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## Solvent-Free Benzylation of 1, 3-Dicarbonyl Compounds with Benzylic Alcohols Catalysed by $\text{Bi}(\text{NO}_3)_3 \cdot 5\text{H}_2\text{O}$

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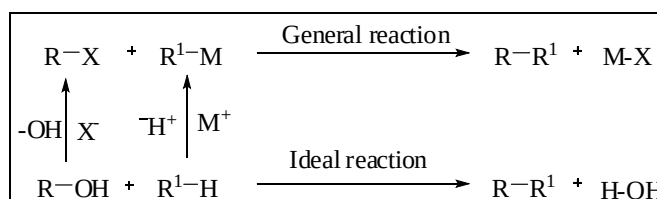
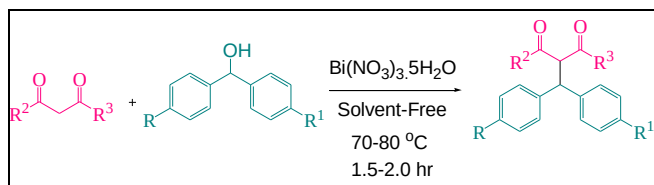
### Abstract

$\text{Bi}(\text{NO}_3)_3 \cdot 5\text{H}_2\text{O}$  is found to be an efficient catalyst for benzylation of secondary benzylic alcohols with 1,3-dicarbonyl compounds under solvent-free conditions at 80 °C. The present protocol exhibits an excellent substrates scope for various secondary benzylic alcohols with 1,3-dicarbonyl compounds. Eco-friendly, efficient, mild reaction conditions and a wide range of applicability to various substrates with high yield are the major advantages of the present protocol.

**Keywords:** Advertising, consumer, effect, problems, education, government

### Introduction

The formation of carbon-carbon bonds is one of the widely used fundamental reactions in organic transformations [1, 2]. Generally, this type of reaction occurs via a coupling reaction between active nucleophiles such as organometallic ( $\text{R}^1\text{M}$ ) and alkyl halides ( $\text{RX}$ ), or their analogs are some of the highly used protocols in organic synthesis. The coupling reaction between  $\text{R}^1\text{M}$  and  $\text{RX}$  produces  $\text{R-R}^1$  along with huge amounts of salt by-products (Scheme 1). In recent years the usage of eco-friendly, prevention of waste or by-products, atom economy, highly efficient, heterogeneous catalysts, green solvents, solvent-free, and safer chemical synthesis are received greater attention in organic synthesis. The development of direct catalytic carbon-carbon bond formation reactions of prior unmodified alcohols with various nucleophiles is considered to be an ideal protocol due to the generation of  $\text{H}_2\text{O}$  as the only side-product.



### Scheme 1: C

1,3-Dicarbonyl compounds and their analogs are widely used for the construction of carbon-carbon formation reactions in organic synthesis. The benzylation of 1,3-dicarbonyl derivatives leads to the generation of many bioactive structural motifs such as warfarin (oral coagulant), reglitazar (diabetes drug), and tipranavir (HIV protease inhibitor) being representative examples [3, 4]. Propargylation of 1,3-dicarbonyl derivatives provides access to valuable synthetic intermediates and heterocycles such as furans and pyrroles [5]. Similarly, allylic alkylations of 1,3-dicarbonyl compounds are an important type of carbon-carbon bond formation reaction that provides a convenient strategy for the construction of complex molecular structures from simple building blocks [6].

Recently, benzylation of 1,3-dicarbonyl compounds with secondary alcohols by using various catalysts such as Lewis

acids [7, 8] sulfamic acid supported on silica [9],  $\text{La}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$ , [10]  $\text{Fe}(\text{ClO}_4)_3 \cdot x\text{H}_2\text{O}$ , [11]  $\text{FeCl}_3$ , [12] trifluoromethanesulfonic acid, [13a] *p*-toluenesulfonic acid, [13b] polymer-supported *p*-toluenesulfonic acid, [13c] Metal triflate, [13d]  $\text{Bi}(\text{OTf})_3$ , [13e] H-Montmorillonite [13f] and  $\text{EMIOTf}$  [13g] have been reported.

Moreover, bismuth salts have attracted the attention of synthetic organic chemists and have been found to show promising catalytic abilities in many organic transformations. In continuation of the construction of C-C bond forming reactions, herein we report an efficient solvent-free benzylation of 1,3-dicarbonyl compounds with benzylic alcohols.

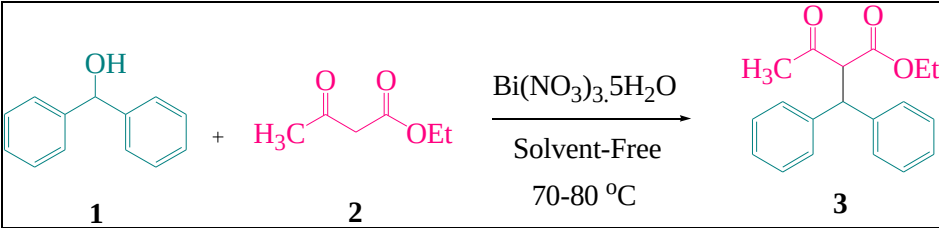
The solvent-free reactions are highly useful in the present research community because of simple to handle, reduce pollution, are comparatively economical to operate, and are especially important in industries. It is understood that solvent-free organic syntheses and transformations are industrially constructive and largely green. The solvent-free or neat reactions are shown the following advantages (a) Eco-friendly, (b) Not required to collect, purify, recycle and

remove solvent after completion of the reaction, (c) Due to more availability of reactants reaction rate is generally high i.e. reduces reaction time, (d) Economic viable (cost saving, save money on solvent), (e) Decreased energy consumption, (f) Large reduction in batch size volume (reactor size) and capital investment.

## Results and Discussion

Initially, we examined the benzylation of benzhydrol (1) with ethyl acetoacetate (2) in the absence of a catalyst in  $\text{CH}_3\text{CN}$  offered the only traces of desired product. Later, we have screened various catalysts for optimization for the benzylation of benzhydrol (1) with ethyl acetoacetate (2) and shown as in Table 1 (Entries 2-6). Among the various tested catalysts,  $\text{Bi}(\text{NO}_3)_3 \cdot 5\text{H}_2\text{O}$  was found to be the most effective catalyst by considering the amount of the catalyst, reaction time, and yield. After that, the effects of various solvents such as  $\text{CH}_3\text{CN}$ ,  $\text{CHCl}_3$ ,  $\text{CH}_3\text{OH}$ , THF, acetone, and solvent-free conditions have been studied (Table 1, entries 8-17). The solvent-free reaction is found to be the choice in terms of yield and reaction time (Table 1, entries 17).

**Table 1:** Optimization of reaction conditions for Benzylation of ethyl acetoacetate with benzhydrol<sup>a</sup>

|  |                                                      |                        |             |                     |                                 |
|-------------------------------------------------------------------------------------|------------------------------------------------------|------------------------|-------------|---------------------|---------------------------------|
| S. No.                                                                              | Catalyst                                             | Solvent                | Temperature | Reaction time (Hr.) | Isolated yield (%) <sup>b</sup> |
| 1                                                                                   | No catalyst                                          | $\text{CH}_3\text{CN}$ | rt          | 8.0                 | Trace                           |
| 2                                                                                   | $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$           | $\text{CH}_3\text{CN}$ | rt.         | 3.0                 | 46                              |
| 3                                                                                   | $\text{Rh}(\text{acac})_3$                           | $\text{CH}_3\text{CN}$ | rt          | 3.0                 | 24                              |
| 4                                                                                   | $\text{Co}(\text{acac})_3$                           | $\text{CH}_3\text{CN}$ | rt          | 3.0                 | 33                              |
| 5                                                                                   | $\text{In}(\text{acac})_3$                           | $\text{CH}_3\text{CN}$ | rt          | 3.0                 | 21                              |
| 6                                                                                   | $\text{Fe}(\text{NO}_3)_3$                           | $\text{CH}_3\text{CN}$ | rt          | 3.0                 | 48                              |
| 7                                                                                   | $\text{BiBr}_3$                                      | $\text{CH}_3\text{CN}$ | rt          | 3.0                 | 57                              |
| 8                                                                                   | $\text{Bi}(\text{NO}_3)_3 \cdot 5\text{H}_2\text{O}$ | $\text{CH}_3\text{CN}$ | rt          | 2.0                 | 72                              |
| 9                                                                                   | $\text{Bi}(\text{NO}_3)_3 \cdot 5\text{H}_2\text{O}$ | $\text{CHCl}_3$        | rt          | 2.0                 | 59                              |
| 10                                                                                  | $\text{Bi}(\text{NO}_3)_3 \cdot 5\text{H}_2\text{O}$ | $\text{MeOH}$          | rt          | 3.0                 | 46                              |
| 11                                                                                  | $\text{Bi}(\text{NO}_3)_3 \cdot 5\text{H}_2\text{O}$ | THF                    | rt          | 3.0                 | 43                              |
| 12                                                                                  | $\text{Bi}(\text{NO}_3)_3 \cdot 5\text{H}_2\text{O}$ | Acetone                | rt          | 3.0                 | 31                              |
| 13                                                                                  | $\text{Bi}(\text{NO}_3)_3 \cdot 5\text{H}_2\text{O}$ | $\text{CH}_3\text{CN}$ | 60 °C       | 2.0                 | 78                              |
| 14                                                                                  | $\text{Bi}(\text{NO}_3)_3 \cdot 5\text{H}_2\text{O}$ | $\text{CH}_3\text{CN}$ | 80 °C       | 2.0                 | 82                              |
| 15                                                                                  | $\text{Bi}(\text{NO}_3)_3 \cdot 5\text{H}_2\text{O}$ | Solvent-Free           | rt          | 4.0                 | 36                              |
| 16                                                                                  | $\text{Bi}(\text{NO}_3)_3 \cdot 5\text{H}_2\text{O}$ | Solvent-Free           | 60 °C       | 2.0                 | 71                              |
| 17                                                                                  | $\text{Bi}(\text{NO}_3)_3 \cdot 5\text{H}_2\text{O}$ | Solvent-Free           | 80 °C       | 2.0                 | 94                              |

<sup>a</sup>Reaction condition: Benzhydrol (1.0 mmol), ethyl acetoacetate (1.5 mmol), and catalyst (10 mol%) is used; <sup>b</sup>Yield of the isolated product after column chromatography.

Under optimized conditions, we explored the generality and substrate scope of various benzhydrol with active methylene substrate including keto esters, and diketone, and the results are depicted in Table 2 (Entries 1-9). When benzhydrol (1a) reacts with ethyl acetoacetate (2a) is carried out at 80 °C in solvent-free or neat conditions to produce the corresponding benzylation product (3a) in 94% yield (Entry 1). The benzhydrol (1a), 4,4'-dichloro- (1b), and 4,4'-difluorobenzhydrol (1c) are also reacted with ethyl acetoacetate (2a) and methyl acetoacetate (2b) smoothly proceeded to give the corresponding benzylated products

(3a and 3b) in excellent yields (Entries 2-4). The 2,4-pentanedione (2c) to afford the corresponding benzylated products in excellent yield (entries 5-7). The benzylation of 1-phenylbutane-1,3-dione (2d) with benzhydrol (1a), and 4,4'-dimethoxy benzhydrol (1c) give the desired benzylation product in 95% and 97%, respectively (Entry 8-9). Irrespective of the nature and position electron-donating or electron-withdrawing group of substituents on benzhydrol has been produced the desired products in excellent yield (Entries 1-9).

**Table 2:** The substrate scope of Benzylation of 1,3-dicarbonyl compounds with various secondary benzyl alcohols<sup>b</sup>

|                                                  |                                                                                 |               |
|--------------------------------------------------|---------------------------------------------------------------------------------|---------------|
|                                                  |                                                                                 |               |
| <b>1a- 1d</b>                                    | <b>2a- 2d</b>                                                                   | <b>3a- 3i</b> |
| <b>1a:</b> R = R <sup>1</sup> = H                | <b>2a:</b> R <sup>2</sup> = CH <sub>3</sub> , R <sup>3</sup> = OEt              |               |
| <b>1b:</b> R = R <sup>1</sup> = Cl               | <b>2b:</b> R <sup>2</sup> = CH <sub>3</sub> , R <sup>3</sup> = OCH <sub>3</sub> |               |
| <b>1c:</b> R = R <sup>1</sup> = F                | <b>2c:</b> R <sup>2</sup> = CH <sub>3</sub> , R <sup>3</sup> = CH <sub>3</sub>  |               |
| <b>1d:</b> R = R <sup>1</sup> = OCH <sub>3</sub> | <b>2d:</b> R <sup>2</sup> = Ph, R <sup>3</sup> = CH <sub>3</sub>                |               |

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|  |  |  |

<sup>a</sup>Reaction condition: Benzhydryl alcohols (1.0 mmol) and 1,3-dicarbonyl compound (1.5 mmol) are used at 80 °C; <sup>b</sup>Yield of isolated product after flash column chromatography.

We further extended our studies towards benzylation of secondary benzyl alcohol derivatives with various 1,3-dicarbonyl compounds that proceeded smoothly to afford the respective benzylation products in excellent yields. The results are summarized in Table 3 (Entries 1-9). The 1-(4-methyl phenyl) ethanol(4b), and 1-(4-methoxy phenyl) ethanol (4c) interact with ethyl acetoacetate(2a) to produce the corresponding benzylation products in 95, and 98%, respectively (Entries 1-2). 1-Phenyl ethanol(4a), 1-(4-methylphenyl) ethanol(4b), 1-(4-methoxy phenyl) ethanol (4c), 1-(2-methylphenyl) ethanol(4d), 1-(4-chlorophenyl) ethanol (4e) reacts with 2,4-pentanedione (2c) to afford the desired products in excellent yields (Entries 3-7). The

reaction of 1-phenyl-propanol (4f), and 1-(2-methoxy phenyl)-1-propanol (4g) with 2,4-pentanedione (2a) gave the desired products in 97% and 94%, respectively (Entries 7 and 8). Irrespective of the nature and position electron-donating or electron-withdrawing group of substituents on the benzene ring of secondary alcohols afforded the desired benzylation products in excellent yield (Entries 1-8). Whereas the electron-donating methoxy group at *ortho* position on the benzene ring of alcohol moiety showed slightly lower reactivity towards benzylation. This is due to steric crowding or steric hindrance of the electron-donating group, *ortho*-methoxy group towards benzylation.

**Table 3:** Benzylation of 1,3-dicarbonyl compounds with various secondary alcohols<sup>a,b</sup>

|                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                               |                      |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                               |                      |
| <p><b>4a- 1d</b></p> <p>4a: R = H, R<sup>1</sup> = CH<sub>3</sub></p> <p>4b: R = 4-CH<sub>3</sub>, R<sup>1</sup> = CH<sub>3</sub></p> <p>4c: R = 4-OCH<sub>3</sub>, R<sup>1</sup> = CH<sub>3</sub></p> <p>4d: R = 2-CH<sub>3</sub>, R<sup>1</sup> = CH<sub>3</sub></p> <p>4e: R = 4-Cl, R<sup>1</sup> = CH<sub>3</sub></p> <p>4f: R = H, R<sup>1</sup> = CH<sub>2</sub>CH<sub>3</sub></p> <p>4g: R = H, R<sup>1</sup> = CH<sub>2</sub>CH<sub>3</sub></p> | <p><b>2a- 2d</b></p> <p>2a: R<sup>2</sup> = CH<sub>3</sub>, R<sup>3</sup> = OEt</p> <p>2c: R<sup>2</sup> = CH<sub>3</sub>, R<sup>3</sup> = CH<sub>3</sub></p> | <p><b>5a- 5i</b></p> |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                               |                      |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                               |                      |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                               |                      |

<sup>a</sup>Reaction condition: Secondary benzyl alcohol (1.0 mmol) and 1,3-dicarbonyl compound (1.5 mmol) are used at 80 °C; <sup>b</sup>Yield of isolated product after flash column chromatography.

## Conclusion

In summary, we have successfully demonstrated an efficient, eco-friendly, solvent-free Bi(NO<sub>3</sub>)<sub>3</sub>·5H<sub>2</sub>O catalysed benzylation of β-ketoesters and 1,3-diketone. Eco-friendly, economically viable, decreased energy consumption, mild reaction conditions, and a wide range of applicability to various substrates with excellent yield are the major advantages of the present protocol. Simplicity of operation since water is the only side product and inexpensiveness of our procedure makes it a practical alternative.

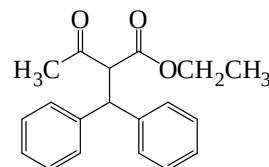
## General procedures

In all the cases the <sup>1</sup>H NMR spectra were recorded with Varian Gemini 200 or 400 MHz instruments. Chemical shifts are reported in ppm in CDCl<sub>3</sub> with tetramethyl silane as an internal standard. <sup>13</sup>C NMR data were collected on Varian Gemini 200 or 400 MHz instruments (50 or 100 MHz). Compounds have been also identified by HRMS (EI) with Jeol DMX 303.

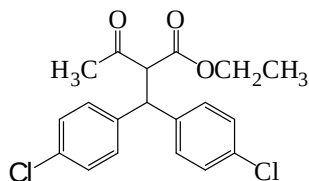
## General experimental procedure for the benzylation of 1,3-dicarbonyl compounds:

To a mixture of secondary benzyl alcohol (1 mmol) and 1,3-dicarbonyl compound (1.5 mmol), Bi(NO<sub>3</sub>)<sub>3</sub>·5H<sub>2</sub>O (10 mol %) was added and stirred under the solvent-free condition at 80 °C. The progress of the reaction mixture was monitored by TLC. After completion of the reaction, the mixture was quenched with distilled water (5 mL) and the mixture was extracted with EtOAc (3X 8 mL). The combined organic portions were washed with water (10 mL) saturated aqueous NH<sub>4</sub>Cl (2 X 10 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under vacuum. The crude product was subjected to column chromatography to obtain pure benzylation product.

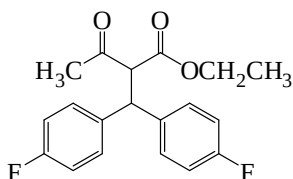
## Characterization data for the benzylation products



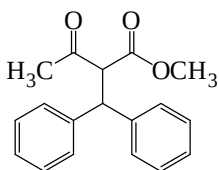
**3a:** White solid,  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.30-7.22 (m, 8H), 7.17-7.12 (m, 2H), 4.77 (d,  $J = 12.0$  Hz, 1H), 4.52 (d,  $J = 12.0$  Hz, 1H), 3.96 (q,  $J = 7.0$  Hz, 4H), 2.08 (s, 3H), 0.98 (t,  $J = 7.0$  Hz, 4H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 201.7, 167.6, 141.5, 141.2, 128.7, 128.5, 127.7, 127.6, 126.9, 126.7, 65.1, 61.4, 50.8, 29.9, 13.7.



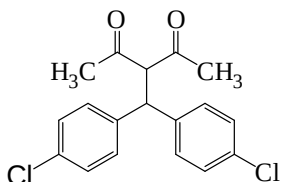
**3b:** White solid,  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.26-7.15 (m, 8H), 4.73 (d,  $J = 12.0$  Hz, 1H), 4.43 (d,  $J = 12.0$  Hz, 1H), 4.00 (q,  $J = 7.0$  Hz, 4H), 2.11 (s, 3H), 1.04 (t,  $J = 7.0$  Hz, 4H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 200.8, 167.2, 139.6, 139.4, 133.0, 132.9, 129.1, 129.0, 128.9, 128.8, 64.8, 61.7, 49.2, 30.1, 13.8; HRMS-FAB ( $m/z$ ):  $[\text{M}]^+$  calcd for  $\text{C}_{19}\text{H}_{19}\text{Cl}_2\text{O}_3$ : 365.0711, found: 365.0711.



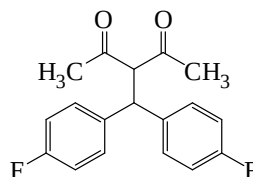
**3c:** White solid,  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.27-7.21 (m, 4H), 6.95 (t,  $J = 8.8$  Hz, 4H), 4.79 (d,  $J = 12.0$  Hz, 1H), 4.46 (d,  $J = 12.0$  Hz, 1H), 4.00 (q,  $J = 7.0$  Hz, 4H), 2.11 (s, 3H), 1.03 (t,  $J = 7.0$  Hz, 4H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 201.1, 167.3, 162.8, 160.4, 137.1, 136.9, 129.1, 129.0, 115.7, 115.4, 65.3, 61.6, 49.1, 29.9, 13.7; HRMS-FAB ( $m/z$ ):  $[\text{M}]^+$  calcd for  $\text{C}_{19}\text{H}_{19}\text{F}_2\text{O}_3$ : 333.1304, found: 333.1302.



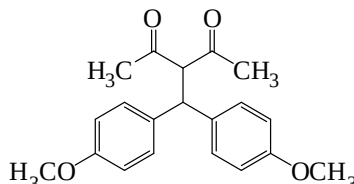
**3d:** White solid,  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.27-7.25 (m, 8H), 7.18-7.14 (m, 2H), 4.77 (d,  $J = 12.0$  Hz, 1H), 4.54 (d,  $J = 12.0$  Hz, 1H), 3.53 (s, 3H), 2.08 (s, 3H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 201.7, 168.1, 141.4, 141.0, 128.8, 128.6, 127.8, 127.5, 126.9, 126.8, 64.9, 52.5, 50.8, 30.0.



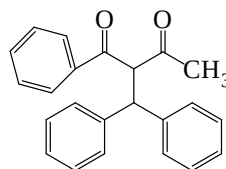
**3e:** White solid,  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.23 (d,  $J = 8.5$  Hz, 4H), 7.15 (d,  $J = 8.5$  Hz, 4H), 4.80 (d,  $J = 12.5$  Hz, 1H), 4.59 (d,  $J = 12.0$  Hz, 1H), 2.0 (s, 3H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 202.0, 139.3, 133.0, 129.1, 129.0, 74.3, 49.5, 29.6.



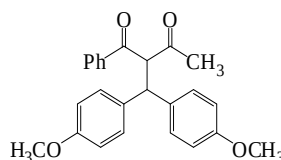
**3f:** White solid,  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.20 (d,  $J = 8.6$  Hz, 2H), 7.18 (d,  $J = 8.6$  Hz, 2H), 6.95 (d,  $J = 8.6$  Hz, 4H), 4.80 (d,  $J = 12.5$  Hz, 1H), 4.64 (d,  $J = 12.0$  Hz, 1H), 1.99 (s, 3H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 203.0, 164.8, 159.8, 137.5, 129.9, 129.7, 116.7, 116.3, 75.4, 50.1, 30.2.



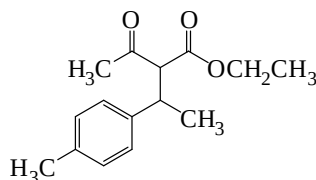
**3g:** White solid,  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.15 (d,  $J = 8.4$  Hz, 4H), 6.78 (d,  $J = 8.6$  Hz, 4H), 4.70 (d,  $J = 12.0$  Hz, 1H), 4.63 (d,  $J = 12.0$  Hz, 1H), 2.72 (s, 3H), 1.98 (s, 3H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 203.3, 158.3, 133.7, 128.6, 114.3, 74.9, 55.1, 49.7, 29.7.



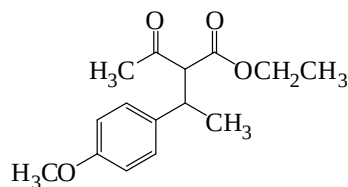
**3h:** White solid,  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.95 (d,  $J = 8.4$  Hz, 2H), 7.50-7.54 (m, 1H), 7.41 (d,  $J = 6.5$  Hz, 2H), 7.37 (d,  $J = 7.0$  Hz, 2H), 7.32-7.28 (m, 2H), 7.26-7.20 (m, 3H), 7.15-7.11 (m, 2H), 7.05-7.02 (m, 1H), 5.02 (d,  $J = 12.0$  Hz, 1H), 5.11 (d,  $J = 12.0$  Hz, 1H), 2.04 (s, 3H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 202.9, 194.2, 141.6, 141.2, 136.8, 133.6, 128.9, 128.7, 128.6, 128.0, 127.7, 127.0, 126.6, 68.8, 51.4, 27.8.



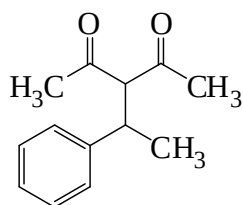
**3i:** White solid,  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.95 (d,  $J = 8.4$  Hz, 2H), 7.54-7.52 (m, 1H), 7.44-7.39 (m, 2H), 7.26 (d,  $J = 8.8$  Hz, 2H), 7.13 (d,  $J = 8.8$  Hz, 2H), 6.84 (d,  $J = 8.8$  Hz, 2H), 6.67 (d,  $J = 8.8$  Hz, 2H), 5.52 (d,  $J = 11.7$  Hz, 1H), 5.02 (d,  $J = 12.0$  Hz, 1H), 3.75 (s, 3H), 3.65 (s, 3H), 2.04 (s, 3H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 203.2, 194.4, 158.4, 158.0, 136.9, 134.2, 133.6, 133.5, 129.0, 128.7, 128.5, 114.3, 113.9, 69.3, 55.1, 55.0, 49.9, 27.6.



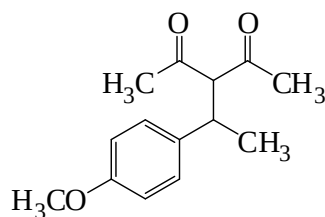
**5a:** White solid,  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.11-7.06 (m, 4H), 4.20 (t,  $J = 7.6$  Hz, 2H), 3.72 (d,  $J = 11.3$  Hz, 1H), 2.27 (s, 3H), 1.92 (s, 3H), 1.27 (t,  $J = 7.6$  Hz, 3H), 1.20 (d,  $J = 7.0$  Hz, 3H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 202.5, 168.6, 140.2, 136.4, 129.4, 127.2, 67.6, 61.4, 39.7, 29.8, 21.0, 20.7, 14.1.



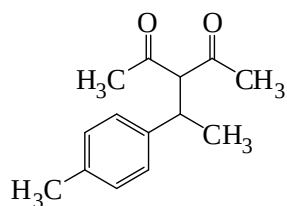
**5b:** White solid,  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.06 (d,  $J = 7.5$  Hz, 2H), 6.74 (d,  $J = 7.5$  Hz, 2H), 4.14 (t,  $J = 7.6$  Hz, 2H), 3.68 (s, 3H), 3.67 (d,  $J = 11.0$  Hz, 1H), 2.21 (s, 3H), 1.27 (t,  $J = 7.6$  Hz, 3H), 1.14 (d,  $J = 7.0$  Hz, 3H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 202.2, 168.3, 158.1, 135.0, 128.1, 113.7, 67.6, 61.1, 54.8, 39.0, 29.6, 20.4, 13.8.



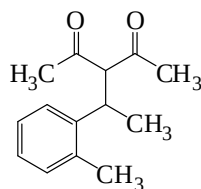
**5c:** White solid,  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.24-7.22 (m, 2H), 7.15-7.12 (m, 3H), 3.99 (d,  $J = 7.8$  Hz, 1H), 3.60-3.54 (m, 1H), 2.20 (s, 3H), 1.77 (s, 3H), 1.15 (d,  $J = 7.5$  Hz, 3H);  $^{13}\text{C-NMR}$  (50 MHz,  $\text{CDCl}_3$ )  $\delta$ : 203.3, 143.0, 128.7, 127.2, 126.9, 76.5, 49.4, 29.8, 20.8.



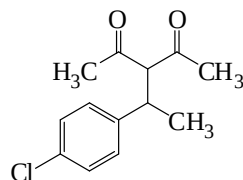
**5d:** White solid,  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.07 (d,  $J = 7.6$  Hz, 2H), 6.79 (d,  $J = 7.6$  Hz, 2H), 3.95 (d,  $J = 7.8$  Hz, 1H), 3.73 (s, 3H), 3.57-3.48 (m, 1H), 2.22 (s, 3H), 1.80 (s, 3H), 1.15 (d,  $J = 7.5$  Hz, 3H);  $^{13}\text{C-NMR}$  (50 MHz,  $\text{CDCl}_3$ )  $\delta$ : 203.7, 158.4, 134.9, 128.2, 114.1, 76.9, 55.1, 39.7, 29.8, 20.9.



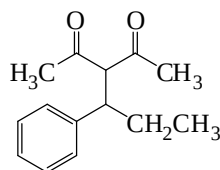
**5e:** White solid,  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 7.07-7.03 (m, 4H), 3.99 (d,  $J = 7.6$  Hz, 1H), 3.58-3.48 (m, 1H), 2.27 (s, 3H), 2.24 (s, 3H), 1.82 (s, 3H), 1.16 (d,  $J = 7.5$  Hz, 3H);  $^{13}\text{C-NMR}$  (50 MHz,  $\text{CDCl}_3$ )  $\delta$ : 203.6, 139.9, 136.5, 129.5, 127.1, 76.5, 40.1, 29.7, 20.9.



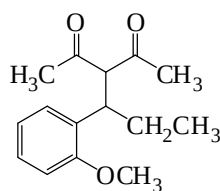
**5f:** White solid,  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$ ;  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 203.3, 203.2, 141.3, 135.3, 130.8, 126.5, 126.4, 125.4, 75.9, 34.9, 29.7, 29.3, 20.5, 19.5.



**5g:** White solid,  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$ ; 7.26 (d,  $J = 8.4$  Hz, 2H), 7.13 (d,  $J = 8.4$  Hz, 2H), 3.99 (d,  $J = 11.3$  Hz, 1H), 3.63-3.55 (m, 1H), 2.26 (s, 3H), 1.86 (s, 3H), 1.18 (d,  $J = 7.0$  Hz, 3H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$ :



**5h:** White solid,  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$ ; 7.31-7.26 (m, 2H), 7.22-7.19 (m, 1H), 7.15 (d,  $J = 7.6$  Hz, 2H), 4.11 (d,  $J = 11.0$  Hz, 1H), 3.35 (td,  $J = 11.0, 3.0$  Hz, 1H), 2.27 (s, 3H), 1.80 (s, 3H), 1.62-1.54 (m, 1H), 1.52-1.44 (m, 1H), 0.69 (t,  $J = 7.0$  Hz, 3H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 204.5, 204.2, 141.4, 129.5, 129.1, 127.9, 77.0, 48.5, 30.7, 30.5, 21.5.



**5i:** White solid,  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$ ; 7.20-7.15 (m, 1H), 7.07 (d,  $J = 7.6$  Hz, 2H), 6.90-6.84 (q,  $J = 7.6$  Hz, 2H), 4.31 (d,  $J = 11.0$  Hz, 1H), 3.83 (s, 3H), 2.26 (s, 3H), 1.85 (s, 3H), 1.60-1.51 (m, 2H), 0.68 (t,  $J = 7.4$  Hz, 3H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 204.2, 203.6, 157.5, 129.4, 128.4, 128.0, 120.6, 110.9, 74.5, 55.2, 41.5, 30.4, 28.3, 26.7, 11.5; HRMS-FAB ( $m/z$ ):  $[\text{M}]^+$  calcd for  $\text{C}_{15}\text{H}_{20}\text{O}_3$ : 248.1412, found: 248.1412.

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