Synthesis, Structure, and Nucleophile-Induced Rearrangements of Spiroketones

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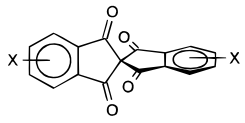
Three tetraketones based on the 2,2′-spirobiindan-1,1′,3,3′-tetraone skeleton were prepared and investigated. All three compounds show spiroconjugation between their perpendicular π-networks. The interaction results in lowering of the energy of the LUMO of the systems by ca. 0.2−0.3 eV as compared to non-spiroconjugated models. The spiroketones are susceptible to nucleophile-induced retro-Claisen condensations that lead to molecular rearrangements destroying spiro connectivity.

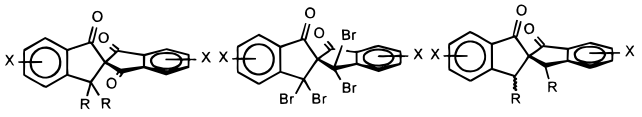
In connection with our investigation of new three-dimensional acceptors[1] we have prepared several spiroketones. The design of these acceptors was based on the phenomenon of spiroconjugation,[2,3] i.e., the ability of two perpendicular π-networks to interact. In the case of the tetraketones **1**−**3** we were interested in their acceptor properties.[1] The π orbitals serving as the LUMOs of these compounds may be considered as the bonding combination of the LUMOs of the corresponding indandiones. The antibonding combination[4] gives the next higher-energy orbital (LUMO+1), and the separation between these two spiro orbitals spanning the entire molecule depends on the strength of the spiroconjugation. That interaction depends mainly on the overlap of the corresponding "half-molecule" orbitals, which in turn is governed to a large degree by the size of the coefficient on the carbonyl-carbons. The larger these coefficients, the larger the interaction between the "halves". As shown by semiempirical calculations[5] in all three tetraketones, the LUMO spans the entire molecule. In **1** and **2** the HOMO is also spiroconjugated, but the interaction is rather small due to the fact that the coefficients on the carbonyl-carbons are very small.[4] In **3**, because of the change in symmetry of the subunit orbitals, the HOMO is no longer spiroconjugated. We report here on the syntheses of these ketones, exploration of their structure, and investigation of their nucleophile-induced reactivity.



1: X = H
2: X = 4,7-diMeO
3: X = 5,6-diMeO

Synthesis of the spiro network for all the acceptors was accomplished using the chemistry[6] illustrated in Scheme 1. In each case the synthesis started with the dialkylation of diethyl malonate with the appropriate benzyl chloride to produce the corresponding diethyl dibenzylmalonate in high yields (90% or better). The diesters were hydrolyzed to the corresponding diacids (**4**−**6**) in very good yields (70% or better). Since all the diacids decarboxylated slowly over time, they were stored in the form of the disodium salts. The free acids were obtained, just before use, by acidification of a cold aqueous solution of the salts with equivalent amounts of concentrated hydrochloric acid.

The spiro network was formed by an intramolecular Friedel−Crafts acylation of the diacids or the diacid chlorides (**7**−**9**). We found that phosphorus pentoxide was the agent of choice to affect the spiro-closure of all the diacids: **4** gave **10** in 42% yield, and **6** lead to **12** in 33% yield, but the reaction of **5** was irreproducible, giving **11** in only 10% yield in the best runs. The cyclization of acid chlorides worked almost as well for the preparation of **10** (in 30% overall yield from the diacid), but it was a preferred method for the preparation of **11** (27% overall yield from the diacid). All the reactions with phosphorus pentoxide worked best on gram/subgram quantities of the diacids. Multigram-scale reactions seemed to lead to larger proportions of undesired decarboxylated side products. On the other hand, closures of the acid chlorides required careful purification of the chlorides (especially in the case of **8**) and precise control of the reaction conditions (catalyst and temperature). The alternative methods of cyclization of the esters or acids (using for example polyphosphoric acid or sulfuric acid) were unsuccessful.



13: X = H, R = H
14: X = H R = Br
15: X = H
16: X = 5,6-diMeO
17: X = 4,7-diMeO R = Br
18: X = 4,7-diMeO R = OH

Once the spiro network was obtained, the benzylic positions were further functionalized by a combination of bromination, hydrolysis, and oxidation reactions.

(1) (a) Maslak, P.; Augustine, M. P.; Burkey, J. D. *J. Am. Chem. Soc.* **1990**, *112*, 5360. (b) Maslak, P. *Adv. Mater.* **1994**, *6*, 405. (c) Maslak, P.; Chopra, A.; Moylan, C. R.; Wortmann, R.; Lebus, S.; Rheingold, A. L.; Yap, G. P. A. *J. Am. Chem. Soc.* **1996**, *118*, 1471. (d) Maslak, P.; Chopra, *J. Am. Chem. Soc.* **1993**, *115*, 9331.

(2) (a) Simmons, H. E.; Fukunaga, T. *J. Am. Chem. Soc.* **1967**, *89*, 5208. (b) Hoffmann, R.; Imamura, A.; Zeiss, G. D. *J. Am. Chem. Soc.* **1967**, *89*, 5215.

(3) For a review see: Durr, H.; Gleiter, R. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 559.

(4) All orbitals of the "halves" that are antisymmetric vs both molecular planes can interact giving the lower-energy bonding and the higher-energy antibonding combinations that span the entire molecule. The frontier orbitals, and specifically here for the electron acceptors the LUMOs, are of main interest. For the purpose of this discussion, the HOMO−LUMO designation refers only to the π system. The nonbonding electrons are treated separately.

(5) The semiempirical MNDO-PM3 calculations (Stewart, J. J. P. *J. Comp-Aid. Mol. Des.* **1990**, *4*, 1) were carried out using Spartan 5 (Wavefunction Inc.).

(6) The synthetic strategy followed that used to prepare dione **10** and a related spirosystem: (a) Langer, E.; Lehner, H. *Tetrahedron* **1973**, *29*, 375. (b) Dynesen, E. *Acta Chem. Scand.* **1972**, *26*, 850. (c) Semmelhack, J.; Foos, S.; Katz, S. *J Am. Chem. Soc.* **1973**, *95*, 7325.

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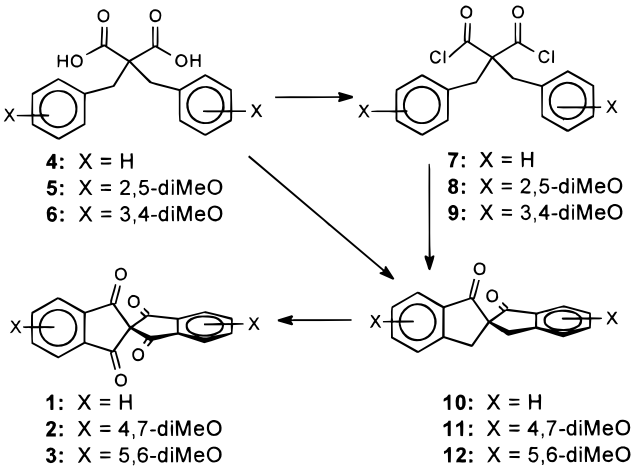
Scheme 1



Direct oxidation of **10** with chromium(VI) oxide produced 2,2′-spirobiindan-1,1′,3-trione (**13**) in 52% yield. The oxidation reaction, however, could not be pushed to completion without destroying the desired product, and it proved difficult to separate **13** from the unreacted **10**. Bromination of **13**, followed by hydrolysis of the dibromotrione (**14**), afforded the target tetraone **1** in a 26% overall yield, starting from **10**. An alternative procedure, involving extensive bromination of **10**, followed by hydrolysis of the tetrabromo compound (**15**), produced the desired tetraone (**1**) in a higher yield (36%) and in fewer steps. A similar exhaustive bromination procedure when applied to **12** gave the corresponding tetrabromide (**16**) that was hydrolyzed to **3** in 80% overall yield. NBS bromination of **11** produced only the corresponding dibromo compound **17**, probably due to the steric hindrance caused by the methoxy groups. Surprisingly, only one diastereoisomer was obtained. Hydrolysis of **17** to the dialcohol **18** (obtained as a mixture of two diastereoisomers) followed by oxidation gave the target tetramethoxytetraone (**2**) in 61% yield (from **11**).

The structure of the spiroketones **1** and **2** was confirmed by X-ray analysis.[7] The molecules possess 2-fold symmetry axes and planes as expected. There are no unusual bond lengths or bond angles present, and the observed and calculated (MNDO-PM3)[5] geometrical parameters are in excellent agreement. The chemical shift equivalence of the signals in the NMR spectra of the compounds also confirms the same high symmetry: the two halves of each molecule are contained in two perpendicular planes, and no significant distortions are seen. This is in contrast to what is observed for spiro donor−acceptor systems, where the aromatic rings of the donor components are bent away from the plane perpendicular to the plane containing the acceptor half.[1c]

A characteristic trend was observed in the ^{13}C chemical shifts of the carbonyl carbons, wherein all the spirodiones (**10**−**12**) and the model compounds **19**−**22** (see below) exhibited shifts ranging from 200 to 205 ppm, while all the spirotetraones had shifts approximately 10 ppm lower (190−191 ppm). The spirotrione **13** showed shifts of intermediate value (ca. 196 ppm). It is unlikely that this trend is related to spiroconjugation; it is probably due to the cumulative inductive effects of the carbonyl groups.

(7) The details of the crystal structure and the crystal packing of **1** and **2** will be presented elsewhere: Maslak, P.; Varadarajan S.; Rheingold, A. L.; Yap, G. P. Manuscript in preparation.

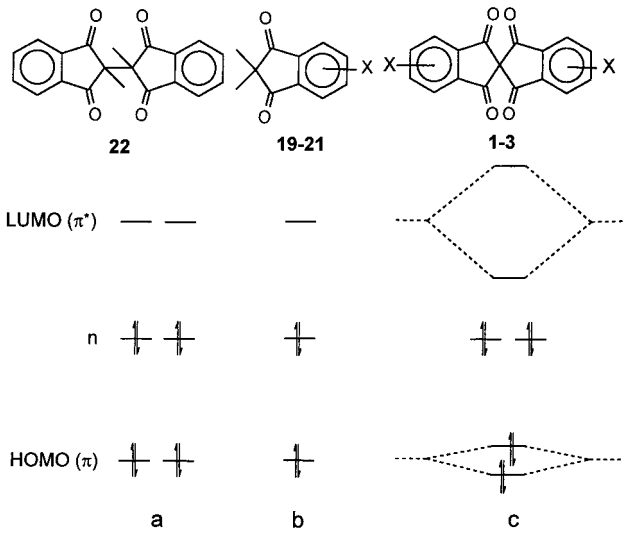


Figure 1. Schematic representation of the orbitals available for electronic transition in model compounds (a, b) and the spiroconjugated tetraones (c). In **3** the HOMO is not spiroconjugated. The HOMO−LUMO designation refers only to the π system.

Also inspection of the infrared carbonyl frequencies did not reveal any significant spiroconjugation effects. The frequencies for the carbonyl absorptions in the spiro molecules were slightly less than those in the corresponding models (**19**−**22**), but these differences were less than 3 cm^{-1}.

The spiroconjugation effects were most visible in the comparison of the UV−visible spectra of the tetraones with those of the corresponding models. The interpretation of the various features in the spectra can be better understood by first considering the interactions of the frontier orbitals in the systems (Figure 1). It should be noted that the figure represents only the orbital picture, while we are dealing with state-to-state transitions in the actual systems. As has been mentioned earlier, both the HOMO and the LUMO of the π subsystems of the spiro compounds can interact (except for **3**, whose HOMO has incorrect symmetry for spiroconjugation). However, since the carbonyl-carbon orbital coefficients on the HOMO are small, these interactions of the subsystem HOMOs are not expected to be significant. Therefore, the HOMO in the spiroconjugated molecules (Figure 1) will not be much different from the HOMO in the model. However, the stronger LUMO−LUMO interactions (due to larger orbital coefficients on the carbonyl-carbons) would lead to a lowering of the LUMO in the spiroconjugated molecule, as compared to the model. Additionally, the probability of the HOMO−LUMO transitions is doubled in the case of the spiro compounds (and the dimer, **22**), as compared to the indandione models since there are two degenerate (or nearly degenerate) HOMOs in the spiro-molecules and the dimer, whereas there is only one such orbital in the models.

The UV−visible spectra of the systems investigated are shown in Figures 2−4. In all cases, there is a striking similarity between the absorption spectra of the spiroketones and the corresponding models. All the absorption bands seen in the spiro compounds are also present in the model compounds.

Compounds **19** and **22** show two $\pi-\pi^*$ transitions at ca. 225 and 245 nm and an $n-\pi^*$ transition at 290−310

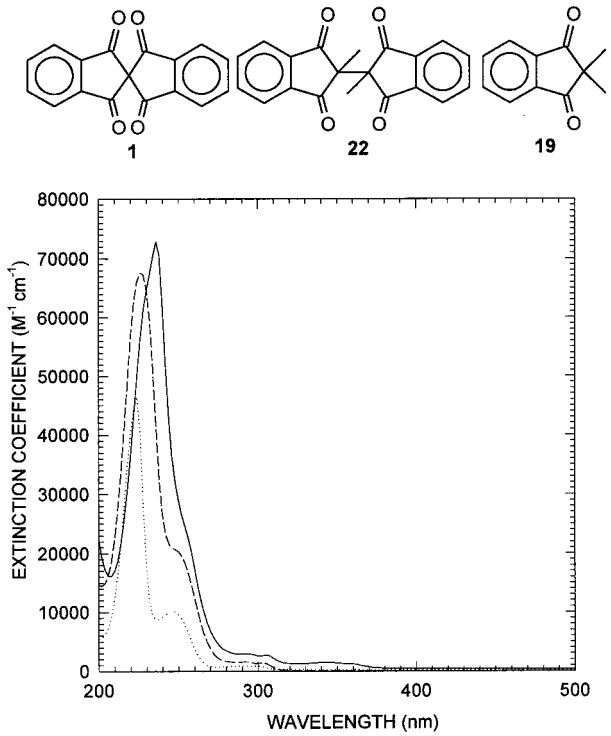


Figure 2. UV−visible spectra of the spiroconjugated acceptor **1** (solid line) and model diones **22** (broken line) and **19** (dotted line) in acetonitrile at room temperature.

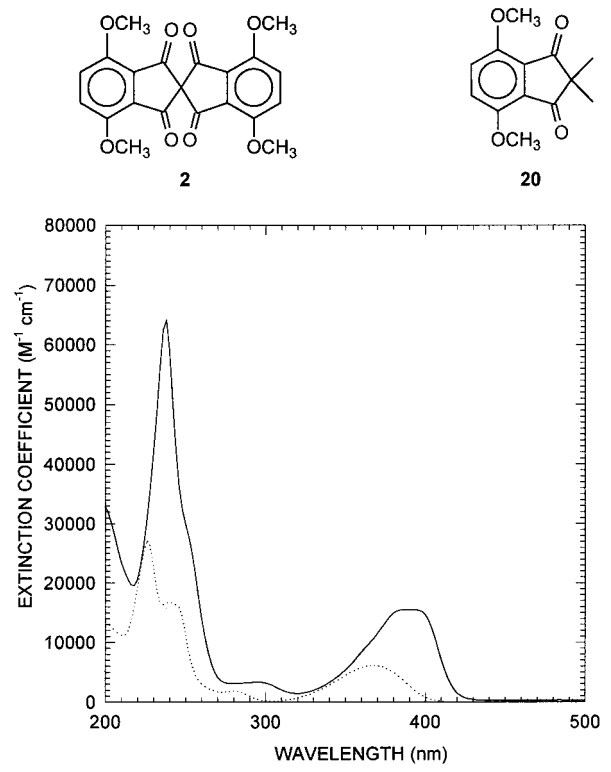


Figure 3. UV−visible spectra of the spiroconjugated acceptor **2** (solid line) and model dione **20** (dotted line) in acetonitrile at room temperature.

nm. The same transitions are seen in the case of the spiro compound **1**, but they are shifted to longer wavelengths, due to the lowering of the π^* level (Figure 1b). Additionally, **1** shows another weak absorption band between 320

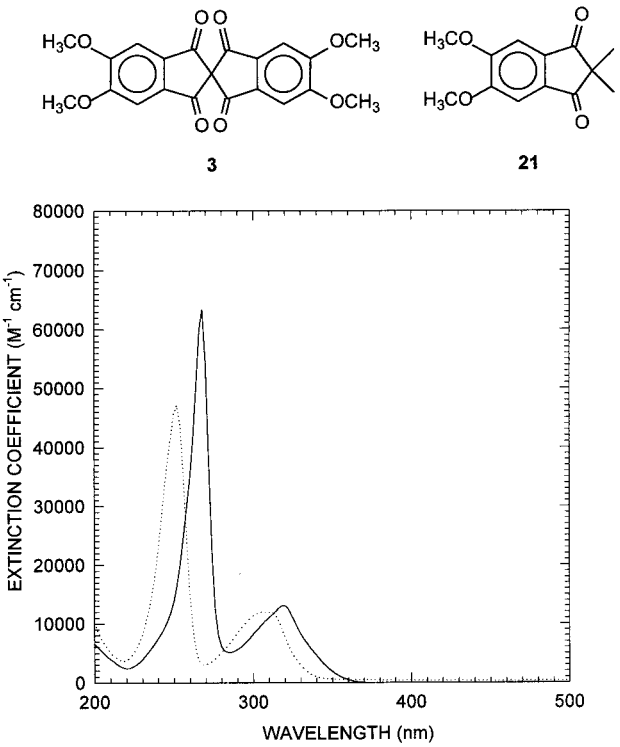


Figure 4. UV−visible spectra of the spiroconjugated acceptor **3** (solid line) and model dione **21** (dotted line) in acetonitrile at room temperature.

and 370 nm. This could be a second n−π^* transition, possible in this case due to the presence of a split LUMO.

In the case of the ketones with methoxy substituents (**2**, **3**, **20**, and **21**), there is an additional absorption band in the near-UV−visible region of the spectrum, which is absent in the unsubstituted ketones (**1**, **19**, and **22**). These bands are present in both the spiro compounds and the corresponding models, and they could be attributed to CT transitions within the subchromophores, arising due to the transfer of charge from the lone pairs on the methoxy oxygens to the carbonyls.

This CT band, in the case of **2** and **20**, is shifted to a longer wavelength as compared to **3** and **21**. Such differences are not unusual for ortho versus para substitution in CT systems. For example, the absorption maxima for ortho- and para-nitroaniline occur at 398 and 354 nm, respectively, in dioxane. This difference can be attributed to the difference in the electrostatic interaction between the two end groups involved in the CT interaction. Since the end groups are closer in **2** and **20**, than in **3** and **21**, the electrostatic interactions are stronger in **2** and **20**, and therefore, the excited state in **2** and **20** is lower in energy. Hence the absorption of the CT transition in **2** and **20** is at a lower energy (longer wavelength).

Compounds **2** and **20** also show two $\pi-\pi^*$ transitions and one n−π^* transition, besides the CT band discussed above, all of which are shifted to longer wavelength in **2** as compared to **20**. As in the case of **1**, this red shift is consistent with the lowering of the LUMO in the spiroconjugated system. The CT band in **2** shows two absorption maxima at ca. 380 and 400 nm. A red shift is also seen in the case of **3** versus **21**; however, both these compounds seem to have only one absorption band ($\pi-\pi^*$) besides the CT band. It is possible that other bands are hidden under the intense $\pi-\pi^*$ band.

The integrated intensities of the absorption bands in the two-chromophore systems (spiro molecules **1** and **2** and the dimer **22**) are nearly double the value for the corresponding single-chromophore systems (models **19** and **20**). This is to be expected, since the probability of transitions should be nearly doubled in the bichromophoric systems (Figure 1).

There is an apparent deviation from this behavior in the case of **3** versus **21**. The intensities of the absorption of the bichromophore **3** are not double the corresponding values for the single chromophore **21** (though they are all higher). The reason for this deviation is not yet clear. One possibility is that some distortion of the chromophore affects the local transition dipole. An experimental error due to the low solubility of the spiro compound in the solvent used (acetonitrile) is unlikely, since precautions were taken to ensure dissolution. The extinction coefficient for the main transition in **3** is slightly lower than the corresponding values for **1** and **2**, while the extinction coefficient for the main transition in the model **21** is higher than the corresponding values for **19** and **20**. It is possible, therefore, that the observed apparent deviation in the relative absorption of **3** and **21** is simply the combined effect of an enhanced extinction coefficient of **21** and a diminished extinction coefficient of **3**.

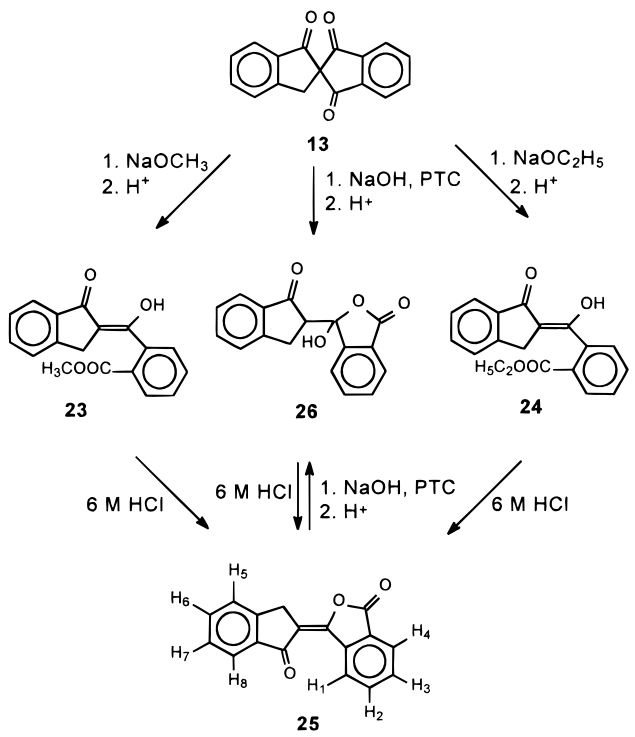
The extent of red shift in the absorption bands of the spiro molecules versus the corresponding absorptions in the appropriate models (converted to energy units) gives us a measure of spiroconjugation in these systems. A comparison of the values (ca. 0.28 eV) for the main $\pi-\pi^*$ transitions in all three systems indicates that the spiroconjugation effects are very similar and that the introduction of the methoxy groups in **2** and **3** does not seem to significantly affect the overlap between the carbonyl-carbon orbitals. This is to be expected, on the basis of similar values of the LUMO orbital coefficients (obtained from semiempirical calculations) for all three compounds.

The differences obtained for the n$-\pi^*$ (for **2**) and the CT transitions (for **2** and **3**) of 0.20−0.24 eV are slightly lower than the differences obtained for the $\pi-\pi^*$ transitions, possibly because the values for the $\pi-\pi^*$ transitions may reflect the combined effect of the lowering of the LUMO and the slight raising of the HOMO in the spiro molecules (except for **3**) due to spiroconjugation effects. This effect is not possible in the case of the n$-\pi^*$ and the CT transitions since the n orbitals are not affected by spiroconjugation. Thus, the UV−visible data on the acceptors clearly indicate the presence of spiroconjugation effects in all the neutral spiro molecules. These effects seem to be quantitatively similar in all the systems investigated and amount to ca. 0.2−0.3 eV in terms of lowering of the LUMO energy as compared to non-spiroconjugated models.

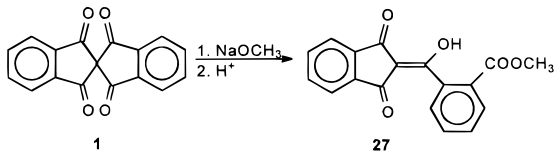
Nucleophile-induced rearrangements were observed during the course of our studies of the spiroketones on several occasions. The electronic structure of these compounds makes them very susceptible to nucleophilic attack. By design, they are electron deficient, and additionally, the carbon−carbon bonds of the spiro carbon are almost perfectly aligned to overlap with the π orbitals of the carbonyl groups. We have briefly probed the nature of these nucleophile-induced reactions using trione **13** and tetraone **1** as convenient models.

2,2′-Spirobiindan-1,3,1′-trione (**13**) was reacted on a preparative scale with several oxygen bases, including sodium methoxide, sodium ethoxide, and sodium hydroxide. When treated with sodium methoxide in methanol, **13** yielded the yellow enolate of β-diketone ester (**23**$^-$). The reaction was complete upon mixing. The UV/visible spectrum of the reaction mixture showed only the enolate (see the Experimental Section for details). Protonation of the mixture with HCl_{aq} yielded enol **23** as the exclusive product (Scheme 2). Analogously, when **13** was treated with sodium ethoxide, **24** was isolated after acidification. Both **23** and **24** exist predominantly in the enol form, but the keto form was detectable by ^{13}C NMR spectroscopy. Acid hydrolysis of either **23** or **24** in aqueous hydrochloric acid produced lactone **25**. All the transformations were nearly quantitative.

Scheme 2



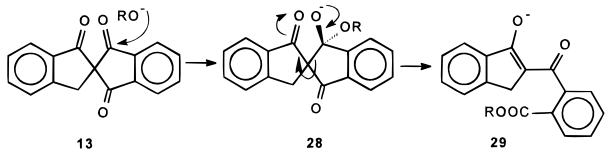
Scheme 3



When **13** was treated with sodium hydroxide under phase-transfer catalysis (PTC) conditions, hemiketal lactone **26** resulted (after acidification). Lactone **25** when treated with sodium hydroxide under PTC conditions was also converted to hemiketal lactone **26**. The stereochemistry of the double bonds in the enol forms of **23** and **24** has not been experimentally determined, but the geometry of **25** was established via decoupling and NOE experiments (see the Experimental Section). The hydrogen assignments are based on chemical shifts and decoupling experiments. The geometry shown is based on the absence of NOE effects between the benzylic hydrogens and H_1. Only one isomer was detected in this case. Again, all the transformations were nearly quantitative.

When **1** was treated with sodium ethoxide in ethanol, compound **27** was obtained (Scheme 3). Hydrolysis of **27** in 6 N hydrochloric acid resulted in 1,3-indandione. These results convey the reactive nature of these compounds.

Scheme 4



Although for convenience our studies concentrated on the trione (**13**), the reactivity of the tetraketone (**1**) and the other tetraones seems to follow similar patterns.

The observed products can be readily rationalized in terms of standard carbonyl chemistry (Scheme 4). Thus, a nucleophile adds rapidly to the electron-deficient indandione moiety. The tetrahedral intermediate formed (**28**) undergoes facile carbon−carbon bond cleavage. Such carbon−carbon bond cleavages in retro-aldol and Claisen condensations are well-known.[8] As is usually the case, the facility of this type of cleavage is dependent upon the stability of the resulting carbanion. In the case of **1** or **13**, the anion **29** is a highly delocalized enolate. In addition, the scissile bond in **28** overlaps very well with the π-system of the indanone moiety. Under such circumstances, the carbon−carbon bond cleavage is favored by both thermodynamic and stereoelectronic factors.

The spectral data indicate that when R = Me or Et, the product from quenching the reaction with aqueous acid is present predominantly as the enol tautomer. The usual hydrogen bonding within the enols of β-dicarbonyl compounds[9] should "lock" the double bond in **23** and **24** in the *Z* configuration, as shown in Scheme 2; however, the stereochemistry of the double bonds in these enols has not been established. The presence of a single peak for the methylene group in the ^{1}H NMR spectra of **23** and **24** and a single resonance for the corresponding α-carbon in the ^{13}C NMR spectrum of **23** suggests that only one isomer is present or that the isomers exchange rapidly on the NMR time scale.

In the case when R = H, the enolate originally produced undergoes a secondary reaction. A proton transfer within enolate **29** (R = H, Scheme 4) yields the carboxylate anion, which adds intramolecularly to the carbonyl group, giving (after protonation) hemiketal-lactone **26**. Lactone **25** and hemiketal-lactone **26** were easily interconvertible. Thus, addition of hydroxide to **25** followed by acidification gave **26**, while treatment of the latter with concentrated acid at elevated temperature regenerated the unsaturated lactone (**25**).

As expected, **1** reacted rapidly with ethoxide in a manner analogous to **13**, yielding after acidification enol **27**. In this system the resulting enolate is even more stable than that observed for **13**, additionally increasing the driving force for the ring opening.

We conclude that both the spirotrione and spirotetraone are very susceptible to attack by charged nucleophiles. Analogous base- or nucleophile-induced reactivity is most likely responsible for some of the difficulties observed in investigation of spiroconjugation effects in all spiroconjugated ketones.

Experimental Section

General Procedures. Infrared (IR) spectra were recorded on samples in the form of films on NaCl plates, solutions in $CHCl_3$, or in KBr. UV/visible spectra were recorded using quartz cuvettes. Mass spectral analyses (MS and HRMS) were recorded using a double-focusing spectrometer. Only structurally significant and the strongest IR frequency and MS fragment-ion peaks are reported. Melting points were determined in open capillary tubes and are uncorrected. Preparative flash chromatography[10] was carried out using Machery Nagel silica gel 60 or Merck silica gel 60, 230−400 mesh. Analytical thin-layer chromatography was performed using EM Reagents precoated silica gel (0.25 mm) F_{254} plates. The mixed solvents used for chromatography are reported as volume/volume ratios.

Diethyl Bis(2,5-dimethoxybenzyl)malonate. Diethyl malonate (49.5 mL, 0.326 mol) was added to a mechanically stirred solution of sodium ethoxide (0.74 mol, prepared in situ by the slow addition of 17.1 g sodium to absolute alcohol) in absolute alcohol (300 mL), under argon. The mixture was stirred for 30 min and then cooled to 0 °C, when a white solid precipitated. **25** (122 g, 0.656 mol) was added as a solid in one installment, and the stirring was continued for 1 h before the temperature was allowed to rise to 25 °C. The mixture was stirred overnight at room temperature. Dilute hydrochloric acid was added to the milky white reaction mixture until the solution was acidic. The solution was extracted with dichloromethane, and the combined extracts were subjected to standard workup. The colorless liquid obtained upon removal of solvent was placed under vacuum (0.1 Torr) for 2 h (145 g, 97%). No further purification was necessary. ^{1}H NMR (200 MHz): 6.78−6.68 (m, 6 H), 4.03 (q, J = 7 Hz, 4 H), 3.68 (s, 12 H), 3.27 (s, 4 H), 1.09 (t, J = 7 Hz, 6 H). ^{13}C NMR (75 MHz): 171.2, 153.0, 152,5, 126.6, 117.7, 112.3, 110.6, 60.8, 58.7, 55.6, 33.5. FTIR (film): 2983 (w), 2941 (w), 2834 (w), 1729 (s), 1610 (w), 1590 (w), 1501 (s), 1465 (m), 1224 (s). EI-MS (*m*/*z*, relative intensity): 460 (M^+, 0.3), 310 (11), 238 (15), 151 (17), 84 (87), 49 (100).

Diethyl bis(3,4-dimethoxybenzyl)malonate was obtained as described above using diethyl malonate and 3,4-dimethoxybenzyl chloride. The colorless liquid obtained on removal of solvent was dissolved in a minimum quantity of hot ethanol. The white crystals that fell out upon cooling were filtered off and dried (118 g, 96%), mp 115−116 °C. ^{1}H NMR (360 MHz): 6.78 (d, J = 8.2 Hz, 2 H), 6.72 (dd, J = 8.2 Hz, J = 1.9 Hz, 2 H), 6.69 (d, J = 1.9 Hz, 2 H) 4.13 (q, J = 7.1 Hz, 4 H), 3.86 (s, 6 H), 3.83 (s, 6 H), 3.18 (s, 4 H), 1.19 (t, J = 7.1 Hz, 6 H). ^{13}C NMR (90 MHz): 171.0, 148.4, 147.8, 128.7, 122.1, 113.3, 110.8, 61.0, 60.0, 55.7, 55.6, 38.7, 13.8. FTIR (KBr): 2976 (w), 2942 (w), 2839 (w), 1736 (s), 1608 (w), 1592 (w), 1518 (s), 1464 (m), 1194 (s). EI-MS (*m*/*z*, relative intensity): 460 (M^+, 22), 263 (24), 152 (15), 151 ($C_9H_{11}O_2$, 100).

Diethyl dibenzylmalonate[11] was prepared as described above from diethylmalonate and benzyl chloride The colorless liquid obtained upon solvent removal was 110.9 g (98%) and was used in the next step without further purification. ^{1}H NMR (200 MHz): 7.30−7.22 (m, 10 H), 4.10 (q, J = 7 Hz, 4 H), 3.24 (s, 4 H), 1.16 (t, J = 7 Hz, 6 H). ^{13}C NMR (50 MHz): 170.6, 136.1, 129.9, 128.6, 128.2, 127.9, 126.6, 60.9, 60.0, 39.0, 13.6. IR (film): 3080−2860 (m) 1725 (s), 1600 (m), 1580 (w), 1485 (m), 1440 (s), 1360 (s), 1280−1140 (s), 1060 (s), 1020 (s). EI-MS (*m*/*z*, relative intensity): 340 (M^+ 1), 295 (2), 249 (53), 204 (14), 203 (100), 193 (11), 192 (18), 131 (10%), 115 (20).

Bis(2,5-dimethoxybenzyl)malonic Acid (5). A viscous mixture of the corresponding diethyl ester (131.5 g, 0.29 mol) and pulverized sodium hydroxide (47 g, 1.18 mol) was mechanically stirred and heated to 90 °C in a flask equipped with an air condenser. Absolute alcohol (5 mL) was added at this temperature, and immediately a white solid fell out of solution. The solid paste was thinned by the periodic addition of water (2−3 mL) when necessary, and the mixture stirred for 6 h at 90 °C. After cooling to room temperature, the mixture was diluted with water (500 mL) and washed with dichloromethane (2 × 200 mL) to remove organic impurities. The aqueous layer was acidified with concentrated HCl keeping the temperature

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below 25 °C by the addition of ice. The yellow solid that fell out of solution was extracted with dichloromethane. The combined organic extracts were subjected to the standard workup. The solution was concentrated by evaporation of solvent when a white solid started falling out. This mixture was cooled in a refrigerator for 1 h, and the resulting white precipitate was filtered out at the aspirator and dried, 81.0 g (70%). A second crop of white solid was obtained on further concentration of the filtrate, followed by cooling and filtration, 14.0 g (12%), mp 159−160 °C. ^{1}H NMR (360 MHz): 6.76 (s, 6 H), 3.74 (s, 6 H), 3.70 (s, 6 H), 3.47 (s, 4 H); (300 MHz, $(CD_3)_2$-CO): 6.82 (d, J = 8.9 Hz, 2 H), 6.78 (s, 2 H), 6.72 (dd, J = 8.7 Hz, J = 3.0 Hz, 2 H), 3.66 (s, 6 H), 3.55 (s, 6 H), 3.33 (s, 4 H). ^{13}C NMR (50 MHz, $(CD_3)_2CO$): 174.0, 154.1, 153.2, 127.3, 117.7, 112.7, 111.8, 58.2, 55.7, 55.6, 35.3. FTIR (KBr): 3001 (m), 2946 (m), 2835 (m), 1701 (s), 1616 (w), 1592 (m), 1503 (s), 1465 (s), 1281 (s), 1225 (s), 1179 (s). EI-MS (*m*/*z*, relative intensity): 404 (M^+, 1), 360 ($M^+ - CO_2$, 75), 191 (18), 151 (100), 137 (18), 121 (55).

Bis(3,4-dimethoxybenzyl)malonic acid (**6**) was preapred as described above from the corresponding diethyl ester. The pale yellow solid that fell out of solution was filtered off at the aspirator, washed with cold dichloromethane (2 × 50 mL), and dried, 80 g (79%), mp 168−170 °C. ^{1}H NMR (300 MHz, $(CD_3)_2CO$): 6.83 (d, J = 8.3 Hz, 2 H), 6.82 (s, 2 H), 6.78 (dd, J = 8.1 Hz, J = 2.1 Hz, 2 H), 3.75 (s, 6 H), 3.74 (s, 6 H), 3.21 (s, 4 H). ^{13}C NMR (75 MHz, $(CD_3)_2CO$): 174.1, 149.7, 149.2, 129.4, 122.6, 114.4, 112.3, 60.9, 55.7, 55.6, 40.8. FTIR (KBr): 3319 (m), 3012 (w), 2968 (w), 2940 (w), 2840 (w), 1753 (m), 1708 (s), 1691 (m), 1517 (s) 1259 (s) 1141 (s). EI-MS (*m*/*z*, relative intensity): 404 (M^+, 1), 361 (11), 360 ($M^+ - CO_2$, 47), 152 (36), 151 ($C_9H_{11}O_2$, 100).

Dibenzylmalonic acid[11] (**4**) was prepared as described above from the corresponding diethyl ester. The white solid that was obtained was 53.4 g (85%) and did not require further purification; mp 174−175 °C (lit.[11] 175 °C). ^{1}H NMR (200 MHz): 7.25−7.23 (m, 10 H), 3.46 (s, 4 H). IR (KBr): 3060−2260 (m), 1720 (s), 1590 (s), 1470 (s), 1430 (s), 1220 (s), 1190 (s). EI-MS (*m*/*z*, relative intensity): 284 (M^+, 0.1), 240 (10), 193 (14), 175 (21), 149 (46), 131 (39), 115 (19), 103 (18), 92 (41), 91 (100).

Bis(2,5-dimethoxybenzyl)malonyl Chloride (**8**)**.** Thionyl chloride (10 mL, 137 mmol) was cooled to 0 °C under argon, and **5** (0.2 g, 0.5 mmol) was added as a solid in one installment. The heterogeneous mixture was stirred at 0 °C for 1 h and then allowed to warm to room temperature over 3 h, during which the solution became homogeneous. The reaction was monitored by NMR, and the stirring was continued until the reaction was complete. The excess thionyl chloride was distilled off under vacuum at room temperature, and the resultant brown oil was dissolved in warm hexane, decanted into a clean flask, and cooled overnight in a refrigerator. The buff-colored solid that fell out was filtered and recrystallized from dry hexane to yield 0.125 g (57%) of white crystals, mp 84−85 °C. ^{1}H NMR (300 MHz): 6.8−6.7 (m, 4 H), 6.6 (s, 2 H), 3.67 (s, 12 H), 3.45 (s, 4 H). ^{13}C NMR (75 MHz): 171.9, 154.0, 153.0, 124.0, 118,6, 114.3, 111.5, 77.3, 55.9, 55.2, 35.3. FTIR (KBr): 2940 (w), 2835 (w), 1788 (s), 1503 (s), 1225 (s), 1045 (s). CI-MS (*m*/*z*, relative intensity): 442 ($M^+ + 2$, 14), 440 (M^+, 19), 369 (26), 219 (35), 151 (100).

Dibenzylmalonic Acid Dichloride[11] (**7**)**.** In a flask equipped with a condenser, drying tube, and $NaOH_{aq}$ trap, **43** (32.04 g, 0.113 mol) was suspended in 50 mL of chloroform. The temperature was lowered to 0 °C, and phosphorus pentachloride (51.78 g, 0.249 mol) was added over a 20 min period. After stirring at room temperature for 1 h, the reaction mixture was heated at reflux for 15 min and cooled to room temperature. The solvent was then removed by rotary evaporation, leaving behind a pale yellow liquid. This liquid was distilled under vacuum (0.7 Torr) to yield 25.93 g (72%) of product (bp 145−150 °C (0.7 Torr), lit.[11] 216−218 °C, 17 Torr). ^{1}H NMR (200 MHz): 7.20−7.05 (m, 10 H), 3.30 (s, 4 H). EI-MS (*m*/*z*, relative intensity): 320 (M^+, 3), 249 (5), 194 (20), 131 (12), 117 (13), 92 (14), 91 (100).

2,2′-Spirobiindan-4,4′,7,7′-tetramethoxy-1,1′-dione (**11**)**.** A mixture of **8** (0.5 g, 1.14 mmol) and a catalytic amount of ferric chloride (0.01 g, 0.06 mmol) was stirred under vacuum (1 Torr) for 5 min in a preheated oil bath at 160 °C. The solid melted to form a dark brown liquid with the evolution of a gas. The mixture was allowed to cool to room temperature, and the resultant solid was stirred with dilute HCl (25 mL) and dichloromethane (25 mL) for 30 min. The organic layer was then separated, and the aqueous layer extracted with dichloromethane. The combined organic layers were subjected to the standard workup. The brown solid left behind on removal of solvent contained the desired product, which was isolated by flash chromatography, eluting with 10% ethyl acetate in dichloromethane. Recrystallization from ethyl acetate yielded 0.2 g (48%) of white crystals, mp 265−267 °C; R_f = 0.35 (10% ethyl acetate in dichloromethane). ^{1}H NMR (200 MHz): 7.02 (d, J = 8.7 Hz, 2 H), 6.74 (d, J = 8.7 Hz, 2 H), 3.86 (s, 6 H), 3.85 (s, 6 H), 3.57 (d, J = 17.5 Hz, 2 H), 2.96 (d, J = 17.5 Hz, 2 H); ^{13}C NMR (50 MHz): 200.1, 152.3, 150.1, 144.2, 124.7, 117.3, 110.0, 65.6, 56.0, 55.9, 34.6. FTIR (KBr): 1714 (m), 1688 (s), 1594 (m), 1499 (s), 1275 (s). EI-MS (*m*/*z*, relative intensity): 369 ($M^+ + 1$, 26), 368 (M^+, 100), 353 (11), 338 (15), 323 (15), 309 (41), 192 (19), 191 (24), 189 (15), 151 (13). Anal. Calcd for $C_{21}H_{20}O_6$: C, 68.47; H, 5.47. Found: C, 68.55; H, 5.61.

2,2′-Spirobiindan-5,5′,6,6′-tetramethoxy-1,1′-dione (**12**)**.** A suspension of **6** (0.50 g, 1.24 mmol) in dry toluene (50 mL) was cooled to 0 °C, and phosphorus pentoxide (0.5 g, 3.52 mmol) was added with vigorous stirring. The solution, which slowly turned deep red, was allowed to warm to room temperature, and it was stirred for 6 h. It was then cooled again to 0 °C and another installment of phosphorus pentoxide (0.5 g, 3.52 mmol) was added, and the mixture was stirred again for 6 h with slow warming to room temperature. The whole process was repeated once more with a third installment of phosphorus pentoxide (0.5 g, 3.52 mmol). The red-colored reaction mixture was quenched with dilute NaOH (50 mL). The resulting white suspension was allowed to settle, and the toluene layer was separated out and washed with water. The aqueous white suspension was extracted with dichloromethane, and the combined extracts were washed with water. The toluene and dichloromethane layers were then combined together and dried over anhydrous sodium sulfate, and the solvent was evaporated off, leaving behind a white solid (0.25 g), which was a mixture containing the desired product. The solid was washed with ethyl acetate, and the residue (0.10 g, 22%) left behind was determined to be pure **12** by ^{1}H NMR. The ethyl acetate washings were combined together, concentrated, and chromatographed on silica gel (eluting with 10% ethyl acetate in dichloromethane) to yield another 0.05 g (11%) of pure product, mp 257−260 °C; R_f = 0.34 (10% ethyl acetate in dichloromethane). ^{1}H NMR (300 MHz): 7.17 (s, 2 H), 6.98 (s, 2 H), 4.01 (s, 6 H), 3.91 (s, 6 H), 3.61 (d, J = 16.7 Hz, 2 H), 3.09 (d, J = 16.8 Hz, 2 H). ^{13}C NMR (75 MHz): 201.6, 155.9, 149.7, 149.4, 128.2, 107.2, 105.1, 65.7, 56.3, 56.1, 37.7. FTIR (KBr): 3415 (m), 2924 (m), 1694 (s), 1605 (m), 1592 (m), 1502 (s), 1310 (s), 1279 (s). EI-MS (*m*/*z*, relative intensity): 369 ($M^+ + 1$, 24), 368 (M^+, 100), 340 ($M^+ - CO$, 15), 339 (12%). Anal. Calcd for $C_{21}H_{20}O_6$: C, 68.47; H, 5.47. Found: C, 68.44; H, 5.57.

2,2′-Spirobiindan-1,1′-dione[6ab] (**10**)**.** Aluminum chloride (0.660 g, 4.95 mmol) and ferric chloride (0.052 g, 0.32 mmol) were added to **7** (12.29 g, 38.3 mmol). The reaction vessel was placed in a Kugelrohr (Aldrich) and heated from 25 °C to 225 °C at a rate of 5 °C/min and at a pressure maintained between 3 and 5 Torr. The desired material distilled over between 180 and 210 °C and solidified in the trap. Recrystallization of the distilled material twice from ethyl acetate yielded 2.89 (30%) of the product as white crystals, mp 168−169 °C (lit.[6a] 174 °C, lit.[6b] 173.6−176 °C); R_f = 0.23 (dichloromethane). ^{1}H NMR (300 MHz, CD_2Cl_2): 7.77−7.42 (m, 8 H), 3.69 (d, J = 14 Hz, 2 H), 3.22 (d, J = 14 Hz, 2 H). ^{13}C NMR (50 MHz): 202.6, 153.7, 135.3, 135.1, 127.6, 126.2, 124.7, 65.2, 37.9. IR (KBr): 1710

(11) Leuchs, H.; Radulescu, D. *Chem. Ber.* **1912**, *45*, 189.

(m), 1680 (s), 1595 (m), 1580 (m), 1255 (s). EI-MS (*m*/*z*, relative intensity): 249 ($M^+ + 1$, 1), 248 (M^+, 100), 247 ($M^+ - 1$, 11), 231 (13), 220 (64), 219 (57), 203 (14), 191 (57), 189 (43), 165 (27), 118 (21).

An alternative procedure, giving better yields, was also used to prepare **10**. Phosphorus pentoxide (3 × 0.5 g, 10.56 mmol) and **4** (0.5 g, 1.76 mmol) were reacted together in dry toluene (50 mL), and the product was worked up, as described for **12**. The white solid obtained upon solvent removal contained **10** and 2-benzyl-1,3-indandione ($R_f = 0.7$, dichloromethane). The desired product was isolated using flash chromatography (eluting with dichloromethane) as a white solid, 0.2 g (46%). No attempt was made to recover any unreacted starting material present in the base extracts.

2,2′-Spirobiindan-1,3,1′-trione (13). A solution of chromium oxide (8.08 g, 80.8 mmol) in 8 mL of water and 50 mL of glacial acetic acid was added to a suspension of **10** (2.49 g, 10.1 mmol) in 50 mL of glacial acetic acid. The reaction mixture was heated at 50−55 °C for 2 h. The reaction was cooled to room temperature, poured into 100 mL of ice−water, and then extracted with dichloromethane. The combined organic layers were washed with water until the aqueous layer was no longer acidic. Due to the reactivity of the product, a basic wash was avoided. After drying over anhydrous sodium sulfate, the solvent was removed by rotary evaporation, leaving behind a mixture of starting material and the desired product, as determined by TLC. The materials were separated by flash chromatography eluting with 20% hexane in dichloromethane. Starting material was recovered, 0.47 g (17%), along with 1.57 g (52%) of the desired product. The product was further purified by recrystallization from ethyl acetate, mp 164−165 °C; $R_f = 0.38$ (dichloromethane). ^{1}H NMR (200 MHz): 8.11−7.89 (m, 4 H), 7.76−7.40 (m, 4 H), 3.63 (s, 2 H). ^{13}C NMR (50 MHz): 196.7, 195.8, 144.2, 143.8, 135.9, 135.8, 134.4, 128.1, 126.5, 125.3, 124.1, 73.0, 31.9. IR (KBr): 3020 (w), 1745 (m), 1700 (s), 1585 (s), 1450 (m), 1400 (m), 1310 (m), 1235 (s), 1185 (m), 965 (m), 890 (m) 830 (m), 740 (s). EI-MS (*m*/*z*, relative intensity): 263 ($M^+ + 1$, 18), 262 (M^+, 100), 234 (15), 233 (30), 206 (32), 205 (24). HREI-MS: calculated for $C_{17}H_{10}O_3$ 262.0630, found 262.0629. Anal. Calcd C, 77.86; H, 3.84. Found: C, 77.99; H, 3.92.

3,3′-Dibromo-2,2′-spirobiindan-4,4′,7,7′-tetramethoxy-1,1′-dione (17). NBS (0.484 g, 2.72 mmol) and a catalytic amount of AIBN (10 mg) were added to **11** (0.5 g, 1.36 mmol) in deoxygenated carbon tetrachloride (25 mL) and refluxed. After 6 h more NBS (0.484 g, 2.72 mmol) and AIBN (10 mg) were added, and reflux was continued. The reaction was monitored by TLC. The monobromo and dibromo products could also be identified by ^{1}H NMR. Catalytic amounts of AIBN (10 mg) were added every 6 h until the reaction was complete (24 h). The reaction mixture was cooled to room temperature, diluted with dichloromethane (50 mL), and subjected to the standard workup, leaving behind a yellow liquid. On addition of ethyl acetate (10 mL), a yellow solid fell out. The solid was filtered and washed with a minimal amount of cold ethyl acetate (10 mL), leaving behind 0.640 g (90%) of **17** (single isomer) as a pale yellow powder. No further purification was necessary: $R_f = 0.4$ (dichloromethane); mp 223−225 °C. ^{1}H NMR (200 MHz): 7.14 (d, $J = 9.0$ Hz, 2 H), 6.82 (d, $J = 8.9$ Hz, 2 H), 5.75 (s, 2 H), 4.0 (s, 6 H), 3.80 (s, 6 H). ^{13}C NMR (50 MHz): 190.7, 152.1, 148.7, 143.4, 121.0, 119.6, 112.7, 82.4, 56.5, 56.0, 46.4. FTIR (KBr): 1712 (s), 1503 (s), 1271 (s). EI-MS (*m*/*z*, relative intensity): 528 ($M^+ + 4$, 4), 526 ($M^+ + 2$, 7), 524 (M^+, 4), 447 ($M^+ - Br + 2$, 71), 445 ($M^+ - Br$, 70), 366 ($M^+ - 2 Br$, 100), 351 (48).

3,3′-Dihydroxy-2,2′-spirobiindan-4,4′,7,7′-tetramethoxy-1,1′-dione (18). A solution of **17** (0.50 g, 0.95 mmol) in a 50% dioxane/water mixture (50 mL) was refluxed for 12 h, during which time the reaction was monitored by TLC. When the reaction was complete, the mixture was cooled to room temperature, and the solvents were removed by rotary evaporation, leaving behind a mixture of the two isomers of **18** as a pale yellow solid, 0.37 g (97%). No further purification was necessary. A small sample of the mixture was separated on a preparative scale TLC plate using 25% ethyl acetate in dichloromethane as the eluting solvent. First isomer, major component (70%): $R_f = 0.27$ (25% ethyl acetate in dichloromethane). ^{1}H NMR (360 MHz): 7.14 (d, $J = 9.2$ Hz, 2 H), 6.85 (d, $J = 9.3$ Hz, 2 H), 5.81 (s, 2 H), 3.94 (s, 6 H), 3.85 (s, 2 H), 3.83 (s, 6 H); EI-MS (*m*/*z*, relative intensity): 400 (M^+, 36), 383 ($M^+ - OH$, 13), 382 (48), 367 (27), 207 (100). Second isomer, minor component (30%): $R_f = 0.1$ (25% ethyl acetate in dichloromethane). ^{1}H NMR (360 MHz): 7.12 (m, 2 H), 6.86 (m, 2 H), 5.99 (s, 1 H), 5.71 (s, 1 H), 3.94 (s, 3 H), 3.92 (s, 3 H), 3.88 (s, 3 H), 3.85 (s, 3 H), 3.42 (s, 1 H), 2.90 (s, 1 H). EI-MS (*m*/*z*, relative intensity): 400 (M^+, 36), 382 (39), 367 (15), 323 (16), 207 (100).

2,2′-Spirobiindan-4,4′,7,7′-tetramethoxy-1,1′,3,3′-tetraone (2). Cold chromic acid solution (0.25 mL, 0.17 mmol, prepared by dissolving sodium dichromate dihydrate (1.0 g, 3.36 mmol) in water (3 mL), slowly adding concentrated H_2SO_4 (1.34 g, 0.73 mL, 13.67 mmol), cooling the solution and diluting it to 5 mL with water) was added to an ice cold solution of **18** (0.100 g, 0.25 mmol, mixture of isomers) in acetone (50 mL) and stirred. The reaction was monitored by TLC. Stirring was continued at 0 °C until the reaction was complete (3 h). The reaction mixture was diluted with dichloromethane (100 mL) and subjected to standard workup. The yellow solid obtained upon solvent removal was recrystallized from dichloromethane (slow evaporation) to yield 0.069 g (70%) of **2** as small, needle-shaped yellow crystals, mp 325−328 °C; $R_f = 0.58$ (20% ethyl acetate in dichloromethane). ^{1}H NMR (300 MHz): 7.34 (s, 4 H), 3.97 (s, 12 H); (200 MHz, CD_2Cl_2): 7.35 (s, 4 H), 3.97 (s, 12 H). FTIR (KBr): 1693 (s), 1279 (s), 1211 (s). EI-MS (*m*/*z*, relative intensity): 397 ($M^+ + 1$, 23), 396 (M^+, 27), 382 (72), 381 (33), 369 (30), 368 (33), 367 (45), 353 (40), 338 (28), 337 (18), 323 (34), 309 (22). Anal. Calcd for $C_{21}H_{16}O_8$: C, 63.64; H, 4.07. Found: C, 63.52; H, 4.30.

2,2′-Spirobiindan-3,3,3′,3′-tetrabromo-5,5′,6,6′-tetramethoxy-1,1′-dione (16). NBS (0.918 g, 3.44 mmol) and **12** (0.50 g, 1.36 mmol) were reacted together as described for **17** using AIBN as initiator. The reaction was monitored by ^{1}H NMR. The dibromo and the tribromo compounds could be identified as intermediates. NBS (0.230 g, 0.86 mmol) and AIBN (10 mg) were added every 12 h until the reaction was complete (96 h). The reaction mixture was worked up as described for **17**, and the pure product obtained after washing with ethyl acetate was 0.830 g (90%). No further purification was necessary; mp > 350 °C (decomp). ^{1}H NMR (300 MHz): 7.52 (s, 2 H), 6.99 (s, 2 H), 4.16 (s, 6 H), 3.91 (s, 6 H). ^{13}C NMR (50 MHz): 186.0, 157.4, 152.5, 152.1, 122.4, 106.9, 104.5, 57.5, 56.6, 55.2. FTIR (KBr): 3480 (w), 3414 (w), 1708 (s), 1616 (w), 1501 (s), 1294 (s). EI-MS (*m*/*z*, relative intensity): 607 ($M^+ - Br + 6$, 11), 605 ($M^+ - Br + 4$, 23), 604 (10), 603 ($M^+ - Br + 2$, 24), 601 ($M^+ - Br$, 11), 526 ($M^+ - 2 Br + 4$, 9), 525 (14), 524 ($M^+ - 2 Br + 2$, 10), 522 ($M^+ - 2 Br$, 6), 447 ($M^+ - 3 Br + 4$, 25), 446 (81), 445 ($M^+ - 3 Br + 2$, 52), 444 (75), 443 ($M^+ - 3 Br$, 35).

2,2′-Spirobiindan-5,5′,6,6′-tetramethoxy-1,1′,3,3′-tetraone (3). Silver acetate (0.100 g, 0.599 mmol) was added to a suspension of **16** (0.100 g, 0.147 mmol) in glacial acetic acid (10 mL), and the mixture refluxed for 4 h. The hot reaction mixture was filtered at the aspirator, and the residue was washed with dichloromethane. The combined organic layers were washed with water until the washings were no longer acidic and dried over anhydrous sodium sulfate. (A base wash was avoided due to the reactivity of the tetraone.) The yellow solid obtained upon solvent evaporation was recrystallized from dichloromethane (slow evaporation) to give 0.052 g (89%) of white crystals, mp > 350 °C (decom); $R_f = 0.63$ (10% ethyl acetate in dichloromethane). ^{1}H NMR (200 MHz): 7.43 (s, 4 H), 4.06 (s, 12 H). ^{13}C NMR (50 MHz): 191.0, 156.4, 140.1, 104.1, 56.8. FTIR (KBr): 2938 (w), 2838 (w), 1718 (m), 1693 (s), 1300 (s). EI-MS (*m*/*z*, relative intensity): 397 ($M^+ + 1$, 23), 396 (M^+, 100), 164 (10), 136 (20), 93 (13), 28 (CO, 75). Anal. Calcd for $C_{21}H_{16}O_8$: C, 63.64; H, 4.07. Found: C, 63.75; H, 4.24.

3′,3′-Dibromo-2,2′-spirobiindan-1,3,1′-trione (14). NBS (0.780 g, 4.34 mmol), a catalytic amount of AIBN (10 mg), and

0.5 mL of bromine were added to **13** (0.563 g, 2.15 mmol) in 25 mL of deoxygenated carbon tetrachloride. The reaction was carried out as described for **15**, with further additions of AIBN (10 mg) every 12 h and NBS (0.780 g, 4.34 mmol) every 24 h, until the reaction was complete (90 h), as indicated by TLC. The reaction mixture was worked up as described for **15**, and the pure product was isolated by flash chromatography eluting with 20% hexane in dichloromethane, yielding 0.529 g (58%); mp 120 °C (decomp); R_f = 0.56 (dichloromethane). ^{1}H NMR (360 MHz): 8.18−7.58 (m, 8 H). IR (KBr): 3000−2900 (m), 1770 (m), 1700 (s), 1170 (s). EI-MS (*m*/*z*, relative intensity): 342 (18), 341 (100), 340 (18), 339 (99), 313 (12), 311 (12), 261 (17), 260 (13), 232 (20), 204 (26), 176 (44).

2,2′-Spirobiindantetraone (1). Silver acetate (0.451 g, 2.70 mmol) was added to a suspension of **14** (0.450 g, 1.07 mmol) in 30 mL of glacial acetic acid. The reaction was carried out and the product was worked up as described for **3**, to yield 0.281 g of a white solid. The product was purified by recrystallization from ethyl acetate to yield 0.260 g (88%); mp 244−246 °C; R_f = 0.57 (dichloromethane). ^{1}H NMR (200 MHz): 8.11−7.91 (m, 8 H). ^{13}C NMR (50 MHz): 191.4, 144.6, 136.2, 124.3, 78.5. IR (KBr): 3020 (w), 1700 (s), 1575 (s), 1210 (s), 1140 (s). EI-MS (*m*/*z*, relative intensity): 277 (M^+ + 1, 18), 276 (M^+, 100), 248 (30), 220 (14). HREI-MS: calculated for $C_{17}H_8O_4$ 276.0423, found 276.0426. Anal. Calcd: C, 73.91; H, 2.92. Found: C, 73.72; H, 3.28.

An alternative procedure (starting from **15**, see below) was developed that gave a better yield of **1** in fewer steps. Silver acetate (0.601 g, 3.599 mmol) was added to a suspension of **15** (0.493 g, 0.880 mmol) in 25 mL of glacial acetic acid. The reaction was carried out and the product was worked up as described for **3**, to yield 0.207 g (85%) of pure **1** as a white solid.

2,2′-Spirobiindan-3,3,3′,3′-tetrabromo-1,1′-dione (15). NBS (0.750 g, 4.213 mmol), a catalytic amount of AIBN (10 mg), and bromine (0.5 mL) were added to **10** (0.501 g, 2.02 mmol) in deoxygenated carbon tetrachloride (25 mL). The reaction was heated at reflux and monitored by TLC. More NBS (0.750 g, 4.213 mmol) was added after 24, 48, and 72 h. Catalytic amounts of AIBN (10 mg) were added every 6 h until the reaction was complete (100 h, no change by TLC over the last 6 h). Also, bromine (0.5 mL) was added if the solution had noticeably decreased in bromine concentration (indicated by decrease in color intensity of the solution). The reaction mixture was cooled to room temperature, diluted with dichloromethane (50 mL), and subjected to the standard workup, leaving behind a yellow liquid containing the desired product. The product was isolated as a pale yellow solid using flash column chromatography (eluting with dichloromethane), yielding 0.475 g (42%); mp > 200 °C (decomp); R_f = 0.69 (dichloromethane). ^{1}H NMR (360 MHz): 8.10 (d, J = Hz, 2 H), 7.85 (t, J = Hz, 2 H), 7. 58 (d, J = Hz, 2 H), 7.45 (t, J = Hz, 2 H). EI-MS (*m*/*z*, relative intensity): 487 (M^+ − Br + 6, 5), 485 (M^+ − Br + 4, 15), 483 (M^+ − Br + 2, 55), 481 (M^+ −Br, 5), 406 (M^+ − 2 Br + 4, 5), 404 (M^+ − 2 Br + 2, 11), 402 (M^+ − 2 Br, 6), 326 (100), 325 (M^+ − 3 Br + 2, 51), 324 (97), 323 (M^+ − 3 Br, 34).

2,2-Dimethylindan-1,3-dione[12] (**19**) was prepared by using the procedure described by Wislicenus and Kotzle.[12] Triethylbenzylammonium chloride (0.050 g) and sodium hydroxide solution (75 mL, 0.6 M) were added to a solution of iodomethane (0.9 mL, 14.31 mmol) and 1,3-indandione (1.03 g, 6.84 mmol) in dichloromethane (75 mL), and the mixture was stirred for 100 h. The organic layer was then separated and washed with a 5% sodium hydroxide solution and subjected to the standard workup. The black oily solid obtained after solvent removal was dissolved in the minimum quantity of hexane. Upon cooling to −78 °C, white crystals fell out of solution and were quickly filtered and dried: 0.272 g (22%); mp 104−105 °C (lit.[12] 107−108 °C). ^{1}H NMR (200 MHz): 8.03−7.86 (m, 4 H), 1.29 (s, 6 H). FTIR (KBr): 3435 (w), 3087 (w), 2974 (s), 2904 (w), 2883 (w), 1744 (s), 1703 (s), 1594 (m), 1286 (s), 1200 (s). EI-MS (*m*/*z*, relative intensity): 176 (M^+ + 2, 1), 175 (M^+ +1, 12), 174 (M^+, 100), 159 (96), 146 (16).

4,7-Dimethoxy-2,2-dimethylindan-1,3-dione[13] (**20**). Polyphosphoric acid (10.0 g) was added to a mixture of 2,2-dimethylmalonic acid (0.60 g, 4.55 mmol) and 1,4-dimethoxybenzene (0.50 g, 3.62 mmol), and the viscous mixture was mechanically stirred and heated to 70 °C. The reaction mixture turned yellow and then bright red. Stirring was continued at 70 °C for 3 h. The reaction was then cooled to room temperature, quenched with ice−water (100 mL), and stirred until the red reaction mixture turned white. The aqueous mixture was extracted with dichloromethane, and the combined organic extracts were given a base wash and then subjected to the standard workup. The desired product was isolated from the pale yellow solid obtained upon solvent removal by flash column chromatography using 10% ethyl acetate in dichloromethane as the eluting solvent. The white powder obtained was recrystallized from 95% ethanol to yield 0.720 g (85%) of white crystals: mp 167−168 °C (lit.[13] mp 170−171 °C); R_f = 0.31 (10% ethyl acetate in hexane). ^{1}H NMR (200 MHz): 7.28 (s, 2 H), 3.99 (s, 6 H), 1.27 (s, 6 H). ^{13}C NMR (50 MHz): 203.9, 152.2, 128.2, 120.7, 56.8, 50.6, 20.6. FTIR (KBr): 2969 (m), 1737 (s), 1701 (s), 1580 (s), 1499 (s), 1054 (s), 1018 (s). CI-MS (*m*/*z*, relative intensity): 236 (M^+ + 2, 15), 235 (M^+ + 1, 100), 234 (M^+, 20), 233 (1), 219 (M^+ − CH_3, 2).

5,6-Dimethoxy-2,2-dimethylindan-1,3-dione (21). Polyphosphoric acid (10.0 g) was added to a mixture of 2,2-dimethylmalonic acid (0.60 g, 4.55 mmol) and 1,2-dimethoxybenzene (0.50 g, 3.62 mmol), the reaction was carried out, and the product was worked up as described for **20**. The desired product was isolated by flash column chromatography eluting with 5% ethyl acetate in dichloromethane in the form of a white powder. The product was recrystallized from 95% ethanol in the form of white needles: 0.570 g (67%); mp 224−226 °C; R_f = 0.46 (10% ethyl acetate in dichloromethane). ^{1}H NMR (300 MHz): 7.34 (s, 2 H), 4.03 (s, 6 H), 1.28 (s, 6 H). ^{13}C NMR (50 MHz): 203.5, 156.0, 135.1, 103.5, 56.6, 49.4, 20.3. FTIR (KBr): 2985 (w), 1729 (s), 1698 (s), 1583 (s), 1502 (s), 1381 (s), 1317 (s), 1108 (s), 1006 (s). EI-MS (*m*/*z*, relative intensity): 235 (M^+ + 1, 9), 234 (M^+, 42), 220 (10), 219 (M^+ − CH_3, 34), 206 (17), 205 (10), 191 (M^+ − CH_3 − CO, 28), 175 (M^+ − CH_3 − 2 CO, 12). Anal. Calcd for $C_{13}H_{14}O_4$: C, 66.66; H, 6.02. Found: C, 66.51; H, 6.33.

2,2′-Dimethyl-[2,2′]-biindenyl-1,3,1′,3′-tetraone (22) was prepared by a modification of the procedure described by Spencer et al.,[14] who obtained **22** as a side product in a reaction used to prepare 2-acetoxy-2-methylindan-1,3-dione. Lead tetraacetate (3.0 g, 6.77 mmol) was added to a suspension of 2-methylindan-1,3-dione[15] (1.00 g, 6.25 mmol) in benzene (5 mL) and stirred for 20 h. A white precipitate was formed. The reaction was quenched with dilute HCl (50 mL), diluted with dichloromethane (50 mL), and stirred for 30 min. The organic layer was separated, and the aqueous layer was extracted with dichloromethane. The organic layers were combined and subjected to the standard workup. The desired product was isolated from the yellow solid obtained upon solvent removal by flash column chromatography using dichloromethane as eluant and recrystallized from 95% ethanol to give white needles (0.64 g, 32%): mp 203−205 °C (lit.[14] 204−205 °C); R_f = 0.27 (dichloromethane). ^{1}H NMR (200 MHz): 7.95−7.75 (m, 8 H), 1.71 (s, 6 H). ^{13}C NMR (50 MHz): 201.2, 140.5, 135.9, 123.6, 55.4, 15.7. FTIR (KBr): 2977 (w), 1748 (m), 1737 (m), 1705 (s), 1592 (m). EI-MS (*m*/*z*, relative intensity): 319 (M^+ + 1, 22), 318 (M^+, 100), 275 (M^+ − CH_3 − CO, 5), 160 (16), 132 (13).

Treatment of 13 with Sodium Ethoxide or Sodium Methoxide. Under argon 2 sodium spheres (0.043 g, 1.87 mmol) were added to 5 mL of ROH (reagent grade methanol or absolute ethanol). After the spheres had completely reacted,

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(14) Spencer, T. A.; Hall, A. L.; Fordham von Reyn, C. *J. Org. Chem.* **1968**, *33*, 3369.

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13 (0.608 g, 0.232 mmol) was added to the NaOR solution. The reaction mixture turned yellow immediately. The UV/vis spectrum showed the presence of the enolate (in CH_3CN λ_{max} = 360 nm, $\epsilon = 8.1 \times 10^4\ M^{-1}\ cm^{-1}$). For comparison, the trione (**13**) has the longest wavelength transition at 290 nm ($\epsilon = 7.8 \times 10^3\ M^{-1}\ cm^{-1}$ in CH_3CN). The solution was neutralized with dilute HCl, which caused the yellow color to disappear. Water, 50 mL, was added, the solution was extracted with dichloromethane, and the extract was subjected to the standard workup. Removal of solvent gave an oily solid residue, approximately 50 mg of **23** for R = Me or of **24** for R = Et. The materials were not further purified for spectral analyses, nor for the hydrolysis reactions. The UV/vis spectrum of the product (**23**) showed the presence of the conjugated chromophore (enol: $\lambda_{max} = 328$ nm, $\epsilon = 1.4 \times 10^5\ M^{-1}\ cm^{-1}$ in CH_3CN).

23: ^{1}H NMR (200 MHz): 7.96−7.80 (m, 2 H), 7.60−7.33 (m, 6 H), 3.69 (s, 3 H), 3.45 (s, 2 H). ^{13}C NMR (50 MHz, k = minor keto form): 201.3(k), 200.1(k), 189.6, 178.4, 167.0, 154.7(k), 147.7, 143.0(k), 137.7, 136.6, 135.4(k), 135.1(k), 132.6, 131.9, 130.2, 129.8, 129.7(k), 129.6, 128.3, 127.6(k), 127.4(k), 127.2, 127.0(k), 125.5, 124.2(k), 123.0, 111.0, 61.2(k), 52.4, 31.1, 30.3(k). EI-MS (*m*/*z*, relative intensity): 295 ($M^+ + 1$, 2), 294 (M^+, 11), 262 (20), 235 (8), 233 (6), 205 (4), 178 (6), 164 (10), 163 (100). HREI-MS: calculated for $C_{18}H_{14}O_4$, 294.0892, found 294.0877.

24: ^{1}H NMR (300 MHz): 8.01−7.84 (m, 2 H), 7.64−7.41 (m, 6 H), 4.27 (q, J = 7 Hz, 2 H), 3.47 (s, 2 H), 1.22 (t, J = 7 Hz, 3 H). IR (in $CHCl_3$): 3010−2920 (w), 1720 (s), 1650 (s), 1610 (s), 1590 (s). EI-MS (*m*/*z*, relative intensity): 308 (M^+, 6.6), 263 (13), 262 (40), 235 (11), 233 (11), 178 (16), 177 (60), 150 (10), 149 (100).

Hydrolysis of 23 and 24. Approximately 50 mg of **23** or **24** and 10 mL of 6 M aqueous hydrochloric acid were combined and refluxed for 1 h. During the reaction, a white solid formed, which was suspended on top of the solution. Water, 50 mL, was added, and the reaction material was extracted with dichloromethane and was subjected to the standard workup. The residue obtained upon solvent removal, approximately 50 mg, was not further purified for spectral analyses nor for further reactions. The hydrolyses of both (**23** and **24**) gave **25**. ^{1}H NMR (360 MHz, for proton labeling see Scheme 2): 9.42 (dd, $J_{1-2} = 7.5$ Hz, $J_{1-3} = 1.0$ Hz, H_1), 7.92 (dd, $J_{3-4} = 7.6$ Hz, $J_{2-4} = 1.0$ Hz, H_4), 7.80 (ddd, $J_{1-2} = J_{2-3} = 7.5$ Hz, $J_{2-4} = 1.0$ Hz, H_2), 7.805 (dd, $J_{7-8} = 7.5$ Hz, $J_{6-8} = 1.0$ Hz, H_8), 7.64 (ddd, $J_{2-3} = J_{3-4} = 7.5$ Hz, $J_{1-3} = 1.0$ Hz, H_3), 7.58 (ddd, $J_{5-6} = J_{6-7} - 7.4$ Hz, $J_{6-8} = 1.0$ Hz, H_6), 7.48 (dd, $J_{5-6} = 7.4$ Hz, $J_{5-7} = 1.0$ Hz, H_5), 7.38 (ddd, $J_{6-7} = J_{7-8} = 7.4$ Hz, $J_{5-7} = 1.0$ Hz, H_7), 4.03 (s, CH_2). NOE effect (^{1}H NMR) was observed between H_5 and the CH_2 group, H_1 and H_2, as well as H_3 and H_4. No NOE effects were observed between the CH_2 group and H_1 or H_4. ^{13}C NMR (75 MHz, CD_2Cl_2): 193.1, 166.8, 148.6, 140.0, 137.3, 136.0, 135.2, 132.7, 128.0, 127.6, 126.2, 125.7, 124.1, 120.0, 31.9. IR (KBr): 3110−3080 (w), 1785 (s), 1685 (s), 1630 (s), 1600 (m), 925 (s). EI-MS (*m*/*z*, relative intensity): 264 ($M^+ + 2$, 2), 263 ($M^+ + 1$, 18), 262 (M^+ 100), 234 (10), 233 (21), 206 (20). HREI-MS: calculated for $C_{17}H_{10}O_3$ 262.0630, found 262.0627.

Treatment of 25 with Sodium Hydroxide. Compound **25** (0.050 g, 0.19 mmol) and a catalytic amount of benzyltriethylammonium chloride (10 mg) were dissolved in 10 mL of dichloromethane and 10 mL of 10% aqueous sodium hydroxide, and the solution was stirred overnight. The aqueous layer was separated and acidified with 5% aqueous hydrochloric acid, causing a white oily material to fall out of the solution. The oil was taken up in ether, and the ether layer was separated. The aqueous layer was extracted twice with ether. The combined ether layers were subjected to the standard workup. The residue obtained upon solvent removal, **26** (approximately 50 mg), was not further purified. ^{1}H NMR (360 MHz): 7.92−7.30 (m, 8 H), 3.47 (dd, J = 9 Hz, J = 15 Hz, 1 H), 2.96 (dd, J = 15 Hz, J = 31 Hz, 1 H), 2.41 (dd, J = 9 Hz, J = 31 Hz, 1 H). ^{13}C NMR (70 MHz): 207.1, 168.0, 153.8, 147.0, 136.2, 135.8, 134.9, 131.0, 128.1, 127.3, 126.5, 125.6, 124.6, 122.5, 107.1, 51.2, 29.0. IR (KBr): 3200−2800 (w), 1695 (s), 1650 (s), 1605 (s), 1285 (s), 1235 (s). EI-MS (*m*/*z*, relative intensity): 280 (M^+, 2), 263 (11), 262 (58), 234 (8%), 233 (15), 206 (15), 205 (11), 178 (18), 176 (9), 149 (32), 133 (11), 132 (100). HREI-MS, calculated for $C_{17}H_{12}O_4$ 280.0736, found 280.0742.

Treatment of 13 with Sodium Hydroxide. Compound **13** (13.2 mg, 0.050 mmol) was added to 15 mL of 10% aqueous sodium hydroxide and 10 mL of dichloromethane. A catalytic amount of benzyltriethylammonium chloride (2 mg) was added, and the solution was stirred for 4 h, after which the aqueous layer was removed and acidified with concentrated hydrochloric acid. The cloudy solution was extracted twice with dichloromethane. The combined organic layers were subjected to the standard workup. The residue obtained upon solvent removal, **26** (approximately 15 mg), was not further purified.

Treatment of 1 with Sodium Ethoxide. Two sodium spheres (0.043 g, 1.87 mmol) were added to 10 mL of absolute ethanol, and after they had completely reacted, **1** (0.044 g, 0.16 mmol) was added at 25 °C. After stirring for 2 h, the solution was acidified with concentrated hydrochloric acid. Water, 50 mL, was added, and the mixture was extracted with dichloromethane. The combined organic layers were subjected to the standard workup, yielding a solid residue of **27** (approximately 40 mg), which was characterized without further purification. ^{1}H NMR (360 MHz): 8.11−8.07 (m, 1 H), 7.90−7.86 (m, 1 H), 7.79−7.55 (m, 6 H), 4.27 (q, J = 7 Hz, 2 H), 1.25 (t, J = 7 Hz, 3 H). ^{13}C NMR (90 MHz): 197.4, 186.7, 180.1, 165.7, 140.4, 138.4, 135.1, 134.1, 132.5, 131.6, 131.0, 130.4, 130.1, 129.5, 122.8, 122.4, 108.6, 61.4, 13.8. IR (in $CHCl_3$): 3020−2840 (w), 1715 (s), 1650 (s), 1610 (s), 1590 (s). EI-MS (*m*/*z*, relative intensity): 322 (M^+, 1), 277 (8), 249 (100), 226 (15), 211 (47). HREI-MS, calculated for $C_{17}H_9O_4$ (M^+ − OEt) 277.0501, found 277.0489. Hydrolysis of **27** in refluxing 6 M hydrochloric acid gave 1,3-indandione.

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Supporting Information Available: ^{1}H NMR and ^{13}C NMR spectra of **13**, **23**−**26**. This material is available free of charge via the Internet at http://pubs.acs.org.

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