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Accessing Polycyclic Terpenoids from Zerumbone via Lewis Acid Catalyzed Synthetic Strategies

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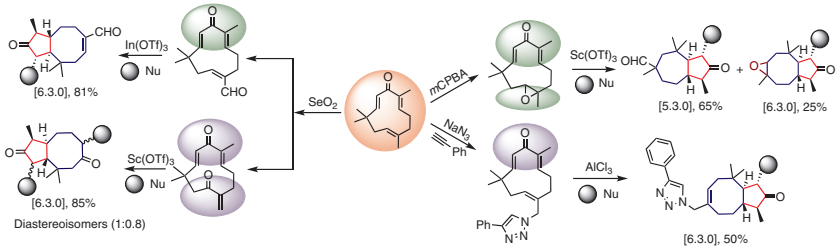

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Abstract We herein disclose an effective strategy for the synthesis of [5.3.0] and [6.3.0] fused polycyclic terpenoids, which are important structural elements of natural products and biologically active compounds. The method comprises of Lewis acid catalyzed interrupted Nazarov cyclization of zerumbone derivatives such as zerumbone epoxide, triazole-appended zerumbone, zerumbal, and zerumbenone with a wide substrate scope with different indoles. Zerumbone epoxide furnished [5.3.0] and [6.3.0] fused structurally diverse sesquiterpenoids and all other zerumbone derivatives furnished the [6.3.0] fused motifs.

Key words zerumbone, zerumbone epoxide, zerumbal, zerumbenone, Lewis acid catalysis, cyclization, polycyclic terpenoids

Natural-product-based drug discovery, especially phytochemical-focused drug development programs, holds an undeniable position in the present drug research scenario.[1–6] In between 1999–2013, only 34% of FDA approved drugs were from natural product origin.[7] Even though natural products have high structural diversity and biological activity, further structural modifications are needed in many cases to develop novel scaffolds with specific properties. The structural reconstruction of natural products (NPs) delivers highly relevant molecular changes, which provide insights into the bioactivities and structure–activity relationships against specific targets that are critical for the exploration of a still-unknown chemical space.

Our group mainly focuses on the phytochemical investigation of medicinal plants from Western Ghats of India[8] and the utilization of naturally abundant molecules to generate structurally diverse bioactive molecules. *Zingiber zerumbet* Smith is one among such plants having natural moieties showing interesting biological activities.[9] Zerumbone, the marker compound present in the rhizome oil of this tropical ginger,[10] comprises 3% of its dry weight. It is a crystalline achiral 11-membered monocyclic sesquiterpene with a flexible skeleton structure with a conjugated dienone part and an isolated olefin part. Within the last few decades, the diverse reactivity of zerumbone was extensively explored by various research groups. Mainly Kitayama and co-workers established various synthetic modifications of zerumbone, including transannular ring contraction,[11] cyclization,[12] regio- and diastereoselective conjugate additions,[13] various regiospecific ring cleavage reactions,[14] ring expansion reaction,[15] asymmetric epoxidation, and so forth.[16]

Our interest in zerumbone chemistry began in 2013 with the report on transition metal catalyzed 1,4-conjugate addition of boronic acids to zerumbone.[17a] In the very next year, we reported a new synthetic methodology for Pd-catalyzed decarboxylative reactions of arenecarboxylic acid with zerumbone.[17b] Later we described the metal-free trans-aziridation of zerumbone and the evaluation of their antidiabetic properties.[17c] In the same year, our group reported the synthesis of zerumbone pendant derivatives via a palladium-catalyzed Tsuji–Trost coupling reaction for the first time.[17d] Recently we have utilized Lewis acid chemistry for the synthesis of [5.7.0], [5.8.0], and [5.8.3] ring-fused structurally diverse natural sesquiterpenoids.[17e] In continuation of our interest in the Lewis acid catalyzed transformations of zerumbone towards highly functionalized sesquiterpenoids, we have extended our work to other zerumbone derivatives, such as zerumbone epoxide and synthetically prepared triazole-linked zerumbone, zerumbal, and zerumbenone, where zerumbone epoxide is a naturally occurring

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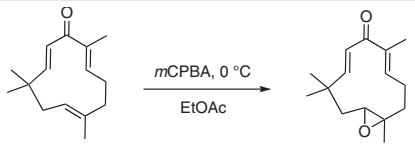
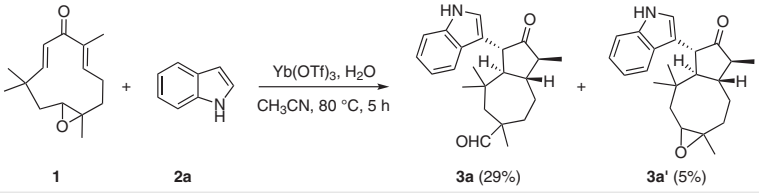


Scheme 1 Epoxidation of zerumbone

humulene epoxide, a component of *Zingiber zerumbet* Smith, and have been reported as precursors for many naturally relevant fused cyclic sesquiterpenoid motifs.[11,12]

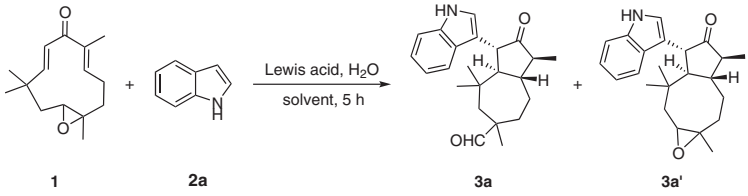
We hypothesized that, just like zerumbone, the zerumbone epoxide could also be activated with a Lewis acid, resulting in transannular cyclization reactions leading to the formation of structurally diverse motifs. We already observed the same while doing the zerumbone activation reactions.[17e] With this concept in mind, we synthesized the epoxide **1** by following a reported procedure in which *m*CPBA selectively reacted at the isolated double bond of zerumbone (**Z**) to afford 97% of zerumbone epoxide **1** (Scheme 1).[16] The structure of the epoxide was confirmed by using various spectroscopic techniques and in comparison with previous reports.

We initiated our studies[17e] with the reaction of zerumbone epoxide and indole as nucleophile in the presence of water and $Yb(OTf)_3$ at room temperature. The reaction after 5 hours at 80 °C afforded a mixture of [5.3.0] (**3a**) and [6.3.0] (**3a'**) fused ring systems (Scheme 2). The structures of the products were confirmed by various spectroscopic



Scheme 2 Lewis acid catalyzed transformation of zerumbone epoxide **1**

Table 1 Optimization of Lewis Acid Catalyzed Transformation of Zerumbone Epoxide **1** with Indole[a]



Entry	Lewis acid	Solvent	Temp (°C)	Yield (%)[b]	
				3a	**3a'**
1	$Yb(OTf)_3$	CH_3CN	RT	NR	NR
2	$Yb(OTf)_3$	CH_3CN	80	29	5
3	$Sc(OTf)_3$	CH_3CN	80	65	25
4	$In(OTf)_3$	CH_3CN	80	29	trace
5	$Cu(OTf)_2$	CH_3CN	80	40	trace
6	$Hf(OTf)_4$	CH_3CN	80	40	10
7	$La(OTf)_3$	CH_3CN	80	32	trace
8	$Zn(OTf)_2$	CH_3CN	80	trace	trace
9	$Sn(OTf)_2$	CH_3CN	80	32	trace
10	$Sn(OTf)_2$	DMF	153	trace	trace
11	$Sn(OTf)_2$	THF	66	32	trace
12	$Sn(OTf)_2$	DCE	83	32	trace
13	$Sn(OTf)_2$	toluene	110	38	trace

[a] Reaction conditions: **1** (1.0 equiv), **2a** (1.0 equiv), Lewis acid (30 mol%), H_2O (10.0 equiv), solvent (2.0 mL), 5 h.
[b] NR = no reaction.

techniques and the stereochemistry of the molecules were confirmed from NOE methods; this was similar to our own previous reports.[17e]

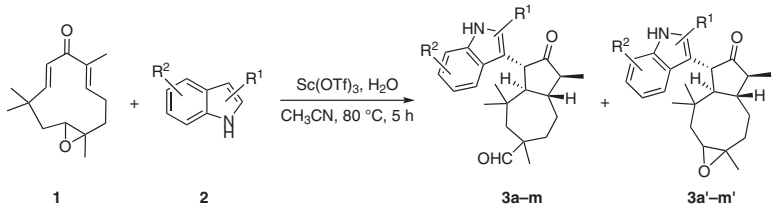
On the basis of the structural analysis of the product, we confirmed that the transformation of zerumbone epoxide to **3a′** had taken place via an interrupted Nazarov cyclization followed by a nucleophilic attack of indole, but the isodaucane system **3a** was formed via an interrupted Nazarov cyclization followed by a pinacol–pinacolone rearrangement of the diol formed through the epoxide ring opening. A similar type of rearrangement was reported by Luu et al. in 1981, where they reported the acid-catalyzed transannular cyclization of zerumbone epoxide to bicyclic derivatives.[12]

The reaction conditions were optimized further by examining various Lewis acids, solvents, and temperatures (Table 1). From the optimization studies, the best conditions were found to consist of a combination of zerumbone epoxide **1** (1.0 equiv), indole **2a** (1.0 equiv), $Sc(OTf)_3$ (30 mol%), and water (10 equiv) in MeCN (2.0 mL) at 80 °C for 5 hours; this led to the products being isolated in yields of 65% for **3a** and 25% for **3a′**.

With the optimal conditions in hand, we checked the scope and generality of this reaction with indoles **2** featuring both electron-withdrawing and -donating substituents. The results are summarized in Table 2. In almost all cases (entries 1–7 and 10–13), except in the case of hydroxy- and amino-substituted indoles (entries 8 and 9), the reactions proceeded smoothly and were completed within 5 hours at 80 °C. Indoles bearing electron-donating and -withdrawing groups afforded comparable yields. In the case of substituted indoles, formation of two more side products resulted; these include polymerized products of indole and indole–acetonitrile products.

We also checked the reactivity of C2-substituted indoles (Table 2, entries 14–16); with 2-phenylindole, we obtained the expected products **3n** and **3n′** in 25% and 23% yield, but 2-formylindole and indole-2-carboxylic acid failed to afford

Table 2 Generality of Lewis Acid Catalyzed Transformation of Zerumbone Epoxide **1** with Indoles **2**[a]



1 **2** **3a–m** **3a′–m′**

Entry	R^1	R^2	Products		Yield (%)[b]	
					3	**3′**
1	H	H	**3a**	**3a′**	65	25
2	H	5-CH_3	**3b**	**3b′**	33	22
3	H	5-Br	**3c**	**3c′**	27	23
4	H	5-NO_2	**3d**	**3d′**	32	20
5	H	5-CHO	**3e**	**3e′**	31	20
6	H	5-CN	**3f**	**3f′**	31	11
7	H	5-F	**3g**	**3g′**	20	15
8	H	5-OH	**3h**	**3h′**	NR	NR
9	H	5-NH_2	**3i**	**3i′**	NR	NR
10	H	5-OCH_3	**3j**	**3j′**	35	20
11	H	7-CH_3	**3k**	**3k′**	37	15
12	H	6-CH_3	**3l**	**3l′**	34	13
13	H	5-Cl	**3m**	**3m′**	25	18
14	2-Ph	H	**3n**	**3n′**	25	23
15	2-CHO	H	**3o**	**3o′**	NR	NR
16	2-COOH	H	**3p**	**3p′**	NR	NR
17	3-CH_3	H	**3q**	**3q′**	NR	NR

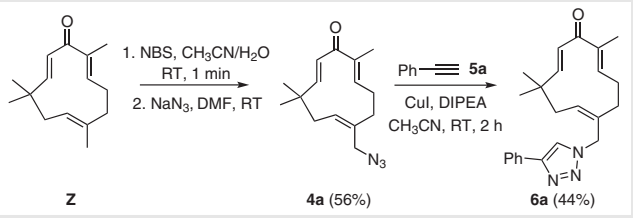
[a] Reaction conditions: **1** (1.0 equiv), **2** (1.0 equiv), $Sc(OTf)_3$ (30 mol%), H_2O (10.0 equiv), CH_3CN (2 mL), 80 °C, 5 h.
[b] NR = no reaction.

the corresponding products, possibly due to the lower nucleophilicity at the C3 position. Reaction with C3-substituted indole also failed to afford the expected products (entry 17).

Next, the scope of this reaction was explored with various nucleophiles such as pyrrole, thiophene, imidazole, sulfonamide, oxazolidine, and pyrazole, but the expected products were not obtained under the optimized conditions.

Our next aim was to check the feasibility of Nazarov cyclization on zerumbone derivatives (functionalized at the isolated double bond). Triazole is an important class of nitrogen-containing heterocycles prevalent in many pharmaceuticals, agrochemicals, and so on.[18] These compounds exhibit various biological activities, such as antimicrobial, antiviral, anti-histaminic, anti-tubercular, etc., and this has attracted various research groups to develop promising synthetic approaches towards these heterocycles.[19] The synthesis of these bioactive motifs can be achieved via the click chemistry approach.[20] Herein, we describe the synthesis of triazole-linked zerumbone derivatives.

We commenced our investigation with the synthesis of azido zerumbone derivative **4a** via the activation of the allylic methyl group of zerumbone by using *N*-bromosuccinimide, followed by azidation using sodium azide, which furnished the product in 56% overall yield[21] (Scheme 3). Azide **4a** was subsequently treated with phenylacetylene (**5a**; 1.5 equiv), in the presence of CuI (20 mol%) as catalyst, and by using DIPEA (3.0 equiv) as the base in acetonitrile (2 mL) at room temperature for 2 hours. The reaction afforded the corresponding triazole-linked product **6a** in 44% yield (Scheme 3). The structure and stereochemistry of the product was confirmed by various spectroscopic techniques such as ^{1}H NMR, ^{13}C NMR, and HRMS analysis.



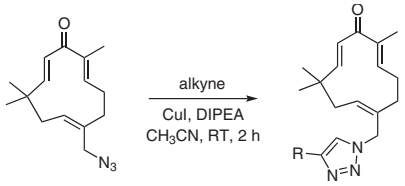
Z **4a** (56%) **6a** (44%)

Scheme 3 CuAAC of zerumbone azide **4a** with phenylacetylene (**5a**)

The scope of the reaction was checked with various aromatic as well as aliphatic alkynes (Table 3). Variously substituted alkynes reacted smoothly with **4a** affording the corresponding triazole-linked products **6a–f** in moderate to good yields (Table 3). The reaction with propargyl alcohol (**5e**) gave the highest yield of 89% (entry 5), but the reaction with propargyl bromide (**5g**) failed (entry 7).

To check our Nazarov cyclization hypothesis, we started our investigations with the reaction of **6a** with the external nucleophile indole **2a** in the presence of various Lewis acids

Table 3 Substrate Scope of CuAAC of Zerumbone Azide **4a** with Alkynes[a]



4a **6a–g**

Entry	Alkyne	Product	Yield (%)[b]
1	Ph—	**6a**	44
2	*p*-Tol—	**6b**	41
3	Ph	**6c**	36
4	Ph	**6d**	38
5	HO	**6e**	89
6	$(CH_2)_4$	**6f**	48
7	Br	**6g**	NR

[a] Reaction conditions: **4a** (1.0 equiv), alkyne (1.5 equiv), CuI (20 mol%), DIPEA (3.0 equiv), CH_3CN (2.0 mL), RT, 2 h.
[b] NR = no reaction.

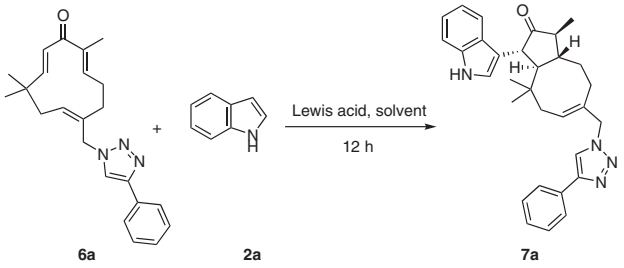
as catalyst in different solvents at 80 °C for 12 hours (Table 4). From the optimization studies, the best conditions were found to consist of a combination of **6a** (1.0 equiv), indole **2a** (1.0 equiv), and $AlCl_3$ (5 mol%), in CH_3CN at 80 °C for 12 hours, delivering the triazole-appended [6.3.0] fused product **7a** in 50% yield (entry 10).

With the optimal conditions in hand, we investigated the scope of reaction with substituted indoles **2** (Table 5). Indoles bearing both electron-donating and electron-withdrawing groups afforded the corresponding products in moderate to good yields.

Next, we turned our attention to the oxidation reactions of zerumbone (**Z**). In 2016, Kumar et al. reported the allylic oxidation of the isolated olefin of **Z** when using selenium dioxide (Scheme 4).[22] They synthesized new zerumbone–bicarbonyl analogues by selective oxidation of the methyl at C13, leading to an aldehyde (zerumbal, **8**) and a ketone (zerumbenone, **9**) with an exocyclic double bond between the C13 and C6 positions.

With our persistent curiosity in constructing polycyclic frameworks, here also we checked the possibility of Lewis acid catalyzed cyclization reactions of the bicarbonyl zerumbone derivatives **8** and **9**. Reaction of zerumbal **8** with indole (1.0 equiv) in the presence of $In(OTf)_3$ (5 mol%) in acetonitrile at room temperature resulted in the formation of the 6–3 ring-fused system **10a** in 81% yield

Table 4 Optimization of Lewis Acid Catalyzed Transformation of Triazole-Appended Zerumbone **6a** with Indole

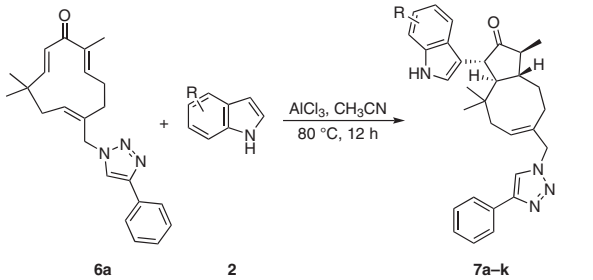


6a **2a** **7a**

Entry	Lewis acid	Solvent	Temp (°C)	Yield (%)[b]
1	$Sc(OTf)_3$	CH_3CN	RT	NR
2	$Sc(OTf)_3$	CH_3CN	80	38
3	$In(OTf)_3$	CH_3CN	80	45
4	$Cu(OTf)_2$	CH_3CN	80	NR
5	$Hf(OTf)_4$	CH_3CN	80	trace
6	$La(OTf)_3$	CH_3CN	80	NR
7	$Zn(OTf)_2$	CH_3CN	80	23
8	$Yb(OTf)_3$	CH_3CN	80	38
9	Ag(OTf)	CH_3CN	80	NR
10	$AlCl_3$	CH_3CN	80	50
11	$AlCl_3$	DMF	153	trace
12	$AlCl_3$	THF	66	NR
13	$AlCl_3$	DCE	83.5	NR
14	$AlCl_3$	toluene	110	NR

[a] Reaction conditions: **6a** (1.0 equiv), **2a** (1.0 equiv), Lewis acid (5 mol%), solvent (2.0 mL), 12 h.
[b] NR = no reaction.

Table 5 Scope of Lewis Acid Catalyzed Transformation of Triazole-Appended Zerumbone **6a** with Indoles **2**[a]



6a **2** **7a–k**

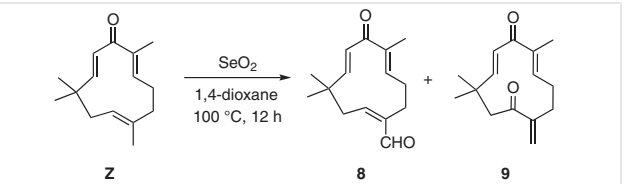
Entry	R	Product	Yield (%)[b]
1	H	**7a**	50
2	5-CH_3	**7b**	30
3	5-Br	**7c**	43
4	5-NO_2	**7d**	39
5	5-CHO	**7e**	32
6	5-OCH_3	**7f**	40
7	7-CH_3	**7g**	39
8	6-CH_3	**7h**	41
9	5-Cl	**7i**	37
10	5-F	**7j**	35
11	5-CN	**7k**	33
12	5-NH_2	**7l**	NR
13	5-OH	**7m**	NR

[a] Reaction conditions: **6a** (1.0 equiv), **2** (1.0 equiv), $AlCl_3$ (5 mol%), CH_3CN (2.0 mL), 80 °C, 12 h.
[b] NR = no reaction.

(Scheme 5), eventuated via the same interrupted Nazarov cyclization followed by nucleophilic attack, as described earlier. The structure and the stereochemistry were confirmed using various spectroscopic techniques.

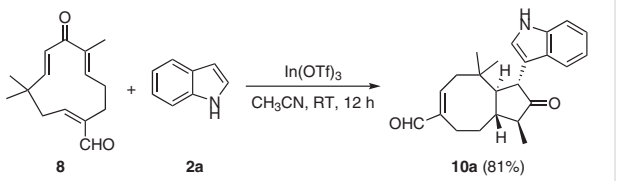
In the detailed optimization studies, the catalytic activity of different Lewis acids and the effect of different solvents and conditions for the reaction were studied; it was found out that the reaction with $In(OTf)_3$ (5 mol%) at room temperature in acetonitrile (2.0 mL) for 12 hours under an argon atmosphere gave the best yield of 81% for **10a** (Table 6, entry 3). Since zerumbal contains two carbonyl groups, we also performed the reaction with 2.0 equivalents of indole, but no desired product was obtained.

To extend the scope and generality of the synthetic methodology, we carried out the reaction with different substituted indoles and the results are listed in Table 7. We first studied the effect of substitution at the C2 position of indole (**10b**, **10c**). Interestingly, 2-phenylindole delivered the expected product (entry 2) but 2-formylindole failed (entry 3). Further, we checked the possibility of C2 activation using C3-substituted indoles (**10d**). Only a trace amount of the desired product was obtained (entry 4). A



Z **8** **9**

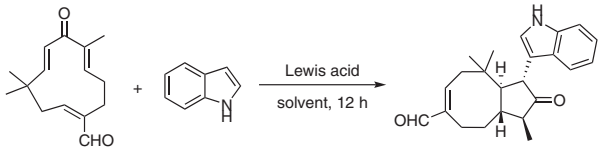
Scheme 4 Allylic oxidation of zerumbone



8 **2a** **10a** (81%)

Scheme 5 Lewis acid catalyzed interrupted Nazarov cyclization of zerumbal **8** with indole

Table 6 Optimization of Lewis Acid Catalyzed Transformation of Zerumbal **8** with Indole[a]



8 **2a** **10a**

Entry	Lewis acid	Solvent	Temp (°C)	Yield (%)[b]
1	$Sc(OTf)_3$	CH_3CN	RT	44
2	$Sc(OTf)_3$	CH_3CN	80	20
3	$In(OTf)_3$	CH_3CN	RT	81
4	$Cu(OTf)_2$	CH_3CN	RT	trace
5	$Fe(OTf)_3$	CH_3CN	RT	trace
6	$La(OTf)_3$	CH_3CN	RT	NR
7	$Zn(OTf)_2$	CH_3CN	RT	NR
8	$Yb(OTf)_3$	CH_3CN	RT	trace
9	$AlCl_3$	CH_3CN	RT	80
10	$BF_3{\cdot}OEt_2$	CH_3CN	RT	NR
11	$In(OTf)_3$	CH_3CN	80	78
12	$In(OTf)_3$	DCE	RT	trace
13	$In(OTf)_3$	DCE	80	75
14	$In(OTf)_3$	THF	RT	trace
15	$In(OTf)_3$	DMSO	RT	NR
16	$In(OTf)_3$	DCE/toluene	RT	trace

[a] Reaction conditions: **8** (1.0 equiv), **2a** (1.0 equiv), Lewis acid (5.0 mol%), solvent (2 mL), 12 h.
[b] NR = no reaction.

detailed substrate scope was checked with C5- and C6-substituted indoles (**10e–n**); the products were obtained in similar yield, which indicates that substitutions have no effect on the outcome of the reaction. The final confirmation of the structure and stereochemistry was obtained from a single-crystal X-ray structure of compound **10g** (Figure 1).

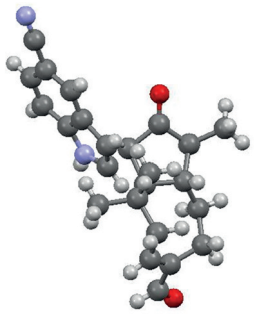
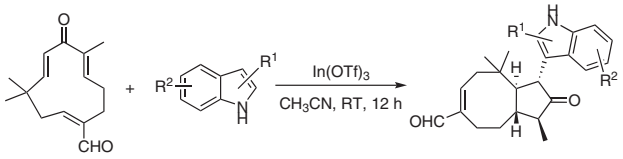


Figure 1 Single-crystal X-ray crystal structure of compound **10g**

Table 7 Scope of Lewis Acid Catalyzed Transformation of Zerumbal **8** with Indoles **2**[a]

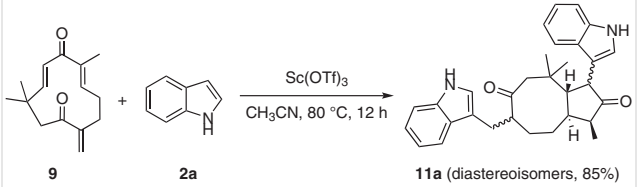


8 **2** **10a–n**

Entry	R^1	R^2	Product	Yield (%)[b]
1	H	H	**10a**	81
2	2-Ph	H	**10b**	73
3	2-CHO	H	**10c**	NR
4	3-CHO	H	**10d**	NR
5	H	5-CHO	**10e**	71
6	H	$5\text{-}NO_2$	**10f**	82
7	H	5-CN	**10g**	78
8	H	$5\text{-}CH_3$	**10h**	62
9	H	$5\text{-}OCH_3$	**10i**	64
10	H	5-F	**10j**	74
11	H	5-Cl	**10k**	75
12	H	$5\text{-}NH_2$	**10l**	NR
13	H	5-OH	**10m**	NR
14	H	$6\text{-}CH_3$	**10n**	63

[a] Reaction conditions: **8** (1.0 equiv), **2** (1.0 equiv), $In(OTf)_3$ (5.0 mol%), CH_3CN (2.0 mL), RT, 12 h.
[b] NR = no reaction.

In the case of zerumbenone, we also started our investigations with $Sc(OTf)_3$ as the Lewis acid. To our dismay, the reaction failed to proceed at room temperature. We noticed that when the reaction temperature was increased to 80 °C, a diastereoisomeric mixture (1:0.8) of a [6.3.0] ring-fused system appended to two indole moieties was formed, probably via an interrupted Nazarov cyclization and allylic carbocation formation (Scheme 6).



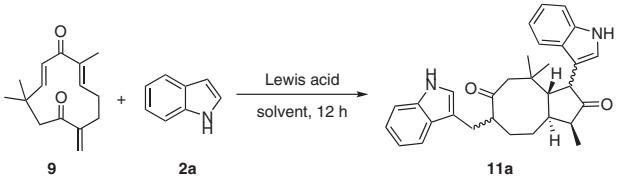
9 **2a** **11a** (diastereoisomers, 85%)

Scheme 6 Lewis acid catalyzed interrupted Nazarov cyclization of zerumbenone **9** with indole

We have carried out detailed optimization studies for the formation of the bis-indole derivative with different Lewis acids, solvents, and reaction conditions. All the Lewis acid tested furnished the desired product in good yield, but $Sc(OTf)_3$ emerged as the best Lewis acid in CH_3CN at 80 °C under an argon atmosphere, with 85% yield (Table 8, entry

2). The structure of the product was established using various spectroscopic techniques such as ^{1}H, ^{13}C, and other 2-D NMR techniques and finally by HRMS analysis.

Table 8 Optimization Studies of Lewis Acid Catalyzed Interrupted Nazarov Cyclization of Zerumbenone **9** with Indole[a]



9 **2a** **11a**

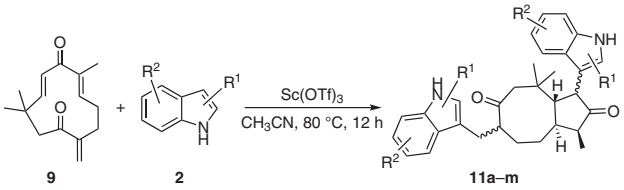
Entry	Lewis acid	Solvent	Temp (°C)	Yield (%)[b,c]
1	$Sc(OTf)_3$	CH_3CN	RT	NR
2	$Sc(OTf)_3$	CH_3CN	80	85
3	$AlCl_3$	CH_3CN	RT	NR
4	$AlCl_3$	CH_3CN	80	65
5	$In(OTf)_3$	CH_3CN	80	79
6	$Fe(OTf)_3$	CH_3CN	80	73
7	$La(OTf)_3$	CH_3CN	80	66
8	$Zn(OTf)_2$	CH_3CN	80	80
9	$BF_3{\cdot}OEt_2$	CH_3CN	80	NR
10	$Sc(OTf)_3$	DCE	80	60
11	$Sc(OTf)_3$	THF	80	trace
12	$Sc(OTf)_3$	DMSO	80	NR
13	$Sc(OTf)_3$	toluene	80	NR
14	$Sc(OTf)_3$	CH_3CN	RT	NR

[a] Reaction conditions: **9** (1.0 equiv), **2a** (2.0 equiv), Lewis acid (5.0 mol%), solvent (2 mL), 12 h.
[b] NR = no reaction.
[c] Diastereoisomers obtained.

With the optimum reaction condition in hand, we checked the feasibility of the reaction with different indoles; the results are listed in Table 9. The substrate scope was tested with different indoles, both with electron-withdrawing and electron-releasing groups, which afforded the products in similar yields In the case of 2-phenyl indole (entry 2), only a trace amount of product was obtained, possibly due to the steric hindrance. Indole-2-carboxylic acid failed to form the product (entry 3), possibly due to the lower nucleophilicity furnished by the carboxylic group at the C3 position. Like in the previous case, here also C5-substituted aminoindole and hydroxyindole failed to deliver the product (entries 12 and 13).

A plausible mechanism for the trans-annular cyclization is shown in Scheme 7. The mechanism of formation of **3a′** can be explained by path A which follows the Nazarov-type cyclization pathway (path A; Scheme 7). Initially, the Lewis acid coordinates to the carbonyl oxygen atom of **Z**, thereby creating an allylic carbocation intermediate $\mathbf{C_2}$. Then, the

Table 9 Scope and Generality of Lewis Acid Catalyzed Interrupted Nazarov Cyclization of Zerumbenone **9** with Indoles[a]



9 **2** **11a–m**

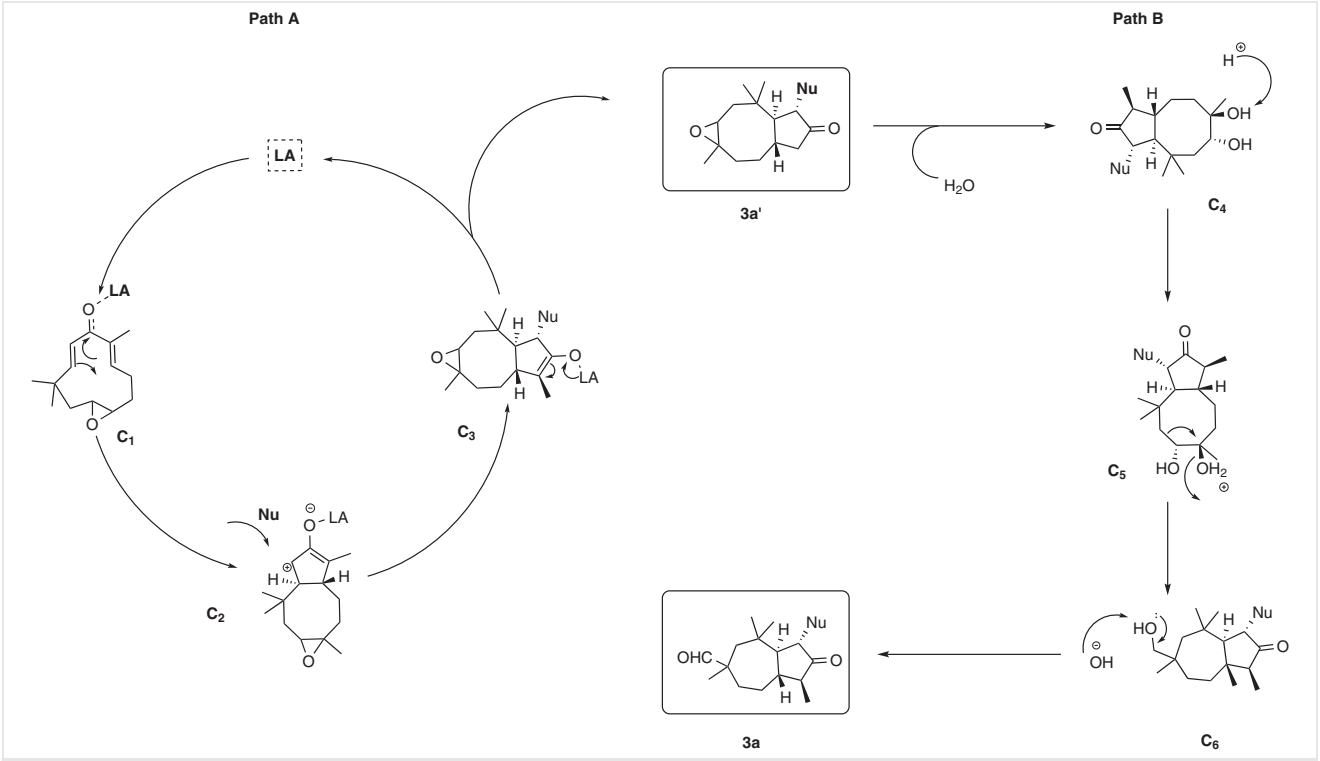
Entry	R^1	R^2	Product	Yield (%)[b,c]
1	H	H	**11a**	85
2	2-Ph	H	**11b**	trace
3	2-COOH	H	**11c**	NR
4	H	5-CN	**11d**	50
5	H	5-CHO	**11e**	35
6	H	5-NO_2	**11f**	56
7	H	5-OCH_3	**11g**	55
8	H	5-CH_3	**11h**	50
9	H	5-F	**11i**	53
10	H	5-Cl	**11j**	45
11	H	5-Br	**11k**	20
12	H	5-NH_2	**11l**	NR
13	H	5-OH	**11m**	NR

[a] Reaction conditions: **9** (1.0 equiv), **2** (2.0 equiv), $Sc(OTf)_3$ (5mol%), CH_3CN (2.0 mL), 80 °C, 12 h.
[b] NR = no reaction.
[c] Diasteroisomers (1:0.8).

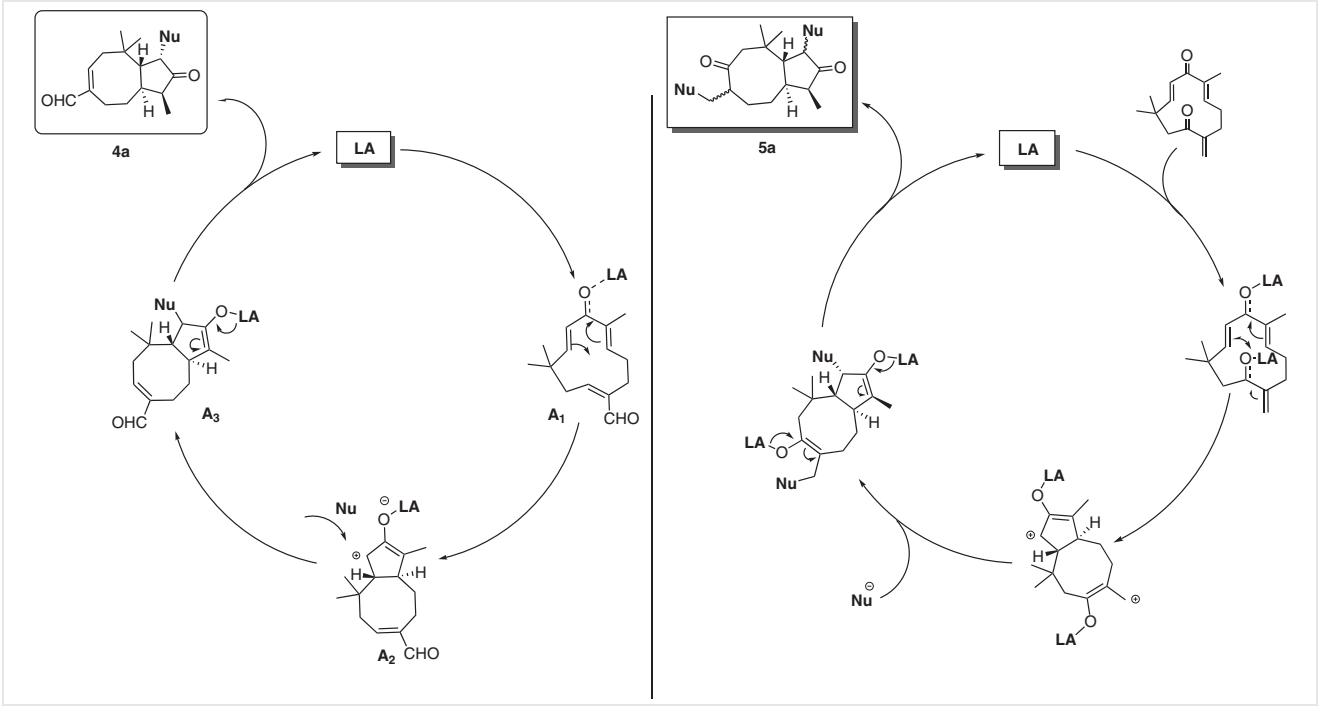
carbocation is trapped by an external nucleophile (indole), followed by tautomeric rearrangement to afford the product **3a′** (Scheme 7). Product **3a′** again undergoes ring opening by a water molecule to afford the diol intermediate $\mathbf{C_4}$, which upon pinacol–pinacolone rearrangement affords product **3a**, which is a [5.3.0] fused ring system.

The formation of **4a** follows the same mechanistic pathway as **3a′**, but for **5a**, there is an interrupted Nazarov cyclization followed by conjugate addition of the nucleophile which results in the formation of the bis-indole derivative (Scheme 8).

In conclusion, we have described a straightforward method for the preparation of polycyclic terpenoid systems from the naturally abundant sesquiterpene zerumbone. Lewis acid catalyzed transannular cyclization of zerumbone derivatives furnished [5.3.0] and [6.3.0] fused ring systems via interrupted Nazarov cyclization. Zerumbone epoxide delivered biologically relevant [5.3.0] and [6.3.0] systems, while all other derivatives, such as triazole-appended zerumbone derivatives, zerumbenone, and zerumbal furnished [6.3.0] fused sesquiterpenoid motifs. Furthermore, the synthetic scope of the polycyclics prepared were tested with a wide variety of substrates, which gave moderate to



Scheme 7 Plausible mechanism for Lewis acid catalyzed transannular cyclization of zerumbone epoxide



Scheme 8 Plausible mechanism for Lewis acid catalyzed transannular cyclization of zerumbal and zerumbenone

good yields. Further, the biological evaluation of various scaffolds is in progress in our laboratory, and will be reported in due course.

All chemicals were of the best grade commercially available and were used without further purification. All solvents were purified according to standard procedures; anhydrous solvents were obtained according to literature methods and stored over molecular sieves. Analytical TLC was performed with Merck TLC Silica gel F_{254} coated on aluminum sheets. Gravity column chromatography was performed using 100–200 or 230–400 mesh silica gel and mixtures of hexane–EtOAc were used for elution. Melting points were determined on a Buchi melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX 500 spectrophotometer ($CDCl_3$, CCl_4 or their mixtures were used as solvent). Chemical shifts δ of the ^{1}H and ^{13}C NMR spectra were referenced against $SiMe_4$ (δ = 0.0) or the signal of the NMR solvent. ESI-HRMS spectra were recorded at 60,000 resolution by using a Thermo Scientific Exactive mass spectrometer. IR spectra were recorded on a Bruker FT-IR alpha spectrophotometer.

Preparation of [5.3.0] and [6.3.0] Fused Cyclic Products 3 and 3′ from Zerumbone Epoxide 1; General Procedure

Zerumbone epoxide **1** (1.0 equiv), indole **2** (1.0 equiv), $Sc(OTf)_3$ (30 mol%), and H_2O (10.0 equiv) were placed in a reaction tube. CH_3CN (2 mL) was added and the reaction mixture was stirred at 80 °C for 5 h. The solvent was evaporated in vacuo and the residue was purified by column chromatography (silica gel, 230–400 mesh, hexane–EtOAc) to yield the product.

3-(1*H*-Indol-3-yl)-1,4,4,6-tetramethyl-2-oxodecahydroazulene-6-carbaldehyde (3a)

Yield: 49 mg (65%); brown pasty mass; R_f = 0.37 (EtOAc–hexane, 3.5:6.5).

IR (neat): 3360, 2961, 2927, 1731, 1691, 1621, 1459, 1370, 1340, 1263, 1158, 1102, 1012, 653, 590 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.46 (s, 1 H), 8.15 (s, 1 H), 7.53 (d, *J* = 8.0 Hz, 1 H), 7.31 (d, *J* = 8.0 Hz, 1 H), 7.16 (t, *J* = 7.5 Hz, 1 H), 7.09 (t, *J* = 7.5 Hz, 1 H), 6.90 (d, *J* = 2.0 Hz, 1 H), 3.40 (d, *J* = 11.0 Hz, 1 H), 2.25–2.21 (m, 2 H), 2.14–2.05 (m, 2 H), 1.88 (d, *J* = 15.5 Hz, 1 H), 1.74 (dd, J_1 = 14.5, J_2 = 7 Hz, 1 H), 1.57 (d, *J* = 15.5 Hz, 1 H), 1.50 (dd, J_1 = 23.0, J_2 = 12.0 Hz, 2 H), 1.17 (d, *J* = 6.5 Hz, 3 H), 1.07 (s, 3 H), 0.88 (s, 3 H), 0.65 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 218.1, 206.1, 136.6, 126.4, 122.4, 122.1, 119.5, 119.1, 115.8, 111.4, 59.2, 50.8, 50.5, 49.5, 49.0, 47.7, 36.6, 33.1, 32.7, 27.3, 25.3, 21.5, 12.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{30}NO_2$: 352.22711; found: 352.22712.

6-(1*H*-Indol-3-yl)-1a,4,7,7-tetramethyldecahydro-5*H*-cyclopenta-[5,6]cycloocta[1,2-*b*]oxiren-5-one (3a′)

Yield: 19 mg (25%); brown pasty mass; R_f = 0.28 (EtOAc–hexane, 3.5:6.5).

IR (neat): 3337, 2964, 2930, 1696, 1574, 1464, 1437, 1376, 1340, 1262, 1141, 1104, 1074, 750, 650 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.13 (s, 1 H), 7.77 (d, *J* = 8.0 Hz, 1 H), 7.33 (t, *J* = 8.0 Hz, 1 H), 7.21 (t, *J* = 7.0 Hz, 1 H), 7.15 (t, *J* = 7.5 Hz, 1 H), 7.01 (d, *J* = 1.5 Hz, 1 H), 3.68 (d, *J* = 5.0 Hz, 1 H), 2.72 (d, *J* = 11.5 Hz, 1 H), 2.41–2.37 (m, 1 H), 2.33 (dd, J_1 = 14.0, J_2 = 7.2 Hz, 1 H), 2.17–2.12(m, 2 H), 2.05 (d, *J* = 11.5 Hz, 1 H), 1.87–1.84 (m, 1 H), 1.75 (dd, J_1 = 17.5, J_2 = 7.5 Hz, 1 H), 1.63 (s, 3 H), 1.23 (dd, J_1 = 13.0, J_2 = 5.0 Hz, 2 H), 1.12 (d, *J* = 7.0 Hz, 3 H), 1.04 (s, 3 H), 1.02 (s, 3 H), 0.88 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 214.6, 134.7, 133.8, 131.0, 130.2, 129.9, 128.3, 112.1, 53.5, 52.4, 49.4, 49.3, 48.3, 41.2, 40.3, 39.6, 34.1, 31.2, 29.7, 25.1, 20.3, 18.8, 13.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{30}NO_2$: 352.22711; found: 352.22712.

1,4,4,6-Tetramethyl-3-(5-methyl-1*H*-indol-3-yl)-2-oxodecahydro-azulene-6-carbaldehyde (3b)

Yield: 26 mg (33%); brown viscous liquid; R_f = 0.35 (EtOAc–hexane, 3.5:6.5).

IR (neat): 3370, 2962, 2927, 1730, 1691, 1583, 1460, 1374, 1343, 1265, 1155, 1102, 920, 795, 735, 621 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.47 (s, 1 H), 7.98 (br s, 1 H), 7.29 (d, *J* = 0.5 Hz, 1 H), 7.21 (d, *J* = 8.0 Hz, 1 H), 6.99 (dd, J_1 = 7.0, J_2 = 1.0 Hz, 1 H), 6.91 (d, *J* = 2.0 Hz, 1 H), 3.38 (d, *J* = 11.0 Hz, 1 H), 2.44 (s, 3 H), 2.23–2.20 (m, 2 H), 2.19–2.09 (m, 2 H), 1.89 (d, *J* = 15.0 Hz, 1 H), 1.75–1.72 (m, 2 H), 1.56–1.43 (m, 2 H), 1.16 (d, *J* = 7.0 Hz, 3 H), 1.08 (s, 3 H), 0.89 (s, 3 H), 0.67 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 216.6, 205.9, 134.8, 129.2, 124.3, 122.2, 121.0, 119.3, 110.8, 59.6, 52.3, 49.8, 48.7, 47.9, 39.7, 34.2, 31.1, 29.8, 25.4, 21.6, 20.0, 19.0, 13.0, 12.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{31}NNaO_2$: 388.22525; found: 388.22638.

1a,4,7,7-Tetramethyl-6-(5-methyl-1*H*-indol-3-yl)decahydro-5*H*-cyclopenta[5,6]cycloocta[1,2-*b*]oxiren-5-one (3b′)

Yield: 17 mg (22%); brown viscous liquid; R_f = 0.18 (EtOAc–hexane, 3.5:6.5).

IR (neat): 3386, 2924, 2855, 1701, 1577, 1458, 1377, 1263, 1180, 1099, 1071, 796, 708, 644, 622 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.80 (br s, 1 H), 7.60 (s, 1 H), 7.21 (d, *J* = 8.0 Hz, 1 H), 7.00 (dd, J_1 = 8.0, J_2 = 1.2 Hz, 1 H), 6.88 (d, *J* = 2.0 Hz, 1 H), 3.12 (d, *J* = 11.0 Hz, 1 H), 2.73 (d, *J* = 11.0 Hz, 1 H), 2.59 (d, *J* = 7.0 Hz, 1 H), 2.46 (s, 3 H), 2.07–1.99 (m, 2 H), 1.91 (dd, J_1 = 14.0, J_2 = 6.5 Hz, 2 H), 1.77–1.73 (m, 2 H), 1.32 (s, 3 H), 1.29 (s, 3 H), 1.26 (s, 3 H), 1.10 (d, *J* = 7.0 Hz, 1 H), 1.03 (d, *J* = 7.0 Hz, 1 H), 0.95 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 214.6, 123.7, 120.3, 119.0, 116.2, 110.5, 62.8, 60.9, 50.8, 50.0, 49.9, 47.0, 45.3, 37.9, 36.7, 36.6, 35.0, 30.8, 29.9, 25.7, 23.5, 21.5, 19.8, 18.5, 14.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{31}NNaO_2$: 388.22525; found: 388.22632.

3-(5-Bromo-1*H*-indol-3-yl)-1,4,4,6-tetramethyl-2-oxodecahydro-azulene-6-carbaldehyde (3c)

Yield: 25 mg (27%); brown viscous liquid; R_f = 0.27 (EtOAc–hexane, 3.5:6.5).

IR (neat): 3346, 2964, 2930, 1730, 1688, 1457, 1375, 1266, 1154, 1104, 884, 795, 734, 702, 636, 614 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = δ 9.47 (s, 1 H), 8.29 (br s, 1 H), 7.61 (d, *J* = 1.0 Hz, 1 H), 7.22 (dd, J_1 = 8.5, J_2 = 1.5 Hz, 1 H), 7.13 (d, *J* = 8.5 Hz, 1 H), 6.85 (d, *J* = 2.0 Hz, 1 H), 3.33 (d, *J* = 11.0 Hz, 1 H), 2.22–2.18 (m, 1 H), 2.14–2.10 (m, 2 H), 1.89 (d, *J* = 15.0 Hz, 1 H), 1.74 (dd, J_1 = 15.0, J_2 = 6.5 Hz, 1 H), 1.58–1.49 (m, 2 H), 1.25 (d, *J* = 7.0 Hz, 2 H), 1.18 (d, *J* = 6.5 Hz, 3 H), 1.08 (s, 3 H), 0.87 (s, 3 H), 0.62 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 217.1, 206.1, 135.2, 128.1, 125.0, 123.7, 121.5, 115.3, 112.9, 59.4, 50.8, 50.5, 49.4, 48.9, 47.9, 36.6, 33.1, 27.1, 25.5, 21.4, 14.2, 12.2.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{28}BrNNaO_2$: 452.12011; found: 452.12076.

6-(5-Bromo-1*H*-indol-3-yl)-1a,4,7,7-tetramethyldecahydro-5*H*-cyclopenta[5,6]cycloocta[1,2-*b*]oxiren-5-one (3c′)

Yield: 21 mg (23%); brown viscous liquid; R_f = 0.18 (EtOAc–hexane, 3.5:6.5).

IR (neat): 3357, 2962, 2929, 1703, 1573, 1457, 1364, 1287, 1226, 1101, 884, 797, 753, 703, 647 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.28 (br s, 1 H), 7.89 (d, *J* = 12.0 Hz, 1 H), 7.26 (t, *J* = 4.0 Hz, 1 H), 7.17 (d, *J* = 8.5 Hz, 1 H), 6.96 (d, *J* = 8.0 Hz, 1 H), 3.59 (t, *J* = 5.0 Hz, 1 H), 2.68 (d, *J* = 11.5 Hz, 1 H), 2.52–2.38 (m, 1 H), 2.36–2.25 (m, 2 H), 2.12 (d, *J* = 11.5 Hz, 1 H), 1.96–1.80 (m, 2 H), 1.79–1.71 (m, 1 H), 1.65 (s, 2 H), 1.61–1.50 (m, 2 H), 1.13 (s, 3 H), 1.04 (s, 7 H), 0.99 (d, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 206.1, 135.2, 128.1, 125.0, 123.7, 121.5, 115.3, 112.9, 60.4, 59.4, 50.8, 50.5, 49.5, 48.9, 47.9, 36.6, 33.1, 27.1, 25.5, 21.3, 14.2, 12.2.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{28}BrNNaO_2$: 452.12011; found: 452.12076.

1,4,4,6-Tetramethyl-3-(5-nitro-1*H*-indol-3-yl)-2-oxodecahydroazulene-6-carbaldehyde (3d)

Yield: 27 mg (32%); yellow pasty mass; R_f = 0.33 (EtOAc–hexane, 3.5:6.5).

IR (neat): 3335, 2961, 2928, 1728, 1696, 1623, 1519, 1470, 1373, 1332, 1248, 1106, 914, 816, 739, 651 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.48 (s, 1 H), 8.51 (s, 1 H), 8.11 (dd, J_1 = 9.0, J_2 = 2.0 Hz, 1 H), 8.00–7.95 (m, 1 H), 7.37 (d, *J* = 9.0 Hz, 1 H), 7.13 (d, *J* = 2.0 Hz, 1 H), 3.44 (d, *J* = 11.0 Hz, 1 H), 3.19–3.05 (m, 1 H), 2.95–2.74 (m, 1 H), 2.66–2.45 (m, 1 H), 2.26–2.20 (m, 1 H), 2.13–2.11 (m, 1 H), 1.93 (d, *J* = 15.0 Hz, 1 H), 1.26 (d, *J* = 3.0 Hz, 2 H), 1.19 (d, *J* = 6.5 Hz, 3 H), 1.09 (s, 3 H), 0.91 (s, 3 H), 0.64 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 217.4, 205.9, 141.9, 139.4, 133.5, 130.2, 125.3, 118.1, 116.6, 111.4, 59.6, 50.7, 50.5, 49.3, 48.9, 47.9, 44.8, 40.2, 39.7, 36.6, 33.0, 30.9, 27.0, 25.5, 23.3, 21.3, 12.2.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{28}N_2NaO_4$: 419.19468; found: 419.19461.

1a,4,7,7-Tetramethyl-6-(5-nitro-1*H*-indol-3-yl)decahydro-5*H*-cyclopenta[5,6]cycloocta[1,2-*b*]oxiren-5-one (3d′)

Yield: 17 mg (20%); yellow viscous liquid; R_f = 0.24 (EtOAc–hexane, 3.5:6.5).

IR (neat): 3077, 2963, 2926, 1728, 1624, 1575, 1520, 1471, 1432, 1376, 1334, 1305, 1262, 1142, 1074, 898, 749, 721, 669 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.74 (dd, J_1 = 15.0, J_2 = 2.0 Hz, 1 H), 8.51 (s, 1 H), 8.15–8.11 (m, 1 H), 7.57 (s, 1 H), 7.38 (d, *J* = 8.5 Hz, 1 H), 3.69 (d, *J* = 6.0 Hz, 1 H), 2.64 (dd, J_1 = 11.5, J_2 = 4.5 Hz, 1 H), 2.49 (dd, J_1 = 10.0, J_2 = 3.0 Hz, 1 H), 2.41–2.36 (m, 1 H), 2.32–2.27 (m, 2 H), 2.23 (d, *J* = 11.5 Hz, 1 H), 1.94–1.88 (m, 5 H), 1.81 (dd, J_1 = 13.0, J_2 = 8.0 Hz, 3 H), 1.65–1.60 (m, 1 H), 1.49–1.39 (m, 1 H), 1.26 (s, 3 H), 1.09 (s, 6 H), 1.00 (d, *J* = 12.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 219.5, 134.7, 133.8, 130.2, 129.8, 128.3, 68.6, 64.2, 54.9, 52.8, 48.9, 41.7, 39.4, 34.1, 30.9, 29.4, 28.6, 21.3, 18.1, 14.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{28}N_2NaO_4$: 419.19468; found: 419.19447.

3-(6-Formyl-3,6,8,8-tetramethyl-2-oxodecahydroazulen-1-yl)-1*H*-indole-5-carbaldehyde (3e)

Yield: 25 mg (31%); brown viscous liquid; R_f = 0.32 (EtOAc–hexane, 3.5:6.5).

IR (neat): 3333, 2961, 2929, 1714, 1679, 1612, 1576, 1459, 1365, 1267, 1175, 1100, 896, 811, 735, 663 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.03 (s, 1 H), 9.48 (s, 1 H), 8.36 (br s, 1 H), 8.09 (s, 1 H), 7.75 (dd, J_1 = 8.5 Hz, J_2 = 1.5 Hz, 1 H), 7.42 (d, *J* = 8.5 Hz, 1 H), 7.08 (d, *J* = 2.0 Hz, 1 H), 3.46 (d, *J* = 11.5 Hz, 1 H), 2.26–2.23 (m, 2 H), 2.26–2.23 (m, 2 H), 2.21–2.10 (m, 2 H), 1.92 (d, *J* = 15.5 Hz, 1 H), 1.79–1.74 (m, 1 H), 1.28–1.25 (m, 2 H), 1.18 (d, *J* = 6.5 Hz, 3 H), 1.15–1.14 (m, 1 H), 1.08 (s, 3 H), 0.90 (d, *J* = 7.0 Hz, 3 H), 0.65 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 216.8, 206.0, 192.3, 140.0, 129.6, 123.9, 118.1, 111.9, 59.6, 50.4, 49.3, 48.9, 47.9, 36.6, 33.0, 27.1, 25.5, 21.3, 12.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{30}NO_3$: 380.22202; found: 380.22328.

3-(3,3,6,8a-Tetramethyl-5-oxodecahydro-2*H*-cyclopenta[5,6]-cycloocta[1,2-*b*]oxiren-4-yl)-1*H*-indole-5-carbaldehyde (3e′)

Yield: 16 mg (20%); brown pasty mass; R_f = 0.29 (EtOAc–hexane, 3:7).

IR (neat): 3335, 2961, 2929, 1714, 1612, 1562, 1464, 1365, 1267, 1175, 1100, 896, 811, 735, 663 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.06 (s, 1 H), 8.40 (s, 1 H), 8.33 (d, *J* = 11.0 Hz, 1 H), 8.07 (t, *J* = 1.5 Hz, 1 H), 7.80 (d, *J* = 8.5 Hz, 1 H), 7.43 (d, *J* = 7.5 Hz, 1 H), 3.72 (d, *J* = 5.5 Hz, 1 H), 2.68 (d, *J* = 11.5 Hz, 1 H), 2.53–2.43 (m, 1 H), 2.39 (t, *J* = 6.0 Hz, 1 H), 2.32–2.28 (m, 1 H), 2.21–2.13 (m, 1 H), 2.09–2.03 (m, 1 H), 1.91 (d, *J* = 5.5 Hz, 1 H), 1.41 (d, *J* = 5.5 Hz, 1 H), 1.25 (d, *J* = 7.5 Hz, 2 H), 1.13 (s, 3 H), 1.07 (s, 6 H), 1.02 (d, *J* = 8.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 217.1, 192.5, 139.9, 133.7, 130.2, 129.8, 128.3, 122.5, 111.9, 53.3, 52.1, 50.1, 49.4, 48.6, 48.4, 31.1, 30.7, 29.7, 20.5, 18.7, 13.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{30}NO_3$: 380.22202; found: 380.22333.

3-(6-Formyl-3,6,8,8-tetramethyl-2-oxodecahydroazulen-1-yl)-1*H*-indole-5-carbonitrile (3f)

Yield: 25 mg (31%); brown viscous liquid; R_f = 0.52 (EtOAc–hexane, 3:7).

IR (neat): 3325, 2962, 2931, 2220, 1728, 1691, 1619, 1469, 1370, 1265, 1173, 1102, 809, 736, 640 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.47 (s, 1 H), 8.52 (br s, 1 H), 7.87 (s, 1 H), 7.38 (d, *J* = 1.5 Hz, 1 H), 7.35 (d, *J* = 0.5 Hz, 1 H), 7.06 (d, *J* = 2.5 Hz, 1 H), 3.39 (d, *J* = 11.5 Hz, 1 H), 2.20–2.09 (m, 5 H), 1.92 (d, *J* = 15.5 Hz, 1 H), 1.18–1.74 (m, 1 H), 1.54–1.49 (m, 3 H), 1.19 (d, *J* = 7.0 Hz, 3 H), 1.14 (s, 3 H), 1.09 (s, 3 H), 0.89 (s, 3 H), 0.61 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 216.4, 204.9, 137.2, 125.1, 124.2, 123.9, 123.6, 115.8, 111.3, 101.9, 58.4, 49.7, 49.5, 48.5, 46.9, 35.6, 31.9, 31.9, 25.9, 24.5, 20.2, 11.2.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{28}N_2NaO_2$: 399.20485; found: 399.20572.

3-(3,3,6,8a-Tetramethyl-5-oxodecahydro-2*H*-cyclopenta[5,6]-cycloocta[1,2-*b*]oxiren-4-yl)-1*H*-indole-5-carbonitrile (3f')

Yield: 9 mg (11%); brown viscous liquid; R_f = 0.41 (EtOAc–hexane, 3.5:6.5).

IR (neat): 3330, 2961, 2927, 2220, 1729, 1621, 1459, 1370, 1340, 1263, 1158, 1102, 1012, 653, 640 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.43 (br s, 1 H), 8.15 (d, J = 13.0 Hz, 1 H), 7.44–7.42 (m, 1 H), 7.40 (s, 1 H), 7.14 (dd, J_1= 10.5, J_2 = 1.5 Hz, 1 H), 3.64 (dd, J_1= 8.5, J_2 = 5.0 Hz, 1 H), 2.65 (d, J = 11.5 Hz, 1 H), 2.55–2.43 (m, 2 H), 2.34 (dd, J_1= 11.0, J_2 = 5.0 Hz, 1 H), 2.31–2.24 (m, 2 H), 2.19 (d, J = 11.5 Hz, 1 H), 2.05 (d, J = 10.5 Hz, 1 H), 1.89 (d, J = 3.5 Hz, 1 H), 1.44–1.39 (m, 1 H), 1.25 (s, 3 H), 1.05 (s, 6 H), 1.00 (d, J = 9.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 216.5, 143.4, 137.9, 133.5, 130.9, 129.1, 122.9, 111.8, 52.1, 49.6, 47.7, 41.5, 40.0, 29.7, 20.6, 17.6, 12.1.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{24}H_{28}N_2NaO_2$: 399.20485; found: 399.20517.

3-(5-Fluoro-1*H*-indol-3-yl)-1,4,4,6-tetramethyl-2-oxodecahydro-azulene-6-carbaldehyde (3g)

Yield: 16 mg (20%); brown viscous liquid; R_f = 0.43 (EtOAc–hexane, 3.5:6.5).

IR (neat): 3350, 2964, 2931, 2874, 1792, 1629, 1580, 1486, 1457, 1375, 1292, 1233, 1168, 936, 843, 794, 735, 700 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 9.46 (s, 1 H), 8.33 (s, 2 H), 7.40 (dd, J_1 = 12.0, J_2 = 8.5 Hz, 1 H), 7.15 (s, 1 H), 6.90 (d, J = 9.5 Hz, 1 H), 3.33 (d, J = 11.0 Hz, 1 H), 2.68 (d, J = 11.5 Hz, 1 H), 2.49–2.41 (m, 1 H), 2.35–2.29 (m, 1 H), 2.21 (dd, J_1 = 13.5, J_2 = 7.0 Hz, 1 H), 1.88 (d, J = 14.0 Hz, 1 H), 1.76–1.72 (m, 1 H), 1.57 (d, J = 13.5 Hz, 1 H), 1.50–1.47 (m, 2 H), 1.07 (s, 3 H), 1.04 (s, 3 H), 1.00 (d, J = 6.5 Hz, 3 H), 0.88 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 215.9, 206.4, 134.6, 133.5, 130.1, 129.8, 128.2, 123.1, 123.0, 116.7, 53.3, 52.2, 49.4, 48.8, 48.6, 48.3, 41.1, 40.1, 39.6, 34.0, 30.9, 29.7, 25.4, 20.3, 18.8, 13.2, 12.2.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{23}H_{28}FNNaO_2$: 392.20018; found: 392.20019.

6-(5-Fluoro-1*H*-indol-3-yl)-1a,4,7,7-tetramethyldecahydro-5*H*-cyclopenta[5,6]cycloocta[1,2-*b*]oxiren-5-one (3g')

Yield: 12 mg (15%); brown viscous liquid; R_f = 0.40 (EtOAc–hexane, 3.5:6.5).

IR (neat): 3366, 2964, 2932, 1728, 1580, 1486, 1458, 1375, 1236, 1167, 1101, 936, 844, 796, 734, 700, 614 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.30 (br s, 1 H), 8.08 (s, 1 H), 7.41 (dd, J_1= 8.5, J_2 = 6.5 Hz, 1 H), 7.21 (dd, J_1= 8.5, J_2 = 4.0 Hz, 1 H), 6.93 (t, J = 9.0 Hz, 1 H), 3.58 (d, J = 5.0 Hz, 1 H), 2.71 (dd, J_1= 21.0, J_2 = 11.5 Hz, 1 H), 2.53–2.39 (m, 1 H), 2.33–2.28 (m, 2 H), 2.10 (d, J = 11.5 Hz, 1 H), 1.88 (d, J = 11.0 Hz, 1 H), 1.73 (dd, J_1= 17.0, J_2 = 7.5 Hz, 1 H), 1.55–1.49 (m, 2 H), 1.11 (s, 3 H), 1.09–0.95 (m, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 216.2, 134.7, 133.7, 133.0, 130.2, 129.8, 128.3, 122.9, 112.0, 111.9, 52.2, 50.0, 49.4, 48.6, 48.3, 41.1, 39.6, 34.0, 31.1, 29.7, 20.3, 18.8, 13.2.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{23}H_{28}FNNaO_2$: 392.20018; found: 392.20019.

3-(5-Methoxy-1*H*-indol-3-yl)-1,4,4,6-tetramethyl-2-oxodecahydro-azulene-6-carbaldehyde (3j)

Yield: 28 mg (35%); brown viscous liquid; R_f = 0.84 (EtOAc–hexane, 3.5:6.5).

IR (neat): 3360, 2962, 2930, 1733, 1689, 1625, 1583, 1485, 1459, 1374, 1295, 1264, 1214, 1172, 1032, 925, 799, 735, 698, 632 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 9.46 (s, 1 H), 8.04 (br s, 1 H), 7.22–7.19 (m, 2 H), 6.99 (s, 1 H), 6.87–6.83 (m, 2 H), 3.85 (s, 3 H), 3.36 (d, J = 11.0 Hz, 1 H), 2.18 (t, J = 9.0 Hz, 2 H), 2.12–2.09 (m, 2 H), 2.06 (d, J = 10.0 Hz, 1 H), 1.89 (d, J = 15.5 Hz, 1 H), 1.76–1.72 (m, 1 H), 1.59–1.52 (m, 1 H), 1.49–1.46 (m, 2 H), 1.16 (d, J = 6.5 Hz, 3 H), 1.07 (s, 3 H), 0.88 (s, 3 H), 0.66 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 218.3, 206.2, 153.9, 131.8, 126.9, 123.1, 115.5, 112.0, 111.8, 101.7, 59.2, 50.8, 50.4, 49.2, 49.0, 47.7, 36.6, 33.0, 32.8, 27.3, 25.4, 21.5, 12.2.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{24}H_{31}NNaO_3$: 404.22016; found: 404.22034.

6-(5-Methoxy-1*H*-indol-3-yl)-1a,4,7,7-tetramethyldecahydro-5*H*-cyclopenta[5,6]cycloocta[1,2-*b*]oxiren-5-one (3j')

Yield: 16 mg (20%); brown viscous liquid; R_f = 0.82 (EtOAc–hexane, 3.5:6.5).

IR (neat): 3362, 2961, 2930, 1729, 1625, 1583, 1485, 1459, 1372, 1296, 1214, 1170, 1038, 912, 832, 800, 731, 696, 645 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.05 (br s, 1 H), 7.26 (s, 1 H), 7.21 (s, 1 H), 6.99 (s, 1 H), 6.86 (d, J = 8.5 Hz, 1 H), 3.88 (s, 3 H), 3.62 (d, J = 4.0 Hz, 1 H), 2.72 (d, J = 11.5 Hz, 1 H), 2.40–2.37 (m, 1 H), 2.35–2.30 (m, 1 H), 2.18–2.13 (m, 2 H), 1.91–1.83 (m, 2 H), 1.77–1.70 (m, 2 H), 1.64 (s, 3 H), 1.52–1.48 (m, 1 H), 1.13 (s, 3 H), 1.03 (d, J = 4.0 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 215.5, 154.3, 133.6, 130.2, 129.8, 128.3, 121.7, 113.1, 112.0, 101.2, 55.9, 52.0, 49.8, 49.4, 48.8, 41.1, 39.7, 34.3, 31.1, 29.8, 20.1, 19.0, 13.0, 12.8.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{24}H_{31}NNaO_3$: 404.22016; found: 404.22034.

1,4,4,6-Tetramethyl-3-(7-methyl-1*H*-indol-3-yl)-2-oxodeca-hydroazulene-6-carbaldehyde (3k)

Yield: 27 mg (37%); brown viscous liquid; R_f = 0.64 (EtOAc–hexane, 3.5:6.5).

IR (neat): 3368, 2960, 2924, 2854, 1733, 1689, 1617, 1458, 1375, 1266, 1156, 1102, 782, 738, 703 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 9.46 (s, 1 H), 8.08 (s, 1 H), 7.98 (d, J = 8.0 Hz, 2 H), 7.03–6.98 (m, 2 H), 3.40 (d, J = 11.0 Hz, 1 H), 2.47 (d, J = 4.5 Hz, 1 H), 2.44 (s, 3 H), 2.23 (d, J = 10.0 Hz, 2 H), 2.08 (d, J = 13.5 Hz, 2 H), 1.88 (d, J = 15.0 Hz, 1 H), 1.74 (d, J = 7.5 Hz, 1 H), 1.56 (s, 1 H), 1.47 (d, J = 11.0 Hz, 1 H), 1.16 (d, J = 6.5 Hz, 3 H), 1.07 (s, 3 H), 0.89 (s, 3 H), 0.67 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 218.2, 206.2, 134.7, 133.7, 131.1, 130.2, 129.8, 128.3, 122.8, 122.1, 120.5, 119.8, 116.9, 59.2, 50.5, 49.7, 49.0, 47.7, 36.6, 27.3, 25.3, 21.5, 16.6, 12.2.

HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{24}H_{32}NO_2$: 366.24276; found: 366.24302.

1a,4,7,7-Tetramethyl-6-(7-methyl-1*H*-indol-3-yl)decahydro-5*H*-cyclopenta[5,6]cycloocta[1,2-*b*]oxiren-5-one (3k')

Yield: 12 mg (15%); brown viscous liquid; R_f = 0.61 (EtOAc–hexane, 3.5:6.5).

IR (neat): 3366, 2962, 2930, 1724, 1617, 1457, 1436, 1372, 1230, 1160, 1070, 784, 741 702, 673, 646 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.01 (br s, 11 H), 7.62 (t, J = 8.5 Hz, 1 H), 7.07 (t, J = 7.0 Hz, 1 H), 7.03 (d, J = 6.5 Hz, 1 H), 6.99 (d, J = 12.0 Hz, 1 H), 3.67 (d, J = 3.0 Hz, 1 H), 2.71 (d, J = 11.5 Hz, 1 H), 2.46 (s, 3 H),

2.42–2.36 (m, 2 H), 2.31 (dd, J_1= 15.0, J_2 = 7.0 Hz, 1 H), 2.19 (dd, J_1= 16.0, J_2 = 4 Hz, 1 H), 2.13 (d, J = 12.5 Hz, 1 H), 2.05 (s, 1 H), 1.86 (d, J = 10.5 Hz, 1 H), 1.74 (d, J = 13.5 Hz, 2 H), 1.26 (s, 6 H), 1.04 (d, J = 3.0 Hz, 3 H), 1.02 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 216.6, 136.1, 123.1, 120.8, 120.3, 120.1, 117.4, 116.9, 52.4, 49.4, 48.9, 48.8, 48.3, 41.0, 34.3, 31.1, 20.1, 19.0, 16.5, 13.2.

HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{24}H_{32}NO_2$: 366.24276; found: 366.24302.

1,4,4,6-Tetramethyl-3-(6-methyl-1*H*-indol-3-yl)-2-oxodecahydroazulene-6-carbaldehyde (3l)

Yield: 27 mg (34%); brown viscous liquid; R_f = 0.78 (EtOAc–hexane, 3.5:6.5).

IR (neat): 3370, 2962, 2930, 1733, 1690, 1630, 1548, 1459, 1375, 1339, 1156, 1101, 1032, 912, 800, 733, 648 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.45 (s, 1 H), 8.01 (br s, 1 H), 7.99 (s, 1 H), 7.08 (d, J = 13.0 Hz, 1 H), 6.80 (s, 1 H), 3.36 (d, J = 11.0 Hz, 1 H), 2.71–2.67 (m, 1 H), 2.43 (s, 3 H), 2.22–2.16 (m, 2 H), 2.10 (d, J = 12.0 Hz, 2 H), 1.88 (s, 1 H), 1.76–1.71 (m, 1 H), 1.57 (s, 1 H), 1.48 (d, J = 11.0 Hz, 1 H), 1.16 (d, J = 6.5 Hz, 3 H), 1.06 (s, 3 H), 0.87 (s, 3 H), 0.65 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 216.7, 206.3, 137.0, 131.9, 124.2, 121.6, 121.2, 118.7, 111.4, 103.5, 59.2, 50.8, 50.5, 49.6, 49.0, 47.7, 36.6, 33.1, 32.6, 27.3, 25.3, 21.7, 12.2.

HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{24}H_{32}NO_2$: 366.24276; found: 366.24334.

1a,4,7,7-Tetramethyl-6-(6-methyl-1*H*-indol-3-yl)decahydro-5*H*-cyclopenta[5,6]cycloocta[1,2-*b*]oxiren-5-one (3l′)

Yield: 10 mg (13%); brown viscous liquid; R_f = 0.89 (EtOAc–hexane, 3.5:6.5).

IR (neat): 3275, 2978, 2930, 1702, 1605, 1479, 1443, 1368, 1224, 1166, 1105, 1011, 860, 736, 650 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.92 (br s, 1 H), 7.57 (d, J = 8.0 Hz, 1 H), 7.06 (t, J = 9.0 Hz, 2 H), 6.91 (d, J = 8.0 Hz, 1 H), 3.57 (d, J = 4.5 Hz, 1 H), 2.64 (d, J = 11.5 Hz, 1 H), 2.37 (s, 3 H), 2.32–2.28 (m, 1 H), 2.25 (dd, J_1= 8.5, J_2= 7.0 Hz, 1 H), 2.18–2.09 (m, 1 H), 2.07–2.02 (m, 1 H), 1.97 (d, J = 11.4 Hz, 1 H), 1.78 (d, J = 6.2 Hz, 1 H), 1.69–1.64 (m, 2 H), 1.26 (s, 1 H), 1.04 (d, J = 7.0 Hz, 3 H), 0.95 (d, J = 6.0 Hz, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 216.6, 137.0, 132.5, 124.1, 121.7, 120.4, 119.3, 116.3, 111.1, 52.6, 52.3, 50.5, 49.4, 48.8, 48.2, 41.0, 39.7, 35.2, 34.3, 31.2, 29.8, 21.7, 20.1, 19.0, 13.1.

HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{24}H_{32}NO_2$: 366.24276; found: 366.24334.

3-(5-Chloro-1*H*-indol-3-yl)-1,4,4,6-tetramethyl-2-oxodecahydroazulene-6-carbaldehyde (3m)

Yield: 21 mg (25%); brown pasty mass; R_f = 0.56 (EtOAc–hexane, 3.5:6.5).

IR (neat): 3337, 2963, 2922, 1708, 1689, 1629, 1574, 1433, 1289, 1259, 1139, 1105, 1073, 896, 802, 752, 703, 672 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.47 (s, 1 H), 8.24 (br s, 1 H), 8.08 (t, J = 2.0 Hz, 1 H), 7.59–7.57 (m, 1 H), 7.46 (d, J = 2.0 Hz, 1 H), 6.91 (d, J = 2.5 Hz, 1 H), 3.34 (d, J = 11.5 Hz, 1 H), 2.69–2.64 (m, 1 H), 2.34–2.32 (m, 1 H), 2.30–2.28 (m, 1 H), 2.14–2.10 (m, 2 H), 1.89 (d, J = 15.5 Hz, 1 H), 1.77–1.72 (m, 1 H). 1.56–1.46 (m, 1 H), 1.20–1.25 (m, 1 H), 1.18 (d, J = 7.0 Hz, 3 H), 1.08 (s, 3 H), 0.88 (s, 3 H), 0.63 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 216.0, 209.1, 144.4, 135.4, 133.8, 133.1, 130.5, 127.8, 68.4, 66.1, 58.3, 51.9, 50.0, 48.3, 37.0, 36.8, 34.1, 29.8, 25.5, 24.2, 18.6, 14.3.

HRMS(ESI): m/z [M + H]$^+$ calcd for $C_{23}H_{29}ClNO_2$: 386.18813; found: 386.18806.

6-(5-Chloro-1*H*-indol-3-yl)-1a,4,7,7-tetramethyldecahydro-5*H*-cyclopenta[5,6]cycloocta[1,2-*b*]oxiren-5-one (3m′)

Yield: 15 mg (18%); brown pasty mass; R_f = 0.53 (EtOAc–hexane, 3.5:6.5).

IR (neat): 3337, 2963, 2922, 1708, 1629, 1581, 1486, 1460, 1362, 1291, 1222, 1184, 1102, 937, 799, 754, 701 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.16 (s, 1 H), 8.02–7.97 (m, 1 H), 7.59 (ddd, J_1 = 8.0, J_2 = 2.0, J_3 = 1.0 Hz, 1 H), 7.25 (d, J = 8.5 Hz, 1 H), 7.19–7.12 (m, 1 H), 3.60 (d, J = 5.0 Hz, 1 H), 2.68 (d, J = 11.5 Hz, 1 H), 2.54–2.39 (m, 1 H), 2.37–2.30 (m, 1 H), 2.30–2.26 (m, 1 H), 2.24 (d, J = 11.5 Hz, 1 H), 2.11 (d, J = 11.5 Hz, 1 H), 2.09–1.99 (m, 1 H), 1.93–1.82 (m, 1 H), 1.74 (dd, J_1 = 12.5, J_2= 8.5 Hz, 1 H), 1.59–1.50 (m, 1 H), 1.13 (s, 3 H), 1.06 (m, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 214.6, 134.7, 133.8, 131.2, 129.9, 128.3, 112.1, 53.5, 52.4, 49.4, 49.4, 41.2, 40.3, 39.6, 34.1, 31.2, 29.7, 25.1, 20.3, 18.8, 13.1.

HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{23}H_{29}ClNO_2$: 386.18813; found: 386.18806.

1,4,4,6-Tetramethyl-2-oxo-3-(2-phenyl-1*H*-indol-3-yl)decahydroazulene-6-carbaldehyde (3n)

Yield: 23 mg (25%); colorless liquid; R_f = 0.58 (EtOAc–hexane, 2.5:7.5).

IR (neat): 3369, 2926, 2858, 1730, 1690, 1457, 1339, 1161, 1073, 923, 765, 742, 703 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.36 (s, 1 H), 8.08 (s, 1 H), 7.57 (d, J = 7.0 Hz, 1 H), 7.45 (dd, J_1 = 13.0, J_2 = 5.5 Hz, 3 H), 7.41 (d, J = 7.0 Hz, 1 H), 7.36 (d, J = 8.0 Hz, 1 H), 7.17 (t, J = 7.5 Hz, 1 H), 7.08 (t, J = 7.5 Hz, 1 H), 3.57 (d, J = 11.5 Hz, 1 H), 2.60–2.50 (m, 1 H), 2.27 (dd, J_1 = 16.0, J_2= 9.0 Hz, 1 H), 2.08 (dd, J_1= 13.5, J_2 = 7.0 Hz, 2 H), 2.02–1.96 (m, H), 1.86–1.72 (m, 1 H), 1.70 (d, J = 15.0 Hz, 1 H), 1.42 (dd, J_1 = 13.0, J_2 = 7.6 Hz, 1 H), 1.26 (s, 3 H), 1.23 (d, J = 6.5 Hz, 3 H), 1.09 (d, J = 6.5 Hz, 1 H), 0.99 (s, 3 H), 0.40 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 219.9, 206.0, 128.9, 128.8, 128.4, 122.2, 119.7, 119.4, 111.4, 57.3, 51.2, 50.6, 49.7, 48.9, 47.9, 36.4, 33.0, 31.6, 27.3, 25.1, 21.5, 12.6.

HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{29}H_{34}NO_2$: 428.25841; found: 428.25792.

1a,4,7,7-Tetramethyl-6-(2-phenyl-1*H*-indol-3-yl)decahydro-5*H*-cyclopenta[5,6]cycloocta[1,2-*b*]oxiren-5-one (3n′)

Yield: 21 mg (23%); colorless liquid; R_f = 0.55 (EtOAc–hexane, 2.5:7.5).

IR (neat): 3369, 2927, 2874, 1730, 1607, 1456, 1338, 1371, 1310, 1160, 913, 843, 737, 702, 652 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.12 (s, 1 H), 7.58 (dd, J_1 = 8.0, J_2 = 1.3 Hz, 2 H), 7.50–7.45 (m, 2 H), 7.44–7.41 (m, 3 H), 7.38 (d, J = 8.0 Hz, 1 H), 7.21–7.18 (m, 1 H), 7.14–7.10 (m, 1 H), 3.87 (d, J = 9.0 Hz, 1 H), 2.54 (dd, J_1 = 9.0, J_2 = 7.0 Hz, 1 H), 2.46 (d, J = 11.5 Hz, 1 H), 2.40–2.32 (m, 1 H), 2.27–2.22 (m, 1 H), 1.97 (s, 2 H), 1.81 (d, J = 11.0 Hz, 3 H), 1.67 (d, J = 11.0 Hz, 1 H), 1.59 (d, J = 2.0 Hz, 1 H), 1.20 (d, J = 7.0 Hz, 3 H), 1.06 (dd, J_1 = 7.0, J_2 = 2.5 Hz, 1 H), 1.01 (d, J = 7.0 Hz, 3 H), 0.83 (s, 3 H), 0.51 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 217.5, 136.4, 132.9, 128.9, 128.8, 128.4, 122.2, 119.7, 119.4, 111.3, 52.9, 50.6, 49.6, 48.9, 36.4, 33.1, 31.7, 29.7, 27.4, 21.6, 12.6.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{29}H_{33}NNaO_2$: 450.24090; found: 450.24222.

(2*E*,6*Z*,10*E*)-6-(Azidomethyl)-2,9,9-trimethylcycloundeca-2,6,10-trienone (4a)

Allylic bromination of zerumbone: NBS (1.0 mmol) was added to a solution of zerumbone (0.92 mmol) and CH_3CN/H_2O (1:1, 15 mL), and the mixture was stirred vigorously at RT for 1 min. H_2O (30 mL) was poured into the solution, which was filtrated immediately, and washed with H_2O several times; this afforded 7-bromo-2,9,9-trimethyl-6-methylenecycloundeca-2,10-dienone as a colorless solid.

Azidation: NaN_3 (1.0 mmol) and Cs_2CO_3 (5 mol%) were added to a solution of 7-bromo-2,9,9-trimethyl-6-methylenecycloundeca-2,10-dienone (0.67 mmol) in DMF (20 mL) at RT and the mixture was stirred for 12 h. The progress of the reaction was monitored by TLC (hexane–EtOAc, 3:2). The DMF solution was extracted with CH_2Cl_2 (3 × 30 mL) and the combined organic extracts were washed with brine (2 × 30 mL), dried over anhydrous Na_2SO_4, and concentrated on a rotary evaporator. Chromatography (silica gel, hexane–EtOAc, 2:1) afforded **4a**.

Yield: 245 mg (56%); colorless viscous liquid; R_f = 0.71 (EtOAc–hexane, 3:7).

IR (neat): 2960, 2924, 2854, 2095, 1653, 1451, 1386, 1364, 1265, 1105, 968, 903, 831, 777, 698, 631 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.00 (s, 1 H), 5.96 (t, *J* = 7.0 Hz, 1 H), 5.76 (d, *J* = 8.0 Hz, 1 H), 5.50 (t, *J* = 8.5 Hz, 1 H), 4.06 (br s, 1 H), 3.44 (br s, 1 H), 2.69 (s, 1 H), 2.55–2.21 (m, 5 H), 1.79 (s, 3 H), 1.25 (s, 3 H), 1.11 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 203.0, 159.3, 148.4, 138.9, 138.6, 129.0, 127.4, 57.8, 48.8, 43.1, 38.3, 29.3, 25.8, 12.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{21}N_3NaO$: 282.15823; found: 282.15758.

Triazole-Linked Zerumbones 6; General Procedure

Zerumbone azide **4a** (1.0 equiv), the appropriate alkyne (1.5 equiv), CuI (20 mol%) as catalyst, and DIPEA (3 equiv) as base were weighed in a reaction tube. CH_3CN (2 mL) was added and the mixture was allowed to stir at RT for 2 h. The solvent was evaporated in vacuo and the residue was purified by column chromatography (silica gel, 100–200 mesh, hexane–EtOAc).

(2*E*,6*Z*,10*E*)-2,9,9-Trimethyl-6-[(4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl]cycloundeca-2,6,10-trienone (6a)

Yield: 31 mg (44%); white solid; R_f = 0.42 (EtOAc–hexane, 3:7); mp 189–190 °C.

IR (neat): 3432, 3058, 2970, 2928, 2858, 2119, 1709, 1647, 1430, 1363, 1266, 1224, 1047, 973, 898, 739, 611, 557 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.84–7.76 (m, 2 H), 7.70 (s, 1 H), 7.44–7.41 (m, 2 H), 7.35–7.27 (m, 1 H), 6.05 (d, *J* = 16.5 Hz, 1 H), 6.03–5.94 (m, 1 H), 5.85 (d, *J* = 16.5 Hz, 1 H), 5.63–5.60 (m, 1 H), 4.81 (br s, 1 H), 5.06 (br s, 1 H), 2.56–2.42 (m, 2 H), 2.28–2.14 (m, 3 H), 1.90–1.86 (m, 1 H), 1.79 (s, 3 H), 1.29 (s, 3 H), 0.93 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 203.4, 158.9, 148.6, 148.2, 139.0, 133.6, 131.7, 130.4, 128.9, 128.3, 127.7, 125.7, 119.3, 47.8, 42.3, 37.7, 34.7, 24.3, 12.0.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{27}N_3NaO$: 384.20518; found: 384.20580.

(2*E*,6*Z*,10*E*)-2,9,9-Trimethyl-6-[(4-*p*-tolyl-1*H*-1,2,3-triazol-1-yl)methyl]cycloundeca-2,6,10-trienone (6b)

Yield: 30 mg (41%); pale yellow solid: R_f = 0.48 (EtOAc–hexane, 3:7); mp 205–208 °C.

IR (neat): 3407, 3138, 2959, 2925, 2861, 1716, 1647, 1497, 1453, 1364, 1268, 1223, 1183, 1108, 1075, 1064, 973, 908, 820, 734, 699, 660 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.70 (d, *J* = 8.5 Hz, 2 H), 7.61 (s, 1 H), 7.21 (d, *J* = 7.5 Hz, 2 H), 6.03 (d, *J* = 16.5 Hz, 1 H), 6.00–5.98 (m, 1 H), 5.82 (d, *J* = 16.5 Hz, 1 H), 5.61–5.58 (m, 1 H), 5.06–5.03 (m, 1 H), 4.79 (br s, 1 H), 2.55–2.41 (m, 2 H), 2.40 (s, 3 H), 2.38–2.04 (m, 4 H), 1.87 (s, 3 H), 1.33 (s, 3 H), 1.16 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 203.0, 158.6, 148.3, 139.1, 138.0, 133.8, 131.5, 129.5, 127.8, 125.6, 118.7, 47.8, 42.3, 37.7, 34.8, 29.7, 29.4, 24.3, 21.3, 12.0.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{29}N_3NaO$: 398.22083; found: 398.22180.

(2*E*,6*Z*,10*E*)-2,9,9-Trimethyl-6-[(4-phenethyl-1*H*-1,2,3-triazol-1-yl)methyl]cycloundeca-2,6,10-trienone (6c)

Yield: 27 mg (36%); amorphous viscous solid; R_f = 0.27 (EtOAc–hexane, 3:7).

IR (neat): 3425, 2960, 2927, 2105, 1644, 1453, 1368, 1268, 1218, 1053, 749, 701, 558 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.27–7.24 (m, 3 H), 7.19–7.14 (m, 2 H), 6.99 (s, 1 H), 6.02 (d, *J* = 16.5 Hz, 1 H), 6.00–5.96 (m, 1 H), 5.77 (d, *J* = 16.5 Hz, 1 H), 5.55–5.52 (m, 1 H), 4.97–4.90 (m, 1 H), 4.69–4.66 (m, 1 H), 3.05–2.97 (m, 4 H), 2.42–2.37 (m, 1 H), 2.32–2.26 (m, 2 H), 2.10–2.07 (m, 3 H), 1.81 (s, 3 H), 1.27 (s, 3 H), 1.13 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 202.9, 158.5, 148.2, 147.6, 141.0, 139.0, 133.9, 131.1, 128.5, 128.4, 127.7, 126.1, 120.6, 47.5, 42.2, 37.7, 35.5, 34.7, 27.5, 24.3, 12.0.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{25}H_{31}N_3NaO$: 412.23648; found: 412.24168.

(2*E*,6*Z*,10*E*)-6-[(4-Benzyl-1*H*-1,2,3-triazol-1-yl)methyl]-2,9,9-trimethylcycloundeca-2,6,10-trienone (6d)

Yield: 27 mg (38%); pale yellow liquid; R_f = 0.28 (EtOAc–hexane, 3:7).

IR (neat): 3410, 2185, 1645, 1454, 1362, 1267, 1210, 1054, 752, 712, 554 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.31–7.21 (m, 5 H), 7.12 (s, 1 H), 6.02 (d, *J* = 16.5 Hz, 1 H), 6.00–5.97 (m, 1 H), 5.79 (d, *J* = 16.5 Hz, 1 H), 5.56–5.29 (m, 1 H), 4.96 (br s, 1 H), 4.71 (br s, 1 H), 4.08–4.05 (m, 2 H), 2.46–2.44 (m, 2 H), 2.24–2.06 (m, 4 H), 1.79 (s, 3 H), 1.29 (s, 3 H), 1.16 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 203.5, 159.0, 148.7, 148.1, 139.0, 138.9, 133.6, 131.5, 128.6, 128.4, 127.6, 126.5, 121.2, 47.6, 42.2, 37.7, 34.7, 32.2, 29.3, 24.3, 24.0, 12.0.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{29}N_3NaO$: 398.22083; found: 398.21868.

(2*E*,6*Z*,10*E*)-6-[(4-(Hydroxymethyl)-1*H*-1,2,3-triazol-1-yl)methyl]-2,9,9-trimethylcycloundeca-2,6,10-trienone (6e)

Yield: 54 mg (89%); colorless solid; R_f = 0.45 (EtOAc–hexane, 3:7); mp 152–154 °C.

IR (neat): 3417, 2960, 2928, 2127, 1641, 1442, 1268, 1223, 1122, 1047, 1010, 971, 755, 699, 557, 538 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.48 (s, 1 H), 6.05 (d, *J* = 16.5 Hz, 1 H), 6.02–5.99 (m, 1 H), 5.80 (d, *J* = 16.5 Hz, 1 H), 5.62–5.59 (m, 1 H), 5.04–4.96 (m, 1 H), 4.80 (s, 2 H), 4.76–4.75 (m, 1 H), 2.47–2.41 (m, 2 H), 2.28–2.27 (m, 1 H), 2.20–2.19 (m, 3 H), 1.83 (s, 3 H), 1.26 (s, 3 H), 1.15 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 203.4, 158.8, 148.5, 139.0, 133.5, 131.8, 127.7, 121.3, 56.6, 47.6, 42.2, 37.7, 34.7, 24.3, 12.0.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{25}N_3NaO_2$: 338.18445; found: 338.18424.

(2*E*,6*Z*,10*E*)-2,9,9-Trimethyl-6-[(4-pentyl-1*H*-1,2,3-triazol-1-yl)methyl]cycloundeca-2,6,10-trienone (6f)

Yield: 33 mg (48%); colorless viscous liquid; R_f = 0.42 (EtOAc–hexane, 3:7).

IR (neat): 3438, 2958, 2930, 2863, 2097, 1646, 1460, 1366, 1267, 1217, 1048, 971, 780, 558 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.21 (s, 1 H), 6.04 (d, *J* = 16.5 Hz, 1 H), 6.02–6.00 (m, 1 H), 5.82 (d, *J* = 16.5 Hz, 1 H), 5.60–5.56 (m, 1 H), 4.99 (br s, 1 H), 4.74 (br s, 1 H), 2.72–2.68 (m, 2 H), 2.52–2.23 (m, 4 H), 2.18–2.04 (m, 2 H), 1.88 (s, 3 H), 1.82–1.64 (m, 2 H), 1.40–1.20 (m, 7 H), 1.14 (s, 3 H), 0.92–0.86 (m, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 203.2, 158.9, 148.8, 148.5, 138.9, 133.9, 131.2, 127.6, 120.2, 47.5, 42.2, 37.6, 34.7, 31.4, 29.6, 29.3, 29.1, 25.6, 24.3, 24.0, 22.4, 14.0, 12.0.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{33}N_3NaO$: 378.25213; found: 378.25278.

Triazole-Appended [6.3.0] Fused Cyclic Products 7; General Procedure

Triazole-appended zerumbone **6a** (1.0 equiv), indole **2** (1.0 equiv), and $AlCl_3$ (5 mol%) were placed in a reaction tube. CH_3CN (2 mL) was added and the reaction mixture was stirred at 80 °C for 5 h. The solvent was evaporated in vacuo and the residue was purified by column chromatography (silica gel, 100–200 mesh, hexane–EtOAc).

(*E*)-3-(1*H*-Indol-3-yl)-1,4,4-trimethyl-7-[(4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl]-1,3,3a,4,5,8,9,9a-octahydro-2*H*-cyclopenta-[8]annulen-2-one (7a)

Yield: 33 mg (50%); brown viscous liquid; R_f = 0.66 (EtOAc–hexane, 2:3).

IR (neat): 3327, 2959 2928, 2869, 1730, 1619, 1459, 1338, 1265, 1224, 1077, 1048, 764, 737, 696 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.0 Hz, 2 H), 7.84 (s, 1 H), 7.78 (d, *J* = 8.0 Hz, 1 H), 7.52 (t, *J* = 7.5 Hz, 2 H), 7.48 (d, *J* = 7.0 Hz, 1 H), 7.43 (s, 1 H), 7.17 (t, *J* = 7.5 Hz, 1 H), 7.14 (d, *J* = 7.0 Hz, 1 H), 7.09 (t, *J* = 8.0 Hz, 1 H), 6.71 (s, 1 H), 5.93 (dd, J_1 = 6.5, J_2 = 10 Hz, 1 H), 5.06 (d, *J* = 14.0 Hz, 1 H), 4.75 (d, *J* = 14.0 Hz, 1 H), 3.53 (d, *J* = 3.5 Hz, 1 H), 2.58–2.52 (m, 1 H), 2.41–2.34 (m, 3 H), 2.26–2.20 (m, 2 H), 2.05–2.02 (m, 1 H), 1.95–1.85 (m, 2 H), 1.25 (s, 6 H), 0.92 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 215.8, 148.1, 136.9, 136.2, 130.7, 129.8, 129.1, 128.5, 126.2, 126.1, 122.4, 121.3, 119.7, 119.6, 116.7, 110.9, 59.0, 48.0, 46.4, 43.7, 39.7, 38.5, 34.9, 31.9, 29.7, 29.3, 24.8, 22.7, 14.1, 12.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{31}H_{35}N_4O$: 479.28054; found: 479.27464.

(*E*)-1,4,4-Trimethyl-3-(5-methyl-1*H*-indol-3-yl)-7-[(4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl]-1,3,3a,4,5,8,9,9a-octahydro-2*H*-cyclopenta[8]annulen-2-one (7b)

Yield: 20 mg (30%); colorless viscous liquid; R_f = 0.69 (EtOAc–hexane, 2:3).

IR (neat): 3332, 2957, 2925, 2856, 1732, 1623, 1464, 1372, 1265, 1224, 1181, 1078, 1048, 975, 917, 798, 765, 737, 696 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.5 Hz, 2 H), 7.83 (s, 2 H), 7.56 (s, 1 H), 7.51 (t, *J* = 7.5 Hz, 2 H), 7.47 (d, *J* = 7.0 Hz, 1 H), 7.06 (d, *J* = 4.0 Hz, 1 H), 6.96 (d, *J* = 8.0 Hz, 1 H), 6.64 (s, H), 5.92 (t, *J* = 8.0 Hz, 1 H), 5.06 (d, *J* = 13.5 Hz, 1 H), 4.98 (d, *J* = 14.0 Hz, 1 H), 3.49 (s, 1 H), 2.54–2.51 (m, 2 H), 2.43 (s, 3 H), 2.39–2.33 (m, 3 H), 2.22 (d, *J* = 5.0 Hz, 1 H), 1.94–1.85 (m, 3 H), 1.26 (s, 6 H), 0.92 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 215.9, 148.1, 134.5, 130.7, 129.8, 129.1, 128.9, 128.5, 126.5, 126.1, 124.0, 121.4, 119.7, 119.2, 116.3, 110.6, 59.0, 48.0, 46.3, 38.6, 34.9, 31.9, 29.7, 29.4, 22.7, 21.5, 15.0, 14.1, 12.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{32}H_{37}N_4O$: 493.29619; found: 492.29605.

(*E*)-3-(5-Bromo-1*H*-indol-3-yl)-1,4,4-trimethyl-7-[(4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl]-1,3,3a,4,5,8,9,9a-octahydro-2*H*-cyclopenta[8]annulen-2-one (7c)

Yield: 33 mg (43%); brown viscous liquid; R_f = 0.33 (EtOAc–hexane, 3:7).

IR (neat): 3331, 2958, 2926, 2856, 1732, 1613, 1459, 1362, 1265, 1222, 1149, 1077, 1048, 976, 884, 797, 764, 735, 695, 655 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.92 (s, 1 H), 7.90–7.87 (m, 2 H), 7.85 (s, 1 H), 7.65 (s, 1 H), 7.52 (d, *J* = 6.5 Hz, 2 H), 7.47 (d, *J* = 7.0 Hz, 1 H), 7.22 (d, *J* = 8.5 Hz, 1 H), 7.05 (d, *J* = 8.5 Hz, 1 H), 6.78 (s, 1 H), 5.99–5.89 (m, 1 H), 5.05 (d, *J* = 14.0 Hz, 1 H), 5.00 (d, *J* = 14.0 Hz, 1 H), 3.44 (d, *J* = 3.5 Hz, 1 H), 2.57 (t, *J* = 13.0 Hz, 1 H), 2.39–2.34 (m, 2 H), 2.27–2.14 (m, 3 H), 2.09–1.99 (m, 1 H), 1.94–1.87 (m, 2 H), 1.26 (s, 3 H), 0.93 (d, *J* = 6.5 Hz, 3 H), 0.90 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 216.2, 148.0, 136.6, 134.9, 130.5, 129.2, 129.8, 128.5, 128.0, 126.0, 125.2, 122.8, 122.2, 120.1, 112.9, 112.5, 59.1, 47.8, 46.5, 39.6, 38.5, 34.8, 29.7, 22.8, 14.1, 12.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{31}H_{34}BrN_4O$: 557.19105; found: 557.19170.

(*E*)-1,4,4-Trimethyl-3-(5-nitro-1*H*-indol-3-yl)-7-[(4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl]-1,3,3a,4,5,8,9,9a-octahydro-2*H*-cyclopenta[8]annulen-2-one (7d)

Yield: 28 mg (39%); yellow viscous liquid; R_f = 0.30 (EtOAc–hexane, 3:7).

IR (neat): 3348, 2959, 2920, 2851, 1710, 1623, 1520, 1469, 1361, 1332, 1267, 1222, 1092, 1048, 975, 912, 815, 766, 733, 698, 649 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.62 (br s, 1 H), 8.53 (s, 1 H), 8.10 (d, *J* = 9.0 Hz, 1 H), 7.82 (d, *J* = 7.5 Hz, 2 H), 7.72 (s, 1 H), 7.43 (d, *J* = 7.0 Hz, 2 H), 7.38 (d, *J* = 9.0 Hz, 1 H), 7.35 (d, *J* = 7.0 Hz, 1 H), 7.20 (s, 1 H), 5.63–5.55 (m, 1 H), 4.92 (d, *J* = 15.0 Hz, 1 H), 4.80 (d, *J* = 14.5 Hz, 1 H), 3.02

(d, *J* = 5.5 Hz, 1 H), 2.50–2.44 (m, 1 H), 2.26–2.22 (m, 1 H), 2.14–2.10 (m, 2 H), 2.06–2.03 (m, 2 H), 1.93–1.86 (m, 2 H), 1.26 (s, 3 H), 0.89 (d, *J* = 7.0 Hz, 1 H), 0.82 (s, 3 H), 0.36 (s, 3 H)..

^{13}C NMR (125 MHz, $CDCl_3$): δ = 218.6, 148.0, 141.7, 138.8, 136.4, 130.4, 128.9, 128.3, 127.8, 127.5, 126.4, 125.7, 119.8, 117.6, 115.9, 111.3, 56.6, 52.6, 39.8, 38.0, 35.1, 30.9, 29.7, 22.9, 21.9, 21.5, 15.0, 10.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{31}H_{34}N_5O_3$: 524.26562; found: 524.265760.

(*E*)-3-(3,9,9-Trimethyl-2-oxo-6-[(4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl]-2,3,3a,4,5,8,9,9a-octahydro-1*H*-cyclopenta[8]annulen-1-yl)-1*H*-indole-5-carbaldehyde (7e)

Yield: 22 mg (32%); brown viscous liquid; R_f = 0.82 (EtOAc–hexane, 2:3).

IR (neat): 3317, 2958, 2927, 2871, 1735, 1690, 1627, 1578, 1465, 1367, 1316, 1226, 1177, 1078, 1048, 974, 920, 810, 766, 697, 625 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.96 (s, 1 H), 7.82 (s, 1 H), 7.81 (s, 1 H), 7.77 (d, *J* = 8.0 Hz, 2 H), 7.74 (d, *J* = 8.0 Hz, 1 H), 7.69 (s, 1 H), 7.45 (t, *J* = 8.0 Hz, 1 H), 7.36 (t, *J* = 7.0 Hz, 1 H), 7.28 (t, *J* = 7.0 Hz, 1 H), 5.76 (t, *J* = 8.5 Hz, 1 H), 4.89 (d, *J* = 14.0 Hz, 1 H), 4.83 (d, *J* = 14.0 Hz, 1 H), 3.51 (d, *J* = 3.5 Hz, 1 H), 2.93 (t, *J* = 16.0 Hz, 1 H), 2.84 (d, *J* = 5.5 Hz, 1 H), 2.79–2.75 (m, 1 H), 2.64–2.60 (m, 1 H), 2.27 (d, *J* = 6.0 Hz, 1 H), 2.24 (d, *J* = 6.5 Hz, 1 H), 2.10–2.01 (m, 1 H), 1.87–1.83 (m, 2 H), 1.59 (s, 3 H), 0.95 (s, 3 H), 0.86 (s, 3 H), 0.59 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 209.0, 192.2, 148.2, 138.4, 136.3, 130.4, 129.2, 128.9, 128.3, 127.1, 126.0, 125.7, 119.3, 111.7, 58.8, 47.1, 46.6, 39.2, 38.5, 38.3, 30.0, 28.3, 27.8, 22.4, 12.1, 8.2.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{32}H_{34}N_4NaO_2$: 529.25795; found: 529.25932.

(*E*)-3-(5-Methoxy-1*H*-indol-3-yl)-1,4,4-trimethyl-7-[(4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl]-1,3,3a,4,5,8,9,9a-octahydro-2*H*-cyclopenta[8]annulen-2-one (7f)

Yield: 28 mg (40%); blackish viscous liquid; R_f = 0.69 (EtOAc–hexane, 3:7).

IR (neat): 3398, 2958, 2928, 2869, 1732, 1626, 1583, 1485, 1464, 1371, 1292, 1263, 1215, 1174, 1051, 912, 799, 766, 735, 696, 619 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 7.0 Hz, 2 H), 7.86 (s, 1 H), 7.51 (t, *J* = 7.5 Hz, 2 H), 7.47 (d, *J* = 7.0 Hz, 1 H), 7.31 (s, 1 H), 7.23 (d, *J* = 2.5 Hz, 1 H), 7.06 (d, *J* = 8.5 Hz, 1 H), 6.80 (dd, J_1 = 8.5, J_2 = 2.0 Hz, 1 H), 6.68 (s, 1 H), 6.03–5.89 (m, 1 H), 5.07 (d, *J* = 13.5 Hz, 1 H), 4.99 (d, *J* = 14.0 Hz, 1 H), 3.87 (s, 3 H), 3.46 (d, *J* = 3.5 Hz, 1 H), 2.54 (d, *J* = 13.5 Hz, 1 H), 2.43–2.31 (m, 2 H), 2.23 (dd, J_1 = 10, J_2 = 5.0 Hz, 2 H), 1.99–1.80 (m, 2 H), 1.29 (dd, J_1 = 8.0, J_2 = 3.0 Hz, 2 H), 1.26 (d, *J* = 1.0 Hz, 3 H), 0.93 (d, *J* = 3.5 Hz, 3 H), 0.91 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 218.9, 154.2, 148.1, 136.8, 129.8, 129.2, 128.5, 126.6, 126.1, 122.0, 112.9, 111.7, 101.1, 58.9, 55.9, 48.2, 46.2, 38.5, 35.1, 31.4, 29.6, 29.4, 22.9, 11.9.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{35}H_{36}N_4NaO_2$: 531.27360; found: 531.27363.

(*E*)-1,4,4-Trimethyl-3-(7-methyl-1*H*-indol-3-yl)-7-[(4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl]-1,3,3a,4,5,8,9,9a-octahydro-2*H*-cyclopenta[8]annulen-2-one (7g)

Yield: 27 mg (39%); colorless viscous liquid; R_f = 0.69 (EtOAc–hexane, 2:3).

IR (neat): 3334, 2956, 2923, 2868, 1727, 1625, 1462, 1340, 1225, 1191, 1076, 1048, 910, 802, 765, 732, 695, 648 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.5 Hz, 2 H), 7.83 (s, 1 H), 7.56 (s, 1 H), 7.51 (t, *J* = 7.0 Hz, 2 H), 7.47 (d, *J* = 7.5 Hz, 1 H), 7.29 (br s, 1 H), 7.06 (d, *J* = 8.0 Hz, 1 H), 6.96 (d, *J* = 8.0 Hz, 1 H), 6.64 (s, 1 H), 5.92 (t, *J* = 8.0 Hz, 1 H), 5.06 (d, *J* = 13.5 Hz, 1 H), 4.98 (d, *J* = 14.0 Hz, 1 H), 3.49 (s, 3 H), 2.57–2.51 (m, 2 H), 2.37 (s, 3 H), 2.35–2.31 (m, 3 H), 2.25–2.17 (m, 2 H), 1.94–1.85 (m, 3 H), 1.25 (s, 3 H), 0.92 (s, 3 H), 0.91 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 216.2, 148.1, 134.5, 130.7, 129.8, 129.1, 128.9, 128.4, 126.5, 126.1, 124.0, 121.4, 119.7, 119.2, 116.3, 110.6, 59.0, 48.0, 46.3, 38.6, 34.9, 31.9, 29.7, 29.4, 22.7, 21.5, 14.1, 12.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{32}H_{37}N_4O$: 493.29619; found: 493.29605.

(*E*)-1,4,4-Trimethyl-3-(6-methyl-1*H*-indol-3-yl)-7-[(4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl]-1,3,3a,4,5,8,9,9a-octahydro-2*H*-cyclopenta[8]annulen-2-one (7h)

Yield: 28 mg(41%); colorless viscous liquid; R_f = 0.69 (EtOAc–hexane, 2:3).

IR (neat): 3338, 2958, 2930, 2863, 1719, 1625, 1460, 1366, 1267, 1217, 1048, 971, 780, 558 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 7.0 Hz, 1 H), 7.76 (s, 2 H), 7.62 (d, *J* = 5.0 Hz, 1 H), 7.57 (d, *J* = 8.0 Hz, 1 H), 7.51 (s, 1 H), 7.46–7.41 (m, 2 H), 7.36 (t, *J* = 7.5 Hz, 2 H), 6.89 (s, 1 H), 6.00 (t, *J* = 16.0 Hz, 1 H), 4.97 (d, *J* = 14.0 Hz, 1 H), 4.90 (d, *J* = 13.5 Hz, 1 H), 3.42 (s, 1 H), 2.48 (s, 1 H), 2.36 (d, *J* = 4.0 Hz, 1 H), 2.34 (s, 3 H), 2.26 (d, *J* = 7.5 Hz, 2 H), 2.15 (d, *J* = 5 Hz, 2 H), 1.98 (d, *J* = 10.5 Hz, 1 H), 1.53–1.46 (m, 2 H), 1.05 (s, 3 H), 1.01 (d, *J* = 7.0 Hz, 3 H), 0.83 (d, *J* = 6.5 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 216.2, 148.1, 134.5, 130.7, 129.8, 129.1, 128.9, 128.5, 126.5, 126.1, 124.0, 121.4, 119.7, 119.2, 116.3, 110.6, 59.0, 48.0, 46.3, 38.6, 34.9, 31.9, 29.7, 29.4, 22.7, 21.5, 14.1, 12.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{32}H_{37}N_4O$: 493.29610; found: 493.29701.

(*E*)-3-(5-Chloro-1*H*-indol-3-yl)-1,4,4-trimethyl-7-[(4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl]-1,3,3a,4,5,8,9,9a-octahydro-2*H*-cyclopenta[8]annulen-2-one (7i)

Yield: 26 mg (37%); brownish viscous liquid; R_f = 0.63 (EtOAc–hexane, 2:3).

IR (neat): 3332, 2930, 2871, 1731, 1627, 1463, 1368, 1224, 1076, 1048, 908, 799, 764, 730, 694, 648, 614 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.0 Hz, 2 H), 7.85 (s, 1 H), 7.76 (s, 1 H), 7.49 (d, *J* = 7.5 Hz, 2 H), 7.33 (d, *J* = 8.5 Hz, 1 H), 7.09 (s, 2 H), 6.82 (s, 1 H), 5.93 (t, *J* = 14.0 Hz, 1 H), 5.04 (d, *J* = 14.0 Hz, 1 H), 4.99 (d, *J* = 14.0 Hz, 1 H), 3.44 (d, *J* = 3.0 Hz, 1 H), 2.55 (t, *J* = 12.5 Hz, 1 H), 2.39 (t, *J* = 12.0 Hz, 1 H), 2.32–2.24 (m, 2 H), 2.19–2.15 (m, 1 H), 1.93–1.88 (m, 1 H), 1.62–1.57 (m, 1 H), 1.42–1.25 (m, 2 H), 0.93 (d, *J* = 6.5 Hz, 3 H), 0.90 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 216.2, 151.3, 148.0, 136.5, 134.6, 130.5, 129.8, 129.2, 128.6, 126.0, 125.8, 123.0, 122.6, 120.2, 119.1, 116.2, 112.1, 59.0, 51.8, 46.6, 41.2, 39.5, 38.5, 37.3, 34.8, 32.7, 29.1, 25.7, 20.2, 12.0, 7.8.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{34}ClN_4O$: 513.24157; found: 513.24171.

(*E*)-3-(5-Fluoro-1*H*-indol-3-yl)-1,4,4-trimethyl-7-[(4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl]-1,3,3a,4,5,8,9,9a-octahydro-2*H*-cyclopenta[8]annulen-2-one (7j)

Yield: 24 mg (35%); brown viscous liquid; R_f = 0.63 (EtOAc–hexane, 2:3).

IR (neat): 3323, 2960, 2928, 2869, 2097, 1731, 1693, 1602, 1485, 1451, 1265, 1173, 1078, 937, 851, 799, 765, 738, 696, 619 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 7.0 Hz, 1 H), 7.85 (s, 1 H), 7.64 (s, 1 H), 7.51 (t, *J* = 7.5 Hz, 2 H), 7.44 (d, *J* = 11.5 Hz, 2 H), 7.08 (d, *J* = 4.0 Hz, 1 H), 6.88 (t, *J* = 8.5 Hz, 1 H), 6.81 (s, 1 H), 5.97–5.90 (m, 1 H), 5.04 (d, *J* = 13.5 Hz, 1 H), 5.00 (d, *J* = 14.0 Hz, 1 H), 3.43 (s, 1 H), 2.55 (t, *J* = 13.5 Hz, 1 H), 2.43–2.37 (m, 1 H), 2.34 (d, *J* = 8.0 Hz, 1 H), 2.25 (s, 1 H), 2.18 (d, *J* = 10.5 Hz, 1 H), 2.06 (d, *J* = 10.0 Hz, 1 H), 1.88 (d, *J* = 14.0 Hz, 2 H), 1.62–1.53 (m, 1 H), 1.25 (s, 6 H), 0.90 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 215.8, 158.9, 157.0, 148.0, 132.7, 129.8, 129.1, 128.5, 126.0, 123.1, 119.9, 111.6, 111.5, 110.9, 110.7, 104.7, 104.5, 59.1, 47.9, 46.5, 38.5, 34.9, 29.7, 22.8, 14.1, 12.0.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{31}H_{34}FN_4O$: 497.27112; found: 497.27491.

(*E*)-3-(3,9,9-Trimethyl-2-oxo-6-[(4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl]-2,3,3a,4,5,8,9,9a-octahydro-1*H*-cyclopenta[8]annulen-1-yl)-1*H*-indole-5-carbonitrile (7k)

Yield: 23 mg (33%); brown viscous liquid; R_f = 0.93 (EtOAc–hexane, 2:3).

IR (neat): 3438, 2923, 2853, 1689, 1587, 1501, 1465, 1431, 1381, 1328, 1224, 1114, 867, 804, 770, 721 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.64 (br s, 1 H), 8.19 (s, 1 H), 7.88 (t, *J* = 5.0 Hz, 2 H), 7.50 (t, *J* = 7.0 Hz, 2 H), 7.44 (t, *J* = 7.0 Hz, 2 H), 7.36 (d, *J* = 8.5 Hz, 2 H), 7.12 (s, 1 H), 5.97 (t, *J* = 9.5 Hz, 1 H), 5.05 (d, *J* = 14.0 Hz, 1 H), 5.01 (d, *J* = 14.0 Hz, 1 H), 3.49 (d, *J* = 3.0 Hz, 1 H), 2.59 (t, *J* = 14.0 Hz, 1 H), 2.48–2.35 (m, 2 H), 2.31–2.26 (m, 2 H), 2.14–2.10 (m, 1 H), 1.67–1.61 (m, 2 H), 1.27–1.25 (m, 1 H), 0.93 (s, 3 H), 0.91 (s, 3 H), 0.89 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 215.8, 148.1, 136.9, 136.2, 130.7, 129.8, 129.1, 128.5, 126.2, 126.1, 122.4, 121.3, 119.7, 119.6, 116.7, 110.9, 59.0, 47.9, 46.4, 43.7, 39.7, 38.5, 34.9, 31.9, 29.7, 29.3, 24.8, 22.7, 14.1, 12.0.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{32}H_{34}N_5O$: 504.27579; found: 504.28834.

Synthesis of [6.3.0] Fused Ring System 10 from Zerumbal 8; General Procedure

Zerumbal **8** (1.0 equiv), indole **2** (1.0 equiv), and $In(OTf)_3$ (5 mol%) were placed in a reaction tube. CH_3CN (2 mL) was added and the reaction mixture was stirred at room temperature for 12 h. The solvent was evaporated in vacuo and the residue was purified by column chromatography (silica gel, 100–200 mesh, hexane–EtOAc).

(*E*)-1-(1*H*-Indol-3-yl)-3,9,9-trimethyl-2-oxo-2,3,3a,4,5,8,9,9a-octahydro-1*H*-cyclopenta[8]annulene-6-carbaldehyde (10a)

Yield: 35 mg (81%); white solid; R_f = 0.20 (EtOAc–hexane, 1:4); mp 145–150 °C.

IR (neat): 3354, 2959, 2928, 2872, 1732, 1679, 1640, 1458, 1372, 1337, 1266, 1206, 1168, 1109, 1012, 739 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 9.50 (s, 1 H), 8.07 (br s, 1 H), 7.78 (d, *J* = 7.5 Hz, 1 H), 7.32 (d, *J* = 8.0 Hz, 1 H), 7.20–7.17 (m, 1 H), 7.15–7.12 (m, 1 H), 6.89 (d, *J* = 2.5 Hz, 1 H), 6.77–6.73 (m, 1 H), 3.60 (d, *J* = 4.0 Hz, 1 H), 3.00–2.96 (m, 1 H), 2.73 (t, *J* = 11.0 Hz, 1 H), 2.41–2.35 (m, 1 H), 2.22–2.15 (m, 4 H), 1.76–1.70 (m, 1 H), 1.52–144 (m, 1 H), 1.05 (d, *J* = 7.0 Hz, 3 H), 1.03 (s, 3 H), 0.97 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 216.0, 194.1, 152.7, 146.0, 136.4, 126.2, 122.7, 120.9, 119.9, 119.7, 116.8, 111.2, 52.1, 48.2, 47.4, 44.0, 40.9, 39.5, 35.2, 27.3, 23.2, 22.7, 12.5.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{23}H_{27}NNaO_2$: 372.19398; found: 372.19468.

(*E*)-3,9,9-Trimethyl-2-oxo-1-(2-phenyl-1*H*-indol-3-yl)-2,3,3a,4,5,8,9,9a-octahydro-1*H*-cyclopenta[8]annulene-6-carbaldehyde (10b)

Yield: 67 mg (73%); white solid; R_f = 0.17 (EtOAc–hexane, 1:4); mp 215–220 °C.

IR (neat): 3350, 2961, 2931, 2336, 1736, 1681, 1640, 1459, 1374, 1281, 1207, 1168, 1112, 886, 799, 764, 670 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 9.43 (s, 1 H), 8.05 (br s, 1 H), 7.86 (d, *J* = 1.5 Hz, 1 H), 7.21–7.19 (m, 1 H), 7.12 (d, *J* = 8.5 Hz, 1 H), 6.81 (d, *J* = 2.5 Hz, 1 H), 6.70–6.67 (m, 1 H), 3.46 (d, *J* = 4.5 Hz, 1 H), 2.93–2.89 (m, 1 H), 2.65 (t, *J* = 11.5 Hz, 1 H), 2.30–2.24 (m, 1 H), 2.15–2.11 (m, 2 H), 1.68–1.63 (m, 2 H), 1.41–1.34 (m, 2 H), 0.99 (d, *J* = 7.0 Hz, 3 H), 0.95 (s, 3 H), 0.88 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 217.4, 193.1, 151.5, 145.7, 136.5, 135.5, 133.9, 128.9, 128.6, 127.5, 121.8, 119.0, 119.0, 111.1, 109.8, 56.0, 44.8, 43.1, 40.1, 39.0, 38.3, 35.9, 26.6, 24.2, 21.8, 21.6.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{29}H_{31}NNaO_2$: 448.22528; found: 448.21853.

(*E*)-3-(6-Formyl-3,9,9-trimethyl-2-oxo-2,3,3a,4,5,8,9,9a-octahydro-1*H*-cyclopenta[8]annulen-1-yl)-1*H*-indole-5-carbaldehyde (10e)

Yield: 70 mg (71%); white solid; R_f = 0.24 (EtOAc–hexane, 1:4); mp 190–194 °C.

IR (neat): 3351, 2959, 2929, 2872, 1733, 1677, 1611, 1571, 1439, 1392, 1371, 1314, 1283, 1176, 1112, 809, 735 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 10.23 (br s, 1 H), 9.61 (s, 1 H), 9.08 (s, 1 H), 7.96 (s, 1 H), 7.26 (d, *J* = 8.5 Hz, 1 H), 7.08 (d, *J* = 8.5 Hz, 1 H), 6.92 (d, *J* = 1.5 Hz, 1 H), 6.48–6.44 (m, 1 H), 3.32 (d, *J* = 4.5 Hz, 1 H), 2.72–2.61 (m, 1 H), 2.51–2.47 (m, 1 H), 2.00–1.96 (m, 1 H), 1.92 (t, *J* = 5.0 Hz, 1 H), 1.88–1.83 (m, 1 H), 1.83–1.77 (m, 2 H), 1.50–1.44 (m, 1 H), 1.15–1.08 (m, 1 H), 0.65 (s, 3 H), 0.60 (d, *J* = 7.0 Hz, 3 H), 0.59 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 220.3, 198.7, 197.0, 157.1, 151.1, 145.4, 134.7, 131.7, 130.1, 129.2, 123.5, 119.8, 117.3, 57.1, 53.1, 52.6, 48.9, 45.6, 44.4, 40.3, 31.8, 27.5, 27.2, 17.0.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{24}H_{27}NNaO_3$: 400.18889; found: 400.18302.

(*E*)-3,9,9-Trimethyl-1-(5-nitro-1*H*-indol-3-yl)-2-oxo-2,3,3a,4,5,8,9,9a-octahydro-1*H*-cyclopenta[8]annulene-6-carbaldehyde (10f)

Yield: 67 mg (82%); yellow solid; R_f = 0.28 (EtOAc–hexane, 1:4); mp 210–215 °C.

IR (neat): 3324, 2958, 2923, 2852, 1723, 1671, 1624, 1516, 1469, 1373, 1370, 1252, 1205, 1168, 1105, 1047, 811, 732 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 9.52 (s, 1 H), 8.79 (d, *J* = 1.5 Hz, 1 H), 8.52 (br s, 1 H), 8.11 (dd, J_1 = 9.0, J_2 = 2.0 Hz, 1 H), 7.36 (d, *J* = 9.0 Hz, 1 H), 7.04 (s, 1 H), 6.79–6.75 (m, 1 H), 3.64 (d, *J* = 4.5 Hz, 1 H), 2.99 (dd,

J_1 = 7.5, J_2 = 5.5 Hz, 1 H), 2.75 (t, J = 11.5 Hz, 1 H), 2.36–2.30 (m, 1 H), 2.22–2.17 (m, 3 H), 1.81–1.76 (m, 1 H), 1.51–1.41 (m, 2 H), 1.08 (d, J = 7.0 Hz, 3 H), 1.06 (s, 3 H), 0.97 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 214.9, 193.3, 151.7, 146.0, 141.5, 139.8, 125.9, 125.5, 118.8, 117.1, 116.8, 111.7, 52.2, 47.8, 47.4, 43.7, 40.4, 39.2, 35.2, 26.6, 22.3, 22.0, 11.8.

HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{23}H_{26}N_2HO_4$: 395.19726; found: 395.19089.

(*E*)-3-(6-Formyl-3,9,9-trimethyl-2-oxo-2,3,3a,4,5,8,9,9a-octahydro-1*H*-cyclopenta[8]annulen-1-yl)-1*H*-indole-5-carbonitrile (10g)

Yield: 38 mg (78%); white solid; R_f = 0.24 (EtOAc–hexane, 1:4); mp 210–214 °C.

IR (neat): 3348, 2961, 2930, 2873, 2220, 1734, 1678, 1640, 1619, 1471, 1439, 1372, 1206, 1168, 1112, 810, 735, 634 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.52 (s, 1 H), 8.58 (br s, 1 H), 8.19 (s, 1 H), 7.42–7.36 (m, 2 H), 7.00 (s, 1 H), 6.79–6.75 (m, 1 H), 3.58 (d, J = 4.5 Hz, 1 H), 3.03–2.97 (m, 2 H), 2.74 (t, J = 11.5 Hz, 1 H), 2.35–2.29 (m, 1 H), 2.22–2.15 (m, 4 H), 1.78–1.73 (m, 1 H), 1.47–1.40 (m, 1 H), 1.07 (d, J = 6.5 Hz, 3 H), 1.04 (s, 3 H), 0.96 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 215.5, 194.1, 152.5, 146.0, 138.0, 126.2, 125.6, 125.6, 122.7, 120.6, 117.7, 112.1, 103.2, 60.4, 52.3, 47.8, 47.5, 44.0, 40.8, 39.4, 35.3, 27.3, 23.1, 22.6, 21.1, 14.2, 12.4.

HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{24}H_{26}N_2HO_2$: 375.20743; found: 375.20224.

(*E*)-3,9,9-Trimethyl-1-(5-methyl-1*H*-indol-3-yl)-2-oxo-2,3,3a,4,5,8,9,9a-octahydro-1*H*-cyclopenta[8]annulene-6-carbaldehyde (10h)

Yield: 48 mg (62%); white solid; R_f = 0.55 (EtOAc–hexane, 1:4); mp 145–147 °C.

IR (neat): 3400, 2960, 2928, 2871, 1732, 1678, 1640, 1465, 1374, 1267, 1180, 1150, 1111, 1049, 1003, 921, 796, 766, 736 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.01 (br s, 1 H), 9.52 (s, 1 H), 7.54 (d, J = 1.0 Hz, 1 H), 7.24 (d, J = 8.0 Hz, 1 H), 7.11 (d, J = 2.5 Hz, 1 H), 6.95 (s, 1 H), 6.94 (dd, J_1 = 8.5, J_2 = 1.5 Hz, 1 H), 6.91–6.87 (m, 1 H), 3.60 (d, J = 4.0 Hz, 1 H), 2.95–2.90 (m, 1 H), 2.86–2.83 (m, 2 H), 2.40 (s, 3 H), 2.31–2.29 (m, 2 H), 2.24–2.18 (m, 2 H), 1.88–1.82 (m, 1 H), 1.58–1.50 (m, 1 H), 1.06 (s, 3 H), 1.03–1.01 (m, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 216.0, 194.0, 152.6, 146.0, 134.8, 129.3, 126.5, 124.3, 120.9, 119.3, 116.4, 110.8, 52.1, 48.2, 47.2, 44.0, 40.9, 39.5, 35.2, 27.2, 23.1, 22.7, 21.5, 12.4.

HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{24}H_{29}NHO_2$: 364.22783; found: 364.22223.

(*E*)-1-(5-Methoxy-1*H*-indol-3-yl)-3,9,9-trimethyl-2-oxo-2,3,3a,4,5,8,9,9a-octahydro-1*H*-cyclopenta[8]annulene-6-carbaldehyde (10i)

Yield: 39 mg (64%); brown solid; R_f = 0.44 (EtOAc–hexane, 1:4); mp 170–172 °C.

IR (neat): 3383, 2958, 2930, 2872, 1733, 1678, 1638, 1584, 1485, 1457, 1374, 1287, 1214, 1173, 1032, 925, 799, 765, 736, 630 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.99 (br s, 1 H), 9.52 (s, 1 H), 7.25–7.24 (m, 2 H), 7.14 (d, J = 2.0 Hz, 1 H), 6.91–6.87 (m, 1 H), 6.76 (dd, J_1 = 8.5, J_2 = 2.5 Hz, 1 H), 3.81 (s, 3 H), 3.59 (d, J = 4.5 Hz, 1 H), 2.95–2.91 (m, 1 H), 2.85–2.81 (m, 1 H), 2.42–2.37 (m, 1 H), 2.32–2.28 (m, 2 H), 2.24–2.19 (m, 2 H), 1.87–1.83 (m, 1 H), 1.56–1.50 (m, 1 H), 1.06 (s, 3 H), 1.04–1.02 (m, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 215.1, 193.4, 154.0, 151.9, 145.9, 132.0, 126.8, 122.5, 115.9, 112.0, 101.0, 55.0, 52.3, 48.2, 47.3, 43.8, 40.5, 39.2, 35.1, 26.6, 22.4, 22.1, 11.9.

HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{24}H_{29}NHO_3$: 380.22274; found: 380.21707.

(*E*)-1-(5-Fluoro-1*H*-indol-3-yl)-3,9,9-trimethyl-2-oxo-2,3,3a,4,5,8,9,9a-octahydro-1*H*-cyclopenta[8]annulene-6-carbaldehyde (10j)

Yield: 49 mg (74%); white solid; R_f = 0.27 (EtOAc–hexane, 1:4); mp 214–216 °C.

IR (neat): 3367, 2960, 2928, 2872, 1732, 1678, 1640, 1582, 1487, 1457, 1375, 1285, 1207, 1172, 1091, 1014, 937, 855, 798, 764, 737, 620 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.10 (br s, 1 H), 9.37 (s, 1 H), 7.32 (dd, J_1 = 10.0, J_2 = 2.5 Hz, 1 H), 7.22–7.20 (m, 1 H), 7.11 (d, J = 2.0 Hz, 1 H), 6.78–6.74 (m, 2 H), 3.45 (d, J = 4.0 Hz, 1 H), 2.80–2.76 (m, 1 H), 2.27–2.21 (m, 1 H), 2.16–2.13 (m, 2 H), 2.10–2.03 (m, 2 H), 1.74–1.68 (m, 1 H), 1.40–1.33 (m, 1 H), 0.92 (s, 3 H), 0.88–0.87 (m, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 215.5, 193.5, 151.9, 145.9, 133.5, 123.9, 112.3, 112.2, 109.9, 109.7, 104.1, 103.9, 52.4, 48.0, 47.1, 43.7, 40.4, 39.1, 35.2, 26.6, 22.3, 22.0, 11.7.

HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{23}H_{26}FHNO_2$: 368.20276; found: 368.19702.

(*E*)-1-(5-Chloro-1*H*-indol-3-yl)-3,9,9-trimethyl-2-oxo-2,3,3a,4,5,8,9,9a-octahydro-1*H*-cyclopenta[8]annulene-6-carbaldehyde (10k)

Yield: 59 mg (75%); brown solid; R_f = 0.48 (EtOAc–hexane, 1:4); mp 210–214 °C.

IR (neat): 3347, 2960, 2930, 2872, 1732, 1678, 1625, 1578, 1518, 1470, 1373, 1330, 1108, 902, 815, 739 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.19 (br s, 1 H), 9.37 (s, 1 H), 7.65 (d, J = 2.0 Hz, 1 H), 7.23 (d, J = 8.5 Hz, 1 H), 7.12 (d, J = 2.5 Hz, 1 H), 6.94 (dd, J_1 = 8.5, J_2 = 2.0 Hz, 1 H), 6.77–6.74 (m, 1 H), 3.49 (d, J = 4.5 Hz, 1 H), 2.80–2.76 (m, 1 H), 2.71–2.66 (m, 1 H), 2.26–2.20 (m, 1 H), 2.17–2.15 (m, 1 H), 2.10–2.03 (m, 1 H), 1.75–1.69 (m, 1 H), 1.40–1.33 (m, 1 H), 0.92 (s, 3 H), 0.88–0.87 (m, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 214.9, 193.3, 151.8, 145.9, 135.3, 127.7, 124.3, 123.6, 121.8, 118.8, 116.1, 112.7, 52.3, 47.8, 47.1, 43.7, 40.4, 39.2, 35.1, 26.6, 22.3, 22.0, 11.7.

HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{23}H_{27}ClNO_2$: 384.17321; found: 384.16729.

Synthesis of [6.3.0] Fused Ring System 11 from Zerumbenone 9; General Procedure

A mixture of zerumbenone **9** (1.0 equiv), indole **2** (1.0 equiv), and $Sc(OTf)_3$ (5 mol%) in CH_3CN (2 mL) as solvent in a Schlenk tube was stirred at 80 °C for 12 h. The completion of the reaction was confirmed by TLC, after which the reaction mixture was concentrated and the crude product was purified by column chromatography (silica gel, 100–200 mesh, hexane–EtOAc), to give **11** as a diastereoisomeric mixture.

7-[(1*H*-Indol-3-yl)methyl]-3-(1*H*-indol-3-yl)-1,4,4-trimethyloctahydro-1*H*-cyclopenta[8]annulene-2,6-dione (11a)

Yield: 52 mg (85%); white solid; R_f = 0.33 (EtOAc–hexane, 3:7); mp 123–127 °C.

IR (neat): 3363, 2960, 2926, 1729, 1686, 1569, 1460, 1341, 1288, 1235, 1156, 1100, 892, 793 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.19–8.11 (m, 4 H), 7.78–7.74 (m, 2 H), 7.63–7.58 (m, 1 H), 7.36–7.29 (m, 4 H), 7.19–7.12 (m, 9 H), 7.00–6.93 (m, 4 H), 3.69 (d, *J* = 4.5 Hz, 1 H), 3.66 (d, *J* = 4.5 Hz, 1 H), 2.84–2.68 (m, 4 H), 2.60 (d, *J* = 11.5 Hz, 1 H), 2.45–2.41 (m, 2 H), 2.38–2.34 (m, 5 H), 1.76–1.67 (m, 3 H), 1.54–1.48 (m, 3 H), 1.07–0.99 (m, 16 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 217.4, 217.0, 216.2, 215.6, 139.3, 136.6, 136.4, 136.3, 127.5, 127.4, 126.2, 126.2, 122.6, 122.5, 122.0, 121.3, 121.3, 119.8, 119.6, 119.3, 118.8, 116.3, 114.1, 113.6, 112.7, 111.3, 111.3, 56.0, 53.9, 53.8, 53.7, 52.4, 51.3, 51.0, 48.8, 48.7, 48.4, 48.3, 42.2, 41.3, 40.0, 39.8, 34.3, 33.9, 33.2, 33.2, 32.0, 31.2, 31.0, 30.4, 27.1, 21.1, 20.1, 13.2, 12.9.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{34}N_2NaO_2$: 489.25183; found: 489.24449.

3-[(1-(5-Cyano-1*H*-indol-3-yl)-3,9,9-trimethyl-2,7-dioxodecahydro-1*H*-cyclopenta[8]annulen-6-yl)methyl]-1*H*-indole-5-carbonitrile (11d)

Yield: 56 mg (50%); white solid; R_f = 0.28 (EtOAc–hexane, 2:3); mp 145–148 °C.

IR (neat): 3341, 2928, 2219, 1733, 1686, 1618, 1472, 1436, 1365 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.77 (br s, 1 H), 8.65 (br s, 1 H), 8.62 (br s, 1 H), 8.14 (s, 1 H), 8.10 (s, 1 H), 7.96 (s, 1 H), 7.94 (s, 1 H), 7.42–7.36 (m, 8 H), 7.16–7.11 (m, 4 H), 3.65–3.62 (m, 2 H), 2.87–2.83 (m, 1 H), 2.80–2.72 (m, 3 H), 2.65 (d, *J* = 7.0 Hz, 1 H), 2.38–2.33 (m, 3 H), 2.29–2.18 (m, 4 H), 2.00–1.97 (m, 2 H), 1.61–1.51 (m, 4 H), 1.08–1.03 (m, 11 H), 0.99–0.98 (m, 5 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 216.6, 216.2, 215.0, 214.8, 138.2, 138.0, 137.9, 127.4, 127.3, 126.2, 126.1, 125.5, 125.4, 125.0, 124.8, 124.5, 123.4, 123.3, 120.9, 120.7, 120.6, 117.2, 117.1, 114.6, 114.0, 112.3, 103.0, 102.6, 102.5, 56.0, 54.2, 53.8, 51.8, 51.4, 50.9, 48.9, 48.5, 48.4, 48.3, 42.5, 41.5, 39.6, 39.4, 33.7, 33.2, 31.1, 30.2, 28.2, 27. 3, 21.4, 20.7, 13.1, 13.0.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{33}H_{32}N_4NaO_2$: 539.24233; found: 539.24357.

3-[(1-(5-Formyl-1*H*-indol-3-yl)-3,9,9-trimethyl-2,7-dioxodecahydro-1*H*-cyclopenta[8]annulen-6-yl)methyl]-1*H*-indole-5-carbaldehyde (11e)

Yield: 40 mg (35%); white solid; R_f = 0.65 (EtOAc–hexane, 2:3); mp 235–240 °C.

IR (neat): 3335, 2923, 2852, 2738, 1732, 1677, 1611, 1576, 1438, 1367, 1313, 1180, 1100 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 10.06 (s, 1 H), 10.05 (s, 1 H), 10.04 (s, 1 H), 10.04 (s, 1 H), 8.70 (br s, 2 H), 8.57 (br s, 1 H), 8.55 (br s, 1 H), 8.31 (d, *J* = 10.5 Hz, 2 H), 8.16 (d, *J* = 12.0 Hz, 2 H), 7.78–7.75 (m, 3 H), 7.46–7.43 (m, 2 H), 7.41–7.39 (m, 2 H), 7.13–7.09 (m, 3 H), 3.72–3.70 (m, 2 H), 2.92–2.87 (m, 1 H), 2.83–2.81 (m, 1 H), 2.79–2.74 (m, 2 H), 2.68 (d, *J* = 11.5 Hz, 1 H), 2.49–2.37 (m, 5 H), 2.31–2.27 (m, 2 H), 2.02–1.96 (m, 3 H), 1.60–1.54 (m, 4 H), 1.09–1.00 (m, 16 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 216.7, 216.3, 215.2, 215.2, 192.3, 140.0, 139.8, 129.8, 129.8, 129.4, 129.3, 127.6, 127.4, 126.3, 126.2, 124.4, 123.3, 122.9, 122.8, 118.3, 118.2, 115.8, 115.1, 112.0, 111.8, 55.9, 54.0, 53.7, 52.0, 51.2, 48.8, 48.5, 48.4, 42.3, 41.4, 39.8, 39.5, 33.3, 31.1, 30.3, 29.7, 28.4, 27.3, 20.6, 20.5, 13.1, 13.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{33}H_{34}N_2O_4$: 545.24166; found: 545.24327.

1,4,4-Trimethyl-3-(5-nitro-1*H*-indol-3-yl)-7-[(5-nitro-1*H*-indol-3-yl)methyl]octahydro-1*H*-cyclopenta[8]annulene-2,6-dione (11f)

Yield: 40 mg (56%); yellow solid; R_f = 0.34 (EtOAc–hexane, 3:7); mp 238–245 °C.

IR (neat): 3351, 2922, 2852, 1730, 1686, 1623, 1579, 1516, 1466, 1372, 1330, 1099, 893, 813, 737 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 10.77 (br s, 2 H), 10.66 (br s, 2 H), 8.67 (d, *J* = 2.5 Hz, 1 H), 8.65 (d, *J* = 2.0 Hz, 1 H), 8.46 (d, *J* = 2.5 Hz, 1 H), 8.45 (d, *J* = 2.0 Hz, 1 H), 7.92–7.90 (m, 2 H), 7.90–7.89 (m, 2 H), 7.46–7.42 (m, 5 H), 7.36 (d, *J* = 2.0 Hz, 1 H), 7.30 (d, *J* = 2.0 Hz, 1 H), 3.72–3.70 (m, 2 H), 2.99–2.94 (m, 1 H), 2.89–2.85 (m, 2 H), 2.50–2.48 (m, 2 H), 2.46–2.44 (m, 1 H), 2.27–2.15 (m, 5 H), 1.80–1.74 (m, 2 H), 1.56–1.44 (m, 3 H), 0.96 (s, 2 H), 0.92–0.90 (m, 11 H), 0.84 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 215.5, 215.3, 214.0, 213.7, 141.4, 141.2, 141.2, 139.9, 139.7, 127.0, 126.0, 125.8, 125.7, 118.6, 118.5, 117.1, 117.0, 116.9, 116.6, 115.7, 115.7, 111.7, 111.6, 56.1, 53.3, 51.5, 50.6, 48.3, 48.2, 48.1, 48.0, 41.4, 39.5, 39.1, 33.1, 30.4, 29.8, 27.9, 26.9, 20.3, 20.0, 12.3, 12.2.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{32}N_4NaO_6$: 579.22198; found: 579.21372.

3-(5-Methoxy-1*H*-indol-3-yl)-7-[(5-methoxy-1*H*-indol-3-yl)methyl]-1,4,4-trimethyloctahydro-1*H*-cyclopenta[8]annulene-2,6-dione (11g)

Yield: 62 mg (55%); white solid; R_f = 0.37 (EtOAc–hexane, 1:3); mp 185–189 °C.

IR (neat): 3410, 2925, 2855, 2098, 1643, 1457, 1367, 1291, 1211, 1167, 1098, 1043, 792, 735 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 10.04 (br s, 2 H), 9.92 (br s, 2 H), 7.30–7.24 (m, 8 H), 7.16 (dd, J_1 = 17.5, J_2 = 2.5 Hz, 2 H), 7.09 (dd, J_1 = 12.5, J_2 = 2.5 Hz, 2 H), 6.80–6.78 (m, 2 H), 6.78–6.77 (m, 2 H), 3.82 (s, 3 H, OCH_3), 3.82 (s, 3 H), 3.81 (d, *J* = 2.0 Hz, 6 H), 3.65 (d, *J* = 4.0 Hz, 2 H), 2.88–2.82 (m, 2 H), 2.76–2.72 (m, 1 H), 2.56–2.49 (m, 3 H), 2.38–2.24 (m, 5 H), 2.00–1.81 (m, 4 H), 1.66–1.59 (m, 1 H), 1.55–1.48 (m, 2 H), 1.05–1.02 (m, 15 H), 0.95 (d, *J* = 7.0 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 215.8, 215.5, 214.7, 214.2, 154.0, 153.8, 153.8, 132.0, 132.0, 132.0, 128.1, 128.0, 126.9, 126.9, 123.9, 123.8, 122.7, 122.6, 115.7, 115.6, 112.6, 112.0, 111.9, 111.4, 111.3, 101.1, 100.5, 100.3, 56.0, 55.1, 55.0, 55.0, 53.4, 53.2, 51.9, 50.9, 50.4, 48.7, 48.7, 47.7, 47.6, 41.9, 41.3, 39.6, 39.2, 33.9, 32.6, 30.4, 29.8, 26.8, 20.3, 19.6, 12.2, 12.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{33}H_{38}N_2NaO_4$: 549.27296; found: 549.26495.

1,4,4-Trimethyl-3-(6-methyl-1*H*-indol-3-yl)-7-[(6-methyl-1*H*-indol-3-yl)methyl]octahydro-1*H*-cyclopenta[8]annulene-2,6-dione (11h)

Yield: 61 mg (50%); white solid; R_f = 0.55 (EtOAc–hexane, 1:4); mp 217–225 °C.

IR (neat): 3399, 2961, 2923, 2858, 1730, 1688, 1625, 1456, 1369, 1337, 1241, 1153, 1098, 800 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.92–7.88 (m, 4 H), 7.66–7.62 (m, 2 H), 7.51 (d, *J* = 8.0 Hz, 1 H), 7.46 (d, *J* = 8.0 Hz, 1 H), 7.17 (br s, 2 H), 7.12 (d, *J* = 6.0 Hz, 2 H), 6.99–6.91 (m, 7 H), 3.63 (d, *J* = 4.5 Hz, 2 H), 2.78–2.70 (m, 4 H), 2.53 (d, *J* = 12.0 Hz, 1 H), 2.46 (s, 5 H), 2.44–2.43 (m, 5 H), 2.38–2.26 (m, 7 H), 1.93–1.85 (m, 3 H), 1.51–1.44 (m, 3 H), 1.05–1.03 (m, 7 H), 1.02–1.00 (m, 7 H), 0.98 (d, *J* = 7.0 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 216.9, 216.5, 215.9, 215.3, 137.0, 136.8, 136.8, 132.5, 132.0, 131.9, 125.4, 125.3, 124.1, 124.1, 121.8, 121.8, 121.7, 121.3, 121.2, 120.4, 119.4, 119.3, 118.5, 118.5, 116.5, 113.6, 112.8, 111.2, 111.1, 111.1, 55.9, 53.9, 53.6. 52.3, 51.3, 51.0, 48.8, 48.8, 48.4, 48.2, 42.1, 41.2, 39.9, 39.8, 34.4, 33.2, 31.2, 30.3, 29.7, 29.2, 27.2, 27.1, 21.7, 21.6, 21.0, 20.0, 13.1, 12.8.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{33}H_{38}N_2NaO_2$: 517.28313; found: 517.28496.

3-(5-Fluoro-1*H*-indol-3-yl)-7-[(5-fluoro-1*H*-indol-3-yl)methyl]-1,4,4-trimethyloctahydro-1*H*-cyclopenta[8]annulene-2,6-dione (11i)

Yield: 52 mg (53%); gummy brown solid; R_f = 0.44 (EtOAc–hexane, 3:7).

IR (neat): 3361, 3057, 2963, 2927, 1730, 1687, 1627, 1582, 1484, 1457, 1351, 1294, 1236, 1172, 1098, 935 796 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.33 (br s, 1 H), 8.32 (br s, 1 H), 8.23 (br s, 1 H), 8.21 (br s, 1 H), 7.42–7.37 (m, 2 H), 7.25–7.16 (m, 6 H), 7.01 (d, *J* = 2.0 Hz, 1 H), 6.99–6.98 (m, 2 H), 6.94 (d, *J* = 2.5 Hz, 1 H), 6.92–6.90 (m, 2 H), 3.56 (d, *J* = 5.0 Hz, 2 H), 2.79–2.67 (m, 5 H), 2.39–2.23 (m, 6 H), 1.94–1.88 (m, 3 H), 1.51–1.46 (m, 3 H), 1.05–0.98 (m, 16 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 217.2, 216.8, 215.7, 158.9, 158.7, 158.7, 157.0, 156.9, 156.8, 133.0, 132.8, 132.7, 127.9, 127.8, 127.7, 126.6, 126.5, 126.5, 124.4, 124.4, 122.9, 122.9, 116.3, 113.8, 113.7, 113.0, 112.9, 112.0, 111.9, 111.1, 110.9, 110.6, 110.5, 110.4, 110.3, 55.9, 53.6, 52.1, 51.0, 48.7, 48.6, 48.6, 48.4, 41.3, 39.8, 39.6, 33.9, 31.2, 30.3, 28.9, 27.2, 20.2, 13.2, 13.0.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{32}N_2F_2NaO_2$: 525.23298; found: 525.23212.

3-(5-Chloro-1*H*-indol-3-yl)-7-[(5-chloro-1*H*-indol-3-yl)methyl]-1,4,4-trimethyloctahydro-1*H*-cyclopenta[8]annulene-2,6-dione (11j)

Yield: 51 mg (45%); white solid; R_f = 0.20 (EtOAc–hexane, 1:4); mp 232–235 °C.

IR (neat): 3363, 2960, 2926, 1729, 1686, 1569, 1460, 1341, 1288, 1235, 1156, 1100, 892, 793 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.90 (br s, 2 H), 7.88 (br s, 2 H), 7.64 (d, *J* = 8.0 Hz, 1 H), 7.46 (d, *J* = 8.0 Hz, 1 H), 7.17 (s, 2 H), 7.12 (s, 2 H), 6.97–6.94 (m, 5 H), 6.91 (d, *J* = 2.0 Hz, 1 H), 3.63 (d, *J* = 4.5 Hz, 2 H), 3.34 (d, *J* = 10.5 Hz, 1 H), 2.76–2.70 (m, 4 H), 2.53 (d, *J* = 12.0 Hz, 2 H), 2.46 (s, 5 H), 2.43 (s, 6 H), 2.36–2.30 (m, 4 H), 2.20–2.14 (m, 3 H), 1.91–1.85 (m, 2 H), 1.52–1.41 (m, 5 H), 1.05–1.03 (m, 11 H), 1.02 (s, 5 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 217.4, 217.1, 216.1, 215.7, 135.0, 134.8, 134.7, 134.5, 128.5, 127.2, 125.4, 125.0, 124.2, 124.1, 122.7, 122.6, 122.2, 122.1, 119.0, 118.9, 118.1, 115.6, 115.6, 112.4, 112.3, 56.0, 52.2, 51.0, 48.5, 48.3, 41.2, 39.7, 33.9, 31.1, 30.9, 29.7, 28.8, 27.1, 20.1, 13.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{32}N_2Cl_2NaO_2$: 557.17388; found: 557.16589.

3-(5-Bromo-1*H*-indol-3-yl)-7-[(5-bromo-1*H*-indol-3-yl)methyl]-1,4,4-trimethyloctahydro-1*H*-cyclopenta[8]annulene-2,6-dione (11k)

Yield: 20 mg (20%); gummy brown mass; R_f = 0.48 (EtOAc–hexane, 3:7).

IR (neat): 3417, 2960, 2926, 1730, 1685, 1614, 1544, 1455, 1399, 1369, 1331, 1236, 1156, 1099, 1051, 894, 801, 736 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.30 (br s, 2 H), 8.21 (br s, 2 H), 7.60–7.56 (m, 2 H), 7.55–7.42 (m, 3 H), 7.40–7.39 (m, 2 H), 7.21–7.19 (m, 4 H), 6.93–6.84 (m, 4 H), 3.59 (d, *J* = 5.0 Hz, 2 H), 2.81–2.74 (m, 2 H), 2.69–2.65 (m, 3 H), 2.46 (d, *J* = 12 Hz, 1 H), 2.32 (t, *J* = 6.0 Hz, 2 H), 2.30–2.22 (m, 3 H), 1.72–1.67 (m, 2 H), 1.53–1.47 (m, 4 H), 1.05–1.04 (m, 5 H), 1.02–0.99 (m, 6 H), 0.97–0.96 (m, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 216.9, 216.5, 215.6, 215.2, 137.3, 137.3, 137.1, 137.0, 129.6, 126.3, 125.2, 125.1, 123.3, 123.1, 123.0, 122.9, 122.7, 121.7, 121.6, 121.0, 120.9, 120.1, 120.0, 118.3, 116.6, 116.6, 116.3, 115.7, 115.7, 115.3, 114.2, 114.2, 114.1, 113.9, 113.1, 55.8, 53.8, 53.7, 52.2, 51.1, 48.6, 48.5, 48.4, 41.2, 39.8, 39.6, 34.0, 31.9, 31.8, 31.2, 31.0, 30.3, 30.0, 29.7, 29.4, 29.3, 28.8, 27.2, 22.7, 21.2, 20.2, 13.2, 12.9.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{32}N_2Br_2NaO_2$: 624.41700; found: 647.07138.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0039-1690840.

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