Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Palladium-Catalyzed Carbonylations of Highly Substituted Olefins using CO-Surrogates

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Content

General Considerations

All manipulations were carried out under an argon atmosphere using Schlenk-techniques, unless stated otherwise. All glass devices used for synthesis were dried and cooled under vacuum before use. Chemicals were purchased from commercial sources and used as received, if not stated otherwise. Oxygen-free and dry solvents were prepared by distillation or using a solvent purification system by Innovative Technologies.
Catalytic experiments were performed in 25 mL sealable glass tubes. Placed in a heating block and stirred with a magnetic stirring bar.
GC measurements were carried out either on a 7890A GC-System with a HP-5 column (polydimethylsiloxane with 5% phenyl groups, length 30 m, i.d. 0.32 mm, film 0.25 µm) from Agilent Technology or a Trace 1310 chromatograph from Thermo Fisher Scientific with a HP-5 column.

Catalytic Experiments with Paraformaldehyde and Methanol

In a typical catalytic experiment, the reaction were performed in 25 mL sealable glass tube with $Pd(OAc)_2$ (1.0 mol%), LIKat Ligand (4.0 mol%), PTSA·H_2O (5.0 mmol), and paraformaldehye (200 mg) rapidly weighed in the air. If used, solid substrates (1.0 mmol) were also weighed in the air and added into the tube. The atmosphere in the vial was then changed to argon and 2.0 mL MeOH were added. Next, liquid substrates (1.0 mmol) were added and the tube was fitted with a sealed cap. The reaction mixture was stirred at 120 °C for 72 hours. The reaction solution was analysed by gas chromatography using isooctane as internal standard.

Data for the Optimization of Reaction Conditions

Tab. S1: [Pd] precursor

[Pd]	yield (l/b)
$Pd(acac)_2$	37 % (>99/1)
$PdCl_2$	0 %
$Pd_2(dba)_3$	0 %
$Pd(TFA)_2$	34 % (>99/1)
$Pd(OAc)_2$	56 % (>99/1)

Conditions: 1.0 mmol 1a, 1 mol% [Pd], 4 mol% L1, 5 mol% PTSA·H_2O, 200 mg $(CH_2O)_n$, in 2 mL MeOH, 120 °C, 20 h.

Tab. S2: Acid studies

acid (x mol%)	yield (l/b)
CF_3SO_3H (5)	42 % (>99/1)
CH_3SO_3H (5)	0 %
H_2SO_4 (5)	53 % (>99/1)
HOAc (5)	0 %
PTSA·H_2O (4)	43 % (>99/1)
PTSA·H_2O (6)	34 % (>99/1)
PTSA·H_2O (7)	19 % (>99/1)

Conditions: 1.0 mmol 1a, 1 mol% [Pd], 4 mol% L1, X mol% acid, 200 mg $(CH_2O)_n$, in 2 mL MeOH, 120 °C, 20 h.

Tab. S3: Time

time	yield (l/b)
48h	78 % (>99/1)
72h	93 % (>99/1)

Conditions: 1.0 mmol 1a, 1 mol% [Pd], 4 mol% L1, 5 mol% PTSA·H_2O, 200 mg $(CH_2O)_n$, in 2 mL MeOH, 120 °C, X h.

Product Characterization

methyl 3,4-dimethylpentanoate[1] (**2a/2a'**): ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.65 (s, 3H), 2.33 (dd, *J* = 20.0, 8.0 Hz, 1H), 2.06 (dd, *J* = 20.0, 8.0 Hz, 1H), 1.89-1.83 (m, 1H), 1.59-1.53 (m, 1H), 0.87-0.81 (m, 9H) ppm. ^{13}C NMR (100 MHz, CDCl3): δ = 174.3, 51.5, 39.1, 36.0, 32.2, 19.9, 18.8, 15.9 ppm.

methyl 3-phenylbutanoate[2] (**2b/2b'**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.18-7.34 (m, 5H), 3.63 (s, 3H), 3.25-3.33 (m, 1H), 2.51-2.68 (m, 2H), 1.31 (d, *J* = 6.0 Hz, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.0, 145.8, 128.6, 126.8, 126.5, 51.6, 42.9, 36.6, 21.9 ppm.

methyl 3-p-tolylbutanoate[3] (**2c/2c'**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.04 – 7.03 (m, 4H), 3.55 (s, 3H), 3.19-3.16 (m, 1H), 2.58-2.41 (m, 2H), 2.24 (s, 3H), 1.21 (d, *J* = 9.0 Hz, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.9, 142.7, 135.9, 129.2, 126.6, 77.5, 77.1, 76.6, 51.5, 42.8, 36.0, 21.9, 21.0 ppm.

methyl 3-(4-fluorophenyl)butanoate[4] (**2d/2d'**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.14-7.21 (m, 2H), 6.93-7.01 (m, 2H), 3.61 (s, 3H), 3.23-3.31 (m, 1H), 2.49-2.63 (m, 2H), 1.28 (d, *J* = 6.0 Hz, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.8, 161.6 (d, J = 242.3 Hz, 1C), 141.4 (d, J = 3.8 Hz, 1C), 128.3 (d, J = 8.3 Hz, 1C), 115.6 (d, J = 21.0 Hz, 1C), 51.7, 43.0, 35.9, 22.1 ppm.

methyl 3-(4-chlorophenyl)butanoate[5] (**2e/2e'**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.24-7.28 (m, 2H), 7.12-7.17 (m, 2H), 3.61 (s, 3H), 3.22-3.32 (m, 1H), 2.49-2.63 (m, 2H), 1.28 (d, *J* = 9.0 Hz, 3H)ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.7, 144.2, 132.2, 128.7, 128.2, 51.7, 42.7, 36.0, 21.9 ppm.

methyl 3-(o-tolyl)butanoate[1] (**2f/2f'**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.24-7.12 (m, 4H), 3.68 (s, 3H), 3.64-3.55 (m, 1H), 2.70 (dd, *J* = 15.0, 6.0 Hz, 1H), 2.59 (dd, *J* = 15.0, 9.0 Hz, 1H), 2.44 (s, 3H), 1.32 (d, *J* = 6.0 Hz, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.8, 143.7, 135.0, 130.3, 126.1, 125.9, 124.8, 124.7, 51.3, 41.7, 31.2, 21.1, 19.2 ppm.

methyl 3-(naphthalen-2-yl)butanoate[3] (**2g/2g'**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.73-7.70 (m, 3H), 7.57 (s, 1H), 7.39-7.27 (m, 3H), 3.53 (s, 3H), 3.40- 3.35 (m, 1H), 2.68- 2.53 (m, 2H), 1.31 (d, *J* = 6 Hz, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.9, 143.1, 133.6, 132.4, 128.2, 127.7, 127.6, 126.0, 125.5, 125.4, 125.0, 77.4, 77.1, 76.8, 51.6, 42.7, 36.6, 21.8 ppm.

methyl 3,3-diphenylpropanoate[6] (**2h/2h'**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39-7.23 (m, 10H), 4.64 (t, *J* = 9.0 Hz, 1H), 3.65 (s, 3H), 3.15 (d, *J* = 9.0 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.4, 143.6, 128.7, 127.8, 126.7, 51.8, 47.1, 40.7 ppm.

dimethyl 3,3'-(1,3-phenylene)dibutyrate[1] (**2i/2i'**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39-7.33 (m, 1H), 7.27-7.17 (m, 3H), 3.74 (s, 6H), 3.42-3.33 (m, 2H), 2.78-2.62 (m, 4H), 1.41 (d, *J* = 6.0 Hz, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.7, 145.8, 128.5, 125.2, 124.5, 51.4, 42.7, 36.3, 21.6 ppm.

methyl cyclohexanecarboxylate[7] (**2k/2k'**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.60 (s, 3H), 2.24 (tt, *J* = 12.3 Hz, 1H), 1.86-1.81 (m, 2H), 1.71-1.55 (m, 3H), 1.44-1.20 (m, 5H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.5, 51.4, 43.1, 29.1, 25.8, 25.5 ppm.

methyl cycloheptanecarboxylate[8] (**2l/2l'**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.65 (s, 3H), 2.44-2.51 (m, 1H), 1.61- 1.74 (m, 4H), 1.39-1.59 (m, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.7, 51.6, 45.1, 31.0, 28.4, 26.5 ppm.

methyl cyclooctanecarboxylate[9] (**2m/2m'**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.65 (s, 3H), 2.47-2.56 (m, 1H), 1.83-1.92 (m, 2H), 1.72-1.75 (m, 4H),1.49-1.63 (m, 8H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.7, 51.7, 43.6, 28.9, 26.9, 26.3, 25.4 ppm.

methyl 2,3-dihydro-1H-indene-1-carboxylate[10] (**2n/2n'**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.23 (d, *J* = 9.0 Hz, 1H), 7.12 (d, *J* = 9.0 Hz, 1H), 6.85 (t, *J* = 9.0 Hz, 2H), 3.78 (s, 3H), 3.67 (s, 3H), 2.90 (t, *J* = 6.0 Hz, 2H), 2.60 (t, *J* = 6.0 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.5, 144.2, 140.8, 127.7, 126.6, 124.9, 124.8, 55.3, 51.7, 36.1, 31.2 ppm.

methyl 3-(1,3-dioxoisoindolin-2-yl)propanoate[11] (**2o/2o'**): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.79-7.76 (m, 2H), 7.66-7.64 (m, 2H), 3.93 (t, *J* = 6.0 Hz, 2H), 3.61 (s, 3H), 2.67 (t, *J* = 7.5 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.2, 170.0, 134.1, 132.0, 123.4, 77.5, 77.1, 76.6, 51.9, 33.8, 32.8 ppm.

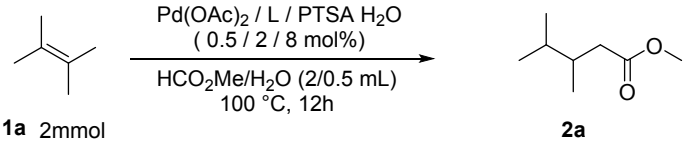
methyl 3-(triethylsilyl)propanoate[12] (**2q/2q'**): 1 H NMR (300 MHz, $CDCl_3$): δ = 3.67 (s, 3H), 2.31-2.25 (m, 2H), 0.96-0.84 (m, 11H), 0.56-0.48 (m, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.6, 51.5, 28.6, 7.3, 6.5, 3.0 ppm.

methyl 3,5,5-trimethylhexanoate[13] (**2s/s'**): ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.65 (s, 3 H), 2.30 (m, 1 H), 2.12 (m, 1 H), 2.02 (m, 1 H), 1.165 (m, 2 H), 0.97 (d, *J* = 9.0 Hz, 3 H), 0.90 (s, 9 H) ppm. ^{13}C NMR ($CDCl_3$, 300 MHz): δ = 173.7, 51.4, 50.7, 44.0, 31.2, 30.1, 27.2, 22.8 ppm.

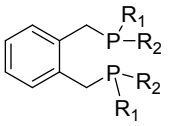
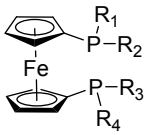
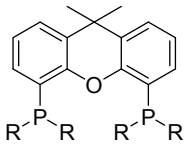
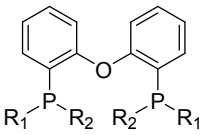
methyl 4,5-bis(4-hydroxyphenyl)heptanoate[1] (**2t**) ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.02-6.61 (m, 8H), 5.85 (s, br, 2H), 3.61 (s, 1H), 3.52 (s, 2H), 2.73-2.42 (m, 2H), 2.14-1.24 (m, 6H, CH2), 0.72 (t, *J* = 6.0 Hz, 1H), 0.53 (t, *J* = 6.0 Hz, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 175.45, 175.43, 154.20, 153.98, 153.85, 153.59, 135.58, 135.08, 134.18, 133.34, 130.02, 129.97, 129.24, 115.36, 115.21, 114.66, 114.49, 53.48, 52.65, 51.79, 51.71, 50.86, 49.93, 32.54, 32.45, 29.53, 28.62, 27.25, 26.00 ppm.

CO Surrogate Reactions Using Methyl formate

Ligand Investigations



1a 2mmol **2a**

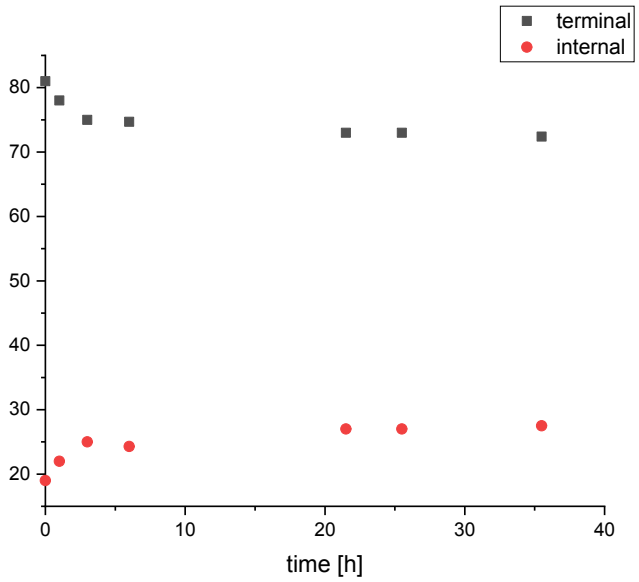
Ligand		Yield
no ligand	-	0 %
	**L1**: R_1=R_2 = ^{t}Bu	0 %
	L2: R_1=R_2 = Ph	0 %
	L3: R_1= ^{t}Bu R_2= 2-py	87 %
	**L4**: R_1=R_4= ^{t}Bu R_2=R_3 = 2-py	9 %
	L5: R_1=R_2=R_3=R_4 = Ph	0 %
	**L6**: R= Ph	0 %
	**L7**: R_1=R_2 = Ph	0 %
	**L8**: R_1=R_2=R_3 = Ph	0 %
	L9: R_1=R_3 = Ph R_2= 2-py	0 %
	L10: R_1=Ph R_2= 2-py R_3 = ^{t}Bu	0 %

Conditions: 2.0 mmol 1a, 1 mol% [Pd], 2 mol% L, 8 mol% PTSA·H_2O, in 2 mL HCO_2Me, 0.5 mL H_20, 100 °C, 12 h.

Catalytic Experiments with Methyl formate

In a typical catalytic experiment, the reaction were performed in 25 mL sealable glass tube with $Pd(OAc)_2$ (0.5 mol%), LIKat Ligand (2.0 mol%), and PTSA·H_2O (8.0 mmol) rapidly weighed in the air. If used, solid substrates (1.0 mmol) were also weighed in the air and added into the tube. The atmosphere in the vial was then changed to argon and 2.0 mL methyl formate, 1.0 mL MeOH, and 0.2 mL H_2O were added. Next, liquid substrates (1.0 mmol) were added and the tube was fitted with a sealed cap. The reaction mixture was stirred at 120 °C for 20 hours. The reaction solution was analysed by gas chromatography using isooctane as internal standard.

DIB ratio of Internal to Terminal during the Reaction



Reference

1. K. Dong, X Fang, S. Gülak, R. Franke, A. Spannenberg, H. Neumann, R. Jackstell, M. Beller, Highly active and efficient catalysts for alkoxycarbonylation of alkenes, *Nat. Commun.*, 2017, **8**, 14117.

2. Y. Nakao, J. Chen, H. Imanaka, T Hiyama, Y. Ichikawa, W-L. Duan, R. Shintani, T. Hayashi, Organo[2-(hydroxymethyl)phenyl]dimethylsilanes as Mild and Reproducible Agents for Rhodium-Catalyzed 1,4-Addition Reactions *J. Am. Chem. Soc.*, 2007, **129**, 9137.

3. Q. Liu, L. Wu, R. Jackstell, M. Beller, Ruthenium-Catalyzed Alkoxycarbonylation of Alkenes with Paraformaldehyde as a Carbon Monoxide Substitute, *ChemCatChem*, 2014, **6**, 2805.

4. W. Tang, W. Wang, X. Zhang, Phospholane–Oxazoline Ligands for Ir-Catalyzed Asymmetric Hydrogenation *Angew. Chem.Int. Ed.*, 2003, **42**, 943.

5. T.O. Vieira, M.J. Green, H. Alper, Highly Regioselective Anti-Markovnikov Palladium-Borate-Catalyzed Methoxycarbonylation Reactions: Unprecedented Results for Aryl Olefins *Org. Lett.*, 2006, **8**, 6143.

6. S. Oi, Y. Honma, Y. Inoue, Conjugate Addition of Organosiloxanes to α,β-Unsaturated Carbonyl Compounds Catalyzed by a Cationic Rhodium Complex *Org. Lett.*, 2002, **4**, 667.

7. Y.N. Cui, J.M. Yin, D.B. Gao, Y.P. Jia, G.Y. Zhou, S.M. Li, Photopromoted methoxycarbonylation of olefin with methyl formate by $Co(OAc)_2$, *Chin. Chem. Lett.,* 2007, **18**, 17.

8. K. Dong, R. Sang, J. Liu, R. Razzaq, R. Franke, R. Jackstell, M. Beller, Palladium-Catalyzed Carbonylation of sec- and tert-Alcohols, *Angew. Chem. Int. Ed.*, 2017, **56**, 6203.

9. L. Wu, Q. Liu, R. Jackstell, M. Beller, Ruthenium-catalyzed alkoxycarbonylation of alkenes using carbon monoxide, *Org. Chem. Front.,* 2015, **2**, 771.

10. C.E. Katz, J. Aubé, Unusual Tethering Effects in the Schmidt Reaction of Hydroxyalkyl Azides with Ketones: Cation−π and Steric Stabilization of a Pseudoaxial Phenyl Group, *J. Am. Chem. Soc.,* 2003, **125**, 13948.

11. B.C. Zhu, X.Z. Jiang, Palladium-catalyzed selective alkoxycarbonylation of N-vinylphthalimide, *Appl. Organomet. Chem.,* 2006, **20**, 277.

12. D. Seyferth, R.E. Mammarella, H.A. Klein, New functional allylic lithium reagents: gem-dialkoxyallyllithium reagents: a useful route to β-silyl- and β-stannylpropionate esters, *J. Organomet. Chem.,* 1980, **194**, 1.

13. R. Sang, P. Kucmierczyk, K. Dong, R. Franke, H. Neumann, R. Jackstell, M. Beller, Palladium-Catalyzed Selective Generation of CO from Formic Acid for Carbonylation of Alkenes, *J. Am. Chem. Soc.*, 2018, **140**, 5217-5223.