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# Palladium-Catalyzed Decarboxylative 1,2-Addition of Carboxylic Acids to Glyoxylic Acid Esters

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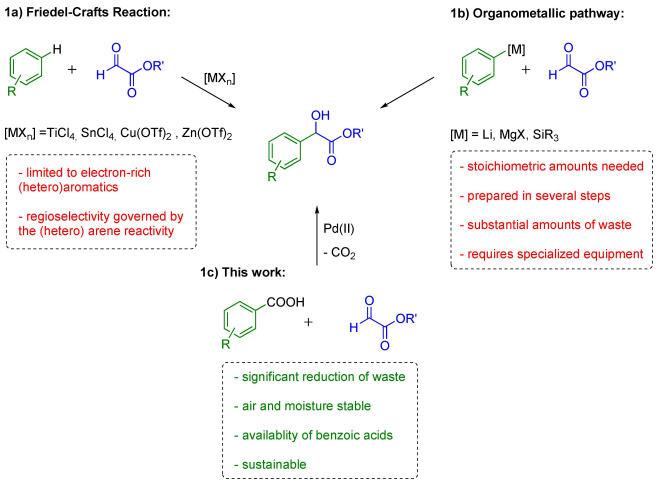
*In memory of Prof. Klaus Hafner.*

The formation of C–C-bonds constitutes one of the most fundamental synthetic operations in organic chemistry. The nucleophilic addition of preformed organometallic reagents to an electrophilic carbonyl functionality represents a classical method for the selective construction of a C–C-bond. However, the synthesis and utilization of an organometallic reagent is associated with an unfavorable environmental profile. Herein, we disclose a Palladium-catalyzed decarboxylative 1,2-addition of carboxylic acids to glyoxylic acid esters. This novel method provides access to the mandelic acid scaffold in good yields. Easy-to-handle and readily available benzoic acids are utilized as more sustainable alternative to preformed organometallic nucleophiles.

## Introduction

Alpha-Hydroxy acids in general and mandelic acids in particular constitute a class of versatile synthetic intermediates and a common structural motif in biological active components (Figure 1 1a).[1,2] Indeed, the parent mandelic acid itself displays some antibacterial activities and has been used against various indications.[3] The vasodilator cyclandelate, is applied in the treatment of claudication or arteriosclerosis.[4] Homatropine, a muscarinic acetylcholine receptor antagonist, is commonly used in eye drops.[5] The stimulant pemoline and the antiplatelet agent clopidogrel can be prepared from the corresponding mandelic acid building blocks.[6,7] Therefore, the efficient synthesis of mandelic acids has received considerable attention. The addition of nucleophiles to glyoxylic acid esters offers an attractive and highly flexible approach for the construction of the mandelic acid scaffold (Scheme 1 1).[8,9] In general, two types of nucleophiles are utilized for this type of transformation. The Friedel-Crafts type addition of (hetero)arenes enables a highly atom-efficient synthesis of the desired α-hydroxy acids (Scheme 1a).[10,11] However, this method is limited to reactive, electron-rich (hetero)aromatics. In addition, the regioselectivity of this reaction is governed by the inherent reactivity of the (hetero)arene. The addition of preformed organometallic nucleophiles offers a more flexible and regioselective approach to mandelic acids (Scheme 1b).[12,13] Unfortunately, the use of stoichiometric amounts of an organometallic reagent is not very sustainable. Usually, organometallic reagents must be prepared in several steps, leading to the generation of substantial amounts of waste both in the production and the




**Scheme 1.** Approaches and opportunities in synthesis of mandelic acids. (a) Synthesis of mandelic acid derivatives via Friedel-Crafts reaction. (b) Synthesis of mandelic acid derivatives via an organometallic precursor. (c) Decarboxylative pathway (this work) for a more sustainable synthesis of mandelic acid derivatives.

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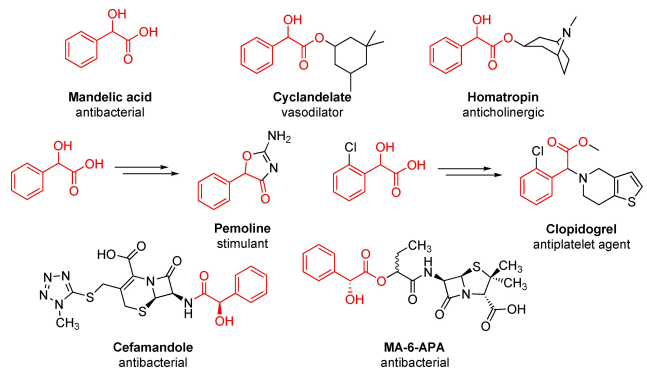



**Figure 1.** Biologically active mandelic acid derivatives and precursors for active pharmaceutical ingredients.

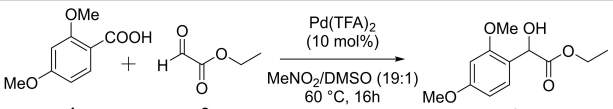
final use of such compounds. In addition, organometallic reagents, either the final reagent itself and/or intermediates for their production, are often very reactive and require specialized equipment and additional safety procedures.[13]

In the last twenty years, carboxylic acids have evolved as highly attractive and more sustainable alternative to preformed organometallics.[14–16] Decarboxylative coupling reactions have emerged as valuable synthetic tool for the construction of carbon-carbon and carbon-heteroatom bonds. Contrary to their organometallic counterparts, aryl carboxylic acids are benchstable, easy-to-handle solids with a wide commercial availability. Utilization of carboxylic acids in metal-catalyzed decarboxylative coupling reactions leads to a significant reduction of waste, viz. only one equivalent of $CO_2$ instead of metal salts. In the last years decarboxylative cross-couplings between benzoic acids and aryl halides[17–21] as well as decarboxylative couplings as carbon-heteroatom bond forming reactions have received considerable attention.[22] On the other hand, replacement of organometallic nucleophiles with carboxylic acids in classical 1,2-addition reactions to electrophilic aldehydes or imines have been only sparsely studied. The group of Wu disclosed a palladium-catalyzed decarboxylative 1,2-addition of benzoic acids to electron-deficient arylaldehydes and their corresponding N-tosyl imines.[23] Larhed and coworkers reported palladium-catalyzed decarboxylative addition reactions of benzoic acids to nitriles and cyanamides for the synthesis of aryl ketones and amidines, which proceed under quite forcing conditions.[24–26] Our group has recently described a palladium-catalyzed three-component synthesis of alpha-arylglycines based on the decarboxylative addition of benzoic acids to in situ generated N-sulfonyl imines.[27] The extension of such 1,2-addition reactions to a broader range of aldehyde or imine electrophiles as more sustainable alternative to classical organometallic chemistry would be highly desirable. Herein we report a palladium-catalyzed decarboxylative addition reaction of benzoic acids to glyoxylic acid esters as a novel approach towards a more sustainable synthesis of mandelic acid derivatives (Scheme 1c).

## Results and Discussion

During our studies on the three-component synthesis of alpha-arylglycines, we became aware, that the same reaction system, consisting of 10 mol% $Pd(TFA)_2$ in $MeNO_2$/DMSO mixture (5 vol% DMSO) also efficiently mediated the decarboxylative addition of 2,4-dimethoxybenzoic acid **1a** to ethyl glyoxylate **2a**. The desired mandelic acid derivative **3a** could be isolated in 72% yield after 16 h reaction time at 60 °C (Table 1, entry 1). Interestingly, commercially available, technical ethyl glyoxylate (a solution of the polymer form in toluene) can be used directly without prior purification. Replacing $MeNO_2$ with DCE, DMF, ethyl acetate or THF led to slightly reduced yields of 53–68% (entries 2–5). Reactions in protic solvents, such as MeOH or EtOH did not furnish any desired product at all (entry 6). DMSO as cosolvent is crucial for an efficient transformation. Reducing the amount to only 2,5 vol% resulted in a significant decrease of the isolated yield (entry 9). Without DMSO the desired product is formed in only 15% yield (entry 11). We assume, that DMSO acts as a ligand, stabilizing the active palladium(II) catalyst and preventing reduction/precipitation of palladium black.[28] A similar beneficial effect of DMSO has been already observed by Myers and Diao.[17,29] Decreasing the temperature or the amount of $Pd(TFA)_2$ had a negative impact on the

**Table 1.** Optimization and effect of deviations from optimized conditions.




1a 1.0 equiv | 2a 1.5 equiv | *Standard Conditions* | 3a 82%

| Entry | Deviations from optimized conditions | Yield [%][a] |
|---|---|---|
| 1 | Solvent nitromethane (not dry) | **72**[b] |
| 2 | Solvent DCE | 68 |
| 3 | Solvent DMF | 62 |
| 4 | Solvent ethyl acetate | 55 |
| 5 | Solvent THF | 53 |
| 6 | Solvent MeOH or EtOH | NR |
| 7 | With 10 vol% DMSO | 60 |
| 8 | With 5 vol% DMSO | 72 |
| 9 | With 2.5 vol% DMSO | 45 |
| 10 | With 1 vol% DMSO | 35 |
| 11 | Without DMSO | 15 |
| 12 | 40 °C | 24 |
| 13 | 25 °C | 15 |
| 14 | With 7.5 mol% Pd | 43 |
| 15 | With 5 mol% Pd | 31 |
| 16 | With 2.5 mol% Pd | 10 |
| 17 | $Pd(OAc)_2$ or $PdCl_2$ | traces |
| 18 | Benzoquinone 1.0 eq[c] | NR |
| 19 | 1,2-bis(phenylsulfinyl)ethane (15 mol%)[c] | NR |
| 20 | With 5 vol% tetramethylene sulfoxide[c] | 49 |
| 21 | Irradiation with a 390–400 nm LED; 10 watts | NR |
| 22 | With pre-dried nitromethane and DMSO | 82[b] |
| 23 | With 1 mol% $H_2O$ | 51 |
| 24 | With 5 mol% $H_2O$ | traces |
| 25 | With MS 4 Å | 50 |
| 26 | Inert gas conditions | 75 |
| 27 | 1.0 mmol reaction | 41[b] |

[a] Determined by GC analysis using biphenyl as internal standard. [b] Isolated yield. [c] without DMSO. NR – no reaction; DCE = 1,2-dichloroethane; DMF = dimethylformamide; THF = tetrahydrofuran; MeOH = methanol; EtOH = ethanol; DMSO = dimethyl sulfoxide; MS = molecular sieve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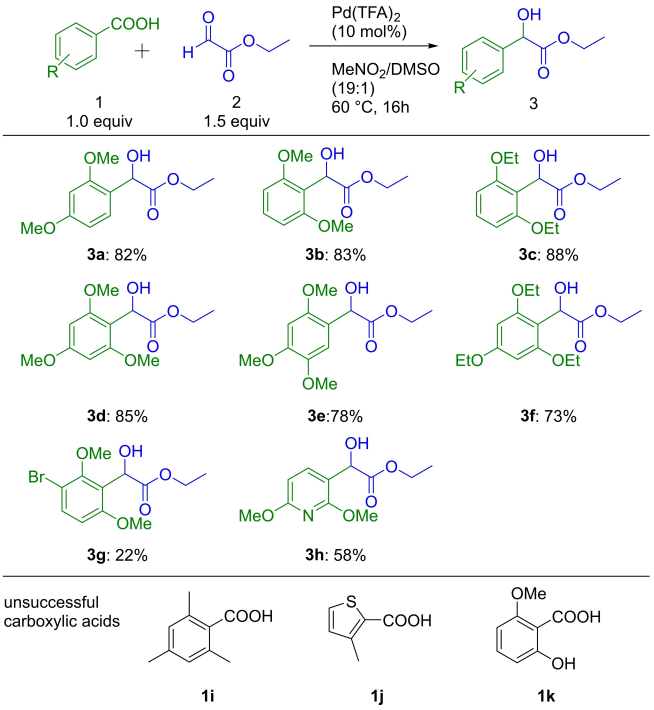
isolated yield (entry 12 to 16). Reactions with other palladium(II) sources, such as $Pd(OAc)_2$ or $PdCl_2$ furnished only traces of the desired product (entry 17). Addition of other ligands, which have been reported to stabilize Pd(II) species, such as benzoquinone or 1,2-bis(phenylsulfinyl)ethane, instead of DMSO did not display any beneficial effects (entries 18 and 19). Only replacement of DMSO with 5 vol% tetramethylene sulfoxide afforded the desired product in a slightly lower yield of 49% (entry 20). Irradiation of the reaction mixture with blue LEDs instead of heating did not furnish any product at all (entry 21). Further studied revealed a detrimental effect of $H_2O$ on the reaction outcome. If all used solvents were stored over MS 4 Å for 48 hours prior to use, the isolated yield increased to 82% (entry 22). Control experiments with pre-dried solvents, show a significant reduction of the yield in the presence of small amount s of water. In the presence of only 1 mol% of $H_2O$, the yield of mandelic acid derivative **3a** decreased to 51% (entry 23). With 5 mol% of $H_2O$ only traces of the desired product are formed (entry 24). Control experiments show that in the presence of water a rapid protodecarboxylation of the benzoic acid **1a** takes place. Therefore, it is mandatory to use dry solvents for this reaction. Unfortunately, the direct addition of molecular sieves to the reaction mixture leads to a sluggish outcome (entry 25). However, storage of all solvents over MS 4 Å for 48 hours prior to their use is sufficient. Air/oxygen does not interfere in the reaction. Performing the reaction under a $N_2$ atmosphere did not lead to any improvements (entry 26). Indeed, all reaction in this study were performed without an inert atmosphere. Performing the reaction on a 1 mmol scale led to a diminished yield (entry 27).

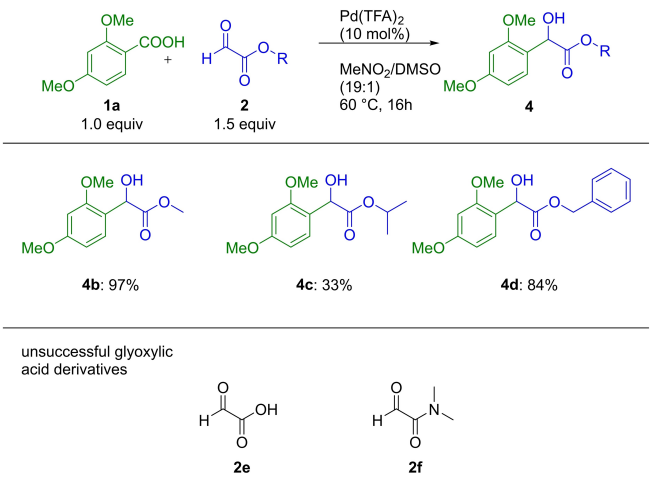
With the optimized reaction conditions, we investigated the decarboxylative addition of various benzoic acid derivatives **1** to ethyl glyoxylate **2a** (Scheme 2). As already observed for similar transformations, this reaction is limited to electron-rich benzoic acids containing at least one substituent in ortho-position.[25–30] Studies by the Larhed group have shown, that substituents in ortho-position can push the plane of the carboxylic acid group in an orthogonal position to the aromatic ring, a requirement for the rate-determining decarboxylation step.[26] Both the 2,4- and the 2,6-dimethoxybenzoic acid **1a** and **1b** afforded the desired mandelic acid derivatives **3a** and **3b** in 82% and 83% yield. One must emphasize, that contrary to the expected outcome of an analogous Friedel-Crafts-reaction with 1,3-dimethoxybenzene, only one single regioisomer is formed in both cases. The corresponding 2,6-diethoxy benzoic acid (**1c**) performed equally well, furnishing the desired product **3c** in 88% yield. Reactions with the trisubstituted benzoic acids **1d–f** lead to the α-hydroxy acid derivatives **3d–f** in 73–85% yield. The decarboxylative addition of 3-bromo-2,6-dimethoxybenzoic acid **1g** to ethyl glyoxylate **2a** afforded product **3g** in only 22% yield. A competitive, unproductive protodecarboxylation led to low yield of the desired addition product in this case. To our delight, also 2,6-dimethoxynicotinic acid **1h** took part in the palladium-catalyzed addition, furnishing the heterocyclic product **3h** in 58% yield. Unfortunately, reactions with other benzoic acids, did not afford any desired product. A couple of selected




**Scheme 2.** Reaction scope – carboxylic acid component.

unsuccessful examples, including 2,4,6-trimethylbenzoic acid (**1i**), 3-methylthiophene-2-carboxylic acid (**1J**) or the phenolic acid (**1k**), are depicted in Scheme 2. Even after extensive investigations, no other suitable benzoic acids or improved reaction conditions could be identified. Interestingly, a fast protodecarboxylation of the acid was observed via GC/MS for most of the unsuccessful compounds.

Afterwards, we examined the addition of 2,4-dimethoxybenzoic acid **1a** to several glyoxylic acid esters **2b–f** (Scheme 3). In general, these reactions proceeded smoothly affording the corresponding mandelic acid ester **4a–4d** in 33–




**Scheme 3.** Reaction scope – glyoxylic acid ester component.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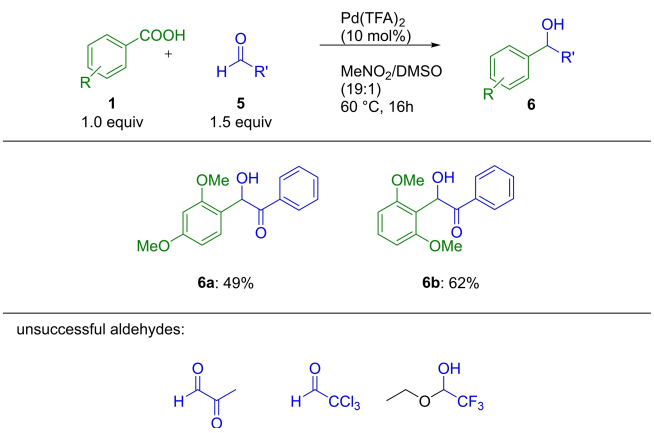
97% yield. Unfortunately, no addition was observed with the parent glyoxylic acid (**2e**) itself or an amide derivative (**2f**).

Next, we turned our attention towards extending the decarboxylative 1,2-addition to other types of aldehydes. Since glyoxylic acid esters can be regarded as activated aldehydes, we focused on reactions with other substrates bearing electron-withdrawing groups near the carbonyl functionality. During this study, we explored the Pd-catalyzed decarboxylative addition of 2,4-dimethoxy- and 2,6-dimethoxybenzoic acid to phenylglyoxal and methylglyoxal as well as trichloroacetaldehyde and the ethyl hemiacetal of trifluoroacetaldehyde (Scheme 4). To our delight, the reactions with phenylglyoxal proceeded smoothly under our standard conditions, affording the desired alpha-hydroxy-ketones **6a** in 49% and **6b** 62% yield. Although, the yield is only moderate, these transformations show, that our method can be extended to other types of aldehydes. Unfortunately, the addition to all other three activated aldehydes furnished only traces of the expected addition products. These results clearly show that more efficient catalyst systems are required for further extension of the substrate scope towards structurally more diverse aldehydes.

## Conclusion

The mandelic acid scaffold an important structural motif in biological active compounds. In this study, we have developed a novel palladium-catalyzed decarboxylative 1,2-addition of benzoic acids to glyoxylic acid esters. This method enables a straightforward synthesis of mandelic acids using readily available benzoic acids as replacement for classical organometallic reagents. Thereby this transformation offers the opportunity to develop more sustainable methods for to the synthesis of this important scaffold. However, certain issues, such as high catalyst loading, or more benign solvents systems still have to be addressed in the future. Studies to extend the scope of this transformations to other aldehyde and imine components and for the development of more active catalysts are currently performed in our laboratories.




**Scheme 4.** Reaction scope – activated aldehyde component.

## Experimental Section

### General Remarks

**Experimental**: Unless otherwise mentioned, all reactions were carried out without any precautions to exclude ambient air or moisture. Thin layer chromatography (TLC) was performed on precoated aluminium sheets (TLC silica gel 60 $F_{254}$). The spots were visualized by ultraviolet light. Flash column chromatography was performed using a puriflash XS 420+ Flash purifier machine from Interchim with prepacked flash columns (Puriflash_Silica HP_15 µm_F0012 or Puriflash_Silica HP_15 µm_F0025) and the respectively solvent mixture. All yields refer to isolated yields of compounds estimated to be >95% pure as determined by $^1$H NMR.

**Materials**: Unless noted, all starting materials including carboxylic acids and glyoxylates were purchased from different commercial sources and used without further purification. The glyoxylates **2b**–**2d** were prepared according to published procedure.[31] $Pd(TFA)_2$ was purchased from Sigma Aldrich, nitromethane from Sigma Aldrich, ethyl glyoxylate (50 w% in toluene) from Alfa Aesar and dimethyl sulfoxide from VWR. Benzoic acids were purchased from TCI, Sigma Aldrich and ABCR. All solvents for purification and flash column chromatography were obtained from VWR and Fisher Scientific in p.a. purity and used as received. Solvents for reactions were stored over MS 4 Å (>48 hr prior to use) without any further precautions to exclude air/Oxygen. MS 4 Å was purchased from Carl-Roth and dried at 120 °C for 72 hr prior to use.

**Analytical Data and Instrumentation**: Proton nuclear magnetic resonance spectra ($^1$H NMR) and carbon spectra ($^{13}$C NMR) were recorded at a frequency of 400 MHz ($^1$H) and 101 MHz ($^{13}$C), respectively. Chemical shifts are expressed as parts per million downfield shift on the δ scale and are referenced to the solvent peak (Chloroform-$d_1$: δ = 7.26 ppm for $^1$H, δ = 77.16 ppm for $^{13}$C). Coupling constants (*J*) are quoted in Hz and the observed signal multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Mass spectra (MS) were measured using ESI (electrospray ionization) techniques. High resolution mass spectra (HRMS) were measured using mass spectroscopy (EI-MS-TOF). Infrared spectra (IR) were recorded on a FT-IR (Fourier transform infrared spectroscopy) spectrometer including a diamond universal ATR sampling technique (attenuated total reflectance) from 4000–400 $cm^{-1}$. The absorption bands were reported in wave numbers ($cm^{-1}$). Melting Points are uncorrected.

### General procedures (GP)

#### *GP1 (Carboxylic Acid Variation)*

A 10 mL screw cap glass vial was charged with a magnetic stirring bar, carboxylic acid (0.2 mmol, 1.0 equiv), ethyl glyoxylate (60 µL (50 w% in toluene), 0.3 mmol,1.5 equiv), $Pd(TFA)_2$ (6.7 mg, 0.02 mmol, 10 mol%) and a mixture of nitromethane and DMSO (5% v/v) (2 mL, 0.1 M referring to 0.2 mmol carboxylic acid) as solvent. The vial was closed with a PE-screw cap and the resulting reaction mixture was stirred vigorously at 40 °C for 16 h. Afterwards the reaction mixture was filtered through a short plug celite and silica gel. The filter pad was rinsed with additional 25 mL acetone and the combined filtrates were concentrated under reduced pressure. Purification of the crude residue by flash column chromatography afforded the analytically pure product.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*GP2 (Glyoxylate Acid Variation)*

A 10 mL screw cap glass vial was charged with a magnetic stirring bar, 2,4-dimethoxybenzoic acid (36 mg, 0.2 mmol, 1.0 equiv), glyoxylate (0.3 mmol, 1.5 equiv), $Pd(TFA)_2$ (6.7 mg, 0.02 mmol, 10 mol%) and a mixture of nitromethane and DMSO (5% v/v) (2 mL, 0.1 M referring to 0.2 mmol carboxylic acid) as solvent. The vial was closed with a PE-screw cap and the resulting reaction mixture was stirred vigorously at 40 °C for 16 h. Afterwards the reaction mixture was filtered through a short plug celite and silica gel. The filter pad was rinsed with additional 25 mL acetone and the combined filtrates were concentrated under reduced pressure. Purification of the crude residue by flash column chromatography afforded the analytically pure product.

**Ethyl 2-(2,4-dimethoxyphenyl)-2-hydroxyacetate (3 a)**

Prepared from 2,4-dimethoxycarboxylic acid (36 mg, 0.2 mmol, 1.0 equiv) according to **GP1**. Purification via puriflash XS 420+ Flash purifier machine, HP_15 μm_F0012 flash column (*n*-Hexane/EtOAc = 9:1→4:1) afforded the analytically pure product as colorless oil (39 mg, 82%). $R_f$: 0.48 (1:1 *n*-Hexane/EtOAc). $^1$H NMR (400 MHz, $CDCl_3$): δ = 7.17 (d, *J* = 8.0 Hz, 1H), 6.48–6.46 (m, 2H), 5.19 (s, 1H), 4.25–4.18 (m, 2H), 3.81 (s, 6 H), 1.21 (t, *J* = 8.0 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ = 174.1, 161.3, 158.4, 130.4, 119.9, 104.4, 99.1, 70.0, 61.8, 55.5, 14.2. IR (ṽ in $cm^{-1}$): 2940 (w), 2843 (w), 1735 (s), 1595 (s), 1478 (s), 1438 (m), 1332 (w), 1269 (s), 1208 (s), 1109 (s), 1061 (s), 935 (w), 863 (w), 786 (m), 607 (m). MS (ESI) m/z: calcd for $C_{12}H_{16}O_5$: 240.1 $[M]^+$, found 263.1 $[M+Na]^+$. HRMS (TOF MS EI+): m/z $[M]^+$ calcd for $C_{12}H_{16}O_5$: 240.0998, found 240.0993.

**Ethyl 2-(2,6-dimethoxyphenyl)-2-hydroxyacetate (3 b)**

Prepared from 2,6-dimethoxycarboxylic acid (36 mg, 0.2 mmol, 1.0 equiv) according to **GP1**. Purification via puriflash XS 420+ Flash purifier machine, HP_15 μm_F0012 flash column (*n*-Hexane/EtOAc = 9:1→4:1) afforded the analytically pure product as slightly yellow solid (40 mg, 83%). $R_f$: 0.47 (1:1 *n*-Hexane/EtOAc). $^1$H NMR (400 MHz, $CDCl_3$): δ = 7.30–7.28 (m, 1H), 6.59 (d, *J* = 8.0 Hz, 2H), 5.69 (s, 1H), 4.29–4.20 (m, 2H), 3.85 (s, 6H), 1.24 (t, *J* = 8.0 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ = 174.5, 158.4, 130.1, 115.8, 104.3, 64.6, 61.5, 56.0, 14.3. IR (ṽ in $cm^{-1}$): 2947 (w), 2842 (w), 1740 (s), 1595 (s), 1461 (s), 1414 (w), 1332 (m), 1298 (s), 1205 (s), 1148 (s), 1111 (s), 1062 (s), 1022 (s), 948 (m), 818 (m), 633 (w), 542 (w). Melting point: 92–93 °C. MS (ESI) m/z: calcd for $C_{12}H_{16}O_5$: 240.1 $[M]^+$, found 263.1 $[M+Na]^+$. HRMS (TOF MS EI+): m/z $[M]^+$ calcd for $C_{12}H_{16}O_5$: 240.0998, found 240.0996.

**Ethyl 2-(2,6-diethoxyphenyl)-2-hydroxyacetate (3 c)**

Prepared from 2,6-diethoxycarboxylic acid (42 mg, 0.2 mmol, 1.0 equiv) according to **GP1**. Purification via puriflash XS 420+ Flash purifier machine, HP_15 μm_F0012 flash column (*n*-Hexane/EtOAc = 9:1→4:1) afforded the analytically pure product as a colorless solid (47 mg, 88%). $R_f$: 0.68 (1:1 *n*-Hexane/EtOAc). $^1$H NMR (400 MHz, $CDCl_3$): δ = 7.19 (t, *J* = 8.0 Hz, 1H), 6.52 (d, *J* = 8.0 Hz, 2H), 5.70 (s, 1H), 4.21 (q, *J* = 8.0 Hz, 2H), 4.12–3.97 (m, 4H), 1.39 (t, *J* = 8.0 Hz, 6H), 1.21 (t, *J* = 8.0 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ = 174.5, 157.7, 129.9, 116.2, 105.0, 64.8, 64.4, 61.4, 14.8, 14.3. IR (ṽ in $cm^{-1}$): 2976 (w), 2935 (w), 1734 (s), 1592 (s), 1462 (s), 1368 (s), 1292 (m), 1244 (s), 1218 (s), 1113 (m), 1085 (s), 1052 (s), 1009 (m), 863 (w), 776 (w), 758 (w), 735 (w), 639 (w), 617 (w), 513 (w). Melting point: 78–79 °C. MS (ESI) m/z: calcd for $C_{14}H_{20}O_5$: 268.1 $[M]^+$, found 291.2 $[M+Na]^+$. HRMS (TOF MS EI+): m/z $[M]^+$ calcd for $C_{14}H_{20}O_5$: 268.1311, found 268.1308.

**Ethyl 2-hydroxy-2-(2,4,6-trimethoxyphenyl) acetate (3 d)**

Prepared from 2,4,6-trimethoxycarboxylic acid (42 mg, 0.2 mmol, 1.0 equiv) according to **GP1**. Purification via puriflash XS 420+ Flash purifier machine, HP_15 μm_F0012 flash column (*n*-Hexane/EtOAc = 9:1→4:1) afforded the analytically pure product as slightly yellow solid (46 mg, 85%). $R_f$: 0.47 (1:1 *n*-Hexane/EtOAc). $^1$H NMR (400 MHz, $CDCl_3$): δ = 6.12 (s, 2H), 5.56 (s, 1H), 4.26–4.16 (m, 2H), 3.81 (s, 3H), 3.79 (s, 6H), 1.21 (t, *J* = 8.0 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ = 174.8, 161.7, 159.2, 108.7, 91.0, 64.4, 61.5, 55.9, 55.5, 14.4. IR (ṽ in $cm^{-1}$): 2945 (w), 2842 (w), 1738 (s), 1592 (s), 1457 (s), 1418 (m), 1332 (s), 1299 (m), 1201 (s), 1149 (m), 1073 (s), 1052 (s), 1029 (s), 952 (m), 810 (w), 763 (m), 742 (m), 665 (w), 636 (w), 545 (w). Melting point: 74–75 °C. MS (ESI) m/z: calcd for $C_{13}H_{18}O_6$: 270.1 $[M]^+$, found 293.2 $[M+Na]^+$. HRMS (TOF MS EI+): m/z $[M]^+$ calcd for $C_{13}H_{18}O_6$: 270.1103, found 270.1109.

**Ethyl 2-hydroxy-2-(2,4,5-trimethoxyphenyl) acetate (3 e)**

Prepared from 2,4,5-trimethoxycarboxylic acid (42 mg, 0.2 mmol, 1.0 equiv) according to **GP1**. Purification via puriflash XS 420+ Flash purifier machine, HP_15 μm_F0012 flash column (*n*-Hexane/EtOAc = 9:1→4:1) afforded the analytically pure product as colorless oil (42 mg, 78%). $R_f$: 0.30 (1:1 *n*-Hexane/EtOAc). $^1$H NMR (400 MHz, $CDCl_3$): δ = 6.80 (s, 1H), 6.52 (s, 1H), 5.24 (s, 1H), 4.25–4.16 (m, 2H), 3.88 (s, 3H), 3.82 (s, 3H), 3.80 (s, 3H), 1.21 (t, *J* = 8.0 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ = 174.1, 151.7, 150.0, 143.3, 118.6, 112.6, 97.9, 69.5, 61.9, 56.6, 56.2, 14.2. IR (ṽ in $cm^{-1}$): 2932 (w), 2839 (w), 1732 (s), 1607 (s), 1512 (s), 1459 (s), 1399 (s), 1314 (m), 1208 (s), 1121 (m), 1069 (s), 1032 (s), 938 (m), 868 (w), 823 (w), 753 (w), 702 (w), 656 (w), 616 (w), 565 (w). MS (ESI) m/z: calcd for $C_{13}H_{18}O_6$: 270.1 $[M]^+$, found 293.2 $[M+Na]^+$. HRMS (TOF MS EI+): m/z $[M]^+$ calcd for $C_{13}H_{18}O_6$: 270.1103, found 270.1100.

**Ethyl 2-hydroxy-2-(2,4,6-triethoxyphenyl) acetate (3 f)**

Prepared from 2,4,6-triethoxycarboxylic acid (51 mg, 0.2 mmol, 1.0 equiv) according to **GP1**. Purification via puriflash XS 420+ Flash purifier machine, HP_15 μm_F0012 flash column (*n*-Hexane/EtOAc = 9:1→4:1) afforded the analytically pure product as a colorless solid (46 mg, 73%). $R_f$: 0.53 (1:1 *n*-Hexane/EtOAc). $^1$H NMR (400 MHz, $CDCl_3$): δ = 6.08 (s, 2H), 5.59 (s, 1H), 4.20 (q, *J* = 8.0 Hz, 2H), 4.08–3.93 (m, 6H), 1.39 (q, *J* = 8.0 Hz, 9H), 1.21 (t, *J* = 8.0 Hz). $^{13}$C NMR (101 MHz, $CDCl_3$): δ = 174.8, 160.8, 158.4, 109.0, 92.2, 64.7, 64.3, 63.6, 61.4, 14.9, 14.8, 14.3. IR (ṽ in $cm^{-1}$): 2979 (w), 2929 (w), 2890 (w), 1732 (s), 1601 (s), 1445 (s), 1392 (s), 1332 (m), 1259 (m), 1224 (s), 1159 (m), 1122 (m), 1068 (s), 1013 (s), 796 (w), 662 (w), 626 (w), 522 (w). Melting point: 78–79 °C. MS (ESI) m/z: calcd for $C_{16}H_{24}O_6$: 312.2 $[M]^+$, found 335.3 $[M+Na]^+$. HRMS (TOF MS EI+): m/z $[M]^+$ calcd for $C_{16}H_{24}O_6$: 312.1573, found 312.1578.

**Ethyl 2-(3-bromo-2,6-dimethoxyphenyl)-2-hydroxyacetate (3 g)**

Prepared from 3-brom-2,6-dimethoxycarboxylic acid (52 mg, 0.2 mmol, 1.0 equiv) according to **GP1**. Purification via puriflash XS 420+ Flash purifier machine, HP_15 μm_F0012 flash column (*n*-Hexane/EtOAc = 9:1→4:1) afforded the analytically pure product as colorless oil (14 mg, 22%). $R_f$: 0.53 (1:1 *n*-Hexane/EtOAc). $^1$H NMR (400 MHz, $CDCl_3$): δ = 7.47 (d, *J* = 8.0 Hz, 1H), 6.60 (d, *J* = 8.0 Hz, 1H), 5.54 (s, 1H), 4.23 (q, *J* = 8.0 Hz, 2H), 3.88 (s, 3H), 3.80 (s, 3H), 1.21 (t, *J* = 8.0 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ = 173.9, 157.9, 156.3, 133.7, 123.3, 108.6, 108.5, 65.4, 62.0, 14.3. IR (ṽ in $cm^{-1}$): 2939 (w), 2846 (w), 1734 (s), 1579 (s), 1464 (s), 1407 (s), 1282 (m), 1222 (s), 1182 (s), 1129 (s), 1079 (s), 1013 (s), 929 (w), 866 (w), 803 (w), 638


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(w), 566 (w). MS (ESI) m/z: calcd for $C_{12}H_{15}BrO_5$: 312.2 $[M]^+$, found 335.3 $[M+Na]^+$. HRMS (TOF MS EI+): m/z $[M]^+$ calcd for $C_{12}H_{15}BrO_5$: 312.1573, found 312.1578.

#### Ethyl 2-(2,6-dimethoxypyridin-3-yl)-2-hydroxyacetate (3 h)

Prepared from 2,6-dimethoxynicotinic acid (37 mg, 0.2 mmol, 1.0 equiv) according to **GP1**. Purification via puriflash XS 420+ Flash purifier machine, HP_15 µm_F0012 flash column (*n*-hexane/ethyl acetate 9:1→4:1) afforded the analytically pure product as slightly yellow oil (28 mg, 58%). $R_f$: 0.77 (1:1 *n*-Hexane/EtOAc). $^1$H NMR (400 MHz, $CDCl_3$): δ = 7.46 (d, *J* = 8.0 Hz, 1H), 6.29 (d, *J* = 8.0 Hz, 1H), 5.16 (s, 1H), 4.21 (q, *J* = 8.0 Hz, 2H), 3.94 (s, 3H), 3.90 (s, 3H), 1.21 (t, *J* = 8.0 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ = 173.7, 163.2, 160.2, 140.8, 140.7, 112.4, 101.1, 101.0, 69.2, 69.1, 62.0, 53.8, 53.7, 53.6, 53.5, 14.2. IR (ν̃ in $cm^{-1}$): 2982 (w), 2949 (w), 1734 (s), 1594 (s), 1471 (s), 1457 (s), 1388 (s), 1319 (m), 1248 (s), 1204 (s), 1098 (m), 1068 (s), 1015 (s), 952 (m), 860 (w), 808 (w), 786 (w), 683 (w), 660 (w), 575 (w), 519 (w). MS (ESI) m/z: calcd for $C_{11}H_{15}NO_5$: 241.1 $[M]^+$, found 264.1 $[M+Na]^+$. HRMS (TOF MS EI+): m/z $[M]^+$ calcd for $C_{11}H_{15}NO_5$: 241.0950, found 241.0951.

#### Methyl 2-(2,4-dimethoxyphenyl)-2-hydroxyacetate (4 b)

Prepared from methyl glyoxylate (26 mg, 0.3 mmol, 1.5 equiv) according to **GP2**. Purification via puriflash XS 420+ Flash purifier machine, HP_15 µm_F0012 flash column (*n*-hexane/ethyl acetate 9:1→4:1) afforded the analytically pure product as slightly yellow oil (44 mg, 97%). $R_f$: 0.47 (1:1 *n*-Hexane/EtOAc). $^1$H NMR (400 MHz, $CDCl_3$): δ = 7.17 (d, *J* = 8.0 Hz, 1H), 6.49–6.46 (m, 2H), 5.22 (d, *J* = 8.0 Hz, 1H), 3.80 (d, *J* = 3.2 Hz, 6H), 3.73 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ = 174.6, 161.4, 158.3, 130.3, 119.7, 104.5, 99.2, 69.8, 55.7, 52.9. IR (ν̃ in $cm^{-1}$): 2952 (w), 2842 (w), 1735 (s), 1609 (s), 1559 (s), 1505 (m), 1449 (s), 1334 (s), 1291 (m), 1262 (s), 1205 (s), 1161 (m), 1122 (s), 1069 (s), 1033 (s), 978 (m), 932 (w), 833 (w), 769 (w), 723 (w), 638 (w), 566 (w). MS (ESI) m/z: calcd for $C_{11}H_{14}O_5$: 226.12 $[M]^+$, found 249.2 $[M+Na]^+$. HRMS (TOF MS EI+): m/z $[M]^+$ calcd for $C_{11}H_{14}O_5$: 226.0841, found 226.0826.

#### Isopropyl 2-(2,4-dimethoxyphenyl)-2-hydroxyacetate (4 c)

Prepared from isopropyl glyoxylate (35 mg, 0.3 mmol, 1.5 equiv) according to **GP2**. Purification via puriflash XS 420+ Flash purifier machine, HP_15 µm_F0012 flash column (*n*-hexane/ethyl acetate 9:1→4:1) afforded the analytically pure product as slightly yellow oil (17 mg, 33%). $R_f$: 0.63 (1:1 *n*-Hexane/EtOAc). $^1$H NMR (400 MHz, $CDCl_3$): δ = 7.15 (d, *J* = 8.0 Hz, 1H), 6.46 (d, *J* = 4 Hz, 2H), 5.14 (d, *J* = 8 Hz, 1H), 5.10–5.06 (m, 1H), 3.80 (d, *J* = 4.0 Hz, 6H), 1.23 (d, *J* = 8.0 Hz, 3H), 1.14 (d, *J* = 8.0 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ = 173.7, 161.3, 158.4, 130.4, 120.2, 104.3, 99.1, 70.2, 69.6, 55.5, 21.8. IR (ν̃ in $cm^{-1}$): 2977 (w), 2936 (w), 2840 (w), 1727 (s), 1608 (s), 1505 (s), 1459 (s), 1378 (s), 1344 (m), 1291 (m), 1261 (s), 1206 (s), 1158 (m), 1108 (s), 1066 (s), 1035 (s), 951 (w), 830 (w), 638 (w), 565 (w). MS (ESI) m/z: calcd for $C_{13}H_{18}O_5$: 254.1 $[M]^+$, found 277.1 $[M+Na]^+$. HRMS (TOF MS EI+): m/z $[M]^+$ calcd for $C_{13}H_{18}O_5$: 254.1154, found 254.1159.

#### Benzyl 2-(2,4-dimethoxyphenyl)-2-hydroxyacetate (4 d)

Prepared from benzyl glyoxylate (49 mg, 0.3 mmol, 1.5 equiv) according to **GP2**. Purification via puriflash XS 420+ Flash purifier machine, HP_15 µm_F0012 flash column (*n*-hexane/ethyl acetate 9:1→4:1) afforded the analytically pure product as colorless oil (51 mg, 84%). $R_f$: 0.74 (1:1 *n*-Hexane/EtOAc). $^1$H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.28 (m, 3H), 7.24–7.21 (m, 2H), 7.16 (d, *J* = 8.0 Hz, 1H), 6.47–6.42 (m, 2H), 5.24 (s, 1H), 5.19 (d, *J* = 2.4 Hz, 2H), 3.80 (s, 3H), 3.65 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ = 173.9, 161.4, 158.4, 135.7, 130.5, 128.6, 128.4, 128.2, 119.8, 104.4, 99.1, 70.4, 67.2, 55.6, 55.4. IR (ν̃ in $cm^{-1}$): 2945 (w), 2839 (w), 1734 (s), 1609 (s), 1559 (s), 1505 (m), 1457 (s), 1291 (m), 1264 (s), 1204 (s), 1162 (m), 1122 (s), 1068 (s), 1032 (s), 935 (w), 832 (w), 742 (w), 696 (w), 635 (w), 590 (w), 570 (w). MS (ESI) m/z: calcd for $C_{17}H_{18}O_5$: 302.1 $[M]^+$, found 325.1 $[M+Na]^+$. HRMS (TOF MS EI+): m/z $[M]^+$ calcd for $C_{17}H_{18}O_5$: 302.1154, found 302.1158.

#### Phenyl 2-(2,4-dimethoxyphenyl)-2-hydroxyacetate (6 a)

Prepared from phenylglyoxal hydrate (40 mg, 0.3 mmol, 1.5 equiv) according to **GP2**. Purification via puriflash XS 420+ Flash purifier machine, HP_15 µm_F0012 flash column (*n*-hexane/ethyl acetate 9:1→4:1) afforded the analytically pure product as colorless oil (28 mg, 49%). $R_f$: 0.69 (1:1 *n*-Hexane/EtOAc). $^1$H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, *J* = 8.0 Hz, 2H), 7.48 (t, *J* = 8.0 Hz, 1H), 7.36 (t, *J* = 8.0 Hz, 2H), 7.06 (d, *J* = 8.0 Hz, 1H), 6.42 (d, *J* = 8.0 Hz, 2H), 6.18 (s, 1H), 3.83 (s, 3H), 3.75 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ = 199.7, 161.4, 157.8, 133.7, 130.0, 128.9, 128.6, 120.6, 105.3, 99.3, 70.8, 55.7, 55.5. IR (ν̃ in $cm^{-1}$): 2937 (w), 2837 (w), 1678 (s), 1608 (s), 1592 (s), 1504 (s), 1452 (m), 1419 (m), 1292 (s), 1266 (s), 1208 (m), 1158 (m), 1141 (m), 1067 (w), 1031 (s), 973 (m), 935 (w), 835 (w), 800 (w), 760 (w), 692 (m). MS (ESI) m/z: calcd for $C_{16}H_{16}O_4$: 272.1 $[M]^+$, found 295.1 $[M+Na]^+$. HRMS (TOF MS EI+): m/z $[M]^+$ calcd for $C_{16}H_{16}O_4$: 272.1049, found 272.1046.

#### Phenyl 2-(2,6-dimethoxyphenyl)-2-hydroxyacetate (6 b)

Prepared from phenylglyoxal hydrate (40 mg, 0.3 mmol, 1.5 equiv) according to **GP2**. Purification via puriflash XS 420+ Flash purifier machine, HP_15 µm_F0012 flash column (*n*-hexane/ethyl acetate 9:1→4:1) afforded the analytically pure product as colorless oil (36 mg, 62%). $R_f$: 0.60 (1:1 *n*-Hexane/EtOAc). $^1$H NMR (400 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 8.0 Hz, 2H), 7.44 (t, *J* = 8.0 Hz, 1H), 7.31 (t, *J* = 8.0 Hz, 2H), 7.19 (t, *J* = 8.0 Hz, 1H), 6.48 (d, *J* = 8.0 Hz, 2H), 6.27 (s, 1H), 3.76 (s, 6H). $^{13}$C NMR (101 MHz, $CDCl_3$): δ = 200.2, 158.1, 134.4, 133.1, 130.4, 128.4, 128.1, 116.8, 104.5, 68.4, 55.9. IR (ν̃ in $cm^{-1}$): 2972 (w), 2940 (w), 2902 (w), 2842 (w), 1677 (s), 1593 (s), 1475 (s), 1452 (m), 1439 (m), 1384 (m), 1341 (w), 1301 (w), 1285 (w), 1252 (s), 1214, 1170 (s), 1103 (s), 1070 (m), 973 (s), 866 (w), 783 (m), 762 (m), 738 (m), 719 (m), 692 (m), 678 (w), 640 (w), 617 (w). MS (ESI) m/z: calcd for $C_{16}H_{16}O_4$: 272.1 $[M]^+$, found 295.1 $[M+Na]^+$. HRMS (TOF MS EI+): m/z $[M]^+$ calcd for $C_{16}H_{16}O_4$: 272.1049, found 272.1048.

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## Conflict of Interest

The authors declare no conflict of interest.

**Keywords:** Carboxylic acids · Decarboxylation · Nucleophilic addition · Palladium · Synthetic Methods


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[1] G. M. Coppola, H. F. Schuster in *α-Hydroxy Acids in Enantioselective Syntheses*, Wiley-VCH, Weinheim, **1997**, pp. 137–164.
[2] H. Gröger, *Adv. Synth. Catal.* **2001**, *343*, 547–558.
[3] P. L. van Putten, *Antonie van Leeuwenhoek* **1979**, *45*, 622–623.
[4] E. Mutschler in *Mutschler Arzneimittelwirkungen, Vol. 11* (G. Geisslinger, S. Menzel, T. Gudermann, B. Hinz, P. Ruth), Wissenschatftliche Verlagsgesellschaft Stuttgart, **2020**.
[5] A. Gore, R. Brandeis, I. Egoz, J. Turetz, U. Nili, E. Grauer, E. Bloch-Shilderman, *Toxological Sciences* **2015**, *146(2)*, 301–310.
[6] M. Poterala, M. Dranka, P. Borowiecki, *Eur. J. Org. Chem.* **2017**, *2017*, 2290–2304.
[7] P. H. Huy, S. Motsch, S. M. Kappler, *Angew. Chem. Int. Ed.* **2016**, *55*, 10145–10149; *Angew. Chem.* **2016**, *128*, 10300–10304.
[8] a) R. A. Firestone, J. L. Fahey, N. S. Maciejewicz, G. S. Patel, B. G. Christensen, *J. Med. Chem.* **1977**, *20*, 551–556; b) M. Terreni, G. Pagani, D. Ubiali, R. Fernández-Lafuente, C. Mateo, J. M. Guisán, *Bioorg. Med. Chem. Lett.* **2001**, *11*, 2429–2432.
[9] A. Fulenmeier, P. Quitt, K. Vogler, P. Lanz, Hoffmann-La Roche Inc., U. S. Pat. 3957758, **1976**.
[10] N. Gathergood, W. Zhuang, K. A. Jorgensen, *J. Am. Chem. Soc.* **2000**, *122*, 12517–12522.
[11] F. Bigi, G. Sartori, R. Maggi, E. Cantarelli, G. Galaverna, *Tetrahedron: Asymmetry* **1993**, *4*, 2411–2414.
[12] K. Aikawa, Y. Hioki, K. Mikami, *Chem. Asian J.* **2010**, *5*, 2346–2350.
[13] M. Schlosser in *Organometallic in Synthesis – Third Manual*, John Wiley & Sons, Inc, Hoboken, **2013**, 5–222.
[14] L. J. Goossen, F. Collet, K. Goossen, *Isr. J. Chem.* **2010**, *50*, 617–629.
[15] N. Rodriguez, L. J. Goossen, *Chem. Soc. Rev.* **2011**, *40*, 5030–5048.
[16] J. Cornella, I. Larrosa, *Synthesis* **2012**, *44*, 653–676.
[17] A. G. Myers, D. Tanaka, M. R. Mannion, *J. Am. Chem. Soc.* **2002**, *124*, 11250–11251.
[18] L. J. Goossen, G. Deng, L. M. Levy, *Science* **2006**, *313*, 662–664.
[19] L. J. Gooßen, N. Rodriguez, P. P. Lange, C. Linder, *Angew. Chem.* **2010**, *122*, 1129–1132; *Angew. Chem. Int. Ed.* **2010**, *49*, 1111–1114.
[20] F. Bilodeau, M.-C. Brochu, N. Guimond, K. H. Thesen, P. Forgione, *J. Org. Chem.* **2010**, *75*, 1550–1560.
[21] F. Chacon-Huete, D. Mangel, M. Ali, A. Sudano, P. Forgione, *ACS Sustainable Chem. Eng.* **2017**, *5*, 7071–7076.
[22] Z. Zeng, A. Feceu, N. Sivendran, L. J. Gooßen, *Adv. Synth. Catal.* **2021**, *363*, 2678–2722.
[23] Y. Luo, J. Wu, *Chem. Commun.* **2010**, *46*, 3785–3787.
[24] J. Lindh, P. J. R. Sjöberg, M. Larhed, *Angew. Chem. Int. Ed.* **2010**, *49*, 7733–7737; *Angew. Chem.* **2010**, *122*, 7899–7903.
[25] J. Rydfjord, F. Svensson, A. Trejos, P. J. R. Sjöberg, C. Sköld, J. Sävmarker, L. R. Odell, M. Larhed, *Chem. Eur. J.* **2013**, *19*, 13803–13810.
[26] F. Svensson, R. S. Mane, J. Sävmarker, M. Larhed, C. Sköld, *Organometallics* **2013**, *32*, 490–497.
[27] A. M. Diehl, G. Manolikakes, *ChemCatChem* **2020**, *12*, 3463–3466.
[28] J. S. Dickstein, J. M. Curto, O. Gutierrez, C. A. Mulrooney, M. C. Kozlowski, *J. Org. Chem.* **2013**, *78*, 4744–4761.
[29] T. Diao, P. White, I. Guzei, S. S. Stahl, *Inorg. Chem.* **2012**, *51*, 11898–11909.
[30] J. S. Dickstein, C. A. Mulrooney, E. M. O'Brien, B. J. Morgan, M. C. Kozlowski, *Org. Lett.* **2007**, *9*, 2441–2444.
[31] B. Sklarz, *Q. Rev. Chem. Soc.* **1967**, *21*, 3–28.

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