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SYNTHESIS OF AZULEN-3-YLHETEROCYCLIC COMPOUNDS USING 2-(3-METHOXYCARBONYLAZULEN-1-YL)ETHYNYLTRIPHENYL-PHOSPHONIUM BROMIDE

Noboru Morita,[a)]* Shiro Moriyama,[a)] Taku Shoji,[a)] Masashi Nakashima,[a)] Masataka Watanabe,[b)] Shigeru Kikuchi,[c)] Shunji Ito,[d)] and Kunihide Fujimori.[e)]

[a)] Department of Chemistry, Graduate School of Science, Tohoku University, 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)] Department of Chemistry, Kumamoto University, Kurokami 2-39-1, Kumamoto 860-8555, Japan
[d)] Department of Materials 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

Abstract – 3-(3-methoxycarbonylazulen-1-yl)ethynyltriphenylphosphonium bromide was prepared from methyl 3-formylazulenecarboxylate. Its resonance structures were discussed on the basis of the ^{1}H and ^{13}C NMR spectroscopy. Furthermore, its reactivity with *o*-substituted aniline was examined. We found that 2-(1-methoxycarbonyl-azulen-3-yl)ethynyltri-phenylphosphonium bromide reacted with *o*-substituted aniline except 2-aminophenol to give corresponding methyl 3-(benzazol-2-yl)azulene-1-carboxylate.†

INTRODUCTION

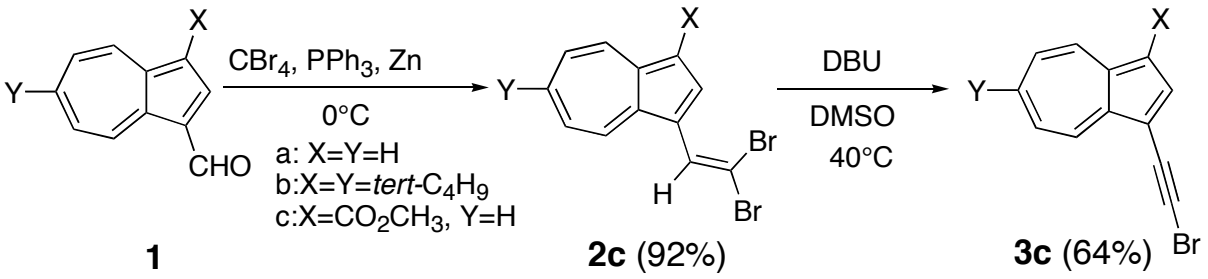
The well-known Corey-Fuchs reaction[1] originally developed by Makekvie[2] has been used largely for the synthesis of variety of ethynyl derivatives. It is also a convenient method for preparation of bromoethynyl derivatives which could convert to ethynylphosphonium bromide.[3] As part of our effort to design novel scaffolds for polyfunctionalyzed azulenes,[4] we have

† This paper is dedicated to Dr. Pierre Potier on the occasion of his 70th birthday.

previously reported the synthesis of 2-(2-azulenyl)ethynyltriphenylphosphonium bromide from 2-formylazulene and its reactivity with *o*-substituted anilines and relativecompounds.[5] We found that 2-formylazulene could be easily access to 2-(2-azulenyl)ethynyltriphenylphosphonium bromide by Corey-Fuchs reaction and subsequent treatment with triphenylphosphine. Moreover, the phosphonium salt was transformed into azulenylbenzoazoles. However, such approaches are expected to take more advantage in the synthesis of 2-(1- or 3-azulenyl)-ethynyltriphenylposponium bromide because 1- or 3-formylazulen is easy to access from azulene or 1-substituted azulenes by the Vilsmeier reaction. Our focus has been to explore novel 1-azulenylethynyltriphenylposponium bromides and the synthetic routes to heterocyclic compounds comprised azulene and benzoazol rings with functional properties.

RESULTS AND DISCUSSION

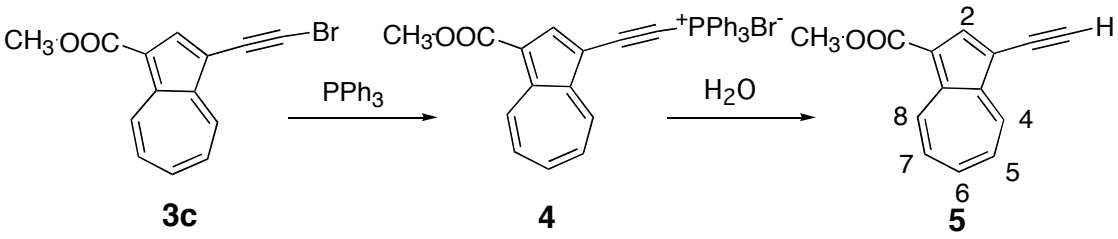
Synthesis of 2-(3-methoxycarbonylazulen-1-yl)ethynyltriphenylphosphonium bromide (4)



Scheme 1.

It was well known that compound (**1a**) could be easily obtained in high yields by formylation of parent azulene by Vilsmeier reaction. The reaction of **1a** with tetrabromomethane in the presence of triphenylphosphine seems to give a corresponding bromide (**2a**), which could not be isolated due to polymerization during concentration of reaction mixture. Therefore, without isolation, a solution of reaction mixture of dibromide (**2a)** was treated with DBU, but **3**a could not be isolated because of complex mixture. Due to decreasing a reaction site and increasing electron density of azulenyl ring, **1b** was use as a 1-formylazulene. Similar results were obtained. On the other hand, when methyl 3-formylazulene-1-carboxylate (**1c)** was used as a substrate, reaction was smoothly proceed to give dibromide (**2c)** in good yields and dehydrobromination was also occurred smoothly by treatment of DBU to give a corresponding bromoethynylazulene derivative (**3c**). The compound (**3c**) reacted with triphenylphosphine in

refluxing ether for 21 h to give 2-(3-methoxycarbonylazulen-1-yl)ethynyltriphenylphosphonium bromide (**4**) in 85% yield.



Scheme 2.

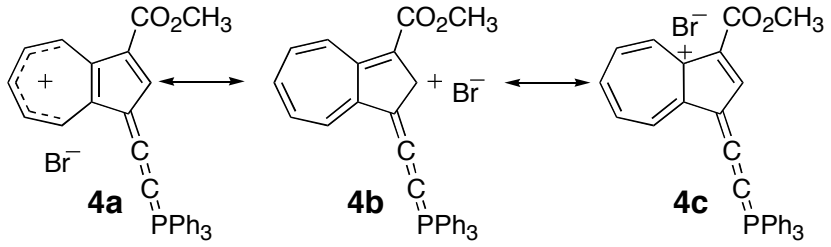
Table 1 Chemical shift of ^{1}H NMR spectrum of **3c**, **4**, and **5**

	5	**3c**	**4**
H-2	8.45	8.42	8.69
H-4	8.72	8.69	9.03
H-5	7.55	7.55	7.87-7.97
H-6	7.86	7.87	8.34
H-7	7.61	7.61	8.22
H-8	9.63	9.62	9.78
OCH_3	3.95	3.95	3.98
Ph			7.87-7.93
≡C-H	3.45		

Table 2 Chemical shift of ^{13}C NMR spectrum of **3c**, **4**, and **5**

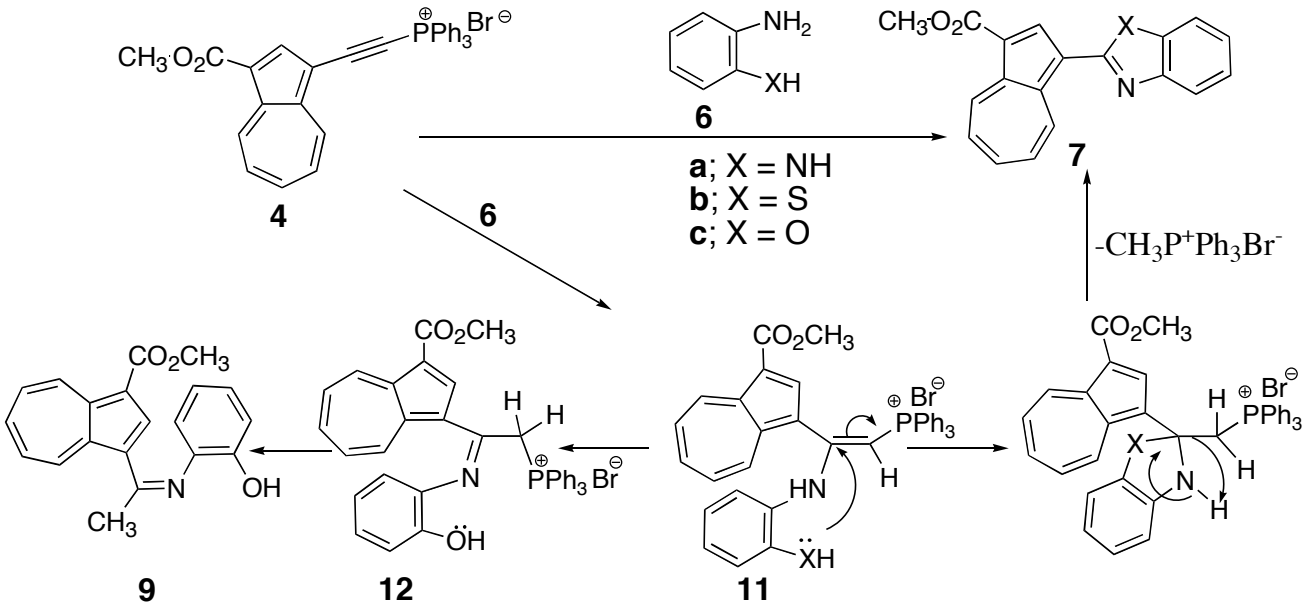
	5	**3c**	**4**
C-1	119.10	109.72	117.61
C-2	140.28	140.41	144.92(J=2.1)
C-3	115.97	115.97	101.79(J=5.4)
C-3a	143.12	143.03	142.96
C-4	137.79	137.82	139.11
C-5	127.79	127.81	132.52
C-6	140.96	140.85	142.86
C-7	129.19	129.24	132.54
C-8	138.61	138.67	142.85
C-8a	145.52	145.58	147.82
—C≡C—X	81.58	53.07	72.93(J=190.95)
—C≡C—X	78.87	75.43	116.96(J=33.9)
p-C_6H_4-			135.78(J=3.15)
m- C_6H_4-			133.07(J=12.75)
o- C_6H_4-			130.83(J=14.85)
ipso- C_6H_4-			118.84(J=99.75)
CH_3-O-	51.28	51.33	51.49
O-CO-	165.18	165.15	164.23

In order to clarify the substituent effect of triphenylphosphonium group in **4**, assignments of the signals in ^{1}H and ^{13}C-NMR spectra were carried out with aid of HMBC and HMQC NMR techniques. Phenyl protons and H-5 of azulene ring overlapped as shown in Tables 1. Coupling constants of phosphorus and carbon decreased according to the increasing distance between them ($J_{P,\ C\text{-}1sp}$ = 190.95 Hz – $J_{P,\ C\text{-}2Az}$=2.1 Hz). The signals of azulene protons and carbons linked to hydrogen in **4** as compared with **5** showed down field shift by 0.24-0.61 ppm and 1.32-4.73 ppm, respectively. Furthermore, the signal at C-2_{sp} showed too much lower field shift by 38.09 ppm. In contrast, the signals of C-1_{az}, C-3_{az}, C-$3a_{az}$ and C-1_{sp} in **4** as compared with **5** showed higher field shift by 1.49, 14.18, 2.56 and 9.28 ppm, respectively. These observations suggest that electron density of each carbon of azulene with hydrogen and C-$8a_{az}$ decreased by the combination with triphenylphosphonium group due to contributions of **4a**, **4b**, and **4c**. However, large down field shift of C-2_{sp} suggested to a possibility of nucleophilic attack at C-2_{sp} of **4**.



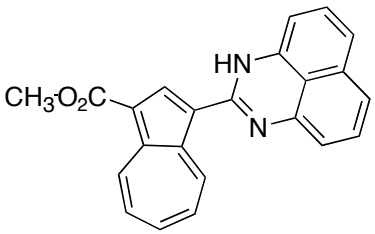
Synthesis of heterocyclic compounds using 4

As shown in Scheme 3, the reactivity of **4** with the dinuleophilic groups, such as *o*-phenylenediamine and related compounds (**6a-c**), was examined. As a result, a nucleophilic addition of Michael type and the subsequent of nucleophilic cyclization like 2-(2-azulenyl)ethynyltriphenylphosphonium bromide[5] gave benzazoles such as methyl 3-(*1H*-benzimidazol-2-yl)azulene-1-carboxylate (**7a**) and methyl 3-(benzothiazol-2-yl)azulene-1-carboxylate (**7b**) in 46 and 71% yields, respectively, except **6c**. However, extremely long reaction time was needed. The reason for its slow reaction rate is the increasing electron density at acetylenic carbon C-2_{sp} by the contributions of **4a-c**. The reaction of 1,8-diaminonaphthalene with **4** also gave corresponding methyl 3-(1*H*-perimidin-2-yl)azulene-1-carboxylate **(8)** in 79 % yield.



Scheme 3.

In the case of thereaction of **4** with **6c**, only a mixture of 3-[1-(2-hydroxyphenylimino)ethyl]azulene-1-carboxylate (**9**) and methyl 3-acetylazulene-1-carboxylate (**10**)[6] was obtained. The imine (**9**) easily converted to **10** during purification. Although the reaction mechanism to give **9** is not clear, we think that *N*-hydrogen of the first Michael reaction product (**11**) shits to C-1 to give imine intermediate (**12**) and undergoes elimination of the triphenylphosphonium group to give **9**, because second Michael reaction of **11** did not proceed smoothly due to weak nucleophilicity of the hydroxy group**.** Similar results have been observed in the reaction of 2-(2-azulenyl)ethynyltriphenylphosphonium bromide with **6c**.[5]



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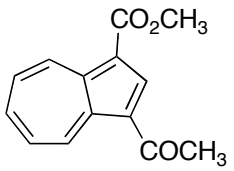

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Comparing with ring protons of 3-ethynylazulene (**5**) with azulenylated heterocyclic compounds (**7a-b** and **8**), by the connecting with these heterocyclic rings at C-3 position of azulene, the ring protons of azulene shifted to lower field in the order of H-4 > H-2 > H-8 > H-6 > H-5 and 7 (see EXPERIMENTAL) due to the anisotropy and electron withdrawing character of heterocyclic ring.

CONCLUSION

This study has shown the preparation of 2-(3-methoxycarbonylazulen-1-yl)ethynyltriphenylphosphonium bromide (**4**) and its application to the synthesis of azulenylated benzazoles at 3-position of azulene ring (**7a**-**b**) and a related compound (**8**) although longer reaction time is necessary comparing with 2-position of azulene and there is a limitation of this reaction in the case of *o*-aminophenol (**6c**).

EXPERIMENTAL

General Information. Melting points were determined on a Yanaco micro melting point apparatus and are uncorrected. IR spectra were taken on a Shimazu FTIR-8100M and ES 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 (125 MHz). MS spectra were measured on a JEOL HX-110 or a Hitachi M-2500 instrument usually at 70 eV. Elemental analyses were performed at the Instrumental Analysis Center of Chemistry, Faculty of Science, Tohoku University.

Synthesis of methyl 3-(2,2-dibromovinyl)azulene-1-carboylate (2c)

A suspension of triphenylphosphine (5.16 g, 19.7 mmol), carbon tetrabromide (6.52 g, 19.7 mmol), and zinc powder (1.28 g, l9.7 mmol) in dry dichloromethane (40 mL) was stirred for 24 h under argon at rt. A solution of methyl 3-formylazulene-1-carboxylate (526 mg, 2.5 mmol) in dry dichloromethane (10 mL) was added to the suspension at rt and stirred at same temperature for 20 min. The deep brown reaction mixture was filtered. After the solvent was removed under reduced pressure, the residue was purified by column chromatography on silica gel using dichloromethane as a solvent to afford methyl 3-(2,2-dibromovinyl)azulene-1-carboxylate (**2c**) (840 mg, 92.3%). **2c;** Green needles (CH_2Cl_2/hexane), mp 158.8-160.2 °C; IR (KBr) ν_{max} 3054 (w), 3021 (w), 2996 (w), 2950 (w), 2363 (w), 1688 (s), 1576 (w), 1536 (w), 1509 (w), 1455 (s), 1439 (m), 1424 (m), 1412 (m), 1393 (w), 1375 (w), 1323 (w), 1229 (m), 1213 (s), 1184 (w), 1152 (w), 1053 (w), 1040 (w), 885 (w), 872 (w), 845 (m), 776 (w), 758 (w), 743 (w), 698 (w), 579 (w), 532 (w) cm^{-1}; ES (CH_2Cl_2) λ_{max} 214.8 (log ε 5.00), 218.6 (5.05), 219.9 (4.94), 226.3 (5.00), 250.0 (4.33) sh, 260.6 (4.29) sh, 300.2 (4.62), 324.6 (4.38), 390.8 (3.97), 408.4 (3.81) sh, 564.2 nm (2.69); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.66 (1H, d, *J*=9.6 Hz, Az-8), 9.01 (1H, s, Az-2), 8.44 (1H, d, *J*=9.6 Hz, Az-4), 7.94 (1H, s, -CH=CBr_2), 7.83 (1H, dd, *J*=10.0, 9.6 Hz, Az-6), 7.58 (1H, dd, *J*=10.0, 9.6 Hz, Az-7), 7.50 (1H, dd, *J*=10.0, 9.6 Hz, Az-5), 3.97 (3H, s, CO_2CH_3); ^{13}C

NMR ($CDCl_3$, 100 MHz) δ 165.46 (<u>C</u>O_2Me), 141.33 (Az-8a), 141.22 (Az-3a), 140.08 (Az-6), 139.09 (Az-2), 138.44 (Az-8), 134.88 (Az-4), 129.32 (<u>C</u>H=CBr_2), 129.0 (Az-7), 127.22 (Az-5), 122.51 (Az-1 or 3), 116.63 (Az-1 or 3), 88.44 (CH=<u>C</u>Br_2), 51.33 (CO_2<u>C</u>H_3); MS (EI, 70eV) m/z 371.9 (M^++2, 50.24%), 370.9 (M^++1, 15.41), 369.8 (M^+, 100), 368.8 (8.71), 367.9 (51.34), 340.8 (16.51), 338.8 (35.3), 336.8 (17.19), 231.9 (11.66), 229.9 (14.15), 210.0 (44.76), 179.0 (33.83), 166.1 (10.42), 152.1 (10.93), 151.1 (29.34), 150.0 (25.86), 89.5 (24.25), 75.5 (14.76), 75.0 (14.59); *Anal.* Calcd for $C_{14}H_{10}O_2Br_2$: C, 45.44; H, 2.72; Br, 43.19. Found: C, 45.38; H, 2.84; Br, 43.38.

Synthesis of methyl 3-(2-bromoethynyl)azulene -1-carboylate (3c)

To a stirred solution of **2c** (740 mg, 2.0 mmol) in DMSO (40 mL), DBU (3.04 g, 20.0 mmol) in DMSO (20 mL) was added dropwise over a period of 7 min under argon at 40°C. After stirring for 23 min at 40°C, the reaction mixture was quenched with water, neutralized with 2N HCl and extracted with toluene. The extract was washed with brine, dried over anhydrous $MgSO_4$. After the solvent was removed under reduced pressure, the resulting residue was purified by column chromatography (silica gel, toluene) to afford methyl 3-(2-bromoethynyl)azulene-1-carboxylate (**3c**) (370.5 mg, 64.1%). **3c**; Deep green needles (CH_2Cl_2 / hexane); mp 142.3-144.1 °C; IR (KBr) ν_{max} 2998 (w), 2953 (w), 1684 (s), 1636 (w), 1580 (w), 1536 (w), 1514 (w), 1455 (s), 1443 (s), 1424 (m), 1410 (m), 1393 (w), 1372 (w), 1293 (w), 1231 (s), 1219 (s), 1181 (w), 1163 (w), 1142 (w), 1053 (m), 893 (w), 876 (w), 779 (m), 747 (m), 602 (w), 575 (w), 471 (w) cm^{-1}; ES (CH_2Cl_2) λ_{max} 221.8 (log ε 4.72), 226.3 (4.84)、243.6 (4.54) sh, 276.6 (4.47), 296.4 (4.44) sh, 303.1 (4.49), 315.6 (4.58), 381.2 (3.91), 397.2 (3.93), 558.8 (2.71), 600.7 (2.62) sh, 655.1 nm (2.17) sh; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.62 (1H, d, *J*=10.0 Hz, Az-8), 8.69 (1H, d, *J*=10.0 Hz, Az-4), 8.42 (1H, s Az-2), 7.87 (1H, t, *J*=9.6 Hz, Az-6), 7.61 (1H, dd, *J*=10.0, 9.6 Hz, Az-7), 7.55 (1H, dd, *J*=10.0, 9.6 Hz, Az-5), 3.95 (3H, s, CO_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.15 (<u>C</u>O_2Me), 145.58 (Az-8a), 143.03 (Az-3a), 140.85 (Az-6), 140.41 (Az-2), 138.67 (Az-8), 137.82 (Az-4), 129.24 (Az-7), 127.81 (Az-5), 115.97 (Az-1), 109.72 (Az-3), 75.43 (Az-<u>C</u>≡CBr), 53.07 (Az-C≡<u>C</u>Br), 51.33 (CO_2<u>C</u>H_3); MS (EI, 70eV) m/z 289.9 (M^++2, 99.15%), 288.9 (M^++1, 15.15), 287.9 (M^+, 100), 259.8 (9.64), 258.8 (70.39), 257.8 (10.41), 256.9 (72.55), 230.9 (8.18), 229.9 (5.92), 228.9 (7.95), 151.1 (13.03), 150.0 (78.2), 149.0 (7.18), 129.4 (6.78), 128.4 (7.53), 98.0 (7.07), 74.9 (32.21), 73.9 (8.64), 61.9 (5.26); *Anal.* Calcd for $C_{14}H_9O_2Br$: C, 58.16; H, 3.14; Br, 27.64. Found: C, 58.25; H, 3.24; Br, 28.12.

Synthesis of 2-(3-methoxycarbonylazulen-1-yl)ethynyltriphenylphosphonium bromide (4)

To a suspension of **3c** (370.5 mg, 1.28 mmol) in abs. ether (20 mL), triphenylphosphine (403.3 mg, 1.54 mmol) was added. It was refluxed for 21 days under argon. The red precipitate was collected by filtration, washed with ether and dried thoroughly in vacuo to give 2-(3-methoxycarbonylazulen-1-yl)ethynyltriphenylphosphonium bromide (**4**) (600.4 mg, 85%). **4**; Red powder; mp 219.6-221.4 °C (decomp.); IR (KBr) ν_{max} 3049 (w), 2947 (w), 2139 (s), 1695 (s), 1583 (w), 1514 (w), 1441 (s), 1412 (m), 1390 (w), 1371 (m), 1294 (w), 1215 (s), 1178 (w), 1111 (m), 1057 (m), 997 (w), 787 (m), 752 (w), 725 (m), 688 (m), 530 (m), 520 (s), 484 (w) cm^{-1}; ES (CH_2Cl_2) λ_{max} 227.9 nm (log ε 4.89), 262.5 (4.13) sh, 270.5 (4.20) sh, 294.8 (4.56), 310.8 (4.45) sh, 315.6 (4.46), 324.9 (4.38) sh, 379.3 (4.19), 394.3 (4.19), 511.8 (2.93), 549.2 (2.83) sh, 597.2 nm (2.37) sh; ^{1}H NMR (400M Hz, $CDCl_3$) δ 9.78 (1H, d, *J*=10.0 Hz, Az-4), 9.03 (1H, d, *J*=10.0 Hz, Az-8), 8.69 (1H, s, Az-2), 8.34 (1H, t, *J*=8.8 Hz, Az-6), 8.22 (1H, dd, *J*=10.0, 8.8 Hz, Az-5), 7.87-7.93 (16H, m, Ph-H and Az-7), 3.98 (3H, s, CO_2Me); ^{13}C NMR (100MHz, $CDCl_3$) δ 164.23 ($\underline{C}O_2Me$), 147.82 (Az-4a), 144.92 (Az-2, d, *J*=2.1 Hz), 142.96 (Az-8a), 142.86 (Az-6), 142.85 (Az-4), 139.11 (Az-8), 135.78 (Ph-*p*, d, *J*=3.15 Hz), 133.07 (Ph-*m*, d, *J*=12.75 Hz), 132.52 (Az-7), 132.54 (Az-5), 130.83 (Ph-*o*, d, *J*=14.85 Hz), 118.84 (Ph-ipso, d, *J*=99.75 Hz), 117.61 (Az-3), 116.96 (Az-$\underline{C}$≡C-P, d, *J*=33.9 Hz), 101.79 (Az-1, d, *J*=5.4 Hz), 72.93 (Az-C≡$\underline{C}$-P, d, *J*=190.95 Hz), 51.49 ($CO_2\underline{Me}$); *Anal*. Calcd for $C_{32}H_{24}O_2BrP\cdot 1/5H_2O$: C, 69.25; H, 4.43. Found: C, 69.20; H, 4.54.

Synthesis of methyl 3-ethynylazulene-1-carboxylate (**5**)

2-(1-Methoxycarbonylazulen-3-yl)ethynyltriphenylphosphonium bromide (**4**) (106.3 mg, 0.192 mmol) was dissolved in a mixture of 0.4 M of aqueous sodium hydroxide (10 mL) and methanol (10 mL). It was stirring at rt for 15 min. The occurring solid product was collected by filtration. From the filtrate, the product was also obtained by extraction with ethyl acetate. The combined product was purified by column chromatography (silica gel, hexane and ethyl acetate (4:1)) to give methyl 3-ethynylazulene-1-carbonylate (**5**) (37.9 mg, 93.8%). **5**; Dark violet plates (EtOH); mp 105–106°C; IR (KBr) ν_{max} 3546 (m), 3467 (m), 3416 (m), 3243 (s), 2091 (w), 1696 (s), 1686 (s), 1458 (s), 1439 (s), 1422 (s), 1412 (s), 1393 (m), 1314 (m), 1226 (s), 1210 (s), 1048 (s), 774 (m), 772 (m), 742 (s), 712 (m), 702 (m), 660 (m), 579 (m) cm^{-1}; ES (EtOH) λ_{max} 240.4 nm (log ε 4.58), 270.2 (4.48), 298.3 (4.51), 310.8 (4.59), 376.1 (3.90), 391.8 (3.92), 555.9 (2.75), 595.0 sh (2.68), 637.2 sh (2.40), 749.5 (1.90), 814.8 (1.91); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (1H, d, *J*=10.0 Hz, Az-8), 8.72 (1H, d, *J*=10.0 Hz, Az-4), 8.45 (1H, s, Az-2), 7.86 (1H, t, *J*=10.0 Hz, Az-6), 7.61 (1H, t, *J*= 10.0 Hz, Az-7), 7.55 (1H, t, *J*=10.0 Hz, Az-5), 3.95 (3H, s, CO_2CH_3), 3.45 (1H, s, Az-C≡C-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.18 ($\underline{C}O_2CH_3$), 145.52 (C-

3a), 143.12 (C-8a), 140.96 (C-6), 140.28 (C-2), 138.61 (C-4), 137.79 (C-8), 129.19 (C-5), 127.79 (C-7), 119.10 (C-1), 115.97 (C-3), 81.58 (-C≡C-H), 78.87 (-C≡C-H), 51.28 ($\underline{C}H_3O$-); MS (EI, 70eV) m/ 210 (M^+, 100 %), 180 (11), 179 (74.6), 152 (7.6), 151 (24.7), 150 (19.7), 90 (4), 75 (5.8); *Anal*. Calcd for $C_{14}H_{10}O_2 \cdot 3/4H_2O$: C, 75.15; H, 5.18. Found: C, 74.99; H, 4.96.

Synthesis of methyl 3-(*1H*-benzimidazol-2-yl)azulene-1-carboxylate (7a)

To a stirred solution of **4** (100 mg, 0.18 mmol) in $CHCl_3$ (10 mL), *o*-phenylenediamine (**6a**) (23.5 mg, 0.22 mmol) was added. The mixture was refluxed for 11 days under argon. The solvent was removed under reduced pressure. The residue was purified by column chromatography (silica gel, ethyl acetate) and GPC ($CHCl_3$) to give methyl 3-(*1H*-benzimidazol-2-yl)azulene-1-carboxylate (**7a**) (25 mg, 45.7%). **7a**; Deep purple needles (toluene); mp 121.7 – 123.9°C; IR (KBr) ν_{max} 3135 (w), 3058 (w), 3002 (w), 2903 (w), 2857 (w), 2795 (w), 1694 (s), 1622 (w), 1593 (w), 1580 (w), 1559 (s), 1539 (w), 1507 (w), 1485 (w), 1458 (m), 1439 (s), 1426 (m), 1414 (s), 1401 (s), 1341 (m), 1316 (w), 1306 (w), 1293 (w), 1271 (m), 1242 (m), 455* (m), 1204 (s), 1129 (w), 1113 (w), 1055 (m), 1036 (w), 1013 (w), 932 (w), 889 (w), 880 (w), 781 (m), 764 (w), 745 (s), 563 (w) cm^{-1}; ES (THF) λ_{max} 230.8 nm (log ε 4.57) sh, 271.4 (4.52), 282.0 (4.48) sh, 313.0 (4.65), 331.0 (4.41) sh, 397.8 (4.11), 416.7 (4.00) sh, 561.4 (2.80) sh, 599.4 (2.71) sh, 667.61 nm (2.12) sh; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.92 (1H, s, NH), 10.39 (1H, d, *J*=10.0 Hz, Az- 8), 9.65 (1H, d, *J*=10.0, Az-4), 9.08 (1H, s, Az-2), 8.14 (1H, dd, *J*=10.0, 9.6 Hz, Az-6), 7.92 (1H, dd, *J*=10.4, 9.2 Hz, Az-7), 7.85 (1H, dd, *J*=9.6, 10.0 Hz, Az-5), 7.62-7.72 (1H, m, Benzo-H_a), 7.50-7.53 (1H, m, Benzo-H_a), 7.25-7.35 (2H, m, Benzo-H_b), 3.94 (3H, s, CO_2CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.54 ($\underline{C}O_2Me$), 149.10 (Az-$\underline{C}$=N), 144.14 (Az-8a), 142.17 (Az-3a), 141.94 (Az-6), 140.39 (Az-8), 140.37 (Benzo), 138.98 (Az-2), 138.32 (Az-4), 133.99 (Benzo), 130.01 (Az-7), 129.93 (Az-5), 122.23 (Benzo), 121.47 (Benzo), 118.43 (Benzo), 116.63 (Benzo), 115.24 (Az-3 or 1), 110.81 (Az-1 or 3), 51.23 ($CO_2\underline{C}H_3$); MS (EI, 70eV) m/z 302.1 (M^+, 100%), 301.1 (39.6), 287.1 (25.8), 271.0 (10.4), 244.1 (14.2), 243.1 (71.5), 242.1 (30.5), 241.1 (7.0), 151.1 (5.1), 135.1 (11.1); *Anal*. Calcd for $C_{19}H_{14}N_2O_2 \cdot 1/5H_2O$: C, 74.59; H, 4.74; N, 9.16. Found: C, 74.53; H, 4.77; N, 8.94.

Synthesis of methyl 3-(benzothiazol-2-yl)azulene-1-carboxylate (7b)

To a stirred solution of **4** (100 mg, 0.181 mmol) in $CHCl_3$ (10 mL), *o*-aminobenzenethiol (**6b**) (27.24 mg, 0.218 mmol) was added. The reaction mixture was refluxed for 14 days under Ar. The solvent was removed under reduced pressure. The residue was purified by column chromatography (silica gel,

CH_2Cl_2) to give methyl 3-(benzothiazol-2-yl)azulene-1-carboxylate (**7b**) (41.1 mg, 71%).

7b; Brown needles (CH_2Cl_2/hexane); mp 178.2-179.9 °C; IR (KBr) ν_{max} 3054 (w), 2994 (w), 2950 (w), 1701 (s), 1578 (w), 1530 (s), 1505 (w), 1456 (m), 1441 (s), 1418 (m), 1402 (s), 1358 (m), 1304 (w), 1275 (w), 1225 (m), 1210 (s), 1193 (m), 1175 (m), 1159 (w), 1152 (w), 1053 (m), 1013 (w), 922 (m), 887 (w), 880 (w), 777 (m), 762 (w), 747 (s), 722 (m), 706 (w), 691 (w), 577 (w), 444 (w) cm^{-1}; ES (CH_2Cl_2) λ_{max} 217.4 nm (log ε 4.88), 220.0 (4.77), 222.8 (4.80), 226.6 (4.91), 275.3 (4.35), 313.7 (4.53), 330.0 (4.43) sh, 345.4 (4.29) sh, 397.8 (4.16), 420.6 (3.97) sh, 545.0 (2.80), 584.4 (2.69) sh, 634.6 nm (2.19) sh; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.20 (1H, d, *J*=10.0 Hz, Az-8), 9.77 (1H, d, *J*=10.0 Hz, Az-4), 8.80 (1H, s, Az-2), 8.12 (1H, dd, *J*=7.6, 0.8 Hz, Benzo-H_a), 7.97 (1H, dd, *J*=9.6, 9.2 Hz, Az-6), 7.92 (1H, dd, *J*=8.0, 0.8 Hz, Benzo-H_a), 7.79 (1H, dd, *J*=10.0, 9.2 Hz, Az-7), 7.71 (1H. dd, *J*=10.0, 9.6 Hz, Az-5), 7.50 (1H, ddd, *J*=8.4, 7.2, 1.2 Hz, Benzo-H_b), 7.38 (1H, ddd, *J*=8.0, 7.2, 1.2 Hz, Benzo-H_b); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.3 ($\underline{C}O_2Me$), 164.3 (Az-$\underline{C}$=N), 154.2 (Az-3a), 143.8 (Az-8a), 141.5 (Az-2), 141.2 (Az-6), 140.6 (Benzo), 140.2 (Az-8), 139.3 (Az-4), 134.0 (Benzo), 130.4 (Az-7), 130.0 (Az-5), 126.2 (Benzo), 124.8 (Benzo), 122.6 (Benzo), 121.3 (Benzo), 120.3 (Az-1 or 3), 116.7 (Az-1 or 3), 51.4 ($CO_2\underline{C}H_3$); MS (EI, 70eV) m/z 319.0 (M^+, 100%), 318.0 (34.2), 304.1 (21.4), 288.1 (17.7), 260.9 (13.8), 260.0 (64.8), 259.0 (25.2), 143.6 (11.6), 130.1 (11.3); *Anal.* Calcd for $C_{19}H_{13}NO_2S$: C, 71.45; H, 4.10; N, 4.39; S, 10.04. Found: C, 71.15; H, 4.19; N, 4.30; S, 10.07.

Synthesis of methyl 3-(1*H*-perimidin-2-yl)azulene-1-carboxylate (8)

To a stirred solution of **4** (100 mg, 0.181 mmol) in $CHCl_3$ (10 mL), 1,8-diaminonaphyhalene (34.4 mg, 0.217 mmol) was added and refluxed for 23 h under argon. The solvent was removed under reduced pressure and the resulting residue was purified by column chromatography (silica gel, CH_2Cl_2 / ethyl acetate) to give methyl 3-(1*H*-perimidin-2-yl)azulene-1-carboxylate (**8**) (50.7 mg, 79.4 %). **8**: Reddish brown crystals (CH_2Cl_2 / hexane); mp 114.4-117.0 °C; IR (KBr) ν_{max} 3594 (w), 3586 (w), 3565 (w), 3551 (w), 3544 (w), 3046 (w), 2946 (m), 1696 (s), 1674 (m), 1634 (s), 1590 (s), 1536 (m), 1520 (m), 1449 (s), 1441 (s), 1418 (s), 1372 (s), 1337 (m), 1285 (w), 1238 (s), 1225 (s), 1204 (s), 1177 (m), 1163 (m), 1132 (w), 1051 (m), 1034 (w), 907 (w), 876 (w), 824 (m), 770 (s), 750 (s), 629 (w), 571 (w), 532 (w) cm^{-1}; ES (THF) λ_{max} 236.2 nm (log ε 4.71), 289.7 (4.59), 301.8 (4.55), 307.9 (4.54) sh, 345.0 (4.28), 357.5 (4.26) nm sh; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.66 (1H, s, NH), 10.17 (1H, d, *J*=10.0 Hz, Az-8), 9.71 (1H, d, *J*=10.0 Hz, Az-4), 8.95 (1H, s, Az-2), 8.18 (1H, t, *J*=9.6 Hz, Az-6), 7.92 (1H, dd, *J*=10.0, 9.6, Az-7 or 5), 7.91 (1H, dd, *J*=10.0, 9.6 Hz, Az-5 or 7), 7.20-7.00 (4H, m, perimidine-H), 6.76 (1H, d, *J*=6.8 Hz, perimidine-H), 6.56 (1H, d, *J*=7.2 Hz, perimidine-H), 3.93 (3H, s, CO_2CH_3); ^{13}C

NMR (100 MHz, DMSO-d_6) δ 164.5 ($\underline{C}O_2Me$), 150.50 (Az-$\underline{C}$=N), 144.96 (Az-8a), 142.57 (Az-3a), 142.03 (Az-6), 141.56 (perimidine), 140.65 (Az-8), 139.14 (Az-2), 138.68 (perimidine), 138.41 (Az-4), 135.01 (perimidine), 130.43 (Az-5 and 7), 128.90 (perimidine), 127.99 (perimidine), 120.99 (perimidine), 119.11 (Az-1 or 3), 118.92 (perimidine), 117.40 (perimidine), 114.36 (Az-3 or 1), 113.71 (perimidine), 102.42 (perimidine), 51.20 ($CO_2\underline{C}H_3$); MS (EI, 70eV) m/z 352.1 (M^+, 100%), 351.1 (20.3), 337.1 (9.9), 321.0 (7.1), 320.0 (12.1), 294.1 (7.9), 293.1 (34.3), 292.1 (29.0), 291.1 (9.9), 290.1 (5.7), 176.0 (6.5), 160.5 (21.1), 146.0 (15.5); *Anal.* Calcd for $C_{23}H_{16}N_2O_2 \cdot 1/4H_2O$: C, 77.40; H, 4.66; N, 7.85. Found: C, 77.46; H, 4.96; N, 7.71.

Reaction of 4 with *o*-aminophenol (6c)

To a stirred solution of 2-(3-methoxycarbonylazulen-1-yl)ethynyltriphenylphosphonium bromide (**4**) (100 mg, 0.181 mmol) in $CHCl_3$ (10 mL), *o*-aminophenol (23.7 mg, 0.218 mmol) was added. The reaction mixture was refluxed for 3 days under Ar. The solvent was removed under reduced pressure. The residue was purified by GPC ($CHCl_3$), to give a mixture of methyl 3-[1-(2-hydroxyphenylimino)ethyl]azulene-1-carboxylate (**9**) (27.0 mg, 46.7%) and a small amount of methyl 3-acetylazulene-1-carboxylate (**10**)[6] (detected on ^{1}H NMR). Because the imine (**9**) easily converted to **10** during purification, we could not obtain analytically pure **9**. **9**; Brown needles (CH_2Cl_2/hexane); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.19 (1H, d, *J*=10.0 Hz, Az-8), 9.80 (1H, d, *J*=10.0 Hz, Az-4), 8.74 (1H, s, Az-2), 7.95 (1H, t, *J*=9.8 Hz, Az-6), 7.72 (1H, dd, *J*= 10.0, 9.8 Hz, Az-7), 7.69 (1H, dd, *J*=10.0, 9.8 Hz, Az-5), 6.87-7.14 (4H, m, Ph-H), 3.99 (3H, s, CO_2CH_3), 2.61 (3H, s, CH_3C=N); MS (EI, 70eV) m/z 319.1 (M^+, 100%), 318.1 (45.4), 305.0 (20.6), 304.0 (97.6), 288.1 (8.1), 261.1 (11.4), 260.1 (54.3), 245.1 (5.4), 244.0 (11.2), 212.0 (12.2), 211.1 (26.0), 186.0 (19.4), 180.0 (8.4), 155.0 (9.8), 153.1 (5.6), 152.1 (14.2), 136.5 (10.1), 133.1 (5.0), 126.0 (5.1), 65.0 (5.3). **10**;[6] Brown crystals (CH_2Cl_2 / hexane); mp 115.0-116.8 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.04 (1H, d, *J*=10.0 Hz, Az-4 or 8), 9.82 (1H, d, *J*= 10.0 Hz, Az-4 or 8), 8.79 (1H, t, *J* = 9.8 Hz, Az-6), 7.78-7.85 (2H, m, Az-5, 7), 3.98 (3H, s, CO_2CH_3), 2.73 (3H, s, $COCH_3$); MS (EI, 70eV) m/z 228.1 (M^+, 44.4%), 214.0 (13.6), 213.1 (100), 197.0 (11.5), 127.0 (5.0), 126.0 (6.0), 91.0 (8.8).

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