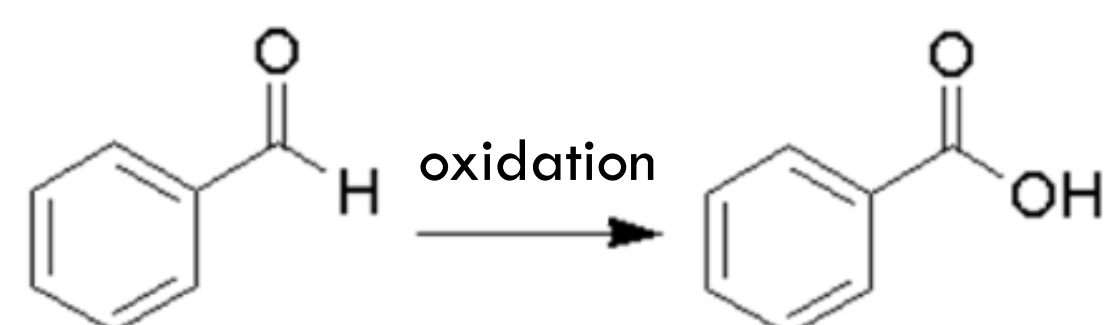


Green Chemistry: The Oxidation of Benzaldehyde by NHCs

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Background and Introduction

Oxidation is an extremely important process among organic and biochemical reactions.¹ Specifically, the oxidation of aromatic aldehydes into esters is a vital part of food chemistry in particular. Here we are researching the oxidation of benzaldehyde into a carboxylic acid, benzoic acid.

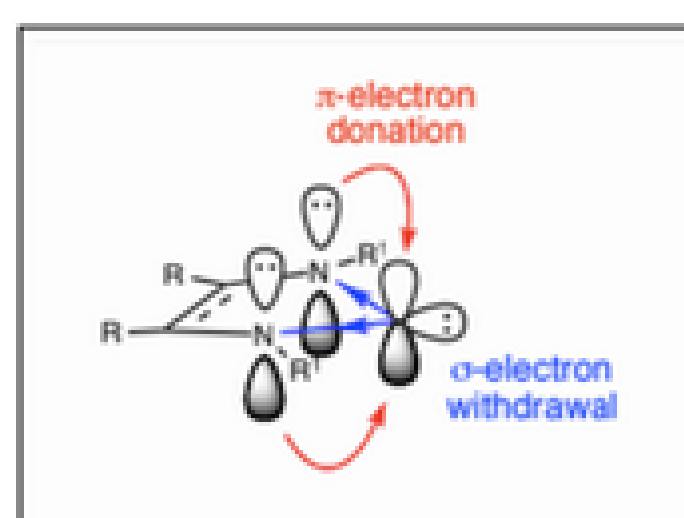
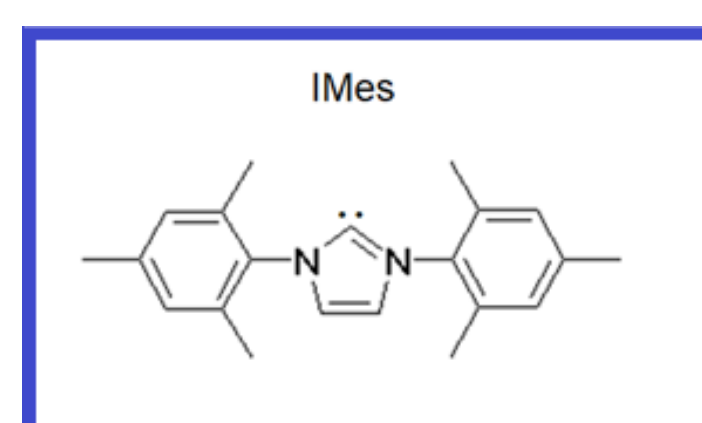
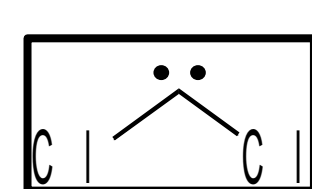


Benzaldehyde (above left) is an aromatic aldehyde commonly used as almond flavoring. Benzoic Acid (above right) is a carboxylic acid, and a versatile chemical used in food preservatives, cosmetics, acne medication, and as an antipsychotic. The USA produces almost 100,000 tons of it every year.

¹Shibley, I. A.; Amaral, K. E.; Aurentz, D. J.; McCaully, R. J. *Chem. Ed.* **2010**, *87*, 1351-1354.

N-Heterocyclic Carbenes (NHCs)

N-heterocyclic carbenes (NHCs) are our catalysts for this reaction, facilitating the otherwise extremely slow oxidation using only atmospheric oxygen as an oxidant. While carbenes themselves are an extremely unstable class of molecules, NHCs have various features that help stabilize them while they retain enough reactivity to be catalytically useful.²



Left to Right: a typical carbene (dichlorocarbene), an NHC, and a stability diagram for an NHC. The lone pairs on nitrogen atoms help stabilize an empty p orbital on the carbene carbon by pi-donation, while the nitrogen's high electronegativity stabilizes the carbene by withdrawing electron density from the carbene carbon through sigma bonds.

²Arduengo, III, A. J.; Harlow, R. L.; Kline, M. *J. Am. Chem. Soc.* **1991**, *113*, 361.

Using a Microwave

While atmospheric oxidation reactions on their own may be inefficient, we have found that microwave irradiation can speed up the process dramatically.

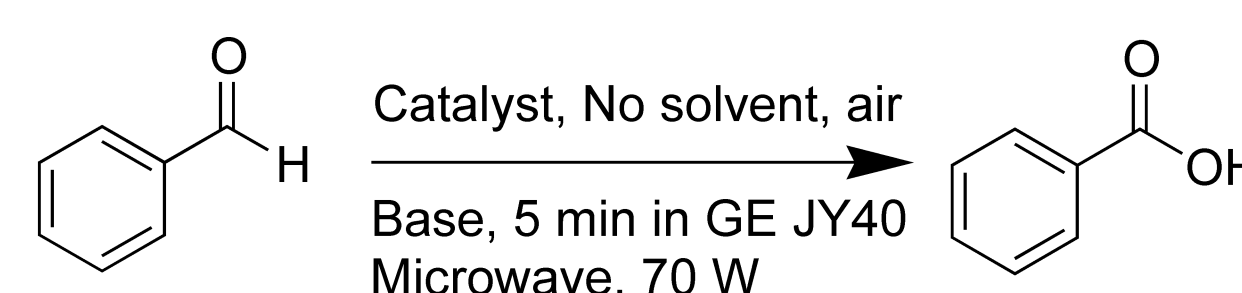
However, a household microwave on high power (1100 W) was found to rapidly boil the reaction mixture, causing the container to explode and the product to be lost. To avoid this, we had the microwave set at the lowest power (70 W). This also helps with heat distribution, allowing the entire sample to be uniformly exposed to the microwave waves.



Current Processes and Our Approach

Currently, the oxidation of benzaldehyde into benzoic acid on the industrial scale employs the use of solvents and highly charged heavy metals as oxidants, such as manganese(VII) and chromium(VI) ions.³ Because of their high charges, these ions are extremely reactive. While this is good news for reaction times, it is also bad news for the environment. When they are disposed of, these chemicals can wreck havoc on their surroundings, upsetting any ecosystem they enter.

To remedy this, we proposed using non-metallic N-heterocyclic carbenes as catalysts for oxidation using atmospheric oxygen, in a domestic microwave. We used two different catalysts, Vitamin B1 (thiamine) and IMes, shown to the left. Our reaction was also mostly solvent free, eliminating another source of waste from the process. Importantly, the process uses the cleanest possible oxidant, atmospheric oxygen.⁴

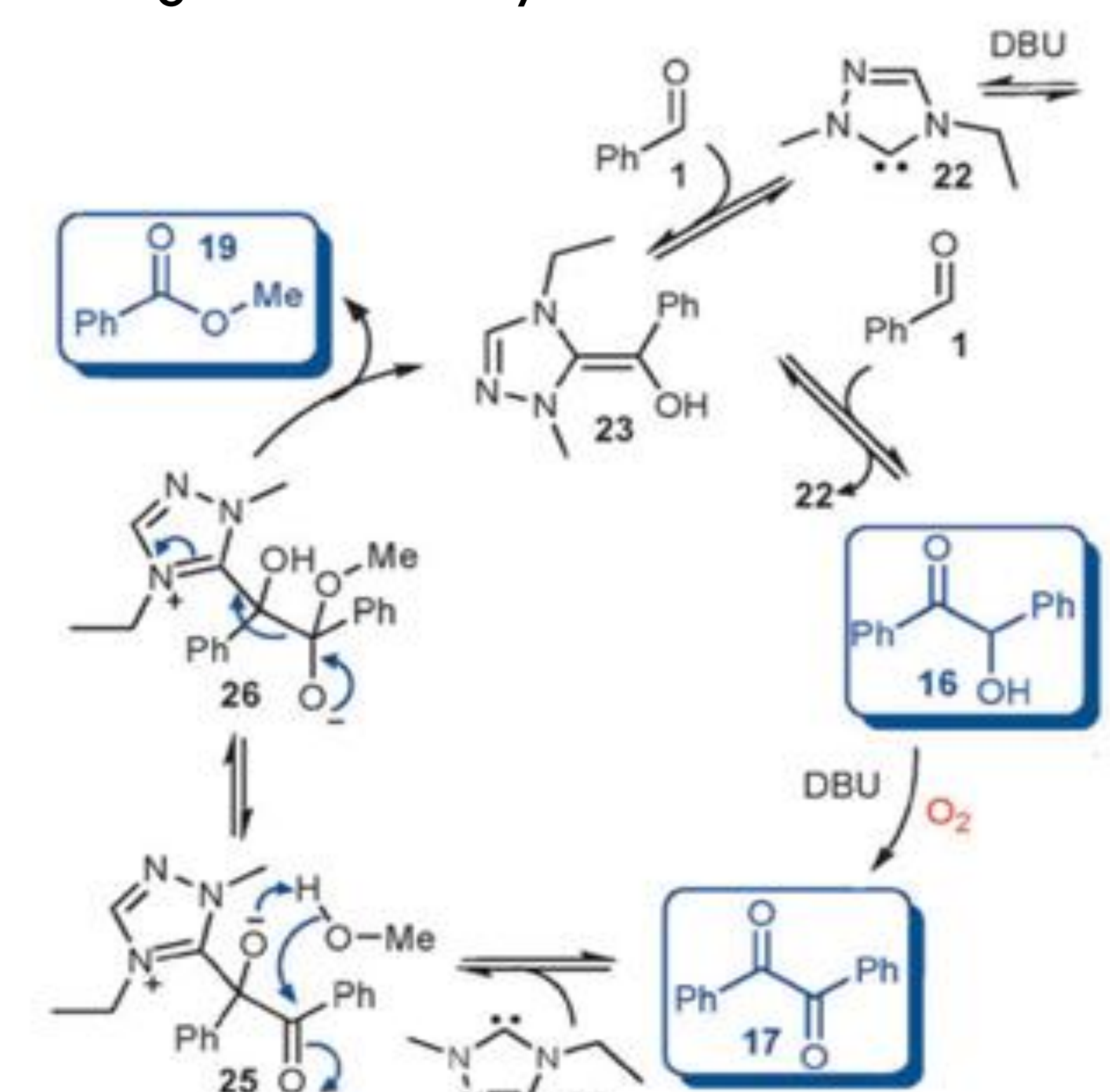


In the diagram above, a base is included in the reaction. The base is required because it deprotonates the partially oxidized molecule, allowing the oxidation to go to completion, as can be seen in the mechanism on the right. We experimented with different bases, and our results are listed below.

³Zhang, X., et. al. *ACS Sustainable Chem. Eng.* **2013**, *1* (8), 974-981.

⁴Our procedure was modified from Estager, J.; Lévêque, J. M.; Turgis, R.; Draye, J. *Mol. Catal. A: Chem.* **2006**, *256*, 261-264.

Proposed Mechanism from Connon, et al. Leading to the Methyl Ester of Benzoic Acid⁶



In this mechanism the presence of benzoin (structure 16) is an intermediate product. This proposed mechanism suggests that we will see benzoin as a byproduct if the reaction does not go to completion (see DBU results below left).

⁶Delany, E. G.; Fagan, C.-L.; Gundala, S.; Zeitler, K.; Connon, S. J. *Chem. Commun.* **2013**, *49*, 6513.

Our Results

Results when using the base Potassium Carbonate (K_2CO_3) in DMSO solvent

NHC Catalyst	Base	Solvent	Sparge O_2	Yield	Notes
Thiamine HCl (0.5 mol%)	K_2CO_3 (2 equiv)	DMSO 10mL	No	0%	IR showed acetic acid
IMesHCl (50 mol%)	K_2CO_3 (2 equiv)	DMSO 10mL	No	0%	

Results when using the base Sodium Methoxide ($NaOCH_3$)

NHC Catalyst	Base	Solvent	Sparge O_2	Yield	Notes
Thiamine HCl (0.5 mol%)	$NaOCH_3$ (1 equiv)	None	No	16%	
Thiamine HCl (0.5 mol%)	$NaOCH_3$ (1 equiv)	None	Yes	21%	
Thiamine HCl (5 mol%)	$NaOCH_3$ (1 equiv)	DME (2 mL)	Yes	31%	
Thiamine HCl (5 mol%)	$NaOCH_3$ (1 equiv)	None	Yes	32%	High Power

Results when using the base 1,8-Diazabicyclo(5.4.0)undec-7-ene (DBU)

NHC Catalyst	Base	Solvent	Sparge O_2	Yield	Notes
IMesHCl (5 mol%)	DBU (1.1 equiv)	None	No	88%	Acid, then water
IMesHCl (5 mol%)	DBU (1.1 equiv)	None	No	14%	Benzoic Acid, then acid

Conclusions and Future Work

- Using NHC catalysts in a domestic microwave for very short reaction times produces moderate yields of oxidized product, using atmospheric oxygen as oxidant.
- The production of benzoic acid depends critically on both the catalyst and base used in the reaction, with highest yields requiring thiamine HCl and sodium methoxide.
- Benzoic acid is observed as a byproduct in many of these reactions, and can be isolated preferentially by varying the workup conditions using DBU base.
- Further survey of NHC catalysts and bases is required to improve benzoic acid yields over 32%.

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