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Article

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Construction of Complex Bisether-bridged Medium-sized Cyclic Compounds from *o*-(1-(Acyloxy)propargyl)benzaldehydes under Base and Acid Catalysis

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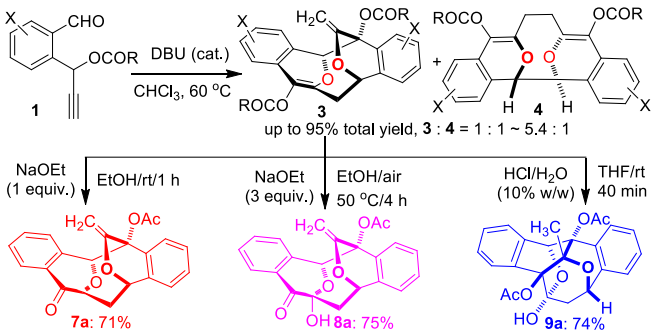


ABSTRACT: We report herein our serendipitous discovery of the rapid and straightforward accesses to unprecedented diverse complex molecular structures from readily available starting materials. Catalyzed by 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) under mild conditions, *o*-(1-(acyloxy)propargyl)benzaldehydes **1** underwent efficient and selective dimerization reactions to produce novel complex bisether-bridged tricyclic products **3** and **4**. The reactions proceeded most probably through dimerizations between 3-methylene-3*H*-isochromene intermediate and its zwitterionic resonance structures which were generated from a concerted 6-π electrocyclic ring closure reaction from the initially formed (2-formylphenyl)allene intermediates derived directly from *o*-(1-(acyloxy)propargyl)benzaldehydes. Treatment of the resulting product simply with NaOEt in ethanol and aqueous HCl, respectively, enabled further development of complex molecular diversities.

INTRODUCTION

Rapid construction of complex molecules of novel bridge bicyclic and tricyclic structures is attractive and important as the creation of diverse three-dimensional molecular entities would provide great opportunity for the discovery of promising drug leads, biological probes and functional materials. Ether-bridged medium rings, for instance, constitute the core skeletons of a large number of naturally occurring products including austroliolide (I),[1] badgerin (II),[1] abyssomicin C (III)[2] and abyssomicin 2 (IV),[2] which possess attractive antibacterial and antiviral activities. The synthetic ether-bridged bicyclic structures such as compound **V** is a potent HIV-1 inhibitor[3] while **VI-VIII** exhibit sedative and analgesic effects in central nervous system[4] (Figure 1). Synthesis of the ether-bridged medium ring-bearing natural and unnatural compounds still remains a formidable challenge. Tedious multistep reactions employing expensive catalysts and reagents under harsh conditions are usually required. We report herein our serendipitous discovery of an efficient and practical protocol to synthesize unprecedented ether-bridged tricyclic medium ring compounds from a very convenient DBU-catalyzed one-pot dimerization of readily available o-(1-(acyloxy)propargyl)benzaldehydes under very mild conditions.

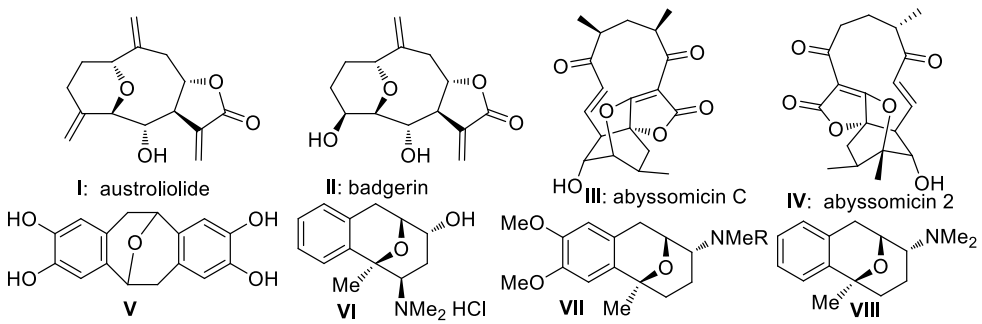


Figure 1. Structures of selected bioactive compounds which contain ether-bridged medium rings.

o-(1-(Acyloxy)propargyl)benzaldehydes are prepared conveniently from commercially available *o*-bromobenzaldehydes and ethynyl Grignard reagent.[5] Despite their multifunctionality and easy availability, *o*-(1-(acyloxy)propargyl)benzaldehydes have been used only scarcely in organic synthesis.[5-7] In a 2010 paper, Liu reported a gold-catalyzed reaction of *o*-(1-acyloxy-2-propynyl)benzaldehydes with vinyl ethers, which proceeded through a formal [4 + 2] cycloaddition between s-*trans*-methylene(vinyl)oxonium intermediate and electron-rich alkenes to produce 5,6,7,10-tetrahydro-5,9-epoxybenzo[8]annulene derivatives.[6] The other documented application is the synthesis of indeno[1,2-*b*]quinolines from the reaction between *o*-(1-acyloxy-2-propynyl)benzaldehydes and anilines based on Povarov reaction.[7]

To continue our recent endeavors in developing new reactions by means of N-heterocyclic carbene and transition metal cascade catalysis,[8] we attempted initially the reaction of *o*-(1-(acetyloxy)propargyl)benzaldehyde **1a** with *N*-boc-phenylimine. Upon the treatment of an NHC catalyst which was generated in situ from the interaction of a triazolium salt and DBU, the reaction of **1a** and imine gave no anticipated azabenzoin product. Occasionally, two product spots were observed on TLC plate, and they were separated by means of silica gel column chromatography. To our surprise and pleasure, two products **3a** and **4a**, whose molecular structures were determined unambiguously with various spectroscopy and X-ray crystallography, were stunning bis-ether-bridged tricyclic compounds (Figure 2). Evidently, they were resulted from distinct dimerization reactions of **1a**.

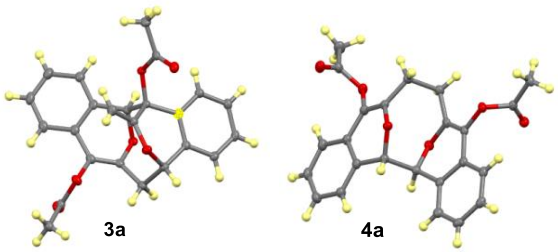


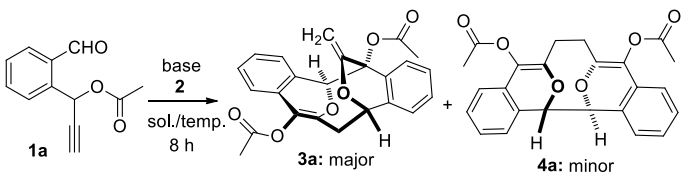
Figure 2. X-ray molecular structures of products **3a** and **4a.** The ellipsoid contour probability level is 50%.

RESULTS AND DISCUSSION

To establish the method for the synthesis of complex bis-ether-bridged medium ring compounds, we started optimization of reaction conditions. After excluding the involvement of N-heterocyclic carbene as the catalyst, we then focused on the base-promoted dimerization reactions of **1a**. In the presence of one equivalent of DBU, reactant **1a** at ambient temperature (~ 25 °C) in dichloromethane (DCM) was transformed within 8 h into 16-methylene-6,14-epoxy-8,13-(epoxymethano)dibenzo[*a*,*e*][10]annulene-5,13-diacetate **3a** and 6,16:9,15-diepoxydibenzo[*a*,*e*][12]annulene-5,10-diacetate **4a** in a total yield of 56% with a **3a : 4a** ratio being 4.6 : 1 (Table 1, entry 1). Both chemical yield and selectivity were slightly improved when DBU was decreased to 50 mol% and 30 mol% (Table 1, entries 2 and 3). DBU-catalyzed reaction of **1a** with a 30 mol % catalyst loading at 40 °C in DCM led to an even better conversion in terms of efficiency and selectivity (Table 1, entry 4). It should be addressed that other organic and inorganic bases including DBN, TDB, DIPEA, DABCO, TMG (tetramethylguanidine), Cs_2CO_3 and *t*-BuOK were not effective to catalyze dimerization reaction (Table 1, entries 5-11). Noticeably, while it did not influence the total chemical yields considerably, the reaction media did change the selectivity of dimerization reaction. For example, the combined

yields for **3a** and **4a** remained comparable when DCM was replaced by chloroform, 1,2-dichloroethane (DCE), toluene, THF, acetone and acetonitrile, the ratio of **3a** over **4a** varied between 6.6 : 1 to 3.2 : 1 with toluene as the least favorably solvent to give the lowest selectivity (Table 1, entries 12 – 17). To our delight, the total chemical yield increased significantly to 91% with the selectivity remaining at a satisfactory level (**3a : 4a** = 5.2 : 1) when the DBU-catalyzed dimerization of **1a** was conducted at 60 °C in chloroform (Table 1, entry 18). Further increase of reaction temperature to 80 °C in DCE, however, did not have a beneficial effect (Table 1, entry 19).

Table 1. Development of DBU-catalyzed dimerization reactions.[a]



Entry	Base	Mol %	solvent	Temp. (°C)	yield of **3a+4a** (%)[c]	**3a** : **4a**[d]
1	DBU	100	CH_2Cl_2	rt	56	4.6 : 1
2	DBU	50	CH_2Cl_2	rt	65	5 : 1
3	DBU	30	CH_2Cl_2	rt	67	5.6 : 1
4	DBU	30	CH_2Cl_2	40	83	6 : 1
5	DBN[b]	30	CH_2Cl_2	40	13	
6	TBD[b]	30	CH_2Cl_2	40	trace	
7	DIPEA	30	CH_2Cl_2	40	--	
8	DABCO	30	CH_2Cl_2	40	--	
9	TMG[b]	30	CH_2Cl_2	40	trace	
10	Cs_2CO_3	30	CH_2Cl_2	40	16	
11	*t*-BuOK	30	CH_2Cl_2	40	22	
12	DBU	30	$CHCl_3$	40	84	5.8 : 1
13	DBU	30	DCE	40	80	6.6 : 1
14	DBU	30	THF	40	76	3.6 : 1
15	DBU	30	toluene	40	73	3.2 : 1
16	DBU	30	CH_3CN	40	74	5.8 : 1
17	DBU	30	Me_2CO	40	67	4.8 : 1
18	DBU	30	$CHCl_3$	60	91	5.2 : 1

19	DBU	30	DCE	80	80	5.4 : 1

[a] A mixture of **1a** (0.5 mmol) and base in solvent (10 mL) was stirred for 8 h at a specified temperature.

[b] DBN = 2,3,4,6,7,8-hexahydropyrrolo[1,2-*a*]pyrimidine;

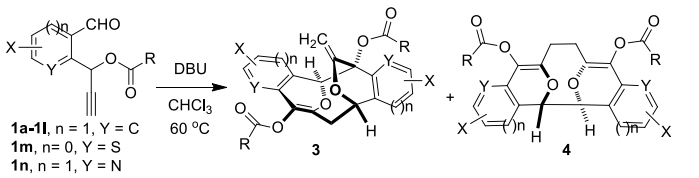
TBD = 2,3,4,6,7,8-hexahydro-1H-pyrimido[1,2-*a*]pyrimidine; TMG = tetramethylguanidine.

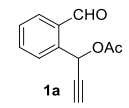
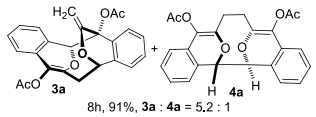
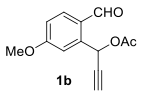
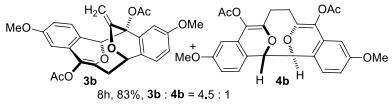
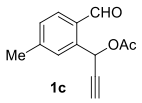
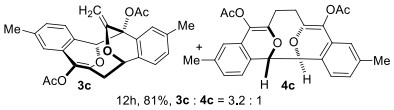
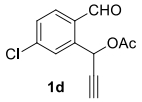
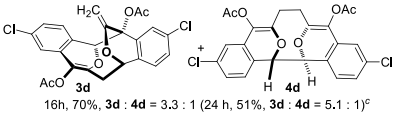
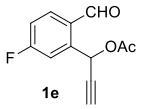
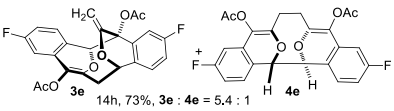
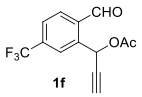
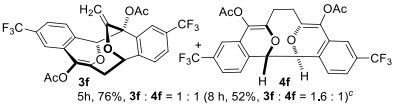
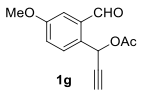
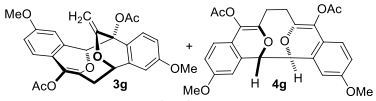
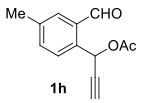
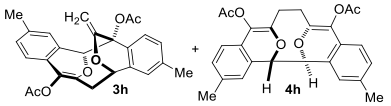
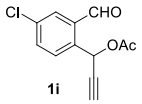
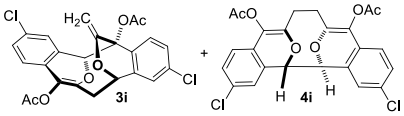
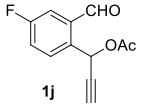
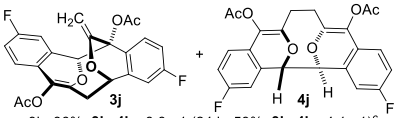
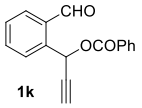
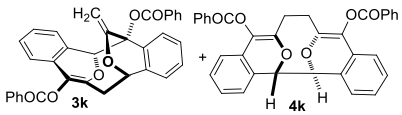
[c] Isolated yields. [d] Determined by ^{1}H NMR in the mixture of products.

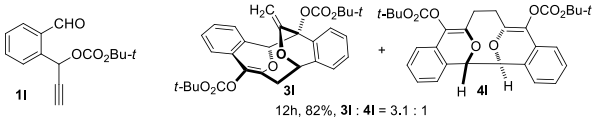
We prepared various *o*-(1-(acyloxy)propargyl)benzaldehyde substrates **1** to assess the scope of dimerization reaction under DBU catalysis (Table 2). It was found that this base-catalyzed reaction tolerated both electron-donating and electron-withdrawing groups on the aromatic ring of benzaldehydes. As summarized in Table 2, irrespective of the electronic nature of the substituent X, all substrates tested underwent transformations to afford the corresponding bis-ether-bridged tricyclic products **3** and **4**. The reactivity and efficiency of transformations were, however, governed by the electronic nature and substitution pattern of the substituents. 2-(1-(Acetyloxy)propargyl)benzaldehydes **1b-f** which bear either an electron-donating group or an electron-withdrawing substituent at *para*-position of carbonyl underwent efficient dimerizations within 5-16 h to afford products **3** and **4** in 70-83% total yields (Table 2, entries 2-6). In the case of *meta*-substituted 2-(1-(acetyloxy)propargyl)benzaldehyde substrates **1g-1j**, replacement of an electron-withdrawing group such as chloro and fluoro by an electron-donating methoxy and methyl group resulted in the decrease of reactivity. A longer reaction time was required and lower chemical yields were observed for the reactions of **1g** and **1h** (24-36 h, 69-75% total yields) than that of **1i** and **1j** (8-9 h, 83-86% total yields) (Table 2, entries 7-10). It is worth noting that in comparison to the substituent dependence on reactivity, substituents exhibited a much more pronounced effect on selectivity or the reaction pathways. For example, when reacting at 60 ^{o}C, substrate **1a** along with its 4-methoxy (**1b**), 4-fluoro (**1e**) and 5-chloro (**1i**) containing analogs yielded products **3** and **4** in a ratio around 5 : 1 (Table 2, entries 1, 2, 5 and 9). On the contrary,

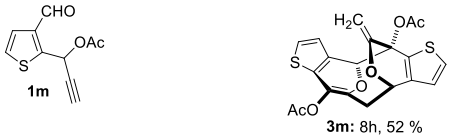
virtually no selectivity (**3** : **4** ~ 1 : 1) was obtained from the reactions of 4-trifluoromethylated (**1f**) and 5-methoxylated (**1g)** benzaldehydes (Table 2, entries 6 and 7). It should be noted that the selectivities of the reactions of **1c, 1d** and **1j** were found to improve slightly from 1 : 1, 3.3 : 1 and 3.3 : 1 to 1.6 : 1, 4.1 : 1 and 5.1 : 1, respectively, when reaction was carried out at a lower temperature as 25-30 ^{o}C with the expense of chemical yields (Table 2, entries 4, 6 and 10). The DBU catalysis also accepted substrates which contain benzoyl (**1k**) and *t*-butoxycarbonyl (Boc) (**1l**) in addition to acetyl attached on propargylic alcohol. Reactions produced analogously bis-oxa-bridged tricyclic products in 82-95% total yields with moderate selectivity (**3** : **4** ~ 3 : 1) (Table 2, entries 11 and 12). The products **3** and **4** have very similar molecular polarities. Successfully separation between them was achieved only by repetitive column chromatography using different eluting solvents with the exception of **3b** and **4b** which were not completely separated. The isolated yields of products **3** and **4** were 30-70% and 13-35%, respectively. In addition to the reaction of *o*-(1-(acyloxy)propargyl)benzaldehydes **1a-1l**, the DBU-catalyzed reactions of 2-(1-(acetyloxy)propargyl)thiophene-3-carbaldehyde **1m** and 2-(1-(acetyloxy)propargyl)nicotinaldehyde **1n** were also examined. Under the similar conditions as that for benzaldehyde **1a**, the DBU-catalyzed reactions of thiophene-3-carbaldehyde **1m** and pyridine-3-carbaldehyde **1n** produced the tricyclic bis-thiophene- and bis-pyridine-fused-[10]annulenes **3m** and **3n** in 52% and 34% yields, respectively (Table 2, entries 13 and 14). No analogous product of **4** was detected in these reactions.

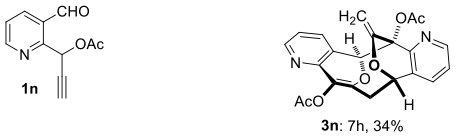
Table 2. Scope of DBU-Catalyzed Reaction of *o*-(1-(Acyloxy)propargyl) Substituted Aromatic Aldehydes **1**.



Entry	Substrate **1**	Products **3** and **4** Time (h), total yield[a], **3** : **4**[b]
1		 8h, 91%, **3a** : **4a** = 5.2 : 1
2		 8h, 83%, **3b** : **4b** = 4.5 : 1
3		 12h, 81%, **3c** : **4c** = 3.2 : 1
4		 16h, 70%, **3d** : **4d** = 3.3 : 1 (24 h, 51%, **3d** : **4d** = 5.1 : 1)[c]
5		 14h, 73%, **3e** : **4e** = 5.4 : 1
6		 5h, 76%, **3f** : **4f** = 1 : 1 (8 h, 52%, **3f** : **4f** = 1.6 : 1)[c]
7		 36h, 69%, **3g** : **4g** = 1 : 1
8		 24h, 75%, **3h** : **4h** = 2.9 : 1
9		 8h, 83%, **3i** : **4i** = 4.6 : 1
10		 9h, 86%, **3j** : **4j** = 3.3 : 1 (24 h, 59%, **3j** : **4j** = 4.1 : 1)[c]
11		 5h, 95%, **3k** : **4k** = 3.2 : 1

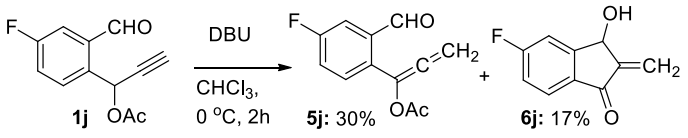
12 

13 

14 

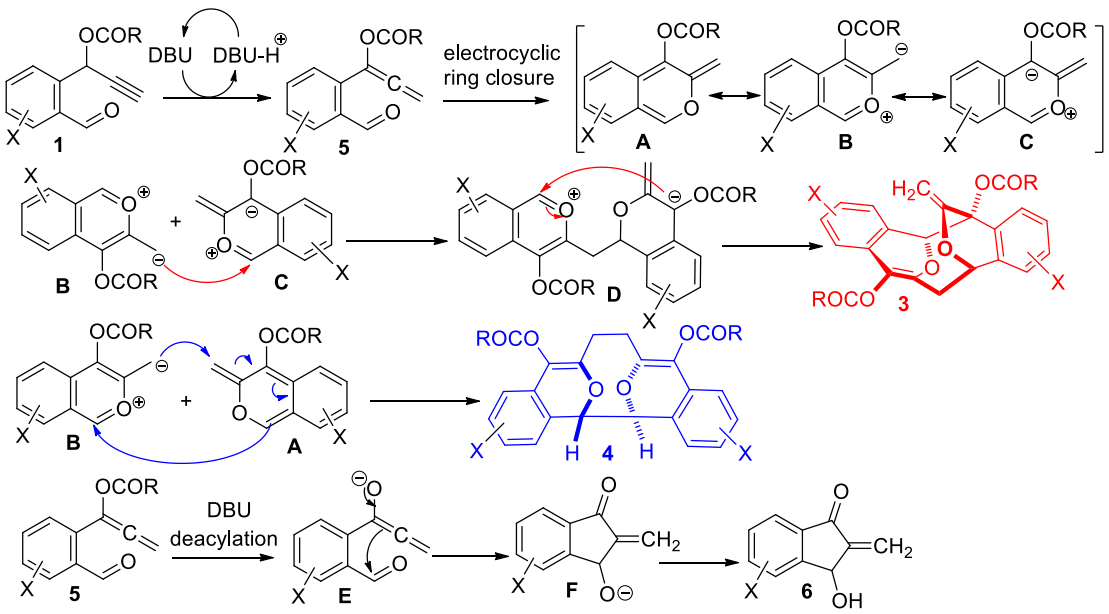
[a] Isolated yields. [b] Determined by ^{1}H NMR in the mixture of products **3** and **4**. [c] The data in the parentheses were obtained from the reactions conducted at 25-30 °C.

The formation of two complex bis-ether-bridged tricyclic compounds **3** and **4** from 2-(1-(acyloxy)propargyl)benzaldehydes **1** is very intriguing. To shed light on the reaction mechanism, the reaction process was carefully monitored with TLC. The reaction was found to form initially other two products which underwent further transformation or decomposition in a prolonged time either at 25 °C or at a higher temperature. To isolate presumably unstable intermediates and to characterize their structures, the reaction of 2-(1-(acetyloxy)propargyl)-5-fluorobenzaldehyde **1j** was executed at 0 °C for a short period of time (2 h). All work-up including silica gel column chromatography at or below 0 °C enabled isolation of compounds **5j** and **6j** (Scheme 1). Confirmed by spectroscopic data, compounds **5j** (30%) and **6j** (17%) turned out to be 1-(4-fluoro-2-formylphenyl)propa-1,2-dienyl acetate and 5-fluoro-3-hydroxy-2-methylene-1-indanone, respectively.



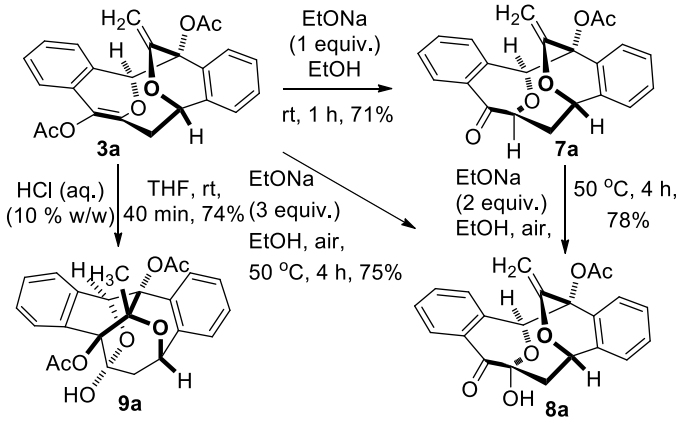
Scheme 1. Isolation of reaction intermediates.

Base on the formation of allene intermediates **5**, we proposed the most plausible reaction pathways of aldehydes **1** under DBU catalysis which are delineated in Scheme 2. Treated with DBU, a strong organic base in solution, *o*-(1-(acyloxy)propargyl)benzaldehydes **1** are transformed into (2-formylphenyl)allene intermediates **5**.[9] Under the thermal condition, allenes **5** would undergo a concerted 6-π electrocyclic ring closure reaction to form 3-methylene-3*H*-isochromene intermediate **A** and its resonance structures **B** and **C**. Dimerization between **B** and **C** gives rise to the formation of products **3** via intermediate **D**, while dimerization between **A** and **B** furnishes products **4**. Although compounds **3** and **4** contain three and two stereogenic centers, respectively, no other diastereomeric isomers were observed. It suggested that the dimerization reactions proceeded in highly diastereoselective manners because of the steric requirement for the assembly of bis-oxa-bridged tricyclic structures. The 1-indanone derivatives **6**, which were unstable in the presence of DBU, should be derived from the base-catalyzed deacylation of allenes **5**, followed by an intramolecular addition of the enolates to aldehyde group (Scheme 2).



Scheme 2. Proposed mechanisms for DBU-catalyzed dimerization reactions of 2-(1-(acyloxy)propargyl)benzaldehydes **1.**

To extend the synthetic application of the methods, further transformations of the resulting major product **3** were attempted. Upon the treatment with one equivalent of sodium ethoxide for 1 h in ethanol at room temperature, compound **3a** underwent selective deacetylation efficiently to afford bisether-bridged tricyclic ketone **7a** in 71% yield (Scheme 3). Employment of an excess amount of EtONa (3 equiv.) did not cause the cleavage of the other acetyl group. Surprisingly, compound **3a** was transformed into α-hydroxylated ketone **8a** in 75% yield within 4h at 50 °C under atmosphere. Under the similar conditions, α-hydroxylated ketone **8a** was also obtained in 78% yield from the reaction of ketone **7a** with EtONa (Scheme 3). On the contrary, when compound **3a** was reacted with aqueous hydrochloric acid (10 % w/w, 1 equiv. HCl) in THF at room temperature, a much more sophisticated tri-bridged tetracyclic compound **9a** was generated in 74% yield (Scheme 3) (See X-ray molecular structures of **7a**, **8a** and **9a** in Figure 3).



Scheme 3. Synthetic applications of the major product **3.**

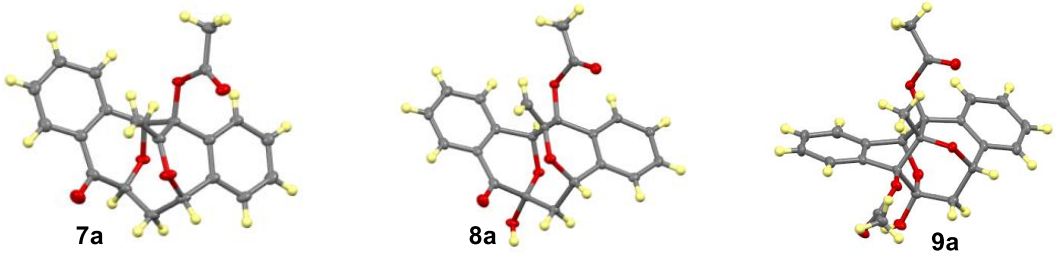
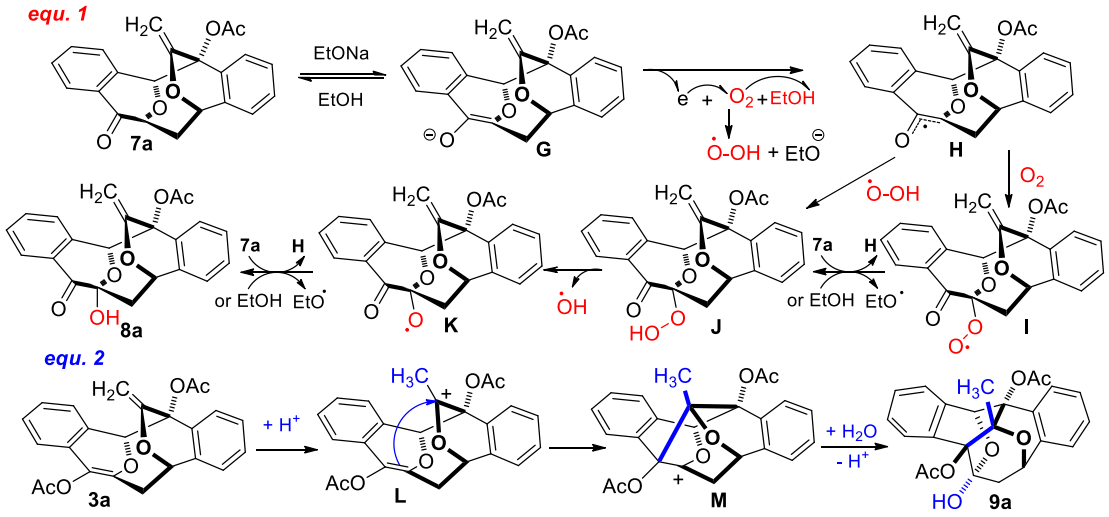


Figure 3. X-ray molecular structures of compounds **7a, 8a** and **9a.** The ellipsoid contour probability level is 50%.

To shed light on the formation of hydroxy group in ketone **8a**, both the reactions of compounds **3a** and **7a** with EtONa were carried out under strictly oxygen-free condition in a glovebox. In these cases, no α-hydroxyketone **8a** was formed. To further trace the origin of the oxygen of hydroxy group in product **8a**, reaction of **7a** under strong basic condition was exposed to $^{18}O_2$. Under this circumstance, an oxygen-18 labelled product **8a'** was yielded, indicating the oxidation of **7a** by molecular oxygen. The α-hydroxyketone **8a** could be obtained from **7a** in the presence of EtONa and O_2 under dark condition excluding the photocatalysis. On the contrary, no α-hydroxyketone **8a** was formed when **7a** was exposed to oxygen gas in the absence of EtONa. Very recently, Yang and coworkers reported a visible-light-mediated iodine-catalyzed α-hydroxylation of α-methylene ketones under aerobic conditions.[10] They demonstrated that the reaction proceeded via a radical pathway. Based on our experimental evidences and Yang's report, a most plausible reaction pathway for the formation of *α*-hydroxyketone **8a** was suggested in Scheme 4. In the presence of EtONa and O_2 (air), ketone **7a** is converted into a radical intermediate **H**, probably via a single electron transfer from the enolate intermediate **G** to oxygen molecule. The resulting enolate radical **H** and hydrogen peroxide radical coupled to form peroxide intermediate **J.** Alternatively, the radical **H** reacts with molecular oxygen to form peroxy radical **I** which subsequently abstracted the hydrogen atom from ethanol or ketone **7a** to afford peroxide intermediate **J**. Decomposition of peroxide **J** led to the formation of α-hydroxyketone **8a (**Scheme 4, *equ.1*)**.** In the presence of aqueous hydrochloric acid, the formation of tetracyclic compound **9a** was most probably started from the protonation of the methene of **3a** followed consecutively by intramolecular addition of the resulting carbocation **L** to the enol moiety and the hydroxylation of the carbocation **M** (Scheme 4, *equ.2*)**.**



Scheme 4. Proposed mechanisms for the formation of compounds **8a** and **9a.**

CONCLUSION

In conclusion, we have established the DUB-catalyzed reactions of *o*-(1-(acyloxy)propargyl) substituted aromatic aldehydes to construct complex molecular structures. The reaction proceeded most probably through the conversion of the reactant into (2-formylphenyl)allene intermediates which underwent a concerted 6-π electrocyclic ring closure reaction to form 3-methylene-3*H*-isochromene intermediate **A** and its zwitterionic resonance structures **B** and **C**. Dimerizations between intermediates **B** and **C** and between **A** and **B** afforded bis-ether-bridged tricyclic compounds **3** and **4,** respectively. We have also demonstrated that the reactions of **3** with NaOEt and hydrochloric acid enabled the further development of complex molecule diversities. The easy availability of starting materials, environmentally benign catalytic reaction without using any transition metals, and efficient construction of diverse complex molecular structures that are not accessible by other means would render the method an invaluable tool in study of organic synthesis and medicinal chemistry.

EXPERIMENTAL SECTION

1. Preparation of the reactants 1.

(1). Preparation of 2-(1-(acetyloxy)propargyl)benzaldehydes 1a-1j (see Scheme S1 and Table S1 in Supporting Information).

A typical experimental procedure for the synthesis of 2-(1-(acetyloxy)propargyl)benzaldehyde 1a.[5] At room temperature, 2-bromobenzaldehyde **Ia** (3.7 g, 20 mmol), triethyl orthoformate (6 g, 40 mmol) and $TsOH \cdot H_2O$ (76 mg, 2 mol%) were dissolved in anhydrous ethanol (20 mL). The reaction mixture was refluxed in ethanol for 6 h in an oil bath. After removal of the solvent, the residue was chromatographed on a silica gel column eluting with a mixture of petroleum ether and ethyl acetate (PE : EA = 30 : 1) to give 1-bromo-2-(diethoxymethyl)benzene **IIa** as colorless oil (4.96 g, 95 %).

Under nitrogen atmosphere, to a solution of acetal **IIa** (4.92 g, 19 mmol) in anhydrous THF (40 mL) was added dropwise *n*-BuLi (2.5 M in hexane, 8.4 mL, 20.9 mmol) at -78 ˚C. After stirring for 30 min at -78 ˚C, anhydrous DMF (3.47 g, 47.5 mmol) was added dropwise to the solution. The resulting mixture was kept stirring at -78 ˚C for 30 min and then at room temperature for another 1 h. The reaction was then quenched by adding a saturated aqueous solution of NH_4Cl (20 mL). The resulting mixture was extracted with ethyl acetate (20 × 3 mL). The combined organic layer was dried over anhydrous $MgSO_4$. After filtration and removal of solvents, the residue was chromatographed on a silica gel column eluting with a mixture of petroleum ether and ethyl acetate (PE : EA = 10 : 1) to give 2-(diethoxymethyl)benzaldehyde **IIIa** as pale yellow oil (3.44 g, 87 %).

Under nitrogen atmosphere and at 0 ˚C, to a solution of 2-(diethoxymethyl)benzaldehyde **IIIa** (2.08 g, 10 mmol) in anhydrous THF (30 mL) was added dropwise ethynylmagnesium bromide

(26 mL, 0.5M in THF, 13 mmol). After the resulting solution was kept stirring at 0 ˚C for 40 min, acetic anhydride (3.06 g, 30 mmol) was added. The reaction mixture was then warmed to room temperature and was stirred for another 2 h. The reaction was quenched by the addition of a saturated aqueous solution of $NaHCO_3$ (30 mL) and the resulting mixture was extracted with ethyl acetate (20 × 3 mL). The combined organic layer was dried over anhydrous $MgSO_4$. After filtration and removal of solvents, the residue was chromatographed on a silica gel column eluting with a mixture of petroleum ether and ethyl acetate (PE : EA = 10 : 1) to give 2-(1-(acetyloxy)propargyl)benzaldehyde diethyl acetal **IVa** as pale yellow oil (2.51 g, 91 %).

Acetal **IVa** (2.49 g, 9 mmol) was hydrolyzed with hydrochloric acid (1 mol/L, 27 mL, 27 mmol) in THF (20 mL) for 3 h at room temperature. The reaction mixture was then neutralized by the addition of a saturated aqueous solution of $NaHCO_3$ (10 mL) and was extracted with ethyl acetate (20 × 3 mL). The combined organic layer was dried over anhydrous $MgSO_4$. After filtration and removal of solvents, the residue was chromatographed on a silica gel column eluting with a mixture of petroleum ether and ethyl acetate (PE : EA = 8 : 1) to give 2-(1-(acetyloxy)propargyl)benzaldehyde **1a** as pale yellow oil (1.57 g, 86%).

2-(1-(Acetyloxy)propargyl)benzaldehyde 1a[6]: pale yellow oil, IR *v* (cm^{-1}) 3285, 2124 (w), 1744, 1697, 1599, 1580; ^{1}H NMR (400 MHz, CD_3Cl_3) δ (ppm) 10.3 (s, 1H), 7.90 (d, *J* = 7.6 Hz, 1H), 7.80 (d, *J* = 7.7 Hz, 1H), 7.63 (dt, *J* = 7.5, 1.2 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.10 (d, *J* = 2.2 Hz, 1H), 2.68 (d, *J* = 2.3 Hz, 1H), 2.10 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 191.6, 169.0, 137.5, 133.9, 133.0, 132.6, 129.3, 128.6, 79.8, 76.1, 62.1, 20.6.

Substrates **1b-1j** were prepared from the substituted 2-bromobenzaldehydes **I** using the same procedures as that for **1a.** The chemical yields of 1-bromo-2-(diethoxymethyl)benzenes **II,**

2-(diethoxymethyl)benzaldehydes **III,** 2-(1-(acetyloxy)propargyl)benzaldehyde diethyl acetals **IV** and compounds **1a-1j** were summarized in Scheme S1 and Table S1 in Supporting Information.

2-(1-(Acetyloxy)propargyl)-4-methoxybenzaldehyde 1b: pale yellow solid, mp 51-52 ^{o}C; IR *v* (cm^{-1}) 3285, 2124 (w), 1746, 1688, 1602, 1570; ^{1}H NMR (400 MHz, CD_3Cl_3) δ (ppm) 10.1 (s, 1H), 7.82 (d, *J* = 8.4 Hz, 1H), 7.30 (d, *J* = 2.8 Hz, 1H), 7.13 (d, *J* = 2.0 Hz, 1H), 6.99 (dd, *J* = 8.8, 2.8 Hz, 1H), 3.90 (s, 3H), 2.65 (d, *J* = 2.4 Hz, 1H), 2.10 (s, 3H). ^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ (ppm) 190.2, 168.9, 163.8, 139.7, 136.0, 126.2, 114.7, 113.4, 79.7, 75.8, 61.8, 55.5, 20.6. HRMS (TOF-ESI): $[M + Na]^+$ calcd for $C_{13}H_{12}O_4Na$: 255.0627, found: 255.0631.

2-(1-(Acetyloxy)propargyl)-4-methylbenzaldehyde 1c: pale yellow oil; IR *v* (cm^{-1}) 3289, 2124 (w), 1748, 1697, 1606; ^{1}H NMR (400 MHz, CD_3Cl_3) δ (ppm): 10.2 (s, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 7.58 (s, 1H), 7.34 (d, *J* = 7.6 Hz, 1H), 7.08 (d, *J* = 2.4 Hz, 1H), 2.66 (d, *J* = 2.4 Hz, 1H), 2.45 (s, 3H), 2.10 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm) 191.3, 168.9, 145.1, 137.3, 133.1, 130.7, 129.9, 129.2, 79.9, 76.0, 62.0, 21.6, 20.6. HRMS (TOF-ESI): $[M + Na]^+$ calcd for $C_{13}H_{12}O_3Na$: 239.0678, found: 239.0681.

2-(1-(Acetyloxy)propargyl)-4-chlorobenzaldehyde 1d: pale yellow oil; IR *v* (cm^{-1}) 3289, 2126 (w), 1746, 1695, 1593, 1566; ^{1}H NMR (400 MHz, CD_3Cl_3) δ (ppm) 10.3 (s, 1H), 7.84 (d, *J* = 8.2 Hz, 1H), 7.78 (s, 1H), 7.54 (d, *J* = 8.3 Hz, 1H), 7.08 (d, *J* = 1.6 Hz, 1H), 2.7 (d, *J* = 1.8 Hz, 1H), 2.13 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ (ppm):190.2, 168.8, 140.3, 139.3, 133.9, 131.3, 129.4, 128.7, 79.2, 76.5, 61.4, 20.6. HRMS (TOF-ESI): $[M + Na]^+$ calcd for $C_{12}H_9ClO_3Na$: 259.0132; found: 259.0134.

2-(1-(Acetyloxy)propargyl)-4-fluorobenzaldehyde 1e: pale yellow oil; IR *v* (cm^{-1}) 3289, 2126 (w), 1746, 1701, 1606, 1587; ^{1}H NMR (400 MHz, CD_3Cl_3) δ (ppm) 10.2 (s, 1H), 7.92 (dd, *J* = 8.5,

5.8 Hz, 1H), 7.52 (dd, *J* = 9.4, 2.2 Hz, 1H), 7.21-7.26 (m, 1H), 7.12 (d, *J* = 1.6 Hz, 1H), 2.69 (d, *J* = 2.1 Hz, 1H), 2.13 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm): 189.9, 168.8, 165.5 (d, *J* = 260 Hz), 140.9 (d, *J* = 8 Hz), 135.6 (d, *J* = 9 Hz), 129.5, 116.0 (d, *J* = 51 Hz), 116.0, 79.2, 76.2, 61.3, 20.5. HRMS (TOF-ESI): $[M + Na]^+$ calcd for $C_{12}H_9FO_3Na$: 243.0427; found: 243.0431.

2-(1-(Acetyloxy)propargyl)-4-(trifluoromethyl)benzaldehyde 1f: pale yellow solid, mp 45-46 °C; IR *v* (cm^{-1}) 3291, 2126 (w), 1751, 1703; ^{1}H NMR (400 MHz, CD_3Cl_3) δ (ppm) 10.4 (s, 1H), 8.03 (s, 1H), 8.03 (d, *J* = 6.5 Hz, 1H), 7.81 (d, *J* = 8 Hz, 1H), 7.09 (d, *J* = 2.2 Hz, 1H), 2.73 (d, *J* = 2.2 Hz, 1H), 2.12 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm): 190.5, 169.0, 138.8, 135.6, 135.2 (q, *J* = 33 Hz), 132.6, 126.3 (q, *J* = 4 Hz), 125.7 (q, *J* = 3 Hz), 123.1 (q, *J* = 272 Hz), 79.2, 77.0, 61.7, 20.7. HRMS (TOF-ESI): $[M + Na]^+$ calcd for $C_{13}H_9F_3O_3Na$: 293.0396; found: 293.0400.

2-(1-(Acetyloxy)propargyl)-5-methoxybenzaldehyde 1g: pale yellow solid, mp 57-58 °C; IR *v* (cm^{-1}) 3285, 2124 (w), 1744, 1689, 1607, 1576; ^{1}H NMR (400 MHz, CD_3Cl_3) δ (ppm) 10.4 (s, 1H), 7.68 (d, *J* = 8.5 Hz, 1H), 7.39 (d, *J* = 2.8 Hz, 1H), 7.13 (dd, *J* = 8.5, 2.8 Hz, 1H), 6.96 (d, *J* = 2.2 Hz, 1H), 3.86 (s, 3H), 2.70 (d, *J* = 2.2 Hz, 1H), 2.07 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 191.0, 169.0, 160.2, 134.5, 130.6, 129.8, 119.6, 115.9, 80.2, 76.1, 61.9, 55.4, 20.6. HRMS (TOF-ESI): $[M + Na]^+$ calcd for $C_{13}H_{12}O_4Na$: 255.0627, found: 255.0631.

2-(1-(Acetyloxy)propargyl)-5-methylbenzaldehyde 1h: pale yellow oil; IR *v* (cm^{-1}) 3287, 2124 (w), 1744, 1695, 1609, 1574; ^{1}H NMR (400 MHz, CD_3Cl_3) δ (ppm): 10.3 (s, 1H), 7.69 (d, *J* = 1.6 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.04 (d, *J* = 2.4 Hz, 1H), 2.66 (d, *J* = 2 Hz, 1H), 2.43 (s, 3H), 2.09 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 191.7, 169.0, 139.5, 134.6, 134.5, 133.0, 132.95, 128.7, 80.0, 76.0, 62.0, 20.8, 20.6. HRMS (TOF-ESI): $[M + Na]^+$ calcd for $C_{13}H_{12}O_3Na$:

239.0678, found: 239.0677.

2-(1-(Acetyloxy)propargyl)-5-chlorobenzaldehyde 1i: pale yellow oil; IR *v* (cm^{-1}) 3291, 2126 (w), 1746, 1695, 1593, 1570; ^{1}H NMR (400 MHz, CD_3Cl_3) δ (ppm) 10.3 (s, 1H), 7.86 (d, *J* = 2 Hz, 1H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.59 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.99 (d, *J* = 2 Hz, 1H), 2.69 (d, *J* = 2.4 Hz, 1H), 2.10 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm):189.9, 168.9, 136.0, 135.7, 134.4, 133.6, 131.6, 130.3, 79.4, 76.6, 61.6, 20.6. HRMS (TOF-ESI): $[M + Na]^+$ calcd for $C_{12}H_9ClO_3Na$: 259.0132; found: 259.0135.

2-(1-(Acetyloxy)propargyl)-5-fluorobenzaldehyde 1j: pale yellow oil; IR *v* (cm^{-1}) 3291, 2126 (w), 1746, 1695, 1609, 1589; ^{1}H NMR (400 MHz, CD_3Cl_3) δ (ppm) 10.3 (s, 1H), 7.76 (dd, *J* = 8.4, 5.1 Hz, 1H), 7.57 (dd, *J* = 8.4, 1.9 Hz, 1H), 7.27-7.32 (m, 1H), 6.96 (s, 1H), 2.73 (s, 1H), 2.08 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm): 189.8, 168.9, 162.8 (d, *J* = 251 Hz), 135.2 (d, *J* = 6 Hz), 133.7,, 131.2 (d, *J* = 7 Hz), 120.6 (d, *J* = 21 Hz), 117.8 (d, *J* = 22 Hz), 79.7, 76.7, 61.6, 20.5. HRMS (TOF-ESI): $[M + Na]^+$ calcd for $C_{12}H_9FO_3Na$ 243.0427; found: 243.0426.

(2). Preparation of 2-(1-(benzoyloxy)propargyl)benzaldehyde 1k (see Scheme S2 in Supporting Information).

To a solution of 2-(diethoxymethyl)benzaldehyde **IIIa** (1.66 g, 8 mmol) in anhydrous THF (30 mL) at 0 °C and under nitrogen protection was added dropwise ethynylmagnesium bromide (21 mL, 0.5 M in THF, 13 mmol). After stirring at 0 ˚C for 40 min, the reaction was quenched by the addition of a saturated aqueous solution of NH_4Cl (20 mL) and the mixture was extracted with ethyl acetate (20 × 3 mL). The combined organic layer was dried over anhydrous $MgSO_4$. After filtration and removal of solvents, the residue was dissolved in anhydrous dichloromethane (10 mL). To this solution, benzoyl chloride (1.35 g, 9.6 mmol), DMAP (0.489 g, 4 mmol) and Et_3N

(1.62 g, 16 mmol) were added at 0 °C under nitrogen atmosphere. After the resulting mixture was stirred for 2 h at ambient temperature, the reaction was then quenched by the addition of water (10 mL). The mixture was extracted with CH_2Cl_2 (10 × 3 mL) and the combined organic layer was dried over anhydrous $MgSO_4$. After filtration and removal of solvents, the residue was chromatographed on a silica gel column eluting with a mixture of petroleum ether and ethyl acetate (PE : EA = 12 : 1) to give 1-(2-(diethoxymethyl)phenyl)propargyl benzoate **IVk** as pale yellow solid (2.19 g, 81 %). The obtained acetal **IVk** was then hydrolyzed with hydrochloric acid (1 mol/L, 20 mL) in THF (15 mL) for 3 h at room temperature. The reaction mixture was neutralized by the addition of a saturated aqueous solution of $NaHCO_3$ (10 mL). After extracting with ethyl acetate (10 × 3 mL), drying and evaporating of solvent, the residue was chromatographed on a silica gel column eluting with a mixture of petroleum ether and ethyl acetate (PE : EA = 20 : 1) to give 2-(1-(benzoyloxy)propargyl)benzaldehyde **1k** as a white solid (1.3 g, 77%).

2-(1-(Benzoyloxy)propargyl)benzaldehyde 1k: white solid, mp 90-91 °C; IR *v* (cm^{-1}) 3289, 2124 (w), 1722, 1697, 1599, 1580; ^1H NMR (600 MHz, CD_3Cl_3) δ (ppm) 10.4 (s, 1H), 8.04 (dd, *J* = 7.8, 1.8 Hz, 2H), 7.92 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.87 (d, *J* = 7.8 Hz, 1H), 7.65 (dt, *J* = 7.2, 1.2 Hz, 1H), 7.57 (t, *J* = 7.8 Hz, 1H), 7.56 (t, *J* = 7.8 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 2H), 7.35 (d, *J* = 1.8 Hz, 1H), 2.73 (d, *J* = 1.8 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm): 191.6, 164.7, 137.7, 134.0, 133.3, 133.2, 132.5, 129.7, 129.4, 129.1, 128.6, 128.3, 79.9, 76.4, 62.8. HRMS (TOF-ESI): $[M + Na]^+$ calcd for $C_{17}H_{12}O_3Na$ 287.0678; found: 287.0682.

(3). Preparation of 2-(1-((*t*-butoxycarbonyl)oxy)propargyl)benzaldehyde 1l (see Scheme S3 in Supporting Information).

To a solution of 2-(diethoxymethyl)benzaldehyde **IIIa** (2.08 g, 10 mmol) in anhydrous THF (30 mL) at 0 °C and under nitrogen protection was added dropwise ethynylmagnesium bromide (26 mL, 0.5 M in THF, 13 mmol). After stirring at 0 ˚C for 40 min, a saturated aqueous solution of NH_4Cl (20 mL) was added, and the resulting mixture was extracted with ethyl acetate (20 × 3 mL). The combined organic layer was dried over anhydrous $MgSO_4$. After filtration and removal of solvents, the residue was dissolved in anhydrous acetonitrile (10 mL). To this solution at 0 °C and under nitrogen protection were added di-*t*-butyl dicarbonate (2.84 g, 13 mmol) and DMAP (0.122 g, 1 mmol). The resulting mixture was kept stirring at 0 °C for 4 h. The reaction was quenched by adding water (10 mL). The mixture was extracted with CH_2Cl_2 (10 × 3 mL) and the combined organic layer was dried over anhydrous $MgSO_4$. After filtration and removal of solvents, the residue was chromatographed on a silica gel column eluting with a mixture of petroleum ether and ethyl acetate (PE : EA = 12 : 1) to give *t*-butyl (1-(2-(diethoxymethyl)phenyl)propargyl) carbonate **IVl** as pale yellow oil (2.41 g, 72 %). The resulting acetal **IVl** was hydrolyzed with hydrochloric acid (1 mol/L, 21mL) in THF (15 mL) at room temperature for 6 h. Then the reaction mixture was neutralized by the addition of a saturated aqueous solution of $NaHCO_3$ (10 mL). After extracting with ethyl acetate (10 × 3 mL), drying and evaporating of solvent, the residue was chromatographed on a silica gel column eluting with a mixture of petroleum ether and ethyl acetate (PE : EA = 15 : 1) to give 2-(1-((*t*-butoxycarbonyl)oxy)propargyl)benzaldehyde **1l** as a pale yellow solid (1.39 g, 74 %).

2-(1-((*t*-Butoxycarbonyl)oxy)propargyl)benzaldehyde 1l: pale yellow solid, mp 51-52 °C; IR *v* (cm^{-1}) 3288, 2126 (w), 1746, 1697, 1601, 1580; δ (ppm) 10.3 (s, 1H), 7.87 (d, *J* = 8 Hz, 1H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.63 (dt, *J* = 7.6, 1.6 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.0 (d, *J* = 1.6 Hz, 1H),

2.69 (d, J = 2.4 Hz, 1H), 1.48 (s, 9H). $^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ (ppm): 191.7, 151.8, 137.2, 133.9, 133.0, 132.9, 129.3, 128.4, 83.1, 79.6, 76.4, 64.5, 27.5. HRMS (TOF-ESI): $[M + Na]^+$ calcd for $C_{15}H_{17}O_4$ 261.1121; found: 261.1118.

(4) Preparation of 2-(1-(acetyloxy)propargyl)thiophene-3-carbaldehyde 1m (see Scheme S4 in Supporting Information).

Substrate **1m** was prepared from thiophene-3-carbaldehyde **Im** using the similar procedures as that for substrate **1a.** The chemical yields of 3-(diethoxymethyl)thiophene **IIm**, 3-(diethoxymethyl)thiophene-2-carbaldehyde **IIIm,** 2-(1-(acetyloxy)propargyl)thiophene-3-carbaldehyde diethyl acetal **IVm** and compound **1m** were summarized in Scheme S4 in Supporting Information.

2-(1-(Acetyloxy)propargyl)thiophene-3-carbaldehyde 1m: pale yellow oil; IR ν (cm^{-1}) 3287, 2127 (w), 1746, 1685, 1528; ^{1}H NMR (400 MHz, CD_3Cl_3) δ (ppm) 10.16 (s, 1H), 7.46 (d, J = 4.9 Hz, 1H), 7.33 (d, J = 4.8 Hz, 1H), 7.14 (s, 1H), 2.71 (s, 1H), 2.13 (s, 3H);$^{13}C\{^{1}H\}$NMR (100 MHz, $CDCl_3$) δ (ppm) 184.1, 168.8, 147.8, 137.6, 128.1, 126.0, 78.9, 75.8, 58.3, 20.5. HRMS (TOF-ESI): $[M + Na]^+$ calcd for $C_{10}H_8O_3SNa$: 231.0086, found: 231.0089.

(5) Preparation of 2-(1-(acetyloxy)propargyl)pyridine-3-carbaldehyde 1n (see Scheme S5 in Supporting Information).

Substrate **1n** was prepared from 2-bromopyridine-3-carbaldehyde **In** using the similar procedures as that for **1a.** The chemical yields of 2-bromo-3-(diethoxymethyl)pyridine **IIn**, 3-(diethoxymethyl)pyridine-2-carbaldehyde **IIIn,** 2-(1-(acetyloxy)propargyl)pyridine-3-carbaldehyde diethyl acetal **IVn** and compound **1n** were summarized in Scheme S5 in Supporting Information.

2-(1-(acetyloxy)propargyl)pyridine-3-carbaldehyde 1n: pale yellow solid; mp 48-49 °C; IR *v* (cm^{-1}) 3280, 2125 (w), 1700, 1584, 1572; ^{1}H NMR (400 MHz, CD_3Cl_3) δ (ppm) 10.56 (s, 1H), 8.79 (d, *J* = 2.7 Hz, 1H), 8.25 (d, *J* = 7.5 Hz, 1H), 7.51 (t, *J* = 4.9 Hz, 1H), 6.99 (s, 1H), 2.75 (s, 1H), 2.15 (s, 3H);^{13}C{^{1}H}NMR (100 MHz, $CDCl_3$) δ (ppm) 189.9, 168.9, 156.3, 153.0, 138.3, 129.2, 124.1, 78.8, 77.3, 64.7, 20.5. HRMS (TOF-ESI): $[M + Na]^+$ calcd for $C_{11}H_9NO_3SNa$: 226.0474, found: 231.0477.

2. General procedure for the DBU-catalyzed reaction of 2-(1-(acyloxy)propargyl) substituted aromatic aldehydes 1.

To a solution of aldehyde **1** (1 mmol) in dry chloroform (20 mL) at room temperature and under nitrogen protection was added DBU (45 μL, 0.3 mmol, 30 mol%) through a syringe. The reaction mixture was warmed up slowly to 60 °C in an oil bath and was then kept stirring for 5 - 36 h. The reaction was then quenched by removal of the solvent. The residue was chromatographed on a silica gel column eluting with a mixture of petroleum ether, dichloromethane and ethyl acetate (PE : DCM : EA from 8 : 1 : 1 to 3 : 1 : 1) to give a mixture of products **3** and **4** in 69-95% total yields. After determining the ratios of **3** over **4** by ^{1}H NMR, the products **3** and **4** were obtained as pure products in 30-70% and 11-35% yields after repetitive silica gel column chromatography eluting with the solvents indicated below. Since compounds **3b** and **4b** were not completely separated by column chromatography, pure **3b** and **4b** were obtained by recrystallization. In the reaction of 2-(1-(acyloxy)propargyl)thiophene-3-carbaldehyde **1m** and 2-(1-(acyloxy)propargyl)pyridine-3-carbaldehyde **1n**, the bis-thiophene- and bis-pyridine-fused-[10]annulene products **3m** and **3n** were isolated in 52% and 34% yields, respectively, by silica gel column chromatography eluting with a mixture of solvents (**3m:** PE :

DCM : EA = 5 : 1 : 1; **3n:** from PE : EA = 1 : 1 to 1 : 3 and then to pure EA), and no analogous product of **4** was detected.

Eluting solvents used for silica gel column chromatography to separate products **3** and **4** are as follows.

3a and **4a**, PE : acetone = 5 : 1; **3c** and **4c**, PE : DCM : EA = 10 : 1 : 1 − 8 : 1 : 1; **3d** and **4d**, PE : acetone = 8 : 1 − 5 : 1; **3e** and **4e**; PE : acetone = 3:1; **3f** and **4f**, PE : DCM : EA = 8 : 1 : 1; **3g** and **4g**, PE : acetone = 3:1; **3h** and **4h**, PE : DCM : EA = 10 : 1 : 1 − 8 : 1 : 1; **3i** and **4i**, PE : DCM : EA = 8 : 1 : 1; **3j** and **4j**, PE : DCM : EA = 8 : 1 : 1; **3k** and **4k**, PE : acetone = 8 : 1; **3l** and **4l**, PE : DCM : EA = 12 : 1 : 1.

16-Methylene-7,8,13,14-tetrahydro-6,14-epoxy-8,13-(epoxymethano)dibenzo[*a*,*e*][10]annulene-5,13-diacetate 3a: white solid, 123.3 mg, 61%, mp 193-194 °C (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1761, 1653, 1620; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.47 (dd, *J* = 6.1, 2.4 Hz, 1H),7.36-7.44 (m, 4H), 7.33 (d, *J* = 7.9 Hz, 1H), 7.23 (d, *J* = 7.2 Hz, 1H), 7.11 (dd, *J* = 6.3, 2.2 Hz, 1H), 5.58 (d, *J* = 5.9 Hz, 1H), 4.69 (s, 1H), 4.08 (d, *J* = 1.8 Hz, 1H), 3.22 (dd, *J* = 13.5, 6.1 Hz, 1H), 3.11 (d, *J* = 1.7 Hz, 1H), 2.49 (d, *J* = 13.4 Hz, 1H), 2.38 (s, 3H), 2.15 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 169.4, 166.9, 153.9, 139.2, 138.4, 137.3, 132.9, 131.3, 129.8, 128.5, 128.2, 127.8, 127.4, 126.9, 123.9, 122.0, 121.5, 85.4, 81.7, 77.8, 74.9, 38.4, 21.7, 20.6; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{24}H_{21}O_6$: 405.1332; found:405.1335.

7,8,15,16-Tetrahydro-6,16:9,15-diepoxydibenzo[*a*,*e*][12]annulene-5,10-diacetate 4a: white solid, 28.3 mg, 14%, mp 217-218 °C (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1759, 1680; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.27 (t, *J* = 8.9 Hz, 2H), 7.22 (t, *J* = 7.3 Hz, 2H), 7.0 (d, *J* = 7.0 Hz, 2H), 6.92 (d, *J* = 7.4 Hz, 2H), 5.25 (s, 2H), 2.62-2.70 (m, 2H), 2.35 (s, 6H),

2.31-2.33 (m, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 169.1, 148.5, 133.0, 131.3, 128.3, 127.53, 127.50, 123.9, 119.1, 84.5, 29.0, 20.3; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{24}H_{21}O_6$: 405.1332; found:405.1335.

3,11-Dimethoxy-16-methylene-7,8,13,14-tetrahydro-6,14-epoxy-8,13-(epoxymethano)dibenzo[*a*,*e*][10]annulene-5,13-diacetate 3b: white solid, mp 203-204 °C (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1759, 1755, 1614; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.38 (d, *J* = 8.3 Hz, 1H), 7.14 (d, *J* = 8.3 Hz, 1H), 6.86-6.91 (m, 2H), 6.82 (d, *J* = 2 Hz, 1H), 6.61 (d, *J* = 2 Hz, 1H), 5.54 (d, *J* = 5.7 Hz, 1H), 4.66 (s, 1H), 4.07 (d, *J* = 1.1 Hz, 1H), 3.84 (s, 3H), 3.83 (s, 3H), 3.16 (dd, *J* = 13.4, 6 Hz, 1H), 3.12 (d, *J* = 1.4 Hz, 1H), 2.42 (d, *J* = 13.4 Hz, 1H), 2.36 (s, 3H), 2.13 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 169.5, 167.0, 159.9, 159.7, 140.0, 138.3, 134.7, 131.3, 129.9, 128.1, 125.2, 123.8, 112.9, 112.4, 108.4, 107.6, 85.5, 81.6, 78.1, 74.8, 55.4, 55.3, 38.8, 21.9, 20.7; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{26}H_{25}O_8$: 465.1543; found: 465.1547.

3,12-Dimethoxy-7,8,15,16-tetrahydro-6,16:9,15-diepoxydibenzo[*a*,*e*][12]annulene-5,10-diacetate 4b: white solid, mp 224-225 °C (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1755, 1682, 1611; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 6.92 (d, *J* = 8.2 Hz, 2H), 6.73 (dd, *J* = 8.2, 2.4 Hz, 2H), 6.46 (d, *J* = 2.4 Hz, 2H), 5.17 (s, 2H), 3.80 (s, 6H), 2.60-2.68 (m, 2H), 2.34 (s, 6H), 2.26-2.32 (m, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 169.3, 159.8, 149.2, 131.3, 129.0, 125.7, 125.2, 112.0, 105.7, 84.8, 55.4, 29.3, 20.5; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{26}H_{25}O_8$: 465.1543; found: 465.1546.

3,11-Dimethyl-16-methylene-7,8,13,14-tetrahydro-6,14-epoxy-8,13-(epoxymethano)dibenzo[*a*,*e*][10]annulene-5,13-diacetate 3c: white solid, 114.6 mg, 53%, mp 211-212 °C (recrystallization

from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1757, 1647; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.35 (d, *J* = 7.7 Hz, 1H), 7.19 (d, *J* = 7.7 Hz, 1H), 7.16 (d, *J* = 7.8 Hz, 1H), 7.11 (d, *J* = 6.8 Hz, 1H), 7.10 (s, 1H), 6.70 (s, 1H); 5.55 (d, *J* = 5.8 Hz, 1H), 4.65 (s, 1H), 4.07 (d, *J* = 1.4 Hz, 1H), 3.19 (dd, *J* = 13.4, 6 Hz, 1H), 3.11 (d, *J* = 1.2 Hz, 1H), 2.44 (d, *J* = 13.5 Hz, 1H), 2.41 (s, 3H), 2.40 (s, 3H), 2.39 (s, 3H), 2.15 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 168.8, 167.2, 154.3, 139.5, 138.63, 138.58, 138.2, 134.7, 133.0, 129.9, 128.8, 128.5, 127.0, 124.0, 122.6, 122.2, 85.4, 81.9, 78.2, 75.1, 38.8, 22.0, 21.7, 21.6, 20.9; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{26}H_{25}O_6$: 433.1645; found: 433.1642.

3,12-Dimethyl-7,8,15,16-tetrahydro-6,16:9,15-diepoxydibenzo[*a,e*][12]annulene-5,10-diacetate 4c: white solid, 34.6 mg, 16%, mp 225-226 °C (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1753, 1676, 1611; ^1H NMR (600 MHz, $CDCl_3$) δ (ppm) 7.0 (d, *J* = 6.6 Hz, 2H), 6.87 (dd, *J* = 7.8 Hz, 2H), 6.69 (s, 2H), 5.17 (s, 2H), 2.59-2.65 (m, 2H), 2.34 (s, 6H), 2.31 (s, 6H), 2.26-2.29 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 169.2, 148.5, 138.0, 131.4, 130.4, 128.1, 127.3, 123.8, 119.7, 84.6, 29.0, 21.2, 20.4; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{26}H_{25}O_6$: 433.1645; found: 433.1648.

3,11-Dichloro-16-methylene-7,8,13,14-tetrahydro-6,14-epoxy-8,13-(epoxymethano)dibenzo[*a, e*][10]annulene-5,13-diacetate 3d: white solid, 108.9 mg, 46%, mp 217-219 °C (recrystallization from *n*-hexane/CH_2Cl_2): IR *v* (cm^{-1}) 1761, 1620; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.36-7.40 (m, 2H), 7.34 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.28 (d, *J* = 1.9 Hz, 1H), 7.17 (d, *J* = 8.2 Hz, 1H), 7.07 (s, 1H), 5.55 (d, *J* = 5.8 Hz, 1H), 4.66 (s, 1H), 4.11 (d, *J* = 2 Hz, 1H), 3.19 (dd, *J* = 13.4, 6 Hz, 1H), 3.15 (d, *J* = 2 Hz, 1H), 2.45 (d, *J* = 13.4 Hz, 1H), 2.39 (s, 3H), 2.16 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, CD_3COCD_3) δ (ppm) 168.9, 166.5, 153.9, 140.4, 137.4, 136.6, 135.6, 133.9, 133.2, 131.8,

129.9, 129.0, 127.7, 127.2, 125.8, 122.5, 121.2, 84.7, 80.5, 76.9, 74.1, 38.0, 20.7, 19.6; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{24}H_{19}Cl_2O_6$: 473.0553; found: 473.0556.

3,12-Dichloro-7,8,15,16-tetrahydro-6,16:9,15-diepoxydibenzo[*a,e*][12]annulene-5,10-diacetate 4d: white solid, 35.5 mg, 15%, mp 236-238 °C (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1774, 1759, 1678; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.18 (dd, *J* = 7.9, 1.6 Hz, 2H), 6.91 (d, *J* = 8 Hz, 2H), 6.88 (d, *J* = 1.3 Hz, 2H), 5.19 (s, 2H), 2.61-2.69 (m, 2H), 2.36 (s, 6H), 2.26-2.32 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 168.9, 149.7, 134.5, 130.8, 130.4, 129.4, 127.3, 125.2, 119.3, 84.0, 29.0, 20.3; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{24}H_{19}Cl_2O_6$: 473.0553; found:473.055.

3,11-Difluoro-16-methylene-7,8,13,14-tetrahydro-6,14-epoxy-8,13-(epoxymethano)dibenzo[*a, e*][10]annulene-5,13-diacetate 3e: white solid, 125.5 mg, 57 %, mp 227-228 °C (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1761, 1751, 1616; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.42 (dd, *J* = 8.3, 5.4 Hz, 1H), 7.20 (dd, *J* = 8.4, 5.3 Hz, 1H), 7.03-7.11(m, 2H), 7.0 (dd, *J* = 9.1, 2.3 Hz, 1H), 6.80 (dd, *J* = 9.1, 2.4 Hz, 1H), 5.57 (d, *J* = 5.8 Hz, 1H), 4.67 (s, 1H), 4.10 (d, *J* = 2 Hz, 1H), 3.19 (dd, *J* = 13.5, 6.0 Hz, 1H), 3.12 (d, *J* = 1.9 Hz, 1H), 2.44 (d, *J* = 13.4 Hz, 1H), 2.38 (s, 3H), 2.14 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d6) δ (ppm) 170.0, 167.6, 162.8 (d, *J* = 243.4 Hz), 162.5 (d, *J* = 241.5 Hz), 154.2, 140.7, 137.8, 135.9 (d, *J* = 7.6 Hz), 134.4, 132.3 (d, *J* = 9.6 Hz), 130.0 (d, *J* = 8.6 Hz), 127.5, 126.9 (d, *J* = 8.6 Hz), 115.3(d, *J* = 22 Hz), 114.9 (d, *J* = 21.1 Hz), 110.2 (d, *J* = 23 Hz), 109.1 (d, *J* = 23 Hz), 85.3, 80.2, 77.3, 74.1, 39.7, 22.0, 21.2; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{24}H_{19}F_2O_6$: 441.1144; found: 441.1142.

3,12-Difluoro-7,8,15,16-tetrahydro-6,16:9,15-diepoxydibenzo[*a,e*][12]annulene-5,10-diacetate 4e: white solid, 24.2 mg, 11%, mp 236-237 °C (recrystallization from *n*-hexane/CH_2Cl_2); IR *v*

(cm^{-1}) 1774, 1751, 1682, 1610; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 6.87-6.96 (m, 4H) 6.63 (dd, *J* = 9.3, 2.2 Hz, 2H), 5.20 (s, 2H), 2.62-2.70 (m, 2H), 2.35 (s, 6H), 2.27-2.33 (m, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 169.1, 163.0 (d, *J* = 245 Hz), 149.8, 130.8 (d, *J* = 2 Hz), 130.0 (d, *J* = 9 Hz), 128.4 (d, *J* = 4 Hz), 125.6 (d, *J* = 9 Hz), 114.1 (d, *J* = 23 Hz), 106.8 (d, *J* = 24 Hz), 84.3, 29.2, 20.5; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{24}H_{19}F_2O_6$: 441.1144; found: 441.1142.

3,11-Di(trfluoromethyl)-16-methylene-7,8,13,14-tetrahydro-6,14-epoxy-8,13-(epoxymethano) dibenzo[*a,e*][10]annulene-5,13-diacetate 3f: white solid, 97.3 mg, 36%, mp 205-206 °C (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1761, 1633; ^{1}H NMR (400 MHz, CD_3COCD_3) δ (ppm) 7.89 (d, *J* = 8.4 Hz, 1H), 7.77 (d, *J* = 8 Hz, 1H), 7.76 (s, 1H), 7.71 (d, *J* = 7.6 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.49 (s, 1H), 5.76 (d, *J* = 6 Hz, 1H), 5.05 (s, 1H), 3.94 (d, *J* = 2 Hz, 1H), 3.32 (dd, *J* = 14, 6 Hz, 1H), 3.16 (d, *J* = 1.2 Hz, 1H), 2.52 (d, *J* = 13.6 Hz, 1H), 2.37 (s, 3H), 2.17 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, CD_3COCD_3) δ (ppm) 169.0, 166.8, 154.1, 142.0, 140.7, 137.7, 135.3, 134.7, 131.1, 130.5 (q, *J* = 32 Hz), 129.8 (q, *J* = 32 Hz), 128.5, 125.3, 124.8 (q, *J* = 4 Hz), 124.2 (q, *J* = 4 Hz), 124.3 (q, *J* = 270 Hz), 124.2 (q, *J* = 270 Hz), 119.8 (q, *J* = 4 Hz), 118.2 (q, *J* = 4 Hz), 85.1, 80.5, 77.1, 74.4, 38.1, 20.8, 19.8; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{26}H_{19}F_6O_6$: 541.108; found: 541.1084.

3,12-Di(trifluoromethyl)-7,8,15,16-tetrahydro-6,16:9,15-diepoxydibenzo[*a,e*][12]annulene-5,10-diacetate 4f: white solid, 94.6 mg, 35%, mp 261-263 °C (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1778, 1757, 1678; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.49 (d, *J* = 7.7 Hz, 2H), 7.14 (s, 2H), 7.11 (d, *J* = 7.8 Hz, 2H), 5.30 (s, 2H), 2.64-2.72 (m, 2H), 2.38 (s, 6H), 2.31-2.36 (m, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 169.1, 150.2, 135.9, 131.3 (q, *J* =

33 Hz), 130.7, 128.9, 124.6 (q, *J* = 4 Hz), 124.5, 123.7 (q, *J* = 271 Hz), 116.2 (q, *J* = 4 Hz), 83.9, 29.1, 20.5; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{26}H_{19}F_6O_6$: 541.108; found: 541.1083.

2,10-Dimethoxy-16-methylene-7,8,13,14-tetrahydro-6,14-epoxy-8,13-(epoxymethano)dibenzo[*a*,*e*][10]annulene-5,13-diacetate 3g: white solid, 70 mg, 30 %, mp 186-187 °C (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1771, 1612; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.22 (d, *J* = 8.5 Hz, 1H), 7.04 (d, *J* = 8.5 Hz, 1H), 7.01 (d, *J* = 2.4 Hz, 1H), 6.95 (dd, *J* = 8.5, 2.4 Hz, 1H), 6.91 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.75 (d, *J* = 2.4 Hz, 1H), 5.49 (d, *J* = 5.9 Hz, 1H), 4.59 (s, 1H), 4.08 (d, *J* = 1.8 Hz, 1H), 3.89 (s, 3H), 3.84 (s, 3H), 3.17 (dd, *J* = 13.5, 6.1 Hz, 1H), 3.14 (d, *J* = 1.4 Hz, 1H), 2.47 (d, *J* = 13.5 Hz, 1H), 2.36 (s, 3H), 2.15 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 169.8, 167.1, 159.5, 159.0, 154.1, 138.9, 138.7, 137.5, 133.7, 125.1, 123.6, 123.2, 114.3, 113.5, 113.3, 109.5, 85.7, 82.6, 78.1, 75.2, 55.55, 55.47, 38.4, 22.1, 20.9; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{26}H_{25}O_8$: 465.1543; found: 465.1546.

2,13-Dimethoxy-7,8,15,16-tetrahydro-6,16:9,15-diepoxydibenzo[*a*,*e*][12]annulene-5,10-diacetate 4g: white solid, 66 mg, 28 %, mp 222 °C (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1755, 1610; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 6.85 (d, *J* = 8.8 Hz, 2H), 6.76 (dd, *J* = 8.8, 2.4 Hz, 2H), 6.53 (d, *J* = 2.8 Hz, 2H), 5.17 (s, 2H), 3.80 (s, 6H), 2.55-2.60 (m, 2H), 2.31 (s, 6H), 2.23-2.28 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 169.5, 159.3, 146.6, 135.2, 131.5, 120.9, 120.8, 112.6, 111.0, 84.3, 55.6, 28.8, 20.6; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{26}H_{25}O_8$: 465.1543; found: 465.1546.

2,10-Dimethyl-16-methylene-7,8,13,14-tetrahydro-6,14-epoxy-8,13-(epoxymethano)dibenzo[*a*,*e*][10]annulene-5,13-diacetate 3h: white solid, 101.6 mg, 47 %, mp 226-227 °C (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1765, 1651, 1618; ^1H NMR (400 MHz,

$CDCl_3$) δ (ppm) 7.26 (s, 1H), 7.18-7.23 (m, 3H), 7.04 (s, 1H), 6.99 (d, *J* = 7.8 Hz, 1H), 5.51 (d, *J* = 5.9 Hz, 1H), 4.61 (s, 1H), 4.06 (d, *J* = 1.8 Hz, 1H), 3.18 (dd, *J* = 13.5, 6.1 Hz, 1H), 3.11 (d, *J* = 1.8 Hz, 1H), 2.45 (d, *J* = 12.8 Hz, 1H), 2.44 (s, 3H), 2.39 (s, 3H), 2.36 (s, 3H), 2.14 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 169.7, 167.1, 154.2, 138.7, 138.6, 137.9, 137.4, 137.3, 131.6, 130.2, 129.3, 129.2, 127.8, 127.4, 124.7, 122.0, 121.5, 85.3, 82.1, 78.0, 75.1, 38.6, 21.9, 21.6, 21.2, 20.8; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{26}H_{25}O_6$: 433.1645; found:433.1648.

2,13-Dimethyl-7,8,15,16-tetrahydro-6,16:9,15-diepoxydibenzo[*a,e*][12]annulene-5,10-diacetate 4h: white solid, 28 mg, 13 %, mp 220-221 °C (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1771, 1684; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.05 (d, *J* = 7.6 Hz, 2H), 6.81 (s, 2H), 6.80 (d, *J* = 7.6 Hz, 2H), 5.17 (s, 2H), 2.57-2.65 (m, 2H), 2.35 (s, 6H), 2.32 (s, 6H), 2.23-2.29 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 169.1, 147.6, 137.4, 133.3, 131.5, 128.8, 124.9, 124.6, 119.1, 84.5, 28.8, 21.1, 20.3; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{26}H_{25}O_6$: 433.1645; found: 433.1649.

2,10-Dichloro-16-methylene-7,8,13,14-tetrahydro-6,14-epoxy-8,13-(epoxymethano)dibenzo[*a, e*][10]annulene-5,13-diacetate 3i: white solid, 142 mg, 60%, mp 195 °C (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1769, 1751, 1626; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.42 (d, *J* = 1.6 Hz, 1H), 7.34-7.38 (m, 2H), 7.20-7.22 (m, 2H), 7.02 (d, *J* = 8.4 Hz, 1H), 5.49 (d, *J* = 6.0 Hz, 1H), 4.58 (s, 1H), 4.09 (d, *J* = 1.6 Hz, 1H), 3.16 (s, 1H), 3.15-3.20 (m, 1H), 2.45 (d, *J* = 13.2 Hz, 1H), 3.13 (s, 3H), 3.12 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 169.4, 167.0, 153.6, 139.5, 139.2, 138.1, 133.8, 133.0, 131.6, 129.0, 128.8, 128.6, 127.2, 124.4, 123.9, 123.2, 86.2, 81.3, 77.6, 74.6, 38.4, 21.9, 20.8; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{24}H_{19}Cl_2O_6$: 473.0553; found: 473.0551.

2,13-Dichloro-7,8,15,16-tetrahydro-6,16:9,15-diepoxydibenzo[*a,e*][12]annulene-5,10-diacetat e 4i: white solid, 33 mg, 14%, mp 225 ºC (dec.) (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1765, 1680; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.25 (dd, *J* = 8.4, 2.0 Hz, 2H), 6.99 (d, *J* = 1.7 Hz, 2H), 6.86 (d, *J* = 8.3 Hz, 2H), 5.20 (s, 2H), 2.60-2.68 (m, 2H), 2.34 (s, 6H), 2.26-2.31 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 169.1, 149.0, 134.4, 133.0, 131.0, 128.7, 126.3, 124.3, 120.8, 83.8, 29.0, 20.5; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{24}H_{19}Cl_2O_6$: 473.0553; found:473.0550.

2,10-Difluoro-16-methylene-7,8,13,14-tetrahydro-6,14-epoxy-8,13-(epoxymethano)dibenzo[*a, e*][10]annulene-5,13-diacetate 3j: white solid, 127.7 mg, 58%, mp 206-208 ºC (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1773, 1753, 1622; ^1H NMR (400 MHz, CD_3COCD_3) δ (ppm) 7.47 (dd, *J* = 8.4, 5.3 Hz, 1H), 7.41 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.14-7.26 (m, 4H), 5.63 (d, *J* = 6 Hz, 1H), 4.80 (s, 1H), 3.92 (d, *J* = 1.6 Hz, 1H), 3.25 (dd, *J* = 13.7, 6.1 Hz, 1H), 3.18 (d, *J* = 1.6 Hz, 1H), 2.48 (d, *J* = 13.6 Hz, 1H), 2.35 (s, 3H), 2.17 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 169.5, 167.1, 162.3 (d, *J* = 248 Hz), 162.1 (d, *J* = 247 Hz), 153.7, 139.6 (d, *J* = 8 Hz), 138.6, 138.2, 133.9 (d, *J* = 8 Hz), 128.7 (d, *J* = 2.9 Hz), 126.4 (d, *J* = 2.9 Hz), 124.3 (d, *J* = 7.6 Hz), 123.8 (d, *J* = 8.6 Hz), 115.8 (d, *J* = 22.1 Hz), 115.7 (d, *J* = 22 Hz), 114.5 (d, *J* = 23 Hz), 111.3 (d, *J* = 22 Hz), 86.1, 81.7, 77.7, 74.7, 38.3, 21.9, 20.8; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{24}H_{19}F_2O_6$: 441.1144; found: 441.1146.

2,13-Difluoro-7,8,15,16-tetrahydro-6,16:9,15-diepoxydibenzo[*a,e*][12]annulene-5,10-diacetate 4j: white solid, 39.6 mg, 18%, mp 236-237 ºC (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1775, 1751, 1687, 1610; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 6.96 (td, *J* = 8.5, 2.4 Hz, 2H), 6.89 (dd, *J* = 8.5, 5.3 Hz, 2H), 6.72 (d, *J* = 8.4, 2.3 Hz, 2H), 5.20 (s, 2H), 2.58-2.67 (m, 2H), 2.34

(s, 6H), 2.25-2.31 (m, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 169.2, 162.0 (d, *J* = 247 Hz), 147.9 (d, *J* = 3 Hz), 135.0 (d, *J* = 7 Hz), 131.0, 124.0 (d, *J* = 3 Hz), 121.3 (d, *J* = 8 Hz), 115.3 (d, *J* = 22 Hz), 111.5 (d, *J* = 23 Hz), 83.7, 28.8, 20.5; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{24}H_{19}F_2O_6$: 441.1144; found: 441.1146.

16-Methylene-7,8,13,14-tetrahydro-6,14-epoxy-8,13-(epoxymethano)dibenzo[*a*,*e*][10]annulene-5,13-dibenzoate 3k: white solid, 185 mg, 70%, mp 154-155 °C (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1740, 1734, 1600; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.24 (d, *J* = 7.2 Hz, 2H), 8.09 (d, *J* = 7.2 Hz, 2H), 7.61-7.72 (m, 3H), 7.46-7.56 (m, 5H), 7.35-7.41 (m, 4H), 7.26 (d, *J* = 4.8 Hz, 1H), 7.20 (d, *J* =7.2 Hz, 1H), 5.62 (d, *J* = 6 Hz, 1H), 4.93 (s, 1H), 4.18 (d, *J* = 2 Hz, 1H), 3.30 (dd, *J* = 13.2, 6 Hz, 1H), 3.25 (d, *J* = 2 Hz, 1H), 2.54 (d, *J* = 13.2 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 165.2, 163.3, 154.4, 140.0, 138.9, 137.6, 134.1, 133.6, 133.5, 131.6, 130.6, 130.4, 129.8, 129.1, 128.9, 128.8, 128.6, 128.2, 127.8, 127.1, 124.2, 122.4, 122.2, 85.8, 82.3, 78.6, 75.3, 38.8; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{34}H_{25}O_6$: 529.1645; found: 529.1643.

7,8,15,16-Tetrahydro-6,16:9,15-diepoxydibenzo[*a*,*e*][12]annulene-5,10-dibenzoate 4k: white solid, 55.5 mg, 21%, mp 244-246 °C (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1742, 1684; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) 8.24 (d, *J* = 7.8 Hz, 4H), 7.65 (t, *J* = 7.2 Hz, 2H), 7.65 (t, *J* = 8.4 Hz, 4H), 7.22-7.23 (m, 4H), 7.05 (t, *J* = 4.2 Hz, 2H), 6.97 (t, *J* = 4.8 Hz, 2H), 5.35 (s, 2H), 2.67-2.72 (m, 2H), 2.36-2.41 (m, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 164.8, 148.8, 133.6, 133.1, 131.6, 130.1, 128.9, 128.5, 128.4, 127.8, 127.5, 123.9, 119.3, 84.7, 29.2; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{34}H_{25}O_6$: 529.1645; found: 529.1649.

Di-*t*-butyl

16-Methylene-7,8,13,14-tetrahydro-6,14-epoxy-8,13-(epoxymethano)dibenzo[*a*,*e*][10]annulene-5,13-dicarbonate 3l: white solid, 145.8 mg, 56%, mp 183-184 °C (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1761, 1622; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.47 (dd, *J* = 6.6, 4.0 Hz, 1H), 7.38-7.47 (m, 4H), 7.35 (dd, *J* = 7.0, 1.8 Hz, 1H), 7.20 (d, *J* = 7.6 Hz, 1H), 7.17 (dd, *J* = 6.9, 4.0 Hz, 1H), 5.56 (d, *J* = 5.8 Hz, 1H), 4.68 (s, 1H), 4.09 (d, *J* = 1.8 Hz, 1H), 3.30 (dd, *J* = 13.4, 6.1 Hz, 1H), 3.23 (d, *J* = 1.8 Hz, 1H), 2.48 (d, *J* = 13.3 Hz, 1H), 1.59 (s, 9H), 1.35 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 154.6, 152.1, 149.8, 139.6, 139.2, 137.6, 133.9, 131.3, 129.9, 128.6, 128.3, 128.1, 127.6, 127.5, 123.9, 122.1, 121.4, 85.7, 83.8, 82.9, 81.6, 78.6, 75.0, 38.4, 27.7, 27.6; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{30}H_{33}O_8$: 521.2169; found: 521.2168.

Di-*t*-butyl-7,8,15,16-tetrahydro-6,16:9,15-diepoxydibenzo[*a*,*e*][12]annulene-5,10-dicarbonate 4l: white solid, 49.5 mg, 19%, mp 163-164 °C (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1761; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.28 (t, *J* = 7.3 Hz, 2H), 7.22 (t, *J* = 7.3 Hz, 2H), 7.04 (d, *J* = 7.4 Hz, 2H), 6.99 (d, *J* = 7.2 Hz, 2H), 5.23 (s, 2H), 2.78-2.86 (m, 2H), 2.31-2.39 (m, 2H), 1.53 (s, 18H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 151.6, 148.7, 133.0, 132.2, 128.3, 127.9, 127.4, 123.8, 118.8, 84.4, 83.4, 28.7, 27.4; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{30}H_{33}O_8$: 521.2169; found:521.2167.

13-Methylene-4,5,11,12-tetrahydro-6,11-epoxy-4,12-(epoxymethano)cyclodeca[1,2-*b*:5,6-*b*']dithiophene-7,12-diacetate 3m: white solid, 108.3 mg, 52%, mp 189 °C (dec.) (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1769, 1760, 1628; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.35 (d, *J* = 5 Hz, 1H), 7.33 (d, *J* = 4.8 Hz, 1H), 7.14 (d, *J* = 4.7 Hz, 1H), 6.94 (d, *J* = 4.7 Hz, 1H), 5.69 (d, *J* = 5.4 Hz, 1H), 4.84 (s, 1H), 4.13 (s, 1H), 3.29 (dd, *J* = 13.4, 5.8 Hz, 1H), 3.12 (s, 1H), 2.42 (d,

J = 13.4 Hz, 1H), 2.32 (s, 3H), 2.13 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 169.0, 167.0, 152.8, 140.7, 136.5, 135.5, 133.9, 133.5, 132.7, 125.5, 125.2, 124.8, 123.3, 85.6, 79.0, 78.9, 72.0, 38.0, 21.5, 20.4; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{20}H_{17}O_6S_2$: 417.0461; found:417.0445.

15-Methylene-5,6,13,14-tetrahydro-7,13-epoxy-5,14-(epoxymethano)cyclodeca[1,2-*b*:5,6-*b*']di pyridine-8,14-diacetate 3n: white solid, 69 mg, 34%, mp 226-227 °C (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1766, 1748, 1654, 1620; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.63 (d, *J* = 2.9 Hz, 2H), 7.80 (d, *J* = 7.3 Hz, 1H), 7.55 (d, *J* = 7.4 Hz, 1H), 7.30-7.33 (m, 2H), 5.63 (d, *J* = 5.5 Hz, 1H), 4.99 (s, 1H), 4.19 (s, 1H), 3.41 (dd, *J* = 13.4, 6 Hz, 1H), 3.23 (s, 1H), 2.48 (d, *J* = 13.4 Hz, 1H), 2.41 (s, 3H), 2.17 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 169.3, 167.0, 154.3, 150.9, 150.85, 150.83, 149.7, 149.2, 148.0, 143.2, 138.8, 134.2, 132.8, 131.4, 126.9, 122.5, 86.5, 79.6, 77.1, 74.2, 38.1, 21.4, 20.5; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{22}H_{19}N_2O_6$: 407.1237; found:407.1261.

3. The isolation of reaction intermediates.

To a solution of 2-(1-(acetyloxy)propargyl)-5-fluorobenzaldehyde **1j** (220 mg, 1 mmol) in dry chloroform (20 mL) at 0 °C and under nitrogen atmosphere was added DBU (45μL, 0.3 mmol, 30 mol%) through a syringe. After the mixture was stirred at 0 °C for 2 h, the solvent was removed under vacuum at 0 °C. Compounds 1-(4-fluoro-2-formylphenyl)propa-1,2-dienyl acetate **5j** (30%) and 5-fluoro-3-hydroxy-2-methylene-1-indanone **6j** (17%) were isolated by silica gel column chromatography eluting with a cold mixture of *n*-pentane and acetone (*n*-pentane : acetone from 10 : 1 to 3 : 1). Substrate **1j** was also recovered in 36% yield.

1-(4-Fluoro-2-formylphenyl)propa-1,2-dienyl acetate 5j: colorless oil, 66 mg, 30%; IR *v* (cm^{-1})

1757, 1694; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 10.38 (s, 1H), 7.50-7.55 (m, 2H), 7.27 (td, *J* = 8.2, 2.8 Hz, 1H), 5.56 (s, 2H), 2.18 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 204.9, 190.1, 168.4, 162.7 (d, *J* = 249 Hz), 135.4 (d, *J* = 7 Hz), 132.1 (d, *J* = 4 Hz), 130.4 (d, *J* = 7 Hz), 120.7 (d, *J* = 22 Hz), 118.9, 114,2 (d, *J* = 23 Hz), 87.8, 20.9; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{12}H_{10}FO_3$: 221.0608; found: 221.0610.

5-fluoro-3-hydroxy-2-methylene-1-indanone 6j: white solid, 30 mg, 17 %, mp 97-98 °C (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 3451, 1692, 1645; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.87 (dd, *J* = 8, 4.8 Hz, 1H), 7.38 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.16 (td, *J* = 9.3 Hz, 1H), 6.38 (d, *J* = 1.8 Hz, 1H), 5.92 (d, *J* = 1.2 Hz, 1H), 5.54 (s, 1H), 2.76 (bs, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 189.7, 167.6 (d, *J* = 257 Hz), 154.6 (d, *J* = 8.7 Hz), 148.1, 133.7, 126.6 (d, *J* = 10.1 Hz), 121.9, 118.1 (d, *J* = 22.7 Hz), 112.9 (d, *J* = 23.1 Hz), 69.3; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{10}H_8FO_2$: 179.0502; found:179.0504.

4. Synthesis of ketone 7a from 3a.

Under atmosphere and at room temperature, a mixture of compound **3a** (202 mg, 0.5 mmol) and EtONa (34 mg, 0.5 mmol) in ethanol (10 mL) was stirred for 1 h. After removal of ethanol under vacuum, dichloromethane (10 mL) was added to the reaction mixture. The precipitate (EtONa) was filtrated off and the filtrate was concentrated. The residue was chromatographed on a silica gel column eluting with a mixture of petroleum ether, dichloromethane and ethyl acetate (PE : DCM : EA = 5 : 1 : 1) to give ketone **7a** in 71% yield.

16-Methylene-5-oxo-5,6,7,8,13,14-hexahydro-6,14-epoxy-8,13-(epoxymethano)dibenzo[*a*,*e*][10]annulene-13-diacetate 7a: white solid, 128.6 mg, 71%, mp 199-200 °C (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 1761, 1692, 1649, 1603; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.99

(d, *J* = 7.2 Hz, 1H), 7.66 (td, *J* = 7.7, 1.2 Hz, 1H), 7.52 (t, *J* = 6.9 Hz, 2H), 7.35-7.42 (m, 2H), 7.30 (dd, *J* = 7.3, 1.2 Hz, 1H), 7.22 (d, *J* = 7.1 Hz, 1H), 5.46 (d, *J* = 6.3 Hz, 1H), 4.93 (s, 1H), 4.61 (d, *J* = 8.3 Hz, 1H), 4.17 (d, *J* = 2 Hz, 1H), 3.32 (dd, *J* = 14.4, 6.5 Hz, 1H), 3.04 (d, *J* = 2.0 Hz, 1H), 2.44 (dd, *J* = 14.2, 8.5 Hz, 1H), 2.19 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 194.0, 166.6, 151.9, 139.0, 137.3, 132.9, 132.2, 130.6, 128.6, 127.8, 127.6, 126.7, 125.5, 124.0, 121.9, 90.4, 82.0, 80.7, 77.0, 74.5, 42.1, 21.7; HRMS (TOF-ESI): $[M + H]^+$ calcd for $C_{22}H_{19}O_5$: 363.1227; found: 363.1230.

5. Synthesis of α-hydroxy ketone 8a from 3a.

Under atmosphere, compound **3a** (101 mg, 0.25 mmol) and EtONa (51 mg, 0.75 mmol) were dissolved in ethanol (5 mL). After the reaction mixture was kept stirring at 50 °C for 4 h in an oil bath, the reaction was quenched by removing ethanol under vacuo followed by the addition of a saturated aqueous solution of NH_4Cl (10 mL). The resulting mixture was extracted with dichloromethane (20 × 3 mL). The combined organic layer was dried over anhydrous $MgSO_4$. After filtration and removal of dichloromethane, the residue was chromatographed on a silica gel column eluting with a mixture of petroleum ether and ethyl acetate (PE : EA = 4 : 1) to give α-hydroxy ketone **8a** in 75% yield.

6-Hydroxy-16-methylene-5-oxo-5,6,7,8,13,14-hexahydro-6,14-epoxy-8,13-(epoxymethano)dibenzo[*a,e*][10]annulene-13-diacetate 8a: white solid, 71 mg, 75%, mp 208-209 °C (recrystallization from *n*-hexane/acetone); IR *v* (cm^{-1}) 3433, 1763, 1697, 1658, 1631, 1600; ^{1}H NMR (400 MHz, CD_3COCD_3) δ (ppm) 7.86 (d, *J* = 7.6 Hz, 1H), 7.73 (td, *J* = 7.3, 0.7 Hz, 1H), 7.69 (d, *J* = 6.8 Hz, 1H), 7.56 (td, *J* = 7.8, 1.2 Hz, 1H), 7.34-7.41 (m, 4H), 5.88 (s, 1H), 5.43 (d, *J* = 6.3 Hz, 1H), 4.99 (s, 1H), 3.97 (d, *J* = 1.6 Hz, 1H), 3.56 (dd, *J* = 14.4, 6.5 Hz, 1H), 3.05 (d, *J* =

1.6 Hz, 1H), 2.18 (s, 3H), 2.18 (dd, *J* = 14.3, 0.8 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, CD_3COCD_3) δ (ppm) 194.5, 166.3, 152.7, 139.1, 137.9, 133.3, 132.8, 131.0, 128.6, 127.5, 127.4, 127.2, 125.7, 124.1, 122.4, 98.4, 90.2, 80.4, 80.3, 74.4, 47.5, 20.8; HRMS (TOF-ESI): $[M + Na]^+$ calcd for $C_{22}H_{18}O_6Na$: 401.0995; found: 401.0993.

Preparation of α-^{18}OH- ketone 8a' from 7a.

At room temperature, compound **7a** (91 mg, 0.25 mmol) and EtONa (34 mg, 0.5 mmol) were dissolved in ethanol (5 mL) in a Schlenk tube. The Schlenk tube was then evacuated and backfilled with $^{18}O_2$. Under $^{18}O_2$ atmosphere, the reaction mixture was kept stirring for 4 h at 50 °C in an oil bath. After work-up with the same procedures as that for compound **8a**, α-^{18}OH-ketone **8a'** was obtained in 74% yield.

α-HO^{18}-Ketone **8a'**: white solid, 70 mg, 74%, mp 206-207 °C (recrystallization from *n*-hexane/acetone); IR *v* (cm^{-1}) 3429, 1763, 1697, 1657, 1626, 1601; ^{1}H NMR (600 MHz, CD_3COCD_3) δ (ppm) 7.83 (d, *J* = 6.6 Hz, 1H), 7.70 (t, *J* = 9 Hz, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 1H), 7.31-7.36 (m, 4H), 5.83 (s, 1H), 5.39 (d, *J* = 5.4 Hz, 1H), 4.96 (s, 1H), 3.94 (d, *J* = 1.8 Hz, 1H), 3.53 (dd, *J* = 13.8, 5.4 Hz, 1H), 3.01 (d, *J* = 2.4 Hz, 1H), 2.14 (s, 3H), 2.14 (d, *J* = 12.6 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, CD_3COCD_3) δ (ppm) 190.3, 166.2, 152.5, 138.9, 137.7, 133.1, 132.6, 130.9, 128.5, 127.4, 127.2, 127.1, 125.5, 124.0, 122.2, 98.2, 90.0, 80.24, 80.18, 74.3, 47.4, 20.6; HRMS calcd for $C_{22}H_{19}O_5O^{18}$ $[M + H]^+$: 381.1224, found: 381.1221.

6. Synthesis of tri-bridged tetracyclic compound 9a from 3a.

To a solution of **3a** (101 mg, 0.25 mmol) in THF (10 mL) was added dropwise hydrochloric acid (84 μL, 10 % w/w, 0.25 mmol HCl). After the mixture was stirred at room temperature for 40 min,

the reaction was quenched by adding brine (10 mL). The resulting mixture was extracted with dichloromethane (20 × 3 mL). The combined organic layer was dried over anhydrous $MgSO_4$. After filtration and removal of solvents, the residue was chromatographed on a silica gel column eluting with a mixture of petroleum ether, dichloromethane and ethyl acetate (PE : DCM : EA = 3 : 1 : 1) to give product **9a** in 74 % yield.

14-Hydroxy-6a-methyl-6a,7,12,12a-tetrahydro-12,7,5-(epoxyethane[1,1,2]triyl)dibenzo[c,g]chromene-7,12a-diacetate 9a. white solid, 78.2 mg,74%, mp 181-182 °C (recrystallization from *n*-hexane/CH_2Cl_2); IR *v* (cm^{-1}) 3356, 1751, 1721; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.42-7.44 (m, 3H), 7.28-7.37 (m, 3H), 7.18-7.22 (m, 2H), 5.62 (s, 1H), 5.16 (d, *J* = 6.4 Hz, 1H), 4.61 (brs, 1H), 2.56 (dd, *J* = 13.9, 6.5 Hz, 1H), 2.49 (s, 3H), 2.24 (d, *J* = 13.9 Hz, 1H), 1.94 (s, 3H), 1.06 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, CD_3COCD_3) δ (ppm) 173.9, 169.6, 141.3, 136.7, 136.2, 132.4, 128.9, 128.7, 128.2, 127.5, 126.5, 126.2, 124.9, 124.7, 95.7, 87.0, 82.7, 80.0, 78.2, 72.7, 41.3, 22.4, 21.6, 18.7; HRMS (TOF-ESI): $[M + Na]^+$ calcd for $C_{24}H_{22}O_7Na$: 445.1257; found: 445.1260.

ASSOCIATED CONTENT

Supporting Information Available. The reaction schemes for the preparation of reactants **1**, copies of ^1H NMR and ^{13}C NMR spectra for reactants **1** and products **3-9**; HRMS of ^{18}OH- ketone **8a';** single crystal data of **3a**, **4a**, **7a**, **8a** and **9a** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org

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The authors declare no competing financial interest**.**

Crystallographic data (CIF files) for **3a** (CCDC 1919071), **4a** (CCDC 1919076), **7a** (CCDC 1919079), **8a** (1919096) and **9a** (CCDC 1919100) have been deposited at the Cambridge Crystallographic Data Center.

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REFERENCES

1 (a) Fraga, B. M.; Terrero, D.; Cabrera, I.; Reina, M. Studies on the Sesquiterpene Lactones from Laurus Novocanariensis Lead to the Clarification of the Structures of 1-Epi-tatridin B and Its Epimer Trtridin B. *Phytochemistry*, **2018**, *153*, 48-52. (b) Goren, N.; Jakupovic, J.; Topal, S. Sesquiterpene Lactones with Antibacterial Activity from Tanacetum Argyrophyllum var. Argyrophyllum. *Phytochemistry*, **1990**, *29*, 1467-1469. (c) Jakupovic, J.; Baruah, R. N.; Bohlmann, F.; King, R. M.; Robinson, H. New Types of Germacranolides from *Austroliabum candidum*. *Planta Medica* **1986**, *52*, 304-206. (d) Shafizadeh, F.; Bhadane, N. R. Badgerin, a New Germacranolide from *Artemisia arbuscula ssp. arbuscula. J. Org. Chem*. **1972**, *37*, 274-277.

2. (a) Li, Q.; Ding, W.; Yao, Z.; Tu, J.; Wang, L.; Huang, H.; Li, S.; Ju, J. AbmV Catalyzes Tandem Ether Installation and Hydroxylation during Neoabyssomicin/Abyssomicin Biosynthesis. *Org. Lett.* **2018**, *20*, 4854−4857. (b) Riedlinger, J.; Reicke, A.; Zähner, H.; Krismer, B.; Bull, A. T.; Maldonado, L. A.; Ward, A. C.; Goodfellow, M.; Bister, B.; Bischoff, D.; Süssmuth, R. D.; Fiedler, H. P. Abyssomicins, Inhibitors of the

para-Aminobenzoic Acid Pathway Produced by the Marine Verrucosispora Strain AB-18-032. *J. Antibiot.* **2004**, *57*, 271−279. (c) Gottardi, E. M.; Krawczyk, J. M.; von Suchodoletz, H.; Schadt, S.; Mühlenweg, A.; Uguru, G. C.; Pelzer, S.; Fiedler, H. P.; Bibb, M. J.; Stach, J. E.; Süssmuth, R. D. Abyssomicin Biosynthesis: Formation of an Unusual Polyketide, Antibiotic-Feeding Studies and Genetic Analysis. *ChemBioChem* **2011**, *12*, 1401−1410. (d) Savic, V. Chapter 5-Abyssomicins: Isolation, Properties, and Synthesis. *Stud. Nat. Prod. Chem.* **2013**, *40*, 133-172.

3. Dupont, R.; Jeanson, L.; Mouscadet, J.-F.; Cotelle, P. Synthesis and HIV-1 Integrase Inhibitory Activities of Catechol and Bis-Catechol Derivatives. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 3175-3178.

4. (a) Wünsch, B.; Zott, M.; Höfner, G. Synthese Enantiomerenreiner 6,10-Epoxybenzocycloocten-7-amine mit ZNS-Aktivität. *Arch. Pharm*. **1992**, *325*, 733-739. (b) Wünsch, B.; Zott, M.; Höfner, G. Synthese Homochiraler 5,9-Epoxybenzocyclooctene mit Aminsubstituenten: Zusammenhang zwischen Struktur und ZNS-Aktivität. *Arch. Pharm*. **1993**, *326*, 823-830.

5. Shibata, M.; Nakajima, K.; Nishibayashi, Y. Enantioselective Intramolecular Propargylic Amination using Chiral Copper–pybox Complexes as Catalysts. *Chem. Commun*. **2014**, *50*, 7874-7877.

6. Teng, T.-M.; Das, A.; Huple, D. B.; Liu, R.-S. Gold-Catalyzed Stereoselective Synthesis of 9-Oxabicyclo[3.3.1]nona-4,7-dienes from Diverse 1-Oxo-4-oxy-5-ynes: A Viable Formal [4 + 2] Cycloaddition on an s-trans-Heterodiene Framework. *J. Am. Chem. Soc.* **2010**, *132*, 12565-12567.

7. Chen, M.; Sun, N.; Liu, Y. Environmentally Benign Synthesisof Indeno[1,2‑b]quinolines via an Intramolecular Povarov Reaction. *Org. Lett.* **2013**, *15*, 5574-5577.

8. (a) Ding, Y.-L.; Li, S.-N.; Cheng, Y. Selective Synthesis of Multifunctionalized 2,3-Dihydroinden-1-ones and 1,3-Dihydroisobenzofurans from the Reaction of *o*‑Alkynylbenzaldehydes with Imines Steered by N‑Heterocyclic Carbene/Copper(II) and N‑Heterocyclic Carbene/Base Cascade Catalysis. *J. Org. Chem.* **2018**, *83*, 8971–8983. (b) Liu, Y.-J.; Ding, Y.-L.; Niu, S.-S.; Ma, J.-T.; Cheng, Y. N‑Heterocyclic Carbene/Palladium Cascade Catalysis:

Construction of 2,2-Disubstitiuted Benzofuranones from the Reaction of 3-(2-Formylphenoxy)propenoates with Allylic Esters. *J. Org. Chem*. **2018**, *83*, 1913−1923.

9. Examples for the DBU-catalyzed allene formation from the propargyl substrates: (a) Xiong, M.; Xie, X.; Liu, Y. Copper-Catalyzed Borylative Cyclization of in Situ Generated *o*-Allenylaryl Nitriles with Bis(pinacolato)diboron. *Org. Lett*. **2017**, *19*, 3398-3401. (b) Sun, N.; Xie, X.; Wang, G.; Chen, H.; Liu, Y. Base-Catalyzed Cyclization of 1,6-Diynyl Carboxylates Involving Propargyl-Allenyl Isomerization: Efficient Synthesis of Benzo[*b*]fluorene and Its Analogues. *Adv. Synth. Catal.* **2017**, *359*, 1394-1401.

10. Yang, J.; Xie, D.; Zhou, H.; Chen, S.; Huo, C.; Li, Z. Visible-light-mediated Iodine-catalyzed α-Hydroxylation of α-Methylene Ketones under Aerobic Conditions. *Org. Chem. Front.*, **2018**, *5*, 1325-1329.