Synthesis of Azulenone Skeletons by Reaction of 2-Phenyl-2-acylketenes [RCO(Ph)C=C=O] with Alkynyl Ethers: Mechanistic Aspects and Further Transformations

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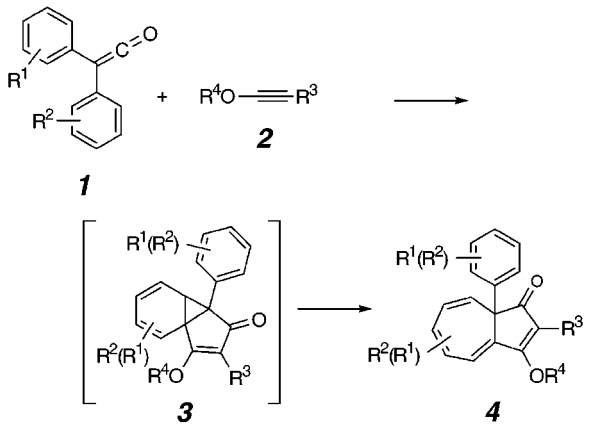
Received October 20, 1997

A method is described for a mild and efficient synthesis of azulenone skeletons via the addition reactions of 2-phenyl-2-acylketenes with 1-alkynyl ethers. A mechanism is presented to account for both azulenone formation as well as the solvent and substrate dependency of a competitive pyrone formation. The azulenone rings have been subsequently transformed into both substituted azulenes or hydroazulenes by derivatization and/or decarboxylation of an angular carboxyl substituent or by hydrogenation.

Introduction

Reaction of diarylketenes **1** with alkynyl ethers **2** is known to produce azulenone derivatives **4**.[1] Previous work has focused primarily on the aromatic substituent effects (i.e. R_1 vs R_2) in the competing formation of postulated norcaradiene derivatives **3**,[2] which undergo ring-opening expansion to **4**. The formation of norcaradiene derivatives **3** has been discussed as a symmetry-allowed [$\pi_a^2 + \pi_a^2 + \pi_s^2$] cycloaddition.[1c,3] Despite the relative ease with which this tandem cycloaddition/electrocyclic opening accesses azulenone derivatives, its synthetic potential appears to have gone largely unexplored.[4] This is likely a function of the angular aryl moieties present in **4**, which impose limits on the options available for further modification of the azulenone skeleton.



In the course of our investigations of acylketene/alkynyl ether reactivity directed toward the synthesis of γ-pyrones,[5] we have observed that arylacylketenes **5** react like diarylketenes (cf. **1**) to yield azulenone derivatives **6** (Table 1). This result intrigued us because of the potentially greater synthetic versatility offered by the angular acyl substituent in **6** (vis-à-vis the aryl substituent present in **4**). Herein we report our initial results on the scope of arylacylketene/alkynyl ether reactions, as well as various transformations of the azulenone products.

Results and Discussion

Substituent Effects in Ketene 5. At the outset of our studies, the series of ketenes **5a**−**c**, derived from thermolysis of the diazoketones **7a-c**,[6] as well as the stable ketene acid chloride **5d**[7] were reacted with 1-methoxy-1-butyne (**2a**). The nature of the acyl moiety in **5** plays a critical role in controlling the efficiency of azulenone **6** formation (Table 1), which is always accompanied by one or more competing reactions. These include competitive pyrone formation and decarboxylation [e.g., to form $PhCH_2PO(OMe)_2$]. As judged by independent trapping experiments with methanol, ketenes **5a** and **5b** (entries 1 and 2) are the sole Wolff rearrangement products[8] accompanying decomposition of **7a** and **7b**. In the case of entry 3, however, **5c** is one of two ketenes generated in approximately equal amounts because the migratory aptitudes for phenyl vs methyl are approximately equal.[9] Ketene **5c** is the only one that can give rise to **6c**. The increasing selectivity for azulenone formation vis-à-vis pyrone formation for **5c** vs **5a** (entries 3 vs 1) suggested that the selectivity for azulenone

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(1) (a) Nieuwenhuis, J.; Arens, J. F. *Rec. Trav. Chem.* **1958**, *77*, 761. (b) Vieregge, H.; Bos, H. J. T.; Arens, J. F. *Rec. Trav. Chem.* **1959**, *78*, 664. (c) Jenny, E. F.; Schenker, K.; Woodward, R. B. *Angew. Chem.* **1961**, *73*, 756.

(2) Teufel, H.; Jenny, E. F. *Tetrahedron Lett.* **1971**, *21*, 1769.

(3) Direct evidence of norcaradienes derived from naphthylketenes and ethoxyacetylene has been reported: Wuest, J. D. *Tetrahedron* **1980**, *36*, 2291.

(4) (a) Barton, D. H. R.; Gardner, J. N.; Petterson, R. C.; Stamm, O. A. *J. Chem. Soc.* **1962**, 2708. (b) Druey, J.; Schenker, K.; Woodward, R. B. *Helv. Chim. Acta* **1962**, *71*, 600.

(5) We have also studied the (formal) [4 + 2] cycloaddition reactions of nonaryl substituted acylketenes with alkynyl ethers to generate γ-pyrones. These results will be published elsewhere.

(6) Baum, J. S.; Shook, D. A.; Davies, H. M. L.; Smith, H. D. *Synth. Commun.* **1987**, *17*, 1709.

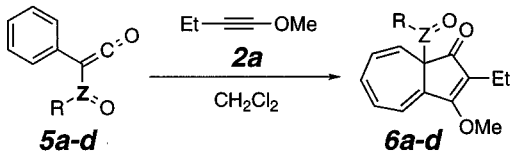
(7) Nakanishi, S.; Butler, K. *Org. Prep. Proc. Intl.* **1975**, *7*, 155−158.

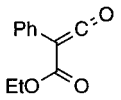
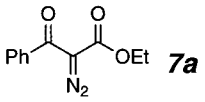
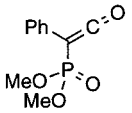
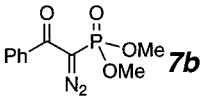
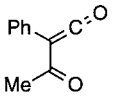
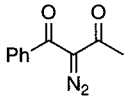
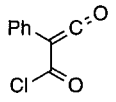
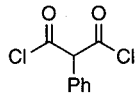
(8) For characterization of ketene **5b,** see: Tomioka, H.; Komatsu, K.; Shimizu, M. *J. Org. Chem.* **1992**, *57*, 6216.

(9) Meier, H.; Zeller, K.-P. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 32.

S0022-3263(97)01931-2 CCC: $15.00
Published on Web 02/11/1998

Table 1. Influence of Acyl Substituent on the Efficiency of Azulenone Formation



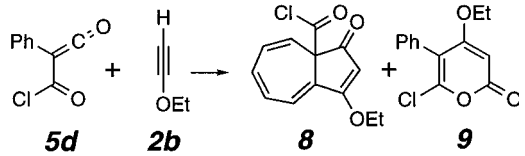
Entry	Ketene	Ketene Precursor	R	Z	Temp (°C)	Product	% Yield	%**6** : %Pyrones
1	 **5a**	 **7a**	EtO	C	130[a]	***6a***	< 5[b]	<1 : 12
2	 **5b**	 **7b**	$(MeO)_2$	P	130[a]	***6b***	10	na
3	 **5c**	 **7c**	Me	C	120[a]	***6c***	20	1.1 : 1
4	 **5d**	 **7d**	Cl	C	0	***6d***	70	>19 : 1[c]

[a] Reactions were performed on a ca. 10−100 mg scale in a capped culture tube behind a blast shield at the indicated bath temperature. [b] As judged by diagnostic ^{1}H NMR ($CDCl_3$) signals for vinylic protons at 5.8−6.6 ppm and GC−MS data (t_R = 9.98 min) at 274 (6, M^+), 201 (100, $M^+ - CO_2Et$), 171 (9), and 115 (6). [c] No pyrone resonances were observed in the ^{1}H NMR spectrum of the crude product mixture for the reaction performed in CH_2Cl_2. The **6d**:α-pyrone ratio was 6:1 when the reaction was performed in benzene.

formation increases with greater electron-withdrawing ability of the acyl moiety. Therefore, we turned to the use of (chlorocarbonyl)phenylketene **5d**. Consistent with this hypothesis, **5d** gave the highest ratio of azulenone/pyrone formation of any of the ketenes studied (entry 4). The 70% yield of **6d** and the mild reaction conditions (0 °C) render this reaction preparatively useful.[10] All subsequent studies were therefore carried out with ketene **5d** and products derived therefrom.

Solvent Effects. Nearly all of the byproducts observed for the reactions of **5a**, **5c**, and **5d** with **2a** (Table 1) were either α- or γ-pyrones.[5] We explored the solvent effect on the efficiency of formation of azulenone **8** vis-à-vis the α-pyrone **9** (Table 2) using (chlorocarbonyl)-phenyl ketene (**5d**) and ethoxyacetylene (**2b**). The ratio of **8** to **9** can be modulated somewhat (i.e., by about a factor of 3) by the choice of solvent. Specifically, more polar solvents support the formation of **8** (entry 1), whereas less polar solvents suppress formation of **8** (entries 3 and 4). For substituted analogues of ethoxyacetylene (**2a**), the ratio of azulenone to pyrone formation is even greater (e.g., entry 4, Table 1), occasionally even to the exclusion of pyrone formation. Finally, the result

Table 2. Solvent Effect on Azulenone vs α-Pyrone Formation



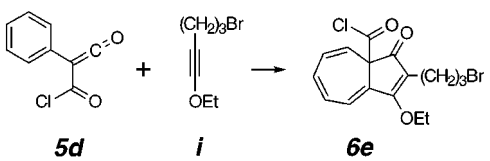
Entry	Solvent	**8** : **9**[a]
1	CH_2Cl_2	2.8[b]
2	Ph-CF_3	2.5
3	benzene	1.5
4	cyclohexane	1.0

[a] As determined by ^{1}H NMR analysis. [b] 48% isolated yield of **8**.

in entry 2 is notable because it adds to the repertoire of reactions for which Curran and co-workers have reported α,α,α-trifluorotoluene to be an adequate, higher boiling, less toxic substitute for dichloromethane.[11]

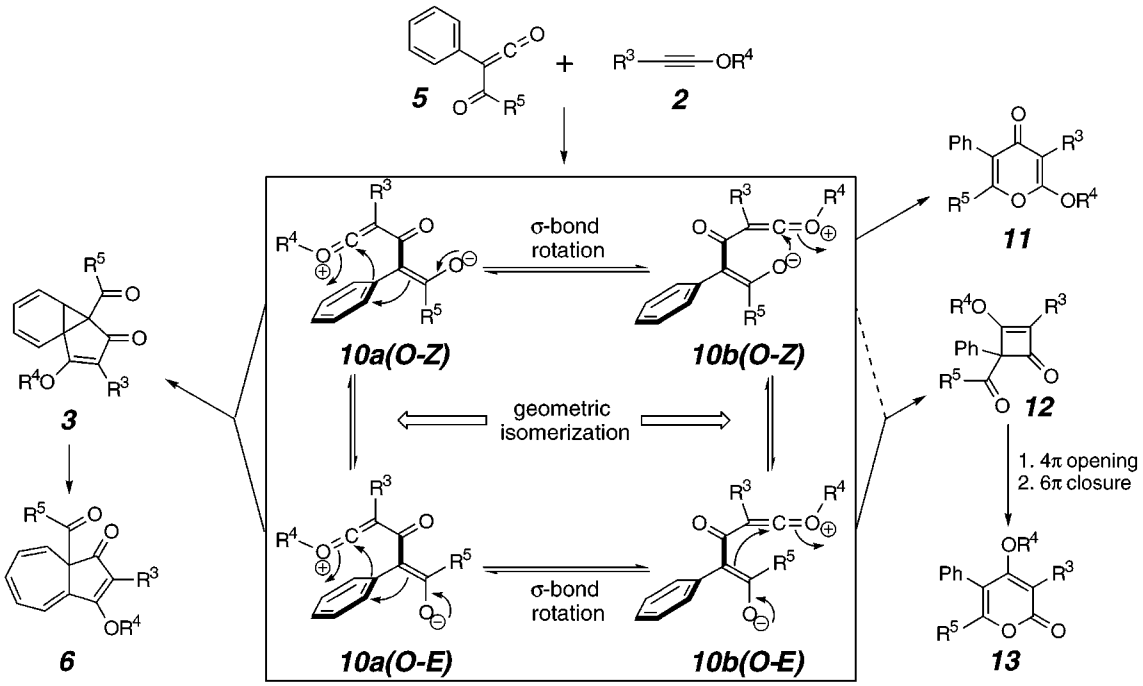
Mechanism. As noted above, previous reports on diarylketene/alkynyl ether reactions have postulated formation of an intermediate norcaradiene derivative **3** formed via a symmetry-allowed [$\pi_a^2 + \pi_a^2 + \pi_s^2$] cycloaddition.[1c,3] Subsequent ring-opening leads to the azulenone products. Although our primary interest has been the exploration of synthetic aspects of these azulenone products **6**, the substituent (Table 1) and solvent

(10) Another example that demonstrates the variety of azulenone acid chlorides that can be prepared by this route is compound **6e** containing a functional side chain, which was prepared from the bromopentynyl ether **i** and **5d**. Once again, the analogous γ-pyrone was not observed (**6e**/pyrone > 19:1).



(11) Ogawa, A.; Curran, D. P. *J. Org. Chem.* **1997**, *62*, 450.

Scheme 1



(Table 2) effects and the competing pathways to pyrone formation invite mechanistic speculation. Perhaps in the reactions of arylacylketenes **5** and alkynyl ethers **2** a stepwise rather than concerted process may be operating to lead to the norcaradiene precursor **3** (Scheme 1). We speculate that initial attack of **2** on **5** gives rise to zwitterionic intermediate **10**.

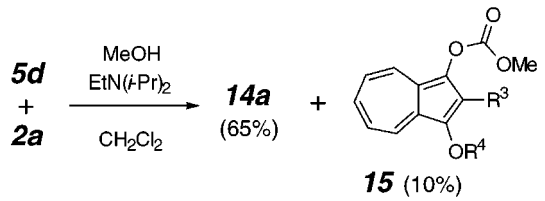
Rotamers of zwitterion **10** capable of cyclization to either azulenone (from **10a**) or pyrone (**10b**) products are considered in Scheme 1. Each can exist as two enolate geometric isomers (**O-*Z*** and **O-*E***). Either **10a(O-*Z*)** or **10a(O-*E*)** could cyclize to norcaradiene intermediate **3**. γ-Pyrones **11** could arise directly via **10b(O-*Z*)** by intramolecular O-acylation. α-Pyrones **13** could arise from cyclobutenones **12**,[12] formed by C-acylation within **10b**.

A plausible argument can be offered to account for the observed solvent effects. Recall that azulenone formation was suppressed in highly nonpolar solvents (Table 2). Rotamers **10a**, the azulenone precursors, should have a larger dipole moment than **10b**, the pyrone precursors. Thus, the equilibrium population of **10a** relative to **10b** should be higher in methylene chloride than in, e.g., cyclohexane, consistent with the observed product ratios (entries 1 vs 4).

Consider the effect of changing the substituent R^5 in ketene **5**. The most electron-withdrawing chlorine atom in **5d** resulted in the greatest preference for the norcaradiene/azulenone pathway compared with the ethoxy and methyl substituents present in **5a** and **5c** (Table 1). The nucleophilicity of the enolate-like character in zwitterions **10** is attenuated when R^5 = Cl. Therefore, *O*-acylation of **10b(O-*Z*)** to give γ-pyrone **11** as well as *C*-acylation of **10b** to give cyclobutenone/α-pyrone **12**/**13** should be suppressed. On the other hand, cyclization of **10a** to **3** is initiated by intramolecular, electrophilic acylation of the phenyl ring, which should be less affected by the electronic character of the substituent R.[5] In other words, cyclization of **10a** to **3** would be expected to occur at more or less similar rates for each of the various R^5 groups. The presence of the chlorine atom therefore is envisioned to slow pyrone formation more than azulenone formation, consistent with the observed trend in substituent effects.

Reactions of Azulenones 6. We have studied three types of reactions that transform azulenones **6** into products of further interest. These involve substitution of the acid chloride at C(8a), deacylation of the COCl group, and some selective hydrogenation reactions of alkenes in the cycloheptatriene moiety.

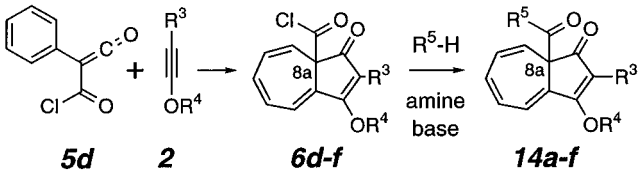
The acid chloride in azulenones **6** was reacted with alcohols and amines to give the corresponding ester and amide derivatives (Table 3). This could be done either starting from isolated **6** (entry 1) or, more conveniently, in a one-pot procedure in which **5d** is reacted sequentially with the appropriate alkynyl ether and trapping nucleophile (entries 2−6). A single-crystal X-ray structure of azulenone **14f** was obtained, providing confirmation of the core skeletal structure of azulenones **6** and **14**.[13] Methyl ester **14a** was the sole product isolated upon methanolysis of **6d** using triethylamine as the basic catalyst. However, when Hünig's base was used, the reaction solution took on an intense dark blue color. The azulene **15** was isolated as a minor product accompanying



(12) For examples of cyclobutenones formed via alkynyl ethers and ketenes see: (a) Wasserman, H. H.; Piper, J. U.; Dehmlow, E. V. *J. Org. Chem.* **1973**, *38*, 1451. (b) Danheiser, R. L.; Gee, S. K.; Sard, H. *J. Am. Chem. Soc.* **1982**, *104*, 26.

(13) The authors have deposited atomic coordinates for **14f** with the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U. K.

Table 3. Preparation of 8a-Substituted Azulenone Esters and Amides

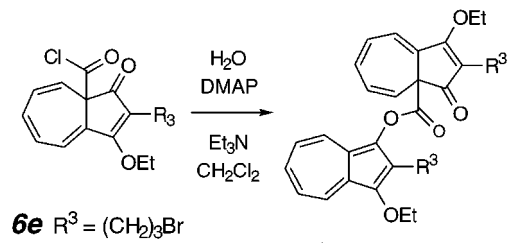


5d *2* *6d-f* *14a-f*

Entry	R_3	R_4	R_5	Product	% Yield
1	Et	Me	MeO	***14a***	65
2	$H_3C(CH_2)_2$	Me	MeO	***14b***	58
3	$Ph(CH_2)_3$	Me	MeO	***14c***	35
4	H	Et	MeO	***14d***	25
5	Et	Me	*p*-NO_2PhCH_2O	***14e***	27
6	Et	Me	*p*-BrPhNH	***14f***	35

14a. This intriguing result demonstrated the potential for mild removal of the angular acyl moiety in azulenones **6**, rendering 1,3-hydroxy azulene derivatives accessible in two steps from readily available precursors.

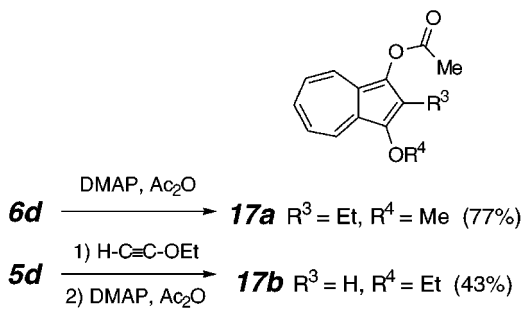
Initial attempts to deacylate azulenones **6** and obtain free 1-hydroxyazulenes by a simple hydrolysis/decarboxylation strategy were unsuccessful. Although dramatic color changes rapidly accompanied the reaction of **6e** or **8** with water, only the *coupled* azulene/azulenone products **16a** and **16b** were isolated. We next conducted the



6e $R^3 = (CH_2)_3Br$ or ***6f*** $R^3 = H$

16a $R^3 = (CH_2)_3Br$ (70%) or ***16b*** $R^3 = H$ (45%)

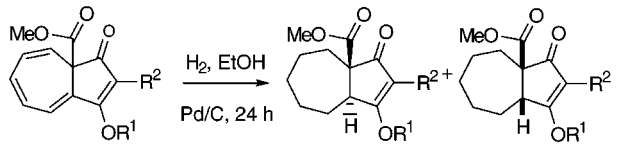
deacylation of **6** in the presence of trapping agents for the transient 1-hydroxyazulene intermediates that are implicated by the formation of products **16**. Use of DMAP/acetic anhydride (5 equiv) provided 1-acetoxy-3-alkoxyazulenes **17a** and **17b** as the predominant products. These results demonstrate that 1-acetoxy-3-alkoxyazulene derivatives **17** are indeed accessible, in reasonable yields, in two steps from readily available starting materials.



6d → ***17a*** $R^3 = Et$, $R^4 = Me$ (77%)

5d → ***17b*** $R^3 = H$, $R^4 = Et$ (43%)

As demonstrated by Barton et al.,[4] azulenones can be selectively hydrogenated to various hydroazulenone analogues. Similarly, we have reduced **14a** by catalytic hydrogenation over 10% palladium on carbon to give the hydroazulenones **18a** and **19a** in a 2:1 ratio. The relative



14a $R^1 = Me$, $R^2 = Et$ ***14d*** $R^1 = Et$, $R^2 = H$

18 ***19***

a $R^1 = Me$, $R^2 = Et$ ***b*** $R^1 = Et$, $R^2 = H$

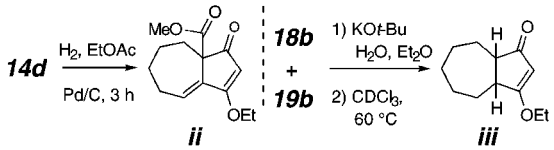
stereochemistry of the ring fusion was assigned by comparing the experimentally determined coupling constants for H(3a) with calculated values. Thus, a Monte Carlo based conformational search using the MM2* force field as implemented in MacroModel[14] (version 6.0) was used to generate a conformer family containing all geometries within 50 kJ/mol of the global minimum for each of the diastereomers. The Boltzmann weighted, calculated, vicinal coupling constants for H(3a) matched well the experimental values **[18a**: $J_{3a/4\alpha}$(calc vs exp) = 5.3 vs 6.0 Hz and $J_{3a/4\beta}$(calc vs exp) = 11.3 vs 11.5 Hz. **19a**: $J_{3a/4\alpha}$(calc vs exp) = 10.3 vs 9.2 Hz and $J_{3a/4\beta}$(calc vs exp) = 2.1 vs 2.7 Hz]. The analogue **14d**, which lacks a substituent at C(2), was similarly reduced and also gave the hexahydro azulenones **18b** and **19b**, this time in a 3:1 ratio. On the basis of these and related[15] results, this methodology could serve as a convenient access to hydroazulenone natural products skeletons.

Experimental Section

Materials. CH_2Cl_2 was distilled from CaH_2, diethyl ether from sodium benzophenone. All reaction vessels were flame-dried under vacuum and back-filled with nitrogen, and all reactions were carried out under a N_2 atmosphere. All diazo

(14) Mohamadi, F.; Richards, N. G. J.; Guida, W. C.; Liskamp, R.; Lipton, M.; Caufield, C.; Chang, G.; Hendrickson, T.; Still, W. C. *J. Comput. Chem.* **1990**, *11*, 440.

(15) In one instance, when the hydrogenation was carefully monitored, the tetrahydroazulenone **ii** was cleanly produced, implying that the disubstituted alkenes are reduced quickly, the trisubstituted C(3a)-C(4) alkene slowly, and the C(2)−C(3) vinylogous ester alkene very slowly (if at all). An additional transformation of **18b**/**19b** is also relevant. Gassman hydrolysis (Gassman, P. G.; Schenk, W. N. *J. Org. Chem.* **1977**, *42*, 918) was accompanied by decarboxylation to give **iii** as a single diastereomer. **ii:** ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.19-1.23 (m, 2H), 1.45 (t, 3H, J = 7.0 Hz), 1.76-1.82 (m, 2H), 1.90−1.94 (m, 2H), 2.32-2.37 (m, 1H), 2.48-2.53 (m, 1H), 3.71 (s, 3H), 4.08−4.14 (m, 2H), 5.37 (s, 1H), and 6.59 (dd, 1H, J = 8.9, and 5.0 Hz); LRMS (EI, 70 eV) *m/z* (rel int) 250 (68), 191 (52), 190 (100), 163 (26), 69 (52). **iii**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22−1.26 (m, 2H), 1.32−1.36 (m, 2H), 1.40 (t, 3H, J = 7.0 Hz), 1.52−1.69 (m, 4H), 1.96−2.00 (m, 2H), 2.63 (ddd, 1H, J = 10.5, 6.0, 3.5 Hz), 2.98 (dddd, 1H, J = 10.5, 7.0, 3.7, 1.3 Hz), 3.96−4.02 (m, 2H), 5.26 (s, 1H); IR (CDCl3) 1711 (s), 1224 (m); MS (EI, 70 eV): *m/z* (rel int) 194 (30, M^+), 179 (30), 151 (25), 139 (100), 111 (24).



14d → ***ii*** + ***18b*** / ***19b*** → ***iii***

compounds were prepared using *p*-acetamidobenzenesulfonyl azide as the diazo transfer reagent following the protocol of Davies (Et_3N, MeCN, 0 °C to rt, ~4 h).[6] Each has been prepared previously by alternative methods: ethyl 2-diazoacetoacetate (**7a**),[16] dimethyl (1-diazo-2-oxo-2-phenyl)ethylphosponate (**7b**),[17] and 2-diazo-1-phenyl-1,3-butanedione (**7c**).[18]

5-Bromo-1-ethoxy-1-pentyne.[19] To a cold (0 °C) stirred solution of ethoxyacetylene (7.13 mmol, 0.500 g of a 50 wt %/wt solution in hexanes) in THF was slowly added *n*-BuLi (7.13 mmol, 2.97 mL, 2.4 M). After 30 min, 1,3-dibromopropane (1.43 g, 0.73 mL, 7.13 mmol, purified by passing through Al_2O_3) was added. This solution was allowed to warm to room temperature and stirred overnight. Solvent was removed in vacuo, and the product purified by silica gel chromatography (SiO_2, 95/5 hexanes/ethyl acetate; R_f = 0.80 in 95/5 hexanes/ethyl acetate and 0.35 in hexanes) and then again with hexanes as the eluent (colorless oil, 0.420 g, 31%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (t, 3H, J = 7.0 Hz), 2.00 (tt, 2H, J = 7.0, 6.6 Hz), 2.29 (t, 2H, J = 6.6 Hz), 3.55 (t, 2H, J = 6.6 Hz), and 4.06 (q, 2H, J = 7.0 Hz); IR (neat) 2258 (s) and 1224 (s) cm^{-1}.

1-Methoxy-5-phenyl-1-pentyne.[20] A flame-dried three neck flask was fitted with a glass-paddled mechanical stirrer and oil bubbler and charged with freshly ground $Fe(NO_3)_3 \cdot 9H_20$ (~500 mg). The flask was cooled (−78 °C) and anhydrous ammonia was condensed (~300 mL). Freshly shaved sodium (5.97 g, 26 mmol) was slowly added over 30 min. After sodium amide was formed (~4 h, indicated by color change from blue to gray), chloroacetaldehyde dimethyl acetal (10.0 g, 80 mmol, freshly distilled) was added via syringe, and the mixture was stirred an additional 90 min. To this was added 1-bromo-3-phenylpropane (14.33 g, 70 mmol) and the suspension stirred for 4 h. The flask was removed from the cold bath and the mixture was carefully quenched with saturated NH_4Cl (50 mL). Pentane (300 mL) was added followed by an additional portion of saturated NH_4Cl (150 mL). The pentane layer was removed, washed with brine, and dried over $MgSO_4$. Removal of pentane by careful distillation led to a yellow oil. Bulb-to-bulb distillation (bath temp = 60−100 °C at 12 mmHg) of this material led to the crude alkynyl ether. Further purification by flash chromatography (SiO_2, 1% ethyl acetate in hexanes) gave pure 1-methoxy-5-phenyl-1-pentyne (4.2 g, 32%): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.80 (tt, 2H, J = 6.9 Hz), 2.16 (t, 2H, J = 6.9 Hz), 2.73 (t, 2H, J = 7.0 Hz), 3.82 (s, 3H), 7.17−7.31 (m, 5H); ^{13}C NMR ($CDCl_3$, 50.32 MHz) δ 16.58, 31.19, 34.76, 35.87, 65.33, 91.37, 125.71, 128.25, 128.48, 141.95; IR (neat) 3026 (m), 2941 (s), 2272 (s), 1244 (s) cm^{-1}. Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.70; H, 7.96.

Dimethyl (±)-2-Ethyl-1,8a-dihydro-3-methoxy-1-oxo-8a-azulenephosphonate (6b). Diazophosphonate **7b** (0.07 g, 0.31 mmol) was heated with 1-methoxy-1-butyne (**2a**, 0.100 g, 0.87 mmol) in CH_2Cl_2 (2 mL) at 110 °C for 5 h. Solvent was removed in vacuo, and products were purified by flash chromatography (SiO_2, ethyl acetate, R_f = 0.25) to give **6b** as a yellow oil (0.009 g, 10%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.14 (t, 3H, J = 7.5 Hz), 2.50 (dq, 1H, J = 14.0, 7.5 Hz), 2.53 (dq, 1H, J = 14.0, 7.5 Hz), 3.70 (d, 3H, J = 11.0 Hz), 3.72 (d, 3H, J = 11.0 Hz), 5.79 (dd, 1H, J = 10.3, 5.0 Hz), 6.13−6.18 (m, 1H), 6.29−6.35 (m, 2H), 6.57 (dd, 1H, J = 7.8, 2.5 Hz); IR ($CDCl_3$) 1734 (s), 1696 (s), 1592 (s), 1035 (m) cm^{-1}; HRMS (EI) calcd for $C_{15}H_{19}O_5P$ 310.0971, found 310.0975.

(±)-1-(8a*H*)-2-Ethyl-3-methoxy-8a-(1-oxoethyl)azulenone (6c). 2-Diazobenzoylacetone (**7c**, 0.100 g, 0.53 mmol) was heated with 1-methoxy-1-butyne (**2a**, 0.100 g, 1.06 mmol) in CH_2Cl_2 (2 mL) at 110 °C for 5 h. Solvent was removed in vacuo and the residue was purified by MPLC (80/20 hexanes/ethyl acetate) to give **6c** as a yellow oil (0.025 g, 20%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.07 (t, 3H, J = 7.5 Hz), 2.19 (s, 3H), 2.46 (q, 2H, J = 7.5 Hz), 4.22 (s, 3H), 6.14 (d, 1H, J = 10.0 Hz), 6.31 (dd, 1H, J = 10, 6.5 Hz), 6.34 (dd, 1H, J = 11.0, 6.5 Hz), 6.44 (dd, 1H, J = 11.0, 6.5 Hz), 6.66 (d, 1H, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$, 125.69 MHz) δ 14.81, 16.71, 26.39, 58.84, 69.38, 118.76, 119.63, 127.87, 128.14, 129.61, 130.62, 133.18, 174.03, 196.97, 200.25; IR ($CDCl_3$) 1719 (m), 1686 (s), 1585 (s) cm^{-1}. Anal. Calcd for $C_{15}H_{16}O_3$: C; 73.75, H: 6.60. Found: C, 73.74; H: 6.57.

(±)-2-Ethyl-1,8a-dihydro-3-methoxy-1-oxo-8a-azulencarboxylic Acid Chloride (6d). To a cold (0 °C) stirred solution of chloroketene **5d**[7] (0.075 g, 0.415 mmol) in CH_2Cl_2 (5 mL) was added 1-methoxy-1-butyne (**2a**, 0.052 g, 0.623 mmol) in CH_2Cl_2 (5 mL) over 30 min. The mixture was allowed to stir at room temperature for 5 h, at which time the solution had turned slightly green. The solvent was removed in vacuo and **6d** was isolated by column chromatography (SiO_2, R_f = 0.30 in 70/30 hexanes/ethyl acetate) as a yellow oil (0.109 g, 70%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.10 (t, 3H, J = 7.5 Hz), 2.50 (q, 2H, J = 7.5 Hz), 4.25 (s, 3H), 5.92 (d, 1H, J = 9.9 Hz), 6.40−6.57 (m, 3H), 6.69 (d, 1H, J = 6.0 Hz); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 14.54, 16.85, 59.11, 69.13, 119.96, 120.40, 126.38, 129.06, 130.15, 131.26, 132.12, 169.13, 174.34, 194.32; IR (neat) 1795 (s), 1699 (m), 1584 (s) cm^{-1}; HRMS calcd for $C_{14}H_{13}ClO_3$ 264.0553, found 264.0563. Anal. Calcd for $C_{14}H_{13}ClO_3$: C, 63.52; H, 4.95. Found: C, 63.68; H, 5.05.

(±)-3-Ethoxy-1,8a-dihydro-1-oxo-8a-azulenecarboxylic Acid Chloride (8) and 6-Chloro-4-ethoxy-5-phenyl-2*H*-pyran-2-one (9). To a cold (0 °C) stirred solution of chloroketene **5d** (0.179 g, 0.99 mmol) in CH_2Cl_2 (5 mL) was added ethoxyacetylene (0.166 mL of a 50 wt %/wt solution in hexanes, 1.1 mmol) in CH_2Cl_2 (5 mL) over 30 min. The mixture was allowed to stir at room temperature for 5 h, at which time the solution had turned slightly green. The solvent was removed in vacuo and purification by column chromatography (SiO_2, R_f = 0.25 in 70/30 hexanes/ethyl acetate) gave, in order of elution, **9** (0.042 g, 17%) and **8** (0.128 g, 48%) as yellow oils. **9**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.46 (t, 3H, J = 7.0 Hz), 4.28 (q, 2H, J = 7.0 Hz), 5.59 (s, 1H), 7.28−7.37 (m, 5H); ^{13}C NMR ($CDCl_3$, 125.69 MHz) δ 14.27, 65.87, 85.62, 115.71, 128.18, 128.25, 130.27, 132.35, 152.05, 159.18, 161.82; IR (KBr) 1728 (s), 1617 (m), 1544 (s), 1332 (s) cm^{-1}. Anal. Calcd for $C_{13}H_{11}ClO_3$: C, 62.29; H, 4.42. Found: C, 61.51; H, 4.42. **8**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.50 (t, 3H, J = 7.0 Hz), 4.15−4.29 (m, 2H), 5.41 (s, 1H), 6.03 (d, 1H, J = 9.4 Hz), 6.48−6.58 (m, 3H), 6.81−6.84 (m, 1H); ^{13}C NMR (125.69 MHz, $CDCl_3$) δ 14.14, 68.52, 70.14, 103.01, 121.29, 126.67, 128.76, 129.93, 130.53, 133.26, 169.24, 180.08, 192.92; IR (neat) 1792 (m), 1694 (s), 1567 (s), cm^{-1}. The methyl ester derivative **14d** (vide infra) gave satisfactory HRMS data.

(±)-2-(3-Bromopropyl)-3-ethoxy-1,8a-dihydro-1-oxo-8a-azulencarboxylic Acid Chloride (6e). To a cold (0 °C) stirred solution of chloroketene **5d** (0.123 g, 0.684 mmol) in CH_2Cl_2 (5 mL) was added 1-ethoxy-5-bromo-1-pentyne (0.156 g, 0.82 mmol) in CH_2Cl_2 (5 mL) over 30 min. The mixture was allowed to stir at room temperature for 5 h, at which time the solution had turned slightly green. MPLC (80/20 hexanes/ethyl acetate, R_f = 0.25 in 1:1 hexanes/ ethyl acetate) provided **6e** (0.127 g, 50%) as a yellow oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.48 (t, 3H, J = 7.0 Hz), 2.08−2.11 (m, 2H), 2.53−2.72 (m, 2H), 3.44 (t, 2H, J = 6.2 Hz), 4.51−4.63 (m, 2H), 5.90 (d, 1H, J = 9.3 Hz), 6.44−6.49 (m, 1H), 6.49−6.59 (m, 3H), 6.76 (d, 1H, J = 5.8 Hz); ^{13}C NMR ($CDCl_3$, 125.69 MHz) δ 13.92, 15.34, 22.20, 33.27, 61.67, 67.70, 115.39, 116.75, 118.56, 118.70, 126.87, 128.45, 131.86, 135.41, 167.25, 174.06, 197.68; IR ($CDCl_3$) 1733 (s), 1694 (m), 1583 (s) cm^{-1}; HRMS (EI) calcd for $C_{16}H_{16}BrCO_2$ (M^+ loss of ClCO) 309.0335, found 309.0333.

Methyl (±)-2-Ethyl-1,8a-dihydro-3-methoxy-1-oxo-8a-azulenecarboxylate (14a). To a cold (0 °C) stirred solution of azulene **6d** (0.80 g, 0.45 mmol) in CH_2Cl_2 (5 mL) was added MeOH (0.015 g, 0.49 mmol), followed by DMAP (0.050 g, 0.40 mmol). This solution was stirred at room temperature for an additional 90 min. The solvents were then removed in vacuo, and the resultant green oil was subjected to column chroma-

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(17) Regitz, M.; Martin, R. *Tetrahedron* **1985**, *41*, 819.
(18) Regitz, M.; Liedhegener, A. *Chem. Ber.* **1966**, *99*, 3128.
(19) See Pons, J.-M.; Kocienski, P. *Tetrahedron Lett.* **1989**, *30*, 1833 for a general procedure for alkylation of lithioethoxyacetylene.
(20) For a general procedure for in situ generation and alkylation of alkoxy acetylides, see: Newman, M. S.; Geib, J. R.; Stalick, W. M. *Org. Prep. Proc. Intl.* **1972**, *4*, 89.

tography (R_f = 0.25 in 70/30 hexanes/ethyl acetate) to give **14a** as a yellow oil (0.076 g, 65%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.05 (t, 3H, J = 7.5 Hz), 2.49 (q, 2H, J = 7.5 Hz), 3.57 (s, 3H), 4.19 (s, 3H), 5.95 (d, 1H, J = 10.0 Hz), 6.33 (dd, 1H, J = 10.0, 5.5 Hz), 6.41 (dd, 1H, J = 10.5, 6.0 Hz), 6.44 (dd, 1H, J = 11.0, 5.5 Hz), 6.60 (d, 1H, J = 6.0 Hz); ^{13}C NMR ($CDCl_3$, 75.4 MHz) δ 14.8, 16.9, 52.9, 59.1, 61.5, 118.6, 120.1, 127.1, 128.7, 128.9, 131.8, 131.9, 168.8, 173.8, 197.3; IR (neat) 1746 (s), 1696 (s), 1585 (s), 1362 (s), 1340 (s), 1232 (s) cm^{-1}; HRMS (EI) calcd for $C_{15}H_{16}O_4$ 260.1048, found 260.1028.

Methyl (±)-1,8a-Dihydro-3-methoxy-1-oxo-2-propyl-8a-azulenecarboxylate (14b). To a cold (0 °C) stirred solution of chloroketene **5d** (0.400 g, 2.2 mmol) in CH_2Cl_2 (15 mL) was added 1-methoxy-1-pentyne (0.281 g, 2.8 mmol) in CH_2Cl_2 (5 mL) over 30 min. The mixture was allowed to stir at room temperature for 5 h, at which time dry MeOH was added (0.073 g, 0.092 mL, 2.3 mmol). The mixture was cooled again (0 °C), and to this solution was added pyridine (0.183 g, 0.187 mL, 2.3 mmol) followed by DMAP (ca. 20 mg). The mixture was stirred at room temperature for an additional 90 min. The volatiles were then removed in vacuo, and the resultant green oil was subjected to column chromatography (R_f = 0.25 in 70/30 in hexanes/ethyl acetate) to give **14b** as a yellow oil (0.35 g, 58%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.92 (t, J = 3H, 7.3 Hz), 1.42−1.58 (m, 2H), 2.41−2.46 (m, 2H), 3.58 (s, 3H), 4.18 (s, 3H), 5.94 (d, 1H, J = 10.0 Hz), 6.33 (dd, 1H, J = 10.0, 5.0 Hz), 6.41−6.48 (m, 2H), 6.50 (d, 1H, J = 6.0 Hz); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 13.83, 23.58, 25.19, 52.82, 58.59, 61.16, 118.42, 118.64, 126.95, 128.54, 128.75, 131.68, 131.90, 168.05, 174.25, 197.44; IR (neat) 1746 (s), 1695 (s), 1585 (s), 1365 (s), 1335 (s), 1232 (s) cm^{-1}. Anal. Calcd for $C_{16}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.11; H, 6.44.

Methyl (±)-1,8a-Dihydro-2-(3-phenylpropyl)-3-methoxy-1-oxo-8a-azulenecarboxylate (14c). To a cold (0 °C) stirred solution of chloroketene **5d** (0.200 g, 1.10 mmol) in CH_2Cl_2 (15 mL) was added 1-methoxy-5-phenyl-1-pentyne (0.270 g, 1.55 mmol) in CH_2Cl_2 (5 mL) over 30 min. The mixture was allowed to stir at room temperature for 5 h, at which time dry MeOH was added (0.070 g, 2.2 mmol). The mixture was cooled again (0 °C), and to this solution was added DMAP (0.161 g, 1.31 mmol). The mixture was stirred at room temperature for an additional 90 min. The volatiles were then removed in vacuo, and the resultant green oil was subjected to column chromatography (R_f = 0.25 in 70/30 in hexanes/ethyl acetate) to give **14c** as a yellow oil (0.135 g, 35%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.81 (m, 2H), 2.47 (t, 2H, J = 8.0 Hz), 2.64 (t, 2H, J = 7.5 Hz), 3.58 (s, 3H), 4.01 (s, 3H), 5.94 (d, 1H, J = 10.0 Hz), 6.32 (dd, 1H, J = 5.5, 10.0 Hz), 6.42 (dd, 1H, J = 10.0, 5.5 Hz), 6.45 (dd, 1H, J = 10.0, 6.0 Hz), 6.58 (d, 1H, J = 5.5 Hz), 7.16−7.25 (m, 5H); ^{13}C NMR (125.69 MHz, $CDCl_3$) δ 22.78, 31.68, 35.46, 52.82, 58.79, 61.13, 118.28, 118.54, 125.86, 126.88, 128.30, 128.40, 128.55, 128.70, 131.78, 131.79, 141.68, 167.96, 174.23, 197.39; IR ($CDCl_3$) 1746 (s), 1694 (s), 1584 (s), 1231 (m) cm^{-1}. Anal. Calcd for $C_{22}H_{22}O_4$: C, 75.41; H, 6.33. Found: C, 74.93; H, 6.24.

Methyl (±)-3-Ethoxy-1,8a-dihydro-1-oxo-8a-azulenecarboxylate (14d). To a cold (0 °C) stirred solution of chloroketene **5d** (0.778 g, 4.3 mmol) in CH_2Cl_2 (50 mL) was added ethoxyacetylene (0.391 g of a 50 wt %/wt solution in hexanes, 5.59 mmol) in CH_2Cl_2 (5 mL) over 30 min. The mixture was stirred at room temperature for 5 h, at which time dry MeOH was added (0.206 g, 6.45 mmol MeOH), followed by Et_3N (6.45 mmol, 0.652 g, 0.898 mL, 1.5 equiv) and DMAP (ca. 50 mg). This was stirred at room temperature for an additional 90 min. The volatiles were then removed in vacuo, and the resultant green oil was subjected to column chromatography (R_f = 0.45 in 70/30 hexanes/ethyl acetate) to give **14d** as a yellow solid (mp 116−118 °C, 0.250 g, 25%): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.47 (t, 3H, J = 7.0 Hz), 3.61 (s, 3H), 4.17−4.21 (m, 2H), 5.37 (s, 1H), 6.00 (d, 1H, J = 9.8 Hz), 6.35−6.48 (m, 3H), 6.90 (d, 1H, J = 5.0 Hz); ^{13}C NMR (75.42 MHz, $CDCl_3$) δ 14.19, 52.39, 62.27, 68.11, 102.74, 119.95, 127.15, 128.38, 128.44, 131.0, 132.85, 167.93, 179.86, 196.23; IR (KBr) 1722 (m), 1689 (s), 1561 (s), 1031 (m) cm^{-1}; HRMS (EI) calcd for $C_{14}H_{14}O_4$ 246.0892, found 246.0889.

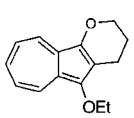
(4-Nitrophenyl)methyl (±)-2-Ethyl-1,8a-dihydro-3-methoxy-1-oxo-8a-azulenecarboxylate (14e). To a cold (0 °C) stirred solution of chloroketene **5d** (0.350 g, 1.93 mmol) was added 1-methoxy-1-butyne (**2a**, 0.163 g, 1.93 mmol) in CH_2Cl_2 (5 mL) over 30 min. The mixture was stirred at room temperature for 5 h, at which time *p*-nitrobenzyl alcohol (0.236 g, 1.54 mmol) in CH_2Cl_2 (5 mL) was added, followed by DMAP (0.235 g, 1.93 mmol). This was stirred at room temperature for 3 h and the solvent removed in vacuo. The black residue was subjected to chromatography (SiO_2, 80/20 ethyl acetate/hexanes, R_f = 0.15 in 75/25 hexanes/ethyl acetate) to give **14e** (0.200 g, 27%) as a yellow solid (mp 135−137 °C): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.07 (t, 3H, J = 7.5 Hz), 2.49 (q, 2H, J = 7.5 Hz), 4.20 (s, 3H), 5.13 (s, 2H), 5.97 (d, 1H, J = 9.0 Hz), 6.34−6.41 (m, 3H), 6.61 (d, 1H, 6.0 Hz), 7.37 (d, 2H, J = 8.6 Hz), 8.14 (d, 2H, J = 8.6 Hz); ^{13}C NMR (75.47 MHz, $CDCl_3$) δ 14.38, 16.80, 58.94, 60.97, 65.49, 118.75, 119.92, 123.62, 126.73, 127.72, 128.71, 128.93, 131.57, 143.17, 147.52, 167.19, 174.04, 196.83; IR ($CDCl_3$) 1739 (s), 1695 (s), 1585 (s), 1524 (s), 1348 (s) cm^{-1}. Anal. Calcd for $C_{21}H_{19}NO_6$: C: 66.14, H: 5.02, N: 3.67. Found: C, 66.05; H, 5.23, N, 3.49.

***N*-(4-Bromophenyl) (±)-2-Ethyl-1,8a-dihydro-3-methoxy-1-oxo-8a-azulenecarboxamide (14f)**. To a cold (0 °C) stirred solution of chloroketene **5d** (0.300 g, 1.63 mmol) was added 1-methoxy-1-butyne (**2a**, 0.139 g, 1.66 mmol) in CH_2Cl_2 (5 mL) over 30 min. The mixture was stirred at room temperature for 5 h, at which time 4-bromoaniline (0.236 g, 1.54 mmol) in CH_2Cl_2 (5 mL) was added, followed by Et_3N (0.254 mL, 0.184 g, 1.82 mmol) and DMAP (0.060 g, 0.49 mmol). This mixture was stirred at room temperature for 3 h and the solvent removed in vacuo. The residue was subjected to chromatography (SiO_2, 70/30 ethyl acetate/hexanes, R_f = 0.15 in 75/25 hexanes/ethyl acetate) to give **14f** as a light yellow solid [0.230 g, 35%, needles, mp 135−137 °C (CH_2Cl_2/pentane)]: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.10 (t, 3H, J = 7.5 Hz), and 2.50 (q, 2H, J = 7.5 Hz), 4.23 (s, 3H), 6.05−6.09 (m, 1H), 6.37−6.39 (m, 1H), 6.52−6.61 (m, 1H), 6.77 (d, 1H, J = 6.6 Hz), 7.35−7.78 (m, 5H), 7.78 (s, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 14.84, 16.77, 58.97, 68.92, 109.97, 116.74, 119.45, 122.16, 126.03, 129.73, 130.51, 130.55, 131.76, 132.07, 136.81, 164.28, 174.26, 199.05; IR ($CDCl_3$) 1687 (s), 1581 (s), 1516 (s) cm^{-1}; HRMS (CI) calcd for $C_{20}H_{18}BrNO_3$ [M + H]$^+$ 400.0548, found 400.0554.

2-(3-Bromopropyl)-3-ethoxy-1-azulenyl (±)-2-(3-Bromopropyl)-3-ethoxy-1,8a-dihydro-1-oxo-8a-azulenecarboxylate (16a). To a cold (0 °C) stirred solution of azulenone acid chloride **6e** (0.032 g, 0.08 mmol) in CH_2Cl_2 (10 mL) was added Et_3N (0.015 mL, 0.010 g, 0.10 mmol) and DMAP (0.001 g, 0.008 mmol). The mixture was stirred for 5 min and H_2O (0.015 mL, 0.86 mmol) added. After several minutes the reaction color turned deep blue. The mixture was stirred at room temperature for 5 h, the volatiles were removed in vacuo, and the product was purified by chromatography (SiO_2, R_f = 0.30 in 70/30 hexanes/ethyl acetate) to give **16a** as a blue oil (0.019 g, 70%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.41 (t, 3H, J = 6.9 Hz), 1.47 (t, 3H, J = 6.9 Hz), 2.10−2.15 (m, 4H), 2.67−2.77 (m, 3H), 3.38 (t, 2H, J = 6.7 Hz), 3.45 (t, 2H, J = 6.5 Hz), 3.71−3.73 (m, 1H), 4.09 (q, 2H, J = 6.9 Hz), 4.55−4.58 (m, 2H), 6.09 (d, 1H, J = 9.8 Hz), 6.44−6.47 (m, 1H), 6.61 (m, 2H), 6.77−6.81 (m, 1H), 6.86 (t, 2H, J = 9.7 Hz), 7.38 (t, 1H, J = 9.8 Hz), 7.71 (d, 1H, J = 9.7 Hz), 8.14 (d, 1H, J = 9.6 Hz).[21]

3-Ethoxy-1-azulenyl (±)-3-Ethoxy-1,8a-dihydro-1-oxo-8a-azulenecarboxylate (16b). To a cold (0 °C) stirred solution of azulenone acid chloride **8** (0.070 g, 0.27 mmol) in CH_2Cl_2 (10 mL) was added H_2O (0.010 g, 0.55 mmol). The mixture was stirred for 20 min, followed by the addition of

(21) Upon GC−MS analysis, this compound underwent thermal cleavage to a smaller fragment to which we assign structure **iv** on the basis of the its mass spectral data: LRMS 228 (35), 199 (100), 171 (83), 115 (24).



iv

Et_3N (0.034 g, 0.046 mL, 0.33 mmol) and DMAP (ca. 5 mg). After several minutes the reaction color turned deep blue. The mixture was stirred at room temperature for 5 h, the volatiles were removed in vacuo, and the product was purified by chromatography (SiO_2, 80/20 hexanes/ethyl acetate, $R_f = 0.25$ in 70/30 hexanes/ethyl acetate) to give **16b** as a blue oil (0.026 g, 45%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.43 (t, 3H, $J = 7.0$ Hz), 1.50 (t, 3H, $J = 7.0$ Hz), 4.14 (q, 2H, $J = 7.0$ Hz), 4.19−4.34 (m, 2H), 5.44 (s, 1H), 6.19 (d, 1H, $J = 10.0$ Hz), 6.48 (dd, 1H, $J = 10.0$, 5.5 Hz), 6.56−6.61 (m, 2H), 6.64 (t, 1H, $J = 9.5$ Hz), 6.83 (dd, 1H, $J = 5.0$, 2.5 Hz), 7.14 (s, 1H), 7.27 (t, 2H, $J = 10.0$ Hz), 7.78 (d, 1H, $J = 9.5$ Hz), 8.12 (d, 1H, $J = 9.0$ Hz); ^{13}C NMR ($CDCl_3$, 125.69 MHz) δ 14.19, 14.95, 62.48, 66.44, 68.21, 99.98, 109.26, 119.10, 119.17, 119.56, 120.22, 121.71, 127.13, 128.66, 128.80, 131.00, 133.10, 133.75, 134.15, 139.86, 140.50, 145.06, 165.80, 179.95, 195.83; IR ($CDCl_3$) 1745 (m), 1695 (s), 1565 (s), 1032 (m) cm^{-1}; UV [EtOH, λ_{max} (log ϵ)] 222 (3.4), 240 (4.13), 286 (4.28), 360 (3.49), and 368 (3.41) nm; HRMS (FAB) calcd for $C_{25}H_{22}O_5$ 402.1467, found 402.1473.

2-Ethyl-3-methoxy-1-azulenyl Ethanoate (17a). To a cold (0 °C) stirred solution of azulenone acid chloride **6d** (0.040 g, 0.15 mmol) in CH_2Cl_2 (5 mL) was added acetic anhydride (0.078 g, 0.75 mmol), the mixture was stirred for 20 min, and DMAP (0.021 g, 0.18 mmol) was added in one portion. The reaction mixture quickly turned deep blue in color and was stirred for 3 h. Solvent was removed in vacuo, and products were purified by chromatography (SiO_2, $R_f = 0.20$ in 90/10 hexanes/ethyl acetate) to give **17a** (0.28 g, 77%) as a blue oil: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.30 (t, 3H, $J = 7.5$ Hz), 2.44 (s, 3H), 2.83 (q, 2H, $J = 7.$ 5 Hz), 3.99 (s, 3H), 6.86 (t, 1H, $J = 9.6$ Hz), 6.90 (t, 1H, $J = 9.3$ Hz), 7.41 (t, 1H, $J = 9.9$ Hz), 7.86 (t, 1H, $J = 9.6$ Hz), 8.21 (t, 1H, $J = 9.6$ Hz); ^{13}C NMR ($CDCl_3$, 75.44 MHz): δ 13.46, 18.38, 20.64, 63.51, 120.67, 121.02, 122.15, 123.54, 130.71, 131.72, 132.70, 135.80, 137.76, 143.65, 169.93; IR (neat) 1767 (s), 1575 (m), 1198 (s) cm^{-1}; UV [EtOH, λ_{max} (log ϵ)] 240 (4.24), 284 (4.80), 336 (3.50), and 352 (3.67) nm. Anal. Calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60. Found: C, 74.02; H, 6.66.

3-Ethoxy-1-azulenyl Ethanoate (17b). To a cold (0 °C) stirred solution of chloroketene **5d** (0.098 g, 1.08 mmol) in CH_2Cl_2 (15 mL) was added ethoxyacetylene (0.075 mL of a 50 wt %/wt solution in hexanes, 5.59 mmol) in CH_2Cl_2 (5 mL) over 30 min, and the mixture was stirred for 6 h. The reaction was cooled to 0 °C and acetic anhydride (2.71 mmol, 0.276 g, 5 equiv) added. After a few minutes, DMAP (0.55 mmol, 0.068 g, 1.01 equiv) was added in one portion, and the mixture turned bright blue. This was stirred for an additional 2 h, adsorbed onto SiO_2, and chromatographed (SiO_2, 90/10 hexanes/ethyl acetate) to provide **17b** as a blue oil ($R_f = 0.25$ in 90/10 hexanes/ethyl acetate, 0.050 g, 40%): ^{1}H NMR (CDCl3, 300 MHz) δ 1.47 (t, 3H, $J = 7.0$ Hz), 2.38 (s, 3H), 4.20 (q, 2H, $J = 7.0$ Hz), 6.60 (t, 1H, $J = 9.9$ Hz), 6.67 (t, 1H, $J = 9.6$ Hz), 7.28 (t, 1H, $J = 9.9$ Hz), 7.90 (d, 1H, $J = 9.9$ Hz), 8.16 (d, 1H, $J = 9.0$ Hz); ^{13}C NMR ($CDCl_3$, 75.44 MHz) δ 14.98, 21.02, 66.44, 109.34, 118.83, 118.92, 119.56, 121.69, 132.75, 133.80, 134.25, 139.91, 145.26, 169.23; IR ($CDCl_3$) 1755 (s), 1581 (s), 1514 (s), 1374 (s), 1358 (s), 1219 (s), 1207 (s) cm^{-1}; UV [EtOH, λ_{max} (log ϵ)] 236 (4.06), 286 (4.51), 360 (3.56), 378 (3.51). Anal. Calcd for $C_{14}H_{14}O_3$: C, 73.03; H, 6.13. Found: C, 73.10; H, 5.82.

2-Ethyl-3-methoxy-1-azulenyl Methyl Carbonate (15). To a cold (0 °C) stirred solution of azulenone **6d** (0.100 g, 0.05 mmol) in CH_2Cl_2 (5 mL) were added ethyl diisopropylamine (0.05 mmol, 0.071 g, 0.095 mL, 1 equiv) and DMAP (0.002 mmol, 0.013 g, 0.2 equiv). This was stirred for 10 min followed by the addition of MeOH (0.031 mL, 0.024 g, 0.07 mmol). The reaction was stirred for 12 h, and the volatiles were then removed in vacuo. The resultant blue oil was subjected to column chromatography ($R_f = 0.25$ in 70/30 hexanes/ ethyl acetate) to give **15** as a blue oil (0.015 g, 10%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.30 (t, 3H, $J = 7.5$ Hz), 2.86 (q, 2H, $J = 7.5$ Hz), 3.95 (s, 3H), 3.98 (s, 3H), 6.91 (t, 1H, $J = 9.8$ Hz), 6.92 (t, 1H, $J = 9.8$ Hz), 7.44 (t, 1H, $J = 10.0$ Hz), 7.96 (d, 1H, $J = 9.5$ Hz), 8.21 (d, 1H, $J = 9.4$ Hz).

Methyl (±)-(3aa,8ab)- and (±)-(3aa,8aa)-2-Ethyl-1,3a,4,5,6,7,8,8a-octahydro-3-methoxy-1-oxo-8a-azulenecarboxylate (18a and 19a). Methyl ester **14a** (0.165 g, 0.66 mmol) was dissolved in ethanol, and 10% Pd/C was added to this solution. The reaction flask was fitted with a balloon filled with H_2, and the mixture was stirred for 24 h. The mixture was filtered through Celite and the solvent was removed in vacuo to provide crude diastereomers (0.150 g, crude 2:1). Chromatographic purification (SiO_2, 70/30 hexanes/ethyl acetate) provided analytical samples of each. Major **18a**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.01 (t, 3H, $J = 7.5$ Hz), 1.05−1.09 (m, 1H), 1.25 (ddd, $J = 1$H, 13.8, 12.0, 5.5 Hz), 1.36 (ddd, 1H, $J = 12.5$, 12.0, 12.0 Hz), 1.62−1.69 (m, 2H), 1.81−1.97 (m, 3H), 1.93−1.96 (m, 1H), 2.35 (q, 2H, $J = 7.5$ Hz,), 2.70 (ddd, $J = 1$H, 13.8, 5.0, 3.0 Hz), 2.98 (dd, 1H, $J = 11.5$, 6.0 Hz), 3.65 (s, 3H), 4.13 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.44 MHz) δ 14.96, 16.33, 23.28, 24.90, 26.11, 27.77, 48.75, 52.23, 58.80, 63.66, 115.98, 170.09, 184.04, 200.91; IR ($CDCl_3$) 1733 (w), 1608 (s), 1347 (m) cm^{-1}. Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.64; H, 8.32. Found: C, 67.04; H, 8.05. Minor **19a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.01 (t, 3H, $J = 7.5$ Hz), 1.40−1.57 (m, 7H), 1.84−1.95 (m, 2H), 2.30 (q, 2H, $J = 7.5$ Hz), 2.33−2.39 (m, 1H), 3.42 (dd, $J = 1$H, $J = 9.15$, 2.7 Hz), 3.68 (s, 3H), 4.09 (s, 3H); ^{13}C NMR ($CDCl_3$, 75.44 MHz) δ 14.35, 15.78, 25.30, 27.15, 28.81, 30.62, 31.22, 48.13, 52.75, 57.99, 63.33, 118.87, 172.65, 185.62, 201.75; IR ($CDCl_3$) 1734 (w), 1616 (s) cm^{-1}. Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.64; H, 8.32. Found: C, 67.07; H, 8.16.

Methyl (±)-(3aα,8aβ)- and (±)-(3aα,8aα)-(±)-3-Ethoxy-1,3a,4,5,6,7,8,8a-octahydro-1-oxo-8a-azulenecarboxylate (18b and 19b). Methyl ester **14d** (0.060 g, 0.2 mmol) was hydrogenated according to the same procedure as for **14a**. The products (∼3:1 ratio of diastereomers by ^{1}H NMR analysis of the crude product mixture) were purified by MPLC (SiO_2, 70:30 hexanes/ethyl acetate) to give a fraction containing a 2.5:1 ratio of major/minor diastereomers and a later fraction containing a 9:1 ratio of major/minor diastereomers (60 mg total recovery, 99% yield). Major **18b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.08−1.16 (m, 1H), 1.29−1.39 (m, 3H), 1.43 (t, $J = 7.5$ Hz, 3H), 1.61−1.66 (m, 1H), 1.67−1.71 (m, 1H), 1.83−1.94 (m, 2H), 2.01−2.10 (m, 1H), 2.71 (ddd, 1H, $J = 14.0$, 5.0, 3.5 Hz), 3.12 (ddd, 1H), $J = 11.7$, 5.8, 1.5 Hz), 3.70 (s, 3H), 4.04−4.11 (m, 2H), 5.18 (d, $J = 1.5$ Hz, 1H); ^{13}C NMR (125.69 Hz, $CDCl_3$) δ 14.05, 22.59, 24.87, 26.00, 27.80, 31.94, 49.43, 52.40, 64.75, 68.00, 100.56, 170.01, 191.57, 199.99; IR ($CDCl_3$) 1733 (s), 1688 (s), 1583 (s) cm^{-1}. Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.64; H, 7.99. Found: C, 66.78; H, 7.76. Minor **19b:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.43 (t, $J = 7.0$ Hz, 3H), 1.60−2.01 (m, 9H), 2.27−2.32 (m, 1H), 3.53 (ddd, 1H, $J = 9.5$, 3.5, 1.0 Hz), 3.71 (s, 3H), 4.04−4.14 (m, 2H), 5.25 (d, $J = 1.5$ Hz, 1H).

Acknowledgment. This work was supported by an NSF-Presidential Faculty Fellowship to R.G.B. (CHE 9350393). We thank Dr. Victor G. Young, Jr. (University of Minnesota) for the X-ray crystallographic analysis.

JO9719315