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Phosphotungstic Acid Catalyzed Direct Benzylation of β-Dicarbonyl Compounds

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Keywords: Phosphotungstic acid / Benzylation / Alcohols / β-Dicarbonyl compounds / Atom-economical reactions

12-Phosphotungstic acid was used as an efficient, ecofriendly, and air- and moisture-stable catalyst to promote the direct substitution of the hydroxy group of benzylic and allylic alcohols with various β-dicarbonyl compounds. This powerful protocol for carbon–carbon bond-forming reactions provides monoalkylated dicarbonyl compounds in high yields with great efficiency.

Introduction

The construction of carbon–carbon bonds is a fundamental task in organic synthesis.[1] One important protocol to accomplish this goal is the alkylation of active methylene compounds such as β-diketones, β-keto esters, and malonic esters.[2] Typically, this transformation is performed with alkyl halides in the presence of at least an equimolar amount of base, which results in the generation of large quantities of waste salts.[3] This is the significant drawback of this protocol. As green chemistry becomes a crucial concern in contemporary chemistry, a synthetic approach with environmental benignity, simple manipulation, and high atom economy is extremely desirable.[4] The catalytic direct alkylation of β-dicarbonyl compounds with unmodified electrophiles such as alcohols, providing water as the only byproduct, would be a suitable alternative. However, because of the poor leaving ability of the hydroxy group, excess amount of Brønsted or Lewis acids is required for this kind of transformation.[5]

Recent examples have shown that the direct alkylation of β-dicarbonyl compounds with allylic alcohols catalyzed by Pd,[6] Co,[7] and Cu[8] in the presence of various additives has been well developed. Very recently, many chemists have focused their attention on the acid-catalyzed alkylation processes that are considered to be the most promising approaches in this field. In this context, various Lewis acids such as $InCl_3$,[9] $InBr_3$,[10] $FeCl_3$,[11] $Bi(OTf)_3$,[12] $Ln(OTf)_3$ (Ln = La, Yb, Sc, Hf),[13] a Lewis acidic ruthenium complex,[14] as well as Brønsted acids including proton-exchanged montmorillonite,[15] *p*-toluenesulfonic acid,[16] triflic acid,[16c] and dodecylbenzenesulfonic acid[17] have been demonstrated to facilitate the dehydrative substitution of allylic and benzylic alcohols with β-dicarbonyl compounds. Furthermore, molecular iodine has also been found to be effective in this transformation.[18]

The heteropoly acids (HPAs) such as 12-phosphotungstic acid (PWA) and 12-phosphomolybdic acid (PMA) are often employed as efficient and green catalysts in many organic processes.[19] Recently, we reported the PWA-catalyzed amidation of alcohols[20a] and hydroalkylation of olefins with 1,3-diketones.[20b] Herein we describe a direct carbon–carbon bond forming reaction of benzylic alcohols with various β-dicarbonyl compounds catalyzed by PWA.

Results and Discussion

As a starting point for reaction conditions optimizations, the reaction of acetylacetone (**1a**) and benzhydryl alcohol (**2a**) was chosen as the prototype reaction and various conditions were screened. The results are listed in Table 1. When the two reactants were mixed with PWA in toluene at 20 °C, only a trace amount of product was observed after 20 h (Table 1, entry 1). Elevating the reaction temperature proved helpful, and the yield of desired product **3aa** increased considerably (Table 1, entries 2 and 3). We were pleased to find that the reaction proceeded with the highest efficiency at 80 °C, affording **3aa** in 92% yield with shorter reaction time (Table 1, entry 4). Further increasing the reaction temperature was unnecessary as a slight decrease in yield was observed (Table 1, entry 5). Then other protic and aprotic solvents of different polarities were examined. *n*-Heptane was also employed as the reaction medium in this transformation; however, in our protocol only a moderate yield was obtained (Table 1, entry 6). A similar result was found in cyclohexane (Table 1, entry 7), whereas the reaction in the halogenated solvent 1,2-dichloroethane (DCE)

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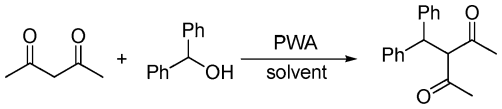
proceeded with higher efficiency (86% yield; Table 1, entry 8). A high yield (85%) was also achieved with acetonitrile as the solvent (Table 1, entry 9). Surprisingly, the reaction proceeded smoothly and efficiently in ethyl acetate, affording the alkylated diketone in 90% yield (Table 1, entry 10). No expected reaction was observed with ethanol and PEG-400 as the reaction media (Table 1, entries 11 and 12). An attempt to perform the reaction in water was also unsuccessful (Table 1, entry 13).

Table 1. Optimizing the reaction conditions for the direct alkylation of acetylacetone (**1a**) with benzhydryl alcohol (**2a**) catalyzed by PWA.[a]



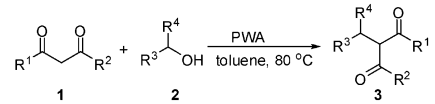
1a **2a** **3a**

Entry	Solvent	*T* [°C]	Time [h]	Yield [%][b]
1	toluene	20	20	trace
2	toluene	40	16	24
3	toluene	60	16	68
4	toluene	80	10	92
5	toluene	90	8	89
6	*n*-heptane	80	12	75
7	cyclohexane	reflux	14	79
8	DCE	80	8	86
9	CH_3CN	reflux	10	85
10	EtOAc	reflux	9	90
11	EtOH	reflux	12	NR[c]
12	PEG-400	80	12	NR[c]
13	H_2O	80	12	NR[c]

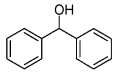
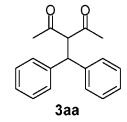
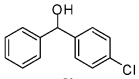
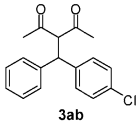
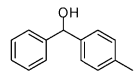
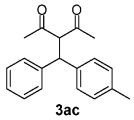
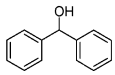
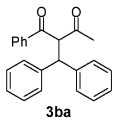
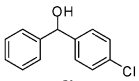
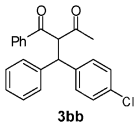
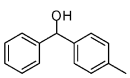
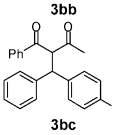
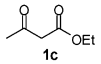
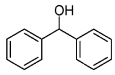
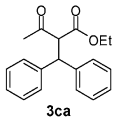
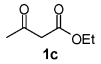
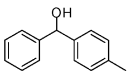
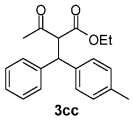
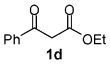
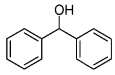
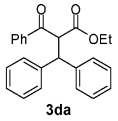
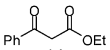
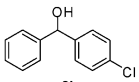
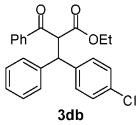
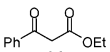
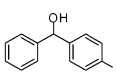
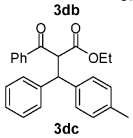
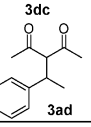
[a] All reactions were performed with acetylacetone (**1a**; 0.25 mmol), benzhydryl alcohol (**2a**; 0.25 mmol), and PWA (5 mg) in the indicated solvent. [b] Isolated yield after flash column chromatography. [c] No expected reaction was observed.

After optimizing the reaction conditions, we commenced to test the substrate generality of this protocol with regard to both coupling partners. These results are summarized in Table 2. At 80 °C in toluene, the reaction of acetylacetone with benzhydrylic alcohols proceeded in excellent yields (90–96%), and the electron-withdrawing group on the phenyl ring of alcohols improved the yield slightly (Table 2, entries 1–3). High yields (83–94%) of the corresponding products were also obtained when benzoylacetone was employed (Table 2, entries 4–6). The unsymmetric benzhydrylic alcohols gave the final products as mixtures of two inseparable diastereomers (Table 2, entries 5 and 6). To our delight, ethyl acetoacetate was also tolerable under the present conditions, giving the alkylated β-keto esters in high yields (85–89%; Table 2, entries 7 and 8). Similarly, the reactions of ethyl benzoylacetate with the benzhydrylic alcohols proceeded smoothly and efficiently (Table 2, entries 9–11). Diastereomers were also observed when unsymmetric benzhydrylic alcohols were employed. Unfortunately, when 1-phenylethanol was utilized as the alkylating agent in the reaction with acetylacetone, desired product **3ad** was isolated in poor yield even when the reaction time was prolonged (Table 2, entry 12).

Table 2. PWA-catalyzed direct alkylation of β-dicarbonyl compounds with benzylic alcohols.[a]



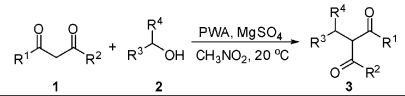
1 **2** **3**

Entry	β-Dicarbonyl compound	Alcohol	Time [h]	Product	Yield [%][b]
1	 **1a**	 **2a**	10	 **3aa**	92
2	 **1a**	 **2b**	8	 **3ab**	96
3	 **1a**	 **2c**	12	 **3ac**	90
4	 **1b**	 **2a**	10	 **3ba**	92
5	 **1b**	 **2b**	7	 **3bb**	94 (1:1)[c]
6	 **1b**	 **2c**	11	 **3bc**	83 (1:1)[c]
7	 **1c**	 **2a**	11	 **3ca**	89
8	 **1c**	 **2c**	10	 **3cc**	85 (2:1)[c]
9	 **1d**	 **2a**	9	 **3da**	92
10	 **1d**	 **2b**	12	 **3db**	87 (2:1)[c]
11	 **1d**	 **2c**	12	 **3dc**	84 (1:1)[c]
12	 **1a**	 **2d**	24	 **3ad**	32

[a] All reactions were performed with β-dicarbonyl compound **1** (0.25 mmol), benzylic alcohol **2** (0.25 mmol), and PWA (5 mg) in toluene (1 mL) at 80 °C. [b] Isolated yield after flash column chromatography. [c] Ratio of the two diastereomers determined by ^{1}H NMR spectroscopic analysis.

Accordingly, the above reaction system was not suitable for 1-phenylethanol, and further improvement was required urgently. Delightfully, after screening various solvents and additives, we finally discovered that the reactions of β-diketones with 1-phenyethanol were highly efficient in nitromethane at 20 °C, delivering the corresponding alkylated products in excellent yields. The dehydration agent $MgSO_4$ played a crucial role in the high conversion of the reaction. The results are shown in Table 3. Obviously, the reaction of β-diketones including acetylacetone, benzoylacetone, and dibenzoylmethanes with 1-phenylethanol gave the corresponding products in high yields, ranging from 84 to 95% within 2 h (Table 3, entries 1–6). The allylic alcohol derived from chalcone was also tolerable under the current reaction conditions, affording the allylated diketones in excellent yields (91–97%) within 30 min (Table 3, entries 7 and 8). Because PWA is soluble in nitromethane, the homogeneous reaction system might increase the reaction rate. In contrast, the reaction of acetylacetone with benzhydryl alcohol in nitromethane was disadvantageous, and product **3aa** was isolated in low yield along with a large quantity of benzophenone derived from the alcohol (Table 3, entry 9). As a result, the reactions in toluene and in nitromethane were complementary to each other, offering the alkylation reactions of β-dicarbonyl compounds with both benzylic and allylic alcohols in high yields.

Table 3. PWA-catalyzed direct alkylation of β-dicarbonyl compounds with alcohols in nitromethane.[a]



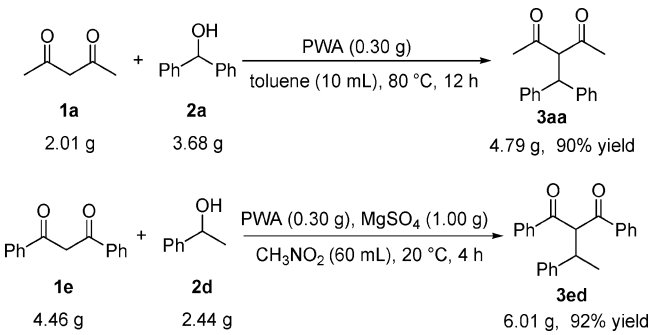
1 2 3

Entry	β-Dicarbonyl compound	Alcohol	Time [min]	Product	Yield [%][b]
1[c]	1a	2d	120	3ad	84
2	1b	2d	120	3bd	95 (4:3)[d]
3	1e	2d	120	3ed	92
4	1f	2d	120	3fd	88
5	1g	2d	90	3gd	95
6	1h	2d	120	3hd	93 (3:2)[d]
7	1e	2e	30	3ee	97
8	1a	2e	30	3ae	91
9	1a	2a	120	3aa	40

[a] Unless otherwise specified, all reactions were performed with β-dicarbonyl compound **1** (0.25 mmol), benzylic alcohol **2** (0.25 mmol), $MgSO_4$ (50 mg), and PWA (5 mg) in CH_3NO_2 (1 mL) at 20 °C. [b] Isolated yield after flash column chromatography. [c] A larger amount of alcohol (0.4 mmol) was employed, and the reaction was performed at 80 °C. [d] Ratio of the two diastereomers determined by ^1H NMR spectroscopic analysis.

It should be mentioned that in the above reactions the catalyst loading of PWA ($H_3PW_{12}O_{40}{\cdot}nH_2O$) was very low, that is, only 5 mg (≈0.6 mol-%), reflecting the high efficiency of PWA.

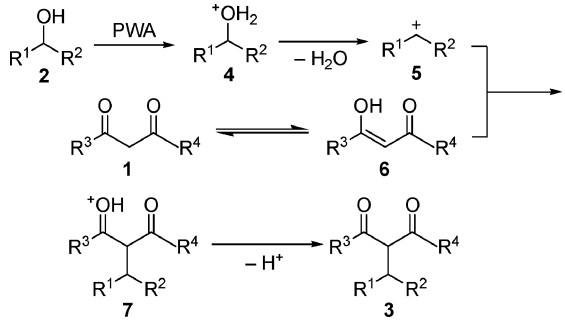
To further highlight the advantage of our protocol, the gram-scale synthesis of the monoalkylated dicarbonyl compounds under different conditions was performed (Scheme 1). After optimizing the reaction conditions, we were pleased to find that the reaction of acetylacetone (**1a**) with benzhydryl alcohol (**2a**) in toluene was able to proceed on a 20-mmol scale, giving final product **3aa** in 90% yield. The reaction of dibenzoylmethane (**1e**) with 1-phenylethanol (**2d**) in nitromethane was also examined, and alkylated product **3ed** was obtained in 92% yield. It is important to emphasize that these reactions should be performed in higher concentrations relative to those performed on small scale. The yield decreased obviously when the reaction was carried out in a more dilute solution. Noteworthy is that the catalyst loading of PWA could be further reduced in the multigram synthesis.



Scheme 1. Gram-scale synthesis of **3aa** and **3ed**.

According to our previous work on the PWA-catalyzed direct amidation of benzylic alcohols,[20a] we hypothesized that an S_N1 pathway would be reasonable for this alkylation

reaction. By action of PWA, the alcohol was protonated to generate a stable benzyl cation after dehydration. This carbocation could quickly combine with the employed β-dicarbonyl compound to produce, after the release of H^+, the final alkylated product (Scheme 2).



Scheme 2. Proposed mechanism for the catalytic addition of β-dicarbonyl compounds to alcohols.

Conclusions

In summary, we have demonstrated a highly efficient methodology for the direct alkylation of β-dicarbonyl compounds with various benzylic and allylic alcohols as alkylating agents catalyzed by cheap 12-phosphotungstic acid. This protocol provides a clean, efficient, synthetically competitive, and cheap alternative to the existing catalytic systems.

Experimental Section

General: Reagents and solvents were obtained from commercial sources and were not further purified before use. All melting points are uncorrected. Infrared spectra were recorded in KBr pellets and reported in cm^{-1}. ^1H NMR spectra were recorded at 300 MHz and are reported in parts per million (ppm) relative to tetramethylsilane (δ = 0.00 ppm). ^{13}C NMR spectra were recorded at 75 MHz and are reported in parts per million (ppm) relative to $CDCl_3$ (δ = 77.16 ppm). High-resolution mass spectra (HRMS) were recorded in the EI mode.

General Procedure for the Direct Alkylation of β-Dicarbonyl Compounds with Benzylic Alcohols in Toluene: To a small vial was added β-dicarbonyl compound **1** (0.25 mmol), alcohol **2** (0.25 mmol), and 12-phosphotungstic acid (5 mg) in toluene (1 mL). The mixture was stirred at 80 °C for the indicated time (monitored by TLC). Upon completion, the solvent was removed under reduced pressure, and the residue was purified by column chromatography (silica gel; petroleum ether/ethyl acetate, 4:1) to obtain desired product **3**. **3aa** (61.2 mg, 92%); **3ab** (72.1 mg, 96%); **3ac** (63.0 mg, 90%); **3ba** (75.5 mg, 92%); **3bb** (85.5 mg, 94%); **3bc** (71.2 mg, 83%); **3ca** (66.4 mg, 89%); **3cc** (66.3 mg, 85%); **3da** (82.4 mg, 92%); **3db** (85.2 mg, 87%); **3dc** (78.2 mg, 84%); **3ad** (16.1 mg, 32%).

General Procedure for the Direct Alkylation of β-Dicarbonyl Compounds with Benzylic Alcohols in Nitromethane: To a small vial was added β-dicarbonyl compound **1** (0.25 mmol), alcohol **2** (0.25 mmol), $MgSO_4$ (50 mg), 12-phosphotungstic acid (5 mg), and CH_3NO_2 (1 mL). The vial was sealed, and the reaction mixture was stirred at 20 °C for the indicated time (monitored by TLC). Upon completion, the solvent was removed under reduced pressure, and the residue was purified by column chromatography (silica gel; petroleum ether/ethyl acetate, 4:1) to obtain desired product **3**. **3ad** (42.4 mg, 84%); **3bd** (63.2 mg, 95%); **3ed** (75.0 mg, 92%); **3fd** (78.3 mg, 88%); **3gd** (94.1 mg, 95%); **3hd** (84.2 mg, 93%); **3ee** (100.9 mg, 97%); **3ae** (66.4 mg, 91%); **3aa** (26.6 mg, 40%).

Procedure for the Gram-Scale Synthesis of Alkylated Product 3aa in Toluene: To a 50-mL round-bottom flask was added acetylacetone (2.01 g, 20 mmol), benzhydryl alcohol (3.68 g, 20 mmol), 12-phosphotungstic acid (0.30 g), and toluene (10 mL). The mixture stirred at 80 °C for 12 h (monitored by TLC). Upon completion, the solvent was removed under reduced pressure, and the residue was was purified by column chromatography (silica gel; petroleum ether/ethyl acetate, 4:1) to obtain desired product **3aa** (4.79 g, 90%).

Procedure for the Gram-scale Synthesis of Alkylated Product 3ed in Nitromethane: To a 100-mL round-bottom flask was added dibenzoylmethane (4.46 g, 20 mmol), 1-phenylethanol (2.44 g, 20 mmol), $MgSO_4$ (1.00 g), 12-phosphotungstic acid (0.30 g), and nitromethane (60 mL). The mixture was allowed to stir at 20 °C for 4 h (monitored by TLC). Upon completion, the solvent was removed under reduced pressure, and the residue was purified by column chromatography (silica gel; petroleum ether/ethyl acetate, 4:1) to obtain desired product **3ed** (6.01 g, 92%).

Compounds **3aa**,[9a,16c] **3ab**,[16c] **3ba**,[21] **3ca**,[5b,16c] **3da**,[22] **3ad**,[9a,12,16c] **3bd**,[12,16c] **3ed**,[12,16c] **3ee**,[23] and **3ae**[9a] were previously reported and their structures were confirmed by comparison of their spectroscopic data with the reported data. Characterization data for new compounds **3ac**, **3bb**, **3bc**, **3cc**, **3 db**, **3dc**, **3fd**, **3gd** and **3hd** are given below.

3-[Phenyl(*p*-tolyl)methyl]pentane-2,4-dione (3ac): ^1H NMR (300 MHz, $CDCl_3$): δ = 7.25–7.23 (m, 4 H, ArH), 7.17–7.12 (m, 3 H, ArH), 7.06 (d, J = 7.5 Hz, 2 H, ArH), 4.76 (d, J = 12.3 Hz, 1 H, CH), 4.69 (d, J = 12.3 Hz, 1 H, CH), 2.25 (s, 3 H, $ArCH_3$), 1.99 (s, 3 H, $COCH_3$), 1.98 (s, 3 H, $COCH_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 203.09, 141.66, 138.40, 136.70, 129.69, 128.98, 127.77, 127.68, 127.01, 74.69, 51.00, 29.79, 29.69, 21.01 ppm. IR (KBr): $\tilde{\nu}$ = 3024, 2924, 1730, 1704, 1513, 1494, 1452, 1417, 1358, 1283, 1238, 1187, 1167, 1143, 956, 831, 796, 777, 738, 697, 618, 583, 535, 489 cm^{-1}. HRMS (EI–TOF): calcd. for $C_{19}H_{20}O_2$ $[M]^+$ 280.1463; found 280.1461.

2-[(4-Chlorophenyl)(phenyl)methyl]-1-phenylbutane-1,3-dione (3bb): Characterized as a 1:1 diastereomeric mixture. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.90–7.85 (m, 2 H, ArH), 7.53–7.45 (m, 1 H, ArH), 7.39–7.33 (m, 2 H, ArH), 7.26–7.00 (m, 9 H, ArH), 5.48 (d, J = 12.0 Hz, 1 H, CH), 5.02 (d, J = 12.0 Hz, 1 H, CH), 1.98 (s, 1.5 H, $COCH_3$), 1.95 (s, 1.5 H, $COCH_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 202.63, 202.56, 194.07, 141.31, 140.85, 140.48, 139.99, 136.97, 136.89, 133.97, 133.86, 133.11, 132.64, 129.59, 129.26, 129.22, 128.99, 128.96, 128.92, 128.89, 128.82, 128.18, 127.79, 127.45, 127.03, 68.94, 50.93, 50.88, 28.03, 27.94 ppm. IR (KBr): $\tilde{\nu}$ = 2922, 1721, 1668, 1596, 1491, 1449, 1358, 1263, 1207, 1154, 1091, 1014, 769, 755, 697, 546 cm^{-1}. HRMS (EI–TOF): calcd. for $C_{23}H_{19}O_2{}^{35}Cl$ $[M]^+$ 362.1074; found 362.1080.

1-Phenyl-2-[phenyl(*p*-tolyl)methyl]butane-1,3-dione (3bc): Characterized as a 1:1 diastereomeric mixture. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.95–7.90 (m, 2 H, ArH), 7.52–7.48 (m, 1 H, ArH), 7.42–6.98 (m, 10 H, ArH), 6.92 (d, J = 7.8 Hz, 1 H, ArH), 5.57 (d, J = 12.0 Hz, 0.5 H, CH), 5.56 (d, J = 12.0 Hz, 0.5 H, CH), 5.04 (d, J = 12.0 Hz, 1 H, CH), 2.26 (s, 1.5 H, $ArCH_3$), 2.14 (s, 1.5 H, $ArCH_3$), 2.02 (s, 1.5 H, $COCH_3$), 2.00 (s, 1.5 H, $COCH_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 203.15, 203.12, 194.52, 194.36,

142.10, 141.64, 138.91, 138.36, 137.16, 137.04, 136.82, 136.32, 133.70, 129.78, 129.47, 129.06, 128.88, 128.83, 128.74, 128.22, 128.11, 127.80, 127.66, 127.12, 126.71, 69.19, 69.15, 51.28, 51.24, 27.88, 21.12, 20.98 ppm. IR (KBr): $\tilde{\nu}$ = 3058, 3027, 2921, 1722, 1671, 1596, 1449, 1357, 1265, 1153, 974, 770, 697, 538 cm^{-1}. HRMS (EI–TOF): calcd. for $C_{24}H_{22}O_2$ $[M]^+$ 342.1620; found 342.1626.

Ethyl 3-Oxo-2-[phenyl(*p*-tolyl)methyl]butanoate (3cc): Characterized as a 2:1 diastereomeric mixture. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.24–6.99 (m, 9 H, ArH), 4.67 (d, J = 12.2 Hz, 1 H, CH), 4.44 (d, J = 12.2 Hz, 1 H, CH), 3.97–3.88 (m, 2 H, OCH_2CH_3), 2.21 (s, 3 H, $ArCH_3$), 2.05 (s, 1 H, $COCH_3$), 2.03 (s, 2 H, $COCH_3$), 0.98 (t, J = 7.1 Hz, 2 H, OCH_2CH_3), 0.94 (t, J = 7.1 Hz, 1 H, OCH_2CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 201.90, 167.86, 167.82, 141.95, 141.65, 138.73, 138.39, 136.63, 136.46, 129.63, 129.39, 128.91, 128.68, 127.88, 127.77, 127.65, 126.96, 126.84, 65.44, 65.40, 61.53, 50.69, 50.65, 30.03, 29.98, 21.05, 13.90, 13.86 ppm. IR (KBr): $\tilde{\nu}$ = 2981, 2921, 1738, 1710, 1513, 1495, 1453, 1362, 1299, 1276, 1215, 1163, 1019, 802, 701, 538 cm^{-1}. HRMS (EI–TOF): calcd. for $C_{20}H_{22}O_3$ $[M]^+$ 310.1569; found 310.1574.

Ethyl 2-Benzoyl-3-(4-chlorophenyl)-3-phenylpropanoate (3db): Characterized as a 2:1 diastereomeric mixture. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.99–7.94 (m, 2 H, ArH), 7.53–7.49 (m, 1 H, ArH), 7.43–7.37 (m, 2 H, ArH), 7.29–7.02 (m, 9 H, ArH), 5.33–5.28 (m, 1 H, CH), 5.02 (d, J = 11.7 Hz, 1 H, CH), 3.94–3.83 (m, 2 H, OCH_2CH_3), 0.93 (t, J = 7.1 Hz, 2 H, OCH_2CH_3), 0.88 (t, J = 7.1 Hz, 1 H, OCH_2CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 192.70, 192.65, 167.71, 167.61, 141.35, 140.52, 136.68, 136.61, 133.88, 133.77, 132.83, 132.51, 129.74, 129.22, 128.83, 128.76, 128.29, 127.77, 127.21, 126.92, 61.83, 61.79, 59.59, 59.41, 50.38, 13.89, 13.81 ppm. IR (KBr): $\tilde{\nu}$ = 2925, 1720, 1675, 1492, 1450, 1368, 1299, 1248, 1211, 1095, 1023, 984, 806, 697, 595 cm^{-1}. HRMS (EI–TOF): calcd. for $C_{24}H_{21}O_3{}^{35}Cl$ $[M]^+$ 392.1179; found 392.1175.

Ethyl 2-Benzoyl-3-phenyl-3-*p*-tolylpropanoate (3dc): Characterized as a 1:1 diastereomeric mixture. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.03–7.98 (m, 2 H, ArH), 7.52–7.47 (m, 1 H, ArH), 7.46–7.38 (m, 2 H, ArH), 7.36 (d, J = 7.2 Hz, 1 H, ArH), 7.29–7.01 (m, 7 H, ArH), 6.94 (d, J = 8.1 Hz, 1 H, ArH), 5.38 (d, J = 11.7 Hz, 1 H, CH), 5.03 (d, J = 11.7 Hz, 1 H, CH), 3.94–3.89 (m, 2 H, OCH_2CH_3), 2.27 (s, 1.5 H, $ArCH_3$), 2.17 (s, 1.5 H, $ArCH_3$), 0.95 (t, J = 7.2 Hz, 1.5 H, OCH_2CH_3), 0.92 (t, J = 7.2 Hz, 1.5 H, OCH_2CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 193.09, 192.93, 167.92, 142.13, 138.93, 138.90, 136.87, 136.83, 136.47, 136.16, 133.61, 129.40, 129.36, 128.83, 128.79, 128.76, 128.65, 128.34, 128.15, 127.80, 127.65, 126.88, 126.58, 61.62, 59.67, 50.67, 21.11, 20.99, 13.85, 13.81 ppm. IR (KBr): $\tilde{\nu}$ = 2980, 2923, 1739, 1674, 1449, 1294, 1264, 1249, 1211, 1153, 1026, 986, 802, 741, 698, 599, 569 cm^{-1}. HRMS (EI–TOF): calcd. for $C_{25}H_{24}O_3$ $[M]^+$ 372.1725; found 372.1732.

1,3-Bis(4-methylphenyl)-2-(1-phenylethyl)propane-1,3-dione (3fd): ^1H NMR (300 MHz, $CDCl_3$): δ = 7.95 (d, J = 8.1 Hz, 2 H, ArH), 7.66 (d, J = 8.1 Hz, 2 H, ArH), 7.28–7.06 (m, 9 H, ArH), 5.54 (d, J = 10.2 Hz, 1 H, CH), 4.07 (dq, J = 10.2, 6.9 Hz, 1 H, $CHCH_3$), 2.38 (s, 3 H, $ArCH_3$), 2.29 (s, 3 H, $ArCH_3$), 1.32 (d, J = 6.9 Hz, 3 H, $CHCH_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 194.78, 194.29, 144.59, 144.32, 143.99, 134.92, 134.66, 129.66, 129.28, 129.17, 128.84, 128.51, 127.87, 126.64, 65.00, 41.21, 21.77, 21.68, 20.44 ppm. IR (KBr): $\tilde{\nu}$ = 2962, 1689, 1654, 1606, 1450, 1408, 1317, 1273, 1224, 1179, 1119, 1024, 977, 908, 815, 699, 614, 594, 562, 533 cm^{-1}. HRMS (EI–TOF): calcd. for $C_{25}H_{24}O_2$ $[M]^+$ 356.1776; found 356.1774.

1,3-Bis(4-chlorophenyl)-2-(1-phenylethyl)propane-1,3-dione (3gd): ^1H NMR (300 MHz, $CDCl_3$): δ = 7.95 (d, J = 8.4 Hz, 2 H, ArH), 7.66 (d, J = 8.4 Hz, 2 H, ArH), 7.42 (d, J = 8.4 Hz, 2 H, ArH), 7.26 (d, J = 8.4 Hz, 2 H, ArH), 7.20–7.09 (m, 5 H, ArH), 5.42 (d, J = 10.2 Hz, 1 H, CH), 4.04 (dq, J = 10.2, 6.9 Hz, 1 H, $CHCH_3$), 1.33 (d, J = 6.9 Hz, 3 H, $CHCH_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 193.74, 193.61, 143.46, 140.52, 139.93, 135.40, 135.24, 130.38, 130.05, 129.40, 129.01, 128.68, 127.83, 127.00, 65.91, 41.28, 20.33 ppm. IR (KBr): $\tilde{\nu}$ = 2964, 1695, 1660, 1587, 1489, 1399, 1273, 1219, 1200, 1094, 982, 910, 847, 831, 756, 696, 615, 530 cm^{-1}. HRMS (EI–TOF): calcd. for $C_{23}H_{18}O_2{}^{35}Cl_2$ $[M]^+$ 396.0684; found 396.0678.

1-(4-Chlorophenyl)-3-phenyl-2-(1-phenylethyl)propane-1,3-dione (3hd): Characterized as a 3:2 diastereomeric mixture. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.02 (d, J = 8.1 Hz, 1.2 H, ArH), 7.96 (d, J = 8.1 Hz, 0.8 H, ArH), 7.72 (d, J = 8.1 Hz, 0.8 H, ArH), 7.67 (d, J = 8.1 Hz, 1.2 H, ArH), 7.59–7.09 (m, 10 H, ArH), 5.53–5.48 (m, 1 H, CH), 4.09–4.03 (m, 1 H, $CHCH_3$), 1.34 (d, J = 6.9 Hz, 3 H, $CHCH_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 194.86, 194.66, 193.95, 193.68, 143.71, 140.29, 139.70, 137.20, 136.96, 135.53, 135.37, 133.82, 133.31, 130.37, 130.03, 129.29, 129.05, 128.93, 128.62, 127.84, 126.87, 65.51, 65.42, 41.35, 41.21, 20.41, 20.23 ppm. IR (KBr): $\tilde{\nu}$ = 2964, 1695, 1659, 1588, 1491, 1448, 1399, 1270, 1220, 1199, 1094, 981, 907, 846, 760, 695, 615, 531 cm^{-1}. HRMS (EI–TOF): calcd. for $C_{23}H_{19}O_2{}^{35}Cl$ $[M]^+$ 362.1074; found 362.1070.

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