cyclohexane:EtOAc) to provide 11c (0.384 g, 93%) as a thick, colorless oil. $\nu_{\text{max}}$/cm$^{-1}$ 3088, 3065, 3032, 3006, 2978, 2935, 1698, 1496, 1482, 1455, 1395, 1366. $^1$H NMR (CDCl$_3$): δ 7.27 – 7.14 (m, 10H), 3.50 – 3.30 (br m, 2H), 3.02 (d, J=14.1 Hz, 2H), 2.83 (d, J=14.1 Hz, 2H), 2.66 (s, 3H), 1.78 – 1.65 (br m, 2H), 1.45 (s, 9H), 1.34 (s, 9H). $^1$C NMR (CDCl$_3$): δ 174.5, 155.5, 137.3, 130.4, 128.0,
126.4, 81.1, 79.5, 50.2, 44.6 & 43.9 (rotamers), 42.0, 33.6, 31.1 & 30.4 (rotamers), 28.5, 27.9.

HRMS: calc’d [M]^+ (C_{28}H_{39}NO_{4}): 453.2879 Found: (EI) 453.2866.

**Synthesis of acid 12a.** The same procedure described above for the preparation of compound 9a was followed except that 11a was used as a starting material. The product was purified by column chromatography (85:15 cyclohexane:EtOAc) to provide 12a (0.166 g, 97%) as a thick, colorless oil. \( v_{\text{max}}/\text{cm}^{-1} \) 3454, 3200, 2980, 2935, 1700, 1694, 1481, 1405, 1368. \(^1\)H NMR (CDCl\(_3\)): \( \delta \) 3.24 (br t, \( J = 7.8 \) Hz, 2H), 2.83 (s, 3H), 1.82 – 1.74 (m, 2H), 1.46 (s, 9H), 1.25 (s, 6H). \(^{13}\)C NMR (CDCl\(_3\)): \( \delta \) 182.9, 155.6, 79.4, 45.4 & 44.9 (rotamers), 40.6, 37.7, 34.0, 28.3, 24.9. HRMS: calc’d [M]^+ (C_{12}H_{23}NO_{4}): 245.1627. Found: (EI) 245.1618.

**Synthesis of acid 12b.** The same procedure described above for the preparation of compound 9a was followed except that 11b was used as a starting material. The product was purified by column chromatography (5:1 cyclohexane:EtOAc) to provide 12b (0.092 g, 90%) as a thick, colorless oil. \( v_{\text{max}}/\text{cm}^{-1} \) 3430, 3270, 3080, 3010, 2980, 2935, 1730, 1700, 1488, 1454, 1404, 1368. \(^1\)H NMR (CDCl\(_3\)): \( \delta \) 5.84 – 5.70 (m, 2H), 5.19 – 5.11 (m, 4H), 3.25 (br t, \( J = 7.4 \) Hz, 2H), 2.82 (s, 3H), 2.38 (d, \( J = 7.4 \) Hz, 4H), 1.84 – 1.76 (m, 2H), 1.46 (s, 9H). \(^{13}\)C NMR (CDCl\(_3\)): \( \delta \) 181.0, 155.6, 132.6, 118.8, 80.3, 47.6, 38.7, 34.1, 32.1, 28.3. HRMS: calc’d [M]^+ (C_{16}H_{27}NO_{4}): 297.1940. Found: (EI) 297.1949.

**Synthesis of acid 12c.** The same procedure described above for the preparation of compound 9a was followed except that 11c was used as a starting material. The product was purified by column chromatography (85:15 cyclohexane:EtOAc) to provide 12c (0.139 g, 94%) as a sticky
white solid. \( \nu_{\text{max}} / \text{cm}^{-1} \) 3460, 3210, 3090, 3067, 3031, 2979, 2935, 1697, 1665, 1497, 1456, 1404, 1368. \(^1\)H NMR (CDCl\(_3\)): \( \delta \) 7.33 – 7.19 (m, 10H), 3.55 – 3.31 (m, 2H), 3.13 (d, \( J = 13.7 \) Hz), 2.93 (d, \( J = 14.0 \) Hz), 2.69 (s, 3H), 1.80 – 1.70 (m, 2H), 1.47 (s, 9H). \(^{13}\)C NMR (CDCl\(_3\)): \( \delta \) 181.2, 155.9, 136.8, 130.2, 128.2, 126.8, 80.1, 50.3, 44.8 & 43.9 (rotamers), 42.1, 43.7, 30.6 & 29.4 (rotamers), 28.5. HRMS: calc’d \([M]^+ \) (C\(_{24}\)H\(_{31}\)NO\(_4\)): 397.2253. Found: (EI) 397.2241.

**Synthesis of acid 12d.** The same procedure described above for the preparation of compound 9a was followed except that 11d was used as a starting material. The product was purified by column chromatography (85:15 cyclohexane:EtOAc) to provide 12d (0.095 g, 88%) as a thick, colorless oil. \( \nu_{\text{max}} / \text{cm}^{-1} \) 3470, 2975, 2876, 1698, 1674, 1468, 1454, 1403, 1368. \(^1\)H NMR (CDCl\(_3\)): \( \delta \) 3.30 – 3.13 (m, 2H), 2.83 (s, 3H), 2.22 – 2.10 (m, 2H), 1.92 – 1.80 (m, 2H), 1.76 – 1.63 (m, 4H), 1.62 – 1.50 (m, 2H), 1.45 (s, 9H). \(^{13}\)C NMR (CDCl\(_3\)): \( \delta \) 182.4, 155.5, 79.3, 51.7, 46.2 & 45.7 (rotamers), 36.4, 36.1, 34.0, 28.3, 24.9. HRMS: calc’d \([M]^+ \) (C\(_{14}\)H\(_{25}\)NO\(_4\)): 271.1784. Found: (EI) 271.1776.

**Synthesis of phenyl ester 13b.** The same procedure described above for the preparation of compound 13a was followed except that 12b was used as a starting material. The product was purified by column chromatography (97:3 cyclohexane:EtOAc) to provide 13b (0.085 g, 74%) as a colorless oil. \( \nu_{\text{max}} / \text{cm}^{-1} \) 3080, 2979, 2934, 1752, 1697, 1642, 1594, 1494, 1457, 1396, 1367. \(^1\)H NMR (CDCl\(_3\)): \( \delta \) 7.38 (t, \( J = 7.4 \) Hz, 2H), 7.23 (t, \( J = 7.4 \) Hz, 1H), 7.06 (br d, \( J = 7.4 \) Hz, 2H), 5.94 – 5.78 (m, 2H), 5.26 – 5.16 (m, 4H), 3.42 – 3.26 (m, 2H), 2.86 (s, 3H), 2.52 (d, \( J = 7.8 \) Hz, 4H), 1.98 – 1.87 (m, 2H), 1.47 (s, 9H). \(^{13}\)C NMR (CDCl\(_3\)): \( \delta \) 174.0, 155.5, 150.7, 132.8, 129.4,
125.8, 121.6, 119.1, 79.6, 48.0, 44.7 & 44.3 (rotamers), 39.1, 34.1, 32.2 & 31.9 (rotamers), 28.5.
HRMS: calc’d [M]+ (C_{22}H_{31}NO_{4}): 373.2253. Found: (EI) 373.2267.

**Synthesis of phenyl ester 13c.** The same procedure described above for the preparation of compound 13a was followed except that 12c was used as a starting material. The product was purified by column chromatography (97:3 cyclohexane:EtOAc) to provide 13c (0.092 g, 60%) as a colorless oil. ν_{max}/cm^{-1} 3091, 3066, 3032, 2980, 2934, 2874, 1750, 1693, 1594, 1495, 1456, 1398, 1367. ¹H NMR (CDCl₃): δ 7.44 – 7.26 (m, 12H), 7.23 (t, J = 7.4 Hz, 1H), 6.88 (d, J = 7.4 Hz), 3.66 – 3.44 (m, 2H), 3.28 (d, J = 13.7 Hz, 2H), 3.05 (d, J = 14.0 Hz, 2H), 2.73 (s, 3H), 2.02 – 1.86 (m, 2H), 1.49 (s, 9H). ¹³C NMR (CDCl₃): δ 173.9, 155.5, 150.5, 136.8, 130.3, 129.3, 128.3, 126.9, 125.8, 121.4, 79.6, 50.8, 44.7 & 43.7 (rotamers), 42.3, 36.7, 30.5 & 29.5 (rotamers), 28.5. HRMS: calc’d [M]+ (C_{30}H_{35}NO_{4}): 473.2566. Found: (EI) 473.2557.

**Synthesis of phenyl ester 13d.** The same procedure described above for the preparation of compound 13a was followed except that 12d was used as a starting material. The product was purified by column chromatography (98:2 cyclohexane:EtOAc → 97:3 cyclohexane:EtOAc) to provide 13d (0.135 g, 76%) as a colorless oil. ν_{max}/cm^{-1} 3103, 3095, 3047, 2974, 2934, 2878, 1750, 1699, 1597, 1494, 1458, 1399, 1367. ¹H NMR (CDCl₃): δ 7.38 (t, J = 7.8 Hz, 2H), 7.22 (t, J = 7.4 Hz, 1H), 7.07 (br d, J = 7.4 Hz, 2H), 3.38 – 3.24 (m, 2H), 2.87 (s, 3H), 2.38 – 2.26 (m, 2H), 2.00 (br t, J = 7.8 Hz, 2H), 1.83 – 1.60 (m, 6H), 1.46 (s, 9H). ¹³C NMR (CDCl₃): δ 175.8, 155.5, 150.9, 129.3, 125.6, 121.4, 79.4, 52.3, 46.3 & 45.9 (rotamers), 36.6 & 36.2 (rotamers), 36.4, 34.2, 28.4, 25.0. HRMS: calc’d [M+H]+ (C_{20}H_{30}NO_{4}): 348.2169. Found: (EI) 348.2169.
Synthesis of phenyl ester 17b. The same procedure described above for the preparation of compound 17a was followed except that 16b was used as a starting material. The product was purified by column chromatography (93:7 cyclohexane:EtOAc) to provide 17b (0.096 g, 58%) as a colorless oil. $\nu_{\text{max}}/\text{cm}^{-1}$ 3120, 3084, 3024, 3008, 2982, 2938, 2898, 1778, 1747, 1698, 1593, 1493, 1476, 1396, 1369. $^1$H NMR (CDCl$_3$): $\delta$ 7.38 (t, $J = 7.8$ Hz, 2H), 7.23 (t, $J = 7.4$ Hz, 1H), 7.11 (d, $J = 7.8$ Hz, 2H), 5.05 (dd, $J = 4.3$ & 8.6 Hz, 1H), 3.64 – 3.48 (m, 1H), 3.43 – 3.29 (m, 1H), 2.89 (s, 3H), 2.38 – 2.13 (m, 2H), 1.51 (s, 9H), 1.46 (s, 9H). $^{13}$C NMR (CDCl$_3$): $\delta$ 168.7, 155.6, 152.8, 150.2, 129.5, 126.1, 121.2, 83.3, 79.8, 72.2, 45.0, 34.5, 29.7, 28.4, 27.7. HRMS: calc’d [M+H]$^+$ (C$_{21}$H$_{31}$NO$_7$): 410.2173. Found: (EI) 410.2173.
Figure S1. $^1$H NMR Spectrum of Compound 5 (400 MHz, CDCl$_3$)

Figure S2. $^1$H NMR Spectrum of Compound 6a (400 MHz, CDCl$_3$)
Figure S3. $^1$H NMR Spectrum of Compound 6b (400 MHz, CDCl$_3$)

Figure S4. $^1$H NMR Spectrum of Compound 7a (400 MHz, CDCl$_3$)
Figure S5. $^1$H NMR Spectrum of Compound 7b (400 MHz, CDCl$_3$)

Figure S6. $^1$H NMR Spectrum of Compound 8a (400 MHz, CDCl$_3$)
**Figure S7.** $^1$H NMR Spectrum of Compound 8b (400 MHz, CDCl$_3$)

**Figure S8.** $^1$H NMR Spectrum of Compound 8c (400 MHz, CDCl$_3$)
Figure S9. $^1$H NMR Spectrum of Compound 9a (400 MHz, CDCl$_3$)

Figure S10. $^1$H NMR Spectrum of Compound 9b (400 MHz, CDCl$_3$)
Figure S11. $^1$H NMR Spectrum of Compound 9c (400 MHz, CDCl$_3$)

Figure S12. $^1$H NMR Spectrum of Compound 10a (400 MHz, CDCl$_3$)
Figure S13. $^1$H NMR Spectrum of Compound 10b (400 MHz, CDCl$_3$)

Figure S14. $^1$H NMR Spectrum of Compound 10c (400 MHz, CDCl$_3$)
Figure S15. $^1$H NMR Spectrum of Compound 11a (400 MHz, CDCl$_3$)

Figure S16. $^1$H NMR Spectrum of Compound 11b (400 MHz, CDCl$_3$)
**Figure S17.** $^1$H NMR Spectrum of Compound 11c (400 MHz, CDCl$_3$)

**Figure S18.** $^1$H NMR Spectrum of Compound 11d (400 MHz, CDCl$_3$)
Figure S19. $^1$H NMR Spectrum of Compound 12a (400 MHz, CDCl$_3$)

Figure S20. $^1$H NMR Spectrum of Compound 12b (400 MHz, CDCl$_3$)
Figure S21. $^1$H NMR Spectrum of Compound 12c (400 MHz, CDCl$_3$)

Figure S22. $^1$H NMR Spectrum of Compound 12d (400 MHz, CDCl$_3$)
Figure S23. $^1$H NMR Spectrum of Compound 13a (400 MHz, CDCl$_3$)

Figure S24. $^1$H NMR Spectrum of Compound 13b (400 MHz, CDCl$_3$)
Figure S25. $^1$H NMR Spectrum of Compound 13c (400 MHz, CDCl$_3$)

Figure S26. $^1$H NMR Spectrum of Compound 13d (400 MHz, CDCl$_3$)
Figure S27. $^1$H NMR Spectrum of Compound 15 (400 MHz, CDCl$_3$)

Figure S28. $^1$H NMR Spectrum of Compound 16a (400 MHz, CDCl$_3$)
Figure S29. $^1$H NMR Spectrum of Compound 16b (400 MHz, CDCl$_3$)

Figure S30. $^1$H NMR Spectrum of Compound 17a (400 MHz, CDCl$_3$)
Figure S31. $^1$H NMR Spectrum of Compound 17b (400 MHz, CDCl$_3$)

Figure S32. $^{13}$C NMR Spectrum of Compound 5 (100 MHz, CDCl$_3$)
Figure S33. $^{13}$C NMR Spectrum of Compound 6a (100 MHz, CDCl$_3$)

Figure S34. $^{13}$C NMR Spectrum of Compound 6b (100 MHz, CDCl$_3$)
Figure S35. $^{13}$C NMR Spectrum of Compound 7a (100 MHz, CDCl$_3$)

Figure S36. $^{13}$C NMR Spectrum of Compound 7b (100 MHz, CDCl$_3$)
Figure S37. $^{13}$C NMR Spectrum of Compound 8a (100 MHz, CDCl$_3$)

Figure S38. $^{13}$C NMR Spectrum of Compound 8b (100 MHz, CDCl$_3$)
Figure S39. $^{13}$C NMR Spectrum of Compound 8c (100 MHz, CDCl$_3$)

Figure S40. $^{13}$C NMR Spectrum of Compound 9a (100 MHz, CDCl$_3$)
Figure S41. $^{13}$C NMR Spectrum of Compound 9b (100 MHz, CDCl₃)

Figure S42. $^{13}$C NMR Spectrum of Compound 9c (100 MHz, CDCl₃)
Figure S43. $^{13}$C NMR Spectrum of Compound 10a (100 MHz, CDCl$_3$)

Figure S44. $^{13}$C NMR Spectrum of Compound 10b (100 MHz, CDCl$_3$)
Figure S45. $^{13}$C NMR Spectrum of Compound 10c (100 MHz, CDCl$_3$)

Figure S46. $^{13}$C NMR Spectrum of Compound 11a (100 MHz, CDCl$_3$)
Figure S47. $^{13}$C NMR Spectrum of Compound 11b (100 MHz, CDCl$_3$)

Figure S48. $^{13}$C NMR Spectrum of Compound 11c (100 MHz, CDCl$_3$)
Figure S49. $^{13}$C NMR Spectrum of Compound 11d (100 MHz, CDCl$_3$)

Figure S50. $^{13}$C NMR Spectrum of Compound 12a (100 MHz, CDCl$_3$)
Figure S51. $^{13}$C NMR Spectrum of Compound 12b (100 MHz, CDCl$_3$)

Figure S52. $^{13}$C NMR Spectrum of Compound 12c (100 MHz, CDCl$_3$)
Figure S53. $^{13}$C NMR Spectrum of Compound 12d (100 MHz, CDCl$_3$)

Figure S54. $^{13}$C NMR Spectrum of Compound 13a (100 MHz, CDCl$_3$)
Figure S55. $^{13}$C NMR Spectrum of Compound 13b (100 MHz, CDCl$_3$)

Figure S56. $^{13}$C NMR Spectrum of Compound 13c (100 MHz, CDCl$_3$)
**Figure S57.** $^{13}$C NMR Spectrum of Compound 13d (100 MHz, CDCl$_3$)

**Figure S58.** $^{13}$C NMR Spectrum of Compound 15 (100 MHz, CDCl$_3$)
Figure S59. $^{13}$C NMR Spectrum of Compound 16a (100 MHz, CDCl$_3$)

Figure S60. $^{13}$C NMR Spectrum of Compound 16b (100 MHz, CDCl$_3$)
Figure S61. $^{13}$C NMR Spectrum of Compound 17a (100 MHz, CDCl$_3$)

Figure S62. $^{13}$C NMR Spectrum of Compound 17b (100 MHz, CDCl$_3$)
Figure S63. $^1$H NMR Spectrum of 3a·TFA (400 MHz, CDCl$_3$)

Figure 64. $^1$H NMR Spectrum of 18a (400 MHz, CDCl$_3$). HRMS calc’d [M]$^+$ (C$_4$H$_7$NO): 85.0528. Found: (EI) 85.0530.

Figure S65. $^1$H NMR Spectrum of 3b·TFA (400 MHz, CDCl$_3$)
Figure S66. $^1$H NMR Spectrum of a) Commercial NMP and b) 18b (400 MHz, CDCl$_3$). HRMS calc’d [M$^+$] (C$\text{$_5$}$H$_9$NO): 99.0684. Found: (EI) 99.0681.

Figure S67. $^1$H NMR Spectrum of 3c-TFA (400 MHz, CDCl$_3$). Upon addition of H$_2$O immediately prior to freeze drying, some material cyclized to form 18c and PhOH.
Figure S68. $^1$H NMR Spectrum of 18c (400 MHz, CDCl$_3$). HRMS calc’d [M]$^+$ (C$_6$H$_{11}$NO): 113.0841. Found: (EI) 113.0841.

Figure S69. $^1$H NMR Spectrum of 3d·TFA (400 MHz, CDCl$_3$)

Figure S70. $^1$H NMR Spectrum of 18d (400 MHz, CDCl$_3$). HRMS calc’d [M+H]$^+$ (C$_8$H$_{14}$NO)$^+$: 140.1070. Found: (EI) 140.1079.
Figure S71. $^1$H NMR Spectrum of 3e⋅TFA (400 MHz, CDCl$_3$)

Figure S72. $^1$H NMR Spectrum of 18e (400 MHz, CDCl$_3$). HRMS calc’d [M]$^+$ ($C_{12}H_{15}NO$): 189.1154. Found: (EI) 181.1156.

Figure S73. $^1$H NMR Spectrum of 3f⋅TFA (400 MHz, CDCl$_3$)
Figure S74. $^1$H NMR Spectrum of 18f (400 MHz, CDCl$_3$). HRMS calc’d [M+H]$^+$ (C$_7$H$_{14}$NO): 128.1070. Found: (EI) 128.1079.

Figure S75. $^1$H NMR Spectrum of 3g $\cdots$ TFA (400 MHz, CDCl$_3$)

Figure S76. $^1$H NMR Spectrum of 18g (400 MHz, CDCl$_3$). HRMS calc’d [M]$^+$ (C$_{11}$H$_{17}$NO): 179.1310. Found: (EI) 179.1308.
Figure S77. $^1$H NMR Spectrum of 3h·TFA (400 MHz, CDCl$_3$)

Figure S78. $^1$H NMR Spectrum of 18h (400 MHz, CDCl$_3$). HRMS calc’d [M]$^+$ (C$_{19}$H$_{21}$NO): 279.1623. Found: (EI) 279.1623.

Figure S79. $^1$H NMR Spectrum of 3i·TFA (400 MHz, CDCl$_3$)
Figure S80. $^1$H NMR Spectrum of $^{18i}$ (400 MHz, CDCl$_3$). HRMS calc’d [M]$^+$ (C$_9$H$_{15}$NO): 153.1154. Found: (EI) 153.1156.

Figure S81. $^1$H NMR Spectrum of $^{3j} \cdot$TFA (400 MHz, Acetone-$d_6$)

Figure S82. $^1$H NMR Spectrum of $^{18j}$ (400 MHz, Acetone-$d_6$). HRMS calc’d [M]$^+$ (C$_4$H$_7$NO$_2$): 101.0477. Found: (EI) 101.0479.
Figure S83. $^1$H NMR Spectrum of 3k TFA (400 MHz, Acetone-$d_6$). Upon addition of H$_2$O immediately prior to freeze drying, some material cyclized to form 18k and PhOH.

Figure S84. $^1$H NMR Spectrum of 18k (400 MHz, Acetone-$d_6$). HRMS calc’d [M]$^+$ (C$_5$H$_9$NO$_2$): 115.0633. Found: (EI) 115.0633.
Figure S85. Cyclization kinetics for compounds 3a and 3b.

Figure 86. Determination of first order rate constant by ln[A]₀/[A] vs t graph for compounds 3a and 3b.
Figure S87. Cyclization kinetics for compounds 3c, 3d, and 3e.

Figure 88. Determination of first order rate constant by ln[A]₀/[A] vs t graph for compounds 3c, 3d, and 3e.
Figure S89. Cyclization kinetics for compounds 3f, 3g, 3h, and 3i.

Figure 90. Determination of first order rate constant by ln[A]₀/[A] vs t graph for compounds 3f, 3g, and 3i.
Figure 91. Determination of first order rate constant by $\ln[A_0]/[A]$ vs t graph for compound 3h.

Figure S92. Cyclization kinetics for compounds 3j and 3k.
Figure 93. Determination of first order rate constant by ln[A]₀/[A] vs t graph for compounds 3j and 3k.

Figure S94. Cyclization rate of 3i at pH 7.0 and 6.0.
Figure 95. Determination of first order rate constant by $\ln[A]/[A]$ vs $t$ graph for compounds 3i at pH 7.0 and 6.0.

Figure 96. Cyclization of 3i and pH 5.0 and 4.0.
Figure 97. Determination of first order rate constant by ln[A]₀/[A] vs t graph for compounds 3i at pH 5.0 and 4.0.

Figure S98. pH dependence of the cyclization rate of 3i.