Organic LETTERS

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CO_2 as a C1 Source: $B(C_6F_5)_3$-Catalyzed Cyclization of *o*-Phenylenediamines To Construct Benzimidazoles in the Presence of Hydrosilane

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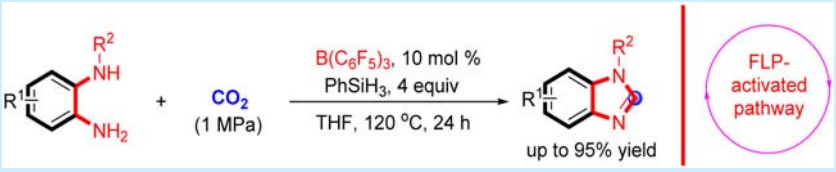
Supporting Information



ABSTRACT: The catalytic construction of benzimidazoles using CO_2 as a carbon source represents a facile and sustainable approach to obtaining these valuable compounds. Herein, we describe the $B(C_6F_5)_3$-catalyzed synthesis of benzimidazoles via cyclization of *o*-phenylenediamines with CO_2 and $PhSiH_3$. This metal-free catalytic route achieves the desired products in high yield under convenient reaction conditions and is applicable to a broad substrate scope. A plausible mechanism for the reaction involving a frustrated Lewis pair pathway is proposed based on spectroscopic characterization (e.g., ^{13}C NMR) of the reaction intermediates.

Carbon dioxide (CO_2) has increasingly been used in synthetic chemistry applications as one of the most economical, abundant, and nontoxic C_1 sources.[1] Meanwhile, CO_2 fixation has become a significant area of research due to global warming concerns.[2] In the past decade, many studies have been conducted on reactions using CO_2 as a raw material for the preparation of formic acid, methanol, carbonates, and amides.[3] These methods usually involve expensive transition-metal catalysts, such as ruthenium,[4] rhodium,[5] nickel,[6] cobalt,[7] iridium,[8] and palladium.[9] However, since CO_2 is relatively unreactive, reactions that can efficiently convert CO_2 into valuable organic compounds are still long-standing goals in chemistry.

Benzimidazoles are ubiquitous motifs in natural products and biologically active molecules. As a result of their wide application in many areas such as in antimicrobial compounds, anthelmintic and antipsychotic drugs, and antiulcer and anticancer agents, benzimidazoles have gained considerable attention.[11−15] Generally, benzimidazoles are prepared from *o*-phenylenediamine and carbonyl compounds. The construction of benzimidazoles using CO_2 as the carbon sourceis an environmentally friendly method, for which several approaches have been reported. N-heterocyclic carbene IPr-catalyzed imidazole formation starting from *o*-diamines and CO_2 in the presence of hydrosilanes was reported by Cantat and co-workers. The use of metal catalysts, such as $RuCl_2(dppe)_2$ and Au/TiO_2, has been documented for the cyclization of *o*-phenylenediamines/2-nitroanilines to produce benzimidazoles under a CO_2/H_2 atomosphere.[17] Liu and co-workers further developed an efficient route to prepare benzimidazoles from CO_2 and *o*-phenylenediamines following a metal-free method; however, 1 equiv of ionic liquid [Bmim][OAc] was required for this transformation.[18] Very recently, a moderate yield of benzimidazole was obtained from a reaction in DMSO or γ-valerolactone, in which the solvent plays a vital role in promoting the reaction between CO_2 and *o*-phenylenediamine.[19]

A remarkable increase in the development of frustrated Lewis pairs (FLPs) toward the activation of small molecules (e.g., H_2 and olefins), even in the development of metal-free homogeneous catalysis, has occurred in recent years.[20−22] FLPs based on amine-borane compounds have been shown to be especially effective at activating CO_2.[23] Therefore, we hypothesized that $B(C_6F_5)_3$ would react with *o*-phenylenediamine and form an amine-borane Lewis pair. Accordingly, thermodynamically stable CO_2 can be converted into useful benzimidazoles by the *in situ* formed FLP. As part of our ongoing interest in homogeneous catalysis promoted by FLPs,[24] we herein describe the $B(C_6F_5)_3$ catalyzed cyclization of *o*-phenylenediamines and CO_2 in the presence of hydrosilanes (Scheme 1b).

Initially, we began our studies by testing the reactions between commercially available 1,2-diaminobenzene **1a** and hydrosilane in the presence of 10 mol % $B(C_6F_5)_3$ under a CO_2 atmosphere in a PTFE-lined autoclave. First, various solvents, including aprotic and protonic media, were surveyed at 140 °C (Table 1, entries 1−5). The solvent used in the reaction greatly affected the

Received: October 26, 2016
Published: December 2, 2016

DOI: 10.1021/acs.orglett.6b03030
Org. Lett. 2016, 18, 6316−6319

Scheme 1. Synthesis of Benzimidazoles

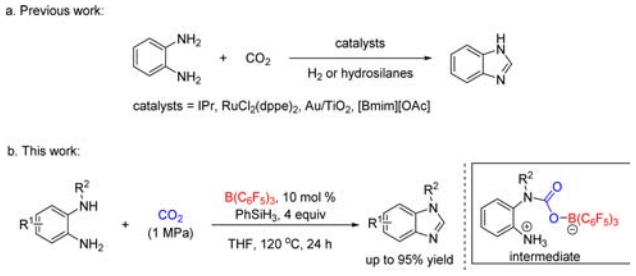
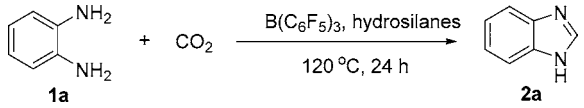


Table 1. Optimization of Reaction Conditions[a]



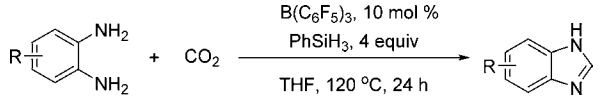
entry	hydrosilane (equiv)	temp (°C)	solvent	yield (%)[b]
1[c]	$PhSiH_3$ (4)	140	Et_2O	trace
2[c]	$PhSiH_3$ (4)	140	EtOH	trace
3[c]	$PhSiH_3$ (4)	140	toluene	no reaction
4[c]	$PhSiH_3$ (4)	140	CH_3CN	46
5[c]	$PhSiH_3$ (4)	140	THF	81
6	$PhSiH_3$ (4)	140	THF	84
7[d]	$PhSiH_3$ (4)	140	THF	51 (45)
8	$PhSiH_3$ (4)	120	THF	83
9	$PhSiH_3$ (4)	100	THF	16 (73)
10	$PhSiH_3$ (3)	120	THF	72
11[e]	$PhSiH_3$ (4)	120	THF	84
12	–	120	THF	no reaction
13[f]	$PhSiH_3$ (4)	120	THF	trace
14[g]	Ph_3SiH (4)	120	THF	10 (32)
15	Ph_2SiH_2 (4)	120	THF	28 (51)

[a]The reactions were carried out in a PTFE-lined autoclave with **1a** (0.2 mmol), hydrosilane (0.8 mmol), and $B(C_6F_5)_3$ (0.02 mmol) in 2 mL of solvent under 1.0 MPa of a CO_2 atmosphere. [b]Isolated yields; recovery of substrate in parentheses. [c]Under 3 MPa of CO_2. [d]Under 0.5 MPa of CO_2. [e]36 h. [f]Without $B(C_6F_5)_3$. [g]1,3-Dihydro-2*H*-benzo[*d*]imidazol-2-one was formed in 50% yield.

outcome. When Et_2O or EtOH was used as the solvent, only trace products were detected (Table 1, entries 1 and 2). No reaction occurred in toluene (Table 1, entry 3). The cyclization proceeded smoothly using CH_3CN or THF as the solvent, giving 46% and 81% yields, respectively (Table 1, entries 4 and 5). Next, we tested the influence of the CO_2 pressure on the reaction. The yield of benzimidazole was slightly improved from 81% to 84% by reducing the pressure of CO_2 from 3 to 1 MPa (Table 1, entry 5 vs 6). The reaction in the presence of 0.5 MPa of CO_2 resulted in a moderate yield (Table 1, entry 7). Further optimization showed that lowering the reaction temperature or reducing the amount of $PhSiH_3$ decreased the yield of compound **2a** (Table 1, entries 9 and 10). Additionally, a longer reaction time did not obviously improve the yield (Table 1, entry 11). When the reaction was performed in the absence of $PhSiH_3$ or $B(C_6F_5)_3$, no reaction occurred (Table 1, entries 12 and 13). Under these optimized conditions, the use of Ph_3SiH or Ph_2SiH_2 in place of $PhSiH_3$ resulted in poor reactivity in this transformation (Table 1, entries 14 and 15), and the main product was 1,3-dihydro-2*H*-benzo-[*d*]imidazol-2-one in the presence of Ph_3SiH.

Using the optimized reaction conditions, a variety of *o*-phenylenediamines were evaluated (Table 2). The *o*-phenylenediamines bearing electron-donating and -withdrawing groups

Table 2. Scope of Cyclization of *o*-Phenylenediamines with CO_2[a]



entry	substrate	product	yield (%)[b]
1	1a	2a	83
2	1b	2b	85
3	1c	2c	58
4	1d	2d	61
5	1e	2e	62
6	1f	2f	76
7	1g	2g	25
8	1h	2h	87
9	1i	2i	95
10	1j	2j	94
11	1k	2k	53
12	1l	2l	79
13	1m	2m	88
14	1n	2n	-

[a]The reactions were carried out in a PTFE-lined autoclave with **1a** (0.2 mmol), $PhSiH_3$ (0.8 mmol), and $B(C_6F_5)_3$ (0.02 mmol, 10 mol %) in 2 mL of THF under 1 MPa of CO_2 at 120 °C. [b]Isolated yields.

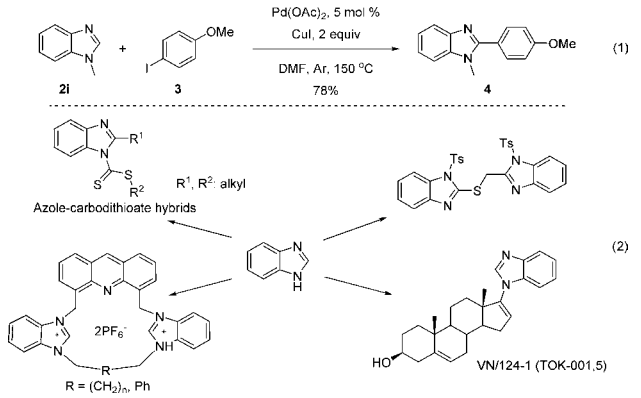
were tolerated well under the reaction conditions, affording the desired benzimidazoles in moderate to good yields (Table 2, entries 1–6). Notably, the steric hindrance of substituted

DOI: 10.1021/acs.orglett.6b03030
Org. Lett. 2016, 18, 6316–6319

diaminobenzene had a noteworthy impact on the reaction outcome: the reaction of *para*-substituted diaminobenzene (**1b**) led to an 85% yield, whereas the *ortho*-substituted diaminobenzene (**1c**) furnished the corresponding product in a 58% yield. Additionally, the nitro-substituted **1g** resulted in an inferior yield of benzimidazole **2g** (Table 2, entry 7). In addition, the heterocyclic compound **2h** was produced as the sole product in 87% yield, when pyridine-3,4-diamine (**1h**) was employed under the optimized reaction conditions (Table 2, entry 8). The cyclization of *N*-methyl- or *N*-ethyl-substituted *o*-phenylenediamine (**1i**, **1j**, and **1m**) with CO_2 proceeded smoothly, affording the *N*-substituted-benzimidazoles in excellent yields (Table 2, entries 9, 10, and 13). In addition, the substrate with an *N*-isopropyl group (**1k**) gave the product in moderate yield because of steric hindrance of the substituent, whereas *N*-benzyl-*o*-phenylenediamine (**1l**) was transformed into benzimidazole (**2l**) in 79% yield. However, the reaction did not occur when *N*-phenyl-*o*-phenylenediamine (**1n**) was tested (Table 2, entry 14).

To show the utility of the benzimidazole product, further transformations were studied. The arylation of 1-methyl-1*H*-benzo[*d*]imidazole (**2i**) with 1-iodo-4-methoxybenzene (**3**) yielded the desired coupling product **4** in 78% yield in the presence of $Pd(OAc)_2$ and CuI (Scheme 2, eq 1).[25] According to

Scheme 2. Transformations of Benzimidazole Products



reported methods, benzimidazoles can also be transformed into a number of bioactive compounds that can be used as antitumor, antibacterial, and antifungal agents, etc. (Scheme 2, eq 2).[26]

We next focused on elucidating the mechanism of the cyclization of *o*-phenylenediamines. Reportedly, CO_2 reacts with *N*,*N*′-(1,4-phenylenebis(methylene))-bis(2-methylpropan-2-amine) (**5**) in the presence of $B(C_6F_5)_3$, resulting in a N-bound CO_2 adduct (**6**) (Figure 1a: ^{13}C NMR, 159.4 ppm).[23a] Therefore, we carried out a similar ^{13}C NMR experiment to prove that the reaction was achieved via the FLP mechanism. A 3-ppm downfield shift of the aromatic resonance was observed upon mixing of *o*-phenylenediamine and $B(C_6F_5)_3$, indicating the formation of an FLP (Figure 1b vs c). Subsequent introduction of CO_2 resulted in a new resonance at 163.14 ppm attributable to the N-bound CO_2 adduct (Figure 1d).[23a] A similar shift was also observed in ^{11}B NMR spectra (Figures S2 and S4, Supporting Information). Based on these observations, a plausible mechanism for the formation of benzimidazoles via an FLP pathway from *o*-phenylenediamine (**1a**) and CO_2 in the presence of $B(C_6F_5)_3$ is depicted in Scheme 3. First, *o*-phenylenediamine (**1a**) and $B(C_6F_5)_3$ react with CO_2 to form the N-bound CO_2 adduct **7**. Next, $PhSiH_3$ is activated by $B(C_6F_5)_3$ and then coordinates with adduct **7** to provide the intermediate **8**.[27] Then,

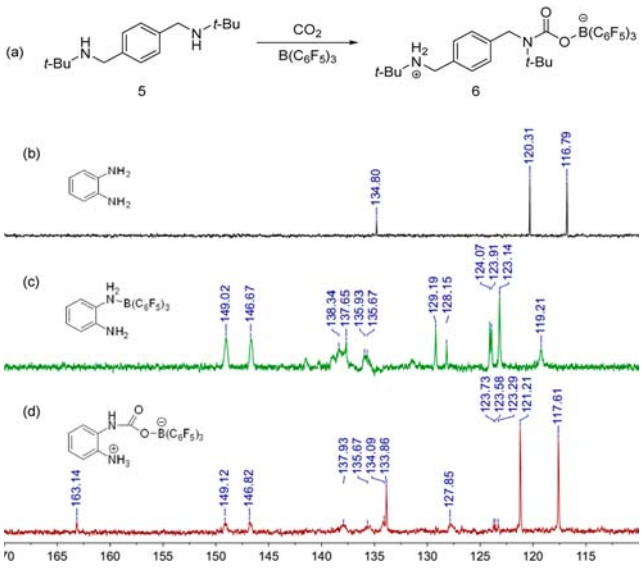
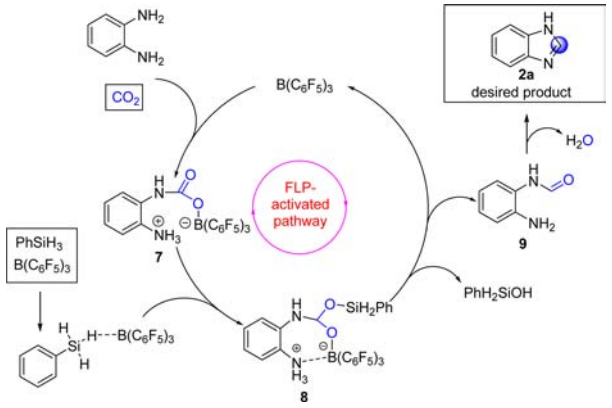


Figure 1. ^{13}C NMR analysis of the reaction.

Scheme 3. Plausible Mechanism of the $B(C_6F_5)_3$ Catalyzed Synthesis of Benzimidazole from *o*-Phenylenediamine, CO_2, and $PhSiH_3$



$B(C_6F_5)_3$ is removed to provide the intermediate formamide **9**. Next, the dehydration and cyclization of the resulting species **9** occurs to provide the desired product benzimidazole (**2a**).

In summary, we have described a metal-free and efficient approach to the preparation of benzimidazoles from *o*-phenylenediamines and CO_2 catalyzed by $B(C_6F_5)_3$ in the presence of hydrosilane via an FLP pathway. Notably, CO_2 is utilized as a C_1 source, and a metal-free method is involved in the synthesis of potentially medicinal benzimidazoles, thereby making it an environmentally benign process. Further studies are underway to understand the role of $B(C_6F_5)_3$ in the activation of CO_2 and to explore new applications of $B(C_6F_5)_3$.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b03030.

Experimental details and NMR data (PDF)

DOI: 10.1021/acs.orglett.6b03030
Org. Lett. 2016, 18, 6316−6319

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work was supported by the National Natural ScienceFoundation of China (21473226 and 21133011).

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DOI: 10.1021/acs.orglett.6b03030
Org. Lett. 2016, 18, 6316−6319