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Palladium-Catalyzed α-Arylation of Zinc Enolates of Esters: Reaction Conditions and Substrate Scope

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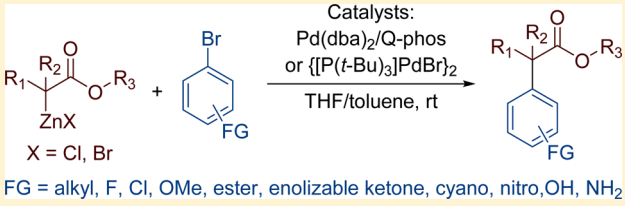
Supporting Information

ABSTRACT: The intermolecular α-arylation of esters by palladium-catalyzed coupling of aryl bromides with zinc enolates of esters is reported. Reactions of three different types of zinc enolates have been developed. α-Arylation of esters occurs in high yields with isolated Reformatsky reagents, with Reformatsky reagents generated from α-bromo esters and activated zinc, and with zinc enolates generated by quenching alkali metal enolates of esters with zinc chloride. The use of zinc enolates, instead of alkali metal enolates, greatly expands the scope of the arylation of esters. The reactions occur at room temperature or at 70 °C with bromoarenes containing cyano, nitro, ester, keto, fluoro, enolizable hydrogen, hydroxyl, or amino functionality and with bromopyridines. The scope of esters encompasses acyclic acetates, propionates, and isobutyrates, α-alkoxyesters, and lactones. The arylation of zinc enolates of esters was conducted with catalysts bearing the hindered pentaphenylferrocenyl di-*tert*-butylphosphine (Q-phos) or the highly reactive dimeric Pd(I) complex $\{[P(t\text{-Bu})_3]PdBr\}_2$.



INTRODUCTION

The α-aryl ester unit is present in many pharmaceuticals and biologically active compounds. Best known are the nonsteroidal anti-inflammatory agents, such as flurbiprofen, ibuprofen, ketoprofen, and naproxen. More recently, Allegra (fexofenadine hydrochloride), which contains the α-arylisobutyric acid moiety, has been developed as an antihistamine.[1] Besides these molecules, α-aryl esters are valuable building blocks because they can be precursors to aryl alcohols, amines, and nitriles. The ester functionality in α-aryl esters can be used to further build the carbon skeleton containing an aryl unit.

The uncatalyzed formation of the C−C bond between an aryl electrophile and an ester enolate is a useful transformation to prepare α-aryl esters. However, methods for this type of C−C bond formation are limited in scope and are often incompatible with auxiliary functionalities or require toxic reagents. Such C−C bonds have been formed by photochemical reactions,[2] reactions via benzyne intermediates,[3] and reactions with arylbismuth[4−6] or aryllead reagents.[7−13] The addition of aryl Grignard reagents to the salt of α-bromopropionic acid is conducted on industrial scale,[14] but it would be difficult to form a quaternary center by this reaction, and the scope of this reaction has not been expanded to encompass substrates containing reactive functional groups.

The palladium-catalyzed α-arylation of carbonyl compounds has been introduced as a mild, catalytic method to form the C−C bond between an aryl ring and the α-position of a carbonyl compound.[15,16] A variety of reactions of ketone,[17−22] ester,[23−28] amide,[29−32] and aldehyde[33,34] enolates have now been reported, but the use of strongly basic and nucleophlic alkali metal enolates limits the scope of these reactions. In addition, the arylated product, which is more acidic than the reactant, quenches the starting enolate, and products from undesired diarylation are formed. Furthermore, the strongly basic conditions prevent asymmetric α-arylations that would form tertiary stereocenters. To overcome these problems, we have begun to develop milder conditions to use zinc enolates generated from α-halo carbonyl compounds (Reformatsky reagents).[26,31] Because Reformatsky reagents are milder bases and nucleophiles than alkali metal enolates, we anticipate that the coupling of Reformatsky reagents could improve the functional group tolerance of the arylation of esters.

The zinc enolates of esters are common reagents used for Reformatsky reactions, and they can be generated from reactions of α-halo esters with zinc metal or by quenching the alkali metal enolates of esters with zinc halides. However, only a few examples of palladium-catalyzed α-arylation of zinc ester enolates have been reported.[35−38] Three decades ago, the palladium-catalyzed α-arylation of zinc ester enolates was reported using the isolated Reformatsky reagents of *tert*-butyl acetate and propionate.[35,36] These arylation reactions, in general, occurred in low yields with high palladium loading (10 mol %), in part because of the use of triarylphosphine ligands. In 2003, we reported, in communication form, the effective coupling of aryl bromides with the isolated Reformatsky reagents with 1 mol % palladium loading.[31] This coupling process tolerates a variety of potentially reactive

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electrophilic and protic functional groups, such as cyano, nitro, ester, keto, hydroxyl, and amino groups. However, these reactions are still limited to esters that can form stable and isolable Reformatsky reagents. In 2004, Moloney reported microwave assisted palladium-catalyzed α-arylation of the zinc enolate of *tert*-butyl acetate in the presence of stoichiometric amounts of $Pd(PPh_3)_4$.[39] Most recently, Knochel reported three examples of palladium-catalyzed α-arylation reactions of zinc ester enolates.[40] These zinc enolates are formed by reaction of ethyl butyrate or isobutyrate with (TMP)ZnCl·LiCl. Because palladium-catalyzed α-arylation of alkali metal enolates occurred in high yields in the presence of catalyst systems bearing sterically hindered, electron-rich alkylphosphines,[24,26−28,31] we sought to develop general procedures for the palladium-catalyzed α-arylation of Reformatsky reagents.

Here, we present a full account of the scope and limitation of a mild and more general palladium-catalyzed coupling of zinc enolates of esters that are generated in situ from α-bromoesters or by quenching the alkali metal ester enolates. The scope of these reactions now encompasses the coupling of acyclic acetates, propionates, and isobutyrates, α-alkoxyesters, and lactones with electronically varied aryl bromides that contain typically reactive protic and electrophilic functional groups.

RESULTS AND DISCUSSION

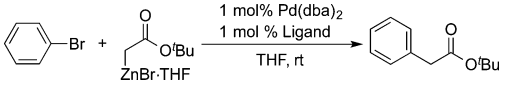
1. α-Arylation of Isolated Reformatsky Reagents. Our initial studies of palladium-catalyzed α-arylation of the zinc enolates of esters were conducted with isolated Reformatsky reagents. The Reformatsky reagents were prepared by reaction of zinc (granular 20-mesh beads) with α-bromo *tert*-butyl acetate and α-bromo *tert*-butyl propionate in THF at 0 °C. The zinc enolates of *tert*-butyl acetate and *tert*-butyl propionate were isolated as THF adducts as white powder in 80% and 55% yields, respectively.

1.1. Conditions and Scope of the α-Arylation of the Isolated Reformatsky Reagent from tert-Butyl Acetate. Arylation reactions of the isolated Reformatsky reagent of *tert*-butyl acetate with phenyl bromide catalyzed by complexes generated from $Pd(dba)_2$ and a series of monodentate phosphine and *N*-heterocyclic carbene ligands are summarized in Table 1. The reactions catalyzed by the single-component catalyst precursor $\{[P(t\text{-}Bu)_3]PdBr\}_2$[41−43] or the combination of $Pd(dba)_2$ and $P(t\text{-}Bu)_3$ or Q-phos formed the coupled product quantitatively (entries 1, 2, and 7). The coupled product was formed in lower yield with less sterically demanding trialkylphosphine ligands (entries 3−6). In sharp contrast to the high-yielding arylation of the lithium enolate of *tert*-butyl acetate catalyzed by $Pd(dba)_2$ and SIPr·HBF_4,[23,25] the reaction of the isolated Reformatsky reagent with PhBr catalyzed by this Pd-SIPr system (entries 8 and 9) afforded the coupled product in very low yields.

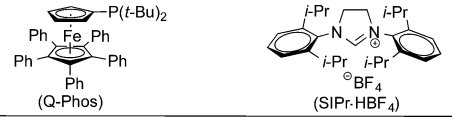
The combination of $Pd(dba)_2$ and unsubstituted ferrocenyl dialkyl or monoalkyl phosphine ligands formed less active catalysts (entries 10−12) than did $Pd(dba)_2$/Q-phos (entry 7). A subset of biphenyldialkylphosphine ligands developed by Buchwald[44,45] were also tested for this arylation reaction, and only modest yields were obtained (entry 13−15). Thus, catalysts generated from $Pd(dba)_2$ and either $P(t\text{-}Bu)_3$ or Q-phos were chosen to study the scope of the palladium-catalyzed α-arylation of zinc enolates of esters.

With an active catalyst in hand and reliable conditions for this coupling process, we investigated the scope of the α-arylation of the isolated Reformatsky reagent of *tert*-butyl acetate. Our results are summarized in Table 2. These reactions were catalyzed by the combination of $Pd(dba)_2$ and Q-phos or the single-component catalyst precursor $\{[P(t\text{-}Bu)_3]$-

Table 1. Effect of Ligands on the Pd-Catalyzed α-Arylation of the Isolated Zinc Enolate of *tert*-Butyl Acetate[a]

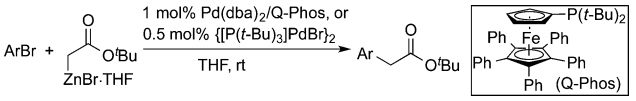


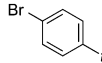
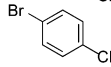
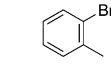
entry	Ligand	GC Yield	entry	Ligand	GC Yield
1	{[P(*t*-Bu)$_3$]PdBr}$_2$	100%	9	SIPr	21%
2	P(*t*-Bu)$_3$	100%	10	PR(*t*-Bu) R = Ad	45%
3	PCy$_3$	0%	11	Ph	25%
4	Cy$_2$P(*t*-Bu)	6%	12	Mes	7%
5	CyP(*t*-Bu)$_2$	36%			
6	AdP(*t*-Bu)$_2$	68%	13	PR'$_2$ R' = Ad Ar = Ph	75%
7	Q-Phos	100%	14	Cy Ph	51%
8	SIPr·HBF$_4$	12%	15	Cy Mes	64%



[a]Conditions: 1.1 equiv of enolate, 1 equiv of aryl bromide in THF (2 mL), 4 h at room temperature. [b]Yields were determined by GC with dodecane as an internal standard.

Table 2. Pd-Catalyzed α-Arylation of the Isolated Zinc Enolate of *tert*-Butyl Acetate[a]



Entry	ArBr	Cond[a]	Yield[h]	Entry	ArBr	Cond[a]	Yield[h]
1		A	94%	16	 4-CO$_2$Me	A	90%
				17		B	90%
2		A	71%	18	 4-CO$_2$Et	A	86%
				19		B	84%
3		A[f]	86%	20	3-CO$_2$*t*-Bu	A	76%
4		B[f]	88%	21	 4-CN	A	90%
5		A[f]	77%	22	3-CN	A	90%
6		B[f]	56%	23	2-CN	A[c]	86%
7		B[b]	67%	24		B	84%
8		B[c]	95%	25	 4-NO$_2$	A	96%
9		A	86%	26	2-NO$_2$	A	87%
				27	 4-OH	B[d]	88%
10		A	84%	28		B[e]	91%
				29	3-OH	B[e]	82%
11		A	83%	30	2-OH	B[e]	83%
				31	 4-NH$_2$	B[d,f]	92%
12		A	91%	32		B[e,g]	85%
				33	3-NH$_2$	B[e,f]	83%
13	 R = Ph	A[c]	72%	34	3-Br	A[b]	90%
				35		B[b]	80%
14	Ph	B[c]	67%	36	4-Br	A[b]	79%
15	Et	A	94%	37		B[b]	66%

[a]Conditions: zinc enolate of *tert*-butyl acetate (0.550 mmol), aryl bromide (0.500 mmol) in THF at room temperature, reaction time: 4 h; (A) 1 mol % $Pd(dba)_2$, 1 mol % Q-phos; (B) 0.5 mol % $\{[P(t\text{Bu})_3]PdBr\}_2$. [b]70 °C. [c]Twice catalyst loadings. [d]2 equiv of enolate. [e]1.05 equiv of KH, 1.1 equiv of enolate. [f]Reaction time: 12 h. [g]Reaction time: 24 h. [h]Average yield for two runs.

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PdBr}$_2$.[41−43] The α-arylation of this isolated zinc enolate occurred in high isolated yields with a wide range of electronically varied bromoarenes at room temperature and a few cases at elevated temperature (70 °C). In none of these reactions were products from the diarylation process of the enolate observed.

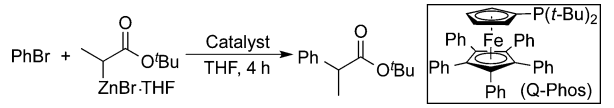
The scope of bromoarenes for this arylation process encompassed electron-neutral, electron-rich, and electron-poor bromoarenes bearing relatively reactive substituents. The coupling was selective for reaction with bromide over chloride and fluoride, and reactions of 1-bromo-4-chlorobenzene (entries 3 and 4) and 1-bromo-2-fluorobenzene (entry 11) formed products resulting from replacement of bromide. Moreover, the arylation reactions occurred smoothly with bromoarenes containing functional groups that are incompatible with strongly basic and nucleophilic alkaline enolates of esters.[24,25,27,28] For example, 4-bromoaryl ketones (entries 13−15), methyl or ethyl 4-bromobenzoate and *tert*-butyl 3-bromobenzoate (entries 16−20), 2-, 3-, and 4-bromobenzonitrile (entries 21−24), and 2- and 4-bromonitrobenzene (entries 25−26) reacted in high isolated yields. The coupling also occurred with *ortho*-substituted bromoarenes (entries 10−12, 23−24, 26, and 30). Moreover, the coupling of 3- or 4-bromopyridine (entries 34−37) occurred in modest to good yields (66−90%) at 70 °C.

Bromoarenes containing protic functionality also reacted to form α-aryl esters. In addition to the reaction with enolizable 4-bromopropiophenone (entry 15), the coupling of the zinc enolate with 2-, 3-, and 4-bromophenol and 3- and 4-bromoaniline occurred and afforded the corresponding α-aryl ester (entries 27−33). Use of 2 equiv of zinc enolate (entries 27 and 31) or use of 1.05 equiv of KH to deprotonate the hydroxyl or amino group prior to addition of the zinc enolate (entries 28−30 and 32−33) allowed these coupling reactions to occur. High yields were achieved when the single-component catalyst precursor {[P(*t*-Bu)$_3$]PdBr}$_2$ was used.

Although the scope of these coupling reactions was broad, the coupling of the isolated Reformatsky reagent of *tert*-butyl acetate does have some limitations. For example, reactions of this isolated Reformastky reagent with 2-bromopyridine did not occur either at room temperature or at 70 °C with both catalysts, even though the coupling reactions with 3- or 4-bromopyridine occurred in high yields. The coupling of this Reformatsky reagent showed high tolerance toward cyano, nitro, ester, ketone, hydroxyl, and amino functionalities, but bromoarenes containing strong electrophiles, e.g., 4-bromobenzaldehyde and 4-bromobenzyl bromide, did not react to give the coupling products.

1.2. Conditions and the Scope of α-Arylation of the Isolated Reformatsky Reagent of tert-Butyl Propionate. Table 3 summarizes selected experiments to identify conditions for the coupling of the isolated Reformatsky reagent of *tert*-butyl propionate with bromobenzene. The combination of Pd(dba)$_2$ and P(*t*-Bu)$_3$ was a highly active catalyst for coupling of the isolated Reformatsky reagent of *tert*-butyl acetate and was also employed for the arylation of the isolated Reformatsky reagent of *tert*-butyl propionate (entries 1−3). When 1.1 equiv of the zinc enolate was used, only modest GC yields were obtained either at room temperature or at 70 °C; however, quantitative yield was achieved at 70 °C when a large excess (e.g., 5 equiv) of the zinc enolate was used (entry 3). When the combination of Pd(dba)$_2$ and Q-phos or the single-component catalyst precursor {[P(*t*-Bu)$_3$]PdBr}$_2$ was used, this coupling occurred in quantitative yield at room temperature with only 1.1 equiv of the enolate (entries 4 and 5).

Table 3. Identification of Conditions for Pd-Catalyzed α-Arylation of the Isolated Zinc Enolate of *tert*-Butyl Propionate[a]

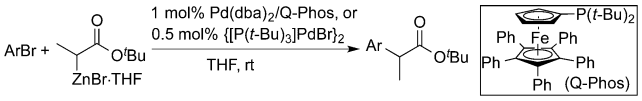


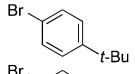
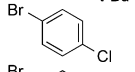
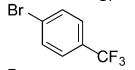
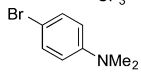
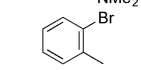
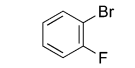
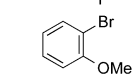
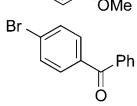
entry	catalyst	enolate (equiv)	temp (°C)	yield[b] (%)
1	Pd(dba)$_2$/P(*t*-Bu)$_3$ (1 mol %)	1.1	rt	60
2	Pd(dba)$_2$/P(*t*-Bu)$_3$ (1 mol %)	1.1	70	45
3	Pd(dba)$_2$/P(*t*-Bu)$_3$ (1 mol %)	5	70	100
4	Pd(dba)$_2$/Q-phos (1 mol %)	1.1	rt	100
5	{[P(*t*-Bu)$_3$]PdBr}$_2$ (0.5 mol %)	1.1	rt	100

[a]Conditions: aryl bromide (0.500 mmol), Pd(dba)$_2$ (5.00 μmol) and P(*t*-Bu)$_3$ or Q-Phos (5.00 μmol), {[P(*t*-Bu)$_3$]PdBr}$_2$ (0.250 μmol), THF (2 mL), 4 h. [b]Yields were determined by GC with dodecane as internal standard.

The coupling of the isolated Reformatsky reagent of *tert*-butyl propionate with aryl bromides is summarized in Table 4. These reactions were catalyzed by the combination of Pd(dba)$_2$ and Q-phos or {[P(*t*-Bu)$_3$]PdBr}$_2$. This arylation occurred with a scope that was similar to that of the isolated Reformatsky reagent of *tert*-butyl acetate. Most of these couplings with aryl bromides occurred at room temperature; only a few cases

Table 4. Pd-Catalyzed α-Arylation of the Isolated Reformatsky Reagent of *tert*-Butyl Acetate[a]



Entry	ArBr	Cond[a]	Yield[h]	Entry	ArBr		Cond[a]	Yield[h]
1		A	88%	12		R' = Me	A	87%
2		B	83%	13			B	81%
3		A[f]	86%	14		R' = Et	A	88%
4		B[f]	79%	15			B	84%
5		A[f]	69%	16		4-CN	A	83%
6		B[f]	61%	17		3-CN	A	80%
7		B[b]	91%	18		2-CN	A[c]	85%
8		A	91%	19		4-NO$_2$	A	88%
				20		2-NO$_2$	A	81%
9		A	81%	21		4-OH	B[d]	92%
				22			B[e]	95%
				23		3-OH	B[e]	87%
10		A	90%	24		4-NH$_2$	B[d,f]	70%
				25			B[e,g]	66%
				26		3-NH$_2$	B[e,f]	74%
11		B[c]	67%	27			A[b]	90%
				28			B[b]	80%

[a]Conditions: zinc enolate of *tert*-butyl acetate (0.550 mmol), aryl bromide (0.500 mmol) in THF at room temperature, reaction time: 4 h; (A) 1 mol % Pd(dba)$_2$, 1 mol % of Q-phos; (B) 0.5 mol % of {[P(*t*-Bu)$_3$]PdBr}$_2$. [b]70 °C. [c]Twice catalyst loadings. [d]2 equiv of enolate. [e]1.05 equiv of KH, 1.1 equiv of enolate. [f]Reaction time: 12 h. [g]Reaction time: 24 h. [h]Average yield for two runs.

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required heating at 70 °C to ensure full conversion of aryl bromides.

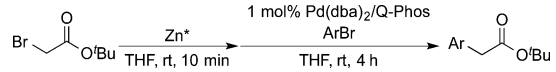
In general, the coupling of this isolated zinc enolate of *tert*-butyl propionate occurred with electron-neutral, electron-rich, and electron-poor aryl bromides in high yields. This enolate underwent coupling in high yields with aryl bromides containing electron-donating (entries 8 and 10) and electron-withdrawing substituents at the *ortho*-position (entries 9, 18, and 20). This arylation reaction also occurred selectively at an aryl bromide over an aryl chloride (entries 3 and 4) or aryl fluoride (entry 9). The reactions catalyzed by the combination of $Pd(dba)_2$ and Q-phos formed the coupled products in higher yields (entries 1, 3, 5, 12, 14, and 27) than those catalyzed by $\{[P(t\text{-}Bu)_3]PdBr\}_2$ (entries 2, 4, 6, 13, 15, and 28).

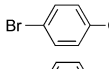
Like the coupling of *tert*-butyl acetate, the coupling of *tert*-butyl propionate occurred in high yields with aryl bromides containing reactive functional groups such as ketones (entry 11), esters (entries 12−15), cyano groups (entries 16−18), and nitro groups (entries 19−20). Remarkably, these couplings also tolerated the hydroxyl and amino groups, provided that these groups were deprotonated by an additional 1 equiv of the Reformatsky reagent (entries 21 and 24) or 1.1 equiv of KH (entries 22−23 and 25−26); however, higher yields were achieved with the single-component catalyst precursor $\{[P(t\text{-}Bu)_3]PdBr\}_2$ than with the combination of $Pd(dba)_2$ and Q-phos for these reactions. The arylation with 3-bromopyridine occurred at 70 °C in high yield in the presence of both catalysts (entries 27−28); however, no coupling occurred with 2- or 4-bromopyridine under these conditions.

2. Arylation of Reformatsky Reagents Generated in Situ from α-Bromoesters and Rieke's Activated Zinc. Even though α-arylation reactions of the isolated Reformatsky reagents of *tert*-butyl acetate and propionate catalyzed by Pd(0)/Q-phos or $\{[P(t\text{-}Bu)_3]PdBr\}_2$ occur with high tolerance toward functional groups under mild conditions, this methodology does have some drawbacks. For example, excess zinc was employed during the generation of the isolated Reformatsky reagents, and this excess zinc would likely interfere with the Pd(II) intermediates during catalysis by oxidation−reduction processes.[46] Furthermore, the substrate scope was limited to esters that form stable and isolable Reformatsky reagents, e.g., methyl isobutyrate does not form an isolable Reformatsky reagent, precluding α-arylation reactions of methyl isobutyate with an isolated reagent. To overcome these drawbacks, we developed conditions for the α-arylation of Reformatsky reagents generated in situ by conducting reactions of α-bromo esters with stoichiometric highly active zinc powder. This highly active zinc powder was prepared by reduction of zinc chloride with lithium metal according to the procedure described by Rieke.[47]

2.1. Scope of the α-Arylation of the Reformatsky Reagent Generated in Situ from tert-Butyl Bromoacetate. The selected examples of α-arylation of this Reformatsky reagent generated in situ are summarized in Table 5. These reactions were conducted with 1 mol % of $Pd(dba)_2$ and 1 mol % of Q-phos. Like the α-arylation of the isolated Reformatsky reagent of *tert*-butyl acetate, the arylation of this Reformtsky reagent generated in situ occurred with electron-neutral, electron-rich, and electron-poor bromoarenes in high yields. Aryl bromides containing an ortho substituent reacted in high isolated yields (entries 1−4). Entries 4−6 illustrate that this α-arylation occurs with aryl bromides bearing the potentially reactive cyano group at the ortho-, meta-, or para-position. This coupling also occurs

Table 5. Pd-Catalyzed α-Arylation of the Reformatsky Reagent Generated in Situ from *tert*-Butyl Bromoacetate[a]



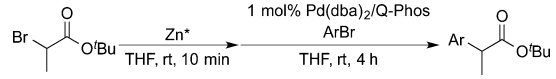
Entry	ArBr	Yield[b]	Entry	ArBr	Yield[b]
1		88%	5		95%
2		98%	6		97%
3		92%	7		83%
4		98%	8		90%
			9		93%

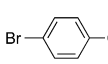
[a]Conditions: *tert*-butyl bromoacetate (0.550 mmol), activated zinc (0.750 mmol), aryl bromide (0.500 mmol), $Pd(dba)_2$ (5.00 μmol), Q-Phos (5.00 μmol), THF (2 mL), room temperature, 4 h. [b]Average yield for two runs.

in high yields with aryl bromides containing ketone functionality (entries 7−9), even with enolizable hydrogens (entries 7 and 8).

2.2. Scope of the α-Arylation of the Reformatsky Reagent Generated in Situ from tert-Butyl 2-Bromopropionate. Table 6 summarizes selected examples of Pd-catalyzed α-arylations of

Table 6. Pd-Catalyzed α-Arylation of the Reformatsky Reagent Generated in Situ from *tert*-Butyl 2-Bromopropionate[a]



Entry	ArBr	Yield[b]	Entry	ArBr	Yield[b]
1		88%	4		86%
2		98%	5		85%
3		92%			

[a]Conditions: *tert*-butyl 2-bromopropionate (0.550 mmol), activated zinc (0.750 mmol), aryl bromide (0.500 mmol), $Pd(dba)_2$ (5.00 μmol), Q-Phos (5.00 μmol), THF (2 mL), room temperature, 4 h. [b]Average yield for two runs.

the Reformatsky reagent generated in situ from *tert*-butyl 2-bromopropionate and the Rieke activated zinc. These reactions were performed with catalysts generated from 1 mol % of $Pd(dba)_2$ and 1 mol % of Q-phos. Because the scope of the α-arylation of the Reformatsky reagent of *tert*-butyl acetate that was generated in situ was similar to that of the reactions of the Reformatsky reagent that was isolated, we investigated a selection of the reactions of *tert*-butyl propionate to determine if this trend also applied to the reactions of the Reformatsky reagent of *tert*-butyl propionate generated in situ. Indeed, the reactions of these two zinc enoaltes occurred with similar scope of aryl bromides. High yields were again obtained for reactions of *ortho*-substituted aryl bromides (entries 1−3). Entries 4 and

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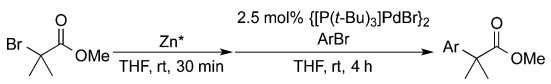
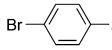
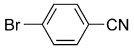
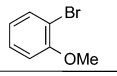
5 illustrate that reactions occurred in high yields with the bromoarenes containing cyano functionality at the *meta*- or *para*-position. However, the reaction of 2-bromobenzonitrile with the enolate generated in situ was different from the reaction with the isolated enolate. In contrast to the reaction of 2-bromobenzonitrile with the isolated enolate, which afforded the coupled product in 85% isolated yield, the corresponding reaction with the enolate generated in situ afforded only trace amount of the coupled product (<5% by GC analysis).

2.3. Scope of the α-Arylation of the Reformatsky Reagent Generated in Situ from Methyl α-Bromoisobutyrate. At first, we attempted α-arylation reactions of the zinc enolate of methyl isobutyrate generated in situ from the Rieke activated zinc and methyl α-bromoisobutyrate under the conditions described for the arylation of the Reformatsky reagents of *tert*-butyl acetate and propionate. However, reactions of the Reformatsky reagent of methyl isobutyrate generated in situ occurred in low yields under these conditions. For example, the coupling of this zinc enolate with 1-bromo-4-*tert*-butylbenzene afforded the desired product in only 32% yield in the presence of 5 mol % of $Pd(dba)_2$ and Q-phos. However, the same reaction conducted with 2.5 mol % of $\{[P(t\text{-}Bu)_3]PdBr\}_2$ occurred in 88% isolated yield. Such enhanced reactivity can be rationalized by the slightly more open structure of the arylpalladium halide intermediate containing $P(t\text{-}Bu)_3$, relative to the structure of the arylpalladium halide containing Q-phos.[48] The Pd(I) dimer, $\{[P(t\text{-}Bu)_3]PdBr\}_2$ was chosen as catalyst precursor to study the scope of arylation of the in situ generated zinc enolate of methyl isobutyrate.

Our experiments on the scope of arylation of the zinc enolate of methyl isobutyrate focused on reactions of bromoarenes that do not couple with alkali metal enolates of methyl isobutyrate. Although a variety of electronically varied aryl bromides reacted with the alkali metal enolates in good yields,[25,27,28] the coupling of alkali metal enolates of methyl isobutyrate with *ortho*-substituted aryl bromides do not occur. Furthermore, the high nucleophilicity of alkali metal enolates of methyl isobutyrate limits reactions of aryl bromides containing electrophilic functionality. The scope of the coupling of this Reformatsky reagent generated in situ was briefly screened and is summarized in Table 7. Like the alkali metal enolates of methyl isobutyrate,[25,27,28] this zinc enolate coupled with the relatively electron-neutral 4-bromo-1-*tert*-butylbenzene at room temperature in 88% isolated yield (entry 1). The coupling of this zinc enolate with *ortho*-substituted aryl bromides occurred in high yields as well (entries 2 and 4). 4-Bromobenzonitrile reacted in 95% isolated yield without any apparent interference with the cyano group (entry 3). The extended scope of arylation of this zinc enolate will be further studied in the next section on the arylation of zinc enolates generated in situ by quenching alkali metal enolates with zinc chloride.

Table 7. Pd-Catalyzed α-Arylation of the Zinc Enolate Generated in Situ from Methyl α-Bromoisobutyrate[a]



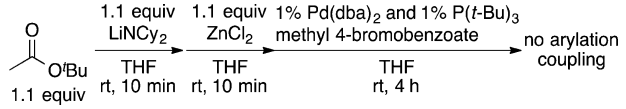
Entry	ArBr	Yield[b]	Entry	ArBr	Yield[b]
1		88%	3		95%
2		98%	4		97%

[a]Conditions: methyl α-bromoisobutyrate (0.550 mmol), activated zinc (0.750 mmol), aryl bromide (0.500 mmol), $\{[P(t\text{-}Bu)_3]PdBr\}_2$ (12.5 μmol), THF (2 mL), room temperature, 4 h. [b]Average yield for two runs.

3. α-Arylation of Zinc Enolates Generated by Quenching Alkali Metal Enolates with $ZnCl_2$. A procedure to couple a zinc ester enolate that is generated directly from the ester, rather than from the α-bromoester, would combine the functional group tolerance of the Reformatsky reagents and the convenience of the coupling of the alkali metal enolates of esters. In addition, a procedure that generates zinc enolates from $ZnCl_2$ is simpler to conduct than a procedure that generates the zinc enolates from activated zinc metal. Thus, we sought to develop conditions for the α-arylation of the zinc ester enolate by quenching the alkali metal enolate of an ester with $ZnCl_2$. The reactivity of zinc ester enolates generated by quenching alkali metal enolates of esters with $ZnCl_2$ and the reactivity of Reformatsky reagents generated from α-bromoesters are different. The use of certain bases to generate the alkali metal ester enolate that would be converted to the zinc ester enolate led to the development of a general coupling of esters with aryl bromides. Thus, the palladium-catalyzed α-arylation of these zinc enolates required careful choice of reaction stoichiometry, temperature, and base.

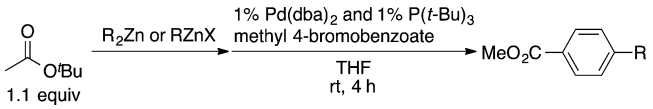
3.1. Evaluation of Conditions for α-Arylation of the Zinc Enolate of tert-Butyl Acetate by Quenching the Alkali Metal Enolate with $ZnCl_2$. To study the arylation of the zinc enolate of *tert*-butyl acetate generated in situ by quenching the alkali metal enolate with $ZnCl_2$, we first attempted to add zinc chloride to the enolate of *tert*-butyl acetate generated under the conditions we have developed for the arylation of alkali metal enolates.[25,27,28] These alkali metal enolates were generated by reaction of the ester with LiHMDS or $LiNCy_2$ in toluene at room temperature. Because $ZnCl_2$ is soluble in THF and the palladium-catalyzed α-arylation of zinc enolates occurs in THF, the alkali metal enolate was first generated in THF instead of toluene and then quenched with $ZnCl_2$ (Scheme 1). Methyl 4-bromobenzoate was chosen as electrophile because this aryl bromide does not couple with the lithium enolate of *tert*-butyl acetate.[25,27,28] However, the arylation of this zinc enolate generated in situ in THF with methyl 4-bromobenzoate did not occur. Alternative conditions needed to be developed for the arylation of the zinc enolate generated in situ.

Scheme 1



Zinc enolates have been reported to form from reactions of carbonyl compounds with alkylzinc reagents.[49] Thus, we attempted to generate the zinc enolate of *tert*-butyl acetate by reaction of *tert*-butyl acetate with diethylzinc or butylzinc bromide (Scheme 2). When diethylzinc was used as base to

Scheme 2



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generate the zinc enolate, the reaction of the resulting mixture with methyl 4-bromobenzoate in the presence of $Pd(dba)_2$ and $P(t\text{-}Bu)_3$ did not yield the desired α-aryl ester. In contrast, the product from the Negishi coupling, methyl 4-ethylbenzoate, was detected by GC−-MS analysis. These results indicated that either diethylzinc was not basic enough to generate the zinc enolate of *tert*-butyl acetate or the ethyl group transferred faster to the palladium center than the enolate in the mixed ethylzinc enolate of *tert*-butyl acetate. The corresponding reaction with butylzinc bromide as base yielded methyl 4-butylbenzoate, the product from the Negishi coupling. This reaction suggested that butylzinc bromide was not a sufficiently strong base to generate the zinc enolate of *tert*-butyl acetate.

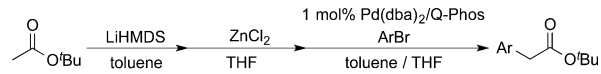
We also attempted to generate the zinc enolate of *tert*-butyl acetate by allowing *tert*-butyl acetate to react with a zinc amide generated in situ by combining 1 or 2 equiv of LiHMDS with $ZnCl_2$. However, this mixture of ester and zinc amide did not react with 4-bromo ethylbenzoate to form the α-aryl ester in the presence of the palladium catalyst containing Q-phos or $P(t\text{-}Bu)_3$ ligand.

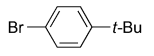
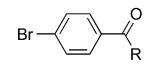
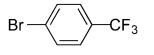
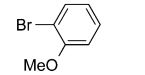
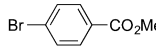
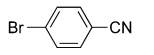
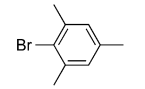
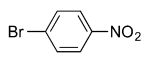
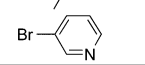
Ultimately, we found that quenching of the lithium enolate generated from *tert*-butyl acetate and LiHMDS at room temperature after only 1 min or at −78 °C after 1 h in a mixed solvent of toluene and THF (volume ratio of 4:1) enabled the coupling of ethyl 4-bromobenzoate with the zinc enolate of *tert*-butyl acetate in high yield. A series of experiments was conducted to evaluate the conditions for the coupling of ethyl 4-bromobenzoate with the zinc enolate generated in situ from *tert*-butyl acetate, lithium bases, and $ZnCl_2$. When LDA or $LiNCy_2$ were used as bases, the coupling did not occur. However, the α-aryl ester was detected by GC−MS analysis when LiHMDS was used as base to generate the lithium enolate in THF, provided that the lithium enolate was quenched with $ZnCl_2$ after a short time (1 min) at room temperate. This reaction was studied in different solvents, such as dioxane, ether, and the mixture of toluene and THF with varied volume ratios; the coupling reaction performed in the mixture of toluene and THF with a 4:1 volume ratio yielded the desired α-aryl ester in nearly quantitative yield.

Finally, to ensure greater reproducibility on larger scales, and to evaluate the need for excess $ZnCl_2$, the lithium enolate of *tert*-butyl acetate was generated with LiHMDS at −78 °C and quenched with $ZnCl_2$ at −78 °C, and the resulting enolate was allowed to react with 1-bromo-4-*tert*-butylbenzene. The conversion of the bromoarene was highly dependent on the amount of $ZnCl_2$ used to quench the lithium enolate. When 1.1 equiv of $ZnCl_2$, relative to the bromoarene, was used to quench the lithium enolate, only 50% conversion of 1-bromo-4-*tert*-butylbenzene was achieved. When 2.2 equiv of $ZnCl_2$ was used, 1-bromo-4-*tert*-butylbenzene was fully converted to the desired α-aryl ester.

3.2. Scope of the Coupling of the Zinc Enolate of tert-Butyl Acetate Generated by Quenching the Lithium Enolate with $ZnCl_2$. With reliable reaction conditions in hand for the α-arylation of the zinc enolate of *tert*-butyl acetate generated in situ by quenching of the lithium enolate with $ZnCl_2$, we studied the scope of this process, and the results are summarized in Table 8. These reactions were conducted with the catalyst generated from 1 mol % of $Pd(dba)_2$ and 1 mol % of Q-phos. The zinc enolate was generated after reaction of *tert*-butyl acetate with LiHMDS at −78 °C for 1 h, followed by quenching the resulting lithium enolate with $ZnCl_2$ at −78 °C for 0.5 h. The scope of the α-arylation of this zinc enolate was

Table 8. Pd-Catalyzed α-Arylation of the Zinc Enolate Generated in Situ by Quenching Lithium Enolate of *tert*-Butyl Acetate with $ZnCl_2$[a]



Entry	ArBr	Yield[c]	Entry	ArBr	Yield[c]
1		95%	6		91%
			7		92%
2		96%	8		89%
3		95%			
4		92%	9		94%
5		92%	10		90%[b]

[a]Standard conditions: *tert*-butyl acetate (0.550 mmol), LiHMDS (0.550 mmol), $ZnCl_2$ (1.10 mmol), aryl bromide (0.500 mmol), $Pd(dba)_2$ (5.00 μmol), Q-Phos (5.00 μmol), in mixed solvent of THF (30%) and toluene (70%), room temperature, 4 h. [b]At 70 °C. [c]Average yield for two runs.

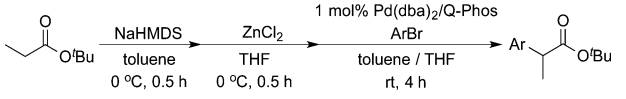
similar to that of the α-arylation of the corresponding isolated Reformatsky reagent. The arylation reactions of this zinc enolate occurred in high isolated yields (89−96%) with electron-neutral (entry 1), electron-poor (entries 2−7), and electron-rich (entry 8) bromoarenes. This coupling tolerated electrophilic functionalities, such as ester (entry 3), cyano (entry 4), nitro (entry 5), and ketone moieties with or without enolizable hydrogen atoms (entries 6 and 7). A sterically hindered 2,6-substituted bromoarene also reacted in high yield (entry 9). Finally, this zinc enolate of *tert*-butyl acetate reacted with 3-bromopyridine at 70 °C in 90% yield (entry 10).

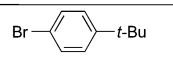
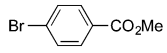
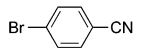
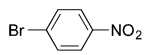
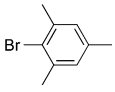
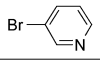
3.3. Conditions for the Coupling of the Zinc Enolate of tert-Butyl Propionate Generated from the Alkali Metal Enolate. The coupling of the zinc enolate of *tert*-butyl propionate generated in situ by quenching of the alkali metal enolate required somewhat different conditions than the coupling of the analogous enolate of *tert*-butyl acetate. A series of arylation reactions of this enolate with 4-bromobenzonitrile showed that high yields were obtained when the enolate was generated from an excess (2 equiv) of LiHMDS and quenched with 2 equiv of $ZnCl_2$. Therefore, we tested reactions with stronger lithium bases. However, no coupled product was observed when either $LiNCy_2$ (effective for arylation of esters with base-stable bromoarenes in the absence of zinc[25,28]) or *s*-BuLi (effective for arylation of propionamides[26]) was used as base instead of LiHMDS. Also, no coupled product was observed with the enolate generated from these bases in THF or a 3:1 mixture of toluene and THF at either room temperature or −78 °C. However, the simple substitution of NaHMDS for LiHMDS in the protocol, deprotonation at 0 °C, quenching of this enolate at 0 °C, and the use of a 3:1 mixture of toluene and THF as solvent led to the coupling of the zinc enolate of *tert*-butyl propionate with 4-bromobenzonitrile in almost quantitative yield.

3.4. Scope of the Coupling of the Zinc Enolate of tert-Butyl Propionate Generated in Situ from NaHMDS and $ZnCl_2$. Table 9 summarizes examples of palladium-catalyzed α-arylations of the zinc enolate of *tert*-butyl propionate formed in situ by quenching the sodium enolate generated from

dx.doi.org/10.1021/jo401476f | J. Org. Chem. 2013, 78, 8250−8266

Table 9. Pd-Catalyzed α-Arylation of the Zinc Enolate Generated in Situ by Quenching Sodium Enolate of *tert*-Butyl Propionate with $ZnCl_2$[a]



Entry	ArBr	Yield[b]	Entry	ArBr	Yield[b]
1		94%	7		87%
2		84%	8		74%[d,e]
3		86%	9		92%[c]
4		88%			
5		89%	10		82%
6		89%	11		90%[f]

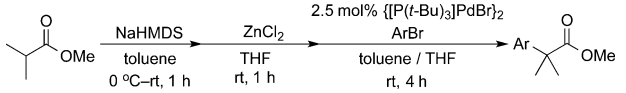
[a]Standard conditions: 1.1 equiv of ester, 1.3 equiv of base, 2.6 equiv of zinc chloride, 1 equiv of aryl bromide (0.5 mmol), 1 mol % of $Pd(dba)_2$, 1 mol % of Q-phos in mixed solvent of toluene and THF at room temperature. [b]Average yield for two runs. [c]2 mol % of $Pd(dba)_2$ and 2 mol % of Q-phos. [d]4 mol % of $Pd(dba)_2$ and 4 mol % of Q-phos. [e]Isolated by distillation (one isolation). [f]70 °C.

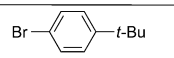
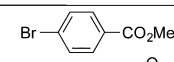
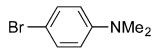
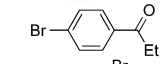
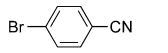
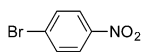
NaHMDS in toluene at 0 °C with $ZnCl_2$. The catalyst used for these reactions was the combination of $Pd(dba)_2$ and Q-phos. A range of electronically varied para-substituted (entries 1–4) and ortho-substituted (entries 5–9) aryl bromides underwent the coupling with this enolate in high yields (74–94%). These reactions are compatible with bromoarenes bearing reactive functional groups, such as carboalkoxy (entry 2), cyano (entries 3 and 9), and nitro (entries 4 and 8) groups on either the para- or ortho-position. The sterically hindered 2,6-substituted 2-bromomesitylene reacted with this enolate in 82% yield (entry 10). The coupling with 3-bromopyridine also occurred in high yield (entry 11), although a higher temperature of 70 °C was required. Coupling reactions of bromoarenes containing enolizable keto functionality did not occur.

3.5. Conditions for Coupling of the Zinc Enolate of Methyl Isobutyrate Generated in situ by Quenching of the Alkali Metal Enolate with $ZnCl_2$. Our studies to develop conditions for the α-arylation of the zinc enolate of methyl isobutyrate generated in situ by quenching the alkali metal enolate with $ZnCl_2$ were conducted primarily with the dimeric Pd(I) catalyst $\{[P(t\text{-}Bu)_3]PdBr\}_2$, instead of a combination of $Pd(dba)_2$ and Q-phos. This Pd(I) catalyst was selected because arylation reactions of the zinc enolate generated from methyl α-bromoisobutyrate and Rieke activated zinc occurred in higher yield when catalyzed by the Pd(I) dimer $\{[P(t\text{-}Bu)_3]PdBr\}_2$ than when catalyzed by a combination of $Pd(dba)_2$ and Q-phos. Like the reactions of *tert*-butyl propionate, the reactions of methyl isobutyrate occurred in high yields when the zinc enolate was generated by deprotonation with NaHMDS, followed by quenching the resulting sodium enolate with an excess of $ZnCl_2$. Consistent with the reaction of 1-bromo-4-*tert*-butylbenzene with the zinc enolate generated from methyl α-bromoisobutyrate and Rieke's activated zinc, the reaction of the zinc enolate generated by quenching of the sodium enolate with $ZnCl_2$ occurred in only 37% yield when a combination of $Pd(dba)_2$ and Q-phos was used as catalyst.

3.6. Scope of the Coupling of the Zinc Enolate of Methyl Isobutyrate Generated in Situ by Quenching of the Alkali Metal Enolate with $ZnCl_2$. Table 10 summarizes the scope of

Table 10. Pd-Catalyzed α-Arylation of the Zinc Enolate Generated in Situ by Quenching the Sodium Enolate of Methyl Isobutyrate with $ZnCl_2$.[a]



Entry	ArBr	Yield[b]	Entry	ArBr	Yield[b]
1		93%	5		92%
2		84%	6		87%
3		90%	7		90%[c]
4		89%	8		91%[c]

[a]Standard conditions: 1.5 equiv of ester, 1.7 equiv of base, 3.4 equiv of zinc chloride, 1 equiv of aryl bromide (0.5 mmol), 2.5 mol % of $\{[P(t\text{-}Bu)_3]PdBr\}_2$ in mixed solvent of toluene and THF at room temperature. [b]Average yield for two runs. [c]70 °C.

the palladium-catalyzed arylation of the zinc enolate of methyl isobutyrate generated in situ by quenching the sodium enolate with $ZnCl_2$. Reactions occurred in high yields with electron-neutral (entry 1), electron-rich (entry 2), and electron-poor (entries 3–6) para-substituted bromoarenes at room temperature. However, reactions with both electron-neutral (entry 7) and electron-rich (entry 8) ortho-substituted bromoarenes required high temperature (70 °C) to go to completion. These coupling reactions were compatible with reactive functionalities, such as nitrile (entry 3), nitro (entry 4), ester (entry 5), and ketone (entry 6) groups. Different from arylation reactions of the zinc enolates of tert-butyl acetate and propionate, reactions of this hindered enolate with 2,6-disubstituted arenes did not form the coupled product, and reactions with arenes containing reactive functional groups, such as cyano and nitro groups, at the *ortho*-position did not occur.

3.7. Scope of the Coupling of the Zinc Enolate of Methyl Propionate Generated in Situ by Quenching of the Alkali Metal Enolate with $ZnCl_2$. Methyl esters are the most common esters, and they easily undergo hydrolysis to generate the corresponding acids. Thus, the sequential reaction of the arylation of methyl esters followed by hydrolysis will provide a valuable route to α-aryl acids. α-Aryl methyl esters can be prepared by nickel-catalyzed Suzuki coupling of α-haloesters with arylboronic acids or nickel-catalyzed reductive coupling of aryl halides with α-haloesters in the presence of manganese.[50,51] However, the direct arylation of methyl esters with aryl halides has been limited to sterically hindered esters such as methyl isobutyrate catalyzed by palladium complexes.[25,27] It is challenging to conduct the arylation of less hindered methyl esters, such as methyl acetate and propionate because the enolates of these esters are thermodynamically unstable and readily undergo the Claisen condensation reaction.

To address this limitation, we sought to develop conditions for the arylation of zinc enolate of methyl propionate. First, we attempted to generate the zinc enolate of methyl propionate under the conditions that we developed to generate the zinc enolate of *tert*-butyl propionate involving deprotonation of the

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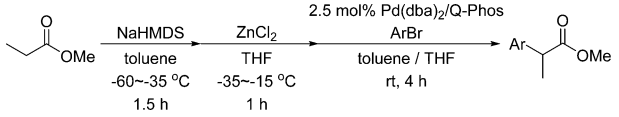
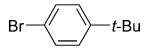
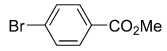
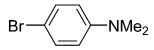
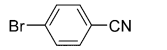
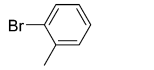
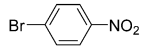
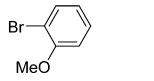
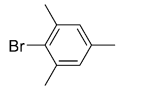
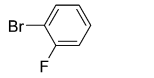
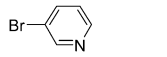
ester with NaHMDS at 0 °C in toluene, followed by quenching of the sodium enolate with $ZnCl_2$ in THF. The coupling of this zinc enolate with 1-bromo-4-*tert*-butylbenzene catalyzed by 2.5 mol % of $Pd(dba)_2$ and 2.5 mol % of Q-phos did not afford any arylation product. Generation of the zinc enolate at −78 °C or between −40 and −15 °C in toluene, followed by quenching with $ZnCl_2$ in THF at the same temperature, gave coupled product, but in less than 50% yield. However, when the sodium enolate was generated by reaction of methyl propionate with NaHMDS in toluene at −60 °C and quenched with $ZnCl_2$ at −35 °C, the coupling of the resulting enolate with 1-bromo-4-*tert*-butylbenzene afforded the desired product in 86% isolated yield.

Under these conditions, we studied the scope of the arylation of the zinc enolate of methyl propionate, and selected examples are listed in Table 11. The coupling occurred with a range of

Table 11. Pd-Catalyzed α-Arylation of the Zinc Enolate Generated in Situ by Quenching the Sodium Enolate of Methyl Propionate with $ZnCl_2$[a]



Entry	ArBr	Yield[b]	Entry	ArBr	Yield[b]
1		86%	6		91%
2		84%	7		80%
3		87%	8		73%
4		91%	9		90%
5		83%	10		84%[c]

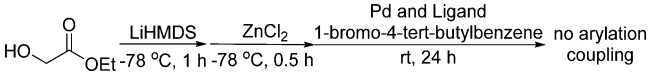
[a]Standard conditions: 1.5 equiv of ester, 1.7 equiv of NaHMDS, 3.4 equiv of zinc chloride, 1 equiv of aryl bromide (0.5 mmol), 2.5 mol % of $Pd(dba)_2$, 2.5 mol % of Q-phos, in mixed solvent of toluene and THF, 4 h at room temperature. [b]Average yield for two runs. [c]Performed at 70 °C.

electronically varied aryl bromides in high isolated yields. It also occurred with *ortho*-substituted (entries 3−5) and di-*ortho*-substituted (entry 9) aryl bromides in high isolated yields and with aryl bromides containing ester (entry 6), cyano (entry 7), and nitro (entry 8) groups. This zinc enolate coupled with 3-bromopyridine at 70 °C to afforded the product in 84% isolated yield. For all of these reactions, the Claisen condensation products between the α-aryl ester products and the remaining zinc enolate were not observed.

3.8. Coupling of the Zinc Enolate of Methyl 2-Benzyloxyacetate Generated in Situ by Quenching of the Alkali Metal Enolate with $ZnCl_2$. α-Hydroxy or alkoxy acids are biologically important compounds,[52] and they can be used as auxiliaries or synthons for the synthesis of chiral ligands.[53−59] However, the methods for preparation of these compounds are limited. Derivatives of mandelic acid or atrolactic acid are generally prepared by oxidation of the α-carbon of α-arylcarbonyl compounds or by reduction of α-dicarbonyl compounds. Fu and co-workers reported an enantioselective O−H insertion to generate various sets of α-alkoxy esters, but this route requires α-aryl esters as the reactant.[60] A reaction sequence comprising the arylation of α-alkoxyesters and hydrolysis of the coupled product would provide an alternative route to prepare α-aryl-α-alkoxy acids. This route would expand the number of derivatives of mandelic acid or atrolactic acids to derivatives containing diverse functionalities on the aryl group.

The palladium-catalyzed arylation of alkali-metal enolates of α-alkoxy esters has been studied,[61] and these reactions occurred in poor yields. The use of the silyl enolates of α-alkoxy esters greatly increased the yields of these reactions.[61] However, isolated silyl enolates are needed for these reactions to occur in high yields. To further simplify the reaction procedure by avoiding the isolation step of the silyl enolate, we attempted to develop the conditions for the coupling of aryl halides with the zinc enolates of α-alkoxy esters. We first studied the arylation of the dianionic zinc enolate of ethyl α-hydroxyacetate (Scheme 3), but no successful coupling was achieved. Subsequently, we

Scheme 3[a]

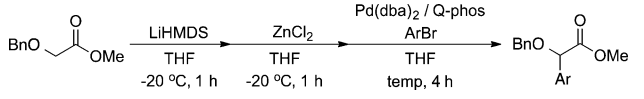


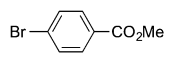
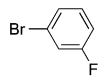
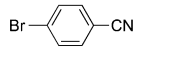
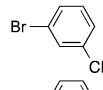
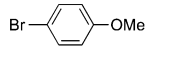
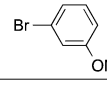
[a]Solvent: THF or 25% THF in toluene; Reagents (equiv): 2.2 equiv LiHMDS/4.4 equiv $ZnCl_2$, or 4.4 equiv LiHMDS/4.4 equiv $ZnCl_2$; Catalysts: 1% $Pd(dba)_2$/1% Q-phos, or 0.5% $\{[P(t\text{-}Bu)_3]PdBr\}_2$.

attempted the arylation of α-alkoxy esters that can be readily converted to α-hydroxyesters, and we chose methyl 2-benzyloxyacetate as the target substrate.

We developed two sets of conditions for the arylation of zinc enolates of α-alkoxy esters. The zinc enolate of methyl 2-benzyloxyacetate generated in situ by quenching its lithium enolate with $ZnCl_2$ in THF at −20 °C coupled with a series of aryl bromides in the presence of 3 mol % Pd and 4.5 mol % Q-phos at room temperature or 1 mol % of Pd and 1.5 mol % of Q-phos at 40 °C. Selected examples of the reaction scope are summarized in Table 12. A range of electron-poor (entries 1−4, 7−9) and electron-rich (entries 5 and 6) aryl bromides reacted

Table 12. Pd-Catalyzed α-Arylation of the Zinc Enolate Generated in Situ by Quenching the Lithium Enolate of Methyl 2-Benzyloxyacetate with $ZnCl_2$[a]



Entry	ArBr	Conditions	Yield[b]	Entry	ArBr	Conditions	Yield[b]
1		A	77%	7		B	78%
2		B	91%				
3		A	81%	8		B	84%
4		B	84%				
5		A	86%	9		B	87%
6		B	92%				

[a]Standard conditions: (A) 1.3 equiv of ester, 1.5 equiv of LiHMDS, 3 equiv of zinc chloride, 1 equiv of aryl bromide (0.5 mmol), 3 mol % of $Pd(dba)_2$, 4.5 mol % of Q-phos, in THF, 4 h at room temperature; (B) 1.5 equiv of ester, 1.7 equiv of LiHMDS, 3.4 equiv of zinc chloride, 1 equiv of aryl bromide (0.5 mmol), 1 mol % of $Pd(dba)_2$, 1.5 mol % of Q-phos, in THF, 4 h at 40 °C. [b]Average yield for two runs.

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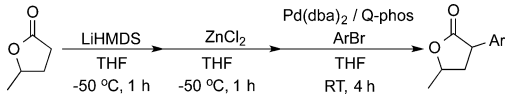
in high yields. The arylation of this zinc enolate tolerates the ester (entries 1 and 2) and cyano (entries 3, 4, and 8) groups. Under both conditions, the coupling with *ortho*-substituted aryl bromides and heteroaryl bromides did not occur.

3.9. Coupling of the Zinc Enolate of Valerolactone Generated in Situ by Quenching of the Alkali Metal Enolate with $ZnCl_2$. α-Aryl lactones are intermediates of biologically or pharmaceutically important molecules.[62] However, methods to prepare such cyclic esters are limited, and the synthesis of these molecules generally takes several steps. Pour reported the multiple-step syntheses of various α-aryl-α-valerolactones as intermediates of Incrustoporine derivatives starting from α-arylacetic acids.[63,64] Lei reported the synthesis of α-aryl-γ-butyrolactones by nickel-catalyzed Suzuki coupling of PhB-$(OH)_2$ and α-bromo-γ-butyrolactone,[51] but a metal-catalyzed coupling of aryl halides with lactones would be an alternative, more direct, approach to α-aryl lactones. Buchwald reported palladium- and nickel-catalyzed enantioselective α-arylation of α-substituted γ-butyrolactones.[65] These nickel-catalyzed reactions occurred in good yields and in high ee's in the presence of 5−30 mol % $ZnBr_2$. However, these reactions were inhibited when stoichiometric Zn(II) salts were used, due to the formation of less reactive zinc enolates. We studied the palladium-catalyzed arylation of the zinc enolate of γ-valerolactone to generate tertiary α-aryl lactones.[65b]

The zinc enolate of γ-valerolactone was generated by reaction of 1.5 equivalents of γ-valerolactone (relative to the aryl bromide added after the generation of the enolate) and 1.7 equiv of LiHMDS followed by quenching with 3.4 equiv of $ZnCl_2$ at −50 °C. The catalyst was generated from 1 mol % of $Pd(dba)_2$ and 1.5 mol % of Q-phos. Selected examples of this coupling reaction are summarized in Table 13. Starting from racemic γ-valerolactone, the products were obtained as mixtures of *cis*- and *trans*-isomers. Aryl bromides having a range of electronic properties reacted in high yields with modest *cis*/*trans* selectivities, and this arylation tolerates the ester (entry 4), cyano (entry 5), and nitro (entry 6) groups. Reactions of electron-poor *para*-substituted aryl bromides (entries 4−6) occurred in slightly higher cis/trans selectivity than reactions of electron-rich, *para*-substituted aryl bromides (entries 1 and 2). The electron-rich, ortho-substituted 2-bromotoluene reacted in 84% isolated yield with a cis/trans of 28/72 (entry 3).

Table 13. Pd-Catalyzed α-Arylation of the Zinc Enolate Generated in Situ by Quenching the Lithium Enolate of Valerolactone with $ZnCl_2$[a]



Entry	ArBr	Yield	cis/trans	Entry	ArBr	Yield	cis/trans
1	Br–C6H4–*t*-Bu	90%	57/43	4	Br–C6H4–CO_2Me	92%	68/32
2	Br–C6H4–OMe	81%	57/43	5	Br–C6H4–CN	84%	63/37
3	Br–C6H4–	84%	28/72	6	Br–C6H4–NO_2	77%	67/33

[a]Standard conditions: 1.5 equiv of ester, 1.7 equiv of LiHMDS, 3.4 equiv of zinc chloride, 1 equiv of aryl bromide (0.5 mmol), 1 mol % of $Pd(dba)_2$, 1.5 mol % of Q-phos, in mixed solvent of toluene and THF, 4 h at room temperature. Ratio of isomers was determined from ^1H NMR integrated ratio.

■ CONCLUSION

We have developed convenient and efficient protocols for the palladium-catalyzed coupling of zinc enolates of esters with aryl bromides. The zinc enolates of esters for this process can be the isolated Reformatsky reagents, zinc enolates generated in situ by reactions of α-bromoesters with Rieke's activated zinc, or the related (but not identical) zinc enolate generated in situ by quenching the alkali metal enolates with $ZnCl_2$. These coupling reactions were conducted with palladium catalysts bearing hindered monophosphines that allow fast oxidative addition of electronically varied aryl bromides and coupling reactions at room temperature. The scope of the reaction of zinc ester enolates encompasses aryl bromides with functionality that does not tolerate the strongly basic or nucleophilic alkali metal enolates, such as ketones with enolizable hydrogens, esters, nitriles, and nitro groups. The scope of esters encompasses acyclic acetates, propionates, and isobutyrates, α-alkoxyesters, and lactones. Considering the high functional group tolerance of zinc enolates, the use of relatively nonpolar solvents for this coupling process, and the high yields of monoarylation products and absence of diarylation products from the reactions of zinc ester enolates, we anticipate that these procedures will provide valuable routes to a wide range of α-aryl carboxylic acid derivatives, including a series of such compounds that were inaccessible through coupling of the alkali metal enolates.

■ EXPERIMENTAL SECTION

General Methods. All reactions were performed in a nitrogen-filled drybox or with Schlenk techniques under N_2. THF and toluene were distilled from sodium/benzophenone. Dichloromethane was distilled from calcium hydride. Anhydrous dioxane was purchased from commercial suppliers and was used and stored in a nitrogen-filled drybox. All aryl bromides, α-bromo esters, bases, zinc halides, lithium, and naphthalene were obtained from commercial suppliers and used without further purification. Zinc metal (granular, 20 mesh) was obtained from Mallinckrodt and activated according to literature procedures.[66] Rieke activated zinc was prepared according to literature procedures.[47] P(*t*-Bu)$_3$ was purchased from Strem, and other ligands were purchased from commercial suppliers. {[P(*t*-Bu)$_3$]PdBr}$_2$ and Q-phos were obtained as a gift from Johnson-Matthey. $Pd(dba)_2$ was prepared according to literature procedures.[67] ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded on 400 or 500 MHz spectrometers, with shifts reported in parts per million downfield from tetramethylsilane and referenced to residual protiated (^1H) or deuterated solvent (^{13}C).

General Procedure for the Arylation of the Reformatsky Reagents of Esters. In a drybox, a 4-mL screw-capped vial was charged with $Pd(dba)_2$ (2.9 mg, 5.0 μmol), Q-phos (3.6 mg, 5.0 μmol), aryl halide (0.500 mmol), the corresponding Reformatsky reagent (0.550 mmol), THF (2 mL), and a magnetic stirring bar. The vial was sealed with a cap containing a PTFE septum and removed from the drybox. The reaction mixture was then stirred at room temperature or 70 °C for 4−24 h. The reaction mixture was then adsorbed onto silica gel, loaded on a silica column, and eluted with a mixture of ethyl acetate in hexanes. The compounds obtained after column chromatography are generally pale yellow or clear oils, which solidified upon standing. Detailed procedures on the purification and data on characterization of products were listed below.

General Procedure for the Arylation of the Reformatsky Reagents of Esters with Bromophenols. In a drybox, a solution of bromophenol (86.5 mg, 0.500 mmol) in THF (1 mL) was added to KH (21.1 mg, 0.525 mmol). Gas evolution occurred immediately. The suspension was stirred at room temperature for 10 min and then transferred to a 4-mL screw-capped vial containg {[P(*t*-Bu)$_3$]PdBr}$_2$

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(2.0 mg, 2.5 μmol), the corresponding Reformatsky reagent (0.550 mmol), THF (1 mL), and a magnetic stirring bar. The vial was sealed with a cap containing a PTFE septum and removed from the drybox. The reaction mixture was stirred at room temperature for 4 h. The reaction mixture was then adsorbed onto silica gel, loaded on a silica column, and eluted with 20% ethyl acetate in hexanes. The compounds obtained after column chromatography are generally pale yellow or clear oils.

General Procedure for the Arylation of the Reformatsky Reagents of Esters with Bromoanilines. In a drybox, a solution of bromoaniline (86.0 mg, 0.500 mmol) in THF (1 mL) was added to KH (21.1 mg, 0.525 mmol). Gas evolution occurred immediately. The suspension was stirred at room temperature for 30 min and then transferred to a 4-mL screw-capped vial containing $\{[P(t\text{-}Bu)_3]PdBr\}_2$ (2.0 mg, 2.50 μmol), the corresponding Reformatsky reagent (0.550 mmol), THF (1 mL), and a magnetic stirring bar. The vial was sealed with a cap containing a PTFE septum and removed from the drybox. The reaction mixture was then stirred at room temperature for 12−24 h and then diluted with Et_2O (30 mL). The resulting solution was washed with 0.1 N HCl (7 mL), with saturated $NaHCO_3$ aqueous solution (20 mL), and then with H_2O (20 mL). The organic phase was dried over $MgSO_4$, filtered, and concentrated at reduced pressure. The crude product was then adsorbed onto silica gel, loaded on a silica column, and eluted with 20% ethyl acetate in hexanes. The compounds obtained after column chromatography are generally pale yellow or clear oils.

Procedure for the Arylation of Zinc Enolates Generated from *tert*-Butyl Bromoacetate and *tert*-Butyl Bromopropionate with Rieke Activated Zinc. In a nitrogen-filled drybox, Rieke activated zinc dust (49.0 mg, 0.750 mmol) was suspended in THF (1 mL) in a 4 mL screw-capped vial containing a stir bar. To this suspension was added dropwise the α-bromoester (0.550 mmol) by syringe, and the vial was sealed. The mixture was stirred at room temperature for 10 min. To the resulting suspension was added a solution of aryl bromide (0.500 mmol), $Pd(dba)_2$ (2.9 mg, 5.0 μmol), and Q-phos (3.6 mg, 5.0 μmol) in THF (1 mL). The vial was sealed with a cap containing PTFE septum and removed from the drybox. The mixture was stirred at room temperature for 4 h. The crude product was adsorbed on silica gel, loaded on a silica column, and eluted with a mixture of ethyl acetate and hexanes. The compounds obtained after column chromatography are generally pale yellow or clear oils. Detailed procedures on the purification and data on characterization of products were listed below.

Procedure for the Arylation of Zinc Enolate Generated from Methyl 2-Bromoisobutyrate with Rieke-Activated Zinc. In a nitrogen-filled drybox, Rieke-activated zinc dust (49.0 mg, 0.750 mmol) was suspended in THF (1 mL) in a 4 mL screw-capped vial containing a stir bar. To this suspension was added dropwise 2-bromoisobutyrate (99.6 mg, 0.550 mmol) by syringe, and the vial was sealed. The mixture was stirred at room temperature for 30 min. To the resulting suspension was added a solution of aryl bromide (0.500 mmol) and $\{[P(t\text{-}Bu)_3]PdBr\}_2$ (9.7 mg, 12.5 μmol) in THF (1 mL). The vial was sealed with a cap containing PTFE septum and removed from the drybox. The resulting solution was stirred at room temperature for 4 h. The crude product was adsorbed on silica gel, loaded on a silica column, and eluted with a mixture of ethyl acetate and hexanes. The compounds obtained after column chromatography are generally pale yellow or clear oils. Detailed procedures on the purification and data on characterization of products were listed below.

General Procedure for the Arylation of the Zinc Enolate of *tert*-Butyl Acetate by Quenching of the Lithium Enolate with $ZnCl_2$. The reactions were conducted under a nitrogen atmosphere. In a nitrogen-filled drybox, a 10 mL round-bottom flask was charged with LiHMDS (92.0 mg, 0.550 mmol), toluene (4 mL), and a magnetic stirring bar. The flask was sealed with a rubber septum, removed from the drybox, connected to a supply of nitrogen, and cooled at −78 °C. To solution was added *tert*-butyl acetate (75 μL, 0.55 mol) dropwise at −78 °C, and the mixture was stirred at this temperature for 1 h. To the resulting suspension of lithium enolate was added a solution of $ZnCl_2$ (150 mg, 1.10 mmol) in THF (2 mL), and the resultant mixture was stirred for 30 min at −78 °C. To the suspension of zinc enolate was added a solution of aryl bromide (0.500 mmol), $Pd(dba)_2$, and Q-phos in toluene (1 mL). The amounts of catalyst components are provided in Table 8. The reaction mixture was allowed to warm to room temperature and stirred at room temperature or at 70 °C for 4 h. The crude product was adsorbed on silica gel, loaded on a silica column, and eluted with a mixture of ethyl acetate and hexanes. The compounds obtained after column chromatography are generally pale yellow or clear oils. Detailed procedures on the purification and data on characterization of products were listed below.

General Procedure for the Arylation of Zinc Enolate of *tert*-Butyl Propionate by Quenching Sodium Enolate with $ZnCl_2$. The reactions were conducted under a nitrogen atmosphere. In a nitrogen-filled drybox, a 10 mL round-bottom flask was charged with NaHMDS (119 mg, 0.650 mmol), toluene (2 mL), and a magnetic stirring bar. The flask was sealed with a rubber septum, removed from the drybox, connected to a supply of nitrogen, and cooled at 0 °C. To this solution was added *tert*-butyl propionate (83 μL, 0.55 mol) dropwise and the mixture was stirred for 0.5 h at 0 °C. To the suspension of sodium enolate was added a solution of $ZnCl_2$ (177 mg, 1.30 mmol) in THF (1.5 mL), and the resultant mixture was stirred for 0.5 h at 0 °C. To the suspension of zinc enolate was added a solution of aryl bromide (0.500 mmol), $Pd(dba)_2$ and Q-phos in toluene (2.5 mL). The amounts of catalyst components are provided in Table 9. The reaction mixture was allowed to warm to room temperature and stirred at room temperature or at 70 °C for 4 h. The crude product was adsorbed on silica gel, loaded on a silica column, and eluted with a mixture of ethyl acetate and hexanes. The compounds obtained after column chromatography are generally pale yellow or clear oils. Detailed procedures on the purification and data on characterization of products were listed below.

General Procedure for the Arylation of Zinc Enolate of Methyl Isobutyrate by Quenching Sodium Enolate with $ZnCl_2$. The reactions were conducted under a nitrogen atmosphere. In a nitrogen-filled drybox, a 10 mL round-bottom flask was charged with NaHMDS (156 mg, 0.850 mmol), toluene (2 mL), and a magnetic stirring bar. The flask was sealed with a rubber septum, removed from the drybox, connected to a supply of nitrogen, and cooled at 0 °C. To this solution was added methyl isobutyrate (86 μL, 0.75 mmol) dropwise and the mixture was stirred for 1 h at 0 °C. After the flask was removed from the ice−water bath, a solution of $ZnCl_2$ (232 mg, 1.70 mmol) in THF (1.5 mL) was added, and the resultant mixture was stirred for 1 h at room temperature. To the suspension of zinc enolate was added a solution of aryl bromide (0.500 mmol) and $\{[P(t\text{-}Bu)_3]PdBr\}_2$ in toluene (2.5 mL). The amounts of catalyst components are provided in Table 10. The reaction mixture was allowed to warm to room temperature and stirred at room temperature or at 70 °C for 4 h. The crude product was adsorbed on silica gel, loaded on a silica column, and eluted with a mixture of ethyl acetate and hexanes. The compounds obtained after column chromatography are generally pale yellow or clear oils. Detailed procedures on the purification and data on characterization of products were listed below.

General Procedure for the Arylation of Zinc Enolate of Methyl Propionate Generated from Quenching Sodium Enolate with $ZnCl_2$. The reactions were conducted under a nitrogen atmosphere. In a drybox, A 10 mL round-bottom flask was charged with NaHMDS (156 mg, 0.850 mmol), toluene (2 mL), and a magnetic stirring bar. The flask was sealed with a rubber septum, removed from the drybox, connected to a supply of nitrogen, and cooled to −60 °C. To the cooled solution was added methyl propionate (72 μL, 0.75 mmol) dropwise and the mixture was stirred for 1.5 h. After this time, temperature of the cold bath was measured as −35 °C. To the suspension of sodium enolate was added a solution of $ZnCl_2$ (232 mg, 1.70 mmol) in THF (1.5 mL), and the resulting mixture was stirred for 1 h. After this time, temperature of the cold bath was measured as −15 °C. To the suspension of zinc enolate was added a solution of aryl bromide (0.500 mmol), $Pd(dba)_2$, and Q-phos in toluene (2.5 mL). The amounts of catalyst components are provided in Table 11. The reaction mixture was allowed to warm to room temperature and stirred for 4 h at room temperature or 70 °C.

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The crude product was adsorbed on silica gel, loaded on a silica column, and eluted with a mixture of ethyl acetate and hexanes. The compounds obtained after column chromatography are generally pale yellow or clear oils. Detailed procedures on the purification and data on characterization of products were listed below.

General Procedure for the Arylation of Zinc Enolate of Methyl Benzyloxyacetate Generated from Quenching Lithium Enolate with $ZnCl_2$. The reactions were conducted under a nitrogen atmosphere. In a drybox, a 10 mL round-bottom flask was charged with LiHMDS, THF (2 mL), and a magnetic stirring bar. The flask was sealed with a rubber septum, removed from the drybox, connected to a supply of nitrogen, and cooled to −20 °C. To this cold solution of LiHMDS in THF was added methyl benzyloxyacetate dropwise and the mixture was stirred for 1 h at −20 °C. To the suspension of lithium enolate was added a solution of $ZnCl_2$ in THF (1.5 mL) amd the mixture was then stirred for 1 h at −20 °C. To the suspension of resulting zinc enolate was added a solution of aryl bromide (0.500 mmol), $Pd(dba)_2$ and Q-phos in THF (2 mL). The amounts of reagents and catalyst components are provided in the Table 12. The reaction mixture was allowed to warm to room temperature and stirred for 4 h at room temperature or 40 °C. After this time, the solvent was evaporated, the residue was dissolved in methylene chloride with application of sonication, and this methylene chloride solution was loaded directly onto a silica gel column. The products were purified by flash column chromatography on silica gel. The compounds obtained after column chromatography are generally pale yellow or clear oils. Conditions for elution are provided along with the spectroscopic and analytical data for each product.

General Procedure for the Arylation of Zinc Enolate of γ-Valerolactone Generated from Quenching Lithium Enolate with $ZnCl_2$. The reactions were conducted under a nitrogen atmosphere. In a drybox, a 10 mL round-bottom flask was charged with LiHMDS (142 mg, 0.850 mmol), THF (2 mL), and a magnetic stirring bar. The flask was sealed with a rubber septum, removed from the drybox, connected to a supply of nitrogen, and cooled to −50 °C. To this cold solution of LiHMDS in THF was added γ-valerolactone (72 μL, 0.75 mmol) dropwise and the mixture was stirred for 1 h at −50 °C. To the suspension of lithium enolate was added a solution of $ZnCl_2$ (232 mg, 1.70 mmol) in THF (1.5 mL) and the mixture was stirred for 1 h at −50 °C. To the suspension of resulting zinc enolate was added a solution of aryl bromide (0.500 mmol), $Pd(dba)_2$ and Q-phos in THF (2.5 mL). The amounts of catalyst components are provided in the Table 13. The reaction mixture was allowed to warm to room temperature, and was stirred for 4 h at room temperature. The crude product was adsorbed on silica gel, loaded on a silica column, and eluted with a mixture of ethyl acetate and hexanes. The compounds obtained after column chromatography are generally pale yellow or clear oils. Detailed procedures on the purification and data on characterization of products were listed below.

***tert*-Butyl 2-Phenylacetate (CAS: 16537-09-0).**[25] (Table 2, entry 1) Purified by chromatography on silica gel (hexane/ethyl acetate = 95/5). Yield: 90.4 mg, 94%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33−7.24 (5H, m), 3.52 (2H, s), 1.43 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 171.1, 134.9, 129.4, 128.6, 127.0, 81.0, 42.9, 28.2.

***tert*-Butyl 2-(4-(*tert*-Butyl)phenyl)acetate (CAS: 255837-00-4).**[25] (Table 2, entry 2; Table 8, entry 1) Purified by chromatography on silica gel (hexane/ethyl acetate = 95/5). Yield: 88.2 mg, 71%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (2H, d, J = 8.4 Hz), 7.20 (2H, d, J = 8.0 Hz), 3.50 (2H, s), 1.45 (9H, s), 1.31 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 171.4, 149.8, 131.8, 129.1, 125.6, 80.9, 42.2, 34.7, 31.6, 28.3.

***tert*-Butyl 2-(4-Chlorophenyl)acetate (CAS: 33155-59-8).**[37] (Table 2, entries 3 and 4) Purified by chromatography on silica gel (hexane/ethyl acetate = 90/10). Yield: 97.5 mg, 86%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (2H, d, J = 8.8 Hz), 7.20 (2H, d, J = 8.8 Hz), 3.49 (2H, s), 1.43 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 170.8, 133.4, 133.0, 130.8, 128.8, 81.3, 42.1, 28.2.

***tert*-Butyl 2-(4-(Trifluoromethyl)phenyl)acetate (CAS: 417709-55-8).**[25] (Table 2, entries 5 and 6; Table 8, entry 2) Purified by chromatography on silica gel (hexane/ethyl acetate = 90/10). Yield: 100 mg, 77%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (2H, d, J = 8.0 Hz), 7.39 (2H, d, J = 8.0 Hz), 3.59 (2H, s), 1.44 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 170.1, 138.7, 129.7, 129.1 (q, J = 32.1 Hz), 125.6 (q, J = 3.6 Hz), 122.8 (q, J = 270.5 Hz), 81.4, 42.4, 28.4.

***tert*-Butyl 2-(4-(Dimethylamino)phenyl)acetate (CAS:1141493-94-8).**[68] (Table 2, entries 7 and 8) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 112 mg, 95%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.13 (2H, d, J = 8.8 Hz), 6.70 (2H, d, J = 8.8 Hz), 3.42 (2H, s), 2.92 (6H, s), 1.43 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 171.9, 149.8, 123.0, 122.9, 113.0, 80.6, 41.8, 41.0, 28.3.

***tert*-Butyl 2-(6-Methoxynaphthalen-2-yl)acetate (CAS: 362523-40-8).**[25] (Table 2, entry 9) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 117 mg, 86%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (2H, broad d, J = 8.6 Hz), 7.67 (1H, d, J = 0.7 Hz), 7.40 (1H, dd, J = 8.4 Hz, 1.6 Hz), 7.14 (1H, dd, J = 8.8 Hz, 2.4 Hz), 7.11 (1H, d, J = 2.4 Hz), 3.91 (3H, s), 3.67 (2H, s), 1.44 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 175.0, 157.6, 135.5, 133.6, 129.2, 128.9, 127.1, 126.1, 125.9, 119.0, 105.4, 80.6, 55.0, 42.4, 27.8.

***tert*-Butyl 2-(*o*-Tolyl)acetate (CAS: 62381-17-3).**[24] (Table 2, entry 10; Table 5, entry 1) Purified by chromatography on silica gel (hexane/ethyl acetate = 90/10). Yield: 86.6 mg, 84%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16−7.12 (2H, broad m), 7.05−6.99 (2H, broad m), 3.51 (2H, s), 2.17 (3H, s), 1.44 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 170.8, 137.5, 134.6, 131.0 (two peaks overlap), 127.2, 126.8, 81.9, 53.7, 28.7, 20.4.

***tert*-Butyl 2-(2-Fluorophenyl)acetate (CAS: 476429-08-0).**[25] (Table 2, entry 11; Table 5, entry 2) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 87.3 mg, 83%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27−7.22 (2H, m), 7.11−7.01 (2H, m), 3.57 (2H, s), 1.45 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 170.1, 160.3 (d, J = 243.3), 130.6 (d, J = 3.7), 128.0 (d, J = 8.6 Hz), 123.1 (d, J = 3.7 Hz), 121.3 (d, J = 15.8 Hz), 114.5 (d, J = 21.2 Hz), 80.3, 35.0, 27.2.

***tert*-Butyl 2-(2-Methoxyphenyl)acetate (CAS: 63730-75-6).**[25] (Table 2, entry 12; Table 5, entry 3; Table 8, entry 8) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 101 mg, 91%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25−7.22 (1H, broad m), 7.16 (1H, broad d, J = 7.3 Hz), 6.92−6.85 (2H, broad m), 3.81 (3H, s), 3.53 (2H, s), 1.44 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 171.5, 157.7, 131.0, 128.5, 124.0, 120.6, 110.5, 80.6, 55.5, 37.5, 28.2.

***tert*-Butyl 2-(4-Benzoylphenyl)acetate (CAS: 595570-50-6).**[31] (Table 2, entries 13 and 14; Table 5, entry 9; Table 8, entry 7) Purified by chromatography on silica gel (hexane/ethyl acetate = 90/10). Yield: 107 mg, 72%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81−7.77 (4H, m), 7.58 (1H, t of t, J = 7.4 Hz, 1.6 Hz), 7.47 (2H, dd, J = 8.0 Hz, 7.2 Hz), 7.39 (2H, broad d, J = 8.4 Hz), 3.62 (2H, s), 1.46 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 196.5, 170.3, 139.6, 137.8, 136.3, 132.5, 130.5, 130.1, 129.4, 128.4, 81.4, 42.7, 28.2. Anal. Calcd for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 77.21; H, 6.70.

***tert*-Butyl 2-(4-Propionylphenyl)acetate (CAS: 595570-52-8).**[31] (Table 2, entry 15; Table 5, entry 8) Purified by chromatography on silica gel (hexane/ethyl acetate = 90/10). Yield: 117 mg, 94%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (2H, d, J = 8.4 Hz), 7.36 (2H, d, J = 8.4 Hz), 3.59 (2H, s), 3.00 (2H, q, J = 7.2 Hz), 1.44 (9H, s), 1.22 (3H, t, J = 7.4 Hz). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 200.7, 170.4, 140.0, 135.8, 129.7, 128.4, 81.5, 42.8, 32.0, 28.2, 8.5. Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.60; H, 8.05.

Methyl 4-(2-*tert*-Butoxy-2-oxoethyl)benzoate (CAS: 219320-15-7).[25] (Table 2, entries 16 and 17; Table 8, entry 3) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 113 mg, 90%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (2H, d, J = 8.0 Hz), 7.35 (2H, d, J = 8.0 Hz), 3.91 (3H, s), 3.58 (2H, s), 1.43 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 170.3, 167.2, 140.1, 130.0, 129.5, 129.0, 81.4, 52.3, 42.9, 28.2.

Ethyl 4-(2-*tert*-Butoxy-2-oxoethyl)benzoate (CAS: 790714-66-8).[39] (Table 2, entries 18 and 19) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 114 mg, 86%. ^{1}H

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NMR (400 MHz, $CDCl_3$): δ 8.00 (2H, d, J = 8.4 Hz), 7.34 (2H, d, J = 8.0 Hz), 4.37 (2H, q, J = 7.2 Hz), 3.58 (2H, s), 1.43 (9H, s), 1.39 (3H, t, J = 7.2 Hz). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 170.2, 166.5, 139.8, 129.7, 129.2, 129.1, 81.2, 61.0, 42.7, 28.0, 14.3.

***tert*-Butyl 3-(2-*tert*-Butoxy-2-oxoethyl)benzoate.** (Table 2, entry 20) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 111 mg, 76%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.89 (1H, d, J = 7.6 Hz), 7.88 (1H, s), 7.44 (1H, d, J = 7.6 Hz), 7.37 (1H, dd, 8.0 Hz, 8.0 Hz), 3.57 (2H, s), 1.59 (9H, s), 1.45 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 170.7, 165.8, 135.0, 133.5, 132.4, 130.4, 128.5, 128.2, 81.3, 81.2, 42.6, 28.4, 28.2.

***tert*-Butyl 2-(4-Cyanophenyl)acetate (CAS: 790714-68-0).**[39] (Table 2, entry 21; Table 5, entry 6; Table 8, entry 4) Purified by chromatography on silica gel (hexane/ethyl acetate = 70/30). Yield: 97.8 mg, 90%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.63 (2H, d, J = 8.2 Hz), 7.42 (2H, d, J = 8.2 Hz), 3.70 (2H, s), 1.44 (9H, s). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 169.3, 146.9, 132.7, 128.8, 119.2, 111.3, 81.8, 42.0, 28.2. Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.87; H, 6.96; N, 6.45. Found: C, 71.63; H, 6.74; N, 6.27.

***tert*-Butyl 2-(3-Cyanophenyl)acetate.** (Table 2, entry 22; Table 5, entry 5) Purified by chromatography on silica gel (hexane/ethyl acetate = 70/30). Yield: 97.8 mg, 90%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.58−7.51 (3H, m), 7.43 (1H, dd, J = 7.6 Hz, 7.6 Hz), 3.57 (2H, s), 1.45 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 169.8, 136.3, 134.0, 133.0, 130.8, 129.4, 118.8, 112.8, 81.7, 42.1, 28.2.

***tert*-Butyl 2-(2-Cyanophenyl)acetate (CAS: 595570-54-0).**[31] (Table 2, entries 23 and 24; Table 5, entry 4) Purified by chromatography on silica gel (hexane/ethyl acetate = 90/10). Yield: 93.4 mg, 86%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.66 (1H, dd, J = 7.6 Hz, 1.2 Hz), 7.56 (1H, ddd, J = 7.7 Hz, 7.7 Hz, 1.2 Hz), 7.38 (2H, m), 3.80 (2H, s), 1.46 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 169.1, 138.6, 132.91, 132.9, 130.7, 127.7, 117.8, 113.6, 82.0, 41.1, 28.1. Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.87; H, 6.96; N, 6.45. Found: C, 71.72; H, 7.15; N, 6.41.

***tert*-Butyl 2-(4-Nitrophenyl)acetate (CAS: 29704-38-9).**[69] (Table 2, entry 25; Table 8, entry 5) Purified by chromatography on silica gel (hexane/ethyl acetate = 70/30). Yield: 114 mg, 96%. ^1H NMR (400 MHz, $CDCl_3$): δ 8.18 (2H, d, J = 8.4 Hz), 7.45 (2H, d, J = 8.4 Hz), 3.64 (2H, s), 1.44 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 169.6, 147.2, 142.3, 130.4, 123.8, 81.9, 42.5, 28.2.

***tert*-Butyl 2-(2-Nitrophenyl)acetate (CAS: 180150-74-7).**[70] (Table 2, entry 26) Purified by chromatography on silica gel (hexane/dichloromethane = 75/25). Yield: 103 mg, 87%. ^1H NMR (400 MHz, $CDCl_3$): δ 8.09 (1H, dd, J = 8.2 Hz, 1.4 Hz), 7.58 (1H, ddd, J = 7.4 Hz, 7.4 Hz, 1.6 Hz), 7.45 (1H, ddd, J = 7.8 Hz, 7.8 Hz, 1.6 Hz), 7.34 (1H, dd, J = 7.6 Hz, 1.2 Hz), 3.94 (2H, s), 1.44 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 169.3, 149.0, 133.6, 133.5, 130.6, 128.5, 125.3, 82.0, 41.2, 28.1.

***tert*-Butyl 2-(4-Hydroxyphenyl)acetate (CAS: 16010-88-1).**[71] (Table 2, entries 27 and 28) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 94.8 mg, 91%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.08 (2H, d, J = 8.4 Hz), 6.70 (2H, d, J = 8.0 Hz), 5.90 (1H, s), 3.46 (2H, s), 1.45 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 172.4, 155.0, 130.5, 126.5, 115.7, 81.4, 41.9, 28.2.

***tert*-Butyl 2-(3-Hydroxyphenyl)acetate (CAS: 82548-54-7).**[72] (Table 2, entry 29) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 85.4 mg, 82%. ^1H NMR (500 MHz, $CDCl_3$, TMS): δ 7.13 (1H, dd, J = 8.0 Hz, 8.0 Hz), 6.78 (1H, broad d, J = 8.0 Hz), 6.73 (1H, s), 6.69 (1H, dd, J = 8.3 Hz, 2 Hz), 6.59 (1H, broad s), 3.46 (2H, s), 1.44 (9H, s). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 172.1, 156.3, 136.0, 129.8, 121.4, 116.5, 114.4, 81.7, 42.8, 28.2.

***tert*-Butyl 2-(2-Hydroxyphenyl)acetate (CAS: 258331-10-1).**[73] (Table 2, entry 30) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 86.4 mg, 83%. ^1H NMR (400 MHz, $CDCl_3$): δ 8.05 (1H, s), 7.19 (1H, ddd, J = 7.6 Hz, 7.6 Hz, 1.4 Hz), 7.08 (1H, dd, J = 7.2 Hz, 1 Hz), 6.96 (1H, dd, J = 8.0 Hz, 1.2 Hz), 6.87 (1H, ddd, J = 7.4 Hz, 7.4 Hz, 1.2 Hz), 3.60 (2H, s), 1.47 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 173.9, 155.7, 131.2, 129.3, 121.2, 120.9, 118.1, 83.2, 39.9, 28.1.

***tert*-Butyl 2-(4-Aminophenyl)acetate (CAS: 174579-31-8).**[74] (Table 2, entries 31 and 32) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 95.3 mg, 92%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.05 (2H, d, J = 8.0 Hz), 6.65 (2H, d, J = 8.4 Hz), 3.42 (2H, broad s), 3.40 (2H, s), 1.43 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 171.8, 145.2, 130.2, 124.9, 115.5, 80.7, 42.0, 28.4.

***tert*-Butyl 2-(3-Aminophenyl)acetate (CAS: 183180-53-2).**[75] (Table 2, entry 33) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 86.0 mg, 83%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.08 (1H, dd, J = 8.0 Hz, 7.6 Hz), 6.64 (1H, broad d, J = 7.6 Hz), 6.58 (1H, s), 6.55 (1H, dd, J = 8.0 Hz, 2.0 Hz), 3.57 (2H, broad s), 3.42 (2H, s), 1.43 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 171.2, 146.7, 135.8, 129.4, 119.5, 116.1, 113.8, 80.8, 42.7, 28.2.

***tert*-Butyl 2-(Pyridin-3-yl)acetate (CAS: 69713-27-5).**[76] (Table 2, entries 34 and 35; Table 8, entry 10) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 87.0 mg, 90%. ^1H NMR (400 MHz, $CDCl_3$): δ 8.52 (2H, m), 7.65 (1H, m), 7.27 (1H, dd, J = 5.2, 2.4 Hz), 3.54 (2H, s), 1.44 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 170.1, 150.5, 148.5, 136.9, 130.6, 123.5, 81.6, 40.0, 28.2.

***tert*-Butyl 2-(Pyridin-4-yl)acetate (CAS: 79757-20-3).**[77] (Table 2, entries 36 and 37) Purified by standard conditions. Yield: 76.3 mg, 79%. ^1H NMR (500 MHz, $CDCl_3$): δ 8.56 (2H, d, J = 6.0 Hz), 7.21 (2H, d, J = 6.0 Hz), 3.53 (2H, s), 1.45 (9H, s). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 169.5, 150.1, 143.7, 124.7, 81.8, 42.2, 28.2.

***tert*-Butyl 2-(4-*tert*-Butylphenyl)propanoate (CAS: 1020539-67-6).**[28] (Table 4, entries 1 and 2; Table 9, entry 1) Purified by chromatography on silica gel (hexane/ethyl acetate = 95/5). Yield: 115 mg, 88%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.32 (2H, d, J = 8.4 Hz), 7.22 (2H, d, J = 8.0 Hz), 3.59 (1H, q, J = 7.2 Hz), 1.44 (3H, d, J = 7.6 Hz), 1.31 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 174.3, 149.7, 138.2, 127.2, 125.5, 80.6, 46.1, 34.6, 31.6, 28.2, 18.9. Anal. Calcd for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99. Found: C, 77.89; H, 10.15.

***tert*-Butyl 2-(4-Chlorophenyl)propanoate (CAS: 465529-75-3).**[78] (Table 4, entries 3 and 4) Purified by chromatography on silica gel (hexane/ethyl acetate = 90/10). ^1H NMR (400 MHz, $CDCl_3$): δ 7.28 (2H, d, J = 9.2 Hz), 7.22 (2H, d, J = 8.8 Hz), 3.58 (1H, q, J = 7.6 Hz), 1.43 (3H, d, J = 7.6 Hz), 1.39 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 173.4, 139.6, 132.7, 128.8, 128.6, 80.7, 45.9, 28.3, 18.4.

***tert*-Butyl 2-(4-(Trifluoromethyl)phenyl)propanoate (CAS: 476429-10-4).**[25] (Table 4, entries 5 and 6) Purified by chromatography on silica gel (hexane/ethyl acetate = 90/10). Yield: 104 mg, 86%. ^1H NMR (500 MHz, $CDCl_3$): δ 7.57 (2H, d, J = 8.0 Hz), 7.41 (2H, d, J = 8.0 Hz), 3.67 (1H, q, J = 7.0 Hz), 1.47 (3H, d, J = 7.5 Hz), 1.40 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): 173.6, 145.7, 129.8 (q, J = 32.0 Hz), 128.4, 125.9 (q, J = 3.8 Hz), 124.7 (q, J = 274 Hz), 81.5, 47.0, 28.3, 18.8.

***tert*-Butyl 2-(4-(Dimethylamino)phenyl)propanoate.** (Table 4, Entry 7) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 113 mg, 91%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.16 (2H, d, J = 8.8 Hz), 6.69 (2H, d, J = 8.8 Hz), 3.51 (1H, q, J = 7.2 Hz), 2.92 (6H, s), 1.40 (3H, d, J = 6.8 Hz), 1.39 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 174.7, 149.7, 129.4, 128.2, 112.9, 80.3, 45.7, 40.9, 28.2, 18.8.

***tert*-Butyl 2-(*o*-Tolyl)propanoate (CAS: 362523-41-9).**[25] (Table 4, entry 8; Table 6, entry 1; Table 9, entry 5) Purified by chromatography on silica gel (hexane/ethyl acetate = 90/10). Yield: 110 mg, 91%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.27−7.25 (1H, broad m), 7.19−7.12 (3H, m), 3.85 (1H, q, J = 7.2 Hz), 2.36 (3H, s), 1.42 (3H, d, J = 7.2 Hz), 1.38 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 174.2, 139.7, 135.7, 130.3, 126.6, 126.5, 126.2, 80.4, 42.2, 27.9, 19.6, 17.7.

***tert*-Butyl 2-(2-Fluorophenyl)propanoate.** (Table 4, entry 9; Table 6, entry 2; Table 9, entry 7) Purified by chromatography on silica gel (hexane/ethyl acetate = 90/10). Yield: 90.8 mg, 81%. ^1H NMR (400 MHz, $CDCl_3$): δ 7.29 (1H, ddd, J = 7.6 Hz, 7.6 Hz, 1.6 Hz), 7.24−7.19 (1H, m), 7.10 (1H, ddd, J = 7.6 Hz, 7.2 Hz, 1.2 Hz), 7.03 (1H, ddd, J = 9.8 Hz, 8.6 Hz, 1.2 Hz), 3.92 (1H, q, J = 7.2 Hz), 1.45 (3H, d, J = 7.2 Hz), 1.41 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 173.4, 160.5 (d, J = 244 Hz), 128.7 (d, J = 4.2 Hz), 128.6

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(d, J = 15.0 Hz), 128.5 (d, J = 8.2 Hz), 124.3 (d, J = 3.5 Hz), 115.5 (d, J = 22.2 Hz), 80.9, 39.6 (d, J = 2.5 Hz), 28.1, 17.6. Anal. Calcd for $C_{13}H_{17}FO_2$: C, 69.62; H, 7.64. Found: C, 69.82; H, 7.55.

***tert*-Butyl 2-(2-Methoxyphenyl)propanoate (CAS: 725262-38-4).**[79] (Table 4, entry 10; Table 6, entry 3; Table 9, entry 6) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 106 mg, 90%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27−7.25 (1H, broad m), 7.19−7.12 (3H, m), 3.92 (1H, q, J = 7.5 Hz), 3.81 (3H, s), 1.44 (3H, d, J = 7.6 Hz), 1.41 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 174.7, 157.0, 130.4, 128.0 (two peaks overlap), 120.8, 110.6, 80.2, 55.0, 40.5, 28.2, 17.3. Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.25; H, 8.43.

***tert*-Butyl 2-(4-Benzoylphenyl)propanoate (CAS: 595570-51-7).**[31] (Table 4, entry 11) Purified by chromatography on silica gel (hexane/ethyl acetate = 95/5). Yield: 104 mg, 67%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82−7.77 (4H, m), 7.59 (1H, t of t, J = 7.4 Hz, 1.6 Hz), 7.49 (2H, dd, J = 8.0 Hz, 7.2 Hz), 7.41 (2H, broad d, J = 8.0 Hz), 3.70 (1H, q, J = 7.2 Hz), 1.49 (3H, d, J = 6.8 Hz), 1.44 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 196.6, 173.3, 146.3, 137.9, 136.4, 132.6, 130.6, 130.2, 128.5, 127.6, 81.2, 46.8, 28.1, 18.6. Anal. Calcd for $C_{20}H_{22}O_3$: C, 77.39; H, 7.14. Found: C, 77.10; H, 7.05.

Methyl 4-(1-*tert*-Butoxy-1-oxopropan-2-yl)benzoate (CAS: 595570-47-1).[31] (Table 4, entries 12 and 13; Table 9, entry 2) Purified by chromatography on silica gel (hexane/ethyl acetate = 90/10). Yield: 115 mg, 87%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (2H, d, J = 8.4 Hz), 7.36 (2H, d, J = 8.0 Hz), 3.91 (3H, s), 3.67 (1H, q, J = 7.2 Hz), 1.46 (3H, d, J = 7.2 Hz), 1.38 (9H, s). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 173.3, 167.2, 146.6, 130.0, 129.0, 127.7, 81.1, 52.3, 46.8, 28.1, 18.5. Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 67.96; H, 7.63.

Ethyl 4-(1-*tert*-Butoxy-1-oxopropan-2-yl)benzoate (CAS: 1334591-49-9).[80] (Table 4, entries 14 and 15) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 122 mg, 88%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.99 (2H, d, J = 8.5 Hz), 7.36 (2H, d, J = 8.0 Hz), 4.37 (2H, q, J = 7.0 Hz), 3.67 (1H, q, J = 7.5 Hz), 1.46 (3H, d, J = 7.0 Hz), 1.39 (3H, t, J = 7.0 Hz), 1.38 (9H, s). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 173.5, 166.9, 146.6, 130.2, 129.5, 127.8, 81.2, 61.3, 46.9, 28.3, 18.7, 14.7. Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 69.28; H, 8.04.

***tert*-Butyl 2-(4-Cyanophenyl)propanoate.** (Table 4, Entry 16; Table 6, Entry 5; Table 9, Entry 3) Purified by chromatography on silica gel (hexane/ethyl acetate = 75/25). Yield: 96.0 mg, 83%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63 (2H, d, J = 8.3 Hz), 7.42 (2H, d, J = 8.3 Hz), 3.69 (1H, q, J = 7.2 Hz), 1.48 (3H, d, J = 7.2 Hz), 1.41 (9H, s). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 173.0, 146.9, 132.7, 128.8, 119.2, 111.3, 81.7, 47.0, 28.3, 18.6. Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.72; H, 7.14; N, 5.70.

***tert*-Butyl 2-(3-Cyanophenyl)propanoate (CAS: 595570-65-3).**[31] (Table 4, entry 17; Table 6, entry 4). Purified by chromatography on silica gel (hexane/ethyl acetate = 75/25). Yield: 92.5 mg, 80%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (1H, s), 7.57−7.55 (2H, m), 7.44 (1H, dd, J = 7.8 Hz, 7.8 Hz), 3.66 (1H, q, J = 7.2 Hz), 1.48 (3H, d, J = 7.2 Hz), 1.41 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 173.1, 142.9, 132.5, 131.7, 131.1, 129.7, 119.2, 113.0, 81.7, 46.5, 28.0, 18.7. Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.59; H, 7.46; N, 6.21.

***tert*-Butyl 2-(2-Cyanophenyl)propanoate (CAS: 595570-55-1).**[31] (Table 4, entry 18; Table 9, entry 9) Purified by chromatography on silica gel (hexane/ethyl acetate = 90/10). Yield: 98.3 mg, 85%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (1H, dd, J = 7.6 Hz, 1.2 Hz), 7.57 (1H, ddd, J = 7.7 Hz, 7.7 Hz, 1.6 Hz), 7.46 (1H, dd, J = 7.6 Hz, 1 Hz), 7.35 (1H, ddd, J = 7.7 Hz, 7.7 Hz, 1.2 Hz), 4.11 (1H, q, J = 7.2 Hz), 1.51 (3H, d, J = 7.2 Hz), 1.41 (9H, s). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 172.3, 145.2, 133.2, 133.1, 127.6, 127.5, 117.9, 112.9, 81.7, 44.7, 28.1, 18.2. Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.68; H, 7.29; N, 5.94.

***tert*-Butyl 2-(4-Nitrophenyl)propanoate (CAS: 89278-22-8).**[69] (Table 4, entry 19; Table 9, entry 4) Purified by chromatography on silica gel (hexane/ethyl acetate = 70/30). Yield: 111 mg, 88%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (2H, d, J = 8.7 Hz), 7.47 (2H, d, J = 8.7 Hz), 3.74 (1H, q, J = 7.2 Hz), 1.50 (3H, d, J = 7.2 Hz), 1.40 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 172.8, 148.9, 147.4, 128.8, 124.1, 81.8, 46.8, 28.3, 18.7. Anal. Calcd for $C_{13}H_{17}NO_4$: C, 62.14; H, 6.82; N, 5.57. Found: C, 62.32; H, 6.98; N, 5.74.

***tert*-Butyl 2-(2-Nitrophenyl)propanoate (CAS: 344438-61-5).** (Table 4, entry 20; Table 9, entry 8) Purified by chromatography on silica gel (hexane/ethyl acetate = 70/30). Yield: 102 mg, 81%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (1H, d, J = 8.0 Hz), 7.59 (1H, dd, J = 7.6 Hz, 7.6 Hz), 7.49 (1H, d, J = 8.0 Hz), 7.41 (1H, dd, J = 7.6 Hz, 7.6 Hz), 4.22 (1H, q, J = 7.2 Hz), 1.57 (3H, d, J = 7.2 Hz), 1.39 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 172.5, 149.3, 135.8, 133.3, 129.7, 127.9, 124.9, 81.6, 42.3, 28.0, 17.7. Anal. Calcd for $C_{13}H_{17}NO_4$: C, 62.14; H, 6.82. Found: C, 62.52; H, 7.06.

***tert*-Butyl 2-(4-Hydroxyphenyl)propanoate (CAS: 595570-57-3).**[31] (Table 4, entries 21 and 22) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 102 mg, 92%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.12 (2H, d, J = 8.0 Hz), 6.74 (2H, d, J = 7.5 Hz), 6.13 (1H, s), 3.56 (1H, q, J = 7.0 Hz), 1.43 (3H, d, J = 7 Hz), 1.40 (9H, s). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 175.1, 155.0, 132.9, 128.7, 115.6, 81.1, 45.9, 28.1, 18.6. Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 69.99; H, 8.10.

***tert*-Butyl 2-(3-Hydroxyphenyl)propanoate.** (Table 4, entry 23) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 96.7 mg, 87%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.17 (1H, dd, J = 8.0 Hz, 7.6 Hz), 6.84 (1H, broad d, J = 7.6 Hz), 6.80 (1H, dd, J = 2.0 Hz, 2.0 Hz), 6.73 (1H, ddd, J = 8.0 Hz, 2.4 Hz, 0.8 Hz), 5.84 (1H, broad s), 3.57 (1H, q, J = 7.2 Hz), 1.42 (3H, d, J = 7.2 Hz), 1.40 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 174.5, 156.2, 142.8, 129.9, 120.0, 114.4, 114.2, 81.2, 46.6, 28.1, 18.6. Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.35; H, 8.43.

***tert*-Butyl 2-(4-Aminophenyl)propanoate (CAS: 595570-58-4).**[31] (Table 4, entries 24 and 25) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 77.5 mg, 70%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08 (2H, d, J = 8.4 Hz), 6.64 (2H, d, J = 8.0 Hz), 3.49 (1H, q, J = 7.0 Hz), 3.49 (2H, broad s), 1.39 (3H, d, J = 7 Hz), 1.38 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 174.6, 145.2, 131.4, 128.4, 115.4, 80.4, 45.8, 28.1, 18.7. Anal. Calcd for $C_{13}H_{15}NO_2$: C, 70.56; H, 8.65; N, 6.33. Found: C, 70.36; H, 8.91; N, 6.20.

***tert*-Butyl 2-(3-Aminophenyl)propanoate (CAS: 183180-55-4).**[75] (Tabel 4, entry 26) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 81.9 mg, 74%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08 (1H, dd, J = 8.0 Hz, 7.6 Hz), 6.68 (1H, broad d, J = 8.0 Hz), 6.63 (1H, broad s), 6.56 (1H, broad dd, J = 8.0 Hz, 2.4 Hz), 3.50 (1H, q, J = 6.8 Hz), 3.50 (2H, broad s), 1.40 (3H, d, J = 6.8 Hz), 1.39 (9H, s). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 174.5, 147.6, 142.3, 129.5, 117.4, 115.7, 113.3, 81.2, 46.3, 28.1, 18.6.

***tert*-Butyl 2-(Pyridin-3-yl)propanoate (CAS: 595570-59-5).**[31] (Table 4, entries 27 and 28; Table 9, entry 11) Purified by chromatography on silica gel (hexane/ethyl acetate = 70/30). Yield: 93.3 mg, 90%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.54 (1H, d, J = 2.0 Hz), 8.50 (1H, dd, J = 8.0 Hz, 1.5 Hz), 7.65 (1H, ddd, J = 8.0 Hz, 8.0 Hz, 1.5 Hz), 7.25 (1H, m), 3.63 (1H, q, J = 7.0 Hz), 1.48 (3H, d, J = 7.0 Hz), 1.40 (9H, s). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 173.2, 149.5, 148.6, 136.8, 134.9, 123.6, 81.3, 44.3, 28.1, 18.5. Anal. Calcd for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.38; H, 8.42; N, 6.67.

Methyl 2-(4-*tert*-Butylphenyl)-2-methylpropanoate (CAS: 157444-69-4).[25] (Table 7, entry 1; Table 10, entry 1) Purified by chromatography on silica gel (hexane/ethyl acetate = 95/5). Yield: 103 mg, 88%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (2H, d, J = 8.6 Hz), 7.26 (2H, d, J = 8.6 Hz), 3.65 (3H, s), 1.57 (6H, s), 1.31 (9H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 177.6, 149.6, 141.8, 125.5, 125.4, 52.4, 46.3, 34.6, 31.5, 26.8.

Methyl 2-Methyl-2-(*o*-tolyl) propanoate (CAS: 77846-89-0). (Table 7, entry 2; Table 10, entry 7) Purified by chromatography on silica gel (hexane/ethyl acetate = 90/10). Yield: 94.2 mg, 96%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41−7.39 (1H, broad m), 7.26−7.16 (3H, m), 3.71 (3H, s), 2.24 (3H, s), 1.61 (6H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 178.8, 142.8, 135.9, 131.8, 126.8, 126.1, 125.0, 52.3,

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46.3, 26.9, 20.0. Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.10; H, 8.48.

Methyl 2-(4-Cyanophenyl)-2-methylpropanoate (CAS: 444807-47-0).[81] (Table 7, entry 3; Table 10, entry 3) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 96.5 mg, 95%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (2H, d, J = 8.6 Hz), 7.44 (2H, d, J = 8.6 Hz), 3.67 (3H, s), 1.59 (6H, s). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 176.4, 150.1, 132.5, 126.9, 118.9, 111.0, 52.7, 47.1, 26.5.

Methyl 2-(2-Methoxyphenyl)-2-methylpropanoate (CAS: 40801-03-4).[82] (Table 7, entry 4; Table 10, entry 8) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 101 mg, 96%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 (1H, d, J = 7.7 Hz), 7.28 (1H, dd, J = 7.9 Hz, 7.7 Hz), 7.00 (1H, dd, J = 7.6 Hz, 7.6 Hz), 6.89 (1H, d, J = 8.1 Hz), 3.80 (3H, s), 3.65 (3H, s), 1.55 (6H, s). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 178.9, 157.1, 134.5, 128.3, 125.8, 121.1, 111.4, 55.7, 52.3, 44.6, 26.1.

***tert*-Butyl 2-(4-Acetylphenyl)acetate (CAS: 219320-14-6).**[83] (Table 5, entry 7; Table 8, entry 6) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 97.2 mg, 83%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (2H, d, J = 8.0 Hz), 7.22 (2H, d, J = 8.0 Hz), 3.45 (2H, s), 2.44 (3H, s), 1.29 (9H, s). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 197.8, 170.1, 140.2, 135.8, 129.6, 128.6, 81.3, 42.6, 28.0, 26.7.

***tert*-Butyl 2-Mesitylacetate (CAS: 366018-72-6).**[25] (Table 8, entry 9) Purified by chromatography on silica gel (hexane/ethyl acetate = 95/5). Yield: 110 mg, 94%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.84 (2H, s), 3.55 (2H, s), 2.29 (6H, s), 2.25 (3H, s), 1.42 (9H, s). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 171.3, 137.3, 136.6, 129.7, 129.2, 81.0, 36.7, 28.5, 21.3, 20.6.

***tert*-Butyl 2-Mesitylpropanoate (CAS: 366018-73-7).**[25] (Table 9, entry 10) Purified by chromatography on silica gel (hexane/ethyl acetate = 95/5). Yield: 102 mg, 82%. ^{1}H NMR (400 MHz, $CDCl_3$): 6.81 (2H, s), 3.96 (1H, q, J = 7.2 Hz), 2.26 (6H, s), 2.24 (3H, s), 1.40 (9H, s), 1.38 (3H, d, J = 7.3 Hz). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 174.6, 136.1, 136.1, 135.8, 129.7, 80.5, 41.3, 28.2, 21.0, 20.6, 15.7.

Methyl 2-(4-Dimethylaminophenyl)-2-methylpropanoate (CAS: 476429-12-6).[25] (Table 10, entry 2) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 92.4 mg, 84%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22 (2H, d, J = 8.9 Hz), 6.70 (2H, d, J = 8.9 Hz), 3.63 (3H, s), 2.93 (6H, s), 1.55 (6H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 177.9, 149.5, 132.6, 126.5, 112.6, 52.3, 45.6, 40.8, 26.8.

Methyl 2-Methyl-2-(4-nitrophenyl)propanoate (CAS: 59115-08-1).[25] (Table 10, entry 4) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 99.3 mg, 89%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.20 (2H, d, J = 8.8 Hz), 7.52 (2H, d, J = 8.8 Hz), 3.70 (3H, s), 1.64 (6H, s). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 176.4, 152.3, 147.2, 127.2, 124.0, 52.9, 47.4, 26.8.

Methyl 4-(1-Methoxy-2-methyl-oxopropan-2-yl)benzoate (CAS: 105235-96-9).[84] (Table 10, entry 5) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 109 mg, 92%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.02 (2H, d, J = 8.6 Hz), 7.42 (2H, d, J = 8.5 Hz), 3.93 (3H, s), 3.68 (3H, s), 1.62 (6H, s). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 177.0, 167.2, 150.2, 130.1, 129.1, 126.2, 52.7, 52.4, 47.2, 26.8.

Methyl 2-Methyl-2-(4-propionylphenyl)propanoate. (Table 10, entry 6) Purified by chromatography on silica gel (hexane/ethyl acetate = 80/20). Yield: 102 mg, 87%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (2H, d, J = 8.4 Hz), 7.45 (2H, d, J = 8.4 Hz), 3.69 (3H, s), 3.02 (2H, q, J = 7.3 Hz), 1.63 (6H, s), 1.25 (3H, t, J = 7.3 Hz). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 200.4, 176.7, 149.7, 135.4, 128.2, 126.0, 52.4, 46.8, 31.8, 26.4, 8.3. Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.60; H, 7.84.

Methyl 2-(4-*tert*-Butylphenyl)propanoate (CAS: 154320-48-6).[85] (Table 11, entry 1) Purified by chromatography on silica gel (hexane/ethyl acetate = 90/10). Yield: 94.7 mg, 86%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37 (2H, d, J = 8.4 Hz), 7.25 (2H, d, J = 8.4 Hz), 3.73 (1H, q, J = 7.2 Hz), 3.69 (3H, s), 1.52 (3H, d, J = 7.2 Hz), 1.34 (9H, s). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 175.6, 150.3, 137.9, 127.5, 125.9, 52.3, 45.3, 34.8, 31.7, 19.0.

Methyl 2-(4-(Dimethylamino)phenyl)propanoate (CAS: 96943-11-2).[2] (Table 11, entry 2) Purified by chromatography on silica gel (hexane/ethyl acetate = 85/15). Yield: 87.1 mg, 84%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.17 (2H, d, J = 8.5 Hz), 6.70 (2H, d, J = 8.0 Hz), 3.64 (3H, s), 3.63 (1H, q, J = 7.5 Hz), 2.93 (6H, s), 1.46 (3H, d, J = 7.0 Hz). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 175.9, 150.0, 128.6, 128.3, 112.9, 52.1, 44.6, 40.8, 18.8.

Methyl 2-(*o*-Tolyl)propanoate (CAS: 74082-02-3).[86] (Table 11, entry 3) Purified by chromatography on silica gel (hexane/ethyl acetate = 85/15). Yield: 77.5 mg, 87%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26−7.24 (1H, broad m), 7.20−7.13(3H, broad m), 3.96 (1H, q, J = 7.5 Hz), 3.65 (3H, s), 2.37 (3H, s), 1.47 (3H, d, J = 7.0 Hz). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 175.6, 139.3, 135.9, 130.7, 127.2, 126.7, 126.7, 52.2, 41.4, 19.8, 18.1.

Methyl 2-(2-Methoxyphenyl)propanoate (CAS: 60779-19-3).[87] (Table 11, entry 4) Purified by chromatography on silica gel (hexane/ethyl acetate = 85/15). Yield: 88.4 mg, 91%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.25−7.20 (2H, m), 6.94 (1H, ddd, J = 7.5 Hz, 7.5 Hz, 1.0 Hz), 6.87 (1H, dd, J = 8.0 Hz, 1.0 Hz), 4.05 (1H, q, J = 7.0 Hz), 3.82 (3H, s), 3.65 (3H, s), 1.45 (3H, d, J = 7.5 Hz). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 175.8, 156.8, 129.7, 128.3, 128.2, 120.9, 110.9, 55.7, 52.1, 39.3, 17.6.

Methyl 2-(2-Fluorophenyl)propanoate (CAS: 145983-09-1).[88] (Table 11, entry 5) Purified by chromatography on silica gel (hexane/ethyl acetate = 85/15). Yield: 75.6 mg, 83%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29 (1H, ddd, J = 7.5 Hz, 7.5 Hz, 1.5 Hz), 7.26−7.21 (1H, m), 7.12 (1H, ddd, J = 7.5 Hz, 7.5 Hz, 1.0 Hz), 7.04 (1H, ddd, J = 8.5 Hz, 8.5 Hz, 1.5 Hz), 4.03 (1H, q, J = 7.5 Hz), 3.68 (3H, s), 1.50 (3H, d, J = 7.5 Hz). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 174.6, 160.5 (d, J = 246 Hz), 128.9, 128.9 (d, J = 2.5 Hz), 128.0 (d, J = 14.6 Hz), 124.5 (d, J = 3.8 Hz), 115.7 (d, J = 22.3 Hz), 52.4 (d, J = 1.8 Hz), 38.5 (d, J = 2.5 Hz), 17.7.

Methyl 4-(1-Methoxy-1-oxopropan-2-yl)benzoate (CAS: 77959-48-9).[50] (Table 11, entry 6) Purified by chromatography on silica gel (hexane/ethyl acetate = 85/15). Yield: 101 mg, 91%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.02 (2H, d, J = 8.3 Hz), 7.39 (2H, d, J = 8.3 Hz), 3.93 (3H, s), 3.81 (1H, q, J = 7.2 Hz), 3.69 (3H, s), 1.54 (3H, d, J = 7.2 Hz). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 174.7, 167.2, 146.0, 130.4, 129.5, 128.0, 52.6, 52.5, 45.9, 18.8.

Methyl 2-(4-Cyanophenyl)propanoate (CAS: 125670-62-4).[89] (Table 11, entry 7) Purified by chromatography on silica gel (hexane/ethyl acetate = 85/15). Yield: 75.7 mg, 80%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (2H, d, J = 8.3 Hz), 7.44 (2H, d, J = 8.2 Hz), 3.81 (1H, q, J = 7.2 Hz), 3.70 (3H, s), 1.54 (3H, d, J = 7.2 Hz). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 173.9, 145.7, 132.5, 128.5, 118.7, 111.2, 52.4, 45.5, 18.4.

Methyl 2-(4-Nitrophenyl)propanoate (CAS: 50415-69-5).[90] (Table 11, entry 8) Purified by chromatography on silica gel (hexane/ethyl acetate = 85/15). Yield: 76.4 mg, 73%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.21 (2H, d, J = 8.8 Hz), 7.50 (2H, d, J = 8.8 Hz), 3.87 (1H, q, J = 7.2 Hz), 3.71 (3H, s), 1.57 (3H, d, J = 7.2 Hz). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 174.1, 148.1, 147.6, 129.0, 124.3, 52.8, 45.7, 18.8.

Methyl 2-Mesitylpropanoate (CAS: 134381-05-8). (Table 11, entry 9) Purified by chromatography on silica gel (hexane/ethyl acetate = 90/10). Yield: 92.8 mg, 90%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.85 (2H, s), 4.03 (1H, q, J = 7.0 Hz), 3.67 (3H, s), 2.25 (3H, s), 2.24 (6H, s), 1.43 (3H, d, J = 7.0 Hz). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 176.2, 136.4, 136.1, 135.5, 130.0, 52.3, 40.1, 21.0, 20.3, 15.7.

Methyl 2-(Pyridin-3-yl)propanoate (CAS: 154369-12-7).[91] (Table 11, entry 10) Purified by chromatography on silica gel (hexane/ethyl acetate = 85/15). Yield: 69.4 mg, 84%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.76 (1H, broad s), 8.72 (1H, broad d, J = 5.0 Hz), 7.98 (1H, broad d, J = 7.8 Hz), 7.56 (1H, broad dd, J = 6.7 Hz, 6.3 Hz), 3.85 (1H, q, J = 7.2 Hz), 3.67 (3H, s), 1.54 (3H, d, J = 7.2 Hz). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 173.3, 148.1, 147.4, 139.7, 138.6, 125.5, 52.6, 42.7, 18.4.

Methyl 4-(1-(Benzyloxy)-2-methoxy-2-oxoethyl)benzoate. (Table 12, entries 1 and 2) Purified by chromatography on silica gel (hexane/ethyl acetate = 85/15). Yield: 143 mg, 91%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (2H, d, J = 8.4 Hz), 7.55 (2H, d, J = 8.2 Hz), 7.35−7.29 (5H, m), 5.00 (1H, s), 4.61 (2H, s), 3.91 (3H, s), 3.71 (3H, s). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 170.8, 166.8, 141.3, 136.9, 130.6, 130.1, 128.7, 128.3, 128.3, 127.4, 79.3, 71.7, 52.7, 52.4. Anal. Calcd for $C_{18}H_{18}O_5$: C, 68.78; H, 5.77. Found: C, 68.60; H, 5.50.

Methyl 2-(Benzyloxy)-2-(4-cyanophenyl)acetate. (Table 12, entries 3 and 4) Purified by chromatography on silica gel (hexane/ethyl acetate = 85/15). Yield: 118 mg, 84%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (2H, d, J = 8.0 Hz), 7.59 (2H, d, J = 8.0 Hz), 7.37−7.32 (5H, m), 4.99 (1H, s), 4.63 (2H, dd, J = 23.4 Hz, 12.0 Hz), 3.73 (3H, s). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 170.3, 141.5, 136.5, 132.4, 128.6, 128.3, 128.1, 127.9, 118.5, 112.6, 78.9, 71.8, 52.7. Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98. Found: C, 72.82; H, 5.11; N, 4.77.

Methyl 2-(Benzyloxy)-2-(4-methoxyphenyl)acetate (CAS: 835914-69-7).[92] (Table 12, entries 5 and 6) Purified by chromatography on silica gel (hexane/ethyl acetate = 85/15). Yield: 132 mg, 92%. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 7.37 (2H, d, J = 8.4 Hz), 7.34−7.28 (5H, m), 6.90 (2H, d, J = 9.2 Hz), 4.88 (1H, s), 4.56 (2H, dd, J = 21.0 Hz, 12.0 Hz), 3.81 (3H, s), 3.70 (3H, s). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 171.7, 160.15, 137.4, 129.0, 128.7, 128.5, 128.3, 128.1, 114.3, 79.2, 71.0, 55.5, 52.5.

Methyl 2-(Benzyloxy)-2-(3-fluorophenyl)acetate. (Table 12, entry 7) Purified by chromatography on silica gel (hexane/ethyl acetate = 85/15). Yield: 107 mg, 78%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.30 (6H, m), 7.25−7.19 (2H, m), 7.04 (1H, dddd, J = 8.4 Hz, 8.4 Hz, 2.8 Hz, 0.8 Hz), 4.93 (1H, s), 4.60 (2H, s), 3.72 (3H, s). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 172.4, 163.4 (d, J = 178.5 Hz), 138.7 (d, J = 7.2 Hz), 136.8, 130.2 (d, J = 8.1 Hz), 128.6, 128.5, 128.1, 123.0 (d, J = 3.8 Hz), 115.7 (d, J = 21.4 Hz), 114.3 (d, J = 22.4 Hz), 78.9 (d, J = 1.9 Hz), 71.4, 52.5. Anal. Calcd for $C_{16}H_{15}FO_3$: C, 70.06; H, 5.51. Found: C, 70.31; H, 5.23.

Methyl 2-(Benzyloxy)-2-(3-cyanophenyl)acetate. (Table 12, entry 8) Purified by chromatography on silica gel (hexane/ethyl acetate = 85/15). Yield: 118 mg, 84%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (1H, broad s), 7.71 (1H, broad d, J = 7.6 Hz), 7.63 (1H, broad d, J = 7.6 Hz), 7.50−7.46 (1H, m), 7.37−7.27 (5H, m), 4.96 (1H, s), 4.63 (2H, dd, J = 25.6 Hz, 12.0 Hz), 3.74 (3H, s). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 170.6, 138.2, 136.6, 132.5, 131.7, 131.1, 129.7, 128.8, 128.6, 128.5, 128.3, 113.1, 78.7, 72.1, 52.9. Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98. Found: C, 72.84; H, 5.49; N, 4.72.

Methyl 2-(Benzyloxy)-2-(3-methoxyphenyl)acetate. (Table 12, entry 9) Purified by chromatography on silica gel (hexane/ethyl acetate = 85/15). Yield: 125 mg, 87%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35−7.25 (6H, m), 7.04−7.02 (2H, broad m), 6.90−6.87 (1H, broad m), 4.91 (1H, s), 4.58 (2H, dd, J = 21.2 Hz, 12.0 Hz), 3.80 (3H, s), 3.70 (3H, s). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 171.3, 160.1, 137.9, 137.2, 129.9, 128.7, 128.3, 128.2, 120.0, 114.7, 112.7, 79.6, 71.3, 55.5, 52.5. Anal. Calcd for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.06; H, 6.59.

3-(4-*tert*-Butylphenyl)-5-methyldihydrofuran-2(3*H*)-one (Mixture of Cis and Trans). (Table 13, entry 1) Purified by chromatography on silica gel (hexane/ethyl acetate = 90/10). Yield: 105 mg, 90%. ^{1}H NMR (500 MHz, $CDCl_3$): δ (A) 7.38 (2H, d, J = 7.5 Hz), (B) 7.37 (2H, d, J = 7.5 Hz), (C) 7.22 (2H, d, J = 7.0 Hz), (D) 7.21 (2H, d, J = 7.5 Hz), (E) 4.83−4.77 (1H, m), (F) 4.65−4.58 (1H, m), (G) 3.92−3.85 (1H, m), (H) 2.79−2.73 (1H, m), (I) 2.57−2.51 (1H, m), (J) 2.35−2.30 (1H, m), (K) 2.06−1.99 (1H, m), (L) 1.50 (3H, broad d, J = 6.5 Hz), (M) 1.46 (3H, broad d, J = 6.0 Hz), (N) 1.31 (9H, s). Integrations: 2.0 for overlapped peaks of A and B; 2.0 for overlapped peaks of C and D; 0.47 for E; 0.65 for F; 1.0 for overlapped peaks of G; 0.61 for H; 0.46 for I; 0.47 for J; 0.62 for K; 1.7 for L; 1.3 for M; 9.0 for overlapped peaks of N. cis/trans =57/43 calculated from H (cis) and J (trans). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 177.8, 177.5, 150.9 (two peaks overlap), 134.3, 133.9, 128.1, 127.7, 126.3, 126.2, 75.5, 75.3, 47.7, 45.7, 40.2, 38.4, 34.9 (two peaks overlap), 31.7 (two peaks overlap), 21.5, 21.3. Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.57; H, 8.83.

3-(4-Methoxyphenyl)-5-methyldihydrofuran-2(3*H*)-one (CAS: 301854-24-0)[64] (Mixture of Cis and Trans). (Table 13, entry 2) Purified by chromatography on silica gel (hexane/ethyl acetate = 85/15). Yield: 83.5 mg, 81%. ^{1}H NMR (500 MHz, $CDCl_3$): δ (A) 7.21 (2H, d, J = 8.5 Hz), (B) 7.20 (2H, d, J = 8.5 Hz), (C) 6.90 (2H, d, J = 9.5 Hz), (D) 6.89 (2H, d, J = 8.5 Hz), (E) 4.82−4.74 (1H, m), (F) 4.64−4.58 (1H, m), (G) 3.90−3.76 (1H, m), (H) 3.80 (3H, s), (I) 2.78−2.73 (1H, m), (J) 2.54−2.46 (1H, m), (K) 2.35−2.28 (1H, m), (L) 2.02−1.95 (1H, m), (M) 1.50 (3H, d, J = 5.5 Hz), (N) 1.46 (3H, d, J = 6.5 Hz), (N) 1.31 (9H, s). Integrations: 2.0 for overlapped peaks of A and B; 2.0 for overlapped peaks of C and D; 0.81 for E; 0.33 for F; 1.0 for overlapped peaks of G; 3.0 for overlapped peaks of H; 0.31 for I; 0.82 for J; 0.80 for K; 0.31 for L; 0.72 for M; 1.9 for N. cis/trans =28/72 calculated from I (cis) and K (trans). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 177.8, 177.5, 159.4 (two peaks overlap), 129.5, 129.4, 129.1, 129.0, 114.8, 114.7, 75.4, 75.2, 55.7 (two peaks overlap), 47.4, 45.2, 40.3, 38.4, 21.4, 21.3.

5-Methyl-3-(*o*-tolyl)dihydrofuran-2(3*H*)-one (Mixture of Cis and Trans). (Table 13, entry 3) Purified by chromatography on silica gel (hexane/ethyl acetate = 85/15). Yield: 79.9 mg, 84%. ^{1}H NMR (500 MHz, $CDCl_3$): δ (A) 7.22−7.11 (4H, m), (B) 4.83−4.76 (1H, m), (C) 4.68−4.61 (1H, m), (D) 4.12−4.03 (1H, m), (E) 2.79−2.73 (1H, m), (F) 2.39−2.31 (1H, m), (G) 2.35 (3H, s), (H) 3.92−3.85 (1H, m), (H) 1.98−1.90 (1H, m), (I) 1.50 (3H, d, J = 6.5 Hz), (J) 1.47 (3H, d, J = 6.0 Hz). Integrations: 4.1 for overlapped peaks of A; 0.45 for B; 0.63 for C; 1.1 for overlapped peaks of D; 0.65 for E; 4.0 for overlapped peaks of F and G; 0.64 for H; 1.7 for I; 1.3 for J. cis/trans =57/43 calculated from I (cis) and J (trans). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 178.1, 177.4, 136.8, 136.6, 136.5, 135.8, 131.3, 131.1, 128.1, 128.0, 127.2 (two peaks overlap), 127.1, 127.0, 75.5, 75.4, 45.6, 43.9, 39.6, 38.3, 21.5, 21.4, 20.1, 20.1. Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.82; H, 7.44.

Methyl 4-(5-Methyl-2-oxotetrahydrofuran-3-yl)benzoate (Mixture of Cis and Trans). (Table 13, entry 4) Purified by chromatography on silica gel (hexane/ethyl acetate = 85/15). Yield: 108 mg, 92%. ^{1}H NMR (400 MHz, $CDCl_3$): δ (A) 8.01 (2H, d, J = 8.4 Hz), (B) 7.38 (2H, d, J = 8.4 Hz), (C) 7.37 (2H, d, J = 8.4 Hz), (D) 4.86−4.78 (1H, m), (E) 4.70−4.61 (1H, m), (F) 4.02−3.94 (1H, m), (G) 3.91 (3H, s), (H) 2.84−2.78 (1H, m), (I) 2.59−2.52 (1H, m), (J) 2.43−2.36 (1H, m), (K) 2.08−1.99 (1H, m), (L) 1.51 (3H, d, J = 6.0 Hz), (M) 1.48 (3H, d, J = 6.4 Hz). Integrations: 2.0 for overlapped peaks of A; 2.0 for overlapped peaks of B and C; 0.34 for D; 0.71 for E; 1.2 for overlapped peaks of F; 2.7 for overlapped peaks of G; 0.71 for H; 0.35 for I; 0.33 for J; 0.73 for K; 2.0 for L; 0.92 for M. cis/trans =68/32 calculated from H (cis) and J (trans). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 176.4, 176.1, 166.7, 166.7, 142.1, 141.6, 130.2, 130.1, 129.5 (two peaks overlap), 128.3, 128.1, 75.2, 75.1, 52.2 (two peaks overlap), 47.6, 45.5, 39.5, 37.6, 20.8, 20.7. Anal. Calcd for $C_{13}H_{14}O_4$: C, 66.66; H, 6.02. Found: C, 66.53; H, 6.00.

4-(5-Methyl-2-oxotetrahydrofuran-3-yl)benzonitrile (Mixture of Cis and Trans). (Table 13, entry 5) Purified by chromatography on silica gel (hexane/ethyl acetate = 85/15). Yield: 84.5 mg, 84%. ^{1}H NMR (400 MHz, $CDCl_3$): δ (A) 7.67 (2H, d, J = 8.8 Hz), (B) 7.44 (2H, d, J = 8.0 Hz), (C) 7.43 (2H, d, J = 8.4 Hz), (D) 4.87−4.79 (1H, m), (E) 4.72−4.63 (1H, m), (F) 4.03−3.95 (1H, m), (G) 2.86−2.80 (1H, m), (H) 2.60−2.52 (1H, m), (I) 2.45−2.38 (1H, m), (J) 2.07−1.98 (1H, m), (K) 1.53 (3H, d, J = 6.4 Hz), (L) 1.50 (3H, d, J = 6.4 Hz). Integrations: 2.0 for overlapped peaks of A; 2.0 for overlapped peaks of B and C; 0.44 for D; 0.71 for E; 1.1 for overlapped peaks of F; 0.70 for G; 0.43 for H; 0.41 for I; 0.75 for J; 1.9 for K; 1.0 for L. cis/trans =63/37 calculated from G (cis) and I (trans). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 172.2, 171.9, 143.7 (two peaks overlap), 132.3, 132.2, 131.3, 131.2, 118.6 (two peaks overlap), 112.6 (two peaks overlap), 75.3, 74.7, 50.3, 49.7, 33.6, 32.5, 21.4, 21.2. Anal. Calcd for $C_{12}H_{11}NO_2$: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.34; H, 5.46; N, 6.66.

5-Methyl-3-(4-Nitrophenyl)dihydrofuran-2(3*H*)-one (CAS: 301854-31-9)[64] (Mixture of Cis and Trans). (Table 13, entry 6)

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Purified by chromatography on silica gel (hexane/ethyl acetate = 85/15). Yield: 85.2 mg, 77%. ^{1}H NMR (400 MHz, $CDCl_3$): δ (A) 8.23 (2H, d, J = 8.8 Hz), (B) 7.51 (2H, d, J = 8.8 Hz), (C) 7.50 (2H, d, J = 8.4 Hz), (D) 4.90−4.82 (1H, m), (E) 4.74−4.64 (1H, m), (F) 4.10−4.01 (1H, m), (G) 2.90−2.83 (1H, m), (H) 2.62−2.56 (1H, m), (I) 2.49−2.42 (1H, m), (J) 2.11−2.02 (1H, m), (K) 1.54 (3H, d, J = 6.0 Hz), (L) 1.51 (3H, d, J = 6.4 Hz). Integrations: 2.0 for overlapped peaks of A; 1.9 for overlapped peaks of B and C; 0.36 for D; 0.72 for E; 1.0 for overlapped peaks of F; 0.72 for G; 0.37 for H; 0.36 for I; 0.74 for J; 2.1 for K; 0.98 for L. cis/trans =67/33 calculated from G (cis) and I (trans). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 175.7, 175.4, 147.4 (two peaks overlap), 144.1, 143.6, 129.2, 128.8, 124.2, 124.0, 75.3, 75.2, 47.3, 45.1, 39.3, 37.3, 21.0, 20.7.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C{^{1}H} NMR spectra of all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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