Total Synthesis of the Phenalenone Diterpene Salvilenone

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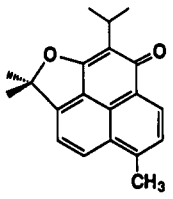
Abstract: The application of a photochemical aromatic annulation strategy in a highly efficient total synthesis of the phenalenone diterpene salvilenone is reported. The pivotal step in the synthesis involves the assembly of the key dihydrophenalene **29** in one step via an annulation involving the siloxyalkyne **28** and either diazo ketone **8** or **9**. The synthesis of the α-benzosuberone **8** was achieved in three steps beginning with 2-methylcyclopentanone by a route featuring an "aryne–enolate condensation" reaction. The alternative aromatic annulation substrate, the β-benzosuberone **9**, was prepared in four steps by a route based on the regiocontrolled ring expansion of the α-methylenetetralin **27**. The key aromatic annulation was then accomplished by irradiating a mixture of either diazo ketone **8** or **9** and 1.4 equiv of the siloxyalkyne **28** in 1,2-dichloroethane at 20–25 °C using a standard Rayonet photochemical reactor. The reaction mixture was next diluted with an equal volume of solvent and heated overnight at 80 °C to complete the annulation; concentration and chromatographic purification furnished the tricyclic phenol **29** as colorless crystals in 60–71% yield. Finally, annulation of the furan ring and oxidation required three steps and provided the phenalenone diterpene in good yield. The synthetic routes described herein provide access to salvilenone in only seven or eight steps (via the α- and β-benzosuberone strategies, respectively), half the number of steps required using the classical linear substitution approach reported previously. These highly efficient syntheses demonstrate the ability of the photochemical aromatic annulation strategy to dramatically streamline the synthesis of polycyclic aromatic compounds.

The phenalenes and phenalenones constitute an unusual class of nonbenzenoid aromatic compounds which have attracted considerable theoretical interest, in part due to the remarkable stability of phenalenyl radicals, anions, and cations.[1] Although phenalenones rarely occur in nature, recently a number of oxygenated derivatives have been isolated from plants and fungi, and several of these compounds have been found to exhibit interesting biological activity.[2,3] Herein we report the application of a photochemical aromatic annulation strategy in two efficient synthetic routes to salvilenone (**1**), a phenalenone diterpene isolated from the Chinese red-rooted sage *Salvia miltiorrhiza*.



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The dried roots of *Salvia miltiorrhiza* Bunge are the source of Dan Shen, one of the most important drugs in Chinese traditional medicine.[4] Today Dan Shen is used principally for the treatment of various heart disorders, but the drug has also been reported to exhibit antipyretic, antineoplastic, antimicrobial, and antiinflammatory properties.[4b,5] In the course of their investigation of minor constituents of Dan Shen, Kakisawa and co-workers isolated trace quantities of a bright yellow substance identified by spectroscopic analysis as possessing the furanophenalenone structure **1**.[6] Interestingly, Eugster had previously reported obtaining a compound with the same structure as salvilenone through the acid-promoted rearrangement of several royleanone derivatives.[7] One total synthesis of salvilenone has been described to date: in 1988, Zheng, Kojima, and Kakisawa reported the synthesis of salvilenone in 14 steps via a classical route featuring two Friedel–Crafts cyclization reactions.[8]

The research described here was undertaken in connection with our program aimed at the development of efficient strategies for the synthesis of highly substituted aromatic systems. Classically, the synthesis of substituted benzenoid compounds has most often been achieved by employing *linear substitution strategies* based on sequential electrophilic substitution and metalation–alkylation reactions. A more effective approach to highly substituted aromatic compounds, however, involves the application of *annulation methods*: convergent strategies in which the aromatic system is assembled from acyclic precursors in a single step, with all (or most) substituents already in place. Annulation strategies enjoy significant advantages over classical linear substitution strategies, especially when applied to the preparation of highly substituted target molecules. For example, annulation routes generally avoid the regiochemical ambiguities associated with aromatic substitution reactions, and their intrinsic convergent character facilitates the efficient assembly of highly substituted aromatics that would require long, multistep routes using classical substitution methodology.

We have previously shown that the addition of vinylketenes to acetylenes provides the basis for a very efficient annulation route to highly substituted aromatic systems.[9,10] In connection with

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(1) For reviews of the chemistry of phenalenes and phenalenones, see: (a) Reid, D. H. *Q. Rev. Chem. Soc.* **1965**, *19*, 274. (b) Murata, I. *Top. Nonbenzenoid Aromat. Chem.* **1973**, *1*, 159.

(2) For a review of naturally occurring phenalenones, see: Cooke, R. G.; Edwards, J. M. *Prog. Chem. Org. Nat. Prod.* **1981**, *40*, 153.

(3) Phenalene derivatives have also received attention as templates in drug design. See: Tang, A. H.; Franklin, S. R.; Code, R. A.; Althaus, J. S.; VonVoigtlander, P. F.; Darlington, W. H.; Szmuszkovicz, J. *Drug Dev. Res.* **1990**, *21*, 53 and references cited therein.

(4) (a) Duke, J. A.; Ayensu, E. S. *Medicinal Plants of China*; Reference Publications, Inc.: Algonac, MI, 1985; Vol. 2, p 38. (b) *Pharmacology and Applications of Chinese Materia Medica*; Chang, H. M., But, P. P. H., Eds.; World Scientific Publishing Co.: Singapore, 1986; Vol. 1, pp 255–268.

(5) For additional references documenting the biological activity of Dan Shen, see: (a) Footnotes 3–5 in Lee, J.; Snyder, J. K. *J. Org. Chem.* **1990**, *55*, 4995. (b) References cited in Chang, H. M.; Cheng, K. P.; Choang, T. F.; Chow, H. F.; Chui, K. Y.; Hon, P. M.; Tan, F. W. L.; Yang, Y.; Zhong, Z. P.; Lee, C. M.; Sham, H. L.; Chan, C. F.; Cui, Y. X.; Wong, H. N. C. *J. Org. Chem.* **1990**, *55*, 3537.

(6) Kusumi, T.; Ooi, T.; Hayashi, T.; Kakisawa, H. *Phytochemistry* **1985**, *24*, 2118.

(7) Hensch, M.; Eugster, C.-H.; Weber, H.-P. *Helv. Chim. Acta* **1975**, *58*, 1934.

(8) (a) Zheng, G.-C.; Kojima, T.; Kakisawa, H. *Heterocycles* **1988**, *27*, 1341. (b) Zheng, G.-C.; Kakisawa, H. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 1117.

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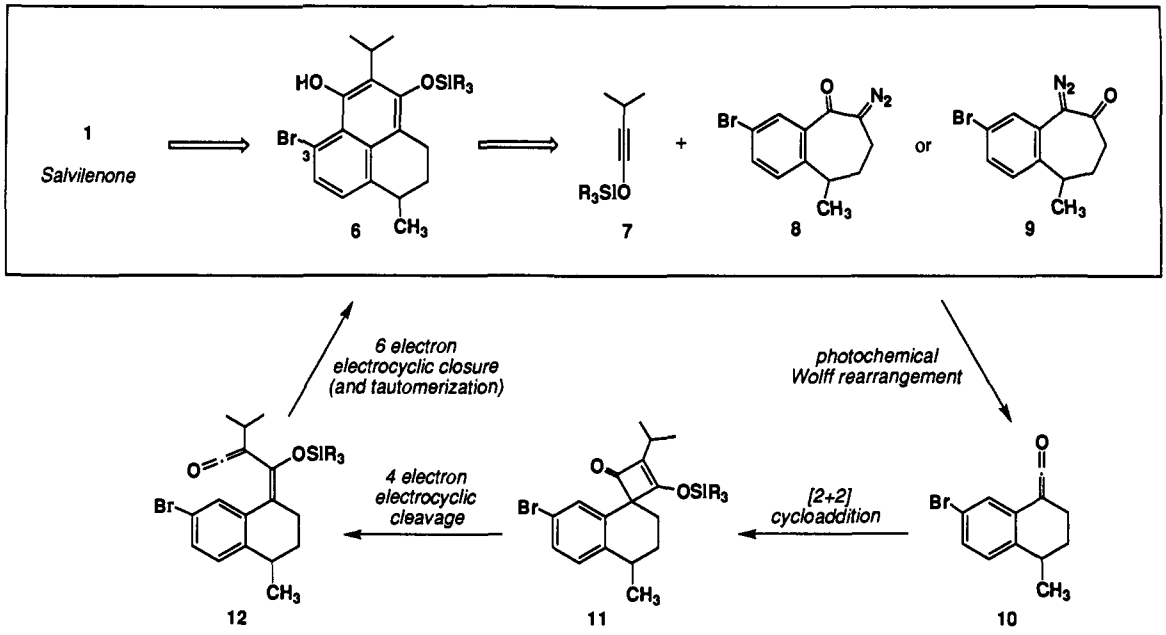
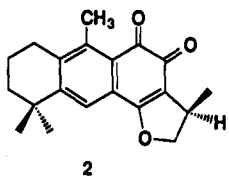
Scheme 1



our interest in defining the scope of this methodology as applied to *polycyclic* compounds, we have examined its application to the construction of each of the three possible tricyclic arrangements of fused six-membered rings. Recently we demonstrated the utility of this strategy in the assembly of the linearly-fused and angularly-fused tricyclic systems, and we have successfully applied this chemistry in extremely direct synthetic routes to the diterpenes aegyptinone A (**2**)[11] and danshexinkun A (**3**).[12] In this paper we now describe the application of our aromatic annulation strategy to the third possible juxtaposition of six-membered rings, the condensed tricyclic system of the phenalenone diterpene salvilenone.



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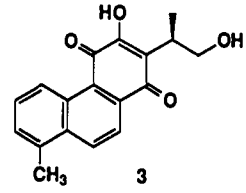

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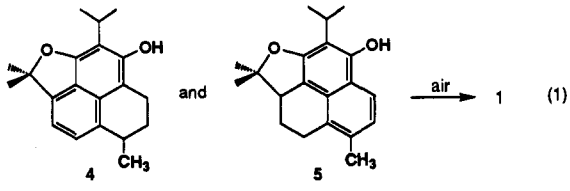
Synthetic Plan

In the course of his studies on the isolation and structure elucidation of salvilenone, Kakisawa found that both **4** and **5** (derived from hydrogenation of salvilenone) undergo spontaneous air oxidation to regenerate the phenalenone system in quantitative yield (eq 1).[6] With this observation in mind, we selected the



dihydrophenalene **6** (Scheme 1) as the target for the key aromatic annulation step in our synthetic plan. Several alternative routes could be envisioned for the installation of the requisite three-carbon appendage at C-3 of this tricycle, and subsequent cyclization and oxidation to generate the furanophenalenone was expected to be a facile process.

The pivotal step in our synthetic approach to salvilenone involves the recently developed "second-generation" version of our aromatic annulation strategy[9d] which has expanded the scope of the method to include the synthesis of *polycyclic* compounds which were not readily available using the original cyclobutenone-based reaction. Our retrosynthetic plan for the key dihydrophenalene **6** called for its assembly in one step via an annulation involving the siloxyalkyne **7** and either diazo ketone **8** or **9**. Scheme 1 outlines the mechanistic course of the proposed annulation reaction. Irradiation of either α-diazo ketone triggers a photochemical Wolff rearrangement producing the same arylketene **10**, which combines with acetylene **7** in a regiospecific [2 + 2] cycloaddition to form **11**. Further irradiation then induces 4π electrocyclic opening of the cyclobutenone ring, thus generating the vinylketene **12** which undergoes rapid 6π electrocyclization to afford, after tautomerization, the desired tricyclic phenol.

An issue crucial to the success of the proposed annulation scheme is the stereochemical course of the ring opening of cyclobutenone **11**. Electrocyclic closure of the resultant vinylketene would only be possible if this ring opening produced the isomer **12** in which the ketene and arene moieties are cis about the enol ether double bond. Even if this were not the case, however, we considered it possible that **6** might still be obtained in good yield if the annulation could be carried out under conditions in which the electrocyclic cleavage of **11** was a reversible process.

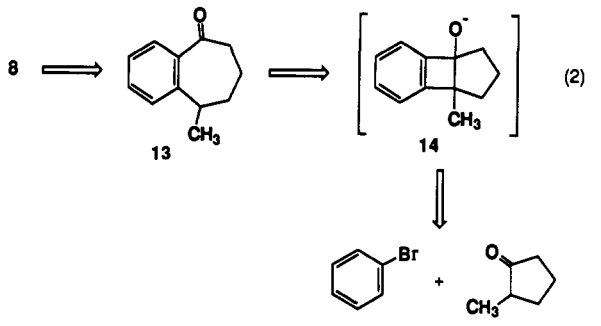
As outlined above, retrosynthetic analysis identified both the α-benzosuberone **8** and the β-benzosuberone **9** as possible substrates for the key aromatic annulation reaction. We therefore set out to synthesize each of these diazo ketones in order to test and compare their suitability as photo-Wolff precursors to the arylketene **10**. Equation 2 outlines our initial plan for the synthesis of the α-benzosuberone intermediate **8** based on an "aryne–enolate condensation" reaction. In the proposed transformation, the more

(9) (a) Danheiser, R. L.; Gee, S. K. *J. Org. Chem.* **1984**, *49*, 1672. (b) Danheiser, R. L.; Gee, S. K.; Perez, J. J. *J. Am. Chem. Soc.* **1986**, *108*, 806. (c) Danheiser, R. L.; Nishida, A.; Savariar, S.; Trova, M. P. *Tetrahedron Lett.* **1988**, *29*, 4917. (d) Danheiser, R. L.; Brisbois, R. G.; Kowalczyk, J. J.; Miller, R. F. *J. Am. Chem. Soc.* **1990**, *112*, 3093. (e) Danheiser, R. L.; Cha, D. D. *Tetrahedron Lett.* **1990**, *31*, 1527.

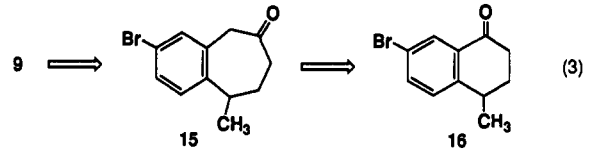
(10) Related methodology for the synthesis of substituted quinones beginning with squaric acid derivatives has been developed independently in the laboratories of Liebeskind and Moore. See: (a) Edwards, J. P.; Krysan, D. J.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1993**, *115*, 9868. (b) Lee, K. H.; Moore, H. W. *Tetrahedron Lett.* **1993**, *34*, 235 and references cited therein.

(11) Danheiser, R. L.; Casebier, D. S.; Huboux, A. H. *J. Org. Chem.* In press.

(12) Danheiser, R. L.; Casebier, D. S.; Loebach, J. L. *Tetrahedron Lett.* **1992**, *33*, 1149.

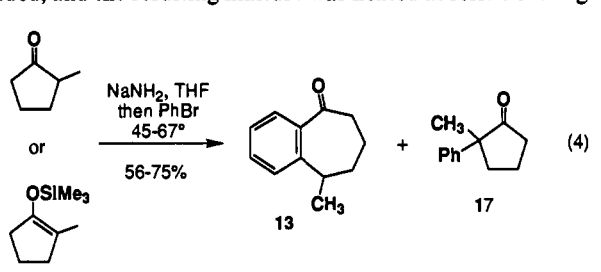


substituted enolate derived from 2-methylcyclopentanone would add to benzyne to afford the benzocyclobutenol anion **14**, which we anticipated would then undergo fragmentation to produce the desired benzosuberone. Regioselective bromination at the less hindered position meta to the ketone carbonyl followed by diazo transfer would then provide the annulation substrate **8**. For the synthesis of the alternative diazo ketone **9**, we chose to exploit the ready availability of the known tetralone **16**[13] and employ a regiocontrolled ring expansion to transform this compound to the requisite β-benzosuberone (eq 3).



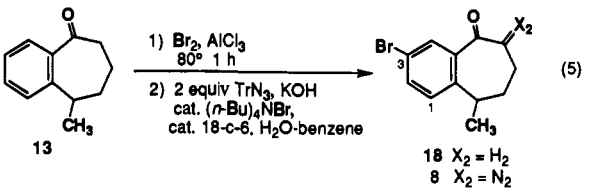
Aryne–Enolate Condensation Approach to α-Benzosuberone 8. Several reports of the synthesis of the α-benzosuberone **13** have appeared previously;[14] however, we felt a more attractive route to **13** might be possible based on the aryne–enolate condensation discussed above. In principle, this expeditious approach could deliver **13** in a single step beginning with 2-methylcyclopentanone. Caubere has pioneered the use of related "arynic condensations" as synthetic routes to benzocyclobutenols, which in certain cases undergo fragmentation providing efficient access to various benzocycloalkanones.[15,16] The mechanism of these sodamide-promoted reactions is complex and is believed to involve the intermediacy of a sodamide–enolate aggregate which acts as a base to deprotonate bromobenzene and generate benzyne.

Satisfactory conditions for achieving the desired transformation were arrived at only after considerable experimentation. As outlined in eq 4, 2-methylcyclopentanone was treated with 2 equiv of $NaNH_2$ in THF at 45 °C for 2 h, bromobenzene was then added, and the resulting mixture was heated at reflux overnight.



In this fashion the desired benzosuberone could be obtained in 56–75% yield as a ca. 70:30 mixture with the isomeric cyclopentanone **17**. Improved results were obtained beginning with the TMS enol ether derivative of 2-methylcyclopentanone;[17,18] this condensation produced **13** and **17** in a ratio of 85:15 and afforded the desired benzosuberone in 42% yield after separation of the isomeric byproduct.[19] Attempts to employ alternative methods for benzyne formation in the context of this aryne–enolate condensation were not successful. For example, none of the desired benzosuberone was obtained when benzyne was generated from either 2-(trimethylsilyl)phenyl triflate[20] or *o*-bromofluorobenzene[21] in the presence of the cyclopentanone enolate.

Although the efficiency of the aryne–enolate condensation was somewhat disappointing, this reaction did provide convenient access to **13** in reasonable yield and in a single step from commercially available starting materials. With the desired benzosuberone in hand, we turned our attention to its conversion to annulation substrate **8** via aromatic bromination and diazo transfer. As shown in eq 5, regioselective bromination was



accomplished by exploiting the "swamping catalyst effect" to suppress reaction at the methylene α to the carbonyl group.[22] Thus, heating a mixture of **13**, 1.2 equiv of bromine, and 2.8 equiv of $AlCl_3$ (without solvent) at 80 °C for 1 h furnished the aryl bromide **18** in 81% yield after chromatographic purification. As expected, bromination occurs exclusively meta to the carbonyl group at the C-3 position of the aromatic ring; steric repulsion by the methyl group disfavors substitution at C-1. Diazo transfer was then best achieved by reaction of **18** with 2,4,6-triisopropylbenzenesulfonyl azide under Mander's phase transfer conditions;[23] in this fashion the aromatic annulation substrate **8** was obtained as yellow crystals in 71–82% yield. This α-diazo ketone could also be produced somewhat less efficiently (55% yield) using our improved "detrifluoroacetylative" diazo transfer procedure.[24]

Friedel–Crafts Cyclization Approach to α-Benzosuberone 8. Although the aryne–enolate condensation approach to diazo ketone **8** is extremely direct (three steps from 2-methylcyclopentanone), the modest yield of the key step in the sequence led us to consider alternative routes to this aromatic annulation substrate. Initially we focused our attention on the Friedel–Crafts annulation of benzene and δ-caprolactone (**19**),[25] a reaction which could again provide access to the α-benzosuberone in a single step. Note that the related annulation of benzene with γ-valerolactone is well-documented and provides 4-methyl-1-

(13) (a) Adachi, K.; Tanaka, J. *Yuki Gosei Kagaku Kyokai Shi* **1973**, *31*, 322. (b) Newman, M. S.; Prabhu, V. S.; Veeraraghavan, S. *J. Org. Chem.* **1983**, *48*, 2926.

(14) (a) Julia, S.; Bonnet, Y. *Bull. Soc. Chim. Fr.* **1957**, 1347. (b) Omar, M. T.; Proctor, G. R.; Scopes, D. I. C. *J. Chem. Res. (M)* **1988**, 2918.

(15) For a review, see: Caubère, P. *Top. Curr. Chem.* **1978**, *73*, 49.

(16) (a) Caubère, P.; Derozier, N.; Loubinoux, B. *Bull. Soc. Chim. Fr.* **1971**, 302. (b) Caubère, P.; Guillaumet, G.; Mourad, M. S. *Tetrahedron Lett.* **1971**, 4673. (c) Carre, M.-C.; Gregoire, B.; Caubere, P. *J. Org. Chem.* **1984**, *49*, 2050 and references cited therein.

(17) House, H. O.; Czuba, L. J.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1969**, *34*, 2324.

(18) Silyl enol ethers are cleaved by NH_2^- to generate enolates: Binkley, E. S.; Heathcock, C. H. *J. Org. Chem.* **1975**, *40*, 2156.

(19) Chromatographic separation of **13** from **17** proved difficult and on a large scale was facilitated by prior sulfonation of the aromatic ring in **17** (which is more nucleophilic). This was accomplished by brief heating of the mixture of **13** and **17** in concentrated H_2SO_4.

(20) Himeshima, Y.; Sonoda, T.; Kobayashi, H. *Chem. Lett.* **1983**, 1211.

(21) (a) Wittig, G.; Pohmer, L. *Angew. Chem.* **1955**, *67*, 348. (b) Gilman, H.; Gorsich, R. D. *J. Am. Chem. Soc.* **1956**, *78*, 2217. (c) Gilman, H.; Gorsich, R. D. *J. Am. Chem. Soc.* **1957**, *79*, 2625.

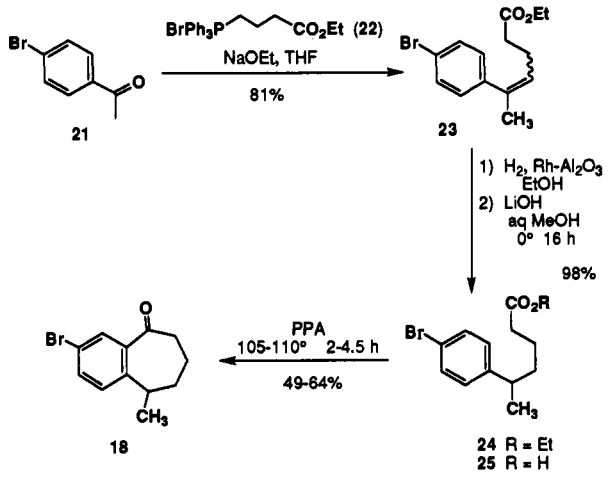
(22) (a) Pearson, D. E.; Pope, H. W.; Hargrove, W. W.; Stamper, W. E. *J. Org. Chem.* **1958**, *23*, 1412. (b) Pearson, D. E.; Pope, H. W.; Hargrove, W. W. *Organic Syntheses;* Wiley: New York, 1973; Collect. Vol. V, p 117.

(23) Lombardo, L.; Mander, L. N. *Synthesis* **1980**, 368.

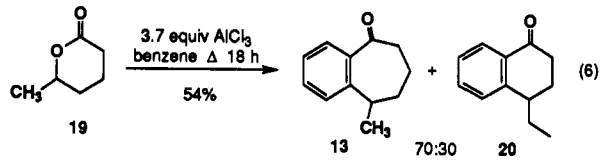
(24) Danheiser, R. L.; Miller, R. F.; Brisbois, R. G.; Park, S. Z. *J. Org. Chem.* **1990**, *55*, 1959.

(25) Taub, D.; Girotra, N. N.; Hoffsommer, R. D.; Kuo, C. H.; Slates, H. L.; Weber, S.; Wendler, N. L. *Tetrahedron* **1968**, *24*, 2443.

Scheme 2



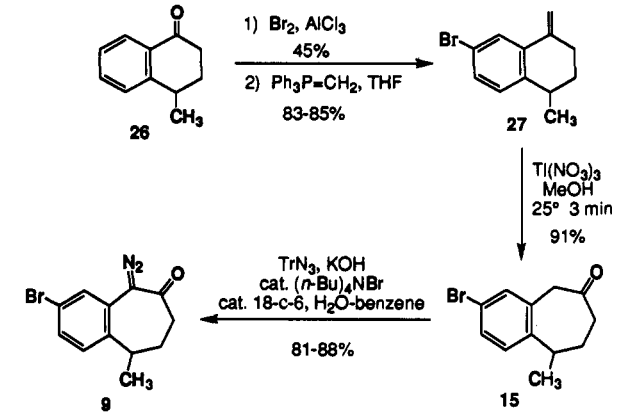
tetralone in excellent yield.[26] Unfortunately, under all conditions examined, the desired α-benzosuberone was generated as an inseparable mixture with the isomeric ketone 4-ethyl-1-tetralone[27] (e.g., eq 6).



We next turned our attention to a more conventional alternative route to **8** based on the intramolecular Friedel–Crafts cyclization of the carboxylic acid **25**. The preparation of this acid was accomplished in three steps as summarized in Scheme 2. Wittig olefination of 4-bromoacetophenone with the phosphorane derived from **22**[28] (THF, reflux, 3 d) produced **23** as a 70:30 mixture of *Z* and *E* olefin isomers in 81% yield. Hydrogenation proceeded smoothly without competing cleavage of the aryl bromide using 5% Rh on alumina in ethanol (25 °C, 36 h), and saponification then afforded the substrate for the Friedel–Crafts cyclization as colorless crystals in 98% overall yield from **23**.

Intramolecular Friedel–Crafts acylations to form seven-membered rings are well-documented,[29] but generally proceed with less facility compared to cyclizations leading to indanones and tetralones. Optimal conditions for effecting the cyclization of **25** to **18** were established only after considerable experimentation. Best results were obtained by heating **25** in polyphosphoric acid (80 g of PPA/g of **25**) at 105–110 °C for 2–4.5 h; column chromatography then provided the 3-bromo-α-benzosuberone in 49–64% yield. Significantly lower yields were obtained if less PPA was used or if the reaction was conducted at lower temperatures. Methanesulfonic acid (MSA)[30] and MSA–P_2O_5[31]

Scheme 3



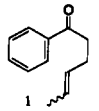
were not effective at promoting this reaction, and cyclizations of the acid chloride corresponding to **25** proceeded in only 10–28% yield. Overall, the five-step Friedel–Crafts cyclization route furnished the aromatic annulation substrate **8** in 32–43% yield beginning with commercially available 4-bromoacetophenone.

Synthesis of β-Benzosuberone 9. As outlined earlier (eq 3), our plan for the synthesis of the alternative aromatic annulation substrate **9** involved a ring expansion strategy beginning with the known bromo-α-tetralone **16**. Scheme 3 describes the synthesis of the diazo ketone **9** via this approach. Since we viewed the literature routes[32] to **16** as being rather lengthy (five to seven steps), we chose instead to prepare this compound by bromination of commercially available 4-methyl-1-tetralone (**26**). Reaction of **26** with bromine and $AlCl_3$ under the conditions of the "swamping catalyst effect"[22] (vide supra) thus provided **16** as colorless crystals in 45% yield.

For the critical ring expansion step, we decided to focus our efforts on the application of the oxidative rearrangement strategy pioneered in the laboratories of Taylor and McKillop.[33] Alternative ring expansion protocols such as the classic diazomethane-based procedure are not very effective when applied to relatively unreactive carbonyl compounds such as tetralone derivatives.[34] The requisite substrate for the oxidative ring expansion, the α-methylenetetralin **27**, was readily obtained in excellent yield by Wittig methylenation of **16** in THF (25 °C, 18 h) as outlined in Scheme 3. Upon exposure to 1.1 equiv of thallium(III) nitrate trihydrate in methanol at 25 °C, **27** was instantly transformed to the desired β-benzosuberone, contaminated only with a small amount of the corresponding dimethyl ketal.[35] None of the isomeric α-benzosuberone could be detected in the crude rearrangement product, as expected based on the higher migratory aptitude of aryl groups in cationic rearrangements. The β-benzosuberone was obtained in 91% yield in this fashion and was easily converted to the desired aromatic annulation substrate **9** by diazo transfer using the Lombardo–Mander protocol.[23] The diazo ketone could also be prepared, albeit in somewhat lower yield (55%), by treatment of **15** with 1.1 equiv each of tosyl azide and DBU in acetonitrile (25 °C, 16 h).[36]

(26) Olson, C. E.; Bader, A. R. *Organic Syntheses*; Wiley: New York, 1963; Collect. Vol. IV, p 898.

(27) The formation of **20** probably proceeds via acylation of benzene by **19**, dehydration of the resulting alcohol to form the alkene **1**, and intramolecular Friedel–Crafts alkylation.



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(28) For the preparation of the corresponding methyl ester, see Sorenson, J. S.; Sorenson, N. A. *Acta Chem. Scand.* **1966**, *20*, 992. We found that by omitting the solvent, better yields of the phosphonium salt **22** could be obtained.

(29) For a review of Friedel–Crafts cyclization reactions, see: Heaney, H. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 2, pp 753–768.

(30) Premasagar, V.; Palaniswamy, V. A.; Eisenbraun, E. J. *J. Org. Chem.* **1981**, *46*, 2974.

(31) Eaton, P. E.; Carlson, G. R.; Lee, J. T. *J. Org. Chem.* **1973**, *38*, 4071.

(32) (a) Adachi, K.; Tanaka, J. *Yuki Gosei Kagaku Kyokai Shi* **1973**, *31*, 322. (b) Newman, M. S.; Prabhu, V. S.; Veeraraghavan, S. *J. Org. Chem.* **1983**, *48*, 2926.

(33) Taylor, E. C.; Chiang, C.-S.; McKillop, A. *Tetrahedron Lett.* **1977**, 1827.

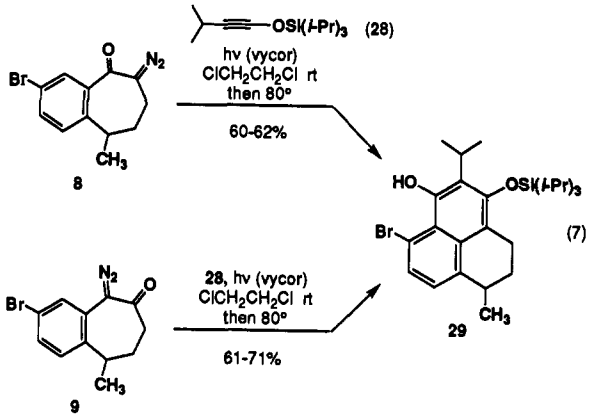
(34) For reviews of ring expansion methods, see: (a) Wovkulich, P. M. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 1, pp 843–899. (b) Hesse, M. *Ring Enlargement in Organic Chemistry*; VCH: Weinheim, 1991. (c) Gutsche, C. D.; Redmore, D. *Carbocyclic Ring Expansions Reactions*; Academic Press: New York, 1968. (d) Haufe, G.; Mann, G. *The Chemistry of Alicyclic Compounds*; Elsevier: Berlin, 1989, pp 240–372.

(35) Treatment with H_2SO_4 in H_2O–CH_2Cl_2 converted this byproduct to **15**.

Photochemical Aromatic Annulation Step

With efficient routes to both α- and β-benzosuberones **8** and **9** in hand, the stage was set for examination of the pivotal aromatic annulation step. As discussed earlier, our retrosynthetic plan called for the deployment of an alkoxy derivative of isopropylacetylene as the alkyne component in this key transformation. We chose to employ the siloxyalkyne derivative **28**,[9c,d] which is readily available in one step from ethyl isobutyrate using the Kowalski reaction.[37] Previous studies in our laboratory[9c,d] and that of Kowalski[38] have demonstrated that siloxyalkynes function as particularly outstanding ketenophiles in our aromatic annulation strategy.

Optimal conditions for effecting the key annulation step are outlined in eq 7. A degassed 0.3 M solution of either diazo ketone **8** or **9** and 1.4 equiv of **28** in 1,2-dichloroethane was irradiated at 254 nm in a vycor tube at 20–25 °C using a standard Rayonet photochemical reactor. After 4–20 h (depending on scale), TLC analysis indicated that the diazo ketone was no longer present and that two new products had formed: the desired tricyclic phenol (**29**), and a second compound believed to be the cyclobutenone intermediate **30** (present as a mixture of two diastereomers). In this case, as in several other annulations studied



previously,[9d,12] the accumulation of colored polymers on the walls of the reaction vessel apparently impedes the complete photochemical conversion of the cyclobutenone intermediate to final product. Consequently, the reaction mixture was next diluted with an equal volume of solvent and heated overnight at 80 °C to complete the conversion of the cyclobutenone intermediate to **29** thermally. Concentration and chromatographic purification furnished the tricyclic phenol **29** as colorless crystals in 60–71% yield; no other characterizable products could be isolated from the reaction. Interestingly, essentially identical results were obtained regardless of which diazo ketone was employed as the ketene precursor for the annulation.

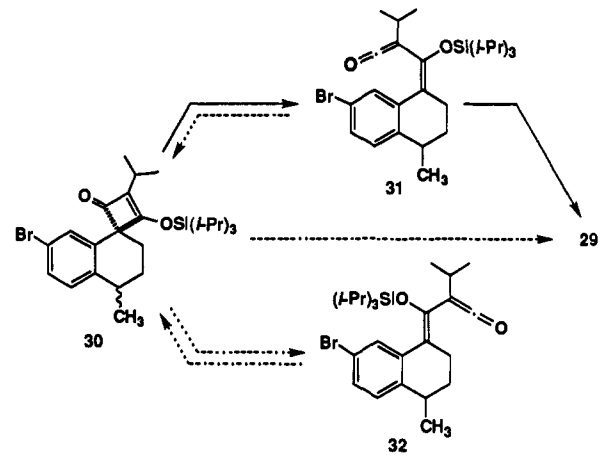
A variety of conditions were examined in the course of determining the optimal procedure for effecting the photochemical aromatic annulation. Conducting the photolysis at 50–60 °C resulted in a lower yield (30–50%) of **29**, and the tricyclic phenol was also obtained in diminished yield (30–50%) when the reaction was carried out using higher (0.7 M) or lower (0.15 M) concentrations of diazo ketone. No change in the efficiency of the annulation was observed when the reaction mixture was irradiated with 300 nm light, and the annulation also proceeded smoothly employing a medium-pressure Hanovia lamp (which is more suitable for large scale work).

(36) For the previous use of DBU for diazo transfer, see: Baum, J. S.; Shook, D. A.; Davies, H. M. L.; Smith, H. D. *Synth. Commun.* **1987**, *17*, 1709.

(37) Kowalski, C. J.; Lal, G. S.; Haque, M. S. *J. Am. Chem. Soc.* **1986**, *108*, 7127.

(38) Kowalski, C. J.; Lal, G. S. *J. Am. Chem. Soc.* **1988**, *110*, 3693.

Scheme 4



The gratifying efficiency of this aromatic annulation reaction raises several intriguing questions concerning the stereochemical course of the process. In principle, the 4π electrocyclic ring opening of the intermediate cyclobutenone **30** can give rise to two stereoisomeric vinylketenes, **31** and **32** (Scheme 4),[39] among which only **31** can undergo direct electrocyclization to afford the desired tricyclic product. Several possible explanations can account for the fact that **29** is nonetheless produced in yields of up to 70% in the aromatic annulation step. For example, one possibility is that the electrocyclic ring opening of **30** is a reversible process. Certain highly substituted vinylketenes are known to undergo electrocyclic closure to form cyclobutenones,[40] and it is thus conceivable that the undesired vinylketene isomer **32** may be interconverting with **31** (via cyclobutenone **30**) under the conditions of the aromatic annulation reaction.[41]

An alternative possibility is that the electrocyclic ring opening is a stereoselective process, leading predominantly to the formation of vinylketene **31**. The stereochemical course of the thermal ring opening of *cyclobutenes* has been the subject of recent investigations by Houk[42] and others,[43] but the related reactions of *cyclobutenones* have received less attention. Baldwin has studied the electrocyclic cleavage of 2,4-dichloro-3-phenylcyclobutenone, and found that this reaction is stereoselective with the C-4 chlorine rotating "outward" in the thermal ring opening and "inward" in the photochemical process.[44] The electrocyclic ring openings of 4-aryl-4-hydroxycyclobutenones are likewise highly stereoselective; in thermal reactions the aryl group prefers to "rotate inward",[10] due to the preference of the strongly donating hydroxyl group to "rotate outward".[42] The stereochemical course of these ring openings is reversed when the reaction is conducted

(39) For reviews of cyclobutene ring opening reactions, see: (a) Durst, T.; Breau, L. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 5, pp 675–697. (b) Marvell, E. *Thermal Electrocyclic Reactions*; Academic Press: New York, 1980; pp 124–213. (c) Bellus, D.; Ernst, B. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 797.

(40) For examples, see: (a) Lee, S. Y.; Kulkarni, Y. S.; Burbaum, B. W.; Johnston, M. I.; Snider, B. B. *J. Org. Chem.* **1988**, *53*, 1848. (b) Maahs, G. *Liebigs Ann. Chem.* **1965**, *686*, 55. (c) Silversmith, E. F.; Kitahara, Y.; Roberts, J. D. *J. Am. Chem. Soc.* **1958**, *80*, 4088.

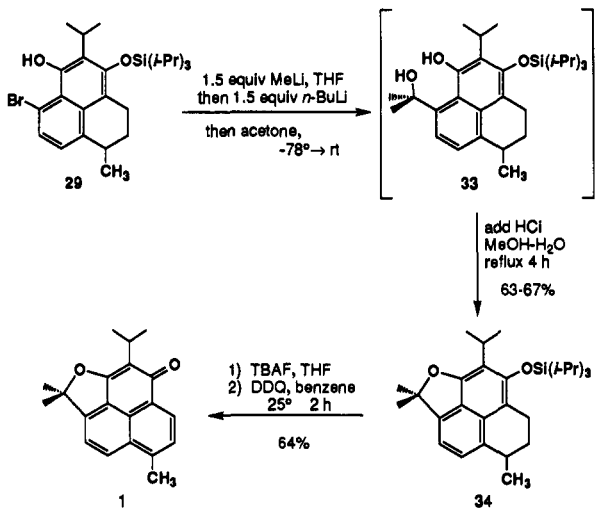
(41) For evidence of reversibility in electrocyclic ring openings of 4-aryl-4-hydroxycyclobutenones, see: Moore, H. W.; Perri, S. T. *J. Org. Chem.* **1988**, *53*, 996.

(42) (a) Kirmse, W.; Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1984**, *106*, 7989. (b) Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1985**, *107*, 2099. (c) Rudolf, K.; Spellmeyer, D. C.; Houk, K. N. *J. Org. Chem.* **1987**, *52*, 3708. (d) Houk, K. N.; Spellmeyer, D. C.; Jefford, C. W.; Rimbault, C. G.; Wang, Y.; Miller, R. D. *J. Org. Chem.* **1988**, *53*, 2125. (e) Buda, A. B.; Wang, Y.; Houk, K. N. *J. Org. Chem.* **1989**, *54*, 2264. (f) Niwayama, S.; Houk, K. N. *Tetrahedron Lett.* **1992**, *33*, 883. (g) Niwayama, S.; Houk, K. N. *Tetrahedron Lett.* **1993**, *34*, 1251.

(43) (a) Dolbier, Jr., W. R.; Koroniak, H.; Burton, D. J.; Bailey, A. R.; Shaw, G. S.; Hansen, S. W. *J. Am. Chem. Soc.* **1984**, *106*, 1871. (b) Piers, E.; Lu, Y.-F. *J. Org. Chem.* **1989**, *54*, 2267. (c) Hayes, R.; Ingham, S.; Saengchantara, S. T.; Wallace, T. W. *Tetrahedron Lett.* **1991**, *32*, 2953 and references cited therein.

(44) Baldwin, J. E.; McDaniel, M. C. *J. Am. Chem. Soc.* **1968**, *90*, 6118.

Scheme 5



photochemically.[45] Unfortunately, the implications of these results in the case of the electrocyclic ring opening of **30** are difficult to evaluate. Cyclobutenone **30** bears neither a strongly donating nor withdrawing substituent at the C-4 position of the cyclobutenone ring, and to further complicate matters, under the conditions of our annulation step this electrocyclic opening may be taking place via either photochemical or thermal activation.

Finally, it should be noted that alternative pathways for the conversion of **30** to **29** that do not involve the intermediacy of the vinylketene **31** cannot be excluded. For example, this transformation might take place via direct [1,3] sigmatropic rearrangement or, alternatively, via a biradical generated through photochemical type I α-cleavage of the cyclobutenone ring.

An obvious experiment which would illuminate the mechanistic course of this key transformation would be to examine the electrocyclic opening of the cyclobutenone **30** in a nucleophilic solvent capable of intercepting any vinylketene intermediates present. Unfortunately, the instability of **30** to silica gel frustrated all attempts to isolate this intermediate in sufficiently pure form to permit us to pursue these studies.

Conversion of Intermediate 29 to Salvilenone

The final manipulations required for the total synthesis of salvilenone involved annulation of the furan ring onto the tricyclic phenalene nucleus, cleavage of the silyl ether group, and oxidation. Scheme 5 outlines the most expeditious route devised for achieving this final stage of the synthesis. Installation of the requisite three-carbon appendage at C-3 was best achieved by addition of the dilithium derivative of **29** to acetone.[46] Thus, sequential treatment of the bromophenol at −78 °C with 1.5 equiv of MeLi (to form the phenolate salt) and 1.5 equiv of BuLi gave an aryllithium intermediate, which was quenched by addition of excess acetone to afford the diol **33**. In practice, this diol was not isolated but was converted directly to the furanophenalene **34** in the same flask by the addition of aqueous HCl and methanol followed by heating for 4 h. Using this protocol **34** was obtained as a white solid in 63–67% yield after chromatographic purification. The success of this transformation proved to be critically dependent on the quality of the acetone, with best results obtained using acetone that had been dried over powdered boric anhydride for 24 h and then freshly distilled prior to use.[47]

Exposure of **34** to 1.5 equiv of tetra-*n*-butylammonium fluoride in THF at 25 °C rapidly cleaved the silyl ether group and produced the expected phenol **4** in excellent yield. It will be recalled that this same phenol had previously been prepared by Kakisawa by hydrogenation of salvilenone and found to undergo air oxidation to regenerate the diterpene in quantitative yield (eq 1).[6] Unfortunately, in our hands exposure of **4** to air or oxygen under a variety of conditions failed to provide salvilenone in satisfactory yield. Recourse was therefore made to chemical oxidants, among which DDQ proved most suitable for effecting the desired transformation. Treatment of the crude product of the silyl ether cleavage step with 1.1 equiv of DDQ in benzene at 25 °C for 2 h thus furnished salvilenone as bright yellow crystals, mp 141–142 °C. Synthetic salvilenone was indistinguishable from an authentic sample of the natural product by mp and TLC comparison and by infrared and ^{1}H NMR spectroscopic analyses.

Conclusions

Heathcock has recently discussed the current status of synthetic organic chemistry and attributed certain misconceptions concerning the maturity of the field to confusion with regard to the difference between the terms "effective" and "efficient".[48] Whereas modern synthetic methodology provides chemists with the ability to devise routes *adequate* to reach many synthetic goals, *practical* and *efficient* syntheses of the same target molecules often are not possible using existing methodology. In this paper we have reported a highly efficient synthesis of the phenalenone diterpene salvilenone which demonstrates the ability of our aromatic annulation strategy to dramatically streamline the synthesis of polycyclic aromatic compounds. The synthetic routes described herein provide access to salvilenone in only seven or eight steps (via the α- and β-benzosuberone strategies, respectively), half the number of steps required using the classical linear substitution approach reported earlier.[8] In addition, this work serves to highlight the special advantages of the diazo ketone-based annulation strategy, since the phenalene and phenalenone systems cannot be readily generated employing the alternative and related cyclobutenone and squaric acid-based aromatic annulation methods.

Experimental Section

General Procedures. All reactions were performed in flame-dried glassware under a positive pressure of argon or nitrogen. Reaction mixtures were stirred magnetically with a Teflon-covered stirbar unless otherwise indicated except for photochemical reactions which were not stirred. Air- and moisture-sensitive liquids and solutions were transferred via syringe or cannula and were introduced into reaction vessels through rubber septa. Reaction product solutions were concentrated by using a Büchi rotary evaporator at ca. 20 mmHg. Column chromatography was performed on Baker silica gel (230–400 mesh).

Materials. Commercial grade reagents and solvents were used without further purification except as indicated below. Ethyl isobutyrate, 2,2,6,6-tetramethylpiperidine, dibromomethane, dichloroethane, and triisopropylsilyl chloride were distilled from calcium hydride. Acetone was stirred over powdered boric anhydride for 24 h and then distilled immediately prior to use.[47] Benzene and tetrahydrofuran were distilled from sodium benzophenone ketyl or its dianion. Methyltriphenylphosphonium bromide was dried at 100 °C (0.1 mmHg) for 24 h prior to use.

Instrumentation. Photolyses were performed in a Rayonet Photochemical Reactor Model RPR-100 or RPR-200 containing 16 253.7-nm low-pressure mercury vapor bulbs (Southern New England Ultraviolet Co.). The photolyses were performed with an internal fan in operation, and the temperature of the reactor was never higher than 35 °C. Melting points were determined with a Fisher-Johns melting point apparatus and are uncorrected. Infrared spectra were recorded using a Perkin-Elmer 1320 grating spectrophotometer. Ultraviolet–visible spectra were measured on a Varian DMS 100 spectrophotometer. ^{1}H NMR spectra were recorded with Varian XL-300 (300 MHz) and Varian Unity 300 (300 MHz) spectrophotometers. ^{13}C NMR spectra were determined on a Varian XL-300 (75 MHz) spectrophotometer. Chemical shifts are expressed in parts per million (δ) downfield from tetramethylsilane. High-

(45) Perri, S. T.; Foland, L. D.; Moore, H. W. *Tetrahedron Lett.* **1988**, *29*, 3529.

(46) Treatment of *o*-bromophenol with 2 equiv of BuLi produces a dilithium derivative which reacts with ketones to form tertiary alcohols in good yield: Talley, J. J.; Evans, I. A. *J. Org. Chem.* **1984**, *49*, 5267.

(47) Burfield, D. R.; Smithers, R. H. *J. Org. Chem.* **1978**, *43*, 3966.

(48) Heathcock, C. H. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 665.

resolution mass spectra (HRMS) were measured on a Finnegan Matt-8200 spectrometer. Elemental analyses were performed by Robertson Microlit Laboratories, Inc., Madison, NJ.

9-Methyl-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-5-one (13). A 100-mL, three-necked, round-bottomed flask equipped with an argon inlet adapter, glass stopper, and rubber septum was charged with $NaNH_2$ (1.58 g, 40.5 mmol) and 30 mL of THF. A solution of 2-methyl-1-[(trimethylsilyl)oxy]-1-cyclopentene (3.46 g, 20.3 mmol) in 16 mL of THF was transferred via cannula to the sodamide suspension over 2 min, and the resulting yellow mixture was stirred at room temperature for 30 min. Bromobenzene (0.849 g, 0.570 mL, 5.41 mmol) was added dropwise via syringe over 1 min, and the reaction mixture was stirred at 45 °C for 4 h and then at reflux for 48 h. The resulting mixture was allowed to cool to room temperature and then poured into a mixture of 50 mL of concentrated HCl and 50 g of ice. The aqueous layer was separated and extracted with three 30-mL portions of diethyl ether, and the combined ether extracts were washed with two 30-mL portions of water and 30 mL of brine, dried over $MgSO_4$, filtered, and concentrated to give 0.929 g of a yellow oil. Column chromatography on 30 g of silica gel (elution with 3% ethyl acetate–hexanes) afforded 0.531 g of an 85:15 mixture of ketones **13** and **17**.

A 25-mL, round-bottomed flask equipped with an argon inlet adapter was charged with the mixture of ketones **13** and **17** (0.471 g) prepared in the previous reaction and 1 mL of concentrated sulfuric acid. The mixture was heated at 120 °C (oil bath temperature) for 45 min and then allowed to cool to room temperature. The resulting mixture was carefully added dropwise to an Erlenmeyer flask containing 20 mL of water. Saturated aqueous $NaHCO_3$ (30 mL) was added until the mixture reached pH 9, and the resulting mixture was extracted with three 20-mL portions of diethyl ether and three 20-mL portions of ethyl acetate. The combined organic phases were washed with 20 mL of water, 20 mL of saturated aqueous $NaHCO_3$, and 20 mL of brine, dried over $MgSO_4$, filtered, and concentrated to give 0.355 g (42% overall yield from bromobenzene) of **13** as a yellow oil. Spectral data was identical to that previously reported for this compound:[14b] IR (neat) 3060, 2920, 1675, 1600, 1450, 1405, 1375, 1355, 1315, 1285, 1250, 1220, 1180, 1110, 1020, 930, 820, and 760 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, J = 7.5 Hz, 1 H), 7.43 (ddd, J = 7.5, 7.5, 1.5 Hz, 1 H), 7.22–7.27 (m, 2 H), 3.07 (m, 1 H), 2.51–2.74 (m, 2 H), 1.79–1.98 (m, 2 H), 1.44–1.64 (m, 2 H), and 1.35 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.1, 143.0, 139.3, 131.8, 127.7, 126.3, 125.1, 41.2, 34.4, 34.2, 20.4, and 19.3.

3-Bromo-9-methyl-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-5-one (18). A 50-mL, three-necked, round-bottomed flask equipped with a mechanical stirrer, argon inlet adapter fitted with rubber tubing leading to a water bubbler, and a Claisen head fitted with an argon inlet adapter and a rubber septum was charged with finely powdered $AlCl_3$ (0.214 g, 1.60 mmol). The $AlCl_3$ was stirred rapidly as the ketone **13** (0.100 g, 0.574 mmol) was added dropwise by syringe over 10 min, and the resulting reddish mass was stirred at 80 °C (oil bath temperature) for 30 min. Bromine (0.110 g, 0.035 mL, 0.688 mmol) was then added dropwise via syringe over 5 min, and the resulting mixture was stirred for 1 h at 80 °C and then poured into 10 g of ice and 10 mL of water. The aqueous layer was separated and extracted with three 20-mL portions of diethyl ether, and the combined organic phases were washed with 20 mL of water, 20 mL of saturated $NaHCO_3$, 20 mL of water, and 20 mL of brine, dried over $MgSO_4$, filtered, and concentrated to provide 0.135 g of a yellow-brown oil. Column chromatography on 10 g of silica gel (elution with 5% ethyl acetate–hexanes) afforded 0.117 g (81%) of **18** as a yellow oil: IR (neat) 3060, 2920, 1675, 1585, 1555, 1460, 1390, 1350, 1315, 1280, 1245, 1220, 1180, 1125, 1080, 1020, 935, 875, 820, and 785 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.66 (d, J = 2.0 Hz, 1 H), 7.58 (dd, J = 8.2, 2.1 Hz, 1 H), 7.16 (d, J = 8.2 Hz, 1 H), 3.04–3.07 (m, 1 H), 2.55–2.73 (m, 2 H), 1.87–2.00 (m, 2 H), 1.52–1.64 (m, 2 H), and 1.37 (d, J = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.5, 142.0, 140.9, 134.6, 130.6, 127.2, 120.3, 41.2, 34.1, 34.0, 20.3, and 19.3; HRMS, *m/e* calcd for $C_{12}H_{13}BrO$ 252.0150, found 252.0147.

3-Bromo-6-diazo-9-methyl-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-5-one (8). A 250-mL, three-necked, round-bottomed flask equipped with two glass stoppers and dropping funnel fitted with an argon inlet adapter was charged with the ketone **18** (0.692 g, 2.73 mmol), triisopropylbenzenesulfonyl azide (0.965 g, 3.12 mmol), tetrabutylammonium bromide (0.247 g, 0.766 mmol), 18-crown-6 (0.024 g, 0.091 mmol), and 48 mL of benzene. Aqueous KOH (66% w/v, 48 mL) was then added dropwise over 10 min. The reaction mixture was stirred vigorously for 80 min and then treated with a second portion of triisopropylbenzenesulfonyl azide (0.727 g, 2.35 mmol). The resulting mixture was stirred at room temperature for 22 h and then poured into 40 mL of diethyl ether and 40 mL of water. The aqueous layer was separated and extracted with three 40-mL portions of diethyl ether, and the combined organic phases were washed with 40 mL of water and 40 mL of brine, dried over Na_2SO_4, filtered, and concentrated to give 2.50 g of a yellow-brown oil. Column chromatography on 100 g of silica gel (elution with 10% ethyl acetate–hexanes) afforded 0.590 g (77%) of **8** as a yellow solid. An analytical sample was prepared by recrystallization from ca. 5 mL of 1:1 diethyl ether–pentane: mp 110–111 °C; IR (CCl_4) 2970, 2930, 2095, 1625, 1465, 1425, 1400, 1355, 1320, 1280, 1230, and 1150 cm^{-1}; UV max (CH_3CN) 307 (ϵ = 9300) and 215 (19 600) nm; ^1H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, J = 2.2 Hz, 1 H), 7.55 (dd, J = 8.3, 2.2 Hz, 1 H), 7.15 (d, J = 8.4 Hz, 1 H), 3.10 (m, 1 H), 2.54 (m, 1 H), 2.29 (m, 2 H), 1.62 (m, 1 H), and 1.37 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.5, 141.0, 140.2, 134.1, 129.7, 126.8, 120.5, 65.1, 37.1, 33.6, 22.1, and 18.3. Anal. Calcd for $C_{12}H_{11}BrN_2O$: C, 51.64; H, 3.97; N, 10.04. Found: C, 51.67; H, 3.96; N, 10.18.

(4-Carbethoxybutyl)triphenylphosphonium bromide (22). A 100-mL, three-necked, round-bottomed flask equipped with a mechanical stirrer, glass stopper, and argon inlet adapter was charged with triphenylphosphine (22.4 g, 85.4 mmol) and ethyl 4-bromobutyrate (20.0 g, 14.7 mL, 103 mmol). The mixture was stirred at 100 °C for 2 h, during which time an additional portion of ethyl 4-bromobutyrate (2.04 g, 1.50 mL, 10.5 mmol) was used to rinse triphenylphosphine from the walls of the flask. The resulting white solid mass was recrystallized from ca. 300 mL of 3:1 ethanol–diethyl ether to afford 33.5 g (86%) of the phosphonium salt **22** as white crystals: mp 173–174 °C; IR (Nujol) 2900, 1720, 1455, 1375, 1235, 1175, 1105, and 720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.68–7.91 (m, 15 H), 3.93–4.13 (m, 4 H), 2.88 (t, J = 7.6 Hz, 2 H), 1.87–2.00 (m, 2 H), and 1.22 (t, J = 7.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.0, 134.4 (J_{CP} = 2.8 Hz), 132.9 (J_{CP} = 10.1 Hz), 129.8 (J_{CP} = 12.4 Hz), 117.2 (J_{CP} = 86.0 Hz), 59.8, 32.6 (J_{CP} = 18.0 Hz), 21.0 (J_{CP} = 51.7 Hz), 17.2 (J_{CP} = 3.2 Hz), and 13.4. Anal. Calcd for $C_{24}H_{26}BrO_2P$: C, 63.03; H, 5.73. Found: C, 62.63; H, 5.96.

(*Z,E*)-Ethyl 5-(4-Bromophenyl)-4-hexenoate (23). A 1-L, three-necked, round-bottomed flask equipped with a mechanical stirrer, reflux condenser fitted with an argon inlet adapter, and rubber septum was charged with the phosphonium salt **22** (29.2 g, 63.8 mmol) and 100 mL of THF. A 500-mL, three-necked, round-bottomed flask equipped with an argon inlet adapter, glass stopper, and rubber septum was charged with sodium (cut into small pieces, 1.42 g, 61.8 mmol) and 150 mL of THF. Absolute ethanol (40 mL) was added slowly to this mixture over a period of 30 min, and the resulting clear solution of sodium ethoxide was transferred via cannula to the phosphonium salt suspension over 20 min. The resulting cloudy yellow solution was heated at reflux for 4 h. A solution of 4-bromoacetophenone (8.48 g, 42.6 mmol) in 20 mL of THF was added via cannula to the ylide mixture over 5 min, and the resulting yellow mixture was then heated at reflux for 72 h. The reaction mixture was allowed to cool to room temperature and then poured into 200 mL of 0.05 M aqueous KH_2PO_4. The aqueous layer was separated and extracted with four 100-mL portions of diethyl ether, and the combined organic phases were washed with 100 mL of water and 100 mL of brine, dried over Na_2SO_4, filtered, and concentrated to afford 36.2 g of an oily orange solid. Column chromatography on 125 g of silica gel (elution with 50% ethyl acetate–hexanes) gave 18.4 g of a yellow oil, which was further purified by chromatography on 500 g of silica gel (elution with 0–5% ethyl acetate–hexanes) to furnish 6.99 g (55%) of **23** as a pale yellow oil (3:1 mixture of *Z:E* isomers) and 3.86 g of **23** contaminated with a small amount of ketone **21**. Column chromatography of the latter fraction on 150 g of silica gel (elution with 3% ethyl acetate–hexanes) gave an additional 2.75 g (22%) of **23**; total yield 9.74 g (77%) of **23** as a 3:1 mixture of *Z:E* isomers used in the next step without separation.

5-(4-Bromophenyl)hexanoic Acid (25). A 250-mL, round-bottomed flask equipped with a rubber septum, a long gas inlet needle, and a short gas outlet needle was charged with the mixture of olefins **23** (16.0 g, 53.8 mmol), 5% rhodium on alumina (4.04 g), and 64 mL of absolute ethanol. Argon was bubbled through the solution for 20 min, and then hydrogen was slowly bubbled through the reaction mixture for 36 h. The reaction mixture was degassed with argon for 20 min and then filtered through Celite with the aid of 100 mL of ethanol and 100 mL of diethyl ether. Concentration of the filtrate afforded 16.9 g of the ester **24** as an orange oil, used in the next step without further purification.

A 500-mL, round-bottomed flask equipped with an argon inlet adapter was charged with the ester **24** (16.1 g of the product of the preceding reaction), 130 mL of methanol, 30 mL of water, and $LiOH \cdot H_2O$ (11.9 g, 283 mmol). The reaction mixture was stirred at 0 °C for 16 h and

then acidified by addition of 10 mL of concentrated HCl. The resulting mixture was extracted with five 100-mL portions of methylene chloride, and the combined organic phases were washed with 100 mL of brine, dried over $MgSO_4$, filtered, and concentrated to give 14.3 g (98% overall from **23**) of **25** as a white solid: mp 71–72 °C; IR (CCl_4) 3020, 2970, 2930, 1715, 1495, 1455, 1415, 1295, 1250, 1110, 1080, 1015, and 935 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 11.69 (br s, 1 H), 7.39 (d, J = 8.6 Hz, 2 H), 7.04 (d, J = 8.6 Hz, 2 H), 2.62–2.66 (m, 1 H), 2.29 (t, J = 6.8 Hz, 2 H), 1.46–1.62 (m, 4 H), and 1.21 (d, J = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.1, 146.0, 131.4, 128.7, 119.6, 39.3, 37.4, 34.0, 22.7, and 22.1. Anal. Calcd for $C_{12}H_{15}BrO_2$: C, 53.16; H, 5.58. Found: C, 53.38; H, 5.70.

3-Bromo-9-methyl-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-5-one (18). A 1-L, three-necked, round-bottomed flask equipped with a thermometer, mechanical stirrer, and powder addition funnel fitted with an argon inlet adapter was charged with polyphosphoric acid (1.0 kg). The contents of the flask were heated to 106 °C, and the carboxylic acid **25** (15.7 g, 0.058 mol) was added through the powder addition funnel over 15 min. After 4.5 h at 106 °C, the reaction mixture was cooled to room temperature, poured into 2 L of water, and carefully brought to approximately pH 4 by addition of 1 kg of NaOH. The resulting mixture was extracted with six 150-mL portions of diethyl ether and four 100-mL portions of CH_2Cl_2. The combined ether extracts were washed with 150 mL of water and 150 mL of brine, dried over $MgSO_4$, filtered, and concentrated to afford a brown oil. The combined CH_2Cl_2 extracts were washed with 150 mL of water and 150 mL of brine, dried over $MgSO_4$, filtered, concentrated, and combined with the product of the ether extracts to afford 14.6 g of a brown oil. The crude product was divided in two equal portions, which were then purified by column chromatography on 250 g of silica gel (elution with 5% ethyl acetate–hexanes) to afford a total of 7.23 g (49%) of **18** as an orange oil with spectral characteristics identical to those described above.

7-Bromo-4-methyl-1,2,3,4-tetrahydro-1*H*-naphthalen-1-one (16). A 50-mL, three-necked, round-bottomed flask equipped with a mechanical stirrer, gas inlet adapter (fitted with Tygon tubing leading to a water bubbler), and a Claisen head (fitted with a rubber septum and an argon inlet adapter) was charged with finely powdered aluminum chloride (15.5 g, 116 mmol). The aluminum chloride was stirred rapidly as 4-methyl-1-tetralone (6.67 g, 6.19 mL, 41.6 mmol) was added dropwise by syringe over 20 min. The resulting dark-red mass was heated with an oil bath at 80–90 °C until it melted, at which point bromine (7.97 g, 2.57 mL, 50.0 mmol) was added dropwise by syringe over 40 min. After 1.5 h, the reaction mixture was allowed to cool to room temperature and then added to 800 g of ice and 800 mL of concentrated HCl. The resulting mixture was extracted with four 300-mL portions of diethyl ether, and the combined organic layers were filtered through Celite. The filtrate was washed with 250 mL of saturated $NaHCO_3$ solution, 250 mL of water, and 250 mL of brine, dried over Na_2SO_4, filtered, and concentrated to afford 9.17 g of a brown oil. Column chromatography on 275 g of silica gel (gradient elution with 5–10% ethyl acetate–hexanes) yielded 4.82 g of a yellow solid which was recrystallized from ca. 20 mL of pentane to afford 4.43 g (45%) of **16** as off-white crystals: mp 54–55 °C (lit.[13a] mp 57.5–58.5 °C); IR (CCl_4) 2940, 2920, 1680, 1580, 1460, 1390, 1320, 1245, 1185, and 895 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.15 (d, J = 2.6 Hz, 1 H), 7.61 (dd, J = 7.5, 2.6 Hz, 1 H), 7.22 (d, J = 7.5 Hz, 1 H), 3.09 (m, 1 H), 2.70 (m, 2 H), 2.24 (m, 1 H), 1.90 (m, 1 H), and 1.40 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.8, 147.6, 136.3, 133.4, 130.0, 129.4, 120.7, 36.1, 32.5, 30.3, and 20.5. Anal. Calcd for $C_{11}H_{11}BrO$: C, 55.25; H, 4.64. Found: C, 55.53; H, 4.69.

7-Bromo-4-methyl-1-methylidene-1,2,3,4-tetrahydro-1*H*-naphthalene (27). A 100-mL, three-necked, round-bottomed flask equipped with a mechanical stirrer, argon inlet adapter, and rubber septum was charged with methyltriphenylphosphonium bromide (3.06 g, 8.57 mmol) and 46 mL of THF and then cooled at 0 °C while a solution of *n*-BuLi (2.54 M in hexanes, 3.17 mL, 8.05 mmol) was added dropwise via syringe over 5 min. The ice bath was then removed, and the resulting orange solution containing a small amount of excess solid phosphonium salt was stirred for an additional 5 min. A solution of **16** (1.28 g, 5.36 mmol) in 7 mL of THF was transferred via cannula over 5 min into the ylide solution, and the resulting cloudy yellow-brown mixture was allowed to stir at 25 °C for 18 h. Aqueous KH_2PO_4 (0.05 M, 30 mL) was then added, and the aqueous layer was separated and extracted with four 40-mL portions of diethyl ether. The combined organic phases were washed with 20 mL of water and 20 mL of brine, dried over Na_2SO_4, filtered, and concentrated to afford 3.40 g of an oily, light brown solid. Column chromatography on 100 g of silica gel (elution with hexanes) afforded 1.08 g (85%) of **27** as a clear, colorless oil: IR (neat) 3080, 2930, 2860, 1625, 1590, 1550, 1465, 1410, 1375, 1090, 1020, 885, and 810 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, J = 2.5 Hz, 1 H), 7.36 (dd, J = 7.5, 2.5 Hz, 1 H), 7.14 (d, J = 7.5 Hz, 1 H), 5.50 (s, 1H), 5.04 (s, 1 H), 2.97 (m, 1 H), 2.60 (m, 2 H), 2.03 (m, 1 H), 1.67 (m, 1 H), and 1.33 (d, J = 7.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.5, 140.9, 136.4, 130.4, 129.7, 127.0, 119.6, 109.1, 32.9, 31.1, 29.6, and 22.0. Anal. Calcd for $C_{12}H_{13}Br$: C, 60.78; H, 5.53. Found: C, 60.77; H, 5.53.

3-Bromo-9-methyl-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-6-one (15). A 100-mL, three-necked, round-bottomed flask equipped with an argon inlet adapter, rubber septum, and glass stopper was charged with $Tl(NO_3)_3 \cdot 3H_2O$ (8.20 g, 18.4 mmol) and 68 mL of methanol. To this solution was then added the methylenetetralin **27** (3.88 g, 16.4 mmol) dropwise via syringe over 1 min. A white precipitate formed immediately. The reaction mixture was stirred for an additional 2 min, diluted with 20 mL of chloroform, and then filtered. The filtrate was diluted with 60 mL of saturated $NaHCO_3$ solution, and the aqueous layer was separated and extracted with three 40-mL portions of chloroform. The combined organic phases were washed with 80 mL of brine, dried over $MgSO_4$, filtered, and concentrated to give 4.46 g of a pale yellow oil. Column chromatography on 140 g of silica gel (elution with 5% ethyl acetate–hexanes) afforded 3.17 g (76%) of the benzosuberone **15** and 0.896 g of the corresponding dimethyl ketal. The ketal was dissolved in 20 mL of methylene chloride and stirred vigorously with 20 mL of 25% aqueous sulfuric acid for 48 h. The aqueous phase of the resulting mixture was separated and extracted with three 20-mL portions of methylene chloride, and the combined organic extracts were washed with 20 mL of brine, dried over $MgSO_4$, filtered, and concentrated to afford 0.767 g of a yellow oil. Column chromatography on 25 g of silica gel (elution with 5% ethyl acetate–hexanes) afforded an additional 0.615 g (15%) of **15**: total yield 3.79 g (91%): IR (neat) 2960, 2920, 1710, 1590, 1480, 1410, 1355, 1205, 895, and 820 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.31 (dd, J = 8.2, 2.2 Hz, 1 H), 7.19 (d, J = 2.2 Hz, 1 H), 7.07 (d, J = 8.2 Hz, 1 H), 3.76 (d, J = 17.6 Hz, 1 H), 3.39 (d, J = 17.3 Hz, 1 H), 3.00–3.08 (m, 1 H), 2.24–2.45 (m, 2 H), 1.99–2.08 (m, 1 H), 1.45–1.56 (m, 1 H), and 1.32 (d, J = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.7, 142.0, 136.1, 132.0, 130.4, 126.8, 119.9, 48.8, 41.0, 34.0, 33.6, and 19.2. Anal. Calcd for $C_{12}H_{13}BrO$: C, 56.94; H, 5.18. Found: C, 56.71; H, 5.14.

3-Bromo-5-diazo-9-methyl-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-6-one (9). A 500-mL, three-necked, round-bottomed flask equipped with an addition funnel fitted with an argon inlet adapter, a rubber septum, and glass stopper was charged with **15** (1.00 g, 3.95 mmol), triisopropylbenzenesulfonyl azide (1.40 g, 4.52 mmol), tetrabutylammonium bromide (0.36 g, 1.1 mmol), 18-crown-6 (0.034 g, 0.13 mmol), and 70 mL of benzene. Aqueous KOH (30% w/v, 70 mL) was added dropwise over 10 min via the addition funnel, and after 30 min, additional triisopropylbenzenesulfonyl azide (1.05 g, 3.39 mmol) was added in one portion. The brownish-green reaction mixture was stirred an additional 90 min and then partitioned between 70 mL of water and 70 mL of diethyl ether. The aqueous layer was separated and extracted with four 50-mL portions of diethyl ether, and the combined organic phases were washed with 60 mL of water and 60 mL of brine, dried over $MgSO_4$, filtered, and concentrated to afford 4.13 g of a brown oil. Column chromatography on 100 g of silica gel (elution with 5% ethyl acetate–hexanes) gave 1.06 g (96%) of a yellow solid which was recrystallized from ca. 10 mL of 1:1 diethyl ether–pentane to afford 0.896 g (81%) of the diazo ketone **9** as yellow crystals. An analytical sample was prepared by recrystallization from diethyl ether–pentane to give dark yellow crystals: mp 102–104 °C; IR (CCl_4) 2950, 2920, 2070, 1645, 1580, 1470, 1300, 1280, 1240, 1215, 1160, 1015, and 865 cm^{-1}; UV max (CH_3CN) 261 (ϵ = 10 700) and 202 (23 200) nm; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40 (dd, J = 8.3, 2.5 Hz, 1 H), 7.32 (d, J = 2.5 Hz, 1 H), 7.21 (d, J = 8.3 Hz, 1 H), 3.08 (m, 1 H), 2.25–2.46 (m, 3 H), 1.68 (m, 1 H), and 1.34 (d, J = 7.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.3, 141.1, 137.9, 130.8, 129.5, 128.2, 127.9, 120.2, 38.5, 36.5, 34.0, and 18.9. Anal. Calcd for $C_{12}H_{11}BrN_2O$: C, 51.64; H, 3.97; N, 10.04. Found: C, 51.38; H, 3.95; N, 9.98.

3-Methyl-1-(triisopropylsiloxy)-1-butyne (28). A 500-mL, three-necked, round-bottomed flask equipped with a rubber septum, glass stopper, and an argon inlet adapter was charged with dibromomethane (7.98 g, 3.22 mL, 45.9 mmol) and 70 mL of THF and cooled to –78 °C with a dry ice–acetone bath. A 100-mL, three-necked, round-bottomed flask equipped with a rubber septum, glass stopper, and argon inlet adapter was charged with 2,2,6,6-tetramethylpiperidine (7.34 g, 8.77 mL, 52.0 mmol) and 63 mL of THF and cooled at 0 °C while *n*-BuLi (2.54 M in

hexanes, 19.3 mL, 49.0 mmol) was added dropwise via syringe over 5 min. The resulting solution was stirred for 10 min at 0 °C, cooled to −78 °C, and transferred via cannula to the dibromomethane solution (allowing it to drip down the side of the flask) over 5 min. The resulting yellow solution was stirred for an additional 10 min at −78 °C, and a precooled (−78 °C) solution of ethyl isobutyrate (2.41 g, 2.78 mL, 20.8 mmol) in 14 mL of THF was then added via cannula over 2 min. The yellow solution was stirred an additional 10 min at −78 °C, after which *n*-BuLi (2.54 M in hexanes, 40.9 mL, 104 mmol) was added dropwise via syringe over 3 min. The resulting orange-brown solution was stirred for 10 min, the dry ice–acetone bath was replaced with a room temperature water bath, and stirring was continued for an additional 35 min. The reaction mixture was then recooled to −78 °C, and a solution of triisopropylsilyl chloride (20.1 g, 22.3 mL, 104 mmol) in 21 mL of THF was added via cannula over 5 min. The resulting solution was stirred for 45 min at −78 °C and then at 0 °C for 5 h.

The reaction mixture was next cooled to −78 °C, and 200 mL of petroleum ether and 100 mL of saturated $NaHCO_3$ were added. The dry ice–acetone bath was removed, and the reaction mixture was allowed to warm slowly to room temperature. The aqueous layer was separated and extracted with three 100-mL portions of petroleum ether, and the combined organic phases were washed with two 100-mL portions of water and 100 mL of brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. *Note: It is essential to remove excess triisopropylsilyl chloride from the crude product prior to purification by column chromatography. This is best accomplished by first removing the silyl chloride in vacuo, and then via a rapid filtration through silica gel.* The resulting murky yellow liquid was further concentrated at ≤0.001 mmHg for 11.5 h at room temperature to give 5.12 g of a shimmery, orange oil. This was divided into two equal portions, each of which was rapidly filtered through ca. 10 g of silica gel, washing with ca. 300 mL of petroleum ether. The combined filtrates were concentrated to give 4.18 g of a clear, pale yellow oil. This material was divided into three equal portions, and each portion was purified by column chromatography on 100 g of silica gel (elution with hexanes). The desired product from all three columns was combined to afford 2.45 g (49%) of **28** as a clear, colorless oil with spectral characteristics identical to those previously reported for this compound:[9c,d] IR (neat) 2960, 2860, 2270, 1460, 1340, 1255, 1145, 1080, 880, and 765 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.46 (septet, J = 6.8 Hz, 1 H), 1.21–1.28 (m, 3 H), and 1.09–1.14 (m, 24 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 86.6, 36.5, 24.3, 19.4, 17.4, and 11.9.

7-Bromo-2,3-dihydro-6-hydroxy-5-isopropyl-1-methyl-4-(triisopropylsiloxy)-1*H*-phenalene (29). A 28-cm vycor tube (16-mm o.d., 14-mm i.d.) fitted with a rubber septum was charged with the diazo ketone **8** (1.63 g, 5.84 mmol), the siloxyacetylene **28** (2.04 g, 8.48 mmol), and 20 mL of 1,2-dichloroethane. A second rubber septum (inverted) was secured with wire to the tube to ensure a good seal, and the solution was degassed with a stream of argon for 20 min and then irradiated at 254 nm for 91 h in a Rayonet photochemical reactor. The reaction mixture was then transferred to a 100-mL, round-bottomed flask fitted with a reflux condenser and an argon inlet adapter, diluted with 40 mL of dichloroethane, and heated at reflux. After 12 h, the reaction mixture was allowed to cool to room temperature and then concentrated to afford 3.52 g of a red-brown oil. Column chromatography on 120 g of silica gel (elution with hexanes) gave 1.79 g (62%) of **29** as a viscous, colorless oil which crystallized upon standing to a white solid: mp 85–87 °C; IR ($CDCl_3$) 3480, 2940, 2870, 1590, 1560, 1455, 1410, 1375, 1360, 1330, 1270, 1180, 1110, 1040, 1010, and 815 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.06 (s, 1 H), 7.41 (d, J = 7.6 Hz, 1 H), 6.97 (d, J = 7.5 Hz, 1 H), 3.56 (septet, J = 7.2 Hz, 1 H), 3.04–3.12 (m, 1 H), 2.98–3.03 (m, 2 H), 1.90–2.02 (m, 1 H), 1.75–1.84 (m, 1 H), 1.45 (d, J = 6.8 Hz, 3 H), 1.43 (d, J = 7.4 Hz, 3 H), 1.32–1.40 (m, 3H), 1.29 (d, J = 7.0 Hz, 3 H), and 1.16 (d, J = 6.9 Hz, 18 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.6, 150.5, 140.8, 131.4, 129.2, 124.9, 122.9, 116.7, 114.9, 112.1, 34.3, 28.9, 26.1, 22.5, 21.3, 20.3, 20.3, 18.2, and 14.3. Anal. Calcd for $C_{26}H_{39}BrO_2Si$: C, 63.52; H, 8.00. Found: C, 63.08; H, 8.11.

7-Bromo-2,3-dihydro-6-hydroxy-5-isopropyl-1-methyl-4-(triisopropylsiloxy)-1*H*-phenalene (29). A 30-cm vycor tube (16-mm o.d., 14-mm i.d.) fitted with a rubber septum was charged with the diazo ketone **9** (1.00 g, 3.58 mmol), the siloxyacetylene **28** (1.21 g, 5.03 mmol), and 12 mL of 1,2-dichloroethane. A second rubber septum (inverted) was secured with wire to the tube to ensure a good seal, and the solution was degassed with a stream of argon for 10 min and then irradiated at 254 nm for 19.5 h in a Rayonet photochemical reactor. The solution was then transferred to a 100-mL, round-bottomed flask fitted with a reflux condenser and an argon inlet adapter, diluted with 24 mL of dichloroethane, and heated at reflux. After 16.5 h, the reaction mixture was allowed to cool to room temperature and then concentrated to afford 2.22 g of a red-brown oil. Column chromatography on 100 g of silica gel (elution with hexanes) gave 1.19 g (68%) of **29** as a viscous, colorless oil, which crystallized on standing to a white solid: mp 85–87 °C. Spectral data was identical to that described above for this compound.

2,2,5-Trimethyl-9-isopropyl-2,5,6,7-tetrahydro-8-(triisopropylsiloxy)-phenaleno[1,9-*bc*]furan (34). A 50-mL, three-necked, round-bottomed flask equipped with an argon inlet adapter, glass stopper, and rubber septum was charged with **29** (0.464 g, 0.944 mmol) and 15 mL of THF. The solution was cooled to −78 °C and then treated sequentially with MeLi (1.49 M in diethyl ether, 0.953 mL, 1.42 mmol) and, after 5 min, *n*-BuLi (2.49 M in hexanes, 0.569 mL, 1.42 mmol). After 10 min, a solution of acetone (2.84 g, 3.59 mL, 48.9 mmol) in 3 mL of THF was added dropwise via cannula, and the reaction mixture was stirred at −78 °C for 25 min. The reaction mixture was allowed to warm to 25 °C over 15 min and then stirred for 30 min. Methanol (6 mL) and aqueous HCl (10%, v/v, 3 mL) were then added, and the reaction mixture was heated at reflux for 4 h. The resulting mixture was allowed to cool to room temperature and then partitioned between 50 mL of diethyl ether and 50 mL of water. The aqueous layer was separated and extracted with three 50-mL portions of diethyl ether, and the combined organic phases were washed with 50 mL of water, 50 mL of saturated $NaHCO_3$, and 50 mL of brine, dried over $MgSO_4$, filtered, and concentrated to give 0.518 g of a blue-green oil. Column chromatography on 20 g of silica gel (elution with hexanes) afforded 0.271 g (63%) of **34** as a clear, colorless oil, which partially crystallized on standing at 14 °C to a white solid: mp 98–99 °C; IR (CCl_4) 2970, 2875, 1630, 1590, 1485, 1460, 1395, 1380, 1325, 1310, 1255, 1230, 1130, 1110, 1040, 885, and 865 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.18 (d, J = 6.5 Hz, 1 H), 6.88 (d, J = 6.5 Hz, 1 H), 3.77 (septet, J = 7.0 Hz, 1 H), 2.91–3.09 (m, 3 H), 2.06–2.13 (m, 1 H), 1.78–1.83 (m, 1 H), 1.70 (s, 6 H), 1.30–1.45 (m, 12 H), and 1.19 (d, J = 7.3 Hz, 18 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.9, 151.6, 143.5, 137.4, 126.2, 122.7, 117.6, 111.5, 111.3, 92.5, 32.4, 31.6, 28.5, 28.3, 25.5, 22.7, 21.4, 21.3, 20.6, 18.2, and 14.5; HRMS *m/e* calcd for $C_{29}H_{44}O_2Si$ 452.3111, found 452.3112.

Salvilenone (1). A 25-mL, round-bottomed flask equipped with an argon inlet adapter was charged with **34** (0.186 g, 0.411 mmol), 8 mL of THF, and tetrabutylammonium fluoride (1.0 M in THF, 0.617 mL, 0.617 mmol). The resulting yellow solution was stirred at room temperature for 15 min and then poured into 20 mL of water. The aqueous layer was separated and extracted with 20 mL of diethyl ether, and the combined organic phases were washed with 20 mL of water and 20 mL of brine, dried over $MgSO_4$, filtered, and concentrated to give a yellow oil which was immediately dissolved in 400 mL of benzene and degassed with a stream of argon for 20 min. 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (0.102 g, 0.449 mmol) was then added, and the reaction mixture was stirred at room temperature for 2 h and then concentrated to give 0.380 g of a dark yellow oil. Column chromatography on 25 g of silica gel (elution with 5% ethyl acetate–hexanes) afforded 0.089 g of a yellow oil. Further purification on 20 g of silica gel (elution with 0–5% ethyl acetate–hexanes) provided 0.077 g (64%) of salvilenone (**1**) as yellow crystals: mp 142–143 °C (lit.[6] mp 141.2 °C); IR ($CHCl_3$) 2955, 2920, 1600, 1555, 1520, 1440, 1370, 1305, 1175, 1075, 975, and 900 cm^{-1}; UV max (CH_3CN) 352 (ε = 9600), 328 (10 500), 236 (36 500), 211 (31 700), and 194 (32 800) nm; ^1H NMR (300 MHz, $CDCl_3$) δ 8.34 (d, J = 7.7 Hz, 1 H), 8.11 (d, J = 8.5 Hz, 1H), 7.54 (d, J = 7.7 Hz, 1 H), 7.43 (d, J = 8.5 Hz, 1 H), 3.43 (septet, J = 6.9 Hz, 1 H), 2.78 (s, 3 H), 1.76 (s, 6 H), and 1.33 (d, J = 7.5 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.5, 165.4, 145.9, 140.4, 129.8, 129.3, 128.6, 127.8, 127.5, 125.4, 122.9, 119.4, 118.2, 96.1, 26.9, 24.2, 21.0, and 19.2. Anal. Calcd for $C_{20}H_{20}O_2$: C, 82.16; H, 6.89. Found: C, 81.89; H, 6.92.

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