

Supporting Information

Palladium-Catalyzed Direct *ortho*-C–H Ethoxycarboxylation of Anilides at Room Temperature

*Yumin Huang, Gaocan Li, Jingsheng Huang, and Jingsong You**

Key Laboratory of Green Chemistry and Technology of Ministry of Education,
College of Chemistry, and State Key Laboratory of Biotherapy, West China Hospital,
West China Medical School, Sichuan University, 29 Wangjiang Road, Chengdu
610064, PR China. Fax: 86-28-85412203; E-mail: jsyou@scu.edu.cn

Table of contents

I. General Remarks	S1
II. Optimization of the coupling reaction of acetanilide 1a with DEAD	S1
III. General procedure for the reaction.....	S5
IV. Procedure for preparation of palladacycle 4	S5
V. Procedure for reaction using stoichiometric palladacycle 4.....	S6
VI. Procedure for esterification of acetanilide using palladacycle 4 as the catalyst....	S6
VII. Characterization of compounds 3a-3r	S7
VIII. References	S19
IX. ¹H and ¹³C NMR spectra of compounds 3a-3r, 4	S20

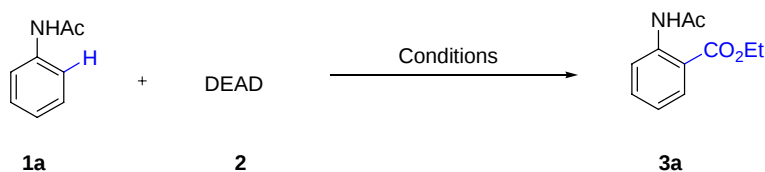
I. General Remarks

NMR spectra were obtained on a Bruker AMX-400. The ^1H NMR (400 MHz) chemical shifts were measured using CDCl_3 or $\text{DMSO}-d_6$ as the internal reference (CDCl_3 : $\delta = 7.26$ ppm; $\text{DMSO}-d_6$: $\delta = 2.50$ ppm). The ^{13}C NMR (100 MHz) chemical shifts are given using CDCl_3 or $\text{DMSO}-d_6$ as the internal standard (CDCl_3 : $\delta = 77.16$ ppm; $\text{DMSO}-d_6$: $\delta = 39.52$ ppm). High-resolution mass spectra (HR-MS) were obtained with a Waters-Q-TOF-Premier (ESI). Melting points were determined with XRC-1 and are uncorrected.

Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. Acetanilide substrates were prepared according to the literature procedure.¹ Unless otherwise indicated, all reactions were carried out under air atmosphere.

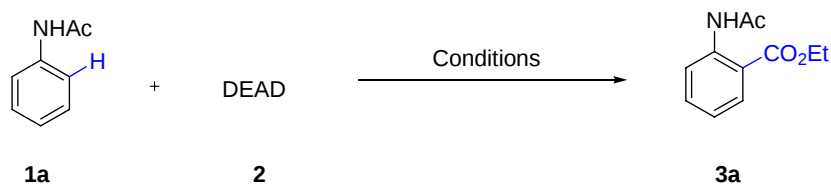
II. Optimization of the coupling reaction of acetanilide 1a with DEAD

Table S1 Screening of oxidants^a



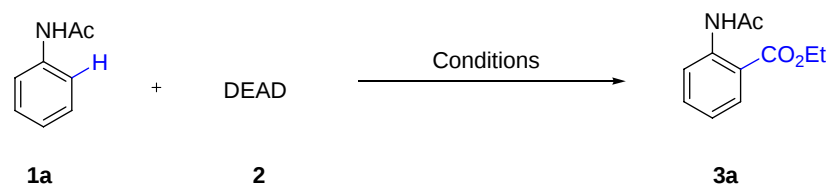
Entry	Oxidant	Yield ^b (%)
1	Oxone	n. d.
2	IBX	n. d.
3	CAN	n. d.
4	TBHP	n. d.
5	$\text{Cu}(\text{OAc})_2$	n. d.
6	$\text{PhI}(\text{OAc})_2$	n. d.
7	$\text{Na}_2\text{S}_2\text{O}_8$	n. d.
8	$\text{K}_2\text{S}_2\text{O}_8$	n. d.
9	BQ	n. d.
10	$(\text{NH}_4)_2\text{S}_2\text{O}_8$	28%

^a Reactions were carried out by using acetanilide (0.3 mmol), DEAD (2.5 equiv), $\text{Pd}(\text{OAc})_2$ (10 mol%), oxidant (2.0 equiv), $p\text{-TsOH}\cdot\text{H}_2\text{O}$ (0.5 equiv) in DCM (1 mL) for 24 h at rt. ^b Isolated yield.

Table S2 Influence of the amount of DEAD^a

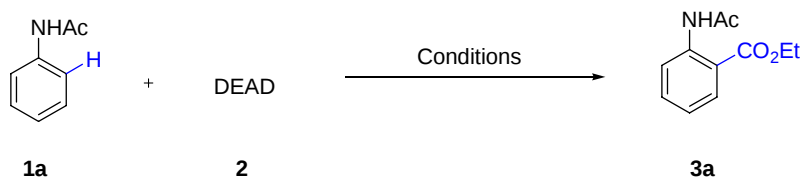
Entry	DEAD (equiv)	Yield ^b (%)
1	2.5	28%
2	3	34%
3	4	34%

^a Reactions were carried out by using acetanilide (0.3 mmol), DEAD, Pd(OAc)₂ (10 mol%), (NH₄)₂S₂O₈ (2.0 equiv), *p*-TsOH·H₂O (0.5 equiv) in DCM (1 mL) for 24 h at rt. ^b Isolated yield.

Table S3 Screening of additives^a

Entry	Additive	Yield ^b (%)
1	-	trace
2	<i>p</i> -TsOH·H ₂ O (0.5 equiv)	34%
3	<i>p</i> -TsOH·H ₂ O (1.0 equiv)	26%
4	CH ₃ SO ₃ H (0.5 equiv)	13%
5	TfOH (0.5 equiv)	27%

^a Reactions were carried out by using acetanilide (0.3 mmol), DEAD (3.0 equiv), Pd(OAc)₂ (10 mol%), (NH₄)₂S₂O₈ (2.0 equiv), additive in DCM (1 mL) for 24 h at rt. ^b Isolated yield.

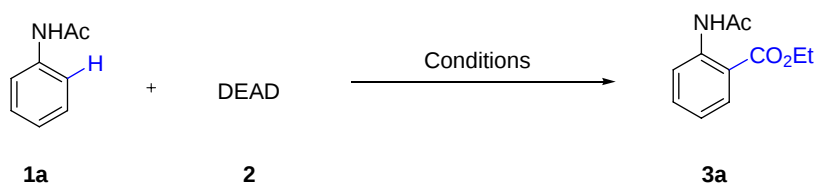
Table S4 Screening of solvents^a

Entry	Solvent	Yield ^b (%)
1	DCM	34%

2	dioxane	29%
3	THF	21%
4	DCE	16%
5	DME	trace
6	DMF	n. d.
7	MeCN	n. d.
8	DMSO	n. d.
9	TFA	n. d.

^a Reactions were carried out by using acetanilide (0.3 mmol), DEAD (3.0 equiv), Pd(OAc)₂ (10 mol%), (NH₄)₂S₂O₈ (2.0 equiv), *p*-TsOH·H₂O (0.5 equiv) in Solvent (1 mL) for 24 h at rt. ^b Isolated yield.

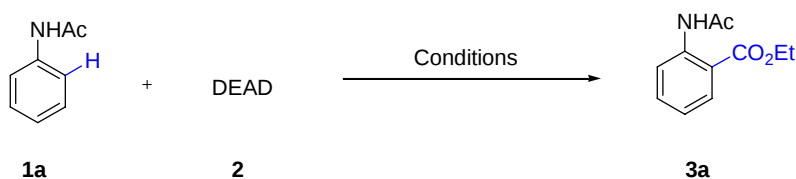
Table S5 Effect of copper salts^a



Entry	Cu salt	Yield ^b (%)
1	CuI	n. d.
2	CuBr	24%
3	CuCl	n. d.
4	Cu(OAc) ₂ ·H ₂ O	37%
5	Cu(OTf) ₂	37%
6	Cu(TFA) ₂ ·H ₂ O	43%
7	CuCl ₂	23%
8	CuBr ₂	40%
9	-	34%

^a Reactions were carried out by using acetanilide (0.3 mmol), DEAD (3.0 equiv), Pd(OAc)₂ (10 mol%), Cu salt (10 mol%), (NH₄)₂S₂O₈ (2.0 equiv), *p*-TsOH·H₂O (0.5 eq) in DCM (1 mL) for 24 h at rt. ^b Isolated yield.

Table S6 Screening of Pd sources^a



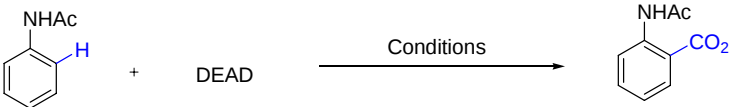
Entry	Pd	Yield ^b (%)
1	Pd(OAc) ₂	34%

2 ^c	Pd(OAc) ₂	32%
3	Pd(TFA) ₂	48%
4	PdCl ₂	n. d.
5	Pd(PhCN) ₂ Cl ₂	trace
6	Pd(PPh ₃) ₂ Cl ₂	n. d.
7	Pd(acac) ₂	39%
8	Pd(cod)Cl ₂	n. d.

^a Reactions were carried out by using acetanilide (0.3 mmol), DEAD (3.0 equiv), Pd (10 mol%), (NH₄)₂S₂O₈ (2.0 equiv), *p*-TsOH·H₂O (0.5 eq) in DCM (1 mL) for 24 h at rt. ^b Isolated yield.

^c Pd (20 mol%).

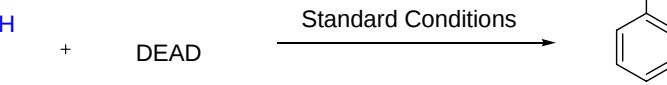
Table S7 Further optimization of C–H esterification^a



Entry	Pd	Cu	Yield (%) ^b
1	-	Cu(TFA) ₂ ·H ₂ O	n. d.
2	Pd(TFA) ₂	-	48%
3	Pd(TFA) ₂	Cu(TFA) ₂ ·H ₂ O	68%
4 ^c	Pd(TFA) ₂	Cu(TFA) ₂ ·H ₂ O	66%

^a Reactions were carried out by using acetanilide (0.3 mmol), DEAD (3.0 equiv), Pd(TFA)₂ (10 mol%), Cu(TFA)₂·H₂O (10 mol%), (NH₄)₂S₂O₈ (2.0 equiv), *p*-TsOH·H₂O (0.5 equiv) in DCM (1 mL) at rt. ^b Isolated yield. ^c 48 h.

Table S8 Effect of radical scavengers^a



Reaction scheme showing the conversion of **1a** (acetanilide) to **3a** (ethyl 2-acetamidobenzoate) using DEAD under Standard Conditions.

Entry	Inhibitor	Yield (%) ^b
1	3.0 equiv TEMPO	n. d.
2	3.0 equiv hydroquinone	n. d.
3	50 mol% BHT	trace

^a Reactions were carried out by using acetanilide (0.3 mmol), DEAD (3.0 equiv), Pd(TFA)₂ (10 mol%), Cu(TFA)₂·H₂O (10 mol%), (NH₄)₂S₂O₈ (2.0 equiv), *p*-TsOH·H₂O (0.5 equiv) in DCM (1 mL) at rt. ^b Isolated yield.

Table S9 Screening of different directing groups^a



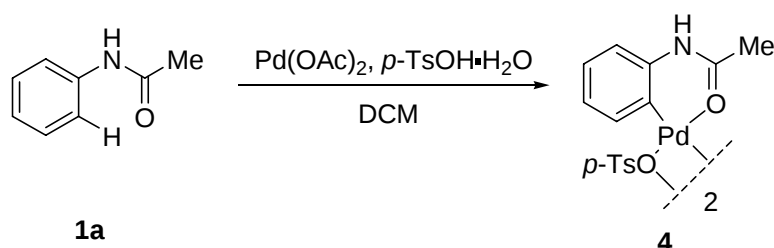
Entry	Direacting group (DG)	Yield (%) ^b
1	COOEt	n. d.
2	CHO	n. d.
3	Ac	83%
4	COEt	84%
5	Piv	73%
6	Ts	n. d.
7	CONMe ₂	trace

^a Reactions were carried out by using acetanilide (0.3 mmol), DEAD (3.0 equiv), Pd(TFA)₂ (10 mol%), Cu(TFA)₂·H₂O (10 mol%), (NH₄)₂S₂O₈ (2.0 equiv), *p*-TsOH·H₂O (0.5 equiv) in DCM (1 mL) at rt. ^b Isolated yield.

III. General procedure for the reaction

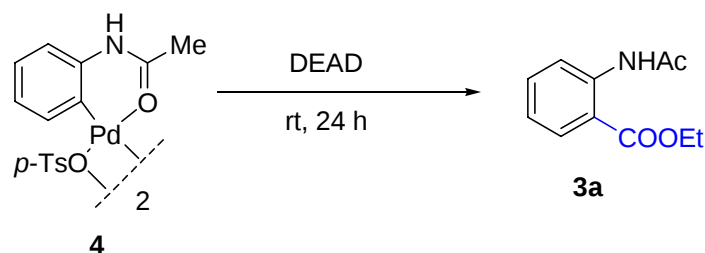
A Schlenk tube with a magnetic stir bar was charged with Pd(TFA)₂ or Pd(OAc)₂, (NH₄)₂S₂O₈ (136.9 mg, 0.6 mmol) or Selectfluor (212.6 mg, 0.6 mmol), acetanilide (0.3 mmol), Cu(TFA)₂·H₂O (8.7 mg, 0.03 mmol), *p*-TsOH·H₂O (28.5 mg, 0.15 mmol) and DCM (1 mL). After the reaction mixture was stirred for 1 min at room temperature, DEAD (156.7 mg, 0.9 mmol) was added. The resulting mixture was stirred at 25 °C for indicated time. The solvent was evaporated and the residue was diluted with 30 mL CH₂Cl₂, filtered through a Celite pad, and washed with CH₂Cl₂ (10-20 mL). The combined organic phases were concentrated and the resulting residue was purified by column chromatography on silica gel to provide the desired product.

IV. Procedure for preparation of palladacycle 4²



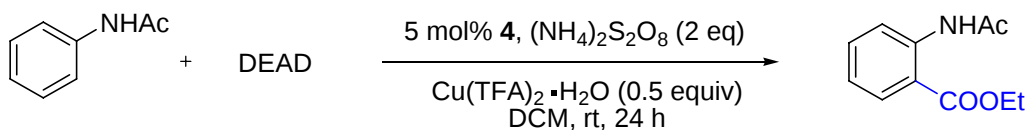
A solution of acetanilide (27 mg, 0.2 mmol), *p*-TsOH·H₂O (38 mg, 0.2 mmol) and Pd(OAc)₂ (45 mg, 0.2 mmol) in DCM was heated at 40 °C for 1 min. The mixture was filtered and dried under vacuum to afford the complex **4** as a pale green solid, which was existed as a dimer (82 mg, 99%). ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.28 (s, 3H), 2.40 (s, 3H), 7.00-7.06 (m, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 7.17-7.21 (m, 1H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 8.0 Hz, 1H), 12.02 (s, 1H) ppm. ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 20.8, 21.2, 117.5, 120.6, 124.8, 125.5, 126.6, 128.1, 131.7, 134.4, 137.7, 145.7, 168.4 ppm. Anal. calcd. for C₃₀H₃₀N₂O₈Pd₂S₂·H₂O: C 42.82, H 3.83, N 3.33; Found: C 42.97, H 3.39, N 2.84.

V. Procedure for reaction using stoichiometric palladacycle **4**



A Schlenk tube with a magnetic stir bar was charged with **4** (123.5 mg, 0.15 mmol), (NH₄)₂S₂O₈ (136.9 mg, 0.6 mmol), Cu(TFA)₂·H₂O (8.7 mg, 0.03 mmol) and DCM (1 mL). After the reaction mixture was stirred for 1 min at room temperature, DEAD (156.7 mg, 0.9 mmol) was added. The resulting mixture was stirred at 25 °C for 24 h. Purification via silica gel column chromatography (petroleum ether/ EtOAc = 7/1-5/1, v/v) afforded the desired product as a white solid (30 mg, 48% yield).

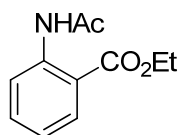
VI. Procedure for esterification of acetanilide using palladacycle **4** as the catalyst



A Schlenk tube with a magnetic stir bar was charged with **4** (12.3 mg, 0.015 mmol),

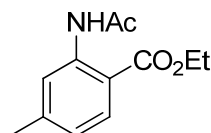
(NH₄)₂S₂O₈ (136.9 mg, 0.6 mmol), *N*-phenylacetamide (40.5 mg, 0.3 mmol), Cu(TFA)₂·H₂O (8.7 mg, 0.03 mmol), *p*-TsOH·H₂O (28.5 mg, 0.15 mmol) and DCM (1 mL). After the reaction mixture was stirred for 1 min at room temperature, DEAD (156.7 mg, 0.9 mmol) was added. Purification via silica gel column chromatography (petroleum ether/ EtOAc = 7/1-5/1, v/v) afforded the desired product as a white solid (39 mg, 63% yield).

VII. Characterization of compounds 3a-3s



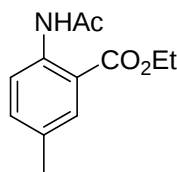
Ethyl 2-acetamidobenzoate (3a)

A Schlenk tube with a magnetic stir bar was charged with Pd(TFA)₂ (10.0 mg, 0.03 mmol), (NH₄)₂S₂O₈ (136.9 mg, 0.6 mmol), *N*-phenylacetamide (40.5 mg, 0.3 mmol), Cu(TFA)₂·H₂O (8.7 mg, 0.03 mmol), *p*-TsOH·H₂O (28.5 mg, 0.15 mmol) and DCM (1 mL). After the reaction mixture was stirred for 1 min at room temperature, DEAD (156.7 mg, 0.9 mmol) was added. The resulting mixture was stirred at 25 °C for 24 h. Purification via silica gel column chromatography (petroleum ether/ EtOAc = 7/1-5/1, v/v) afforded the desired product as a white solid (42 mg, 68% yield). M.p.: 58-61 °C; ¹H NMR (400 MHz, CDCl₃): δ = 1.42 (t, *J* = 7.2 Hz, 3H), 2.24 (s, 3H), 4.38 (q, *J* = 7.2 Hz, 2H), 7.07 (t, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 8.69 (d, *J* = 8.4 Hz, 1H), 11.10 (s, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 14.3, 25.6, 61.5, 115.2, 120.4, 122.5, 130.9, 134.7, 141.8, 168.5, 169.2 ppm. HRMS (ESI⁺): calcd for C₁₁H₁₃NNaO₃ [M+Na]⁺ 230.0793, found 230.0797.



Ethyl 2-acetamido-4-methylbenzoate (3b)

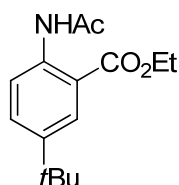
A Schlenk tube with a magnetic stir bar was charged with Pd(OAc)₂ (6.7 mg, 0.03 mmol), Selectfluor (212.6 mg, 0.6 mmol), *N-m*-tolylacetamide (44.7 mg, 0.3 mmol), Cu(TFA)₂·H₂O (8.7 mg, 0.03 mmol), *p*-TsOH·H₂O (28.5 mg, 0.15 mmol) and DCM (1 mL). After the reaction mixture was stirred for 1 min at room temperature, DEAD (156.7 mg, 0.9 mmol) was added. The resulting mixture was stirred at 25 °C for 48 h. Purification via silica gel column chromatography (petroleum ether/ EtOAc = 7/1-5/1, v/v) afforded the desired product as a white solid (38 mg, 57% yield). M.p.: 70-72 °C; ¹H NMR (400 MHz, CDCl₃): δ = 1.40 (t, *J* = 7.2 Hz, 3H), 2.22 (s, 3H), 2.38 (s, 3H), 4.35 (q, *J* = 7.2 Hz, 2H), 6.87 (d, *J* = 8.0 Hz, 1H), 7.91 (d, *J* = 8.4 Hz, 1H), 8.53 (s, 1H), 11.10 (s, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 14.3, 22.2, 25.6, 61.3, 112.6, 120.7, 123.5, 130.8, 141.7, 145.9, 168.5, 169.2 ppm. HRMS (ESI⁺): calcd for C₁₂H₁₅NNaO₃ [M+Na]⁺ 244.0950, found 244.0950.



Ethyl 2-acetamido-5-methylbenzoate (3c)

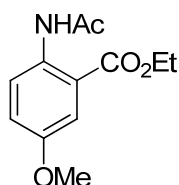
A Schlenk tube with a magnetic stir bar was charged with Pd(TFA)₂ (10.0 mg, 0.03 mmol), (NH₄)₂S₂O₈ (136.9 mg, 0.6 mmol), *N-p*-tolylacetamide (44.7 mg, 0.3 mmol), Cu(TFA)₂·H₂O (8.7 mg, 0.03 mmol), *p*-TsOH·H₂O (28.5 mg, 0.15 mmol) and DCM (1 mL). After the reaction mixture was stirred for 1 min at room temperature, DEAD (156.7 mg, 0.9 mmol) was added. The resulting mixture was stirred at 25 °C for 24 h. Purification via silica gel column chromatography (petroleum ether/ EtOAc = 7/1-5/1, v/v) afforded the desired product as a white solid (55 mg, 83% yield). M.p.: 98-100 °C; ¹H NMR (400 MHz, CDCl₃): δ = 1.42 (t, *J* = 7.2 Hz, 3H), 2.21 (s, 3H), 2.32 (s, 3H), 4.36 (q, *J* = 7.2 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.82 (s, 1H), 8.57 (d, *J* = 8.8 Hz, 1H), 10.98 (s, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 14.3, 20.8, 25.6, 61.4,

115.1, 120.4, 130.9, 132.0, 135.4, 139.3, 168.5, 169.0 ppm. HRMS (ESI⁺): calcd for C₁₂H₁₅NNaO₃ [M+Na]⁺ 244.0950, found 244.0953.



Ethyl 2-acetamido-5-*tert*-butylbenzoate (3d)

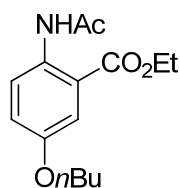
A Schlenk tube with a magnetic stir bar was charged with Pd(TFA)₂ (10.0 mg, 0.03 mmol), (NH₄)₂S₂O₈ (136.9 mg, 0.6 mmol), *N*-(4-*tert*-butylphenyl)acetamide (57.4 mg, 0.3 mmol), Cu(TFA)₂·H₂O (8.7 mg, 0.03 mmol), *p*-TsOH·H₂O (28.5 mg, 0.15 mmol) and DCM (1 mL). After the reaction mixture was stirred for 1 min at room temperature, DEAD (156.7 mg, 0.9 mmol) was added. The resulting mixture was stirred at 25 °C for 24 h. Purification via silica gel column chromatography (petroleum ether/ EtOAc = 7/1-5/1, v/v) afforded the desired product as a white solid (58 mg, 73% yield). M.p.: 88-89 °C; ¹H NMR (400 MHz, CDCl₃): δ = 1.31 (s, 9H), 1.43 (t, *J* = 7.2 Hz, 3H), 2.22 (s, 3H), 4.39 (q, *J* = 7.2 Hz, 2H), 7.57 (dd, *J* = 2.4 Hz, 8.8 Hz, 1H), 8.02 (d, *J* = 2.4 Hz, 1H), 8.59 (d, *J* = 8.8 Hz, 1H), 10.98 (s, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 14.4, 25.6, 31.3, 34.4, 61.4, 114.9, 120.4, 127.2, 131.9, 139.2, 145.4, 168.6, 169.1 ppm. HRMS (ESI⁺): calcd for C₁₅H₂₁NNaO₃ [M+Na]⁺ 286.1419, found 286.1422.



Ethyl 2-acetamido-5-methoxybenzoate (3e)

A Schlenk tube with a magnetic stir bar was charged with Pd(OAc)₂ (6.7 mg, 0.03

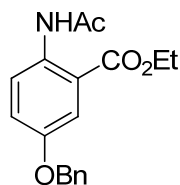
mmol), $(\text{NH}_4)_2\text{S}_2\text{O}_8$ (136.9 mg, 0.6 mmol), *N*-(4-methoxyphenyl)acetamide (49.6 mg, 0.3 mmol), $\text{Cu}(\text{TFA})_2 \cdot \text{H}_2\text{O}$ (8.7 mg, 0.03 mmol), *p*-TsOH $\cdot\text{H}_2\text{O}$ (28.5 mg, 0.15 mmol) and DCM (1 mL). After the reaction mixture was stirred for 1 min at room temperature, DEAD (156.7 mg, 0.9 mmol) was added. The resulting mixture was stirred at 25 °C for 48 h. Purification via silica gel column chromatography (petroleum ether/ EtOAc = 7/1-5/1, v/v) afforded the desired product as a white solid (44 mg, 62% yield). M.p.: 88-91 °C; ^1H NMR (400 MHz, CDCl_3): δ = 1.41 (t, J = 7.2 Hz, 3H), 2.21 (s, 3H), 3.81 (s, 3H), 4.38 (q, J = 7.2 Hz, 2H), 7.11 (dd, J = 2.8 Hz, 9.2 Hz, 1H), 7.52 (d, J = 2.8 Hz, 1H), 8.61 (d, J = 9.2 Hz, 1H), 10.80 (s, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 14.3, 25.4, 55.7, 61.6, 114.9, 116.2, 120.6, 121.9, 135.3, 154.4, 168.0, 168.7 ppm. HRMS (ESI $^+$): calcd for $\text{C}_{12}\text{H}_{15}\text{NNaO}_4$ $[\text{M}+\text{Na}]^+$ 260.0899, found 260.0897.



Ethyl 2-acetamido-5-butoxybenzoate (3f)

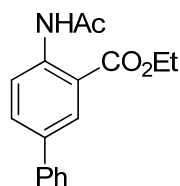
A Schlenk tube with a magnetic stir bar was charged with $\text{Pd}(\text{OAc})_2$ (6.7 mg, 0.03 mmol), $(\text{NH}_4)_2\text{S}_2\text{O}_8$ (136.9 mg, 0.6 mmol), *N*-(4-butoxyphenyl)acetamide (62.2 mg, 0.3 mmol), $\text{Cu}(\text{TFA})_2 \cdot \text{H}_2\text{O}$ (8.7 mg, 0.03 mmol), *p*-TsOH $\cdot\text{H}_2\text{O}$ (28.5 mg, 0.15 mmol) and DCM (1 mL). After the reaction mixture was stirred for 1 min at room temperature, DEAD (156.7 mg, 0.9 mmol) was added. The resulting mixture was stirred at 25 °C for 48 h. Purification via silica gel column chromatography (petroleum ether/ EtOAc = 7/1-5/1, v/v) afforded the desired product as a white solid (50 mg, 60% yield). M.p.: 68-70 °C; ^1H NMR (400 MHz, CDCl_3): δ = 0.97 (t, J = 7.6 Hz, 3H), 1.41 (t, J = 7.2 Hz, 3H), 1.46-1.52 (m, 2H), 1.74-1.77 (m, 2H), 2.20 (s, 3H), 3.95 (t, J = 6.4 Hz, 2H), 4.37 (q, J = 7.2 Hz, 2H), 7.09 (dd, J = 2.8 Hz, 9.2 Hz, 1H), 7.51 (d, J = 2.8 Hz, 1H), 8.59 (d, J = 9.2 Hz, 1H), 10.80 (s, 1H) ppm. ^{13}C NMR (100 MHz,

CDCl₃): δ = 14.0, 14.3, 19.3, 25.5, 31.4, 61.6, 68.2, 115.8, 116.3, 121.1, 121.9, 135.2, 154.0, 168.1, 168.8 ppm. HRMS (ESI⁺): calcd for C₁₅H₂₁NNaO₄ [M+Na]⁺ 302.1368, found 302.1373.



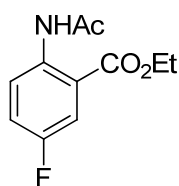
Ethyl 2-acetamido-5-(benzyloxy)benzoate (3g)

A Schlenk tube with a magnetic stir bar was charged with Pd(OAc)₂ (6.7 mg, 0.03 mmol), (NH₄)₂S₂O₈ (136.9 mg, 0.6 mmol), *N*-(4-(benzyloxy)phenyl)acetamide (72.4 mg, 0.3 mmol), Cu(TFA)₂·H₂O (8.7 mg, 0.03 mmol), *p*-TsOH·H₂O (28.5 mg, 0.15 mmol) and DCM (1 mL). After the reaction mixture was stirred for 1 min at room temperature, DEAD (156.7 mg, 0.9 mmol) was added. The resulting mixture was stirred at 25 °C for 48 h. Purification via silica gel column chromatography (petroleum ether/ EtOAc = 7/1-5/1, v/v) afforded the desired product as a white solid (49 mg, 52% yield). M.p.: 88-90 °C; ¹H NMR (400 MHz, CDCl₃): δ = 1.41 (t, *J* = 7.2 Hz, 3H), 2.21 (s, 3H), 4.37 (q, *J* = 7.2 Hz, 2H), 5.06 (s, 2H), 7.17 (dd, *J* = 2.8 Hz, 8.8 Hz, 1H), 7.33-7.44 (m, 5H), 7.62 (d, *J* = 2.8 Hz, 1H), 8.61 (d, *J* = 9.2 Hz, 1H), 10.82 (s, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 14.3, 25.5, 61.6, 70.6, 116.3, 116.4, 121.4, 122.0, 127.7, 128.3, 128.8, 135.6, 136.7, 153.6, 168.0, 168.8 ppm. HRMS (ESI⁺): calcd for C₁₈H₁₉NNaO₄ [M+Na]⁺ 336.1212, found 336.1208.



Ethyl 4-acetamidobiphenyl-3-carboxylate (3h)

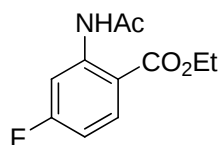
A Schlenk tube with a magnetic stir bar was charged with Pd(TFA)₂ (10.0 mg, 0.03 mmol), Selectfluor (212.6 mg, 0.6 mmol), *N*-(biphenyl-4-yl)acetamide (63.4 mg, 0.3 mmol), Cu(TFA)₂·H₂O (8.7 mg, 0.03 mmol), *p*-TsOH·H₂O (28.5 mg, 0.15 mmol) and DCM (1 mL). After the reaction mixture was stirred for 1 min at room temperature, DEAD (156.7 mg, 0.9 mmol) was added. The resulting mixture was stirred at 25 °C for 24 h. Purification via silica gel column chromatography (petroleum ether/ EtOAc = 7/1-5/1, v/v) afforded the desired product as a white solid (56 mg, 66% yield). M.p.: 116-118 °C; ¹H NMR (400 MHz, CDCl₃): δ = 1.44 (t, *J* = 7.2 Hz, 3H), 2.26 (s, 3H), 4.42 (q, *J* = 7.2 Hz, 2H), 7.34-7.38 (m, 1H), 7.44-7.47 (m, 2H), 7.57-7.60 (m, 2H), 7.77 (dd, *J* = 2.0 Hz, 8.8 Hz, 1H), 8.26 (d, *J* = 2.4 Hz, 1H), 8.78 (d, *J* = 8.8 Hz, 1H), 11.12 (s, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 14.4, 25.7, 61.7, 115.5, 120.9, 126.9, 127.6, 129.0, 129.2, 133.2, 135.4, 139.8, 140.9, 168.4, 169.2 ppm. HRMS (ESI⁺): calcd for C₁₇H₁₇NNaO₃ [M+Na]⁺ 306.1106, found 306.1106.



Ethyl 2-acetamido-5-fluorobenzoate (3i)

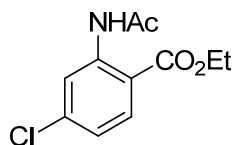
A Schlenk tube with a magnetic stir bar was charged with Pd(OAc)₂ (6.7 mg, 0.03 mmol), Selectfluor (212.6 mg, 0.6 mmol), *N*-(4-fluorophenyl)acetamide (45.9 mg, 0.3 mmol), Cu(TFA)₂·H₂O (8.7 mg, 0.03 mmol), *p*-TsOH·H₂O (28.5 mg, 0.15 mmol) and DCM (1 mL). After the reaction mixture was stirred for 1 min at room temperature, DEAD (156.7 mg, 0.9 mmol) was added. The resulting mixture was stirred at 25 °C for 24 h. Pd(OAc)₂ (3.4 mg, 0.015 mmol) was then added, and the reaction mixture was stirred for another 24 h. Purification via silica gel column chromatography (petroleum ether/ EtOAc = 7/1-5/1, v/v) afforded the desired product as a white solid (30 mg, 44% yield). M.p.: 83-84 °C; ¹H NMR (400 MHz, CDCl₃): δ = 1.43 (t, *J* = 7.2 Hz, 3H), 2.23 (s, 3H), 4.39 (q, *J* = 7.2 Hz, 2H), 7.25-7.28 (m, 1H), 7.71 (dd, *J* = 3.2

Hz, 9.2 Hz, 1H), 8.71 (dd, $J = 5.2$ Hz, 9.2 Hz, 1H), 10.94 (s, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 14.3, 25.5, 62.0, 116.8, 117.0, 121.6, 121.8, 122.2, 122.3, 138.1, 156.1, 158.5, 167.42, 167.44, 169.1$ ppm. HRMS (ESI^+): calcd for $\text{C}_{11}\text{H}_{12}\text{FNNaO}_3$ $[\text{M}+\text{Na}]^+$ 248.0699, found 248.0701.



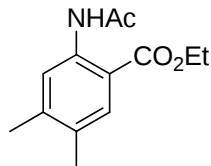
Ethyl 2-acetamido-4-fluorobenzoate (3j)

A Schlenk tube with a magnetic stir bar was charged with $\text{Pd}(\text{TFA})_2$ (10.0 mg, 0.03 mmol), Selectfluor (212.6 mg, 0.6 mmol), *N*-(3-fluorophenyl)acetamide (45.9 mg, 0.3 mmol), $\text{Cu}(\text{TFA})_2 \cdot \text{H}_2\text{O}$ (8.7 mg, 0.03 mmol), *p*-TsOH $\cdot$ H_2O (28.5 mg, 0.15 mmol) and DCM (1 mL). After the reaction mixture was stirred for 1 min at room temperature, DEAD (156.7 mg, 0.9 mmol) was added. The resulting mixture was stirred at 25 °C for 24 h. $\text{Pd}(\text{TFA})_2$ (5.0 mg, 0.015 mmol) was then added, and the reaction mixture was stirred for another 24 h. Purification via silica gel column chromatography (petroleum ether/ EtOAc = 7/1-5/1, v/v) afforded the desired product as a white solid (34 mg, 50% yield). M.p.: 76-78 °C; ^1H NMR (400 MHz, CDCl_3): $\delta = 1.41$ (t, $J = 7.2$ Hz, 3H), 2.24 (s, 3H), 4.37 (q, $J = 7.2$ Hz, 2H), 6.73-6.77 (m, 1H), 8.03-8.07 (m, 1H), 8.52 (d, $J = 12.0$ Hz, 1H), 11.26 (s, 1H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 14.3, 25.7, 61.6, 107.3, 107.6, 109.7, 109.9, 111.3, 133.1, 133.2, 143.8, 144.0, 165.1, 167.6, 167.8, 169.4$ ppm. HRMS (ESI^+): calcd for $\text{C}_{11}\text{H}_{12}\text{FNNaO}_3$ $[\text{M}+\text{Na}]^+$ 248.0699, found 248.0700.



Ethyl 2-acetamido-4-chlorobenzoate (3k)

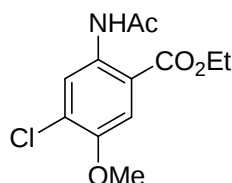
A Schlenk tube with a magnetic stir bar was charged with Pd(OAc)₂ (6.7 mg, 0.03 mmol), Selectfluor (212.6 mg, 0.6 mmol), *N*-(3-chlorophenyl)acetamide (50.9 mg, 0.3 mmol), Cu(TFA)₂·H₂O (8.7 mg, 0.03 mmol), *p*-TsOH·H₂O (28.5 mg, 0.15 mmol) and DCM (1 mL). After the reaction mixture was stirred for 1 min at room temperature, DEAD (156.7 mg, 0.9 mmol) was added. The resulting mixture was stirred at 25 °C for 24 h. Pd(OAc)₂ (3.4 mg, 0.015 mmol) was then added, and the reaction mixture was stirred for another 24 h. Purification via silica gel column chromatography (petroleum ether/ EtOAc = 7/1-5/1, v/v) afforded the desired product as a white solid (35 mg, 48% yield). M.p.: 68-70 °C; ¹H NMR (400 MHz, CDCl₃): δ = 1.41 (t, *J* = 7.2 Hz, 3H), 2.23 (s, 3H), 4.37 (q, *J* = 7.2 Hz, 2H), 7.04 (d, *J* = 8.8 Hz, 1H), 7.96 (d, *J* = 8.8 Hz, 1H), 8.81 (s, 1H), 11.15 (s, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 14.3, 25.6, 61.8, 113.3, 120.3, 122.8, 132.0, 141.0, 142.6, 167.9, 169.3 ppm. HRMS (ESI⁺): calcd for C₁₁H₁₂ClNNaO₃ [M+Na]⁺ 264.0403, found 264.0402.



Ethyl 2-acetamido-4,5-dimethylbenzoate (3l)

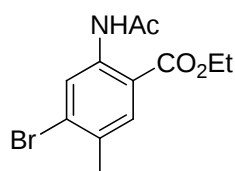
A Schlenk tube with a magnetic stir bar was charged with Pd(TFA)₂ (10.0 mg, 0.03 mmol), (NH₄)₂S₂O₈ (136.9 mg, 0.6 mmol), *N*-(3,4-dimethylphenyl)acetamide (49.0 mg, 0.3 mmol), Cu(TFA)₂·H₂O (8.7 mg, 0.03 mmol), *p*-TsOH·H₂O (28.5 mg, 0.15 mmol) and DCM (1 mL). After the reaction mixture was stirred for 1 min at room temperature, DEAD (156.7 mg, 0.9 mmol) was added. The resulting mixture was stirred at 25 °C for 24 h. Purification via silica gel column chromatography (petroleum ether/ EtOAc = 7/1-5/1, v/v) afforded the desired product as a white solid (53 mg, 75% yield). M.p.: 108-110 °C; ¹H NMR (400 MHz, CDCl₃): δ = 1.41 (t, *J* = 7.2 Hz, 3H), 2.21 (s, 3H), 2.23 (s, 3H), 2.30 (s, 3H), 4.35 (q, *J* = 7.2 Hz, 2H), 7.76 (s, 1H), 8.48 (s, 1H), 10.96 (s, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 14.4, 19.2, 20.6,

25.6, 61.2, 112.8, 121.3, 130.9, 131.3, 139.6, 144.5, 168.6, 169.0 ppm. HRMS (ESI⁺): calcd for C₁₃H₁₇NNaO₃ [M+Na]⁺ 258.1106, found 258.1110.



Ethyl 2-acetamido-4-chloro-5-methoxybenzoate (3m)

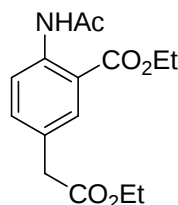
A Schlenk tube with a magnetic stir bar was charged with Pd(OAc)₂ (6.7 mg, 0.03 mmol), Selectfluor (212.6 mg, 0.6 mmol), *N*-(3-chloro-4-methoxyphenyl)acetamide (59.9 mg, 0.3 mmol), Cu(TFA)₂·H₂O (8.7 mg, 0.03 mmol), *p*-TsOH·H₂O (28.5 mg, 0.15 mmol) and DCM (1 mL). After the reaction mixture was stirred for 1 min at room temperature, DEAD (156.7 mg, 0.9 mmol) was added. The resulting mixture was stirred at 25 °C for 24 h. Pd(OAc)₂ (3.4 mg, 0.015 mmol) was then added, and the reaction mixture was stirred for another 24 h. Purification via silica gel column chromatography (petroleum ether/ EtOAc = 7/1-5/1, v/v) afforded the desired product as a white solid (43 mg, 53% yield). M.p.: 119-121 °C; ¹H NMR (400 MHz, CDCl₃): δ = 1.43 (t, *J* = 7.2 Hz, 3H), 2.21 (s, 3H), 3.90 (s, 3H), 4.40 (q, *J* = 7.2 Hz, 2H), 7.51 (s, 1H), 8.83 (s, 1H), 10.88 (s, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 14.4, 25.5, 56.5, 61.9, 112.9, 114.2, 122.5, 129.6, 135.9, 150.0, 167.6, 168.9 ppm. HRMS (ESI⁺): calcd for C₁₂H₁₄ClNNaO₄ [M+Na]⁺ 294.0509, found 294.0508.



Ethyl 2-acetamido-4-bromo-5-methylbenzoate (3n)

A Schlenk tube with a magnetic stir bar was charged with Pd(TFA)₂ (10.0 mg, 0.03

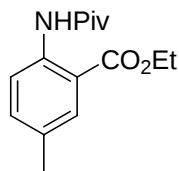
mmol), Selectfluor (212.6 mg, 0.6 mmol), *N*-(3-bromo-4-methylphenyl)acetamide (68.4 mg, 0.3 mmol), Cu(TFA)₂·H₂O (8.7 mg, 0.03 mmol), *p*-TsOH·H₂O (28.5 mg, 0.15 mmol) and DCM (1 mL). After the reaction mixture was stirred for 1 min at room temperature, DEAD (156.7 mg, 0.9 mmol) was added. The resulting mixture was stirred at 25 °C for 24 h. Pd(TFA)₂ (5.0 mg, 0.015 mmol) was then added, and the reaction mixture was stirred for another 24 h. Purification via silica gel column chromatography (petroleum ether/ EtOAc = 7/1-5/1, v/v) afforded the desired product as a white solid (38 mg, 42% yield). M.p.: 108-111 °C; ¹H NMR (400 MHz, CDCl₃): δ = 1.42 (t, *J* = 7.2 Hz, 3H), 2.22 (s, 3H), 2.37 (s, 3H), 4.37 (q, *J* = 7.2 Hz, 2H), 7.85 (s, 1H), 8.97 (s, 1H), 10.98 (s, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 14.3, 22.4, 25.6, 61.7, 114.1, 124.0, 131.9, 132.0, 132.1, 140.0, 168.0, 169.0 ppm. HRMS (ESI⁺): calcd for C₁₂H₁₄BrNNaO₃ [M+Na]⁺ 322.0055, found 322.0057.



Ethyl 2-acetamido-5-(2-ethoxy-2-oxoethyl)benzoate (3o)

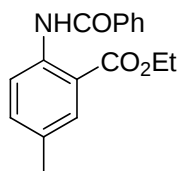
A Schlenk tube with a magnetic stir bar was charged with Pd(TFA)₂ (10.0 mg, 0.03 mmol), Selectfluor (212.6 mg, 0.6 mmol), ethyl 2-(4-acetamidophenyl)acetate (66.4 mg, 0.3 mmol), Cu(TFA)₂·H₂O (8.7 mg, 0.03 mmol), *p*-TsOH·H₂O (28.5 mg, 0.15 mmol) and DCM (1 mL). After the reaction mixture was stirred for 1 min at room temperature, DEAD (156.7 mg, 0.9 mmol) was added. The resulting mixture was stirred at 25 °C for 24 h. Purification via silica gel column chromatography (petroleum ether/ EtOAc = 7/1-5/1, v/v) afforded the desired product as colorless oil (55 mg, 62% yield). ¹H NMR (400 MHz, CDCl₃): δ = 1.24 (t, *J* = 7.2 Hz, 3H), 1.40 (t, *J* = 7.2 Hz, 3H), 2.21 (s, 3H), 3.58 (s, 2H), 4.14 (q, *J* = 7.2 Hz, 2H), 4.36 (q, *J* = 7.2 Hz, 2H), 7.44 (dd, *J* = 2.4 Hz, 8.8 Hz, 1H), 7.94 (d, *J* = 2.4 Hz, 1H), 8.65 (d, *J* = 8.8 Hz, 1H), 11.05 (s, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 14.27, 14.31, 25.6, 40.6, 61.1, 61.6,

115.2, 120.6, 128.2, 131.4, 135.5, 140.7, 168.2, 169.1, 171.4 ppm. HRMS (ESI⁺): calcd for C₁₅H₁₉NNaO₅ [M+Na]⁺ 316.1161., found 316.1167.



Ethyl 5-methyl-2-pivalamidobenzoate (3p)

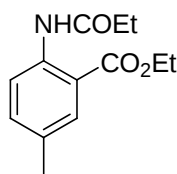
A Schlenk tube with a magnetic stir bar was charged with Pd(TFA)₂ (10.0 mg, 0.03 mmol), (NH₄)₂S₂O₈ (136.9 mg, 0.6 mmol), *N*-*p*-tolylpivalamide (57.4 mg, 0.3 mmol), Cu(TFA)₂·H₂O (8.7 mg, 0.03 mmol), *p*-TsOH·H₂O (28.5 mg, 0.15 mmol) and DCM (1 mL). After the reaction mixture was stirred for 1 min at room temperature, DEAD (156.7 mg, 0.9 mmol) was added. The resulting mixture was stirred at 25 °C for 24 h. Purification via silica gel column chromatography (petroleum ether/ EtOAc = 7/1-5/1, v/v) afforded the desired product as a white solid (58 mg, 73% yield). M.p.: 103-105 °C; ¹H NMR (400 MHz, CDCl₃): δ = 1.34 (s, 9H), 1.42 (t, *J* = 7.2 Hz, 3H), 2.33 (s, 3H), 4.38 (q, *J* = 7.2 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.84 (s, 1H), 8.66 (d, *J* = 8.4 Hz, 1H), 11.24 (s, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 14.4, 20.8, 27.7, 40.4, 61.4, 115.2, 120.4, 130.9, 131.7, 135.4, 139.7, 168.6, 177.9 ppm. HRMS (ESI⁺): calcd for C₁₅H₂₁NNaO₃ [M+Na]⁺ 286.1419, found 286.1417.



Ethyl 2-benzamido-5-methylbenzoate (3q)

A Schlenk tube with a magnetic stir bar was charged with Pd(TFA)₂ (10.0 mg, 0.03 mmol), (NH₄)₂S₂O₈ (136.9 mg, 0.6 mmol), *N*-*p*-tolylbenzamide (63.4 mg, 0.3 mmol),

Cu(TFA)₂·H₂O (8.7 mg, 0.03 mmol), *p*-TsOH·H₂O (28.5 mg, 0.15 mmol) and DCM (1 mL). After the reaction mixture was stirred for 1 min at room temperature, DEAD (156.7 mg, 0.9 mmol) was added. The resulting mixture was stirred at 25 °C for 24 h. Purification via silica gel column chromatography (petroleum ether/ EtOAc = 7/1-5/1, v/v) afforded the desired product as a white solid (61 mg, 72% yield). M.p.: 103-105 °C; ¹H NMR (400 MHz, CDCl₃): δ = 1.44 (t, *J* = 7.2 Hz, 3H), 2.37 (s, 3H), 4.42 (q, *J* = 7.2 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 1H), 7.52-7.55 (m, 3H), 7.90 (s, 1H), 8.05 (d, *J* = 7.2 Hz, 2H), 8.82 (d, *J* = 8.4 Hz, 1H), 11.99 (s, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 14.4, 20.9, 61.6, 115.5, 120.5, 127.5, 128.9, 131.1, 131.9, 132.3, 135.1, 135.6, 139.6, 165.7, 168.8 ppm. HRMS (ESI⁺): calcd for C₁₇H₁₇NNaO₃ [M+Na]⁺ 306.1106, found 306.1105.



Ethyl 5-methyl-2-propionamidobenzoate (3r)

A Schlenk tube with a magnetic stir bar was charged with Pd(TFA)₂ (10.0 mg, 0.03 mmol), (NH₄)₂S₂O₈ (136.9 mg, 0.6 mmol), *N*-*p*-tolylpropionamide (49.0 mg, 0.3 mmol), Cu(TFA)₂·H₂O (8.7 mg, 0.03 mmol), *p*-TsOH·H₂O (28.5 mg, 0.15 mmol) and DCM (1 mL). After the reaction mixture was stirred for 1 min at room temperature, DEAD (156.7 mg, 0.9 mmol) was added. The resulting mixture was stirred at 25 °C for 24 h. Purification via silica gel column chromatography (petroleum ether/ EtOAc = 7/1-5/1, v/v) afforded the desired product as a white solid (59 mg, 84% yield). M.p.: 71-73 °C; ¹H NMR (400 MHz, CDCl₃): δ = 1.26 (t, *J* = 7.6 Hz, 3H), 1.41 (t, *J* = 7.2 Hz, 3H), 2.32 (s, 3H), 2.46 (q, *J* = 7.6 Hz, 2H), 4.36 (q, *J* = 7.2 Hz, 2H), 7.34 (d, *J* = 7.6 Hz, 1H), 7.82 (s, 1H), 8.61 (d, *J* = 8.8 Hz, 1H), 11.00 (s, 1H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 9.8, 14.3, 20.8, 31.8, 61.4, 115.0, 120.4, 130.9, 131.8, 135.4, 139.4, 168.5, 172.8 ppm. HRMS (ESI⁺): calcd for C₁₃H₁₇NNaO₃ [M+Na]⁺ 258.1106, found

258.1105.

VIII. References

- (1) B. S. Kim, C. Jang, D. J. Lee and S. W. Youn, *Chem. Asian. J.*, 2010, **5**, 2336.
- (2) R. Giri, J. K. Lam and J.-Q. Yu, *J. Am. Chem. Soc.*, 2010, **132**, 686.

IX. ¹H and ¹³C NMR spectra of compounds 3a-3r, 4

