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Note

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Nucleophilic and electrophilic double aroylation of chalcones with benzils promoted by the dimsyl anion as a route to all carbon tetrasubstituted olefins

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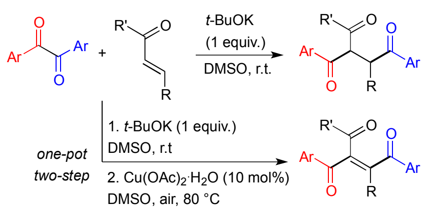
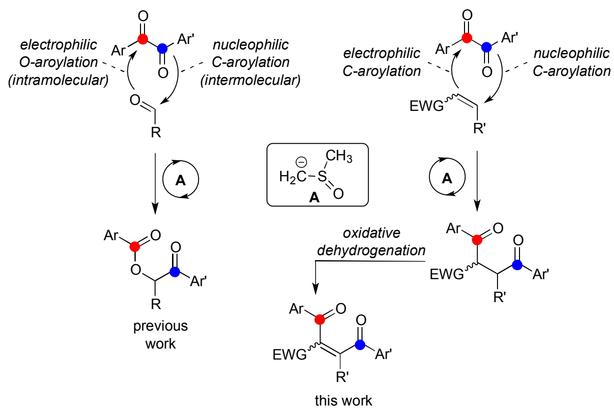


Abstract: Dimsyl anion promoted the polarity reversal of benzils in a Stetter-like reaction with chalcones to give 2-benzoyl-1,4-diones (double aroylation products), which in turn were converted into the corresponding tetrasubstituted olefins via aerobic oxidative dehydrogenation catalyzed by $Cu(OAc)_2$.

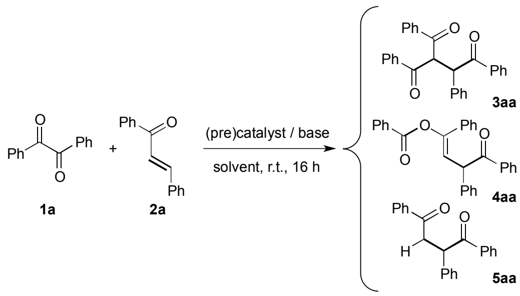
Atom-economical reactions represent a powerful tool in synthetic organic chemistry and a means to mitigate its negative effects on the environment.[1] In this context, the formation of multiple bonds in a single organocatalytic transformation is of great significance to readily access diverse structural motifs displaying all portions of the starting materials.[2] Bi-functional molecules constitute valuable substrates for the design of organocatalytic domino sequences; nevertheless, the use of highly reactive α-diketones has been rarely investigated in this type of approach,[3] in which the double carbonyl functionality of 1,2-diones exhibits electrophilic behavior at the carbonyl carbon and nucleophilic character at the alpha position. A complementary mode of carbonyl reactivity is, however, possible for this class of substrates; as demonstrated by our group, α-diketones can be rendered nucleophilic at carbonyl carbon (umpolung reactivity) through the catalysis of thiamine diphosphate (ThDP)-dependent enzymes[4] and *N*-heterocyclic carbenes (NHCs)[5] in nucleophilic acylations. Recently, we also discovered the capability of methylsulfinyl (dimsyl) carbanion **A** to induce the polarity reversal of diaryl α-diketones (benzils) in chemoselective cross-benzoin condensations with aldehydes.[6] Dimsyl anion, generated by deprotonation of the DMSO solvent, served as surrogate of hazardous cyanide ion promoting the formation of benzoylated benzoins in a atom-economic fashion through sequential nucleophilic *C*- and electrophilic *O*-aroylations (Scheme 1). As a logical extension of the study on the benzoin reaction, we reasoned that utility of dimsyl anion catalysis could be further enhanced by conducting a double *C*-aroylation process on activated alkenes, thus providing a novel variant of the parent Stetter reaction (hydroacylation process).[7] We also envisaged that the resulting activated 1,4-dicarbonyls could be further elaborated going back to the alkene stage via a catalytic oxidative dehydrogenation step to produce all carbon tetrasubstituted olefins from chalcones through a simple and effective one-pot process (Scheme 1). On the other hand, tetrasubstituted alkenes with conjugated systems are challenging synthetic targets[8] with unique structural and electronic features in material science[9] as well as useful building blocks for synthetic chemistry.[10]



SCHEME 1. Double aroylation of aldehydes and activated alkenes with benzils promoted by the dimsyl anion **A**.

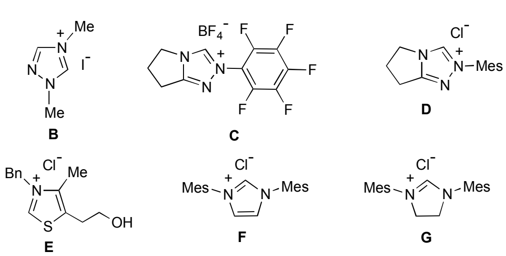
The reaction of benzil **1a** with chalcone **2a** was initially investigated to verify the feasibility of the project (Table 1). Reaction selectivity was a major issue to be addressed since formation of the desired double *C*-aroylation product **3aa** could be accompanied by generation of by-products **4aa** and **5aa** via competitive double *C*,*O*-aroylation and hydroacylation pathways, respectively (*vide infra*). Gratifyingly, under the conditions previously described for the generation of dimsyl anion **A** (anhydrous DMSO, 30 mol% *t*-BuOK, r.t.), the reaction of equimolar **1a** and **2a** gave the expected compound **3aa** (34%, entry 1) with only trace amounts of the Stetter product **5aa** and no evidence of **4aa**. While a mild heating (50 °C) of the reaction mixture had a negative effect on the reaction output (entry 2), an increase of *t*-BuOK amount (100 mol%) improved the yield of **3aa** (46%, entry 3), thus highlighting the importance of the excess of base to produce the necessary quantity of dimsyl anion (pK_a [DMSO] = 35.0; pK_a [*t*-BuOK] = 32.2).[11] In line with our previous findings, the reaction output was strictly correlated to the strength of the base in DMSO, that is *t*-BuOK > Cs_2CO_3 ≈ CsOH > DBU >> Et_3N (entries 4-7). Optimal reaction conditions delivering **3aa** in 75% yield (entry 8) were finally established using an excess of benzil **1a** (2 equiv.). For the sake of comparison, the catalytic activity of cyanide anion was also tested detecting the same reaction selectivity and a comparable but appreciably higher yield of **3aa** (83-82%, entries 10-11).

TABLE 1. Optimization of the model double *C*-aroylation of chalcone **2a** with benzil **1a**.[a]



Entry	Solvent	(Pre)catalyst (mol %)	Base (mol %)	Yield (%)
1[b]	DMSO	-	*t*-BuOK (30)	34
2[b,c]	DMSO	-	*t*-BuOK (30)	28
3[b]	DMSO	-	*t*-BuOK (100)	46
4	DMSO	-	DBU (100)	24
5	DMSO	-	Cs_2CO_3 (100)	32
6[d]	DMSO	-	CsOH (100)	35
7	DMSO	-	Et_3N (100)	-
8	DMSO	-	*t*-BuOK (100)	75
9[e]	DMSO	-	*t*-BuOK (100)	32
10	DMSO	KCN (25)	-	83
11	DMSO	TBACN (25)	-	82
12	CH_2Cl_2	**B** (20)	DBU (50)	15
13	CH_2Cl_2	**C** (20)	DBU (50)	-
14	CH_2Cl_2	**D** (20)	DBU (50)	-
15	DMSO	**E** (20)	NEt_3 (50)	-
16	DMSO	**F** (20)	DBU(50)	28
17	DMSO	**G** (20)	DBU (50)	25

[a]Reaction conditions: benzil **1a** (0.50 mmol), chalcone **2a** (0.25 mmol), and anhydrous solvent (1.0 mL). [b]**2a**: 0.50 mmol. [c]Temperature: 50 °C. [d]Reaction performed in the presence of 4 Å MS. [e]**2a**: 1.00 mmol.

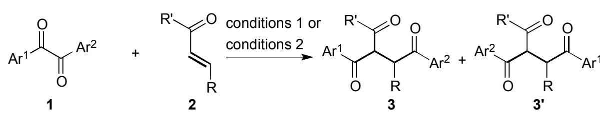


In addition, commercially available NHC salts **B-G** were screened under suitable conditions evaluating the effects of altering the solvent, temperature, and base. After some experimentation, it was found that the sole triazolium salt **B**-DBU couple catalyzed the reaction in CH_2Cl_2 affording **3aa** in modest yield (15%, entry 12). Indeed, the more hindered triazolium salts **C-D** (entries 13-14) and thiazolium,[12] imidazolium, and imidazolium pre-catalysts **E-G** (entries 15-17) proved to be totally inactive, being the observed formation of **3aa** in DMSO the result of a background activity of the dimsyl anion.

The substrate scope of the disclosed double *C*-aroylation reaction was initially examined with benzils **1a-h** and chalcones **2a-g** displaying various substitution patterns under two sets of conditions (Table 2). In general, the process promoted by the dimsyl anion (100 mol% *t*-BuOK, DMSO; conditions 1) provided a safe and environmentally benign access to 2-benzoyl-1,4-diones **3** and **3'**, albeit with slightly diminished yields (2-18%) compared to the same process catalyzed by the toxic KCN (25 mol%, DMSO; conditions 2). Relative efficiencies of reactions between benzil **1a** and chalcones **2a-g** bearing electron-withdrawing, -neutral, and -donating groups indicated a more pronounced effect of substituents on the benzoyl ring of chalcone, obtaining higher yields of **3** with electron poor aromatic rings (entries 1-7). Investigation on the electronic requirements for the α-diketone **1** showed the 2,2'-pyridyl **1b** with an electron-withdrawing moiety as a highly reactive substrate (entries 8-9); unexpectedly, the use of electron-deficient 4,4'-ditrifluoromethylbenzil **1c** and 4,4'-difluorobenzil **1d** led to a significant reduction of reaction efficiency (entries 10-11) mainly because of the diketone self-condensation side-reaction.[13] Combination of the electron-rich 4,4'-dimethylbenzil **1e** and activated chalcone **2b** rendered the corresponding product **3eb** with good conversion (entry 12).

The employment of unsymmetrical benzils **1f-h** produced the two regioisomers **3** and **3'** in variable isomeric ratios. The mono-substituted 2-chloro benzil **1f** exhibited the highest capability in controlling the chemoselectivity (**3**:**3'** cr) of the double *C*-aroylation process as it reacted with chalcone **2b** yielding almost exclusively the isomer **3fb**' (5:95 cr; entry 13). This result implied that dimsyl/cyanide anion favorably added to the less hindered carbonyl carbon of **1f**. Similarly, a comparison of the reactivity of mono-substituted 4-Cl and 4-OMe benzils **1g** and **1h** toward chalcone **2a** indicated the preferential attack of the catalyst to the diketone carbonyl carbon with lower electron density (entries 14-15). A limitation of the dimsyl anion-based methodology appeared evident from the representative couplings of enone **2h** (R = H) with benzil **1a** and activated 2,2'-pyridyl **1b** (entries 16-17). The expected products **3ah** and **3bh** were, in fact, detected in only trace amounts by MS analysis of the crude reaction mixtures;[14] by contrast, the cyanide-catalyzed couplings proceeded smoothly affording **3ah** and **3bh** in moderate and good yield, respectively.

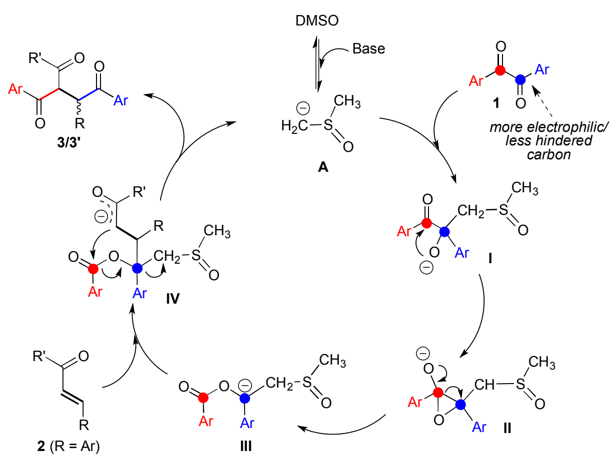
TABLE 2. Scope of the double *C*-aroylation reaction.[a]



Entry	Ar[1]	Ar[2]	1	R	R'	2	3 (dr)[b]	3' (dr)[b]	3+3' (%, %)[c]	3:3' (cr)[d]
1	Ph	Ph	**1a**	Ph	Ph	**2a**	**3aa**	[e]	75, 83	-
2	Ph	Ph	**1a**	4-ClC$_6$H$_4$	Ph	**2b**	**3ab**	[e]	77, 89	-
3	Ph	Ph	**1a**	4-BrPh	Ph	**2c**	**3ac**	[e]	70, 88	-
4	Ph	Ph	**1a**	4-MePh	Ph	**2d**	**3ad**	[e]	63,75	-
5	Ph	Ph	**1a**	Ph	4-ClC$_6$H$_4$	**2e**	**3ae** (1:1)	[e]	70, 86	-
6	Ph	Ph	**1a**	Ph	4-OMePh	**2f**	**3af** 1:1)	[e]	40, 44	-
7	Ph	Ph	**1a**	4-ClC$_6$H$_4$	4-OMePh	**2g**	**3ag** (1:1)	[e]	55, 70	-
8[f]	2-pyridyl	2-pyridyl	**1b**	Ph	Ph	**2a**	**3ba** (1.5:1)	[e]	79, 81	-
9[f]	2-pyridyl	2-pyridyl	**1b**	4-ClC$_6$H$_4$	Ph	**2b**	**3bb** (1.5:1)	[e]	77, 84	-
10	4-CF$_3$C$_6$H$_4$	4-CF$_3$C$_6$H$_4$	**1c**	Ph	Ph	**2a**	**3ca** (19:1)	[e]	30, 32	-
11	4-FC$_6$H$_4$	4-FC$_6$H$_4$	**1d**	Ph	Ph	**2a**	**3da** (1:1)	[e]	22, 29	-
12[f]	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	**1e**	4-ClC$_6$H$_4$	Ph	**2b**	**3eb** (1:1)	[e]	67, 82	-
13	Ph	2-ClC$_6$H$_4$	**1f**	4-ClC$_6$H$_4$	Ph	**2b**	**3fb**	**3fb'** (1.5:1)	44, 51	5:95
14	Ph	4-ClC$_6$H$_4$	**1g**	Ph	Ph	**2a**	**3ga**	**3ga'**[g] (1:1)	52, 64	70:30
15	Ph	4-OMeC$_6$H$_4$	**1h**	Ph	Ph	**2a**	**3ha**	**3ha'**[h] (1:1)	47, 58	16:84
16	Ph	Ph	**1a**	H	Ph	**2h**	**3ah**	[e]	<5, 28	-
17[f]	2-pyridyl	2-pyridyl	**1b**	H	Ph	**2h**	**3bh**	[e]	<5, 75	-

[a]Conditions 1: *t*-BuOK (100 mol%), DMSO, r.t, 16 h. Conditions 2: KCN (25 mol%), DMSO, r.t. 16 h. [b]Diastereomeric ratio determined by ^{1}H NMR analysis of crude reaction mixtures. [c]Yields (conditions 1/conditions 2). [d]Chemoselectivity ratio determined by ^{1}H NMR analysis of crude reaction mixtures. [e]**3' = 3**. [f]Conditions 1 with Cs_2CO_3 (100 mol%) as the base. [g]**3ga'= 3ae**. [h]**3ha' = 3af**.

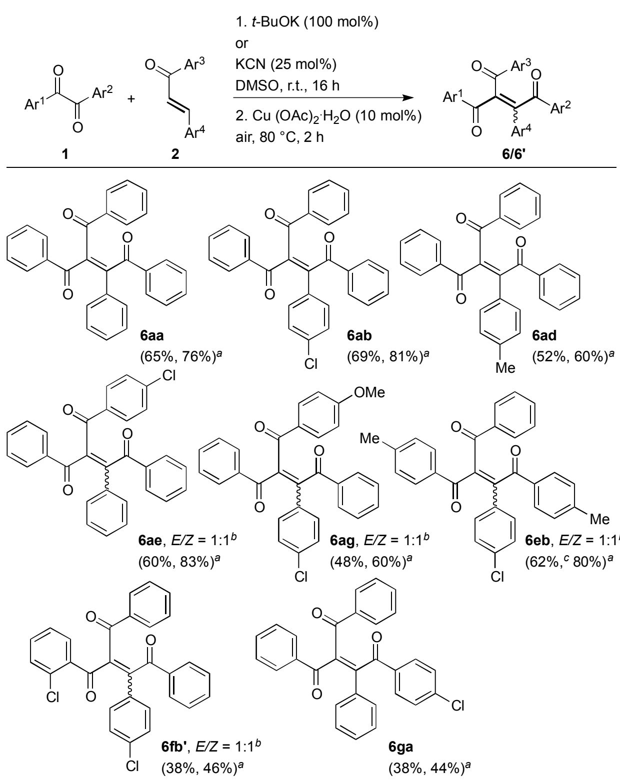
All these findings are in agreement with the following mechanistic proposal. Similarly to what reported for the cyanide catalysis,[15] addition of dimsyl anion **A** to the more electrophilic carbon (blue colored) of α-diketone **1** forms the intermediate **I**, which in turn evolves to the carbanion **III** via the epoxide **II**. Then, conjugate addition of **III** to chalcone **2** (R = Ar) affords the anion **IV**, which finally liberates the double *C*-aroylation product **3/3'** and the promoter **A** through an intramolecular Claisen-type reaction. Carbonyl group formation is supposed to be the driving force for the elimination of dimsyl anion in the final step of the proposed mechanism;[16] on the other hand, regeneration of the promoter **A** requires the presence of stoichiometric *t*-BuOK because of the higher acidity of the product **3/3'** compared to that of DMSO.[17] It can also be speculated that formation of the hydroacylation product of type **5aa** (Table 1), occasionally detected in trace amounts in some substrate combinations, originates from partial hydrolysis of the species **IV** with benzoyl group elimination. It is important to emphasize that involvement in the catalytic cycle of the acyl anion equivalent **III** and dimsyl anion **A** has been previously supported by ESI-MS/MS experiments and trapping of **A** with benzophenone.[6]



SCHEME 2. Proposed mechanism of the double *C*-aroylation reaction promoted by the dimsyl anion **A**.

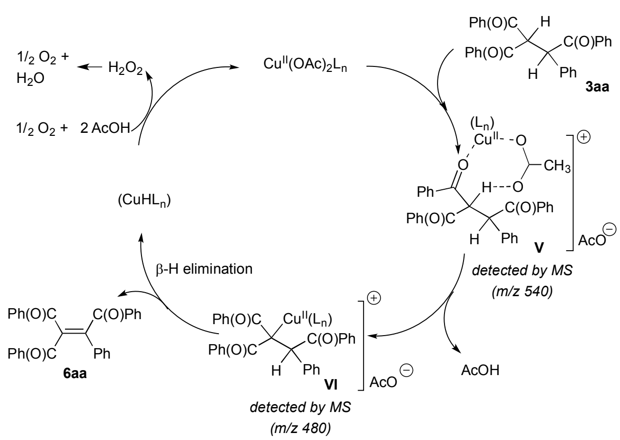
Next, to demonstrate the utility of the double *C*-aroylation process we showed that the 2-benzoyl-1,4-diones **3/3'** could be converted into the corresponding all carbon substituted olefins **6/6'** in a straightforward manner. Accordingly, the copper-catalyzed oxidative dehydrogenation of isolated **3/3'** was briefly investigated in DMSO; full conversions in **6/6'** were achieved using 10 mol% of $Cu(OAc)_2 \cdot H_2O$, *t*-BuOK (1 equiv.), and air as the terminal oxidant (80 °C, 2 h).[18] This result paved the way for the development of a convenient one-pot two-step process for the direct elaboration of chalcones **2** into the doubly aroylated olefins **6/6'**. Hence, to the solution of benzil **1** and chalcone **2** in DMSO was initially added *t*-BuOK (100 mol%) or KCN (25 mol%); then, after having established the completion of the reaction by TLC analysis, the reaction mixture containing the 2-benzoyl-1,4-dione **3/3'** was treated at 80 °C with $Cu(OAc)_2 \cdot H_2O$ (10 mol%) giving the desired tetrasubstituted olefins **6/6'** in satisfactory overall yields (Table 3).

TABLE 3. One-pot two-step synthesis of tetrasubstituted olefins **6/6'**.



[a]Yields (dimsyl catalysis/cyanide catalysis). [b]Diastereomeric ratio determined by ^1H and ^{13}C NMR analyses of crude reaction mixtures. [c]First step performed using Cs_2CO_3 (100 mol%) as the base.

To provide an insight into the mechanism of aerobic oxidative dehydrogenation,[19] **3aa** oxidation was initially performed in the presence of the radical scavenger TEMPO; **6aa** was obtained as the major product, thus suggesting that radicals were not involved in this reaction. Also, it was verified that **3aa** dehydrogenation could proceed in the absence of *t*-BuOK (or KCN) with lower kinetics but still high conversion efficiency. A parallel ESI-MS investigation on **3aa** oxidation without the base was then carried out to identify key intermediates of the catalytic cycle. When an acetonitrile solution of **3aa** was treated with $Cu(OAc)_2 \cdot H_2O$, formation of the ionic cluster **V** corresponding to [**3aa**+Cu^{II}(AcO)]$^+$ was observed at *m/z* 540 (^{63}Cu).[20] Relevant is the fact that **V** released AcOH during the MS/MS fragmentation with formation of the species **VI** (*m/z* 480), in which copper(II) replaces the lost proton.[20] Elimination of AcOH in the presence of deuterated acetonitrile unequivocally confirmed the proton abstraction from the substrate. It can be hypothesized that a similar mechanism of copper-mediated C-H activation may also occur in solution;[19a] β-hydride elimination should then complete the formation of the double bond in **6aa** with generation of a copper species,[21] which is converted to the active catalyst by molecular oxygen.



SCHEME 3. Proposed mechanism for the copper-catalyzed aerobic dehydrogenation of **3/3'** based on an ESI-MS/MS study.

In conclusion, we have developed a novel umpolung reaction consisting in the double aroylation of chalcones with benzils promoted by dimsyl or cyanide anion. The utility of the resulting 2-benzoyl-1,4-diones has been also demonstrated by their facile conversion into the corresponding tetrasubstituted olefins.

Experimental Section

Potassium *tert*-butoxide was purified by sublimation (200-220 °C at 1 mmHg) before utilization. Reactions were monitored by TLC on silica gel 60 F_{254} with detection by charring with phosphomolybdic acid. Flash column chromatography was performed on silica gel 60 (230-400 mesh). ^{1}H (300 MHz), ^{13}C (75 MHz), and ^{19}F (282 MHz) NMR spectra were recorded in $CDCl_3$ solutions at room temperature. Peaks assignments were aided by ^{1}H-^{1}H COSY and gradient-HMQC experiments. ESI-MS routine analyses were performed in positive ion mode with samples dissolved in 10 mM solution of ammonium formate in 1:1 MeCN/H_2O. For accurate mass measurements, the compounds were detected in positive ion mode by HPLC-Chip Q/TOF-MS (nanospray) analysis using a quadrupole, a hexapole, and a time-of-flight unit to produce spectra. Residual water of commercially available anhydrous DMSO (0.016% w/w) was determined by Karl Fisher analysis. Diketones **1a,b**, **1d**, **1e, 1h** and chalcones **2a-d** are commercially available compounds. Diketones **1c**,[22] **1f**,[6] **1g**,[6] chalcones **2e-g**,[23] and enone **2h**[24] were synthesized as described. The 2-benzoyl-1,4-dione **3ah** is a known compound.[7a]

Optimization of the model double *C*-aroylation of chalcone 2a with benzil 1a.

Entries 1-9. To a vigorously stirred mixture of benzil **1a** (105 mg, 0.50 mmol), the stated amount of chalcone **2a**, and anhydrous DMSO (1 mL), the stated amount of base (mol% based on **1a**) was added in one portion. Then, the mixture was degassed under vacuum and saturated with argon (by an argon-filled balloon) three times. The mixture was stirred at the stated temperature for 16 h, then diluted with H_2O (5 mL), extracted with CH_2Cl_2 (2 × 25 mL). The combined organic phases were washed with brine (5 mL), dried (Na_2SO_4), concentrated, and eluted from a column of silica gel with 10:1 cyclohexane-AcOEt to give **3aa**.

Entries 10-11. To a vigorously stirred mixture of benzil **1a** (105 mg, 0.50 mmol), **2a** (54 mg, 0.25 mmol), and anhydrous DMSO (1 mL), potassium cyanide (8.1 mg, 0.13 mmol) or tetrabutylammonium cyanide (34 mg, 0.13 mmol) was added in one portion. Then, the mixture was degassed under vacuum and saturated with argon (by an argon-filled balloon) three times. The mixture was stirred at the stated temperature for 16 h, then diluted with H_2O (5 mL), extracted with CH_2Cl_2 (2 × 25 mL). The combined organic phases were washed with brine (5 mL), dried (Na_2SO_4), concentrated, and eluted from a column of silica gel with 10:1 cyclohexane-AcOEt to give **3aa**.

Entries 12-17. To a vigorously stirred mixture of benzil **1a** (105 mg, 0.50 mmol), **2a** (54 mg, 0.25 mmol), stated amount of azolium salt (20 mol% based on **1a**) and anhydrous DMSO (1 mL), the stated base (0.25 mmol) was added in one portion. Then, the mixture was degassed under vacuum and saturated with argon (by an argon-filled balloon) three times. Then, the mixture was degassed under vacuum and saturated with argon (by an argon-filled balloon) three times. The mixture was stirred at the stated temperature for 16 h, then diluted with H_2O (5 mL), extracted with CH_2Cl_2 (2 × 25 mL). The combined organic phases were washed with brine (5 mL), dried (Na_2SO_4), concentrated, and eluted from a column of silica gel with 10:1 cyclohexane-AcOEt to give **3aa** (no product formation in entries 13-15).

General procedure for the double *C*-aroylation of activated alkenes 2 with benzils 1 promoted by the dimsyl anion (Conditions 1, Table 2). To a vigorously stirred mixture of benzil **1** (1.00 mmol), alkene **2** (0.50 mmol), and anhydrous DMSO (2 mL), potassium *tert*-butoxide (112 mg, 1.00 mmol) was added in one portion. Then, the mixture was degassed under vacuum and saturated with argon (by an argon-filled balloon) three times. The mixture was stirred at room temperature until complete disappearance or best conversion of the starting alkene (TLC analysis, ca. 2-16 h).

The mixture was then diluted with H_2O (5 mL), and extracted with CH_2Cl_2 (2 × 35 mL). The combined organic phases were washed with brine (8 mL), dried (Na_2SO_4), concentrated, and eluted from a column of silica gel with the suitable elution system to give **3/3'**.

General procedure for the double *C*-aroylation of activated alkenes 2 with benzils 1 catalyzed by potassium cyanide (Conditions 2, Table 2). To a vigorously stirred mixture of benzil **1** (1.00 mmol), alkene **2** (0.50 mmol), and anhydrous DMSO (2 mL), potassium cyanide (16 mg, 0.25 mmol) was added in one portion. Then, the mixture was degassed under vacuum and saturated with argon (by an argon-filled balloon) three times. The mixture was stirred at room temperature until complete disappearance or best conversion of the starting alkene (TLC analysis, ca. 2-16 h). The mixture was then diluted with H_2O (5 mL), and extracted with CH_2Cl_2 (2 × 35 mL). The combined organic phases were washed with brine (8 mL), dried (Na_2SO_4), concentrated, and eluted from a column of silica gel with the suitable elution system to give **3/3'**.

*2-Benzoyl-1,3,4-triphenylbutane-1,4-dione (**3aa**).* Column chromatography with 10:1 cyclohexane-AcOEt afforded **3aa** (155 mg, 75%; conditions 1) as a white amorphous solid. Conditions 2: **3aa** (174 mg, 83%). ^{1}H NMR: δ = 8.08-7.98 (m, 2 H, Ar), 7.95-7.89 (m, 2 H, Ar), 7.70-7.65 (m, 2 H, Ar), 7.54-7.44 (m, 2 H, Ar), 7.43-7.32 (m, 4 H, Ar), 7.31-7.21 (m, 5 H, Ar), 7.14-7.06 (m, 2 H, Ar), 7.05-6.95 (m, 1 H, Ar), 6.38 (d, *J* = 10.7 Hz, 1 H, H-2), 5.80 (d, *J* = 10.7 Hz, 1 H, H-3); ^{13}C{^{1}H} NMR: δ = 198.1, 195.9, 194.2, 136.6, 136.2, 135.9, 134.8, 133.4, 133.3, 133.1, 129.1, 129.0, 128.6, 128.5, 128.4, 127.8, 60.5, 55.2; IR ($CDCl_3$) ν: 3031, 2937, 1704, 1634, 1630, 1532 cm^{-1}. ESI MS (418.4): 441.6 (M + Na$^+$). HRMS (ESI/Q-TOF) calcd for $C_{29}H_{22}NaO_3$ ([M + Na]$^+$) 441.1467, found: 441.1474.

*2-Benzoyl-3-(4-chlorophenyl)-1,4-diphenylbutane-1,4-dione (**3ab**).* Column chromatography with 13:1 cyclohexane-AcOEt afforded **3ab** (174 mg, 77%; conditions 1) as a white amorphous solid.

Conditions 2: **3ab** (202 mg, 89%). ^{1}H NMR: δ = 8.04-7.96 (m, 2 H, Ar), 7.94-7.87 (m, 2 H, Ar), 7.74-7.67 (m, 2 H, Ar), 7.54-7.44 (m, 3 H, Ar), 7.44-7.35 (m, 3 H, Ar), 7.35-7.27 (m, 3 H, Ar), 7.24-7.19 (m, 2 H, Ar), 7.12-7.03 (m, 2 H, Ar), 6.36 (d, J = 10.7 Hz, 1 H, H-2), 5.79 (d, J = 10.7 Hz, 1 H, H-3); ^{13}C{^{1}H} NMR: δ = 197.8, 195.5, 194.0, 136.5, 136.1, 135.7, 133.8, 133.6, 133.5, 133.3, 130.3, 129.2, 129.0, 128.7, 128.7, 128.6, 60.4, 54.3; IR ($CDCl_3$) ν: 3061, 2960, 1689, 1660, 1659, 1596 cm^{-1}. ESI MS (452.9): 475.7 (M + Na^{+}). HRMS (ESI/Q-TOF) calcd for $C_{29}H_{21}ClNaO_3$ ([M + Na]$^{+}$) 475.1077, found: 475.1084.

*2-Benzoyl-3-(4-bromophenyl)-1,4-diphenylbutane-1,4-dione (**3ac**).* Column chromatography with 13:1 cyclohexane-AcOEt afforded **3ac** (173 mg, 70%; conditions 1) as a white amorphous solid. Conditions 2: **3ac** (218 mg, 88%). ^{1}H NMR: δ = 8.04-7.96 (m, 2 H, Ar), 7.95-7.88 (m, 2 H, Ar), 7.73-7.67 (m, 2 H, Ar), 7.53-7.43 (m, 3 H, Ar), 7.42-7.36 (m, 3 H, Ar), 7.35-7.27 (m, 3 H, Ar), 7.26-7.20 (m, 2 H, Ar), 7.18-7.12 (m, 2 H, Ar), 6.35 (d, J = 10.7 Hz, 1 H, H-2), 5.78 (d, J = 10.7 Hz, 1 H, H-3); ^{13}C{^{1}H} NMR: δ = 197.8, 195.5, 194.0, 136.5, 136.1, 135.7, 134.0, 133.6, 133.5, 133.3, 132.2, 130.7, 129.0, 128.7, 128.7, 128.6, 122.0, 60.4, 54.4; IR ($CDCl_3$) ν: 3062, 2924, 1690, 1663, 1661, 1595 cm^{-1}. ESI MS (497.4): 520.6 (M + Na^{+}). HRMS (ESI/Q-TOF) calcd for $C_{29}H_{21}BrNaO_3$ ([M + Na]$^{+}$) 519.0572, found: 519.0585.

*2-Benzoyl-1,4-diphenyl-3-(p-tolyl)butane-1,4-dione (**3ad**).* Column chromatography with 14:1 cyclohexane-AcOEt afforded **3ad** (136 mg, 63%; conditions 1) as a white amorphous solid. Conditions 2: **3ad** (163 mg, 75%). ^{1}H NMR: δ = 8.05-7.98 (m, 2 H, Ar), 7.95-7.88 (m, 2 H, Ar), 7.73-7.64 (m, 2 H, Ar), 7.52-7.39 (m, 4 H, Ar), 7.38-7.33 (m, 3 H, Ar), 7.32-7.27 (m, 2 H, Ar), 7.18-7.09 (m, 2 H, Ar), 6.93-6.88 (m, 2 H, Ar), 6.36 (d, J = 10.7 Hz, 1 H, H-2), 5.77 (d, J = 10.7 Hz, 1 H, H-3), 2.11 (s, 3 H, CH_3); ^{13}C{^{1}H} NMR: δ = 198.2, 195.9, 194.3, 137.5, 136.8, 136.3, 136.0, 133.3, 133.1, 133.0, 131.7, 129.7, 129.0, 128.9, 128.7, 128.7, 128.6, 128.5, 128.4, 60.7, 54.8, 20.9; IR ($CDCl_3$) ν: 3063, 2919, 1691, 1688, 1687, 1595 cm^{-1}. ESI MS (432.5): 455.5 ($M + Na^+$). HRMS (ESI/Q-TOF) calcd for $C_{30}H_{24}NaO_3$ ($[M + Na]^+$) 455.1623, found: 455.1614.

*2-Benzoyl-1-(4-chlorophenyl)-3,4-diphenylbutane-1,4-dione **(3ae)***. Column chromatography with 10:1 cyclohexane-AcOEt afforded **3ae** (158 mg, 70%; conditions 1) as a 1:1 mixture of diastereoisomers. Conditions 2: **3ae** (194 mg, 86%; dr = 1:1). Separation of the two diastereoisomers was carried by a second column chromatography using toluene as the elution system . First eluted diastereoisomer slightly contaminated by uncharacterized by-products: ^1H NMR: δ = 8.05-7.96 (m, 2 H, Ar), 7.89-7.82 (m, 2 H, Ar), 7.66-7.58 (m, 2 H, Ar), 7.53-7.22 (m, 10 H, Ar), 7.14-7.08 (m, 2 H, Ar), 7.07-7.00 (m, 1 H, Ar), 6.31 (d, *J* = 10.7 Hz, 1 H, H-2), 5.78 (d, *J* = 10.7 Hz, 1 H, H-3); $^{13}C\{^1H\}$ NMR: δ = 198.0, 195.6, 193.0, 139.9, 136.5, 135.8, 134.7, 134.5, 133.5, 133.2, 130.0, 129.1, 129.0, 129.0, 128.8, 128.6, 128.5, 128.4, 128.0, 127.8, 60.4, 55.3; IR ($CDCl_3$) ν: 3067, 2924, 1697, 1667, 1665, 1589 cm^{-1}. ESI MS (452.9): 475.8 ($M + Na^+$). HRMS (ESI/Q-TOF) calcd for $C_{29}H_{21}ClNaO_3$ ($[M + Na]^+$) 475.1077, found: 475.1083. Second eluted diastereoisomer: ^1H NMR: δ = 8.05-7.96 (m, 2 H, Ar), 7.92-7.85 (m, 2 H, Ar), 7.66-7.58 (m, 2 H, Ar), 7.52-7.43 (m, 2 H, Ar), 7.41-7.32 (m, 4 H, Ar), 7.29-7.22 (m, 4 H, Ar), 7.18-7.08 (m, 2 H, Ar), 7.07-7.00 (m, 1 H, Ar), 6.31 (d, *J* = 10.7 Hz, 1 H, H-2), 5.77 (d, *J* = 10.7 Hz, 1 H, H-3); $^{13}C\{^1H\}$ NMR: δ = 197.9, 194.8, 193.8, 139.9, 136.1, 135.8, 134.9, 134.7, 133.5, 133.2, 130.0, 129.2, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 127.9, 60.4, 55.1; IR ($CDCl_3$) ν: 3063, 2923, 1692, 1661, 1587 cm^{-1}. ESI MS (452.9): 475.7 ($M + Na^+$). HRMS (ESI/Q-TOF) calcd for $C_{29}H_{21}ClNaO_3$ ($[M + Na]^+$) 475.1077, found: 475.1092.

*2-Benzoyl-1-(4-methoxyphenyl)-3,4-diphenylbutane-1,4-dione **(3af)***. Column chromatography with 6:1 cyclohexane-AcOEt afforded **3af** (89 mg, 40%; conditions 1) as an inseparable 1:1 mixture of diastereoisomers. Conditions 2: **3af** (98 mg, 44%; dr = 1:1). ^1H NMR: δ = 8.05-7.98 (m, 2 H, Ar), 7.95-7.88 (m, 2 H, Ar), 7.73-7.64 (m, 2 H, Ar), 7.52-7.41 (m, 2 H, Ar), 7.41-7.32 (m, 4 H, Ar), 7.31-7.26 (m, 2 H, Ar), 7.15-7.06 (m, 2 H, Ar), 7.06-6.98 (m, 1 H, Ar), 6.85-6.69 (m, 2 H, Ar), 6.32 (d, *J* = 10.8 Hz, 0.5 H, H-2’), 6.31 (d, *J* = 10.8 Hz, 0.5 H, H-2”), 5.79 (d, *J* = 10.8 Hz, 0.5 H, H-3’), 5.78 (d, *J* = 10.8 Hz, 0.5H, H-3”), 3.80 (s, 1.5 H, CH_3’), 3.78 (s, 1.5 H, CH_3”); $^{13}C\{^1H\}$ NMR: δ = 198.3 (0.5 C), 198.1 (0.5 C), 196.0 (0.5 C), 194.4 (0.5 C), 194.0 (0.5 C), 192.4 (0.5 C), 163.7 (0.5 C), 163.4 (0.5 C), 136.7, 136.2, 136.0, 134.9, 133.3, 133.2, 133.0, 131.1, 130.3, 129.7, 129.6, 129.0, 128.7, 128.6, 128.5, 128.4, 127.7, 113.8 (0.5 C), 113.6 (0.5 C), 60.4 (0.5 C), 60.2 (0.5 C), 55.4, 55.1 (0.5 C), 55.0 (0.5 C); IR ($CDCl_3$) ν: 3062, 2936, 1672, 1669, 1667, 1596 cm^{-1}. ESI MS (448.5): 471.7 (M + Na^+). HRMS (ESI/Q-TOF) calcd for $C_{30}H_{24}NaO_4$ ([M + Na]$^+$) 471.1572, found: 471.1559.

2-Benzoyl-3-(4-chlorophenyl)-1-(4-methoxyphenyl)-4-phenylbutane-1,4-dione ***(3ag)***. Column chromatography with 7:1 cyclohexane-AcOEt afforded **3ag** (134 mg, 55%; conditions 1) as an inseparable 1:1 mixture of diastereoisomers. Conditions 2: **3ag** (169 mg, 70%; dr = 1:1). ^{1}H NMR: δ = 8.03-7.95 (m, 2 H, Ar), 7.94-7.85 (m, 2 H, Ar), 7.76-7.68 (m, 2 H, Ar), 7.53-7.36 (m, 4 H, Ar), 7.35-7.17 (m, 4 H, Ar), 7.11-7.04 (m, 2 H, Ar), 6.84-6.73 (m, 2 H, Ar), 6.29 (d, *J* = 10.7 Hz, 0.5 H, H-2’), 6.28 (d, *J* = 10.7 Hz, 0.5 H, H-2”), 5.78 (d, *J* = 10.7 Hz, 0.5 H, H-3’), 5.76 (d, *J* = 10.7 Hz, 0.5 H, H-3”), 3.81 (s, 1.5 H, CH_3’), 3.78 (s, 1.5 H, CH_3”); $^{13}C\{^1H\}$ NMR: δ = 198.0 (0.5 C), 197.9 (0.5 C), 195.7 (0.5 C), 194.3 (0.5 C), 193.6 (0.5 C), 192.2 (0.5 C), 163.8 (0.5 C), 136.6, 136.2, 135.8, 133.8, 133.5, 133.4, 133.3, 131.1, 130.4, 130.3, 129.4, 129.2, 129.0, 128.6, 113.9 (0.5 C), 113.8 (0.5 C), 60.3 (0.5 C), 60.1 (0.5 C), 55.5 (0.5 C), 55.4 (0.5 C), 54.3 (0.5 C), 54.1 (0.5 C); IR ($CDCl_3$) ν: 3061, 2924, 1671, 1669, 1667, 1596 cm^{-1}. ESI MS (482.9): 506.3 (M + Na^+). HRMS (ESI/Q-TOF) calcd for $C_{30}H_{23}ClNaO_4$ ([M + Na]$^+$) 505.1183, found: 505.1175.

2-Benzoyl-3-phenyl-1,4-di(pyridin-2-yl)butane-1,4-dione ***(3ba)***. Column chromatography with 4:1 cyclohexane-AcOEt afforded **3ba** (166 mg, 79%; conditions 1) as an inseparable 1.5:1 mixture of diastereoisomers. Conditions 2: **3ba** (170 mg, 81%; dr = 1.5:1). ^{1}H NMR: δ = 8.71-8.66 (m, 1 H, Ar), 8.66-8.60 (m, 0.4 H, Ar”), 8.41-8.34 (m, 0.6 H, Ar’), 8.23-8.12 (m, 1 H, Ar), 8.06-7.94 (m, 1 H, Ar), 7.88-7.80 (m, 1 H, Ar), 7.78-7.65 (m, 2 H, Ar), 7.62-7.52 (m, 0.6 H, Ar’), 7.48-7.41 (m, 0.4 H, Ar”), 7.41-7.12 (m, 8 H, Ar), 7.01-6.84 (m, 3 H, Ar), 6.90 (d, *J* = 11.5 Hz, 0.4 H, H-2”), 6.66 (d, *J* = 11.5 Hz, 0.6 H, H-2’), 6.42 (d, *J* = 11.5 Hz, 0.4 H, H-3”), 6.30 (d, *J* = 11.5 Hz, 0.6 H, H-3’); $^{13}C\{^1H\}$ NMR: δ = 199.1 (0.6 C), 198.6 (0.4 C), 198.2 (0.6 C), 197.9 (0.4 C), 196.3 (0.6 C), 195.1 (0.5 C), 152.3, 151.4, 149.1, 149.1, 148.5, 148.4, 138.0, 136.9, 136.6, 134.3, 133.1, 132.0, 130.2, 129.8, 129.1, 129.0, 128.4, 128.2, 127.9, 127.6, 127.3, 127.1, 127.0, 126.9, 126.9, 122.8, 122.7, 122.5, 59.7 (0.6 C), 58.1 (0.4 C), 52. 6 (0.4 C), 52.1 (0.6 C); IR ($CDCl_3$) ν: 3057, 2916, 1691, 1690, 1685, 1581 cm^{-1}. ESI MS (420.5): 421.9 (M + H^+). HRMS (ESI/Q-TOF) calcd for $C_{27}H_{21}N_2O_3$ ($[M + H]^+$) 421.1552, found: 421.1541.

*2-Benzoyl-3-(4-chlorophenyl)-1,4-di(pyridin-2-yl)butane-1,4-dione (**3bb**).* Column chromatography with 4:1 cyclohexane-AcOEt afforded **3bb** (175 mg, 77%) as an inseparable 1.5:1 mixture of diastereoisomers. Conditions 2: **3bb** (191 mg, 84%; dr = 1.5:1). ^1H NMR: δ = 8.71-8.64 (m, 1.4 H, Ar), 8.44-8.37 (m, 0.6 H, Ar’), 8.18-8.11 (m, 1 H, Ar), 8.05-7.96 (m, 1.6 H, Ar), 7.89-7.82 (m, 1.4 H, Ar), 7.81-7.70 (m, 2 H, Ar), 7.66-7.59 (m, 1 H, Ar), 7.47-7.20 (m, 7 H, Ar), 6.98-6.87 (m, 2 H, Ar) 6.91 (d, *J* = 11.5 Hz, 0.4 H, H-2”), 6.63 (d, *J* = 11.5 Hz, 0.6 H, H-2’), 6.40 (d, *J* = 11.5 Hz, 0.4 H, H-3”), 6.28 (d, *J* = 11.5 Hz, 0.6 H, H-3’); $^{13}C\{^1H\}$ NMR: δ = 198.8 (0.6 C), 198.3 (0.4 C), 198.0 (0.6 C), 197.6 (0.4 C), 196.0 (0.6 C), 194.8 (0.4 C), 152.2, 152.1, 151.3, 149.1, 149.0, 148.6, 148.5, 137.9, 137.0, 136.8, 136.7, 136.4, 133.2, 133.1, 133.0, 132.2, 131.5, 131.1, 129.1, 129.0, 128.5, 128.4, 128.1, 127.8, 127.3, 127.2, 127.1, 127.0, 122.9, 122.8, 122.6, 122.6, 59.6 (0.6 C), 57.9 (0.4 C), 51.9 (0.4 C), 51.4 (0.6 C); IR ($CDCl_3$) ν: 3057, 2920, 1692, 1670, 1669, 1581 cm^{-1}. ESI MS (454.9): 456.3 (M + H^+). HRMS (ESI/Q-TOF) calcd for $C_{27}H_{20}ClN_2O_3$ ($[M + H]^+$) 455.1162, found: 455.1150.

2-Benzoyl-3-phenyl-1,4-bis(4-(trifluoromethyl)phenyl)butane-1,4-dione ***(3ca)***. Column chromatography with 16:1 cyclohexane-AcOEt afforded **3ca** (83 mg, 30%; conditions 1) as a 19:1 mixture of diastereoisomers slightly contaminated by uncharacterized by-products. Conditions 2: **3ca** (88 mg, 32%; dr = 19:1). ^{1}H NMR: δ = 8.12-8.06 (m, 2 H, Ar), 8.02-7.96 (m, 2 H, Ar), 7.78-7.70 (m, 2 H, Ar), 7.69-7.58 (m, 4 H, Ar), 7.52-7.43 (m, 2 H, Ar), 7.32-7.27 (m, 2 H, Ar), 7.25-7.21 (m, 2 H, Ar), 7.16-7.10 (m, 2 H, Ar), 6.35 (d, *J* = 10.7 Hz, 1 H, H-2), 5.75 (d, *J* = 10.7 Hz, 1 H, H-3). ^{13}C{^{1}H} NMR: δ = 197.2, 195.2, 193.4, 138.7, 138.5, 136.2, 133.8, 130.5, 129.4, 129.3, 128.9, 128.6, 128.6, 128.3, 128.3, 126.5, 125.8, 125.7, 123.1 (q, *J* = 270 Hz, 2 CF_3), 60.5, 55.6. ^{19}F NMR: δ = -63.0, -63.2, -63.3, -63.4; IR ($CDCl_3$) ν: 3071, 2918, 1700, 1681, 1679, 1582 cm^{-1}. ESI MS (554.5): 577.1 (M + Na^+). HRMS (ESI/Q-TOF) calcd for $C_{31}H_{20}F_6NaO_3$ ([M + Na]$^+$) 577.1214, found: 577.1231.

2-Benzoyl-1,4-bis(4-fluorophenyl)-3-phenylbutane-1,4-dione ***(3da)***. Column chromatography with 18:1:1 cyclohexane-AcOEt-dichloromethane afforded **3da** (50 mg, 22%; conditions 1) as an inseparable 1:1 mixture of diastereoisomers. Conditions 2: **3da** (66 mg, 29%; dr = 1:1). Separation of the two diastereoisomers was carried by a second column chromatography using toluene as the elution system. First eluted diastereoisomer: ^{1}H NMR: δ = 8.09-7.98 (m, 2 H, Ar), 7.97-7.89 (m, 2 H, Ar), 7.68-7.61 (m, 2 H, Ar), 7.47-7.40 (m, 1 H, Ar), 7.32-7.22 (m, 4 H, Ar), 7.16-6.96 (m, 7 H, Ar), 6.30 (d, *J* = 10.7 Hz, 1 H, H-2), 5.72 (d, *J* = 10.7 Hz, 1 H, H-3); ^{13}C{^{1}H} NMR: δ = 196.5, 195.6, 192.6, 165.7 (d, *J* = 255 Hz, 2 *C*F), 136.5, 134.6, 133.5, 131.8, 131.7, 131.4, 131.3, 129.2, 128.9, 128.6, 128.0, 115.7, 115.6, 60.4, 55.2; ^{19}F NMR: δ = -103.8–-104.0 (m), -104.7–-104.9 (m); IR ($CDCl_3$) ν: 3065, 2920, 1693, 1667, 1593 cm^{-1}. ESI MS (454.5): 477.1 (M + Na^+). HRMS (ESI/Q-TOF) calcd for $C_{29}H_{20}F_2NaO_3$ ([M + Na]$^+$) 477.1278, found: 477.1293. Second eluted diastereoisomer: ^{1}H NMR: δ = 8.09-7.98 (m, 2 H, Ar), 7.93-7.84 (m, 2 H, Ar), 7.77-7.63 (m, 2 H, Ar), 7.53-7.45 (m, 1 H, Ar), 7.40-7.30 (m, 2 H, Ar), 7.27-7.20 (m, 2 H, Ar), 7.17-7.01 (m, 5 H, Ar), 7.01-6.88 (m, 2 H, Ar), 6.29 (d, *J* = 10.7 Hz, 1 H, H-2), 5.70 (d, *J* = 10.6 Hz, 1 H, H-3); ^{13}C{^{1}H}

NMR: δ = 196.6, 194.5, 194.2, 165.9 (d, *J* = 255 Hz, *C*F), 136.3, 134.8, 133.8, 133.2, 132.5, 132.0, 131.9, 131.7, 131.5, 129.5, 129.1, 129.0, 128.8, 128.25, 116.1, 115.8, 60.5, 55.3; ^{19}F NMR: δ = -104.2–-104.3 (m), -104.7–-104.9 (m); IR ($CDCl_3$) ν: 3075, 2919, 1691, 1666, 1593 cm^{-1}. ESI MS (454.5): 477.9 (M + Na$^+$). HRMS (ESI/Q-TOF) calcd for $C_{29}H_{20}F_2NaO_3$ ([M + Na]$^+$) 477.1278, found: 477.1296.

*2-Benzoyl-3-(4-chlorophenyl)-1,4-di-p-tolylbutane-1,4-dione (**3eb**).* Column chromatography with 12:1 cyclohexane-AcOEt afforded **3eb** (161 mg, 67%; conditions 1) as an inseparable 1:1 mixture of diastereoisomers. Conditions 2: **3eb** (197 mg, 82%; dr = 1:1). ^{1}H NMR: δ = 7.95-7.86 (m, 2 H, Ar), 7.85-7.78 (m, 1 H, Ar), 7.74-7.66 (m, 1 H, Ar), 7.65-7.57 (m, 1 H, Ar), 7.50-7.40 (m, 1 H, Ar), 7.39-7.27 (m, 2 H, Ar), 7.23-7.15 (m, 5 H, Ar), 7.14-7.04 (m, 4 H, Ar), 6.32 (d, *J* = 10.7, 0.5 H, H-2'), 6.31 (d, *J* = 10.7, 0.5 H, H-2''), 5.77 (d, 1 H, *J* = 10.7 Hz, H-3' and H-3''), 2.34 (s, 3 H, CH_3), 2.32 (s, 3 H, CH_3); ^{13}C{^{1}H} NMR: δ = 197.5 (0.5 C), 197.4 (0.5 C), 195.7 (0.5 C), 195.0 (0.5 C), 194.1 (0.5 C), 193.4 (0.5C), 144.7, 144.4, 144.2, 136.6, 136.2, 134.0, 133.8, 133.7, 133.6, 133.5, 133.4, 133.2, 130.3, 129.3, 129.1, 128.9, 128.8, 128.7, 128.6, 60.3 (0.5 C), 60.2 (0.5 C), 54.2 (0.5 C), 54.1 (0.5 C), 21.6; IR ($CDCl_3$) ν: 3032, 2920, 1690, 1667, 1604, 1572 cm^{-1}. ESI MS (481.0): 504.2 (M + Na$^+$). HRMS (ESI/Q-TOF) calcd for $C_{31}H_{25}ClNaO_3$ ([M + Na]$^+$) 503.1390, found: 503.1388.

*2-Benzoyl-4-(2-chlorophenyl)-3-(4-chlorophenyl)-1-phenylbutane-1,4-dione (**3fb**) and 2-benzoyl-1-(2-chlorophenyl)-3-(4-chlorophenyl)-4-phenylbutane-1,4-dione (**3fb'**).* Column chromatography with 13:1 cyclohexane-AcOEt afforded **3fb** and **3fb'** (107 mg, 44%; conditions 1) as a 1:19 mixture of isomers. Conditions 2: **3fb** and **3fb'** (124 mg, 51%; cr =1:19). **3fb**: ^{1}H NMR (selected data): δ = 6.38 (d, *J* = 10.7 Hz, 1 H, H-2), 5.98 (d, *J* = 10.7 Hz, 1 H. H-3). **3fb'**: ^{1}H NMR (1.5:1 mixture of diastereoisomer): δ = 7.98-7.92 (m, 2 H, Ar), 7.75-7.65 (m, 1 H, Ar), 7.62-7.53 (m, 1 H, Ar), 7.52-7.42 (m, 2 H, Ar), 7.41-7.28 (m, 6 H, Ar), 7.26-7.13 (m, 4 H, Ar), 7.12-7.02 (m, 2 H, Ar), 6.42-6.27

(m, 1 H, H-2' and H-2"), 5.79 (d, J = 10.7 Hz, 0.4 H, H-3'), 5.64 (d, J = 10.7 Hz, 0.6 H. H-3"). $^{13}C\{^{1}H\}$ NMR (1.5:1 mixture of diastereoisomer): δ = 198.6 (0.6 C), 198.0 (0.4 C), 194.9 (0.6 C), 194.4 (0.4 C), 194.1 (0.6 C), 193.2 (0.4 C), 137.2, 136.4, 136.2, 134.2, 134.1, 133.8, 133.6, 133.6, 133.4, 132.9, 132.2, 131.9, 131.4, 130.90, 130.8, 130.5, 130.3, 130.0, 129.6, 129.2, 129.0, 128.7, 128.6, 128.5, 126.7, 64.3 (0.4 C), 59.9 (0.6 C), 57.6 (0.6 C), 53.4 (0.4 C); IR ($CDCl_3$) ν: 3063, 2920, 1688, 1686, 1665, 1594 cm^{-1}. ESI MS (487.4): 510.9 (M + Na^+). HRMS (ESI/Q-TOF) calcd for $C_{29}H_{20}Cl_2NaO_3$ ($[M + Na]^+$) 509.0687, found: 509.0677.

*2-Benzoyl-4-(4-chlorophenyl)-1,3-diphenylbutane-1,4-dione (**3ga**).* Column chromatography with 10:1 cyclohexane-AcOEt afforded **3ga** and **3ga'** (117 mg, 52%; conditions 1) as a 2.3:1 mixture of isomers. Conditions 2: **3ga** and **3ga'** (144 mg, 64%; cr = 2.3:1). First eluted was **3ga'** (= **3ae**). Second eluted was **3ga** as a white amorphous solid. ^{1}H NMR: δ = 7.98-7.92 (m, 2 H, Ar), 7.91-7.85 (m, 2 H, Ar), 7.70-7.64 (m, 2 H, Ar), 7.50-7.39 (m, 3 H, Ar), 7.38-7.32 (m, 3 H, Ar), 7.28-7.21 (m, 4 H, Ar), 7.14-7.07 (m, 2 H, Ar), 7.06-6.98 (m, 1 H, Ar), 6.35 (d, J = 10.7 Hz, 1 H, H-2), 5.72 (d, J = 10.7 Hz, 1 H, H-3); $^{13}C\{^{1}H\}$ NMR: δ = 196.9, 195.7, 194.1, 139.6, 136.5, 136.0, 134.5, 134.2, 133.5, 133.4, 130.4, 129.2, 128.9, 128.9, 128.7, 128.6, 128.5, 128.2, 127.9, 60.3, 55.2; IR ($CDCl_3$) ν: 3065, 2928, 1692, 1666, 1664, 1588 cm^{-1}. ESI MS (452.9): 475.6 (M + Na^+); HRMS (ESI/Q-TOF) calcd for $C_{29}H_{21}ClNaO_3$ ($[M + Na]^+$) 475.1077, found: 475.1098.

*2-Benzoyl-4-(4-methoxyphenyl)-1,3-diphenylbutane-1,4-dione (**3ha**).* Column chromatography with 6:1 cyclohexane-AcOEt afforded **3ha** and **3ha'** (105 mg, 47%; conditions 1) as 1:5.3 mixture of isomers slightly contaminated by uncharacterized by-products. Conditions 2: **3ha** and **3ha'** (130 mg, 58%; cr =1:5.3). **3ha**: ^{1}H NMR (selected data): δ = 6.39 (d, J = 10.7 Hz, 1 H, H-2), 5.80 (d, J = 10.7 Hz, 1 H, H-3), 3.86 (s, 3 H, OCH_3); $^{13}C\{^{1}H\}$ NMR (selected data): δ = 55.0; IR ($CDCl_3$) ν: 3063, 2927, 1673, 1671, 1597, 1575 cm^{-1}. ESI MS (448.5): 471.6 (M + Na^+); HRMS (ESI/Q-TOF) calcd for $C_{30}H_{24}NaO_4$ ($[M + Na]^+$) 471.1572, found: 471.1573. **3ha'** = **3af**.

2-Benzoyl-1,4-diphenylbutane-1,4-dione ***(3ah)***. Conditions 1: trace amounts of **3ah** as determined by MS analysis of the crude reaction mixture; ESI MS (342.4): 365.6 (M + Na^+). Conditions 2: column chromatography with 5:1 cyclohexane-AcOEt afforded **3ah**[7a] (48 mg, 28%) as a yellow solid: mp 154-155 °C. ^{1}H NMR: δ = 8.06- 7.94 (m, 6 H, Ar), 7.62-7.54 (m, 3 H, Ar), 7.51-7.40 (m, 6 H, Ar), 6.12 (t, *J* = 7.0 Hz, 1 H, H-2), 3.78 (d, *J* = 7.0 Hz, 2 H, 2 H-3); IR ($CDCl_3$) ν: 3062, 2924, 1731, 1678, 1663, 1596 cm^{-1}.

2-Benzoyl-1,4-di(pyridin-2-yl)butane-1,4-dione ***(3bh)***. Conditions 1: trace amounts of **3bh** as determined by MS analysis of the crude reaction mixture; ESI MS (344.4): 345.8 (M + H^+). Conditions 2: column chromatography with 3:1 cyclohexane-AcOEt afforded **3bh** (129 mg, 75%;) as a yellow foam ^{1}H NMR: δ = 8.68-8.64 (m, 1 H, Ar), 8.58-8.54 (m, 1 H, Ar), 8.14-8.00 (m, 4 H, Ar), 7.86-7.78 (m, 2 H, Ar), 7.60-7.52 (m, 1 H, Ar), 7.50-7.39 (m, 4 H, Ar), 6.47 (dd, 1 H, *J* = 5.0, 8.0 Hz, H-2), 4.17 (dd, 1 H, *J* = 8.0, 18.5 Hz, H-3a), 3.75 (dd, 1 H, *J* = 5.0, 18.5 Hz, H-3b); $^{13}C\{^1H\}$ NMR: δ = 198.5, 197.3, 197.0, 152.8, 151.7, 149.0, 148.9, 137.0, 136.9, 136.0, 133.2, 128.9, 128.7, 127.3, 122.6, 121.9, 50.6, 37.0; IR ($CDCl_3$) ν: 3057, 2924, 1695, 1673, 1596, 1582 cm^{-1}. HRMS (ESI/Q-TOF) calcd for $C_{21}H_{17}N_2O_3$ ($[M + H]^+$) 345.1239, found: 345.1255.

Model aerobic oxidative dehydrogenation of 3aa.

To a vigorously stirred mixture of **3aa** (209 mg, 0.50 mmol), potassium *tert*-butoxide (56 mg, 0.50 mmol), and anhydrous DMSO (2 mL), $Cu(OAc)_2 \cdot H_2O$ (10 mg, 0.05 mmol) was added in one portion. The mixture was stirred at 80 °C for 2 h under atmospheric air (balloon), then cooled to room temperature, diluted with H_2O (5 mL), and extracted with CH_2Cl_2 (2 x 35 mL). The combined organic phases were washed with brine (8 mL), dried (Na_2SO_4), concentrated, and eluted from a column of silica gel with 10:1 cyclohexane-AcOEt to give **6aa** (197 mg, 95%).

General procedure for the one-pot two step synthesis of tetrasubstituted olefins 6/6' (Conditions 1, Table 3). To a vigorously stirred mixture of benzil **1** (1.00 mmol), alkene **2** (0.50 mmol), and anhydrous DMSO (2 mL), potassium *tert*-butoxide (112 mg, 1.00 mmol) was added in one portion. Then, the mixture was degassed under vacuum and saturated with argon (by an argon-filled balloon) three times. The mixture was stirred at room temperature until complete disappearance or best conversion of the starting alkene (TLC analysis, ca. 2-16 h), then $Cu(OAc)_2 \cdot H_2O$ (20 mg, 0.10 mmol) was added in one portion. The mixture was stirred at 80 °C for 2 h under atmospheric air (balloon), then cooled to room temperature, diluted with H_2O (5 mL), and extracted with CH_2Cl_2 (2 × 35 mL). The combined organic phases were washed with brine (8 mL), dried (Na_2SO_4), concentrated, and eluted from a column of silica gel with the suitable elution system to give **6/6'**.

General procedure for the one-pot two step synthesis of tetrasubstituted olefins 6/6' (Conditions 2, Table 3). To a vigorously stirred mixture of benzil **1** (1.00 mmol), alkene **2** (0.50 mmol), and anhydrous DMSO (2 mL), potassium cyanide (16 mg, 0.25 mmol) was added in one portion. Then, the mixture was degassed under vacuum and saturated with argon (by an argon-filled balloon) three times. The mixture was stirred at room temperature until complete disappearance or best conversion of the starting alkene (TLC analysis, ca. 2-16 h), then $Cu(OAc)_2 \cdot H_2O$ (20 mg, 0.10 mmol) was added in one portion. The mixture was stirred at 80 °C for 2 h under atmospheric air (balloon), then cooled to room temperature, diluted with H_2O (5 mL), and extracted with CH_2Cl_2 (2 × 35 mL). The combined organic phases were washed with brine (8 mL), dried (Na_2SO_4), concentrated, and eluted from a column of silica gel with the suitable elution system to give **6/6'**.

2-Benzoyl-1,3,4-triphenylbut-2-ene-1,4-dione ***(6aa)***. Column chromatography with 10:1 cyclohexane-AcOEt afforded **6aa** (135 mg, 65%; conditions 1) as a white amorphous solid. Conditions 2: **6aa** (158 mg, 76%). ^{1}H NMR: δ = 8.01-7.93 (m, 2 H, Ar), 7.89-7.84 (m, 2 H, Ar), 7.84-7.77 (m, 2 H, Ar), 7.50-7.38 (m, 3 H, Ar), 7.37-7.32 (m, 3 H, Ar), 7.31-7.24 (m, 5 H, Ar), 7.17-7.10 (m, 3 H, Ar); $^{13}C\{^{1}H\}$ NMR: δ = 195.0, 194.3, 193.1, 151.7, 141.9, 136.6, 136.1, 135.7, 134.0, 133.7, 133.4, 133.3, 129.8, 129.7, 129.6, 129.4, 128.8, 128.6, 128.6, 128.5, 128.3; IR ($CDCl_3$) ν: 3063, 2923, 1662, 1646, 1595, 1578 cm^{-1}. ESI MS (416.5): 439.1 ($M + Na^+$); HRMS (ESI/Q-TOF) calcd for $C_{29}H_{20}NaO_3$ ($[M + Na]^+$) 439.1310, found: 439.1318.

2-Benzoyl-3-(4-chlorophenyl)-1,4-diphenylbut-2-ene-1,4-dione ***(6ab)***. Column chromatography with 13:1 cyclohexane-AcOEt afforded **6ab** (155 mg, 69%; conditions 1) as a white amorphous solid. Conditions 2: **6ab** (184 mg, 82%). ^{1}H NMR: δ = 8.01-7.94 (m, 2 H, Ar), 7.88-7.85 (m, 4 H, Ar), 7.54-7.44 (m, 2 H, Ar), 7.44-7.33 (m, 5 H, Ar), 7.33-7.20 (m, 4 H, Ar), 7.18-7.08 (m, 2 H, Ar); $^{13}C\{^{1}H\}$ NMR: δ = 194.8, 193.9, 192.8, 150.2, 142.6, 136.4, 136.0, 135.9, 135.5, 134.1, 133.6, 133.5, 132.4, 129.9, 129.8, 129.7, 129.4, 129.16, 128.8, 128.6, 128.4; IR ($CDCl_3$) ν: 3062, 2924, 1652, 1595, 1579 cm^{-1}. ESI MS (450.9): 473.4 ($M + Na^+$). HRMS (ESI/Q-TOF) calcd for $C_{29}H_{19}ClNaO_3$ ($[M + Na]^+$) 473.0920, found: 473.0917.

2-*Benzoyl-1,4-diphenyl-3-(p-tolyl)but-2-ene-1,4-dione* ***(6ad)***. Column chromatography with 14:1 cyclohexane-AcOEt afforded **6ad** (112 mg, 52%; conditions 1) as a white amorphous solid. Conditions 2: **6ad** (129 mg, 60%). ^{1}H NMR: δ = 8.02-7.93 (m, 2 H, Ar), 7.89-7.83 (m, 2 H, Ar), 7.82-7.76 (m, 2 H, Ar), 7.51-7.39 (m, 3 H, Ar), 7.39-7.30 (m, 4 H, Ar), 7.30-7.21 (m, 2 H, Ar), 7.21-7.11 (m, 2 H, Ar), 6.99-6.87 (m, 2 H, Ar), 2.17 (s, 3 H, CH_3); $^{13}C\{^{1}H\}$ NMR: δ = 195.2, 194.5, 193.2, 152.2, 141.1, 140.0, 136.7, 136.2, 135.8, 133.6, 133.3, 133.2, 131.0, 129.8, 129.7, 129.6, 129.3, 128.6, 128.5, 128.5, 128.3, 21.2; IR ($CDCl_3$) ν: 3063, 2921, 1663, 1643, 1595, 1578 cm^{-1}. ESI MS (430.5): 453.1 ($M + Na^+$). HRMS (ESI/Q-TOF) calcd for $C_{30}H_{22}NaO_3$ ($[M + Na]^+$) 453.1467, found: 453.1470.

(E/Z)-2-Benzoyl-1-(4-chlorophenyl)-3,4-diphenylbut-2-ene-1,4-dione ***(6ae)***. Column chromatography with 10:1 cyclohexane-AcOEt afforded **6ae** (129 mg, 60%; conditions 1) as a 1:1 mixture of diastereoisomers. Conditions 2: **6ae** (186 mg, 83%; *E/Z* = 1:1). ^{1}H NMR: δ = 8.01-7.94 (m, 1 H, Ar'), 7.94-7.88 (m, 1 H, Ar''), 7.87-7.73 (m, 4 H, Ar), 7.52-7.40 (m, 2 H, Ar), 7.40-7.32 (m, 3 H, Ar), 7.32-7.21 (m, 5 H, Ar), 7.21-7.08 (m, 3 H, Ar); ^{13}C{^{1}H} NMR: δ = 194.9 (0.5 C), 194.8 (0.5 C), 194.2 (0.5 C), 193.2 (0.5 C), 193.0 (0.5 C), 192.0 (0.5 C), 151.9 (0.5 C), 151.7 (0.5 C), 141.6 (0.5 C), 141.4 (0.5 C), 140.3 (0.5 C), 139.9 (0.5 C), 136.5, 135.9, 135.6, 134.9, 134.4, 133.9, 133.8, 133.6, 133.5, 133.4, 131.1, 130.8, 129.9, 129.8, 129.7, 129.3, 129.0, 128.9, 128.9, 128.8, 128.7, 128.4, 128.5, 128.4; IR ($CDCl_3$) ν: 3061, 2928, 1653, 1652, 1586, 1582 cm^{-1}. ESI MS (450.9): 473.6 (M + Na$^+$). HRMS (ESI/Q-TOF) calcd for $C_{29}H_{19}ClNaO_3$ ([M + Na]$^+$) 473.0920, found: 473.0903.

(E/Z)-2-Benzoyl-3-(4-chlorophenyl)-1-(4-methoxyphenyl)-4-phenylbut-2-ene-1,4-dione ***(6ag)***. Column chromatography with 7:1 cyclohexane-AcOEt afforded **6ag** (115 mg, 48%; conditions 1) as a 1:1 mixture of diastereoisomers. Conditions 2: **6ag** (144 mg, 60%; *E/Z* = 1:1). ^{1}H NMR: δ = 8.05-7.99 (m, 1 H, Ar'), 7.99-7.92 (m, 1 H, Ar''), 7.84-7.80 (m, 4 H, Ar), 7.53-7.43 (m, 2 H, Ar), 7.42-7.31 (m, 3 H, Ar), 7.29-7.19 (m, 3 H, Ar), 7.18-7.07 (m, 2 H, Ar), 6.89-6.81 (m, 1 H, Ar), 6.81-6.72 (m, 1 H, Ar), 3.83 (s, 1.5 H, CH_3), 3.78 (s, 1.5 H, CH_3); ^{13}C{^{1}H} NMR: δ = 194.9 (0.5 C), 194,9 (0.5 C), 194.0 (0.5 C), 192.9 (0.5 C), 192.1 (0.5C), 190.9 (0.5 C), 164.3 (0.5 C), 164.0 (0.5 C), 149.2 (0.5 C), 149.0 (0.5 C), 143.3 (0.5 C), 143.1 (0.5 C), 136.4, 136.0, 135.6, 134.1, 133.6, 133.4, 132.5, 132.4, 132.1, 129.8, 129.7, 129.4, 129.3, 129.1, 128.8, 128.6, 128.4,114.1 (0.5 C), 113.7 (0.5 C), 55.5 (0.5 C), 55.4 (0.5 C); IR ($CDCl_3$) ν: 3060, 2920, 1652, 1650, 1581, 1579 cm^{-1}. ESI MS (480.9): 503.6 (M + Na$^+$). HRMS (ESI/Q-TOF) calcd for $C_{30}H_{21}ClNaO_4$ ([M + Na]$^+$) 503.1026, found: 503.1032.

(E/Z)-2-Benzoyl-3-(4-chlorophenyl)-1,4-di-p-tolylbut-2-ene-1,4-dione ***(6eb)***. Column chromatography with 12:1 cyclohexane-AcOEt afforded **6eb** (148 mg, 62%; conditions 1) as a 1:1 mixture of diastereoisomers. Conditions 2: **6eb** (191 mg, 80%; *E/Z* = 1:1). ^{1}H NMR: δ = 8.01-7.94 (m, 1 H, Ar'), 7.92-7.85 (m, 1 H, Ar''), 7.85-7.69 (m, 4 H, Ar), 7.59-7.43 (m, 1 H, Ar), 7.43-7.33 (m, 1 H, Ar), 7.33-7.25 (m, 1 H, Ar), 7.25-7.19 (m, 2 H, Ar), 7.18-7.05 (m, 6 H, Ar), 2.35 (s, 1.5 H, CH_3), 2.34 (s, 3 H, CH_3), 2.29 (s, 1.5 H, CH_3); ^{13}C{^{1}H} NMR: δ = 194.5 (0.5 C), 194.4 (0.5 C), 194.0 (0.5 C), 193.5 (0.5 C), 192.8 (0.5 C), 192.3 (0.5 C), 149.8, 145.2, 144.7, 144.5, 142.7, 136.5, 136.0, 135.7, 134.0, 133.6, 133.4, 133.2, 132.7, 130.1, 130.0, 129.9, 129.8, 129.7, 129.6, 129.5, 129.3, 129.1, 129.1, 128.8, 128.3, 127.0, 21.7 , 21.6; IR ($CDCl_3$) ν: 3039, 2920, 1651, 1650, 1602, 1580 cm^{-1}. ESI MS (479.0): 502.3 (M + Na$^+$). HRMS (ESI/Q-TOF) calcd for $C_{31}H_{23}ClNaO_3$ ([M + Na]$^+$) 501.1233, found: 501,1250.

(E/Z)-2-Benzoyl-1-(2-chlorophenyl)-3-(4-chlorophenyl)-4-phenylbut-2-ene-1,4-dione ***(6fb')***. Column chromatography with 13:1 cyclohexane-AcOEt afforded **6fb'** (92 mg, 38%) as a 1:1 mixture of diastereoisomers. Conditions 2: **6fb'** (111 mg, 46%; *E/Z* = 1:1). ^{1}H NMR: δ 7.99-7.91 (m, 4 H, Ar), 7.59-7.53 (m, 1 H, Ar), 7.52-7.45 (m, 2 H, Ar), 7.41-7.33 (m, 4 H, Ar), 7.24-7.17 (m, 5 H, Ar), 7.13-7.05 (m, 2 H, Ar); ^{13}C{^{1}H} NMR: δ = 194.1, 193.2, 192.7, 146.7 (0.5 C) , 146.6 (0.5 C), 136.2, 135.9, 135.6 (0.5 C), 135.5 (0.5 C), 134.2, 133.8, 132.9, 132.7, 131.8, 131.6, 130.8, 130.5, 130.2, 130.0, 129.8, 129.6, 129.5, 128.9, 128.7, 128.6, 128.5, 126.7; IR ($CDCl_3$) ν: 3067, 2923, 1655, 1651, 1594, 1590 cm^{-1}. ESI MS (485.4): 508.0 (M + Na$^+$). HRMS (ESI/Q-TOF) calcd for $C_{29}H_{18}Cl_2NaO_3$ ([M + Na]$^+$) 507.0531, found: 507.0520.

2-Benzoyl-4-(4-chlorophenyl)-1,3-diphenylbut-2-ene-1,4-dione ***(6ga)***. Column chromatography with 10:1 cyclohexane-AcOEt afforded **6ga** (85 mg, 38%; conditions 1) as a white amorphous solid. Conditions 2: **6ga** (99 mg, 44%). ^{1}H NMR: δ = 7.99-7.92 (m, 2 H, Ar), 7.82-7.74 (m, 4 H, Ar), 7.50-7.39 (m, 2 H, Ar), 7.38-7.30 (m, 5 H, Ar), 7.29-7.22 (m, 3 H, Ar), 7.19-7.12 (m, 3 H, Ar);

$^{13}C\{^1H\}$ NMR: δ = 194.2, 194.0, 193.1, 151.8, 142.0, 140.0, 136.5, 136.0, 134.1, 133.9, 133.6, 133.5, 131.1, 130.0, 129.9, 129.4, 129.0, 128.8, 128.7, 128.6, 128.5; IR ($CDCl_3$) ν: 3063, 2920, 1653, 1651, 1588, 1585 cm^{-1}. ESI MS (450.9): 473.8 (M + Na^+). HRMS (ESI/Q-TOF) calcd for $C_{29}H_{19}ClNaO_3$ ($[M + Na]^+$) 473.0920, found: 473.0922.

Aerobic oxidative dehydrogenation of 3aa in presence of TEMPO.

To a vigorously stirred mixture of **3aa** (209 mg, 0.50 mmol), potassium *tert*-butoxide (112 mg, 1.00 mmol), (2,2,6,6-tetramethyl-piperidin-1-yl)oxyl (78 mg, 0.50 mmol) and anhydrous DMSO (2 mL), $Cu(OAc)_2 \cdot H_2O$ (20 mg, 0.10 mmol) was added in one portion. The mixture was stirred at 80 °C for 2 h under atmospheric air (balloon), then cooled to room temperature, diluted with H_2O (5 mL), and extracted with CH_2Cl_2 (2 x 35 mL). The combined organic phases were washed with brine (8 mL), dried (Na_2SO_4), concentrated, and eluted from a column of silica gel with 10:1 cyclohexane-AcOEt to give **6aa** (135 mg, 65%).

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Supporting Information. NMR spectra of **3/3’**, **6/6’** and ESI-MS spectra of **V-VI**. This material is available free of charge via the Internet at http://pubs.acs.org.

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