铁催化 1,3-共轭烯烃的 Heck 型脱羧烷基化反应

王凯凯^a 陈绍维^b 李亚军^b 李达谅^{*,a} 鲍红丽^{*,b}^(a) 福建师范大学南方生物医学研究中心&化学与材料学院 福州 350007)^(b) 中国科学院福建物质结构研究所 煤制乙二醇重点实验室 福州 350002)

摘要 报道了铁催化的烷基过氧酯或者叔丁基过氧酯对 1,3-共轭烯烃的 Heck 型脱羧烷基化反应。这个方法提供了一个有效的对 1,3-共轭烯烃进行 Heck 型烷基化的途径,不但收率高,而且有些情况下具有很高的区位选择性。此方法也可以用来对生物活性分子进行后期 Heck 型烷基化修饰。

关键词 铁催化; 1,3-共轭烯烃; Heck 型烷基化; 脱羧反应; 过氧酯; 过氧酯

Iron-Catalyzed Decarboxylative Heck-Type Alkylation of Conjugate 1,3-Dienes

Wang, Kaikai^a Chen, Shaowei^b Li, Yajun^b Li, Daliang^{*,a} Bao, Hongli^{*,b}^(a) Biomedical Research Center of South China & College of Chemistry and Materials Science, Fujian Normal University, Fuzhou 350007)^(b) Key Laboratory of Coal to Ethylene Glycol and Its Related Technology, Fujian Institute of Research on the Structure of Matter, Chinese Academy of Sciences, Fuzhou 350002)

Abstract An iron-catalyzed decarboxylative Heck-type alkylation of conjugate 1,3-dienes with alkyl diacyl peroxides and *t*-butyl peresters is reported. This method offers an efficient approach to alkylation of 1,3-dienes with good yields, and in some cases with high selectivities. Late-stage alkylation of bioactive compounds was also found to be effective.

Keywords iron catalysis; 1,3-dienes; Heck-type alkylation; decarboxylation; peresters; diacyl peroxides

1 Introduction

The 1,3-diene motif is widely prevalent as a key structure in many natural products, pharmaceuticals, and other bioactive agents.^[1] It also plays a significant role in synthetic chemistry, including the state-of-the-art Diels-Alder [4+2] cycloaddition reaction.^[2] The 1,3-diene motifs are commonly constructed either by the Wittig reaction of α,β -unsaturated aldehydes with Wittig reagents,^[3] or the Heck-Mizoroki cross-coupling of vinyl iodides with alkenes.^[4] However, notwithstanding the advances that have been achieved, the documented methods for the synthesis of 1,3-dienes are limited by the lack of readily available reagents and harsh reaction conditions, and convenient approaches for the synthesis of 1,3-dienes are still needed.

Diacyl peroxides and *t*-butyl peresters are ancient chemicals as shown in reports which can be traced back

over centuries. Because of their explosive potential however, these compounds are frequently used with great care as oxidants or radical initiators in industry and academia. In recent years, our work^[5] and other studies^[6] have revealed that these peroxides can serve as good alkylating reagents. For example, in the presence of a copper catalyst, 1,3-dienes can react with diacyl peroxides to deliver 1,2-alkylesterification products^[7] as well as diesterification products^[8] (Scheme 1a). Alternatively, with iron catalysis, the alkyl Heck reaction affords the corresponding cross-coupling products.^[5f,5h,9] Zhu *et al.*^[10] reported a stereospecific synthesis of polyenes via a radical-mediated Heck-type alkylation with multifunctionalized tertiary alkyl bromides (Scheme 1b). Continuing our interest in the difunctionalization of unsaturated carbon-carbon bonds,^[11] we report herein an iron-catalyzed decarboxylative alkylation of 1,3-dienes with diacyl peroxides and *t*-butyl perest-

* Corresponding authors. E-mail: daliangli@fjnu.edu.cn; hlbao@fjirsm.ac.cn

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ers as the alkylating reagents (Scheme 1c).

(a) Our previous work on 1,3-dienes and alkyl peroxides

(b) Zhu's work on 1,3-dienes and multifunctionalized tertiary alkyl bromides

(c) This work: Iron-catalyzed decarboxylative alkylation of 1,3-dienes

Scheme 1 Alkylation of 1,3-dienes

2 Results and discussion

Our initial studies were focused on metal-catalyzed Heck-type alkylation of the conjugate 1,3-diene (**1a**) as shown in Table 1. Based on our previous work, we began the investigation with an iron salt as catalyst and tetrahydrofuran (THF) as solvent. The reaction between the 1,3-diene **1a** and the alkyl diacyl peroxide **2a** in the presence of $\text{Fe}(\text{OTf})_3$ (2 mol%) in THF (2.5 mL) at 80 °C gave the desired product **3aa** in 40% yield (Table 1, Entry 1). Other transition-metal catalysts, such as $\text{Mn}(\text{OAc})_2$, MnBr_2 , $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$, $\text{Ni}(\text{acac})_2$, CoBr_2 , and CuBr were also tested but were found to give low efficiencies (Table 1, Entries 2~7).^[12] While $\text{Fe}(\text{acac})_3$ and FeCl_2 provided very small amount of the desired product **3aa**, $\text{Fe}(\text{OTf})_3$ gave a yield as high as 67% (Table 1, Entries 8~10). The reaction temperature was scoped but no improvement was obtained by increasing or decreasing the reaction temperature (Table 1, Entries 11~14). The yield could be improved to 74% when the peroxide **2a** was added in three portions, and the *E/Z* value of the desired product was approximately 2 : 1 (Table 1, Entry 15).

With the optimal conditions in hand, the scope of the diacyl peroxides and peresters were investigated, and the results shown in Table 2 were obtained. The diacyl peroxides with functionalities such as an aryl group or chloride, reacted to give the corresponding products (**3ab**, **3ac**, and **3ag**) in moderate to high yields (82%~86%). Generic alkyl diacyl peroxides afforded the corresponding products (**3ad**~**3af** and **3aj**) in moderate to good yields (70%~82%). The diacyl peroxides that contain a five-membered ring and a 1-adamantyl group afforded the corresponding products **3ah** and **3ai**, respectively.

Next, alkylating reagents containing a secondary alkyl source were explored. The perester containing a five-membered ring afforded the corresponding product (**5aa**) in 73% yield. Simple peresters also reacted well to give the corresponding products (**5ab** and **5ac**) in 75% and 61% yield, respectively.

The scope of conjugate 1,3-dienes with different substituents

Table 1 Optimization of reaction conditions^a

Entry	Catalyst	Solvent	Temp/°C	Yield ^b /%
1	$\text{Fe}(\text{OTf})_3$	THF	80	40 (2 : 1)
2	$\text{Mn}(\text{OAc})_2$	THF	80	Trace
3	MnBr_2	THF	80	Trace
4	$\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$	THF	80	Trace
5	$\text{Ni}(\text{acac})_2$	THF	80	Trace
6	CoBr_2	THF	80	Trace
7	CuBr	THF	80	4
8	$\text{Fe}(\text{acac})_3$	THF	80	4
9	FeCl_2	THF	80	10
10	$\text{Fe}(\text{OTf})_3$	THF	80	67 (2 : 1)
11	$\text{Fe}(\text{OTf})_3$	THF	60	65 (2 : 1)
12	$\text{Fe}(\text{OTf})_3$	THF	70	60 (2 : 1)
13	$\text{Fe}(\text{OTf})_3$	THF	90	63 (2 : 1)
14	$\text{Fe}(\text{OTf})_3$	THF	100	64 (2 : 1)
15	$\text{Fe}(\text{OTf})_3$	THF	80	74 (2 : 1) ^c

^a Reaction was conducted with 1,3-diene (**1a**) (0.5 mmol), alkyl diacyl peroxide (**2a**) (1 mmol), and catalyst (2 mol%) in THF (2.5 mL) at the stated temperature for 2 h under an N_2 atmosphere. ^b Yield of isolated product and ratio of *E* and *Z* (shown in parentheses). ^c **2a** was added in 3 equal portions at intervals of 15 min.

was studied as shown in Table 3. Conjugate 1,3-dienes with a chlorine on the benzene ring reacted with **2a**, delivering products **3ba** and **3ca** in high yields and with low *E/Z* values. A 1,3-diene containing an electron-donating group, such as methoxy group or methyl group, reacts with **2a** to give the corresponding products (**3da** and **3ea**) in 40% and 71% yields. Next, the reactions of different conjugate 1,3-dienes with peresters were investigated. Chlorine-substituted 1,3-dienes reacted with **4a** to deliver the corresponding products (**5ba** and **5ca**) in high yields. 1,3-Dienes with an electron-donating group gave the desired products (**5da** and **5ea**) with relatively low yields. Interestingly, presumably due to the steric hindrance effect, 1,3-dienes with a bromine offered the desired products (**5fa**~**5ha**) as single isomers, respectively.

To exemplify the synthetic applications of this method, the use of the reaction in the late-stage modification of bioactive compounds was examined (Scheme 2). The alkylation of exemestane, an aromatase inhibitor used in the treatment of breast cancer, delivered the modified product (**7**) in 69% yield with excellent regioselectivity. The exocyclic carbon-carbon double bond was found to be translocated into an internal position. This example demonstrates that the method is a useful means of functionalizing complex molecules at the late stage.

Based on the previous works^[5-10], an iron-catalyzed plausible mechanism involving a single electron-transfer is

Table 2 Scope of alkyl diacyl peroxides or peresters with 1,3-diene (**1a**)^a

^a Reaction was conducted with 1,3-diene (**1a**) (0.5 mmol), **2** or **4** (1 mmol), and $\text{Fe}(\text{OTf})_3$ (2 mol%) in THF (2.5 mL) at 80 °C for 2 h under an N_2 atmosphere.

Scheme 2 Late-stage functionalization of complex molecules**Table 3** Scope of 1,3-dienes^a

^a Reaction was conducted with 1,3-diene **1** (0.5 mmol), **2a** or **4a** (1 mmol), and $\text{Fe}(\text{OTf})_3$ (2 mol%) in THF (2.5 mL) at 80 °C for 2 h under an N_2 atmosphere.

proposed (Scheme 3). $\text{Fe}(\text{OTf})_3$ is reduced by an alkyl radical or a 1,3-diene to form an iron(II) species (**A**), which transfers an electron to a perester to afford an iron(III) species (**B**) and an alkyl radical. The alkyl radical reacts with a 1,3-diene to form a delocalized allylic carbon radical **C**, which can be oxidized by the iron(III) species (**B**) to produce a delocalized allylic carbocation (**D**) and regenerates the iron(II) (**A**). Upon deprotonation by a base, the carbocation (**D**) would deliver the desired product.

3 Conclusion

In conclusion, we have developed an iron-catalyzed decarboxylative alkylation of conjugate 1,3-dienes with alkyl

Scheme 3 A plausible mechanism

diacyl peroxides and *t*-butyl peresters. This is an efficient way to alkylate 1,3-dienes with good yields and in at least some cases, high selectivity. A moderate substrate scope was observed and the alkylation of bioactive compounds at a late stage was also achieved.

4 Experimental section

4.1 Instruments and agents

The thin-layer chromatography (TLC) plate was used to track the reaction, and the UV light waves are 254 and 365 nm. ^1H NMR and ^{13}C NMR were recorded on a Bruker advance 400 NMR spectrometer. All the reagent were purchased from commercially available sources, and the alkyl diacyl peroxides and *t*-butyl peresters were synthesized by our group.

4.2 Experiment method

A flame-dried flask with stir bar was charged with $\text{Fe}(\text{OTf})_3$ (5 mg, 2 mol%) in the glove box, sealed with a septum, and brought out of the glovebox. THF (2 mL) was added and then conjugate 1,3-diene (0.5 mmol) was added into the solution. Diacyl peroxide or perester (1 mmol) was added in 3 portions (interval time was 15 min). The reaction mixture was warmed to 80 °C gradually after the first portion was added. And then the reaction mixture stirred for 2 h after the last two portions was added. After completion as detected by TLC, the reaction mixture was cooled to ambient temperature and concentrated by rotary evaporation under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether) to yield the desired product.

((*E*)-6,6-Dimethylhepta-1,3-dien-1-yl)benzene (**3aa**): A clear liquid, 83 mg, 74% yield, *E* : *Z* = 2.0 : 1. ^1H NMR (600 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 7.42~7.35 (m, 2H), 7.33~7.26 (m, 2H), 7.23~7.17 (m, 1H), 7.08~7.02 (m, 0.31H), 6.79~6.72 (m, 0.69H), 6.56~6.33 (m, 1H), 6.24~6.12 (m, 1H), 5.87~5.76 (m, 0.69H), 5.59~5.48 (m, 0.29H), 2.20~2.14 (m, 0.62H), 2.06~

1.99 (m, 1.45H), 1.78~1.60 (m, 5H), 1.37~1.11 (m, 4H), 0.97~0.85 (m, 2H); ^{13}C NMR (151 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 137.77, 134.77, 132.14, 131.98, 131.56, 129.96, 129.53, 129.44, 128.67, 128.64, 127.39, 127.14, 126.41, 126.20, 124.75, 41.05, 38.50, 38.28, 35.90, 33.33, 33.28, 26.65, 26.46; MS (EI) m/z : 226.34 [M^+]. These data matches with the reported value.^[13]

((*E*)-Hexa-1,3-diene-1,6-diyl)dibenzene (**3ab**): A clear liquid, 96 mg, 82% yield, *E* : *Z* = 1.7 : 1. ^1H NMR (400 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 7.39~7.36 (m, 2H), 7.33~7.29 (m, 4H), 7.26~7.16 (m, 4H), 7.07~6.93 (m, 0.38H), 6.83~6.67 (m, 0.66H), 6.58~6.39 (m, 1H), 6.32~6.12 (m, 1H), 5.94~5.77 (m, 0.67H), 5.66~5.45 (m, 0.36H), 2.75~2.73 (t, *J* = 7.4 Hz, 2H), 2.67~2.56 (m, 0.7H), 2.54~2.41 (m, 1.3H); ^{13}C NMR (100 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 141.73, 137.56, 134.60, 132.42, 131.80, 131.08, 130.44, 129.28, 129.23, 128.58, 128.47, 128.37, 127.44, 127.19, 126.37, 126.18, 125.98, 125.90, 124.23, 35.92, 35.77, 34.72, 29.91. HRMS (EI^+) calcd for $\text{C}_{18}\text{H}_{18}$: 234.1409; found 234.1418.

((*E*)-Hepta-1,3-diene-1,7-diyl)dibenzene (**3ac**): A clear liquid, 100 mg, 80% yield, *E* : *Z* = 3 : 2. ^1H NMR (400 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 7.43~7.34 (m, 2H), 7.33~7.25 (m, 4H), 7.24~7.14 (s, 4H), 7.07~6.90 (m, 0.43H), 6.79~6.72 (m, 0.60H), 6.57~6.41 (m, 1H), 6.33~6.12 (m, 1H), 5.94~5.75 (m, 0.61H), 5.61~5.49 (m, 0.41H), 2.74~2.57 (t, *J* = 7.4, 2H), 2.35~2.27 (m, 0.8H), 2.25~2.14 (m, 1.2H), 1.85~1.69 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 142.36, 142.25, 137.61, 137.58, 135.29, 132.66, 132.15, 130.97, 130.17, 129.35, 129.20, 128.57, 128.49, 128.33, 127.39, 127.14, 126.36, 126.16, 125.75, 124.42, 35.41, 35.28, 32.40, 31.31, 31.01, 27.40. HRMS (EI^+) calcd for $\text{C}_{19}\text{H}_{20}$: 248.1565; found 248.1568.

((*E*)-6-Methylhepta-1,3-dien-1-yl)benzene (**3ad**): A clear liquid, 70 mg, 75% yield, *E* : *Z* = 4 : 1. ^1H NMR (400 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 7.43~7.35 (m, 2H), 7.34~7.25 (m, 2H), 7.23~7.16 (m, 1H), 7.12~6.99 (m, 0.20H), 6.83~6.69 (m, 0.79H), 6.63~6.38 (m, 1H), 6.27~6.12 (m, 1H), 5.89~5.72 (m, 0.8H), 5.60~5.49 (m, 0.2H), 2.21~2.07 (m, 0.67H), 2.03 (m, 1.30H), 1.72~1.63 (m, 0.7H), 1.48~1.42 (m, 0.35H), 1.01~0.84 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 137.72, 134.74, 132.13, 132.04, 131.64, 130.03, 129.49, 128.62, 128.59, 127.36, 127.11, 126.37, 126.17, 124.66, 42.34, 37.14, 28.90, 28.66, 22.49, 22.44. HRMS (EI^+) calcd for $\text{C}_{14}\text{H}_{18}$: 186.1409; found 186.1407.

((*E*)-6-Methylocta-1,3-dien-1-yl)benzene (**3ae**): A clear liquid, 71 mg, 71% yield, *E* : *Z* = 3 : 2. ^1H NMR (400 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 7.44~7.34 (m, 2H), 7.35~7.27 (m, 2H), 7.24~7.17 (m, 1H), 7.11~7.01 (m, 0.4H), 6.86~6.71 (m, 0.6H), 6.56~6.39 (m, 1H), 6.26~5.99 (m, 1H), 5.89~5.74 (m, 0.6H), 5.61~5.47 (m, 0.4H), 2.32~2.24 (m, 0.33H), 2.20~2.09 (m, 1H), 2.03~1.93 (m, 0.66H), 1.49~1.34 (m, 2H), 1.22~1.13 (m, 1H), 0.93~0.86 (m, 6H); ^{13}C NMR (100

MHz, CDCl₃, a mixture of *E* and *Z* isomers) δ : 137.70, 137.69, 134.70, 132.13, 131.95, 131.61, 129.89, 129.48, 129.43, 128.58, 128.54, 127.31, 127.05, 126.31, 126.12, 124.65, 40.04, 35.28, 34.99, 34.93, 29.25, 29.18, 19.22, 19.17, 11.59, 11.50. HRMS (EI⁺) calcd for C₁₅H₂₀: 200.1565; found 200.1569.

((1*E*)-6,8,8-Trimethylnona-1,3-dien-1-yl)benzene (**3af**): A clear liquid, 99 mg, 82% yield, *E* : *Z* = 2.3 : 1. ¹H NMR (400 MHz, CDCl₃, a mixture of *E* and *Z* isomers) δ : 7.43~7.34 (m, 2H), 7.34~7.25 (m, 2H), 7.23~7.14 (m, 1H), 7.10~7.01 (m, 0.3H), 6.82~6.68 (m, 0.7H), 6.57~6.37 (m, 1H), 6.29~6.09 (m, 1H), 5.88~5.72 (m, 0.7H), 5.63~5.45 (m, 0.3H), 2.32~2.21 (m, 0.3H), 2.19~2.08 (m, 1H), 2.06~1.94 (m, 0.7H), 1.72~1.54 (m, 1H), 1.32~1.25 (m, 1H), 1.10~1.00 (m, 1H), 0.97~0.88 (m, 12H); ¹³C NMR (100 MHz, CDCl₃, a mixture of *E* and *Z* isomers) δ : 137.70, 134.80, 132.28, 132.01, 131.78, 129.97, 129.51, 129.48, 128.59, 128.56, 127.32, 127.08, 126.32, 126.14, 124.70, 50.66, 50.54, 42.80, 37.60, 31.16, 30.18, 30.08, 29.80, 22.65, 22.60. HRMS (EI⁺) calcd for C₁₈H₂₆: 242.2035; found 242.2039.

((1*E*)-8-Chloroocta-1,3-dien-1-yl)benzene (**3ag**): A clear liquid, 95 mg, 86% yield, *E* : *Z* = 2.2 : 1. ¹H NMR (400 MHz, CDCl₃, a mixture of *E* and *Z* isomers) δ : 7.44~7.35 (m, 2H), 7.35~7.26 (m, 2H), 7.25~7.17 (m, 1H), 7.09~6.98 (m, 0.31H), 6.80~6.68 (m, 0.69H), 6.60~6.37 (m, 1H), 6.37~5.98 (m, 1H), 5.88~5.69 (m, 0.69H), 5.56~5.41 (m, 0.31H), 3.66~3.36 (m, 2H), 2.35~2.23 (m, 0.6H), 2.21~2.16 (m, 1.4H), 1.89~1.74 (m, 2H), 1.67~1.55 (m, 2H); ¹³C NMR (100 MHz, CDCl₃, a mixture of *E* and *Z* isomers) δ : 137.53, 134.69, 132.49, 132.07, 131.14, 130.43, 129.36, 129.15, 128.61, 128.57, 127.48, 127.20, 126.36, 126.17, 124.11, 44.96, 32.09, 32.06, 32.03, 27.18, 26.88, 26.50. HRMS (EI⁺) calcd for C₁₄H₁₇Cl: 220.1019; found 220.1025.

((1*E*)-5-Cyclopentylpenta-1,3-dien-1-yl)benzene (**3ah**): A clear liquid, 77 mg, 73% yield, *E* : *Z* = 2.2 : 1. ¹H NMR (600 MHz, CDCl₃, a mixture of *E* and *Z* isomers) δ : 7.42~7.35 (m, 2H), 7.33~7.27 (m, 2H), 7.23~7.16 (m, 1H), 7.09~7.01 (m, 0.17H), 6.78~6.71 (m, 0.83H), 6.55~6.40 (m, 1H), 6.22~6.14 (m, 1H), 5.86~5.79 (m, 0.83H), 5.59~5.52 (m, 0.16H), 2.32~2.24 (m, 0.47H), 2.17~2.11 (m, 1.73H), 1.93~1.85 (m, 1H), 1.80~1.71 (m, 2H), 1.66~1.47 (m, 4H), 1.19~1.12 (m, 2H); ¹³C NMR (151 MHz, CDCl₃, a mixture of *E* and *Z* isomers) δ : 137.76, 135.53, 132.81, 131.98, 130.97, 129.99, 129.60, 128.92, 128.66, 128.63, 127.14, 126.40, 126.20, 124.69, 40.41, 40.06, 39.38, 32.41, 25.25; MS (EI) *m/z*: 212.31 [M⁺]. HRMS (FI) calcd for C₁₆H₂₀: 212.1563; found 212.1560.

(1*S*,3*S*)-1-((4*E*)-5-Phenylpenta-2,4-dien-1-yl)adamantane (**3ai**): A clear liquid, 110 mg, 79% yield, *E* : *Z* = 3.2 : 1. ¹H NMR (600 MHz, CDCl₃, a mixture of *E* and *Z* isomers) δ : 7.42~7.35 (m, 2H), 7.33~7.26 (m, 2H), 7.23~7.16 (m, 1H), 7.08~7.02 (m, 0.26H), 6.81~6.73 (m, 0.78H), 6.54~6.39 (m, 1H), 6.29~6.12 (m, 1H), 5.88~5.81 (m, 0.77H), 5.63~5.57 (m, 0.22H), 2.06~2.02 (m, 0.61H), 1.96~1.92 (m, 3H), 1.91~1.87 (m, 1.59H), 1.70~1.59

(m, 6H), 1.53~1.47 (m, 6H); ¹³C NMR (151 MHz, CDCl₃, a mixture of *E* and *Z* isomers) δ : 137.75, 132.74, 132.14, 132.08, 130.49, 129.99, 129.53, 129.31, 128.66, 128.63, 127.14, 126.42, 126.20, 124.78, 48.10, 42.61, 42.56, 37.18, 33.62, 28.84. HRMS (FI) calcd for C₂₁H₂₆: 278.2028; found 278.2029.

((1*E*)-Pentadeca-1,3-dien-1-yl)benzene (**3aj**): A clear liquid, 99 mg, 70% yield, *E* : *Z* = 2.1 : 1. ¹H NMR (600 MHz, CDCl₃, a mixture of *E* and *Z* isomers) δ : 7.42~7.35 (m, 2H), 7.32~7.27 (m, 2H), 7.23~7.16 (m, 1H), 7.09~7.02 (m, 0.21H), 6.78~6.71 (m, 0.75H), 6.54~6.38 (m, 1H), 6.23~6.11 (m, 1H), 5.86~5.79 (m, 0.74H), 5.56~5.49 (m, 0.20H), 2.32~2.24 (m, 0.50H), 2.16~2.08 (m, 1.65H), 1.44~1.37 (m, 2H), 1.32~1.22 (m, 16H), 0.90~0.84 (m, 3H); ¹³C NMR (151 MHz, CDCl₃, a mixture of *E* and *Z* isomers) δ : 137.76, 136.22, 131.97, 130.52, 129.95, 129.58, 128.71, 128.66, 128.63, 127.39, 127.13, 126.39, 126.19, 124.60, 33.00, 32.03, 29.81, 29.79, 29.75, 29.72, 29.63, 29.47, 29.40, 29.34, 22.81, 14.25. HRMS (FI) calcd for C₂₁H₃₂: 284.2494; found 284.2499.

1-Chloro-3-((1*E*)-6,6-dimethylhepta-1,3-dien-1-yl)benzene (**3ba**): A clear liquid, 99 mg, 85% yield, *E* : *Z* = 2 : 1. ¹H NMR (400 MHz, CDCl₃, a mixture of *E* and *Z* isomers) δ : 7.37 (d, *J* = 11.0 Hz, 1H), 7.27~7.20 (m, 2H), 7.20~7.13 (m, 1H), 7.09~7.00 (m, 0.37H), 6.86~6.68 (m, 0.66H), 6.50~6.32 (m, 1H), 6.32~6.08 (m, 1H), 5.94~5.79 (m, 0.66H), 5.71~5.60 (m, 0.35H), 2.19~2.17 (d, *J* = 8.0 Hz, 0.69H), 2.03~2.01 (d, *J* = 7.7 Hz, 1.31H), 0.95 (s, 3H), 0.91 (s, 6H); ¹³C NMR (100 MHz, CDCl₃, a mixture of *E* and *Z* isomers) δ : 139.63, 134.50, 134.38, 132.21, 131.51, 130.83, 130.65, 129.83, 129.78, 129.74, 128.53, 127.19, 126.95, 126.03, 125.92, 125.87, 124.62, 124.34, 47.49, 41.91, 31.65, 31.49, 29.39. HRMS (EI⁺) calcd for C₁₅H₁₉Cl: 234.1175; found 234.1171.

1-Chloro-4-((1*E*)-6,6-dimethylhepta-1,3-dien-1-yl)benzene (**3ca**): A clear liquid, 95 mg, 81% yield, *E* : *Z* = 2.3 : 1. ¹H NMR (400 MHz, CDCl₃, a mixture of *E* and *Z* isomers) δ : 7.35~7.23 (m, 4H), 7.08~6.96 (m, 0.3H), 6.81~6.69 (m, 0.7H), 6.52~6.34 (m, 1H), 6.29~6.06 (m, 1H), 5.95~5.82 (m, 0.7H), 5.71~5.56 (m, 0.3H), 2.18~2.16 (d, *J* = 8.1 Hz, 0.59H), 2.03~2.01 (d, *J* = 7.7 Hz, 1.44H), 0.95 (s, 2.7H), 0.91 (s, 6.3H); ¹³C NMR (100 MHz, CDCl₃, a mixture of *E* and *Z* isomers) δ : 136.19, 133.83, 132.55, 132.32, 130.97, 130.80, 130.03, 129.93, 128.70, 127.47, 127.26, 125.12, 47.48, 41.90, 31.63, 31.47, 29.37. HRMS (EI⁺) calcd for C₁₅H₁₉: 234.1175; found 234.1183.

1-((1*E*)-6,6-Dimethylhepta-1,3-dien-1-yl)-2-methoxybenzene (**3da**): A clear liquid, 46 mg, 40% yield, *E* : *Z* = 3.2 : 1. ¹H NMR (400 MHz, CDCl₃, a mixture of *E* and *Z* isomers) δ : 7.43~7.37 (m, 1H), 7.12~7.09 (m, 1H), 7.07~6.94 (m, 0.28H), 6.89~6.81 (m, 1H), 6.79~6.77 (d, *J* = 8.0 Hz, 1H), 6.73~6.71 (m, 1.45H), 6.25~6.11 (m, 1H), 5.79~5.72 (m, 0.77H), 5.53~5.47 (m, 0.24H), 3.78 (s, 3H), 2.11~2.09 (d, *J* = 8.1 Hz, 0.53H), 1.95~1.93 (d, *J* = 7.7 Hz, 1.59H), 0.87 (s, 2.26H), 0.84 (s, 6.79H); ¹³C NMR (100 MHz, CDCl₃, a mixture of *E* and *Z* isomers) δ :

156.58, 133.38, 132.43, 130.94, 130.15, 129.65, 128.32, 128.07, 126.72, 126.67, 126.38, 126.22, 125.31, 124.78, 120.66, 110.88, 110.83, 67.99, 55.47, 47.49, 41.86, 31.46, 29.38, 25.63. HRMS (EI^+) calcd for $\text{C}_{16}\text{H}_{22}\text{O}$: 230.1671; found 230.1666.

1-((1*E*)-6,6-Dimethylhepta-1,3-dien-1-yl)-4-methylbenzene (**3ea**): A clear liquid, 76 mg, 71% yield, $E : Z = 2.3 : 1$. ^1H NMR (400 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 7.31~7.26 (m, 2H), 7.12~7.09 (m, 2H), 7.04~7.00 (m, 0.3H), 6.76~6.69 (m, 0.7H), 6.52~6.39 (m, 1H), 6.24~6.13 (m, 1H), 5.87~5.78 (m, 0.7H), 5.60~5.50 (m, 0.3H), 2.32 (s, 3H), 2.18~2.16 (d, $J=8.0$ Hz, 0.55H), 2.02~2.00 (d, $J=7.7$ Hz, 1.45H), 0.94 (s, 2.80H), 0.91 (s, 6.20H); ^{13}C NMR (100 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 137.18, 136.90, 134.96, 134.90, 132.75, 132.44, 132.14, 130.36, 130.07, 129.69, 129.32, 129.30, 128.52, 126.27, 126.07, 123.72, 47.51, 41.88, 31.65, 31.48, 29.40, 21.25. HRMS (EI^+) calcd for $\text{C}_{16}\text{H}_{22}$: 214.1722; found 214.1723.

((1*E*)-4-Cyclopentylbuta-1,3-dien-1-yl)benzene (**5aa**): A clear liquid, 72 mg, 73% yield, $E : Z = 1.9 : 1$. ^1H NMR (400 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 7.43~7.33 (m, 2H), 7.31~7.26 (m, 2H), 7.22~7.15 (m, 1H), 7.12~7.05 (m, 0.35H), 6.81~6.68 (m, 0.65H), 6.55~6.38 (m, 1H), 6.25~6.04 (m, 1H), 5.88~5.71 (m, 0.65H), 5.53~5.38 (m, 0.29H), 3.02~2.96 (m, 0.3H), 2.55~2.49 (m, 0.7H), 1.89~1.77 (m, 2H), 1.73~1.54 (m, 4H), 1.39~1.26 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 140.62, 138.72, 137.77, 131.85, 129.95, 129.57, 128.68, 128.59, 128.56, 127.40, 127.30, 127.05, 126.33, 126.14, 124.84, 43.69, 39.02, 34.07, 33.27, 25.51, 25.26. HRMS (EI^+) calcd for $\text{C}_{15}\text{H}_{18}$: 198.1409; found 198.1410.

((1*E*)-5-Ethylhepta-1,3-dien-1-yl)benzene (**5ab**): A clear liquid, 75 mg, 75% yield, $E : Z = 3 : 1$. ^1H NMR (400 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 7.41~7.34 (m, 2H), 7.31~7.26 (m, 2H), 7.21~7.15 (m, 1H), 7.10~6.98 (m, 0.23H), 6.81~6.69 (m, 0.76H), 6.55~6.40 (m, 1H), 6.30~6.09 (m, 1H), 5.62~5.48 (m, 0.75H), 5.31~5.16 (m, 0.25H), 2.49~2.35 (m, 0.2H), 1.92~1.81 (m, 0.8H), 1.51~1.40 (m, 2H), 1.33~1.24 (m, 2H), 0.91~0.82 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 140.25, 138.17, 137.79, 137.76, 131.94, 130.63, 129.86, 129.63, 129.20, 128.60, 128.57, 127.29, 127.06, 126.33, 126.14, 125.19, 46.64, 41.56, 28.37, 27.78, 11.98, 11.88. HRMS (EI^+) calcd for $\text{C}_{15}\text{H}_{20}$: 200.1565; found 200.1573.

((1*E*)-5-Propylocta-1,3-dien-1-yl)benzene (**5ac**): A clear liquid, 70 mg, 61% yield, $E : Z = 4 : 1$. ^1H NMR (400 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 7.42~7.35 (m, 2H), 7.32~7.26 (m, 2H), 7.21~7.15 (m, 1H), 7.08~6.96 (m, 0.2H), 6.81~6.71 (m, 0.8H), 6.57~6.39 (m, 1H), 6.28~6.07 (m, 1H), 5.68~5.46 (m, 0.8H), 5.28~5.18 (m, 0.2H), 2.57~2.43 (m, 0.18H), 2.02~1.86 (m, 0.82H), 1.50~1.38 (m, 2H), 1.33~1.21 (m, 6H), 0.92~0.83 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 140.62, 138.53, 137.74, 131.91, 130.41,

129.82, 129.62, 128.93, 128.61, 128.57, 127.29, 127.06, 126.32, 126.13, 125.14, 44.96, 39.86, 35.38, 34.85, 29.72, 29.68, 28.72, 28.20, 22.98, 22.94, 14.18, 12.00, 11.89. HRMS (EI^+) calcd for $\text{C}_{17}\text{H}_{24}$: 228.1878; found 228.1880.

1-Chloro-3-((1*E*)-5-ethylnona-1,3-dien-1-yl)benzene (**5ba**): A clear liquid, 111 mg, 85% yield, $E : Z = 3 : 1$. ^1H NMR (400 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 7.37~7.34 (m, 1H), 7.25~7.19 (m, 2H), 7.18~7.13 (m, 1H), 7.06~6.98 (m, 0.25H), 6.82~6.66 (m, 0.75H), 6.48~6.31 (m, 1H), 6.24~6.08 (m, 1H), 5.68~5.52 (m, 0.75H), 5.36~5.22 (m, 0.25H), 2.53~2.44 (m, 0.2H), 2.00~1.89 (m, 0.8H), 1.49~1.38 (m, 2H), 1.31~1.20 (m, 6H), 0.91~0.84 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 141.84, 139.68, 139.65, 134.54, 134.51, 131.00, 130.42, 130.00, 129.77, 129.72, 128.53, 128.26, 127.12, 126.88, 126.38, 125.99, 125.91, 124.58, 124.28, 44.95, 39.91, 35.29, 34.75, 29.68, 29.64, 28.64, 28.11, 22.96, 22.90, 14.13, 11.94, 11.84. HRMS (EI^+) calcd for $\text{C}_{17}\text{H}_{23}\text{Cl}$: 262.1488; found 262.1494.

Chloro-4-((1*E*)-5-ethylnona-1,3-dien-1-yl)benzene (**5ca**): A clear liquid, 118 mg, 90% yield, $E : Z = 4 : 1$. ^1H NMR (400 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 7.32~7.18 (m, 4H), 7.04~6.94 (m, 0.2H), 6.84~6.63 (m, 0.8H), 6.49~6.30 (m, 1H), 6.25~6.04 (m, 1H), 5.68~5.45 (m, 0.8H), 5.31~5.19 (m, 0.2H), 2.55~2.40 (m, 0.2H), 1.99~1.90 (m, 0.8H), 1.48~1.37 (m, 2H), 1.31~1.20 (m, 6H), 0.89~0.83 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 141.29, 139.13, 136.28, 136.26, 132.76, 132.51, 130.58, 130.20, 130.13, 128.73, 128.70, 128.65, 128.46, 127.43, 127.23, 125.64, 44.96, 39.88, 35.29, 34.77, 29.68, 29.65, 28.64, 28.13, 22.94, 22.90, 14.13, 11.95, 11.85. HRMS (EI^+) calcd for $\text{C}_{17}\text{H}_{23}$: 262.1488; found 262.1487.

1-((1*E*)-5-Ethylnona-1,3-dien-1-yl)-2-methoxybenzene (**5da**): A clear liquid, 77 mg, 60% yield, $E : Z = 4 : 1$. ^1H NMR (400 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 7.48~7.44 (m, 1H), 7.18~7.14 (m, 1H), 7.10~7.01 (m, 0.22H), 6.96~6.82 (m, 2.32H), 6.80~6.76 (m, 1.46H), 6.32~6.11 (m, 1H), 5.63~5.43 (m, 0.79H), 5.28~5.12 (m, 0.21H), 3.84 (s, 3H), 2.57~2.41 (m, 0.2H), 2.02~1.87 (m, 0.8H), 1.49~1.35 (m, 2H), 1.32~1.15 (m, 6H), 0.92~0.82 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 156.57, 139.95, 137.88, 131.17, 130.33, 129.63, 128.25, 128.01, 126.86, 126.74, 126.47, 126.40, 126.21, 125.90, 124.48, 120.67, 110.88, 110.81, 55.46, 44.89, 39.77, 35.38, 34.85, 29.69, 29.64, 28.73, 28.20, 22.93, 22.90, 14.14, 11.97, 11.86. HRMS (EI^+) calcd for $\text{C}_{18}\text{H}_{26}\text{O}$: 258.1984; found 258.1994.

1-((1*E*)-5-Ethylnona-1,3-dien-1-yl)-4-methylbenzene (**5ea**): A clear liquid, 61 mg, 50% yield, $E : Z = 3.4 : 1$. ^1H NMR (400 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 7.22~7.16 (m, 2H), 7.04~7.00 (m, 2H), 6.93~6.87 (m, 0.23H), 6.70~6.54 (m, 0.77H), 6.46~6.28 (m, 1H), 6.19~6.01 (m, 1H), 5.58~5.36 (m, 0.77H), 5.21~5.03 (m, 0.23H), 2.44~2.37 (m, 0.2H), 2.25 (s, 3H), 1.92~1.79 (m, 0.8H), 1.41~1.30 (m, 2H), 1.24~1.13 (m, 6H), 0.84~0.77 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3 , a mixture of *E* and *Z* isomers) δ : 140.62, 138.53, 137.74, 131.91, 130.41,

ture of *E* and *Z* isomers) δ : 139.97, 137.92, 137.10, 136.81, 135.02, 134.96, 131.85, 130.49, 129.77, 129.30, 129.27, 129.01, 128.68, 126.22, 126.03, 124.25, 44.91, 39.79, 35.36, 34.85, 29.69, 29.65, 28.71, 28.20, 22.96, 22.91, 21.22, 14.14, 11.95, 11.85. HRMS (EI^+) calcd for $\text{C}_{18}\text{H}_{26}$: 242.2035; found 242.2033.

((1*Z*,3*E*)-2-Bromo-5-ethylnona-1,3-dien-1-yl)benzene (**5fa**): A clear liquid, 128 mg, 71% yield. ^1H NMR (400 MHz, CDCl_3) δ : 7.66~7.64 (d, $J=7.2$ Hz, 2H), 7.36~7.33 (m, 2H), 7.30~7.26 (m, 1H), 6.86 (s, 1H), 6.18~6.14 (d, $J=14.6$ Hz, 1H), 6.01~5.96 (dd, $J=14.6, 9.0$ Hz, 1H), 2.08~1.99 (m, 1H), 1.51~1.44 (m, 2H), 1.34~1.25 (m, 6H), 0.92~0.87 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ : 141.54, 136.07, 130.24, 129.43, 128.06, 127.79, 123.74, 44.54, 34.76, 29.65, 28.13, 22.87, 14.12, 11.88. HRMS (EI^+) calcd for $\text{C}_{17}\text{H}_{23}\text{Br}$: 306.0983; found 306.0993.

1-((1*Z*,3*E*)-2-Bromo-5-ethylnona-1,3-dien-1-yl)-4-fluorobenzene (**5ga**): A clear liquid, 118 mg, 73% yield. ^1H NMR (600 MHz, Chloroform-*d*) δ : 7.67~7.61 (m, 2H), 7.06~7.01 (m, 2H), 6.81 (s, 1H), 6.14 (d, $J=14.6$ Hz, 1H), 5.97 (dd, $J=14.6, 9.1$ Hz, 1H), 2.08~2.00 (m, 1H), 1.53~1.41 (m, 2H), 1.35~1.25 (m, 6H), 0.91~0.83 (m, 6H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ : 162.17 (d, $J=248.4$ Hz), 141.77, 132.19 (d, $J=3.4$ Hz), 131.26 (d, $J=8.0$ Hz), 130.13, 128.34, 123.75, 115.16 (d, $J=21.7$ Hz), 44.64, 34.84, 29.73, 28.21, 22.94, 14.20, 11.97; MS (EI) m/z : 324.25 [$\text{M}]^+$.

1-((1*Z*,3*E*)-2-Bromo-5-ethylnona-1,3-dien-1-yl)-4-chlorobenzene (**5ha**): A clear liquid, 119 mg, 70% yield. ^1H NMR (600 MHz, Chloroform-*d*) δ : 7.64~7.55 (m, 2H), 7.35~7.28 (m, 2H), 6.80 (s, 1H), 6.14 (d, $J=14.6$ Hz, 1H), 5.99 (dd, $J=14.6, 9.1$ Hz, 1H), 2.09~2.01 (m, 1H), 1.51~1.43 (m, 2H), 1.37~1.24 (m, 6H), 0.92~0.81 (m, 6H); ^{13}C NMR (151 MHz, Chloroform-*d*) δ : 142.23, 134.57, 133.56, 130.76, 130.13, 128.37, 128.24, 124.47, 44.67, 34.82, 29.73, 28.19, 22.94, 14.21, 11.98; MS (EI) m/z : 340.22 [$\text{M}]^+$.

(8*R*,9*S*,10*R*,13*S*,14*S*)-6-Isopentyl-10,13-dimethyl-9,10,11,12,13,14,15,16-octahydro-3*H*-cyclopenta[*a*]phenanthrene-3,17(8*H*)-dione (**7**): A clear liquid, 121 mg, 69% yield. ^1H NMR (400 MHz, CDCl_3) δ : 7.09 (d, $J=8.0$ Hz, 1H), 6.30 (d, $J=12.0$ Hz, 1H), 6.24 (s, 1H), 5.87 (s, 1H), 2.56~2.50 (m, 1H), 2.43~2.38 (m, 2H), 2.24~2.09 (m, 3H), 1.93~1.90 (m, 2H), 1.75~1.64 (m, 2H), 1.60~1.42 (m, 3H), 1.35~1.29 (m, 3H), 1.19 (s, 3H), 1.00 (s, 3H), 0.92 (t, $J=8.0$ Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3) δ : 219.24, 186.48, 162.12, 153.66, 137.26, 131.48, 127.69, 121.64, 49.03, 48.80, 47.76, 41.26, 37.82, 37.25, 35.57, 31.28, 30.53, 28.03, 22.66, 22.33, 21.43, 21.39, 20.17, 13.84. HRMS (EI^+) calcd for $\text{C}_{24}\text{H}_{32}\text{O}_2$: 352.2402; found 352.2405.

Supporting Information ^1H NMR and ^{13}C NMR spectra of compounds **3**, **4**, and **7**. The Supporting Information is available free of charge via the Internet at <http://sioc-journal.cn/>.

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(Li, L.; Fan, Y.)