35. The Decomposition of *cis*-Fused Cyclopenteno-1,2,4-trioxanes Induced by Ferrous Salts and Some Oxophilic Reagents

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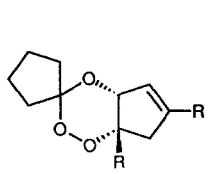
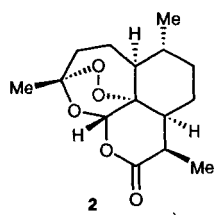
Two *cis*-fused cyclopenteno-1,2,4-trioxanes, **1a** and **1b**, were subjected to Zn in AcOH or $FeCl_2 \cdot 4H_2O$ in MeCN. In the first case, the main course was deoxygenation to give cyclopentanone (**18**) and the 1,4-diphenyl- or 1,4-bis(4-fluorophenyl)cyclopent-3-ene-1,2-diol **10** (*Scheme 5*). In the second case, isomerization chiefly occurred resulting in the formation of a dimer **9** of the respective 3,5-diaryl-5-hydroxycyclopent-2-enyl 5-hydroxypentanoates **8** (*Scheme 3*).

The *cis*-fused cyclopenteno-1,2,4-trioxanes **1a** and **1b**, like artemisinin (**2**), display potent antimalarial activity [1]. It was suggested that they share a common mode of action against *Plasmodium* at the intraerythrocytic stage [2]. Heme, which is produced by



1a R = Ph
b R = 4-F-C_6H_4



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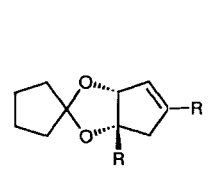
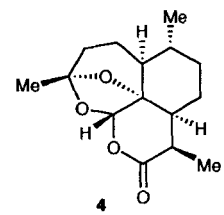


3a R = Ph
b R = 4-F-C_6H_4



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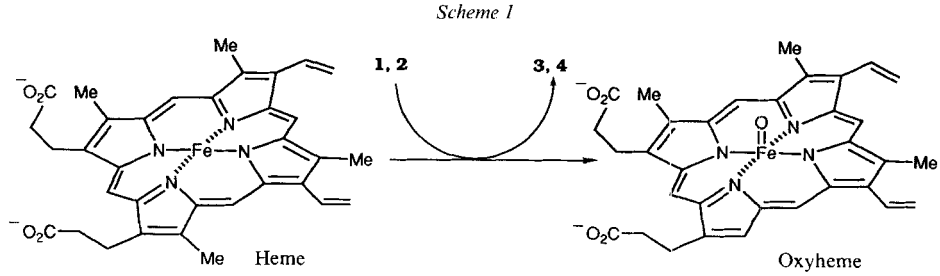
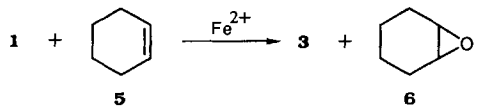
proteolysis of ingested hemoglobin, is toxic to the parasite, but is normally removed by enzyme-catalyzed oxidative polymerization to hemozoin [3]. We speculated that **1** and **2** could interrupt this detoxification process by transferring an O-atom to heme to create an iron-oxene intermediate or oxyheme which subsequently disables the parasite (*Scheme 1*). The complement of this process would be the formation of the 1,3-dioxolanes **3** and **4**, respectively. In an attempt to evaluate 1,2,4-trioxanes as O-atom transfer agents, we

Scheme 1



Scheme 2



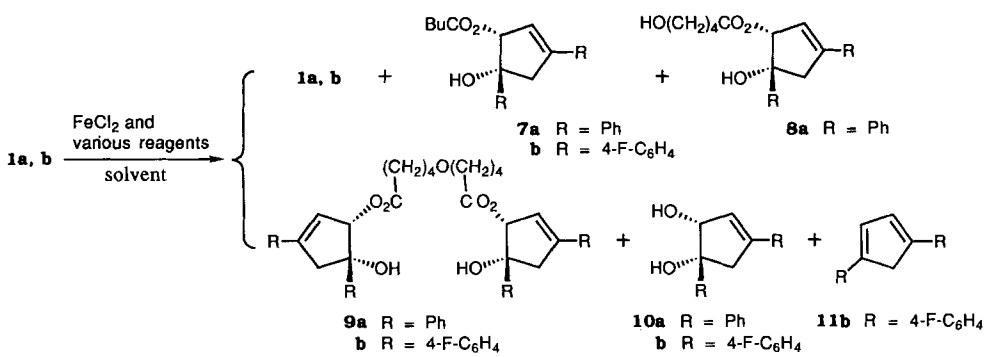
decided to treat **1a** and **1b** with $FeCl_2$ under a variety of conditions in the presence of cyclohexene (**5**), expecting that cyclohexene epoxide (**6**) and **3** might be produced if an iron-oxene species were implicated (*Scheme 2*).

Results. – It is immediately seen from the first set of experiments that transfer of an O-atom did not occur. No cyclohexene epoxide (**6**) or 1,3-dioxolane (**3a**) was detected. To be absolutely sure, an independently prepared sample of **3a** and commercially available **6** were compared with the product composition. Despite their structural similarity, **3a** can be clearly distinguished from **1a** by its characteristic NMR spectrum. The action of $FeCl_2$ on **1a** gave only products arising from the opening of the trioxane and cyclopentane rings (*Table 1*, *Scheme 3*). In all cases (*Entries 9* and *10* excepted), just two esters were formed.

Table 1. *Reaction of Ferrous Chloride with* cis-*Fused Cyclopenteno-1,2,4-trioxane* **1a** *to Give Cyclopentene Products* **7a–10a**

Entry	Ferrous salt (equiv.)	Solvent	Temp. [°C]	Reaction time	Product composition				
					1a	**7a**	**8a**	**9a**	**10a**
1	$FeCl_2$ (0.001)	MeCN	22	45 min	74	3	–	7	–
2	$FeCl_2$ (0.20)	MeCN	22	2 h 20 min	28	–	–	20	–
3	$FeCl_2 \cdot 4H_2O$ (0.05)	MeCN	22	40 min	28	14	–	31	–
4	$FeCl_2 \cdot 4H_2O$ (0.19)	MeCN	–40	5 h	49	2	–	14	–
5	$FeCl_2 \cdot 4H_2O$ (0.20)	MeCN	–10	1 h 30 min	29	2	–	34	–
6	$FeCl_2 \cdot 4H_2O$ (0.20)	MeCN	22	2 h	22	2	–	38	–
7	$FeCl_2 \cdot 4H_2O$ (0.35)	MeCN	22	2 h	–	2	–	66	–
8	$FeCl_2 \cdot 4H_2O$ (0.35)	AcOH	22	1 h	–	1	–	31	–
9	$FeCl_2 \cdot 4H_2O$ (0.20)	THF	–78	1 h 30 min	69	–	8	–	–
10	$FeCl_2 \cdot 4H_2O$ (0.15)	THF	–78	24 h	80	–	–	6	–
11	Zn (10.0)	THF/AcOH/H_2O	22	3 h	–	6	–	–	82

Scheme 3[1])



[1]) All products are racemic mixtures, but for the sake of clarity only one enantiomer is shown in the schemes.

Oxybis(pentanoate) **9a** was obtained in varying amounts as the major product, but always accompanied by pentanoate **7a** as the minor product in consistently low yields[1]). Anhydrous $FeCl_2$ in MeCN as solvent, regardless of its concentration, brought about inefficient conversion of **1a** to **9a** (*Entries 1* and *2*). The use of the tetrahydrate improved the yield of **9a** even at low concentration (*Entry 3*). Increasing the concentration and the temperature was more effective. The starting trioxane was progressively converted to completion giving **9a** in an optimum yield of 66% (*Entries 4–7*). The balance of product in all these reactions was uncharacterized polymeric material. By changing the solvent to AcOH, the yield of **9a** was reduced although the starting trioxane was entirely consumed (*Entry 8*). When tetrahydrofuran (THF) was employed as solvent at low temperature, the origin of dimeric product **9a** was revealed. At a short reaction time, a single product was isolated, the 5-hydroxypentanoate **8a** in low yield (*Entry 9*). By allowing the reaction to run for 24 h, **9a** was obtained instead in equally low yield (*Entry 10*). In a separate experiment, a solution of **8a** in $CDCl_3$ was allowed to stand for 3 days at −30°, during which time the ^{1}H-NMR spectrum changed completely to that of **9a**.

By way of comparison, the action of Zn powder in a mixture of aqueous AcOH and THF resulted in the reduction of **1a** to diol **10a** in high yield producing some pentanoate **7a** as well (*Entry 11*). The balance of material was cyclopentanone (**18**; see below).

Further experiments were undertaken with fluoro derivative **1b**. No epoxidation of cyclohexene (**5**) as an addendum was detected in the presence of $FeCl_2 \cdot 4H_2O$, and **3b** was not obtained (*cf. Scheme 2*). Typically, **1b** behaved like **1a**; **9b** was the main product accompanied by minor amounts of **7b** (*Scheme 3*). Zn Dust in AcOH gave essentially the same result as with **1a** (*Table 2, Entry 1*). However, on prolonging the reaction time, pentanoate **7b** was no longer observed, probably owing to its hydrolysis *in situ* to the diol

Table 2. *Reaction of Various Reagents with* cis*-Fused Cyclopenteno-1,2,4-trioxane* **1b** *to Give Cyclopentene Products* **7b**–**11b**

Entry	Reagent	Solvent	Temp. [°C]	Reaction time	Product composition				
					1b	**7b**	**9b**	**10b**	**11b**
1	Zn (10 equiv.)	AcOH	22	3.5 h	–	13	–	78	–
2	Zn (10 equiv.)	AcOH	22	7 h	–	–	–	58	–
3	Fe (10 equiv.)	AcOH	22	30 min	–	58	–	–	–
4	WCl_6/BuLi (1.5/3.0 equiv.)	THF	50	40 min	–	3	19	4	70
5	Ph_3P/Et_3N (10/5 equiv.)	$CDCl_3$	70	18 h	100	–	–	–	–
6	thiourea (10 equiv.)	$CDCl_3$/MeOH 1:2	40	16 h	100	–	–	–	–

10b (*Entry 2*). The action of Fe powder was remarkably different from that of Zn and gave exclusively pentanoate **7b** in high yield (*Entry 3*). Low-valent tungsten chloride, previously exploited for reducing epoxides to olefins [4], behaved similarly with **1b**. The chief result was complete deoxygenation to cyclopentadiene **11b** (*Entry 4*) which was easily identified by its spectral similarity to 1,4-diphenylcyclopenta-1,3-diene [5]. At the same time, the usual decomposition products **7b**, **9b**, and **10b** were also obtained in small quantities. In contrast, exposure of **1b** to triphenylphosphine [6] or thiourea [7], which are traditionally used for abstracting an O-atom from peroxides, was entirely without effect (*Entries 5* and *6*).

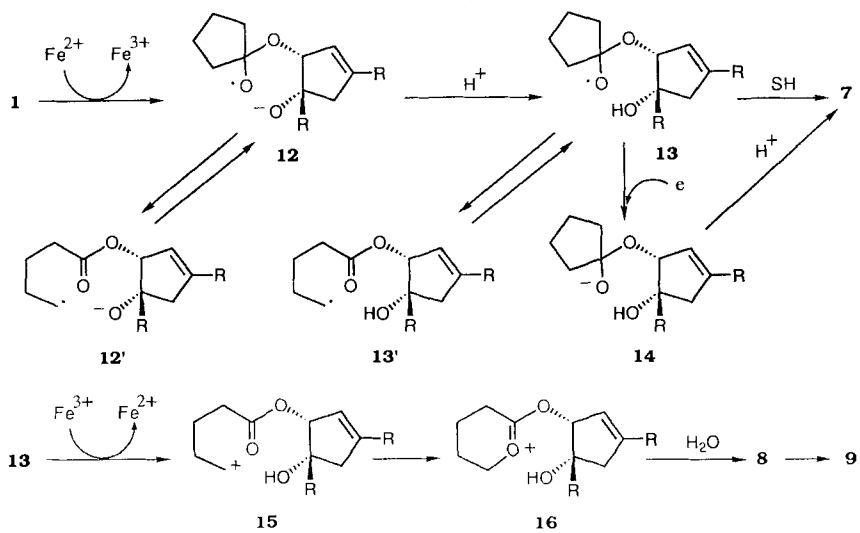
Discussion. – As the formation of the foregoing products is unusual, a brief description of the proof of their structure is appropriate.

The essential features of **7a** were revealed by its ^{1}H-NMR spectrum. The cyclopentene moiety was unambiguously evident from the signals at 3.25 (*AB*), 5.89 (*dt*, RCO_2CH), and 6.22 ppm (*dd*, C=C*H*). The pentanoate moiety was clearly indicated by the multiplicities (*t*, *sext.*, *quint.*, and *t*, resp.) observed at 0.9, 1.36, 1.64, and 2.41 ppm. The attribution of the remaining signals to the OH and Ph groups was straightforward. The presence of the ester group followed from its IR spectrum (1735 cm^{-1}), and the molecular weight was confirmed by the peak at 336 in the MS. The spectral properties of **7b** were similar to those of **7a**.

The structure of **9a** was more difficult to assign since no M^+ appeared at 686 in the MS. Nevertheless, the presence of a peak at 532 ruled out a monomeric cyclopentenol structure and corresponded to the loss of 2 Ph groups in keeping with **9a**. The fact that the ^{1}H- and ^{13}C-NMR spectra displayed 23 ^{1}H- and 18 ^{13}C-resonances, respectively, may be reconciled by the symmetric dimeric ether formula. The attribution of the ^{1}H-signals was confirmed by a ^{1}H,^{13}C correlation. The ester function was characterized by its IR absoption (1735 cm^{-1}). The MS of **9b** also failed to give a M^+ at 759. However, significant peaks were registered at 569, 637, 643, and 659 indicating loss of 2 4-FC_6H_4 radicals, a 4-FC_6H_4 radical plus CO, and $C_4H_8O_3$, and $C_4H_8O_2$ fragments, respectively. Fluoro analogue **9b** gave spectral data comparable to those of **9a**.

The origin of the esters **7** and **9** is best rationalized by rupture of the peroxide bond of **1** as the first step. A single-electron transfer by the Fe^{2+} ion gives radical anion **12** which by protonation affords oxy radical **13** (*Scheme 4*). Subsequent capture of a H-atom from the medium (SH) would account for the formation of pentanoate **7**. This reaction course

Scheme 4[1])



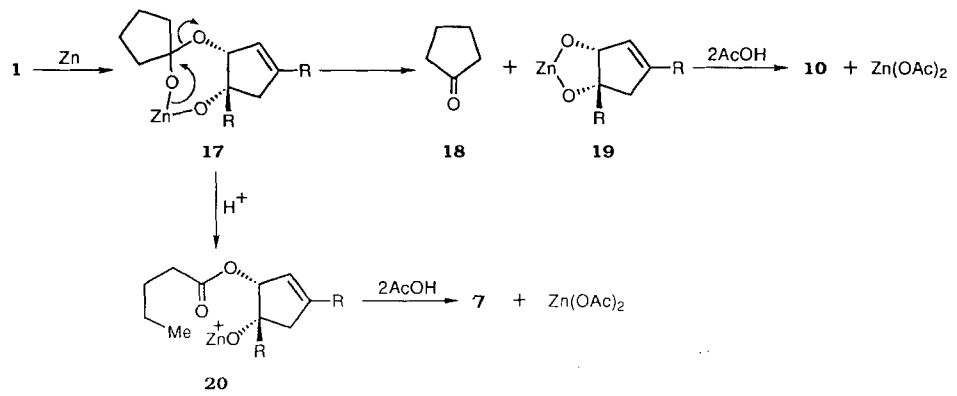
may be regarded as a minor noncatalytic event, since the production of **7** appears to diminish at higher concentrations of Fe^{2+} ion. When dissolving Fe metal is employed (*Entry 3*, *Table 2*), it appears that radical **13** is continually formed and reduced further to anion **14** which immediately undergoes protonation in the acidic medium. Under these strong reducing conditions, the formation of large amounts of **7** is understandable.

When greater amounts of Fe^{2+} ion are present, a second, oxidative step intervenes. Radical **13** returns an electron to the previously generated Fe^{3+} ion thereby producing primary cation **15**, most probably stabilized as bicyclic oxonium species **16**. Annihilation of **16** by a molecule of H_2O gives alcohol **8**. Thereafter, two molecules of **8** or **8** and **16** combine to produce dimeric species **9**.

Thus it is seen that the Fe^{2+} ion, through its redox behavior, catalyzes isomerization as the main reaction pathway; two molecules of **1** give **9** by rearrangement and condensation.

In contrast, the treatment of **1** with dissolving Zn brings about reduction by transfer of two electrons [8]. Once again, the peroxidic link of **1** is the focus of attack (*Scheme 5*).

Scheme 5[1])



In view of the oxophilic nature of the Zn cation [9], the primary intermediate is best represented as the bidentate species **17**. Disproportionation to cyclopentanone (**18**) and the zinc diolate **19** affords by acetolysis **10** and zinc acetate. A minor avenue of reaction is preemptive protonation to the monodentate pentanoate **20** which subsequently gives **7** and zinc acetate.

Interestingly, low-valent tungsten favors outright deoxygenation but also embraces the mechanistically disparate processes of isomerization and reduction to a minor degree.

Lastly, the inertness of **1b** towards reagents which avidly abstract O-atoms confirms the implausibility of the formation of oxyheme (*Scheme 2*).

Conclusion. – The present findings permit a clarification of mechanisms proposed earlier to account for the dichotomous reaction courses, deoxygenation and isomerization, of a related tricyclic 1,2,4-trioxane [10]. It is now realized that deoxygenation is a consequence of two-electron reduction, whereas isomerization is catalyzed by single-electron exchange. Nevertheless, this distinction raises yet another question about the mode of action of **1** and artemisinin (**2**) in killing the intraerythrocytic parasite, which is presumably the same. On the one hand, the Fe^{2+} ion as well as heme undoubtedly interact with the peroxide bond in **1** and **2** to produce an incipient radical anion. In the case of **2**, the radical was characterized by its EPR spectrum [11]. The subsequent evolution of these radical anions produces toxic radicals, which if not intercepted, lead to isomerization. On the other hand, the malaria parasite, when treated with **2**, metabolizes it to deoxyartemisinin (**4**), which is clearly the consequence of two-electron reduction[2]), probably effected by a dehydrogenase. In other words, the metabolite **4** is an artefact unrelated to the parasiticidal action of **2**.

We also conclude that the anti-malarial potency of the bicyclic trioxanes **1a**, **b** resides in the masked ester group which is revealed when the peroxide bond breaks on accepting

[2]) Artemisinin (**2**), on treatment with powdered Zn in AcOH, gives **4** exclusively (unpublished).

an electron (*Scheme 4*). The oxy radical anion **12** so formed will open to the δ-pentanoate radical anion **12′**. Likewise, the oxy radical **13**, obtained by protonation of **12**, will be in equilibrium with its C-centered radical **13′**.

It should now be possible, in the light of these mechanistic considerations, to further modify bicyclic trioxanes such as **1** and render them even more potent.

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Experimental Part

General. Reactions requiring anh. conditions were carried out under N_2 or Ar. Anh. $FeCl_2$ was stored under Ar [12]. Solvent and reagents were purchased from *Fluka, Merck*, or *Aldrich* and were dried and distilled prior to use [13]. IR Spectra: *Perkin-Elmer-1600-FTIR* spectrometer; in $CHCl_3$ or $CDCl_3$. NMR Spectra: *Bruker-AMX-400* (400 (^{1}H) and 100 MHz (^{13}C)) and *Varian-Gemini* (200 (^{1}H) and 50 MHz (^{13}C)) instruments; in $CDCl_3$; chemical shifts δ in ppm with reference to Me_4Si, coupling constants J in Hz; ^{13}C multiplicities refer to proton coupling off-resonance; the different kinds of C-atoms were determined by APT or DEPT pulse sequence methods. MS: *Finnigan-4000, VG-70-70E*, and *VG Autospec* spectrometers.

Typical Procedure. Trioxanes **1a** and **1b** [14] were allowed to react with $FeCl_2$ and other reagents. To the reagent ($FeCl_2$, *etc.*) in the solvent (5 ml) were added cyclohexene (**6**; 60 µl) and the trioxane (100 mg) at a set temp. and then stirred for a certain period of time (see *Tables 1* and *2* for details). The resulting yellow or brown mixture was filtered over *Celite* which was rinsed with CH_2Cl_2. The resulting filtrate and washings were evaporated, and the residue so obtained was subjected to column chromatography (CC; SiO_2, CH_2Cl_2/hexane 9:1) thereby providing the pure products **7–9** as oils and **10** as solids.

(1RS,5RS)-5-Hydroxy-3,5-diphenylcyclopent-2-en-1-yl Pentanoate (**7a**). IR ($CHCl_3$): 3692*w*, 3579*m*, 3066*m*, 3015*s*, 2961*s*, 2861*m*, 1735*vs*, 1600*m*, 1495*m*, 1447*s*, 1338*m*, 1167*vs*, 1105*s*. ^{1}H-NMR ($CDCl_3$, 400 MHz): 7.54–7.49 (*m*, 4 H); 7.4–7.29 (*m*, 6 H); 6.22 (*dt*, J = 1.84, 1.84, 1 H); 5.89 (*dd*, J = 1.08, 0.76, 1 H); 3.25 (*AB*, J_{AB} = 16.5, δ_A 3.28 (*t*, J = 1.48), δ_B 3.22, 2 H); 2.97 (*s*, 1 H); 2.41 (*t*, J = 7.36, 2 H); 1.64 (*quint.*, J = 7.36, 2 H); 1.36 (*sext.*, J = 7.36, 2 H); 0.92 (*t*, J = 7.36, 3 H). MS: 336 (1, M^+), 318 (2), 251 (8), 234 (32), 217 (4), 149 (6), 130 (13), 120 (13), 105 (100), 91 (7), 85 (26), 77 (35), 57 (47).

(1RS,5RS)-5-Hydroxy-3,5-diphenylcyclopent-2-en-1-yl 5-Hydroxypentanoate (**8a**). IR ($CDCl_3$): 3583*w*, 3062*w*, 3030*w*, 2960*m*, 1735*vs*, 1495*m*, 1448*s*, 1261*vs*, 1172*s*, 1015*s*. ^{1}H-NMR: 7.55–7.5 (*m*, 4 H); 7.41–7.28 (*m*, 6 H); 6.22 (*dt*, J = 1.84, 1.84, 1 H); 5.89 (*dd*, J = 1.12, 1.08, 1 H); 3.56–3.54 (*m*, 2 H); 3.5 (*s*, 1 H); 3.26 (*AB*, J_{AB} = 16.56, δ_A 3.28 (*t*, J = 1.48), δ_B 3.23, 2 H); 2.92 (*s*, 1 H); 2.48–2.44 (*m*, 2 H); 1.84–1.81 (*m*, 4 H).

Bis[(1RS,5RS)-5-hydroxy-3,5-diphenylcyclopent-2-en-1-yl] Oxybis(pentanoate) (**9a**). IR ($CDCl_3$): 3582*m*, 3063*m*, 2959*m*, 1735*vs*, 1600*w*, 1495*m*, 1448*s*, 1342*m*, 1172*s*, 1070*s*. ^{1}H-NMR: 7.52–7.48 (*m*, 8 H); 7.4–7.27 (*m*, 12 H); 6.22 (*dt*, J = 1.84, 1.84, 2 H); 5.89 (*dd*, J = 1.08, 0.76, 2 H); 3.56–3.53 (*m*, 4 H); 3.24 (*AB*, J_{AB} = 16.8, δ_A 3.21 (*t*, J = 1.48), δ_B 3.27, 4 H); 2.93 (*s*, 2 H); 2.48–2.44 (*m*, 4 H); 1.84–1.81 (*m*, 8 H). ^{13}C-NMR: 172.6 (CO); 146.1 (C); 144.9 (C); 134.5 (C); 128.8 (CH); 128.6 (CH); 128.4 (CH); 127.4 (CH); 126.1 (CH); 124.9 (CH); 121.1 (CH); 84.6 (CH); 80.6 (C); 48.1 (CH_2); 44.4 (CH_2); 33.5 (CH_2); 31.7 (CH_2); 22.2 (CH_2). MS: 532 (1), 352 (1), 252 (5), 234 (69), 205 (19), 191 (14), 178 (11), 157 (11), 128 (6), 105 (100), 91 (31), 77 (100), 51 (77).

(1RS,2RS)-1,4-Diphenylcyclopent-3-ene-1,2-diol (**10a**). M.p. 114°. IR ($CDCl_3$): 3590*s*, 3528*s*, 3887*s*, 3062*s*, 3028*s*, 2916*m*, 1631*w*, 1601*m*, 1495*vs*, 1447*vs*, 1379*s*, 1340*s*, 1241*s*, 1208*s*, 1068*vs*, 1040*vs*. ^{1}H-NMR: 7.57–7.48 (*m*, 4 H); 7.39–7.26 (*m*, 6 H); 6.19 (*dt*, J = 1.84, 1.84, 1 H); 4.97 (*dd*, J = 7.7, 1.84, 1 H); 3.3 (*s*, 1 H); 3.24 (br. *s*, 2 H); 2.39 (*d*, J = 7.7, 1 H). ^{13}C-NMR: 145.7 (C); 143.5 (C); 135 (C); 128.6 (CH); 128.5 (CH); 128.4 (CH); 127.2 (CH); 126.1 (CH); 125.1 (CH); 124.8 (CH); 83.8 (CH); 80.5 (C); 48.5 (CH_2). MS: 252 (5, M^+), 235 (3), 224 (5), 209 (5), 191 (2), 157 (2), 145 (3), 133 (34), 120 (77), 105 (100), 91 (17), 77 (68), 51 (25).

(1RS,5RS)-3,5-Bis(4-fluorophenyl)-5-hydroxycyclopent-2-en-1-yl Pentanoate (**7b**). IR ($CHCl_3$): 3694*w*, 3579*m*, 3029*w*, 2961*m*, 2932*m*, 2874*w*, 1736*s*, 1603*s*, 1510*vs*, 1412*w*, 1328*m*, 1225*vs*, 1159*vs*, 1090*s*, 1014*m*. ^{1}H-NMR: 7.51–7.44 (*m*, 4 H); 7.09–7.01 (*m* 4 H); 6.13 (*dt*, J = 1.84, 1.84, 1 H); 5.82 (*s*, 1 H); 3.18 (*AB*, J_{AB} = 16.56, δ_A 3.23 (*t*, J = 1.47), δ_B 3.14, 2 H); 2.96 (*s*, 1 H); 2.4 (*t*, J = 7.32, 2 H); 1.63 (*quint.*, J = 7.36, 2 H); 1.34 (*sext.*, J = 7.36, 2 H); 0.91 (*t*, J = 7.36, 3 H). ^{13}C-NMR: 173.2 (CO); 163 (*d*, ^1J(C,F) = −247.4, C); 162.1 (*d*, ^1J(C,F) = −244.9, C); 144.8 (C); 140.7 (*d*, ^4J(C,F) = 3.2, C); 130.7 (*d*, ^4J(C,F) = 3.3, C); 127.9 (*d*, ^3J(C,F) = 8, CH); 126.7 (*d*, ^3J(C,F) = 8, CH); 121 (*d*, ^6J(C,F) = 2.2, CH); 115.6 (*d*, ^2J(C,F) = 21.3, CH); 115.2 (*d*, ^2J(C,F) = 19.9, CH); 84.2 (CH); 80.3 (C); 48.4 (CH_2); 34.1 (CH_2); 26.9 (CH_2); 22.2 (CH_2); 13.7 (Me). MS: 372 (0.3, M^+), 354 (1), 287 (5), 270 (16), 253 (5), 220 (1), 175 (3), 148 (8), 138 (9), 123 (100), 109 (9), 95 (24), 85 (53), 75 (6), 57 (90), 51 (2).

Bis[(1RS,5RS)-3,5-bis(4-fluorophenyl)-5-hydroxycyclopent-2-en-1-yl] Oxybis(pentanoate) (**9b**). IR ($CHCl_3$): 3580*m*, 3020*m*, 2959*m*, 1736*s*, 1603*s*, 1510*vs*, 1412*m*, 1234*vs*, 1159*s*, 1089*m*, 1014*m*. ^{1}H-NMR ($CDCl_3$, 400 MHz): 7.5–7.44 (*m*, 8 H); 7.09–7.02 (*m*, 8 H); 6.13 (*dt*, J = 1.84, 1.84, 2 H); 5.82 (br. *s*, 2 H); 3.56–3.52 (*m*, 4 H); 3.18 (*AB*, J_{AB} = 16.52, δ_A 3.23 (*t*, J = 1.47), δ_B 3.14, 4 H); 2.9 (*s*, 2 H); 2.45–2.43 (*m*, 4 H); 1.84–1.80 (*m*, 8 H). ^{13}C-NMR ($CDCl_3$, 50 MHz): 172.6 (CO); 163.1 (*d*, ^1J(C,F) = –247.6, C); 162.1 (*d*, ^1J(C,F) = –244.9, C); 145.1 (C); 140.6 (*d*, ^4J(C,F) = 3.25, C); 130.6 (*d*, ^4J(C,F) = 3.55, C); 127.9 (*d*, ^3J(C,F) = 8.2, CH); 126.7 (*d*, ^3J(C,F) = 8, CH); 120.8 (*d*, ^6J(C,F) = 1.8, CH); 115.6 (*d*, ^2J(C,F) = 21.2, CH); 115.3 (*d*, ^2J(C,F) = 20.9, CH); 84.5 (CH); 80.3 (C); 48.4 (CH_2); 44.4 (CH_2); 33.5 (CH_2); 31.7 (CH_2); 22.2 (CH_2). CI-MS (selected peaks): 687 (14), 673 (32), 659 (20), 653 (39), 643 (14), 637 (50), 569 (12), 480 (50), 405 (50), 287 (34), 271 (100), 254 (40), 175 (35), 137 (30), 123 (60), 101 (75), 83 (50), 69 (88), 55 (50), 41 (90).

(1RS,2RS)-1,4-Bis(4-fluorophenyl)cyclopent-3-ene-1,2-diol (**10b**). M.p. 133–134°. IR ($CHCl_3$): 3694*w*, 3596*w*, 3531*w*, 3019*s*, 1603*m*, 1509*s*, 1409*w*, 1327*w*, 1233*m*, 1208*s*, 1159*m*, 1087*w*, 1011*w*. ^{1}H-NMR: 7.53–7.43 (*m*, 4 H); 7.08–7.03 (*m*, 4 H); 6.11 (*dt*, J = 1.84, 1.84, 1 H); 4.91 (*d*, J = 8, 1 H); 3.35 (*s*, 1 H); 3.18 (*AB*, J_{AB} = 16.52, δ_A 3.19, δ_B 3.17, 2 H); 2.37 (*d*, J = 8, 1 H). ^{13}C-NMR: 161.8 (*d*, ^1J(C,F) = –243.9, C); 160.9 (*d*, ^1J(C,F) = –240.8, C); 143.6 (*d*, ^4J(C,F) = 2.7, C); 139.5 (C); 131.9 (*d*, ^4J(C,F) = 3.35, C); 127.8 (*d*, ^3J(C,F) = 8.1, CH); 127.2 (*d*, ^3J(C,F) = 8.1, CH); 126.7 (*d*, ^6J(C,F) = 2.3, CH); 115.3 (*d*, ^2J(C,F) = 21.1, CH); 114.4 (*d*, ^2J(C,F) = 20.8, CH); 82.9 (CH); 79.7 (C); 48.1 CH_2). MS: 288 (8, M^+), 271 (17), 260 (3), 245 (6), 220 (2), 151 (49), 138 (88), 123 (100), 109 (20), 95 (47), 75 (18), 55 (13).

1,4-Bis(4-fluorophenyl)cyclopenta-1,3-diene (**11b**). IR ($CHCl_3$): 3019*s*, 1505*m*, 1423*w*, 1216*vs*, 1158*w*, 1045*w*, 928*m*. ^{1}H-NMR: 7.53–7.49 (*m*, 4 H); 7.06–7.02 (*m*, 4 H); 6.85 (*s*, 2 H); 3.73 (*s*, 2 H). ^{13}C-NMR: 161.9 (*d*, ^1J(C,F) = –245, C); 144.4 (*d*, ^5J(C,F) = 2.1, C); 132.2 (*d*, ^4J(C,F) = 3.5, C); 127.8 (CH); 126.4 (*d*, ^3J(C,F) = 8, CH); 115.6 (*d*, ^2J(C,F) = 21.8, CH). MS: 254 (100, M^+), 233 (24); 220 (3), 207 (3), 159 (10), 133 (21), 120 (5), 107 (9), 83 (7), 75 (8), 57 (9).

3a,5-Diphenylspiro[4H-cyclopenta-1,3-dioxole-2,1'-cyclopentane] (**3a**). To a soln. of diol **10a** (105 mg) in dry cyclopentanone (3 ml) was added dry anh. $CuSO_4$ (400 mg). After stirring for 4 h at 22°, the mixture was filtered over *Celite* and evaporated to give a residue which was purified by CC (*Florisil*, CH_2Cl_2): **3a** (42% yield). M.p. 87–90°. IR ($CHCl_3$): 3019*vs*, 2972*m*, 1600*w*, 1495*m*, 1447*m*, 1333*m*, 1223*vs*, 1104*s*, 1046*m*, 928*m*. ^{1}H-NMR: 7.5–7.44 (*m*, 4 H); 7.39–7.24 (*m*, 6 H); 6.27 (*dt*, J = 1.8, J = 2.24, 1 H); 5.29 (*s*, 1 H); 3.27 (*AB*, J_{AB} = 17.28, δ_A 3.39 (*t*, J = 1.84), δ_B 3.14 (*d*, J = 1.48), 2 H); 1.89–1.64 (*m*, 8 H). ^{13}C-NMR: 145.5 (C); 144.9 (C); 135.2 (C); 128.6 (CH); 128.5 (CH); 128.3 (CH); 127 (CH); 126.2 (CH); 124.5 (CH); 124 (CH); 120.8 (C); 92.8 (CH); 90 (C); 49.4 CH_2); 38.6 (CH_2); 37.7 (CH_2) 23.6 (CH_2); 23.1 (CH_2). HR-MS: 318.1610260 ($C_{22}H_{22}O_2^+$, calc. 318.1619800).

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