CHAPTER 6

IDENTIFICATION OF SIDE PRODUCTS IN THE PRODUCTION OF METHYL 4-(METHOXYMETHYL) BENZENE CARBOXYLATE (MMBC) FROM METHYL 5-(METHOXYMETHYL)-FURAN-2-CARBOXYLATE (MMFC) AND ETHYLENE

6.1 Identification of side products in the synthesis of MMBC

As shown in the previous chapter, MMBC can be produced with high selectivity (70-80+ %) from MMFC under high ethylene pressures using Zr-Beta. This chapter summarizes the main side products that have been identified in the reaction system. These findings may help in future investigations for improving catalyst selectivity or for discovering more selective (and active) catalytic materials for the ethylene Diels-Alder-dehydration reaction of HMFA-derived dienes. The methods used to elucidate these side products include GC/FID, GC/MS, prep-thin layer chromatography (prep-TLC), and ^{1}H NMR.

GC/FID was used to analyze the reaction product mixtures to determine the number of side products being produced in the MMFC/MMBC system using the Zr-Beta and Sn-Beta catalysts. Typical chromatograms of product solutions, along with the reaction results (conversion, yield, selectivity), are shown in Fig. 6.1. A chromatogram from an Al-Beta (Bronsted acid zeolite) catalyzed reaction is included for comparison.

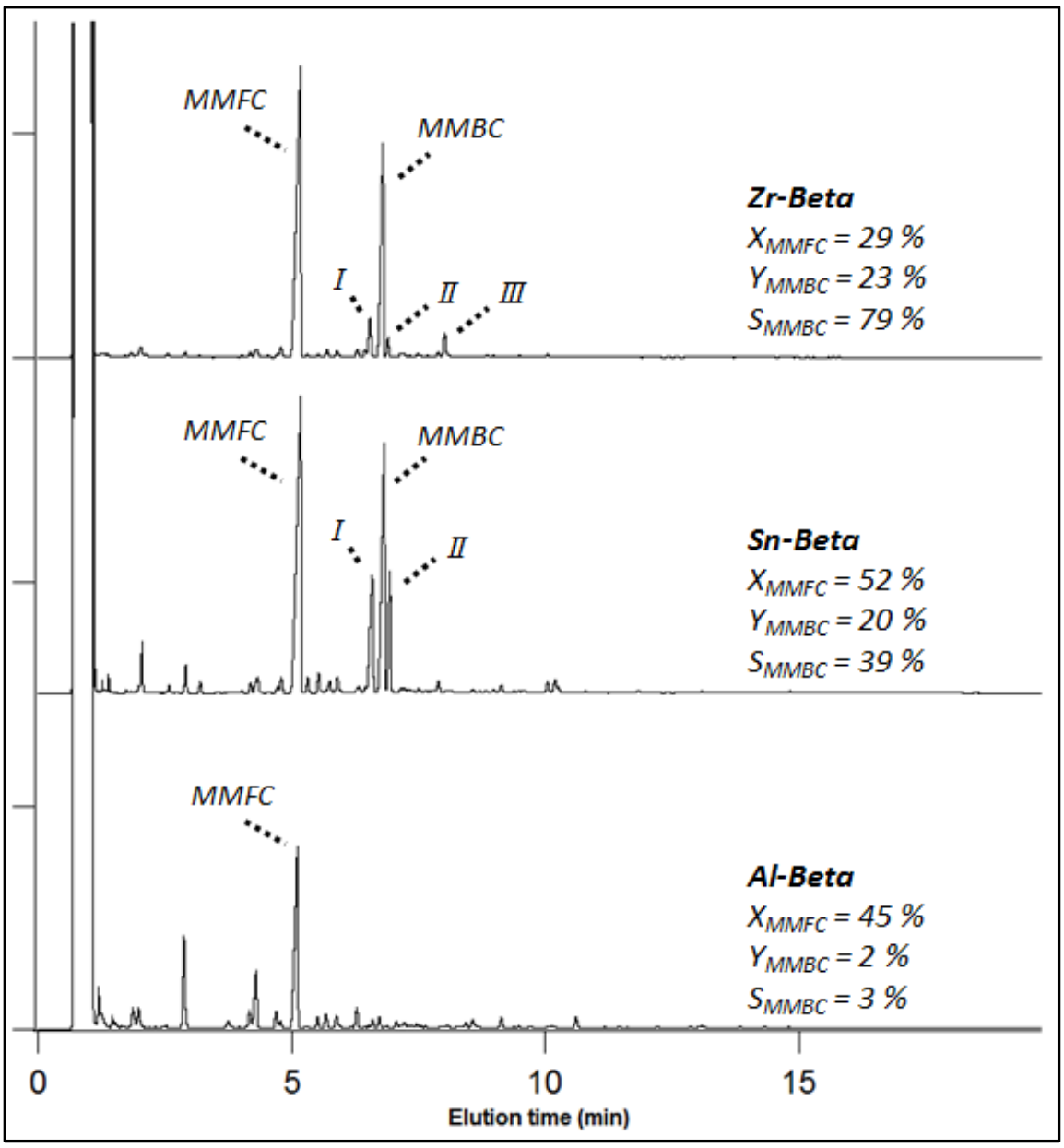

Fig. 6.1 GC-FID chromatograms of product solutions in the Diels-Alder-dehydration reaction of MMFC and ethylene using Zr-Beta, Sn-Beta, and Al-Beta catalysts. Reaction conditions: 0.1 M MMFC in dioxane, 100 mg catalyst, 190^{o}C, 1000 psig C_2H_4, 6 hrs. Al-Beta reaction time was 3 hr. Conversions and yields determined by ^{1}H NMR.

As shown in the previous chapter only the Zr-Beta and Sn-Beta molecular sieves were found to produce the Diels-Alder-dehydration product, MMBC, with

reasonable yield and selectivity, and the Bronsted acid zeolite produces only small amounts of the desired product with very low selectivity. The largest side product peaks in the Zr-Beta chromatogram are identified as products I, II, and III. In the Sn-Beta system, these same products also appear along with many additional side products. Interestingly, the products I and II in the Zr-Beta system are produced in a significantly higher amount by the Sn-Beta. Further investigation was mainly focused on identifying side products I and II.

The Sn-Beta and Zr-Beta product solutions were analyzed by GC/MS to obtain EI mass spectra of the side products. The mass spectra of the three main side products in the Zr-Beta system (I, II, and III) are shown in Fig. 6.2-6.4. Compounds I, II, and III have molecular weights of 166, 194, and 194, respectively. MS libraries of known compounds were screened and no match was found for any of these three spectra.

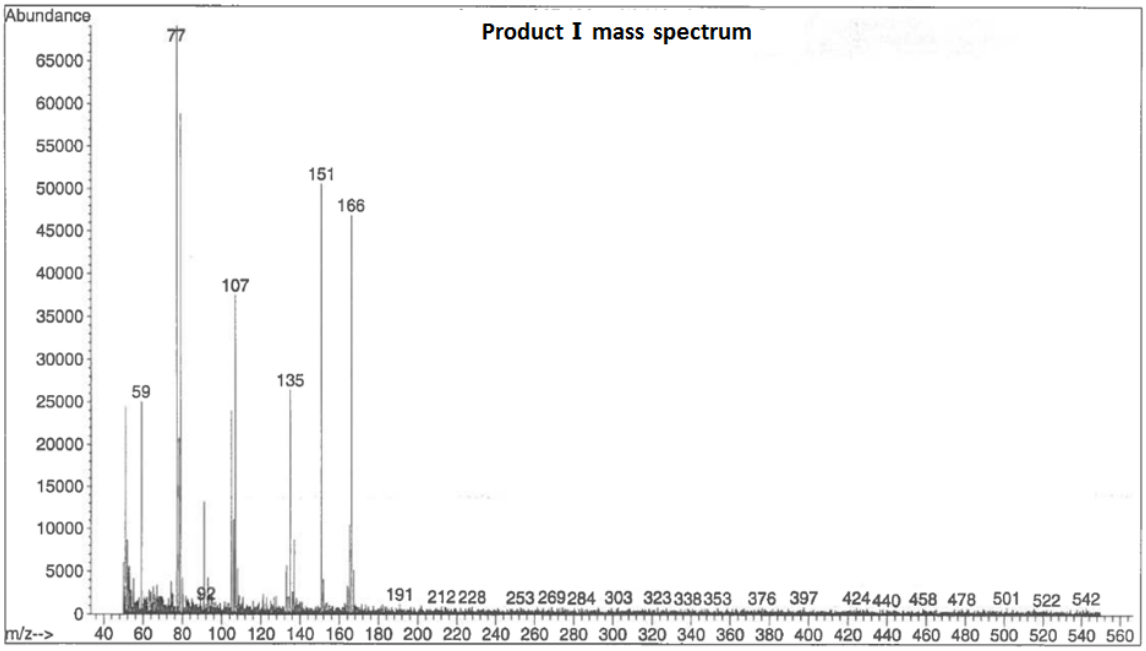

Fig. 6.2 EI mass spectrum of Product I.

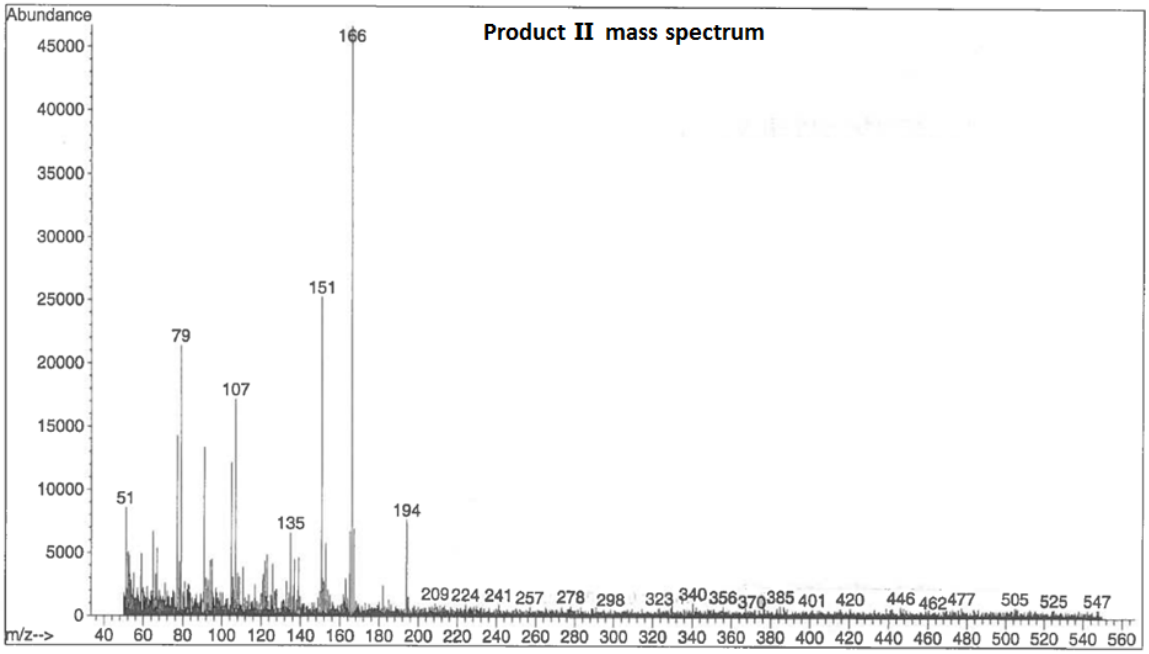

Fig. 6.3 EI mass spectrum of Product II.

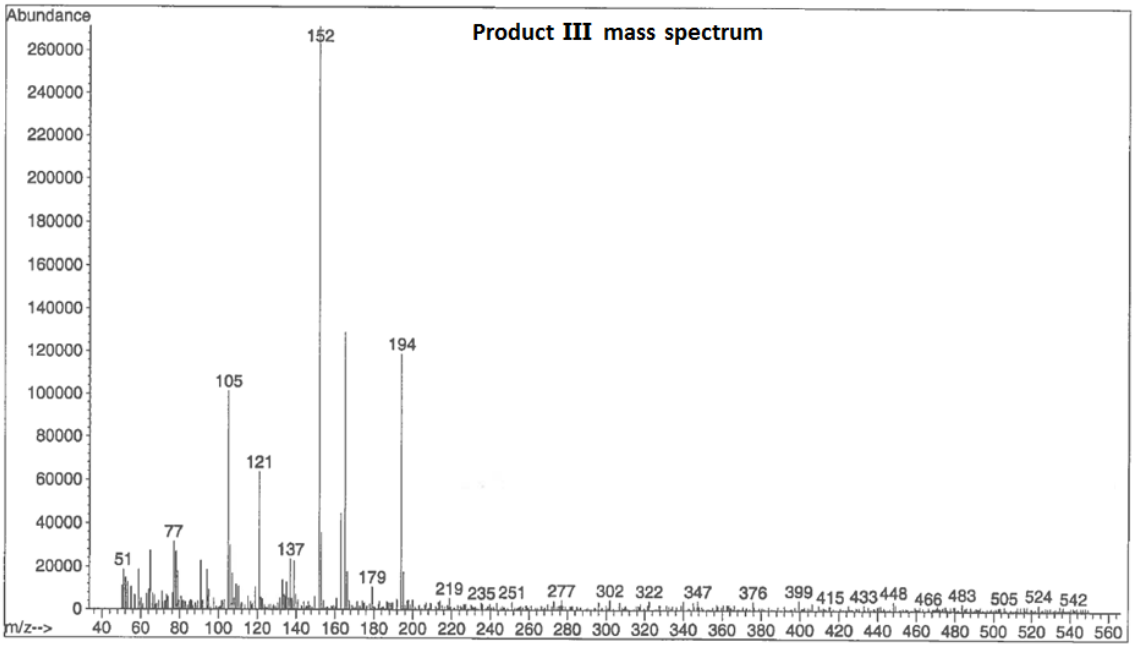

Fig. 6.4 EI mass spectrum of Product III.

To provide additional information that would be helpful for determining the identity of these compounds, more accurate fragment masses and chemical formula predictions were obtained by collecting time of flight mass spectra (TOF-MS). The EI mass spectra and predicted chemical formulas were obtained for products I and II (Fig. 6.5). The masses of products I and II are 166.063 and 194.094, respectively, and based on the fragment weights the predicted chemical formulas were determined as $C_9H_{10}O_3$ and $C_{11}H_{14}O_3$.

When comparing the spectra in Fig. 6.5, it is clear that the masses of all the fragments in the two spectra are very similar, if not identical. Additionally, the difference in the predicted chemical formulas is one ethylene molecule (C_2H_4) and the mass of the first molecular ion fragment peak (166.063) in the product II mass spectrum corresponds to a loss of one ethylene molecule. This information

suggests that a close relationship between the two compounds exist and that an ethylene molecule is reacting in some way with I to form II.

As mentioned, mass spectra libraries have been searched to find a match to either of these spectra but no match was found. Therefore, to provide further information to identity of these compounds, efforts were made to separate the product mixture and isolate the unknowns for NMR analysis.

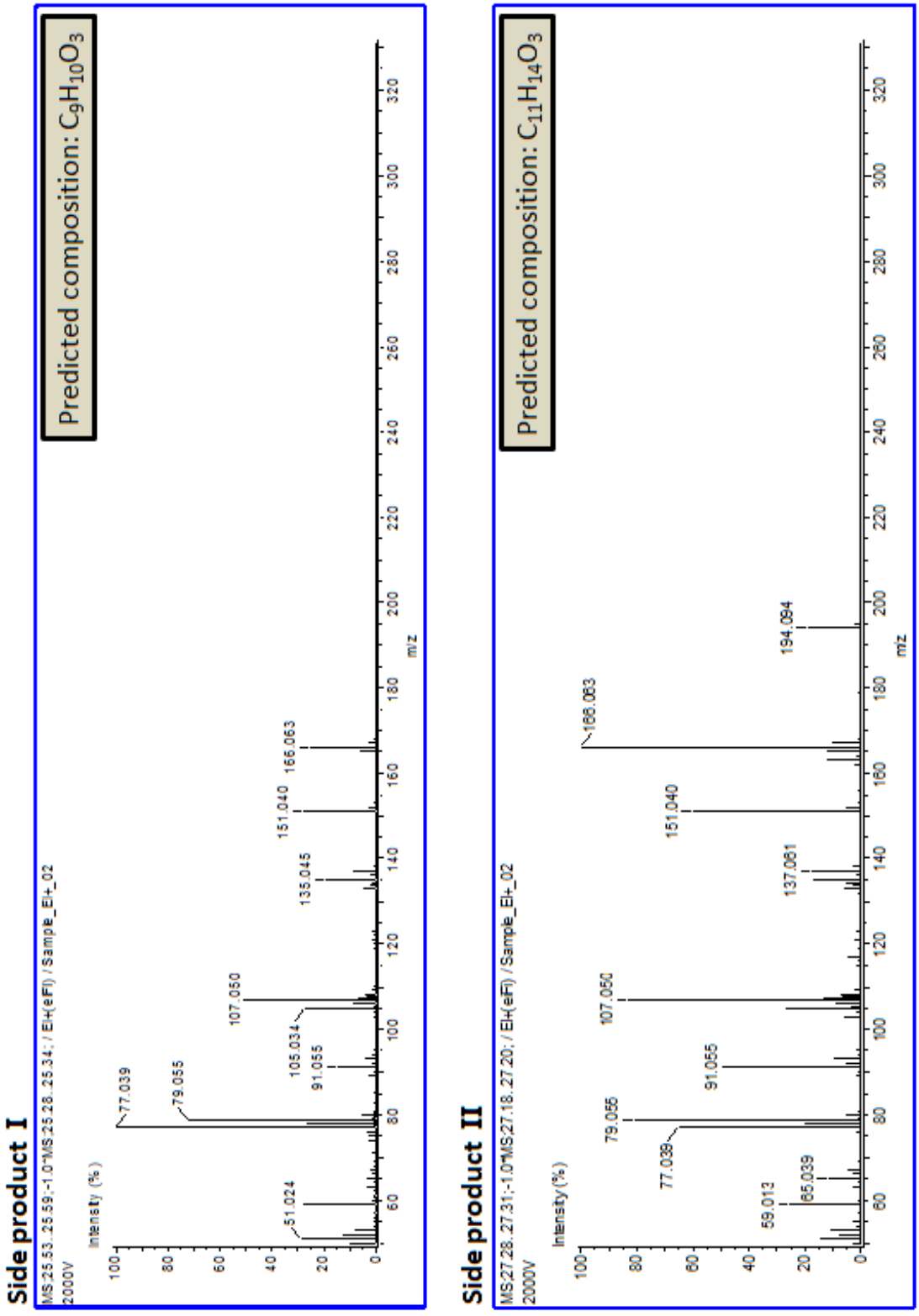

Fig. 6.5 TOF EI mass spectra and predicted chemical formulas of side products I and II.

To isolate the unknown side products, thin layer chromatography (TLC) was used as a method to separate the reaction product mixtures. Since larger amounts of products I and II are produced using Sn-Beta as catalyst, the product solutions made from the Sn-Beta catalyzed reactions were used in the TLC experiments. The product mixture was filtered to remove catalyst and deposited onto silica plates using a needle syringe. Using a 1 ethyl acetate:3 hexanes v/v mobile phase, the product mixture was separated into multiple bands (visible under UV light) on the silica plates. The organics in each of the bands were collected by scratching away the silica from the plates and collecting into separate vials. The silica was contacted in dichloromethane (DCM) and the DCM was then collected, filtered, and analyzed by GC/FID.

Contained in one of the TLC bands was both MMFC and the side product I. The gas chromatogram of the DCM solution containing the compounds in the TLC band is shown in Fig. 6.6, and essentially only MMFC and side product I are present. Several TLC plates were prepared, and enough of the separated band was collected and redissolved in $CDCl_3$ to obtain a ^1H NMR spectrum (Fig. 6.7). The MMFC peaks are indicated by "*", and six additional peaks are labeled corresponding to side product I.

The ^1H NMR spectrum supports the proposed cyclohexadiene molecular structure (Fig. 6.8), namely methyl 4-formylcyclohexa-1,3-diene-1-carboxylate. The relative areas and chemical shifts of the six numbered peaks in the NMR (Table 6.1) can be related to each of the protons in methyl 4-formylcyclohexa-1,3-diene-1-carboxylate. Additionally, this molecule has a chemical formula of

$C_9H_{10}O_3$ which is consistent with the predicted formula from the TOF/MS experiment, and the EI mass spectrum of side product I can be interpreted from this structure .

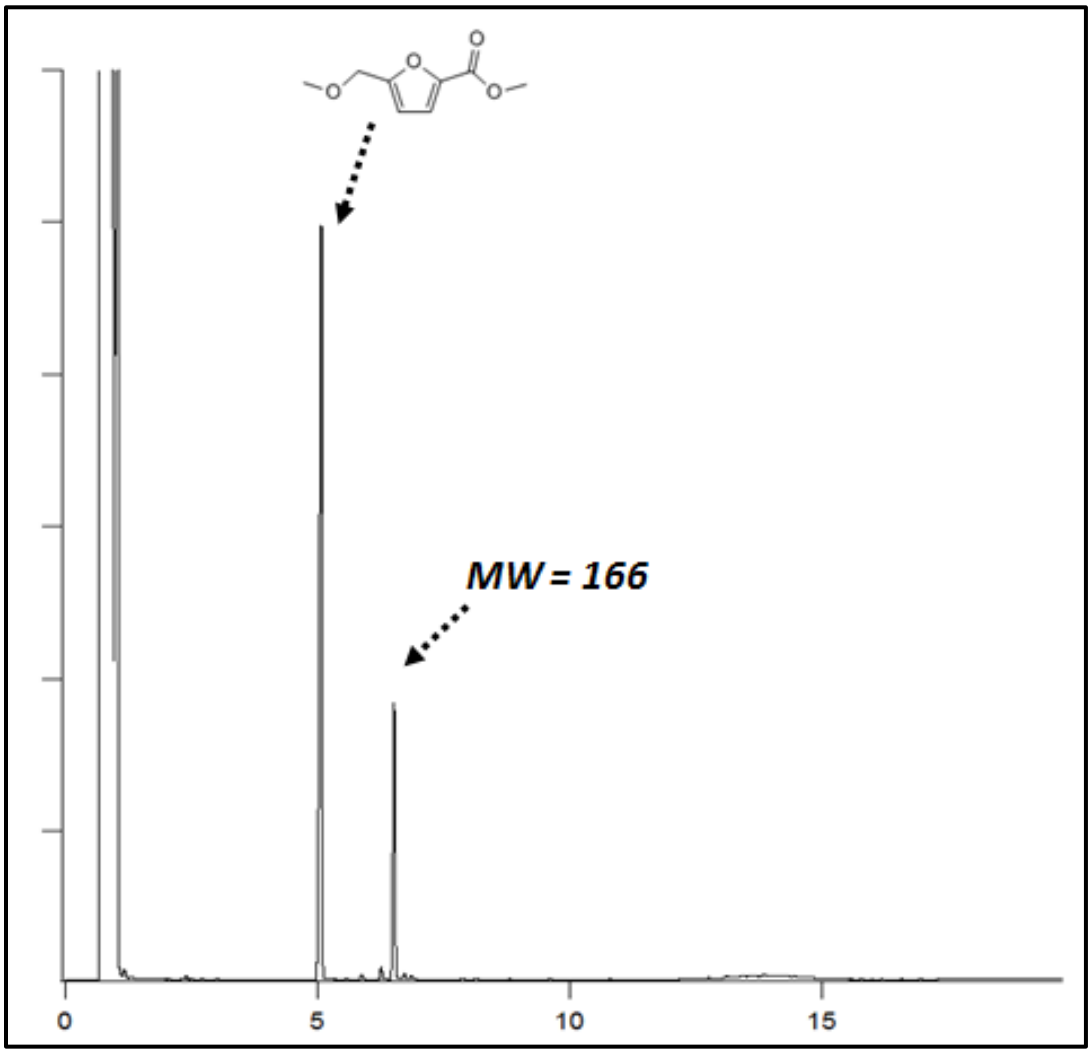

Fig. 6.6 GC-FID chromatogram of TLC fraction containing I (MW=166) and MMFC.

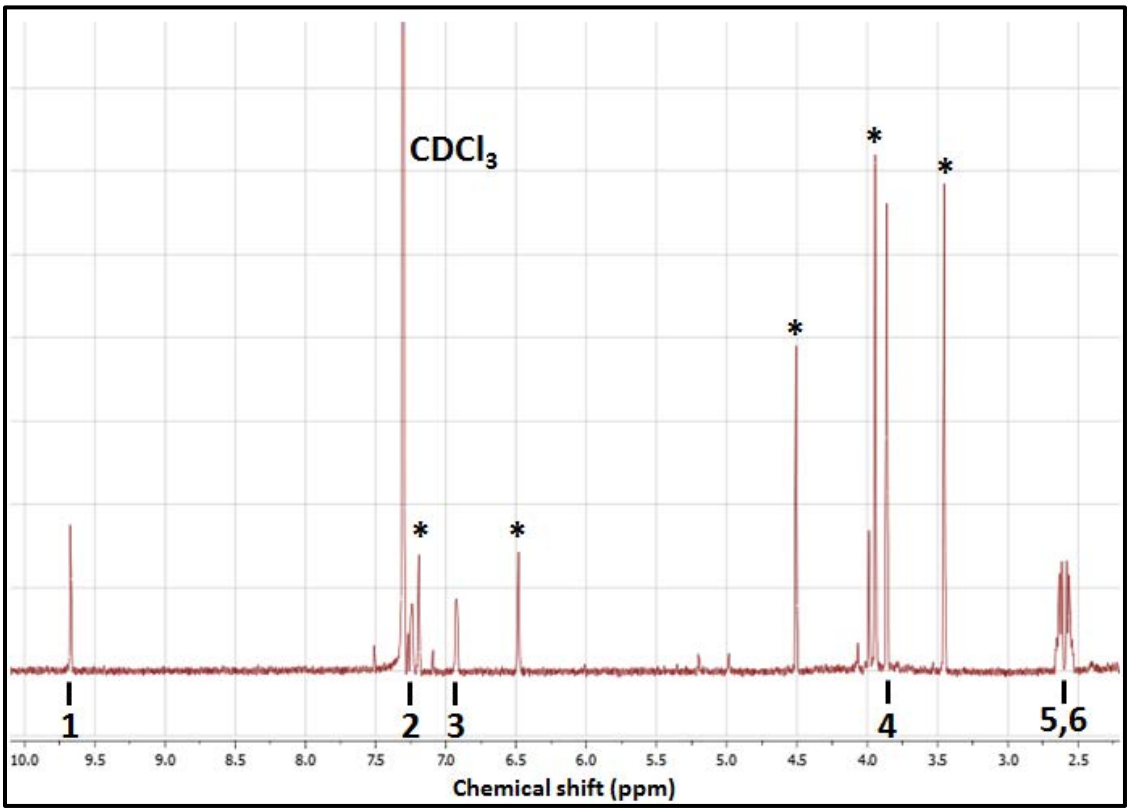

Fig. 6.7 ^{1}H NMR spectrum of TLC fraction containing product I and MMFC (∗).

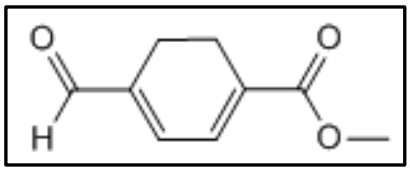

Fig. 6.8 Proposed molecular structure of product I (MW = 166), methyl 4-formylcyclohexa-1,3-diene-1-carboxylate.

Table 6.1 Relative areas of numbered peaks corresponding to I in Fig. 6.7.

Peak No.	Area
1	1
2	0.93
3	1.03
4	3.22
5	2.09
6	2.08

The TLC method was also able to isolate a fraction containing side product II by GC/FID and GC/MS, although several other compounds were also present in the fraction and very little material was collected on each plate which prevented a satisfactory ^{1}H NMR spectrum from being collected.

Since the mass spectrum of II is similar to I with the main difference being an additional ethylene fragment, and since the proposed structure of I has a cyclohexadiene functionality to it, there is a reasonable possibility that II is a Diels-Alder product between I and ethylene. One likely structure of II is methyl 4-formylbicyclo[2.2.2]oct-2-ene-1-carboxylate (Fig. 6.9). The thermally induced retro-Diels-Alder reaction to produce ethylene and I is probably the first dissociation reaction that occurs during ionization in the MS to produce a fragmentation pattern similar to I. Another example of the similarity in mass spectra between a cyclohexadiene and the Diels-Alder adduct of the diene with ethylene is seen when comparing the mass spectra of 1,3- cyclohexadiene and bicyclo[2.2.2]oct-2-ene (Mass spectra available on webbook.nist.gov). The formation of a bicyclo[2.2.2]oct-2-ene product from the Diels-Alder addition of

ethylene to a cyclohexadiene side product was also observed by Do, et al. in the elucidation of the reaction network for the ethylene Diels-Alder-dehydration reaction of DMF and ethylene to PX (Fig. 6.10).[1]

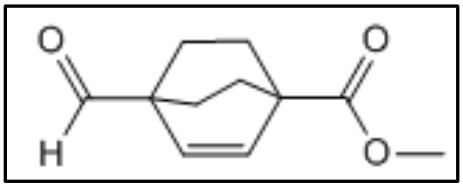

Fig. 6.9 Proposed molecular structure of product II (MW = 194), methyl 4-formylbicyclo[2.2.2]oct-2-ene-1-carboxylate.

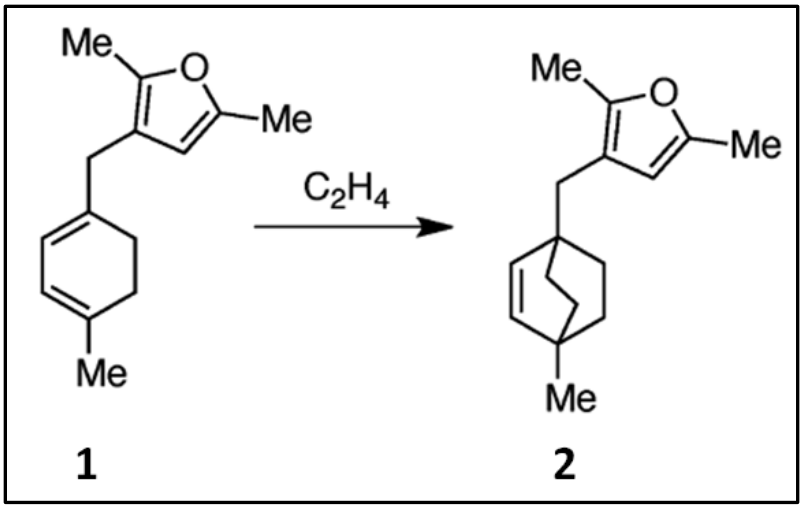

Fig. 6.10 Formation of a bicyclo[2.2.2]oct-2-ene product from the Diels-Alder addition of ethylene with a cyclohexadiene side product observed by Do, et al.[1]

After several weeks of storing in vials at ambient conditions, the Sn-Beta and Zr-Beta catalyzed product solutions were analyzed again and the formation of different side products were observed. In addition to MMFC and MMBC, methyl 4-formyl benzoate, dimethyl 2,5-furandicarboxylate, and dimethyl

terephthalate were the main products, as shown in the GC/FID chromatogram in Fig. 6.11. The compounds were confirmed by comparing the GC elution times and mass spectra with known product standards (mass spectra in Fig. 6.1-6.3-A of appendix). Along with the formation of these new side products was the disappearance of the initially formed side products, methyl 4-formylcyclohexa-1,3-diene-1-carboxylate and methyl 4-formylbicyclo[2.2.2]oct-2-ene-1-carboxylate.

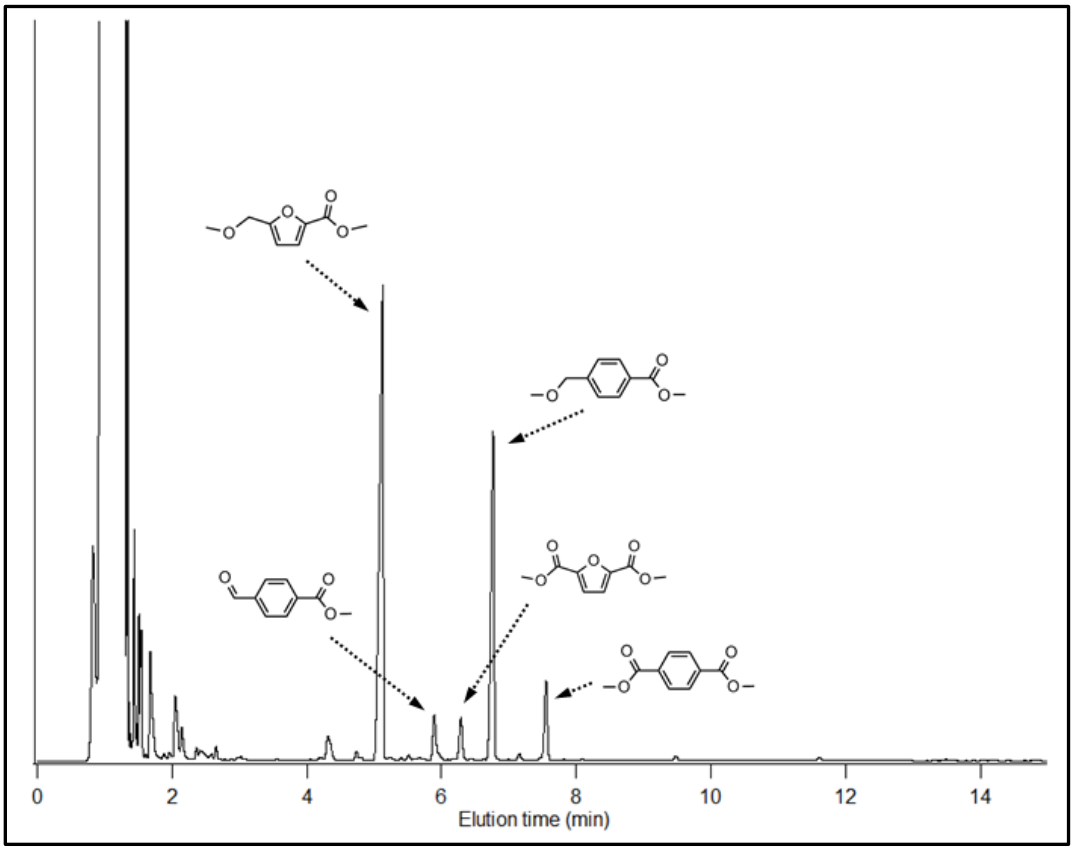

Fig. 6.11 Example of gas chromatogram of MMFC/ethylene Diels-Alder product solution after storing for several weeks at room temperature.

It is highly probable that methyl 4-formyl benzoate forms from the methyl 4-formylcyclohexa-1,3-diene-1-carboxylate side product by an air oxidation as shown in Fig. 6.12. Similar types of oxidations from cyclohexadiene side products to the aromatics were also reported by Do, et al.[1] Specifically, isolated samples of **1** and **3** converted to **2** and **4**, respectively, upon standing in air (Fig. 6.13). In another example, Mcgraw, et al. reported the thermally induced oxidation at 120 ^{o}C of α-terpinene to p-cymene, thymol, and carvacrol (Fig. 6.14).[2]

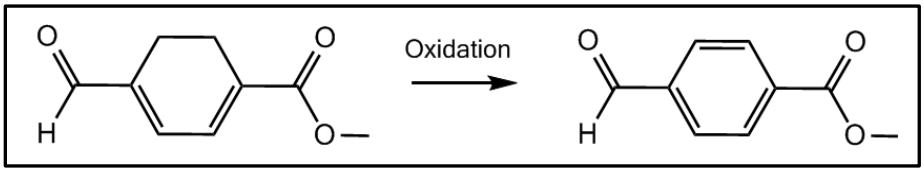

Fig. 6.12 Proposed oxidation of methyl 4-formylcyclohexa-1,3-diene-1-carboxylate to methyl 4-formyl benzoate at ambient conditions.

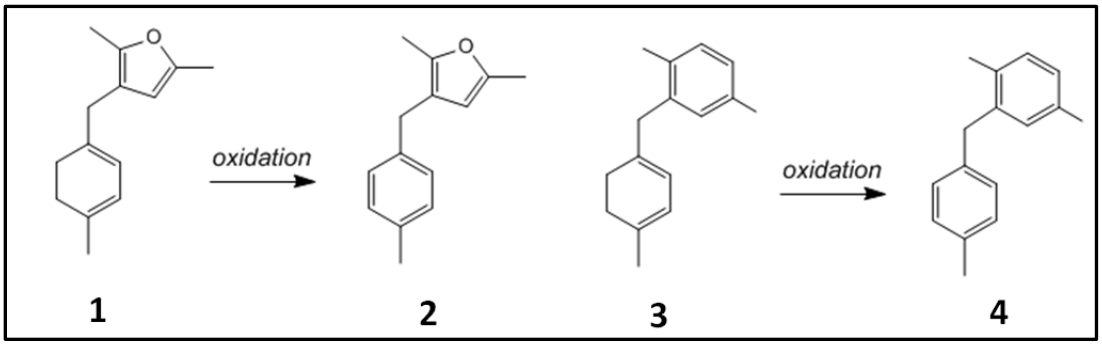

Fig. 6.13 Oxidation of cyclohexadiene side products to the corresponding aromatics observed by Do, et al.[1]

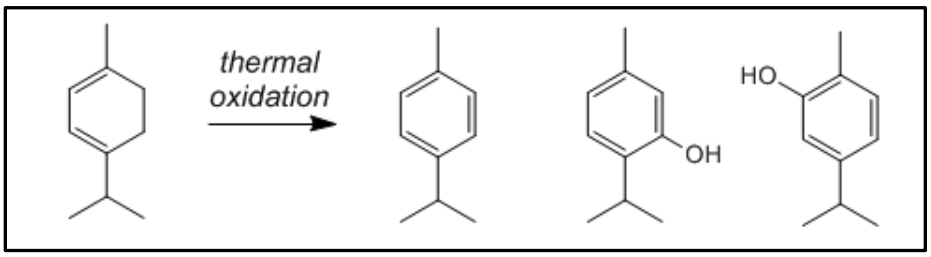

Fig. 6.14 Thermal oxidation of α-terpinene to p-cymene, thymol, and carvacrol reported by Mcgraw, et al.[2]

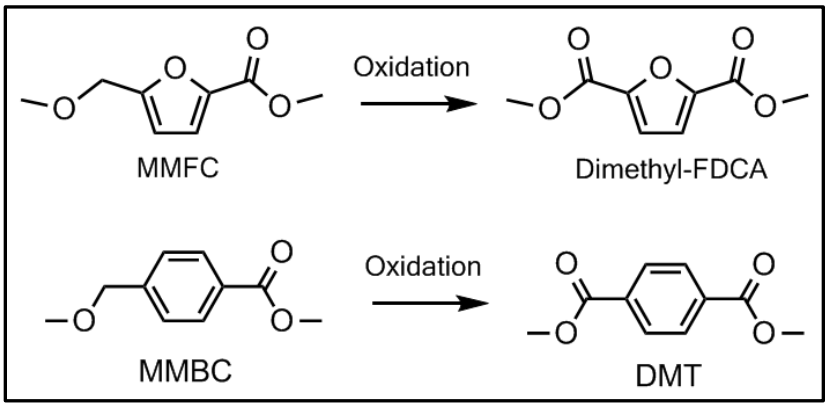

Fig. 6.15 Possible formation of dimethyl-FDCA and DMT from oxidation of MMFC and MMBC, respectively.

The dimethyl ester of FDCA (dimethyl-FDCA) and DMT are likely formed from MMFC and MMBC, respectively, by oxidation (Fig. 6.15).

The proposed overall reaction network for the system based on the findings of this investigation is shown in Fig. 6.16. The Lewis acid catalyst is involved in catalyzing the Diels-Alder-dehydration of MMFC (**1**) and ethylene to MMBC (**4**) under reaction conditions (190^{o}C, 1000 psig C_2H_4) via the ring-opened Diels-Alder adduct **3**. The formation of the side product methyl 4-formylcyclohexa-1,3-diene-1-carboxylate (**10**) could also be formed via a Lewis

acid-catalyzed pathway. One possible mechanism for the formation of **10** involves an alternate ring-opened Diels-Alder adduct (**6**) and the formation of methanol. The product **10** then reacts with ethylene to form the product **12**. The conversion of **10** to **12** is expected to be reversible, therefore as **10** oxidizes to form **11**, both **10** and **12** are consumed. This would reasonably explain the formation of **11** at the expense of **10** and **12** in the GC chromatogram after the solutions are stored at long times. Dimethyl-FDCA (**13**) and DMT (**5**) are likely formed from the oxidation of MMFC (**1**) and MMBC (**4**), respectively, while being stored at room temperature.

Alternate acid-catalyzed pathways for the ring-opening of the Diels-Alder adduct between ethylene and DMF have also been proposed and observed in some recent investigations.[1,3] When the DMF/PX reaction is catalyzed by Bronsted acid zeolites, the different ring-opening pathways are shown in Fig. 6.17. The acidic proton attacks the oxygen atom to induce the breaking of a bridging C-O bond that forms a hydroxyl group and a cationic charge. The acid zeolite abstracts a proton from one of the saturated carbons adjacent to the cationic charge to produce two different PX precursors (**16** and **17**) that further dehydrate/isomerize to PX (**18**). Do, et al. observed experimentally the formation of **17**[1] which supports the proposed formation of intermediate **6** in the MMFC/MMBC system. Additionally, Bell et al. used computational methods to predict the formation of both **16** and **17** in the DMF/PX system[3] which provides further supporting evidence for the proposed ring-opening pathways for the MMFC/ethylene adduct (**2**).

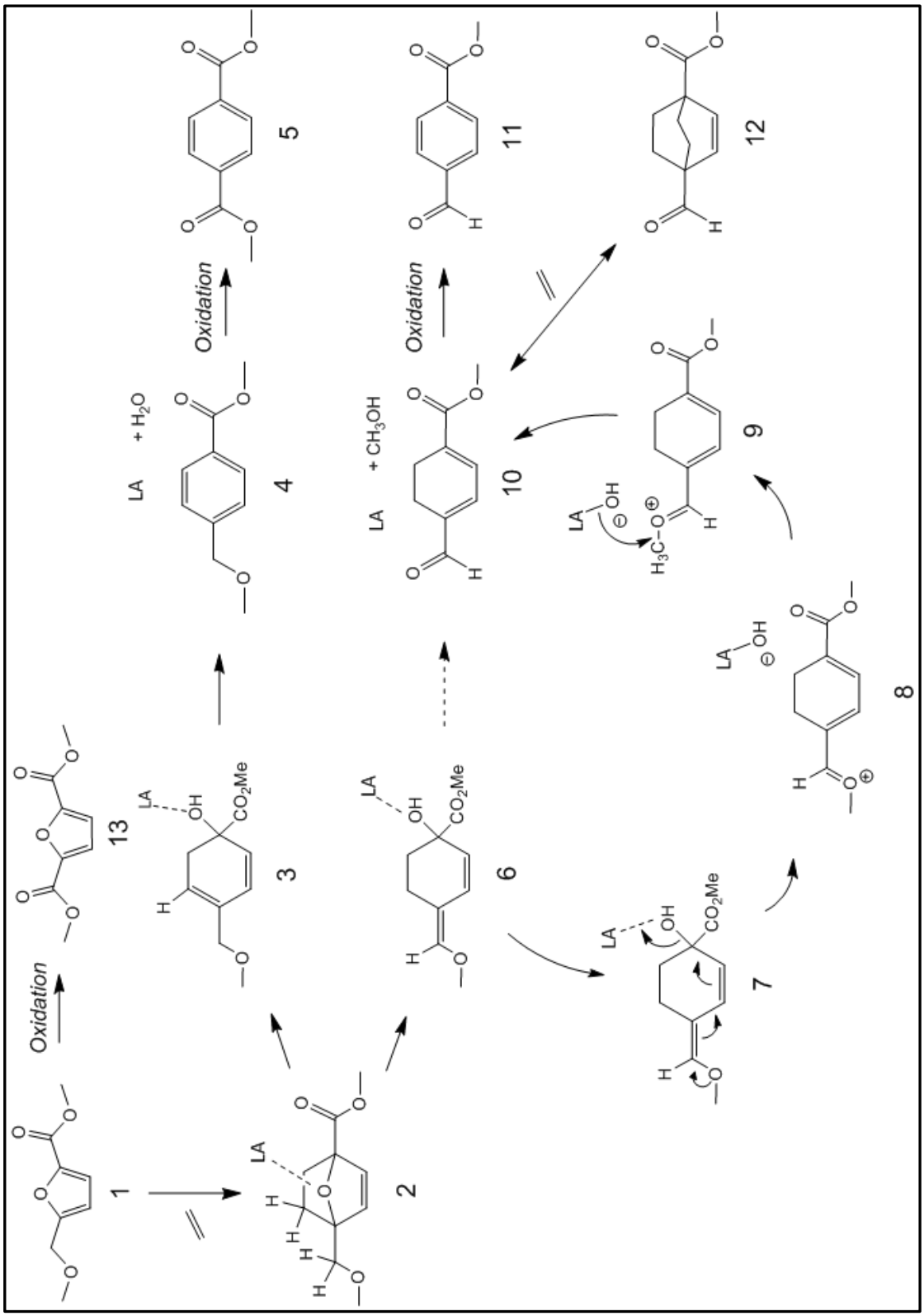

Fig. 6.16 Proposed reaction network for the Diels-Alder-dehydration of MMFC and ethylene to MMBC with Lewis acid Beta molecular sieve catalysts.

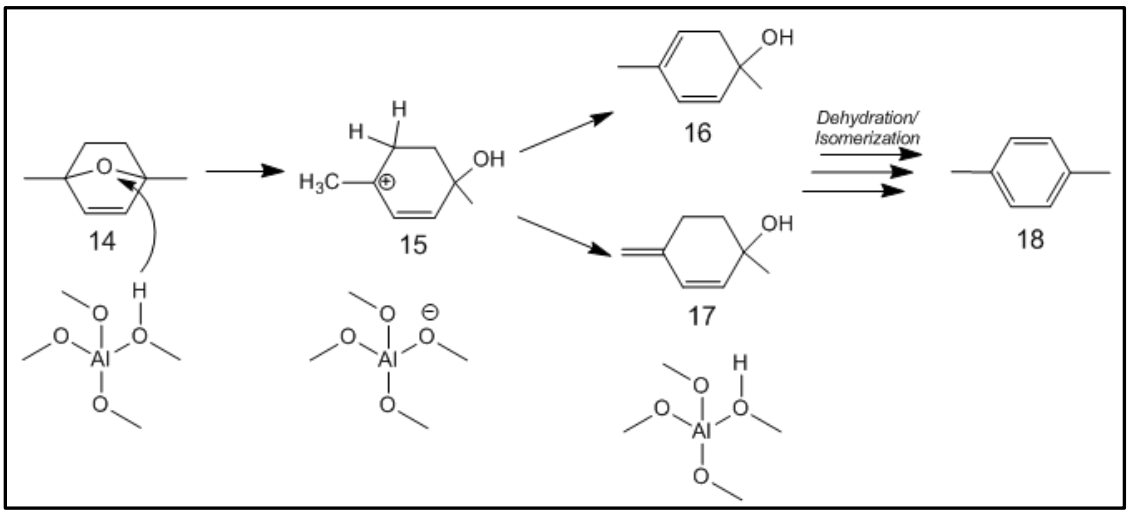

Fig. 6.17 Alternate acid-catalyzed pathways for the ring-opening of the Diels-Alder adduct between ethylene and the DMF.

6.2 References

[1] Do, P.T.M.; McAtee, J.R.; Watson, D.A.; Lobo, R.F.; *ACS Catal.* **2013**, *3*, 41 – 46.

[2] Mcgraw, W.B., et al.; *Environ.Sci. Technol.* **1999**, *33*, 4029.

[3] Li, Y-P.; Head-Gordon, M.; Bell, A.T.; *J. Phys. Chem. C* **2014**, *118*, 22090 – 22095.