Construction of Highly-Substituted Aromatics Bearing Acyl Substituents Using Cyclobutenedione Technology: Vinylketene-Based Benzannulations Using 3-Acyl-4-(substituted amino)cyclobutenediones

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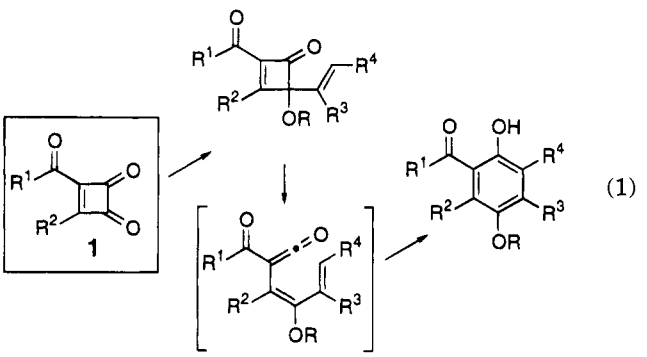
Highly-substituted acylated aromatics were efficiently synthesized from 3-acylcyclobutenediones via vinylketene-based benzannulations. Aryl and alkenyl lithiates added regioselectively to 3-acyl-4-(substituted amino)-3-cyclobutene-1,2-diones at −78 °C to produce the corresponding 4-aryl- and 4-alkenyl-3-(substituted amino)-2-acylcyclobutenones in good yields. Substrates lacking the vinylogous amide functionality were not preparable by this route, because the acylcyclobutenedione starting materials are not sufficiently stable to manipulate. Benzannulations of 4-(3-furyl)-, 4-(2-thienyl)-, 4-(2-dihydropyranyl)-, 4-(2-dihydrofuranyl)-, 4-(1-naphthyl)-, and 4-(2-naphthyl)-substituted cyclobutenones proceeded in refluxing mesitylene to give the corresponding acyl aromatics in 80–90% yield. Of all the 4-*aryl*cyclobutenones synthesized (*aryl* = phenyl and substituted phenyl), only those with an electron-donating substituent (OMe, NMe_2) at the meta position of phenyl group underwent benzannulation in refluxing mesitylene to afford acyl aromatics in moderate yields.

Introduction

In the last decade cyclobutenediones have emerged as powerful synthetic precursors used for the regiocontrolled synthesis of highly substituted quinones, hydroquinones, and catechols.[1-3] Modifications of this chemistry have led to novel methods for the construction of highly substituted naphthalenes,[4] phenols,[5,6] catechols,[7] heterocycles,[8,9] and highly-oxygenated angularly-fused polycyclic aromatics.[10]

Of the many reported studies of cyclobutenedione-based benzannulations and quinone constructions, there are no examples using cyclobutenediones bearing electron-withdrawing substituents. A recent report from this laboratory described the synthesis of 3-acylcyclobutenediones (**1**),[11] thus allowing a study of an acyl substituent in vinylketene-based benzannulation technology. If successfully implemented, benzannulation using acylcyclobutenediones would allow the regiocontrolled incorporation of an acyl group into highly substituted aromatics (eq 1). Subsequent manipulation of the acyl group in the products would offer access to more complex molecules.

Two fundamental questions were addressed in the present study: the regioselectivity of carbanion addition to the "trione" system of the acylcyclobutenedione, and the influence of the electron-withdrawing acyl group on the cyclobutenone ring-opening and electrocyclization of the resulting vinylketene to a substituted aromatic. Described herein is the synthesis of acyl aromatics by the regioselective addition of carbon nucleophiles to acylcyclobutenediones **1** (R^2 = 1-piperidinyl, NH*t*-Bu, N,N-dibenzylamino) followed by thermolysis of the adducts (eq 1).



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Results and Discussion

The synthesis of acyl aromatics via acylcyclobutenediones requires the regioselective addition of an unsaturated carbon nucleophile to one of the cyclobutenedione carbonyl groups and not to the acyl substituent. The release of ring strain that attends nucleophilic addition to a CO group on the cyclobutenedione ring should favor attack there, leaving only selective addition at one of the two cyclobutenedione carbonyl groups to complete the regiocontrol. It is well established in cyclobutenedione chemistry that a heteroatom substituent (alkoxy or amino) deactivates the *nonadjacent* carbonyl group through resonance delocalization and directs nucleophilic addition to the more reactive *adjacent* carbonyl group.[12] Of those acylcyclobutenediones available by Stille cross-coupling of (tri-*n*-butylstannyl)cyclobutenediones with acid chlorides, only 3-acyl-4-(substituted amino)-3-cyclobutene-1,2-diones are sufficiently stable to allow syn-

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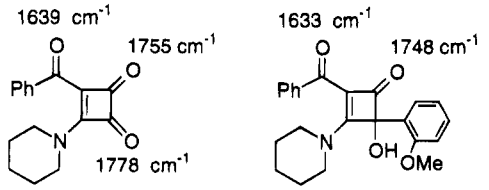
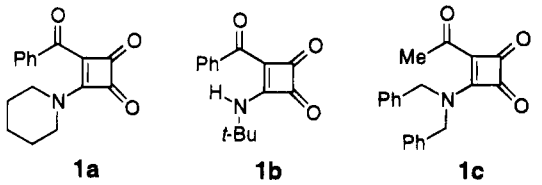


Figure 1.

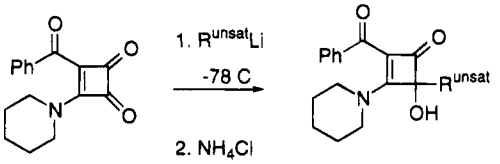
thetic manipulation.[11] Accordingly, substrates **1a–c**, which possess the requisite heteroatom substituent, were chosen to commence the study. Regiospecific addition of a carbon nucleophile to the more reactive cyclobutenedione CO group adjacent to the nitrogen substituent was anticipated.



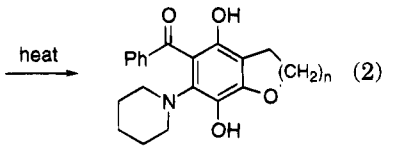
Treatment of cyclobutenedione **1a** with 1-hexynyllithium, (2-methoxyphenyl)lithium, [5-(2,3-dihydrofuranyl)]lithium, and [6-(3,4-dihydro-2*H*-pyranyl)]lithium followed by low temperature quench with NH_4Cl afforded a single product in each case in very good to excellent yield (eq 2). (2-Methoxyphenyl)lithium was generated by lithium–halogen exchange from the corresponding aryl bromide with 2 equiv of *t*-BuLi, while tin–lithium exchange was used to generated the lithiated vinyl ethers.[13,14] Assignment of the regiochemistry of the adducts relied on precedented addition to the nonvinylogous amide cyclobutenedione carbonyl group and was deduced from IR data (Figure 1): acylcyclobutenedione **1a** showed three CO stretches at 1778, 1755, and 1639 cm^{-1} assigned to the CO adjacent to the nitrogen substituent, the CO opposite the nitrogen substituent, and the benzoyl CO, respectively. The product resulting from addition of the nucleophile lacked the highest frequency absorption, indicating addition to the nonvinylogous amide cyclobutenedione carbonyl group.

Though isolable in high yield, not all 4-hydroxy-4-substituted-2-benzoyl-3-(1-piperidinyl)cyclobutenones converted into substituted aromatics on thermolysis. Thus, heating a mesitylene or xylene solution of the alkynyl and aryl adducts **2a** and **2b** at reflux under nitrogen resulted in complete decomposition. In contrast, adducts **2c** and **2d**, obtained from dihydrofuran and dihydro-2*H*-pyran, underwent benzannulation in refluxing mesitylene within 10 min to afford acylhydroquinones **3a** and **3b** in good yields (eq 2).

To simplify the method development and minimize complications from untimely oxidation of sensitive hydroquinones, acetylation of the 4-hydroxyl substitutent of the adducts **2** was conducted (Table 1). Treatment of **1a** with different aryl and alkenyl lithiates at −78 °C followed by *in situ* quenching with Ac_2O gave the adducts **4** in good to excellent yields. Thermolysis of the aryl adducts was very sluggish in refluxing *m*-xylene; no benzannulation products could be isolated after heating a *m*-xylene solution of **4a**, **4b**, or **4d** for more than 48 h. Thermolysis of 1-naphthyl adduct **4f** in *m*-xylene for 45 h gave only 33% of the desired product **5f** with efficient recovery of starting material. However, **5f** was obtained in 91% yield when a mesitylene solution of **4f** was heated to reflux (162 °C) for 10 h (entry 6, Table 1). In refluxing mesitylene, the 2-naphthyl adduct **4g** underwent benzannulation at a comparable rate to give **5g** in 83% yield (entry 7, Table 1). Further supporting the initial assignment of regiochemistry to the cyclobutenedione adducts **2** and **4**, all benzannulation products **5** and **6** listed in Table 1 have a strong intramolecular hydrogen bond between the phenolic OH group and the adjacent benzoyl group as evidenced by the phenolic chemical shifts between 9 and 13 ppm in the ^1H NMR spectra.



2a, R^{unsat} = 1-hexynyl, 94%
2b, R^{unsat} = 2-methoxyphenyl, 86%
2c, R^{unsat} = 2-(4,5-dihydrofuranyl), 73%
2d, R^{unsat} = 2-(5,6-dihydro-6H-pyranyl), 75%



(2)

3a, n = 1, 86%
3b, n = 2, 86%

The thermolysis of regioisomeric methoxyphenyl adducts **4b**, **4c**, and **4d** in mesitylene was informative (Table 1, entries 2–4). Only minor traces of the rearrangment products were formed from the *o*- (**4b**) and *p*-methoxyphenyl (**4d**) adducts after prolonged refluxing in mesitylene. However, thermolysis of the *m*-methoxyphenyl adduct **4c** was slow but efficient in refluxing mesitylene and gave a 4 to 1 mixture of **5c** and **5c′** in 71% combined yield after 72 h. This observation, combined with the rapid rearrangement of nonaromatic substrates under identical conditions (see below), suggests that opening of the cyclobutenone ring is fast and reversible and that electrocyclization of the vinylketene is the rate determining step (Scheme 1). Disruption of aromaticity raises the barrier of the electrocyclization step for simple aromatic substituents relative to nonaromatic substituents (compare Table 1, entries 10–12) and relative to the 1-naphthyl and 2-naphthyl derivatives, **4f** and **4g**.

Of the three regioisomeric methoxyphenyl derivatives **4b**, **4c**, and **4d** only the *m*-methoxyphenyl derivative, **4c**, participated in the benzannulation, suggesting that resonance donation of the *m*-OCH_3 group ($\sigma^+ = -0.78$)[15] to the point of attack on the aromatic ring by the electrophilic ketene is important. The predominance of the "*para*"-cyclization product **5c** over the "*ortho*"-cyclization product **5c′** is attributed to simple steric effects. It is of interest that 4-arylcyclobutenones bearing 2-alkyl, 2-aryl, or 2-alkoxy substituents undergo facile thermal rearrangement to benzannulated aromatics, while most of the 2-acyl-4-arylcyclobutenones of the present study

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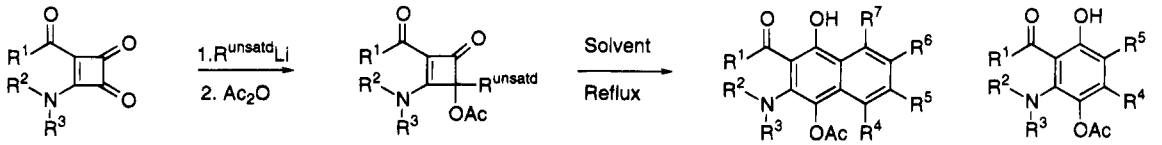
Table 1. Regioselective Synthesis of Acyl Aromatics form 3-Acyl-4-amino-3-cyclobutene-1,2-dione



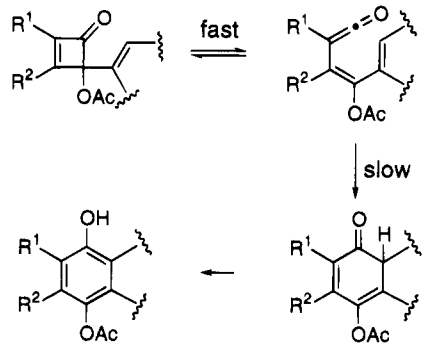
1a, R^1 = Ph, R^2-R^3 = -$(CH_2)_5$-

1b, R^1 = Ph, R^2 = H, R^3 = *t*-Bu

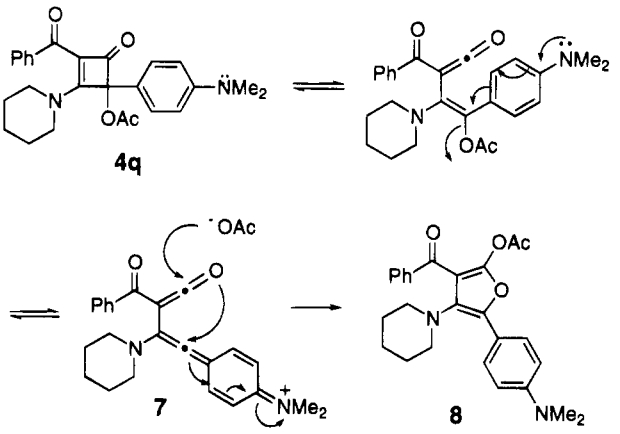
1c, R^1 = Me, R^2 = R^3 = CH_2Ph

entry	R^{unsatd} Li	1a–c	4/%	solvent/time	R^1	R^2	R^3	Cmpd	R^4	R^5	R^6	R^7	% yield
1	phenyl	**1a**	**4a**/71	mesitylene/24 h	Ph	1-piperidinyl		**5a**	H	H	H	H	0
2	2-methoxyphenyl	**1a**	**4b**/55	mesitylene/72 h	Ph	1-piperidinyl		**5b**	MeO	H	H	H	0
3	3-methoxyphenyl	**1a**	**4c**/66	mesitylene/72 h	Ph	1-piperidinyl		**5c**	H	MeO	H	H	56
								5c′	H	H	H	MeO	15
4	4-methoxyphenyl	**1a**	**4d**/59	mesitylene/48 h	Ph	1-piperidinyl		**5d**	H	H	MeO	H	0
5	3-(dimethylamino)phenyl	**1a**	**4e**/52	mesitylene/11 h	Ph	1-piperidinyl		**5e**	H	Me_2N	H	H	46
6	1-naphthyl	**1a**	**4f**/79	mesitylene/10 h	Ph	1-piperidinyl		**5f**	benzo		H	H	91
7	2-naphthyl	**1a**	**4g**/76	mesitylene/29 h	Ph	1-piperidinyl		**5g**	H	H	benzo		83
8	3-furyl	**1a**	**4h**/64	mesitylene/5 h	Ph	1-piperidinyl		**6a**	$-CH{=}CHO-$	–	–		90
9	2-thienyl	**1a**	**4i**/69	mesitylene/16 h	Ph	1-piperidinyl		**6b**	$-SCH{=}CH-$	–	–		87
10	(*E*/*Z*)-1-propenyl	**1a**	**4j**/75	mesitylene/1.5 h	Ph	1-piperidinyl		**6c**	H	Me	–	–	87
11	5-(2,3-dihydrofuranyl)	**1a**	**4k**/77	mesitylene/10 min	Ph	1-piperidinyl		**6d**	$-OCH_2CH_2-$		–	–	94
12	6-(3,4-dihydro-2*H*-pyranyl)	**1a**	**4l**/77	mesitylene/10 min	Ph	1-piperidinyl		**6e**	$-O(CH_2)_3-$		–	–	100
13	5-(2,3-dihydrofuranyl)	**1b**	**4m**/55	mesitylene/5 min	Ph	H	*t*-butyl	**6f**	$-OCH_2CH_2-$		–	–	82
14	6-(3,4-dihydro-2*H*-pyranyl)	**1b**	**4n**/54	mesitylene/5 min	Ph	H	*t*-butyl	**6g**	$-O(CH_2)_3-$		–	–	97
15	5-(2,3-dihydrofuranyl)	**1c**	**4o**/72	mesitylene/5 min	Me	benzyl	benzyl	**6h**	$-OCH_2CH_2-$		–	–	92
16	6-(3,4-dihydro-2*H*-pyranyl)	**1c**	**4p**/55	xylene/10 min	Me	benzyl	benzyl	**6j**	$-O(CH_2)_3-$		–	–	86

Scheme 1. Benzannulation Mechanism



Scheme 2. Formation of Furan Derivative 8



rearrange only with reticence or not at all. Relative to other carbon substituted ketenes, acylketenes are thermodynamically stabilized.[16] Assuming the acyl substituent does not similarly stabilize the transition state for electrocyclization, the systems in the current study would show diminished rates of the reaction, relative to benzannulations using cyclobutenones bearing nonacyl substituents at the 2-position.

Thermolysis of the *m*-(*N*,*N*-dimethylamino)phenyl adduct **4e** in mesitylene proceeded faster than *m*-methoxyphenyl analog (11 h vs 72 h) and gave only the less hindered rearrangement product **5e**. Surprisingly, the *p*-(*N*,*N*-dimethylamino)phenyl adduct **4q** was not inert to thermolysis and in refluxing mesitylene gave the furan derivative **8** in 83% yield as the only product. The formation of **8** is thought to proceed through the iminium ion intermediate **7** (Scheme 2), and compared to the methoxy analog **4d** which is inert to thermolysis, the rearrangement of **4q** to the furan is attributed to the greater electron-releasing ability of the dimethylamino substituent.

Consistent with the notion that aromatic stabilization of the unsaturated substituent raises the barrier to electrocyclization, those cyclobutenedione adducts bearing less-stabilized heteroaromatic substituents (3-furyl, **4h**, and 2-thienyl, **4i**) rearranged readily to the corresponding benzannulation products **6a** and **6b** in good yields (entries 8, 9; Table 1). Not surprisingly, rearrangement of the 1-propenyl adduct **4j**, the dihydrofuranyl adduct **4k**, and dihydropyranyl adduct **4l** proceeded faster than any of the aryl adducts (entries 10–12). Consistent with the polar character of the electrocyclization, the latter two substrates, both electron-rich enol ether derivatives, transformed into products within minutes in refluxing mesitylene at 162 °C, providing very high yields of **6d** and **6e**.

The above strategy had been extended to the 2-acyl-3-(substituted amino)cyclobutenediones **1b** and **1c** (entries 13–16; Table 1). Addition of 2.5 equiv of [5-(2,3-dihydrofuranyl)]lithium and [6-(3,4-dihydro-2*H*-pyranyl)]-lithium to the vinylogous secondary amide **1b** gave the desired adducts **4m** and **4n** in moderate yields (Table 1). Excellent yields of benzannulation products **6f** and **6g** were obtained when mesitylene solutions of these two adducts were heated at reflux for 5 min. The adducts

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4o and **4p** obtained by adding 5-(2,3-dihydrofuranyl)-lithium and 6-(3,4-dihydro-2*H*-pyranyl)lithium to **1c** rearranged readily in either refluxing xylene or mesitylene to give the ring expansion products **6h** and **6j** in high yields.

Conclusions

In conclusion, an efficient synthesis of acyl substituted aromatics from acylcyclobutenediones has been demonstrated. Aryl, heteroaryl, and vinyl lithiates add regioselectively to 3-acyl-4-(substituted amino)-3-cyclobutene-1,2-diones and after treatment with acetic anhydride, the 4-acetoxy adducts can be isolated in good yields. Thermolysis of the cyclobutenedione adducts possessing 4-alkenyl substituents proceeds quickly in either refluxing mesitylene or xylene to produce the desired benzannulation products in excellent yields. Thermolysis of the 4-aryl adducts requires an electron-donating group at the meta position on the phenyl ring for efficient rearrangement. 4-Heteroaryl and 4-naphthyl adducts undergo rearrangement more readily than the 4-substituted phenyl derivatives. An alternate and regiospecific synthesis of highly-substituted acylated aromatics has been realized using dithiane derivatives of acylcyclobutenediones, which are stable without the amino substituent required in the present study. These results will be published separately.

Experimental Section

General Experimental. Analytical thin-layer chromatography (TLC) was performed on Merck silica gel plates with F-354 indicator. Visualization was accomplished by one or more of the following methods: UV light, phosphomolybdic acid stain, vanillin stain, and anisaldehyde stain. Solvents for extraction and chromatography were reagent grade and used as received. Flash column chromatography was conducted using 32–63 μm Flash silica gel obtained from EM. Solvents (THF, xylene, mesitylene) used as reaction media were dried over 5 Å molecular sieves before use and had no more than 50 ppm of H_2O as measured by Karl Fischer titration. Reagents purchased from commercial sources were used directly without further purification. All reactions were performed under a dry argon or nitrogen atmosphere in base-washed, flame-dried glassware. "Brine" refers to a saturated aqueous solution of NaCl. Unless otherwise specified, solutions of NH_4Cl and $NaHCO_3$ refer to saturated aqueous solutions.

Starting Materials. 3-Isopropoxy-4-(tri-*n*-butylstannyl)-3-cyclobutene-1,2-dione,[17] 3-benzoyl-4-(1-piperidinyl)-3-cyclobutene-1,2-dione (**1a**),[11] 5-(tri-*n*-butylstannyl)-2,3-dihydrofuran,[13,14] and 6-(tri-*n*-butylstannyl)-3,4-dihydro-2*H*-pyran[13,14] were prepared according to literature procedures.

3-Benzoyl-4-(*tert*-butylamino)-3-cyclobutene-1,2-dione (1b). According to the literature procedure followed for **1a**,[11] 3-benzoyl-4-(*tert*-butylamino)-3-cyclobutene-1,2-dione, a yellow microcrystalline solid (1.07 g, 4.160 mmol, 89%), was prepared from 3-isopropoxy-4-(tri-*n*-butylstannyl)-3-cyclobutene-1,2-dione (2.00 g, 4.660 mmol, 1.00 equiv), benzoyl chloride (0.66 g, 4.700 mmol, 1.01 equiv), benzylchlorobis(triphenylphosphine)palladium (67 mg, 0.088 mmol, 2.0 mol %), CuI (17 mg, 0.089 mmol, 2.0 mol %), and *tert*-butylamine (670 mg, 8.90 mmol, 2.00 equiv). TLC (silica gel, 30% ethyl acetate in hexanes, R_f = 0.45); chromatographic purification (flash column, silica gel, 50% ether in hexanes); mp 113–114 °C (ether/hexanes). IR (CH_2Cl_2, KCl, cm^{-1}): 3442 (m), 3298 (m), 3066 (m), 2972 (s), 1772 (s), 1761 (s), 1656 (s), 1617 (s), 1512 (s), 1451 (s), 1219 (s), 1163 (s). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.89 (br s, 1 H), 8.46 (d, J = 7.5 Hz, 2 H), 7.64 (t, J = 7.5 Hz, 1 H), 7.55 (t, J = 7.5 Hz, 2 H), 1.55 (t, J = Hz, 9 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 194.6, 187.3, 185.9, 182.8, 156.0, 135.8, 134.4, 129.7, 128.8, 55.5, 30.0. Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44. Found: C, 69.85; H, 5.92; N, 5.43.

3-Acetyl-4-(*N*,*N*-dibenzylamino)-3-cyclobutene-1,2-dione (1c). According to the literature procedure followed for **1a**, 3-acetyl-4-(*N*,*N*-dibenzylamino)-3-cyclobutene-1,2-dione was analogously prepared as yellow crystals (1.26 g, 3.950 mmol, 89%) from 3-isopropyl-4-(tri-*n*-butylstannyl)-3-cyclobutene-1,2-dione (1.90 g, 4.430 mmol, 1.00 equiv), acetyl chloride (0.69 g, 4.9 mmol), benzylchlorobis(triphenylphosphine)palladium (80 mg, 0.106 mmol, 2.0 mol %), copper iodide (40 mg, 0.106 mmol, 5.0 mol %), and dibenzylamine (1.0 g, 5.0 mmol, 1.13 equiv). TLC (silica gel, 30% ethyl acetate in hexanes, R_f = 0.40); chromatographic purification (Flash column, silica gel, 1 cm x 10 cm, 10% ethyl acetate in hexanes); mp 137–138 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 3055 (m), 2988 (w), 1785 (m), 1770 (s), 1668 (s), 1615 (s), 1422 (m), 1143 (w), 1046 (w), 895 (m), 957 (w). ^1H NMR ($CDCl_3$, 300 MHz): δ 7.40 (m, 6 H), 7.20 (m, 4 H), 5.07 (s, 2 H), 4.94 (s, 2 H), 2.64 (s, 3 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 196.9, 191.9, 186.9, 178.6, 156.1, 134.1, 133.6, 129.2, 129.1, 128.9, 128.6, 128.5, 128.3, 56.4, 52.0, 30.6. Anal. Calcd for $C_{20}H_{17}NO_3$: C, 75.22; H, 5.37; N, 4.39. Found: C, 75.15; H, 5.39; N, 4.31.

Preparation of 4-Hydroxycyclobutenones, 2. Representative Procedure. 2-Benzoyl-4-(1-hexynyl)-4-hydroxy-3-(1-piperidinyl)-2-cyclobuten-1-one, 2a. Into a THF (5 mL) solution of 1-hexyne (45 mg, 0.548 mmol, 1.37 equiv) at −78 °C was added dropwise *n*-butyllithium (0.30 mL, 1.50 M in hexanes, 0.450 mmol, 1.12 equiv). The resulting solution was stirred for 10 min at −78 °C and then cannulated into a THF (10 mL) solution of 3-benzoyl-4-(1-piperidinyl)-3-cyclobutene-1,2-dione (108 mg, 0.401 mmol, 1.00 equiv) held at −78 °C. After 10 min the reaction was quenched with NH_4Cl (0.5 mL) and the mixture warmed to rt. The reaction mixture was poured into water (15 mL) and extracted with ether (3 × 25 mL). The combined ether layers were washed once with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated to give an off-white solid. Recrystallization from methylene chloride and pentane afforded 132 mg (0.376 mmol, 94%) of 2-benzoyl-4-(1-hexynyl)-4-hydroxy-3-(1-piperidinyl)-2-cyclobuten-1-one as a white microcrystalline solid. TLC (silica gel, 50% ethyl acetate in hexanes, R_f = 0.40); mp 134–135 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 3553 (w), 3235 (w), 2948 (m), 2862 (m), 2232 (w), 1749 (m), 1633 (s), 1602 (s), 1430 (s), 1137 (m). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.00 (d, J = 7.2 Hz, 2 H), 7.50 (m, 3 H), 5.65 (br s, 1 H), 4.16 (m, 1 H), 3.90 (m, 1 H), 3.70 (m, 2 H), 2.20 (dt, J = 7.2, 1.8 Hz, 2 H), 1.77 (m, 6 H), 1.35 (m, 4 H), 0.84 (dt, J = 7.2, 1.8 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 185.7, 181.4, 170.4, 137.7, 132.4, 129.4, 127.8, 114.6, 90.4, 81.2, 74.6, 52.7, 51.6, 30.2, 26.2, 25.9, 23.3, 21.7, 18.5, 13.3. Anal. Calcd for $C_{22}H_{25}NO_3$: C, 75.19; H, 7.17; N, 3.99. Found: C, 75.11; H, 7.17; N, 3.95.

4-(2-Anisyl)-2-benzoyl-4-hydroxy-3-(1-piperidinyl)-2-cyclobuten-1-one, 2b. By the representative procedure, 2-bromoanisole (110 mg, 0.588 mmol, 1.08 equiv) in THF (5 mL), *n*-butyllithium (0.40 mL, 1.50 M in hexanes, 0.600 mmol, 1.11 equiv), and a THF (10 mL) solution of 3-benzoyl-4-(1-piperidinyl)-3-cyclobutene-1,2-dione (146 mg, 0.542 mmol, 1.00 equiv) gave an off-white solid. Recrystallization from methylene chloride and pentane afforded 175 mg (0.464 mmol, 86%) of 4-(2-anisyl)-2-benzoyl-4-hydroxy-3-(1-piperidinyl)-2-cyclobuten-1-one as a white microcrystalline solid. TLC (silica gel, 50% ethyl acetate in hexanes, R_f = 0.30); mp 179–180 °C dec (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 3485 (w), 2949 (m), 1748 (m), 1633 (s), 1602 (s), 1490 (m), 1450 (m), 1434 (m), 1242 (m), 1023 (m). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.06 (d, J = 7.5 Hz, 2 H), 7.50 (t, J = 7.2 Hz, 1 H), 7.41 (t, J = 7.8 Hz, 2 H), 7.27 (m, 2 H), 6.98 (t, J = 7.8 Hz, 2 H), 5.20 (s, 1 H), 4.20 (m, 2 H), 3.93 (s, 3 H), 3.65 (m, 1 H), 3.50 (m, 1 H), 1.90 (m, 2 H), 1.70 (m, 2 H), 1.60 (m, 2 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 185.7, 182.9, 171.3, 157.5, 138.0, 132.5, 129.7, 129.6, 127.9, 127.1, 125.0, 121.5, 112.4, 105.2, 91.6, 56.5, 52.7, 52.0, 26.1, 25.8, 23.5. Anal. Calcd for $C_{23}H_{23}NO_4$: C, 73.19; H, 6.14; N, 3.71. Found: C, 73.50; H, 6.08; N, 3.63.

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2-Benzoyl-4-(2,3-dihydrofuran-5-yl)-4-hydroxy-3-(1-piperidinyl)-2-cyclobuten-1-one, 2c. By the representative procedure, 5-(tri-*n*-butylstannyl)-2,3-dihydrofuran (200 mg, 0.557 mmol, 1.12 equiv) in THF (5 mL), *n*-butyllithium (0.38 mL, 1.60 M in hexanes, 0.610 mmol, 1.22 equiv), and a THF (10 mL) solution of 3-benzoyl-4-(1-piperidinyl)-3-cyclobutene-1,2-dione (134 mg, 0.498 mmol, 1.00 equiv) gave a yellow solid. Chromatographic purification (flash column, silica gel, 1 cm x 12 cm, 20–50% ethyl acetate in hexanes) afforded 124 mg (0.365 mmol, 73%) of 2-benzoyl-4-(2,3-dihydrofuran-5-yl)-4-hydroxy-3-(1-piperidinyl)-2-cyclobuten-1-one as a white microcrystalline solid. TLC (silica gel, 50% ethyl acetate in hexanes, R_f = 0.20); mp 167–168 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 3560 (w), 3260 (w), 2959 (w), 2864 (w), 1748 (m), 1633 (s), 1601(s), 1434 (s), 1256 (s), 1065 (m). ^1H NMR ($CDCl_3$, 300 MHz): δ 7.99 (d, J = 7.8 Hz, 2 H), 7.50 (t, J = 7.2 Hz, 1 H), 7.41 (t, J = 7.5 Hz, 2 H), 5.23 (t, J = 2.4 Hz, 1 H), 4.83 (br s, 1 H), 4.45 (m, 2 H), 4.22 (m, 1 H), 3.98 (m, 1 H), 3.66 (m, 2 H), 2.70 (m, 2 H), 1.75 (m, 6 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 185.5, 182.4, 170.7, 153.5, 137.9, 132.6, 129.6, 128.0, 116.1, 99.1, 87.1, 71.0, 53.0, 51.6, 30.2, 26.3, 26.0, 23.6. HRMS (EI) Calcd for $C_{20}H_{21}NO_4$: 339.1470. Found: 339.1485.

2-Benzoyl-4-(3,4-dihydro-2*H*-pyran-6-yl)-4-hydroxy-3-(1-piperidinyl)-2-cyclobuten-1-one, 2d. By the representative procedure, 6-(tri-*n*-butylstannyl)-3,4-dihydro-2*H*-pyran (150 mg, 0.402 mmol, 1.08 equiv) in THF (5 mL), *n*-butyl lithium (0.30 mL, 1.45 M in hexanes, 0.440 mmol, 1.19 equiv), and a THF (10 mL) solution of 3-benzoyl-4-(1-piperidinyl)-3-cyclobutene-1,2-dione (100 mg, 0.371 mmol, 1.00 equiv) gave a yellow solid. Chromatographic purification (flash column, silica gel, 1 cm x 12 cm, 20–50% ethyl acetate in hexanes) afforded 98 mg (0.277 mmol, 75%) of 2-benzoyl-4-(3,4-dihydro-2*H*-pyran-6-yl)-4-hydroxy-3-(1-piperidinyl)-2-cyclobuten-1-one as an off-white microcrystalline solid. TLC (silica gel, 50% ethyl acetate in hexanes, R_f = 0.20); mp 150–151 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 3565 (w), 3280 (w), 2949 (w), 2864 (w), 1748 (m), 1631 (s), 1602 (s), 1434 (s), 1266 (s), 1066 (m), 979 (w). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.02 (m, 2 H), 7.45 (m, 3 H), 5.17 (t, J = 3.6 Hz, 1 H), 4.32 (br s, 1 H), 4.10 (m, 4 H), 3.63 (m, 2 H), 2.10 (m, 2 H), 1.80 (m, 8 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 185.3, 182.3, 171.3, 148.8, 138.0, 132.6, 129.6, 128.0, 116.9, 99.0, 89.4, 66.8, 52.9, 51.5, 26.3, 26.1, 23.6, 22.1, 20.1. Anal. Calcd for $C_{21}H_{23}NO_4$: C, 71.37; H, 6.56; N, 3.96. Found: C, 71.19; H, 6.63; N, 3.91.

Thermolysis of 4-Hydroxycyclobutenones, 2. Representative Procedure. 5-Benzoyl-4,7-dihydroxy-6-(1-piperidinyl)dihydro[*b*]benzofuran, 3a. A mesitylene (2.5 mL) solution of 2-benzoyl-4-(2,3-dihydrofuran-5-yl)-4-hydroxy-3-(1-piperidinyl)-2-cyclobuten-1-one (28 mg, 0.083 mmol, 1.00 equiv) was sparged with argon and then heated to reflux under an argon atmosphere. Starting material was consumed after 10 min, as evidenced by TLC (silica gel, 50% ethyl acetate in hexanes). The reaction mixture was cooled to rt and concentrated on a rotary evaporator to give 28 mg of a yellow solid that was recrystallized from methylene chloride/pentane to afford 24 mg (0.071 mmol, 86%) of 5-benzoyl-4,7-dihydroxy-6-(1-piperidinyl)dihydro[*b*]benzofuran as an orange solid. TLC (silica gel, 50% ethyl acetate in hexanes, R_f = 0.58); mp 182–183 °C (methylene chloride/pentane); IR (CH_2Cl_2, KCl, cm^{-1}): 3557 (w), 2938 (m), 2854 (w), 1633 (s), 1608 (m), 1462 (s), 1332 (s), 995 (s). ^1H NMR ($CDCl_3$, 300 MHz): δ 9.66 (br s, 1 H), 7.57 (d, J = 7.2 Hz, 2 H), 7.47 (t, J = 6.9 Hz, 1 H), 7.37 (t, J = 7.5 Hz, 2 H), 4.71 (t, J = 8.7 Hz, 2 H), 4.60 (br s, 1 H), 3.23 (t, J = 8.7 Hz, 2 H), 2.70 (m, 4 H), 2.00 (m, 6 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 199.9, 153.7, 150.3, 141.6, 141.4, 131.4, 130.9, 128.7, 127.8, 112.8, 108.1, 73.7, 52.7, 27.3, 26.2, 23.8. HRMS (EI) Calcd for $C_{20}H_{21}NO_4$: 339.1470. Found: 339.1460.

6-Benzoyl-5,8-dihydroxy-7-(1-piperidinyl)-3,4-dihydro-2*H*-benzo[*b*]pyran, 3b. 2-Benzoyl-4-(3,4-dihydro-2*H*-pyran-6-yl)-4-hydroxy-3-(1-piperidinyl)-2-cyclobuten-1-one (27 mg, 0.076 mmol, 1.00 equiv) in refluxing *m*-xylene (2.5 mL) after 10 min gave a red solid. Recrystallization from methylene chloride and pentane afforded 23 mg (0.065 mmol, 86%) of 6-benzoyl-5,8-dihydroxy-7-(1-piperidinyl)-3,4-dihydro-2*H*-benzo[*b*]pyran as an orange microcrystalline solid. TLC (silica gel, 50% ethyl acetate in hexanes, R_f = 0.60); mp 183–184 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 3536 (m), 2939 (m), 1618 (s), 1456 (s), 1395 (m), 1334 (s), 1217 (s), 1127 (s), 1005 (m), 953 (m). ^1H NMR ($CDCl_3$, 300 MHz): δ 10.10 (s, 1 H), 7.55 (d, J = 7.8 Hz, 2 H), 7.46 (t, J = 7.2 Hz, 1 H), 7.37 (t, J = 7.8 Hz, 2 H), 5.15 (s, 1 H), 4.30 (t, J = 5.1 Hz, 2 H), 2.79 (m, 4 H), 2.72 (t, J = 6.6 Hz, 2 H), 2.04 (t, J = 5.7 Hz, 2 H), 1.80 (m, 6 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 200.8, 152.3, 147.9, 142.1, 136.9, 135.1, 131.0, 129.3, 128.3, 127.7, 105.9, 67.4, 52.5, 25.8, 23.9, 21.6, 18.6. Anal. Calcd for $C_{21}H_{23}NO_4$-H_2O: C, 67.92; H, 6.74; N, 3.77. Found: C, 68.07; H, 6.72; N, 3.55.

Preparation of 4-Acetoxycyclobutenones, 4. Representative Procedure. 4-Acetoxy-2-benzoyl-3-(1-piperidinyl)-4-phenyl-2-cyclobuten-1-one, 4a. Bromobenzene (172 mg, 1.095 mmol, 1.10 equiv) in THF (5 mL) at −78 °C was treated dropwise with *t*-BuLi (1.3 mL, 1.70 M in pentane, 2.210 mmol, 2.21 equiv). The resulting solution was stirred for 10 min at −78 °C and then cannulated into a THF (10 mL) solution of 3-benzoyl-4-(1-piperidinyl)-3-cyclobutene-1,2-dione (265 mg, 0.999 mmol, 1.00 equiv) held at −78 °C. After 10 min the reaction was quenched with Ac_2O (0.20 mL, 2.120 mmol, 2.12 equiv) and warmed to rt. The reaction mixture was poured into $NaHCO_3$ (15 mL) and extracted with ether (3 × 25 mL). The combined ether layers were washed once with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated to give an off-white solid. Recrystallization from methylene chloride and pentane gave 276 mg (0.709 mmol, 71%) of 4-acetoxy-2-benzoyl-3-(1-piperidinyl)-4-phenyl-2-cyclobuten-1-one as an off-white solid. TLC (silica gel, 50% ethyl acetate in hexanes, R_f = 0.50); mp 169–170 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 3066 (w), 2948 (w), 2863 (w), 1753 (s), 1637 (s), 1604 (s), 1452 (s), 1433 (m), 1369 (m), 1218 (s), 1144 (m), 1020 (w). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.09 (d, J = 7.8 Hz, 2 H), 7.42 (m, 8 H), 4.16 (m, 1 H), 4.10 (m, 1 H), 3.44 (sept, J = 7.2 Hz, 1 H), 3.39 (sept, J = 7.2 Hz, 1 H), 2.26 (s, 3 H), 1.85 (m, 2 H), 1.70 (m, 2 H), 1.51 (m, 2 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 185.1, 178.4, 169.6, 169.4, 143.3, 137.9, 134.2, 132.7, 129.8, 128.9, 128.8, 128.0, 125.2, 93.5, 52.7, 51.5, 25.7 (2C), 23.2, 21.2. HRMS (EI) Calcd for $C_{24}H_{23}NO_4$: 389.1627. Found: 389.1618.

4-Acetoxy-2-benzoyl-4-(2-anisyl)-3-(1-piperidinyl)-2-cyclobuten-1-one, 4b. By the representative procedure, 2-bromoanisole (208 mg, 1.112 mmol, 1.09 equiv) in THF (5 mL), *t*-BuLi (1.30 mL, 1.70 M in pentane, 2.210 mmol, 2.17 equiv), 3-benzoyl-4-(1-piperidinyl)-3-cyclobutene-1,2-dione (270 mg, 1.018 mmol, 1.00 equiv) in THF (10 mL), and Ac_2O (0.20 mL, 2.120 mmol, 4.67 equiv) quench gave a yellow oil. Chromatographic purification (flash column, silica gel, 1 cm x 12 cm, 30% ethyl acetate in hexanes) afforded 236 mg (0.563 mmol, 55%) of 4-acetoxy-2-benzoyl-4-(2-anisyl)-3-(1-piperidinyl)-2-cyclobuten-1-one as a white microcrystalline solid. TLC (silica gel, 30% ethyl acetate in hexanes, R_f = 0.35); mp 187–189 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 3065 (w), 2945 (s), 2862 (m), 1747 (s), 1627 (s), 1492 (s), 1450 (s), 1367 (s), 1284 (s), 1221 (s). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.10 (d, J = 7.5 Hz, 2 H), 7.48 (t, J = 7.2 Hz, 2 H), 7.41 (t, J = 7.2 Hz, 2 H), 7.29 (t, J = 8.1 Hz, 1 H), 7.00 (t, J = 7.5 Hz, 1 H), 6.89 (d, J = 8.4 Hz, 1 H), 4.07 (m, 2 H), 3.79 (s, 3 H), 3.54 (m, 1 H), 3.48 (m, 1 H), 2.21 (s, 3 H), 1.86 (m, 2 H), 1.71 (m, 2 H), 1.57 (m, 2 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 184.9, 177.6, 171.2, 169.3, 156.5, 138.1, 132.3, 130.0, 129.7, 128.6, 127.9, 122.4, 121.1, 116.4, 112.5, 92.2, 56.3, 52.5, 51.8, 25.8, 25.7, 23.4, 21.4. Anal. Calcd for $C_{25}H_{25}NO_5$: C, 71.58; H, 6.01; N, 3.34. Found: C, 71.51; H, 5.82; N, 3.52.

4-Acetoxy-2-benzoyl-4-(3-anisyl)-3-(1-piperidinyl)-2-cyclobuten-1-one, 4c. By the representative procedure, 3-bromoanisole (103 mg, 0.551 mmol, 1.12 equiv) in THF (5 mL), *t*-BuLi (0.65 mL, 1.7 M in pentane, 1.110 mmol, 2.25 equiv), 3-benzoyl-4-(1-piperidinyl)-3-cyclobutene-1,2-dione (133 mg, 0.494 mmol, 1.00 equiv) in THF (10 mL), and Ac_2O (0.20 mL, 2.120 mmol, 4.29 equiv) gave an orange oil. Chromatographic purification (flash column, silica gel, 1 cm x 10 cm, 10–50% ethyl acetate in hexanes) gave 137.5 mg (0.328 mmol, 66%) of 4-acetoxy-2-benzoyl-4-(3-anisyl)-3-(1-piperidinyl)-2-cyclobuten-1-one as an off-white solid. TLC (silica gel, 50% ethyl acetate

in hexanes, R_f = 0.20); mp 175–176 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 3065 (w), 2950 (m), 1753 (s), 1636 (s), 1604 (s), 1451 (s), 1434 (s), 1220 (s), 1028 (m), 965 (w). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.06 (d, J = 7.2 Hz, 2 H), 7.42 (m, 3 H), 7.27 (t, J = 7.8 Hz, 1 H), 7.05 (m, 2 H), 6.84 (dd, J = 8.1, 2.7 Hz, 1 H), 4.18 (m, 1 H), 4.06 (m, 1 H), 3.78 (s, 3 H), 3.38 (m, 2 H), 2.23 (s, 3 H), 1.83 (m, 2 H), 1.65 (m, 2 H), 1.50 (m, 2 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 185.0, 178.2, 169.4, 169.3, 159.9, 137.9, 135.7, 132.6, 129.9, 129.7, 128.0, 117.3, 116.8, 113.7, 111.6, 93.4, 55.3, 52.7, 51.5, 25.8, 25.8, 23.3, 21.2. HRMS (EI) Calcd for $C_{25}H_{25}NO_5$: 419.1732. Found: 419.1720.

4-Acetoxy-2-benzoyl-4-(4-anisyl)-3-(1-piperidinyl)-2-cyclobuten-1-one, 4d. By the representative procedure, 4-bromoanisole (75 mg, 0.401 mmol, 1.06 equiv) in THF (5 mL), t-BuLi (0.50 mL, 1.70 M in pentane, 0.850 mmol, 2.25 equiv), 3-benzoyl-4-(1-piperidinyl)-3-cyclobutene-1,2-dione (100 mg, 0.377 mmol, 1.00 equiv) in THF (10 mL), and Ac_2O (0.15 mL, 1.590 mmol, 4.22 equiv) gave a yellow solid. Chromatographic purification (flash column, silica gel, 1 cm x 12 cm, 20% ethyl acetate in hexanes) afforded 93 mg (0.222 mmol, 59%) of 4-acetoxy-2-benzoyl-4-(4-anisoyl)-3-(1-piperidinyl)-2-cyclobuten-1-one as an off-white solid. TLC (silica gel, 40% ethyl acetate in hexanes, R_f = 0.32); mp 186–187 °C (methylene chloride/pentane); IR (CH_2Cl_2, KCl, cm^{-1}): 3059 (w), 2950 (w), 2865 (w), 1751 (s), 1636 (s), 1603 (s), 1512 (m), 1452 (s), 1436 (m), 1216 (s), 1142 (w), 1023 (m). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.08 (d, J = 7.2 Hz, 2 H), 7.42 (m, 5 H), 6.90 (d, J = 8.7 Hz, 2 H), 4.15 (m, 1 H), 4.10 (m, 1 H), 3.78 (s, 3 H), 3.44 (sept, J = 7.2 Hz, 1 H), 3.42 (sept, J = 5.7 Hz, 1 H), 2.24 (s, 3 H), 1.85 (m, 2 H), 1.68 (m, 2 H), 1.55 (m, 2 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 185.1, 178.9, 169.9, 169.4, 159.9, 137.9, 132.6, 129.7, 128.0, 126.5, 126.1, 117.4, 114.2, 93.2, 55.3, 52.6, 51.4, 25.9 (2C), 23.3, 21.2. HRMS (EI) Calcd for $C_{25}H_{25}NO_5$: 419.1732. Found: 419.1712. Anal. Calcd for $C_{25}H_{25}NO_5$: C, 71.58; H, 6.01; N, 3.34. Found: C, 71.60; H, 6.06; N, 3.32.

4-Acetoxy-2-benzoyl-4-(3-(*N*,*N*-dimethylamino)phenyl))-3-(1-piperidinyl)-2-cyclobuten-1-one, 4e. By the representative procedure, 3-bromo-*N*,*N*-dimethylaniline (80 mg, 0.400 mmol, 1.08 equiv) in THF (5 mL), t-BuLi (0.63 mL, 1.40 M in pentane, 0.880 mmol, 2.37 equiv), 3-benzoyl-4-(1-piperidinyl)-3-cyclobutene-1,2-dione (100 mg, 0.371 mmol, 1.00 equiv) in THF (10 mL), and Ac_2O (0.20 mL, 2.120 mmol, 4.30 equiv) gave a yellow oil. Chromatographic purification (Flash column, silica gel, 1 cm x 10 cm, 20–50% ethyl acetate in hexanes) gave 84 mg (0.194 mmol, 52%) of 4-acetoxy-2-benzoyl-4-(3-(*N*,*N*-dimethylamino)phenyl)-3-(1-piperidinyl)-2-cyclobuten-1-one as a white solid. TLC (silica gel, 50% ethyl acetate in hexanes, R_f = 0.20); mp 195–196 °C (methylene chloride/pentane); IR (CH_2Cl_2, KCl, cm^{-1}): 3064 (w), 2949 (w), 2866 (w), 1751 (s), 1634 (s), 1500 (m), 1450 (s), 1435 (m), 1219 (s), 959 (w). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.08 (d, J = 7.2 Hz, 2 H), 7.47 (m, 3 H), 7.22 (t, J = 7.2 Hz, 1 H), 6.85 (s, 1 H), 6.78 (d, J = 7.8 Hz, 1 H), 6.69 (d, J = 7.5 Hz, 1 H), 4.20 (m, 1 H), 4.08 (m, 1 H), 3.45 (m, 2 H), 2.94 (s, 6 H), 2.24 (s, 3 H), 1.86 (m, 2 H), 1.70 (m, 2 H), 1.55 (m, 2 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 185.0, 178.6, 169.8, 169.4, 150.8, 138.0, 134.8, 132.5, 129.7, 129.4, 128.0, 116.6, 113.1, 112.9, 109.2, 93.7, 52.6, 51.5, 40.5, 25.9, 25.8, 23.3, 21.3. Anal. Calcd for $C_{26}H_{28}N_2O_4$: C, 72.20; H, 6.53; N, 6.48. Found: C, 72.06; H, 6.46; N, 6.22.

4-Acetoxy-2-benzoyl-4-(1-naphthyl)-3-(1-piperidinyl)-2-cyclobuten-1-one, 4f. By the representative procedure, 1-bromonaphthalene (113 mg, 0.546 mmol, 1.09 equiv) in THF (5 mL), t-BuLi (0.65 mL, 1.70 M in pentane, 1.110 mmol, 2.22 equiv), 3-benzoyl-4-(1-piperidinyl)-3-cyclobutene-1,2-dione (135 mg, 0.501 mmol, 1.00 equiv) in THF (10 mL), and Ac_2O (0.15 mL, 1.590 mmol, 3.17 equiv) gave a yellow oil. Crystallization from methylene chloride and pentane gave 175 mg (0.398 mmol, 79%) of 4-acetoxy-2-benzoyl-4-(1-naphthyl)-3-(1-piperidinyl)-2-cyclobuten-1-one as an off-white microcrystalline solid. mp 152–154 °C (methylene chloride/pentane); IR (CH_2Cl_2, KCl, cm^{-1}): 3052 (w), 2950 (w), 1750 (s), 1635 (s), 1602 (s), 1451 (s), 1435 (s), 1291 (s), 1218 (m), 1050 (m), 949 (w). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.57 (d, J = 8.4 Hz, 1 H), 8.06 (d, J = 7.2 Hz, 2 H), 7.83 (t, J = 6.9 Hz, 2 H), 7.45 (m, 7 H), 4.28 (m, 1 H), 4.20 (m, 1 H), 3.70 (m, 2 H), 2.23 (s, 3 H), 2.00–1.65 (m, 6 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 185.5, 170.2, 169.7, 169.4, 137.9, 134.5, 132.5, 131.4, 131.0, 130.3, 129.6, 128.2, 127.9, 127.3, 126.2, 124.6, 124.0, 114.5, 107.6, 96.2, 53.0, 51.2, 25.9, 25.8, 23.4, 21.3. HRMS (EI) Calcd for $C_{28}H_{25}NO_4$: 439.1783. Found: 439.1784.

4-Acetoxy-2-benzoyl-4-(2-naphthyl)-3-(1-piperidinyl)-2-cyclobuten-1-one, 4g. By the representative procedure, 2-bromonaphthalene (85 mg, 0.410 mmol, 1.11 equiv) in THF (5 mL), t-BuLi (0.54 mL, 1.70 M in pentane, 0.920 mmol, 2.48 equiv), 3-benzoyl-4-(1-piperidinyl)-3-cyclobutene-1,2-dione (100 mg, 0.371 mmol, 1.00 equiv) in THF (10 mL), and Ac_2O (0.20 mL, 2.120 mmol, 4.30 equiv) gave a yellow oil. Chromatographic purification (flash column, silica gel, 1 cm x 10 cm, 30% ethyl acetate in hexanes) gave 124 mg (0.282 mmol, 76%) of 4-acetoxy-2-benzoyl-4-(2-naphthyl)-3-(1-piperidinyl)-2-cyclobuten-1-one as a white microcrystalline solid. TLC (silica gel, 50% ethyl acetate in hexanes, R_f = 0.40); mp 155–157 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 2951 (w), 2864 (w), 1751 (s), 1637 (s), 1604 (s), 1451 (m), 1227 (m), 965 (w). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.12 (d, J = 7.2 Hz, 2 H), 8.00 (s, 1 H), 7.85 (m, 3 H), 7.50 (m, 6 H), 4.16 (m, 2 H), 3.45 (m, 2 H), 2.32 (s, 3 H), 1.90 (m, 2 H), 1.68 (m, 2 H), 1.50 (m, 2 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 185.1, 178.3, 169.5, 169.4, 137.9, 133.2, 132.7, 131.5, 129.7, 128.8, 128.2, 128.0, 127.6, 126.6, 126.5, 124.7, 122.4, 116.9, 104.9, 93.8, 52.7, 51.5, 25.9 (2C), 23.3, 21.3. Anal. Calcd for $C_{28}H_{25}NO_4 \cdot {}^1/_2H_2O$: C, 75.17; H, 6.04; N, 3.13. Found: C, 75.47; H, 5.81; N, 3.10. HRMS (EI) Calcd for $C_{28}H_{25}NO_4$: 439.1783. Found: 439.1779.

4-Acetoxy-2-benzoyl-4-(3-furanyl)-3-(1-piperidinyl)-2-cyclobuten-1-one, 4h. By the representative procedure, 3-bromofuran (90 mg, 0.612 mmol, 1.32 equiv) in THF (5 mL), t-BuLi (0.65 mL, 1.70 M in pentane, 1.110 mmol, 2.39 equiv), 3-benzoyl-4-(1-piperidinyl)-3-cyclobutene-1,2-dione (125 mg, 0.464 mmol, 1.00 equiv) in THF (10 mL), and Ac_2O (0.20 mL, 2.120 mmol, 4.57 equiv) gave a yellow oil. Chromatographic purification (flash column, silica gel, 1 cm x 10 cm, 30% ethyl acetate in hexanes) gave 112 mg (0.295 mmol, 64%) of 4-acetoxy-2-benzoyl-4-(3-furanyl)-3-(1-piperidinyl)-2-cyclobuten-1-one as an off-white solid. TLC (silica gel, 30% ethyl acetate in hexanes, R_f = 0.17); mp 127–130 °C dec (methylene chloride/pentane); IR (CH_2Cl_2, KCl, cm^{-1}): 2950 (w), 2865 (w), 1755 (s), 1639 (s), 1604 (s), 1451 (s), 1433 (m), 1219 (s), 1169 (m). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.07 (d, J = 7.8 Hz, 2 H), 7.57 (s, 1 H), 7.44 (m, 4 H), 6.40 (s, 1 H), 4.15 (m, 1 H), 4.02 (m, 1 H), 3.50 (m, 2 H), 2.21 (s, 3 H), 1.85 (m, 2 H), 1.70 (m, 2 H), 1.58 (m, 2 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 185.3, 178.5, 170.1, 169.3, 158.1, 143.9, 140.3, 137.9, 132.7, 129.7, 128.1, 120.9, 107.9, 89.4, 52.7, 51.1, 26.1, 25.9, 23.4, 21.1. Anal. Calcd for $C_{22}H_{21}NO_5$-1/3 H_2O: C, 68.55; H, 5.54; N, 3.64. Found: C, 68.53; H, 5.47; N, 3.53. HRMS (EI) Calcd for $C_{22}H_{21}NO_5$: 379.1419. Found: 379.1405.

4-Acetoxy-2-benzoyl-3-(1-piperidinyl)-4-(2-thienyl)-2-cyclobuten-1-one, 4i. By the representative procedure, 2-bromothiophene (184 mg, 1.129 mmol, 1.15 equiv) in THF (5 mL), t-BuLi (1.30 mL, 1.70 M in pentane, 2.210 mmol, 2.25 equiv), 3-benzoyl-4-(1-piperidinyl)-3-cyclobutene-1,2-dione (265 mg, 0.984 mmol, 1.00 equiv) in THF (10 mL), and Ac_2O (0.20 mL, 2.120 mmol, 4.57 equiv) gave a yellow oil. Chromatographic purification (flash column, silica gel, 1 cm x 12 cm, 20–30% ethyl acetate in hexanes) gave 269 mg (0.680 mmol, 69%) of 4-acetoxy-2-benzoyl-3-(1-piperidinyl)-4-(2-thienyl)-2-cyclobuten-1-one as an off-white solid. TLC (silica gel, 50% ethyl acetate in hexanes, R_f = 0.33); mp 153–154 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 3066 (m), 2949 (m), 2863 (m), 1755 (s), 1636 (s), 1605 (s), 1450 (s), 1433 (s), 1370 (s), 1291 (s), 1216 (s), 1100 (m), 960 (m). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.07 (d, J = 7.8 Hz, 2 H), 7.52 (t, J = 7.2 Hz, 1 H), 7.44 (t, J = 7.5 Hz, 2 H), 7.32 (d, J = 5.1 Hz, 1 H), 7.14 (d, J = 3.0 Hz, 1 H), 7.01 (t, J = 4.0 Hz, 1 H), 4.20 (m, 1 H), 4.02 (m, 1 H), 3.51 (s, 2 H), 2.24 (s, 3 H), 1.84 (m, 2 H), 1.72 (m, 2 H), 1.59 (m, 2 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 185.3, 178.0, 169.6, 169.0, 137.9, 137.6, 132.7, 129.7, 128.0, 127.2, 126.2, 124.8, 116.2, 91.8, 52.8, 51.5, 25.9, 25.8, 23.3, 21.1. Anal. Calcd for $C_{22}H_{21}NO_4S$: C, 66.82; H, 5.35; N, 3.54; S, 8.11. Found: C, 66.78; H, 5.35; N, 3.51.

4-Acetoxy-2-benzoyl-3-(1-piperidinyl)-4-(1-propenyl)-2-cyclobuten-1-one, 4j. By the representative procedure, (*E*/*Z*)-1-(tri-*n*-butylstannyl)propene (135 mg, 0.393 mmol, 1.06 equiv) in THF (5 mL), *n*-BuLi (0.32 mL, 1.45 M in hexanes, 0.460 mmol, 1.24 equiv), 3-benzoyl-4-(1-piperidinyl)-3-cyclobutene-1,2-dione (100 mg, 0.371 mmol, 1.00 equiv) in THF (10 mL), and Ac_2O (0.20 mL, 2.120 mmol, 5.71 equiv) gave a yellow oil. Chromatographic purification (flash column, silica gel, 1 cm x 10 cm, 30−50% ethyl acetate in hexanes) afforded 98 mg (0.277 mmol, 75%) of 4-acetoxy-2-benzoyl-3-(1-piperidinyl)-4-(1-propenyl)-2-cyclobuten-1-one as a yellow oil. TLC (silica gel, 50% ethyl acetate in hexanes, $R_f = 0.35$). IR (CH_2Cl_2, KCl, cm^{-1}): 3060 (w), 2949 (w), 2864 (w), 1750 (s), 1635 (s), 1602 (s), 1451 (s), 1435 (m), 1226 (s), 963 (w). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.05 (d, $J = 7.2$ Hz, 2 H), 7.44 (m, 3 H), 5.80 (m, 1 H), 5.43 (dd, $J = 8.4$, 1.5 Hz, 1 H), 4.05 (m, 2 H), 3.55 (m, 2 H), 2.13 (s, 3 H), 1.85 (dd, $J = 7.2$, 1.5 Hz, 3 H), 1.69 (m, 6 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 185.1, 178.4, 171.0, 169.4, 137.9, 132.9, 132.5, 129.6, 127.9, 122.3, 115.7, 91.7, 52.4, 51.3, 26.1, 25.7, 23.3, 21.1, 14.5. HRMS (EI) Calcd for $C_{21}H_{23}NO_4$: 353.1627. Found: 353.1628.

4-Acetoxy-2-benzoyl-4-(2,3-dihydrofuran-5-yl)-3-(1-piperidinyl)-2-cyclobuten-1-one, 4k. By the representative procedure, 5-(tri-*n*-butylstannyl)-2,3-dihydrofuran (200 mg, 0.557 mmol, 1.15 equiv) in THF (5 mL), *n*-BuLi (0.38 mL, 1.60 M in hexanes, 0.610 mmol, 1.26 equiv), 3-benzoyl-4-(1-piperidinyl)-3-cyclobutene-1,2-dione (130 mg, 0.483 mmol, 1.00 equiv) in THF (10 mL), and Ac_2O (0.30 mL, 3.180 mmol, 6.58 equiv) gave a yellow oil. Chromatographic purification (flash column, silica gel, 1 cm x 10 cm, 10−50% ethyl acetate in hexanes) afforded 142 mg (0.372 mmol, 77%) of 4-acetoxy-2-benzoyl-4-(2,3-dihydrofuran-5-yl)-3-(1-piperidinyl)-2-cyclobuten-1-one as a white microcrystalline solid. TLC (silica gel, 50% ethyl acetate in hexanes, $R_f = 0.22$); mp 144−145 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 3063 (w), 2953 (m), 2865 (w), 1754 (s), 1636 (s), 1451 (s), 1436 (s), 1218 (s), 1143 (w), 934 (w). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.05 (d, $J = 7.8$ Hz, 2 H), 7.45 (m, 3 H), 5.25 (t, $J = 2.7$ Hz, 1 H), 4.39 (t, $J = 9.3$ Hz, 2 H), 4.17 (m, 1 H), 3.94 (m, 1 H), 3.64 (m, 2 H), 2.69 (dt, $J = 9.6$, 2.4 Hz, 2 H), 2.16 (s, 3 H), 1.70 (m, 6 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 185.1, 177.0, 169.0, 168.9, 150.7, 138.0, 132.6, 129.7, 128.0, 116.4, 100.4, 89.2, 70.8, 52.8, 51.7, 30.0, 26.2, 25.8, 23.5, 22.1. Anal. Calcd for $C_{22}H_{23}NO_5$: C, 69.28; H, 6.08; N, 3.67. Found: C, 69.38; H, 6.09; N, 3.64.

4-Acetoxy-2-benzoyl-4-(3,4-dihydro-2*H*-pyran-6-yl)-3-(1-piperidinyl)-2-cyclobuten-1-one, 4l. By the representative procedure, 6-(tri-*n*-butylstannyl)-3,4-dihydro-2*H*-pyran (240 mg, 0.643 mmol, 1.33 equiv) in THF (5 mL), *n*-BuLi (0.45 mL, 1.60 M in hexanes, 0.720 mmol, 1.49 equiv), 3-benzoyl-4-(1-piperidinyl)-3-cyclobutene-1,2-dione (130 mg, 0.483 mmol, 1.00 equiv) in THF (10 mL), and Ac_2O (0.30 mL, 3.180 mmol, 6.58 equiv) gave a yellow oil. Chromatographic purification (flash column, silica gel, 1 cm x 10 cm, 10−50% ethyl acetate in hexanes) afforded 148 mg (0.374 mmol, 77%) of 4-acetoxy-2-benzoyl-4-(3,4-dihydro-2*H*-pyran-6-yl)-3-(1-piperidinyl)-2-cyclobuten-1-one as a white microcrystalline solid. TLC (silica gel, 50% ethyl acetate in hexanes, $R_f = 0.30$); mp 134−135 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 3063 (w), 2948 (s), 2864 (m), 1752 (s), 1635 (s), 1600 (s), 1453 (s), 1435 (s), 1220 (s), 1142 (m), 1070 (s), 1022 (m). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.05 (dd, $J = 7.2$, 1.2 Hz, 2 H), 7.50 (m, 3 H), 5.22 (t, $J = 3.9$ Hz, 1 H), 4.15 (m, 1 H), 4.01 (m, 2 H), 3.90 (m, 1 H), 3.60 (m, 2 H), 2.16 (s, 3 H), 2.05 (m, 2 H), 1.82 (m, 4 H), 1.70 (m, 4 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 184.5, 177.8, 169.3, 169.0, 146.8, 138.1, 132.5, 129.7, 127.9, 117.0, 100.7, 91.8, 66.8, 52.7, 51.6, 26.1, 25.8, 23.4, 21.9, 21.2, 20.1. Anal. Calcd for $C_{23}H_{25}NO_5$: C, 69.86; H, 6.37; N, 3.54. Found: C, 69.60; H, 6.36; N, 3.47.

4-Acetoxy-2-benzoyl-3-(*tert*-butylamino)-4-(2,3-dihydrofuran-5-yl)-2-cyclobuten-1-one, 4m. By the representative procedure, 5-(tri-*n*-butylstannyl)-2,3-dihydrofuran (688 mg, 1.916 mmol, 2.24 equiv) in THF (5 mL), *n*-BuLi (1.25 mL, 1.60 M in hexanes, 2.000 mmol, 2.34 equiv), 3-benzoyl-4-(*tert*-butylamino)-3-cyclobutene-1,2-dione (220 mg, 0.855 mmol, 1.00 equiv) in THF (10 mL), and Ac_2O (0.60 mL, 6.360 mmol, 7.44 equiv) gave a yellow oil. Chromatographic purification (flash column, silica gel, 1 cm x 12 cm, 20−40% ethyl acetate in hexanes) afforded 173 mg (0.468 mmol, 55%) of 4-acetoxy-2-benzoyl-3-(*tert*-butylamino)-4-(2,3-dihydrofuran-5-yl)-2-cyclobuten-1-one as a white microcrystalline solid. TLC (silica gel, 30% ethyl acetate in hexanes, $R_f = 0.22$); mp 147−148 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 3250 (br, w), 3062 (m), 2982 (m), 1756 (s), 1614 (s), 1568 (s), 1460 (s), 1370 (s), 1226 (s), 1184 (s), 1130 (m), 988 (w). ^1H NMR ($CDCl_3$, 300 MHz): δ 9.64 (br s, 1 H), 8.42 (dd, $J = 7.8$, 1.2 Hz, 2 H), 7.47 (m, 3 H), 5.32 (t, $J = 2.4$ Hz, 1 H), 4.36 (m, 2 H), 2.72 (m, 2 H), 2.16 (s, 3 H), 1.43 (s, 9 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 186.6, 176.4, 174.9, 168.6, 150.8, 136.2, 133.0, 129.3, 128.4, 119.4, 99.5, 91.0, 70.8, 55.4, 30.1, 29.7, 21.2. Anal. Calcd for $C_{21}H_{23}NO_5$: C, 68.28; H, 6.28; N, 3.79. Found: C, 67.63; H, 6.30; N, 3.72. HRMS (EI) Calcd for $C_{21}H_{23}NO_5$: 369.1576. Found: 369.1573.

4-Acetoxy-2-benzoyl-3-(*tert*-butylamino)-4-(3,4-dihydro-2*H*-pyran-6-yl)-2-cyclobuten-1-one, 4n. By the representative procedure, 6-(tri-*n*-butylstannyl)-3,4-dihydro-2*H*-pyran (930 mg, 2.492 mmol, 2.51 equiv) in THF (5 mL), *n*-BuLi (1.60 mL, 1.60 M in hexanes, 2.560 mmol, 2.58 equiv), 3-benzoyl-4-(*tert*-butylamino)-3-cyclobutene-1,2-dione (255 mg, 0.991 mmol, 1.00 equiv) in THF (10 mL), and Ac_2O (0.60 mL, 6.360 mmol, 6.42 equiv) gave a yellow oil. Chromatographic purification (flash column, silica gel, 1 cm x 12 cm, 20−40% ethyl acetate in hexanes) afforded 205 mg (0.535 mmol, 54%) of 4-acetoxy-2-benzoyl-3-(*tert*-butylamino)-4-(3,4-dihydro-2*H*-pyran-6-yl)-2-cyclobuten-1-one as a white microcrystalline solid. TLC (silica gel, 40% ethyl acetate in hexanes, $R_f = 0.32$); mp 133−134 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 3058 (m), 2987 (w), 1754 (s), 1613 (s), 1586 (s), 1465 (m), 1372 (m), 1228 (s), 1072 (w). ^1H NMR ($CDCl_3$, 300 MHz): δ 9.61 (br s, 1 H), 8.43 (d, $J = 7.5$ Hz, 2 H), 7.50 (m, 3 H), 5.29 (dd, $J = 3.9$, 3.3 Hz, 1 H), 3.95 (m, 2 H), 2.13 (s, 3 H), 2.10 (m, 2 H), 1.81 (m, 2 H), 1.42 (s, 9 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 186.3, 177.3, 175.2, 168.4, 146.3, 136.3, 132.9, 129.3, 128.4, 120.2, 99.4, 92.9, 66.7, 55.3, 29.7, 21.9, 21.2, 20.1. HRMS (EI) Calcd for $C_{22}H_{25}NO_5$: 383.1732. Found: 383.1732.

4-Acetoxy-2-acetyl-3-(*N*,*N*-dibenzylamino)-4-(2,3-dihydrofuran-5-yl)-2-cyclobuten-1-one, 4o. By the representative procedure, 5-(tri-*n*-butylstannyl)-2,3-dihydropyran (210 mg, 0.563 mmol, 1.24 equiv) in THF (5 mL), *n*-BuLi (0.38 mL, 1.60 M in hexanes, 0.610 mmol, 1.34 equiv), 3-acetyl-4-(*N*,*N*-dibenzylamino)-3-cyclobutene-1,2-dione (145 mg, 0.454 mmol, 1.00 equiv) in THF (10 mL), and Ac_2O (0.20 mL, 2.120 mmol, 4.67 equiv) gave a yellow oil. Chromatographic purification (flash column, silica gel, 1 cm x 12 cm, 20−40% ethyl acetate in hexanes) afforded 142 mg (0.329 mmol, 72%) of 4-acetoxy-2-acetyl-3-(*N*,*N*-dibenzylamino)-4-(2,3-dihydrofuran-5-yl)-2-cyclobuten-1-one as a white microcrystalline solid. TLC (silica gel, 30% ethyl acetate in hexanes, $R_f = 0.19$); mp 141−143 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 2930 (w), 2865 (w), 1759 (s), 1657 (s), 1602 (s), 1583 (s), 1454 (s), 1246 (m), 1217 (m), 1048 (m). ^1H NMR ($CDCl_3$, 300 MHz): δ 7.35 (m, 6 H), 7.15 (m, 4 H), 5.41 (A of AB quartet, $J = 17.7$ Hz, 1 H), 5.23 (t, $J = 2.7$ Hz, 1 H), 5.13 (B of AB quartet, $J = 17.4$ Hz, 1 H), 4.46 (pent, $J = 15.3$ Hz, 2 H), 4.35 (m, 2 H), 2.65 (s, 2 H), 2.50 (s, 3 H), 1.98 (s, 3 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 190.2, 180.2, 170.0, 168.6, 150.2, 135.0, 133.7, 129.0, 128.8, 128.5, 128.4, 128.1, 127.5, 118.5, 100.4, 90.8, 70.7, 56.5, 53.4, 30.1, 30.0, 20.9. Anal. Calcd for $C_{26}H_{25}NO_5$·1/3 H_2O: C, 71.40; H, 5.80. Found: C, 71.40; H, 5.95. HRMS (EI) Calcd for $C_{26}H_{25}NO_5$: 431.1732. Found: 431.1737.

4-Acetoxy-2-acetyl-3-(*N*,*N*-dibenzylamino)-4-(3,4-dihydro-2*H*-pyran-6-yl)-2-cyclobuten-1-one, 4p. By the representative procedure, 6-(tri-*n*-butylstannyl)-3,4-dihydro-2*H*-pyran (410 mg, 1.270 mmol, 1.33 equiv) in THF (5 mL), *n*-BuLi (0.85 mL, 1.49 M in hexanes, 0.610 mmol, 1.34 equiv), 3-acetyl-4-(*N*,*N*-dibenzylamino)-3-cyclobutene-1,2-dione (305 mg, 0.955 mmol, 1.00 equiv) in THF (10 mL), and Ac_2O (0.20 mL, 2.120 mmol, 4.67 equiv) gave a yellow oil. Chromatographic purification (flash column, silica gel, 1 cm x 12 cm, 30% ethyl acetate in hexanes) afforded 234 mg (0.525 mmol, 55%) of 4-acetoxy-2-acetyl-3-(*N*,*N*-dibenzylamino)-4-(3,4-dihydro-2*H*-pyran-6-yl)-2-cyclobuten-1-one as a white microcrystalline solid. TLC (silica gel, 50% ethyl acetate in hexanes, $R_f = 0.35$);

mp 72–73 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 2937 (w), 1759 (s), 1655 (s), 1600 (s), 1454 (s), 1369 (m), 1222 (m), 1115 (m), 1072 (m). ^1H NMR ($CDCl_3$, 300 MHz): δ 7.36 (m, 6 H), 7.16 (m, 4 H), 5.26 (m, 2 H), 5.22 (t, J = 3.9 Hz, 1 H), 4.48 (m, 2 H), 3.98 (m, 2 H), 2.48 (s, 3 H), 2.05 (m, 2 H), 1.95 (s, 3 H), 1.80 (m, 2 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 190.1, 181.1, 170.4, 168.6, 146.0, 135.2, 133.8, 129.0, 128.8, 128.5, 128.3, 128.1, 127.5, 119.2, 100.6, 92.9, 66.8, 56.4, 53.4, 30.1, 21.8, 20.9, 20.0. Anal. Calcd for $C_{27}H_{27}NO_5$: C, 72.79; H, 6.11; N, 3.14. Found: C, 72.87; H, 6.19; N, 3.11.

4-Acetoxy-2-benzoyl-4-(4-(*N*,*N*-dimethylamino)phenyl)-3-(1-piperidinyl)-2-cyclobuten-1-one, 4q. By the representative procedure, 4-bromo-*N*,*N*-dimethylaniline (110 mg, 0.550 mmol, 1.12 equiv) in THF (5 mL), *t*-BuLi (0.65 mL, 1.70 M in pentane, 1.110 mmol, 2.27 equiv), 3-benzoyl-4-(1-piperidinyl)-3-cyclobutene-1,2-dione (130 mg, 0.490 mmol, 1.00 equiv) in THF (10 mL), and Ac_2O (0.20 mL, 2.120 mmol, 4.67 equiv) gave a yellow oil. Chromatographic purification (flash column, silica gel, 1 cm x 12 cm, 50% ethyl acetate in hexanes) afforded 131 mg (0.303 mmol, 62%) of 4-acetoxy-2-benzoyl-4-(4-(*N*,*N*-dimethylamino)phenyl)-3-(1-piperidinyl)-2-cyclobuten-1-one as a white solid. TLC (silica gel, 50% ethyl acetate in hexanes, R_f = 0.22); mp 229–231 °C (methylene chloride/pentane); IR (CH_2Cl_2, KCl, cm^{-1}): 2945 (m), 2862 (m), 1747 (s), 1627 (s), 1601 (s), 1523 (s), 1450 (s), 1435 (s), 1367 (s), 1289 (m), 1221 (s), 1143 (m). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.08 (d, J = 7.5 Hz, 2 H), 7.50 (t, J = 6.6 Hz, 1 H), 7.42 (t, J = 7.5 Hz, 2 H), 7.33 (d, J = 8.7 Hz, 2 H), 6.70 (d, J = 8.7 Hz, 2 H), 4.15 (m, 2 H), 3.47 (m, 2 H), 2.94 (s, 6 H), 2.23 (s, 3 H), 1.88 (m, 2 H), 1.69 (m, 2 H), 1.57 (m, 2 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 185.1, 179.5, 170.4, 169.6, 150.6, 138.1, 132.5, 129.7, 127.9, 126.2, 121.2, 116.1, 112.3, 93.3, 52.6, 51.4, 40.2, 25.9 (2C), 23.4, 21.3. Anal. Calcd for $C_{26}H_{28}N_2O_4$: C, 72.20; H, 6.53; N, 6.48. Found: C, 71.99; H, 6.54; N, 6.47.

Thermolysis of 4-Acetoxycyclobutenones, 4. Representative Procedure. 4-Acetoxy-2-benzoyl-6-methoxy-3-(1-piperidinyl)naphth-1-ol, 5c and 4-Acetoxy-2-benzoyl-8-methoxy-3-(1-piperidinyl)naphth-1-ol, 5c′. A mesitylene (2.5 mL) solution of 4-acetoxy-2-benzoyl-4-(3-anisyl)-3-(1-piperidinyl)-2-cyclobuten-1-one (22 mg, 0.052 mmol, 1.00 equiv) was sparged with argon and then heated to reflux under an argon atmosphere. Monitoring by TLC indicated consumption of starting material after 72 h. The reaction mixture was cooled to rt and concentrated on a rotary evaporator to give a red oil. ^1H NMR analysis indicated a 78:22 mixture of **5c**:**5c′**. Chromatographic purification (preparative TLC, silica gel, 40% ethyl acetate in hexanes) afforded 12 mg (0.029 mmol, 56%) of 4-acetoxy-2-benzoyl-6-methoxy-3-(1-piperidinyl)naphth-1-ol as an orange microcrystalline solid and 3.5 mg (0.008 mmol, 15%) of 4-acetoxy-2-benzoyl-8-methoxy-3-(1-piperidinyl)naphth-1-ol as a red microcrystalline solid. Data for **4-acetoxy-2-benzoyl-6-methoxy-3-(1-piperidinyl)naphth-1-ol:** TLC (silica gel, 50% ethyl acetate in hexanes, R_f = 0.70); mp 173–174 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 3052 (w), 2942 (m), 2857 (w), 1762 (s), 1624 (s), 1603 (s), 1578 (m), 1494 (s), 1425 (s), 1205 (s), 1012 (m), 909 (w), 888 (w). ^1H NMR ($CDCl_3$, 300 MHz): δ 11.00 (br s, 1 H), 8.27 (d, J = 9.0 Hz, 1 H), 7.60 (d, J = 7.2 Hz, 2 H), 7.49 (t, J = 7.2 Hz, 1 H), 7.39 (t, J = 7.2 Hz, 2 H), 7.06 (dd, J = 9.0, 2.4 Hz, 1 H), 6.83 (d, J = 2.1 Hz, 1 H), 3.92 (s, 3 H), 2.85 (m, 4 H), 2.43 (s, 3 H), 1.19 (m, 2 H), 0.98 (m, 4 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 200.2, 170.1, 161.3, 157.5, 140.9, 140.8, 133.4, 132.9, 131.7, 128.9, 127.9, 126.5, 117.1, 116.0, 113.1, 100.0, 55.3, 52.8, 25.4, 23.8, 21.1. Anal. Calcd for $C_{25}H_{25}NO_5$: C, 71.58; H, 6.01; N, 3.34. Found: C, 71.66; H, 6.07; N, 3.34. Data for **4-acetoxy-2-benzoyl-8-methoxy-3-(1-piperidinyl)naphth-1-ol**: TLC (silica gel, 50% ethyl acetate in hexanes, R_f = 0.57); mp 192–194 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 3375 (w), 3053 (m), 2937 (s), 2857 (w), 1764 (s), 1673 (m), 1627 (s), 1600 (s), 1448 (s), 1370 (s), 1039 (m). ^1H NMR ($CDCl_3$, 300 MHz): δ 9.44 (s, 1 H), 7.88 (d, J = 7.2 Hz, 2 H), 7.53 (t, J = 7.2 Hz, 1 H), 7.41 (m, 3 H), 7.24 (m, 1 H), 6.79 (d, J = 7.8 Hz, 1 H), 4.01 (s, 3 H), 2.90 (m, 4 H), 2.44 (s, 3 H), 1.30 (m, 2 H), 1.19 (m, 4 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 195.8, 170.0, 156.8, 150.0, 141.2, 138.3, 134.7, 132.7, 130.6, 129.1, 128.4, 127.3, 114.6, 112.8, 104.9, 104.3, 56.3, 52.4, 26.2, 24.1, 21.9. Anal. Calcd for $C_{25}H_{25}NO_5$: C, 71.58; H, 6.01; N, 3.34. Found: C, 71.53; H, 5.98; N, 3.27.

4-Acetoxy-2-benzoyl-6-(*N*,*N*-dimethylamino)-3-(1-piperidinyl)naphth-1-ol, 5e. 4-Acetoxy-2-benzoyl-4-(3-(*N*,*N*-dimethylamino)phenyl)-3-(1-piperidinyl)-2-cyclobuten-1-one (40 mg, 0.092 mmol, 1.00 equiv) in refluxing mesitylene (2.5 mL) after 11 h gave a red oil. Chromatographic purification (flash column, silica gel, 1 cm x 10 cm, 20% ethyl acetate in hexanes) afforded 18 mg (0.042 mmol, 46%) of 4-acetoxy-2-benzoyl-6-(*N*,*N*-dimethylamino)-3-(1-piperidinyl)naphth-1-ol as a yellow microcrystalline solid. TLC (silica gel, 30% ethyl acetate in hexanes, R_f = 0.50); mp 177–178 °C (methylene chloride/pentane); IR (CH_2Cl_2, KCl, cm^{-1}): 2945 (s), 2850 (m), 1768 (s), 1638 (s), 1610 (s), 1450 (s), 1336 (s), 1212 (s), 1130 (s), 1065 (m). ^1H NMR ($CDCl_3$, 300 MHz): δ 11.53 (s, 1 H), 8.17 (d, J = 9.3 Hz, 1 H), 7.59 (d, J = 7.2 Hz, 2 H), 7.47 (t, J = 7.2 Hz, 1 H), 7.40 (t, J = 7.8 Hz, 2 H), 6.98 (dd, J = 9.3, 2.4 Hz, 1 H), 6.47 (d, J = 2.4 Hz, 1 H), 3.10 (s, 6 H), 2.84 (m, 4 H), 2.41 (s, 3 H), 1.30 (m, 2 H), 0.95 (m, 4 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 200.0, 170.2, 158.7, 151.6, 141.6, 140.6, 133.6, 132.2, 131.2, 128.7, 127.7, 126.0, 114.0, 113.3, 111.2, 98.1, 52.7, 40.2, 25.4, 23.8, 21.1. Anal. Calcd for $C_{26}H_{28}N_2O_4$: C, 72.20; H, 6.53; N, 6.48. Found: C, 72.39; H, 6.62; N, 6.41.

4-Acetoxy-2-benzoyl-1-hydroxy-3-(1-piperidinyl)-phenanthrene, 5f. 4-Acetoxy-2-benzoyl-4-(1-naphthyl)-3-(1-piperidinyl)-2-cyclobuten-1-one (36 mg, 0.082 mmol, 1.00 equiv) in refluxing mesitylene (2.5 mL) after 10 h gave a red oil. Chromatographic purification (preparative TLC, silica gel, 30% ethyl acetate in hexanes) afforded 33 mg (0.075 mmol, 91%) of 4-acetoxy-2-benzoyl-1-hydroxy-3-(1-piperidinyl)phenanthrene as a red microcrystalline solid. TLC (silica gel, 30% ethyl acetate in hexanes, R_f = 0.44); mp 151–153 °C (methylene chloride/pentane); IR (CH_2Cl_2, KCl, cm^{-1}): 2942 (m), 2853 (w), 1761 (s), 1612 (s), 1592 (s), 1444 (m), 1325 (s), 1200 (s), 1185 (s). ^1H NMR ($CDCl_3$, 300 MHz): δ 10.58 (s, 1 H), 9.07 (d, J = 8.4 Hz, 1 H), 8.28 (d, J = 9.0 Hz, 1 H), 7.89 (d, J = 6.9 Hz, 1 H), 7.70 (m, 3 H), 7.60 (m, 3 H), 7.44 (t, J = 7.5 Hz, 2 H), 2.91 (m, 4 H), 2.38 (s, 3 H), 1.63 (m, 6 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 200.2, 169.4, 155.8, 143.1, 140.3, 136.6, 134.8, 132.3, 129.9, 129.3, 129.0, 128.4, 128.1, 127.6, 127.0, 126.2, 126.0, 120.9, 120.4, 115.5, 53.4, 25.7, 23.8, 21.6. Anal. Calcd for $C_{28}H_{25}NO_4$: C, 76.52; H, 5.73; N, 3.19. Found: C, 76.42; H, 5.72; N, 3.16.

1-Acetoxy-3-benzoyl-4-hydroxy-2-(1-piperidinyl)-phenanthrene, 5g. 4-Acetoxy-2-benzoyl-4-(2-naphthyl)-3-(1-piperidinyl)-2-cyclobuten-1-one (36 mg, 0.082 mmol, 1.00 equiv) in refluxing mesitylene (2.5 mL) after 29 h gave a red oil. Chromatographic purification (preparative TLC, silica gel, 40% ethyl acetate in hexanes) afforded 30 mg (0.068 mmol, 83%) of 1-acetoxy-3-benzoyl-4-hydroxy-2-(1-piperidinyl)phenanthrene as an orange microcrystalline solid. TLC (silica gel, 40% ethyl acetate in hexanes, R_f = 0.60); mp 194–195 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 3057 (w), 2942 (m), 2857 (w), 1764 (s), 1609 (s), 1596 (s), 1447 (m), 1331 (m), 1198 (s), 907 (w). ^1H NMR ($CDCl_3$, 300 MHz): δ 11.35 (s, 1 H), 9.72 (d, J = 8.7 Hz, 1 H), 7.86 (dd, J = 5.4, 3.6 Hz, 2 H), 7.59 (m, 6 H), 7.42 (t, J = 7.5 Hz, 2 H), 2.90 (m, 4 H), 2.48 (s, 3 H), 1.52 (m, 2 H), 1.05 (m, 4 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 201.0, 170.2, 158.6, 158.4, 141.7, 132.1, 131.8, 131.7 (2C), 129.1, 128.5, 128.3, 128.1, 128.0, 127.7, 126.6, 118.6, 116.7 (2C), 53.1, 25.5, 23.8, 21.2. HRMS (EI) Calcd for $C_{28}H_{25}NO_4$: 439.1783. Found: 439.1778.

4-Acetoxy-6-benzoyl-7-hydroxy-5-(1-piperidinyl)benzo[*b*]furan, 6a. 4-Acetoxy-2-benzoyl-4-(3-furanyl)-3-(1-piperidinyl)-2-cyclobuten-1-one (95 mg, 0.250 mmol, 1.00 equiv) in refluxing mesitylene (5 mL) after 5 h gave a red oil. Chromatographic purification (preparative TLC, silica gel, 30% ethyl acetate in hexanes) afforded 85 mg (0.224 mmol, 90%) of 4-acetoxy-6-benzoyl-7-hydroxy-5-(1-piperidinyl)benzo[*b*]furan as an orange microcrystalline solid. TLC (silica gel, 30% ethyl acetate in hexanes, R_f = 0.40); mp 110–111 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 2942 (m), 2855 (w), 1763 (s), 1645 (m), 1597 (m), 1460 (s), 1297 (s), 1198 (s), 1050 (s), 978 (m), 909 (m). ^1H NMR ($CDCl_3$, 300 MHz): δ 9.37 (br s, 1 H), 7.69 (d, J = 2.1 Hz, 1 H), 7.61 (d, J = 7.8 Hz, 2 H), 7.52 (t, J = 7.5 Hz, 1 H), 7.38 (t, J = 7.5 Hz, 2 H), 5.57

(d, J = 2.1 Hz, 1 H), 2.79 (m, 4 H), 2.38 (s, 3 H), 1.18 (m, 2 H), 0.92 (m, 4 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 200.0, 169.4, 147.6, 143.0, 140.8, 140.5, 139.5, 132.7, 131.8, 128.5, 127.9, 127.8, 117.7, 104.8, 53.1, 25.4, 23.7, 21.0. Anal. Calcd for $C_{22}H_{21}NO_5$: C, 69.65; H, 5.58; N, 3.69. Found: C, 69.40; H, 5.85; N, 3.55.

7-Acetoxy-5-benzoyl-4-hydroxy-6-(1-piperidinyl)benzo[*b*]thiophene, 6b. 4-Acetoxy-2-benzoyl-3-(1-piperidinyl)-4-(2-thienyl)-2-cyclobuten-1-one (52 mg, 0.131 mmol, 1.00 equiv) in refluxing mesitylene (5 mL) after 16 h gave a red solid. Chromatographic purification (flash column, silica gel, 1 cm x 10 cm, 30% ethyl acetate in hexanes) afforded 45 mg (0.114 mmol, 87%) of 7-acetoxy-5-benzoyl-4-hydroxy-6-(1-piperidinyl)-benzo[*b*]thiophene as a yellow microcrystalline solid. TLC (silica gel, 40% ethyl acetate in hexanes, R_f = 0.40); mp 129–130 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 3058 (s), 2987 (m), 2940 (m), 1769 (s), 1609 (s), 1444 (s), 1190 (s), 1041 (m), 894 (s). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.17 (s, 1 H), 7.62 (d, J = 7.2 Hz, 2 H), 7.55 (d, J = 5.7 Hz, 1 H), 7.50 (t, J = 7.2 Hz, 1 H), 7.40 (t, J = 7.5 Hz, 2 H), 7.26 (d, J = 5.4 Hz, 1 H), 2.82 (t, J = 5.1 Hz, 4 H), 2.39 (s, 3 H), 1.25 (m, 2 H), 0.98 (m, 4 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 200.5, 169.1, 153.6, 141.1, 140.8, 133.8, 131.9, 128.9, 127.9, 126.9, 123.9, 122.2, 115.9, 53.1, 25.4 (2C), 23.7, 21.0. Anal. Calcd for $C_{22}H_{21}NO_4S$: C, 66.82; H, 5.35; N, 3.54; S, 8.11. Found: C, 66.64; H, 5.41; N, 3.47.

4-Acetoxy-2-benzoyl-3-(1-piperidinyl)-6-methylphenol, 6c. 4-Acetoxy-2-benzoyl-4-(1-propenyl)-3-(1-piperidinyl)-2-cyclobuten-1-one (54 mg, 0.153 mmol, 1.00 equiv) in refluxing mesitylene (5 mL) after 1.5 h gave a red oil. Chromatographic purification (preparative TLC, silica gel, 50% ethyl acetate in hexanes) afforded 47 mg (0.133 mmol, 87%) of 4-acetoxy-2-benzoyl-3-(1-piperidinyl)-6-methylphenol as a orange oil. TLC (silica gel, 50% ethyl acetate in hexanes, R_f = 0.55). IR (CH_2Cl_2, KCl, cm^{-1}): 3056 (m), 2987 (m), 2942 (m), 2857 (w), 1760 (s), 1614 (s), 1448 (s), 1214 (s), 1193 (s), 1034 (w), 897 (m). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.85 (br s, 1 H), 7.62 (d, J = 7.2 Hz, 2 H), 7.50 (t, J = 7.2 Hz, 1 H), 7.39 (t, J = 7.8 Hz, 2 H), 6.91 (s, 1 H), 2.72 (m, 4 H), 2.29 (s, 3 H), 2.23 (s, 3 H), 1.17 (m, 2 H), 0.97 (m, 4 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 200.5, 170.2, 154.5, 142.4, 140.4, 139.0, 132.0, 129.8, 128.7, 128.0, 126.9, 121.7, 52.9, 25.5, 23.7, 21.3, 15.4. Anal. Calcd for $C_{21}H_{23}NO_4$: C, 71.37; H, 6.56; N, 3.96. Found: C, 71.67; H, 7.00; N, 3.54.

7-Acetoxy-5-benzoyl-4-hydroxy-6-(1-piperidinyl)dihydrobenzo[*b*]furan, 6d. 4-Acetoxy-2-benzoyl-4-(2,3-dihydrofuran-5-yl)-3-(1-piperidinyl)-2-cyclobuten-1-one (52 mg, 0.136 mmol, 1.00 equiv) in refluxing mesitylene (2.5 mL) after 10 min gave a bright yellow solid. Recrystallization from methylene chloride and pentane afforded 48.7 mg (0.128 mmol, 94%) of 7-acetoxy-5-benzoyl-4-hydroxy-6-(1-piperidinyl)dihydrobenzo[*b*]furan as a yellow microcrystalline solid. TLC (silica gel, 50% ethyl acetate in hexanes, R_f = 0.60); mp 175–176 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 3066 (w), 2942 (m), 2856 (w), 1763 (s), 1635 (s), 1605 (s), 1572 (m), 1447 (s), 1324 (s), 1196 (s), 1103 (s), 994 (m), 930 (m). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.30 (br s, 1 H), 7.57 (d, J = 7.2 Hz, 2 H), 7.47 (t, J = 6.9 Hz, 1 H), 7.38 (t, J = 7.5 Hz, 2 H), 4.71 (t, J = 8.7 Hz, 2 H), 3.23 (t, J = 8.7 Hz, 2 H), 2.70 (m, 4 H), 2.30 (s, 3 H), 1.18 (m, 2 H), 1.03 (m, 4 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 199.5, 169.1, 158.6, 155.1, 147.7, 141.1, 131.4, 128.8, 127.8, 124.2, 111.8, 108.2, 73.9, 53.3, 26.9, 25.6, 23.7, 20.8. Anal. Calcd for $C_{22}H_{23}NO_5$: C, 69.28; H, 6.08; N, 3.67. Found: C, 69.14; H, 6.07; N, 3.61.

7-Acetoxy-5-benzoyl-4-hydroxy-6-(1-piperidinyl)-3,4-dihydro-2*H*-benzo[*b*]pyran, 6e. 4-Acetoxy-2-benzoyl-4-(3,4-dihydro-2*H*-pyran-6-yl)-3-(1-piperidinyl)-2-cyclobuten-1-one (24 mg, 0.061 mmol, 1.00 equiv) in refluxing mesitylene (2 mL) after 10 min gave a bright yellow solid. Chromatographic purification (preparative TLC, silica gel, 50% ethyl acetate in hexanes) afforded 24 mg (0.061 mmol, 100%) of 7-acetoxy-5-benzoyl-4-hydroxy-6-(1-piperidinyl)-3,4-dihydro-2*H*-benzo[*b*]-pyran as a yellow microcrystalline solid. TLC (silica gel, 50% ethyl acetate in hexanes, R_f = 0.40); mp 159–160 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 2940 (s), 2856 (m), 1763 (s), 1635 (s), 1605 (s), 1575 (m), 1451 (s), 1364 (m), 1332 (s), 1210 (s), 1132 (s), 1069 (m). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.60 (s, 1 H), 7.57 (d, J = 7.5 Hz, 2 H), 7.47 (t, J = 6.6 Hz, 1 H), 7.38 (t, J = 7.5 Hz, 2 H), 4.22 (t, J = 5.1 Hz, 2 H), 2.70 (t, J = 6.3 Hz, 6 H), 2.30 (s, 3 H), 2.01 (m, 2 H), 1.16 (pent, J = 5.7 Hz, 2 H), 0.98 (m, 4 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 200.0, 169.7, 157.4, 152.8, 144.5, 141.3, 131.3, 128.7, 127.8 (2C), 110.7, 106.1, 67.2, 53.1, 25.5, 23.8, 21.3, 20.9, 18.7. Anal. Calcd for $C_{23}H_{25}NO_5$: C, 69.86; H, 6.37; N, 3.54. Found: C, 69.81; H, 6.06; N, 3.63.

7-Acetoxy-5-benzoyl-6-(*tert*-butylamino)-4-hydroxy-2,3-dihydrobenzo[*b*]furan, 6f. 4-Acetoxy-2-benzoyl-3-(*tert*-butylamino)-4-(2,3-dihydrofuran-5-yl)-2-cyclobuten-1-one (82 mg, 0.222 mmol, 1.00 equiv) in refluxing *m*-xylene (5 mL) after 5 min gave a bright yellow solid. Recrystallization from methylene chloride and pentane afforded 67 mg (0.181 mmol, 82%) of 7-acetoxy-5-benzoyl-6-(*tert*-butylamino)-4-hydroxy-2,3-dihydrobenzo[*b*]furan as a yellow microcrystalline solid. TLC (silica gel, 20% ethyl acetate in hexanes, R_f = 0.22); mp 126–127 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 3349 (w), 2974 (m), 1770 (s), 1637 (s), 1612 (s), 1483 (m), 1327 (s), 1199 (s), 1105 (s), 1020 (s), 924 (m). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.64 (s, 1 H), 7.61 (d, J = 7.2 Hz, 2 H), 7.45 (t, J = 7.2 Hz, 1 H), 7.34 (t, J = 7.5 Hz, 2 H), 4.75 (t, J = 9.0 Hz, 2 H), 3.28 (t, J = 9.0 Hz, 2 H), 2.64 (br s, 1 H), 2.30 (s, 3 H), 0.81 (s, 9 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 200.3, 168.3, 157.4, 154.8, 140.9, 140.2, 131.5, 129.9, 127.6, 124.4, 114.0, 109.9, 74.0, 55.8, 30.0, 27.0, 20.6. Anal. Calcd for $C_{21}H_{23}NO_5$: C, 68.28; H, 6.28; N, 3.79. Found: C, 68.18; H, 6.29; N, 3.72.

8-Acetoxy-6-benzoyl-7-(*tert*-butylamino)-5-hydroxy-3,4-dihydro-2*H*-benzo[*b*]pyran, 6g. 4-Acetoxy-2-benzoyl-3-(*tert*-butylamino)-4-(3,4-dihydro-2*H*-pyran-6-yl)-2-cyclobuten-1-one (70 mg, 0.183 mmol, 1.00 equiv) in refluxing mesitylene (2.5 mL) after 5 min gave a bright yellow solid. Chromatographic purification (flash column, silica gel, 1 cm x 10 cm, 10% ethyl acetate in hexanes) afforded 68 mg (0.177 mmol, 97%) of 8-acetoxy-6-benzoyl-7-(*tert*-butylamino)-5-hydroxy-3,4-dihydro-2*H*-benzo[*b*]pyran as a yellow microcrystalline solid. TLC (silica gel, 30% ethyl acetate in hexanes, R_f = 0.43); mp 135–137 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 2943 (m), 1764 (s), 1613 (s), 1574 (m), 1366 (s), 1329 (s), 1203 (s), 1139 (s), 1045 (m), 960 (m). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.97 (s, 1 H), 7.61 (d, J = 7.2 Hz, 2 H), 7.44 (t, J = 7.2 Hz, 1 H), 7.33 (t, J = 7.5 Hz, 2 H), 4.25 (t, J = 5.1 Hz, 2 H), 2.73 (t, J = 6.6 Hz, 2 H), 2.57 (br s, 1 H), 2.30 (s, 3 H), 2.05 (m, 2 H), 0.79 (s, 9 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 200.5, 168.8, 157.0, 152.1, 140.3, 137.6, 131.5, 130.0, 128.3, 127.5, 112.3, 107.0, 67.1, 55.5, 30.0, 21.2, 20.7, 18.7. Anal. Calcd for $C_{22}H_{25}NO_5$: C, 68.91; H, 6.57; N, 3.65. Found: C, 68.71; H, 6.58; N, 3.70.

7-Acetoxy-5-acetyl-6-(*N*,*N*-dibenzylamino)-4-hydroxy-2,3-dihydrobenzo[*b*]furan, 6h. 4-Acetoxy-2-acetyl-3-(*N*,*N*-dibenzylamino)-4-(2,3-dihydrofuran-5-yl)-2-cyclobuten-1-one (73 mg, 0.169 mmol, 1.00 equiv) in refluxing mesitylene (2.5 mL) after 5 min gave a bright yellow solid. Chromatographic purification (flash column, silica gel, 1 cm x 10 cm, 10–20% ethyl acetate in hexanes) afforded 67 mg (0.155 mmol, 92%) of 7-acetoxy-5-acetyl-6-(*N*,*N*-dibenzylamino)-4-hydroxy-2,3-dihydrobenzo[*b*]furan as a yellow microcrystalline solid. TLC (silica gel, 10% ethyl acetate in hexanes, R_f = 0.14); mp 114–115 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 3057 (w), 2984 (w), 2866 (w), 1766 (s), 1630 (s), 1606 (s), 1430 (s), 1360 (m), 1316 (s), 1200 (s), 1028 (m), 987 (m). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 12.55 (s, 1 H), 7.30 (m, 6 H), 7.20 (m, 4 H), 4.73 (t, J = 8.7 Hz, 2 H), 4.18 (s, 4 H), 3.23 (t, J = 8.7 Hz, 2 H), 2.51 (s, 3 H), 2.13 (s, 3 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 204.2, 168.2, 158.8, 157.4, 146.2, 136.9, 129.6, 128.3, 127.6, 125.5, 113.6, 110.0, 73.9, 57.1, 30.3, 26.9, 20.6. Anal. Calcd for $C_{26}H_{25}NO_5$: C, 72.37; H, 5.84; N, 3.25. Found: C, 72.23; H, 5.87; N, 3.27.

8-Acetoxy-6-acetyl-7-(*N*,*N*-dibenzylamino)-5-hydroxy-3,4-dihydro-2*H*-benzo[*b*]pyran, 6j. 4-Acetoxy-2-acetyl-3-(*N*,*N*-dibenzylamino)-4-(3,4-dihydro-2*H*-pyran-6-yl)-2-cyclobuten-1-one (90.4 mg, 0.203 mmol, 1.00 equiv) in refluxing *m*-xylene (2.5 mL) after 10 min gave a yellow solid. Chromatographic purification (flash column, silica gel, 1 cm x 10 cm, 10–20%

ethyl acetate in hexanes) afforded 78 mg (0.175 mmol, 86%) of 8-acetoxy-6-acetyl-7-(*N*,*N*-dibenzylamino)-5-hydroxy-3,4-dihydro-2*H*-benzo[*b*]pyran as a yellow microcrystalline solid. TLC (silica gel, 30% ethyl acetate in hexanes, $R_f = 0.34$); mp 135–136 °C (methylene chloride/pentane); IR (CH_2Cl_2, KCl, cm^{-1}): 3032 (w), 2929 (m), 2856 (m), 1765 (s), 1607 (s), 1428 (m), 1363 (s), 1206 (s), 1175 (s), 1064 (m), 974 (m), 906 (m). ^1H NMR ($CDCl_3$, 300 MHz): δ 13.00 (s, 1 H), 7.30 (m, 6 H), 7.20 (m, 4 H), 4.18 (m, 6 H), 2.70 (m, 2 H), 2.53 (s, 3 H), 2.16 (s, 3 H), 2.03 (m, 2 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 204.4, 168.9, 159.9, 153.1, 143.0, 137.1, 129.6, 128.3 (2C), 127.5, 112.1, 107.7, 67.2, 57.6, 30.6, 21.2, 20.8, 18.6. Anal. Calcd for $C_{27}H_{27}NO_5$: C, 72.79; H, 6.11; N, 3.14. Found: C, 72.54; H, 6.14; N, 3.12.

4-Acetoxy-3-benzoyl-1-(4-(*N*,*N*-dimethylamino)phenyl)-2-(1-piperidinyl)furan, 8. 4-Acetoxy-2-benzoyl-4-(4-(*N*,*N*-dimethylamino)phenyl)-3-(1-piperidinyl)-2-cyclobuten-1-one (20 mg, 0.046 mmol, 1.00 equiv) in refluxing mesitylene (2 mL) after 12 h gave a yellow solid. Chromatographic purification (preparative TLC, silica gel, 50% ethyl acetate in hexanes) afforded 16.5 mg (0.038 mmol, 83%) of 4-acetoxy-3-benzoyl-1-(4-(*N*,*N*-dimethylamino)phenyl)-2-(1-piperidinyl)furan as a yellow solid. TLC (silica gel, 50% ethyl acetate in hexanes, $R_f = 0.50$); mp 229–231 °C (methylene chloride/pentane). IR (CH_2Cl_2, KCl, cm^{-1}): 2937 (s), 2854 (m), 1772 (m), 1694 (s), 1630 (s), 1611 (s), 1538 (s), 1515 (s), 1447 (s), 1194 (s), 1129 (s). ^1H NMR ($CDCl_3$, 300 MHz): δ 7.80 (m, 2 H), 7.42 (m, 3 H), 7.17 (d, $J = 8.1$ Hz, 2 H), 6.76 (d, $J = 8.1$ Hz, 2 H), 2.99 (s, 6 H), 2.80 (m, 4 H), 2.20 (s, 3 H), 1.45 (m, 6 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 167.7, 163.4, 155.4, 150.4, 149.8, 148.6, 131.5, 130.5, 130.0, 129.8, 128.4, 128.1, 122.7, 112.0, 52.4, 40.5, 26.4, 23.8, 21.2. HRMS (EI) Calcd for $C_{26}H_{28}N_2O_4$: 432.2049. Found: 432.2054.

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Supporting Information Available: In lieu of microanalyses for compounds **3a**, **4a**, **5g**, and **8**, photocopies of their ^1H NMR spectra are available (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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