Electronic Supplementary Information

Metal-Free Oxidative Decarbonylative Coupling of Aromatic

Aldehydes with Arenes: Direct Access to Biaryls

Ren-Jin Tang^{*a*}, Qing He^{*b*}, and Luo Yang^{**a*}

a Key Laboratory for Environmentally Friendly Chemistry and Application of the Ministry of Educati on, College of Chemistry, Xiangtan University, Hunan, 411105, China Fax: +86-731-58292251; Tel: +86-731-58298351;E-mail: yangluo@xtu.edu.cn

b Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences, Beijing, 100190, China

Table of Contents

1.	General information	S1-S2
2.	General experimental procedures	S2
3.	Detailed optimization of the reaction conditions	S2-S4
4.	The preliminary competition reaction	S4-S5
5.	Experimental data for the ODC mechanism	S5-S6
6.	Kinetic isotope effect experiment	S6-S7
7.	DFT calculations	S7-S14
8.	Characterization data of products 3a-o, 4a-m, 5-7	S15-S24
9.	Copies of ¹ H and ¹³ C NMR spectra of 3a-o, 4a-m, 5-7	S25-S86

1. General information

Thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 precoated plates (0.25 mm) or Sorbent Silica Gel 60 F254 plates. The developed chromatography was analyzed by UV lamp (254 nm). High-resolution mass spectra (HRMS) were obtained from a JEOL JMS-700 instrument (ESI). Melting points are uncorrected. Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance 400 spectrometer at ambient temperature. Chemical shifts for ¹H NMR spectra are reported in parts per million (ppm) from tetramethylsilane with the solvent resonance as the internal standard (chloroform: δ 7.26 ppm). Chemical shifts for ¹³C NMR spectra are reported in parts per million (ppm) from tetramethylsilane with the solvent as the internal standard (CDCl₃: δ 77.16 ppm). Data are reported as following: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, m = multiplet, br = broad signal), coupling constant (Hz), and integration.

Reagents: Unless otherwise noted, all commercially available compounds were used as provided without further purification. Dry solvents: 1,2-dichloroethane, acetonitrile were dried by CaH_2 ; benzene and dioxane were dried by sodium metal using benzophenone as the indicator.

2. General experimental procedures

A general experimental procedure is described as following:

An oven-dried reaction vessel was charged with 1,2-dinitrobenzene (0.2 mmol, 33.6 mg), *p*-methoxycarbonyl benzaldehyde (**1a**, 0.2 mmol, 32.8 mg), benzene (1.5 mL), and TBP (2.5 equiv, 0.5 mmol, 94 μ L) under argon. The vessel was sealed and heated at 150 °C (oil bath temperature) for 12 h. The resulting mixture was cooled to room temperature, transferred to silica gel column directly and eluted with petroleum ether and ethyl acetate (30:1) to give products **3a** (28.8 mg, 68 % yield).

3. Detailed optimization of the reaction conditions



~~

	Ar-CHO + H - $(140 \circ C, 12 h)$ 1a , Ar = p MeO ₂ C-C ₆ H ₄	Ar
Entry	Additive (equiv)	Yield (%) ^[b]
1		<2%
2	Nitrobenzene (2.0)	22
3	4-Nitrobenzoic acid (2.0)	38
4	4-Nitrobenzoyl chloride (2.0)	54
5	Nitromethane (2.0)	trace
6	Sodium nitrite (2.0)	trace
7	4-Nitroaniline (2.0)	trace
8	1,2-Dinitrobenzene (2.0)	60
9	1,3-Dinitrobenzene (2.0)	56
10	1,4-Dinitrobenzene (2.0)	48
11	1,2-Dinitrobenzene (1.5)	62
12	1,2-Dinitrobenzene (1.0)	64
13	1,2-Dinitrobenzene (0.2)	38

^[a] Reaction conditions: **1a** (0.2 mmol), TBP (0.5 mmol) and additive in benzene (1.5 mL) for 12 h at 140°C under argon atmosphere. ^[b] Isolated yields.

Table S2. Optimization of the oxidants^[a]



Entry	Oxidant (equiv)	Yield (%) ^[b]
1	TBP (2.5)	64
2	TBHP (2.5)	63
3	O_2	< 2%
4	Ag ₂ CO ₃ (2.5)	n.d.
5	Cu(OAc) ₂ (2.5)	n.d.
6	$PhI(OAc)_2(2.5)$	n.d.
7	Fe(acac) ₂ (0.05)+TBP(2.5)	trace ^[c]
8	CuCl ₂ (0.05)+TBP(2.5)	trace ^[c]
9	Ni(COD) ₂ (0.05)+TBP(2.5)	trace ^[c]
10	TBP (2.0)	57
11	TBP (3.0)	60

^[a] Reaction conditions: **1a** (0.2 mmol), oxidant/additive in benzene (1.5 mL) for 12 h at 140°C under argon atmosphere. ^[b] Isolated yields. n.d. = not detected. ^[c] tert-butyl methyl terephthalate was the main product.

	Ar-CHO + H- (O) Additive, [O] 140 °C, 12 h Ar-	
Entry	Solvent (mL)	Yield $(\%)^{[b]}$
1	Benzene (1.5)	64
2	Benzene (0.75)+1,2-dichloroethane (0.75)	43
3	Benzene (0.75)+dioxane (0.75)	trace
4	Benzene (0.75)+acetonitrile (0.75)	35
5	Benzene (0.75)+dimethyl sulfoxide (0.75)	n.d.
6	Benzene (0.75)+dimethylformamide (0.75)	n.d.
7	Benzene (1.0)	57
8	Benzene (2.0)	65

Table S3. Optimization of the solvents^[a]

^[a] Reaction conditions: **1a** (0.2 mmol), TBP (0.5 mmol) and DNB (0.2 mmol) in solvent for 12 h at 140°C under argon atmosphere. ^[b] Isolated yields. n.d. = not detected.

Table S4. Optimization of the temperature^[a]

	Ar-CHO + H - $(-)$ 1a , Ar = p MeO ₂ C-C ₆ H ₄	-CO Additive, [O] 140 °C, 12 h 3a
Entry	Temperature (°C)	Yield (%) ^[b]
1	130	55
2	140	64
3	150	68
4	160	67

^[a] Reaction conditions: **1a** (0.2 mmol), TBP (0.5 mmol) and DNB (0.2 mmol) in benzene (1.5 mL) for 12 h at given temperature under argon atmosphere. ^[b] Isolated yields.

4. The preliminary competition reactions

			1.0 equiv DNB	
	n- ^t Bu-C-H-CHO		2.5 equiv TBP	p^{t} Bu-CoHa-Ph + p -CEo-CoHa-Ph
(a)	<i>p</i> Bu 0 ₆ n ₄ 0no	p 01 3 061 401 10	benzene	
	1I , 0.1 mmol	1d , 0.1 mmol	150 °C, 2 h	3I : 3d = 1.1 : 1.0

Experimental procedures:

An oven-dried reaction vessel was charged with 1,2-dinitrobenzene (0.2 mmol, 1 equiv), 4-*tert*-butyl benzaldehyde (0.1 mmol, 0.5 equiv), 4-trifluoromethyl benzaldehyde (0.1 mmol, 0.5 equiv), benzene (1.5 mL) and TBP (0.5 mmol, 2.5 equiv) under argon. The vessel was sealed and heated at 150 % (oil bath temperature) for 2 h. The work up procedure was the same as model reaction.

The ratio of product **3l** to **3d** was **1.1:1.0**, determined by the ¹H NMR. **NMR spectrum of products 3l/3d:**



-1.372

Experimental procedures:

An oven-dried reaction vessel was charged with 1,2-dinitrobenzene (0.2 mmol, 1.0 equiv), aromatic aldehyde (**11**, 0.2 mmol, 1.0 equiv), benzene (40 equiv), p-(CF₃)₂-C₆H₄ (40 equiv) and TBP (0.5 mmol, 2.5 equiv) under argon. The vessel was sealed and heated at 150 °C (oil bath temperature) for 2 h. The work up procedure was the same as model reaction.

The ratio of product **3l** to **4o** was **1.2:1.0**, determined by the ¹H NMR. This result suggests that the aldehydes and arenes with different electron densities showed comparable reaction rate.

NMR spectrum of products 31/40:



5. Experimental data for the reaction mechanism

To further understand this metal free oxidative decarbonylative coupling of aromatic aldehydes with arenes, we tested such a transformation in the presence of various radical scavengers. We found that, 1) in the presence of TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl, 1.0 equiv), the ODC reaction still led to 41% yield of product **3a** (scheme **3a**), thus a chain radical mechanism should be excluded; 2) in the presence of 2.0 equivalent of 1,1-diphenylethylene, the product methyl 4-(2,2-diphenylvinyl)benzoate **5** was detected in 3% yield (equation 2), which further strongly supports the generation of aryl radical during the reaction.



6. Kinetic isotope effect experiment

$$\begin{array}{r} \textbf{Ar-CHO} + \textbf{C}_{6}\textbf{H}_{6} + \textbf{C}_{6}\textbf{D}_{6} & \underbrace{\begin{array}{c} 1.0 \text{ equiv DNB} \\ 2.5 \text{ equiv TBP} \\ 40 \text{ equiv 40 equiv} & 150 \ ^{\circ}\textbf{C}, \ \textbf{2} \ \textbf{h} \end{array}}_{\textbf{Ar} - \textbf{C}_{6}\textbf{H}_{5} + \textbf{Ar} - \textbf{C}_{6}\textbf{D}_{5} \\ \textbf{Ar} = 4 - \textbf{Bu}^{t} - \textbf{C}_{6}\textbf{H}_{4}, \qquad \textbf{3I-H} : \textbf{3I-D} = 1.4 : 1.0, 37 \ \% \text{ total yield} \end{array}$$

 $\zeta^{1.370}_{1.366}$

Experimental procedures:

h1-2014-06-13

An oven-dried reaction vessel was charged with 1,2-dinitrobenzene (0.2 mmol, 1equiv), aromatic aldehyde (**1l**, 0.2 mmol, 1equiv), benzene (0.75 mL), benzene-D⁶ (0.75 mL) and TBP (0.5 mmol, 2.5 equiv) under argon. The vessel was sealed and heated at 150 $^{\circ}$ C (oil bath temperature) for 2 h. The work up procedure was the same as model reaction.

The ratio of product **3l-H** to **3l-D** was **1.4:1.0**, determined by the ¹H NMR. This result suggested that the benzene C-H bond cleavage step was not the rate-determining step.

NMR spectrum of products 31-H /31-D:

77.586 77.587 77.587 77.587 77.484 77.449 77.449 77.449 77.449 77.449 77.508 77.7325 77.73577 77.73577777777777777777777777	-1.373
--	--------



7. DFT calculations

(1) Full authorship of Gaussian 09:

Gaussian 09, Revision A.01,

M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria,

M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci,

G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian,

A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada,

M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima,

Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr.,

J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers,

K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand,

K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi,

M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross,

V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann,

O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski,

R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth,

P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels,O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski,and D. J. Fox, Gaussian, Inc., Wallingford CT, 2009.

(2) Free energy reaction profiles for the metal-free ODC

B3LYP/6-31+G (d) basis set was used for geometry optimizations and solvation corrections were computed with an integral equation formalism-polarizable continuum model (IEF-PCM) for benzene at 298K. Harmonic frequency calculations were performed for all stationary points to determine a local minima or transition structures. The transition state showed **only one** imaginary vibration, which were further confirmed by IRC analysis of Gaussian.

The mechanism of this ODC of benzaldehyde (1j) with chlorobenzene (2m) was studied using calculations at the B3LYP/6-31+G (d) level of theory. Single-point solvation corrections were computed with a integral equation formalism-polarizable continuum model (IEF-PCM) for chlorobenzene.



Figure 1. Free energy profiles for the proposed mechanism of this ODC. Calculated at the B3LYP/6-31+G (d) basis with IEF-PCM solvation corrections for chlorobenzene at 298K.

	ΔG ^{act} TS1	∆G ^{act} _{TS2}	∆G ^{act} _{TS3}	∆G ^{act} _{SET}	∆G ^{act} _{TS4}
Activation Energy	12.4	26.5	17.9	35.7	0.9
(kcal/mol)					

As shown in **Figure 1**, acyl radical **I** is generated through transition state **TS1** by the direct aldehyde hydrogen abstraction of benzaldehyde (**1j**) by *tert*-butyl radical with an activation energy of 12.4 kcal/mol. The subsequent decarbonylation and addition to benzene through **TS2** and **TS3** afford phenyl radical **II** and phenylcyclohexadienyl radical **III**. These two steps require an activation energy of 26.5 and 17.9 kcal/mol, respectively.

The DFT calculation on the details of SET step was complicated. The phenylcyclohexadienyl cation **IV** is 35.7 Kcal/mol higher in free energy than the radical **III**. The activation energies for SET are often close to the reaction free energies using Marcus theory, thus the activation barrier of SET is roughly estimated as $\Delta G^{act}_{SET} \approx 35.7$ Kcal/mol. By comparing ΔG^{act}_{SET} with the energy barriers of transition states (**TS1-TS4**) obtained by DFT calculation, the rate-determine step might be the SET step. The low KIE value (1.41) obtained from the competition reaction between C₆H₆ and C₆D₆ with aldehyde **11** further confirmed the deprotonation was not the rate-determine step.

(3) Absolute Calculation Energies, Enthalpies and Free Energies (Hartree)

Geometry	E (elec)	H (in benzene)	G (in benzene)
PhCHO	-345.594463	-345.477170	-345.515051
^t BuO•	-233.020808	-232.890813	-232.927838
TS1	-578.609246	-578.365003	-578.423038
^t BuOH	-233.688138	-233.544889	-233.581591
$PhCO \bullet (I)$	-344.941217	-344.836333	-344.874894
TS2	-344.891335	-344.789798	-344.832628
$Ph\bullet$ (II)	-231.574202	-231.481482	-231.514877
СО	-113.317919	-113.309608	-113.332050
chlorobenzene	-691.857491	-691.760017	-691.796279
TS3	-923.420991	-923.230302	-923.282721
radical III	-923.462566	-923.271027	-923.319113
DNB	-641.268964	-641.153453	-641.200348
DNB ^{•-}	-641.402551	-641.289635	-641.336013
cation IV	-923.277564	-923.083200	-923.132882
^t BuO-	-233.162914	-233.034233	-233.070088
V	-1156.500739	-1156.176007	-1156.242639
TS4	-1156.497074	-1156.174447	-1156.241219
Ph-C ₆ H ₄ -Cl ^p	-922.922897	-922.739820	-922.787762

(4) Geometries for all the optimized transition states



TS1:			
С	3.12056	0.58964	-1.26924
С	2.88717	-0.24899	0.00014
Н	2.94392	-0.01792	-2.16415
Н	2.44459	1.45182	-1.29741
Н	4.14956	0.96717	-1.30467
С	3.11857	0.58669	1.27184
С	3.82058	-1.48104	-0.00053
Н	2.94076	-0.02301	2.16505
Н	4.14743	0.96435	1.30963
Н	2.44238	1.44866	1.30107
Н	4.86561	-1.1488	0.00099
Н	3.64826	-2.09626	0.88892
Н	3.6501	-2.09393	-0.89195

0	1.5789	-0.81122	-0.00152
С	-2.958	-1.68849	-0.00038
С	-1.70616	-1.07208	-0.00065
С	-1.6216	0.3307	-0.0003
С	-2.79155	1.11588	0.00033
С	-4.03581	0.49247	0.00061
С	-4.11881	-0.90782	0.00025
Н	-3.02902	-2.7722	-0.00065
Н	-0.79664	-1.66478	-0.00113
Н	-2.71067	2.19858	0.0006
Н	-4.94213	1.09129	0.0011
Н	-5.09308	-1.38905	0.00047
С	-0.29744	0.97462	-0.0006
0	-0.05541	2.15868	-0.00043
Н	0.64593	0.15503	-0.00108



TS2:

С	3.12056	0.58964	-1.26924
С	2.88717	-0.24899	0.00014
Н	2.94392	-0.01792	-2.16415
Н	2.44459	1.45182	-1.29741
Н	4.14956	0.96717	-1.30467
С	3.11857	0.58669	1.27184
С	3.82058	-1.48104	-0.00053
Н	2.94076	-0.02301	2.16505
Н	4.14743	0.96435	1.30963
Н	2.44238	1.44866	1.30107
Н	4.86561	-1.1488	0.00099
Н	3.64826	-2.09626	0.88892
Н	3.6501	-2.09393	-0.89195
0	1.5789	-0.81122	-0.00152
С	-2.958	-1.68849	-0.00038
С	-1.70616	-1.07208	-0.00065
С	-1.6216	0.3307	-0.0003
С	-2.79155	1.11588	0.00033
С	-4.03581	0.49247	0.00061

С	-4.11881	-0.90782	0.00025
Н	-3.02902	-2.7722	-0.00065
Н	-0.79664	-1.66478	-0.00113
Н	-2.71067	2.19858	0.0006
Н	-4.94213	1.09129	0.0011
Н	-5.09308	-1.38905	0.00047
С	-0.29744	0.97462	-0.0006
0	-0.05541	2.15868	-0.00043
Н	0.64593	0.15503	-0.00108



TS3: С 2.37017 1.52452 -0.03422 С 0.00992 3.46238 0.64687 С 3.25502 -0.73739 0.0441 С 1.94736 -1.2539 0.03214 С 0.89092 -0.014 -0.35694 С 1.06019 1.01829 -0.04818 С -1.18897 -1.18728 -0.0199 С -1.7162 -0.70933 1.21189 С 1.22748 -2.62011 0.34828 С -3.07504 0.91172 0.02198 С -2.63216 0.38809 -1.20346 С -1.72825 -0.66951 -1.23175 Η 2.53497 2.60006-0.06036 Η 4.47481 1.0426 0.01988 Η 4.10475 -1.41709 0.0782Η 1.78428 -2.33034 0.05828 Η 0.20658 1.69288 -0.08429 Η -0.68586 -2.1498 -0.03784 Η -1.38092 -1.15444 2.145 Η -2.99179 0.73042 2.17593 -3.78574 1.73399 0.03993 Η -3.01188 0.7981 -2.13595

-1.40101

H H

-2.1808

-1.08676



IV:			
С	3.02089500	1.62317000	-0.00028100
С	4.14419500	0.78988500	-0.00022600
С	3.98167900	-0.59796800	0.00000000
С	2.69926500	-1.15520000	0.00017600
С	1.57609900	-0.32113700	0.00012400
С	1.73782700	1.07132800	-0.00011200
С	0.15462300	-0.91941800	0.00028600
С	-0.59495000	-0.64269800	1.24942900
С	-1.89157900	-0.21184100	1.24653900
С	-2.53623600	-0.00294600	-0.00001500
С	-1.89152800	-0.21251600	-1.24642700
С	-0.59490100	-0.64337400	-1.24903100
Н	3.14079600	2.70286100	-0.00046200
Н	5.14127600	1.22095800	-0.00036600
Н	4.84993900	-1.25080400	0.00003400
Н	2.58039500	-2.23585600	0.00033800
Н	0.86932000	1.72601300	-0.00016700
Н	0.29812100	-2.02261400	0.00058400
Н	-0.07841700	-0.81148500	2.19005600
Н	-2.43089300	-0.02182400	2.16776200
Н	-2.43081100	-0.02301200	-2.16777400
Н	-0.07833600	-0.81267500	-2.18954600
Cl	-4.15845500	0.52145400	-0.00019000



V:

V:				
С	4.30945000	-1.32668000	-0.18777000	
С	4.85935000	-0.04810900	-0.31456300	
С	4.02676200	1.07362100	-0.23223900	
С	2.65664800	0.91398400	-0.01652800	
С	2.09564400	-0.36710900	0.11247300	
С	2.93464100	-1.48515900	0.02100200	
С	0.60184700	-0.49808600	0.38432800	
С	-0.31533500	-0.21915500	-0.77981100	
С	-1.42148100	-1.09548600	-1.02890200	
С	-1.74831100	-2.05105800	-0.10303200	
С	-0.96637000	-2.30618100	1.07797500	
С	0.18510400	-1.61857900	1.26336000	
Н	4.94821500	-2.20403000	-0.25220700	
Н	5.92758200	0.07396000	-0.47427400	
Н	4.44590000	2.07249600	-0.32499100	
Н	2.01055700	1.78455700	0.06283200	
Н	2.51588800	-2.48437800	0.11639500	
Н	0.34890000	0.40286600	1.00581000	
Н	0.10339600	0.30618500	-1.62912300	
Н	-2.00345700	-0.98368300	-1.93784100	
Н	-1.29578800	-3.06506600	1.77968000	
Н	0.80314200	-1.81758900	2.13529000	
С	-3.10524000	2.31348900	0.01203100	
С	-1.60421300	2.65071800	0.07215200	
Н	-3.33544900	1.74541500	-0.89771400	
Н	-3.39233900	1.70337300	0.87645300	
Н	-3.72049200	3.22274400	0.01028300	
С	-1.31444300	3.43561000	1.37984700	
С	-1.19987800	3.52024300	-1.13391600	
Н	-0.24910000	3.68280000	1.45023400	
Н	-1.89033000	4.37014200	1.40297900	
Н	-1.58990700	2.83585600	2.25462600	
Н	-1.77687600	4.45360600	-1.16709900	
Н	-0.13493300	3.77623500	-1.07980800	
Н	-1.37435800	2.98149000	-2.07394100	
Ο	-0.81107600	1.47264400	0.16240200	
Cl	-3.16570600	-3.05826600	-0.33619200	



TS4			
С	4.29344200	-1.35591200	-0.15653100
С	4.85511400	-0.08347700	-0.29750900
С	4.03299800	1.04596500	-0.22589300
С	2.65935300	0.90415700	-0.01071600
С	2.08737500	-0.36871500	0.13077500
С	2.91812500	-1.49693800	0.05329700
С	0.58756500	-0.52638800	0.33452800
С	-0.25152800	-0.38145700	-0.87412300
С	-1.39311400	-1.17330600	-1.06857200
С	-1.76136600	-2.07042600	-0.08423800
С	-1.00400900	-2.26758900	1.10781300
С	0.15239400	-1.56400800	1.27886500
Н	4.92260300	-2.24059600	-0.21427700
Н	5.92390100	0.02726800	-0.46150700
Н	4.46146700	2.03955700	-0.33117400
Н	2.02176500	1.78217200	0.04989600
Н	2.48758500	-2.49092800	0.15101500
Н	0.19889100	0.48534500	0.81332400
Н	0.13159700	0.20804600	-1.69624500
Н	-1.97316300	-1.08569200	-1.98103600
Н	-1.34131700	-2.98990600	1.84347700
Н	0.75658000	-1.72453600	2.16796700
С	-3.07734300	2.36118800	0.01285200
С	-1.57141600	2.69661900	0.08474900
Н	-3.29338200	1.78658800	-0.89617800
Н	-3.37251800	1.75415600	0.87712700
Н	-3.69545700	3.26900500	-0.00056700
С	-1.28127600	3.48301000	1.38328300
С	-1.16810500	3.55022400	-1.13708400

8. Spectra data of products 3a-3a, 4a-4m: (3a) methyl biphenyl-4-carboxylate ¹

The title compound was prepared according to the general procedure described above by the reaction between *p*-methoxycarbonyl benzaldehyde (1a) with benzene, and purified by flash column chromatography as white solid (28.8 mg, 68%).

M.p. 113-115 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.11 (d, J = 8.2 Hz, 2H), 7.68-7.62 (m, 4H), 7.47 (t, J = 7.4 Hz, 2H), 7.41 (d, J = 7.2 Hz, 1H), 3.94 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 167.10, 145.74, 140.10, 130.21, 129.04, 129.02, 128.25, 127.39, 127.16, 52.23; MS (EI) m/z (%): 212(81)[M]⁺, 181(100), 152(79), 76(38); IR(cm⁻¹): 1709, 1284, 1267, 1111, 857, 746, 699.

(3b) biphenyl-4-carbonitrile²



The title compound was prepared according to the general procedure described above by the reaction between 4-formylbenzonitrile (**1b**) with benzene, and purified by flash column chromatography as white solid (22.5 mg, 63%).

M.p. 84-86 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.74-7.68 (m, 4H), 7.59 (d, *J* = 7.3 Hz, 2H), 7.49 (t, *J* = 7.3 Hz, 2H), 7.43(t, *J* = 7.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 145.75, 139.25, 132.69, 129.22, 128.78, 127.83, 127.33, 119.06, 110.99; MS (EI) m/z (%): 179(100)[M]⁺, 151(23), 126(5), 89(8), 76(12); IR(cm⁻¹): 842, 766, 722, 695.

(3c) biphenyl-3-carbonitrile ³

The title compound was prepared according to the general procedure described above by the reaction between 3-formylbenzonitrile (1c) with benzene, and purified by flash column chromatography as light yellow oil (18.4 mg, 45%).

¹H NMR (400 MHz, CDCl₃) δ 7.86 (s, 1H), 7.81 (d, *J* = 7.7 Hz, 1H), 7.63 (d, *J* = 7.5 Hz, 1H), 7.57-7.53 (m, 3H), 7.48 (t, *J* = 7.4 Hz, 2H), 7.42 (t, *J* = 7.2 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 142.55, 138.97, 131.58, 130.79, 129.70, 129.23, 128.99, 128.50, 127.18, 118.94, 113.07; MS (EI) m/z (%): 179(100)[M]⁺, 151(28), 126(11), 76(17); IR(cm⁻¹): 2228, 1475, 895, 802, 756, 692.

(3d) 4-(trifluoromethyl)biphenyl⁴

The title compound was prepared according to the general procedure described above by the reaction between 4-(trifluoromethyl)benzaldehyde (1d) with benzene, and purified by flash column chromatography as white solid (25.3 mg, 57%).

¹ S. M. Raders, J. V. Kingston, and J. G. Verkade, J. Org. Chem. 2010, 75, 1744.

² C.-L. Sun, H. Li, D.-G. Yu, M. Yu, S.-F. Zheng, B.-J. Li, Z.-J. Shi, *Nat. Chem.* **2010**, *2*, 1044.

³ Z. Xi, Y. Zhou, W. Chen, J. Org. Chem. 2008, 73, 8497.

⁴ J.-H. Li, W.-J. Liu, Org. Lett. 2004, 6, 2809.

M.p. 135 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.70 (s, 4H), 7.60 (d, J = 7.2 Hz, 2H), 7.50-7.41 (m, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 139.97, 136.46, 129.14, 128.91, 128.35, 127.59, 127.44, 127.33, 125.88 (q, J = 3.6 Hz); MS (EI) m/z (%): 222(100)[M]⁺, 201(18), 172(12), 152(28); IR(cm⁻¹): 1324, 1164, 1117, 1069, 765, 732, 695.

(3e) 4-bromobiphenyl⁵

The title compound was prepared according to the general procedure described above by the reaction between 4-bromobenzaldehyde (1e) with benzene, and purified by flash column chromatography as white solid (30.2 mg, 65%).

M.p. 82-84 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.55 (d, J = 2.6 Hz, 4H), 7.44 (t, J = 8.2 Hz, 4H), 7.37 (d, J = 7.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 140.28, 140.14, 132.00, 129.04, 128.88, 127.78, 127.08, 121.69; MS (EI) m/z (%): 232 (87) [M]+, 152(100), 126(21), 76(45); IR(cm⁻¹): 2361, 1469, 1389, 1073, 995, 827, 689.

(3f) 4-fluorobiphenyl²



The title compound was prepared according to the general procedure described above by the reaction between 4-fluorobenzaldehyde (**1f**) with benzene, and purified by flash column chromatography as white solid (21.3 mg, 62%).

M.p. 70-72 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.54 (t, *J* = 4.0 Hz, 4H), 7.43 (t, *J* = 8.0 Hz, 2H), 7.34 (t, *J* = 8.0 Hz, 1H), 7.12 (t, *J* = 8.0 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 140.46, 128.96, 128.88 (d, *J* = 1.5 Hz), 128.80, 127.40, 127.32, 127.17, 115.75 (d, *J* = 21.4 Hz); MS (EI) m/z (%): 172(100)[M]⁺, 146(7), 133(8), 85(12); IR(cm⁻¹): 1227, 835, 815, 757, 734, 687.

(3g) 4-chlorobiphenyl²

Cl-Ph

The title compound was prepared according to the general procedure described above by the reaction between 4-chlorobenzaldehyde (1g) with benzene, and purified by flash column chromatography as white solid (24.4 mg, 65%).

M.p. 71-73 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.61-7.51 (m, 4H), 7.46-7.40 (m, 4H), 7.37 (d, J = 7.3 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 140.19, 139.88, 133.58, 129.06, 129.02, 128.54, 127.73, 127.14; MS (EI) m/z (%): 188(100) [M]⁺, 152(51), 126(10), 76(22); IR(cm⁻¹): 2923, 2853, 1475, 1092, 829, 757, 737, 695.

(3h) 3-chlorobiphenyl⁶

⁵ J.-F. Wei, J. Jiao, J.-J. Feng, J. Lv, X.-R. Zhang, X.-Y. Shi, Z.-G. Chen, J. Org. Chem. 2009, 74, 6283.

⁶ J. T. Reeves, D. R. Fandrick, Z. Tan, J. J. Song, H. Lee, N. K. Yee C. H. Senanayake, Org. Lett. 2010 12, 4388.

The title compound was prepared according to the general procedure described above by the reaction between 3-chlorobenzaldehyde (**1h**) with benzene, and purified by flash column chromatography as colorless oil (21.8 mg, 58%).

¹H NMR (400 MHz, CDCl₃) δ 7.57 (d, J = 7.9 Hz, 3H), 7.44 (d, J = 7.5 Hz, 3H), 7.39-7.33 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 143.29, 130.11, 129.03, 128.89, 128.01, 127.47, 127.41, 127.27, 125.44, 110.11; MS (EI) m/z (%): 188(100)[M]⁺, 152(65), 126(8), 94(7), 76(22); IR(cm⁻¹): 1591, 1563, 1471, 1404, 1099, 790, 751, 691.

(3i) 2-chlorobiphenyl⁷

The title compound was prepared according to the general procedure described above by the reaction between 2-chlorobenzaldehyde (1i) with benzene, and purified by flash column chromatography as colorless oil (15.8 mg, 42%).

¹H NMR (400 MHz, CDCl₃) δ 7.60 (d, J = 7.4 Hz, 1H), 7.49 – 7.40(m, 5H), 7.37 – 7.29 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 131.52, 130.10, 129.59, 128.89, 128.64, 128.18, 127.73, 127.39, 127.32, 126.93; MS (EI) m/z (%): 188(100)[M]⁺, 152(60), 126(8), 76(22); IR(cm⁻¹): 1466, 1424, 1073, 1035, 742, 696.

(3j) biphenyl²



The title compound was prepared according to the general procedure described above by the reaction between benzaldehyde (1j) with benzene, and purified by flash column chromatography as white solid (20.3 mg, 66%).

M.p. 68-70 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.60 (d, *J*= 7.3 Hz, 4H), 7.44 (t, *J*= 7.4 Hz, 4H), 7.35 (t, *J*= 7.1 Hz, 2H); ¹³C NMR (100MHz, CDCl₃) δ 141.46, 128.89, 127.39, 127.32. MS (EI) m/z (%): 154(100)[M]⁺, 139(5), 128(7), 115(8), 76(18); IR(cm⁻¹): 2361, 1427, 1003, 901, 724, 692.

(3k) 4-methylbiphenyl²



The title compound was prepared according to the general procedure described above by the reaction between 4-methylbenzaldehyde (1k) with benzene, and purified by flash column chromatography as white solid (20.5 mg, 61%).

M.p. 41-43 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.58 (t, *J* = 7.1 Hz, 2H), 7.49 (d, *J* = 7.7 Hz, 2H), 7.42 (t, *J* = 7.4 Hz, 2H), 7.36-7.30 (m, 1H), 7.25 (d, *J* = 7.2 Hz, 2H), 2.39 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 141.39, 138.59, 137.14, 129.63, 128.85, 127.39, 127.32, 127.13, 21.20; MS (EI) m/z (%): 168(100)[M]⁺, 152(22), 139(7), 128(7), 115(12), 91(8), 82(10); IR(cm⁻¹): 1484, 820, 755, 736, 695.

⁷ E. Ullah, J. McNulty, and A. Robertson, *Eur. J. Org. Chem.* **2012**, 2012, 2127.

(3l) 4-*tert*-butylbiphenyl⁸



The title compound was prepared according to the general procedure described above by the reaction between 4-(*tert*-butyl)benzaldehyde (11) with benzene, and purified by flash column chromatography as colorless oil (26.5 mg, 63%).

¹H NMR (400 MHz, CDCl₃) δ 7.59 (d, J = 6.8 Hz, 2H), 7.54 (d, J = 8.0 Hz, 2H), 7.48– 7.41 (m, 4H), 7.34 (t, J = 7.4Hz, 1H), 1.36 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 150.42, 141.27, 138.51, 128.83, 127.17, 127.12, 126.94, 125.84, 34.67, 31.54; MS (EI) m/z (%): 211(35)[M+1]⁺, 195(100), 167(32), 151(18); IR(cm⁻¹): 1483, 835, 764, 733, 695.

(3m) 4-methoxybiphenyl²



The title compound was prepared according to the general procedure described above by the reaction between 4-methoxybenzaldehyde (**1m**) with benzene, and purified by flash column chromatography as light yellow solid (19.5 mg, 53%).

M.p. 80-82 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.54 (t, J = 8.2 Hz, 4H), 7.41 (t, J = 7.4 Hz, 2H), 7.30 (t, J = 7.2 Hz, 1H), 6.98 (d, J = 8.4 Hz, 2H), 3.85 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 146.54, 141.04, 134.02, 128.85, 128.30, 126.90, 126.80, 114.43, 55.49; MS (EI) m/z (%): 184(100)[M]⁺, 169(48), 152(15), 141(44), 115(38); IR(cm⁻¹): 1246, 1197, 1183, 1035, 832, 757, 685.

(3n) 1-phenylnaphthalene ⁹



The title compound was prepared according to the general procedure described above by the reaction between 1-naphthaldehyde (1n) with benzene, and purified by flash column chromatography as colorless oil (18.4 mg, 45%).

¹H NMR (400 MHz, CDCl₃) δ 7.92-7.86 (m, 2H), 7.59 (d, J = 7.4 Hz, 1H), 7.55-7.33 (m, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 133.99, 130.23, 128.89, 128.41, 128.39, 127.78, 127.38, 127.31, 127.06, 126.32, 126.20, 126.15, 125.89, 125.51; MS (EI) m/z (%): 204(100)[M]⁺, 189(5), 176(8), 101(35), 88(16); IR(cm⁻¹): 800, 776, 760, 737, 698.

(30) 2-phenylnaphthalene²



The title compound was prepared according to the general procedure described above by the reaction between methyl 2-naphthaldehyde (10) with benzene, and purified by flash column

⁸ C. M. So, C. P. Lau, A. S. C. Chan, F. Y. Kwong, J. Org. Chem. 2008, 73, 7731.

⁹ N. Asao, T. Nogami, S. Lee, Y. Yamamoto, J. Am. Chem. Soc. 2003, 125, 10921.

chromatography as white solid (24.9 mg, 61%).

M.p. 95-97 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.05 (s, 1H), 7.94 – 7.86 (m, 3H), 7.75 (t, J = 8.0 Hz, 3H), 7.53 – 7.48 (m, 4H), 7.39 (t, J = 8.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 141.35, 138.75, 133.90, 132.81, 128.99, 128.55, 128.35, 127.80, 127.58, 127.49, 126.42, 126.06, 125.96, 125.75; MS (EI) m/z (%): 204(100)[M]⁺, 189(5), 176(8), 101(15), 89(8), 76(5); IR(cm⁻¹): 2361, 857, 818, 753, 734, 686.

(4a) methyl 2',5'-bis(trifluoromethyl)-biphenyl-4-carboxylate ¹⁰



The title compound was prepared according to the general procedure described above by the reaction between *p*-methoxycarbonyl benzaldehyde (**1a**) with 1,4-bis(trifluoromethyl)benzene (**2a**, 1.5 mL, as solvent), and purified by flash column chromatography as light yellow solid (41.7 mg, 60%).

M.p. 81-83 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.11 (d, J = 8.0 Hz, 2H), 7.91 (d, J = 8.0 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.60 (s, 1H), 7.41 (d, J = 8.0 Hz, 2H), 3.96 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 166.77, 142.91, 130.37 (d, J = 1.9 Hz), 129.74, 129.47, 129.14, 129.13, 128.74 (d, J = 3.7 Hz), 128.30, 128.22, 127.23(q, J = 5.2 Hz), 125.02(q, J = 3.3 Hz), 52.39; MS (EI) m/z (%): 348(35)[M]⁺, 317(100), 269(42), 219(18), 201(5); IR(cm⁻¹): 1719, 1312, 1278, 1174, 1087, 1024, 840, 707.

(4b) methyl 2',5'-dichloro-biphenyl-4-carboxylate¹⁰



The title compound was prepared according to the general procedure described above by the reaction between *p*-methoxycarbonyl benzaldehyde (**1a**) with 1,4-dichlorobenzene (**2b**, 1.5 mL, as solvent), and purified by flash column chromatography as white solid (32.5 mg, 58%). M.p. 80-82 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.11 (d, *J* = 8.2 Hz, 2H), 7.50 (d, *J* = 8.2 Hz, 2H), 7.42 (d, *J* = 8.5 Hz, 1H), 7.34 (d, *J* = 2.2 Hz, 1H), 7.31-7.28 (m, 1H), 3.95 (s, 3H); ¹³C NMR (100

7.42 (d, J = 8.5 Hz, 1H), 7.34 (d, J = 2.2 Hz, 1H), 7.31-7.28 (m, 1H), 3.95 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 166.84, 142.82, 141.19, 132.98, 131.35, 131.09, 130.92, 130.08, 129.66, 129.53, 129.23, 52.31; MS (EI) m/z (%): 280(65)[M]⁺, 249(100), 186(76), 151(23), 124(15), 93(28); IR(cm⁻¹): 1713, 1285, 1100, 1022, 792, 770, 699.

(4c) methyl 2',5'-dimethyl-biphenyl-4-carboxylate ¹¹

¹⁰ HRMS was been tested.

¹¹ T. E. Storr, M. F. Greaney, Org. Lett. 2013, 15, 1410.



The title compound was prepared according to the general procedure described above by the reaction between *p*-methoxycarbonyl benzaldehyde (**1a**) with *p*-xylene (**2c**, 1.5 mL, as solvent), and purified by flash column chromatography as light yellow oil (22.5 mg, 47%).

¹H NMR (400 MHz, CDCl₃) δ 8.08 (d, *J* = 8.1 Hz, 2H), 7.39 (d, *J* = 8.1 Hz, 2H), 7.17 (d, *J* = 7.7 Hz, 1H), 7.10 (d, *J* = 7.7 Hz, 1H), 7.04 (s, 1H), 3.94 (s, 3H), 2.35 (s, 3H), 2.22 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 167.24, 147.18, 140.94, 135.53, 132.17, 130.59, 130.36, 129.55, 129.41, 128.78, 128.69, 52.18, 21.01, 19.96; MS (EI) m/z (%): 240(100)[M]⁺, 225(7), 209(78), 181(52), 165(76), 152(8), 97(21); IR(cm⁻¹): 1720, 1434, 1272, 1179, 1102, 812, 778.



The title compounds were prepared according to the general procedure described above by the reaction between *p*-methoxycarbonyl benzaldehyde (**1a**) with 1-chloro-4-(trifluoromethyl)benzene (**2d**, 1.5 mL, as solvent), and purified by flash column chromatography as light yellow solid (34.5 mg, 55%).¹⁰

M.p. 76-78 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.15-8.08 (m, 2H), 7.74 – 7.46 (m, 4H), 7.37 (t, J = 8.0 Hz, 1H), 3.96 (d, J = 2.7 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 166.79, 143.08, 142.57, 140.47, 137.77, 136.42, 131.79, 130.84, 130.18, 129.72, 129.56, 129.35, 129.05, 128.18, 128.10 (q, J = 3.6 Hz), 127.87 (q, J = 5.9 Hz), 125.97 (q, J = 3.4 Hz), 125.11, 122.40, 52.38; MS (EI) m/z (%): 314(45)[M]⁺, 283(100), 255(4), 235(15), 220(52), 186(8); MS (EI) m/z (%): 314(32)[M]⁺, 283(100), 235(28), 220(18), 201(7), 141(10); IR(cm⁻¹): 1720, 1309, 1277, 1167, 1106, 1022, 820, 774, 704.



The title compounds were prepared according to the general procedure described above by the reaction between *p*-methoxycarbonyl benzaldehyde (**1a**) with 1,3-bis(trifluoromethyl)benzene (**2e**, 1.5 mL, as solvent) as solvent, and purified by flash column chromatography as light yellow solid (37.5 mg, 54%).¹²

¹² C5 isomer: P. Harrisson, J. Morris, P. G. Steel, T. B. Marder, *Synlett* 2009, 20, 147.

M.p. 89-91 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.18– 8.03(m, 3H), 7.98– 7.84 (m, 1H), 7.68 (t, J = 8.7 Hz, 1H), 7.49– 7.33 (m, 2H), 3.96 (d, J = 3.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 166.77, 142.98, 142.57, 142.37, 132.61, 130.68, 130.39, 130.28 129.45, 128.98, 128.49-128.39 (m), 127.57-127.51 (m), 127.43, 123.72-123.63 (m), 121.92-121.87 (m), 52.40; MS (EI) m/z (%): 348(38)[M]⁺, 317(100), 269(54), 219(17), 201(7), 149(8), 125(10); IR(cm⁻¹): 1718, 1378, 1169, 1119, 1061, 849, 771, 706.



The title compounds were prepared according to the general procedure described above by the reaction between *p*-methoxycarbonyl benzaldehyde (**1a**) with m-xylene (**2f**, 1.5 mL, as solvent), and purified by flash column chromatography as light yellow oil (23.0 mg, 48%).¹³

¹H NMR (400 MHz, CDCl₃) δ 8.12-8.06 (m, 2H), 7.38 (d, J = 8.2 Hz, 1H), 7.25 – 7.06 (m, 4H), 3.94 (d, J = 4.2 Hz, 3H), 2.38 (d, J = 4.8 Hz, 2H), 2.24 (s, 1H), 2.01 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 167.24, 147.03, 146.44, 141.01, 138.27, 137.72, 135.74, 135.12, 131.43, 130.15, 129.97, 129.65, 129.55, 129.50, 129.44, 127.63, 127.60, 127.21, 126.78, 125.35, 52.17 21.50, 21.17, 20.80, 20.39; MS (EI) m/z (%): 240(100)[M]⁺, 209(82), 181(35), 165(68), 97(21); IR(cm⁻¹): 1720, 1435, 1272, 1178, 1101, 820, 771, 708.



The title compounds were prepared according to the general procedure described above by the reaction between *p*-methoxycarbonyl benzaldehyde (**1a**) with 1,2-dichlorobenzene (**2g**, 1.5 mL, as solvent), and purified by flash column chromatography as light yellow solid (34.1 mg, 61%).¹⁴ M. p. 77-79 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.11 (d, *J* = 8.0 Hz, 2H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.54 – 7.43(m, 2H), 7.29 – 7.22 (m, 2H), 3.95 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 166.87, 143.92, 143.22, 142.08, 140.22, 134.03, 131.03, 130.45, 130.14, 129.92, 129.59, 129.53, 129.35, 129.26, 127.40, 127.04, 126.59, 52.28; MS (EI) m/z (%): 280(46)[M]⁺, 249(100), 186(78), 151(26), 124(18), 93(35); IR(cm⁻¹): 1716, 1430, 1286, 1189, 1117, 1033, 764, 701.

¹³ C2 isomer: C. M. So, W. K. Chow, P. Y. Choy, C. P. Lau, and F. Y. Kwong, *Chem. Eur. J.* **2010**, *16*, 7996.

C5 isomer: B.-T. Guan, Y. Wang, B.-J. Li, D.-G. Yu, Z.-J. Shi, J. Am. Chem. 2008, 130, 14468.

¹⁴ C4 isomer: D. Qiu, H. Meng, L. Jin, Y. Zhang, J.-B. Wang, Angew. Chem. Int. Ed. 2013, 125, 11795.



The title compounds were prepared according to the general procedure described above by the reaction between *p*-methoxycarbonyl benzaldehyde (**1a**) with 1,2-difluorobenzene (**2h**, 1.5 mL, as solvent), and purified by flash column chromatography as light yellow solid (25.8 mg, 52%).¹⁵ M. p. 63-65°C; ¹H NMR (400 MHz, CDCl₃) δ 8.11 (t, *J* = 7.8 Hz, 2H), 7.61 (t, *J* = 8.0 Hz, 2H), 7.46 – 7.33 (m, 1H), 7.23 – 7.13 (m, 2H), 3.95 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 166.86, 130.42, 129.98, 129.85, 129.13, 129.10, 127.03, 125.39 (dd, *J* = 3.4, 1.9 Hz), 124.65 (d, *J* = 3.4 Hz), 124.42 (dd, *J* = 6.9, 4.7 Hz), 123.43 (dd, *J* = 6.1, 3.5 Hz), 117.90 (d, *J* = 17.7 Hz), 117.00 (d, *J* = 7.4 Hz), 116.40 (d, *J* = 18.1 Hz), 52.28; MS (EI) m/z (%): 248(55)[M]⁺, 230(16), 217(100), 200(23), 188(48), 170(17); IR(cm⁻¹): 1720, 1477, 1276, 1184, 1111, 1094, 761, 703.

MeO₂C
$$4i$$
, 50%
(C3/C4 = 1.4:1.0)

The title compounds were prepared according to the general procedure described above b by the reaction between *p*-methoxycarbonyl benzaldehyde (**1a**) with o-xylene (**2i**, 1.5 mL, as solvent), and purified by flash column chromatography as light yellow oil (24.0 mg, 50%).¹⁶

¹H NMR (400 MHz, CDCl₃) δ 8.08 (d, *J* = 7.9 Hz, 2H), 7.65 (d, *J* = 8.3 Hz, 1H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.24 – 7.14 (m, 1H), 7.07 (d, *J* = 6.9 Hz, 1H), 3.94 (d, *J* = 3.7 Hz, 3H), 2.33 (d, *J* = 11.0 Hz, 4H), 2.14 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 167.23, 147.68, 145.93, 141.46, 137.51, 137.26, 136.90, 133.91, 130.39, 130.19, 129.62, 129.55, 129.50, 128.73, 128.65, 127.51, 126.95, 125.53, 124.79, 52.17, 20.69, 19.98, 19.56, 17.02; MS (EI) m/z (%): 240(100)[M]⁺, 225(7), 209(82), 181(54), 165(74), 152(8); IR(cm⁻¹): 1719, 1434, 1272, 1179, 1102, 1019, 860, 768;



(*o/m/p* =1.7:2.3:1.0)

The title compounds were prepared according to the general procedure described above by the reaction between *p*-methoxycarbonyl benzaldehyde (**1a**) with (trifluoromethyl)benzene (**2j**, 1.5 mL, as solvent), and purified by flash column chromatography as light yellow solid (35.8 mg, 64%).¹⁷

M. p. 55-57 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.15-8.07 (m, 2H), 7.86 – 7.48 (m, 5H), 7.41-7.31

¹⁵ C3 isomer: MERCK SERONO S.A., WO2010/115736 A2, **2010**.

C4 isomer: ELI LILLY AND COMPANY, WO2004/94363 A1, 2004.

¹⁶ C4 isomer: T. Ishiyama, K. Sato, Y. Nishio, N. Miyaura, Angew. Chem. Int. Ed. 2003, 42, 5346.

¹⁷ ortho isomer : J-H. Wu, D-Y. Zhang, L. Chen, J-N. Li, H. Liu, D-X. Liu, J. Med. Chem. 2013, 56, 761. meta and para isomers: Amatore Muriel, Gosmini Corinne, Angew. Chem. Int. Ed. 2008, 47, 2089.

(m, 1H), 3.95 (d, J = 2.7 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 166.96, 166.87, 144.66, 144.20, 141.06, 131.75, 131.53, 130.67, 130.44, 130,41, 120.10, 129.97, 129.56, 129.56, 129.23, 129.21, 128.00, 127.74, 127.38, 127.28, 126.30 (q, J = 5.3 Hz), 126.00 (q, J = 3.8 Hz), 124.90 (q, J = 3.7 Hz), 124.20 (q, J = 3.8 Hz), 52.25, 52.19; MS (EI) m/z (%): 280(45)[M]⁺, 249(100), 219(7), 201(46), 152(8); IR(cm⁻¹): 1714, 1330, 1318, 1277, 1160, 1109, 1069, 767, 702.



4k, 61% (o/m/p = 8.0:4.5:1.0)

The title compounds were prepared according to the general procedure described above by the reaction between p-methoxycarbonyl benzaldehyde (1a) with fluorobenzene (2k, 1.5 mL, as solvent), and purified by flash column chromatography as light yellow oil (28.0 mg, 61%).¹⁸ ¹H NMR (400 MHz, CDCl₃) δ 8.11 (d, J = 8.1 Hz, 2H), 7.65-7.62 (m, 2H), 7.54 – 7.32 (m, 2H), 7.32 – 7.04 (m, 2H), 3.95 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 167.02, 164.64, 161.21, 144.46, 140.58, 130.80 (d, J = 3.2 Hz), 130.61, 130.53, 130.35, 129.98, 129.89, 129.85, 129.16 (d, J = 3.2 Hz), 127.19, 124.65 (d, J = 3.7 Hz), 123.07 (d, J = 3.0 Hz), 116.42 (d, J = 22.6 Hz), 114.58 (d, J = 2.6 Hz), 114.58 (d, J = 3.0 Hz), 126.07 (d, J = 3.0 Hz), 116.42 (d, J = 22.6 Hz), 114.58 (d, J = 3.0 Hz), 126.07 (d, J = 3.0 Hz), 127.07 (d, J = 3.0 Hz), 126.07 (d, J = 3.0 Hz), 12 21.1 Hz), 114.36 (d, J = 22.1 Hz), 52.22; MS (EI) m/z (%): 230(68)[M]⁺, 199(100), 170(55), 151(12), 99(15), 85(21); IR(cm⁻¹): 1718, 1295, 1189, 1104, 755, 727, 698.



(o/m/p = 3.0:1.4:1.0)

The title compounds were prepared according to the general procedure described above by the reaction between p-methoxycarbonyl benzaldehyde (1a) with toluene (2l, 1.5 mL, as solvent), and purified by flash column chromatography as light yellow oil (24.4 mg, 54%).¹⁹

¹H NMR (400 MHz, CDCl₃) δ 8.09(t, J = 8.0 Hz, 2H), 7.65 (d, J = 8.2 Hz, 1H), 7.54 - 7.33 (m, 3H), 7.33-7.23 (m, 2H), 3.94 (s, 3H), 2.42 (d, J = 10.0 Hz, 1H), 2.26 (s, 2H); ¹³C NMR (100 MHz, CDCl₃) & 167.18, 146.98, 145.99, 141.09, 140.22, 138.70, 135.31, 130.63, 130.23, 130.20, 129.79, 129.66, 129.58, 129.41, 129.03, 128.97, 128.87, 128.29, 128.18, 127.98, 127.26, 127.19, 126.93, 126.04, 124.55, 52.17, 21.61, 21.24, 20.45; MS (EI) m/z (%): 226(87)[M]⁺, 195(100), 167(38), 152(46), 97(12), 82(10); IR(cm⁻¹): 1718, 1434, 1274, 1180, 1104, 755, 728, 702.

¹⁸ ortho isomer: T. Blümke, Y.-H. Chen, Z. Peng, P. Knochel, Nat. Chem. 2010, 2, 313.

para isomers: B.-T. Guan, Y. Wang, B.-J. Li, D.-G. Yu, Z.-J. Shi, J. Am. Chem. Soc. **2008**, 130, 14468. ortho and meta isomers: P. Leowanawat, N. Zhang, A.-M. Resmerita, B. M. Rosen, and V. Percec, J. Org. Chem. 2011, 76, 9946.

para isomer: B.-T. Guan, Y. Wang, B.-J. Li, D.-G. Yu, Z.-J. Shi, J. Am. Chem. Soc. 2008, 130, 14468.



The title compounds were prepared according to the general procedure described above by the reaction between *p*-methoxycarbonyl benzaldehyde (1a) with chlorobenzene (2m, 1.5 mL, as solvent), and purified by flash column chromatography as light yellow oil (29.0 mg, 59%).²⁰ ¹H NMR (400 MHz, CDCl₃) δ 8.11 (d, J = 8.1 Hz, 2H), 7.64-7.61 (m, 1H), 7.56-7.48 (m, 2H), 7.44 – 7.31(m, 3H), 3.95 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 167.01, 144.15, 139.77, 132.55, 131.27, 130.35, 130.28, 130.26, 129.68, 129.50, 129.26, 128.65, 128.27, 127.57, 127.19, 127.07, 127.02, 125.56, 52.22; MS (EI) m/z (%): 246(76)[M]⁺, 215(100), 152(82), 119(18), 91(15), 76(28); IR(cm⁻¹): 1717, 1434, 1273, 1184, 1102, 753, 699.

(2-(4-methoxyphenyl)ethene-1,1-diyl)dibenzene²¹



¹H NMR (400 MHz, CDCl₃) δ 7.42 - 7.15 (m, 10H), 6.94 (t, J= 8.4 Hz, 3H), 6.67 (d, J= 8.5 Hz, 2H), 3.75 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 158.54, 143.74, 140.80, 140.76, 130.94, 130.56, 130.23, 128.85, 128.30, 127.81, 127.54, 127.41, 127.33, 113.57, 55.29.

2-nitroaniline²²



¹H NMR (400 MHz, CDCl₃) δ 8.12 (d, J= 8.5 Hz, 1H), 7.36 (t, J= 7.5 Hz, 1H), 6.81 (d, J= 8.3 Hz, 1H), 6.81 (d, J= 8 1H), 6.71 (t, J= 7.7 Hz, 1H), 6.06 (s, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 144.82, 135.78, 132.30, 126.24, 118.88, 117.02.

4-methyl-N-(2-nitrophenyl)benzamide²³



¹H NMR (400 MHz, CDCl₃) δ 11.32 (s, 1H), 9.01 (d, J = 8.5 Hz, 1H), 8.28 (d, J = 8.2 Hz, 1H), 7.90 (d, J = 8.0 Hz, 2H), 7.71 (t, J = 7.7 Hz, 1H), 7.34 (d, J = 7.9 Hz, 2H), 7.21 (t, J = 7.8 Hz, 1H), 2.45 (s, J = 7.0 Hz, 2Hz), 7.21 (t, J = 7.8 Hz, 1Hz), 7.45 (s, J = 7.8 Hz, 1Hz), 7.11 (t, J = 7.8 Hz, 1Hz), 7.45 (s, J = 7.8 Hz), 7.45 (s

²⁰ ortho isomer: Matsushita, Sakamoto, Murakami, Matsui, Synthetic Commun. 1994, 24, 3307. meta isomer: L-T. Niu, H. Zhang, H-J. Yang and H. Fu, Synlett 2014, 25, 995.

para isomer: C. I. Traficante, C. M. L. Delpiccolo, E. G. Mata, *ACS Comb Sci.* **2014**, *16*, 211. ²¹ C.-L.Sun, Y.-F. Gu, B. Wang, and Z.-J. Shi, *Chem. Eur. J.* **2011**, *17*, 10844.

²² H.-J. Xu, Y.-F. Liang, Z.-Y. Cai, H.-X. Qi, C.-Y. Yang, Y.-S. Feng, J. Org. Chem. **2011**, 76, 2296.

²³ P. K. Sasmal, S. Sridhar, J. Iqbal, *Tetrahedron Lett.* **2006**, 47, 8661.

3H). ¹³C NMR (101 MHz, CDCl₃) δ 165.89, 143.53, 136.60, 136.29, 135.71, 131.43, 129.87, 127.56, 126.03, 123.26, 123.30, 21.68.













(**3c**)







S32





S34



(**3f**)



h1-2014-07-03






CI





(**3g**)











































(**4**a)



















(**4e**)











(**4h**)














h1-2014-05-30









(**4l**)



S79



(**4m**)



(1----)



S82



S83







