136. Photo-oxygenation of Styrenic Estrogens: Structural Analysis of 8,9-Didehydro-, 6,7-Didehydro-, and 9,11-Didehydroestrone Derivatives and Their Reactivity towards Singlet Oxygen

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Dedicated to Prof. Dr. *Kurt Schaffner* on the occasion of his 60th birthday

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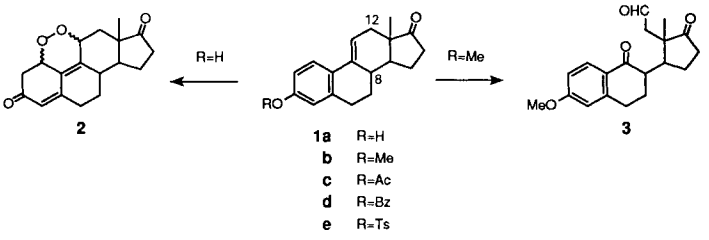
A series of didehydro-3-*O*-methyl-estrones having a styrenic framework, with the ring-A-conjugated double bond in all three possible positions (8,9-didehydro- (**6**), 9,11-didehydro- (**1b**), 6,7-didehydro- (**9**), and the 12,18-dinor-8,9-didehydroestrone analog **11**), were compared for their reactivity towards singlet oxygen. Under dye-sensitized photo-oxygenation conditions, both, products derived from ene-type reactions with the isolation of a stable hydroperoxide and a fragmentation product, were obtained from **6** (see *Scheme 3*), while only fragmentation took place for **1b** (*Scheme 1*). Kinetic studies indicated that **6** is more reactive towards $^1O_2$ than **1b** ($\beta = 9.2 \cdot 10^{-3}$ mol·l^{-1} *vs* $3.3 \cdot 10^{-2}$ mol·l^{-1}, resp.). The observed reactivity, apparently, does not match with ene-type reaction and [2 + 2]cycloaddition being in competition, since the most activated substrate **6** preferentially yields ene-type products and their derivatives. Conformational analysis on the structure of **6** and **1b**, both calculated by molecular-mechanic techniques (MMPMI) and determined by X-ray diffraction, show that the allylic H-atoms satisfy the orthogonality rule for ene-type reactions. The product distribution is best rationalized by applying *Fukui*'s rule which takes into account a combination of electronic and geometric factors. Substrates **9** and **11** yielded photoproducts arising from ene-type reaction with no stable primary products isolated (*Scheme 4*). Geometric considerations based on the calculated structures by molecular mechanics are consistent with the observed results.

1. Introduction. – Since the first report of the dye-sensitized photo-oxygenation of a steroidal compound by *Windaus* and *Brunken* in 1928 [1], singlet-oxygen chemistry has been extensively studied to understand the physical chemistry of excited oxygen and its interaction with electron-rich organic molecules and as a synthetic tool in organic chemistry.

The behaviour of natural estrogenic steroids under dye-sensitized photo-oxygenation conditions has been previously studied. Initial data about the reaction products arising from estrone and estradiol showed the formation of 10-hydroperoxides as primary products which easily evolved to *p*-quinols [2]. Reactive hydroperoxides from estrogens in contraceptive agents have been implicated in the photoallergic side effects of oral contraceptives through their direct interaction to DNA [3]. We extended the study to styrenic estranes with the aim of shifting the reactive moiety of the steroid skeleton to rings B and C in order to functionalize these new positions and rationalize the reactivity pattern towards singlet oxygen. The first family of tetraenic steroids tested was the

Scheme 1

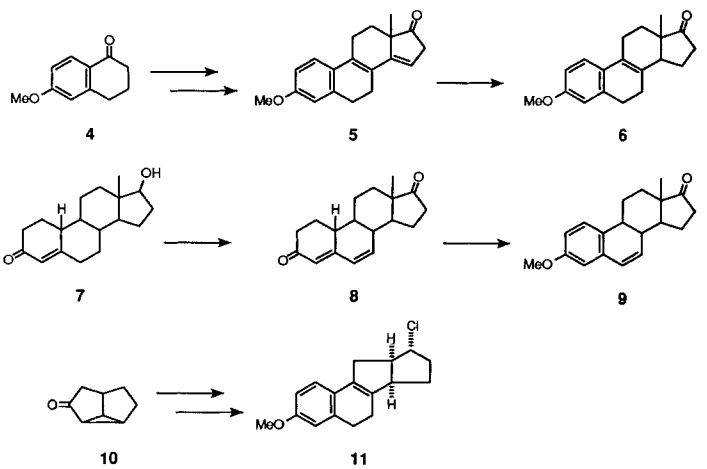


9,11-didehydroestrone derivatives **1a–e** (*Scheme 1*) [4] [5]. These activated *p*-substituted styrene substrates showed different reactivity and yielded different products depending on the substitution at C(3), *e.g.* **2** and **3** when R was H and Me, respectively. The C-seco-aldehyde **3** arises from an oxidative cleavage of the C(9)=C(11) bond of **1b**; the intermediacy of a 1,2-dioxetane as primary photo-oxygenation product was suggested, although no direct evidence was provided. This oxidative fragmentation allowed the design of a short synthesis of 11-oxaestrogens from estrone in nine steps [6].

In the present study, we report the behaviour towards singlet oxygen of other styrenic estranes with the ring-A-conjugated double bond in positions 8,9 or 6,7. Conformational calculations and X-ray structures of a set of styrenic substrates are described in order to rationalize their differential reactivity in terms of geometric and electronic factors.

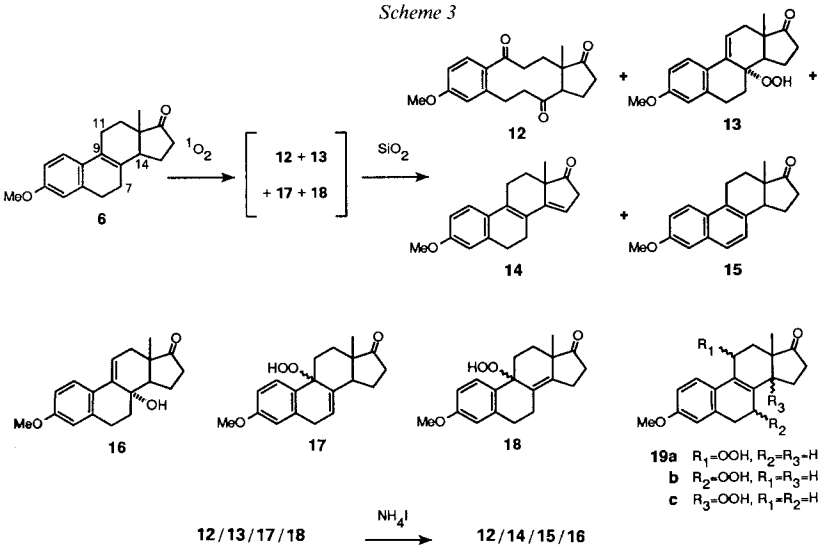
2. Results. – 2.1. *Synthesis of Estratetraene Substrates.* The (±)-3-methoxyestra-1,3,5(10),8-tetraen-17-one (**6**) was prepared by *Torgov* synthesis from 3,4-dihydro-6-methoxynaphthalen-1(2*H*)-one (**4**; *Scheme 2*) [7]. The regioselective reduction of the pentaene **5** to **6** was done according to *Hainaut* and *Bucourt* by catalytic hydrogenation with $Pd/CaCO_3$ [8]. The 3-methoxyestra-1,3,5(10),6-tetraen-17-one (**9**) was synthetized as described previously by our group [9] from 17β-hydroxyestr-4-en-3-one (**7**) through selective microbial aromatization of **8**, and (±)-17α-chloro-3-methoxy-12,18-dinor-13α-estra-1,3,5(10),8-tetraene (**11**) was obtained by total synthesis as reported by *Demuth* [10] (*Scheme 2*).

Scheme 2



2.2. *Dye-Sensitized Photo-oxygenation of the Estratetraene Derivatives. Estratetraenone* **6**: The photo-oxygenation of **6** was carried out by following the experimental conditions reported previously for the 9,11-didehydroestrone derivative **1b** [5]: a solution of **6** in MeOH at 0° was irradiated in a tubular photo-oxygenation reactor using rose bengal as sensitizer. TLC and HPLC monitoring showed the complete disappearance of **6** after 40 min with the concomitant formation of four products. Chromatographic separation on SiO_2 afforded **12** (16%), **13** (24%), **14** (16%), and **15** (4%; *Scheme 3*).

Scheme 3



The allylic hydroperoxide **13** was stable at room temperature. In addition to spectroscopic data, its reactivity provided further evidence of the structure (hydroperoxide function) and the configuration at C(8). Acid treatment in $MeOH/H_2SO_4$ solution at room temperature for 12 h yielded triketone **12** (50% conversion) as a result of a *Hock*-type rearrangement [11]. Under reductive conditions (NH_4I/MeOH), **13** gave the corresponding allylic alcohol **16**. The 8α-OH configuration was assigned to **16** by comparison of its ^{1}H-NMR spectra to that of a sample synthetized independently by epoxidation of **6** followed by acid ring opening as described by *Stein et al.* [12]. Since the hydroperoxide reduction to an alcohol (**13**→**16**) does not involve the C–O bond, the same 8α-OOH configuration was assigned to **13**.

While **12** and **13** are expected photo-oxygenation products (**12** from 1,2-dioxetane cleavage and **13** as primary ene-type product), **14** and **15** might arise from some oxygenated intermediates which are not stable either under the reaction conditions or during purification. To identify their primary products, the photo-oxygenation was carefully monitored by HPLC/UV. Neither **14** nor **15** were observed in the mixture prior to SiO_2 chromatography, thus assessing that they are secondary products. Instead, two new compounds **17** and **18** (*Scheme 3*) were detected besides **12** and **13**. The HPLC retention times and the UV spectra suggested that they are allylic hydroperoxides. From the ^{1}H-NMR spectra of the crude reaction mixture (*Table 1*) and from the UV absorption of

Table 1. *^{1}H-NMR Data of the Crude Photo-oxygenation Mixture and of the Reduced* (NH_4I) *Crude Photo-oxygenation Mixture from (±)-3-Methoxyestra-1,3,5(10),8-tetraen-17-one* (**6**)

	Compound[a])	δ(Me(18)) [ppm]	δ(olef. H) [ppm] (*J* [Hz])
Crude photo-oxygenation mixture	**12** (14%)	1.13	
	13 (21%)	0.96	6.20 (*dd*, *J* = 5.8, 3.2, H–C(11))
	17 (19%)	0.78	5.90 (*ddd*, *J* = 3.6, 3.6, 1.7, H–C(7))
	18 (18%)	1.08	
Reduced crude photo-oxygenation mixture	**12** (14%)	1.13	
	16 (18%)	0.95	6.00 (*dd*, *J* = 5.8, 3.8, H–C(11))
	14 (11%)	1.13	5.85 (*dd*, *J* = 2.7, 2.7, H–C(15))
	15 (19%)	0.79	

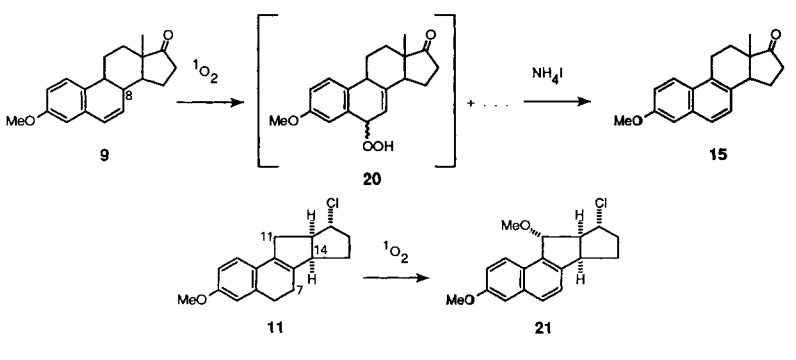
[a]) Yields (in parenthesis) were determined by comparison of the Me(18) integrals with that of 3-methoxyestrone (δ(Me(18)) 0.90) which was used as internal standard.

the HPLC peaks, the tentative structures **17** and **18** were assigned. Other allylic hydroperoxides such as **19a–c** are discarded because of the absence of a *ca.* 280 nm peak in the UV spectra, characteristic of 1,3,5(10),8-tetraene derivatives.

Treatment of the crude photo-oxygenation mixture **12**/**13**/**17**/**18** with NH_4I afforded **12**/**14**/**15**/**16**. No allylic alcohols derived from **17** or **18** were detected by ^{1}H-NMR. Only their dehydration products **14** and **15** were directly formed and isolated; **14** and **15** were also obtained after direct SiO_2 chromatography of the crude photo-oxygenation mixture.

Estratetraenone **9**: Irradiation of **9** under the same conditions as those described for **1b** and **6** produced a very slow reaction. After 10 h, a mixture of starting material and two products in a 3:1:1 molar ratio (^{1}H-NMR) had formed. Longer reaction times showed extensive degradation of the crude mixture. NH_4I treatment of the crude material in MeOH solution followed by chromatographic separation gave equilenin (**15**; 25%; *Scheme 4*), which was not detected in the crude reaction mixture, starting material **9** (44%), and a complex mixture of degradation products (31%). Attempts to isolate primary photo-oxygenation products failed. A primary product, however, was tentatively identified as the allylic hydroperoxide **20** by ^{1}H-NMR analysis of the crude photo-oxygenation mixture prior to reduction (5.42 ppm (*m*, H–C(6)) and 5.77 ppm (*d*, *J* = 4 Hz, H–C(7))). Similar spectra of hydroperoxides from the dye-sensitized photo-oxygenation

Scheme 4



of 1,2-dihydronaphthalenes have been described [13]. Therefore, equilenin (**15**) is the only stable product arising from reduction and dehydration of hydroperoxide **20**.

Chlorodinorestratetraene **11**: Steroid analog **11** [10] was irradiated in $MeOH/CH_2Cl_2$ solution at 0° for 5 h as reported [14]. $NaBH_4$ reduction of the mixture and SiO_2 chromatography gave **21** in 40% yield (*Scheme 4*). The configuration at C(11) was inferred from its ^{1}H-NMR spectra (5.08 ppm *s*, H–C(11), *i.e.* no vicinal coupling to H–C(13), dihedral angle H–C(11)–C(13)–H *ca.* 90°). Provided a 13α-H configuration, an 11α-MeO configuration was assigned.

2.3. *Kinetics of (±)-3-Methoxyestra-1,3,5(10),8-tetraen-17-one* (**6**). In order to have a physical parameter to compare the different reactivities of compounds **1b** and **6** towards oxidation with singlet oxygen, we evaluated the index of reactivity (β) of **6** by applying kinetic technics as previously reported for the studies of the 9,11-didehydroestrone series **1a–e** [5]. The general *Eqn. 1* is used to derive the kinetic constants[1]),

$$\Phi(AO_2) = \Phi(^1O_2)\frac{k_r[A]}{k_d + k_r[A]} \quad (1)$$

were k_r is the rate constant of chemical reaction with the substrate A, and k_d is the rate constant of physical deactivation by the solvent.

Kinetic measurements were carried out using a steroid concentration [A] ranging from $7.08 \cdot 10^{-4}$ M to $3.66 \cdot 10^{-3}$ M. A fixed rose-bengal concentration [RB] = $3.27 \cdot 10^{-6}$ M

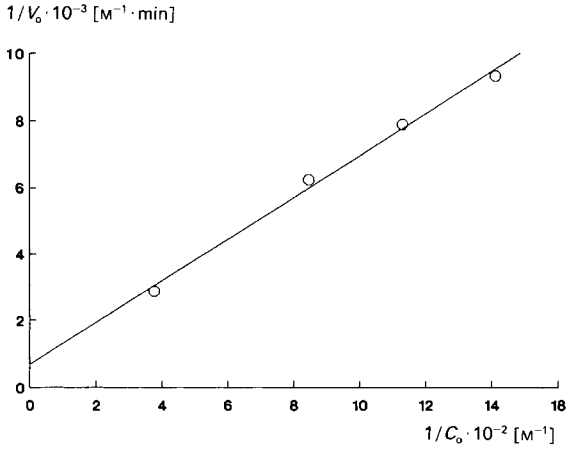


Fig. 1. $1/V_0$ vs. $1/C_0$ *plot for* **6** *at constant sensitizer concentration.* [RB] = $3.27 \cdot 10^{-6}$ M (data from *Table 2*). Fitting curve: $1/V_0 = 6.80 \cdot 10^2 + 6.26 \cdot (1/C_0)$, $\beta = 9.2 \cdot 10^{-3}$ mol·l^{-1}.

[1]) It is assumed that physical quenching of $^1O_2$ by the substrate is negligible compared to chemical quenching to yield photoproducts. Also, it is known that in reactive cyclic olefines, physical quenching (k_q) does not take place at all or does it with efficencies lower than quenching by the solvent (*i.e.* $k_q[A] < k_d$) [15]. From the above considerations, *Eqn. 2* simplifies to *Eqn. 1*.

$$\Phi(AO_2) = \Phi(^1O_2)\frac{k_r[A]}{k_d + (k_r + k_q)[A]} \quad (2)$$

Furthermore, it has been proved for **1b** that $(k_r + k_q) \approx k_r$ by measuring the half life of singlet oxygen under the reaction conditions (unpublished results).

Table 2. *Kinetic Parameters for the Dye-Sensitized Photo-oxygenation of* **6** *and* **1b** *at Constant Sensitizer Concentration.* [RB] = $3.27 \cdot 10^{-6}$ M and $9.8 \cdot 10^{-5}$ M, respectively[a]).

6				**1b**			
C_0 [M]	V_0 [M·min^{-1}]	K [min^{-1}]	e_r [%]	C_0 [M]	V_0 [M·min^{-1}]	K [min^{-1}]	e_r [%]
$7.08 \cdot 10^{-4}$	$1.1 \cdot 10^{-4}$	0.15	2.2	$1.77 \cdot 10^{-3}$	$3.2 \cdot 10^{-5}$	0.018	1.7
$8.85 \cdot 10^{-4}$	$1.3 \cdot 10^{-4}$	0.14	3.1	$2.48 \cdot 10^{-3}$	$4.2 \cdot 10^{-5}$	0.017	2.1
$1.18 \cdot 10^{-3}$	$1.6 \cdot 10^{-4}$	0.14	2.2	$3.55 \cdot 10^{-3}$	$6.2 \cdot 10^{-5}$	0.017	5.7
$3.66 \cdot 10^{-3}$	$3.5 \cdot 10^{-4}$	0.13	2.9	$7.09 \cdot 10^{-3}$	$1.1 \cdot 10^{-4}$	0.016	3.6
$\beta = 9.2 \cdot 10^{-3}$ mol·l^{-1}				$\beta = 3.3 \cdot 10^{-2}$ mol·l^{-1}			

[a]) C_0 = initial steroid concentration; V_0 = initial rate in steroid disappearance; K = pseudo-first-order rate constant; e_r [%] = average relative error of the fitting curve.

was empirically determined to ensure diffusion-controlled conditions in all experiments. It was done by plotting the initial reaction rate V_0 at constant steroid concentration against sensitizer concentration; while V_0 increases proportional to sensitizer concentration at low [RB], a plateau is reached at high concentrations because mass transfer of molecular oxygen becomes limiting [5]. The value of [RB] chosen represents 1/30 of that used for **1b** due to the higher reactivity of substrate **6**. The plot $1/V_0$ *vs.* $1/C_0$ at different initial steroid concentration C_0 fits to a straight line (*Fig. 1* and *Table 2*) from which the value $\beta = 9.2 \cdot 10^{-3}$ mol·l^{-1} (calculated as the ratio of slope to intercept) was obtained. Assuming a half lifetime $\tau_{1/2}$ for singlet oxygen in MeOH of 7 μs [16], the rate constant $k_r = 1.6 \cdot 10^7$ M^{-1}·s^{-1} ($k_r = 1/(\beta \cdot \tau_{1/2})$) was deduced.

2.4. *Geometry of the Substrates: Conformational Calculations and X-Ray Structures.* Conformational analysis of the photo-oxygenation substrates were carried out by molecular-mechanic calculations using *Allinger*'s MMPMI program (QCPE 395; a MM2 force field with *Brown*'s VESCF procedure for π calculations) [17]. Crystal structures were solved by X-ray diffraction for substrates **6** and **1b** using direct methods (see *Exper. Part*). Selected data are summarized in *Table 3* and the structures represented in *Fig. 2*. Of special interest for further discussions are the torsional angles between the styrenic double-bond plane and the allylic H-atoms. As shown in *Figs. 2a* and *2b*, both 8,9-didehydro derivatives **6** and **11** gave two energy-minimized ring-B conformations **A** and **B**. Differences in calculated heats of formation ($\Delta\Delta H_f^\circ$) for the two couples of conformers were less than 0.5 kcal/mol. Conformer **6B**, the one with the lower calculated strain

Table 3. *Selected Dihedral Angles* [°] *and Calculated Energies*[a]) *for Compounds* **1b**, **6**, **9**, *and* **11**

	6B		**6A**	**11B**	**11A**
	MMPMI	X-Ray[b])	MMPMI	MMPMI	MMPMI
C(9)–C(8)–C(7)–H_α	151	153	82	152	90
C(9)–C(8)–C(7)–H_β	–92	–90	–161	–91	–153
C(8)–C(9)–C(11)–H_α	127	129	122	111	–109
C(8)–C(9)–C(11)–H_β	–116	–112	–122	–128	–129
C(9)–C(8)–C(14)–H	–89	–87	–84	–112	–112
Aromatic torsion [°] C(5)–C(10)–C(9)–C(8)	–18	–20	20	–15	12
Strain energy E_s [kcal·mol^{-1}]	37.16		37.58	31.32	31.05
Heat of formation ΔH_f° [kcal·mol^{-1}]	–48.53		–48.05	–21.76	–22.07

Table 3 (cont.)

	1b			**9**
	MMPMI	X-Ray[b])		MMPMI
C(11)–C(9)–C(8)–H	108	102	C(6)–C(7)–C(8)–H	81
C(9)–C(11)–C(12)–H_α	110	98		
C(9)–C(11)–C(12)–H_β	–133	–132		
Aromatic torsion [°]			Aromatic torsion [°]	
C(1)–C(10)–C(9)–C(11)	–19	–16	C(10)–C(5)–C(6)–C(7)	19
Strain energy E_s (kcal·mol^{-1})	30.23		Strain energy E_s [kcal·mol^{-1}]	37.14
Heat of formation ΔH_f° [kcal·mol^{-1}]	–54.82		Heat of formation ΔH_f° [kcal·mol]	–47.61

[a]) Calculated according to *Allinger*'s MMPMI (QCPE 395).
[b]) Complete X-ray data available from the *Cambridge Crystallographic Data Centre*.

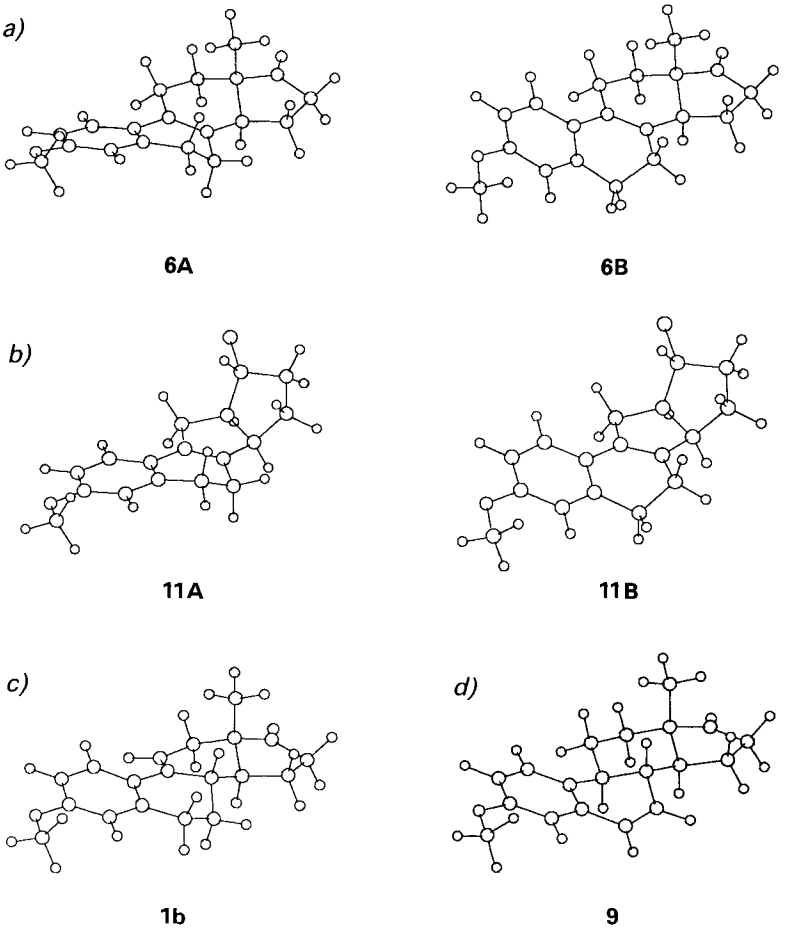


Fig. 2. *Molecular geometries as calculated by MMPMI:* a) *energy-minimized conformations for* **6**, b) *conformations for* **11**, *and* c) *and* d) *calculated stable conformations for* **1b** *and* **9**, *respectively*. Selected geometric data are given in *Table 3*. $\Delta\Delta H_f^\circ = [\Delta H_f^\circ(\mathbf{6A}) - \Delta H_f^\circ(\mathbf{6B})] = 0.5\,\text{kcal}\cdot\text{mol}^{-1}$; $\Delta\Delta H_f^\circ = [\Delta H_f^\circ(\mathbf{11A}) - \Delta H_f^\circ(\mathbf{11B})] = -0.3\,\text{kcal}\cdot\text{mol}^{-1}$.

energy, matched the X-ray-determined structure. *Figs. 2c* and *2d* show the most stable calculated conformations for compounds **1b** and **9** (no other local minima of equivalent strain energy were found). Again, it should be noted that there is a very good correspondence between the calculated and the X-ray structures for **1b**.

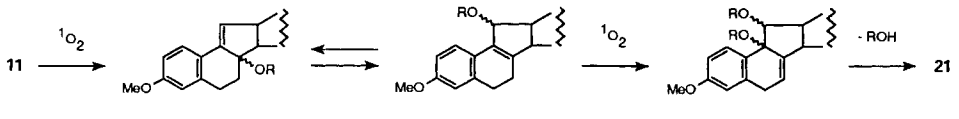
3. Discussion. – 3.1. *Photo-oxygenation Products.* Essentially, singlet oxygen adds to olefinic systems according to three reaction modes which give rise to distinct photoproducts: *a*) [2 + 2] cycloaddition yielding 1,2-dioxetanes which are usually thermally or photochemically cleaved to dicarbonilic fragments, *b*) ene-type reaction yielding allylic hydroperoxides which often tend to be reduced to allylic alcohols and dehydrated to conjugated olefins, and *c*) [2 + 4] cycloaddition to conjugated olefins to give endoperoxides. Assigning a reaction path is difficult since the primary photoproducts (often not detected) may evolve to common final products through thermal rearrangements [18].

The 9,11-didehydroestrone **1b** yields the fragmentation product **3** as the only isolated compound in 50% yield. The kinetics of the reaction gave a β value of $3.3 \cdot 10^{-2}$ mol·l^{-1} (*Table 2*) which indicates that **1b** is an activated olefin for the electrophilic addition of $^1O_2$. A 1,2-dioxetane was suggested as a primary product [5].

The 8,9-didehydroestrone **6** is structurally analog to **1b** but has a higher degree of substitution at the styrenic double bond. Both allylic hydroperoxides and their derivatives as well as a fragmentation product are obtained. The result suggests a competition between ene-type reaction and [2 + 2] cycloaddition. Out of the three hydroperoxides **13**, **17**, and **18** initially formed, only one turns out to be stable (**13**; *Scheme 3*). It is worth noting that it is the only primary ene-type photoproduct that maintains the styrenic conjugation as opposed to the other transient hydroperoxides **17** and **18** which contain an isolated double bond. Hydroperoxide **13** undergoes a *Hock*-type rearrangement to triketone **12** (50% yield) upon acid treatment ($MeOH/H_2SO_4$). The specific conditions and long reaction times required for this rearrangement indicate that the fragmentation product **12** obtained on irradiation of **6** is not formed from a hydroperoxide by acid rearrangement. Moreover, no **12** was detected when purified **13** was subjected to photo-oxygenation. It should be emphasized that we have no evidence of oxidative cleavage products arising from rearrangement of ene-type products in the photo-oxygenation reaction itself. Consistently, we assume that both processes, ene-type reaction and [2 + 2] cycloaddition, compete as primary processes.

Steroid analog **11**, although structurally close to **6** in having the same double-bond substitution pattern, is less reactive. But no direct comparison between **6** and **11** can be done since **11** was photo-oxygenated in $MeOH/CH_2Cl_2$ 2:1 instead of MeOH, the solvent of choice for **1b**, **6**, and **9**. The formation of **21** from **11** may be easily rationalized as the result of a double ene-type reaction where the initial allylic hydroperoxide rearranges to a more activated olefinic system which adds a second molecule of singlet oxygen [14] (see *Scheme 5*).

Scheme 5



R = OH, Me

The 6,7-didehydroestrone **9** is the slower reacting substrate: after a 15-fold longer irradiation time than for **6**, only 40% conversion was observed (by ^{1}H-NMR). An ene-type reaction takes place leading to the unstable allylic hydroperoxide **20**. As in the case of **6** and **11**, the tendency of the primary ene-type products to aromatize or extend conjugation drives the reaction through a reductive dehydration to yield equilenin (**15**).

3.2. *Factors Directing Product Distribution.* Provided the same reaction conditions (solvent, temperature, sensitizer and oxygen concentration, except for **11** with regard to solvent), the different behaviour of the substrates, both observed in the reaction rates and product distribution, should be rationalized in terms of intrinsic electronic and geometric factors.

3.2.1. *Electronic Factors.* The set of styrenic compounds described differ in the double-bond position and degree of substitution. Thus, **1b**, **6**, and **11** are *p*-methoxy-substituted styrenes, while **9** has a *m*-methoxy substitution. On the other hand, **6** and **11** are tetrasubstituted olefins, while **1b** is trisubstituted and **9** is disubstituted. These structural considerations allow a first classification attending to general criteria directing electrophilic additions to double bonds.

Of special interest are the different rate constants and reaction patterns for the two *p*-methoxy-derivatives **1b** and **6**. Both are activated acceptors of $^1O_2$ when compared to other described compounds [11] [19], with rate constants of $1.6 \cdot 10^7$ $M^{-1} \cdot s^{-1}$ ($\beta = 9.2 \cdot 10^{-3}$ $mol \cdot l^{-1}$) for **6** and $4.3 \cdot 10^6$ $M^{-1} \cdot s^{-1}$ ($\beta = 3.3 \cdot 10^{-2}$ $mol \cdot l^{-1}$) for **1b** (k_r is *ca.* 4-fold higher for the former). Other authors have documented an increase in reactivity between 3- and 20-fold when a H-atom is replaced by an alkyl group at the olefinic system [16] [20]. The distribution of reaction products, however, does not match the trend of observed reactivities. If ene-type reaction and [2 + 2] cycloaddition are in competition for a given substrate, the rate constant ratio $k_{[2+2]}/k_{ene}$ will increase with double-bond activation. Nevertheless, while **1b** gives the fragmentation product **3** in 50% yield, **6** affords three allylic hydroperoxides with a global yield of 60% (in addition to 16% of isolated triketone **12**). Therefore, the ratio fragmentation/ene-type products for **6** is lower than that expected for its increased reactivity relative to **1b**.

3.2.2. *Geometric Factors.* It is often argued that ene-type processes require the allylic H-atom to be orthogonal to the π-system plane in order to be withdrawn during the reaction. In principle, in cyclohexene systems with no sterical interferences, the more axial the H-atoms are, the easier the abstraction.

The preferred calculated conformations of **6** are **6A** and **6B** (see *Table 3* and *Fig. 2a*), the latter being close to the solid-state structure as determined by X-ray crystallography (*Chapt. 2.4*). The allylic hydroperoxide **17** (configuration at C(9) unknown) is generated by H–C(7) abstraction from **6**. Both conformers **6A** and **6B** have an axial H-atom at C(7); thus **6A** would give the 9α-hydroperoxide by H_α–C(7) abstraction and **6B** the 9β-hydroperoxide by H_β–C(7) abstraction. Hydroperoxide **18** arises from H–C(14) abstraction which is axial on the α-face of both **6A** and **6B**. This geometric view, however, fails to explain the formation of 8α-hydroperoxide **13**. H-Abstraction would operate on the pseudoequatorial H–C(11) (dihedral angle 122–127° (calculated) or 129° (X-ray)). Even assuming a less favourable conformation in this case, the observed 1:1:1 molar ratio for hydroperoxides **13**/**17**/**18** has no explanation on the basis of substrate geometry.

The X-ray-determined and calculated stable conformation of **1b** (*Table 3, Fig. 2c*) has a half-chair conformation for ring C where two allylic H-atoms, H_α–C(12) and H–C(8),

are quasiorthogonal to the olefinic π-system plane. This geometry would predict some extend of ene-type reaction, which, however, was not observed (only seco-aldehyde **3** was detected and isolated). While abstraction of the pseudo-axial H_β–C(8) could be prevented by the developing 1,3-diaxial interaction with the 18β-Me group, the lack of ene-type products arising from H_α–C(12) abstraction is more surprising. This H-atom lays on the α-face with a dihedral angle of 98° (X-ray; calculated 110°), relative to the C(9)=C(11) bond and has no apparent steric hindrance with any neighbouring group. The deviation from orthogonality seems not large enough to justify the lack of this type of reaction by solely attending to geometric factors.

Last, the behaviour of **9** and **11** satisfies the predictions from geometric considerations. Since the two conformers **11A** and **11B** are expected to be present in solution (*Table 3*, *Fig. 2b*), both having an axial allylic H–C(7), the geometric considerations made for the parent didehydroestrane **6** are applicable. Other pseudoaxial positions are also found for the α-face allylic H-atoms at C(11) and C(14) in both **11A** and **11B**. Therefore, an ene-type reaction has the proper requirements to take place. Regarding to **9**, the single allylic H_β–C(8) occupies an axial position (*Table 3*, *Fig. 2d*). Its abstraction might be prevented by 1,3-diaxial interaction with the 18β-Me as argued for **1b** above. Here, however, the lower substrate activation due to the *m*-substitution makes it unlikely that [2 + 2] cylcoaddition can compete. Upon extended reaction time, the abstraction occurs to yield the unstable hydroperoxide **20**.

Summarizing, the product distribution for **9** and **11** is satisfactorily rationalized by simple geometric and electronic factors. On the other hand, no easy explanation justifies the results obtained for **1b** and **6**. Both, formation of the hydroperoxide **13** from **6** and the lack of ene-type reaction for **1b** disagree with the above considerations.

3.2.3. Fukui's *Rule*. The apparent inconsistency observed in the behaviour of **1b** and **6** can be best explained by applying *Fukui*'s rule [21] [18]. It states that the orientation of $^1O_2$ attack on an olefin is determined by the factors that control the orientation of the initially attacking O-atom and the tail O-atom in a perepoxide structure. When applying the rule to **1b**, it predicts that the attacking O-atom will add to the end of the styrenic dipole (C(11)). Attack on the β-face is unlikely due to the sterical hindrance by 18β-Me which will prevent either $^1O_2$ approach or H_β–C(8) abstraction. Therefore, O-attack occurs preferentially on the α-face and then, since no α-allylic H-atom is available, the formation of a 1,2-dioxetane is expected provided the substrate is an electron-rich olefin. Therefore, the preference for oxidative fragmentation of **1b** agrees with *Fukui*'s rule.

In the case of **6**, the rule would predict a preferential abstraction of a H-atom at C(11) following O-attack at C(8). The low accessibility of the pseudoequatorial H_α–C(11) justifies that the resulting hydroperoxide **13** is not the major reaction product. Instead, other hydroperoxides and a compound from [2 + 2] cycloaddition are also formed.

Work on compound **11** was done in the laboratory of Dr. *Martin Demuth* during a collaboration programme between the *Max-Plank-Institut für Strahlenchemie*, D-4330 Mülheim, a.d. Ruhr, and the *Institut Químic de Sarrià*, E-08017 Barcelona.

Experimental Part

General. TLC: plates from *Merck* (silica gel *60F-254*). Column chromatography (CC): *Merck* 70–230 mesh. HPLC: *Hewlett-Packard-1090* coupled to a *Hewlett-Packard-3390-A* integrator; *Spherisorb ODS 2* column, 15 cm length, 0.39 cm diameter, 5 or 10 µl injection loop. GC: *Hewlett-Packard-5890-A* equipped with a FID detector and coupled to a *Hewlett-packard-3392-A* integrator; capillar *OV 101* column, 27 m length. M.p.: *Gallenkamp* apparatus; uncorrected. UV: *Hewlett-Packard-8450-A* spectrophotometer; λ_{max} in nm, ε in $l \cdot cm^{-1} \cdot mol^{-1}$. IR (in cm^{-1}): *Perkin-Elmer-683* instrument. ^{1}H-NMR: *Bruker-AC-80* or *Varian-XL-200* spectrometer; δ in ppm. rel. to TMS as internal standard. MS: *Hewlett-Packard-5995-A* instrument; *m/z* for the main peaks (rel. intensity).

General Irradiation Procedure. For the prep. photo-oxygenations, a soln. of the substrate and the sensitizer (rose bengal) in dry MeOH was placed in a 300-ml tubular *Pyrex* photoreactor and irradiated with a halogen lamp (*Sylvania*, 500 W) fitted with a cooling jacket. O_2 was bubbled through the soln. at constant flux (0.5 $ml \cdot s^{-1}$). Temp. was kept at 0° by an auxiliary external cooling system and solvent evaporation avoided by means of a gas trap. Anal.-scale photo-oxygenations were carried out in a 30-ml *Pyrex* tube attached to the lamp and fitted with an inlet of O_2.

Kinetic Measurements. The general method previously described [5] was used for the kinetics of **6**. Samples were taken at regular time intervals directly from the reaction vessel through a rubber septum. Analysis was performed by HPLC with MeCN/H_2O 7:3 (1.5 $ml \cdot min^{-1}$ at 25°) and UV detector at 280 nm. Absolute concentration of the substrate was calculated by calibrating the detector in each run with standardized solns. Kinetic parameters were calculated by linear least-square fitting of experimental data to *Eqn. 1*, and relative errors by standard statistical methods.

Crystal Structures. Colourless crystals of **1b** were obtained by slow evaporation from an acetone/Et_2O soln. A suitable monocrystal was mounted on an *Enraf-Nonius-CAD4* diffractometer. Graphite-monochromated MoK_α radiation ($\lambda = 0.71069$ Å) was used. Cell dimensions were determined by least-squares methods from 25 reflections ($5 < \theta < 16°$). $a = 7.051(3)$, $b = 14.580(4)$, $c = 14.886(7)$ Å, $\alpha = \beta = \gamma = 90$. The $P2_12_12_1$ space group was uniquely determined from the observed extinctions. $Z = 4$, $D_x = 1.255$ $g \cdot cm^{-3}$ in good agreement with related steroid crystals. Using $\omega/2\theta$ scan up to $2\theta = 50\sigma$, 1349 unique reflections were measured; of the total, 572 were considered as observed ($I \geq 2.5\sigma(I)$). After the *Lorentz* and polarization corrections were applied, normalized structure factor amplitudes were computed using the MULTAN program [22]. Initial standard procedure did not give any recognizable fragment. A subsequent run using BFAC = 5 gave rings A and B of the steroid framework, posterior weighted *Fourier*'s afforded the whole molecule. The refinement was carried out by full-matrix least-squares on *F* using the program SHELLX [23]. H-Atom positions (except those corresponding to allylic H-atoms) were calculated riding on the adjacent C-atoms asuming C–H = 1.08 Å and refined with an overall temp. factor. Final conventional *R* was 0.038.

Colourless crystals of **6** were obtained by the same procedure as described for **1b**. An isometric monocrystal suitable for X-ray analysis was mounted on a *CAD4* diffractometer. Cell dimensions determined as above ($5 < \theta < 13°$) gave: $a = 8.613(4)$, $b = 9.205(3)$, $c = 10.579(4)$ Å, $\alpha = 98.46(4)$, $\beta = 98.08(4)$, $\gamma = 111.57(3)$. The space group is $P\bar{1}$, $Z = 2$, $D_x = 1.226$ $g \cdot cm^{-3}$. Using $\omega/2\theta$ scan up to $2\theta_{max} = 50°$, 2657 unique reflections were measured of which 1996 were considered as observed ($I \geq 2.5\sigma(I)$). After the *Lorentz* and polarization corrections were applied, normalized structure factor amplitudes were computed using the MULTAN program. All non-H atoms were located from the phase set with the highest figure of merit. The refinement was performed by full-matrix least-squares methods (SHELLX). All H-atoms were located in subsequent difference *Fourier* syntheses. Final conventional *R* was 0.045. Both enantiomers are present in the unit cell.

Atomic coordinates and equivalent isotropic thermal parameters of **1b** and **6** have been deposited at the *Cambridge Crystallographic Data Centre.*

1. *Photo-oxygenation of (±)-3-Methoxyestra-1,3,5(10),8-tetraen-17-one* (**6**). 1.1. *Photo-oxygenation of* **6** *and Isolation of Products.* Compound **6** (374 mg) and rose bengal (34 mg) in 300 ml of dry MeOH were irradiated at 0° for 40 min while O_2 was bubbled through the soln. Solvent evaporation and chromatographic purification (silica gel, cyclohexane/AcOEt 20:3→2:1) yielded four main fractions (in order of increasing polarity).

Fraction 1 (16 mg) was identified as *(±)-3-methoxyestra-1,3,5(10),8,14-pentaen-17-one* (**14**), identical by its spectral data with authentic material. M.p. 108–110° (from Et_2O). UV: 312 (28000). IR: 1740, 1610, 1595, 1565, 1500, 1250, 1040.

Fraction 2 (58 mg) was crystallized from acetone/light petroleum ether: 42 mg of *(±)-3-methoxyestra-1,3,5(10),6,8-pentaen-17-one* (**15**). M.p. 187–189°. UV (EtOH): 267 (5300), 278 (5500), 289 (4000), 323 (2500), 337 (2600). IR: 1740, 1625, 1600, 1510, 1490. ^{1}H-NMR ($CDCl_3$, 200 MHz): 7.86 (*d*, $J = 9.0$, H–C(1)); 7.62 (*d*, $J = 8.2$, H–C(7)); 7.26 (*d*, $J = 8.2$, H–C(6)); 7.19 (*dd*, $J = 9.0, 2.8$, H–C(2)); 7.13 (*d*, $J = 2.8$, H–C(4)); 3.91 (*s*, MeO); 0.79 (*s*, Me). MS: 280 (81, M^+), 224 (57), 223 (47).

Fraction 3 (99 mg) was rechromatographed (SiO_2, cyclohexane/AcOEt 4:1) and crystallized from Et_2O: 30 mg of pure *(±)-8α-hydroperoxy-3-methoxyestra-1,3,5(10),9(11)-tetraen-17-one* (**13**). M.p. 153–155° (dec.) UV (EtOH): 262 (14800), 294 (3700). IR 3360, 1740, 1630, 1610, 1570, 1240. ^{1}H-NMR ($CDCl_3$, 200 MHz): 7.65 (br., OOH, disappears after shaking with D_2O); 7.40 (*d*, *J* = 8.6, H–C(1)); 6.73 (*dd*, *J* = 8.6, 2.8, H–C(2)); 6.65 (*d*, *J* = 2.8, H–C(4)); 6.20 (*dd*, *J* = 5.8, 3.2, H–C(11)); 3.79 (*s*, MeO); 0.95 (*s*, Me). MS: 314 (7, M^+), 298 (20), 280 (35), 237 (44), 223 (40), 211 (38), 165 (70), 152 (40). Anal. calc. for $C_{19}H_{22}O_4$ (314.38): C 72.59, H 7.05; found: C 72.26, H 6.99.

Fraction 4 (66 mg) was rechromatographed (SiO_2, cyclohexane/AcOEt 4:1) and crystallized from acetone/light petroleum ether: 38 mg of *(±)-3-methoxy-8,9-secoestra-1,3,5(10)-trien-8,9,17-trione* (**12**). M.p. 162–164°. UV (EtOH): 272 (7800). IR: 1740, 1710, 1680, 1605, 1570, 1500, 1255. ^{1}H-NMR ($CDCl_3$, 200 MHz): 7.28 (*d*, *J* = 9.2, H–C(1)); 6.76 (*m*, H–C(2), H–C(4)); 3.83 (*s*, MeO); 1.14 (*s*, Me). MS: 314 (21, M^+), 190 (17), 176 (29), 162 (100). Anal. calc. for $C_{19}H_{22}O_4$ (314.38): C 72.59, H 7.05; found: C 72.86, H 7.00.

Pentaenes **14** and **15** were not detected in the crude photo-oxygenation mixture from **6** by HPLC/UV (linear gradient MeCN/H_2O 4:6 from 0 to 8 min and 7:3 from 8 to 17 min, 1.5 ml·min^{-1}, 25°), even when the mixture was kept at r.t. for 1 or 2 h after irradiation. Besides **12** and **13**, the products **17** and **18** were detected (no intense absorption at 280 nm; similar polarity than **13**). Upon treatement of crude **12**/**13**/**17**/**18** with NH_4I or after extended contact with SiO_2 **17** and **18** were easily converted to **14** and **15**. Structures *(±)-9-hydroperoxy-3-methoxyestra-1,3,5(10),7-tetraen-17-one* (**17**) and *(±)-9-hydroperoxy-3-methoxyestra-1,3,5(10),8(14)-tetraen-17-one* (**18**) were tentatively assigned based on the ^{1}H-NMR of crude **12**/**13**/**17**/**18** (see *1.2.1*).

1.2. *^{1}H-NMR Data.* 1.2.1. *Crude Reaction Mixture* **12**/**13**/**17**/**18**. To a soln. of **6** (40.4 mg) in 25 ml of dry MeOH in a *Pyrex* tube, 1 ml of rose bengal soln. (3.8 mg/ml) was added. The soln. was cooled at 0° and photo-oxygenated for 35 min. Then 3-methoxyestrone (8.1 mg) was added as internal standard, and the solvent was evaporated. The residue was disolved in $CDCl_3$, the rose bengal filtered off and the ^{1}H-NMR recorded immediately. ^{1}H-NMR: **12** (14%), **13** (21%), **17** (19%), and **18** (18%); yields calculated from the Me integrals referred to the internal standard (δ = 0.90); no **14** or **15**. ^{1}H-NMR ($CDCl_3$, 80 MHz): 6.20 (*dd*, *J* = 5.8, 3.2, H–C(11), **13**); 5.90 (*ddd*, *J* = 3.6, 3.6, 1.7, H–C(7), **17**); 3.83 (*s*, MeO, **12**); 3.81 (*s*, MeO, **18**); 3.80 (*s*, MeO, **17**); 3.79 (*s*, MeO, **13**); 1.13 (*s*, Me, **12**); 1.08 (*s*, Me, **18**); 0.96 (*s*, Me, **13**); 0.78 (*s*, Me, **17**).

1.2.2. *Reduced Crude Mixture.* As described in *1.2.1*, **6** (35.7 mg) was photo-oxygenated (25 ml of MeOH, 3.3 mg of rose bengal). After 35 min, 3-methoxyestrone (6.6 mg) was added as internal standard and the soln. treated with NH_4I (100 mg) at r.t. for 1 h. After evaporation, the residue was taken up in $CHCl_3$ and the soln. washed with aq. $Na_2S_2O_3$ soln., dried ($MgSO_4$), and evaporated. ^{1}H-NMR: no **13**, **17**, or **18**; **12** (14%), **16** (18%), **14** (11%), and **15** (19%). ^{1}H-NMR ($CDCl_3$, 80 MHz): 7.85 (*d*, *J* = 9, H–C(1), **15**); 7.62 (*d*, *J* = 8, H–C(7), **15**); 6.00 (*dd*, *J* = 5.0, 3.8, H–C(11), **16**); 5.85 (*dd*, *J* = 2.7, 2.7, H–C(15), **14**); 1.13 (*s*, Me, **12** and **14**); 0.95 (*s*, Me, **16**); 0.79 (*s*, Me, **15**).

1.3. *Reduction of* **13** *with NH_4I.* A soln. of **13** (7.4 mg) in MeOH (1 ml) was treated with aq. 0.5N NH_4I (0.5 ml) and the soln. stirred at r.t. for 1 h. After dilution with 25 ml of AcOEt, the org. phase was washed with aq. $Na_2S_2O_3$ soln., dried ($MgSO_4$), and evaporated: 6.8 mg of a white solid, identified as *(±)-8α-hydroxy-3-methoxyestra-1,3,5(10),9(11)-tetraen-17-one* (**16**) by comparison of its spectral data with an authentic sample synthesized independently by epoxidation of **6** [12]. UV (EtOH): 260 (13600), 291 (2900). IR: 3480, 1740, 1610, 1570, 1500, 1230. ^{1}H-NMR ($CDCl_3$, 80 MHz): 7.41 (*d*, *J* = 8.3, H–C(1)); 6.74 (*dd*, *J* = 8.3, 2.7, H–C(2)); 6.68 (*d*, *J* = 2.7, H–C(4)); 6.00 (*dd*, *J* = 5.0, 3.8, H–C(11)); 3.79 (*s*, MeO); 0.95 (*s*, Me).

1.4. Hock *Cleavage of* **13**. Hydroperoxide **13** (5.3 mg) was added to MeOH (1 ml) and 20% H_2SO_4 (0.5 ml) and stirred overnight. The coloured soln. was diluted with AcOEt, washed with aq. $NaHCO_3$ soln. and H_2O, dried ($MgSO_4$), and evaporated: greenish oil, **13**/**12** *ca.* 1:1 (TLC). IR: strongly absorptions of **12** at 1740, 1710, 1680.

2. *Photo-oxygenation of 3-Methoxyestra-1,3,5(10),6-tetraen-17-one* (**9**). 2.1. A soln. of **9** (126 mg) in MeOH (150 ml) at 0° was photo-oxygenated using rose bengal (12 mg) as sensitizer. TLC and ^{1}H-NMR after 10 h: 2 main products and **9**, 1:1:3. Structure *(±)-6-hydroperoxy-3-methoxyestra-1,3,5(10),7-tetraen-17-one* (**20**) was tentatively assigned to one of the photoproducts. The structure of the second photoproduct remains still unknown. ^{1}H-NMR ($CDCl_3$, 80 MHz): 6.05 (*d*, *J* = 11.8, H–C(7), **9**); 5.77 (br. *d*, *J* = 4.0, H–C(7,), **20**); 5.42 (*m*, H–C(6), **20**); 4.65 (*d*, *J* = 2.2, unknown); 4.38 (*dd*, *J* = 7.0, 2.2, unknown); 0.90 (*s*, Me, **9**); 0.86 (*s*, Me, **20** or unknown); 0.84 (*s*, Me, unknown or **20**).

Extensive degradation of the crude product was observed upon longer reaction times or upon standard chromatographic procedures (SiO_2) for separation.

2.2. As described in *2.1*, **9** (102 mg) was photo-oxygenated for 10 h (100 ml of MeOH, 10 mg of rose bengal). The resulting soln. was treated with 200 mg of NH_4I at r.t. for 3 h and then evaporated. The residue was diluted with $CHCl_3$, the soln. washed with aq. $Na_2S_2O_3$ soln., dried ($MgSO_4$), and evaporated, and the residue purified by CC

(SiO_2, cyclohexane/AcOEt 2:1): 2 main fractions. The less polar one (70 mg) was identified by GC (260°) and ^{1}H-NMR as a mixture of **9** (64%) and *3-methoxyestra-1,3,5(10),6,8-pentaen-17-one* (**15**; 36%), which could not be further separated by standard CC (silica gel). ^{1}H-NMR ($CDCl_3$, 80 MHz): 7.86 (*d*, J = 9.0, H–C(1), **15**); 7.62 (*d*, J = 8.2, H–C(7), **15**); 6.51 (*d*, J = 11.8, H–C(6), **9**); 6.06 (*d*, J = 11.8, H–C(7), **9**); 3.91 (*s*, MeO, **15**); 3.80 (*s*, MeO, **9**); 0.90 (*s*, Me, **9**); 0.78 (*s*, Me, **15**).

Attempts to identify other components from the remaining fractions were unsuccessful.

3. *Photo-oxygenation of (±)-17α-Chloro-3-methoxy-12,18-dinor-13α-estra-1,3,5(10),8-tetraene* (**11**). A soln. of **11** (300 mg) in MeOH (16 ml) and CH_2Cl_2 (8 ml) was irradiated for 5 h in the presence of *Sensitox* (220 mg), while O_2 was bubbled through the soln. The photosensitizer was separated by filtration, the filtrate diluted with MeOH, and the soln. treated with excess $NaBH_4$ at 0° for 30 min. After evaporation, the residue was taken up in CH_2Cl_2, the soln. washed several times with H_2O, dried ($MgSO_4$), and evaporated, and the oily residue (287 mg) submitted to CC (SiO_2, toluene/Et_2O 98:2): *(±)-17α-chloro-3,11α-dimethoxy-12,18-dinor-13α-estra-1,2,5(10),6,8-pentaene* (**21**), 40% yield. IR: 2980–2750, 1470, 1430, 1290, 1170–1050. ^{1}H-NMR ($CDCl_3$, 200 MHz): 7.85 (*d*, J = 9.0, H–C(1)); 7.68 (*d*, J = 8.5, H–C(7) or H–C(6)); 7.25 (*d*, J = 8.5, H–C(6) or H–C(7)); 7.16 (*dd*, J = 9.0, 2.5, H–C(2)); 7.11 (*d*, J = 2.5, H–C(4)); 5.08 (*s*, H–C(11)); 4.15 (*m*, H–C(17)); 4.07 (*m*, H–C(14)); 3.90 (*s*, MeO–C(3)); 3.45 (*s*, MeO–C(11)); double-resonance experiments were carried out for the unequivocal chemical-shift assignment of arom. protons and for the calculation of coupling constants (see [14]). MS: 302 (M^+), 271 (100).

REFERENCES

[1] A. Windaus, J. Brunken, *Justus Liebigs Ann. Chem.* **1928,** *460,* 225.

[2] P. Lupón, J. Gómez, J.-J. Bonet, *Angew. Chem.* **1983,** *95,* 757; *ibid. Suppl.* **1983,** 1025–1034; *ibid. Int. Ed.* **1983,** *22,* 711.

[3] A. Sedee, G. Beijersbergen van Henegouwen, *Arch. Pharm. (Weinheim, Ger.)* **1985,** *318,* 111; A. Sedee, G. Beijersbergen van Henegouwen, N. J. DeMol, G. Lodder, *Chem. Biol. Interact.* **1984,** *51,* 357.

[4] P. Lupón, F. Grau, J.-J. Bonet, *Helv. Chim. Acta* **1984,** *67,* 332.

[5] A. Planas, P. Lupón, M. Cascalló, J.-J. Bonet, *Helv. Chim. Acta* **1989,** *72,* 715.

[6] A. Planas, N. Sala, J.-J. Bonet, *Helv. Chim. Acta* **1989,** *72,* 725.

[7] S. N. Ananchenko, I. V. Torgov, *Tetrahedron Lett.* **1963,** 1553; T. A. Serebryakova, A. V. Zakharychev, M. A. Nekrasova, S. N. Ananchenko, I. V. Torgov, London Patent Office, 1971, 1308121.

[8] D. Hainaut, R. Bucourt, *Bull. Soc. Chim. Fr.* **1977,** 119.

[9] C. Brosa, J. C. Ferrer, C. Malet, J. M. Amézaga, *J. Org. Chem.* **1989,** *54,* 3984.

[10] M. Demuth, *Chimia* **1984,** *38,* 257.

[11] A. P. Scaap, K. A. Zaklika, in 'Singlet Oxygen', Eds. H. H. Wasserman and R. W. Murray, Academic Press, New York, 1979, Chapt. 6; E. Wistuba, C. Ruchardt, *Tetrahedron Lett.* **1981,** *22,* 3389.

[12] R. P. Stein, G. C. Buzby, H. Smith, *Tetrahedron* **1970,** *26,* 1917.

[13] P. A. Burns, C. S. Foote, *J. Org. Chem.* **1976,** *41,* 908.

[14] A. Planas, J.-J. Bonet, M. Demuth, in preparation.

[15] K. Gollnik, H. J. Kuhn, in 'Singlet Oxygen', Eds. H. H. Wasserman and R. W. Murray, Academic Press, New York, 1979, Chapt. 8, p. 288.

[16] P. B. Merkel, D. A. Kearns, *J. Am. Chem. Soc.* **1972,** *94,* 1029; *ibid.* **1972,** *94,* 7244.

[17] N. Allinger, 'QCPE-395 + QCPE-318 Molecular Mechanics Package: STRPI, MAKESTM, MMPMI, MDRAWI', Serena Software, University of Georgia.

[18] A. A. Frimer, *Chem. Rev.* **1979,** *79,* 359.

[19] B. Stevens, S. R. Perez, *Mol. Photochem.* **1974,** *6,* 1; J. C. Carmier, X. Deglise, *C. R. Hebd. Séances Acad. Sci., Ser. C* **1973,** *277,* 1187.

[20] D. Brkic, P. Forzatti, I. Pasquon, F. Trifiro, *J. Photochem.* **1976,** *5,* 23; K. Gollnick, *Adv. Chem. Ser.* **1968,** *3,* 77.

[21] S. Inagaki, H. Fujimoto, K. Fukui, *Chem. Lett.* **1976,** 749.

[22] P. Main, S. J. Fiske, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq, M. M. Woolfson, 'MULTAN, 1980', Universities of York, England, and Louvain, Belgium.

[23] G. M. Sheldrick, 'SHELLX76', University of Cambridge, England, 1976.