

Carbocation Lewis Acid Catalyzed Diels-Alder Reactions of Anthracene Derivatives

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(5) Supporting Information

ABSTRACT: The carbocation salt [Ph₃C][BArF] has been identified as a viable Lewis acid catalyst for the Diels–Alder reactions between anthracene derivatives and unsaturated carbonyl compounds with good selectivity and high efficiency.



ue to the high energy barrier on dearomatization, intermolecular Diels-Alder reactions of the arene ring are generally difficult to achieve and require harsh conditions with prolonged heating or UV irradiation.¹ Anthracene is an exception and is amenable to both thermal² and photochemical³ cycloadditions, since the initial disclosure by Diels and Alder in 1931.^{2a} The resulted anthracene Diels-Alder adducts are of significant interest as organic functional materials.^{4,5} To address the synthetic need, catalytic strategies have been actively pursued for an anthracene Diels-Alder reaction.⁶⁻⁹ In Lewis base catalysis based on HOMO activation, specific anthracene derivatives such as anthracen-9-ones and 2-anthracen-9-yl acetaldehydes are activated to react with electro-deficient dienophiles in a highly stereocontrolled manner.⁹ Lewis acid catalysis has also been widely reported to promote the Diels-Alder reaction of 9-substituted anthracenes via LUMO activation of the dienophiles (Scheme 1A).⁷ However, stoichiometric or excess Lewis acid catalysts were normally required, and the reactions were limited in the scopes of both anthracenes and dienophiles.

Since the discovery of the first trityl cation in 1901,¹⁰ stable carbocations have been explored as organic Lewis acid catalysts in organic synthesis.^{11,12} However, the application of carbocation Lewis acid catalysis is still rather limited in terms of the reaction scopes and catalytic efficiency. Recently, we have developed latent carbocation with chiral trityl phosphate for Lewis acid catalysis in the Friedel–Crafts reaction, HDA reaction, and carbonyl-ene reaction.¹³ Herein, we report that tritylium salt [Ph₃C][BArF], in situ generated by Ph₃CBr and NaBArF, could effectively promote a Diels–Alder reaction with anthracenes with broad scopes under mild conditions (Scheme 1B).

The model reaction of anthracenes 1a and β , γ -unsaturated α keto ester 2a was investigated with different Lewis acid catalysts (Table 1). We were delighted to find that Diels–Alder product 3a was obtained in 60% yield as a single stereoisomer when 10% Ph₃CClO₄ was used as the catalyst in toluene at 50 °C (Table 1, entry 2). No reaction was observed in the absence of any catalyst

Scheme 1. Diels-Alder Reaction of Anthracenes



(Table 1, entry 1). A survey of different carbocation Lewis acid was then followed, and the best results were obtained with tritylium salt [Ph₃C][BArF] *in situ* generated by Ph₃CBr (1 equiv) and NaBArF (1 equiv) in 67% yield (Table 1, entry 6 vs entries 2–5). We found that Ph₃CBr or NaBArF itself has no or very weak activity (Table 1, entries 4 and 7). Further improvement on the reaction activity could be achieved by conducting the reaction in DCE (Table 1, entries 6, 8–13). In addition, the catalyst loading of [Ph₃C][BArF] can be reduced from 10 mol % to 5 mol % while maintaining a similar performance (Table 1, entry 14). Further lowering the loading to 2 mol % led to serious reduction of yield (60% yield, Table 1, entry 15). The reaction at 50 °C was preferred, and conducting the reaction at ambient temperature gave only 34% yield (Table 1, entry 16).

Other metal Lewis acid, such as $InBr_3$, $FeBr_3$, $AlCl_3$, and BF_3 · OEt₂, could catalyze the reactions, albeit with lower productivity

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Table 1. Optimization of the Reaction Conditions^a



13	Ph ₃ CBr/NaBArF	CH_3CN	trace
14 ^c	Ph ₃ CBr/NaBArF	DCE	90
15 ^d	Ph ₃ CBr/NaBArF	DCE	60
16 ^{<i>c</i>,<i>e</i>}	Ph ₃ CBr/NaBArF	DCE	34
17 ^c	InBr ₃	DCE	65
18 ^c	FeBr ₃	DCE	77
19 ^c	AlCl ₃	DCE	16
20 ^c	$BF_3 \bullet OEt_2$	DCE	46
21 ^c	$HBF_4 \bullet OEt_2$	DCE	NR
'General co	nditions: 1a (0.2 mmol)	, 2a (0.1 mmol),	and catalyst (10
nol %) in solvent (0.2 M) at 50 °C, for 24 h. ^b Determined by 1 H			
NMR analy	sis with an internal sta	ndard, 1,3,5-trmet	hyloxylbenzene.
Ph_2CBr (5 mol %) and NaBArF (5 mol %). $^{d}Ph_2CBr$ (2 mol %) and			

NMR analysis with an internal standard, 1,3,5-trmethyloxylbenzene. ^cPh₃CBr (5 mol %) and NaBArF (5 mol %). ^dPh₃CBr (2 mol %) and NaBArF (2 mol %). ^eAt room temperature. NR = no reaction. BArF = $[3,5-(CF_3)_2C_6H_3]_4B$. DCM = dichloromethane. DCE = 1,2-dichloroethane.

(Table 1, entries 17–20). It was also noted that a retro-Diels– Alder process also existed in an non-neglectable portion in metal Lewis acid catalysis due to the strong aromatization tendency of the Diels–Alder adducts. In control experiments, when the purified Diels–Alder adduct **3a** was treated with Lewis acid catalyst at room temperature, significant retro reaction (15–22% conversion) was observed for all the metal Lewis acids, but not with the carbocation Lewis acid (Scheme 2), highlighting the

Scheme 2. Retro-Diels-Alder Reaction in the Presence of Lewis Acid



unique performance of carbocation catalysis. Steric effect would be a possible reason to account for the irreversible nature of carbon cation catalysis at room temperature. In addition, when Brønsted acid such as $HBF_4 \cdot OEt_2$ was used, the reaction did not work (Table 1, entry 21) at all, excluding the possibility of free acid catalysis.

With the optimized reactions in hand, the substrate scope of $[Ph_3C][BArF]$ catalysis was investigated. The results are

presented in Scheme 3. A number of β , γ -unsaturated α -keto esters 2 were examined, and aromatic keto esters bearing either

Scheme 3. Substrate Scope in Diels–Alder Reaction of Anthracenes 1 and β , γ -Unsaturated α -Keto Esters 2^{*a*}



^{*a*}General conditions: **1** (0.6 mmol), **2** (0.3 mmol), Ph₃CBr (5 mol %), and NaBArF (5 mol %) in DCE (0.2 M) at 50 °C, for 24 h. ^{*b*}One mmol scale of **2a**. Diastereoselectivity was determined by ¹H NMR.

an electron-withdrawing group (F, Cl, Br, Ph) or electrondonating group (CH_3) at the ortho- or meta-position of the phenyl group can be equally applied with high yields (Scheme 3, 3a-e, 3g-k), while a strong electron-withdrawing group (CF₃) gave a relatively lower yield (Scheme 3, 3f). An ortho-fluoride substituted group also worked well, providing a much better yield than its chloride- and bromide-substituted counterparts (Scheme 3, 31 vs 3m and 3n). Gratifyingly, dichloride and naphthylsubstituted groups could also react with anthracene 1a, giving 76% and 69% yields, respectively. Different ester groups (Et, i-Pr) on α -keto ester were tolerated to give the Diels-Alder adducts in excellent yields (Scheme 3, 3q and 3r). In addition, 9,10-dimethylanthracene has also been examined in the reaction, providing 99% yields of the Diels-Alder product 3s. When 9methylanthracene was used, two regioisomeric 3t and 3t' (7.7:1) were obtained in 86% yield at 50 °C, while a single regioisomer 3t' was obtained in 99% yield at room temperature. When 3t' was treated with trityl catalyst at 50 $^{\circ}$ C, its transformation to 3t was clearly observed accompanying the retro-Diel-Alder process. This observation indicates 3t' is kinetically favored, while **3t** is thermodynamically preferred.^{7e} In addition, 9-bromoanthracene could not react at all as a result of its electrondeficient nature.

The reactions could also be applied to other α,β -unsaturated carbonyl compounds 4 (Scheme 3). For Z-configured α,β -enones such as cyclopent-2-enone and cyclohex-2-enone, moderate yields of the Diels–Alder products were obtained (Scheme 4, 5a and 5b). Methyl vinyl ketone and methyl styryl





^{*a*}General conditions: 1 (0.6 mmol), 4 (0.3 mmol), Ph₃CBr (5 mol %), and NaBArF (5 mol %) in DCE (0.2 M) at 50 °C, for 24 h. ^{*b*}With InBr₃ (5 mol %). Diastereoselectivity was determined by 2D-NOESY.

ketones worked well in the reactions (Scheme 4, 5c–f). Heterocycle, e.g., thiophene, can also be incorporated to deliver the Diels–Alder adduct 5g in 79% yield (Scheme 4, 5g). In addition, chalcones bearing either an electron-withdrawing or electron-donating group can be equally applied to give the desired Diels–Alder adducts in up to 99% yields (Scheme 4, 5h–k).¹⁴ In contrast, the use of a typical metal Lewis acid such as InBr₃ gave only 36% yield under otherwise identical conditions. Moreover, α,β -unsaturated aldehyde, such as (*E*)-but-2-enal, also reacted smoothly with anthracene 1a to give the expected adduct in 86% yield (Scheme 4, 5l). Unfortunately, the reaction did not work with acrylate and acrylonitrile.

Furthermore, we also examined the reactions with pentacene **6** (Scheme 5). To our delight, β , γ -unsaturated α -keto esters, methyl styryl ketone, and α , β -unsaturated aldehyde were tolerated to give the Diels–Alder adducts in good to excellent yields (Scheme 5, 7**a**–**n**).

A proposed reaction pathway of the Diels–Alder is shown in Scheme 6. The unsaturated carbonyl compounds were activated by a trityl cation to form the intermediate **A**, thus lowering the LUMO of dienophile and enabling the Diels–Alder reaction with anthracene **2a** to give the final product after catalyst release. The capability of a trityl cation in differentiating the starting

Scheme 5. Substrate Scope in Diels–Alder Reaction of Pentacene 6^a



^{*a*}General conditions: pentacene **6** (0.6 mmol), **2** or **4** (0.3 mmol), Ph₃CBr (5 mol %), and NaBArF (5 mol %) in DCE (0.2 M) at 50 °C, for 24 h. Diastereoselectivity was determined by ¹H NMR.





enone/enal and the product via coordination (A vs B) makes the retro-Diels–Alder process unfavorable, thus facilitating the forward reactions.

In summary, we have developed a carbocation Lewis acidcatalyzed Diels—Alder reaction of anthracene derivatives and a number of unsaturated carbonyl compounds under mild conditions with high to excellent yields. Further studies are currently underway to disclose the mechanistic details and to develop asymmetric carbocation catalysis of anthracene Diels— Alder reactions.

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ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.8b00619.

Experimental details and spectroscopic data for all new compounds (PDF)

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Notes

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(14) When a mixture of *E*- and *Z*-chalcone **4a** (3.3:1) was used, a single diastereoisomer **5h** was obtained in 99% yield. In a control experiment, *Z*-chalcone **4a** was completely transformed into *E*-chalcone **4a** in 1 h when treated with trityl catalyst at 50 °C.