

NHC Catalyzed Transformation of Aromatic Aldehydes to Acids by Carbon Dioxide: An Unexpected Reaction[†]

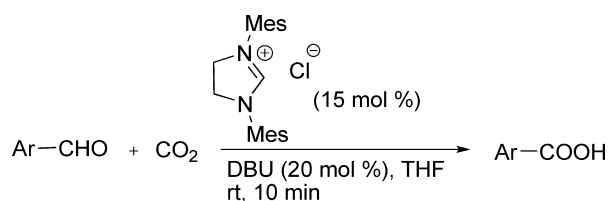
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Received April 19, 2010

ABSTRACT



A facile NHC-mediated reaction of aromatic aldehydes with carbon dioxide leading to carboxylic acids is described. The present protocol is mechanistically important, and it can serve as a tool for the sequestration of carbon dioxide.

In nature, decarboxylation of pyruvic acid to an acetal anion equivalent¹ is initiated by the coenzyme thiamine pyrophosphate (TPP), the modus operandi as elucidated by Breslow² involves the deprotonation of the thiazolium ring of TPP and addition of the resulting ylide to pyruvate to form a tetrahedral intermediate. The latter, by virtue of the thiazolium moiety serving as an “electron sink”, undergoes isomerization to an enamino. In his seminal work, Breslow has shown that a variety of azolium species afford the ylides which react with aldehydes to form the corresponding enamino (Breslow intermediate), and the latter participate in benzoin condensation in a manner akin to the acetoin synthesis in nature. In recent years, the chemistry of azolium ylides, popularly known as nucleophilic heterocyclic carbenes (NHC),³ has received considerable attention as ligands for

transition metals,⁴ building blocks in heterocyclic construction,⁵ and catalysts in a number of synthetic transformations⁶ especially in the area of homoenolate reactions.^{7,8} During the course of our work involving NHCs, we were intrigued by the possibility of trapping the Breslow intermediate with CO₂ to afford aryl glyoxylic acids (Scheme 1). Notwithstanding the unfavorable thermodynamic factors, this seemingly simple idea was considered worthy of pursuit because of the known facile transformation of the latter to mandelic acids⁹ and arylglycine derivatives which are building blocks for pharmaceuticals and other valuable materials.¹⁰

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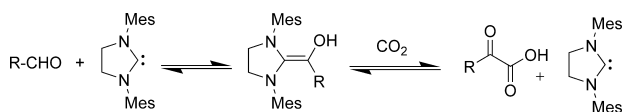
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Scheme 1. Concept of Glyoxylic Acid Synthesis



Conceivably, the carboxylation envisioned above would provide a simple route for the synthesis of value-added products and in turn open up a potentially useful approach to the sequestration of CO₂,^{11,12} culpable for the green house effect and global warming. In this context, it is noteworthy that the reaction of NHCs and imidazoles with CO₂ resulting in the carboxylates is known in the literature,¹³ and the latter have been proposed as carriers of NHCs as well as CO₂. NHC-catalyzed reaction of CO₂ with propargylic alcohols and epoxides leading to carbonates is also known.¹⁴ Recently, Zhang and coworkers have reported the NHC-catalyzed reduction CO₂ to methanol.¹⁵ Subsequently, while this work was under completion, the same group reported the NHC-catalyzed reaction of CO₂ with aldehydes leading to carboxylic acids.¹⁶

In a prototype experiment designed to test the validity of the concept outlined above (Scheme 1), *p*-fluorobenzaldehyde (1 equiv) and 1,3-dimesityl-4,5-dihydro-1*H*-imidazol-3-ium (SIMes) chloride (0.15 equiv) were taken in THF. After the addition of DBU (0.2 equiv), the solution was stirred in a CO₂ atmosphere (balloon). After 16 h, the reaction mixture was quenched with hydrochloric acid (1 N, 5 mL) and extracted with DCM. The organic layer on usual processing and chromatography afforded a colorless crystalline solid that to our surprise was found to be *p*-fluorobenzoic acid (mp

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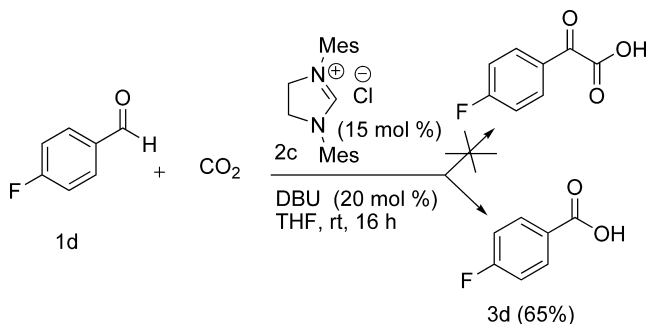
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182–184 °C). Interestingly, not even a trace of *p*-fluorophenylglyoxylic acid was obtained from the reaction mixture (Scheme 2). Although the conceptualization of a novel

Scheme 2



synthesis of phenyl glyoxylic acid did not materialize, the preparative value of this transformation proceeding under mild conditions and its mechanistic importance prompted us to pursue the reaction in some detail.

Subsequent to the preliminary experiments, it was found that the reaction worked more efficiently when a slow stream of CO₂ was passed through the solution of the aldehyde and the catalyst for 10 min; the product was obtained in 72% yield. A number of commonly used NHC catalysts were screened for assessing their utility in optimizing this reaction, and the results are summarized in Table 1.

Table 1. Catalyst Screening

entry	catalyst	condition	yield ^a (%)
1	2a	THF, rt, 10 min	0
2	2b	THF, rt, 10 min	61
3	2c	THF, rt, 10 min	72
4	2d	THF, rt, 10 min	5

^a Isolated yield. **2a**: R = phenyl. **2b**: R = 2,4,6-trimethylphenyl. **2c**: R = 2,4,6-trimethylphenyl.

The reaction was extended to a number of aldehydes, and the products were characterized by conventional spectroscopic methods and by comparison to the data available in the literature.^{17,18} The results are presented in Table 2. From our studies, it was found that in general best results were obtained when THF was used as the solvent, the exception being benzaldehyde and 3,4-dimethoxybenzaldehyde which gave better results in acetonitrile.

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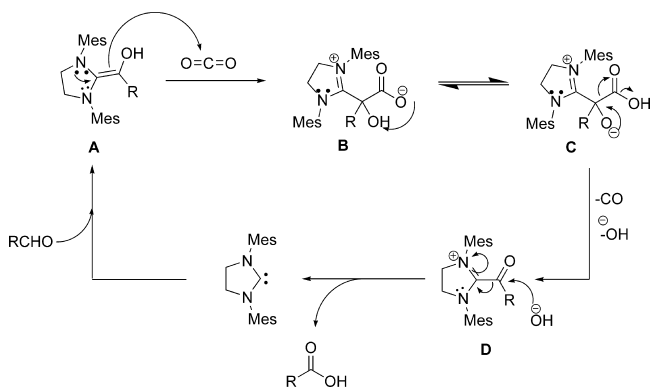
(17) All of the compounds reported here in are known in the literature; most of them are commercially available.

Table 2. Substrate Scope

R-CHO + CO ₂		2c (15 mol %)		DBU (20 mol %), THF		R-COOH	
1				rt, 10 min		3	
entry	R-	product	yield ^{a,b} (%)				
1	3,4-dichlorophenyl	3a	92 (95)				
2	4-trifluoromethylphenyl	3b	90 (94)				
3	phenyl	3c	86 ^c (88)				
4	4-fluorophenyl	3d	72 (84)				
5	4-nitrophenyl	3e	76 (85)				
6	2-thienyl	3f	72 (78)				
7	4-bromophenyl	3g	71 (79)				
8	4-chlorophenyl	3h	70 (85)				
9	2-furyl	3i	65 (72)				
10	4-methylphenyl	3j	62 (71)				
11	3,4-dimethoxyphenyl	3k	60 ^c (69)				
12	2-bromophenyl	3l	56 (70)				
13	4-methoxyphenyl	3m	36 (57)				

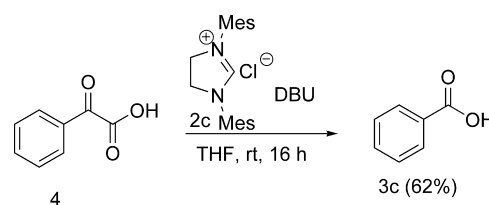
^a Isolated yield. ^b Yield based on recovered aldehyde. ^c CH₃CN (80 °C, 30 min).

In the absence of any oxidant or source of oxygen in the reaction mixture, it was surmised that carbon dioxide is undergoing reduction to CO and in the process the aldehyde is getting oxidized to acid. Mechanistically, the reaction may be viewed as occurring via the addition of carbon dioxide to the readily formed Breslow intermediate A to afford the hydroxycarboxylate B and the tautomer C. Conceivably, the latter can lose CO and hydroxide (cf. decomposition of formate) to afford the benzoic acid (Scheme 3). Support for

Scheme 3. Proposed Mechanistic Pathway

this hypothesis was obtained by the detection of CO in the reaction mixture.¹⁹

It may be mentioned that species D is generally invoked as an intermediate in the oxidative esterification of aldehydes. Gratifyingly, indirect evidence for the mechanistic postulate outlined above was accrued by the formation of benzoic acid when phenylglyoxylic acid was exposed to NHC under the same experimental conditions in which benzaldehyde was transformed to benzoic acid (Scheme 4).

Scheme 4

It is noteworthy that Gu and Zhang also have identified CO in the effluent gases, and a mechanistic scheme for the reduction of CO₂ has been presented.¹⁶ However, it is unlikely that their postulate is correct, since a preformed NHC-carboxylate depicted as intermediate in their work failed to react with aldehyde to afford the acid.

In conclusion, we have encountered a facile NHC-mediated reaction of carbon dioxide and aldehyde leading to carboxylic acid under simple, mild, experimental conditions. In addition to the preparative utility of the present protocol, its potential value in the sequestration of CO₂ cannot be underestimated, especially in the current era of global warming.

Acknowledgment. V.N. thanks the Department of Science and Technology (DST), New Delhi, for the Raja Ramanna Fellowship. We also thank CSIR, New Delhi, for financial assistance.

Supporting Information Available: Experimental details and spectral data for all compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(19) CO in the reaction mixture was detected by reduction of PdCl₂ in solution to palladium metal (see the Supporting Information).