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Ring Expansion-Annulation Strategy for the Synthesis of Substituted Azulenes and Oligoazulenes. 2. Synthesis of Azulenyl Halides, Sulfonates, and Azulenylmetal Compounds and Their Application in Transition-Metal-Mediated Coupling Reactions

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A "ring expansion-annulation strategy" for the synthesis of substituted azulenes is described based on the reaction of β'-bromo-α-diazo ketones with rhodium carboxylates. The key transformation involves an intramolecular Büchner reaction followed by β-elimination of bromide, tautomerization, and in situ trapping of the resulting 1-hydroxyazulene as a carboxylate or triflate ester. Further synthetic elaboration of the azulenyl halide and sulfonate annulation products can be achieved by employing Heck, Negishi, Stille, and Suzuki coupling reactions. Reaction of the azulenyl triflate **84** with pinacolborane provides access to the azulenylboronate **91**, which participates in Suzuki coupling reactions with alkenyl and aryl iodides. The application of these coupling reactions to the synthesis of biazulenes, terazulene **101**, and related oligoazulenes is described, as well as the preparation of the azulenyl amino acid derivative **110**.

Introduction

This paper describes a general "ring expansion-annulation strategy" for the synthesis of substituted azulenes. The method is particularly well suited for the preparation of azulenes bearing halogen and sulfonate substituents, and the resultant annulation products can be employed in a variety of transition-metal-catalyzed carbon−carbon bond-forming reactions. Together, these processes provide a powerful tandem strategy for the preparation of a wide range of azulenes substituted on both the five- and seven-membered rings.[1]

The azulenes constitute the best known class of polycyclic nonbenzenoid aromatic compounds and have long fascinated chemists with their beautiful colors and unusual electronic properties.[2] Guaiazulene, a naturally occurring azulene, has a long history as an additive in cosmetics and lotions, and more recently, azulenes have attracted interest in medicine as antiulcer drugs,[3] anticancer agents,[4] and as antioxidant therapeutics for neurodegenerative conditions.[5] Other important applications of azulene derivatives exploit their unique electronic characteristics, and considerable attention has recently been focused on their potential utility as components in "advanced materials" with novel electronic and optical properties.[6]

Few general methods for the synthesis of substituted azulenes have been reported to date, and consequently nearly all commercial applications of azulenes have relied on the availability of the naturally occurring sesquiterpene guaiazulene. Early approaches to the synthesis of azulenes required low-yield dehydrogenation steps and were limited to the preparation of relatively simple derivatives. More recently, however, powerful annulation strategies have been developed that provide access to azulenes of more complex structure. Particularly useful annulation methods include the Ziegler−Hafner synthesis,[7] annulation methods based on 2*H*-cyclohepta[*b*]furan-2-ones,[8] [6+4] cycloadditions,[9] and [3+2] annulations involving the reaction of tropylium cation with allenylsilanes.[10] Unfortunately, while these methods provide

(1) For a preliminary account of part of this work, see: Kane, J. L., Jr.; Shea, K. M.; Crombie, A. L.; Danheiser, R. L. *Org. Lett.* **2001**, *3*, 1081.

(2) For reviews, see: (a) Zeller, K.-P. In *Methoden der Organischen Chemie* (*Houben-Weyl*); Kropf, H., Ed.; Georg Thieme Verlag: Stuttgart, Germany, 1985; Vol. V/2c, p 127. (b) Lloyd, D. *Nonbenzenoid Conjugated Carbocyclic Compounds*; Elsevier: Amsterdam, The Netherlands, 1984; pp 352−377. (c) Lloyd, D. *The Chemistry of Conjugated Cyclic Compounds*; John Wiley and Sons: Chichester, UK, 1989; Chapter 13. (d) Mochalin, V. B.; Porshnev, Yu. N. *Russ. Chem. Rev.* **1977**, *46*, 530.

(3) Yanagisawa, T.; Wakabayashi, S.; Tomiyama, T.; Yasunami, M.; Takase, K. *Chem. Pharm. Bull.* **1988**, *36*, 641.

(4) (a) Asato, A. E.; Peng, A.; Hossain, M. Z.; Mirzadegan, T.; Bertram, J. S. *J. Med. Chem.* **1993**, *36*, 3137. (b) Hong, B.-C.; Jiang, Y.-F.; Kumar, E. S. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 1981. (c) Hidetsugu, W.; Kana, H.; Keiko, Y.; Ken, H.; Hirotaka, K.; Hirofumi, N.; Teruo, K.; Kazue, S.; Seiji, S.; Susumu, S.; Shuichi, K.; Hidecki, N.; Noboru, M.; Hiroshi, S. *Anticancer Res.* **2003**, *23*, 4747.

(5) Becker, D. A.; Ley, J. J.; Echegoyen, L.; Alvarado, R. *J. Am. Chem. Soc.* **2002**, *124*, 4678.

(6) For recent representative examples, see: (a) Ito, S.; Inabe, H.; Okujima, T.; Morita, N.; Watanbe, M.; Imafuku, K. *Tetrahedron Lett.* **2000**, *41*, 8343. (b) Ohta, A.; Yamaguchi, K.; Fujisawa, N.; Yamashita, Y.; Fujimori, K. *Heterocycles* **2001**, *54*, 377. (c) Wang, F.; Lai, Y.-H. *Macromolecules* **2003**, *36*, 536. (d) Wang, F.; Lai, Y.-H.; Han, M.-Y. *Org. Lett.* **2003**, *5*, 4791. (e) Ito, S.; Inabe, H.; Morita, N.; Ohta, K.; Kitamura, T.; Imafuku, K. *J. Am. Chem. Soc.* **2003**, *125*, 1669 and references therein.

(7) (a) Hafner, K.; Meinhardt, K.-P. *Organic Syntheses*; Wiley: New York, 1990; Collect. Vol. VII, p 15. (b) Reviewed in: Jutz, J. C. *Top. Curr. Chem.* **1978**, *73*, 125.

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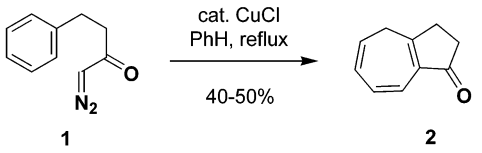
efficient access to azulenes substituted on the five-membered ring and to azulene itself, they have limited utility for the synthesis of derivatives bearing substituents on the *seven-membered ring*.

The goal of our research has been the design of a general strategy for the synthesis of azulenes substituted on both the five- *and* seven-membered rings. Since a wide variety of substituted benzene derivatives are easily prepared or are commercially available, we have focused our attention on approaches that might employ these readily obtained compounds as starting materials. Most attractive to us in this regard have been "*ring-expansion-annulation strategies*": cascade ("tandem") processes[11] in which a benzene ring is expanded to seven carbon atoms concomitant with the creation of a five-membered ring. Specifically, our investigations have focused on intramolecular variants of the Büchner cycloheptatriene synthesis, which has previously been applied to the synthesis of *hydro*azulenes by Julia, Scott, and McKervey,[12] among others. Pioneering work in this area was carried out in the laboratories of Scott, who in 1973 reported the copper-catalyzed cyclization of diazo ketone **1** to afford the bicyclic trienone **2** in moderate yield.[13,14] Although exposure of **2** to alumina and then P_2O_5 in methanesulfonic acid at 60 °C effects its transformation to azulene, unfortunately this process proceeds in only 30−50% yield, and attempts to apply a similar strategy to the synthesis of *substituted* azulenes gave the desired compounds in very low yield.[13b]



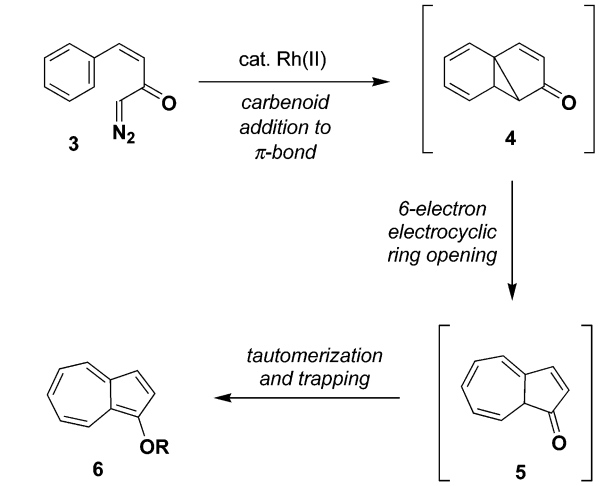
1 2 (1)

Results and Discussion

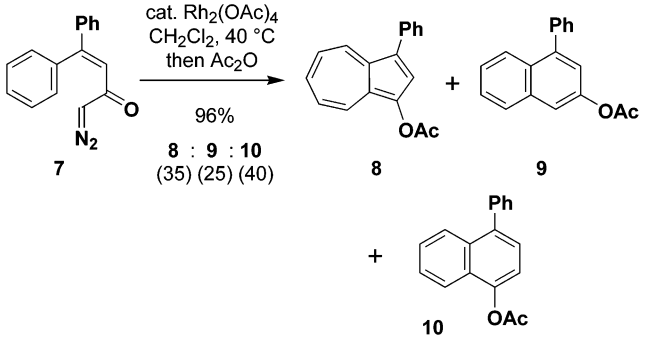
The aim of our studies in this area has been the design of a variant of the intramolecular Büchner strategy that would deliver azulene derivatives directly and without the need for elevated temperatures or harsh reagents to effect elimination and/or dehydrogenation steps.

Diazo Enone Strategy. Our first attempt to circumvent the need for a dehydrogenation step involved the cyclization of α′-diazo derivatives of α,β-unsaturated ketones of general type **3** (Scheme 1). Intramolecular

SCHEME 1



SCHEME 2



Büchner reaction of substrates of this type could afford enones of type **5**, which we expected would tautomerize to furnish 1-hydroxyazulenes (**6**, R = H). 1-Hydroxyazulenes are known to be quite unstable, readily undergoing polymerization,[15] and we therefore planned to trap this intermediate in situ as a carboxylate or sulfonate ester. Thus, as an added bonus, this strategy would provide azulenes functionalized with hydroxy derivatives at the C-1 position that potentially could be elaborated via transition-metal-catalyzed coupling reactions to a wide variety of functionalized and substituted azulenes.

Unfortunately, all attempts to achieve the desired transformation produced the desired azulenes accompanied by isomeric naphthalene byproducts. For example, treatment of diazo enone **7**[16] with a catalytic amount of rhodium acetate followed by acetic anhydride led in near-quantitative yield to a mixture of azulene **8** and the naphthol derivatives **9** and **10** (Scheme 2). The 2-naphthol derivative **9** may arise via an acid-promoted rearrangement of the norcaradiene intermediate of type **4**,[17,18] while the 1-naphthol **10** most likely is formed via Wolff

(8) (a) Yang, P.-W.; Yasunami, M.; Takase, K. *Tetrahedron Lett.* **1971**, 4275. (b) Wakabayashi, H.; Yang, P.-W.; Wu, C.-P.; Shindo, K.; Ishikawa, S.; Nozoe, T. *Heterocycles* **1992**, *34*, 429 and references therein.

(9) Mukherjee, D.; Dunn, L. C.; Houk, K. N. *J. Am. Chem. Soc.* **1979**, *101*, 251 and references therein.

(10) Becker, D. A.; Danheiser, R. L. *J. Am. Chem. Soc.* **1989**, *111*, 389.

(11) Reviews: (a) Ho, T.-L. *Tandem Organic Reactions*; Wiley: New York, 1992. (b) Tietze, L. F.; Beifuss, U. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 131. (c) Bunce, R. A. *Tetrahedron* **1995**, *51*, 13103.

(12) For a review, see: Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; John Wiley & Sons: New York, 1998; pp 289−324.

(13) (a) Scott, L. T. *J. Chem. Soc., Chem. Commun.* **1973**, 882. (b) Scott, L. T.; Minton, M. A.; Kirms, M. A. *J. Am. Chem. Soc.* **1980**, *110*, 6311. (c) Scott, L. T.; Sumpter, C. A. *Organic Syntheses*; Wiley: New York, 1993, Collect. Vol. VIII, p 196.

(14) In subsequent studies, McKervey found that this process proceeds more efficiently when catalyzed by rhodium(II) acetate dimer. See ref 13c and: McKervey, M. A.; Tuladhar, S. M.; Twohig, M. F. *J. Chem. Soc., Chem. Commun.* **1984**, 129.

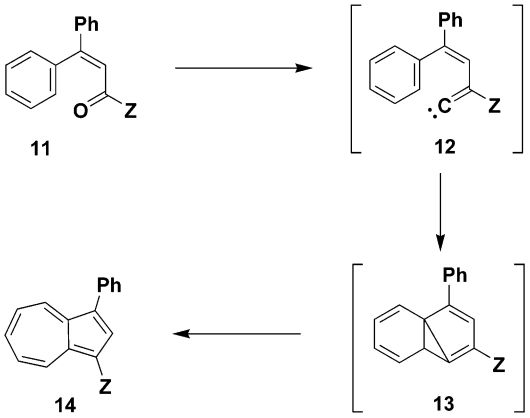
(15) (a) Asao, T.; Ito, S.; Morita, N. *Tetrahedron Lett.* **1989**, *30*, 6693. (b) Asao, T. *Pure Appl. Chem.* **1990**, *62*, 507.

(16) Prepared from 4,4-diphenylbut-3-en-2-one in 85% yield via detrifluoroacetylative diazo transfer according to the method of Danheiser et al.: Danheiser, R. L.; Miller, R. F.; Brisbos, R. G.; Park, S. Z. *J. Org. Chem.* **1990**, *55*, 1959.

(17) See: McKervey, M. A.; Tuladhar, S. M.; Twohig, M. F. *J. Chem. Soc., Chem. Commun.* **1984**, 129.

(18) For the formation of 2-naphthols in the cyclization of related diazo derivatives of β-keto esters, see: Taylor, E. C.; Davies, H. M. L. *Tetrahedron Lett.* **1983**, *24*, 5453.

SCHEME 3

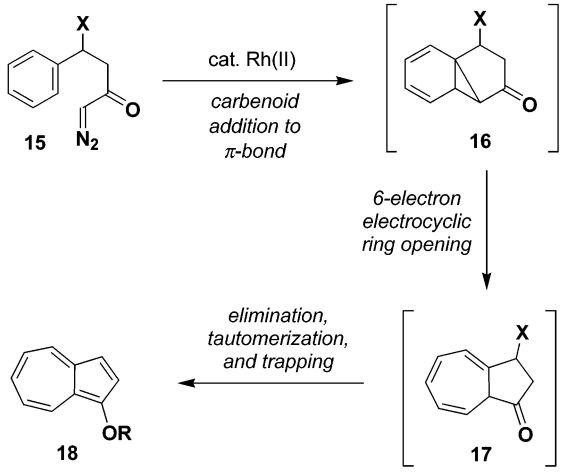


rearrangement of **7** to generate a vinylketene which then undergoes 6π electrocylic closure.[19]

Alkylidenecarbene Strategy. We next turned our attention to a variant of the Büchner cyclization based on alkylidenecarbenes of type **12** (Scheme 3). Many methods are available for the generation of alkylidenecarbenes from carbonyl compounds,[20] and Brown has previously reported the formation of benzazulene in a reaction in which a related alkylidenecarbene is generated by vapor phase pyrolysis.[21] We focused our attention on the convenient generation of alkylidenecarbenes by reaction of carbonyl compounds with diazomethylphosphonate (DAMP).[22] Unfortunately, reactions of ketones of type **11** (e.g., **11**, Z = CH_3) with DAMP failed to take place under a variety of conditions, and not unexpectedly, aldehydes (**11**, Z = H) reacted with DAMP to form conjugated enynes via the very facile 1,2 C−H shift that is well documented for alkylidenecarbenes derived from aldehydes.[20a−b,23,24]

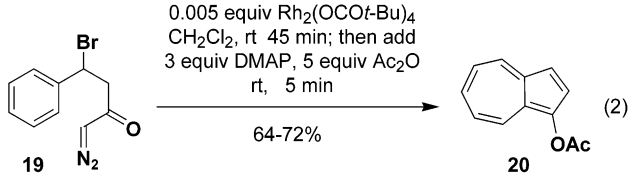
***β*-Halo Diazo Ketone Strategy.** With the failure of the exploratory studies summarized above, we turned our attention to the strategy outlined in Scheme 4 in which the intramolecular Büchner reaction is carried out with use of a substrate bearing a suitable leaving group "X". We anticipated that this process would deliver a bicyclic ketone of type **17** that would undergo β-elimination and subsequent tautomerization to afford a 1-hydroxyazulene derivative. As mentioned earlier, it was hoped that this type of ring expansion-annulation product could be

SCHEME 4



trapped as a sulfonate derivative, which could then be elaborated via transition-metal-catalyzed coupling reactions to furnish a variety of 1-substituted azulenes. At the outset we recognized, however, that for this approach to be successful it would be necessary to identify a leaving group that would be stable to the conditions of the carbenoid addition step, that would not undergo premature elimination at the stage of **15** or intermediate **16**, and whose elimination from **17** would take place more rapidly than isomerization of the β,γ-double bond to form a trienone analogous to **2** (eq 1).

Our initial studies focused on β-hydroxy ketone derivatives (e.g., **15**, X = OAc), and in these cases isomerization indeed proved competitive with the desired elimination. Ultimately we found that halogens, particularly bromine, function as the best leaving groups for the desired transformation. The feasibility of the ring expansion-annulation strategy was initially demonstrated by using the known diazo ketone **19**.[25] Optimal conditions involve dropwise addition of the diazo ketone over 45 min to 0.5 mol % of rhodium(II) pivalate[26,27] in dichloromethane at room temperature. Elimination of bromide and trapping of the resulting unstable hydroxyazulene is then accomplished by addition of excess 4-(dimethylamino)-pyridine and acetic anhydride. As outlined in eq 2, 1-acetoxyazulene[28] is obtained as blue needles in up to 72% overall yield with use of this convenient "one-flask" procedure.



Preparation of *β*′-Bromo-α-Diazo Ketones. Several synthetic approaches to the requisite diazo ketone ring expansion-annulation substrates were examined. For most substrates, the most efficient route begins with readily available cinnamic acids and employs hydrobro-

(19) Marvell, E. N. *Thermal Electrocyclic Reactions*; Academic Press: New York, 1980.

(20) For examples, see: (a) Colvin, E. W.; Hamill, B. J. *J. Chem. Soc., Chem. Commun.* **1973**, 151. (b) Colvin, E. W.; Hamill, B. J. *J. Chem. Soc., Perkin Trans. 1* **1977**, 869. (c) Trahanovsky, W. S.; Emeis, S. L.; Lee, A. S. *J. Org. Chem.* **1976**, *41*, 4044. (d) Brown, R. F. C.; Eastwood, F. W. *J. Org. Chem.* **1981**, *46*, 4588.

(21) Brown, R. F. C.; Eastwood, F. W.; Harrington, K. J.; McMullen, G. L. *Aust. J. Chem.* **1974**, *27*, 2393.

(22) (a) Seyferth, D.; Marmor, R. S. *J. Org. Chem.* **1971**, *36*, 128. (b) Seyferth, D.; Marmor, R. S.; Hilbert, P. *J. Org. Chem.* **1971**, *36*, 1379. (c) Regitz, M. *Liebigs Ann. Chem.* **1971**, *748*, 207.

(23) After our study, Aoyama and co-workers reported the synthesis of 2,3-dihydroazulenes via a related strategy involving intramolecular reactions of alkylidenecarbenes. In their approach, a 4-aryl-2-oxobutanoic ester ($ArCH_2CH_2COCO_2R$) is reacted with $Me_3SiCH(Li)N_2$ to generate a carbene that furnishes a 1-carboalkoxy-2,3-dihydroazulene in moderate yield. See: Hari, Y.; Tanaka, S.; Takuma, Y.; Aoyama, T. *Synlett* **2003**, 2151.

(24) For earlier, related intramolecular Büchner reactions for the synthesis of cycloheptapyrrolones, see: (a) Gilbert, J. C.; Blackburn, B. K. *J. Org. Chem.* **1986**, *51*, 4087. (b) Ogawa, H.; Aoyama, T.; Shioiri, T. *Synlett* **1994**, 757.

(25) Rosenquist, N. R.; Chapman, O. L. *J. Org. Chem.* **1976**, *41*, 3326.

(26) Legzdins, P.; Mitchell, R. W.; Rempel, G. L.; Ruddick, J. D.; Wilkinson, G. *J. Chem. Soc.* **1970**, 3322.

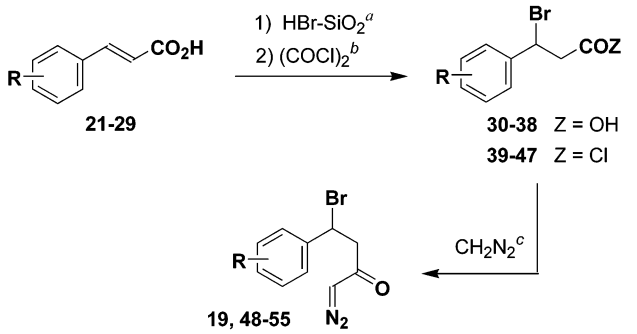
mination to install the β-bromine atom followed by elaboration of the carboxylic acids to diazo ketones with use of standard Arndt−Eistert conditions. An attractive feature of this approach is that many cinnamic acids are commercially available, and others are easily prepared in one step from benzaldehydes by using the Knoevenagel reaction.[29]

Initial attempts to add either HCl or HBr to cinnamic acids were not fruitful, and led to mixtures of the desired product and recovered starting material. After considerable experimentation, a successful protocol was finally developed based on the general method of Kropp.[30] Optimal conditions involve treatment of the cinnamic acid with a solution of anhydrous HBr in dichloromethane in the presence of silica gel[31] (10 g per 0.6−2 g of alkene) at room temperature. Purification of the resulting β-bromo carboxylic acids is not necessary, and reaction with oxalyl chloride and then diazomethane furnishes the expected β-bromo diazo ketones in good overall yield (Table 1).

Addition of HBr to cinnamic acids with alkyl-substituted and electron-rich aryl groups proceeded smoothly to completion in 22−48 h;[32] however, electron-deficient substrates (Table 1, entries 2−6, 9) were found to require extended reaction times (90−192 h). For the synthesis of even more highly electron-deficient systems, an alternative synthetic route was developed based on the benzylic bromination of 3-phenylpropionic acids[33] (Table 2). This alternative protocol also proved useful for the preparation of diazo ketone **67** (entry 3), as 2-methylcinnamic acid was recovered unchanged from attempted hydrobromination with $HBr-SiO_2$.

Scope of the Ring Expansion-Annulation Strategy. Table 3 delineates the scope of the ring expansion-annulation strategy. In a typical reaction, a solution of the diazo ketone is added dropwise over 45−90 min to a solution of 0.005 to 0.01 equiv of rhodium(II) pivalate at room temperature. Base (e.g., 4-DMAP) and a trapping agent are then added, and after 5 min the reaction is quenched by addition of methanol. Workup and purification by column chromatography then furnishes the desired azulenes. The overall yields for this multistep cascade process are generally good, except in the case of some of the more electron-deficient substrates (e.g., entries 9 and 10) where the desired azulenes are produced in ca. 20% overall yield accompanied by several uncharacterizable byproducts. Noteworthy is the success

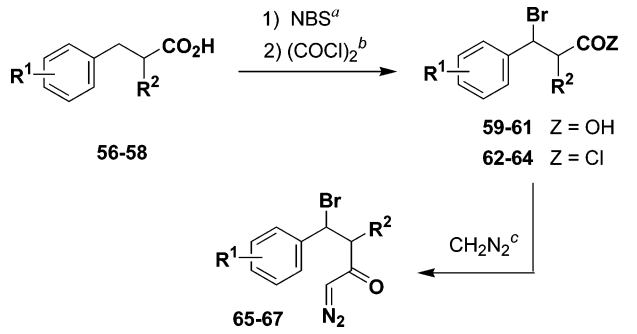
TABLE 1. Preparation of β-Bromo Diazo Ketones from Cinnamic Acids



entry	R	cinnamic acid	β-bromo acid	β-bromo acid chloride	diazo ketone (overall yield[d])
1	H	**21**	**30**	**39**	**19** (60%)
2	2-Cl	**22**	**31**	**40**	**48** (51%)
3	2-I	**23**[e]	**32**	**41**	**49** (53%)
4	3-*i*-Pr	**24**[f]	**33**	**42**	**50** (51−60%)
5	3-Br	**25**	**34**	**43**	**51** (55%)
6	3-CF_3	**26**	**35**	**44**	**52** (30%)
7	4-CH_3	**27**	**36**	**45**	**53** (47%)
8	4-Cl	**28**	**37**	**46**	**54** (61%)
9	3,4-di-Cl	**29**	**38**	**47**	**55** (45%)

[a] $HBr-SiO_2$, CH_2Cl_2, rt, 22−192 h. [b] 1.2 equiv of $(COCl)_2$, PhH, 65 °C, 15−18 h. [c] 4.0 equiv of CH_2N_2, Et_2O, 0 °C to rt, 1−3 h. [d] Overall isolated yield (from corresponding cinnamic acids) of products purified by chromatography on silica gel. [e] Prepared in 88% yield by Knoevenagel reaction of malonic acid with 2-iodobenzaldehyde (piperidine, pyridine, reflux, 16 h) as previously described by Larock and Doty (Larock, R. C.; Doty, M. J. *J. Org. Chem.* **1993**, *58*, 4579). [f] See Supporting Information and ref 1.

TABLE 2. Preparation of β-Bromo Diazo Ketones from 3-Arylpropionic Acids



entry	R^1	R^2	propionic acid	β-bromo acid	β-bromo acid chloride	diazo ketone (overall yield[d])
1	4-NO_2	H	**56**[e]	**59**	**62**	**65** (28%)
2	4-CN	H	**57**[f]	**60**	**63**	**66** (41%)
3	H	CH_3	**58**[g]	**61**	**64**	**67** (60%)

[a] 1.2 equiv of NBS, cat. AIBN, CCl_4, *hν*, 80 °C, 2−4 h. [b] 1.2 equiv of $(COCl)_2$, PhH, 65 °C, 15−18 h. [c] 4.0 equiv of CH_2N_2, Et_2O, 0 °C to rt, 1−4 h. [d] Overall isolated yield (from corresponding arylpropionic acids) of products purified by chromatography on silica gel. [e] Walter, M.; Besendorf, H.; Schnider, O. *Helv. Chim. Acta* **1963**, *46*, 1127. [f] Wagner, G.; Garbe, C.; Richter, P. *Pharmazie* **1973**, *28*, 724. Also available in 77% yield by alkylation of *tert*-butyl acetate (LDA, THF, α-iodo-*p*-tolunitrile) followed by cleavage of the *tert*-butyl ester (TMSCl, NaI, CH_3CN). [g] Brunner, H.; Leitner, W. *J. Organomet. Chem.* **1990**, *387*, 209. Also available in 52% yield by alkylation of ethyl propionate (LDA, THF, benzyl bromide) followed by hydrolysis of the ester (KOH, H_2O).

(27) Other rhodium(II) catalysts proved to be inferior to the pivalate for this transformation. Reactions with rhodium(II) acetate, perfluorobutyrate, triphenylacetate, and octanoate provided **20** in 19−46% yield. For a review of the effect of ligands on Rh(II)-catalyzed reactions, see: Doyle, M. P.; Ren, T. In *Progress in Inorganic Chemistry*; Karlin, K. D., Ed.; John Wiley & Sons: New York, 2001; Vol. 49, pp 113−168 and references therein.

(28) Asao, T.; Ito, S.; Morita, N. *Tetrahedron Lett.* **1989**, *30*, 6693.

(29) For a review, see: Jones, G. *Org. React.* **1967**, *15*, 204.

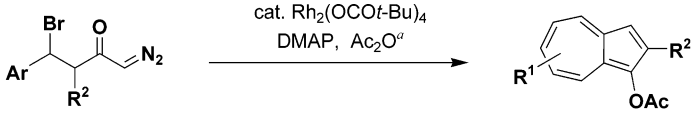
(30) Kropp, P. J.; Daus, K. A.; Tubergen, M. W.; Kepler, K. D.; Wilson, V. P.; Craig, S. L.; Baillargeon, M. M.; Breton, G. W. *J. Am. Chem. Soc.* **1993**, *115*, 3071.

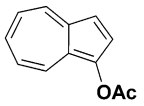
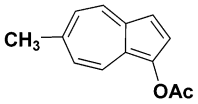
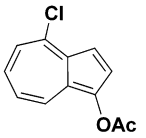
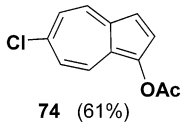
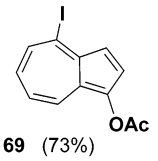
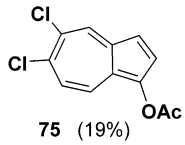
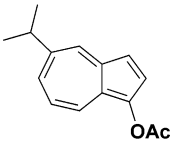
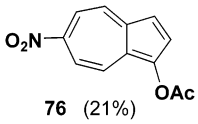
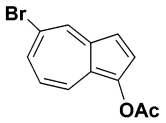
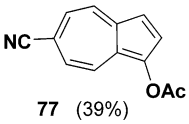
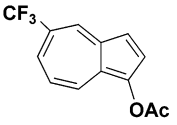
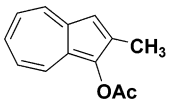
(31) Merck, Baker, and Silicycle silica gel 60 (230−400 mesh), and ICN silica gel (32−60 μm) were dried at 200 °C for 48 h at 0.1 mmHg prior to use.

(32) Although benzylic bromides derived from cinnamic acids with highly electron-rich aryl groups (e.g., 2-OMe-C_6H_4) can be prepared by this method, these compounds proved to be highly unstable toward elimination and polymerization.

(33) For benzylic bromination of 3-phenylpropionic acid itself, see: McGarvey, J. E. B.; Knipe, A. C. *J. Chem. Educ.* **1980**, *57*, 155.

TABLE 3. Synthesis of Substituted Azulenes



entry	diazo ketone[b] (Ar)	azulene (% yield)[c]	entry	diazo ketone[b] (Ar)	azulene (% yield)[c]
1	**19** (C_6H_5)	 **20**[d] (64-72%)	7	**53** (4-Me-C_6H_4)	 **73** (47%)[e]
2	**48** (2-Cl-C_6H_4)	 **68** (58-61%)	8	**54** (4-Cl-C_6H_4)	 **74** (61%)
3	**49** (2-I-C_6H_4)	 **69** (73%)	9	**55** (3,4-di-Cl-C_6H_3)	 **75** (19%)
4	**50** (3-*i*-Pr-C_6H_4)	 **70** (54%)[f]	10	**65** (4-NO_2-C_6H_4)	 **76** (21%)
5	**51** (3-Br-C_6H_4)	 **71** (39%)	11	**66** (4-CN-C_6H_4)	 **77** (39%)
6	**52** (3-CF_3-C_6H_4)	 **72** (40%)	12	**67** (C_6H_5, R^2 = CH_3)	 **78** (58%)

[a] 0.005−0.01 equiv of $Rh_2(OCOt\text{-}Bu)_4$, CH_2Cl_2, rt, 45−90 min; then add 3 equiv of DMAP, 5 equiv of Ac_2O, rt, 5 min. [b] R^2 = H unless otherwise indicated. [c] Isolated yields of products purified by chromatography on silica gel. [d] Asao, T.; Ito, S.; Morita, N. *Tetrahedron Lett.* **1989**, *30*, 6693. [e] Estimated yield; 22% overall yield from 4-methylcinnamic acid (**27**). [f] Et_2O used as solvent.

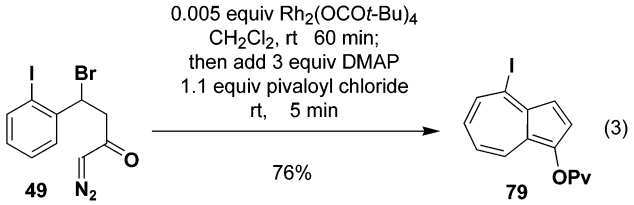
of the ring expansion-annulation in the case of halogenated substrates, which stands in contrast with earlier reports that halobenzenes do not participate in related Büchner reactions in good yield.[13c] These haloazulene annulation products hold particular interest due to their potential utility as substrates for transition-metal-catalyzed coupling reactions (vide infra). In the case of ortho- and meta-substituted substrates (entries 2−6), the ring expansion-annulation was found to proceed with carbenoid addition occurring away from the substituent to afford predominantly a single azulene regioisomer.[34] Only trace amounts (<1%) of byproducts tentatively identified as regioisomeric azulenes were detected in these reactions.[35] Interestingly, attempted ring expansion-annulation with the *m*-isopropyl substrate **50** (entry 4) under the standard conditions produced only traces of the desired azulene, but this reaction proceeded in good yield when diethyl ether was employed in place of dichloromethane as the solvent.

As mentioned earlier, critical to the success of the ring expansion-annulation reaction is the trapping of the initially generated unstable 1-hydroxyazulenes as stable

(34) The regiochemistry of these azulenes was assigned on the basis of ^1H NMR NOE experiments.

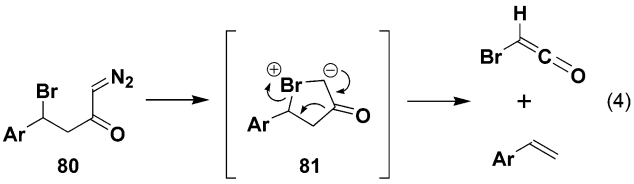
(35) For a review of earlier studies on the regiochemical course of related intramolecular Büchner reactions, see: Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; John Wiley & Sons: New York, 1998; pp 298−319.

ester derivatives. In most cases, acetic anhydride was found to be a convenient esterification agent, reacting in less than 5 min in the presence of 4-DMAP to afford the expected azulenyl acetates. As illustrated in eq 3, in situ esterification can also be accomplished with acyl chlorides, and as discussed later, the application of Tf_2O and Tf_2NPh provides access to 1-azulenyl sulfonates that participate in useful palladium-catalyzed coupling reactions.



(3)

Interestingly, in most ring expansion-annulation reactions styrene derivatives were isolated as minor byproducts in 10−15% yield. One possible mechanism to account for the formation of these side products is outlined in eq 4. The inter- and intramolecular trapping of rhodium carbenoids derived from diazo ketones by heteroatoms is well-documented,[36] and the proposed fragmentation is related to the β-eliminations that have been observed in reactions of sulfonium and oxonium ylides generated in analogous reactions.[37] This mechanism must be regarded as speculative, however, in view of our failure to detect or trap bromoketene in any of these reactions.

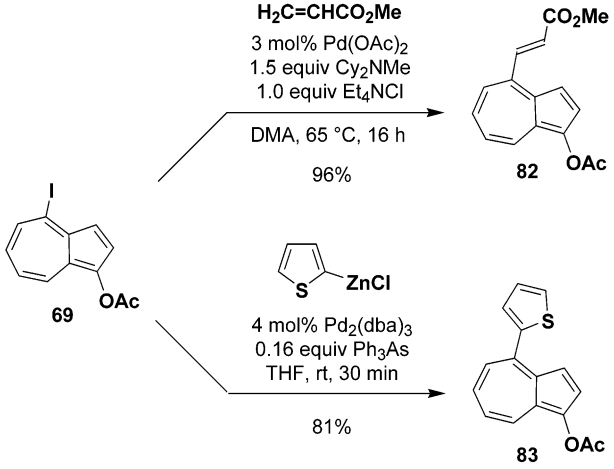


(4)

Synthetic Elaboration of Ring Expansion-Annulation Products. An important consideration in the design of the ring expansion-annulation strategy was the expectation that it would deliver azulenes with hydroxyl derivatives (including sulfonates) at C-1 of the five-membered ring and could also provide products with multiple substituents, including halogen atoms, on the seven-membered ring. The next goal in our investigation was to explore the feasibility of employing these substituents as handles for the further synthetic elaboration of the azulene annulation products.

Of particular interest to us was the possibility of employing azulenyl halides and sulfonates in transition-metal-catalyzed carbon−carbon bond-forming reactions. At the outset of our investigation, the feasibility of achieving such transformations was far from clear. It is well documented that the chemistry of azulenes often differs significantly from that of more familiar benzenoid aromatic systems such as naphthalene, and at the time we began our studies, only four prior reports had appeared describing such reactions. Most significantly, in

SCHEME 5



1986 Dehmlow reported that certain 6-bromoazulenes participate in Sonogashira reactions and Negishi couplings with arylzinc compounds,[38] and in 1991 Horino described the Heck vinylation of several haloazulenes.[39,40] Concurrent with our studies, further reports of coupling reactions involving haloazulenes have appeared, including additional examples of Sonogashira reactions,[41] two examples of a Stille coupling reaction,[5,42] and several Suzuki reactions.[43]

As described earlier, application of the ring expansion-annulation strategy to *o*-halobenzene substrates provides convenient access to 4-haloazulenes such as **69**. We have found that **69** participates smoothly in Heck[44] and Negishi[45] reactions to afford 4-vinyl- and 4-aryl-substituted azulenes in excellent yield (Scheme 5). In the case of the Heck reaction, best results are obtained by employing the indicated modified version of the Jeffery phase transfer protocol.[46]

(36) For a review, see: Padwa, A.; Hornbuckle, S. F. *Chem. Rev.* **1991**, *91*, 263.

(37) For examples, see: (a) Moody, C. J.; Taylor, R. J. *Tetrahedron Lett.* **1988**, *29*, 6005. (b) Roskamp, E. J.; Johnson, C. R. *J. Am. Chem. Soc.* **1986**, *108*, 6062.

(38) Balschukat, D.; Dehmlow, E. V. *Chem. Ber.* **1986**, *119*, 2272.

(39) Horino, H.; Asao, T.; Inoue, N. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 183.

(40) See also: (a) Homocoupling of 1- and 2-haloazulenes with copper metal: Morita, T.; Takase, K. *Bull. Chem. Soc. Jpn.* **1982,** *55*, 1144. (b) Formation of oligo- and polyazulenes by Ni-catalyzed coupling of 1-bromo- and 1,3-dibromoazulene: Iyoda, M.; Sato, K.; Oda, M. *Tetrahedron Lett.* **1985**, *26*, 3829.

(41) See ref 6e and: (a) Fabian, K. H. H.; Elwahy, A. H. M.; Hafner, K. *Tetrahedron Lett.* **2000**, *41*, 2855. (b) Elwahy, A. H. M.; Hafner, K. *Tetrahedron Lett.* **2000**, *41*, 4079. (c) Ito, S.; Inabe, H.; Okujima, T.; Morita, N.; Watanbe, M.; Imafuku, K. *Tetrahedron Lett.* **2000**, *41*, 8343. (d) Ito, S.; Inabe, H.; Okujima, T.; Morita, N.; Watanabe, M.; Harada, N.; Imafuku, K. *J. Org. Chem.* **2001**, *66*, 7090. (e) Elwahy, A. H. M. *Tetrahedron Lett.* **2002**, *43*, 711.

(42) Ito, S.; Okujima, T.; Morita, N. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1896.

(43) Kurotobi, K.; Tabata, H.; Miyauchi, M.; Murafuji, T.; Sugihara, Y. *Synthesis* **2002**, 1013.

(44) For reviews, see: (a) Jeffery, T. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; JAI: London, UK, 1996; Vol. 5, pp 153−260. (b) Brase, S.; de Meijere, A. In *Metal-catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: New York, 1998; pp 99−166. (c) Crisp, G. T. *Chem. Soc. Rev.* **1998**, *27*, 427. (d) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009. (e) Beller, M.; Riermeier, T. H.; Stark, G. In *Transition Metals for Organic Synthesis*: *Building Blocks and Fine Chemicals*; Beller, M., Bolm, C., Eds.; Wiley-VCH: Weinheim, Germany, 1998; Vol. 1, pp 208−240. (f) *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E.-i., de Meijere, A., Eds.; Wiley-Interscience: New York, 2002; Vol 1, pp 1133−1367.

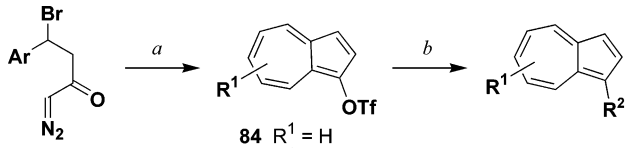
(45) For a review of coupling reactions with organozinc reagents, see: Negishi, E.-i.; Liu, F. In *Metal-catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: New York, 1998; pp 1−48.

(46) Gürtler, C.; Buchwald, S. L. *Chem. Eur. J.* **1999**, 3107.

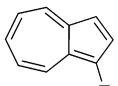
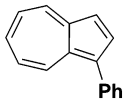
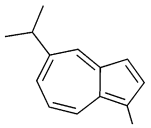
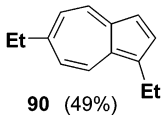
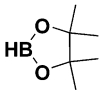
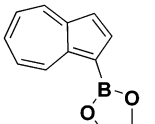
We next turned our attention to the key issue of effecting transition-metal-catalyzed coupling reactions at the C-1 position of the ring expansion-annulation products. In situ trapping of the annulation products with *N*-phenyltriflimide[47] provided the expected triflates (e.g., **84**−**86**), but initial attempts to utilize these azulenes in efficient coupling reactions with various organotin, boron, zinc, aluminum, copper, silicon, and magnesium reagents met with dismal failure. The azulenyl triflate **84** is formed in 91% yield (as estimated by ^{1}H NMR analysis) and is stable to storage at 0 °C in dichloromethane or diethyl ether. However, this triflate was found to rapidly decompose upon concentration and also upon exposure to dipolar aprotic solvents such as NMP, DMF, and DMA, which are often preferred solvents for Pd-catalyzed coupling reactions.[48] To our dismay, conditions that led to efficient coupling reactions in control experiments with the triflate derivative of 1-naphthol resulted only in the formation of uncharacterizable polymeric products in the case of azulenyl triflate **84**.

Successful coupling was ultimately realized by exploiting recent advances in the development of highly active catalysts for palladium-mediated cross-coupling and amination reactions. In particular, we have found that Suzuki coupling reactions[49] of azulenyl triflates to afford 1-alkyl- and 1-arylazulenes can be achieved in high yield by using Buchwald's *o*-(dicyclohexylphosphino)biphenyl ligand.[50,51] Our preliminary report[1] of this process disclosed the first successful examples of Suzuki coupling reactions involving azulenyl halides or sulfonates. Table 4 summarizes the results of our studies to date. Best overall yields are obtained by employing azulenyl triflates in the Suzuki coupling reaction without prior purification. Alkylboranes are superior to boronic acid and ester derivatives for this coupling, and complete reaction takes place in THF under the indicated conditions either at room temperature for several hours or alternatively at reflux for several minutes. Cesium carbonate proved to be the optimal base for the reaction, although KF and CsF are equally effective in some cases. Interestingly, coupling was found to take place at similar rates at C-1 and C-6 of the 6-chloroazulenyl triflate **86**; reaction with excess triethylborane provided the diethylazulene **90** in good overall yield (entry 4). The Suzuki reaction leading to **89** (entry 3) comprises the key step in our synthesis of the antiulcer drug egualen sodium ("KT1-32", **92**).[52]

TABLE 4. Suzuki Coupling Reactions of Azulenyl Triflates

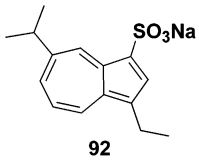


84 R^1 = H
85 R^1 = 4-*i*-Pr
86 R^1 = 6-Cl

entry	diazo ketone (Ar)	borane (conditions)	azulene (overall yield[c])
1	**19** (C_6H_5)	*B*-Et-9-BBN (5 equiv, rt, 2 h)	 **87** (56%)
2	**19** (C_6H_5)	*B*-Ph-9-BBN (1.4 equiv, 65 °C, 15 min)	 **88** (60%)
3	**50** (3-*i*-Pr-C_6H_4)	*B*-Et-9-BBN (5 equiv, rt, 5 h)	 **89** (36%)
4	**54** (4-Cl-C_6H_4)	Et_3B (2.4 equiv, rt, 2 h)	 **90** (49%)
5	**19** (C_6H_5)	 (2 equiv, rt, 16 h)	 **91** (45-51%)

[a] 1 mol % of $Rh_2(OCOt\text{-}Bu)_4$, CH_2Cl_2, rt, 45 min; then add 3 equiv of DMAP, 1 equiv of Tf_2NPh, rt, 10 min. [b] Borane, 5 mol % of $Pd(OAc)_2$, 7.5−10 mol % of (*o*-biphenyl)PCy_2 (20 mol % in entry 5), 3 equiv of Cs_2CO_3, (4.0 equiv of Et_3N in entry 5), THF. [c] Overall isolated yield (from diazo ketone) of products purified by column chromatography on silica gel.

Overall, our approach delivers **92** in eight steps beginning with commercially available *m*-isopropylphenol, a considerable improvement over the previously published route.[52]

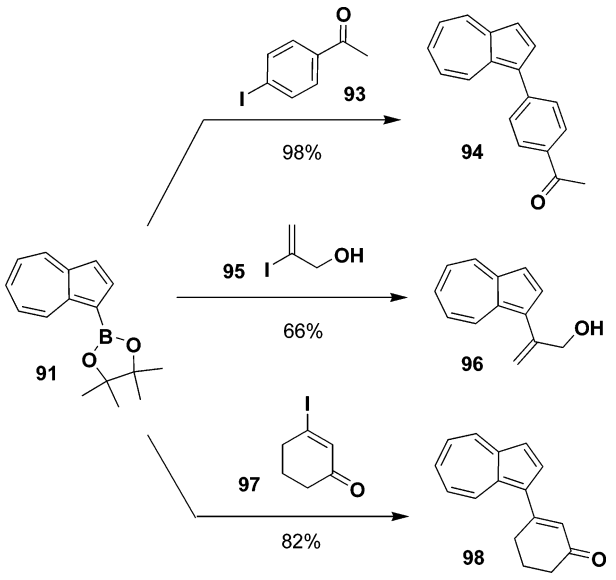


92

Particularly noteworthy in Table 4 is the palladium-catalyzed borylation of **84** to afford the 1-azulenylboronate **91**. Because of the instability of C-1 azulenyl triflates to long-term storage, we sought a more robust azulene derivative that could serve as an intermediate for the synthesis of a variety of 1-substituted derivatives.

(47) Hendrickson, J. B.; Bergeron, R. *Tetrahedron Lett.* **1973**, 4607.
(48) The decomposition of aryl triflates in dipolar aprotic solvents has been observed previously. See: Eschavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 5478 and references therein.
(49) For reviews, see: (a) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147. (b) Miyaura, N. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; JAI: London, UK, 1998; Vol. 6, pp 187−243. (c) Suzuki, A. In *Metal-catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: New York, 1998; pp 49−97. (d) Stanforth, S. P. *Tetrahedron* **1998**, *54*, 263. (e) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.
(50) Wolfe, J. P.; Singer, R. A.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9550.
(51) Exploratory studies on Heck and Stille couplings of **84** were not fruitful and were not pursued further once successful Suzuki reactions had been achieved.
(52) (a) Yanagisawa, T.; Wakabayashi, S.; Tomiyama, T.; Yasunami, M.; Takase, K. *Chem. Pharm. Bull.* **1988**, *36*, 641. See also: (b) Yanagisawa, T.; Kosakai, K.; Tomiyama, T.; Yasunami, M.; Takase, K. *Chem. Pharm. Bull.* **1990**, *38*, 3355. (c) Yanagisawa, T.; Kosakai, K.; Izawa, C.; Tomiyama, T.; Yasunami, M. *Chem. Pharm. Bull.* **1991**, *39*, 2429. (d) Mochizuki, S.; Matsumoto, M.; Wakabayashi, S.; Kosakai, K.; Tomiyama, A.; Kishimoto, S. *J. Gastroenterol.* **1996**, *31*, 785.

SCHEME 6[a]



[a] Reagents and conditions: 1.5 equiv of **91**, 5 mol % of $Pd(OAc)_2$, 20 mol % of (*o*-biphenyl)PCy_2, 3.0 equiv of $Ba(OH)_2$, dioxane−H_2O, 65 °C, 15 min.

Initially, we attempted to effect borylation of **84** using bis(pinacolato)diboron according to the general method of Miyuara.[53] Unfortunately, only decomposition of **84** was observed upon attempted reaction with the diboron reagent under a variety of conditions and with a wide range of phosphine ligands.[54,55] Successful borylation of **84** was finally achieved by employing the much less expensive borylation agent pinacolborane.[56] Best results were obtained by using Buchwald's ligand (*o*-biphenyl)-PCy_2 as recommended by Baudoin,[57] and in this fashion the azulenylboronate **91** could be isolated in 45−51% overall yield from the diazo ketone **19** (Table 4, entry 5). The azulenylboronate is a dark purple solid, stable to purification by column chromatography and to storage at 0 °C in CH_2Cl_2 or benzene.

As illustrated in Scheme 6, the azulenyl boronate **91** reacts smoothly in Suzuki coupling reactions with 4-iodoacetophenone and alkenyl iodides **95**[58] and **97**[59] to afford the expected 1-substituted azulenes. These coupling reactions were generally carried out employing the iodide as the limiting reagent; alternatively, reaction of 1.0 equiv of **91** with 1.1−1.5 equiv of the organoiodine compound provided the desired azulenes in 73%, 44%, and 37% yield, respectively.

(53) (a) Ishiyama, T.; Murata, M.; Miyaura, N. *J. Org. Chem.* **1995**, *60*, 7508. (b) Ishiyama, T.; Itoh, Y.; Kitano, T.; Miyaura, N. *Tetrahedron Lett.* **1997**, *38*, 3447. (c) Reviewed in: Ishiyama, T.; Miyaura, N. *J. Organomet. Chem.* **2000**, *611*, 392.

(54) In contrast, borylation of the triflate derivative of 1-naphthol was achieved in high yield under similar conditions.

(55) During the course of our work, Sugihara reported the borylation of 2- and 6-haloazulenes using this reagent. See ref 43 and: Kurotobi, K.; Miyauchi, M.; Takakura, K.; Murafuji, T.; Sugihara, Y. *Eur. J. Org. Chem.* **2003**, 3663.

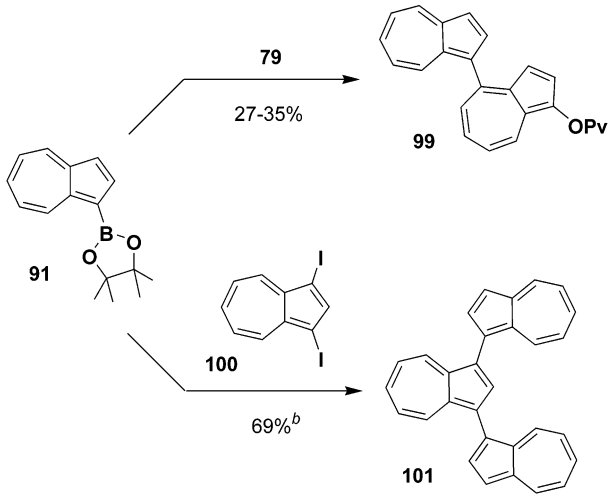
(56) Murata, M.; Oyama, T.; Watanabe, S.; Masuda, Y. *J. Org. Chem.* **2000**, *65*, 164.

(57) Baudoin, O.; Guénard, D.; Guéritte, F. *J. Org. Chem.* **2000**, *65*, 9268.

(58) Irifune, S.; Kibayashi, T.; Ishii, Y.; Ogawa, M. *Synthesis* **1988**, 366.

(59) Piers, E.; Grierson, J. R.; Lau, C. K.; Nagakura, I. *Can. J. Chem.* **1982**, *60*, 210.

SCHEME 7[a]



[a] Reagents and conditions: 1.0 equiv of **79**, 5 mol % of $Pd(OAc)_2$, 20 mol % of (*o*-biphenyl)PCy_2, 3.0 equiv of $Ba(OH)_2$, dioxane−H_2O, 45−65 °C, 30 min. [b]2.0 equiv of **91** relative to 1,3-diiodoazulene was employed for this reaction.

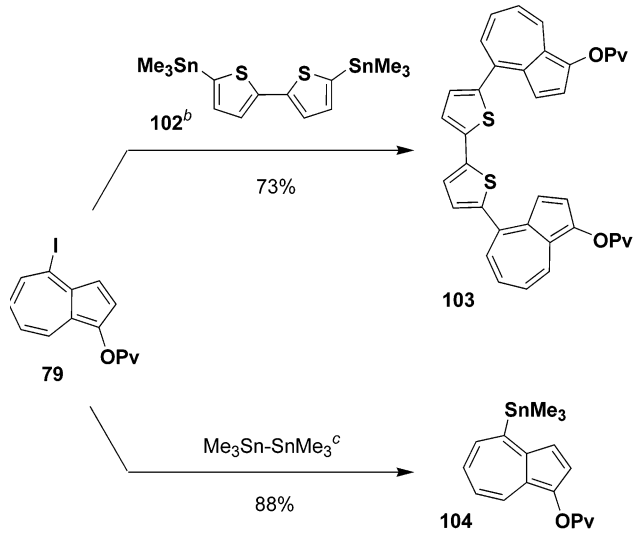
Synthesis of Oligoazulenes. π-Conjugated organic oligomers and polymers have attracted enormous attention in recent years due to their utility as advanced materials for the construction of molecular devices.[60] The unusual electronic and optical properties of azulenes has led to significant interest in the design and synthesis of oligomers and polymers incorporating these novel aromatic systems.[6] For the most part, research in this area to date has relied on the availability of the natural product guaiazulene and a very limited suite of substituted azulenes available by de novo synthetic routes. In our view, the ability of our ring expansion-annulation strategy to provide efficient access to a variety of azulenes substituted on *both* the five- and seven-membered ring makes it an especially powerful method for the preparation of azulene building blocks for the construction of advanced materials. To demonstrate the potential utility of the ring expansion-annulation strategy in this connection, we undertook the synthesis of several representative bi-, tri-, and related oligoazulenes.

The importance of biaryls as components in liquid crystals and other novel materials is well established. The Suzuki coupling of the azulenylboronate **91** with iodoazulene **79** (Scheme 7) illustrates one approach to the preparation of *biazulenes* based on our ring expansion-annulation products. To our knowledge, **99** represents the first example of a biazulene with a C-1 to C-4 linkage. In a similar fashion, reaction of boronate **91** with 1,3-diiodoazulene[41a] provides the terazulene **101** as metallic green crystals in good yield. This route to **101** is markedly superior to the prior synthesis of this compound that generated the terazulene in only 13% yield as one component of a mixture of oligoazulenes.[40b]

We next turned our attention to the application of the ring expansion-annulation products in the synthesis of azulenyl thiophene oligomers. The goal of this model

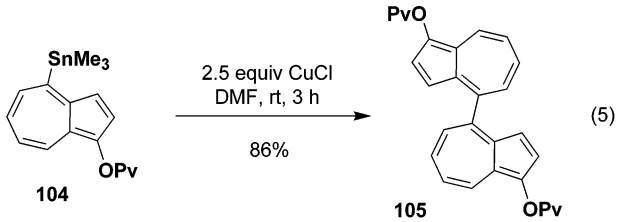
(60) (a) *Handbook of Conducting Polymers*; Skotheim, T. A., Elsenbaumer, P. L., Reynolds, J. R., Eds.; Marcel Decker: New York, 1998. (b) *Electronic Materials*: *The Oligomer Approach*; Müllen, K., Wegner, G., Eds.; Wiley-VCH: Weinheim, Germany, 1997.

SCHEME 8[a]



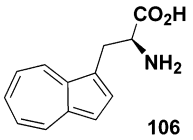
[a] Reagents and conditions: 10 mol % of $Pd(Ph_3P)_4$, toluene, reflux, 24 h. [b] 2.0 equiv of **79** relative to **102** was employed for this reaction. [c] 1.6 equiv.

study was to develop synthetic chemistry with potential utility for the preparation of conducting polymers and other electroactive materials. Our initial efforts focused on coupling reactions involving haloazulenes and thiophenylboron derivatives, but when these approaches proved inefficient, we turned our attention to the application of Stille couplings with thiophenylstannanes.[61] In the event, we were pleased to find that iodoazulene **79** undergoes efficient Stille coupling with the bis-stannane **102**[62] to furnish **103** as a dark green solid in 73% yield (Scheme 8). Also noteworthy is the successful reaction of **79** with hexamethylditin[63,64] to afford the azulenylstannane **104**. Our interest in **104** derived from the expectation that it might serve as a useful precursor to the 4,4′-biazulene system. Only one inefficient previous synthesis of this biazulene has been reported previously.[65] In fact, treatment of **104** with CuCl in DMF according to the general method of Piers[66] furnished the desired biazulene **105** as turquoise crystals in excellent yield (eq 5). Interestingly, to date our attempts to effect Stille coupling of **104** with iodoazulene **79** have not been successful, and these experiments have led to recovery of the unreacted azulenes accompanied by 1-trimethylacetoxy-4-methylazulene.

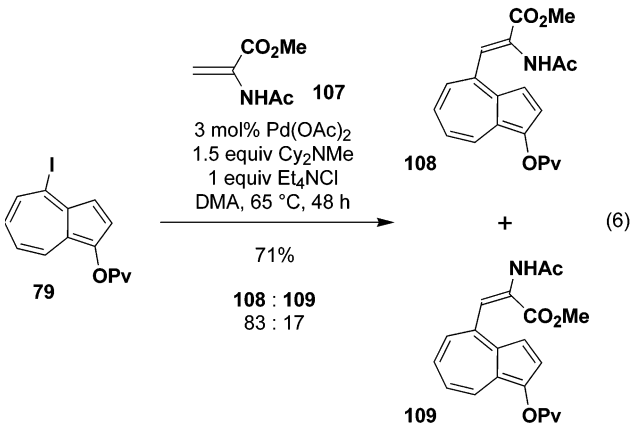


(5)

Synthesis of Azulenyl Amino Acids. The design and synthesis of "unnatural" amino acids incorporating azulene moieties is an interesting problem that has received surprisingly little attention to date.[67] Azulenyl amino acids have potential utility as fluorescent probes, and azulenyl analogues of tryptophan and phenylalanine are expected to exhibit unusual behavior due to the unique electronic characteristics of the azulenyl system. Loidl's six-step synthesis of β-(1-azulenyl)-L-alanine **106**[67c] (from expensive azulene itself) represents the most significant work in this area to date. It occurred to us that the azulenyl halides, sulfonates, boronates, and stannane derivatives available via our ring expansion-annulation methodology might serve as valuable building blocks for the synthesis of azulenyl amino acids. Particularly attractive to us was the prospect of employing our azulenes in Negishi couplings with Jackson's iodoalanine derivatives[68] and in Heck reactions with amidoacrylates.[69]



To explore the feasibility of the latter approach, we examined the reaction of iodoazulene annulation product **79** with the readily available amidoacrylate **107**.[70] As outlined in eq 6, the desired Heck reaction can be



(6)

achieved in good yield, but surprisingly affords a mixture of *Z* and *E* dehydroamino acids in a ratio of 83:17.[71] The stereochemistry of the isomeric esters was assigned based

(61) For a review of Pd-catalyzed coupling reactions of thiophene derivatives, see: Li, J. J.; Gribble, G. W. *Palladium in Heterocyclic Chemistry*; Pergamon: Oxford, UK, 2000; Chapter 5.

(62) Prepared from 2,2′-dithiophene by metalation with *n*-BuLi followed by reaction with trimethylstannyl chloride. We thank Phoebe Kwan and Professor Timothy Swager for providing us with a sample of this compound.

(63) For reviews of the Stille coupling reaction, see: (a) Farina, V.; Krishnamurthy, V.; Scott, W. J. *Org. React.* **1997**, *50*, 1. (b) Mitchell, T. N. In *Metal-catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: New York, 1998; pp 167−202.

(64) Concurrent with our studies, Ito reported the preparation of 6-(tributylstannyl)azulene and its reaction with aryl halides. See: Okujima, T.; Ito, S.; Morita, N. *Tetrahedron Lett.* **2002**, *43*, 1261 and ref 42.

(65) Huenig, S.; Ort, B. *Liebigs Ann.* **1984**, *12*, 1905.

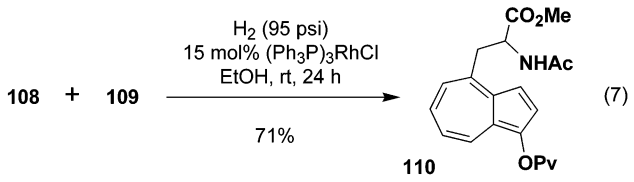
(66) Piers, E.; Yee, J. G. K.; Gladstone, P. L. *Org. Lett.* **2000**, *2*, 481.

(67) (a) Anderson, A. G., Jr.; Gale, D. J.; McDonald, R. N.; Anderson, R. G.; Rhodes, R. C. *J. Org. Chem.* **1964**, *29*, 1373. (b) Klemm, L. H.; Hudson, B. S.; Lu, J. *Org. Prep. Proced. Int.* **1989**, *21*, 633. (c) Loidl, G.; Musiol, H.-J.; Budisa, N.; Huber, R.; Poirot, S.; Fourmy, D.; Moroder, L. *J. Peptide Sci.* **2000**, *6*, 139.

(68) Review: Gair, S.; Jackson, R. F. W. *Curr. Org. Chem.* **1998**, *2*, 527.

(69) (a) Carlström, A.-S.; Frejd, T. *Synthesis* **1989**, 414. (b) Carlström, A.-S.; Frejd, T. *Acta Chem. Scand.* **1992**, *46*, 163.

on ^{1}H NMR chemical shifts and was confirmed by NOE experiments. Initially, the formation of isomeric dehydroamino acids was not a concern, since Burk has reported conditions for the asymmetric hydrogenation of related isomeric mixtures to afford a single amino acid enantiomer.[72] Unfortunately, to date we have not identified conditions under which hydrogenation of **108** and **109** with Burk's DuPhos catalyst system proceeds at a reasonable rate. On the other hand, hydrogenation of the mixture of dehydroamino acids in the presence of Wilkinson's catalyst proceeds as expected to afford the desired azulenyl amino acid deriviative **110** in good yield (eq 7). Separation of enantiomers can be effected by HPLC with use of a Daicel Chiracel OD column, thus providing access to both the D- and L-azulenyl amino acids in pure form.



Conclusions

The ring expansion-annulation strategy described herein provides efficient access to a variety of azulenes substituted on both the five and seven-membered rings. This method is particularly well suited for the preparation of azulenyl halides, sulfonates, and boronates, and these annulation products function as valuable and versatile building blocks for the construction of highly substituted azulenes and oligoazulenes.

Experimental Section

Materials. Commercial grade reagents and solvents were used without further purification except as indicated below. Acetonitrile, benzene, *N*,*N*-dicyclohexylmethylamine, and triethylamine were distilled under argon from calcium hydride. Diethyl ether and tetrahydrofuran were distilled under argon from sodium benzophenone ketyl or dianion or purified by pressure filtration through activated alumnia. Dichloromethane and toluene were purified by pressure filtration through activated alumina and Cu(II) oxide. Oxalyl chloride was distilled under argon. Acetic anhydride was distilled from quinoline. Activated silica gel was prepared by heating at 200 °C for 48 h at 0.1 mmHg prior to use.

General Procedure for the Synthesis of *β*-Bromo Diazo Ketones via Hydrobromination with HBr: 4-Bromo-1-diazo-4-phenyl-2-butanone (19). A 500-mL, three-necked, round-bottomed flask was equipped with a glass stopper, gas dispersion tube attached to a cylinder of HBr, and a gas outlet adapter attached via Tygon tubing to an Erlenmeyer flask filled with water. The reaction flask was charged with cinnamic acid **21** (7.04 g, 47.2 mmol), 70 g of activated silica gel, and 240 mL of dichloromethane. HBr was bubbled through the reaction mixture for 40 min, and then the gas inlet and outlet were replaced by glass stoppers. The orange suspension was stirred at room temperature for 20 h. The two glass stoppers were replaced with the gas inlet and outlet used previously, and HBr was again bubbled through the reaction mixture for 40 min. The flask was stoppered and stirred for 4 h and then the orange suspension was filtered with the aid of 400 mL of diethyl ether. The filtrate was washed with two 300-mL portions of water and 300 mL of brine, dried over $MgSO_4$, filtered, and concentrated to provide 9.36 g of 3-bromo-3-phenylpropionic acid (**30**) as a white solid used in the next step without purification.

A 250-mL, one-necked, flask equipped with a reflux condenser fitted with an argon inlet adapter was charged with the bromo acid **30** prepared as described above (4.50 g, ca. 19.6 mmol), oxalyl chloride (3.59 g, 2.40 mL, 28.3 mmol, ca. 1.40 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 16 h at 65 °C. After this time, the reaction mixture was 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[73] (ca. 67 mmol, 3.4 equiv, generated from Diazald (21.5 g, 100.5 mmol) 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 pipet 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 and quenched by addition of acetic acid. The bright yellow reaction mixture was concentrated to provide 5.24 g of a yellow oil, which was dissolved in 15 mL of CH_2Cl_2, concentrated onto 10.4 g of silica gel, and transferred to the top of a column of 100 g of silica gel. Elution with 20% ethyl acetate−hexanes afforded 4.09 g (71% overall from cinnamic acid **21**) of 4-bromo-1-diazo-4-phenyl-2-butanone (**19**) as a yellow solid with spectral data consistent with that previously reported for this compound:[25] mp 65−66 °C; IR ($CHCl_3$) 3087, 2110, and 1627 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42−7.44 (m, 2 H), 7.34−7.38 (m, 2 H), 7.29−7.33 (m, 1 H), 5.48 (dd, J = 5.8, 9.15 Hz, 1 H), 5.31 (br s, 1 H), and 3.23 (ABX, J_{ax} = 9.3, J_{bx} = 5.5, J_{ab} = 15.4 Hz, δ_a = 3.31, δ_b = 3.15, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.3, 141.1, 129.1, 128.9, 127.4, 56.1, 50.2, and 48.3.

General 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 (67). 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[74] (**58**) (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

(70) Yokoyama, Y.; Takahashi, M.; Takashima, M.; Mitsuru, K.; Kohno, Y.; Kobayashi, H. *Chem. Pharm. Bull.* **1994**, *42*, 832.

(71) Heck reactions of aryl halides with **107** normally produce exclusively Z dehydroamino acid derivatives. For an exception, see ref 69a.

(72) (a) Burk, M. J.; Feaster, J. E.; Nugent, W. A.; Harlow, R. L. *J. Am. Chem. Soc.* **1993**, *115*, 10125. See also: (b) Burk, M. J.; Gross, M. F.; Martinez, J. P. *J. Am. Chem. Soc.* **1995**, *117*, 9375. (c) Burk, M. J.; Wang, Y. M.; Lee, J. R. *J. Am. Chem. Soc.* **1996**, *118*, 5142.

(73) Diazomethane was generated from Diazald by using a mini-diazomethane apparatus as described in: Black, T. H. *Aldrichim. Acta* **1983**, *16*, 3.

(74) Prepared in 52% yield by alkylation of ethyl propionate (LDA, THF, benzyl bromide) followed by ester hydrolysis (KOH, H_2O). For a previous synthesis of this compound, see: Brunner, H.; Leitner, W. *J. Organomet. Chem.* **1990**, *387*, 209.

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-phenylpropionic acid) of 4-bromo-1-diazo-3-methyl-4-phenyl-2-butanone (**67**) (mixture of diastereomers) as a yellow solid: mp 51.0−61.0 °C; IR (CCl_4) 2890, 2080, 1635, and 1535 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} (ϵ) 247 (20 145), 192 (35 500) nm; HRMS (EI) *m/z* calcd for $C_{11}H_{11}BrN_2O$ 266.0055, found 266.0048.

General Procedure for the Synthesis of Acetoxyazulenes: 1-Acetoxyazulene (20). 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[75] (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 (**19**) (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-DMAP (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 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.[28] mp 47.5−50.2 °C); IR (CCl_4) 3030, 2810, 1765, 1580, 1545, and 1500 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} (ϵ) 732 (101), 663 (258), 608 (292), 586 (252), 347 (2933), 277 (30 166), 238 (8845), 213 (3352) nm.

1-Acetoxy-4-chloroazulene (68). Application of the general procedure gave 0.157 g (58%) of **68** as a blue-gray solid, mp 55.5−56.5 °C. IR (CCl_4) 3020, 1760, 1585, and 1550 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} (ϵ) 657 (267), 605 (311), 520 (114), 351 (4130), 337 (2970), 284 (35 440), 245 (23 670), 219 (8960) nm. Anal. Calcd for $C_{12}H_9ClO_2$: C, 65.32; H, 4.11. Found: C, 65.31; H, 3.99.

1-Acetoxy-4-iodoazulene (69). Application of the general procedure gave 0.792 g (73%) of **69** as a metallic blue solid, mp 76.0−77.0 °C. IR (CCl_4) 2950, 2920, 1754, and 1550 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.18 (d, J = 9.5 Hz, 1 H), 7.87−7.89 (m, 2 H), 7.39 (d, J = 4.3 Hz, 1 H), 7.20 (app t, J = 10.1 Hz, 1 H), 7.13 (app t, J = 9.6 Hz, 1 H), and 2.45 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.3, 140.4, 136.6 (2 C), 135.0, 132.2, 129.2, 125.7, 123.0, 121.9, 117.2, and 21.3; UV−vis (hexane) λ_{max} (ϵ) 611 (380), 352 (7075), 316 (15 710), 296 (53 475), 279 (47 230), 261 (61 175), 231 (15 810), and 192 (22 260) nm. Anal. Calcd for $C_{12}H_9IO_2$: C, 46.18; H, 2.91. Found: C, 46.08; H, 2.83.

1-Acetoxy-5-isopropylazulene (70). Application of the general procedure (except that Et_2O was employed as solvent in place of dichloromethane) gave 0.151 g (54%) of **70** as a blue oil. IR (thin film) 2960, 2920, 2860, 1755, and 1580 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.20 (d, J = 1.8 Hz, 1H), 8.08 (d, J = 10.0 Hz, 1H), 7.75 (d, J = 4.3 Hz, 1H), 7.49 (d, J = 9.5 Hz, 1H), 7.17 (d, J = 4.3 Hz, 1H), 7.01 (app t, J = 9.5, 10.0 Hz, 1H), 3.03 (sept, J = 6.9 Hz, 1H), 2.40 (s, 3H), and 1.33 (d, J = 6.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 142.7, 138.1, 137.0, 135.7, 130.6, 127.9, 125.6, 121.6, 121.5, 112.9, 38.4, 24.4, and 21.0; UV−vis max (hexane) λ_{max} (ϵ) 614 (119), 352 (2170), 279 (21 570), and 225 (67 000) nm. Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 79.14; H, 6.87.

1-Acetoxy-5-bromoazulene (71). Application of the general procedure gave 0.109 g (39%) of **71** as an olive green solid, mp 60.5−61.5 °C. IR (CCl_4) 2900, 1765, 1580, and 1545 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} (ϵ) 690 (273), 632 (302), 601 (250), 371 (3230), 362 (2440), 351 (3980), 347 (2860), 337 (2070), 278 (28 900) nm. Anal. Calcd for $C_{12}H_9BrO_2$: C, 54.37; H, 3.42. Found: C, 54.59; H, 3.29.

1-Acetoxy-5-(trifluoromethyl)azulene (72). Application of the general procedure gave 0.109 g (40%) of **72** as a blue solid, mp 43.5−44.5 °C. IR (CCl_4) 2920, 2840, 1770, 1580, and 1500 cm^{-1}; ^1H 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} (ϵ) 608 (255), 583 (221), 352 (8474), 278 (61 858), 215 (11 863) nm. Anal. Calcd for $C_{13}H_9F_3O_2$: C, 61.42; H, 3.56. Found: C, 61.43; H, 3.63.

1-Acetoxy-6-methylazulene (73). Application of the general procedure gave 0.076 g (22% overall from 4-methylcinnamic acid **27**, estimated 47% yield for ring expansion-annulation step) of **73** as a blue solid, mp 67.0−67.5 °C. IR (CCl_4) 3030, 2920, 2880, 1765, and 1580 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} (ϵ) 714 (105), 645 (270), 596 (300), 368 (3000), 352 (5700), 349 (5890), 335 (4390), 281 (72 290), 234 (18 120) nm. Anal. Calcd for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04. Found: C, 77.84; H, 6.04.

1-Acetoxy-6-chloroazulene (74). Application of the general procedure gave 0.569 g (61%) of **74** as metallic blue flakes, mp 66.5−67.0 °C. IR (CCl_4) 2880, 1750, 1565, and 1510 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} (ϵ) 777 (100), 664 (252), 606 (290), 582 (250), 561 (212), 304 (6730), 283 (61 500), 237 (9270), 217 (10 205) nm. 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.

1-Acetoxy-5,6-dichloroazulene (75). Application of the general procedure gave 0.054 g (19%) of **75** as a green solid, mp 73.0−76.0 °C. IR (CCl_4) 3020, 2920, 1770, 1570, and 1505 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.89 (d, J = 11.0 Hz, 1H), 7.82 (d, J = 4.4 Hz, 1H), 7.27 (d, J = 11.0 Hz, 1H), 7.22 (d, J = 4.4 Hz, 1H), and 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.6, 142.7, 140.0, 137.3, 132.5, 130.3, 128.1, 126.6, 125.5, 121.8, 116.4, and 21.1; UV−vis max (hexane) λ_{max}

(75) Rhodium(II) pivalate was prepared by reaction of rhodium(III) chloride with 5.0 equiv of trimethylacetic acid and 2.0 equiv of trimethylacetic acid sodium salt in EtOH (reflux, 3 h) according to the procedure of: Legzdins, P.; Mitchell, R. W.; Rempel, G. L.; Ruddick, J. D.; Wilkinson, G. *J. Chem. Soc.* **1970**, 3322.

(ϵ) 797 (110), 626 (320), 352 (7780), and 287 (81 050) nm. Anal. Calcd for $C_{12}H_8Cl_2O_2$: C, 56.50; H, 3.16. Found: C, 56.24; H, 2.98.

1-Acetoxy-6-nitroazulene (76). Application of the general procedure gave 0.065 g (21%) of **76** as a brown solid, mp 97.0−97.5 °C. IR (CCl_4) 2920, 1770, and 1535 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} (ϵ) 686 (310), 352 (565), 291 (51 500), 246 (19 850), 221 (16 700), 205 (16 300), 198 (26 900), 193 (29 300) nm. 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.

1-Acetoxy-6-cyanoazulene (77). Application of the general procedure gave 0.111 g (39%) of **77** as a green solid, mp 112.0−113.0 °C. IR (CCl_4) 3010, 2930, 2190, 1765, and 1575 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} (ϵ) 662 (342), 283 (86 600) nm. 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.

1-Acetoxy-2-methylazulene (78). Application of the general procedure gave 0.149 g (58%) of **78** as blue needles, mp 58.5−59.5 °C. IR (CCl_4) 3020, 2970, 2870, 1765, 1580, 1540, and 1500 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} (ϵ) 684 (120), 641 (270), 621 (270), 585 (310), 573 (280), 550 (250), 346 (4270), 283 (49 840), 279 (47 465), 274 (45 570) nm. Anal. Calcd for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04. Found: C, 77.73; H, 5.66.

1-Trimethylacetoxy-4-iodoazulene (79). A 250-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[75] (0.017 g, 0.030 mmol, 0.01 equiv) and 45 mL of dichloromethane. A solution of diazo ketone **49** (1.08 g, 2.80 mmol) in 30 mL of dichloromethane was added dropwise via the addition funnel over 1 h to the rapidly stirred green solution of rhodium catalyst, and the resulting dark green mixture was stirred for 5 min. Trimethylacetyl chloride (0.37 g, 0.38 mL, 3.08 mmol) was then rapidly added via syringe, and then 4-DMAP (1.03 g, 8.40 mmol) was added in one portion. The resulting deep green solution was stirred at room temperature for 5 min and then poured into 60 mL of diethyl ether and 30 mL of 1 M aq HCl solution. The organic phase was separated and washed with two 30-mL portions of 1 M aq HCl solution and 30 mL of brine, dried over $MgSO_4$, filtered, and concentrated to yield 1.06 g of a green oil. Column chromatography on 30 g and then 10 g of silica gel (gradient elution with 0−2% EtOAc−hexane) afforded 0.756 g (76%) of **79** as a green solid: mp 39−40 °C; IR (CH_2Cl_2) 2973, 1751, and 1552 cm^{-1}; UV (CH_2Cl_2) λ_{max} 353 nm; ^1H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, J = 9.5 Hz, 1 H), 7.85−7.88 (m, 2 H), 7.39 (d, J = 4.3 Hz, 1 H), 7.19 (app t, J = 9.8 Hz, 1 H), 7.11 (app t, J = 9.5 Hz, 1 H), and 1.48 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.7, 140.7, 136.6, 136.5, 134.8, 132.0, 129.2, 125.8, 123.0, 121.8, 117.1, 39.7, and 27.6; HRMS-ESI (m/z) [M + H] calcd for $C_{15}H_{15}IO_2$ 355.0189, found 355.0179.

Methyl 3-[4-(1-Acetoxyazulenyl)]acrylate (82). A 10-mL, two-necked, round-bottomed flask equipped with two rubber septa and an argon inlet needle was charged with azulenyl iodide **69** (0.172 g, 0.55 mmol), $Pd(OAc)_2$ (0.003 g, 0.015 mmol, 0.03 equiv), Et_4NCl (0.083 g, 0.50 mmol), 2.0 mL of dimethylacetamide, *N,N*-dicyclohexylmethylamine (0.147 g, 0.160 mL, 0.75 mmol), and methyl acrylate (0.043 g, 0.045 mL, 0.50 mmol) in that order. One of the rubber septa was replaced with a glass stopper and the other septum was replaced with a reflux condenser fitted with an argon inlet adapter, and the suspension was stirred at 65 °C for 16 h. The resulting dark green suspension was allowed to cool to room temperature, diluted with 10 mL of diethyl ether, and washed with 20 mL of H_2O. The aqueous layer was back-extracted with two 10-mL portions of ether, and the combined organic layers were washed with 10 mL of H_2O and 10 mL of brine, dried over $MgSO_4$, filtered, and concentrated to yield 0.221 g of a dark green oil. Column chromatography on 22 g of silica gel (elution with 15% EtOAc−hexane) afforded 0.129 g (96%) of **82** as a green solid: mp: 56−57 °C; IR (CCl_4) 2940, 1760, 1720, and 1540 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.57 (d, J = 15.9 Hz, 1 H), 8.26 (d, J = 9.8 Hz, 1 H), 7.86 (d, J = 4.6 Hz, 1 H), 7.57 (app t, J = 10.1 Hz, 1 H), 7.53 (d, J = 4.6 Hz, 1 H), 7.35 (t, J = 10.7 Hz, 1 H), 7.12 (t, J = 9.6 Hz, 1 H), 6.69 (d, J = 15.9 Hz, 1 H), 3.89 (s, 3 H), and 2.45 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.5, 167.1, 144.6, 142.0, 139.5, 137.8, 133.2, 132.8, 128.2, 127.6, 124.3, 122.4, 121.6, 111.6, 52.4, and 21.4; UV−vis (hexane) λ_{max} (ϵ) 649 (378), 352 (4080), 292 (63 520), 257 (58 035), and 192 (6505) nm. Anal. Calcd for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 70.97; H, 5.05.

1-Acetoxy-4-(2-thienyl)azulene (83). A 50-mL, three-necked, round-bottomed flask equipped with a rubber septum, glass stopper, and an argon inlet adapter was charged with 2-thienyllithium (1.0 M in THF, 0.96 mL, 0.960 mmol) and 5 mL of THF. $ZnCl_2$ (0.131 g, 0.961 mmol) was then added, and the resulting mixture was stirred for 30 min. To the greenish-gray mixture was then added tris(dibenzylideneacetone)-dipalladium (0.023 g, 0.026 mmol) and triphenylarsine (0.031 g, 0.103 mmol). A 10-mL, one-necked, pear-shaped flask was charged with 1-acetoxy-4-iodoazulene (**69**) (0.200 g, 0.641 mmol) and 4 mL of THF. The azulene solution was transferred dropwise via cannula into the reaction mixture over 1 min and the flask was rinsed with two 1.5-mL portions of THF. After 30 min, the reaction mixture was poured into 30 mL of saturated ammonium chloride solution and 50 mL of diethyl ether. The organic phase was separated and washed with 30 mL of saturated ammonium chloride solution and 30 mL of brine, dried over $MgSO_4$, filtered, and concentrated to provide 0.223 g of a greenish brown oil. Column chromatography on 20 g of silica gel (elution with 5% ethyl acetate−hexanes, compound applied adsorbed onto 0.500 g silica gel) afforded 0.140 g (81%) of 1-acetoxy-4-(2-thienyl)azulene (**83**) as an olive green solid. An analytical sample was prepared by recrystallization from hexanes at −20 °C: mp 98.0−99.0 °C; IR (CCl_4) 3020, 2910, 1760, 1585, and 1535 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.25 (d, J = 9.4 Hz, 1H), 7.76 (d, J = 4.6 Hz, 1H), 7.48−7.53 (m, 4 H), 7.28 (d, J = 10.6 Hz, 1H), 7.18 (dd, J = 3.8, 4.2 Hz, 1H), 7.04 (app t, J = 9.4, 9.8 Hz, 1H), and 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.3, 160.5, 144.0, 143.8, 138.9, 137.1, 132.6, 132.2, 128.4, 127.3, 127.1, 126.8, 126.2, 120.9, 114.4, and 21.1; UV−vis (hexane) λ_{max} (ϵ) 625 (438), 599 (377), 352 (4725), 280 (28 350), and 239 (3,30) nm. Anal. Calcd for $C_{16}H_{12}O_2S$: C, 71.62; H, 4.51. Found: C, 71.45; H, 4.59.

General Procedure for the Preparation of 1-(Trifluoromethanesulfonyloxy)azulene (84). 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[75] (0.006 g, 0.010 mmol) and 18 mL of dichloromethane. The addition funnel was charged with diazo ketone **19** (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 stirred green solution of catalyst. After 5 min, Tf_2NPh (0.357 g, 1.00 mmol) was added in one portion, and then a solution of 4-DMAP (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 being stirred 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 that 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 the azulenyl triflate **84** as an unstable purple-blue oil: IR (CCl_4) 3000, 1580, and 1550 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.35 (d, J = 9.7 Hz, 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.

1-Ethylazulene (87). A solution of azulenyl triflate **84** (ca. 1.00 mmol) in diethyl ether−dichloromethane prepared according to the general procedure was concentrated with use of 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.[76] 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 Cs_2CO_3 (0.977 g, 3.0 mmol) were then added, followed by a solution of *B*-ethyl-9-BBN[77] (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 **19**) of 1-ethylazulene[78] as a dark blue oil: IR (thin film) 3010, 2960, 2920, 2860, 1570, 1530, and 1500 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.

1-Phenylazulene (88). A solution of azulenyl triflate **84** (ca. 1.00 mmol) in diethyl ether−dichloromethane prepared according to the general procedure was concentrated with use of 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.[76] 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), Cs_2CO_3 (0.977 g, 3.0 mmol), and *B*-phenyl-9-BBN[79] (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 **19**) of 1-phenylazulene as a dark blue solid: mp 51−53 °C (lit.[80] mp 58 °C); IR (thin film) 3050, 3000, 2960, 1600, and 1570 cm^{-1}; ^1H 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 (89). A solution of azulenyl triflate **85** (ca. 1.05 mmol) in diethyl ether prepared according to the general procedure (except that Et_2O was employed as solvent in place of dichloromethane) was concentrated with use of a rotary evaporator to a volume of ca. 5 mL. The flask was then equipped with a stir bar and argon inlet adapter and the remaining solvent was removed at 0.1 mmHg with vigorous stirring.[76] 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. $Pd(OAc)_2$ (0.012 g, 0.053 mmol), *o*-(dicyclohexylphosphino)biphenyl (0.028 g, 0.079 mmol), and Cs_2CO_3 (1.03 g, 3.15 mmol) were then added, followed by a solution of *B*-ethyl-9-BBN[77] (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 5 h. The black suspension was diluted with 15 mL of diethyl ether and washed with 15 mL of 2 M NaOH solution and 15 mL of brine, dried over $MgSO_4$, filtered, and concentrated to yield 1.18 g of a green oil. Purification by column chromatography on 36 g and then on 20 g of silica gel (elution each time with pentane) afforded 0.075 g (36% overall from diazo ketone **50**) of 1-ethyl-5-isopropylazulene as a dark blue oil: IR (thin film): 2950, 2920, 2860, 1570, and 1505 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.

1,6-Diethylazulene (90). A solution of azulenyl triflate **86** (ca. 1.00 mmol) in diethyl ether−dichloromethane prepared according to the general procedure was concentrated to a volume of ca. 5 mL in a 25-mL, one-necked, round-bottomed flask. The flask was then equipped with a rubber septum and argon inlet needle and the remaining solvent was removed with vigorous stirring at 0.02 mmHg.[76] THF (1.0 mL) was immediately added to produce a dark purple solution. $Pd(OAc)_2$ (0.011 g, 0.05 mmol, 0.05 equiv), *o*-(dicyclohexylphosphino)-biphenyl (0.026 g, 0.075 mmol, 0.075 equiv), Cs_2CO_3 (0.977 g, 3.0 mmol), and 2.4 mL of Et_3B solution (1.0 M in THF, 2.4 mmol) were added, and the dark purple suspension was stirred at room temperature for 2 h. The resulting dark green suspension was diluted with 20 mL of diethyl ether and extracted with two 10-mL portions of aq 2 M NaOH solution and 10 mL of brine, dried over $MgSO_4$, filtered, and concentrated to yield 0.265 g of a dark green oil. Column chromatography on 26 g of silica gel (elution with pentane) afforded 0.091 g (49% overall from diazo ketone **54**) of **90** as a dark blue oil: IR (CH_2Cl_2) 2964, 2930, 2869, 1579, 1401, and 832 cm^{-1}; UV (CH_2Cl_2) λ_{max} 351 nm; ^1H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, J = 10.1 Hz, 1 H), 8.17 (d, J = 10.1 Hz, 1 H), 7.71 (d, J = 3.7 Hz, 1 H), 7.27 (d, J = 2.8 Hz, 1 H), 7.01 (d, J = 9.8 Hz, 1 H), 6.98 (d, J = 9.5 Hz, 1 H), 3.09 (q, J = 7.5 Hz, 2 H), 2.81

(76) Though stable in solution, the azulenyl triflate is unstable in concentrated form where it has a tendency to decompose to form an intractable black solid. Concentration to dryness on the rotary evaporator usually led to decomposition; this could be avoided by removing the last several milliliters of solvent under high vacuum and then venting the flask to argon.

(77) (a) Knights, E. F.; Brown, H. C. *J. Am. Chem. Soc.* **1968**, *90*, 5283. For alternative methods for the preparation of this reagent, see: (b) Kramer, G. W.; Brown, H. C. *J. Organomet. Chem.* **1974**, *73*, 1. (c) Brown, C. A. *J. Org. Chem.* **1975**, *40*, 3154.

(78) Anderson, A. G.; Breazeale, R. D. *J. Org. Chem.* **1969**, *34*, 2375.

(79) Prepared by reaction of 9-BBN with 1 equiv of phenyllithium and 1 equiv of methyl iodide according to the procedure of Brown (ref 77b).

(80) Plattner, P. A.; Furst, A.; Gordon, M.; Zimmermann, K. *Helv. Chim. Acta* **1950**, *33*, 1910. See also: Oda, M.; Kajioka, T.; Haramoto, K.; Miyatake, R.; Kuroda, S. *Synthesis* **1999**, *8*, 1349.

(q, J = 7.5 Hz, 2 H), 1.39 (t, J = 7.5 Hz, 3 H), and 1.34 (t, J = 7.6 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.3, 139.3, 136.1, 135.0, 134.2, 133.2, 133.1, 122.7, 122.1, 116.7, 35.6, 20.6, 17.1, and 16.0; HRMS-ESI (*m/z*) [M^+] calcd for $C_{14}H_{16}$ 184.1247, found 184.1244.

2-(1-Azulenyl)-4,4,5,5-tetramethyl-[1,3,2]-dioxaborolane (91). A solution of azulenyl triflate **84** (ca. 3.00 mmol) in diethyl ether−dichloromethane prepared according to the general procedure was concentrated to a volume of ca. 5 mL in a 50-mL, one-necked, round-bottomed flask. The flask was then equipped with a rubber septum and argon inlet needle and the remaining solvent was removed with vigorous stirring at 0.02 mmHg.[76] THF (8.4 mL) was immediately added to produce a dark purple solution. $Pd(OAc)_2$ (0.034 g, 0.15 mmol, 0.05 equiv), *o*-(dicyclohexylphosphino)biphenyl (0.21 g, 0.60 mmol, 0.20 equiv), triethylamine (1.69 mL, 1.22 g, 12.0 mmol), and 6.0 mL of 4,4,5,5-tetramethyl-1,3,2-dioxaborolane solution (1.0 M in THF, 6.0 mmol) were added, and the dark purple suspension was stirred at room temperature for 16 h. The resulting deep purple suspension was diluted with 15 mL of diethyl ether and extracted with 10 mL of H_2O and 10 mL of brine, dried over $MgSO_4$, filtered, and concentrated to yield 1.93 g of a deep purple oil. Column chromatography on 50 g of silica gel (gradient elution 0−5% EtOAc−hexane) afforded 0.477 g of a purple oil that was repurified on 15 g of silica gel (gradient elution with 0−3% EtOAc−hexane) to afford 0.368 g (48% overall from diazo ketone **19**) of **91** as a dark purple solid: mp 56−58 °C; IR (CH_2Cl_2) 2977, 2930, 1579, and 1500 cm^{-1}; UV (CH_2Cl_2) λ_{max} 345 and 362 nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.18 (d, J = 9.5 Hz, 1 H), 8.43 (d, J = 9.5 Hz, 1 H), 8.35 (d, J = 3.7 Hz, 1 H), 7.68 (app t, J = 9.8 Hz, 1 H), 7.38−7.42 (m, 2 H), 7.31 (app t, J = 9.8 Hz, 1 H), and 1.42 (s, 12 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.3, 145.8, 144.8, 138.5, 137.6, 136.9, 136.7, 125.4, 124.9, 119.3, 83.1, and 25.2; HRMS-ESI (*m/z*) [M + H] calcd for $C_{16}H_{19}BO_2$ 255.1551, found 255.1555.

General Procedure A for Suzuki Coupling Reactions of Azulenyl Boronate 91: 4-(1-Azulenyl)acetophenone (94). A 25-mL, one-necked, pear-shaped flask equipped with a rubber septum and argon inlet needle was charged with azulenyl boronate **91** (0.168 g, 0.66 mmol), *p*-iodoacetophenone (0.108 g, 0.44 mmol), $Pd(OAc)_2$ (0.005 g, 0.02 mmol, 0.05 equiv), *o*-(dicyclohexylphosphino)biphenyl (0.031 g, 0.088 mmol, 0.20 equiv), barium hydroxide (0.226 g, 1.32 mmol), 2.75 mL of 1,4-dioxane, and 1.65 mL of H_2O. The rubber septum was replaced with a reflux condenser fitted with an argon inlet adapter and the suspension was stirred at 65 °C for 15 min. The resulting dark blue-green suspension was allowed to cool to room temperature, filtered through 1 g of silica gel in a glass pipet with the aid of diethyl ether, and concentrated to yield 0.357 g of a dark blue-green oil. Column chromatography on 36 g and then 11 g of silica gel (gradient elution with 5−10% MTBE−pentane) afforded 0.106 g (98%) of **94** as a dark blue-green semisolid: IR (CH_2Cl_2) 3028, 1675, 1600, and 1573 cm^{-1}; UV (CH_2Cl_2) λ_{max} 306, 328, and 383 nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (d, J = 10.1 Hz, 1 H), 8.40 (d, J = 9.2 Hz, 1 H), 8.10−8.11 (m, 2 H), 8.07 (d, J = 4.0 Hz, 1 H), 7.73−7.75 (m, 2 H), 7.66 (app t, J = 9.8 Hz, 1 H), 7.48 (d, J = 4.0 Hz, 1 H), 7.24 (app t, J = 9.8 Hz, 2 H), and 2.68 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.1, 142.7, 142.6, 138.8, 137.9, 137.4, 135.8, 135.7, 134.9, 130.0, 129.7, 129.0, 124.3, 124.1, 118.2, and 26.9; HRMS-ESI (*m/z*) [M + H] calcd for $C_{18}H_{14}O$ 247.1117, found 247.1111.

General Procedure B for Suzuki Coupling Reactions of Azulenyl Boronate 91: 4-(1-Azulenyl)acetophenone (94). A 10-mL, one-necked, pear-shaped flask equipped with a rubber septum and argon inlet needle was charged with azulenyl boronate **91** (0.076 g, 0.30 mmol), *p*-iodoacetophenone (0.081 g, 0.33 mmol), $Pd(OAc)_2$ (0.003 g, 0.02 mmol, 0.05 equiv), *o*-(dicyclohexylphosphino)biphenyl (0.021 g, 0.060 mmol, 0.20 equiv), barium hydroxide (0.154 g, 0.900 mmol), 1.9 mL of 1,4-dioxane, and 1.1 mL of H_2O. The rubber septum was replaced with a reflux condenser fitted with an argon inlet adapter and the suspension was stirred at 65 °C for 15 min. The resulting dark blue-green suspension was cooled to room temperature, filtered through 1 g of silica gel in a glass pipet with the aid of diethyl ether, and concentrated to yield 0.163 g of a dark blue-green oil. Column chromatography on 16 g of silica gel (gradient elution with 0−10% EtOAc−hexane) afforded 0.054 g (73%) of **94** as a dark blue-green semisolid.

2-(1-Azulenyl)prop-2-en-1-ol (96). Reaction of azulenyl boronate **91** (0.110 g, 0.29 mmol) with vinyl iodide **95**[58] (0.053 g, 0.29 mmol) in the presence of $Pd(OAc)_2$ (0.003 g, 0.01 mmol, 0.050 equiv), *o*-(dicyclohexylphosphino)biphenyl (0.020 g, 0.058 mmol, 0.20 equiv), and barium hydroxide (0.149 g, 0.870 mmol) in 1.8 mL of 1,4-dioxane and 1.0 mL of H_2O according to general procedure A provided 1.67 g of a blue green oil. Column chromatography on 15 g of silica gel (gradient elution with 10−20% EtOAc−hexane) afforded 0.035 g (66%) of **96** as a green oil.

Alternatively, reaction of azulenyl boronate **91** (0.277 g, 1.09 mmol) with vinyl iodide **95** (0.302 g, 1.64 mmol) in the presence of $Pd(OAc)_2$ (0.012 g, 0.055 mmol, 0.050 equiv), *o*-(dicyclohexylphosphino)biphenyl (0.076 g, 0.22 mmol, 0.20 equiv), and barium hydroxide (0.560 g, 3.27 mmol) in 6.0 mL of 1,4-dioxane and 3.6 mL of H_2O according to general procedure B provided 2.09 g of a dark green oil. Column chromatography on 30 g of silica gel (gradient elution with 10−20% EtOAc−hexane) afforded 0.089 g (44%) of **96** as a green oil: IR (CH_2Cl_2) 3356, 2920, 1570, and 1559 cm^{-1}; UV (CH_2Cl_2) λ_{max} 280, 238, and 345 nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (d, J = 9.8 Hz, 1 H), 8.33 (d, J = 9.5 Hz, 1 H), 7.91 (d, J = 4.0, 1 H), 7.61 (app t, J = 9.8 Hz, 1 H), 7.38 (d, J = 4.0, 1 H), 7.18 (app q, J = 10.0 Hz, 2 H), 5.64 (app q, J = 1.6 Hz, 1 H), 5.37 (td, J = 0.9 and 1.8 Hz, 1 H), 4.61 (s, 2 H), and 1.72 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.8, 141.7, 138.5, 137.3, 136.9, 135.8, 135.3, 128.4, 123.6, 123.4, 117.4, 113.6, and 67.0; HRMS-ESI (*m/z*) [M + H] calcd for $C_{13}H_{12}O$ 185.0961, found 185.0965.

3-(1-Azulenyl)cyclohex-2-enone (98). Reaction of azulenyl boronate **91** (0.057 g, 0.22 mmol) with vinyl iodide **97**[59] (0.33 g, 0.15 mmol) in the presence of $Pd(OAc)_2$ (0.002 g, 0.008 mmol, 0.050 equiv), *o*-(dicyclohexylphosphino)biphenyl (0.011 g, 0.030 mmol, 0.20 equiv), and barium hydroxide (0.077 g, 0.45 mmol) in 1.0 mL of 1,4-dioxane and 0.5 mL of H_2O according to general procedure A provided 0.093 g of a dark green oil. Column chromatography on 10 g of silica gel (gradient elution with 20−25% EtOAc−hexane) afforded 0.027 g (82%) of **98** as a dark green solid.

Alternatively, reaction of azulenyl boronate **91** (0.229 g, 0.900 mmol) with vinyl iodide **97** (0.306 g, 1.35 mmol) in the presence of $Pd(OAc)_2$ (0.010 g, 0.045 mmol, 0.050 equiv), *o*-(dicyclohexylphosphino)biphenyl (0.063 g, 0.18 mmol, 0.20 equiv), and barium hydroxide (0.463 g, 2.70 mmol) in 5.0 mL of 1,4-dioxane and 3.0 mL of H_2O according to general procedure B provided 0.578 g of a dark green oil. Column chromatography on 30 g of silica gel (elution with 20% EtOAc−hexane) afforded 0.073 g (37%) of **98** as a dark green solid: mp 62−63 °C; IR (CH_2Cl_2) 2943, 1646, and 1575 cm^{-1}; UV (CH_2Cl_2) λ_{max} (ϵ) 249 (33 933), 280 (20 898), 316 (22 795), 328 (21 890), and 392 (19 824) nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.73 (d, J = 9.9 Hz, 1 H), 8.38 (d, J = 9.6 Hz, 1 H), 8.03 (d, J = 4.1 Hz, 1 H), 7.70 (t, J = 9.8 Hz, 1 H), 7.41 (d, J = 4.1 Hz, 1 H), 7.27−7.33 (m, 2 H), 6.47 (s, 1 H), 2.97 (t, J = 5.8 Hz, 2 H), 2.58 (t, J = 6.71 Hz, 2 H), and 2.22−2.27 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.9, 157.2, 143.9, 139.3, 138.1, 136.7, 136.45, 136.48, 128.6, 126.0, 125.6, 125.3, 118.6, 37.7, 31.2, and 23.3; HRMS-ESI (*m/z*) [M + H] calcd for $C_{16}H_{14}O$ 223.1117, found 223.1116.

1′-Trimethylacetoxy-1,4′-biazulene (99). Reaction of azulenyl boronate **91** (0.197 g, 0.775 mmol) with azulenyl iodide **79** (0.274 g, 0.775 mmol) in the presence of $Pd(OAc)_2$ (0.009 g, 0.04 mmol, 0.05 equiv), *o*-(dicyclohexylphosphino)biphenyl (0.054 g, 0.16 mmol, 0.20 equiv), and barium hydroxide (0.398 g, 2.33 mmol) in 4.3 mL of 1,4-dioxane and 2.6 mL of H_2O at 45 °C for 30 min according to the general procedure B provided

0.616 g of a dark green oil. Purification by preparative HPLC on a Waters Prep Nova Pak HR column (6 μ silica, 19 mm × 30 cm; gradient elution with 5−10% EtOAc−hexane) afforded 0.073 g (27%) of **99** as a green oil: IR (CH_2Cl_2) 2973, 1749, and 1546 cm^{-1}; UV (CH_2Cl_2) λ_{max} (ϵ) 240 (27 893), 278 (45 314), and 424 (5768) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 8.46 (d, J = 9.5 Hz, 1 H), 8.36 (d, J = 9.8 Hz, 1 H), 8.30 (d, J = 9.5 Hz, 1 H), 8.22 (d, J = 4.0 Hz, 1 H), 7.72 (d, J = 4.3 Hz, 1 H), 7.66 (app t, J = 9.6 Hz, 1 H), 7.59 (app t, J = 9.8 Hz, 1 H), 7.54 (d, J = 3.7 Hz, 1 H), 7.35 (d, J = 10.4 Hz, 1 H), 7.27 (t, J = 9.8 Hz, 1 H), 7.08−7.15 (m, 2 H), 7.00 (d, J = 4.6 Hz, 1 H), and 1.52 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.1, 147.6, 142.1, 138.93, 138.85, 138.6, 137.7, 136.90, 136.85, 136.0, 134.0, 132.5, 131.9, 127.8, 126.93, 126.86, 124.1, 123.9, 120.6, 117.6, 115.1, 39.6, and 27.7; HRMS-ESI (*m/z*) [M + H] calcd for $C_{15}H_{22}O_2$ 355.1693, found 355.1685.

[1,1′,3′,1″]-Terazulene (101). Reaction of azulenyl boronate **91** (0.259 g, 1.02 mmol) with 1,3-diiodoazulene[81] (0.194 g, 0.51 mmol) in the presence of $Pd(OAc)_2$ (0.006 g, 0.026 mmol, 0.05 equiv), *o*-(dicyclohexylphosphino)biphenyl (0.035 g, 0.100 mmol, 0.20 equiv), and barium hydroxide (0.262 g, 1.53 mmol) in 2.8 mL of 1,4-dioxane and 1.7 mL of H_2O according to the general procedure B provided 0.259 g of a green oil. Column chromatography on 26 g of silica gel (gradient elution with 0−2% EtOAc−hexane) afforded 0.165 g of a green solid that was further purified on 8 g of silica gel (gradient elution with 0−5% EtOAc−hexane) to afford 0.135 g (69%) of **101** as a metallic green solid with spectral data consistent with that previously reported for this compound:[40b] mp 97−98 °C; IR (CH_2Cl_2) 1569, 1447, and 1393 cm^{-1}; UV (CH_2Cl_2) λ_{max} (ϵ) 242 (186 900), 264 (240 372), 312 (190 778), and 400 (93 016) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 8.50 (d, J = 9.5 Hz, 2 H), 8.41 (d, J = 9.5 Hz, 4 H), 8.36 (s, 1 H), 8.22 (d, J = 3.4 Hz, 2 H), 7.54−7.62 (m, 5 H), 7.18 (d, J = 9.6 Hz, 2 H), 7.07 (app td, J = 9.8, 20.8 Hz, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.7, 139.9, 139.2, 138.8, 138.5, 137.9, 137.3, 136.9, 136.8, 136.6, 126.6, 126.3, 123.15, 123.11, 117.9 (one resonance corresponds to two overlapping carbons); HRMS-ESI (*m/z*) [M^+] calcd for $C_{30}H_{20}$ 380.1560, found 380.1558.

5,5′-Bis(1-trimethylacetoxyazulen-4-yl)-2,2′-bithiophene (103). A 10-mL, one-necked, round-bottomed flask equipped with a rubber septum and argon inlet needle was charged with azulenyl iodide **79** (0.143 g, 0.400 mmol), 5,5′-bis(trimethylstannyl)-2,2′-bithiophene[62] (0.099 g, 0.20 mmol), $(Ph_3P)_4Pd$ (0.023 g, 0.020 mmol, 0.10 equiv), and 3.6 mL of toluene. The rubber septum was replaced with a reflux condenser fitted with an argon inlet adapter and the suspension was heated at reflux for 24 h. The resulting dark green suspension was allowed to cool to room temperature, filtered through 5 g of silica gel with the aid of 100 mL of methylene chloride, and concentrated to yield 0.192 g of a dark green oil. Column chromatography on 20 g of silica gel (gradient elution with 0−10% CH_2Cl_2−benzene) afforded 0.091 g (73%) of **103** as a dark green solid: mp 218−219 °C; IR (CH_2Cl_2) 2973, 1750, and 1506 cm^{-1}; UV (CH_2Cl_2) λ_{max} (ϵ) 244 (85 407), 286 (129 967), and 424 (53 225) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, J = 9.4 Hz, 2 H), 7.82 (d, J = 4.4 Hz, 2 H), 7.62 (d, J = 4.4 Hz, 2 H), 7.58 (app t, J = 10.1 Hz, 2 H), 7.50 (d, J = 3.7 Hz, 2 H), 7.32−7.36 (m, 4 H), 7.06 (app t, J = 9.6 Hz, 2 H), and 1.50 (s, 18 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.9, 143.6, 143.1, 139.6, 138.7, 137.4, 132.8, 132.0, 129.8, 127.7, 127.6, 125.9, 124.4, 121.1, 114.6, 39.7, and 27.7; HRMS-ESI (*m/z*) [M^+] calcd for $C_{38}H_{34}O_4S_2$ 618.1893, found 618.1894.

1-Trimethylacetoxy-4-trimethylstannylazulene (104). A threaded Pyrex tube (ca. 20 mL capacity) equipped with a rubber septum and argon inlet needle was charged with azulenyl iodide **79** (0.350 g, 0.990 mmol), hexamethylditin (0.518 g, 1.58 mmol), $(Ph_3P)_4Pd$ (0.114 g, 0.099 mmol, 0.100 equiv), and 9 mL of toluene. The solution was degassed by 4 freeze−pump−thaw cycles (−196 °C, 0.02 mmHg), and the tube was then sealed under argon with a threaded Teflon cap. The reaction mixture was heated in an oil bath at 120 °C for 24 h. The resulting blue suspension was allowed to cool to room temperature, filtered through 5 g of silica gel with the aid of 75 mL of diethyl ether, and concentrated to yield 0.635 g of a blue oil. Column chromatography on 30 g of silica gel (gradient elution with 0−5% EtOAc−hexane) afforded 0.339 g (88%) of **104** as a blue solid: mp 51−53 °C; IR (CH_2Cl_2) 2975, 1751, and 1480 cm^{-1}; UV (CH_2Cl_2) λ_{max} (ϵ) 246 (21 919), 285 (35 105), and 347 (5057) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, J = 9.5 Hz, 1 H), 7.84 (d, J = 4.3 Hz, 1 H), 7.49 (app t, J = 9.8 Hz, 1 H), 7.31 (d, J = 9.8 Hz, 1 H), 7.23 (d, J = 4.1 Hz, 1 H), 7.05 (app t, J = 9.5 Hz, 1 H), 1.48 (s, 9 H), and 0.50 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.0, 161.8, 141.1, 138.1, 136.9, 132.2, 130.0, 127.4, 125.4, 121.8, 116.2, 39.6, 27.7, and −7.2; HRMS-ESI (*m/z*) [M + H] calcd for $C_{18}H_{24}O_2Sn$ 393.0871, found 393.0859.

1,1′-Bis(trimethylacetoxy)-4,4′-biazulene (105). A 25-mL, two-necked, round-bottomed flask equipped with a rubber septum and an argon inlet adapter was charged with azulenyl stannane **104** (0.175 g, 0.450 mmol), CuCl (0.111 g, 1.12 mmol), and 5.0 mL of DMF. The resulting blue suspension was stirred at room temperature for 3 h. The resulting turquoise suspension was diluted with 20 mL of diethyl ether and washed with two 10-mL portions of H_2O and 10 mL of brine. The combined aqueous layers were back-extracted with two 10-mL portions of ether, and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated to yield 0.230 g of a turquoise oil. Column chromatography on 12 g of silica gel (gradient elution with 0−5% EtOAc−hexane) afforded 0.088 g (86%) of **105** as a turquoise solid: mp 200−201 °C; IR (CH_2Cl_2) 2974, 1751, and 1555 cm^{-1}; UV (CH_2Cl_2) λ_{max} (ϵ) 247 (62 915), 278 (81 548), 349 (11 119), and 369 (7632) nm; ^1H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, J = 9.6 Hz, 2 H), 7.67 (d, J = 4.4 Hz, 2 H), 7.61 (app t, J = 10.0 Hz, 2 H), 7.22 (d, J = 10.4 Hz, 2 H), 7.15 (app t, J = 9.6 Hz, 2 H), 6.80 (d, J = 4.3 Hz, 2 H), and 1.49 (s, 18 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.9, 151.0, 139.0, 137.7, 133.0, 132.7, 128.0, 127.8, 125.2, 121.6, 114.5, 39.7, and 27.6; HRMS-ESI (*m/z*) [M^+] calcd for $C_{30}H_{30}O_4$ 454.2139, found 454.2157.

(*Z*)-2-Acetylamino-3-[1-trimethylacetoxyazulen-4-yl]-acrylic Acid Methyl Ester (108) and (*E*)-2-Acetylamino-3-[1-trimethylacetoxyazulen-4-yl]-acrylic Acid Methyl Ester (109). A 25-mL, one-necked, round-bottomed flask equipped with a rubber septum and an argon inlet needle was charged sequentially with azulenyl iodide **79** (0.584 g, 1.65 mmol), $Pd(OAc)_2$ (0.010 g, 0.045 mmol, 0.03 equiv), Et_4NCl (0.249 g, 1.50 mmol), 6.5 mL of dimethylacetamide, *N*,*N*-dicyclohexylmethylamine (0.440 g, 0.480 mL, 2.25 mmol), and methyl-2-acetamidoacrylate[82] (0.215 g, 1.50 mmol). The rubber septum was replaced with a reflux condenser fitted with an argon inlet adapter and the suspension was stirred at 65 °C for 48 h. The resulting blue suspension was allowed to cool to room temperature, diluted with 20 mL of diethyl ether, washed with two 15-mL portions of H_2O and 15 mL of brine, dried over $MgSO_4$, filtered, and concentrated to yield 0.979 g of a blue oil. Column chromatography on 90 g of silica gel (elution with 40−60% EtOAc−hexane) afforded 0.393 g (71%) of a 5:1 mixture of **108** and **109** as a blue solid:[83] mp 59−61 °C; IR (CH_2Cl_2) 2975, 1734, 1675, and 1506 cm^{-1}; UV (CH_2Cl_2) λ_{max} 244, 285, and 623 nm; ^1H NMR (500 MHz, $CDCl_3$) δ 8.69 (s, 1 H, minor isomer), 8.21 (d, J = 9.2, 1 H, major isomer), 8.18 (d, J = 9.8 Hz, 1 H, minor isomer), 7.80 (d, J = 4.3 Hz, 1 H, major isomer), 7.72−7.77 (m, 3 H, both isomers), 7.55 (app t, J =

(81) 1,3-Diiodoazulene was prepared by the reaction of azulene with 2.1 equiv of NIS in methylene chloride (rt, 12 h) according to the procedure of Hafner, see ref 41a.

(82) Methyl-2-acetamidoacrylate was prepared by reaction of methyl pyruvate with 2.0 equiv of acetamide in benzene (reflux, 2.5 h) according to the procedure of Yokoyama, see ref 70.

(83) Partial separation of this mixture was accomplished by preparative HPLC (Waters Prep Nova Pak HR column, 6 μm silica, 19 mm × 30 cm; gradient elution with 40−60% EtOAc−hexane).

10.1 Hz, 1 H, major isomer), 7.50 (app t, J = 10.4 Hz, 1 H, minor isomer), 7.21−7.23 (m, 2 H, both isomers), 7.08−7.13 (m, 2 H, major isomer), 6.97−7.06 (m, 3 H, minor isomer), 3.93 (s, 3 H, major isomer), 3.37 (s, 3 H, minor isomer), 2.21 (s, 3 H, minor isomer), 1.91 (br s, 3 H, major isomer), and 1.48 (s, 18 H, both isomers); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.0, 176.9, 169.2, 168.7, 165.2, 164.9, 145.8, 142.5, 139.3, 138.8, 137.7, 136.8, 132.5, 132.1, 131.9, 131.7, 129.3, 129.1, 128.1, 127.6, 127.5, 127.1, 125.9, 124.7, 123.2, 122.3, 121.2, 112.5, 112.0, 53.2, 52.7, 39.65, 39.62, 27.62, 27.60, 25.0, and 23.2 (one resonance corresponds to two overlapping carbons); HRMS-ESI (m/z) [M + Na] calcd for $C_{21}H_{23}NO_5$ 392.1468, found 392.1451.

2-Acetylamino-3-(1-trimethylacetoxyazulen-4-yl)-propionic Acid Methyl Ester (110). A 500-mL Parr hydrogenation bottle was charged with a 5:1 mixture of azulenyl pivalates **108** and **109** (0.080 g, 0.22 mmol), $(PPh_3)_3RhCl$ (0.030 g, 0.032 mmol, 0.15 equiv), and 20 mL of degassed ethanol. The bottle was evacuated and filled with hydrogen three times, and then shaken under 95 psi of hydrogen for 24 h. The reaction mixture was then concentrated to yield 0.115 g of a blue oil. Column chromatography on 10 g of silica gel (elution with 5−10% IPA−hexane) afforded 0.057 g (71%) of **110** as a blue oil:[84] IR (CH_2Cl_2) 3282, 2973, 1748, 1658, 1562, and 1504 cm^{-1}; UV (CH_2Cl_2) λ_{max} 245, 285, and 348 nm; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, J = 9.5 Hz, 1 H), 7.79 (d, J = 4.6 Hz, 1 H), 7.51 (app t, J = 10.1 Hz, 1 H), 7.39 (d, J = 4.6 Hz, 1 H), 7.05 (app t, J = 9.6 Hz, 1 H), 6.99 (d, J = 10.4 Hz, 1 H), 6.01 (d, J = 7.6 Hz, 1 H), 5.06 (q, J = 6.9 Hz, 1 H), 3.66 (dd, J = 1.5, 6.7 Hz, 2 H), 3.59 (s, 3 H), 1.91 (s, 3 H), and 1.48 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.9, 172.2, 169.9, 145.7, 139.2, 137.7, 133.9, 132.6, 127.2, 127.0, 125.7, 121.5, 111.4, 53.7, 52.6, 39.64, 39.61, 27.6, and 23.4; HRMS-ESI (m/z) [M + Na] calcd for $C_{21}H_{25}NO_5$ 394.1625, found 394.1607.

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Supporting Information Available: Experimental procedures and characterization data for diazo ketones **48**−**55**, **65**, and **66** and ^{1}H NMR spectra for all azulene and diazo ketone products. This material is available free of charge via the Internet at http://pubs.acs.org.

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(84) Separation of enantiomers could be effected by HPLC, using a Daicel Chiracel OD column (elution with 10% IPA-hex); t_R = 14.164 and 17.796 min; $[\alpha]_D$ −24 (c 2.86, CH_2Cl_2); $[\alpha]_D$ +22 (c 2.76, CH_2Cl_2).