A Facile Access to Medium- and Large-Size Naphthalenacarbocycles via Lewis Acid Mediated Ring-Expansion Reaction of Bicyclic Vinylidenecyclopropanes

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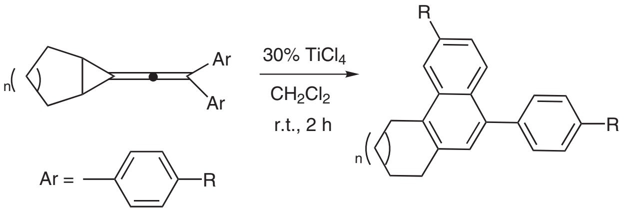
Received 25 September 2007

Abstract: Ring-expansion reactions of bicyclic vinylidenecyclopropanes in the presence of Lewis acid was investigated, providing an efficient method for the synthesis of naphthalenes with annulated carbocycles of various ring sizes in good to excellent yields under mild conditions.

Key words: bicyclic vinylidenecyclopropanes, ring expansion, Lewis acids

The synthesis of medium- and large-size ring systems is still a challenge for organic chemists as they are widespread, ranging from naturally occurring compounds to macrocyclic synthetic receptors or ligands.[1] A number of reactions such as Wurtz coupling,[2] Friedel–Crafts reaction,[3] acyloin condensation,[4] samarium diiodide promoted reaction[5] and metal-mediated coupling reactions[6] were applied to synthesize carbocyclic skeletons. Ring-expansion reaction from smaller cyclic units is also a facile method for the synthesis of medium- and large-size ring compounds. Many interesting and useful medium- and large-size ring compounds have been synthesized through these methods.[7]

Methylenecyclopropanes (MCPs) are highly strained but readily available molecules which have served as useful building blocks in organic synthesis.[8] Recently, we have investigated the cyclization reactions of MCPs to synthesize aromatic compounds.[9] Compared with MCPs, vinylidenecyclopropanes (VCPs) have an allene structure unit instead of the vinyl bonds adjacent to the cyclopropyl ring, which might lead to more possible reactive positions than classical MCPs, and yet they are thermally stable and reactive substances. Therefore, thermal and photochemical skeletal conversions of VCPs have attracted much attention from theoretical, spectroscopic, synthetic and mechanistic viewpoints.[10]

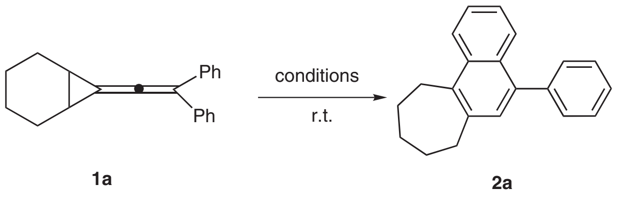


Scheme 1

Recently, Shi et al. have developed the reaction of vinylidenecyclopropanes catalyzed by Lewis acids to afford a series of naphthalene and indene derivatives.[10g–i] Herein, we wish to report a ring-expansion reaction of bicyclic vinylidenecyclopropanes mediated by $TiCl_4$ for the synthesis of medium- and large-size naphthalenacarbocycles (Scheme 1).

Initially, we examined the reaction of 0.5 mmol of bicyclic vinylidenecyclopropane **1a** with 10% of $BF_3{\cdot}OEt_2$ as a catalyst in CH_2Cl_2 at room temperature. After stirring for 12 hours, the desired product **2a** was obtained in 55% yield (Table 1, entry 1). To optimize the reaction conditions, a series of Lewis acids and solvents were employed.

Table 1 Optimization of Conditions for the Synthesis of Naphthalenacarbocycle **2a**[a]

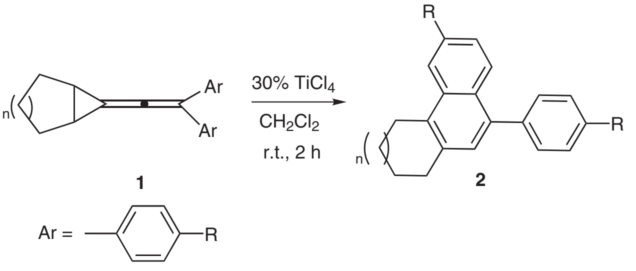


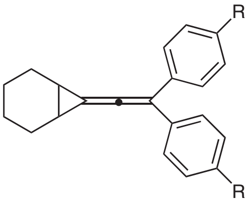
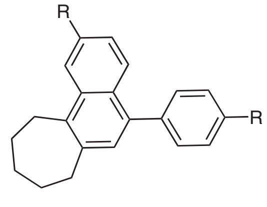
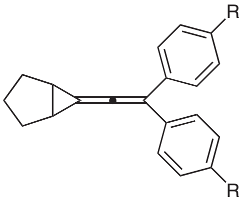
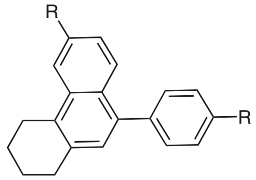
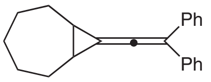
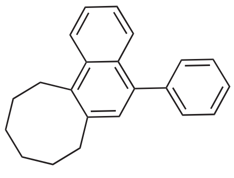
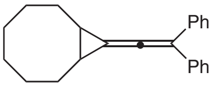
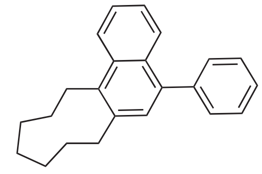
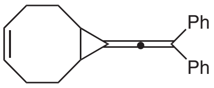
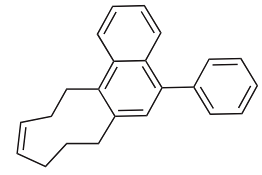
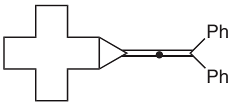
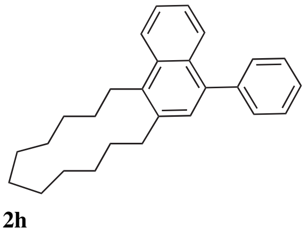
Entry	Lewis acid	Solvent	Time (h)	Yield (%)[b]
1	10% $BF_3{\cdot}EtO_2$	CH_2Cl_2	12	55
2	10% $AlCl_3$	CH_2Cl_2	48	10
3	10% CF_3COOH	CH_2Cl_2	48	33
4	10% $ZrCl_4$	CH_2Cl_2	24	58
5	10% $TiCl_4$	CH_2Cl_2	5	66
6	20% $TiCl_4$	CH_2Cl_2	2	74
7	**30% $TiCl_4$**	**CH_2Cl_2**	**2**	**85**
8	30% $TiCl_4$	toluene	2	78
9	30% $TiCl_4$	THF	5	trace[c]
10	30% $TiCl_4$	MeCN	5	trace[d]

[a] The reaction was carried under a nitrogen atmosphere on a 0.5-mmol scale.
[b] Isolated yield.
[c] Compound **1a** (83%) was recovered.
[d] Compound **1a** (77%) was recovered.

SYNLETT 2008, No. 2, pp 0229–0232
Advanced online publication: 21.12.2007
DOI: 10.1055/s-2007-1000844; Art ID: W18007ST

Table 2 Synthesis of Medium- and Large-Size Naphthalenacarbocycles[a]



Entry	Vinylidenecyclopropanes	Product	Yield (%)[b]
			
1	**1a** (R = H)	**2a** (R = H)	85
2	**1b** (R = Cl)	**2b** (R = Cl)	87
			
3	**1c** (R = H)	**2c** (R = H)	82
4	**1d** (R = Cl)	**2d** (R = Cl)	83
5	 **1e**	 **2e**	78
6	 **1f**	 **2f**	86
7	 **1g**	 **2g**	85
8	 **1h**	 **2h**	82

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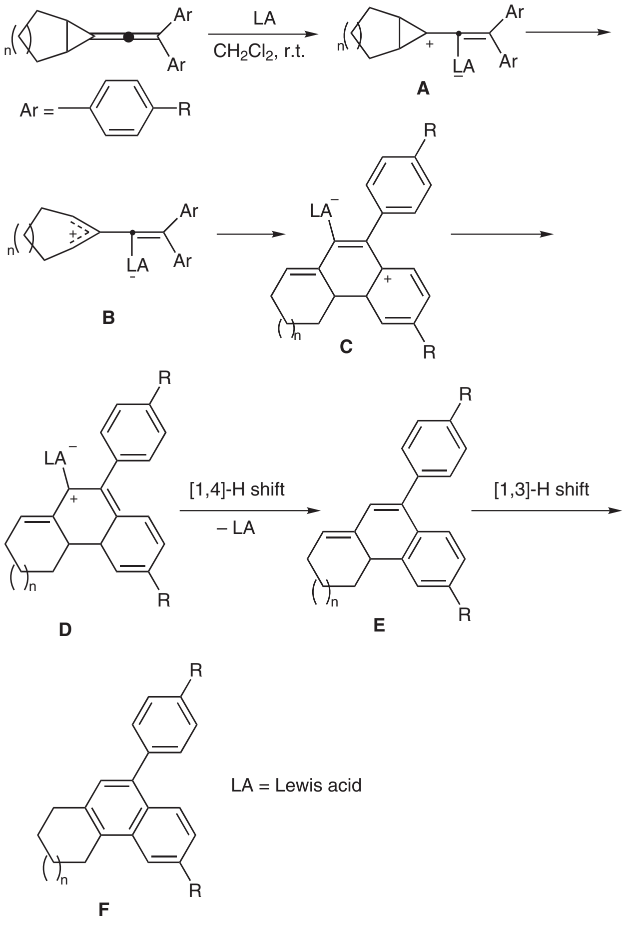
[a] The reaction was carried out under nitrogen atmosphere on a 0.5-mmol scale.

[b] Isolated yield.

The experimental results showed that $TiCl_4$ was a better Lewis acid than the other Lewis acid tested and in this case, the corresponding product **2a** was obtained in 66% yield (Table 1, entry 5). Further investigations indicated that when the catalyst amount was enhanced to 30%, the yield of product was efficiently improved and CH_2Cl_2 was found to be the best solvent (Table 1, entry 7).

With these results in hand, the scope of this reaction was investigated and the typical results are summarized in Table 2.[11] As can be seen from Table 2, the corresponding rearranged product **2**, six-membered ring and medium-size naphthalenacarbocycles derivatives were obtained in good to high yields (Table 2, entries 1–6). For bicyclic vinylidenecyclopropane **1g**, the corresponding product **2g** was obtained in 85% yield (Table 2, entry 7), which showed that the C=C double bond was tolerated in this reaction. For large-size bicyclic vinylidenecyclopropane **1h**, the reaction happened smoothly to afford **2h** in 82% yield (Table 2, entry 8).

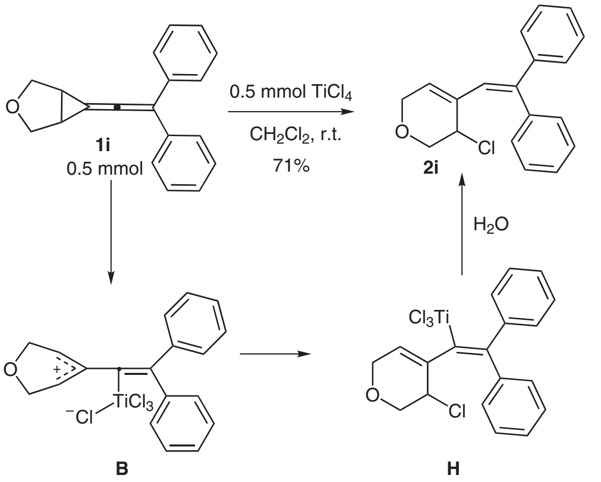
A plausible mechanism for the ring-expansion reaction is shown in Scheme 2.[10i] Coordination of compound **1** to Lewis acid gives the intermediate **A**, which produces the ring-expansion intermediate **B**. The intramolecular Friedel–Crafts reaction of **B** gives the cyclized intermediate **C**, which is smoothly transformed to the intermediate **D** through further rearrangement. The Lewis acid is released via a 1,4-proton shift to give the corresponding intermediate **E**, while a further 1,3-proton shift finally affords the aromatic product **F** (Scheme 2).



Scheme 2

When the bicyclic vinylidenecyclopropane **1i** was employed, a similar ring-expansion reaction happened to give the intermediate **B**. However, chlorination of **B** instead of the intramolecular Friedel–Crafts reaction occurred to give the intermediate **H**, which could be transformed to the final product 3,6-dihydro-2*H*-pyran derivative **2i** in 71% yield when quenched with water (Scheme 3).[12]

In conclusion, we have disclosed that the Lewis acid mediated ring-expansion reaction of bicyclic vinylidenecyclopropanes would give a convenient approach to the synthesis of naphthalenes with annulated carbocycles of various ring sizes. Due to the easily accessible starting materials, the simple reaction procedure and the mild conditions, this method could prove very attractive for the building of common-, medium- and large-size rings. The reaction mechanism and synthetic applications of this methodology are being further studied in our laboratory.



Scheme 3

Acknowledgment

We are grateful to the National Natural Science Foundation of China (Project No. 20472072, 20332060 and 20672095) for financial support.

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(11) **Typical Procedure for the Preparation of 2**: To a solution of bicyclic vinylidenecyclopropanes (0.5 mmol) in anhyd CH_2Cl_2 (3 mL) under N_2 was added $TiCl_4$ (28.4 mg, 0.15 mmol) under a nitrogen atmosphere. The mixture was stirred at r.t. for 2 h. After the reaction was complete, the mixture was concentrated and the residue was purified by flash chromatography to afford medium- and large-size naphthalenacarbocycles **2**. Selected spectral data for **2h**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (d, J = 8.0 Hz, 1 H), 7.87 (d, J = 8.4 Hz, 1 H), 7.42–7.53 (m, 5 H), 7.36–7.42 (m, 1 H), 7.30–7.36 (m, 1 H), 7.25 (s, 1 H), 3.00–3.09 (m, 2 H), 2.70–2.80 (m, 2 H), 1.74–1.89 (m, 4 H), 1.64–1.73 (m, 2 H), 1.48–1.64 (m, 6 H), 1.34–1.48 (m, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.2, 23.4, 24.5, 24.6, 26.4, 26.6, 26.9, 27.0, 27.1, 27.8, 32.3, 123.9, 124.5, 125.6, 126.6, 126.9, 128.1, 129.8, 130.2, 130.6, 132.8, 135.1, 137.4, 138.2, 141.1. IR (KBr): 2929, 2856, 1461, 1383, 762, 707 cm^{-1}. MS (70 eV, EI): m/z = 356 [M$^+$], 356 (100). HRMS (EI): m/z [M$^+$] calcd for $C_{27}H_{32}$: 356.2504; found: 356.2512.

(12) Spectral data for **2i**: ^{1}H NMR (400 MHz, $CDCl_3$): = 7.33–7.41 (m, 3 H), 7.27–7.32 (m, 7 H), 6.42 (s, 1 H), 5.57 (t, J = 2.6 Hz, 1 H), 4.24 (d, J = 2.2 Hz, 1 H), 4.17 (dd, J_1 = 3.7 Hz, J_2 = 18.0 Hz, 1 H), 4.08 (dd, J_1 = 1.8 Hz, J_2 = 17.8 Hz, 1 H), 3.98 (dd, J_1 = 2.9 Hz, J_2 = 12.4 Hz, 1 H), 3.87 (dd, J_1 = 3.0 Hz, J_2 = 12.4 Hz, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 54.0, 65.5, 70.0, 125.1, 127.4, 127.5, 127.6, 128.1, 128.3, 129.8, 132.7, 140.0, 142.5, 143.9. IR (film): 3056, 3024, 2925, 2852, 1658, 1598, 1491, 1445, 1380, 1135, 1080, 758, 700 cm^{-1}. MS (70 eV, EI): m/z = 296 [M$^+$], 231 (100).