Iodine-Catalyzed C–N Cleavage of Tertiary Amines: Synthesis of Methylene-Bridged Bis-1,3-dicarbonyl Compounds

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Abstract: A novel and efficient iodine-catalyzed C–N cleavage of tertiary amines via an sp^3 C–H bond oxidative coupling reaction is described. A wide range of methylene-bridged bis-1,3-dicarbonyl compounds were synthesized in up to 92% yield by using an environmentally benign catalytic system in combination with 1,3-dicarbonyl compounds.

Key words: iodine, oxidative coupling, C–N cleavage, tertiary amines, methylene-bridged bis-1,3-dicarbonyl compounds

The cleavage of C–N bonds has attracted much attention from organic chemists due to the wide existence of nitro-containing compounds in natural products and numerous organisms.[1] However, since C–N bonds are usually inert, harsh conditions are generally required for their cleavage.[2,3] During the past decades, much effort has been devoted to the design of efficient protocols to solve this problem,[3] including (1) conversion of nitro groups into better leaving groups, such as diazonium salts,[1b,4] ammonium salts and azaheterocycles,[5] to facilitate the C–N bond cleavage, and (2) use of transition metals to directly catalyze the C–N bond cleavage.[6] Recently, oxidative coupling reactions have been developed to construct C–C and C–N bonds via C–N cleavage based on sp^3 C–H bond activation of secondary or tertiary amine derivatives. For example, iron,[7] copper,[8] gold,[9] ruthenium[10] and palladium[11] have been employed as catalysts or photocatalysts in the construction of 1,3-dicarbonyl compounds and alkyl aryl ketones, and in the C3-selective formylation of indoles using *N*-methylaniline or *N*,*N*-dimethylaniline as the formylating reagent under oxidation conditions,[10,12] thus avoiding many side reactions which occur when formaldehyde and dihalomethanes are used as a methylene source.[13] Besides C–C bond formation, new C–N bond formation via C–N bond cleavage of tertiary amines has also been reported by the groups of Huang,[14] Wang[15] and Xu.[16] However, in the above transformations, expensive and toxic transition-metal catalysts are essential. Thus, new catalytic systems capable of performing the C–N bond cleavage both in an environmentally friendly manner and with high efficiency are highly desirable.

Iodine is an inexpensive, environmentally benign reagent with a low toxicity.[17] In the past decade, iodine sources have proved useful as catalysts in oxidative coupling reactions. For example, the groups of Itoh and Prabhu have independently successfully developed a molecular iodine catalyzed cross-dehydrogenative coupling reaction between *N*-phenyltetrahydroisoquinoline and a series of nucleophiles (e.g., carbonyl derivatives, phenols, indoles, amides, nitroalkanes),[17g,18] while Yan and Wang have reported the intramolecular oxidative decarboxylative amination of primary α-amino acids for the synthesis of quinazolines.[19] However, little attention has been paid to the use of iodine as a catalyst to realize the C–N bond cleavage of amines.[12] Herein, we present an iodine-catalyzed oxidative coupling reaction via C–N bond cleavage of tertiary amines.

Initially, the reaction was conducted with *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) as substrate and ethyl 3-oxo-3-phenylpropanoate as the reaction partner, without the addition of catalyst, at 100 °C in the presence of di-*tert*-butyl peroxide (DTBP) as oxidant for 12 hours; however, as shown in Table 1, the desired methylene-bridged bis-1,3-dicarbonyl compound was not obtained (entry 1). When potassium iodide or sodium iodide was used as the catalyst, the desired product was isolated in 61% and 34% yield, respectively (Table 1, entries 2 and 3). The reaction with iodine as catalyst gave the best result, affording the product in 86% yield (Table 1, entry 4). Then, a series of other oxidants was screened; it was found that air, *tert*-butyl hydroperoxide (TBHP), oxygen and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) were less efficient for this transformation, providing lower yields of product (Table 1, entries 5–8). Other oxidants, such as *m*-chloroperoxybenzoic acid, benzoyl peroxide (BPO) and 1,4-benzoquinone (BQ), were barely able to promote the reaction (Table 1, entries 9–11). Further screening of the solvent indicated its key role in the reaction outcome. Tetrahydrofuran, *N*,*N*-dimethylformamide, dimethyl sulfoxide, benzene, toluene, xylene and 1,2-dichloroethane gave the corresponding product in moderate yield (Table 1, entries 12–18), and were thus less productive than the use of acetonitrile as solvent. The reaction temperature was also explored; when the temperature was raised to 120 °C, the product was obtained in 63% yield, while lowering the temperature to 60 °C resulted in 33% yield of product (Table 1, entries 19 and 20). When the reaction time was prolonged to 16 hours, the yield was 82%, while this reaction gave the desired product in 72% yield when the time was shortened to 8 hours (Table 1, entries 21 and 22). The use of other tertiary amines, such as *N*,*N*-dimethylaniline (Table 1, entry 23), was investigated

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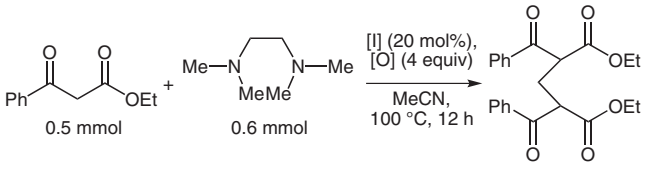
which resulted in lower yields of the methylene-bridged bis-1,3-dicarbonyl compound.

Table 1 Optimization of the Reaction Conditions

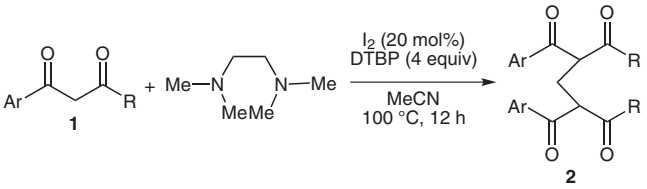


Entry	[I]	Oxidant	Solvent	Yield[a] (%)
1	–	DTBP	MeCN	trace
2	KI	DTBP	MeCN	61
3	NaI	DTBP	MeCN	34
4	I_2	DTBP	MeCN	86
5	I_2	air (1 atm)	MeCN	64
6	I_2	TBHP (70% aq)	MeCN	20
7	I_2	O_2 (1 atm)	MeCN	52
8	I_2	DDQ	MeCN	23
9	I_2	MCPBA	MeCN	trace
10	I_2	BPO	MeCN	trace
11	I_2	BQ	MeCN	trace
12	I_2	DTBP	THF	47
13	I_2	DTBP	DMF	45
14	I_2	DTBP	DMSO	48
15	I_2	DTBP	benzene	41
16	I_2	DTBP	toluene	40
17	I_2	DTBP	xylene	37
18	I_2	DTBP	DCE	42
19[b]	I_2	DTBP	MeCN	63
20[c]	I_2	DTBP	MeCN	33
21[d]	I_2	DTBP	MeCN	82
22[e]	I_2	DTBP	MeCN	72
23[f]	I_2	DTBP	MeCN	23

[a] Isolated yield.
[b] Reaction temperature: 120 °C.
[c] Reaction temperature: 60 °C.
[d] Reaction time: 16 h.
[e] Reaction time: 8 h.
[f] *N*,*N*-Dimethylaniline was used as the methylene source.

With the optimized conditions in hand, we then explored the scope of the reaction; the results are summarized in Table 2. Firstly, when methyl 3-oxo-3-phenylpropanoate was used as the substrate, the yield of the corresponding product **2b** was slightly lower than that of the ethyl ester **2a** (Table 2, entries 1 and 2). For substrates with electron-donating groups on the phenyl ring, the corresponding methylene-bridged compounds were obtained in excellent yields. For example, when a 4-methoxy, 4-ethoxy or 4-morpholino group was present on the phenyl ring, the corresponding products **2d**–**f** were obtained in up to 92% yield (Table 2, entries 4–6). Moreover, *meta*-substituted substrates also gave the corresponding products, **2g** and **2h**, in 86% and 82% yield, respectively (Table 2, entries 7 and 8). However, for the reactions of substrates with an electron-withdrawing substituent on the phenyl ring, there was a clear decrease in the yield of product (**2i**–**k**; Table 2, entries 9–11). 1,3-Diketones such as 1,3-diphenylpropane-1,3-dione and 1-phenylbutane-1,3-dione could be transformed into the corresponding products **2l** and **2m** in moderate yields under the optimized conditions (Table 2, entries 12 and 13). Methyl 3-(2-naphthyl)-3-oxopropanoate and a β-keto amide also participated in the reaction, and gave the desired products **2n** and **2o** in 68% and 71% yield, respectively (Table 2, entries 14 and 15).

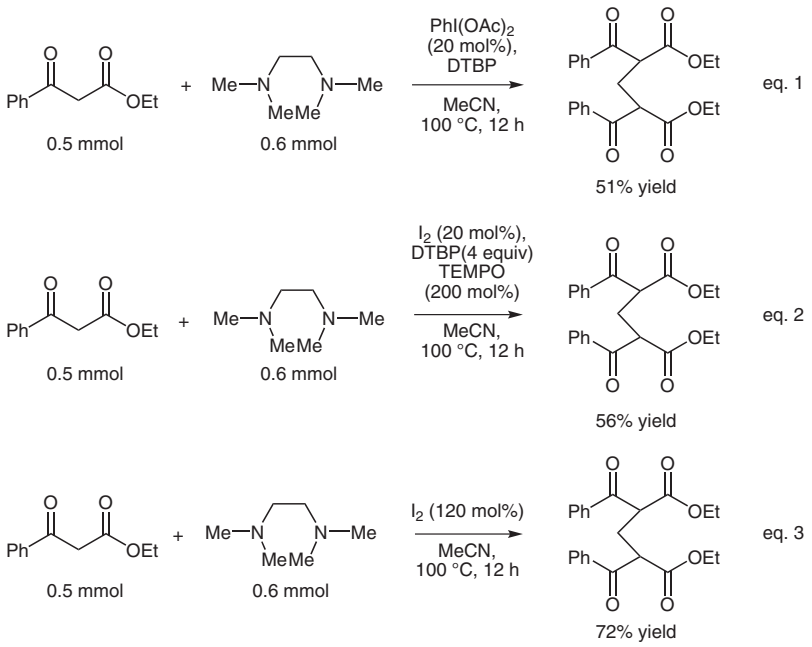
Table 2 Reaction Scope



Entry	Ar	R	Product	Yield[a] (%)
1	Ph	OEt	**2a**	86
2	Ph	OMe	**2b**	78
3	4-Tol	OMe	**2c**	67
4	4-$MeOC_6H_4$	OMe	**2d**	88
5	4-$EtOC_6H_4$	OMe	**2e**	91
6	morpholino	OMe	**2f**	92
7	3-$MeOC_6H_4$	OMe	**2g**	86
8	3,4-OCH_2O-	OMe	**2h**	82
9	4-FC_6H_4	OMe	**2i**	69
10	4-ClC_6H_4	OMe	**2j**	73
11	4-BrC_6H_4	OMe	**2k**	51
12	Ph	Ph	**2l**	46
13	Ph	Me	**2m**	41
14	2-Naph	OMe	**2n**	68
15	Ph	morpholino	**2o**	71

[a] Isolated yield.

To obtain more information about the reaction mechanism, (diacetoxyiodo)benzene [$PhI(OAc)_2$] instead of iodine was used as a catalyst under the optimized reaction conditions; the corresponding product **2a** was isolated in

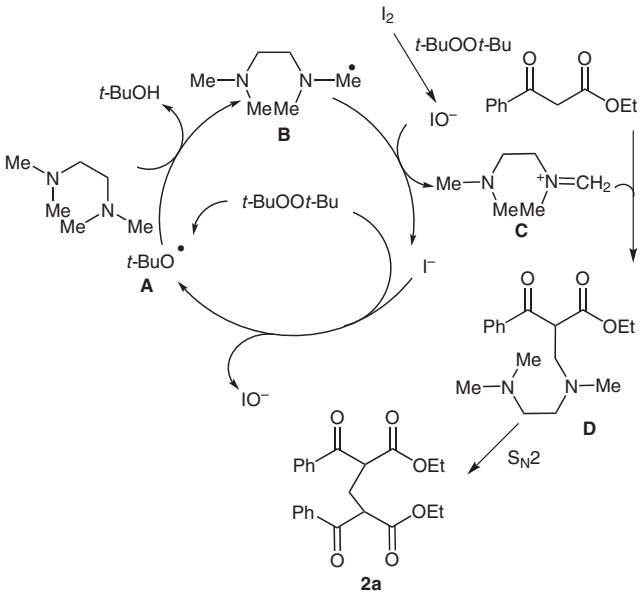


Scheme 1 Probe of the reaction mechanism

51% yield (Scheme 1, eq 1), which indicates that the catalyst might go through a hypervalent iodine process. Next, a radical inhibitor (TEMPO) was added to the reaction mixture under the optimized conditions; in this case, the yield of product decreased dramatically (to 56%; Scheme 1, eq 2), suggesting a process with a radical intermediate. Taking into account that iodine may undergo homolysis and heterolysis reactions, which could generate $I^{\bullet}$, I^{+} and I^{-}, we then increased the amount of iodine to 1.2 equivalents under nitrogen atmosphere without DTBP as oxidant, and found that the reaction took place smoothly, giving the product in 72% yield (Scheme 1, eq 3). This suggests that the reaction goes through a radical process and a hypervalent iodine process.

Based on our studies and previous literature,[8a,b,12,19] we propose a possible mechanism for this reaction (Scheme 2). First, thermal homolysis of di-*tert*-butyl peroxide would generate the *tert*-butoxy radical **A** (*t*-BuO$^{\bullet}$). Then, occurrence of a single-electron transfer procedure between TMEDA and the *tert*-butoxy radical would result in formation of the TMEDA radical **B**. On the other hand, iodine would be oxidized by di-*tert*-butyl peroxide to afford hypervalent iodine, which could then oxidize radical **B** to produce iminium ion **C** and iodine. Attack of the β-keto ester at the iminium ion would give intermediate **D**, which could then undergo a nucleophilic substitution reaction to afford the desired product **2a**.

In conclusion, we have described a general and efficient iodine-catalyzed C–N cleavage of tertiary amines under mild conditions. This protocol provides a practical and green method for the synthesis of bis-1,3-dicarbonyl compounds in moderate to excellent yields using DTBP as an oxidant. Studies of the mechanism showed that the reaction proceeds via a radical process. Further study is currently underway in our laboratory.



Scheme 2 Proposed reaction mechanism

^{1}H and ^{13}C NMR spectra were determined for solutions in $CDCl_3$ with TMS as internal standard on BRUKER DRX 600 spectrometers or agilent 400 spectrometers. ESI-HRMS data were measured on a Bruker Compass DataAnalysis 4.0 mass instrument (ESI).

Methylene-Bridged Bis-1,3-dicarbonyl Compounds 2a–o; General Procedure

A 1,3-dicarbonyl compound **1** (0.5 mmol), I_2 (25.4 mg, 20 mol%), TMEDA (1.2 equiv), DTBP (4 equiv) and MeCN (2 mL) were added to a 25-mL flame-dried Schlenk tube under air. The Schlenk tube

was sealed with a rubber septum and stirred for 12 h at 100 °C. The reaction progress was monitored by TLC. After completion of the reaction, the mixture was allowed to cool to r.t., the solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (EtOAc–hexane, 1:40, 1:20) to afford the desired product.

Diethyl 2,4-Dibenzoylpentanedioate (2a)
White solid; yield: 85 mg (86%); two diastereomers (1.2:1).

^{1}H NMR (601 MHz, $CDCl_3$): δ = 8.06–8.05 (m, 4 H), 7.62–7.61 (m, 2 H), 7.52–7.46 (m, 4 H), 4.64 (t, *J* = 7.2 Hz, 1 H), 4.55 (t, *J* = 7.2 Hz, 1 H), 4.24–4.21 (m, 2 H), 4.11–4.09 (m, 2 H), 2.78–2.52 (m, 2 H), 1.22 (t, *J* = 7.2 Hz, 3 H), 1.11 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 195.29, 194.92, 169.80, 169.44, 135.95, 135.46, 133.93, 133.92, 129.01, 128.92, 61.77, 61.75, 51.65, 51.39, 28.30, 27.75, 14.10, 13.97.

Dimethyl 2,4-Dibenzoylpentanedioate (2b)
White solid; yield: 72 mg (78%); two diastereomers (1.8:1).

^{1}H NMR (601 MHz, $CDCl_3$): δ = 8.05 (dd, J_1 = 7.2 Hz, J_2 = 1.2 Hz, 4 H), 7.63–7.58 (m, 2 H), 7.52–7.47 (m, 4 H), 4.67 (t, *J* = 7.2 Hz, 1 H), 4.58 (t, *J* = 7.2 Hz, 1 H), 3.75 (s, 4 H), 3.64 (s, 2 H), 2.77–2.55 (m, 2 H).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 195.22, 194.82, 170.33, 169.93, 135.89, 135.42, 134.05, 134.03, 129.08, 129.01, 128.98, 128.87, 52.78, 51.41, 51.16, 28.47, 27.93.

Dimethyl 2,4-Bis(4-methylbenzoyl)pentanedioate (2c)
White solid; yield: 66 mg (67%); two diastereomers (1.2:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 8.0 Hz, 4 H), 7.27 (d, *J* = 8.0 Hz, 4 H), 4.64–4.52 (m, 2 H), 3.74 (s, 5 H), 3.63 (s, 1 H), 2.74–2.52 (m, 2 H), 2.42 (d, *J* = 8.8 Hz, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.82, 170.44, 145.03, 132.99, 129.68, 129.21, 52.72, 51.36, 28.59, 21.85.

Dimethyl 2,4-Bis(4-methoxybenzoyl)pentanedioate (2d)
White solid; yield: 94 mg (88%); two diastereomers (1.4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 8.8 Hz, 4 H), 6.99–6.93 (m, 4 H), 4.60 (t, *J* = 7.2 Hz, 1 H), 4.52 (t, *J* = 7.6 Hz, 1 H), 3.89 (d, *J* = 7.6 Hz, 6 H), 3.75 (s, 3 H), 3.64 (s, 3 H), 2.75–2.51 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.79, 193.34, 170.63, 170.17, 164.29, 131.57, 131.47, 128.92, 128.41, 114.20, 55.70, 55.68, 52.71, 51.25, 50.96, 28.86, 28.20.

Dimethyl 2,4-Bis(4-ethoxybenzoyl)pentanedioate (2e)
White solid; yield: 104 mg (91%); two diastereomers (1.1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04 (d, *J* = 8.8 Hz, 4 H), 6.93 (dd, J_1 = 15.2 Hz, J_2 = 8.8 Hz, 4 H), 4.60 (t, *J* = 7.2 Hz, 1 H), 4.51 (t, *J* = 7.2 Hz, 1 H), 4.11 (dq, J_1 = 14.2 Hz, J_2 = 7.2 Hz, 4 H), 3.75 (s, 3 H), 3.64 (s, 3 H), 2.75–2.51 (m, 2 H), 1.45 (m, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.77, 193.32, 170.63, 170.19, 163.72, 131.55, 131.45, 128.70, 128.20, 114.60, 114.59, 64.01, 63.98, 52.68, 51.20, 50.92, 28.88, 28.21, 14.78, 14.77.

HRMS (ESI): *m*/*z* [M^+ + 23] calcd for $C_{25}H_{28}NaO_8$: 479.1676; found: 479.1687.

Dimethyl 2,4-Bis(4-morpholinobenzoyl)pentanedioate (2f)
White solid; yield: 124 mg (92%); two diastereomers (1.2:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 9.2 Hz, 4 H), 6.87 (dd, J_1 = 12.8 Hz, J_2 = 8.8 Hz, 4 H), 4.58 (t, *J* = 7.2 Hz, 1 H), 4.50 (t, *J* = 7.2 Hz, 1 H), 3.85 (d, *J* = 3.6 Hz, 8 H), 3.74 (s, 3 H), 3.63 (s, 3 H), 3.35–3.32 (m, 8 H), 2.74–2.50 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.27, 192.82, 170.82, 170.34, 154.68, 154.66, 131.28, 131.20, 126.28, 125.75, 113.30, 66.56, 52.53, 51.09, 50.69, 47.30, 29.01, 28.33.

HRMS (ESI): *m*/*z* [M^+ + 23] calcd for $C_{29}H_{34}N_2NaO_8$: 561.2207; found: 561.2210.

Dimethyl 2,4-Bis(3-methoxybenzoyl)pentanedioate (2g)
White solid; yield: 92 mg (86%); two diastereomers (1.3:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66–7.61 (m, 2 H), 7.57 (s, 2 H), 7.42–7.36 (m, 2 H), 7.16–7.11 (m, 2 H), 4.63 (t, *J* = 7.2 Hz, 1 H), 4.54 (t, *J* = 7.2 Hz, 1 H), 3.88 (d, *J* = 8.8 Hz, 6 H), 3.75 (s, 3 H), 3.64 (s, 3 H), 2.77–2.53 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.08, 194.64, 170.31, 169.93, 160.14, 160.11, 137.19, 136.71, 130.00, 121.70, 121.58, 120.96, 120.85, 55.65, 52.80, 52.78, 51.61, 51.34, 28.65, 28.08.

HRMS (ESI): *m*/*z* [M^+ + 23] calcd for $C_{23}H_{24}NaO_8$: 451.1363; found: 451.1382.

Dimethyl 2,4-Bis(1,3-benzodioxol-5-ylcarbonyl)pentanedioate (2h)
White solid; yield: 93 mg (82%); two diastereomers (1.5:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72–7.66 (m, 2 H), 7.50 (dd, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 2 H), 6.87 (dd, J_1 = 9.6 Hz, J_2 = 8.4 Hz, 2 H), 6.07 (d, *J* = 6.0 Hz, 4 H), 4.54 (t, *J* = 7.2 Hz, 1 H), 4.45 (t, *J* = 7.6 Hz, 1 H), 3.75 (s, 4 H), 3.65 (s, 2 H), 2.72–2.50 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 193.32, 192.83, 170.41, 170.01, 152.68, 152.66, 148.59, 148.53, 130.69, 130.22, 125.92, 125.74, 108.63, 108.59, 108.27, 102.20, 102.17, 52.76, 51.24, 50.99, 28.89, 28.26.

HRMS (ESI): *m*/*z* [M^+ + 23] calcd for $C_{23}H_{20}NaO_{10}$: 479.0949; found: 479.0969.

Dimethyl 2,4-Bis(4-fluorobenzoyl)pentanedioate (2i)
White solid; yield: 70 mg (69%); two diastereomers (2.1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14–8.08 (m, 4 H), 7.20–7.14 (m, 4 H), 4.63 (t, *J* = 8.0 Hz, 1 H), 4.53 (t, *J* = 8.0 Hz, 1 H), 3.76 (s, 4 H), 3.65 (s, 2 H), 2.75–2.50 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.70, 193.22, 170.25, 169.74, 167.67, 165.12, 131.98, 131.88, 116.35, 116.14, 52.90, 51.31, 51.08, 28.45, 27.77.

Dimethyl 2,4-Bis(4-chlorobenzoyl)pentanedioate (2j)
White solid; yield: 80 mg (73%); two diastereomers (5.4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, *J* = 8.4 Hz, 4 H), 7.47 (t, *J* = 8.8 Hz, 4 H), 4.60 (t, *J* = 7.2 Hz, 2 H), 3.75 (s, 6 H), 2.73–2.50 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.03, 170.09, 140.78, 133.72, 130.50, 129.40, 73.08, 52.98, 51.29, 28.30.

Dimethyl 2,4-Bis(4-bromobenzoyl)pentanedioate (2k)
White solid; yield: 67 mg (51%); two diastereomers (2.5:1).

^{1}H NMR (601 MHz, $CDCl_3$): δ = 7.92–7.90 (m, 4 H), 7.66–7.62 (m, 4 H), 4.59 (t, *J* = 7.2 Hz, 1 H), 4.50 (t, *J* = 7.2 Hz, 1 H), 3.75 (s, 4 H), 3.64 (s, 2 H), 2.72–2.51 (m, 2 H).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 194.23, 193.82, 170.05, 169.61, 134.60, 134.17, 132.41, 130.55, 130.45, 129.59, 129.53, 52.92, 51.24, 51.08, 28.24, 27.64.

2,4-Dibenzoyl-1,5-diphenylpentane-1,5-dione (2l)
White solid; yield: 53 mg (46%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 (d, *J* = 7.6 Hz, 7 H), 7.58 (t, *J* = 6.8 Hz, 4 H), 7.48 (t, *J* = 7.6 Hz, 9 H), 5.75 (t, *J* = 6.8 Hz, 2 H), 2.76 (t, *J* = 6.8 Hz, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 196.72, 135.54, 134.03, 129.17, 128.95, 54.11, 29.06.

3,5-Dibenzoylheptane-2,6-dione (2m)
White solid; yield: 35 mg (41%); two diastereomers (1:1).

^{1}H NMR (601 MHz, $CDCl_3$): δ = 8.07 (dd, J_1 = 7.2 Hz, J_2 = 1.2 Hz, 2 H), 8.03 (dd, J_1 = 7.2 Hz, J_2 = 0.6 Hz, 2 H), 7.64–7.61 (m, 2 H), 7.58–7.48 (m, 4 H), 4.71 (t, J = 6.6 Hz, 1 H), 4.64 (t, J = 6.6 Hz, 1 H), 2.61–2.46 (m, 2 H), 2.19 (s, 3 H), 2.15 (s, 3 H).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 204.07, 203.53, 196.79, 196.57, 136.15, 135.84, 134.22, 129.20, 129.15, 129.08, 128.99, 59.57, 59.40, 29.56, 29.25, 27.59, 27.23.

Dimethyl 2,4-Di(2-naphthoyl)pentanedioate (2n)
White solid; yield: 80 mg (68%); two diastereomers (1.1:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.63 (d, J = 12.0 Hz, 2 H), 8.12 (d, J = 20.0 Hz, 1 H), 8.05–8.02 (m, 2 H), 7.94–7.92 (d, J = 8.0 Hz, 2 H), 7.89–7.82 (m, 3 H), 7.65–7.49 (m, 4 H), 4.85 (t, J = 8.0 Hz, 1 H), 4.79 (t, J = 8.0 Hz, 1 H), 3.78 (s, 3 H), 3.64 (s, 3 H), 2.93–2.69 (m, 2 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 195.22, 194.74, 170.36, 170.06, 136.04, 135.97, 133.21, 132.78, 132.65, 132.56, 131.43, 131.25, 130.08, 130.04, 129.15, 129.08, 128.91, 128.85, 127.89, 127.79, 127.10, 126.98, 124.20, 124.11, 52.87, 52.81, 51.46, 51.33, 28.83, 28.24.

2,4-Dibenzoyl-1,5-dimorpholinopentane-1,5-dione (2o)
White solid; yield: 85 mg (71%); two diastereomers (3:1).

^{1}H NMR (601 MHz, $CDCl_3$): δ = 8.15 (d, J = 1.2 Hz, 1 H), 8.12–8.08 (m, 3 H), 7.63 (t, J = 7.2 Hz, 1 H), 7.58 (t, J = 7.2 Hz, 1 H), 7.54 (t, J = 7.8 Hz, 1 H), 7.49 (t, J = 7.8 Hz, 3 H), 4.90–4.84 (m, 2 H), 3.74–3.56 (m, 16 H), 2.75–2.25 (m, 2 H).

^{13}C NMR (151 MHz, $CDCl_3$): δ = 196.32, 196.25, 168.70, 168.65, 135.61, 135.41, 134.01, 129.21, 129.16, 128.68, 66.87, 66.76, 66.67, 49.56, 49.52, 46.49, 46.36, 42.67, 42.55, 29.06, 28.94.

HRMS (ESI): m/z [M^+ + 23] calcd for $C_{27}H_{30}N_2NaO_6$: 501.1996; found: 501.2001.

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