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Palladium-Catalyzed [3+2] Cycloaddition of Carbon Dioxide and Trimethylenemethane under Mild Conditions

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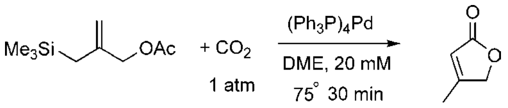
ABSTRACT



Carbon dioxide undergoes a Pd-catalyzed [3+2] cycloaddition with trimethylenemethane (TMM) under mild conditions (1 atm, 75 °C, 30 min) to produce a γ-butyrolactone product in 63% yield, when the Pd–TMM complex is generated from 2-(acetoxymethyl)-3-(trimethylsilyl)propene. The reaction reported here is more rapid than the all-carbon [3+2] cycloaddition, and only the γ-butyrolactone is produced in a competition experiment. With substituted substrates, the reaction is completely regioselective, producing the product derived from the kinetic Pd–TMM complex.

The development of new methods for the utilization of carbon dioxide is an area of considerable current interest because carbon dioxide is both a greenhouse gas and a cheap and abundant source of carbon atoms.[1,2] Transition metals have been shown to be effective at activating the relatively unreactive CO_2 molecule,[3,4] and reactions in which a metal complex *catalyzes* a transformation of carbon dioxide are especially appealing.[5] Some recently reported examples include the reaction of CO_2 with epoxides[6−8] or aziridines,[9] the nickel-catalyzed carboxylation of 1,3-dienes with CO_2 and dialkylzinc reagents,[10−12] and the cycloaddition of diynes with CO_2 to give α-pyrones.[13,14] The drawback of many of these methods is the requirement for high pressures of carbon dioxide, thus limiting their synthetic utility. In addition, most research into cycloaddition reactions has focused on the incorporation of CO_2 into even sized rings since 2 carbon and 4 carbon components are readily available. Herein we report a Pd-catalyzed [3+2] cycloaddition reaction between carbon dioxide and a series of 2-trimethylsilylmethyl-2-propenyl acetates to produce substituted γ-butyrolactones that takes place efficiently under 1 atm of carbon dioxide (eq 1).

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(1) Arakawa, H.; Aresta, M.; Armor, J. N.; Barteau, M. A.; Beckman, E. J.; Bell, A. T.; Bercaw, J. E.; Creutz, C.; Dinjus, E.; Dixon, D. A.; Domen, K.; Du Bois, D. L.; Eckert, J.; Fujita, E.; Gibson, D. H.; Goddard, W. A.; Goodman, D. W.; Keller, J.; Kubas, G. J.; Kung, H. H.; Lyons, J. E.; Manzer, L. E.; Marks, T. J.; Morokuma, K.; Nicholas, K. M.; Periana, R.; Que, L.; Rostrup-Nielson, J.; Sachtler, W. M. H.; Schmidt, L. D.; Sen, A.; Somorjai, G. A.; Stair, P. C.; Stults, B. R.; Tumas, W. *Chem. Rev.* **2001**, *101*, 953−996.

(2) Sakakura, T.; Choi, J. C.; Yasuda, H. *Chem. Rev.* **2007**, *107*, 2365−2387.

(3) Yin, X.; Moss, J. R. *Coord. Chem. Rev.* **1999**, *181*, 27−59.

(4) Aresta, M.; Quaranta, E.; Tommasi, I.; Giannoccaro, P.; Ciccarese, A. *Gazz. Chim. Ital.* **1995**, *125*, 509−538.

(5) Louie, J. *Curr. Org. Chem.* **2005**, *9*, 605−623.

(6) Coates, G. W.; Moore, D. R. *Angew. Chem., Int. Ed.* **2004**, *43*.

(7) Darensbourg, D. J. *Chem. Rev.* **2007**, *107*, 2388−2410.

(8) Paddock, R. L.; Nguyen, S. T. *J. Am. Chem. Soc.* **2001**, *123*, 11498−11499.

(9) Miller, A. W.; Nguyen, S. T. *Org. Lett.* **2004**, *6*, 2301−2304.

(10) Takimoto, M.; Mori, M. *J. Am. Chem. Soc.* **2001**, *123*, 2895−2896.

(11) Takimoto, M.; Mori, M. *J. Am. Chem. Soc.* **2002**, *124*, 10008−10009.

(12) Takimoto, M.; Nakamura, Y.; Kimura, K.; Mori, M. *J. Am. Chem. Soc.* **2004**, *126*, 5956−5957.

(13) Tekavek, T. N.; Arrif, A. M.; Louie, J. *Tetrahedron* **2004**, *60*, 7431−7437.

(14) Louie, J.; Gibby, J. E.; Farnworth, M. V.; Tekavek, T. N. *J. Am. Chem. Soc.* **2002**, *124*, 15188−15189.

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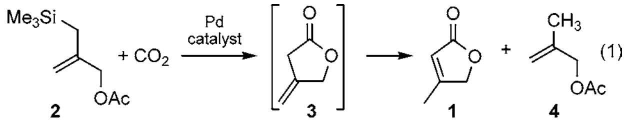
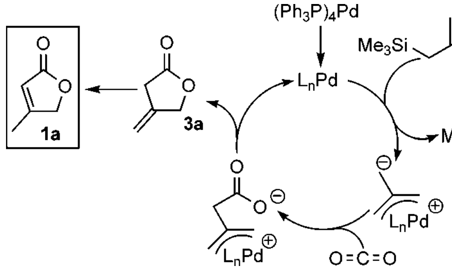


(1)

The Pd-catalyzed [3+2] cycloaddition of methylenecyclopropane (MCP) with carbon dioxide to form γ-butyrolactones was initially reported by Inoue in 1979[15] and further studied by Binger.[16] While yields of compound **1a** as high as 80% can be obtained under the proper conditions, the reaction only succeeds under CO$_2$ pressures of 40 atm and temperatures greater than 130 °C, thus severely limiting its utility. It is also plagued by the fact that Pd catalyzes the reaction of product **1a** with more MCP, leading to higher oligomers.[16] It is believed that the mechanism of this reaction involves oxidative addition of Pd(0) into the cyclopropane ring to produce an η^3-Pd trimethylenemethane (TMM) complex, which is an excellent all-carbon 1,3-dipole (see Scheme 1 for a drawing of the Pd−TMM complex). The electron-rich end can attack the carbonyl carbon of CO$_2$, while the electron-poor end can accept electron density from the oxygen. Pd−TMM complexes have been implicated as intermediates in a wide variety of catalytic reactions,[17] but they are too unstable to isolate and characterize. As a result, they must always be generated from an appropriate precursor as an initial step in a catalytic cycle.

Scheme 1. Possible Catalytic Cycle



Another precursor to Pd−TMM complexes is commercially available and readily prepared 2-(acetoxymethyl)-3-(trimethylsilyl)propene (**2a**). This molecule has been extensively used by Trost as a 3-atom partner in [3+2] cycloadditions with both C=C and C=O double bonds as the two-atom component.[17−21] Compound **2a** participates in many of the same reactions as MCP, but the conditions are generally milder, and product selectivity can be realized if substituted versions of **2** are employed.

Heating a THF solution of **2a** under reflux overnight with 8 mol % of (PPh$_3$)$_4$Pd under 1 atm of carbon dioxide results in the smooth formation of γ-butyrolactone **1a** in which the carbon and one oxygen atom from CO$_2$ have been incorporated into the 5-membered ring. The initial cycloadduct is almost certainly compound **3a**, but it is never detected; the C=C double bond presumably undergoes a facile isomerization to an endocyclic position in conjugation with the carbonyl group under the reaction conditions. A possible mechanism for this reaction is depicted in Scheme 1.

On the basis of NMR and GC/MS analysis of the crude product mixture, other products that could be identified were "higher order" cycloadducts in which more than one molecule of **1a** was co-oligomerized with CO$_2$ (Figure 1), oligomers of compound **2a** that do not contain CO$_2$, and methallyl acetate (**4**) obtained through protodesilylation of **2a**.

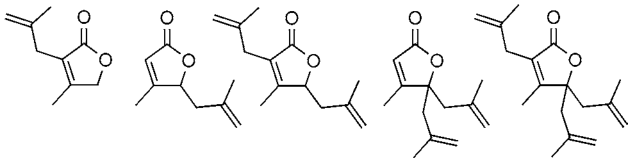


Figure 1. Higher order cycloadducts of TMM and CO$_2$.

These byproducts were not unexpected: the "higher order" cycloadducts were observed by Binger when methylenecyclopropane was used as the Pd−TMM precursor, and compound **4** was present in many of Trost's reactions.

Having demonstrated the feasibility of the [3+2] cycloaddition with carbon dioxide as the 2-atom component, we sought to optimize the reaction. In our initial experiments, which employed typical conditions for [3+2] cycloaddition reactions of **2a**,[22] the isolated yield of **1a** was 25%. Variables that we investigated included the concentration, temperature, reaction time, stirring rate, solvent, and ligands around palladium. We found that concentration was the factor most responsible for higher order cycloadducts, and their formation was suppressed at lower concentrations, until they were barely detectable at a substrate concentration of 20 mM. Since no further improvement was observed with additional dilution, a concentration of 20 mM was employed in all subsequent studies.

The suppression of non-CO$_2$ containing products required maximum exposure of the reaction solution to CO$_2$. When the reaction was stirred *rapidly* under a CO$_2$ atmosphere for 5 min at room temperature, then heated to 60 °C for 1.5 h, **1a** and **4** were the only products detected by GC. The isolated yield of **1a** under these conditions was 62% (Table 1, entry 1). Using NMR spectroscopy, we determined the yield for this reaction to be 69% by integrating the NMR signal for the methyl groups of durene (1,2,4,5-tetramethylbenzene)

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(15) Inoue, Y.; Hibi, T.; Satake, M.; Hashimoto, H. *J. Chem. Soc., Chem. Commun.* **1979**, 982.

(16) Binger, P.; Weintz, H. J. *Chem. Ber.* **1984**, *117*, 654−665.

(17) Trost, B. M. *Angew. Chem., Int. Ed.* **1986**, *25*, 1−20.

(18) Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1979**, *101*, 6429−6432.

(19) Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1979**, *101*, 6432−6433.

(20) Trost, B. M.; Mignani, S. M.; Nanninga, T. N. *J. Am. Chem. Soc.* **1986**, *108*, 6051−6053.

(21) Trost, B. M.; Stambuli, J. P.; Silverman, S. M.; Schworer, U. *J. Am. Chem. Soc.* **2006**, *128*, 13328−13329.

(22) Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1983**, *105*, 2315−2325.

Table 1. Optimization of the Pd-Catalyzed Cycloaddition of **2a** and Co$_2$ To Produce **1a**

entry	catalyst	conditions	yield (%)
1	$(Ph_3P)_4Pd$	THF, 1.5 h, 60 °C	69,[b] 62[c]
2	$(Ph_3P)_4Pd$	THF, 3 h, 50 °C	45[a]
3	$(Ph_3P)_4Pd$	DME, 0.5 h, 75 °C	72,[a] 69,[b] 55[c]
4	$(Ph_3P)_4Pd$	PhH, 20 h, 60 °C	63[c]
5	$(Ph_3P)_4Pd$	PhMe, 24 h, 75 °C	31[b]
6	$(Ph_3P)_4Pd$	DMF, 18 h, 55 °C	19[a]
7	$Pd(OAc)_2 + 4\ PPh_3$	THF,18 h, 55 °C	42[a]
8	$Pd(OAc)_2 + 3\ PPh_3$	THF, 18 h, 55 °C	46[a]
9	$Pd(OAc)_2 + 2\ PPh_3$	THF, 3.5 h, 55 °C	0[a]
10	$Pd(OAc)_2 + 3\ P(OiPr)_3$	THF, 18 h, 55 °C	0[a]
11	$Pd(OAc)_2 + 5\ P(OiPr)_3$	THF, 18 h, 50 °C	minimal[a]
12	$Pd(OAc)_2 + 8\ P(OiPr)_3$	THF, 21 h, 50 °C	minimal[a]
13	$Pd(OAc)_2 + 4\ PCy_3$	THF, 18 h, 55 °C	0[a]
14	$Pd(OAc)_2 + 4\ P(o\text{-tol})_3$	THF, 72 h, 55 °C	0[a]
15	$Pd(OAc)_2$ + 2 dppe	THF, 48 h, 55 °C	minimal[a]
16	$Pd(OAc)_2$ + 2 BINAP	THF, 18 h, 55 °C	0[a]

[a] GC yield. [b] NMR yield. [c] Isolated yield

against the signal for the methyl group of **1a**. Presumably, carrying out the reaction at a temperature below the boiling point of the solvent allows a greater partial pressure of CO_2 above the solution, and an increased concentration of CO_2 in solution. However, we also observed that if the temperature is reduced too much, the amount of undesired **4** increases at the expense of **1a**. In a reaction run at 50 °C, the GC yield of **1a** determined with mesitylene as an internal standard and correcting for the response factor of mesitylene was 45% (entry 2).

The need to keep the temperature close to, but below the boiling point of THF proved inconvenient, so we screened several higher boiling solvents. Similar yields were obtained in DME at 75 °C; at this temperature the reaction is complete in 30 min (entry 3). Benzene or toluene could be used as solvents (entries 4 and 5), but the rate is much slower—requiring overnight reaction at 75 °C to go to completion, and the yield is reduced in toluene. DMF is also an acceptable solvent, but once again, the GC yield is lower (entry 6).

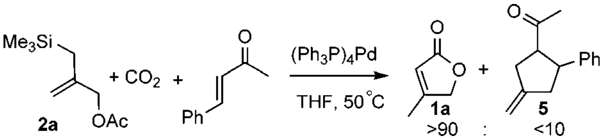
To vary the phosphine ligands, we generated a catalyst in situ by mixing palladium(II) acetate with the desired phosphine. We validated the in situ catalyst generation by carrying out experiments with triphenylphosphine and comparing the results to those obtained with $(Ph_3P)_4Pd$. With 3 or 4 equiv of PPh_3 relative to Pd, the yields are slightly lower than with $(Ph_3P)_4Pd$, but the reaction is clearly successful (entries 7 and 8). In contrast, if only 2 equiv of PPh_3 are added, there is no conversion of substrate **2a**, and palladium black is observed in the flask (entry 9).

Trost reported that triisopropyl phosphite is another successful ligand in Pd-catalyzed all-carbon [3+2] cycloaddition reactions.[23] However, the same is not true for the reaction with carbon dioxide (entries 10−12). Even with 8 equiv of $P(OiPr)_3$ relative to Pd, there is minimal conversion of **2a** to **1a**. No reaction was observed at all when the larger ligands PCy_3 and $P(o\text{-tol})_3$ were added to Pd (entries 13 and 14), and the bidentate phosphines dppe and BINAP were equally unsuccessful (entries 15 and 16). Presumably, ligands that are too large or coordinate to the metal too tightly are unsuccessful because they do not permit both CO_2 and the substrate to approach the coordination sphere. Given that this ligand screen sampled phosphines with a variety of steric and electronic properties, and none were nearly as successful as triphenylphosphine, no other ligands were screened.

On the basis of the conditions we screened, the optimal procedure for substrate **2a** consists of using 8 mol % of $Pd(PPh_3)_4$ as the catalyst with a substrate concentration of 20 mM in DME as the solvent.

Several control experiments were carried out to demonstrate that the use of **2a** as a Pd−TMM precursor is required for the formation of **1a** under such mild conditions. Specifically, **2a** was recovered unchanged after a THF solution was heated overnight under CO_2 in the absence of palladium. Interestingly, the formation of byproduct **4** also requires palladium, since none of it was formed in the absence of palladium. Furthermore, when diphenylmethylenecyclopropane, a substrate known to undergo the [3+2] reaction with CO_2 under high temperatures and pressures,[16] was synthesized and subjected to the mild reaction conditions, there was no reaction. In another experiment, a solution of substrate **2a** was stirred with $Pd(PPh_3)_4$ under nitrogen instead of under CO_2. Complete consumption of **2a** in the absence of CO_2 requires 2 h instead of 30 min; the products are various sized oligomers of TMM.

Of particular interest is the fact that the [3+2] cycloaddition between **2a** and CO_2 is more rapid than the cycloaddition between **2a** and an alkene, which suggests that CO_2 is involved in the rate-limiting step of the mechanism. In a competition experiment, an equimolar ratio of **2a** and benzylideneacetone (an alkene typically employed by Trost as a 2-atom component in the [3+2] cycloaddition)[22] was heated to 50 °C under a CO_2 atmosphere in the presence of the palladium catalyst. The reaction is slower than in the absence of benzylideneacetone: 6 h are required for complete consumption of **2a**, but most importantly, the ratio of CO_2 cycloadduct **1a** to the all carbon cycloadduct (**5**) is >9:1 by GC, and most of the benzylideneacetone was not consumed (eq 2).



(2)

To examine the scope and regioselectivity of the reaction, we synthesized methylated substrates **2b**,[24] **2c**,[24] and **2d** as described in the Supporting Information. All three methylated

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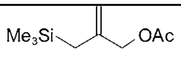
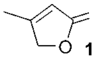
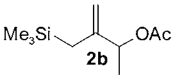
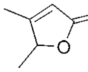
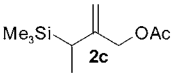
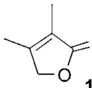
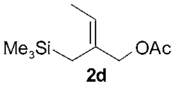
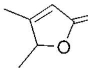
(23) Trost, B. M.; Nanninga, T. N.; Satoh, T. *J. Am. Chem. Soc.* **1985**, *107*, 721−723.

(24) Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1981**, *103*, 5972−5974.

substrates participate in the cycloaddition as shown in Table 2. However, the reaction conditions for the cycloaddition were not individually optimized for each substituted substrate.

Table 2. Substrates for Pd-Catalyzed Cycloaddition

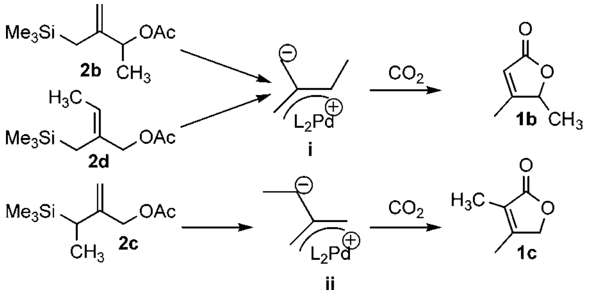
entry	substrate	product	% yield
1	 **2a**	 **1a**	69[a], 62[b]
2	 **2b**	 **1b**	46[b]
3	 **2c**	 **1c**	47[a], 35[b]
4	 **2d**	 **1b**	32[a], 27[b]

[a] NMR yield. [b] Isolated yield.

Unlike in the case of the all-carbon [3+2] cycloaddition,[24] the product depends on the structure of the starting material. Specifically, the product obtained from reaction of **2b** or **2d** contains the methyl group at the 5-position of the furanone ring (**1b**), whereas reaction of substrate **2c** gives a product with the methyl group at the 3-position of the ring (**1c**).

The rate of the reaction also depends on the structure of the starting material. Reactions starting with **2c** are faster than those starting with **2a**, while reactions starting with **2b** or **2d** are slower (but still not as slow as the all-carbon [3+2]). On the basis of the product regiochemistry and the relative rate observations, we believe that in all cases the product is formed from attack of the kinetic Pd−TMM complex (**i** or **ii**) on CO_2 (Scheme 2), and that cycloaddition is faster than isomerization. This is in contrast with the all-carbon reaction where isomerization to the thermodynamic Pd−TMM complex (**ii**) with the methyl group on the anionic carbon precedes cycloaddition,[24] but consistent with a recently reported [3+3] cycloaddition involving compounds **2b** and **2c**.[25] The formation of product **1b** from either **2b** or **2d** suggests that complex **i** is formed from each of these substrates, and unlike in the case of the all-carbon [3+2], this intermediate is competent to undergo the cycloaddition with CO_2, albeit more slowly than complex **ii** does.

Scheme 2. Kinetic Pd−TMM Complexes



In summary, we have developed an efficient Pd-catalyzed [3+2] cycloaddition of 2-(trimethylsilylmethyl)allyl acetates with carbon dioxide to produce γ-butyrolactones under mild conditions (1 atm of CO_2, 75 °C, 30 min). Further investigations of the scope and mechanism of this reaction are in progress.

Acknowledgment. We thank the donors of the American Chemical Society Petroleum Research Fund and Goucher College for financial support of this research.

Supporting Information Available: Discussion of substrate synthesis, and full experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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(25) Shintani, R.; Hayashi, T. *J. Am. Chem. Soc.* **2006**, *128*, 6330−6331.