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Synthesis of the Indene, THF, and Pyrrolidine Skeletons by Lewis Acid Mediated Cycloaddition of Methylenecyclopropanes with Aldehydes, *N*-Tosyl Aldimines, and Acetals

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Abstract: Methylenecyclopropanes (MCPs **1**) react with aldehydes, *N*-tosyl aldimines, and acetals to give the corresponding indene, THF, and pyrrolidine cycloaddition products in the presence of $BF_3{\cdot}OEt_2$ under mild reaction conditions. Some special transformations of MCPs **1** with aldehydes have been reported in this paper. A plausible reaction mechanism has been discussed, which is based on a deuterium-labeling experiment and the Prins-type reaction mechanism.

Keywords: cycloaddition · indene · methylenecyclopropanes · synthetic methods · THF

Introduction

Over the past few decades, there has been a mounting interest in the application of methylenecyclopropanes (MCPs **1**) to synthetic transformations. An attractive feature of these compounds is their surprising stability, despite a high level of conformational strain.[1,2] In particular, increasing attention has been paid to the transition-metal-mediated reactions of MCPs, which have been used in the construction of interesting complex organic molecules.[3] Thus far, it has been established that in the presence of transition metals, such as Pd catalyst, MCPs **1** can react with aldehydes[4] or imines[5] to give the corresponding [3+2] cycloaddition products.

In addition, we and others have reported both Lewis acid mediated and thermo-induced cycloaddition reactions of MCPs **1** with aldehydes or ketones to give other types of cyclic products.[6–8] However, either activated aldehydes, ketones, or MCPs **1** are required to render this type of cycloaddition possible.

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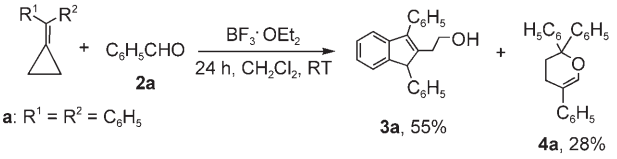
Recently, Yamamoto and co-workers reported the synthesis of indenes by ytterbium(III) triflate catalyzed carboalkoxylation/Friedel–Crafts reactions of arylidenecyclopropanes with acetals. In this study, they reported that the reaction was inert in solvents such as 1,2-dichloroethane (DCE) or toluene and temperature sensitive, with 80 °C being a suitable temperature for its completion.[9] However, in a preliminary communication, we described the Lewis acid $BF_3{\cdot}OEt_2$-mediated novel cycloaddition reactions of MCPs **1** with nonactivated aldehydes and *N*-tosyl aldimines under milder reaction conditions (room temperature). By using this novel [3+2] annulation or intramolecular Friedel–Crafts reaction, the indene, THF, and pyrrolidine skeletons were generated.[10] In this paper, we report the full details of the $BF_3{\cdot}OEt_2$-mediated cycloaddition reactions of MCPs **1** with aldehydes and *N*-tosyl aldimines, because of their potential application for the synthesis of several biologically important products. The $BF_3{\cdot}OEt_2$-mediated cycloaddition reactions of MCPs **1** with acetals at room temperature in 1,2-dichloroethane has also been discussed. In addition, we have disclosed some special transformations of MCPs **1** with aldehydes in the presence of $BF_3{\cdot}OEt_2$. A plausible reaction mechanism for these transformations has been discussed, based on both a deuterium-labeling experiment and the Prins-type reaction mechanism.

Results and Discussion

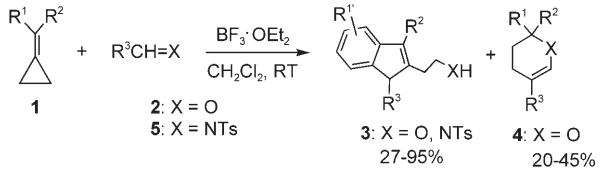
Lewis acid mediated cycloaddition reactions of MCPs 1 with aldehydes and *N*-tosyl aldimines: Initial attempts at cycloaddition were made with MCP **1a** (diphenylmethylenecyclo-

propane) and benzaldehyde **2a** as the substrates. Of the Lewis acids and solvents screened, the combination of $BF_3{\cdot}OEt_2$ and dichloromethane or 1,2-dichloroethane produced the best results for this transformation, and the corresponding indene product **3a** was obtained in a 55% yield, along with 2,2,5-triphenyl-3,4-dihydro-2*H*-pyran (**4a**) in a 28% yield (dichloromethane, room temperature), rather than the expected [3+2] cycloaddition product (Scheme 1).[6a]



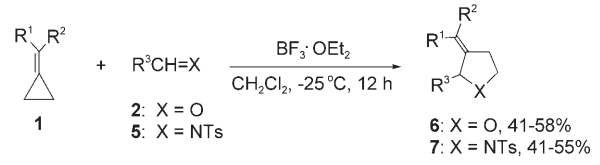
Scheme 1. The cycloaddition reaction of MCP **1a** with aldehyde **2a**.

A series of MCPs **1** and aldehydes **2** or *N*-tosyl aldimines **5** were then subjected to the optimal reaction conditions described above. For most cases, a wide range of indene derivatives **3** were obtained as the major products in moderate to high yields by using this methodology. For the reactions of MCP **1a** with *N*-tosyl aldimines (ArCH=NTs) **5**, the corresponding indenes **3** were formed as the sole products in good yields (Scheme 2).[10]



Scheme 2. $BF_3{\cdot}OEt_2$-mediated (0.1 mmol) reactions of MCPs **1** (0.5 mmol) with aldehydes **2** (1.0 mmol) or *N*-tosyl aldimines **5** (0.75 mmol) at room temperature.

On the other hand, we found that when the reactions of MCPs **1** with aliphatic aldehydes **2** or *N*-tosyl aldimines **5** were carried out at low temperatures (−25 °C), the corresponding [3+2] cycloaddition products **6** (THF skeleton) and **7** (pyrrolidine skeleton) were produced in moderate yields, without the formation of indene products (Scheme 3). This result suggests that the corresponding indene products might be derived from the further transformation of the cycloaddition products **6** and **7** at a higher temperature than that described above.

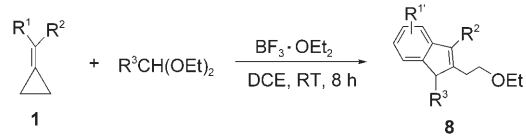


Scheme 3. $BF_3{\cdot}OEt_2$-mediated (0.1 mmol) reactions of MCPs **1** (0.5 mmol) with aliphatic aldehydes **2** (1.0 mmol) and *N*-tosyl aldimines **5** (0.75 mmol) at −25 °C.

Therefore, on the basis of the above investigations, it can be concluded that a broad spectrum of MCPs **1**, aldehydes **2**, and *N*-tosyl aldimines **5** are able to undergo several types of cycloaddition reaction to give the corresponding annulation products in moderate to good yields under mild conditions.

Lewis acid mediated cycloaddition reactions of MCPs 1 with acetals: The reactions of MCPs **1** with selected acetals were carried out in 1,2-dichloroethane under similar conditions to those described previously (Table 1). The reactions proceeded smoothly to give the corresponding indene derivatives **8** in moderate to good yields at room temperature. The use of either electron-donating or electron-withdrawing substituents on the benzene ring of the MCPs **1** had a slight affect upon the yields of the indenes **8** produced. For example, decreased yields of the indenes **8** were obtained when using MCPs **1** with electron-donating groups on the benzene ring (in most cases these reactions were conducted under identical conditions, entries 4–8). The use of electron-donating or electron-withdrawing groups on the phenyl ring of the acetals also had a slight affect upon the yields of indenes **8** produced, depending on which MCP **1** was employed. Reactions of MCP **1a** (diphenylmethylenecyclopropane) with acetals containing electron-withdrawing groups on the phenyl ring produced the indenes **8** in lower yields relative to those obtained when MCP **1d** (di(4-chlorophenyl)methylenecyclopropane) was reacted with these acetals (compare: entries 1–3 with 9–11). For MCP **1b** (di(4-methoxyphenyl)methylenecyclopropane, entries 4–7), the substituents on the phenyl ring of the acetals did not significantly affect the yields of indenes **8** produced (entries 4, 5 and 7), with the exception of the indene **8f** (entry 6), for which the

Table 1. $BF_3{\cdot}OEt_2$-mediated (0.1 mmol) reactions of MCPs **1** (0.4 mmol) with acetals (0.4 mmol) at room temperature.



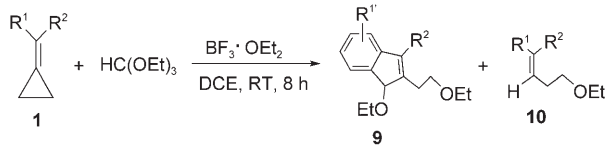
Entry	MCPs **1**[a]	Acetals [R^3]	Yield [%][b]
1	**1a**	C_6H_5	**8a**, 78
2	**1a**	4-ClC_6H_4	**8b**, 70
3	**1a**	4-$NO_2C_6H_4$	**8c**, 61
4	**1b**	4-$CH_3C_6H_4$	**8d**, 50
5	**1b**	C_6H_5	**8e**, 50
6	**1b**	4-ClC_6H_4	**8f**, 67
7	**1b**	4-$NO_2C_6H_4$	**8g**, 50
8	**1c**	C_6H_5	**8h**, 71
9	**1d**	C_6H_5	**8i**, 60
10	**1d**	4-ClC_6H_4	**8j**, 74
11	**1d**	4-$NO_2C_6H_4$	**8k**, 84

[a] For **1a** $R^1=R^2=C_6H_5$, **1b** $R^1=R^2=$4-$MeOC_6H_4$, **1c** $R^1=R^2=$4-MeC_6H_4, and **1d** $R^1=R^2=$4-ClC_6H_4. [b] Isolated yields.

acetal employed contained a chlorine atom on the benzene ring.

Lewis acid mediated cycloaddition reactions of MCPs 1 with triethylorthoformate: For the next step in our study, we treated the MCPs **1** with triethylorthoformate (Table 2). The

Table 2. $BF_3{\cdot}OEt_2$-mediated (0.1 mmol) reactions of MCPs **1** (0.8 mmol) with triethylorthoformate (0.4 mmol) at room temperature.



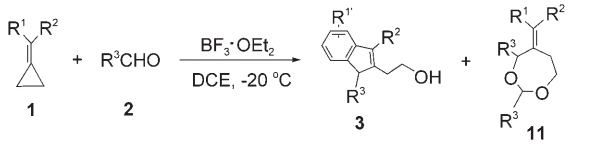
Entry	MCPs **1**[a]	Yield [%][b]	
1	**1a**	**9a**, 28	**10a**, 10
2	**1b**	trace	**10b**, 13
3	**1d**	**9b**, 9	**10c**, 20
4	**1e**	**9c**, 19	**10d**, 59

[a] For **1a** $R^1=R^2=C_6H_5$, **1b** $R^1=R^2=4$-$MeOC_6H_4$, **1d** $R^1=R^2=4$-ClC_6H_4, and **1e** $R^1=R^2=4$-FC_6H_4. [b] Isolated yields.

reactions proceeded smoothly at room temperature producing the corresponding indene derivatives **9** in trace-to-low yields, along with the ring-opened products **10** and ethanol for each case.[8a] This result can be explained as follows: in the presence of the Lewis acid $BF_3{\cdot}OEt_2$, triethylorthoformate can easily release one molecule of ethanol, which can then further react with the MCPs **1** to produce the ring-opened products **10**.[8a] For MCP **1b**, which contains electron-donating groups on its phenyl rings, the corresponding indene product was formed in trace amounts (entry 2).

Some interesting results based on the reactions of special substrates: For the reactions of MCPs **1** with arylaldehydes, bearing a strongly electron-withdrawing group such as NO_2 on the benzene ring (nitrobenzaldehyde), we found that 1,3-dioxepanes **11** and the corresponding indene products were obtained at −20 °C for all cases (Table 3). In fact, for some

Table 3. $BF_3{\cdot}OEt_2$-mediated (0.1 mmol) reactions of MCPs **1** (0.6 mmol) with nitrobezadehydes (0.4 mmol).



Entry	MCPs **1**[a]	Aldehydes **2**[b]	Yield [%][c]	
1	**1a**	**2b**	**3b**, 39%	**11a**, 21%
2	**1a**	**2c**	**3c**, 12%	**11b**, 56%
3	**1a**	**2d**	**3d**, 22%	**11c**, 12%
4	**1f**	**2c**	–	**11d**, 28% (3:4)[d]
5	**1d**	**2c**	**3e**, 19%	**11e**, 43%
6	**1e**	**2c**	**3f**, 15%	**11f**, 17%

[a] For **1a** $R^1=R^2=C_6H_5$, **1d** $R^1=R^2=4$-ClC_6H_4, **1e** $R^1=R^2=4$-FC_6H_4, and **1f** $R^1=C_6H_5$ and $R^2=2$-ClC_6H_4. [b] For **2b** $R^3=3$-NO_2, **2c** $R^3=4$-NO_2, and **2d** $R^3=2$-NO_2. [c] Isolated yields. [d] Ratio of the two isomers see Supporting Information.

cases (entries 2 and 4–6), the corresponding 1,3-dioxepanes **11** were obtained as the major products. For the unsymmetrical MCP **1f**, the corresponding 1,3-dioxepane **11d** was formed as a mixture of the *cis* and *trans* isomers (entry 4, see also the Supporting Information). The structure of **11b** was confirmed by single crystal X-ray diffraction analysis (Figure 1).[11] For reactions involving nitrobenzaldehyde, it

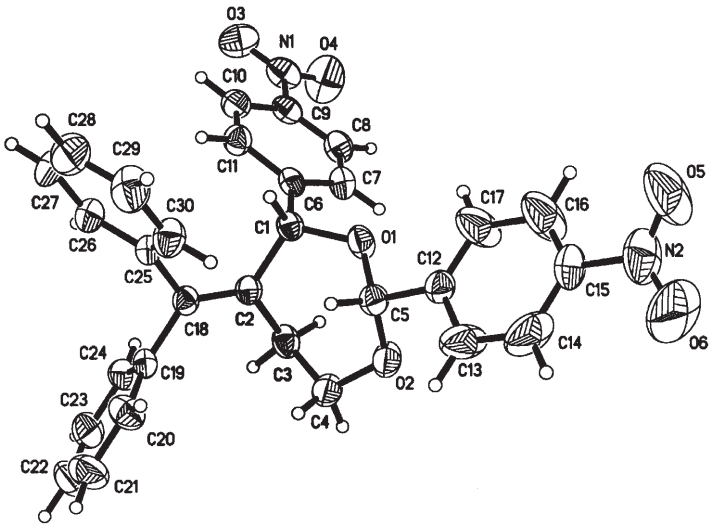
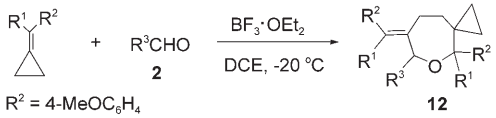


Figure 1. The ORTEP drawing of **11b**.

should be emphasized that the 1,3-dioxepane **11** can only be isolated as a substrate at low temperatures (−20 °C) and isolation of this product at room temperature is difficult.

For the reactions of MCPs **1** substituted with strongly electron-donating groups, for example di(4-methoxyphenyl)-methylenecyclopropane (**1b**), with various arylaldehydes, the corresponding oxepanes **12** bearing a cyclopropyl group at the 3,3′-position were obtained as the sole products (Table 4). The formation of the oxepanes **12** is sensitive to the reaction time. In the control experiments, we found that by varying the reaction time from 1.5 h to 3 h, for the reaction of MCP **1b** with 4-nitrobenzaldehyde, the yield of **12a** was increased from 24% to 33%, with the conversion of MCP **1b** increasing dramatically from 50% to 77% (entries 1 and 2). When the reaction time was prolonged to 5 h the yield of **12a** did not increase, but the conversion of MCP **1b** was increased by a further 5% (entries 2 and 3). The slight increase in the isolated yield of **12a** versus the dramatic increase in the percentage conversion of MCP **1b** suggests that oxepane **12a** is labile under the reaction conditions. None of the desired products were obtained when reaction time was prolonged to 24 h. Similar results were obtained for the reaction of MCP **1b** with the nitrobenzaldehydes **2b** and **2d** (entries 4–7). Therefore, for the remaining arylaldehydes tested, the reactions of MCP **1b** were carried out within 2 h under otherwise identical conditions to the reactions described above (entries 8–13). As elucidated in Table 4, the reactions proceeded smoothly to give the de-

Table 4. $BF_3{\cdot}OEt_2$-mediated (0.06 mmol) reactions of MCP **1b** (0.8 mmol) with various aldehydes (0.4 mmol).



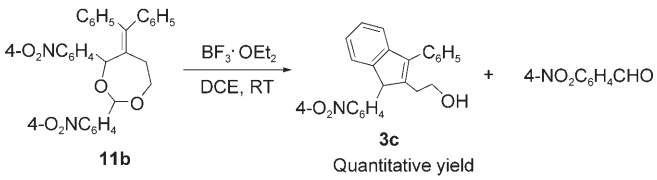
1b: $R^1 = R^2 = 4\text{-}MeOC_6H_4$ **12**

Entry	Aldehydes **2**[a]	Time [h]	Yield [%][b]
1	**2c**	1.5	**12a**, 24 (50)
2	**2c**	3	**12a**, 33 (77)
3	**2c**	5	**12a**, 33 (82)
4	**2b**	2	**12b**, 31 (56)
5	**2b**	5	**12b**, 34 (86)
6	**2d**	2	**12c**, 34 (58)
7	**2d**	5	**12c**, 34 (93)
8	**2e**	2	**12d**, 38 (80)
9	**2f**	2	**12e**, 47 (89)
10	**2g**	2	**12f**, 48 (74)
11	**2h**	2	**12g**, 30 (72)
12	**2i**	2	**12h**, 37 (55)
13	**2a**	2	**12i**, 30 (52)

[a] For **2a** $R^3 = C_6H_5$, **2b** $R^3 = 3\text{-}NO_2C_6H_4$, **2c** $R^3 = 4\text{-}NO_2C_6H_4$, **2d** $R^3 = 2\text{-}NO_2C_6H_4$, **2e** $R^3 = 4\text{-}ClC_6H_4$, **2f** $R^3 = 2,4\text{-}Cl_2C_6H_3$, **2g** $R^3 = 2,3\text{-}Cl_2C_6H_3$, **2h** $R^3 = 3\text{-}FC_6H_4$, and **2i** $R^3 = 2\text{-}ClC_6H_4$. [b] Isolated yields (percentage conversions are shown in parentheses).

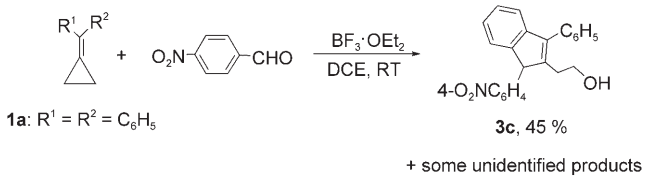
sired oxepane products **12** in moderate yields at >50% conversion. Arylaldehydes with electron-withdrawing groups, such as NO_2, F, or Cl, on the phenyl ring are necessary for this transformation to produce the corresponding oxepanes **12** in moderate yields (Table 4). The reaction of MCP **1b** with benzaldehyde also takes place, under identical conditions, to produce oxepane **12i** in 30% yield (entry 13). However, none of the desired products were obtained when arylaldehydes bearing electron-donating groups on the benzene ring such as 4-methoxybenzaldehyde and 4-methylbenzaldehyde were used for this reaction. Therefore, the choice of substituent on the benzene ring of the MCPs **1** or arylaldehydes drastically affects the products produced from these reactions.

Exploration of the reaction mechanism: In the following investigation, we found that the 1,3-dioxepane product **11b** was completely transformed to the indene product **3c** (quantitative yield) within 1 h in the presence of $BF_3{\cdot}Et_2O$ at room temperature. 4-Nitrobenzaldehyde was also formed during this reaction (Scheme 4).



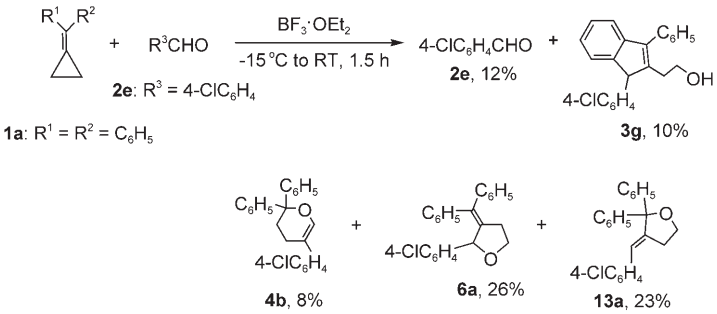
Scheme 4. BF_3OEt_2-mediated transformation of **11b** to indene **3c** at room temperature.

Moreover, we also found that when the reaction of MCP **1a** with 4-nitrobenzaldehyde was carried out at room temperature for 16 h, the indene product **3c** was obtained in 45% yield, although some unidentified products were also formed (Scheme 5).



Scheme 5. $BF_3{\cdot}OEt_2$-mediated reaction of MCP **1a** with 4-nitrobenzaldehyde at room temperature.

To further clarify the reaction pathway, we also investigated the reaction of MCP **1a** with 4-chlorobenzaldehyde by using a short reaction time (1.5 h) and temperatures ranging from −15 °C to room temperature. The THF products **6a** and **13a**, the starting substrate **2e**, the indene product **3g**, and the pyran product **4b** were all isolated from this reaction, with the indene product **3g** and the pyran product **4b** requiring careful isolation procedures (Scheme 6). The structure of **13a** was confirmed by single-crystal X-ray diffraction analysis (Figure 2).[12] We further, unambiguously, confirmed that both **6a** and **13a** can be completely transformed into



Scheme 6. Reaction of MCP **1a** with 4-chlorobenzaldehyde at −15 °C to room temperature.

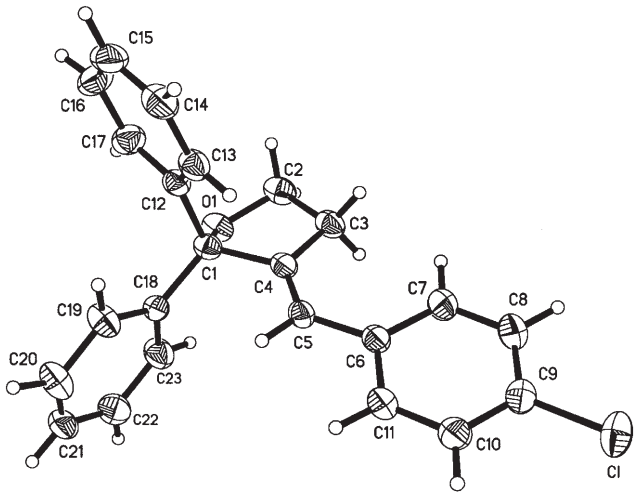
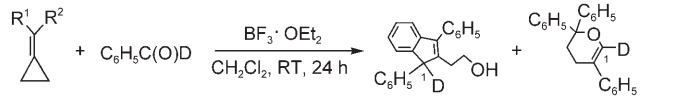


Figure 2. The ORTEP drawing of **13a**.

indene **3g** within 0.5 h, in the presence of $BF_3{\cdot}Et_2O$ at room temperature (intramolecular Friedel–Crafts reaction).

Thus, based on the results described above, we can conclude that the indenes **3** can also be derived from the further reaction of the THF products **6** and **13** or 1,3-dioxepane products **11** in the presence of $BF_3{\cdot}OEt_2$ at room temperature.

A deuterium-labeling experiment was also carried out, under the same reaction conditions, by conducting the reaction of MCP **1a** with $C_6H_5C(O)D$ (Scheme 7). The products

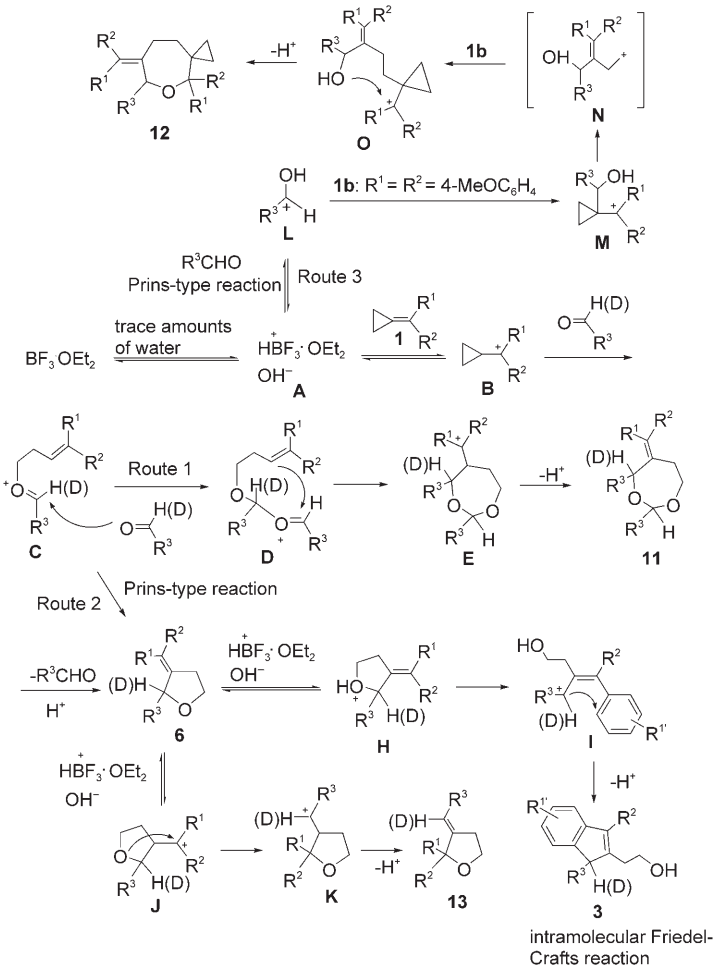


1a: $R^1 = R^2 = C_6H_5$ [D]**3a**, 46%, 99% D [D]**4a**, 30%, 99% D

Scheme 7. Lewis acid promoted reaction of MCP **1a** with $C_6H_5C(O)D$.

[D]**3a** and [D]**4a** were obtained in 46 and 30% yields, respectively, with 99% D content at the C-1 position (^1H NMR and ^{13}C NMR spectroscopic data is detailed in the Supporting Information). Deuterium incorporation did not occur at any other position in [D]**3a** and [D]**4a**.

On the basis of the deuterium-labeling experiment and the fact that the indenes **3** can either be derived from the THF products **6** and **13** or the 1,3-dioxepane products **11** in the presence of $BF_3{\cdot}OEt_2$, a plausible reaction mechanism for the cycloaddition of MCPs **1** with aldehydes has been proposed (Schemes 8 and 9). This reaction mechanism differs from that proposed in our preliminary communication.[10] Initially, reaction of $BF_3{\cdot}OEt_2$ with trace amounts of water in the reaction system generates the Brønsted acid type catalyst **A**.[13] The reaction of catalyst **A** with MCPs **1** produces the zwitterionic intermediate **B** (the corresponding counter ion of $BF_3{\cdot}OEt_2$, that is OH^-, has been omitted in all of the intermediates for convenience). Intermediate **B** can probably form an oxonium type cationic intermediate **C** with an aldehyde by a Prins-type reaction.[14] The intermediate **C** can then further react with another molecule of aldehyde to form the intermediate **D**, another oxonium-type cationic intermediate.[15] The intramolecular cyclization of **D** (also a Prins-type reaction) affords the intermediate **E**, and the release of a proton from this intermediate produces the 1,3-dioxepane product **11**.[16] For nitrobenzaldehyde, which contains a strongly electron-withdrawing group on its benzene ring, the reaction of the intermediate **C** with an aldehyde and the intramolecular Prins-type reaction (Route 2) can take place more easily than for other intermediates, as the carbon atom of the carbonyl group is more positively charged for this case. In the presence of Brønsted acid type catalyst **A**, 1,3-dioxepane **11** liberates one molecule of the corresponding aldehyde to give the corresponding THF product **6**.[16] Protonation at the oxygen atom of **6** by the Brønsted acid type catalyst **A** affords the cationic intermediate **H**, which when followed by the intramolecular Friedel–Crafts reaction, presumably via the intermediate **I**, furnishes



Scheme 8. Proposed reaction mechanism for the $BF_3{\cdot}OEt_2$-mediated cycloadditions of MCPs with aldehydes.

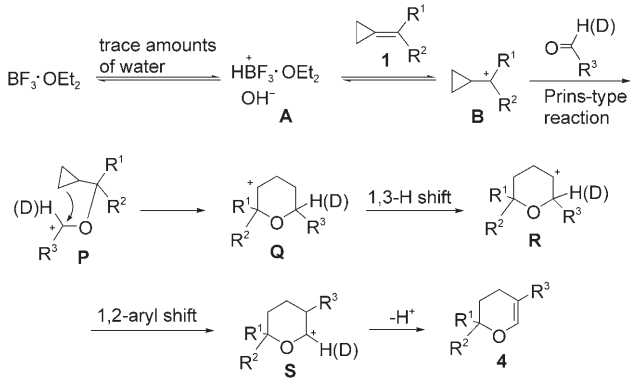
the indene product **3** (for arylaldehydes the intramolecular Friedel–Crafts reaction occurs by the means of Route 1, Scheme 8). In another route, protonation of the carbon–carbon double bond of **6** affords the cationic intermediate **J**, which when followed by the intramolecular Prins-type reaction gives the cationic intermediate **K**. The subsequent release of a proton from **K** produces another THF product **13** (for aliphatic aldehydes by the means of Route 1 in Scheme 8).

Alternatively, the intramolecular Prins-type reaction of intermediate **C** directly gives THF product **6** which can form the indene **3** and THF product **13** in the similar way (Route 2 in Scheme 8).

On the other hand, the Prins-type reaction of an arylaldehyde with MCP **1b** ($R^1 = R^2 = 4\text{-}MeOC_6H_4$) can give the cationic intermediate **M**, probably via intermediate **L**, in the presence of the Brønsted acid type catalyst **A**.[13] This cationic intermediate **M** should be the most stable intermediate in this reaction system as it is stabilized by the cyclopropyl ring and the two phenyl groups, which both bear a strongly electron-donating methoxy group.[17] This intermediate can give the reactive cationic intermediate **N** by the means of a

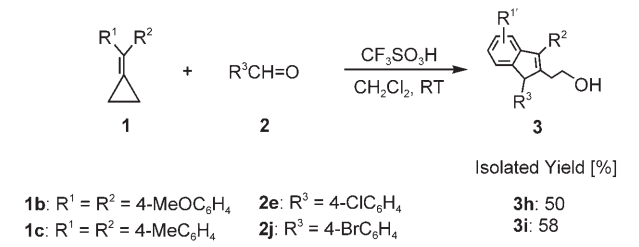
homoallylic rearrangement,[18] which can then react with another molecule of MCP **1b** to produce another stabilized cationic intermediate **O**. The intramolecular Prins-type reaction produces the product **12** and regenerates a proton (Route 3 in Scheme 8).

Moreover, the intermediate **B** can also form the oxonium-type cationic intermediate **P** with a molecule of the aldehyde by a Prins-type reaction, which when followed by a further intramolecular Prins-type reaction furnishes the cationic intermediate **Q**.[17] A 1,3-hydrogen shift[19] in intermediate **Q** gives the cationic intermediate **R**. The subsequent 1,2-aryl shift[20] and the liberation of a proton produces the corresponding pyran product **4** (Scheme 9).



Scheme 9. Proposed reaction mechanism for the $BF_3{\cdot}OEt_2$-mediated formation of product **4**.

In the above mentioned mechanism, the Prins-type reaction is a key reaction pathway, and the deuterium-labeled proton did not migrate during the reaction. To verify this Prins-type reaction mechanism, we carried out the same reaction in the presence of a Brønsted acid, under otherwise identical conditions. In fact, we found that the corresponding indene derivatives were obtained when trifluoromethanesulfonic acid (CF_3SO_3H, TfOH, 0.1 equiv) was used as the catalyst in dichloromethane at room temperature, although in somewhat lower yields. The results from these experiments suggest that the above mentioned transformations were involved in the Brønsted acid catalyzed reaction of an olefin with an aldehyde, a Prins-type reaction (Scheme 10).



Scheme 10. Reaction of MCPs **1** (0.5 mmol) with aldehydes (1.0 mmol) in the presence of CF_3SO_3H (0.1 mmol) at room temperature.

Conclusion

In conclusion, we have developed some facile and effective Lewis acid $BF_3{\cdot}OEt_2$-mediated cycloaddition reactions of MCPs **1** with nonactivated aldehydes, *N*-tosyl aldimines, and acetals, which can be utilized for the synthesis of the indene, THF, and pyrrolidine skeletons under mild conditions. For the reactions of aryl-substituted MCPs **1** with aryl aldehydes, acetals or *N*-tosyl aldimines at room temperature, the corresponding indene products **3** and **8** are the major products formed; however, for the reactions of MCPs **1** with aliphatic aldehydes or *N*-tosyl aldimines at lower temperatures and with relatively shorter reaction times, the corresponding THF products **6** or the pyrrolidine products **7** are the major products formed.

Several special transformations have also been reported in this paper. For example: 1) For the low-temperature reactions of aryl-substituted MCPs **1** with aryl aldehydes, which contain strongly electron-withdrawing groups, the corresponding 1,3-dioxepanes **11** and the indenes **3** are formed (1,3-dioxepanes **11** can be transformed into the indenes **3** at room temperature in the presence of $BF_3{\cdot}OEt_2$). 2) For the low-temperature reactions of aryl-substituted MCPs **1**, which contain strongly electron-donating groups on their benzene rings, with aryl aldehydes, the corresponding oxepanes **12** are obtained at $>50\,\%$ conversion of the employed MCP **1**.

The reaction mechanism has been discussed on the basis of deuterium-labeling and control experiments outlined in this paper. The Prins-type reaction is a key reaction pathway in this mechanism. At low reaction temperatures and with short reaction times, indenes **3**, pyranes **4**, and the THF products **6** and **13** can be isolated. The THF products **6** and **13** can be completely transformed into indenes **3** at room temperature or during a prolonged reaction time at low temperature, in the presence of $BF_3{\cdot}OEt_2$. Therefore, the indenes **3** are the most stable products produced in these reactions. As a result of the ready availability of the starting materials and the ease of operation of these novel reactions, they have the potential to be applied to the construction of several biologically important products. Efforts to determine the scope and limitations of these reactions are currently underway in this laboratory.

Experimental Section

General methods: Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively. Mass spectra were recorded by using EI, ESI or Maldi methods, and HRMS was conducted on a Finnegan MA$^+$ mass spectrometer. The organic solvents used were dried by standard methods when necessary. Satisfactory CHN microanalyses were obtained by using a Carlo–Erba 1106 analyzer. For purification purposes, the commercially obtained aldehydes were recrystallized or dissolved in dichloromethane, washed with $NaHCO_3$ aqueous solution, and redistilled in vacuo. All reactions were monitored by TLC analysis with Huanghai GF254 silica-gel-coated plates. Flash column chromatography was carried out using 300–400 mesh silica gel under increased pressure. Deuterated benzaldehyde ($C_6H_5C(O)D$) was purchased from Aldrich.

General procedure for the reaction of MCPs 1 with aldehydes to produce indene systems (Method A): $BF_3{\cdot}Et_2O$ (0.1 mmol) was added to a solution of the MCP **1** (0.5 mmol) and aldehyde (1.0 mmol) in dichloromethane (1.5 mL), under an argon atmosphere. The resulting reaction mixture was then stirred for 24 h at room temperature. After this time, the mixture was quenched by the addition of aqueous $NaHCO_3$ solution, and the product was extracted with dichloromethane (3×10 mL). The organic layers produced were then dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure. Purification of the crude product was achieved by silica-gel column chromatography.

General procedure for the reaction of MCPs 1 with acetals to produce indene systems (Method B): $BF_3{\cdot}Et_2O$ (0.1 mmol) was added to a solution of the MCP **1** (0.4 mmol) and acetal (0.4 mmol) in 1,2-dichloroethane (1.0 mL), under an argon atmosphere. The resulting reaction mixture was then stirred for 24 h at room temperature. After this time, the mixture was quenched by the addition of aqueous $NaHCO_3$ solution, and the product was extracted with dichloromethane (3×10 mL). The organic layers produced were then dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure. Purification of the crude product was achieved by silica-gel column chromatography.

Compound 3a: A yellow liquid; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): $\delta=$ 2.26–2.35 (m, 1H), 2.73–2.83 (m, 1H), 3.63 (t, $J=6.6$ Hz, 2H), 4.61 (s, 1H), 7.08–7.48 ppm (m, 14H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=30.6$, 57.4, 62.2, 119.8, 123.8, 125.1, 126.7, 126.9, 127.4, 128.2, 128.5, 128.8, 129.1, 134.8, 139.6, 141.5, 144.6, 144.9, 148.1 ppm; IR (Nujol): $\tilde{\nu}=3564$, 3388, 3061, 3024, 2952, 2882, 2237, 1734, 1598, 1493, 1452, 1443, 1247, 1073, 1044, 909, 774, 750, 737, 701 cm^{-1}; MS (EI): *m/z* (%): 312 (100) $[M]^+$, 294 (56), 281 (62), 203 (84); HRMS: *m/z* calcd for $C_{23}H_{20}O$: 312.1514; found: 312.1505 $[M]^+$.

Compound 4a: A white solid; m.p. 142–144 °C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS): $\delta=2.31$ (t, $J=6.6$ Hz, 2H), 2.67 (t, $J=6.6$ Hz, 2H), 7.10–7.34 (m, 12H, Ar, CH=), 7.43–7.46 ppm (m, 4H, Ar); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=20.9$, 31.8, 81.1, 113.0, 123.9, 125.8, 125.9, 127.1, 128.27, 128.33, 139.0, 140.7, 144.5 ppm; IR (Nujol): $\tilde{\nu}=3081$, 3058, 3021, 2966, 2919, 2844, 1941, 1648, 1596, 1494, 1447, 1376, 1165, 1058, 1007, 892, 757, 746, 694 cm^{-1}; MS (EI): *m/z* (%): 312 (13) $[M]^+$, 180 (100), 179 (34), 165 (39); HRMS: calcd for $C_{23}H_{20}O$: 312.1514; found: 312.1526 $[M]^+$.

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[12] Crystal data of **13a**: formula: $C_{23}H_{19}OCl$; M_r: 346.83; color, habit: colorless, prismatic; crystal system: monoclinic; lattice type: primitive; lattice parameters: $a=10.0390(7)$, $b=19.8339(14)$, $c=9.2205(7)$ Å, $\alpha=90°$, $\beta=104.7300(10)°$, $\gamma=90°$, $V=1775.6(2)$ Å^3; space group: $P2_1/c$; $Z=4$; $\rho_{calcd}=1.297$ g cm^{-3}; $F_{000}=728$; diffractometer: Rigaku AFC7R; residuals: *R*/*wR*: 0.0545/0.1228. CCDC-210599 contains the supplementary crystallographic data for this

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