Cycloadducts of *C*-Nitrosocarbonyl Compounds and Ergosteryl Acetate; [3,3]Sigmatropic Rearrangements of *N*-Aroyl-3,6-dihydro-1,2-oxazines

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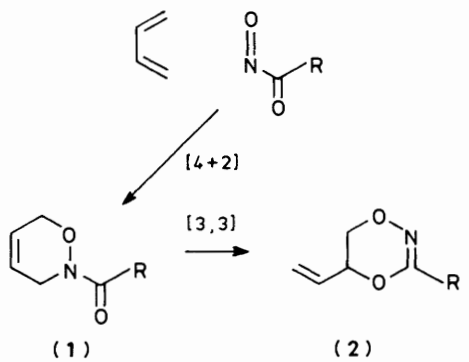
Oxidation of acetohydroxamic acid with tetraethylammonium periodate in the presence of ergosteryl acetate (**3**) gave a single cycloadduct (**4a**) arising from 1,4-addition of the nitroso group of nitrosocarbonylmethane to the diene system of (**3**). In contrast, nitrosocarbonylbenzene, generated by oxidation of benzohydroxamic acid or by thermal dissociation of the 9,10-dimethylanthracene adduct (**12**; R = Ph), gave two 1,4-adducts, (**4b**) and (**5b**), with (**3**). The adduct (**5b**) isomerised at 60 °C to give a dioxazine (**6b**), *formally* an adduct of nitrosocarbonylbenzene, acting as a 4π-electron component, with the 5,6-double bond of (**3**). However, the isomerisation still took place in the presence of triphenylphosphine, an efficient trap for *C*-nitroso-compounds, and must therefore have occurred by an intramolecular, [3,3]sigmatropic rearrangement. 4-Bromo-, 4-methoxy-, and 4-nitro-nitrosocarbonylbenzene reacted similarly with (**3**) whereas 2,4,6-trimethylnitrosocarbonylbenzene gave (**4f**) as the sole adduct. Adducts of pyrocalciferyl acetate (**21**) and isopyrocalciferyl acetate (**22**) with nitrosocarbonylbenzene and of ergosteryl acetate with the nitrosoimine (**26**) have also been prepared.

Oxidation of hydroxamic acids, RCONHOH, with, for example, tetraethylammonium periodate is believed[1] to generate transient *C*-nitrosocarbonyl compounds, RCONO. When the oxidations are conducted in the presence of conjugated dienes, cycloadducts of the type (**1**) (Scheme 1) are formed in high yield.[2] In this paper we record experiments which have led to the discovery[3] of a new class of [3,3]sigmatropic rearrangement, (**1**) → (**2**).



Scheme 1.

Ergosteryl acetate (**3**) reacts with nitrosyl cyanide to form two cycloadducts (**4**; RCO = CN) and (**5**; RCO = CN) in similar amounts.[4] We expected, therefore, that nitrosocarbonyl compounds would add similarly to ergosteryl acetate to form two series of adducts. However, oxidation of acetohydroxamic acid in the presence of ergosteryl acetate gave a single cycloadduct (**4a**) in high yield (84%). Clearly, 1,4-addition to the conjugated diene had occurred, since the ^{1}H n.m.r. spectrum of (**4a**) showed an AB quartet (*J* 9 Hz) arising from 6-H and 7-H together with signals of the usual type expected for an ergosteryl derivative. The structure (**4a**), rather than (**5a**), was indicated by a one-proton signal at δ 3.47 (dd, *J* 14 and 5 Hz) which could only be attributed to 4α-H. The lowfield position of this signal must be due to the proximity of the *N*-acetyl group [see (**7**)] since neither of the adducts of nitrosyl cyanide and ergosteryl acetate showed any correspondingly deshielded proton. In contrast, oxidation of benzohydroxamic acid in the presence of (**3**), followed by work-up of the reaction mixture without special precautions (see below), gave two cycloadducts. The minor (33%), oily adduct was recognised as (**4b**) by spectroscopic comparison with (**4a**). The major (50—56%), crystalline adduct (**6b**), however, was of an unexpected type. The ^{1}H n.m.r. spectrum of this product lacked the AB quartet expected for 6-H and 7-H in a 1,4-cycloadduct but showed instead two broad singlets, δ 4.63 and 5.50. The presence of a dioxazine ring in (**6b**) was deduced spectroscopically with the aid of the model compound[5] (**8**), the ^{13}C n.m.r. spectrum being especially informative (Table). The complete structure (**6b**) was then defined by the following degradation.

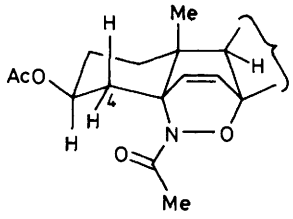
Treatment of the model compound (**8**) with methyl fluorosulphonate in benzene at room temperature gave the corresponding quaternary ammonium salt in high yield; this was readily hydrolysed with hydrochloric acid to give the hydroxylamine (**9**). Similarly, the adduct (**6b**) was converted into the hydroxylamine (**10**). This, with zinc in acetic acid, then yielded the benzoate (**11**), which was identical with material prepared from ergosterol by oxidation with perbenzoic acid.[6] Ergosterol behaved like ergosteryl acetate in forming two adducts (**4b**; Ac = H) and (**6b**; Ac = H) with nitrosocarbonylbenzene. The major (52%), crystalline adduct (**6b**; Ac = H) was characterised by acetylation to give (**6b**) which, in turn, was hydrolysed to regenerate (**6b**; Ac = H).

In principle, the dioxazine (**6b**) might arise directly by cycloaddition of nitrosocarbonylbenzene, acting as a 4π-component, to the 5,6-double-bond of ergosteryl acetate (**3**). However, cholesteryl acetate did not react with nitrosocarbonylbenzene, generated either directly by oxidation of benzohydroxamic acid, or indirectly by thermal dissociation of its adduct (**12**; R = Ph) with 9,10-dimethylanthracene. An alternative explanation for the formation of (**6b**) emerged from the following experiments.

Table. ^{13}C N.m.r. spectra of the dioxazines (**8**) and (**6b**) (δ p.p.m. in $CDCl_3$)

	Carbon atoms (dioxazine numbering)						
	3	5	6	1′	2′	3′	4′
(**8**)	153.9	63.8*	64.6*	130.9	128.2	125.6	130.3
(**6b**)	150.8	72.6	75.5	130.9	128.1	125.6	130.1

* Assignments may need to be interchanged.



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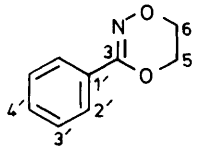

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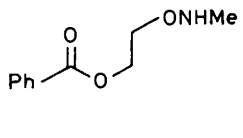

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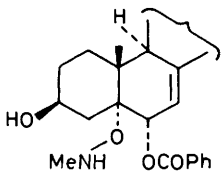

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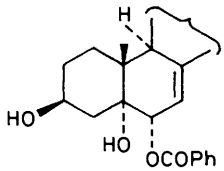

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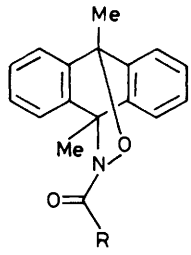

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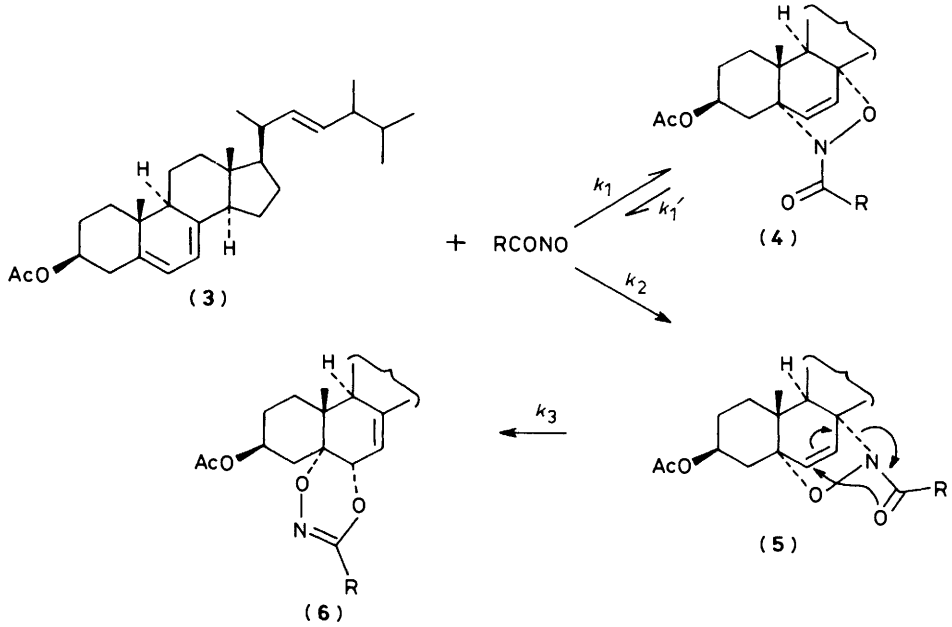
Ergosteryl acetate was treated, as before, with benzohydroxamic acid and periodate, but the total reaction mixture was examined by ^{1}H n.m.r. spectroscopy after evaporation of the solvent at 0 °C. No signals for the dioxazine (**6b**) were observed. Instead, the AB quartet, δ 6.57 and 6.23 (*J* 9 Hz), arising from the adduct (**4b**) was accompanied by a new AB quartet, δ 6.49 and 6.29 (*J* 8 Hz), attributed to the adduct (**5b**). When the mixture was heated in benzene at 60 °C the signals attributed to (**5b**) disappeared and were replaced by those for (**6b**) while the signals for (**4b**) remained unchanged. It was clear, therefore, that in the original preparation of (**6b**), isomerisation of the labile adduct (**5b**) had occurred during the normal operations of separation and crystallisation. This isomerisation was shown to be intramolecular by heating the foregoing mixture of (**4b**) and (**5b**) in benzene at 60 °C with an excess of triphenylphosphine, an efficient trapping agent for nitrosocarbonyl compounds.[7] The isomerisation proceeded as before and at qualitatively the same rate. In contrast, when the adduct (**4b**) was heated with triphenylphosphine in toluene at 111 °C, slow but efficient (78% isolated) conversion into ergosteryl acetate (**3**) was observed. In the absence of triphenylphosphine the adduct (**4b**) isomerised slowly at 111 °C to give (**6b**), presumably *via* dissociation (retro-Diels–Alder reaction) and recombination of the components to afford, initially, the labile adduct (**5b**). Finally, the dioxazine (**6b**) was stable at 111 °C in the presence of triphenylphosphine. The various reactions leading ultimately to the thermodynamically stable adduct (**6b**) are summarised in Scheme 2. Similarly, ergosteryl acetate reacted with 4-bromo-, 4-methoxy-, and 4-nitro-nitrosocarbonylbenzene to afford, initially, pairs of adducts of the type (**4**) and (**5**) (see the Experimental section for details). In no case could the adducts (**5**) be obtained completely pure owing to their ready isomerisation to the stable dioxazines (**6**). Oxidation of 2,4,6-trimethylbenzohydroxamic acid in the presence of ergosteryl acetate gave (**4f**) as the sole product. To this extent, 2,4,6-trimethylnitrosocarbonylbenzene behaves like nitrosocarbonylmethane, perhaps reflecting diminished conjugation between the phenyl and carbonyl groups.

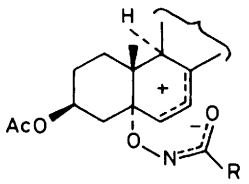
The intramolecular isomerisation, (**5**) → (**6**), formally constitutes a new class of [3,3]sigmatropic rearrangement [*cf.* (**1**) → (**2**)]. For a concerted process, as shown in Scheme 2, the amide nitrogen must become pyramidal in the transition state. However, an alternative, two-step mechanism involving the



For the b, c, d, and e series, $k_2 > k_1 \gg k_3 \gg k_1'$

a; R = Me
b; R = Ph
c; R = 4-BrC_6H_4
d; R = 4-$MeOC_6H_4$
e; R = 4-$NO_2C_6H_4$
f; R = 2,4,6-$Me_3C_6H_2$

Scheme 2.



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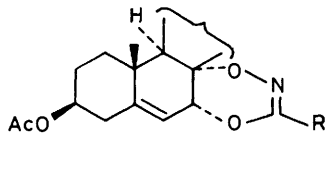

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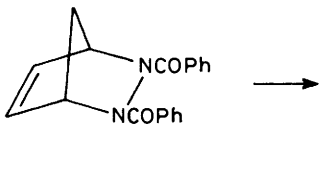

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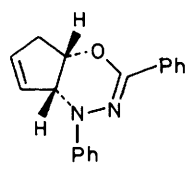

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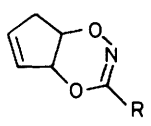

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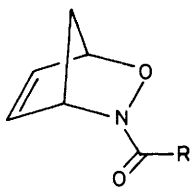
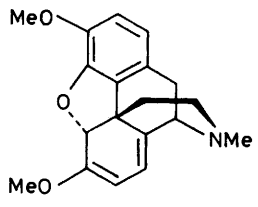


(18)

dipolar species (**13**) cannot be excluded. The facility of this rearrangement may well reflect relief of the steric interactions associated with the *cis*-fused, B/C ring system [*cf.* (**7**)]. The corresponding rearrangement of (**4**) would lead to the sterically congested isomer of type (**14**), which, so far, has not been detected. A closely related [3,3]sigmatropic rearrangement, namely the thermal isomerisation of the bridged diazine (**15**) to the fused oxadiazine (**16**), has been described by Mackay *et al.*[8] More recently Dao *et al.*[9] have made the interesting observation that dioxazines of the type (**17**) may arise directly by reaction between cyclopentadiene and nitrosocarbonyl compounds. For example, oxidation of pivalohydroxamic acid in the presence of cyclopentadiene gave a *ca.* 9:1 mixture of (**18**; R = Bu^t) and (**17**; R = Bu^t) at a temperature too low to permit rearrangement of the former to the latter. The ability of nitrosoalkenes to act similarly as 4π-components (heterodienes) in cycloaddition reactions with conjugated dienes (acting as 2π-components) has been discussed by Faragher and Gilchrist.[10] They found that vinyloxazines are indeed formed readily from nitrosoalkenes and dienes although it is not clear whether the final products arise directly or *via* a [3,3]sigmatropic rearrangement.

We had earlier shown[2] that thebaine (**19**) is converted into adducts of the type (**20**) either by treatment with hydroxamic acids, RCONHOH, in the presence of periodate or by heating with the adducts (**12**). This was taken as evidence for the involvement of a common, reactive intermediate, RCONO. A more discriminating test is possible with ergosteryl acetate (**3**) since two types of adduct, (**4**) and (**6**), were formed by the 'direct' oxidative method and, importantly, their ratio was controlled kinetically. A comparison with the 'indirect' method was therefore of interest. Accordingly, ergosteryl acetate (**3**) was heated with (**12**; R = Ph) in benzene and the products were separated by thin layer chromatography. The isomeric adducts (**4b**) and (**6b**) were obtained in yields of 27 and 44%, respectively (ratio 1:1.6) whereas, by the 'direct' method, the corresponding yields were 33 and 56% (ratio 1:1.7). This close agreement in product ratios supports the idea that the 'direct' and 'indirect' methods involve a common intermediate. Confirmatory evidence was obtained from analogous experiments involving oxidation of 4-bromobenzohydroxamic acid or heating (**12**; R = 4-BrC_6H_4). The first, 'direct' method gave the adducts (**4c**) (33%) and (**6c**) (57%) (ratio 1:1.7) while the 'indirect' methods gave (**4c**) (25%) and (**6c**) (53%) (ratio 1:2.1).



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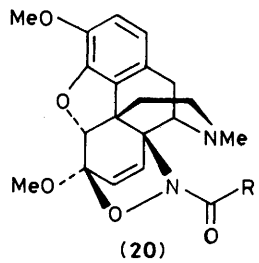

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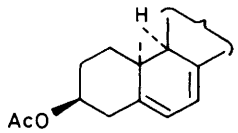

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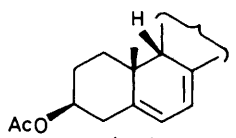

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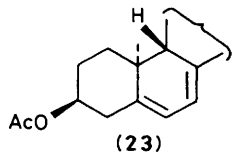

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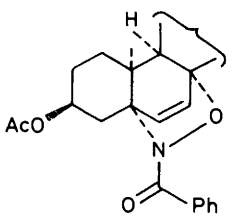

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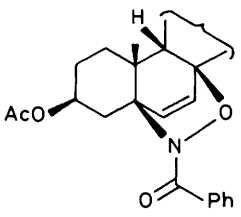

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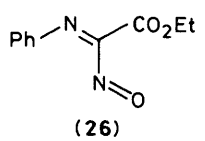

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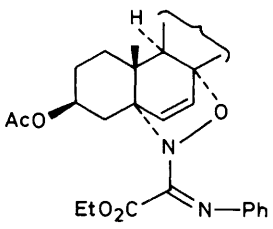

(27)

The reactions of nitrosocarbonylbenzene, generated by oxidation of benzohydroxamic acid, with pyrocalciferyl acetate (**21**), isopyrocalciferyl acetate (**22**), and lumisteryl acetate (**23**) were briefly studied. The first two isomers gave single adducts, formulated tentatively* as (**24**) (67%) and (**25**) (63%), respectively. Lumisteryl acetate (**23**) did not yield any adduct under these conditions, a result which reflects the low reactivity of this isomer towards dienophiles.[11] Finally, generation of the transient nitroso imine (**26**), by oxidation of the appropriate

* In the ^{1}H n.m.r. spectra (see the Experimental section) of the adducts (**24**) and (**25**) signals for both 4-methylene protons appear at low field (near δ 3), an observation best accommodated by the regio- and stereochemistries shown.

amidoxime[12] in the presence of ergosteryl acetate, gave the adduct (**27**) as the only steroidal product.

Experimental

M.p.s were determined with a Kofler hot-stage apparatus. N.m.r. spectra were recorded for deuteriochloroform solutions and i.r. spectra, except where otherwise stated, for KBr discs. Light petroleum refers to the fraction b.p. 60—80 °C except where otherwise stated. For a CAUTIONARY note on the preparation of tetraethylammonium periodate see Ref. 2.

Adduct (**4a**) *of Ergosteryl Acetate and Nitrosocarbonylmethane.*—Acetohydroxamic acid (1.3 mmol) was added in portions during 10 min with stirring to ergosteryl acetate (**3**) (0.5 mmol) and tetraethylammonium periodate[13] (0.7 mmol) in dichloromethane (25 ml) at 0 °C. After 1 h, the mixture was washed successively with aqueous sodium thiosulphate, saturated aqueous sodium hydrogen carbonate, and water and was then dried ($MgSO_4$) and evaporated. Crystallisation of the residue from methanol gave 8α,5α-(N-*acetylepoxyimino*)-5,8-*dihydroergosteryl acetate* (**4a**) as needles [84% based on (**3**)], m.p. 142—145 °C (Found: C, 75.1; H, 9.6; N, 3.0. $C_{32}H_{49}NO_4$ requires C, 75.15; H, 9.6; N, 2.7%); $\nu_{max.}$ 1 743 and 1 675 cm^{-1}; δ 1.85 (s, NAc), 2.01 (s, OAc), 3.47 (dd, *J* 14 and 5 Hz, 4α-H), 5.20 (m, 22-H and 23-H), 5.26 (m, 3-H), and 6.22 and 6.36 (ABq, *J* 9 Hz, 6-H and 7-H); *m/z* 511.

Adducts (**4b**) *and* (**6b**) *of Ergosteryl Acetate* (**3**) *and Nitrosocarbonylbenzene.*—Benzohydroxamic acid (1.5 mmol) was oxidised in the presence of (**3**) (1.0 mmol) as described for the preparation of (**4a**). The reaction mixture was chromatographed on silica plates developed with chloroform. The faster-running fraction [56% based on (**3**)] gave the *dioxazine* (**6b**) as needles (50%), m.p. 190—191 °C (from methanol) (Found: C, 77.3; H, 9.0; N, 2.7. $C_{37}H_{51}NO_4$ requires C, 77.45; H, 9.0; N, 2.4%); $\nu_{max.}$ 1 728 cm^{-1}; δ 1.96 (s, OAc), 4.63 (br s, 6-H), 5.05 (br s, 7-H), 5.20 (m, 22-H and 23-H), *ca.* 5.2 (m, 3-H), 7.40 (3 H, m, ArH), and 7.85 (2 H, m, ArH); *m/z* 573. The slow-running fraction gave the adduct (**4b**) as an undistillable oil (33%); $\nu_{max.}$ (liquid film) 1 733 and 1 654 cm^{-1}; δ 2.05 (s, OAc), 3.67 (dd, *J* 14 and 5 Hz, 4α-H), *ca.* 5.1 (3 H, m, 3-H, 22-H, and 23-H), 6.23 and 6.57 (ABq, *J* 9 Hz, 6-H and 7-H), and 7.2—7.6 (m, Ph); *m/z* 438 (*M* − PhCONO).

Adducts (**4b**) *and* (**5b**) *of Ergosteryl Acetate and Nitrosocarbonylbenzene.*—The foregoing preparation of (**4b**) and (**6b**) was repeated but the ice-cooled reaction mixture in dichloromethane was washed successively with ice-cooled, aqueous solutions of sodium thiosulphate, 10% sodium hydroxide, and sodium chloride and was then dried ($MgSO_4$) and evaporated under reduced pressure at 0 °C. The n.m.r. spectrum of the residual oil was recorded immediately. No signals attributable to (**6b**) were observed. Instead signals for (**4b**) were accompanied by the following, attributed to (**5b**): δ 1.91 (s, OAc), and 6.29 and 6.49 (ABq, *J* 8 Hz, 6-H and 7-H). When this mixture was heated in benzene at 60 °C, smooth conversion of (**5b**) into (**6b**) was observed by n.m.r. spectroscopy, the conversion being complete after 7 h. The conversion proceeded at qualitatively the same rate in the presence of triphenylphosphine (2 mol equiv.).

Adducts (**4b**; Ac = H) *and* (6b: Ac = H) *of Ergosterol and Nitrosocarbonylbenzene.*—Benzohydroxamic acid (0.4 mmol) was oxidised in the presence of ergosterol (0.25 mmol), as before, to give the *dioxazine* (**6b**; Ac = H), m.p. 170—172 °C (from methanol) (Found: C, 79.1; H, 9.1; N, 2.85. $C_{35}H_{49}NO_3$ requires C, 79.05; H, 9.3; N, 2.6%); $\nu_{max.}$ 3 240 cm^{-1}; δ 4.02 (m, 3-H), 4.62 (br s, 6-H), 5.03 (br s, 7-H), 5.17 (m, 22-H and 23-H), 7.35 (3 H, m, ArH), and 7.80 (2 H, m, ArH); *m/z* 531, and the oily adduct (**4b**; Ac = H) (38%); $\nu_{max.}$ (liquid film) 3 390 and 1 662 cm^{-1}; δ 3.57 (dd, *J* 14 and 5 Hz, 4α-H), 4.16 (m, 3-H), 5.19 (m, 22-H and 23-H), 6.23 and 6.52 (ABq, *J* 9 Hz, 6-H and 7-H), 7.32 (3 H, m, ArH), and 7.80 (2 H, m, ArH); *m/z* 396 (*M* − PhCONO). The dioxazine (**6b**; Ac = H) was converted with acetic anhydride in pyridine into (**6b**) which was hydrolysed with methanolic sodium hydroxide to regenerate (**6b**; Ac = H).

Preparation of (**4b**) *and* (**6b**) *Using the Adduct* (**12**; R = Ph).—Ergosteryl acetate (0.1 mmol) and the adduct[2] (**12**; R = Ph) (0.1 mmol) were heated in benzene (15 ml) under reflux for 4.5 h. Chromatography of the mixture gave (**4b**) (27%) and (**6b**) (44%).

Degradation of the Dioxazine (**8**).—The dioxazine[5] (**8**) (2.0 mmol) in dry benzene (10 ml) was treated with methyl fluorosulphonate (2.0 mmol) at room temperature. After 10 min the solution had become cloudy and after 2 h a substantial precipitate of *2-methyl-3-phenyl-5,6-dihydro-1,4,2-dioxazinium fluorosulphonate* had formed (91%). This salt had m.p. 135—137 °C (decomp.) (Found: C, 43.5; H, 4.6; N, 5.1. $C_{10}H_{12}FNO_5S$ requires C, 43.4; H, 4.3; N, 5.05%). The salt was hydrolysed in 10% hydrochloric acid at room temperature overnight. The mixture was made alkaline and extracted with chloroform to give the hydroxylamine (**9**) as an oil; $\nu_{max.}$ (liquid film) 3 420 and 1 727 cm^{-1}; δ 2.67 (s, Me), 3.94 (m, $NOCH_2$), 4.50 (m, $COOCH_2$), 4.92 (br s, NH, exchangeable with D_2O), 7.4 (3 H, m, ArH), and 8.0 (2 H, m, ArH); *m/z* 195.

Degradation of the Adduct (**6b**).—The adduct (**6b**) (0.35 mmol) was treated with methyl fluorosulphonate (0.35 mmol) in benzene (10 ml). No precipitate formed but methylation was complete (t.l.c. control) after 45 min at room temperature. Methanol (10 ml), water (0.1 ml), and concentrated hydrochloric acid (0.1 ml) were added directly to the reaction mixture. After 12 h at room temperature the mixture was diluted with water (100 ml), adjusted to pH 11 with sodium hydroxide, and extracted with ether (3 × 25 ml). The extracts were dried ($MgSO_4$) and evaporated to give the oily hydroxylamine (**10**) (56%); $\nu_{max.}$ (liquid film) 3 400 and 1 721 cm^{-1}; δ 2.65 (s, NMe), 3.63 (m, 3-H), 4.89 (br s, 7-H), 5.16 (m, 22-H and 23-H), 5.44 (br s, 6-H), 7.4 (3 H, m, ArH), and 8.0 (2 H, m, ArH); *m/z* 563. This was hydrolysed at room temperature in methanolic sodium hydroxide to give *5,6-dihydro-6α-hydroxy-5α-methylamino-oxyergosterol* (**10**; PhCO=H), m.p. 179—181 °C (from methanol) (Found: C, 76.0; H, 10.8; N, 2.8. $C_{29}H_{49}NO_3$ requires C, 75.9; H, 10.7; N, 3.05%); $\nu_{max.}$ (liquid film) 3 400 cm^{-1}; δ 2.60 (s, NMe), 3.85 (m, 3-H), 4.10 (br s, 6-H), and 5.17 (m, 7-H, 22-H, and 23-H); *m/z* 459. The hydroxylamine benzoate (**10**) (50 mg) was reduced with zinc powder (195 mg) in acetic acid (5 ml) for 14 h at room temperature. The mixture was diluted with water (50 ml), treated with an excess of sodium hydrogen carbonate, and extracted with chloroform. The extracts yielded the known[6] benzoate (**11**) (74%), m.p. and mixed m.p. 194—195 °C. Similarly, the hydroxylamine (**10**; PhCO=H) was reduced with zinc to give the known[6] triol (**11**; PhCO=H) (59%), m.p. and mixed m.p. 241—242 °C.

Isomerisation of the Adduct (**4b**).—The adduct (**4b**) (0.1 mmol) was heated in toluene (5 ml) at 111 °C under nitrogen. Isomerisation to give the adduct (**6b**) was complete (t.l.c. control) in 16 h (55% yield after purification). When the adduct (**4b**) was heated in toluene with triphenylphosphine (2 mol equiv.) ergosteryl acetate (**3**) (78%) was isolated after 4 h. The adduct (**4b**) was unaffected by heating in benzene at 80 °C for 2 h.

Adduct (**12**; R = 4-BrC_6H_4) *of* 9,10-*Dimethylanthracene and* 4-*Bromonitrosocarbonylbenzene.*—Prepared by the standard method,[2] 9,10-(N-4-*bromobenzoylepoxyimino*)-9,10-*dihydro-*

9,10-*dimethylanthracene* (**12**, R = 4-BrC_6H_4) formed plates, m.p. 125—128 °C (from benzene–light petroleum) (Found: C, 66.0; H, 4.5; N, 3.2. $C_{23}H_{18}BrNO_2$ requires C, 65.7; H, 4.3; N, 3.3%); $\nu_{max.}$ 1 680 cm^{-1}; δ 2.04 (s, 9 or 10-Me), 2.75 (s, 10 or 9-Me), and 7.2—7.7 (12 H, m, ArH); *m/z* 206 (*M* − $C_7H_4BrNO_2$).

Adducts (**4c**) *and* (**6c**) *of Ergosteryl Acetate* (**3**) *and* 4-*Bromonitrosocarbonylbenzene*.—Oxidation of 4-bromobenzohydroxamic acid (0.9 mmol) in the presence of (**3**) (0.5 mmol) gave the *dioxazine* (**6c**) (57%), m.p. 224—226 °C (decomp.) (from methanol) (Found: C, 66.9; H, 7.75; N, 2.4. $C_{37}H_{50}BrNO_4$ requires C, 67.0; H, 7.9; N, 2.2%); $\nu_{max.}$ 1 735 cm^{-1}; δ 1.97 (s, Ac), 4.60 (br s, 6-H), 4.98 (br s, 7-H), 5.08 (m, 3-H), 5.15 (m, 22-H and 23-H), and 7.42 and 7.63 (ABq, *J* 8 Hz, ArH); *m/z* 652, and 8α,5α-(N-4-*bromobenzoylepoxyimino*)-5,8-*dihydroergosteryl acetate* (**4c**) (33%), m.p. 143—146 °C (from methanol) (Found: C, 67.2; H, 7.65; N, 1.8. $C_{37}H_{50}BrNO_4$ requires C, 67.0; H, 7.9; N, 2.2%); $\nu_{max.}$ 1 735 and 1 653 cm^{-1}; δ 2.07 (s, Ac), 3.65 (dd, *J* 14 and 5 Hz, collapsed to d, *J* 14 Hz upon irradiation at δ 5.15, 4α-H), 5.15 (m, 3-H), 5.18 (m, 22-H and 23-H), 6.21 and 6.52 (ABq, *J* 8 Hz, 6-H and 7-H) and 7.40 (br s, ArH); *m/z* 438 (*M* − $C_7H_4BrNO_2$).

Preparation of (**4c**) *and* (**6c**) *Using the Adduct* (**12**; R = 4-BrC_6H_4).—Ergosteryl acetate (0.25 mmol) and the adduct (**12**; R = 4-BrC_6H_4) (0.25 mmol) were heated in benzene under reflux for 7 h to give (**6c**) (53%) and (**4c**) (25%).

Adducts (**4d**), (**5d**), *and* (**6d**) *of Ergosteryl Acetate* (**3**) *and* 4-*Methoxynitrosocarbonylbenzene*.—Oxidation of 4-methoxybenzohydroxamic acid (1.5 mmol) in the presence of (**3**) (1.0 mmol) gave the *dioxazine* (**6d**) (47%), m.p. 216—218 °C (from methanol) (Found: C, 75.9; H, 8.8; N, 2.6. $C_{38}H_{53}NO_5$ requires C, 75.6; H, 8.8; N, 2.3%); $\nu_{max.}$ 1 740 cm^{-1}; δ 1.97 (s, Ac), 3.80 (s, OMe), 4.60 (br s, 6-H), 5.04 (br s, 7-H), 5.11 (m, 3-H), 5.20 (m, 22-H and 23-H), and 6.87 and 7.76 (ABq, *J* 9 Hz, ArH); *m/z* 603, and 5,8-*dihydro*-8α,5α-(N-4-*methoxybenzoylepoxyimino*)*ergosteryl acetate* (**4d**) (23%), m.p. 153—156 °C (from benzene–light petroleum) (Found: C, 75.4; H, 8.9; N, 2.6. $C_{28}H_{53}NO_5$ requires C, 75.6; H, 8.8; N, 2.3%); $\nu_{max.}$ 1 737 and 1 655 cm^{-1}; δ 2.01 (s, Ac), 3.67 (dd, *J* 14 and 5 Hz, 4α-H), 3.82 (s, OMe), 5.19 (m. 22-H and 23-H), 5.26 (m, 3-H), 6.17 and 6.55 (ABq, *J* 9 Hz, 6-H and 7-H), and 6.82 and 7.59 (ABq, *J* 9 Hz, ArH); *m/z* 438 (*M* − $C_8H_7NO_3$). This preparation was repeated and the products were isolated at 0 °C as before, to give, after chromatography on silica plates, (**4d**) and a fraction containing a little (**6d**) and the unstable adduct (**5d**); δ 1.95 (s, Ac), 3.84 (s, OMe), 6.28 and 6.46 (ABq, *J* 9 Hz, 6-H and 7-H), and 6.94 and 7.75 (ABq, *J* 9 Hz, ArH). This mixture was heated in benzene at 60 °C and the conversion of (**5d**) into (**6d**), monitored by n.m.r. spectroscopy, was judged to be complete in 6 h.

Adducts (**4e**), (**5d**), *and* (**6e**) *of Ergosteryl Acetate* (**3**) *and* 4-*Nitronitrosocarbonylbenzene*.—Oxidation of 4-nitrobenzohydroxamic acid (0.8 mmol) in the presence of (**3**) (0.25 mmol) gave the *dioxazine* (**6e**) (58%), m.p. 201—203 °C (from methanol) (Found: C, 72.1; H, 8.0; N, 4.3. $C_{37}H_{50}N_2O_6$ requires C, 71.85; H, 8.1; N, 4.5%); $\nu_{max.}$ 1 740 cm^{-1}; δ 1.97 (s, Ac), 4.71 (br s, 6-H), 5.05 (br s, 7-H), 5.11 (m, 3-H), 5.20 (m, 22-H and 23-H), and 7.98 and 8.21 (ABq, *J* 9 Hz, ArH); *m/z* 618, and 5,8-*dihydro*-8α,5α-(N-4-*nitrobenzoylepoxyimino*)*ergosteryl acetate* (**4e**) (17%), m.p. 147—148 °C (from aqueous methanol) (Found: C, 71.8; H, 7.9; N, 4.3. $C_{37}H_{50}N_2O_6$ requires C, 71.9; H, 8.9; N, 4.5%); $\nu_{max.}$ 1 738 and 1 660 cm^{-1}; δ 2.02 (s, Ac), 3.67 (dd, *J* 14 and 5 Hz, 4α-H), 5.18 (m, 22-H and 23-H), 5.23 (m, 3-H), 6.25 and 6.51 (ABq, *J* 9 Hz, 6-H and 7-H), and 7.56 and 8.15 (ABq, *J* 9 Hz, ArH); *m/z* 438 (*M* − $C_7H_4N_2O_4$). This preparation was repeated and the products were isolated at 0 °C, as before, to give a mixture of (**4e**) and (**5e**). Chromatography on silica plates afforded a pure sample of (**5e**); $\nu_{max.}$ (liquid film) 1 745 and 1 660 cm^{-1}; δ 1.90 (s, Ac), 5.11 (m, 3-H), 5.21 (m, 22-H and 23-H), 6.31 and 6.48 (ABq, *J* 9 Hz, 6-H and 7-H), and 7.73 and 8.24 (ABq, *J* 9 Hz, ArH). Attempts to crystallise this adduct caused isomerisation to (**6e**). This isomerisation was complete (n.m.r. control) in benzene at 60 °C in 18 h.

Adduct (**4f**) *of Ergosteryl Acetate* (**3**) *and* 2,4,6-*Trimethylnitrosocarbonylbenzene*.—Oxidation of 2,4,6-trimethylbenzohydroxamic acid (1.5 mmol) in the presence of (**3**) (0.5 mmol) gave 5,8-*dihydro*-8α,5α-(N-2,4,6-*trimethylbenzoylepoxyimino*)-*ergosteryl acetate* (**4f**) (80%) as a glassy solid (Found: C, 78.3; H, 9.35; N, 2.4. $C_{40}H_{57}NO_4$ requires C, 78.05; H, 9.3; N, 2.3%); $\nu_{max.}$ 1 736 and 1 658 cm^{-1}; δ 1.96 (s, Ac), 2.04 (s, ArMe), 2.24 (s, ArMe), 2.32 (s, ArMe), 3.73 (dd, *J* 14 and 5 Hz, 4α-H), 5.24 (m, 22-H and 23-H), 5.25 (m, 3-H), 6.25 and 6.46 (ABq, *J* 9 Hz, 6-H and 7-H), 6.67 (s, ArH), and 6.78 (s, ArH); *m/z* 438 (*M* − $C_{10}H_{11}NO_2$).

Adduct (**24**) *of Pyrocalciferyl Acetate* (**21**) *and Nitrosocarbonylbenzene*.—Oxidation of benzohydroxamic acid (0.15 mmol) in the presence of (**21**)[14] (0.05 mmol) gave 8α,5α-(N-*benzoylepoxyimino*)-5,8-*dihydropyrocalciferyl acetate* (**24**) (tentative structure) (67%), m.p. 95—98 °C (from methanol) (Found: C, 77.3; H, 8.8; N, 2.8. $C_{37}H_{51}NO_4$ requires C, 77.5; H, 9.0; N, 2.4%); $\nu_{max.}$ 1 738 and 1 655 cm^{-1}; δ 2.04 (s, Ac), 2.68 (dd, *J* 15 and 4 Hz, 4-H), 3.25 (br d, *J* 15 Hz, 4-H), 5.11 (m, 22-H and 23-H), 5.23 (m, 3-H), 6.25 and 6.96 (ABq, *J* 8 Hz, 6-H and 7-H), and 7.1—7.6 (m, Ph); *m/z* 438 (*M* − PhCONO).

Adduct (**25**) *of Isopyrocalciferyl Acetate* (**22**) *and Nitrosocarbonylbenzene*.—Oxidation of benzohydroxamic acid (0.15 mmol) in the presence of (**22**)[14] (0.05 mmol) gave 8α,5α-(N-*benzoylepoxyimino*)-5,8-*dihydroisopyrocalciferyl acetate* (**25**) (tentative structure) (63%), m.p. 124—126 °C (from methanol) (Found: C, 77.7; H, 8.9; N, 2.4. $C_{37}H_{51}NO_4$ requires C, 77.5; H, 9.0; N, 2.4%); $\nu_{max.}$ 1 735 and 1 628 cm^{-1}; δ 2.07 (s, Ac), 2.7—3.2 (2 H, m, 4-H), 5.03 (m, 3-H), 5.11 (m, 22-H and 23-H), 6.19 and 6.53 (ABq, *J* 8 Hz, 6-H and 7-H), and 7.2—7.7 (m, Ph); *m/z* 438 (*M* − PhCONO).

Adduct (**27**) *of Ergosteryl Acetate* (**3**) *and the Nitrosoimine*[12] (**26**).—Lead tetra-acetate (0.25 mmol) was added in portions with stirring to (**3**) (0.25 mmol) and ethyl 2-oximino-2-phenylaminoacetate (0.33 mmol) in dichloromethane (25 ml) at 0 °C. After 1 h, the mixture was washed with 5% aqueous sodium hydroxide and then brine. The dichloromethane solution was dried ($MgSO_4$) and evaporated to give, after chromatography on silica plates developed with chloroform, the *adduct* (**27**) (65%), m.p. 153—154.5 °C (from methanol) (Found: C, 74.6; H, 8.7; N, 4.2. $C_{40}H_{56}N_2O_5$ requires C, 74.5; H, 8.7; N, 4.3%); $\nu_{max.}$ 1 738, 1 725, and 1 643 cm^{-1}; δ 1.98 (s, Ac), 3.70 (dd, *J* 14 and 5 Hz, 4α-H), 3.91 (q, *J* 7 Hz, OCH_2), 5.21 (m, 22-H and 23-H), 5.42 (m, 3-H), 6.32 and 6.50 (ABq, *J* 9 Hz, 6-H and 7-H), and 6.7—7.4 (m, Ph); *m/z* 438 (*M* − $C_{10}H_{10}N_2O_3$).

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