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Carbene Carbonylation

Synthesis of Amido Esters and Amido Phosphonates through Carbonylation of Diazo Compounds Followed by Nucleophilic Addition Reaction

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Abstract: We report a method to produce amido esters and amido phosphonates. Octacarbonyldicobalt [$Co_2(CO)_8$] was found to be an efficient nongaseous CO source that could be used as a reagent for the carbonylation of diazo esters and diazo phosphonates under mild reaction conditions. A number of diazo esters and diazo phosphonates smoothly underwent the reaction with CO, which was generated from $Co_2(CO)_8$, to produce the corresponding ketenes. The subsequent reaction with an amine afforded the expected amido esters and phosphonates. By applying the developed protocol, we synthesized a number of amido esters and amido phosphonates. Characterization of these compounds was achieved by using standard spectroscopic and analytical techniques as well as crystal structure analysis for four of the products.

Introduction

Amides are an important functional group in organic chemistry and biochemistry.[1–3] The amide functionality can serve as a directing group in a synthetic method[4–6] and is related to other groups such as esters and phosphonates, which are more useful in total synthesis.[7–10] Because of its importance, several synthetic methods have been developed to prepare different types of amides, most of which start from carbonyl compounds and amines.[11–13] Widely used methods include: (i) carbonylation followed by amidation and (ii) the hydroamidation of alkynes and nitriles.[14–17] These known methods, however, are not fully suitable to the synthesis of amido esters and amido phosphonates because of their low functional-group tolerance.[11,15] Under certain reaction conditions, the Ritter reaction, the reaction of isonitriles and compounds with active methylene groups, and an amino carbonylation strategy can be employed for the synthesis of amido esters.[18–20] Nonetheless, these methods also suffer from harsh reaction conditions, low yields, and narrow substrate scopes.[18,20]

In contrast, because of their diverse and reactive nature, ketenes are widely used as key intermediates in synthetic organic chemistry.[21,22] Ketenes are known to participate in cycloadditions as well as nucleophilic and electrophilic addition reactions, which result in the formation of β-lactones, β-lactams, and many other synthetic and biologically important molecules.[23–25] Many methods are known for the preparation of ketenes, including the use of chemical, photochemical, and thermal conditions.[21,26] The synthesis of ketenes by the carbonylation of carbenes using carbon monoxide offers several advantages when other known methods suffer from low yields and harsh reaction conditions.[27]

Similarly, the carbonylation of carbenes from diazo compounds or tosyl hydrazones by using carbon monoxide catalyzed by Pd or Co^{II} catalysts offers both advantages and disadvantages.[28–30] These reactions (catalysts) are moderately successful at higher temperature but result in low yields. Another inevitable drawback includes the use of carbon monoxide gas, which is highly flammable and poisonous. Because of the colorless and odorless nature of CO, its handling can become extremely dangerous. The adequate equipment that is necessary presents a challenge for a common synthetic laboratory and also in chemical industry.[31–33] Although there are difficulties in the handling of CO, few alternate methods have been developed for the carbonylation of alkyl or aryl halides by using nongaseous carbon monoxide sources.[34–36] Considering the importance of amido esters and amido phosphonates, and in continuation of our research on carbenes,[37–40] we herein report an efficient method for the synthesis of amido esters and amido phosphonates that proceeds through the carbonylation of carbenes by using a nongaseous CO source followed by a nucleophilic addition reaction using different amines.

Results and Discussion

Among all of the nongaseous carbon monoxide sources, carbonylmetal and typical organic carbonyl compounds have gained much attention.[41,42] In general, organic carbonyl compounds decompose and generate CO above room temperature or in the presence of a strong base.[32,34,41] Carbene-related reactions, however, must be carried out at or below room temperature to achieve maximum yields (and to minimize the carbene-

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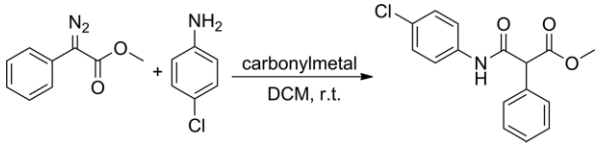
dimerized products).[43–45] Thus, if we use an organic carbonyl compound as a nongaseous CO source, we will need a separate catalyst to activate the diazo compound and yield the carbene. In the case of carbonylmetal compounds, the same complex can simultaneously produce CO and activate diazo compounds to produce the carbenes. Herein, we have chosen carbonylmetal compounds as a nongaseous carbon monoxide source. Among the majority of these complexes, octacarbonyldicobalt [$Co_2(CO)_8$] is one of the more interesting ones, as it is not only a nongaseous CO source[46] but can also decompose diazo compounds to produce ketenes under mild reaction conditions.[47–49]

For the initial screening of different carbonylmetal compounds, we chose commercially less expensive $Co_2(CO)_8$ and $Fe_2(CO)_9$ as solid CO sources. First, we employed $Co_2(CO)_8$ with methyl 2-diazo-2-phenylacetate and 4-chloroaniline as the model substrates. The desired amido ester product was successfully produced after 6 h in 81 % yield (Table 1, Entry 1). Encouraged by this result, we then carried out similar reactions with $Fe_2(CO)_9$ and $Mn_2(CO)_{10}$ as the CO sources. In case of $Fe_2(CO)_9$, we obtained a moderate product yield (47 %) after 24 h (Table 1, Entry 2). However, $Mn_2(CO)_{10}$ did not provide the expected product (Table 1, Entry 3).

Table 1. Screening of various carbonylmetal compounds for the amido ester synthesis.[a]

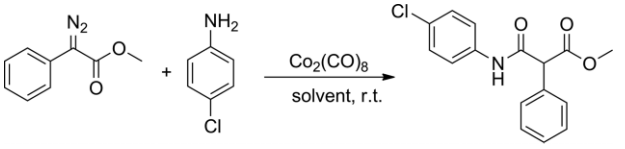


Entry	Carbonylmetal compound[b]	Time [h]	Yield [%][c]
1	$Co_2(CO)_8$	6	81
2	$Fe_2(CO)_9$	24	47
3	$Mn_2(CO)_{10}$	24	n.d.

[a] Reagents and conditions: aniline (0.5 mmol) and diazo compound (0.55 mmol) in solvent (5 mL). [b] We used 0.25 mmol of the carbonylmetal compound. [c] Pure compound after column chromatography (n.d. = not detected).

From the results of screening different carbonylmetal compounds, we found that $Co_2(CO)_8$ was the most suitable nongaseous CO source for the carbonylation of carbenes from diazo compounds. Next, we screened other reaction conditions such as solvent and catalyst loading. When the reaction was carried out in tetrahydrofuran (THF), we observed a 61 % yield of the amido ester along with 13 % of the N–H insertion product after 12 h (Table 2, Entry 2). When we conducted the reaction in acetonitrile and methanol, only a trace amount of the expected product was produced along with the recovery of the unreacted starting materials (Table 2, Entries 3 and 4). In the case of toluene, we did observe the expected product (79 % yield; Table 2, Entry 5), and the yield and reaction times were similar to those that occurred when the transformation was carried out in dichloromethane (DCM). For the sake of operational convenience and to obtain maximum yields, we employed DCM for our remaining investigations.

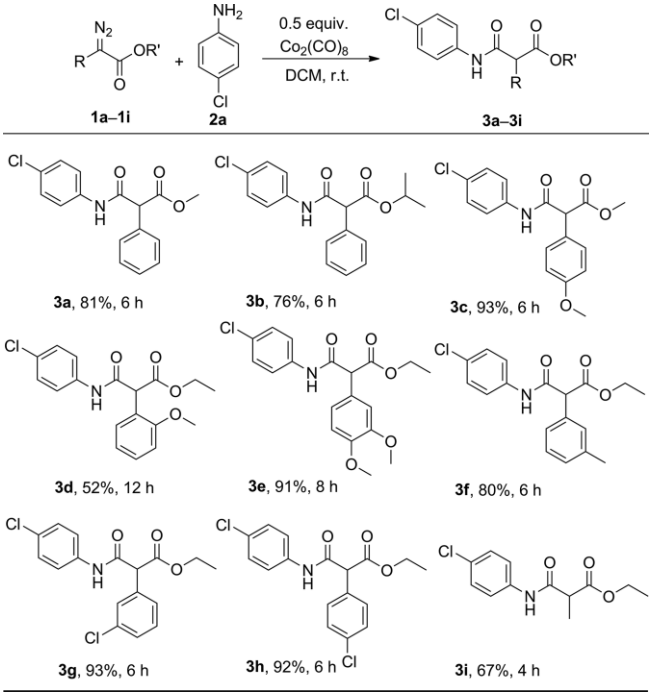
Table 2. Optimization of solvent and carbonylmetal loading.[a]



Entry	Solvent	$Co_2(CO)_8$ [equiv.]	Time [h]	Yield [%][b]
1	DCM	0.5	6	81
2	THF	0.5	12	61 (13 % N-H IP)
3[c]	CH_3OH	0.5	24	trace
4[c]	CH_3CN	0.5	24	trace
5	toluene	0.5	6	79
6	DCM	0.25	12	43 (8 % N-H IP)
7	DCM	0.75	4	85
8	DCM	1	3	82
9[d]	DCM	0.02	24	trace

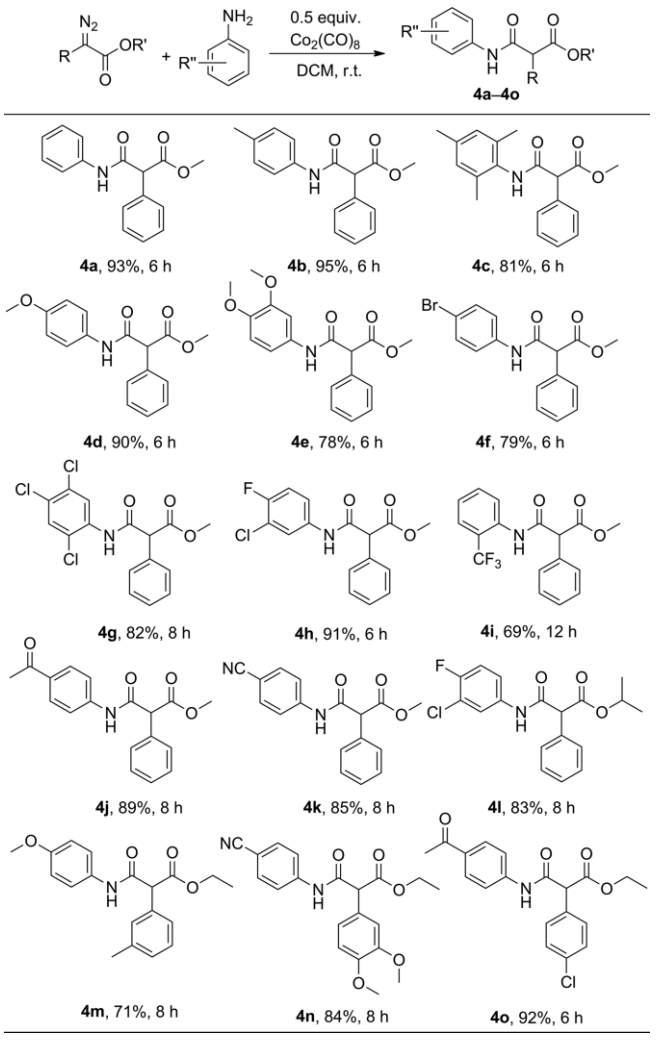
[a] Reagents and conditions: aniline (0.5 mmol) and diazo compound (0.55 mmol) in solvent (5 mL). [b] Pure compound after column chromatography. IP = insertion product. [c] Unreactive diazo compound and aniline were recovered. [d] Reaction was carried out under 1 atm CO pressure (CO was generated by dehydration of formic acid using sulfuric acid and was used after purification).

Experiments were also conducted to optimize the concentration of $Co_2(CO)_8$ for the above-mentioned reaction. The desired product was produced in 81 % yield when the reaction was carried out with 0.5 equiv. of $Co_2(CO)_8$, (Table 2, Entry 1). By employing 0.75 equiv. of $Co_2(CO)_8$ over 4 h, we observed a slight increase in the yield of the desired product to 85 % (Table 2, Entry 7). Using 1 equiv. of $Co_2(CO)_8$ afforded the expected product in 82 % yield after 3 h (Table 2, Entry 8). When the reaction was conducted with a catalytic amount of $Co_2(CO)_8$ under 1 atm of CO for 24 h, we obtained a trace amount of the

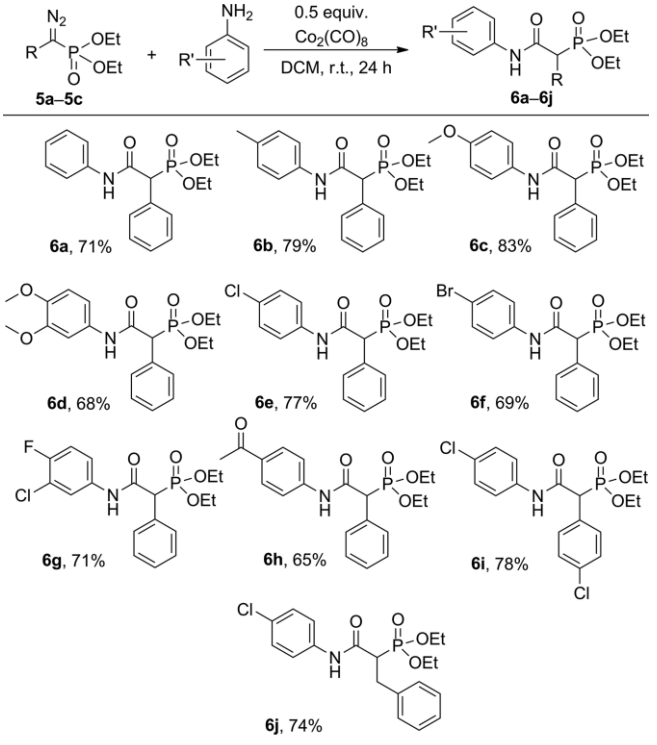


Scheme 1. Scope of diazo compounds for the amido ester synthesis.

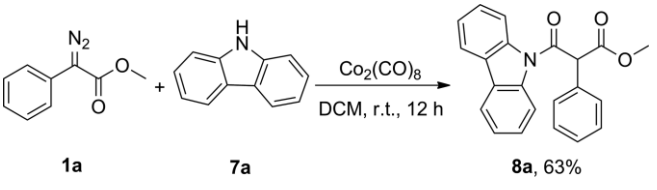
amido ester (Table 2, Entry 9). On the basis of the above results, we decided to use 0.5 equiv. of $Co_2(CO)_8$ and DCM as a solvent for further studies (Schemes 1, 2, 3, and 4).



Scheme 2. Scope of anilines for the amido ester synthesis.



Scheme 3. Scope of diazo phosphonates and anilines for the amido phosphonate synthesis.



Scheme 4. Carbazole as a heterocyclic amine source in the amido ester synthesis.

To explore the substrate scope of the reaction, we screened various diazo acetates and treated them with 4-chloroaniline (Scheme 1). Isopropyl 2-diazo-2-phenylacetate provided a decreased yield and afforded 76 % of the expected product **3b** after 6 h. The diazo(phenyl)acetates that contain electron-donating groups at the *para* position of the aromatic ring gave excellent yields. For example, methyl 2-diazo-2-(4-methoxyphenyl)acetate produced the expected product **3c** in 93 % yield after 6 h of reaction time. In the case of ethyl 2-diazo-2-(3,4-dimethoxyphenyl)acetate, we observed a very good yield of 91 % of **3e** after 8 h. When we used ethyl 2-diazo-2-(2-methoxyphenyl)acetate, however, only a 52 % yield of **3d** was obtained after 12 h, which may be caused by the bulkiness of the 2-OMe group. We also screened various diazo(phenyl)acetates that have electron-withdrawing groups, including ethyl 2-(3-chlorophenyl)-2-diazoacetate and ethyl 2-(4-chlorophenyl)-2-diazoacetate, which gave **3g** and **3h** in very good yields of 93 and 92 %, respectively, after 6 h. Ethyl 2-diazopropanoate, however, only afforded a moderate yield of 67 % after a reaction time of 4 h.

Next, we screened a number of anilines under the optimized reaction conditions to examine their scope in our developed protocol (Scheme 2). Both anilines that have electron-donating (to give **4b**–**4e**) as well as those that have electron-withdrawing groups (to give **4f**–**4k**) underwent the reaction and afforded good to very good yields. Aniline provided **4a** in a very good yield of 93 % after 6 h, and anilines that contain moderately electron-donating groups produced very good yields (i.e., **4b** and **4d**). Anilines that have strong electron-donating groups, however, provided lower yields (i.e., **4c** and **4e**). From the above studies, we noted that among the anilines that contain electron-withdrawing groups, those halo-substituted anilines afforded good yields (i.e., **4f**–**4h**). In addition, *ortho*-substituted anilines tended to give lower yields compared with *meta*- and *para*-substituted anilines (e.g., **4i**). Anilines that contain other functional groups such as carbonyl or nitrile also produced

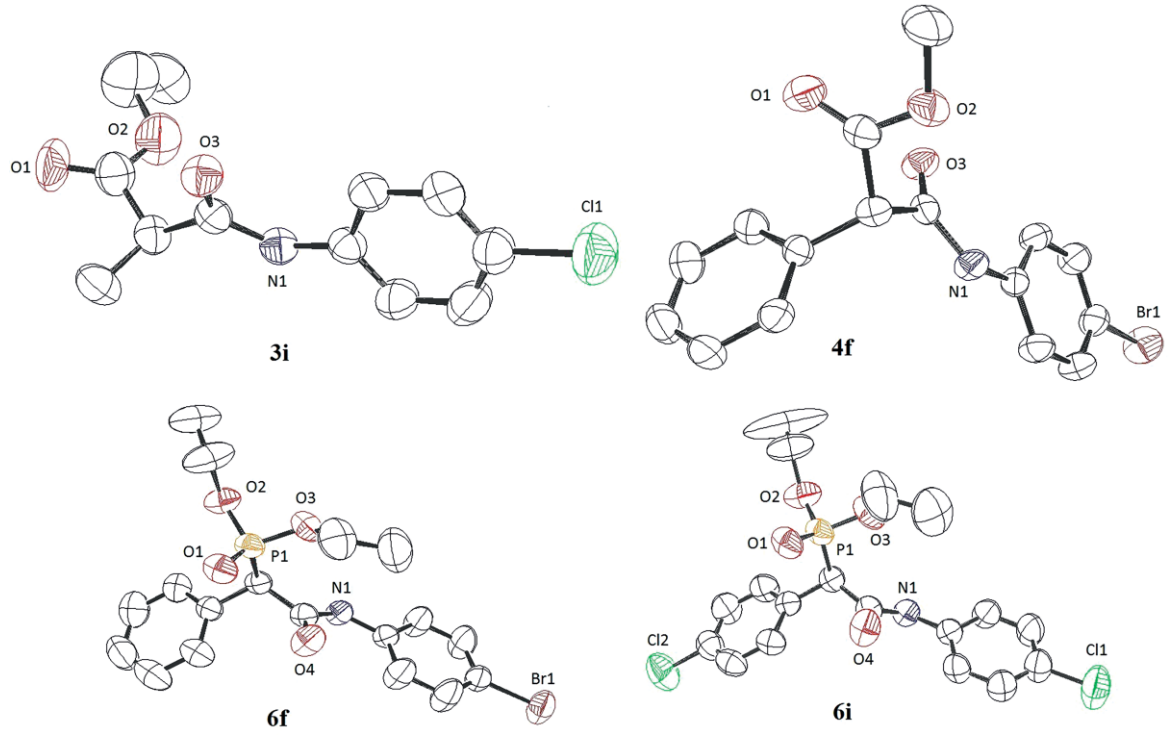


Figure 1. Molecular structures of **3i**, **4f**, **6f**, and **6i** (hydrogen atoms are omitted for clarity). Thermal ellipsoids are set at 50 % probability.

good yields [i.e., 89 % (**4j**) and 85 % (**4k**)] after 8 h of reaction time. Additional reactions also provided good to very good yields of **4l**–**4o**.

Taking into consideration the importance of amido phosphonates, we then applied our developed protocol for their synthesis by using diazo phosphonates and anilines (Scheme 3). In this regard, we screened various anilines and diazo phosphonates. The reaction of aniline with a diazo phosphonate afforded the expected product **6a** in 71 % yield after 24 h. Stirring of the reaction mixture for a longer period of time did not improve the yield. We also screened different anilines that contain electron-donating and electron-withdrawing groups (to give **6b**–**6h**) and observed good yields by employing anilines that have moderately electron-donating groups (i.e., to give **6b** and **6c**). A decrease in the yield was observed with anilines that contain strong electron-donating groups (i.e., to give **6d**). When we used anilines that contain electron-withdrawing groups, moderate to good yields resulted (i.e., to give **6e**–**6h**). The reaction of benzyl diazo phosphonate with 4-chloroaniline afforded a good yield (78 %) of **6i** after 24 h.

After successfully demonstrating the scope of the anilines and diazo phosphonates, we examined the use of both aliphatic (i.e., benzylamine) and heterocyclic (i.e., carbazole) amines in the amido ester synthesis (Scheme 4). In the case of the heterocyclic amine, we observed a moderate 63 % yield of **8a** after 12 h, whereas the use of benzylamine afforded only a trace amount of the product.

As a part of the characterization of these new products, crystals of **3i**, **4f**, **6f**, and **6i** were analyzed by single-crystal XRD studies to confirm their molecular structures (Figure 1).

Conclusions

We developed an efficient method for the synthesis of amido esters and amido phosphonates from the reactions of diazo compounds with anilines in the presence of $Co_2(CO)_8$ as a non-gaseous carbon monoxide source. Various carbonylmetal compounds and different organic solvents were screened to determine the optimal reaction conditions. By applying the developed protocol, we synthesized and characterized a number of important amido esters and amido phosphonates. Further studies on the formation of ketenes from diazo compounds and CO are in progress in our laboratory.

Experimental Section

General Methods: Unless otherwise mentioned, all reactions were conducted under dry nitrogen with oven-dried glassware. All solvents were distilled and stored under nitrogen prior to use according to standard procedures. Methanol, dichloromethane, and acetonitrile were dried with and distilled from CaH_2. THF and toluene were dried with and distilled from sodium/benzophenone. Unless otherwise mentioned, commercially available chemicals were used as received. All diazo compounds were prepared by applying the standard reported procedures.[37–40] TLC analysis was performed on precoated silica gel 60 F_{254} plates, and the developed plates were visualized under UV light (254 nm). Column chromatography was performed on silica gel (100–200 mesh). The ^1H and ^{13}C NMR spectroscopic data were recorded at 400 and 100 MHz, respectively. Chemical shifts (δ) are reported in ppm. The residual solvent signal was used as a reference for ^1H NMR data, and the solvent signal

was used as a reference for the ^{13}C NMR data. HRMS data were recorded with a UHD Q-TOF mass spectrometer. CCDC 1529619 (for **3i**), 1521410 (for **4f**), 1529617 (for **6f**), and 1529618 (for **6i**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

General Procedures for the Synthesis of the Amido Esters and Amido Phosphonates: An oven-dried 20 mL Schlenk tube (not a pressure tube) was charged with aniline (0.5 mmol) and $Co_2(CO)_8$ (0.25 mmol), and then the solvent (4 mL) was added through the septum. The diazo compound (0.55 mmol) was dissolved in the solvent (1 mL), and the solution was added to the reaction mixture at 0 °C. The reaction mixture was warmed to room temperature and stirred for the reported time. The progress of the reaction was monitored by TLC analysis (hexane/ethyl acetate). Upon completion of the reaction, the solvent was evaporated under reduced pressure, and the crude residue was purified by column chromatography on silica gel (hexane/ethyl acetate) to yield the desired product.

Methyl 3-[(4-Chlorophenyl)amino]-3-oxo-2-phenylpropanoate (3a): White solid (124 mg, 81 % yield); m.p. 171–173 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.11 (s, 1 H), 7.45 (dd, J = 11.8, 8.6 Hz, 4 H), 7.36 (q, J = 5.6 Hz, 3 H), 7.24 (d, J = 8.6 Hz, 2 H), 4.64 (s, 1 H), 3.78 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.7, 165.3, 136.1, 133.7, 129.7, 129.4, 129.1, 128.7, 128.2, 121.4, 58.7, 53.2 ppm. IR (film): $\tilde{\nu}$ = 3344, 3311, 3069, 2952, 2831, 1753, 1660, 1603, 1540, 1491, 1397, 1353, 1311, 1209, 1155, 1011, 973, 827, 775 cm^{-1}. HRMS (ESI): calcd. for $C_{16}H_{15}ClNO_3$ $[M + H]^+$ 304.0740; found 304.0746.

Isopropyl 3-[(4-Chlorophenyl)amino]-3-oxo-2-phenylpropanoate (3b): Off-white solid (127 mg, 76 % yield); m.p. 107–109 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.25 (s, 1 H), 7.51–7.47 (m, 2 H), 7.44 (dd, J = 8.0, 1.5 Hz, 2 H), 7.40–7.33 (m, 3 H), 7.28–7.24 (m, 2 H), 5.11 (dt, J = 12.5, 6.3 Hz, 1 H), 4.58 (s, 1 H), 1.31 (d, J = 6.3 Hz, 3 H), 1.19 (d, J = 6.2 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.1, 165.5, 136.2, 134.1, 129.6, 129.3, 129.1, 128.6, 128.0, 121.4, 70.4, 59.0, 21.8, 21.5 ppm. IR (film): $\tilde{\nu}$ = 3298, 3195, 3131, 2831, 1740, 1654, 1609, 1548, 1492, 1401, 1364, 1207, 1172, 1103, 833, 776, 735 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{19}ClNO_3$ $[M + H]^+$ 332.1053; found 332.1058.

Methyl 3-[(4-Chlorophenyl)amino]-2-(4-methoxyphenyl)-3-oxopropanoate (3c): Light brown semisolid (155 mg, 93 % yield). ^1H NMR (400 MHz, $CDCl_3$): δ = 9.04 (s, 1 H), 7.47–7.40 (m, 2 H), 7.37–7.30 (m, 2 H), 7.23 (d, J = 8.7 Hz, 2 H), 6.90–6.85 (m, 2 H), 4.58 (s, 1 H), 3.77 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.6, 165.8, 159.8, 136.1, 129.6, 129.5, 129.0, 125.6, 121.4, 114.6, 58.0, 55.3, 53.0 ppm. IR (film): $\tilde{\nu}$ = 3319, 3124, 3001, 2953, 2833, 1738, 1667, 1630, 1600, 1539, 1512, 1492, 1399, 1364, 1250, 1178, 1154, 1092, 1031, 1012, 828, 775 cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{17}ClNO_4$ $[M + H]^+$ 334.0846; found 334.0844.

Ethyl 3-[(4-Chlorophenyl)amino]-2-(2-methoxyphenyl)-3-oxopropanoate (3d): White solid (91 mg, 52 % yield); m.p. 114–116 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.78 (s, 1 H), 7.51–7.43 (m, 2 H), 7.41 (dd, J = 7.6, 1.6 Hz, 1 H), 7.33 (td, J = 8.2, 1.7 Hz, 1 H), 7.25 (dd, J = 7.4, 1.4 Hz, 2 H), 7.00 (td, J = 7.5, 1.0 Hz, 1 H), 6.94 (d, J = 8.2 Hz, 1 H), 4.89 (s, 1 H), 4.24 (q, J = 7.1 Hz, 2 H), 3.86 (s, 3 H), 1.25 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.8, 165.9, 156.8, 136.5, 130.2, 129.9, 129.4, 129.0, 122.9, 121.5, 121.2, 111.4, 62.0, 55.9, 54.0, 14.2 ppm. IR (film): $\tilde{\nu}$ = 3308, 3125, 2940, 2831, 2710, 1735, 1665, 1603, 1543, 1493, 1462, 1399, 1365, 1248, 1213, 1228, 1158, 1093, 1031, 839, 826, 775, 754 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{19}ClNO_4$ $[M + H]^+$ 348.1003; found 348.1000.

Ethyl 3-[(4-Chlorophenyl)amino]-2-(3,4-dimethoxyphenyl)-3-oxopropanoate (3e): White solid (172 mg, 91 % yield); m.p. 125–127 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.04 (s, 1 H), 7.49–7.44 (m, 2 H), 7.27–7.21 (m, 2 H), 6.97 (dd, J = 11.0, 2.0 Hz, 2 H), 6.84 (d, J = 8.1 Hz, 1 H), 4.56 (s, 1 H), 4.30–4.20 (m, 2 H), 3.86 (s, 3 H), 3.85 (s, 3 H), 1.28 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.1, 165.7, 149.4, 149.3, 136.1, 129.6, 129.0, 126.1, 121.3, 120.4, 111.5, 111.4, 62.3, 58.4, 55.98, 55.93, 14.0 ppm. IR (film): $\tilde{\nu}$ = 3292, 2975, 2831, 1739, 1655, 1593, 1522, 1400, 1365, 1349, 1261, 1203, 1182, 1168, 1146, 1024, 818, 768, 760 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{21}ClNO_5$ $[M + H]^+$ 378.1108; found 378.1111.

Ethyl 3-[(4-Chlorophenyl)amino]-3-oxo-2-(*m*-tolyl)propanoate (3f): White solid (133 mg, 80 % yield); m.p. 121–123 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.17 (s, 1 H), 7.48 (d, J = 8.8 Hz, 2 H), 7.25 (m, 5 H), 7.15 (d, J = 6.8 Hz, 1 H), 4.57 (s, 1 H), 4.33–4.18 (m, 2 H), 2.35 (s, 3 H), 1.28 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.5, 165.5, 139.2, 136.2, 133.8, 129.6, 129.5, 129.2, 129.1, 128.9, 125.0, 121.4, 62.4, 58.8, 21.6, 14.1 ppm. IR (film): $\tilde{\nu}$ = 3351, 2981, 2834, 1724, 1693, 1599, 1536, 1488, 1393, 1366, 1250, 1192, 1167, 1093, 1029, 837, 816, 776, 748 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{19}ClNO_3$ $[M + H]^+$ 332.1053; found 332.1052.

Ethyl 2-(3-Chlorophenyl)-3-[(4-chlorophenyl)amino]-3-oxopropanoate (3g): White solid (165 mg, 93 % yield); m.p. 95–97 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.26 (s, 1 H), 7.48 (dd, J = 8.9, 2.8 Hz, 2 H), 7.43 (d, J = 1.0 Hz, 1 H), 7.36–7.28 (m, 3 H), 7.27 (d, J = 2.5 Hz, 1 H), 7.26 (d, J = 1.7 Hz, 1 H), 4.57 (s, 1 H), 4.34–4.16 (m, 2 H), 1.28 (td, J = 7.1, 1.1 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9, 164.6, 136.0, 135.7, 135.1, 130.5, 129.9, 129.1, 128.9, 128.4, 126.4, 121.5, 62.7, 58.2, 14.1 ppm. IR (film): $\tilde{\nu}$ = 3295, 3132, 2831, 1748, 1655, 1607, 1548, 1492, 1400, 1364, 1205, 1176, 1095, 1029, 825, 775 cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{16}Cl_2NO_3$ $[M + H]^+$ 353.0507; found 352.0505.

Ethyl 2-(4-Chlorophenyl)-3-[(4-chlorophenyl)amino]-3-oxopropanoate (3h): Off-white solid (162 mg, 92 % yield); m.p. 122–124 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.22 (s, 1 H), 7.50–7.44 (m, 2 H), 7.39–7.31 (m, 4 H), 7.28–7.24 (m, 2 H), 4.57 (s, 1 H), 4.31–4.18 (m, 2 H), 1.27 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.1, 164.9, 136.0, 134.7, 132.4, 129.9, 129.6, 129.4, 129.1, 121.4, 62.7, 58.0, 14.0 ppm. IR (Film): $\tilde{\nu}$ = 3330, 2988, 2832, 2717, 1749, 1661, 1600, 1538, 1492, 1397, 1365, 1335, 1303, 1213, 1165, 1088, 1017, 827, 775 cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{16}Cl_2NO_3$ $[M + H]^+$ 352.0507; found 352.0511.

Ethyl 3-[(4-Chlorophenyl)amino]-2-methyl-3-oxopropanoate (3i): White solid (86 mg, 67 % yield); m.p. 89–91 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.80 (s, 1 H), 7.50 (d, J = 8.7 Hz, 2 H), 7.31–7.25 (m, 2 H), 4.24 (q, J = 7.1 Hz, 2 H), 3.43 (q, J = 7.3 Hz, 1 H), 1.54 (d, J = 7.3 Hz, 3 H), 1.31 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.9, 167.3, 136.3, 129.5, 129.1, 121.3, 62.1, 47.4, 15.6, 14.1 ppm. IR (film): $\tilde{\nu}$ = 3301, 3190, 3123, 2983, 2831, 1745, 1677, 1651, 1600, 1543, 1490, 1455, 1396, 1362, 1326, 1293, 1243, 1209, 1176, 1092, 1037, 1010, 934, 838, 818, 775, 721 cm^{-1}. HRMS (ESI): calcd. for $C_{12}H_{15}ClNO_3$ $[M + H]^+$ 256.0740; found 256.0731.

Methyl 3-Oxo-2-phenyl-3-(phenylamino)propanoate (4a): Off-white solid (126 mg, 93 % yield); m.p. 102–104 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.00 (s, 1 H), 7.51 (d, J = 7.9 Hz, 2 H), 7.45 (d, J = 6.6 Hz, 2 H), 7.40–7.32 (m, 3 H), 7.29 (t, J = 7.9 Hz, 2 H), 7.10 (d, J = 7.4 Hz, 1 H), 4.66 (d, J = 1.3 Hz, 1 H), 3.78 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.7, 165.2, 137.5, 133.9, 129.3, 129.1, 128.6, 128.3, 124.8, 120.1, 58.9, 53.1 ppm. IR (film): $\tilde{\nu}$ = 3288, 3064, 2951, 2831, 1750, 1652, 1598, 1535, 1496, 1444, 1362, 1310, 1274, 1243, 1207, 1159, 1075, 1009, 986, 774, 737 cm^{-1}. HRMS (ESI): calcd. for $C_{16}H_{16}NO_3$ $[M + H]^+$ 270.1130; found 270.1136.

Methyl 3-Oxo-2-phenyl-3-(*p*-tolylamino)propanoate (4b): White solid (135 mg, 95 % yield); m.p. 148–150 °C. ^1H NMR (400 MHz,

$CDCl_3$): δ = 8.91 (s, 1 H), 7.46 (dd, J = 7.9, 1.5 Hz, 2 H), 7.42–7.32 (m, 5 H), 7.10 (d, J = 8.3 Hz, 2 H), 4.66 (s, 1 H), 3.79 (s, 3 H), 2.30 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.6, 165.1, 135.0, 134.4, 134.0, 129.5, 129.3, 128.6, 128.3, 120.2, 58.9, 53.1, 21.0 ppm. IR (film): $\tilde{\nu}$ = 3342, 2954, 2716, 1753, 1656, 1539, 1363, 1270, 1208, 1156, 1012, 816, 774, 708 cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{18}NO_3$ [M + H]$^+$ 284.1287; found 284.1293.

Methyl 3-(Mesitylamino)-3-oxo-2-phenylpropanoate (4c): White solid (126 mg, 81 % yield); m.p. 151–153 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03 (s, 1 H), 7.50 (d, J = 6.9 Hz, 2 H), 7.42–7.32 (m, 3 H), 6.82 (s, 2 H), 4.72 (s, 1 H), 3.79 (s, 3 H), 2.22 (s, 3 H), 2.03 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.3, 165.7, 137.0, 135.0, 134.1, 130.7, 129.2, 128.9, 128.5, 128.3, 58.9, 52.9, 21.0, 18.2 ppm. IR (film): $\tilde{\nu}$ = 3347, 3261, 2956, 2831, 2717, 1750, 1730, 1643, 1596, 1437, 1363, 1249, 1255, 1171, 1015, 842, 775, 731, 703 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{22}NO_3$ [M + H]$^+$ 312.1600; found 312.1605.

Methyl 3-[(4-Methoxyphenyl)amino]-3-oxo-2-phenylpropanoate (4d): Light brown solid (135 mg, 90 % yield); m.p. 132–133 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.90 (s, 1 H), 7.45–7.27 (m, 7 H), 6.80 (d, J = 9.0 Hz, 2 H), 4.64 (s, 1 H), 3.76 (s, 3 H), 3.74 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.5, 165.1, 156.6, 133.9, 130.6, 129.2, 128.5, 128.4, 121.9, 114.1, 58.7, 55.5, 53.0 ppm. IR (film): $\tilde{\nu}$ = 3343, 3078, 2953, 2834, 1752, 1657, 1608, 1545, 1511, 1438, 1409, 1361, 1320, 1299, 1272, 1249, 1208, 1154, 1034, 971, 831, 757, 711 cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{17}NNaO_4$ [M + H]$^+$ 322.1055; found 322.1062.

Methyl 3-[(3,4-Dimethoxyphenyl)amino]-3-oxo-2-phenylpropanoate (4e): Off-white solid (129 mg, 78 % yield); m.p. 125–127 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.94 (s, 1 H), 7.45 (d, J = 6.6 Hz, 2 H), 7.42–7.29 (m, 4 H), 6.89 (dd, J = 8.6, 2.3 Hz, 1 H), 6.77 (d, J = 8.6 Hz, 1 H), 4.64 (s, 1 H), 3.83 (s, 3 H), 3.83 (s, 3 H), 3.79 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.7, 165.2, 149.0, 146.1, 133.9, 131.2, 129.3, 128.6, 128.3, 111.9, 111.2, 104.8, 58.8, 56.1, 55.9, 53.1 ppm. IR (film): $\tilde{\nu}$ = 3431, 3286, 2954, 2832, 1747, 1650, 1602, 1518, 1459, 1363, 1266, 1229, 1199, 1168, 1133, 1024, 773, 702 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{20}NO_5$ [M + H]$^+$ 330.1341; found 330.1346.

Methyl 3-[(4-Bromophenyl)amino]-3-oxo-2-phenylpropanoate (4f): White solid (138 mg, 79 % yield); m.p. 51–53 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.09 (s, 1 H), 7.51–7.31 (m, 9 H), 4.64 (s, 1 H), 3.80 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.9, 165.2, 136.6, 133.7, 132.1, 129.4, 128.8, 128.2, 121.7, 117.4, 58.8, 53.3 ppm. IR (film): $\tilde{\nu}$ = 3443, 3345, 2952, 2831, 2716, 1753, 1662, 1602, 1537, 1486, 1391, 1362, 1311, 1209, 1157, 1070, 1009, 972, 823, 775, 725 cm^{-1}. HRMS (ESI): calcd. for $C_{16}H_{15}BrNO_3$ [M + H]$^+$ 348.0235; found 348.0232.

Methyl 3-Oxo-2-phenyl-3-[(2,4,5-trichlorophenyl)amino]propanoate (4g): White solid (153 mg, 82 % yield); m.p. 100–102 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.64 (s, 1 H), 8.59 (d, J = 4.7 Hz, 1 H), 7.48–7.37 (m, 6 H), 4.69 (s, 1 H), 3.82 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.4, 165.5, 133.9, 133.3, 131.9, 129.9, 129.6, 129.0, 128.2, 127.8, 122.5, 121.9, 59.0, 53.4 ppm. IR (film): $\tilde{\nu}$ = 3430, 3208, 3091, 2995, 2831, 1739, 1662, 1601, 1517, 1457, 1361, 1316, 1296, 1272, 1211, 1152, 1080, 1013, 895, 774, 714 cm^{-1}. HRMS (ESI): calcd. for $C_{16}H_{13}Cl_3NO_3$ [M + H]$^+$ 371.9961; found 371.9960.

Methyl 3-[(3-Chloro-4-fluorophenyl)amino]-3-oxo-2-phenylpropanoate (4h): White solid (147 mg, 91 % yield); m.p. 141–143 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.17 (s, 1 H), 7.68 (dd, J = 6.5, 2.5 Hz, 1 H), 7.48–7.23 (m, 6 H), 7.03 (t, J = 8.8 Hz, 1 H), 4.63 (s, 1 H), 3.79 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.6, 165.5, 155.0 (d, $J_{C,F}$ = 246.5 Hz), 134.1 (d, $J_{C,F}$ = 3.3 Hz), 133.5, 129.4, 128.7, 128.2, 122.4, 121.2 (d, $J_{C,F}$ = 18.6 Hz), 119.9 (d, $J_{C,F}$ = 6.9 Hz), 116.6 (d, $J_{C,F}$ = 22.1 Hz), 58.55, 53.22 ppm. IR (film): $\tilde{\nu}$ = 3425, 3309, 2830, 2716, 1741, 1675, 1605, 1498, 1355, 1301, 1221, 1199, 1154, 1024, 877, 825, 773, 728 cm^{-1}. HRMS (ESI): calcd. for $C_{16}H_{14}ClFNO_3$ [M + H]$^+$ 322.0646; found 322.0643.

Methyl 3-Oxo-2-phenyl-3-{[2-(trifluoromethyl)phenyl]amino}propanoate (4i): White solid (117 mg, 69 % yield); m.p. 105–107 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.20 (s, 1 H), 8.21 (d, J = 8.3 Hz, 1 H), 7.59 (d, J = 7.9 Hz, 1 H), 7.54–7.46 (m, 3 H), 7.43–7.35 (m, 3 H), 7.20 (t, J = 7.7 Hz, 1 H), 4.71 (s, 1 H), 3.81 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.1, 165.7, 135.0, 133.13 (d, $J_{C,F}$ = 47.2 Hz), 129.5, 128.9, 128.3, 126.43–125.88 (m), 124.8, 124.2, 122.5, 120.56 (d, $J_{C,F}$ = 29.9 Hz), 59.2, 53.2 ppm. IR (film): $\tilde{\nu}$ = 3426, 3270, 2956, 2831, 2716, 1749, 1659, 1600, 1531, 1455, 1363, 1321, 1277, 1215, 1163, 1117, 1060, 1036, 989, 772, 710 cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{15}F_3NO_3$ [M + H]$^+$ 338.1004; found 338.1007.

Methyl 3-[(4-Acetylphenyl)amino]-3-oxo-2-phenylpropanoate (4j): White solid (139 mg, 89 % yield); m.p. 113–115 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.41 (s, 1 H), 7.90 (d, J = 8.7 Hz, 2 H), 7.63 (d, J = 8.7 Hz, 2 H), 7.47–7.42 (m, 2 H), 7.39–7.32 (m, 3 H), 4.70 (s, 1 H), 3.79 (s, 3 H), 2.55 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.1, 171.3, 165.6, 141.9, 133.5, 133.2, 129.7, 129.3, 128.7, 128.3, 119.4, 58.8, 53.2, 26.5 ppm. IR (film): $\tilde{\nu}$ = 3323, 2955, 2834, 1748, 1680, 1665, 1598, 1522, 1500, 1435, 1403, 1362, 1271, 1245, 1208, 1155, 1014, 976, 848, 819, 775, 741, 700 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{18}NO_4$ [M + H]$^+$ 312.1236; found 312.1240.

Methyl 3-[(4-Cyanophenyl)amino]-3-oxo-2-phenylpropanoate (4k): White solid (126 mg, 85 % yield); m.p. 144–146 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.44 (s, 1 H), 7.67 (d, J = 8.6 Hz, 2 H), 7.58 (d, J = 8.6 Hz, 2 H), 7.46–7.34 (m, 5 H), 4.67 (s, 1 H), 3.81 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.6, 165.6, 141.5, 133.4, 133.3, 129.5, 128.9, 128.1, 120.0, 118.9, 107.6, 58.7, 53.3 ppm. IR (film): $\tilde{\nu}$ = 3426, 3318, 3198, 3120, 2954, 2223, 1737, 1681, 1596, 1536, 1503, 1405, 1360, 1324, 1296, 1251, 1153, 1025, 851, 774, 700 cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{15}N_2O_3$ [M + H]$^+$ 295.1083; found 295.1072.

Isopropyl 3-[(3-Chloro-4-fluorophenyl)amino]-3-oxo-2-phenylpropanoate (4l): White solid (146 mg, 83 % yield); m.p. 105–107 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.32 (s, 1 H), 7.71 (dd, J = 6.6, 2.6 Hz, 1 H), 7.44–7.30 (m, 6 H), 7.04 (t, J = 8.8 Hz, 1 H), 5.17–5.06 (m, 1 H), 4.57 (s, 1 H), 1.31 (d, J = 6.3 Hz, 3 H), 1.19 (d, J = 6.3 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9, 165.6, 156.2, 153.7, 134.23 (d, $J_{C,F}$ = 3.4 Hz), 133.9, 128.64 (d, $J_{C,F}$ = 133.8 Hz), 128.6, 122.3, 121.16 (d, $J_{C,F}$ = 18.6 Hz), 119.80 (d, $J_{C,F}$ = 6.9 Hz), 116.62 (d, $J_{C,F}$ = 22.1 Hz), 70.4, 58.8, 21.7, 21.4 ppm. IR (film): $\tilde{\nu}$ = 3266, 3096, 2990, 2813, 1726, 1673, 1599, 1501, 1383, 1350, 1304, 1258, 1211, 1169, 1105, 908, 873, 823, 774, 733 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{18}ClFNO_3$ [M + H]$^+$ 350.0959; found 350.0964.

Ethyl 3-[(4-Methoxyphenyl)amino]-3-oxo-2-(*m*-tolyl)propanoate (4m): Off-white solid (117 mg, 71 % yield); m.p. 51–53 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.91 (s, 1 H), 7.47–7.39 (m, 2 H), 7.25 (d, J = 4.7 Hz, 3 H), 7.14 (dd, J = 6.6, 2.9 Hz, 1 H), 6.87–6.76 (m, 2 H), 4.58 (s, 1 H), 4.32–4.16 (m, 2 H), 3.77 (s, 3 H), 2.35 (s, 3 H), 1.27 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.47, 165.19, 156.65, 139.08, 134.05, 130.78, 129.29, 129.12, 128.96, 125.11, 121.81, 114.17, 62.21, 58.92, 55.57, 21.55, 14.08 ppm. IR (film): $\tilde{\nu}$ = 3293, 2981, 2832, 1740, 1650, 1602, 1531, 1364, 1314, 1254, 1189, 1167, 1031, 823, 774 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{22}NO_4$ [M + H]$^+$ 328.1549; found 328.1543.

Ethyl 3-[(4-Cyanophenyl)amino]-2-(3,4-dimethoxyphenyl)-3-oxopropanoate (4n): White solid (155 mg, 84 % yield); m.p. 51–53 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.35 (s, 1 H), 7.67 (d, J = 8.7 Hz, 2 H), 7.59 (d, J = 8.7 Hz, 2 H), 6.97 (d, J = 6.6 Hz, 2 H), 6.86 (d, J =

8.9 Hz, 1 H), 4.58 (s, 1 H), 4.27 (dddd, *J* = 17.9, 10.8, 7.2, 3.7 Hz, 2 H), 3.88 (s, 3 H), 3.87 (s, 3 H), 1.29 (t, *J* = 7.1 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.18, 166.07, 149.51, 149.46, 141.58, 133.30, 125.76, 120.22, 119.95, 118.84, 111.59, 111.37, 107.52, 62.53, 58.41, 56.07, 56.00, 14.05 ppm. IR (film): $\tilde{\nu}$ = 3300, 2997, 2940, 2833, 2234, 1734, 1666, 1593, 1515, 1467, 1409, 1364, 1304, 1257, 1207, 1181, 1146, 1024, 877, 829, 776 cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{21}N_2O_5$ $[M + H]^+$ 369.1450; found 369.1438.

Ethyl 3-[(4-Acetylphenyl)amino]-2-(4-chlorophenyl)-3-oxopropanoate (4o): Off-white solid (166 mg, 92 % yield); m.p. 51–53 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.53 (s, 1 H), 7.90 (d, *J* = 8.4 Hz, 2 H), 7.63 (d, *J* = 8.1 Hz, 2 H), 7.35 (dd, *J* = 22.8, 8.0 Hz, 4 H), 4.64 (s, 1 H), 4.34–4.19 (m, 2 H), 2.56 (s, 3 H), 1.27 (t, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.2, 170.6, 165.3, 141.8, 134.7, 133.3, 132.1, 129.7, 129.7, 129.3, 119.4, 62.6, 58.1, 26.5, 14.0 ppm. IR (film): $\tilde{\nu}$ = 3337, 2987, 2831, 2713, 1725, 1669, 1594, 1526, 1489, 1407, 1363, 1274, 1210, 1176, 1145, 1094, 1019, 836, 775 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{19}ClNO_4$ $[M + H]^+$ 360.1003; found 360.1003.

Diethyl [2-Oxo-1-phenyl-2-(phenylamino)ethyl]phosphonate (6a): White solid (124 mg, 71 % yield); m.p. 119–121 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.37 (s, 1 H), 7.54 (d, *J* = 7.9 Hz, 4 H), 7.40–7.30 (m, 3 H), 7.27 (dd, *J* = 9.8, 6.2 Hz, 2 H), 7.07 (t, *J* = 7.2 Hz, 1 H), 4.31 (dd, $J_{H,P}$ = 23.3 Hz, $J_{H,H}$ = 2.5 Hz, 1 H), 4.17–4.01 (m, 3 H), 3.89 (m, 1 H), 1.27 (t, *J* = 7.1 Hz, 3 H), 1.16 (t, *J* = 7.0 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.4, 138.0, 131.82 (d, $J_{C,P}$ = 7.4 Hz), 129.62 (d, $J_{C,P}$ = 6.9 Hz), 129.0, 128.9, 128.2, 124.5, 120.0, 64.22 (d, $J_{C,P}$ = 6.9 Hz), 63.29 (d, $J_{C,P}$ = 7.2 Hz), 54.11 (d, $J_{C,P}$ = 130.9 Hz), 16.40 (d, $J_{C,P}$ = 6.0 Hz), 16.31 (d, $J_{C,P}$ = 5.8 Hz) ppm. IR (film): $\tilde{\nu}$ = 3359, 2980, 2934, 2831, 1680, 1598, 1521, 1495, 1439, 1361, 1325, 1294, 1236, 1163, 1098, 1034, 970, 944, 806, 757, 732 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{23}NO_4P$ $[M + H]^+$ 348.1365; found 348.1369.

Diethyl [2-Oxo-1-phenyl-2-(*p*-tolylamino)ethyl]phosphonate (6b): White solid (143 mg, 79 % yield); m.p. 122–124 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.20 (s, 1 H), 7.56–7.49 (m, 2 H), 7.43 (d, *J* = 8.4 Hz, 2 H), 7.39–7.29 (m, 3 H), 7.09 (d, *J* = 8.3 Hz, 2 H), 4.24 (d, $J_{H,P}$ = 23.4 Hz, 1 H), 4.18–4.07 (m, 2 H), 4.06–3.98 (m, 1 H), 3.86 (m, 1 H), 2.29 (s, 3 H), 1.28 (t, *J* = 7.1 Hz, 3 H), 1.15 (d, *J* = 7.1 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.1, 135.4, 134.2, 131.89 (d, $J_{C,P}$ = 7.2 Hz), 129.63 (d, $J_{C,P}$ = 6.9 Hz), 129.5, 128.93 (d, $J_{C,P}$ = 1.9 Hz), 128.18 (d, $J_{C,P}$ = 2.6 Hz), 120.1, 64.17 (d, $J_{C,P}$ = 7.0 Hz), 63.28 (d, $J_{C,P}$ = 7.1 Hz), 54.12 (d, $J_{C,P}$ = 130.4 Hz), 21.0, 16.43 (d, $J_{C,P}$ = 6.0 Hz), 16.30 (d, $J_{C,P}$ = 5.8 Hz) ppm. IR (film): $\tilde{\nu}$ = 3426, 3256, 3122, 2982, 2832, 1677, 1605, 1515, 1362, 1236, 1161, 1054, 1031, 964, 819, 776 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{25}NO_4P$ $[M + H]^+$ 362.1521; found 362.1521.

Diethyl {2-[(4-Methoxyphenyl)amino]-2-oxo-1-phenylethyl}phosphonate (6c): White solid (157 mg, 83 % yield); m.p. 129–131 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.20 (s, 1 H), 7.53 (dd, *J* = 6.3, 1.3 Hz, 2 H), 7.45 (d, *J* = 8.5 Hz, 2 H), 7.38–7.29 (m, 3 H), 6.84–6.78 (m, 2 H), 4.26 (d, $J_{H,P}$ = 23.3 Hz, 1 H), 4.17–3.97 (m, 3 H), 3.89 (m, 1 H), 3.76 (s, 3 H), 1.28 (t, *J* = 7.1 Hz, 3 H), 1.15 (t, *J* = 7.1 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.1, 156.5, 131.95 (d, $J_{C,P}$ = 7.3 Hz), 131.1, 129.61 (d, $J_{C,P}$ = 6.9 Hz), 128.9, 128.2, 121.7, 114.1, 64.18 (d, $J_{C,P}$ = 7.0 Hz), 63.25 (d, $J_{C,P}$ = 7.2 Hz), 55.5, 53.97 (d, $J_{C,P}$ = 130.5 Hz), 16.42 (d, $J_{C,P}$ = 6.1 Hz), 16.31 (d, $J_{C,P}$ = 5.9 Hz) ppm. IR (film): $\tilde{\nu}$ = 3426, 3262, 3208, 3134, 3076, 2981, 2926, 2832, 1679, 1605, 1553, 1510, 1412, 1298, 1246, 1213, 1179, 1159, 1045, 974, 830, 759 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{25}NO_5P$ $[M + H]^+$ 378.1470; found 378.1471.

Diethyl {2-[(3,4-Dimethoxyphenyl)amino]-2-oxo-1-phenylethyl}phosphonate (6d): Light brown solid (139 mg, 68 % yield); m.p. 51–53 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.37 (s, 1 H), 7.59–7.46 (m, 2 H), 7.32 (m, 4 H), 6.99 (dd, *J* = 8.6, 2.4 Hz, 1 H), 6.78–6.71 (m, 1 H), 4.33 (d, $J_{H,P}$ = 23.4 Hz, 1 H), 4.19–4.02 (m, 3 H), 4.01–3.89 (m, 1 H), 3.84 (s, 3 H), 3.82 (s, 3 H), 1.27 (t, *J* = 6.9 Hz, 3 H), 1.19 (t, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.12, 148.97 (d, $J_{C,P}$ = 7.4 Hz), 145.86 (d, $J_{C,P}$ = 8.9 Hz), 133.21–130.76 (m), 129.63 (d, $J_{C,P}$ = 6.9 Hz), 128.91 (d, $J_{C,P}$ = 3.0 Hz), 128.2, 111.7, 111.23 (d, $J_{C,P}$ = 3.7 Hz), 104.5, 64.27 (d, $J_{C,P}$ = 7.1 Hz), 63.26 (d, $J_{C,P}$ = 7.1 Hz), 56.1, 55.9, 54.00 (d, $J_{C,P}$ = 131.2 Hz), 19.40–12.79 (m) ppm. IR (film): $\tilde{\nu}$ = 3427, 3264, 2962, 2831, 1674, 1604, 1514, 1450, 1363, 1233, 1140, 1024, 979, 774 cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{27}NO_6P$ $[M + H]^+$ 408.1576; found 408.1574.

Diethyl {2-[(4-Chlorophenyl)amino]-2-oxo-1-phenylethyl}phosphonate (6e): Light brown semisolid (147 mg, 77 % yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.53 (s, 1 H), 7.52 (dd, *J* = 6.2, 1.5 Hz, 2 H), 7.49–7.41 (m, 2 H), 7.38–7.29 (m, 3 H), 7.24–7.11 (m, 2 H), 4.35 (d, $J_{H,P}$ = 23.4 Hz, 1 H), 4.17–4.02 (m, 3 H), 4.01–3.93 (m, 1 H), 1.27 (t, *J* = 7.0 Hz, 3 H), 1.19 (t, *J* = 7.1 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.5, 136.6, 131.7, 131.6, 129.61 (d, $J_{C,P}$ = 6.8 Hz), 129.3, 128.9, 128.28 (d, $J_{C,P}$ = 2.6 Hz), 121.1, 63.90 (dd, $J_{C,P}$ = 110.3, 7.1 Hz), 54.01 (d, $J_{C,P}$ = 131.3 Hz), 16.38 (t, $J_{C,P}$ = 5.5 Hz) ppm. IR (film): $\tilde{\nu}$ = 3458, 3240, 2984, 2931, 2831, 1673, 1601, 1545, 1493, 1400, 1365, 1232, 1206, 1051, 1025, 973, 960, 832, 775, 701 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{22}ClNO_4P$ $[M + H]^+$ 382.0975; found 382.0973.

Diethyl {2-[(4-Bromophenyl)amino]-2-oxo-1-phenylethyl}phosphonate (6f): White solid (148 mg, 69 % yield); m.p. 176–178 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.50 (s, 1 H), 7.55–7.49 (m, 2 H), 7.45–7.40 (m, 2 H), 7.39–7.30 (m, 5 H), 4.32 (d, $J_{H,P}$ = 23.4 Hz, 1 H), 4.18–4.03 (m, 3 H), 4.00–3.91 (m, 1 H), 1.28 (t, *J* = 7.1 Hz, 3 H), 1.19 (t, *J* = 7.1 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.1, 131.9, 131.64 (d, $J_{C,P}$ = 7.5 Hz), 129.62 (d, $J_{C,P}$ = 6.9 Hz), 128.96 (d, $J_{C,P}$ = 2.0 Hz), 128.3, 121.5, 117.0, 64.45 (d, $J_{C,P}$ = 7.0 Hz), 63.35 (d, $J_{C,P}$ = 7.3 Hz), 54.08 (d, $J_{C,P}$ = 130.9 Hz), 20.85–14.85 (m) ppm. IR (film): $\tilde{\nu}$ = 3426, 3243, 3182, 3112, 3058, 2984, 2831, 2713, 1674, 1602, 1542, 1498, 1392, 1362, 1323, 1233, 1050, 1025, 973, 775 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{22}BrNO_4P$ $[M + H]^+$ 426.0470; found 426.0461.

Diethyl {2-[(3-Chloro-4-fluorophenyl)amino]-2-oxo-1-phenylethyl}phosphonate (6g): White solid (142 mg, 71 % yield); m.p. 180–182 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.84 (d, $J_{H,P}$ = 15.1 Hz, 1 H), 7.69 (d, *J* = 6.5 Hz, 1 H), 7.55 (d, *J* = 6.2 Hz, 2 H), 7.40–7.27 (m, 4 H), 6.94 (td, *J* = 8.8, 4.6 Hz, 1 H), 4.46 (dd, $J_{H,P}$ = 23.4 Hz, $J_{H,H}$ = 8.5 Hz, 1 H), 4.25–4.01 (m, 4 H), 1.29 (dt, *J* = 10.0, 7.0 Hz, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.7, 155.9, 153.4, 134.9, 131.65 (d, *J* = 8.3 Hz), 129.59 (d, *J* = 6.8 Hz), 128.9, 128.3, 121.8, 120.88 (d, $J_{C,F}$ = 17.4 Hz), 119.25 (d, $J_{C,P}$ = 7.1 Hz), 116.33 (d, $J_{C,F}$ = 22.2 Hz), 64.73 (d, $J_{C,P}$ = 6.6 Hz), 63.35 (d, $J_{C,P}$ = 7.4 Hz), 53.91 (d, $J_{C,P}$ = 131.9 Hz), 16.48–16.38 (m) ppm. IR (film): $\tilde{\nu}$ = 3254, 3063, 2831, 2710, 1686, 1606, 1556, 1498, 1395, 1363, 1236, 1215, 1034, 978, 774 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{21}ClFNO_4P$ $[M + H]^+$ 400.0881; found 400.0874.

Diethyl {2-[(4-Acetylphenyl)amino]-2-oxo-1-phenylethyl}phosphonate (6h): White solid (127 mg, 65 % yield); m.p. 180–182 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.98 (d, *J* = 8.3 Hz, 1 H), 7.77 (dd, *J* = 8.7, 3.5 Hz, 2 H), 7.58 (dd, *J* = 10.8, 3.7 Hz, 4 H), 7.41–7.31 (m, 3 H), 4.54 (dd, $J_{H,P}$ = 23.5 Hz, $J_{H,H}$ = 6.3 Hz, 1 H), 4.24–4.02 (m, 4 H), 2.51 (d, *J* = 1.5 Hz, 3 H), 1.32–1.22 (m, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.1, 165.1, 142.6, 132.7, 131.6, 129.63 (d, $J_{C,P}$ = 6.8 Hz), 129.5, 128.84 (d, $J_{C,P}$ = 6.3 Hz), 128.3, 119.0, 64.63 (d, $J_{C,P}$ = 6.7 Hz), 63.39 (d, $J_{C,P}$ = 7.3 Hz), 54.06 (d, $J_{C,P}$ = 133.6 Hz), 26.4, 16.4, 16.3 ppm. IR (film): $\tilde{\nu}$ = 3432, 3254, 3188, 3107, 3059, 2979, 2831, 1679, 1600, 1541, 1362, 1270, 1240, 1211, 1024, 975, 840,

774 cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{25}NO_5P$ $[M + H]^+$ 390.1470; found 390.1465.

Diethyl {1-(4-Chlorophenyl)-2-[(4-chlorophenyl)amino]-2-oxoethyl}phosphonate (6i): White solid (163 mg, 78 % yield); m.p. 51–53 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.63 (s, 1 H), 7.47 (dd, J = 8.6, 2.1 Hz, 2 H), 7.45–7.40 (m, 2 H), 7.33 (d, J = 8.4 Hz, 2 H), 7.20–7.12 (m, 2 H), 4.41 (d, $J_{H,P}$ = 23.7 Hz, 1 H), 4.22–4.04 (m, 4 H), 1.28 (m, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.2, 136.6, 134.30 (d, $J_{C,P}$ = 3.4 Hz), 131.00 (d, $J_{C,P}$ = 6.8 Hz), 130.27 (d, $J_{C,P}$ = 8.2 Hz), 129.4, 128.97 (d, $J_{C,P}$ = 2.1 Hz), 128.9, 121.0, 64.63 (d, $J_{C,P}$ = 6.9 Hz), 63.46 (d, $J_{C,P}$ = 7.3 Hz), 53.15 (d, $J_{C,P}$ = 131.9 Hz), 16.46 (d, $J_{C,P}$ = 4.1 Hz), 16.41 (d, $J_{C,P}$ = 4.3 Hz) ppm. IR (film): $\tilde{\nu}$ = 3425, 3243, 3185, 3117, 3060, 2985, 2831, 2713, 1676, 1601, 1545, 1490, 1396, 1363, 1234, 1207, 1094, 1049, 1025, 974, 832, 776 cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{21}Cl_2NO_4P$ $[M + H]^+$ 416.0585; found 416.0579.

Diethyl {1-[(4-Chlorophenyl)amino]-1-oxo-3-phenylpropan-2-yl}phosphonate (6j): White solid (147 mg, 74 % yield); m.p. 147–149 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 9.55 (s, 1 H), 7.30 (d, J = 8.8 Hz, 2 H), 7.26–7.15 (m, 5 H), 7.01 (d, J = 8.8 Hz, 2 H), 4.30–4.01 (m, 4 H), 3.48–3.35 (m, 2 H), 3.14–3.01 (m, 1 H), 1.38 (t, J = 7.1 Hz, 3 H), 1.30 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.4, 139.04 (d, $J_{C,P}$ = 14.1 Hz), 136.9, 128.8, 128.7, 128.6, 128.5, 126.7, 120.8, 64.06 (d, $J_{C,P}$ = 6.3 Hz), 62.37 (d, $J_{C,P}$ = 7.0 Hz), 48.97 (d, $J_{C,P}$ = 127.9 Hz), 32.86 (d, $J_{C,P}$ = 4.9 Hz), 16.55 (d, $J_{C,P}$ = 5.9 Hz), 16.44 (d, $J_{C,P}$ = 6.2 Hz) ppm. IR (film): $\tilde{\nu}$ = 3262, 3121, 3068, 2983, 1690, 1605, 1547, 1492, 1398, 1359, 1250, 1222, 1088, 1050, 1026, 980, 885, 826, 775 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{24}ClNO_4P$ $[M + H]^+$ 396.1131; found 396.1119.

Methyl 3-(9*H*-Carbazol-9-yl)-3-oxo-2-phenylpropanoate (8a): White solid (109 mg, 63 % yield); m.p. 121–123 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.19 (d, J = 8.2 Hz, 2 H), 7.99 (d, J = 7.7 Hz, 2 H), 7.52–7.36 (m, 9 H), 5.80 (s, 1 H), 3.81 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.9, 167.6, 138.5, 132.6, 129.5, 129.2, 128.7, 127.7, 126.8, 124.3, 120.1, 116.25, 59.8, 53.3 ppm. IR (film): $\tilde{\nu}$ = 2949, 2831, 2716, 1725, 1667, 1595, 1494, 1445, 1368, 1334, 1255, 1236, 1199, 1161, 1018, 982, 865, 826, 775, 753 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{18}NO_3$ $[M + H]^+$ 344.1287; found 344.1305.

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