Triphenylphosphine catalyzed novel one-pot multicomponent synthesis of functionalized β -acetamido carbonyl compounds

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Full experimental detail

Benzaldehydes **1** (1.1mmol) was allowed to react with ethyl acetoacetate/ enolizable ketones or β -keto esters **2** (1 mmol) and acetyl chloride **3** (1.5 mmol) in the presence of PPh₃ (10 mol%) in acetonitrile (3 mL) at room temperature. The progress of reaction was monitored by TLC. The corresponding β -acetamido ketones **4** were obtained after 5-7 h in 74-94% yield. The mixture was extracted with ethyl acetate (3×10ml), washed with water (3×10ml), dried over Na₂SO₄. Then the solvent was removed in vacuo and the crude product was recrystallized from ethyl acetate-hexane to afford product. The product was characterized by NMR and mass spectroscopy. Syn/anti ratio of product was established by ¹H NMR studies. The spectral data of all the compounds match fairly with that reported in literature (references 14, 20, 24(d) and 25 of main text).

Melting points, ¹H NMR, ¹³C NMR and HRMS data

Compound 4a: mp 104–106 °C. ¹H NMR (500 MHz, CDCl₃): δ 7.83 (2H, d, J=7.4 Hz), 7.46 (1H, d, J=7.4 Hz), 7.37 (2H, t, J=7.8 Hz), 7.11–7.27 (5H, m), 6.77 (1H, d, J=7.5 Hz), 5.48 (1H, m), 3.64 (1H, dd, J=5.3 Hz, 11.5 Hz), 3.35 (1H, dd, J=6.1 Hz, 10.7 Hz), 1.93 (3H, s). ¹³C NMR (125 MHz, CDCl₃): δ 198.9, 169.7, 141.3, 136.8, 133.8, 128.9, 128.5, 127.7, 126.8, 50.3, 43.5, 23.6. HRMS (ESI): ([M]⁺): Calcd for C₁₇H₁₇NO₂: 267.126; Found: 267.126.

Compound 4b: mp 111–115 °C. ¹H NMR (500 MHz, CDCl₃): δ 7.90 (2H, t, J=7.2 Hz), 7.54 (1H, t, J=7.4 Hz), 7.46 (2H, t, J=7.9 Hz), 7.20 (2H, d, J=8.1 Hz), 7.11 (2H, d, J=8.4 Hz), 6.76 (1H, d, J=7.4 Hz), 5.49 (1H, m), 3.74 (1H, dd, J=5.3 Hz, 11.5 Hz), 3.42 (1H, dd, J=6.3 Hz, 10.5 Hz), 2.29 (3H, s), 2.02 (3H, s). ¹³C NMR (125 MHz, CDCl₃): δ 198.9, 169.7, 138.3, 137.3, 136.8, 133.8, 129.5, 128.9, 128.1, 126.6, 50.0, 43.3, 23.6, 21.2. HRMS (ESI): ([M]⁺): Calcd for C₁₈H₁₉NO₂: 281.142; Found: 281.140.

Compound 4c: mp 110–113 °C. ¹H NMR (500 MHz, CDCl₃): δ 7.92 (2H, d, J=7.3 Hz), 7.58 (1H, t, J=7.3 Hz), 7.44 (2H, t, J=8.2 Hz), 7.30–7.46 (2H, m), 6.94–7.00 (2H, m), 6.74 (1H, d, J=7.5 Hz), 5.53 (1H, m), 3.72 (1H, dd, J=5.0 Hz, 12.0 Hz), 3.44 (1H, dd, J=6.0 Hz, 10.9 Hz), 2.07 (3H, s), 2.00 (3H, s). ¹³C NMR (125 MHz, CDCl₃): δ 198.8, 169.7, 163.0, 161.2, 137.2, 136.8, 133.7, 129.0, 128.6, 115.8, 49.7, 43.3, 29.9, 23.5. HRMS (ESI): ([M]⁺): Calcd for C₁₇H₁₆FNO₂: 285.117; Found: 285.119.

Compound 4d: mp 145–148 °C. ¹H NMR (500 MHz, CDCl₃): δ 7.83 (2H, d, J=7.3 Hz), 7.52 (1H, t, J=6.5 Hz), 7.36 (2H, t, J=8.0 Hz), 7.16–7.19 (4H, m), 6.71 (1H, d, J=7.2 Hz), 5.48 (1H, m), 3.65 (1H, dd, J=5.0 Hz, 12.2 Hz), 3.37 (1H, dd, J=6.4 Hz, 11.3 Hz), 1.94 (3H, s). ¹³C NMR (125 MHz, CDCl₃): δ 198.9, 169.7, 139.7, 136.5, 134.2, 133.4, 129.2, 129.0, 128.5, 128.0, 49.5, 43.0, 23.7. HRMS (ESI): ([M]⁺): Calcd for C₁₇H₁₆ClNO₂: 321.087; Found: 321.085.

Compound 4e: mp 145–148 °C. ¹H NMR (500 MHz, CDCl₃): δ 7.82 (2H, d, J=7.2 Hz), 7.52 (1H, t, J=7.3 Hz), 7.46 (2H, t, J=8.0 Hz), 7.37 (2H, d, J=8.3 Hz), 7.20 (2H, d, J=8.4 Hz), 6.72 (1H, d, J=7.0 Hz), 5.48 (1H, m), 3.70 (1H, dd, J=5.3 Hz, 16.0 Hz), 3.43 (1H, dd, J=6.2 Hz, 16.8 Hz), 2.01 (3H, s). ¹³C NMR (125 MHz, CDCl₃): δ 196.7, 166.7, 140.0, 136.6, 134.0, 131.6, 129.3, 129.0, 128.0, 128.3, 49.6, 43.0, 23.9. HRMS (ESI): ([M]⁺): Calcd for C₁₇H₁₆BrNO₂: 345.036; Found: 345.038.

Compound 4f: mp 110–112 °C. ¹H NMR (500 MHz, CDCl₃): δ 7.93 (2H, d, J=7.2 Hz), 7.53 (1H, d, J=7.4 Hz), 7.47 (2H, t, J=7.9 Hz), 7.23 (2H, t, J=5.1 Hz), 6.80 (2H, t, J=7.4 Hz), 5.53 (1H, m), 3.75 (3H, s), 3.71 (1H, dd, J=5.3 Hz, 11.5 Hz), 3.40 (1H, dd, J=6.5 Hz, 10.3 Hz), 1.97 (3H, s). ¹³C NMR (125 MHz, CDCl₃): δ 199.0, 169.4, 159.0, 136.4, 133.6, 133.0, 128.9, 128.5, 127.8, 114.3, 55.5, 49.6, 43.5, 23.8. HRMS (ESI): ([M]⁺): Calcd for C₁₈H₁₉NO₃: 297.136; Found: 297.135.

Compound 4g: mp 190–193 °C. ^1H NMR (500 MHz, CDCl_3): δ 7.96 (1H, d, $J=6.8$), 7.90 (2H, d, $J=7.2$ Hz), 7.73 (1H, d, $J=8.0$ Hz), 7.57 (2H, t, $J=7.6$ Hz), 7.44 (2H, t, $J=8.0$ Hz), 7.39 (1H, t, $J=8.0$ Hz), 7.05 (1H, d, $J=5.6$ Hz), 5.91–5.99 (1H, m), 3.71 (1H, dd, $J=6.4$, 17.2 Hz), 3.65 (1H, dd, $J=5.6$, 16.8 Hz), 2.02 (3H, s); ^{13}C NMR (125 MHz, CDCl_3) 198.7, 169.3, 148.7, 137.3, 136.5, 134.3, 133.7, 130.1, 129.2, 128.6, 128.7, 125.3, 47.5, 42.4, 23.7. HRMS (ESI): ($[\text{M}]^+$): Calcd for $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}_4$: 312.111; Found: 312.110.

Compound 4h: mp 137–140 °C. ^1H NMR (500 MHz, CDCl_3) 8.19 (1H, s), 8.04 (1H, d, $J=6.8$ Hz), 7.85 (2H, d, $J=7.6$ Hz), 7.68 (1H, d, $J=7.6$ Hz), 7.55 (1H, t, $J=7.6$ Hz), 7.40–7.47 (3H, m), 6.93 (1H, d, $J=7.6$ Hz), 5.60–5.67 (1H, m), 3.77 (1H, dd, $J=5.2$, 17.6 Hz), 3.51 (1H, dd, $J=5.6$, 17.6 Hz), 2.06 (3H, s); ^{13}C NMR (125 MHz, CDCl_3) 198.1, 169.9, 143.5, 136.4, 134.0, 133.1, 130.6, 129.8, 129.1, 128.5, 122.6, 121.3, 49.3, 42.7, 23.6. HRMS (ESI): ($[\text{M}]^+$): Calcd for $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}_4$: 312.111; Found: 312.114.

Compound 4i: mp 131–133 °C. ^1H NMR (500 MHz, CDCl_3): ^1H NMR 7.14–7.27 (5H, m), 7.05 (1H, d, $J=8.5$ Hz), 5.76 (1H, dd, $J=5.0$ Hz, 9.3 Hz), 4.25 (1H, d, $J=5.5$ Hz), 2.19 (3H, s), 2.02 (3H, s), 1.93 (3H, s). ^{13}C NMR (125 MHz, CDCl_3): δ 205.2, 202.6, 169.7, 139.5, 129.2, 128.0, 126.8, 126.5, 70.5, 52.3, 31.2, 30.3, 23.5. HRMS (ESI): ($[\text{M}]^+$): Calcd for $\text{C}_{14}\text{H}_{17}\text{NO}_3$: 247.121; Found: 247.119.

Compound 4j: mp 149–152 °C. ^1H NMR (500 MHz, CDCl_3): δ 7.17 (2H, d, $J=8.3$ Hz), 7.06 (2H, d, $J=8.2$ Hz), 5.83 (1H, dd, $J=6.5$ Hz, 2.7 Hz), 4.26 (1H, d, $J=6.3$ Hz), 2.27 (3H, s), 2.20 (3H, s), 2.12 (3H, s), 1.95 (3H, s). ^{13}C NMR (125 MHz, CDCl_3): δ 205.5, 202.8, 169.7, 137.6, 136.4, 129.8, 126.4, 71.2, 52.0, 31.2, 30.0, 23.2, 21.2. HRMS (ESI): ($[\text{M}]^+$): Calcd for $\text{C}_{15}\text{H}_{19}\text{NO}_3$: 261.136; Found: 261.138.

Compound 4k: mp 136–139 °C. ^1H NMR (500 MHz, CDCl_3): δ 7.16–7.20 (2H, m), 7.15 (2H, d, $J=9.1$ Hz), 6.92–6.96 (2H, m), 5.72 (1H, dd, $J=6.5$ Hz, 2.7 Hz), 4.23 (1H, d, $J=6.4$ Hz), 2.17 (3H, s), 2.02 (3H, s), 1.87 (3H, s). ^{13}C NMR (125 MHz, CDCl_3): δ 205.3, 202.5, 169.7, 163.5, 161.3, 135.6, 128.4, 115.7, 71.0, 51.6, 30.7, 30.2, 23.4. HRMS (ESI): ($[\text{M}]^+$): Calcd for $\text{C}_{14}\text{H}_{16}\text{FNO}_3$: 265.111; Found: 265.111.

Compound 4l: mp 165–168 °C. ^1H NMR (500 MHz, CDCl_3): δ 7.30 (2H, d, $J=8.4$ Hz), 7.20 (2H, d, $J=8.4$ Hz), 7.06 (2H, d, $J=8.2$ Hz), 5.80 (1H, dd, $J=6.5$ Hz, 2.7 Hz), 4.28 (1H, d, $J=5.6$ Hz), 2.26 (3H, s), 2.12 (3H, s), 2.00 (3H, s). ^{13}C NMR (125 MHz, CDCl_3): δ 205.5, 202.3, 170.0, 138.3, 133.9, 129.0, 128.3, 70.2, 51.5, 31.2, 30.3, 23.7. HRMS (ESI): ($[\text{M}]^+$): Calcd for $\text{C}_{14}\text{H}_{16}\text{ClNO}_3$: 281.082; Found: 281.080.

Compound 4m: mp 146–149 °C. ^1H NMR (500 MHz, CDCl_3): δ 7.32 (2H, d, $J=8.4$ Hz), 7.20 (2H, d, $J=8.4$ Hz), 7.04 (2H, d, $J=8.2$ Hz), 5.80 (1H, dd, $J=6.5$ Hz, 2.7 Hz), 4.28 (1H, d, $J=5.6$ Hz), 3.76 (3H, s), 2.26 (3H, s), 2.12 (3H, s), 2.02 (3H, s). ^{13}C NMR (125 MHz, CDCl_3): δ 205.1, 202.3, 170.0, 138.3, 133.7, 129.2, 128.3, 70.4, 51.7, 31.4, 30.1, 23.7. HRMS (ESI): ($[\text{M}]^+$): Calcd for $\text{C}_{15}\text{H}_{19}\text{NO}_4$: 277.131; Found: 277.133.

Compound 4n: mp 106–109 °C. Data for major isomer (anti): ^1H NMR (500 MHz, CDCl_3): δ 7.14–7.23 (5H, m), 7.03 (1H, d, $J=8.0$ Hz), 5.64 (1H, dd, $J=6.3$ Hz, 3.3 Hz), 4.06 (2H, q, $J=3.6$ Hz), 4.07 (1H, d, $J=6.8$ Hz), 2.11 (3H, s), 1.93 (3H, s), 1.13 (3H, t, $J=7.1$ Hz). ^{13}C NMR (125

MHz, CDCl₃): δ 204.2, 169.5, 167.6, 139.2, 128.8, 127.7, 126.7, 63.3, 62.1, 52.4, 30.6, 23.5, 14.3. HRMS (ESI): ([M]⁺): Calcd for C₁₅H₁₉NO₄: 277.131; Found: 377.130.

Compound 4o: mp 97–100 °C. Data for major isomer(anti): ¹H NMR(500 MHz, CDCl₃): δ 7.08 (2H, d, J=8.5 Hz), 7.03 (2H, d, J=8.5 Hz), 5.62 (1H, dd, J=6.7 Hz, 2.5 Hz), 4.05 (2H, q, J=3.7 Hz), 3.97 (1H, d, J=6.7 Hz), 2.24 (3H, s), 2.12 (3H, s), 1.88 (3H, s), 1.09 (3H, t, J=7.0 Hz). ¹³C NMR (125 MHz, CDCl₃): δ 204.2, 169.9, 167.6, 137.4, 136.6, 129.5, 126.0, 63.9, 62.2, 52.3, 30.4, 23.4, 21.3, 14.1. HRMS (ESI): ([M]⁺): Calcd for C₁₆H₂₁NO₄: 291.147; Found: 291.146.

Compound 4p: mp 100–103 °C. Data for major isomer (anti): ¹H NMR (500 MHz, CDCl₃): δ 8.41 (1H, d, J 8.9 Hz), 7.31–7.37 (2H, m), 7.11–7.14 (2H, m), 5.45 (1H, dd, J=9.1 Hz, 2.4 Hz), 4.06 (1H, d, J=11.2 Hz), 3.85 (2H, q, J=7.1 Hz), 2.52 (3H, s), 1.76 (3H, s), 0.90 (3H, t, J=7.1 Hz). ¹³C NMR (125 MHz, CDCl₃): δ 202.4, 169.5, 168.1, 161.4, 137.7, 130.2, 116.0, 65.9, 62.2, 52.5, 30.7, 23.5, 14.7. HRMS (ESI): ([M]⁺): Calcd for C₁₅H₁₈FNO₄: 295.122; Found: 295.122.

Compound 4q: mp 104–107 °C. Data for major isomer (anti): ¹H NMR (500 MHz, CDCl₃): δ 7.16–7.19 (4H, m), 5.41 (1H, dd, J=6.9 Hz, 1.9 Hz), 4.08 (2H, q, J=2.7 Hz), 3.96 (1H, d, J=6.7 Hz), 2.13 (3H, s), 1.87 (3H, s), 1.11 (3H, t, J=7.2 Hz). ¹³C NMR (125 MHz, CDCl₃): δ 203.8, 170.2, 167.1, 138.3, 133.7, 129.0, 127.7, 63.2, 61.6, 51.9, 30.1, 23.3, 14.1. HRMS (ESI): ([M]⁺): Calcd for C₁₅H₁₈ClNO₄: 311.092; Found: 311.090.

Compound 4r: mp 104–106 °C. Data for major isomer (anti): ¹H NMR (500 MHz, CDCl₃): δ 7.22 (2H, d, J=3.4 Hz), 6.82 (2H, d, J=1.5 Hz), 5.64 (1H, dd, J=6.7 Hz, 2.3 Hz), 4.10 (2H, q, J=2.9 Hz), 4.04 (1H, d, J=6.6 Hz), 3.78 (3H, s), 2.15 (3H, s), 1.93 (3H, s), 1.13 (3H, t, J=7.1 Hz). ¹³C NMR (125 MHz, CDCl₃): δ 204.3, 169.6, 167.7, 159.5, 131.6, 128.2, 114.3, 63.7, 62.2, 55.6, 52.3, 30.6, 23.5, 14.1. HRMS (ESI): ([M]⁺): Calcd for C₁₆H₂₁NO₅: 307.142; Found: 307.142.