Diamine–Mediated Degradative Dimerisation of Morita–Baylis–Hillman Ketones

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General

The aldehydes and diamine used in the study were purchased from Sigma-Aldrich. Ethylenediamine was distilled prior to use. Anhydrous ethylenediamine was prepared following a literature protocol.¹ Solvents were distilled for the reactions. IBX was synthesised from 2-iodobenzoic acid following a literature protocol.² Synthesis of Morita-Baylis-Hillman adducts and their oxidation were performed using reported protocols.³ Silica gel (100-200 mesh) and other common reagents were procured from local suppliers. Proton and carbon nuclear magnetic resonance spectra were recorded on a Bruker Avance 500 MHz and 400 MHz NMR spectrometer. Elemental analysis was recorded on Thermo Finnigan FLASH EA 1112. High resolution mass spectral analysis (HRMS) was performed on a XEVO G2-S QT instrument of Waters Corporation, USA.

Experimental Section

General procedure for the synthesis of methylene-bridged bis-1,3-dicarbonyl compounds:

MBH ketone 1 (0.5 mmol) was dissolved in dioxane (500 µL) followed by the addition of ethylene-1,2-diamine (2c, 0.6 mmol) to the reaction flask. The resulting reaction mixture was allowed to stir at room temperature for the time mentioned in Table 2 of the manuscript for the respective adducts. The crude residue was directly subjected to the silica gel chromatography (EtOAc: petroleum ether) to obtain pure 3 (as a mixture of two diastereomers; ratio mentioned for each adduct in the tabulation section below).

One pot protocol for the synthesis of dimethyl 2,4-dibenzoylpentanedioate (3a) from Morita-Baylis-Hillman adduct 4:

MBH adduct 4 (96 mg, 0.5 mmol) was dissolved in CH₂CN (4 mL) followed by the addition IBX (210 mg, 0.75 mmol). The resulting mixture was allowed to stir at 80 °C and the progress of the reaction was monitored using thin layer chromatography. After 5 h, upon complete consumption of 4, the reaction mixture was cooled to room temperature followed by the addition of ethylene-1, 2-diamine (2c, 40 µL, 0.6 mmol) to the reaction flask. The resulting reaction mixture was allowed to stir at room temperature for 40 min. The reaction mixture was filtered and the solvent was removed under reduced pressure. The crude residue was subjected to the silica gel chromatography (EtOAc: petroleum ether, 2:8) to obtain pure 3a as a white solid; yield (mixture of two diastereomers): 67 mg (73%).
Tabulated data of the synthesised products:

Dimethyl 2,4-dibenzoylpentanedioate (3a):^4

Purified by silica gel chromatography (EtOAc: petroleum ether, 2:8)
Yield: 81 mg (88%); White solid; The ratio of the two diastereomers is 1.4:1; Two diastereomers: \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 2.54-2.79 (m, 2H), 3.62 (s, 2.47H), 3.74 (s, 3.54H), 4.59 (t, \(J = 7.5\) Hz, 0.82H), 4.68 (t, \(J = 7.5\) Hz, 1.14H), 7.44-7.53 (m, 4H), 7.55-7.63 (m, 2H), 8.02-8.09 (m, 4H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 27.80, 28.35, 51.03, 51.28, 52.66, 128.85, 128.88, 128.95, 133.91, 133.93, 135.30, 135.76, 169.80, 170.20, 194.70, 195.09; HRMS (ESI-TOF): m/z [M+Na]\(^+\) calculated for C\(_{21}\)H\(_{20}\)O\(_6\)Na: 391.1152; found 391.1285.

Dimethyl 2,4-bis(4-fluorobenzoyl)pentanedioate (3b):^4

Purified by silica gel chromatography (EtOAc: petroleum ether, 1.5:8.5)
Yield: 95 mg (94%); Light yellow semi-solid; The ratio of the two diastereomers is 2.6:1; Two diastereomers: \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 2.49-2.75 (m, 2H), 3.64 (s, 1.68H), 3.75 (s, 4.32H), 4.53 (t, \(J = 7.5\) Hz, 0.61H), 4.63 (t, \(J = 7.5\) Hz, 1.46H), 7.11-7.21 (m, 4H), 8.05-8.14 (m, 4H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): 27.65, 28.30, 50.96, 51.19, 52.73, 116.09 (d, \(J = 22.0\) Hz), 131.64 (d, \(J = 9.0\) Hz), 131.78 (d, \(J = 10.0\) Hz), 132.15 (d, \(J = 3.0\) Hz), 166.26 (d, \(J = 255.0\) Hz), 169.61, 170.10, 193.09, 193.54.

Dimethyl 2,4-bis(4-chlorobenzoyl)pentanedioate (3c):^4

Purified by silica gel chromatography (EtOAc: petroleum ether, 1.5:8.5)
Yield: 93 mg (85%); White solid; The ratio of the two diastereomers is 1.7:1; Two diastereomers: \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 2.49-2.74 (m, 2H), 3.64 (s, 2.19H), 3.74 (s, 3.81H), 4.51 (t, \(J = 7.5\) Hz, 0.79H), 4.61 (t, \(J = 7.5\) Hz, 1.30 H), 7.42-7.50 (m, 4H), 7.96-8.03 (m, 4H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): 
27.52, 28.15, 50.94, 51.73, 52.79, 129.26, 130.26, 130.37, 133.56, 140.57, 140.62, 169.51, 169.97, 193.47, 193.91.

**Dimethyl 2,4-bis(4-bromobenzoyl)pentanedioate (3d):**

![Chemical Structure](image)

Purified by silica gel chromatography (EtOAc: petroleum ether, 1.5:8.5)
Yield: 111 mg (85%); Light yellow solid; The ratio of the two diastereomers is 1.9:1; **Two diastereomers:**

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 2.49-2.74 (m, 2H) 3.64 (s, 2.09H), 3.74 (s, 3.91H), 4.50 (t, $J = 7.5$ Hz, 0.76H), 4.60 (t, $J = 7.0$ Hz, 1.34H), 7.61-7.66 (m, 4H), 7.87-7.94 (m, 4H); $^{13}$C NMR (125 MHz, CDCl$_3$): 27.49, 28.10, 50.93, 51.10, 52.79, 52.80, 129.38, 129.44, 130.31, 130.42, 132.26, 134.01, 134.45, 169.47, 169.90, 193.67, 194.09.

**Dimethyl 2,4-bis(4-methoxylbenzoyl)pentanedioate (3e):**

![Chemical Structure](image)

Purified by silica gel chromatography (EtOAc: petroleum ether, 2:8)
Yield: 80 mg (74%); light yellow gum; The ratio of the two diastereomers is 1.4:1; **Two diastereomers:**

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 2.49-2.74 (m, 2H) 3.63 (s, 2.47H), 3.74 (s, 3.52H), 3.85 (s, 3.59H), 3.87 (s, 2.51H), 4.52 (t, $J = 7.5$ Hz, 0.83H), 4.60 (t, $J = 7.5$ Hz, 1.15H), 6.93 (d, $J = 8.5$ Hz, 2.38H), 6.96 (d, $J = 9.0$ Hz, 1.75H), 8.04 (d, $J = 8.5$ Hz, 4H); $^{13}$C NMR (125 MHz, CDCl$_3$): 28.06, 28.70, 50.93, 51.08, 52.52, 55.52, 55.54, 114.05, 114.06, 128.31, 128.80, 131.30, 131.40, 164.16, 170.02, 170.46, 193.18, 193.61.

**Dimethyl 2,4-bis(4-methylbenzoyl)pentanedioate (3f):**

![Chemical Structure](image)

Purified by silica gel chromatography (EtOAc: petroleum ether, 1.5:8.5)
Yield: 82 mg (82%); White semi-solid; The ratio of the two diastereomers is 1.6:1; **Two diastereomers:**

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 2.40 (s, 3.74H), 2.42 (s, 2.50H), 2.52-2.76 (m, 2H), 3.63 (s, 2.31H), 3.74 (s, 3.69H), 4.55 (t, $J = 7.5$ Hz, 0.82H), 4.63 (t, $J = 7.5$ Hz, 1.26H), 7.26 (d, $J = 8.0$ Hz, 2.52H), 7.30 (d, $J
= 8.5 Hz, 1.68H), 7.94 (d, J = 8.0 Hz, 4H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): 21.70, 27.90, 28.46, 50.96, 51.22, 52.58, 129.00, 129.09, 129.56, 129.58, 132.87, 133.32, 144.91, 169.94, 170.31, 194.30, 194.70.

**Dimethyl 2,4-bis(4-nitrobenzoyl)pentanedioate (3g):**

![Chemical Structure Image]

Purified by silica gel chromatography (EtOAc: petroleum ether, 2:8)

Yield: 42 mg (37%); yellow gum; The ratio of the two diastereomers is 1.2:1; Two diastereomers: \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 2.54-2.80 (m, 2H), 3.67 (s, 2.79H), 3.78 (s, 3.20H), 4.61 (t, J = 7.0 Hz, 0.94H), 4.72 (t, J = 7.0 Hz, 1.10H), 8.21 (d, J = 9.0 Hz, 1.91H), 8.26 (d, J = 8.5 Hz, 2.25H), 8.34-8.39 (m, 4H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): 27.06, 27.66, 51.24, 51.39, 53.04, 53.05, 124.10, 129.83, 130.00, 139.70, 140.14, 150.78, 150.81, 169.02, 169.50, 193.29, 193.62.; Anal. calculated for C\(_{21}\)H\(_{18}\)N\(_2\)O\(_{10}\): C, 55.03; H, 3.96; N, 6.11; found C, 55.12; H, 3.91; N, 6.18.

**Dimethyl 2,4-bis(4-cyanobenzoyl)pentanedioate (3h):**

![Chemical Structure Image]

Purified by silica gel chromatography (EtOAc: petroleum ether, 2:8)

Yield: 30 mg (29%); white semi-solid; The ratio of the two diastereomers is 1.2:1; Two diastereomers: \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 2.50-2.76 (m, 2H), 3.66 (s, 2.73H), 3.76 (s, 3.28H), 4.56 (t, J = 7.0 Hz, 0.94H), 4.68 (t, J = 7.0 Hz, 1.12H), 7.80-7.84 (m, 4H), 8.14 (d, J = 8.5 Hz, 1.87H), 8.18 (d, J = 8.5 Hz, 2.35H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): 27.10, 27.73, 51.02, 51.19, 53.00, 53.02, 117.22, 117.26, 117.68, 129.17, 129.33, 132.75, 132.77, 138.18, 138.64, 169.08, 169.60, 193.46, 193.82; Anal. calculated for C\(_{23}\)H\(_{18}\)N\(_2\)O\(_6\): C, 66.03; H, 4.34; N, 6.70; found C, 66.12; H, 4.38; N, 6.65.

**Dimethyl 2,4-bis(3-chlorobenzoyl)pentanedioate (3i):**

![Chemical Structure Image]

Purified by silica gel chromatography (EtOAc: petroleum ether, 1.5:8.5)
Yield: 73 mg (66%); transparent oil; The ratio of the two diastereomers is 1.4:1; **Two diastereomers:** $^1$H NMR (500 MHz, CDCl$_3$): $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 2.52-2.76 (m, 2H), 3.66 (s, 2.53H), 3.76 (s, 3.46H), 4.51 (t, $J$ = 7.0 Hz, 0.87H), 4.60 (s, 1.15H), 7.40-7.49 (m, 2H), 7.58 (t, $J$ = 9.5 Hz, 2H), 7.90-7.96 (m, 2H), 8.00 (d, $J$ = 10.0 Hz, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$): 27.48, 28.02, 51.00, 51.19, 52.87, 126.93, 127.06, 128.82, 128.88, 130.25, 133.89, 133.91, 135.30, 135.33, 136.84, 137.25, 169.40, 169.72, 193.45, 193.84; Anal. calculated for C$_{21}$H$_{18}$Cl$_2$O$_6$: C, 57.68; H, 4.15; found C, 57.76; H, 4.19.

**Dimethyl 2,4-bis(3-methoxybenzoyl)pentanedioate (3j):**

Purified by silica gel chromatography (EtOAc: petroleum ether, 2:8)

Yield: 107 mg (90%); white gum; The ratio of the two diastereomers is 1.4:1; **Two diastereomers:** $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 2.54-2.79 (m, 2H), 3.65 (s, 2.53H), 3.75 (s, 3.47H), 3.86 (s, 3.64H), 3.89 (s, 2.69H), 4.55 (t, $J$ = 7.5 Hz, 0.89H), 4.64 (t, $J$ = 7.0 Hz, 1.22H), 7.10-7.18 (m, 2H), 7.39 (dt, $J$ = 8.0 Hz, 2H), 7.55-7.59 (m, 2H), 7.62 (d, $J$ = 8.0 Hz, 0.91H), 7.65 (d, $J$ = 7.5 Hz, 1.24H); $^{13}$C NMR (125 MHz, CDCl$_3$): 27.96, 28.51, 51.12, 51.48, 52.62, 55.50, 112.82, 112.84, 120.70, 120.79, 121.55, 129.86, 136.33, 137.10, 160.10, 160.03, 169.79, 170.16, 194.51, 194.93.

**Dimethyl 2,4-di(furan-2-carbonyl)pentanedioate (3k):**

Purified by silica gel chromatography (EtOAc: petroleum ether, 2:8)

Yield: 47 mg (54%); light yellow-orange semi-solid; The ratio of the two diastereomers is 1.2:1; **Two diastereomers:** $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 2.62 (dt, $J$ = 7.5 Hz, 2H), 3.68 (s, 2.76H), 3.72 (s, 3.24H), 4.30 (t, $J$ = 7.5 Hz, 0.94H), 4.34 (t, $J$ = 7.5 Hz, 1.07H), 6.54-6.56 (m, 1.02H), 6.57-6.60 (m, 0.96H), 7.37 (d, $J$ = 3.5 Hz, 2H), 7.59 (s, 0.99H), 7.63 (s, 0.91H); $^{13}$C NMR (125 MHz, CDCl$_3$): 26.92, 27.39, 51.23, 51.27, 52.70, 112.74, 112.75, 119.40, 119.49, 147.52, 147.54, 151.41, 151.60, 169.33, 169.45, 182.85, 182.97; Anal. calculated for C$_{17}$H$_{16}$O$_6$: C, 58.62; H, 4.63; found C, 58.72; H, 4.68.
Diethyl 2,4-dibenzoylpentanedioate (3l):\(^4\)

![Image of molecule](image)

Purified by silica gel chromatography (EtOAc: petroleum ether, 1.5:8.5)

Yield: 74 mg (75\%); white solid; The ratio of the two diastereomers is 1.7:1; **Two diastereomers:** \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 1.10 (t, \(J = 7.0\) Hz, 2.23H), 1.21 (t, \(J = 7.5\) Hz, 3.77H), 2.54-2.80 (m, 2H), 4.05-4.14 (m, 0.73H), 4.55 (t, \(J = 7.5\) Hz, 2.52H), 4.63 (t, \(J = 7.5\) Hz, 1.23H), 7.44-7.52 (m, 4H), 7.55-7.62 (m, 2H), 8.05 (d, \(J = 7.5\) Hz, 4H); \(^13\)C NMR (125 MHz, CDCl\(_3\)): 13.88, 14.00, 27.68, 28.21, 51.35, 51.59, 61.64, 61.67, 128.80, 128.82, 128.89, 128.91, 133.77, 133.82, 135.43, 135.91, 169.34, 169.69, 194.82, 195.17.

Diethyl 2,4-bis(4-fluorobenzoyl)pentanedioate (3m):\(^5\)

![Image of molecule](image)

Purified by silica gel chromatography (EtOAc: petroleum ether, 1.5:8.5)

Yield: 97 mg (90\%); light yellow gum; The ratio of the two diastereomers is 1.1:1; **Two diastereomers:** \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 1.12 (t, \(J = 7.5\) Hz, 3.13H), 1.22 (t, \(J = 7.5\) Hz, 0.92H), 4.59 (t, \(J = 7.5\) Hz, 1.02H), 7.11-7.20 (m, 4H), 8.05-8.13 (m, 4H); \(^13\)C NMR (125 MHz, CDCl\(_3\)): 13.89, 13.99, 27.52, 28.15, 51.26, 51.47, 61.76, 61.78, 116.01 (d, \(J = 22.0\) Hz), 131.59 (d, \(J = 9.5\) Hz), 131.73 (d, \(J = 9.0\) Hz), 131.81 (d, \(J = 3.0\) Hz), 132.31 (d, \(J = 3.0\) Hz), 166.20 (d, \(J = 254.0\) Hz), 169.14, 169.57, 193.19, 193.60.

Diethyl 2,4-bis(4-chlorobenzoyl)pentanedioate (3n):\(^5\)

![Image of molecule](image)

Purified by silica gel chromatography (EtOAc: petroleum ether, 1.5:8.5)

Yield: 85 mg (73\%); white solid; The ratio of the two diastereomers is 1.3:1; **Two diastereomers:** \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 1.13 (t, \(J = 7.5\) Hz, 2.60H), 1.22 (t, \(J = 7.0\) Hz, 3.60H), 2.50-2.75 (m, 2H), 4.06-4.16 (m, 1.82H), 4.18-4.27 (m, 2.09H), 4.49 (t, \(J = 7.5\) Hz, 0.92H), 4.59 (t, \(J = 7.5\) Hz, 1.02H), 7.45 (d, \(J = 9.0\) Hz, 2.17H), 7.48 (d, \(J = 8.5\) Hz, 1.63H), 7.99 (d, \(J = 9.0\) Hz, 4H); \(^13\)C NMR (125 MHz, CDCl\(_3\)): 

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13.90, 13.99, 27.41, 28.00, 51.26, 51.43, 61.81, 61.83, 129.16, 129.18, 130.22, 130.33, 133.75, 134.20, 140.46, 140.48, 169.04, 169.43, 193.57, 193.96.

**Diethyl 2,4-bis(4-bromobenzoyl)pentanedioate (3o):**

![Diagram of Diethyl 2,4-bis(4-bromobenzoyl)pentanedioate (3o)](image)

Purified by silica gel chromatography (EtOAc: petroleum ether, 1.5:8.5)

Yield: 127 mg (92%); light yellow solid; The ratio of the two diastereomers is 1.2:1; **Two diastereomers:**

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.12 (t, $J = 7.5$ Hz, 2.66H), 1.21 (t, $J = 7.0$ Hz, 3.39H), 2.49-2.74 (m, 2H), 4.08-4.15 (m, 1.88 H), 4.16-4.26 (m, 2.25H), 4.47 (t, $J = 7.5$ Hz, 0.88H), 4.55 (t, $J = 7.5$ Hz, 1.09H), 7.58-7.66 (m, 4H), 7.91 (d, $J = 8.0$ Hz, 4H); $^{13}$C NMR (125 MHz, CDCl$_3$): 13.91, 14.00, 27.38, 27.96, 51.22, 51.38, 61.84, 129.23, 129.28, 130.29, 130.39, 132.18, 134.17, 134.60, 169.00, 169.38, 193.76, 194.15.

**Diethyl 2,4-bis(4-methoxybenzoyl)pentanedioate (3p):**

![Diagram of Diethyl 2,4-bis(4-methoxybenzoyl)pentanedioate (3p)](image)

Purified by silica gel chromatography (EtOAc: petroleum ether, 2:8)

Yield: 83 mg (73%); light yellow semi-solid; The ratio of the two diastereomers is 1.1:1; **Two diastereomers:** $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.12 (t, $J = 7.0$ Hz, 2.74H), 1.22 (t, $J = 7.5$ Hz, 3.20H), 2.50-2.74 (m, 2H), 3.85 (s, 3.09H), 3.87 (s, 2.79H), 4.05-4.14 (m, 2.01H), 4.16-4.25 (m, 2.07H), 4.48 (t, $J = 7.5$ Hz, 0.90H), 4.56 (t, $J = 7.5$ Hz, 1.02H), 6.92 (d, $J = 8.5$ Hz, 2.14H), 6.96 (d, $J = 8.5$ Hz, 1.83H), 8.01-8.06 (m, 4H); $^{13}$C NMR (125 MHz, CDCl$_3$): 13.93, 14.03, 27.95, 28.58, 51.11, 51.36, 55.50, 55.53, 64.48, 61.51, 113.99, 128.44, 128.94, 131.27, 131.36, 164.08, 164.09, 169.56, 169.94, 193.29, 193.69.

**Diethyl 2,4-bis(4-methylbenzoyl)pentanedioate (3q):**

![Diagram of Diethyl 2,4-bis(4-methylbenzoyl)pentanedioate (3q)](image)

Purified by silica gel chromatography (EtOAc: petroleum ether, 1.5:8.5)

Yield: 84 mg (79%); white solid; The ratio of the two diastereomers is 1.2:1; **Two diastereomers:** $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 1.12 (t, $J = 7.0$ Hz, 2.66H), 1.22 (t, $J = 7.5$ Hz, 3.35H), 2.40 (s, 3.20H), 2.42 (s, 2.70H), 2.52-2.76 (m, 2H), 4.05-4.15 (m, 1.75 H), 4.16-4.26 (m, 2.19H), 4.51 (t, $J = 7.5$ Hz, 0.87H),
4.59 (t, \( J = 7.5 \) Hz, 1.05H), 7.25 (d, \( J = 8.5 \) Hz, 2.21H), 7.29 (d, \( J = 8.0 \) Hz, 1.74H), 7.94 (t, \( J = 8.5 \) Hz, 4H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): 13.91, 14.02, 21.68, 21.70, 27.80, 28.33, 51.26, 51.52, 61.53, 61.56, 128.97, 129.05, 129.48, 129.49, 133.02, 133.47, 144.75, 144.76, 169.47, 169.79, 194.41, 194.76.

Diethyl 2,4-bis(4-nitrobenzoyl)pentanedioate (3r):\(^5\)

\[
\text{O}_2\text{N}
\]

Purified by silica gel chromatography (EtOAc: petroleum ether, 2:8)

Yield: 49 mg (40%); light yellow gum The ratio of the two diastereomers is 1:1; Two diastereomers: \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta \) 1.13 (t, \( J = 7.5 \) Hz, 3H), 1.23 (t, \( J = 7.0 \) Hz, 3H), 2.54-2.80 (m, 2H), 4.08-4.16 (m, 2H), 4.18-4.30 (m, 2H), 4.57 (t, \( J = 7.0 \) Hz, 1H), 4.68 (t, \( J = 7.0 \) Hz, 1H), 8.19-8.27 (m, 4H), 8.33-8.40 (m, 4H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): 13.88, 13.96, 26.93, 27.51, 51.55, 51.68, 62.20, 124.02, 124.04, 129.79, 129.96, 139.89, 140.33, 150.72, 150.75, 168.56, 168.98, 193.40, 193.72.

Diethyl 2,4-bis(3-chlorobenzoyl)pentanedioate (3s):

\[
\text{Cl}
\]

Purified by silica gel chromatography (EtOAc: petroleum ether, 2:8)

Yield: 57 mg (49%); light yellow gum; The ratio of the two diastereomers is 1:1; Two diastereomers: \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta \) 1.14 (t, \( J = 7.0 \) Hz, 2.71 H), 1.22 (t, \( J = 7.0 \) Hz, 3.30H), 2.53-2.76 (m, 2H), 4.06-4.17 (m, 2.04H), 4.17-4.28 (m, 2.19H), 4.47 (t, \( J = 7.5 \) Hz, 0.90H), 4.55 (t, \( J = 7.5 \) Hz, 1.01H), 7.40-7.48 (m, 2H), 7.54-7.60 (m, 2H), 7.91-7.95 (m, 2H), 7.98-8.00 (m, 1.07H), 8.00-8.03 (m, 0.87H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): 13.87, 13.97, 27.32, 27.82, 51.34, 51.49, 61.90, 126.89, 127.00, 128.80, 128.84, 130.15, 133.74, 133.76, 135.23, 135.25, 137.05, 137.43, 168.92, 169.19, 193.50, 193.84; HRMS (ESI-TOF): m/z [M + Na]\(^+\) calculated for C\(_{23}\)H\(_{22}\)Cl\(_2\)O\(_6\)Na: 487.0686; found: 487.0688.
Diethyl 2,4-bis(3-methoxybenzoyl)pentanedioate (3t).

![Chemical structure of 3t]

Purified by silica gel chromatography (EtOAc: petroleum ether, 2:8)
Yield: 89 mg (78%); light yellow gum; The ratio of the two diastereomers is 1:1; Two diastereomers:

\[ ^1H \text{ NMR (500 MHz, CDCl}_3)\]: \( \delta \) 1.14 (t, \( J = 7.0 \) Hz, 2.72H), 1.23 (t, \( J = 7.5 \) Hz, 3.20H), 2.54-2.79 (m, 2H), 3.86 (s, 3.18H), 3.89 (s, 2.64H), 4.07-4.16 (m, 1.81H), 4.17-4.27 (m, 2.11H), 4.51 (t, \( J = 7.5 \) Hz, 0.92H), 4.59 (t, \( J = 7.5 \) Hz, 1.03H), 7.11-7.18 (m, 2H), 7.35-7.43 (m, 2H), 7.55-7.60 (m, 2H), 7.64 (t, \( J = 6.5 \) Hz, 2H);

\[ ^{13}C \text{ NMR (125 MHz, CDCl}_3)\]: 13.90, 14.00, 27.84, 28.37, 51.53, 51.76, 55.49, 55.50, 61.64, 112.80, 120.58, 120.69, 121.43, 121.53, 129.78, 136.80, 137.26, 159.98, 160.00, 169.33, 169.65, 194.62, 195.00.

Diethyl 2,4-difuran-2-carbonyl)pentanedioate (3u).

![Chemical structure of 3u]

Purified by silica gel chromatography (EtOAc: petroleum ether, 2:8)
Yield: 78 mg (83%); Light yellow semi-solid; The ratio of the two diastereomers is 1:1; Two diastereomers:

\[ ^1H \text{ NMR (500 MHz, CDCl}_3)\]: \( \delta \) 1.15 (t, \( J = 7.5 \) Hz, 3H), 1.20 (t, \( J = 7.0 \) Hz, 3H), 2.56-2.66 (m, 2H), 4.10-4.21 (m, 4H), 4.24-4.31 (m, 2H), 6.52-6.55 (m, 1H), 6.55-6.57 (m, 1H), 7.35 (t, \( J = 3.5 \) Hz, 2H), 7.58 (s, 1H), 7.61 (s, 1H);

\[ ^{13}C \text{ NMR (125 MHz, CDCl}_3)\]: 13.93, 13.97, 26.78, 27.23, 51.50, 51.58, 61.66, 61.67, 112.62, 112.65, 119.18, 119.27, 147.29, 147.34, 151.48, 151.68, 168.84, 168.94, 182.97, 183.10.
Experimental details of the Nash test

General procedure for the Nash test:

Formation of formaldehyde in the reaction was assessed using the Nash Test. The Nash reagent was prepared by dissolving NH₄OAc (7.5 g, 95 mmol), 2,4-pentanedione (0.1 mL, 1 mmol) and acetic acid (0.15 mL, 2.5 mmol) in 50 mL of water. After obtaining a clear solution, it was stored in the dark.

A typical reaction with the model substrate was set up under the optimised conditions; after completion of the reaction, an aliquot (50 µL) was taken out from the reaction mixture and Nash reagent added (5 mL) was added to it. The resulting mixture was allowed to stir on a pre-heated oil-bath at 60 °C for 5 min; it was allowed to cool to room temperature. The UV spectrum of the mixture was then recorded, which showed a $\lambda_{\text{max}}$ at 411 nm. A control test UV spectrum was similarly recorded for formaldehyde treated with the Nash reagent, and a $\lambda_{\text{max}}$ of 412 nm was observed, to confirm the generation of formaldehyde in the reaction.

References:

$^1$H and $^{13}$C NMR spectra of the synthesised products