HETEROCYCLES, Vol. 82, No. 2, 2011, pp. 1283 - 1296. © The Japan Institute of Heterocyclic Chemistry
Received, 27th June, 2010, Accepted, 4th August, 2010, Published online, 6th August, 2010
DOI: 10.3987/COM-10-S(E)74

2-[1,3-BIS(ETHOXYCARBONYL)AZULEN-6-YL]ETHYNYLTRIPHENYL-PHOSPHONIUM BROMIDE †

Noboru Morita,[a]* Shiro Moriyama,[a] Kozo Toyota,[a] Masataka Watanabe,[b] Shigeru Kikuchi,[c] Shunji Ito,[d] and Kunihide Fujimori[e]

[a] Department of Chemistry, Graduate School of Science, Tohoku University, Aoba-ku, Sendai 980-8578, Japan
[b] Institute of Multidisiplinary research for advanced Materials, Tohoku University, Katahira 2-1-1, Aoba-ku, Sendai 980-8577, Japan
[c] Graduate School of Science and Technology, Kumamoto University, Kurokami 2-39-1, Kumamoto 860-8555, Japan
[d] Department of Material Science and Technology, Faculty of Science and Technology, Hirosaki University, Bunkyocho 3, Hirosaki 036-8561, Japan
[e] Department of Chemistry, Faculty of Science, Shinshu University, 3-1-1, Asahi, Matsumoto, 390-8621, Japan
*Corresponding author: Tel. & Fax +81-22-378-5491
E-mail: nmorita-kamo@hb.tp1.jp

Abstract – 2-[1,3-Bis(ethoxycarbonyl)azulen-6-yl]ethynyltriphenylphosphonium bromide was prepared from diethyl 6-ethynyl-1,3-azulenedicarboxylate. Its NMR spectroscopic property was made clear. Furthermore, its reactivity with *o*-substituted aniline was studied, comparing with 1- and 2-ethynyl azulene derivatives. We found that 2-[3-(methoxycarbonyl)azulen-1-yl]ethynyltriphenylphosphonium bromide also reacted with *o*-substituted anilines in $CHCl_3$ to give corresponding 2-[1,3-bis(ethoxycarbonyl)azulen-6-yl]benzoazoles. However, in DMSO another products were obtained.

INTRODUCTION

During the investigation of reaction of phenylethynyltriphenylphosphonium bromide with vicinal dinucleophiles such as *o*-phenylenediamine, *o*-aminobenzenethiol, *o*-aminophenol, and 1,8-diaminonaphthalene, we found nucleophilic addition of these nucreophiles to β-alkyne carbon of phenylethynyltriphenylphosphonium bromide which attached to the phenyl ring, proceeded and followed

---

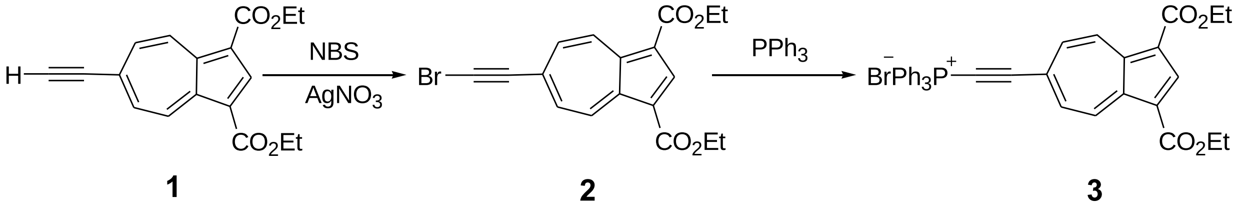
† Dedicated to Professor Dr. Albert Eschenmoser, ETH Zürich on his 85th birthday.

by secondary nucleophilic attack to the same carbon by another functional group to give a corresponding phenyl benzazole or related heterocyclic compound along with methyltriphenylphosphonium bromide.[1] Azulene is characterized as an aromatic hydrocarbon with polarity. In its derivatives, the electronic contribution of azulenyl ring depends on the position of connecting to its functional group. As part of our effort to design novel scaffolds for polyfunctionalyzed azulenes,[2] syntheses and reactivities of similar azulene derivatives to phenylethynyltriphenylphosphonium bromide were carried out. Syntheses of 1- and 2-substituted azulene derivatives such as 2-(2-azulenyl)ethynyltriphenylphosphonium bromide (**6**)[3] and 2-[3-(methoxycrbonyl)azulen-1-yl]ethynyltriphenylphosphonioum bromide (**9**)[4] from the corresponding formylazulene and their reactivity with *o*-substituted anilines and a related compound have been reported.[3,4] Therefore, we have investigated on the corresponding 6-substituted azulene as a part of syntheses of a variety of azulenylethynyltriphenylphosphonium bromides and 2-azulenylbenzoazoles. 6-Ethynyl-1,3-diethoxycarbonylazulene (**1**) could be easily prepared by the palladium-catalyzed coupling reaction of diethyl 6-bromoazulene-1,3-dicarboxylate with trimethylsilylacetylene, followed by desilylation with KF.[2c] We will report herein about the preparation and some interesting properties of 2-[1,3-bis(ethoxycarbonyl)azulen-6-y]ethynyltriphenylphosphonium bromide (**3**).

RESULTS AND DISCUSSION

Synthesis and spectral data of 2-[bis(1,3-ethoxycarbonyl)azulen-6-yl]ethynyltriphenylphosphonium bromide (3)

Due to prepare 6-(2-bromoethynyl)azulene by bromination of corresponding ethynylazulene, C-1 and C-3 positions in azulene ring need to be protected. In addition to this from the synthetic point of view, we select 6-ethynyl-1,3-bis(ethoxycarbonyl)azulene (**1**)[2c] as a starting material. The compound **1** was treated with NBS in the presence of silver nitrate to give 6-(2-bromoethynyl)-1,3-bis(ethoxycarbonyl)azulene (**2**) in 68% yield. It was treated with triphenylphosphine in diethyl ether at room temperature for 3 days to give 2-[1,3-bis(ethoxycarbonyl)azulen-6-yl]ethynyltriphenylphosphonium bromide (**3**) in 99.6% yield.

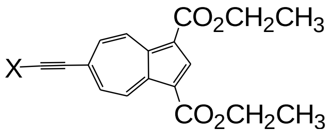


Scheme 1

The IR spectrum of **3** exhibits a strong characteristic absorption of the triple bond at 2174 cm^{-1}. Its wave number is the highest among these of 2-(2-azulenyl)ethynyltriphenylphosphonium bromide (**6**) (2160 cm^{-1}) and 2-[3-(methoxycarbonyl)azulen-1-yl)ethynyltriphenylphosphonium bromide (**9**) (2139 cm^{-1}).

The total polarity of its molecule is the lowest because the azulenyl group works as an electron-withdrawing group. The chemical shifts in ^{1}H- and ^{13}C-NMR spectra of compounds **1**, **2**, and **3** are shown in Tables 1 and 2, respectively. As expected, the chemical shifts of azulene ring protons in **3**

Table 1. Chemical shift in the ^{1}HNMR spectrum of diethyl 6-ethynylazulene-1,3-dicarboxylate derivatives



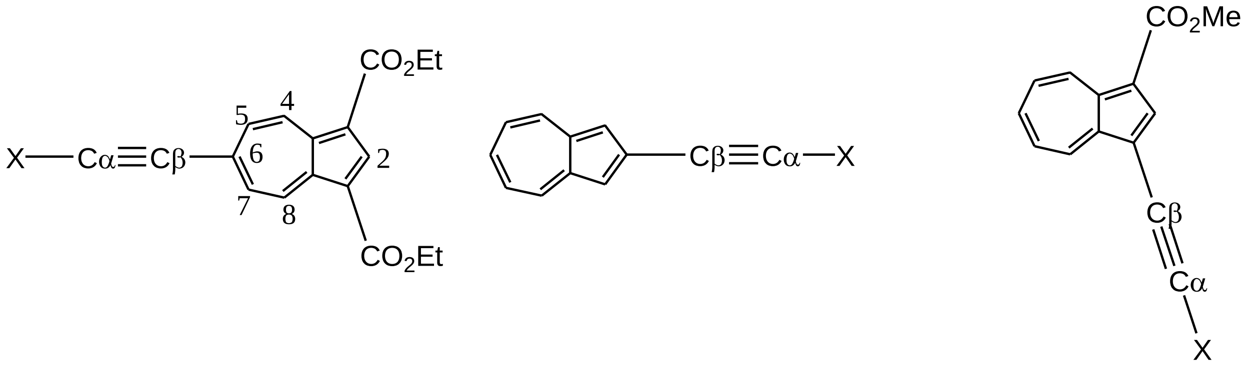
X=	H	Br	PPh_3 Br
2	8.79	8.81	8.98
4 and 8	9.64	9.65	9.79
5 and 7	7.85	7.82	8.23
CH_2	4.43	4.43	4.43
CH_3	1.45	1.45	1.44
Ph			7.78-7.88
≡C−H	3.48		

Table 2. Chemical shift in the ^{13}C NMR spectrum of diethyl 6-ethynylazulene-1,3-dicarboxylate derivatives

X=	H	Br	PPh_3Br
1 and 3	117.13	117.18.	118.76
2	144.09	143.98	147.07
3a and 8a	143.61	143.54	144.46
4 and 8	137.50	135.32	137.69
5 and 7	133.50	133.44	133.45
6	134.68	137.41	127.90(*J*=8.8)
$-C\equiv\underline{C}-X$	82.28	60.20	71.87(*J*=190.95)
$-\underline{C}\equiv C-X$	86.20	83.16	118.43(*J*=28.9)
p-Ph-			136.35(*J*=3.0)
m-Ph-			133.02(*J*=12.1)
o-Ph-			131.14(*J*=14.5)
ipso-Ph -			117.34(*J*=99.7)
$\underline{C}H_3$-CH_2O-	14.52		14.49
CH_3-$\underline{C}H_2O$-	60.20		60.61
-$\underline{C}O_2CH_2CH_3$	164.74		164.23

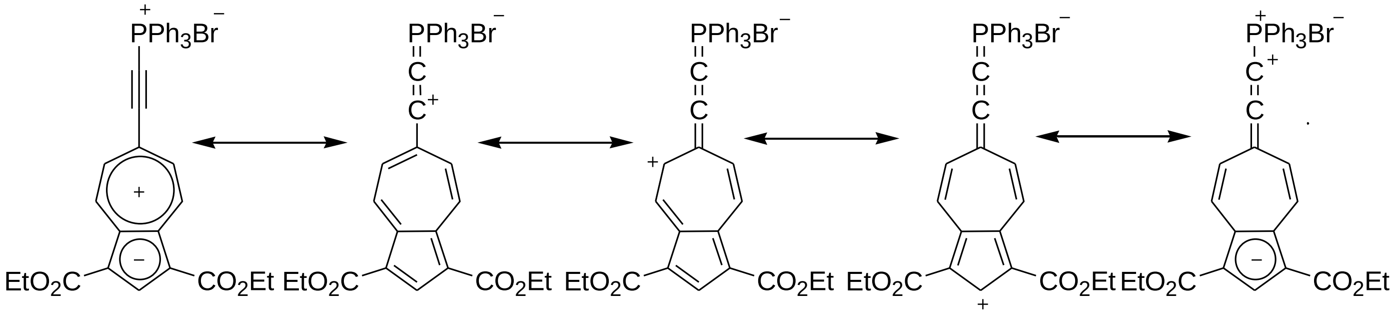
comparing with those of **1** and **2** were shifted to lower field character by 0.14~0.41 ppm. Triphenylphosphonium moiety works as an electron withdrawing group. Especially ring protons of C-5,7 characteristically shifted to lower field by 0.38-0.41 ppm. A similar result has been obtained in 2-(3-methyloxycarbonylazulene-1-yl)ethynyltriphenylphosphonium bromide. The ^{13}C NMR spectrum shows beside C-6 and C-P lower field shifts compared with **1** was observed. These observations were due to the contribution of resonance structures **3b** and **3c**. Electron density of C-2 (Cβ) acetylenic carbon is the lowest among azulenylethynyltriphenylphosphonium bromides. We expect compound **3** was attacked the most easily by nucleophiles.

Table 3. Chemical shifts of acetylenic carbons (Cα and Cβ) of compounds **1**-**9**



	Cα	Cβ
1: X=H,	82.28,	86.20
2: X=Br,	60.20,	83.16
3: $X=P^+(Ph)_3Br^-$	71.87,	118.43
4: X=H,	83.02,	81.80
5: X=Br,	55.77,	78.53
6: $X=P^+(Ph)_3Br^-$,	72.42,	117.67
7: X=H,	81.58,	78.87
8: X=Br,	53.07,	75.43
9: $X=P^+(Ph)_3Br^-$,	72.93,	116.90

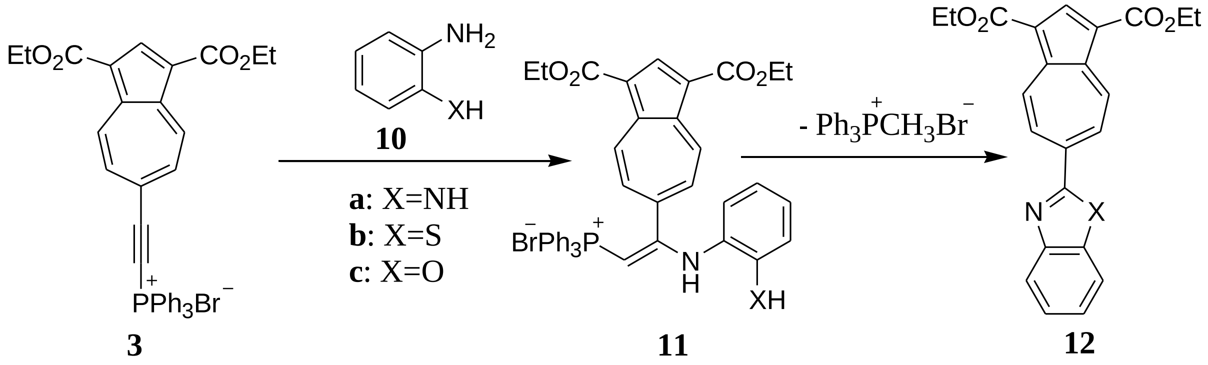
Figure 1. The resonance structures of compound **3**



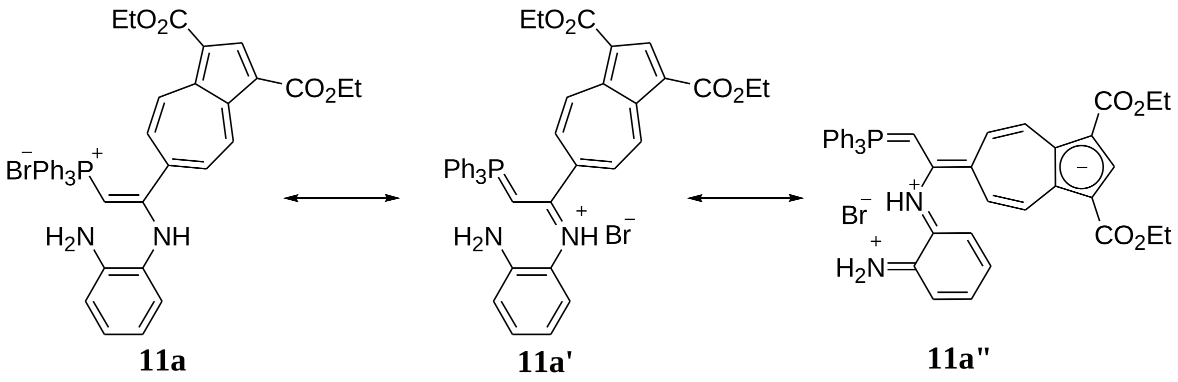
3a **3b** **3c** **3d** **3e**

Reaction of 1,3-diethoxycarbonylazulen-6-ylethynyltriphenylphosphonium bromide (3) with *o*-phenylenediamine and its related compounds in $CHCl_3$

Compounds **3** reacts with *o*-phenylenediamine in dry $CHCl_3$ at refluxing temperature to give a nucleophilic adduct **11a** quantitatively which is easily crystalized. Other nuclophilic adducts in the reaction of azulenylethynyltriphenylphosphonium bromides with *o*-substituted aniline salts were not crystallized. Azulene ring peaks in NMR spectrum of **11a** show little broadening at ca. 30 ˚C due to the contribution of **11a”**. When the temperature was raised to 50 ˚C, broadening peaks become sharp due to increasing the contribution of **11a** and **11a’**. When the refluxing was continued for 50 hrs without isolation of **11a**, **11a** underwent intramolecular cyclization to give a 6-(1*H*-benzimidazol-2-yl)azulene derivative (**12a**) in 34% yield.



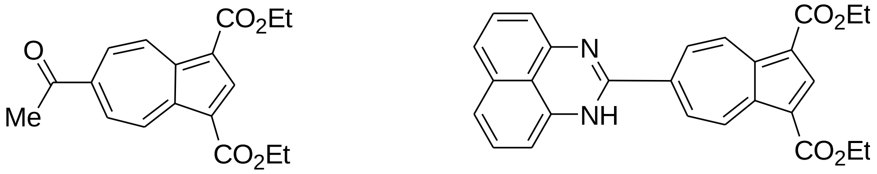
Scheme 2



Scheme 3

The investigation of the reaction of **3** with *o*-aminothiophenol (**10b**) to be expected to give a 6-(benzothiazol-2-yl)azulene derivative (**12b**) was carried out. Consumption of the starting material was observed by thin layer chromatography, but the generation of **12b** and methyltriphenylphosphonium bromide could not be observed. On the contrast to **10b**, *o*-aminophenol (**10c**) gave a

6-(benzoxazol-2-yl)azulene derivative (**12c)** in 29% yield along with 6-acetylazulene (**13**)[5] in 13% yield. By the treatment of the intermediate of the first nucleophilic addition product with sodium hydride or Et_3N, we succeeded to improve a yield of **12c** (44-48%). The phosphonium salt **3** reacts with 1,8-diaminonaphthalene the most smoothly in refluxing $CHCl_3$ under Ar to give diethyl 6-(*1H*-perimidin-2-yl)azulene-1,3-dicarboxylate (**14**) in 87% yield.



13 **14**

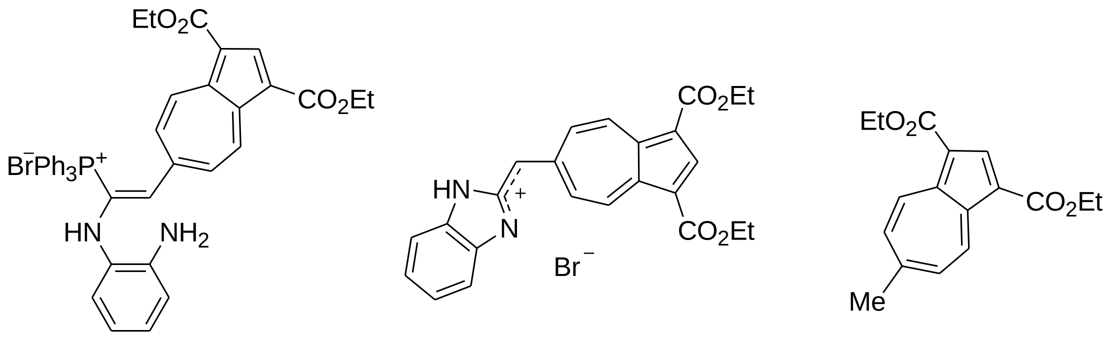
Figure 2

Cyclic voltammetry of heteroaryl azulenes

To clarify the effect to electrochemical behavior of azulene ring by the benzoazol, by using cyclic voltammetry (CV) and differential pulse voltammetry (DPV), obtained heteroaryl azulenes **12a**, **12c**, and **14** were examined. One reversible reducing waves of the azulene itself exhibits at -1.54 V at should correspond to one single-electron transfers. 6,6'-Biazulenyl exhibits two half-waves at -1.09 and -1.32 V.[6] Although the CV spectrum in **12a** could not be observed a clear redox wave, **12c** and **14** exhibited the reduction potentials $E_{1/2}$ (1) at -1.15 and -1.23 V, respectively. They also exhibit irreversible reduction potential higher voltage at -1.73 (**12c**), -1.59 and -1.90 volt (**14**), respectively. That is there is a possibility of stable anion radicals in compounds **12c** and **14**.

Reaction of 3 with 10a in DMSO

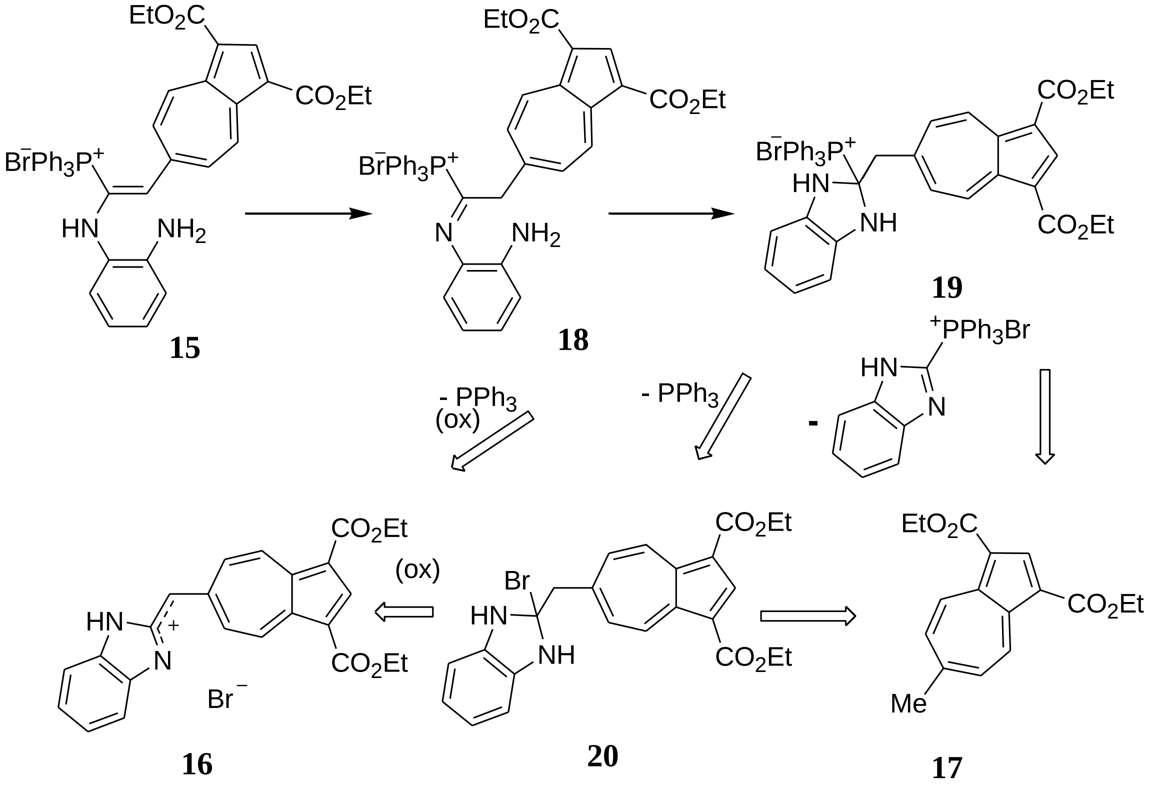
In order to investigate the cyclization of **11a** over the temperature 60 ˚C, dimethylsulfoxide was used as a reaction solvent. After mixing **3** and **10a** in DMSO, a heterocyclic product was not observed until 80 ˚C on the TLC. After heating at 100 ˚C for 2h, three compounds were isolated by column chromatography on silica gel and GPC. One of them is recovered compound **3** (6%). Although the other products could not be purified completely, we assigned compounds **15** (7%) and **16** (18%) as these structures shown in Figure 3 on the basis of their ^1H NMR spectra as shown in **Experimental** section. Heating was carried out higher temperature at 120˚C for 2 h to give known diethyl 6-methylazulene-1,3-dicarboxylate (**17**)[7] in 8% yield. These observations suggested that nucleophilic attack of **10a** to **3** occurred at different acetylene carbon C_α in DMSO.



15 **16** **17**

Figure 3

Since the contribution of resonance structure **3e** in DMSO increases, we could suppose that there ia a possibility of following reaction as shown in Scheme 4. The strong nucreophile **10a** attacks to Cα of **3** followed by the second attack to the same Cα to give **19** or isomerization to **18** then nucreophilic attack at the same carbon to give **19**. Elimination of triphenylphosphonium part from **19** along with oxidation directly or via **20** gives **16**. Then the elimination of benzimidazole part from **19** or via **16** or **20** gives **17**. At least compound **3** undergoes another reaction with **10a** in DMSO compared with the experiment in $CHCl_3$



Scheme 4

CONCLUSION

2-[1,3-Bis(ethoxycarbonyl)azulen-6-yl]ethynyltriphenylphosphonium bromide was prepared from corresponding 6-ethynylazulene by two steps in an excellent total yield. Michael type adducts could be isolated for the first time in azulene derivatives. We find that reaction of **3** with **10a** is depends on the solvent effect. The position of nucleophilic addition is different between the case of $CHCl_3$ and DMSO. We supposed that the polarity of azulene regulates the position of nucleophilic addition in DMSO. The yield of cyclized products increases by the addition of sodium hydride or Et_3N to reaction intermediate. The some obtained compounds exhibit a reversible reduction wave. This procedure is applicable for the synthesis of heteroarylazulenes.

EXPERIMENTAL

General Information. Melting points were determined on a Yanaco micro melting point apparatus and are uncorrected. IR spectra were taken on a Shimadzu FTIR-8100M or a Hitachi 270-30 spectrophotometer and UV spectra were measured on a Hitachi U-3410 spectrophotometer. ^{1}H NMR spectra (^{13}C NMR spectra) were recorded on JEOL LAMBDA 400 (100 MHz) and 600 (150 MHz). MS spectra were measured on a JEOL HX-110 or a Hitachi M-2500 instrument usually at 70 eV. Voltammetry measurements were carried out with a BAS 100B/W electrochemical workstation equipped with Pt working and auxiliary electrodes and a reference electrode formed from $Ag/AgNO_3$ (0.01 M) in acetonitrile containing tetrabutylammonium perchlorate (0.1 M). These results were described in **Results and Discussion**. Elemental analyses were performed at the Instrumental Analysis Center of Chemistry, Faculty of Science, Tohoku University.

Diethyl 6-(2-bromoethynyl)azulene-1, 3-dicarboxylate (2)

To a stirred solution of diethyl 6-ethynylazulene-1,3-dicarboxylate (1) (1.0 mg, 3.37 mmol) in acetone (85 ml), $AgNO_3$ (688 mg, 4.05 mmol) was added at rt under Ar and the solution was stirred for 30 min under Ar. The solution of *N*-bromosuccinimide (721 mg, 4.05 mmol) in acetone (170 mL) was added and stirred for 5 h. After addition of Et_2O (40 mL) to the suspension, precipitates were removed by filtration and the residue was washed with acetone until the washing was no longer colored. The ice water (40 mL) was added to the filtrate with stirring and extracted with 200 mL portion of Et_2O twice, then dried with anhydrous $MgSO_4$, evaporated under reduced pressure. Purification of resulting residue by column chromatography (silica gel, CH_2Cl_2) gave diethyl 6-(2-bromoethynyl)azulene-1,3-dicarboxylate (**2**) as purple crystals (858 mg, 68%).

2: Violet needles (CH_2Cl_2/*n*-hexane); mp 165.8-166.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.65 (2H, d, J =

11.2 Hz, H-4, 8), 8.81 (1H, s, H-2), 7.82 (2H, d, *J* = 11.2 Hz, H-5, 7), 4.43 (4H, q, *J* = 7.2 Hz, $\text{-CO}_2\text{C}\underline{\text{H}_2}\text{CH}_3$), 1.45 (6H, t, *J* = 7.2 Hz, $\text{-CO}_2\text{CH}_2\text{C}\underline{\text{H}_3}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.76 ($\underline{\text{C}}\text{O}_2\text{Et}$), 143.98 (Az-2), 143.54 (Az-3a, 8a), 137.41 (Az-6), 135.32 (Az-4, 8), 133.44 (Az-5, 7), 117.18 (Az-1, 3), 83.16 (Az-$\underline{\text{C}}$CBr), 60.20 (Az-C$\underline{\text{C}}$Br), 57.14 ($\text{CO}_2\underline{\text{C}}\text{H}_2\text{CH}_3$), 14.52 ($\text{CO}_2\text{CH}_2\underline{\text{C}}\text{H}_3$); IR (KBr) ν_{max} 2974 (w), 2187 (m), 1699 (s), 1686 (s), 1583 (w), 1568 (w), 1543 (w), 1477 (w), 1464 (m), 1433 (s), 1414 (w), 1390 (m), 1377 (w), 1356 (w), 1307 (w), 1240 (w), 1207 (s), 1186 (s), 1107 (w), 1089 (m), 1082 (m), 1045 (m), 1032 (w), 981 (m), 871 (w), 852 (w), 763 (w), 661 cm^{-1} (w); MS (EI, 70eV) m/z 376 (M^++1, 100%), 375 (M^+, 19.64), 374 (99.5), 331.9 (9.0), 330.9 (48.7), 329.9 (9.5), 328.9 (47.7), 304 (16.7), 303 (38.6), 302 (18.5), 301 (39.8), 296 (10.5), 258.9 (7.9), 257 (9.2), 251.2 (6.5), 230 (6.4), 218.9 (6.8), 216.9 (8.3), 150 (8.9), 138.1 (7.8); ES (CH_2Cl_2) 218.6 (log ε 4.85), 220.9 (4.89), 227.0 (4.50), 263.8 (4.25) sh, 270.2 (4.25) sh, 328.1 (4.87), 347.0 (4.30), 358.8 (4.27) sh, 367.1 (4.28), 380.9 (3.61), 539.0 (2.78), 574.2 (2.70) sh, 626.0 nm (2.20); Anal. Calcd (%) for $C_{18}H_{15}BrO_4$: C, 57.62, H, 4.03, Br, 21.30. Found: C, 57.76, H, 4.15, Br, 21.53.

2-[1,3-Bis(ethoxycarbonyl)azulen-6-yl]ethynyltriphenylphosphonium bromide (3)

A suspension of diethyl 6-bromoethynylazulene-1,3-dicarboxylate (**2**) (416 mg, 1.11 mmol) and triphenylphosphine (349 mg, 1.33 mmol) in absolute Et_2O (20 mL) was stirred for 3 days at rt under Ar. The green precipitate was collected by filtration, washed with Et_2O and dried thoroughly in vacuo to give pure **3** (705.5 mg, 99.6%).

3: Green powder; mp 129.3-132.9 °C (decomp.); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (2H, d, *J* = 10.0 Hz, Az-4,8), 8.98 (1H, s, Az-2), 8.23 (2H, d, *J* = 10.0 Hz, Az-5,7), 7.78-7.88 (15H, m, Ph-H), 4.43 (4H, q, *J* = 7.2 Hz, $\text{-CO}_2\text{C}\underline{\text{H}_2}\text{CH}_3$), 1.44 (6H, t, *J* = 7.2 Hz, $\text{-CO}_2\text{CH}_2\text{C}\underline{\text{H}_3}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.23 ($\underline{\text{C}}\text{O}_2\text{Et}$), 147.07 (Az-2), 144.46 (Az-3a, 8a), 137.69 (Az-4, 8), 136.35 (d, *J* = 3.0 Hz, *p*-Ph), 133.02 (d, *J* = 12.1 Hz, *m*-Ph), 131.14 (d, *J* = 14.5 Hz, *o*-Ph), 133.45 (Az-5 or 7), 127.90 (d, *J* = 8.8 Hz, Az-6), 118.76 (Az-1, 3), 118.43 (d, *J* = 28.9 Hz, Az-$\underline{\text{C}}$≡C-P), 117.34 (d, *J* = 99.7 Hz, *ipso*-Ph), 71.87 (d, *J* = 190.95 Hz, Az-C≡$\underline{\text{C}}$-P), 60.61 ($\text{CO}_2\underline{\text{C}}\text{H}_2\text{CH}_3$), 14.49 ($\text{CO}_2\text{CH}_2\underline{\text{C}}\text{H}_3$); IR (KBr) ν_{max} 3055 (w), 2984 (w), 2174 (s), 1693 (s), 1583 (w), 1568 (w), 1543 (w), 1477 (w), 1464 (w), 1437 (s), 1406 (w), 1390 (m), 1236 (m), 1213 (s), 1188 (s), 1111 (s), 1068 (w), 1037 (m), 995 (w), 850 (w), 827 (m), 762 (m), 727 (m), 688 (m), 571 (w), 542 (w), 524 (s), 482 cm^{-1} (w); ES (CH_2Cl_2) λ_{max} 219.3 (log ε 5.15), 226.3 (5.21), 261.8 (4.44) sh, 269.5 (4.34) sh, 315.3 (4.77) sh, 327.8 (5.01), 350.5 (4.15) sh, 361.0 (4.22), 369.4 (4.26), 591.1(2.67), 640.1 (2.55) sh, 720.4 nm (1.97) sh; Anal. Calcd (%) for $C_{36}H_{30}BrO_4P\cdot4/5H_2O$: C, 66.33, H, 4.89. Found: C, 66.50, H, 5.13.

2-(2-Aminophenylamino)-2-[1,3-di(ethoxycarbonyl)azulen-6-yl]ethynyl]triphenylphosphonium bromide (11a)

To a stirred solution of **3** (100 mg, 0.157 mmol) in $CHCl_3$ (10 mL), *o*-phenylenediamine (**10a**) (22.8 mg, 0.211mmol) was added and stirred for 1 h at rt. The reaction mixture was evaporated under reduced pressur. Resulting residue was dissolved in a small portion of CH_2Cl_2 and Et_2O was added. Aroused brown precipitate was collected by filtration and dried in vacuo to produce **11a** (122.9 mg, 94%).

11a: Brown powder (CH_2Cl_2 / Et_2O), mp 146-147.5 ˚C (decomp.), ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.07 (2H, d, *J* = 10.4 Hz, Az-4, 8), 8.73 (1H, s, Az-2), 7.27-7.75 (21H, m), 4.38 (4H, q, *J* = 7.2 Hz, $-CO_2C\underline{H_2}CH_3$), 1.43 (6H, *J* = 7.2 Hz, $-CO_2CH_2C\underline{H_3}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.67, 164.39, 144.47, 143.55, 143.26, 138.05, 137.31, 135.01, 33.51, 133.27, 133.22, 133.16, 133.11, 130.39, 130.26, 129.59, 129.46, 124.10, 121.03, 119.47, 118.59, 117.80, 116.66, 60.16, 14.43; IR (KBr) ν_{max}3400 (m), 3206 (w), 3058 (w), 2980 (m), 2938 (w), 2905 (w), 1690 (s), 1624 (m), 1578 (m), 1560 (m), 1541 (m), 1512 (m), 1501(m), 1483 (m), 1435 (s), 1412 (m),1391 (m), 1364 (w), 1352 (w), 1341 (w), 1314 (w), 1238 (m), 1212 (s), 1161 (w), 1107 (m), 1076, 1036 (m), 997 (w), 988 (w), 930 (w), 907 (w), 853 (w), 820 (w), 750 (m), 721 (m), 693 (m), 669 (w), 633 (w), 615 (w), 572 (w), 556 (w), 542 (w), 519 (m), 498 (w), 478 (w), 409 cm^{-1} (w); ES (CH_2Cl_2) λ_{max} 268 (log ε 4.49), 314 (4.61), 382 (4.06), 430 (3.05) sh, 466 (2.99) sh, 523 (2.88) sh, 565 nm (2.70); Anal. Calcd (%) for $C_{42}H_{38}N_2O_4BrP \cdot 4/5H_2O$: C, 66.47, H, 5.37, N, 3.73. Found: C, 66.37, H, 5.25, N, 3.69.

Diethyl 6-(*1H*-benzimidazol-2-yl)azulene-1,3-dicarboxylate (12a)

To a stirred solution of **3** (200 mg, 0.314 mmol) in $CHCl_3$ (10 mL), **10a** (40.8 mg, 0.377 mmol) was added and refluxed for 50 h under Ar. The reaction mixture was evaporated under reduced pressure and small portion of THF was added. The resulting suspension was filtered and the filtrate was evaporated under reduced pressure. The resulting residue was purified by column chromatography (silica gel, AcOEt), followed by GPC ($CHCl_3$) afford crude cyclized compound diethyl 6-(*1H*-benzimidazol-2-yl)azulene-1,3-dicarboxylate (**12a**). Recrystallization of this crude product from toluene gave **12a** (41.1 mg, 34%).

12a: Brown crystals (toluene); mp 256.8-259.2 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.47 (1H, br, NH), 9.71 (2H, d, *J* = 11.2 Hz, Az-4,8), 8.80 (2H, d, *J* = 11.2 Hz, Az-5,7), 8.60 (1H, s, Az-2), 7.78 (1H, d, *J* = 6.4 Hz, Benzo-H$_a$), 7.63 (1H, d, *J* = 6.8 Hz, Benzo-H$_a$), 7.33-7.28 (2H, m, Benzo-H$_b$), 4.36 (4H, q, *J* = 7.2 Hz, $CO_2C\underline{H_2}CH_3$), 1.38 (6H, t, *J* = 7.2 Hz, $CO_2CH_2C\underline{H_3}$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.76 ($-\underline{C}O_2Et$), 151.31, 144.08, 142.60, 142.42, 141.40, 137.96, 135.88, 128.91, 124.30, 122.77, 119.77, 115.99, 112.07, 51.90 (-CO$_2$<u>C</u>H$_2$CH$_3$), 14.34 (-CO$_2$CH$_2$<u>C</u>H$_3$); MS (EI, 70eV) m/z 389.1 (M$^+$+1, 7.77 %), 388.1 (M$^+$, 100), 343 (31.5), 316.1 (12.8), 315 (14.9), 270.9 (5.7), 242 (5.3); IR (KBr) ν_{max} 3544 (w), 3333 (m), 3056 (w), 2984 (m), 2940 (w), 2905 (w), 2872 (w), 1696 (s), 1661 (s), 1590 (s), 1520 (w), 1480 (w), 1435 (s), 1393 (s), 1364 (w), 1350 (w), 1314 (w), 1262 (w), 1213 (s), 1148 (w), 1109 (w), 1084 (m), 1069 (m), 1040 (s), 995 (w), 866 (w), 801 (w), 766 (m), 743 (m), 654 (w), 604 (w), 505 (w), 450 cm^{-1} (w); ES (THF) λ_{max} 236.2 (log ε 4.58), 261.8 (4.18) sh, 307.0 (4.28), 359.1 (4.52), 374.8 (4.50), 404.2 (4.43), 567.4 (2.83), 630.5 nm (2.15) sh; Anal. Calcd (%) for $C_{23}H_{20}N_2O_4$: C, 71.12, H, 5.19, N, 7.21. Found: C, 71.27, H, 5.34, N, 7.21.

Diethyl 6-(benzoxazol-2-yl)azulene-1,3-dicarboxylate (12c)

To a stirred solution of **3** (100 mg, 0.157 mmol) in CHCl$_3$ (10 mL), *o*-aminophenol (**10c**) (20.6 mg, 0.188 mmol) was added and refluxed for 13 days under Ar. The reaction mixture was evaporated under reduced pressure. The resulting residue was purified by column chromatography (silica gel, AcOEt) and GPC (CHCl$_3$) to give diethyl 6-(benzoxazol-2-yl)azulene-1,3-dicarboxylate (**12c**) (17.4 mg, 29%) and diethyl 6-acetylazulene-1,3-dicarboxylate (**13**) (6.3 mg, 13%).

12c: Brown-purple needles (CH$_2$Cl$_2$/*n*-hexane); mp 207.2-210.1 °C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.88 (2H, d, *J* = 10.4 Hz, Az-4, 8), 8.89 (1H, s, Az-2), 8.82 (2H, d, *J* = 10.4 Hz, Az-5,7), 7.86 (1H, d, *J* = 6.8 Hz, Benzo-H$_a$), 7.67 (1H, d, *J* =7 .6 Hz, Benzo-H$_a$), 7.46-7.41 (2H, m, Benzo-H$_b$), 4.46 (4H, q, *J* = 7.2 Hz, CO$_2$C<u>H</u>$_2$CH$_3$), 1.48 (6H, t, *J* = 7.2 Hz, CO$_2$CH$_2$C<u>H</u>$_3$); ^{13}C NMR (100 MHz, CDCl$_3$) δ 164.75 (-<u>C</u>O$_2$Et), 163.11 (Az-<u>C</u>=N), 151.54, 145.29, 144.17, 142.27, 138.14, 136.87, 128.63, 126.67, 125.37, 120.89, 117.43, 111.06, 60.31 (-CO$_2$<u>C</u>H$_2$CH$_3$), 14.56 (-CO$_2$CH$_2$<u>C</u>H$_3$); IR (KBr) ν_{max} 3586 (w), 3565 (w), 3061 (w), 2982 (w), 2940 (w), 2905 (w), 2872 (w), 1688 (s), 1586 (w), 1528 (w), 1474 (w), 1431 (s), 1391 (m), 1379 (w), 1350 (w), 1235 (s), 1204 (s), 1111 (w), 1075 (m), 1046 (s), 988 (m), 868 (w), 801 (w), 769 (w), 743 (m), 659 (w), 602 cm^{-1} (w); ES (CH$_2$Cl$_2$) λ_{max} 240.4 (log ε 4.54), 271.1 (4.09), 311.1 (4.32) sh, 352.4 (4.59), 372.6 (4.52), 395.0 (4.35), 498.6 (2.76) sh, 547.3 (2.83), 591.8 nm (2.71) sh; MS (EI, 70eV) m/z 389.0 (M$^+$, 100%), 345.0 (9.99), 344.1 (38.12), 317.0 (16.02), 316.0 (29.58), 272.0 (7.51), 232.0 (4.57), 158.0 (4.23); Anal. Calcd (%) for $C_{23}H_{19}NO_5$: C, 70.94, H, 4.92, N, 3.60. Found: C, 70.94, H, 4.99, N, 3.63.

13:[6] mp 129-130 ˚C (from EtOH); ^{1}H NMR (400 MHz, CDCl$_3$) δ 9.87 (2H, d, *J* = 11.0 Hz, Az-4, 8), 8.94 (1H, s, Az-2), 8.33 (2H, d, *J* = 11.3 Hz, Az-5, 7), 4.46 (4H, q, *J* = 7.2 Hz, CO$_2$C<u>H</u>$_2$CH$_3$), 2.82 (3H, s, COC<u>H</u>$_3$), 1.47 (6H, t, *J* = 7.2 Hz, CO$_2$CH$_2$C<u>H</u>$_3$); MS (EI, 70eV) m/z 314.1 (M$^+$, 100), 270.1 (10.7), 269.0 (59.8), 242.1 (18.0), 241.1 (31.6), 197.1 (9.6), 170.1 (5.9).

Reaction of 3 and 10c in presence of sodium hydride

To a stirred solution of **3** (50 mg, 0.079 mmol) in $CHCl_3$ (10 mL), **10c** (10.5 mg, 0.094 mmol) was added and refluxed for 2 h under Ar. To the reaction mixture, after cooling to rt, was added sodium hydride (50%, 4.6 mg, 0.096 mmol) and refluxed for 8 h. Reaction mixture was evaporated under reduced pressure and resulting residue was purified by column chromatography (silica gel, AcOEt) and GPC ($CHCl_3$) to give **12c** (13.3 mg, 44%).

Reaction of 3 and 10c in the presence of triethylamine

To a stirred solution of **3** (50 mg, 0.079 mmol) in dry CH_2Cl_2 (10 mL), **10c** (10.3 mg, 0.094 mmol) was added and refluxed for 1 h under Ar. To the reaction mixture, after cooling to rt, triethylamine (9.4 mg, 0.095 mmol) was added and refluxed for 22 h. Reaction mixture was evaporated under reduced pressure and resulting residue was purified by column chromatography (silica gel, AcOEt) and GPC ($CHCl_3$) to give **12c** (14.8 mg, 0.038 mmol, 48%).

Diethyl 6-(*1H*-perimidin-2-yl)azulene-1,3-dicarboxylate (14)

To a stirred solution of **3** (100 mg, 0.157 mmol) in $CHCl_3$ (10 mL), 1,8-diaminonaphyhalene (29.8 mg, 0.188 mmol) was added and refluxed for 1 h under Ar. The reaction mixture was evaporated under reduced pressure and small portion of THF was added. The resulting suspension was filtered and the filtrate was evaporated under reduced pressure. The resulting residue was purified by column chromatography (silica gel, CH_2Cl_2), to give diethyl 6-(*1H*-perimidin-2-yl)azulene-1,3-dicarboxylate (**14**) (59.9 mg, 0.137 mmol, 87%).

14: Deep green crystals (CH_2Cl_2 / *n*-hexane) mp 129.0-131.7 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.74 (2H, d, *J* = 11.2 Hz, Az-4, 8), 8.67 (1H, s, Az-2), 8.40 (2H, d, *J* = 10.8 Hz, Az-5. 7), 7.19-7.07 (4H, m, perimidine-$H_{b,\,c}$), 6.61 (2H, br, perimidine-H_a), 4.37 (4H, q, *J* = 7.2 Hz, $CO_2C\underline{H}_2CH_3$), 1.38 (6H, t, *J* = 7.2 Hz, $CO_2CH_2C\underline{H}_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.68 (-$\underline{C}O_2Et$), 154.73, 145.11, 143.41, 143.10, 138.02, 134.99, 129.63, 128.51, 121.46, 119.20, 116.00, 59.95 (-$CO_2\underline{C}H_2CH_3$), 14.32 (-$CO_2CH_2\underline{C}H_3$); MS (EI, 70 eV) m/z 438.0 (M^+, 100%), 365.1 (3.69), 292.0 (6.25), 291.0 (3.88), 182.5 (14.89); IR (KBr) ν_{max} 3366 (w), 3052 (w), 2980 (w), 2932 (w), 2905 (w), 1694 (s), 1678 (s), 1657 (m), 1636 (m), 1595 (s), 1566 (w), 1526 (w), 1478 (m), 1435 (s), 1410 (m), 1393 (m), 1374 (m), 1354 (w), 1339 (w), 1291 (w), 1240 (m), 1211 (s), 1165 (w), 1098 (w), 1073 (w), 1042 (m), 1034 (m), 986 (w), 871 (w), 837 (w), 824 (w), 764 (m), 719 (w), 666 (w), 648 (w), 586 cm^{-1} (w); ES (THF) λ_{max} 235.9 (log ε 4.79), 270.2 (4.30), 320.7 (4.78), 350.2 (4.42) sh, 377.0 (4.06) sh, 553.4 nm (3.41); Anal. Calcd (%) for $C_{27}H_{22}N_2O_4$: C, 73.96, H, 5.06, N, 6.39. Found: C, 73.66, H, 5.34, N, 6.35.

Reaction of 3 with 10a in DMSO at 100 ˚C

To a stirred solution of **3** (100 mg, 0.157 mmol) in DMSO (10 mL), **10a** (20.4 mg, 0.188 mmol) was added and stirred at 100 °C for 8 h. The reaction mixture was poured into the water and extracted with AcOEt. The extract was dried with anhydrous $MgSO_4$ and evaporated under reduced pressure. The resulting residue was purified by column chromatography (silica gel, AcOEt), followed by GPC ($CHCl_3$). However, we could not get pure **15** and **16** enough for elemental analysis. Crude 1-(2-aminophenylamino)-2-(1,3-diethoxycarbonylazulen-6-yl)vinyltriphenylphosphonium bromide (**15**) (8 mg, 6%) and cyclized compound **16** (13 mg, 17%).

15: ^{1}H NMR (400MHz, $CDCl_3$) δ 9.80 (2H, d, *J* = 10.8 Hz, Az-4,8), 8.80 (1H, s, Az-2), 8.20-8.23 (1H, m, vinyl-H), 7.99 (2H, d, *J*=10.8 Hz, Az-5,7), 7.52-7.75 (19H, m, Benzo-H, Ph-H), 5.27 (br, NH or NH_2), 4.43 (4H, q, *J* = 7.2 Hz, $CO_2C\underline{H}_2CH_3$), 1.45 (6H, t, *J* = 7.2 Hz, $-CO_2CH_2C\underline{H}_3$).

16: ^{1}H NMR (400MHz, $CDCl_3$) δ 9.95 (2H, d, *J* = 11.2 Hz, Az- 4, 8), 9.45 (1H, s, vinyl-H), 8.92 (1H, s, Az-2), 8.51 (2H, d, *J* = 11.2 Hz, Az-5, 7), 8.38 (1H, s, NH), 8.20-8.27 (1H, m, Benzo-H), 8.11 (1H, d, *J*=9.0 Hz, Benzo-H), 7.95 (1H, d, *J* = 8.8 Hz, Benzo-H), 7.84-7.91 (1H, m, Benzo-H); MS (EI, 70eV) m/z 481 (M^++1, 27.5%), 480.1 (M^+, 100), 479.2 (27.8), 478.1 (98.5), 435.0 (30.4), 432.8 (28.4), 407.8 (13.2), 406.9 (22.2), 406.0 (13.4), 404.8 (20.8), 401.1 (19.5), 400.1 (75.2), 355.1 (24.5), 328.0 (10.9), 327.0 (16.7), 253.1 (10.6).

Reaction of 3 with 10a in DMSO at 120 °C

To a stirred solution of **3** (100 mg, 0.157 mmol) in DMSO (10 mL), **10a** (20.4 mg, 0.188 mmol) was added and stirred at 120 °C for 2 h. The reaction mixture was poured into the water and extracted with AcOEt. The extract was dried with anhydrous $MgSO_4$ and evaporated under reduced pressure to give 27.3 mg of reaction mixture. It was purified by short column chromatography (silica gel, AcOEt) to give diethyl 6-methyl-1,3-azulenedicarboxylate (**17**) (3.7 mg, 8%).[7]

17: MS (EI, 70eV) m/z 287.0 (M^++1, 18.1 %), 286.1 (M^+, 100), 271 (2.6), 258 (5.4), 242 (12.4), 241.1 (68.8), 215.1 (3.7), 214.1 (24.1), 213.1 (50.9), 187 (1), 186 (6.5), 169 (10.3), 142.1 (5.1), 139 (11.1).

REFERENCES

1. (a) H. G. Viehe and Franchimont, *Chem. Ber.*, 1962, **95**, 319; (b) S. I. Miller, C. E. Orzech, C. A. Welch, G. R. Ziegler, and J. I. Dickstein, *J. Am. Chem. Soc.*, 1962, **84**, 2020; (c) H. Hoffmann and H. Förster, *Tetrahrdron Lett.*, 1964, **5**, 983; (d) S. I. Miller and J. Dickstein, *Acc. Chem. Res.*, 1976, **9**,

358; (e) N. Morita, J. Dickstein, and S. I. Miller, *J. Chem. Soc., Perkin Trans. 1*, 1979, 2103.

2. (a) T. Asao, S. Ito, and N. Morita, *Tetrahedron Lett.*, 1988, **29**, 2839; (b) S. Ito, S. Kikuchi, N. Morita, and T. Asao, *J. Org. Chem.*, 1999, **64**, 5815; (c) S. Ito, H. Inabe, T. Okujima, N. Morita, M. Watanabe, N. Harada, and K. Imafuku, *J. Org. Chem.*, 2001, **66**, 7090; (d) S. Ito, T. Okujima, and N. Morita, *J. Chem. Soc., Perkin Trans. 1*, 2002, 1896; (e) S. Ito, A. Nomura, N. Morita, C. Kabuto, H. Kobayashi, S. Maejima, K. Fujimori, and M. Yasunami, *J. Org. Chem.*, 2002, **67**, 7295; (f) S. Ito, H. Inabe, N. Morita, K. Ohta, T. Kitamura, and K. Imafuku, *J. Am. Chem. Soc.*, 2003, **125**, 1669; (g) S. Ito, M. Ando, A. Nomura, N. Morita, C. Kabuto, H. Mukai, K. Ohta, J. Kawakami, A. Yoshizawa, and A. Tajiri, *J. Org. Chem.*, 2005, **70**, 3939.
3. S. Ito, S. Moriyama, T. Shoji, M. Nakashima, M. Watanabe, T. Kubo, M. Yasunami, K. Fujimori, and N. Morita, *Heterocycles*, 2003, **61**, 339.
4. N. Morita, S. Moriyama, T. Shoji, M. Nakashima, M. Watanabe, S. Kikuchi, M. Yasunami, S. Ito, and K. Fujimori, *Heterocycles*, 2004, **64**, 305.
5. T. Nozoe, K. Takase, and M. Tada, *Bull. Chem. Soc. Jan.*, 1963, **36**, 1010.
6. S. Hünig, and B. Ort, M. Hanke, C. Jutz, T. Morita, K. Takase, Y. Fukazawa, M. Aoyagi, and S. Itô, *Liebigs Ann. Chem.*, 1984, 1952.
7. (a) N. Abe, T. Morita, and K. Takase, *Tetrahedron Lett.*, 1973, 3883; (b) T. Morita, N. Abe, and K. Takase, *J. Chem. Soc., Perkin Trans. 1*, 2000, 3063.