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Synthetic Scope of Brønsted Acid-Catalyzed Reactions of Carbonyl Compounds and Ethyl Diazoacetate

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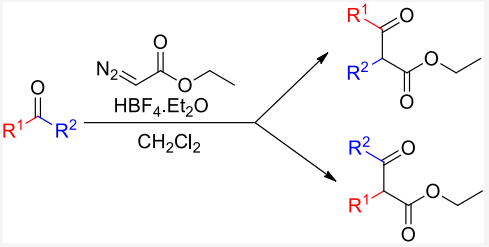
ABSTRACT: The comprehensive study of the reactions of carbonyl compounds and ethyl diazoacetate in the presence of a Brønsted acid catalyst is described. In result, a broad range of 3-oxo-esters were synthesized from a variety of ketones and aliphatic aldehydes by 1,2-aryl/alkyl/hydride shift. Aryl−methyl ketones produced only aryl-migrated products, whereas other ketones yielded a mixture of products. For diaryl ketones, the identity of two inseparable migrated products was confirmed by two-dimensional NMR spectroscopy.



INTRODUCTION

3-Oxo-esters and related 3-hydroxy acrylates are useful precursors for synthesizing biologically active and pharmaceutically important compounds due to their expandable functionality and wide range of substrate scope.[1−4] The presence of prochirality of such synthons promotes the construction of a quaternary carbon center.[5] They are also exploited as common monomers in the polymer industry.[6] Moreover, such oxo-esters and their related acrylates contribute to very unusual Michael and Mannich type reactions.[7−10] Therefore, increasing efforts have been devoted to developing efficient protocols for the synthesis of these vital scaffolds using commercially available starting materials.[11]

In our previous work, we reported the formation of 3-hydroxy-2-aryl acrylates by 1,2-aryl migration from the reactions of aromatic aldehydes with ethyl diazoacetate (EDA) in the presence of an iron Lewis acid catalyst.[12] Later on, other groups also reported the similar type of reactions using different Lewis acid catalysts.[13,14] In 2004, our group explored the catalyst scopes to produce 3-hydroxy-2-aryl acrylates and 3-oxo-esters with Brønsted type acids using similar substrates.[15] However, reactions of more sterically hindered and less electrophilic aromatic/aliphatic ketones or aliphatic aldehydes with EDA in the presence of a Brønsted acid catalyst are certainly rare. Herein, we present the unexplored reaction of various carbonyl compounds and EDA in the presence of $HBF_4{}^{\bullet}OEt_2$ for the formation of 3-oxo-esters (Scheme 1). During this study, we also characterized the ratio of the isolated migrated products from diaryl ketones by the heteronuclear multiple bond correlation (HMBC) method.

RESULTS AND DISCUSSION

Based on our published work with acetophenone and EDA using $HBF_4{}^{\bullet}OEt_2$ catalyst, we decided to expand the scope of this reaction using several substituted acetophenones.[15] The results are summarized in Table 1. The reaction of acetophenones and EDA provided a good yield of product, ethyl 3-oxo-2-arylbutanoate which was in equilibrium with enol tautomer, ethyl 3-hydroxy-2-arylbut-2-enoate (**3a−h**). The enol products were found exclusively as *Z*-form, which was confirmed by two-dimensional (2D) NMR (see the Supporting Information, SI). The *Z*-enol form might be stable due to the presence of intramolecular hydrogen bonding between the hydroxy and carbonyl group as observed in ethyl 3-hydroxy-2-phenyl-acrylate.[16] In the substituted acetophenones, the *para*-substituted acetophenones bearing a weak electron-withdrawing group such as chloro (**1b**), a strong electron-donating group such as methoxy (**1c**), and a weak electron-donating group such as methyl (**1d**) were provided almost similar yields of products. The methyl substituent on *meta*- and *ortho*- positions (**1e** and **1f**) yielded lower amount of products compared to the methyl substituent on *para*-position (**1d**). Substrates bearing strong electron-withdrawing groups on the aromatic rings provided low yield, for example, when the 4-nitroacetophenone (**1g**) was subjected to the standard reaction conditions, the desired product (**3g**) was isolated in only 15% yield, and most of the starting material was recovered. Interestingly, tautomeric 3-oxo-esters derived from 2-acetonaphthone showed good tolerances in the catalytic system, giving the desired product (**3h**) with a 55% yield. It should be noted that no methyl-migrated products were observed from the reactions of acetophenones and EDA.

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Scheme 1. Formation of 3-Oxo-Esters in Presence of a Brønsted Acid Catalyst by 1,2-Migration

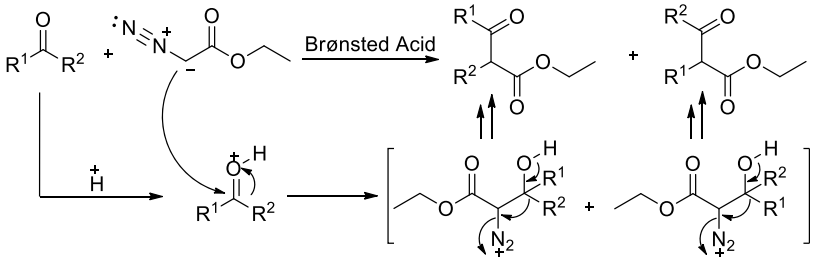
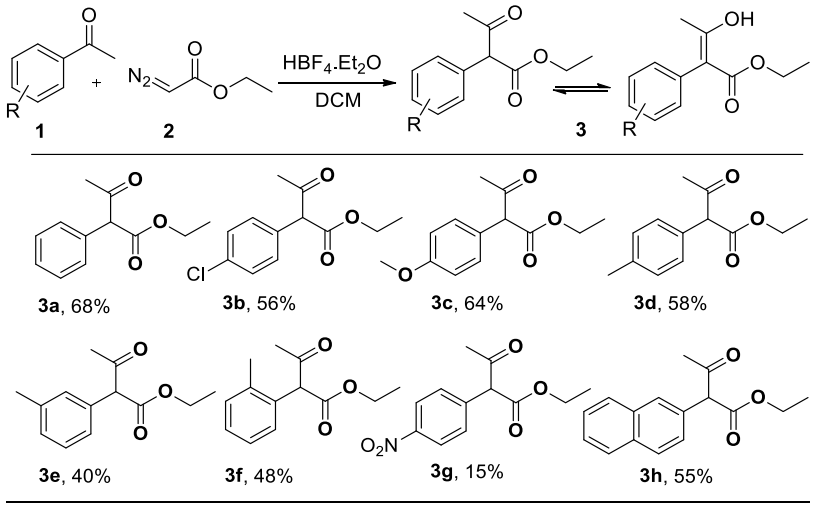


Table 1. Migratory Aptitude of Methyl−Aryl Groups[a]



[a]Reaction conditions: **1** (3.0−5.0 mmol), **2** (6.0−10.0 mmol), $HBF_4{}^{\bullet}OEt_2$ (0.6−1.0 mmol), and CH_2Cl_2 (10−15 mL) at −78 °C to room-temperature (rt) for 3 days.

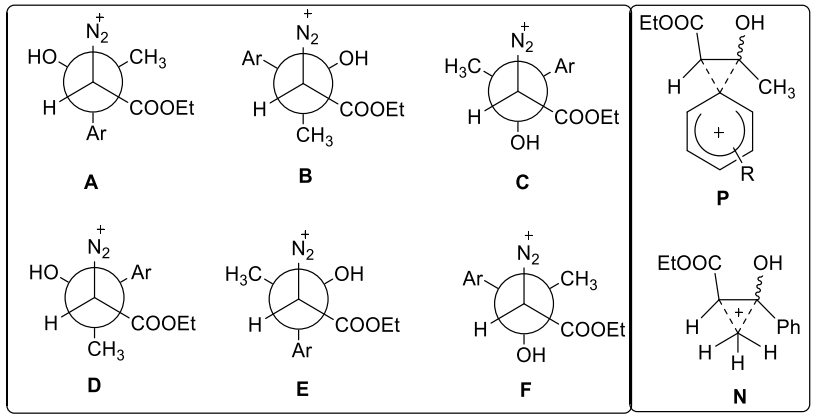


Figure 1. Newman projections of six possible rotamers (**A**−**F**) and a phenonium ion intermediate (**P**) along with nonclassical carbocation intermediate (**N**).

The above findings could be explained with respect to six probable rotamers **A**−**F** (Figure 1) from the reaction of acetophenones and EDA in the presence of $HBF_4{}^{\bullet}OEt_2$. Rotamers **A**−**C** are interconvertible due to the rotation of C−C bonds and their diastereomeric form of rotamers, **D**−**F** are also interconvertible. In both rotamers **A** and **E**, migrating aryl group and leaving diazonium group were anti to each other; thus, the formation of 3-oxo-ester **3** was favorable. On the other hand, in rotamers **B** and **D**, the methyl migrating group was anti to the leaving group, which could favor the formation of methyl-migrated product. However, the aryl migration from rotamer **A**/**E** was more favorable over methyl from rotamer **B**/**D** due to its ability to stabilize an intermediate phenonium ion (Figure 1, **P**) by six-electron resonance participation, whereas two electrons participating in nonclassical carbocation intermediate (Figure 1, **N**) are not stable enough to facilitate any methyl migration. The predominant phenyl over methyl migration is consistent with the pinacol rearrangement, which also involved carbocation intermediate.[17] In our discussion, we did not consider rotamers **C** and **F** which are prerequisite for the formation of epoxide, not observed in our reactions.

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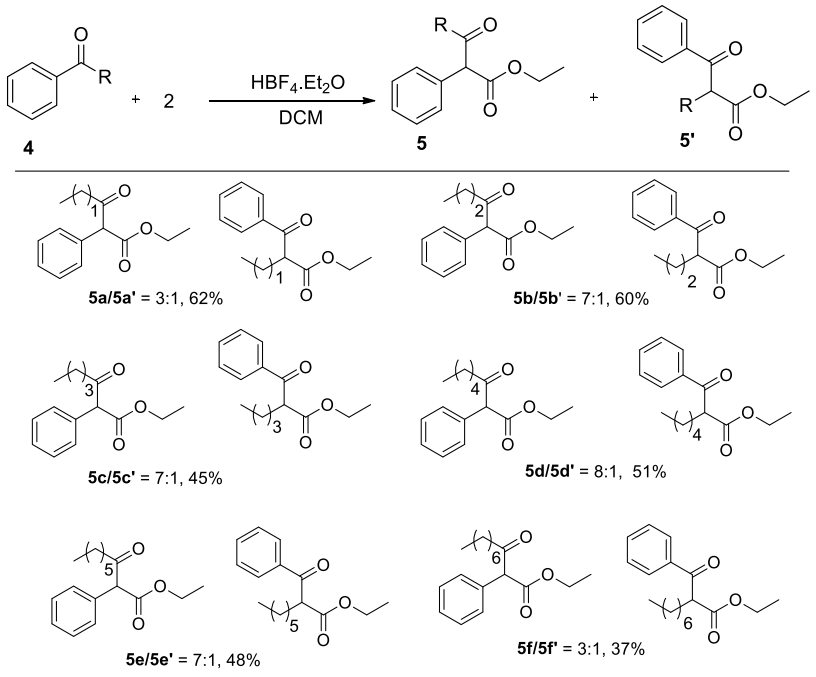
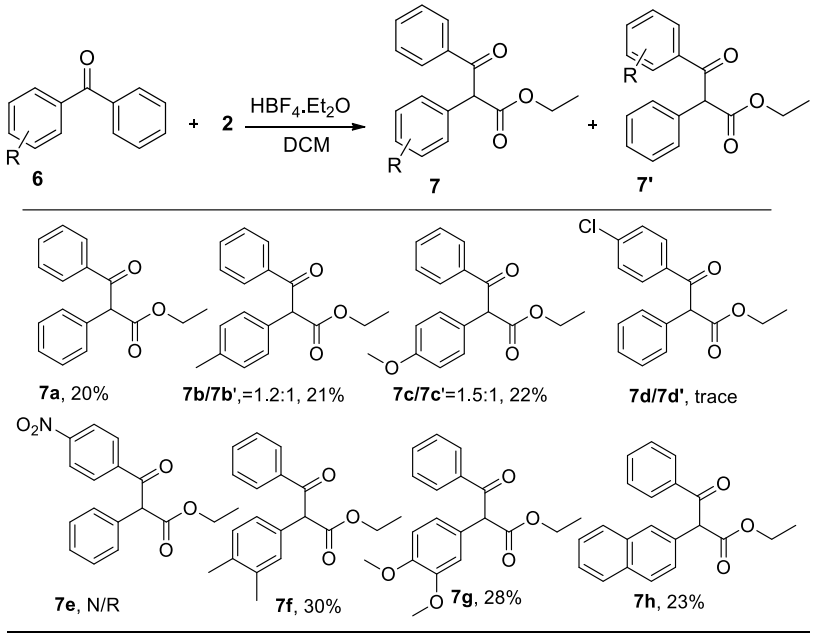
Table 2. Migratory Aptitude of Alkyl−Phenyl Groups[a,b]



[a]Reaction conditions: **4** (2.0−5.0 mmol), **2** (4.0−10.0 mmol), $HBF_4{}^{\bullet}OEt_2$ (0.4−1.0 mmol), and CH_2Cl_2 (10−15 mL) at −78 °C to room-temperature (rt) for 3 days. [b]The ratios of the products are calculated from the NMR of the crude mixtures.

Table 3. Migratory Aptitude of Aryl−Phenyl Groups[a,b]



[a]Reaction conditions: **6** (5.0−10.0 mmol), **2** (10.0−20 mmol), $HBF_4{}^{\bullet}OEt_2$ (1.0−2.0 mmol), and CH_2Cl_2 (15−20 mL) at −78 °C to room-temperature (rt) for 3 days. [b]The ratios of the products are calculated from the NMR of the crude mixtures.

From the perceived nature of the phenyl and methyl groups of acetophenone, the reactions were extended to other aromatic ketones by varying alkyl groups (Table 2). In the case of increasing alkyl chain length, both phenyl- and alkyl-migrated products were formed. For example, when propiophenone (**4a**) was employed as a substrate, both phenyl- and ethyl-migrated products (**5a**/**5a**′ = 3:1) were obtained with 62% isolated yield. With increasing alkyl chain length, the migratory tendency of phenyl group relative to alkyl migration was constant (**5b**/**5b**′−**5e**/**5e**′ ∼ 7:1). However, when the reaction was carried out with octanophenone (**4f**), the ratio of the migrated products was **5f**/**5f**′ = 3:1 and the yield was 37%. Although we did not observe any methyl migration in acetophenone (**1a**), the migration of ethyl or other longer chain alkyl groups happened may be due to their ability to stabilize the developing carbocation intermediate by hyperconjugation compared to a methyl group.[17]

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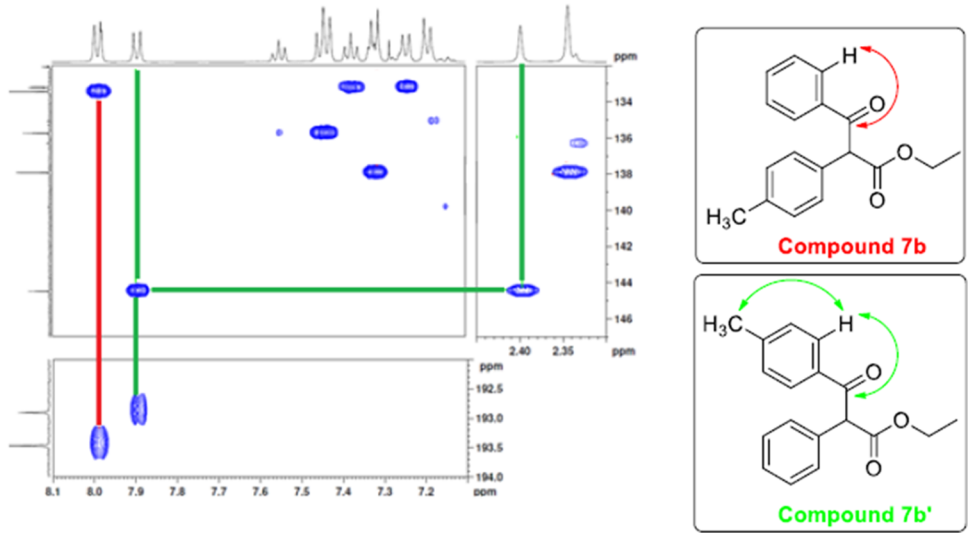

Figure 2. HMBC cross-peak spectra for the products of *para*-methylbenzophenone.

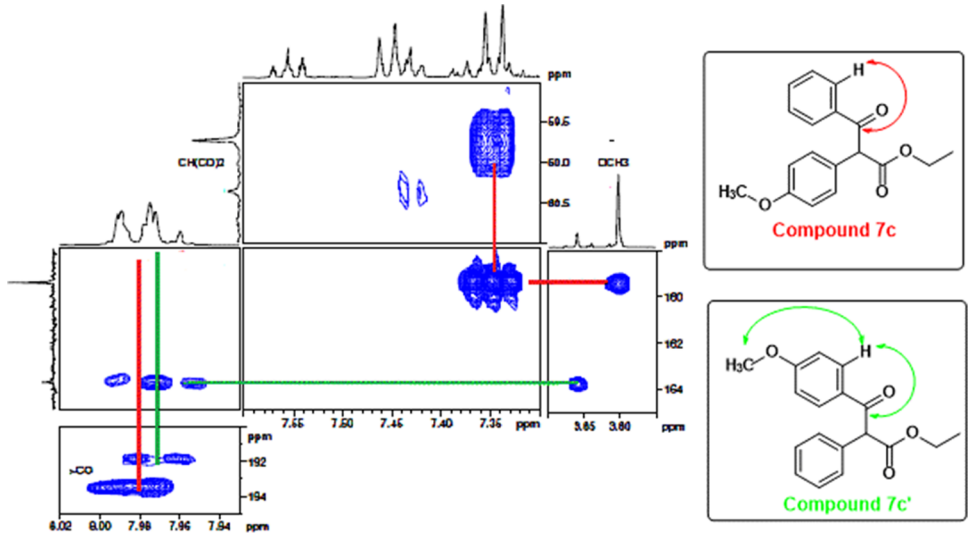

Figure 3. HMBC cross-peak spectra for the products of *para*-methoxybenzophenone.

For further investigations, we turned our attention to benzophenone and substituted benzophenones (Table 3). From our inquiry, it was revealed that when an electron-donating group such as methyl was present in the mono-substituted benzophenone (**6b**), both phenyl- and *para*-tolyl-migrated products (**7b**/**7b**′′) were formed in a ratio of 1:1.2. Our result agrees with the value (1.28 ± 0.09) reported by Curtin and Crew in the acid-catalyzed deamination reaction of 2-amino-L-phenyl-L-*p*-tolylethanol involving carbocation intermediate.[18] Moreover, in our study, the *para*-anisyl group in compound **6c** provided the relatively better migration (1.5/1) might be because of the additional interaction energy in the transition state induce by the *para*-methoxy group during carbocation formation.[19] In the case of electron-rich 3,4-disubstituted benzophenone (**6f** and **6g**), we obtained exclusively the disubstituted phenyl-migrated products (**7f** and **7g**). This type of migration was also found in naphthyl phenyl ketone (**6h**) where electron-rich naphthyl group was migrated to give the desired product (**7h**). The exclusive formation of (**7f**), (**7g**), and (**7h**) may be due to the better stability of the corresponding phenonium carbocation intermediate. On the other hand, when an electron-withdrawing group (**6d** and **6e**) was present in the monosubstituted benzophenone, trace or no product was observed, which could be due to the instability of carbocation intermediate.[15]

As we obtained a mixture of products from the reactions of *para*-methyl (**6b**) and *para*-methoxybenzophenone (**6c**) and EDA, we undertook 2D NMR studies to confirm the structure of the products. After analyzing HMBC spectra, we observed a cross-peak signal between the *ortho*-proton of the benzene ring (a doublet at δ 7.99) and the carbonyl carbon of ester (δ 193.7) (red line in Figure 2), which correlates with the structure of **7b** generated by *para*-methyl phenyl migration. On the other hand, a cross-peak signal was identified among the *ortho*-proton (a doublet at δ 7.89) and the *para*-methyl carbon of the benzene ring (δ 2.39) as well as with the carbonyl carbon of ester (δ 192.9) (green line in Figure 2). This cross-coupling nicely correlates with **7b**′ formed by phenyl migration. By comparing the peaks at δ 7.89 and δ 7.99 in the crude mixture (see the SI), we concluded that this reaction yielded slightly more product of **7b** than **7b**′ due to the favorable migration of electron-donating *para*-methyl phenyl over the phenyl group.

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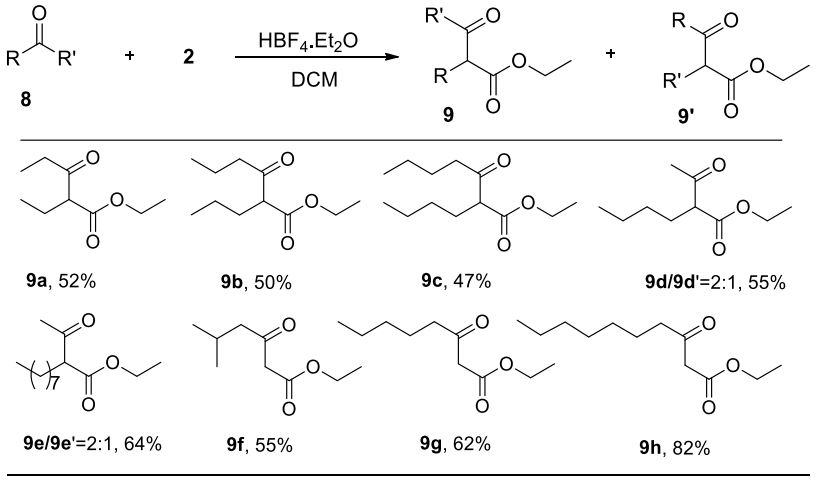
Table 4. Migratory Aptitude of Alkyl-Hydride Groups[a,b]



[a]Reaction conditions: **8** (2.0−8.0 mmol), **2** (4.0−16.0 mmol), $HBF_4{}^{\bullet}OEt_2$ (0.4−1.6 mmol), and CH_2Cl_2 (10−15 mL) at −78 °C to room-temperature (rt) for 3 days. [b]The ratios of the products are calculated after isolation.

Similarly, we have confirmed the structure of **7c** by 2D NMR by comparing a cross-peak signal between the *ortho*-proton of the benzene ring (a doublet at δ 7.98) and the carbonyl carbon of ester (δ 194.0) (red line in Figure 3) and the structure of **7c′** from the cross-peak signal among the *ortho*-proton (a doublet at δ 7.97) and the *para*-methoxy carbon of the benzene ring (δ 3.86) with the carbonyl carbon of ester (δ 192.0) (green line in Figure 3) (see also the SI).

Finally, to demonstrate the further utility of the reaction, transformation of the aliphatic aldehydes and ketones were explored. The results of these reactions are summarized in Table 4. For the migratory aptitude of unsymmetrical aliphatic ketones, increasing the steric bulk of the alkyl group increases its tendency to migrate. The longer alkyl chain-migrated products dominated over the methyl-migrated products (**9d**/**9d′** and **9e**/**9e′** = 2:1) due to the hyperconjugation effect with a longer chain alkyl group, triggered better stability of the carbocation intermediate.[17] In the case of aliphatic aldehydes, the hydride-migrated products (**9f**, **9g**, and **9h**) formed exclusively as observed with an aromatic aldehyde.[20]

In summary, we investigated the reaction of less explored aromatic/aliphatic ketones as well as aliphatic aldehydes with EDA employed as the reaction partner. The distinct reactivity between carbonyl compounds and EDA has allowed the incorporation of a diverse range of substituent patterns into the product formation. Depending on the migratory aptitudes of hydride, alkyl, phenyl, and aryl groups, a wide range of 3-oxo-esters are formed. We anticipate that these valuable synthons will further prove their utility in preparing important building blocks of biologically active natural and synthetic compounds.

EXPERIMENTAL SECTION

All reactions were performed under a dry nitrogen atmosphere using standard Schlenk techniques unless otherwise noted. All reaction vessels were flame dried under vacuum and filled with nitrogen prior to use. Reagents and solvents were purchased from Sigma-Aldrich, Milwaukee. All ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ (internal standard: 7.26 ppm, ^1H; 77.16 ppm, $^{13}C\{^1H\}$) at room temperature with a Bruker 300 and 500 MHz spectrometers. The chemical shifts (δ) are given in parts per million (ppm) and the coupling constants in Hertz (Hz). The following abbreviations are used: s-singlet, d-doublet, t-triplet, q-quartet, and m-multiplet. Previously reported compounds were identified by ^1H NMR. All new compounds were additionally characterized by ^1H NMR, ^{13}C NMR, and high-resolution mass spectrometry (HRMS). HRMS were obtained using Shimadzu liquid chromatography-ion trap-time of flight tandem mass spectrometry (LCMS-IT-TOF) by the electrospray ionization (ESI) technique. For the column chromatography, silica gel (35−70 μm) was used. The thin-layer chromatography (TLC) was performed on aluminum-backed plates precoated (0.25 mm) with Silica Gel 60 F254 with a suitable solvent system and was visualized using UV fluorescence and/or iodine chamber.

General Procedure for the One-Pot Synthesis of 3-Oxo-Esters. For each experiment, carbonyl compounds (2.0−8.0 mmol, 1.0 equiv) were dissolved in 10−20 mL of freshly distilled dichloromethane under nitrogen at −78 °C. A Brønsted acid, $HBF_4{}^{\bullet}OEt_2$ catalyst (0.4−1.6 mmol, 0.2 equiv) was added, and the reaction mixture was stirred for 1 h at the same temperature. Ethyl diazoacetate (EDA) (4.0−16.0 mmol, 2.0 equiv) was diluted in 5 mL of freshly distilled dichloromethane and added to the solution over a period of 0.5−1 h. Then, the reaction mixture was allowed to stir for 72 h at room temperature. After completion of the reaction, it was quenched by adding tetrahydrofuran (THF). The reaction mixture was filtered through a silica plug using dichloromethane as a solvent and the solvent was removed by rotary evaporation. Pure products were isolated by silica gel column chromatography with 0−10% ethyl acetate in hexane except, **5j** (50% dichloromethane in hexane) and **5k** (100% dichloromethane).

*Ethyl 3-Oxo-2-phenylbutanoate (Keto-enol = 1:1) (**3a**).*[15,21] The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 100:1). The title product was isolated as a colorless oil (0.52 g, 68%) from the reaction of acetophenone (0.51 g, 4.25 mmol, 1.0 equiv) and EDA (1.03 mL, 8.50 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.12 mL, 0.85 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 13.15 (s, 1H), 7.40−7.29 (m, 8H), 7.19−7.16 (m, 2H), 4.71 (s, 1H), 4.26−4.16 (m, 4H), 2.21 (s, 3H), 1.87 (s, 3H), 1.30 (t, J = 7.5 Hz, 3H), and 1.21 (t, J = 7.5 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 201.6, 173.9, 172.6, 168.5, 135.3, 132.7, 131.2, 129.3, 128.9, 128.3, 128.0, 126.9, 104.4, 65.8, 61.6, 60.6, 28.8, 19.9, 14.2, and 14.1.

*Ethyl 2-(4-Chlorophenyl)-3-oxobutanoate (Keto-enol = 9:8) (**3b**).*[21] The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 50:1). The title product was isolated as a colorless oil (0.46 g, 56%) from the reaction of 4′-chloroacetophenone (0.52 g, 3.38 mmol, 1.0 equiv) and EDA (0.82 mL, 6.78 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.09 mL, 0.68 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 500 MHz): δ 13.14 (s, 1H), 7.38 (d, J = 10.0 Hz, 2H), 7.32 (t, J = 10.0 Hz, 4H), 7.11 (d, J = 10.0 Hz, 2H), 4.69 (s, 1H),

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4.26−4.17 (m, 4H), 2.22 (s, 3H), 1.87 (s, 3H), 1.30 (t, J = 7.5 Hz, 3H), and 1.21 (t, J = 7.5 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 200.9, 174.1, 172.3, 168.2, 134.5, 133.7, 132.9, 132.6, 131.1, 130.7, 129.1, 128.3, 103.3, 64.9, 61.7, 60.8, 28.9, 19.9, 14.2, and 14.1.

*Ethyl 2-(4-Methoxyphenyl)-3-oxobutanoate (Keto-enol = 4:3) (**3c**).*[21] The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 50:1). The title product was isolated as a colorless oil (0.52 g, 64%) from the reaction of 4′-methoxyacetophenone (0.51 g, 3.41 mmol, 1.0 equiv) and EDA (0.82 mL, 6.82 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.09 mL, 0.68 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 13.11 (s, 1H), 7.28 (d, J = 6.0 Hz, 2H), 7.08 (t, J = 4.5 Hz, 2H), 7.28 (t, J = 9.0 Hz, 4H), 4.65 (s, 1H), 4.20 (q, J = 7.5 Hz, 4H), 3.82 (s, 3H), 3.81 (s, 3H), 2.18 (s, 3H), 1.86 (s, 3H), 1.28 (t, J = 7.5 Hz, 3H), and 1.19 (t, J = 7.5 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 201.8, 174.0, 172.8, 168.8, 159.6, 158.5, 132.2, 130.4, 127.9, 127.5, 124.8, 114.3, 113.5, 103.8, 64.9, 61.5, 60.6, 55.2, 55.1, 28.6, 19.8, 14.2, and 14.1.

*Ethyl 3-Oxo-2-(p-tolyl)butanoate (Keto-enol = 2:1) (**3d**).*[22] The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 100:1). The title product was isolated as a colorless oil (0.30 g, 58%) from the reaction of 4′-methylacetophenone (0.53 g, 3.91 mmol, 1.0 equiv) and EDA (0.95 mL, 7.83 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.11 mL, 0.78 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 13.14 (s, 1H), 7.27−7.15 (m, 8H), 7.06 (d, J = 6.0 Hz, 2H), 4.67 (s, 1H), 4.28−4.16 (m, 4H), 2.38 (s, 3H), 2.37 (s, 3H), 2.20 (s, 3H), 1.87 (s, 3H), 1.30 (t, J = 7.5 Hz, 3H), and 1.22 (t, J = 6.0 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 201.8, 173.8, 172.8, 168.7, 138.1, 136.5, 132.2, 131.1, 129.7, 129.6, 129.1, 128.8, 104.1, 65.4, 61.6, 60.6, 28.7, 21.2, 21.1, 20.0, 14.2, and 14.1.

*Ethyl 3-Oxo-2-(m-tolyl)butanoate (Keto-enol = 3:4) (**3e**).*[23] The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 100:1). The title product was isolated as a colorless oil (0.21 g, 40%) from the reaction of 3′-methylacetophenone (0.52 g, 3.85 mmol, 1.0 equiv) and EDA (0.93 mL, 7.69 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.11 mL, 0.77 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 13.15 (s, 1H), 7.28−7.10 (m, 8H), 7.06 (d, J = 9.0 Hz, 2H), 4.68 (s, 1H), 4.27−4.17 (m, 4H), 2.38 (s, 6H), 2.21 (s, 3H), 1.88 (s, 3H), 1.30 (t, J = 7.5 Hz, 3H), and 1.22 (t, J = 7.5 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 201.7, 173.8, 172.7, 168.6, 138.6, 137.5, 135.1, 132.6, 131.9, 129.9, 129.0, 128.8, 128.3, 127.9, 127.7, 126.3, 104.4, 65.7, 61.5, 60.6, 28.7, 21.4, 19.9, 14.2, and 14.1.

*Ethyl 3-Oxo-2-(o-tolyl)butanoate (Keto-enol = 1:4) (**3f**).*[22] The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 100:1). The title product was isolated as a colorless oil (0.26 g, 48%) from the reaction of 2′-methylacetophenone (0.53 g, 4.00 mmol, 1.0 equiv) and EDA (0.95 mL, 7.90 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.11 mL, 0.79 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 13.10 (s, 0.8H), 7.72 (d, J = 9.0 Hz, 2H), 7.39 (d, J = 6.0 Hz, 2H), 7.25 (d, J = 6.0 Hz, 4H), 7.09 (s, 1H), 4.94 (s, 0.2H), 4.29−4.23 (m, 2H), 4.16−4.10 (m, 1H), 2.61 (s, 3H), 2.57 (s, 3H), 2.20 (s, 3H), 1.78 (s, 3H), 1.30 (s, 3H), and 1.22 (t, J = 7.5 Hz, 3H).

*Ethyl 2-(4-Nitrophenyl)-3-oxobutanoate (Keto-enol = 4:5) (**3g**).*[21] The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 25:1). The title product was isolated as a colorless oil (0.078 g, 15%) from the reaction of 4′-nitroacetophenone (0.52 g, 3.12 mmol, 1.0 equiv) and EDA (0.75 mL, 6.24 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.085 mL, 0.62 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 13.25 (s, 1H), 8.36−8.20 (m, 3H), 7.83 (t, J = 4.5 Hz, 1H), 7.61−7.48 (m, 3H), 7.37 (d, J = 9.0 Hz, 1H), 4.85 (s, 1H), 4.30−4.18 (m, 4H), 2.29 (s, 3H), 1.91 (s, 3H), 1.31 (t, J = 7.5 Hz, 3H), and 1.21 (t, J = 7.5 Hz, 3H).

*Ethyl 2-(Naphthalen-2-yl)-3-oxobutanoate (Keto-enol = 5:3) (**3h**).*[23] The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 50:1). The title product was isolated as a colorless oil (0.29 g, 55%) from the reaction of 2-acetonaphthone (0.52 g, 3.04 mmol, 1.0 equiv) and EDA (0.73 mL, 6.07 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.084 mL, 0.61 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 500 MHz): δ 13.22 (s, 1H), 7.90−7.83 (m, 7H), 7.65 (s, 1H), 7.55−7.49 (m, 5H), 7.31 (d, J = 10.0 Hz, 1H), 4.89 (s, 1H), 4.31−4.19 (m, 4H), 2.25 (s, 3H), 1.92 (s, 3H), 1.32 (t, J = 7.5 Hz, 3H), and 1.19 (t, J = 7.5 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 201.7, 174.2, 172.7, 168.6, 133.4, 133.3, 133.0, 132.8, 132.4, 130.2, 130.0, 129.6, 128.7, 128.7, 128.0, 127.9, 127.7, 127.5, 126.7, 126.5, 126.4, 126.0, 125.9, 104.3, 65.9, 61.7, 60.7, 28.9, 20.0, 14.2, and 14.1.

*Ethyl 3-Oxo-2-phenylpentanoate (Keto-enol = 6:5) (**5a**).* The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 100:1). The title product was isolated as a colorless oil (0.58 g, 34%) from the reaction of propiophenone (0.52 g, 3.88 mmol, 1.0 equiv) and EDA (0.94 mL, 7.75 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.11 mL, 0.78 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 13.23 (s, 1H), 7.37−28 (m, 8H), 7.18 (t, J = 4.5 Hz, 2H), 4.76 (s, 1H), 4.26−4.14 (m, 4H), 2.53 (q, J = 6.0 Hz, 2H), 2.15 (q, J = 6.0 Hz, 2H), 1.28 (t, J = 7.5 Hz, 3H), 1.18 (t, J = 7.5 Hz, 3H), and 1.12−1.01 (m, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 204.2, 178.1, 172.8, 168.7, 135.2, 133.0, 131.2, 129.4, 128.8, 128.1, 128.0, 126.9, 103.6, 64.8, 61.5, 60.5, 34.9, 26.3, 14.2, 14.0, 11.1, and 7.8. HRMS (ESI/Q-TOF): calculated (m/z) for $C_{13}H_{17}O_3$ $(M + H)^+$: 221.1172; found 221.1164.

*Ethyl 2-Benzoylbutanoate (**5a′**).*[24] The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 100:1). The title product was isolated as a colorless oil (0.48 g, 28%) from the reaction of propiophenone (0.52 g, 3.88 mmol, 1.0 equiv) and EDA (0.94 mL, 7.75 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.11 mL, 0.78 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 7.98 (d, J = 9.0 Hz, 2H), 7.55 (t, J = 6.0 Hz, 1H), 7.48 (t, J = 6.0 Hz, 2H), 4.21 (t, J = 6.0 Hz, 1H), 4.12 (q, J = 9.0 Hz, 2H), 2.07−1.98 (m, 2H), 1.14 (t, J = 6.0 Hz, 3H), and 0.98 (t, J = 7.5 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 195.2, 169.9, 136.4, 133.4, 128.7, 128.5, 61.2, 55.8, 22.4, 14.0, and 12.1.

*Ethyl 3-Oxo-2-phenylhexanoate (Keto-enol = 2:3) (**5b**).* The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 100:1). The title product was isolated as a colorless oil (0.59 g, 36%) from the reaction of butyrophenone (0.52 g, 3.50 mmol, 1.0 equiv) and EDA (0.85 mL, 7.0 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.096 mL, 0.70 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 13.20 (s, 1H), 7.40−7.30 (m, 8H), 7.18 (d, J = 5.0 Hz, 2H), 4.74 (s, 1H), 4.27−4.17 (m, 4H), 2.48 (t, J = 7.5 Hz, 2H), 2.11 (t, J = 8.0 Hz, 2H), 1.63−1.55 (m, 4H), 1.29 (t, J = 6.0 Hz, 3H), 1.19 (t, J = 6.0 Hz, 3H), and 0.89−0.83 (m, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 203.7, 176.9, 172.9, 168.6, 135.2, 132.8, 131.4, 129.5, 128.8, 128.2, 128.0, 126.9, 104.3, 65.0, 61.6, 60.6, 43.5, 34.7, 20.1, 17.1, 14.2, 14.1, 13.8, and 13.4. HRMS (ESI/Q-TOF): calculated (m/z) for $C_{14}H_{19}O_3$ $(M + H)^+$: 235.1329; found 235.1312.

*Ethyl 2-Benzoylpentanoate (**5b′**).*[25] The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 100:1). The title product was isolated as a colorless oil (0.39 g, 24%) from the reaction of butyrophenone (0.52 g, 3.50 mmol, 1.0 equiv) and EDA (0.85 mL, 7.0 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.096 mL, 0.70 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 7.98 (t, J = 4.5 Hz, 2H), 7.55 (t, J = 7.5 Hz, 1H), 7.48 (t, J = 7.5 Hz, 2H), 4.31 (t, J = 7.5 Hz, 1H), 4.15 (q, J = 6.0 Hz, 2H), 2.04−1.95 (m, 2H), 1.43−1.33 (m, 2H), 1.17 (t, J = 7.5 Hz, 3H), and 0.95 (t, J = 7.5 Hz, 3H).

*Ethyl 3-Oxo-2-phenylheptanoate (Keto-enol = 7:2) (**5c**).* The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 100:1). The title product was isolated as a colorless oil (0.24 g, 30%) from the reaction of valerophenone (0.53 g, 3.27 mmol, 1.0 equiv) and EDA (0.79 mL, 6.53 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.089 mL, 0.65 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 13.20 (s, 0.4H), 8.15 (d, J = 5.0 Hz, 1H), 7.51 (t, J = 5.0 Hz, 1H), 7.51−7.35 (m, 7H), 7.17 (d, J = 5.0 Hz, 1H), 4.73 (s, 1.3H), 4.30−4.16 (m, 4H), 2.49 (t, J = 7.5 Hz, 2H), 2.12 (t, J = 7.5 Hz, 2H), 1.56−1.53 (m,

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4H), 1.30−1.24 (m, 7H), 1.22 (t, J = 4.5 Hz, 3H), and 0.93−0.80 (m, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 203.8, 177.2, 171.1, 168.6, 132.7, 131.3, 129.4, 128.8, 128.2, 128.0, 126.9, 104.1, 65.0, 61.6, 60.4, 41.3, 32.5, 31.9, 29.7, 29.4, 28.8, 25.7, 22.3, 14.2, 14.1, 14.1, and 13.7. HRMS (ESI/Q-TOF): calculated (m/z) for $C_{15}H_{21}O_3$ $(M + H)^+$: 249.1485; found 249.1464.

*Ethyl 2-Benzoylhexanoate (**5c′**).*[26] The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 100:1). The title product was isolated as a colorless oil (0.12 g, 15%) from the reaction of valerophenone (0.53 g, 3.27 mmol, 1.0 equiv) and EDA (0.79 mL, 6.53 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.089 mL, 0.65 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.01 (d, J = 9.0 Hz, 2H), 7.55 (d, J = 6.0 Hz, 1H), 7.48 (t, J = 7.5 Hz, 2H), 4.30 (t, J = 7.5 Hz, 1H), 4.12 (q, J = 15.9, 9.0 Hz, 2H), 2.03 (q, J = 12.0, 6.0 Hz, 2H), 1.36−1.28 (m, 4H), 1.19 (t, J = 7.5 Hz, 3H), and 0.92 (t, J = 7.5 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 195.3, 170.1, 136.4, 133.4, 128.7, 128.6, 61.3, 54.4, 29.8, 28.7, 22.5, 14.0, and 13.8.

*Ethyl 3-Oxo-2-phenyloctanoate (Keto-enol = 2:3) (**5d**).* The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 100:1). The title product was isolated as a colorless oil (0.24 g, 32%) from the reaction of hexanophenone (0.50 g, 2.84 mmol, 1.0 equiv) and EDA (0.74 mL, 5.67 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.078 mL, 0.57 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 13.26 (s, 1H), 7.41−28 (m, 8H), 7.19 (t, J = 6.0 Hz,2H), 4.77 (s, 1H), 4.26−4.14 (m, 4H), 2.51 (t, J = 7.5 Hz, 2H), 2.14 (t, J = 7.5 Hz, 2H), 1.63−1.54 (m, 4H), 1.43−1.32 (m, 14H), and 0.89−0.83 (m, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 203.6, 177.2, 172.8, 168.5, 135.2, 132.9, 131.3, 129.5, 128.7, 127.9, 126.9, 104.1, 65.0, 61.4, 60.5, 41.5, 32.7, 31.3, 31.1, 26.4, 23.3, 22.3, 22.3, 22.2, 14.1, and 14.0. HRMS (ESI/Q-TOF): calculated (m/z) for $C_{16}H_{23}O_3$ $(M + H)^+$: 263.1642; found 263.1642.

*Ethyl 2-Benzoylheptanoate (**5d′**).* The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 100:1). The title product was isolated as a colorless oil (0.14 g, 19%) from the reaction of hexanophenone (0.50 g, 2.84 mmol, 1.0 equiv) and EDA (0.74 mL, 5.67 mmol, 0.2 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.078 mL, 0.57 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.01 (d, J = 9.0 Hz, 2H), 7.59 (t, J = 7.5 Hz, 1H), 7.46 (t, J = 7.5 Hz, 2H), 4.30 (t, J = 7.5 Hz, 1H), 4.16 (q, J = 7.5 Hz, 2H), 2.05−1.98 (m, 2H), 1.39−1.27 (m, 6H), 1.18 (t, J = 7.5 Hz, 3H), and 0.88 (t, J = 7.5 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 195.3, 170.1, 136.4, 133.4, 128.7, 128.7, 128.6, 128.5, 61.3, 54.4, 31.6, 28.9, 27.3, 22.4, and 13.9. HRMS (ESI/Q-TOF): calculated (m/z) for $C_{16}H_{23}O_3$ $(M + H)^+$: 263.1642; found 263.1649.

*Ethyl 3-Oxo-2-phenylnonanoate (Keto-enol = 2:1) (**5e**).* The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 100:1). The title product was isolated as a colorless oil (0.23 g, 31%) from the reaction of heptanophenone (0.52 g, 2.73 mmol, 1.0 equiv) and EDA (0.66 mL, 5.46 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.075 mL, 0.55 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 13.20 (s, 1H), 7.39−7.29 (m, 9H), 7.18−7.15 (m, 1H), 4.74 (s, 1H), 4.26−4.17 (m, 4H), 2.50 (t, J = 7.5 Hz, 3H), 2.12 (t, J = 7.5 Hz, 2H), 1.58−1.54 (m, 4H), 1.31−1.18 (m, 18H), and 0.89−0.84 (m, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 203.7, 177.2, 172.9, 168.6, 135.2, 132.8, 131.3, 129.6, 129.4, 129.0, 128.8, 128.1, 128.0, 126.9, 104.1, 65.0, 61.5, 60.5, 41.9, 32.7, 31.5, 28.8, 28.5, 26.6, 23.6, 22.4, 14.2, 14.1, and 14.0. HRMS (ESI/Q-TOF): calculated (m/z) for $C_{17}H_{25}O_3$ $(M + H)^+$: 277.1798; found 277.1783.

*Ethyl 2-Benzoyloctanoate (**5e′**).*[27] The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 100:1). The title product was isolated as a colorless oil (0.13 g, 17%) from the reaction of heptanophenone (0.52 g, 2.73 mmol, 1.0 equiv) and EDA (0.66 mL, 5.46 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.075 mL, 0.55 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.01 (d, J = 9.0 Hz, 2H), 7.60 (t, J = 6.0 Hz, 1H), 7.49 (t, J = 7.5 Hz, 2H), 4.30 (t, J = 7.5 Hz, 1H), 4.16 (q, J = 7.5 Hz, 2H), 2.03 (d, J = 3.0 Hz, 2H), 1.36−1.27 (m, 8H), 1.19 (t, J = 6.0 Hz, 3H), and 0.88 (t, J = 6.0 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 195.3, 170.1, 136.4, 133.4, 128.7, 128.6, 61.3, 54.4, 31.5, 29.7, 29.1, 29.0, 27.6, 22.5, and 14.0.

*Ethyl 3-Oxo-2-phenyldecanoate (Keto-enol = 5:3) (**5f**).* The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 100:1). The title product was isolated as a colorless oil (0.23 g, 30%) from the reaction of octanophenone (0.54 g, 2.64 mmol, 1.0 equiv) and EDA (0.64 mL, 5.29 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.073 mL, 0.53 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 13.18 (s, 1H), 7.37−28 (m, 8H), 7.16 (d, J = 6.0 Hz, 2H), 4.73 (s, 1H), 4.27−4.15 (m, 4H), 2.49 (t, J = 7.5 Hz, 2H), 2.11 (t, J = 7.5 Hz, 2H), 1.62−1.55 (m, 4H), 1.31−1.17 (m, 22H), and 0.89−0.85 (m, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 203.8, 177.2, 172.9, 168.6, 135.2, 132.8, 131.3, 129.4, 128.8, 128.1, 127.9, 126.9, 104.1, 65.0, 61.5, 60.6, 41.6, 32.7, 31.6, 29.1, 28.9, 28.8, 26.7, 23.6, 22.6, 22.6, and 14.2. HRMS (ESI/Q-TOF): calculated (m/z) for $C_{18}H_{27}O_3$ $(M + H)^+$: 291.1955; found 291.1945.

*Ethyl 2-Benzoylnonanoate (**5f′**).* The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 100:1). The title product was isolated as a colorless oil (0.054 g, 7%) from the reaction of octanophenone (0.54 g, 2.64 mmol, 1.0 equiv) and EDA (0.64 mL, 5.29 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.073 mL, 0.53 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.01 (d, J = 9.0 Hz, 2H), 7.59 (t, J = 7.5 Hz, 1H), 7.49 (t, J = 7.5 Hz, 2H), 4.29 (t, J = 7.5 Hz, 1H), 4.15 (q, J = 7.5 Hz, 2H), 2.03−1.98 (m, 2H), 1.34−1.27 (m, 10H), 1.18 (t, J = 7.5 Hz, 3H), and 0.88 (t, J = 6.0 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 195.3, 170.1, 136.4, 133.4, 128.7, 128.5, 61.3, 54.4, 31.7, 29.4, 29.0, 29.0, 27.6, 22.6, 14.0, and 14.0. HRMS (ESI/Q-TOF): calculated (m/z) for $C_{18}H_{27}O_3$ $(M + H)^+$: 291.1955; found 291.1927.

*Ethyl 3-Oxo-2,3-diphenylpropanoate (**7a**).*[28] The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 50:1). The title product was isolated as a colorless oil (0.37 g, 20%) from the reaction of benzophenone (1.25 g, 6.86 mmol, 1.0 equiv) and EDA (1.67 mL, 13.72 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.19 mL, 1.37 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.00 (d, J = 6.0 Hz, 2H), 7.56 (t, J = 7.5 Hz, 1H), 7.47−7.32 (m, 7H), 5.66 (s, 1H), 4.25 (q, J = 7.5 Hz, 2H), and 1.27 (t, J = 7.5 Hz, 3H).

*Ethyl 3-Oxo-3-phenyl-2-(p-tolyl)propanoate (**7b**) and Ethyl 3-Oxo-2-phenyl-3-(p-tolyl)propanoate (**7b′**).* The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 13:1). The title product was isolated as a colorless oil (0.36 g, 21%) from the reaction of 4-methylbenzophenone (1.18 g, 6.01 mmol, 1.0 equiv) and EDA (1.45 mL, 12.02 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.17 mL, 1.20 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 500 MHz): δ 7.98 (d, J = 10.0 Hz, 2H), 7.88 (d, J = 5.0 Hz, 1H), 7.55 (t, J = 7.5 Hz, 1H), 7.44 (q, J = 7.5 Hz, 4H), 7.37 (t, J = 7.5 Hz, 1H), 7.31 (d, J = 10.0 Hz, 3H), 7.24 (d, J = 10.0 Hz, 2H), 7.18 (d, J = 5.0 Hz, 2H), 5.61 (s, 1H), 5.59 (s, 1H), 4.26−4.22 (m, 4H), 2.40 (s, 2H), 2.34 (s, 3H), and 1.26 (t, J = 6.0 Hz, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 193.5, 192.9, 169.0, 168.9, 144.5, 137.9, 135.8, 133.5, 133.3, 133.2, 130.0, 129.6, 129.4, 129.1, 128.9, 128.8, 128.8, 128.1, 66.1, 66.0, 61.7, 60.5, 60.2, 21.7, 21.2, 14.1, and 14.0. HRMS (ESI/Q-TOF): calculated (m/z) for $C_{18}H_{19}O_3$ $(M + H)^+$: 283.1329; found 283.1264.

*Ethyl 2-(4-Methoxyphenyl)-3-oxo-3-phenylpropanoate (**7c**) and Ethyl 3-(4-Methoxyphenyl)-3-oxo-2-phenylpropanoate (**7c′**).*[28] The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 9:1). The title product was isolated as a colorless oil (0.36 g, 22%) from the reaction of 4-methoxybenzophenone (1.15 g, 5.42 mmol, 1.0 equiv) and EDA (1.31 mL, 10.84 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.15 mL, 1.08 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 7.99−7.95 (m, 4H), 7.55 (t, J = 6.0 Hz, 2H), 7.44 (t, J = 6.0 Hz, 4H), 7.37−7.28 (m, 4H), 6.90 (d, J = 9.0 Hz, 4H), 5.58 (s, 1H), 5.57 (s, 1H), 4.24 (q, J = 7.5 Hz, 4H), 3.86 (s, 3H), 3.80 (s, 3H), and

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1.29−1.24 (m, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 193.6, 191.8, 169.1, 169.0, 163.8, 159.4, 135.7, 133.4, 133.4, 131.3, 130.7, 129.5, 129.9, 128.8, 128.7, 128.6, 128.0, 125.0, 114.3, 113.9, 61.7, 60.3, 59.7, 55.5, 55.2, 14.1, and 14.0.

*Ethyl 3-(4-Chlorophenyl)-3-oxo-2-phenylpropanoate (**7d**) and Ethyl 2-(4-Chlorophenyl)-3-oxo-3-phenylpropanoate (**7d′**).*[28] The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 9:1). The title product was isolated as a colorless oil (trace amount) from the reaction of 4-chlorobenzophenone (1.21 g, 5.58 mmol, 1.0 equiv) and EDA (1.35 mL, 11.16 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.15 mL, 1.12 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 500 MHz): δ 7.98−7.90 (m, 2H), 7.46−7.35 (m, 8H), 5.60 (s, 0.3H), 5.55 (s, 0.7H), 4.28−4.21 (m, 3H), and 1.29−1.24 (m, 5H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 192.1, 168.5, 140.0, 134.0, 133.7, 132.7, 130.9, 130.3, 129.5, 129.1, 129.0, 128.9, 128.9, 128.8, 128.3, 128.2, 62.0, 61.9, 60.6, 59.7, and 14.0.

*Ethyl 2-(3,4-Dimethylphenyl)-3-oxo-3-phenylpropanoate (**7f**).* The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/dichloromethane = 1:1). The title product was isolated as a colorless oil (0.50 g, 30%) from the reaction of 3,4-dimethylbenzophenone (1.18 g, 5.61 mmol, 1.0 equiv) and EDA (1.36 mL, 10.22 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.15 mL, 1.12 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 500 MHz): δ 7.49−7.31 (m, 6H), 7.15−7.07 (m, 2H), 5.24 (s, 1H), 4.38−4.24 (m, 2H), 2.24 (s, 3H), 2.28 (s, 3H), and 1.21 (t, J = 7.5 Hz, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 169.8, 168.2, 153.4, 152.2, 139.6, 138.3, 137.1, 136.9, 130.3, 130.2, 130.0, 130.0, 129.8, 129.7, 129.4, 129.2, 128.7, 128.6, 128.6, 127.1, 126.9, 126.4, 126.2, 124.8, 99.6, 99.5, 64.2, 19.8, 19.7, and 13.8. HRMS (ESI/Q-TOF): calculated (m/z) for $C_{19}H_{21}O_3$ (M + H)+: 297.1485; found 297.1474.

*Ethyl 2-(3,4-Dimethoxyphenyl)-3-oxo-3-phenylpropanoate (**7g**).*[29] The compound was prepared according to the general procedure and purified by silica gel column chromatography (dichloromethane). The title product was isolated as a colorless oil (0.43 g, 28%) from the reaction of 3,4-dimethoxybenzophenone (1.15 g, 4.75 mmol, 1.0 equiv) and EDA (1.15 mL, 9.50 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.13 mL, 0.95 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 500 MHz): δ 7.99 (d, J = 5.0 Hz, 2H), 7.56 (t, J = 7.5 Hz, 2H), 7.45 (t, J = 7.5 Hz, 4H), 6.95 (d, J = 10.0 Hz, 2H), 6.86 (d, J = 10.0 Hz, 4H), 5.56 (s, 1H), 4.24 (q, J = 5.0 Hz, 4H), 3.89 (s, 3H), 3.87 (s, 3H), and 1.27 (t, J = 5.0 Hz, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 193.5, 169.0, 149.2, 149.0, 135.8, 133.5, 128.9, 128.7, 125.4, 122.1, 112.5, 111.2, 61.7, 60.0, 56.0, 55.8, 30.9, and 14.1.

*Ethyl 2-(Naphthalen-2-yl)-3-oxo-3-phenylpropanoate (**7h**).* The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 20:1). The title product was isolated as a colorless oil (0.34 g, 23%) from the reaction of 2-naphthyl phenyl ketone (1.08 g, 4.65 mmol, 1.0 equiv) and EDA (1.12 mL, 9.30 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.13 mL, 0.93 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 500 MHz): δ 8.29 (s, 1H), 7.97−7.88 (m, 6H), 7.65−7.60 (m, 2H), 7.58−7.7.51 (m, 3H), 4.29−4.23 (m, 3H), and 1.31 (t, J = 7.5 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 196.7, 169.8, 137.9, 135.3, 134.8, 132.4, 132.3, 131.9, 130.1, 129.4, 128.4, 128.3, 127.8, 126.8, 125.8, 68.2, 61.1, and 14.2. HRMS (ESI/Q-TOF): calculated (m/z) for $C_{21}H_{19}O_3$ (M + H)+: 319.1329; found 319.1365.

*Ethyl 2-Ethyl-3-oxopentanoate (**9a**).*[30] The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 50:1). The title product was isolated as a colorless oil (0.53 g, 52%) from the reaction of 3-pentanone (0.51 g, 5.92 mmol, 1.0 equiv) and EDA (1.43 mL, 11.84 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.16 mL, 1.18 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 4.09 (q, J = 6.0 Hz, 2H), 3.28 (t, J = 7.5 Hz, 1H), 2.49−2.42 (m, 2H), 1.78 (t, J = 7.5 Hz, 2H), 1.17 (t, J = 6.0 Hz, 3H), 0.97 (t, J = 7.5 Hz, 3H), and 0.82 (t, J = 7.5 Hz, 3H).

*Ethyl 3-Oxo-2-propylhexanoate (**9b**).* The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 50:1). The title product was isolated as a colorless oil (0.45 g, 50%) from the reaction of 4-heptanone (0.52 g, 4.53 mmol, 1.0 equiv) and EDA (1.43 mL, 9.06 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.13 mL, 0.91 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 4.15 (q, J = 7.5 Hz, 2H), 3.41 (t, J = 6.0 Hz, 1H), 2.52−2.43 (m, 2H), 1.82−1.78 (m, 2H), 1.59 (q, J = 7.5 Hz, 2H), 1.24 (t, J = 6.0 Hz, 5H), and 0.91−0.86 (m, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 205.3, 169.9, 61.1, 58.9, 43.6, 30.2, 20.7, 16.9, 14.0, 13.8, and 13.5. HRMS (ESI/Q-TOF): calculated (m/z) for $C_{11}H_{21}O_3$ (M + H)+: 201.1485; found 201.1478.

*Ethyl 2-Butyl-3-oxoheptanoate (**9c**).*[31] The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 50:1). The title product was isolated as a colorless oil (0.38 g, 47%) from the reaction of 5-nonanone (0.51 g, 3.59 mmol, 1.0 equiv) and EDA (0.87 mL, 7.18 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.10 mL, 0.72 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 500 MHz): δ 4.14−4.11 (m, 2H), 3.36 (t, J = 7.5 Hz, 1H), 2.51−2.41 (m, 2H), 2.33 (t, J = 5.0 Hz, 1H), 1.78−1.75 (m, 2H), 1.51−1.47 (m, 2H), 1.27−1.24 (m, 3H), 1.22−1.18 (m, 3H), and 0.85−0.81 (m, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 205.3, 169.9, 61.0, 59.1, 42.4, 41.4, 29.5, 27.8, 25.9, 25.5, 22.3, 22.1, 14.0, and 13.7.

*Ethyl 2-Acetylhexanoate (**9d**) and Ethyl 2-Methyl-3-oxoheptanoate (**9d′**).*[32] The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 50:1). The title product was isolated as a colorless oil (0.51 g, 55%) from the reaction of 2-hexanone (0.50 g, 4.99 mmol, 1.0 equiv) and EDA (1.20 mL, 9.98 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.14 mL, 1.0 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 4.24−4.20 (m, 4H), 3.53 (q, J = 7.5 Hz, 1H), 3.41 (t, J = 7.5 Hz, 1H), 2.63−2.48 (m, 1H), 2.25 (s, 3H), 1.85−1.81 (m, 2H), 1.61−1.57 (m, 3H), 1.36−1.28 (m, 15H), and 0.94−0.91 (m, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 206.0, 203.4, 170.6, 169.9, 61.2, 59.9, 41.0, 29.5, 28.7, 27.9, 25.6, 22.4, 22.2, 14.1, 14.0, and 13.8.

*Ethyl 2-Acetyldecanoate (**9e**).*[33] The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 50:1). The title product was isolated as a colorless oil (0.36 g, 44%) from the reaction of 2-decanone (0.53 g, 3.39 mmol, 1.0 equiv) and EDA (0.89 mL, 6.78 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.09 mL, 0.68 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 4.21 (q, J = 7.5 Hz, 2H), 3.41 (t, J = 7.5 Hz, 1H), 2.23 (s, 3H), 1.85 (s, 2H), 1.31−1.27 (m, 15H), and 0.89 (t, J = 6.0 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 203.4, 170.0, 61.2, 60.0, 31.8, 29.3, 29.3, 29.2, 28.7, 28.2, 27.4, 22.6, 14.1, and 14.1.

*Ethyl 2-Acetyldecanoate (**9e′**).* The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 50:1). The title product was isolated as a colorless oil (0.16 g, 20%) from the reaction of 2-decanone (0.53 g, 3.39 mmol, 1.0 equiv) and EDA (0.89 mL, 6.78 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.09 mL, 0.68 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 5.32 (s, 1H), 4.32−4.13 (m, 2H), 3.52 (q, J = 7.5 Hz, 2H), 2.24 (s, 3H), 1.62 (s, 4H), 1.38−1.36 (m, 13H), and 1.38 (t, J = 7.5 Hz, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz): δ 203.3, 170.0, 61.2, 60.0, 32.0, 29.3, 29.2, 28.7, 28.2, 27.4, 22.6, and 14.1. HRMS (ESI/Q-TOF): calculated (m/z) for $C_{14}H_{27}O_3$ (M + H)+: 243.1955; found 243.1940.

*Ethyl 5-Methyl-3-Oxohexanoate (**9f**).*[34] The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 50:1). The title product was isolated as a colorless oil (0.56 g, 55%) from the reaction of 3-methylbutanal (0.51 g, 5.92 mmol, 1.0 equiv) and EDA (1.43 mL, 11.84 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.16 mL, 1.2 mmol, 0.2 equiv). ^1H NMR ($CDCl_3$, 300 MHz): δ 4.20−4.08 (m, 2H), 3.38 (s, 2H), 2.39 (d, J = 6.0 Hz, 2H), 2.18−2.11 (m, 1H), 1.25 (t, J = 6.0 Hz, 3H), and 0.92−0.88 (m, 6H).

*Ethyl 3-Oxooctanoate (**9g**).*[35] The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 50:1). The title product was isolated as a colorless oil with hexane (0.60 g, 62%) from the reaction of hexanal (0.52 g, 5.19 mmol, 1.0 equiv) and EDA (1.43 mL, 10.38 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.14 mL, 1.04 mmol, 0.2

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equiv). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.19 (q, J = 6.0 Hz, 2H), 3.42 (s, 2H), 2.53 (t, J = 7.5 Hz, 2H), 1.61−1.59 (m, 2H), 1.29−1.25 (m, 4H), and 0.88−0.82 (m, 3H). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 203.0, 167.3, 61.3, 49.3, 43.0, 31.9, 31.2, 29.7, 23.2, 22.7, 22.4, 14.1, and 13.9.

*Ethyl 3-Oxodecanoate (**9h**).*[36] The compound was prepared according to the general procedure and purified by silica gel column chromatography (hexane/ethyl acetate = 50:1). The title product was isolated as a colorless oil with hexane (0.70 g, 82%) from the reaction of octanal (0.51 g, 3.98 mmol, 1.0 equiv) and EDA (0.96 mL, 7.96 mmol, 2.0 equiv) in the presence of $HBF_4{}^{\bullet}OEt_2$ (0.11 mL, 0.80 mmol, 0.2 equiv). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.91 (q, J = 7.5 Hz, 2H), 3.16 (s, 1H), 2.28 (t, J = 7.5 Hz, 1H), 1.32 (s, 2H), 1.03−0.98 (m, 15H), and 0.62 (d, J = 6.0 Hz, 6H). ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz): δ 201.7, 166.5, 88.2, 60.1, 48.3, 41.9, 31.0, 28.4, 28.3, 28.3, 22.7, 21.9, 13.2, and 13.2.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02972.

Copies of the ^{1}H NMR, ^{13}C{^{1}H} NMR, and HRMS for all new products, and 2D NMR for ethyl 3-oxo-2-phenylbutanoate (keto-enol) (**3a**), ethyl 3-oxo-2-phenylpentanoate (keto-enol) (**5a**), ethyl 3-oxo-3-phenyl-2-(*p*-tolyl)propanoate and ethyl 3-oxo-2-phenyl-3-(*p*-tolyl)propanoate (**7b**/**7b**′), and ethyl 2-(4-methoxyphenyl)-3-oxo-3-phenylpropanoate and ethyl 3-(4-methoxyphenyl)-3-oxo-2-phenylpropanoate (**7c**/**7c**′) (PDF)

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Notes

The authors declare no competing financial interest.

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