A Thermolytic Azulene Synthesis from Dimethyl 4-Morpholino-3,3a,8,8a-tetrahydroazulene-5,6-dicarboxylates and Its 1-Substituted Derivatives

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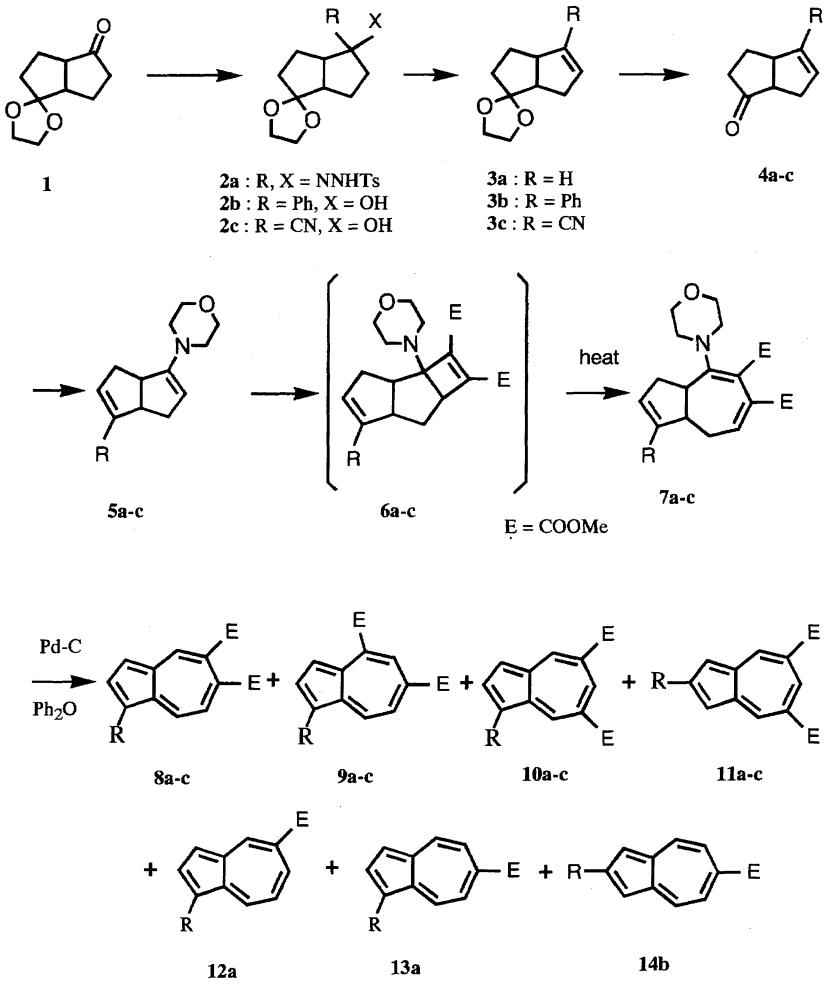
The thermolysis of 1-substituted 4-morpholino-3,3a,8,8a-tetrahydroazulene-5,6-dicarboxylates derivatives (**7a—c**) under catalytic dehydrogenation conditions was studied. The reaction substrates were prepared by a several-step sequence involving the [2+2] cycloaddition of bicyclc morpholino enamines with dimethyl acetylenedicarboxylate, and a subsequent electrocyclic opening of the cyclobutene ring as a key skeletal construction, starting from bicyclo[3.3.0]octane-2,6-dione mono(ethylene acetal). Refluxing of a diphenyl ether solution of dimethyl 4-morpholino-3,3a,8,8a-tetrahydroazulene-5,6-dicarboxylate (**7a**) containing a catalytic amount of Pd–C gave a 10% yield of dimethyl azulene-5,6-dicarboxylate (**8a**), accompanied by a 10% yield of dimethyl azulene-4,6-dicarboxylate (**9a**), trace amounts of dimethyl azulene-5,7-dicarboxylate (**10a**), methyl azulene-5-carboxylate (**12a**), and methyl azulene-6-carboxylate (**13a**). Under the same thermolytic conditions, a 1-phenyl-substituted compound **7b** gave corresponding similar types of phenyl-substituted azulenes (**8b**, **9b**, **10b**, **11b**, and **14b**), and a 1-cyano-substituted compound **7c** gave a mixture of corresponding similar types of cyano-substituted azulenes (**8c**, **9c**, **10c**, and **11c**). This sequence provides a new method for synthesizing substituted azulenes suffering from migration and removal of one ester group. Also the thermolysis of a similar system of dimethyl 3-(1-pyrrolidinyl)-2,7-cycloheptadiene-1,2-dicarboxylate (**15**), even in the absence of a catalyst, gave cycloheptatriene derivatives of dimethyl 1,3,5-cycloheptatriene-dicarboxylate (**16**, **17**, **18**, and **19**), bearing no morpholine molecule.

Among many azulene syntheses,[1] mechanistically interesting skeletal rearrangements in the formation of azulenes from saturated bicyclic hydrocarbons under catalytic dhydrogenation conditions have been reported.[2] Meanwhile, during the course of our synthetic investigation of azuleno [2,1-*a*]azulene, we found an alternate type of rearrangement,[3] in which an ester group on a seven-membered ring rearranged to neighboring positions along with a loss of the morpholine molecule under catalytic dehydrogenation conditions. It is of interest to clarify the generality of the reaction for the preparing azulenes and its application. Thus, we explored these reactions in detail using two types of model compounds of 1-substituted tetrahydroazulene having substituents, such as a morpholino and two methoxycarbonyl groups at the 4-, 5-, and 6-positions, and dimethyl 3-(1-pyrrolidinyl)-2,7-cycloheptadiene-1,2-dicarboxylate (**15**). In the work reported here, it was found that the thermolysis of these compounds proved to be a new method for preparing azulene derivatives and cycloheptatriene derivatives accompanied by the rearrangement of substituents and the cleavage of the morpholine or pyrrolidine molecule, depending upon the applied conditions.[3] Based upon some additional experiments concerning these reactions, a plausible mechanism of the rearrangements is discussed.

Results and Discussion

For the purpose of examining of the rearrangement in the formation of azulenes, three types of reaction substrates, such as dimethyl 4-morpholino-3,3a,8,8a-tetrahydroazulene-5,6-dicarboxylate (**7a**), 1-phenyl derivative **7b**, and 1-cyano derivative **7c**, were prepared from the same starting material of mono(ethylene acetal) of bicyclo[3.3.0]octane-2,6-dione (**1**),[4] as illustrated in Scheme 1. Since the known methods for synthesizing of bicyclo[3.3.0]octa-6-ene-2-one (**4a**) are tedious, and are not appropriate for a preparative scale,[5] in this study an alternative synthetic pathway was devised starting from **1**, as follows. The reaction of **1** with tosylhydrazine in methanol at r.t. for 3 h gave tosylhydrazone **2a** in over 90% yield. The reaction of **2a** with sodium hydride in refluxing diglyme for 3 h furnished **3a** in 70% yield, and the subsequent acid-catalyzed hydrolysis gave **4a** in 90% yield. On the other hand, the 1-phenyl derivative **4b** was prepared by a three-step sequence from **1**, as follows: The reaction of **1** with phenylmagnesium bromide gave the alcohol **2b**, and a following treatment of **2b** with acid yielded **4b** through **3b** in 46% total yield based on **1**. The 1-cyano derivative **4c** was prepared by cyanohydrin formation, following dehydration and hydrolysis under acidic conditions in a similar manner as above gave **4c** in 36% total yield based on **1**. All of the spectral data of



Scheme 1.

4a—**c** are consistent with the assigned structures. The reaction of **4a**—**c** with morpholine in the presence of *p*-TsOH in refluxing benzene for 5—10 h gave the corresponding moisture-sensitive enamines **5a**—**c** in moderate yields. Because of their instability, these enamines were immediately treated with dimethyl acetylenedicarboxylate (DMAD) in refluxing toluene for 3—5 h to give **7a**—**c** in the ring-opened forms through the cyclobutene-fused intermediate **6a**—**c**, in 35—45% yields based on **5a**—**c**. Enamines **7a**—**c** were obtained as crystallines, and their structures were confirmed based on the spectral properties and elemental analyses. The IR spectra of **7a**—**c** showed the characteristic strong absorption band around 1720—1690 cm^{-1} assigned for the ester groups. The ^1H NMR spectra of these compounds showed characteristic signals for the olefinic proton at the 7-position resonated at $\delta = 6.80$—6.90 as a triplet. The dehydrogenation reaction was performed as follows. A mixture of tetrahydroazulene **7a**—**c** and a catalytic amount of Pd–C in diphenyl ether was refluxed until the starting material was completely consumed (about 7—9 min). The rearranged compounds, besides the expected unrearranged compounds, were obtained after purification by column chromatography. The products and their yields are given in Table 1, and no other isolable product was obtained. The best total yield of the products was

Table 1. The Yields of Azulenes Formed by Rearrangements under the Catalytic Dehydrogenation Conditions

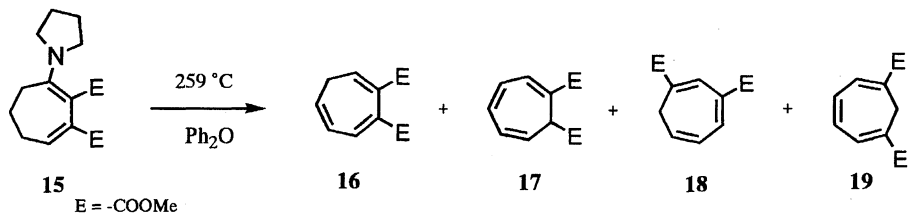
8a	**9a**	**10a**	**11a**	**12a**	**13a**	**14a**
10.2%	10.1%	0.1%	(=**10a**)	Trace	Trace	—
8b	**9b**	**10b**	**11b**	**12b**	**13b**	**14b**
16.3%	4.5%	3.8%	5.5%	—	—	Trace
8c	**9c**	**10c**	**11c**	**12c**	**13c**	**14c**
14.0%	6.5%	12.8%	7.0%	—	—	—

obtained in the case of **7c**, used as starting material, that is about 40%. The electron-withdrawing cyano group at the 1-position might suppress any undesirable reactions, such as polymerization.

All of the spectral data of these azulene products are consistent with the assigned structures. The IR spectra of the products show the characteristic absorption bands at around 1720 cm^{-1}, indicating the conjugated ester groups on the azulenes; in the case of cyano-substituted azulenes, those observed at around 2200 cm^{-1} indicate a conjugated cyano group. Their ^1H NMR spectra show a similar signal pattern, depending upon the type of substitution on an azulene ring. The ^1H NMR spectrum of **8a** shows that the signals observed at $\delta = 8.31$ and 7.30 as a doublet can be assigned for the pro-

tons at the 8- and 7-positions based on their chemical shifts and the same coupling constants of $J = 11.0$ Hz, indicating the vicinal position. Also, the signals observed at $\delta = 7.97$ as a triplet and at $\delta = 7.60$ as a doublet are assigned for protons at the 2-position, and the 1- and 3-positions by their coupling constants of $J = 3.0$ Hz, indicating typical vicinal protons of a five-membered ring, respectively.[6] The signal observed at the lowest field, $\delta = 8.89$, as a singlet was assigned for protons at the 4-position, because it is perhaps due to the anisotropic effect of ester group and deshielding effect of the ring current of the five-membered ring. Similarly, all of the protons of the compounds of the same types of **8b** and **8c** are assigned as follows: signals observed as a doublet at $\delta = 8.30$ and 7.39 in **8b**, and $\delta = 8.69$ and 7.71 in **8c**, with coupling constants of $J = 10.4$ and 9.9 Hz, are assigned for the protons at the 8- and 7-positions of these compounds, respectively. Also, the signals which resonated as a doublet at $\delta = 7.99$ and 7.80 in **8b**, and $\delta = 8.21$ and 7.52 in **8c**, with coupling constants of $J = 1.5$ and 4.1 Hz, are assigned for the protons at their 2- and 3-positions, respectively. The signal for the proton at the 4-position was observed as a singlet at $\delta = 8.85$ for **8b**, and 9.01 for **8c**, respectively. The smallest coupling constants of the protons at the 7- and 8-positions and the lowest chemical shift at the 4-position of **8c** compared to those of **8a** and **8b** maybe due to the least bond alternation caused by the higher dipolar structure in **8c** by the strong electron-withdrowing cyano group at the 1-position on the azulene system. Similarly, the structural assignments of the series of **9**, **10**, and **11** based on the ^{1}H NMR spectra were performed by a comparison with their analogous patterns, as follows. The compounds analogous to **9** showed similar signals in their ^{1}H NMR spectra; that is, the signal observed at the lowest field as a singlet was assigned for the proton at the 5-position by the anisotropic effects of two ester groups at the 4- and 6-positions, at $\delta = 8.41$ for **9a**, $\delta = 8.45$ for **9b**, and $\delta = 8.68$ for **9c**, respectively. Also, the signals of the ^{1}H NMR spectrum of **9a**, separately observed at $\delta = 7.54$ and 7.79 as a doublet, were assigned for the protons at the 1- and 3-positions and the signal at $\delta = 8.19$ as a triplet for the 2-position, respectively, based on their same coupling constants of $\delta = 3.0$ Hz. This showed the unsymmetrical structure of **9a**. Also, the signals observed at $\delta = 8.47$ and 8.15 with the same coupling constants as those of **8a** were assigned for the protons at the 8- and 7-positions. Similarly, the signals of **9b** observed at $\delta = 8.19$ and 7.79 as a doublet were assigned for the protons at the 2- and 3-positions, and the protons at the 2- and 3-positions of **9c** were resonated at $\delta = 8.29$ and 7.82 with coupling constants of $J = 2.0$ and 4.1 Hz, respectively. Also, the signals observed at $\delta = 8.39$ and 8.13 as a doublet with coupling constants of $J = 9.8$ Hz, and at $\delta = 8.78$ as a double doublet and $\delta = 8.44$ as a doublet with coupling constants of $J = 9.9$ Hz, were assigned for the protons at 7- and 8-positions of **9b** and **9c**, respectively. In the type of **10**, the ^{1}H NMR spectra showed characteristic signals for the protons on seven-membered ring having small coupling constants indicating the *meta* positions of each other, e. g., for **10a**, at $\delta = 9.41$ as triplet for the proton at the 6-position and $\delta = 9.25$ as a doublet for those at the 4- and 8-positions with coupling constant of $J = 1.7$ Hz; for **10b**, at $\delta = 9.38$ as a triplet for the 6-positions, $\delta = 9.35$ as a doublet for the 4-position, and $\delta = 9.19$ as a doublet for the 8-position with the same coupling constants as that of **10a**; for **10c**, at $\delta = 9.58$ as a double doublet ($J = 1.4$ and 1.9 Hz) for the 6-position, $\delta = 9.51$ as a doublet ($J = 1.4$ Hz) for the 8-position, and $\delta = 9.38$ as a doublet ($J = 1.9$ Hz) for the 4-position, respectively. The signals of the protons at the 1- and 3-positions resonated at $\delta = 7.60$ as a doublet and the 2-position at $\delta = 7.78$ as a triplet with a coupling constant of $J = 3.5$ Hz, and those of the 2- and 3-positions of **10b** and **10c** were observed at $\delta = 8.07$ and 7.78 as a doublet for **10b**, and $\delta = 8.18$ and 7.69 for **10c** with the same coupling constants of $J = 4.1$ Hz, respectively. The simple ^{1}H NMR spectrum of **11b** showed a symmetrical structure, and the protons on a seven-membered ring resonated at $\delta = 9.31$ as a triplet assigned for the protons at the 6-position, and at $\delta = 9.20$ as a doublet for those at the 4- and 8-positions with coupling constants of $J = 1.7$ Hz, respectively; the signal resonated at $\delta = 8.30$ as a singlet is assigned for the protons at the 1- and 3-positions, indicating the 2-phenyl substituted azulene structure. All of the chemical shifts of the ring protons of **10a—c** were observed in a similar region, which indicates that the electron-withdrawing cyano group at the 2-position contributes to the polarization of azulene less than that of the 1-position.

Some additional experiments under various conditions were performed by using a simplified compound of dimethyl 3-(1-pyrrolidinyl)-2,7-cycloheptadiene-1,2-dicarboxylate (**15**), which constitutes nearly the same structure as the seven-membered ring moiety of **7**. A treatment of **15** under the same conditions gave four main products (**16**,[7] **17**,[7] **18**, and **19**[8]) in 4.3, 3.8, 15, and 16% yields, respectively. Also, it was accidentally found that a similar reaction of **15** in the absence of a catalyst gave the same result, as shown in Scheme 2. Complete consumption of the starting material took 7—15 min, though additional reaction times did not improve the yields, but caused decomposition, as shown in Table 2. The structures of these compounds, **16** and **17**, were confirmed by a direct comparison of the spectral data with those of the authentic samples; those of **18** and **19** were determined based on the spectral data. The ^{1}H NMR spectrum of **18** shows that the signals observed at $\delta = 7.87$ as a doublet and at $\delta = 7.74$ as a singlet are assigned for the protons at the 4- and 2-positions, respectively. Also, that of **19** was confirmed by a comparison of the spectral data with those of a sample derived from authentic diacid.[8] Especially, in the UV-vis spectra, **19** has a longer absorption maximum than that of **18**, clearly showing the greater conjugation of the ester groups through the triene moiety in **19**. The above results indicate that the migration of a methoxycarbonyl group only requires the structure of the seven-membered ring moiety. Additional experimentals giving some information about the reaction sequence were performed as follows. When **8a** was heated under the same conditions employed in the transformation of **7a** to **8a**, no further change of **8a** was observed.



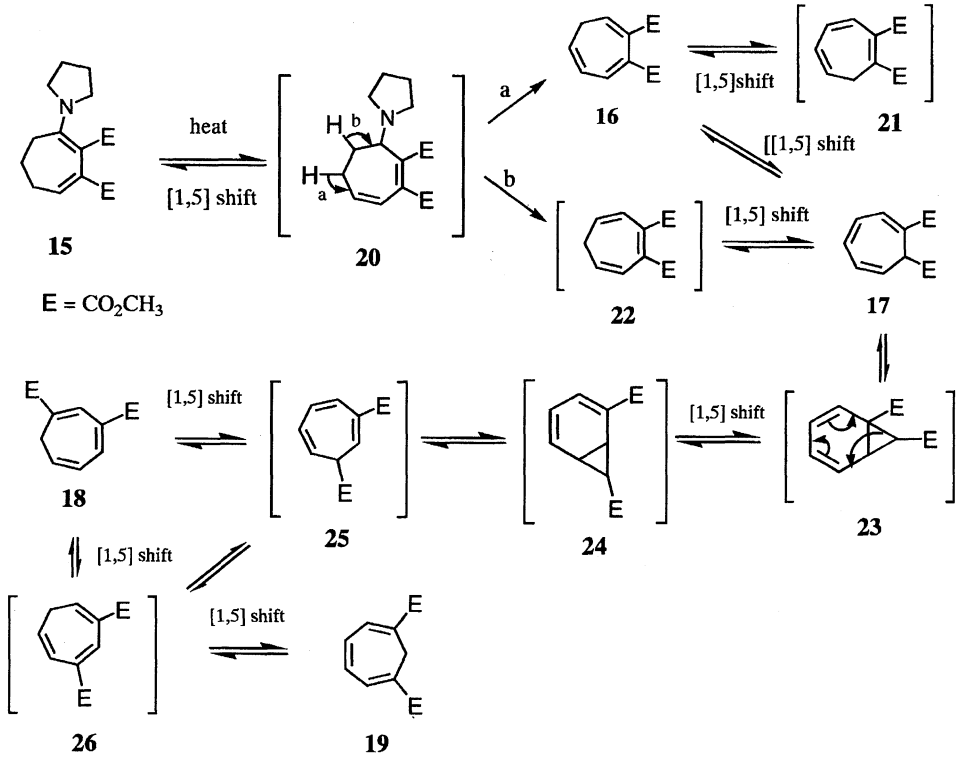
Scheme 2.

Table 2. The Yields (%) of Products by Pyrolysis of Dimethyl 3-(1-Pyrrolidinyl)-1,3-cycloheptadiene-2,3-dicarboxylate

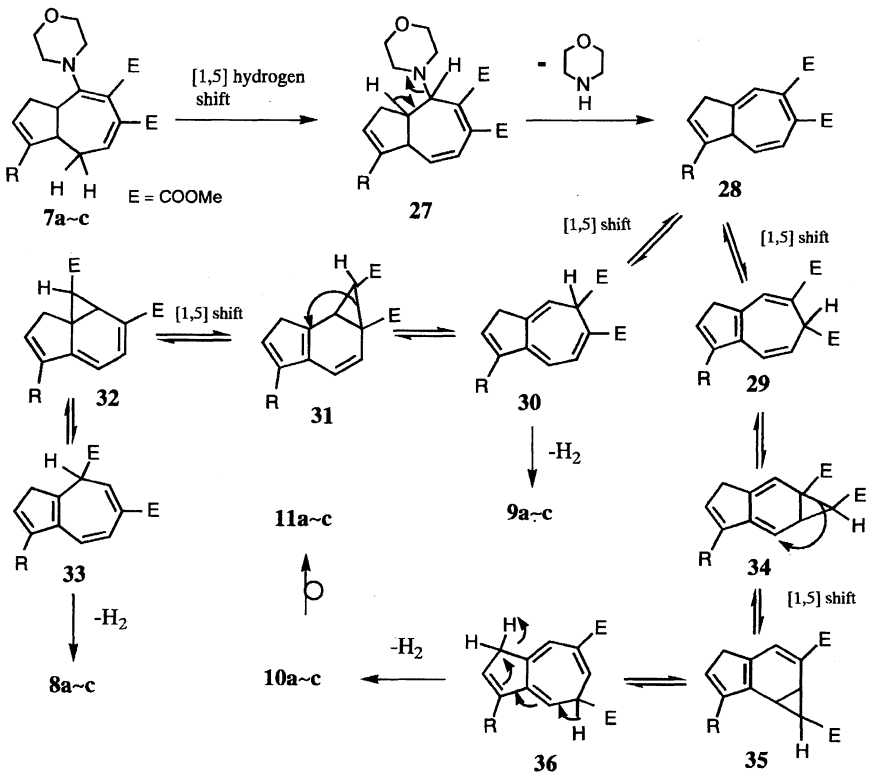
Reaction time	Product			
(min)	**16**	**17**	**18**	**19**
7	5.1	4.8	16.3	16.8
15	4.3	3.8	14.8	16.6

Also, the thermal reactions of **7a** in the presence of 2,5-di-*t*-butylphenol, nitrobenzene, or *p*-benzoquinone, as a radical scavenger, in the reaction mixture, caused no changes in the yields or ratios of the products indicating an exclusion of the radical process. Based upon the results mentioned above, one of the possible mechanism for this rearrangement, as illustrated in Scheme 3, can be considered. The reaction was initiated by a [1,5] hydrogen shift from the 6- to 3-position precedent to the elimination of a pyrrolidine molecule from **15** via compound **20**, which is an intermediate, but is unable to be detect in the products to give cycloheptatriene **21** and/or **22**. They were followed by a successive interconversion of isomers by the [1,5] hydrogen shifts and [1,5] migration of three-membered ring, as suggested in the literature,[7] to give **23**, **24**, **25**; the final tautomerization gave the corresponding cycloheptatriene products, respectively.[9]

Because of the facts that **8a** is not an intermediate for either a rearranged or deesterified product, it is considered that the reactions of **7** and **15**, having the same partial structure, passed through a similar type of process. Then, a plausible reaction mechanism for azulene formation is proposed as illustrated in Scheme 4. That is, the initial step and successive rearrangement are similar to the case of **15**; e. g., the skeletal rearrangement of the seven-membered ring occurs in its norcaradiene forms **31** by the [1,5] migration of the three-membered ring to give **32** and **35**. Finally dehydrogenation of the cycloheptatriene forms, such as **36** by Pd–C yields azulenes (**10a—c**), and is followed by the migration



Scheme 3.



Scheme 4.

of substituents on a five-membered ring to give (**11a—c**).

In conclusion, the thermolytic reaction of compounds such as **7** and **15** pave a new way to the synthesis of azulene and cycloheptatriene derivatives accompanied by rearrangements and removal of the substituents on their seven-membered ring.

Experimental

All of the melting points were uncorrected. The IR spectra were taken on a Hitachi IR-810 spectrometer and the UV-vis spectra were recorded on a Shimadzu UV-265FS. The ^{1}H NMR spectra were taken on Hitachi R-24 (60 MHz) on JEOL-FX90 (90 MHz), and JEOLα400 (400 MHz) spectrometers, in chloroform-*d* (TMS as internal standard). The ^{13}C NMR spectra were taken on a JEOL-FX90 (23 MHz) and a JEOLα400 (100 MHz) in chloroform-*d* (TMS as the internal standard). The Mass spectra were taken on a JEOL-OISG-2 mass spectrometer.

Preparation of Bicyclo[3.3.0]octan-6-ene-2-one 4a. The reaction of half acetal of bicyclo[3.3.0]octane-2,6-dione (**1**) (18 g, 99 mmol) with tosylhydrazine (18.6 g, 95 mmol) in methanol (100 mL) at r.t. overnight gave crystals, which were collected by suction filteration; These were washed well with ethanol and dried to give **2a** in 97% yield (34 g). **2a**: Colorless needles, mp 168—169 °C (methanol); IR (KBr) 3210vs, 2950m, 1600m, 1170vs, 820s, 675s cm^{-1}; ^{1}H NMR (60 MHz) δ = 7.82 (d, J = 6.0 Hz, 2H), 7.35 (d, J = 6.0 Hz, 2H), 7.30 (m, 2H), 3.88 (s, 4H), 2.42 (s, 3 H), 3.20—1.10 (m, 10H); MS *m/z* 350 (M$^+$; 100%). Found: C, 58.12; H, 6.29; N, 7.88%. Calcd for $C_{17}H_{22}N_2SO_4$: C, 58.27; H, 6.33; N, 7.99%.

To a solution of **2a** (31 g, 90 mmol) in anhydrous diglyme (300 mL) was added sodium hydride (7.4 g, 310 mmol) in ca. 1 g portions at r.t. for 20 min. The mixture was refluxed for 3 h under a nitrogen atmosphere. After being cooled, the mixture was poured into water and extracted with ether (100 mL×3). The combined extracts were washed with a small amount of 3 M HCl (1 M = 1 mol dm^{-3}), water, and brine twice each, and dried over anhydr. $MgSO_4$. After removing the solvent in vacuo, the residue was column chromatographed on silica gel to give a colorless oil of the ene acetal **3a** in 57% yield (5.4 g). **3a**: Colorless oil; IR (film) 3050m, 2950s, 1620w, 1100m, 620m cm^{-1}; ^{1}H NMR δ = 5.47 (m, 1H), 3.81 (s, 4H), 1.98—0.70 (m, 8H); MS *m/z* 166 (M$^+$; 4%), 122 (17%), 99 (100%). HRMS Found: *m/z* 166.0969. Calcd for $C_{10}H_{14}O_2$: M, 166.0992.

To a solution of **3a** (4.2 g, 25.3 mmol) in acetone (80 mL) was added 3 M HCl (10 mL); the mixture was stirred at r.t. for 3 h. After sat. sodium hydrogencarbonate (15 mL) was added to this reaction mixture, acetone was removed in vacuo. The residue was extracted with benzene (50 mL×3); then, the combined extracts were washed with water and brine twice each, and dried over anhydr. $MgSO_4$. The solvent was removed by evaporation, and the residue was chromatographed on silica gel to give **4a** in 58% yield (1.8 g).

Preparation of Phenyl Derivative 4b. To a solution of phenylmagnesium bromide prepared from the bromobenzene (20.3 g, 129 mmol) and magnesium (4.10 g, 170 mmol), in dry ether (130 mL) was added half acetal **1** (16.8 g, 92.3 mmol) in dry ether (10 mL) dropwise at r.t.; the resulted mixture was stirred for 1 h. The reaction mixture was poured into a saturated ammonium chloride solution (50 mL) and extracted with ether (20 mL×3). The extracts were combined, washed with water and brine three times each, and dried over anhydr. $MgSO_4$. After removing the solvent, the residue was chromatographed on silica gel to give **2b** in 88% yield (21.2 g). **2b**: Colorless needles, mp 67—68 °C (CH_2Cl_2–hexane); IR (KBr) 3490s, 3070w, 1511w, 1228m, 1130s, 760m cm^{-1}; ^{1}H NMR (60 MHz) δ = 7.37 (m, 5H), 3.99 (m, 4H), 3.36 (s, 1H), 2.81 (m, 2H), 1.95 (m, 8H); MS *m/z* 260 (M$^+$; 23%), 242 (100%), 197 (85%). HRMS Found: *m/z* 260.1406. Calcd for $C_{16}H_{20}O_3$: M, 260.1409.

A benzene solution (250 mL) of **2b** (16.0 g, 61.5 mmol) in the

presence of TsOH (500 mg) was refluxed for 6 h gave **3b** in 75% yield (11.2 g) as a pale-yellow oil. **3b**: IR (film) 3050w, 2950m, 1635m, 1602m, 1498m, 1445m, 987m cm^{-1}; ^1H NMR δ = 7.20 (m, 5H), 5.88 (m, 1H), 3.78 (s, 4H), 2.64 (m, 4H), 2.02 (m, 2H), 1.61 (m, 2H). MS *m/z* 242 (M^+; 100%), 197 (95%), 155 (58%). The acid hydrolysis of acetal **2b** was also performed under the same conditions for a longer reaction time to give **4b** in 75% yield. **4b**: IR (film) 3040w, 2995m, 1632m, 1601m, 1500m, 1450m, 1272m, 1118m, 838m, 756m cm^{-1}; ^1H NMR (90 MHz) δ = 7.20 (m, 5H), 5.88 (m, 1H), 3.78 (s, 4H), 2.64 (m, 4H), 2.02 (m, 2H), 1.61 (m, 2H); MS *m/z* 198 (M^+; 76%), 170 (90%), 142 (100%). HRMS Found: *m/z* 198.1040. Calcd for $C_{14}H_{14}O$: M, 198.1042. Found: C, 63.21; H, 4.81; N, 14.94%. Calcd for $C_{20}H_{18}N_4O_4$ as 2,4-DNP: C, 63.45; H, 4.80; N, 14.81%.

Preparation of Cyano Derivative 4c. To a solution of **1** (12 g, 58 mmol) and sodium cyanide (14 g, 22 mmol) in aqueous THF (THF : water = 5 : 2) (50 mL) was added H_2SO_4 (1 mol dm^{-3}) dropwise at ice cooling temperature for 30 min, and then stirred for 1 h. The reaction mixture was poured into ice water (50 mL) and extracted with ether (30 mL×3). The combined organic layer was washed with water and brine three times each, and dried over anhydr. $MgSO_4$. The solvent was evaporated in vacuo, and the residue was chromatographed on silica gel to give **2c** in 75% yield (14.0 g). **2c**: Pale-yellow oil, IR (film) 3410vs, 2950s, 2217w, 1455m, 1340s, 1206s, 1110vs, 1025s, 940s, 888m, 726w cm^{-1}; ^1H NMR (60 MHz) δ = 4.50 (m, 1H), 3.80 (s, 4H), 3.20 (m, 1H), 2.60—2.30 (m, 2H), 1.80 (m, 6H); MS *m/z* 209 (M^+; 5.5%), 140 (34%), 99 (100%). HRMS Found: *m/z* 209.1009. Calcd for $C_{11}H_{15}NO_3$: M, 209.1008.

To a solution of **2c** (12 g, 58 mmol) in pyridine (45 mL) was added thionyl chloride (30 mL) dropwise at r.t. for 30 min; the mixture was stirred at 50 °C for 30 min. The resulting reaction mixture was poured into H_2SO_4 (1.5 mol dm^{-3}) and extracted with ether (30 mL×3). After the combined organic layer were worked up as mentioned above, column chromatography of the residue on silica gel gave **3c** in 68% yield (6.5 g). **3c**: Colorless oil; IR (film) 3050w, 2958m, 2200vs, 1630m, 1580m, 1230m cm^{-1}; ^1H NMR (60 MHz) δ = 6.39 (m, 1H), 3.74 (s, 4H), 2.68 (m, 2H), 1.58 (m, 6H); MS *m/z* 191 (M^+; 76%). HRMS Found: *m/z* 191.1040. Calcd for $C_{11}H_{13}NO_2$: M, 191.1042.

The hydrolysis of **3c** was carried out in the similar manner to that described above, and gave **4c** in 75% yield. **4c**: Colorless oil; IR (film) 3050w, 2958m, 2208vs, 1727s, 1630m, 1604m, 1428m, 1161m, 923m, 824m cm^{-1}; ^1H NMR (60 MHz) δ = 6.39 (m, 1H), 2.68 (m, 2H), 1.58 (m, 6H); MS *m/z* 147 (M^+; 100%). HRMS Found: *m/z* 147.1360. Calcd for C_9H_9NO: M, 147.1342.

General Procedure for the Preparation of Enamines and the Subsequent Cycloaddition Reaction of Enamines with Dimethyl Acetylenedicarboxylate (DMAD). To a solution of ketone **4a** (50 mmol) and morpholine (10.3 g, 150 mmol) in dry benzene (130 mL) was added titanium tetrachloride (15.2 g, 80 mmol) in dry benzene (15 mL) dropwise at ice cooling temperature over a period of 30 min. After being stirred for 3 h, the reaction mixture was filtered. The solids collected were well washed with benzene three times (15 mL×3). The filterates were combined and concentrated to dryness to give the enamine **5a**. The enamine and an equivalent molar of DMAD were dissolved in dry toluene (ca. 20—30 times of weight) and refluxed for 5 h. The reaction mixture was cooled and the solvent was removed in vacuo. The residue was chromatographed on silica gel to give tetrahydroazulene derivative **7a**. Analytical pure samples were obtained by recrystallization from CH_2Cl_2–hexane.

7a: (16%), colorless needles, mp 190.5—191 °C (CH_2Cl_2–hexane); IR (KBr) 3200w, 2945m, 1720vs, 1690s, 1120m, 900s, 700m cm^{-1}; ^1H NMR (90 MHz) δ = 6.80 (t, *J* = 7.5 Hz, 1H), 5.51 (m, 2H), 4.12—3.83 (m, 3H), 3.59 (s, 3H, OMe), 3.56 (s, 3H, OMe), 3.83—2.73 (m, 4H), 3.38 (m, 2H), 2.40—0.85 (m, 5H); HRMS Found: *m/z* 333.1563. Calcd for $C_{18}H_{23}NO_5$: M, 333.1573. Found: C, 64.62; H, 6.84; N, 4.40%. Calcd for $C_{18}H_{23}NO_5$: C, 64.84; H, 6.91; N, 4.20%.

7b: (30%), colorless needles, mp 201—205 °C (CH_2Cl_2–hexane); IR (KBr) 3075w, 2960m, 1718vs, 1698s, 1621m, 1565m, 1421m, 1270s, 1229s, 1119m, 1078m, 908m, 776m, 760m, 701m cm^{-1}; ^1H NMR (90 MHz) δ = 7.34 (m, 5H), 6.80 (t, *J* = 7.5 Hz, 1H), 6.09 (m, 1H), 4.26 (m, 1H), 3.80 (m, 4H), 3.70 (s, 3H, OMe), 3.65 (s, 3H, OMe), 3.58—2.82 (m, 5H), 2.58 (m, 2H), 2.33 (m, 2H); HRMS Found: *m/z* 409.1889. Calcd for $C_{24}H_{27}NO_5$: M, 409.1889. Found: C, 70.47; H, 6.60; N, 3.50%. Calcd for $C_{24}H_{27}NO_5$: C, 70.42; H, 6.60; N, 3.40%.

7c: (42%), colorless needles, mp 186—188 °C (CH_2Cl_2–hexane); IR (KBr) 3060w, 2920m, 1717vs, 1683s, 1609m, 1534m, 1422m, 1350m, 1246s, 1110m, 1032m, 942m, 850m, 821m, 762m, 735m, 703m cm^{-1}; ^1H NMR (90 MHz) δ = 6.91 (t, *J* = 7.5 Hz, 1H), 6.68 (m, 1H), 3.92 (m, 1H), 3.74 (m, 4H), 3.71 (s, 3H, OMe), 3.65 (s, 3H, OMe), 3.19 (m, 5H), 2.60 (m, 2H), 2.39 (m, 2H); MS *m/z* 358 (M^+; 11%), 299 (99.5%), 86 (100%). Found: C, 63.39; H, 6.05; N, 7.90%. Calcd for $C_{19}H_{22}N_2O_5$: C, 63.69; H, 6.15; N, 7.82%.

General Procedure for Dehydrogenation Reaction of 7a—c in the Presence of Pd–C. A mixture of **7** (ca. 20—30 mmol) and Pd–C (3—5 mg) in diphenyl ether (10 mL) was refluxed for 7—9 min. After being cooled, the mixture was chromatographed on silica gel to give azulene derivatives **8—14** by benzene elution. The products and their yields are shown in Table 1.

8a: Blue needles, mp 134—135 °C (CH_2Cl_2–hexane); IR (KBr) 3050w, 2950m, 1720vs, 1575m, 1250vs, 765m cm^{-1}; ^1H NMR (90 MHz) δ = 8.89 (s, 1H, H-4), 8.31 (d, *J* = 11.0 Hz, 1H, H-8), 7.97 (t, *J* = 3.0 Hz, 1H, H-2), 7.60 (d, *J* = 3.0 Hz, 1H, H-3), 7.50 (d, *J* = 3.0 Hz, 1H, H-1), 7.30 (d, *J* = 11.0 Hz, 1H, H-7), 3.92 (s, 6H, 2×OMe); MS *m/z* 244 (M^+; 100%), 155 (14%). HRMS Found: *m/z* 244.0730. Calcd for $C_{14}H_{12}O_4$: M, 244.0733. Found: C, 68.69; H, 4.97%. Calcd for $C_{14}H_{12}O_4$: C, 68.85; H, 4.92%.

8b: Blue needles, mp 118—119 °C (hexane); IR (KBr) 3050w, 2950m, 1758vs, 1748s, 1250vs, 765m cm^{-1}; ^1H NMR (90 MHz) δ = 8.85 (s, 1H, H-4), 8.30 (d, *J* = 10.4 Hz, 1H, H-8), 7.99 (d, *J* = 1.5 Hz, 1H, H-2), 7.95 (m, 2H on Ph), 7.80 (d, *J* = 1.5 Hz, H-3), 7.50 (m, 3H on Ph), 7.39 (d, *J* = 10.4 Hz, 1H, H-7), 3.95 (s, 6H, 2×OMe); MS *m/z* 320 (M^+; 100%). Found: C, 74.84; H, 5.12%. Calcd for $C_{20}H_{16}O_4$: C, 74.99; H, 5.03%.

8c: Purple needles, mp 128—129 °C (hexane); IR (KBr) 3050w, 2200vs, 1722vs, 1250vs, 765m cm^{-1}; ^1H NMR (90 MHz) δ = 9.01 (s, 1H, H-4), 8.69 (d, *J* = 9.9 Hz, 1H, H-8), 8.21 (d, *J* = 4.1 Hz, 1H, H-2), 7.71 (d, *J* = 9.9 Hz, 1H, H-7), 7.52 (d, *J* = 4.1 Hz, H-3), 3.98 (s, 6H, 2×OMe); MS *m/z* 269 (M^+; 100%). Found: C, 67.14; H, 4.10; N, 5.45%. Calcd for $C_{15}H_{11}NO_4$: C, 66.91; H, 4.09; N, 5.20%.

9a: Green needles, mp 46—47 °C (CH_2Cl_2–hexane); IR (KBr) 1723vs, 1198vs, 760m cm^{-1}; ^1H NMR (90 MHz) δ = 8.47 (d, *J* = 11.0 Hz, 1H, H-8), 8.41 (s, 1H, H-5), 8.19 (t, *J* = 3.0 Hz, 1H, H-3), 8.15 (d, *J* = 11.0 Hz, 1H, H-7), 7.84 (d, *J* = 3.0 Hz, 1H, H-3), 7.54 (d, *J* = 3.0 Hz, H-1), 4.09 (s, 6H, 2×OMe); HRMS Found: *m/z* 244.0792. Calcd for $C_{14}H_{12}O_4$: M, 244.0733. Found: C, 68.87; H, 4.78%. Calcd for $C_{14}H_{12}O_4$: C, 68.85; H, 4.92%.

9b: Green needles, mp 93—95 °C (CH_2Cl_2–hexane); IR (KBr) 1711vs, 1699s, 1198vs, 760m cm^{-1}; ^1H NMR (90 MHz) δ = 8.45 (s, 1H, H-5), 8.39 (d, *J* = 9.8 Hz, 1H, H-8), 8.19 (d, *J* = 2.0 Hz, 1H,

H-2), 8.13 (d, J = 9.8 Hz, 1H, H-7), 8.00 (m, 2H on Ph), 7.79 (d, J = 2.0 Hz, 1H, H-3), 7.43 (m, 3H on Ph), 4.11 (s, 3H, OMe), 4.00 (s, 3H, OMe); MS m/z 320 (M^+; 100%), 289 (49%). Found: C, 74.73; H, 5.24%. Calcd for $C_{20}H_{16}O_4$: C, 74.99; H, 5.03%.

9c: (mixture with **11c**); ^{1}H NMR (90 MHz) δ = 8.78 (d, J = 9.9 Hz, 1H, H-8), 8.68 (d, J = 1.3 Hz, 1H, H-5), 8.44 (dd, J = 1.3 and 9.9 Hz, 1H, H-7), 8.29 (d, J = 4.1 Hz, 1H, H-2), 7.82 (d, J = 4.1 Hz, 1H, H-3), 4.04 (s, 3H, OMe), 4.02 (s, 3H, OMe); MS m/z 269 (M^+; 100%). HRMS Found: m/z 269.2039. Calcd for $C_{15}H_{11}O_4$: M, 269.2089.

10a (= **11a**): Blue needles, mp 147—149 °C (hexane); IR (KBr) 3080w, 3000m, 1717vs, 1592m, 1433m, 1315m, 1235vs, 1171m, 1085m, 1000m, 968m, 773m cm^{-1}; ^{1}H NMR (90 MHz) δ = 9.41 (t, J = 1.7 Hz, 1H, H-6), 9.25 (d, J = 1.7 Hz, 2H, H-4 and 8), 7.99 (t, J = 3.5 Hz, 1H, H-2), 7.60 (d, J = 3.5 Hz, 2H, H-1 and 3), 3.92 (s, 6H, 2×OMe); MS m/z 244 (M^+; 100%), 155 (14%). HRMS Found: m/z 244.0720. Calcd for $C_{14}H_{12}O_4$: M, 244.0733. Found: C, 68.79; H, 4.67%. Calcd for $C_{14}H_{12}O_4$: C, 68.85; H, 4.92%.

10b: Violet needles, mp 216—218 °C (hexane); IR (KBr) 3050w, 1719vs, 1250vs, 765m cm^{-1}; ^{1}H NMR (90 MHz) δ = 9.38 (t, J = 1.7 Hz, 1H, H-6), 9.35 (d, J = 1.7 Hz, 1H, H-4), 9.19 (d, J = 1.7 Hz, 1H, H-8), 8.07 (d, J = 4.1 Hz, 1H, H-2), 7.96 (m, 2H on Ph), 7.78 (d, J = 4.1 Hz, H-3), 7.50 (m, 3H on Ph), 4.20 (s, 3H, –Me), 3.96 (s, 3H, –OMe); MS m/z 320 (M^+; 100%). Found: C, 75.00; H, 5.06%. Calcd for $C_{20}H_{16}O_4$: C, 74.99; H, 5.03%.

10c: Reddish needles, mp 200—202 °C (hexane); IR (KBr) 3050w, 2210vs, 1720vs, 1250vs, 760m cm^{-1}; ^{1}H NMR (90 MHz) δ = 9.58 (dd, J = 1.4 and 1.9 Hz, 1H, H-6), 9.51 (d, J = 1.4 Hz, 1H, H-8), 9.38 (d, J = 1.9 Hz, 1H, H-4), 8.18 (d, J = 4.1 Hz, 1H, H-2), 7.69 (d, J = 4.1 Hz, H-3), 4.07 (s, 3H, OMe), 4.06 (s, 3H, OMe); MS m/z 269 (M^+; 86%), 195 (100%). Found: C, 66.63; H, 4.20; N, 5.25%. Calcd for $C_{15}H_{11}NO_4$: C, 66.91; H, 4.09: N, 5.20%.

11b: Purple needles, mp 213—214 °C (hexane); IR (KBr) 3050w, 1720vs, 1245vs cm^{-1}; ^{1}H NMR (90 MHz) δ = 9.31 (t, J = 1.7 Hz, 1H, H-6), 9.20 (d, J = 1.7 Hz, 2H, H-4 and 8), 8.30 (s, 2H, H-1,3), 7.95 (m, 2H on Ph), 7.51 (m, 3H on Ph), 4.03 (s, 6H, 2×OMe); ^{13}C NMR (23 MHz) δ = 168.0 (C=O); 151.6, 138.8, 138.2, 138.0, 135.8, 129.4, 127.7, 123.8, 122.9, 52.6; MS m/z 320 (M^+; 100%). Found: C, 74.73; H, 5.24%. Calcd for $C_{20}H_{16}O_4$: C, 74.99; H, 5.03%.

12a: Blue oil; IR (film) 3030w, 2950m, 1718vs, 1604s, 1592m, 1493m, 1241m, 1151m, 814m, 750m cm^{-1}; ^{1}H NMR (90 MHz) δ = 9.12 (d, J = 9.18 Hz, 1H, H-8), 8.45 (d, J = 6.15 Hz, 1H, H-6), 8.40 (d, J = 9.18 Hz, 1H, H-7), 7.95 (t, J = 1.70 Hz, 1H, H-2), 7.59 (d, J = 1.70 Hz, 1H, H-3), 7.55 (d, J = 1.70 Hz, 1H, H-1), 7.17 (m, 1H, H-7), 3.92 (s, 3H, OMe); MS m/z 186 (M^+; 100%), 155 (80%). HRMS Found: m/z 186.0659. Calcd for $C_{12}H_{10}O_2$: M, 186.0679.

13a: Reddish oil; IR (film) 3030w, 2925m, 1712vs, 1438m, 1263m, 1238m, 1081m, 771m cm^{-1}; ^{1}H NMR (90 MHz) δ = 8.41 (d, J = 7.20 Hz, 2H, H-4 and 8), 8.00 (t, J = 4.50 Hz, 1H, H-2), 7.95 (d, J = 7.20 Hz, 2H, H-5 and 7), 7.39 (d, J = 4.50 Hz, 2H, H-1 and 3), 3.95 (s, 3H, OMe); MS m/z 186 (M^+; 100%), 127 (53%). HRMS Found: m/z 186.0670. Calcd for $C_{12}H_{10}O_2$: M, 186.0679.

14b: Reddish oil; IR (film) 3015w, 2925m, 1720vs, 1438m, 1245m, 771m cm^{-1}; ^{1}H NMR (90 MHz) δ = 8.34 (d, J = 10.6 Hz, 2H, H-4 and 8), 8.03 (d, J = 10.6 Hz, 2H, H-5 and 7), 7.96 (m, 2H on Ph), 7.73 (s, 2H, H-1 and 3), 7.35 (s, 3H on Ph), 3.98 (s, 3H, OMe); MS m/z 262 (M^+; 100%). HRMS Found: m/z 262.0820. Calcd for $C_{18}H_{14}O_2$: M, 262.0879.

18: Pale yellow oil; IR (film) 2940w, 1720vs, 1715vs, 1618w, 1535w, 1435w, 1340w, 1280s, 1220s, 1195m, 1095m, 1055m, 755m, 740m cm^{-1}; ^{1}H NMR (400 MHz) δ = 7.87 (d, J = 5.99 Hz, 1H, H-4), 7.74 (s, 1H, H-2), 6.43 (dd, J = 9.00 and 5.99 Hz, 1H, H-5), 5.88 (dt, J = 9.00 and 7.19 Hz, 1H, H-6), 3.87 (s, 3H, –OMe), 3.81 (s, 3H, –OMe), 2.69 (d, J = 7.19 Hz, 2H, H-7); ^{13}C NMR (100 MHz) δ = 167.2, 166.2, 141.0, 131.3, 131.1, 130.2, 126.6, 122.5, 52.4, 52.2, 26.9; MS m/z 208 (M^+; 32%), 193 (72%), 177 (42%), 149 (75%), 105 (21%), 991 (47%), 90 (30%), 89 (35%), 63 (23%). HRMS Found: m/z 208.0759. Calcd for $C_{11}H_{12}O_4$: M, 208.0735. UV-vis λ_{max} (EtOH) 226 (log ε = 4.32), 293 nm (3.77).

19: Pale yellow oil; IR (film) 2950w, 1719vs, 1615w, 1435w, 1355w, 1275s, 1205s, 1100m, 1055m, 740m cm^{-1}; ^{1}H NMR (400 MHz) δ = 7.28 (m, 2H), 6.87 (m, 2H), 3.81 (s, 6H, –OMe), 3.05 (s, 2H, H-7); ^{13}C NMR (100 MHz) δ = 165.9, 133.5, 133.1, 125.2, 52.2, 25.6; MS m/z 208 (M^+; 48%), 193 (M^+ – Me, 100%), 177 (20%), 149 (58%), 133 (28%), 119 (20%), 91 (72%), 90 (30%), 89 (45%). HRMS Found: m/z 208.0714. Calcd for $C_{11}H_{12}O_4$: M, 208.0735. UV-vis λ_{max} (EtOH) 229 (log ε = 4.16), 306 nm (3.69).

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