Synthesis of Steroidal Azides. Part 2.[1] Reaction of 4,6-Dien-3-ones with Lead Tetra-acetate and Trimethylsilyl Azide

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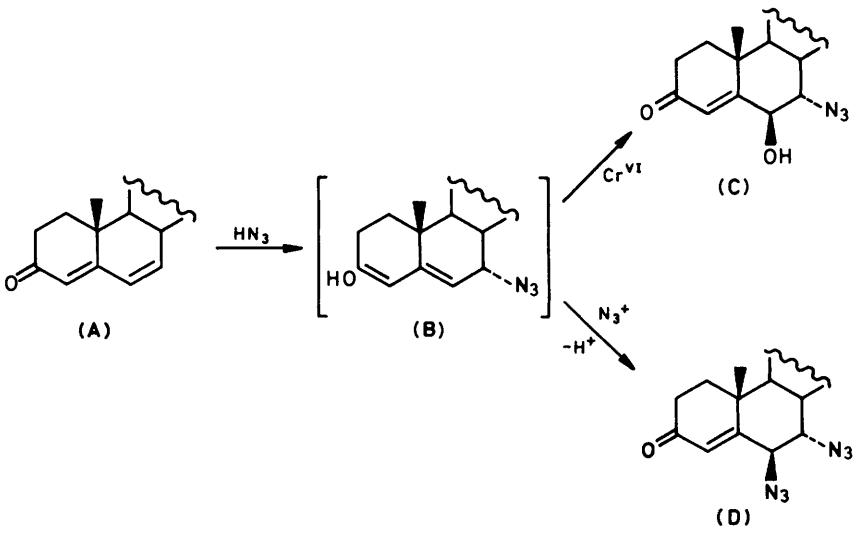
The reaction of steroidal 4,6-dien-3-ones with lead tetra-acetate and trimethylsilyl azide is shown to give predominantly 6β,7α-diazido-4-en-3-ones together with minor amounts of 7α-azido-4-ene-3,6-diones. With lead tetra-acetate and a mixture of trimethylsilyl azide and trimethyl silyl bromide, the same substrates yield exclusively 7α-azido-6β-bromo-4-en-3-ones. Reaction mechanisms are proposed to interpret these results. The 6β,7α-diazido-4-en-3-ones may be readily converted into 6-azido-4,6-dien-3-ones.

In the preceding paper [1] we showed that reaction of steroidal 4,6-dien-3-ones (A) with chromium trioxide and sodium azide in glacial acetic acid leads to the formation of the corresponding 7α-azido-6β-hydroxy-4-en-3-ones (C), together with small amounts of 6β,7α-diazido-4-en-3-ones (D). In addition, we proposed a mechanism by which both products might be formed *via* 7α-azidodienol intermediates (B) (Scheme 1). In anticipation that elimination of hydrazoic acid from these 6β,7α-diazides would generate the pharmaceutically valuable 6-azido-4,6-dien-3-ones,[2,3] we sought an alternative reagent which would generate, and preferentially deliver electrophilic azide to, the 7α-azidodienol intermediate (B) at the expense of forming an azidohydrin.

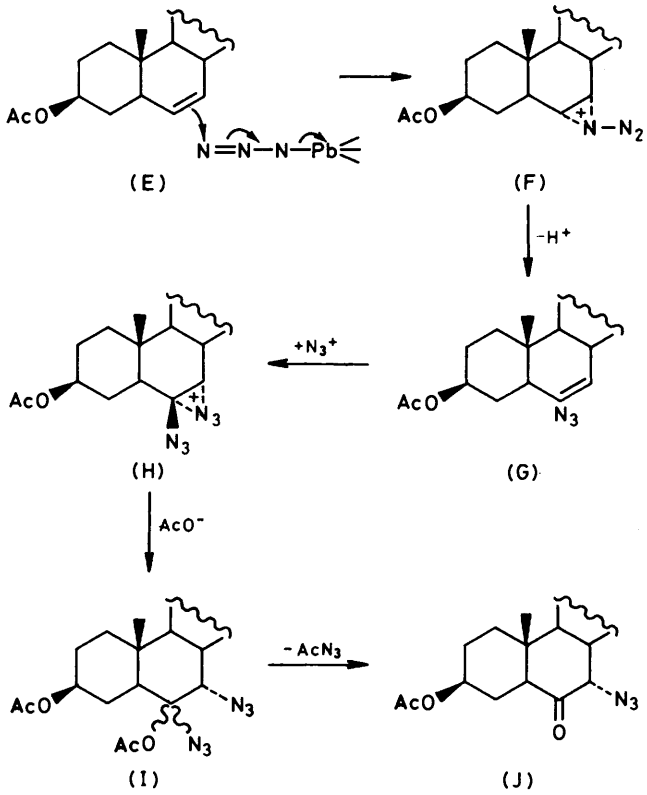
In a number of papers Zbiral and his co-workers have shown that the azide-transfer reagent system lead tetra-acetate–trimethylsilyl azide represents an elegant method of introducing positive azide to a large variety of olefinic and acetylenic compounds.[4] In general the reaction of lead tetra-acetate and trimethylsilyl azide with isolated trisubstituted steroidal olefins yields allylic azides [5] or seco keto nitriles,[6] depending upon temperature, whereas with isolated disubstituted olefins the major products are α-azidoketones.[7] The latter products were considered to arise by the mechanism which is illustrated for the case of a Δ^6-steroid in Scheme 2. Nucleophilic attack of the double bond in the substrate (E) on a lead azide ligand would lead to the 6α,7α-azidonium [8] ion (F) which, upon equilibration to a free carbonium ion and loss of a proton, can afford the vinyl azide (G). Owing to the electron-donating properties of the azide group, intermediate (G) is now more nucleophilic than the starting olefin (E) and thus a further positive azide ion can be delivered giving (H). Saturation with acetate ion and subsequent 1,1-elimination of acetyl azide from (I) would yield the observed product (J).

Interestingly, in the steroidal olefin cases studied by Zbiral *et al.*, vicinal diazides which would result from attack of an azide group on azidonium ions such as (F) were not observed (except as a minor product in one instance [6]), although they are common products from acyclic olefins [9] and bridged compounds.[10] This we assume is a reflection of the rapidity with which steroidal intermediates of type (F) collapse to vinyl azides.

We are not aware of any published examples of the reaction between lead tetra-acetate–trimethylsilyl azide and conjugated enones. However, in the light of our experience with chromium trioxide and sodium azide,[1] we felt that a 4,6-dien-3-one might undergo an analogous reaction, that is an initial nucleophilic conjugate addition of azide to give the 7α-azido-3,5-dienol intermediate (K) (Scheme 3), perhaps assisted by co-ordination of lead to the carbonyl oxygen. A similar mechanism is proposed for the zinc chloride-catalysed reaction of trimethylsilyl azide with aldehydes.[11] Intermediate (K) can subsequently undergo an electrophilic addition of positive azide delivered by lead. Furthermore, reduced nucleophilicity of the 6,7-double bond, imparted by the conjugated ketone,



Scheme 1.

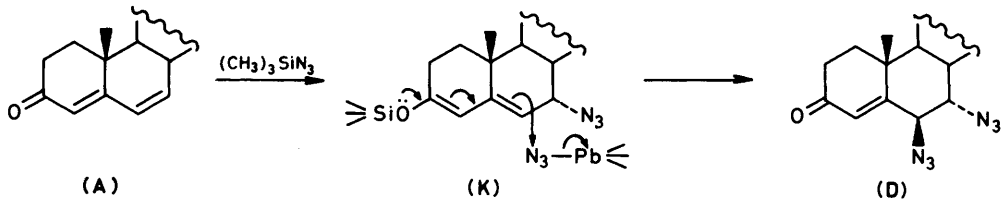


Scheme 2.

ring B, *viz.* the 6β,7α-diazido-1,4-dien-3-one (9) and traces of the 7α-azido-1,4-diene-3,6-dione (10). We did not observe any products arising from conjugate addition of azide to C-1. Similarly, the 6β,7α-diazido adducts (13) and (14) could be prepared from the 9α-fluoro-substituted 1,4,6-trien-3-ones (11) and (12) respectively, although in much reduced yield (17 and 19% respectively). This we assume is a reflection of the steric hindrance imposed by a 1,3-diaxial interaction between fluorine at C-9 and the incoming azide group at C-7.

An intriguing result was obtained when 17α-acetoxy-6,7-dehydroprogesterone (1) in methylene dichloride was treated with lead tetra-acetate in the presence of both trimethylsilyl azide and trimethylsilyl bromide in an 8 : 2 molar ratio. A single product was obtained in excellent yield whose structure was deduced from the following data. The mass spectrum exhibited molecular ions at *m/z* 491 and 493 corresponding to the addition of BrN_3. The presence of an azide function was confirmed by the i.r. spectrum (2 120 cm^{-1}). The u.v. spectrum revealed a maximum at 245 nm (ε 11 700) indicating that addition had taken place in ring B. The ^1H n.m.r. spectrum in [$^2H_6$]DMSO * displayed a doublet at δ 5.34 ($J_{6,7}$ 3 Hz, 6-H) and a broad singlet at δ 4.20 ($w_{\frac{1}{2}}$ 7 Hz). Furthermore, the 4-H signal at δ 6.14 appeared as a sharp singlet, indicating the 6-substituent to be axially oriented.[12] The absence of any axial–axial coupling to 7-H shows the 7-substituent to be similarly axially positioned. This information defines the structure as the 6β-bromo-7α-azido adduct (6). In addition, the latter compound could also be obtained by the treatment of (1) with bromine azide.[13]

Similarly, when (1) was treated with lead tetra-acetate, trimethylsilyl azide, and trimethylsilyl chloride, there was



Scheme 3.

should reduce the tendency to form a 6α,7α-cyclic azidonium ion which would be expected to lead to unwanted 6-keto-7α-azide.

In the event, when 17α-acetoxy-6,7-dehydroprogesterone (1) was treated at 0 °C with two equivalents of lead tetra-acetate and eight equivalents of trimethylsilyl azide in methylene dichloride, two main products were formed, together with a number of minor contaminants. The major component, obtained in 55% yield, proved to be the desired 6β,7α-diazide (4), whereas the minor component (24%) was the unstable 6-keto-7α-azide (5). The structures of both these compounds were determined by comparison of their physical properties with those of authentic specimens.[1] Similarly 6,7-dehydro-17α-hydroxyprogesterone (2) gave primarily the diazide (8).

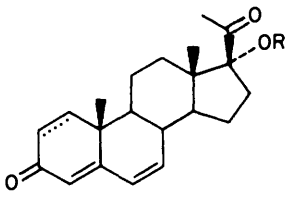
It should be noted that the 6-keto-7α-azides prepared during the course of this work decomposed with time to a number of products. T.l.c. evidence indicated that these decomposition products were responsible for most of the contaminants in the lead tetra-acetate–trimethylsilyl azide reactions. Those keto azides which were isolated usually did not crystallise and gave unsatisfactory combustion analyses.

Treatment of 1,2:6,7-didehydro-17α-hydroxyprogesterone (3) with lead tetra-acetate–trimethylsilyl azide under the same conditions led only to products resulting from reaction in obtained the analogous 6β-chloro-7α-azide (7) together with smaller amounts of the previously isolated 7α-azido-6-ketone (5). The chloro azide adduct (7) could be converted into the previously described [14] 17α-acetoxy-6-chloro-6,7-dehydroprogesterone (15) with tetramethylammonium fluoride [2] in acetonitrile.

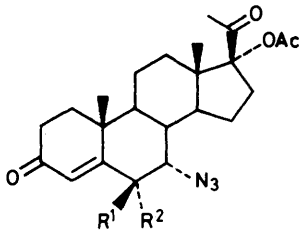
The exclusive formation of these 6β-halogeno-7α-azides can be rationalised in terms of the weaker nucleophilicity of chlorine and bromine relative to that of azide. Thus products arising from conjugate addition of halide to C-7 are not observed. Conversely, the electrophilicity of bromine and chlorine is greater than that of azide, and apparently only positive halogen is transferred to the 7α-azido-3,5-dien-3-ol intermediates.

Finally, the 6β,7α-diazido-4-en-3-ones could be converted into the desired 6-azido-4,6-dien-3-ones, either by treatment with sodium azide in dimethylformamide (DMF), or by tetramethylammonium fluoride in acetonitrile.[2] For example, 17α-acetoxy-6β,7α-diazidoprogesterone (4) gave the known [15] 17α-acetoxy-6-azido-6,7-dehydroprogesterone (16) in good yield. However, prolonged heating (three days at 65 °C) with tetramethylammonium fluoride in acetonitrile was required to

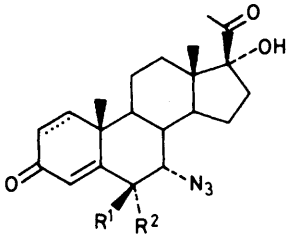
* DMSO is dimethyl sulphoxide.



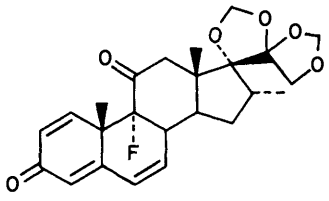
(1) R = Ac, $\Delta^{4,6}$
(2) R = H, $\Delta^{4,6}$
(3) R = H, $\Delta^{1,4,6}$



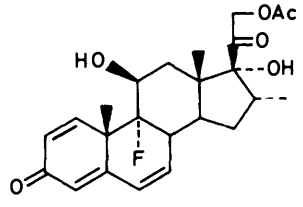
(4) $R^1 = N_3$, $R^2 = H$
(5) $R^1R^2 = O$
(6) $R^1 = Br$, $R^2 = H$
(7) $R^1 = Cl$, $R^2 = H$



(8) $R^1 = N_3$, $R^2 = H$, Δ^4
(9) $R^1 = N_3$, $R^2 = H$, $\Delta^{1,4}$
(10) $R^1R^2 = O$, $\Delta^{1,4}$



(11)



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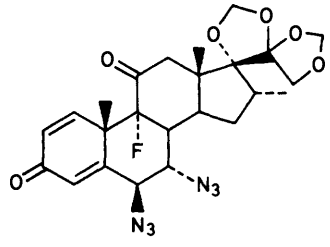

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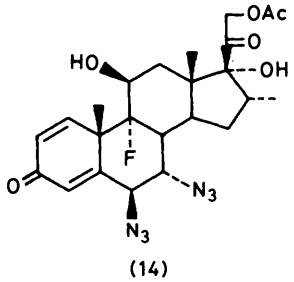
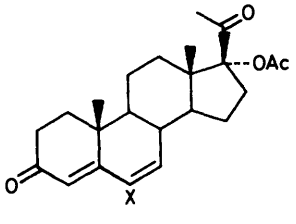
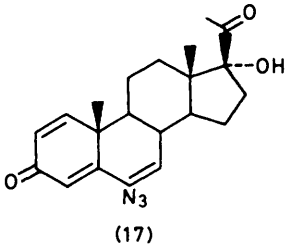


(14)



(15) X = Cl
(16) X = N_3



(17)

convert the Δ^1-analogue, 6β,7α-diazido-17α-hydroxy-1,2-dehydroprogesterone (9) into 6-azido-17α-hydroxypregna-1,4,6-triene-3,20-dione (17).

Experimental

General experimental details are described in the preceding paper.[1] Lead tetra-acetate was freed from acetic acid before use by storage over sodium hydroxide under vacuum. **CAUTION! The reactions utilizing lead tetra-acetate in the presence of trimethylsilyl azide generate lead azide species as by-products. Although we did not experience any explosions, the well documented [16] explosive properties of lead azide demand appropriate safety precautions, including the use of remotely controlled equipment and adequate shielding. The lead azide was destroyed by dissolution in 50% aqueous sodium hydroxide.**

Reaction of 3,20-*Dioxopregna*-4,6-*dien*-17α-*yl Acetate* (1) *with Lead Tetra-acetate and Trimethylsilyl Azide*.—A solution of dry lead tetra-acetate (2.66 g, 6 mmol) in methylene dichloride (50 ml) was added dropwise to a stirred solution of 3,20-dioxopregna-4,6-dien-17α-yl acetate (1.11 g, 3 mmol) and trimethylsilyl azide (3.18 ml, 24 mmol) in methylene dichloride (50 ml) at 5 °C. The mixture was stirred for an additional 18 h during which time it warmed to room temperature. The precipitated lead salts were removed by filtration through Celite and the filtrate was washed in turn with 5% aqueous sodium hydrogen carbonate and water, and dried. Evaporation of the solvent gave an oil which was chromatographed over a silica gel column. Gradient elution with light petroleum–ether gave first 6β,7α-diazido-3,20-dioxopregn-4-en-17α-yl acetate (4) (750 mg, 55%), crystallised from ether (345 mg), m.p. 161—162 °C; $[\alpha]_D$ −100°; identical with an authentic specimen,[1] followed by 7α-azido-3,6,20-trioxopregn-4-en-17α-yl acetate (5) (310 mg, 24%) as an unstable oil, identified by comparison with a previously obtained [1] sample.

6β,7α-*Diazido*-17α-*hydroxypregn*-4-*ene*-3,20-*dione* (8).—In a manner similar to that above, reaction of 17α-hydroxypregna-4,6-diene-3,20-dione (2) (328 mg, 1 mmol) with lead tetra-acetate (886 mg, 2 mmol) and trimethylsilyl azide (1.06 ml, 8 mmol) gave 6β,7α-*diazido*-17α-*hydroxypregn*-4-*ene*-3,20-*dione* (8) (250 mg, 61%), crystallised from ether (102 mg, m.p. 170—171 °C (decomp.); $[\alpha]_D$ −104°; $\lambda_{max.}$ 235 (nm ε 12 600); $\nu_{max.}$ 3 450, 2 100, 1 700, 1 670, and 1 640 cm^{-1}; δ 6.01 (1 H, s, 4-H), 5.29 (1 H, s, exchanges with ^2H_2O, 17α-OH), 4.70 (1 H, d, $J_{6,7}$ 3 Hz, 6-H), 3.82 (1 H, t, $J_{7,8}$ 3 Hz, 7-H), 2.10 (3 H, s, 21-H_3), 1.26 (3 H, s, 19-H_3), and 0.55 (3 H, s, 18-H_3) (Found: C, 60.9; H, 6.8; N, 20.2%; M^+, 412. $C_{21}H_{28}N_6O_3$ requires C, 61.14; H, 6.84; N, 20.38%; *M*, 412).

6β,7α-*Diazido*-17α-*hydroxypregna*-1,4-*diene*-3,20-*dione* (9) *and* 7α-*Azido*-17α-*hydroxypregna*-1,4-*diene*-3,6,20-*trione* (10).—In a manner similar to that above, reaction of 17α-hydroxypregna-1,4,6-triene-3,20-dione (3) (326 mg, 1 mmol) with lead tetra-acetate (886 mg, 2 mmol) and trimethylsilyl azide (1.06 ml, 8 mmol) gave, after column chromatography

on silica gel, 6β,7α-*diazido*-17α-*hydroxypregna*-1,4-*diene*-3,20-*dione* (9), crystallised from ether (233 mg, 57%), m.p. 188—190 °C; $[\alpha]_D$ −166°; $\lambda_{max.}$ 244 nm (ε 16 500); $\nu_{max.}$ 3 400, 2 100, 1 720, 1 670, and 1 630 cm^{-1}; δ 7.21 (1 H, d, $J_{1,2}$ 10 Hz, 1-H), 6.43 (1 H, d, $J_{2,4}$ 2 Hz, 4-H), 6.16 (1 H, dd, 2-H), 5.30 (1 H, s, exchanges with ^2H_2O, 17α-OH), 4.89 (1 H, d, $J_{6,7}$ 3 Hz, 6-H), 3.95 (1 H, br s, $w_{\frac{1}{2}}$ 7 Hz, 7-H), 2.10 (3 H, s, $COCH_3$), 1.32 (3 H, s, 19-H_3), and 0.58 (3 H, s, 18-H_3) (Found: C, 61.15; H, 6.35; N, 20.75%; M^+, 410. $C_{21}H_{26}N_6O_3$ requires C, 61.44; H, 6.39; N, 20.48%; *M*, 412), and 7α-azido-17α-hydroxypregna-1,4-diene-3,6,20-trione (10) as a gum (37 mg, 10%), $\lambda_{max.}$ 250 nm; $\nu_{max.}$ 3 550, 2 120, 1 730, 1 720, 1 680, and 1 640 cm^{-1}; δ 7.29 (1 H, d, $J_{1,2}$ 10 Hz, 1-H), 6.30 (1 H, s, 4-H), 6.23 (1 H, dd, $J_{2,4}$ 2 Hz, 2-H), 5.31 (1 H, s, exchanges with ^2H_2O, 17α-OH), 4.20 (1 H, d, $J_{7,8}$ 3 Hz, 7-H), 2.11 (3 H, s, $COCH_3$), 1.20 (3 H, s, 19-H_3), and 0.57 (3 H, s, 18-H_3).

6β,7α-*Diazido*-9α-*fluoro*-16α-*methyl*-17α,20:20,21-*bis*(*methylenedioxy*)*pregna*-1,4-*diene*-3,11-*dione* (13).—In a manner similar to that above, reaction of 9α-fluoro-16α-methyl-17α,20:20,21-bis(methylenedioxy)pregna-1,4,6-triene-3,11-dione (11) (430 mg, 1.0 mmol) with lead tetra-acetate (886 mg, 2 mmol) and trimethylsilyl azide (1.06 ml, 8 mmol) gave, after column chromatography on silica gel, 6β,7α-*diazido*-9α-*fluoro*-16α-*methyl*-17α,20:20,21-*bis*(*methylenedioxy*)*pregna*-1,4-*diene*-3,11-*dione* (13), crystallised from ether (88 mg, 17%), m.p. 208—209 °C; $[\alpha]_D$ −109°; $\lambda_{max.}$ 234 nm (ε 15 800); $\nu_{max.}$ 2 100, 1 720, 1 670, and 1 625 cm^{-1}; δ (C^2HCl_3) 7.46 (1 H, d, $J_{1,2}$ 10 Hz, 1-H), 6.42 (1 H, s, 4-H), 6.32 (1 H, dd, $J_{2,4}$ 2 Hz, 2-H), 5.0—5.25 (4 H, m, 2 × OCH_2O), 4.52 (1 H, d, $J_{6,7}$ 3 Hz, 6-H), 3.98 (2 H, s, 21-H_2), 3.65 (1 H, br s, $w_{\frac{1}{2}}$ 8 Hz, 7-H), 1.71 (3 H, s, 19-H_3), 1.03 (3 H, d, *J* 7 Hz, 16α-CH_3), and 0.90 (3 H, s, 18-H_3) (Found: C, 56.3; H, 5.3; N, 16.2%; M^+, 514. $C_{24}H_{27}FN_6O_6$ requires C, 56.02; H, 5.29; N, 16.34%; *M*, 514).

6β,7α-*Diazido*-9α-*fluoro*-16α-*methyl*-3,20-*dioxopregna*-1,4-*diene*-11β,17α,21-*triol* 21-*Acetate* (14).*—In a manner similar to that described above, reaction of 9α-fluoro-16α-methyl-3,20-dioxopregna-1,4,6-triene-11β,17α,21-triol 21-acetate (12) (432 mg, 1 mmol) with lead tetra-acetate (886 mg, 2 mmol) and trimethylsilyl azide (1.06 ml, 8 mmol) gave, after column chromatography on silica gel, 6β,7α-*diazido*-9α-*fluoro*-16α-*methyl*-3,20-*dioxopregna*-1,4-*diene*-11β,17α,21-*triol* 21-*acetate* (14) (100 mg, 19%), crystallised from ether (52 mg), m.p. 208—210 °C; $[\alpha]_D$ −50°; $\lambda_{max.}$ 237 nm (ε 15 300); $\nu_{max.}$ 3 500, 2 100, 1 760, 1 725, 1 670, 1 630, and 1 240 cm^{-1}; δ (C^2HCl_3) 7.32 (1 H, d, $J_{1,2}$ 10 Hz, 1-H), 6.38 (1 H, s, 4-H), 6.30 (1 H, dd, $J_{2,4}$ 2 Hz, 2-H), 4.94 (2 H, s, 21-H_2), 4.62 (1 H, d, $J_{6,7}$ 2 Hz, 6-H), 4.33 (1 H, d, *J* 13 Hz, 11α-H), 3.64 (1 H, br s, $w_{\frac{1}{2}}$ 8 Hz, 7-H), 2.11 (3 H, s, 21-$OCOCH_3$), 1.70 (3 H, s, 19-H_3), 1.00 (3 H, s, 18-H_3), and 0.90 (3 H, d, *J* 7 Hz, 16α-CH_3) (Found: C, 55.75; H, 5.7; N, 16.1%; M^+, 516. $C_{24}H_{29}FN_6O_6$ requires C, 55.80; H, 5.66; N, 16.27%; *M*, 516).

7α-*Azido*-6β-*bromo*-3,20-*dioxopregn*-4-*en*-17α-*yl Acetate* (6).—Reaction of 3,20-dioxopregna-4,6-dien-17-yl acetate (1) (185 mg, 0.5 mmol) with lead tetra-acetate (443 mg, 1 mmol), trimethylsilyl azide (0.53 ml, 4 mmol), and trimethylsilyl bromide (0.13 ml, 1 mmol) as described above gave, after column chromatography on silica gel, 7α-*azido*-6β-*bromo*-3,20-*dioxopregn*-4-*en*-17α-*yl acetate* (6), crystallised from ether (123 mg, 50%), m.p. 151—152 °C (decomp.); $[\alpha]_D$ −38°; $\lambda_{max.}$ 245 nm (ε 11 700); $\nu_{max.}$ 2 120, 1 730, 1 710, 1 670, 1 610, and 1 250 cm^{-1}; δ 6.14 (1 H, s, 4-H), 5.34 (1 H, d, $J_{6,7}$ 3 Hz, 6-H), 4.20 (1 H, br s, $w_{\frac{1}{2}}$ 7 Hz, 7-H), 2.09 (3 H, s, $COCH_3$), 1.98 (3 H, s, $COCH_3$), 1.43 (3 H, s, 19-H_3), and 0.64 (3 H, s, 18-H_3) [Found: C, 56.0; H, 5.9; N, 8.75%; (M^+ − 43), 448 and 450. $C_{23}H_{30}BrN_3O_4$ requires C, 56.10; H, 6.14; N, 8.53%; *M*, 491 and 493].

7α-*Azido*-6β-*chloro*-3,20-*dioxopregn*-4-*en*-17α-*yl Acetate* (7).—Reaction of compound (1) (740 mg, 2.0 mmol) with trimethylsilyl azide (2.12 ml, 16 mmol), trimethylsilyl chloride (0.51 ml, 4 mmol), and lead tetra-acetate (1.77 g, 4 mmol) as described above gave, after column chromatography on silica gel, 7α-*azido*-6β-*chloro*-3,20-*dioxopregn*-4-*en*-17α-*yl acetate* (7), crystallised from ether (451 mg, 50%), m.p. 192—194 °C; $[\alpha]_D$ −78°; $\lambda_{max.}$ 237 nm (ε 14 400); $\nu_{max.}$ 2 120, 1 740, 1 710, 1 670, and 1 250 cm^{-1}; δ 6.19 (1 H, s, 4-H), 5.19 (1 H, d, $J_{6,7}$ 3 Hz, 6-H), 4.12 (1 H, br s, $w_{\frac{1}{2}}$ 7 Hz, 7-H), 2.08 (3 H, s, $COCH_3$), 1.96 (3 H, s, $COCH_3$), 1.36 (3 H, s, 19-H_3), and 0.62 (3 H, s, 18-H_3) (Found: C, 61.55; H, 6.7; Cl, 7.35; N, 10.65; M^+, 447 and 449. $C_{23}H_{30}ClN_3O_4$ requires C, 61.66; H, 6.75; Cl, 7.92; N, 9.38%; *M*, 447 and 449).

6-*Chloro*-3,20-*dioxopregna*-4,6-*dien*-17α-*yl Acetate* (15).—(i) *Using sodium azide*. A mixture of 7α-azido-6β-chloro-3,20-dioxopregn-4-en-17α-yl acetate (7) (113 mg, 0.25 mmol), sodium azide (20 mg, 0.31 mmol), and DMF (10 ml) was maintained at 80 °C for 3 h. The reaction mixture was cooled, diluted with ether, washed with water, and dried. Evaporation of the solvent left a solid residue which was crystallised from ether to give 6-chloro-3,20-dioxopregna-4,6-dien-17α-yl acetate (15) (55 mg, 54%), m.p. 208—210 °C; $[\alpha]_D$ +2° (lit.,[14] m.p. 211—212 °C; $[\alpha]_D$ +6°); δ 6.39 (1 H, d, $J_{7,8}$ 2 Hz, 7-H), 6.00 (1 H, s, 4-H), 2.05 (3 H, s, $COCH_3$), 1.97 (3 H, s, $COCH_3$), 1.10 (3 H, s, 19-H_3), and 0.63 (3 H, s, 18-H_3).

(ii) *Using tetramethylammonium fluoride*. A solution of compound (7) (50 mg) in acetonitrile (25 ml) was stirred with tetramethylammonium fluoride pentahydrate (50 mg) at room temperature overnight. The reaction mixture was diluted with ether, washed with water, and dried. Evaporation of the solvent and crystallisation of the residue gave compound (15) (23 mg, 51%), identical with the previously obtained material.

6-*Azido*-3,20-*dioxopregna*-4,6-*dien*-17α-*yl Acetate* (16).—(i) *Using sodium azide*. A mixture of 6β,7α-diazido-3,20-dioxopregn-4-en-17α-yl acetate (4) (454 mg, 1.0 mmol), sodium azide (650 mg, 10 mmol), and DMF (20 ml) was maintained at 80 °C for 5 h. After being cooled to room temperature the reaction mixture was diluted with ether, washed with water, and dried. The ethereal solution was concentrated to leave a brown oil which was chromatographed on a silica gel column. Gradient elution with light petroleum–ether gave 6-azido-3,20-dioxopregna-4,6-dien-17α-yl acetate (16), crystallised from ether–light petroleum (225 mg, 55%), m.p. 172—175 °C; $[\alpha]_D$ +70° (lit.,[15] m.p. 169—192 °C; $[\alpha]_D$ +75°); $\lambda_{max.}$ 251 (ε 13 100) and 298 nm (12 700); $\nu_{max.}$ 2 100, 1 730, 1 720, 1 670, and 1 270 cm^{-1}; δ 5.85 (2 H, s, 4- and 7-H), 2.04 (3 H, s, $COCH_3$), 1.98 (3 H, s, $COCH_3$), 1.32 (3 H, s, 19-H_3), and 0.65 (3 H, s, 18-H_3) (Found: C, 67.15; H, 6.8; N, 10.1%; M^+, 411. $C_{23}H_{29}N_3O_4$ requires C, 67.13; H, 7.10; N, 10.21%; *M*, 411).

(ii) *Using tetramethylammonium fluoride*. A mixture of compound (4) (113 mg, 0.25 mmol) and tetramethylammonium fluoride pentahydrate (113 mg) in acetonitrile (10 ml) was stirred at 65 °C for 2 h. The reaction mixture was cooled, diluted with ethyl acetate, washed with water, and dried. Evaporation of the solvent gave a yellow oil. Decolourisation with charcoal and crystallisation from ether gave compound (16) (48 mg, 47%), identical with the previously obtained material.

* 6β,7α-Diazido-9α-fluoro-1,2-dehydro-16α-methylcortisol acetate.

6-*Azido*-17α-*hydroxypregna*-1,4,6-*triene*-3,20-*dione* (17).—A solution of 6β,7α-diazido-17α-hydroxypregna-1,4-diene-3,20-dione (9) (65 mg, 0.16 mmol) in acetonitrile (5 ml) containing tetramethylammonium fluoride pentahydrate (65 mg) was heated in an oil-bath at 65 °C for 3 d. The mixture was cooled, diluted with ethyl acetate, and washed with water. The organic phase was dried and evaporated to give a brown gum which was chromatographed on 2 × 1 000 μ silica gel preparative plates [developer chloroform–ethyl acetate (4 : 1)]. Extraction of the least polar band with ethyl acetate gave starting material (12 mg) and extraction of the more polar band with ethyl acetate gave 6-*azido*-17α-*hydroxypregna*-1,4,6-*triene*-3,20-*dione* (17), crystallised from ether–light petroleum (16 mg, 27%), m.p. 145—146 °C (decomp.); $[\alpha]_D$ +28°; $\lambda_{max.}$ 249 (ε 15 000) and 311 nm (6 500); $\nu_{max.}$ 3 400, 2 100, 1 710, 1 675, and 1 650 cm^{-1}; δ 7.20 (1 H, d, $J_{1,2}$ 10 Hz, 1-H), 6.17 (1 H, dd, $J_{2,4}$ 2 Hz, 2-H), 6.13 (1 H, d, 4-H), 5.78 (1 H, d, $J_{7,8}$ 2 Hz, 7-H), 5.26 (1 H, s, exchanges with ^2H_2O, 17-OH), 2.10 (3 H, s, 21-H_3), 1.18 (3 H, s, 19-H_3), and 0.63 (3 H, s, 18-H_3) (Found: C, 68.6; H, 6.8; N, 11.35%; M^+, 367. $C_{21}H_{25}N_3O_3$ requires C, 68.64; H, 6.86; N, 11.44%; *M*, 367).

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