Triflic imide-catalyzed cascade cycloaddition and Friedel–Crafts reaction of diarylvinylidenecyclopropanes with ethyl 5,5-diarylpenta-2,3,4-trienoate†

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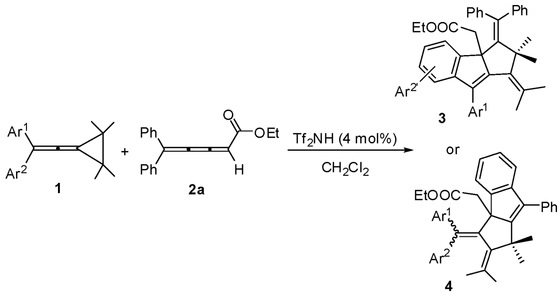
Triflic imide-catalyzed cascade cycloaddition and Friedel–Crafts reaction of diarylvinylidenecyclopropanes with ethyl 5,5-diarylpenta-2,3,4-trienoates provided a variety of novel polycyclic ester derivatives in moderate to good yields under mild conditions.

1,2,3-Butatriene derivatives have attracted much attention from organic chemists for a long time and their novel chemical properties have been extensively explored thus far. For example, it has been known that substituted 1,2,3-butatrienes could be used to construct [4]radialenes upon heating[1] or under catalysis by transition metal complexes.[2] Moreover, the cycloaddition reactions of 1,2,3-butatrienes with diazomethane,[3] 1,3-dithiol-4-ones,[4] nitrones,[5] and cyclopentadiene[6] could regioselectively provide the corresponding cycloadducts in high yields under mild conditions. Other reactions, such as oxidation,[7] reduction,[8] halogenation[9] and free-radical reactions,[10] have also been extensively studied during the last two decades. Very interestingly, the complexation of 1,2,3-butatriene with a variety of metals can enable the formation of five- and seven-membered metallacyclic alkyne complexes and double bridged lithium bisallylic structures.[11,12] Although great progress has been made on the intramolecular annulation reactions of specific substrates containing 1,2,3-butatriene,[13] the intermolecular cycloaddition of 1,2,3-butatriene with allene is unprecedented in the literature to the best of our knowledge. In this paper, we wish to report a novel cascade cycloaddition and Friedel–Crafts reaction of diarylvinylidenecyclopropanes with ethyl 5,5-diarylpenta-2,3,4-trienoates catalyzed by triflic imide (Tf_2NH, 4 mol%) to produce the polycyclic ester products **3** or **4** in good to excellent yields (eqn 1).

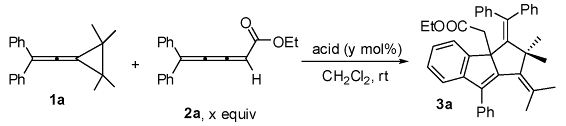
Vinylidenecyclopropanes (VDCPs) **1**, which have an allene moiety connected by a cyclopropane ring and yet are thermally stable and reactive substances in organic synthesis, are among the most attractive compounds.[14] Significant work has been conducted on using these compounds in the presence of metal catalysts, Lewis acids and Brønsted acids.[15] These results stimulated us to investigate the reaction of diarylvinylidenecyclopropanes with ethyl 5,5-diarylpenta-2,3,4-trienoates catalyzed by Brønsted acids.



(1)

The initial examination was performed by using diphenylvinylidenecyclopropane **1a** and ethyl 5,5-diphenylpenta-2,3,4-trienoate **2a** (1.0 equiv.) as the substrates in the presence of *p*-toluenesulfonic acid (10 mol%) in dichloromethane (DCM) at room temperature (25 °C). We found that the cascade cycloaddition and Friedel–Crafts reaction took place slowly to give the annulation product **3a** in 33% yield after 5 days (Table 1, entry 1). Using CF_3CO_2H as the catalyst resulted in the formation of intractable product mixtures (Table 1, entry 2). Triflic acid (TfOH) and boron fluoride etherate ($BF_3{\cdot}OEt_2$) were equally efficient catalysts for this annulation reaction, producing **3a** in 73% yield, respectively (Table 1, entries 3 and 4). We were pleased to find that triflic imide (Tf_2NH) resulted in **3a** in a higher yield (82%) under identical conditions (Table 1, entry 5). In order to accelerate the reaction and to further enhance the yield of **3a**, we attempted to elevate the temperature to 40 °C

Table 1 Reaction of diphenylvinylidenecyclopropanes with ethyl 5,5-diphenylpenta-2,3,4-trienoate: effect of the catalysts, solvents and temperatures



entry[a]	acid	x	y	temp (°C)	time	yield (%)[b] 3a
1	*p*-TSA	1.0	10	25	5 d	33
2	CF_3COOH	1.0	10	25	5 d	complex
3	TFOH	1.0	10	25	5 d	73
4	$BF_3{\cdot}OEt_2$	1.0	20	25	5 d	73
5	***Tf₂NH***	***1.0***	***4***	***25***	***5 d***	***82***
6	Tf_2NH	1.0	4	40	20 h	64
7	***Tf₂NH***	***1.2***	***4***	***40***	***5 h***	***76***
8	Tf_2NH	1.5	4	40	5 h	77
9[c]	Tf_2NH	1.5	4	80	5 h	50

[a] Reaction conditions: VDCP **1a** (0.18 mmol) and **2a** (x equiv.) were dissolved in CH_2Cl_2 (2 ml). Acid (y mol%) was added then the mixtures were stirred for different times at rt or under reflux. [b] Isolated yield. [c] 1,2-Dichloroethane was used as the solvent.

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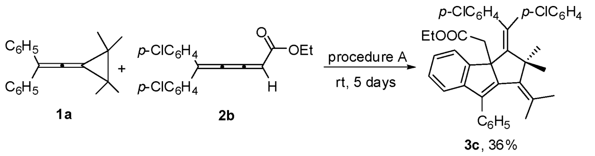
† Electronic supplementary information (ESI) available: Detailed description of experimental procedures, full characterization of new compounds **3a–3c**, **3f–3i** and **4c–4e** shown in Tables 1,2 and eqn 2, X-ray crystal analysis data of **3a**, **4c** and **4e** (CIF). CCDC reference numbers 689419, 700829 and 719328. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b903965a

and found that the reaction can be completed within 20 hours to give **3a** in 64% yield (Table 1, entry 6). Using 1.2 and 1.5 equivalent of ethyl 5,5-diphenylpenta-2,3,4-trienoate **2a** in the reaction provided **3a** in 76% and 77% yield within 5 hours at 40 °C, respectively (Table 1, entries 7 and 8). Raising the reaction temperature to 80 °C in 1,2-dichloroethane (DCE) led to **3a** in 50% yield within 5 hours (Table 1, entry 9). The structure of **3a** has been further confirmed by X-ray diffraction and its CIF data have been presented in the ESI.†[16]

Based on the above modifications, we found two general procedures: procedure **A**, in which the reaction is performed at 25 °C in dichloromethane and procedure **B** in which temperature was raised to 40 °C in dichloromethane. In the above two procedures, **1a** (1.0 equiv.) and **2a** (1.2 equiv.) were found necessary.

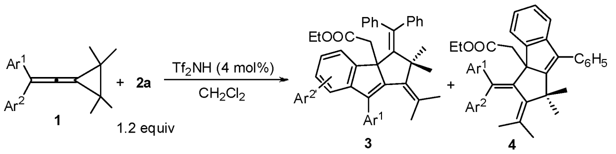
With these optimal conditions identified, we next examined the scope of this interesting cascade annulation reaction and the results of these experiments are summarized in Table 2. Using diarylvinylidenecyclopropane **1b** bearing moderately electron-donating methyl groups on the benzene rings afforded the corresponding annulation product **3b** in 38% yield with procedure **A** and in 40% yield within 10 hours with procedure **B** (Table 2, entries 1 and 2). As for diarylvinylidenecyclopropanes **1c–1e** bearing electron-withdrawing groups on both of their benzene rings, the annulation reactions proceeded smoothly to provide the corresponding polycyclic ester products **4** in moderate to good yields within 4–5 days at 25 °C or within several hours at 40 °C (Table 2, entries 3–7). Unexpectedly, for the substrate **1e** bearing an *ortho*-chloro atom on one benzene ring and a *para*-chloro atom on the other, the corresponding annulation product **4e** was obtained exclusively in the *E*-configuration in 34% yield (Table 2, entry 7). The structures of **4c** and **4e** were further confirmed by X-ray diffraction and their CIF data are presented in the ESI.†[17,18] Moreover, this annulation reaction appears to be of good regioselectivity. As for the unsymmetrical diarylvinylidenecyclopropanes **1f**, **1g** and **1i** bearing electron-withdrawing groups on one of the benzene rings, the corresponding annulation products **3f**, **3g** and **3i** were obtained in moderate to good yields, suggesting that the intramolecular Friedel–Crafts reactions occurred on the electron-rich aromatic rings of diarylvinylidenecyclopropanes **1** exclusively (Table 2, entries 8–11 and 14). Only in the reaction of **1h** with **2a** was **3h** produced, along with some of product **4h** (Table 2, entries 12 and 13). Generally, procedure **B** facilitates the production of **4c–4d** and **3f–3h** (Table 2, entries 3 and 4, 5 and 6, 8 and 9, 10 and 11, 12 and 13). In the case of ethyl 5,5-diarylpenta-2,3,4-trienoate **2b** bearing a moderately electron-withdrawing chloro atom at the *para*-position of the benzene ring, the corresponding annulation derivative **3c** was obtained in 36% yield under the standard procedure **A** (eqn 2).



(2)

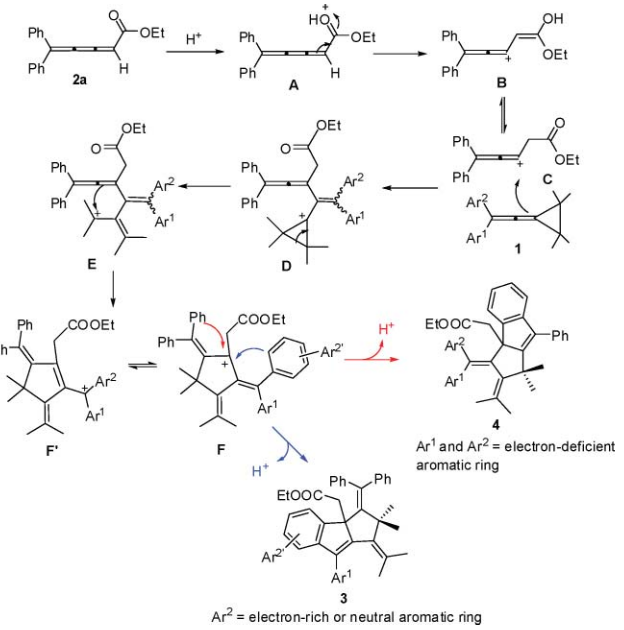
A plausible mechanism of this reaction is proposed in Scheme 1. Firstly, Brønsted acid Tf_2NH activates 5,5-diphenylpenta-2,3,4-trienoate **2a** producing intermediate **A**, which can isomerize to the carbocationic intermediate **C** *via* an enolate intermediate **B**. Subsequently, diarylvinylidenecyclopropane **1** undergoes a nucleophilic attack on intermediate **C** to generate intermediate **D**, which produces intermediate **E** *via* the ring opening of

Table 2 Tf_2NH-catalyzed cascade cycloaddition and Friedel–Crafts reactions of diarylvinylidenecyclopropanes **1** with ethyl 5,5 diphenylpenta-2,3,4-trienoate **2a**



				yield(%)[b]	yield(%)[b]
entry[a]	Ar^1/Ar^2	procedure	time	3	4
1	$p\text{-}CH_3C_6H_4/p\text{-}CH_3C_6H_4$, **1b**	A	5 d	**3b**, 38	
2		B	10 h	**3b**, 40	
3	$p\text{-}ClC_6H_4/p\text{-}ClC_6H_4$, **1c**	A	4 d		**4c**, 58
4		B	4 h		**4c**, **84**
5	$p\text{-}FC_6H_4/p\text{-}FC_6H_4$, **1d**	A	5 d		**4d**, 63
6		B	9 h		**4d**, 80
7	$o\text{-}ClC_6H_4/p\text{-}ClC_6H_4$, **1e**	A	12 h		**4e**, 34[c]
8	$p\text{-}ClC_6H_4/C_6H_5$, **1f**	B	5 d	**3f**, 50	
9		A	6 h	**3f**, 65	
10	$m,p\text{-}Cl_2C_6H_3/C_6H_5$, **1g**	B	5 d	**3g**, 54	
11		A	9 h	**3g**, 58	
12	$p\text{-}FC_6H_4/C_6H_5$, **1h**	B	5 d	**3h**, 68[d]	
13		A	6 h	**3h**, 68[e]	
14	$m,p\text{-}F_2C_6H_3/C_6H_5$, **1i**	B	12 h	**3i**, 42	

[a] Conditions A: VDCP **1** (0.18 mmol) and **2a** (0.216 mmol, 1.2 equiv.) were dissolved in CH_2Cl_2 (2.0 ml). Tf_2NH (2.0 mg, 4.0 mol%) was added and then the mixtures were stirred for several days at rt; conditions B: VDCP **1** (0.18 mmol) and **2a** (0.216 mmol, 1.2 equiv.) were stirred for several hours at 40 °C. [b] Isolated yield. [c] This compound was formed exclusively in the E-configuration on the basis of the X-ray crystal structure (ESI).† [d] This contains some of product **4** which can not be separated from the major product by flash chromatography on silica get and the ratio of **3h**:**4h** = 3:1 was determined by ^1H NMR spectroscopic data. [e] A ratio of **3h**:**4h** = 10:1 was determined by ^1H NMR spectroscopic data.



Scheme 1 Plausible mechanism of the annulation reactions.

cyclopropane. An intramolecular nucleophilic attack generates intermediate **F**, which should be in an equilibrium with intermediate **F′** *via* allylic rearrangement. It is understandable that the intramolecular Friedel–Crafts reaction is favored for the electron-rich aromatic rings of intermediate **F**. Thus, there are two pathways for the intramolecular Friedel–Crafts reaction. For the diarylvinylidenecyclopropanes **1** bearing moderately electron-donating groups on the benzene rings or neutral benzene ring (for example **1a** and **1b**), the intramolecular Friedel–Crafts reaction occurs on the aromatic ring of diarylvinylidenecyclopropanes **1** to give the products **3** since Ar[1] and Ar[2] are in a larger conjugate system which can stabilize the cationic intermediate generated in the Friedel–Crafts reaction to consequently produce the product **3** in a highly stereo- and regioselective manner (Table 1, entries 1, 2 and 8–14 of Table 2, eqn 2). On the other hand, for the diarylvinylidenecyclopropanes **1** bearing electron-withdrawing groups on both of the benzene rings, the intramolecular Friedel–Crafts reaction occurs on the aromatic ring of 5,5-diphenylpenta-2,3,4-trienoate **2a** to generate products **4** (Table 2, entries 3–7) (Scheme 1).

In conclusion, we have developed novel synthetic methods for the cascade cycloaddition and Friedel–Crafts reactions of diarylvinylidenecyclopropanes **1** with ethyl 5,5-diarylpenta-2,3,4-trienoates **2** to provide a variety of polycyclic esters **3** and **4** in moderate to good yields catalyzed by triflic imide (Tf_2NH). This work is particularly useful to research on the reactivity of 1,2,3-butatriene containing derivatives. Efforts are in progress to elucidate further mechanistic details of these reactions and to understand their scope and limitations.

Acknowledgements

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16 The crystal data of **3a** have been deposited in the CCDC with number 689419 (see the ESI†).

17 The crystal data of **4c** have been deposited in the CCDC with number 700829 (see the ESI†).

18 The crystal data of **4e** have been deposited in the CCDC with number 719328 (see the ESI†).