Oximation of 2-Azido-4,4-dimethyl-3-oxo Steroids: Formation of α-Keto Oximes and Dioximes[1]

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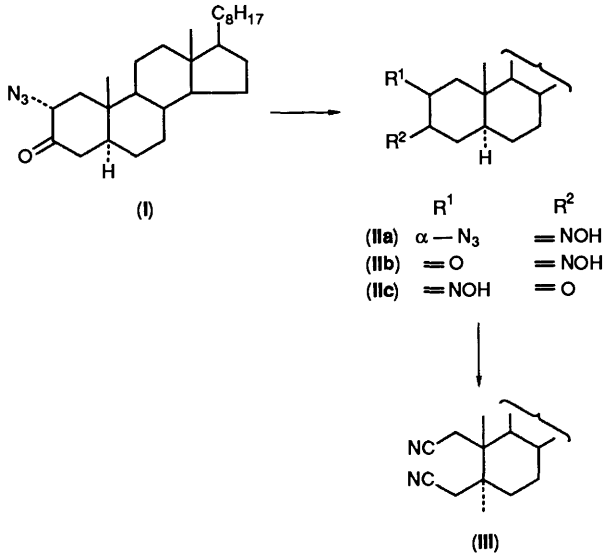
Treatment of 2-azido-4,4-dimethyl-3-oxo steroids (**1a, b**) with an excess of hydroxylamine hydrochloride in the presence of sodium acetate give the corresponding 2α-azido-3-hydroxyimino (**2a, b**) and 2,3-bishydroxyimino derivatives (**3a, b**). In the case of the Δ^5-analogue (**1c**), the 2-hydroxyimino-3-oxo compound (**4c**) is formed in addition to the 2-azido-3-hydroxyimino (**2c**) and 2,3-bishydroxyimino (**3c**) derivatives. The bishydroxyimino compounds (**3**) were converted into the oxadiazole (furazan) derivatives (**6**).

Our interest in new synthetic approaches to biologically active steroids possessing a nitrogen functional group led us to investigate the reactions of α-azido steroidal ketones[2] and their oximes.[1]

We recently reported[1] on the oximation of 2α-azido-3-oxo-5α-steroids (**I**) and on the conversion of oximes (**IIa**) into 1,4-dicyano-2,3-seco-5α-steroids (**III**). (Scheme 1). 2α-Azido-5α-cholestan-3-one was condensed with excess of hydroxylamine hydrochloride to give 2α-azido-5α-cholestan-3-one oxime (**IIa**) in almost quantitative yield. However, it was found that the sterically hindered 2α-azido-4,4-dimethyl-3-oxo derivatives (**1a** and **b**) give dioximes (**3a** and **b**) as abnormal products in addition to the normal oximation products (**2a** and **b**).

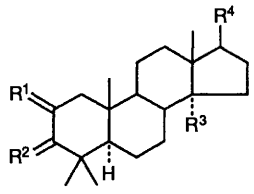


Scheme 1.

We describe here the details of this abnormal oximation reaction. Furthermore, we attempted the synthesis of some new ring-A-fused oxadiazoles in the 4,4-dimethyl steroid field.

Results and Discussion

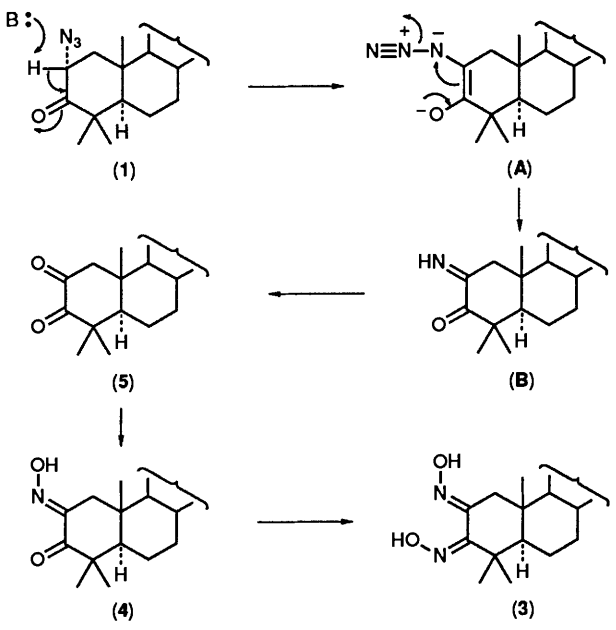
The oximation of 2α-azido-4,4-dimethyl-3-oxo steroids (**1a** and **b**) with an excess of hydroxylamine in refluxing methanol give 2α-azido-3-hydroxyimino derivatives (**2a**) (38%) and (**2b**) (26%) and 2,3-bishydroxyimino derivatives (**3a**) (48%) and (**3b**) (46%). The probable mechanism of the bishydroxyimination is outlined in Scheme 2. The conversion of azido ketones (**1**) into bishydroxyimino derivatives (**3**) presumably involves a base-catalysed enolizaton of substrates (**1**) to give the intermediates (**A**), which decompose to give the imines (**B**). The sensitive imino ketones (**B**) are rapidly hydrolysed to the diketones (**5**), which were oximinated to monohydroxyimino derivatives (**4**), followed by further oximation to dioximes (**3**) with excess of hydroxylamine.



	R^1	R^2	R^3	R^4	Δ
(1a)	α-N_3, β-H	O	H	C_8H_{17}	
(1b)	α-N_3, β-H	O	Me	C_8H_{17}	$\Delta^{8,9}$
(1c)	~N_3, ~H	O	H	OAc	$\Delta^{5,6}$
(2a)	α-N_3, β-H	NOH	H	C_8H_{17}	
(2b)	α-N_3, β-H	NOH	Me	C_8H_{17}	$\Delta^{8,9}$
(2c)	~N_3, ~H	NOH	H	OAc	$\Delta^{5,6}$
(3a)	NOH	NOH	H	C_8H_{17}	
(3b)	NOH	NOH	Me	C_8H_{17}	$\Delta^{8,9}$
(3c)	NOH	NOH	H	OAc	$\Delta^{5,6}$
(4a)	NOH	O	H	C_8H_{17}	
(4c)	NOH	O	H	OAc	$\Delta^{5,6}$
(5)	O	O	H	C_8H_{17}	
(6a)	N—O—N		H	C_8H_{17}	
(6b)	N—O—N		Me	C_8H_{17}	$\Delta^{8,9}$
(6c)	N—O—N		H	OAc	$\Delta^{5,6}$

As to this probable mechanism, we consider that hindrance around the carbonyl group restricting its oximation allows formation of enolate (A), and consequent azido fragmentation effectively competes with oximation of the 3-keto group. In the case of 2α-azido-3-oxo steroids without the 4,4-dimethyl moiety, the bishydroxyimino derivative was not detected.[1] This fact can be explained by the lack of such hindrance of the carbonyl group.

The formation of bishydroxyimino derivatives (**3a** and **b**) is



Scheme 2.

slightly preferred to the formation of 2-azido-3-hydroxyimino derivatives (**2a** and **b**). These results are attributable to faster enolization with base (NH_2OH) as compared with the oximation at the 3-oxo group. As expected, compound (**1a**) has been converted, *via* the 2,3-diketone, into 2-hydroxyimino-4,4-dimethyl-5α-cholestan-3-one (**4a**) as the sole product, on treatment with an equimolar amount of hydroxylamine. In this case the products, other than ketone (**4a**) and the starting ketone (**1a**), were not detected by TLC.

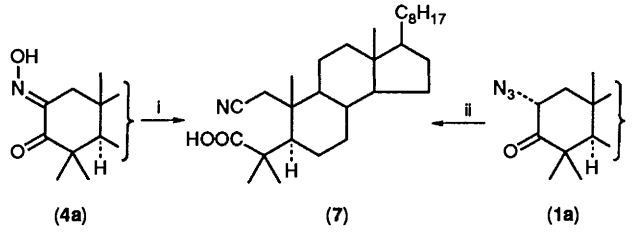
The above mentioned mechanism is also rationalized by the fact that oximation occurs on use of a stronger base (MeO^-). Treatment of a methanolic solution of compound (**1a**) including hydroxylamine hydrochloride (15 mol equiv.) and sodium methoxide (30 mol equiv.) under reflux for 2 h gave 2-hydroxyimino 3-ketone (**4a**) in 63% yield. However, TLC analysis of this reaction mixture showed that the oximes (**2a**) and (**3a**) were not formed. More prolonged treatment of the above solution gave a complex mixture containing seven constituents, from which the main product (**4a**) was isolated in 37% yield by column chromatography on silica gel. Unfortunately, we were unable to isolate other constituents in a pure form. However, TLC analysis of the reaction mixture again showed that the oximes (**2a**) and (**3a**) were not formed. The absence of α-azido oxime (**2a**) in the reaction mixture implies that the enolization occurred nearly quantitatively with the strong base and that enolate-induced azido fragmentation then follows. These reactions also involve enolate-induced fragmentation to give intermediate (**B**), hydrolysis of which gives diketone intermediate (**5**); oximation of dione (**5**) then gives mono-oxime (**4a**) (Scheme 2). However, further oximation of keto oxime (**4a**) to dioxime (**3a**) has not been observed.

As mentioned above, when the reaction is carried out in the presence of a strong base, α-hydroxyimino ketone (**4a**) tends to decompose to several products, which have not yet been identified.

We have briefly explored an aspect of the intermediacy of the diketone (**5**) (Scheme 2). Treatment of compound (**1a**) with sodium methoxide (Na/MeOH) (15 mol equiv.) in the absence of hydroxylamine at room temperature led to evolution of N_2, and isolation of the diketone (**5**) (as diosphenol) in 51% yield. From this result the formation of diketone (**5**) as an intermediate in the formation of dioximes (**3**) is postulated. However, the conversion of the α-keto imine (**B**) (Scheme 2) into the oxime may take place by attack of the hydroxylamine directly on the imine so that the diketone might not be involved.

We attempted a further experiment that could both clear up this matter and possibly demonstrate a greater versatility since a sterically hindered ketone might not be required when NaOMe is present as the base. Thus, treatment of the 2α-azido-3-oxo-5α-steroids (**I**) without 4,4-dimethyl substituents with a hydroxylamine–NaOMe combination gave a mixture of keto oximes (**IIb**) and (**IIc**) (Scheme 1). Two products were isolated in 22% (**IIb**) and 13% (**IIc**) yield from the mixture by preparative TLC (PLC). Formation of 2-keto 3-oxime (**IIb**) would lend further support to the intermediacy of diketone (**5**).

The location of the carbonyl group in the 2-hydroxyimino 3-ketone (**4a**) is consistent with an unequivocal synthesis of the cyano carboxylic acid (**7**) by C–C bond-cleavage reaction of compounds (**4a**) and (**1a**) with thionyl chloride[3] and bromine,[2] respectively (Scheme 3). From these results it appeared



Scheme 3. *Reagents:* i, $SOCl_2$; ii, Br_2 AcOH.

that monohydroxyimination of 2,3-diketone intermediates (**5**) occurs at the less hindered C-2 carbonyl group. In the case of 17β-acetoxy-2-azido-4,4-dimethylandrost-5-en-3-one (**1c**), a small amount of 2-hydroxyimino-3-oxo compound (**4c**) was isolated in additon to compounds (**2c**) and (**3c**). The formation of compound (**4c**) can be rationalized in the following way. It is thought that the presence of a $\Delta^{5,6}$ double bond affects the conformation of the A-ring.[4] This deformation of the A ring makes oximation at C-3 more difficult compared with the case for the saturated analogues.

Structures of compounds (**2**), (**3**), and (**4**) followed from their analytical and spectra data (see Experimental section).

The *anti*-configuration of the 2-hydroxyimino group to the C-3 carbonyl group in compounds (**4**) was established by the formation of a dark green complex with copper(II) ion.[5] The ^1H NMR spectrum of compound (**4**) showed a doublet at δ 3.15 (**4a**), 3.30 (**4c**) which was assigned to 1-H^B, also suggesting that the 2-hydroxyimino group has the *anti*-configuration to the carbonyl group.[6]

The 2,3-bishydroxyimino steroids without the 4,4-dimethyl group, as prepared by Shimizu *et al.*,[7] all exist in the *anti*-form. Such compounds furnished a coloured precipitate with nickel ion, indicating an *anti*-configuration.[7b] However, 4,4-dimethyl derivatives (**3**) failed to form the bright red nickel complex characteristic of *anti*-compounds. The ^1H NMR spectra of compounds (**3**) exhibited a one-proton doublet at δ 3.10–3.40 (1-H^B). On this basis, the *amphi*-form (Scheme 2) is the probable structure for compound (**3**).

The incorporation of an oxadiazole ring fused at the 2,3-position of androstanes has been shown to lead to compounds therapeutically useful as anabolic agents.[7] In connection with our continuing interest in biologically active steroids, we undertook the synthesis of a number of ring-A-fused oxadiazoles of 4,4-dimethyl steroids. 2,3-Bishydroxyimino compounds (**3**) were converted into oxadiazole derivatives by treatment with neat $SOCl_2$. These products had spectral data characteristic of a fused oxadiazole system and were assigned the structures (**6a–c**) (see Experimental section). The total yields of (**6a**), (**6b**), and (**6c**)

based on (**1a**), (**1b**), and (**1c**) used were 32.5, 33.3, and 34.6%, respectively. For compound (**6c**), this conversion was accomplished by use of the crude residue resulting from oximation (without isolation of 2,3-bishydroxyimino derivative). Studies designed to determine the biological activity of these oxadiazoles are in progress and will be reported elsewhere.

Experimental

M.p.s were determined with a Yanagimoto apparatus and are uncorrected. IR spectra were recorded in KBr on a Hitachi Model 215 spectrophotometer. ^1H NMR (90 MHz) and ^{13}C NMR (22.6 MHz) spectra were recorded in $CDCl_3$ with tetramethylsilane as internal standard, on a Hitachi FT-NMR spectrometer. Mass spectra were measured with a direct inlet at 70 eV on a Hitachi M-80 instrument. PLC was carried out on Merck Kieselgel 60 F_{254}.

α-Azido ketones (**1**) were synthesized from the corresponding α-bromo ketones according to the procedure of Zbiral.[8]

2α-*Azido*-4,4-*dimethyl*-5α-*cholestan*-3-*one* (**1a**).—72.5% yield; m.p. 106–107 °C (from diethyl ether–MeOH); ν_{max} 2 112, 1 716, and 1 268 cm^{-1}; δ_H 4.25 (1 H, dd, *J* 5.6 and 13.8 Hz, 2-H$^\beta$); δ_C 60.91 (C-2) and 210.37 (C-3) (Found: C, 76.5; H, 10.7; N, 9.3. $C_{29}H_{49}N_3O$ requires C, 76.43; H, 10.83; N, 9.22%).

2α-*Azidolanost*-8-*en*-3-*one* (**1b**).—73.3% yield; m.p. 144–147 °C (from diethyl ether–MeOH); ν_{max} 2 112 and 1 718 cm^{-1}; δ_H 4.27 (1 H, dd, *J* 6.0 and 13.5 Hz, 2-H$^\beta$); δ_C 48.41 (C-4), 61.04 (C-2), and 210.18 (C-3) (Found: C, 77.2; H, 10.7; N, 9.1. $C_{30}H_{49}N_3O$ requires C, 77.03; H, 10.55; N, 8.98%).

17β-*Acetoxy*-2-*azido*-4,4-*dimethylandrost*-5-*en*-3-*one** (**1c**).—38.5% yield; m.p. 133–134 °C (from MeOH–$CHCl_3$); ν_{max} 2 104, 1 744, 1 716, 1 242, 1 060, and 1 048 cm^{-1}; δ_H 2.05 (3 H, s, OAc), 4.27 (1 H, dd, *J* 4.9 and 9.0 Hz, 2-H), 4.62 (1 H, br t, 17-H$^\alpha$), and 5.62 (1 H, m, 6-H); δ_C 47.92 (C-4), 59.70 (C-2), and 212.17 (C-3) (Found: C, 68.9; H, 8.4; N, 10.3. $C_{23}H_{33}N_3O_3$ requires C, 69.14; H, 8.32; N, 10.51%).

Typical Procedure for Preparation of Oximes.—A stirred mixture of the α-azido ketone (**1**) (2.34 mmol), methanol (100 ml), hydroxylamine hydrochloride (35.1 mmol), and sodium acetate (25 mmol) was heated under reflux for 9 h. After work-up, the resulting residue was purified by silica gel column chromatography.

2α-*Azido*-4,4-*dimethyl*-5α-*cholestan*-3-*one oxime* (**2a**) *and* 4,4-*dimethyl*-5α-*cholestane*-2,3-*dione dioxime* (**3a**). Elution with benzene gave *mono-oxime* (**2a**) (38%); m.p. 175–179 °C (from MeOH–diethyl ether); ν_{max} 3 300, 2 100, 1 258, and 920 cm^{-1}; δ_H 5.60 (1 H, m, 2-H$^\beta$) (Found: C, 74.1; H, 10.9; N, 12.1. $C_{29}H_{50}N_4O$ requires C, 73.99; H, 10.70; N, 11.90%). Further elution with the same solvent afforded *dioxime* (**3a**) (48%), m.p. 212–215 °C (decomp.) (from MeOH–diethyl ether); ν_{max} 3 304, 1 638, 1 542, and 952 cm^{-1}; δ_H 2.16 (1 H, d, *J* 18 Hz, 1-H$^\alpha$) and 3.36 (1 H, d, *J* 18 Hz, 1-H$^\beta$) (Found: M^+, 458.3875. $C_{29}H_{50}N_2O_2$ requires *M*, 458.3875).

2α-*Azidolanost*-8-*en*-3-*one oxime* (**2b**) *and lanost*-8-*ene*-2,3-*dione dioxime* (**3b**) Elution with benzene gave *mono-oxime* (**2b**) (26%); m.p. 174–176 °C (from MeOH–diethyl ether); ν_{max} 3 304, 2 112, 1 246, and 950 cm^{-1}; δ_H 5.22 (1 H, dd, *J* 6.0 and 10.0 Hz, 2-H$^\beta$) and 9.13 (1 H, br s, NOH); δ_C 38.39 (C-4), 41.58 (C-1), 49.13 (C-2), and 163.17 (C-3) (Found: C, 74.8; H, 10.3; N, 11.3. $C_{30}H_{50}N_4O$ requires C, 74.64; H, 10.43; N, 11.60%). Further elution with benzene–diethyl ether (9:1) afforded dioxime (**3b**) (46%); m.p. 204–208 °C (from MeOH–diethyl ether) (lit.,[5] 202–205 °C); ν_{max} 3 324, 1 694, 1 548, and 948 cm^{-1}; δ_H 3.10 (1 H, d, *J* 18 Hz, 1-H$^\beta$) and 8.75 (2 H, m, NOH); δ_C 36.41 (C-1), 153.82 (C=NOH), and 154.36 (C=NOH) (Found: M^+, 470.3888. Calc. for $C_{30}H_{50}N_2O_2$: *M*, 470.3875).

17β-*Acetoxy*-2-*azido*-4,4-*dimethylandrost*-5-*en*-3-*one oxime* (**2c**), 17β-*acetoxy*-4,4-*dimethylandrost*-5-*ene*-2,3-*dione dioxime* (**3c**), *and* 17β-*acetoxy*-4,4-*dimethylandrost*-5-*ene*-2,3-*dione* 2-*oxime* (**4c**).† The reaction of azido ketone (**1c**) (300 mg) gave a mixture containing compounds (**2c**), (**3c**), and (**4c**) after 9 h reflux, from which azido oxime (**2c**) (55 mg, crude crystals), dioxime (**3c**) (15 mg), and keto oxime (**4c**) (10 mg) were obtained by silica gel chromatography. Elution with benzene gave crude crystals of compound (**2c**); m.p. 140–157 °C (from acetone); ν_{max} 3 404, 2 108, 1 740, 1 716, 1 252, and 952 cm^{-1}; δ_H 2.05 (3 H, s, OAc), 4.60 (1 H, br t, 17-H$^\alpha$), 5.00 (1 H, m, 2-H), 5.62 (1 H, m, 6-H), and 9.17 (1 H, br s, NOH).

Further elution with benzene–diethyl ether (9:1) gave three fractions. The first fraction afforded dioxime (**3c**) (15 mg). The second fraction (190 mg) was a mixture of products (**3c**) and (**4c**), and the final fraction gave keto oxime (**4c**) (10 mg). The *bishydroxyimino derivative* (**3c**) was recrystallized from acetone–hexane (9:1), m.p. 209–212 °C (decomp.); ν_{max} 3 344, 1 740sh, 1 630, 1 550, 1 250, 1 046, and 956 cm^{-1}; δ_H 2.08 (3 H, s, OAc), 3.40 (1 H, d, *J* 18 Hz, 1-H$^\beta$), 4.65 (1 H, 17-H$^\alpha$), 5.65 (1 H, m, 6-H), 10.00 (1 H, br m, NOH), and 12.65 (1 H, br m, NOH); δ_C 41.67 (C-4), 120.10 (C-6), 146.60 (C-5), 152.92 (C=NOH), 153.46 (C=NOH), and 171.74 (C=O) (Found: M^+, 402.2528. $C_{23}H_{34}N_2O_4$ requires *M*, 402.2520).

The 2-*hydroxyimino*-3-*keto derivative* (**4c**) was recrystallized from aq. acetone, m.p. 215–222 °C (decomp.); ν_{max} 3 328, 1 738, 1 708, 1 610, 1 250, 1 056, 1 034, 960, and 880 cm^{-1}; δ_H 2.04 (3 H, s, OAc), 3.30 (1 H, d, *J* 18 Hz, 1-H$^\beta$), 4.60 (1 H, br t, 17-H$^\alpha$), and 5.60 (1 H, m, 6-H); δ_C 48.09 (C-4), 152.78 (C=NOH), and 201.28 (C-3) (Found: M^+, 387.2413. $C_{23}H_{33}NO_4$ requires *M*, 387.2411).

4,4-*Dimethyl*-5α-*cholestane*-2,3-*dione* 2-*Oxime* (**4a**).—(a) *With equimolar hydroxylamine hydrochloride.* A mixture of the α-azido ketone (**1a**) (425 mg, 0.93 mmol), methanol (50 ml), hydroxylamine hydrochloride (60 mg, 0.86 mmol), and sodium acetate (77 mg, 0.94 mmol) was heated under reflux for 9 h. After work-up, the residue was chromatographed on a silica gel column. Elution with benzene gave the unchanged starting material (**1a**) (190 mg). Further elution with benzene–diethyl ether (9:1) gave the *title compound* (**4a**), which was crystallized from MeOH–diethyl ether as needles (135 mg, 32.6%), m.p. 193–198 °C (decomp.); ν_{max} 3 300, 1 704, 1 618, and 964 cm^{-1}; δ_H 3.15 (1 H, d, *J* 18 Hz, 1-H$^\beta$); δ_C 153.47 (C=NOH) and 203.86 (C-3) (Found: M^+, 443.3793. $C_{29}H_{49}NO_2$ requires *M*, 443.3766). Compound (**4a**) gave a dark green precipitate with 5% copper sulphate in ethanol.

(b) *With hydroxylamine hydrochloride in the presence of sodium methoxide.* A mixture of the α-azido ketone (**1a**) (500 mg, 1.1 mmol), hydroxylamine hydrochloride (1.144 g, 16.5 mmol), methanol (100 ml), and sodium metal (757 mg, 32.9 mmol) was heated under reflux for 2 h. After work-up, the residue was chromatographed on a silica gel column. Elution with benzene–diethyl ether (9:1) gave compound (**4a**) (305 mg, 63%).

(c) *Prolonged treatment of the above mixture.* The above mixture was heated under reflux for 9 h. After the usual work-up, a residue (453 mg) was obtained, which was chromatographed on a silica gel column. Elution with benzene–diethyl ether (9:1) gave compound (**4a**) (183 mg, 37%).

4,4-*Dimethyl*-5α-*cholestane*-2,3-*dione* (*as Diosphenol*) (**5**).—α-Azido ketone (**1a**) (250 mg, 0.55 mmol) was dissolved in a

* 2-Azido-4,4-dimethyl-3-oxoandrost-5-en-17β-yl acetate.

† 2-Azido-3-hydroxyimino-4,4-dimethyl-, 2,3-bishydrodroxy imino-4,-4-dimethyl-, and 2-hydroxyimino-4,4-dimethyl-3-oxo-androst-5-en-17β-yl acetates, respectively.

mixture of methanol (50 ml) and sodium metal (190 mg, 8.3 mmol). The mixture was continuously stirred at room temperature for 50 min, and was then poured into water and extracted with diethyl ether. After evaporation of the solvent, the residue was chromatographed on a silica gel column. Elution with benzene–light petroleum (b.p. range 40–70 °C) (1:1) gave dione (**5**), which was recrystallized from methanol as plates (124 mg, 51%), m.p. 164–165 °C (lit.,[9] 168 °C).

5α-Cholestane-2,3-dione 3-Oxime (**IIb**)[6a] *and 5α-Cholestane-2,3-dione 2-Oxime* (**IIc**).[6a,10]—A solution of the azido ketone (**I**) (200 mg, 0.47 mmol), hydroxylamine hydrochloride (32 mg, 0.47 mmol), and sodium metal (188 mg, 8.15 mmol) in methanol (32 ml) was heated under reflux for 2 h. After work-up, PLC of the residue with benzene–ethyl acetate (2:1) gave the 2-keto-3-oxime (**IIb**) (42 mg, 22%) and 3-keto-2-oxime (**IIc**) (26 mg, 13%) as the less polar fraction. An analytical specimen of compound (**IIb**) was obtained by recrystallization from aq. ethanol, m.p. 197–199 °C (decomp.) (lit.,[6a] 196–198 °C); ν_{max} 3 580sh, 3 420sh, 3 250, 1 708, 1 685sh, 1 608, 1 000, 980, and 940 cm^{-1}. An analytical specimen of compound (**IIc**) was obtained by recrystallization from methanol–diethyl ether, m.p. 237–240 °C (decomp.) (lit.,[10] 240–242 °C,[6a] 271–274 °C); ν_{max} 3 260, 1 720, 1 619, 970sh, and 955 cm^{-1}.

4,4-Dimethyl-2-nitrilo-2,3-seco-5α-cholestan-3-oic Acid (**7**).—(a) *From compound* (**1a**). To a stirred solution of α-azido ketone (**1a**) (205 mg) in acetic acid (35 ml) was added a solution of bromine (72 mg) in acetic acid (5 ml) at room temperature and the mixture was stirred for 40 min. After work-up, the resulting residue was chromatographed on a silica gel column with benzene–diethyl ether (9:1) as eluant to give the *carboxylic acid* (**7**), which was crystallized from methanol–diethyl ether as needles (155 mg, 77.8%), m.p. 207–210 °C (decomp.); ν_{max} 3 600–3 100, 2 670, 2 248, 1 700, and 960 cm^{-1}; δ_H 2.55 (2 H, m, 1-H) and 10.35 (1 H, m, CO_2H); δ_C 117.90 (CN) and 184.62 (CO_2H) (Found; M^+, 443.3737. $C_{29}H_{49}NO_2$ requires *M*, 443.3766).

(b) *From compound* (**4a**). To solid α-keto-oxime (**4a**) (98 mg) at 0 °C was slowly added neat thionyl chloride (2.5 ml), and the mixture was stirred for 20 min. Quenching of the reaction mixture in ice–water followed by extraction with diethyl ether afforded a crude residue, which was chromatographed on silica gel. Elution with benzene–diethyl ether (9:1) gave acid (**7**), which was crystallized from methanol–diethyl ether as needles (80 mg, 82%).

Typical Procedure for Preparation of Furazans (**6**).—To solid (**3**) (0.22 mmol) at 0 °C was slowly added neat thionyl chloride (2 ml), and the mixture was stirred for 15 min. Quenching of the reaction mixture in ice–water followed by extraction with diethyl ether afforded a crude residue, which was chromatographed on a silica gel column. The following compounds were thus prepared.

4,4-Dimethyl-5α-cholestano[2,3-c][1,2,5]*oxadiazole* (**6a**). Elution with benzene gave *compound* (**6a**), which was recrystallized from MeOH–diethyl ether as plates (69%); m.p. 182–185 °C; ν_{max} 1 004 and 880 cm^{-1}; λ_{max} (EtOH) 216 nm (ε 3 875); δ_H 2.19 (1 H, d, *J* 16.5 Hz, 1-H$^\alpha$) and 3.16 (1 H, d, *J* 16.5 Hz, 1-H$^\beta$); δ_C 150.68 (C=N) and 159.93 (C=N) (Found: M^+, 440.3776. $C_{29}H_{48}N_2O$ requires *M*, 440.3769).

Lanost-8-eno[2,3-c][1,2,5]*oxadiazole* (**6b**). Elution with benzene gave *compound* (**6b**), which was recrystallized from MeOH–diethyl ether as plates (71.4%; m.p. 151–153 °C; ν_{max} 1 004 and 882 cm^{-1}; λ_{max} (EtOH) 215 nm (ε 7 180); δ_H 2.35 (1 H, d, *J* 15.8 Hz, 1-H$^\alpha$) and 3.20 (1 H, d, *J* 15.8 Hz, 1-H$^\beta$); δ_C 151.03 (C=N) and 159.93 (C=N) (Found: M^+, 452.3774. $C_{30}H_{48}N_2O$ requires *M*, 452.3769).

17β-Acetoxy-4,4-dimethyl-androst-5-eno[2,3-c][1,2,5]*-oxadiazole* (**6c**).* An unseparated mixture of compounds (**3c**) and (**4c**) (305 mg) as described above was dissolved in neat thionyl chloride (5 ml) at 0 °C, and the reaction mixture was stirred for 20 min. After work-up, the resulting residue was chromatographed on a silica gel column. Elution with benzene gave *compound* (**6c**), which was recrystallized from MeOH–diethyl ether as plates (126 mg); ν_{max} 1 734, 1 256, 1 004, 880, and 870 cm^{-1}; λ_{max} (EtOH) 215 nm (ε 5 480); δ_H 2.04 (3 H, s, Ac), 2.30 (1 H, d, *J* 16.5 Hz, 1-H$^\alpha$), 3.25 (1 H, d, *J* 16.5 Hz, 1-H$^\beta$), 4.63 (1 H, m, 17-H$^\alpha$), and 5.82 (1 H, m, =CH); δ_C 150.27 (C=N) and 159.44 (C=N) (Found: M^+, 384.2419. $C_{23}H_{32}N_2O_3$ requires *M*, 384.2415).

* 4,4-Dimethylandrost-5-eno[2,3-*c*][1,2,5]oxadiazole-17β-yl acetate.

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