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Bismuth- and Iron-Catalyzed Three-Component Synthesis of α-Amino Acid Derivatives: A Simple and Convenient Route to α-Arylglycines

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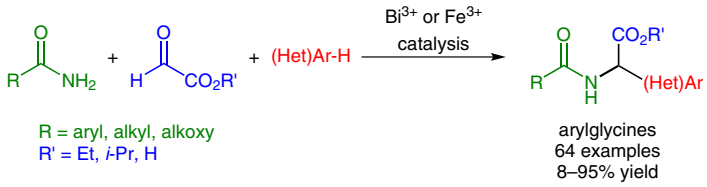

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Abstract Efficient bismuth- and iron-catalyzed three-component syntheses of α-arylglycines have been developed. These methods provide a general, atom-economic route to various N-protected α-arylglycines starting from readily available amides (or carbamates), glyoxalates, and (hetero)arenes with water as the only by-product. Scope and limitations of bismuth- and iron-catalyzed reactions are discussed and compared. In addition, mechanistic investigations as well as initial forays into stereoselective three-component reactions are presented.

Key words multicomponent reactions, iron, bismuth, aza-Friedel–Crafts reaction, amino acids, homogeneous catalysis

α-Amino acids are of fundamental importance for biology, biochemistry, and chemistry.[1,2] They form the backbone of proteins, an essential part of every living organism, and are used as common feedstock for the production of biodegradable plastics, fertilizers, nutritional supplements, or drugs.[1,2] Many proteinogenic and nonproteinogenic α-amino acids have important biological, nonprotein-related functions, such as glutamate,[1] an important neurotransmitter or glycine,[3] the starting material for the biosynthesis of porphyrin-type cofactors. With the expansion of the genetic code and the discovery of protein-based drugs, nonproteinogenic (or unnatural) α-amino acids have gained increasing attention.[1,2] Among these nonproteinogenic α-amino acids, α-arylglycines are of particular importance, as they are building blocks for various drugs, such as cardiovascular agents[4] and β-lactam antibiotics[5] like amoxicillin and norcardicin A (Figure 1). The α-arylglycine moiety is also part of numerous natural products, such as vancomycin[6] or chloropeptin I[7] (Figure 1). Expanding the organic chemist's tool box with novel efficient, modular and practical methods for the synthesis of the α-arylglycine structure is therefore of great interest.[8,9] Common procedures for the preparation of these compounds are based on the addition of a nucleophile to an imine species, such as the Mannich reaction,[10] the Strecker reaction,[11] the Petasis–(Borono–Mannich) reaction,[12] or aza-Friedel–Crafts-type reactions[13] (Scheme 1).

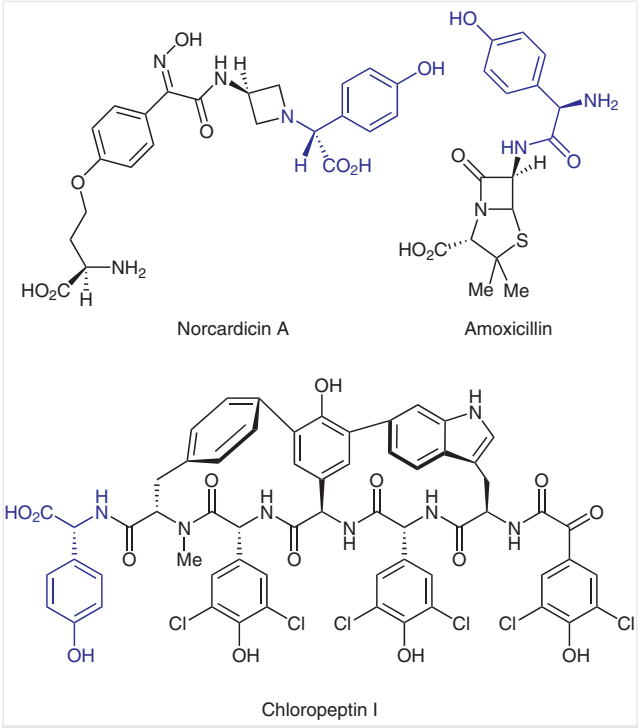

Figure 1 α-Arylglycine moiety in biologically active substances

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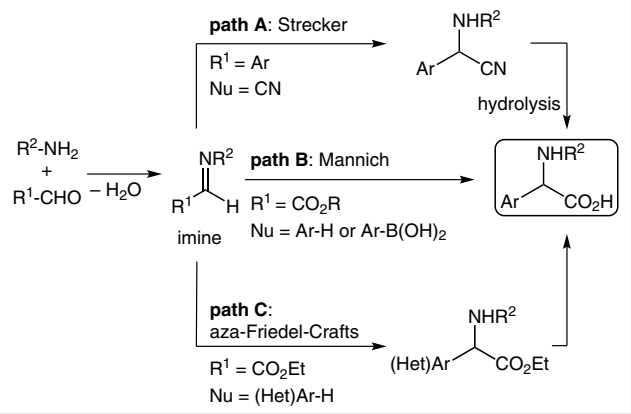


Scheme 1 Different synthetic routes to α-arylglycines

However, these methods have some decisive drawbacks. Cyanides used in the Strecker reaction are highly toxic and the subsequent hydrolysis of the nitrile function under acidic conditions curtails the functional group tolerance (Scheme 1, path A). The Petasis–(Borono–Mannich) reaction and related processes require prefunctionalized and often expensive boronic acid derivatives (Scheme 1, path B). Another important approach is the direct amino- and amidoalkylation of unfunctionalized (hetero)arenes (Scheme 1, path C).[13,14] These aza-Friedel–Crafts-type reactions are based on nucleophilic addition of arenes to highly electrophilic imines and especially *N*-acylimines. In combination with the in situ formation of the reactive *N*-acylimine species via condensation of an aldehyde and an amide, these methods enable the preparation of α-arylglycines with water as only by-product and offer a promising opportunity for the sustainable and atom-economic synthesis of this important compound class.[15] However, reported aza-Friedel–Crafts-type reactions are often limited to very reactive (hetero)arenes or require stoichiometric amounts of strong Brønsted or Lewis acids.[14] These restrictions lead to a rather small substrate scope and the formation of considerable amounts of waste and by-products.

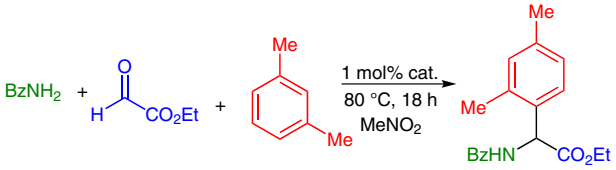
In the course of our research on imine-based multicomponent reactions,[16] we were able to develop three-component reactions for the synthesis of α-arylglycines using inexpensive and nontoxic bismuth and iron catalysts.[16a,b] These reactions provide straightforward access to a broad scope of α-(hetero)arylglycines. They utilize readily available starting materials and water is generated as the only by-product. Herein we report the full scope and limitations of both methods, together with comparison of the specific advantages and disadvantages as well as detailed mechanistic investigations.

Optimization and Scope

At the onset of our studies, we hypothesized that an ideal catalyst should be able to catalyze both the formation of a reactive *N*-acylimine via condensation of an amide with a glyoxylic acid derivative and the addition of an unreactive arene to the in situ formed *N*-acylimine. Small quantities of water formed in the condensation step should not lead to a significant catalyst deactivation. For the sake of practicality the glyoxalate was used in its more stable polymeric or hydrated form.[17]

To identify a suitable catalyst system, the reaction of benzamide (**1a**) with commercially available ethyl glyoxalate (**2a**)[18] and the moderately reactive *m*-xylene (**3a**)[19] was chosen using only 1 mol% of the catalyst (Table 1). Preliminary results revealed that several Lewis and Brønsted acids are able to catalyze this reaction, albeit with various degrees of efficiency (Table 1). Water-sensitive Lewis acids, such as $BF_3{\cdot}OEt_2$ and $AlCl_3$, or weak Brønsted acids, for example, TFA or $(PhO)_2P(O)OH$, did not catalyze the reaction at all (yields <10%, results not shown).

Table 1 Initial Screening of Different Catalysts



1a **2a** **3a** **4a**

Entry	Catalyst	Yield (%)[a]
1	$Fe(ClO_4)_3{\cdot}xH_2O$	91
2	$Bi(OTf)_3$	88
3	$In(OTf)_3$	72
4	$Yb(OTf)_3$	54
5	$Sc(OTf)_3$	16
6	TfOH	18
7	TfOH (5 mol%)	49
8	TsOH	12

[a] Yields are given for the isolated product. The product was obtained as a 98:2 mixture of regioisomers. Only the major regioisomer is shown.

The stronger Brønsted acids TfOH and TsOH provided the desired product in <20% yield (Table 1, entries 6 and 8). A higher loading of TfOH did not lead to a greatly improved yield (entry 7). Most promising results were obtained with $Bi(OTf)_3$, $In(OTf)_3$, and $Yb(OTf)_3$ (entries 2–4). Other metal triflates such as $Sc(OTf)_3$, $Mg(OTf)_2$, or $Zn(OTf)_2$ did not show a similar catalytic activity. Surprisingly, 1 mol% $Fe(ClO_4)_3$ furnished the α-arylglycine **4a** in 91% yield (entry 1).

From an ecological and economic point of view, readily available, cheap, and nontoxic iron salts would be an ideal catalyst system for this three-component reaction.[20,21] Therefore, iron-based catalysts were investigated in more detail. During our previous research on amidoalkylation reactions, $Bi(OTf)_3$ was identified as a very active, nontoxic, and relatively cheap catalyst.[22,23] Thus, we decided to take

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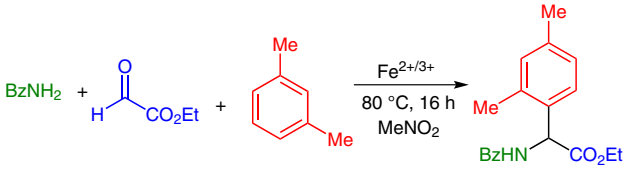
focus on bismuth-catalyzed reactions as well. Although $In(OTf)_3$ and $Yb(OTf)_3$ showed promising catalytic activity (Table 1, entries 3 and 4), In- and Yb-based catalysts were not examined due to the toxicity and teratogenic potential of In(III) and Yb(III) salts.[24]

To optimize the reaction conditions for both bismuth- and iron-based conversions, the initial model reaction between benzamide (**1a**), ethyl glyoxalate (**2a**), and *m*-xylene (**3a**) was chosen. The results for the optimization of the iron catalyst are depicted in Table 2. Both, iron chloride either in its anhydrous form or as hexahydrate, as well as iron perchlorate displayed high catalytic activities. Despite the fact that both $Fe(ClO_4)_3$ and $FeCl_3{\cdot}6H_2O$ gave similar yields during the initial optimization reactions (Table 2, entries 1 and 7), $Fe(ClO_4)_3$ led to higher yields in general. Additionally, for $Fe(ClO_4)_3$ the catalyst loading can be decreased without significant loss of efficiency (entry 9). Whereas 1 mol% $Fe(ClO_4)_3$ led to the desired product in 91% yield (entry 8), the yield with 1 mol% $FeCl_3$ dropped to 18% (entry 5). The corresponding Fe^{2+} salts could catalyze the model reaction with similar efficiency (entries 6 and 11). However, as judged by the observed rapid color change, we assume a fast oxidation of Fe^{2+} to Fe^{3+} under our aerobic reaction conditions. To rule out a possible 'hidden' catalysis by Brønsted acids, the reaction was performed in the presence of the proton scavenger 2,6-di-*tert*-butylpyridine (dbpy, entry 12).[25] No significant decrease in yield was observed. Therefore, we concluded that a Fe^{3+} species is the active catalyst.

Next, different solvents were examined for our three-component reaction (Table 2, entries 13–16). Best results were obtained in nitromethane. All other tested solvents led to lower yields (1,2-dichloroethane, dichloromethane, or 1,4-dioxane) or complete shutdown of the reaction (THF, H_2O, EtOAc). A similar screening of reaction parameters was performed with the Bi-catalyzed three-component synthesis. As shown in Table 3, $Bi(OTf)_3$ proved to be the optimal catalyst. Other bismuth salts like $BiCl_3$ or $BiBr_3$ afforded the product in lower yields (Table 3, entries 5 and 6). Notably, the catalyst loading of $Bi(OTf)_3$ could be reduced to only 1 mol% without a significant change in yield and even with only 0.5 mol% of $Bi(OTf)_3$ the product could be isolated in 77%. As shown in Table 1, TfOH, a possible by-product from the hydrolysis of $Bi(OTf)_3$, did not display a similar catalytic activity. To further exclude a possible Brønsted acid catalysis a control reaction with the proton scavenger dbpy was performed also in the case of $Bi(OTf)_3$ (entry 7). Again no significant decrease in the catalytic activity was observed, indicating a Bi(III)-species as the active catalyst. In the case of the Bi-catalyzed reaction, nitromethane also proved to be

Table 2 Optimization of the Reaction Parameters for Fe-Catalyzed Three-Component Reaction for the Synthesis of α-Arylglycine **4a**

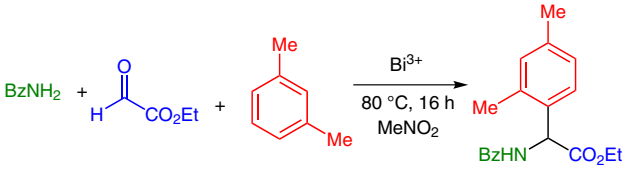


1a **2a** **3a** **4a**

Entry	Catalyst	Solvent	Yield (%)[a]
1	$FeCl_3{\cdot}6H_2O$ (5 mol%)	$MeNO_2$	84
2	$FeCl_3{\cdot}6H_2O$ (2 mol%)	$MeNO_2$	84
3	anhyd $FeCl_3$ (5 mol%)	$MeNO_2$	86
4	anhyd $FeCl_3$ (2 mol%)	$MeNO_2$	87
5	anhyd $FeCl_3$ (1 mol%)	$MeNO_2$	18
6	$FeCl_2{\cdot}4H_2O$ (2 mol%)	$MeNO_2$	82
7	$Fe(ClO_4)_3{\cdot}xH_2O$ (5 mol%)	$MeNO_2$	91
8	$Fe(ClO_4)_3{\cdot}xH_2O$ (1 mol%)	$MeNO_2$	91
9	$Fe(ClO_4)_3{\cdot}xH_2O$ (0.5 mol%)	$MeNO_2$	75
10	$Fe(ClO_4)_3{\cdot}xH_2O$ (0.1 mol%)	$MeNO_2$	37
11	$Fe(ClO_4)_2{\cdot}xH_2O$ (2 mol%)	$MeNO_2$	82
12	$Fe(ClO_4)_3{\cdot}xH_2O$ (5 mol%) + dbpy (10 mol%)	$MeNO_2$	86
13	$FeCl_3{\cdot}6H_2O$ (2 mol%)	DCE	39
14	$FeCl_3{\cdot}6H_2O$ (2 mol%)	CH_2Cl_2	23
15	$FeCl_3{\cdot}6H_2O$ (2 mol%)	1,4-dioxane	<10
16	$FeCl_3{\cdot}6H_2O$ (2 mol%)	MeCN	10

[a] Yields are given for the isolated product. The product was obtained as a 98:2 mixture of regioisomers. Only the major regioisomer is shown.

Table 3 Optimization of the Reaction Parameters for Bi-Catalyzed Three-Component Reaction for the Synthesis of α-Arylglycine **4a**



1a **2a** **3a** **4a**

Entry	Catalyst	Solvent	Yield (%)[a]
1	$Bi(OTf)_3$ (5 mol%)	$MeNO_2$	84
2	$Bi(OTf)_3$ (2 mol%)	$MeNO_2$	89
3	$Bi(OTf)_3$ (1 mol%)	$MeNO_2$	88
4	$Bi(OTf)_3$ (0.5 mol%)	$MeNO_2$	77
5	$BiCl_3$ (5 mol%)	$MeNO_2$	72
6	$BiBr_3$ (5 mol%)	$MeNO_2$	69
7	$Bi(OTf)_3$ (5 mol%) + dbpy (10 mol%)	$MeNO_2$	84
8	$Bi(OTf)_3$ (5 mol%)	DCE	52

[a] Yields are given for the isolated product. The product was obtained as a 98:2 mixture of regioisomers. Only the major regioisomer is shown.

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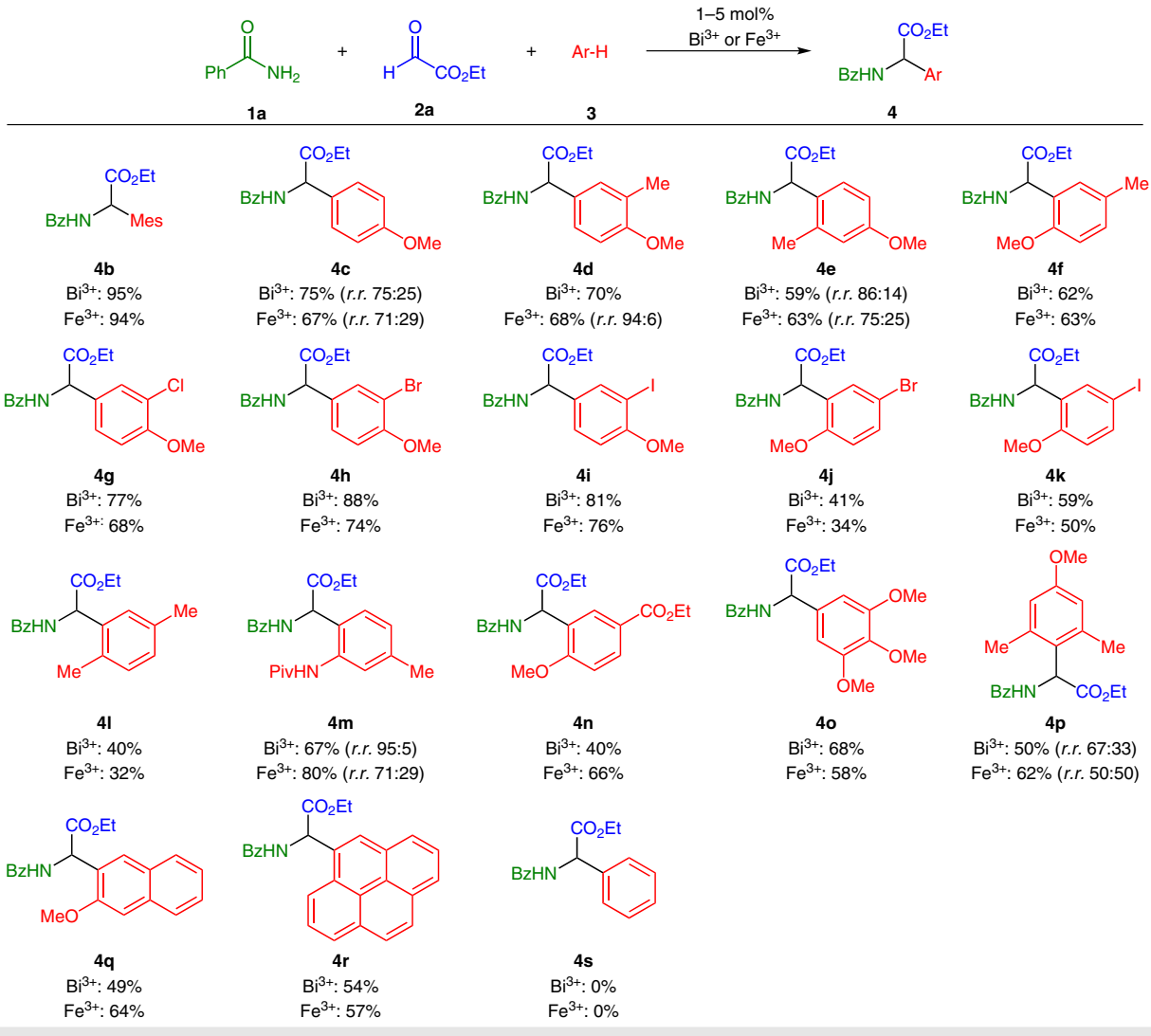
the ideal solvent. While yields in 1,2-dichloroethane were still acceptable (entry 8), the use of other solvents led to significant lower yields (results not shown).

Scope of (Hetero)Arenes, Amides, and Glyoxalates

After identification of the ideal reaction conditions, the scope of our methods was explored. First, reactions of different arenes with benzamide (**1a**), and ethyl glyoxalate (**2a**) were investigated. Various electron-rich arenes are suitable substrates for both the Fe- and the Bi-catalyzed aza-Friedel–Crafts reaction (Scheme 2). The combined results are shown in Scheme 2. Both types of catalyst furnished different α-arylglycine derivatives in good to excellent yields. Interestingly *N*-pivalolyl-protected aniline **3m** reacted chemoselectively and α-arylglycine **4m** was isolated in 67% (Bi) and 80% (Fe) yield. The reactions of polycyclic arenes led to the formation of glycine derivatives **4q** and **4r**, useful building blocks for the synthesis of fluorescence labels,[26] in 49–64% yield. Less reactive arenes, such as benzene, did not react, even under harsh reaction conditions. In most cases only one regioisomer was obtained. However, in some cases, such as in the reaction with anisole, a mixture of regioisomers was isolated. To our surprise, the use of $Bi(OTf)_3$, supposedly the more active catalyst, always led to higher regioselectivities. In certain cases, such as with anisole, only a small, negligible difference in the regioselectivity was observed (75:25 vs. 71:29 *para*/*ortho*). However, for reactions with other arenes, $Bi(OTf)_3$ furnished the desired products with a significantly higher regioselectivity. This fact is exemplified by the arylglycines **4e** (86:14 vs.



Scheme 2 Substrate scope: arene component. Yields are given for isolated products. Unless otherwise mentioned, the corresponding α-arylglycine was observed as one single regioisomer (*d.r.* >98:2). In the case of regioisomers, only the major one is shown. Bz = benzoyl, Piv = pivalolyl.

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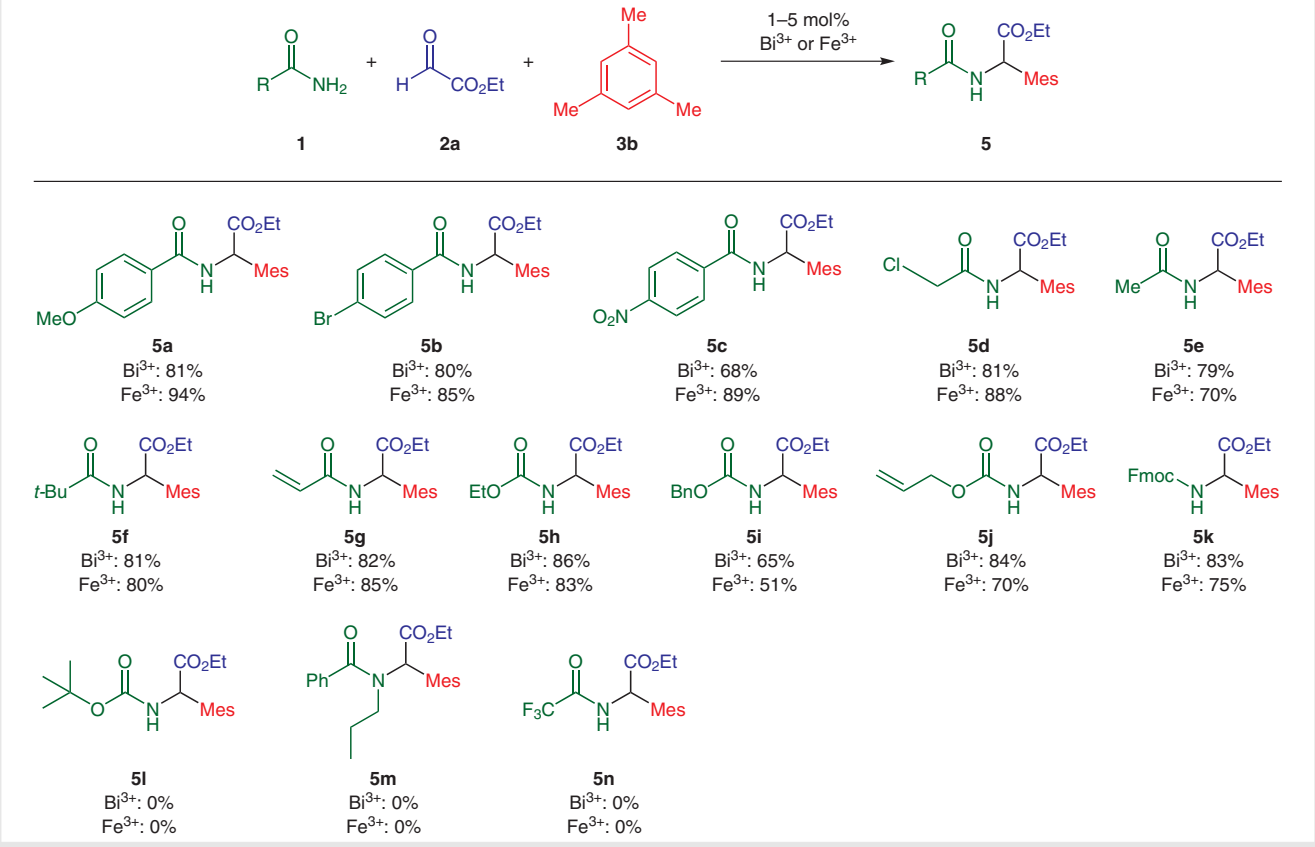
75:25), **4m** (95:5 vs. 71:29), or **4p** (67:33 vs 50:50). So far we do not have a conclusive explanation for this phenomenon.

Next, the reactions of different amides and carbamates with ethyl glyoxalate (**2a**) and mesitylene (**3b**) were examined (Scheme 3). To our delight different benzamide derivatives were compatible with both catalysts systems and the desired products **5a–c** were obtained in excellent yields (68–94%). Alkyl-substituted primary amides are also suitable substrates and arylglycine derivatives **5d–f** were obtained in 70–88% yield with iron catalysis and in 79–81% yield with bismuth catalysis. Even acid-sensitive amides such as acrylamide were transformed into the desired product **5g** in 82% (Bi) or 85% (Fe) yield. Carbamates are suitable substrates for the bismuth- and the iron-catalyzed three-component reactions. Different *N*-protected α-arylglycines **5h–k**, such as **5i** bearing a Cbz-protecting group or the Fmoc-derivative **5k**, were obtained in high yields. Unfortunately reaction with *tert*-butyl carbamate did not furnish the desired Boc-protected arylglycine **5l**. Sterically more demanding secondary amides or electron-deficient trifluoroacetyl amide proved to be unsuitable for our method and the desired products **5m** and **5n** could not be obtained.

Not only arenes but also heteroaromatic compounds are suitable substrates for the three-component reaction (Scheme 4). The corresponding heteroarylglycines **7a–l** were obtained in good to excellent yields with both Fe and Bi catalysis. In general, lower reaction temperatures were necessary to avoid direct addition of the heteroarene to the aldehyde (Scheme 5).[27] Reaction of benzamide (**1a**) with ethyl glyoxalate (**2a**) and a heteroarene **6** as the nucleophilic component furnished different heteroarylglycines in 47 to 88% yield (Scheme 4). Interestingly, reactions with carbamates, such as urethane, as the amide component, led to overall higher yields as well as improved regioselectivities. Improved regioselectivities can be rationalized by the decreased reactivity of the in situ formed *N*-carbamoylimine compared to the *N*-acylimine in the benzamide case. The low yields with benzamides are most probably associated with the instability of the formed amidoalkylated products under acidic conditions. We assume that these compounds decompose under acidic conditions via dissociation of the benzamide, thereby forming a stabilized heterobenzylic cation **9**, which can react with excess of the heteroarene to the corresponding diarylmethane derivative **10**.



Scheme 3 Substrate scope: amide component. Yields are given for the isolated products. Mes = mesityl (2,4,6-trimethylphenyl), Bn = benzyl, Fmoc = [9*H*-fluoren-9-yl)methoxy]carbonyl.

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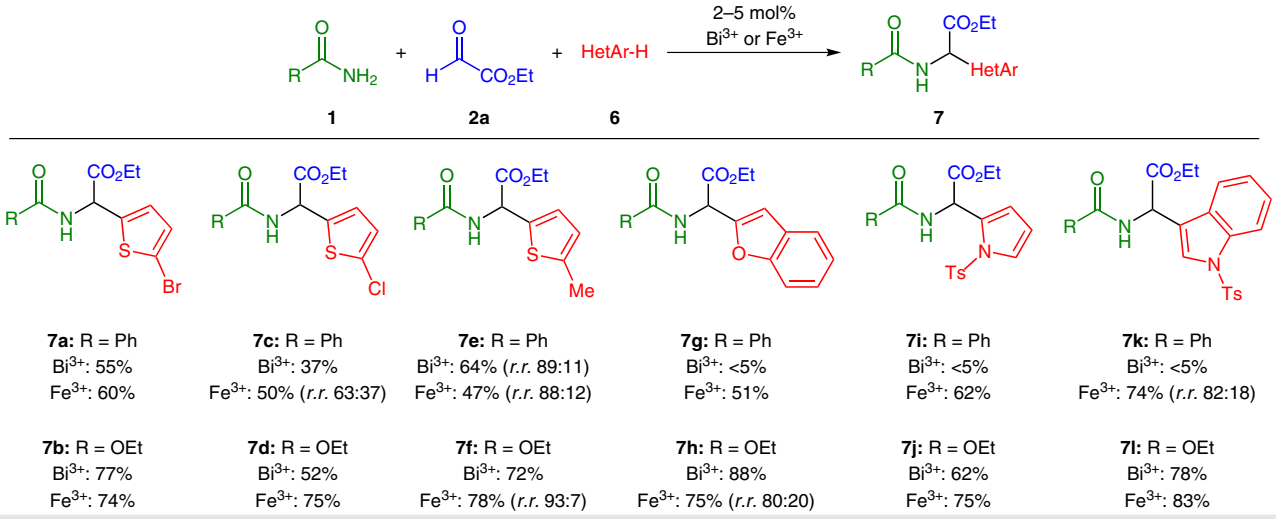
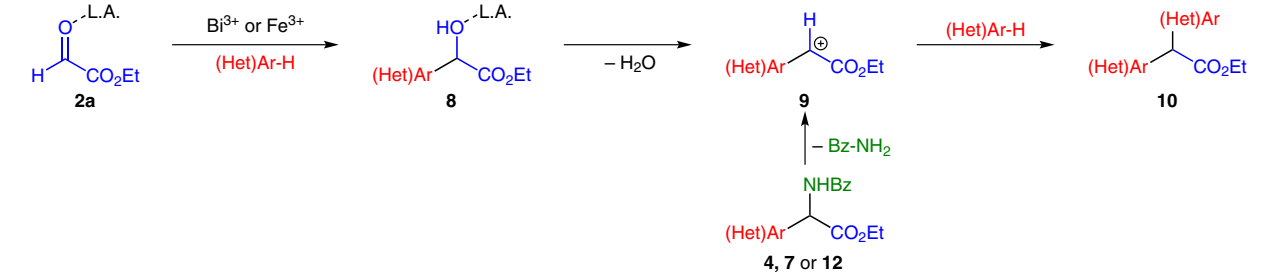
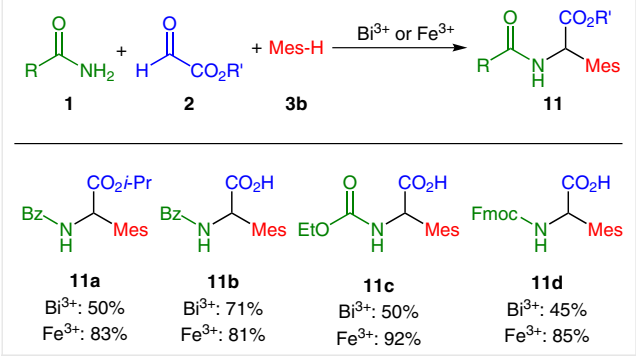


Scheme 4 Substrate scope: heteroarenes. Yields are given for isolated products. Unless otherwise mentioned, the corresponding α-arylglycine was observed as one single regioisomer (*d.r.* >98:2). Yields are given for the isolated product. In the case of regioisomers, only the major one is shown. Ts = tosyl.



Scheme 5 Mechanistic rationale for the formation of the observed by-products with very electron-rich (hetero)arenes

Indeed, $Bi(OTf)_3$-catalyzed reactions of very electron-rich heterocycles, such as benzofuran, *N*-tosylpyrrole, or -indole, with benzamide (**1a**) and ethyl glyoxalate (**2a**) led to the selective formation of the double addition products of type **10** (Scheme 5). Using the less active iron catalyst, heteroarylglycines **7g**, **7i**, and **7k** could be isolated in 51, 62, and 74% yield, respectively. Both methods are not limited to ethyl glyoxalate as the aldehyde component (Scheme 6).[28] Reactions with different glyoxalates, such as isopropyl glyoxalate (**2b**) furnished the desired amino acid derivative **11a** in 50 and 83% yield. Even free glyoxylic acid, used as aqueous solution, can be employed as aldehyde source, thereby providing the free acid **11b** in 71 and 81% yield. Reactions with carbamates, such as urethane or the Fmoc-derivative, afforded the *N*-protected arylglycines **11c** and **11d** in 45–92% yield. Especially, the Fmoc-protected acid **11d** would be an ideal starting material for solid-phase peptide synthesis with unnatural amino acid derivatives. In the case of the carbamates, iron catalysis proved to be more reliable and furnished the desired products in higher yields and purity.



Scheme 6 Reaction of benzamide (**1a**) and different carbamates with glyoxylic acid derivatives **2** and mesitylene (**3b**). Yields are given for isolated products.

Limitations

In general, similar yields were obtained with bismuth and iron catalysis. In the case of competing regioisomer formation, reactions with $Bi(OTf)_3$ gave consistently higher regioselectivities. During our studies on the scope of the

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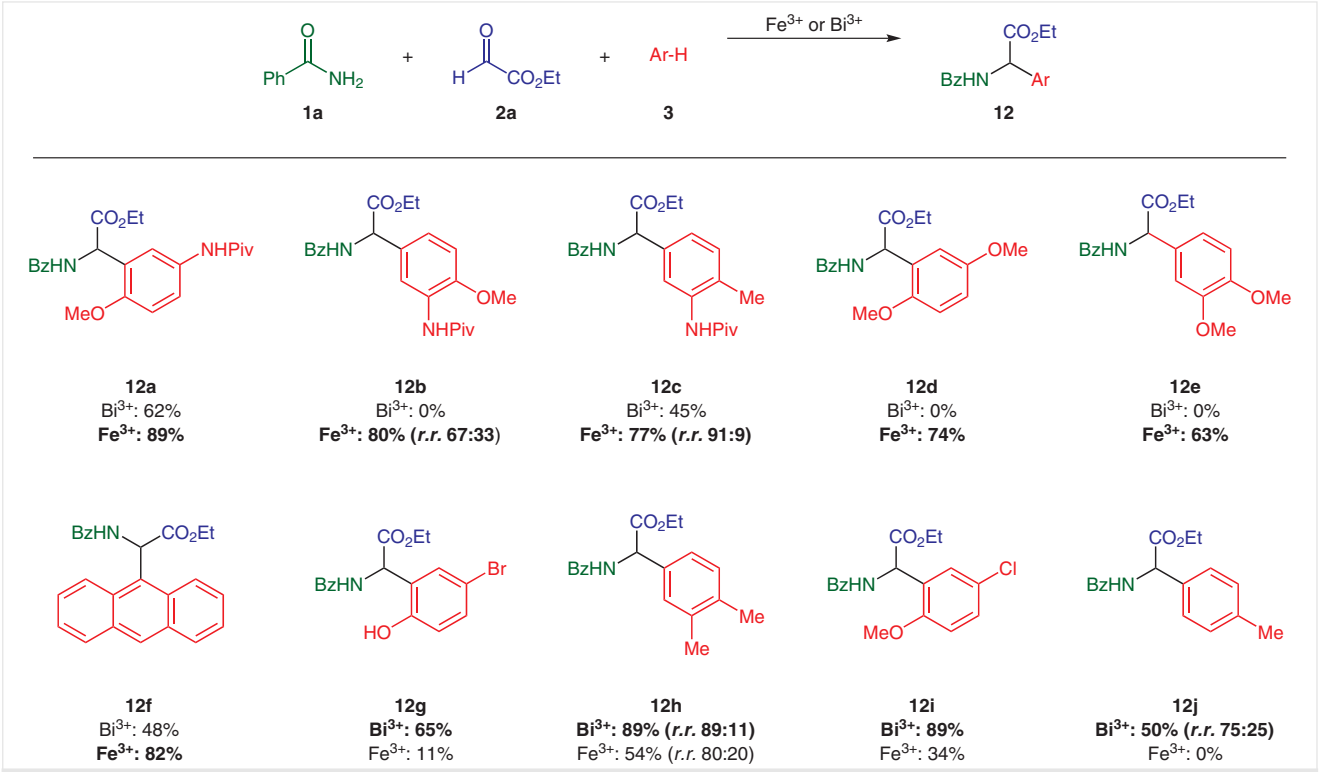
arene component, a significant difference was observed in the reactivity for very electron-rich as well as for unreactive aromatics (Scheme 7). These differences in reactivity are most probably associated with the activity of the used catalyst. For very reactive, electron-rich arenes, such as dimethoxybenzenes, anthracene, or anisidine derivatives, the less active iron catalyst proved to be advantageous. The amidoalkylated arenes **12a–j** were obtained in 63–89% yield. Reactions of electron-rich arenes in combination with the more active $Bi(OTf)_3$ gave the corresponding products in lower yields or did not afford the product at all. In these cases, the competing formation of diarylmethane derivatives was observed in significant quantities (cf. Scheme 5). For free phenols, such as 4-bromophenol, bismuth catalysis proved to be advantageous and furnished the glycine derivative **12g** in 65% yield (vs 11% with Fe^{3+}). With iron catalysts oxidative coupling reactions of the phenol were observed. In the case of less reactive arenes, such as *o*-xylene, the more active bismuth catalyst proved to be more efficient and afforded the arylglycine in 89% yield (vs 54% with Fe^{3+} catalysis). $Bi(OTf)_3$ could even catalyze the reaction of toluene, furnishing product **12j** in 50% yield. In the case of iron catalysis no product formation was observed with toluene. Although the lower catalytic activity of the iron salts might look like a disadvantage at the first glance, it proved to be a major advantage in terms of practicability. Commercially available, technical ethyl glyoxalate, is commonly provided as a solution of the polymer form in toluene. In the case of Bi-catalyzed reactions, toluene has to be removed prior to the reaction to avoid the formation of **12j** as side-product. For iron-catalyzed reactions the commercially available solution can be used without further processing, thereby leading to a more straightforward procedure.

Also in the case of less reactive amide components, the higher catalytic activity of $Bi(OTf)_3$ proved to be beneficial (Scheme 8). $Bi(OTf)_3$-catalyzed reactions with cyclic secondary amides or carbamates afforded the desired products **14a** and **14b** in 63 and 80% yield. No product formation

Scheme 8 Substrate scope: reactions with cyclic secondary amides and carbamates. Yields are given for the isolated products.



Scheme 7 Substrate scope: limitation for Bi^{3+} and Fe^{3+}. Yields are given for the isolated products. Unless otherwise mentioned, the corresponding α-arylglycine was observed as one single regioisomer (*d.r.* >98:2). In the case of regioisomers, only the major one is shown.

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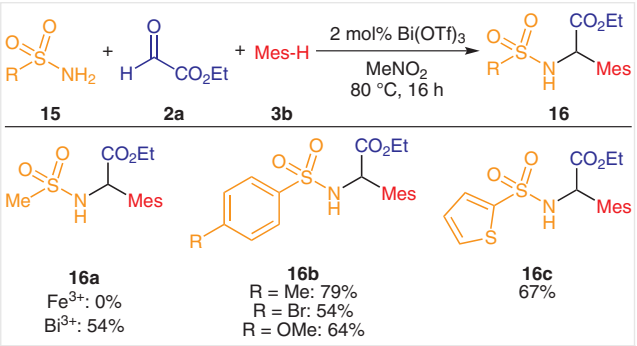
with iron catalysts was observed. Acyclic secondary amides or carbamates proved to be unreactive using either bismuth or iron catalysis.

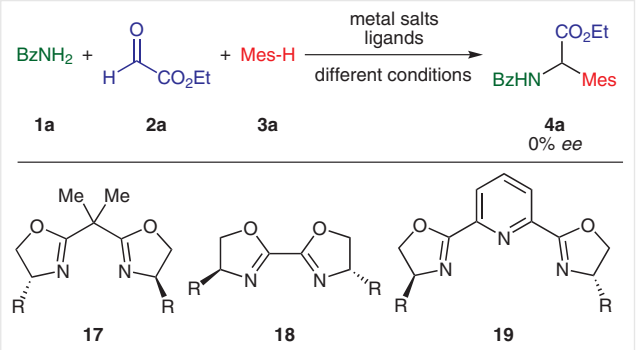
Interestingly, $Bi(OTf)_3$ was able to catalyze reactions with different sulfonamides as amide component (Scheme 9). The corresponding *N*-sulfonylated arylglycines **16a–c** were obtained in 54–79% yield. Presumably, $Bi(OTf)_3$ is active enough to catalyze the addition of arenes to in situ less electrophilic *N*-sulfonylimines.[14]



Scheme 9 Substrate scope with sulfonamides. Yields are given for the isolated products.

Investigations into Stereoselective Reactions

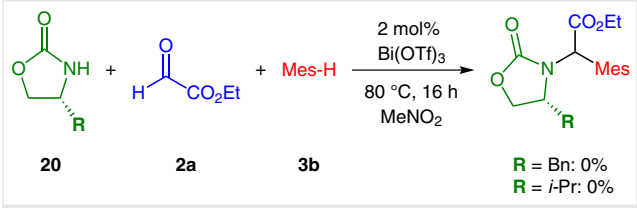
Since most of the natural α-arylglycines exist in one enantiomeric form, stereoselective synthesis of these compounds would be highly desirable. Therefore, we decided to investigate a possible asymmetric version of our three-component reactions (Scheme 10). The most obvious approach would be the use of chiral ligands in our transformation. Hence various common chiral ligands were tested in combination with different Bi^{3+} or Fe^{3+} salts (Scheme 10).[29] Unfortunately, no asymmetric induction was observed using various metal–ligand combinations, solvents, or temperatures (Scheme 10). In further studies using different ligands and variations of the amide or arene component as well as In^{3+} and Yb^{3+}, promising Lewis acids in our initial screening, were studied. Again no asymmetric induction was observed.



Scheme 10 Unsuccessful enantioselective approaches

Since no enantioselective version of the three-component reaction could be realized with chiral catalysts, we decided to explore diastereoselective reactions with chiral amide components (Schemes 11–13).

For first tests chiral carbamates based on the Evans auxiliary were selected (Scheme 11).[30] However, chiral oxazolidinones, such as **20a** or **20b**, did not furnish the desired products under our standard reaction conditions. Whereas **20b** did not react at all, an interesting reactivity was observed for oxazolidinone **20a**. The bismuth-catalyzed reaction of **20a** furnished cyclic amino acid derivative **21** in 84% yield as single diastereomer (Scheme 12). Formation of the cyclic product can be rationalized by an intramolecular addition of the phenyl moiety to the formed *N*-acylimine. Even in the presence of excess of mesitylene no intermolecular addition was observed. Therefore, we next selected chiral primary amides as potential chiral starting materials for our three-component reaction.



Scheme 11 Unsuccessful diastereoselective approach using Evans-type carbamates

Scheme 12 Intramolecular amidoalkylation of **20a**. Yield is given for the isolated product.

Reaction of phthalimide-protected valine amide **22** with ethyl glyoxalate (**2a**) and mesitylene (**3b**) furnished the expected product **23** in 84% with $Bi(OTf)_3$ and 78% yield with $FeCl_3 \cdot 6H_2O$ (Scheme 13). Only moderate diastereoselectivities (67:33 and 65:35) were observed. Variation of the temperature, solvent, or catalyst did not improve the stereoselectivity. Replacing the amide protecting group by a carbamate, led to a diminished diastereoselectivity and a drastic decrease in isolated yields. Reactions with amide-protected valine amides did not furnish any desired product at all. In summary, all our approaches to stereoselective reactions did not lead to the expected results. Only in the case of chiral amide components moderate stereoselectivi-

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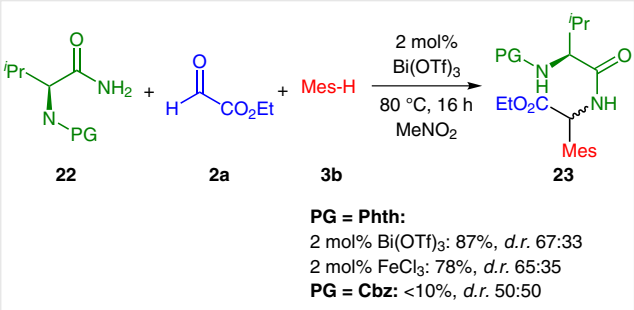
ties could be achieved. Therefore, further studies into the field of asymmetric three-component reactions were not pursued.

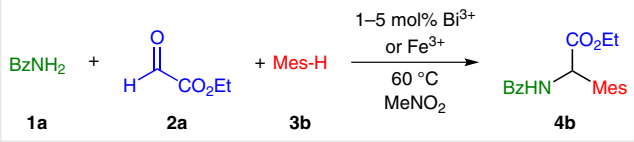


22 2a 3b 23

Scheme 13 Reaction of *N*-protected valine amide **22**. Yields are given for the isolated products. Phth = phthaloyl, PG = protecting group.

Mechanistic Investigations

In order to gain further insight into the reaction mechanism and the different catalytic activities of $Bi(OTf)_3$ and Fe^{3+} salts, a series of experiments were performed. First the progress of the reaction between benzamide (**1a**), ethyl glyoxalate (**2a**), and mesitylene (**3b**) in the presence of different catalysts as well as catalyst loadings was monitored by gas chromatographic analysis (Scheme 14, Figures 2 and 3).



1a 2a 3b 4b

Scheme 14 Model reaction for kinetic experiments

In order to obtain a clearer distinction between the different systems, the reaction was performed at a slightly decreased temperature of 60 °C. Initially we compared the rates for conversion of the limiting starting material, benzamide (**1a**), and product formation with 5 mol% of $Bi(OTf)_3$ and 5 mol% $Fe(ClO_4)_3$. In both cases an interesting observation was made: the rates of benzamide conversion and product formation deviate significantly from each other at the onset of the reaction (Figure 2).

In the case of $Fe(ClO_4)_3$, a fast conversion of the benzamide (20% conversion after 10 min and 70% after 45 min) was observed. However, the rate of product formation was slower (<1% yield after 10 min and 50% yield after 45 min). Similar observations were made with 5 mol% of $Bi(OTf)_3$ (20% and 45% conversion vs 2% yield and 30% yield after 10 and 45 min, respectively). Since in both cases the yield of α-arylglycine **4b** exceeded 90% after 24 hours reaction time, no unproductive side-reactions of benzamide can account for the fast conversion of the amide component. Therefore, formation of some kind of productive intermediate, most probably by the reaction of two of the three components, has to take place.

As can be seen from Figure 3, $Fe(ClO_4)_3$ catalyzes the reaction with a higher efficiency than $Bi(OTf)_3$, both at high (5 mol%) and low (1 mol%) catalyst loading. With 5 mol% $Fe(ClO_4)_3$ 64% of the amidoalkylated product is observed after 60 minutes, compared to only 28% with 5 mol% $Bi(OTf)_3$. As expected, reduction of the catalyst loading to 1 mol% leads to a considerable decrease in the reaction rate (Figure 3).

Interestingly, $FeCl_3{\cdot}6H_2O$ displays the lowest catalytic activity. After 50 minutes at 60 °C, only 5% product formation was observed with 5 mol% $FeCl_3{\cdot}6H_2O$. Presumably, a facile dissociation of the noncoordinating counterions to form an active metal catalyst is crucial for a high activity.[31] We have to emphasize that under our standard reaction conditions (80 °C; 16 h, 24 h, respectively) all three catalysts [$Fe(ClO_4)_3$, $FeCl_3{\cdot}6H_2O$, and $Bi(OTf)_3$] give similar yields at 5 mol% and even 2 mol% loadings (>90% in all cases). To our surprise, $Bi(OTf)_3$, the catalyst with the best performance with less reactive arenes, displayed an inferior activity compared to $Fe(ClO_4)_3$ in the reaction with mesitylene

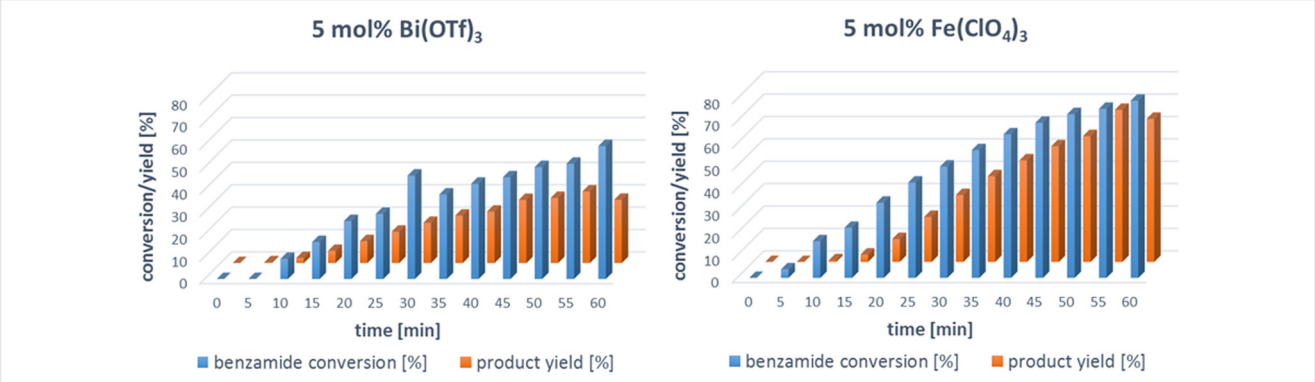


Figure 2 Comparison of the rates of benzamide conversion and product formation

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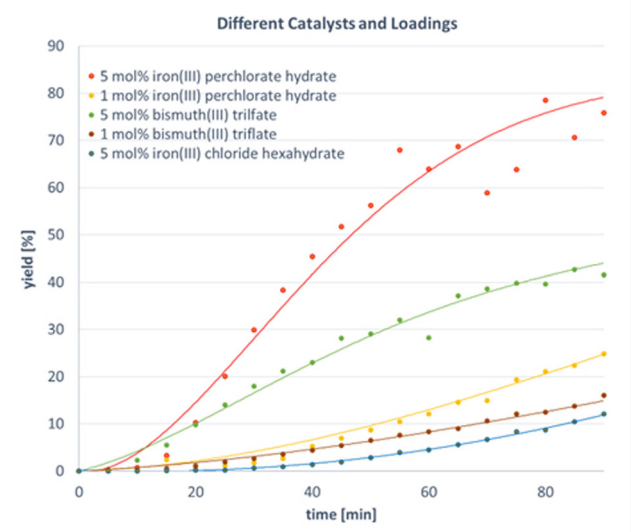

Figure 3 Rates of product formation with different catalyst loadings

(Figure 3). Therefore, $Fe(ClO_4)_3$ is the catalyst of choice for more reactive arenes, considering the activity and the economic and ecologic aspects of iron(III) salts.

As outlined in the introduction, our first rationale for the development of these three-component reactions was the in situ formation of a reactive *N*-acylimine species. Initial experiments indicated the formation of a two-component adduct of benzamide with one of the other starting materials (Figure 2). Therefore, we examined the reaction between benzamide (**1a**) and ethyl glyoxalate (**2a**) in the presence of 5 mol% $Fe(ClO_4)_3$ or 5 mol% $Bi(OTf)_3$ (Scheme 15). At room temperature quantitative formation of *N*,*O*-hemiaminal **24a** is observed within 24 hours (Scheme 15). Longer reaction times (96 h) or heating to 80 °C led to the formation of bisamide **25a**, insoluble in most common organic solvents, in almost quantitative yields. Indeed, the formation and precipitation of bisamide **25** could be observed in some of our three-component reactions. During the reaction bisamide **25a** is consumed completely and at the end the reaction mixture becomes homogenous again. Due to the insolubility of bisamide **25a** and the instability of bisamide **25a** and hemiaminal **24a**, we were not able to quantify the amount of both intermediates during the course of the reaction with the analytical methods available at our department (GC, HPLC, React-IR, or NMR). Neither were we able to detect any reactive *N*-acylimine species.[32] As expected, the reaction of benzamide (**1a**) and mesitylene (**3b**) in the presence of an iron or bismuth catalyst did not furnish any new product at all (Scheme 15). Treatment of either hemiaminal **24a** or bisamide **25a**, both known precursors for acylimines,[14] with $Bi(OTf)_3$ or $Fe(ClO_4)_3$ and mesitylene (**3b**) led to the expected formation of the aryl glycine derivative **4b** in 85 and 83% yield. To elucidate further reaction pathways, the two-component reaction of mesitylene (**3b**) with ethyl glyoxalate (**2a**) was investigated next. Both 2 mol% $Bi(OTf)_3$ and 2 mol% $Fe(ClO_4)_3$ furnished the double addition product **26** in 70–74% yield. Formation of such diarylmethane products was already observed in the case of more reactive (hetero)arenes (cf. Scheme 5) and is described in the literature.[27] Addition of a ligand, 2,2′-bipyridine (bipy) to the iron-catalyzed reaction, enabled the controlled synthesis of monoaddition product **27** in 66% yield. Alcohol **27** is the presumed intermediate in the synthesis of diarylmethane products of type **26**. We next examined alcohol **27** as a possible intermediate in our three-component reaction. Treatment of **27** with 1.0 equivalent of benzamide and 2.0 equivalents of mesitylene under our standard reaction conditions did furnish the expected product **4b** and diarylmethane derivative **26** in less than 5% yield, using either $Bi(OTf)_3$ or $Fe(ClO_4)_3$. These experiments indicate that alcohol **27** is not involved in the main reaction pathway. On the basis of these results, we assume the following mechanism (Scheme 15). In the first step, the amide adds to the glyoxylic acid derivative **2** to form hemiaminal **24**. Elimination of water furnishes a reactive acylimine species **28**. Trapping of this highly electrophilic imine with a second molecule of the amide gives bisamide **25**, observed intermediate in some of our three-component reactions. The fast addition of a second amide is not surprising, if one considers the higher nucleophilicity of the amide nitrogen.[18] Under the reaction conditions, bisamide **25**, favored under kinetic control, can decompose to yield the reactive *N*-acylimine **28**. In the presence of a suitable, nucleophilic arene, the *N*-acylimine can undergo an aza-Friedel–Crafts type reaction to afford the desired α-arylglycine product **4** containing a thermodynamically more stable C–C bond. The catalytic activity of the used catalyst greatly depends on two factors. On the one hand, the catalyst has to be stable in the presence of significant amounts of water, since up to 100 equivalents of water are generated during the course of the reaction (with respect to the catalyst).

On the other hand the catalyst has to promote the addition of the amide **1** to the glyoxalate **2** over the direct addition of the arene **3** to the aldehyde **2**. Only the right combination of both reactivities leads to an efficient catalyst for these three-component reactions. In addition, the Lewis acidic catalyst could further activate the *N*-acylimine towards the addition of a nucleophile. This might partially explain the higher activity of $Bi(OTf)_3$, a strong Lewis acid, in reactions with less nucleophilic arenes.[28] Another possible explanation for the high catalytic efficiency of bismuth as well as the observed improved regioselectivities is the activation of the arene component by the bismuth catalyst. Although Bi(III)-arene complexes have been reported in literature, we do not have any solid experimental evidence for an additional activation of the arene component.[33] We assume that two factors contribute to the observed low stereoselectivities in our asymmetric approaches. The high intrin-

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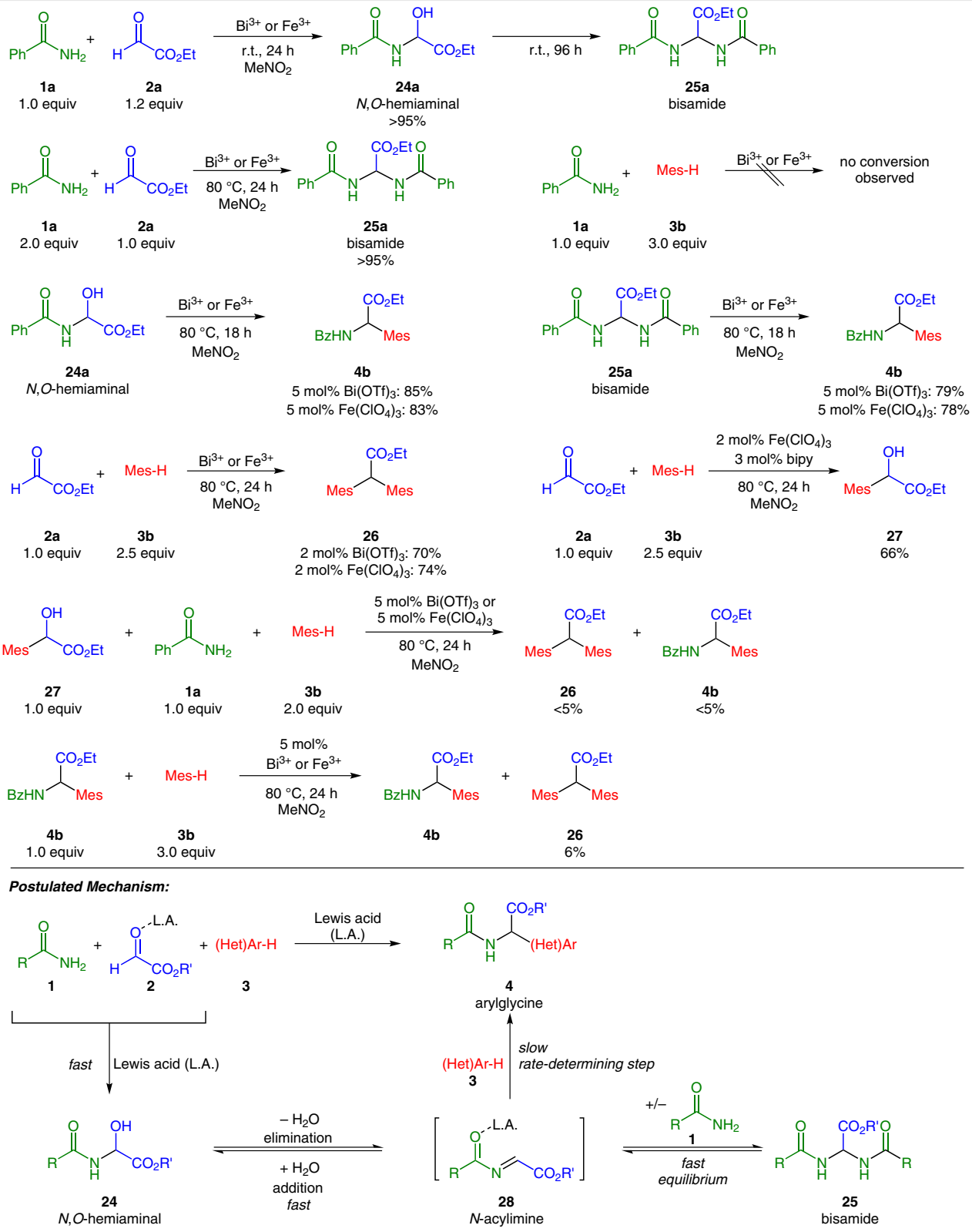

Scheme 15 Mechanistic studies and postulated reaction pathway

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sic reactivity of *N*-acylimines leads to a low selectivity in general, both for the diastereoselective and enantioselective reactions. As reported in the literature, coordination of a Lewis acid to the *N*-acylimine takes place at the oxygen atom.[34] This places the catalyst far away from the reactive center, thereby severely hampering any stereochemical induction by the ligand. Based on this assumption, one can rationalize that tailor-made sterically very demanding ligands should offer a solution to this problem. However, the catalytic activity of such encumbered systems might be too low for these types of multicomponent reactions.

Conclusion and Outlook

In summary, two general $Bi(OTf)_3$- and Fe^{3+}-catalyzed three-component reactions between amides, (hetero)arenes, and glyoxylic acid derivatives have been developed. Scope and limitations as well as advantages and disadvantages of both catalyst systems were investigated in detail. These investigations show that very cheap Fe^{3+} salts are the catalysts of choice in most reactions. The lower activity of iron-based catalysts offers an additional advantage in the case of very reactive arene components. On the other hand, the high activity of $Bi(OTf)_3$ significantly expands the scope of the three-component reaction and allows the utilization of less reactive arenes and sulfonamides. Investigations into potential asymmetric versions of the three-component reaction were unsuccessful. No enantioselective reaction was realized and the diastereoselective induction with chiral amide components was low to moderate. Mechanistic investigations indicate a reaction pathway via formation of a reactive, highly electrophilic acylimine followed by an aza-Friedel–Crafts-type reaction with the arene as nucleophilic component. These practical and operationally simple reactions enable the efficient and straightforward synthesis of N-protected arylglycines from simple commercial available starting materials and nontoxic catalysts. With water as the only generated side-product, these methods constitute a promising approach towards the sustainable synthesis of important α-amino acids.

For reactions and column chromatography, solvents were obtained from different commercial suppliers in >97% purity and used as received.

All reactions were performed without any precautions to exclude ambient air or moisture. TLC was performed on precoated aluminum sheets (silica gel 60 F254). The spots were visualized by using UV radiation, I_2, or cerium(IV) ammonium molybdate. Flash column chromatography was performed by using Silica 60 (0.04–0.063 mm, 230–400 mesh). All yields refer to isolated yields of compounds estimated to be >95% pure, as determined by ^1H NMR spectroscopy. Melting points are uncorrected.

N-(*m*-Tolyl)pivalamide, *N*-(3-methoxyphenyl)pivalamide, 1-methoxy-3,5-dimethylbenzene, 2-methoxy-naphthalene, 1-tosyl-1*H*-pyrrole, 1-tosyl-1*H*-indole, *N*-(*o*-tolyl)pivalamide, *N*-(2-methoxy-phenyl)pivalamide, *N*-(4-methoxyphenyl)pivalamide, methanesulfonamide, 4-methylbenzenesulfonamide, 4-methoxybenzenesulfonamide, 4-bromobenzenesulfonamide, thiophene-2-sulfonamide, and 2-(1,3-dioxoisoindolin-2-yl)-3-methylbutanamide were synthesized according to literature.[16] Ethyl glyoxalate was obtained as 50 wt% solution in toluene. Glyoxylic acid was obtained as 50 wt% solution in H_2O and used as received. All other starting materials were purchased from commercial sources and used without further purification. $Fe(ClO_4)_3$ was obtained as undefined hydrate ($Fe(ClO_4)_3{\cdot}xH_2O$, yellow form, reagent grade) from different providers. The exact H_2O content was determined by elemental analysis. Depending on the provider and storage time (or even the time for weighting out a defined amount for elemental analysis) $Fe(ClO_4)_3$ contained from one up to ten molecules of H_2O. Therefore, the amount of $Fe(ClO_4)_3$ used is always calculated on anhyd $Fe(ClO_4)_3$. No changes in catalytic activity were observed for different batches of $Fe(ClO_4)_3$ or upon prolonged storage times. No special precautions were taken to avoid exposure of $Fe(ClO_4){\cdot}xH_2O$ to moisture. **Caution!** Perchlorate salts are known to be shock-sensitive and are potential explosives. They should be handled with care and the necessary precautions. Since most of these properties are associated with anhyd perchlorate salts, we strongly advise to **use the hydrated form of $Fe(ClO_4)_3$. Under no circumstances should $Fe(ClO_4)_3$ be dried or handled in its anhydrous form**. Since similar yields are obtained even with the decahydrate $Fe(ClO_4)_3{\cdot}10H_2O$, this is not necessary. Special precautions should be taken to avoid accidental drying of the perchlorate, for example, by accidental evaporation of the solvent from the reaction. During our studies we never encountered problems associated with $Fe(ClO_4)_3$. Even prolonged heating of $Fe(ClO_4)_3$ in $MeNO_2$ up to 120 °C did not lead to any decomposition. (In fact it is known the anhydrous $LiClO_4$ is stable in Et_2O at temperatures up to 140–150 °C. For further information on perchlorate safety and stability, we recommend the article of Long.[35]

Anhyd $Bi(OTf)_3$ was obtained from different providers and used directly. No special precautions were taken to avoid exposure of $Bi(OTf)_3$ to moisture. Therefore, we cannot rule out the formation of $Bi(OTf)_3{\cdot}xH_2O$ during storage. Indeed, depending on the provider and storage time (or even the time for weighting out a defined amount for elemental analysis) $Bi(OTf)_3$ contained up to six molecules of water. However, no changes in catalytic activity and yield even upon prolonged storage (>1 year) were observed. Therefore, the amount of $Bi(OTf)_3$ used is always calculated on anhyd $Bi(OTf)_3$. The actual catalyst loading for particular reactions might be slightly lower, depending on the batch quality and storage time.

^1H and ^{13}C NMR spectra were recorded at 300, 400, or 500 MHz and 75, 101, or 126 MHz, respectively. Chemical shifts are reported as δ-values relative to the residual $CDCl_3$ or DMSO-d_6 peak (δ = 7.26 for ^1H and δ = 77.16 for ^{13}C; δ = 2.50 for ^1H and δ = 39.52 for ^{13}C). Coupling constants (*J*) are given in Hz and standard abbreviations are used for signal multiplicities.

Mass spectra (MS) were measured using ESI (electrospray ionization) techniques. High-resolution mass spectra (HRMS) were measured using MALDI (Matrix-assisted Laser Desorption/Ionization) techniques.

IR spectra were recorded on an FTIR (Fourier transform infrared spectroscopy) spectrophotometer including a diamond universal ATR sampling technique (attenuated total reflectance) from 4000–400 cm^{-1}. The absorption bands were reported in wave numbers (cm^{-1}).

Three-Component Synthesis of α-Arylglycines; General Procedure (GP)

A 10 mL screw cap vial was charged with the respective iron salt (1–5 mol%) or $Bi(OTf)_3$ (1–5 mol%), the appropriate amide (1.0 equiv), and $MeNO_2$ (4.0 mL/mmol amide) (or DCE wherever applicable). Ethyl glyoxalate (1.2 equiv) and the appropriate aromatic compound

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(3.0 equiv) were added under vigorous stirring. Ethyl glyoxalate was used as a 50 wt% solution in toluene (technical form) and used as received for the reactions with iron(III) salts. For the reaction with $Bi(OTf)_3$ toluene was removed in vacuo (1 mbar, 3 h) in order to avoid side reactions. The resulting oil was redissolved in $MeNO_2$. The reaction mixture was heated to 40–100 °C and stirred at this temperature. After cooling to r.t., the reaction mixture was diluted with EtOAc and filtered through a short plug of Celite and silica gel. The plug was rinsed with additional EtOAc. The combined filtrates were concentrated under reduced pressure. Purification of the crude residue by column chromatography (cyclohexane/EtOAc, then *n*-hexane/EtOAc) afforded the analytically pure product.

Ethyl 2-Benzamido-2-(2,4-dimethylphenyl)acetate (4a)

Bi Catalysis: Compound **4a** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (122 mg, 1.2 mmol, 1.2 equiv), *m*-xylene (0.37 mL, 3.0 mmol, 3.0 equiv), and $Bi(OTf)_3$ (13 mg, 0.02 mmol, 2 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as a colorless solid [276 mg, 89%; ratio of regioisomers (*r.r.*) = >98:2].

Fe Catalysis: Compound **4a** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), *m*-xylene (0.18 mL, 1.5 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (9 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless solid (141 mg, 91%; *r.r.* = >98:2). Further purification of the major regioisomer could be achieved by precipitation from hexane/CH_2Cl_2 (only major regioisomer, as judged by ^{1}H NMR). Analytical data were obtained for this purified regioisomer.

Mp 98.2 °C; R_f = 0.54 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3304 (w), 2985 (w), 2360 (w), 1745 (s), 1635 (s), 1601 (w), 1580 (w), 1523 (s), 1487 (m), 1371 (w), 1348 (m), 1324 (w), 1212 (s), 1189 (m), 1150 (m), 1095 (m), 1021 (m), 929 (w), 872 (w), 810 (w), 774 (w), 722 cm^{-1} (m).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (dd, *J* = 5.3, 3.3 Hz, 2 H), 7.52–7.40 (m, 3 H), 7.17 (d, *J* = 7.8 Hz, 1 H), 7.07–6.96 (m, 3 H), 5.93 (d, *J* = 7.1 Hz, 1 H), 4.31–4.11 (m, 2 H), 2.52 (s, 3 H), 2.30 (s, 3 H), 1.23 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.8, 166.7, 138.4, 136.9, 133.9, 132.5, 131.9, 131.8, 128.7, 127.33, 127.3, 126.4, 62.0, 53.5, 21.2, 19.6, 14.2.

MS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{22}NO_3$: 312.2; found: 312.2.

HRMS (MALDI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{22}NO_3$: 312.1594; found: 312.1596.

Ethyl 2-Benzamido-2-mesitylacetate (4b)

Bi Catalysis: Compound **4b** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 1.2 mmol, 1.2 equiv), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 1 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as a colorless solid (308 mg, 95%).

Fe Catalysis: Compound **4b** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv), and $FeCl_3{\cdot}6H_2O$ (3 mg, 0.010 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless solid (153 mg, 94%).

Mp 77.6 °C; R_f = 0.50 (cyclohexane/EtOAc = 7:3)

IR (ATR): 3320 (m), 2980 (w), 1727 (s), 1632 (s), 1579 (m), 1525 (s), 1488 (m), 1382 (w), 1339 (w), 1311 (m), 1242 (s), 1136 (m), 1082 (m), 1020 (s), 929 (m), 852 (m), 800 (m), 713 (m), 689 (s), 622 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 7.5 Hz, 2 H), 7.47 (dt, *J* = 15.0, 7.2 Hz, 3 H), 7.18 (d, *J* = 6.1 Hz, 1 H), 6.85 (d, *J* = 7.8 Hz, 2 H), 6.19 (d, *J* = 6.6 Hz, 1 H), 4.34–4.12 (m, 2 H), 2.48 (s, 6 H), 2.25 (s, 3 H), 1.22 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.9, 166.6, 137.8, 137.1, 134.1, 131.8, 131.0, 130.2, 128.7, 127.2, 62.2, 52.8, 21.0, 20.5, 14.2.

MS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{24}NO_3$: 326.2; found: 326.1.

HRMS (MALDI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{24}NO_3$: 326.1751; found: 326.1751.

Ethyl 2-Benzamido-2-(4-methoxyphenyl)acetate (4c)

Bi Catalysis: Compound **4c** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (122 mg, 1.2 mmol, 1.2 equiv), anisole (0.32 mL, 3.0 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 1 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as a colorless solid (236 mg, 75%; *r.r.* = 75:25).

Fe Catalysis: Compound **4c** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), anisole (0.16 mL, 1.5 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (9 mg, 0.050 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless solid (105 mg, 67%; *r.r.* = 75:25). Further purification of the major regioisomer could be achieved by precipitation from hexane/CH_2Cl_2 (*r.r.* = 78:22, as judged by ^{1}H NMR analysis). Analytical data were obtained for this purified mixture.

Mp 65.6 °C; R_f = 0.49 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3319 (w), 2964 (w), 1737 (s), 1633 (s), 1578 (w), 1530 (m), 1512 (s), 1490 (m), 1462 (w), 1366 (w), 1317 (m), 1248 (s), 1022 (m), 801 (m), 762 (m), 692 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ (major regioisomer) = 7.78–7.72 (m, 2 H), 7.47–7.28 (m, 5 H), 7.03 (d, *J* = 6.6 Hz, 1 H), 6.85–6.79 (m, 2 H), 5.63 (d, *J* = 7.0 Hz, 1 H), 4.24–4.07 (m, 2 H), 3.72 (s, 3 H), 1.20–1.14 (m, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.3, 166.5, 159.7, 133.8, 131.8, 131.6, 130.8, 129.8, 128.9, 128.7, 128.5 128.4, 127.1, 121.1, 114.4, 111.1, 62.0, 61.6, 56.3, 55.6, 55.3, 53.9, 14.0 (peaks not assigned to regioisomers).

MS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{19}NO_4Na$: 336.1; found: 336.4.

HRMS (MALDI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{20}NO_4$ 314.1387, found 314.1384.

Ethyl 2-Benzamido-2-(4-methoxy-3-methylphenyl)acetate (4d)

Bi Catalysis: Compound **4d** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), 1-methoxy-2-methylbenzene (0.19 mL, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 5 mol%) in

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$MeNO_2$ (4.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless solid (115 mg, 70%; *r.r.* = >98:2).

Fe Catalysis: Compound **4d** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.24 mL, 1.2 mmol, 1.2 equiv), 1-methoxy-2-methylbenzene (0.37 mL, 3.0 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (18 mg, 0.05 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless solid (223 mg, 68%; *r.r.* = 94:6). Further purification of the major regioisomer could be achieved by precipitation from hexane/CH_2Cl_2 (only major regioisomer, as judged by ^{1}H NMR analysis). Analytical data were obtained for this purified regioisomer.

Mp 95.0 °C; R_f = 0.51 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3323 (w), 2361 (w), 1733 (s), 1635 (s), 1579 (m), 1531 (m), 1508 (m), 1451 (w), 1347 (m), 1315 (m), 1278 (m), 1249 (s), 878 (m), 800 (m), 751 (m), 691 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 7.4 Hz, 2 H), 7.51 (t, *J* = 7.3 Hz, 1 H), 7.43 (t, *J* = 7.5 Hz, 2 H), 7.26 (m, 2 H), 7.06 (d, *J* = 6.6 Hz, 1 H), 6.80 (d, *J* = 8.4 Hz, 1 H), 5.66 (d, *J* = 7.0 Hz, 1 H), 4.34–4.13 (m, 2 H), 3.82 (s, 3 H), 2.21 (s, 3 H), 1.25 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.5, 166.6, 158.1, 134.0, 131.9, 129.7, 128.7, 128.4, 127.5, 127.3, 126.1, 110.3, 62.0, 56.5, 55.5, 16.4, 14.2.

MS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{21}NO_4Na$: 350.1; found: 350.3.

HRMS (MALDI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{22}NO_4$: 328.1543; found: 328.1543.

Ethyl 2-Benzamido-2-(4-methoxy-2-methylphenyl)acetate (4e)

Bi Catalysis: Compound **4e** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), 1-methoxy-3-methylbenzene (0.19 mL, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless solid (97 mg, 59%; *r.r.* = 80:20).

Fe Catalysis: Compound **4e** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), 1-methoxy-3-methylbenzene (0.19 mL, 1.5 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (9 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless solid (121 mg, 63%; *r.r.* = 75:25). Further purification of the major regioisomer could be achieved by precipitation from hexane/CH_2Cl_2 (84:16 mixture of regioisomers, as judged by ^{1}H NMR analysis). Analytical data were obtained for this purified mixture.

Mp 90.2 °C; R_f = 0.51 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3343 (w), 2937 (w), 1732 (s), 1638 (s), 1611 (m), 1579 (m), 1486 (m), 1347 (m), 1293 (m), 1252 (s), 1111 (m), 1079 (m), 925 (w), 862 (m), 761 (m), 691 (s), 626 cm^{-1} (m).

^{1}H NMR (400 MHz, $CDCl_3$): δ (major regioisomer) = 7.89–7.73 (m, 2 H), 7.55–7.38 (m, 3 H), 7.23–7.15 (m, 1 H), 7.00 (d, *J* = 6.5 Hz, 1 H), 6.82–6.70 (m, 2 H), 5.89 (d, *J* = 6.9 Hz, 1 H), 4.32–4.11 (m, 2 H), 3.79 (s, 3 H), 2.53 (s, 3 H), 2.35 (s, 1 H), 1.27–1.16 (m, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.8, 166.7, 159.6, 138.7, 133.9, 131.9, 131.7, 130.7, 128.7, 128.6, 128.6, 127.8, 127.7, 127.3, 127.3, 121.8, 116.6, 112.2, 111.9, 62.0, 55.7, 55.4, 53.3, 21.8, 19.9, 14.2 (peaks not assigned to regioisomers).

MS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{22}NO_4$: 328.2; found: 328.3.

HRMS (MALDI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{22}NO_4$: 328.1543; found: 328.1543.

Ethyl 2-Benzamido-2-(2-methoxy-5-methylphenyl)acetate (4f)

Bi Catalysis: Compound **4f** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), 1-methoxy-4-methylbenzene (0.19 mL, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless solid (102 mg, 62%; *r.r.* = >98:2).

Fe Catalysis: Compound **4f** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.24 mL, 1.2 mmol, 1.2 equiv), 1-methoxy-4-methylbenzene (0.38 mL, 3.0 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (18 mg, 0.05 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless solid (205 mg, 63%; *r.r.* = >98:2).

Mp 100.3 °C; R_f = 0.51 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3263 (m), 2908 (w), 2832 (w), 1732 (s), 1637 (s), 1579 (w), 1524 (m), 1506 (m), 1461 (m), 1390 (w), 1365 (m), 1323 (s), 1254 (s), 1206 (s), 1135 (s), 1091 (s), 1033 (s), 978 (w), 874 (m), 805 (s), 761 (m), 717 (s), 690 (s), 604 cm^{-1} (m).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82–7.77 (m, 2 H), 7.52–7.46 (m, 1 H), 7.42 (t, *J* = 7.4 Hz, 2 H), 7.29 (d, *J* = 8.1 Hz, 1 H), 7.25 (d, *J* = 1.9 Hz, 1 H), 7.10 (dd, *J* = 8.3, 1.7 Hz, 1 H), 6.80 (d, *J* = 8.3 Hz, 1 H), 5.89 (d, *J* = 8.3 Hz, 1 H), 4.25–4.16 (m, 2 H), 3.83 (s, 3 H), 2.30 (s, 3 H), 1.21 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.3, 166.7, 155.1, 134.4, 131.7, 131.6, 130.6, 130.2, 128.6, 127.3, 125.5, 111.2, 61.7, 55.8, 54.1, 20.6, 14.3.

MS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{21}NO_4Na$: 350.1; found: 350.2.

HRMS (MALDI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{22}NO_4$: 328.1543; found: 328.1543.

Ethyl 2-Benzamido-2-(3-chloro-4-methoxyphenyl)acetate (4g)

Bi Catalysis: Compound **4g** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (122 mg, 1.2 mmol, 1.2 equiv), 2-chloroanisole (0.38 mL, 3.0 mmol, 3.0 equiv), and $Bi(OTf)_3$ (13 mg, 0.02 mmol, 2 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless solid (266 mg, 77%; *r.r.* = >98:2).

Fe Catalysis: Compound **4g** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.24 mL, 1.2 mmol, 1.2 equiv), 2-chloroanisole (0.38 mL, 3.0 mmol, 3.0 equiv) and $FeCl_3{\cdot}6H_2O$ (14 mg, 0.05 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as colorless solid (235 mg, 68%; *r.r.* = >98:2).

Mp 89.0 °C; R_f = 0.49 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3310 (w), 2976 (w), 1730 (s), 1634 (s), 1604 (m), 1578 (m), 1525 (s), 1489 (s), 1372 (w), 1342 (m), 1292 (s), 1255 (s), 1188 (s), 1093 (s), 1063 (s), 1023 (s), 919 (w), 875 (m), 795 (m), 689 cm^{-1} (s).

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^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85–7.79 (m, 2 H), 7.55–7.41 (m, 4 H), 7.33 (dd, *J* = 8.5, 2.2 Hz, 1 H), 7.19 (d, *J* = 6.6 Hz, 1 H), 6.93–6.89 (m, 1 H), 5.67 (d, *J* = 6.8 Hz, 1 H), 4.32–4.15 (m, 2 H), 3.89 (s, 3 H), 1.25 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.8, 166.4, 155.1, 133.5, 131.9, 130.0, 128.9, 128.7, 127.2, 127.0, 123.0, 112.2, 62.3, 56.2, 55.9, 14.03.

MS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{19}ClNO_4$: 348.1; found: 348.0.

HRMS (MALDI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{19}ClNO_4$: 348.0997; found: 348.0996.

Ethyl 2-Benzamido-2-(3-bromo-4-methoxyphenyl)acetate (4h)

Bi Catalysis: Compound **4h** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol), ethyl glyoxalate (122 mg, 1.2 mmol), 2-bromoanisole (0.37 mL, 3.0 mmol, 3.0 equiv), and $Bi(OTf)_3$ (13 mg, 0.02 mmol, 2 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as a colorless solid (344 mg, 88%; *r.r.* = >98:2).

Fe Catalysis: Compound **4h** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.30 mL, 1.5 mmol, 1.5 equiv), 2-bromoanisole (0.37 mL, 3.0 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (18 mg, 0.05 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a colorless solid (289 mg, 74%; *r.r.* = >98:2).

Mp 103.7 °C; R_f = 0.51 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3387 (w), 2992 (w), 2942 (w), 1739 (s), 1654 (s), 1602 (w), 1580 (w), 1519 (m), 1498 (m), 1484 (s), 1443 (m), 1367 (w), 1342 (w), 1286 (m), 1261 (s), 1213 (s), 1179 (s), 1152 (m), 1096 (w), 1055 (m), 799 (m), 713 (s), 688 (m), 665 cm^{-1} (m).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85–7.80 (m, 2 H), 7.61 (d, *J* = 2.2 Hz, 1 H), 7.52 (m, 1 H), 7.44 (dd, *J* = 10.2, 4.6 Hz, 2 H), 7.38 (dd, *J* = 8.5, 2.2 Hz, 1 H), 7.18 (d, *J* = 6.6 Hz, 1 H), 6.90–6.86 (m, 1 H), 5.68 (d, *J* = 6.7 Hz, 1 H), 4.32–4.16 (m, 2 H), 3.89 (s, 3 H), 1.25 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.9, 166.6, 156.2, 133.7, 132.1, 132.1, 130.6, 128.8, 127.9, 127.3, 112.3, 112.2, 62.4, 56.5, 55.9, 14.2.

MS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{19}BrNO_4$: 392.0; found: 392.9.

HRMS (MALDI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{19}BrNO_4$: 392.0492; found: 392.0491.

Ethyl 2-Benzamido-2-(3-iodo-4-methoxyphenyl)acetate (4i)

Bi Catalysis: Compound **4i** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (122 mg, 1.2 mmol, 1.2 equiv), 2-iodoanisole (0.40 mL, 3.0 mmol, 3.0 equiv), and $Bi(OTf)_3$ (13 mg, 0.02 mmol, 2 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as a colorless solid (355 mg, 81%; *r.r.* = >98:2).

Fe Catalysis: Compound **4i** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (122 mg, 1.2 mmol, 1.2 equiv), 2-iodoanisole (0.40 mL, 3.0 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (7 mg, 0.02 mmol, 2 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless solid (333 mg, 76%; *r.r.* = >98:2).

Mp 120.6 °C; R_f = 0.54 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3390 (w), 2362 (w), 1840 (s), 1655 (s), 1600 (w), 1579 (w), 1518 (m), 1483 (s), 1367 (w), 1343 (w), 1286 (m), 1259 (m), 1214 (s), 1180 (s), 1153 (m), 1097 (w), 1048 (m), 1012 (s), 927 (w), 799 (m), 714 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86–7.78 (m, 3 H), 7.56–7.38 (m, 4 H), 7.17 (d, *J* = 6.6 Hz, 1 H), 6.80 (d, *J* = 8.5 Hz, 1 H), 5.65 (d, *J* = 6.8 Hz, 1 H), 4.32–4.15 (m, 2 H), 3.87 (s, 3 H), 1.25 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.0, 166.6, 158.4, 138.2, 133.7, 132.1, 131.1, 129.0, 128.8, 127.3, 111.1, 86.5, 62.4, 56.6, 55.7, 14.1.

MS (ESI): *m*/*z* $[M]^+$ calcd for $C_{18}H_{18}INO_4$: 439.0; found: 439.2.

HRMS (MALDI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{19}INO_4$: 440.0353; found: 440.0345.

Ethyl 2-Benzamido-2-(5-bromo-2-methoxyphenyl)acetate (4j)

Bi Catalysis: Compound **4j** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol), ethyl glyoxalate (122 mg, 1.2 mmol), 4-bromoanisole (0.38 mL, 3.0 mmol, 3.0 equiv), and $Bi(OTf)_3$ (33 mg, 0.05 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 16 h at 100 °C. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as a colorless solid (161 mg, 41%; *r.r.* = >98:2).

Fe Catalysis: Compound **4j** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol), ethyl glyoxalate (0.24 mL, 1.2 mmol), 4-bromoanisole (0.38 mL, 3.0 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (18 mg, 0.05 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 16 h at 100 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a colorless solid (132 mg, 34%; *r.r.* = >98:2).

Mp 129.2 °C; R_f = 0.56 (cyclohexane/EtOAc = 7:3).

IR (ATR): 1738 (m), 1638 (s), 1576 (m), 1520 (m), 1486 (s), 1365 (s), 1337 (m), 1315 (s), 1247 (s), 1188 (s), 1176 (s), 1131 (m), 1087 (s), 1026 (s), 900 (m), 868 (m), 801 (s), 759 (w), 718 (m), 688 (s), 669 (s), 653 (s), 618 (s), 590 (s), 539 (m), 500 cm^{-1} (w).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (d, *J* = 7.3 Hz, 2 H), 7.56 (d, *J* = 2.4 Hz, 1 H), 7.53–7.38 (m, 4 H), 7.28–7.24 (m, 1 H), 6.82–6.75 (m, 1 H), 5.88 (d, *J* = 8.0 Hz, 1 H), 4.27–4.17 (m, 2 H), 3.84 (s, 3 H), 1.21 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.7, 166.7, 156.4, 134.1, 133.5, 132.5, 131.9, 128.7, 128.0, 127.3, 113.3, 113.0, 62.0, 56.1, 53.4, 14.2.

MS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{19}BrNO_4$ 392.1; found: 392.1.

Anal. Calcd for $C_{18}H_{18}BrNO_4$: C, 55.12; H, 4.63; N, 3.57. Found: C, 54.86; H, 4.50; N, 3.42.

Ethyl 2-Benzamido-2-(5-iodo-2-methoxyphenyl)acetate (4k)

Bi Catalysis: Compound **4k** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (122 mg, 1.2 mmol, 1.2 equiv), 4-iodoanisole (702 mg, 3.0 mmol, 3.0 equiv), and $Bi(OTf)_3$ (33 mg, 0.05 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 16 h at 100 °C. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as a colorless solid (261 mg, 59%; *r.r.* = >98:2).

Fe Catalysis: Compound **4k** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.24 mL, 1.2 mmol, 1.2 equiv), 4-iodoanisole (702 mg, 3.0 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (18 mg, 0.05 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless solid (221 mg, 50%; *r.r.* = >98:2).

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Mp 102.4 °C; R_f = 0.46 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3277 (w), 3054 (w), 2933 (w), 2835 (w), 1739 (s), 1637 (s), 1602 (w), 1578 (w), 1523 (m), 1486 (s), 1456 (m), 1391 (w), 1366 (w), 1336 (m), 1317 (m), 1294 (m), 1247 (s), 1188 (s), 1134 (m), 1093 (m), 1025 (s), 800 (m), 689 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.83–7.75 (m, *J* = 13.0, 7.6 Hz, 2 H), 7.75–7.68 (m, 1 H), 7.63–7.37 (m, 4 H), 7.31–7.20 (m, 1 H), 6.71–6.64 (m, 1 H), 5.86 (d, *J* = 8.0 Hz, 1 H), 4.26–4.15 (m, 2 H), 3.82 (s, 3 H), 1.21 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.7, 166.7, 157.2, 139.2, 138.6, 134.1, 131.9, 128.7, 128.4, 127.3, 113.5, 83.2, 62.0, 55.9, 53.3, 14.3.

MS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{18}H_{18}INO_4Na$: 462.0; found: 462.2.

HRMS (MALDI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{19}INO_4$: 440.0353; found: 440.0347.

Ethyl 2-Benzamido-2-(2,5-dimethylphenyl)acetate (4l)

Bi Catalysis: Compound **4l** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), *p*-xylene (0.19 mL, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless oil (62 mg, 40%).

Fe Catalysis: Compound **4l** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), *p*-xylene (0.19 mL, 1.5 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (9 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless oil (53 mg, 32%); R_f = 0.38 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3338 (w), 2977 (w), 2925 (w), 2869 (w), 1737 (s), 1638 (s), 1578 (w), 1531 (s), 1489 (m), 1366 (w), 1344 (s), 1285 (m), 1219 (m), 1198 (s), 1077 (w), 1021 (m), 808 (w), 689 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 7.4 Hz, 2 H), 7.55–7.41 (m, 3 H), 7.13–7.01 (m, 4 H), 5.93 (d, *J* = 7.0 Hz, 1 H), 4.35–4.11 (m, 2 H), 2.51 (s, 3 H), 2.30 (s, 3 H), 1.29–1.19 (m, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.6, 166.5, 136.1, 135.0, 133.8, 133.7, 131.8, 130.9, 129.2, 128.6, 127.2, 127.0, 61.9, 53.6, 21.0, 19.1, 14.0.

MS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{22}NO_3$: 312.2; found: 312.2.

HRMS (MALDI): *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{22}NO_3$: 312.1594; found 312.1595.

Ethyl 2-Benzamido-2-(3-methyl-5-pivalamidophenyl)acetate (4m)

Bi Catalysis: Compound **4m** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), 3-methylpivalanilide (287 mg, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (16 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 100 °C. Purification by chromatography (*n*-hexane/EtOAc 4:1) yielded the product as a yellow solid (13 mg, 67%; *r.r.* = >98:2).

Fe Catalysis: Compound **4m** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.0 equiv), 3-methylpivalanilide (287 mg, 1.5 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (9 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 100 °C. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as a yellow solid (158 mg, 80%; *r.r.* = 71:29).

Mp 157–159 °C; R_f = 0.5 (*n*-hexane/EtOAc = 1:1).

IR (ATR): 3244 (w), 2962 (w), 1742 (s), 1666 (m), 1638 (s), 1600 (m), 1582 (w), 1524 (s), 1505 (s), 1481 (m), 1443 (m), 1399 (m), 1387 (m), 1369 (m), 1335 (s), 1252 (m), 1194 (s), 1158 (s), 1105 (m), 1076 (m), 1019 (m), 949 (w), 911 (m), 872 (m), 839 (w), 829 (w), 814 (w), 796 (w), 769 (m), 691 (s), 665 (m), 596 (m), 567 (w), 519 (w), 489 cm^{-1} (w).

^1H NMR (400 MHz, $CDCl_3$): δ (major regioisomer) = 7.80–7.78 (m, 2 H), 7.52–7.48 (m, 1 H), 7.44–7.37 (m, 4 H), 7.31 (br s, 1 H), 7.23 (d, *J* = 8.2 Hz, 1 H), 7.08 (br d, *J* = 6.7 Hz, 1 H), 5.90 (d, *J* = 6.9 Hz, 1 H), 4.27–4.12 (m, 2 H), 2.53 (s, 3 H), 1.30 (s, 9 H), 1.22 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ (major regioisomer) = 176.8, 171.6, 166.7, 138.2, 138.1, 133.8, 131.9, 131.2, 128.7, 127.2, 127.2, 122.3, 118.1, 62.1, 53.4, 39.7, 27.7, 19.7, 14.1.

MS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{28}N_2O_4$: 396.2; found: 419.1.

HRMS (MALDI): *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{28}N_2O_4$: 397.2122; found: 397.2182.

Ethyl 3-(1-Benzamido-2-ethoxy-2-oxoethyl)-4-methoxybenzoate (4n)

Bi Catalysis: Compound **4n** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), ethyl 4-methoxybenzoate (360 mg, 2.0 mmol, 4.0 equiv), and $Bi(OTf)_3$ (16 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 72 h at 100 °C. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as a yellow oil (77 mg, 40%; *r.r.* = >98:2).

Fe Catalysis: Compound **4n** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.0 equiv), ethyl 4-methoxybenzoate (270 mg, 1.5 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (9 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 100 °C. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as a yellow oil (128 mg, 66%; *r.r.* = 71:28); R_f = 0.3 (hexane/EtOAc = 7:3).

IR (ATR): 3342 (w), 2981 (w), 2843 (w), 1741 (m), 1711 (s), 1650 (s), 1608 (m), 1580 (m), 1506 (m), 1484 (m), 1465 (m), 1445 (m), 1391 (w), 1368 (m), 1322 (m), 1297 (m), 1265 (s), 1238 (s), 1204 (s), 1188 (s), 1130 (s), 1103 (m), 1023 (s), 913 (m), 862 (m), 831 (m), 801 (m), 771 (m), 713 (s), 692 (m), 647 (m), 630 (m), 589 (m), 541 (m), 473 cm^{-1} (m).

^1H NMR (300 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 2.1 Hz, 1 H), 8.04 (dd, *J* = 8.6, 2.2 Hz, 1 H), 7.82–7.79 (m, 2 H), 7.53–7.43 (m, 3 H), 7.27 (br s, 1 H), 6.93 (d, *J* = 8.7 Hz, 1 H), 6.00 (d, *J* = 8.0 Hz, 1 H), 4.35 (q, *J* = 7.1 Hz, 2 H), 4.20 (q, *J* = 7.1 Hz, 2 H), 3.92 (s, 3 H), 1.38 (t, *J* = 7.1 Hz, 3 H), 1.20 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.86, 166.73, 166.11, 160.76, 134.16, 132.20, 132.13, 131.84, 128.69, 127.31, 125.93, 123.56, 110.71, 61.98, 61.01, 56.06, 53.61, 14.53, 14.23.

MS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{21}H_{23}NO_6Na$: 408.1; found: 408.1.

HRMS (MALDI): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{24}NO_6$ 386.1598; found: 386.1600.

Ethyl 2-Benzamido-2-(3,4,5-trimethoxyphenyl)acetate (4o)

Bi Catalysis: Compound **4o** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), 1,2,3-trimethoxybenzene (253 mg, 3.0 mmol, 3.0 equiv), $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%), and in $MeNO_2$

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(2.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 7:3) yielded the product as a colorless oil (127 mg, 68%; *r.r.* = >98:2).

Fe Catalysis: Compound **4o** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.24 mL, 1.2 mmol, 1.2 equiv), 1,2,3-trimethoxybenzene (505 mg, 3.0 mmol, 3.0 equiv), $Fe(ClO_4)_3$ (18 mg, 0.05 mmol, 5 mol%), and 2,2′-bipyridine (0.06 mmol, 6 mol%, 9 mg) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 100 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 7:3) yielded the product as a colorless oil (216 mg, 58%; *r.r.* = >98:2); R_f = 0.23 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3347 (w), 2979 (w), 2939 (w), 2837 (w), 1721 (m), 1670 (m), 1600 (m), 1581 (m), 1516 (m), 1494 (s), 1465 (w), 1418 (m), 1369 (m), 1313 (m), 1278 (s), 1244 (s), 1203 (s), 1172 (s), 1092 (s), 1055 (s), 1015 (s), 964 (m), 909 (m), 873 (m), 798 (m), 746 (m), 713 (m), 692 (m), 667 (m), 570 (m), 514 cm^{-1} (m).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.83–7.79 (m, 2 H), 7.52–7.47 (m, 1 H), 7.45–7.40 (m, 2 H), 7.32 (d, *J* = 7.8 Hz, 1 H), 7.12 (d, *J* = 8.6 Hz, 1 H), 6.67–6.64 (m, 1 H), 5.86 (d, *J* = 7.9 Hz, 1 H), 4.31–4.15 (m, 2 H), 3.95 (s, 3 H), 3.86 (s, 3 H), 3.86 (s, 3 H), 1.23 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.5, 166.7, 154.3, 151.8, 142.2, 134.3, 131.8, 128.7, 127.3, 124.6, 123.5, 107.3, 61.9, 61.1, 60.9, 56.1, 53.6, 14.3.

MS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{23}NO_6Na$: 396.1; found: 396.3.

HRMS (MALDI): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{24}NO_6$: 374.1598; found: 374.15988.

Ethyl 2-Benzamido-2-(4-methoxy-2,6-dimethylphenyl)acetate (4p)

Bi Catalysis: Compound **4p** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), 1-methoxy-3,5-dimethylbenzene (204 mg, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (*n*-hexane/EtOAc = 9:1 → 4:1) yielded the product as a colorless oil (84 mg, 50%; *r.r.* = 67:33).

Fe Catalysis: Compound **4p** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), 1-methoxy-3,5-dimethylbenzene (204 mg, 1.5 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (9 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 100 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a yellowish oil (106 mg, 62%; *r.r.* = 50:50); R_f = 0.57 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3449 (w), 3319 (s), 2977 (m), 2840 (w), 2099 (s), 1739 (s), 1655 (s), 1651 (s), 1624 (m), 1599 (m), 1580 (m), 1512 (s), 1482 (s), 1446 (m), 1367 (m), 1318 (s), 1251 (s), 1207 (s), 1186 (s), 1147 (s), 1094 (s), 1024 (s), 1002 (m), 973 (m), 931 (m), 906 (m), 887 (m), 862 (m), 848 (m), 810 (s), 745 (m), 709 (s), 691 (s), 672 (m), 645 (m), 608 (m), 590 (m), 546 (m), 526 (m), 502 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.82–7.77 (m, 2 H), 7.50–7.39 (m, 3 H), 7.17 (d, *J* = 6.1 Hz, 1 H), 6.75–6.44 (m, 2 H), 6.23–6.12 (m, 1 H), 4.32–4.10 (m, 2 H), 3.85–3.74 (m, 3 H), 2.56 (s, 2 H), 2.49 (s, 2 H), 2.31 (s, 2 H), 1.28–1.15 (m, 3 H) (peaks not assigned to regioisomers).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.9, 171.5, 166.6, 166.4, 158.7, 157.5, 139.0, 138.3, 134.5, 133.9, 131.7, 131.5, 128.6, 128.5, 127.2, 127.1, 126.3, 124.2, 122.2, 114.4, 109.7, 62.0, 61.4, 55.5, 55.0, 52.5, 50.2, 21.5, 20.8, 19.9, 14.2, 14.1 (peaks not assigned to regioisomers).

MS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{24}NO_4$: 342.1; found: 342.2.

HRMS (MALDI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{24}NO_4$: 342.1053; found: 342.1696.

Ethyl 2-Benzamido-2-(2-methoxynaphthalen-1-yl)acetate (4q)

Bi Catalysis: Compound **4q** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), 2-methoxynaphthalene (237 mg, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as an orange oil (89 mg, 49%).

Fe Catalysis: Compound **4q** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), 2-methoxynaphthalene (237 mg, 1.5 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (9 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as an orange oil (123 mg, 64%); R_f = 0.31 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3446 (w), 2979 (w), 2841 (w), 2099 (w), 1739 (s), 1651 (s), 1626 (m), 1598 (m), 1580 (m), 1560 (m), 1512 (s), 1482 (s), 1473 (s), 1445 (m), 1386 (s), 1367 (m), 1319 (m), 1267 (s), 1251 (s), 1204 (s), 1185 (s), 1147 (s), 1086 (s), 1024 (s), 906 (m), 888 (w), 864 (m), 848 (m), 810 (s), 783 (m), 709 (s), 692 (s), 672 (m), 645 (m), 605 (m), 589 (m), 546 (m), 526 (m), 502 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 8.36 (d, *J* = 8.7 Hz, 1 H), 7.88 (d, *J* = 9.0 Hz, 1 H), 7.84–7.78 (m, 3 H), 7.62–7.57 (m, 1 H), 7.50–7.36 (m, 5 H), 7.30 (d, *J* = 9.0 Hz, 1 H), 6.86 (d, *J* = 8.9 Hz, 1 H), 4.23–4.16 (m, 2 H), 3.99 (s, 3 H), 1.16 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.8, 167.0, 155.3, 134.4, 132.6, 131.7, 130.8, 129.6, 128.7, 128.6, 127.8, 127.4, 124.1, 123.1, 119.5, 113.1, 61.7, 56.6, 49.0, 14.3.

MS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{22}NO_4$: 364.2; found: 364.3.

HRMS (MALDI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{22}NO_4$: 364.1543; found: 364.1544.

Ethyl 2-Benzamido-2-(pyren-4-yl)acetate (4r)

Bi Catalysis: Compound **4r** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), pyrene (303 mg, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as a colorless solid (111 mg, 54%; *r.r.* = >98:2).

Fe Catalysis: Compound **4r** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), pyrene (303 mg, 1.5 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (9 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 20:1 → 9:1 → 4:1) yielded the product as a colorless solid (115 mg, 57%; *r.r.* = >98:2).

Mp 207.3 °C; R_f = 0.48 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3331 (w), 2985 (w), 2360 (w), 2342 (w), 1740 (s), 1635 (s), 1602 (w), 1579 (w), 1517 (w), 1489 (m), 1374 (w), 1349 (m), 1313 (w), 1204 (s), 1183 (m), 1150 (m), 1089 (m), 1021 (m), 845 (s), 824 (m), 692 cm^{-1} (s).

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^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.61–8.54 (m, 1 H), 8.25–8.01 (m, 8 H), 7.86–7.79 (m, 2 H), 7.49 (dd, *J* = 14.0, 6.6 Hz, 1 H), 7.40 (t, *J* = 7.5 Hz, 2 H), 7.26 (s, 1 H), 6.83 (d, *J* = 7.3 Hz, 1 H), 4.36–4.15 (m, 2 H), 1.18 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.8, 166.9, 133.8, 132.0, 131.8, 131.4, 130.9, 130.1, 129.3, 128.9, 128.7, 128.2, 127.4, 127.3, 126.4, 125.8, 125.7, 125.4, 125.2, 125.1, 124.8, 122.8, 62.3, 54.3, 14.2.

MS (ESI): *m*/*z* $[M]^+$ calcd for $C_{27}H_{21}NO_3$: 407.2; found: 407.2.

HRMS (MALDI): *m*/*z* $[M]^+$ calcd for $C_{27}H_{21}NO_3$: 407.1516; found: 407.1513.

Ethyl 2-Mesityl-2-(4-methoxybenzamido)acetate (5a)

Bi Catalysis: Compound **5a** was synthesized according to the GP from 4-methoxybenzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless solid (145 mg, 81%).

Fe Catalysis: Compound **5a** was synthesized according to the GP from 4-methoxybenzamide (73 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv), and $FeCl_3{\cdot}6H_2O$ (3 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1 → 7:3) yielded the product as a colorless solid (166 mg, 94%).

Mp 109.8 °C; R_f = 0.36 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3432 (w), 2921 (m), 2851 (m), 1726 (m), 1652 (s), 1605 (m), 1524 (w), 1486 (s), 1366 (m), 1349 (m), 1306 (m), 1252 (s), 1214 (w), 1193 (s), 1175 (s), 1088 (m), 1021 (s), 845 (m), 767 cm^{-1} (m).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 8.7 Hz, 2 H), 7.08 (d, *J* = 6.3 Hz, 1 H), 6.92 (d, *J* = 8.7 Hz, 2 H), 6.85 (s, 2 H), 6.18 (d, *J* = 6.5 Hz, 1 H), 4.32–4.11 (m, 2 H), 3.84 (s, 3 H), 2.47 (s, 6 H), 2.25 (s, 3 H), 1.22 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.1, 166.1, 162.5, 137.7, 137.1, 131.1, 130.1, 129.0, 126.3, 113.9, 62.1, 55.5, 52.8, 21.0, 20.5, 14.2.

MS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{26}NO_4$ 356.2; found: 356.2.

HRMS (MALDI): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{26}NO_4$ 356.1856; found: 356.1856.

Ethyl 2-(4-Bromobenzamido)-2-mesitylacetate (5b)

Bi Catalysis: Compound **5b** was synthesized according to the GP from 4-bromobenzamide (100 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless solid (161 mg, 80%).

Fe Catalysis: Compound **5b** was synthesized according to the GP from 4-bromobenzamide (100 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv), and $FeCl_3{\cdot}6H_2O$ (3 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a colorless solid (172 mg, 85%).

Mp 89.5 °C; R_f = 0.70 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3427 (w), 2969 (w), 1731 (s), 1660 (s), 1607 (w), 1588 (m), 1566 (w), 1506 (s), 1473 (s), 1366 (m), 1352 (w), 1309 (s), 1256 (m), 1212 (w), 1189 (s), 1159 (m), 881 (m), 848 (m), 777 (m), 751 (s), 613 cm^{-1} (m).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71–7.51 (m, 4 H), 7.14 (d, *J* = 6.2 Hz, 1 H), 6.86 (s, 2 H), 6.15 (d, *J* = 6.5 Hz, 1 H), 4.33–4.12 (m, 2 H), 2.46 (s, 6 H), 2.25 (s, 3 H), 1.22 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.8, 165.6, 137.9, 137.1, 132.89, 132.0, 130.8, 130.2, 128.8, 126.6, 62.3, 52.9, 21.0, 20.5, 14.2.

MS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{20}H_{22}BrNO_3Na$: 428.1; found 428.2.

HRMS (MALDI): *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{23}BrNO_3$: 404.0856; found: 404.0854.

Ethyl 2-Mesityl-2-(4-nitrobenzamido)acetate (5c)

Bi Catalysis: Compound **5c** was synthesized according to the GP from 4-nitrobenzamide (83 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless solid (125 mg, 68%).

Fe Catalysis: Compound **5c** was synthesized according to the GP from 4-nitrobenzamide (166 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.24 mL, 1.2 mmol, 1.2 equiv), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv), and $FeCl_3{\cdot}6H_2O$ (14 mg, 0.050 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a colorless solid (329 mg, 89%).

Mp 119.2 °C; R_f = 0.36 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3349 (w), 2978 (w), 1731 (s), 1634 (m), 1598 (m), 1525 (s), 1488 (m), 1460 (w), 1343 (m), 1297 (m), 1240 (s), 1148 (w), 1077 (m), 1024 (m), 928 (w), 876 (m), 853 (m), 799 (m), 761 (w), 720 (s), 679 cm^{-1} (m).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.28 (d, *J* = 8.7 Hz, 2 H), 7.95 (d, *J* = 8.7 Hz, 2 H), 7.27–7.22 (m, 1 H), 6.87 (s, 2 H), 6.15 (d, *J* = 6.4 Hz, 1 H), 4.34–4.12 (m, 2 H), 2.46 (s, 6 H), 2.26 (s, 3 H), 1.23 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.6, 164.6, 149.9, 139.6, 138.2, 137.1, 130.4, 130.3, 128.4, 124.0, 62.5, 53.1, 21.0, 20.5, 14.2.

MS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{20}H_{22}N_2O_5Na$: 393.1; found: 393.3.

HRMS (MALDI): *m*/*z* $[M + Na]^+$ calcd for $C_{20}H_{22}N_2O_5Na$: 393.1421; found: 393.1421.

Ethyl 2-(2-Chloroacetamido)-2-mesitylacetate (5d)

Bi Catalysis: Compound **5d** was synthesized according to the GP from 2-chloroacetamide (47 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv), $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1 → 7:3) yielded the product as a colorless oil (121 mg, 81%).

Fe Catalysis: Compound **5d** was synthesized according to the GP from 2-chloroacetamide (47 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv), and $FeCl_3{\cdot}6H_2O$ (3 mg, 0.010 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1 → 7:3) yielded the product as a colorless oil (131 mg, 88%); R_f = 0.30 = (cyclohexane/EtOAc = 7:3).

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IR (ATR): 3307 (w), 2975 (w), 1733 (s), 1660 (m), 1519 (m), 1463 (w), 1370 (w), 1311 (m), 1195 (s), 1150 (m), 1096 (m), 1017 (s), 925 (w), 853 (m), 769 cm^{-1} (m).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.59 (d, *J* = 6.2 Hz, 1 H), 6.87–6.82 (m, 2 H), 5.99 (d, *J* = 7.2 Hz, 1 H), 4.32–3.97 (m, 4 H), 2.40 (s, 6 H), 2.25 (s, 3 H), 1.21 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.1, 165.3, 138.4, 137.1, 130.4, 130.2, 129.9, 69.3, 62.2, 52.5, 42.7, 21.0, 20.4, 20.1, 14.2.

MS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{20}ClNO_3Na$: 320.1; found: 320.2.

HRMS (MALDI): *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{21}ClNO_3$: 298.1205; found: 298.1202.

Ethyl 2-Acetamido-2-mesitylacetate (5e)

Bi Catalysis: Compound **5e** was synthesized according to the GP from acetamide (59 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (122 mg, 1.2 mmol, 1.2 equiv), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv), and $Bi(OTf)_3$ (33 mg, 0.05 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1 → 1:1) yielded the product as a colorless solid (209 mg, 79%).

Fe Catalysis: Compound **5e** was synthesized according to the GP from acetamide (30 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv), and $FeCl_3{\cdot}6H_2O$ (7 mg, 0.020 mmol, 2 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1 → 1:1) yielded the product as a colorless solid (93 mg, 70%).

Mp 95.8 °C; R_f = 0.29 (cyclohexane/EtOAc = 1:1).

IR (ATR): 3302 (m), 2976 (w), 2360 (w), 1748 (s), 1649 (s), 1524 (s), 1366 (m), 1310 (w), 1281 (w), 1211 (s), 1192 (s), 1149 (m), 1124 (m), 1022 (m), 855 (m), 832 (w), 797 (w), 644 cm^{-1} (m).

^1H NMR (400 MHz, $CDCl_3$): δ = 6.84 (s, 2 H), 6.40 (d, *J* = 6.4 Hz, 1 H), 6.02 (d, *J* = 7.2 Hz, 1 H), 4.28–4.07 (m, 2 H), 2.38 (s, 6 H), 2.25 (s, 3 H), 2.01 (s, 3 H), 1.19 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.9, 169.4, 137.8, 137.0, 131.2, 130.1, 62.0, 52.2, 23.2, 21.0, 20.4, 14.2.

MS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{21}NO_3Na$: 286.1; found: 286.2.

HRMS (MALDI): *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{22}NO_3$: 264.1594; found: 264.1597.

Ethyl 2-Mesityl-2-pivalamidoacetate (5f)

Bi Catalysis: Compound **5f** was synthesized according to the GP from pivalamide (100 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (122 mg, 1.2 mmol, 1.2 equiv), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 1 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless oil (248 mg, 81%).

Fe Catalysis: Compound **5f** was synthesized according to the GP from pivalamide (50 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv) and $FeCl_3{\cdot}6H_2O$ (3 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless oil (122 mg, 80%); R_f = 0.44 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3448 (w), 2961 (m), 1731 (s), 1670 (s), 1611 (w), 1494 (s), 1395 (w), 1366 (m), 1308 (m), 1257 (m), 1185 (s), 1100 (m), 1016 (m), 907 (w), 852 (m), 770 cm^{-1} (w).

^1H NMR (300 MHz, $CDCl_3$): δ = 6.83 (s, 2 H), 6.68 (d, *J* = 6.0 Hz, 1 H), 5.96 (d, *J* = 6.7 Hz, 1 H), 4.30–4.06 (m, 2 H), 2.40 (s, 6 H), 2.24 (s, 3 H), 1.24–1.16 (m, 12 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.7, 172.0, 137.60, 137.0, 131.1, 130.1, 62.0, 52.4, 38.9, 27.7, 21.0, 20.4, 14.2.

MS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{28}NO_3$: 306.2; found: 306.2.

HRMS (MALDI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{28}NO_3$: 306.2064; found: 306.2064.

Ethyl 2-Acrylamido-2-mesitylacetate (5g)

Bi Catalysis: Compound **5g** was synthesized according to the GP from acrylamide (71 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (122 mg, 1.2 mmol, 1.2 equiv), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 1 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless solid (226 mg, 82%).

Fe Catalysis: Compound **5g** was synthesized according to the GP from acrylamide (71 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.24 mL, 1.2 mmol, 1.2 equiv), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv), and $FeCl_3{\cdot}6H_2O$ (7 mg, 0.02 mmol, 2 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 7:3) yielded the product as a colorless solid (233 mg, 85%).

Mp 117.2 °C; R_f = 0.43 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3304.43 (s), 2983 (s), 1748 (s), 1652 (m), 1614 (m), 1519 (s), 1404 (m), 1368 (s), 1311 (s), 1209 (m), 1187 (s), 1148 (m), 1113 (m), 1072 (s), 1023 (m), 990 (m), 958 (s), 856 (m), 810 (m), 604 cm^{-1} (m).

^1H NMR (400 MHz, $CDCl_3$): δ = 6.84 (s, 2 H), 6.59 (t, *J* = 16.2 Hz, 1 H), 6.29 (dd, *J* = 16.9, 1.0 Hz, 1 H), 6.16 (dd, *J* = 17.0, 10.1 Hz, 1 H), 6.07 (d, *J* = 6.9 Hz, 1 H), 5.66 (dd, *J* = 10.1, 1.0 Hz, 1 H), 4.30–4.09 (m, 2 H), 2.40 (s, 6 H), 2.24 (s, 3 H), 1.20 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.8, 164.7, 137.8, 137.1, 130.9, 130.4, 130.1, 127.4, 62.1, 52.4, 21.0, 20.4, 14.2.

MS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{22}NO_3$: 276.2; found: 276.2.

HRMS (MALDI): *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{22}NO_3$: 276.1594; found: 276.1595.

Ethyl 2-[(Ethoxycarbonyl)amino]-2-mesitylacetate (5h)

Bi Catalysis: Compound **5h** was synthesized according to the GP from ethyl carbamate (45 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as colorless crystals (126 mg, 86%).

Fe Catalysis: Compound **5h** was synthesized according to the GP from ethyl carbamate (45 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv), and $FeCl_3{\cdot}6H_2O$ (3 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a colorless solid (121 mg, 83%).

Mp 54.1 °C; R_f = 0.40 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3374 (m), 2964 (s), 1705 (s), 1612 (w), 1509 (m), 1391 (w), 1366 (m), 1308 (s), 1263 (w), 1220 (m), 1173 (w), 1091 (m), 1053 (s), 947 (w), 847 (w), 781 (m), 732 (w), 694 (w), 639 cm^{-1} (w).

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^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.84 (s, 2 H), 5.83–5.71 (m, 1 H), 5.67 (d, *J* = 6.1 Hz, 1 H), 4.16 (d, *J* = 91.0 Hz, 4 H), 2.37 (s, 6 H), 2.25 (s, 3 H), 1.27–1.17 (m, 6 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.6, 155.8, 137.5, 136.7, 131.2, 129.8, 61.7, 61.0, 53.3, 20.7, 20.0, 14.4, 14.0.

MS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{24}NO_4$: 294.2; found: 294.2.

HRMS (MALDI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{24}NO_4$: 294.1700; found: 294.1700.

Ethyl 2-{[Benzyloxy)carbonyl]amino}-2-mesitylacetate (5i)

Bi Catalysis: Compound **5i** was synthesized according to the GP from benzyl carbamate (76 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a colorless solid (116 mg, 65%).

Fe Catalysis: Compound **5i** was synthesized according to the GP from benzyl carbamate (76 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv), and $FeCl_3{\cdot}6H_2O$ (3 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a colorless solid (91 mg, 51%).

Mp 73.5 °C; R_f = 0.38 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3363 (m), 2957 (s), 2360 (m), 1728 (m), 1701 (s), 1521 (s), 1479 (w), 1455 (w), 1370 (w), 1306 (m), 1231 (s), 1048 (s), 986 (m), 916 (w), 824 (m), 794 (m), 752 (s), 700 (s), 606 cm^{-1} (m).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43–7.01 (m, 5 H), 6.85 (s, 2 H), 5.88–5.55 (m, 2 H), 5.17–4.99 (m, 2 H), 4.29–4.06 (m, 2 H), 2.38 (s, 6 H), 2.26 (s, 3 H), 1.19 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.7, 155.8, 137.8, 136.9, 136.4, 131.3, 130.1, 130.1, 128.7, 128.3, 67.2, 62.0, 53.7, 21.0, 20.3, 14.2.

MS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{25}NO_4Na$: 378.2; found: 378.3.

HRMS (MALDI): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{25}NO_4Na$: 378.1677; found: 378.1681.

Ethyl 2-{[(Allyloxy)carbonyl]amino}-2-mesitylacetate (5j)

Bi Catalysis: Compound **5j** was synthesized according to the GP from allyloxycarbamate (51 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as a colorless oil (128 mg, 84%).

Fe Catalysis: Compound **5j** was synthesized according to the GP from allyloxycarbamate (102 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.24 mL, 1.2 mmol, 1.2 equiv), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv), and $FeCl_3{\cdot}6H_2O$ (14 mg, 0.05 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 20:1 → 9:1 → 4:1) yielded the product as a colorless oil (215 mg, 70%); R_f = 0.63 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3376 (w), 2981 (w), 1831 (w), 1718 (s), 1649 (w), 1611 (w), 1498 (m), 1369 (m), 1305 (m), 1195 (s), 1093 (m), 1053 (s), 932 (m), 852 (m), 775 cm^{-1} (m).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.84 (s, 2 H), 5.98–5.68 (m, 3 H), 5.35–5.15 (m, 2 H), 4.63–4.47 (m, 2 H), 4.30–4.07 (m, 2 H), 2.37 (s, 6 H), 2.25 (s, 3 H), 1.20 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.8, 155.6, 137.8, 136.9, 132.8, 131.3, 130.1, 118.0, 66.0, 62.0, 53.7, 21.0, 20.3, 14.2.

MS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{24}NO_4$: 306.2; found: 306.2.

HRMS (MALDI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{24}NO_4$: 306.1700; found: 306.1700.

Ethyl 2-({[(9*H*-Fluoren-9-yl)methoxy]carbonyl}amino)-2-mesitylacetate (5k)

Bi Catalysis: Compound **5k** was synthesized according to the GP from (9*H*-fluoren-9-yl)methyl carbamate (120 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 3.0 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as a colorless oil (185 mg, 83%).

Fe Catalysis: Compound **5k** was synthesized according to the GP from (9*H*-fluoren-9-yl)methyl carbamate (239 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.24 mL, 1.2 mmol, 1.2 equiv), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv), and $FeCl_3{\cdot}6H_2O$ (5 mg, 0.020 mmol, 2 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1) yielded the product as a colorless oil (332 mg, 75%); R_f = 0.69 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3368 (w), 2956 (w), 1718 (s), 1611 (w), 1498 (m), 1448 (m), 1305 (m), 1195 (s), 1050 (s), 852 (m), 739 (s), 621 cm^{-1} (m).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 7.5 Hz, 2 H), 7.63–7.47 (m, 2 H), 7.45–7.26 (m, 4 H), 6.86 (s, 2 H), 5.90–5.49 (m, 2 H), 4.44–4.11 (m, 5 H), 2.35 (s, 6 H), 2.27 (s, 3 H), 1.21 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.7, 155.7 144.1, 143.9, 141.4, 137.9, 137.0, 131.1, 130.2, 127.8, 127.2, 125.2, 120.1, 67.3, 62.1, 53.8, 47.3, 21.0, 20.4, 14.2.

MS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{28}H_{29}NO_4Na$: 466.2; found: 466.0.

HRMS (MALDI): *m*/*z* [M + Na]$^+$ calcd for $C_{28}H_{29}NO_4Na$: 466.1989; found: 466.1993.

Ethyl 2-Benzamido-2-(5-bromothiophen-2-yl)acetate (7a)

Bi Catalysis: Compound **7a** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), 2-bromothiophene (0.15 mL, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 16 h at 60 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a yellow solid (102 mg, 55%; *r.r.* = >98:2).

Fe Catalysis: Compound **7a** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.24 mL, 1.2 mmol, 1.2 equiv), 2-bromothiophene (0.29 mL, 3.0 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (18 mg, 0.05 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a yellow solid (219 mg, 60%; *r.r.* = >98:2).

Mp 95.2 °C; R_f = 0.58 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3309 (w), 2995 (w), 2929 (w), 1738 (s), 1636 (s), 1604 (w), 1570 (w), 1525 (s), 1488 (m), 1371 (m), 1292 (s), 1205 (s), 1171 (m), 1123 (w), 1083 (m), 1012 (m), 810 (m), 755 (m), 716 (s), 691 cm^{-1} (s).

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^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 7.7 Hz, 2 H), 7.57–7.51 (m, 1 H), 7.49–7.43 (m, 2 H), 7.16–7.08 (m, 1 H), 6.94–6.77 (m, 2 H), 5.99–5.92 (m, 1 H), 4.37–4.23 (m, 2 H), 1.32 (t, *J* = 7.1 Hz, 3 H) (peaks not assigned to regioisomers).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.6, 166.7, 140.7, 137.8, 133.4, 132.3, 130.0, 128.8, 127.3, 126.6, 126.2, 125.7, 112.7, 62.8, 52.6, 14.2 (peaks not assigned to regioisomers).

MS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{14}BrNO_3SNa$: 390.0; found: 390.1.

HRMS (MALDI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{14}BrNO_3S$: 367.9952; found: 367.9951.

Ethyl 2-(5-Bromothiophen-2-yl)-2-[(ethoxycarbonyl)amino]acetate (7b)

Bi Catalysis: Compound **7b** was synthesized according to the GP from urethane (67 mg, 0.75 mmol, 1.5 equiv), ethyl glyoxalate (51 mg, 0.5 mmol, 1.0 equiv), 2-bromothiophene (0.16 mL, 1.5 mmol), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (1.0 mL). The reaction mixture was stirred for 16 h at 60 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a yellow solid (130 mg, 77%; *r.r.* = >98:2).

Fe Catalysis: Compound **7b** was synthesized according to the GP from urethane (89 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.24 mL, 1.2 mmol, 1.2 equiv), 2-bromothiophene (0.28 mL, 3.0 mmol), and $Fe(ClO_4)_3$ (18 mg, 0.05 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 48 h at 40 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a yellow solid (249 mg, 74%; *r.r.* = >98:2).

Mp 48.8 °C; R_f = 0.56 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3305 (m), 2983 (w), 2951 (w), 2904 (w), 1741 (s), 1686 (s), 1526 (m), 1499 (w), 1433 (m), 1372 (m), 1312 (m), 1295 (m), 1257 (m), 1216 (s), 1107 (s), 1061 (s), 1038 (s), 963 (s), 810 (w), 800 (w), 780 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.91 (d, *J* = 3.8 Hz, 1 H), 6.82 (d, *J* = 3.7 Hz, 1 H), 5.68 (s, 1 H), 5.53 (d, *J* = 7.4 Hz, 1 H), 4.31–4.20 (m, 2 H), 4.19–4.11 (m, 2 H), 1.31–1.23 (m, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.5, 155.6, 141.1, 129.9, 126.3, 112.6, 62.6, 61.7, 53.8, 14.6, 14.2.

MS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_{14}BrNO_4SNa$: 358.0; found: 358.1.

HRMS (MALDI): *m*/*z* [M + K]$^+$ calcd for $C_{11}H_{14}BrNO_4SK$: 373.9464; found: 373.9453.

Ethyl 2-Benzamido-2-(5-chlorothiophen-2-yl)acetate (7c)

Bi Catalysis: Compound **7c** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), 2-chlorothiophene (0.15 mL, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 16 h at 60 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a yellow solid (119 mg, 37%; *r.r.* = >98:2).

Fe Catalysis: Compound **7c** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.24 mL, 1.2 mmol, 1.2 equiv), 2-chlorothiophene (0.28 mL, 3.0 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (18 mg, 0.05 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a yellow low-melting solid (161 mg, 50%; *r.r.* = 63:37).

R_f = 0.58 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3300 (w), 2978 (w), 2929 (w), 1983 (w), 1983 (w), 1739 (s), 1635 (s), 1604 (w), 1579 (w), 1525 (s), 1587 (m), 1443 (m), 1369 (m), 1324 (m), 1290 (s), 1204 (s), 1166 (m), 1125 (m), 1086 (m), 1021 (m), 989 (m), 881 (m), 810 (m), 754 (m), 715 (s), 690 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 7.6 Hz, 2 H), 7.57–7.42 (m, 3 H), 7.12 (d, *J* = 6.3 Hz, 1 H), 6.95–6.76 (m, 2 H), 5.99–5.91 (m, 1 H), 4.37–4.23 (m, 2 H), 1.32 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.7, 166.7, 140.7, 137.8, 133.4, 132.3, 130.5, 130.0, 128.9, 127.3, 126.6, 126.2, 125.7, 62.8, 52.6, 52.6, 14.2 (peaks not assigned to regioisomers).

MS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{14}ClNO_3SNa$: 346.0; found: 346.2.

HRMS (MALDI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{15}ClNO_3S$: 324.0456; found: 324.0454.

Ethyl 2-(5-Chlorothiophen-2-yl)-2-[(ethoxycarbonyl)amino]acetate (7d)

Bi Catalysis: Compound **7d** was synthesized according to the GP from urethane (67 mg, 0.75 mmol, 1.5 equiv), ethyl glyoxalate (51 mg, 0.5 mmol, 1.0 equiv), 2-chlorothiophene (0.16 mL, 1.5 mmol), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (1.0 mL). The reaction mixture was stirred for 16 h at 60 °C. Purification by chromatography (cyclohexane/EtOAc 9:1 → 4:1) yielded the product as a yellow solid (76 mg, 52%; *r.r.* = >98:2).

Fe Catalysis: Compound **7d** was synthesized according to the GP from urethane (89 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.24 mL, 1.2 mmol, 1.2 equiv), 2-chlorothiophene (0.29 mL, 3.0 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (18 mg, 0.05 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 48 h at 40 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a yellow solid (219 mg, 75%; *r.r.* = >98:2).

Mp 46.9 °C; R_f = 0.56 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3310 (m), 2985 (w) 1741 (s), 1686 (s), 1528 (m), 1443 (m), 1371 (m), 1355 (m), 1206 (s), 1045 (s), 986 (s), 964 (w), 869 (w), 780 (m), 664 cm^{-1} (m).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.84–6.82 (m, 1 H), 6.77 (d, *J* = 3.8 Hz, 1 H), 5.68 (s, 1 H), 5.51 (d, *J* = 7.3 Hz, 1 H), 4.31–4.10 (m, 4 H), 1.34–1.14 (m, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.5 155.6, 138.2, 130.4, 126.2, 125.4, 62.6, 61.7, 53.9, 14.6, 14.1.

MS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_{14}ClNO_4SNa$: 314.0; found: 314.2.

HRMS (MALDI): *m*/*z* [M + K]$^+$ calcd for $C_{11}H_{14}ClNO_4SK$: 329.9964; found: 329.9970.

Ethyl 2-Benzamido-2-(5-methylthiophen-2-yl)acetate (7e)

Bi Catalysis: Compound **7e** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), 2-methylthiophene (0.15 mL, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (1.0 mL). The reaction mixture was stirred for 16 h at r.t. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless solid (97 mg, 64%; *r.r.* = 89:11).

Fe Catalysis: Compound **7e** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), 2-methylthiophene (0.15 mL, 1.5 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (9 mg, 0.025 mmol, 5 mol%) in $MeNO_2$

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(2.0 mL). The reaction mixture was stirred for 24 h at 60 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a yellow solid (72 mg, 47%; *r.r.* = 88:12).

Mp 66–68 °C; R_f = 0.3 (cyclohexane/EtOAc = 4:1).

IR (ATR): 3315 (w), 2981 (w), 2917 (w), 1737 (s), 1637 (s), 1603 (m), 1579 (m), 1523 (s), 1486 (s), 1446 (m), 1369 (m), 1327 (m), 1294 (m), 1229 (m), 1204 (s), 1172 (s), 1122 (m), 1083 (m), 1019 (s), 976 (m), 929 (w), 883 (w), 803 (m), 754 (m), 714 (s), 691 (s), 672 (s), 622 (m), 601 (s), 579 (s), 557 (s), 537 (s), 522 (s), 505 (m), 480 (m), 472 cm^{-1} (m).

^1H NMR (300 MHz, $CDCl_3$): δ (major regioisomer) = 7.83–7.79 (m, 2 H), 7.54–7.41 (m, 3 H), 7.05 (br d, *J* = 5.5 Hz, 1 H), 6.92–6.89 (m, 1 H), 6.64–6.60 (m, 1 H), 5.95 (d, *J* = 7.4 Hz, 1 H), 4.36–4.18 (m, 2 H), 2.44 (s, 3 H), 1.32–1.22 (m, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ (major regioisomer) = 171.21, 170.29, 166.66, 140.68, 136.33, 133.80, 133.68, 132.04, 131.94, 128.73, 127.32, 127.25, 126.37, 125.81, 125.26, 122.71, 62.39, 62.09, 52.63, 50.95, 15.43, 14.17, 13.25.

MS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{18}NO_3$: 303.1; found: 304.3.

HRMS (MALDI): *m*/*z* $[M + Na]^+$ calcd for $C_{16}H_{17}NO_3SNa$: 326.0821; found: 326.0821.

Ethyl 2-[(Ethoxycarbonyl)amino]-2-(5-methylthiophen-2-yl)acetate (7f)

Bi Catalysis: Compound **7f** was synthesized according to the GP from urethane (67 mg, 0.75 mmol, 1.5 equiv), ethyl glyoxalate (51 mg, 0.5 mmol, 1.0 equiv), 2-methylthiophene (0.15 mL, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in DCE (4.0 mL). The reaction mixture was stirred for 16 h at 60 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a colorless oil (97 mg, 72%; *r.r.* = >98:2).

Fe Catalysis: Compound **7f** was synthesized according to the GP from urethane (89 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.24 mL, 1.2 mmol, 1.2 equiv), 2-methylthiophene (0.29 mL, 3.0 mmol, 3.0 equiv) and $Fe(ClO_4)_3$ (18 mg, 0.050 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 48 h at 40 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a yellow oil (211 mg, 78%; *r.r.* = 93:7); R_f = 0.56 cyclohexane/EtOAc = 7:3).

IR (ATR): 3326 (w), 2985 (w), 2933 (w), 1710 (s), 1506 (s), 1370 (m), 1317 (m), 1200 (s), 1094 (w), 1053 (s), 862 (w), 798 (m), 778 cm^{-1} (m).

^1H NMR (300 MHz, $CDCl_3$): δ (major regioisomer) = 6.87–6.77 (m, 1 H), 6.62–6.51 (m, 1 H), 5.66–5.41 (m, 2 H), 4.31–4.09 (m, 4 H), 2.44 (s, 3 H), 1.29–1.19 (m, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ (major regioisomer) = 170.3, 155.7, 140.6, 136.6, 126.1, 125.2, 62.2, 61.5, 53.8, 15.4, 14.6, 14.2.

MS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{12}H_{17}NO_4SNa$: 294.1; found: 294.4.

HRMS (MALDI): *m*/*z* $[M + K]^+$ calcd for $C_{12}H_{17}NO_4SK$: 310.0510; found: 310.0511.

Ethyl 2-Benzamido-2-(benzofuran-2-yl)acetate (7g)

Fe Catalysis: Compound **7g** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.24 mL, 1.2 mmol, 1.2 equiv), benzofuran (0.33 mL, 3.0 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (18 mg, 0.050 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 60 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1) yielded the product as a yellow solid (166 mg, 51%, *r.r.* = >98:2).

Mp 79.4 °C; R_f = 0.59 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3299 (w), 3057 (w), 2991 (w), 1751 (s), 1639 (s), 1602 (w), 1579. (w), 1526 (s), 1488 (m), 1454 (m), 1369 (w), 1336 (m), 1241 (m), 1206 (s), 1156 (s), 1094 (m), 1016 (m), 961 (m), 820 (m), 749 (s), 716 (s), 689 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.89–7.82 (m, 2 H), 7.60–7.42 (m, 5 H), 7.35–7.19 (m, 3 H), 6.85 (s, 1 H), 6.09 (d, *J* = 7.7 Hz, 1 H), 4.37–4.21 (m, 2 H), 1.28 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.7, 166.8, 155.1, 151.5, 133.6, 132.2, 128.8, 128.1, 127.4, 124.9, 123.3, 121.5, 111.5, 106.1, 62.8, 51.3, 14.2.

MS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{19}H_{17}NO_4Na$: 346.1; found: 346.2.

HRMS (MALDI): *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{18}NO_4$: 324.1230; found: 324.1229.

Ethyl 2-(Benzofuran-2-yl)-2-[(ethoxycarbonyl)amino]acetate (7h)

Bi Catalysis: Compound **7h** was synthesized according to the GP from urethane (46 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), benzofuran (0.16 mL, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 16 h at 60 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a yellow solid (128 mg, 88%; *r.r.* = >98:2).

Fe Catalysis: Compound **7h** was synthesized according to the GP from urethane (89 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.24 mL, 1.2 mmol, 1.2 equiv), benzofuran (0.32 mL, 3.0 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (18 mg, 0.05 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 60 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a yellow solid (219 mg, 75%; *r.r.* = 80:20). Further purification of the major regioisomer could be achieved by precipitation from hexane/CH_2Cl_2 (91:9 mixture of regioisomers, as judged by ^1H NMR analysis). Analytical data were obtained for this purified mixture.

Mp 60.3 °C; R_f = 0.56 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3263 (w), 2983 (w), 1742 (m), 1688 (s), 1605 (w), 1533 (m), 1453 (m), 1369 (m), 1319 (s), 1245 (s), 1200 (s), 1093 (m), 1049 (s), 953 (m), 937 (m), 753 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ (major regioisomer) = 7.57–7.52 (m, 1 H), 7.49–7.42 (m, 1 H), 7.32–7.19 (m, 2 H), 6.76 (s, 1 H), 5.85–5.72 (m, 1 H), 5.71–5.58 (m, 1 H), 4.32–4.10 (m, 4 H), 1.29–1.22 (m, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.7, 155.8, 155.0, 151.8, 128.0, 124.9, 123.2, 121.4, 111.5, 105.5, 62.6, 61.7, 52.6, 14.6, 14.2 (peaks not assigned to regioisomers).

MS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{17}NO_5Na$: 314.1; found: 314.2.

HMRS (MALDI): *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{18}NO_5$: 292.1180; found: 292.1177.

Ethyl 2-(Benzamido)-2-(1-tosyl-1*H*-pyrrol-2-yl)acetate (7i)

Fe Catalysis: Compound **7i** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.24 mL, 1.2 mmol, 1.2 equiv), *N*-tosylpyrrole (664 mg, 3.0 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (18 mg, 0.05 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 60 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1) yielded the product as a yellow oil (265 mg, 62%; *r.r.* = >98:2); R_f = 0.57 (cyclohexane/EtOAc = 7:3).

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IR (ATR): 3365 (w), 1725 (m), 1662 (m), 1599 (w), 1505 (w), 1482 (m), 1404 (w), 1363 (m), 1345 (m), 1281 (w), 1246 (w), 1211 (m), 1188 (m), 1172 (s), 1155 (s), 1123 (m), 1091 (m), 1056 (m), 1017 (m), 864 (w), 808 (m), 750 (s), 716 (m), 702 (m), 673 (s), 627 (m), 584 (s), 562 (s), 542 (s), 511 cm^{-1} (m).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.68–7.58 (m, 4 H), 7.53–7.36 (m, 3 H), 7.33–7.28 (m, 1 H), 7.18–7.11 (m, 2 H), 6.88 (d, *J* = 7.5 Hz, 1 H), 6.48–6.41 (m, 1 H), 6.31–6.22 (m, 2 H), 4.23–4.06 (m, 2 H), 2.26 (s, 3 H), 1.19 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.6, 166.5, 145.2, 136.4, 133.5, 131.9, 130.1, 129.7, 128.6, 127.3, 126.8, 124.6, 116.9, 112.1, 62.3, 50.1, 21.6, 14.1.

MS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{22}N_2O_5SNa$: 449.1; found: 449.1.

HRMS (MALDI): *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{22}N_2O_5SNa$: 449.1142; found: 449.1146.

Ethyl 2-[(Ethoxycarbonyl)amino]-2-(1-tosyl-1*H*-pyrrol-2-yl)acetate (7j)

Bi Catalysis: Compound **7j** was synthesized according to the GP from urethane (46 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), *N*-tosylpyrrole (332 mg, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in DCE (2.0 mL). The reaction mixture was stirred for 16 h at 60 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4.1) yielded the product as a yellow solid (123 mg, 62%; *r.r.* = >98:2).

Fe Catalysis

Compound **7j** was synthesized according to the GP from urethane (89 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.24 mL, 1.2 mmol, 1.2 equiv), *N*-tosylpyrrole (664 mg, 3.0 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (18 mg, 0.05 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 40 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a yellow solid (302 mg, 75%; *r.r.* = >98:2).

Mp 138.9 °C; R_f = 0.63 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3367 (w), 3161 (w), 2985 (w), 1722 (m), 1709 (s), 1596 (w), 1515 (m), 1469 (m), 1407 (w), 1364 (m), 1329 (m), 1213 (m), 1176 (s), 1154 (s), 1124 (m), 1090 (m), 1048 (s), 899 (m), 813 (m), 739 (m), 702 cm^{-1} (m).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.70 (d, *J* = 8.3 Hz, 2 H), 7.31–7.21 (m, 3 H), 6.30 (s, 1 H), 6.25–6.22 (m, 1 H), 5.84 (d, *J* = 8.1 Hz, 1 H), 5.43 (d, *J* = 6.5 Hz, 1 H), 4.22–4.03 (m, 4 H), 2.40 (s, 3 H), 1.20 (m, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.9, 155.7, 145.2, 136.3, 130.0, 129.9, 127.1, 124.3, 116.1, 111.9, 62.1, 61.4, 51.3, 21.7, 14.7, 14.1.

MS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{22}N_2O_6SNa$: 417.1; found: 417.2.

HRMS (MALDI): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{22}N_2O_6SNa$: 417.1096; found: 417.1099.

Ethyl 2-Benzamido-2-(1-tosyl-1*H*-indol-3-yl)acetate (7k)

Fe Catalysis: Compound **7k** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), *N*-tosylindole (407 mg, 1.5 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (9 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 60 °C. Purification by chromatography (*n*-hexane/EtOAc = 9:1 → 4.1 → 7:3) yielded the product as a white low-melting foam (177 mg, 74%; *r.r.* = 82:18).

R_f = 0.40 (*n*-hexane/EtOAc = 7:3).

IR (ATR): 1739 (w), 1644 (w), 1520 (w), 1486 (w), 1447 (w), 1367 (m), 1171 (s), 1120 (m), 1089 (m), 1019 (m), 979 (m), 812 (w), 746 (m), 703 (s), 666 (s), 570 (s), 536 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 8.00–6.90 (m, 15 H), 6.05 (d, *J* = 7.4 Hz, 1 H), 4.40–4.12 (m, 2 H), 2.33 (s, 3 H), 1.23 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.6, 166.9, 145.4, 135.3, 135.1, 133.6, 132.1, 130.1, 129.9, 128.8, 127.3, 127.1, 125.4, 125.1, 123.8, 120.2, 118.0, 113.9, 62.4, 49.6, 21.7, 14.2.

MS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{24}N_2O_5SNa$: 499.1; found: 499.1.

HRMS (MALDI): *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{24}N_2O_5SNa$: 499.1298; found: 499.1291.

Ethyl 2-[(Ethoxycarbonyl)amino]-2-(1-tosyl-1*H*-indol-3-yl)acetate (7l)

Bi Catalysis: Compound **7l** was synthesized according to the GP from urethane (46 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), *N*-tosylindole (203 mg, 0.75 mmol, 1.5 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in DCE (4.0 mL). The reaction mixture was stirred for 16 h at 60 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4.1) yielded the product as a colorless oil (171 mg, 78%; *r.r.* = >98:2).

Fe Catalysis: Compound **7l** was synthesized according to the GP from urethane (89 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.24 mL, 1.2 mmol, 1.2 equiv), *N*-tosylindole (814 mg, 3.0 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (18 mg, 0.05 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 60 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4.1) yielded the product as a colorless oil (369 mg, 83%; *r.r.* = >98:2). Compound **7l** is very sensitive, especially towards light or acid and decomposes rapidly. Partial decomposition (<5%) is observed upon silica gel chromatography. Analytically pure **7l** could be obtained by preparative HPLC (column: Machery Nagel Nuc 50-100/250 × 20 mm, hexane/EtOAc/CH_2Cl_2 = 10:1.5:2, flow rate 8 mL/min) and has to be stored under argon, protected from light at or below –20 °C.

R_f = 0.59 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3383 (w), 2981 (w), 1714 (m), 1596 (w), 1514 (w), 1446 (m), 1368 (m), 1301 (m), 1218 (m), 1171 (s), 1200 (m), 1093 (m), 1050 (m), 1019 (m), 976 (m), 856 (w), 812 (m), 745 (s), 704 (m), 663 cm^{-1} (s).

^1H NMR (500 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 8.3 Hz, 1 H), 7.75 (d, *J* = 8.4 Hz, 2 H), 7.64 (d, *J* = 7.9 Hz, 1 H), 7.58 (s, 1 H), 7.27 (t, *J* = 32.8 Hz, 4 H), 5.68–5.42 (m, 2 H), 4.27–4.08 (m, 4 H), 2.34 (s, 3 H), 1.27–1.16 (m, 6 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 170.5, 155.8, 145.3, 135.3, 135.1, 130.1, 128.6, 127.0, 125.3, 124.8, 123.6, 120.2, 118.2, 113.8, 62.2, 61.5, 50.8, 21.7, 14.6, 14.1.

MS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{24}N_2O_6SNa$: 467.1; found: 467.2.

HRMS (MALDI): *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{24}N_2O_6SNa$: 467.1247; found: 467.1239.

Isopropyl 2-Benzamido-2-mesitylacetate (11a)

Bi Catalysis: Compound **11a** was synthesized according to the GP from benzamide (66 mg, 0.55 mmol, 1.0 equiv), isopropyl 2-oxoacetate (75 mg 0.65 mmol, 1.18 equiv), mesitylene (0.21 mL, 3.0 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1 → 1:1) yielded the product as colorless solid (94 mg, 50%).

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Fe Catalysis: Compound **11a** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), isopropyl 2-oxoacetate (174 mg, 1.5 mmol, 1.5 equiv), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (18 mg, 0.050 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 60 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1 → 1:1) yielded the product as a colorless solid (281 mg, 83%).

Mp 101.2 °C; R_f = 0.56 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3317 (m), 2975 (w), 2932 (w), 1747 (s), 1633 (s), 1579 (w), 1530 (s), 1490 (m), 1462 (m), 1360 (m), 1212 (s), 1154 (m), 1108 (s), 1089 (s), 973 (w), 852 (m), 828 (w), 787 cm^{-1} (m).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.82–7.78 (m, 2 H), 7.53–7.39 (m, 3 H), 7.18 (d, *J* = 6.2 Hz, 1 H), 6.83 (s, 2 H), 6.15 (d, *J* = 6.6 Hz, 1 H), 5.08 (hept, *J* = 6.3 Hz, 1 H), 2.47 (s, 6 H), 2.25 (s, 3 H), 1.25 (d, *J* = 6.3 Hz, 3 H), 1.12 (d, *J* = 6.2 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.4, 166.6, 137.6, 137.0, 134.2, 131.8, 131.1, 130.1, 128.7, 127.2, 69.9, 53.0, 21.8, 21.6, 21.0, 20.5.

MS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{21}H_{25}NO_3Na$: 362.2; found: 362.3.

HRMS (MALDI): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{26}NO_3$: 340.1907; found: 340.1905.

2-Benzamido-2-mesitylacetic Acid (11b)

Fe Catalysis: Compound **11b** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), glyoxylic acid (50% w/w in H_2O, 0.07 mL, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv), and $FeCl_3·6H_2O$ (7 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (CH_2Cl_2/MeOH = 20:1 → 9:1) yielded the product as a low-melting solid (120 mg, 81%).

Bi Catalysis: Compound **11b** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), glyoxylic acid (50% w/w in H_2O, 0.13 mL, 1.2 mmol, 1.2 equiv), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv), and $Bi(OTf)_3$ (13 mg, 0.02 mmol, 2 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 21 h at 80 °C. After cooling to r.t., aq 1 M NaOH (15 mL) was added to the reaction mixture. The aqueous phase was washed with EtOAc (2 × 10 mL), acidified with aq 2 N HCl to pH 4, and extracted with EtOAc (3 × 10 mL). The combined organic layers were dried (anhyd $MgSO_4$), filtered, and evaporated to dryness. Purification by chromatography (CH_2Cl_2/MeOH = 20:1 → 9:1) yielded the product as a low-melting solid (211 mg, 71%).

Mp <30 °C; R_f = 0.41 (CH_2Cl_2/MeOH = 9:1).

IR (ATR): 3412 (w), 2920 (w), 2520 (w), 1732 (m), 1612 (s), 1575 (m), 1514 (s), 1485 (s), 1344 (w), 1308 (w), 1240 (m), 1193 (m), 1085 (w), 976 (w), 851 (m), 746 (m), 713 cm^{-1} (s).

^1H NMR (300 MHz, DMSO-d_6): δ = 8.50 (d, *J* = 6.7 Hz, 1 H), 7.88 (d, *J* = 7.0 Hz, 2 H), 7.56–7.42 (m, 3 H), 6.85 (s, 2 H), 5.94 (d, *J* = 6.7 Hz, 1 H), 2.35 (s, 6 H), 2.21 (s, 3 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 172.5, 166.4, 137.2, 136.5, 133.8, 131.4, 131.4, 129.3, 128.2, 127.7, 52.2, 20.4, 20.1.

MS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{20}NO_3$: 298.1; found: 298.5.

HRMS (MALDI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{20}NO_3$: 298.1438; found: 298.1440.

2-[(Ethoxycarbonyl)amino]-2-mesitylacetic Acid (11c)

Bi Catalysis: Compound **11c** was synthesized according to the GP from urethane (45 mg, 0.5 mmol, 1.0 equiv), glyoxylic acid (0.07 mL, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (CH_2Cl_2/MeOH = 50:1 → 20:1) yielded the product as a colorless solid (66 mg, 50%).

Fe Catalysis: Compound **11c** was synthesized according to the GP from urethane (45 mg, 0.5 mmol, 1.0 equiv), glyoxylic acid (0.07 mL, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv), and $FeCl_3·6H_2O$ (7 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (CH_2Cl_2/MeOH = 50:1 → 20:1) yielded the product as a colorless solid (122 mg, 92%).

Mp 144.5 °C; R_f = 0.23 (CH_2Cl_2/MeOH = 9:1).

IR (ATR): 3267 (w), 3027 (w), 2918 (w), 2530 (w), 1725 (s), 1655 (m), 1613 (m), 1513 (w), 1426 (w), 1336 (m), 1226 (w), 1196 (m), 1067 (m), 925 (m), 851 cm^{-1} (m).

^1H NMR (400 MHz, DMSO): δ = 12.78 (s, 1 H), 7.42 (d, *J* = 7.2 Hz, 1 H), 6.81 (s, 2 H), 5.52 (d, *J* = 7.7 Hz, 1 H), 4.09–3.94 (m, 2 H), 2.26 (s, 6 H), 2.19 (s, 3 H), 1.16 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (101 MHz, DMSO): δ = 172.8, 156.1, 136.7, 136.4, 132.0, 129.2, 60.0, 52.9, 20.4, 19.9, 14.6.

MS (ESI): *m*/*z* $[M]^+$ calcd for $C_{14}H_{19}NO_4$: 265.1; found: 264.2.

HRMS (MALDI): *m*/*z* $[M + Na]^+$ calcd for $C_{14}H_{19}NO_4Na$: 288.1206; found: 288.1208.

2-({[(9*H*-Fluoren-9-yl)methoxy]carbonyl}amino)-2-mesitylacetic Acid (11d)

Bi Catalysis: Compound **11d** was synthesized according to the GP from 9*H*-fluoren-9-yl carbamate (113 mg, 0.5 mmol, 1.0 equiv), glyoxylic acid (0.07 mL, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc =7:3 → 1:1) yielded the product as a colorless oil (94 mg, 45%).

Fe Catalysis: Compound **11d** was synthesized according to the GP from 9*H*-fluoren-9-yl carbamate (113 mg, 0.5 mmol, 1.0 equiv), glyoxylic acid (0.07 mL, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv), and $FeCl_3·6H_2O$ (9 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc =7:3 → 1:1) yielded the product as a colorless oil (177 mg, 85%); R_f = 0.35 (EtOAc).

IR (ATR): 3347 (w), 2953 (w), 1717 (s), 1598 (w), 1512 (m), 1443 (m), 1323 (m), 1194 (s), 1052 (s), 853 (m), 747 (s), 616 cm^{-1} (m).

^1H NMR (500 MHz, DMSO-d_6): δ = 12.84 (s, 1 H), 7.90–7.86 (m, 2 H), 7.86–7.81 (m, 1 H), 7.81–7.70 (m, 2 H), 7.44–7.38 (m, 2 H), 7.35–7.26 (m, 2 H), 6.83 (s, 2 H), 5.52 (d, *J* = 7.6 Hz, 1 H), 4.32–4.16 (m, 3 H), 2.28 (s, 6 H), 2.20 (s, 3 H).

^{13}C NMR (126 MHz, DMSO-d_6): δ = 172.8, 156.1, 144.0, 143.7, 140.7, 136.9, 136.5), 131.9, 129.3, 127.7, 127.1, 127.0, 125.5, 120.1, 65.9, 53.1, 46.7, 20.4, 20.0.

MS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{26}H_{26}NO_4$: 416.2; found: 416.4.

HRMS (MALDI): *m*/*z* $[M + Na]^+$ calcd for $C_{26}H_{25}NO_4Na$: 438.1676; found: 438.1674.

Ethyl 2-Benzamido-2-(2-methoxy-5-pivalamidophenyl)acetate (12a)

Fe Catalysis: Compound **12a** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), *N*-(4-methoxyphenyl)pivalamide

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(311 mg, 1.5 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (9 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1 → 7:3 → 1:1) yielded the product as a colorless solid (184 mg, 89%; *r.r.*= >98:2).

Bi Catalysis: Compound **12a** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), *N*-(4-methoxyphenyl)pivalamide (311 mg, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1 → 7:3 → 1:1) yielded the product as a colorless solid (128 mg, 62%; *r.r.* = >98:2).

Mp 90.2 °C; R_f = 0.20 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3302 (w), 2948 (w), 1743 (m), 1638 (s), 1603 (w), 1526 (s), 1414 (w), 1369 (w), 1328 (m), 1216 (s), 1149 (m), 1096 (m), 1029 (m), 932 (w), 859 (w), 806 (w), 725 (m), 693 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.84–7.76 (m, 3 H), 7.52–7.39 (m, 3 H), 7.34–7.30 (m, 2 H), 6.86 (d, *J* = 8.9 Hz, 1 H), 5.84 (d, *J* = 8.0 Hz, 1 H), 4.25–4.16 (m, 2 H), 3.83 (s, 3 H), 1.30 (s, 9 H), 1.20 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 176.7, 171.9, 166.7, 153.8, 134.2, 131.8, 131.5, 128.7, 127.3, 126.1, 123.2, 122.2, 111.7, 61.9, 56.0, 53.9, 39.6, 27.8, 14.3.

MS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{29}N_2O_5$: 413.2; found: 413.9.

HRMS (MALDI): *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{29}N_2O_5$: 413.2071; found: 413.2071.

Ethyl 2-Benzamido-2-(4-methoxy-3-pivalamidophenyl)acetate (12b)

Fe Catalysis: Compound **12b** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), *N*-(2-methoxyphenyl)pivalamide (311 mg, 1.5 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (9 mg, 0.025 mol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 100 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1 → 7:3 → 1:1) yielded the product as a colorless solid (164 mg, 80%, obtained as a 1.6:1 mixture of regioisomers). Further purification of the major regioisomer could be achieved by precipitation from hexane/CH_2Cl_2 (92:8 mixture of regioisomers, as judged by ^1H NMR analysis). Analytical data were obtained for this purified mixture.

Mp 127.6 °C; R_f = 0.34 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3443 (w), 3283 (w), 2959 (w), 2361 (w), 1743 (m), 1668 (m), 1632 (m), 1600 (w), 1579 (w), 1525 (s), 1484 (s), 1430 (m), 1394 (w), 1339 (m), 1267 (m), 1198 (m), 1153 (m), 1122 (m) 1093 (w), 1027 cm^{-1} (m).

^1H NMR (400 MHz, $CDCl_3$): δ = 8.54 (d, *J* = 2.2 Hz, 1 H), 8.10 (s, 1 H), 7.85–7.79 (m, 2 H), 7.52–7.39 (m, 3 H), 7.19–7.11 (m, 2 H), 6.86 (d, *J* = 8.4 Hz, 1 H), 5.68 (d, *J* = 7.0 Hz, 1 H), 4.33–4.12 (m, 2 H), 3.89 (s, 3 H), 1.31 (s, 9 H), 1.24 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 176.6, 171.1, 166.7, 148.1, 134.0, 131.8, 129.7, 128.7, 128.5, 127.4, 123.10, 118.2, 110.1, 62.1, 56.9, 56.1, 40.2, 27.8, 14.2.

MS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{23}H_{28}N_2O_5Na$: 435.2; found: 435.3.

HRMS (MALDI): *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{29}N_2O_5$: 413.2071; found: 413.2072.

Ethyl 2-Benzamido-2-(4-methyl-3-pivalamidophenyl)acetate (12c)

Bi Catalysis: Compound **12c** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), 2-methylpivalanilide (287 mg, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (16 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 100 °C. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as a yellow solid (89 mg, 45%; *r.r.* = >98:2).

Fe Catalysis: Compound **12c** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), 2-methylpivalanilide (287 mg, 1.5 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (9 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 100 °C. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as a yellow solid (152 mg, 77%; *r.r.* = 91:9).

Mp 123–125 °C; R_f = 0.5 (*n*-hexane/EtOAc = 1:1).

IR (ATR): 2959 (w), 2923 (m), 2853 (w), 1744 (s), 1661 (s), 1643 (s), 1615 (w), 1602 (w), 1580 (w), 1519 (s), 1489 (s), 1446 (m), 1417 (w), 1399 (w), 1367 (m), 1340 (s), 1299 (s), 1265 (s), 1218 (m), 1194 (s), 1170 (s), 1092 (m), 1023 (m), 947 (w), 923 (w), 880 (w), 800 (w), 777 (m), 749 (w), 714 (s), 691 (s), 620 (s), 608 (s), 584 (s), 540 cm^{-1} (m).

^1H NMR (300 MHz, $CDCl_3$): δ = 7.91 (d, *J* = 9.0 Hz, 1 H), 7.82–7.79 (m, 2 H), 7.51–7.41 (m, 3 H), 7.28 (s, 2 H), 7.23 (br s, 1 H), 7.12 (br d, *J* = 6.8 Hz, 1 H), 5.68 (d, *J* = 6.9 Hz, 1 H), 4.30–4.13 (m, 2 H), 2.26 (s, 3 H), 1.33 (s, 9 H), 1.24 (t, *J* = 5.8 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.6, 171.2, 166.6, 136.3, 133.9, 133.1, 132.0, 129.7, 129.14, 128.7, 127.3, 125.8, 123.2, 62.2, 56.6, 40.0, 27.8, 17.8, 14.2.

MS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{23}H_{28}N_2O_4Na$: 420.0; found: 420.0.

HRMS (MALDI): *m*/*z* $[M + K]^+$ calcd for $C_{23}H_{28}N_2O_4K$: 435.1681; found: 435.1674.

Ethyl 2-Benzamido-2-(2,5-dimethoxyphenyl)acetate (12d)

Fe Catalysis: Compound **12d** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), 1,4-dimethoxybenzene (207 mg, 1.5 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (9 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless solid (128 mg, 74%).

Mp 75.4 °C; R_f = 0.33 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3299 (w), 2954 (w), 2835 (w), 1727 (m), 1636 (m), 1581 (w), 1503 (s), 1458 (m), 1327 (m), 1207 (s), 1153 (s), 1045 (s), 1022 (s), 925 (m), 822 (m), 755 (m), 715 (m), 635 cm^{-1} (m).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.82–7.78 (m, 2 H), 7.51–7.46 (m, 1 H), 7.42 (t, *J* = 7.4 Hz, 2 H), 7.31 (d, *J* = 8.1 Hz, 1 H), 7.01 (s, 1 H), 6.84 (d, *J* = 1.3 Hz, 2 H), 5.90 (d, *J* = 8.3 Hz, 1 H), 4.26–4.16 (m, 2 H), 3.82 (s, 3 H), 3.78 (s, 3 H), 1.21 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.1, 166.7, 153.9, 151.4, 134.3, 131.7, 128.7, 127.3, 126.7, 116.7, 114.5, 112.4, 61.8, 56.3, 55.9, 54.1, 14.3.

MS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{19}H_{21}NO_5Na$: 366.1; found: 366.2.

HRMS (MALDI): *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{22}NO_5$: 344.1493; found: 344.1491.

Anal. Calcd for $C_{19}H_{21}NO_5$: C, 66.46; H, 6.16; N, 4.08. Found: C, 66.20, H, 6.11; N, 3.80.

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Ethyl 2-Benzamido-2-(3,4-dimethoxyphenyl)acetate (12e)

Fe Catalysis: Compound **12e** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.24 mL, 1.2 mmol, 1.2 equiv), veratrole (0.38 mL, 3.0 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (18 mg, 0.05 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a colorless oil (216 mg, 63%; *r.r.* = >98:2).

R_f = 0.32 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3338 (w), 2980 (w), 1732 (s), 1634 (s), 1595 (w), 1578 (w), 1520 (s), 1488 (m), 1467 (m), 1356 (m), 1332 (m), 1255 (s), 1238 (m), 1203 (m), 1183 (m), 1165 (m), 1139 (s), 1097 (m), 1017 (s), 923 (w), 878 (w), 851 (m), 799 (m), 752 (m), 714 (s), 691 (m), 633 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 7.3 Hz, 2 H), 7.51 (t, *J* = 7.3 Hz, 1 H), 7.44 (t, *J* = 7.5 Hz, 2 H), 7.11 (d, *J* = 6.7 Hz, 1 H), 7.02–6.94 (m, 2 H), 6.85 (d, *J* = 8.2 Hz, 1 H), 5.69 (d, *J* = 7.0 Hz, 1 H), 4.33–4.15 (m, 2 H), 3.89 (s, 3 H), 3.87 (s, 3 H), 1.25 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.3, 166.7, 149.4, 149.4, 133.9, 132.0, 129.3, 128.8, 127.3, 119.7, 111.5, 110.7, 62.1, 56.7, 56.1, 56.1, 14.2.

MS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{19}H_{21}NO_5Na$: 366.1; found: 366.3.

HRMS (MALDI): *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{22}NO_5$: 344.1493; found: 344.1490.

Anal. Calcd for $C_{19}H_{21}NO_5$: C, 66.46; H, 6.16; N, 4.08. Found: C, 66.31; H, 6.18; N, 3.98.

Ethyl 2-(Anthracen-9-yl)-2-benzamidoacetate (12f)

Bi Catalysis: Compound **12f** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), anthracene (267 mg, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 20:1 → 9:1 → 4:1) yielded the product as a yellow solid (92 mg, 48%; *r.r.* = >98:2).

Fe Catalysis: Compound **12f** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), anthracene (267 mg, 1.5 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (9 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 20:1 → 9:1 → 4:1) yielded the product as a yellow solid (157 mg, 82%; *r.r.* = >98:2).

Mp 128.6 °C; R_f = 0.59 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3355 (w), 3058 (w), 2979 (w), 1721 (s), 1640 (s), 1579 (w), 1520 (s), 1488 (m), 1450 (m), 1367 (w), 1314 (s), 1210 (s), 1142 (m), 1092 (m), 1044 (m), 901 (m), 845 (m), 727 (s), 713 (s), 690 cm^{-1} (s).

^1H NMR (500 MHz, $CDCl_3$): δ = 8.55–8.43 (m, 3 H), 8.06 (d, *J* = 8.4 Hz, 2 H), 7.78 (d, *J* = 8.5 Hz, 2 H), 7.64–7.34 (m, 9 H), 7.31 (d, *J* = 7.2 Hz, 1 H), 4.25–4.09 (m, 2 H), 1.04 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 172.3, 167.3, 133.8, 131.9, 131.8, 130.3, 129.8, 129.4, 128.7, 128.1, 127.37, 127.3, 125.3, 123.6, 62.3, 51.4, 14.1.

MS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{25}H_{22}NO_3$: 384.2; found: 385.0.

HRMS (MALDI): *m*/*z* [M] calcd for $C_{25}H_{21}NO_3$: 383.1521; found: 383.1501.

Ethyl 2-Benzamido-2-(5-bromo-2-hydroxyphenyl)acetate (12g)

Bi Catalysis: Compound **12g** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), 4-bromophenol (260 mg, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (3 mg, 0.005 mmol, 1 mol%) in DCE (2.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a low-melting solid (123 mg, 65%; *r.r.* = >98:2).

Fe Catalysis: Compound **12g** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.24 mL, 1.2 mmol, 1.2 equiv), 4-bromophenol (516 mg, 3.0 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (7 mg, 0.02 mmol, 2 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a low-melting solid (39 mg, 11%; *r.r.* = >98:2).

R_f = 0.46 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3368, 3099, 2920, 2852, 1736, 1622, 1576, 1530 (s), 1488 (m), 1430 (m), 1363, 1344 (m), 1310 (m), 1278 (s), 1236 (m), 1198 (m), 1120 (m), 1090 (s), 1022 (m), 877 (m), 813 (s), 727 (s), 692 cm^{-1} (m).

^1H NMR (400 MHz, $CDCl_3$): δ = 9.47 (s, 1 H), 7.86–7.76 (m, 2 H), 7.61 (d, *J* = 6.7 Hz, 1 H), 7.58–7.52 (m, 1 H), 7.49–7.43 (m, 2 H), 7.35–7.31 (m, 1 H), 7.13 (d, *J* = 2.4 Hz, 1 H), 6.92 (d, *J* = 8.7 Hz, 1 H), 5.83 (d, *J* = 6.9 Hz, 1 H), 4.39–4.30 (m, 2 H), 1.30 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.6, 168.3, 155.0, 133.3, 132.7, 132.0, 129.9, 128.8, 127.3, 126.1, 121.3, 112.6, 62.9, 51.8, 14.0.

MS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_{16}BrNO_4Na$: 400.0; found: 400.1.

HRMS (MALDI): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{17}BrNO_4$: 378.0335; found: 378.0335.

Ethyl 2-Benzamido-2-(3,4-dimethylphenyl)acetate (12h)

Bi Catalysis: Compound **12h** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (122 mg, 1.2 mmol, 1.2 equiv), *o*-xylene (0.36 mL, 3.0 mmol, 3.0 equiv), and $Bi(OTf)_3$ (13 mg, 0.02 mmol, 2 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as a colorless solid (278 mg, 89%; *r.r.* = 89:11).

Fe Catalysis: Compound **12h** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), *o*-xylene (0.18 mL, 1.5 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (9 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless solid (88 mg, 54%; *r.r.* = 80:20). Further purification of the major regioisomer could be achieved by precipitation from hexane/CH_2Cl_2 (87:13 mixture of regioisomers, as judged by ^1H NMR analysis). Analytical data were obtained for this purified mixture.

Mp 70–72 °C; R_f = 0.31 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3285 (w), 2981 (w), 1741 (s), 1635 (s), 1602 (w), 1579 (w), 1527 (s), 1488 (s), 1446 (w), 1370 (w), 1345 (m), 1302 (m), 1263 (m), 1189 (s), 1153 (s), 1093 (m), 1022 (m), 819 (w), 689 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ (major regioisomer) = 7.82 (d, *J* = 7.3 Hz, 2 H), 7.54–7.39 (m, 3 H), 7.22–6.95 (m, 4 H), 5.71 (d, *J* = 7.1 Hz, 1 H), 4.34–4.10 (m, 2 H), 2.26 (s, 3 H), 2.25 (s, 3 H), 1.27–1.21 (m, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ (major regioisomer) = 171.4, 166.6, 137.5, 137.2, 134.3, 134.0, 131.9, 130.3, 128.7, 127.3, 124.8, 124.4, 62.1, 56.8, 20.0, 19.6, 14.2.

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MS (ESI): m/z [M + H]$^+$ calcd for $C_{19}H_{22}NO_3$: 312.2; found: 312.2.

HRMS (MALDI): m/z [M + H]$^+$ calcd for $C_{19}H_{22}NO_3$: 312.1594; found: 312.1595.

Ethyl 2-Benzamido-2-(5-chloro-2-methoxyphenyl)acetate (12i)

Bi Catalysis: Compound **12i** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (122 mg, 1.2 mmol, 1.2 equiv), 4-chloroanisole (0.49 mL, 4.0 mmol, 4.0 equiv), and $Bi(OTf)_3$ (32 mg, 0.05 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 16 h at 100 °C. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as a colorless solid (310 mg, 89%; *r.r.* = >98:2).

Fe Catalysis: Compound **12i** was synthesized according to the GP from benzamide (121 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.24 mL, 1.2 mmol, 1.2 equiv), 4-chloroanisole (0.37 mL, 3.0 mmol, 3.0 equiv), and $Fe(ClO_4)_3$ (18 mg, 0.05 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 9:1 → 4:1) yielded the product as a colorless solid (116 mg, 34%; *r.r.* = >98:2).

Mp 88.8 °C; R_f = 0.55 (cyclohexane/EtOAc = 7:3).

IR (ATR): 3257 (w), 2959 (w), 1737 (s), 1638 (s), 1602 (w), 1579 (w), 1523 (m), 1488 (s), 1458 (m), 1365 (w), 1320 (m), 1247 (s), 1190 (s), 1130 (m), 1093 (s), 1026 (s), 979 (w), 804 (m), 719 (m), 658 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79 (dd, J = 5.2, 3.3 Hz, 2 H), 7.53–7.40 (m, 4 H), 7.30–7.23 (m, 2 H), 6.83 (d, J = 8.8 Hz, 1 H), 5.88 (d, J = 8.0 Hz, 1 H), 4.24–4.17 (m, 2 H), 3.85 (s, 3 H), 1.21 (t, J = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 170.6, 166.5, 155.7, 134.0, 131.7, 130.6, 129.4, 128.6, 127.4, 127.2, 125.9, 112.3, 61.9, 56.0, 53.3, 14.1.

MS (ESI): m/z [M + H]$^+$ calcd for $C_{18}H_{19}ClNO_4$: 348.1; found: 348.2.

HRMS (MALDI): m/z [M + H]$^+$ calcd for $C_{18}H_{19}ClNO_4$: 348.0997; found: 348.0995.

Ethyl 2-Benzamido-2-(*p*-tolyl)acetate (12j)

Bi Catalysis: Compound **12j** was synthesized according to the GP from benzamide (61 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), toluene (0.22 mL, 2.1 mmol, 4.2 equiv), and $Bi(OTf)_3$ (7 mg, 0.005 mmol, 2 mol%) in DCE (2.0 mL). The reaction mixture was stirred for 16 h at 100 °C. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as a colorless solid (74 mg, 50%; *r.r.* = 75:25).

Mp 99–101 °C; R_f = 0.4 (*n*-hexane/EtOAc 4:1).

IR (ATR): 3290 (w), 1743 (s), 1636 (s), 1603 (m), 1581 (m), 1527 (s), 1488 (s), 1447 (m), 1372 (m), 1348 (m), 1330 (m), 1300 (w), 1275 (w), 1252 (m), 1206 (s), 1178 (s), 1153 (s), 1096 (m), 1075 (w), 1021 (s), 928 (w), 815 (m), 803 (w), 791 (w), 759 (m), 723 (s), 711 (s), 691 (s), 634 (m), 615 (m), 587 (s), 573 (m), 512 (m), 487 (m), 459 cm^{-1} (w).

^{1}H NMR (300 MHz, $CDCl_3$): δ (major regioisomer) = 7.83–7.80 (m, 2 H), 7.54–7.40 (m, 3 H), 7.35–7.32 (m, J = 8.1 Hz, 2 H), 7.24–7.16 (m, J = 15.2, 5.8 Hz, 2 H), 7.11 (br d, J = 6.9 Hz, 1 H), 5.73 (d, J = 7.0 Hz, 1 H), 4.33–4.11 (m, 2 H), 2.34 (s, 3 H), 1.29–1.19 (m, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.33, 166.61, 138.51, 137.19, 135.48, 133.94, 131.93, 131.17, 129.81, 128.73, 128.60, 127.34, 127.28, 126.67, 126.45, 62.12, 56.75, 53.71, 21.30, 19.68, 14.18. (peaks are not assigned to regioisomers).

MS (ESI): m/z [M + H]$^+$ calcd for $C_{18}H_{20}NO_3$: 298.5; found: 298.5.

HRMS (MALDI): m/z [M + H]$^+$ calcd for $C_{18}H_{20}NO_3$: 298.1438; found: 298.1439.

Ethyl 2-Mesityl-2-(2-oxopyrrolidin-1-yl)acetate (14a)

Bi Catalysis: Compound **14a** was synthesized according to the GP from pyrrolidin-2-one (85 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (122 mg, 1.2 mmol, 1.2 equiv), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv), and $Bi(OTf)_3$ (13 mg, 0.02 mmol, 2 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless solid (182 mg, 63%).

Fe Catalysis: Compound **14a** was synthesized according to the GP from pyrrolidin-2-one (43 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv), and $FeCl_3{\cdot}6H_2O$ (3 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless solid (12 mg, 8%).

Mp 141–142 °C; R_f = 0.2 (cyclohexane/EtOAc = 7:3).

IR (ATR): 2988 (w), 2926 (w), 1743 (s), 1681 (s), 1610 (m), 1491 (m), 1460 (m), 1245 (m), 1187 (s), 1023 (m), 903 (w), 860 (m), 673 cm^{-1} (m).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.87 (s, 2 H), 6.12 (s, 1 H), 4.33–4.11 (m, 2 H), 3.66 (m, 1 H),

2.93 (m, 1 H), 2.56–2.35 (m, 2 H), 2.26 (d, J = 4.5 Hz, 9 H), 2.10–1.99 (m, 1 H), 1.86–1.79 (m,

1 H), 1.24 (t, J = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.3, 171.7, 138.1, 130.1, 128.2, 61.8, 54.0, 44.2, 30.8, 21.0, 20.6, 18.3, 14.2.

MS (ESI): m/z [M + H]$^+$ calcd for $C_{17}H_{24}NO_3$: 290.2; found: 290.2.

Anal. Calcd for $C_{17}H_{23}NO_3$: C, 70.56; H, 8.01; N, 4.84. Found: C, 70.47; H, 7.97; N, 4.66.

Ethyl 2-Mesityl-2-(2-oxooxazolidin-3-yl)acetate (14b)

Bi Catalysis: Compound **14b** was synthesized according to the GP from oxazolidin-2-one (87 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (122 mg, 1.2 mmol, 1.2 equiv), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv), and $Bi(OTf)_3$ (13 mg, 0.02 mmol, 2 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless solid (234 mg, 80%).

Mp 127–128 °C; R_f = 0.2 (cyclohexane/EtOAc = 7:3).

IR (ATR): 2921 (w), 1732 (s), 1611 (w), 1486 (w), 1447 (m), 1239 (m), 1144 (w), 1023 (s), 884 (m), 738 (w), 699 (m), 676 cm^{-1} (m).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.89 (s, 2 H), 5.88 (s, 1 H), 4.45–4.14 (m, 4 H), 3.93 (m, 1 H), 3.13 (m, 1 H), 2.28 (d, J = 2.7 Hz, 9 H), 1.26 (t, J = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.4, 158.4, 138.6, 137.9, 130.3, 127.8, 62.5, 62.1, 55.6, 41.9, 21.0, 20.5, 14.3.

MS (ESI): m/z [M + H]$^+$ calcd for $C_{16}H_{22}NO_4$: 292.2; found: 292.2.

Anal. Calcd for $C_{16}H_{21}NO_4$: C, 65.96; H, 7.27; N, 4.81. Found: C, 65.82; H, 7.25; N, 4.69.

Ethyl 2-Mesityl-2-(methylsulfonamido)acetate (16a)

Bi Catalysis: Compound **16a** was synthesized according to the GP from methanesulfonamide (49 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL).

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The reaction mixture was stirred for 20 h at 80 °C. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as a colorless solid (81 mg, 54%).

Mp 126–128 °C; R_f = 0.5 (*n*-hexane/EtOAc 7:3).

IR (ATR): 3298 (w), 2966 (w), 2927 (w), 2111 (w), 1732 (s), 1609 (w), 1464 (w), 1413 (m), 1401 (m), 1366 (w), 1327 (s), 1311 (s), 1289 (s), 1254 (m), 1219 (s), 1199 (s), 1161 (s), 1145 (s), 1096 (s), 1021 (m), 987 (s), 970 (s), 909 (w), 872 (m), 855 (s), 827 (m), 784 (w), 762 (s), 721 (w), 636 (w), 602 (m), 555 (m), 528 (s), 513 (s), 475 cm^{-1} (m).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.86 (s, 2 H), 5.64 (d, *J* = 4.0 Hz, 1 H), 5.41 (br d, *J* = 3.5 Hz, 1 H), 4.29–4.13 (m, 2 H), 2.61 (s, 3 H), 2.35 (s, 6 H), 2.26 (s, 3 H), 1.20 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.21, 138.51, 137.35, 130.28, 129.78, 62.68, 55.24, 42.03, 21.04, 20.10, 14.20.

MS (ESI): *m*/*z* [M + Na] calcd for $C_{14}H_{21}NO_4SNa$: 322.1; found: 322.0.

HRMS (MALDI): *m*/*z* [M + K]$^+$ calcd for $C_{14}H_{21}NO_4SK$: 338.0823; found: 338.0823.

Ethyl 2-Mesityl-2-(4-methylphenylsulfonamido)acetate (16b, R = Me)

Bi Catalysis: Compound **16b** was synthesized according to the GP from 4-methylbenzenesulfonamide (87 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (*n*-hexane/EtOAc = 9:1 → 4:1) yielded the product as a colorless solid (148 mg, 79%).

Mp 138–140 °C; R_f = 0.3 (cyclohexane/EtOAc = 4:1).

IR (ATR): 3275 (w), 2923 (w), 1735 (s), 1611 (w), 1597 (w), 1451 (w), 1407 (w), 1367 (w), 1330 (m), 1289 (m), 1265 (m), 1228 (m), 1187 (w), 1163 (s), 1119 (w), 1095 (w), 1065 (m), 1023 (m), 972 (w), 938 (w), 911 (m), 870 (m), 838 (w), 825 (w), 809 (s), 778 (w), 721 (m), 705 (w), 670 (m), 586 (s), 552 (s), 530 (m), 486 cm^{-1} (w).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.44 (d, *J* = 8.3 Hz, 2 H), 7.07 (d, *J* = 8.1 Hz, 2 H), 6.65 (s, 2 H), 5.69 (d, *J* = 4.6 Hz, 1 H), 5.51 (d, *J* = 4.7 Hz, 1 H), 4.20–4.03 (m, 2 H), 2.34 (s, 3 H), 2.21 (s, 6 H), 2.21 (s, 3 H), 1.12 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.93, 143.13, 137.99, 137.18, 137.13, 129.84, 129.46, 129.17, 126.99, 62.55, 55.01, 21.59, 20.92, 20.12, 14.10.

MS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{25}NO_4SNa$: 398.1; found: 398.1.

HRMS (MALDI): *m*/*z* [M + K]$^+$ calcd for $C_{20}H_{25}NO_4SK$: 414.1136; found: 414.1133.

Ethyl 2-(4-Bromophenylsulfonamido)-2-mesitylacetate (16b, R = Br)

Bi Catalysis: Compound **16b** (R = Br) was synthesized according to the GP from 4-bromobenzenesulfonamide (120 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 16 h at 100 °C. Purification by chromatography (*n*-hexane/EtOAc 4:1 → 7:3) yielded the product as a colorless solid (118 mg, 54%).

Mp 114–116 °C; R_f = 0.6 (*n*-hexane/EtOAc = 4:1).

IR (ATR): 3309 (w), 2965 (w), 1732 (s), 1610 (w), 1577 (w), 1473 (w), 1449 (w), 1391 (m), 1370 (m), 1323 (s), 1299 (m), 1278 (s), 1247 (m), 1223 (m), 1200 (m), 1159 (s), 1147 (s), 1090 (s), 1071 (s), 1033 (m), 1012 (m), 975 (w), 925 (m), 852 (m), 818 (s), 764 (w), 740 (s), 724 (m), 703 (w), 615 (s), 593 (m), 562 (s), 553 (s), 532 (m), 475 cm^{-1} (m).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.37–7.30 (m, 4 H), 6.63 (s, 2 H), 5.84 (br d, *J* = 4.2 Hz, 1 H), 5.57 (d, *J* = 4.3 Hz, 1 H), 4.23–4.06 (m, 2 H), 2.20 (s, 6 H), 2.19 (s, 3 H), 1.14 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.65, 139.23, 138.40, 137.17, 131.58, 129.83, 128.78, 128.32, 127.12, 62.68, 55.01, 20.88, 20.01, 14.09.

MS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{22}BrNO_4SNa$: 462.0; found: 462.0.

HRMS (MALDI): *m*/*z* [M + K]$^+$ calcd for $C_{19}H_{22}BrNO_4SK$: 478.0085; found: 478.0069.

Ethyl 2-Mesityl-2-(4-methoxyphenylsulfonamido)acetate (16b, R = OMe)

Bi Catalysis: Compound **16b** (R = OMe) was synthesized according to the GP from 4-methoxybenzenesulfonamide (196 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 3.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 18 h at 80 °C. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as a colorless solid (126 mg, 64%).

Mp 173–175 °C; R_f = 0.5 (*n*-hexane/EtOAc 4:1).

IR (ATR): 3274 (w), 2923 (w), 1738 (m), 1594 (m), 1496 (m), 1437 (w), 1412 (m), 1329 (m), 1311 (w), 1288 (w), 1263 (s), 1228 (m), 1183 (m), 1157 (m), 1119 (w), 1096 (m), 1063 (m), 1024 (s), 939 (w), 913 (m), 870 (m), 828 (s), 801 (m), 779 (m), 722 (m), 674 (s), 628 (w), 585 (s), 559 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.50–7.45 (m, 2 H), 6.75–6.70 (m, 2 H), 6.66 (s, 2 H), 5.67 (br d, *J* = 4.5 Hz, 1 H), 5.51 (d, *J* = 4.6 Hz, 1 H), 4.20–4.04 (m, 2 H), 3.80 (s, 3 H), 2.21 (s, 6 H), 2.19 (s, 3 H), 1.13 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.95, 162.74, 137.90, 137.17, 131.85, 129.87, 129.42, 129.09, 113.71, 62.55, 55.66, 55.00, 20.92, 20.13, 14.12.

MS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{25}NO_5SNa$: 414.1; found: 414.08.

HRMS (MALDI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{25}NO_5SNa$: 414.1346; found: 414.1338.

Ethyl 2-Mesityl-2-(thiophene-2-sulfonamido)acetate (16c)

Bi Catalysis: Compound **16c** was synthesized according to the GP from 2-thiophenesulfonamide (82 mg, 0.5 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 1.2 equiv), mesitylene (0.21 mL, 1.5 mmol, 1.5 equiv) and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 16 h at 80 °C. Purification by chromatography (*n*-hexane/EtOAc 9:1 → 4:1) yielded the product as a colorless solid (123 mg, 67%).

Mp 158–160 °C; R_f = 0.3 (*n*-hexane/EtOAc = 4:1).

IR (ATR): 3314 (w), 3115 (w), 2967 (w), 2083 (w), 1739 (s), 1612 (w), 1509 (w), 1480 (w), 1463 (w), 1407 (m), 1367 (w), 1329 (s), 1287 (s), 1225 (m), 1197 (m), 1157 (s), 1144 (s), 1091 (s), 1033 (m), 1014 (s), 976 (w), 925 (w), 852 (s), 828 (m), 782 (w), 739 (m), 729 (s), 666 (s), 641 (w), 608 (s), 589 (s), 570 (s), 546 (s), 528 (s), 468 cm^{-1} (m).

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^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.44 (dd, *J* = 5.0, 1.2 Hz, 1 H), 7.24 (dd, *J* = 3.8, 1.3 Hz, 1 H), 6.88–6.85 (m, 1 H), 6.72 (s, 2 H), 5.87 (br d, *J* = 4.9 Hz, 1 H), 5.59 (d, *J* = 5.0 Hz, 1 H), 4.22–4.05 (m, 2 H), 2.26 (s, 6 H), 2.21 (s, 3 H), 1.14 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.78, 141.13, 138.13, 137.21, 132.19, 131.93, 129.96, 129.35, 127.00, 62.67, 55.28, 20.96, 20.16, 14.11.

MS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{22}NO_4S_2$: 368.1; found: 368.5.

HRMS (MALDI): *m*/*z* [M + K]$^+$ calcd for $C_{17}H_{21}NO_4S_2K$: 406.0544; found: 406.0543.

Ethyl 3,5,10,10a-Tetrahydro-3-oxo-1*H*-oxazolo[3,4-*b*]isoquinoline-5-carboxylate (21)

Bi Catalysis: Compound **21** was synthesized according to the GP from (*R*)-4-benzyloxazolidin-2-one (59 mg, 0.3 mmol, 1.0 equiv), ethyl glyoxalate (61 mg, 0.6 mmol, 2.0 equiv), and $Bi(OTf)_3$ (7 mg, 0.01 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (cyclohexane/EtOAc = 4:1) yielded the product as a colorless solid (72 mg, 84%).

Mp 58–59 °C; R_f = 0.2 (cyclohexane/EtOAc = 7:3).

IR (ATR): 2980 (w), 2936 (w), 2084 (w), 1760 (s), 1726 (s), 1477 (m), 1454 (m), 1408 (m), 1393 (m), 1365 (m), 1340 (m), 1322 (m), 1272 (s), 1237 (s), 1227 (s), 1205 (s), 1186 (s), 1167 (m), 1115 (m), 1099 (m), 1063 (s), 1017 (s), 983 (m), 938 (m), 917 (w), 892 (m), 876 (m), 824 (m), 810 (m), 759 (s), 745 (m), 715 (w), 697 (m), 671 (m), 620 (w), 585 (w), 534 (m), 509 (w), 495 cm^{-1} (m).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.61–7.56 (m, 1 H), 7.28–7.25 (m, 3 H), 7.18–7.15 (m, 1 H), 5.46 (s, 1 H), 4.72–4.67 (m, 1 H), 4.52–4.45 (m, 1 H), 4.27–4.12 (m, 3 H), 3.06–2.99 (m, 1 H), 2.93–2.84 (m, 1 H), 1.31 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.09, 157.14, 132.04, 129.88, 128.95, 128.31, 127.65, 127.31, 69.38, 62.16, 55.07, 49.62, 33.78, 14.25.

The structure was assigned by COSY.

MS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{16}NO_4$: 262.1; found: 262.2.

Anal. Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 63.95; H, 5.82; N, 5.20.

Ethyl 2-(3-Methyl-(1,3-dioxoisoindolin-2-yl)butanamido)-2-mesitylacetate (23, PG = Phth)

Bi Catalysis: Compound **23** (PG = Phth) was synthesized according to the GP from 3-methyl-2(1,3-dioxoisoindolin-2-yl)butanamide (246 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (122 mg, 1.2 mmol, 1.2 equiv), mesitylene (0.41 mL, 3.0 mmol, 3.0 equiv), and $Bi(OTf)_3$ (13 mg, 0.02 mmol, 2 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as a colorless solid (393 mg, 87%; *r.r.* = 67:33).

IR (ATR): 3348 (w), 2966 (w), 2873 (w), 2050 (w), 1979 (w), 1776 (w), 1765 (w), 1730 (m), 1705 (s), 1676 (s), 1608 (w), 1525 (s), 1466 (m), 1383 (s), 1360 (m), 1331 (m), 1279 (m), 1240 (s), 1153 (m), 1099 (m), 1063 (s), 1026 (s), 982 (w), 947 (w), 908 (w), 885 (m), 868 (w), 854 (m), 827 (w), 806 (w), 766 (w), 725 (s), 708 (m), 688 (w), 613 (s), 604 cm^{-1} (s).

Diastereomer a

Mp 63–65 °C; R_f = 0.2 (*n*-hexane/EtOAc = 4:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.10 (br d, *J* = 7.2 Hz, 1 H), 7.90–7.88 (m, 2 H), 7.77–7.74 (m, 2 H), 6.83 (s, 2 H), 5.99 (d, *J* = 7.3 Hz, 1 H), 4.44 (d, *J* = 11.5 Hz, 1 H), 4.20–4.03 (m, 2 H), 2.86–2.74 (m, 1 H), 2.39 (s, 6 H), 2.25 (s, 3 H), 1.11 (t, *J* = 7.1 Hz, 3 H), 0.92 (d, *J* = 6.7 Hz, 3 H), 0.83 (d, *J* = 6.6 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.38, 168.61, 168.33, 137.69, 137.05, 134.54, 131.57, 130.90, 130.01, 123.88, 63.58, 61.85, 52.40, 27.89, 21.01, 20.29, 19.62, 14.11.

Diastereomer b

Mp 136–138 °C; R_f = 0.3 (*n*-hexane/EtOAc = 4:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.95 (br d, *J* = 7.4 Hz, 1 H), 7.85–7.82 (m, 2 H), 7.74–7.71 (m, 2 H), 6.79 (s, 2 H), 6.04 (d, *J* = 7.5 Hz, 1 H), 4.45 (d, *J* = 11.3 Hz, 1 H), 4.24–4.09 (m, 2 H), 3.03–2.90 (m, 1 H), 2.36 (s, 6 H), 2.21 (s, 3 H), 1.20–1.14 (m, 6 H), 0.86 (d, *J* = 6.6 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.43, 168.54, 168.50, 137.72, 137.08, 134.52, 131.51, 130.82, 129.99, 123.84, 63.29, 61.88, 52.10, 27.96, 20.97, 20.28, 19.91, 19.72, 14.18.

MS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{31}N_2O_5$: 451.2; found: 451.4.

HRMS (MALDI): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{31}N_2O_5$: 451.2228; found: 451.2224.

Ethyl 2-Benzamido-2-hydroxyacetate (24a)

Fe Catalysis: Compound **24a** was synthesized according to the GP from benzamide (61 mg, 1.0 mmol, 1.0 equiv), ethyl glyoxalate (0.12 mL, 1.2 mmol, 1.2 equiv), and $FeCl_3{\cdot}6H_2O$ (13 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at r.t. Purification by chromatography (*n*-hexane/EtOAc = 4:1) yielded the product as a colorless solid (96 mg, 99%).

Mp 54.8 °C; R_f = 0.30 (*n*-hexane/EtOAc = 7:3).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84–7.79 (m, 2 H), 7.51 (d, *J* = 51.2 Hz, 3 H), 7.36 (d, *J* = 5.8 Hz, 1 H), 5.78 (dd, *J* = 6.9, 6.0 Hz, 1 H), 4.35 (q, *J* = 7.1 Hz, 2 H), 4.15 (d, *J* = 5.8 Hz, 1 H), 1.36 (t, *J* = 7.1 Hz, 3 H).

Analytical and spectral data are consistent with those reported in the literature.[36]

Ethyl 2,2-Bis(benzamido)acetate (25a)

Fe Catalysis: Compound **25a** was synthesized according to the GP from benzamide (242 mg, 2.0 mmol, 2.0 equiv), ethyl glyoxalate (0.10 mL, 1.0 mmol, 1.0 equiv), and $FeCl_3{\cdot}6H_2O$ (13 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (2.0 mL). After stirring for 24 h at 80 °C, the white precipitate was filtered, and dried under reduced pressure. The desired product was isolated as a white solid (325 mg, ~100%).

Mp (decomp.); R_f = 0.26 (*n*-hexane/EtOAc = 7:3).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00–7.70 (m, 6 H), 7.55–7.42 (m, 6 H), 5.88 (t, *J* = 6.7 Hz, 1 H), 4.33 (dd, *J* = 14.1, 7.0 Hz, 2 H), 1.30 (t, *J* = 7.1 Hz, 3 H).

Analytical and spectral data are consistent with those reported in the literature.[37]

Ethyl 2,2-Dimesitylacetate (26)

Fe Catalysis: Compound **26** was synthesized according to the GP from ethyl glyoxalate (0.10 mL, 1.0 mmol, 1.0 equiv), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv), and $FeCl_3{\cdot}6H_2O$ (13 mg, 0.025 mmol, 5 mol%) in $MeNO_2$ (4.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (*n*-hexane/EtOAc = 20:1 → 9:1) yielded the product as a colorless solid (320 mg, 99%).

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Mp 100–106 °C; R_f = 0.72 (*n*-hexane/EtOAc = 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.79 (s, 4 H), 4.24 (q, *J* = 7.1 Hz, 2 H), 2.24 (s, 6 H), 2.07 (s, 12 H), 1.27 (t, *J* = 7.1 Hz, 3 H).

Analytical and spectral data are consistent with those reported in the literature.[38]

Ethyl 2-Hydroxy-2-mesitylacetate (27)

Fe Catalysis: Compound **27** was synthesized according to the GP from ethyl glyoxalate (0.24 mL, 1.2 mmol, 1.0 equiv), mesitylene (0.42 mL, 3.0 mmol, 3.0 equiv), 2,2′-bipyridine (5 mg, 0.03 mmol, 3 mol%), and $Fe(ClO_4)_3$ (7 mg, 0.02 mmol, 2 mol%) in $MeNO_2$ (2.0 mL). The reaction mixture was stirred for 24 h at 80 °C. Purification by chromatography (hexane/EtOAc = 4:1) yielded the product as a colorless oil (176 mg, 66%).

R_f = 0.51 (*n*-hexane/EtOAc = 7:3).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.84 (s, 2 H), 5.52 (d, *J* = 2.8 Hz, 1 H), 4.34–4.11 (m, 2 H), 3.22 (d, *J* = 2.8 Hz, 1 H), 2.33 (s, 6 H), 2.26 (s, 3 H), 1.22 (t, *J* = 7.1 Hz, 3 H).

Analytical data are consistent with those reported in the literature.[39]

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1561499.

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(17) Monomeric glyoxalates are prepared from the corresponding polymers by pyrolysis. The monomers are so reactive that they polymerize easily and react readily with water to generate the hydrated forms. Therefore, they have to be distilled just prior to use, after pyrolysis, and used under nonaqueous conditions.
(18) Ethyl glyoxalate was obtained in the polymer form (50 wt% solution) in toluene. Toluene was removed prior to the initial experiments by applying vacuum (1 mbar) for 2 h.
(19) For an excellent overview of the nucleophilicity of arenes as well as the reactivity of various other molecules, we recommend the database of Prof. H. Mayr (LMU Munich): http://www.cup.lmu.de/oc/mayr/reaktionsdatenbank/.
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