JOC The Journal of Organic Chemistry

Article

Fe(II)/Fe(III)-catalyzed Intramolecular Didehydro-Diels-Alder Reaction of Styrene-ynes

Hyeon Jin Mun, Eun Young Seong, Kwang-Hyun Ahn, and Eun Joo Kang

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.7b02672 • Publication Date (Web): 20 Dec 2017

Just Accepted

ACS Publications

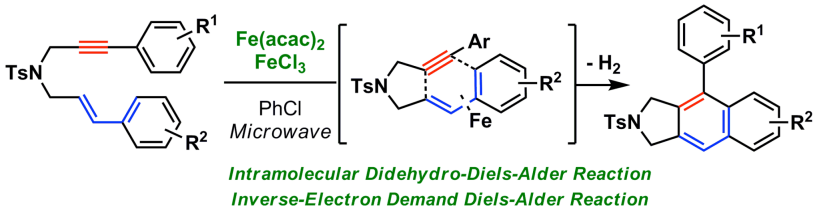
The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

Fe(II)/Fe(III)-catalyzed Intramolecular Didehydro-Diels-Alder Reaction of Styrene-ynes

Hyeon Jin Mun, Eun Young Seong, Kwang-Hyun Ahn*, and Eun Joo Kang*

Department of Applied Chemistry, Kyung Hee University, Yongin 17104, Korea

*E-mail: khahn@khu.ac.kr, ejkang24@khu.ac.kr



ABSTRACT: The intramolecular didehydro-Diels-Alder reaction of styrene-ynes was catalyzed by Fe(II) and Fe(III) to produce various naphthalene derivatives under microwave heating conditions. Mechanistic calculations found that the Fe(II) catalyst activates the styrenyl diene in an inverse-electron-demand Diels-Alder reaction, and the consecutive dehydrogenation reaction can be promoted by either Fe(II)-catalyzed direct dehydrogenation or an Fe(III)-catalyzed rearomatization/dehydrogenation pathway.

INTRODUCTION

The Diels−Alder reaction is one of the most useful cycloaddition reactions to construct six-membered ring compounds.[1] The Diels−Alder reaction normally combines the 4π-component of a conjugated diene with the 2π-component of a dienophile to synthesize cyclohexenes. However the diverse variants in the oxidation levels of the reactant pairs and products have been investigated for venerable [4+2] cycloadditions, which effectively accompanied with the consecutive transformations such as dehydrogenation, hydrogen atom shift and further C-X bond formation of highly reactive cycloadducts. Among those strategies, having one of the C-C double bonds participating in the Diels-Alder reaction replaced by a triple bond, the reaction of the diene with a dienophilic alkyne can afford

cyclohexadiene, which process has been called the didehydro-Diels-Alder reaction. Another involvement of alkyne; the combination of 1,3-enyne as the 4π-component with alkyne results cyclic allene adduct, which rapidly rearranges via a [1,5] hydrogen shift to benzene in tetradehydro-Diels-Alder reaction.[2] The cycloaddition between 1,3-diyne and diynophilic alkyne generates a highly oxidized and constrained benzyne via hexadehydro-Diels-Alder reaction, and this versatile intermediate participates in the trapping sequence to develop the structural complexity.[2d-f]

In particular, the didehydro-Diels-Alder reaction of styrenes with alkynes is an efficient strategy to promote further dehydrogenation (aromatization) resulting a naphthalene core without additional oxidants.[3] However, utilizing styrene as the 4π-component has been considered challenging, due to the unfavored dearomatization during the reaction and the competing polymerization and [2+2] cycloaddition reactions.[3a,4] These problems necessitate the use of harsh reaction conditions or highly reactive dienophiles, and under these conditions the cycloadducts are sometimes more reactive as dienes than their styrene precursors leading to further Diels-Alder reactions. Intramolecular cycloaddition system of styrene-ynes and various strategies for increasing the reactivities of the styrene or alkyne have been developed for the efficient and effective synthesis of polycyclic aromatic compounds.[5] Most strategies involve the preparation of electron-deficient alkyne dienophiles that have an electron-withdrawing group on the alkyne terminus or within the tether,[6] or utilize a Lewis acid ($ZnCl_2$) to coordinate with the carbonyl oxygen of the alkynone decreasing the energy of the LUMO of the dienophile, accelerating the intermolecular Diels−Alder reaction.[7] Alternatively, HOMO activation of the diene by the in-situ generation of a formal trienamine species was reported by Chen in the asymmetric dearomatic Diels−Alder reaction.[8] In the inverse-electron-demand Diels−Alder (iEDDA) reaction, 1,3-heterodienes are triggered to undergo cycloaddition by Lewis acid ($CuBr_2$, Cu_2O) coordination increasing the electron-deficiency.[9] These available methods, however, need for an additional functional group to accelerate reactivities of the Diels-Alder and consecutive reaction, and more versatile approach was considered necessary. Inspired by our recent studies on Fe-catalyzed C-C multiple bond (allene and diene) activation,[10] we envisaged that the relatively

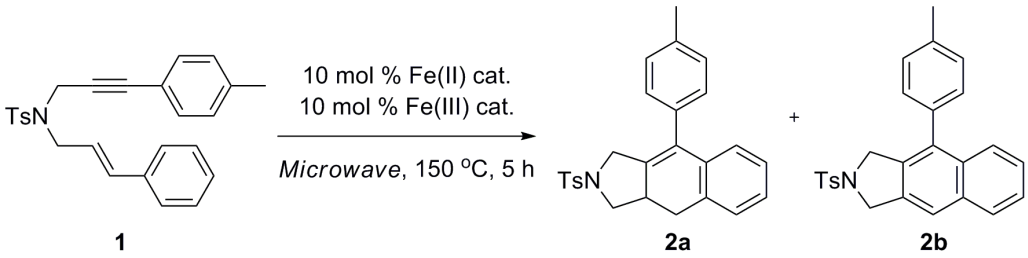
unactivated styrene-ynes could participate in didehydro-Diels-Alder reaction. Thus, polycyclic aromatic frameworks could be prepared using the π activation ability of the green and non-toxic iron catalysts. A thorough understanding of the mechanism as well as the role of the Fe catalyst as determined by theoretical studies is provided herein.

RESULTS AND DISCUSSION

Initial experiments were directed towards the didehydro-Diels-Alder reaction of styrene-yne substrate **1**. Upon irradiating under microwave reactor (150 W) and maintain the reaction temperature at 150 ^{o}C for 5 h, the product mixture of dihydronaphthalene **2a** and the desired naphthalene **2b** was observed in 29% yield (Table 1, entry 1). Using iron(II) catalysts such as $FeCl_2$ and $Fe(acac)_2$, higher yields were obtained with decreased selectivity between the two products **2a** and **2b** (Table 1, entries 2-4). Encouraged by the increased reactivity afforded by the Fe(II) catalysts, we turned to the optimization of the solvent and the use of an Fe(III) catalyst. Chlorobenzene (PhCl) provided the best yield (Table 1, entries 4-7), but various Fe(III) catalysts showed no dramatic influence on the yield or product distribution (Table 1, entries 8-10).[11] In an attempt to promote full conversion to **2b**, and to check the role of the Fe(II) and Fe(III) catalysts, the product mixture of **2a** and **2b** was subjected to further reaction (Table 2). Subjecting the product mixture (**2a**:**2b**; around 50:50) to either 50 mol % of $Fe(acac)_2$ or 20 mol % of $FeCl_3$ showed that the Fe(III) catalyst effectively promoted the dehydrogenation reaction of **2a** affording an 8:92 ratio of **2a**:**2b** (Table 2, entries 1-2). When utilizing isoprene or diphenyl ethylene as the hydrogen acceptor with Fe complex, a slightly higher ratio of **2b** was observed, which is difficult to conclude that the hydrogen acceptor has affected (Table 2, entries 3-5).[12] As in the Brummond's report on the intramolecular didehydro-Diels-Alder reaction of styrene-ynes containing heteroatom tethers,[6a] the dihydronaphthalene could not be oxidized to the corresponding naphthalene by dichlorodicyanobenzoquinone (DDQ), or O_2, moreover, several reactions with DDQ under vigorous conditions or longer reaction time gave the decomposition of the naphthalene product (Table 2, entries 6-9).[5c,13] The use of hypervalent iodine(III) reagent,

PhI(OTs)OH (hydroxyl(tosyloxy)iodobenzene, HTIB, Koser reagent) didn't give an acceptable result, even with the sequential treatment of oxidant at the end of the Diels-Alder reaction (Table 2, entry 10).[13f]

Consequently, further optimization of the reaction conditions focused on using a dual catalytic system of Fe(II) and Fe(III) to efficiently promote this didehydro-Diels-Alder reaction. Investigation of several Fe(III) catalysts, catalyst loading, and heating methods (Table 1, entries 11-17) revealed that 10 mol % of each $Fe(acac)_2$ and $FeCl_3$ under microwave irradiation afforded the highest efficiency and selectivity for naphthalene **2b** synthesis (Table 1, entry 12).

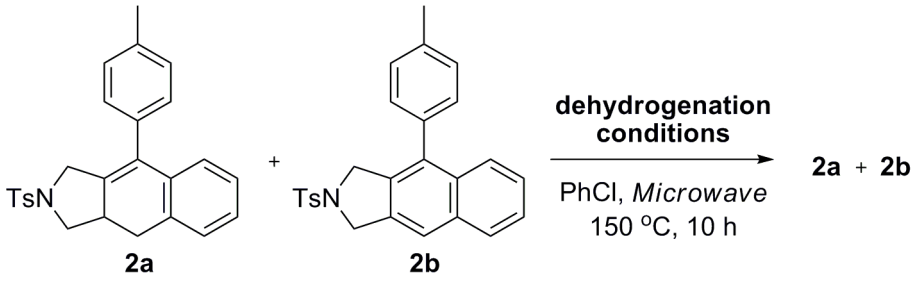


1 **2a** **2b**

entry	Fe(II) cat.	Fe(III) cat.	solvent	yield (%)	[**2a** : **2b**]
1	-	-	PhCl	29	14 : 86
2	$FeCl_2$	-	PhCl	74	55 : 45
3	$FeCl_2\ 4H_2O$	-	PhCl	66	52 : 48
4	$Fe(acac)_2$	-	PhCl	79	59 : 41
5	$Fe(acac)_2$	-	toluene	71	49 : 51
6	$Fe(acac)_2$	-	*o* - xylene	48	23 : 77
7	$Fe(acac)_2$	-	benzene	42	57 : 43
8	-	$Fe(OTs)_3$	PhCl	54	72 : 28
9	-	$FeCl_3$	PhCl	66	62 : 38
10	-	$FeBr_3$	PhCl	58	31 : 69
11	$Fe(acac)_2$	$Fe(OTs)_3$	PhCl	47	13 : 87
12	$Fe(acac)_2$	$FeCl_3$	PhCl	74	22 : 78
13[a]	$Fe(acac)_2$	$FeCl_3$	PhCl	56	5 : 95
14[b]	$Fe(acac)_2$	$FeCl_3$	PhCl	71	18 : 82
15[c]	$Fe(acac)_2$	$FeCl_3$	PhCl	59	12 : 88
16	$Fe(acac)_2$	$FeBr_3$	PhCl	50	- : 100
17[a]	$Fe(acac)_2$	$FeBr_3$	PhCl	63	41 : 59

[a] 5 mol % of Fe(III) catalyst, [b] 20 mol % of Fe(III) catalyst, [c] reflux for 16 h

Table 1. Optimization of didehydro-Diels-Alder reaction conditions



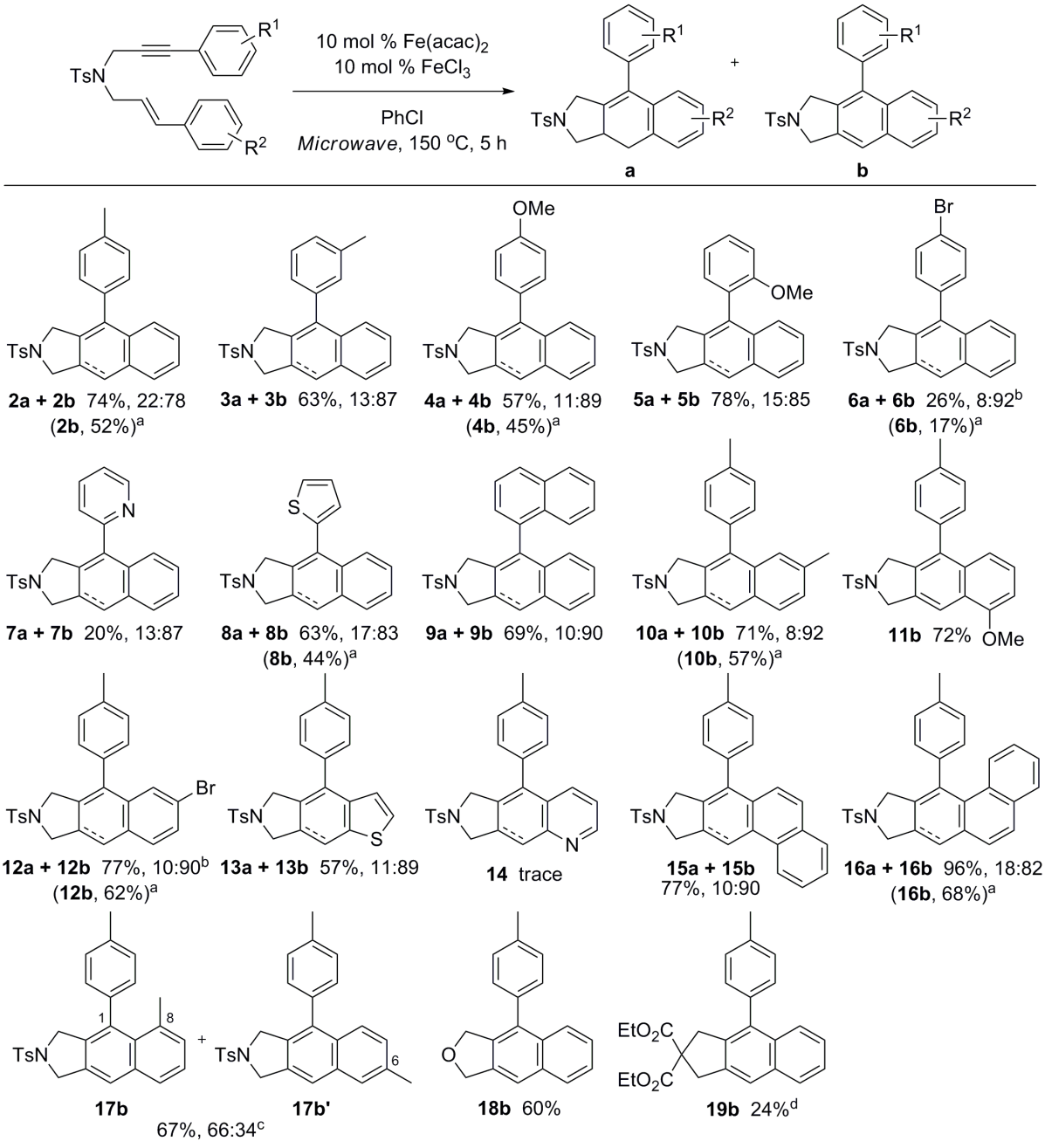
entry	initial, **2a** : **2b**	conditions	final, **2a** : **2b**
1	50 : 50	50 mol % $Fe(acac)_2$	41 : 59
2	41 : 59	20 mol % $FeCl_3$	8 : 92
3	41 : 59	50 mol % $Fe(acac)_2$, 1 equiv. isoprene	32 : 68
4	48 : 52	50 mol % $Fe(acac)_2$, 1 equiv. diphenyl ethylene	37 : 63
5	57 : 43	20 mol % $FeCl_3$, 1 equiv. isoprene	52 : 48
6	50 : 50	1 equiv. DDQ[a]	decomposed
7	47 : 53	2.1 equiv. DDQ[b]	80 : 20[c]
8	44 : 56	10 mol % DDQ, 10 mol % $NaNO_2$, O_2 (1 atm)[d]	47 : 53
9	38 : 62	5 mol % $Pd(TFA)_2$, O_2 (1 atm)[e]	30 : 70
10	61 : 39	1 equiv. HTIB[f]	46 : 54

[a] reflux, 24 h, [b] reflux, 12 h, [c] 45% isolated yield, [d] toluene, reflux, 12 h, [e] acetone, r.t. 12 h, [f] CH_2Cl_2, r.t. 5 h

Table 2. Dehydrogenation experiments

The styrene-yne substrates were reacted under optimized conditions, and the results are summarized in Table 3. Substrates containing electron-donating groups (CH_3 and OCH_3) on the alkynyl benzene ring produced the desired products **2-5** in good yield. In contrast, the yields of products **6** containing a bromo substituent, and **7** containing a pyridine, were considerably lower, which is thought to be the reduced reactivity of electron-deficient alkyne moiety. Heteroaromatic and fused aromatic ring-containing products **8-9** were obtained in good yield. Additionally, *p*-methyl and *o*-methoxy substituents on styrenyl benzene rings have been introduced, resulting their respective products. Compound **11b** was exclusively produced without the corresponding dihydronaphthalene, and the corresponding dihydronaphthalene product were not detectable by ^{1}H-NMR analysis of the

crude reaction mixture. This result observed in the case of **11b** was understood by the slightly more congested structure due to *ortho*-methoxy substituents, resulting to promote the consecutive dehydrogenation process. In contrast with the reaction forming product **6**, the bromo substituted styrenyl benzene ring did not affect the formation of **12**, which suggests that the LUMO of the styrene interacts with the HOMO of the alkyne in an iEDDA reaction.[2d,9a,14] Furthermore, the Br atom was maintained, providing a handle for further manipulation to produce a range of useful compounds. The pyridine moiety seemed to deactivate the Fe catalysts through coordination, however thiophene and naphthalene substituents afforded benzothiophene **13** and phenanthrene compounds **15-16** in great yields and regioselectivities. Reaction of *m*-methyl substituted styrene-yne gave a 1.9:1 mixture of the 8-methyl and 6-methylnaphthalenes, **17b** and **17b′** in 67% yield. Structural changes in the tether were also examined; the precursor having an ether tether produced only one product **18b** in 60% yield, and the precursor with an all-carbon tether possessing a diester moiety afforded **19b** in 24% yield with the recovery of starting material. The preferred formation of the naphthalene products (**18b** and **19b**) may be explained by the tendency to gradually decrease the H-H distance in the boat conformation of didehydro-Diels-Alder cycloadduct, depending on the element of tether.[6c]

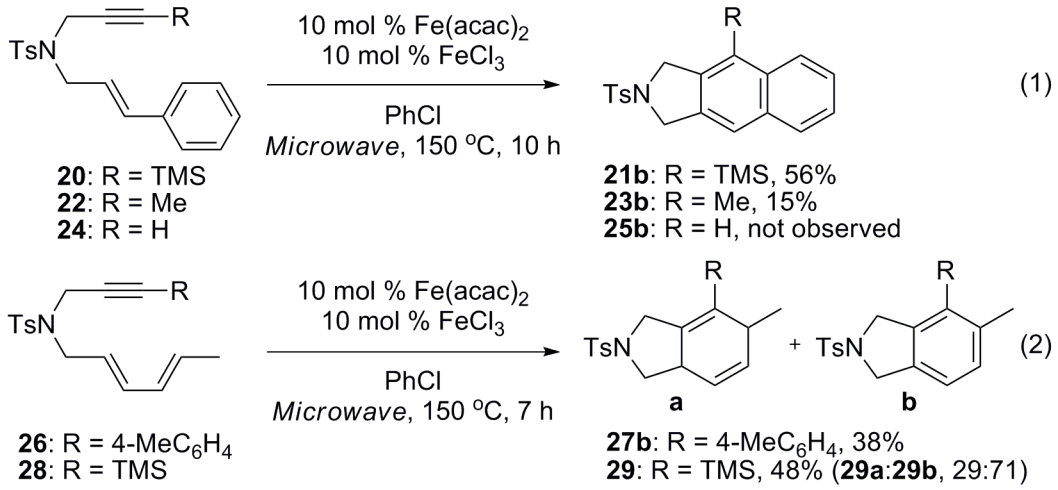


[a]isolated yield of naphthalene compound after recrystallization, [b]reaction for 7 h, [c]mixture of regioisomers (**17b** + **17b'**) [d]determined by ^{1}H NMR spectra of mixture with sm and **19b**

Table 3. Substrate scope of the didehydro-Diels-Alder reaction

Next, other functional groups on the terminus of the alkyne were investigated in this intramolecular didehydro-Diels-Alder reaction (Scheme 1). Substitution of the alkyne with TMS provided naphthalene **21b** in 56% yield after a prolonged reaction time, and the CH_3 and H substituents in **22** and **24** impeded the reaction considerably. Matsubara has also reported the dehydrogenation reaction

when a silyl group is utilized as the bulky trimethylsilyl group can induce steric repulsion bringing the two hydrogen atoms into spatial proximity.[5g] Other non-styrene diene substrates were also expected to be converted to cyclohexadienes or benzene derivatives through this intramolecular didehydro-Diels-Alder reaction. The methylated internal diene **26** bearing an aryl alkyne moiety afforded benzene product **27b** in 38% yield, while diene **28** containing a silyl alkyne moiety resulted in a product mixture of cyclohexadiene **29a** and benzene derivative **29b**.



Scheme 1. Additional substrates of the didehydro-Diels-Alder reaction

To demonstrate the mechanism of this Fe-catalyzed didehydro-Diels-Alder reaction,[15] DFT calculations were carried out to analyze the energy levels and molecular structures of the theoretical reactions. Figure 1 presents the structures and energy profiles of the Diels-Alder reaction pathways in the presence or absence of an iron(II) catalyst.[16] The coordination of the $FeCl_2$ catalyst forming the pre-reaction complex **A-$FeCl_2$** can decrease the energy level of reactant (**A**) by a considerable amount (-30.15 kcal/mol). Furthermore, the free energy barrier in the presence of $FeCl_2$ was 14.06 kcal/mol, which is 15.07 kcal/mol lower than the TS without catalyst. It can be concluded that the Fe(II) catalyst accelerates the reaction via the formation of the thermodynamically more stable and preorganized complex (**A-$FeCl_2$**), and the activation of the styrene towards dearomatization by

partially localizing the arene π system.[17]

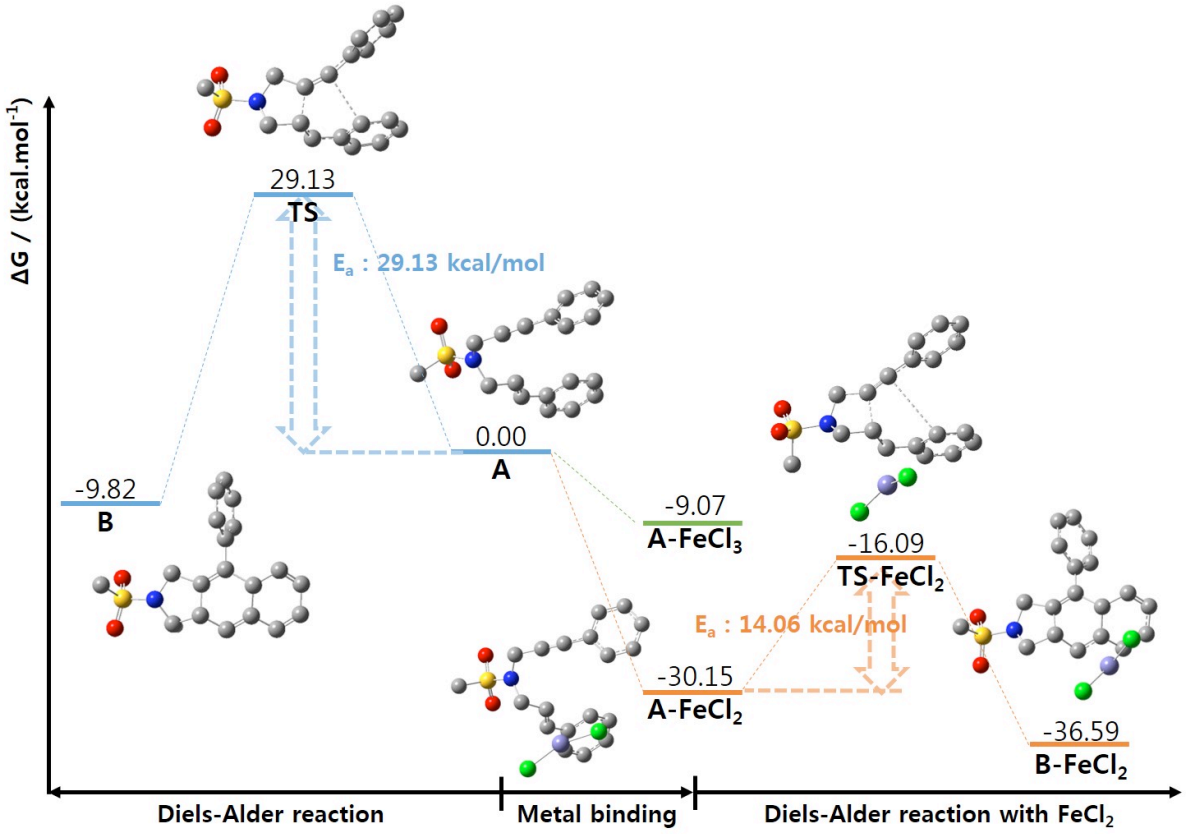


Figure 1. Energy profile for the two Diels-Alder reaction pathways

The detailed data of pre-reaction complexes **A-FeCl$_2$** and **A-FeCl$_3$** is shown in Figure 2, and the different effect of Fe(II) or Fe(III) complex is shown to be characteristic. First of all, it is worth noting that iron is shown to interact with the styrene moiety and not with the alkyne or arene, supporting the proposed iEDDA reaction pathway. The structure of **A-FeCl$_2$** complex exhibits the shorter Fe···C(16) or Fe···C(18) distances (2.157 Å and 2.070 Å respectively) than those of **A-FeCl$_3$** complex (2.466 Å and 2.427 Å respectively). Unlike the bent-shaped $FeCl_2$, a nearly planar structure of $FeCl_3$ hinders the Fe(III) center from approaching the styrenyl unit, thus making the relative minimum high (-30.15 vs -9.07 kcal/mol).

Similar to Brummond's result,[6c] which supported that the naphthalene product was formed through the loss of hydrogen gas from the initially formed cycloadduct, the cyclohexadiene intermediate **B** in our DFT calculations exists in a boat-like structure showing a H(17)···H(26) distance of 3.204 Å.

Upon a close interaction with Fe complexes, the corresponding distance was significantly reduced to 2.536 Å in the **B-FeCl$_2$** complex and 2.779 Å in the **B-FeCl$_3$** complex (Figure 2). Here again, two iron catalysts showed the clear differences of Fe···C(18) or Fe···C(20) distance; the distances in **B-FeCl$_2$** complex was 1.4~1.6 Å shorter than those in **B-FeCl$_3$** complex and this seems to be a factor that makes the whole structure more congested to render the direct dehydrogenation by loss of H_2. In Figure 2e, on the other hand, the structure of **B-FeCl$_3$** complex exhibits the shorter H(26)···Cl distance (2.225 Å) and the longer C(22)-H(26) distance (1.146 Å), which verifies that $FeCl_3$ might be involved in the proton transfer of H(26) through a weakening of the C(22)-H(26) bond to promote the aromatization toward dihydronaphthalene **2a** or intermediate **C** in Figure 3. The result of deuterium labeling experiment also supported the deuterium transfer of D(26) toward dihydronaphthalene ***d*-2a** (84% D-incorporated) during the aromatization process (Scheme 2).

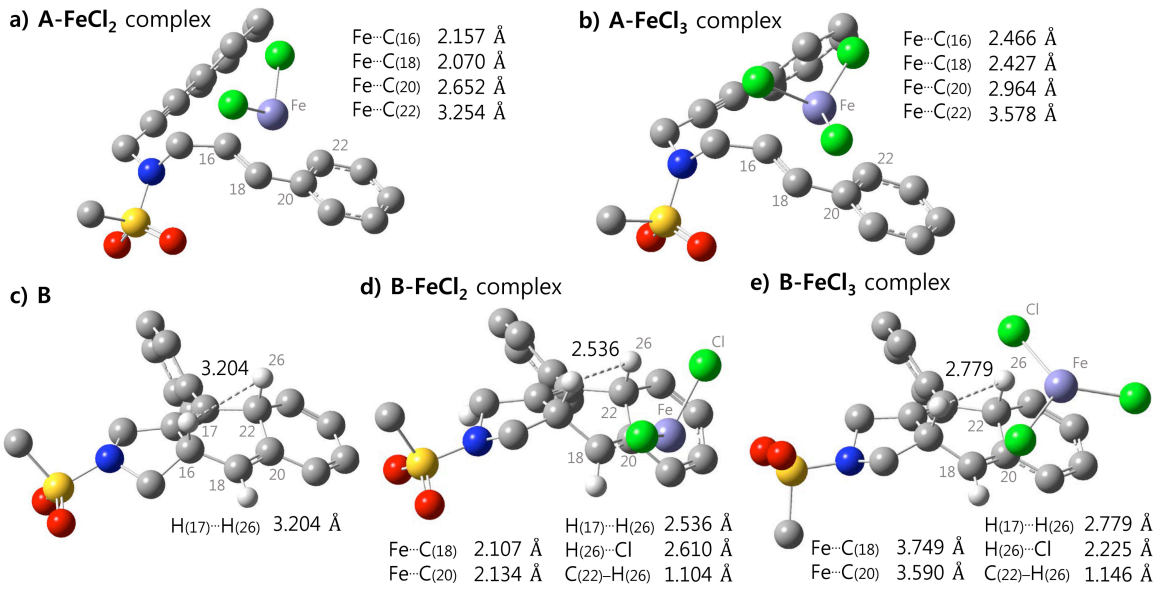
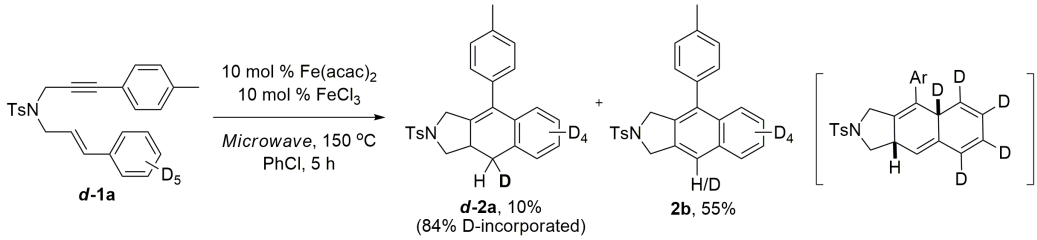


Figure 2. DFT calculation result of related Fe complexes of **A** and **B**



Scheme 2. Deuterium labeling experiment

The following mechanism is proposed according to the reaction results and mechanistic studies.

First, the rate acceleration of the Diels-Alder reaction arises by the lowering of the styrene LUMO energy level in Fe-coordinated complex **I**, even though this process is accompanied by the disruption of aromaticity. The resulting [4+2] cycloadduct **B** can proceed toward the two feasible pathways; (1) the Fe(II) catalyst might induce a direct dehydrogenation of the two hydrogen atoms in spatial proximity, resulting in the naphthalene derivative **D**, and (2) aromatization by the proton-transfer of H(26) is promoted by the Fe(III) catalyst and consecutive dehydrogenation affords naphthalene derivative **D**.

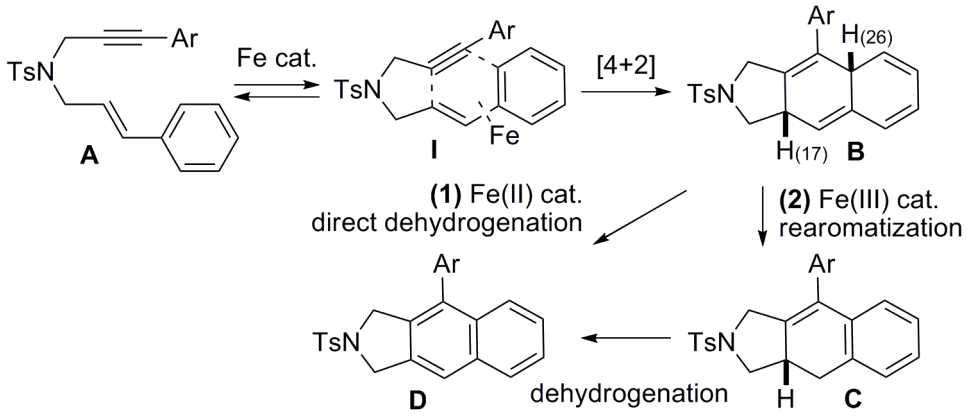


Figure 3. Plausible mechanisms of the Fe-catalyzed IMDDA reaction

CONCLUSION

In this study, the combined system of Fe(II) and Fe(III) was found to catalyze the didehydro-Diels-Alder reaction of styrenyl alkyne substrates to produce polyaromatic cycloadducts. In spite of the challenges associated with the use of a styrene as a conjugated diene (dearomatization and further dehydrogenation), the distinguishing feature of this catalytic system is that there is no need for any other functional groups to modulate the electronic environment of diene-ynes. The experimental results and mechanistic DFT calculations show the following two facts; (1) the coordination of Fe(II) to the styrene reduces both the energy level of the substrate and the activation energy of the Diels-Alder reaction step, and (2) the dehydrogenation process can be promoted by both Fe(II) via direct dehydrogenation and Fe(III) via aromatization. Further efforts to expand the scope of this Fe(II)/Fe(III)-catalyzed didehydro-Diels-Alder reaction for synthesizing complex molecules are in

progress.

EXPERIMENTAL SECTION

General Information. The reaction was conducted in the CEM Discover microwave reactor using sealed reaction vessels. The reaction temperature (150 ^{o}C) was reached by 150 W after 5 min and maintained by the infrared temperature control. All solvents used in the preparation and fractionation of samples were reagent grade and were not purified further. Flash chromatography was carried out using silica gel (70-230 mesh ASTM). All other commercially available reagents were used as received. Reactions were monitored by thin layer chromatography (TLC) using 0.25-mm E. Merck pre-coated silica gel plates, and the spots were visualized under 254 nm UV light and/or charring after dipping the TLC plate into anisaldehyde solution. NMR spectra were recorded in $CDCl_3$ using JEOL (300 MHz) spectrometers (^{1}H frequency, ^{13}C frequency MHz). Residual solvent signals were used for reference ($CHCl_3$ at δ 7.26 ppm for ^{1}H, δ 77.0 for ^{13}C NMR). Mass spectra were recorded using JEOL (JMS-700, quadruple doublet based lens system, EI) or Thermo (Q Exactive, hybrid quadruple orbitrap system, ESI) mass spectrometer.

General procedure for Fe-catalyzed didehydro-Diels-Alder reaction: A styrene-yne (0.1 mmol) was added in the chlorobenzene solution (1 mL) of $Fe(acac)_2$ (2.5 mg, 0.01 mmol) and $FeCl_3$ (1.6 mg, 0.01 mmol). The reaction mixture was reacted in the sealed reaction vessel under the microwave reactor at 150 ^{o}C and 150 W. The reaction temperature was monitored by the infrared temperature control for 5 h. After cooled, it was purified through flash chromatography to give products. Some solid products are purified by recrystallization with DCM and hexane to obtain a single naphthalene product.

4-*p*-tolyl-2-tosyl-2,3-dihydro-1*H*-benzo[*f*]isoindole (2b). Yield after column chromatography 31 mg, 74% as a 22:78 mixture of **2a** and **2b**. Yield after recrystallization 22 mg, 52%; white powder; m.p. 233-234 ^{o}C; R_f = 0.53 (Hex:EtOAc, 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.80 (d, *J* = 8.1 Hz, 1

H), 7.74 (d, *J* = 8.3 Hz, 2 H), 7.64 - 7.56 (m, 2 H), 7.47 - 7.40 (m, 1 H), 7.37 - 7.28 (m, 5 H), 7.15 (d, *J* = 8.1 Hz, 2 H), 4.79 (s, 2 H), 4.49 (s, 2 H), 2.47 (s, 3 H), 2.39 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 143.9, 137.8, 134.68, 134.67, 134.5, 133.8, 133.74, 133.69, 132.2, 130.0, 129.6, 129.4, 128.1, 127.9, 126.14, 126.08, 126.06, 120.7, 53.7, 53.3, 21.5, 21.3 ppm; HRMS (EI) calcd for $C_{26}H_{23}NO_2S$ (M^+) 413.1449, found 413.1450.

9-*m*-tolyl-2-tosyl-2,3,3a,4-tetrahydro-1H-benzo[*f*]isoindole (3a) and 4-*m*-tolyl-2-tosyl-2,3-dihydro-1*H*-benzo[*f*]isoindole (3b). Yield after column chromatography 26 mg, 63% as a 13:87 mixture of **3a** and **3b**; white powder; R_f = 0.57 (Hex:EtOAc, 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.79 (d, *J* = 8.1 Hz, 1 H), 7.74 (d, *J* = 8.3 Hz, 2 H), 7.68 (d, *J* = 8.3 Hz, 0.3 H), 7.62 (s, 1 H), 7.56 (d, *J* = 8.4 Hz, 1 H), 7.46 - 7.33 (m, 3 H), 7.29 (d, *J* = 8.4 Hz, 3 H), 7.18 - 7.09 (m, *J* = 6.4 Hz, 0.5 H), 7.08 - 7.01 (m, 2 H), 6.95 (br. s., 0.1 H), 6.74 (d, *J* = 7.3 Hz, 0.1 H), 4.87 - 4.71 (m, 2 H), 4.56 - 4.42 (m, 2 H), 4.28 (dd, *J* = 1.4, 15.9 Hz, 0.1 H), 3.97 (t, *J* = 8.7 Hz, 0.1 H), 3.62 (dd, *J* = 2.3, 15.7 Hz, 0.1 H), 3.11 (qd, *J* = 7.8, 15.4 Hz, 0.1 H), 2.92 - 2.81 (m, *J* = 6.8 Hz, 0.2 H), 2.66 - 2.58 (m, 0.1 H), 2.42 (s, 3 H), 2.38 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 143.9, 143.8, 138.6, 137.8, 137.7, 136.7, 134.8, 134.4, 134.3, 133.8, 133.7, 133.5, 132.1, 130.2, 130.0, 129.9, 128.8, 128.7, 128.6, 128.1, 127.9, 127.8, 127.2, 126.9, 126.6, 126.2, 126.1, 125.9, 120.7, 54.4, 53.7, 53.5, 53.2, 50.7, 39.0, 32.8, 31.6, 21.55, 21.53 ppm; HRMS (EI) calcd for $C_{26}H_{25}NO_2S$ (**3a**, M^+) 415.1606, found 415.1610 and $C_{26}H_{23}NO_2S$ (**3b**, M^+) 413.1449, found 413.1450.

4-(4-methoxyphenyl)-2-tosyl-2,3-dihydro-1*H*-benzo[*f*]isoindole (4b).[18] Yield after column chromatography 25 mg, 57% as a 11:89 mixture of **4a** and **4b**. Yield after recrystallization 19 mg, 45%; light yellow powder; m.p. 225-226 °C; R_f = 0.45 (Hex:EtOAc, 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.80 (d, *J* = 8.1 Hz, 1 H), 7.75 (d, *J* = 8.3 Hz, 2 H), 7.60 (d, *J* = 7.3 Hz, 2 H), 7.47 - 7.40 (m, 1 H), 7.36 (d, *J* = 7.2 Hz, 1 H), 7.30 (d, *J* = 8.1 Hz, 2 H), 7.18 (d, *J* = 8.6 Hz, 2 H), 7.03 (d, *J* = 8.6 Hz, 2 H), 4.79 (s, 2 H), 4.49 (s, 2 H), 3.91 (s, 3 H), 2.38 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 159.5, 143.9, 134.4, 134.3, 133.9, 133.8, 132.3, 130.7, 130.0, 129.8, 128.1, 127.8, 126.2, 126.1,

126.0, 120.6, 114.4, 55.5, 53.7, 53.3, 21.5 ppm; HRMS (EI) calcd for $C_{26}H_{23}NO_3S$ (M^+) 429.1399, found 429.1399.

9-(2-methoxyphenyl)-2-tosyl-2,3,3a,4-tetrahydro-1H-benzo[*f*]isoindole (5a) and 4-(2-methoxyphenyl)-2-tosyl-2,3-dihydro-1*H*-benzo[*f*]isoindole (5b). Yield after column chromatography 34 mg, 78% as a 15:85 mixture of **5a** and **5b**; light yellow powder; R_f = 0.49 (Hex:EtOAc, 2:1); ^{1}H NMR (300 MHz,$CDCl_3$) δ = 7.81 - 7.71 (m, 3 H), 7.70 - 7.65 (m, 0.48 H), 7.61 (s, 1 H), 7.49 - 7.39 (m, 3 H), 7.38 (br. s., 0.32 H), 7.36 - 7.28 (m, 3 H), 7.11 - 7.03 (m, 3 H), 6.99 (d, *J* = 8.1 Hz, 0.32 H), 6.96 - 6.89 (m, 0.32 H), 6.63 (d, *J* = 6.6 Hz, 0.17 H), 4.86 - 4.73 (m, 2 H), 4.53 - 4.39 (m, 2 H), 4.25 - 4.04 (m, 0.32 H), 3.99 (t, *J* = 8.5 Hz, 0.16 H), 3.78 - 3.54 (m, 3.48 H), 3.10 (tt, *J* = 8.3, 16.2 Hz, 0.16 H), 2.96 - 2.80 (m, *J* = 12.8 Hz, 0.32 H), 2.74 - 2.57 (m, *J* = 2.9 Hz, 0.16 H), 2.41 (br. s., 0.48 H), 2.37 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 157.0, 143.84, 143.79, 143.77, 138.4, 137.5, 134.5, 134.3, 134.1, 133.8, 133.7, 133.6, 132.2, 131.6, 131.5, 131.0, 130.6, 129.92, 129.86, 129.6, 129.4, 128.1, 127.9, 127.8, 127.0, 126.9, 126.84, 126.79, 126.0, 125.9, 125.6, 124.5, 121.1, 121.0, 120.8, 111.5, 55.6, 55.5, 54.9, 53.8, 53.4, 51.0, 38.9, 38.8, 32.7, 21.5 ppm; HRMS (EI) calcd for $C_{26}H_{25}NO_3S$ (**5a**, M^+) 431.1555, found 431.1559 and $C_{26}H_{23}NO_3S$ (**5b**, M^+) 429.1399, found 429.1402.

4-(4-bromophenyl)-2-tosyl-2,3-dihydro-1*H*-benzo[*f*]isoindole (6b). Yield after column chromatography 12 mg, 26% as a 8:92 mixture of **6a** and **6b**. Yield after recrystallization 8 mg, 17%; light yellow powder; m.p. 257-258 ^{o}C; R_f = 0.59 (Hex:EtOAc, 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.82 (d, *J* = 8.1 Hz, 1 H), 7.75 (d, *J* = 8.1 Hz, 2 H), 7.65 (d, *J* = 8.1 Hz, 3 H), 7.54 - 7.42 (m, 3 H), 7.38 (d, *J* = 7.3 Hz, 1 H), 7.32 (d, *J* = 8.1 Hz, 2 H), 7.15 (d, *J* = 8.3 Hz, 2 H), 4.80 (s, 2 H), 4.45 (s, 2 H), 2.40 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 144.0, 136.6, 134.5, 133.71, 133.68, 133.2, 132.3, 131.8, 131.3, 130.1, 130.0, 128.2, 127.94, 127.87, 126.5, 126.3, 125.7, 125.6, 122.4, 121.3, 53.6, 53.1, 21.6 ppm; HRMS (EI) calcd for $C_{25}H_{20}BrNO_2S$ (M^+) 477.0398, found 477.0400.

9-(thiophen-2-yl)-2-tosyl-2,3,3a,4-tetrahydro-1H-benzo[*f*]isoindole (7a) and 4-(thiophen-2-yl)-2-tosyl-2,3-dihydro-1*H*-benzo[*f*]isoindole (7b). Yield after column chromatography 8 mg, 20% as a

13:87 mixture of **7a** and **7b**; brown solid; R_f = 0.40 (Hex:EtOAc, 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.83 - 7.74 (m, 4 H), 7.71 (d, *J* = 8.1 Hz, 0.48 H), 7.65 (s, 1 H), 7.53 - 7.39 (m, 3 H), 7.39 - 7.36 (m, 0.48 H), 7.31 (d, *J* = 7.9 Hz, 2 H), 7.23 - 7.19 (m, 1 H), 7.13 (s, 0.32 H), 7.05 - 7.01 (m, 1 H), 6.93 (d, *J* = 3.7 Hz, 0.16 H), 4.80 (s, 2 H), 4.62 (s, 2 H), 4.39 (d, *J* = 16.5 Hz, 0.16 H), 3.98 (t, *J* = 8.9 Hz, 0.16 H), 3.80 (d, *J* = 14.7 Hz, 0.16 H), 3.19 - 3.02 (m, *J* = 9.4 Hz, 0.16 H), 2.91 - 2.81 (m, *J* = 9.4 Hz, 0.32 H), 2.65 - 2.57 (m, 0.16 H), 2.42 (s, 0.48 H), 2.39 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.7, 150.4, 144.0, 136.8, 134.7, 134.4, 133.8, 133.6, 132.8, 131.3, 130.0, 128.4, 128.3, 127.9, 126.6, 126.2, 125.4, 125.3, 122.8, 121.9, 53.4, 53.1, 21.5 ppm; HRMS (EI) calcd for $C_{23}H_{21}NO_2S_2$ (**7a**, M^+) 407.1014, found 407.1015 and $C_{23}H_{19}NO_2S_2$ (**7b**, M^+) 405.0857, found 405.0856.

4-(pyridin-2-yl)-2-tosyl-2,3-dihydro-1*H*-benzo[*f*]isoindole 8b. Yield after column chromatography 25 mg, 63% as a 17:83 mixture of **8a** and **8b**. Yield after recrystallization 18 mg, 44%; brown solid; m.p. 215-217 ^{o}C; R_f = 0.49 (Hex:EtOAc, 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.79 (d, *J* = 4.0 Hz, 1 H), 7.90 - 7.79 (m, 2 H), 7.75 (d, *J* = 8.1 Hz, 2 H), 7.71 - 7.61 (m, 2 H), 7.48 - 7.36 (m, 4 H), 7.30 (d, *J* = 8.1 Hz, 2 H), 4.77 (s, 2 H), 4.60 (s, 2 H), 2.38 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 144.00, 143.97, 139.6, 138.4, 137.5, 135.7, 134.4, 134.2, 133.7, 133.6, 133.0, 130.05, 130.01, 128.3, 128.1, 128.0, 127.9, 127.8, 127.64, 127.59, 127.3, 127.1, 126.8, 126.6, 126.3, 126.0, 125.82, 125.79, 121.9, 54.2, 53.7, 53.6, 51.2, 39.3, 32.5, 21.6, 21.5 ppm; HRMS (EI) calcd for $C_{24}H_{20}N_2O_2S$ (M^+) 400.1245, found 400.1245.

9-(naphthalen-1-yl)-2-tosyl-2,3,3a,4-tetrahydro-1H-benzo[f]isoindole (9a) and 4-(naphthalen-1-yl)-2-tosyl-2,3-dihydro-1*H*-benzo[*f*]isoindole (9b). Yield after column chromatography 31 mg, 69% as a 10:90 mixture of **9a** and **9b**; light brown solid; R_f = 0.51 (Hex:EtOAc, 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.98 (dd, *J* = 4.6, 8.3 Hz, 2 H), 7.85 (d, *J* = 8.4 Hz, 1 H), 7.73 (s, 1 H), 7.67 (d, *J* = 8.3 Hz, 2 H), 7.60 (dd, *J* = 7.0, 8.3 Hz, 1 H), 7.50 (ddd, *J* = 1.1, 6.9, 8.2 Hz, 1 H), 7.43 (ddd, *J* = 2.8, 5.3, 8.1 Hz, 1 H), 7.33 (dd, *J* = 1.1, 7.0 Hz, 1 H), 7.28 (t, *J* = 3.3 Hz, 3 H), 7.24 (d, *J* = 1.1 Hz, 2 H), 7.10 (d, *J* = 8.4 Hz, 1 H), 6.98 - 6.87 (m, 0.1 H), 6.47 (d, *J* = 2.4 Hz, 0.1 H), 4.91 - 4.78 (m, 2 H), 4.45 - 4.35 (m, 1 H), 4.26 - 4.17 (m, 1 H), 4.06 (qd, *J* = 4.0, 9.5 Hz, 0.1 H), 3.85 - 3.76 (m, *J* = 1.7 Hz, 0.1

H), 3.51 - 3.40 (m, *J* = 2.8 Hz, 0.1 H), 3.28 - 3.14 (m, 0.1 H), 3.05 - 2.87 (m, *J* = 5.0, 5.0 Hz, 0.2 H), 2.84 - 2.72 (m, *J* = 15.6 Hz, 0.1 H), 2.43 (s, 0.3 H), 2.38 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 143.9, 135.2, 134.8, 134.6, 134.1, 133.8, 133.6, 132.8, 132.7, 131.9, 129.99, 129.96, 128.8, 128.7, 128.62, 128.59, 128.1, 128.02, 127.98, 127.9, 127.8, 127.5, 127.3, 127.2, 126.7, 126.4, 126.32, 126.27, 126.2, 126.14, 126.10, 126.0, 125.9, 125.8, 125.7, 121.2, 54.8, 53.8, 53.1, 50.7, 50.6, 39.1, 38.9, 32.9, 32.7, 21.5 ppm; HRMS (EI) calcd for $C_{29}H_{25}NO_2S$ (**9a**, M^+) 451.1606, found 451.1604 and $C_{29}H_{23}NO_2S$ (**9b**, M^+) 449.1449, found 449.1451.

6-methyl-4-*p*-tolyl-2-tosyl-2,3-dihydro-1*H*-benzo[*f*]isoindole (10b). Yield after column chromatography 30 mg, 71% as a 8:92 mixture of **10a** and **10b**. Yield after recrystallization 24 mg, 57%; light yellow powder; m.p. 187-188 °C; R_f = 0.63 (Hex:EtOAc, 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.76 - 7.67 (m, 3 H), 7.57 (s, 1 H), 7.31 (dd, *J* = 5.2, 8.0 Hz, 6 H), 7.14 (d, *J* = 8.1 Hz, 2 H), 4.77 (s, 2 H), 4.46 (s, 2 H), 2.48 (s, 3 H), 2.38 (d, *J* = 6.6 Hz, 6 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 143.9, 137.7, 136.0, 134.9, 134.0, 133.81, 133.79, 133.7, 133.4, 132.3, 132.0, 130.0, 129.6, 129.4, 128.4, 127.91, 127.85, 124.9, 120.4, 53.7, 53.3, 31.6, 22.7, 21.9, 21.5, 21.4, 14.1 ppm; HRMS (EI) calcd for $C_{27}H_{25}NO_2S$ (M^+) 427.1606, found 427.1606.

8-methoxy-4-*p*-tolyl-2-tosyl-2,3-dihydro-1*H*-benzo[*f*]isoindole (11b). Yield after column chromatography 32 mg, 72%; brown solid; m.p. 226-229 °C; R_f = 0.62 (Hex:EtOAc, 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.08 (s, 1 H), 7.73 (d, *J* = 8.3 Hz, 2 H), 7.29 (d, *J* = 7.9 Hz, 4 H), 7.22 (d, *J* = 7.5 Hz, 1 H), 7.17 - 7.10 (m, 3 H), 6.79 (d, *J* = 7.3 Hz, 1 H), 4.79 (s, 2 H), 4.48 (s, 2 H), 3.99 (s, 3 H), 2.46 (s, 3 H), 2.38 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 155.5, 143.9, 137.7, 135.0, 134.3, 134.1, 133.8, 133.7, 133.2, 130.0, 129.6, 129.4, 127.9, 127.8, 126.0, 125.9, 118.4, 115.0, 104.0, 55.7, 54.0, 53.4, 21.5, 21.3 ppm; HRMS (EI) calcd for $C_{27}H_{25}NO_3S$ (M^+) 443.1555, found 443.1552.

6-bromo-4-*p*-tolyl-2-tosyl-2,3-dihydro-1*H*-benzo[*f*]isoindole (12b). Yield after column chromatography 38 mg, 77% as a 10:90 mixture of **12a** and **12b**. Yield after recrystallization 30 mg, 62%; white solid; m.p. 218-221 °C; R_f = 0.58 (Hex:EtOAc, 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.76 - 7.71 (m, 3 H), 7.67 (d, *J* = 8.8 Hz, 1 H), 7.59 (s, 1 H), 7.51 (dd, *J* = 1.8, 8.8 Hz, 1 H), 7.32 (t, *J*

= 6.7 Hz, 4 H), 7.12 (d, *J* = 7.9 Hz, 2 H), 4.76 (s, 2 H), 4.47 (s, 2 H), 2.48 (s, 3 H), 2.39 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 144.0, 138.2, 135.0, 134.9, 134.0, 133.9, 133.7, 133.6, 133.3, 132.2, 130.0, 129.9, 129.7, 129.5, 129.3, 128.2, 127.8, 120.6, 120.5, 53.6, 53.2, 21.5, 21.4 ppm; HRMS (EI) calcd for $C_{26}H_{22}BrNO_2S$ (M^+) 491.0555, found 491.0551.

4-p-tolyl-6-tosyl-6,7,7a,8-tetrahydro-5*H*-thieno[3,2-*f*]isoindole (13a) and 4-*p*-tolyl-6-tosyl-6,7-dihydro-5*H*-thieno[3,2-*f*]isoindole (13b). Yield after column chromatography 24 mg, 57% as a 11:89 mixture of **13a** and **13b**; brown solid; R_f = 0.63 (Hex:EtOAc, 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.74 (d, *J* = 8.3 Hz, 2 H), 7.69 (d, *J* = 8.3 Hz, 0.3 H), 7.62 (s, 1 H), 7.35 - 7.27 (m, 5 H), 7.25 - 7.19 (m, 2 H), 7.17 (s, 0.1 H), 7.12 (d, *J* = 5.5 Hz, 1 H), 7.10 - 7.05 (m, 0.2 H), 6.96 (d, *J* = 5.1 Hz, 0.1 H), 6.59 (d, *J* = 5.1 Hz, 0.1 H), 4.75 (s, 2 H), 4.56 (s, 2 H), 4.34 (d, *J* = 15.6 Hz, 0.1 H), 3.94 (t, *J* = 8.7 Hz, 0.1 H), 3.69 (dd, *J* = 2.5, 15.3 Hz, 0.1 H), 3.41 - 3.24 (m, 0.1 H), 3.01 (dd, *J* = 8.0, 15.3 Hz, 0.1 H), 2.89 (t, *J* = 9.4 Hz, 0.1 H), 2.66 - 2.57 (m, *J* = 16.1 Hz, 0.1 H), 2.44 (s, 3 H), 2.41 (br. s., 0.6 H), 2.39 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 143.9, 140.3, 138.8, 137.9, 135.1, 133.8, 133.5, 132.7, 131.6, 130.0, 129.6, 128.9, 127.8, 126.6, 123.2, 115.4, 53.7, 53.0, 21.5, 21.3 ppm; HRMS (EI) calcd for $C_{24}H_{23}NO_2S_2$ (**13a**, M^+) 421.1170, found 421.1171 and $C_{24}H_{21}NO_2S_2$ (**13b**, M^+) 419.1014, found 419.1017.

7-p-tolyl-9-tosyl-9,10,10a,11-tetrahydro-8*H*-naphtho[2,1-*f*]isoindole (15a) and 7-*p*-tolyl-9-tosyl-9,10-dihydro-8*H*-naphtho[2,1-*f*]isoindole (15b). Yield after column chromatography 36 mg, 77% as a 10:90 mixture of **15a** and **15b**; white powder; R_f = 0.53 (Hex:EtOAc, 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.62 (d, *J* = 8.1 Hz, 1 H), 8.48 (s, 1 H), 8.01 (d, *J* = 8.4 Hz, 0.2 H), 7.83 (d, *J* = 7.7 Hz, 1 H), 7.76 (d, *J* = 8.1 Hz, 2 H), 7.64 - 7.48 (m, 4 H), 7.42 (d, *J* = 7.7 Hz, 0.2 H), 7.31 (t, *J* = 8.0 Hz, 4 H), 7.25 - 7.19 (m, 0.8 H), 7.16 (d, *J* = 7.7 Hz, 2 H), 7.05 (br. s., 0.4 H), 6.97 (d, *J* = 8.4 Hz, 0.2 H), 4.89 (s, 2 H), 4.53 (s, 2 H), 4.38 (d, *J* = 15.6 Hz, 0.2 H), 4.06 (t, *J* = 8.5 Hz, 0.2 H), 3.75 - 3.59 (m, 0.4 H), 3.26 - 3.09 (m, *J* = 7.4, 7.4, 15.2 Hz, 0.2 H), 3.05 - 2.95 (m, 0.2 H), 2.72 - 2.62 (m, 0.2 H), 2.48 (s, 3 H), 2.40 (d, *J* = 5.0 Hz, 1.2 H), 2.37 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 143.9, 137.8, 137.6, 136.3, 135.5, 135.2, 135.0, 134.8, 134.3, 133.93, 133.91, 133.5, 133.4, 133.3, 133.1,

132.6, 131.9, 131.3, 130.8, 130.4, 130.2, 130.01, 129.97, 129.74, 129.68, 129.6, 129.5, 129.3, 128.8, 128.7, 127.9, 127.8, 127.0, 126.9, 126.6, 126.5, 125.6, 124.6, 124.4, 123.6, 122.9, 115.7, 54.6, 54.3, 53.6, 50.8, 39.0, 27.8, 21.6, 21.5, 21.4, 21.3 ppm; HRMS (EI) calcd for $C_{30}H_{27}NO_2S$ (**15a**, M^+) 465.1762, found 465.1760 and $C_{30}H_{25}NO_2S$ (**15b**, M^+) 463.1606, found 463.1609.

11-*p*-tolyl-9-tosyl-9,10-dihydro-8*H*-naphtho[1,2-*f*]isoindole (16b). Yield after column chromatography 54 mg, 96% as a 18:82 mixture of **16a** and **16b**. Yield after recrystallization 32 mg, 68%; white powder; m.p. 188-191 ^oC; R_f = 0.63 (Hex:EtOAc, 2:1); ^1H NMR (300 MHz, $CDCl_3$) δ = 7.79 (dd, *J* = 1.3, 7.9 Hz, 1 H), 7.73 (d, *J* = 8.4 Hz, 2 H), 7.69 - 7.62 (m, 4 H), 7.40 (ddd, *J* = 1.1, 7.0, 7.9 Hz, 1 H), 7.31 (t, *J* = 8.7 Hz, 4 H), 7.11 (d, *J* = 7.9 Hz, 3 H), 4.84 (s, 2 H), 4.41 (s, 2 H), 2.51 (s, 3 H), 2.38 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 143.9, 139.0, 137.7, 136.6, 135.5, 134.3, 134.0, 133.9, 133.6, 130.85, 130.76, 130.0, 128.7, 128.5, 128.2, 128.1, 128.0, 127.81, 127.78, 127.4, 126.3, 126.2, 125.5, 122.0, 54.3, 54.1, 21.5, 21.5 ppm; HRMS (EI) calcd for $C_{30}H_{25}NO_2S$ (M^+) 463.1606, found 463.1609.

5-methyl-4-*p*-tolyl-2-tosyl-2,3-dihydro-1*H*-benzo[*f*]isoindole (17b) and 7-methyl-4-*p*-tolyl-2-tosyl-2,3-dihydro-1*H*-benzo[*f*]isoindole (17b'). Yield after column chromatography 29 mg, 67% as a 66:34 mixture of **17b** and **17b'**; brown powder; R_f = 0.59 (Hex:EtOAc, 2:1); ^1H NMR (300 MHz, $CDCl_3$) δ = 7.76 - 7.68 (m, 2 H), 7.68 - 7.63 (m, 1 H), 7.60 (s, 1 H), 7.57 - 7.46 (m, 1 H), 7.33 - 7.26 (m, 4 H), 7.21 (d, *J* = 7.7 Hz, 1 H), 7.16 - 7.12 (m, 1 H), 7.06 (d, *J* = 7.9 Hz, 1 H), 4.77 (s, 2 H), 4.47 (s, 1 H), 4.31 (s, 1 H), 2.46 (d, *J* = 2.9 Hz, 4 H), 2.38 (s, 3 H), 1.95 (s, 2 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 143.8, 138.8, 137.4, 135.9, 135.1, 134.8, 134.5, 133.3, 130.0, 129.6, 129.4, 129.2, 128.9, 128.4, 127.9, 127.8, 127.5, 127.1, 125.9, 125.7, 122.0, 120.0, 54.0, 53.8, 24.8, 22.7, 21.5, 21.4 ppm; HRMS (EI) calcd for $C_{27}H_{25}NO_2S$ (M^+) 427.1606, found 427.1603.

4-*p*-tolyl-1,3-dihydronaphtho[2,3-*c*]furan (18b). Yield after column chromatography 16 mg, 60%; yellow viscous liquid; R_f = 0.56 (Hex:EtOAc, 2:1); ^1H NMR (300 MHz, $CDCl_3$) δ = 7.86 (d, *J* = 7.9 Hz, 1 H), 7.73 - 7.66 (m, 2 H), 7.45 (t, *J* = 7.4 Hz, 1 H), 7.36 (dt, *J* = 1.1, 7.6 Hz, 2 H), 7.32 - 7.29 (m, 2 H), 7.25 - 7.23 (m, 1 H), 5.29 (s, 2 H), 5.03 (s, 2 H), 2.45 (s, 3 H) ppm; ^{13}C NMR (75 MHz,

$CDCl_3$) δ = 137.9, 137.5, 137.1, 135.3, 133.9, 132.8, 132.1, 129.54, 129.49, 129.3, 129.1, 128.2, 126.0, 125.9, 125.8, 118.8, 73.5, 73.1, 21.3 ppm; HRMS (EI) calcd for $C_{19}H_{16}O$ (M^+) 260.1201, found 260.1202.

diethyl 4-p-tolyl-1H-cyclopenta[b]naphthalene-2,2(3H)-dicarboxylate (19b). Yield (determined by ^{1}H-NMR) after column chromatography 32 mg, 78% from a 30:70 mixture of **19b** (24%) and starting material (54%); colorless liquid; R_f = 0.53 (Hex:EtOAc, 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.79 (d, *J* = 8.1 Hz, 1 H), 7.66 (s, 1 H), 7.59 (d, *J* = 8.4 Hz, 1 H), 7.43-7.36 (m, 4 H), 7.31 (d, *J* = 5.5 Hz, 4 H), 7.24 (br. s., 1 H), 4.17 (q, *J* = 7.2 Hz, 4 H), 3.78 (s, 2 H), 3.48 (s, 2 H), 2.46 (s, 3 H), 1.22 (t, *J* = 7.1 Hz, 6 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 171.6, 170.0, 138.5, 138.1, 137.6, 137.2, 137.1, 136.9, 135.7, 135.1, 134.5, 134.1, 133.6, 132.0, 131.6, 129.8, 129.2, 129.01, 128.97, 128.6, 128.5, 127.8, 127.4, 126.3, 126.2, 125.9, 125.2, 125.1, 124.0, 123.6, 121.9, 120.2, 83.7, 83.6, 61.60, 61.58, 61.3, 60.6, 57.4, 40.4, 39.8, 36.5, 36.0, 23.7, 21.3, 21.2, 14.0, 13.9 ppm; HRMS (ESI) calcd for $C_{26}H_{26}O4$ ($M + H^+$) 403.1909, found 403.1903.

2-tosyl-4-(trimethylsilyl)-2,3-dihydro-1H-benzo[f]isoindole (21b).[5g] Yield after column chromatography 22 mg, 56%; orange liquid; R_f = 0.53 (Hex:EtOAc, 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.12 (d, *J* = 6.8 Hz, 1 H), 7.80 (d, *J* = 8.3 Hz, 2 H), 7.76 (d, *J* = 2.8 Hz, 1 H), 7.63 (s, 1 H), 7.49-7.41 (m, 2 H), 7.33 (d, *J* = 8.1 Hz, 2 H), 4.78 (s, 2 H), 4.68 (s, 2 H), 2.40 (s, 3 H), 0.50 (s, 9 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 143.8, 141.6, 136.9, 134.1, 133.0, 129.9, 129.0, 128.2, 127.8, 125.5, 125.4, 123.2, 55.0, 52.4, 21.4, 2.2 ppm; HRMS (ESI) calcd for $C_{22}H_{25}NO_2SSi$ ($M + H^+$) 396.1448, found 396.1447.

4-methyl-2-tosyl-2,3-dihydro-1H-benzo[f]isoindole (23b).[19] Yield after column chromatography 5 mg, 15%; light yellow liquid; R_f = 0.60 (Hex:EtOAc, 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.77 (d, *J* = 8.1 Hz, 2 H), 7.34 - 7.29 (m, 5 H), 6.53 (s, 1 H), 6.58 (s, 1 H), 6.08 (dt, *J* = 6.8 Hz, 1 H), 4.05 (d, *J* = 2.4 Hz, 2 H), 3.96 (d, *J* = 6.8 Hz, 2 H), 2.43 (s, 3 H), 1.59 - 1.54 (m, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 143.8, 134.2, 133.6, 133.45, 133.38, 132.1, 129.9, 128.5, 128.1, 127.7, 125.9, 125.8,

123.6, 119.3, 53.6, 53.0, 21.4, 15.1 ppm; HRMS (ESI) calcd for $C_{20}H_{19}NO_2S$ ($M + H^+$) 338.1209, found 338.1190.

5-methyl-4-*p*-tolyl-2-tosylisoindoline (27b). Yield after column chromatography 14 mg, 56%; yellow solid; m.p. 175-177 ^oC; R_f = 0.61 (Hex:EtOAc, 2:1); ^1H NMR (300 MHz , $CDCl_3$) δ = 7.70 (d, *J* = 8.3 Hz, 2 H), 7.29 (d, *J* = 8.1 Hz, 2 H), 7.23 (d, *J* = 7.7 Hz, 2 H), 7.15 (d, *J* = 7.7 Hz, 1 H), 7.06 - 6.97 (m, 3 H), 4.63 (s, 2 H), 4.32 (s, 2 H), 2.41 (d, *J* = 3.9 Hz, 6 H), 2.08 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 143.7, 137.4, 137.3, 135.8, 135.7, 134.0, 133.6, 129.95, 129.91, 129.6, 128.5, 127.8, 121.3, 54.1, 53.7, 21.5, 21.3, 19.8 ppm; HRMS (EI) calcd for $C_{23}H_{23}NO_2S$ (M^+) 377.1449, found 377.1452.

5-methyl-2-tosyl-4-(trimethylsilyl)isoindoline (29b).[5g] Yield after column chromatography 17 mg, 48% as a 29:71 mixture of **29a** and **29b**. Yield after recrystallization 10 mg, 29%; colorless oil; R_f = 0.51 (Hex:EtOAc, 2:1); ^1H NMR (300 MHz, $CDCl_3$) δ = 7.76 (d, *J* = 8.4 Hz, 1 H), 7.72 (d, *J* = 8.1 Hz, 2 H), 7.37 - 7.25 (m, 3 H), 7.03 (s, 0.84 H), 5.66 - 5.52 (dd, *J* = 8.8 Hz, 2 H), 4.62 (s, 0.84 H), 4.52 (s, 0.84 H), 3.97 (d, *J* = 13.0 Hz, 1 H), 3.82 - 3.71 (m, 2 H), 2.98 - 2.76 (m, 2 H), 2.72 - 2.61 (m, 1 H), 2.46 - 2.36 (m, 6 H), 1.04 (d, *J* = 6.8 Hz, 3 H), 0.34 (s, 3 H), 0.12 (s, 9 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 143.82, 143.80, 141.9, 133.8, 133.11, 133.05, 130.1, 130.0, 127.8, 123.4, 55.5, 52.9, 23.7, 21.5, 1.9 ppm; HRMS (ESI) calcd for $C_{19}H_{25}NO_2SSi$ ($M + H^+$) 360.1448, found 360.1446.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:

DFT calculation data for all compounds and Fe complexes in Figure 1 and 2.

^1H NMR and ^{13}C NMR for all synthesized compounds.

■ AUTHOR INFORMATION

Corresponding Authors

***E-mail:** khahn@khu.ac.kr, ejkang24@khu.ac.kr

ORCID

Eun Joo Kang: 0000-0002-7600-3609

Kwang-Hyun Ahn: 0000-0002-2812-4895

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This study was supported by the Ministry of Education, Science and Technology, National Research Foundation (grant numbers NRF-2015R1D1A1A01060349) and the GRRC program of Gyeonggi province (GRRCKyungHee2017-A01, Novel and original technology research for platform synthesis of incrementally modified synthetic global drug candidates).

■ REFERENCES

1. (a) Diels, O.; Alder, K. *Ann. Chem*. **1928**, *460*, 98. (b) Dewar, M. J. S.; Olivella, S.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1986**, *108,* 5771. (c) Winkler, J. D. *Chem. Rev.* **1996**, *96*, 167. (d) Jørgensen, K. A. *Angew. Chem. Int. Ed.* **2000**, *39,* 3558. (e) Takao, K.; Munakata, R.; Tadano, K. *Chem. Rev.* **2005**, *105,* 4779. (f) Jiang, X.; Wang, R. *Chem. Rev.* **2013**, *113,* 5515.
2. This process has been generally called the dehydro-Diels-Alder (DDA) reaction, which suggested by P. Wessig; (a) Wessig, P.; Müller, G. *Chem. Rev.* **2008**, *108,* 2051. (b) Wessig, P.; Matthes, A.; Pick, C. *Org. Biomol. Chem*. **2011**, *9*, 7599. (c) Wessig, P.; Matthes, A.; Schilde, U.; Kelling, A. *Eur. J. Org. Chem*. **2013**, 2123. (d) Hoye, T. R.; Baire, B.; Niu, D.; Willoughby, P. H.; Woods, B. P. *Nature* **2012**, *490*, 208. (e) Wang, T.; Hoye, T. R. *J. Am. Chem. Soc.* **2016**, *138,* 13870. (f) Vandavasi, J. K.; Hu, W.-P.; Hsiao, C.-T.; Senadi, G. C.; Wang, J.-J. *RSC Adv.* **2014**, *4,* 57547.
3. (a) Wagner-Jauregg, T. *Synthesis* **1980**, 769. (b) Parker, K. A.; Ruder, S. M. *J. Am. Chem. Soc.* **1989**, *111,* 5948.

4. Stille, J. K.; Chung, D. C. *Macromolecules* **1975**, *8,* 83.

5. (a) Klemm, L. H.; Gopinath, K. W. *Tetrahedron Lett.* **1963**, *19,* 1243. (b) Klemm, L. H.; Klemm, R. A.; Santhanam, P. S.; White, D. V. *J. Org. Chem.* **1971**, *36,* 2169. (c) Klemm, L. H.; McGuire, T. M.; Gopinath, K. W. *J. Org. Chem.* **1976**, *41,* 2571. (d) Toyota, M.; Terashima, S. *Tetrahedron Lett.* **1989**, *30,* 829. (e) Chackalamannil, S.; Doller, D.; Clasby, M.; Xia, Y.; Eagen, K.; Lin, Y.; Tsai, H.-A.; McPhail, A. T. *Tetrahedron Lett.* **2000**, *41,* 4043. (f) Ruijter, E.; Garcia-Hartjes, J.; Hoffmann, F.; van Wandelen, L.; de Kanter, F.; Janssen, E.; Orru, R. *Synlett* **2010**, *2010,* 2485. (g) Ozawa, T.; Kurahashi, T.; Matsubara, S. *Org. Lett.* **2011**, *13,* 5390. (h) Fang, Z.; Liu, Y.; Barry, B.-D.; Liao, P.; Bi, X. *Org. Lett.* **2015**, *17,* 782. (i) For an extensive review on the recent progress in dehydro-Diels-Alder reactions, see Li, W.; Zhou, L.; Zhang, J. *Chem. Eur. J.* **2016**, *22*, 1558.

6. (a) Kocsis, L. S.; Benedetti, E.; Brummond, K. M. *Org. Lett.* **2012**, *14,* 4430. (b) Kocsis, L. S.; Brummond, K. M. *Org. Lett.* **2014**, *16,* 4158. (c) Kocsis, L. S.; Kagalwala, H. N.; Mutto, S.; Godugu, B.; Bernhard, S.; Tantillo, D. J.; Brummond, K. M. *J. Org. Chem.* **2015**, *80,* 11686. (d) Brummond, K. M.; Kocsis, L. S. *Acc. Chem. Res*. **2015**, *48*, 2320.

7. Zheng, M.; Wu, F.; Chen, K.; Zhu, S. *Org. Lett.* **2016**, *18,* 3554.

8. Xiao, Y.-C.; Yue, C.-Z.; Chen, P.-Q.; Chen, Y.-C. *Org. Lett.* **2014**, *16,* 3208.

9. (a) Muthukrishnan, I.; Vinoth, P.; Vivekanand, T.; Nagarajan, S.; Maheswari, C. U.; Menendez, J. C.; Sridharan, V. *J. Org. Chem.* **2016**, *81,* 1116. (b) Yu, X.; Wang, J.; Xu, Z.; Yamamoto, Y.; Bao, M. *Org. Lett.* **2016**, *18,* 2491.

10. (a) Jung, M. S.; Kim, W. S.; Shin, Y. H.; Jin, H. J.; Kim, Y. S.; Kang, E. J. *Org. Lett.*, **2012**, *14*, 6262. (b) Kim, J. H.; Kim, S. W.; Jung, M. S.; Ahn, K-H.; Kang, E. J. *Bull. Korean Chem. Soc*. **2015**, *36*, 2846.

11. Other Lewis acids such as $InCl_3$, AgOTf, and $Sn(OTf)_2$ were tested in this styrenyl didehydro-Diels-Alder reaction, however all reactions resulted either C-N bond cleavage or decomposition of styren-yne substrate.

12. (a) Göttker-Schnetmann, I.; Brookhart M. *J. Am. Chem. Soc.* **2004**, *126,* 9330. (b) Ahuja, R.; Punji, B.; Findlater, M.; Supplee, C.; Schinski, W.; Brookhart, M.; Goldman, A. S. *Nat. Chem.* **2011**, *3,* 167. (c) Lyons, T. W.; Bézier, D.; Brookhart, M. *Organometallics* **2015**, *34,* 4058. (d) Liu, X.-J.; Wang, W.-P.; Huo, C.-D.; Wang, X.-C.; Quan, Z.-J. *Catal. Sci. Technol*. **2017**, *7*, 565.

13. (a) Ilhan, F.; Tyson, D. S.; Meador, M. A. *Org. Lett.* **2006**, *8,* 577. (b) Zhang, W.; Ma, H.; Zhow, L.; Sun, Z.; Du, Z.; Miao, H.; Xu, J. *Molecules* **2008**, *13*, 3236. (c) Ruijter, E.; Garcia-Hartjes, J.; Hoffmann, F.; van Wandelen, L. T. M.; de Kanter, F. J. J.; Janssen, E.; Orru, R. V. A. *Synlett* **2010**, *16*, 2485. (d) Abdelhamid, I. A.; Butenschön, H. *Eur. J. Org. Chem.* **2015**, 226. (e) Bercaw, J. E.; Hazari, N.; Labinger, J. A. *J. Org. Chem*. **2008**, *73*, 8654. (f) Silva, L. F.; Siqueira, F. A.; Pedrozo, E. C.; Vieira, F. Y. M.; Doriguetto, A. C. *Org. Lett.* **2007**, *9,* 1433.

14. (a) Sundararajan, G.; Prabagaran, N.; Varghese, B. *Org. Lett.* **2001**, *3,* 1973. (b) Gademann, K.; Chavez, D. E.; Jacobsen, E. N. *Angew. Chem. Int. Ed.* **2002**, *41,* 3095. (c) Li, P.; Yamamoto, H. *J. Am. Chem. Soc.* **2009**, *131,* 16628. (d) Jiang, X.; Wang, R. *Chem. Rev.* **2013**, *113,* 5515. (e) Yan, X.; Ling, F.; Zhang, Y.; Ma, C. *Org. Lett.* **2015**, *17,* 3536. (f) Duret, G.; Quinlan, R.; Martin, R. E.; Bisseret, P.; Neuburger, M.; Gandon, V.; Blanchard, N. *Org. Lett.* **2016**, *18,* 1610.

15. To investigate the reaction mechanism, we checked the possibility of radical pathway in the didehydro-Diels-Alder reaction. The addition of 1.5 equivalents of TEMPO resulted in decreasing of the overall yield without any significant difference in the product ratio (32% yield, **2a**:**2b** = 16:84), which cannot strongly support the radical mechanism.

16. We employed a model catalyst as $FeCl_2$ instead of $Fe(acac)_2$ and *N*-mesyl functional group instead of *N*-tosyl group to simplify the calculation.

17. Kolis, S. P.; Chordia, M. D.; Liu, R.; Kopach, M. E.; Harman, W. D. *J. Am. Chem. Soc.* **1998**, *120,* 2218.

18. Das, J.; Mukherjee, R.; Basak, A. *J. Org. Chem*. **2014**, *79*, 3789.

19. Wang, F.; Tong, X.; Cheng, J.; Zhang, Z. *Chem. Eur. J*. **2004**, *10*, 5338.