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Molecular Transformation of 2-Methylazulenes: An Efficient and Practical Synthesis of 2-Formyl- and 2-Ethynylazulenes

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Abstract: 2-Formylazulene derivatives were obtained in good yields by the reaction of 2-methylazulenes with *N,N*-dimethylformamide dimethyl acetal, followed by oxidative cleavage of intermediately formed enamines with $NaIO_4$. Vilsmeier formylation of 1-phenyl-3-methylazulenes also afforded the corresponding 2-formylazulenes in moderate yields. In a 2-methylazulene derivative having a formyl group at the 1-position, self-condensation reaction was also observed by the treatment with sodium methoxide to produce a trans-1-(azulen-1-yl)-2-(azulen-2-yl)ethylene derivative, of which structure was clarified by single crystal X-ray analysis. 2-Formylazulenes obtained by the reaction were also transformed to 2-ethynylazulenes in good yields by modified Seyferth−Gilbert reaction. The reactivity of 1-iodoazulene bearing 2-formyl function toward palladium-catalyzed cross-coupling reactions was also examined.

Introduction

Azulene, which is one of the non-alternating 10π electron aromatic compounds, has attracted the interest of many research groups owing to its unusual properties as well as its beautiful blue color. Thus, various functionalization methods for azulene and its derivatives have been reported by many researchers.[1] Functionalization of 1- and/or 3-positions of azulene derivatives have readily achieved by electrophilic substitution reactions because these sites have high reactivity toward a variety of electrophiles.[1,2] On the other hand, introduction of functional groups to the other positions of azulene

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ring has often encountered some difficulties, although the effective functionalization methods at their 5- and/or 7-positions have reported.[3,4]

2-Formylazulene derivatives are versatile starting materials that can be converted into azulene-substituted α-hydroxyketones, diketones, imines, hydrazones, alkenes, alkynes, and heterocyclic compounds.[5] Even the synthesis of 2-formylazulenes with a simple structure, there is no straightforward method because of the difficult availability of the starting materials and/or the multi-step synthesis required in addition to the low product yields. In early years of azulene chemistry, Hafner and Moritz reported that 1,3-dimethylazulene undergoes the electrophilic substitution reaction under the Vilsmeier formylation conditions to afford the corresponding 2-formylazulene derivative in 21% yield.[6] In 1980, Takase and co-workers reported the preparation of 2-formylazulene by using OsO_4 oxidation of 2-styrylazulene.[7] However, this method requires the starting material which is difficult to synthesize, and the yield of the product is quite low (13%). Although Murafuji *et al*. have also reported the synthesis of 2-formylazulene by the reduction of azulene-2-carboxamide with diisobutylalminium hydride (DIBAL) in 42% yield, preparation of the azulene-2-carboxamide precursor required multiple-step synthetic pathway.[8] We have also reported the preparation of 2-formylazulene by the reaction with 2-azulenyllithium and magnesium reagents with DMF in excellent yields (89% and 99% yields, respectively), but preparation of 2-iodoazulene, which is difficult to access, is required to prepare the azulenyl metal reagents.[9] 2-Formylazulene have also been prepared by Yasunami−Takase's azulene synthesis,4d but the preparation method is not applicable to the other functional derivatives, straightforwardly, because of the quite low applicability of the functional group on the 2*H*-cyclohepta[*b*]furan-2-one precursors. When electron-withdrawing group is substituted to the precursor, the reaction competes with the side reaction to give aminopentafulvenes.[10] From the situation mentioned above, the development of a synthetic procedure by a short step with readily available starting materials should bring great benefits to the practical synthesis of 2-formylazulenes.

Oxidative cleavage of the enamines, which have been prepared by the reaction of electron-deficient aromatic compounds at their methyl function with *N,N*-dimethylformamide dimethyl acetal (DMFDMA), with $NaIO_4$ is a general procedure for the transformation of the methyl group to formyl function in the aromatic compounds.[11] In azulene chemistry, 4-formyl-[12] and 6-formylazulene[13] derivatives have been prepared from the corresponding methylazulenes by using the similar procedure. However, there is no example adopting this method to the synthesis of 2-formylazulenes, despite the electron-withdrawing nature at the 2-position as
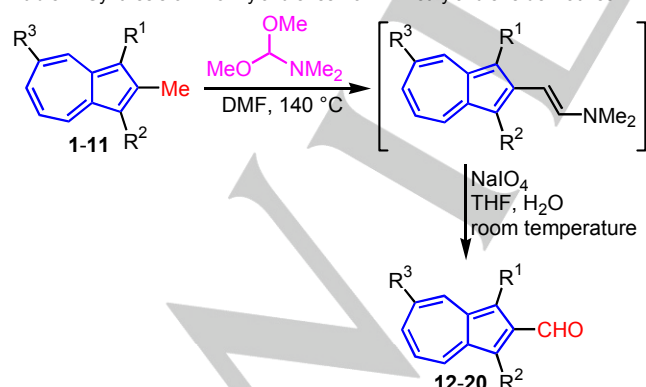
similar with that at the 4- and 6-positions. Since 2-methylazulenes could be readily synthesized in high yields by Yasunami−Takase's procedure, an efficient and practical synthetic procedure of 2-formylazulenes should be established, if the method can be applied.

Herein, we describe a novel synthetic approach to 2-formylazulenes by the reaction of 2-methylazulenes with DMFDMA, followed by the oxidative cleavage of intermediately formed enamines with $NaIO_4$. As another method, the synthesis of 2-formylazulenes by the Vilsmeier reaction of 1-phenyl-3-methylazulene derivatives was also investigated. Furthermore, we found the formation of trans-alkene derivative substituted by two-azulenyl groups by the self-condensation reaction under basic conditions in the course of studying the reactivity of 1-formyl-2-methylazulene derivative. Transformation of 2-formylazulenes to 2-ethynylazulenes was also examined by modified Seyferth−Gilbert reaction conditions. These results demonstrate the usefulness of the 2-methylazulene derivatives as starting materials that can be converted to various functional azulene derivatives.

Results and Discussion

Synthesis of 2-formylazulenes: For the synthesis of 2-formylazulenes, we adopted the reaction of several 2-methylazulenes with DMFDMA to give the enamine intermediates, followed by the oxidative cleavage of intermediately formed enamines with $NaIO_4$. Since the enamine intermediates obtained by the reaction were instable and readily decomposed by chromatographic purification process, the oxidative cleavage with $NaIO_4$ was performed without the isolation of the enamine intermediates. However, in the case of the reaction of **5**, suitable single crystal for single crystal X-ray structure analysis was exceptionally obtained from the crude enamine product. Thus, the crystal structure of the enamine intermediate was clarified by the single crystal X-ray structure analysis (Figure 1). The yield and structure of 2-formylazulenes obtained by the reaction are summarized in Table 1.

Table 1. Synthesis of 2-formylazulenes from 2-methylazulene derivatives.

Entry	Substrate	Product	Yield [%][a]
1	**1** (i-Pr, CO2Me, Me)	**12** (i-Pr, CO2Me, CHO)	54
2	**2** (CO2Me, Me)	**13** (CO2Me, CHO)	67
3	**3** (CO2Me, Me, CO2Me)	**14** (CO2Me, CHO, CO2Me)	61
4	**4** (CO2Me, Me, CHO)	**15** (CO2Me, CHO, CHO)	83
5	**5** (i-Pr, CO2Me, Me, CHO)	**16** (i-Pr, CO2Me, CHO, CHO)	85
6	**6** (CHO, Me, CHO)	**17** (CHO, CHO, CHO)	80
7	**7** (CO2Me, Me, F)	**18** (CO2Me, CHO, F)	90
8	**8** (CO2Me, Me, Cl)	**19** (CO2Me, CHO, Cl)	62
9	**9** (CO2Me, Me, Br)	**20** (CO2Me, CHO, Br)	25
10	**10** (CO2Me, Me, I)	**21** (CO2Me, CHO, I)	decomposition
11	**11** (Me)	**22** (CHO)	no reaction

[a] Two-step yield from 2-methylazulenes **1−9**.

In general, the reaction of 2-methylazulene derivatives having electron-withdrawing substituents at their 1,3-positions produced the corresponding 2-formylazulenes in good yields. On the other hand, this reaction was not effective in the cases of 2-methylazulenes with either bromine or iodine substituent, since the reaction competed with the decomposition of the substrate.

The reaction of **1** with DMFDMA at 140 ºC gave crude enamine intermediate as brown oil (Table 1). The oxidative cleavage of the enamine intermediate with $NaIO_4$ afforded 2-formylazulene **12** in 54% yield (entry 1). As shown in Table 1, 2-formylazulenes **13−19** were also obtained by the reaction of 2-methylazulene derivatives **2−8** with DMFDMA, followed by the oxidative cleavage with $NaIO_4$ in good to excellent yields

(61−90%, entries 2−8). In particular, two-step reaction of 2-methylazulene derivatives **4**−**7**, in which the electron-withdrawing group was substituted at their 1,3-positions, produced the corresponding 2-formylazulenes in excellent yields. These results suggested that the enamine intermediates formed by the reaction of **4**−**7** are more likely formed compared to those of the other derivatives, since the acidity of the methyl group at the 2-position was increased by the electron-withdrawing groups at their 1,3-positions. On the other hand, the reaction of **9** and **10** having either bromine or iodine substituent with DMFDMA resulted in decomposition, owing to the thermal instability of the precursors **9** and **10** (entries 9 and 10). Moreover, no reaction was observed to form an enamine intermediate in 2-methylazulene (**11**) (entry 11). This implies the requirement of an electron-withdrawing group at least on azulene ring to afford the enamine intermediate.

These new 2-formylazulenes were fully characterized on the basis of their spectral data, as summarized in the Experimental Section. The signal assignment of ^{1}H NMR was accomplished by COSY experiment. HRMS of the new compounds ionized by MALDI, EI or FAB showed the expected molecular ion peaks. The structure of **16** was also confirmed by single-crystal X-ray structural analysis, since the suitable single crystals were obtained by slow evaporation from MeOH (Figure 2). These results show the correctness of the structure of synthesized 2-formylazulenes.
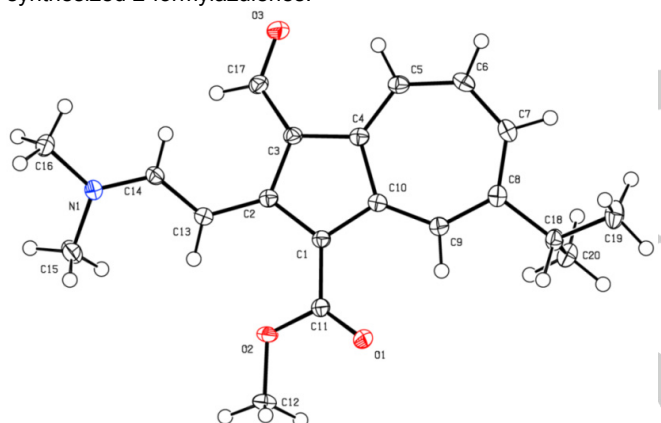

Figure 1. ORTEP Drawing for the enamine intermediate obtained from the reaction of **5**; Ellipsoids are drawn at 50% probability.[14]
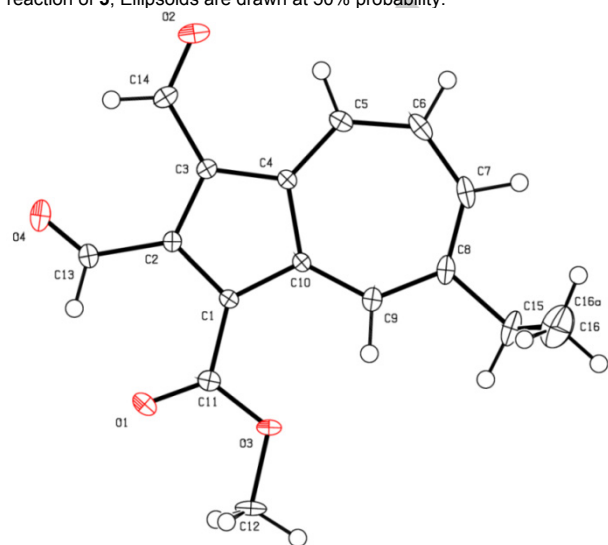

Figure 2. ORTEP Drawing for 2-formylazulene **16**; Ellipsoids are drawn at 50% probability.[14]

By utilizing the high acidity of the methyl proton at the 2-position, the synthesis of cyclooctatetraene derivative fused by two azulene rings was investigated by the aldol-type condensation reaction on the 1-formyl group. In order to prevent the solubility problem of the product by π-π stacking, 2-methylazulene derivative **5**, which was substituted by the bulky isopropyl group, was selected as a starting material.

Contrary to the expectation, the reaction of compound **5** with sodium methoxide in methanol afforded *trans*-alkene **23** with two-azulenyl substituents as a single product in 70% yield, instead of the presumed cyclooctatetraene derivative (Scheme 1). This fact indicates that the self-condensation reaction of the methyl and formyl groups between the two azulene rings produces the thermodynamically stable *trans*-alkene product prior to the *cis*-alkene product. Therefore, the cyclooctatetraene derivative, which requires the formation of *cis*-alkene intermediate, should not be generated under this condition.
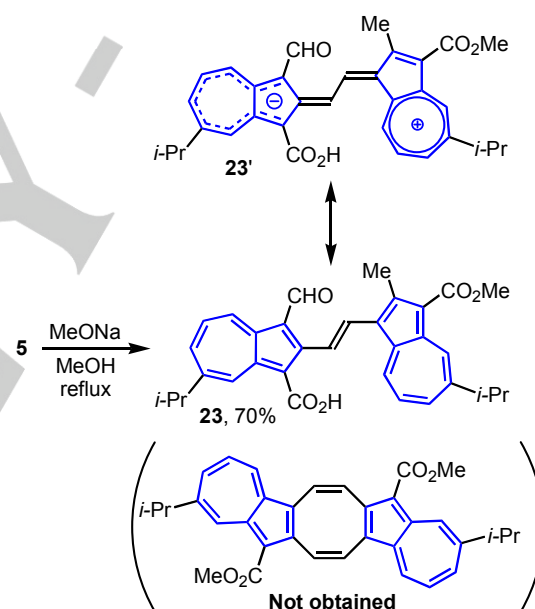
Scheme 1. Synthesis of **23** by the self-condensation reaction of **5**.

The ^{1}H NMR spectrum of alkene **23** showed proton signals of the both azulene rings, individually. The coupling constant of the alkene protons was observed as J = 16.6 Hz, which supported the *trans*-alkene structure of **23**. Furthermore, the *trans*-alkene structure of **23** was also confirmed by single crystal X-ray structure analysis (Figure 3). Although the bond length between the azulene ring and the methyl carbon at the 2-position showed almost the same length (C14−C28, 1.501 Å) toward the ordinary single bond, the single bonds (i.e. C2−C11 and C12−C13) exhibited shorter bond length. This result indicates the resonance effect between the 1-azulenyl and 2-azulenyl groups to form **23'** through the alkene moiety as shown in Scheme 1.
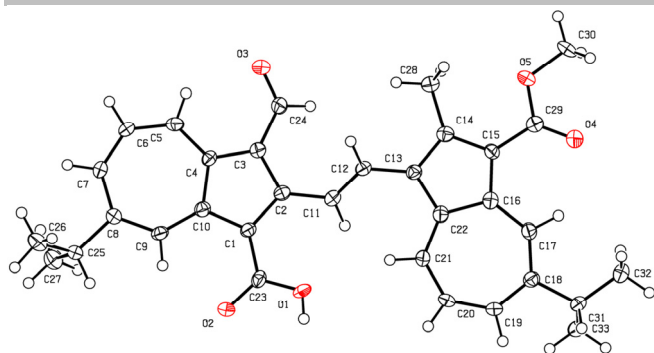
Figure 3. ORTEP Drawing of **23**; Ellipsoids are drawn at 50% probability. C2−C11 1.459(3) Å, C12−C13 1.454(3) Å, C14−C28 1.501(3) Å. [14]

Although the precursor **5** showed a weak absorption band at λ_{max} =489 nm, the UV/Vis spectra of **23** in CH_2Cl_2 revealed a broad and strong absorption band in the visible region center at λ_{max} = 476 nm (Figure 4). Since such absorption band cannot be observed in the UV/Vis spectrum of the precursor **5**, the strong absorption band of **23** in the visible region might be originated from the intramolecular charge transfer (ICT) between the two azulene rings.
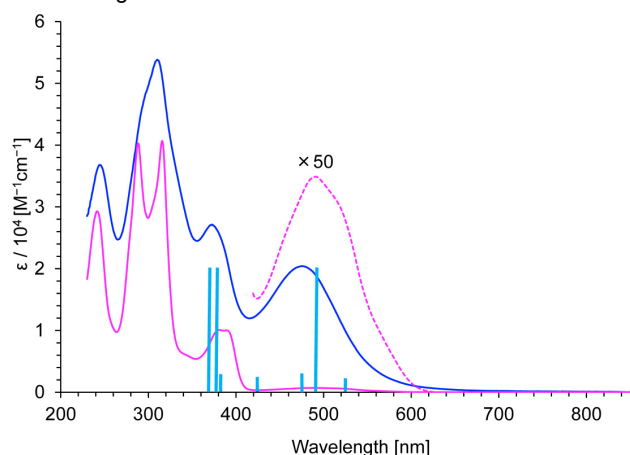

Figure 4. The UV/Vis spectra of **23** (blue line) and **5** (pink line) in CH_2Cl_2, and calculated spectrum of **23** (light-blue bar); the dotted line represents that of 50 magnifications.

In order to interpret these differences theoretically, orbital calculations of **5** and **23** were carried out by using time-dependent density functional theory (TD−DFT) at B3LYP/6-31G** level (Table 2). The absorption band of **5** at λ_{max} = 489 nm can be assigned to the transition originated from HOMO to LUMO. Thus, the longest wavelength absorption band of **5** should be attributed to the π-π* transition of the azulene ring itself (see Supporting Information, Figure S107). The calculations revealed that the strong absorption band of **23** in the visible region arises from the transition from HOMO to LUMO and LUMO+1 (Figure 5). However, the transition from HOMO to LUMO (ICT from 1-azulenyl group to 2-azulenyl moiety) has much more pronounced effect on the absorption band than that from HOMO to LUMO+1 (π-π* transition of the 2-azulenyl moiety). The calculation also suggested the transition from 2-azulenyl group to 1-azulenyl moiety (i.e., HOMO−1 → LUMO),

but the contribution to the absorption band is lower than that from the former two transitions (from HOMO to LUMO and LUMO+1), since the oscillator strength of the transition is rather small. Although the π-π* transition of the 1-azulenyl group itself at λ_{max} = 525 nm is shown by the calculation, this absorption band is probably overlapped with edge of the broad absorption band. Therefore, the results can be concluded that the strong and broad absorption band observed at λ_{max} = 476 nm in the UV/Vis spectrum is ICT from the electron-rich 1-azulenyl group to the electron-deficient 2-azulenyl moiety as illustrated by the resonance structure in Scheme 1.[15]

Table 1. Electronic transitions for **5** and **23** derived from the computed values based on the TD−DFT calculations at the B3LYP/6-31G** level and experimental results.

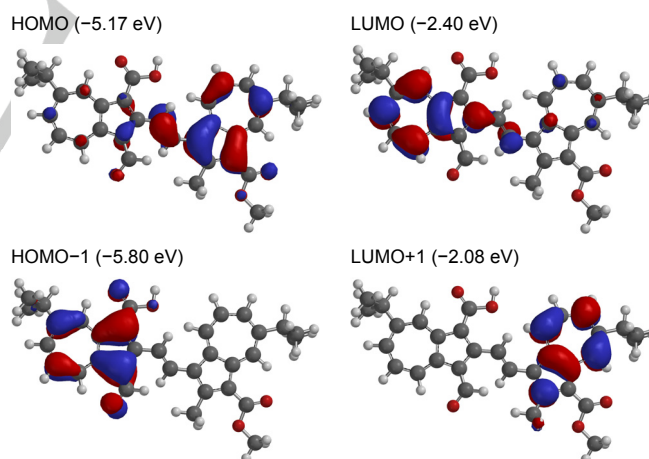| Compound	Experimental	Computed values	
	λ_{max} (log ε)	λ_{max} (strength)	Composition of band[a] (amplitude)
5	489 (2.84)	464 (0.0059)	H → L (0.9665)
23	476 (4.31)	477 (0.0273)	H−1 → L (0.8775)
		493 (0.4873)	H → L (0.9301) H → L+1 (0.2417)
		525 (0.0091)	H → L+1 (0.9345)

[a] H = HOMO; L = LUMO

Figure 5. Frontier Kohn–Sham orbitals of **23** at the B3LYP/6-31G** level.

For the further development of 2-formylazulene synthesis, Vilsmeier formylation was also applied to 1,3-disubstituted azulenes. Although the preparation of 2-formylazulene derivatives by the Vilsmeier formylation of 1,3-dialkylazulenes was previously reported by Hafner and Moritz, yield of the products was relatively low because of the competition of the *ipso*-substitution at the alkyl substituent.[5] We have also tried the formylation of 1,3,6-tri-*tert*-butylazulene by the same method, but 1-formylazulene derivative was exclusively obtained in excellent yield (98%) by the *ipso*-substitution, instead of the

formation of 2-formylazulene derivative.[16] Therefore, methyl and phenyl groups were introduced to the 1,3-positions of azulene ring prior to the Vilsmeier reaction, since the secondary and tertiary alkyl groups could be replaced by the *ipso*-substitution (Scheme 2).

Precursors **24** and **25** were prepared by the reduction of ester function of methyl 3-phenylazulene-1-carboxylate derivatives[17] with DIBAL. Although the transformation from ester to methyl group by DIBAL reduction is usually difficult, compounds **24** and **25** were obtained from the corresponding precursors in excellent yields (**24**: 91%, **25**: 93%). Treatment of **24** with $POCl_3$ in DMF afforded the corresponding 2-formylazulene **26** in 27% yield, along with the recovery of **24** (69%). The reaction showed almost the same yield as that of 1,3-dimethylazulene reported by Hafner *et al*.[5] On the other hand, higher yield of the product **27** (52%) was observed in the Vilsmeier formylation of 6-isopropylazulene derivative **25**. These results suggest that isopropyl group at the 6-position of azulene ring increases the reactivity at the 2-position toward the electrophilic substitution reaction, owing to the electron-donating inductive effect.
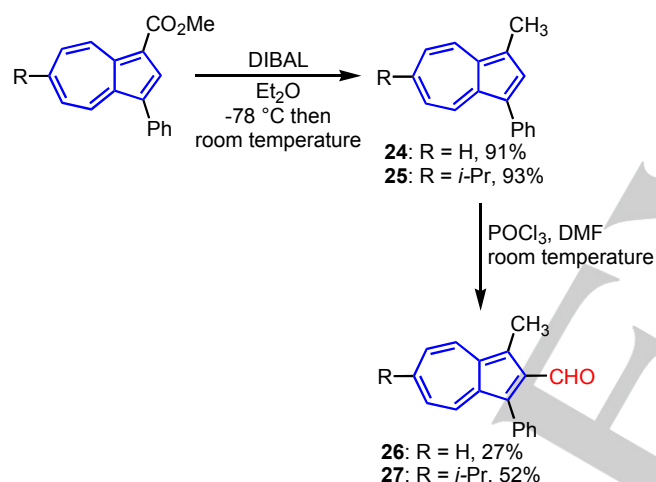
Scheme 2. Synthesis of 2-formylazulenes **26** and **27** by Vilsmeier reaction of **24** and **25**.

Reactivity of 2-formylazulenes: 1-Iodoazulene derivative **21** could not be obtained by the two-step transformation of **10**, but the iodination of **12** and **13** with *N*-iodosuccinimide (NIS) afforded the corresponding 1-iodoazulenes **28** (90%) and **21** (99%) in excellent yields (Scheme 3). To test the reactivity toward the palladium-catalyzed coupling reaction, we have investigated the Suzuki−Miyaura and Sonogashira−Hagihara reactions by using **28** as a substrate. The Sonogashira−Hagihara reaction of **28** with ethynylbenzene in the presence of [Pd(PPh₃)₄] catalyst gave the corresponding 1-ethynylazulene **29** in 92% yield. The Suzuki−Miyaura coupling of **28** with phenylboronic acid in refluxing 1,4-dioxane also afforded the cross-coupled product **30** in 95% yield. Although preparations of 1-arylazulenes by the Suzuki−Miyaura coupling of 1-haloazulenes[18] or 1-azulenyl triflates[19] with arylbronic acids have been represented in the literatures, the reported yields of the products were relatively low. Although the efficient Suzuki−Miyaura coupling at the 1-position of azulene ring was

reported by Oda *et al*, the procedure required expensive and electron-rich phosphine ligands (i.e., BINAP and dppf) for the successful reaction.[20] The high yield of the product **30** was ascribed to the electron-withdrawing group at the 1- and 2-positions of **28**, which should increase the reactivity toward the oxidative addition of the palladium catalyst.
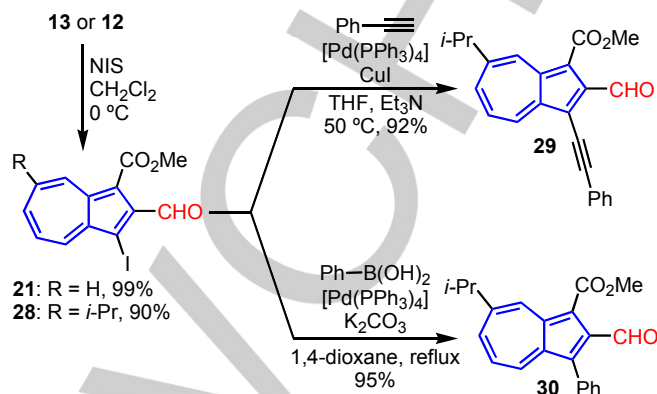
Scheme 3. Cross-coupling reactions of 1-iodoazulenes **21** and **28**.

2-Ethynylazulene derivatives are important building blocks for the construction of the extended π-electron systems. Usually, 2-ethynylazulenes have been prepared by Sonogashira−Hagihara reaction of 2-haloazulenes.[21] However, preparation of the 2-haloazulene precursors is relatively difficult due to the tedious synthetic pathway as mentioned above.[4d] Even though we have previously reported the synthesis of 2-ethynylazulene from 2-formylazulene *via* Corey−Fuchs reaction in moderate yield, the procedure required a four-step synthetic pathway.[4c] In this context development of facile and short step method is indispensable for establishing the practical synthesis of 2-ethynylazulene derivatives.

Seyferth−Gilbert reaction, which is a reaction of α-diazophosphonate with aldehyde, is one of the efficient procedures to transform aldehyde to alkyne derivative in one-step.[22] Since the method requires a strong base, the α-diazophosphonate derivatives such as Ohira−Bestmann reagent, whose reaction proceeds under milder basic conditions, has been developed.[23] In 2008, Taber and co-workers have reported the modified Seyferth−Gilbert reaction with dimethyl 1-diazo-2-oxo-2-phenylethylphosphonate (**31**).[24] The reagent **31** is easy to prepare and has almost same reactivity compared to the Ohira−Bestmann reagent. However, there are no reports of this alkynylation reaction applied to the azulene derivatives, so far, in spite of the much promise of the reagent. For the development of novel synthetic route to 2-ethynylazulene derivatives, we adopted the modified Seyferth−Gilbert reaction to 2-formylazulenes under the similar conditions reported by Taber *et al*.

The yield and structure of 2-ethynylazulene derivatives obtained by the reaction are appeared in Table 3. The yield of 2-ethynylazulene derivatives by the Seyferth−Gilbert reaction of 2-formylazulenes was depended on the substituent on the seven-membered ring. When the reaction was carried out with the substrates having isopropyl group on the seven-membered ring, the reaction afforded the 2-ethynylazulene derivatives **32** (85%) and **37** (80%) in good yields (entries 1 and 6). Meanwhile,

absence of the isopropyl group on the seven-membered ring resulted in low to moderate yields of the products **33−36** (18−58%), due to the competing decomposition reaction (entries 2−5). Alkynes **32−35** were relatively stable under the ambient conditions, but compounds **36** and **37** are readily decomposed even when stored at −30 °C.

Table 3. Modified Seyferth−Gilbert reaction of 2-formylazulenes with **31**.

Entry	Substrate	Product	Yield [%][a]
1	**12**	**32**	85
2	**13**[4d]	**33**	58
3	**18**	**34**	18
4	**22**[25]	**35**	46
5	**26**	**36**	41
6	**27**	**37**	80

[a] Two-step yield from 2-methylazulenes **1−9**.

Presumed reaction mechanism of the Seyferth−Gilbert reaction is illustrated in Scheme 4. In the case of the 2-formylazulene derivatives without isopropyl group, anion intermediate generated from **31** might attack not only the formyl group but also electron-deficient seven-membered ring leading to the decomposition of the substrate (Path B). Whereas, the bulkiness of isopropyl group on 2-formylazulenes **32** and **37** might prevent the nucleophilic attack of the anion to the seven-membered ring resulting to 2-ethynylazulenes in good yields (Path A).
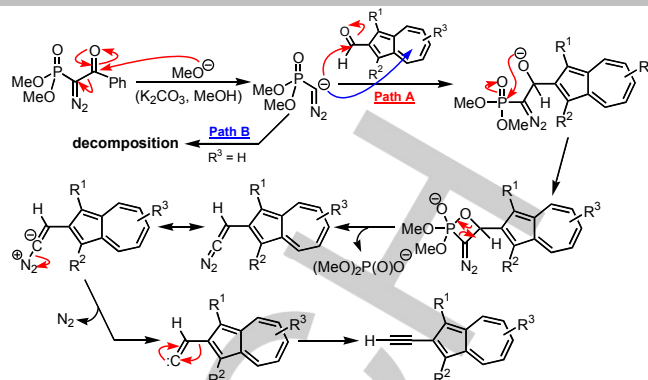
Scheme 4. Presumed reaction mechanism for the Seyferth−Gilbert reaction of 2-formylazulenes.

Conclusions

In conclusion, we have described the novel and effective synthetic procedure of 2-formyl- and 2-ethynylazulene derivatives from 2-methylazulenes, which are readily available by Yasunami−Takase's procedure.

The reaction of 2-methylazulenes with DMFDMA, followed by the oxidative cleavage of intermediately formed enamines with $NaIO_4$ gave 2-formylazulenes in good to excellent yields, except for 2-methylazulene itself, and 1-bromo- and 1-iodoazulene derivatives. As another synthetic method for 2-formylazulenes, Vilsmeier reaction of 1-phenyl-3-methylazulenes was also examined. This study revealed that the isopropyl group at the seven-membered ring increased the reactivity toward the electrophilic reaction at the 2-position. Since the preparation of 2-formylazulene and its derivatives is relatively difficult so far, our methods should become one of the efficient and practical procedures. In order to prepare further functionalized 2-formylazulenes, palladium-catalyzed cross-coupling reaction of **28**, which prepared by the reaction of 2-formylazulene **12** with NIS, was investigated. As a result, both Suzuki−Miyaura and Sonogashira−Hagihara reaction of **28** gave the corresponding cross-coupling products in excellent yields.

Furthermore, 2-formylazulenes could be transformed to 2-ethynylazulenes **32−37** by modified Seyferth−Gilbert reaction with 1-diazo-2-oxo-2-phenylethylphosphonate (**31**). Although the yield of the products depends on the substituent on the azulene ring, this is the first example of the molecular transformation starting from 2-methylazulenes to 2-ethynylazulenes. Since the preparation of 2-formyl- and 2-ethynylazulene derivatives have difficult by the conventional methods, the results described in this paper should become one of the practical and effective methods for the synthesis of these derivatives.

Experimental Section

General: Melting points were determined with a Yanagimoto MPS3 micromelting apparatus. The HRMS data were obtained with a Bruker Daltonics APEX III instrument or a JEOL JMS-700 instrument. The IR and UV/Vis spectra were recorded with JASCO FTIR-4100 and Shimadzu UV-2550 spectrophotometers. The ^1H and ^{13}C NMR spectra were recorded with a JEOL ECA500 spectrometer at 500 and 125 MHz, respectively.

Methyl 3-formyl-7-isopropyl-2-methylazulene-1-carboxylate (5): POCl$_3$ (4.61 g, 30.1 mmol) was added at 0 °C to a solution of **1** (2.44 g, 10.1 mmol) in DMF (100 mL). The resulting mixture was stirred at room temperature for 3 h. The reaction mixture was poured into aq. K$_2$CO$_3$ and extracted with toluene. The organic layer was washed with brine, dried with Na$_2$SO$_4$, and concentrated under reduced pressure. The crude product was purified by recrystallization from CH$_2$Cl$_2$/hexane to give **5** (2.53 g, 93%) as purple crystals. M.p. 149.5−150 °C; IR (ATR): ν$_{max}$= 2960 (w), 2927 (w), 2869 (w), 2731 (w), 1686 (s), 1647 (s), 1601 (w), 1574 (w), 1522 (w), 1506 (w), 1470 (m), 1439 (s), 1407 (w), 1382 (w), 1374 (w), 1342 (w), 1280 (w), 1230 (m), 1200 (m), 1135 (w), 1110 (m), 1090 (m), 1071 (w), 1047 (w), 991 (w), 960 (w), 930 (w), 874 (w), 807 (w), 794 (w), 783 (m), 666 (m) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ$_H$= 10.53 (s, 1H, CHO), 9.73 (d, 1H, J = 1.4 Hz, H$_8$), 9.68 (d, 1H, J = 9.7 Hz, H$_4$), 7.88 (d, 1H, J = 10.3 Hz, H$_6$), 7.75 (t, 1H, J = 10.0 Hz, H$_5$), 4.00 (s, 3H, CO$_2$Me), 3.26 (sept, 1H, J = 6.9 Hz, i-Pr), 3.03 (s, 3H, Me), 1.43 (d, 6H, J = 6.9 Hz, i-Pr) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ$_C$= 186.7, 166.5, 158.7, 154.2, 145.1, 143.5, 139.5, 137.8, 136.1, 132.8, 121.7, 115.8, 51.3, 39.6, 24.7, 14.5 ppm; HRMS (MALDI-TOF): calcd for C$_{17}$H$_{18}$O$_3$+H$^+$ [M + H]$^+$ 271.1329; found: 271.1334.

1,3-diformyl-2-methylazulene (6): POCl$_3$ (4.60 g, 30.0 mmol) was added at 0 °C to a solution of **11** (1.42 g, 10.0 mmol) in DMF (50 mL). The resulting mixture was stirred at 100 °C for 12 h. The reaction mixture was poured into aq. K$_2$CO$_3$ and extracted with AcOEt. The organic layer was washed with brine, dried with Na$_2$SO$_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with toluene/AcOEt (10 : 1) to give **6** (1.76 g, 8.90 mmol, 89%) as red needles. M.p. 194−195 °C; IR (ATR): ν$_{max}$= 2782 (w), 2751 (w), 1632 (s), 1594 (w), 1537 (w), 1508 (m), 1457 (m), 1435 (s), 1399 (m), 1375 (m), 1322 (w), 1292 (m), 1138 (w), 1092 (w), 1035 (w), 978 (s), 917 (m), 873 (w), 744 (s), 707 (w), 681 (w), 654 (s) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ$_H$= 10.53 (s, 2H, CHO), 9.75 (d, 2H, J = 9.8 Hz, H$_{4,8}$), 8.00 (t, 1H, J = 9.8 Hz, H$_6$), 7.87 (t, 2H, J = 9.8 Hz, H$_{5,7}$), 3.06 (s, 3H, Me) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ$_C$= 186.4, 159.8, 144.6, 141.1, 138.4, 134.3, 122.6, 74.2, 11.9 ppm; HRMS (MALDI-TOF): calcd for C$_{13}$H$_{10}$O$_2$+H$^+$ [M + H]$^+$ 199.0754; found: 199.0736.

Methyl 3-chloro-2-methylazulene-1-carboxylate (8): To a solution of **2** (407 mg, 2.03 mmol) in CHCl$_3$ (10 mL) and Et$_3$N (1 mL) was added N-chlorosuccinimide (549 mg, 4.11 mmol) at room temperature. The resulting mixture was stirred at the same temperature for 2 h under an Ar atmosphere. The reaction mixture was poured into a sat.Na$_2$SO$_3$ solution and extracted with CHCl$_3$. The organic layer was washed with brine, dried with Na$_2$SO$_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel with CH$_2$Cl$_2$ to give **8** (399 mg, 84 %) as green solid. m.p. 93−95 °C; IR (AT−R) ν$_{max}$= 2947 (w), 2829 (w), 1678 (s), 1581 (w), 1534 (w), 1497 (w), 1453 (m), 1436 (m), 1410 (s), 1381 (w), 1359 (w), 1289 (w), 1241 (m), 1213 (s), 1149 (w), 1116 (s), 1083 (s), 1071 (s), 1047 (s), 1014 (w), 971 (w), 924 (w), 902 (w), 876 (w), 844 (w), 782 (m), 741 (m), 718 (w), 693 (w), 656 (w) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ$_H$= 9.49 (d, 1H, J = 9.9 Hz, H$_8$), 8.45 (d, 1H, J = 9.9 Hz, H$_4$), 7.74 (t, 1H, J = 9.9 Hz, H$_6$), 7.53-7.45 (m, 2H, H$_{5,7}$), 3.98 (s, 3H, CO$_2$Me), 2.83 (s, 3H, Me) ppm;

^{13}C NMR (125 MHz, CDCl$_3$): δ$_C$= 166.0, 149.4, 139.8, 138.6, 137.0, 136.7, 133.9, 128.2, 127.1, 118.4, 113.6, 51.2, 15.4 ppm; HRMS (EI-MS, positive): calcd for C$_{13}$H$_{11}$ClO$_2$$^+$ [M]$^+$ 234.0443; found: 234.0442.

Methyl 1-bromo-2-methylazulene-3-carboxylate (9): To a solution of **2** (411 mg, 2.05 mmol) in CHCl$_3$ (10 mL) and Et$_3$N (1 mL) was added N-bromosuccinimide (743 mg, 4.17 mmol) at room temperature. The resulting mixture was stirred at the same temperature for 1 h under an Ar atmosphere. The reaction mixture was poured into a sat.Na$_2$SO$_3$ solution and extracted with CHCl$_3$. The organic layer was washed with brine, dried with Na$_2$SO$_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel with CH$_2$Cl$_2$ to give **9** (366 mg, 64%) as green solid. m.p. 92−93 °C; IR (AT−R) ν$_{max}$= 3006 (w), 2957 (w), 2918 (w), 1691 (s), 1593 (w), 1581 (w), 1540 (w), 1499 (w), 1460 (m), 1433 (s), 1411 (m), 1393 (m), 1364 (w), 1297 (w), 1232 (m), 1202 (s), 1076 (s), 1017 (w), 1007 (w), 953 (w), 834 (w), 778 (m), 739 (m), 655 (w) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ$_H$= 9.48 (d, 1H, J = 9.9 Hz, H$_4$), 8.45 (d, 1H, J = 9.9 Hz, H$_8$), 7.75 (t, 1H, J = 9.9 Hz, H$_6$), 7.55-7.49 (m, 2H, H$_{5,7}$), 3.98 (s, 3H, CO$_2$Me), 2.85 (s, 3H, Me) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ$_C$= 166.0, 151.4, 140.9, 138.8, 138.5, 136.5, 135.7, 128.3, 127.4, 114.7, 108.7, 51.2, 17.2 ppm; HRMS (EI-MS, positive): calcd for C$_{13}$H$_{11}$BrO$_2$$^+$ [M]$^+$ 277.9937; found: 277.9934.

Methyl 2-formyl-7-isopropylazulene-1-carboxylate (12): DMFDMA (3.57 g, 30.0 mmol) was added to a solution of **1** (2.43 g, 10.0 mmol) in DMF (7 mL). The resulting mixture was refluxed for 20 h. The reaction mixture was poured into water and extracted with hexane/AcOEt. The organic layer was washed with brine, dried with Na$_2$SO$_4$, and concentrated under reduced pressure to give crude enamine product as dark brown oil. To this crude enamine product (2.83 g) in a mixed solvent of THF (25 mL) and H$_2$O (25 mL) was added sodium periodate (6.12 g, 28.6 mmol) and the mixture was stirred at room temperature for 1 day. After the reaction mixture was filtered, the filtrate was extracted with CH$_2$Cl$_2$. The organic layer was dried over Na$_2$SO$_4$ and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel with CH$_2$Cl$_2$ to give **12** (1.39 g, 54%) as green solid. M.p. 94−95 °C; IR (ATR): ν$_{max}$ = 3104 (w), 2954 (w), 2885 (w), 1678 (s), 1666 (s), 1578 (w), 1468 (m), 1442 (m), 1420 (m), 1389 (w), 1362 (w), 1349 (m), 1332 (w), 1313 (w), 1263 (w), 1230 (s), 1192 (m), 1178 (w), 1143 (w), 1132 (w), 1068 (m), 1050 (w), 1024 (m), 978 (w), 955 (w), 936 (w), 875 (w), 849 (m), 799 (m), 779 (m), 730 (w), 678 (w), 655 (w) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ$_H$ = 10.93 (s, 1H, CHO), 9.86 (d, 1H, J = 1.1 Hz, H$_8$), 8.48 (d, 1H, J = 9.7 Hz, H$_4$), 7.86 (d, 1H, J = 10.3 Hz, H$_6$), 7.67 (s, 1H, H$_3$), 7.45 (t, 1H, J = 9.9 Hz, H$_5$), 4.03 (s, 3H, CO$_2$Me), 3.23 (sept, 1H, J = 6.9 Hz, i-Pr), 1.43 (d, 6H, J = 6.9 Hz, i-Pr) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ$_C$ = 192.7, 165.5, 150.1, 145.1, 142.4, 142.2, 141.6, 141.2, 127.6, 117.4, 114.3, 51.5, 39.3, 24.7 ppm, one signal is overlapped with the other; HRMS (MALDI-TOF): calcd for C$_{16}$H$_{16}$O$_3$ + Ag$^+$ [M + Ag]$^+$ 363.0145; found: 363.0122.

Methyl 2-formylazulene-1-carboxylate (13): DMFDMA (359 mg, 3.01 mmol) was added to a solution of **2** (203 mg, 1.01 mmol) in DMF (2 mL). The resulting mixture was refluxed for 38

h. The reaction mixture was poured into water and extracted with hexane/AcOEt. The organic layer was washed with brine, dried with Na_2SO_4, and concentrated under reduced pressure to give crude enamine product as dark red oil. To this crude enamine product (258 mg) in a mixed solvent of THF (5 mL) and H_2O (5 mL) was added sodium periodate (647 mg, 3.02 mmol) and the mixture was stirred at room temperature for 1 day. After the reaction mixture was filtered, the filtrate was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel with CH_2Cl_2 to give **13** (145 mg, 67%) as green solid. M.p. 110−111 °C (lit. 119−120 °C);[6] ^1H NMR (500 MHz, $CDCl_3$): δ_H = 10.94 (s, 1H, CHO), 9.74 (d, 1H, J = 10.0 Hz, H_8), 8.58 (d, 1H, J = 9.5 Hz, H_4), 7.91 (t, 1H, J = 9.7 Hz, H_6), 7.76 (s, 1H, H_3), 7.59 (t, 1H, J = 10.0 Hz, H_7), 7.49 (t, 1H, J = 9.7 Hz, H_5), 4.03 (s, 3H, CO_2Me) ppm; Data are in agreement with those previously reported in reference 6.

Dimethyl 2-formylazulene-1,3-dicarboxylate (14): DMFDMA (267 mg, 2.24 mmol) was added to a solution of **3** (259 mg, 1.00 mmol) in DMF (1.5 mL). The resulting mixture was refluxed for 4 h. The reaction mixture was poured into water and extracted with hexane/AcOEt. The organic layer was washed with brine, dried with Na_2SO_4, and concentrated under reduced pressure to give crude enamine product as dark red solid. To this crude enamine product (313 mg) in a mixed solvent of THF (5 mL) and H_2O (5 mL) was added sodium periodate (647 mg, 3.02 mmol) and the mixture was stirred at room temperature for 16 h. After the reaction mixture was filtered, the filtrate was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel with CH_2Cl_2 to give **14** (166 mg, 61%) as red solid. M.p. 170−171 °C; (lit. 167−168 °C);[6] IR (ATR): v_{max} = 3004 (w), 2957 (w), 1694 (s), 1537 (w), 1490 (w), 1455 (m), 1442 (s), 1434 (s), 1421 (m), 1395 (m), 1300 (w), 1243 (m), 1209 (s), 1174 (s), 1084 (s), 1065 (m), 1012 (w), 992 (w), 951 (w), 895 (w), 800 (m), 779 (w), 743 (m), 680 (w), 661 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ_H = 10.80 (s, 1H, CHO), 9.76 (d, 2H, J = 10.0 Hz, $H_{4,8}$), 8.07 (t, 1H, J = 9.9 Hz, H_6), 7.83 (t, 2H, J = 10.0 Hz, $H_{5,7}$), 3.95 (s, 6H, CO_2Me) ppm. Data are in agreement with those previously reported in reference 6.

Methyl 2,3-diformylazulene-1-carboxylate (15): DMFDMA (490 mg, 4.11 mmol) was added to a solution of **4** (456 mg, 2.00 mmol) in DMF (4 mL). The resulting mixture was refluxed for 4 h. The reaction mixture was poured into water and extracted with CH_2Cl_2. The organic layer was washed with brine, dried with Na_2SO_4, and concentrated under reduced pressure to give crude enamine product as dark red solid. To this crude enamine product (567 mg) in a mixed solvent of THF (8 mL) and H_2O (8 mL) was added sodium periodate (1.28 g, 6.00 mmol) to and the mixture was stirred at room temperature for 3 h. After the reaction mixture was filtered, the filtrate was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel with toluene/AcOEt (5 : 1) to give **15** (400 mg, 83%) as purple solid. M.p. 163−164 °C; IR (ATR): v_{max} = 2964 (w), 2874 (w), 1701 (m), 1685 (m), 1662 (s), 1579 (w), 1531 (w), 1497 (w), 1457 (s), 1425

(s), 1389 (m), 1317 (w), 1297 (w), 1239 (m), 1212 (s), 1194 (m), 1157 (w), 1119 (s), 1067 (m), 997 (w), 987 (m), 930 (m), 892 (w), 874 (w), 805 (w), 785 (w), 761 (w), 746 (w), 725 (w), 700 (w), 665 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ_H = 10.98 (s, 1H, CHO), 10.55 (s, 1H, CHO), 10.10 (d, 1H, J = 10.0 Hz, H_8), 9.88 (d, 1H, J = 10.0 Hz, H_4), 8.16 (t, 1H, J = 9.7 Hz, H_6), 7.93−7.89 (m, 2H, $H_{5,7}$), 4.05 (s, 3H, CO_2Me) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ_C = 192.9, 189.2, 164.7, 148.7, 144.1, 143.8, 143.7, 142.9, 142.2, 133.5, 132.4, 122.9, 117.4, 52.3 ppm; HRMS (MALDI-TOF): calcd for $C_{14}H_{10}O_4$ + Ag^+ [M + Ag]$^+$ 348.9625; found: 348.9663.

Methyl 2,3-diformyl-7-isopropylazulene-1-carboxylate (16): DMFDMA (1.53 g, 12.8 mmol) was added to a solution of **5** (2.47 g, 9.15 mmol) in DMF (15 mL). The resulting mixture was refluxed for 4 h. The reaction mixture was poured into water and extracted with CH_2Cl_2. The organic layer was washed with brine, dried with Na_2SO_4, and concentrated under reduced pressure to give crude enamine product as dark red solid. To this crude enamine product (2.91 g) in a mixed solvent of THF (22 mL) and H_2O (22 mL) was added sodium periodate (5.77 g, 27.0 mmol) and the mixture was stirred at room temperature for 3 h. After the reaction mixture was filtered, the filtrate was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel with CH_2Cl_2 to give **16** (2.16 g, 85%) as dark purple solid. M.p. 207−208 °C; IR (ATR): v_{max} = 2965 (w), 2872 (w), 1752 (w), 1682 (s), 1650 (s), 1573 (w), 1494 (m), 1465 (m), 1440 (s), 1421 (m), 1404 (m), 1382 (m), 1341 (w), 1316 (w), 1284 (w), 1229 (s), 1211 (m), 1136 (m), 1117 (m), 1093 (m), 1067 (w), 1048 (w), 1005 (m), 984 (m), 933 (m), 893 (w), 818 (m), 782 (m), 730 (w), 695 (w), 662 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ_H = 10.95 (s, 1H, CHO), 10.49 (s, 1H, CHO), 9.99−9.96 (m, 2H, $H_{4,8}$), 8.10 (d, 1H, J = 10.2 Hz, H_6), 7.86 (t, 1H, J = 10.2 Hz, H_5), 4.04 (s, 3H, CO_2Me), 3.32 (sept, 1H, J = 6.9 Hz, i-Pr), 1.46 (d, 6H, J = 6.9 Hz, i-Pr) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ_C = 193.1, 188.9, 164.9, 154.7, 149.0, 143.8, 143.5, 142.3, 142.2, 142.0, 133.3, 122.1, 116.2, 52.1, 39.5, 24.6 ppm; HRMS (MALDI-TOF): calcd for $C_{17}H_{16}O_4$ + Ag^+ [M + Ag]$^+$ 391.0094; found: 391.0093.

Enamine intermediate: M.p. 91−93 °C; IR (ATR): v_{max} = 2963 (w), 1673 (m), 1624 (s), 1610 (s), 1599 (s), 1566 (m), 1516 (w), 1500 (w), 1463 (s), 1444 (s), 1426 (s), 1417 (s), 1389 (s), 1366 (m), 1339 (w), 1293 (m), 1272 (m), 1233 (w), 1220 (w), 1198 (m), 1134 (s), 1113 (s), 1102 (s), 1080 (m), 1030 (w), 999 (w), 978 (m), 957 (w), 920 (w), 895 (w), 882 (w), 852 (m), 826 (m), 806 (m), 794 (m), 781 (w), 734 (w), 689 (w), 673 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ_H = 10.05 (s, 1H, CHO), 9.39 (dd, 1H, J = 11.0, 3.5 Hz, H_8), 9.33 (s, 1H, H_4), 7.56−7.54 (m, 2H, $H_{6,7}$), 6.91 (d, 1H, J = 13.1 Hz, CH=CH), 6.41 (d, 1H, J = 13.1 Hz, CH=CH), 3.98 (s, 3H, CO_2Me), 3.15 (sept, 1H, J = 6.9 Hz, i-Pr), 3.05 (s, 6H, NMe_2), 1.38 (d, 6H, J = 6.9 Hz, i-Pr) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ_C = 187.44, 167.02, 158.41, 153.90, 152.42, 146.55, 145.40, 136.05, 134.23, 132.91, 132.30, 119.24, 112.12, 92.52, 51.01, 40.97, 39.51, 24.55 ppm; HRMS (EI-MS, positive): calcd for $C_{20}H_{23}NO_3^+$ [M]$^+$ 325.1673; found: 325.1680.

1,2,3-Triformylazulene (17): DMFDMA (1.07 g, 8.96 mmol) was added to a solution of **6** (833 mg, 4.20 mmol) in DMF (6 mL). The resulting mixture was refluxed for 4 h. The reaction mixture

was poured into water and extracted with CH_2Cl_2. The organic layer was washed with brine, dried with Na_2SO_4, and concentrated under reduced pressure to give crude enamine product as brown solid. To this crude enamine product (1.06 g) in a mixed solvent of THF (12 mL) and H_2O (12 mL) was added sodium periodate (2.70 g, 12.6 mmol) and the mixture was stirred at room temperature for 3 h. After the reaction mixture was filtered, the filtrate was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel with CH_2Cl_2/AcOEt (50 : 1) to give **17** (712 mg, 80%) as reddish purple solid. M.p. 242−243 °C (lit. 242−243 °C);[6] ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 11.22 (s, 1H, CHO), 10.84 (s, 2H, CHO), 10.00 (d, 2H, J = 9.7 Hz, H$_{4,8}$), 8.25 (t, 1H, J = 9.7 Hz, H$_6$), 8.01 (t, 2H, J = 9.9 Hz, H$_{5,7}$) ppm; Data are in agreement with those previously reported in reference 6.

Methyl 3-fluoro-2-formylazulene-1-carboxylate (18): DMFDMA (515 mg, 4.32 mmol) was added to a solution of **7** (471 mg, 2.16 mmol) in DMF (3 mL). The resulting mixture was refluxed for 3 h. The reaction mixture was poured into water and extracted with CH_2Cl_2. The organic layer was washed with brine, dried with Na_2SO_4, and concentrated under reduced pressure to give crude enamine product as brown solid. To this crude enamine product (590 mg) in a mixed solvent of THF (8 mL) and H_2O (8 mL) was added sodium periodate (1.39 g, 6.50 mmol) and the mixture was stirred at room temperature for 3 h. After the reaction mixture was filtered, the filtrate was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel with CH_2Cl_2 to give **18** (454 mg, 90%) as green solid. M.p. 136−137 °C; IR (ATR): v_{max} = 2965 (w), 2892 (w), 1682 (s), 1577 (w), 1513 (w), 1472 (w), 1438 (s), 1421 (m), 1409 (w), 1400 (m), 1381 (w), 1315 (w), 1298 (w), 1236 (w), 1202 (s), 1181 (m), 1138 (s), 1044 (m), 1017 (w), 1006 (w), 963 (m), 899 (m), 876 (m), 800 (w), 777 (s), 768 (m), 740 (m), 679 (w), 655 (w) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 10.83 (s, 1H, CHO), 9.67 (dd, 1H, J = 10.0, 2.0 Hz, H$_4$), 8.60 (d, 1H, J = 10.0 Hz, H$_8$), 7.90 (t, 1H, J = 10.0 Hz, H$_6$), 7.50 (t, 1H, J = 10.0 Hz, H$_5$), 7.42 (t, 1H, J = 10.0 Hz, H$_7$), 4.02 (s, 3H, CO$_2$Me) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ_C = 190.3, 165.0, 150.6, 148.4, 144.0, 143.3, 138.0, 134.0, 128.4, 127.3, 127.2, 126.9, 110.0, 51.9 ppm; HRMS (MALDI-TOF): calcd for $C_{13}H_9FO_3 + Ag^+$ [M + Ag]$^+$ 338.9581; found: 338.9594.

Methyl 3-chloro-2-formylazulene-1-carboxylate (19): DMFDMA (413 mg, 3.46 mmol) was added to a solution of **8** (412 mg, 1.75 mmol) in DMF (10 mL). The resulting mixture was refluxed for 3 h. The reaction mixture was poured into water and extracted with AcOEt. The organic layer was washed with brine, dried with Na_2SO_4, and concentrated under reduced pressure to give crude enamine product as brown oil. To this crude enamine product (485 mg) in a mixed solvent of THF (10 mL) and H_2O (10 mL) was added sodium periodate (752 mg, 3.51 mmol) and the mixture was stirred at room temperature for 1 day. After the reaction mixture was filtered, the filtrate was extracted with AcOEt. The organic layer was dried over Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel with hexane/AcOEt (4 : 1) to give **19** (270 mg, 62%) as green solid. M.p. 156−158 °C; IR (ATR): v_{max} = 2958 (w), 1691 (s), 1582 (w),

1541 (w), 1500 (w), 1460 (m), 1433 (s), 1411 (m), 1393 (m), 1365 (m), 1297 (w), 1232 (m), 1202 (s), 1076 (s), 1007 (w), 953 (w), 894 (w), 834 (w), 779 (m), 739 (m), 697 (w), 686 (w), 674 (w), 656 (w) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 10.83 (s, 1H, CHO), 9.64 (d, 1H, J = 10.0 Hz, H$_8$), 8.74 (s, 1H, J = 10.0 Hz, H$_4$), 7.95 (t, 1H, J = 10.0 Hz, H$_6$), 7.61−7.55 (m, 2H, H$_{5,7}$), 4.01 (s, 3H, CO$_2$Me) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ_C = 190.9, 164.6, 143.4, 142.1, 140.0, 139.3, 139.2, 138.0, 129.2, 128.0, 117.3, 114.6, 52.0, ppm; HRMS (EI-MS, positive): calcd for $C_{13}H_9ClO_3^+$ [M]$^+$ 248.0235; found: 248.0242.

Methyl 3-bromo-2-formylazulene-1-carboxylate (20): DMFDMA (161 mg, 1.35 mmol) was added to a solution of **9** (188 mg, 0.673 mmol) in DMF (5 mL). The resulting mixture was refluxed for 3 h. The reaction mixture was poured into water and extracted with AcOEt. The organic layer was washed with brine, dried with Na_2SO_4, and concentrated under reduced pressure to give crude enamine product as brown oil. To this crude enamine product (153 mg) in a mixed solvent of THF (5 mL) and H_2O (5 mL) was added sodium periodate (287 mg, 1.34 mmol) and the mixture was stirred at room temperature for 1 day. After the reaction mixture was filtered, the filtrate was extracted with AcOEt. The organic layer was dried over Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel with hexane/AcOEt (4 : 1) to give **20** (50 mg, 25%) as green solid. M.p. 145−146 °C; IR (ATR): v_{max} = 2954 (w), 2886 (w), 1698 (s), 1684 (s), 1578 (w), 1532 (w), 1455 (m), 1429 (m), 1414 (m), 1379 (w), 1339 (w), 1293 (m), 1230 (w), 1193 (s), 1070 (s), 1050 (s), 1002 (w), 990 (w), 965 (w), 951 (w), 894 (w), 861 (w), 823 (w), 796 (w), 770 (m), 736 (m), 709 (w) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 10.76 (s, 1H, CHO), 9.60 (d, 1H, J = 10.0 Hz, H$_8$), 8.72 (d, 1H, J = 10.0 Hz, H$_8$), 7.94 (t, 1H, J = 10.0 Hz, H$_6$), 7.61 (d, 1H, J = 10.0 Hz, H$_7$), 7.59 (d, 1H, J = 10.0 Hz, H$_5$), 4.00 (s, 3H, CO$_2$Me) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ_C = 191.2, 164.6, 143.1, 141.7, 141.5, 140.3, 139.7, 129.3, 128.3, 115.9, 104.9, 52.0, ppm; HRMS (EI-MS, positive): calcd for $C_{13}H_9BrO_3^+$ [M]$^+$ 291.9730; found: 291.9729.

***trans*-1-(2-Methyl-3-methoxycarbonyl-5-isopropylazulen-1-yl)-2-(1-carboxy-3-formyl-7-isopropylazulen-2-yl)ethylene (23):** To a solution of **5** (811 mg, 3.00 mmol) in MeOH (30 mL) was added Na (367 mg, 15.5 mmol). The resulting mixture was refluxed for 18 h under an Ar atmosphere. The reaction mixture was poured into water and neutralized with HCl. The precipitate was collected by filtration to give **23** (544 mg, 70%) as brown crystals. M.p. 206−208 °C; IR (ATR): v_{max} = 2956 (w), 2865 (w), 1680 (m), 1639 (s), 1611 (m), 1575 (w), 1520 (w), 1437 (s), 1395 (m), 1380 (m), 1364 (w), 1303 (w), 1263 (w), 1238 (m), 1221 (s), 1191 (m), 1143 (w), 1105 (m), 1069 (w), 995 (w), 977 (w), 966 (w), 935 (w), 880 (w), 864 (w), 846 (w), 799 (m), 782 (m), 735 (w), 690 (w), 667 (w) cm^{-1}; UV/Vis (CH$_2$Cl$_2$): λ_{max} (log ε) = 244 (4.57), 295 sh (4.67), 311 (4.73), 373 (4.43), 385 sh (4.38), 476 (4.31) nm; ^{1}H NMR (500 MHz, CD$_2$Cl$_2$): δ_H = 10.48 (s, 1H, CHO), 9.84 (m, 2H, H$_{4',8'}$), 9.51 (s, 1H, H$_4$), 8.76 (d, 1H, J = 9.7 Hz, H$_8$), 8.01 (d, 1H, J = 16.6 Hz, CH=CH), 7.94 (d, 1H, J = 10.3 Hz, H$_{6'}$), 7.83 (t, 1H, J = 10.2 Hz, H$_{5'}$), 7.55 (d, 1H, J = 10.0 Hz, H$_6$), 7.42 (t, 1H, J = 9.9 Hz, H$_7$), 7.35 (d, 1H, J = 16.6 Hz, CH=CH), 3.94 (s, 3H, CO$_2$Me), 3.29 (sept, 1H, J = 6.9 Hz, i-Pr), 3.12 (sept, 1H, J = 6.9 Hz, i-Pr), 2.94 (s, 3H, Me), 1.42 (d, 6H, J = 6.9 Hz, i-Pr), 1.35 (d, 6H, J = 6.9 Hz, i-Pr) ppm, proton signal

of CO$_2$H could not be observed due to the broadening of the signal; ^{13}C NMR (125 MHz, CD$_2$Cl$_2$): δ$_C$ = 188.3, 169.8, 166.5, 158.2, 154.9, 152.4, 149.9, 145.6, 144.1, 142.4, 140.1, 140.0, 138.5, 137.5, 136.9, 136.2, 134.5, 133.4, 133.1, 127.8, 125.2, 124.7, 121.6, 115.4, 112.8, 50.9, 39.6, 39.2, 24.38, 24.36, 16.2 ppm; HRMS (FAB-MS, positive): calcd for C$_{33}$H$_{32}$O$_5^+$ [M]$^+$ 508.2245; found: 508.2249.

1-Methyl-3-phenylazulene (24): To a solution of methyl 3-phenylazulene-1-carboxylate (1.95 g, 7.43 mmol) in Et$_2$O (20 mL) was added 1 M DIBAL (45 mL) at −78 °C under an Ar atmosphere. The resulting mixture was stirred at room temperature for 14 h. The reaction mixture was poured into water and extracted with hexane. The organic layer was washed with brine, dried with Na$_2$SO$_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with hexane to give **24** (1.48 g, 91%) as blue oil. IR (ATR): ν$_{max}$ = 3023 (w), 2918 (w), 1618 (w), 1597 (w), 1569 (m), 1533 (w), 1496 (m), 1433 (m), 1410 (w), 1364 (m), 1311 (w), 1205 (w), 1155 (w), 1069 (m), 1026 (m), 942 (m), 912 (m), 869 (s), 835 (m), 800 (m), 765 (s), 737 (s), 700 (s), 668 (s) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ$_H$ = 8.46 (d, 1H, J = 9.7 Hz, H$_4$), 8.25 (d, 1H, J = 9.7 Hz, H$_8$), 7.88 (s, 1H, H$_2$), 7.62 (d, 2H, J = 7.7 Hz, o-Ph), 7.55-7.49 (m, 3H, H$_6$ and m-Ph), 7.36 (t, 1H, J = 7.4 Hz, p-Ph), 7.09−7.01 (m, 2H, H$_{5,7}$), 2.73 (s, 3H, Me) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ$_C$ = 138.2, 138.1, 137.9, 137.5, 135.4, 135.2, 134.2, 129.8, 129.7, 128.6, 126.2, 125.4, 122.5, 121.5, 12.7 ppm; HRMS (EI-MS, positive): calcd for C$_{17}$H$_{14}^+$ [M]$^+$ 218.1091; found: 218.1094.

6-Isopropyl-1-methyl-3-phenylazulene (25): To a solution of methyl 6-isopropyl-3-phenylazulene-1-carboxylate (2.18 g, 7.18 mmol) in Et$_2$O (20 mL) was added 1.00 M DIBAL (45 mL) at −78 °C under an Ar atmosphere. The resulting mixture was stirred at room temperature for 12 h. The reaction mixture was poured into water and extracted with hexane. The organic layer was washed with brine, dried with Na$_2$SO$_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with hexane to give **25** (1.74 g, 93%) as blue oil. IR (ATR): ν$_{max}$ = 2960 (w), 2926 (w), 2870 (w), 1597 (w), 1577 (s), 1496 (w), 1462 (w), 1437 (w), 1379 (w), 1363 (w), 1325 (w), 1239 (w), 1206 (w), 1156 (w), 1071 (w), 1040 (m), 957 (w), 913 (w), 865 (m), 830 (s), 764 (s), 699 (s), 676 (m), 665 (w), 656 (w) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ$_H$ = 8.48 (d, 1H, J = 10.0 Hz, H$_4$), 8.24 (d, 1H, J = 10.0 Hz, H$_8$), 7.85 (s, 1H, H$_2$), 7.69 (d, 2H, J = 7.4 Hz, o-Ph), 7.55 (t, 2H, J = 7.4 Hz, m-Ph), 7.40 (t, 1H, J = 7.4 Hz, p-Ph), 7.05 (m, 2H, H$_{5,7}$), 3.07 (sept, 1H, J = 6.9 Hz, i-Pr), 2.76 (s, 3H, Me), 1.41 (d, 6H, J = 6.9 Hz, i-Pr) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ$_C$ = 160.1, 137.7, 137.0, 136.7, 134.9, 133.9, 129.7, 129.5, 128.6, 126.0, 125.3, 121.7, 120.6, 39.7, 24.3, 12.6 ppm; HRMS (EI-MS, positive): calcd for C$_{20}$H$_{20}^+$ [M]$^+$ 260.1560; found: 260.1568.

2-Formyl-1-methyl-3-phenylazulene (26): POCl$_3$ (920 mg, 6.00 mmol) was added at 0 °C to a solution of **24** (437 mg, 2.00 mmol) in DMF (10 mL). The resulting mixture was stirred at room temperature for 12 h. The reaction mixture was poured into K$_2$CO$_3$ aq. and extracted with hexane/AcOEt. The organic layer was washed with brine, dried with Na$_2$SO$_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with hexane/AcOEt (4 : 1) to give

26 (133 mg, 27%) as green solid. M.p. 131−132 °C; IR (ATR): ν$_{max}$ = 2833 (w), 2736 (w), 1666 (s), 1599 (w), 1569 (m), 1479 (w), 1450 (m), 1429 (m), 1378 (m), 1293 (w), 1229 (w), 1179 (w), 1147 (m), 1101 (m), 1075 (w), 1041 (w), 1001 (m), 950 (w), 920 (w), 890 (m), 854 (w), 826 (m), 789 (m), 747 (s), 733 (s), 718 (s), 701 (s), 669 (m), 653 (m) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ$_H$ = 10.41 (s, 1H, CHO), 8.43 (d, 1H, J = 10.0 Hz, H$_4$), 8.26 (d, 1H, J = 9.5 Hz, H$_8$), 7.57 (t, 1H, J = 9.7 Hz, H$_6$), 7.51 (t, 2H, J = 7.4 Hz, o-Ph), 7.43−7.46 (m, 3H, m,p-Ph), 7.06 (t, 1H, J = 9.7 Hz, H$_7$), 6.98 (t, 1H, J = 9.7 Hz, H$_5$), 2.90 (s, 3H, Me) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ$_C$ = 193.0, 142.0, 140.3, 139.4, 137.9, 137.6, 136.9, 134.5, 134.2, 132.0, 128.4, 127.4, 126.5, 123.6, 122.7, 11.6 ppm; HRMS (MALDI-TOF): calcd for C$_{18}$H$_{14}$O$^+$ [M]$^+$ 246.1039; found: 246.1045; HRMS (MALDI-TOF): calcd for C$_{18}$H$_{14}$O + Ag$^+$ [M + Ag]$^+$ 353.0090; found: 353.0115. Structure of **26** was also determined by single crystal X-ray analysis (Figure 6).
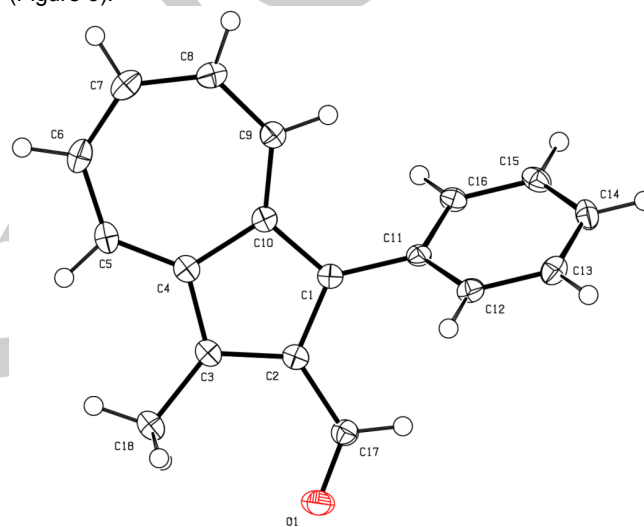

Figure 6. ORTEP Drawing of **26**; Ellipsoids are drawn at 50% probability. [14]

2-Formyl-6-isopropyl-1-methyl-3-phenylazulene (27): POCl$_3$ (1.03 g, 6.72 mmol) was added at 0 °C to a solution of **25** (583 mg, 2.24 mmol) in DMF (15 mL). The resulting mixture was stirred at room temperature for 12 h. The reaction mixture was poured into K$_2$CO$_3$ aq. and extracted with hexane/AcOEt. The organic layer was washed with brine, dried with Na$_2$SO$_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with hexane/AcOEt (4 : 1) to give **27** (335 mg, 52%) as green solid. M.p. 84−86 °C; IR (ATR): ν$_{max}$ = 2967 (w), 2926 (w), 2737 (w), 1670 (s), 1577 (s), 1482 (w), 1446 (m), 1429 (m), 1389 (w), 1378 (w), 1329 (w), 1246 (m), 1179 (w), 1131 (w), 1110 (w), 1074 (w), 1040 (w), 1029 (w), 923 (w), 885 (w), 862 (w), 837 (s), 793 (w), 751 (m), 723 (m), 703 (m), 686 (w), 670 (w), 656 (w) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ$_H$ = 10.38 (s, 1H, CHO), 8.37 (d, 1H, J = 10.3 Hz, H$_4$), 8.21 (d, 1H, J = 10.3 Hz, H$_8$), 7.49−7.52 (t, 2H, J = 7.4 Hz, o-Ph), 7.45−7.41 (m, 3H, m,p-Ph), 7.02 (d, 1H, J = 10.3 Hz, H$_5$), 6.93 (d, 1H, J = 10.0 Hz, H$_7$), 3.00 (sept, 1H, J = 6.9 Hz, i-Pr), 2.88 (s, 3H, Me), 1.33 (d, 6H, J = 6.9 Hz, i-Pr) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ$_C$ = 192.9, 165.1, 140.0, 139.1, 137.0, 136.2, 135.6, 134.5, 134.4, 132.0, 128.3, 127.3, 126.5, 122.7, 122.2, 40.0, 24.0, 11.6 ppm; HRMS (MALDI-TOF): calcd for C$_{21}$H$_{20}$O$^+$

[M]$^+$ 288.1509; found: 288.1516; HRMS (MALDI-TOF): calcd for C$_{21}$H$_{20}$O + Ag$^+$ [M + Ag]$^+$ 395.0560; found: 395.0538.

Methyl 2-formyl-3-iodoazulene-1-carboxylate (21): To a solution of **13** (100 mg, 0.467 mmol) in CH$_2$Cl$_2$ (5 mL) was added *N*-iodosuccinimide (316 mg, 1.41 mmol) at room temperature. The resulting mixture was stirred at room temperature for 18 h under an Ar atmosphere. After the solvent was removed under reduced pressure, the crude product was purified by silica gel column chromatography with CH$_2$Cl$_2$ to give **21** (156 mg, 98%) as green solid. M.p. 145−146 °C; IR (ATR): v_{max} = 2947 (w), 2885 (w), 1686 (s), 1577 (w), 1533 (w), 1455 (m), 1438 (m), 1409 (m), 1379 (w), 1328 (m), 1298 (w), 1289 (w), 1230 (m), 1200 (s), 1154 (w), 1064 (m), 1046 (m), 1003 (w), 982 (w), 951 (w), 893 (m), 862 (w), 816 (w), 794 (w), 769 (m), 735 (m), 712 (w), 695 (w), 678 (w) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 10.74 (s, 1H, CHO), 9.62 (d, 1H, J = 10.0 Hz, H$_8$), 8.73 (d, 1H, J = 10.0 Hz, H$_4$), 7.96 (t, 1H, J = 10.0 Hz, H$_6$), 7.65 (t, 2H, J = 10.0 Hz, H$_{5,7}$), 4.02 (s, 3H, CO$_2$Me) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ_C = 192.0, 164.6, 145.1, 144.8, 143.2, 142.7, 142.0, 141.2, 129.5, 128.6, 118.2, 76.5, 52.0 ppm; HRMS (EI-MS, positive): calcd for C$_{13}$H$_9$IO$_3$$^+$ [M]$^+$ 339.9591; found: 339.9606.

Methyl 2-formyl-3-iodo-7-isopropylazulene-1-carboxylate (28): To a solution of **12** (256 mg, 1.00 mmol) in CH$_2$Cl$_2$ (7 mL) was added *N*-iodosuccinimide (451 mg, 2.00 mmol) at room temperature. The resulting mixture was stirred at room temperature for 2 h under an Ar atmosphere. After the solvent was removed under reduced pressure, the crude product was purified by silica gel column chromatography with toluene/AcOEt (50 : 1) to give **28** (342 mg, 90%) as green solid. M.p. 133−135 °C; IR (ATR): v_{max} = 2948 (w), 2889 (w), 1686 (s), 1672 (s), 1577 (w), 1520 (w), 1446 (m), 1414 (m), 1397 (w), 1376 (w), 1335 (w), 1303 (w), 1279 (w), 1222 (s), 1198 (m), 1171 (w), 1125 (w), 1069 (m), 1015 (m), 975 (m), 930 (w), 890 (w), 824 (m), 806 (m), 772 (m), 745 (w), 685 (w), 675 (w), 667 (w), 657 (w) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 10.73 (s, 1H, CHO), 9.74 (s, 1H, H$_8$), 8.62 (d, 1H, J = 10.0 Hz, H$_4$), 7.92 (d, 1H, J = 10.0 Hz, H$_6$), 7.62 (t, 1H, J = 10.0 Hz, H$_5$), 4.01 (s, 3H, CO$_2$Me), 3.24 (sept, 1H, J = 6.9 Hz, *i*-Pr), 1.43 (d, 6H, J = 6.9 Hz, *i*-Pr) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ_C = 192.3, 164.7, 151.1, 145.0, 143.3, 143.2, 142.13, 142.05, 140.8, 128.4, 116.8, 74.8, 51.9, 39.3, 24.6 ppm; HRMS (MALDI-TOF): calcd for C$_{16}$H$_{15}$IO$_3$ + Ag$^+$ [M + Ag]$^+$ 488.9111; found: 488.9118.

Methyl 2-formyl-7-isopropyl-3-phenylethynylazulene-1-carboxylate (29): To a degassed solution of **21** (336 mg, 0.880 mmol), ethynylbenzene (182 mg, 1.78 mmol), and CuI (20 mg, 0.11 mmol) in THF (5 mL) and triethylamine (5 mL) was added tetrakis(triphenylphosphine)palladium(0) (36 mg, 0.031 mmol). The resulting mixture was stirred at 50 °C for 2 h under an Ar atmosphere. The reaction mixture was poured into a 10% NH$_4$Cl solution and extracted with AcOEt. The organic layer was washed with brine, dried over Na$_2$SO$_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with toluene/AcOEt (50 : 1) to give **29** (288 mg, 92%) as green solid. M.p. 133−133.5 °C; IR (ATR): v_{max} = 2954 (w), 2897 (w), 2197 (w), 1683 (s), 1597 (w), 1578 (w), 1481 (m), 1446 (m), 1401 (w), 1377 (w), 1362 (w), 1337 (w), 1306 (w), 1272 (w), 1241 (m), 1216 (s), 1195 (m), 1108 (m), 1048 (m), 1027 (w), 1003 (w), 962 (w), 933 (w), 873 (w), 833 (w),

804 (m), 762 (m), 695 (m), 668 (w), 656 (w) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 10.92 (s, 1H, CHO), 9.76 (s, 1H, H$_4$), 8.84 (d, 1H, J = 10.0 Hz, H$_8$), 7.90 (d, 1H, J = 10.0 Hz, H$_6$), 7.67 (d, 2H, J = 7.2 Hz, *o*-Ph), 7.56 (t, 1H, J = 10.0 Hz, H$_7$), 7.36 (m, 3H, *m,p*-Ph), 4.03 (s, 3H, CO$_2$Me), 3.23 (sept, 1H, J = 6.9 Hz, *i*-Pr), 1.43 (d, 6H, J = 6.9 Hz, *i*-Pr) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ_C = 191.3, 165.2, 151.5, 144.8, 143.9, 142.6, 141.7, 141.3, 140.2, 131.8, 128.4, 128.3, 123.7, 114.7, 110.1, 96.6, 83.7, 51.8, 39.4, 24.6 ppm, one signal is overlapped with the other; HRMS (MALDI-TOF): calcd for C$_{24}$H$_{20}$O$_3$ + Ag$^+$ [M + Ag]$^+$ 463.0458; found: 463.0469.

Methyl 2-formyl-7-isopropyl-3-phenylazulene-1-carboxylate (30): To a solution of **21** (192 mg, 0.502 mmol), phenylboronic acid (122 mg, 1.00 mmol), and K$_2$CO$_3$ (211 mg, 1.53 mmol) in 1,4-dioxane (5 mL) and H$_2$O (0.5 mL) was added tetrakis(triphenylphosphine)palladium(0) (32 mg, 0.0277 mmol). The resulting mixture was refluxed for 19 h under an Ar atmosphere. The reaction mixture was poured into water and extracted with AcOEt. The organic layer was washed with brine, dried with Na$_2$SO$_4$, and concentrated under reduced pressure. The residue was purified by recrystallization from CH$_2$Cl$_2$/MeOH to give **30** (159 mg, 95%) as green needles. M.p. 107−108 °C; IR (ATR): v_{max} = 2962 (w), 2947 (w), 2871 (w), 1684 (s), 1598 (w), 1577 (w), 1507 (w), 1442 (s), 1401 (w), 1378 (w), 1362 (w), 1309 (w), 1282 (w), 1227 (m), 1188 (m), 1171 (s), 1131 (w), 1119 (w), 1073 (m), 1056 (m), 1036 (w), 1024 (w), 1001 (w), 989 (m), 963 (w), 947 (w), 883 (w), 847 (w), 810 (m), 776 (m), 755 (m), 744 (m), 700 (s), 679 (w), 663 (w) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 10.78 (s, 1H, CHO), 9.76 (d, 1H, J = 1.4 Hz, H$_8$), 8.33 (d, 1H, J = 10.0 Hz, H$_4$), 7.83 (d, 1H, J = 10.0 Hz, H$_6$), 7.48 (t, 2H, J = 7.3 Hz, *o*-Ph), 7.36−7.43 (m, 4H, H$_5$ and *m,p*-Ph), 4.03 (s, 3H, CO$_2$Me), 3.24 (sept, 1H, J = 6.9 Hz, *i*-Pr), 1.44 (d, 6H, J = 6.9 Hz, *i*-Pr) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ_C = 193.0, 165.8, 149.8, 143.1, 141.5, 141.3, 140.7, 140.6, 139.7, 134.3, 131.4, 131.0, 128.2, 127.52, 127.50, 113.8, 51.8, 39.2, 24.7 ppm; HRMS (MALDI-TOF): calcd for C$_{22}$H$_{20}$O$_3$ + Ag$^+$ [M + Ag]$^+$ 439.0458; found: 439.0452. Structure of **30** was also determined by single crystal X-ray analysis (Figure 7).
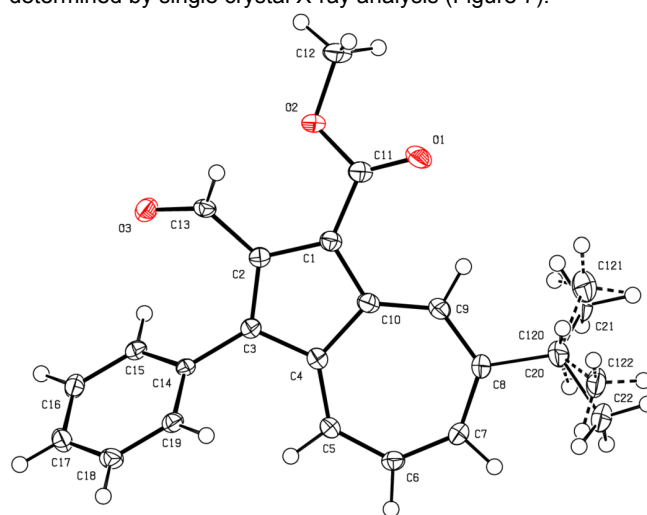

Figure 7. ORTEP Drawing of **30**; Ellipsoids are drawn at 50% probability. [14]

Methyl 2-ethynyl-7-isopropylazulene-1-carboxylate (32): To a solution of **12** (128 mg, 0.500 mmol) and K_2CO_3 (217 mg, 1.57 mmol) in MeOH (5 mL) was added **31** (165 mg, 0.650 mmol). The resulting mixture was stirred at room temperature for 1.5 h under an Ar atmosphere. The reaction mixture was poured into water and extracted with AcOEt. The organic layer was washed with brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with toluene to give **32** (109 mg, 85%) as purple oil. IR (ATR): v_{max} = 2960 (w), 2100 (w), 1683 (s), 1577 (w), 1523 (w), 1466 (m), 1446 (s), 1418 (s), 1380 (m), 1364 (w), 1341 (m), 1303 (w), 1222 (s), 1199 (m), 1181 (m), 1129 (w), 1062 (s), 1030 (m), 1010 (w), 957 (w), 936 (w), 881 (w), 821 (m), 777 (m), 696 (w), 668 (m) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 9.68 (s, 1H, H$_8$), 8.25 (d, 1H, J = 9.7 Hz, H$_4$), 7.72 (d, 1H, J = 10.0 Hz, H$_6$), 7.42−7.37 (m, 2H, H$_{3,5}$), 4.00 (s, 3H, CO$_2$Me), 3.72 (s, 1H, C≡CH), 3.21 (sept, 1H, J = 6.9 Hz, i-Pr), 1.41 (d, 6H, J = 6.9 Hz, i-Pr) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ_C = 165.5, 149.8, 142.8, 141.1, 138.9, 138.4, 136.7, 131.4, 127.4, 122.6, 116.3, 86.5, 81.5, 51.1, 39.4, 24.7 ppm; HRMS (MALDI-TOF): calcd for $C_{17}H_{16}O_2$ + H$^+$ [M + H]$^+$ 253.1223; found: 253.1225.

Methyl 2-ethynylazulene-1-carboxylate (33): To a solution of **13** (100 mg, 0.467 mmol) and K_2CO_3 (211 mg, 1.53 mmol) in MeOH (5 mL) was added **31** (156 mg, 0.614 mmol). The resulting mixture was stirred at room temperature for 4 h under an Ar atmosphere. The reaction mixture was poured into water and extracted with AcOEt. The organic layer was washed with brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with toluene to give **33** (57 mg, 58%) as purple solid. M.p. 99−99.5 °C (lit. 98.5−99.0 °C);[4d] ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 9.56 (d, 1H, J = 10.0 Hz, H$_8$), 8.36 (d, 1H, J = 10.0 Hz, H$_4$), 7.77 (t, 1H, J = 10.0 Hz, H$_6$), 7.56 (t, 1H, J = 10.0 Hz, H$_7$), 7.45 (m, 2H, H$_{3,5}$), 4.00 (s, 3H, CO$_2$Me), 3.74 (s, 1H, C≡CH) ppm; Data are in agreement with those previously reported in reference 4d.

Methyl 2-ethynyl-3-fluoroazulene-1-carboxylate (34): To a solution of **18** (114 mg, 0.491 mmol) and K_2CO_3 (216 mg, 1.56 mmol) in MeOH (5 mL) was added **31** (202 mg, 0.794 mmol). The resulting mixture was stirred at room temperature for 3 h under an Ar atmosphere. The reaction mixture was poured into water and extracted with AcOEt. The organic layer was washed with brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with toluene to give **34** (20 mg, 18%) as blue solid. M.p. 126−128 °C; IR (ATR): v_{max} = 3279 (w), 3007 (w), 2956 (w), 2107 (w), 1681 (s), 1595 (w), 1573 (w), 1540 (w), 1508 (w), 1474 (w), 1456 (m), 1440 (s), 1409 (s), 1392 (w), 1311 (w), 1291 (w), 1235 (m), 1214 (s), 1160 (w), 1115 (w), 1036 (w), 1014 (w), 963 (w), 909 (w), 891 (w), 858 (w), 839 (w), 807 (w), 781 (m), 742 (m), 680 (w), 665 (m) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 9.56 (dd, 1H, J = 10.0, 2.6 Hz, H$_8$), 8.39 (d, 1H, J = 10.0 Hz, H$_4$), 7.77 (t, 1H, J = 10.0 Hz, H$_6$), 7.46 (t, 1H, J = 10.0 Hz, H$_7$), 7.38 (t, 1H, J = 10.0 Hz, H$_5$), 3.99 (s, 3H, CO$_2$Me), 3.90 (s, 1H, C≡CH) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ_C = 164.9, 153.7, 151.6, 141.2, 140.3, 134.1, 133.7, 128.0, 126.5, 115.9, 111.9, 90.7, 76.4, 51.4 ppm; HRMS (EI-MS, positive): calcd for $C_{14}H_9FO_2^+$ [M]$^+$ 228.0582; found: 228.0593.

2-Ethynylazulene (35): To a solution of **22** (78 mg, 0.500 mmol) and K_2CO_3 (213 mg, 1.54 mmol) in MeOH (5 mL) was added **31** (170 mg, 0.669 mmol). The resulting mixture was stirred at room temperature for 2 h under an Ar atmosphere. The reaction mixture was poured into water and extracted with hexane. The organic layer was washed with brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with hexane to give **35** as blue solid. M.p .64−66 °C (lit. 66 °C);[24] ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 8.27 (d, 2H, J = 9.8 Hz, H$_{4,8}$), 7.57 (t, 1H, J = 9.8 Hz, H$_6$), 7.45 (s, 2H, H$_{1,3}$), 7.19 (t, 2H, J = 9.8 Hz, H$_{5,7}$), 3.48 (s, 1H, C≡CH) ppm; Data are in agreement with those previously reported in reference 24.

2-Ethynyl-1-methyl-3-phenylazulene (36): To a solution of **26** (123 mg, 0.500 mmol) and K_2CO_3 (207 mg, 1.50 mmol) in MeOH (5 mL) was added **31** (153 mg, 0.602 mmol). The resulting mixture was stirred at room temperature for 7 h under an Ar atmosphere. The reaction mixture was poured into water and extracted with AcOEt. The organic layer was washed with brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with hexane/AcOEt (50 : 1) to give **36** (50 mg, 41%) as green oil. IR (ATR): v_{max} = 3285 (m), 3052 (w), 3023 (w), 2913 (w), 2094 (w), 1682 (w), 1598 (m), 1569 (m), 1505 (m), 1479 (m), 1440 (m), 1386 (m), 1294 (w), 1228 (m), 1181 (w), 1144 (w), 1074 (m), 1026 (m), 994 (m), 950 (m), 917 (m), 890 (m), 852 (m), 823 (m), 763 (s), 739 (s), 715 (s), 698 (s) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 8.27 (d, 1H, J = 9.7 Hz, H$_4$), 8.21 (d, 1H, J = 9.7 Hz, H$_8$), 7.65 (d, 2H, J = 7.4 Hz, o-Ph), 7.52 (t, 3H, J = 7.4 Hz, m,p-Ph), 7.47 (t, 1H, J = 9.7 Hz, H$_6$), 7.07 (t, 1H, J = 9.7 Hz, H$_5$), 7.01 (t, 1H, J = 9.7 Hz, H$_7$), 3.62 (s, 1H, C≡CH), 2.76 (s, 3H, Me) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ_C = 138.8, 136.6, 136.2, 136.0, 135.5, 134.8, 131.6, 130.7, 128.8, 128.7, 128.3, 126.8, 123.5, 122.5, 87.8, 80.9, 11.5 ppm; HRMS (MALDI-TOF): calcd for $C_{19}H_{14}^+$ [M]$^+$ 242.1090; found: 242.1106.

2-Ethynyl-6-isopropyl-1-methyl-3-phenylazulene (37): To a solution of **27** (144 mg, 0.500 mmol) and K_2CO_3 (211 mg, 1.53 mmol) in MeOH (5 mL) was added **31** (191 mg, 0.751 mmol). The resulting mixture was stirred at room temperature for 5 h under an Ar atmosphere. The reaction mixture was poured into water and extracted with CH$_2$Cl$_2$. The organic layer was washed with brine, dried with Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with hexane/AcOEt (20 : 1) to give **37** (114 mg, 80%) as green oil. IR (ATR): v_{max} = 3293 (s), 3057 (w), 2964 (m), 2928 (w), 2869 (w), 1936 (w), 1599 (w), 1574 (s), 1507 (w), 1461 (s), 1447 (m), 1415 (w), 1389 (m), 1376 (w), 1362 (w), 1329 (w), 1301 (w), 1256 (m), 1245 (w), 1182 (w), 1156 (w), 1121 (w), 1074 (w), 1041 (m), 1026 (w), 1011 (w), 918 (w), 882 (w), 858 (w), 841 (s), 765 (m), 740 (m), 719 (s), 698 (s), 675 (w), 661 (w) cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ_H = 8.23 (d, 1H, J = 10.3 Hz, H$_4$), 8.16 (d, 1H, J = 10.3 Hz, H$_8$), 7.66 (d, 2H, J = 7.5 Hz, o-Ph), 7.51 (t, 2H, J = 7.5 Hz, m-Ph), 7.39 (t, 1H, J = 7.5 Hz, p-Ph), 7.02 (d, 1H, J = 10.3 Hz, H$_5$), 7.02 (d, 1H, J = 10.3 Hz, H$_7$), 3.59 (s, 1H, C≡CH), 3.00 (sept, 1H, J = 6.9 Hz, i-Pr), 2.74 (s, 3H, Me), 1.34 (d, 6H, J = 6.9 Hz, i-Pr) ppm; ^{13}C NMR (125 MHz, CDCl$_3$): δ_C = 161.0, 135.9, 135.7, 135.3, 134.62, 134.56, 131.4, 130.6, 128.6, 128.2, 127.3, 126.7, 122.7, 121.7, 87.1, 81.1, 39.7,

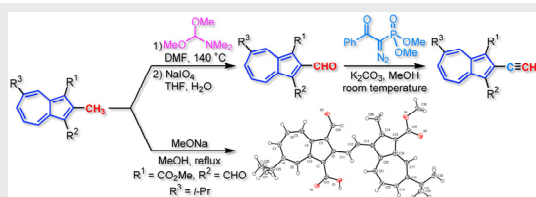24.2, 11.4 ppm; HRMS (MALDI-TOF): calcd for $C_{22}H_{20}^+$ [M]$^+$ 284.1560; found: 284.1557.

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FULL PAPER

2-Formylazulene derivatives were obtained in good yields by the reaction of 2-methylazulenes with *N,N*-dimethylformamide dimethyl acetal, followed by oxidative cleavage of intermediately formed enamines with NaIO$_4$. 2-Formylazulenes obtained by the reaction were also transformed to 2-ethynylazulenes in good yields by modified Seyferth−Gilbert reaction.

Azulene Chemistry

Taku Shoji,* Takanori Araki, Nanami Iida, Yoshiaki Kobayashi, Akira Ohta, Ryuta Sekiguchi, Shunji Ito, Shigeki Mori, Tetsuo Okujima, and Masafumi Yasunami