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A partial synthesis of 13-ethyl-11-methylene-18,19-dinor-17α-pregn-4-en-20-yn-17-ol (desogestrel) based upon intramolecular oxidation of an 11β-hydroxy-19-norsteroid to the 18 → 11β-lactone

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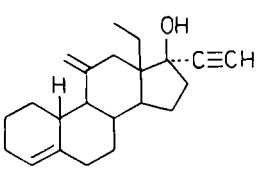
Abstract. A partial synthesis of the 13-ethyl-18-norsteroid desogestrel is reported. The key step in this synthesis is the intramolecular oxidation of 11β-hydroxyestr-5-ene-3,17-dione cyclic bis-(1,2-ethanediyl acetal) **3** with $Pb(OAc)_4$ and iodine to 3,3:17,17-bis[1,2-ethanediylbis(oxy)]-11β--hydroxyestr-5-en-18-oic acid γ-lactone **2**.
The 13-COOH group was then converted into a 13-ethyl group by a Grignard reaction with methylmagnesium bromide followed by Wolff–Kishner reduction of the 13-acetyl group thus formed.

Introduction

The progestagen 13-ethyl-11-methylene-18,19-dinor-17α--pregn-4-en-20-yn-17-ol **1** (desogestrel) is widely used for contraception[1,2,3] and we have developed a partial synthesis of this important steroid via the lactone **2**, which can be prepared using an intramolecular hypoiodite reaction.



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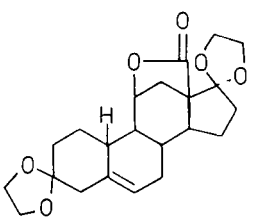
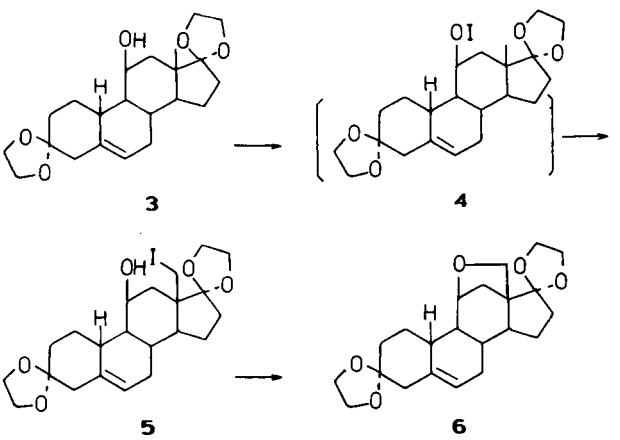


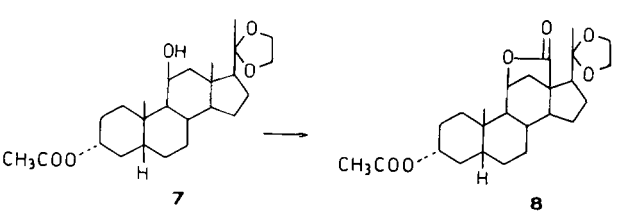
2

Intramolecular hypoiodite reactions are widely used for mono- and di-substitution of otherwise inert angular methyl groups of steroids[4,5]. We have applied this reaction, for example, to convert 11β-hydroxyestr-5-ene-3,17-dione cyclic bis(1,2-ethanediyl acetal) **3** via the hydroxy iodide **5** into 11β,18-epoxyestr-5-ene-3,17-dione cyclic bis(1,2-ethanediyl acetal) **6** (Scheme 1)[6]. By contrast, very few examples of trisubstitution reactions, involving a larger excess of the oxidizing reagent $Pb(OAc)_4$, have been reported[7-10]. *Kalvoda* et al.[11] described the oxidation of 3α-(acetyloxy)--11β-hydroxy-5β-pregnan-20-one cyclic 1,2-ethanediyl acetal **7** with $Pb(OAc)_4$ and I_2, which gave, among other products, the (18 → 11β)-lactone **8** (Scheme 2).



3 **4** **5** **6**

Scheme 1

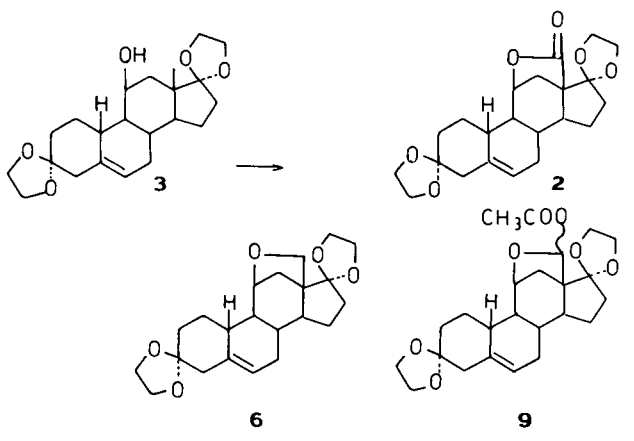


7 **8**

Scheme 2

The lactonization

Treatment of 11β-hydroxyestr-5-ene-3,17-dione cyclic bis(1,2-ethanediyl acetal) **3** in cyclohexane with an excess of $Pb(OAc)_4$ and iodine (molar ratio steroid/$Pb(OAc)_4/I_2$ 1/4 · 2/1) with azobisisobutyronitrile as radical initiator gave, in a small-scale experiment after chromatography, the lactone **2** in *ca.* 44% yield together with the epoxide **6** (*ca.* 3%) and a mixture of isomeric epoxy acetates **9** (*ca.* 6%) (Scheme 3). The yield of the lactone **2** was 40% in large-scale experiments.
Meystre et al.[12] assumed epoxy acetates, such as compounds **9**, to be secondary products in the hypoiodite reaction, formed by acetolysis of the primarily formed unstable epoxy iodides. For this reason, they suggested the



Scheme 3

inclusion of an acetolysis step in the work-up procedure to obtain the maximum yield of epoxy acetates. As an alternative, the inclusion of an acidic oxidation step involving Ag_2CrO_4 and CrO_3 may be used to obtain the lactones in a reasonable yield. These suggestions have been widely accepted.

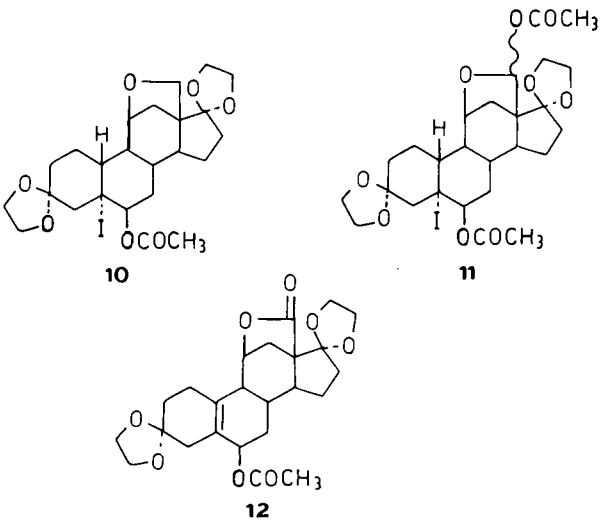
In our case, however, we were unable to isolate any 18-iodo-11β,18-epoxyestr-5-ene-3,17-dione cyclic bis(1,2-ethanediyl acetal). Even *Kalvoda* and *Heusler* state in their 1971 review[4] that no direct proof for the intermediacy of epoxy iodides in this reaction is available. This contrasts with many examples[12-14] where epoxy acetates have been isolated without the inclusion of an acetolysis step in the work-up procedure.

The only iodosteroids isolated as side-products were 11β-hydroxy-18-iodoestr-5-ene-3,17-dione cyclic bis(1,2-ethanediyl acetal) **5**, 6β-(acetyloxy)-11β,18-epoxy-5α-iodoestrane-3,17-dione cyclic bis(1,2-ethanediyl acetal) **10** (Scheme 4) and 6β,18-bis(acetyloxy)-11β,18-epoxy-5α-iodoestrane-3,17-dione cyclic bis(ethanediyl acetal) **11**. Both **10** and **11** result from addition to the 5(6)-double bond. Another side-product isolated, 6β-(acetyloxy)-3,3:17,17-bis[1,2-ethanediylbis(oxy)]-11β-hydroxyestr-5(10)-en-18-oic acid γ-lactone **12**, may have been formed from the corresponding 5α-iodo compound during chromatography.

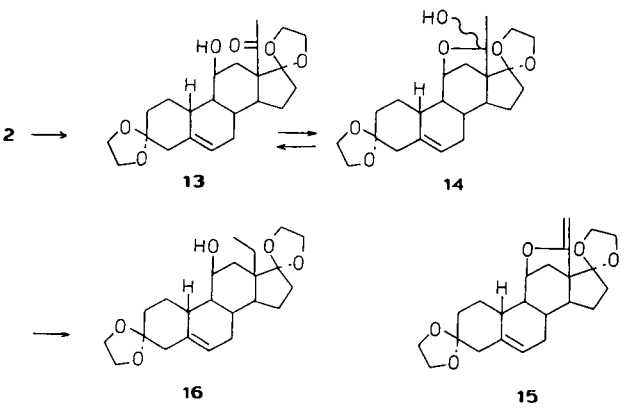
The 5(6)-double bond had, up till now, been considered to be fairly inert under the conditions of the hypoiodite reaction. Allylic oxidation was the only side-reaction reported[12,15,17]. On the basis of the results mentioned, *i.e.* no evidence for the formation of iodooxides but rather for the formation of 5α-iodo 6β-(acetyloxy) steroids, we decided not to introduce an acidic oxidation step, which would also have removed the protecting groups, in the work-up procedure. A zinc-reduction step, which will regenerate the 5(6)-double bond from the 5α-iodo 6β-(acetyloxy) steroids[17] was used as an alternative. It also proved economical to use the lactone **2** as a semi-purified product for the next step of the synthesis.

Conversion into desogestrel

The conversion of the lactone **2** into desogestrel **1** proved to be straightforward. Grignard reaction with methylmagnesium bromide gave, in a virtually quantitative yield, the hydroxy ketone **13**, which in solution occurs in equilibrium with the acetals **14** (Scheme 5). We found no formation of the tertiary alcohol, even under forcing reaction conditions such as higher temperatures or prolonged reaction time. The 11β,18-epoxy-18-hydroxy-18-methylestr-5-ene-3,17-dione cyclic bis(1,2-ethanediyl acetals) **14** were found to dehydrate upon chromatography on



Scheme 4



Scheme 5

silica gel to 11β,18-epoxy-18-methyleneestr-5-ene-3,17-dione cyclic bis(1,2-ethanediyl acetal) **15**. Wolff–Kishner reduction of the mixture of the hydroxy ketone **13** and the acetals **14** gave 13-ethyl-11β-hydroxygon-5-ene-3,17-dione cyclic bis(1,2-ethanediyl acetal) **16** in 83% yield.

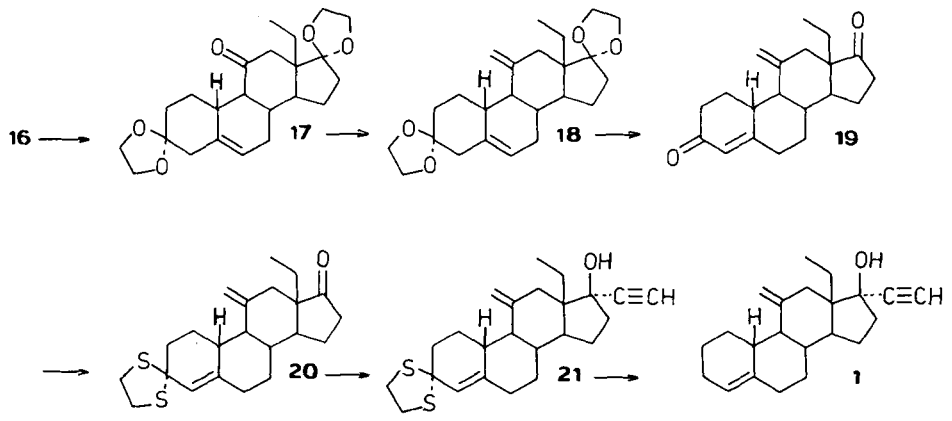
The 11-ketone **17** was obtained in 90% yield by oxidation of **16** with CrO_3/pyridine and converted, by Wittig reaction, as described by *van den Broek* et al., into the known 18-methyl-11-methyleneestr-4-ene-3,17-dione cyclic bis(1,2-ethanediyl acetal) **18** (Scheme 6)[3]. Removal of the protecting acetal groups gave, in 83% yield, the dione **19**, which was converted selectively into the cyclic 3-(1,2-ethanediyl dithioacetal **20** (91% yield). The complete conversion of the 17-ketone into the 17α-ethynyl-17β-hydroxy derivative **21** proved difficult[18]. Reductive removal of the cyclic (1,2-ethanediyl dithioacetal) group followed by purification gave the known 13-ethyl-11-methylene-18,19-dinor-17α-pregn-4-en-20-yn-17-ol (desogestrel) **1**[3] in 58% overall yield from **20**.

Although it has been stated that 13-ethyl-18-norsteroids can only be prepared via total synthesis[19], the results presented above show that desogestrel can be prepared via partial synthesis.

Experimental[20]

3,3:17,17-Bis[1,2-ethanediylbis(oxy)]-11β-hydroxyestr-5-en-18-oic acid γ-lactone **2**

A suspension of $Pb(OAc)_4$ (55.8 g; 126 mmol), $CaCO_3$ (18.6 g; 186 mmol) and iodine (7.62 g; 30 mmol) in cyclohexane (2400 ml) was



Scheme 6

heated to reflux for 10 min with stirring. After cooling to 60°C, **3** (11.22 g; 30 mmol) and azobisisobutyronitrile (1 g) were added and heating to reflux was continued for 2 h. The reaction mixture was cooled and filtered over hyflo. The resulting solution was washed with a saturated solution of sodium thiosulfate, a saturated solution of sodium bicarbonate followed by water, dried over Na_2SO_4 and concentrated *in vacuo*. The residue (16.9 g) was separated by chromatography on silica gel (500 g) using toluene/ethyl acetate/pyridine (1/1/0.02) as eluent. The crude **2** (6.2 g) was crystallized from methylene dichloride/methanol and gave fairly pure **2** (4.47 g; 12 mmol; 40%) with m.p. 147–151°C. An analytical sample was recrystallised from methylene dichloride/diethyl ether; m.p. 157.5–159.5°C; $[\alpha]_D$ −8. Anal. $C_{22}H_{28}O_6$ (388) calcd.: C 68.02, H 7.27, O 24.71; found: C 67.8, H 7.3, O 24.9%. IR (CCl_4): 1785 (C=O), 1670 (C=C), 1102 and 1037 (C–O of the acetals), 870 (C=CH) cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.85 (d, *J* 11.5 Hz, 12α-H), 2.29 (br.s., 4 H's), 2.53 (dd, *J* 11.5 and 6 Hz, 12β-H, 3.8–4.0 (m, OCH_2CH_2O), 4.76 (d, *J* 6 Hz, 11α-H), 5.48 (m, 6-H).

Fairly pure 11β-hydroxy-18-iodoestr-5-ene-3,17-dione cyclic bis(1,2-ethanediyl acetal) **5** (1.4 g, 2.4 mmol, 8%) was also isolated; m.p. 122–136°C. From other experiments we have isolated:

6β-(Acetyloxy)-11β,18-epoxy-5α-iodoestrane-3,17-dione cyclic bis(1,2-ethanediyl acetal) **10**. ^1H NMR ($CDCl_3$): δ 0.30 (td, *J* 12, 12 and 3 Hz, 2β-H), 2.09 (s, $COCH_3$), 2.18 (d, *J* 15 Hz, 4α-H), 2.34 (dd, *J* 15 and 2.5 Hz, 4β-H), 2.61 (ddd, *J* 14, 12 and 3 Hz, 10β-H), 3.73, 3.80 (2 × d, *J* 8 Hz, 18 H's), 3.84–4.07 (m, OCH_2CH_2O), 4.43 (d, *J* 6 Hz, 11α-H), 5.36 (t, *J* 2.6 Hz, 6α-H).

6β,18-Bis(acetyloxy)-11β,18-epoxy-5α-iodoestrane-3,17-dione cyclic bis(1,2-ethanediyl acetal) **11**. ^1H NMR major epimer ($CDCl_3$): δ 0.30 (td, *J* 12, 12 and 3 Hz, 2β-H), 2.06 (s, 18-$OCOCH_3$), 2.12 (s, 6-$OCOCH_3$), 2.59 (ddd, *J* 14, 13 and 2.6 Hz, 10β-H), 3.8–4.0 (m, OCH_2CH_2O), 4.63 (d, *J* 6.2 Hz, 11α-H), 5.36 (t, *J* 2.6 Hz, 6α-H), 6.26 (s, 18 H's).

6β-(Acetyloxy)-3,3:17,17-bis[1,2-ethanediylbis(oxy)]-11β-hydroxyestr-5(10)-en-18-oic acid γ-lactone **12**. ^1H NMR ($CDCl_3$): δ 1.85 (d, *J* 11.5 Hz, 12α-H), 2.04 (s, $COCH_3$), 2.53 (dd, *J* 6 and 11.5 Hz, 12β-H), 3.8–4.0 (m, OCH_2CH_2O), 5.02 (d, *J* 6 Hz, 11α-H), 5.10 (m, 6α-H).

13-Acetyl-11β-hydroxygon-5-ene-3,17-dione cyclic bis(1,2-ethanediyl acetal) **13**

From purified **2**. A suspension of Mg (1.09 g, 45 mmol) in dry ether (30 ml) was saturated with methyl bromide until all the magnesium had reacted. The ether was replaced with dry tetrahydrofuran (30 ml) and a solution of **2** (1.16 g, 3 mmol) in toluene (27 ml) was then added. After 2½ h heating to reflux, the reaction mixture was poured into water (250 ml). Extraction with toluene gave, after washing, drying and evaporation of solvents, a mixture of **13** and the isomeric **14** (1.23 g, 3 mmol, quant.) with m.p. 151–156°C. An analytical sample of **13** could be prepared by careful crystallization from methylene dichloride/diethyl ether; m.p. 177.5–179.5°C; $[\alpha]_D$ −36. IR (CH_2Cl_2): 3611 and 3480 (OH), 1691 (C=O), 1100 (C–O of the acetals) cm^{-1}. ^1H NMR ($CDCl_3$ + pyridine): δ 2.32 (s, $COCH_3$), 3.95 (br.s., OCH_2CH_2O), 4.45 (m, 11α-H), 5.50 (br.m., 6-H).

Without purification of **2**. A suspension of $Pb(OAc)_4$ (14.14 g, 32 mmol), $CaCO_3$ (6.2 g, 62 mmol) and iodine (2.54 g, 10 mmol) in cyclohexane (700 ml) was heated to reflux for 10 min with stirring. **3** (3.76 g, 10 mmol) and azobisisobutyronitrile (0.3 g) in cyclohexane (100 ml) were added and heating to reflux was continued for 40 min. The reaction mixture was cooled to room temperature and prepared for distillation. Ethanol (600 ml, 96%) and zinc dust (37 g, 565 mmol) were added and about 1 l of solvent was distilled for 1½ hours. After filtration, the remaining solvents were removed *in vacuo* and the residue (3.95 g) dissolved in dry toluene (25 ml). This solution was added, with stirring, to a solution of methylmagnesium bromide, prepared from magnesium (0.6 g, 25 mmol), methyl bromide and ether (50 ml). After stirring at room temperature for 1 h, the reaction mixture was cooled to 0°C and a solution of NH_4Cl (3 g, 56 mmol) in water (10 ml) was added slowly. The reaction mixture was steam-distilled until free of organic solvents and cooled to 0°C. The precipitate (3.39 g) was collected, washed with water and dried *in vacuo* at room temperature. The residue was suspended in toluene (2 ml) and ethyl acetate (1 ml) and stirred overnight at −20°C. The crystalline mixture of **13** and the isomeric **14** with m.p. 150–156°C was collected (1.80 g, 4.5 mmol, 45%).

13-Ethyl-11β-hydroxygon-5-ene-3,17-dione cyclic bis(1,2-ethanediyl acetal) **16**

To a suspension of a mixture of **13** and the isomeric acetals **14** (9.3 g, 23 mmol) in triethylene glycol (100 ml) were added hydrazine hydrate (36 ml, 740 mol) and hydrazine dihydrochloride (9.0 g, 85 mmol). The reaction mixture was stirred at 135°C for 1½ hours, cooled to about 80°C and potassium hydroxide (15 g, 265 mmol) added. The reaction mixture was heated to 170°C, whereby lower boiling components were distilled off, and was maintained at this temperature for 3½ hours. It was then cooled and poured into ice water (1 l). The suspension was neutralized with hydrochloric acid and extracted with methylene chloride. The extract was washed, dried and concentrated *in vacuo*. The residue (8.34 g) was crystallized from ethyl acetate to give **16** (7.5 g, 19 mmol, 83%) with m.p. 174–178°C. The analytical sample had a m.p. 179–181°C and an $[\alpha]_D$ +11.5. $C_{23}H_{34}O_5$ (390) calcd.: C 70.74, H 8.78, O 20.49; found: C 70.5, H 9.0, O 20.3%. IR (CCl_4): 3640 and 3520 (OH), 1680 (C=C), 1100 and 1030 (C–O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 3.88 (br.s., 17-acetal), 3.95 (br.s., 3-acetal), 4.20 (q., *J* 3 Hz, 11α-H), 5.45 (br.m., 6-H).

13-Ethylgon-5-ene-3,11,17-trione 3,17-cyclic bis(1,2-ethanediyl acetal) **17**

In a nitrogen atmosphere, powdered chromium trioxide (7.7 g, 77 mmol) was added carefully over a period of 30 min to a well stirred and cooled mixture of dry pyridine (25 ml) and dry methylene chloride (194 ml). Stirring was continued for 30 min followed by the dropwise addition of a solution of **16** (7.7 g, 20 mmol) in methylene dichloride (45 ml). The reaction mixture was stirred at room temperature for 20 h and then filtered over hyflo. The filtrate was washed with a sodium bisulfite solution followed by water, dried and filtered. The solution was concentrated *in vacuo* to a

volume of 15 ml, diluted with diethyl ether (80 ml), treated with charcoal (100 mg) and concentrated *in vacuo*. The residue was crystallized from methylene dichloride/diethyl ether to give **17** (7.0 g, 18 mmol, 90%) with m.p. 173–177°C. The analytical sample had a m.p. 175–177°C and an $[\alpha]_D$ +69. $C_{23}H_{32}O_5$ (388) calcd.: C 71.11, H 8.30, O 20.59; found: C 70.9, H 8.3, O 20.4%. IR (CCl_4): 1707 (C=O), 1672 (C=C), 1100 and 1170 (C–O of the acetals) cm^{-1}. ^1H NMR: δ 2.60 (br.s. 12 H's), 3.88 (m, 17-acetal), 3.94 (br.s., 3-acetal), 5.49 (br.s., 6-H).

13-Ethyl-11-methylenegon-5-ene-3,17-dione cyclic bis(1,2-ethanediyl acetal) **18**

Methyltriphenylphosphonium bromide (39.5 g, 110 mmol) was dissolved in dry dimethyl sulfoxide (200 ml) and, while stirring, sodium hydride dispersion in mineral oil (4.45 g, 57%, 105 mmol) was added. The reaction mixture was heated to 75°C and stirred until the evolution of hydrogen gas had ceased (*ca.* $\frac{3}{4}$–1 h). After cooling, **17** (5 g, 13 mmol) was added. The reaction mixture was heated to 60°C, stirred for 3 h and then poured into ice–water (2 l). The crystals were collected, washed with cold 50% methanol and dried. Crystallization from methylene chloride/ethanol gave **18** (4.63 g, 12 mmol, 92%) with m.p. 190–192°C (lit.[3] m.p. 183–186°C).

13-Ethyl-11-methylenegon-4-ene-3,17-dione **19**

A suspension of **18** (11.65 g, 30 mmol) in acetone (250 ml) and concentrated hydrochloric acid (1.2 ml) was stirred at room temperature for $4\frac{1}{2}$ hours. The reaction mixture was concentrated *in vacuo* to a volume of 25 ml, diluted with water (500 ml) and neutralized with a 2 M NaOH solution (about 7 ml). The precipitate was collected, dried and crystallized from methylene dichloride/ethanol to yield **19** (7.5 g, 25 mmol, 83%) with m.p. 149–151.5°C (lit.[3] m.p. 153–155°C).

13-Ethyl-11-methylenegon-4-ene-3,17-dione cyclic 3-(1,2-ethanediyl dithioacetal) **20**

To a solution of **19** (6.5 g, 22 mmol) in dry tetrahydrofuran (60 ml) were added successively ethanedithiol (3.21 ml, 38 mmol) and boron trifluoride etherate (4.4 ml, 42 mmol). After stirring for $2\frac{3}{4}$ h at reflux temperature, 45 ml of tetrahydrofuran were distilled off *in vacuo*, followed by addition of methanol (150 ml). The mixture was cooled to −20°C and maintained at this temperature for 2 h. The precipitate was collected, washed with cold methanol, aqueous 1 M NaOH solution and water and then dried. This yielded **20** (7.73 g, 20 mmol, 91%) with m.p. 191–193°C (lit.[3] m.p. 192–194°C).

13-Ethyl-11-methylene-18,19-dinor-17α-pregn-4-en-20-yn-17-ol **1**

A stirred suspension of potassium *tert*-butoxide (7 g, 62 mmol) in dry tetrahydrofuran (70 ml) was cooled to 0°C and dry, purified acetylene was passed through for 2 h. The reaction mixture was then cooled to −15/−20°C, followed by the addition over *ca.* 15 min of a solution of **20** (4.8 g, 13 mmol) in dry tetrahydrofuran (30 ml). Acetylene was passed through at −15/−20°C for an additional 2 h. The reaction mixture was then poured into ice–water (1 l) and the mixture neutralized with acid. Extraction with methylene dichloride gave crude **21** (5.75 g). The crude product was dissolved in dry tetrahydrofuran (27.5 ml) and added over 30 min to a suspension of sodium (2.28 g, 99 mmol) in liquid ammonia (85 ml). After stirring for 1 h at −4°C, dry acetonitrile (3 ml) was added slowly. The ammonia was evaporated and the remaining suspension was diluted carefully with water (300 ml). The temperature was maintained below 10°C. Extraction with hexane gave crude **1**, which was purified by chromatography on silica gel. Elution with methylene dichloride-hexane 1/1 and crystallization from pentane gave pure **1** (2.34 g, 7.5 mmol, 58%) with m.p. 109–110°C (lit.[3] m.p. 109–110°C).

Acknowledgement

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References

[1] *E. de Jager*, Contracept. Deliv. Syst. **3**, 11 (1982).
[2] *M. J. Weijers*, Clinical Therapeutics **4**, 359 (1982).
[3] *A. J. v.d. Broek, C. v. Bokhoven, P. M. J. Hobbelen* and *J. Leemhuis*, Recl. Trav. Chim. Pays-Bas **94**, 35 (1975).
[4] *K. Heusler* and *J. Kalvoda*, Synthesis **10**, 501 (1971).
[5] *K. Heusler* and *J. Kalvoda* in "Organic Reactions in Steroid Chemistry", *J. Fried* and *J. A. Edwards*, eds., Van Nostrand Reinhold Company, New York, 1972, Vol. II, p. 237.
[6] *A. J. v.d. Broek, A. I. A. Broess, M. J. v.d. Heuvel, H. P. de Jongh, J. Leemhuis, K. H. Schönemann, J. Smits, J. de Visser, N. P. van Vliet* and *F. J. Zeelen*, Steroids **30**, 481 (1977).
[7] *R. E. Ireland* and *L. N. Mander*, J. Org. Chem. **34**, 142 (1969).
[8] *Y. Shimizu*, Experientia **26**, 588 (1970).
[9] *H. Suginome, H. Ono* and *T. Masamune*, Tetrahedron Lett. 2909 (1969).
[10] *G. Habermehl* and *A. Haaf*, Liebigs Ann. Chem. **723**, 181 (1969).
[11] *J. Kalvoda, K. Heusler, G. Anner* and *A. Wettstein*, Helv. Chim. Acta. **46**, 618 (1963).
[12] *Ch. Meystre, K. Heusler, J. Kalvoda, P. Wieland, G. Anner* and *A. Wettstein*, Helv. Chim. Acta **45**, 1317 (1962).
[13] *K. Heusler, J. Kalvoda, Ch. Meystre, G. Anner* and *A. Wettstein*, Helv. Chim. Acta **45**, 2161 (1962).
[14] *E. Wenkert* and *B. L. Mylari*, J. Am. Chem. Soc. **89**, 174 (1967).
[15] *M. Stefanović, A. Jokić, Z. Maksimović, Lj. Lorenc* and *M. Lj. Mihailović*, Helv. Chim. Acta **53**, 1895 (1970).
[16] *S. Motahasi, M. Satomi, Y. Fujimoto* and *T. Tatsano*, Chem. Pharm. Bull. **31**, 1788 (1983) reported, however, formation of a 5α-iodo-6β-acetoxy derivative upon reaction of cholesteryl acetate with $Pb(OAc)_4$ and sodium iodide.
[17] *J. Kalvoda, K. Heusler, H. Ueberwasser, G. Anner* and *A. Wettstein*, Helv. Chim. Acta **46**, 1361 (1963).
[18] *Cf. H. Smith, G. A. Hughes, G. H. Douglas, G. R. Wendt, G. C. Buzby, R. A. Edgren, J. Fisher, T. Foell, B. Gadsby, D. Hartley, D. Herbst, A. B. A. Phillips, R. Rees, J. Siddall, J. Siuda, L. L. Smith, J. Tokolics* and *D. H. P. Watson*, J. Chem. Soc. II 4472 (1964); *J. C. Blazejewski, R. Dorme* and *C. Wakselman*, J. Chem. Soc. Perkin I 337 (1986).
[19] *H. Baier, G. Dürner* and *G. Quinkert*, Helv. Chim. Acta **68**, 1054 (1985).
[20] For general remarks see: *N. P. van Vliet, A. I. A. Broess, J. A. M. Peters, A. J. van den Broek, J. A. J. Leemhuis* and *F. J. Zeelen*, Recl. Trav. Chim. Pays-Bas **105**, 111 (1986).