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Facile Synthesis of Tetrahydrofurans from Cycloadditions of Vinylidenecyclopropanes with Aldehydes and Further Tunable Transformations for the Construction of Furan, Indene, and Benzo[*c*]fluorene Derivatives

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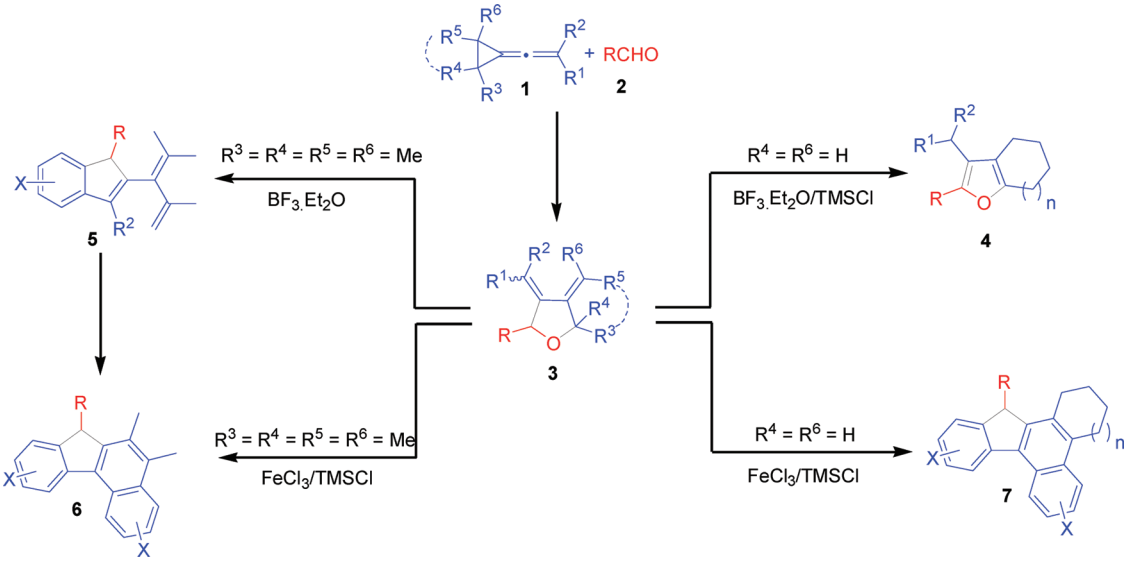

The cycloadditions of vinylidenecyclopropanes with aldehydes for the synthesis of tetrahydrofurans are detailed in this paper. The obtained polysubstituted tetrahydrofurans could serve as versatile intermediates to selectively produce furan, indene, and benzo[*c*]fluorene derivatives depending on the substituents at the tetrahydrofurans' rings and the varied reaction conditions, which clearly exhibit insights into the synthetic applications of tetrahydrofurans. The scope, limitations, and mechanisms of these transformations have been discussed in detail. Attractively, these cycloadditions of vinylidenecyclopropanes with aldehydes and the further transformations of the cycloadducts provide an efficient protocol for the construction of various medium- and large-size ring-fused tetrahydrofuran, furan, and benzo[*c*]fluorene derivatives.

Introduction

As one of the most important classes of heterocyclic compounds, tetrahydrofurans (THFs) are not only significant components in many natural product-like scaffolds[1] but also useful building blocks in organic synthesis.[2] Ring-opening reactions of polysubstituted THFs are meaningful synthetic transformations because they provide effective accesses to monomers, particularly bifunctional intermediates, which could serve as four-carbon building blocks for the formation

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of a variety of useful compounds.[2,3] This has stimulated the development of a number of approaches for the ring-opening of THFs. Nonetheless, most of the known cases have resulted in either monomers,[3b,4] complex mixtures of oligomers,[2b,5] or dimerization of THFs.[3a,6] On the other hand, nowadays increasing attention has been paid to efficient generation of complex structures in the context of diversity-oriented synthesis (DOS), which refers to an area with considerable importance in the disciplines of organic synthesis and chemical biology.[7,8] Thus, the development of tandem reactions utilizing THFs, which might be subsequently transformed to the bifunctional intermediates for the construction of complex molecular skeletons in a diversity-oriented manner, should be an appealing strategy in organic synthesis.

Vinylidenecycloproanes (VCPs),[9−11] which contain an allene moiety and a connected cyclopropane ring, are highly strained but readily available and reactive substances that have served as useful building blocks in organic synthesis. Previously, we have reported the Lewis acid-mediated cycloadditions of VCPs and aldehydes, providing an efficient and selective synthesis of a variety of functionalized tetrahydrofuran, indene, furan, furo[2,3-*b*]furan, and benzo[*c*]fluorene derivatives, which were controlled by the choice of varied reaction conditions and the substituent effects (Figure 1, Scheme 1).[12] During our ongoing investigations, we found that the formed polysubstituted THFs played a crucial role in the transformations of these adducts. Thus, the interesting ring-opening of THFs mediated by Lewis acids and subsequent transformations via controllable pathways could result in a diversity-oriented synthesis of various polycyclic compounds. Herein, we describe the full details on the scope and limitations of the cycloaddition reaction of VCPs with aldehydes for the synthesis of THFs (Figure 1, pattern 1) and report an interesting class of Lewis acid-mediated tandem reactions based on THFs to produce furan, indene, and benzo[*c*]fluorene derivatives in a diversity-oriented manner. The scope, limitations, and mechanistic insights of these cascade transformations of THFs **3** were also discussed in the paper.

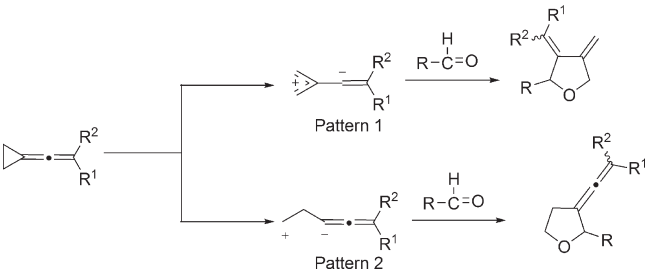

FIGURE 1. Ring-opening models for [3 + 2] cycloadditions of VCPs and aldehydes.

Results and Discussion

Synthesis of Polysubstituted Tetrahydrofurans via $BF_3 \cdot Et_2O$-Catalyzed [3 + 2] Cycloaddition of VCPs 1 with Aldehydes 2. The exploration was carried out by using **1a** and aldehyde **2a** as model substrates. It was found that the use of 0.3 equiv of $BF_3 \cdot Et_2O$ in DCM at −10 °C was suitable in terms of practicality and yield of **3a** (Table 1, entry 1).[12b] The reaction conditions developed above were found to be broadly applicable to a wide variety of VCPs with four methyl groups at the cyclopropane moiety ($R^3 = R^4 = R^5 = R^6 = Me$) and bicyclic VCPs. First, for VCPs with four methyl groups at the cyclopropane moiety, significant substituent effects of aromatic aldehydes on the reaction outcome were found. The intermolecular [3 + 2] cycloaddition reactions proceeded readily for all of the tested aldehydes **2** bearing strong electron-withdrawing groups on the aromatic ring to give the tetrahydrofuran frameworks in good to excellent yields (Table 1, entries 1−4); however, for aldehyde **2d** with an electron-donating group appended on the aromatic ring, the tetrahydrofuran product was observed in a trace amount (Table 1, entry 6). Second, for the unsymmetrical VCP **1d**, the reaction produced **3f** as a mixture of *E*/*Z* isomers in 76% yield (Table 1, entry 7); to our delight, for the unsymmetrical VCP **1e** (R^1 = Ph, R^2 = Me), the reaction furnished (*E*)-**3g** in 78% yield with high selectivity (Table 1, entry 8). Finally, the reaction of bicyclic VCPs **1f**−**i** with variation in ring size also proceeded successfully and gave a variety of ring-expansion products **3** as mixtures of cis/trans isomers in moderate yields under the established conditions (Table 1, entries 9−14).

Synthesis of Medium- and Large-Size Ring-Fused Fully Substituted Furans via Aromatization of the Bicyclic THFs Intermediates. Our previous studies demonstrated that the bicyclic THFs **3** could transform to the corresponding furans **4** via an intramolecular isomerization. In addition, we developed one-pot reactions for the synthesis of furan derivatives **4**.[12a] Encouraged by the above results and considering that the medium- and large-size ring-fused heterocyclic ring systems are core structures of numerous natural

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SCHEME 1. Lewis Acid Mediated Selective Cycloadditions of VCPs and Aldehydes

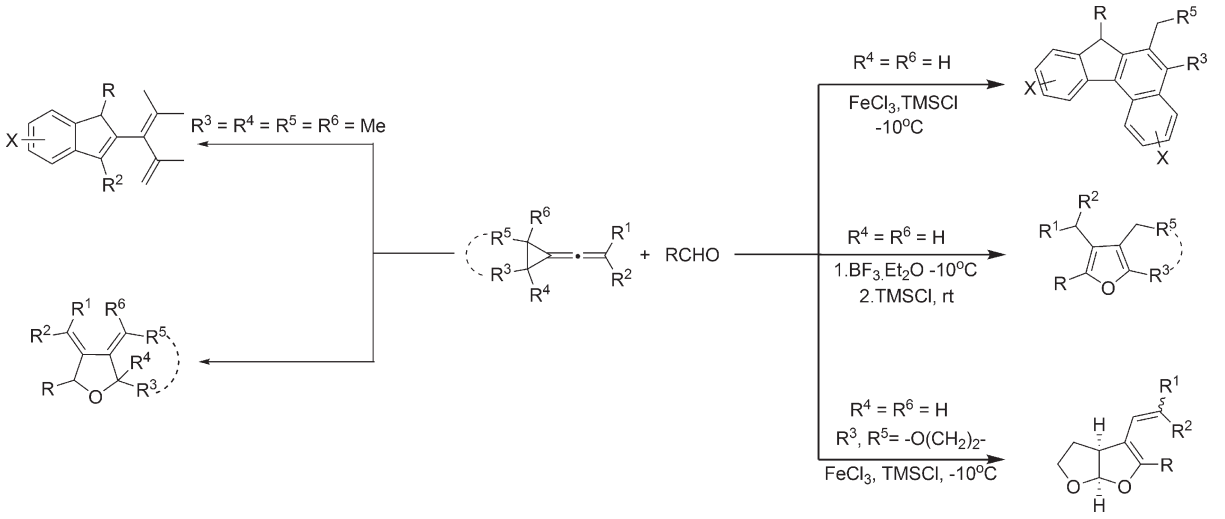
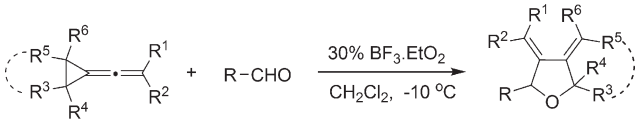


TABLE 1. $BF_3 \cdot Et_2O$-Catalyzed [3 + 2] Cycloaddition of VCPs 1 and Aldehydes 2[a]



1 2 3

entry	$R^3/R^4/R^5/R^6$	R^1/R^2 (**1**)	R (**2**)	time (h)	yield of **3** (%)
1	$R^3 = R^4 = R^5 = R^6$ = Me	C_6H_5/C_6H_5 (**1a**)	*p*-$NO_2C_6H_4$ (**2a**)	12	**3a**, 93
2	$R^3 = R^4 = R^5 = R^6$ = Me	**1a**	*m*-$NO_2C_6H_4$ (**2b**)	12	**3b**, 90
3	$R^3 = R^4 = R^5 = R^6$ = Me	*p*-FC_6H_4/*p*-FC_6H_4 (**1b**)	**2a**	12	**3c**, 87
4	$R^3 = R^4 = R^5 = R^6$ = Me	*p*-MeC_6H_4/*p*-MeC_6H_4 (**1c**)	**2a**	12	**3d**, 82
5	$R^3 = R^4 = R^5 = R^6$ = Me	**1a**	Ph (**2c**)	24	**3e**, 53
6	$R^3 = R^4 = R^5 = R^6$ = Me	**1a**	*p*-OMePh (**2d**)	24	trace[b]
7	$R^3 = R^4 = R^5 = R^6$ = Me	*p*-MeC_6H_4/*p*-ClC_6H_4 (**1d**)	**2a**	12	**3f**, 76 (4:3)[c]
8	$R^3 = R^4 = R^5 = R^6$ = Me	Ph/Me (**1e**)	**2a**	8	**3g**, 78 (*E*)
9	$R^4 = R^6$ = H, $R^3, R^5 = -(CH_2)_3-$	Ph/Ph (**1f**)	**2a**	5	**3h**, 52 (2:1)[d]
10	$R^4 = R^6$ = H, $R^3, R^5 = -(CH_2)_4-$	Ph/Ph (**1g**)	**2a**	24	**3i**, 68 (1:1)[d]
11	$R^4 = R^6$ = H, $R^3, R^5 = -(CH_2)_4-$	**1g**	**2b**	12	**3j**, 67 (1:1)[d]
12	$R^4 = R^6$ = H, $R^3, R^5 = -(CH_2)_4-$	**1g**	*p*-BrC_6H_4 (**2e**)	24	**3k**, 53 (1.1:1)[d]
13	$R^4 = R^6$ = H, $R^3, R^5 = -(CH_2)_6-$	Ph/Ph (**1h**)	**2a**	24	**3l**, 36 (1:1)[d]
14	$R^4 = R^6$ = H, $R^3, R^5 = -(CH_2)_{10}-$	Ph/Ph (**1i**)	**2a**	24	**3m**, 43 (3:2)[d]

[a]Unless otherwise specified, the reaction was carried out using **1** (0.3 mmol) and **2** (0.36 mmol) in CH_2Cl_2 under nitrogen atmosphere. [b]2-(2,4-Dimethylpenta-1,3-dien-3-yl)-1-(4-methoxyphenyl)-3-phenyl-1*H*-indene was obtained in 18% yield along with an unidentified mixture.[12b] [c]Deduced by ^{1}H NMR (*Z*/*E* or *E*/*Z*). [d]Deduced by ^{1}H NMR (cis/trans or trans/cis), and 0.7 equiv of $BF_3 \cdot Et_2O$ was added.

products,[13] we then tried to enlarge their applications for the synthesis of various-size ring fused furan frameworks. As can be seen from Table 2, the corresponding six-, seven-, and eight-membered bicyclic furan derivatives were obtained in acceptable yields (Table 2, entries 1−6). For eight-membered bicyclic vinylidenecyclopropane **1h**, the corresponding product was obtained in slightly lower yield (Table 2, entry 8). Additionally, the large-size ring fused furan could also be obtained in moderate yield (Table 2, entry 9).

A tentative reaction pathway of the cycloadditions of VCPs with aldehydes is outlined in Scheme 2.[12a] The initial electrophilic addition of intermediate **A** with VCPs **1** furnishes cationic intermediate **B**, in which a strain release is favorably accomplished by ring-opening of the intermediate **B** to give **C** or the resonance-stabilized intermediate **C**[1] and **C**[2]. The followed intramolecular O-attacked cyclization of intermediate **C** could produce the polysubstituted THFs **3**. For tetrahydrofurans with annulated carbocycles of various ring sizes, in which R^4 and R^6 are hydrogen atoms, **3** may undergo an intramolecular isomerization to give furan derivatives **4** in the presense of $BF_3 \cdot Et_2O$/TMSCl.

Synthetic Application of Multisubstituted Tetrahydrofurans for the Synthesis of Indenes 5 and Benzo[*c*]fluorenes 6. In the course of our investigations on the applications of THFs, it was surprising but also interesting to observe that the rearrangement of THF **3a**, which was mediated by $FeCl_3$/TMSCl, afforded indene product **5a** in 42% yield together with the benzo[*c*]fluorene **6a** in 38% yield probably via the intramolecular double-Friedel−Crafts reactions (Table 3, entry 1). Efforts were made to optimize the reaction conditions to afford one product predominantly. Gratifyingly, the yield of **6a** was sharply improved to 89%, and the formation

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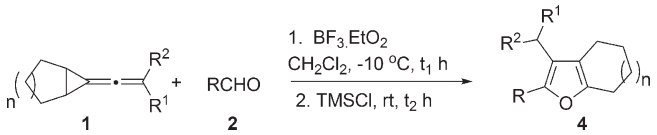
TABLE 2. One-Pot Reactions for the Synthesis of Medium- and Large-Size Ring-Fused Furan Derivatives 4[a]



entry	R^1/R^2	*n* (**1**)	R (**2**)	time t_1/t_2 (h)	yield of **4** (%)
1	Ph/Ph	1 (**1f**)	**2a**	24/24	**4a**, 54
2	*p*-MeC_6H_4/*p*-ClC_6H_4	1 (**1j**)	**2a**	24/36	**4b**, 63
3	Ph/Ph	2 (**1g**)	**2a**	24/24	**4c**, 65
4	Ph/Ph	2 (**1g**)	*o*-$NO_2C_6H_4$ (**2f**)	12/24	**4d**, 56
5	*p*-ClC_6H_4 /*p*-ClC_6H_4	2 (**1k**)	**2a**	24/36	**4e**, 59
6	*p*-MeC_6H_4 /*p*-MeC_6H_4	2 (**1l**)	**2a**	24/36	**4f**, 41
7	Ph/Ph	3 (**1m**)	**2b**	24/24	**4g**, 42
8	Ph/Ph	4 (**1h**)	**2a**	24/36	**4h**, 35[b]
9	Ph/Ph	8 (**1i**)	**2a**	24/36	**4i**, 45

[a]Unless otherwise specified, the reaction was carried out using **1** (0.3 mmol) and **2** (0.36 mmol) in dry CH_2Cl_2 under nitrogen atmosphere, after stirring fot t_1 h, 1.2 eq. TMSCl was added in the reaction, and the mixture was stirring for t_2 h . [b]2.0 eq. TMSCl was added.

SCHEME 2. Proposed Mechanistic Pathway for Cycloadditions of VCPs with Aldehydes

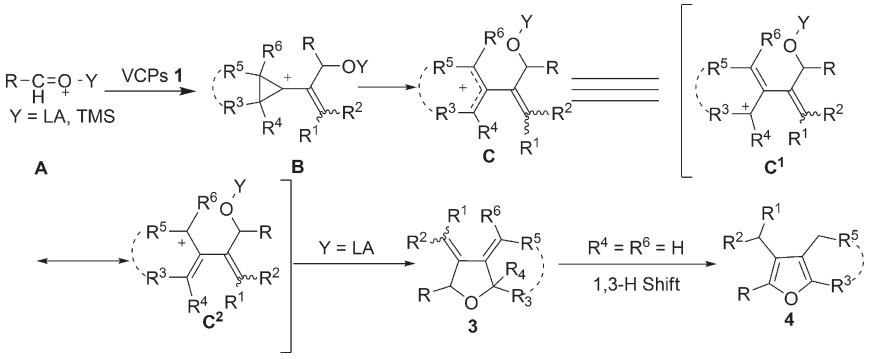
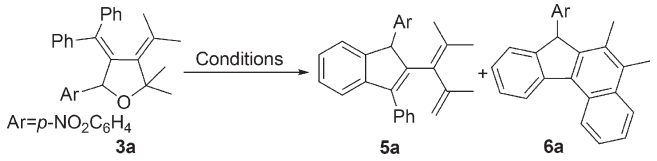


TABLE 3. Optimization of the Reaction Conditions for the Applications of THF Derivatives[a]



entry	LA (equiv)	TMSCl (equiv)	solvent	time (h)	temp (°C)	yield of **5a** (%)	yield of **6a** (%)
1	$FeCl_3$ (0.5)	0	CH_2Cl_2	24	rt	42	38
2	$FeCl_3$ (0.3)	1.2	CH_2Cl_2	18	rt	35	44
3	$FeCl_3$ (0.3)	2	CH_2Cl_2	12	rt	trace	62
4	**$FeCl_3$ (0.5)**	**2**	**CH_2Cl_2**	**12**	**rt**	**trace**	**89**
5	$FeCl_3$ (0.5)	10	CH_2Cl_2	12	rt	trace	85
6	**$BF_3 \cdot Et_2O$ (0.3)**	**0**	**DCE**	**24**	**60**	**76**	**trace**

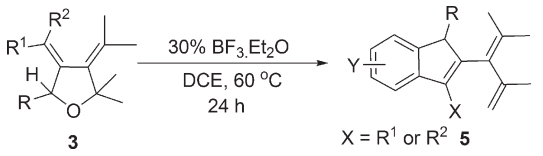
[a]The reaction was carried out under nitrogen atmosphere on a scale of 0.1 mmol.

of **5a** was suppressed to trace yield by the addition of 2.0 equiv of TMSCl (Table 3, entry 4). Decreasing the amount of $FeCl_3$ or TMSCl significantly decreased the yields (Table 3, entries 2 and 3). Furthermore, in $ClCH_2CH_2Cl$ (DCE) at 60 °C, the yield of indene **5a** was improved to 76% and **6a** was observed in trace amount by employing $BF_3 \cdot Et_2O$ as catalyst (Table 3, entry 6).

Various substrates were prepared to test the generality of the $BF_3 \cdot Et_2O$-mediated rearrangement of THFs for the synthesis of polysubstituted indenes **5** under the established conditions, and the results were summarized in Table 4. THFs **3e** ($R^1 = R^2 = R^3 =$ Ph) also readily participated in the reaction and gave a good yield of the corresponding indene compound (Table 4, entry 2). Interestingly, the reaction of stereoisomers **3f** (R^1 = *p*-MeC_6H_4 or *p*-ClC_6H_4, R^2 = *p*-ClC_6H_4 or *p*-MeC_6H_4, R = *p*-$NO_2C_6H_4$, *Z*/*E* or *E*/*Z* = 4:3) was also observed as a clean transformation and produced **5c** exclusively in 85% yield. It should be noted that the intramolecular Friedel–Crafts cyclization occurred preferentially at the *p*-MeC_6H_4 group rather than the *p*-ClC_6H_4 subtituent, probably due to the fact that the intramolecular Friedel–Crafts reaction takes place more easily for the electron-rich aromatic moiety

(Table 4, entry 3). As for the (*E*)-**3g** (R^1 = Me, R^2 = Ph), the reaction provided the corresponding product **5d** in 73% yield even in the presence of $FeCl_3$/TMSCl (Table 4, entry 4).

TABLE 4. Synthesis of Various Polysubstituted Indene Derivatives[a]

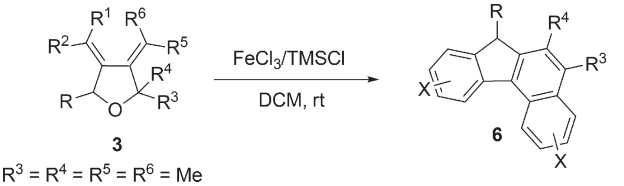


entry	R^1	R^2	R (**3**)	yield of **5** (%)
1	Ph	Ph	*p*-$NO_2C_6H_4$ (**3a**)	**5a**, 76
2	Ph	Ph	Ph (**3e**)	**5b**, 81
3	*p*-Me(Cl)C_6H_4	*p*-Cl(Me)C_6H_4	*p*-$NO_2C_6H_4$ (**3f**, 4:3)	**5c**, 85[b]
4	Me	Ph	*p*-$NO_2C_6H_4$ (**3g**)	**5d**, 73[c]

[a]Unless otherwise specified, the reaction was carried out using **3** (0.1 mmol) and $BF_3.Et_2O$ (0.03 mmol) in DCE. [b]X = *p*-ClC_6H_4, *Y* = Me. [c]X = Me, *Y* = H. the reaction was carried out using **3g** (0.1 mmol), TMSCl (0.2 mmol), $FeCl_3$ (0.05 mmol) in CH_2Cl_2 at rt.

To demonstrate the efficiency and scope of the method for the synthesis of benzo[*c*]fluorenes, we next applied the catalytic system (Table 3, entry 4) to a variety of THFs. As shown in Table 5, substitution the 5-position (R) of THFs including ethyl, phenyl, and substituted phenyl groups were well tolerated (Table 5, entries 1−5). Second, the reactions of THFs **3** bearing the electron-donating substituents (Me) on the aromatic rings of R^1 and R^2 provided the corresponding benzo[*c*]fluorene **6f** in acceptable yield (Table 5, entry 6). However, variation in the electronic character of the substituents (R^1, R^2) had a large influence on this reaction. Indeed, for substrate **3c** ($R^1 = R^2 = p$-FC_6H_5), the reaction gave the benzo[*c*]fluorene **6g** only in 32% yield even with an increasing amount of catalyst and prolonged reaction time (Table 5, entry 7).

TABLE 5. Synthesis of Various Benzo[*c*]fluorene Derivatives[a]

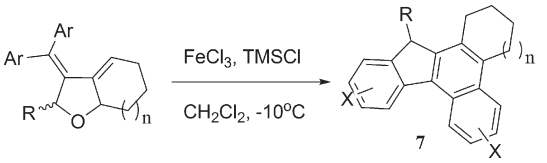


entry	R^1/R^2	R (**3**)	time (h)	yield of **6** (%)
1	C_6H_5/C_6H_5	*p*-$NO_2C_6H_4$ (**3a**)	12	**6a**, 89
2	C_6H_5/C_6H_5	*m*-$NO_2C_6H_4$ (**3b**)	24	**6b**, 81
3	C_6H_5/C_6H_5	*p*-BrC_6H_4 (**3n**)	24	**6c**, 70
4	C_6H_5/C_6H_5	Ph (**3e**)	24	**6d**, 67
5	C_6H_5/C_6H_5	C_2H_5 (**3o**)	24	**6e**, 85
6	*p*-MeC_6H_4/ *p*-MeC_6H_4	*p*-$NO_2C_6H_4$ (**3d**)	24	**6f**, 75
7	*p*-FC_6H_4/*p*-FC_6H_4	*p*-$NO_2C_6H_4$ (**3c**)	48	**6g**, 32[b]

[a]The reaction was carried out under nitrogen atmosphere on a scale of 0.1 mmol. [b]After the mixture was stirred for 24 h, another 0.5 equiv of $FeCl_3$ and 2.0 equiv of TMSCl were added, and an unidentified mixture was obtained along with the product.

Synthetic Application of Multisubstituted Bicyclic Tetrahydrofuran for the Synthesis of Medium- and Large-Size Ring-Fused Benzo[*c*]fluorene Derivatives. Inspired by these observations, we next turned our efforts toward the synthesis of medium- and large-size fused benzo[*c*]fluorene derivatives from THFs. As indicated in Table 6, a variety of THFs with annulated carbocycles of various ring sizes could be applied to produce the corresponding medium- and large-size ring-fused products in moderate to good yields from the mixture substrates.

TABLE 6. Synthesis of Medium- and Large-Size Ring Fused Benzo-[*c*]fluorene Derivatives[a]



entry	Ar	R	*n* (**3**[b])	time (h)	yield of **7** (%)
1	Ph	*p*-$NO_2C_6H_4$	1 (**3h**)	6	**7a**, 71
2	Ph	*o*-$NO_2C_6H_4$	2 (**3p**)	6	**7b**, 68
3	Ph	*p*-BrC_6H_4	2 (**3k**)	6	**7c**, 60
4	*p*-MeC_6H_4	*p*-$NO_2C_6H_4$	2 (**3q**)	6	**7d**, 46
5	Ph	*p*-$NO_2C_6H_4$	3 (**3r**)	6	**7e**, 57
6	Ph	*p*-$NO_2C_6H_4$	4 (**3l**)	6	**7f**, 52
7	Ph	*p*-$NO_2C_6H_4$	8 (**3m**)	6	**7g**, 61

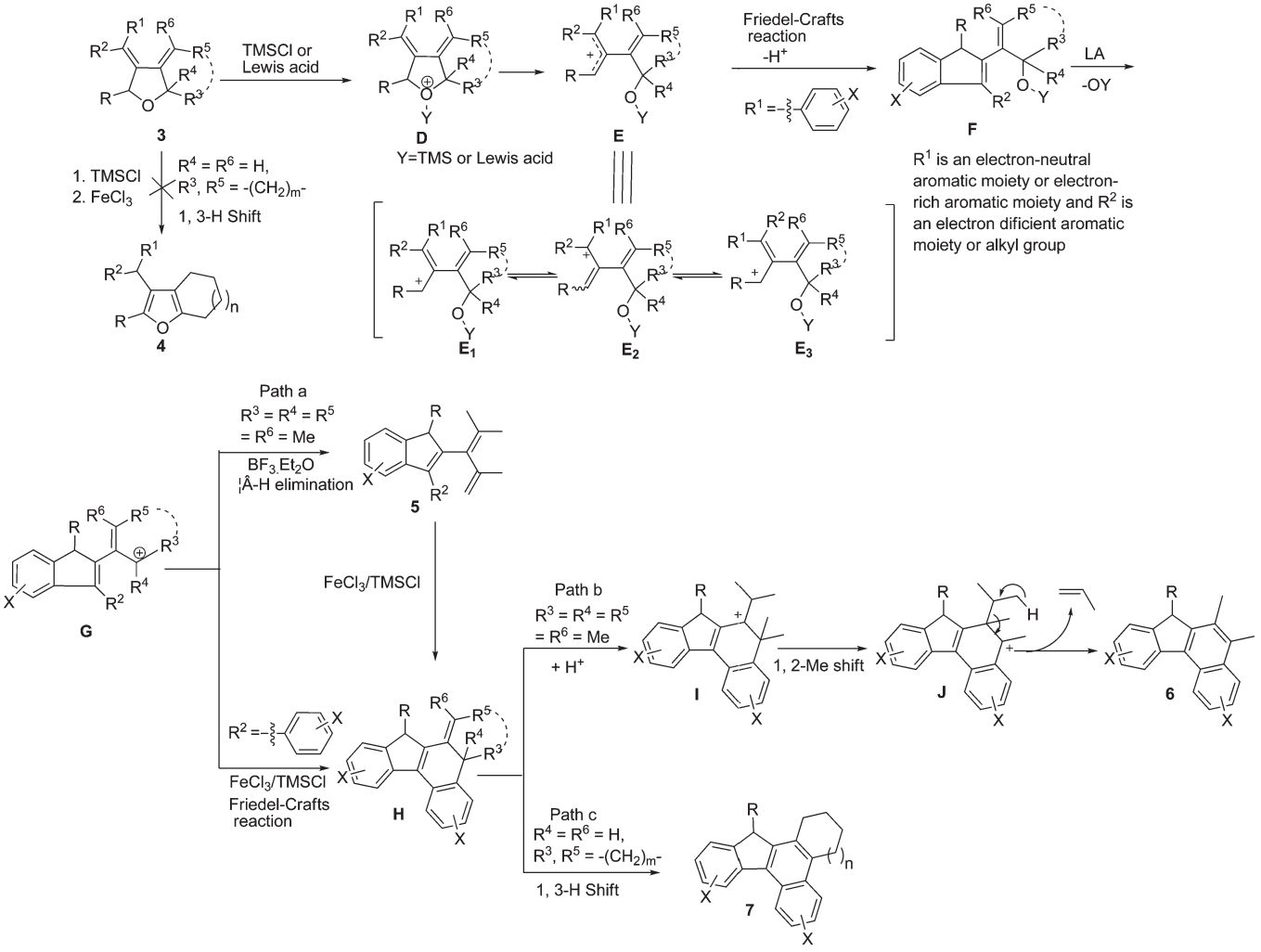
[a]The reaction was carried out under nitrogen atmosphere on a scale of 0.1 mmol. [b]**3** are mixture of cis/trans isomers.

Mechanistic Discussion

One of the proposed mechanisms for the formation of indene and benzo[*c*]fluorene derivatives is outlined in Scheme 3. Initially, the reaction of THFs **3** with Lewis acid or TMSCl generates oxonium intermediate **D**. In this case, furan derivatives **4** are observed in trace yields when R^4 and R^6 are hydrogen atoms. A rational explanation of this drastic difference can be attributed to the fact that the reaction of bicyclic-THFs **3** with TMSCl probably easily forms the oxonium intermediate **D**, which may facilitate the ring-opening step of bicyclic-THFs in the presence of $FeCl_3$. Second, the ring-opening reaction of oxonium intermediate **D** produces δ-allylic cationic intermediate **E** or the reversible cationic intermediate $\mathbf{E_1}$, $\mathbf{E_2}$, and $\mathbf{E_3}$. When R^1 is an electron-rich aromatic moiety or an electron-neutral aromatic moiety (phenyl) and R^2 is an electron-dificient aromatic moiety or alkyl group (methyl), the intramolecular Friedel−Crafts reaction with the aromatic R^1 group exclusively takes place to produce the intermediate **F**, probably due to the nature of Friedel−Crafts reaction (Table 4, entries 3 and 4).[14] The subsequent transformation of **F** leads to the formation of intermediate **G** in the presence of Lewis acid. Then, the varied reaction conditions and the substituent effects might result in dramatic differences in the further transformations of **G**. In the presence of $BF_3 \cdot Et_2O$ in DCE at 60 °C, deprotonation of intermediate **G** takes place to afford the corresponding indenes **5** when R^1, R^2, R^3, and R^4 are methyl groups. However, in a $FeCl_3$/TMSCl catalytic system, intermediate **G** undergoes intramolecular Friedel−Crafts reaction to give intermediate **H**. In addition, the intermediate **H** might also be generated via the intramolecular Friedel−Crafts reaction from the indenes **5** in

(14) (a) Fleming, I. *Chemtracts: Org. Chem.* **2001**, *14*, 405–406. (b) Chevrier, B.; Weis, R. *Angew. Chem.* **1974**, *86*, 12–21.

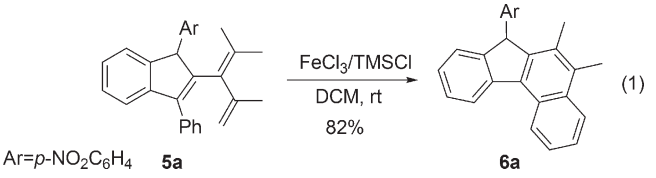
SCHEME 3. Proposed Mechanistic Pathway for the Tunable Sequential Transformations of THFs



the presence of $FeCl_3$/TMSCl (see eq 1). Then the intermediate H is believed to proceed via a consecutive process including protonation, 1,2-migration of the methyl group, and elimination of a propene molecule to afford the aromatized benzo[*c*]fluorene derivatives **6** when R^1, R^2, R^3, and R^4 are methyl groups (path b, see eq 1 below).[15] When R^4 and R^6 are hydrogen atoms, aromatization of the intermediate **H** takes place to produce the corresponding benzo[*c*]fluorenes **7** (path c).

There is still another tentative pathway shown as follows: intermediate **D** might undergo ring-opening step to produce the cationic intermediate **C** (Scheme 2), which then may proceed via a consecutive process including β-H elimination and an intramolecular Friedel−Crafts reaction to give the indene products **5**.[12b] Probably, further transformation of the indene derivatives **5** via a similar consecutive process ultimately gave the benzo[*c*]fluorene derivatives **6** (Scheme 3, path b). Accordingly, the ring-fused benzo[*c*]fluorenes **7** may also be formed via the double-intramolecular Friedel−Crafts reactions from the same cationic intermediate **C**.[12a]

Notably, the hypothesis that the formation of **6** may come from a series of consecutive transformations of **5** is supported by the fact that treatment of indene product **5a** with $FeCl_3$/TMSCl at room temperature in DCM successfully delivered the benzo[*c*]fluorine **6a** in 82% yield (eq 1), indicating the possibility of the mechanism shown as path b in Scheme 3.



Conclusion

In summary, we present the comprehensive study of the Lewis acid mediated cycloadditions of vinylidenecyclopropanes with aldehydes and demonstrate that the afforded THFs could be used as versatile building blocks for the construction of various polycyclic frameworks in controllable ways. It is meaningful in the aspects as follows: (1) It has been revealed that the reaction pathway of Lewis acid catalyzed transformtions of THFs was dramatically changed depending on the varied catalytic systems and significant influence of substituents. (2) These interesting sequential

(15) Li, W.; Shi, M.; Li, Y. X. *Chem.—Eur. J.* **2009**, *15*, 8852.

transformations provide an efficient route to polysubstituted furan, indene, and benzo[*c*]fluorene derivatives in moderate to good yields in a diversity-oriented manner. (3) The corresponding reaction mechanisms have been discussed on the basis of the control experiments and related investigations. (4) These processes provide an efficient protocol for the synthesis of various medium- and large-size ring-fused tetrahydrofurans, furans, and benzo[*c*]fluorenes, which are of current interest.[16] (5) The detailed investigations on the transformations of THFs would also provide insight into the mechanism of the Lewis acid mediated selective reaction of vinylidenecycloproanes with aldehydes.

Experimental Section

General Experimental Procedures for the Synthesis of Tetrahydrofuran Derivatives 3. Under an atmosphere of dry nitrogen, $BF_3 \cdot Et_2O$ (0.09 mmol) was added to a solution of aldehyde **2** (0.36 mmol) in 2 mL of dry CH_2Cl_2 at −10 °C. Then a solution of VCP **1** (0.3 mmol) in 2 mL of CH_2Cl_2 was added slowly. The progress of the reaction was monitored by TLC analysis until the starting material was consumed completely. The reaction mixture was quenched with 5 mL of water and extracted with EtOAc (3 × 5 mL). The combined organic layers were dried over anhydrous $MgSO_4$. Evaporation and column chromatography on silica gel afforded **3**.

4-(Di-*p*-tolylmethylene)-2,2-dimethyl-5-(4-nitrophenyl)-3-(propan-2-ylidene)tetrahydrofuran (3d). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (d, J = 6.8 Hz, 2H), 7.42 (d, J = 6.8 Hz, 2H), 7.02−7.13 (m, 4H), 6.84−6.96 (m, 2H), 6.66−6.80 (m, 2H), 5.12 (s, 1H), 2.33 (s, 3H), 2.28 (s, 3H), 1.65 (s, 3H), 1.59 (s, 3H), 1.31 (s, 3H), 1.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.0, 21.1, 21.7, 25.0, 28.5, 29.51, 79.5, 81.5, 123.5, 128.0, 128.4, 128.7, 128.9, 129.6, 136.2, 136.5, 137.3, 139.6, 140.1, 140.4, 147.0, 152.1. IR (neat): 2953, 2917, 2850, 1599, 1462, 1342, 1180, 1021, 823, 768 cm^{-1}. MS (70 eV, EI): m/z 453 (M^+). HRMS (EI): m/z calcd for $C_{30}H_{31}NO_3$ (M^+) 453.2304, found 453.2309.

General Experimental Procedures for the One-Pot Reaction Synthesis of Furan Derivatives 4. Under an atmosphere of dry nitrogen, bicyclic VCP **1** (0.3 mmol) was added to a solution of aldehyde **2** (0.36 mmol) in 5 mL of dry CH_2Cl_2 at −10 °C. Then $BF_3 \cdot Et_2O$ (70 mmol %) was injected. After stirring the mixture was stirred for the specified time (monitored by TLC), the required TMSCl was injected and the reaction temperature was warmed to rt. After being stirred for another 24−36 h, the reaction mixture was quenched with 5 mL of water and extracted with EtOAc (3 × 5 mL). The combined organic layers were dried over anhydrous $MgSO_4$. After filtration and removal of the solvent in vacuo, the residues were purified with flash chromatography to afford **4**.

3-((4-Chlorophenyl)(*p*-tolyl)methyl)-2-(4-nitrophenyl)-4,5,6,7-tetrahydrobenzofuran (4b). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, J = 9.2 Hz, 2H), 7.54 (d, J = 8.4 Hz, 2H), 7.25 (d, J = 8.4 Hz, 2H), 7.13 (d, J = 7.6 Hz, 2H), 6.98−7.05 (m, 4H), 5.65 (s, 1H), 2.66 (t, J = 5.8 Hz, 2H), 2.34 (s, 3H), 1.69−1.80 (m, 3H), 1.50−1.65 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.0, 22.3, 22.8, 23.5, 29.6, 46.4, 120.6, 123.9, 125.8, 126.0, 128.4, 128.9, 129.3, 130.5, 132.3, 136.5, 137.3, 138.2, 141.0, 145.5, 153.0, 153.3. IR (neat): 2925, 2856, 1591, 1508, 1445, 1333, 1090, 909, 851, 801, 731 cm^{-1}. MS (70 eV, EI): m/z 457 (M^+). HRMS (EI): m/z calcd for $C_{28}H_{24}NO_3Cl$ (M^+) 457.1445, found 457.1452.

General Experimental Procedures for the Synthesis of Indene Derivatives 5. Under an atmosphere of dry nitrogen, $BF_3 \cdot Et_2O$ (30 mmol %) was added to a solution of tetrahydrofuran **3** (0.1 mmol) in 2 mL of dry CH_2Cl_2 at room temperature. Then, the mixture was warmed to 60 °C. After the reaction was complete (monitored by TLC), the reaction mixture was quenched with 4 mL of water and extracted with EtOAc (3 × 4 mL). The combined organic layers were dried over anhydrous $MgSO_4$. After filtration and removal of the solvent in vacuo, the residues were purified with flash chromatography to afford **5**.

3-(4-Chlorophenyl)-2-(2,4-dimethylpenta-1,3-dien-3-yl)-6-methyl-1-(4-nitrophenyl)-1*H*-indene (5c). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (d, J = 8.8 Hz, 2H), 7.40−7.49 (m, 4H), 7.26 (d, J = 7.6 Hz, 1H), 7.21 (d, J = 8.8 Hz, 2H), 7.12 (d, J = 7.6 Hz, 1H), 6.97 (s, 1H), 5.04 (s, 1H), 4.74 (s, 1H), 4.41 (s, 1H), 2.32 (s, 3H), 1.81 (s, 3H), 1.55 (s, 3H), 1.14 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.3, 21.5, 22.4, 23.2, 57.4, 116.2, 119.9, 123.5, 124.9, 128.0, 128.7, 129.5, 129.8, 131.2, 132.6, 133.1, 134.3, 135.8, 140.5, 141.6, 145.3, 146.8, 147.2, 148.2. IR (neat): 2916, 1601, 1521, 1091, 824, 741, 693 cm^{-1}. MS (70 eV, EI) m/z: 455 (M^+). HRMS (EI): m/z calcd for $C_{29}H_{26}ClNO_2$ (M^+) 455.1652, found 455.1647.

General Experimental Procedures for the Synthesis of Benzo[*c*]fluorene Derivatives 6. Under an atmosphere of dry nitrogen, TMSCl (0.2 mmol) was injected to a solution of tetrahydrofuran **3** (0.1 mmol) in 2 mL of dry CH_2Cl_2 at rt. The mixture was stirred for 5 min, and then $FeCl_3$ (0.05 mmol) was added. After being stirred for the specified time (monitored by TLC) at rt, the reaction mixture was quenched with 4 mL of water and extracted with EtOAc (3 × 4 mL). The combined organic layers were dried over anhydrous $MgSO_4$. After filtration and removal of the solvent in vacuo, the residues were purified with flash chromatography to afford **6**.

5,6-Dimethyl-7-(4-nitrophenyl)-7*H*-benzo[*c*]fluorene (6a). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.83 (d, J = 8.0 Hz, 1H), 8.38 (d, J = 7.6 Hz, 1H), 8.19 (d, J = 8.4 Hz, 1H), 8.08 (d, J = 8.8 Hz, 2H), 7.57−7.69 (m, 2H), 7.42−7.49 (m, 1H), 7.16−7.29 (m, 4H), 5.19 (s, 1H), 2.63 (s, 3H), 2.17 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.0, 17.3, 54.4, 123.0, 124.1, 124.3, 124.8, 125.1, 125.6, 125.6, 126.2, 127.8, 128.2, 128.5, 130.4, 132.4, 133.4, 134.4, 141.8, 144.7, 146.8, 147.7, 149.8. IR (neat): 2923, 2852, 1593, 1518, 1342, 1275, 1260, 856, 721 cm^{-1}. MS (70 eV, EI) m/z: 365 (M^+). HRMS (EI): m/z calcd for $C_{25}H_{19}NO_2$ (M^+) 365.1416, found 365.1425.

General Experimental Procedures for the Synthesis of Ring-Fused Benzo[*c*]fluorene Derivatives 7. Under an atmosphere of dry nitrogen, TMSCl (0.2 mmol) was injected to a solution of bicyclic tetrahydrofuran **3** (0.1 mmol) in 2 mL of dry CH_2Cl_2 at rt. The mixture was stirred for 5 min, and then $FeCl_3$ (0.05 mmol) was added. After being stirred for the specified time (monitored by TLC) at rt, the reaction mixture was quenched with 4 mL of water and extracted with EtOAc (3 × 4 mL). The combined organic layers were dried over anhydrous $MgSO_4$. After filtration and removal of the solvent in vacuo, the residues were purified with flash chromatography to afford **7**.

9-(4-Nitrophenyl)-6,7,8,9-tetrahydro-5*H*-indeno[2,1-*l*]phenanthrene (7a). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.81 (d, J = 8.4 Hz, 1H), 8.36 (d, J = 8.0 Hz, 1H), 8.11 (d, J = 8.0 Hz, 1H), 8.06 (d, J = 8.8 Hz, 2H), 7.56−7.68 (m, 2H), 7.41−7.47 (m, 1H), 7.22 (d, J = 7.6 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 5.06 (s, 1H), 3.18−3.28 (m, 1H), 3.03−3.15 (m, 1H), 2.63−2.74 (m, 1H), 2.08−2.19 (m, 1H), 1.94−2.02 (m, 1H), 1.60−1.85 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.5, 22.9, 26.4, 28.1, 53.9, 123.0, 124.0, 124.1, 124.3, 124.9, 125.7, 125.7, 126.2, 127.8, 128.1, 128.7, 131.7, 132.8, 133.2, 134.3, 141.8, 144.3, 146.8, 148.0, 149.5. IR (neat):

(16) (a) Breitenbach, J.; Boosfeld, J.; Vögtle F. In *Comprehensive Supramolecular Chemistry*; Lehn, J. M., Ed.; Pergamon: New York, 1996; Vol. 2, pp 29−67. (b) Dietrich, B.; Viout, P.; Lehn, J. M. *Macrocyclic Chemistry*; VCH: Weinheim, 1993.

2955, 2921, 1596, 1515, 1460, 1344, 1072, 756, 726 cm^{-1}. MS (70 eV, EI) *m*/*z*: 391 (M^+). HRMS (EI): *m*/*z* calcd for $C_{27}H_{21}NO_2$ (M^+) 391.1572, found 391.1568.

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Supporting Information Available: General experimental procedures and spectroscopic data for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.