Photochemical Transformation of Truxones to *C*-Nor-*D*-homo Steroid Systems[1]

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The photolysis of endo head-to-tail truxone *endo*-**3** yields, along with the indenone **2**, a considerable amount of an aromatic *C*-nor-*D*-homo steroid **4**. The mechanism for this steroid formation has been investigated and a mechanism involving a β-cleavage of a cyclobutane bond is proposed (Scheme II). The synthetic applicability of this reaction, as a route to *C*-nor-*D*-homo steroid systems, has been investigated but seems to be of a limited value.

In the synthesis of 6-methoxyindenone **2**, through the $AlCl_3$-catalyzed internal ketovinylation of the corresponding β-chloro vinyl ketone **1**, we observed the formation of small to large amounts of truxones, which were identified as endo head-to-tail dimers (Scheme I).[1]

Starting from the purified indenone, the experimental procedure could be modified to yield nearly exclusively either *endo*-**3** or *exo*-**3**.[3] In an attempt to obtain the indenone **2** through a photocycloreversion (high-pressure Hg lamp, room temperature in $ClCH_2CH_2Cl$) from the dimer *endo*-**3**, along with the indenone **2** (46%) a new product was obtained (54%), which was characterized as an aromatic *C*-nor-*D*-homo steroid with structure **4**;[1] no other products were observed.

In this paper we present our results relating to the mechanism of this reaction. The indenone–steroid ratio (GLC analyses) remained constant from the very start of the reaction. This seems to point out that the formation of indenone and steroid proceeds via a common intermediate. A possible mechanism, for which further evidence will be given, is depicted in Scheme II.

The steps **3** → **5c** are equivalent with a concerted 1,3-suprafacial shift, which is allowed starting from the excited state of **3**.

ESR experiments, proving the formation of radicals during the photolysis, have been done but no identification of the radicals was possible. Capture experiments with α,α′-diphenyl-β-picrylhydrazyl (DPPH) were negative. The proposed pathway from *endo*-**3** to **5c** resembles the pathway proposed in the photolysis of a benzobicyclohexene system adjacent to a carbonyl group.[4] The proven[1] cis junction between the B and the C ring in the steroid **4** follows from the nature of the intermediate **5c**. Our earlier proposed mechanism[1] involved a photodecarbonylation and formation of a benzobicyclohexene system **6**, which then underwent a photochemical disrotatory ring opening, followed by a thermal suprafacial 1,5-sigmatropic benzoyl shift (Scheme III).

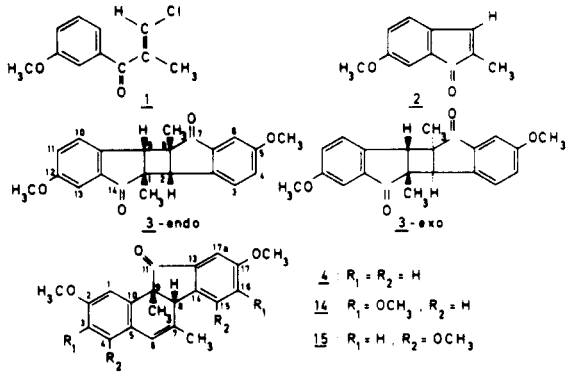
This mechanism can no longer be held as it requires a two-photon process for the steroid formation and a one-photon process for the indenone formation, which is not likely as a constant indenone–steroid ratio is found from the very beginning of the reaction. The rather high quantum yield (0.1) renders the photodecarbonylation also less likely. It has been reported that Norrish I type cleavages occur preferentially from the $\eta\pi^*$ triplet state and not from the $\pi\pi^*$ triplet state.[5]

The phosphorescence spectrum of *endo*-**3** points out that the lowest triplet is a $\pi\pi^*$ triplet state.[6] The quantum yield is more in agreement with a β-cleavage of the strained cyclobutane bond. A β-cleavage with high quantum yield has been observed for small-ring compounds.[7] A thermal ring opening of the benzobicyclohexene system is not to be expected at room temperature as similar benzobicyclohexene systems undergo ring opening only in boiling xylene.[8]

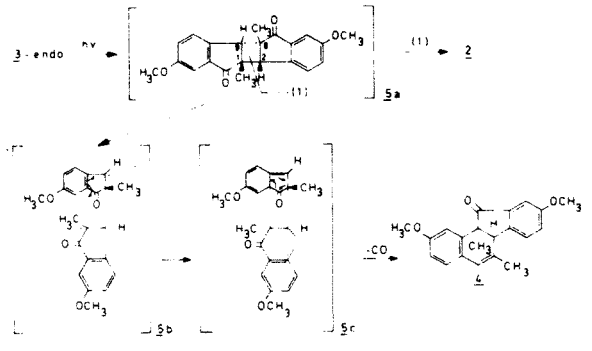
Further evidence for the mechanism in Scheme II has been found in the influence of substituents on the indenone–steroid ratio (Table I). The presence of a methoxyl function para to the carbonyl will facilitate the formation of the intermediate **5c** from **5b** leading to more steroid (see truxone *endo*–**7** in Table I). A methoxyl function meta to the carbonyl supports the stabilization of a radical on C_2 and thereby facilitates the cleavage (1) leading to more indenone (see truxone *endo*-**8** in Table I).

The high quantum yield of *endo*-**9** reflects the destabili-

Scheme I



Scheme II



Scheme III

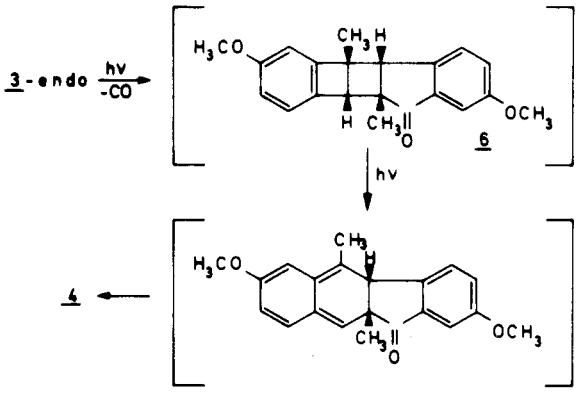


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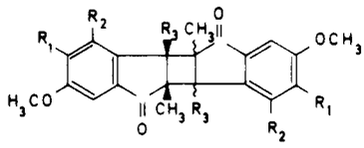
Table I. Photolysis of



trux-one	registry no.	R_1	R_2	R_3	indenone	registry no.	steroid	registry no.	indenone/steroid[a]	quantum yield[b]	irradiation time, h	% truxone recovered
endo-**3**	52102-74-6	H	H	H	**2**	52102-75-7	**4**	65808-95-9	46/54	0.10	1	45
endo-**7**	69027-71-0	OCH_3	H	H	**7a**	4900-43-0	**14**	69027-75-4	30/70	0.13	1	90
endo-**8**	69027-72-1	H	OCH_3	H	**8a**	69027-74-3	**15**	69027-76-5	82/18		0.5	25
endo-**9**	69027-73-2	H	H	CH_3	**9a**	2887-89-0			100/0	0.50	2	20
exo-**3**	65831-79-0	H	H	H	**2**				100/0	0.17	1.5	30
exo-**7**	69087-56-5	OCH_3	H	H	**7a**				100/0	0.18	1	90
ezo-**8**	69088-04-6	H	OCH_3	H	**8a**				100/0	0.19	2	10

[a] GLC analyses after 1 min of irradiation. [b] Quantum yield for truxone disappearance.

zation of the cyclobutane bonds by the neighboring methyl–methyl interactions. This destabilization also brings about exclusive indenone formation as cleavage (1) is favored. This is also the case for all the exo dimers (**3**, **7**, and **8**); instead of a steric CH_3–H interaction on the cyclobutane ring a steric CH_3-aromatic ring interaction occurs, probably leading to a larger destabilization of the remaining cyclobutane bond in intermediate **5a**.[9]

This easy cycloreversion to indenone is also observed in the mass spectra of these products, where a high $(M^+/2)/M^+$ ratio is observed (150–1000). The $(M^+/2)/M^+$ ratio for the endo dimers (except *endo*-**9**) is much lower (10–50) (less steric destabilization of cyclobutane bonds).

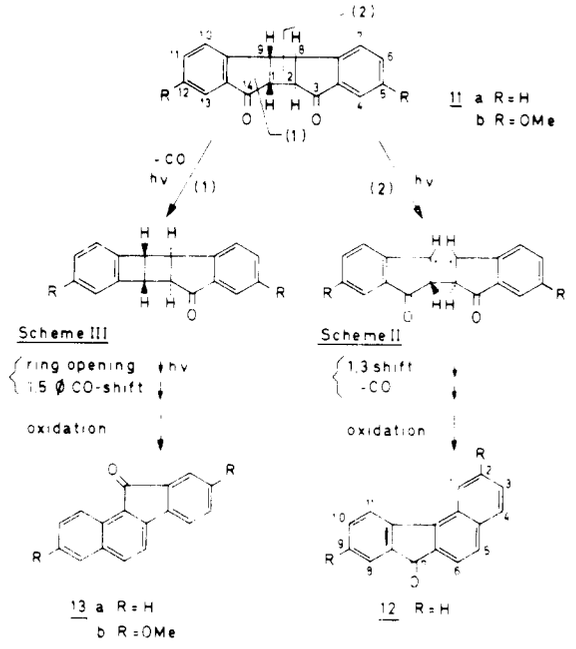
Photolysis of **10**, obtained by reducing one of the carbonyl groups of the truxone *endo*-**3** with lithium aluminium hydride to the hydroxyl stage, also gives exclusively indenone. No steroid was observed. This can be explained by the mechanism of Scheme II, as this would imply the rather difficult expulsion[10] of CHOH instead of CO in the step leading from intermediate **5c** to **4**. No hydroxy indene was observed either, but this can be explained by air oxidation during workup.[11]

Another mechanism which has been envisaged for the steroid formation also implies **5a**, as a common intermediate for indenone and steroid formation. Cleavage of the carbonyl C_1 bond in **5a** and concomitant formation of a double bond between C_1 and C_9 results in a new biradical intermediate. This intermediate can lead to the steroid **4** by recombination of the radical site on C_8 and the phenyl radical created by loss of carbon monoxide. However, no plausible explanation can be given for the cis relationship of H and CH_3 in the new double bond which is created, nor for the exclusive formation of a cis junction between the B and C ring of the steroid **4** in the ring closure of the biradical intermediate.

A further argument against the mechanism of Scheme III is the reaction product of the photolysis of the 5,12-dimethoxy head-to-head truxone **11a** (Scheme IV). As shown in this scheme the mechanism of Scheme III should lead, after air oxidation, to **13a**. Such products could be interesting, as starting from **11b** a product **13b** would be obtained. This skeleton with methoxyl groups in positions 3 and 17 of the A and D rings is appropriate for transformation to natural *C*-nor-*D*-homo steroids. However, photolysis of truxone **11a** affords the benzo[*c*]fluorenone **12**, instead of the benzo[a]-fluorenone **13a**. This result favors the mechanism of Scheme II to that of Scheme III.

Taking into account the influence of substituents and the complex mechanism, we can conclude that the reaction seems to be of limited importance as a synthetic route to *C*-nor-*D*-homo steroid systems.

Scheme IV



Experimental Section

The UV spectra have been recorded with a Perkin-Elmer double-beam spectrophotometer 124 and the IR spectra with a Perkin-Elmer 257 grating spectrophotometer. The NMR spectra have been taken on a Varian XL-100 spectrometer and for the ESR spectra on an ESR spectrometer Varian E-4. For the mass spectra an AEI-MS-12 was used; the ionization energy was 70 eV and samples were injected directly at a temperature between 100 and 200 °C. All melting points are uncorrected.

General Procedure for the Synthesis of Indenones. The indenones **2** and **7a** have been synthesized by $AlCl_3$-catalyzed cyclization of the corresponding β-chlorovinyl ketones, which are accessible from the corresponding propiophenones.[12] The indenone **8a** was obtained by refluxing the corresponding β-chlorovinyl ketone for 15 h in DMF (yield 52%). All indenones were purified by column chromatography on silica gel with hexane–chloroform and crystallization from ether–pentane. The indenone **9a** was obtained via an earlier described procedure.[13]

General Procedure for the Synthesis of the Endo Head-to-Tail Truxones 3, 7, 8, and 9. A solution of indenone (2.9 mol) in 40 mL of dichloromethane is added slowly to a suspension of $AlCl_3$ (2.9 mol) in 40 mL of dichloromethane. When the addition is complete (90 min) the mixture is stirred for 2 h at 20 °C. After working up with ice

water–2 N HCl, aqueous $NaHCO_3$, and water, the solution is dried over $MgSO_4$. Removal of the dichloromethane yields a slightly yellow colored oil. Recrystallization from heptane affords white crystals of endo truxone.

Identification of the Products: Endo Dimer 3 (yield 84%): UV ($ClCH_2CH_2Cl$) 314 (7170), 252 (16 200), 220 (58 000); IR ($CHCl_3$) 1705 cm^{-1} ($\nu_{C=O}$); mp 149 °C; NMR ($CDCl_3$) δ 1.73 (6p, s, 1- and 8-CH_3), 3.37 (2p, s, 2- and 9-H), 3.68 (6p, s, 5- and 12-OCH_3), 6.72 (2p, d, J_m = 2.5 Hz, 6-H and 13-H), 7.06 (2p, d × d, J_o = 8 and J_m = 2.5 Hz, 4-H and 11-H), 7.31 (2p, d, J_o = 8 Hz, 3-H and 10-H); MS 348 (2.0), 320 (1.5), 305 (0.8), 174 (100), 159 (7.7), 131 (12.0). Anal. Calcd for $C_{22}H_{20}O_4$: C, 75.84; H, 5.79. Found: C, 75.65; H, 6.36.

Endo Dimer 7 (yield 82%): UV ($ClCH_2CH_2Cl$) 307 (16 600), 270 (20 000), 231 (33 000); IR ($CHCl_3$) 1695 cm^{-1} ($\nu_{C=O}$); mp 249 °C; NMR ($CDCl_3$) δ 1.69 (6p, s, 1- and 8-CH_3), 3.32 (2p, s, 2- and 9-H), 3.76 (6p, s, 5- and 12-OCH_3), 3.95 (6p, s, 4- and 11-OCH_3), 6.72 and 6.80 (2 × 2p, 2 × s, 3-, 6-, 10-, and 13-H); MS 408 (9.1), 380 (1.1), 204 (100), 189 (15.9), 161 (2.0). Anal. Calcd for M^+: 408.1571. Found: 408.1571.

Endo Dimer 8[14] (yield 10%): UV ($ClCH_2CH_2Cl$) 330 (4000), 266 (8580); IR ($CHCl_3$) 1710 cm^{-1} ($\nu_{C=O}$); mp 170–172 °C; NMR ($CDCl_3$) δ 1.64 (6p, s, 1- and 8-CH_3), 3.40 (2p, s, 2- and 9-H), 3.68 (6p, s, 5- and 12-OCH_3), 3.92 (6p, s, 3- and 10-OCH_3), 6.34 and 6.56 (2 × 2p, 2 × d, J = 2 Hz, 4-, 6-, 11-, and 13-H); MS 408 (2.2), 380 (0.8), 365 (0.6), 204 (100), 189 (18.4), 161 (30.6). Anal. Calcd for M^+: 408.1571. Found: 408.1595.

Endo Dimer 9 (yield 75%): UV ($ClCH_2CH_2Cl$) 315 (6820), 250 (16 540), 228 (28 740); IR ($CHCl_3$) 1715 cm^{-1} ($\nu_{C=O}$); mp 177 °C; NMR ($CDCl_3$) δ 1.38 and 1.42 (2 × 6p, 2 × s, 1-, 2-, 8-, and 9-CH_3), 3.62 (6p, s, 5- and 12-OCH_3), 6.60 (2 p, d, J_m = 2 Hz, 6-H and 13-H), 7.00 (2p, d × d, J_o = 8 and J_m = 2 Hz, 4-H and 11-H), 7.20 (2p, d, J_o = 8 Hz, 3-H and 10-H); MS 376 (0.1), 188 (100). Anal. Calcd for $C_{24}H_{24}O_4$: C, 76.57; H, 6.43. Found: C, 76.56; H, 6.71.

General Procedure for the Synthesis of the Exo Head-to-Tail Truxones 3, 7, and 8. $AlCl_3$ (2.9 mmol) is added slowly to a solution of indenone (2.9 mmol) in 50 mL of dichloromethane. When addition of $AlCl_3$ is complete (90 min), the mixture is stirred for 3 h at room temperature. After being worked up with ice water–2 N HCl, aqueous $NaHCO_3$, and water, the solution is dried over $MgSO_4$. Removal of the dichloromethane yields a slightly yellow colored oil. Recrystallization from ether affords white crystals of the exo truxone.

Identification of the Products: Exo Dimer 3 (yield 82%): UV ($ClCH_2CH_2Cl$) 318 (7400), 250 (24 400), 224 (49 000); IR ($CHCl_3$) 1700 cm^{-1} ($\nu_{C=O}$); mp 243 °C; NMR ($CDCl_3$) δ 0.83 (6p, s, 1- and 8-CH_3), 3.22 (2p, s, 2- and 9-H), 3.90 (6p, s, 5- and 12-OCH_3), 7.22–7.54 (6p, m, Ar–H); MS 348 (0.1), 320 (0.5), 175 (130), 174 (100), 159 (28.6), 131 (57.2). Anal. Calcd for $C_{22}H_{20}O_4$: C, 75.84; H, 5.79. Found: C, 75.83; H, 5.73.

Exo Dimer 7 (yield 84%): UV ($ClCH_2CH_2Cl$) 310 (18 800), 270 (21 600), 236 (39 700); IR ($CHCl_3$) 1685 cm^{-1} ($\nu_{C=O}$); mp 315 °C; NMR ($CDCl_3$) δ 0.85 (6p, s, 1- and 8-CH_3), 3.19 (2p, s, 2- and 9-H), 3.98 and 4.04 (2 × 6p, 2 × s, 4-, 5-, 11-, and 12-OCH_3), 6.98 (2p, s, 3-H and 10-H), 7.30 (2p, s, 6-H and 13-H); MS 408 (0.4), 380 (6.3), 204 (100), 189 (5.2). Anal. Calcd for M^+: 408.1572. Found: 408.1575.

Exo Dimer 8 (yield 80%): UV ($ClCH_2CH_2Cl$) 327 (6700), 264 (15 500), 234 (40 700); IR ($CHCl_3$) 1700 cm^{-1} ($\nu_{C=O}$); mp 316–317 °C; NMR ($CDCl_3$) δ 0.80 (6p, s, 1- and 8-CH_3), 3.24 (2p, s, 2- and 9-H), 3.86 and 3.88 (2 × 6p, 2 × s, 3-, 5-, 10-, and 12-OCH_3), 6.70 (2p, d, J_m = 2 Hz, 4-H and 11-H), 6.88 (2p, d, J_m = 2 Hz, 6- and 13-H); MS 408 (0.2), 380 (2.4), 204 (100), 189 (8.7), 161 (8.7). Anal. Calcd for M^+: 408.1572. Found: 408.1572.

1,8-Dimethyl-5,12-dimethoxy-7-oxo-14-hydroxytruxane (10). To a solution of 1.44 mmol of endo truxone **3** in 30 mL of monoglyme is added a suspension of 1.00 mmol of $LiAlH_4$ in monoglyme. When the addition is complete (20 min), the mixture is refluxed for 90 min. A white precipitate is formed during the reaction. After working up with ice water–2 N HCl, the mixture is extracted three times with ether. The combined organic layers are dried over $MgSO_4$ and the solvent is evaporated. Preparative TLC of the products over SiO_2 (75% hexane–25% acetone) affords 1.03 mmol of the endo truxone **3** and 0.39 mmol of **10**.

Truxane 10 (yield 27%): IR ($CHCl_3$) 3560 (ν_{OH}) and 1705 cm^{-1} ($\nu_{C=O}$); NMR ($CDCl_3$) δ 1.63 and 1.81 (2 × 3p, 2 × s, 1- and 8-CH_3), 2.25 (1p, d, J = 10 Hz, 14-OH), 3.25 (2p, s, 2- and 9-H), 3.63 and 3.68 (2 × 3p, 2 × s, 5- and 12-OCH_3), 4.91 (1p, d, J = 10 Hz, 14-H), 6.40–7.60 (6p, m, Ar–H); MS 350 (2.5), 176 (100), 161 (15.9).

Exo Head-to-Head Truxone 11a. 11a was prepared by oxidation of the corresponding truxane with CrO_3 in acetic acid:[15] UV(EtOH) 346 (<100), 333 (<100), 288 (2200), 245 (12 700); IR ($CHCl_3$) 1720 cm^{-1}; mp 220–222 °C (lit.[16] mp 221–223 °C); NMR ($CDCl_3$) δ 3.12 (2p, d, J = 7 Hz, 1- and 2-H), 3.75 (2p, d, J = 7 Hz, 8- and 9-H), 7.48–8.08 (8p, m, Ar–H); MS 260 (29.0), 232 (12.9), 231 (10.3), 202 (8.7), 130 (100), 102 (38.8).

Irradiation Experiments with 3, 7, 8, and 9. Degassed solutions of 0.3 mmol of truxone (**3, 7, 8,** and **9**) in 20 mL of 1,2-dichloroethane were irradiated in a Pyrex tube with a high-pressure Hg lamp.[17] The product distributions were determined by NMR analyses and GLC analyses. No other products than the starting truxone, the indenone, and the steroid were observed. The reaction mixtures were subjected to preparative TLC on silica gel with $CHCl_3$–hexane (1/1). This resulted in a 80–90% recovery of starting truxone and reaction products. The irradiation time, the percentage of recovered truxone, and the indenone–steroid distribution are summarized in Table I.

Identification of the Products. Steroid 4: UV (EtOH) 277 (1600), 252 (19 000); IR ($CHCl_3$) 1715 cm^{-1} ($\nu_{C=O}$); mp 138 °C; NMR ($CDCl_3$) δ 1.50 (3p, s, 9-CH_3), 2.30 (3 p, d, J = 1.5 Hz, 7-CH_3), 3.55 (1p, s, broad, 8-H), 3.78 (6p, s, 2- and 17-OCH_3), 6.33 (1p, s, broad, 6-H), 6.63 (1p, d × d, J_o = 8.3 and J_m = 2.5 Hz, 3-H), 6.88 (1p, d, J_o = 8.3 Hz, 4-H), 7.11 (1p, d × d, J_o = 8 and J_m = 2.5 Hz, 16-H), 7.16 (2p, broad, 1- and 17a-H), 7.44 (1p, t × d, J_o = 8, J_p = 1, and J_{8-H} = 1 Hz, 15-H); MS 320 (100), 305 (72.0), 290 (6.0), 277 (7.5), 262 (4.8). Anal. Calcd for $C_{21}H_{20}O_3$: C, 78.73; H, 6.29. Found: C, 78.65; H, 6.63.

Steroid 14: UV ($ClCH_2CH_2Cl$) 288 (12 900), 268 (18 200), 235 (38 600); IR ($CHCl_3$) 1700 cm^{-1} ($\nu_{C=O}$); mp 182–183 °C; NMR ($CDCl_3$) δ 1.47 (3p, s, 9-CH_3), 2.34 (3p, d, J = 1.5 Hz, 7-CH_3), 3.55 (1p, s, broad, 8-H), 3.79, 3.87, 3.89, and 3.94 (4 × 3p, 4 × s, 2-, 3-, 16-, and 17-OCH_3), 6.33 (1p, broad, 6-H), 6.50 (1p, s, 4-H), 6.98, 7.17, 7.22 (3 × 1p, 3 × s, 1–15- and 17a-H); MS 380 (100), 365 (44.7), 350 (3.0), 337 (2.8). Anal. Calcd for M^+: 380.1622. Found: 380.1608.

Steroid 15: IR ($CHCl_3$) 1710 cm^{-1} ($\nu_{C=O}$); mp 154–156 °C; NMR ($CDCl_3$) δ 1.44 (3p, s, 9-CH_3), 2.23 (3p, s, broad, 7-CH_3), 3.56 (1p, s, broad, 8-H), 3.72, 3.76, 3.77 (12p, 3 × s, 2-, 4-, 15-, and 17-OCH_3), 6.28 (1p, broad 6-H), 6.60–6.72 (3p, m, 3 Ar-H), 6.79 (1p, d, J = 2 Hz, 1 Ar-H); MS 380 (100), 365 (91.4), 350 (19.4), 337 (13.8). Anal. Calcd for M^+: 380.1622. Found: 380.1613.

Irradiation of the Truxane 10. A degassed solution of 0.35 mmol (123 mg) of **10** in 10 mL of 1,2-dichloroethane was irradiated during 6 h.[17] An NMR analysis of the reaction mixture shows the presence of only the truxane **10** and the indenone **2** in a 40–60 proportion.

Irradiation of the Exo Head-to-Head Truxone 11a. A degassed solution of 1.55 mmol (400 mg) of **11** in 35 mL of 1,2-dichloroethane was irradiated during 6 days.[17] The reaction mixture was purified by preparative TLC on silica gel (benzene–ethyl acetate 90/10). This afforded 80 mg of starting material (25%), 144 mg of endo head-to-tail truxone (35%), which was purified further by crystallization from acetone [mp 191 °C (lit.[16] mp 190–192 °C)], and finally 110 mg of benzo[*c*]fluorenone **12** (31%), which was further purified by repeated preparative TLC (silica gel, benzene–hexane 60/40) and crystallization from heptane: yellow-red crystals, mp 157–158 °C (lit.[18] mp 158–159 °C).

Identification of Benzo[*c*]fluorenone 12: IR ($CHCl_3$) 1710 cm^{-1} ($\nu_{C=O}$); MS 230 (100), 202 (47.3), 201 (21.0), 200 (23.7); NMR ($CDCl_3$) δ 7.17–8.20 (9p, m), 8.43 (1p, m, H_1). Two protons exhibited a great deshielding effect in the presence of Eu(fod); these two protons were recognized as 8-H (d, broad, J_o = 7.5 Hz) and 6-H (d, J_o = 8.5 Hz). The proton at δ 8.43 did not shift significantly with Eu(fod).

Determination of the Quantum Yields. For the determination of the quantum yields, the samples have been irradiated with monochromatic light;[19] hexamethylenebis(maleimide) has been used as an actinometer.[20] All the determinations have been done at 20 °C with degassed samples, the optical density of which was 2.2 at the wavelength of irradiation, so that all light was absorbed. The degree of conversion of a truxone did not exceed 10%. The results are given in Table I.

ESR Experiments. A solution of 10^{-4} M endo truxone **3** in CH_2Cl_2 (suprasil quartz tube) was degassed by subsequent freeze–thaw cycles and irradiated at the temperature of liquid nitrogen with a Hanovia UV gun using a Pyrex filter.

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Registry No.—**10,** 69027-77-6; **11a,** 17062-18-9; **12,** 6051-98-5; *endo*-4b,4c,9a,9b-tetrahydrocyclobuta[1,2-*a*:3,4-*a'*]diindenedione, 17062,22-5; (*E*)-α-methyl-β-chlorovinyl *m*-methoxyphenyl ketone, 69027-78-7; (*E*)-α-methyl-β-chlorovinyl 3,4-dimethoxyphenyl ketone, 69027-79-8; (*E*)-α-methyl-β-chlorovinyl 3,5-dimethoxyphenyl ketone, 69027-80-1.

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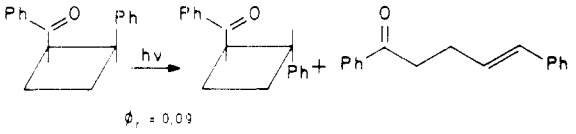

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Stereoselective Synthesis of Racemic Elemanolide Dilactones Related to Vernolepin

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A synthesis of 8-deoxy-9β-hydroxyvernolepin (**16**), an isomer of the elemanolide sesquiterpene dilactone vernolepin, is described. The synthesis employs the monoketal of 1,4-cyclohexanedione as the starting point and proceeds via symmetrical intermediates. Introduction of the requisite acetic acid side chains is achieved via symmetrical dialkylation of the enamine derivative of the aforementioned ketone using 1,3-dichloro-2-propene as an acetic acid chloride equivalent. The second (ketal protected) carbonyl grouping is employed to introduce the geminal hydroxymethyl, vinyl substituents after reduction and protection of the 4-ketone grouping. This is accomplished by carbethoxylation and alkylation of the resulting β-keto ester enolate with ethyl iodoacetate to give a single keto diester of the proper relative stereochemistry at the four contiguous chiral centers. The stereochemistry was confirmed through conversion of this intermediate to bisnordihydro-8-deoxyvernolepin (**21**), a substance of known stereochemistry.

The cytotoxic tumor inhibitory elemanolide sesquiterpene, vernolepin, has occasioned a considerable expenditure of creative synthetic effort in laboratories throughout the world since Kupchan and his associates first described its isolation and structure some ten years ago.[1] Impressive progress has been recorded. Several imaginative total syntheses have evolved[2] and numerous reports describing potential solutions for one or more of the various synthetic problems posed by the vernolepin family have appeared.[3]

Efforts in our own laboratory over the past few years have been directed toward straightforward, efficient stereoselective syntheses of dilactones related to vernolepin. The approach described herein was designed with total synthesis in mind, but unforeseen difficulties at the penultimate stages have thus far kept us from that goal. Nonetheless, the basic plan and the evolved chemistry contain elements of intrinsic interest and applicability to synthetic chemistry which prompt this report.

In our synthetic analysis of vernolepin (Scheme I), we noted that transposition of the C-8 hydroxyl grouping to C-9 (structure I) greatly simplified synthetic and stereochemical problems by permitting the use of a symmetrical intermediate such as III. Furthermore, the expected conformational rigidity imposed by the trans,anti arrangement (all equatorial) of the three substituents in this intermediate and consideration of stereochemical factors controlling enolate alkylations led us

Scheme I