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No Acid Required: 4π and 6π Electrocyclization Reactions of Dienyl Diketones for the Synthesis of Cyclopentenones and 2*H*-Pyrans

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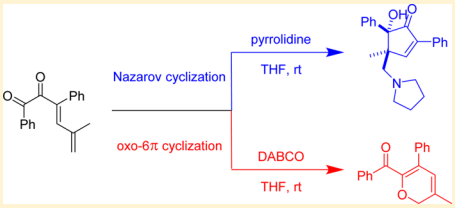
Supporting Information

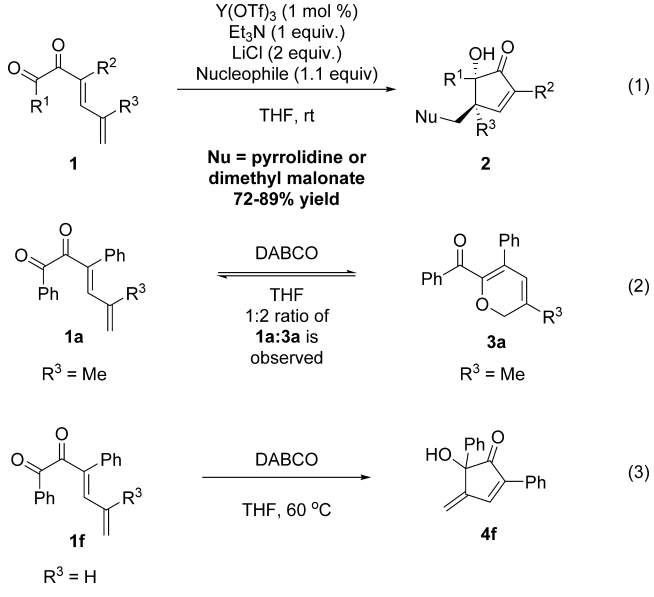
ABSTRACT: The 1,6-conjugate addition of nucleophiles to dienyl diketones produces either cyclopentenone or 2*H*-pyran products with high selectivity through either Nazarov (4π) or 6π electrocyclization, respectively. The outcome of the reaction is dependent upon the nature of the nucleophile used. Nucleophiles that are anionic or easily deprotonated exclusively produce cyclopentenones via Nazarov cyclization, whereas the neutral nucleophile DABCO promotes 6π cyclization to afford 2*H*-pyrans. Experimental evidence is presented for both retro-4π and -6π electrocyclization in these systems, lending support to the bifurcated mechanistic hypothesis proposed for these cyclizations.



INTRODUCTION

Electrocyclic reactions are becoming increasingly valuable in synthesis as chemists continue to develop new methods for catalyzing these cyclizations.[1] In recent years, mild catalytic methods for achieving neutral,[2] cationic,[3] and anionic[4] cyclizations have been reported with a broad set of applications, including efficient synthesis of heterocycles and rapid, stereospecific assembly of densely functionalized carbocyclic systems. As one might expect, neutral cyclizations occur either spontaneously or with heating, cationic reactions typically require catalysis with either a Brønsted or Lewis acid species, and anionic reactions proceed under basic conditions. However, emerging evidence suggests that "cationic" electrocyclizations can occur thermally without the addition of acid.[5] In this paper, we examine cationic 4π and neutral 6π electrocyclic reactions of dienyl diketones, determine the utility of the reactions for the selective synthesis of either cyclopentenones or 2*H*-pyrans, and discuss the apparent contradiction of proposing a cationic electrocyclization mechanism for a reaction that occurs under neutral or even basic conditions.

We previously described a Lewis acid that promoted 1,6-conjugate addition to initiate Nazarov cyclization.[6] For example, treatment of dienyl diketones **1** ($R^3 \neq H$) with catalytic Lewis acid, lithium chloride, and triethylamine as a base, and in the presence of a nucleophile, results in their smooth conversion to cyclopentenones **2** (eq 1). However, treatment of the same dienyl diketones **1** with the nucleophilic tertiary amine DABCO (1,4-diazabicyclo[2.2.2]octane) leads to two different types of cyclization products: either 2*H*-pyrans **3** (eq 2)[7] or 4-methylene cyclopentenones **4** (eq 3), depending upon the R^3 substituent on the dienone. In this paper, we analyze the factors that control cyclization behavior and allow for the efficient synthesis of elusive pyrans **3**, 5-hydroxy γ-alkylidene cyclopentenones **4**, or the highly substituted cyclopentenone systems of type **2**.



RESULTS AND DISCUSSION

Treatment of **1a** (R^3 = Me) with DABCO (10 mol %) at room temperature gave a 1:2 ratio of **1a** and **3a** after 8 h (entry 1, Table 1). Similarly, when pyran **3a** is resubjected to 1 equiv of DABCO for 24 h, **1a** and **3a** are again obtained at a 1:2 ratio. In contrast, formation of pyrans **3** from dienyl diketones **1** is efficient in substrates with bulkier R^3 substituents (entries 2–4, Table 1). As shown in Table 1, rapid, complete conversion to **3** is observed for substrates with larger R^3 substituents (e.g., **1b**, **1c**, **1d**). Interestingly, when **1e** is subjected to the reaction conditions (entry 5), pyran **3e** was generated, but the

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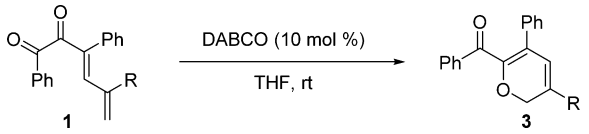
Table 1. DABCO-Induced Cyclizations[a]

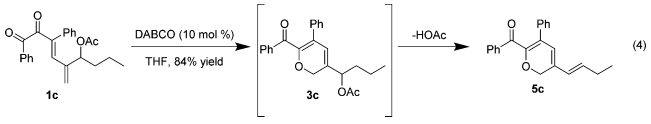


entry	R	product, yield	reaction time
1	**1a**	b	8h
2	**1b**,	3b, 98%	<1h
3	**1c**,	c	<5 min
4	**1d**,	3d, 96%	1h
5	**1e**,	3e, 84%	8h

[a]The diene was dissolved in THF (1 M), and DABCO (10 mol %) was added. The solution was stirred at room temperature until all starting material was consumed by TLC, unless otherwise noted. [b]Conversion to **3a** is incomplete (see eq 2); equilibrium is reached after 2 h. [c]See eq 4.

cyclization was much slower than that of the previous substrates (**1b** or **1d**). Presumably, this is because the steric impact of a methylene group at the homoallylic position is not as strong as that of an acetate. These findings are consistent with previous studies that found that an oxatriene/pyran ratio is affected by substitution pattern and that steric bulk at R^3 favors pyran **3**.[8]

In the case of secondary allylic acetate **1c**, treatment with DABCO rapidly produces **5c** (entry 3, Table 1; eq 4).



Monitoring the reaction by ^{1}H NMR at low concentration, we were able to observe the following reaction sequence: cyclization generates pyran **3c**, followed by net loss of HOAc to afford *trans*-alkene **5c**. We suggest that the acetate is first ionized to generate a stabilized cation and then deprotonated at the homoallylic position.

To further probe this reactivity and the role of the nucleophile, we subjected several dienyl diketones to both pyrrolidine and DABCO (Table 2). When diketones **1a** and **1f** were treated with pyrrolidine, they proceeded rapidly to cyclopentenones **2a** and **2f**, even without a Lewis acid. However, when treated with DABCO, they proceeded to **3a** and **4f**, respectively, as described above. Dienyl diketones **1g** and **1h** showed the same cyclization behavior: When treated with pyrrolidine, both substrates proceeded to cyclopentenone products **2g** and **2h**, respectively, as a mix of diastereomers (entries 3 and 5, Table 2). When treated with DABCO, **1g** and **1h** produced pyrans **3g** and **3h**, respectively (entries 4 and 6, Table 2). This demonstrates that the outcome of the reaction can be controlled by nucleophile choice. X-ray crystallography confirms that product **2a** has the same stereochemistry (Supporting Information) as previously described cyclopentenones produced when a Lewis acid was used to catalyze the reaction.

Previous reports have established that the interconversion between the *cis*-1,3-dienone and 2*H*-pyran by oxa-6π electrocyclization/retro-electrocyclization is facile;[9] however, the

Table 2. Selective 4π and 6π Electrocyclizations of Dienyl Diketones 1[a]

entry	substrate	amine	product	% yield
1	**1a**	HN	**2a**	85
2	**1a**	N	**3a**	66
3	**1f**	HN	**2f**	87
4	**1f**	N	**4f**[b]	93
5[c]	**1g**	HN	**2g**	56[d]
6	**1g**	N	**3g**	86
7	**1h**	HN	**2h**	35[d]
8	**1h**	N	**3h**	92

[a]Reaction conditions: nucleophile (1 equiv) was added to substrate in THF (1 M), and the reaction was monitored by TLC or NMR. [b]Product is formed by Nazarov cyclization followed by DABCO elimination. [c]Twenty percent of 2*H*-pyran product **3g** was also observed. [d]Product obtained as an inseparable mixture of diastereoisomers: 1.2:1 dr (**2g**) and 6:1 dr (**2h**) as determined by ^{1}H NMR spectroscopy.

studies suggest that equilibrium favors the closed form only when the pyran contains sterically demanding substitutents,[10] or is part of a bicyclic system,[11] and is therefore substrate dependent. However, *trans*-1,3-dienone is unreactive unless it can be smoothly isomerized to the *cis* isomer. The isomer-

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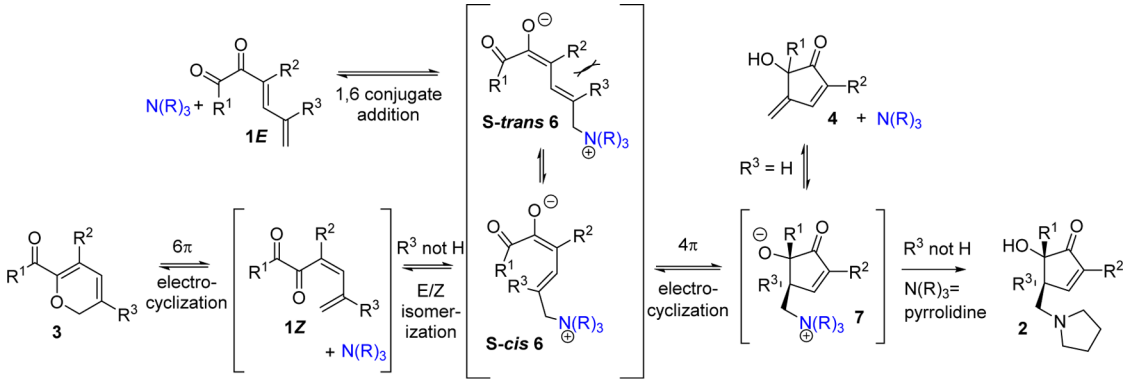
Scheme 1. Mechanistic Hypothesis for a Bifurcated Reaction Pathway



ization is traditionally accomplished by UV irradiation;[12] however, these reactions often have low yields and generate undesired side products. Preparing *cis*-1,3-dienones directly[13−15] is also challenging;[16] thus, the DABCO protocol demonstrated in Table 1 represents an improved method for the synthesis of 2*H*-pyrans, which are found in a number of natural products.[17]

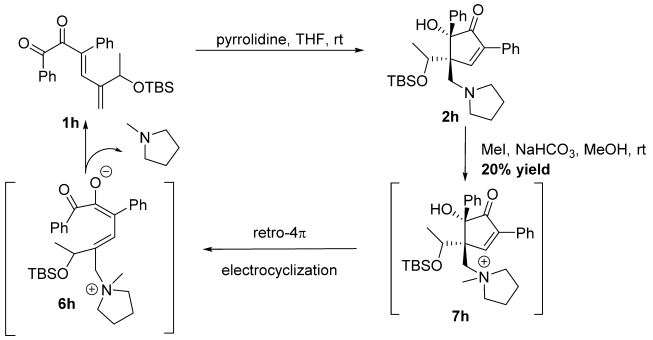
A mechanistic hypothesis for the observed cyclization behavior of dienyl diketones **1** is offered in Scheme 1.[18] Upon 1,6-conjugate addition of an amine nucleophile to **1**, the internal olefin is able to rotate freely in intermediate **6**, enabling the substrate to adopt a conformation in which it can undergo cyclization. When the nucleophile is a secondary amine, 4π electrocyclization (**6** to **7**) is followed by proton transfer to form cyclopentenone adduct **2**.

Using the tertiary amine DABCO as the nucleophile, the outcome and rate of reaction are dependent upon the size of R^3. If R^3 = H, 1,6-addition/Nazarov cyclization produces **7** as usual, and then elimination of DABCO produces methylene cyclopentenone **4**. However, if $R^3 \neq$ H, the high-energy electrocyclization product **7** cannot be deprotonated or otherwise neutralized, so the only available pathway is retro-4π electrocyclization, which regenerates S-*cis* **6**. The elimination of DABCO from **6** can produce either **1*E*** (from the S-*trans* isomer) or **1*Z*** (from the S-*cis* isomer). Since **1*Z*** is never observed by NMR, we surmise that it undergoes rapid 6π electrocyclization to afford pyran **3**.

With respect to the 6π electrocyclization pathway, we propose that the ratio of S-*trans* **6** to S-*cis* **6** increases as R^2 and R^3 become larger, corresponding to a higher proportion of **1*Z***/**3** relative to **1*E*** (see eq 2). Furthermore, larger substituents at R^3 increase the overall rate of pyran formation (see Table 1), suggesting that bond rotation is rate-limiting. These observations lead to the general prediction that in reactions of dienyl diketones **1** with uncharged nucleophiles, 4π cyclization products **2** and **4** will be obtained if intermediate **7** can be deprotonated (i.e., when the nucleophile is a secondary amine or when R^3 = H), whereas 6π cyclization products **3** (or an equilibrium mixture of **1*E*** and **3**) will result when it cannot.[19]

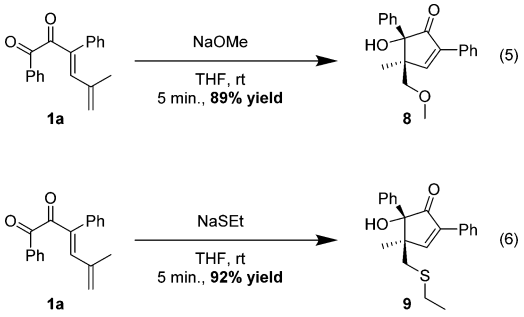
To test the feasibility of the proposed retro-4π electrocyclization,[20] we treated pyrrolidine adduct **2h** (Scheme 2) with iodomethane to give intermediate **7h**. This intermediate is analogous to the zwitterions formed when DABCO is used, and dienyl diketone **1h** is produced. Presumably, a retro-Nazarov-type reaction of **7h** produces **6h**, which can then eliminate to give the dienyl diketone **1h**.

Scheme 2. Execution of Retro-Nazarov Cyclization



Given that in Table 2 and eq 3 4π "cationic" electrocyclizations occur in the presence of neutral nucleophiles alone via a putative zwitterionic intermediate, we treated methyl-substituted dienyl diketone **1a** with anionic nucleophiles to test the limits of nucleophile-initiated cyclizations. Reactions with sodium methoxide (eq 5) and sodium ethanethiolate (eq 6) proceeded very cleanly to afford addition products **8** and **9**, respectively (Scheme 3). Sodium cyanide and sodium azide gave complex mixtures of products, presumably resulting from unselective 1,2-, 1,4-, and 1,6-addition.

Scheme 3. Reactions with Anionic Nucleophiles



The idea that a 4π "cationic" electrocyclization might occur without acid, and without the formation of a discrete pentadienyl cation, leads to the following questions: is this really Nazarov cyclization, and does it conform to pericyclic selection rules? We propose that even though critical intermediate **6** is not cationic (Scheme 1), it can be considered to have "pentadienyl cation character" in the same way cyclopropenone has aromatic character and cyclopentadienone has antiaromatic character. A survey of the literature reveals

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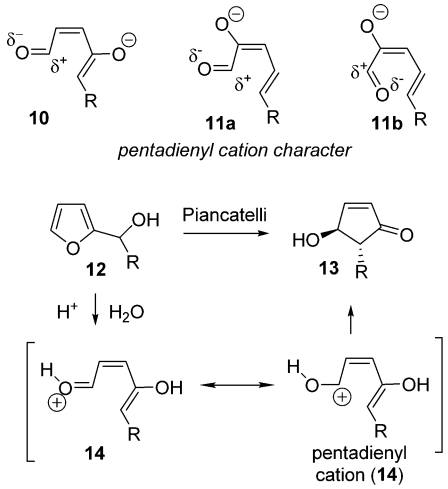
that cyclization of enolates of type **10** and **11** (Scheme 4) generates cyclopentenones with suspiciously high diastereoselectivity under basic conditions.[21] Because a canonical pentadienyl cation intermediate cannot be invoked in these reactions, one could argue that these cyclizations are intramolecular aldol reactions that occur without conservation of orbital symmetry.[22] However, the diastereoselectivity observed is difficult to rationalize unless one invokes conrotatory electrocyclization. Furthermore, the systems have the same substitution pattern as Piancatelli cyclization,[23] which is also an intramolecular aldol reaction (Scheme 4), but one that is acid catalyzed and therefore more easily rationalized as pericyclic.[24,25]

Scheme 4. Cyclization of Enolates



In our system, the 1,6-conjugate-addition-initiated cyclization of dienyl diketones **1** generates cyclopentenones with the same relative stereochemistry (cf. **2a**−**2i**, **8**, and **9**) independent of whether the reaction is catalyzed by a Lewis acid (eq 1), uncatalyzed under neutral conditions (Table 2, entries 1, 3, 5, and 7), or uncatalyzed under basic conditions (eqs 5 and 6). This suggests that 4π conrotatory cyclization occurs in all of the cyclizations of dienyl diketone **1** through either an enol or an enolate intermediate of type **11a** (Scheme 4) with pentadienyl cation character. It is also important to note that while conformer **11b** would undergo 4π conrotatory cyclization to produce the opposite (undetected) diastereoisomer, it is likely that the orientation of the carbonyl could make 6π electrocyclization more favorable for this conformer.

In conclusion, we have described the 1,6-conjugate addition of a nucleophile to dienyl diketones to generate cyclopentenones **2** and **4** and 2*H*-pyrans **3** through a bifurcated mechanism. We have also demonstrated that electrocyclization/retroelectrocyclization pathways control product distribution in these reactions, which suggests that the intermediates undergoing 4π cationic Nazarov electrocyclization need not carry a net positive charge. Further investigations are underway, including asymmetric variants of the 1,6-conjugate-addition/Nazarov-cyclization sequence.

EXPERIMENTAL SECTION

Substrates **1a** and **1d**−**f** are known compounds synthesized following reported procedures.[6]

General Procedure A for the Synthesis of Dienyl Diketones. Dienyl diketone was prepared following a known procedure[26] from *tert*-butyldimethyl((3-methylene-5-phenylpent-4-yn-2-yl)oxy)silane and phenylglyoxal. $Rh(COD)_2OTf$ (0.131 g, 0.28 mmol) and Rac-BINAP (0.208 g, 0.34 mmol) were added to a flame-dried 100 mL round-bottom flask in a glovebox. Dry dichloroethane (DCE) (25 mL) was then added, and the reaction mixture was allowed to stir for 30 min at room temperature in an inert atmosphere; the color changed from red to orange. Phenylglyoxal (1.28 g, 8.4 mmol) and ene-yne (5.6 mmol) were then added to the DCE (25 mL), and the solution was purged with hydrogen gas for 1 h. During this time, it became necessary to flush a clogged needle with DCE. Once all of the solids had dissolved, the outlet was removed and the flask was charged with hydrogen gas overnight, during which time the color changed from dark red to black. Once the starting material was consumed, the reaction products were concentrated and subjected to quick column chromatography (silica gel, 4:1 hexane/EtOAc) to give a yellow product that was impure by TLC. This was then taken up in DMSO, (3 mL) and one portion of IBX (1.18 g, 4.2 mmol) was added. The reaction mixture was allowed to stir until all of the starting material was consumed by TLC. The reaction products were then quenched with water, extracted with diethyl ether, dried with $MgSO_4$, and concentrated. The products were then purified by flash chromatography (silica gel, 9:1 hexane/EtOAc).

*(E)-5-Methyl-1,3-diphenylhexa-3,5-diene-1,2-dione (**1a**).* The product was synthesized according to general procedure A, isolated as a yellow oil, and purified by flash chromatography (9:1 hexane/EtOAc, 1.35 g, 87%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, J = 7.5 Hz, 2H), 7.71 (t, J = 7.4 Hz, 1H), 7.57 (t, J = 7.6 Hz, 2H), 7.47−7.41 (m, J = 3.2 Hz, 3H), 7.31 (dd, J = 6.5, 3.7 Hz, 2H), 5.39 (s, 2H), 1.48 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 196.9, 195.5, 149.2, 141.3, 137.5, 134.8, 134.0, 133.4, 130.3, 129.8, 129.1, 128.6, 128.5, 128.2, 21.3. IR (neat, cm^{-1}): 3460, 2955, 2363, 2335, 1716, 1456, 1439, 1288, 1218, 1153, 1067, 696. LRMS (APCI, m/z): calcd for $C_{19}H_{16}O_2$, 276.1; found, 276.7.

*(E)-2-Methylene-5,6-dioxo-4,6-diphenylhex-3-en-1-yl Acetate (**1b**).* The product was synthesized according to general procedure A and purified by silica gel chromatography using 9:1 hexane/EtOAc as the eluent to give the dienyl diketone **1b** (0.67 g, 72% yield). ^{1}H NMR (400 MHz, CDCl3): δ 7.90 (d, J = 7.9 Hz, 2H), 7.64 (t, J = 7.3 Hz, 1H), 7.49 (dd, J = 17.6, 10.0 Hz, 2H), 7.38 (d, J = 4.8 Hz, 3H), 7.27−7.19 (m, 2H), 7.16 (s, 1H), 5.54 (s, 1H), 5.44 (s, 1H), 4.20 (s, 2H), 1.95 (s, 3H). ^{13}C NMR (126 MHz, CDCl3): δ 196.1, 195.0, 170.0, 148.0, 144.7, 139.4, 138.4, 134.9, 133.6, 133.2, 129.8, 129.7, 129.3, 129.1, 128.9, 128.5, 128.4, 127.5, 126.3, 64.4, 20.8. IR (neat, cm^{-1}): 3059, 2160, 2033, 1975, 1739, 1670, 1597, 1450, 1373, 1226, 1041, 698. LRMS (APCI, m/z): calcd for $C_{21}H_{18}O_4$, 334.4; found, 334.8.

*(E)-5-Methylene-8,9-dioxo-7,9-diphenylnon-6-en-4-yl Acetate (**1c**).* The product was synthesized according to general procedure A. Chromatography (silica gel, 9:1 hexane/EtOAc) afforded **1c** as a bright yellow oil (0.316 g, 15% over two steps). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.97 (dd, J = 8.3, 1.2 Hz, 2H), 7.70 (dd, J = 10.6, 4.3 Hz, 1H), 7.57 (t, J = 7.8 Hz, 2H), 7.48−7.38 (m, 3H), 7.33−7.27 (m, 3H), 7.16 (s, 1H), 5.41 (s, 1H), 5.18−5.10 (m, 2H), 2.03 (s, 3H), 1.54 (m, J = 18.8, 14.0, 9.3, 5.3 Hz, 3H), 1.34−1.23 (m, 2H), 1.15−1.00 (m, 2H), 0.87 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 196.0, 195.1, 170.0, 143.5, 142.7, 139.3, 134.7, 133.4, 133.2, 129.6, 129.6, 129.0, 128.7, 128.5, 123.5, 74.9, 36.1, 21.0, 18.6, 13.6. HRMS (ESI-TOF, m/z): $[M + H]^+$ calcd for $C_{24}H_{24}O_4$, 377.1753; found, 377.1751.

*(E)-3-Methylene-6,7-dioxo-5,7-diphenylhept-4-en-1-yl Acetate (**1d**).* The product was synthesized according to general procedure A, isolated as a yellow oil, and purified by flash chromatography (9:1 hexane/EtOAc, 1.64 g, 84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, J = 7.6 Hz, 2H), 7.64 (t, J = 7.3 Hz, 1H), 7.51 (t, J = 7.6 Hz, 2H), 7.37 (d, J = 6.3 Hz, 3H), 7.24 (d, J = 7.7 Hz, 2H), 7.14 (s, 1H), 5.33 (s, 1H), 5.28 (s, 1H), 3.90 (t, J = 6.5 Hz, 2H), 2.15 (t, J = 6.5 Hz, 2H), 1.94 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 196.4, 195.2, 170.9, 147.7, 140.8, 138.0, 134.9, 133.3, 130.3, 130.0, 129.1, 128.4, 127.3, 62.7, 33.5, 20.9. IR (neat, cm^{-1}): 3441, 3059, 2931, 1747, 1681, 1597, 1492, 1450, 1265, 1172, 1103, 732, 694. LRMS (APCI, m/z): calcd for $C_{22}H_{20}O_4$, 348.1; found, 348.8.

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*(E)-5-Methylene-8,9-dioxo-7,9-diphenylnon-6-en-1-yl Acetate (**1e**).* The product was synthesized according to general procedure A, isolated as a yellow oil, and purified by flash chromatography (9:1 hexane/EtOAc, 1.79 g, 85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, J = 7.2 Hz, 2H), 7.64 (t, J = 7.4 Hz, 1H), 7.51 (t, J = 7.7 Hz, 2H), 7.40−7.34 (m, 3H), 7.26−7.20 (t, 2H), 7.13 (s, 1H), 5.28 (d, J = 1.0 Hz, 1H), 5.22 (s, 1H), 3.87 (t, J = 6.2 Hz, 2H), 2.01 (s, 3H), 1.82 (t, J = 7.1 Hz, 2H), 1.33−1.20 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 196.6, 195.4, 171.2, 148.4, 144.5, 137.8, 134.8, 133.9, 133.4, 130.0, 129.8, 129.1, 128.6, 128.4, 125.9, 64.2, 34.1, 28.1, 25.1, 21.1. IR (neat, cm^{-1}): 2947, 2866, 1735, 1670, 1581, 1450, 1365, 1238, 1203, 1141, 979, 663. LRMS (APCI, m/z): calcd for $C_{24}H_{24}O_4$, 376.2; found, 376.8.

*(E)-1,3-Diphenylhexa-3,5-diene-1,2-dione (**1f**).* The product was synthesized according to general procedure A, obtained as a yellow oil, and carried through to the next reaction without further purification. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, J = 7.2 Hz, 2H), 7.65 (t, J = 10.6 Hz, 1H), 7.52 (t, J = 7.7 Hz, 2H), 7.36−7.46 (m, 3H), 7.26−7.31 (m, 2H), 7.16 (d, J = 11.0 Hz, 1H), 6.48−6.61 (m, 1H), 5.71 (d, J = 16.9 Hz, 1H), 5.56 (d, J = 10.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 196.1, 195.1, 147.0, 138.5, 134.9, 133.3, 133.2, 132.8, 130.3, 129.9, 129.2, 129.1, 128.6, 128.5. IR (neat, cm^{-1}): 3059, 1735, 1677, 1658, 1612, 1450, 1222, 1141, 698. HRMS (ESI-TOF, m/z): $[M + H]^+$ calcd for $C_{18}H_{15}O_2$, 263.1072; found, 263.1072.

*(E)-6-Hydroxy-5-methylene-1,3-diphenylhept-3-ene-1,2-dione (**1g**).* Dienyl diketone **1g** was prepared by dissolving **1h** in MeOH (1 mL) and adding HCl (1 M, aq) dropwise while stirring. If formation of a precipitate was observed, methanol was added until it dissolved. Reaction was observed by TLC until all starting material was consumed. Product was extracted with diethyl ether and concentrated to afford **1g** as a bright yellow oil (0.46 g, 94% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.98 (d, J = 7.4 Hz, 2H), 7.70 (t, J = 7.4 Hz, 1H), 7.57 (t, J = 7.8 Hz, 2H), 7.48−7.37 (m, 4H), 7.30 (dd, J = 6.0, 4.6 Hz, 3H), 7.24 (s, 1H), 5.48 (s, 1H), 5.07 (s, 1H), 4.25 (m, J = 6.4 Hz, 1H), 1.64 (d, J = 18.2 Hz, 1H), 1.26 (d, J = 6.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 196.0, 195.1, 147.2, 144.7, 139.4, 134.8, 133.8, 133.2, 129.62, 129.55, 129.0, 128.7, 128.4, 121.1, 69.4, 22.8. HRMS (ESI-TOF, m/z): $[M + H]^+$ calcd for $C_{20}H_{18}O_3$, 307.1334; found, 307.1336.

*(E)-6-((tert-Butyldimethylsilyl)oxy)-5-methylene-1,3-diphenylhept-3-ene-1,2-dione (**1h**).* The product was synthesized according to general procedure A. Chromatography (silica gel, 9:1 hexane/EtOAc) afforded **1h** as a bright yellow oil (0.71 g, 30% yield over two steps). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.99 (d, J = 7.6 Hz, 2H), 7.69 (d, J = 7.3 Hz, 1H), 7.56 (t, J = 7.7 Hz, 2H), 7.49−7.38 (m, 3H), 7.31 (d, J = 6.7 Hz, 2H), 7.26 (s, 1H), 5.45 (s, 1H), 5.02 (s, 1H), 4.20 (q, J = 6.2 Hz, 1H), 1.17 (d, J = 6.3 Hz, 3H), 0.85 (d, J = 12.0 Hz, 9H), −0.03 (d, J = 11.4 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 196.32, 195.36, 147.66, 145.39, 138.93, 134.66, 134.02, 133.28, 129.7, 129.6, 129.0, 128.6, 128.3, 120.9, 70.1, 25.7, 24.4, 18.0, −5.0. HRMS (ESI-TOF, m/z): $[M + H]^+$ calcd for $C_{26}H_{32}O_3Si$, 421.2199; found, 421.2196.

General Procedure B for the Formation of 2*H*-Pyrans 3a,b,d−h, 4f, and 5c Using DABCO. To a solution of dienyl diketone in THF (1 M) was added DABCO in one portion at room temperature. The reactions were monitored by TLC until the starting material was consumed (in cases where the starting material and product have identical R_f values, the reactions were monitored by ^{1}H NMR). The reaction was then quenched with HCl (1 M, aq), and the mixture was extracted with diethyl ether, dried with magnesium sulfate, and concentrated. The compounds were then purified by silica gel chromatography.

*(3-Methyl-5-phenyl-2H-pyran-6-yl)(phenyl)methanone (**3a**).* The product was obtained from **1a** using general procedure B, isolated as a bright yellow oil, and purified by flash chromatography (9:1 hexane/EtOAc, 33 mg, 66% (equilibrium mix of 2*H*-pyran and dienyl diketone)). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.79 (d, J = 7.4 Hz, 2H), 7.42 (t, J = 7.4 Hz, 1H), 7.29 (dd, J = 16.8, 9.2 Hz, 2H), 7.21−7.06 (m, 5H), 6.00 (d, J = 0.9 Hz, 1H), 4.69 (s, 2H), 1.88 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.5, 144.7, 1370, 136.8, 132.7, 130.4, 129.6, 128.4, 128.2, 128.1, 127.3, 123.3, 121.7, 68.9, 19.2. HRMS (ESI-TOF, m/z): $[M + H]^+$ calcd for $C_{19}H_{16}O_2$, 277.1229; found, 277.1225.

*(6-Benzoyl-5-phenyl-2H-pyran-3-yl)methyl Acetate (**3b**).* The product was obtained from **1b** using general procedure B, isolated as a white solid, and purified by flash chromatography (4:1 hexane/EtOAc, 49 mg, 98%) ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.88−7.84 (m, 2H), 7.59−7.55 (m, 1H), 7.53−7.47 (m, 2H), 7.41−7.35 (m, 3H), 7.26−7.17 (m, 2H), 6.35 (2, 1H), 4.84 (s, 1H), 4.76 (s, 1H), 2.17 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.3, 170.8, 147.2, 136.4, 136.2, 133.3, 129.9, 129.8, 129.1, 128.6, 128.5, 128.4, 128.4, 127.7, 126.4, 125.1, 121.6, 66.3, 64.5, 21.0. IR (neat, cm^{-1}): 3059, 2928, 1739, 1670, 1450, 1234, 1180, 1022. LRMS (APCI, m/z): calcd for $C_{21}H_{18}O_4$, 234.4; found, 234.8.

*2-(6-Benzoyl-5-phenyl-2H-pyran-3-yl)ethyl Acetate (**3d**).* The product was obtained from **1d** using general procedure B as a yellow oil after flash chromatograpy (9:1 hexane/EtOAc, 48 mg, 96%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (t, J = 7.7 Hz, 2H), 7.43 (t, J = 7.4 Hz, 1H), 7.31 (t, J = 7.7 Hz, 2H), 7.21−7.10 (m, 5H), 6.10 (s, 1H), 4.73 (s, 2H), 4.26 (t, J = 6.6 Hz, 2H), 2.52 (t, J = 6.4 Hz, 2H), 2.08 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 191.5, 171.0, 145.8, 136.7, 136.6, 133.1, 129.9, 129.7, 128.5, 128.3, 128.3, 127.6, 123.2, 122.9, 68.1, 62.3, 32.9, 21.1. IR (neat, cm^{-1}): 3425, 3063, 2962, 2935, 1735, 1678, 1581, 1492, 1450, 1365, 1234, 1037, 698. LRMS (APCI, m/z): calcd for $C_{22}H_{20}O_4$, 348.1; found, 348.8.

*4-(6-Benzoyl-5-phenyl-2H-pyran-3-yl)butyl Acetate (**3e**).* The product was obtained from **1e** using general procedure B, isolated as a yellow oil, and purified by flash chromatography (9:1 hexane/EtOAc, 44 mg, 84%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78 (d, J = 7.1 Hz, 2H), 7.41 (t, J = 8.2 Hz, 1H), 7.30 (t, J = 7.7 Hz, 2H), 7.19−7.10 (m, 5H), 6.01 (s, 1H), 4.69 (s, 2H), 4.10 (t, J = 6.4 Hz, 2H), 2.22 (t J = 7.1 Hz, 2H), 2.05 (s, 3H), 1.74−1.56 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.6, 171.3, 145.3, 137.0, 136.8, 136.0, 133.8, 132.9, 130.3, 129.7, 129.2, 128.5, 128.3, 128.2, 127.5, 123.8, 123.5, 121.3, 68.1, 64.2, 58.9, 42.3, 33.1, 28.4, 23.4, 21.1. IR (neat, cm^{-1}): 2935, 2858, 2360, 2341, 1735, 1666, 1597, 1446, 1365, 1242, 1018, 698. LRMS (APCI, m/z): calcd for $C_{24}H_{24}O_4$, 376.2; found, 376.8.

*(3-(1-Hydroxyethyl)-5-phenyl-2H-pyran-6-yl)(phenyl)methanone (**3g**).* The product was obtained from **1g** using general procedure B, isolated as a bright yellow oil, and purified by flash chromatography (9:1 hexane/EtOAc, 43 mg, 86%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.92 (d, J = 7.6 Hz, 2H), 7.43 (t, J = 7.3 Hz, 2H), 7.34−7.17 (m, 5H), 7.15−6.95 (m, 3H), 6.65 (s, 1H), 5.43 (s, 1H), 5.24 (s, 2H), 5.09 (d, J = 6.3 Hz, 1H), 1.54 (d, J = 6.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 195.3, 143.2, 138.2, 136.5, 133.6, 132.7, 130.2, 128.3, 128.0, 128.0, 127.8, 126.8, 113.3, 95.0, 66.6, 18.0. HRMS (ESI-TOF, m/z): $[M + H]^+$ calcd for $C_{20}H_{18}O_3$, 307.1334; found, 307.1336.

*(3-(1-((tert-Butyldimethylsilyl)oxy)ethyl)-5-phenyl-2H-pyran-6-yl)-(phenyl)methanone (**3h**).* The product was obtained from **1h** using general procedure B, isolated as a yellow oil, and purified by flash chromatography (9:1 hexane/EtOAc, 27 mg, 54%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.83−7.78 (m, 2H), 7.43 (t, J = 7.4 Hz, 1H), 7.32 (t, J = 7.7 Hz, 2H), 7.26 (s, 1H), 7.19−7.12 (m, 5H), 6.14 (d, J = 1.0 Hz, 1H), 4.78 (d, J = 7.3 Hz, 2H), 4.47 (d, J = 6.3 Hz, 1H), 1.35 (d, J = 6.4 Hz, 3H), 0.92 (s, 10H), 0.11 (s, 7H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.4, 146.1, 136.81, 136.77, 136.6, 132.9, 129.6, 128.4, 128.2, 128.1, 127.4, 123.0, 119.7, 69.3, 65.4, 25.8, 25.8, 22.9, 18.2, −4.7, −4.8. HRMS (ESI-TOF, m/z): $[M + H]^+$ calcd for $C_{26}H_{32}O_3Si$, 421.2199; found, 421.2184.

*(E)-(3-(But-1-en-1-yl)-5-phenyl-2H-pyran-6-yl)(phenyl)-methanone (**5c**).* The product was obtained from **1c** using general procedure B, isolated as yellow oil, and purified by flash chromatography (9:1 hexane/EtOAc, 35 mg, 84%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.80 (d, J = 7.5 Hz, 2H), 7.43 (t, J = 7.4 Hz, 1H), 7.30 (m, J = 20.1, 12.4 Hz, 3H), 7.23−7.05 (m, 6H), 6.17 (d, J = 16.0 Hz, 1H), 6.11 (s, 1H), 5.76 (dt, J = 15.8, 6.6 Hz, 1H), 4.97 (s, 2H), 2.22 (m, J = 7.0 Hz, 2H), 1.07 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.2, 146.1, 136.9, 136.7, 134.5, 132.8, 129.8, 129.6, 128.5, 128.2, 128.1, 127.4, 126.9, 123.8, 123.2, 65.5, 26.3, 13.5. HRMS (ESI-TOF, m/z): calcd for $C_{22}H_{20}O_2$, 317.1542; found, 317.1544.

*5-Hydroxy-4-methylene-2,5-diphenylcyclopent-2-en-1-one (**4f**).* The product was obtained from **1f** using general procedure B and isolated as a pale yellow solid after flash chromatography (9:1 hexane/

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EtOAc, 44 mg, 88%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.15 (s, 1H), 7.88 (d, J = 7.4 Hz, 2H), 7.52−7.37 (m, 6H), 7.31 (dt, J = 19.4, 6.9 Hz, 3H), 5.61 (s, 1H), 5.49 (s, 1H), 3.39 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 204.3, 152.6, 149.9, 140.1, 139.9, 130.5, 129.6, 128.8, 128.6, 128.1, 127.4, 125.2, 114.3, 79.6. HRMS (ESI-TOF, m/z): $[M + Na]^+$ calcd for $C_{18}H_{14}O_2Na$, 285.0891; found, 285.0899.

General Procedure C for the Addition of Pyrrolidine to Dienyl Diketones 2a and 2h. To a solution of dienyl diketone in THF (1 M) was added pyrrolidine in one portion at room temperature. The reactions were monitored by TLC until the starting material was consumed. The reaction was then quenched with HCl (1 M, aq), and the mixture was extracted with diethyl ether, dried with magnesium sulfate, and concentrated. The compounds were then purified by silica gel chromatography.

*5-Hydroxy-4-methyl-2,5-diphenyl-4-(pyrrolidin-1-ylmethyl)-cyclopent-2-enone (**2a**).* The product was obtained from **1a** using general procedure C and isolated as a red solid by aqueous workup (280 mg, 85%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.00 (s, 1H), 7.87 (d, J = 7.1 Hz, 2H), 7.53−7.43 (m, 5H), 7.37−7.28 (m, 3H), 2.49−2.22 (m, 6H), 1.68 (s, 4H), 1.45 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 207.0, 169.6, 169.2, 158.7, 142.0, 139.4, 130.4, 129.3, 128.8, 128.6, 128.2, 127.0, 125.5, 84.1, 52.9, 52.7, 49.8, 49.2, 28.6. IR (neat, cm^{-1}): 3658−3162, 2966, 2931, 2796, 1712, 1597, 1446, 1307, 1060, 698. LRMS (APCI, m/z): calcd for $C_{23}H_{25}NO_2$, 347.2; found, 347.8.

*5-Hydroxy-2,5-diphenyl-4-(pyrrolidin-1-ylmethyl)cyclopent-2-enone (**2f**).* The product was obtained from **1f** using general procedure C and isolated as a red solid by aqueous workup (275 mg, 87%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.90 (d, J = 3.1 Hz, 1H), 7.86−7.80 (m, 2H), 7.54−7.49 (m, 2H), 7.49−7.41 (m, 3H), 7.38 (t, J = 7.6 Hz, 2H), 3.43−3.36 (m, 1H), 3.05 (dd, J = 17.4, 7.1 Hz, 2H), 2.71−2.57 (m, 4H), 2.09 (s, 1H), 1.84 (d, J = 6.4 Hz, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 205.4, 156.8, 143.6, 142.2, 131.2, 129.1, 128.7, 128.6, 127.5, 127.3, 124.6, 81.7, 57.1, 54.1, 49.9, 29.9, 23.7. IR (neat, cm^{-1}): 3678−3163, 3059, 3028, 2966, 2877, 1716, 1597, 1558, 1492, 1446, 1381, 698. LRMS (APCI, m/z): calcd for $C_{22}H_{23}NO_2$, 333.2; found, 333.9.

*5-Hydroxy-4-(1-hydroxyethyl)-2,5-diphenyl-4-(pyrrolidin-1-ylmethyl)cyclopent-2-en-1-one (**2g**).* The product was obtained from **1g** using general procedure C. Purification of the product was extremely difficult due to its high polarity and instability. The reaction also resulted in a roughly 1.2:1 mix of diastereomers (14 mg, 56%). HRMS (ESI-TOF, m/z): $[M + H]^+$ calcd for $C_{24}H_{27}NO_3$, 378.2069; found, 378.2073.

*(4S,5S)-4-((S)-1-((tert-Butyldimethylsilyl)oxy)ethyl)-5-hydroxy-2,5-diphenyl-4-(pyrrolidin-1-ylmethyl)cyclopent-2-en-1-one (**2h**).* The product was obtained from **1h** using general procedure C and isolated as a pale yellow oil after purification by column chromatography (4:1 hexane/EtOAc, 108 mg, 92%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.79 (d, J = 7.2 Hz, 2H), 7.68 (s, 1H), 7.47−7.40 (m, 5H), 7.39 (d, J = 7.2 Hz, 1H), 7.28−7.18 (m, 4H), 4.56 (d, J = 6.4 Hz, 1H), 4.18 (s, 1H), 2.63 (d, J = 14.0 Hz, 1H), 2.51 (d, J = 14.0 Hz, 2H), 2.33 (d, J = 5.0 Hz, 2H), 2.10 (d, J = 5.2 Hz, 2H), 1.58 (s, 4H), 1.36 (d, J = 6.4 Hz, 3H), 0.85 (s, 9H), 0.11 (d, J = 8.3 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 205.2, 157.6, 143.7, 140.5, 128.8, 128.8, 127.7, 127.1, 127.1, 126.9, 86.0, 72.3, 59.6, 56.5, 55.7, 25.9, 23.9, 20.3, 18.0, −3.6, −4.2. HRMS (ESI-TOF, m/z): $[M + H]^+$ calcd for $C_{30}H_{41}NO_3Si$, 492.2934; found, 492.2928.

*(4S,5S)-5-Hydroxy-4-(methoxymethyl)-4-methyl-2,5-diphenylcyclopent-2-en-1-one (**8**).* To a 1 M solution of **1a** (33 mg) in THF was added sodium methoxide (0.363 mL, 0.5 M in methanol) dropwise at room temperature. Once the starting material was consumed as observed by TLC, the reaction was quenched with water, and the mixture was extracted with ether, dried with $MgSO_4$, and concentrated. The product was isolated as a pale yellow oil and purified by flash chromatography (4:1 hexane/EtOAc, 33 mg, 89%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89 (s, 1H), 7.84 (d, J = 7.3 Hz, 2H), 7.48−7.34 (m, 5H), 7.28 (d, J = 6.2 Hz, 3H), 3.16−3.04 (m, 2H), 3.00 (s, 3H), 2.90 (dd, J = 48.8, 9.0 Hz, 2H), 1.38 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 207.7, 162.6, 141.1, 139.8, 130.7, 129.0, 128.7, 127.9, 127.8, 127.0, 126.6, 83.7, 76.1, 58.9, 51.7, 45.8, 21.1, 8.6. HRMS (ESI-TOF, m/z): $[M + H]^+$ calcd for $C_{20}H_{20}O_3$, 309.1491; found, 309.1496.

*(4R,5S)-4-((Ethylthio)methyl)-5-hydroxy-4-methyl-2,5-diphenylcyclopent-2-en-1-one (**9**).* To a 1 M solution of **1a** (33 mg) in THF was added sodium ethanethiolate (0.015 mg) in one portion at room temperature. Once the starting material was consumed as observed by TLC, the reaction was quenched with water, and the mixture was extracted with ether, dried with $MgSO_4$, and concentrated. The product was isolated as a pale yellow oil and purified by flash chromatography (4:1 hexane/EtOAc, 37 mg, 92%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.04 (s, 1H), 7.94−7.77 (m, 2H), 7.54−7.37 (m, 5H), 7.39−7.17 (m, 4H), 3.17 (s, 1H), 2.31 (m, J = 58.0, 49.6, 12.7 Hz, 4H), 1.43 (s, 3H), 1.09 (t, J = 7.4 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 207.0, 162.9, 141.1, 140.0, 130.5, 129.2, 128.8, 128.2, 127.9, 127.0, 126.4, 85.4, 51.6, 39.8, 28.3, 23.9, 14.7. HRMS (ESI-TOF, m/z): $[M + H]^+$ calcd for $C_{21}H_{22}O_2S$, 339.1419; found, 339.1416.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H NMR and ^{13}C NMR spectra, and X-ray crystallographic data for compound **2a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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