DOI: 10.1002/adsc.201300652

Methylsulfinyl (Dimsyl) Anion as Umpolung Catalyst for the Chemoselective Cross-Benzoin Reaction of α-Diketones with Aldehydes

Olga Bortolini,[a,*] Giancarlo Fantin,[a] Valeria Ferretti,[a] Marco Fogagnolo,[a] Pier Paolo Giovannini,[a] Alessandro Massi,[a,*] Salvatore Pacifico,[a] and Daniele Ragno[a]

[a] Dipartimento di Scienze Chimiche e Farmaceutiche, Università di Ferrara, Via Fossato di Mortara 17, I-44121 Ferrara, Italy
Fax: (+39)-053-224-0709; phone: (+39)-053-245-5183; e-mail: olga.bortolini@unife.it or alessandro.massi@unife.it

Received: July 25, 2013; Revised: September 6, 2013; Published online: November 11, 2013

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201300652.

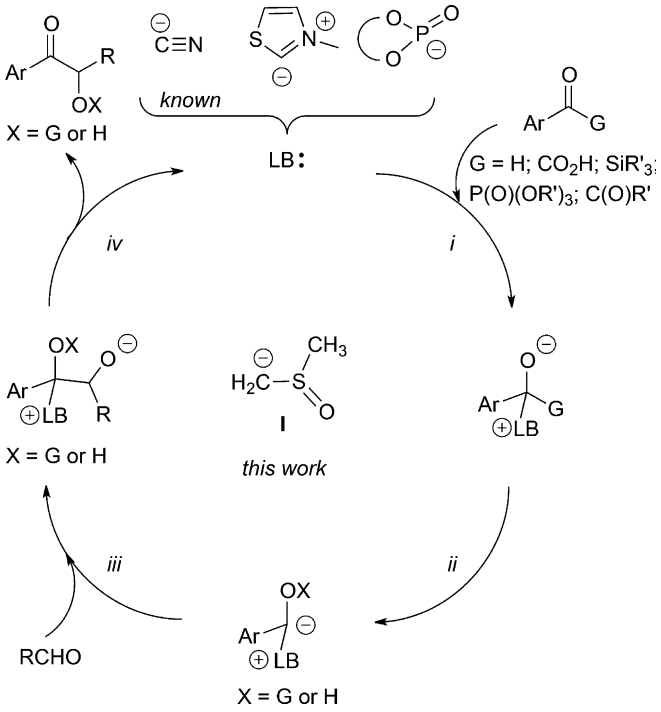
Abstract: The hitherto unreported ability of the methylsulfinyl carbanion (dimsyl anion) to generate acyl anion equivalents is described. The dimsyl anion, in fact, efficiently catalyzes chemoselective intermolecular cross-benzoin condensations of diaryl α-diketones (benzils) with various aromatic and aliphatic aldehydes to give the corresponding aryl-aryl and aryl-alkyl benzoin benzoates in an atom-economic fashion. The dimsyl anion acts as an environmentally friendly alternative to the toxic cyanide anion and it is obtained by *in situ* deprotonation of dimethyl sulfoxide (DMSO) solvent with a catalytic amount of a strong base, potassium *tert*-butoxide (*t*-BuOK) the optimal promoter. The assumption that the methylsulfinyl carbanion is the active catalyst in the title transformation is supported by electrospray ionization mass spectrometry (ESI-MS) experiments.

Keywords: carbanions; C–C coupling; mass spectrometry; synthetic methods

Introduction

The umpolung strategy[1] represents nowadays a powerful tool for the development of new, selective, and efficient routes for the synthesis of target molecules. The benzoin condensation is a classical example of this concept as it proceeds through the generation of an acyl anion equivalent from an aldehyde,[2] pyruvate,[3] acylsilane,[4] acylphosphonate,[5] or α-diketone.[6] So far, non-enzymatic benzoin reactions have been realized catalytically only by the use of the cyanide anion,[2a–c,7] N-heterocyclic carbenes (NHCs),[2d–k,8] or metallophosphites,[9] the efficiency of each class of catalyst being strictly dependent on the family of acyl anion precursors employed. Despite the many successes already achieved in this area of research, the benzoin reaction is continuously attracting great interest in the organic chemistry community.[10] Hence, many efforts have been recently devoted to the development of highly stereoselective versions of this reaction through optimal catalyst design,[11] to the discovery of domino processes based on this reactivity,[12] and to the effective preparation of non-symmetrical products by the chemoselective cross-coupling of suitable donor/acceptor couples.[10,13] In this regards, we succeeded in the racemic, thiazolium carbene-catalyzed condensation of dialkyl α-diketone donors with α-keto ester acceptors,[14] while failing in the access to this same reactivity with diaryl α-diketones (benzils). In this occasion, an unexpected enlargement of the thiazolium ring occurs,[15] which prevents the use of benzils as equivalents of aromatic aldehydes. Diaryl α-diketones, however, are conveniently used to perform cross-benzoin condensations with aryl aldehydes under cyanide catalysis.[16] In general, the mechanism of action of the cyanide ion in benzoin reactions is similar to that of NHCs and phosphite anions, with the catalyst working at different stages in the catalytic cycle as Lewis base (LB; step *i*), as anion-stabilizing group (*ii*), and as leaving group (*iv*; Scheme 1).

In the search of a non-toxic but equally effective alternative to the cyanide ion for the polarity reversal of benzils and taking into consideration the above mechanistic requirements for new catalyst design, we herein introduce the unprecedented reactivity of methylsulfinyl carbanion (dimsyl ion **I**) as new cata-



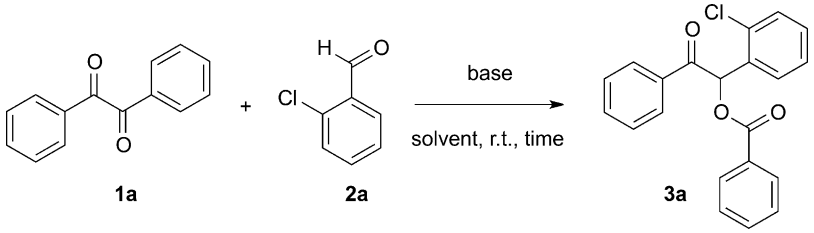
Scheme 1. Catalytic cycle in benzoin-type couplings.

lyst for the umpolung of diaryl α-diketones, and demonstrate its general efficacy in the atom-economic synthesis of racemic benzoylated benzoins using aryl and alkyl aldehyde acceptors.

Results and Discussion

At the beginning of this study, we were aware of the typical use of the dimsyl anion, first reported by Corey and Chaykovsky,[17] as Brønsted base,[18] but also of its ability to act as nucleophilic carbanion in additions to some unsaturated systems.[19] Hence, we envisaged that the dimsyl ion, obtained by direct deprotonation of dimethyl sulfoxide solvent, could also function as a Lewis base for α-dicarbonyl attack, and thus behave as an umpolung catalyst in close analogy to the cyanide ion. This speculation was verified in the reaction of benzil **1a** with *o*-chlorobenzaldehyde **2a** in anhydrous DMSO (4 Å molecular sieves) in the presence of catalytic *t*-BuOK (10 mol%). Indeed, this reaction successfully afforded the cross-coupling derivative **3a** in a short reaction time (1 h) and 95% isolated yield (entry 1, Table 1). Exposure of the reaction mixture to the residual water present in the commer-

Table 1. Optimization of the model benzoin reaction of benzil **1a** with *o*-chlorobenzaldehyde **2a**.[a]



Entry	Solvent	Base (mol%)	Time [h]	Yield [%][b]
1	DMSO[c]	*t*-BuOK (10)	1	95
2	DMSO	*t*-BuOK (10)	1	93
3	DMSO	*t*-BuOK (5)	1	55
4	DMSO	Cs_2CO_3 (10)	1	68
5	DMSO	DBU (10)	1	45
6	DMSO	Et_3N (10)	60	–
7	THF	*t*-BuOK (10)	60	–
8	CH_2Cl_2	*t*-BuOK(10)	60	–
9	DMA	*t*-BuOK(10)	60	–
10	NMP	*t*-BuOK(10)	60	–
11	THF	Bu_4NOH (20)[d]	60	–
12	*THF*[e]	*t*-BuOK (10)	16	5
13	*THF*[f]	*t*-BuOK (10)	16	28

[a] *Reaction conditions:* benzil (0.50 mmol), 2-chlorobenzaldehyde (0.50 mmol), anhydrous solvent (1.0 mL), and the stated amount of base. Residual water content determined by Karl Fischer analysis (see the Experimental Section).
[b] Isolated yield.
[c] Reaction performed in the presence of 4 Å MS.
[d] Bu_4NOH is in the 30' hydrate form.
[e] Reaction performed in the presence of 1 equiv. of anhydrous DMSO.
[f] Reaction performed in the presence of 10 equiv. of anhydrous DMSO.

cial anhydrous DMSO had a negligible effect on the final output (entry 2), while a halving of the *t*-BuOK amount reduced to 55% the isolated yield of **3a** (entry 3). The latter result and the dependence of the reaction efficiency on the strength of the base in DMSO, that is, *t*-BuOK > Cs_2CO_3 > DBU ≫ Et_3N, led us to suppose the actual role of the dimsyl anion as active catalyst (entries 4–6). This conclusion was initially supported by an independent experiment consisting in the generation of **I** from DMSO/*t*-BuOK and its subsequent trapping with benzophenone to produce the $Ph_2C(OH)CH_2S(O)CH_3$ adduct.[17b] Nevertheless, in order to exclude the direct activation of benzil **1a** by *t*-BuOK, the model benzoin condensation was next performed in the 'inactive' solvents THF and dichloromethane, and no product formation was observed under these conditions (entries 7 and 8). The same result was detected using dimethylacetamide (DMA) and *N*-methylpyrrolidone (NMP) as solvents, which are closer to DMSO in terms of stabilization capability of charged intermediates (entries 9 and 10). The possibility of a benzilic-like rearrangement[20] promoted by the hydroxide ion, eventually generated under basic conditions from the residual water of DMSO, was also excluded by an experiment carried out in THF with catalytic (20 mol%) Bu_4NOH (entry 11). To unequivocally prove the catalytic activity of the dimsyl anion in the model benzoin condensation, the **1a**/**2a** coupling was finally performed in THF with increasing amounts of anhydrous DMSO (from 0.2 to 10 equivalents; only selected data are reported). Gratifyingly, a direct correlation between the added DMSO and the yield of **3a** was observed (entries 12 and 13), thus confirming the necessity of an excess of DMSO to generate a quantity of dimsyl anion sufficient for promoting the reaction (pK_a [DMSO] = 35.0; pK_a [*t*-BuOH] = 32.2).[21]

It is widely recognized that the synthesis of cross-benzoin products is still a challenging task;[10,13] therefore, the general applicability of the disclosed dimsyl anion catalysis was next addressed by considering different diketone/aldehyde combinations (Table 2).

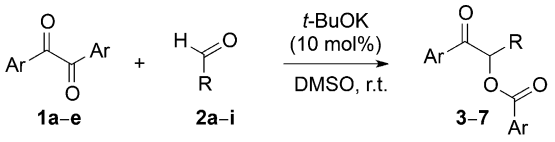
Indeed, the use of DMSO/*t*-BuOK appears as a significant improvement over the reported methodology,[6,16] as it provides a complete chemoselective, practical, economical, and safe access to benzoylated benzoins without the need for toxic cyanide catalysis.[22] Hence, several benzils **1** and aryl/alkyl aldehydes **2** with various substitution patterns that include electron-withdrawing and electron-donating groups were explored using the new catalytic conditions. It was observed that the electronic features of the acceptor aldehyde had a great relevance on the final reaction output. More precisely, electron-deficient aromatic aldehydes afforded the best results (entries 1–4), whereas when electron-donating groups were involved as substituents on either diketone **1** or aldehyde **2**, the reaction outcomes were less remarkable (entries 6 and 7). The substrate scope was subsequently extended to the 2,2′-pyridyl **1d**, which proved to be highly reactive as well (entries 8 and 9). It was also demonstrated that the presence of an *ortho*-substituent on the benzil did not reduce the coupling efficiency (entry 10). Of note, the disclosed process can accommodate the challenging elaboration of non-aromatic aldehydes (entries 11 and 12). While the side aldol reaction of **2h** and **2i** could not be suppressed under the basic reaction conditions, formation of the corresponding aryl-alkyl benzoin adducts **3h** and **3i** was guaranteed by the complete chemoselectivity of the umpolung process (preferential α-dicarbonyl activation), which precluded alkyl aldehydes **2h** and **2i** from participating in homo-benzoin reactions.

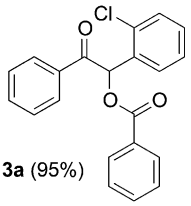
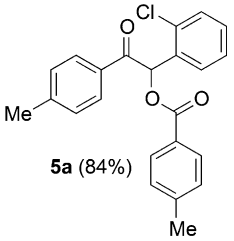
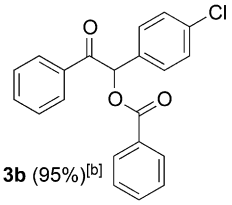
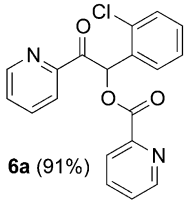
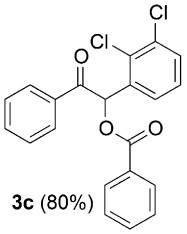
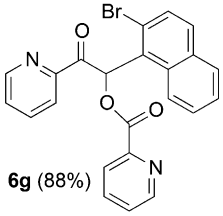
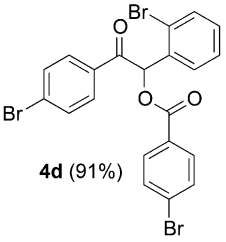
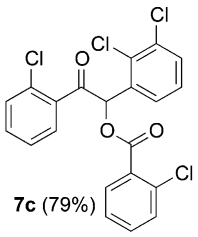
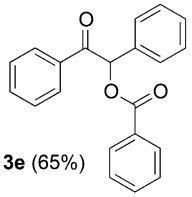
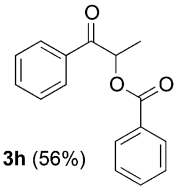
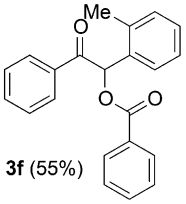
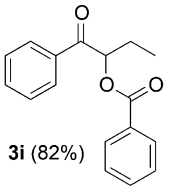
A mechanistic rationalization for the observed new catalysis is proposed as shown in Scheme 2. The direct deprotonation of DMSO with the Brønsted base generates the dimsyl anion **I**.[23] This activated species is able to attack the α-diketone **1** forming the intermediate **II**, which then rearranges to the carbanion **IV** through the epoxide **III** in analogy with what proposed for the cyanide catalysis.[6,24] Then, the carbanion **IV** intercepts the aldehyde electrophilic carbon affording the intermediate **V**, which finally releases the benzoin benzoate product **3** and catalyst **I** through intramolecular trans-esterification.[25]

With the aim to elucidate the postulated mechanism, the capture of the intermediate **IV** was initially attempted through a dedicated experiment performed with benzil **1a** and *t*-BuOK (20 mol%) under strictly anhydrous conditions (DMSO, molecular sieves) and in the absence of the aldehyde acceptor (see the Experimental Section). In this occasion, the only detectable product was the α,α′-stilbenediol dibenzoate **9a**, which was formed by the addition of **IV** to a second molecule of diketone **1a** (homocoupling pathway, Scheme 2). Significantly, this reaction outcome closely resembled that found in a previous study carried out under the same conditions but using the cyanide ion as the catalyst.[6a,24]

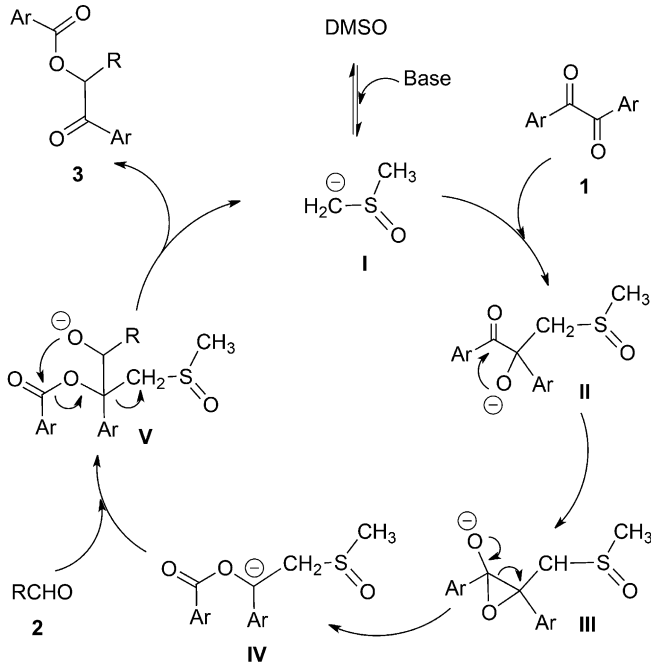
The assumption that **IV** is the key player in the disclosed catalytic system was thus supported by a parallel investigation on its formation in the gas phase from DMSO/*t*-BuOK/**1a** using electrospray ionization mass spectrometry (ESI-MS). This technique, in fact, is considered to be as efficient as low-temperature NMR to detect and characterize elusive intermediates.[26a] The ESI-MS experiments showed the formation of the addition product between the dimsyl anion and benzil, which was detected in negative-ion mode at $m/z = 287$ with DMSO and at $m/z = 292$ with DMSO-d_6. The possibility to distinguish among the isobaric intermediates **II**, **III**, and **IV** came from tandem mass spectrometric (MS/MS) analysis.[26b] Relevant is the fact that when the ion species at $m/z = 287$ was mass

Table 2. Substrate scope.

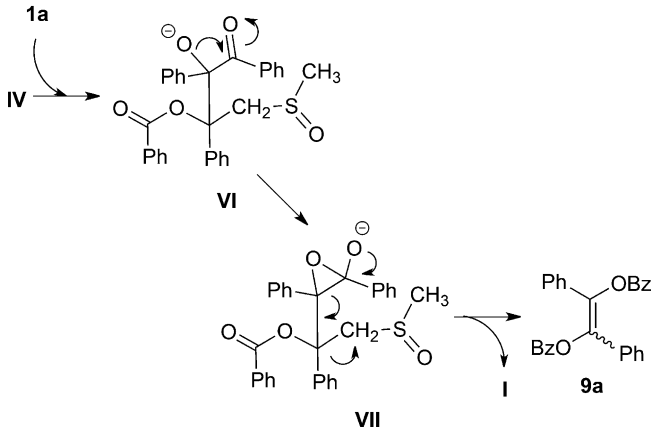


Entry	Diketone	Aldehyde	Product[a]	Entry	Diketone	Aldehyde	Product[a]
1	**1a** (Ar = Ph)	**2a** (R = 2-ClC$_6$H$_4$)	 **3a** (95%)	7[d]	**1c** (Ar = 4-MeC$_6$H$_4$)	**2a** (R = 2-ClC$_6$H$_4$)	 **5a** (84%)
2	**1a** (Ar = Ph)	**2b** (R = 4-ClC$_6$H$_4$)	 **3b** (95%)[b]	8	**1d** (Ar = 2-pyridyl)	**2a** (R =2-ClC$_6$H$_4$)	 **6a** (91%)
3	**1a** (Ar = Ph)	**2c** (R = 2,3-Cl$_2$C$_6$H$_3$)	 **3c** (80%)	9	**1d** (Ar = 2-pyridyl)	**2g** (R = 2-Br-naphthyl)	 **6g** (88%)
4	**1b** (Ar = 4-BrC$_6$H$_4$)	**2d** (R = 2-BrC$_6$H$_4$)	 **4d** (91%)	10	**1e** (Ar = 2-ClC$_6$H$_4$)	**2c** (R = 2,3-Cl$_2$C$_6$H$_3$)	 **7c** (79%)
5[c]	**1a** (Ar = Ph)	**2e** (R = Ph)	 **3e** (65%)	11[e]	**1a** (Ar = Ph)	**2h** (R = Me)	 **3h** (56%)
6[c]	**1a** (Ar = Ph)	**2f** (R = 2-MeC$_6$H$_4$)	 **3f** (55%)	12[e]	**1a** (Ar = Ph)	**2i** (R = Et)	 **3i** (82%)

[a] Isolated yields.
[b] Yield of **3b** containing *ca.* 20% of isomeric **3b** (see the Experimental Section).
[c] Performed at 50 °C with 3 equiv. of **2**.
[d] Performed with 2 equiv. of **1c**.
[e] Performed with 2 equiv. of **2**.



Homocoupling pathway



Scheme 2. Proposed mechanism.

selected and fragmented, we observed the formation of the benzoate anion ($m/z = 121$) together with its counterpart $[PhCCHS(O)CH_3]^-$ ($m/z = 165$)[27] and the methylsulfinyl anion ($m/z = 77$; Figure 1). This result indicated the structure **IV** as the most plausible one,[28] and confirmed the rearrangement of **II** to **IV** as a fast process.[6a]

Conclusions

In summary, we have described a new reactivity of the methylsulfinyl carbanion (dimsyl anion), which consists in its ability to generate acyl anion equivalents from diaryl α-diketones. The dimsyl anion has been conveniently generated from the direct deprotonation of DMSO solvent with the optimal base *t*-BuOK employed in catalytic amounts. The chemoselective activation by dimsyl anion of α-diketones over aldehydes has been exploited for the effective, environmentally benign, and low-cost synthesis of benzoylated benzoin products avoiding the use of hazardous cyanide sources. A mechanistic rationalization of the disclosed unconventional umpolung catalysis has been proposed and an insight into the structure and stability of the postulated acyl anion equivalent (intermediate **IV**) has been provided with the support of ESI-MS experiments.

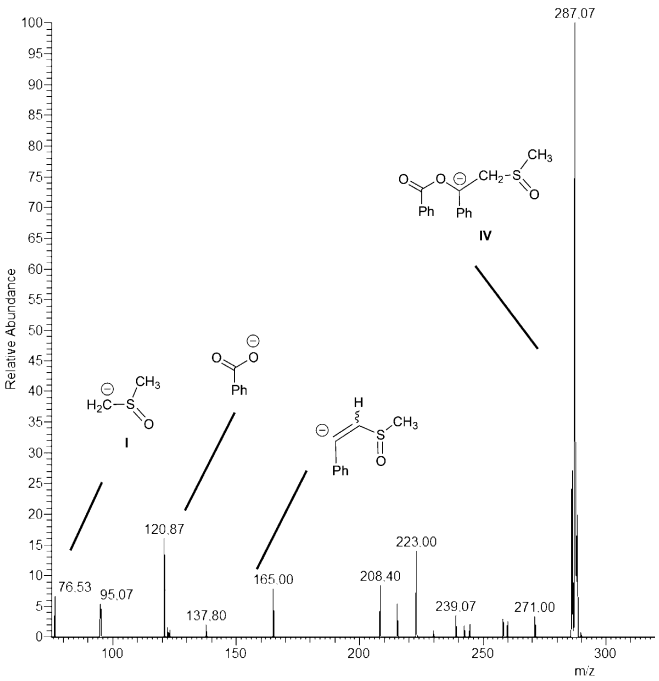


Figure 1. MS/MS of the benzil/dimsyl adduct ($m/z = 287$) and the related signature fragments.

It is important to emphasize that we have herein introduced for the first time sulfinyl carbanions as a new class of catalyst capable of promoting the challenging cross-benzoin reaction, which, so far, has been performed catalytically only by the use of the cyanide anion, N-heterocyclic carbenes, and metallophosphites.

An investigation on the polarity reversal of other classes of acyl anion precursors by the discovered catalytic methodology and the utilization of different unsaturated acceptors[29] is currently underway in our laboratories, and our progress will be reported in due course.

Experimental Section

Potassium *tert*-butoxide was purified by sublimation (200–220 °C at 5 mmHg) using a Büchi glass oven B580 in the

sublimation mode. Liquid aldehydes were freshly distilled before their 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) and ^{13}C (75 MHz) NMR spectra were recorded in $CDCl_3$ solutions at room temperature. Peak assignments were aided by ^{1}H-^{1}H COSY and gradient-HMQC experiments. Elemental analyses were performed with a FLASH 2000 Series CHNS/O analyzer (ThermoFisher Scientific). 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 analyzed in positive ion mode by Agilent 6520 HPLC-Chip Q/TOF-MS (nanospray) using a quadrupole, a hexapole, and a time-of-flight unit to produce spectra. The capillary source voltage was set at 1700 V; the gas temperature and drying gas were kept at 350 °C and 5 L min^{-1}, respectively. The MS analyzer was externally calibrated with ESI-L low concentration tuning mix from m/z = 118 to 2700 to yield accuracy below 5 ppm. Accurate mass data were collected by directly infusing samples in 40/60 H_2O/ACN 0.1% TFA into the system at a flow rate of 0.4 μL min^{-1}. Karl Fisher analysis of commercially available (Sigma–Aldrich) anhydrous solvents was performed with the 756 KF Coulometer (Metrohm) to determine the residual water (% w/w): DMSO (0.016%), DMA (0.009%), and NMP (0.184%). α-Diketones **1a–e** and aldehydes **2a–g** were purchased from Sigma–Aldrich. Spectroscopic data of compounds **3e**,[25] **3h**,[30] **8a**,[13a] and **9a**[6a,24,34] were identical to those reported in the literature.

Optimization Study of the Model Cross-Benzoin Reaction of 1a and 2a (Table 1)

To a vigorously stirred mixture of **1a** (105 mg, 0.50 mmol), 2-chlorobenzaldehyde **2a** (56 μL, 0.50 mmol), and the stated anhydrous solvent (1 mL), the stated amount of base (5–20 mol% referred to **1a**) was added in one portion. The mixture was stirred at room temperature for the stated reaction time. Then, the mixture was diluted with H_2O (5 mL) and extracted with Et_2O (2×25 mL). The combined organic phases were dried (Na_2SO_4), concentrated, and eluted from a column of silica gel with 10:1 cyclohexane-AcOEt to give **3a** as a white foam.

General Procedure for the Cross-Benzoin Reactions of α-Diketones 1 with Aldehydes 2 (Table 2)

To a vigorously stirred mixture of α-diketone **1** (1.00 mmol), aldehyde **2** (1.00 mmol), and anhydrous DMSO (2 mL), potassium *tert*-butoxide (11 mg, 0.10 mmol) was added in one portion. The mixture was stirred at room temperature until complete disappearance of the starting diketone was detected (TLC analysis, *ca.* 1–16 h). Then, the mixture was diluted with H_2O (5 mL) and extracted with Et_2O (2×25 mL). The combined organic phases were dried (Na_2SO_4), concentrated, and eluted from a column of silica gel with the suitable elution system to give the benzoylated benzoins **3**–**7**.

1-(2-Chlorophenyl)-2-oxo-2-phenylethyl benzoate (3a): Column chromatography with 20:1 cyclohexane-AcOEt afforded **3a** as a white foam; yield: 332 mg (95%). ^{1}H NMR: δ = 8.12–8.07 (m, 2H, Ar), 8.02–7.98 (m, 2H, Ar), 7.60–7.40 (m, 8H, Ar), 7.44 (s, 1H, H-1), 7.36–7.24 (m, 2H, Ar); ^{13}C NMR: δ = 193.3, 165.8, 134.9, 134.4, 134.2, 133.8, 133.4, 131.8, 130.8, 130.4, 130.2, 130.1, 130.0, 129.9, 129.5, 129.2, 129.0, 128.8, 128.4, 127.6, 74.0; ESI-MS (M = 350.8): m/z = 373.9 (M + Na$^+$); anal. calcd. for $C_{21}H_{15}ClO_3$: C 71.90, H 4.31; found: C 71.75, H 4.07; HR-MS (ESI/Q-TOF): m/z = 373.0597, calcd. for $C_{21}H_{15}ClO_3Na$ [M + Na]$^+$: 373.0601.

1-(4-Chlorophenyl)-2-oxo-2-phenylethyl benzoate (3b): Column chromatography with 20:1 cyclohexane-AcOEt gave first 2-(4-chlorophenyl)-2-oxo-1-phenylethyl benzoate **3b′**[31,32] as a white amorphous solid; yield: 66 mg (19%). ^{1}H NMR: δ = 8.14–8.08 (m, 2H, Ar), 7.94–7.90 (m, 2H, Ar), 7.60–7.50 (m, 2H, Ar), 7.48–7.32 (m, 8H, Ar), 7.03 (s, 1H, H-1); ^{13}C NMR: δ = 192.6, 166.0, 133.5, 130.2–128.5 (17 C), 77.9; ESI-MS (M = 350.8): m/z = 373.8 (M + Na$^+$); anal. calcd. for $C_{21}H_{15}ClO_3$: C 71.90, H 4.31; found: C 71.63, H 4.55; HR-MS (ESI/Q-TOF): m/z = 351.0779, calcd. for $C_{21}H_{16}ClO_3$ [M + H]$^+$: 351.0782.

Eluted second was **3b**[32] as a white amorphous solid; yield: 266 mg (76%). ^{1}H NMR: δ = 8.14–8.06 (m, 2H, Ar), 8.00–7.94 (m, 2H, Ar), 7.60–7.32 (m, 10H, Ar), 7.06 (s, 1H, H-1); ^{13}C NMR: δ = 193.4, 165.9, 135.4, 134.5, 133.7, 133.5, 130.0–128.4 (14C), 77.3; ESI-MS (M = 350.8): m/z = 373.7 (M + Na$^+$); anal. calcd. for $C_{21}H_{15}ClO_3$: C 71.90, H 4.31; found: C 71.66, H 4.11; HR-MS (ESI/Q-TOF): m/z = 373.0601, calcd. for $C_{21}H_{15}ClO_3Na$ [M + Na]$^+$: 373.0602.

1-(2,3-Dichlorophenyl)-2-oxo-2-phenylethyl benzoate (3c): Column chromatography with 50:1 cyclohexane-AcOEt afforded **3c** as a white amorphous solid; yield: 307 mg (80%). ^{1}H NMR: δ = 8.12–8.04 (m, 2H, Ar), 8.02–7.94 (m, 2H, Ar), 7.62–7.53 (m, 2H, Ar), 7.61 (s, 1H, H-1), 7.52–7.39 (m, 6H, Ar), 7.22 (t, 1H, J = 8.0 Hz, Ar); ^{13}C NMR: δ = 193.2, 165.8, 134.5, 134.2, 133.8, 132.4, 131.7, 130.3, 129.1–128.1 (12C), 74.5; ESI-MS (M = 385.1): m/z = 386.7 (M + H$^+$); anal. calcd. for $C_{21}H_{14}Cl_2O_3$: C 65.47, H 3.66; found: C 65.31, H 3.40; HR-MS (ESI/Q-TOF): m/z = 407.0259, calcd. for $C_{21}H_{14}Cl_2O_3Na$ [M + Na]$^+$: 407.0218.

1-(2-Bromophenyl)-2-(4-bromophenyl)-2-oxoethyl 4-bromobenzoate (4d): For the synthesis of **4d** 6 mL of solvent were used. Column chromatography with 30:1 cyclohexane-AcOEt afforded **4d** as a white amorphous solid; yield: 503 mg (91%); ^{1}H NMR: δ = 7.98–7.90 (m, 2H, Ar), 7.88–7.80 (m, 2H, Ar), 7.70–7.64 (m, 1H, Ar), 7.62–7.52 (m, 4H, Ar), 7.44 (s, 1H, H-1), 7.43–7.38 (m, 1H, Ar), 7.36–7.20 (m, 2H, Ar); ^{13}C NMR: δ = 192.3, 165.1, 133.7, 133.0, 132.2–130.2 (11C), 192.2, 128.7, 128.3, 127.9, 124.7, 77.3; ESI-MS (M = 553.0): m/z = 554.6 (M + H$^+$); anal. calcd. for $C_{21}H_{13}Br_3O_3$: C 45.61, H 2.37; found: C 45.88, H 2.65; HR-MS (ESI/Q-TOF): m/z = 572.8295, calcd. for $C_{21}H_{13}Br_3O_3Na$ [M + Na]$^+$: 572.8307.

2-Oxo-1,2-diphenylethyl benzoate (3e): For the synthesis of **3e** three equiv. of aldehyde **2e** were used and the reaction was performed at 50 °C. Column chromatography with 10:1 cyclohexane-AcOEt afforded **3e**[25] as a white amorphous solid; yield: 205 mg (65%). ^{1}H NMR: δ = 8.14–8.08 (m, 2H, Ar), 8.02–7.94 (m, 2H, Ar), 7.60–7.50 (m, 4H, Ar), 7.48–7.34 (m, 7H, Ar), 7.08 (s, 1H, H-1); ^{13}C NMR: δ = 193.7, 166.0, 134.7, 133.7, 133.5, 133.4, 130.0, 129.3, 129.1–128.4 (12C), 77.9; ESI-MS (M = 316.3): m/z = 339.6 (M + Na$^+$); anal. calcd. for $C_{21}H_{16}O_3$: C 79.73, H 5.10; found: C 79.99, H

5.48; HR-MS (ESI/Q-TOF): $m/z = 339.0925$, calcd. for $C_{21}H_{16}O_3Na$ $[M+Na]^+$: 339.0997.

2-Oxo-2-phenyl-1-(*o*-tolyl)ethyl benzoate (3f): For the synthesis of **3f** three equiv. of aldehyde **2f** were used and the reaction was performed at 50 °C. Column chromatography with 12:1 cyclohexane-AcOEt afforded **3f**[16] as a white amorphous solid; yield: 182 mg (55%). ^{1}H NMR: $\delta = 8.14$–8.08 (m, 2H, Ar), 7.92–7.86 (m, 2H, Ar), 7.60–7.7.37 (m, 8H, Ar), 7.32–7.14 (m, 2H), 7.29 (s, 1H, H-1), 2.50 (s, 3H, CH_3); ^{13}C NMR: $\delta = 194.2$, 166.1, 137.3, 135.0, 133.4, 133.3, 132.3, 131.3, 130.0–128.4 (11C), 126.7, 75.6, 19.5; ESI-MS (M = 330.4): $m/z = 331.9$ $(M+H^+)$; anal. calcd. for $C_{22}H_{18}O_3$: C 79.98, H 5.59; found: C 79.61, H 5.21; HR-MS (ESI/Q-TOF): $m/z = 353.1138$, calcd. for $C_{22}H_{18}O_3Na$ $[M+Na]^+$: 353.1148.

1-(2-Chlorophenyl)-2-oxo-2-(*p*-tolyl)ethyl 4-methylbenzoate (5a): For the synthesis of **5a** two equiv. of diketone **1c** were used. Column chromatography with 9:1 cyclohexane-AcOEt afforded **5a** as a yellow foam; yield: 317 mg (84%). ^{1}H NMR: $\delta = 8.00$–7.94 (m, 2H, Ar), 7.93–7.88 (m, 2H, Ar), 7.54 (s, 1H, H-1), 7.52–7.43 (m, 2H, Ar), 7.38–7.18 (m, 6H), 2.40 (s, 3H, CH_3), 2.36 (s, 3H, CH_3); ^{13}C NMR: $\delta = 193.0$, 165.8, 144.7, 144.1, 134.1, 132.2, 131.9, 130.6–128.9 (10C), 127.5, 126.5, 126.4, 73.7, 21.7 (2C); ESI-MS (M = 378.8): $m/z = 401.5$ $(M+Na^+)$; anal. calcd. for $C_{23}H_{19}ClO_3$: C 72.92, H 5.06; found: C 72.77, H 5.29; HR-MS (ESI/Q-TOF): $m/z = 379.1084$, calcd. for $C_{23}H_{20}ClO_3$ $[M+H]^+$: 379.1095.

1-(2-Chlorophenyl)-2-oxo-2-(pyridin-2-yl)ethyl picolinate (6a): Column chromatography with 2:1 cyclohexane-AcOEt afforded **6a** as a white foam; yield: 320 mg (91%). ^{1}H NMR: $\delta = 8.79$–8.74 (m, 1H, Ar), 8.62–8.56 (m, 1H, Ar), 8.20–8.14 (m, 1H, Ar), 8.09–8.03 (m, 1H, Ar), 8.08 (s, 1H, H-1), 7.86–7.74 (m, 2H, Ar), 7.49–7.36 (m, 4H, Ar), 7.30–7.26 (m, 2H, Ar); ^{13}C NMR: $\delta = 193.9$, 164.3, 151.3, 150.1, 149.1, 147.5, 136.9, 136.8, 135.2, 131.9, 130.4, 130.3, 130.2, 127.6, 127.1, 127.0, 125.7, 122.8, 75.5; ESI-MS (M = 352.7): $m/z = 375.9$ $(M+Na^+)$; anal. calcd. for $C_{19}H_{13}ClN_2O_3$: C 64.69, N 7.94, H 3.71; found: C 64.85, N 7.72, H 3.95; HR-MS (ESI/Q-TOF): $m/z = 353.0690$, calcd. for $C_{19}H_{14}ClN_2O_3$ $[M+H]^+$: 353.0687.

1-(1-Bromonaphthalen-2-yl)-2-oxo-2-(pyridin-2-yl)ethyl picolinate (6g): Column chromatography with 2.5:1 cyclohexane-AcOEt afforded **6g** as a white foam; yield: 393 mg (88%). ^{1}H NMR: $\delta = 8.80$–8.76 (m, 1H, Ar), 8.58–8.55 (m, 1H, Ar), 8.45–8.40 (m, 1H, Ar), 8.38 (s, 1H, H-1), 8.19–8.16 (m, 1H, Ar), 8.10–8.05 (m, 1H, Ar), 7.85–7.73 (m, 4H, Ar), 7.64–7.58 (m, 1H, Ar), 7.57–7.51 (m, 2H, Ar), 7.50–7.44 (m, 1H, Ar), 7.40–7.35 (m, 1H, Ar); ^{13}C NMR: $\delta = 194.2$, 164.2, 151.3, 150.1, 149.5, 149.2, 147.5, 135.9, 136.8, 134.5, 132.7, 131.6, 128.3–127.0 (7C), 126.1, 125.7, 122.8, 79.0; ESI-MS (M = 447.2): $m/z = 448.8$ $(M+H^+)$; anal. calcd. for $C_{23}H_{15}BrN_2O_3$: C 61.76, N 6.26, H 3.38; found: C 61.58, N 6.49, H 3.65; HR-MS (ESI/Q-TOF): $m/z = 447.0330$, calcd. for $C_{23}H_{16}BrN_2O_3$ $[M+H]^+$: 447.0339.

2-(2-Chlorophenyl)-1-(2,3-dichlorophenyl)-2-oxoethyl 2-chlorobenzoate (7c): Column chromatography with 20:1 cyclohexane-AcOEt afforded **7c** as a white foam; yield: 358 mg (79%). ^{1}H NMR: $\delta = 8.00$–7.96 (m, 2H, Ar), 7.74–7.70 (m, 2H, Ar), 7.55.7.50 (m, 2H, Ar), 7.49 (s, 1 H H-1), 7.48–7.44 (m, 1H, Ar), 7.42–7.21 (m, 4H, Ar); ^{13}C NMR: $\delta = 194.4$, 164.2, 136.1, 134.5, 133.8, 133.3, 132.9, 132.5, 132.4, 132.1, 131.7, 131.6, 131.3, 130.6, 129.6, 128.7, 128.4, 127.7, 126.9, 126.7, 77.1; ESI-MS (M = 454.1): $m/z = 455.6$ $(M+H^+)$; anal. calcd. for $C_{21}H_{12}Cl_4O_3$: C 55.54, H 2.66; found: C 55.35, H 2.47; HR-MS (ESI/Q-TOF): $m/z = 455.1344$, calcd. for $C_{21}H_{13}Cl_4O_3$ $[M+H]^+$: 455.1381.

1-Oxo-1-phenylpropan-2-yl benzoate (3h): For the synthesis of **3h** two equiv. of aldehyde **2h** were used. Column chromatography with 10:1 cyclohexane-AcOEt afforded **3h**[30] slightly contaminated by uncharacterized products; yield: 142 mg (56%). ^{1}H NMR: $\delta = 8.12$–8.08 (m, 2H, Ar), 8.03–7.96 (m, 2H, Ar), 7.62–7.56 (m, 2H, Ar), 7.52–7.42 (m, 4H, Ar), 6.21 (q, 1H, $J = 6.8$ Hz, H-2), 1.64 (d, 3H, $J = 6.8$ Hz, CH_3); ^{13}C NMR: $\delta = 196.7$, 166.0, 134.5, 133.6, 133.3, 129.9, 129.5, 128.8–128.4 (7C), 71.9, 17.2; ESI-MS (M = 254.3): $m/z = 255.7$ $(M+H^+)$; HR-MS (ESI/Q-TOF): $m/z = 277.0838$, calcd. for $C_{16}H_{14}O_3Na$ $[M+Na]^+$: 277.0835.

1-Oxo-1-phenylbutan-2-yl benzoate (3i): For the synthesis of **3i** two equiv. of aldehyde **2i** were used. Column chromatography with 9:1 cyclohexane-AcOEt afforded **3i**[33] as a white foam; yield: 219 mg (82%). ^{1}H NMR: $\delta = 8.14$–8.08 (m, 2H, Ar), 8.03–7.96 (m, 2H, Ar), 7.62–7.54 (m, 2H, Ar), 7.53–7.38 (m, 4H, Ar), 6.08 (dd, 1H, $J = 4.6$ Hz, $J = 7.8$ Hz, H-2), 2.15–1.92 (m, 2H, 2 H-3), 1.11 (t, 3H, $J = 7.4$ Hz, CH_3); ^{13}C NMR: $\delta = 196.5$, 166.3, 135.0, 133.6, 133.3, 129.9–128.1 (9C), 76.8, 25.0, 10.1; ESI-MS (M = 268.3): $m/z = 269.9$ $(M+H^+)$; anal. calcd. for $C_{17}H_{16}O_3$: C 76.10, H 5.55; found: C 75.82, H 6.01; HR-MS (ESI/Q-TOF): $m/z = 291.1002$, calcd. for $C_{17}H_{16}O_3Na$ $[M+Na]^+$: 291.0992.

Representative Procedure for the Deprotection of Benzoylated benzoins 3–7

A mixture of benzoylated benzoin **3a** (150 mg, 0.43 mmol) and MeCN (4 mL) was vigorously stirred, degassed under vacuum, and saturated with argon (by an argon-filled balloon) three times. Then, to the refluxed mixture was added a 0.09 M aqueous solution of NaOH (6 mL) by a syringe-pump apparatus during 15 min. At the end of the addition, the mixture was refluxed for an additional 30, cooled to room temperature, and neutralized with 0.1 M aqueous HCl. The resulting mixture was partially concentrated, diluted with H_2O (5 mL), and extracted with AcOEt (2×25 mL). The combined organic phases were dried (Na_2SO_4), concentrated, and eluted from a column of silica gel with 14:1 cyclohexane-AcOEt to give *2-(2-chlorophenyl)-2-hydroxy-1-phenylethanone* (**8a**)[13a] as a white amorphous solid; yield: 89 mg (85%). ^{1}H NMR: $\delta = 7.94$–7.90 (m, 2H, Ar), 7.56–7.50 (m, 1H, Ar), 7.44–7.36 (m, 3H, Ar), 7.24–7.14 (m, 2H, Ar), 7.15–7.08 (m, 1H, Ar), 6.38 (d, 1H, $J = 5.5$ Hz, H-2), 4.57 (d, 1H, $J = 5.5$ Hz, OH); ^{13}C NMR: $\delta = 199.7$, 136.7, 134.1, 136.6, 133.1, 130.3, 130.0, 128.9–128.7 (5C), 127.7, 72.7; ESI-MS (M = 246.7): $m/z = 269.8$ $(M+Na^+)$; anal. calcd. for $C_{14}H_{11}ClO_2$: C 68.16, H 4.49; found: C 68.16, H 6.01; HR-MS (ESI/Q-TOF): $m/z = 269.0330$, calcd. for $C_{14}H_{11}ClO_2Na$ $[M+Na]^+$: 269.0340.

α,α′-Stilbenediol Dibenzoate (9a)

To a vigorously stirred mixture of benzil **1a** (105 mg, 0.50 mmol), 4 Å molecular sieves (50 mg), and anhydrous DMSO (1 mL), potassium *tert*-butoxide (11 mg, 0.10 mmol) was added in one portion. The mixture was stirred at room temperature and analyzed (^{1}H NMR) at regular time intervals (30 min) to eventually detect the formation of diagnostic species. After 8 h reaction time, the mixture was diluted

with H_2O (5 mL) and extracted with Et_2O (2×25 mL). The combined organic phases were dried (Na_2SO_4), concentrated, and eluted from a column of silica gel with 25:1 cyclohexane-AcOEt to give first unreacted **1a**; yield: 61 mg (58%).

Eluted second was **9a**[6a,24,34] as a 2.5:1 mixture of *E*/*Z* diastereoisomers; yield: 37 mg (35%). ^{1}H NMR (selected data for the *E*-isomer): δ = 8.14–8.06 (m, 4H, Ar), 7.72–7.64 (m, 4H, Ar); ^{13}C NMR (selected data for the *E*-isomer): δ = 164.6, 140.0; ^{1}H NMR (selected data for the *Z*-isomer): δ = 8.06–8.00 (m, 4H, Ar), 7.64–7.56 (m, 4H, Ar); ^{13}C NMR (selected data for the *Z*-isomer): δ = 164.2, 138.9; ESI-MS (M = 420.5): *m*/*z* = 443.7 ($M+Na^+$); anal. calcd. for $C_{28}H_{20}O_4$: C 79.98, H 4.79; found: C 79.72, H 4.50; HR-MS (ESI/Q-TOF): *m*/*z* = 443.1232, calcd. for $C_{28}H_{20}O_4Na$ [$M+Na]^+$: 443.1259.

If the reaction is not performed under strictly anhydrous conditions the benzoylated benzoin **3e** is formed in place of **9a**.

Acknowledgements

We gratefully acknowledge University of Ferrara (fondi FAR) and MIUR (Progetto PRIN, grants 2009ZSC5K2 004 and 20098SJX4F 004) for financial support. Thanks are also given to Mr. P. Formaglio for NMR spectroscopic experiments, to Mrs. Ercolina Bianchini for elemental analyses, and to Dr. T. Bernardi for high-resolution mass spectrometric experiments.

References

[1] D. Seebach, *Angew. Chem.* **1979**, *91*, 259–278; *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 239–258.

[2] a) F. Wöhler, J. Liebig, *Ann. Pharm.* **183**2, 3, 249–282; b) T. Ukai, R. Tanakaand, T. Dokawa, *J. Pharm. Soc. Jpn.* **1943**, *63*, 296–300; c) R. Breslow, *J. Am. Chem. Soc.* **1958**, *80*, 3719–3726. For recent reviews, see: d) K. Hirano, I. Piel, F. Glorius, *Chem. Lett.* **2011**, *40*, 786–791; e) A. T. Biju, N. Kuhl, F. Glorius, *Acc. Chem. Res.* **2011**, *44*, 1182–1195; f) V. Nair, R. S. Menon, A. T. Biju, C. R. Sinu, R. R. Paul, A. Jose, V. Sreekumar, *Chem. Soc. Rev.* **2011**, *40*, 5336–5346; g) H. U. Vora, T. Rovis, *Aldrichimica Acta* **2011**, *44*, 3–11; h) J. L. Moore, T. Rovis, *Top. Curr. Chem.* **2010**, *291*, 77–144; i) E. P. Phillips, A. Chan, K. A. Scheidt, *Aldrichimica Acta* **2009**, *42*, 55–65; j) D. Enders, *J. Org. Chem.* **2008**, *73*, 7857–7870; k) D. Enders, O. Niemeier, A. Henseler, *Chem. Rev.* **2007**, *107*, 5606–5655.

[3] A. Stamatis, G. Malandrinos, I. S. Butler, N. Hadjiliadis, M. Louloudi, *J. Mol. Catal. A: Chem.* **2007**, *267*, 120–128.

[4] a) X. Linghu, J. S. Johnson, *Angew. Chem.* **2003**, *115*, 2638–2640; *Angew. Chem. Int. Ed.* **2003**, *42*, 2534–2536; b) A. Ricci, A. Degl′Innocenti, S. Chimichi, M. Fiorenza, G. Rossini, *J. Org. Chem.* **1985**, *50*, 130–133.

[5] a) A. S. Demir, Ö. Reis, A. C. Iğdir, I. Esiringü, S. Eymur, *J. Org. Chem.* **2005**, *70*, 10584–10587; b) C. C. Bausch, J. S. Johnson, *Adv. Synth. Catal.* **2005**, *347*, 1207–1211; c) A. S. Demir, B. Reis, Ö. Reis, S. Eymur, M. Göllü, S. Tural, G. Saglam, *J. Org. Chem.* **2007**, *72*, 7439–7442.

[6] a) H. Kwart, M. M. Baevsky, *J. Am. Chem. Soc.* **1958**, *80*, 580–588; b) J. P. Kuebrich, R. L. Schowen, *J. Am. Chem. Soc.* **1971**, *93*, 1220–1223.

[7] a) X. Linghu, C. C. Bausch, J. S. Johnson, *J. Am. Chem. Soc.* **2005**, *127*, 1833–1840; b) J. C. Tarr, J. S. Johnson, *Org. Lett.* **2009**, *11*, 3870–3872.

[8] a) X. Bugaut, F. Glorius, *Chem. Soc. Rev.* **2012**, *41*, 3511–3522; b) D. Enders, T. Balensiefer, *Acc. Chem. Res.* **2004**, *37*, 534–541; c) C. Burstein, F. Glorius, *Angew. Chem.* **2004**, *116*, 6331–6334; *Angew. Chem. Int. Ed.* **2004**, *43*, 6205–6208; d) T. Dudding, K. N. Houk, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5770–5775; e) D. Enders, O. Niemeier, T. Balensiefer, *Angew. Chem.* **2006**, *118*, 1491–1495; *Angew. Chem. Int. Ed.* **2006**, *45*, 1463–1467; f) A. Berkessel, H. Gröger, in: *Asymmetric Organocatalysis*, Wiley-VCH, Weinheim, **2005**, p 227; g) H. Takikawa, Y. Hachisu, J. W. Bode, K. Suzuki, *Angew. Chem.* **2006**, *118*, 3572–3574; *Angew. Chem. Int. Ed.* **2006**, *45*, 3492–3494; h) C. Burstein, S. Tschan, X. Xie, F. Glorius, *Synthesis* **2006**, 2418–2439; i) D. Enders, O. Niemeier, G. Raabe, *Synlett* **2006**, 2431–2434; j) N. Marion, S. Díez-González, S. P. Nolan, *Angew. Chem.* **2007**, *119*, 3046–3058; *Angew. Chem. Int. Ed.* **2007**, *46*, 2988–3000; k) D. Enders, T. Balensiefer, O. Niemeier, M. Christmann, in: *Enantioselective Organocatalysis. Reactions and Experimental Procedures*, (Ed.: P. I. Dalko), Wiley-VCH, Weinheim, **2007**, pp 331–355.

[9] a) X. Linghu, J. R. Potnick, J. S. Johnson, *J. Am. Chem. Soc.* **2004**, *126*, 3070–3071; b) M. R. Nahm, X. Linghu, J. R. Potnick, C. M. Yates, P. S. White, J. S. Johnson, *Angew. Chem.* **2005**, *117*, 2429; *Angew. Chem. Int. Ed.* **2005**, *44*, 2377; c) A. Gliga, H. Klare, M. Schumacher, F. Soki, J. M. Neudörfl, B. Goldfuss, *Eur. J. Org. Chem.* **2011**, 256–263.

[10] S. E. O'Toole, C. A. Rose, S. Gundala, S. K. Zeitler, S. J. Connon, *J. Org. Chem.* **2011**, *76*, 347–357, and references cited therein.

[11] a) L. Baragwanath, C. A. Rose, K. Zeitler, S. J. Connon, *J. Org. Chem.* **2009**, *74*, 9214–9217; b) T. Dudding, K. N. Houk, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5770–5775; c) D. Enders, U. Kallfass, *Angew. Chem.* **2002**, *114*, 1822–1824; *Angew. Chem. Int. Ed.* **2002**, *41*, 1743–1745.

[12] For a recent review, see: A. Grossmann, D. Enders, *Angew. Chem.* **2012**, *124*, 320–332; *Angew. Chem. Int. Ed.* **2012**, *51*, 314–325.

[13] a) N. Kuhl, F. Glorius, *Chem. Commun.* **2011**, *47*, 573–575; b) I. Piel, M. D. Pawelczyk, K. Hirano, R. Fröhlich, F. Glorius, *Eur. J. Org. Chem.* **2011**, 5475–5484; c) D. Enders, A. Henseler, *Adv. Synth. Catal.* **2009**, *351*, 1749–1752; d) D. Enders, A. Grossmann, J. Fronert, G. Raabe, *Chem. Commun.* **2010**, *46*, 6282–6284.

[14] a) O. Bortolini, G. Fantin, M. Fogagnolo, P. P. Giovannini, V. Venturi, S. Pacifico, A. Massi, *Tetrahedron* **2011**, *67*, 8110–8115. For a highly stereoselective version, see: b) C. A. Rose, S. Gundala, C.-L. Fagan, J. F. Franz, S. J. Connon, K. Zeitler, *Chem. Sci.* **2012**, *3*, 735–740.

[15] V. Bertolasi, O. Bortolini, A. Donvito, G. Fantin, M. Fogagnolo, P. P. Giovannini, A. Massi, S. Pacifico, *Org. Biomol. Chem.* **2012**, *10*, 6579–6586.
[16] A. S. Demir, Ö. Reis, *Tetrahedron* **2004**, *60*, 3803–3811.
[17] a) E. J. Corey, M. Chaykovsky, *J. Am. Chem. Soc.* **1962**, *84*, 866–867; b) E. J. Corey, M. Chaykovsky, *J. Am. Chem. Soc.* **1965**, *87*, 1345–1353; c) P. Speers, K. E. Laidig, A. Steitwieser, *J. Am. Chem. Soc.* **1994**, *116*, 9257–9926.
[18] a) J. J. Bloomfield, *J. Org. Chem.* **1962**, *27*, 2742–2746; b) E. J. Corey, R. B. Mitra, H. Uda, *J. Am. Chem. Soc.* **1964**, *86*, 485–492; c) S. Danishefsky, G. Koppel, R. Levine, *Tetrahedron Lett.* **1968**, *9*, 2257–2260.
[19] a) E. J. Corey, M. Chaykovsky, *J. Am. Chem. Soc.* **1964**, *86*, 1639–1640; b) H. Nozaki, T. Mori, M. Kawanisi, *Can. J. Chem.* **1968**, *46*, 3767–3770; c) C. Walling, L. Bollyky, *J. Org. Chem.* **1964**, *29*, 2699–2701; d) W. A. Boll, *Tetrahedron Lett.* **1968**, 5531–5534.
[20] a) J. Liebig, *Justus Liebigs Ann. Chem.* **1838**, *25*, 1–31; b) S. Yamabe, N. Tsuchida, S. Yamazaki, *J. Org. Chem.* **2006**, *71*, 1777–1783.
[21] Equilibrium acidities in DMSO: F. G. Bordwell, *Acc. Chem. Res.* **1988**, *21*, 456–463.
[22] For the importance of benzoin esters as useful photolabile compounds, see: a) H. B. Lee, S. Balasubramanian, *J. Org. Chem.* **1999**, *64*, 3454–3460; b) M. C. Pirrung, S. W. Shuey, *J. Org. Chem.* **1994**, *59*, 3890–3897; c) G. Papageorgiou, J. E. T. Corrie, *Tetrahedron* **1997**, *53*, 3917–3932.
[23] For previous unconfirmed anomalies related to benzil as single reactant in similar conditions, see: a) J. C. Triesler, C. S. Aaron, J. L. Frye, J. Y. Park, *J. Org. Chem.* **1968**, *33*, 1077–1080; b) J. C. Trisler, J. K. Doty, J. M. Robinson, *J. Org. Chem.* **1969**, *34*, 3421–3425.
[24] J. C. Trisler, J. L. Frye, *J. Org. Chem.* **1965**, *30*, 306–307.
[25] The occurrence of a reduction/hydroacylation pathway was excluded because the formation of isomeric products of **3**, where the R group is on the ester functionality, was not observed (A. Chan, K. A. Scheidt, *J. Am. Chem. Soc.* **2006**, *128*, 4558–4559).
[26] a) F. M. Nachtigall, M. N. Eberlin, *Organic Reaction Studies by ESI-MS*, in: *Reactive Intermediates: MS Investigations in Solution*, (Ed.: L. S. Santos), Wiley-VCH, Weinheim, **2010**; b) K. L. Busch, G. L. Glish, S. A. McLuckey, *Mass Spectrometry/Mass Spectrometry. Techniques and Applications of Tandem Mass Spectrometry*, VCH, New York, **1988**.
[27] This fragmentation occurs with a hydrogen shift.
[28] Density functional theory (DFT) calculations carried out at the B3LYP/6–31G(d,p) level of theory showed the intermediate **IV** as the most stable structure (see the Supporting Information).
[29] O. Bortolini, G. Fantin, M. Fogagnolo, P. P. Giovannini, A. Massi, S. Pacifico, *Org. Biomol. Chem.* **2011**, *9*, 8437–8444.
[30] M. Uyanik, D. Suzuki, T. Yasui, K. Ishihara, *Angew. Chem.* **2011**, *123*, 5443–5446; *Angew. Chem. Int. Ed.* **2011**, *50*, 5331–5334.
[31] D. Armesto, W. M. Horspool, M. J. Ortiz, R. Perez-Ossorio, *Synthesis* **1988**, 799–801.
[32] M. B. Rubin, S. Inbar, *J. Org. Chem.* **1988**, *53*, 3355–3358.
[33] S. Arseniyadis, K. S. Kyler, D. S. Watt, *Org. React.* **1984**, 1–364.
[34] T.-C. Wong, R. D. Rieke, *J. Org. Chem.* **1988**, *53*, 2381–2383.

