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PNNL-32706

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March 2022

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U.S. DEPARTMENT OF ENERGY

Prepared for the U.S. Department of Energy
under Contract DE-AC05-76RL01830

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*under Contract DE-AC05-76RL01830*

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# Abstract

The coupling of oxygenates derived from biomass is critical to the production of sustainable commodity chemicals. However, most current industrial oxygenate condensation processes rely on highly corrosive homogenous basic catalysts. To find greener alternatives, several condensation reactions were screened using a variety of alkaline-doped MgO and MgO-Al2O3 heterogenous catalysts. These include i) the self-condensation of hexanedione to methylcyclopentenone, ii) the self-condensation of methyl ethyl ketone to form C8 or C12 ketones, and iii) the coupling of dimethyl succinate and benzaldehyde. We demonstrate substantial yields for several condensation reactions that typically require homogenous base catalysts.

# Summary

A range of basic catalysts were prepared by modifying MgO and hydrotalcite derived MgO-Al2O3 with potassium, strontium, and cesium. Several of these catalysts were shown to be capable of catalyzing the self-condensation reactions of hexanedione and methyl-ethyl ketone and cross condensation of dimethyl succinate and benzaldehyde. The different pKa values of the tested reactants (hexanedione ≤ MEK < dimethyl succinate) lead to marked differences in the activity of the catalysts for each coupling reaction. For instance, while the self-condensation of MEK occurs readily on non-modified hydrotalcite derived catalysts (base strength sufficient to deprotonate pKa:18–35) the condensation of dimethyl succinate and benzaldehyde occurs only in the presence of stronger base catalysts (base strength sufficient to deprotonate pKa ≥35). However, reactant pKa values alone are clearly not sufficient predictors of the required solid base site strength necessary for reaction. The self-condensation of hexanedione seems to rely on catalytic sites intrinsic to the rehydrated hydrotalcite catalyst which we cannot fully characterize with the techniques employed in this study. As leaching of introduced alkali cations by water produced during condensation has been observed in similar work [24], future work is required to better understand if the catalysts employed in this work will be fully recyclable in practice.

# Acknowledgments

This research was supported by the Energy and Environmental Directorate (EED) Mission Seed, under the Laboratory Directed Research and Development (LDRD) Program at Pacific Northwest National Laboratory (PNNL).  PNNL is a multi-program national laboratory operated for the U.S. Department of Energy (DOE) by Battelle Memorial Institute under Contract No. DE-AC05-76RL01830.

# Acronyms and Abbreviations

C-C Coupling: Carbon-Carbon Coupling reaction
Hydrotalcite: Mg6Al2(CO3)(OH)16·H2O
LDH: Layered double hydroxide
TPD: Temperature programmed desorption
*H_*: Basicity
HD: 2,5 Hexanedione
MCP: Methyl Cyclopentenone
MEK: Mehtyl Ethyl Ketone
MCPBA: 3-methoxycarbonyl-4-phenylbut-3-enoic acid

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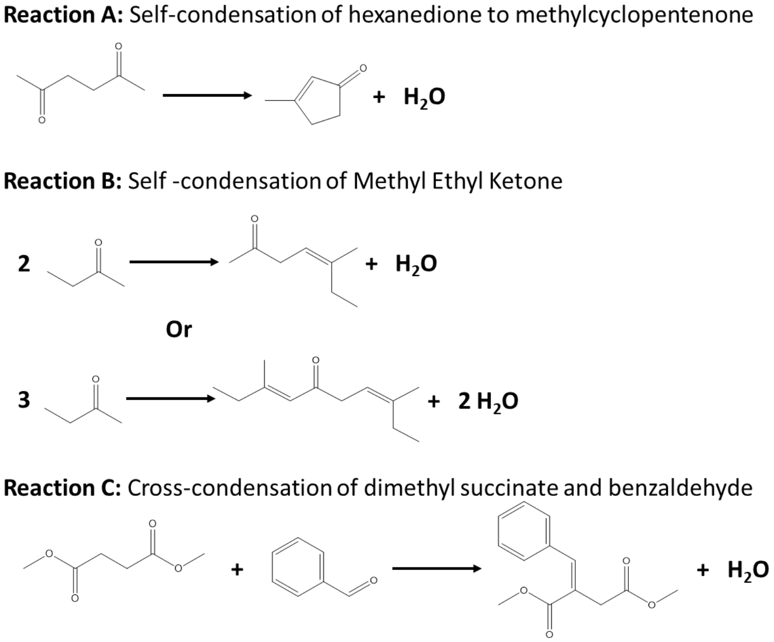
# 1.0 Introduction

Studies have shown that biomass-based fuels and chemicals have lower health and environmental risks compared to traditional fossil carbon sources [1, 2]. Biofuels have been growing steadily as a possible source of carbon-neutral sustainable energy that can reduce greenhouse gases and air pollutants. However, practical use of biomass to make biofuels and bioproducts requires efficient conversion processes and catalysts.

Carbon–carbon coupling reactions between oxygenates, particularly aldol condensations and other coupling reactions involving carbonyls, are a key step in the conversion of biomass to useful fuels and chemicals [3]. However, many base-catalyzed condensation reactions of ketones and esters require the use of prohibitively corrosive homogenous catalysts like alkali hydroxides (NaOH/KOH) and metal alkoxides (CH3ONa) [4]. The use of these strong base catalysts also results in the production of substantial amounts of waste and imposes significant recycling costs [4]. Thus, better conversion technologies are urgently needed to replace homogenous base catalysts with cost effective heterogenous catalyst systems. While solid acid catalysts see extensive use in the refining industry, solid base catalysts, by comparison, are relatively uncommon in industrial processes [5].

This study focuses on condensation reactions leading to coupled ketones and esters derived from biomass using solid base catalysts. A carbonyl condensation reaction takes place between two carbonyl partners, one of which must possess an alpha-hydrogen atom. The first step in the reaction involves the removal of an α-proton by a base. The typical pKa value of a ketone is 20–24 and an ester is ≥ 25 [6]. Therefore, a suitable solid base catalyst must have the appropriate strength to facilitate deprotonation of the reactant under investigation.

We screen condensation reactions between ketones and/or esters with a variety of pKa values. Three reactions (shown in Figure 1): the self-condensation of hexanedione to methylcyclopentenone (Reaction A), the self-condensation of methyl ethyl ketone to form C8 or C12 ketones (Reaction B), and the coupling of dimethyl succinate and benzaldehyde (Reaction C) are chosen for screening as each of these compounds may be produced from biomass resources. Hexadione has been identified as an important intermediate in the production of methylcyclopentenone, a desirable next generation gasoline blend stock, from 2,5-dimethylfuran (DMF) [7]. Methyl ethyl ketone (MEK) may be produced from biomass resources via combined fermentation and catalytic processing [8]. Bio-based succinic acid is one of the twelve most promising bio-based building blocks named by DOE for future biorefineries[9] and offers sustainable options for a wide range of applications in the food, cosmetics, pharmaceutical and chemical industries [10].


**Reaction A:** Self-condensation of hexanedione to methylcyclopentenone

**Reaction B:** Self -condensation of Methyl Ethyl Ketone

**Reaction C:** Cross-condensation of dimethyl succinate and benzaldehyde

***Figure 1:*** Condensation reactions used in this study.

To screen a variety of catalytic systems for these reactions we focus on modifying two known heterogenous catalysts: magnesium oxide (MgO) and hydrotalcite derived MgO-Al2O3. The use of MgO as a base catalyst has been studied extensively for the reactions of organic carbonates, such as the Wittig reaction [11], Claisen-Schmidt condensation [12], and asymmetric Henry and Michael reactions [13]. The base strength of MgO can be altered by pre-treatment temperature and increased by doping with alkali and alkaline-earth metals [14, 15].Hydrotalcite-derived mixed metal oxide catalysts are an emerging class of solid base catalysts.

Hydrotalcite is a layered double hydroxide (LDH) consisting of Mg and Al. Upon thermal treatment the layered structure of hydrotalcite dehydrates to form a mixture of amorphous MgO and Al2O3 with unique catalytic properties [16]. These amorphous oxides also possess a “memory-effect” by which re-introduced water will cause a restructuring of the material, reforming the original LDH phase [16, 17]. Hydrotalcite, or hydrotalcite derived oxides, have been widely reported to be active for several base-catalyzed reactions, including Michael addition [18] and several condensation reactions [19, 20]. Several parameters have been shown to impact the nature of the catalytic sites of hydrotalcite derived catalysts, including the Mg/Al ratio [21, 22], calcination temperature [23], and the introduction of alkali cations [24].

In this work we screen representative biomass-derived oxygenate coupling reactions over a variety of catalysts; specifically typical solid base catalysts (MgO and hydrotalcite derived MgO-Al2O3) modified with alkaline species (Cs, Sr, K). We demonstrate substantial yields of coupling products (>20%) for at least one screened catalyst in each reaction. Via characterization of the base sites of these catalyst via titration with Hammett indicators and CO2 TPD we make preliminary steps towards understanding the catalytic site requirements of each reaction.

# 2.0 Experimental

## 2.1 Materials & Chemicals

Magnesium oxide (MgO) powder (1-5micron) was purchased from Atlantic Equipment Engineers. Hydrotalcite, Mg6Al2(CO3)(OH)16·4H2O powder was purchased from Sigma-Aldrich. The molar Mg/Al ratio of this materials is between 4.0 and 5.0. The alkali metal and alkali earth metals used for doping were purchased as salts - NaNO3, KNO3, CsNO3 and Sr(NO3)2 from Sigma-Aldrich. The indicators—phenolphthalein, 4-nitroaniline, 2,4-dinitroaniline and diphenylmethane—were purchased from TCI America.

## 2.2 Catalyst preparation

Solid base catalysts were prepared via wetness impregnation of nitrate salts on MgO powder (1-5µ) and hydrotalcite powder. Each support was calcined in air at 550 °C for 5 hours prior to impregnation. The alkaline salts, NaNO3, KNO3, CsNO3, and Sr(NO3)2, were dissolved in deionized water and introduced to the solid catalyst by wetness impregnation. The wet catalysts were dried at room temperature for 2 hours and then at 100 °C for 4 hours before calcination at 600 °C for 3 hours under N2. The catalysts were transferred and stored in a glove box. Rehydration of hydrotalcite catalysts was performed by treating the calcined catalyst at room temperature in a nitrogen flow saturated with water vapor for 2 hours prior to dry N2 for 4 hours.

## 2.3 Measurement of catalyst basicity

Two methods were used to characterize the basic properties of the synthesized catalysts. Hammett indicators were used to titrate basic sites according to literature protocols [25]. A 200 mg catalyst sample was added to a 0.5mL solution of indicator diluted in toluene under nitrogen. The color of the solution was observed after 2 hours.

Temperature programmed desorption (TPD) of CO2 was used to characterize the basicity of catalysts. The experiments were performed on an Automated Catalyst Characterization System (AutoChem II) from Micromeritics. 50 mg of a powder sample was heated to 500 °C under N2 for 1 hour. After cooling the sample to room temperature, it was exposed to a 20 mL min-1 flow of CO2 for 1 hour and then purged with N2 for 1 hour to remove physical absorbed CO2. A TPD was then performed using a N¬2 flow of 20 mL min-1 by heating from room temperature to 850 °C at a heating rate of 4 °C min-1. CO2 desorption was tracked via an online mass spectrometer (Pfeiffer Thermostar GSD 301).

## 2.4 Measurement of catalytic activity

All reactions were carried out with neat reactant. 10 wt% of catalyst was added to the substrate for each experiment. All reactions were conducted under nitrogen. The catalyst was first loaded into a Schlenk flask in the glove box. The substrate was then cannulated into the flask under N2. The reaction mixture was heated to reflux at 200 °C for Reaction A and 120 °C for Reaction C. Both reactions A and C were allowed to proceed for 12 h. The reaction of methyl ethyl ketone (Reaction B) was performed in a high-pressure batch reactor under 200 psig of N2 at 120 °C for 4 h. In all cases the catalyst was removed by filtration after the reaction mixture was cooled to room temperature. The products were identified and quantified via gas chromatography (GC-MS and GC-FID; Agilent 7890). In each tested reaction no significant byproducts are observed via GC and reasonably high (>90%) carbon balances are achieved. Thus, we report only coupling product yields for each screened catalyst and reaction.

# 3.0 Results and Discussion

## 3.1 Catalyst Characterization

The base strength of the prepared catalysts was determined using the Hammett indicators phenolphthalein, 4-nitroaniline, 2,4-dinitroaniline and diphenylmethane. The results shown in Table 1 reveal that the H- value (as defined by Paul and Long [25]) of non-modified hydrotalcite (HT-MgO-Al2O3) is ≥ 18.4 and < 35 whereas the H- of non-modified MgO is in the range 9.8–13.0. Generally, the basicity of hydrotalcite based catalysts is stronger than that of MgO based catalysts. The K, Sr, and Cs modified hydrotalcite possess basic sites with pKa values greater than 35, meaning these catalysts are superbases. Superbases exhibit basicity (H-) greater than 26, where H- corresponds to the pKa value of the indicator [4].

**Table 1:** Basicity screening by Hammett indicators:

| | pKa | MgO | K/MgO | Sr/MgO | HT-MgO-$Al_2O_3$ | Sr/ HT-MgO-$Al_2O_3$ | K/ HT-MgO-$Al_2O_3$ | Cs/ HT-MgO-$Al_2O_3$ |
|---|---|---|---|---|---|---|---|---|
| **Phenolphthalein** | 9.8 | + | + | + | + | + | + | + |
| **4-nitroaniline** | 13.0 | - | - | - | + | + | + | + |
| **2,4-dinitroaniline** | 18.5 | - | - | - | + | + | + | + |
| **diphenylmethane** | 35.0 | - | - | - | - | + | + | + |

The base properties of these catalysts were also examined by CO2-temperature programmed desorption (TPD) (Figure 2). For ease of discussion 3 arbitrary temperature regions (25-350 °C, 350-750 °C, and 750-850 °C) are used to define weak, medium, and strong basic sites respectively.

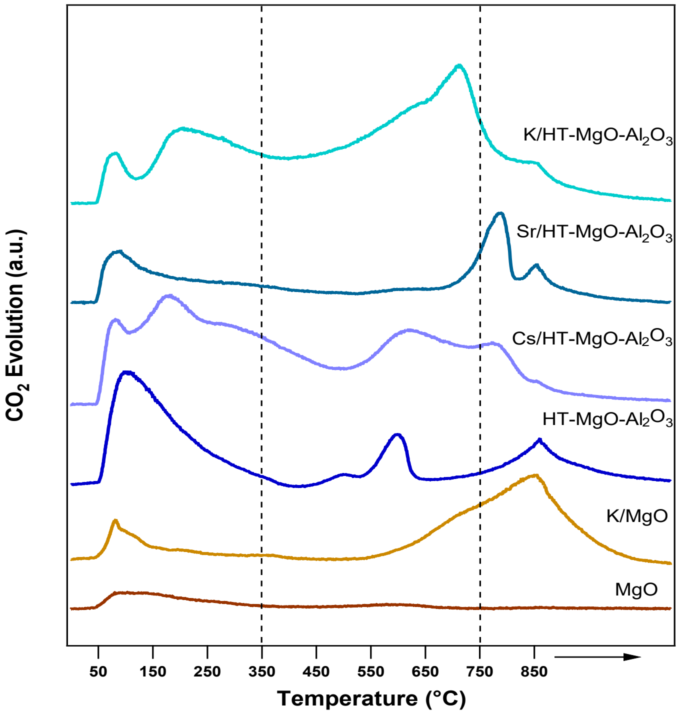


**Figure 2**: $CO_2$ TPD spectra of the prepared catalysts

MgO possesses little to no basic sites compared to the other tested catalysts, however this may simple be due to the relatively low surface area of our tested MgO. Alkali modification introduces a substantial number of strong base sites to the MgO catalyst (K/MgO), in line with previous literature [15]. HT-MgO-Al2O3 has a broad variety of base sites but is characterized by predominantly weakly basic sites. Interestingly, the changes in catalyst basicity upon alkaline modification of the hydrotalcite catalyst with a variety of modifiers (Cs, Sr, K) is highly dependent on the modifier used. While all alkaline species introduce some medium and strong basic sites the proportion and specific temperature region of these sites vary dramatically.

**Table 2:** Basicity screening by TPD:

| **Catalyst** | **Catalyst Basic Site Density (µmol/g)** | | | |
|---|---|---|---|---|
| | Weak (R.T. – 350 °C) | Medium (350 – 750 °C) | Strong (750 – 850 °C) | Total |
| **K/HT-MgO-$Al_2O_3$** | 254 | 490 | 118 | 863 |
| **Sr/HT-MgO-$Al_2O_3$** | 133 | 94 | 117 | 344 |
| **Cs/HT-MgO-$Al_2O_3$** | 392 | 339 | 102 | 833 |
| **HT-MgO-$Al_2O_3$** | 270 | 79 | 110 | 459 |
| **K/MgO** | 64 | 90 | 205 | 359 |
| **MgO** | 50 | 18 | 6 | 74 |

## 3.2 Catalyst Activity Testing

### 3.2.1 Reaction A: Self-condensation of 2,5 hexanedione to methylcyclopentenone

The reaction mechanism for condensation of hexanedione (HD) to methyl cyclopentenone (MCP) is well-established and is generally thought to require both a base to initiate the nucleophile and an acid for dehydration. Homogenous base catalysts have been shown to be able to catalyze this reaction at moderate yields [26]. More recent work has also demonstrated that mixed metal oxide solid base catalysts are also active for this reaction and have been shown to achieve quite high yields [7].

Reactivity testing of the self-condensation of HD to MCP using several catalysts (Table 3) shows that several solid base catalysts can facilitate this reaction. Rehydrated hydrotalcite demonstrates the highest yield of MCP (41.6%) while alkali modified MgO catalysts (K-MgO and Sr-MgO) exhibit middling yields (10-20%). The high product yield with rehydrated hydrotalcite could be attributed to an increase in the available mild Brønsted base sites by reconstruction of its hydroxyl interlayer, which has been demonstrated in the literature [27]. Unfortunately, given that the advanced catalyst characterization that is necessary to discern these specific sites is outside the scope of this work, we cannot comment on whether similar sites may be present on K-MgO and Sr-MgO. This result does indicate, however, that base site strength alone is not a sufficient indicator for catalytic performance in this reaction, as alkali modified catalysts with strong base character deliver poor results compared to the rehydrated hydrotalcite-derived catalyst.

**Table 3**: Product yield of methylcyclopentenone from hexanedione at 200 °C

| Catalyst | % Yield of MCP |
|---|---|
| **HT-MgO-$Al_2O_3$** | 1.5 |
| **HT-MgO-$Al_2O_3$ Rehydrated** | 41.6 |
| **Sr-MgO-$Al_2O_3$** | 4.7 |
| **K-MgO** | 10.2 |
| **Sr-MgO** | 19.3 |

### 3.2.2 Reaction B: Self -condensation of Methyl Ethyl Ketone (MEK)

The condensation of MEK using base catalysts results in primary dimer (C8 ketones) and secondary trimer products (C12 ketone). Reactivity testing of several solid base catalysts reveal several counterintuitive trends in this reaction (Table 4). The yield of MEK coupling products is nearly identical in the case of all tested hydrotalcite derived catalysts (HT-MgO-Al2O3, HT-MgO-Al2O3 rehydrated and K-HT-MgO-Al2O3). Many studies focused on condensation reactions over hydrotalcite catalysts observe higher rates over rehydrated catalysts [28-30]. Rehydrated hydrotalcite catalysts have been shown to possess weaker base sites than calcined hydrotalcite catalysts [29], however they are generally believed to exhibit better catalytic activity due to the formation of Brønsted base sites by water introduction [27]. One potential explanation of the negligible difference between calcined and rehydrated hydrotalcite for MEK condensation is that stronger Lewis base sites intrinsic to the hydrotalcite catalyst are more catalytically relevant than the Brønsted sites formed by rehydration. This is consistent with the slight increase in condensation yield over K-HT-MgO-Al2O3, as K introduction does increase the strong base site density of the hydrotalcite catalyst.

**Table 4**: Product yield of MEK self-condensation at 120 °C and 200 psig

| Catalyst | % Yield of MEK dimers and trimers |
|---|---|
| **HT-MgO-$Al_2O_3$** | 20.7 |
| **HT-MgO-$Al_2O_3$ Rehydrated** | 20.3 |
| **K-HT-MgO-$Al_2O_3$** | 24.6 |
| **K-MgO** | 0.43 |

### 3.2.3 Reaction C: Cross-condensation of dimethyl succinate and benzaldehyde

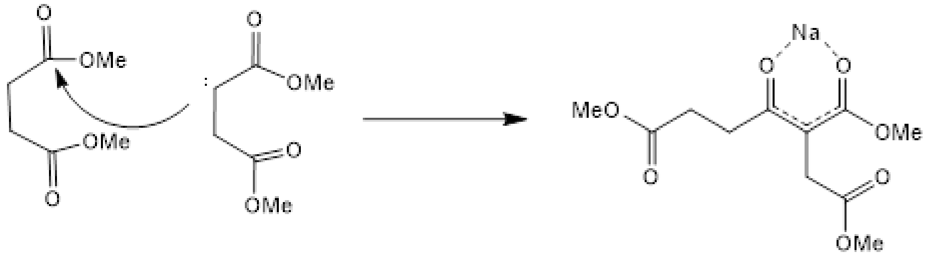
Dimethyl succinate reacts with benzaldehyde to give a Stobbe condensation product of 3-methoxycarbonyl-4phenylbut-3-enoic acid (MCPBA). The condensation of dimethyl succinate and benzaldehyde has been shown to proceed in the presence of strong homogenous base catalysts like potassium tert-butoxide [31] and lithium methoxide [32]. The results of reactivity testing are summarized in Table 5. The K modified hydrotalcite based catalyst (K-HT-MgO-

Al2O3) achieves the highest yield of MCPBA at 38% compared with other tested catalysts. While all tested catalysts exhibit some activity for this reaction, all tested alkali doped hydrotalcite derived catalysts generally possess substantially higher activity. As these catalysts are the only screened catalysts to be titrated by diphenylmethane, this reaction appears to require a high pKa .

**Table 5**: Product yield of the condensation of dimethyl succinate and benzaldehyde

| Catalyst | % Yield of MCPBA |
|---|---|
| **HT-MgO-$Al_2O_3$** | 2.8 |
| **HT-MgO-$Al_2O_3$ Rehydrated** | 3.4 |
| **K-HT-MgO-$Al_2O_3$** | 38.4 |
| **Sr-HT-MgO-$Al_2O_3$** | 13.3 |
| **Cs-HT-MgO-$Al_2O_3$** | 30.2 |
| **MgO** | 2.1 |
| **K-MgO** | 6.6 |

It is also notable that while the catalysts studied here can facilitate condensation between dimethyl succinate and benzaldehyde, none demonstrate measurable activity for the self-condensation of dimethyl succinate under the tested reaction conditions. This can be explained by the ability of the strongly basic sites on alkaline treated hydrotalcite-based catalysts to activate dimethyl succinate as a nucleophile but not complete the corresponding electrophile addition. Similar reactions have been shown to proceed when catalyzed by NaOMe forming an organic Na+ salt product [33]. Thus, we postulate that self-condensation of dimethyl succinates requires a homogenous cation containing catalyst to stabilize the final product. Scheme 1 shows the proposed reaction product stabilized by Na+.



Sheme 1: Dimethyl succinated self-condensation and product stabilization by Na cations

A broad range of yields for the products obtained in Reaction C for the tested catalysts are observed (Table 5). Given the wide variety of weak, medium and strongly basic sites measured by CO2 TPD (Table 2) for the tested catalysts, qualitative correlations to gain insight into which sites are catalytically relevant are shown in Figure 3.

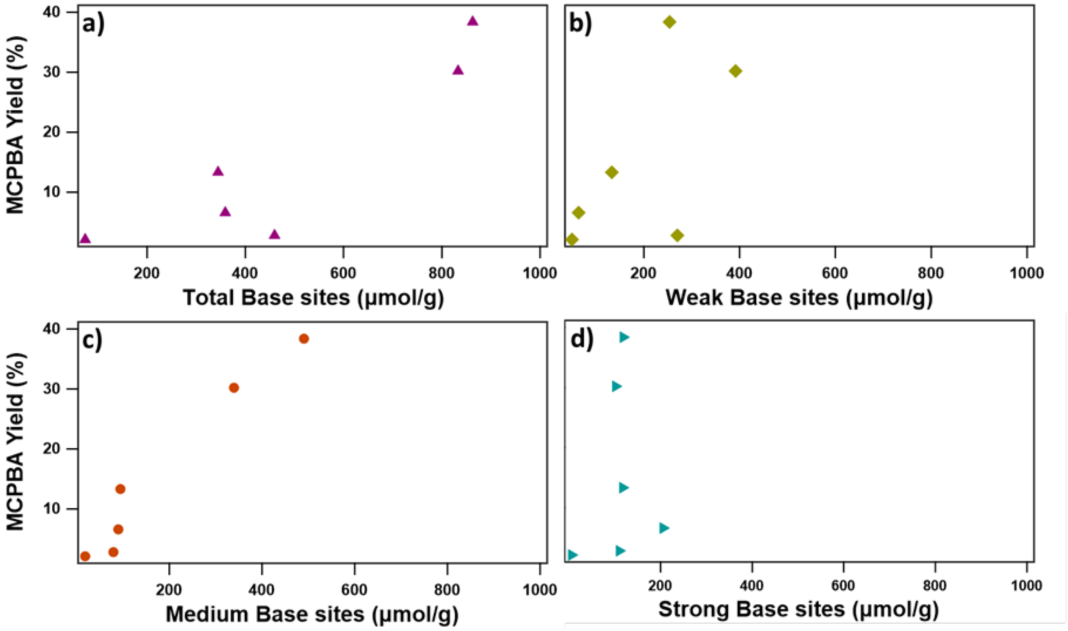


**Figure 3:** Correlations of MCPBA yield in Reaction C with the concentration of different types of basic sites as quantified by $CO_2$ TPD.

The yield of MCPBA varying with the total site density (Figure 3.a), weak site density (Figure 3.b), medium site density (Figure 3.c), and strong site density (Figure 3.d) are plotted. While no discernable correlation between the total (Figure 3.a), weak (Figure 3.b) or strong sites (Figure 3.d) appears to exist, a relatively monotonic trend is observed between the yield of MCPBA and the density of medium strength base sites (Figure 3.c). This implies that base sites that desorb CO2 between 350 and 750 °C are more catalytically relevant in this reaction than very weak or very strong sites.

# 4.0 Conclusions

A range of basic catalysts were prepared by modifying MgO and hydrotalcite derived MgO-Al2O3 with potassium, strontium, and cesium. Several of these catalysts were shown to be capable of catalyzing the self-condensation reactions of hexanedione and methyl-ethyl ketone and cross condensation of dimethyl succinate and benzaldehyde. The different pKa values of the tested reactants (hexanedione ≤ MEK < dimethyl succinate) lead to marked differences in the activity of the catalysts for each coupling reaction. For instance, while the self-condensation of MEK occurs readily on non-modified hydrotalcite derived catalysts (base strength sufficient to deprotonate pKa:18–35) the condensation of dimethyl succinate and benzaldehyde occurs only in the presence of stronger base catalysts (base strength sufficient to deprotonate pKa ≥35). However, reactant pKa values alone are clearly not sufficient predictors of the required solid base site strength necessary for reaction. The self-condensation of hexanedione seems to rely on catalytic sites intrinsic to the rehydrated hydrotalcite catalyst which we cannot fully characterize with the techniques employed in this study. As leaching of introduced alkali cations by water produced during condensation has been observed in similar work [24], future work is required to better understand if the catalysts employed in this work will be fully recyclable in practice.

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