# Microwave-Irradiated Transition-Metal Catalysis: Rapid and Efficient Dehydrative Carbon–Carbon Coupling of Alcohols with Active Methylenes

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Abstract: A rapid and highly productive synthetic microwaveirradiation protocol for transition-metal-catalyzed carbon–carbon coupling of a wide range of benzylic/allylic alcohols with  $\beta$ -diones,  $\beta$ -keto esters, and dialkyl malonates is reported. In a representative screening of transition-metal catalysts, salts of Zn, Cu, Fe, Sc, Ru, Pt, Ta, and Mo were found to furnish the coupling products. In light of the results obtained, among all of these catalysts copper(II) triflate was found to be relatively more effective compared to other catalysts even in the case of a less reactive benzyl alcohol or diester. Interestingly, these MW-irradiated reactions are performed in a more or less MW-transparent medium, such as toluene, having a very low tan $\delta$ , or under neat conditions.

**Key words:** alcohols, alkylations, catalysis, C–C coupling, dicarbonyl compounds, microwave irradiation, transition metals

Driving chemical reactions by microwave irradiation is recognized as, more or less, an ecofriendly alternative to conventional heating methods.<sup>1,2</sup> Especially, the celebrated transition-metal-based reactions under conventional heating, e.g., Suzuki–Miyaura,<sup>3a</sup> Migita–Kosugi–Stille,<sup>3b</sup> Negishi,<sup>3c</sup> Heck,<sup>3d</sup> Sonogashira<sup>3e</sup> C–C and Buchwald– Hartwig<sup>3f</sup> C–N coupling reactions, are very well-emerging transformations at superior speeds under MW irradiation<sup>1–3</sup> than with conventional heating conditions. This is, perhaps, because the rate and efficiency is very high in MW-irradiated protocols, which are cleaner than conventional heating methods.<sup>1–3</sup>

The C–C coupling reaction of alkyl halides and pseudohalides with active methylene compounds is an important protocol in organic syntheses.<sup>4–7</sup> Generally, these processes require the use of a stoichiometric amount of base. Strikingly, organic chemists have envisioned the catalytic addition of alkenes<sup>6</sup> or alcohols<sup>7</sup> with active methylene compounds as an ingenious atom-economical<sup>8</sup> green protocol. Water is the only byproduct if alcohol is employed (as compared to HX in the case of alkyl halides<sup>4</sup>) and alcohols are abundantly available.

In this extremely demanding task, initially we, and subsequently others, have reported Lewis or Brønsted acid catalyzed C–C coupling reactions using alcohols under conventional heating conditions.<sup>9,10</sup> Despite these rapid developments, perhaps due to the poor leaving ability of the hydroxy group and the low activation of the alcohols by catalysts, in most of these methods a very long heating period (5 h to 24 h, for a moderate to very good yield) and often a special solvent, e.g., nitromethane<sup>9c-h</sup> or dichloromethane,<sup>10a</sup> were essential. In some cases, stoichiometric or excess amounts<sup>10</sup> of Lewis acids (BF<sub>3</sub>·OEt<sub>2</sub>),<sup>10a</sup> or Brønsted acids (AcOH<sup>7d</sup> or HCO<sub>2</sub>H<sup>10b</sup>) and alcohols or active methylene compounds<sup>9d</sup> were required even when using extended heating periods.<sup>9,10</sup> Hence, new and efficiently accelerated catalytic protocols with a wide range of applicability and operational simplicity are extremely desirable for this exigent C–C coupling.

Taking impetus from the efficient, well-known MW-accelerated transition-metal-catalyzed C–C and C–N coupling reactions,<sup>1–3</sup> we envisaged the significant coupling of alcohols with active methylene compounds under MWirradiated metal catalysis.

To the best of our knowledge there exists no report on the MW-irradiated cross dehydrative C–C coupling of active methylene compounds with alcohols as nucleophiles.<sup>1–3</sup> Herein, we report a synthetically essential and highly productive MW-induced transition-metal-catalyzed coupling of alcohols with active methylene compounds.

At first, we examined the transition-metal catalysts under MW irradiation with toluene as the medium by using the reactive combination of diphenylmethanol (1a) and acetylacetone (2a) (100 °C, 15 min, Table 1). Several transition-metal catalysts were found to be promising candidates, including, fortunately, some of the common and inexpensive metals such as copper, zinc, and iron. Several other representative transition-metal catalysts salts, listed in Table 1, were ineffective.

Next, in the reaction using low reactive 4-bromobenzyl alcohol (1b) with 1,3-diphenylpropane-1,3-dione (2b), the catalytic activity of copper(II) triflate is apparently higher than that of scandium, zinc, and iron (Table 2) affording 3b in 63% yield. The effect of MW is also obvious because the low efficiency under thermal heating. Although scandium(III) triflate<sup>9e</sup> and iron(III) chloride<sup>9d</sup> catalysts were effective with more reactive substrates 1a and 2a,

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	MW irradiation	ĬĬ
Ph Ph <b>1a 2a</b> (1 mmol) (1.2–1.5 mr	catalyst (5 mol%), toluene, 100 °C, 15 min nol)	Ph Ph
	,	3a
Catalyst	Yield (%) of	3a
none	0 <sup>b</sup>	
NiBr <sub>2</sub>	0	
WCl <sub>4</sub>	0	
SnCl <sub>2</sub> <sup>c</sup>	0	
CoCl <sub>2</sub> <sup>c</sup>	0	
$ZrCl_4$	0	
CrCl <sub>2</sub>	0	
LaCl <sub>3</sub>	0	
MnCl <sub>2</sub>	0	
NbCl <sub>5</sub>	0	
Pd(PPh <sub>3</sub> ) <sub>4</sub> <sup>c</sup>	0	
RhCl(PPh <sub>3</sub> ) <sub>3</sub>	0	
YCl <sub>3</sub>	0	
HfCl <sub>4</sub>	0	
AgClO <sub>4</sub>	8	
$Zn(OTf)_2^{d}$	30	
RuCl <sub>3</sub>	80	
$ZnBr_2^{\ d}$	95	
TaI <sub>5</sub>	99	
$H_2PtCl_6 \cdot 6 H_2O$	99	
Sc(OTf) <sub>3</sub>	98	
Cu(OTf)2 <sup>d</sup>	98	
FeCl <sub>2</sub>	99	

<sup>a</sup> Irradiations were performed in a Biotage Initiator, sealed tube and the temperature ramped to that stated and held there for 15 min at normal absorption.

<sup>c</sup> 3 mol%.

<sup>d</sup> 110 °C.

they were not effective in the case of a less reactive benzyl alcohol **1b**, with the exception of copper(II) triflate.

Next, we screened solvents congenial to MW irradiation for the coupling reaction of diphenylmethanol (1a) with acetylacetone (2a). The copper(II) triflate catalyst system did not effect the reaction in polar solvents, such as ethanol, dimethyl sulfoxide, *N*,*N*-dimethylformamide, which are usually employed to readily achieve higher temperatures, and gave no product (Table 3). Other polar solvents such as tetrahydrofuran, chloroform, and acetone were less favorable. It was observed that even nonpolar solvents such as methylcyclohexane and hexane gave comparable yields to ethyl acetate and acetonitrile. Analogously, the nonpolar solvent toluene afforded **3a** in excellent yield, which is comparable to chlorinated solvents such as 1,2-dichloroethane and chlorobenzene. Naturally, toluene was selected as an ecofriendly solvent.

To attain higher temperatures that effect the chemical reactions of organic functional groups, MW irradiations are usually performed in polar media that has a permanent dipole moment and high tand factor.<sup>11a,b</sup> These characteristics are essential requirements for an efficient absorption of MW and the generation of heat (temperature) to effect the chemical reactions of functional groups present in the solvent medium. However, the MW-irradiated coupling reaction of alcohol 1a with 2a was effective even in a more or less MW transparent nonpolar media (with a very low tan $\delta$  factors) such as hexane, methylcyclohexane, or toluene (Table 3).<sup>11c</sup> This is perhaps because of: (a) a low absorption of MW by these solvents, and (b) relatively enhanced direct contact of MW with the functional groups of reactants (alcohol, ketone, and catalyst) themselves having a permanent dipole moment that might effected the coupling reaction (similar to neat reaction conditions).<sup>1-3,11d</sup> Additionally, in hexane or methylcyclohexane a slightly higher yield of product 3a was observed using MW than under oil bath heating.<sup>11e</sup> Since the theoretical aspects of heating by MW is still a topic of research,<sup>1-3</sup> it could be speculated that either one or both components of MW (electric and magnetic) could be activating the substrates in a medium with a low tan $\delta$  factor.

Taking impetus from these results, the generality of this MW-irradiated coupling was demonstrated for a high efficiency using a variety of 1,3-diones and alcohols (Table 4).<sup>11f</sup> From the point of convenience and efficient productivity, copper, zinc, and iron catalysts were employed in the coupling reactions. The iron(III) chloride catalyzed reactions of diarylmethanols **1a**,**c** with dione **2a** under solvent-free conditions gave 3a,c in quantitative yields (Table 4, entries 1 and 2). 1-Phenylethanol (1d) effectively reacted with the diketones 2a and 2b in the presence of copper(II) triflate and zinc(II) bromide, respectively (Table 4, entries 3 and 4). Then, the couplings of allylic alcohols 1e, f, with 2a, b were effected by copper(II) triflate, scandium(III) triflate, zinc(II) bromide, and iron(III) chloride catalysts to give the respective products effectively (Table 4, entries 5-8). The highly enolizable cyclic dione 2c was MW irradiated with 1a in the presence of copper(II) triflate to give 3i with an all-carbon quaternary center (Table 4, entry 9).

<sup>&</sup>lt;sup>b</sup> 20 min.

1b 2b 3b B **Conditions**<sup>a</sup> Catalyst (5 mol%) Time (min) Yield (%) MW, chlorobenzene, 135 °C Cu(OTf)<sub>2</sub> 30 63<sup>b</sup> MW, chlorobenzene, 135 °C Sc(OTf)<sub>3</sub> 45 29 MW, chlorobenzene, 135 °C Zn(OTf)<sub>2</sub> 0 45 0<sup>c</sup> MW, chlorobenzene, 135 °C FeCl<sub>3</sub> 45 50 MW, chlorobenzene, 135 °C Cu(OTf)<sub>2</sub> 45 chlorobenzene, 100 °C Cu(OTf)<sub>2</sub> 45 <20<sup>d</sup>  $0^d$ toluene, 110 °C Cu(OTf)<sub>2</sub> 45

Table 2 MW-Irradiated and Conventional Heating Reactions of 1b with 2b

<sup>a</sup> See footnote a in Table 1, very high absorption, reactions were carried out using 1b and 2b (1 mmol each), catalyst (5 mol%), solvent (2.5 mL).

<sup>b</sup> 1.5 mmol of **1b** was used.

<sup>c</sup> 4-Chlorobenzyl alcohol or benzyl alcohol was used instead of 1b.

<sup>d</sup> Oil bath heating.

Table 3 Screening of Solvents Suitable for MW Irradiation<sup>a</sup>



Solvent	$tan\delta^b$	Temp (°C)	Time (min)	Yield (%) MW	Oil bath		
EtOH <sup>c</sup>	0.941	100	15	0			
DMSO <sup>c</sup>	0.825	150	15	0			
DMF <sup>c</sup>	0.161	150	15	0			
CHCl <sub>3</sub> <sup>c</sup>	0.091	65	15	<10			
DCE <sup>c</sup>	0.127	90	15	98			
chlorobenzene <sup>c</sup>	0.101	110	12	90			
EtOAc <sup>c</sup>	0.059	85	15	67			
acetone <sup>c</sup>	0.054	60	15	<10			
MeCN <sup>c</sup>	0.062	90	3	70	50		
MeCN <sup>c</sup>	0.062	90	15	79	75		
THF <sup>c</sup>	0.047	70	15	<10	<10		
toluene <sup>d</sup>	0.040	110	15	>98	>98		
hexane <sup>d</sup>	0.020	70	15	55	48		
methylcyclohexaned	_e	90	3	53	32		
methylcyclohexaned	_e	90	15	84	69		

<sup>a</sup> Irradiations performed in a Biotage Initiator, sealed tube and the temperature ramped to that stated and held there for allotted time. <sup>b</sup> Values of tanδ factor as reported.<sup>11a,b</sup>

Reactions performed under very high absorption. <sup>d</sup> Reactions performed under normal absorption.

<sup>e</sup> tanδ value not available.

Table 4 MW-Irradiated Coupling of Alcohols with 1,3-Diones<sup>a</sup>

OH Ph	$R^1$ + $R^2$ $R^3$	$\frac{MW \ \text{irradiation}}{\text{toluene, } MtX_n, \ T \ \ ^{\circ}C,$	time R <sup>2</sup> Ph	2 R <sup>3</sup>			
Entry	Alcohol	Dione	Catalyst (mol%)	Temp (°C)	Time (min)	Product	Yield (%)
1 2	Ph + R $1a: R = Ph$ $1c: R = 4-Tol$	2a	FeCl <sub>3</sub> (5) FeCl <sub>3</sub> (5)	110 110	20 20	$\begin{array}{c} 0 & 0 \\ Ph & R \\ 3a: R = Ph \\ 3c: R = 4-Tol \end{array}$	<b>3a</b> : 99 <sup>b</sup> <b>3c</b> : 98 <sup>b</sup>
3 4	OH Ph	$\mathbf{a}: \mathbf{R} = \mathbf{M}\mathbf{e}$ $\mathbf{2a}: \mathbf{R} = \mathbf{P}\mathbf{h}$	$Cu(OTf)_2(5)$ $ZnBr_2(5)$	110 110	25 25	$\mathbf{3d: } \mathbf{R} = \mathbf{Me}$ $\mathbf{3e: } \mathbf{R} = \mathbf{Ph}$	<b>3d</b> : 75 <b>3e</b> : 92
5 6 7	OH le	2a 2a 2b	Cu(OTf) <sub>2</sub> (3) Sc(OTf) <sub>3</sub> (3) ZnBr <sub>2</sub> (5)	110 110 110	15 15 35	$\mathbf{3f}: \mathbf{R} = \mathbf{Me}$	<b>3f</b> : 67 <b>3f</b> : 75 <b>3g</b> : 77
8	Ph Ph	2a	FeCl <sub>3</sub> (3)	90	1	3f: R = Me $3g: R = Ph$ $0$ $Ph$ $Ph$ $Bh$	90
9	1a	20	Cu(OTf) <sub>2</sub> (5)	110	30	COMe Ph	85°

<sup>a</sup> See footnote a in Table 3, all reactions were carried out using 1 (1 mmol) and 2 (1–1.2 mmol) under normal absorption.

<sup>b</sup> Neat reaction performed using **2a** (1.5 mmol).

<sup>c</sup> Chlorobenzene was used under very high absorption.

Table 5 shows the reactions of alcohols with a variety of  $\beta$ -keto esters or dialkyl malonate; these are less reactive than 1,3-diones. The reaction of  $\beta$ -keto esters **2d**,**g** were promoted by convenient metal catalysts such as copper, iron, and zinc (Table 5, entries 1, 4, 5, 6, and 7). The iron(III) chloride catalyzed reaction of 2d with 1a in neat conditions gave **3j** quantitatively (Table 5, entry 1). The coupling reactions of alcohol **1a** with **2e**,**f** were also catalyzed by scandium(III) triflate (Table 5, entries 2 and 3). The  $\alpha$ -substituted  $\beta$ -keto esters **2f**,**g** afforded the products **31,m** with an all-carbon quaternary center (Table 5, entries 3 and 4). Another less common, demanding reaction is the coupling of an alcohol with the diesters dimethyl or diethyl malonate **2h**,**i**. The scandium(III) triflate or copper(II) triflate catalyzed MW-irradiated reactions of diesters 2h,i with **1a,g,c** gave **3p-r** in very good yields (Table 5, entries 8–10). Similarly, an allylic alcohol 1f with diethyl malonate (2i) gave 3s (Table 5, entries 11 and 12).

Next, to find the relatively high acceleration and efficiency under MW irradiation, we performed a preliminary comparison between conventional heat and MW-irradiated settings using  $\beta$ -keto esters. Representative examples are shown in Table 6. The iron(III) chloride catalyzed reaction of diphenylmethanol (1a) and ethyl 2-methyl-3oxobutanoate (2f) was completed in one minute to give 3l in 81% yield under MW irradiation, while conventional heating gave the same product in 35% yield. The reaction of 1-phenylethanol (1d) and  $\beta$ -keto ester 2d gave a similar result for **3t** in six minutes (44% and 10%). Analogously, the coupling of **1a** and highly enolizable cyclic keto ester 2j showed the same trend in 8 minutes (40% and 0%) in giving **3u**. The coupling of alcohol **1a** with a diester **2i** is difficult for the copper(II) triflate or scandium(III) triflate

MW irradiation OR4 R R3 toluene, cat. (X mol%) Ph R<sup>1</sup> Ŕ Entry Alcohol β-Keto ester MtX<sub>n</sub> Time Product Yield Temp or dialkyl malonate (mol%) (°C) (min) (%) OEt 1  $FeCl_3(5)$ 110 20 M (98)<sup>b</sup> OEt Ph P٢ Ph 1a 2d 3j MeC 2 110 25 OMe 65  $Sc(OTf)_3(3)$ **1**a MeC OMe Ph Ph 2e 3k 3 1a  $Sc(OTf)_3(3)$ 110 5 OEt 82 OEt Me Ме Ph Ph 2f31 Ph COOEt 110 20 95 4 1a  $FeCl_3(5)$ *\_*/0 OEt 2g 3m Ph ŌН Ph COOEt 5 110 15 2g  $ZnBr_{2}(5)$ 78°  $Zn(OTf)_2(5)$ 6 2g 110 15 83° Ph Ph 1f 3n 7 1f 2d  $Cu(OTf)_2(3)$ 110 5 OEt 90° Ph Ph 30 MeO OMe 71<sup>d</sup> 15 8  $Sc(OTf)_3(5)$ 135 Ph H₄CI-p MeC OMe P 2h 1g **3p**,**q 3p**: R = 4-ClC<sub>6</sub>H<sub>4</sub> 9 2h  $Sc(OTf)_3(5)$ 135 15 **3q**: R = 4-Tol 78<sup>d</sup> Ph 1c  $Cu(OTf)_2(5)$ 10 135 15 EtO OEt 71<sup>d</sup> **1**a EtO OEt Ph P٢ 2i 3r  $Sc(OTf)_3(5)$ 11 20 72<sup>d</sup> EtC OFt 1f 2i 135 12  $ZnBr_{2}(5)$ 15 69<sup>d</sup> Ph Pł 3s

Table 5 Coupling of Alcohols with  $\beta$ -Keto Esters or Dialkyl Malonates under MW<sup>a</sup>

<sup>a</sup> See footnote a, Table 3, all reactions were carried out using 1 (1 mmol) and 2 (1-1.1 mmol) under normal absorption.

<sup>b</sup> Neat reaction done using **2d** (1.5 mmol).

<sup>c</sup> ds ratio 1:1.

<sup>d</sup> Chlorobenzene was used under very high absorption.

Table 6 Attempts for Comparing the Efficiency and Rate Acceleration in MW and Conventional Heat Settings<sup>a</sup>



<sup>a</sup> See footnote a in Table 3, normal absorption, reactions were carried out using 1 and 2 (1 mmol each).

<sup>b</sup> Preheated oil bath was used.

<sup>c</sup> Chlorobenzene was used under very high absorption.

<sup>d</sup> Oil bath heating at 100 °C in toluene or chlorobenzene for 20 min.

<sup>e</sup> Oil bath reaction in toluene at 100 °C for 30 min.

<sup>f</sup> Oil bath reaction in chlorobenzene at 100 °C for 20 min.

catalyzed conventional heating reaction and furnishes only trace amounts of **3s**. In contrast, the MW-irradiation protocol gave **3s** in 71% or 93% yield, respectively, in just 15 minutes (Table 6). These investigations apparently revealed that the rate acceleration and efficiency in MW irradiation are far better than conventional heating conditions.

In conclusion, a synthetically essential, rapid and efficient MW-irradiated transition-metal-catalyzed C–C coupling of benzylic or allylic alcohols with  $\beta$ -dicarbonyls has been established. This green protocol offers easy and unlimited access for the coupling products.

MW irradiations were carried out in a Biotage Initiator, in a sealed tube (supplied by Biotage) and the temperature ramped to that stated and held there for allotted time (see the Tables 1–6 for the type of absorption was set for each solvent). IR spectra were recorded as thin films or KBr pellets on a Horiba FT-720 spectrophotometer. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on Jeol JNM-GSX-270 or 400 (270/67.9 or 400/100 MHz) spectrometers, respectively with TMS as internal standard. Carbon types were determined in DEPT <sup>13</sup>C NMR or OFR spectral analyses. MS spectra were recorded on a Jeol JMS-DS303 spectrometer. Column chromatography was performed on silica gel (100–200 mesh, Wako silica gel) or flash column was

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performed. Reactions were carried out either under MW irradiation in a sealed tube or under thermal heating in an inert atmosphere. Solutions were dried with anhydrous  $MgSO_4$ . Reagents were added to the reaction flask through syringe. Analytical TLC was performed on silica plates and components were visualized by observation under I<sub>2</sub> or UV light. Yields were determined from <sup>1</sup>H NMR spectra using internal standards or after isolation by column chromatography. Ratios of diastereomers were determined from <sup>1</sup>H NMR of crude reaction mixture.

Compounds 3a-h,<sup>12-18</sup> 3j,<sup>19</sup> 3m,<sup>20</sup> 3o,<sup>21</sup> 3r,<sup>22</sup> 3s,<sup>23</sup> and 3t<sup>15</sup> have been previously reported in the literature.

#### MW Irradiated Transition-Metal-Catalyzed Dehydrative C–C Coupling of Alcohols with Nucleophiles; General Procedure

To a dry sample tube closed by a septum containing a magnetic bead, alcohol (1 mmol) and  $\beta$ -dicarbonyl compound (1–1.1 mmol) were added under an inert atmosphere. Then an appropriate solvent (toluene or other solvent, see the appropriate Table) and catalyst were added. The sample tube was sealed with a cap and then subjected to MW irradiation (See Tables for the appropriate catalyst, temperature, and time). After the period of irradiation, the mixture was poured into a separating funnel containing H<sub>2</sub>O (2–3 mL) and extracted with Et<sub>2</sub>O (3 ×). The combined organic layers were dried and concentrated to afford the crude mixture, which was then purified by column chromatography. Yields of products were determined after isolation by column chromatography or from <sup>1</sup>H NMR spectra using an internal standard.

### Transition-Metal-Catalyzed Dehydrative C–C Coupling of Alcohols with Nucleophiles Using Conventional Heating; General Procedure

To a dry round-bottom flask were added the alcohol (1 mmol) and  $\beta$ -dicarbonyl compound (1–1.1 mmol) under an inert atmosphere. Then the appropriate solvent (toluene or other solvent) (2.5 mL) and catalyst were added. The flask was then dipped into a preheated oil bath (See Tables for appropriate catalyst, temperature and time). After the appropriate time, the mixture was cooled with a r.t. water bath and poured into a separating funnel containing H<sub>2</sub>O (2–3 mL) and extracted with Et<sub>2</sub>O (3 ×). The combined organic layers were dried and concentrated to afford the crude mixture. Yields of products were determined after isolation by column chromatography or from <sup>1</sup>H NMR spectra using an internal standard.

# Diethyl 2-Benzhydrylmalonate (3r); Typical Procedure for Gram-Scale Preparation

Diphenylmethanol (2 g, 10.8 mmol), diethyl malonate (1.75 g, 10.8 mmol), and Cu(OTf)<sub>2</sub> (195 mg, 5 mol%) in chlorobenzene (15 mL) were subjected to MW irradiation using a CEM discover MW machine for a hold period of 20 min at 110 °C (the temperature ramped to that stated in 9 min). After irradiation, the mixture was subjected to the usual workup procedure as given above to afford **3r** (2.39 g, 67%).

### 2-Acetyl-2-benzhydrylcyclohexanone (3i)

Mp 131–133 °C (hexane–Et<sub>2</sub>O).

IR (CDCl<sub>3</sub>): 1697, 1596, 1492, 1446 cm<sup>-1</sup>.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.23–7.12 (m, 10 H), 5.47 (s, 1 H), 2.81–2.76 (m, 1 H), 2.53–2.49 (m, 1 H), 2.22–2.14 (m, 1 H), 1.91–1.08 (m, 5 H), 1.84 (s, 3 H).

 $^{13}\text{C}$  NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 208.5, 204.3, 140.7, 140.2, 130.4, 130.2, 128.4, 128.0, 126.8, 126.4, 73.4, 53.2, 42.3, 31.1, 26.9, 25.2, 22.2.

GC-MS (CI): m/z (%) = 307 (M<sup>+</sup> + H, 0.48), 263 (3.3), 245 (4.6), 168 (14.1), 167 (100), 141 (2.8).

HRMS (CI):  $m/z \ [M + H]^+$  calcd for  $C_{21}H_{23}O_2$ : 307.1698; found: 307.1695.

## Methyl 2-Benzhydryl-4-methoxy-3-oxobutanoate (3k)

Mp 89–91 °C (hexane–Et<sub>2</sub>O).

IR (CDCl<sub>3</sub>): 1754, 1727, 1496, 1454 cm<sup>-1</sup>.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.31–7.13 (m, 10 H), 4.81 (d, J = 12.4 Hz, 1 H), 4.70 (d, J = 12.4 Hz, 1 H), 3.90 (d, J = 18.0 Hz, 1 H), 3.68 (d, J = 18.0 Hz, 1 H), 3.51 (s, 3 H), 3.18 (s, 3 H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 201.7, 167.5, 141.3, 140.8, 128.8, 128.6, 128.0, 127.4, 127.0, 126.8, 77.6, 59.2, 59.1, 52.5, 50.6.

GC-MS (CI): m/z (%) = 313 (M<sup>+</sup> + H, 0.36), 295 (2.3), 294 (6.2), 209 (5.6), 168 (13.4), 167 (100).

HRMS (CI):  $m/z [M + H]^+$  calcd for  $C_{19}H_{21}O_4$ : 313.1440; found: 313.1444.

## Ethyl 2-Benzhydryl-2-methyl-3-oxobutanoate (3l)

Colorless thick oil.

IR (CDCl<sub>3</sub>): 1712, 1496, 1450, 1230 cm<sup>-1</sup>.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.30–7.13 (m, 10 H), 5.27 (s, 1 H), 4.05–3.93 (m, 2 H), 2.05 (s, 3 H), 1.52 (s, 3 H), 1.01 (t, *J* = 6.8 Hz, 3 H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 204.5, 171.6, 141.1, 140.5, 129.9, 129.7, 128.2, 128.0, 126.6, 126.5, 65.0, 61.6, 53.6, 26.9, 18.2, 13.6.

GC-MS (EI): m/z (%) = 310 (M<sup>+</sup>, 0.02), 292 (29.6), 221 (11.7), 219 (13.33), 168 (13.9), 167 (100), 165 (17.0), 152 (8.1), 115 (6.9).

HRMS (EI): m/z [M]<sup>+</sup> calcd for C<sub>20</sub>H<sub>22</sub>O<sub>3</sub>: 310.1569; found: 310.1577.

Ethyl 1-(1,3-Diphenylallyl)-2-oxocyclopentanecarboxylate (3n) Isolated as a mixture of diastereomers (ds 70:30); colorless thick oil.

IR (CDCl<sub>3</sub>): 1751, 1724, 1600, 1492 cm<sup>-1</sup>.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.33–7.15 (m, 10 H), 6.52–6.34 (m, 2 H), 4.53 (d, *J* = 8.8 Hz, 1 H)\*, 4.43 (d, *J* = 8.8 Hz, 1 H), 4.17–4.07 (m, 2 H)\*, 3.98 (q, *J* = 7.2 Hz, 2 H), 2.73–2.70 (m, 1 H), 2.40–1.68 (s, 5 H), 1.18 (t, *J* = 7.2 Hz, 3 H)\*, 1.04 (t, *J* = 7.2 Hz, 3 H). \*Minor isomer.

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta = 213.3$ , 213.1\*, 168.9, 168.8\*, 139.6, 139.4\*, 136.8, 133.0, 132.8\*, 129.6, 128.8, 128.4\*, 124.4, 128.3, 128.2, 128.32, 127.4, 127.4\*, 66.2, 66.2\*, 61.7\*, 61.5, 52.8, 51.9\*, 38.8, 38.6\*, 29.9, 28.5\*, 19.7, 19.4\*, 14.0\*, 13.8. \*Minor isomer.

MS-FAB: m/z (%) = 371 (M<sup>+</sup> + Na, 77), 193 (100).

HRMS-FAB: m/z [M + Na]<sup>+</sup> calcd for C<sub>23</sub>H<sub>24</sub>NaO<sub>3</sub>: 371.1623; found: 371.1626.

# **Dimethyl 2-[(4-Chlorophenyl)phenylmethyl]malonate (3p)** Mp 87–89 °C (hexane–Et<sub>2</sub>O).

IR (CDCl<sub>3</sub>): 1754, 1735, 1492, 1434 cm<sup>-1</sup>.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.28–7.16 (m, 9 H), 4.75 (d, J = 12.4 Hz, 1 H), 4.32 (d, J = 12.4 Hz, 1 H), 3.56 (s, 3 H), 3.53 (s, 3 H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 167.8, 167.7, 140.5, 139.7, 132.7, 129.0, 128.8, 128.7, 127.5, 127.1, 57.0, 52.7, 52.6, 50.3.

GC-MS (EI): *m*/*z* (%) = 332 (M<sup>+</sup>, 32.5), 274 (28.0), 273 (27.9), 272 (80.4), 271 (13.0), 241 (45.2), 203 (31.4), 201 (100), 165 (57.9).

HRMS (EI): m/z [M]<sup>+</sup> calcd for C<sub>18</sub>H<sub>17</sub>ClO<sub>4</sub>: 332.0815; found: 332.0819.

# Dimethyl 2-[(4-Methylphenyl)phenylmethyl]malonate (3q) Mp 104–106 °C (hexane–Et $_2$ O).

IR (CDCl<sub>3</sub>): 1754, 1735, 1454, 1434 cm<sup>-1</sup>.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.28–7.24 (m, 4 H), 7.17–7.15 (m, 3 H), 7.06 (d, *J* = 7.6 Hz, 2 H), 4.73 (d, *J* = 12.4 Hz, 1 H), 4.34 (d, *J* = 12.4 Hz, 1 H), 3.55 (s, 3 H), 3.53 (s, 3 H), 2.26 (s, 3 H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 168.1, 168.1, 141.3, 138.1, 136.4, 129.3, 128.6, 127.6, 127.5, 126.8, 57.2, 52.6, 52.5, 50.7, 21.0.

GC-MS (EI): *m*/*z* (%) = 312 (M<sup>+</sup>, 23.3), 253 (15.0), 252 (50.0), 221 (28.8), 181 (100), 178 (13.7), 165 (24).

HRMS (EI): m/z [M]<sup>+</sup> calcd for C<sub>19</sub>H<sub>20</sub>O<sub>4</sub>: 312.1362; found: 312.1362.

#### **Ethyl 1-Benzhydryl-2-oxocyclohexanecarboxylate (3u)** Colorless thick oil.

IR (CDCl<sub>3</sub>): 1712, 1600, 1496, 1450 cm<sup>-1</sup>.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 7.42–7.12 (m, 10 H), 5.08 (s, 1 H), 3.93–3.72 (m, 2 H), 2.39–2.65 (m, 1 H), 2.45–2.37 (m, 2 H), 1.95–1.47 (m, 5 H), 0.88 (t, *J* = 6.8 Hz, 3 H).

 $^{13}$ C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 206.2, 170.6, 140.8, 140.4, 130.6, 130.2, 127.8, 126.5, 126.3, 65.8, 61.2, 54.0, 41.8, 34.8, 26.7, 22.6, 13.4.

MS-FAB: m/z (%) = 359 (M<sup>+</sup> + Na, 48), 167 (100).

HRMS-FAB: m/z [M + Na]<sup>+</sup> calcd for C<sub>22</sub>H<sub>24</sub>NaO<sub>3</sub>: 359.1623; found: 359.1627.

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