Synthesis T. Moragas, R. Martin Paper

Nickel-Catalyzed Reductive Carboxylation of Cyclopropyl Motifs with Carbon Dioxide

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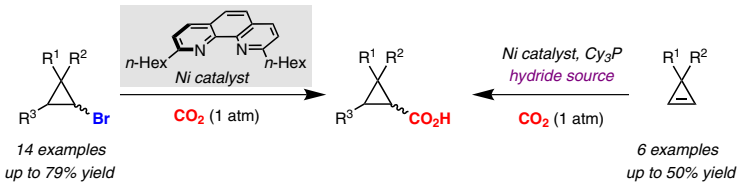
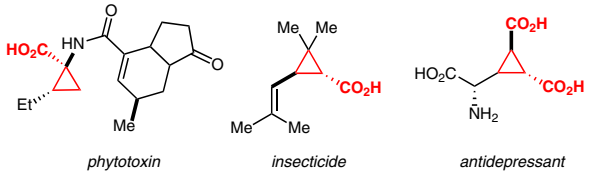


Received: 09.03.2016
Accepted: 13.03.2016
Published online: 11.04.2016
DOI: 10.1055/s-0035-1560439; Art ID: ss-2016-z0171-op

Abstract A nickel-catalyzed reductive carboxylation technique for the synthesis of cyclopropanecarboxylic acids has been developed. This user-friendly and mild transformation operates at atmospheric pressure of carbon dioxide and utilizes either organic halides or alkene precursors, thus representing the first example of catalytic reductive carboxylation of secondary counterparts lacking adjacent π-components.

Key words nickel, carboxylation, cross-coupling, carbon dioxide, catalysis

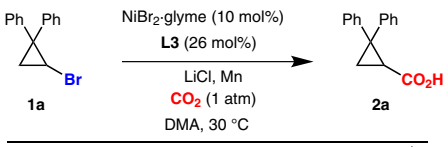
Over the past few years, metal-catalyzed cross-electrophile coupling reactions of organic halides have become powerful alternatives to the well-established cross-coupling reactions based on nucleophilic/electrophilic regimes.[1] Although remarkable levels of sophistication have been reached, the vast majority of these transformations rely on the utilization of homogeneous precursors such as carbonyl compounds or organic halides, among others.[1] Indeed, the employment of heterogeneous coupling partners in these endeavors remains rather unexplored, constituting an opportunity to increase the applicability of these processes. In this context, the design of cross-electrophile coupling reactions based on the utilization of abundant and nontoxic carbon dioxide, probably the greenest C1 source in nature,[2] represents a unique strategy to explore the ability to convert simple precursors into carboxylic acids, molecules of utmost relevance in a wide variety of molecules that display significant biological activities.[3] Unfortunately, the thermodynamic stability and kinetic inertness of carbon dioxide constitute serious drawbacks to be overcome when designing catalytic processes.[2] Driven by the seminal stoichiometric studies reported by Osakada and co-workers,[4] we[5] and others[6] have recently developed a series of metal-catalyzed reductive carboxylation techniques *using organic (pseudo)halides as precursors*. While it might be argued that this field has already reached its full potential, a close look at the developed protocols indicates otherwise. Specifically, while the carboxylation of primary organic (pseudo)halides poses no problems,[5d] the extension to secondary or tertiary motifs is rather problematic, and a solution to this challenge still remains elusive. At present, the catalytic carboxylation of secondary or tertiary organic (pseudo)halides remains limited to substrates containing adjacent π-components such as alkenes,[5c] alkynes[6d] or aromatic motifs.[5e,g,6a,b,e,f] Challenged by such a perception, we wondered whether the ring strain and orbital rehybridization of cyclopropyl rings[7] might facilitate the targeted carboxylation event of secondary cyclopropyl scaffolds, representing a new access to cyclopropanecarboxylic acids, a scaffold that is particularly prevalent in natural products and medicinally important compounds (Scheme 1).[8] Herein, we describe the successful realization of this concept. This transformation is distinguished by its mild reaction conditions and by operating at atmospheric pressure of carbon dioxide, thus constituting a powerful alternative to existing methodologies for preparing cyclopropane-derived carboxylic acids. Interestingly, a different stereoselectivity profile was found when either organic halides or cyclopropenes were employed.



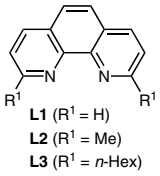
Scheme 1 Representative cyclopropanecarboxylic acids of interest

We started our investigations with bromide **1a** as model substrate (Table 1). After systematic evaluation of all reaction parameters, we found that a combination of $NiBr_2$·glyme (10 mol%), ligand **L3** (26 mol%), manganese as reducing agent and lithium chloride as additive in DMA at 30 °C delivered **2a** in 77% isolated yield. Interestingly, a significant erosion in the yield was observed when the targeted reaction was conducted at higher temperatures (Table 1, entry 2), with ring-opened product **3a** obtained preferentially.[9] Precatalysts other than $NiBr_2$·glyme resulted in a lower efficiency (Table 1, entries 3 and 4). In contrast with other catalytic carboxylation techniques,[5b,d,e] the presence of COD did not significantly inhibit the formation of **2a** (Table 1, entry 3). Although DMF provided nearly identical results as DMA (Table 1, entry 6), further studies demonstrated the superior activity of DMF for less activated substrates. In line with our expectations, the utilization of MeCN, DMSO or the inclusion of zinc as reducing agent resulted in negligible amounts of **2a** (Table 1, entries 5 and 7). Although it might be argued that similar yields were found in the presence or absence of LiCl (Table 1, entries 1 and 8), its presence was crucial for avoiding the formation of **3a**. At present we do not have an explanation for such an observation. In line with other reductive carboxylation techniques,[5,6] the nature of the ligand backbone exerted a profound influence on the reaction outcome. Specifically, we found that while phosphine ligands or bipyridines resulted in lower yields of **2a** (Table 1, entries 14 and 15), phenanthroline backbones were perfectly suited for our purposes (entries 10–13). Furthermore, a subtle balance of electronic and steric effects was critical for success, with ligands possessing *ortho* alkyl motifs and lacking substituents at the *para* positions providing the best results (Table 1, entries 1 and 11 vs 10, 12 and 13). Control experiments revealed that all of the critical reaction parameters [Ni(II) precatalyst, **L3** and Mn] were essential for the reaction.

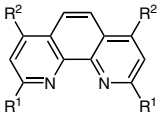
Table 1 Screening of the Reaction Conditions[a]



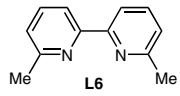
Entry	Deviation from standard conditions	**2a** (%)[b]
1	None	89,77[c]
2	At 60 °C	16
3	$Ni(cod)_2$ (10 mol%) as catalyst	75
4	$Ni(OTf)_2$ (10 mol%) as catalyst	59
5	MeCN (DMSO) as solvent	2(17)
6	DMF as solvent	89
7	Zn as reductant	11
8	No LiCl was added	80
9	Using 10% of **L3**	81
10	Using **L1** as ligand	13
11	Using **L2** as ligand	84
12	Using **L4** as ligand	58
13	Using **L5** as ligand	47
14	Using **L6** as ligand	26
15	Using Cy_3P as ligand	1
16	No $NiBr_2$·glyme or Mn	0



L1 (R^1 = H)
L2 (R^1 = Me)
L3 (R^1 = *n*-Hex)



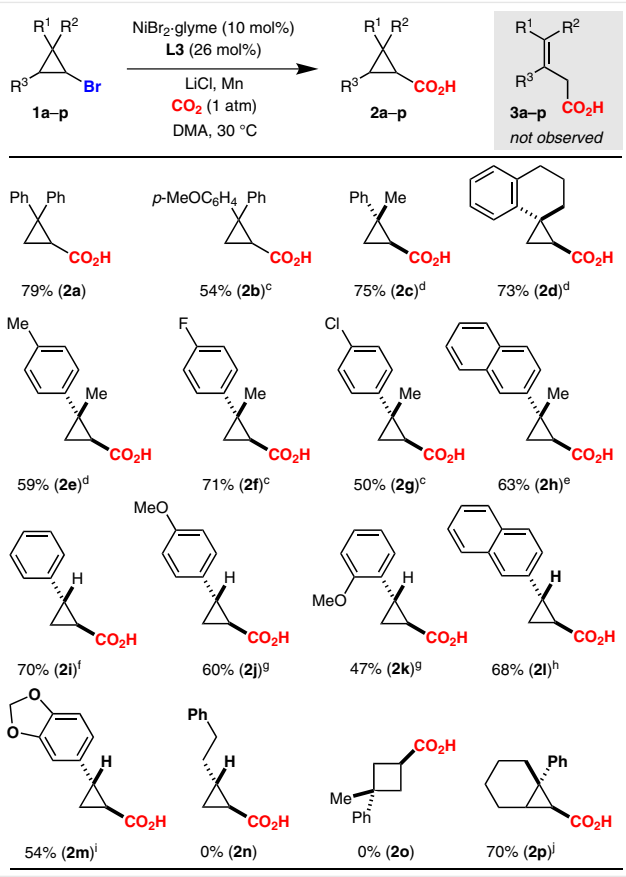
L4 (R^1 = Me; R^2 = Ph)
L5 (R^1 = *n*-Bu; R^2 = Me)



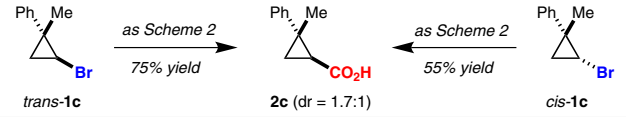
L6

[a] Reaction conditions: **1a** (0.20 mmol), $NiBr_2$·glyme (10 mol%), **L3** (26 mol%), LiCl (0.80 mmol), Mn (0.52 mmol), CO_2 (1 atm), DMA (0.40 M), 30 °C, 40 h.
[b] HPLC yields using anisole as internal standard.
[c] Isolated yield.

With our optimized conditions in hand, we next turned our attention to exploring the generality of our nickel-catalyzed reductive carboxylation of cyclopropyl bromides, precursors that are readily available in multigram quantities from known literature procedures. As shown for **1c**–**h**, cyclopropyl backbones containing alkyl substituents provided similar reactivities to **1a**, resulting in moderate to good yields of the targeted carboxylic acids **2c**–**h** (Scheme 2). It is worth noting, however, that the presence of an aromatic substituent is required for the reaction to occur, as cyclopropyl backbones exclusively containing alkyl residues, such as **1n**, failed to react. Likewise, we found that otherwise related cyclobutyl rings did not deliver the expected carboxylic acid **2o**; while tentative, we believe that the sp^2-like character associated with cyclopropyl rings might be critical,[7] thus allowing for a greater interaction with the nickel precatalyst and enhancing the corresponding carboxylation event. Interestingly, the reaction could be extended to monosubstituted cyclopropyl bromides **1i**–**m**; in all cases, the desired products were obtained in good yields. Notably, these reaction conditions tolerated backbones containing a fluoride (**2f**), chloride (**2g**), methyl ether (**2b**, **2j** and **2k**) or acetal (**2m**) group, residues that are known to participate in nickel-catalyzed cross-coupling reactions.[10] Gratifyingly, the reaction could also be extended to trisubstituted cyclopropyl bromides, as the reaction with **1p** yielded the desired product **2p** in 70% isolated yield. It is worth mentioning that all unsymmetrically substituted cyclopropanecarboxylic acids illustrated in Scheme 2 were obtained as *cis*/*trans* mixtures. In all cases analyzed, the major isomer possessed the aromatic ring and the carboxylic acid in a *trans* configuration, an observation that is in line with other carbometalations of cyclopropyl analogues.[11] Importantly, the *cis*/*trans* ratios observed do not correlate well to the ratios of the starting cyclopropyl bromides, suggesting that radical intermediates might come into play. Such an assumption was further corroborated by the reactions of diastereomerically pure *trans*-**1c** and *cis*-**1c**; invariably, **2c** was obtained with an identical *cis*/*trans* ratio, albeit in different yields (Scheme 3).

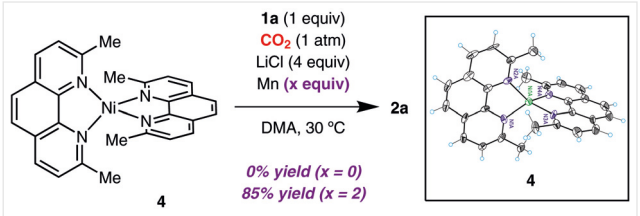


Scheme 2 Carboxylation of cyclopropyl bromides.[a,b] [a] *Reagents and conditions*: **1a–p** (0.20 mmol), $NiBr_2$·glyme (10 mol%), **L3** (26 mol%), LiCl (0.80 mmol), Mn (0.52 mmol), CO_2 (1 atm), DMA (0.40 M), 30 °C, 48 h; [b] Isolated yields, average of at least two independent runs; [c] dr = 1.4:1; [d] dr = 1.7:1; [e] dr = 1.5:1; [f] dr = 5:1; [g] dr = 3.3:1; [h] dr = 4.3:1; [i] dr = 3.6:1; [j] dr = 1.1:1.



Scheme 3 Catalytic carboxylation of *trans*-**1c** and *cis*-**1c**

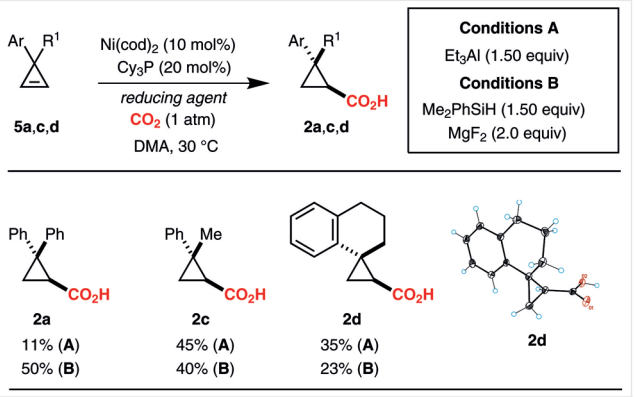
Next, we focused our attention on studying the reactivity of the putative Ni(0)$\mathbf{L_2}$ intermediates. While the isolation of complexes based on **L3** proved particularly cumbersome, we turned our efforts to the synthesis of Ni(0)(**L2**)$_2$ (**4**)[5c,12] as **L2** provided an otherwise analogous reactivity to that observed for **L3** (Table 1, entry 11). In line with our expectations, **4** was found to be competent as precatalyst, delivering **2a** in 66% yield. Stoichiometric experiments revealed that while the presence of 2 equivalents of manganese resulted in an 85% yield of **2a**, no reaction occurred in the absence of manganese (Scheme 4). Whether this result indicates the intermediacy of nickel(I) intermediates[13] or other mechanistic scenarios is a matter of ongoing studies in our laboratories.[14]



Scheme 4 Stoichiometric experiments with **4**

While the successful preparation of cyclopropanecarboxylic acids (Scheme 2) represented the first catalytic reductive carboxylation of secondary organic halides lacking adjacent π-components, the poor stereoselectivity found reinforced a change in strategy. To such end, we wondered whether the use of otherwise related cyclopropenes could promote an analogous hydrocarboxylation event with a higher stereoselectivity profile.[15] After considerable experimentation, we found that a Ni(cod)$_2$/Cy_3P regime based on the employment of Et_3Al or Me_2PhSiH as hydride sources provided the best results (Scheme 5). While moderate yields were generally observed, it is worth noting that the corresponding products **2c**,**d** were obtained as single diastereoisomers. Although careful NMR spectroscopy revealed that the compounds possess a *trans* configuration, the structure of **2d** was unequivocally established by X-ray crystallographic analysis. While the intermediacy of well-defined nickel hydride intermediates might be invoked with a protocol based on Me_2PhSiH,[16] the successful utilization of Et_3Al in these hydrocarboxylation events might suggest the intermediacy of nickelalactones followed by a subsequent transmetalation/β-hydride elimination event.[17,18]

In conclusion, a new nickel-catalyzed reductive carboxylation protocol for the synthesis of cyclopropanecarboxylic acids has been developed using carbon dioxide as C1 synthon. This user-friendly methodology is characterized by its mild conditions at atmospheric pressure of carbon dioxide. This work represents the first time that a catalytic reductive carboxylation of secondary organic halides can be conducted in the absence of adjacent π-components. While poor stereoselectivities were found when utilizing organic halide counterparts, the employment of otherwise related cyclopropenes resulted in single diastereoisomers. Current investigations are focused on extending the scope of these reactions and unraveling the origin of the stereoselectivity found with the cyclopropene analogues.



Scheme 5 Hydrocarboxylation of cyclopropenes **5**. *Reagents and conditions*: A) **5a**,**c**,**d** (0.20 mmol), $Ni(cod)_2$ (10 mol%), Cy_3P (20 mol%), Et_3Al (0.30 mmol), CO_2 (1 atm), DMA (0.40 M), 30 °C, 40 h; B) **5a**,**c**,**d** (0.20 mmol), $Ni(cod)_2$ (10 mol%), Cy_3P (20 mol%), MgF_2 (0.40 mmol), Me_2PhSiH (0.30 mmol), CO_2 (1 atm), DMA (0.40 M), 30 °C, 40 h.

Commercially available materials were used without further purification. Nickel(II) bromide–ethylene glycol dimethyl ether complex ($NiBr_2$·glyme) and manganese powder (99.99% trace metal basis) were purchased from Aldrich. Anhydrous *N*,*N*-dimethylacetamide (DMA, 99.8% purity) was purchased from Acros Organics. Bis(1,5-cyclooctadiene)nickel(0) [$Ni(cod)_2$, 98%+ purity] and tricyclohexylphosphine (Cy_3P) were obtained from Strem. ^1H and ^{13}C NMR spectra were recorded on Bruker 400 MHz and 500 MHz instruments at 20 °C. All ^1H NMR data are reported in parts per million (ppm) downfield of TMS and were measured relative to the signals for $CHCl_3$ (7.26 ppm) or TMS (0.00 ppm). All ^{13}C NMR spectra are reported in ppm relative to residual $CHCl_3$ (77.16 ppm), and were obtained with ^1H decoupling. Coupling constants, *J*, are reported in Hertz. Melting points were measured using open glass capillaries in a Büchi B540 apparatus. Infrared spectra were recorded on a Bruker Tensor 27 spectrometer. Mass spectra were recorded on a Waters LCT Premier spectrometer. High-pressure liquid chromatography (HPLC) was performed on an Agilent Technologies Model 1260 Infinity HPLC instrument equipped with an Agilent Eclipse Plus C18 column (3.5 µm, 4.6 × 100 mm) and UV/vis detector. Flash chromatography was performed with EM Science silica gel 60 (230–400 mesh) and using Hanessian's stain or potassium permanganate as TLC stain. The yields reported in Schemes 2 and 5 refer to isolated yields and represent an average of at least two independent runs.

Nickel-Catalyzed Carboxylation of Cyclopropyl Bromides 1 (Scheme 2); General Procedure

An oven-dried Schlenk tube containing a stirring bar was charged with $NiBr_2$·glyme (0.02 mmol, 10 mol%), **L3** (0.05 mmol, 26 mol%), Mn (0.52 mmol, 2.60 equiv) and LiCl (0.80 mmol, 4 equiv). The Schlenk tube was evacuated and backfilled under CO_2 flow (this procedure was repeated three times). Anhydrous DMA (0.50 mL) and the corresponding cyclopropyl bromide **1** (0.20 mmol, 1 equiv) were then added under CO_2 flow. The Schlenk tube was next closed at atmospheric pressure of CO_2 (1 atm) and the mixture was stirred for 48 h. The mixture was then carefully quenched with 2 M HCl to hydrolyze the resulting carboxylate, and extracted several times with EtOAc and CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The products were purified by flash chromatography (hexanes–EtOAc).

2,2-Diphenylcyclopropanecarboxylic Acid (2a)

Following the general procedure using **1a** (54.6 mg) gave **2a** as a pale yellow solid; yield: 36.7 mg (77%); mp 167–169 °C.

IR ($CDCl_3$): 3027, 1702, 1446, 1221, 903 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.34 (m, 2 H), 7.32–7.14 (m, 8 H), 2.53 (dd, *J* = 8.0, 5.9 Hz, 1 H), 2.14 (dd, *J* = 5.9, 4.8 Hz, 1 H), 1.69 (dd, *J* = 8.1, 4.8 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 176.6, 144.7, 139.9, 129.9, 129.7, 128.7, 128.6, 128.5, 127.7, 127.2, 126.8, 41.2, 28.7, 20.9.

The spectroscopic data for **2a** match those previously reported in the literature.[19]

2-(4-Methoxyphenyl)-2-phenylcyclopropanecarboxylic Acid (2b)

Following the general procedure using **1b** (60.6 mg) gave **2b** as a pale yellow solid; yield: 28.3 mg (53%); *trans*/*cis* = 1.4:1.

IR ($CDCl_3$): 2954, 2929, 1698, 1511, 1245, 1176 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.32 (m, 2 H), 7.31–7.17 (m, 10.11 H), 6.86–6.77 (m, 3.46 H), 3.81 (s, 2.21 H), 3.78 (s, 3 H), 2.49 (ddd, *J* = 14.0, 8.0, 5.9 Hz, 1.73 H), 2.11 (dd, *J* = 5.9, 4.8 Hz, 1.73 H), 1.79–1.57 (m, 1.73 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 176.4, 158.6, 158.4, 145.1, 140.3, 137.0, 132.0, 130.7, 129.5, 128.9, 128.6, 128.5, 127.6, 127.1, 126.7, 114.0, 114.0, 55.4, 55.3, 40.7, 40.4, 28.8, 28.6, 21.1, 20.8.

MS (ESI–): *m*/*z* = 267 [M – H].

HRMS: *m*/*z* calcd for $C_{17}H_{15}O_3$: 267.1027; found: 267.1030.

2-Methyl-2-phenylcyclopropanecarboxylic Acid (2c)

Following the general procedure using **1c** (42.2 mg) gave **2c** as a pale yellow oil; yield: 26.8 mg (76%); *trans*/*cis* = 1.7:1.

IR ($CDCl_3$): 2958, 2928, 1695, 1443, 1427, 1224 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.11 (m, 7.95 H), 2.00 (dd, *J* = 8.1, 6.1 Hz, 1 H), 1.95 (dd, *J* = 7.7, 5.4 Hz, 0.59 H), 1.80 (t, *J* = 5.1 Hz, 0.59 H), 1.59 (s, 3 H), 1.55–1.45 (m, 3.59 H), 1.27 (dd, *J* = 7.7, 4.6 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 178.8, 177.7, 145.6, 141.3, 128.7, 128.5, 128.3, 128.3, 127.4, 126.8, 126.7, 125.8, 33.5, 32.1, 28.7, 28.1, 27.5, 21.5, 20.6, 20.1.

MS (ESI–): *m*/*z* = 175 [M – H].

HRMS: *m*/*z* calcd for $C_{11}H_{11}O_2$: 175.0765; found: 175.0768.

3′,4′-Dihydro-2′*H*-spiro[cyclopropane-1,1′-naphthalene]-2-carboxylic Acid (2d)

Following the general procedure using **1d** (47.4 mg) gave **2d** as a pale yellow solid; yield: 30.8 mg (76%); *trans*/*cis* = 1.7:1.

IR ($CDCl_3$): 2929, 2861, 1690, 1430, 1224 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.24–6.99 (m, 5 H), 6.76–6.62 (m, 1 H), 2.94–2.90 (m, 0.59 H), 2.89 (t, *J* = 6.3 Hz, 2 H), 2.16–2.09 (m, 6.24 H), 2.08–1.73 (m, 6.24 H), 1.67 (dd, *J* = 8.3, 5.4 Hz, 1 H), 1.57 (dd, *J* = 6.5, 5.2 Hz, 1 H), 1.32 (dd, *J* = 7.9, 5.5 Hz, 0.59 H), 1.30–1.19 (m, 0.59 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.5, 176.2, 139.2, 139.1, 138.1, 134.1, 129.3, 128.5, 126.7, 126.4, 126.1, 124.8, 121.9, 35.9, 33.5, 32.2, 32.0, 30.6, 30.4, 29.5, 27.8, 23.3, 22.3, 22.0, 18.6.

MS (ESI–): *m*/*z* = 201 [M – H].

HRMS: *m*/*z* calcd for $C_{13}H_{13}O_2$: 201.0921; found: 201.0923.

2-Methyl-2-(*p*-tolyl)cyclopropanecarboxylic Acid (2e)

Following the general procedure using **1e** (45.0 mg) gave **2e** as a pale yellow oil; yield: 21.7 mg (57%); *trans*/*cis* = 1.7:1.

IR ($CDCl_3$): 2958, 2926, 1695, 1445, 1429, 1223 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.21–7.16 (m, 3.25 H), 7.14–7.02 (m, 3.28 H), 2.33 (s, 3 H), 2.32 (s, 1.88 H), 1.97–1.86 (m, 1.63 H), 1.75 (t, *J* = 5.0 Hz, 0.63 H), 1.55 (s, 3 H), 1.52–1.40 (m, 3.82 H), 1.22 (dd, *J* = 7.7, 4.6 Hz, 0.63 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 178.5, 177.2, 142.8, 138.5, 136.4, 129.3, 129.2, 128.6, 127.4, 33.3, 31.9, 29.0, 28.2, 27.6, 21.6, 21.3, 21.1, 20.7, 20.3.

MS (ESI–): *m*/*z* = 189 [M – H].

HRMS: *m*/*z* calcd for $C_{12}H_{13}O_2$: 189.0921; found: 189.0924.

2-(4-Fluorophenyl)-2-methylcyclopropanecarboxylic Acid (2f)

Following the general procedure using **1f** (45.8 mg) gave **2f** as a pale yellow oil; yield: 30.3 mg (78%); *trans*/*cis* = 1.4:1.

IR ($CDCl_3$): 2958, 2928, 1697, 1512, 1429, 1220 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.22 (m, 3.56 H), 7.09–6.94 (m, 3.28 H), 1.97–1.87 (m, 1.7 H), 1.76 (t, *J* = 5.1 Hz, 0.70 H), 1.56 (s, 3 H), 1.51–1.44 (m, 4.10 H), 1.26 (dd, *J* = 7.7, 4.7 Hz, 0.70 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 178.4, 177.4, 161.8 (d, *J* = 244.8 Hz), 161.7 (d, *J* = 245.2 Hz), 141.5 (d, *J* = 3.2 Hz), 137.2 (d, *J* = 3.2 Hz), 130.3 (d, *J* = 8.0 Hz), 129.2 (d, *J* = 8.0 Hz), 115.4 (d, *J* = 21.5 Hz), 115.3 (d, *J* = 21.3 Hz), 32.8, 31.6, 28.8, 28.3, 27.6, 21.5, 20.8, 20.5.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –116.1.

MS (ESI–): *m*/*z* = 193 [M – H].

HRMS: *m*/*z* calcd for $C_{11}H_{10}FO_2$: 193.0670; found: 193.0672.

2-(4-Chlorophenyl)-2-methylcyclopropanecarboxylic Acid (2g)

Following the general procedure using **1g** (49.1 mg) gave **2g** as a yellow oil; yield: 21.0 mg (50%); *trans*/*cis* = 1.4:1.

IR ($CDCl_3$): 2960, 2927, 1695, 1495, 1448, 1429 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.17 (m, 6.84 H), 2.05–1.91 (m, 1.71 H), 1.76 (t, *J* = 5.1 Hz, 0.71 H), 1.56 (s, 3 H), 1.51–1.42 (m, 4.13 H), 1.28–1.25 (m, 0.71 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.2, 177.2, 144.2, 140.0, 132.6, 132.6, 130.3, 130.2, 129.0, 128.8, 128.6, 126.4, 32.9, 31.6, 28.6, 28.2, 27.6, 21.5, 20.7, 20.2.

MS (ESI–): *m*/*z* = 209 [M – H].

HRMS: *m*/*z* calcd for $C_{11}H_{10}ClO_2$: 209.0375; found: 209.0375.

2-Methyl-2-(naphthalen-2-yl)cyclopropanecarboxylic Acid (2h)

Following the general procedure using **1h** (52.2 mg) gave **2h** as a pale yellow oil; yield: 28.3 mg (63%); *trans*/*cis* = 1.5:1.

IR ($CDCl_3$): 2958, 2925, 1690, 1445, 1427, 1218 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.85–7.77 (m, 4.19 H), 7.77–7.68 (m, 2.21 H), 7.52–7.34 (m, 5.13 H), 2.05 (dd, *J* = 8.1, 6.0 Hz, 1 H), 1.99 (dd, *J* = 7.6, 5.4 Hz, 0.65 H), 1.90 (t, *J* = 5.0 Hz, 0.65 H), 1.63 (s, 3 H), 1.60 (dd, *J* = 8.3, 4.8 Hz, 1 H), 1.56–1.50 (m, 2.95 H), 1.32 (dd, *J* = 7.7, 4.6 Hz, 0.65 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.4, 177.2, 143.1, 139.0, 133.6, 133.5, 132.6, 132.4, 128.4, 128.1, 127.9, 127.8, 127.7, 127.5, 127.0, 126.4, 126.1, 126.0, 125.9, 125.7, 33.7, 32.4, 28.9, 28.3, 27.5, 21.6, 20.9, 20.3.

MS (ESI–): *m*/*z* = 225 [M – H].

HRMS: *m*/*z* calcd for $C_{15}H_{13}O_2$: 225.0921; found: 225.0924.

2-Phenylcyclopropanecarboxylic Acid (2i)

Following the general procedure using **1i** (39.4 mg) gave **2i** as a pale yellow oil; yield: 22.8 mg (70%); *trans*/*cis* = 5.0:1.

IR ($CDCl_3$): 3029, 2927, 1689, 1445, 1231 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.27 (m, 2.98 H), 7.27–7.20 (m, 1.25 H), 7.17–7.10 (m, 1.94 H), 2.70 (td, *J* = 9.0, 7.8 Hz, 0.20 H), 2.62 (ddd, *J* = 9.3, 6.7, 4.1 Hz, 1 H), 2.13 (ddd, *J* = 9.2, 7.7, 5.6 Hz, 0.20 H), 1.93 (ddd, *J* = 8.4, 5.2, 4.1 Hz, 1 H), 1.76 (dt, *J* = 7.8, 5.3 Hz, 0.20 H), 1.68 (dt, *J* = 9.5, 4.9 Hz, 1 H), 1.45–1.40 (m, 1.20 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 179.6, 139.7, 136.0, 129.4, 128.7, 128.1, 127.0, 126.8, 126.4, 27.2, 26.8, 24.1, 21.6, 17.6, 12.3.

The spectroscopic data for **2i** match those previously reported in the literature.[20]

2-(4-Methoxyphenyl)cyclopropanecarboxylic Acid (2j)

Following the general procedure using **1j** (45.4 mg) gave **2j** as a pale yellow solid; yield: 22.9 mg (60%); *trans*/*cis* = 3.3:1.

IR ($CDCl_3$): 2955, 2931, 1694, 1516, 1456, 1249 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.22 (d, *J* = 8.2 Hz, 0.62 H), 7.06 (d, *J* = 8.6 Hz, 2 H), 6.88–6.75 (m, 2.62 H), 3.81 (s, 3.93 H), 2.69–2.61 (m, 0.31 H), 2.57 (ddd, *J* = 9.2, 6.8, 4.2 Hz, 1 H), 2.08 (ddd, *J* = 9.2, 7.9, 5.6 Hz, 0.31 H), 1.83 (ddd, *J* = 8.3, 5.1, 4.0 Hz, 1 H), 1.69 (dt, *J* = 7.7, 5.3 Hz, 0.31 H), 1.63 (ddd, *J* = 9.5, 5.2, 4.5 Hz, 1 H), 1.45–1.40 (m, 0.31 H), 1.39–1.33 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 179.0, 158.5, 158.4, 131.5, 130.3, 127.9, 127.5, 114.0, 113.5, 55.3, 55.2, 26.6, 26.0, 23.5, 21.3, 17.2, 12.2.

The spectroscopic data for **2j** match those previously reported in the literature.[21]

2-(2-Methoxyphenyl)cyclopropanecarboxylic Acid (2k)

Following the general procedure using **1k** (45.4 mg) gave **2k** as a white solid; yield: 18.0 mg (47%); *trans*/*cis* = 3.3:1.

IR ($CDCl_3$): 2928, 1693, 1498, 1459, 1248 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.25–7.12 (m, 1.60 H), 6.96–6.72 (m, 3.60 H), 3.85 (s, 3 H), 3.79 (s, 0.90 H), 2.80 (ddd, *J* = 9.2, 7.0, 4.3 Hz, 1 H), 2.58 (q, *J* = 8.5 Hz, 0.30 H), 2.18–2.07 (m, 0.30 H), 1.82 (dt, *J* = 7.8, 4.8 Hz, 1 H), 1.67–1.54 (m, 1.30 H), 1.49–1.33 (m, 1.30 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 180.4, 178.1, 158.9, 158.5, 130.5, 128.1, 127.9, 127.9, 126.2, 124.9, 120.5, 120.2, 110.5, 110.0, 55.6, 55.4, 22.7, 22.5, 22.3, 20.7, 16.3, 12.6.

The spectroscopic data for **2k** match those previously reported in the literature.[21]

2-(Naphthalen-2-yl)cyclopropanecarboxylic Acid (2l)

Following the general procedure using **1l** (45.4 mg) gave **2l** as a yellow solid; yield: 28.0 mg (66%); *trans*/*cis* = 4.3:1.

IR ($CDCl_3$): 3052, 2927, 1690, 1453, 1435, 1231 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88–7.72 (m, 3.92 H), 7.64–7.57 (m, 1 H), 7.55–7.37 (m, 2.56 H), 7.34–7.14 (m, 1.23 H), 2.90–2.74 (m, 1.23 H), 2.27–2.18 (m, 0.23 H), 2.03 (dt, *J* = 8.7, 4.7 Hz, 1 H), 1.90 (dt, *J* = 7.9, 5.4 Hz, 0.23 H), 1.76 (dt, *J* = 9.5, 4.9 Hz, 1 H), 1.61–1.47 (m, 1.23 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 179.5, 137.1, 133.5, 133.4, 132.7, 132.5, 128.4, 128.2, 127.9, 127.8, 127.7, 127.6, 126.5, 126.0, 125.8, 125.7, 125.1, 124.7, 29.9, 27.5, 27.0, 24.0, 17.6, 12.5.

MS (ESI–): *m*/*z* = 211 [M – H].

HRMS: *m*/*z* calcd for $C_{14}H_{11}O_2$: 211.0765; found: 211.0769.

2-(Benzo[*d*][1,3]dioxol-5-yl)cyclopropanecarboxylic Acid (2m)

Following the general procedure using **1m** (48.2 mg) gave **2m** as a yellow solid; yield: 22.6 mg (55%); *trans*/*cis* = 3.6:1.

IR ($CDCl_3$): 2924, 1689, 1504, 1442, 1233, 1038 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.85–6.68 (m, 1.77 H), 6.68–6.52 (m, 2.06 H), 5.95 (s, 2.56 H), 2.67–2.49 (m, 1.28 H), 2.16–1.99 (m, 0.28 H), 1.89–1.78 (m, 1 H), 1.74–1.52 (m, 1.28 H), 1.44–1.30 (m, 1.28 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 179.4, 176.9, 148.0, 147.4, 146.6, 133.5, 129.9, 122.7, 120.0, 109.9, 108.4, 108.0, 106.9, 101.2, 101.1, 27.2, 26.6, 23.8, 21.5, 17.4, 12.6.

MS (ESI–): *m*/*z* = 205 [M – H].

HRMS: *m*/*z* calcd for $C_{11}H_9O_4$: 205.0506; found: 205.0506.

1-Phenylbicyclo[4.1.0]heptane-7-carboxylic Acid (2p)

Following the general procedure using **1p** (50.2 mg) gave **2p** as a yellow solid; yield: 30.3 mg (70%); *trans*/*cis* = 1.1:1.

IR ($CDCl_3$): 2930, 1692, 1446, 1243 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.26 (m, 4.51 H), 7.25–7.18 (m, 3.45 H), 2.32–2.12 (m, 3.62 H), 2.05 (ddd, *J* = 13.4, 8.4, 6.4 Hz, 0.75 H), 1.96–1.71 (m, 5.57 H), 1.66–1.15 (m, 7.74 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.9, 177.6, 148.9, 144.0, 128.5, 128.3, 128.2, 127.7, 126.4, 126.3, 38.2, 33.4, 32.8, 31.6, 29.2, 27.5, 26.0, 24.2, 22.7, 21.2, 21.13, 21.1, 21.0, 18.5.

The spectroscopic data for **2p** match those previously reported in the literature.[22]

Nickel-Catalyzed Hydrocarboxylation of Cyclopropenes 5 (Scheme 5); General Procedure A

An oven-dried Schlenk tube containing a stirring bar was charged with $Ni(cod)_2$ (0.02 mmol, 10 mol%) and Cy_3P (0.04 mmol, 20 mol%). The Schlenk tube was evacuated and backfilled under CO_2 flow (this procedure was repeated three times). Anhydrous DMA (0.50 mL), the corresponding cyclopropene **5** (0.20 mmol, 1 equiv) and a 1 M solution of Et_3Al in hexanes (0.30 mmol, 1.5 equiv) were then added under CO_2 flow. The Schlenk tube was next closed at atmospheric pressure of CO_2 (1 atm) and the mixture was stirred for 40 h. The mixture was then carefully quenched with 2 M HCl to hydrolyze the resulting carboxylate, and extracted several times with EtOAc and CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The products were purified by flash chromatography (hexanes–EtOAc).

Nickel-Catalyzed Hydrocarboxylation of Cyclopropenes 5 (Scheme 5); General Procedure B

An oven-dried Schlenk tube containing a stirring bar was charged with $Ni(cod)_2$ (0.02 mmol, 10 mol%), Cy_3P (0.04 mmol, 20 mol%) and MgF_2 (0.40 mmol, 2.0 equiv). The Schlenk tube was evacuated and backfilled under CO_2 flow (this procedure was repeated three times). Anhydrous DMA (0.50 mL), the corresponding cyclopropene **5** (0.20 mmol, 1 equiv) and Me_2PhSiH (0.30 mmol, 1.5 equiv) were then added under CO_2 flow. The Schlenk tube was next closed at atmospheric pressure of CO_2 (1 atm) and the mixture was stirred for 40 h. The mixture was then carefully quenched with 2 M HCl to hydrolyze the resulting carboxylate, and extracted several times with EtOAc and CH_2Cl_2. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The products were purified by flash chromatography (hexanes–EtOAc).

***trans*-2-Methyl-2-phenylcyclopropanecarboxylic Acid (*trans*-2c)**

Following general procedure A using **5c** (26.0 mg) gave **2c** as a colorless oil and single stereoisomer; yield: 15.9 mg (45%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.29 (m, 4 H), 7.25–7.18 (m, 1 H), 1.99 (dd, *J* = 8.1, 6.1 Hz, 1 H), 1.58 (s, 3 H), 1.55–1.46 (m, 2 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 178.0, 145.7, 128.7, 127.6, 126.8, 32.2, 27.5, 21.6, 20.3.

***trans*-3′,4′-Dihydro-2′*H*-spiro[cyclopropane-1,1′-naphthalene]-2-carboxylic Acid (*trans*-2d)**

Following general procedure A using **5d** (31.2 mg) gave **2d** as a white solid and single stereoisomer; yield: 14.1 mg (35%); mp 162–164 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.15–7.06 (m, 3 H), 6.81–6.67 (m, 1 H), 2.89 (dd, *J* = 7.1, 5.6 Hz, 2 H), 2.09–1.95 (m, 3 H), 1.89 (dddd, *J* = 12.8, 6.5, 5.6, 3.0 Hz, 1 H), 1.81 (dtd, *J* = 13.2, 7.0, 3.1 Hz, 1 H), 1.68 (dd, *J* = 8.1, 5.2 Hz, 1 H), 1.57 (dd, *J* = 6.5, 5.2 Hz, 1 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 176.7, 139.2, 138.2, 129.3, 126.4, 126.1, 121.9, 31.8, 30.6, 30.4, 27.8, 23.3, 22.3.

Acknowledgment

We thank ICIQ, the European Research Council (ERC-277883), MINECO (CTQ2012-34054 & Severo Ochoa Excellence Accreditation 2014–2018, SEV-2013-0319) and the Cellex Foundation for support. Johnson Matthey, Umicore and Nippon Chemical Industrial are acknowledged for a gift of metal and ligand sources. We sincerely thank M. Martínez for the X-ray crystallographic data.

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1560439.

Primary Data

Primary data for this article are available online at http://www.thieme-connect.com/products/ejournals/journal/10.1055/s-00000084 and can be cited using the following DOI: 10.4125/pd0076th.

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