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Efficient Nickel-Catalyzed [2 + 2 + 2] Cycloaddition of CO_2 and Diynes

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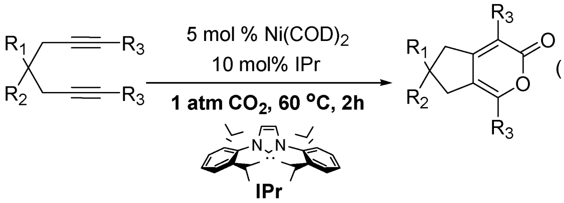
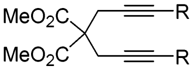
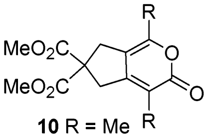
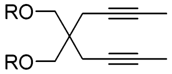
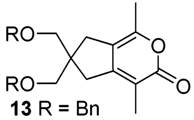
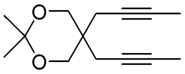
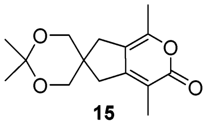
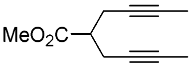
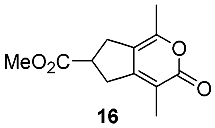
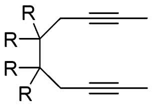
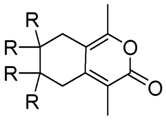
Carbon dioxide is an environmental friendly, nontoxic, nonflammable, and abundant resource.[1] However, because its π orbitals are filled and relatively low in energy, the molecule is highly inert. Thus, the use of CO_2 as a feedstock for forming new carbon−carbon bonds remains a challenging goal for organic chemists. While a number of processes for activating CO_2 exist, they generally involve the use of high pressures, high temperatures, harsh conditions (i.e., Grignard reactions), or all of the above. Some of these obstacles have been overcome with the development of metal (nickel or palladium) complexes that mediate the oxidative couplings of CO_2 with various unsaturated hydrocarbons.[2,3] While they permit the use of CO_2 under atmospheric pressures, stoichiometric amounts of metal are necessary. A few catalytic systems have been developed; however, they require much harsher conditions (high pressures of CO_2 and high temperatures), and only a limited range of substrates can be used.[4] Herein, we report a mild and efficient protocol for catalyzing the [2 + 2 + 2] cycloaddition of diynes and CO_2.[5] The method uses low catalyst loadings and atmospheric pressures of CO_2 and provides a convienent route to pyrones, which are versatile synthetic building blocks[6] and a common structural motif in many natural products.[7]



(1)

The cycloaddition of CO_2 and dimethyl 2,2-*di*-but-2-ynylmalonate (**1**) was chosen as the model reaction, and conditions were limited to using atmospheric pressures of CO_2, low temperatures, and short reaction times. A variety of ligands (amines, phosphines, and imidazolylidenes) in combination with $Ni(COD)_2$[8] were screened for catalytic activity; however, only with the use of *N*-heterocyclic carbenes such as 1,3-bis-(2,6-diisopropylphenyl)-imidazol-2-ylidene) (IPr) or 1,3-bis(1,3,5-trimethyl)-imidazol-2-ylidene (IMes) were appreciable amounts of pyrone detected.[9] Solvent, temperature, concentration, and the initial catalyst-to-ligand ratio were all found to be important factors that affected the yields of pyrone. No reaction was observed in acetone, acetonitrile, methylene chloride, hexanes, pyridine, or diethyl ether which is likely due to the instability or insolubility of Ni intermediates in these solvents. As expected, no product was formed in the absence of either ligand or $Ni(COD)_2$. Ultimately, quantitative yields (as determined using gas chromatography) were obtained using 5 mol % of $Ni(COD)_2$, 10 mol % of IPr,[10] and a substrate concentration of 0.1 M in toluene, benzene, or THF at 60 °C (eq 1).

Table 1. Ni-Catalyzed Cycloaddition of Diynes and Carbon Dioxide[a]

Entry	Substrate	Product	% Yield[b]
1	 **1** R = Me	 **10** R = Me	93%
	2 R = Et	**11** R = Et	94%
	3 R = *i*Pr	**12** R = *i*Pr	86%
2	 **4** R = Bn	 **13** R = Bn	93%
	5 R = TBDMS	**14** R = TBDMS	92%
3	 **6**	 **15**	96%
4	 **7**	 **16**	82%
5	 **8** R = CO_2Et	 **17** R = CO_2Et	97%
	9 R = H	**18** R = H	75%

[a] Reactions conditions: 5 mol % $Ni(COD)_2$, 10 mol % IPr, 0.10 M substrate in toluene at 60 °C, 2 h. [b] Isolated yields (average of at least two runs).

A variety of internal diynes were subjected to the Ni-catalyzed cycloaddition under these optimized conditions (Table 1). The reaction tolerated both acid- and base-sensitive functional groups such as esters, ethers, and siloxanes, and a variety fused five- and six-membered rings were prepared. In addition, the unsubstituted diyne (e.g., **9**) afforded the corresponding pyrone (**18**) in good yield.

All attempts to decrease the catalyst loading below 5 mol % led to incomplete conversion of diyne substrates, even at elevated temperatures and prolonged reaction times. However, using the isolated, well-defined complex $Ni(IPr)_2$ as the catalyst,[11] loadings could be decreased to 1 mol %, although higher substrate concentrations (>0.75 M) were necessary to achieve high conversions.

The mechanism is believed to involve an initial [2 + 2] cycloaddition of CO_2 and a single alkynyl unit of the substrate (**19**) (Scheme 1).[12] Subsequent insertion of the second pendant alkynyl unit followed by a carbon−oxygen bond-forming reductive elimination would then release the pyrone product and regenerate the catalyst (NiL_n). In accord with the proposed mechanism, no con-

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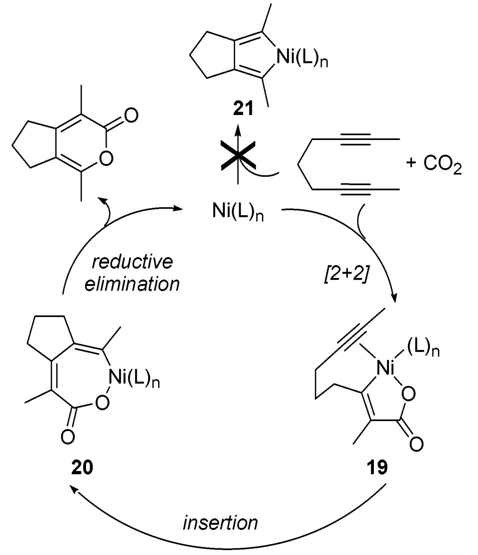
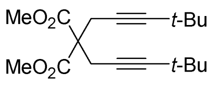
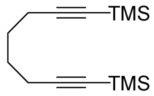
Scheme 1. Proposed Mechanism of Ni-Catalyzed [2 + 2 + 2] Cycloaddition of Diynes and CO_2



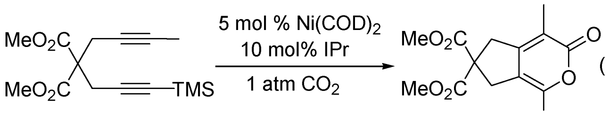
version was observed for sterically hindered diynes **22** and **23**. Interestingly, the proposed mechanism suggested that asymmetrical diynes that possess at least one unhindered alkyne may undergo a regioselective cyclization. This was tested by analyzing the cycloaddition product of the asymmetric diyne **24** with CO_2. Only one pyrone regioisomer (**25**) was observed and isolated in 83% yield (eq 2). Initial [2 + 2] addition of the relatively unhindered methyl-terminated alkyne and CO_2 followed by insertion of the TMS-terminated alkyne explains the observed regioselectivity.



22



23



24 **25**

Further support for this mechanism was obtained from monitoring the reaction between $Ni(IPr)_2$ and diyne or CO_2 by ^1H NMR spectroscopy. Unlike other Ni(0) complexes,[9] $Ni(IPr)_2$ did not readily react with diyne **1** to form nickelole **21** at room temperature. In fact, even under reaction conditions (2 h, 60 °C), the reaction between **1** and $Ni(IPr)_2$ was slow. Furthermore, the addition of CO_2 at this point did not lead to pyrone formation. In contrast, $Ni(IPr)_2$ reacted quantitatively with CO_2 at room temperature.[13] Subsequent addition of diyne (2 h, 60 °C) yielded pyrone quantitatively. It is likely that the steric bulk of the IPr ligand (relative to phosphines, amines, and other imidazolylidenes[9]) shields the Ni(0) complex from an unproductive reaction with the diyne (to form nickelole complexes such as **21**). In addition, the increased steric bulk and electron-donating character of the IPr ligand may facilitate reductive elimination from **20**.[14]

In conclusion, we have developed a mild and efficient method for the preparation of pyrones from diynes and CO_2. The reaction employs catalytic amounts of Ni(0) and IPr ligand, atmospheric pressures of CO_2, and mild reaction conditions. We are currently working toward expanding the substrate scope, enhancing catalyst performance, and increasing our mechanistic understanding of this reaction.

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Supporting Information Available: Detailed experimental procedures and compound characterization (PDF). This material is available free of charge via the Internet at http://pubs.acs.org/.

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(9) Although both IMes and IPr facilitated the formation of product, yields were significantly higher with the use of IPr. Preliminary experiments suggest that $Ni(IMes)_2$ undergoes an unproductive reaction with diynes, both in the presence and absence of CO_2.
(10) Alternatively, a combination of $IPrBF_4$ and KO-t-Bu, *in lieu* of IPr, can be used without loss of catalytic activity.
(11) The preparation of $Ni(IPr)_2$ is not as straightforward as reported (Böhm, V. P. W.; Gstöttmayr, C. W. K.; Weskamp, T.; Herrmann, W. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 3387). We found that $Ni(COD)_2$ and IPr exist in equilibrium with $Ni(IPr)_2$ and COD ($K_{eq} = 1$). Thus, we believe that generation of the catalyst in situ from the combination of $Ni(COD)_2$ and IPr is a more practical approach.
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