Lewis Acid Catalyzed Geminal Acylation Reaction of Ketones with 1,2-Bis((trimethylsilyl)oxy)cyclobutene: Direct Formation of 2,2-Disubstituted 1,3-Cyclopentanediones

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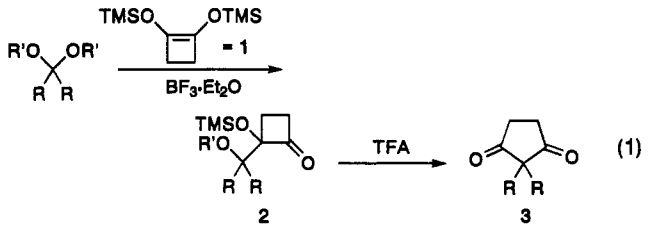
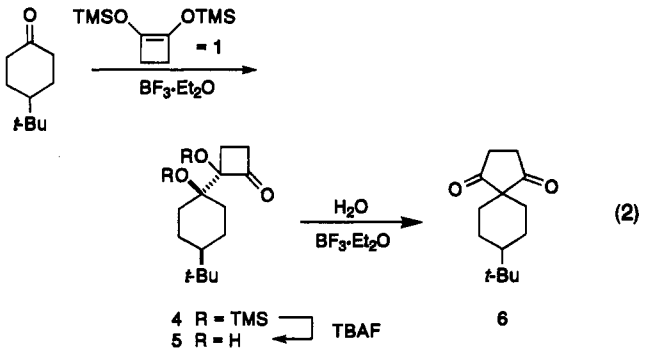
Ketones reacted with 1,2-bis((trimethylsilyl)oxy)cyclobutene (1) under catalysis by boron trifluoride etherate to yield 2,2-disubstituted 1,3-cyclopentanedione products via silylated cyclobutanone intermediates in a two-step, one-pot process. In many instances addition of a small amount of water to the reaction medium after completion of the first step assisted the subsequent rearrangement to the product, such that reversion of the intermediate to the starting ketone became an insignificant process. Yields were best with cyclohexanones (>90%), but steric hindrance and conjugated double bonds reduced yields considerably.

Treatment of the acetal of an unhindered ketone with 1,2-bis((trimethylsilyl)oxy)cyclobutene (1) in the presence of a Lewis acid is an effective method for converting that acetal into a doubly substituted 1,3-cyclopentanedione moiety.[1-5] In essence the process is a geminal acylation on the acetal carbon, and it has appeared as a key step in a number of syntheses.[2,6] Two reactions are involved: the first is the addition of 1 to the substrate, generally in the presence of BF_3·Et_2O as the catalyst, to give a cyclobutanone intermediate (2). In the initial procedure by Kuwajima,[1] the cyclobutanone 2 was isolated prior to rearrangement with trifluoroacetic acid to afford the diketone 3 (eq 1). Subsequent refinement in our laboratories[2,4] showed that both reactions could be effected in a single operation, often in higher overall yield, by the use of 2–3 molar equiv of 1 and a large excess of BF_3·Et_2O. Kuwajima stated that ketones were unreactive under the conditions of the initial aldol step,[1b] which was consistent with an indifference of silyl enol ethers toward reaction with ketones in other systems.[7] Mukaiyama[8] reported that $TiCl_4$-catalyzed reactions of silyl enol ethers with ketones were sluggish.



(1)

Only modest yields of geminally acylated products were realized when we subjected some simple cyclic ketones to the one-pot procedure developed for the acetals of ketones. GC-MS analysis of the reaction mixtures revealed that the starting ketones were largely consumed, but compared to the acetal reactions,[2,4] considerable amounts of unrearranged cyclobutanone intermediates remained. After much experimentation, we found that it was more productive to add initially 1.5 molar equiv of 1[9] and an equivalent of BF_3·Et_2O. The mixtures were stirred until the intermolecular reaction had taken place. It was possible to isolate some intermediates in which the ketone oxygens had become (trimethylsilyl)oxy groups and/or hydroxyls (e.g. 4 and/or 5 in eq 2), but during the workup and/or isolation process significant reversion to the starting ketones was observed. For the system shown in eq 2, NMR analysis indicated that a single bis((trimethylsilyl)oxy) compound was produced, and the X-ray structure revealed it to be the product of equatorial attack onto the carbonyl of the substrate, i.e. 4. This was the same direction of



(2)

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(7) (a) Stork, G.; Hudrlik, P. F. *J. Am. Chem. Soc.* **1968**, *90*, 4464. (b) Nakamura, E.; Shimizu, M.; Kuwajima, I.; Sakata, J.; Yokoyama, K.; Noyori, R. *J. Org. Chem.* **1983**, *48*, 932. (c) Sato, T.; Otera, J.; Nozaki, H. *J. Am. Chem. Soc.* **1990**, *112*, 901.

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(9) Bloomfield, J. J.; Nelke, J. M. *Organic Syntheses*; Wiley: New York, 1988; Collect. Vol. VI, p 167. It was very important that 1 be pure; therefore redistillation of 1 under vacuum is strongly recommended if impurities are evident in its ^1H NMR spectrum.

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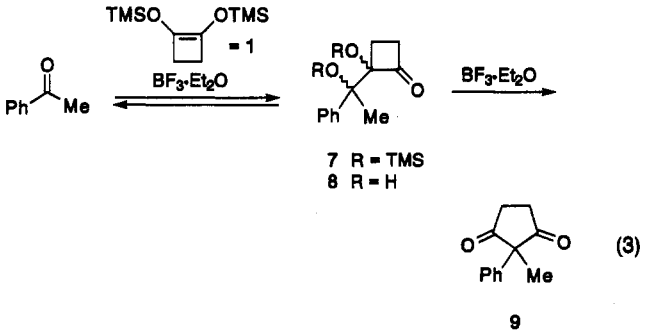
addition as Kuwajima had observed with a corresponding acetal.[1b] However, it was not necessary to isolate intermediates such as 4 if 1,3-cyclopentanediones were desired. A small volume of water (roughly equal to the volume of BF_3·Et_2O) was added to the medium containing the cyclobutanone intermediate, followed shortly thereafter by a large excess of BF_3·Et_2O.[10] In this way the diketone 6 was obtained in 94% yield directly from the starting ketone. One can speculate that the addition of water and acid must have facilitated the rearrangement by hydrolysis of one or both of the (trimethylsilyl)oxy groups of 4. Rearrangement to 6 also took place smoothly when compound 4 was first desilylated with tetrabutylammonium fluoride (TBAF), to provide diol 5, and then treated with BF_3·Et_2O under anhydrous conditions.

The reaction of acetophenone with 1 was followed by ^{1}H NMR. Successive spectra showed that diastereomeric intermediates 7[11] were formed quickly. These went on to disappear almost as quickly (without the addition of water), and signals for the diketone 9 emerged (eq 3). This

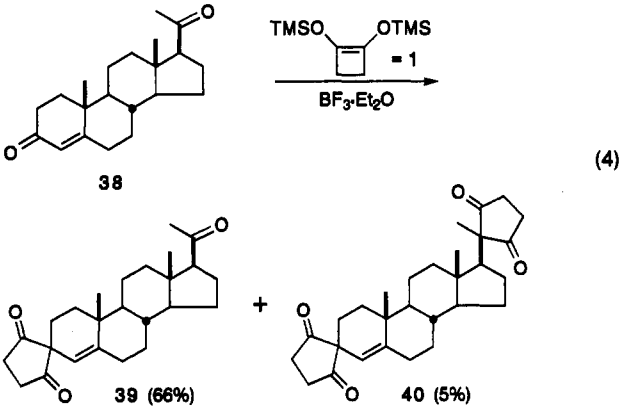


(3)

difference in reactivity between the systems in eq 2 and eq 3 was consistent with benzylic stabilization of the transition state of the rearrangement in eq 3. Thus, it appeared that the hydrolysis of 7 to the diol 8 could offer little advantage, but in a preparative experiment in which water was not added, the yield of 9 was only 45%, and a significant amount of acetophenone was recovered. It seemed that partial reversion of intermediate 7 to acetophenone during the reaction adversely affected the yield of 9. If, under these reaction conditions, there were a significant amount of 7 reverting to the starting ketone instead of proceeding to product, then the effect of the addition of many equivalents of 1 should be to induce the ketone to recycle *in situ*. Indeed, addition of 8 equiv of 1, in portions over many hours, to a reaction medium containing acetophenone and 15 equiv of BF_3·Et_2O was to raise the yield of 9 dramatically to 91%.[12] This was consistent with significant *in situ* recycling of the acetophenone. However, this procedure was very wasteful of 1, and 9 was obtained in 82% yield using only 1.5 equiv of 1 when the procedure that included the addition of a small amount of water was followed.

Geminal acylation reactions of 1 were examined with a variety of ketones, and the best yields of the diketone products are reported in Table 1. Yields were very sensitive to the steric environment of the ketone (compare entries 1–6; also, 2,4-dimethyl-3-pentanone was unreactive). While this ensured that a 2,2-disubstituted 1,3-cyclopentanedione product did not continue to react, it also meant that yields were low except with unencumbered ketones. The best yields, all over 90%, were with cyclohexanones (entries 10, 13–15, and eq 2).[13] The effect of an α-methyl substituent on either cyclopentanone or cyclohexanone was to reduce the yield by roughly 30% (entry 7 versus 8, and 10 versus 11 and 12). Tetrahydrocarvone (entry 12) was a 1:1 epimeric mixture produced by catalytic hydrogenation of (*R*)-carvone. It was interesting that the product of its reaction with 1 under the usual conditions was a 10:1 mixture of which the major epimer was the one with the axial methyl, i.e., **21a**. When the reaction was worked up before the addition of the H_2O/BF_3·Et_2O, a mixture was obtained that consisted largely of diol intermediates **36** and **37** as well as 22% of **21a**, but *none* of **21b**. In contrast, when the same tetrahydrocarvone was acetalized with 1,2-ethanediol and then reacted with 1 under the standard conditions for acetals the predominant product was **21b**, i.e., with the equatorial methyl.[4]

The distant double bonds in entry 16 did not appear to influence the reaction significantly, although a small amount of double-bond migration was evident in the product. However, when there was a double bond in the γ-position, as in entry 17, the NMR spectrum of the crude product was devoid of signals characteristic of the cyclopentanedione moiety. Recently Curran showed that substrates of this type undergo further cyclization.[14] Reactions with simple conjugated enones (entries 18–20) gave very poor yields of the desired diketones and relatively large amounts of intractable material. Steric hindrance about the β-carbon inhibited the destruction of the enones: 4,4-dimethyl-2-cyclohexen-1-one (entry 21) and progesterone **38** (eq 4) gave reasonable yields of spiro-



(4)

annulated products. With the latter, the rate of reaction of the unhindered conjugated ketone at C-3 was much faster than that of the α-substituted ketone (C-20), so **39** was isolated in 66% yield and only 5% of **40** was obtained, but each was contaminated with a small amount of the double-bond-isomerized product. It is important to note that acetals of conjugated ketones do not give any geminal acylation products. Nevertheless, when acetalization is accompanied by double bond migration, e.g., during acid-catalyzed acetalization of isophorone with 1,2-ethanediol,

(10) Rearrangement of 4 to 6 will occur in the presence of a large excess of BF_3·Et_2O, even without the addition of H_2O. Addition of just H_2O, or an aqueous solution of boric acid, in the place of H_2O/BF_3·Et_2O to a solution of 4 did not lead to either hydrolysis or rearrangement.

(11) The diastereoselectivity of this reaction was modest (3.5:1) so no attempt was made to establish the relative stereochemistry of the major isomer. The ratio of diastereomers was similar to that reported for a fluoride-induced reaction of 1 with benzaldehyde (7:3).[7b]

(12) The reaction was heated to hasten rearrangement to 9 and/or reversion to acetophenone, and the progress of the reaction was followed by GC-MS until no acetophenone was evident in the reaction mixture. These harsher reaction conditions did not work well with other substrates.

(13) The reaction conditions used for cyclohexanone (entry 10) proved equally effective for the corresponding 1,3-dioxolane, but the 1,3-dithiane was unreactive.

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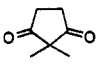
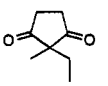
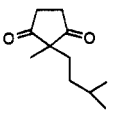
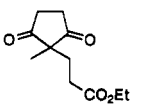
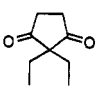
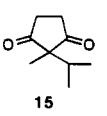
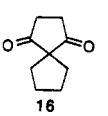
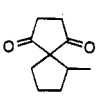
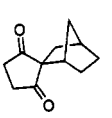
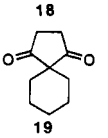
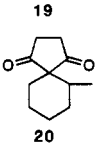
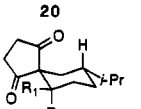
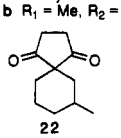
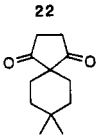
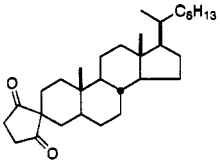
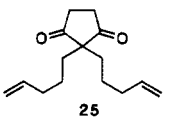
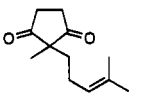
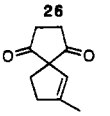
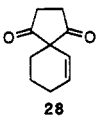
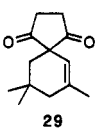
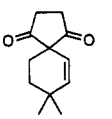
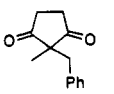
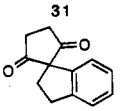
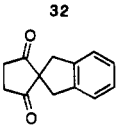
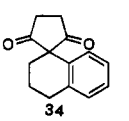
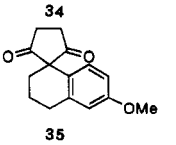
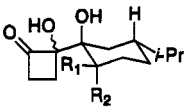
Table 1. Reactions of 1,2-Bis((trimethylsilyl)oxy)cyclobutene (1) and Ketones

entry	substrate	product	yield (%)
1	acetone	 10	84
2	butanone	 11	61
3	6-methyl-2-heptanone	 12	65
4	ethyl levulinate	 13	36
5	3-pentanone	 14	47
6	3-methylbutanone	 15	52
7	cyclopentanone	 16	79
8	2-methylcyclopentanone	 17	55
9	bicyclo[2.2.1]heptan-2-one	 18	75
10	cyclohexanone	 19	94 (96[a])
11	2-methylcyclohexanone	 20	62
12	tetrahydrocarvone (1:1 mixture of epimers)	 21a R_1 = H, R_2 = Me 21b R_1 = Me, R_2 = H	52 3
13	3-methylcyclohexanone	 22	93
14	4,4-dimethylcyclohexanone	 23	90
15	5α-cholestanone	 24	87
16	1,10-undecadien-6-one	 25	78
17	6-methyl-5-hepten-2-one	 26	0
18	3-methyl-2-cyclopenten-1-one	 27	20[b]
19	2-cyclohexen-1-one	 28	2[b]
20	isophorone	 29	33
21	4,4-dimethyl-2-cyclohexen-1-one	 30	71
22	1-phenyl-2-propanone	 31	51
23	1-indanone	 32	74
24	2-indanone	 33	66
25	1-tetralone	 34	55
26	6-methoxy-1-tetralone	 35	52

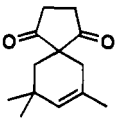
[a] From the corresponding acetal with 1,2-ethanediol. [b] From GC-MS analysis of the crude product.

geminal acylation with **1** proceeds smoothly without further isomerization.[4] Thus, the reaction of **1** directly on isophorone (entry 20) provided the 6-ene isomer **29** whereas from its acetal the 7-ene isomer **41** was the only product.

α-Keto aromatics were somewhat better substrates than β-keto aromatics (eq 3 versus entry 22 of Table I; entry 23 versus 24). Furthermore, the aromatic ketones were superior substrates compared to the corresponding aromatic acetals.[4] 6-Methoxy-2-tetralone decomposed under the reaction conditions, and benzophenone was unreactive.



36 R_1 = H, R_2 = Me
37 R_1 = Me, R_2 = H



41

Overall, yields by this method are competitive with those by the one-pot acetal procedure, especially with aromatic substrates. A clear advantage of this method in total synthesis is a reduction of the number of synthetic steps because there is now no need to form an acetal before a geminal acylation step.

Experimental Section

General. Compound 1 was prepared by the method of Bloomfield and Nelke.[9] All reactions were performed under N_2. BF_3·Et_2O was distilled before use; CH_2Cl_2 (the solvent for all reactions with 1) was distilled from CaH_2. "Workup" consisted of washes with H_2O (×2), reextraction of the aqueous layers with CH_2Cl_2 (×2), washing the combined organic layers with brine, drying over anhydrous $MgSO_4$, and concentration under vacuum with a rotary evaporator. Flash chromatography ("chromatography") used 230–400 mesh silica gel, with hexane containing an increasing proportion of ethyl acetate as the eluent. It should be noted that TLC visualization methods involving acid sprays (ceric ammonium nitrate/H_2SO_4, phosphomolybdic acid, or *p*-anisaldehyde in H_2SO_4) and I_2 are very insensitive toward many of the diketone products, especially the smaller nonaromatic ones. IR spectra (cm^{-1}) were recorded as casts on an FT instrument. ^1H NMR spectra were obtained at 300 MHz in $CDCl_3$; shifts are relative to internal TMS; coupling constants (J) are in hertz. ^{13}C NMR spectra were recorded at 75 MHz, and chemical shifts are relative to solvent (δ 77.0 for $CDCl_3$, 53.8 for CD_2Cl_2); each ^{13}C chemical shift is followed in parentheses by the number of attached protons, as determined by APT and heteronuclear correlation spectra.

(1′α,4′α)-2-(4-*tert*-Butyl-1-((trimethylsilyl)oxy)cyclohexyl)-2-((trimethylsilyl)oxy)cyclobutanone (4). To a solution of 4-*tert*-butylcyclohexanone (215 mg, 1.40 mmol) and BF_3·Et_2O (0.20 mL, 1.6 mmol) in CH_2Cl_2 (10 mL) at rt was added 1 (0.60 mL, 2.3 mmol). The reaction mixture was stirred at rt for 2.7 h. A saturated aqueous boric acid solution (approximately 0.3 mL) was added, and the mixture was stirred overnight. Workup afforded a white solid (355 mg) for which GC-MS analysis included only 4% starting ketone, 8% diketone 6, and 63% 4. Chromatography provided starting ketone (120 mg, 55% recovery) and 4 (99 mg, 32%) as large colorless crystals: mp 62.5–64 °C.[15] IR: 1784. ^1H NMR: δ 2.82–2.59 (2H, m), 2.49 (1H, ddd, J = 6.6, 10.5, 12.3), 1.95 (1H, ddd, $J \approx$ 3.0, 3.0, 10.2), 1.82 (1H, ddd, J = 8.4, 11.1, 12.3), 1.67 (1H, dddd, $J \approx$ 3.0, 3.0, 3.0, 12.3), 1.60–1.47 (2H, m), 1.36 (1H, dddd, $J \approx$ 3.3, 12.3, 12.3, 12.3), 1.29–1.12 (2H, m), 1.04 (1H, br ddd, $J \approx$ 3.8, 12.2, 12.2), 0.89 (1H, partially overlapped m), 0.84 (9H, s), 0.15 (9H, s), 0.11 (9H, s). ^{13}C NMR: δ 212.7 (0), 98.7 (0), 75.8 (0), 47.3 (1), 41.2 (2), 34.6 (2), 32.3 (0), 30.8 (2), 27.5 (3C, 3), 25.1 (2), 22.1 (2), 21.9 (2), 2.4 (3C, 3), 1.5 (3C, 3). MS: 384 (0.5, M^+), 329 (12), 328 (38), 327 (21), 230 (18), 228 (10), 227 (53), 147 (27), 75 (32), 73 (100), 62 (13), 57 (43), 45 (47), 41 (20).

(1′α,4′α)-2-(4-*tert*-Butyl-1-hydroxycyclohexyl)-2-hydroxycyclobutanone (5). To a solution of 4 (20 mg, 0.052 mmol) in CH_2Cl_2 (2.0 mL) was added approximately 0.1 mL of a 1 M solution of tetrabutylammonium fluoride in THF (Aldrich). The solution was stirred at rt for 6 h. Workup provided no 6, just 5 (8.8 mg, 70%) as a colorless solid: mp 147–149.5 °C. IR: 3376, 1757. ^1H NMR: δ 3.41 (1H, br s), 3.02–2.75 (2H, m), 2.33 (1H, ddd, J = 6.4, 11.1, 12.6), 2.03 (1H, ddd, J = 8.7, 11.2, 12.6), 1.90–1.70 (2H, m including br s at 1.81), 1.70–1.50 (4H, m), 1.44–1.21 (3H, m), 0.97 (1H, m), 0.87 (9H, s). ^{13}C NMR: δ 213.1 (0), 96.0 (0), 72.8 (0), 47.6 (1), 42.3 (2), 32.4 (0), 30.5 (2), 27.5 (3C, 3), 23.4 (2), 21.8 (2), 21.7 (2). MS: no M^+, 222 (1.3, $M^+ - H_2O$), 207 (2), 184 (2), 155 (14), 123 (10), 98 (13), 95 (14), 81 (21), 57 (100), 43 (37), 41 (42). HRMS: calcd for $C_{14}H_{22}O_2$ ($M^+ - H_2O$) 222.1619, found 222.1626.

8-*tert*-Butylspiro[4.5]decane-1,4-dione (6) Directly from the Ketone. To a solution of 4-*tert*-butylcyclohexanone (171 mg, 1.11 mmol) and BF_3·Et_2O (0.15 mL, 1.2 mmol) in CH_2Cl_2 (9.0 mL) at −78 °C was added 1 (0.50 mL, 1.9 mmol) in CH_2Cl_2 (4.0 mL) over 20 min. The reaction mixture was stirred for 3 h at −78 °C before it was allowed to attain rt. H_2O (approximately 0.2 mL) was added, and the mixture was cooled again to −78 °C before more BF_3·Et_2O (2.0 mL, 16 mmol) was added. The mixture was allowed to attain rt overnight. Workup provided a brown oil, which was redissolved in ether (15 mL), and decolorizing charcoal (approximately 1 g) was added. This was filtered through a plug containing more charcoal (approximately 2 g) and Florisil (approximately 6 g), and an additional 200 mL of ether was passed through this plug. The combined ether solutions were concentrated under vacuum to provide 6 as colorless crystals (232 mg, 94%): mp 82.5–84 °C. IR: 1753 (m), 1721. ^1H NMR: δ 2.75 (4H, br s), 1.76–1.49 (9H), 0.87 (9H, s). ^{13}C NMR: δ 215.7 (0), 215.6 (0), 55.0 (0), 46.7 (1), 34.3 (2), 34.1 (2), 32.2 (0), 29.9 (2C, 2), 27.2 (3C, 3), 21.5 (2C, 2). MS: 222 (10, M^+), 207 (8), 166 (59), 165 (23), 124 (13), 112 (21), 111 (23), 81 (11), 67 (10), 57 (100), 41 (43). HRMS: calcd for $C_{14}H_{22}O_2$ 222.1619, found 222.1628.

8-*tert*-Butylspiro[4.5]decane-1,4-dione (6) from Intermediate 4. To a solution of 4 (13 mg, 0.033 mmol) in CH_2Cl_2 (2.0 mL) was added a drop of H_2O followed by BF_3·Et_2O (0.06 mL, 0.5 mmol). This was stirred at rt overnight. Workup provided 8.3 mg of a cream-colored solid, which ^1H NMR analysis revealed was composed of 5 and 6, in a 1:1.8 ratio, respectively.

8-*tert*-Butylspiro[4.5]decane-1,4-dione (6) from Diol 5. A solution of 5 (18 mg, 0.075 mmol) and BF_3·Et_2O (0.15 mL, 1.2 mmol) in CH_2Cl_2 (2.0 mL) was stirred at rt for 17.5 h. Workup provided 6 (17 mg, 100%).

2-(1-Phenyl-1-((trimethylsilyl)oxy)ethyl)-2-((trimethylsilyl)oxy)cyclobutanone (7). A solution of acetophenone (229 mg, 1.91 mmol) in CH_2Cl_2 (75 mL) was cooled to −78 °C, and BF_3·Et_2O (0.12 mL, 0.98 mmol) was added followed, dropwise, by a solution of 1 (1.5 mL, 5.7 mmol) in CH_2Cl_2 (6.0 mL) over 30 min. The solution was allowed to warm to rt over the next 2 h, and then it was heated at reflux for 1 h. Workup provided a bright yellow liquid. Chromatography gave 7 (a diastereomeric mixture in a 3.5:1 ratio, by ^1H NMR) as an oil. IR: 1793. ^1H NMR for the major isomer: δ 7.51 (2H, br d, $J \approx$ 7.1), 7.41–7.27 (3H, m), 2.88 (1H, ddd, J = 8.7, 11.7, 17.6), 2.70 (1H, ddd, J = 5.7, 10.8, 17.6), 2.50 (1H, ddd, J = 5.7, 11.7, 12.2), 1.83 (3H, s), 1.66 (1H, ddd, J = 8.7, 10.8, 12.2), 0.15 (9H, s), 0.08 (9H, s); and some discernable signals for the minor isomer: δ 2.70–2.48 (m), 1.94 (1H, m), 1.77 (3H, s). ^{13}C NMR for the major isomer δ 213.6 (0), 143.6 (0), 127.1 (2C, 1), 127.0 (2C, 1), 126.9 (1), 97.1 (0), 79.3 (0), 41.8 (2), 24.2 (2), 22.9 (3), 2.1 (3C, 3), 1.1 (3C, 3); and some discernable signals for the minor isomer δ 211.6 (0), 143.5 (0), 98.0 (0), 79.4 (0), 41.3 (2), 25.5 (2), 24.2 (3), 2.1 (3C, 3), 1.0 (3C, 3). MS: 350 (0.3, M^+), 294 (24), 232 (12), 231 (6), 230 (6), 193 (47), 147 (19), 75 (14), 73 (100), 45 (14). HRMS: calcd for $C_{18}H_{30}O_3Si_2$ 350.1732, found 350.1753.

2-Methyl-2-phenyl-1,3-cyclopentanedione (9) by Multiple Additions of 1. A solution of acetophenone (509 mg, 4.24 mmol) in CH_2Cl_2 (300 mL) was cooled to -78 °C before BF_3·Et_2O (7.7 mL, 63 mmol) was added followed, dropwise, by a solution of 1 (3.4 mL, 13 mmol) in CH_2Cl_2 (10 mL). This was stirred for 15 min before the mixture was allowed to attain rt, and the mixture was heated at reflux. After 12, 16.5, and 38 h, at which times aliquots were removed and analyzed by GC-MS, additional 1 was added (1.0, 1.0 and 3.0 mL, respectively). After heating for a total of 44 h, GC-MS indicated no acetophenone remained. The reaction was allowed to cool, and workup provided a black

(15) Atomic coordinates for the X-ray structure of 4 have been deposited with the Cambridge Crystallographic Data Centre. A request for these coordinates should be addressed to the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CD2 1EZ, U.K.

residue. Vacuum distillation in a Kugelrohr apparatus gave **9** (726 mg, 91%) as a yellow liquid.[16]

2-Methyl-2-phenyl-1,3-cyclopentanedione (9) with Addition of H_2O. To a solution of acetophenone (211 mg, 1.76 mmol) in CH_2Cl_2 (9.0 mL) at rt was added BF_3·Et_2O (0.25 mL, 2.0 mmol) followed by **1** (0.70 mL, 2.7 mmol). After 2 h, GC-MS analysis of the mixture indicated the presence of **9** (73%) and **7** (19%) with only 2% acetophenone remaining; 30 min later H_2O (approximately 0.3 mL) was added followed after 10 min by BF_3·Et_2O (3.3 mL, 27 mmol) and stirring was continued for 1 h. Workup and decolorization (as for **6**) provided **9** as a pale yellow oil (273 mg, 83%), but GC-MS revealed that this was contaminated by approximately 1% acetophenone.

2,2-Dimethyl-1,3-cyclopentanedione (10). Acetone (165 mg, 2.84 mmol), BF_3·Et_2O (0.35 mL, 2.9 mmol), and **1** (1.1 mL, 4.2 mmol), 1 h at rt; H_2O (approximately 0.4 mL), BF_3·Et_2O (5.1 mL, 42 mmol), 1 h at rt; workup and decolorization (as for **6**). **10** (299 mg, 84%, pale yellow solid): mp 36.5-38 °C.[16]

2-Ethyl-2-methyl-1,3-cyclopentanedione (11). Butanone (204 mg, 2.84 mmol) was treated exactly as for acetone to provide **11** (243 mg, 61%) as an oil.[16]

2-Methyl-2-(3-methylbutyl)-1,3-cyclopentanedione (12). 6-Methylheptanone (303 mg, 2.37 mmol), BF_3·Et_2O (4.5 mL, 37 mmol), **1** (1.6 mL, 6.1 mmol), −78 °C to rt and stirred 3 days; workup and chromatography. **12** (300 mg, 65%, oil). IR: 1764 (shoulder), 1724. ^{1}H NMR: δ 2.76 (4H, apparent narrow d, J = 0.6), 1.58 (2H, m), 1.49 (1H, m), 1.22–1.03 (4H, m), 1.09 (3H, s), 0.82 (6H, d, J = 6.6). ^{13}C NMR: δ 216.3 (2C, 0), 56.4 (0), 38.7 (2), 35.7 (2), 34.9 (2C, 2), 27.2 (1), 22.1 (2C, 3), 22.0 (2), 18.5 (3). MS: 196 (1.4, M$^+$), 181 (1), 153 (4), 125 (100), 113 (30), 112 (60), 97 (24), 82 (17), 69 (27), 41 (61). HRMS: calcd for $C_{12}H_{20}O_2$ 196.1462, found 196.1454.

2-(2-Carbethoxyethyl)-2-methyl-1,3-cyclopentanedione (13). Ethyl levulinate (221 mg, 1.54 mmol), BF_3·Et_2O (2.7 mL, 22 mmol), **1** (1.2 mL, 4.6 mmol), −78 °C to rt and stirred 43 h; workup and chromatography. **13** (118 mg, 36%, oil).[16]

2,2-Diethyl-1,3-cyclopentanedione (14). 3-Pentanone (243 mg, 2.83 mmol), BF_3·Et_2O (0.40 mL, 3.4 mmol), **1** (1.1 mL, 4.2 mmol), 3.7 h at rt; H_2O (approximately 0.4 mL), BF_3·Et_2O (5.2 mL, 42 mmol), overnight; workup and decolorization. **14** (204 mg, 47%, oil that crystallized during storage): mp 62–63.5 °C. IR: 1720. ^{1}H NMR: δ 2.74 (4H, s), 1.68 (4H, q, J = 7.5), 0.77 (6H, t, J = 7.5). ^{13}C NMR: δ 217.4 (0), 62.0 (0), 36.2 (2), 27.7 (3). MS (from GC-MS): 154 (82, M$^+$), 139 (100), 126 (27), 125 (91), 111 (24), 97 (33), 83 (48), 69 (20), 55 (59). HRMS: calcd for $C_9H_{14}O_2$ 154.0993, found 154.0983.

2-Methyl-2-(1-methylethyl)-1,3-cyclopentanedione (15). 3-Methylbutanone (276 mg, 3.21 mmol), BF_3·Et_2O (0.50 mL, 3.8 mmol), **1** (1.3 mL, 4.8 mmol), 2 h at rt; H_2O (approximately 0.5 mL), BF_3·Et_2O (5.9 mL, 48 mmol), overnight; workup and decolorization. **15** (258 mg, 52%, oil).[16]

Spiro[4.4]nonane-1,4-dione (16). Cyclopentanone (211 mg, 2.51 mmol), BF_3·Et_2O (0.30 mL, 2.5 mmol), **1** (1.0 mL, 3.8 mmol), 1 h at rt; H_2O (approximately 0.35 mL), BF_3·Et_2O (4.6 mL, 38 mmol), 1 h; workup and decolorization: **16** (300 mg, 79%, solid), mp 54–57.5 °C.[16]

6-Methylspiro[4.4]nonane-1,4-dione (17). 2-Methylcyclopentanone (216 mg, 2.20 mmol), BF_3·Et_2O (0.30 mL, 2.5 mmol), **1** (0.90 mL, 3.4 mmol),1 h at rt; H_2O (approximately 0.3 mL), BF_3·Et_2O (4.5 mL, 37 mmol), 1 h; workup and decolorization. **17** (200 mg, 55%, oil).[16]

Spiro[bicyclo[2.2.1]heptane-2,2′-cyclopentane]-1,3-dione (18). Bicyclo[2.2.1]heptan-2-one (206 mg, 1.87 mmol), BF_3·Et_2O (0.25 mL, 2.0 mmol), **1** (0.75 mL, 2.9 mmol), 1 h at rt; H_2O (approximately 0.3 mL), BF_3·Et_2O (3.4 mL, 28 mmol), 1 h; workup and decolorization. **18** (250 mg, 75%) as colorless crystals, mp 112–113 °C (lit.[1b] mp 109.5–110.5 °C).[16]

Spiro[4.5]decane-1,4-dione (19) from cyclohexanone. Cyclohexanone (212 mg, 2.17 mmol), BF_3·Et_2O (0.30 mL, 2.5 mmol), **1** (0.90 mL, 3.4 mmol), −78 °C for 3 h, then to rt over 2 h; H_2O (approximately 0.4 mL), BF_3·Et_2O (4.0 mL, 33 mmol), −78 °C to rt overnight ; workup and decolorization. **19** (337 mg, 94%) as large white crystals, mp 60–61.5 °C (lit.[1b] mp 61–62 °C).[16]

(16) The spectral data were identical with those of material produced by the acetal route.[2,4]

Spiro[4.5]decane-1,4-dione (19) from the acetal of cyclohexanone. 1,4-Dioxaspiro[4.5]decane (306 mg, 2.16 mmol), BF_3·Et_2O (0.30 mL, 2.5 mmol), **1** (0.9 mL, 3.2 mmol), 2.5 h at rt; H_2O (approximately 0.4 mL), BF_3·Et_2O (4.0 mL, 33 mmol), overnight; workup and decolorization. **19** (343 mg, 96%).

6-Methylspiro[4.5]decane-1,4-dione (20). 2-Methylcyclohexanone (228 mg, 2.03 mmol), BF_3·Et_2O (0.30 mL, 2.5 mmol), **1** (0.80 mL, 3.1 mmol), 1 h at rt; H_2O (approximately 0.4 mL), BF_3·Et_2O (3.7 mL, 30 mmol), overnight; workup and decolorization. **20** (227 mg, 62%, oil).[16]

(6*S*,9*R*)-6-Methyl-9-(methylethyl)spiro[4.5]decane-1,4-dione (21a) and (6*R*,9*R*)-6-Methyl-9-(methylethyl)spiro[4.5]decane-1,4-dione (21b). Tetrahydrocarvone (1:1 mixture of methyl epimers; 340 mg, 2.20 mmol), BF_3·Et_2O (0.30 mL, 2.6 mmol), **1** (0.9 mL, 3.3 mmol), 22.5 h at rt; H_2O (approximately 0.4 mL), BF_3·Et_2O (4.0 mL, 33 mmol), 30 h; workup and decolorization: 408 mg of a yellow oil. GC-MS analysis indicated 2 isomeric products in a ratio of 10:1. Chromatography gave 12 mg of recovered tetrahydrocarvone **21b**[16] (14 mg, 3%) and the more polar isomer **21a** (254 mg, 52%) as a yellow oil. IR: 1759 (m), 1719 (s). ^{1}H NMR: δ 3.01–2.74 (2H, m), 2.66–2.49 (2H, m), 2.07–1.74 (3H, m), 1.70–1.00 (6H, m), 0.91 (3H, d, J = 5.0), 0.874 (3H, d, J = 6.7), 0.869 (3H, d, J = 6.8). ^{13}C NMR: δ 214.6 (0), 214.1 (0), 60.8 (0), 36.6 (1), 34.7 (2), 34.3 (2), 32.7 (1), 31.7 (1), 27.6 (2), 25.2 (2), 22.1 (2), 19.7 (3), 19.4 (3), 14.6 (3). MS: 222 (21, M$^+$), 207 (8), 179 (12), 151 (13), 138 (59), 126 (59), 125 (100), 112 (37), 111 (24), 98 (46), 95 (25), 55 (54), 43 (37), 41 (87). HRMS: calcd for $C_{14}H_{22}O_2$ 222.1618, found 222.1604.

7-Methylspiro[4.5]decane-1,4-dione (22). 3-Methylcyclohexanone (205 mg, 1.83 mmol), BF_3·Et_2O (0.25 mL, 2.0 mmol), **1** (0.75 mL, 2.9 mmol),1 h at rt; H_2O (approximately 0.3 mL), BF_3·Et_2O (3.3 mL, 27 mmol), 1 h; workup and decolorization. **22** (306 mg, 93%, solid): mp 68–70.5 °C. IR: 1714. ^{1}H NMR: δ 2.76 (4H, m), 1.94 (1H, m), 1.90–1.53 (5H, m), 1.41 (1H, ddd, J = 3.9, 12.9, 13.4), 1.13 (1H, dd, J ≈ 12.7, 13.1), 0.89 (1H, m), 0.87 (3H, d, J = 6.6). ^{13}C NMR: δ 215.9 (0), 215.5 (0), 56.7 (0), 36.8 (2), 34.3 (2), 34.2 (2), 33.6 (2), 29.0 (2), 26.2 (1), 22.2 (3), 20.6 (2). MS: 180 (55, M$^+$), 165 (6), 151 (5), 125 (21), 124 (49), 112 (100), 111 (25), 95 (37), 81 (43), 69 (28), 67 (38), 55 (69), 41 (51). HRMS: calcd for $C_{11}H_{16}O_2$ 180.1149, found 180.1162.

8,8-Dimethylspiro[4.5]decane-1,4-dione (23). 4,4-Dimethylcyclohexanone (230 mg, 1.83 mmol), BF_3·Et_2O (0.20 mL, 1.6 mmol), **1** (0.80 mL, 3.1 mmol), -78 °C for 3.5 h, then to rt over 1.5 h; H_2O (approximately 0.3 mL), BF_3·Et_2O (3.3 mL, 27 mmol), overnight; workup and decolorization. **23** (320 mg, 90%, cream-colored crystals): mp 65–66.5 °C. IR: 1756, 1715. ^{1}H NMR: δ 2.76 (4H, s), 1.61 (4H, m), 1.47 (4H, m), 0.95 (6H, s). ^{13}C NMR: δ 215.4 (2C, 0), 55.1 (0), 34.0 (2C, 2), 32.9 (2C, 2), 28.7 (0), 27.6 (2C, 3), 25.2 (2C, 2). MS: 194 (52, M$^+$), 179 (12), 151 (21), 138 (15), 137 (16), 125 (100), 112 (96), 111 (31), 95 (27), 93 (20), 83 (20), 81 (25), 69 (36), 67 (22), 56 (42), 55 (33), 53 (27), 41 (67). HRMS: calcd for $C_{12}H_{18}O_2$ 194.1306, found 194.1300.

Spiro[5α-cholestane-3,2′-cyclopentane]-1,3-dione (24). 5α-Cholestane (304 mg, 0.788 mmol), BF_3·Et_2O (1.5 mL, 12 mmol), **1** (0.53 mL, 2.0 mmol), −78 °C to rt then 48 h at rt; workup and chromatography. **24** (310 mg, 87%, colorless crystals): mp 150.5–152 °C. IR: 1761 (shoulder), 1721. ^{1}H NMR: δ 2.73 (4H, m), 2.0–0.9 (unresolved), 0.90 (3H, d, J = 6.4), 0.863 (3H, d, J = 6.6), 0.859 (3H, d, J = 6.6), 0.82 (3H, s), 0.64 (3H, s). ^{13}C NMR: δ 215.5 (2C, 0), 56.4 (0), 56.2 (1), 56.1 (1), 53.5 (1), 42.4 (0), 39.8 (2), 39.4 (1), 39.4 (2), 36.0 (2), 35.7 (1), 35.3 (1), 35.1 (0), 34.4 (2), 34.0 (2), 32.8 (2), 31.8 (2), 31.5 (2), 28.2 (2), 28.1 (2), 27.9 (1), 24.6 (2), 24.0 (2), 23.7 (2), 22.7 (3), 22.5 (3), 20.7 (2), 18.5 (3), 11.9 (3), 11.0 (3). MS: 454 (29, M$^+$), 439 (30), 330 (18), 329 (13), 301 (26), 300 (47), 299 (100), 231 (41), 191 (32). HRMS: calcd for $C_{31}H_{50}O_2$ 454.3808, found 454.3819.

2,2-Bis(4-pentenyl)-1,3-cyclopentanedione (25). 1,10-Undecadien-6-one (1.75 g, 10.6 mmol), BF_3·Et_2O (1.3 mL, 11 mmol), **1** (4.2 mL, 16 mmol), 11 h at rt; H_2O (approximately 1.3 mL), BF_3·Et_2O (20 mL, 165 mmol), 3.5 h; workup and decolorization: 2.15 g of a brown oil, which GC-MS analysis showed was 90% **25**, some unrearranged material, and less than 5% starting ketone. For a colorless sample obtained by chromatography, IR 1722, 1641. ^{1}H NMR: δ 5.69 (2H, m), 4.95 (4H, m), 2.71 (4H, s), 1.96 (4H, apparent q, J = 7.0), 1.62 (4H, m), 1.20 (4H, m). ^{13}C NMR: δ 217.3 (0), 137.3 (1), 115.1 (2), 60.8 (0), 36.1 (2), 34.6 (2), 33.7 (2), 23.7 (2). MS: no M$^+$, 205 (2), 167 (52), 166 (33), 141 (26), 125

(25), 124 (17), 112 (44), 111 (35), 99 (21), 81 (38), 79 (26), 68 (27), 67 (54), 55 (69), 53 (26), 41 (100).

7-Methylspiro[4.4]non-6-ene-1,4-dione (27). 3-Methyl-2-cyclopenten-1-one (222 mg, 2.31 mmol), BF_3·Et_2O (0.30 mL, 2.5 mmol), 1 (0.95 mL, 3.6 mmol) 1 h at rt; H_2O (approximately 0.4 mL), BF_3·Et_2O (4.2 mL, 34 mmol), 1 h; workup and decolorization: 210 mg of a viscous oil for which GC-MS analysis revealed a mixture of double bond isomers, including the major component (41%) with this MS, 164 (100, M^+ required for $C_{10}H_{12}O_2$), 149 (14), 136 (29), 121 (20), 108 (83), 80 (82), 79 (94), 77 (34). ^1H NMR of the mixture showed olefinic multiplets at δ 5.95, 5.18, and 5.01 in a ratio of 4:1:2.5, respectively.

Spiro[4.5]dec-6-ene-1,4-dione (28). 2-Cyclohexen-1-one (251 mg, 2.61 mmol) as for **29** (below), chromatography; 9.3 mg (approximately 2%) of a yellow oil, which GC-MS suggested contained a mixture of **28** and its double-bond isomer (3:1, respectively). For **28**: MS 164 (96, M^+), 136 (13), 135 (10), 122 (12), 108 (58), 80 (57), 79 (100), 77 (37).

7,9,9-Trimethylspiro[4.5]dec-6-ene-1,4-dione (29). 3,5,5-Trimethyl-2-cyclohexen-1-one (220 mg, 1.62 mmol), BF_3·Et_2O (2.9 mL, 24 mmol),1 (1.3 mL, 5.0 mmol), −78 °C to rt, then 65 h; workup and chromatography. **29** (108 mg, 33%, oil which solidified on standing): mp 58–59.5 °C. IR: 1723. ^1H NMR: δ 5.05 (1H, br s), 2.84 (4H, m), 1.82 (2H, br s), 1.75 (3H, br s), 1.62 (2H, s), 1.00 (6H, s). ^{13}C NMR: δ 212.6 (2C, 0), 139.7 (0), 112.8 (1), 62.9 (0), 43.3 (2), 38.3 (2), 34.7 (2C, 2), 30.2 (0), 29.2 (2C, 3), 24.5 (3). MS: 206 (100, M^+), 191 (49), 163 (24), 150 (28), 135 (20), 121 (22), 107 (94), 91 (42). HRMS: calcd for $C_{13}H_{18}O_2$ 206.1306, found 206.1299.

8,8-Dimethylspiro[4.5]dec-6-ene-1,4-dione (30). 4,4-Dimethylcyclohex-2-en-1-one (214 mg, 1.73 mmol), BF_3·Et_2O (0.20 mL, 1.6 mmol) 1 (0.70 mL, 2.7 mmol), 1 h at rt; H_2O (approximately 0.2 mL), BF_3·Et_2O (3.2 mL, 26 mmol) 70 min; workup and decolorization. **30** (237 mg, 72%, pale yellow crystals): mp 78.5–80 °C. IR: 1755 (shoulder), 1716. ^1H NMR: δ 5.88 (1H, d, J = 9.9), 5.11 (1H, d, J = 9.9), 2.85 (4H, m), 1.79 (2H, m), 1.60 (2H, m), 1.04 (6H, s). ^{13}C NMR: δ 213.3 (2C, 0), 143.3 (1), 117.2 (1), 60.0 (0), 34.6 (2C, 2), 31.7 (2), 31.1 (0), 28.9 (2C, 3), 25.6 (2). MS: 192 (48, M^+), 177 (100), 149 (18), 131 (20), 121 (43), 107 (17), 93 (34), 91 (30), 77 (29). HRMS: calcd for $C_{12}H_{16}O_2$ 192.1149, found 192.1141.

2-Benzyl-2-methyl-1,3-cyclopentanedione (31). 1-Phenyl-2-propanone (260 mg, 1.94 mmol), BF_3·Et_2O (0.30 mL, 2.5 mmol), 1 (0.8 mL, 2.9 mmol),2.3 h at rt; H_2O (approximately 0.4 mL), BF_3·Et_2O (3.6 mL, 29 mmol), overnight; workup, decolorization and chromatography. **31** (200 mg, 51%, waxy yellow crystals): mp 42–43 °C. IR: 1724. ^1H NMR: δ 7.21 (3H, m), 7.03 (2H, m), 2.95 (2H, s), 2.55 (2H, m), 2.05 (2H, m), 1.19 (3H, s). ^{13}C NMR: δ 217.2 (2C, 0), 135.6 (0), 129.4 (2C, 1), 128.4 (2C, 1), 127.0 (1), 58.1 (0), 42.8 (2), 35.6 (2C, 2), 19.8 (3). MS: 202 (33, M^+), 187 (10), 159 (18), 145 (11), 117 (18), 91 (100). HRMS: calcd for $C_{13}H_{14}O_2$ 202.0993, found 202.0989.

2′,3′-Dihydrospiro[cyclopentane-1,1′-[1*H*]indene]-2,5-dione (32). 1-Indanone (210 mg, 1.59 mmol), BF_3·Et_2O (2.9 mL, 24 mmol), 1 (1.7 mL, 6.5 mmol), 20 min at −78 °C, then 1.5 h at rt, and then 1.5 h at reflux. Workup and Kugelrohr distillation: bright yellow oil (247 mg), which GC-MS revealed was 95% **32**. Chromatography of a portion: **32** as colorless crystals: mp 104–105.5 °C. IR: 1754 (shoulder), 1722. ^1H NMR: δ 7.33–7.10 (3H, m), 6.89 (1H, d, J = 7.5), 3.15 (2H, t, J = 7.4), 2.92 (4H, center of complex m), 2.37 (2H, t, J = 7.4). ^{13}C NMR: δ 213.1 (2C, 0), 144.7 (0), 140.6 (0), 128.2 (1), 126.8 (1), 125.3 (1), 122.4 (1), 69.8 (0), 35.4 (2C, 2), 32.8 (2), 31.6 (2). MS: 200 (94, M^+), 144 (56), 130 (15), 129 (15), 116 (82), 115 (100). HRMS: calcd for $C_{13}H_{12}O_2$ 200.0837, found 200.0838.

1′,3′-Dihydrospiro[cyclopentane-1,2′-[2*H*]indene]-2,5-dione (33). 2-Indanone (259 mg, 1.96 mmol), BF_3·Et_2O (0.30 mL, 2.5 mmol), 1 (0.8 mL, 2.9 mmol), 2 h at rt; H_2O (approximately 0.4 mL), BF_3·Et_2O (3.6 mL, 29 mmol), overnight; workup and decolorization. **33** (258 mg, 66%, solid): mp 112–114 °C. IR: 1721. ^1H NMR: δ 7.17 (4H, br s), 3.22 (4H, s), 2.84 (4H, s). ^{13}C NMR: δ 213.7 (0), 139.2 (0), 127.1 (1), 124.2 (1), 62.0 (0), 40.0 (2), 34.7 (2). MS: 200 (56, M^+), 172 (100), 158 (53), 143 (42), 128 (47), 116 (74), 115 (85), 58 (59). HRMS: calcd for $C_{13}H_{12}O_2$ 200.0837, found 200.0826.

1′,2′,3′,4′-Tetrahydrospiro[cyclopentane-1,1′-naphthalene]-2,5-dione (34). 1-Tetralone (296 mg, 2.03 mmol), BF_3·Et_2O (0.30 mL, 2.5 mmol), 1 (0.8 mL, 2.9 mmol), 2.2 h at rt; H_2O (approximately 0.4 mL), BF_3·Et_2O (3.7 mL, 31 mmol), overnight; workup and decolorization: 312 mg of a pale brown solid that GC-MS analysis showed was a 1:3.3 mixture of 1-tetralone and **34**. A colorless, analytical sample was obtained by chromatography: mp 102.5–104 °C. IR: 1719. ^1H NMR: δ 7.21–7.03 (3H, m), 6.53 (1H, d, J = 7.6), 2.91 (4H, center of complex m), 2.82 (2H, narrow m), 1.92 (4H, narrow m). ^{13}C NMR: δ 214.7 (2C, 0), 138.4 (0), 131.7 (0), 129.6 (1), 128.3 (1), 127.4 (1), 126.2 (1), 62.3 (0), 35.1 (2C, 2), 31.4 (2), 28.6 (2), 17.8 (2). MS: 214 (100, M^+), 186 (16), 158 (43), 130 (64), 129 (73), 128 (40), 115 (37). HRMS: calcd for $C_{14}H_{14}O_2$ 214.0993, found 214.0995.

1′,2′,3′,4′-Tetrahydro-6-methoxyspiro[cyclopentane-1,1′-naphthalene]-2,5-dione (35). 6-Methoxy-1-tetralone (198 mg, 1.13 mmol), BF_3·Et_2O (0.40 mL, 3.3 mmol), 1 (0.90 mL, 3.4 mmol), 47 h at rt. A further 0.40 mL (1.5 mmol) of 1 was added, and the mixture was stirred for another 45 h. After addition of H_2O (approximately 0.4 mL) and BF_3·Et_2O (2.1 mL, 17 mmol), the mixture was stirred for 3 days. Workup and decolorization gave 234 mg of yellow, oily crystals that GC-MS revealed contained 1% starting ketone, 86% **35**, and 5% unrearranged intermediates. Chromatography yielded **35** (142 mg, 52%) as colorless crystals: mp 116.5–117.5 °C. IR: 1716. ^1H NMR: δ 6.70-6.64 (2H, m), 6.45 (1H, m), 3.75 (3H, s), 2.94 (4H, center of broad, symmetric m), 2.83 (2H, m), 1.92 (4H, narrow m). ^{13}C NMR: δ 215.0 (2C, 0), 158.6 (0), 139.9 (0), 129.3 (1), 123.9 (0), 114.0 (1), 112.9 (1), 62.0 (0), 55.1 (3), 35.1 (2C, 2), 31.7 (2), 29.1 (2), 17.9 (2). MS: 244 (100, M^+), 188 (42), 174 (21), 160 (89), 159 (23), 145 (23), 115 (27). HRMS: calcd for $C_{15}H_{16}O_3$ 244.1099, found 244.1107.

Intermediates 36 and 37 from Tetrahydrocarvone. To a solution of tetrahydrocarvone (9:1 epimeric mixture; 288 mg, 1.87 mmol) and BF_3·Et_2O (0.30 mL, 2.1 mmol) in CH_2Cl_2 (10 mL) was added 1 (0.80 mL, 2.8 mmol), and this was stirred at rt for 22.5 h. Workup gave a yellow oil from which chromatography provided **21a** (108 mg, 26%), **36** [**(2*R*,1′*S*,2′*S*,5′*R*)-** and **(2*S*,1′*S*,2′*S*,5′*R*)-2-(1-hydroxy-5-isopropyl-2-methylcyclohexyl)-2-hydroxycyclobutanone** in a 1:1 ratio] as a colorless solid (56 mg, 12%), and **37** [**(2*R*,1′*S*,2′*R**R*,5′*R*)-** and **(2*S*,1′*S*,2′*R*,5′*R*)-2-(1-hydroxy-5-isopropyl-2-methylcyclohexyl)-2-hydroxycyclobutanone** in a 2.2:1 ratio] as a colorless solid (106 mg, 24%). Crystallization of **36** from hexane–CH_2Cl_2 gave colorless needles of one of the isomers (**36a**): mp 130–131 °C. IR: 3508, 3341 (br), 1767. ^1H NMR: δ 2.93 (2H, m), 2.67 (1H, br), 2.57 (1H, m), 2.15–1.84 (3H, m), 1.70–1.35 (8H, m), 1.00 (3H, d, J = 7.2), 0.89 (3H, d, J = 5.9), 0.87 (3H, d, J = 6.2). ^{13}C NMR: δ 210.8 (0), 97.9 (0), 76.1 (0), 42.7 (2), 38.3 (1), 34.9 (1), 32.6 (1), 30.4 (2), 29.2 (2), 23.8 (2), 22.3 (2), 20.0 (3), 19.3 (3), 15.6 (3). MS: no M^+, 222 (11), 207 (25), 155 (56), 137 (49), 111 (32), 95 (66), 81 (64), 69 (43), 56 (32), 55 (64), 45 (46), 43 (100), 41 (69). Resolved signals for the other isomer of **36** (from the mixture), ^1H NMR: δ 0.94 (3H, d, J = 7.2), 0.87 (3H, d, J = 6.0), 0.86 (3H, d, J = 6.6). ^{13}C NMR: δ 214.8 (0), 95.8 (0), 77.0 (0), 43.9 (2), 38.1 (1), 32.9 (1), 32.5 (1), 32.1 (2), 28.6 (2), 25.2 (2), 22.7 (2), 19.9 (3), 19.3 (3), 15.2 (3). Crystallization of **37** failed to separate an isomer; from the mixture, ^1H NMR (CD_2Cl_2): δ 3.01–2.77 and 1.81–0.84 (unresolved multiplets), 2.65 (1H, m, major), 2.36 (1H, m, minor), 1.98 (1H, m, minor), 1.86 (1H, m, major), 0.93 (3H, d, J = 6.8, minor), 0.88 (3H, d, J = 6.8, major), 0.85 (3H, d, J = 6.7, major), 0.84 (3H, d, J = 6.7, major). ^{13}C NMR (CD_2Cl_2) for the major isomer δ 213.3 (0), 97.1 (0), 76.0 (0), 43.4 (2), 38.8 (1), 36.6 (2), 36.0 (1), 32.9 (1), 31.3 (2), 28.9 (2), 26.0 (2), 20.1 (3), 19.5 (3), 17.0 (3); for the minor isomer: δ 213.1 (0), 98.7 (0), 75.3 (0), 43.0 (2), 38.6 (1), 37.6 (2), 36.6 (1), 32.8 (1), 31.4 (2), 28.8 (2), 23.8 (2), 20.1 (3), 19.3 (3), 16.9 (3).

Reaction of Progesterone (38) with 1. Progesterone (**38**) (259 mg, 0.824 mmol), BF_3·Et_2O (0.25 mL, 2.0 mmol), 1 (0.70 mL, 2.7 mmol),19 h at rt; H_2O (approximately 0.2 mL), BF_3·Et_2O (1.5 mL, 12 mmol), 2.5 h); workup and chromatography. **39** (208 mg, 66% pale yellow crystals) and, in a more polar fraction, **40** (19 mg, 5%, cream-colored crystals). The NMR spectra revealed that each was contaminated with less than 10% of its 5-ene isomer. For **39**: mp 135.5–138 °C. IR: 1721, 1703. ^1H NMR: δ 4.86 (1H, br s), 2.83 (2H, m), 2.12 (3H, s), 1.07 (3H, s), 0.63 (3H, s) and other signals unresolved 2.9–0.9. NOE results: irradiation at δ 4.86 gave NOE of m at 2.83 (0.5%) and a dm at approximately 2.08 (3%); irradiation at δ 2.83 gave NOE of br s at δ 4.86 (4.5%); and a small signal for a minor isomer at 5.30 (m). ^{13}C NMR: δ

214.8 (0), 213.2 (0), 209.5 (0), 151.4 (0), 111.9 (1), 63.6 (1), 60.5 (0), 56.0 (1), 53.4 (1), 44.0 (0), 38.7 (2), 36.8 (0), 35.7 (1), 34.8 (2), 34.6 (2), 32.6 (2), 32.5 (2), 32.2 (2), 31.5 (3), 25.0 (2), 24.3 (2), 22.7 (2), 21.4 (2), 19.1 (3), 13.3 (3). MS: 382 (100, M^+), 367 (12), 191 (45), 190 (23), 164 (27), 43 (79). HRMS: calcd for $C_{25}H_{34}O_3$ 382.2506, found 382.2513. For **40**: mp 267–268 °C. IR: 1759 (m), 1719 (s). ^1H NMR: δ 4.84 (1H, s), 2.91–2.62 (8H, m), 2.38–0.80 (m), 1.13 (3H, s), 1.03 (3H, s), 0.61 (3H, s), and a small signal for a minor isomer at 5.38 (m). ^{13}C NMR: δ 217.8 (0), 216.8 (0), 214.9 (0), 213.0 (0), 151.4 (0), 111.9 (1), 60.5 (0), 56.9 (1), 55.6 (0), 54.9 (1), 53.3 (1), 42.9 (0), 38.9 (2), 36.7 (0), 35.5 (1), 35.2 (2), 34.2 (2), 34.8 (2), 34.2 (2), 32.5 (2), 32.3 (2), 32.1 (2), 24.9 (2), 22.9 (2), 21.7 (2), 21.0 (2), 20.7 (3), 19.0 (3), 14.9 (3). MS: 450 (100, M^+), 435 (7), 422 (8), 339 (8), 323 (12), 191 (65), 190 (38), 164 (45), 147 (22), 135 (19), 113 (22), 107 (25), 105 (32), 91 (45). HRMS: calcd for $C_{29}H_{38}O_4$ 450.2768, found 450.2761.

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Supplementary Material Available: X-ray structure[15] for **4** and ^1H and ^{13}C NMR spectra of compounds **4–7**, **12**, **14**, **21a**, **22–25**, **29–35**, **36a**, **39**, and **40** (43 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.