Metal-Mediated [6 + 3] Cycloaddition Reactions of Fulvenes. A Novel Approach to Indan Systems

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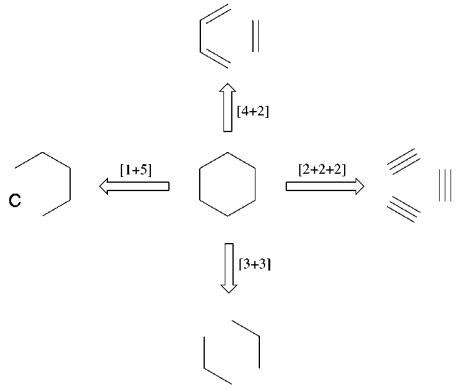
The [6 + 3] cycloaddition of 2-oxyallyl cations to the electron rich fulvene ketene acetal provides an efficient route to the indan skeleton. The structures of these indan adducts were assigned by extensive 2D NMR experiments. Direct hydrolysis of these ketal adducts affords the corresponding diketones or indens. Reaction of the fulvene ketene thioacetal as well as the tandem [6 + 3]−[4 + 3] cycloadditions were also studied. A mechanism is proposed which may account for the origin of stereo- and regioselectivity in this cycloaddition.

Introduction

Cycloaddition reactions provide rapid and elegant methods for the construction of mono and polycyclic systems. Since its discovery at the turn of the century,[1] the Diels−Alder reaction has played a crucial role in the synthesis of 6-membered rings. The search for other novel 6-membered ring-forming cycloaddition reactions is currently an active topic of research in many laboratories. In fact, this is highlighted by recent advances in the cobalt-mediated [2 + 2 + 2] cycloaddition[2] of alkynes to benzene and various [3 + 3] carbocyclizations (Scheme 1).[3,4] Theoretically, there is another possible two-component cycloaddition that could lead to the 6-membered ring: the [5 + 1] cycloaddition. However, to the best of our knowledge, this type of reaction has never been reported.[5]

The fused [5,6] indan ring system is present in many naturally occurring biologically active polycarbocyclic compounds.[6] It has also served as a useful building block for the synthesis of a wide variety of natural and unnatural compounds. A variety of Diels−Alder retrosynthetic approaches to the indan ring system have been outlined and successfully applied to the total synthesis of such skeletons (Scheme 2).[7] However, in certain cases, the presence of bulky substituents at the reacting centers or mismatched electronics of the diene and dienophile dictate harsh reaction conditions. Alternatively, dissection of the indan backbone via a retro-[6 + 3] cyclization provides the two fragments shown in Scheme 2. This strategy is analogous to the [3 + 3] cycloaddition in the synthesis of 6-membered rings. Guided by the recent advances in the pericyclic reactions of fulvenes, we suspected that the [6 + 3] reactions of fulvene ketene acetal **1** and 2-oxyallyl cations could provide a conceptually new synthetic approach to 6-membered ring systems. We herein report the details of the discovery of this novel methodology.[8]

Scheme 1



[⊗] Abstract published in *Advance ACS Abstracts,* September 15, 1997.

(1) For an interesting historical note on the discovery of the Diels−Alder reaction, see: Berson, J. A. *Tetrahedron*, **1992**, *48*, 3.

(2) For examples of [2 + 2 + 2] cycloadditions, see: (a) Vollhardt, K. P. C. *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 539−556. (b) Brown, S.; Clarkson, S.; Grigg, R.; Sridharan, V. *Tetrahedron Lett.* **1993**, *34*, 157−160. (c) Trost, B. M.; Tanoury, G. J. *J. Am. Chem. Soc.* **1987**, *109*, 4753−4755. (d) Hoberg, H.; Oster, B. W. *Synthesis*, **1982**, 324−325. (e) Grigg, R.; Scott, R.; Stevenson, P. *J. Chem. Soc., Perkin Trans 1* **1988**, 1357−1364.

(3) For examples of heteroatom [3 + 3] cycloadditions, see: (a) Mori, M.; Sugiyama, T.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *J. Org. Chem.* **1992**, *57*, 7, 2285−2294. (b) Bambal, R. B.; Kemmitt, R. D. W. *J. Organomet. Chem.* **1989**, *362*, C18−C20. (c) Pearson, W. H.; Fang, W.; Kampf, J. W. *J. Org. Chem.* **1994**, *59*, 2682−2684. (d) Bonini, B. F.; Maccagnani, G.; Mazzanti, G.; Zwanenburg, B. *J. Chem. Soc., Chem. Commun.* **1985**, 237−238. (e) Tominaga, Y.; Ueda, H.; Ogata, K.; Kohra, S. *J. Heterocycl. Chem.* **1992**, *29*, 209−214.

(4) For examples of [3 + 3] annulations, see: (a) Ward, D. E.; Gai, Y.; Kaller, B. F. *J. Org. Chem.* **1995**, *60*, 7830. (b) Seebach, D.; Missbach, M.; Calderari, G.; Eberle, M. *J. Am. Chem. Soc.* **1990**, *112*, 7625−7638. (c) Meyer, W. L.; Brannon, M. J.; Merritt, A.; Seebach, D. *Tetrahedron Lett.* **1986**, *27*, 1449−1452. (d) Chan, T. H.; Kang, G. J. *Terahedron Lett.* **1983**, *24*, 3051−3054. (e) Lu, Xiyan, Huang, Y. *Tetrahedron Lett.* **1986**, *27*, 1615−1616. (f) Sands, R. D. *J. Org. Chem.* **1983**, *48*, 3362−3363. Anzeveno, P. B.; Matthews, D. P. Charlotte, L. B.; Barbuch, R. J. *Tetrahedron Lett.* **1984**, *49*, 3134−3138. Chan, T.-H.; Brownbridge, P. *J. Am. Chem. Soc.* **1980**, *102*, 3534−3538. Molander, G. A.; Shubert, D. C. *J. Am. Chem. Soc.* **1987**, *109*, 576−578.

(5) Alternatively, [6 + 1], [5 + 2], and [4 + 3] cycloadditions lead to 7-membered rings. For examples and lead references, see: (I) [6 + 1]: Ye, T.; McKervey, M. A. *Chem. Rev. (Washington, D.C.)* **1994**, *94*, 1091. (II) [5 + 2]: (a) Sánchez, I. H.; Yáñez, R.; Enríquez, R.; Joseph-Nathan, P. *J. Org. Chem.* **1981**, *46*, 2818. (b) Sammes, P. G. *Gazz. Chim. Ital.* **1986**, *116*, 109. (c) Wender, P. A.; Lee. H. Y.; Wilhelm, R. S.; Williams, P. D. *J. Am. Chem. Soc.* **1989**, *111*, 8954. (d) Padwa, A.; Hornbuckel, S. F.; Fryxell, G. E.; Stull, P. D. *J. Org. Chem.* **1992**, *57*, 5747. (e) Wender, P. A.; Siggel, L.; Nuss, J. M. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Paquette, L. A., Eds.; Pergamon Press: New York, 1991; Vol 5, p 645−673. (f) Wender, P. A.; Takahashi, H.; Witulski, B. *J. Am. Chem. Soc.* **1995**, *117*, 4720. (III) [4 + 3]: (a) Norori, R. *Acc. Chem. Res* **1979**, *12*, 61. (b) Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 1. (c) Mann, J. *Tetrahedron* **1986**, *421*, 4611. (d) Harmata, M.; Elahmad, S. *Tetrahedron Lett.* **1993**, *34*, 789. (e) Giguere, R. J.; Tassely, S. M.; Rose, M. I.; Krishnamurthy, V. V. *Tetrahedron Lett.* **1990**, *31*, 4577. (f) Trost, B. M.; Schneider, S. *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 213. Binger, P.; Büch, H. M. *Top. Curr. Chem.* **1987**, *135*, 77. (g) Davies, H. M. L. *Tetrahedron* **1993**, *49*, 5203. (h) Hosomi, A.; Tominaga, Y. in Comprehensive Organic Synthesis; Trost, B. M., Fleming, I. Paquette, L. A., Eds.; Pergamon Press: New York, 1991; Vol 5, pp 593−615. (i) Boger, D. L.; Brotherton, C. E. *J. Org. Chem.* **1985**, *50*, 3425.

(6) (a) Corey, E. J., Cheng, X.-M. *The Logic of Chemical Synthesis*, Wiley: New York, 1989. (b) Ho, T.-L. *Carbocyclic Construction in Terpenes Synthesis*, VCH: New York, 1988. (c) Heathcock, C. H.; Graham, S. L.; Pirrung, M. C. In *The Total Synthesis of Natural Products*: ApSimon, J. W., Ed.; Wiley: New York, 1983; Vol 5, p 323−333.

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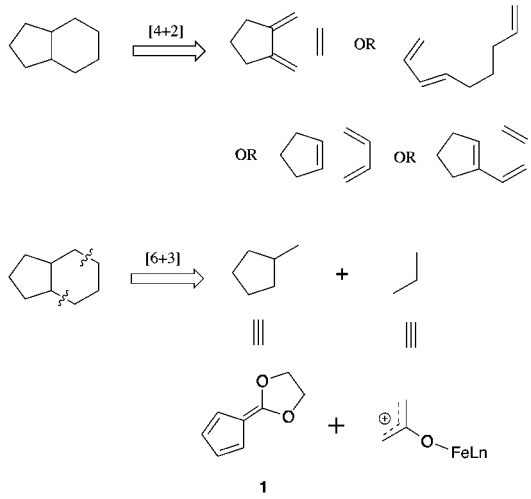
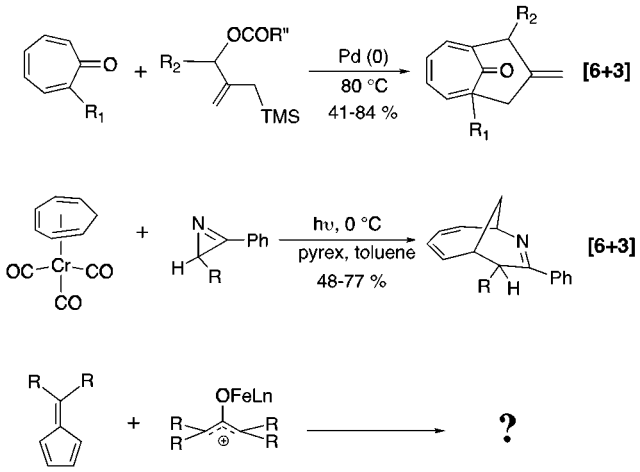
Scheme 2



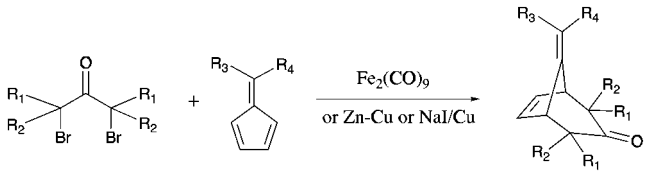
1

Scheme 3



The first practical carbon−carbon bond forming [6 + 3] reaction was reported by Trost and co-workers in 1987 (Scheme 3).[9] They demonstrated that in the presence of Pd(0), tropones react with silyl carboxylates to yield the corresponding [6 + 3] carbocycles exclusively.[10] This methodology was successfully applied to the synthesis of bicyclo[4.3.1]alkenones.[11] The second example of a [6 + 3] cycloaddition is the metal-mediated cycloaddition reaction of azirine and cycloheptatriene reported in 1995.[12]

Scheme 4



R_1 = CH_3, i-Pr, Ph R_3 = Me, *t*-Bu, Ph, OAc 30-85 %

R_2 = H, CH_3, i-Pr R_4 = H, Me, Ph

These researchers found that irradiation of azirines in the presence of Cr(III)-coordinated cycloheptatriene provides heterobicyclo[4.3.1]alkenones.

Encouraged by the success of the [6+3] cycloadditions of tropones and cycloheptatriene, we became intrigued with the possibility that fulvene may also undergo [6 + 3] cyclizations (Scheme 3). Given the fact that fulvenes have six π electron, like tropones and cycloheptatriene, the question was *whether fulvene would react with 2-oxyallyl cation to give the [6 + 3] adduct?*[13]

Unfortunately, 6-mono- or 6,6-dialkylfulvenes react with 2-oxyallyl cations[14] to afford [4 + 3] cycloadducts exclusively.[15]

While studying the mechanism of [4 + 3] cycloadditions, Kanematsu and co-workers found that the reaction of 2-oxyallyl-Fe(II) cation with 6-(dimethylamino)fulvene afforded a novel fulvene adduct **2** in low yield (17%, Scheme 5).[16] The striking difference in the chemoselectivity of this cycloaddition may be attributed to an increase in the electron density of the 6-(dimethylamino)-fulvene system. The formation of the product can be rationalized via a stepwise mechanism: initial addition of the C-1 of fulvene to the electrophilic cation followed by cyclization, 1,5-H shift, and elimination to give the adduct **2**. However, no further studies regarding this unusual chemoselective reaction have been reported. On the basis of this result, we suspected that the yield in this two-step cycloaddition could be enhanced by further increasing the electron density on the fulvene. As a result, we prepared and reacted fulvene ketene acetal **1**[17] with a series of 2-oxyallyl-Fe(II) cations.

Results and Discussion

Although fulvene **1** has been known for quite some time, it has never been used in organic synthesis until our study.[18] The synthesis of **1** starts with nickelocene

(7) (a) de Jong, J. C.; Jansen, J. F.; Feringa, B. L. *Tetrahedron Lett.* **1990**, *31*, 3047−3050. (b) Hoffmann, H.; Bolte, M.; Berger, B.; Hoppe, D. *Tetrahedron Lett.* **1993**, *34*, 6537−6540. Ando, K. Akadegawa, N. Takayama, H. *J. Chem. Soc. Chem. Commun.* **1991**, 1765−1767. (c) Roush, W. R.; Ko, A. I., Gillis, H. *J. Org. Chem.* **1980**. *45*, 4264. (d) Roush, W. R.; Gillis, H. R. *J. Org. Chem.* **1980**, *45*, 5, 4267. (e) For other synthesis of functionalized indans involving cyclopentanone−cyclohexanone annulations or anionic Oxy-Cope rearrangements of bicyclo[2.2.1] systems, see: (i) Dahnke, K. R.; Paquette, L. A. *J. Org. Chem.* **1994**, *59*, 885−889. (i) Suri, S. C. *Tetrahedron Lett.* **1996**, *37*, 2335. (ii) Greene, A. E.; Coelho, F.; Barreiro, E. J.; Costa, P. R. *J. Org. Chem.* **1986**, *51*, 4250. (iii) Greene, A. E.; Serra, A.; Coelho, F.; Barreiro, E. J.; Costa, P. R. *J. Org. Chem.* **1987**, *52*, 1169. (iv) Piers, E.; Yeung, B. W. A. *J. Org. Chem.* **1984**, *49*, 4567. (v) Piers, E.; Yeung, B. W. A. *Can. J. Chem.* **1986**, *64*, 2475. (vi) Jung, M. E.; Hudspeth, J. P. *J. Am. Chem. Soc.*, **1978**, *100*, 4309.

(8) For a preliminary account of some of this work, see: Hong, B.-C.; Sun, S.-S. *Tetrahedron Lett.* **1996**, *37*, 659.

(9) Trost, B. M.; Seoane, P. R. *J. Am. Chem. Soc.* **1987**, *109*, 615.

(10) Prior to this work, several cycloadditions of diphenylnitrileimine or nitrile oxide with tropone were reported. However, these reactions were low yielding and the [6 + 3] adducts were the minor products. See: (a) Bonadeo, M.; De Micheli, C.; Gandolfi, R. *J. Chem. Soc., Perkin Trans. 1* **1977**, 939. (b) Houk, K. N.; Watts, C. R. *Tetrahedron Lett.* **1970**, 4025. (c) De Micheli, C.; Gandolfi, R.; Grünanger, P.; *Tetrahedron*, **1974**, *30*, 3765. (d) Mukherjee, D.; Watts, C. R.; Houk, K. N. *J. Org. Chem.* **1978**, *43*, 817.

(11) A relevant but different chemoselective reaction of tropones was reported earlier. The reaction of the 2-oxyallyl cation (generated from 2,4- dibromoketone and $Fe_2(CO)_9$) with tropones afford the corresponding [8 + 3] cycloaddition adduct. See: Ishizu, T.; Mori, M.; Kanematsu, K. *J. Org. Chem.* **1981**, *46*, 526.

(12) Chaffee, K.; Morcos, H.; Sheridan, J. B. *Tetrahedron Lett.* **1995**, *36*, 1577.

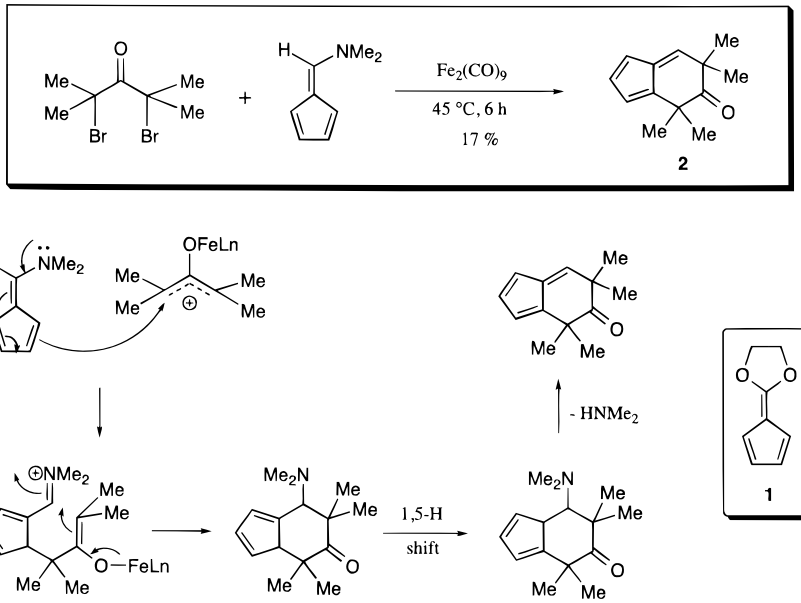
(13) The 1,3-dipolar cycloaddition of diazomethane, azirine, nitrile oxide, or nitropyridyl betaine with fulvenes is known; however, these reactions give low yields. See: (a) Houk, K. N.; Luskus, L. J. *Tetrahedron Lett.* **1970**, 4029. (b) Padwa, A.; Nobs, F. *Tetrahedron Lett.* **1978**, 93. (c) Dennis, N.; Ibrahim, B.; Katritzky, A. R. *J. Chem. Soc., Perkin Trans 1* **1976**, 2307. (d) Caramella, P.; Frattini, P.; Grünanger, P. *Tetrahedron Lett.* **1971**, 3817.

(14) For reviews on the synthetic utility of oxyallyl cations, see: (a) Mann, J. *Tetrahedron* **1986**, *42*, 4611. (b) Hoffmann, H. M. R. *Angew. Chem., Int. Engl.* **1973**, *12*, 819.

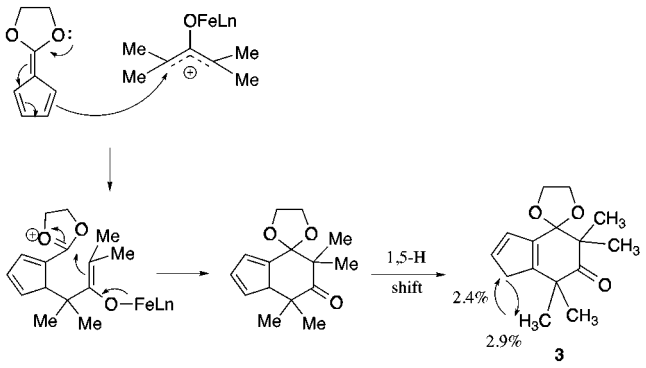
(15) A variety of [4 + 3] cycloadditions have been employed in the total synthesis of natural products. See: (a) Kashman, Y.; Rudi, A. *Tetrahedron* **1974**, *30*, 109. (b) Rawson, D. I.; Carpenter, B. K.; Hoffmann, H. R. *J. Am. Chem. Soc.* **1979**, *101*, 1786. (c) Takaya, H.; Makino, S.; Hayakawa, Y.; Noyori, R. *J. Am. Chem. Soc.* **1978**, *100*, 1765. (d) Noyori, R.; Hayakawa, Y.; Takaya, H.; Murai, S.; Kobayashi, R.; Sonoda, N. *J. Am. Chem. Soc.* **1978**, *100*, 1759.

(16) Ishizu, T.; Mori, M.; Kanematsu, K. *J. Org. Chem.* **1981**, *46*, 526−531.

Scheme 5. Reaction of 6-Aminofulvene



Scheme 6



and CF_3I[19] and involves tedious procedures which have probably contributed to the limited body of research on this intriguing compound.[20] To overcome this problem, we developed a simple and cost-effective method for the synthesis of 2-cyclopentadienyliden-1,3-dioxolane (**1**).[21]

The reactivity of the fulvene ketene acetal **1** was explored next. After stirring a solution of **1**, $Fe_2(CO)_9$, and 2,4-dibromo ketone in dry benzene at 25 °C for 2 h, the [6 + 3] cycloadduct **3** was isolated in 86% yield (Scheme 6). The mechanism for the formation of **3** is unknown. The formation of **3** can be rationalized by a two-step process analogous to that outlined in Scheme 6: initial addition of the 2-oxyallyl cation across C-1 and C-6 of the fulvene ring, followed by a 1,5-H shift to afford the cycloadduct.

The structure of **3** was assigned on the basis of its ^{1}H NMR, ^{13}C NMR, COSY, DEPT, HETCOR, and mass spectral data. The results of the NOE studies carried out on this adduct were consistent with the structure depicted in Scheme 6. Irradiation of the C-1 protons gave rise to a 2.9% enhancement of the neighboring methyl protons, while irradiation of the methyl protons caused a 2.4% enhancement of the C-1 signal.

Other 2-oxyallyl cations react with fulvene ketene acetal **1** with similar chemoselectivity (Table 1). This reaction is relatively insensitive to the steric bulk of the cation substituents, as shown by the high yields of the adducts in entries 1−3. The reaction of disubstituted 2-oxyallyl cations and fulvene **1** results first in the formation of inden isomers **6**, **8**, **10**, and**12**, followed by isomerization to the corresponding indenes **7**, **9**, **11**, and **13**, respectively. This isomerization can also be induced by refluxing intermediates **6**, **8**, **10**, and **12** in benzene or after prolonged storage of these compounds at ambient temperature.[22] On the other hand, as we expected, decreasing the electron density of the fulvene disfavors the [6 + 3] pathway. For example, in the entry 8, reaction of 6-methoxyfulvene with 2-oxyallyl cation yielded the [4 + 3] adduct exclusively.

Products **7**, **9**, and **11** were isolated as single stereoisomers. The relative cis stereochemistries of these adducts can be assigned by examination of the ^{1}H NMR of the corresponding alcohol, which was obtained upon reduction of the ketones **6** (LAH, THF, −78 °C; 91%).[23] The coupling constants between the carbinol methine proton and the two adjacent methine protons are $J = 2.4$, 2.4 Hz. These values are consistent with equatorial−axial coupling constants for the cis isomers. The [6 + 3] cycloaddition of 2-oxyallyl cations and fulvene ketene acetal is categorized as a [6π + 2π] process and must proceed in a stepwise manner as outlined in Scheme 6. Although high stereoselectivity during a cycloaddition

(17) The dipole moment of fulvenes can be enhanced by increasing the electron density on C-6. For previous preparations of this fulvene, see: (a) Olsson, T.; Wennerström, O. *Acta Chem. Scand. B*, **1978**, *32*, 293. (b) Bönzli, P.; Otter, A.; Neuenschwander, M.; Huber, H.; Kellerhals, H. P. *Helv. Chem. Acta* **1986**, *69*, 1052.

(18) For a preliminary account of the [6 + 4] cycloadditions of fulvene **1** and α-pyrones, see: Hong, B.-C.; Sun, S.-S. *Chem. Commun.* **1996**, 937.

(19) Both reagents are expensive: 1 mol of bis(cyclopentadienyl)-nickel costs $1700 and 1 mol of CF_3I gas cost $713 (Aldrich Chemical Co., 1996− 1997).

(20) No detailed procedure was reported for the preparation of fulvene **1** in ref 17b. However, the reaction is quite complicated and gives a lower overall yield than our methodology (vide infra).

(21) The fulvene **1** was prepared on a 100 g scale by reaction of cyclopentadiene with KOH and 2-chloroethyl chloroformate as described: Hong, B.-C.; Hong, J.-S., *Synth. Comm.* **1997**, in press.

(22) Due to 1,5-H shifts, these compounds tend to isomerize further to unseparable mixtures of double bond isomers. Direct hydrolysis of these adducts, however, affords stable indenes (vide infra).

(23)

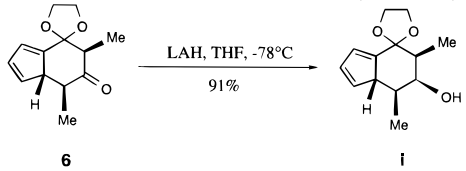
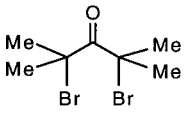
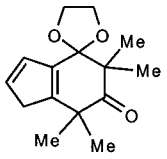
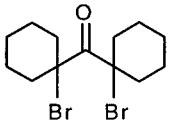
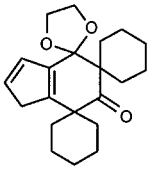
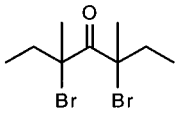
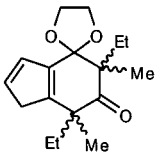
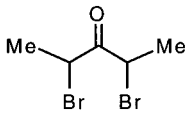
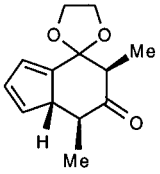
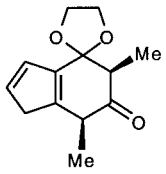
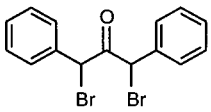
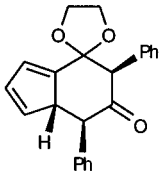
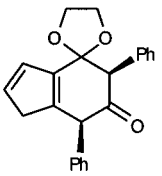
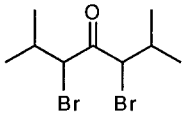
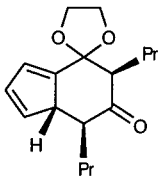
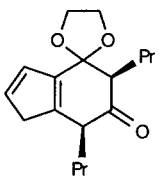
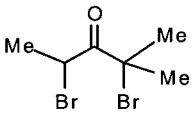
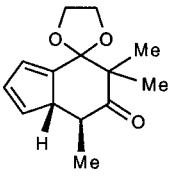
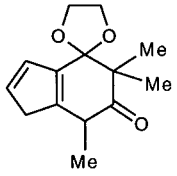
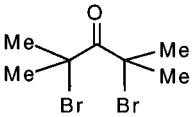
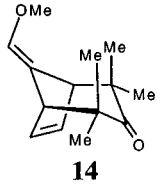


Table 1. Cycloaddition of Fulvenes and Dibromo Ketones

Entry	Dibromoketone	Product	Yield (%)[a]
1		 **3**	86
2		 **4**	66
3		 **5**	70
4		 **6**  **7**	66[b]
5		 **8**  **9**	79[b]
6		 **10**  **11**	59[b]
7		 **12**  **13**	72[b]
8[c]		 **14**	56[d]

[a] Isolated yield. [b] **6**, **8**, **10**, or **12** were obtained first, these products isomerized to **7**, **9**, **11,** or **13** after a few hours at ambient temperature [c] Dibromoketone was reacted with 6-methoxyfulvene. [d] No [6 + 3] product was observed.

may hint at a concerted pathway, some stepwise reactions are known which show high stereoselectivity.[24] In principle, the degree of stereoselectivity in a stepwise process depends on the relative rates of ring closure in the intermediate and the energy barrier for internal rotation which would result in inversion of stereochemistry. The stereoselectivity of the present [6 + 3] reaction is presumably due to formation of intermediate **A,** which results from a cisoid approach of the oxyallyl cation (W

(24) Hayakawa, Y.; Yokoyama, K.; Noyori, R. *J. Am. Chem. Soc.* **1978**, *100*, 0, 1971.

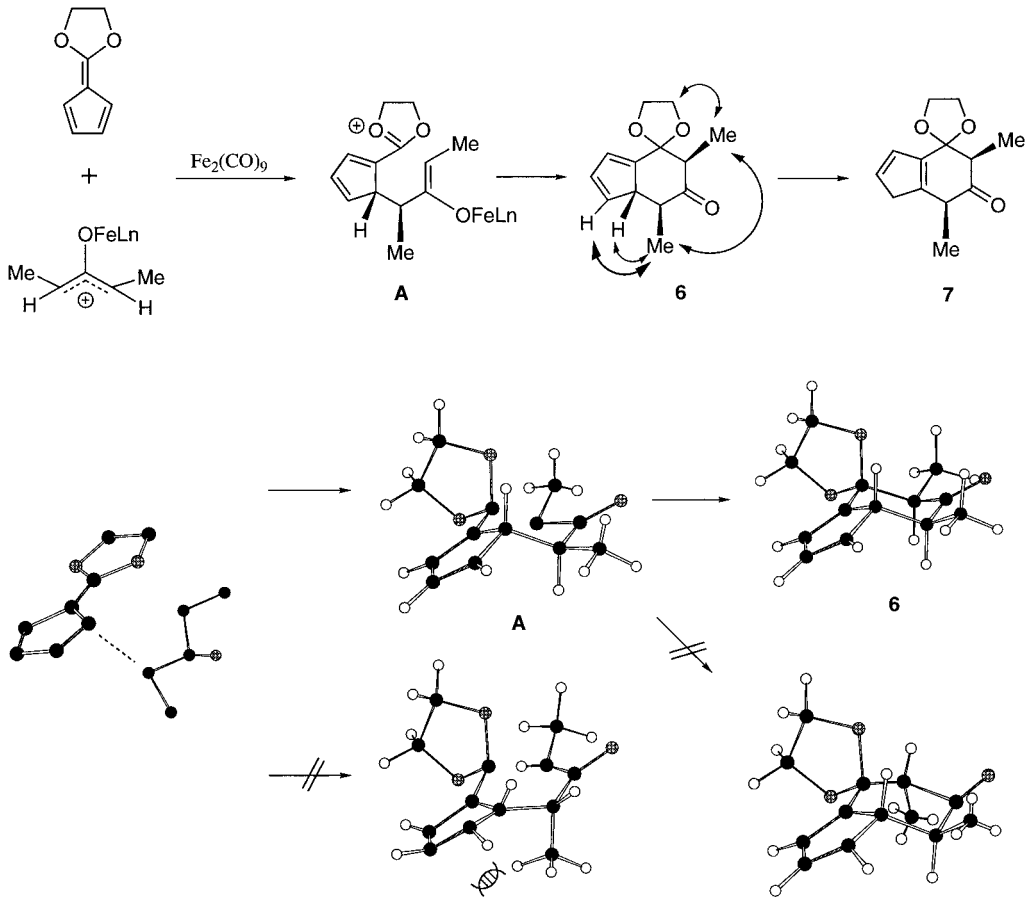


Figure 1.

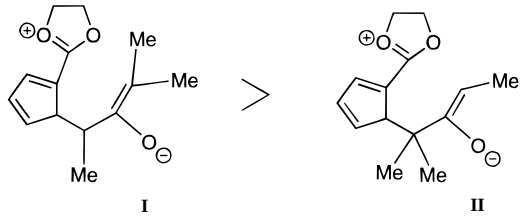


Figure 2.

conformation) toward the fulvene (Figure 1).[25] The ring closure then proceeds through a chairlike 6-membered ring transition state leading to the cis orientation of the two substituents. The other possible boat-form 6-membered ring transition state would lead to the twisted 6-membered ring with trans substituents. The stereochemistry of **6** was assigned by a NOESY experiment unambiguously, as depicted in Figure 1.

On the other hand, when the four substituents of the oxyallyl cation are sterically similar, the ring closure can occur from the three possible stereoisomers of the oxyallyl cation (*EE*, *ZZ*, and *EZ*). Stereoselective reaction of each isomer according to Figure 1 would initially lead to the four possible diastereomeric products and ultimately to the two diasteromers of **5** (Table 1, entry 3). The observed regioselectivity in entry 7 of Table 1 can be interpreted in terms of the stability of the zwitterionic intermediate of **I** vs **II** or a late transition state (Figure 2).[26]

Direct hydrolysis of these ketal adducts gave different products (Scheme 7). The tetrasubstituted adducts **3**, **4**, and **5** afforded the corresponding diketones **15**, **16**, and **17**, respectively. However, under the same conditions, the disubstituted ketals **7**, **9**, and **11** gave the indenes **18**, **19**, and **20**, respectively, This can be rationalized via an acid-catalyzed ring opening of the ketal followed by the enolization of ketone to give the aromatic ring. The results of the NOESY studies carried out on these indenes were consistent with the structures depicted in Scheme 7. Unlike the ketals, these hydrolyzed products were stable at ambient temperature for several months and no isomerization was observed.

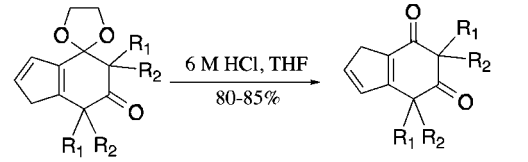
To further extend the scope of this reaction to other fulvene ketene acetals, the thioacetal **21**[27] was employed and reacted with 2-oxyallyl cation (Scheme 8). This led to the formation of both the [4 + 3] adduct **22** and [6 + 3] adduct **23** in a 2.2:1 ratio. As expected, the lower electron density of fulvene **21**, caused by the hyperconjugation of the empty d orbital of sulfur and olefin π electrons, helped favor the [4 + 3] over the [6 + 3] pathway.

The possibility of a tandem [6 + 3]−[4 + 3] cycloaddition of fulvenes prompted us to consider an approach to the synthesis of the stemodane class of compounds depicted in Scheme 9 (e.g. aphidicolin). Such a strategy could allow the rapid construction of a subset of these tricyclic systems starting from a simple fulvene skeleton. Unfortunately, the reaction of adduct **3** and 2-oxyallyl cation afforded the alkylation product isomers **24** and **25** in a ratio of 2.4 to 1 (76% yield). These products may arise from the electrophilic addition of 2-oxyallyl cation to **3** followed by loss of a proton to give an overall electrophilic substitution.[28] Reaction of the fulvene **1** with 2 equiv of 2-oxyallyl cation also afforded similar

(25) Some of the protons in Figure 1 have been omitted for clarity.
(26) For a similar mechanic study of the regioselectivity in the [3 + 2] cycloaddition of 2-oxyallyl cation and alkenes, see: Noyori, R.; Shimizu, F.; Fukuta, K.; Takaya, H.; Hayakawa, Y. *J. Am. Chem. Soc.* **1977**, *99*, 5196.

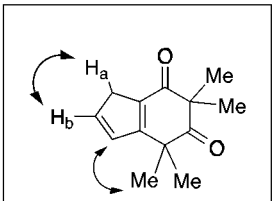
(27) Gompper, R.; Kutter, E. *Chem. Ber.* **1965**, *98*, 2825.

Scheme 7

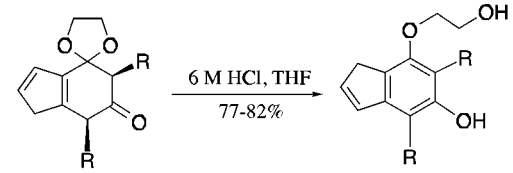


3 $R_1 = R_2 = CH_3$
4 $R_1 = R_2 = -(CH_2)_5-$
5 $R_1 = CH_3, R_2 = C_2H_5$

15 $R_1 = R_2 = CH_3$
16 $R_1 = R_2 = -(CH_2)_5-$
17 $R_1 = CH_3, R_2 = C_2H_5$

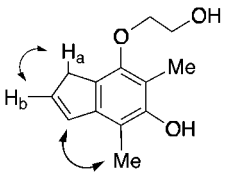


NOE connectivity of 15



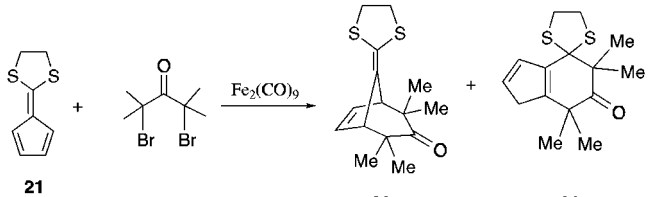
7 R = CH_3
9 R = C_6H_5
11 R = *i*-Pr

18 R = CH_3
19 R = C_6H_5
20 R = *i*-Pr



NOE connectivity of 18

Scheme 8



21 **22** **23**

2.2 : 1

yields of adduct **24** and **25**. Alternatively, treatment of the adducts **23** with 2-oxyallyl cations gave the alkylation product **26** and **27** in a 1:1 ratio and 65% yield. Direct hydrolysis of **24** (or **25**) and **26** (or **27**) afforded the corresponding ketone **28** in quantitative yield. The results of the NOESY studies carried out on **24** and **28** were consistent with the structures depicted in Scheme 9.

Conclusion

In summary, the [6 + 3] cycloaddition of 2-oxyallyl cations to electron rich fulvene ketene acetal provides an efficient route to the indan skeleton. This method establishes the experimental framework for a conceptually new approach to indan systems. Extensions of this work to the total synthesis of xestovanin as well as the possible tandem [6 + 3]−[4 + 3] cycloaddition are currently under active investigation.

Experimental Section

General Procedure. All solvents were reagent grade. Anhydrous tetrahydrofuran was distilled from sodium. All chemicals were purchased from Aldrich Chemical Co. Reactions were normally carried out under argon atmosphere in flame-dried glassware. Merck silica gel 60 (partical size 0.04−0.063 mm) was employed for flash chromatography. HPLC was equipped with the ultraviolet and refractive index detectors. The sample was analyzed and/or separated on a μ-Porasil column (25 cm × 1.0 cm) by elution with gradient of ethyl acetate and hexane. The flow rate of the indicated elution solvent is maintained at 5 mL/min, and the retention time of a compound is recorded. Melting points are uncorrected. ^{1}H NMR, NOE, COSY, and NOESY spectra were obtained in $CDCl_3$ unless otherwise noted at 400 or 200 MHz. ^{13}C NMR spectra, HETCOR, COLOC, and DEPT experiments were obtained at 100 Hz or 50 MHz.

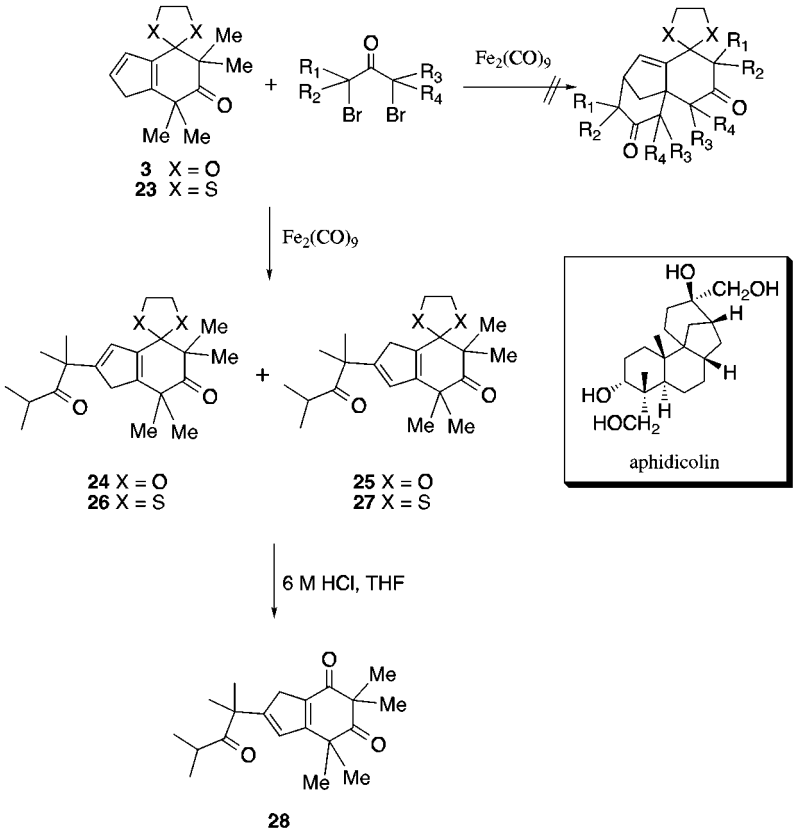
Representative Procedure for the [6 + 3] Cycloaddition: 1′,7′-Dihydro-5′,5′,7′,7′-tetramethylspiro[1,3-dioxolane-2,4′-[4*H*]inden]-6′(5′*H*)-one (3). To a mixture of 2-cyclopenta-2,4-dienylidene-1,3-dioxolane (**1**) (370 mg, 2.7 mmol) and $Fe_2(CO)_9$ (1.49 g, 4.1 mmol) in dry benzene (80 mL) was added 2,4-dibromo-2,4-dimethylpentan-3-one (1.12 g, 4.1 mmol). The suspension was vigorously stirred for 2 h at 25 °C and filtered. The filtrate was concentrated in vacuo and the residue was purified by flash column chromatography with 3% EtOAc−hexane (R_f = 0.68 in 10% EtOAc−hexane) to give indan **3** as a colorless oil (580 mg, 86% yield). IR (neat) 2969, 1712, 1476, 1381, 1212, 1150, 1047, 984, 952 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.12 (s, 6 H), 1.27 (s, 6 H), 3.03 (br s, 2 H), 3.96−4.08 (m, 4 H), 6.33 (d, J = 5.4 Hz, 1 H), 6.46 (d, J = 5.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 20.22 (2 CH_3), 27.90 (2 CH_3), 39.65 (CH_2), 44.95 (C), 53.77 (C), 66.13 (2 CH_2), 108.65 (C), 129.98 (CH), 131.42 (CH), 139.23 (C), 147.21 (C), 216.61 (C); MS (*m*/*z*, relative intensity) 248 (M^+, 38), 233 (7), 178 (100), 163 (65), 149 (57), 119 (29), 107 (49), 105 (29), 91 (68); exact mass calculated for $C_{15}H_{20}O_3$ (M^+) 248.1412, found 248.1421.

Trispiro[biscyclohexane-1,5″:1′,7″(6″*H*)-[5*H*]indene-4″-(1″*H*),2‴-[1,3]dioxolan]-6″-one (4). As described for the preparation of indan **3**, the crude product after purification by flash chromatography with 1.5% EtOAc−hexane (R_f = 0.49 in 5% EtOAc−hexane) gave indan **4** as a colorless oil (80 mg, 66% yield). IR (neat) 2925, 1701, 1449, 1183, 1047, 997 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.90−2.20 (m, 20 H), 3.18 (br s, 2 H), 3.85−4.21 (m, 4 H), 6.32 (d, J = 5.4 Hz, 1 H), 6.43 (d, J = 5.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 22.5 (2 C), 22.9 (2 C), 25.4, 25.9, 28.4 (2 C), 35.7 (2 C), 41.4, 49.2, 58.0, 66.1 (2 C), 109.3, 130.1, 131.5, 140.1, 147.9, 215.5; MS (*m*/*z*, relative intensity) 328 (M^+, 23), 252 (11), 236 (13), 234 (33), 219 (16), 218 (100), 217 (16), 154 (17), 149 (13); exact mass calculated for $C_{21}H_{28}O_3$ (M^+) 328.2038, found 328.2039

5′,7′-Diethyl-1′,7′-dihydro-5′,7′-dimethylspiro[1,3-dioxolane-2,4′-[4*H*]inden]-6′(5′H)-one (5). As described for the preparation of indan **3**, the crude product after purification by flash chromatography with 1.5% EtOAc−hexane (R_f = 0.80 in 10% EtOAc−hexane) gave indan **5** isomers as a colorless oil (72 mg, 70% yield). IR (neat) 2974, 2882, 1704, 1456, 1206, 1090, 1056, 1011 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) (revealed the presence of two isomers in ca. 1:1 ratio): δ 0.58 (t, J = 7.4 Hz, 3 H), 0.73 (t, J = 7.4 Hz, 3 H), 0.75 (t, J = 7.4 Hz, 3 H), 0.81 (t, J = 7.4 Hz, 3 H), 1.07 (s, 3 H), 1.13 (s, 3 H), 1.25 (s, 3 H), 1.26 (s, 3 H), 1.20−2.20 (m, 8 H), 2.96 (ddd, J = 1.6, 1.6, 23.4 Hz, 2 H), 3.08 (ddd, J = 1.6, 1.6, 23.4 Hz, 2 H), 3.95−

(28) For a detailed mechanic study on this type of electrophilic addition of 2-oxyallyl cation to dienes, see: Hoffmann, H. M. R. *Angew. Chem.* **1984**, *23*, 1−88.

Scheme 9



4.20 (m, 8 H), 6.38 (ddd, J = 5.5, 2.8, 1.4 Hz, 2 H), 6.50 (ddd, J = 5.5, 2.4, 1.2 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) (revealed the presence of two isomers in ca. 1:1 ratio): δ 8.7, 8.9, 9.8, 10.0, 12.6, 14.9, 25.7, 27.3, 27.1, 28.0, 32.7, 34.3, 39.7, 39.8, 49.8 (2 C), 57.2, 58.9, 65.5, 65.6, 66.3, 66.5, 109.1, 109.3, 130.1, 130.2, 131.5, 131.6, 140.9, 141.0, 145.3, 146.4, 215.1 (2 C); MS (*m*/*z*, relative intensity) 276 (M^+, 15), 226 (75), 208 (100), 192 (57), 149 (33), 128 (32); exact mass calculated for $C_{17}H_{24}O_3$ (M^+) 276.1725, found 276.1724.

7′,7a′-Dihydro-5′,7′-dimethylspiro[1,3-dioxolane-2,4′-[4*H*]inden]-6′(5′*H*)-one (6). As described for the preparation of indan **3**, the crude product after purification by flash chromatography with 2.5% EtOAc−hexane (R_f = 0.70 in 10% EtOAc−hexane) gave indan **6** as a colorless oil (54 mg, 66% yield). IR (neat) 2977, 2884, 1715, 1453, 1232, 1207, 1069, 941 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.08 (d, J = 6.6 Hz, 3 H), 1.28 (d, J = 6.4 Hz, 3 H), 1.93 (dq, j = 10.5, 6.4 Hz, 1 H), 2.78 (d, J = 10.5 Hz, 1 H), 2.82 (q, J = 6.4 Hz, 1 H), 3.68−4.25 (m, 4 H), 6.30−6.60 (m, 3 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 6.6 (CH_3), 14.2 (CH_3), 47.3 (CH), 52.6 (CH), 55.1 (CH), 64.7 (CH_2), 66.2 (CH_2), 107.7 (C), 125.3 (CH), 131.8 (CH), 137.1 (CH), 148.9 (C), 208.7 (C); MS (*m*/*z*, relative intensity) 220 (M^+, 39), 164 (100), 163 (47), 149 (89), 119 (20), 115 (16), 105 (57), 100 (17); exact mass calculated for $C_{13}H_{16}O_3$ (M^+) 220.1099, found 220.1102

1′,7′-Dihydro-5′,7′-dimethylspiro[1,3-dioxolane-2,4′-[4*H*]-inden]-6′(5′*H*)-one (7). A solution of indan **6** (52 mg, 0.24 mmol) in benzene (15 mL) was heated to 40 °C for 8 h. The solution was concentrated in vacuo and the residue was purified by flash column chromatography with 9% EtOAc−hexane (R_f = 0.26 in 10% EtOAc−hexane) to give indan **7** as a colorless oil (50 mg, 95% yield). mp 89−91 °C; IR (neat) 2979, 2882, 1720, 1452, 1372, 1332, 1192, 1080, 1048, 936 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.12 (d, J = 6.7 Hz, 3 H), 1.28 (d, J = 7.2 Hz, 3 H), 3.02 (br s, 2 H), 3.15 (q, J = 6.7 Hz, 1 H), 3.28 (q, J = 7.2 Hz, 1 H), 3.92−4.27 (m, 4 H),6.36 (d, J = 5.4 Hz, 1 H), 6.47 (d, J = 5.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 7.2 (CH_3), 14.4 (CH_3), 41.6 (CH_2), 44.1 (CH), 53.0 (CH), 66.4 (CH_2), 66.7 (CH_2), 108.1 (C), 129.5 (CH), 132.6 (CH), 134.5 (C), 143.9 (C), 208.3 (C); MS (*m*/*z*, relative intensity) 220 (M^+, 39), 206 (32), 191 (26), 180 (71), 164 (81), 163 (53), 152 (30), 149 (70), 147 (35), 135 (35); exact mass calculated for $C_{13}H_{16}O_3$ (M^+) 220.1099, found 220.1098.

7′,7a′-Dihydro-5′,7′-diphenylspiro[1,3-dioxolane-2,4′-[4*H*]inden]-6′(5′*H*)-one (8) and 1′,7′-Dihydro-5′,7′-diphenylspiro[1,3-dioxolane-2,4′-[4*H*]inden]-6′(5′*H*)-one (9). As described for the preparation of indan **3**, the crude product after purification by flash column chromatography with 3.5% EtOAc−hexane (R_f = 0.50 in 10% EtOAc−hexane) gave indan **8** and **9** as a colorless oil (85 mg, 79% yield). The mixture was further separated by HPLC with 7% EtOAc−hexane to give indans **8** (t_R = 10.6 min) and **9** (t_R = 13.5 min) as colorless oils. However, **8** was isomerized to **9** and other complex isomers during the chromatography purification and spectrum acquisition. A solution of the indan (**8** and **9)** mixtures (85 mg, 0.25 mmol) in benzene (15 mL) was then heated to 40 °C for 8 h. The solution was concentrated in vacuo and the residue was purified by HPLC with 7% EtOAc−hexane to give **9** (t_R = 13.5 min) as a colorless oil (78 mg, 72% yield from fulvene **1**). IR (neat) 3030, 2926, 2857, 1732, 1602, 1494, 1372, 990, 942, 744, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.97 (d, J = 23.5 Hz, 1 H), 3.14 (d, J = 23.5 Hz, 1 H), 3.24−3.31 (m, 1 H), 3.45−3.54 (m, 1 H), 3.86−4.06 (m, 2 H), 4.37 (s. 1 H), 4.62 (s, 1 H), 6.50 (d, J = 5.4 Hz, 1 H), 6.61 (d, J = 5.4 Hz, 1 H), 7.19−7.43 (m, 10 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 42.1, 56.8, 61.1, 66.2, 66.4, 107.8, 127.4, 127.6 (2 C), 128.1 (2 C), 128.3, 128.9 (2 C), 129.2, 131.9 (2 C), 132.2, 133.9, 137.7, 141.1, 143.7, 203.1; MS (*m*/*z*, relative intensity) 344 (M^+, 55), 258 (32); 191 (26), 180 (71), 164 (81), 163 (53), 152 (30), 149 (70), 147 (35), 135 (35); exact mass calculated for $C_{23}H_{20}O_3$ (M^+) 344.1412, found 344.1412.

7′,7a′-Dihydro-5′,7′-bis(1-methylethyl)spiro[1,3-dioxolane-2,4′-[4*H*]inden]-6′(5′*H*)-one (10) and 1′,7′-Dihydro-5′,7′-bis(1-methylethyl)spiro[1,3-dioxolane-2,4′-[4*H*]inden]-6′(5′*H*)-one (11). As described for the preparation of indan **3**, the crude product after purification by flash column chromatography with 1.5% EtOAc−hexane (R_f = 0.82 in 10% EtOAc−hexane) gave indans **10** and **11** as a colorless oil (60 mg, 59% yield). The mixture was further separated by HPLC with 2% EtOAc−hexane to give indans **10** (t_R = 10.5 min) and **11** (t_R = 11.8 min) as colorless oils. However, **10** was isomerized to **11** and other complex isomers during the

chromatography purification and spectrum acquisition. A solution of the indan (**10** and **11)** mixtures (85 mg, 0.25 mmol) in benzene (15 mL) was then heated to 40 °C for 8 h. The solution was concentrated in vacuo and the residue was purified by HPLC with 2% EtOAc−hexane to give **11** (t_R = 11.8 min) as a colorless oil (52 mg, 51% yield from fulvene **1**). IR (neat) 2962, 2876, 1714, 1470, 1372, 1285, 1163, 950, 730 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.81 (d, J = 6.8 Hz, 3 H), 0.85 (d, J = 6.8 Hz, 3 H), 1.06 (d, J = 6.8 Hz, 3 H), 1.09 (d, J = 6.8 Hz, 3 H), 2.08−2.20 (m, 1 H), 3.59−3.73 (m, 1 H), 3.05 (d, J = 24.0 Hz, 1 H), 3.13 (br s, 2 H), 3.24 (d, J = 24.0 Hz, 1 H), 3.78−3.89 (m, 1 H), 4.05−4.23 (m, 2 H), 4.25−4.36 (m, 1 H), 6.38 (d, J = 5.4 Hz, 1 H), 6.49 (d, J = 5.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.9, 19.8, 20.3, 21.6, 28.3, 34.6, 41.2, 43.5, 54.8, 65.1, 67.7, 108.5, 129.3, 132.9, 140.6, 143.2, 200.3; MS (*m*/*z*, relative intensity) 276 (M^+, 10), 275 (41), 265 (21), 248 (60), 219 (25), 206 (68), 178 (77), 163 (27), 149 (40), 129 (67), 113 (100); exact mass calculated for $C_{17}H_{24}O_3$ (M^+) 276.1725, found 276.1730.

7′,7a′-dihydro-5′,5′,7′-trimethylspiro[1,3-dioxolane-2,4′-[4*H*]inden]-6′(5′*H*)-one (12). As described for the preparation of indan **3**, the crude product after purification by flash column chromatography with 5% EtOAc−hexane (R_f = 0.57 in 10% EtOAc−hexane) gave indan **12** as a colorless oil (56 mg, 72% yield). IR (neat) 2995, 1724, 1470, 1388, 1120, 1033, 978 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.05 (s, 3 H), 1.10 (s, 3 H), 1.26 (d, J = 6.4 Hz, 3 H), 2.17 (dq, J = 12.7, 6.4 Hz, 1 H), 2.76 (dd, J = 12.7, 1.2 Hz, 1 H), 3.77−3.82 (m, 1 H), 3.88−3.97 (m, 2 H), 4.03−4.12 (m, 1 H), 6.39−6.53 (m, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.5 (CH_3), 16.1 (CH_3), 23.8 (CH_3), 42.8 (CH), 53.2 (C), 54.7 (CH), 64.7 (CH_2), 66.1 (CH_2), 109.7 (C), 126.7 (CH), 131.7 (CH), 137.2 (CH), 147.6 (C), 212.4 (C); MS (*m*/*z*, relative intensity) 234 (M^+, 30), 206 (22), 191 (32), 180 (65), 164 (81), 163 (53), 152 (30), 149 (70), 147 (35), 135 (35); exact mass calculated for $C_{14}H_{18}O_3$ (M^+) 234.1256; found 234.1260.

1′,7′-dihydro-5′,5′,7′-trimethylspiro[1,3-dioxolane-2,4′-[4*H*]inden]-6′(5′*H*)-one (13). Starting from **12** as described for the preparation of indan **7**, the crude product after purification by flash column chromatography with 8% EtOAc−hexane (R_f = 0.38 in 10% EtOAc−hexane) gave indan **13** as a colorless oil (27 mg, 90% yield). IR (neat) 2995, 1724, 1470, 1388, 1120, 1033, 978 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.11 (s, 3 H), 1.22 (s, 3 H), 1.30 (d, J = 7.2 Hz, 3 H), 2.97 (d, J = 20.8 Hz, 1 H), 3.07 (d, J = 20.8 Hz, 1 H), 3.32 (q, J = 6.4 Hz, 1 H), 3.94−4.09 (m, 4 H), 6.36 (d, J = 5.6 Hz, 1 H), 6.46 (d, J = 5.6 Hz, 1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.6 (CH_3), 17.6 (CH_3), 21.8 (CH_3), 41.4 (CH), 41.7 (CH_2), 54.0 (C), 66.1 (CH_2), 66.7 (CH_2), 109.6 (C), 130.1 (CH), 132.2 (CH), 140.7 (C), 142.8 (C), 212.1 (C); MS (*m*/*z*, relative intensity) 234 (M^+, 39), 206 (32), 191 (26), 180 (71), 164 (81), 163 (53), 152 (30), 149 (70), 147 (35), 135 (35); exact mass calculated for $C_{14}H_{18}O_3$ (M^+) 234.1256, found 234.1257.

8-(Methoxymethylene)-2,2,4,4-tetramethylbicyclo[3.2.1]-oct-6-en-3-one (**14**)**.** To a mixture of cyclopenta-2,4-dienylidenemethoxymethane (**4**) (50 mg, 0.46 mmol) and $Fe_2(CO)_9$ (0.26 g, 0.71 mmol) in dry benzene (15 mL) was added 2,4-dibromo-2,4-dimethylpentan-3-one (191 mg, 0.70 mmol). The suspension was vigorously stirred for 2 h at 25 °C and filtered. The filtrate was concentrated in vacuo and the residue was purified by flash column chromatography with 1.2% EtOAc−CH_2Cl_2 (R_f = 0.88 in 10% EtOAc−CH_2Cl_2) to give the dione as colorless oil (57 mg, 56%). IR (neat) 2972, 2930, 1698, 1470, 1118, cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.02 (s, 3 H), 1.03 (s, 3 H), 1.15 (s, 3 H), 1.16 (s, 3 H), 2.57 (d, J = 2.6 Hz, 1 H), 3.17 (d, J = 2.6 Hz, 1 H), 3.59 (s, 3 H), 5.89 (s 1 H), 6.19 (dd, J = 6.0, 2.6 Hz, 1 H), 6.26 (dd, J = 6.0, 2.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 24.1, 24.2, 27.8, 28.0, 49.6, 52.0, 52.5, 52.8, 59.6, 124.1, 136.1, 136.5 (2 C), 221.0; MS (*m*/*z*, relative intensity) 220 (M^+, 30) 219 (21), 149 (28), 113 (15), 111 (17); exact mass calculated for $C_{14}H_{20}O_2$ (M^+) 220.1463, found 220.1462.

4,4,6,6-Tetramethyl[1*H*]indene-5,7(4*H*,6*H*)-dione (**15**). To a solution of indan **3** (49 mg, 0.2 mmol) in THF (5 mL) was added 6 M HCl (0.5 mL). The solution was stirred for 10 h at 25 °C and diluted with EtOAc (100 mL). The solution was washed with saturate aqueous $NaHCO_3$ solution and brine (20 mL) and concentrated in vacuo. The residue was purified by flash column chromatography with 6% EtOAc−hexane (R_f = 0.65 in 20% EtOAc−hexane) to give indan **15** as a white solid (34 mg, 85% yield). mp 46−48 °C; IR (neat) 2978, 1712, 1660, 1516, 1470, 1408 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.34 (s, 6 H), 1041 (s, 6 H), 3.39 (br s, 2 H), 6.68 (d, J = 5.4 Hz, 1 H), 6.91 (d, J = 5.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 24.3 (2 CH_3), 26.6 (2 CH_3), 39.6 (CH_2), 45.3 (C), 56.4 (C), 131.3 (CH), 134.8 (C), 143.2 (CH), 165.7 (C), 195.1 (C), 215.2 (C); MS (*m*/*z*, relative intensity) 204 (M^+, 34), 161 (11), 135 (12), 134 (100), 119 (56), 106 (14), 105 (14); exact mass calculated for $C_{13}H_{16}O_2$ (M^+) 204.1150, found 204.1147.

Dispiro[biscyclohexane-1,5″:1′,7″-[1*H*]indene]-5″,7″-(4″*H*,6″*H*)-dione (16). Starting from **4** as described for the preparation of **15**, the crude product after purification by flash column chromatography with 3% EtOAc−hexane (R_f = 0.57 in 10% EtOAc−hexane) gave indan **16** as a colorless oil (37 mg, 80% yield). IR (neat) 2928, 1704, 1652, 1514, 1450, 1400, 1366 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.10−2.15 (m, 20 H), 3.33 (br s, 2 H), 6.72 (d, J = 5.4 Hz, 1 H), 6.82 (d, J = 5.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 22.2 (2 CH_2), 22.4 (2 CH_2), 25.3 (CH_2), 25.4 (CH_2), 32.4 (2 CH_2), 34.4 (2 CH_2), 39.6 (CH_2), 49.4 (C), 62.8 (C), 131.8 (CH), 136.6 (C), 141.9 (CH), 165.3 (C), 195.7 (C), 212.8 (C); MS (*m*/*z*, relative intensity) 284 (M^+, 32), 167 (40); 149 (94), 111 (59), 110 (37); exact mass calculated for $C_{19}H_{24}O_2$ (M^+) 284.1776, found 284.1787.

4,6-Diethyl-4,6-dimethyl[1*H*]indene-5,7(4*H*,6*H*)-dione (**17**). Starting from **5** as described for the preparation of **15**, the crude product after purification by flash column chromatography with 4% EtOAc−hexane (R_f = 0.45 in 10% EtOAc−hexane) gave the **17** epimers. The mixture was further separated by HPLC with 4% EtOAc−hexane to give indan **17a** (t_R = 20.95 min, 16 mg, 44% yield) as a colorless oil and **17b** (t_R = 23.60 min, 14 mg, 40% yield) as a colorless solid. For **17a**: IR (neat) 2970, 1708, 1656, 1516, 1456, 1410, 1370 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.56 (t, J = 7.4 Hz, 3 H), 0.69 (t, J = 7.4 Hz, 3 H), 1.25 (s, 3 H), 1.37 (s, 3 H), 1.48−1.72 (m, 1 H), 1.83 (q, J = 7.4 Hz, 2 H), 2.02−2.24 (m, 1 H), 3.44 (d, J = 4 Hz, 2 H), 6.63 (d, J = 5.2 Hz, 1 H), 6.92 (d, J = 5.2 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 9.7 (CH_3), 10.0 (CH_3), 20.4 (CH_3), 25.3 (CH_3), 32.9 (CH_2), 33.3 (CH_2), 39.5 (CH_2), 50.2 (C), 61.2 (C), 131.3 (CH), 137.7 (C), 143.0 (CH), 164.5 (C), 195.3 (C), 215.7 (C); MS (*m*/*z*, relative intensity) 232 (M^+, 10), 204 (29); 175 (28), 149 (29), 148 (61), 147 (21), 133 (100); exact mass calculated for $C_{15}H_{20}O_2$ (M^+) 232.1463, found 232.1460. For **17b**: mp 66−68 °C; IR (neat) 2968, 1708, 1655, 1516, 1460, 1410, 1370 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.60 (t, J = 7.4 Hz, 3 H), 0.67 (t, J = 7.4 Hz, 3 H), 1.28 (s, 3 H), 1.37 (s, 3 H), 1.51−1.74 (m, 1 H), 1.81−2.12 (m, 2 H), 2.18−2.40 (m, 1 H), 3.45 (br s, 2 H), 6.64 (d, J = 5.2 Hz, 1 H), 6.93 (d, J = 5.2 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 10.0 (CH_3), 10.1 (CH_3), 26.9 (CH_3), 27.6 (CH_3), 29.1 (CH_2), 32.0 (CH_2), 39.6 (CH_2), 50.1 (C), 61.4 (C), 131.2 (CH), 137.8 (C), 143.2 (CH), 164.7 (C), 195.1 (C), 215.6 (C); MS (*m*/*z*, relative intensity) 232 (M^+, 10), 204 (44), 175 (14), 149 (25), 148 (76), 147 (17), 133 (100); exact mass calculated for $C_{15}H_{20}O_2$ (M^+) 232.1463, found 232.1461

7-(2-Hydroxyethoxy)-4,6-dimethylinden-5-ol (**18**). Starting from **7** as described for the preparation of **15**, the crude product after purification by flash column chromatography with 13% EtOAc−CH_2Cl_2 (R_f = 0.30 in 15% EtOAc−CH_2Cl_2) gave inden **18** as a colorless oil (33 mg, 82% yield). mp 99−101 °C; IR (neat) 3100−3650, 2918, 1606, 1548, 1454, 1216, 1124, 1074 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.71 (br s, 1 H), 2.20 (s, 3 H), 2.29 (s, 3 H), 3.39 (br s, 2 H), 3.85−4.00 (m, 2 H), 4.06 (t, J = 4.2 Hz, 2 H), 4.75 (s, 1 H), 6.48 (d, J = 5.4 Hz, 1 H), 6.89 (d, J = 5.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 9.2 (CH_3), 11.9 (CH_3), 37.0 (CH_2), 62.4 (CH_2), 73.3 (CH_2), 111.9 (C), 112.7 (C), 125.6 (C), 130.1 (CH), 133.4 (CH), 143.5 (C), 151.0 (C), 151.8 (C); MS (*m*/*z*, relative intensity) 221 (M^+ + 1, 14), 220 (M^+, 100), 176 (97), 175 (37), 161 (90), 147 (16), 131 (13), 128 (13), 115 (24); exact mass calculated for $C_{13}H_{16}O_3$ (M^+) 220.1099, found 220.1102.

7-(2-Hydroxyethoxy)-4,6-diphenylinden-5-ol (**19**). Starting from **9** as described for the preparation of **15**, the crude product after purification by flash chromatography with 25% EtOAc−CH_2Cl_2 (R_f = 0.39 in 30% EtOAc−CH_2Cl_2), and HPLC with 23% EtOAc−hexane (t_R = 13.65) gave inden **19** as a

colorless oil (37 mg, 77% yield). mp 174−176 °C; IR (neat) 3600−3150, 3056, 2934, 1604, 1404, 1360, 1292, 1170, 1052, 912, 750, 730, 702 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.54 (br s, 1 H), 3.42−3.66 (m, 4 H), 3.91 (t, J = 4.4 Hz, 2 H), 5.12 (s, 1 H), 6.56 (d, J = 5.4 Hz, 1 H), 6.72 (d, J = 5.4 Hz, 1 H), 7.28−7.66 (m, 10 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 37.3 (CH_2), 61.9 (CH_2), 73.7 (CH_2), 118.2 (C), 118.6 (C), 125.8 (C), 127.5 (CH), 128.0 (CH), 128.7 (2 CH), 128.9 (2 CH), 130.3 (2 CH), 130.9 (2 CH), 131.1 (CH), 133.7 (C), 135.2 (CH), 135.5 (C), 145.5 (C), 149.5 (C), 151.3 (C); MS (*m*/*z*, relative intensity) 345 (M^+ + 1, 25), 344 (M^+, 100), 301 (13), 300 (53), 299 (15), 252 (14), 165 (14); exact mass calculated for $C_{23}H_{20}O_3$ (M^+) 344.1412, found 344.1415.

7-(2-Hydroxyethoxy)-4,6-bis(methylethyl)inden-5-ol (20). Starting from **11** as described for the preparation of **15**, the crude product after purification by flash column chromatography with 20% EtOAc−CH_2Cl_2 (R_f = 0.23 in 20% EtOAc−CH_2Cl_2) gave inden **20** as a colorless solid (34 mg, 79% yield). mp 98−100 °C; IR (neat) 3050−3650, 2958, 1724, 1598, 1546, 1462, 1444, 1259, 1106, 1056 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.38 (d, J = 7.4 Hz, 12 H), 2.23 (br s, 1 H), 3.35 (br s, 2 H), 3.29−3.47 (m, 1 H), 3.47−3.65 (m, 1 H), 3.87−4.00 (m, 2 H), 4.05 (t, J = 4.5 Hz, 2 H), 4.79 (s, 1 H), 6.48 (d, J = 5.4 Hz, 1 H), 7.02 (d, J = 5.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 21.4 (2 CH_3), 22.2 (2 CH_3), 24.9 (CH), 27.5 (CH), 36.6 (CH_2), 62.4 (CH_2), 73.8 (CH_2),123.5 (C), 123.7 (C), 126.9 (C), 130.8 (CH), 133.4 (CH), 142.4 (C), 150.4 (C), 152.2 (C); MS (*m*/*z*, relative intensity) 277 (M^+ + 1, 22), 276 (M^+, 100), 261 (64), 233 (22), 231 (25), 217 (47), 201 (19), 189 (20), 149 (24), 131 (19); exact mass calculated for $C_{17}H_{24}O_3$ (M^+) 276.1725, found 276.1725.

8-(1,3-Dithiolan-2-ylidene)-2,2,4,4-tetramethylbicyclo-[3.2.1]oct-6-en-3-one (22) and 1′,7′-dihydro-5′,5′,7′,7′-tetramethylspiro[1,3-dithiolane-2,4′-[4*H*]inden]-6′(5′H)-one (23). Starting from fulvene **21** as described for the preparation of **3**, the crude product after purification by flash column chromatography with 1% EtOAc−hexane (R_f = 0.68 in 10% EtOAc−hexane) gave the **22** and **23** epimers. The mixture was further separated by HPLC with 0.8% EtOAc−hexane to give indans **22** (t_R = 18.54 min, 38 mg, 22% yield) and **23** (t_R = 20.33 min, 83 mg, 50% yield) as colorless solids. For **22**: mp 92−94 °C; IR (neat) 2966, 2922, 1700, 1648, 1468, 1378, 1032, 740 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.05 (s, 6 H), 1.22 (s, 6 H), 2.94 (br s, 2 H), 3.24−3.49 (m, 4 H), 6.23 (br s, 2 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 24.3 (2 CH_3), 27.6 (2 CH_3), 37.6 (2 CH_2), 54.0 (2 C), 56.5 (2 CH), 133.4 (2 C), 135.9 (2 CH), 220.0 (C); MS (*m*/*z*, relative intensity) 280 (M^+, 42), 211 (23), 210 (100), 209 (47), 195 (40), 168 (16), 135 (18); exact mass calculated for $C_{15}H_{20}OS_2$ (M^+) 280.0956, found 280.0956. For **23**: mp 90−92 °C; IR (neat) 2980, 1709, 1376, 1048 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.29 (s, 6 H), 1.32 (s, 6 H), 3.08 (br s, 2 H), 3.20−3.48 (m, 4 H), 6.35 (d, J = 5.5 Hz, 1 H), 6.69 (d, J = 5.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 22.6 (2 CH_3), 28.3 (2 CH_3), 40.1 (CH_2), 41.7 (2 CH_2), 44.9 (C), 55.6 (C), 72.6 (C), 131.4 (CH), 132.6 (CH), 140.8 (C), 143.0 (C), 216.2 (C); MS (*m*/*z*, relative intensity) 280 (M^+, 100), 210 (58), 209 (25), 182 (50), 145 (39); exact mass calculated for $C_{15}H_{20}OS_2$ (M^+) 280.0956, found 280.0956.

1′,7′-Dihydro-5′,5′,7′,7′-tetramethyl-2-(1″,1″,3″-trimethyl-2-oxobutyl)spiro[1,3-dioxolane-2,4′-[4*H*]inden]-6′-(5′*H*)-one (24) and 3′7′-dihydro-5′,5′,7′,7′-tetramethyl-2-(1″,1″,3″-trimethyl-2″-oxobutyl)spiro[1,3-dioxolane-2,4′-[4*H*]inden]-6′-(5′*H*)-one (25). To a mixture of **3** (108 mg, 0.44 mmol) and $Fe_2(CO)_9$ (488 mg, 1.35 mmol) in dry benzene (15 mL) was added 2,4-dibromo-2,4-dimethylpentan-3-one (366 mg, 1.35 mmol). The suspension was vigorously stirred for 2 h at 25 °C and filtered. The filtrate was concentrated in vacuo and the residue was purified by flash column chromatography with 6% EtOAc−CH_2Cl_2 (R_f = 0.42 in 10% EtOAc−CH_2Cl_2) to give **24** and **25**. The mixture was further separated by HPLC with 6% EtOAc−hexane to give indans **24** (t_R = 20.30 min, 84 mg, 53% yield) and **25** (t_R = 23.54 min, 36 mg, 23%yield) as colorless oils. For **24**: IR (neat) 2976, 1704, 1470, 1378, 1214, 1146, 1042 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.86 (s, 3 H), 0.90 (s, 3 H), 1.09 (s, 6 H), 1.22 (s, 6 H), 1.37 (s, 6 H), 2.87 (s, 2 H), 2.97−3.17 (m, 1 H), 3.85−4.12 (m, 4 H), 6.32 (s 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 20.3 (2 CH_3), 20.4 (2 CH_3), 24.1 (2 CH_3), 27.8 (2 CH_3), 34.1 (CH), 39.6 (CH_2), 45.0 (C), 51.1 (C), 54.0 (C), 66.3 (2 CH_2), 108.7 (C), 126.0 (CH), 139.1 (C), 146.7 (C), 149.4 (C), 216.3 (C), 216.9 (C); MS (*m*/*z*, relative intensity) 360 (M^+, 10) 290 (21), 289 (100), 219 (59), 175 (16), 147 (63); exact mass calculated for $C_{22}H_{32}O_4$ (M^+) 360.2300, found 360.2318. For **25**: IR (neat) 2977, 1709, 1470, 1380, 1145, 1046 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.88 (s, 3 H), 0.92 (s, 3 H), 1.10 (s, 6 H), 1.25 (s, 6 H), 1.38 (s, 6 H), 2.985−3.12 (m, 1 H), 2.99 (s, 2 H), 3.86−4.08 (m, 4 H), 6.31 (s 1 H); MS (*m*/*z*, relative intensity) 360 (M^+, 6) 290 (26), 289 (100), 220 (17), 219 (88), 175 (29), 147 (36); exact mass calculated for $C_{22}H_{32}O_4$ (M^+) 360.2300, found 360.2312.″

1′,7′-Dihydro-5′,5′,7′,7′-tetramethyl-2-(1″,1″,3″-trimethyl-2″-oxobutyl)spiro[1,3-dithiolane-2,4′-[4*H*]inden]-6′(5′H)-one (26) and 3′,7′-dihydro-5′,5′,7′,7′-tetramethyl-2-(1″,1″,3″-trimethyl-2-oxobutyl)spiro[1,3-dithiolane-2,4′-[4*H*]inden]-6′(5′*H*)-one (27). Starting from **23** as described for the preparation of **22**, the crude product after purification by flash column chromatography with 3% EtOAc−hexane (R_f = 0.47 in 10% EtOAc−hexane) gave **26** and **27**. The mixture was further separated by HPLC with 3% EtOAc−hexane to give indans **26** (t_R = 17.12 min, 22.5 mg, 29% yield) and **27** (t_R = 20.34 min, 28 mg, 36% yield) as colorless oils. For **26**: IR (neat) 2972, 1709, 1470, 1376, 1028, 992 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.89 (s, 3 H), 0.92 (s, 3 H), 1.25 (s, 6 H), 1.29 (s, 6 H), 1.37 (s, 6 H), 2.91−3.14 (m, 1 H), 3.21 (br s, 2 H), 3.17−3.43 (m, 4 H), 6.23 (s, 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 20.5 (2 CH_3), 22.6 (2 CH_3), 23.9 (2 CH_3), 26.8 (2 CH_3), 34.1 (CH), 41.9 (3 CH_2), 43.8 (C), 51.2 (C), 56.3 (C), 74.2 (C), 126.5 (CH), 139.7 (C), 143.9 (C), 150.9 (C), 215.9 (C), 216.7 (C); MS (*m*/*z*, relative intensity) 392 (M^+, 17), 322 (28), 321 (98), 293 (27), 199 (30), 147 (100); exact mass calculated for $C_{22}H_{32}O_2S_2$ (M^+) 392.1844, found 392.1846. For **27**: IR (neat) 2970, 1709, 1470, 1378, 1028, 992 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.87 (s, 3 H), 0.90 (s, 3 H), 1.22 (s, 6 H), 1.28 (s, 6 H), 1.38 (s, 6 H), 2.89 (br s, 2 H), 2.96−3.19 (m, 1 H), 3.21−3.45 (m, 4 H), 6.54 (s, 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 20.4 (2 CH_3), 22.5 (2 CH_3), 23.8 (2 CH_3), 28.1 (2 CH_3), 34.0 (CH), 39.8 (CH_2), 41.7 (2 CH_2), 44.8 (C), 51.2 (C), 55.8 (C), 72.6 (C), 128.8 (CH), 140.6 (C), 142.3 (C), 148.6 (C), 215.8 (C), 217.1 (C); MS (*m*/*z*, relative intensity) 392 (M^+, 12), 323 (13), 322 (26), 321 (100), 293 (37), 201 (47), 199 (20), 147 (23); exact mass calculated for $C_{22}H_{32}O_2S_2$ (M^+) 392.1844, found 392.1845.

4,4,6,6-Tetramethyl-2-(1,1,3-trimethyl-2-oxobutyl)[1*H*]-indene-5,7(4*H*,6*H*)-dione (28). Starting from **24** or **26** as described for the preparation of **15**, the crude product after purification by flash column chromatography with 10% EtOAc−CH_2Cl_2 (R_f = 0.56 in 20% EtOAc−CH_2Cl_2) gave the dione as a colorless oil (36 mg, 78%). IR (neat) 2974, 1712, 1703, 1652, 1538, 1470, 1180, 1044, 996 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.94 (s, 3 H), 0.97 (s, 3 H), 1.33 (s, 6 H), 1.40 (s, 6 H), 1.43 (s, 6 H), 2.83−3.08 (m, 1 H), 3.34 (br s, 2 H), 6.47 (s 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 20.5 (2 CH_3), 24.3 (2 CH_3), 24.5 (2 CH_3), 26.5 (2 CH_3), 35.1 (CH), 39.5 (CH_2), 45.2 (C), 51.7 (C), 56.4 (C), 127.1 (CH), 133.8 (C), 162.6 (C), 165.6 (C), 194.7 (C), 214.9 (C), 215.2 (C); MS (*m*/*z*, relative intensity) 316 (M^+, 6) 247 (22), 246 (100), 245 (17), 231 (18), 175 (12), 163 (12), 147 (31); exact mass calculated for $C_{20}H_{28}O_3$ (M^+) 316.2038, found 316.2039.

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Supporting Information Available: Copies of the spectra for compounds **3**−**20**, **22**−**24**, **26**−**28**, and **i** (86 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.

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