CHAPTER 5

DISCOVERY OF NEW SELECTIVE DIELS-ALDER REACTIONS USING ETHYLENE: PRODUCTION OF PTA FROM HMF VIA OXIDATION ROUTE

5.1 New ethylene Diels-Alder-dehydration reactions using 5-methyl-2-furoic acid (MFA) and methyl 5-methyl-2-furoate (MMF) as dienes

In Chapter 4, the synthesis of PTA from FDCA (fully oxidized HMF) and ethylene was accomplished using the Lewis acid molecular sieve catalysts in dioxane solvent, although maximum PTA yields of only ~3 mol % were obtained. This chapter discusses further efforts to improve the reactivity of the furanic diene containing the electron-withdrawing carboxylic acid groups (–COOH) in the ethylene Diels-Alder-dehydration reaction. These efforts resulted in the discovery of a series of new ethylene Diels-Alder-dehydration reactions catalyzed by Lewis acid-containing molecular sieves and mesoporous silicas, and these new reactions open a new route to renewable PTA from HMF that avoid reduction steps.

As hypothesized in Chapter 4, the slow reactivity of FDCA in the Diels-Alder reaction with ethylene is likely due to the deactivation of the diene function towards cycloadditions with a dienophile by the two carboxylic acid groups (–COOH). Attempts were made to make these groups less deactivating by using the Na^+ salt of FDCA, since the (–COONa) group would be less electron withdrawing than the (–COOH) groups. Here, another strategy was successfully applied and was the use of furanic dienes that contain only one (–COOH) or (–COOR) group on the 2- position and a methyl, hydroxymethyl, or alkoxymethyl group on the 5- position. This substitution of the functionality on the 5- position replaces an electron-withdrawing group (–COOH) with a slightly electron-donating group (-CH_3, -CH_2OH, -CH_2OR), resulting in a more active diene in the Diels-Alder reaction with ethylene.

The next dienes tested were 5-methyl-2-furoic acid (MFA) and the corresponding methyl ester, methyl 5-methyl-2-furoate (MMF). The corresponding Diels-Alder-dehydration products with ethylene are p-toluic acid (TA) and methyl p-toluate (MPT) (Fig. 5.1). These dienes have similar functionality to FDCA and dimethyl-FDCA, but they should be more active in Diels-Alder reactions due to having only one carboxylic acid function. Therefore, these furans were used as model dienes in the effort to understand if the presence of two carboxylic acid functions was the cause of the slow reaction rates with ethylene.

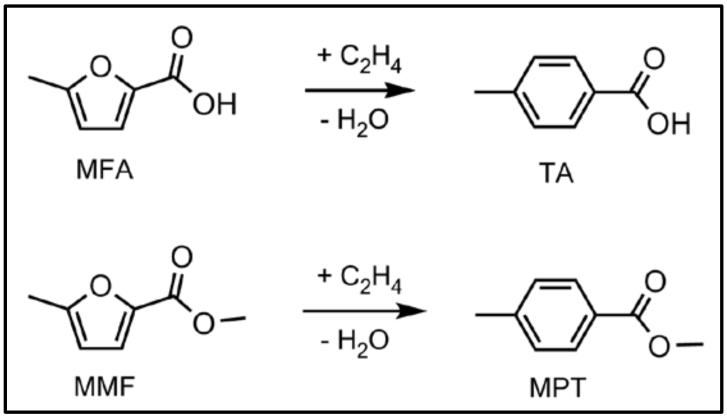


Fig. 5.1 Ethylene Diels-Alder-dehydration reactions of MFA to TA and MMF to MPT.

Table 5.1 Ethylene Diels-Alder-dehydration reaction results for conversion of MFA/MMF to TA/MPT. Reaction conditions: 0.4 M solution in dioxane, 200 mg catalyst, T=225^{o}C, 1000 psig C_2H_4, 6 hours. Results determined by ^{1}H NMR.

Entry	Diene	Product	Catalyst	Conversion (%)	Yield (%)	Selectivity (%)
1	MFA	TA	Sn-BEA	82	14	17
2	MMF	MPT	Sn-BEA	13	13	~100
3	MMF	MPT	Sn-MCM-41	12	12	~100
4	MMF	MPT	Sn-SiO_2 (amorphous)	11	11	~100
5	MMF	MPT	Si-BEA	0	0	n/a

These dienes were tested for reaction with ethylene using dioxane solvent in the presence of various Lewis acid (Sn^{4+})-containing silica materials (Table 5.1). Sn-BEA was found to catalyze the Diels-Alder-dehydration reaction between MFA and ethylene to produce 14 mol % yield of TA at 82% conversion after 6 hours at 225^{o}C and 1000 psig C_2H_4 pressure (entry 1). Although the selectivity to TA in this system was low, the catalyst after reaction was an off-white color and not significantly coked. The methyl ester, MMF, reacted with ethylene in the presence of a variety of Lewis acidic silicas to produce the aromatic product, MPT, with nearly 100% selectivity. Sn-BEA molecular sieve, Sn-MCM-41 mesoporous silica, and a Sn^{4+}-containing amorphous silica (Sn-SiO_2) all produced similar results, that is 11-13 % yield of MPT at nearly 100% selectivity (entries 2-4). A control experiment using a pure silica Beta (Si-BEA, entry 5) confirmed that the Sn^{4+} sites were required for catalysis and that the silica surface is not catalyzing the reaction.

Zirconium (Zr^{4+})-containing Beta molecular sieves were also shown to be effective and selective catalysts for the conversion of MMF and ethylene to MPT

(Table 5.2). Different Zr-Beta samples were used for the two reactions (entries 1-2), both producing MPT with high selectivity. The gas chromatograms of both product solutions (Fig. 5.2 and Fig 5.3) indicate very few side products.

Table 5.2 Reaction results for Zr-Beta as catalyst in ethylene Diels-Alder dehydration of MMF to MPT. Reaction conditions: 0.1 M MMF in dioxane, 100 mg Zr-Beta, 190^{o}C, 1000 psig C_2H_4, 6 hours. A Si/Zr atom ratio of 123 was measured for both Zr-Beta-1 and Zr-Beta-2 samples by energy-dispersive x-ray spectroscopy (EDS). Conversions and yields measured by ^{1}H NMR in entry 1 and by GC-FID (decane as external standard) in entry 2.

Entry	Catalyst Sample	MMF Conversion (%)	MPT Yield (%)	MPT Selectivity (%)
1	Zr-Beta-1	23.0	22.3	97
2	Zr-Beta-2	15.8	16.0	101

The finding that MFA and MMF can react with ethylene in the Diels-Alder-dehydration reaction to produce the aromatic product was a significant breakthrough in the research project. Unfortunately, MFA and MMF are not particularly useful intermediates in the transformation of HMF to PTA. A route involving MFA or MMF would be impractical, mainly because the synthesis of MFA from HMF would be difficult as one of the substituents of HMF would need to be selectively reduced while the other selectively oxidized (Fig. 5.4).

In the next section, a new route is proposed for the transformation of HMF to PTA that avoid reduction steps and utilize Diels-Alder-dehydration reactions similar to those described here.

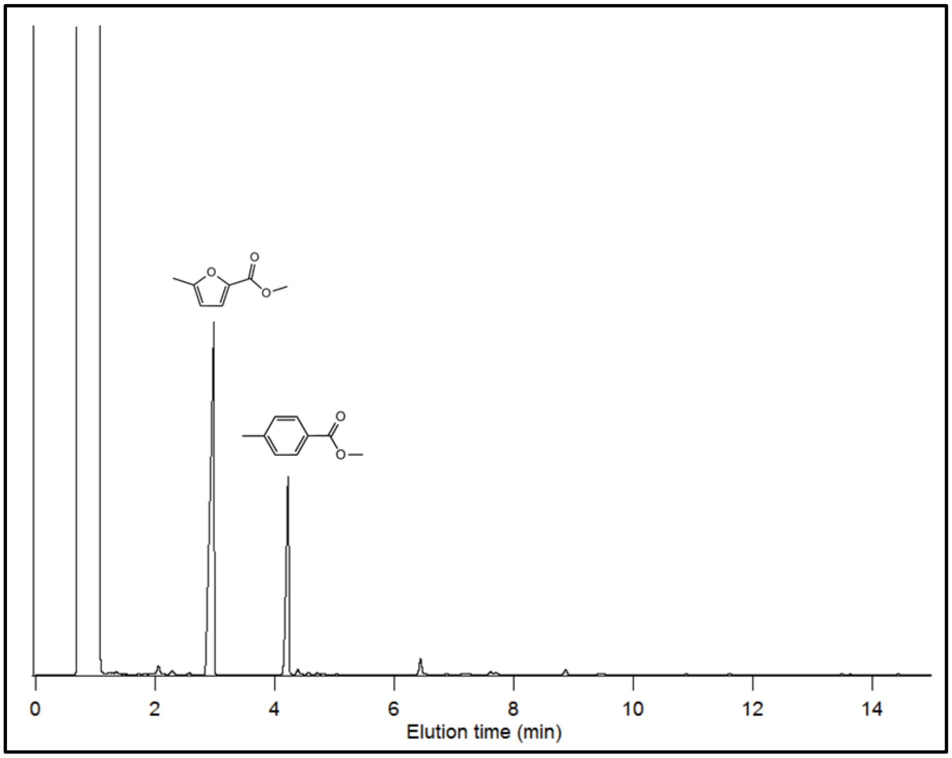


Fig. 5.2 Gas chromatogram of product in Table 5.2, Entry 1.

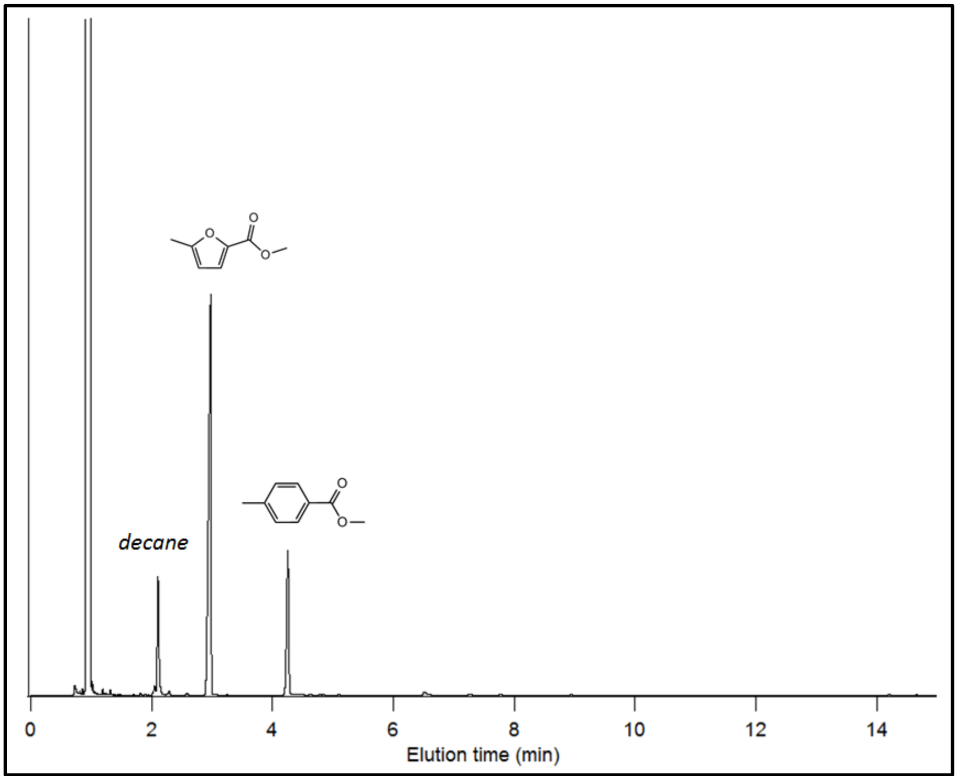


Fig. 5.3 Gas chromatogram of product in Table 5.2, Entry 2.

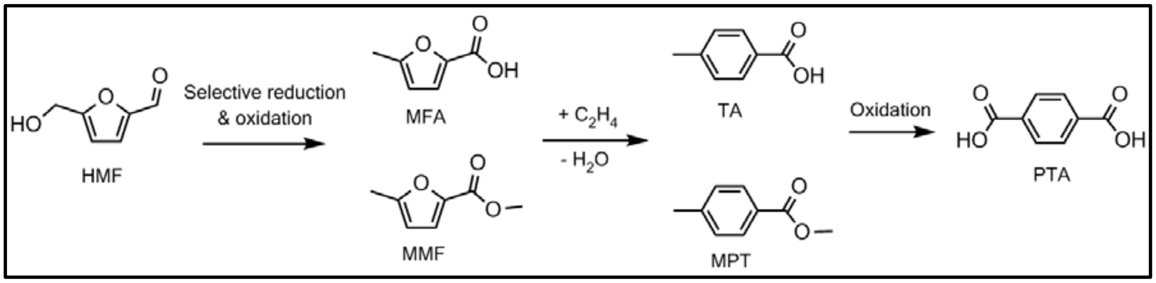


Fig. 5.4 Pathway to PTA from HMF via ethylene Diels-Alder-dehydration of MFA/MMF to TA/MPT.

5.2 Methyl 5-methoxymethyl-furan-2-carboxylate (MMFC) as a diene in the ethylene Diels-Alder-dehydration reaction

The MFA and MMF dienes are unique from the dienes tested in Chapter 4 in that these substrates have one carboxylic acid or carboxylate ester functionality. Based on this observation, a pathway from HMF to PTA was proposed that involved the partial oxidation of HMF to the carboxylic acid, 5-hydroxymethyl-2-furoic acid (HMFA). The HMFA intermediate may then react with ethylene to form the PTA precursor, 4-(hydroxymethyl)benzoic acid (HMBA), that could be further oxidized to PTA (Fig.5.5). Since HMFA can be easily obtained through the air oxidation of HMF,[1] HMFA was a HMF derivative of high interest for the ethylene Diels-Alder-dehydration reaction. Since in the previous section the most selective conversion was achieved when MFA was protected with methanol to form the ester MMF, the methanol protected form of HMFA, methyl 5-methoxymethyl-furan-2-carboxylate (MMFC), was also an attractive substrate for testing. The reaction of MMFC with ethylene would produce methyl 4-(methoxymethyl)benzene carboxylate (MMBC), a precursor to both PTA and dimethylterephthalate (DMT). In this section, the Diels-Alder-dehydration reaction results for the conversion of MMFC to MMBC will be summarized and discussed. The results for using HMFA will be presented in the following section.

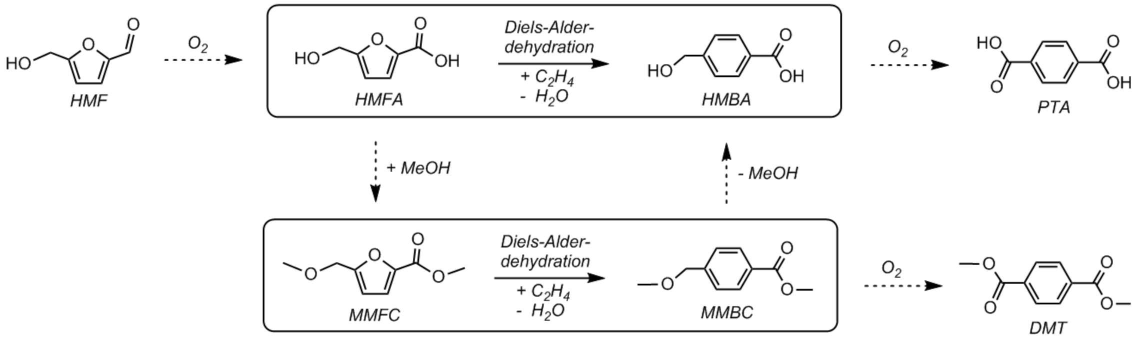


Fig. 5.5 Proposed pathway from HMF to PTA via the Diels-Alder-dehydration of HMFA/MMFC and ethylene.

Several materials were screened for catalytic activity in the conversion of MMFC and ethylene to MMBC (Table 5.3). The MMFC substrate was stable in dioxane solvent at 190^{o}C and stable in the presence of Si-Beta (entries 1 & 2). A series of Lewis acid Beta molecular sieves with different Lewis acid centers in the silica framework were tested (entries 3-7). Out of all five different materials Sn-Beta and Zr-Beta were the only ones active for the Diels-Alder-dehydration reaction, and while both Sn-Beta and Zr-Beta produced MMBC at similar yields (24 and 21 %, respectively) the Zr-Beta was significantly more selective (48 and 81 %, respectively). These results show that the proposed reaction to convert MMFC and ethylene to MMBC is possible, and high selectivity can be achieved using Zr-Beta as catalyst. The Ti-, Ta-, and Nb-containing Beta molecular sieves were essentially inactive. When Sn- and Zr-containing MCM-41 (mesoporous silica), MFI (medium-pore silica molecular sieve), and amorphous silica materials were tested (entries 8-12), little or no MMBC was detected. Recall, Sn-MCM-41 and amorphous Sn-SiO_2 were active catalysts for the conversion of MMF and ethylene to TA. This suggests that a possible effect due to the confinement within the microporous environment of the large-pore Beta molecular sieve may be important for the Diels-Alder-dehydration reaction between MMFC and ethylene. The solid Bronsted acid, H-Al-Beta, was screened (entry 13), and after the 6 hour reaction period MMFC was fully converted with only 2 % yield of MMBC, clearly indicating the importance of using a Lewis acidic material to avoid significant side reaction and degradation of the oxygenated substrate under the reaction conditions.

Table 5.3 Reaction results for ethylene Diels-Alder dehydration of MMFC to MMBC. Reaction conditions: 0.1 M MMFC in dioxane, 100 mg catalyst, 190°C, 1000 psig C_2H_4. Conversions and yields determined by ^{1}H NMR.

Entry	Catalyst	Time (hr)	MMFC conversion (%)	MMBC yield (%)	MMBC selectivity (%)
1	None	6	1	0	0
2	Si-Beta	6	2	0	0
3	Sn-Beta	6	50	24	48
4	Zr-Beta	6	26	21	81
5	Ti-Beta	12	2	1	50
6	Ta-Beta	2	9	1	11
7	Nb-Beta	2	n.d.	0	0
8	Sn-MCM-41	6	5	1	20
9	Zr-MCM-41	6	4	0	0
10	Sn-MFI	6	9	0	0
11	Zr-MFI	2	11	0	0
12	Sn-SiO_2 (amorphous)	6	16	2	13
13	H-Al-Beta	6	100	2	2

The feed solution and product solution ^{1}H NMR spectra for the experiments in entries 3-4 of Table 5.3 are given in Fig. 5.6-5.9. The MMFC and

MMBC peaks are clearly shown, along with the large dioxane peak (~3.6 ppm), DMSO peak (~2.5 ppm, NMR solvent residual signal), and tetraethylsilane (TES) peaks (~0.5 and ~0.9 ppm, external standard). Dissolved ethylene was also observed in the ^{1}H NMR spectrum when the analysis was performed soon after reaction. Note also there is a side band feature from the large dioxane peak at ~8.4 ppm that was observed in most of the spectra. The verification of MMBC formation was also made using GC/MS and comparing the mass spectrum of the product to the known standard (Fig 5.1-A in appendix).

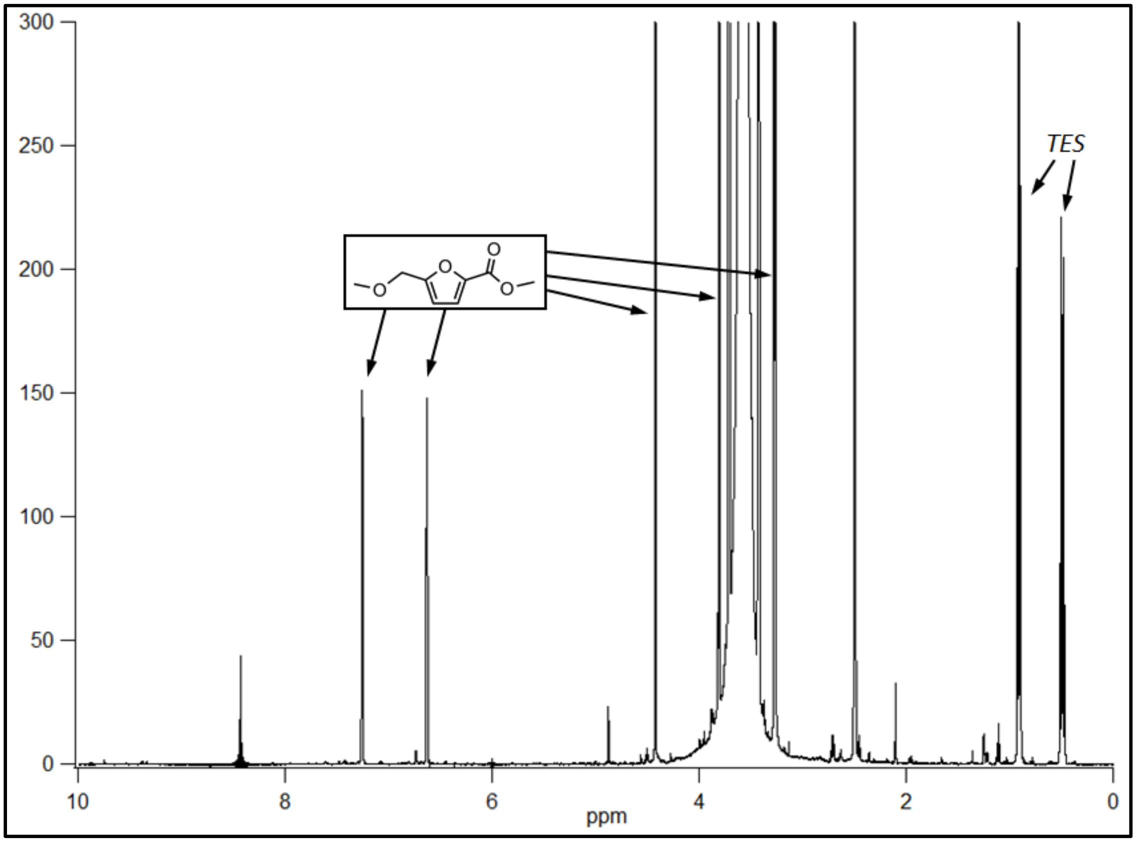


Fig. 5.6 ^{1}H NMR (in DMSO-d_6) of feed solution for experiment in Entry 4, Table 5.3.

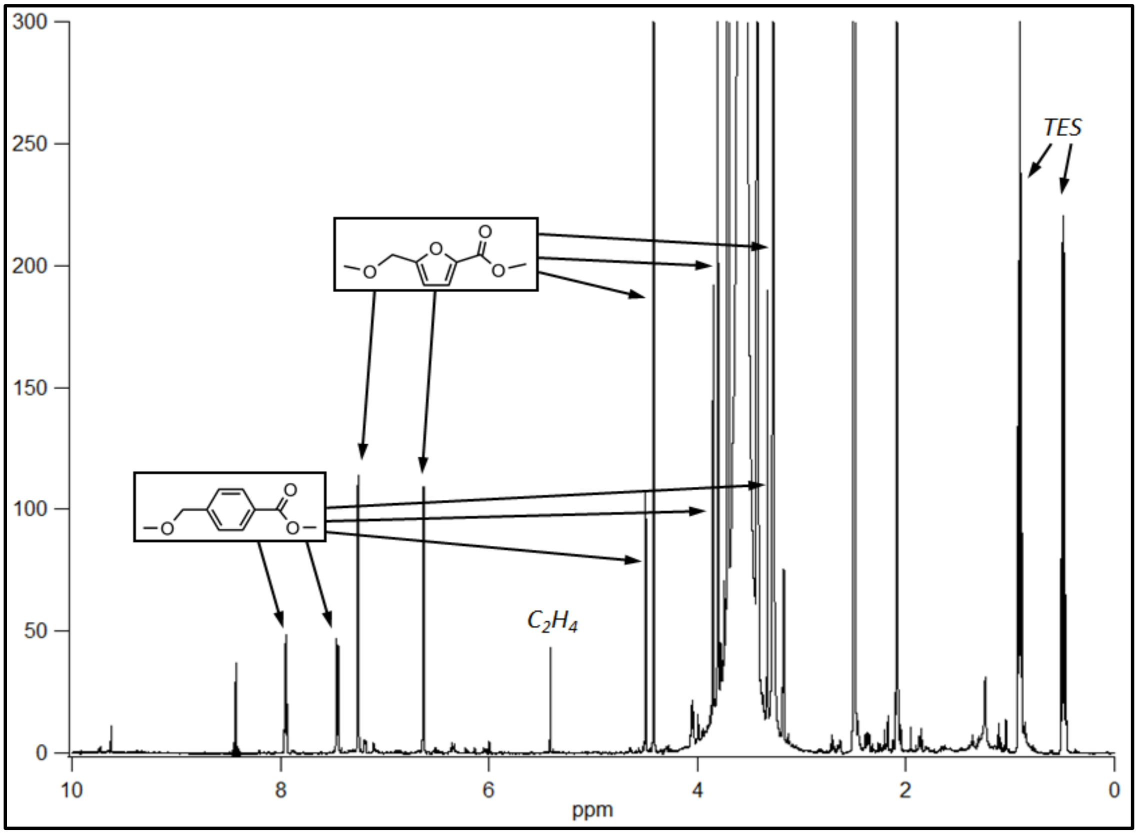


Fig. 5.7 ^{1}H NMR (in DMSO-d_6) of product solution for experiment in Entry 4, Table 5.3.

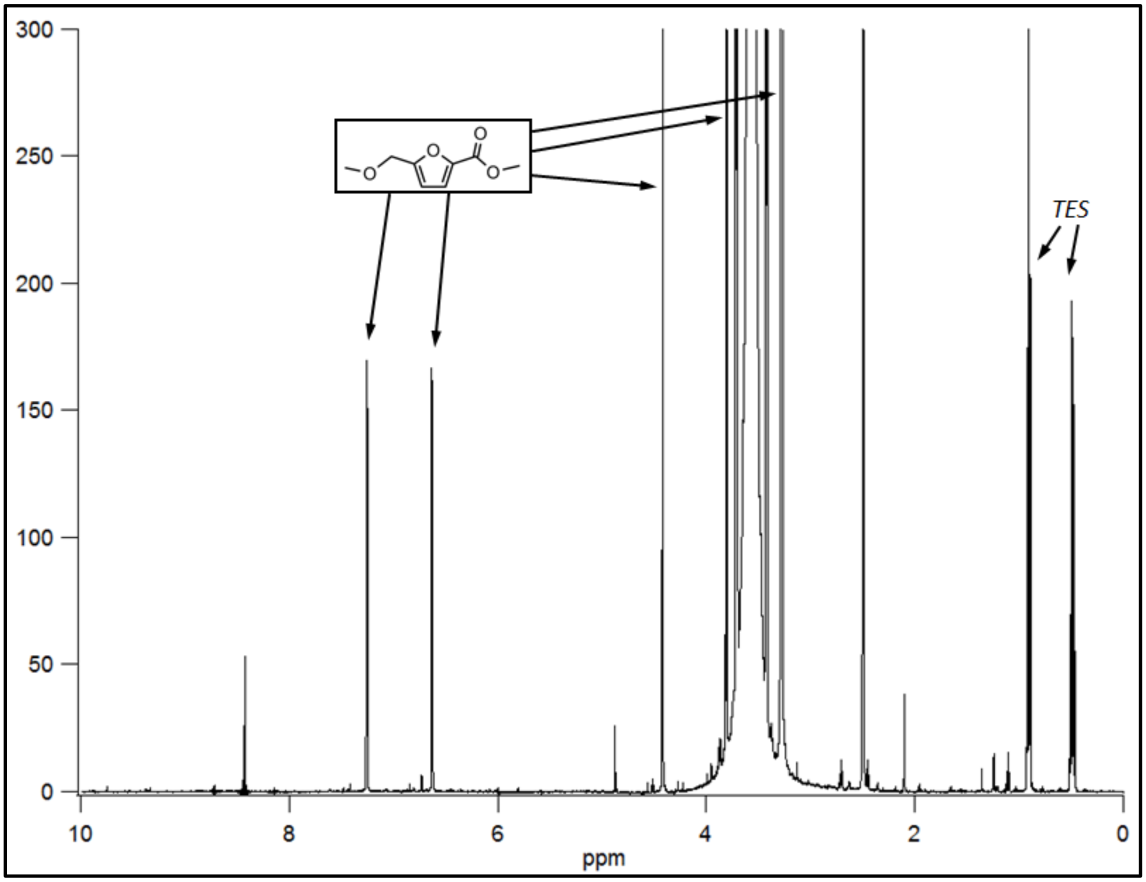


Fig. 5.8 ^{1}H NMR (in DMSO-d_6) of feed solution for experiment in Entry 3, Table 5.3.

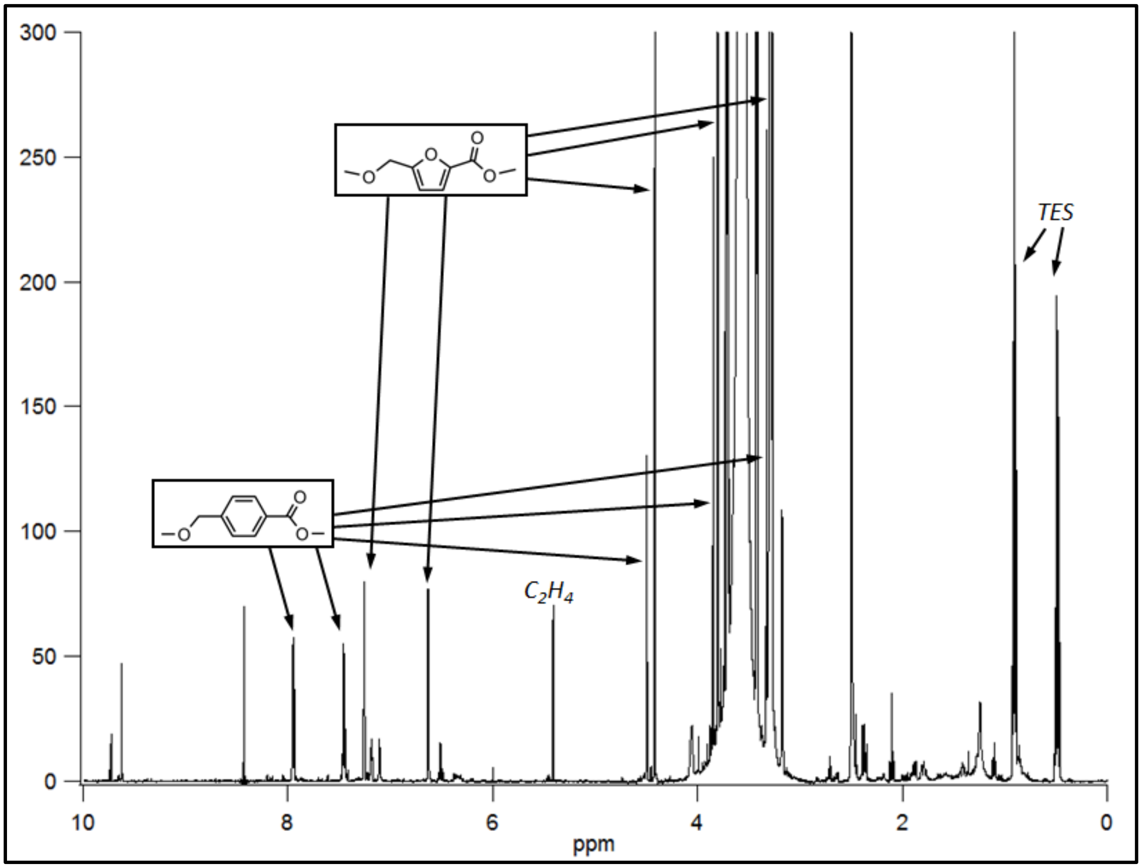


Fig. 5.9 ^{1}H NMR (in DMSO-d_6) of product solution for experiment in Entry 3, Table 5.3.

The product spectra for both the Zr-Beta and Sn-Beta systems look very similar and clearly there are some side products being formed that appear to be the same in both systems. The most significant peaks corresponding to these side products appear in the ^{1}H NMR spectra at 6.51, 7.11, 7.18, 9.62, and 9.73 ppm. The Sn-Beta catalyst produces a higher amount of these side products compared to Zr-Beta. There appears to be aldehyde groups being produced since two of these peaks are in the 9-10 ppm range.

The product solutions from the Sn-Beta and Zr-Beta systems were analyzed by GC/FID to determine the number of side products in addition to

MMBC (Fig. 5.10). The MMFC and MMBC peaks are indicated on the figure and appear at elution times of ~5.1 and ~6.8 minutes, respectively. As expected from the measured selectivities and NMR results, the chromatogram from the Zr-Beta system clearly indicates less side products than the Sn-Beta system.

There are three main side product peaks in the Zr-Beta chromatogram that elute at ~6.6, ~6.9 and ~7.9 minutes in Fig. 5.10. Interestingly, the two products that elute at ~6.6 and ~6.9 minutes in the Zr-Beta system are not only present in the Sn-Beta system as well, but are produced in significantly larger quantities. Chapter 6 provides detailed analysis and discussion of the identification of these main side products.

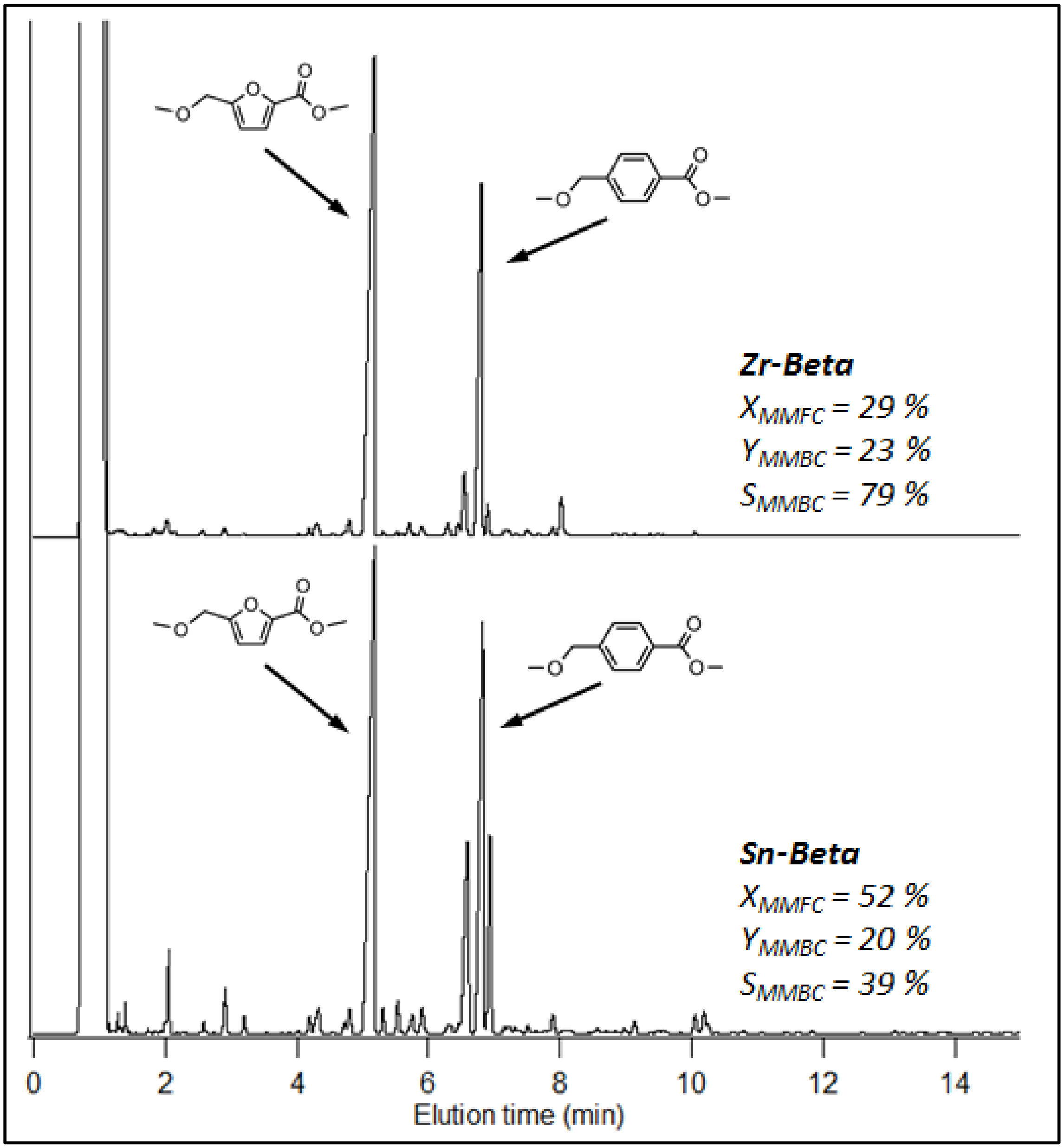


Fig. 5.10 GC-FID chromatograms of product solutions in the Diels-Alder-dehydration reaction of MMFC and ethylene using Zr-Beta and Sn-Beta catalysts. Reaction conditions: 0.1 M MMFC in dioxane, 100 mg catalyst, 190^{o}C, 1000 psig C_2H_4, 6 hrs. Conversions and yields determined by ^{1}H NMR.

The MMFC conversion, MMBC yield, and MMBC selectivity using the Sn-Beta and Zr-Beta catalysts were measured over time (Fig 5.11). The Sn-Beta catalyst produces MMBC at 40-50 % selectivity for the first 6 hours. The yield of MMBC reaches a maximum at ~24 % while the MMFC continues to react to >70% conversion after 12 hours of reaction. The Zr-Beta catalyst is more selective with ~70-80% MMBC selectivities for the entire 12 hour reaction, and appears to remain active after 12 hours.

Further reaction testing was performed by changing various system parameters, such as reaction temperature, solvent, catalyst loading amount, and addition of water (Table 5.4). Comparison of entries 2 and 3 indicate that when using Sn-Beta an increase in temperature from 190^{o}C to 210^{o}C results in a decrease in MMBC selectivity as the conversion increases without any improvement in MMBC yield. When an aliphatic solvent (hexane) was added to the dioxane in a 1:1 v/v ratio, the selectivity decreased slightly (entries 2 and 4). The Zr-Beta catalyst loading was increased from the typical 100 mg to 300 mg in entry 6, and after 6 hours of reaction the selectivity dropped significantly from 85% to 63% while the MMBC yield only increased by 3%. Another ether solvent, triglyme, was tested in entry 7 and very similar performance as dioxane was observed, that is high selectivity and ~30% yield.

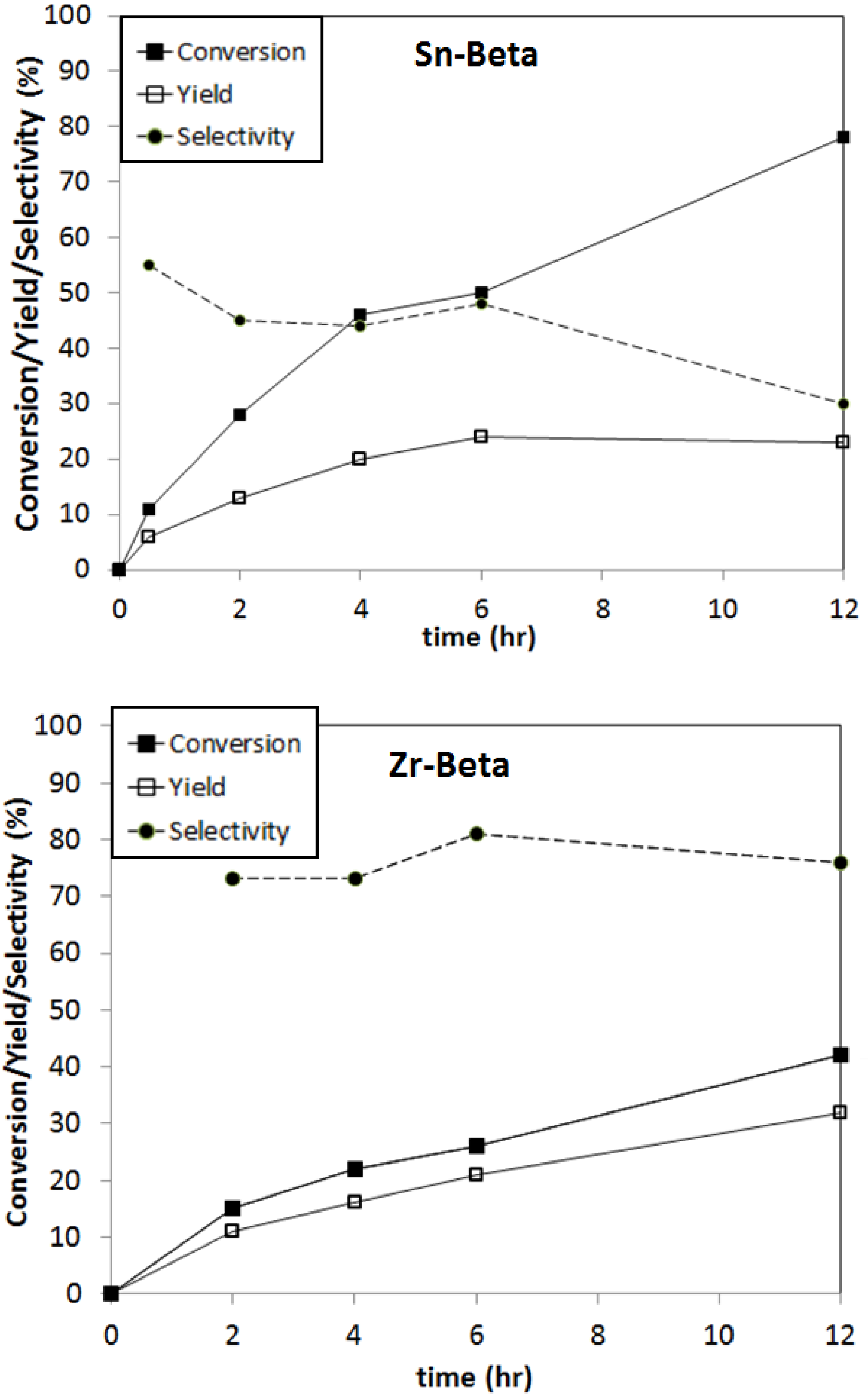


Fig. 5.11 Reaction profiles for the Diels-Alder-dehydration reaction of MMFC and ethylene using Zr-Beta (bottom) and Sn-Beta (top). Reaction conditions: 0.1 M MMFC in dioxane, 100 mg catalyst, 190°C, 1000 psig C_2H_4. Results determined by ^1H NMR.

Table 5.4 Additional reaction results for ethylene Diels-Alder dehydration of MMFC to MMBC. Reaction conditions: 0.1 M MMFC in solvent, 100 mg catalyst, 1000 psig C_2H_4. Results determined by ^{1}H NMR. *300 mg catalyst used.

Entry	Catalyst	Solvent	Temperature (^{o}C)	Time (hr)	MMFC conversion (%)	MMBC yield (%)	MMBC selectivity (%)
1	None	dioxane	190	6	1	0	0
2	Sn-Beta	dioxane	190	2	28	13	46
3	Sn-Beta	dioxane	210	2	44	13	30
4	Sn-Beta	dioxane/hexane 1:1 v/v	190	2	33	12	36
5	Zr-Beta	dioxane	190	6	34	29	85
6	Zr-Beta*	dioxane	190	6	51	32	63
7	Zr-Beta	triglyme	190	6	40	33	83
8	Zr-Beta	triglyme (0.5 wt % water)	190	6	35	22	63
9	Zr-Beta	18-crown-6	190	6	27	3	11

To probe the effect of the water being produced by the Diels-Alder-dehydration reaction, a small amount of water was added to the reaction in entry 8. Both the yield and selectivity drop significantly with just a small addition of water (0.5 wt % water added to triglyme). Since there was a small amount of water present in the dioxane and triglyme solvents used for these reactions, this result suggests that if the initial water were removed then selectivities closer to 100% and higher yields may be achieved. Since these experiments were not carried out in a dry glove box, controlling the exact amount of water, and removing the small amount of water from the feed solutions, while loading the Parr batch reactor was difficult.

An experiment using a large crown ether, 18-crown-6, as solvent was also performed (entry 9) and very low yields/selectivities were observed. This result may be explained by the large amount of water introduced into the system from using the very hydrophilic 18-crown-6.

Another example of the ^{1}H NMR spectra collected for a Zr-Beta catalyzed reaction between MMFC and ethylene is given in Fig. 5.12-5.13, correspond to the experiment reported in entry 5 of Table 5.4. The MMBC yield and selectivity was measured to be 29% and 85%, respectively, when using the TES external standard method. When the quantification was made using the dioxane solvent peak as an internal standard reference (method described in Chapter 2), a MMBC yield and selectivity of 30% and 93%, respectively, was measured. These results were some of the best obtained using any catalyst and reaction condition. The Zr-Beta sample (JP 4-89) used to generate the data in Table 5.4 showed higher activity and selectivity (in dioxane or triglyme) than other Zr-Beta samples prepared using the same or similar synthesis procedures. In an effort to understand how this sample was unique, further investigation was carried out to help elucidate what synthesis parameters are most important for making Zr-Beta catalysts with higher activities and selectivities.

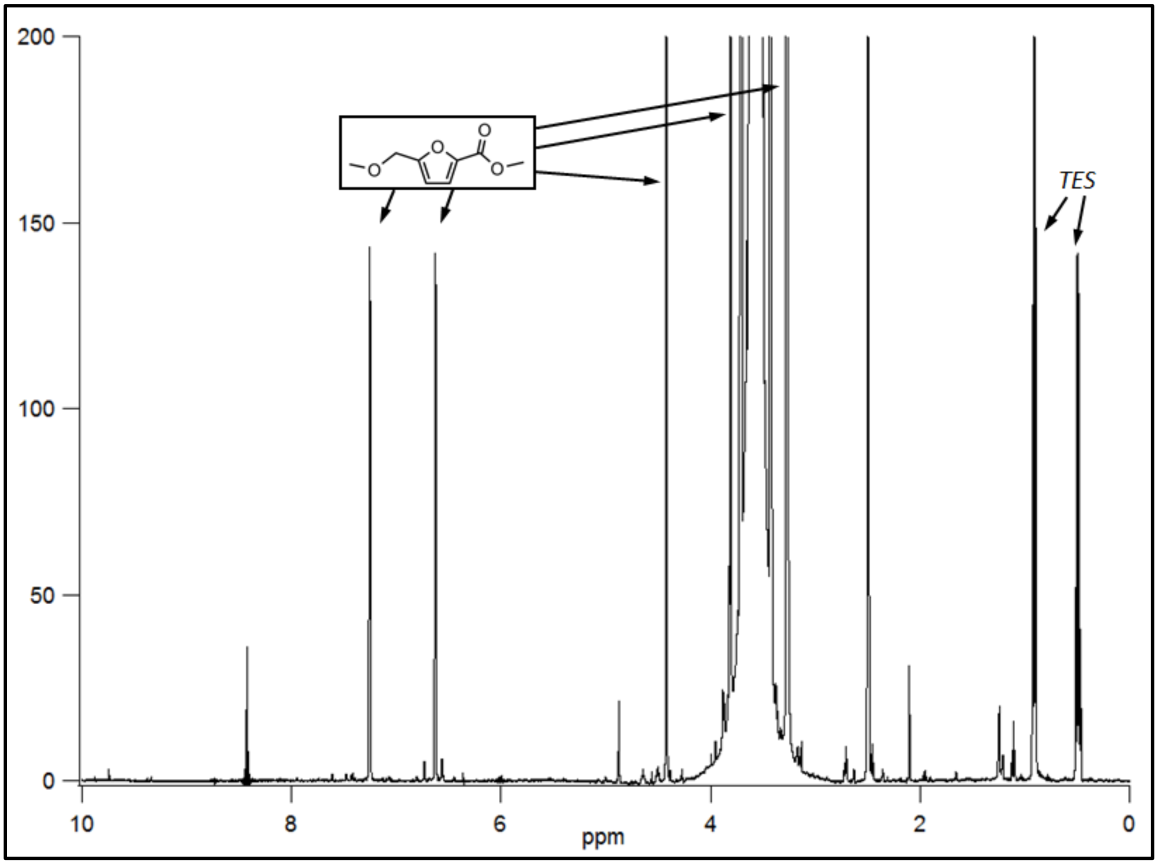


Fig. 5.12 ^{1}H NMR (in DMSO-d_6) of feed solution for experiment in Entry 5, Table 5.4.

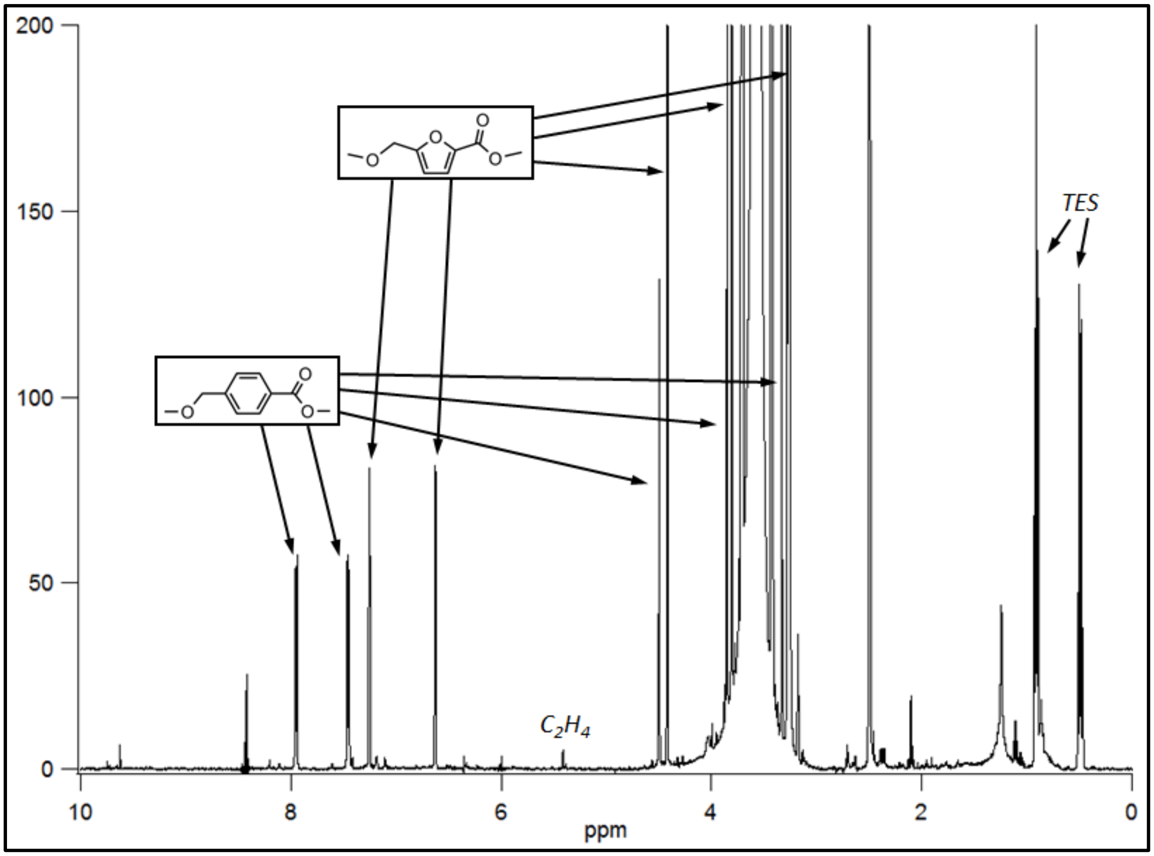


Fig. 5.13 ^{1}H NMR (in DMSO-d_6) of product solution for experiment in Entry 5, Table 5.4.

Reaction results using seven different Zr-Beta catalyst samples are summarized (entries 1-7, Table 5.5). Synthesis details of the samples are listed, including Zr source, gel stir time before addition of Zr source, gel Si/Zr ratio, and final Si/Zr ratio of the catalysts. Two different Zr sources were used – zirconyl chloride ($ZrOCl_2$) and Zr(IV) propoxide. The gel stir time is the time allowed for TEOS hydrolysis in the aqueous TEAOH solution before the addition of the zirconium source (see Chapter 2). “Short” stir times of 37-56 minutes (entries 1-3) are compared to “long” stir times of 94-123 minutes (entries 4-7). The Si/Zr ratio in the synthesis gel was varied between 63 and 400, resulting in final catalyst Si/Zr ratios between 92 and 492. Also included for comparison, is a result using ZrO_2 as catalyst (entry 8).

The result using the JP 4-89 sample with high activity and selectivity is given in entry 1. The Zr source for this catalyst was $ZrOCl_2$ with a high loading of Zr in the gel (Si/Zr = 63). Also, a “short” stir time of 56 minutes was used. After 6 hours of reaction under the typical conditions, the MMBC yield and selectivity was 30% and 93.2%, respectively. When a Zr-Beta sample prepared using the same synthesis method (entry 2) was prepared, only 13.6 % MMBC yield was made at 75.2 % selectivity. The sample in entry 3 was another attempt to replicate entry 1 while using a shorter stir time (37 min), but this catalyst produced another poor reaction result. The exact synthesis and reaction performance observed for the JP 4-89 sample was unable to be reproduced.

Table 5.5 Reaction results for Zr-Beta catalyzed synthesis of MMBC by Diels-Alder-dehydration reaction.

Reaction conditions: 0.1 M MMFC in dioxane, 190°C, 6 hours, 1000 psig C_2H_4. Conversions and yields determined by ^{1}H NMR.

Entry	Catalyst	Zr source in catal. synth.	Gel stir time before addition of Zr source (min)	Gel Si:Zr	Catalyst Si:Zr †	MMFC:Zr molar ratio	MMFC conversion (%)	MMBC yield (%)	MMBC selectivity (%)
1	Zr-Beta-1	$ZrOCl_2$	56	63	116	70	32.2	30.0	93.2
2	Zr-Beta-2	$ZrOCl_2$	56	63	130	78	18.1	13.6	75.2
3	Zr-Beta-3	$ZrOCl_2$	37	63	137	82	13.0	9.5	73.1
4	Zr-Beta-4	$ZrOCl_2$	98	63	123	74	25.4	21.8	86.0
5	Zr-Beta-5	Zr(IV) propoxide	108	63	92	55	29.1	22.7	78.2
6	Zr-Beta-6	Zr(IV) propoxide	123	125	155	58	33.2	25.4	76.6
7	Zr-Beta-7	Zr(IV) propoxide	94	400	492	74	42.5	26.4	62.2
8*	ZrO_2	-	-	-	-	-	-2.0	0	0

* 12 mg ZrO_2 used in reaction; Reaction time: 2 hours.

† Entries 1-4 determined by energy-dispersive x-ray spectroscopy (EDS). Entries 5-7 by Galbraith Laboratories (GLI procedure ME-70).

From the visual appearance of the synthesis gel for the catalysts in entries 2 and 3 it was apparent that at the time the Zr source was added to the gel (after the stir times listed), the gel was not completely homogeneous. That is, the organic TEOS was not hydrolyzed enough to dissolve into the aqueous TEAOH phase to form one homogeneous gel phase. Also, after the addition of the $ZrOCl_2$, white precipitate formed in the gel that was presumably ZrO_2 via TEAOH-catalyzed hydrolysis/condensation of $ZrOCl_2$. The formation of ZrO_2 at this point in the synthesis may result in less incorporation of the Zr into the zeolite framework of the final catalyst and fewer active sites. The time required for the TEOS to fully dissolve in the aqueous TEAOH solution varies and was noticed to depend on the stirring speed setting on the magnetic stir plate (e.g., faster stirring leads to shorter times to reach a homogeneous phase). It is still unclear as to why the JP 4-89 synthesis in entry 1 was not reproduced in entry 2 or 3, but the variable time required for the TEOS to form a single phase with the aqueous TEAOH phase may be an important factor.

Based on this assumption, additional Zr-Beta samples were prepared using “long” stir times (94-123 min) that allowed for a homogeneous phase to form prior to addition of the Zr source (entries 4-7). With the longer stir times the formation of white precipitates upon addition of the Zr source was significantly reduced, and the resulting Zr-Beta materials were more active catalysts with 21.8-26.4% MMBC yields after 6 hours of reaction. One explanation for this result is by allowing more time for the dissolution of the silica source (TEOS) into the aqueous TEAOH phase before introducing Zr into the gel, the Zr source is less likely to condense with itself to form ZrO_2 and more likely to incorporate into the silica networks being formed from the TEOS condensation reactions, and this may ultimately lead to more efficient Zr incorporation into the molecular sieve framework to generate more catalytically active Lewis acid centers.

The Zr source was also varied by using Zr(IV) propoxide and comparison of entries 4 and 5 show that while the MMBC yields are similar between Zr-Beta catalysts made using the different Zr sources (21.8 % vs. 22.7 %), the selectivity is higher for the catalyst made using the $ZrOCl_2$ (86.0 % vs. 78.2 %).

The Si/Zr ratio of the synthesis gel was increased in entries 6 and 7 to produce Zr-Beta with fewer Zr. The Diels-Alder-dehydration reactions were performed by keeping the number of Zr metal atoms (and therefore, the MMFC:Zr ratio) in the reactor relatively constant by using more catalyst (160 mg used in entry 6 and 400 mg used in entry 7). The MMBC yields for entries 5-7 are very similar and ranged between 22.7 %-26.4 %, while the selectivity dropped from 78.2 % to 62.2 % as the Si/Zr ratio in the catalyst was increased from 92 to 492. An explanation for the drop in selectivity with the higher Si/Zr ratio materials may be that as more catalyst was added to keep the number of Zr metal atoms in the system nearly constant, additional water was also introduced into the reactor (there is water adsorbed on the hydrophilic crystal surfaces). As was observed before, addition of water into the system can have a negative effect on MMBC selectivity.

To probe whether the selectivity was being affected by extraframework ZrO_2 on the Zr-Beta catalysts, a two hour reaction was performed using zirconia as catalyst (entry 8). No conversion or MMBC yield was observed. This result does not negate the notion that extraframework ZrO_2 nanoparticles within the molecular sieve pores are contributing to additional conversion of the MMFC to undesired side products, but indicates that bulk ZrO_2 particles are inactive in catalyzing side reactions of MMFC.

This investigation indicates that catalytic performance of Zr-Beta in the ethylene Diels-Alder-dehydration reaction to convert MMFC to MMBC depends significantly on how the catalyst is synthesized. The data suggest that higher MMBC selectivities may be achieved by using $ZrOCl_2$ as the Zr source (rather than Zr(IV) propoxide) and by allowing longer stir times of the TEOS/TEAOH/water mixture before addition of the Zr. Future research directions should be focused on Zr-Beta catalyst synthesis and characterization, and understanding the important characteristics of these materials for achieving high activity and selectivity towards MMBC.

Since a commercially viable process for the conversion of MMFC to MMBC in the liquid phase will likely require higher reaction concentrations than the 2 wt % MMFC concentration used here, an experiment using 10 wt % MMFC was performed to explore the feasibility of using higher MMFC concentrations (Table 5.6). A low loading of Zr-Beta (26 mg) was used since higher conversions were expected with the higher reactant concentrations. After the typical 6 hour reaction, only 4.8 % MMBC yield was produced with a selectivity of 16.4 %. No significant side products were detected by GC/FID (Fig 5.2-A), but the product solution and catalyst turned black. The MMFC had apparently polymerized/converted to insoluble products and had significantly coked/deposited onto the catalyst. This result indicates that the development of methods, reaction conditions, or catalysts that allow for higher MMFC concentrations while maintaining high MMBC selectivity is important for allowing this process to become more commercially viable.

Table 5.6 Ethylene Diels-Alder-dehydration of MMFC to MMBC using high MMFC concentrations. Reaction conditions: 10 wt % MMFC in dioxane, 190^{o}C, 6 hr, 1000 psig C_2H_4. Results determined by ^{1}H NMR.

Catalyst	Catalyst amount (mg)	MMFC conversion (%)	MMBC yield (%)	MMBC selectivity (%)
Zr-Beta	26	29.3	4.8	16.4

To probe whether the MMBC product is participating in secondary reactions as it is being produced in the Diels-Alder-dehydration reaction between ethylene and MMFC, an experiment was performed using a feed solution containing only MMBC dissolved in dioxane. The reactor was charged with a 2 wt% MMBC solution and 100 mg of Zr-Beta, and a 2 hour reaction was performed under the typical reaction conditions (190^{o}C, 1000 psig C_2H_4). No measurable conversion of the MMBC was determined by ^{1}H NMR, suggesting that the MMBC is likely not participating in secondary reactions that would lead to lower selectivities. It is important to note that the Zr-Beta sample used for this experiment was one that was previously found to produce MMBC at lower selectivities (i.e., entry 2, Table 5.5), further suggesting that the MMBC product is not reacting over even the less selective Zr-Beta catalysts and that the loss in selectivity in those reactions are instead due to reactions of the MMFC reactant.

5.3 5-Hydroxymethyl-2-furoic acid (HMFA) as a diene in the ethylene Diels-Alder-dehydration reaction

The use of HMFA as a diene in the ethylene Diels-Alder-dehydration reaction to produce HMBA as a product was investigated (Fig. 5.14) and the reaction testing results will be summarized and discussed here. Reaction conditions that allowed for high selectivities to HMBA were significantly more challenging to find than in the MMFC/MMBC system, and this was clearly due to the higher reactivities of the alcohol and carboxylic acid functionalities.

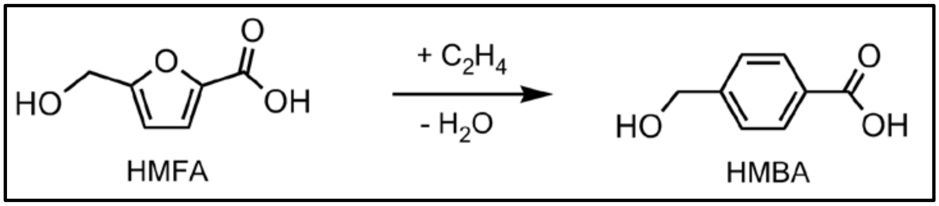


Fig. 5.14 Synthesis of HMBA by Diels-Alder-dehydration reaction of HMFA and ethylene.

Reaction screening results are shown in Table 5.7 for the conversion of HMFA to HMBA using different Lewis acid molecular sieve catalysts and two different HMFA suppliers - Matrix Scientific and Enamine. The Sn-Beta produces the highest yields of HMBA (19 %) at 31 % selectivity when using HMFA supplied by Matrix. The Zr-Beta, Ta-Beta, and Nb-Beta were also found to be active for catalyzing the formation of HMBA, but with less yield and selectivity.

The reactivity was found to also depend on the chosen HMFA supplier. The HMFA from Matrix was found to react more selectivity over Sn-Beta than the HMFA from Enamine. A similar result was found when using the Zr-Beta catalyst, although the effect was less significant. Interestingly, when the control experiments were performed without the addition of catalyst, the Matrix HMFA converted significantly (17 %) over the six hour reaction period while no conversion was measured with the Enamine HMFA. Clearly, there are unknown impurities in the supplied HMFA that are contributing to the observed reactivity.

Table 5.7 Results for ethylene Diels-Alder-dehydration of HMFA to HMBA using Lewis acid molecular sieve catalysts. Reaction conditions: 0.1 M HMFA in dioxane, 190^{o}C, 6 hr, 1000 psig C_2H_4, 100 mg catalyst. Results determined by ^{1}H NMR.

Entry	**Catalyst**	**HMFA supplier**	**HMFA conversion (%)**	**HMBA yield (%)**	**HMBA selectivity (%)**
1	Sn-Beta	Matrix Scientific	61	19	31
2	Zr-Beta	Matrix Scientific	87	9	10
3	Sn-Beta	Enamine	70	12	17
4	Zr-Beta	Enamine	92	6	7
5	Ta-Beta	Enamine	61	6	10
6	Nb-Beta	Enamine	75	3	4
7	None	Matrix Scientific	17	0	0
8	None	Enamine	-1	0	0

An example ^{1}H NMR spectrum of a reaction product solution containing the HMFA diene and HMBA product is shown in Fig. 5.15, along with a spectrum of the same solution spiked with HMBA standard to clearly show which peaks correspond to the HMBA product.

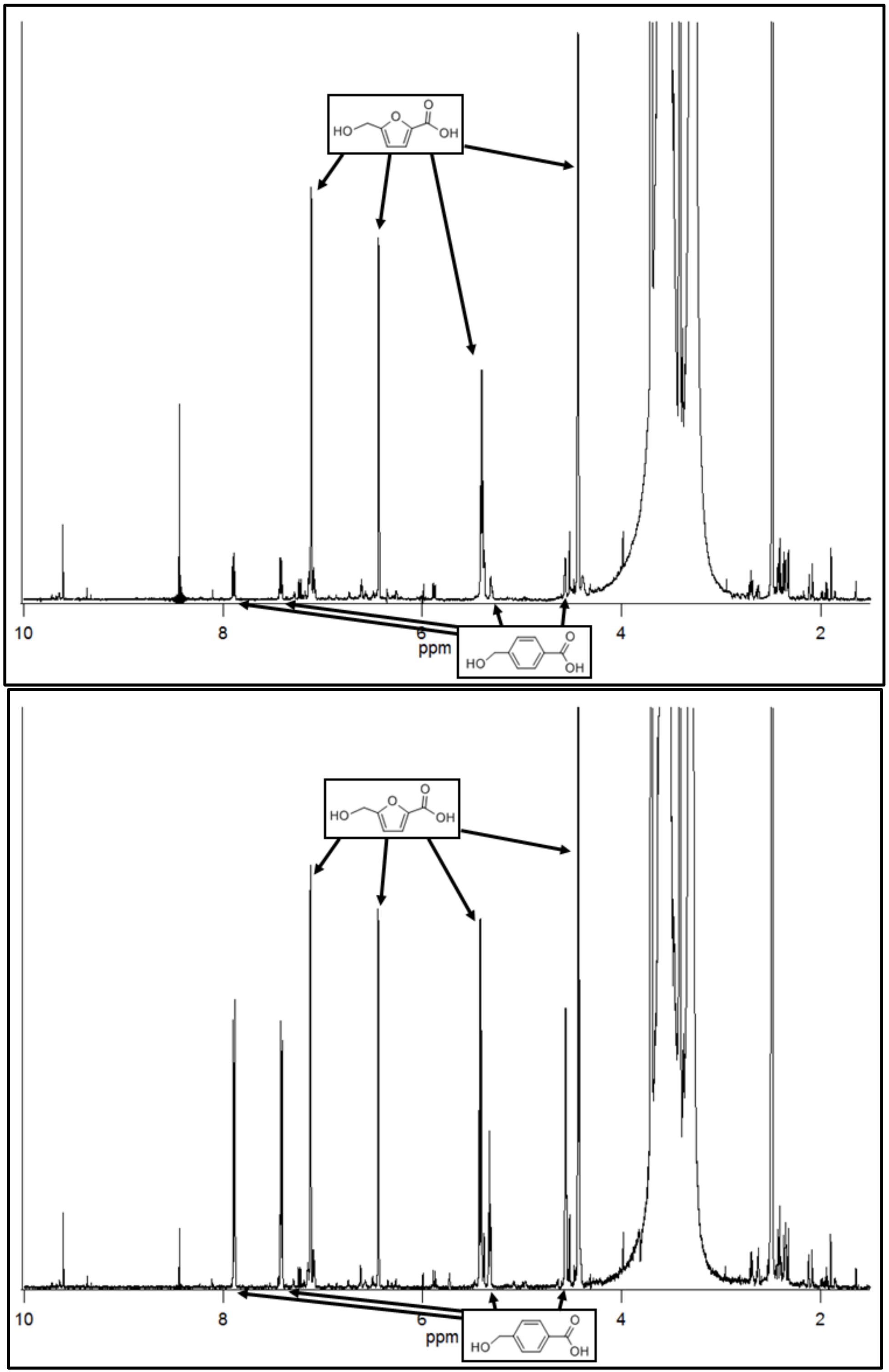


Fig. 5.15 ^{1}H NMR (in DMSO-d_6) of a product solution for the Diels-Alder-dehydration of HMFA and ethylene to form HMBA (top), and the same solution spiked with the HMBA standard (bottom).

Table 5.8 Results for control experiments for ethylene Diels-Alder-dehydration of HMFA. Reaction conditions: 1000 psig C_2H_4, 190°C, 0.1 M HMFA in dioxane, 100 mg catalyst. Results determined by ^{1}H NMR.

Entry	Catalyst	HMFA supplier	Other exp. conditions	Time (hr)	HMFA conversion (%)	HMBA yield (%)	HMBA selectivity (%)
1	None	Matrix Sci.		2	5	0	0
2	None	Matrix Sci.		6	17	0	0
3	None	Matrix Sci.	glass liner in reactor	6	15	0	0
4	None	Matrix Sci.	100 mg $MgSO_4$	2	5	0	0
5	None	Matrix Sci.	100 mg $MgSO_4$	6	12	0	0
6	None	Matrix Sci.	200 mg $MgSO_4$	6	12	0	0
7	None	Enamine		6	-1	0	0
8	Si-Beta	Matrix Sci.		2	20	0	0
9	Si-Beta	Matrix Sci.		6	56	0	0
10	Si-Beta	Enamine		6	14	0	0

Several control experiments were performed to help provide understanding for the reason for the low HMBA selectivities and high conversion of HMFA in the absence of any catalyst (Table 5.8). To test whether side reactions resulting from contact with the steel walls of the Parr reactor were the reason for the high HMFA conversion s in the absence of any catalyst (entries 1 & 2), a glass liner for the Parr reactor was used (entry 3) but the conversion still remained significant. A desiccant, magnesium sulfate, was tested (entries 4-6) to determine if by removing water from solution the HMFA conversion could be slowed, but only a small decrease in HMFA conversion compared to that in entries 1-2 was measured after six hours at reaction conditions. Entry 7 shows that HMFA conversion in the no catalyst control experiment can be avoided by using the Enamine-supplied HMFA. Other control experiments in which Si-Beta was tested (entries 8-10) showed that the pure silica material contributes to

HMFA conversion. Over half of the Matrix HMFA reacted and 14 % of the Enamine HMFA reacted after six hours in the presence of Si-Beta.

These findings suggest that future research directions should focus on understanding the impurities, and the side reactions that these impurities cause, in the HMFA supply. Additionally, the development of methods, reaction conditions, and catalyst modifications that reduce the side reactions and deposition of HMFA onto the silica catalyst surface will be crucial for improving the selectivity to the desired HMBA product.

5.4 5-Methoxymethyl-2-furoic acid (MMFA) and methyl 5-hydroxymethyl furan-2-carboxylate (HMFC) as dienes in the ethylene Diels-Alder-dehydration reaction.

Clearly, the selectivity to the 1,4-substituted aromatic product can be improved substantially by adding methanol to the alcohol and carboxylic acid functions of HMFA before performing the ethylene Diels-Alder-dehydration reaction with the Lewis acid molecular sieve catalyst. This section summarizes experiments that were performed using the dienes shown in Fig. 5.16 that have either the ether *or* the ester function. These dienes are 5-methoxymethyl-2-furoic acid (MMFA) and methyl 5-hydroxymethyl furan-2-carboxylate (HMFC), and the products are 4-methoxymethyl benzoic acid (MMBA) and methyl 4-hydroxymethyl benzene carboxylate (HMBC), respectively.

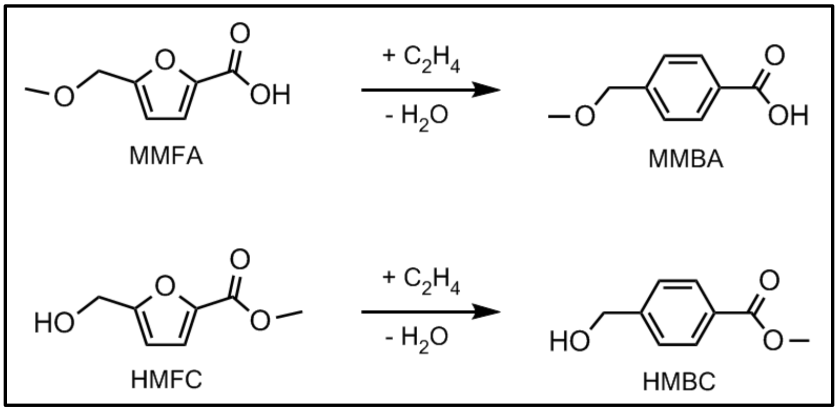
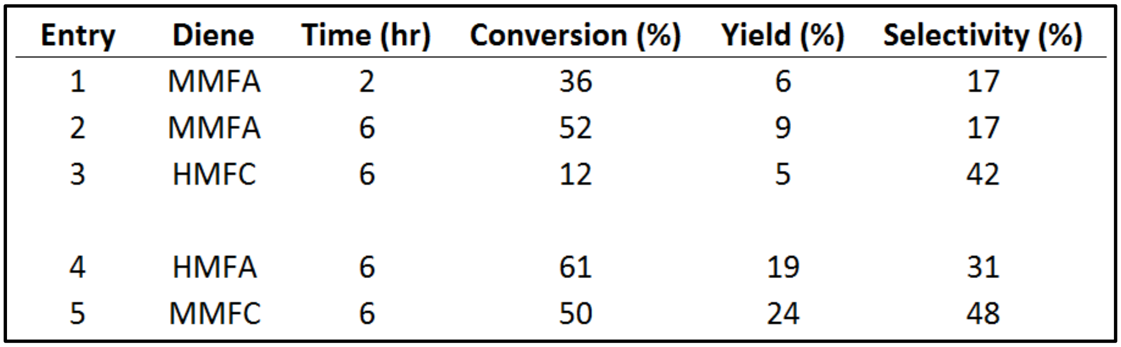


Fig. 5.16 Synthesis of HMBA by Diels-Alder-dehydration reaction of HMFA and ethylene.

Table 5.9 shows reaction results obtained using Sn-Beta as catalyst and compares the reactivity of the four HMFA-derived dienes – HMFA, MMFC, MMFA, and HMFC. Entries 1 and 2 show that the selectivity for the conversion of MMFA to the MMBA product is low (17 %) after two and six hours of reaction, and entry 3 shows that a higher selectivity (42%) is achieved when using the HMFC diene. The yields of the MMBA and HMBC are lower than the yields reported earlier for the conversions of both HMFA to HMBA (entry 4) and MMFC to MMBC (entry 5). It is clear that the highest yields and selectivities are achieved by protecting both the alcohol and acid functions of HMFA (i.e., MMFC).

Table 5.9 Results for ethylene Diels-Alder-dehydration reactions using MMFA, HMFC, HMFA, and MMFC with Sn-Beta. Reaction conditions: 1000 psig C_2H_4, 190^{o}C, 0.1 M diene in dioxane, 100 mg Sn-Beta. Results determined by ^{1}H NMR.



Entry	Diene	Time (hr)	Conversion (%)	Yield (%)	Selectivity (%)
1	MMFA	2	36	6	17
2	MMFA	6	52	9	17
3	HMFC	6	12	5	42
4	HMFA	6	61	19	31
5	MMFC	6	50	24	48

5.5 References

[1] Casanova, O.; Iborra, S.; Corma, A.; *ChemSusChem* **2009** *2*(12), 1138 – 1144.