3. *Massenspektrum von Trisdesaspidin* (**19**) (Fig. 3). Auch in diesem Spektrum tritt eine schwache Spitze bei *m/e* 668 auf, die auch hier auf thermische Bildung von Filixsäure (**1**) durch Rottleron-Umlagerung (Schema c)) deutet. Die Spitze bei *m/e* 446 könnte von Desaspidin-BB (**20**) herrühren, das sich thermisch nach Schema d) bilden kann. Die weiteren Spitzen sind gut verständlich, wenn man auch hier annimmt, dass vorwiegend die in den Formeln angedeuteten Spaltungen nach Schema a) und b) stattfinden.

4. *Massenspektrum von Trispara-aspidin* (**24**) (Fig. 4). Die Spitze höchster Masse liegt hier bei *m/e* 668, was dem Molekel-Ion entspricht. Ob hier daneben auch thermische Rottleron-Umlagerung stattfindet, lässt sich durch Massenspektroskopie nicht entscheiden, weil die Produkte isomer sein würden. Die Spitze bei *m/e* 460 könnte von **25** herrühren, entstanden nach Schema d). Es könnte sich natürlich auch um Albaspidin-BB (**11**) handeln, das aus **25** durch Rottleron-Umlagerung entstehen kann oder auch direkt aus 2 Molekeln **24** durch Vereinigung der zwei linken Kerne. Die weiteren starken Spitzen sind hier wieder am besten verständlich, wenn man annimmt, dass Spaltungen nach dem Schema a) und b) bevorzugt stattfinden.

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307. Steroid Total Synthesis, Part IV[1]); (±)-13β-Ethyl-17α--ethynyl-17β-hydroxy-gon-4-en-3-one[2])

by **M. Rosenberger, T. P. Fraher** and **G. Saucy**

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(27. IX. 71)

Summary. The title compound (*Norgestrel*), a potent progestational agent, has been prepared by a new total synthesis. The scheme is based on earlier work with BCD-tricyclic intermediates, condensation of 2-ethyl-cyclopentane-1,3-dione with 2-[2-diethylamino-ethyl]-6-[4-*t*-butoxy-pentyl]-tetrahydropyran-2-ol being the key step. The synthesis features the addition of acetylene to a $\Delta^{5(10)}$-4-oxa-17-keto intermediate, followed by a novel transformation to the final product.

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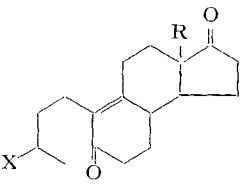
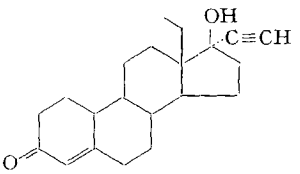
[1]) Part III, see [1].

[2]) Norgestrel; see [2].

In the first publication [3] of this series, a novel and efficient synthesis of (±)-17β-hydroxy-deA-androst-9-en-5-one has been reported. As an extension of this work, we now wish to describe a new synthesis of (±)-13β-ethyl-gon-4-ene-3,17-dione(**17**) [4][3]) and *Norgestrel* (**2**) [2], a very important 18-homo-19-norsteroid. Our plan consisted of first synthesizing an 18-homo-BCD-tricyclic intermediate of type **1b**, (X = precursor for a keto group), utilizing the experience gained in the preparation of simple homologs, such as the one mentioned previously and particularly **1a**, *cf.* [1] and [6]. At the outset, the use of the *t*-butoxy moiety as a precursor for a 3-keto group seemed rather attractive[4]). Thus, we decided to first synthesize the tricyclic compound **1b**. The second part of our plan envisaged the transformation of **1b** into *Norgestrel* [2] by a novel process involving 4-oxa-type intermediates. The preparation



1a, X = H, R = CH_3
(unnatural series)
1b, X = —O—; R = C_2H_5
(racemic series)



2 (racemic; *Norgestrel*)

of **1b** turned out to be straightforward, but we encountered some interesting difficulties in the second part of our synthesis. As will be seen, the major problem could be solved.

Results and Discussion. – The synthesis of the racemic BCD-tricyclic intermediate **12**, our first goal, is illustrated in scheme 1. Starting with the lactol **3**, whose preparation from glutaraldehyde is described in a separate paper [7], the '*Mannich* base' **5** was obtained in 78% yield by the previously elaborated method (vinyl *Grignard* reaction, followed by oxidation of the product **4** with manganese dioxide in the presence of diethylamine) [6]. The base **5** was characterized as its oxalate. Condensation of **5** with 2-ethyl-cyclopentane-1,3-dione [8] in boiling xylene-acetic acid afforded the diene **6** which was purified by chromatography on alumina. The yield **5** → **6** was 86%. In the NMR. spectrum[5]) the product **6** showed the vinyl proton at C–9 as a triplet at δ 5.54 ppm (J = 2–3 Hz; dihedral angle of ~60°), the *t*-butoxy group as a singlet at δ 1.22 ppm, and the CH_3 of the ethyl group as a triplet centered at δ 0.83 ppm (J = 7 Hz). Determination of the stereochemical uniformity of C–3 and C–6a was not possible on the basis of spectral analysis; presumably, the '*trans*'-isomer (ethyl and 4-*t*-butoxypentyl groups *trans* to each other) predominated[6]). Reduction of the ketone **6** with lithium aluminum hydride next gave the unstable alcohol **7**. The NMR. spectrum of this material showed the vinyl proton at C–9 as a triplet at δ 5.17 (J = 2–3 Hz) and the CH_3 of the ethyl group as a triplet at δ 1.0 (J = 7 Hz). The C–7 proton was readily identified as a triplet at δ 4.13 (J = 8 Hz;

[3]) An alternate synthesis of (±)-13β-ethyl-gon-4-ene-3,17-dione (**17**) is recorded in part V; see [5].

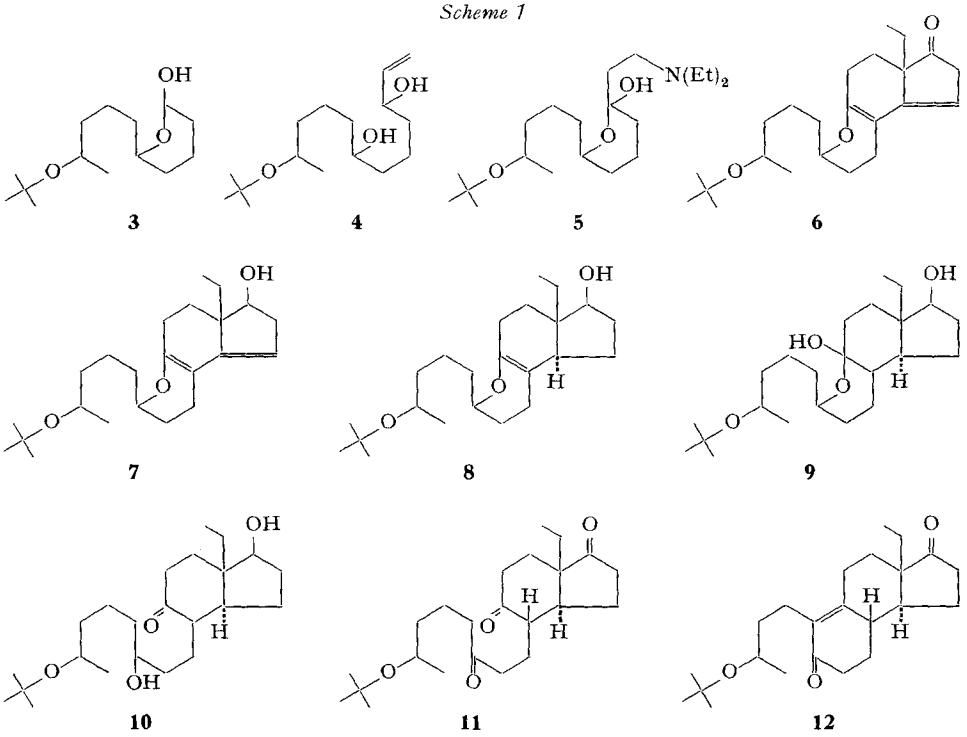
[4]) The use of *G. Stork*'s isoxazole procedure has also been investigated; see [5].

[5]) See experimental section for details.

[6]) Major product by analogy with previous examples; *cf.* [6].

dihedral angle of 25° and 140°). The downfield shift of the methyl part of the C–6a ethyl group was expected for the removal of the shielding effect of the carbonyl π-system.

Scheme 1



(racemic compounds)

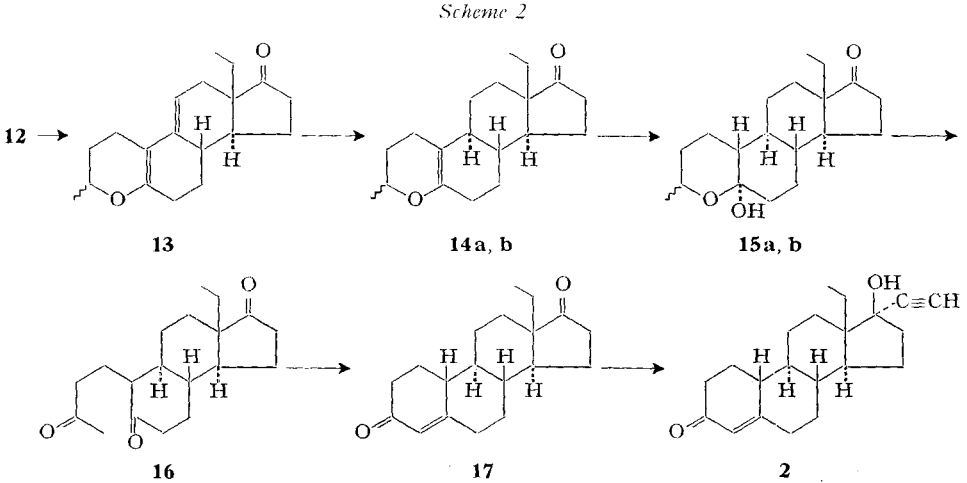
Selective catalytic hydrogenation of the crude diene **7** afforded the CD-*trans*[6]) intermediate **8**. In the NMR. spectrum the CH_3 of the C–6a ethyl group was again shifted downfield and appeared together with the *t*-butyl group at δ 1.17 ppm. Hydration of the enol ether **8** with aqueous acid gave the hemiacetal **9**. This product appears to be in equilibrium with the 'open' form **10**, on the basis of the IR. analysis (carbonyl absorption at 1700 cm^{-1}). No attempt was made to isolate **10** in pure form, since it was found that the mixture of **9** and **10** was well suited for the oxidation with *Jones'* chromic acid reagent [9]. We assume that the hydroxy ketone **10** is the intermediate which undergoes oxidation leading to the desired triketone **11**. This product showed the expected carbonyl bands in the IR spectrum at 1695, 1705 and 1730 cm^{-1}, and in the NMR. spectrum there was observed the characteristic upfield shift of the CH_3 of the ethyl group due to the 1-keto group (triplet at δ 0.87 ppm (J = 6 Hz)).

Treatment of the crude oxidation product **11** with sodium hydroxide in *t*-butyl alcohol finally afforded the pure enone **12** as an oil after purification by column chromatography. The overall yield for the transformation **6** → **12** was 52%. The product displayed the expected UV. absorption maximum at 249 nm (ε_{max} 13.800). The product **12** was a mixture of two racemates due to the chiral center at C–3. The

stereochemistry at C–8, C–13 and C–14 is proven by the transformation into (±)-13β-ethyl-gon-4-ene-3,17-dione (**17**) described below, and follows from our previous results[1]).

Our first synthesis of *Norgestrel* [2] **2** from the BCD-intermediate **12** is illustrated in Scheme 2. Interestingly, the conditions used to cleave the *t*-butoxy group (*p*-toluenesulfonic acid in boiling benzene) led directly to the formation of the novel dienol ether **13** in excellent yield. The unstable, crystalline product **13** was again a mixture at C-3. Thus, in the NMR. spectrum, the methyl group at C–3 appeared as two doublets centered at approximately δ 1.3 ppm (J = 6 Hz) while the proton on the same carbon was seen as two quartets centered at δ 4.03 ppm (J = 6 Hz). The chemical shift difference between the two quartets is about 3 Hz while that of the methyl groups is about 1 Hz. An examination of *Dreiding* models of the two possible isomers (3α-methyl and 3β-methyl) would indicate that because of C–1, C–11 proton interaction, the C–3 proton of the 3β-methyl isomer is displaced from the center of the 5(10)-double bond. One would thus expect a lessening in the shielding effect and can therefore assign the low-field quartet to the β-methyl isomer and the high-field one to the α-isomer. In the crystalline sample examined by NMR. the isomer ratio was about 2:3. Thus the methyl groups at C–3 could also be identified, the high- and low-field methyl doublets belonging to the 3α-methyl and 3β-methyl isomers respectively. Because of the poor stability of the compound **13**, we did not isolate the two isomers in pure form. The UV. spectrum, λ_{max} = 249 nm, is strong evidence for the hetero-annular *trans*-diene system present in structure **13**, and excludes the other alternative (ring B homoannular *cis*-diene). The vinyl proton at C–11 was seen in the NMR. spectrum at δ 5.3 ppm (distorted triplet, J = 2 Hz). As observed for the diene **7**, the dienol ether **13** readily underwent selective hydrogenation preferentially from the alpha side of the 9(11)-double bond over palladium on carbon in toluene containing a small amount of triethylamine. As expected, the resulting enol ether **14** was a mixture of isomers at C–3. This was readily seen in the NMR. spectrum. Thus the C–3

Scheme 2



(racemic compounds)

methyl group gave rise to two doublets centered at δ 1.2 and 1.24 ppm (each with $J = 6$ Hz) with the C–3 proton as a complex series of bands centered at δ 3.9 ppm (spread from δ 3.5–4.2 ppm). Interestingly, the methyl protons of the C–13 ethyl group were more shielded than in the diene **13** (upfield shift of δ 0.8 ppm).

Crystallization of the mixture gave one isomer, **14a** (~85% pure by NMR.), in which the C–3 methyl group was at δ 1.2 ppm ($J = 6$ Hz) and the proton at the same carbon was a complex band centered at δ 4.0 ppm. The mother liquor material, which was rich in the other isomer, showed the low-field split methyl at δ 1.24 ppm and the proton at C–3 at δ 3.75 ppm. The two isomers (**14a, b**) were not completely separated; however, on hydration, the crystalline enol ether **14a** produced the hemiacetal **15a** which was found to be uniform (sharp melting point; NMR. analysis) after crystallization. The higher melting isomer **15b** resulted from the hydration of a fraction rich in the enol ether **14b**. Contrary to our expectations, the oxidation of these hemiacetals **15a, b** did not furnish the desired triketone **16** in good yield. Thus, chromium trioxide in acetone–6N sulfuric acid gave only 9% of the ketone **16**. Variations of the oxidation procedure did not improve the yield[7]). On cyclization with *p*-toluenesulfonic acid in boiling benzene **16** afforded the tetracyclic enone **17** [4]. The crystalline product had all the expected spectral properties. Since physical data for **17** were unavailable from the literature, we also prepared this compound from authentic[8]) *Norgestrel* (**2**) [2] by *Jones'* oxidation [9][9]). The two preparations **17** were found to be identical in all respects. The same diketone **17** was directly obtained in 9% yield from crude hemiacetal **15a, b** by oxidation with an excess of N-bromosuccinimide in aqueous acetone. The final product, *Norgestrel* (**2**) [2], was readily obtained (23% yield) from the diketone **17**, using potassium acetylide in liquid ammonia with benzene/ether as a cosolvent. This selective ethynylation of a 13-ethyl-3,17-dioxo-steroid has precedent in the 13-methyl series [11]. Our preparation **2** was found to be identical with an authentic sample[8]).

An improved route for the transformation of the intermediate **14a, b** into *Norgestrel* **2** [2] is illustrated in Scheme 3. First, the 17-ketone **14a** (containing 15% of isomer **14b**) was ethynylated with lithium acetylide in liquid ammonia-tetrahydrofuran to afford 66% of the acetylenic carbinol **18a**. Similarly, using potassium acetylide, the isomer **18b** was obtained from **14b** (enriched material). Since the hydration-oxidation sequence again (*cf.* the transformation **14a, b** → **16**) was found to be very poor (only the keto lactone **20b** could be isolated from **18b**[10]), a novel scheme was designed. This is based on the reaction of the enol ether **18a, b** with methoxyamine hydrochloride in pyridine to give the oxime ether **21**, followed by oxidation with chromium trioxide in dimethylformamide[11]) to **22** and hydrolysis-cyclization with 4N hydrogen chloride in methanol (reflux) to afford *Norgestrel* **2** [2].

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[7]) Spectral analysis indicated the formation of keto lactones as major by-products, presumably arising from the hemiacetals **15a, b** *via* **14a, b** and subsequent oxidation of the enol ether double bond; *cf.* [10].

[8]) We would like to thank Dr. *Hershel Smith* at Wyeth for a generous sample of *Norgestrel*.

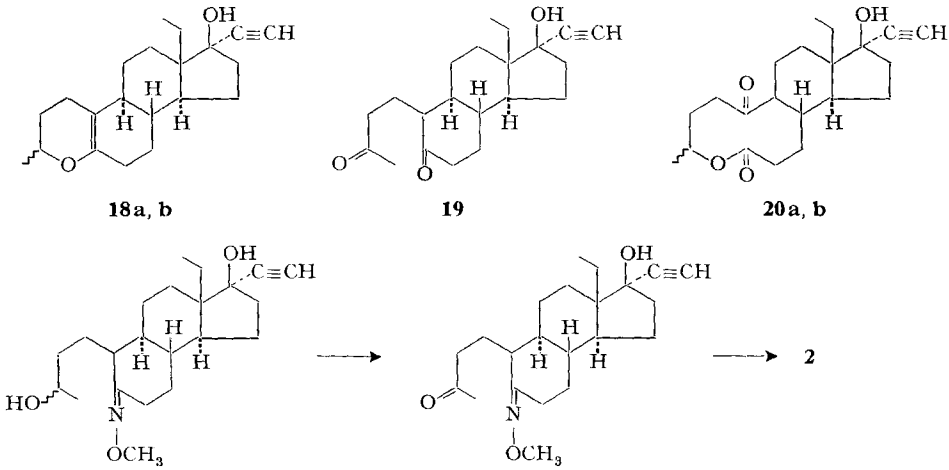
[9]) This convenient procedure resulted as a benefit from our investigations on the preparation of *Norgestrel* **2** [2] from the 17-ethynyl precursor **18a, b** (see Scheme 3)[10]).

[10]) IR. analysis indicated substantial loss of the 17-ethynyl-carbinol moiety with formation of 17-oxo compounds.

[11]) We used somewhat milder conditions than those reported by *Snatzke* [12].

The intermediates **21** and **22** need not be purified for this transformation (**18** → **2**), which gave an overall yield of 31%. In our opinion this sequence should lend itself to further improvement. It is worth noting that the 17-ethynyl-carbinol moiety appears to be quite stable towards chromium trioxide in dimethylformamide (*Snatzke*'s reagent) [12]. In contrast, we found this group to be rather unstable towards chromium trioxide in acetone-sulfuric acid (*Jones*' reagent) [9]. The hydrolysis of the

Scheme 3



18a, b **19** **20a, b**

21 **22**

(racemic compounds)

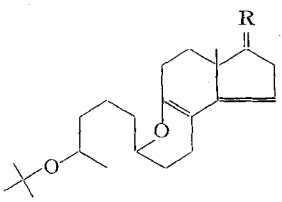
oxime ether **22** to give the diketone **19** was conveniently achieved with 1N hydrogen chloride in chloroform at room temperature, using pyruvic acid as an acceptor. Treatment of the non-crystalline intermediate **19** with *p*-toluenesulfonic acid in boiling benzene smoothly gave the cyclized product **2**.

The novel transformation of the $\Delta^{5(10)}$-4-oxa system was also applied to the synthesis of racemic 19-norandrost-4-ene-3,17-dione (**33**) from the enol ether **27** (see Scheme 4). The latter compound was prepared from the base **5** in a straight-forward manner, *via* the intermediates shown, **23** → **26**. The sequence **5** →**27** is analogous to that described above, *i.e.* **5** → **12** → **14a,b**[12]). Reaction of the dihydropyran **27** (1:1 mixture at C–3) with methoxyamine hydrochloride in pyridine-water at room temperature afforded the dioxime **29** in high yield. The IR. spectrum of the chromatographed product showed the characteristic oxime ether band at 1050 cm^{-1} and a strong hydroxyl band at 3425 cm^{-1}. Oxidation with the silver carbonate reagent [13] in boiling xylene converted the oily alcohol **29** to the crystalline ketone **31** in very good yield. Upon treatment with 6N hydrogen chloride in methanol (reflux) **31** directly furnished (±)-19-norandrost-4-ene-3,17-dione **33** [14]. Hydrolysis-exchange of **31** with levulinic acid in aqueous hydrochloric acid and chloroform was very slow and only the C–5 oxime ether was cleaved. The 19-norsteroid **33** was also readily obtained

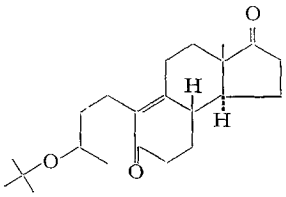
[12]) See Schemes 1 and 2, and the experimental for details.

from the 17-hydroxy intermediate **28** *via* the 3,17-diol **30** and the 3,17-diketone **32** (oxidation with chromium trioxide in dimethylformamide [12].

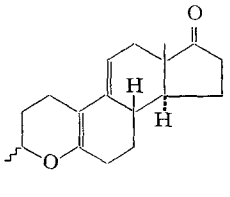
Scheme 4



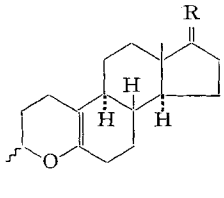
23 R = O
24 R = α–H, β–OH



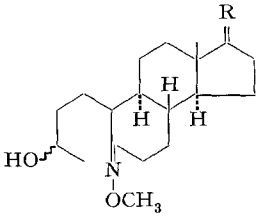
25



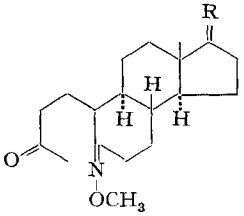
26



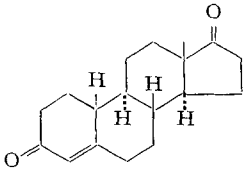
27 R = O
28 R = α–H, β–OH



29 R = N–OCH_3
30 R = α–H, β–OH



31 R = N–OCH_3
32 R = O



33

(racemic compounds)

Experimental Section

General. Melting points (m.p.) were determined in open capillary tubes and are uncorrected, except where noted. For column (elution) chromatography *Merck* silica gel (0.2–0.5 mm mesh) and *Woelm* alumina (grade III, neutral) were used. Thin layer chromatography (TLC.) was carried out on *Brinkmann* F 254 silica plates using a 1:1 mixture of ethyl acetate and benzene. The plates were first viewed under short wavelength UV. light. The spots were developed by spraying with 50% aqueous *p*-toluenesulfonic acid and heating to 120° for 1–3 minutes, followed by exposure to iodine vapours. IR. spectra were determined with a *Beckman* IR 8 and IR 9 spectrophotometer while UV. spectra were determined with a *Cary* Model 14. *Varian* Models A-60 and HA-100 NMR. spectrometers were used to record ^{1}H NMR. spectra at 60 Hz and 100 Hz, respectively. Chemical shifts were determined using tetramethylsilane (TMS) as an internal standard. Mass spectra were determined on *CEC* 21–110 and *Jeolco* 015 G spectrometers.

Removal of solvents '*in vacuo*' refers to removal at 20 Torr and 45° with a rotavapor and finally at 0.5 Torr.

(±)-*11*-(t-*Butoxy*)-*3,7-dihydroxy-dodec-1-ene* (**4**). 6-(4-*t*-Butoxypentyl)-tetrahydropyran-2-ol (212 g; **3**) was dissolved in tetrahydrofuran (925 ml) cooled to 0° and treated during 30 min with a solution of vinylmagnesium chloride in tetrahydrofuran (1397 ml; 20% *w/w*). After stirring a further 2 h at room temperature an aqueous ammonium chloride solution (10%; 1 l) was added and the mixture was extracted into ether.

Removal of the solvents '*in vacuo*' yielded the crude diol **4** (227 g) as a waxy solid. Crystallization of a sample of this material from petroleum ether (b.p. 40–60°) yielded a solid: m.p. 49–52°; IR. (film): 3360 (—OH), 3080, 920 (>C=CH_2), and 1200 cm^{-1} (—O—|—).

$C_{16}H_{32}O_3$ Calc. C 70.60 H 11.83% Found C 70.37 H 11.89%

(±)-*2-(2-Diethylamino-ethyl)-6-(4-*t*-butoxypentyl)-tetrahydropyran-2-ol* (**5**). A solution of the diol **4** (41.3 g) in benzene (100 ml) was added to a slurry of manganese dioxide (320 g; *Sterwin Chemicals Inc.*) in more benzene (1600 ml) containing diethylamine (120 ml). After stirring a further 16 h at room temperature under nitrogen the solids were filtered off, washed with benzene (5 × 200 ml) and the combined filtrates were taken to dryness '*in vacuo*'.

The crude *Mannich* base **5** (50 g) was dissolved in ether (500 ml) and the basic fraction was extracted into dilute aqueous hydrochloric acid (1 N: 3 × 100 ml). Regeneration of the base with aqueous potassium hydroxide solution (2 N) gave pure **5** (45.2 g) after isolation with ether. IR. (film): 3160 (bonded —OH), 1340, 1460 (N—C), and 1200 cm^{-1} (—O—|—).

The *oxalate of* **5** on crystallization from ethyl acetate ether mixture, displayed a double m.p.: 79–83° and 203–205°.

$C_{20}H_{41}NO_3, C_2H_2O_4$ Calc. C 60.80 H 9.99 N 3.23% Found C 60.55 H 9.73 N 3.45%

(±)-*3-(4-*t*-Butoxypentyl)-6aβ-ethyl-1,2,3,5,6,6a-hexahydro-cyclopenta*[f]*chromen-7(8*H*)-one* (**6**). A solution of the *Mannich* base **5** (45.2 g) in xylene (220 ml) was added rapidly under nitrogen to a boiling solution of 2-ethyl-cyclopentane-1,3-dione (22 g) in xylene (440 ml) and acetic acid (220 ml). After heating at reflux for a further hour the mixture was cooled to room temperature and washed with water (5 × 200 ml). Removal of the solvents '*in vacuo*' gave the crude dienol ether **6** as an orange oil (50 g) which was dissolved in petroleum ether (b.p. 40–60°) and absorbed onto a column of alumina (1200 g). Elution with ether-petroleum ether (40–60°) mixtures (2–5%; 1 l cuts) afforded pure **6** (38 g).

A small portion gave on distillation in a bulbe tube a pale yellow oil: b.p. 140–165°/0.01 Torr. UV. (EtOH): λ_{max} 253 nm (ε = 17,600). IR. ($CHCl_3$): 1740 (cyclopentanone), 1640 (dienol ether), and 1200 cm^{-1} (—O—|—). NMR. ($CDCl_3$): δ 5.54 (*t*, 1H, *J* = 2–3 Hz, C9 proton); 1.22 (*s*, 9H, —$C(CH_3)_3$), and 0.83 (*t*, 3H, *J* = 7 Hz, —CH_2—CH_3) ppm.

$C_{23}H_{36}O_3$ Calc. C 76.62 H 10.07% Found C 76.65 H 9.9%

(±)-*3-(4-*t*-Butoxypentyl)-6aβ-ethyl-1,2,3,5,6,6a,7,8-octahydro-cyclopenta*[f]*chromen-7β-ol* (**7**). To a slurry of lithium aluminium hydride (10 g) in ether (500 ml) cooled to −10° was added a solution of the dienol ether **6** (36 g) in ether (150 ml). After stirring a further hour at room temperature, saturated aqueous sodium sulfate solution (25 ml) was added. The solids were filtered off and washed with ether. Removal of the solvents '*in vacuo*' gave the unstable alcohol **7** (38 g).

Crystallization of an aliquot from hexane yielded crystalline material: m.p. 73–77°. IR. ($CHCl_3$): 3625 (—OH), 1642 (dienol ether), and 1200 cm^{-1} (—O—|—). UV. (EtOH): λ_{max} 252 nm (ε = 17,450). NMR. ($CDCl_3$): δ 5.17 (*t*, 1H, *J* = 2–3 Hz, C9 proton); 4.13 (*t*, 1H, *J* = 8 Hz, C7 proton); 1.22 (*s*, 9H, —O—|—); 1.06 (*d*, 3H, *J* = 6 Hz, CH_3—CH—); 1.0 (*t*, 3H, *J* = 7 Hz; CH_3CH_2) ppm.

$C_{23}H_{38}O_2$ Calc. C 76.20 H 10.37% Found C 75.82 H 10.47%

(±)-trans-*3-(4-*t*-Butoxypentyl)-6aβ-ethyl-1,2,3,5,6,6a,7,8,9,9a-decahydro-cyclopenta*[f]*chromene-7β-ol* (**8**). The alcohol **6** (5.35 g) was dissolved in toluene (100 ml), treated with a 5% palladium on carbon catalyst (1.5 g) and hydrogenated at room temperature and pressure until the uptake of hydrogen ceased (approximately 3 h). The solids were filtered off, washed well with toluene, and the combined filtrates were taken to dryness '*in vacuo*' to give **8** as a glass (5.4 g).

A sample of this material yielded on distillation a viscous oil. b.p. 150° at 0.01 Torr (bulb tube). IR. ($CHCl_3$): 3575 (—OH), 1680 (enol ether), and 1200 cm^{-1} (—O—|—). NMR. ($CDCl_3$): δ 1.17 (*t*, 3H, *J* = 7 Hz, CH_3CH_2—), and 1.06 (*d*, 3H, *J* = 6 Hz, CH_3—CH—) ppm.

$C_{23}H_{40}O_3$ Calc. C 75.80 H 11.06% Found C 75.79 H 11.12%

(±)-trans-*3-(4-*t*-Butoxypentyl)-6aβ-ethyl-perhydrocyclopenta*[f]*chromene-4a,7β-diol* (**9**). A solution of the crude enol ether **8** (35.9 g) in acetone (700 ml) was treated with aqueous sulfuric acid (3 N; 200 ml) and left to stand under nitrogen at room temperature for 24 h. Dilution with saturated brine solution (100 ml) and extraction with ether yielded the hydration product **9** (36 g) as a glass. A sample of this material was purified by chromatography on alumina; elution with an ether-

hexane mixture (15%) yielded a pure sample of the hemiacetal **9** as a glass. IR. ($CHCl_3$): 3575 (—OH), 1705 (weak C=O), and 1200 cm^{-1} (—O—|—).

$C_{23}H_{42}O_4$ Calc. C 72.20 H 11.07% Found C 71.97 H 10.70%

(±)-trans-*4-(7-t-Butoxy-3-oxo-octyl)-7aβ-ethyl-perhydroindan-1,5-dione* (**11**). A solution of the crude hydration product **9** (4.55 g) in acetone (200 ml) was cooled to 10° and treated with a fresh solution of *Jones'* chromic acid mixture. After 30 min stirring at room temperature aqueous sodium hydrogen sulfite solution (10%; 10 ml) and brine (500 ml) were added and the products isolated with ether. The ether extracts were washed successively with aqueous sodium carbonate solution (10%), water, and dried over anhydrous magnesium sulfate. Removal of the solvents gave the crude triketone **11** (3.65 g) as a light brown colored oil. An aliquot on distillation yielded an analytical sample: b.p. 205°/0.075 Torr (bulb tube). IR. ($CHCl_3$): 1730 (cyclopentanone), 1695 and 1705 (C=O), and 1200 cm^{-1} (—O—|—). NMR. ($CDCl_3$): δ 3.6 (*q*, 1H, J = 6 Hz, —$\overset{|}{C}$H—O—), 1.07 (*d*, 3H, J = 6 Hz; CH_3—$\overset{|}{C}$H—O), and 0.87 (*t*, 3H, J = 6 Hz, CH_3CH_2—) ppm. The UV. spectrum indicated that a few percent of the material had cyclized to the tricyclic compound **12**.

$C_{23}H_{38}O_4$ Calc. C 72.9 H 10.12% Found C 73.2 H 9.8%

(±)-trans-*3aβ-Ethyl-6-(3-t-butoxybutyl)-2,3,3a,4,5,7,8,9,9a,9b-decahydro-1*H*-cyclopenta*[a]*-naphthalene-3,7-dione* (**12**) [= (±)-*10-(3-t-Butoxybutyl)-13β-ethyl-deA-gon-9-ene-5,17-dione*]. A solution of the crude triketone **11** (25.4 g) in *t*-butyl alcohol (70 ml) was added to a mixture of powdered potassium hydroxide (1 g) in *t*-butyl alcohol (250 ml) at 55° under nitrogen. After stirring 1 h at this temperature, brine (1000 ml) was added and the desired material was isolated by extraction with ether. The crude tricyclic material (23.6 g) was chromatographed on alumina (2 kg) and elution with ether – petroleum ether (40–60°) mixtures (15% → 25%) gave the pure **12** (15.5 g). An aliquot of this material furnished on distillation the analytical sample: b.p. 180°/0.05 Torr (bulb tube). IR. ($CHCl_3$): 1730 (cyclopentanone), 1660 and 1600 (cyclohexenone), and 1195 cm^{-1} (—O—|—). UV. (EtOH): λ_{max} 249 nm (ε = 13,820). NMR. ($CDCl_3$): δ 3.64 (*q*, 1H, J = 6 Hz, —$\overset{|}{C}$H—O—C(CH_3)), 1.18 (*s*, 9H, O—C(CH_3)$_3$), 1.13 (*d*, 3H, J = 6 Hz, CH_3—$\overset{|}{C}$H—O—), and 0.87 (*t*, 3H, J = 7 Hz, CH_3—CH_2—) ppm.

$C_{23}H_{36}O_3$ Calc. C 76.6 H 10.07% Found C 76.54 H 9.97%

(±)-*2-Methyl-6aβ-ethyl-2,3,4,6,6a,9,9a,9b,10,11-decahydro-indeno*[*5,4-f*]*chromen-7*(*8*H)*-one* (**13**) [= (±)-*3ξ-Methyl-13β-ethyl-4-oxa-gona-5(10),9(11)-dien-17-one*]. A solution of the tricyclic material **12** (14.1 g) in benzene (250 ml) containing *p*-toluenesulfonic acid (600 mg) was heated at reflux under nitrogen for 4½ h. After cooling to room temperature the solution was washed with aqueous sodium hydrogencarbonate solution (5%) and the solvents were removed '*in vacuo*' to give the crude unstable dienol ether **13** (11.9 g) as a light orange colored crystalline solid. A portion of this material was crystallized twice from hexane to yield an analytical sample (mixture of 2 isomers): m.p. 109–116°. IR. ($CHCl_3$): 1732 (cyclopentanone) and 1645 cm^{-1} (dienol ether). UV. (EtOH): λ_{max} 249 nm (ε = 17,500). NMR. ($CDCl_3$): δ 5.5 (*m*, 1H, C5 vinyl proton), 4.06 (*q*, J = 6 Hz; O—$\overset{|}{C}$H—CH_3, β-isomer), 4.12 (*q*, J = 6 Hz, O—$\overset{|}{C}$H—CH_3, α-isomer), 1.25 (*d*, J = 6 Hz, CH_3—$\overset{|}{C}$H—O, α-isomer), 1.27 (*d*, J = 6 Hz, CH_3—$\overset{|}{C}$H—O, β-isomer), and 0.82 (*t*, 3H, J = 6 Hz, CH_3—CH_2—). $C_{19}H_{22}O_2$ Calc. C 79.68 H 9.15% Found C 79.25 H 9.08%

(±)-*2-Methyl-6aβ-ethyl-2,3,4,4b,5,6,6a,9,9a,9b,10,11-dodecahydro-indeno*[*5,4-f*]*chromen-7*(*8*H)*-one* (**14a,b**) [= (±)-*3 ξ-Methyl-13β-ethyl-4-oxa-gon-5(10)-en-17-one*]. The crude material **13** (33.3 g; 1:1 mixture at C2) was dissolved in toluene (300 ml) containing triethylamine (2.5 ml), treated with a palladium-on-carbon catalyst (5%; 5 g) and hydrogenated at room temperature and normal pressure until the uptake of hydrogen stopped. The solids were filtered off, washed with toluene, and the combined filtrates were taken to dryness '*in vacuo*' to yield the mixture of enol ethers **14a,b** (33.8 g). Repeated crystallization of this material from hexane and from ethyl acetate gave **14a** (9.7 g) of approximately 85% purity (by NMR.); m.p. 118–112°. IR. ($CHCl_3$): 1730 (cyclopentanone) and 1680 cm^{-1} (enol ether). NMR. ($CDCl_3$): δ 4 (*m*, 1H, —$\overset{|}{C}$H—O—), 1.2 (*d*, 3H, J = 6 Hz; CH_3—$\overset{|}{C}$H—O), and 0.75 (*t*, 3H, J = 7 Hz, CH_3—CH_2—) ppm.

$C_{19}H_{28}O_2$ Calc. C 79.23 H 9.80% Found C 79.15 H 9.66%

The mother liquors from the first crystallization were filtered through alumina (20:1 ratio) in hexane to yield an oil enriched in isomer **14b** (~65% by NMR.). NMR. ($CDCl_3$): δ 4.0 (*m*, CH—O—, **14a**), 3.9 (*m*, —CH—O—, **14b**), 1.2 (*d*, J = 6 Hz, CH_3—CH—O, **14a**), 1.24 (*d*, J = 6 Hz, CH_3—CH—O, **14b**), and 0.75 (*t*, 3 H, J = 7 Hz, CH_3—CH_2—) ppm.

(±)-*2-Methyl-6aβ-ethyl-11a-hydroxy-perhydroindeno[5,4-f]chromene-7-one* (**15a**) *and* (**15b**) [= (±)-*3ξ-Methyl-5α-hydroxy-13β-ethyl-4-oxa-gonan-17-one*]. The enol ether **14a** (1 g, ~85% one isomer) was dissolved in acetone (75 ml), treated with aqueous sulfuric acid (1 N; 35 ml) and left at room temperature for $^1/_2$ h. Dilution with saturated brine solution and extraction into ether yielded the crude *hemiacetal* **15a** as a glass. Crystallization from hexane afforded pure material: m.p. 114–116. IR. ($CDCl_3$): 3580 (—OH) and 1730 cm^{-1} (cyclopentanone). NMR. ($CDCl_3$): δ 4.1 (*m*, 1 H, —CH—O—), 1.13 (*d*, 3 H, J = 6.5 Hz, CH_3—CH—O), and 0.77 (*t*, 3 H, J = 7 Hz; CH_3CH_2—) ppm.

$C_{19}H_{30}O_3$ Calc. C 74.47 H 9.87% Found C 74.28 H 10.05%

Isomer **15b** was isolated as follows: The mother liquor material rich in **14b** (3 g, ~65%) was chromatographed on silica gel (300 g). Elution with ethyl acetate-benzene mixture (20%) gave the hemiacetal (1 g). Crystallization from ether afforded pure material: m.p. 136–139°. IR. ($CHCl_3$): 3575 (—OH) and 1730 cm^{-1} (cyclopentanone). NMR. ($CDCl_3$): δ 4.06 (*m*, 1 H, —CH—O—), 1.11 (*d*, 3 H, J = 6.5 Hz, CH_3—CH—O), and 0.75 (*t*, 3 H, J = 7 Hz, CH_3—CH_2—) ppm.

$C_{19}H_{30}O_3$ Calc. C 74.47 H 9.87% Found C 74.13 H 10.16%

(±)-*3aβ-Ethyl-6-(3-oxobutyl)-perhydrocyclopenta[a]naphthalene-3,7-dione* (**16**) [= (±)-*10-(3-Oxobutyl)-13β-ethyl-deA-gonane-5,17-dione*]. The crude hydration product (from a mixture of **14a** and **14b**) **15a,b** (432 mg) was dissolved in acetone (17 ml), cooled to 20° and treated over 10 min with a solution of chromium trioxide (740 mg) in aqueous sulfuric acid (6 N; 3.7 ml). After stirring for a further hour at room temperature a sodium hydrogensulfite solution (10%) was added, followed by a saturated brine solution. Extraction with ether gave an oil (370 mg) on removal of the solvents. Chromatography on silica gel gave the desired *triketone* **16** (39 mg) on elution with an ethyl acetate-hexane mixture (40%). IR. (film): 1725 (cyclopentanone) and 1700 cm^{-1} (cyclohexanone and methylketone).

Further elution with ethyl acetate-hexane mixture (40%) yielded a *lactone* which was crystallized from hexane, m.p. 177–185° (this was a mixture of isomers). IR. ($CHCl_3$): 1720 (strong band, lactone and cyclopentanone) and 1700 cm^{-1} (large-ring ketone).

(±)-*13β-Ethyl-gon-4-ene-3,17-dione* (**17**). The oily triketone **16** (39 mg) was heated at reflux for 3 h with *p*-toluenesulfonic acid (10 mg) in benzene (25 ml). After washing the benzene with water, the solvents were removed '*in vacuo*' to give an oil which on crystallization from hexane gave the desired material **17** (10 mg): m.p. 155–157°. UV. (EtOH): λ_{max} 236 nm (ε = 17,250). IR. ($CHCl_3$): 1730 (cyclopentanone), 1670 and 1623 cm^{-1} (cyclohexenone).

This same material was also formed as follows: The crude hydration product **15a,b** (574 mg) in acetone (20 ml) was treated with N-bromosuccinimide (900 mg) and water (2 ml) and stirred at room temperature overnight. Dilution with water and extraction into ether yielded an oil which contained at least three components. Chromatography on silica gel and elution with an ethyl acetate-hexane mixture (25%) gave **17** (164 mg). Recrystallization from acetone-hexane mixtures gave pure **17** (50 mg), m.p. 155–157°. UV. (EtOH): λ_{max} 239 nm (ε = 17,900).

$C_{19}H_{26}O_2$ Calc. C 79.68 H 9.15% Found C 79.90 H 8.94%

Both samples prepared above were identical with an authentic sample prepared as follows.

A solution of (±)-13β-ethyl-17α-ethynyl-17β-hydroxy-gon-4-en-3-one (**2**)[8] (500 mg) in acetone (50 ml) was treated at room temperature with *Jones* chromic acid mixture (3 ml) (the reaction is exothermic and cooling is required). After stirring a further 15 min at room temperature aqueous sodium hydrogensulfite solution was added, followed by a saturated brine solution. Extraction of the organic materials into ether yielded an oily solid on removal of the solvents. Chromatography on silica gel as before and recrystallization from an acetone-hexane mixture gave pure **17** (160 mg): m.p. 157–159°. UV. (EtOH): λ_{max} 239 nm (ε = 17,600). IR. ($CHCl_3$): 1730 (cyclopentanone), 1670 and 1620 cm^{-1} (cyclohexenone). NMR. ($CDCl_3$): δ 5.82 (1 H, C4 vinyl proton) and 0.78 (*t*, 3 H, J = 7 Hz, CH_3—CH_2) ppm.

(±)-13β-Ethyl-17α-ethynyl-17β-hydroxy-gon-4-en-3-one (**2**) *from* **17**. A solution of the tetracyclic diketone **17** (500 mg) in a mixture of benzene and ether (1:1; 10 ml) was added to a solution of potassium acetylide (from potassium, 500 mg) in liquid ammonia (50 ml) saturated with acetylene. After stirring for 2 h at −33°, ether (150 ml) was added and the ammonia was distilled off. The organic phase was washed with a saturated brine solution and taken to dryness *'in vacuo'*. Chromatography of the residue (550 mg) on silica gel (50 g) and crystallization from an acetone-hexane mixture yielded the pure compound **2** (116 mg); m.p. 204–206. This material was identical with an authentic sample [2][8]). – UV. (EtOH): λ_{max} 239 nm (ε = 17,350); IR. ($CHCl_3$): 3600 (—OH), 3300 (—C≡CH), 1670 and 1620 cm^{-1} (cyclohexenone). NMR. ($CDCl_3$): δ 5.82 (*s* (broad), 1H, C4 proton), 2.56 (*s*, 1H, —C≡CH), 2.04 (*s*, 1H, —OH), and 1.0 (*t*, 3H, J = 6 Hz, CH_3—CH_2) ppm.

(±)-2-Methyl-6aβ-ethyl-7α-ethynyl-2,3,4,4b,5,6,6a,7,8,9,9a,9b,10,11-tetradecahydro-indeno[5,4-f]chromene-7β-ol (**18a**) *and* (**18b**) [= *(±)-3ξ-Methyl-13β-ethyl-17α-ethynyl-4-oxa-gon-5(10)-en-17β-ol*]. Liquid ammonia (600 ml) was saturated with acetylene (passed through dry ice-acetone trap and concentrated sulfuric acid) for $^1/_2$ h and then treated with potassium metal (3 g) (during the entire reaction the passage of acetylene was never stopped). After the complete addition of the potassium the mixture was stirred for a further $^1/_2$ h and then treated over 20 min with a solution of the enol ether **14a** (8 g; ~85% pure) in tetrahydrofuran (120 ml). The whole mixture was stirred at ~−33° for 2 h and then treated with ether (400 ml). Half the ammonia was distilled off and solid ammonium chloride (20 g) was added, followed after 15 min by water (180 ml). The passage of acetylene was stopped and the ethereal solution was washed with saturated brine solution and then taken to dryness *'in vacuo'*. Recrystallization of the residue from hexane afforded *pure* **18a** (5.8 g); m.p. 138–143°. IR. ($CHCl_3$): 3600 (—OH), 3300 (—C≡CH), and 1675 cm^{-1} (enol ether). NMR. ($CDCl_3$): δ 3.97 (*m*, 1H, —C*H*—O—), 2.58 (*s*, 1H, —C≡C*H*), 1.9 (*s*, 1H, —O*H*), 1.2 (*d*, 3H, J = 6.5 Hz; C2—CH_3), and 0.95 (*t*, 3H, J = 7 Hz, CH_3CH_2—) ppm.

$C_{21}H_{30}O_2$ Calc. C 80.21 H 9.62% Found C 80.19 H 9.48%

The other isomer, **18b**, was prepared in the same fashion as above from material rich in **14b** (~65%). Thus the enol ether mixture (2 g) yielded after repeated crystallization from hexane the *pure isomer* **18b** (1 g): m.p. 143–150°; IR. ($CHCl_3$): 3600 (OH), 3300 (—C≡CH), and 1675 cm^{-1} (enol ether). NMR. ($CDCl_3$): δ 3.76 (*m*, 1H, J_{ae} = 2 Hz; J_{aa} = 10.5 Hz, J_{CHCH_3} = 6.5 Hz, C2 proton), 2.6 (*s*, 1H, —C≡C*H*), 1.9 (*w*, 1H, —O*H*), 1.27 (*d*, 3H, J = 6.5 Hz; C2CH_3), and 0.98 (*t*, 3H, J = 7 Hz, CH_3CH_2—) ppm. Mass spectrum (*m/e*): 314 (theory 314).

$C_{21}H_{30}O_2$ Calc. C 80.21 H 9.62% Found C 79.98 H 9.54%

(Note that less than 5% of the other isomer would be hard to detect in the NMR. spectrum.)

(±)-5-Methyl-10aβ-ethyl-11α-ethynyl-11β-hydroxy-perhydroindeno[4,5-e]oxecane-3,8-dione (**20**). The ethynyl enol ether **18b** (550 mg) was dissolved in acetone (50 ml) and hydrated with dilute aqueous sulfuric acid (1N; 25 ml). After 25 min at room temperature brine was added and the *hemiacetal* isolated with ether (557 mg).

This material, devoid of an enol ether band in the IR. spectrum, was dissolved in acetone (300 ml), cooled to 0–5° and treated with *Jones'* chromic acid mixture (1.8 ml). After stirring for 10 min at 0–5° aqueous sodium hydrogensulfite was added and the products were extracted into ether. Chromatography of the crude oxidation product on alumina (60 g) yielded the *lactone* **20b** on elution with an ether-hexane mixture (1:1). Crystallization from a hexane-benzene mixture gave pure material: m.p. 165–167°. IR. ($CHCl_3$): 3600 (—OH), 3300 (—C≡CH), 1725 (lactone) and 1700 cm^{-1} (large-ring ketone). NMR. ($CDCl_3$): δ 4.85 (*m*, 1H, C5 proton), 2.6 (*s*, 1H, —C≡C*H*), 2.28 (*s*, 1H, —O*H*), 1.41 (*d*, 3H, J = 6 Hz, C5—CH_3), and 1.0 (*t*, 3H, J = 7 Hz, CH_3—CH_2) ppm.

$C_{21}H_{30}O_4$ Calc. C 72.80 H 8.73% Found C 73.45 H 8.36%

Similarly enol ether **18a** yielded the *lactone* **20a**: MP. 197–199°. IR. ($CHCl_3$): 3540 (—OH), 3300 (—C≡CH), 1722 (large-ring lactone) and 1710 (large-ring ketone). NMR. ($CDCl_3$): δ 5 (*m*, 1H, C5 proton), 2.62 (*s*, 1H, —C≡C*H*), 1.24 (*d*, 3H, J = 6.5 Hz, C5—CH_3), and 0.93 (*t*, 3H, J = 7 Hz, CH_3—CH_2—) ppm.

$C_{21}H_{30}O_4$ Calc. C 72.80 H 8.73% Found C 72.92 H 8.83%

(±)-3α-Ethynyl-3β-hydroxy-3aβ-ethyl-6-(3-hydroxybutyl)-7-methoxyimino-perhydrocyclopenta[a] *naphthalene* (**21**). The acetylenic enol ether **18a** (1.5 g) was dissolved in pyridine (5 ml) containing

water (0.25 ml) and treated with methoxyamine hydrochloride (1 g). After standing at room temperature for 20 h the mixture was quenched with brine and extracted with dichloromethane. The organic phase was washed with aqueous sulfuric acid (1N), sodium carbonate solution (10%), water, and dried over anhydrous magnesium sulfate. After filtering off the solids the solvents were removed '*in vacuo*' to yield the oxime ether as a solid (1.65 g). Crystallization from isopropyl ether gave pure **21**: m.p. 163–165°. IR. ($CHCl_3$): 3600 and 3400 (—OH), 3300 (—C≡CH), and 1045 cm^{-1} (oxime ether). NMR. ($CDCl_3$): δ 3.85 (*s*, 3H, —OCH_3), 2.6 (*s*, 1H, —C≡CH), 1.2 (*d*, 3H, J = 6 Hz, CH_3—CH), and 1.12 (*t*, 3H, J = 7 Hz, CH_3—CH_2—) ppm.

$C_{22}H_{35}NO_3$ Calc. C 73.09 H 9.76 N 3.87% Found C 73.23 H 9.81 N 3.81%

(±)-*13β-Ethyl-17α-ethynyl-17β-hydroxy-gon-4-en-3-one* (**2**) *from* **21**. A sample of the crude oxime ether **21** (1 g), dissolved in dimethylformamide (10 ml), was treated at 5° with a solution of chromium trioxide (1 g) in dimethylformamide (13 ml) to which had been added concentrated sulfuric acid (0.5 ml). The mixture was then warmed to room temperature and stirred for 1 h. Dilution with water and isolation of the organic materials with dichloromethane yielded the *ketone* **22** as a glass (850 mg). This material failed to crystallize, even after chromatography on silica gel. IR. ($CHCl_3$): 2580 and 3400 (—OH), 3300 (—C≡CH), 1705 (open-chain ketone), and 1040 cm^{-1} (oxime ether).

A sample of this ketone (140 mg) was dissolved in chloroform (5 ml) and stirred for two days at room temperature with a solution of pyruvic acid and aqueous hydrogen chloride (9:1; 1N; 5 ml). The expected *diketone* **19** was isolated with dichloromethane as an oil (128 mg). When treated with *p*-toluenesulfonic acid (25 mg) in boiling benzene (5 ml) for 1 h it readily yielded the desired product **2**. Crystallization from acetone-hexane mixtures gave the pure material (38 mg): m.p. 204–206°. This material was identical with an authentic sample by mixed m.p., TLC., IR., and UV.

The same product was obtained from **22** as follows. A solution of crude **22** (430 mg) in methanol (15 ml) was heated at reflux for 2 h with hydrochloric acid (4N; 7.5 ml). Dilution with water and extraction with dichloromethane gave the crude product as a cream-colored solid (378 mg). Chromatography of the material on silica gel (40 g) and recrystallization from acetone-hexane mixtures yielded pure **2** (143 mg) indistingusishable from an authentic sample.

(±)-*3-(4-t-Butoxypentyl)-6aβ-methyl-1,2,3,5,6,6a-hexahydro-cyclopenta*[f]*chromen-7*(8H)*-one* (**23**). A solution of 2-methyl-cyclopentane-1,3-dione (13.7 g) in xylene (280 ml) and acetic acid (140 ml) was heated at reflux under nitrogen and treated over 15 min with a solution of the amine **5** (28 g) in xylene (120 ml). After stirring at reflux for $^3/_4$ h longer, the dienol ether was isolated as before. This crude material (29 g) was chromatographed on alumina to yield the pure **23** (22 g). A portion was distilled to yield the analytical sample: b.p. 180°/0.01 Torr. UV. (EtOH): λ_{max} 252 nm (ε = 17,550).

$C_{22}H_{34}O_3$ Calc. C 76.26 H 9.89% Found C 76.49 H 10.03%

(±)-*3-(4-t-Butoxypentyl)-6aβ-methyl-1,2,3,5,6,6a,7,8-octahydro-cyclopenta*[f]*chromen-7β-ol* (**24**). Lithium aluminium hydride (4.6 g) was added to tetrahydrofuran (230 ml) and cooled to −10°. The chromatographed dienol ether **23** (23.1 g), dissolved in tetrahydrofuran (460 ml), was added to the above suspension over 15 min under nitrogen. After stirring a further hour at 0° water was carefully added. The solids were filtered off and washed with ether. Concentration of the combined filtrates to dryness gave the alcohol **24** (23.1 g) as a yellow-colored crystalline solid. A portion was crystallized several times from hexane to yield the analytically pure sample: needles, m.p. 97–101°. UV. (EtOH): λ_{max} 253 nm (ε = 18,700).

$C_{22}H_{36}O_3$ Calc. C 75.78 H 10.41% Found C 76.01 H 10.28%

(±)-trans-*6-(3-t-Butoxybutyl)-3aβ-methyl-2,3,3a,4,5,7,8,9,9a,9b-decahydro-1*H*-cyclopenta*[a]*naphthalene-3,7-dione* (**25**). The crude alcohol **24** (22.5 g) was dissolved in toluene (450 ml) and hydrogenated at room temperature and pressure in the presence of a palladium-on-carbon catalyst (5%; 3.4 g). After the hydrogen uptake stopped (~6 h) the solids were filtered off and the product was obtained as an oil after removal of the solvents (23.1 g). A portion of this material was chromatographed on alumina and finally distilled to yield a colorless liquid: b.p. 200°/0.01 Torr.

$C_{22}H_{38}O_3$ Calc. C 75.38 H 10.93% Found C 75.15 H 10.93%

The crude hydrogenation product (22.1 g) was dissolved in acetone (220 ml) and treated, at room temperature, with aqueous sulfuric acid (110 ml) and left for 3 h. Most of the acetone was

removed at 20 Torr and 35° and the desired *hemiacetal* was isolated by ether extraction. Chromatography on alumina (650 g) yielded the pure material on elution with hexane-ether mixtures (1:1 and 1:4) (14.8 g). The IR. spectrum showed only the bands due to the hydroxy and *t*-butyl ether groups (no enol ether bands).

A solution of the chromatographed hemiacetal (17.4 g) in acetone (700 ml) was treated, over 20 min, with a solution of chromium trioxide (12.7 g) in aqueous sulfuric acid (6N; 63.5 ml). After stirring for 2 h at room temperature the mixture was treated with water and the desired material was extracted with benzene. The combined benzene extracts were washed with a sodium carbonate solution (10%), water, and taken to dryness *'in vacuo'* to give the *triketone* (15.4 g)as an oil. A portion of this material was distilled to give an analytical sample: m.p. 200°/0.01 Torr.

$C_{22}H_{36}O_4$ Calc. C 72.49 H 9.95% Found C 72.21 H 10.00%

This triketone (13.8 g) was dissolved in *t*-butyl alcohol (38 ml) and heated 1 h at 55° under nitrogen with powdered sodium hydroxide (544 mg) in *t*-butyl alcohol (126 ml). Addition of acetic acid (1 ml), removal of most of the *t*-butyl alcohol *'in vacuo'* and isolation of the product with benzene and water yielded the tricyclic material **25** (11.9 g) as an amber-colored oil. UV. (EtOH): λ_{max} 247 nm ($\varepsilon = 12{,}850$).

(±)-*2,6aβ-Dimethyl-2,3,4,4b,5,6,6a,9,9a,10,11-dodecahydro-indeno[5,4-f]chromen-7(8H)-one* (**27** [= (±)-*3ξ-Methyl-4-oxa-ester-5(10)-en-17-one*]. Crude **25** (10 g) was dissolved in benzene (300 ml) containing *p*-toluenesulfonic acid (500 mg) and heated at reflux, under nitrogen, for 4 h. The benzene was washed with water and taken to dryness *'in vacuo'*. The crude *dienol ether* **26** (8.5 g; some solvent residue) failed to crystallize. IR. (film): 1732 (cyclopentanone) and 1636 cm^{-1} (dienol ether).

This unstable material was dissolved in toluene (200 ml) containing triethylamine (5 ml) and hydrogenated at room temperature and pressure in the presence of a palladium-on-carbon catalyst (5%; 1.5 g). After the hydrogen uptake stopped, the solids were filtered off and the solvents removed *'in vacuo'*. The crude enol ether mixture **27** (8.4 g) was chromatographed on alumina (150 g). Elution with benzene yielded the pure *isomer mixture* **27** (5.93 g). IR. ($CHCl_3$): 1740 (cyclopentanone) and 1680 cm^{-1} (enol ether). NMR. ($CDCl_3$): δ 4 (*m*, 1H, $-\overset{|}{C}H-O-$), 1.25 and 1.2 (*d*, 3H, $J = 6$ Hz, isomeric methyl groups at C2), and 0.88 (*s*, 3H, C6a–CH_3) ppm. Mass spectrum (molecular ion) *m/e* 274 (calc. 274).

$C_{18}H_{26}O_2$ Calc. C 78.79 H 9.55% Found C 78.98 H 9.42%

(±)-*3,7-Di-methoxyimino-3aβ-methyl-6-(3-oxobutyl)-perhydrocyclopenta[a]naphthalene* (**31**) [= (±)-*5,17-Di-methoxyimino-10-(3-oxabutyl)-deA-estrane*]. The mixture of isomers **27** (747 mg) was dissolved in pyridine (4 ml) containing water (1 ml), treated with methoxyamine hydrochloride (500 mg) and left at room temperature for two days. Dilution with water and extraction with dichloromethane yielded the *dioxime* **29** as an oil (954 mg). Chromatography on silica gel (50 g) yielded the pure material (643 mg) on elution with ethyl acetate – benzene mixture (10% and 20%). IR. (film): 3425 (–OH) and 1050 cm^{-1} (=N–OCH_3).

This dioxime (640 mg) was dissolved in xylene (30 ml), treated with silver carbonate on celite [13] (3 g) and heated at reflux for one hour under nitrogen. The solids were filtered off and the residue on removal of the solvents was crystallized from hexane to give *pure* **31** (445 mg): m.p. 110–111°. IR. ($CHCl_3$): 1712 cm^{-1} ($\rangle C=O$) and 1050 cm^{-1} (=N–OCH_3). NMR. ($CDCl_3$): δ 3.83 (*s*, 6H, =N–OCH_3), 2.15 (*s*, 3H, –CO–CH_3), and 0.94 (*s*, 3H, $-\overset{|}{C}-CH_3$) ppm. Mass spectrum (parent ion) *m/e* 348 (theory 348).

$C_{20}H_{32}N_2O_3$ Calc. C 68.93 H 9.26 N 8.04% Found C 69.09 H 9.24 N 8.14%

(±)-*19-Norandrost-4-ene-3,17-dione* (**33**) [14] [= (±)-*Estr-4-ene-3,17-dione*]. The dioxime ether **31** (107 mg) was dissolved in a mixture of methanol (5 ml) and aqueous hydrogen chloride (6N; 1 ml) and heated at reflux under nitrogen for 3 h. Dilution with brine and extraction with dichloromethane gave crude **33** (70 mg) on removal of the solvents. Recrystallization from acetone-hexane mixtures gave pure material (30 mg): m.p. 150–154°. This product was identical with authentic **33**, based on IR., UV. and TLC. comparison.

This same compound was also prepared from the enol ether mixture **27** as follows. The mixture **27** was reduced with an excess of lithium aluminium hydride in ether at room temperature for 1 h. Isolation of the *alcohol* **28** (an oil) presented no difficulties and this crude material was converted to the *oxime ether* **30** with methoxyamine as in previous examples.

Chromatography of the crude product on silica gel gave **30** as a glass (837 mg from 837 mg **28**). IR. ($CHCl_3$): 3400 and 3600 (—OH), and 1040 cm^{-1} (=N—OMe).

A solution of this diol **30** (417 mg) in dimethylformamide (5 ml) was treated with a mixture of chromium trioxide (500 mg) and sulfuric acid (0.25 ml) in dimethylformamide (5.5 ml). After 2 h at room temperature the mixture was quenched with water and extracted with dichloromethane. Removal of the solvents *'in vacuo'* gave the crude *diketone* **32** (378 mg). IR. (film): 1735 (cyclopentanone), 1705 (methyl ketone), and 1050 cm^{-1} (=N—OMe).

This material was dissolved in a mixture of methanol (15 ml) and aqueous hydrogen chloride (4N; 7.5 ml) and heated at reflux for 2 h. Isolation of the product with dichloromethane yielded crude **33** as an oil (302 mg). This material was indistinguishable from the pure material by TLC. and IR. analysis. Chromatography on silica gel and recrystallization from hexane-acetone mixtures yielded pure **33** (95 mg), identical with an authentic sample; m.p. 155–157.

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308. Stereochemie der Ringöffnung der σ-Komplexe von 2-Naphtol-1-sulfonsäure mit Diazoniumsalzen und der anschliessenden Phtalazinbildung: Eine Fragmentierung als Konkurrenzreaktion der Abspaltung der Abgangsgruppe bei der elektrophilen Substitution[1])

25. Mitteilung zur Kenntnis der Azokupplung[2])

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(14. X. 71)

Summary. The reaction of 2-naphthol-1-sulfonic acid with diazonium salts was investigated in the pH range 10 to 15. The structures postulated for the reaction products by *Rowe et al.* [3] and by *Koller* [4] were proved by instrumental analysis. In alkaline solutions, instead of the usual diazode-

[1]) Vorträge an der Cork Mechanisms Conference «Structure and Mechanism in Nitrogen Chemistry», Cork (Ireland), 8. April 1971, und an der Herbstversammlung der Schweiz. Chem. Gesellschaft, Fribourg, 9. Oktober 1971.

[2]) 24. Mitteilung: *Penton & Zollinger* [1].