Ni-Catalyzed Site-Selective Dicarboxylation of 1,3-Dienes with CO_2

Andreu Tortajada,[†] Ryo Ninokata[†] and Ruben Martin[†§]*

†Institute of Chemical Research of Catalonia (ICIQ), The Barcelona Institute of Science and Technology, Av. Països Catalans 16, 43007 Tarragona, Spain

§ ICREA, Passeig Lluís Companys, 23, 08010, Barcelona, Spain

Supporting Information Placeholder

ABSTRACT: A site-selective catalytic incorporation of multiple CO_2 molecules into 1,3-dienes en route to adipic acids is described. This protocol is characterized by its mild conditions, excellent chemo- and regioselectivity and ease of execution under CO_2 (1 atm), including the use of bulk butadiene and/or isoprene feedstocks.

The recent years have witnessed an emerging demand for catalytic techniques that forge multiple C–C bonds via the synergistic combination of chemical feedstocks.[1] Among various conceivable scenarios, a site-selective incorporation of carbon dioxide (CO_2)[2] into olefin feedstocks in the absence of stoichiometric organometallic reagents is of particular relevance,[3] holding promise to streamline the synthesis of industrially-relevant carboxylic acids.[4] Despite the elegant advances realized, these carboxylation protocols remain currently confined to *single* CO_2 insertions (Scheme 1, *paths a & b*).[5] Therefore, the ability to expand the catalytic carboxylation portfolio of C=C bonds beyond *single* CO_2 insertions would be a worthwhile endeavour, opening up new strategies for preparing saturated polycarboxylic acids.[6]

Scheme 1. Carboxylation of Olefinic C=C Bonds.
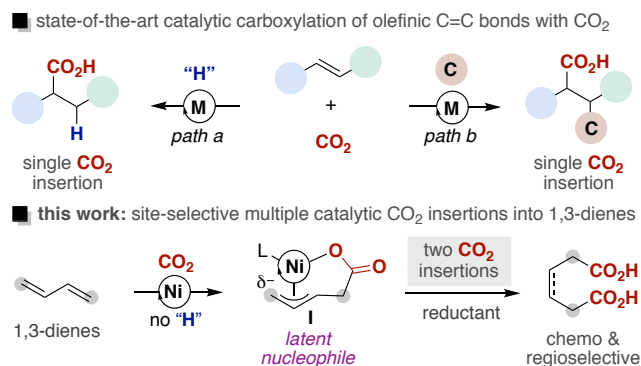
As part of our ongoing interest in CO_2,[7] we questioned whether we could enable a catalytic, site-selective incorporation of *multiple* CO_2 motifs into abundant 1,3-dienes en route to adipic acids,[8] building blocks of particular relevance in the production of plastics and adhesives.[9] If successful, this pathway might also offer an opportunity to complement recent catalytic difunctionalization of 1,3-dienes,[10] as raw materials (CO_2) would be used as electrophilic carbon synthons in lieu of nucleophilic reagents.[11] However, such a scenario bears considerable risk and might seem counterintuitive at first sight due to (a) the proclivity of 1,3-dienes to trigger telomerization reactions[12] and (b) the fact that statistical mixtures of monocarboxylic acids were exclusively observed with hydrocarboxylation conditions previously employed for either alkynes[13] or alkenes,[5b] reinforcing the notion that a multiple, yet controllable, CO_2 insertion event would be particularly problematic. We anticipated that a site-

selective insertion of *multiple* CO_2 units could be rationally controlled in the absence of hydride sources by exploiting the inherent carbogenic nucleophilicity of **I** (Scheme 1, *bottom*).[14] Upon π–σ equilibration, the targeted adipic acids could be obtained by a subsequent regioselective CO_2 incorporation into **I** that precedes a final reduction to recover back the catalytic Ni(0)L$_n$ species. Herein, we report the successful realization of this goal, culminating in a mild method that operates at atmospheric pressure of CO_2 and is characterized by its chemo- and regioselectivity profile, including the ability to use of bulk butadiene and/or isoprene feedstocks.

Table 1. Optimization of the Reaction Conditions.[a]

Entry	Deviation from standard conditions	2a (%)[b,c]
1	*None*	*79, 74[d]*
2	Using NiBr$_2$·glyme	38, 70[e]
3	Using Ni(COD)$_2$	0, 60[e]
4	**L1** instead of **L7**	8
5	**L2** instead of **L7**	46
6	**L3** instead of **L7**	30
7	**L4** instead of **L7**	4
8	**L5** instead of **L7**	56
9	**L6** instead of **L7**	33
10	DMF (NMP) as solvent	30 (44)
11	Zn instead of Mn	41
12	No NiBr$_4$(TBA)$_2$, no **L7** or no Mn	0

[a] **1a** (0.20 mmol), NiBr$_4$(TBA)$_2$ (5 mol%), **L7** (5 mol%), Mn (1.50 equiv), CO_2 (1 bar), DMA (0.5 M), 50 °C. [b] Z/E = 1.4:1 to 5:1. [c] ^{1}H-NMR yields using fluorene as internal standard. [d] Isolated yield. [e] with TBAB (10 mol%). TBAB: tetrabutylammonium bromide, TBA: tetrabutylammonium.

We began our investigations by studying the reaction of **1a** with CO_2 (1 atm). After some experimentation,[15] a cocktail consisting of NiBr$_4$(TBA)$_2$, **L7** and Mn as reductant in DMA at 50 °C furnished **2a** (Z/E = 2.4:1) in 74% isolated yield. It is worth noting that not even traces of **2a'** or telomerization side-products were observed in the crude mixtures. Intriguingly, the absence of ammonium salts resulted in a markedly lower reactivity (entries 2 and 3).[16] A detailed survey of nitrogen-donor ligands revealed that a seemingly trivial modification at C2 was critical for success (entries 4 vs 5-6). Unlike recent reductive carboxylations,[17] the presence of substituents at both 2,2'-positions had a deleterious effect (entry 9 vs 1), thus showing the subtleties of our protocol. The use of other precatalysts (entries 2 and 3), solvents (entry 10) or reductants

(entry 11) had a detrimental impact on reactivity.[18] Notably, identical results were observed regardless of whether (*E*)-**1a** or (*Z*)-**1a** were used, constituting an additional bonus from a synthetic and practical standpoint.[19] As expected, control experiments revealed no product formation when each parameter was omitted from the mixture (entry 12).[15]

Table 2. Ni-catalyzed 1,4-Dicarboxylation of 1,3-Dienes.[a]

[a] As Table 1 (entry 1), followed by exposure to TMSCHN$_2$ and Pd/C (5 mol%), B$_2$(OH)$_4$ (2 equiv) and H$_2$O (5 equiv) at rt. [b] Isolated yields, average of two independent runs, using 1,3-dienes as *E/Z* mixtures. [c] Using **_E_-1a**. [d] dr = 1.5:1. [e] dr = 1:1. [f] 1 mmol scale. [g] Using H$_2$ and Pd/C as reductant. [h] NiBr$_4$(TBA)$_2$ (10 mol%) and **L7** (10 mol%).

Once we established the optimized reaction conditions, we next studied the generality of our catalytic dicarboxylation of 1,3-dienes (Table 2).[19] In situ protection of the carboxylic acid function as the methyl ester and reduction of the pending alkene was necessary to avoid unnecessary purification issues of the resulting adipic acid derivatives.[20] As expected, a host of 1,3-dienes substituted with either aliphatic (**1n-1q**) or aromatic backbones (**1a-1m**) reacted equally well with the NiBr$_4$(TBA)$_2$/**L7** couple. Notably, the outcome of the latter was found to be insensitive to whether electron-rich or electron-poor arenes were employed, even in the

presence of *ortho*-substituents (**1i-1k**). The site-selective incorporation of multiple CO_2 motifs into 1,3-dienes was accompanied by an excellent chemoselectivity, as esters (**3j**, **3k**), nitriles (**3m**), ketones (**3p**) or amides (**3q**) were well-tolerated. Interestingly, the presence of an organo-metallic reagent does not interfere with productive for-mation of **3l**, thus demonstrating the complementarity of our technique with classical nucleophilic/electrophilic regimes.[21,22] Likewise, the reaction could be applied in the presence of heterocyclic cores (**3f**). As illustrated by the successful preparation of **3g** and **3h**, the reaction could also be extended to disubstituted 1,3-dienes, albeit with lower diastereoselectivities. Although C–O electro-philes are inherently predisposed to nickel-catalyzed C–C bond-forming reactions,[23] we found that **3k** could be obtained in 89% yield, leaving ample room for further derivatization via cross-coupling technologies.

Scheme 2. Ni-catalyzed Carboxylation of Diene Feedstocks.
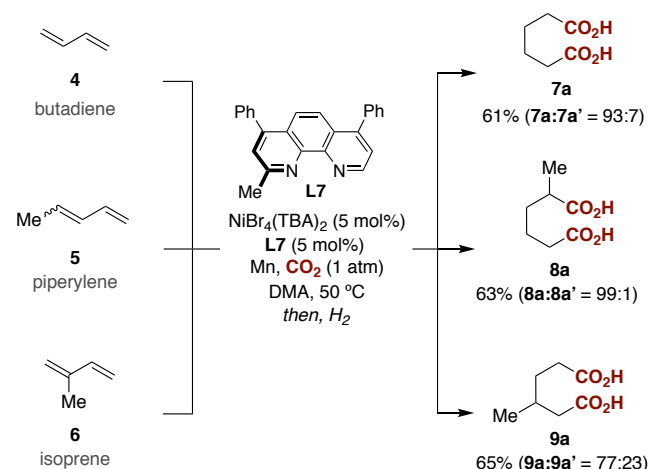
In light of these results, we wondered whether our pro-tocol could be used for the valorization of butadiene, isoprene or piperylene, compounds that are obtained in bulk as byproducts of the steam cracking in the produc-tion of ethylene.[24] As shown in Scheme 2, this turned out to be the case, and **7a-9a** were all obtained in good yields from the corresponding 1,3-diene feedstocks after a subsequent hydrogenolysis event. Strikingly, butadiene **4** resulted in a 93:7 regioselectivity pattern whereas the presence of a methyl group in either **5** or **6** had a non-negligible effect on site-selectivity, with **5** providing the best regiochemical discrimination (**8a**).[25] Although the 1,4–ratio of **7a** and **9a** could partially be improved by using either **L5** or **L2** in lieu of **L7**, significant lower yields were observed in these cases.[15] Taken together, the results summarized in Table 2 and Scheme 2 stand as a testament to the potential of this catalytic technology for enabling a site-selective incorporation of multiple CO_2 units into abundant 1,3-diene precursors.

Scheme 3. Mechanistic Experiments.
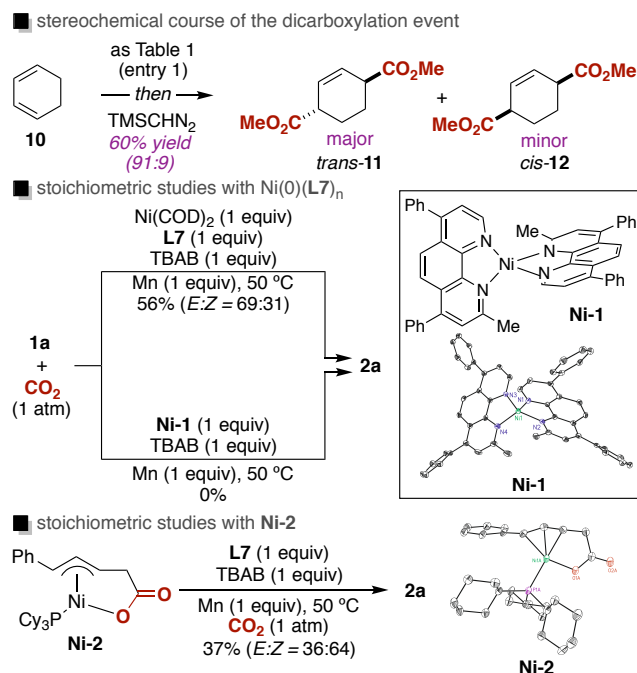
Next, we decided to gather indirect evidence about the mechanism by studying the stereochemical course of **10** with CO_2 (Scheme 3, *top*). Interestingly, *trans*-**11** was preferentially formed over *cis*-**12**, suggesting that the second CO_2 unit is inserted into the π-allyl complex **I** (Scheme 1) via formal backside attack.[26] This seemingly trivial interpretation, however, does certainly not rule out a rapid interconversion of the putative π-allyl nickel complexes upon exposure to Ni(0)(**L7**) prior to CO_2 insertion.[27] Although unraveling the mechanistic under-pinnings of this reaction should await further investiga-tions, we turned our attention to study the reactivity of **Ni-1** (Scheme 3, *middle*). This complex was easily pre-pared by exposure of **L7** and Ni(COD)$_2$ in benzene at 40 ºC, the structure of which was univocally determined by X-ray crystallography.[15] Interestingly, the reactivity of **Ni-1** with **1a** was not comparable to that observed with Ni(COD)$_2$/**L7**, with not even traces of **2a** being observed in the former.[28] While one might attribute this finding to the non-innocent role of COD,[29] the reluctance of coordinatively saturated **Ni-1** to dissociate **L7** prior to 1,3-diene binding seems more likely. Unfortunately, the preparation of π-allyl complex **I** (Scheme 1) in pure analytical form bearing **L7** as ligand proved to be par-ticularly elusive. Gratifyingly, we could prepare struc-turally-related **Ni-2**, and the η³-hapticity of the allyl motif was finally revealed by X-ray structure analysis (*bottom*).[15] Interestingly, we found that **Ni-2** only fur-nished **2a** in the presence of both **L7** and Mn.[15,30] Whether these results suggest that single-electron trans-fer processes come into play via putative Ni(I) species[31] or invoke other mechanistic interpretations is the subject of ongoing studies.

In summary, we have documented a site-selective, catalytic incorporation of *multiple* CO_2 molecules into abundant 1,3-dienes, thus giving access to adipic acids from simple and available precursors. The salient features of this method are its excellent regio- and chemoselectivity, mild conditions and ease of execution. Further extensions to other hydrocarbons, including asymmetric transformations, are currently in progress.

ASSOCIATED CONTENT

Supporting Information. Experimental procedures, crystallographic data and spectral data. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

* rmartinromo@iciq.es

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(19) The mass balance accounts for unreacted starting material and competitive polymerization of the 1,3-diene. Notably, no reaction took place under CO_2 pressure (10 bars).

(20) Regardless of whether aromatic or aliphatic dienes were employed, *Z:E* selectivities ranging from 1.5:1 to 2.5:1 were obtained. Competitive olefin isomerization was prevented by conducting the hydrogenolysis with $B_2(OH)_4$-H_2O: Cummings, S. P.; Le, T.-N.; Fernandez, G. E.; Quiambao, L. G.; Stokes, B. J. *J. Am. Chem. Soc*. **2016**, *138*, 6107.

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Ni catalyst / **Ligand**

1,3-dienes + CO_2 → latent nucleophile → CO_2H / CO_2H

22 examples
up to 90% yield

Site-selective incorporation of multiple CO$_2$ motifs
Excellent chemo- & regioselectivity profile
Wide scope & mild conditions