A Ring Expansion-Annulation Strategy for the Synthesis of Substituted Azulenes. Preparation and Suzuki Coupling Reactions of 1-Azulenyl Triflates

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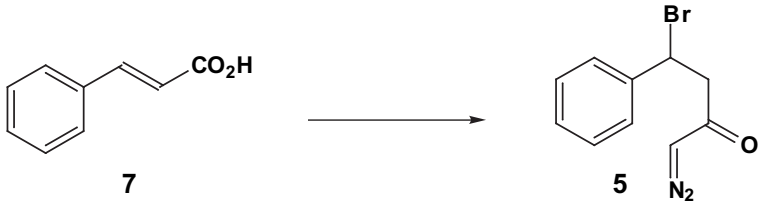
Supporting Information

General Procedures. All reactions were performed in flame-dried glassware under a positive pressure of nitrogen or argon with magnetic stirring. Sensitive liquids and solutions were transferred via syringe or cannula and were introduced into reaction vessels through rubber septa. Reaction product solutions were concentrated using a Büchi rotary evaporator at ca. 20 mmHg. Column chromatography was performed on EM Science silica gel 60 (35-75 μm) or Silicycle silica gel 60.

Materials. Commercial grade reagents and solvents were used without further purification except as indicated below. Benzene and dichloromethane were distilled from calcium hydride. Diethyl ether and tetrahydrofuran were distilled from benzophenone ketyl or dianion. Acetic anhydride was distilled from quinoline. Activated silica gel was prepared by heating at 200 ºC at 0.1 mmHg for 3 d. Diazomethane was generated from Diazald© according to the procedure of Black.[1] Oxalyl chloride was distilled under argon at atmospheric pressure and *N*-bromosuccinimide was recrystallized from water. *B*-Phenyl-9-BBN was prepared from 9-BBN and phenyllithium via the procedure of Brown.[2] Rhodium(II) pivalate was prepared from rhodium(III) chloride by the procedure of Wilkinson.[3] Sulfur trioxide-pyridine complex was purified by the procedure of Shioiri.[4]

Instrumentation. ^{1}H NMR spectra were recorded on Varian XL-300 (300 MHz), Varian Unity 300 (300 MHz), and Varian Inova 500 (500 MHz) spectrometers. ^{13}C NMR spectra were recorded on Varian Unity 300 (75 MHz) and Varian Inova 500 (125 MHz) spectrometers. ^{1}H NMR and ^{13}C NMR chemical shifts are expressed in parts per million (δ) relative to TMS. Infrared spectra were obtained on a Perkin-Elmer 1320 grating or a Perkin-Elmer 1600 series FTIR spectrophotometer. Ultraviolet-visible spectra were recorded with a Perkin-Elmer 552 UV-Vis spectrophotometer. Elemental analyses were performed by E&R Microanalytical Laboratory, Inc. of Parsippany, New Jersey or Robertson Microlit Laboratories, Inc., of Madison, New Jersey.

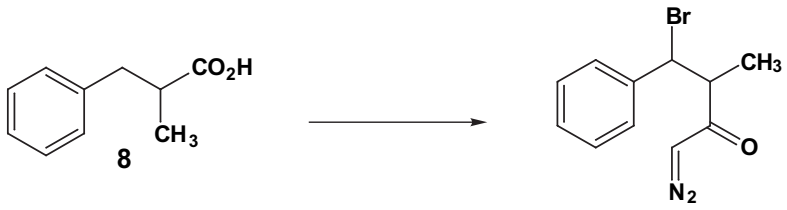


7 5

Representative Procedure for the Synthesis of β'-Bromo-α-diazo Ketones via Hydrobromination with HBr. 4-Bromo-1-diazo-4-phenyl-2-butanone (5). A 250-mL, three-necked, round-bottomed flask equipped with a glass stopper, gas dispersion tube attached to a cylinder of HBr, and a gas outlet adapter attached with Tygon tubing to an Erlenmeyer flask filled with water, was charged with cinnamic acid (3.50 g, 23.6 mmol), 20 g of activated silica gel, and 120 mL of dichloromethane. HBr was bubbled through the reaction mixture for 20 min, and then the gas inlet and outlet were replaced with glass stoppers. The orange suspension was stirred at room temperature for 20 h. The glass stoppers were replaced with the gas adapters used previously, and HBr was bubbled through the reaction mixture for an additional 20 min. The flask was stoppered and stirred for 4 h and then the orange suspension was filtered with the aid of 250 mL of diethyl ether. The filtrate was washed with two 200-mL portions of water and 200 mL of brine, dried over $MgSO_4$, filtered, and concentrated to provide 4.50 g of 3-bromo-3-phenylpropionic acid as a white solid.

A 200-mL, one-necked flask equipped with a reflux condenser and argon inlet adapter was charged with the acid prepared above, oxalyl chloride (3.59 g, 2.40 mL, 28.3 mmol, 1.20 equiv), and 60 mL of benzene. As the suspension was heated to 65 °C, the solid acid dissolved and

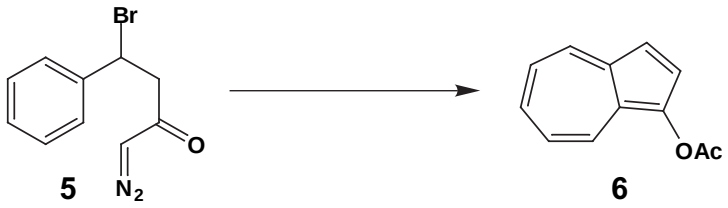
vigorous gas evolution began. After 30 min, gas evolution had ceased, and the reaction mixture was stirred for an additional 15.5 h at 65 °C. The reaction mixture was next allowed to cool to room temperature and then concentrated to a volume of ca. 10 mL. A 500-mL one-necked, round-bottomed flask (note: *clearseal joint*) was charged with a solution of CH_2N_2 (ca. 67 mmol, 2.8 equiv, generated from Diazald (20.2 g, 94.5mmol)) in 300 mL of diethyl ether. The yellow solution was cooled to 0 °C and rapidly stirred while the benzene solution of the acid chloride prepared above was added via pipette over 1 min (the flask containing the acid chloride was rinsed with two 5-mL portions of diethyl ether). The ice bath was removed after 10 min, stirring was stopped, and the reaction mixture was allowed to warm to room temperature. After 1 h, excess diazomethane was distilled off under reduced pressure (ca. 20 mmHg) into an Erlenmeyer flask cooled at -78 °C. The bright yellow reaction mixture was concentrated to provide 5.62 g of a yellow oil, which was deposited on silica gel and purified by column chromatography on silica gel (elution with 20% ethyl acetate-hexanes) to afford 3.91 g (69% from cinnamic acid) of pure 4-bromo-1-diazo-4-phenyl-2-butanone as a yellow solid with spectral data consistent with that previously reported for this compound.[5]



Representative Procedure for the Synthesis of β'-Bromo-α-diazo Ketones via Benzylic Bromination with NBS. 4-Bromo-1-diazo-3-methyl-4-phenyl-2-butanone. A 250-mL, three-necked, round-bottomed flask equipped with an argon inlet adapter, reflux condenser, and glass stopper was charged with 2-methyl-3-phenylpropionic acid[6] (2.00 g, 12.2 mmol), *N*-bromosuccinimide (2.60 g, 14.6 mmol), and 60 mL of carbon tetrachloride. The resulting suspension was heated at 80 °C while being irradiated with a sunlamp. After 2 h, the yellow reaction mixture was filtered (while hot), allowed to cool to room temperature, filtered again, and then concentrated to provide 3.21 g of 3-bromo-2-methyl-3-phenylpropionic acid as a light brown solid.

Conversion of this material to the desired diazo ketone was accomplished according to the general procedure described above by reaction with oxalyl chloride (1.86 g, 1.30 mL, 14.6 mmol) in 60 mL of benzene, followed by treatment with CH_2N_2 (ca. 35 mmol, generated from Diazald (10.4 g,

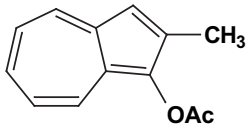
48.8 mmol)) in 150 mL of diethyl ether. The crude diazo ketone (3.57 g of yellow oil) was purified by column chromatography on 60 g of silica gel (compound adsorbed on 8 g of silica gel, elution with 20% ethyl acetate-hexanes) to afford 1.96 g (60% overall yield from 2-methyl-3-phenylproionic acid) of 4-bromo-1-diazo-3-methyl-4-phenyl-2-butanone (mixture of diastereomers) as a yellow solid: mp 51.0-61.0 °C; IR (CCl_4) 2890, 2080, 1635, 1535, 1440, 1345, 1245, 1195, 1130, 990 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.22-7.39 (m, 5 H), 5.42 (br s, 1 H, minor isomer), 5.14 (app t, J = 8.8, 10.3 Hz, 1 H), 5.06 (br s, 1 H, major isomer), 3.03-3.11 (m, 1 H), 1.47 (d, J = 7.1 Hz, 3 H, major isomer), 0.92 (d, J = 7.0 Hz, 3 H, minor isomer); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.4, 194.3, 140.5, 139.4, 128.8, 128.4, 127.8, 127.6, 57.5, 55.1, 55.0, 54.1, 52.8, 17.7, 17.0; UV (CH_3CN) λ_{max}, nm (ε) 247 (20,145), 192 (35,500); HRMS (EI): *m/z* calcd for $C_{11}H_{11}BrN_2O$: 266.0055, found: 266.0048.



5 6

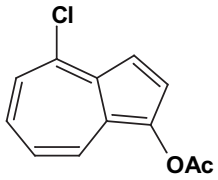
Representative Procedure for the Synthesis of Acetoxyazulenes. 1-Acetoxyazulene (6). A 500-mL, three-necked, round-bottomed flask equipped with a rubber septum, 125-mL pressure-equalizing addition funnel, and an argon inlet adapter was charged with rhodium pivalate (0.022 g, 0.040 mmol) and 120 mL of dichloromethane. The addition funnel was charged with 4-bromo-1-diazo-4-phenyl-2-butanone (2.00 g, 7.89 mmol) and 75 mL of dichloromethane. The solution of the diazo ketone was added dropwise over 1.5 h to the rapidly stirred solution of the catalyst. After 5 min, acetic anhydride (4.02 g, 3.70 mL, 39.5 mmol) was added in one portion via syringe, and then 4-dimethylaminopyridine (2.89 g, 23.7 mmol) was immediately added in one portion. The resulting deep blue solution was stirred for 5 min and then treated with 10 mL of methanol. After stirring an additional 10 min, the reaction mixture was poured into a 1-L separatory funnel containing 100 mL of dichloromethane and 200 mL of 3% HCl solution. The organic phase was separated, washed with 150 mL of 3% HCl solution and 200 mL of brine, dried over $MgSO_4$, filtered, and concentrated to provide 1.40 g of a blue oil. Column chromatography on 50 g of silica gel (elution with 5% ethyl acetate-hexanes) afforded 0.948 g (64%) of 1-acetoxyazulene as blue needles: mp 53.5-54.5 °C (lit.[7] mp 47.5-

50.2 °C); IR (CCl_4) 3030, 2810, 1765, 1580, 1545, 1500, 1400, 1370, 1320, 1220, 1205, 1030 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.25 (d, *J* = 9.3 Hz, 1 H), 8.21 (d, *J* = 10.0 Hz, 1 H), 7.80 (d, *J* = 4.2 Hz, 1 H), 7.58 (app t, *J* = 9.8 Hz, 1 H), 7.27 (d, *J* = 4.2 Hz, 1 H), 7.09 (dt, *J* = 4.2, 10.0 Hz, 2 H), 2.43 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 138.5, 138.1, 137.8, 135.5, 132.1, 127.8, 126.1, 122.6, 121.7, 113.8, 20.9; UV-Vis (hexane) λ_{max}, nm (ε) 732 (101), 663 (258), 608 (292), 586 (252), 347 (2,933), 277 (30,166), 238 (8,845), 213 (3,352).



16

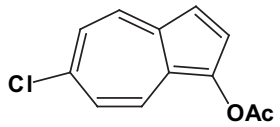
1-Acetoxy-1-methylazulene (16). Blue needles, mp 58.5-59.5 °C. IR (CCl_4) 3020, 2970, 2870, 1765, 1580, 1540, 1500, 1400, 1370, 1350, 1290, 1200, 1110, 1000, 905 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.10 (d, *J* = 9.4 Hz, 1 H), 7.97 (d, *J* = 9.7 Hz, 1 H), 7.48 (app t, *J* = 9.9 Hz, 1 H), 7.03-7.10 (m, 3 H), 2.46 (s, 3 H), 2.43 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 140.2, 136.7, 136.5, 135.9, 135.6, 130.1, 127.3, 123.0, 122.2, 114.5, 20.6, 13.4; UV-Vis (CH_3CN) λ_{max}, nm (ε) 684 (120), 641 (270), 621 (270), 585 (310), 573 (280), 550 (250), 346 (4,270), 283 (49,840), 279 (47,465), 274 (45,570). Anal. Calcd for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04. Found: C, 77.73; H, 5.66.



17

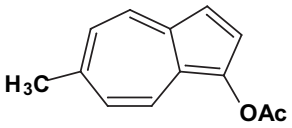
1-Acetoxy-4-chloroazulene (17). Blue-gray solid, mp 55.5-56.5 °C. IR (CCl_4) 3020, 1760, 1585, 1550, 1495, 1450, 1395, 1365, 1310, 1230, 1200, 1060, 1030, 990, 925, 910, 865 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.22 (d, *J* = 9.7 Hz, 1 H), 7.80 (d, *J* = 4.2 Hz, 1 H), 7.52 (d, *J* = 4.2 Hz, 1 H), 7.44 (app t, *J* = 10.2 Hz, 1 H), 7.29 (d, *J* = 10.8 Hz, 1 H), 7.06 (app t, *J* = 9.6 Hz, 1 H), 2.41 (s, 3 H); ^{13}C

NMR (75 MHz, $CDCl_3$) δ 169.1, 144.0, 139.4, 136.0, 132.4, 130.1, 128.0, 126.3, 124.5, 121.1, 114.3, 21.0; UV-Vis (hexane) λ_{max}, nm (ε) 657 (267), 605 (311), 520 (114), 351 (4,130), 337 (2,970), 284 (35,440), 245 (23,670), 219 (8,960. Anal. Calcd for $C_{12}H_9ClO_2$: C, 65.32; H, 4.11. Found: C, 65.31; H, 3.99.



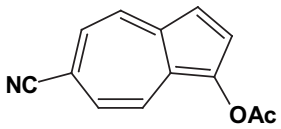
18

1-Acetoxy-6-chloroazulene (18). Metallic blue flakes, mp 66.5-67.0 °C. IR (CCl_4) 2880, 1750, 1565, 1510, 1465, 1375, 1345, 1290, 1230, 1185, 1010, 980 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.01 (d, *J* = 10.2 Hz, 1 H), 8.00 (d, *J* = 10.6 Hz, 1 H), 7.77 (d, *J* = 4.3 Hz, 1 H), 7.27 (d, *J* = 4.3 Hz, 1 H), 7.23-7.16 (m, 2 H), 2.42 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0, 145.6, 139.6, 135.8, 133.9, 130.3, 128.0, 124.7, 122.8, 122.3, 116.1, 21.0; UV-Vis (hexane) λ_{max}, nm (ε) 777 (100), 664 (252), 606 (290), 582 (250), 561 (212), 304 (6,730), 283 (61,500), 237 (9,270), 217 (10,205). Anal. Calcd for $C_{12}H_9ClO_2$: C, 65.32; H, 4.11; Cl, 16.07. Found: C, 65.16; H, 4.17; Cl, 15.88.



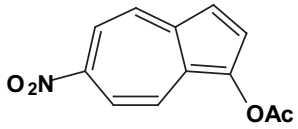
19

1-Acetoxy-6-methylazulene (19). Blue solid, mp 67.0-67.5 °C. IR (CCl_4) 3030, 2920, 2880, 1765, 1580, 1495, 1430, 1400, 1370, 1315, 1210, 1030 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.08 (d, *J* = 9.4 Hz, 1 H), 8.04 (d, *J* = 10.2 Hz, 1 H), 7.67 (d, *J* = 4.3 Hz, 1 H), 7.21 (d, *J* = 4.3 Hz, 1 H), 6.99 (d, *J* = 9.4 Hz, 1 H), 6.98 (d, *J* = 10.2 Hz, 1 H), 2.60 (s, 3 H), 2.41 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 150.5, 138.1, 137.3, 134.1, 131.1, 126.4, 125.0, 123.9, 123.6, 114.0, 28.3, 21.1; UV-Vis (CH_3CN) λ_{max}, nm (ε) 714 (105), 645 (270), 596 (300), 368 (3,000), 352 (5,700), 349 (5,890), 335 (4,390), 281 (72,290), 234 (18,120). Anal. Calcd for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04. Found: C, 77.84; H, 6.04.



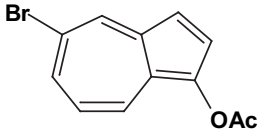
20

1-Acetoxy-6-cyanoazulene (20). Green solid, mp 112.0-113.0 °C. IR (CCl_4) 3010, 2930, 2190, 1765, 1575, 1480, 1415, 1380, 1355, 1300, 1250, 1185, 1015 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.16 (d, *J* = 10.0 Hz, 1 H), 8.14 (d, *J* = 9.5 Hz, 1 H), 8.01 (d, *J* = 4.3 Hz, 1 H), 7.38 (d, *J* = 4.3 Hz, 1 H), 7.26 (d, *J* = 9.5 Hz, 1 H), 7.18 (d, *J* = 10.0 Hz, 1 H), 2.44 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.6, 140.0, 136.7, 136.1, 132.2, 130.9, 126.4, 125.4, 123.3, 120.8, 120.6, 116.9, 20.9; UV-Vis (methanol) λ_{max}, nm (ε) 662 (342), 283 (86,600). Anal. Calcd for $C_{13}H_9NO_2$: C, 73.92; H, 4.29; N, 6.63. Found: C, 73.65; H, 4.04; N, 6.45.



21

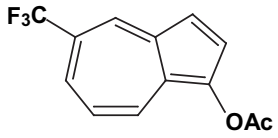
1-Acetoxy-6-nitroazulene (21). Brown solid, mp 97.0-97.5 °C. IR (CCl_4) 2920, 1770, 1535, 1440, 1395, 1330, 1315, 1245, 1205, 1195, 1035, 1005, 980 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.29-8.33 (m, 2 H), 8.00-8.14 (m, 3 H), 7.44 (d, *J* = 4.3 Hz, 1 H), 2.46 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.5, 154.0, 140.2, 136.8, 134.7, 132.8, 129.8, 126.2, 117.1, 116.3, 114.6, 21.0; UV-Vis (CH_3CN) λ_{max}, nm (ε) 686 (310), 352 (565), 291 (51,500), 246 (19,850), 221 (16,700), 205 (16,300), 198 (26,900), 193 (29,300). Anal. Calcd for $C_{12}H_9NO_4$: C, 62.34; H, 3.92; N, 6.06. Found: C, 62.39; H, 3.83; N, 5.74.



22

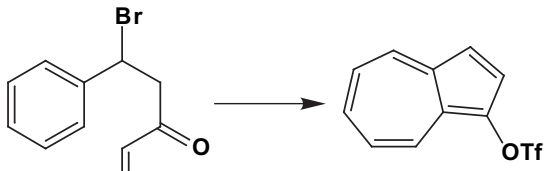
1-Acetoxy-5-bromoazulene (22). Olive green solid, mp 60.5-61.5 °C. IR (CCl_4) 2900, 1765, 1580, 1545, 1420, 1395, 1365, 1300, 1200, 1030, 995, 895 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.49 (d, *J* = 2.1 Hz, 1 H), 8.13 (d, *J* = 9.8 Hz, 1 H), 7.90-7.84 (m, 2 H), 7.24 (d, *J* = 4.3 Hz, 1 H), 6.83 (app t, *J*

= 9.9 Hz, 1 H), 2.42 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.9, 141.0, 140.9, 138.6, 133.6, 131.3, 129.9, 126.2, 120.7, 117.4, 114.7, 21.0; UV-Vis (hexane) λ_{max}, nm (ε) 690 (273), 632 (302), 601 (250), 371 (3,230), 362 (2,440), 351 (3,980), 347 (2,860), 337 (2,070), 278 (28,900). Anal. Calcd for $C_{12}H_9BrO_2$: C, 54.37; H, 3.42. Found: C, 54.59; H, 3.29.



23

1-Acetoxy-5-(trifluoromethyl)azulene (23). Blue solid, mp 43.5-44.5 °C. IR (CCl_4) 2920, 2840, 1770, 1580, 1500, 1460, 1400, 1370, 1330, 1290, 1260, 1200, 1170, 1130, 1055, 1035, 1000, 915 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.45 (d, *J* = 1.4 Hz, 1 H), 8.29 (d, *J* = 9.5 Hz, 1 H), 7.92 (d, *J* = 4.3 Hz, 1 H), 7.83 (d, *J* = 4.3 Hz, 1 H), 7.47 (d, *J* = 4.3 Hz, 1 H), 7.09 (app t, *J* = 9.8 Hz, 1 H), 2.43 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.8, 140.5, 134.8, 134.7, 134.4, 134.1, 134.0, 133.3, 129.4, 126.2, 120.5, 118.6, 21.0; UV-Vis (hexane) λ_{max}, nm (ε) 608 (255), 583 (221), 352 (8,474), 278 (61,858), 215 (11,863). Anal. Calcd for $C_{13}H_9F_3O_2$: C, 61.42; H, 3.56. Found: C, 61.43; H, 3.63.



5 **24**

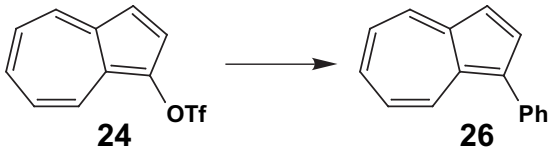
1-(Trifluoromethanesulfonyloxy)azulene (24). A 100-mL, three-necked, round-bottomed flask equipped with a rubber septum, 60-mL pressure-equalizing addition funnel, and an argon inlet adapter was charged with rhodium pivalate (0.006 g, 0.010 mmol) and 18 mL of dichloromethane. The addition funnel was charged with 4-bromo-1-diazo-4-phenyl-2-butanone (0.253 g, 1.00 mmol) and 16 mL of dichloromethane, and the bright yellow solution of the diazo ketone was added dropwise over 45 min to the rapidly stirring green solution of catalyst. After 5 min, *N*-phenyltrifluoromethanesulfonimide (0.357 g, 1.00 mmol) was added in one portion, and then a solution of 4-dimethylaminopyridine (0.367 g, 3.00 mmol) in 2 mL of dichloromethane was immediately added via cannula. The resulting deep blue solution was stirred for 10 min and then treated with 1 mL of piperidine. After stirring for an additional 15 min, the reaction mixture was

poured into a separatory funnel containing 30 mL of diethyl ether and 30 mL of 1 M HCl solution. The organic phase was separated and washed with two 30-mL portions of 1 M HCl and 30 mL of brine, dried over $MgSO_4$, and filtered to afford a blue solution of the triflate which was used immediately in the next reaction without further purification. A sample of the product of another reaction was purified by column chromatography on silica gel (elution with 5% ethyl acetate-hexanes) to afford 1-(trifluoromethanesulfonyloxy)azulene as an unstable purple-blue oil: IR (CCl_4) 3000, 1580, 1550, 1490, 1420, 1400, 1310, 1240, 1210, 1140, 990, 885 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.35 (d, J = 9.7Hz, 1 H), 8.34 (d, J = 9.4 Hz, 1 H), 7.68-7.74 (m, 2 H), 7.22-7.31 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.7, 139.6, 136.1, 134.5, 132.5, 127.2, 126.7, 124.4, 124.1, 116.8, 113.7.

24 **25**

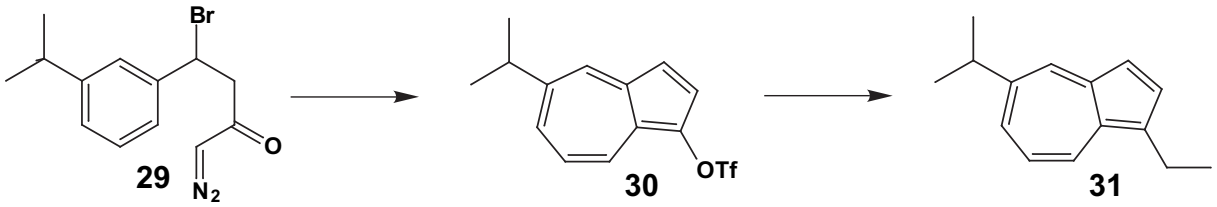
1-Ethylazulene (25). A solution of crude azulene triflate **24** in ether-dichloromethane prepared as described above was transferred to a 25-mL round-bottomed flask and concentrated using a rotary evaporator to a volume of ca. 5 mL. The flask was then equipped with a stirbar and argon inlet adapter and the solution was concentrated further at 0.1 mmHg with vigorous stirring to a volume of 0.2-0.5 mL.[8] The argon inlet adapter was immediately removed and replaced with a rubber septum and argon inlet needle, and 1.0 mL of THF was added to produce a dark purple solution. Palladium acetate (0.011 g, 0.05 mmol), *o*(dicyclohexylphosphino)biphenyl (0.026 g, 0.075 mmol), and cesium carbonate (0.977 g, 3.0 mmol) were then added, followed by a solution of *B*-ethyl-9-BBN[9] (prepared by stirring 10 mL of a 0.5 M solution of 9-BBN in THF under a positive pressure of ethylene for 2 h). The resulting mixture was stirred at room temperature for 2 h and the resulting black suspension was then diluted with 30 mL of diethyl ether and washed with 30 mL of 2 M NaOH solution and 30 mL of brine, dried over $MgSO_4$, filtered, and concentrated to yield 1.17 g of a turquoise oil. Purification by column chromatography on silica gel (elution with pentane) afforded 0.088 g (56% overall from diazo ketone **5**) of 1-ethylazulene[10] as a dark blue oil: IR (thin film) 3010, 2960, 2920, 2860, 1570, 1530, 1500, 1450, 1420, 1390, 1290 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, J = 9.2 Hz, 1 H), 8.25 (d, J = 9.5 Hz, 1 H), 7.82 (d, J = 3.7 Hz, 1 H), 7.53 (t, J = 9.8 Hz, 1

H), 7.35 (d, J = 3.7 Hz, 1 H), 7.08 (t, J = 9.8 Hz, 1 H), 7.06 (t, J = 9.6 Hz, 1 H), 3.12 (q, J = 7.6 Hz, 2 H), 1.40 (t, J = 7.6 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.4, 137.3, 136.3, 136.2, 135.3, 133.2, 133.0, 121.9, 121.2, 116.6, 20.4, 15.7. Anal. Calcd for $C_{12}H_{12}$: C, 92.24; H, 7.76. Found: C, 91.96; H, 8.06.



24 **26**

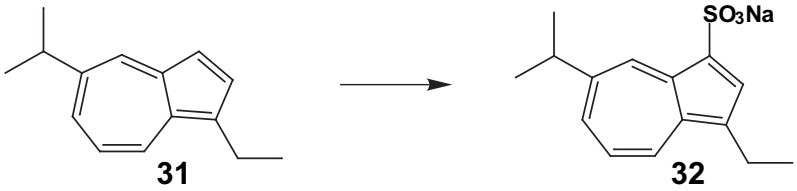
1-Phenylazulene (26). A solution of crude azulene triflate **24** in ether-dichloromethane prepared as described above was transferred to a 25-mL round-bottomed flask and concentrated using a rotary evaporator to a volume of ca. 5 mL. The flask was then equipped with a stirbar and argon inlet adapter and the solution was concentrated further at 0.1 mmHg with vigorous stirring to a volume of 0.2-0.5 mL.[8] The argon inlet adapter was immediately removed and replaced with a rubber septum and argon inlet needle, and 1.0 mL of THF was added to produce a dark purple solution. Palladium acetate (0.011 g, 0.050 mmol), *o*-(dicyclohexylphosphino)biphenyl (0.035 g, 0.100 mmol), cesium carbonate (0.977 g, 3.0 mmol), and *B*-phenyl-9-BBN (0.277 g, 1.4 mmol) were then added, and the septum was replaced with a reflux condenser fitted with an argon inlet adapter. The dark purple suspension was heated at reflux (preheated oil bath) for 15 min and then allowed to cool to room temperature. The resulting black suspension was diluted with 30 mL of diethyl ether and washed with 30 mL of 2 M NaOH solution and 30 mL of brine, dried over $MgSO_4$, filtered, and concentrated to yield 0.345 g of a turquoise oil. Purification by column chromatography on silica gel (elution with pentane) afforded 0.124 g (60% overall from diazo ketone **5**) of 1-phenylazulene as a dark blue solid: mp 51-53 °C (lit.[11] mp 58 °C); IR (thin film) 3050, 3000, 2960, 1600, 1570, 1480, 1390 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (d, J = 9.8 Hz, 1 H), 8.40 (dd, J = 9.8, 0.6 Hz, 1 H), 8.09 (d, J = 4.0 Hz, 1 H), 7.70-7.67 (m, 2 H), 7.63 (t, J = 9.8 Hz, 2 H), 7.55 (appar t, J = 7.8 Hz, 1 H), 7.50 (d, J = 3.7 Hz, 1 H), 7.41 (m, 1 H), 7.19 (t, J = 9.9 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.6, 138.2, 137.5, 137.2, 137.1, 135.6, 135.2, 131.3, 129.7, 128.6, 126.2, 123.3, 123.0, 117.4. Anal. Calcd for $C_{16}H_{12}$: C, 94.08; H, 5.92. Found: C, 94.05; H, 6.28.



1-Ethyl-5-isopropylazulene (31). A 100-mL, three-necked, round-bottomed flask equipped with a rubber septum, 60-mL pressure-equalizing addition funnel, and argon inlet adapter was charged with rhodium pivalate (0.012 g, 0.020 mmol) and 18 mL of diethyl ether. The addition funnel was charged with 4-bromo-1-diazo-4-(3-isopropylphenyl)-2-butanone (0.295 g, 1.00 mmol) and 16 mL of diethyl ether, and the bright yellow solution of diazo ketone was added dropwise over 45 min to the rapidly stirred green solution of catalyst. After 5 min, *N*-phenyltrifluoromethanesulfonimide (0.357 g, 1.00 mmol) was added in one portion, and then a solution of 4-dimethylaminopyridine (0.367 g, 3.00 mmol) in 15 mL of diethyl ether was immediately added via cannula. The resulting deep purple suspension was stirred for 10 min and then treated with 1 mL of piperidine. After stirring an additional 15 min, the reaction mixture was poured into a separatory funnel containing 50 mL of diethyl ether and 50 mL of 1 M HCl solution. The organic phase was separated and washed with two 50-mL portions of 1 M HCl and 50 mL of brine, dried over $MgSO_4$, and filtered to afford a blue solution of the triflate which was used immediately in the next reaction without further purification.

The solution of azulene triflate **30** in diethyl ether prepared as described above was transferred to a 50-mL round-bottomed flask and concentrated using a rotary evaporator to a volume of ca. 5 mL. The flask was then equipped with a stirbar and argon inlet adapter and the remaining solvent was removed at 0.1 mmHg with vigorous stirring.[8] The argon inlet adapter was immediately removed and replaced with a rubber septum and argon inlet needle, and 1.0 mL of THF was added to produce a dark blue solution. Palladium acetate (0.011 g, 0.050 mmol), *o*-(dicyclohexylphosphino)biphenyl (0.026 g, 0.075 mmol), potassium fluoride (0.174 g, 3.00 mmol), and triethylborane (1.40 mL of a 1.0 M solution in THF, 1.40 mmol) were added, and the septum was replaced with a reflux condenser fitted with an argon inlet adapter. The dark blue suspension was heated at reflux (preheated oil bath) for 10 min and then allowed to cool to room temperature. The resulting black suspension was diluted with 30 mL of diethyl ether and washed with 30 mL of 2 M NaOH solution and 30 mL of brine, dried over $MgSO_4$, filtered, and concentrated to yield 0.293 g of a black oil. Purification by column chromatography on silica gel

(elution with pentane) afforded 0.083 g (42% overall from diazo ketone **29**) of 1-ethyl-5-isopropylazulene as a dark blue oil: IR (thin film): 2950, 2920, 2860, 1570, 1505, 1455 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, *J* = 1.9 Hz, 1 H), 8.17 (d, *J* = 9.6 Hz, 1 H), 7.77 (d, *J* = 3.8 Hz, 1 H), 7.43-7.48 (m, 1 H), 7.24 (d, *J* = 3.8 Hz, 1 H), 7.02 (t, *J* = 10.0 Hz, 1 H), 3.02-3.10 (m, 3 H), 1.33-1.39 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.8, 140.5, 136.2, 136.1, 136.0, 134.7, 131.9, 131.8, 120.8, 115.7, 38.3, 24.5, 20.4, 15.8. Anal. Calcd for $C_{15}H_{18}$: C, 90.83; H, 9.17. Found: C, 90.80; H, 9.19.



31 **32**

Sodium 3-Ethyl-7-isopropyl-1-azulenesulfonate (KT1-32) (32). A 10-mL, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with 1-ethyl-5-isopropylazulene **31** (0.086 g, 0.434 mmol) and 3.0 mL of benzene. Sulfur trioxide-pyridine complex (0.414 g, 2.60 mmol, 6.00 equiv) was added, and the septum was replaced with a reflux condenser fitted with an argon inlet adapter. The resulting blue mixture was heated at reflux for 3.5 h and then allowed to cool to room temperature. The reaction mixture was filtered with the aid of 50 mL of absolute ethanol and the filtrate was concentrated using a rotary evaporator to a volume of ca. 5 mL and then cooled at 0 °C while a solution of NaOH (0.100 g) in 5 mL of water was added via pipet. The resulting solution was heated at 30-35 °C for 2 h, allowed to cool to room temperature, and then diluted with 30 mL of 1-butanol. The organic layer was washed with two 30-mL portions of brine, dried over Na_2SO_4, and concentrated to yield 0.280 g of dark blue solid. Purification by column chromatography on silica gel (elution with 10% ethanol-acetonitrile) afforded 0.074 g (57%) of **32** as a blue oil. Repeated concentration of the solid from carbon tetrachloride furnished **32** as a blue-green solid: mp 154.5-156.0 °C (lit.[12] mp 152-154 °C (dec)); IR (KBr) 3448, 2960, 1459, 1420, 1388, 1178, 1049 cm^{-1}; ^1H NMR (500 MHz, DMSO) δ 9.09 (d, *J* = 1.53 Hz, 1 H), 8.22 (d, *J* = 9.5 Hz, 1 H), 7.81 (s, 1 H), 7.61 (d, *J* = 10.4 Hz, 1 H), 7.13 (t, *J* = 9.9 Hz, 1 H), 3.04 (sept, *J* = 6.7 Hz, 1 H), 2.96 (q, *J* = 7.6 Hz, 2 H), 1.30 (d, *J* = 6.7 Hz, 6 H), 1.28 (t, *J* = 7.6 Hz, 3 H); ^{13}C NMR (125 MHz, DMSO) δ 142.4, 136.6, 136.3, 135.9, 135.8,

133.4, 132.8, 132.7, 127.7, 122.1, 38.1, 24.5, 19.5, 15.7; HRMS (FAB): calcd for $C_{15}H_{17}NaO_3S$ $(M+H)^+$ 301.0874, found 301.0869.

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