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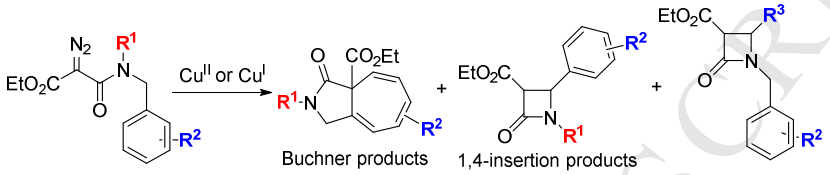

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ABSTRACT

Ethyl 3-alkyl(arylmethyl)amino-2-diazo-3-oxopropanoates (diazo amidoacetates) generate generally both cyclohepta[*c*]pyrrolones (Buchner products) and *β*-lactams (1,4-insertion products), and show obvious *N-substituent-controlled* chemoselectivity between the intramolecular Buchner reaction and aliphatic 1,4-C-H insertion under the catalysis of copper salts. The less steric *N*-alkyl substituents in the amide moiety generally favor the aliphatic 1,4-C-H insertion, while the more steric *N*-alkyl substituents generally favor the Buchner reaction. Compared with rhodium and ruthenium-catalyzed conditions, the current copper-catalyzed conditions improved the Buchner reaction selectivity of ethyl 3-alkyl(arylmethyl)amino-2-diazo-3-oxopropanoates

1. Introduction

The reactions of carbenes derived from diazo compounds provide a powerful tool to construct synthetically and biologically important organic compounds, especially in the intramolecular reactions.[1] Of particular, we are quite interested in the intramolecular Buchner reaction[2] and aliphatic 1,4-C-H insertion of substituted diazoacetamides.[3] The former gives 9-azabicyclo[5.3.0]deca-2,4,6-trien-10-one derivatives, 5,7-bicyclic products, while the latter produces *β*-lactams for *N*-benzyldiazoacetamides. Additionally, the reactions also generate aliphatic 1,5-C-H insertion to afford *γ*-lactams[4] and aromatic 1,6-C-H insertion to yield tetrahydroisoquinolinones in some cases[4d,i,5] (Scheme 1). The chemoselectivity between the Buchner reaction and aliphatic 1,4-C-H insertion has received much attention.[4-9] Previously published results revealed that the substituents adjacent to the diazo group,[4e,f,6] the ligands of rhodium catalysts,[4c,d,6d,7] *N*-substituents,[4b,c,e,f,h,5b,6c,d,e,8] and even the reaction conditions[6e,7b,h,j,9] played important roles in deciding the chemoselectivity. Ethyl 3-alkyl(arylmethyl)amino-2-diazo-3-oxopropanoates (*N*-alkyl-*N*-arylmethyl-diazoaceamides with α-ethoxycarbonyl substituent) produced generally *β*-lactams as major or sole products under the catalysis of rhodium and ruthenium catalysts.[10] Under these conditions, Buchner products were obtained in only a few cases with low selectivity. Recently, our group discovered that the presence of the cyano group adjacent to the diazo group led to a specific Buchner reaction under copper catalysis because of the π-π stacking interaction between the electron-deficient cyano group and the electron-rich *N*-arylmethyl group in diazoacetamides[11] (Scheme 1).

In our further studies, we hope to extend our studies on the reaction of ethyl 3-alkyl(arylmethyl)-2-diazo-3-oxopropanoates (ethyl diazoamidoacetates) under the copper catalysis and to improve the intramolecular Buchner reaction selectivity. Herein, we present the *N-substituent-controlled* intramolecular Buchner reacion to form ethyl 2-alkyl-3-oxo-1,2,3,3a-tetrahydrocyclohepta[*c*]pyrrole-3a-carboxylates and 1,4-insertion into aliphatic C-H bonds to yield ethyl *trans*-β-lactam-3-carboxylates (Scheme 1).

2. Results and Discussion

Ethyl 3-alkyl(arylmethyl)amino-3-oxopropanoates **1** were prepared from coupling of ethyl malonyl chloride and *N*-alkyl-*N*-arylmethylamines and further converted into ethyl 3-alkyl(arylmethyl)amino-2-diazo-3-oxopropanoates **2** by the diazo transformation with *p*-acetamidobenzenesulfonyl azide (*p*-ABSA) in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as base (Scheme 2).

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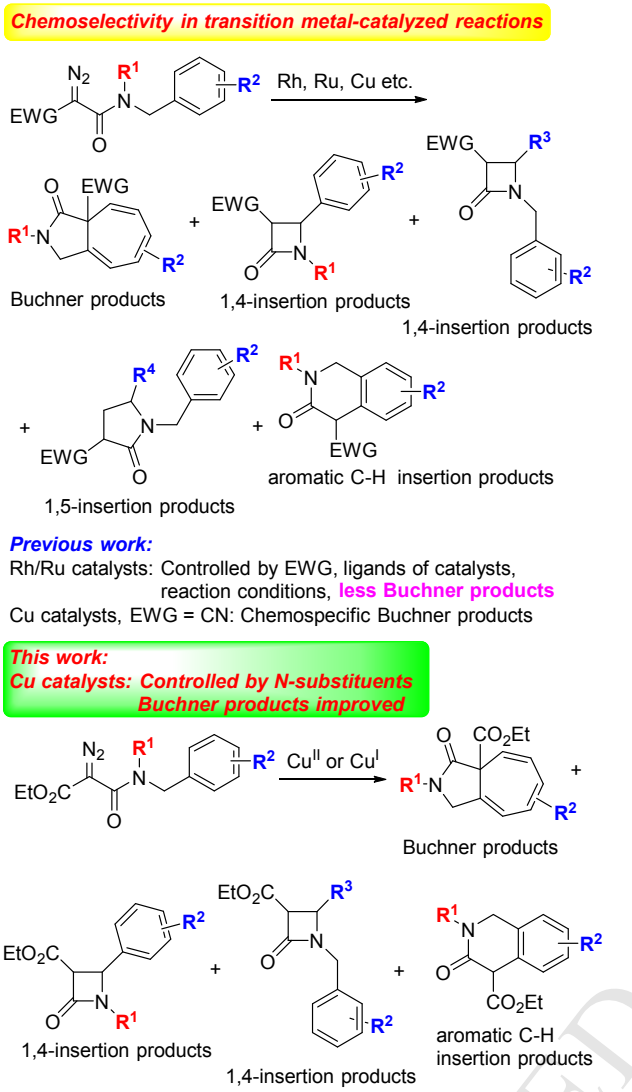
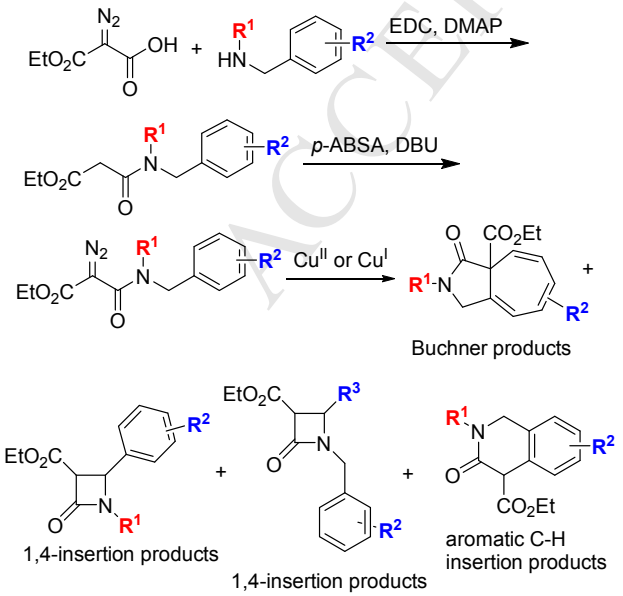


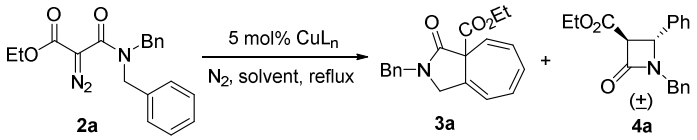
Scheme 1. Transition metal-catalyzed reactions of diazoacetamides with electron-withdrawing substituents.



Scheme 2. Copper-catalyzed reactions of ethyl 3-alkyl(arylmethyl)amino-2-diazo-3-oxopropanoates.

Ethyl 2-diazo-3-dibenzylamino-3-oxopropanoate (**2a**) was selected as a model substrate to optimize the reaction conditions under catalysis of different copper salts. At first, $Cu(acac)_2$ was chosen as the catalyst for the reaction in 1,2-dichloroethane (DCE) as solvent because they showed excellent efficiency in the reaction of 2-cyano-2-diazopropanamides.[33] The desired product ethyl 2-benzyl-3-oxo-1,2,3,3a-tetrahydrocyclohepta[*c*]pyrrole-3a-carboxylate (**3a**) was obtained in 27% yield with aliphatic 1,4-C-H insertion by-product *β*-lactam **4a** in 14% yield after refluxing overnight (Table 1, entry 1). The yields of both products were improved in refluxing toluene overnight (Table 1, entry 2). Further investigation upon various copper catalysts (Table 1, entries 3–12), including CuBr, CuI, CuCl, $Cu(OAc)_2\cdot H_2O$, $CuSO_4\cdot 5H_2O$, $Cu(NO_3)_2\cdot 3H_2O$, $CuBr_2$, $Cu(OTf)_2$, $CuOTf\cdot 1/2C_6H_6$, and $CuCl_2\cdot 2H_2O$ salts, revealed that $CuCl_2\cdot 2H_2O$ was optimal catalyst, showing a quantitative total yield and high Buchner reaction selectivity. Changing addition mode from dropwise to one portion further improved the selectivity from 72:28 to 75:25 (Table 1, entries 12 and 13). When the reaction was carried out under open air, similar selectivity was observed, but the yields decreased obviously, especially for Buchner product (Table 1, entry 14). Different solvents were screened. High chemoselectivity was obtained in refluxing dioxane, but with low total yield (Table 1, entry 15). Low chemoselectivies and total yields were observed in refluxing THF and DCM (Table 1, entries 16 and 17). The results indicated that toluene was good choice of solvent. Different temperatures were further tested in toluene (Table 1, entries 18–20). Compared with the reaction in refluxing toluene, yields decreased but chemoselectivities increased at 100 °C, 80 °C, and 60 °C. Finally, the reaction was attempted in refluxing toluene without catalyst. Low yield and chemoselectivity were obtained (Table 1, entry 21). Thus, the optimal conditions (5 mol % $CuCl_2\cdot 2H_2O$, toluene, reflux) were ascertained, the best yield of 100% and moderate chemoselectivity of 75:25 were achieved (Table 1, entry 13). Although the chemoselectivity was not high, the highest yield of Buchner product was obtained due to the highest total yield.

Table 1 Optimization of copper catalysts and reaction conditions[a]



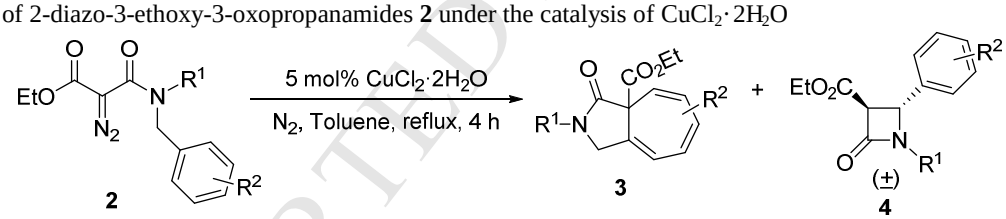
Entry	Catalyst	Solvent	Time (h)	**3a**(%)[b]	**4a**(%)[b]
1	$Cu(acac)_2$	DCE	overnight	27	14
2	$Cu(acac)_2$	Toluene	overnight	35	44
3	CuBr	Toluene	4	42	57
4	CuI	Toluene	4	39	55
5	CuCl	Toluene	4	41	58
6	$Cu(OAc)_2\cdot H_2O$	Toluene	4	45	54
7	$CuSO_4\cdot 5H_2O$	Toluene	4	41	59
8	$Cu(NO_3)_2\cdot 3H_2O$	Toluene	4	39	60
9	$CuBr_2$	Toluene	4	49	50
10	$Cu(OTf)_2$	Toluene	4	5	30
11	$CuOTf\cdot 1/2C_6H_6$	Toluene	4	50	29
12	$CuCl_2\cdot 2H_2O$	Toluene	4	72	28
13[c]	$CuCl_2\cdot 2H_2O$	Toluene	4	**75**	**25**
14[d]	$CuCl_2\cdot 2H_2O$	Toluene	4	65	21
15	$CuCl_2\cdot 2H_2O$	Dioxane	4	74	7

16	$CuCl_2 \cdot 2H_2O$	THF	4	11	3
17	$CuCl_2 \cdot 2H_2O$	DCM	4	26	3
18[e]	$CuCl_2 \cdot 2H_2O$	Toluene	4	66	7
19[f]	$CuCl_2 \cdot 2H_2O$	Toluene	4	35	5
20[g]	$CuCl_2 \cdot 2H_2O$	Toluene	4	5	1
21	-	Toluene	4	37	15

[a] Unless otherwise noted, all reactions were performed on 0.4 mmol scale in 5 mL of the solvent under nitrogen atmosphere. Diazo compound **2a** was dissolved in 5 mL of solvent and added dropwise. The reaction was monitored by TLC until the starting material was completely consumed. [b] Yields were determined by ^{1}H NMR with 4-iodonitrobenzene as an internal standard. [c] Diazo compound **2a** was added in one portion. [d] In open air, diazo compound **2a** was added in one portion. [e] Conducted at 100 °C. [f] Conducted at 80 °C. [g] Conducted at 60 °C.

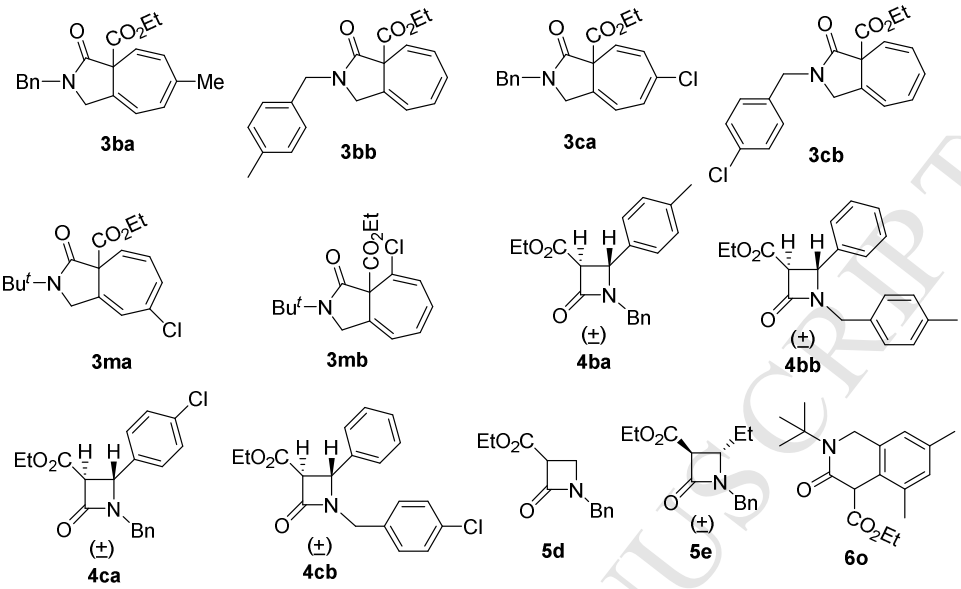
After successful optimization of the reaction conditions, we subsequently investigated the substrate scope. These results were summarized in Table 2. Ethyl 2-diazo-3-dibenzylamino-3-oxopropanoate (**2a**) generated the desired product ethyl 2-benzyl-3-oxo-1,2,3,3a-tetrahydrocyclohepta[*c*]pyrrole-3a-carboxylate (**3a**) in 75% yield with the corresponding aliphatic 1,4-C-H insertion product *β*-lactam **4a** in 25% yield (Table 2, entry 1). Two substituted 2-diazo-3-dibenzylamino-3-oxopropanoates **2b** and **2c** were also screened. Ethyl 3-benzyl[(4-methylphenyl)methyl]amino-2-diazo-3-oxopropanoate (**2b**) gave rise to two different Buchner products **3ba** and **3bb** in the same yield of 30% with the corresponding aliphatic 1,4-C-H insertion product *β*-lactams **4ba** and **4bb** (Table 2, entry 2). Ethyl 3-benzyl[(4-chlorophenyl)methyl]amino-2-diazo-3-oxopropanoate (**2c**) afforded two different Buchner products in yields of 28% and 35%, respectively, with the corresponding *β*-lactams **4ca** and **4cb** (Table 2, entry 3). The Buchner reaction slightly favored on the electron-richer benzyl group as previously reported. However, two different aliphatic 1,4-C-H insertion product *β*-lactams **4ba** and **4bb**, **4ca** and **4cb** in these two reactions cannot be separated due to their similar polarity and property. A series of 3-alkyl(benzyl)amino-2-diazo-3-oxopropanoates **2d-p** were further evaluated. For less bulky 3-benzyl(methyl/propyl)amino-2-diazo-3-oxopropanoates **2d** and **2e**, besides Buchner products **3d** and **3e** and β-lactams **4d** and **4e**, another class of aliphatic 1,4-C-H insertion product β-lactams **5d** and **5e** was obtained (Table 2, entries 4 and 5). While, for more bulky 3-benzyl(isopropyl/*tert*-butyl)amino-2-diazo-3-oxopropanoates **2f** and **2g**, both Buchner products **3f** and **3g** and *β*-lactams **4f** and **4g** were obtained, respectively, without other aliphatic 1,4-C-H insertion product β-lactam **5d** and aliphatic 1,5-C-H insertion product *γ*-lactams (Table 2, entries 6 and 7). Ethyl 3-benzyl(*tert*-butyl)amino-2-diazo-3-oxopropanoates **2h-l** with *para*-substituents on the benzyl group generated both Buchner products **3h-l** and *β*-lactams **4h-l**, with Buchner products as major products in most cases (Table 2, entries 8–12). 3-*tert*-Butyl[(3-chlorophenyl)methyl]amino-2-diazo-3-oxopropanoate **2m** afforded two different regiomeric Buchner products **3ma** and **3mb** in a total yield of 25% with a ratio of 64:36 and the corresponding *β*-lactam **4m** in 64% yield (Table 2, entry 13). However, 3-*tert*-butyl[(2-chlorophenyl)methyl]amino-2-diazo-3-oxopropanoate **2n** gave rise to Buchner product **3n** only in 61% yield (Table 2, entry 14). 3-*tert*-Butyl[(3,5-dimethylphenyl)methyl]amino-2-diazo-3-oxopropanoate **2o** produced both aliphatic 1,4-C-H insertion product *β*-lactam **5o** in 34% yield and aromatic 1,6-C-H insertion product **6o** in 66% yield (Table 2, entry 15). However, 3-*tert*-butyl[(2,4-dimethoxyphenyl)methyl]amino-2-diazo-3-oxopropanoate **2p** did not give Buchner product **3p** nor any insertion products (Table 2, entry 16).

Table 2 Reaction of 2-diazo-3-ethoxy-3-oxopropanamides **2** under the catalysis of $CuCl_2 \cdot 2H_2O$



Entry	R^1	R^2	Yield (%)			
			3	**4**	**5**	**6**
1	CH_2Ph	H	**3a** (75)	**4a** (25)		
2	CH_2Ph	4-Me	**3ba** (30) **3bb** (30)	**4ba+4bb** (14)		
3	CH_2Ph	4-Cl	**3ca** (28) **3cb** (36)	**4ca+4cb** (33)		
4	Me	H	**3d** (15)	**4d** (21)	**5d** (52)	
5	^{n}Pr	H	**3e** (33)	**4e** (15)	**5e** (3)	
6	^{i}Pr	H	**3f** (24)	**4f** (11)		
7	^{t}Bu	H	**3g** (20)	**4g** (64)		
8	^{t}Bu	4-F	**3h** (58)	**4h** (42)		
9	^{t}Bu	4-Cl	**3i** (67)	**4i** (27)		
10	^{t}Bu	4-Br	**3j** (41)	**4j** (46)		
11	^{t}Bu	4-Me	**3k** (52)	**4k** (47)		
12	^{t}Bu	4-OMe	**3l** (34)	**4l** (35)		
13	^{t}Bu	3-Cl	**3ma+3mb** (64:36)(25)	**4m** (64)		
14	^{t}Bu	2-Cl	**3n** (61)	**4n** (0)		
15	^{t}Bu	3,5-	**3o** (0)	**4o** (34)		**6o** (66)

16	^{t}Bu	$(Me)_2$ 2,4-$(OMe)_2$	**3p** (0)	**4p** (0)



Structures in Table 2

The results indicate that substrates with less bulky *N*-alkyl groups undergo not only benzylic aliphatic 1,4-C-H insertion, but also aliphatic 1,4-C-H insertion on the less steric alkyl groups, such as methyl and propyl groups, besides the desired Buchner reaction, because both conformations A and B exist in the reaction mixture. However, substrates with bulky *N*-alkyl groups, for example, isopropyl and *tert*-butyl groups, exist predominantly in conformation B, resulting in only occurrence of the benzylic 1,4-C-H insertion besides the desired Buchner reaction (Figure 1). No aliphatic 1,5-C-H insertion was observed under catalysis of the copper catalyst.

Figure 1. Reactive conformations in reaction mixture.

3. Conclusion

The copper-catalyzed reactions of ethyl 3-alkyl(arylmethyl)amino-2-diazo-3-oxopropanoates have been investigated. They generate generally both cyclohepta[*c*]pyrrolones (Buchner products) and β-lactams (1,4-insertion products), showing obvious *N-substituent-controlled* chemoselectivity between the intramolecular Buchner reaction and aliphatic 1,4-C-H insertion. The less bulky *N*-alkyl substituents generally predominant the aliphatic 1,4-C-H insertion, while the more steric *N*-alkyl substituents generally prefer the Buchner reaction. Compared with rhodium and ruthenium-catalyzed conditions, the current copper-catalyzed conditions improved the Buchner products in the reactions of 2-diazo-3-ethoxy-3-oxopropanamides.

4. Experimental Section

General Information:

Melting points (m.p.) were determined on a Yanaco MP-500 melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 400 NMR spectrometer at 400 MHz and 100 MHz, respectively, in $CDCl_3$ with TMS as an internal standard and chemical shifts were reported in ppm. IR spectra were taken on a Nicolet AVATAR 330 FT-IR spectrometer. HRMS spectra were performed on a Bruker LC/MSD TOF mass spectrometer.

For reactions conducted under anhydrous conditions glassware was dried in oven at 105 °C prior to use and the reactions were carried out under a nitrogen atmosphere. Solvents were refluxed with drying reagents and freshly distilled prior to use. Dichloromethane (DCM) and 1,2-dichloroethane (DCE) were dried over calcium hydride. Toluene was refluxed in the presence of sodium wire with diphenyl ketone as an indicator. Reagents used were obtained from commercial suppliers and used without purification. All reactions were followed by thin-layer chromatography (TLC) where practical, using silica gel GF_{254} fluorescent treated silica gel plates, which were visualized under UV light (254 nm). Column chromatography was performed on silica gel zcx II (200–300 mesh) with petroleum ether (PE, 60 ^{o}C-90 ^{o}C) and ethyl acetate (EA) as the eluent.

4.1. General Procedure for the reductive amination

A primary amine (20 mmol) and aldehyde (20 mmol) were dissolved in MeOH (50 mL) and the resulting solution was stirred for 3 hours at room temperature, then $NaBH_4$ (0.90 g, 24 mmol) was added portionwise. After 1 hour, the solution was added water (50 mL) and extracted with DCM (30 mL) twice.

The combined organic layer was dried over anhydrous Na_2SO_4 and then evaporated under reduced pressure. The crude product was used in the next step without further purification.

4.2. General Procedure for the synthesis of ethyl 3-(benzylamino)-3-oxopropanoates using EDC/DMAP as condensation reagents

To a mixture of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC, 2.88 g, 15 mmol), 4-dimethylaminopyridine (DMAP, 0.183 g, 1.5 mmol) and the corresponding secondary amine (7.5 mmol) in DCM (20 mL) was added ethyl hydrogen malonate (1.3 mL, 11 mmol). The reaction mixture was stirred sufficiently at ambient temperature until amines were disappeared. Then the reaction mixture was diluted with DCM and washed with brine (2×10 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel chromatography (petroleum ether/EtOAc, v/v 10:1) to afford pure amide **1**.

*4.2.1. Ethyl 3-(dibenzylamino)-3-oxopropanoate (**1a**)*

Yellow oil. 47% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.05 (m, 10H, ArH), 4.63 (s, 2H, CH_2), 4.44 (s, 2H, CH_2), 4.20 (q, J = 7.1 Hz, 2H, CH_2), 3.54 (s, 2H, CH_2), 1.27 (t, J = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 166.7, 136.6, 135.7, 128.9, 128.5, 128.1, 127.8, 127.4, 126.3, 61.5, 50.5, 48.2, 41.3, 14.0. IR (DCM) ν (cm^{-1}): 1738 (C=O), 1652 (C=O). HRMS (ESI) calcd. for $C_{19}H_{22}NO_3^+$ $[M+H]^+$ *m/z* 312.1594, found 312.1592.

*4.2.2. Ethyl 3-(benzyl(4-methylbenzyl)amino)-3-oxopropanoate (**1b**)*

Yellow oil. 83% yield. Major isomer (52%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.23 (m, 4H, ArH), 7.18 – 7.09 (m, 4H, ArH), 7.02 (d, J = 7.8 Hz, 1H, ArH), 4.60 (s, 2H, CH_2), 4.37 (s, 2H, CH_2), 4.18 (q, J = 7.1 Hz, 2H, CH_2), 3.52 (s, 2H, CH_2), 2.31 (s, 3H, CH_3), 1.25 (t, J = 7.2 Hz, 3H, CH_3). Major isomer (48%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.23 (m, 4H, ArH), 7.18 – 7.09 (m, 4H, ArH), 7.02 (d, J = 7.8 Hz, 1H, ArH), 4.57 (s, 2H, CH_2), 4.40 (s, 2H, CH_2), 4.18 (q, J = 7.2 Hz, 2H, CH_2), 3.50 (s, 2H, CH_2), 2.33 (s, 3H, CH_3), 1.26 (t, J = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 167.4, 166.62, 166.59, 137.4, 137.0, 136.7, 135.8, 133.5, 132.6, 129.6, 129.1, 128.9, 128.5, 128.1, 128.0, 127.7, 127.3, 126.3, 61.4, 50.23, 50.18, 48.0, 47.8, 41.3, 21.0, 20.9, 14.0. IR (DCM) ν (cm-1): 1738 (C=O), 1651 (C=O). HRMS (ESI) calcd. for $C_{20}H_{24}NO_3^+$ $[M+H]^+$ *m/z* 326.1751, found 326.1741.

*4.2.3. Ethyl 3-(benzyl(4-chlorobenzyl)amino)-3-oxopropanoate (**1c**)*

Colorless oil. 99% yield. ^{1}H NMR (400 MHz, $CDCl_3$) Major isomer (65%): δ 7.38 – 7.25 (m, 5H, ArH), 7.22 – 7.11 (m, 3H, ArH), 7.07 (d, J = 8.0 Hz, 1H, ArH), 4.55 (s, 2H, CH_2), 4.41 (s, 2H, CH_2), 4.18 (q, J = 7.1 Hz, 2H, CH_2), 3.52 (s, 2H, CH_2), 1.26 (t, J = 7.1 Hz, 3H, CH_3). Minor isomer (35%): δ 7.38 – 7.25 (m, 5H, ArH), 7.22 – 7.11 (m, 3H, ArH), 7.07 (d, J = 8.0 Hz, 1H, ArH), 4.58 (s, 2H, CH_2), 4.38 (s, 2H, CH_2), 4.18 (q, J = 7.1 Hz, 2H, CH_2), 3.50 (s, 2H, CH_2), 1.26 (t, J = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 167.3, 166.8, 166.6, 139.6, 136.6, 136.3, 135.4, 135.1, 134.2, 133.6, 133.2, 129.4, 129.1, 129.0, 128.9, 128.63, 128.55, 128.5, 128.4, 128.1, 128.0, 127.9, 127.8, 127.7, 127.5, 127.4, 126.3, 64.1, 61.5, 61.4, 50.6, 50.4, 49.9, 48.2, 48.1, 47.6, 41.22, 41.16, 14.0. IR (DCM) ν (cm^{-1}): 1738 (C=O), 1651 (C=O). HRMS (ESI) calcd. for $C_{19}H_{21}ClNO_3^+$ $[M+H]^+$ *m/z* 346.1204, found 346.1207.

*4.2.4. Ethyl 3-(benzyl(methyl)amino)-3-oxopropanoate (**1d**)*

Yellow oil. 59% yield. ^{1}H NMR (400 MHz, $CDCl_3$) Major isomer (62%): δ 7.45 – 7.10 (m, 5H, ArH), 4.62 (s, 2H, CH_2), 4.22 (q, J = 7.2 Hz, 2H, CH_2), 3.53 (s, 2H, CH_2), 2.92 (s, 3H, CH_3), 1.28 (t, J = 7.2 Hz, 3H, CH_3). Minor isomer (38%): δ 7.45 – 7.10 (m, 5H, ArH), 4.54 (s, 2H, CH_2), 4.18 (q, J = 7.2 Hz, 2H, CH_2), 3.49 (s, 2H, CH_2), 2.97 (s, 3H, CH_3), 1.25 (t, J = 7.2 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 167.5, 166.4, 166.2, 136.7, 135.9, 128.9, 128.6, 127.9, 127.8, 127.4, 126.3, 61.4, 53.9, 50.9, 41.6, 41.2, 35.3, 34.0, 14.1, 14.0. IR (DCM) ν (cm^{-1}): 1736 (C=O), 1654 (C=O). HRMS (ESI) calcd. for $C_{13}H_{18}NO_3^+$ $[M+H]^+$ *m/z* 236.1281, found 236.1277.

*4.2.5. Ethyl 3-(benzyl(propyl)amino)-3-oxopropanoate (**1e**)*

Yellow oil. 79% yield. ^{1}H NMR (400 MHz, $CDCl_3$) Major isomer (56%): δ 7.48 – 7.09 (m, 5H, ArH), 4.64 (s, 2H, CH_2), 4.23 (q, J = 7.2 Hz, 2H, CH_2), 3.53 (s, 2H, CH_2), 3.14 (t, J = 7.6 Hz, 2H, CH_2), 1.67 – 1.52 (m, 2H, CH_2), 1.30 (t, J = 6.0 Hz, 3H, CH_3), 0.89 (t, J = 7.3 Hz, 3H, CH_3). Minor isomer (44%): δ 7.48 – 7.09 (m, 5H, ArH), 4.54 (s, 2H, CH_2), 4.17 (q, J = 7.2 Hz, 2H, CH_2), 3.43 (s, 2H, CH_2), 3.36 (t, J = 7.6 Hz, 2H, CH_2), 1.67 – 1.52 (m, 2H, CH_2), 1.26 (t, J = 5.9 Hz, 3H, CH_3), 0.88 (t, J = 7.4 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.7, 167.6, 166.4, 166.1, 137.1, 136.3, 128.9, 128.5, 127.8, 127.6, 127.2, 126.2, 61.4, 61.3, 51.6, 49.2, 48.1, 47.9, 41.5, 41.1, 21.5, 20.5, 14.04, 14.01, 11.2, 11.1. IR (DCM) ν (cm^{-1}): 1736 (C=O), 1655 (C=O). HRMS (ESI) calcd. for $C_{15}H_{22}NO_3^+$ $[M+H]^+$ *m/z* 264.1594, found 264.1597.

*4.2.6. Ethyl 3-(benzyl(isopropyl)amino)-3-oxopropanoate (**1f**)*

Colorless oil. 53% yield. ^{1}H NMR (400 MHz, $CDCl_3$) Major isomer (55%): δ 7.41 – 7.14 (m, 5H, ArH), 4.86 (hept, J = 6.8 Hz, 1H, CH), 4.48 (s, 2H, CH_2), 4.17 (q, J = 7.2 Hz, 2H, CH_2), 3.30 (s, 2H, CH_2), 1.26 (t, J = 7.2 Hz, 3H, CH_3), 1.14 (t, J = 7.3 Hz, 6H, $2CH_3$). Minor isomer (45%): δ 7.41 – 7.14 (m, 5H, ArH), 4.57 (s, 2H, CH_2), 4.24 (q, J = 7.2 Hz, 2H, CH_2), 4.07 (hept, J = 6.7 Hz, 1H, CH), 3.60 (s, 2H, CH_2), 1.32 (t, J = 7.2 Hz, 3H, CH_3), 1.14 (t, J = 7.3 Hz, 6H, $2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 167.7, 167.0, 166.0, 138.9, 137.8, 128.8, 128.2, 127.3, 126.7, 126.5, 125.7, 61.4, 61.2, 49.9, 46.4, 46.1, 43.8, 42.0, 41.8, 21.3, 20.0, 14.04, 13.97. IR (DCM) ν (cm^{-1}): 1738 (C=O), 1645 (C=O). HRMS (ESI) calcd. for $C_{15}H_{22}NO_3^+$ $[M+H]^+$ *m/z* 264.1594, found 264.1592.

*4.2.7. Ethyl 3-(benzyl(tert-butyl)amino)-3-oxopropanoate (**1g**).*[12]

Colorless oil. 76% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (t, J = 7.5 Hz, 2H, ArH), 7.31 – 7.18 (m, 3H, ArH), 4.59 (s, 2H, CH_2), 4.18 (q, J = 7.1 Hz, 2H, CH_2), 3.37 (s, 2H, CH_2), 1.45 (s, 9H, $3CH_3$), 1.27 (t, J = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 167.7, 138.6, 128.9, 127.2, 125.5, 61.2, 58.4, 49.2, 43.9, 28.6, 14.1.

*4.2.8. Ethyl 3-(tert-butyl(4-fluorobenzyl)amino)-3-oxopropanoate (**1h**).*

White solid, m.p. 78–81 °C. 46% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.17 (m, 2H, ArH), 7.16 – 6.94 (m, 2H, ArH), 4.59 (s, 2H, CH_2), 4.18 (q, J = 7.2 Hz, 2H, CH_2), 3.37 (s, 2H, CH_2), 1.45 (s, 9H, $3CH_3$), 1.27 (t, J = 7.2 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 167.4, 161.7 (d, J = 245.6 Hz), 134.2 (d, J = 3.1 Hz), 126.9 (d, J = 8.0 Hz), 115.6 (d, J = 21.6 Hz), 61.1, 58.2, 48.4, 43.7, 28.4, 13.9. IR (DCM) ν (cm^{-1}): 1742 (C=O), 1658 (C=O). HRMS (ESI) calcd. for $C_{16}H_{23}FNO_3^+$ $[M+H]^+$ *m/z* 296.1656, found 296.1664.

*4.2.9. Ethyl 3-(tert-butyl(4-chlorobenzyl)amino)-3-oxopropanoate (**1i**)*

White solid, m.p. 73–76 °C. 56% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.2 Hz, 2H, ArH), 7.18 (d, *J* = 8.1 Hz, 2H, ArH), 4.56 (s, 2H, CH_2), 4.18 (q, *J* = 7.1 Hz, 2H, CH_2), 3.34 (s, 2H, CH_2), 1.44 (s, 9H, $3CH_3$), 1.27 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 167.6, 137.2, 133.0, 129.1, 126.9, 61.3, 58.4, 48.6, 43.9, 28.6, 14.1. IR (DCM): *v* (cm^{-1}): 1735 (C=O), 1648 (C=O). HRMS (ESI) calcd. for $C_{16}H_{23}ClNO_3^+$ $[M+H]^+$ *m/z* 312.1361, found 312.1358.

*4.2.10. Ethyl 3-((4-bromobenzyl)(tert-butyl)amino)-3-oxopropanoate (**1j**)*

White solid, m.p. 79–80 °C. 71% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.5 Hz, 2H, ArH), 7.12 (d, *J* = 8.5 Hz, 2H, ArH), 4.54 (s, 2H, CH_2), 4.18 (q, *J* = 7.1 Hz, 2H, CH_2), 3.34 (s, 2H, CH_2), 1.44 (s, 9H, $3CH_3$), 1.27 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.0, 167.6, 137.8, 132.1, 127.3, 121.1, 61.4, 58.5, 48.7, 43.9, 28.6, 14.1. IR (DCM) *v* (cm^{-1}): 1741 (C=O), 1655 (C=O). HRMS (ESI) calcd. for $C_{16}H_{23}BrNO_3^+$ $[M+H]^+$ *m/z* 356.0856, found 356.0858.

*4.2.11. Ethyl 3-(tert-butyl(4-methylbenzyl)amino)-3-oxopropanoate (**1k**)*

Yellow oil. 63% yield. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.18 (d, *J* = 8.0 Hz, 2H, ArH), 7.11 (d, *J* = 8.0 Hz, 2H, ArH), 4.55 (s, 2H, CH_2), 4.17 (q, *J* = 7.2 Hz, 2H, CH_2), 3.37 (s, 2H, CH_2), 2.35 (s, 3H, CH_3), 1.45 (s, 9H, $3CH_3$), 1.27 (t, *J* = 7.2 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 167.7, 136.9, 135.6, 129.6, 125.4, 61.2, 58.3, 49.0, 44.0, 29.1, 28.6, 21.0, 14.1. IR (DCM) *v* (cm^{-1}): 1742 (C=O), 1652 (C=O). HRMS (ESI) calcd. for $C_{17}H_{26}NO_3^+$ $[M+H]^+$ *m/z* 292.1907, found 292.1910.

*4.2.12. Ethyl 3-(tert-butyl(4-methoxybenzyl)amino)-3-oxopropanoate (**1l**)*[13]

Colorless oil. 39% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (d, *J* = 8.7 Hz, 2H, ArH), 6.97 – 6.78 (m, 2H, ArH), 4.53 (s, 2H, CH_2), 4.18 (q, *J* = 7.1 Hz, 2H, CH_2), 3.81 (s, 3H, CH_3), 3.38 (s, 2H, CH_2), 1.44 (s, 9H, $3CH_3$), 1.27 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 167.7, 158.8, 130.5, 126.6, 114.3, 61.2, 58.3, 55.3, 48.6, 43.9, 28.6, 14.1. IR (DCM) *v* (cm^{-1}): 1742 (C=O), 1659 (C=O). HRMS (ESI) calcd. for $C_{17}H_{26}NO_4^+$ $[M+H]^+$ *m/z* 308.1856, found 308.1859.

*4.2.13. **Ethyl 3-(tert-butyl(3-chlorobenzyl)amino)-3-oxopropanoate (1m)***

Colorless oil. 65% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.18 (m, 3H, ArH), 7.13 (d, *J* = 7.4 Hz, 1H, ArH), 4.58 (s, 2H, CH_2), 4.17 (q, *J* = 7.1 Hz, 2H, CH_2), 3.34 (s, 2H, CH_2), 1.44 (s, 9H, $3CH_3$), 1.26 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 167.5, 140.9, 134.8, 130.1, 127.4, 125.6, 123.5, 61.2, 58.3, 48.6, 43.8, 28.5, 13.9. IR (DCM) *v* (cm^{-1}): 1736 (C=O), 1655 (C=O). HRMS (ESI) calcd. for $C_{16}H_{23}ClNO_3^+$ $[M+H]^+$ *m/z* 312.1361, found 312.1362.

*4.2.14. Ethyl 3-(tert-butyl(2-chlorobenzyl)amino)-3-oxopropanoate (**1n**)*

Colorless oil. 76% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.30 (m, 3H, ArH), 7.28 – 7.07 (m, 1H, ArH), 4.61 (s, 2H, CH_2), 4.18 (q, *J* = 7.1 Hz, 2H, CH_2), 3.30 (s, 2H, CH_2), 1.46 (s, 9H, $3CH_3$), 1.27 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* = 167.9, 167.9, 135.9, 131.8, 129.7, 128.5, 127.3, 127.0, 61.3, 58.4, 47.2, 43.8, 28.4, 14.1. IR (DCM) *v* (cm^{-1}): 1742 (C=O), 1660 (C=O). HRMS (ESI) calcd. for $C_{16}H_{23}ClNO_3^+$ $[M+H]^+$ *m/z* 312.1361, found 312.1362.

*4.2.15. Ethyl 3-(tert-butyl(3,5-dimethylbenzyl)amino)-3-oxopropanoate (**1o**)*

Colorless oil. 64% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 – 6.68 (m, 4H, ArH), 4.51 (s, 2H, CH_2), 4.18 (q, *J* = 7.1 Hz, 2H, CH_2), 3.37 (s, 2H, CH_2), 2.31 (s, 6H, $2CH_3$), 1.45 (s, 9H, $3CH_3$), 1.27 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 167.7, 138.6, 138.5, 128.8, 128.5, 126.2, 123.2, 61.2, 58.3, 49.1, 44.0, 28.9, 28.6, 21.3, 14.1. IR (DCM) *v* (cm^{-1}): 1742 (C=O), 1654 (C=O). HRMS (ESI) calcd. for $C_{18}H_{28}NO_3^+$ $[M+H]^+$ *m/z* 306.2064, found 306.2059.

*4.2.16. Ethyl 3-(tert-butyl(2,4-dimethoxybenzyl)amino)-3-oxopropanoate (**1p**)*

White solid, m.p. 93–96 °C. 20% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.4 Hz, 1H, ArH), 6.50 (dd, *J* = 8.4, 2.3 Hz, 1H, ArH), 6.45 (d, *J* = 2.3 Hz, 1H, ArH), 4.44 (s, 2H, CH_2), 4.18 (q, *J* = 7.2 Hz, 2H, CH_2), 3.81 (s, 6H, $2CH_3$), 3.33 (s, 2H, CH_2), 1.44 (s, 9H, $3CH_3$), 1.26 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 168.0, 160.1, 156.9, 126.9, 119.0, 103.9, 98.5, 61.1, 58.1, 55.4, 55.2, 44.2, 43.8, 28.4, 14.1. IR (DCM) *v* (cm^{-1}): 1740 (C=O), 1654 (C=O). HRMS (ESI) calcd. for $C_{18}H_{28}NO_5^+$ $[M+H]^+$ *m/z* 338.1962, found 338.1963.

4.3. General Procedure for the synthesis of ethyl 3-(benzylamino)-2-diazo-3-oxopropanoates 2

To a solution of **1** (5 mmol) in dry DCM (20 mL) was added *p*-ABSA (1.32 g, 5.5 mmol) and DBU (5.5 mmol, 0.82 mL) at 0 °C. The resulting mixture was stirred for 18 hours at room temperature. Filtrated to remove the solid. The solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography to afford the pure product **2**.

*4.3.1. Ethyl 2-diazo-3-(dibenzylamino)-3-oxopropanoate (**2a**).*[7d]

Yellow oil. 76% yield. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.38–7.12 (m, 10H, ArH), 4.51 (s, 4H, $2CH_2$), 4.25 (q, *J* = 7.2 Hz, 2H, CH_2), 1.28 (t, *J* = 7.2 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 162.4, 162.3, 136.2, 128.6, 127.7, 127.5, 66.8, 61.4, 50.3, 14.3.

*4.3.2. Ethyl 3-(benzyl(4-methylbenzyl)amino)-2-diazo-3-oxopropanoate (**2b**)*

Yellow oil. 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.24 (m, 3H, ArH), 7.18 – 7.11 (m, 4H, ArH), 7.04 (d, *J* = 8.0 Hz, 2H, ArH), 4.49 (s, 2H, CH_2), 4.45 (s, 2H, CH_2), 4.24 (q, *J* = 7.1 Hz, 2H, CH_2), 2.33 (s, 3H, CH_3), 1.27 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4, 162.2, 137.2, 136.3, 133.1, 129.3, 128.6, 127.8, 127.7, 127.5, 66.8, 61.4, 50.1, 21.1, 14.3. IR (DCM) *v* (cm^{-1}): 2127 (C=N=N), 1709 (C=O), 1626 (C=O). HRMS (ESI) calcd. for $C_{20}H_{22}N_3O_3^+$ $[M+H]^+$ *m/z* 352.1656, found 352.1647.

*4.3.3. Ethyl 3-(benzyl(4-chlorobenzyl)amino)-2-diazo-3-oxopropanoate (**2c**)*

Yellow oil. 93% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.28 (m, 5H, ArH), 7.18 – 7.10 (m, 4H, ArH), 4.48 (s, 2H, CH_2), 4.46 (s, 2H, CH_2), 4.26 (q, *J* = 7.1 Hz, 2H, CH_2), 1.28 (t, *J* = 7.2 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5, 162.3, 136.0, 134.8, 133.4, 129.2, 128.8, 128.7, 127.8, 127.7, 67.0, 61.6, 50.7, 49.7, 14.4. IR (DCM) *v* (cm^{-1}): 2130 (C=N=N), 1709 (C=O), 1626 (C=O). HRMS (ESI) calcd. for $C_{19}H_{19}ClN_3O_3^+$ $[M+H]^+$ *m/z* 372.1109, found 372.1114.

*4.3.4. Ethyl 3-(benzyl(methyl)amino)-2-diazo-3-oxopropanoate **(2d)***

Yellow oil. 93% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.13 (m, 5H, ArH), 4.60 (s, 2H, CH_2), 4.26 (q, *J* = 7.1 Hz, 2H, CH_2), 2.91 (s, 3H, CH_3), 1.29 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3, 162.1, 136.4, 128.6, 127.8, 127.5, 66.5, 61.4, 52.9, 36.0, 14.4. IR (DCM) *ν* (cm^{-1}): 2125 (C=N=N), 1709 (C=O), 1626 (C=O). HRMS (ESI) calcd. for $C_{13}H_{16}N_3O_3^+$ $[M+H]^+$ *m/z* 262.1186, found 262.1182.

*4.3.5. Ethyl 3-(benzyl(propyl)amino)-2-diazo-3-oxopropanoate **(2e)***

Yellow oil. 84% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 – 7.05 (m, 5H, ArH), 4.61 (s, 2H, CH_2), 4.26 (q, *J* = 7.1 Hz, 2H, CH_2), 3.25 (t, *J* = 7.4 Hz, 2H, CH_2), 1.63 – 1.54 (m, 2H, CH_2), 1.29 (t, *J* = 7.1 Hz, 3H, CH_3), 0.86 (t, *J* = 7.4 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5, 161.9, 136.7, 128.6, 127.49, 127.47, 66.4, 61.4, 50.7, 48.9, 20.7, 14.4, 11.1. IR (DCM) *ν* (cm^{-1}): 2124 (C=N=N), 1708 (C=O), 1625 (C=O). HRMS (ESI) calcd. for $C_{15}H_{20}N_3O_3^+$ $[M+H]^+$ *m/z* 290.1499, found 290.1502.

*4.3.6. Ethyl 3-(benzyl(isopropyl)amino)-2-diazo-3-oxopropanoate **(2f)***

Yellow oil. 98% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 6.83 (m, 5H, ArH), 4.54 (s, 2H, CH_2), 4.36 – 4.07 (m, 3H, CH & CH_2), 1.30 (t, *J* = 7.1 Hz, 3H, CH_3), 1.23 (d, *J* = 6.7 Hz, 6H, $2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.6, 161.7, 138.3, 128.4, 126.9, 126.7, 66.8, 61.3, 50.9, 45.9, 21.0, 14.4. IR (DCM) *ν* (cm^{-1}): 2121 (C=N=N), 1707 (C=O), 1623 (C=O). HRMS (ESI) calcd. for $C_{15}H_{20}N_3O_3^+$ $[M+H]^+$ *m/z* 290.1499, found 290.1498.

*4.3.7. Ethyl 3-(benzyl(tert-butyl)amino)-2-diazo-3-oxopropanoate **(2g)**.[12,13]*

Yellow crystals, m.p. 95–96 °C. 72% yield. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.40 – 7.14 (m, 5H, ArH), 4.62 (s, 2H, CH_2), 4.23 (q, *J* = 7.2 Hz, 2H, CH_2), 1.39 (s, 9H, $3CH_3$), 1.28 (t, *J* = 7.2 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 163.3, 162.6, 139.6, 128.7, 127.3, 126.8, 61.3, 58.9, 51.6, 28.8, 14.4.

*4.3.8. Ethyl 3-(tert-butyl(4-fluorobenzyl)amino)-2-diazo-3-oxopropanoate **(2h)***

Yellow crystals, m.p. 90–93 °C. 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (dd, *J* = 8.4, 5.3 Hz, 2H, ArH), 7.02 (t, *J* = 8.6 Hz, 2H, ArH), 4.58 (s, 2H, CH_2), 4.24 (q, *J* = 7.1 Hz, 2H, CH_2), 1.38 (s, 9H, $3CH_3$), 1.29 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 162.4, 162.0 (d, *J* = 246.0 Hz), 135.3 (d, *J* = 3.2 Hz), 128.4 (d, *J* = 8.0 Hz), 115.5 (d, *J* = 21.5 Hz), 61.3, 58.9, 50.9, 28.8, 14.4. IR (DCM) *ν* (cm^{-1}): 2125 (C=N=N), 1707 (C=O), 1654 (C=O). HRMS (ESI) calcd. for $C_{16}H_{21}FN_3O_3^+$ $[M+H]^+$ *m/z* 322.1567, found 322.1571.

*4.3.9. Ethyl 3-[tert-butyl(4-chlorobenzyl)amino]-2-diazo-3-oxopropanoate **(2i)**.[13]*

Yellow crystals, m.p. 54–56 °C. 99% yield. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.30 (d, *J* = 8.4 Hz, 2H, ArH), 7.14 (d, *J* = 8.4 Hz, 2H, ArH), 4.58 (s, 2H, CH_2), 4.23 (q, *J* = 7.2 Hz, 2H, CH_2), 1.38 (s, 9H, $3CH_3$), 1.29 (t, *J* = 7.2 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 162.4, 138.2, 133.1, 128.8, 128.2, 61.3, 59.0, 51.0, 28.8, 14.4.

*4.3.10. Ethyl 3-[(4-bromobenzyl)(tert-butyl)amino]-2-diazo-3-oxopropanoate **(2j)***

Yellow crystals, m.p. 54–57 °C. 94% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.4 Hz, 2H, ArH), 7.08 (d, *J* = 8.4 Hz, 2H, ArH), 4.56 (s, 2H, CH_2), 4.23 (q, *J* = 7.1 Hz, 2H, CH_2), 1.37 (s, 9H, $3CH_3$), 1.28 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 162.4, 138.8, 131.7, 128.5, 121.1, 61.3, 59.0, 51.0, 28.8, 14.4. IR (DCM) *ν* (cm^{-1}): 2124 (C=N=N), 1707 (C=O), 1654 (C=O). HRMS (ESI) calcd. for $C_{16}H_{21}BrN_3O_3^+$ $[M+H]^+$ *m/z* 382.0761, found 382.0764.

*4.3.11. Ethyl 3-[tert-butyl(4-methylbenzyl)amino]-2-diazo-3-oxopropanoate **(2k)***

Yellow crystals, m.p. 73–76 °C. 76% yield. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.13 (d, *J* = 8.0 Hz, 2H, ArH), 7.08 (d, *J* = 8.0 Hz, 2H, ArH), 4.58 (s, 2H, CH_2), 4.23 (q, *J* = 7.2 Hz, 2H, CH_2), 2.33 (s, 3H, CH_3), 1.38 (s, 9H, $3CH_3$), 1.28 (d, *J* = 7.2 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 162.6, 137.0, 136.5, 129.3, 126.7, 61.2, 58.8, 51.3, 28.8, 21.0, 14.4. IR (DCM) ν (cm^{-1}): 2123 (C=N=N), 1709 (C=O), 1629 (C=O). HRMS (ESI) calcd. for $C_{17}H_{24}N_3O_3^+$ $[M+H]^+$ *m/z* 318.1812, found 318.1811.

*4.3.12. Ethyl 3-[tert-butyl(4-methoxybenzyl)amino]-2-diazo-3-oxopropanoate **(2l)**.[13]*

Yellow oil. 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.7 Hz, 2H, ArH), 6.95 – 6.76 (m, 2H, ArH), 4.55 (s, 2H, CH_2), 4.23 (q, *J* = 7.1 Hz, 2H, CH_2), 3.80 (s, 3H, CH_3), 1.37 (s, 9H, $3CH_3$), 1.29 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 162.6, 158.8, 131.4, 128.0, 114.0, 68.1, 61.2, 58.8, 55.3, 51.1, 28.7, 14.4.

*4.3.13. Ethyl 3-(tert-butyl(3-chlorobenzyl)amino)-2-diazo-3-oxopropanoate **(2m)***

Yellow crystals, m.p. 63–67 °C. 73% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.22 (m, 2H, ArH), 7.19 (s, 1H, ArH), 7.10 (d, *J* = 7.1 Hz, 1H, ArH), 4.59 (s, 2H, CH_2), 4.23 (q, *J* = 7.2 Hz, 2H, CH_2), 1.39 (s, 9H, $3CH_3$), 1.29 (t, *J* = 7.2 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 162.4, 141.8, 134.6, 129.9, 127.5, 126.9, 124.9, 61.3, 59.1, 51.1, 28.8, 14.4. IR (DCM) *ν* (cm^{-1}): 2125 (C=N=N), 1708 (C=O), 1630 (C=O). HRMS (ESI) calcd. for $C_{16}H_{21}ClN_3O_3^+$ $[M+H]^+$ *m/z* 338.1266, found 338.1258.

*4.3.14. Ethyl 3-[tert-butyl(2-chlorobenzyl)amino]-2-diazo-3-oxopropanoate **(2n)***

Yellow oil. 66% yield. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.38 – 7.17 (m, 4H, ArH), 4.75 (s, 2H, CH_2), 4.23 (q, *J* = 7.2 Hz, 2H, CH_2), 1.41 (s, 9H, $3CH_3$), 1.28 (t, *J* = 7.0 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.6, 162.6, 136.8, 132.2, 129.9, 128.6, 128.4, 126.8, 61.3, 59.1, 49.0, 28.7, 14.4. IR (DCM) *ν* (cm^{-1}): 2124 (C=N=N), 1708 (C=O), 1631 (C=O). HRMS (ESI) calcd. for $C_{16}H_{21}ClN_3O_3^+$ $[M+H]^+$ *m/z* 338.1266, found 338.1267.

*4.3.15. Ethyl 3-(tert-butyl(3,5-dimethylbenzyl)amino)-2-diazo-3-oxopropanoate **(2o)***

Yellow crystals, m.p. 176–181 °C. 78% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.89 (s, 1H, ArH), 6.79 (s, 2H, ArH), 4.55 (s, 2H, CH_2), 4.23 (q, *J* = 7.1 Hz, 2H, CH_2), 2.29 (s, 6H, $2CH_3$), 1.40 (s, 9H, $3CH_3$), 1.28 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 162.6, 139.5, 138.2, 128.8, 124.4, 67.9, 61.2, 58.9, 51.5, 28.8, 21.3, 14.4. IR (DCM) *ν* (cm^{-1}): 2122 (C=N=N), 1709 (C=O), 1630 (C=O). HRMS (ESI) calcd. for $C_{18}H_{26}N_3O_3^+$ $[M+H]^+$ *m/z* 332.1969, found 332.1971.

*4.3.16. Ethyl 3-(tert-butyl(2,4-dimethoxybenzyl)amino)-2-diazo-3-oxopropanoate **(2p)***

Yellow crystals, m.p. 54-58 °C. 91% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 – 7.03 (m, 1H, ArH), 6.47 – 6.41 (m, 2H, ArH), 4.53 (s, 2H, CH_2), 4.24 (q, *J* = 7.1 Hz, 2H, CH_2), 3.80 (s, 3H, CH_3), 3.77 (s, 3H, CH_3), 1.33 (s, 9H, $3CH_3$), 1.29 (t, *J* = 7.1

Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.7, 162.9, 160.4, 158.9, 129.9, 119.3, 103.8, 98.6, 61.1, 58.1, 55.5, 55.3, 48.3, 28.4, 14.4. IR (DCM) *v* (cm^{-1}): 2120 (C=N=N), 1708 (C=O), 1632 (C=O). HRMS (ESI) calcd. for $C_{18}H_{26}N_3O_5^+$ $[M+H]^+$ *m/z* 364.1867, found 364.1880.

4.4. General Procedure for the reaction of ethyl 3-alkyl(arylmethyl)amino-2-diazo-3-oxopropanoates 2 under the catalysis of $CuCl_2 \cdot 2H_2O$

A two-necked flask charged with 5 mol% $CuCl_2 \cdot 2H_2O$ (3.4 mg, 0.02 mmol) was added dry toluene (5 mL) under N_2 atmosphere and then the solution was heated to reflux. A solution of diazoamidoacetate **2** (0.4 mmol) in 5 mL of dry toluene was added. Upon addition, the solution was refluxed for another 4 hours. Then the internal standard 4-iodonitrobenzene was added. The solvent was removed under reduced pressure and the residue was purified by preparative TLC to afford the products **3** and **4**.

*4.4.1. Ethyl 2-benzyl-3-oxo-1,2,3,3a-tetrahydrocyclohepta[c]pyrrole-3a-carboxylate (**3a**).*[7d]

Colorless crystals, m.p. 97–100 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 – 6.22 (m, 5H, ArH), 6.54 – 6.32 (m, 3H, 3CH), 6.23 (d, *J* = 5.2 Hz, 1H, CH), 5.65 (d, *J* = 9.4 Hz, 1H, CH), 4.79 (d, *J* = 14.9 Hz, 1H in CH_2), 4.44 (d, *J* = 14.8 Hz, 1H in CH_2), 4.27 (d, *J* = 15.0 Hz, 1H in CH_2), 4.15 – 4.00 (m, 2H, CH_2), 4.00 (d, *J* = 15.0 Hz, 1H in CH_2), 1.15 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 167.7, 135.5, 130.4, 129.8, 128.7, 128.3, 128.1, 127.9, 127.8, 122.4, 120.5, 61.7, 59.9, 50.2, 46.7, 14.0.

*4.4.2. Ethyl trans-1-benzyl-4-phenylazetidin-2-one-3-carboxylate (**4a**).*[7d,14]

Colorless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.18 (m, 10H, ArH), 4.87 (d, *J* = 15.2 Hz, 1H in CH_2), 4.70 (s, 1H, CH), 4.24 (q, *J* = 7.2 Hz, 2H, CH_2), 3.91 (s, 1H, CH), 3.83 (d, *J* = 15.3 Hz, 1H in CH_2), 1.29 (t, *J* = 7.2 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 162.4, 135.9, 134.6, 129.1, 129.0, 128.7, 128.2, 127.8, 126.7, 63.4, 61.8, 57.0, 44.8, 14.1.

*4.4.3. Ethyl 2-benzyl-6-methyl-3-oxo-1,2,3,3a-tetrahydrocyclohepta[c]pyrrole-3a-carboxylate (**3ba**)*

Yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.09 (m, 5H, ArH), 6.21 (d, *J* = 6.2 Hz, 2H, 2CH), 5.65 – 5.59 (m, 2H, 2CH), 4.78 (d, *J* = 14.9 Hz, 1H in CH_2), 4.73 (d, *J* = 14.7 Hz, 1H in CH_2), 4.24 (d, *J* = 14.9 Hz, 1H in CH_2), 4.15 – 3.93 (m, 3H, CH_2 & 1H in CH_2), 2.02 (s, 3H, CH_3), 1.14 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 168.0, 139.1, 137.5, 135.5, 132.4, 131.3, 130.5, 129.8, 128.7, 128.3, 128.0, 127.9,125.3, 122.3, 120.4, 61.6, 59.9, 50.1, 46.6, 24.4, 13.9. IR (DCM) *v* (cm^{-1}): *v* = 1747 (C=O), 1698 (C=O). HRMS (ESI) calcd. for $C_{20}H_{22}NO_3^+$ $[M+H]^+$ *m/z* 324.1594, found 324.1599.

*4.4.4. Ethyl 2-(4-chlorobenzyl)-3-oxo-1,2,3,3a-tetrahydrocyclohepta[c]pyrrole-3a-carboxylate (**3bb**)*

Yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.09 (m, 4H, ArH), 6.51 – 6.37 (m, 3H, 3CH), 6.28 (d, *J* = 10.1 Hz, 1H, CH), 6.10 (d, *J* = 6.5 Hz, 1H, CH), 4.42 (d, *J* = 9.4 Hz, 1H in CH_2), 4.38 (d, *J* = 9.2 Hz, 1H in CH_2), 4.24 (d, *J* = 14.9 Hz, 1H in CH_2),4.15 – 3.93 (m, 3H, CH_2 and 1H in CH_2), 2.33 (s, 3H, CH_3), 1.14 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 168.0, 137.5, 135.5, 132.4, 129.8, 129.4, 128.2, 127.9, 127.7, 121.3, 120.2, 61.5, 59.4, 50.0, 46.4, 21.0, 13.9. IR (DCM) *v* (cm^{-1}): *v* = 1747 (C=O), 1698 (C=O). HRMS (ESI) calcd. for $C_{20}H_{22}NO_3^+$ $[M+H]^+$ *m/z* 324.1594, found 324.1599.

*4.4.5. Ethyl trans-1-benzyl-4-(4-methylphenyl)azetidin-2-one-3-carboxylate (**4ba**) and ethyl trans-1-(4-methylbenzyl)-4-phenylazetidin-2-one-3-carboxylate (**4bb**)*

4ba and **4bb** cannot be separated due to similar polarity and property. Yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.28 (m, 6H, ArH), 7.19 – 7.04 (m, 12H, ArH), 4.86 (d, *J* = 15.2 Hz, 1H in CH_2), 4.84 (d, *J* = 15.2 Hz, 1H in CH_2),4.68 (d, *J* = 2.3 Hz, 1H, CH), 4.66 (d, *J* = 2.3 Hz, 1H, CH), 4.23 (m, 4H, $2CH_2$), 3.91 – 3.87 (m, 2H, 1H in CH_2 & 1H in CH_2), 3.79 (d, *J* = 15.2 Hz, 1H in CH_2), 3.76 (d, *J* = 15.1 Hz, 1H in CH_2), 2.36 (s, 3H, CH_3), 2.33 (s, 3H, CH_3), 1.29 (t, *J* = 7.1 Hz, 6H, $2CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.9, 166.8, 162.5, 162.3, 139.0, 137.5, 136.1, 134.8, 132.9, 131.6, 129.8, 129.4, 129.1, 129.0, 128.8, 128.24, 128.21, 127.8, 126.8, 126.7, 63.5, 63.4, 61.77, 61.76, 56.9, 44.7, 44.5, 21.2, 21.1, 14.1. IR (DCM) *v* (cm^{-1}): 1764 (C=O), 1732 (C=O). HRMS (ESI) calcd. for $C_{20}H_{22}NO_3^+$ $[M+H]^+$ *m/z* 324.1594, found 324.1595.

*4.4.6. Ethyl 2-benzyl-6-chloro-3-oxo-1,2,3,3a-tetrahydrocyclohepta[c]pyrrole-3a-carboxylate (**3ca**)*

White solid, m.p. 149-151 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.23 (m, 5H, ArH), 6.61 (d, *J* = 6.9 Hz, 1H, CH), 6.44 (dd, *J* = 10.3, 1.5 Hz, 1H, CH), 6.13 (ddd, *J* = 6.8, 2.0, 2.0 Hz, 1H, CH), 5.68 (d, *J* = 10.3 Hz, 1H, CH), 4.78 (d, *J* = 14.9 Hz, 1H in CH_2), 4.43 (d, *J* = 14.8 Hz, 1H in CH_2), 4.25 (d, *J* = 15.1 Hz, 1H in CH_2), 4.18 (dq, *J* = 10.7, 7.1 Hz, 1H in CH_2), 4.05 (dq, *J* = 10.7, 7.1 Hz, 1H in CH_2), 3.97 (d, *J* = 15.1 Hz, 1H in CH_2), 1.18 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.3, 167.4, 135.3, 135.2, 131.0, 129.9, 128.8, 128.0, 127.9, 126.9, 123.8, 119.0, 62.2, 59.7, 50.1, 46.8, 13.9. IR (DCM) *v* (cm^{-1}): 1743 (C=O), 1693 (C=O). HRMS (ESI) calcd. for $C_{19}H_{19}ClNO_3^+$ $[M+H]^+$ *m/z* 344.1048, found 344.1050.

*4.4.7. Ethyl 2-(4-chlorobenzyl)-3-oxo-1,2,3,3a-tetrahydrocyclohepta[c]pyrrole-3a-carboxylate (**3cb**)*

Yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.4 Hz, 2H, ArH), 7.21 (d, *J* = 8.4 Hz, 2H, ArH), 6.53 – 6.40 (m, 3H, 3CH), 6.24 (d, *J* = 5.7 Hz, 1H, CH), 5.63 (d, *J* = 9.8 Hz, 1H, CH), 4.77 (d, *J* = 15.0 Hz, 1H in CH_2), 4.38 (d, *J* = 15.0 Hz, 1H in CH_2), 4.26 (dd, *J* = 14.9, 2.2 Hz, 1H in CH_2), 4.14 – 3.92 (m, 3H, CH_2 & 1H in CH_2), 1.15 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 167.7, 134.1, 133.7, 130.1, 130.0, 129.3, 129.0, 128.4, 128.2, 122.3, 120.7, 61.8, 59.8, 50.2, 46.1, 14.0. IR (DCM) *v* (cm^{-1}): 1747 (C=O), 1698 (C=O). HRMS (ESI) calcd. for $C_{19}H_{19}ClNO_3^+$ $[M+H]^+$ *m/z* 344.1048, found 344.1050.

*4.4.8. Ethyl trans-1-benzyl-4-(4-chlorophenyl)azetidin-2-one-3-carboxylate (**4ca**) and ethyl trans-1-(4-chlorobenzyl)-4-phenylazetidin-2-one-3-carboxylate (**4cb**)*

4ca and **4cb** cannot be separated from the copper-catalyzed reaction mixture. They cannot be separated each other and were obtained from the $Rh_2(OAc)_4$-catalyzed reaction for verifying their structures. 63% yield. Yellow oil. Major (71%): ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.23 (m, 7H, ArH), 7.11 (d, *J* = 8.4 Hz, 2H, ArH), 4.80 (d, *J* = 15.3 Hz, 1H, 1H in CH_2), 4.69 (d, *J* = 2.4 Hz, 2H, CH), 4.24 (qd, *J* = 7.1, 2.1 Hz, 1H, CH_2), 3.92 (d, *J* = 2.3 Hz, 1H, CH), 3.82 (d, *J* = 15.4 Hz, 1H, 1H in CH_2), 1.30 (t, *J* = 7.1 Hz, 3H, CH_3). Minor (29%): ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.23 (m, 7H, ArH), 7.11 (d, *J* = 8.4 Hz, 2H, ArH), 4.78 (d, *J* = 14.8 Hz, 1H, 1H in CH_2), 4.69 (d, *J* = 2.4 Hz, 2H, CH), 4.24 (qd, *J* = 7.1, 2.1 Hz, 1H, CH_2), 3.87 (d, *J* = 2.2 Hz, 1H, CH), 3.83 (d, *J* = 15.3 Hz, 1H, 1H in CH_2), 1.30 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 166.5, 162.3, 162.1, 135.7, 134.5, 133.7, 133.2, 129.8, 129.5, 129.3, 129.11, 129.09, 128.9,

128.79, 128.76, 128.2, 127.91, 127.86, 126.7, 63.5, 63.4, 61.85, 61.82, 57.1, 56.3, 50.1, 46.8, 44.9, 44.1, 14.1, 13.9. IR (DCM) ν (cm^{-1}): 1765 (C=O), 1731 (C=O). HRMS (ESI) calcd. for $C_{19}H_{19}ClNO_3^+$ $[M+H]^+$ *m/z* 344.1048, found 344.1056.

*4.4.9. Ethyl 2-methyl-3-oxo-1,2,3,3a-tetrahydrocyclohepta[c]pyrrole-3a-carboxylate (**3d**)*

Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.49 – 6.39 (m, 3H, 3CH), 6.31 (s, 1H, CH), 5.60 (d, *J* = 9.7 Hz, 1H, CH), 4.40 (d, *J* = 15.0 Hz, 1H in CH_2), 4.12 (d, *J* = 14.9 Hz, 1H in CH_2), 4.05 (q, *J* = 7.1 Hz, 2H, CH_2), 3.00 (s, 3H, CH_3), 1.14 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 168.1, 130.7, 129.8, 128.5, 127.7, 122.7, 120.4, 61.8, 52.8, 30.0, 29.7, 14.0. IR (DCM) ν (cm^{-1}): 1708 (C=O), 1650 (C=O). HRMS (ESI) calcd. for $C_{13}H_{16}NO_3^+$ $[M+H]^+$ *m/z* 234.1125, found 234.1122.

*4.4.10. Ethyl trans-1-methyl-4-phenylazetidin-2-one-3-carboxylate (**4d**).*[15]

Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.33 (m, 5H, ArH), 4.82 (d, *J* = 2.2 Hz, 1H, CH), 4.27 (q, *J* = 7.2 Hz, 1H in CH_2), 4.26 (q, *J* = 7.2 Hz, 1H in CH_2), 3.89 (d, *J* = 2.2 Hz, 1H, CH), 3.45 (s, 3H, CH_3), 1.27 (t, *J* = 7.2 Hz, 3H, CH_3).

*4.4.11. Ethyl 1-benzyl-2-oxoazetidine-3-carboxylate (**5d**)*

Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.29 (m, 5H, ArH), 4.49 (d, *J* = 15.2 Hz, 1H in CH_2), 4.42 (d, *J* = 15.2 Hz, 1H in CH_2), 4.27 (qd, *J* = 7.2, 1.7 Hz, 2H, CH_2), 4.05 (dd, *J* = 5.3, 2.6 Hz, 1H, CH), 3.49 (dd, *J* = 5.7, 2.6 Hz, 1H in CH_2), 3.29 (t, *J* = 5.5 Hz, 1H in CH_2), 1.33 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 162.3, 134.8, 128.9, 128.1, 127.9, 61.7, 54.1, 46.3, 41.7, 14.1. IR (DCM) ν (cm^{-1}): 1762 (C=O), 1721 (C=O). HRMS (ESI) calcd. for $C_{13}H_{16}NO_3^+$ $[M+H]^+$ *m/z* 234.1125, found 234.1129.

*4.4.12. Ethyl 2-propyl-3-oxo-1,2,3,3a-tetrahydrocyclohepta[c]pyrrole-3a-carboxylate (**3e**)*

Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.49 – 6.40 (m, 3H, 3CH), 6.31 (d, *J* = 4.1 Hz, 1H, CH), 5.60 (d, *J* = 9.6 Hz, 1H, CH), 4.41 (dd, *J* = 14.9, 2.3 Hz, 1H in CH_2), 4.11 (dd, *J* = 14.9, 2.3 Hz, 1H in CH_2), 4.10 – 4.00 (m, 2H, CH_2), 3.52 (dt, *J* = 14.0, 7.1 Hz, 1H in CH_2), 3.28 (dt, *J* = 14.0, 6.9 Hz, 1H in CH_2), 1.68 – 1.58 (m, 2H, CH_2), 1.14 (t, *J* = 7.1 Hz, 3H, CH_3), 0.94 (t, *J* = 7.4 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 167.9, 130.9, 129.8, 128.4, 127.8, 122.7, 120.4, 61.6, 60.0, 50.5, 44.3, 20.3, 14.0, 11.0. IR (DCM) ν (cm^{-1}): 1746 (C=O), 1705 (C=O). HRMS (ESI) calcd. for $C_{15}H_{20}NO_3^+$ $[M+H]^+$ *m/z* 262.1438, found 262.1439.

*4.4.13. Ethyl trans-1-propyl-4-phenylazetidin-2-one-3-carboxylate (**4e**)*

Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.30 (m, 5H, ArH), 4.84 (d, *J* = 2.1 Hz, 1H, CH), 4.25 (qd, *J* = 7.1, 2.5 Hz, 2H, CH_2), 3.84 (d, *J* = 2.0 Hz, 1H, CH), 3.44 (dt, *J* = 14.0, 7.3 Hz, 1H in CH_2), 2.84 (dt, *J* = 14.0, 6.7 Hz, 1H in CH_2). 1.56 – 1.47 (m, 2H, CH_2), 1.30 (t, *J* = 7.1 Hz, 3H, CH_3), 0.92 (t, *J* = 7.4 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 162.5, 136.5, 129.1, 129.0, 126.7, 63.4, 61.8, 57.3, 42.7, 20.9, 14.1, 11.4. IR (DCM) ν (cm^{-1}): 1766 (C=O), 1731 (C=O). HRMS (ESI) calcd. for $C_{15}H_{20}NO_3^+$ $[M+H]^+$ *m/z* 262.1438, found 262.1438.

*4.4.14. Ethyl trans-1-benzyl-4-ethylazetidin-2-one-3-carboxylate (**5e**)*

Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.28 (m, 5H, ArH), 4.71 (d, *J* = 15.4 Hz, 1H in CH_2), 4.23 (q, *J* = 7.1 Hz, 2H, CH_2), 4.13 (d, *J* = 15.5 Hz, 1H in CH_2), 3.71 (ddd, *J* = 8.3, 4.3, 2.4 Hz, 1H, CH), 3.63 (d, *J* = 2.1 Hz, 1H, CH), 1.78 – 1.69 (m, 1H in CH_2), 1.50 – 1.40 (m, 1H in CH_2), 1.30 (t, *J* = 7.1 Hz, 3H, CH_3), 0.88 (t, *J* = 7.4 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 162.1, 135.2, 128.8, 128.0, 127.8, 61.6, 59.0, 56.3, 44.8, 24.9, 14.1, 9.2. IR (DCM) ν (cm^{-1}): 1766 (C=O), 1737 (C=O). HRMS (ESI) calcd. for $C_{15}H_{20}NO_3^+$ $[M+H]^+$ *m/z* 262.1438, found 262.1434.

*4.4.15. Ethyl 2-isopropyl-3-oxo-1,2,3,3a-tetrahydrocyclohepta[c]pyrrole-3a-carboxylate (**3f**)*

Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.47 – 6.39 (m, 3H, 3CH), 6.32 (d, *J* = 3.8 Hz, 1H, CH), 5.60 (d, *J* = 10.3 Hz, 1H, CH), 4.48 (hept, *J* = 6.8 Hz, 1H, CH), 4.34 (dd, *J* = 14.7, 2.4 Hz, 1H in CH_2), 4.14 – 3.96 (m, 3H, 1H in CH_2 & CH_2), 1.23 (d, *J* = 6.8 Hz, 3H, CH_3), 1.19 (d, *J* = 6.8 Hz, 3H, CH_3), 1.14 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 167.9, 131.1, 129.7, 128.3, 127.8, 122.6, 120.5, 61.6, 60.5, 45.7, 43.4, 19.7, 19.5, 14.0. IR (DCM) ν (cm^{-1}): 1751 (C=O), 1698 (C=O). HRMS (ESI) calcd. for $C_{15}H_{20}NO_3^+$ $[M+H]^+$ *m/z* 262.1438, found 262.1441.

*4.4.16. Ethyl trans-1-isopropyl-4-phenylazetidin-2-one-3-carboxylate (**4f**)*

Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.36 (m, 5H, ArH), 4.84 (d, *J* = 2.3 Hz, 1H, CH), 4.30 – 4.17 (m, 2H, CH_2), 3.80 (d, *J* = 2.3 Hz, 1H, CH), 3.77 (hept, *J* = 6.8 Hz, 1H, CH), 1.30 (t, *J* = 7.1 Hz, 3H, CH_3), 1.30 (d, *J* = 6.8 Hz, 3H, CH_3), 1.04 (d, *J* = 6.7 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 162.1, 137.9, 128.4, 126.8, 126.6, 62.7, 61.7, 56.3, 45.7, 21.0, 20.3, 14.1. IR (DCM) ν (cm^{-1}): 1763 (C=O), 1729 (C=O). HRMS (ESI) calcd. for $C_{15}H_{20}NO_3^+$ $[M+H]^+$ *m/z* 262.1438, found 262.1434.

*4.4.17. Ethyl 2-tert-butyl-3-oxo-1,2,3,3a-tetrahydrocyclohepta[c]pyrrole-3a-carboxylate (**3g**)*

White solid, m.p. 80–83 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.47 – 6.39 (m, 3H, 3CH), 6.26 (dd, *J* = 4.6, 2.4 Hz, 1H, CH), 5.60 – 5.58 (m, 1H, CH), 4.46 (dd, *J* = 14.9, 2.3 Hz, 1H in CH_2), 4.24 (dd, *J* = 14.9, 1.6 Hz, 1H in CH_2), 4.11 (dq, *J* = 10.7, 7.1 Hz, 1H in CH_2), 4.00 (dq, *J* = 10.7, 7.1 Hz, 1H in CH_2), 1.46 (s, 9H, $3CH_3$), 1.15 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 168.1, 131.4, 129.6, 128.3, 127.7, 123.1, 120.1, 61.5, 61.2, 54.7, 49.5, 27.4, 14.0. IR (DCM) ν (cm^{-1}): 1746 (C=O), 1722 (C=O). HRMS (ESI) calcd. for $C_{16}H_{22}NO_3^+$ $[M+H]^+$ *m/z* 276.1594, found 276.1600.

*4.4.18. Ethyl trans-1-(tert-butyl)-4-phenylazetidin-2-one-3-carboxylate (**4g**).*[14,15]

Colorless crystals, m.p. 91–94 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.32 (m, 5H, ArH), 4.85 (d, *J* = 2.3 Hz, 1H, CH), 4.27 – 4.19 (m, 2H, CH_2), 3.69 (d, *J* = 2.2 Hz, 1H, CH), 1.29 (t, *J* = 7.6 Hz, 3H, CH_3), 1.27 (s, 9H, $3CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 162.1, 139.1, 128.9, 128.7, 126.6, 62.5, 61.6, 56.4, 55.1, 28.0, 14.1.

*4.4.19. Ethyl 2-tert-butyl-6-fluoro-3-oxo-1,2,3,3a-tetrahydrocyclohepta[c]pyrrole-3a-carboxylate (**3h**)*

Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.39 (ddd, *J* = 10.9, 9.4, 1.8 Hz, 1H, CH), 6.17 – 6.14 (m, 2H, 2CH), 5.75 (dd, *J* = 10.6, 5.1 Hz, 1H, CH), 4.44 (d, *J* = 14.9 Hz, 1H in CH_2), 4.19 (d, *J* = 15.5 Hz, 1H in CH_2), 4.17 – 4.10 (m, 1H in CH_2), 4.03 (dq, *J* = 10.7, 7.1 Hz, 1H in CH_2), 1.46 (s, 9H, $3CH_3$), 1.17 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 167.8, 161.2 (d, *J* = 245.2 Hz), 128.2 (d, *J* = 3.7 Hz), 125.6 (d, *J* = 13.7 Hz), 122.7 (d, *J* = 36.6 Hz), 116.8 (d, *J* = 11.7 Hz), 109.1 (d, *J* = 28.1

Hz), 61.9, 61.1, 54.9, 49.5, 27.4, 13.9. IR (DCM) ν (cm^{-1}): 1745 (C=O), 1701 (C=O). HRMS (ESI) calcd. for $C_{16}H_{21}FNO_3^+$ $[M+H]^+$ *m/z* 294.1500, found 294.1500.

*4.4.20. Ethyl trans-1-(tert-butyl)-4-(4-fluorophenyl)azetidin-2-one-3-carboxylate (**4h**)*

Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.35 (m, 2H, ArH), 7.07 (t, *J* = 8.6 Hz, 2H, ArH), 4.84 (d, *J* = 2.2 Hz, 1H, CH), 4.28 – 4.17 (m, 2H, CH_2), 3.66 (d, *J* = 2.3 Hz, 1H, CH), 1.30 (t, *J* = 7.1 Hz, 3H, CH_3), 1.26 (s, 9H, $3CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 162.8 (d, *J* = 248.0 Hz), 162.0, 135.0 (d, *J* = 3.3 Hz), 128.3 (d, *J* = 8.3 Hz), 116.0 (d, *J* = 21.8 Hz), 62.6, 61.8, 55.7, 55.2, 28.1, 14.1. IR (DCM) ν (cm^{-1}): 1761 (C=O), 1728 (C=O). HRMS (ESI) calcd. for $C_{16}H_{21}FNO_3^+$ $[M+H]^+$ *m/z* 294.1500, found 294.1504.

*4.4.21. Ethyl 2-tert-butyl-6-chloro-3-oxo-1,2,3,3a-tetrahydrocyclohepta[c]pyrrole-3a-carboxylate (**3i**)*

Yellow crystals, m.p. 77–80 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.61 (d, *J* = 6.9 Hz, 1H, CH), 6.40 (d, *J* = 10.3 Hz, 1H, CH), 6.16 (d, *J* = 6.9 Hz, 1H, CH), 5.63 (d, *J* = 10.3 Hz, 1H, CH), 4.44 (d, *J* = 15.1 Hz, 1H in CH_2), 4.28 – 4.12 (m, 3H, CH_2 & 1H in CH_2), 1.46 (s, 9H, $3CH_3$), 1.17 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 170.1, 166.9, 135.0, 132.0, 129.6, 126.9, 124.5, 118.6, 62.6, 61.8, 55.3, 49.4, 28.1, 14.1. IR (DCM) ν (cm^{-1}): 1700 (C=O), 1654 (C=O). HRMS (ESI) calcd. for $C_{16}H_{21}ClNO_3^+$ $[M+H]^+$ *m/z* 310.1204, found 310.1203.

*4.4.22. Ethyl trans-1-(tert-butyl)-4-(4-chlorophenyl)azetidin-2-one-3-carboxylate (**4i**).*[16]

Colorless crystals, m.p. 77–80 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.33 (m, 4H, ArH), 4.83 (d, *J* = 2.2 Hz, 1H, CH), 4.02 (dq, *J* = 10.8, 7.1 Hz, 2H, CH_2), 3.65 (d, *J* = 2.3 Hz, 1H, CH), 1.26 (m, 12H, $4CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 167.7, 162.0, 137.8, 134.6, 129.2, 128.0, 61.6, 55.7, 54.9, 49.4, 27.4, 13.9.

*4.4.23. Ethyl 2-tert-butyl-6-bromo-3-oxo-1,2,3,3a-tetrahydrocyclohepta[c]pyrrole-3a-carboxylate (**3j**)*

White crystals, m.p. 94–97 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86 (d, *J* = 6.8 Hz, 1H, CH), 6.53 (dd, *J* = 10.2, 1.0 Hz, 1H, CH), 6.12 (ddd, *J* = 6.8, 2.0, 2.0 Hz, 1H, CH), 5.54 (d, *J* = 10.2 Hz, 1H, CH), 4.42 (d, *J* = 15.3 Hz, 1H in CH_2), 4.27 – 4.14 (m, 2H, $2CH_2$), 4.03 (dq, *J* = 10.7, 7.1 Hz, 1H in CH_2), 1.47 (s, 9H, $3CH_3$), 1.20 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.0, 167.7, 132.5, 131.4, 130.6, 124.43, 124.39, 119.3, 61.9, 61.0, 54.9, 49.4, 27.4, 14.0. IR (DCM) ν (cm^{-1}): 1767 (C=O), 1733 (C=O). HRMS (ESI) calcd. for $C_{16}H_{21}BrNO_3^+$ $[M+H]^+$ *m/z* 354.0699, found 354.0702.

*4.4.24. Ethyl trans-1-(tert-butyl)-4-(4-bromophenyl)azetidin-2-one-3-carboxylate (**4j**)*

Colorless crystals, m.p. 80-82 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.50 (m, 2H, ArH), 7.32 – 7.25 (m, 2H, ArH), 4.82 (d, *J* = 2.2 Hz, 1H, CH), 4.23 (qd, *J* = 7.0, 2.8 Hz, 2H, CH_2), 3.64 (d, *J* = 2.2 Hz, 1H, CH), 1.270 (t, *J* = 7.0 Hz, 3H, CH_3), 1.266 (s, 9H, $3CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.9, 162.0, 138.4, 132.2, 128.3, 122.7, 62.4, 61.7, 55.7, 48.3, 28.0, 14.1. IR (DCM) ν (cm^{-1}): 1767 (C=O), 1733 (C=O). HRMS (ESI) calcd. for $C_{16}H_{21}BrNO_3^+$ $[M+H]^+$ *m/z* 354.0699, found 354.0702.

*4.4.25. Ethyl 2-tert-butyl-6-methyl-3-oxo-1,2,3,3a-tetrahydrocyclohepta[c]pyrrole-3a-carboxylate (**3k**)*

Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.24 (d, *J* = 10.1 Hz, 1H, CH), 6.21 (d, *J* = 6.5 Hz, 1H, CH), 6.13 (d, *J* = 6.6 Hz, 1H, CH), 5.56 (d, *J* = 10.1 Hz, 1H, CH), 4.43 (d, *J* = 14.8 Hz, 1H in CH_2), 4.20 (d, *J* = 14.7 Hz, 1H in CH_2), 4.13 (dq, *J* = 10.7, 7.1 Hz, 1H in CH_2), 3.98 (dq, *J* = 10.8, 7.1 Hz, 1H in CH_2), 2.02 (s, 3H, CH_3), 1.46 (s, 9H, $3CH_3$), 1.14 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 168.4, 138.9, 131.0, 129.2, 125.2, 122.1, 119.8, 61.4, 60.8, 54.7, 49.3, 27.4, 24.5, 14.0. IR (DCM) ν (cm^{-1}): 1762 (C=O), 1730 (C=O). HRMS (ESI) calcd. for $C_{17}H_{24}NO_3^+$ $[M+H]^+$ *m/z* 290.1751, found 290.1751.

*4.4.26. Ethyl trans-1-(tert-butyl)-4-(4-methylphenyl)azetidin-2-one-3-carboxylate (**4k**)*

Colorless crystals, m.p. 106-108 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.1 Hz, 2H, ArH), 7.18 (d, *J* = 7.9 Hz, 2H, ArH), 4.81 (d, *J* = 2.2 Hz, 1H, CH), 4.28 – 4.16 (m, 2H, CH_2), 3.67 (d, *J* = 2.2 Hz, 1H, CH), 2.36 (s, 3H, CH_3), 1.28 (t, *J* = 7.1 Hz, 3H, CH_3), 1.26 (s, 9H, $3CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2, 162.2, 138.6, 136.1, 129.6, 126.6, 62.5, 61.6, 56.3, 55.1, 28.1, 21.1, 14.1. IR (DCM) ν (cm^{-1}): 1762 (C=O), 1730 (C=O). HRMS (ESI) calcd. for $C_{17}H_{24}NO_3^+$ $[M+H]^+$ *m/z* 290.1751, found 290.1751.

*4.4.27. Ethyl 2-(tert-butyl)-6-methoxy-3-oxo-1,2,3,3a-tetrahydrocyclohepta[c]pyrrole-3a-carboxylate (**3l**)*

Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.27 (dd, *J* = 10.7, 2.1 Hz, 1H, CH), 6.13 (d, *J* = 7.2 Hz, 1H, CH), 5.73 (d, *J* = 10.6 Hz, 1H, CH), 5.61 (d, *J* = 7.1 Hz, 1H, CH), 4.42 (d, *J* = 14.1 Hz, 1H in CH_2), 4.26 – 4.09 (m, 3H, 1H in CH_2 & CH_2), 3.60 (s, 3H, CH_3), 1.45 (s, 9H, $3CH_3$), 1.15 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.3, 166.6, 159.4, 131.1, 129.8, 129.3, 127.9, 114.4, 61.9, 58.2, 55.3, 52.3, 43.4, 27.6, 14.0. IR (DCM) ν (cm^{-1}): ν = 1701 (C=O), 1654 (C=O). HRMS (ESI) calcd. for $C_{17}H_{24}NO_4^+$ $[M+H]^+$ *m/z* 306.1700, found 306.1698.

*4.4.28. Ethyl trans-1-(tert-butyl)-4-(4-methoxyphenyl)azetidin-2-one-3-carboxylate (**4l**).*[17]

Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.6 Hz, 2H, ArH), 6.90 (d, *J* = 8.6 Hz, 2H, ArH), 4.80 (d, *J* = 2.0 Hz, 1H, CH), 4.23 (qd, *J* = 7.2, 3.2 Hz, 2H, CH_2), 3.82 (s, 3H, CH_3), 3.67 (d, *J* = 2.2 Hz, 1H, CH). 1.29 (t, *J* = 7.2 Hz, 3H, CH_3), 1,26 (s, 9H, $3CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2, 162.1, 159.8, 130.9, 127.9, 114.3, 62.5, 61.6, 56.0, 55.3, 55.1, 28.1, 14.1.

*4.4.29. Ethyl 2-tert-butyl-7-chloro-3-oxo-1,2,3,3a-tetrahydrocyclohepta[c]pyrrole-3a-carboxylate (**3ma**)*

White crystals, m.p. 83–87 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.61 (d, *J* = 7.0 Hz, 1H, CH), 6.39 – 6.30 (m, 2H, 2CH), 6.27 (d, *J* = 1.9 Hz, 1H, CH), 4.46 (dd, *J* = 15.4, 2.5 Hz, 1H in CH_2), 4.23 (dd, *J* = 15.3, 2.0 Hz, 1H in CH_2), 4.15 – 4.03 (m, 2H, CH_2), 1.46 (s, 9H, $3CH_3$), 1.17 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 167.4, 133.5, 133.1, 128.1, 126.3, 123.3, 122.1, 61.8, 55.0, 53.4, 49.2, 27.4, 14.0. IR (DCM) ν (cm^{-1}): ν = 1747 (C=O), 1698 (C=O). HRMS (ESI) calcd. for $C_{16}H_{21}ClNO_3^+$ $[M+H]^+$ *m/z* 310.1204, found 310.1208.

*4.4.30. Ethyl 2-tert-butyl-4-chloro-3-oxo-1,2,3,3a-tetrahydrocyclohepta[c]pyrrole-3a-carboxylate (**3mb**)*

White crystals, m.p. 83–87 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.61 (d, *J* = 7.0 Hz, 1H, CH), 6.38 (m, 2H, 2CH), 6.27 (d, *J* = 1.9 Hz, 1H), 6.21 – 6.15 (m, 1H, CH), 5.75 (s, 1H, CH), 4.41 (dd, *J* = 15.4, 2.4 Hz, 1H in CH_2), 4.23 (dd, *J* = 15.4, 1.9 Hz, 1H in CH_2), 4.15 – 4.03 (m, 2H, CH_2), 1.45 (s, 9H, $3CH_3$), 1.17 (t, *J* = 7.1, 3.0 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 167.4,

134.3, 132.3, 130.2, 129.1, 121.1, 119.6, 61.9, 61.0, 59.7, 49.4, 27.4, 14.0. IR (DCM) ν (cm^{-1}): ν = 1747 (C=O), 1698 (C=O). HRMS (ESI) calcd. for $C_{16}H_{21}ClNO_3^+$ $[M+H]^+$ *m/z* 310.1204, found 310.1208.

*4.4.31. Ethyl trans-1-(tert-butyl)-4-(3-chlorophenyl)azetidin-2-one-3-carboxylate (**4m**)*

Yellow crystals, m.p. 74–77 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (s, 1H, ArH), 7.34 – 7.28 (m, 3H, ArH), 4.82 (d, *J* = 2.3 Hz, 1H, CH), 4.27 – 4.21 (m, 2H, CH_2), 3.66 (d, *J* = 2.3 Hz, 1H, CH), 1.30 (t, *J* = 7.2 Hz, 3H, CH_3), 1.28 (s, 9H, $3CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 161.9, 141.5, 135.0, 130.3, 128.9, 126.8, 124.6, 62.5, 61.8, 55.7, 55.3, 28.1, 14.1. IR (DCM) ν (cm^{-1}): ν = 1766 (C=O), 1731 (C=O). HRMS (ESI) calcd. for $C_{16}H_{21}ClNO_3^+$ $[M+H]^+$ *m/z* 310.1204, found 310.1209.

*4.4.32. Ethyl 2-tert-butyl-8-chloro-3-oxo-1,2,3,3a-tetrahydrocyclohepta[c]pyrrole-3a-carboxylate (**3n**)*

Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.48 – 6.36 (m, 3H, 3CH), 5.70 (d, *J* = 9.9 Hz, 1H, CH), 4.33 (d, *J* = 16.2 Hz, 1H in CH_2), 4.23 (d, *J* = 16.0 Hz, 1H in CH_2), 4.13 (dq, *J* = 10.7, 7.1 Hz, 1H in CH_2), 4.03 (dq, *J* = 10.8, 7.1 Hz, 1H in CH_2), 1.48 (s, 9H, $3CH_3$), 1.16 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.9, 162.5, 130.4, 129.6, 129.4, 127.3, 127.2, 125.8, 61.7, 55.2, 49.6, 27.9, 27.4, 14.1. IR (DCM) ν (cm^{-1}): ν = 1709 (C=O), 1659 (C=O). HRMS (ESI) calcd. for $C_{16}H_{21}ClNO_3^+$ $[M+H]^+$ *m/z* 310.1204, found 310.1206.

*4.4.33. Ethyl trans-1-(tert-butyl)-4-(3,5-dimethylphenyl)azetidin-2-one-3-carboxylate (**4o**)*

Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00 – 6.96 (m, 3H, ArH), 4.76 (d, *J* = 2.2 Hz, 1H, CH), 4.22 (qd, *J* = 7.1, 4.8 Hz, 2H, CH_2), 3.67 (d, *J* = 2.2 Hz, 1H, CH), 2.32 (s, 6H, $2CH_3$), 1.28 (t, *J* = 7.1 Hz, 3H, CH_3), 1.28(s, 9H, $3CH_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 162.2, 138.6, 134.2, 130.3, 129.1, 124.3, 123.3, 62.5, 61.6, 56.5, 48.7, 29.7, 28.1, 21.2, 14.1. IR (DCM) ν (cm^{-1}): ν = 1732 (C=O), 1716 (C=O). HRMS (ESI) calcd. for $C_{18}H_{26}NO_3^+$ $[M+H]^+$ *m/z* 304.1907, found 304.1903.

*4.4.34. Ethyl 2-(tert-butyl)-5,7-dimethyl-3-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylate (**6o**)*

Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 (s, 1H, ArH), 6.86 (s, 1H, ArH), 4.65 (s, 1H, CH), 4.63 (d, *J* = 15.8 Hz, 1H in CH_2), 4.42 (d, *J* = 15.1 Hz, 1H in CH_2), 4.11 (q, *J* = 7.1 Hz, 2H, CH_2), 2.37 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 1.53 (s, 9H, $3CH_3$), 1.22 (t, *J* = 7.1 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.8, 167.2, 137.2, 135.8, 133.3, 130.3, 127.1, 124.2, 61.5, 57.9, 54.8, 47.4, 28.2, 21.0, 18.7, 14.0. IR (DCM) ν (cm^{-1}): ν = 1735 (C=O), 1655 (C=O). HRMS (ESI) calcd. for $C_{18}H_{26}NO_3^+$ $[M+H]^+$ *m/z* 304.1907, found 304.1910.

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Supplementary Material

Copies of ^{1}H and ^{13}C NMR spectra of unknown products **1**, **2**, **3**, **4**, **5**, and **6**, copies of ^{1}H NMR spectra of some representative crude reaction mixtures. The Supplementary Material is available free of charge on http://dx. doi: 10.1021/xxxxxx.

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