Preparation and Reactions of Steroidal Cross-conjugated 3-Nitrones

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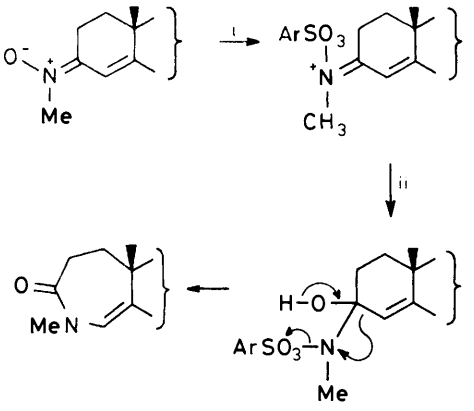
Treatment of the *N*-methylnitrone (1b) of dichlorisone acetate (*E*–*Z*-mixture) with toluene-*p*-sulphonyl chloride in pyridine in the presence of water gave dichlorisone acetate (1a) (88%). In the presence of hydrogen sulphide, however, the nitrone was deoxygenated to give the corresponding imine (1c), which on prolonged reaction with hydrogen sulphide in pyridine afforded the corresponding 1,4-diene-3-thione (1d). Similarly prepared were the unstable imines (2d), (3c), and (4c), which were smoothly converted into the corresponding thiones (2e), (3d), and (4d), respectively. In the absence of strong nucleophiles, dichlorisone acetate nitrone (1b) was treated with toluene-*p*-sulphonyl chloride in pyridine to give the corresponding trienimine (1g) (45%). Under similar conditions, however, prednisolone-21-propionate nitrone (3b) gave the 2-*p*-tolylsulphonyloxy-derivative (3e) as the major product. Separate treatment of both *Z*- and *E*-isomers of dehydrotestosterone acetate nitrone [(2b) and (2c)] afforded, in both cases, the 2-*p*-tolylsulphonyloxy-derivative (2g) (25%), whereas betamethasone nitrone (4b) gave a mixture of the 2-*p*-tolylsulphonyloxy-dienimine (4f) and the trienimine (4h) in low yield.

NITRONES have proved to be versatile intermediates in organic synthesis, as exemplified by their participation in *inter alia* [3 + 2] cycloadditions,[1] the Krohnke reaction,[2] and various rearrangement reactions induced by treatment with esterifying reagents.[3] Our earlier investigations into the chemistry of the nitrone function [4] led to the development of a novel rearrangement reaction whereby saturated and unsaturated steroidal ring-A nitrones could be converted into their A-aza-A-homosteroid analogues on treatment with tosyl chloride in pyridine, which contained traces of water (Scheme 1).

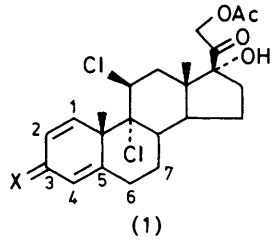


Ar = C_6H_4Me-*p*

SCHEME 1 *Reagents*: i, $ArSO_2Cl$, pyridine; ii, H_2O

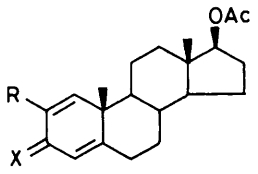
Unlike the analogous Beckmann rearrangement of oximes,[5,6] the nature of the products of the nitrone rearrangement was found to be independent of the configuration of the starting nitrones. Furthermore, in the case of the 4-ene-3-nitrones, exclusive migration of the *vinyl* group occurred. By contrast, Shoppee *et al.*[5] have demonstrated that only the analogous *E*-oximes can undergo the Beckmann rearrangement to afford lactam products that result from preferential alkyl migration. As a logical extension to this work, we have prepared some steroidal 1,4-diene-3-nitrones and studied this and related aspects of their chemistry.

Although less reactive than the steroidal 3-ones and 4-en-3-ones, cross-conjugated 1,4-dien-3-ones may conveniently be converted into the corresponding 3-(*N*-methylnitrone) derivatives in high yield on treatment with an excess of *N*-methylhydroxylamine hydrochloride in pyridine at 40 °C for *ca.* 10 h. In this way, the dienones (1a), (2a), (3a), and (4a) afforded the *N*-methylnitrones (1b), (2b) + (2c), (3b), and (4b), respectively, as mixtures of geometric isomers, except where otherwise specified. In general, those mixtures were obtained as amorphous powders [$\lambda_{max.}$ 316—319 nm (ε 23 400—25 000); δ 3.63—3.87 (s, *N*-methyl)] with indefinite melting points. In the case of 17β-acetoxyandrosta-1,4-dien-3-one (2a), however, fractional crystallization of the derived nitrone mixture from diethyl ether was possible, to give pure samples of the *E*- and *Z*-isomers, both as crystalline solids with characteristic melting points and optical rotations. Configurational assignments followed from n.m.r. considerations; the nitrone with the more deshielded 4-H and the more shielded 2-H



(1)

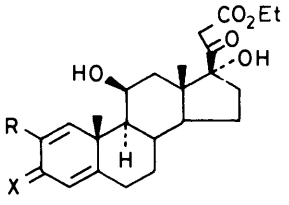
a ; X = O
b ; X = N(O⁻)–Me
c ; X = NMe
d ; X = S
e ; X = NMe · *p* – Me $C_6H_4SO_3H$
f ; X = CPh_2
g ; X = NMe ; 6,7-dehydro
h ; X = O ; 6,7-dehydro



(2)

a ; X = O, R = H
b : X = Me, O⁻, N⁺ (Z)
c ; X = O⁻, N⁺, Me (E)
d ; X = NMe, R = H
e ; X = S, R = H
f ; X = NMe · HCl, R = H
g ; X = NMe, R = $OSO_2C_6H_4Me$-p
h ; X = O, R = $OSO_2C_6H_4Me$-p

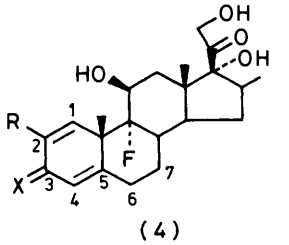
was assigned as the *Z*-isomer, and *vice versa* for the *E*-isomer. The interconversion of the isomers under simulated reaction conditions was readily demonstrated by n.m.r. spectroscopy. Thus, dissolution of the *E*-nitrone (2c) in [$^2H_5$]pyridine which contained pyridinium tosylate



(3)

a ; X = O, R = H
b ; X = N⁺–Me, O⁻, R = H
c ; X = NMe, R = H
d ; X = S, R = H
e ; X = NMe, R = $OSO_2C_6H_4Me$-p
f ; X = S, R = $OSO_2C_6H_4Me$-p
g ; X = O, R = $OSO_2C_6H_4Me$-p

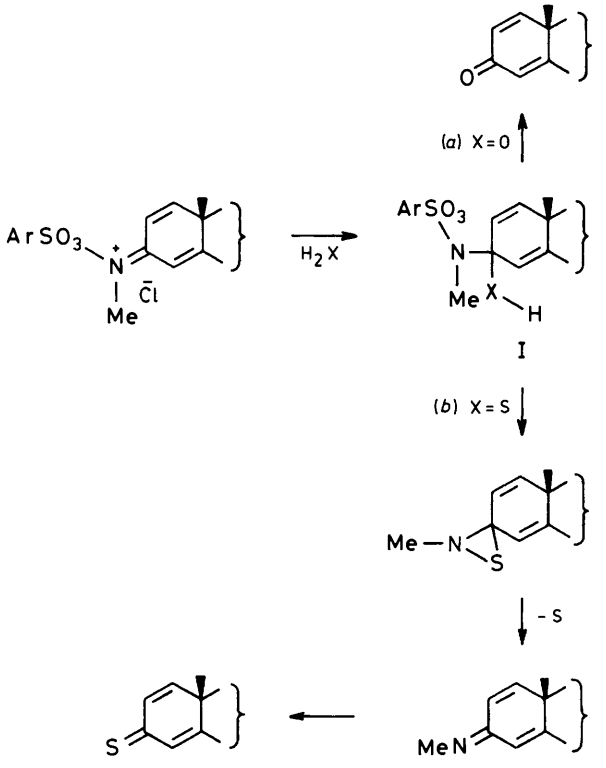
(0.2 equiv.) gave an equilibrium mixture which contained *ca.* equal amounts of each geometric isomer. A similar effect has been observed for 4-ene-3-nitrones.[4] All subsequent discussion will refer to *E*–*Z* mixtures unless stated otherwise.



(4)

a ; X = O, R = H
b ; X = N⁺–Me, O⁻, R = H
c ; X = NMe, R = H
d ; X = S, R = H
e ; X = NMe · *p*-$MeC_6H_4SO_3H$, R = H
f ; X = NMe, R = $OSO_2C_6H_4Me$-p
g ; X = O, R = $OSO_2C_6H_4Me$-p
h ; X = NMe, R = H ; 6,7-dehydro
i ; X = O, R = H ; 6,7-dehydro

On treatment with toluene-*p*-sulphonyl chloride in pyridine which contained water (15 equiv.) the *N*-methylnitrone of dichlorisone acetate (1b) (*E*–*Z* mixture) underwent smooth conversion into the parent dienone (1a) (88%) rather than to either of the expected rearrangement products. Most plausibly, the reaction proceeded *via* initial tosylation of the nitrone function followed by attack by water to give an intermediate of type I (X = O) [Scheme 2, path (*a*)] with breakdown to the original



Ar = C_6H_4Me-p

SCHEME 2

dienone (1a). The apparent reluctance of this system to undergo a rearrangement reaction similar to that of the analogous α,β-unsaturated nitrones under the same conditions may be due to the unfavourable geometry imposed upon intermediate I (X = O) by the presence of an additional ring-A carbon-carbon double bond.

On the basis of this result, replacement of water by hydrogen sulphide in the reaction mixture was expected to lead directly to the formation of the pharmaceutically interesting 1,4-diene-3-thiones [Scheme 2, path (*b*), X = S]. We have shown previously that the direct thionation of diverse α,β-unsaturated ketones and cross-conjugated dienones can be effected using phosphorus pentasulphide in pyridine.[7] In fact, treatment of the *N*-methylnitrone (1b) in pyridine, which contained an excess of hydrogen sulphide, with toluene-*p*-sulphonyl chloride for 1 h at room temperature yielded, after chromatography, a purple, crystalline solid $C_{23}H_{28}Cl_2O_4S$

$\lambda_{max.}$ 330 nm (ε 23 500)], formulated as the desired 1,4-diene-3-thione (1d) (10%) and, in addition, a more polar product identified as the iminiumtoluene-*p*-sulphonate (1e) (60%). An extended reaction time and the presence of an excess of hydrogen sulphide gave a 52% yield of the thione (1d). Moreover, separate treatment of the iminium salt (1e) with hydrogen sulphide also gave the thione (1d), which thus implicates the intermediacy of the salt in the thionation process. The thione (1d) reacted readily with diphenyldiazomethane at room temperature to furnish the corresponding diphenylmethylene derivative (1f) in 83% yield. Careful basification of the iminium salt (1e) yielded the corresponding free *N*-methylimine (1c) as an unstable solid which could not be obtained analytically pure. Similarly prepared were the unstable *N*-methylimines (2d), (3c), and (4c). These were readily converted into the fully characterized thione derivatives (2e), (3d), and (4d), respectively, in moderate to good yields on treatment with hydrogen sulphide in pyridine. The mechanisms of these transformations deserve further comment. We believe that the iminium salt formation proceeds as depicted in Scheme 2.

The direct conversion of simple aryl nitrones into the corresponding thiones using thiolacetic acid has been reported recently.[8] We have found that this method also works well with nitrones of cross-conjugated dienones. Thus dichlorisone acetate nitrone (1b), on treatment with thioacetic acid (6 equiv.) in pyridine over a period of 18 h, afforded the desired thione (1d) in over 80% yield after chromatography.

Nitrone deoxygenation has been effected by treatment with trialkyl phosphite [9] and Si_2Cl_6,[10] conditions which are probably not applicable to unprotected corticoids. Moreover, since cross-conjugated 1,4-dien-3-ones are relatively inert to nucleophilic attack at C-3, few ketimine or enamine derivatives are known.[11] The reaction of the derived nitrones with toluene-*p*-sulphonyl chloride in the presence of hydrogen sulphide thus represents a novel and potentially useful synthetic method for the preparation of steroidal 3-ketimines.

The conversion of diene-thiones into the corresponding dienones has been accomplished in good yield *via* photolysis of the derived thione *S*-oxides.[7] Our interest in selective oxidation processes prompted us to examine the suitability of bis-*p*-methoxyphenyl telluroxide (5)

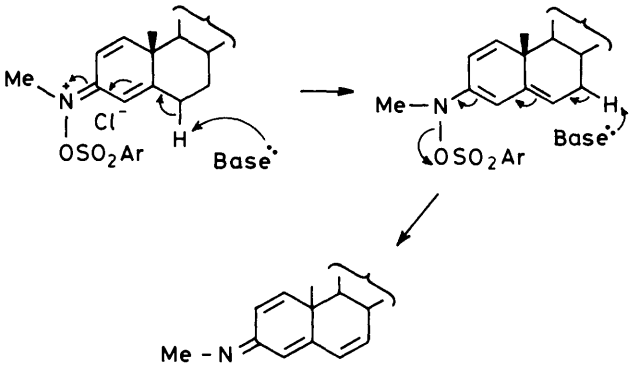
$p\text{-}MeOC_6H_4)_2Te{=}X$

(5) X = O

(6) X = :

towards effecting this transformation. This reagent has previously shown considerable potential as a mild oxidant for a number of diverse thiocarbonyl substrates.[12] Indeed, treatment of dichlorisone acetate thione (1d) in methanol–dichloromethane solution with telluroxide (5) for 21 h at ambient temperature formed the corresponding dienone (1a). Column chromatography afforded unchanged starting material (36%), bis-*p*-methoxyphenyl telluride (6) (44)%, and the desired dienone (1a) (42%).

Under suitably basic conditions and in the *absence* of strong nucleophiles the labile *p*-tolylsulphonylated nitrone was expected to suffer two successive deprotonations with elimination of toluene-*p*-sulphonic acid and the formation of a 1,4,6-trien-3-imine function (Scheme 3). Subsequent hydrolysis would then give the corresponding 1,4,6-trien-3-one; thus this constitutes a novel route to this relatively inaccessible system. Existing methods for the dehydrogenation of 1,4-dien-3-ones includes bromination–dehydrobromination under particularly carefully controlled conditions,[13] high-potential quinone dehydrogenation,[14,15] and DDQ oxidation of a derived 1,3,5-trien-3-ol ester.[16] The latter processes, however, characteristically give low-yields, in part owing to the unfavourable enolization of the dienone substrates and in part to the possible occurrence of alternative reaction pathways, including electrophilic addition of the reagent to the substrate.



SCHEME 3

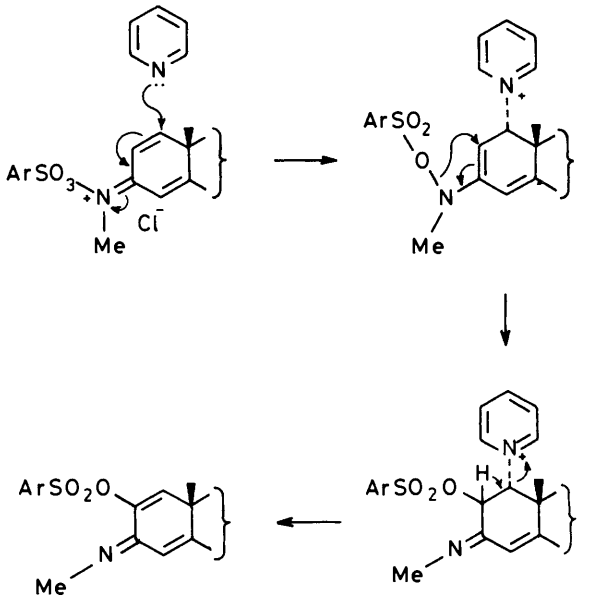
In practice, dichlorisone acetate nitrone (1b) was found to react rapidly with a slight excess of toluene-*p*-sulphonyl chloride in anhydrous pyridine at ambient temperature to give a deep red solution that contained several more polar products (t.l.c. analysis). Treatment of the reaction mixture with aqueous alkali, extraction, and chromatography yielded the desired trienimine (1g) (35%) as an unstable solid [$\lambda_{max.}$ 284 nm (ν 19 200); $\nu_{max.}$ 1 660, 1 730, and 1 750 cm^{-1}] which could not be obtained microanalytically pure. Alternatively, direct chromatographic separation of the product mixture on neutral alumina (eluant, pyridine) afforded the trienimine (1g) in 45% yield. Subsequent hydrolysis in refluxing aqueous ethanol for 18 h gave, after chromatography, the desired trienone (1 h) (61%), the spectra and microanalytical data of which were in complete accord with the assigned structure.

Further experiments, however, revealed that this

reaction pathway was unique to the nitrone (1b). For example, prednisolone-21-propionate nitrone (3b) underwent a rapid reaction with tosyl chloride to give, instead of the expected more polar trienimine, a major product of lower polarity which was readily isolated by chromatography. Although apparently homogeneous by most criteria, the broad melting range of the product indicated the presence of an isomeric mixture. The mass spectrum and elemental analysis of the product were consistent with the formula $C_{32}H_{41}NO_8S$. Moreover, the presence of a *p*-tolylsulphonyloxy-group and a 1,4-dienimine moiety were suggested by u.v. [$\lambda_{max.}$ 254 (t 19 000) and 230 nm (18 200)] and i.r. [1 730 (C-20 ketone), 1 660, 1 620, 1 600, 1 370, 1 190, 1 180, and 1 080 cm^{-1}] spectroscopy. The ^1H n.m.r. spectrum showed *inter alia* the presence of a *p*-tolylsulphonyl group [δ 2.40 (s), 7.22 (d, *J* 8 Hz), and 7.75 (d, *J* 8 Hz)], an *N*-methyl singlet at δ 3.07 and two vinyl singlets at δ 6.03 and 6.50. Most reasonably, the product was either the C-1 or C-2 substituted *p*-tolylsulphonyloxy-1,4-dienimine (*E*–*Z* mixture). The final assignment as the C-2 isomer (3e) was supported by ^{13}C n.m.r. spectroscopy. Thus, a comparison between the spectra of the product and the starting nitrone (3b) indicated essentially no difference in the C-3, -4, and -5 chemical shifts, whereas the C-1 resonance of the tosyloxy-dienimine at δ 136.0 was 13 p.p.m. upfield, and the C-2 resonance at δ 154.2 was 38 p.p.m. downfield of the corresponding resonances of the nitrone (3b). The spectral data of the derived thione (3f) and ketone (3g) were also consistent with this assignment.

When both *Z*- and *E*-isomers of dehydrotestosterone acetate nitrone (2b) and (2c) were treated separately with toluene-*p*-sulphonyl chloride in anhydrous pyridine, both nitrones gave, as the only isolable product, the corresponding 2-*p*-tolylsulphonyloxydienimine (2g) (25%). This was fully characterized by hydrolysis to the corresponding 3-keto-derivative (2h). Similar treatment of betamethasone nitrone (4b), however, yielded a mixture of the 2-*p*-tolylsulphonyloxydienimine (4f) (17%), again characterized as the derived 3-ketone (4g), and the trienimine (4h) (9%). After reflux in aqueous ethanol for 5 h, the trienimine (4h) afforded the known trienone (4i) in 48% yield. Clearly, these results indicate that the outcome of the reaction is strongly influenced by the nature of the C-9 substituent of the substrate, but independent of nitrone configuration.

A plausible mechanism for the formation of the 2-*p*-tolylsulphonyloxy-derivatives is represented in Scheme 4. The initial step is believed to be rapid *O*-*p*-tolylsulphonylation of the nitrone function. Subsequent conjugate addition of pyridine at C-1 to give the 1-pyridinium-3-(*N*-*p*-tolylsulphonyloxymethylamino)-2,4-diene, followed by rearrangement and β-elimination would then afford the observed product. Rearrangement of the 1-pyridinium intermediate has ample precedent in the literature.[3,17] Moreover the key role of pyridine in the reaction was readily demonstrated. Thus, whereas treatment of prednisolone propionate nitrone (3b) with toluene-*p*-sulphonyl chloride in pyridine, which contained pyridinium hydrochloride, gave the expected 2-*p*-tolylsulphonyloxy-derivative (3e) (22%), the reaction in dimethylformamide using triethylamine as base gave only very complex reaction mixtures. When the reaction was carried out in dimethylformamide in the presence of pyridine (5 equiv.), the expected product was isolated in 23% yield. Significantly, use of 4-dimethylaminopyridine (DMAP) gave much higher isolated yields (58%). The relatively hindered 2,4,6-trimethylpyridine, on the other hand, in dimethylformamide solution or as solvent gave only complex product mixtures.



SCHEME 4

Conjugate addition of pyridine was expected to occur from the α-face of the substrate for steric and electronic reasons. Attack at C-5 was considered even less likely. Thus, a relatively bulky α-substituent [such as chlorine in the case of dichlorisone acetate nitrone (1b)] at C-9 would indeed hinder attack at C-1; the alternative mechanism (Scheme 3) which leads to trienimine, would therefore be more favoured. Electronic effects must also be important as the presence of a 9α-fluoro-substituent, as in betamethasone nitrone (4b), led to the formation of both the 2-*p*-tolyl sulphonyloxy-derivative (4f) and the trienimine (4h); the former predominated. In contrast, prednisolone propionate nitrone (3b), which possesses only one hydrogen atom at C-9, afforded the corresponding 2-*p*-tolylsulphonyloxy-2 derivative (3e) as the major product. Similar results were obtained with other esterifying reagents. Thus, for example, the nitrone (3b) on treatment with toluene-*p*-sulphonic anhydride in pyridine gave the *p*-tolylsulphonyloxy-derivative (3e) in 65% yield.

EXPERIMENTAL

Melting points were determined on a Kofler hot stage and are uncorrected. Optical rotations were recorded at room temperature using a Rudolph photoelectric polarimeter, and refer to chloroform solutions (unless otherwise stated). I.r. spectra were recorded on a Perkin-Elmer 137 ' Infracord ' spectrophotometer and are reported for KBr discs (unless otherwise stated). U.v. spectra were recorded on a Carey II spectrophotometer and are reported for ethanol solutions. ^{1}H N.m.r. spectra were recorded on a Varian T60 spectrometer for solutions in $CDCl_3$ (unless otherwise stated) and are reported as downfield shifts from internal Me_4Si (δ). Medium-pressure chromatography was carried out on Merck Kieselgel H silica gel. Preparative and thin layer chromatography (p.l.c. and t.l.c.) were carried out on Merck GF_{254} silica gel. Developing solvents are given in parentheses.

Preparation of Steroidal Nitrones.—General procedure. The steroidal dienone (0.2—0.3M) and *N*-methylhydroxylamine (10 equiv.) in pyridine were stirred at 40 °C for 8–12 h under argon. To isolate the products the reaction mixture was poured into water, followed by filtration if precipitation of the product occurred, or by extraction into chloroform, drying over anhydrous Na_2SO_4, filtration and evaporation under reduced pressure. Further purification was effected by medium-pressure liquid chromatography on silica, with dichloromethane–methanol mixtures as eluant. In this way the following compounds were prepared.

21-*Acetoxy*-9α,11β-*dichloro*-17α-*hydroxy*-3-*methylimino*-*pregna*-1,4-*dien*-20-*one* N-*oxide* (1b) (80%), m.p. 175—180 °C (decomp.) (from acetone); $\nu_{max.}$ 3 300, 3 000, 1 750, 1 730, 1 650, and 1 220 cm^{-1}; $\lambda_{max.}$ 317 nm (ε 24 000); δ [$(CD_3)_2SO$ (30%)–$CDCl_3$ (70%)] 0.90 (s, 18-H), 1.67 (s, 19-H), 2.12 (s, OAc), 3.73 (s, NMe), 4.88 (3 H, m, 11-H, 21-H), and 6.0—7.4 (3 H, m, 1-,2-,4-H); *m/e* 483 ($M^{+\cdot}$), 467, 448, 415, 381, and 379 (Found: C, 57.35; H, 6.6; Cl, 14.1; N, 2.8. $C_{24}H_{32}Cl_2NO_5\cdot H_2O$ requires C, 57.68; H, 6.60; N, 2.72; Cl, 14.31%).

17β-*Acetoxy*-3-*methylimino*-1,4-*androstadiene* N-*oxide* (*Z*-isomer) (2b) (yield of Z : E mixture 84%), m.p. 142—148 °C (from diethyl ether); $[\alpha]_D$ +237° (*c* 4.8); $\nu_{max.}$ 3 000, 1 735, 1 660, 1 650, 1 540, 1 370, 1 260, 1 240, 1 220, and 1 035 cm^{-1}; $\lambda_{max.}$ 318 nm (ε 23 700); δ 0.87 (s, 18-H), 1.20 (s, 19-H), 2.10 (s, OAc), 3.87 (s, NMe), 4.75br t, *J* 8 Hz, 17-H), 6.37 (1 H, d, *J* 10 Hz, 1-H), 6.65 (1 H, dd, *J* 10.2 Hz, 2-H), and 7.18br (1-H, s, 4-H); *m/e* 357 ($M^{+\cdot}$), 341, and 135 (Found: C, 70.6; H, 8.8; N, 3.4. $C_{22}H_{31}NO_3\cdot H_2O$ requires C, 70.4; H, 8.5; N, 3.7%).

17β-*Acetoxy*-3-*methylimido*-1,4-*androstadiene* N-*oxide* (*E*-isomer) (2c), m.p. 170—175 °C (from diethyl ether); $[\alpha]_D$ −18.5° (*c* 3.5); $\nu_{max.}$ 3 000, 1 740, 1 650, 1 530, 1 370, 1 260, 1 240, 1 220, 1 110, 1 035, and 1 020 cm^{-1}; $\lambda_{max.}$ 319 nm (ε 24 000); δ 0.83 (s, 18-H), 1.17 (s, 19-H), 2.03 (s, OAc), 3.73 (s, NMe), 4.58br (1 H, t, *J* 8 Hz, 17-H), 6.17 (1 H, s, 4-H), 6.37 (1 H, d, *J* 10 Hz, 1-H), and 7.10 (1 H, dd, *J* 10.2 Hz, 2-H); *m/e* 357 ($M^{+\cdot}$), 341, and 135 (Found: C, 73.5; H, 8.7; N, 3.9. $C_{22}H_{31}NO_3$ requires C, 73.9; H, 8.9; N, 3.9%).

11β,17α-*Dihydroxy*-3-*methylimino*-21-*propionyloxy*-1,4-*pregnadien*-20-*one* N-*oxide* (3b) (90%), m.p. 188—200 °C (decomp.) (from ethyl acetate); $[\alpha]_D$ +182° (*c* 5.0); $\nu_{max.}$ 3 350, 3 000, 1 750, 1 725, 1 650, 1 350, and 1 200 cm^{-1}; $\lambda_{max.}$ 316 nm (ε 23 400); δ [$(CD_3)_2SO$ (30%)–$CDCl_3$ (70%)] 0.83 (s, 18-H), 1.13 (t, *J* 7 Hz, $MeCH_2CO_2$), 1.40 (s, 19-H), 2.42 (q, *J* 7 Hz, $MeCH_2CO_2$), 3.68 (s, NMe), 4.32 (1 H, m, 11-H), 4.39br (2 H, s, 21-H), and 6.1—7.3 (3 H, m, 1-,2-,4-H); *m/e* 445 ($M^{+\cdot}$), 429, 410, 135, and 134 (Found: C, 67.2; H, 8.0; N, 3.0. $C_{25}H_{35}NO_6$ requires C, 67.4; H, 7.9; N, 3.1%).

9α-*Fluoro*-11β,17α,21-*trihydroxy*-16β-*methyl*-3-*methylimino*-1,4-*pregnadien*-20-*one* N-*oxide* (4b) (87%), m.p. 180—188 °C; $[\alpha]_D$ −21° (*c* 4.4); $\nu_{max.}$ 3 500, 3 000, 1 710, 1 660, 1 100, and 1 040; $\lambda_{max.}$ 318 nm (ε 24 100); δ [$(CD_3)_2SO$] 0.93 (s, 18-H), 1.03 (d, *J* 7 Hz, 16-Me), 1.42 (s, 19-H), 3.63 (s, NMe), 4.22 (m, 11-H, OH), 5.03br (2 H, s, 21-H), and 6.0—7.2 (3 H, m, 1-,2-,4-H); *m/e* 421 ($M^{+\cdot}$), 405, and 135 (Found: C, 62.8; H, 7.8; F, 4.2; N, 3.3. $C_{23}H_{32}FNO_5\cdot H_2O$ requires C, 62.8; H, 7.8; F, 4.3; N, 3.2%).

Reaction of the Nitrone (1b) *with Toluene*-p-*sulphonyl Chloride in the Presence of Water.*—The nitrone (1b) (485 mg) in pyridine (15 ml) and water (0.15 ml) was treated with toluene-*p*-sulphonyl chloride (215 mg) under argon for 15 min. The red reaction mixture was then diluted with ice–water and extracted with chloroform (5 × 30 ml). The combined organic extracts were dried (anhydrous $MgSO_4$), filtered, and evaporated under reduced pressure. P.l.c. of the residue (eluant, 3% methanol in dichloromethane) gave dichlorisone 21-acetate (1a) (396 mg, 88%), identical to an authentic sample.

Reaction of the Nitrone (1b) *with Toluene*-p-*sulphonyl Chloride in the Presence of Hydrogen Sulphide.*—Toluene-*p*-sulphonyl chloride (330 mg) was stirred into a mixture of the nitrone (1b) (730 mg) and hydrogen sulphide (300 mg) in anhydrous pyridine (45 ml) under argon. A red colour immediately formed and, after 1 h, the mixture was diluted with ice–water and then extracted with chloroform (5 × 50 ml). The combined organic extracts were dried (anhydrous Na_2SO_4), filtered, and then concentrated under reduced pressure. P.l.c. of the residue (eluant, methanol–dichloromethane mixtures) gave, in order of increasing polarity, 21-acetoxy-9α,11β-dichloro-17a-hydroxy-20-oxopregna-1,4-diene-3-thione (1d) as purple *needles* (70 mg, 10%), m.p. 148—150 °C (decomp.) (from acetonitrile); $[\alpha]_D$ 220° (*c* 3.6); $\nu_{max.}$ 3 550, 3 000, 1 750, 1 735, 1 640, 1 375, and 1 120 cm^{-1}; $\lambda_{max.}$ 330 nm (ε 23 500); δ 1.0 (3 H, s, 18-H), 1.75 (3 H, s, 19-H), 2.17 (3 H, s, OAc), 4.83br (1 H, s, 11-H), 4.93 (2 H, ABq, *J* 18 Hz, 21-H), 6.92 (1 H, d, *J* 10 Hz, 1-H), 6.92 (1 H, m, 2-H), and 7.0 (1 H, s, 4-H); *m/e* 470 ($M^{+\cdot}$), 468, 251, 151, 137, and 105 (Found: C, 58.4; H, 6.0; Cl, 14.9; S, 6.8. $C_{23}H_{28}Cl_2O_4S$ requires C, 58.59; H, 5.99; Cl, 15.04; S, 6.8%); and 21-acetoxy-9α,11β-dichloro-17α-hydroxy-3-methyliminiopregna-1,4-dien-20-one tosylate (1e) (570 mg, 60%); $\nu_{max.}$ 3550, 3 000, 1 755, 1 740, 1 670, 1 105, and 1 050 cm^{-1}; $\lambda_{max.}$ 251 nm (ε 23 500); δ (CD_3OD–$CDCl_3$) 0.97 (3 H, s, 18-H), 1.68 (3 H, s, 19-H), 2.13 (3 H, s, OAc), 2.37 (3 H, s, Ar-Me), 3.4 (3 H, s, NMe), 4.7br (1 H, s, 11-H), 4.95 (2 H, m, 21-H), 6.7—7.3 (3 H, m, 1-,2-,4-H), 7.18 (2 H, d, *J* 8 Hz, aryl-H), and 7.88 (2 H, d, *J* 7 Hz, aryl-H); *m/e* 469 and 467. A solution of the iminium salt (1e) (160 mg) in chloroform (30 ml) was washed with dilute sodium hydrogencarbonate (0.25N, 15 ml) and then dried (anhydrous Na_2SO_4). Evaporation of the solvent under reduced pressure gave 21-acetoxy-9α,11β-dichloro-17α-hydroxy-3-methyliminopregna-1,4-diene-20-one (1c) (120 mg); $\nu_{max.}$ 3 550, 3 000, 1 750, 1 740, and 1 665 cm^{-1}; $\lambda_{max.}$ 248 nm (ε 19 800); δ 0.98 (3 H, s, 18-H), 1.68 (3 H, s, 19-H), 2.15 (3 H, s, OAc), 3.25 (3 H, s, NMe), 4.75br (1 H, s, 11-H), 4.95 (2 H, m, 21-H), 5.38br (1 H, s, exchanges with D_2O, 17α-OH), and 6.1—6.8 (3 H, m, 1-,2-,4-H); *m/e* 469 ($M^{+\cdot}$ +2) and 467 ($M^{+\cdot}$).

21-*Acetoxy*-9α,11β-*dichloro*-3-(*diphenylmethylene*)-17α-*hydroxypregna*-1,4-*dien*-20-*one* (1f).—The thione (1d) (120 mg) and diphenyldiazomethane (55 mg) in dichloromethane

(20 ml) were stirred under argon at room temperature for 24 h. Work-up, followed by p.l.c. and recrystallization from acetone afforded the title compound (1f) as white *needles* (125 mg, 83%), m.p. 170—172 °C (decomp.); $\nu_{max.}$ 3 500, 3 000, 1 750, 1 730, 1 655, and 1 600 cm^{-1}; $\lambda_{max.}$ 312 (ε 25 500) and 248 nm (12 000); δ 0.98 (3 H, s, 18-H), 1.71 (3 H, s, 19-H), 2.13 (3 H, s, OAc), 4.77br (1 H, s, 11-H), 4.91 (2 H, ABq, *J* 18 Hz, 21-H), 5.95 (1 H, d, *J* 10 Hz, 1-H), 6.18 (1 H, m, 4-H), 6.55 (1 H, m, 2-H), and 7.25 (10 H, m, aryl-H); *m/e* 606 ($M^{+\bullet}$ + 2) and 604 ($M^{+\bullet}$) (Found: C, 69.65; H, 6.25; Cl, 11.0. $C_{36}H_{38}Cl_2O_4 \cdot H_2O$ requires C, 69.34; H, 6.46; Cl, 11.37%).

Deoxygenation of 1,4-*Diene*-3-*nitrones*.—*General procedure*. To a stirred solution of the nitrone (0.02—0.07M) in anhydrous pyridine, which contained hydrogen sulphide (4—5 equiv.), under argon at 20—25 °C was added in one portion, freshly recrystallized toluene-*p*-sulphonyl chloride (1.2—1.5 equiv.). A red colour immediately formed and t.l.c. analysis indicated complete consumption of the starting nitrones within 10 s. After 5 min work-up the reaction mixtures gave the products which were isolated by chromatography.

17β-*Acetoxy*-3-*methyliminoandrosta*-1,4-*diene hydrochloride* (2f). The (*Z*)-nitrone (2b) (359 mg, 1 mmol), treated as above gave after alkaline aqueous work-up, washing with hydrochloric acid, and p.l.c. (eluant, 15% methanol in dichloromethane) the *title compound* (2 f) (216 mg, 58%), m.p. 225—245 °C (decomp.) (from dichloromethane–diethyl ether); $\nu_{max.}$ 3 000, 2 900, 2 600, 1 920, 1 730, 1 665, 1 240, and 1 040 cm^{-1}; $\lambda_{max.}$ 268 nm (ε 15 200); δ 0.88 (s, 18-H), 1.32 (s, 19-H), 205 (s, OAc), 3.38 (3 H, s, NMe), 4.60br (1 H, t, *J* 8 Hz, 17α-H), 6.5—7.8 (3 H, m, 1-,2-,3-H), and 10.15 (1 H, m, NH); *m/e* 341 ($M^{+\bullet}$ − HCl) and 134 (Found: C, 68.9; H, 8.5; Cl, 9.6; N, 3.5. $C_{22}H_{31}NO_2 \cdot HCl \cdot 0.5\ H_2O$ requires C, 68.4; H, 8.5; Cl, 9.2; N, 3.6%). The salt (2f) was converted into the free *N*-methylimine (2d) by passage through a column of alumina (eluant, pyridine). The column eluate was concentrated to 10 ml, and hydrogen sulphide (1.3 equiv.) added. After 1 min the solution was concentrated further and more hydrogen sulphide (2.5 equiv.) was added. Removal of the solvent followed by p.l.c. of the residue (eluant, 5% methanol in dichloromethane) gave 17β-*acetoxyandrosta*-1,4-*diene*-3-*thione* (2e) (42 mg, 45%) (recrystallized from acetone), m.p. 151—153 °C; $[\alpha]_D$ +300° (*c* 0.4); $\nu_{max.}$ 3 000, 1 730, 1 630, 1 250, and 1 130 cm^{-1}; $\lambda_{max.}$ 328 (ε 24 600); δ 0.85 (s, 18-H), 1.27 (s, 19-H), 2.03 (s, OAc), 4.55br (1 H, t, *J* 7 Hz, 17α-H), and 6.78br (3 H, s, 1-,2-,4-H); *m/e* 344 ($M^{+\bullet}$) and 302 (Found: C, 72.9; H, 8.1; S, 9.2. $C_{21}H_{28}O_2S$ requires C, 73.2; H, 8.2; S, 9.3%).

11β,17α-*Dihydroxy*-3-*methylimino*-21-*propionyloxypregna*-1,4-*dien*-20-*one* (3c). Similarly the nitrone (3b) (111 mg, 0.25 mmol) gave, after direct chromatographic work-up, the title compound (3c) (103 mg, 96%); $\nu_{max.}$ 3 550, 2 950, 1 750, 1 730, 1 655, and 1 580 cm^{-1}; $\lambda_{max.}$ 256 nm (ε 15 900); δ 0.92 (s, 18-H), 1.12 (t, *J* 7 Hz, $MeCH_2CO$), 1.38 (s, 19-H), 2.45 (q, *J* 7 Hz, $MeCH_2CO$), 3.35 (s, NMe), 4.47 (m, 11α-H), 4.97br (s, 21-H), 5.7—7.0 (m, 1-,2-,4-H).

11β,17α-*Dihydroxy*-20-*oxo*-21-*propionyloxypregna*-1,4-*diene*-3-*thione* (3d). The nitrone (3b) (223 mg, 0.5 mmol) was dissolved in dry pyridine (15 ml), which contained hydrogen sulphide (5 equiv.), and treated with toluene-*p*-sulphonyl chloride (143 mg, 1.5 equiv.). After 5 min, strong anion exchange resin (10 equiv.), slurried in a small amount of ethanol, was added, followed after 20 min by hydrogen sulphide (5 equiv.) in pyridine. Filtration of the reaction mixture, concentration under reduced pressure, and p.l.c. (eluant, 7.5% methanol in dichloromethane) afforded the *title compound* (3d) (77 mg, 36%), m.p. 137—142 °C (decomp.) (from acetone); $[\alpha]_D$ +236° (*c* 2.75); $\nu_{max.}$ 3 550, 3 000sh, 1 740, 1 720, 1 640, 1 370, 1 200, and 1 120 cm^{-1}; $\lambda_{max.}$ 332 nm (ε 23 800); δ 0.93 (s, 18-H), 1.15 (t, *J* 7 Hz, $MeCH_2CO$), 1.45 (s, 19-H), 2.43 (q, *J* 7 Hz, $MeCH_2CO$), 4.43 (11α-*H*), 4.85br (s, 21-H), 6.70br (s, 4-H), and 6.88br (s, 1-,2-H); *m/e* 432 ($M^{+\bullet}$), 414, 256, 192, 169, 137, 128, and 96 (Found: C, 66.8; H, 7.5; S, 7.2. $C_{24}H_{32}O_5S$ requires C, 66.6; H, 7.5; S, 7.4%).

9α-*Fluoro*-11β,17α,21-*trihydroxy*-16β-*methyl*-3-*methyliminopregna*-1,4-*dien*-20-*one* (4c). Similarly, the nitrone (4b) (100 mg, 0.24 mmol) gave, after direct chromatographic work-up, the title compound (4c) (46 mg, 41%); $\nu_{max.}$ 3 500, 3 000, 1 720, 1 650, and 1 040 cm^{-1}; $\lambda_{max.}$ 250 nm (ε 11 100); δ 0.97br (s, 16-Me and 18-H), 1.50 (s, 19-H), 3.22 (s, NMe), 4.18 (m, 11α-H, OH, and 21-H), and 6.6—7.8 (m, 1-,2-,4-H).

9α-*Fluoro*-11β,17α,21-*trihydroxy*-16β-*methyl*-20-*oxopregna*-1,4-*diene*-3-*thione* (4d). The nitrone (4b) (962 mg, 2.29 mmol) in dry pyridine (20 ml) that contained hydrogen sulphide (4.4 equiv.) was treated with toluene-*p*-sulphonyl chloride (671 mg, 3.5 mmol). After 5 min strong anion exchange resin (11 equiv.) was added to the reaction mixture, which was left for a further 15 min. The mixture was filtered, flushed with argon, and concentrated under reduced pressure. Medium-pressure chromatography (eluant, methanol–dichloromethane mixtures) gave, in order of increasing polarity, the *title compound* (4d) (731 mg, 78%), m.p. 160 °C (decomp.) (from acetone); $[\alpha]_D$ +210° (*c* 1.7); $\nu_{max.}$ 3 550, 3 000, 1 720, 1 640, 1 580, and 1 050 cm^{-1}; $\lambda_{max.}$ 330 nm (ε 24 100); δ [$(CD_3)_2CO$] 1.13 (s, 18-H), 1.20 (d, *J* 7 Hz, 16-H), 1.65 (s, 19-H), 4.30 (m, 11α-H, 21-H, and OH), 6.80br (s, 4-H), 6.88 (dd, *J* 10.2 Hz, 2-H), and 7.12 (d, *J* 10 Hz, 1-H); *m/e* 408 ($M^{+\bullet}$) (Found: C, 64.4; H, 7.4; F, 4.6; S, 7.9. $C_{22}H_{29}FO_4S$ requires C, 64.7; H, 7.2; F, 4.65; S, 7.85%); and 9α,fluoro-11β,17α,21-trihydroxy-16β-methyl-3-methyliminiopregna-1,4-dien-20-one tosylate (4e) (205 mg, 15%); $\nu_{max.}$ 3 500, 3 000, 1 720, 1 660, and 1 630 cm^{-1}; $\lambda_{max.}$ (MeOH) 265 (ε 10 600) and 222 nm (13 200); δ [$(CD_3)_2SO$] 0.97 (s, 18-H), 1.03 (d, *J* 7 Hz, 16-Me), 1.50 (s, 19-H), 2.28 (s, aryl-Me), 3.25 (s, NMe), 4.20 (m, 11α-H, 21-H, and O*H*), 6.4—7.0 (m, 1-,2-,4-H), 7.02 (d, *J* 8 Hz, aryl-H), and 7.53 (d, *J* 8 Hz, aryl-H).

Preparation of the Thione (1d) *from the Nitrone* (1b) *and Thioacetic Acid*.—The nitrone (1b) (240 mg, 0.5 mmol) and thioacetic acid (0.21 ml, 2.8 mmol) in pyridine (15 ml) were stirred under argon in the dark for 18.5 h. The reaction mixture was divided into two equal portions and one half was evaporated to dryness under reduced pressure. P.l.c. of the residue (eluant, 5% methanol in dichloromethane) afforded the thione (1d) (104 mg, 88%), identical with an authentic sample. After 25 h the second portion was treated similarly to give a further 96 mg (81%) of thione (1d).

Oxidation of the Thione (1d) *with Bis*-p-*methoxyphenyl Telluroxide* (5).—The thione (1d) (90 mg, 0.19 mmol), dissolved in 50% methanol–dichloromethane (5 ml), was stirred under argon with bis-*p*-methoxyphenyl telluroxide (5) (90 mg, 0.25 mmol) for 21 h. Removal of the solvent under reduced pressure, and p.l.c. of the residue (eluant, 5% methanol in dichloromethane) gave bis-*p*-methoxyphenyl telluride (6) (38 mg, 44%), the starting thione (1d)

(37 mg, 36k), and dichloroisone acetate (1a) (36 mg, 42%), identical with an authentic sample.

21-*Acetoxy*-9α,11β-*dichloro*-17α-*hydroxy*-3-*methylimino*-*pregna*-1,4,6-*trien*-20-*one* (1g). The nitrone (1b) (1.01 g, 2.08 mmol) in pyridine (50 ml) that contained 4Å molecular sieves (2.0 g) was treated with toluene-*p*-sulphonyl chloride (591 mg, 3.1 mmol) under argon. After 2 min, the deep red mixture was poured into water (80 ml) and dichloromethane (110 ml). Aqueous alkali (1M, 20 ml) was added and extraction into dichloromethane gave a gum (0.96 g). Medium-pressure chromatography (eluant, methanol–dichloromethane mixtures) gave non-polar material (0.12 g), a mixture of the trienimine (1g) and its toluene-*p*-sulphonate salt (0.34 g), and a polar fraction that contained no discrete steroidal products (0.30 g). The major fraction was taken up in dichloromethane and washed with aqueous alkali (0.1M) to give the title compound (1g) (340 mg, 35%) (which was precipitated from dichloromethane with diethyl ether, m.p. 160 °C (decomp.); $\nu_{max.}$ 3 500, 3 000, 1 750, 1 730, 1 660, 1 370, and 1 230 cm^{-1}; $\lambda_{max.}$ 284 nm (ε 19 200); δ 1.02 (s, 18-H), 1.60 (s, 19-H), 2.18 (s, OAc), 3.25 (s, NMe), 4.80 (m, 11α-H), 4.93br (s, 21-H), and 5.5—7.0 (m, 1-,2-,4-,6-,7-H); *m/e* 393, 379, 319, 235, and 234. In another experiment, direct chromatography of the reaction mixture on a column of alumina (neutral, 5 g/100 mg nitrone) afforded the trienimine (1h) (see below) on elution with pyridine (45%).

21-*Acetoxy*-9α,11β-*dichloro*-17α-*hydroxypregna*-1,4,6-*triene*-3,20-*dione* (1h).—The trienimine (1g) (67 mg, 0.14 mmol) in 95% ethanol (20 ml) was refluxed under an atmosphere of argon for 18 h. Removal of the solvent under reduced pressure followed by p.l.c. (eluant, 5% methanol in dichloromethane) gave the trienone (1h) (39 mg, 61%), m.p. 235—239 °C (from methanol) (lit.,[18] m.p. 225 °C); $[\alpha]_D$ +133° (*c* 1.5); $\nu_{max.}$ 3 400, 3 000, 1 750, 1 720, 1 650, 1 630, 1 600, 1 370, 1 230, and 890 cm^{-1}; $\lambda_{max.}$ 298 (ε 13 100), 248 (9 500), and 228 nm (11 200) (lit.,[18] $\lambda_{max.}$ 297 (ε 10 400), 248 (8 000), and 225 nm (10 000); δ [$(CD_3)_2SO$ (50%)–CD_3COCD_3 (50%)] 0.93 (s, 18-H), 1.65 (s, 19-H), 2.12 (s, Ac), 4.95 (m, 11α-H and 21-H), 5.8–6.2 (m, 2-,4-,6-,7-H) and 7.42 (d, *J* 10 Hz,, 1-H); *m/e* 455, 453, 351, 236, and 221 (Found: C, 61.0; H, 5.85; Cl, 15.75. $C_{23}H_{26}Cl_2O_5$ requires C, 60.9; H, 5.8; Cl, 15.6%).

11β,17α-*Dihydroxy*-3-*methylimino*-21-*propionyloxy*-2-p-*tolylsulphonyloxypregna*-1,4-*dien*-20-*one* (3e).—The nitrone (3b) (902 mg, 2.02 mmol), dissolved in pyridine (50 ml) which contained molecular sieves (1.74 g), was treated with toluene-*p*-sulphonyl chloride (577 mg, 1.5 equiv.). After 10 min, the orange mixture was poured into 0.2M aqueous alkali and extracted into dichloromethane to give, after evaporation, a gum. Medium-pressure chromatography (eluant, methanol–dichloromethane mixtures) gave a non-polar mixture (106 mg), the title compound (3e) (428 mg, 35%), and a polar mixture (336 mg). Further purification by high-pressure liquid chromatography (h.p.l.c.) (eluant, 7.5% methanol in chloroform) and crystallization from ethyl acetate–heptane gave the *product* (3e), m.p. 107—119 °C; $\nu_{max.}$ 3 700, 3 000, 1 730, 1 660, 1 620, 1 600, 1 370, 1 190, 1 180, and 1 080 cm^{-1}; $\lambda_{max.}$ 254 (ε 19 000) and 230 nm (18 200); δ 0.90 (s, 18-H), 1.17 (t, *J* 7 Hz, *Me*CH_2CO), 1.40 (s, 19-H), 2.40 (q, *J* 7 Hz, Me*C*H_2CO), 2.40 (s, aryl-Me), 3.07 (s, NMe), 4.32 (1 H, m, 11α-H), 4.90 (2 H, ABq, *J* 19, 2 Hz, 21-H), 6.03 (1 H, s, 4-H), 6.50 (1 H, s, 1-H), 7.22 (2 H, d, *J* 8 Hz, aryl-H), and 7.75 (2 H, d, *J* 8 Hz, aryl-H); *m/e* 599 ($M^{+\bullet}$), 535, 445, 246, 150, 123, and 91 (Found: C, 63.7; H, 7.1; N, 1.8; S, 5.0. $C_{32}H_{41}NO_6S{\cdot}0.5\ H_2O$ requires C, 63.1; H, 7.0; N, 2.3; S, 5.3%). In another experiment, treatment of the nitrone (3b) (80 mg, 0.18 mmol) in pyridine with toluene-*p*-sulphonic anhydride (2.6 equiv.) gave, after the usual work-up, the dienimine (3e) (94 mg, 67%) (82% pure by u.v. analysis).

11β,17α-*Dihydroxy*-20-*oxo*-21-*propionyloxy*-2-p-*tolylsulphonyloxypregna*-1,4-*diene*-3-*thione* (3f).—The dienimine (3e) (99 mg, 0.17 mmol) in pyridine (5 ml) at −5 °C was treated with hydrogen sulphide (1 equiv.). After 15 min the solvent was removed under reduced pressure to afford a dark gum (108 mg). P.l.c. (eluant, 2.5% methanol in dichloromethane) gave unchanged starting material (40 mg, 38%) and the thione (3f) (38 mg, 36%), m.p. 75—79 °C (from diethyl ether); $[\alpha]_D$ +147° (*c* 3.8); $\nu_{max.}$ 3 600, 3 000, 1 725, 1 640, 1 580, 1 370, 1 190, and 1 180 cm^{-1}; $\lambda_{max.}$ 336 (ε 20 200) and 222 nm (16 000); δ 0.93 (s, 18-H), 1.17 (t, *J* 7 Hz, *Me*CH_2CO), 1.50 (s, 19-H), 2.38 (s, aryl-Me), 4.45 (m, 11α-H), 4.87br (s, 21-H), 6.58 (1 H, s, 4-H), 7.97 (1 H, s, 1-H), and 7.18 (2 H, d, *J* 8 Hz, aryl-H).

11β,17α-*Dihydroxy*-21-*propionyloxy*-2-p-*tolylsulphonyloxy*-*pregna*-1,4-*diene*-3,20-*dione* (3g).—The dienimine (3e) (720 mg, 1.2 mmol) in 95% ethanol (10 ml) was refluxed under argon for 6 h. The solvent was removed under reduced pressure, and the residue was separated by p.l.c. (eluant, 50% methanol in dichloromethane) to give starting material (398 mg) and the title compound (3g) (290 mg, 41%). The recovered imine was again subjected to the reaction conditions described above for 20h to afford, after p.l.c., a further 209 mg (29%) of *product*, m.p. 169—172 °C (from diethyl ether); $[\alpha]_D$ +93° (*c* 3.0); $\nu_{max.}$ 3 600, 3 000, 1 730, 1 670, 1 650, 1 370, 1 190, 1 175, 1 130, and 1 080 cm^{-1}; $\lambda_{max.}$ 247 (ε 13 500) and 230 nm (21 000); δ 0.93 (s, 18-H), 1.17 (t, *J* 7 Hz, *Me*CH_2CO), 1.48 (s, 19-H), 2.43 (s, aryl-Me), 4.40 (1 H, m, 11α-H), 4.93br (2 H, s, 21-H), 5.92 (1 H, s, 4-H), 7.18 (s, 1-H), 7.32 (d, *J* 8 Hz, aryl-H), and 7.83 (2 H, d, *J* 8 Hz, aryl-H); *m/e* 586, 137, and 91 (Found: C, 63.5; H, 6.6; S, 5.5. $C_{31}H_{38}O_9S$ requires C, 63.5; H, 6.5; S, 5.5%).

17β-*Acetoxy*-2-*tolylsulphonyloxyandrosta*-1,4-*dien*-3-*one* (2h).—The (*Z*)-nitrone (2b) (357 mg, 1 mmol) in pyridine (20 ml) which contained molecular sieves (0.86 g) was treated with toluene-*p*-sulphonyl chloride (294 mg, 1.5 equiv.). After 5 min, the red reaction mixture was poured into water and extracted with dichloromethane to give, after evaporation, a gum (527 mg). P.l.c. (eluant, 10% methanol in dichloromethane) gave a non-polar mixture (58 mg) of the dienimine (2g) (64 mg, 13%); δ 0.82 (s, 18-H), 1.18 (s, 19-H), 2.05 (s, Ac), 2.42 (s, aryl-Me), 3.17 (3 H, s, NMe), 4.60 (1 H, t, *J* 8 Hz, 17α-H), 6.22 (1 H, s, 4-H), 6.33 (1 H, s, 1-H), 7.35 (2 H, d, *J* 8 Hz, aryl-H), and 7.90 (d, *J* 8 Hz, aryl-H); and a polar mixture (181 mg). Similarly, the (*E*)-nitrone (2c) (364 mg, 1 mmol) gave a non-polar mixture (62 mg), the dienimine (2g) (94 mg, 18%), and a polar mixture (175 mg). A solution of the dienimine (2g) (73 mg, 0.14 mmol) in 95% ethanol was refluxed for 5 h. Removal of the solvent under reduced pressure and separation of the residue by p.l.c. afforded the *title compound* (2h) (31 mg, 44%), m.p. 177—179 °C (from diethyl ether–hexane); $\nu_{max.}$ 3 000, 2 900, 1 720, 1 675, 1 650, 1 370, 1 250, 1 190, 1 180, 1 150, and 1 080 cm^{-1}; $\lambda_{max.}$ 247 (ε 12 000) and 230 nm (15 400); δ 0.85 (s, 18-H), 1.28 (s, 19-H), 2.03 (s, Ac), 2.47 (s, aryl-Me), 4.63 (1 H, t, *J* 7 Hz, 17α-H), 6.05 (1 H, s, 4-H), 7.00 (1 H, s, 1-H), 7.38 (2 H, d, *J* 8 Hz, aryl-H), and 7.92 (2 H, d, *J* 8 Hz, aryl-H); *m/e* 498, 344, 343, 147, 137, and 41 (Found: C, 67.55; H, 6.9; S, 6.35. $C_{28}H_{34}O_6S$ requires C, 67.4; H, 6.9; S, 6.4%).

9α-*Fluoro*-11β,17α,21-*trihydroxy*-16β-*methyl*-2-p-*tolylsulphonyloxypregna*-1,4-*diene*-3,20-*dione* (4g).—The nitrone (4b) (2.8 mmol) in pyridine (50 ml) which contained molecular sieves (4.0 g) was treated with toluene-*p*-sulphonyl chloride (1.5 equiv.). After 5 min, filtration through Celite and aqueous work-up afforded a gum (851 mg). Medium-pressure chromatography (eluant, acetic acid–methanol–dichloromethane mixtures) gave a non-polar mixture (44 mg), the dienimine (4f) (274 mg, 17%), and a polar fraction (530 mg) (see below).

The crude dienimine (4f) was further purified by precipitation from methanol–diethyl ether solution with hexane (170 mg, 10%) and gave $\nu_{max.}$ 3 550, 3 300, 3 000, 1 720, 1 670, 1 630, 1 600, 1 370, 1 190, 1 180, 1 080, and 1 070 cm^{-1}; $\lambda_{max.}$ 251 (ε 19 200) and 231 nm (18 900); δ [$(CD_3)_2SO$ (30%)–$CDCl_3$ (70%)] 1.03 (s, 18-H), 1.10 (d, *J* 7 Hz, 16-Me), 1.52 (s, 19-H), 2.43 (s, aryl-Me), 3.03 (s, NMe), 3.83 (m, 11α-H, OH), 4.40br (2 H, s, 21-H), 6.20 (1 H, s, 4-H), 6.62 (1 H, s, 1-H), 7.32 (2 H, d, *J* 8 Hz, aryl-H), and 7.78 (2 H, d, *J* 8 Hz, aryl-H). A solution of the dienimine (4f) (130 mg, 0.23 mmol) in 95% ethanol (10 ml) was refluxed for 10 h. Removal of the solvent under reduced pressure and chromatography of the residue gave the starting material (47 mg, 36%) and the *title compound* (4g) (65 mg, 50%), m.p. 200—204 °C (from aqueous ethanol); $[\alpha]_D$ +176° (*c* 7.1); $\nu_{max.}$ 3 550, 3 000, 1 720, 1 660, 1 630, 1 370, 1 190, 1 175, 1 130, and 1 080 cm^{-1}; $\lambda_{max.}$ 245 (inflection) (ε 13 800) and 228 nm (20 800); δ 1.12 (s, 18-H), 1.28 (d, *J* 7 Hz, 16-Me), 1.62 (s, 19-H), 2.43 (s, aryl-Me), 4.25 (m, 11α-H), 4.47 s, 21-H), 6.02 (s, 4-H), 7.23 (s, 1-H), 7.33 (d, *J* 8 Hz, aryl-H), and 7.85 (d, *J* 8 Hz, aryl-H); *m/e* 562 ($M^{+\cdot}$), 137, and 91 (Found: C, 61.8; H, 6.3; S, 5.6. $C_{29}H_{35}FO_8S$ requires C, 61.9; H, 6.3; S, 5.7%). The polar reaction was treated with strong anion exchange resin in ethanol followed by p.l.c. (eluant, 20% methanol in dichloromethane) to give 9α-fluoro-11β,17α,21-trihydroxy-16β-methyl-3-methyliminopregna-1,4,6-trien-20-one (4h) (108 mg, 9%); $\lambda_{max.}$ 283 nm (ε 11 400); δ [$(CD_3)_2SO$ (50%)–$CDCl_3$ (50%)] 1.08 (s, 18-H), 1.43 (s, 19-H), 3.52 (s, NMe), 4.32 (11α-H, 21-H, OH), and 5.4—7.4 (m, 1-,2-,4-H). The trienimine (4h) was refluxed in 95% ethanol (10 ml) for 5 h. The solvent was removed under reduced pressure and the residue separated by p.l.c. to afford 9α-fluoro-11β,17α,21-trihydroxy-16β-methylpregna-1,4,6-triene-3,20-dione (4i) (52 mg, 48%), m.p. 220—228 °C; $\lambda_{max.}$ 298 (ε 11 000), 251 (9 400), and 221 nm (11 300); δ [$(CD_3)_2SO$ (30%)–$CDCl_3$ (70%)] 1.10 (s, 18-H), 1.20 (d, *J* 6 Hz, 16-Me), 1.52 (s, 19-H), 4.35 (m, 11α-H, 21-H, OH), 5.60—6.50 (m, 2-,4-,6-,7-H), and 7.27 (d, *J* 10 Hz, 1-H).

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