

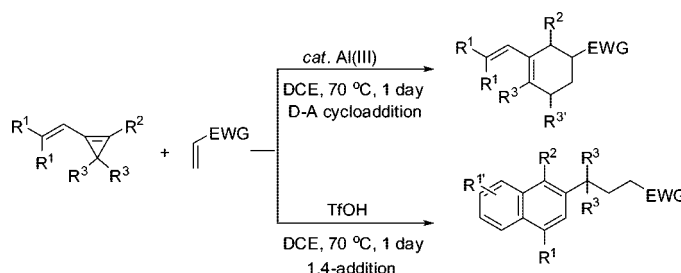
Acid-Catalyzed Cascade Ring-Opening and Addition Reactions of Arylvinylcyclopropenes with α,β -Unsaturated Substrates, Scope and Limitations

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Received December 21, 2008



Catalyzed by Al(III) catalyst, arylvinylcyclopropenes react with α,β -unsaturated substrates smoothly to produce the Diels–Alder adducts in moderate to good yields through a cascade ring-opening reaction/Diels–Alder cycloaddition. On the other hand, strong Brønsted acid TfOH can promote the cascade intramolecular Friedel–Crafts/1,4-addition reaction to produce indene derivatives in moderate to good yields under mild conditions. The acidity of the catalysts plays a key role in these reactions.

Introduction

Cyclopropenes,¹ as highly strained small ring species, have been of continuing interest in the past few decades.² One of the most common behaviors of cyclopropenes is the ring-opening reaction under various conditions. For example, photoirradiation³ of 1,2-diphenyl-3,3-dimethylcyclopropene produced the isomeric dienes in a 3:1 ratio (Scheme 1, reaction a).⁴ Moreover, thermolysis of tetramethylcyclopropene at 490

or 260–298 °C led to dimethylpenta-1,3-dienes (Scheme 1, reaction b).⁵ Alternatively, if there is no methyl group or only one methyl group at the C-3 position, the pyrolysis of cyclopropenes afforded alkyne products (Scheme 1, reactions c and d).⁶ Furthermore, Brønsted acid (TsOH) could promote the ring-opening reaction of cyclopropene to afford the corresponding 1,3-diene product when the β -cationic center is stabilized by the trimethylsilyl group (Scheme 1, reaction e).⁷

These ring-opening products give the probability that cyclopropenes can act as dienes to react with other dienophiles in a cascade reaction process with such ring-opening reaction followed by the Diels–Alder cycloaddition, which was different from the common roles of dienophiles that cyclopropenes acted in most cases.⁸ Namely, as common dienophiles, cyclopropenes can directly react with various dienes under mild conditions to give the corresponding formal Diels–Alder products, six-membered rings with up to four stereogenic centers, in a regio-

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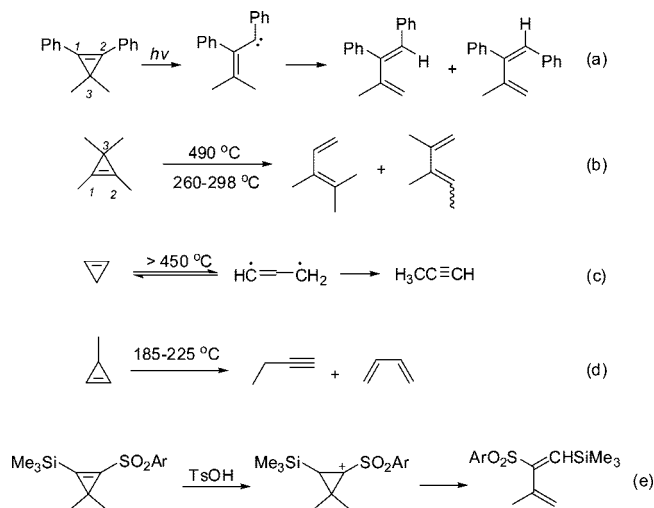
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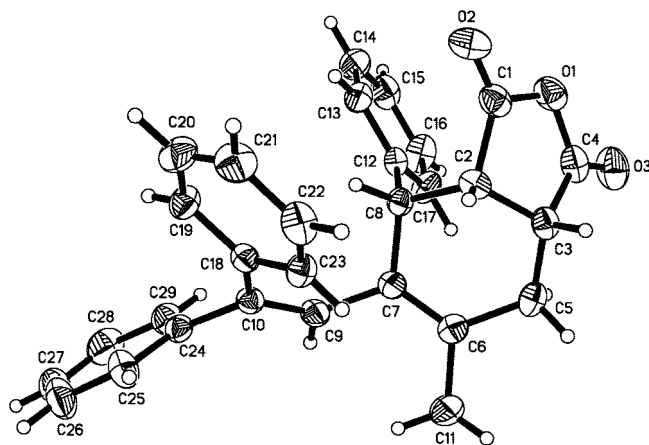
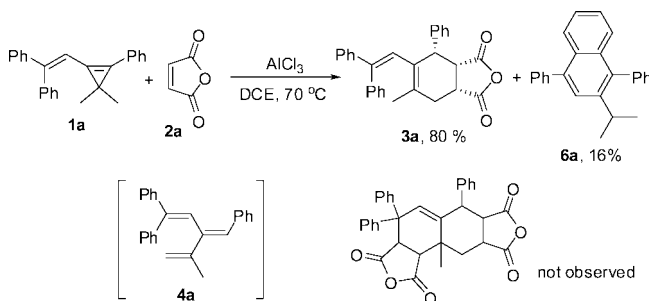
SCHEME 1. Ring-Opening Reactions of Cyclopropanes



and stereocontrolled way and in good yields.⁹ In this paper, we wish to report the acid-catalyzed regioselective ring-opening reaction of arylvinylcyclopropanes **1**¹⁰ followed by Diels–Alder cycloaddition with α,β -unsaturated substrates to construct cyclohexene skeletons, in which cyclopropanes acted as pre-dienes rather than dienophiles to construct six-membered-ring compounds. Moreover by changing the catalyst to a stronger Brønsted acid, a cascade intramolecular Friedel–Crafts/1,4-addition of **1** with α,β -unsaturated substrates took place to produce indene derivatives under identical conditions.

Results and Discussion

To obtain the ring-opening products of phenylvinylcyclopropane **1a**, we initially attempted pyrolysis of **1a** at 260 °C, but it was found that none of the corresponding ring-opening product **4a** was formed. Furthermore, by adding maleic anhydride **2a** under the same condition to trap the in situ formed **4a**, we found that complicated reaction products were obtained, presumably due to both of the reactants and the products are being stable at such high temperature. Then, using 0.1 equiv of AlCl_3 as the catalyst, it was found that the Diels–Alder cycloaddition product **3a**, derived from the reaction of ring-opening product **4a** (the *E*-configuration of **4a** was deduced by the retro-D-A reaction of *endo*-adduct **3a**) with **2a**, was obtained in 80% yield along with the rearrangement product **6a** in 16% yield at 70 °C in 1,2-dichloroethane (DCE). In addition, the product **3a** did not undergo further Diels–Alder cycloaddition with another molecule of **2a**, presumably due to the steric hindrance of the two adjacent phenyl groups (Scheme 2). Compound **3a** was unam-

FIGURE 1. ORTEP drawing of compound **3a**.SCHEME 2. AlCl_3 -Catalyzed Cascade Ring-Opening Diels–Alder ReactionTABLE 1. Ring-Opening Reaction of **1a** in the Presence of Various Lewis or Brønsted Acids

entry ^a	cat.	solvent	<i>T</i> (°C)	yield (%) ^b		
				4a	5a	6a
1	AlCl_3	DCE	20			
2	AlCl_3	DCE	70	49	35	14
3	$\text{CH}_3\text{CO}_2\text{H}$	DCE	70			
4	HCl	DCE	70		56	39
5	ZrCl_4	DCE	70			88
6	TsOH	DCE	20	10	57	25
7	TsOH	DCE	70		40	39
8	cat. Al(III)	DCE	70	97		
9	cat. Al(III)	toluene	70	92		
10	cat. Al(III)	DCM	20			
11	cat. Al(III)	THF	70	17		

^a All reactions were carried out with **1a** (0.2 mmol) in the presence of the listed catalysts (10 mol %) and solvent (1.0 mL). ^b Isolated yields.

biguously determined by an X-ray diffraction (Figure 1) and its CIF data are presented in the Supporting Information.¹¹

To determine the optimal conditions of the ring-opening reaction of **1a**, we carried out the reactions of **1a** in the presence

(11) The crystal data of **3a** have been deposited in CCDC with the number 679736. Empirical formula: $\text{C}_{33}\text{H}_{32}\text{O}_5$; formula weight: 508.59; crystal color, habit: colorless, prismatic; crystal dimensions: $0.457 \times 0.411 \times 0.347$ mm; crystal system: Monoclinic; lattice type: primitive; lattice parameters: $a = 16.4843(15)$ Å, $b = 9.9238(9)$ Å, $c = 16.6985(16)$ Å, $\alpha = 90^\circ$, $\beta = 106.622(2)^\circ$, $\gamma = 90^\circ$, $V = 2617.5(4)$ Å³; space group: $P2(1)/c$; $Z = 4$; $D_{\text{calc}} = 1.291$ g/cm³; $F_{000} = 1080$; diffractometer: Rigaku AFC7R; residuals: $R = 0.0900$, $R_w = 0.2676$.

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TABLE 2. Scope of the Cascade Ring-Opening and Diels–Alder Cycloaddition

entry ^a	1 (R ¹ /R ² /R ³)	2	yield (%) ^b
1	1a (C ₆ H ₅ /C ₆ H ₅ /Me)	2a	3a , 86
2	1a	2b ,	3b , 96
3	1a	2c , EtO ₂ C—C≡C—CO ₂ Et	3c , 80
4	1a	2d , ^c	3d , 32 3d' , 50
5	1a	2e , ^c	3e , 40 3e' , 40
6	1a	2f , ^c	3f , 35 3f' , 57
7	1b (C ₆ H ₅ / <i>p</i> -ClC ₆ H ₄ /Me)	2c	3g , 82
8	1c (C ₆ H ₅ / <i>p</i> -MeC ₆ H ₄ /Me)	2c	3h , 62
9	1d (<i>p</i> -ClC ₆ H ₄ /C ₆ H ₅ /Me)	2c	3i , 79
10	1e (<i>p</i> -MeC ₆ H ₄ /C ₆ H ₅ /Me)	2c	3j , 96
11	1f (C ₆ H ₅ /C ₆ H ₅ /(CH ₂) ₅ -)	2c	3k , 61

^a All reactions were carried out with **1** (0.2 mmol) and **2** (0.3 mmol) in the presence of Al-catalyst (0.02 mmol) and DCE (2.0 mL) at 70 °C for 24 h.
^b Isolated yields. ^c **2** (2 mmol) was used.

of various Lewis and Brønsted acids. At room temperature, no reaction occurred in the presence of AlCl₃ in DCE (Table 1, entry 1). At 70 °C, **4a** was provided in 49% yield along with the rearrangement product 1,4-diphenyl-2-(propan-2-ylidene)-1,2-dihydronaphthalene **5a** in 35% yield and naphthalene derivative **6a** in 14% (Table 1, entry 2). The structure of **5a** was further confirmed by X-ray diffraction and its CIF data are presented in the Supporting Information.¹² With acetic acid as the catalyst at 70 °C, no reaction occurred (Table 1, entry 3). Brønsted acid HCl did not produce **4a**, affording **5a** and **6a** in 56% and 39% yield, respectively (Table 1, entry 4). Using ZrCl₄ as the catalyst provided naphthalene derivative **6a** exclusively in 88% yield, which is very similar as that catalyzed by BF₃·OEt₂ (Table 1, entry 5).¹⁰ Using Brønsted acid TsOH as the catalyst afforded **4a** in 10% yield along with 57% of **5a** and 25% of **6a** at 20 °C (Table 1, entry 6). On the other hand, **5a** and **6a** were formed in 40% and 39% yield, respectively, at 70 °C without the formation of **4a**, which is significantly

different from those reactions shown in Scheme 1 since substrate **1a** does not have a TMS group to stabilize the cationic intermediate¹³ (Table 1, entry 7). Interestingly, although we could not obtain **4a** in 80% yield when AlCl₃ was used as the catalyst (80% of **3a** was formed as shown in Scheme 2), it was found that using AlCl₃ hydrolyzed Al(III) powder¹⁴ as the catalyst [indicated as cat. Al(III) in this paper] produced **4a** in 97% yield in DCE at 70 °C exclusively (Table 1, entry 8). In toluene, **4a** was formed in 92% yield under the standard conditions (Table 1, entry 9). The examination of solvent effects revealed that DCE is the best one for the reaction to give the corresponding ring-opening product **4a** exclusively in higher yield (Table 1, entries 8–11).

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(14) We also found that the AlCl₃ used in Scheme 2 was partially hydrolyzed by water, but if using Al(OH)₃ as the catalyst, no reaction occurred along with the recovery of the starting materials **1a**. Therefore, we found that Al(III) complex [Al(OH)₂Cl]_n, which was prepared by partial hydrolysis of AlCl₃ with water, is the effective catalyst in this reaction. See the Supporting Information for the details.

(15) The crystal data of **7a** have been deposited in CCDC with the number 687327.

(12) The crystal data of **5a** have been deposited in CCDC with the number 672065.

TABLE 3. TfOH-Catalyzed Reactions of **1** with **2f–h**

entry ^a	1 (R ¹ /R ² /R ³)	2	yield (%) ^b
1	1a (C ₆ H ₅ /C ₆ H ₅ /Me)	2f	7a , 70
2	1a	2g , 	7b , 15
3	1c (C ₆ H ₅ / <i>p</i> -MeC ₆ H ₄ /Me)	2f	7c , 70
4	1e (<i>p</i> -MeC ₆ H ₄ /C ₆ H ₅ /Me)	2f	7d , 83
5	1a	2h , 	7e , 60

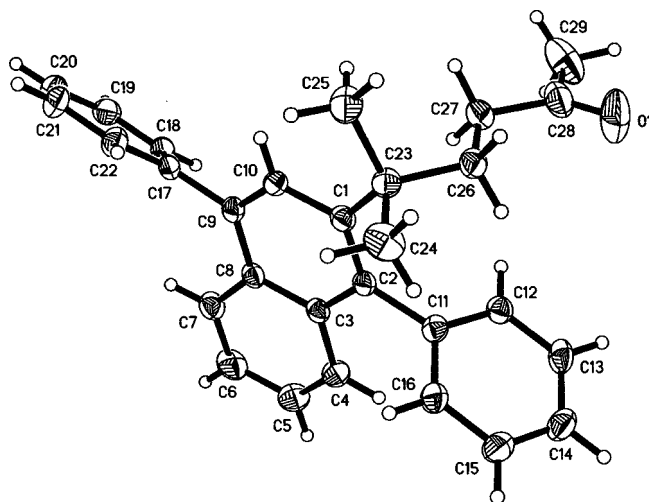
^a All reactions were carried out with **1** (0.2 mmol) and **2** (0.6 mmol) in the presence of TfOH (0.02 mmol) and DCE (2.0 mL) at 70 °C for 24 h. ^b Isolated yields.

With the best reaction conditions in hand, we next examined the cascade ring-opening and Diels–Alder cycloaddition of a variety of arylvinylcyclopropanes **1** with α,β -unsaturated substrates **2** and the results of these experiments are summarized in Table 2. The reactions of **1a** with **2a**, 1-phenyl-1*H*-pyrrole-2,5-dione **2b**, and diethyl but-2-ynedioate **2c** proceeded smoothly to give the corresponding D-A adducts **3a–c** in good to excellent yields (Table 2, entries 1–3). As for unsymmetrical dienophiles **2d–f**, regioisomeric mixtures **3** and **3'** were obtained in good to excellent yields (Table 2, entries 4–6). By using **2c** as the dienophile to examine the reactions with other arylvinylcyclopropanes **1b–f**, the corresponding D-A adducts **3b–f** were obtained in good yields under the standard conditions (Table 2, entries 7–11).

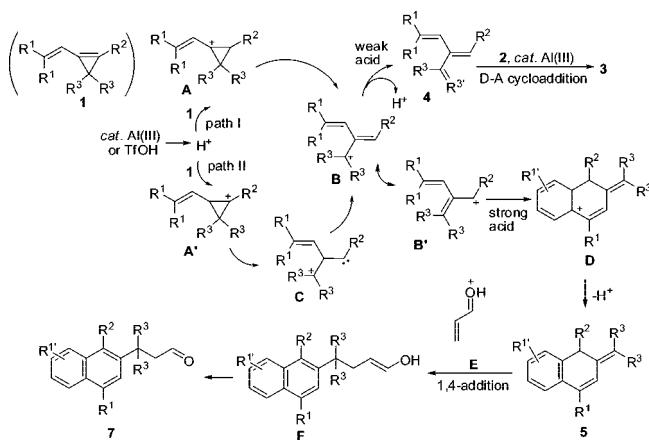
During the examination of the catalytic ability of Brønsted acids in this reaction, it was found that if the strong Brønsted acid trifluoromethanesulfonic acid (CF₃SO₃H, TfOH) was used as the catalyst, the naphthalene derivatives **7** were obtained via the cascade intramolecular Friedel–Crafts/1,4-addition process rather than the expected formal D-A cycloadducts or the ring-opening products **4**. For example, with methyl vinyl ketone **2f** and acrylaldehyde **2g** as the substrates to react with **1a** in DCE in the presence of TfOH (10 mol%), naphthalene derivatives **7a** and **7b** were obtained in 70% and 15% yield, respectively (Table 3, entries 1 and 2). Arylvinylcyclopropanes **1c** and **1e** could also react with **2f** to produce naphthalene derivatives **7c** and **7d** in moderate to good yields and since the substitutions on the aromatic rings are at the para position, only one product can be produced when the intramolecular Friedel–Craft reaction took place (Table 3, entries 3 and 4). As for cyclopent-2-enone **2h**, the corresponding naphthalene derivative **7e** was formed in 60% yield in the reaction with **1a** (Table 3, entry 5).

The structure of compound **7a** was unambiguously determined by X-ray diffraction and its CIF data are presented in the Supporting Information (Figure 2).¹⁵

A plausible mechanism for the formation of cycloadducts **3** and conjugate addition products **7** is outlined in Scheme 3. Initially, the protonation of arylvinylcyclopropane **1** by acid (Al(III) catalyst or TfOH) produces intermediate **A** or **A'** (path I or path II), which undergoes a ring-opening process to give intermediate **B** or **C**. Intermediate **C** can be converted to intermediate **B** via 1,2-proton transfer. Deprotonation of intermediate **B** produces **4**, and followed by a Diels–Alder cycloaddition with **2** catalyzed by Al(III) catalyst to give D-A adduct **3**. In the presence of strong Brønsted acid TfOH, intermediate **B** undergoes intramolecular isomerization to afford the corre-

FIGURE 2. ORTEP drawing of compound **7a**.

SCHEME 3. A Plausible Reaction Mechanism



sponding 1,2-dihydronaphthalene derivative **5** other than deprotonation,¹⁰ which reacts with protonated α,β -unsaturated ketone or aldehyde to produce intermediate **F**. Isomerization of intermediate **F** gives the corresponding naphthalene derivative **7** (Scheme 3).

It should be noted that it is impossible to prepare arylvinylcyclopropanes (both R¹ are alkyl groups or one R¹ is an alkyl group) via the corresponding arylvinylidenecyclopropanes by using our previously reported procedure since the corresponding enynes were produced exclusively (see the Supporting Information for details).¹⁰

In conclusion, we have found an interesting cascade reaction of ring-opening of arylvinylcyclopropanes followed by cyclo- or 1,4-addition with a variety of α,β -unsaturated substrates catalyzed by Brønsted acids, which affords an efficient synthetic protocol for the preparation of functionalized cyclohexene or indene derivatives. Further work directed at elucidation of the detailed mechanism of this process and the application of it to the synthesis of cyclohexene or indene containing natural products is currently in progress.

Experimental Section

General Procedure for the Preparation of Al(III) Catalyst [cat. Al(III): Al(OH)₃Cl]. Water (10 mL) was added dropwise into aluminum chloride (4.0 g, 0.2 mmol) then the solution was dried by a blast oven. This catalyst was indicated as cat. Al(III) in this paper.

Al-Catalyzed Ring-Opening Diels–Alder Reaction of Arylvinylcyclopropenes 1a with Maleic Anhydride 2a. Under an argon atmosphere, 1,1-diphenylvinylcyclopropene (64 mg, 0.2 mmol), maleic anhydride **2a** (30 mg, 0.3 mmol), and cat. Al(III) (2 mg, 0.02 mmol) were added into a Schlenk tube. The reaction mixture was stirred at 70 °C for 24 h to give **3a** in 86% yield after column chromatography.

TfOH-Catalyzed Reaction of Arylvinylcyclopropenes 1a with Methyl Vinyl Ketone 2f. Under an argon atmosphere, 1,1-diphenylvinylcyclopropene **1a** (64 mg, 0.2 mmol), methyl vinyl ketone **2f** (50 μ L, 0.6 mmol), and TfOH (2 μ L, 0.02 mmol) were added into a Schlenk tube. The reaction mixture was stirred at 70 °C for 24 h to give **7a** in 70% yield after column chromatography.

Compound **3a**: white solid, mp 179–181 °C; IR (CH₂Cl₂) ν 3028, 2903, 2849, 1855, 1782, 1711, 1489, 1443, 1219, 1109, 999, 902, 769, 698, 588 cm⁻¹; ¹H NMR (300 MHz, CDCl₃, TMS) δ 1.84 (3H, s, CH₃), 2.49 (1H, dd, J_1 = 11.4 Hz, J_2 = 19.2 Hz, CH₂), 2.88 (1H, d, J = 19.2 Hz, CH₂), 3.02 (1H, dd, J_1 = 7.2 Hz, J_2 = 9.9 Hz, CH), 3.24–3.31 (1H, m, CH), 3.66 (1H, d, J = 7.2 Hz, CH), 6.46 (1H, s, CH), 6.88–6.91 (2H, m, Ar), 7.10–7.24 (10H, m, Ar), 7.34–7.37 (3H, m, Ar); ¹³C NMR (75 MHz, CDCl₃, TMS) δ 20.6, 27.1, 37.5, 43.8, 45.7, 127.0, 127.6, 127.8, 127.9, 128.0, 128.1, 128.3, 128.6, 128.7, 129.5, 129.9, 131.5, 136.5, 140.4, 142.3, 143.8, 171.1, 173.7; MS (EI) m/z (%) 420 (43.73) [M⁺], 378 (31.55), 377 (100), 331 (26.09), 253 (28.80), 231 (69.29), 215 (26.46), 167 (37.70), 91 (38.02); HRMS (EI) calcd for C₂₉H₂₄O₃ (M⁺) requires 420.1725, found 420.1723.

Compound **7a**: white solid, mp 69–70 °C; IR (CH₂Cl₂) ν 3058, 3059, 3002, 2959, 1948, 1716, 1590, 1360, 1165, 1073, 1031, 892, 770, 730, 703 cm⁻¹; ¹H NMR (300 MHz, CDCl₃, TMS) δ 1.22 (6H, s, CH₃), 1.85 (2H, t, J = 8.1 Hz, CH₂), 2.04 (3H, s, CH₃), 2.28 (2H, J = 8.1 Hz, CH₂), 7.12–7.54 (14H, m, Ar), 7.88 (1H, d, J = 8.4 Hz, Ar); ¹³C NMR (75 MHz, CDCl₃, TMS) δ 30.0, 31.3, 37.9, 40.0, 40.1, 125.3, 125.4, 125.5, 127.2, 127.3, 127.7, 127.8, 127.9, 128.3, 129.8, 130.2, 131.2, 134.8, 137.5, 139.5, 141.0, 141.1, 141.2, 209.1; MS (EI) m/z (%) 392 (71.12) [M⁺], 393 (24.65), 322 (31.68), 321 (100), 307 (13.47), 306 (29.67), 305 (13.74), 291 (40.65), 43 (13.76); HRMS (EI) calcd for C₂₉H₂₈O (M⁺) requires 392.2140, found 392.2132.

Acknowledgement. Financial support from the Shanghai Municipal Committee of Science and Technology (06XD14005 and 08dj1400100-2), National Basic Research Program of China (973)-2009CB825300, and the National Natural Science Foundation of China (20872162, 20672127, 20732008, 20821002, and 20702013) is greatly acknowledged.

Supporting Information Available: Spectroscopic data of the compounds shown in Tables 1–3 and detailed descriptions of experimental procedures. This material is available free of charge via the Internet at <http://pubs.acs.org>.

JO802786R