Formation and Reactions of *C*-Nitrosoformate Esters, a New Class of Transient Dienophiles

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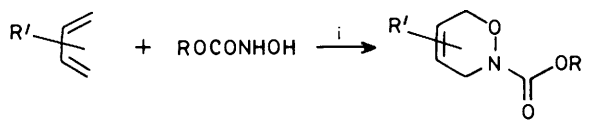
Oxidation of *N*-hydroxycarbamic esters, ROCONHOH, with tetraethylammonium or sodium periodate in the presence of conjugated dienes gave *N*-alkoxycarbonyl-3,6-dihydro-2*H*-1,2-oxazines, formed apparently by cycloaddition of transient *C*-nitrosoformate esters, ROCONO, with the dienes. Cleavage of various *N*-alkoxycarbonyl derivatives under mild conditions is exemplified. The cycloadduct (**10a**) of benzyl nitrosoformate and 9,10-dimethylanthracene decomposed in benzene at 80 °C in the presence of thebaine (**3**) to give the corresponding adduct (**4a**) of thebaine, together with 9,10-dimethylanthracene. Similarly, the adduct (**6b**) of 2,2,2-trichloroethyl nitrosoformate and cyclopentadiene, when heated with ergosteryl acetate, gave the corresponding adduct (**8b**) of the steroid. Benzyl and t-butyl azidoformates decomposed in dimethyl sulphoxide at 115—130 °C in the presence of thebaine to give the adducts (**4a**) and (**4c**) of benzyl and t-butyl nitrosoformate and the alkaloid. The other, major products were the sulphoximides (**20a**) and (**20c**). Alkoxycarbonylnitrenes, therefore, attack dimethyl sulphoxide either on sulphur, to give sulphoximides, or on oxygen, to give nitrosoformates. Benzyl nitrosoformate, generated thermally from either the adduct (**10a**) or (**6a**), reacted with triphenylphosphine to give, apparently, benzyloxycarbonylnitrene which attacked the solvent, benzene, to form *N*-benzyloxycarbonylazepine (**24a**). The adduct (**6c**) of t-butyl nitrosoformate and cyclopentadiene behaved likewise to give the azepine (**24c**). The reaction of (**6c**) with triphenylphosphine in benzene or dichloromethane gave a small quantity of 5,5-dimethyloxazolidin-2-one (**26**), a known cyclisation product of t-butyloxycarbonylnitrene.

Oxidation of hydroxamic acids, RCONHOH, is believed to generate transient *C*-nitrosocarbonyl compounds, RCONO, which may be trapped *in situ* by conjugated dienes to form *N*-acyldihydroxazines.[1] We find [1a,2] that oxidation of *N*-hydroxycarbamic esters (**1**) proceeds similarly (Scheme 1) to afford the oxazine derivatives (**2**) having readily removable, *N*-protecting groups of the type employed in peptide chemistry (Scheme 2).



(**1**) (**2**)

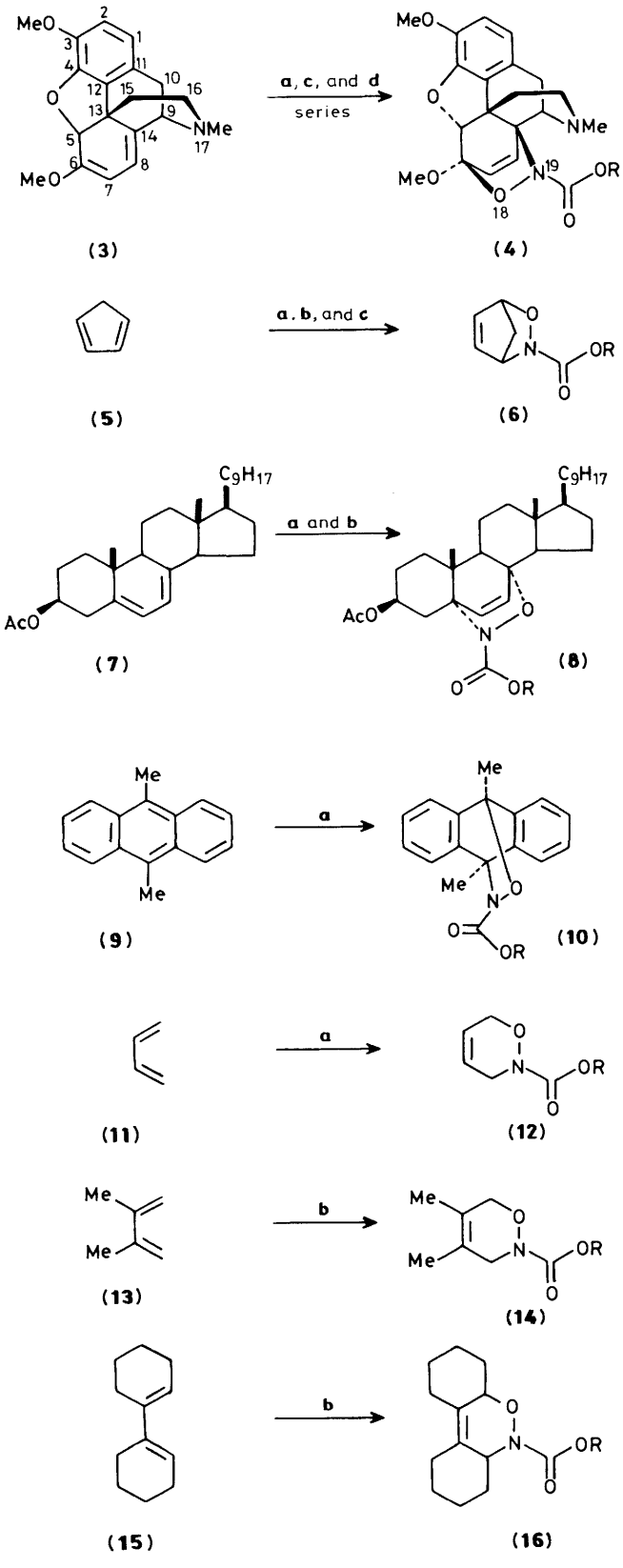
Scheme 1. *Reagents:* i, Et_4NIO_4 or $NaIO_4$

This procedure thus offers a useful preparative route to the parent dihydro-oxazines, and therefrom, by reductive cleavage of the N–O bonds, the related 4-amino alcohols. The experiments described in this paper provide compelling evidence, though not conclusive proof, that oxidation of the hydroxamic derivatives (**1**) forms *C*-nitrosoformate esters (*O*-nitrosocarbonyl compounds), ROCONO. However, these species, like the *C*-nitrosocarbonyl compounds,[1] have so far evaded detection by direct, physical methods.

Oxidation of the *N*-hydroxycarbamic esters (**1a**, **c**, **d**) with tetraethylammonium periodate in the presence of thebaine (**3**) gave the corresponding cycloadducts (**4**) in high yield. Cyclopentadiene (**5**) was converted similarly, using tetraethylammonium or sodium periodate, into the adducts (**6a**—**c**) and ergosteryl acetate (**7**) into (**8a**) and (**8b**). Oxidation of (**1a**) in the presence of 9,10-dimethylanthracene (**9**) or buta-1,3-diene (**11**) gave (**10a**) and (**12a**), respectively, and oxidation of (**1b**) in the presence of 2,3-dimethylbuta-1,3-diene (**13**) or the bicyclohexenyl (**15**) gave (**14b**) and (**16b**), respectively. The structures of the products were readily determined spectroscopically by comparison with the corresponding cycloadducts of nitrosocarbonyl-methane and -benzene.[1] The cycloadduct of (**13**) and nitrosocarbonylbenzene was prepared, in the usual way, to assist identification of (**14b**).

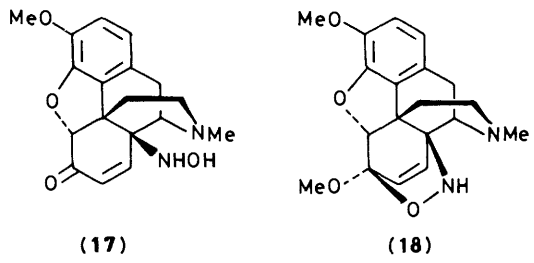
Cleavage of various *N*-alkoxycarbonyl derivatives was achieved readily by standard, literature methods. Thus, the *N*-benzyloxycarbonyl derivative (**12a**), with hydrogen bromide in acetic acid, give the parent dihydro-oxazine[3] as its crystalline hydrobromide. Cleavage of the t-butoxycarbonyl derivative (**4c**) with methanolic hydrogen chloride occurred, as expected, with concomitant opening of the cyclic acetal to give 14β-hydroxyaminocodeinone[4] (**17**). In contrast, when the thebaine derivative (**4d**), having an *N*-protecting group designed[5] for removal under mild, basic conditions, was treated with 1,5-diazabicyclo[4.3.0]non-5-ene, the oily acetal (**18**) was obtained. Unexpectedly, this product decomposed during attempted crystallisation, to give thebaine (**3**), presumably by loss of nitrosyl hydride[6] (HNO). However, it was easily characterised by hydrolysis with hydrochloric acid to give the codeinone (**17**). Similarly, treatment of the *N*-(2,2,2-trichloroethoxycarbonyl) derivative (**8b**) with an excess of zinc powder in acetic acid gave ergosteryl acetate (**7**) in high yield. Again, it would appear that the parent, bridged dihydro-oxazine is inherently unstable. A similar, thermal instability has been reported[7] for 2-oxa-3-azabicyclo[2.2.1]hept-5-ene (**6**; ROCO = H), although the decomposition products were not identified.

When the cycloadducts of 9,10-dimethylanthracene (DMA) (**9**) and *C*-nitrosocarbonyl compounds are heated in benzene in the presence of conjugated dienes, for example thebaine (**3**), the corresponding adducts of the dienes are formed with the release of DMA.[1b,c] Similarly, the adduct (**10a**) reacted with thebaine (**3**) in benzene at 80 °C to give the thebaine adduct (**4a**) in essentially quantitative yield. The release of DMA from (**10a**) was followed (absorption at 385 nm) kinetically in benzene at



a; R = $PhCH_2$
b; R = CCl_3CH_2
c; R = Bu^t
d; R = 4-$MeC_6H_4SO_2CH_2CH_2$

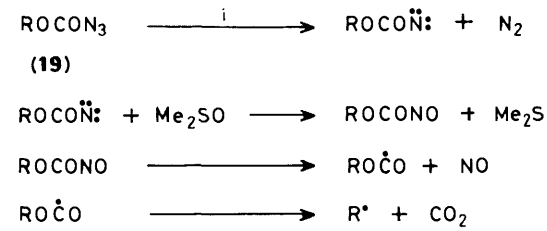
Scheme 2.



(17) (18)

60 °C in the presence of thebaine (1 or 2 mol equiv.). First-order kinetics were observed, $k = 4.3 \times 10^{-4}$ s^{-1}, consistent with slow dissociation of the adduct (**10a**) followed by rapid capture of benzyl nitrosoformate, $PhCH_2OCONO$, by thebaine. The rate of dissociation of (**10a**) is *ca.* 10 times that of the adduct of DMA and nitrosocarbonylmethane.[1b] Attention was then turned to the cyclopentadiene adduct (**6b**) in the hope that it too would dissociate, like the adduct (**6**; RO = Ph) of nitrosocarbonylbenzene,[1d] and thus serve as a convenient precursor for trichloroethyl nitrosoformate. Accordingly, equimolar amounts of (**6b**) and ergosteryl acetate (**7**) were heated under reflux in benzene to give, after 12 h, the adduct (**8b**) in quantitative yield. The reaction was found to proceed more rapidly when benzene was distilled slowly from the reaction mixture, the volume of the mixture being maintained by occasional addition of benzene. Presumably, this procedure succeeds by removing cyclopentadiene, released from the adduct (**6b**), from the reaction mixture where it would otherwise compete with ergosteryl acetate for trichloroethyl nitrosoformate. Again, (**6b**) and (**15**) gave the adduct (**16b**) in good yield, although the reaction was very slow, requiring 4 days for completion in refluxing toluene.

Prosser *et al.*[8] studied the thermal decomposition of octadecyl azidoformate in dimethyl sulphoxide (DMSO) at 120 °C and proposed a 4-step reaction sequence (Scheme 3) to



Scheme 3. i, heat at 120 °C

account for the formation of dimethyl sulphide, carbon dioxide, and nitric oxide. The azidoformate decomposed at a rate similar to that observed in other solvents at this temperature, suggesting that the first step was indeed unimolecular dissociation to produce octadecyloxycarbonylnitrene. To our knowledge, this is the first reference in the literature to the formation of nitrosoformates,* although no direct evidence for their fleeting existence was obtained. We re-investigated the decomposition of azidoformates in the hope that nitrosoformates might be trapped as their cycloadducts with thebaine. Benzyl azidoformate[9] (**19a**) was heated in DMSO at 130 °C for 2 h to give the sulphoximide (**20a**) (50—60%) and benzaldehyde (15%). Prosser *et al.*[8] reported that octadecyl azidoformate gave some solid material which they assumed to be the corresponding sulphoximide but did not fully characterise. When the decomposition of (**19a**) (1.8 mmol) was conducted as

* Prosser *et al.*[8] described their proposed intermediate as a 'nitrite' but the structure, ROCONO, was unambiguously indicated.

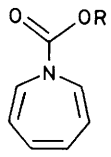
before but in the presence of thebaine (**3**) (0.32 mmol), the adduct (**4a**) was obtained (66% yield based on thebaine) along with (**20a**) and benzaldehyde. Similarly, t-butyl azidoformate (**19c**) decomposed in DMSO at 115 °C to give the sulphoximide (**20c**) (58%). Decomposition of (**19c**) (2.5 mmol) in the presence of thebaine (0.5 mmol) gave the adduct (**4c**) [84% based on (**3**) and 17% on (**19c**)] and the sulphoximide (**20c**) (51%). This last

$ROCON{=}SOMe_2$

(**20**)

experiment was repeated using (**19c**) (0.25 mmol) and thebaine (0.5 mmol) to give thebaine (73%), the adduct (**4c**) [25% based on (**19c**)], and the sulphoximide (**20c**) (40%). Sulphoximide formation was essentially irreversible under the standard conditions since heating (**20a**) with thebaine in DMSO at 130 °C gave no detectable amounts of (**4a**). These experiments strongly suggest that nitrosoformates are indeed formed during the decomposition of azidoformates in DMSO. It appears that alkoxycarbonylnitrenes attack the solvent either on sulphur to give sulphoximides (major pathway) or on oxygen to give nitrosoformates (minor pathway). However, we have, at best, accounted in this way for only 68% of the azide consumed; it is possible that the alkoxycarbonylnitrenes decompose also by a route not involving initial attack on the solvent.

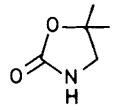
We showed earlier[1c] that *C*-nitrosocarbonyl compounds (**21**), generated by dissociation of their adducts with 9,10-dimethylanthracene (DMA), react with triphenylphosphine and other phosphorus(III) compounds to form isocyanates by deoxygenation with rearrangement (Scheme 4). In contrast, we find that the nitrosoformates (**22**) undergo deoxygenation to give, apparently, alkoxycarbonylnitrenes (**23**), an outcome no doubt reflecting the small migratory tendency of alkoxy groups. The adduct (**10a**) of DMA and benzyl nitrosoformate was largely unchanged by prolonged (24 h) heating in benzene at 80 °C, conditions which lead to the complete decomposition of the corresponding adducts of nitrosocarbonyl-methane and -benzene. However, when (**10a**) was heated in benzene at 60 °C in the presence of triphenylphosphine (1 mol equiv.), decomposition ensued with the formation of triphenylphosphine oxide and DMA. First-order kinetics were observed, as before, for the release of DMA and the rate constant, $k = 4.5 \times 10^{-4}$ s^{-1}, was similar to that measured for the reaction of (**10a**) with thebaine. Furthermore, the reaction of (**10a**) with an excess (2 mol equiv.) of triphenylphosphine proceeded at essentially the same rate, $k = 4.2 \times 10^{-4}$ s^{-1}. Equimolar amounts of (**10a**) and triphenylphosphine were heated in benzene under reflux for 2 h and the products separated chromatographically. The major product (22—32% yield from several experiments), apart from DMA and triphenylphosphine oxide, was *N*-benzyloxycarbonylazepine (**24a**), which was obtained as an unstable, yellow oil and identified by comparison of its ^1H n.m.r. spectrum with that published[10] for (**24**; R = Et). The product (**24a**) is that expected from attack of benzyloxycarbonylnitrene (**23a**) on the solvent, benzene. In agreement with this, heating benzyl azidoformate in benzene at 120 °C gave the same product (**24a**), in similar yield (30%). The azepine (**24a**) was still formed in substantial amounts (25%) from (**10a**) in benzene in the presence of an excess (2 mol equiv.) of triphenylphosphine. Surprisingly, the nitrene (**23a**) must attack the solvent, to give (**24a**), faster than it attacks the phosphine, which gives the phosphine imide (**25**). Similarly, heating the cyclopentadiene adduct (**6a**) in benzene with triphenylphosphine gave the azepine (**24a**) (19%). In an attempt to discover the fate of benzyloxycarbonylnitrene * when formed in an inert solvent, the adduct (**6a**) was heated with triphenylphosphine at 80 °C in dichloromethane. However, the reaction mixture was complex and the only identifiable product, apart from triphenylphosphine oxide, was the phosphine imide (**25**) (2%). The adduct (**6c**) likewise decomposed in benzene in the presence of triphenylphosphine to give small amounts of *N*-t-butoxycarbonylazepine[11] (**24c**) and the oxazolidinone (**26**), a known[12] cyclisation product of t-butoxycarbonylnitrene. When the reaction was carried out in dichloromethane the product mixture was still complex but again contained the oxazolidone (**26**). It appears therefore that nitrosoformates are deoxygenated according to Scheme 4, although competing reactions detract from the preparative value of this new route to alkoxycarbonylnitrenes.



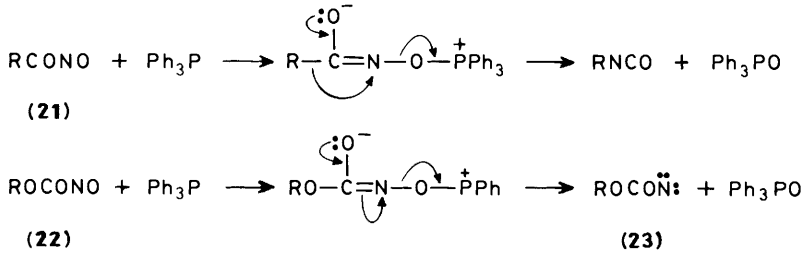
(**24**)

$Ph_3P{=}NCO_2CH_2Ph$

(**25**)



(**26**)



Scheme 4.

The foregoing experiments provide compelling evidence for the independent, if fleeting, existence of nitrosoformate esters formed by (i) oxidation of hydroxamic derivatives, (ii) dissociation of the cycloadducts (**6**) and (**10**), and (iii) oxidation of nitrenes with dimethyl sulphoxide. The use of trichloroethyl nitrosoformate in the synthesis of 14-aminocodeinone will be described in the following paper.[13] An elegant application of benzyl nitrosoformate in the synthesis of tabtoxin has recently been recorded by Baldwin *et al.*[14]

* For a discussion of the unimolecular cyclisation of benzyloxycarbonylnitrene see O. Meth-Cohn, *Heterocycles*, 1980, **14**, 1497.

Experimental

M.p.s were determined with a Kofler hot-stage apparatus. Unless otherwise stated, n.m.r. spectra were recorded for $CDCl_3$ solutions and i.r. spectra for KBr discs. Molecular ion peaks of trichloro derivatives are reported only for the [$^{35}Cl_3$] species. Light petroleum refers to the fraction b.p. 60—80 °C. Tetraethylammonium periodate was prepared by the published method;[15] but see note of **CAUTION** in ref. 1*b*.

2,2,2-*Trichloroethyl* N-*Hydroxycarbamate* (**1b**).—2,2,2-Trichloroethyl chloroformate (4.24 g, 20 mmol) was added dropwise during 10 min with vigorous stirring and cooling in ice to hydroxylamine hydrochloride (6.95 g, 100 mmol) and sodium hydroxide (4.8 g, 120 mmol) in water (80 ml). The mixture was shaken at room temperature for 1 h and then acidified with hydrochloric acid (to pH 5) and extracted with ether (10 × 80 ml). The extracts were washed with brine, dried ($MgSO_4$), and evaporated to afford the *title compound* (**1b**) (3.08 g, 74%), m.p. 87—89 °C (from benzene–light petroleum) (Found: C, 17.5; H, 2.0; Cl, 50.6; N, 7.0. $C_3H_4Cl_3NO_3$ requires C, 17.3; H, 1.9; Cl, 51.1; N, 6.7%); $\nu_{max.}$ 3 350, 3 250, and 1 715 cm^{-1}; δ 4.83 (s, CH_2), and 6.0 and 8.4 (2 × br s, OH and NH, exch. with D_2O); *m/z* 207. The yield of (**1b**) was generally less for larger scale preparations.

2-(*Toluene-4-sulphonyl*)*ethyl* N-*Hydroxycarbamate* (**1d**).—2-(Toluene-4-sulphonyl)ethyl chloroformate[5] (70 mmol) was dissolved in dry methanol (30 ml) and immediately added dropwise with stirring during 5 min to an ice-cooled solution of hydroxylamine (100 mmol) in methanol (150 ml). The mixture was kept at room temperature for 16 h and then diluted with acetone (25 ml) and evaporated. 2-(*Toluene-4-sulphonyl*)*ethyl* N-*hydroxycarbamate* (**1d**) (6.1 g, 60%) had m.p. 123—126 °C (from ethanol) (Found: C, 46.1; H, 5.1; N, 5.65; S, 12.0. $C_{10}H_{13}NO_5S$ requires C, 46.3; H, 5.0; N, 5.4; S, 12.4%); $\nu_{max.}$ 3 405, 3 295, and 1 715 cm^{-1}; δ[$(CD_3)_2CO$] 2.44 (s, Me), 3.53 (t, *J* 7 Hz, SO_2CH_2), 4.36 (t, *J* 7 Hz, OCH_2), 7.47 (2 H, d, *J* 8 Hz, ArH), 7.83 (2 H, d, *J* 8 Hz, ArH), and 9.72 (br s, NH and OH, exch. with D_2O); *m/z* 259.

Preparation of Cycloadducts: General Methods.—Cycloadducts were prepared[1b–e] (method a) by addition of the *N*-hydroxycarbamate (**1**) to the appropriate diene and tetraethylammonium periodate in dichloromethane with stirring at 0 °C. Alternatively (method b), the *N*-hydroxycarbamates were added with vigorous stirring to a 2-phase mixture of the diene in ethyl acetate and sodium periodate in 0.5M-aqueous sodium acetate–acetic acid buffer (pH *ca.* 6) at 0 °C. Exceptionally, the adduct (**12a**) of buta-1,3-diene was prepared using tetraethylammonium periodate in nitromethane at −10 °C (method c). Products were isolated by the *tandard methods.*[1b–e] Yields are quoted for purified materials.

Cycloadducts (**4a**, **c**, **d**) *of Thebaine* (**3**).—19-*Benzyloxycarbonyl*-6,14-*dihydro*-6β,14β-*epoxyiminothebaine* (**4a**) (method a, 76%) had m.p. 104—106 °C (from benzene–light petroleum) (Found: C, 67.9; H, 5.9; N, 5.8. $C_{27}H_{28}N_2O_6$ requires C, 68.1; H, 5.9; N, 5.9%); $\nu_{max.}$ 1 716 cm^{-1}; δ 2.44 (s, NMe), 3.49 (s, 6-OMe), 3.80 (s, 3-OMe), 4.51 (d, *J* 7 Hz, 9-H), 4.57 (s, 5-H), 5.14 (ABq, *J* 12 Hz, PhCH_2), 6.02, (s, 7- and 8-H), 6.63 (ABq, *J* 8 Hz, 1- and 2-H), and 7.31 (br s, Ph); *m/z* 476. 19-*t-Butoxycarbonyl*-6,14-*dihydro*-6β,14β-*epoxyiminothebaine* (**4c**) (method a, 74%) was obtained as a foam (Found: C, 65.1; H, 6.9; N, 6.1. $C_{24}H_{30}N_2O_6$ requires C 65.1; H, 6.8; N, 6.3%); $\nu_{max.}$ (thin film) 1 710 cm^{-1}; δ 1.43 (s, Bu^t), 2.46 (s, NMe), 3.59 (s, 6-OMe), 3.80 (s, 3-OMe), 4.48 (d, *J* 7 Hz, 9-H), 4.52 (s, 5-H), 5.97 and 6.11 (ABq, *J* 8.5 Hz, 8- and 7-H), and 6.56 and 6.70 (ABq, *J* 8 Hz, 1-and 2-H); *m/z* 442. [19-2-(Toluene-4-sulphonyl)ethoxycarbonyl]-6,14-dihydro-6β,14β-epoxyiminothebaine (**4d**) (method a, 72%) was obtained as a glass showing no molecular ion peak in its mass spectrum; $\nu_{max.}$ ($CHCl_3$) 1 713 cm^{-1}; δ 2.40 and 2.41 (2 × s, NMe and ArMe), 3.39 (t, *J* 6.5 Hz, CH_2SO_2), 3.54 (s, 6-OMe), 3.77 (s, 3-OMe), 4.38 (t, *J* 6.5 Hz, CH_2O), 4.50 (s, 5-H), 4.51 (d, *J* 7 Hz, 9-H), 6.08 (s, 7- and 8-H), 6.60 and 6.66 (ABq, *J* 8 Hz, 1- and 2-H), 7.34 (2H, d, *J* 8 Hz, ArH), and 7.76 (2 H, d, *J* 8 Hz, ArH).

Cycloadducts (**6a**—**c**) *of Cyclopentadiene* (**5**).—3-*Benzyloxycarbonyl*-2-*oxa*-3-*azabicyclo*[2.2.1]*hept*-5-*ene* (**6a**) (methods a and b, 71%) had m.p. 33—36 °C (from light petroleum) (Found: C, 67.45; H, 5.8; N, 6.0%; *m/z* 231.0897. $C_{13}H_{13}NO_3$ requires C, 67.5; H, 5.6; N, 6.1%; M^+, 231.0897); $\nu_{max.}$ 1 706 and 1 742 cm^{-1}; δ 1.67 and 1.93 (2 × dm, *J* 9 Hz, 7-CH_2), 5.00 and 5.20 (2 × m, 1- and 4-H), 5.11 (s, PhCH_2), 6.33 (m, 5- and 6-H), and 7.30 (s, Ph). 3-(2,2,2-*Trichloroethoxycarbonyl*)-2-*oxa*-3-*azabicyclo*[2.2.1]*hept*-5-*ene* (**6b**) (method b, 70%) had m.p. 86—87.5 °C (from ethyl acetate) (Found: C, 34.9; H, 2.8; N, 4.9. $C_8H_8Cl_3NO_3$ requires C, 35.2; H, 2.9; N, 5.1%); $\nu_{max.}$ 1 710 cm^{-1}; δ 1.82 and 2.05 (2 × dm, *J* 9 Hz, 7-CH_2), 4.62 and 4.82 (ABq, *J* 11 Hz, OCH_2), 5.08 and 5.36 (2 × m, 1- and 4-H), and 6.45 (m, 5- and 6-H). 3-*t-Butoxycarbonyl*-2-*oxa*-3-*azabicyclo*[2.2.1]*hept*-5-*ene* (**6c**) (method b, 70%) had m.p. 45.5 °C (from light petroleum) (Found: C, 61.0; H, 7.7; N, 7.2. $C_{10}H_{15}NO_3$ requires C, 60.9; H, 7.6; N, 7.1%); $\nu_{max.}$ 1 740 cm^{-1}; δ 1.45 (s, Bu^t), 1.68 and 1.98 (2 × dm, *J* 9 Hz, 7-CH_2), 4.97 and 5.23 (2 × m, 1- and 4-H), and 6.39 (m, 5- and 6-H).

Cycloadducts (**8a**) and (**8b**) *of Ergosteryl Acetate* (**7**).—N-*Benzyloxycarbonyl*-5,8-*dihydro*-8α,5α-*epoxyiminoergosteryl acetate* (**8a**) (method a, 80%) had m.p. 141—143 °C (from methanol) (Found: C, 75.3; H, 8.9; N, 2.5. $C_{38}H_{53}NO_5$ requires C, 75.6; H, 8.8; N, 2.3%); $\nu_{max.}$ 1 738 and 1 712 cm^{-1}; δ 2.01 (s, Ac), 3.32 (dd, *J* 14 and 5 Hz, 4α-H), 4.96 and 5.16 (ABq, *J* 13 Hz, PhCH_2), 5.17 (m, 22- and 23-H), 5.20 (m, 3-H), 6.22 (s, 6- and 7-H), and 7.25 (s, Ph); *m/z* 438 ($M^+ - C_8H_7NO_3$). N-(2,2,2-*Trichloroethoxycarbonyl*)-5,8-*dihydro*-8α,5α-*epoxyiminoergosteryl acetate* (**8b**) (method a, 86%; method b, 80%) had m.p. 157—159 °C (from methanol or ethyl acetate–light petroleum) (Found: C, 61.6; H, 7.6; Cl, 16.3; N, 2.1. $C_{33}H_{48}Cl_3NO_5$ requires C, 61.5; H, 7.45; Cl, 16.5; N, 2.2%); $\nu_{max.}$ 1 728 cm^{-1}; δ 2.02 (s, Ac), 3.35 (dd, *J* 14 and 5 Hz, 4α-H), 4.45 and 4.97 (ABq, *J* 13 Hz, OCH_2), 5.12 (m, 22- and 23-H), 5.27 (m, 3-H), and 6.25 (s, 6- and 7-H); *m/z* 438 ($M^+ - C_3H_2Cl_3NO_3$).

Cycloadduct (**10a**) *of* 9,10-*Dimethylanthracene* (**9**).—N-*Benzyloxycarbonyl*-9,10-*dihydro*-9,10-*dimethyl*-9,10-*epoxyiminoanthracene* (**10a**) (method a, 72%) had m.p. 132—134 °C (from ethyl acetate–light petroleum) (Found: C, 77.4; H, 5.7; N, 3.5. $C_{24}H_{21}NO_3$ requires C, 77.6; H, 5.7; N, 3.8%); $\nu_{max.}$ 1 698 cm^{-1}; δ 2.25 and 2.60 (2 × s, Me), 4.98 (s, PhCH_2), and 6.8—7.6 (13 H, m, ArH); *m/z* 206 ($M^+ - C_8H_7NO_3$).

Cycloadduct (**12a**) *of Buta*-1,3-*diene* (**11**).—2-Benzyloxycarbonyl-3,6-dihydro-2*H*-1,2-oxazine (**12a**) (method c, 72%) was obtained as an oil; $\nu_{max.}$ (liquid film) 1 710 cm^{-1}; δ 4.08 (m, CH_2), 4.32 (m, CH_2), 5.18 (s, PhCH_2), 5.75 (2 H, s, vinyl-H), and 7.31 (s, Ph).

Cycloadducts (**14b**) *and* (**14**; RO = Ph) *of* 2,3-*Dimethylbuta*-1,3-*diene* (**13**).—2-(2,2,2-*Trichloroethoxycarbonyl*)-3,6-*dihydro*-4,5-*dimethyl*-2H-1,2-*oxazine* (**14b**) (method b, 59%) had b.p. 140 °C (0.2 mm Hg) (Found: C, 37.2; H, 4.3; Cl, 36.8. $C_9H_{12}Cl_3NO_3$ requires C, 37.4; H, 4.2; Cl, 36.9%); $\nu_{max.}$ (liquid film) 1 725 cm^{-1}; δ 1.66 (br s, 2 × Me), 4.08 and 4.34 (2 × br s, 2 × CH_2), and 4.88 (s, OCH_2); *m/z* 287. 2-*Benzoyl*-3,6-*dihydro*-4,5-*dimethyl*-2H-1,2-*oxazine* (**14**; RO = Ph) (method b, 89%) had m.p. 62—65 °C (from benzene—light petroleum) (Found:

C, 71.6; H, 6.9; N, 6.8. $C_{13}H_{15}NO_2$ requires C, 71.9; H, 6.9; N, 6.5%); $\nu_{max.}$ (liquid film) 1 649 cm^{-1}; δ 1.60 and 1.75 (2 × br s, 2 × Me), 4.16 (br s, OCH_2 and NCH_2), and 7.2—7.8 (m, Ph); *m/z* 217.

Cycloadduct (**16b**) *of the Bicyclohexenyl*[16] (**15**).—The *cycloadduct* (**16b**) (method b, 61%) had m.p. 88—90 °C (from benzene–light petroleum) (Found: C, 48.8; H, 5.6; Cl, 28.5; N, 3.7. $C_{15}H_{20}Cl_3NO_3$ requires C, 48.8; H, 5.6; Cl, 28.9; N, 3.8%); $\nu_{max.}$ 1 705 cm^{-1}; δ 1.0—3.1 (16 H, m), 4.46 (m, NCH and OCH), and 4.70 and 4.96 (ABq, *J* 12 Hz, OCH_2); *m/z* 367.

Cleavage of the Cycloadduct (**12a**) *with Hydrogen Bromide.*—The oily adduct (**12a**) (1 mmol) was treated with hydrogen bromide in acetic acid (48% w/v, 0.33 ml) at room temperature. After 45 min, evolution of carbon dioxide had ceased and the solution was then diluted with methanol (5 ml) then dry ether (100 ml). 3,6-*Dihydro*-2H-1,2-*oxazine hydrobromide* crystallised from the mixture as needles (65%), m.p. 132—134 °C (Found: C, 28.7; H, 4.9; N, 8.8; Br, 48.6. C_4H_8BrNO requires C, 28.9; H, 4.8; N, 8.4; Br, 48.2%).

Cleavage of the Cycloadduct (**4c**) *with Methanolic Hydrogen Chloride.*—Hydrogen chloride was passed into methanol (2 ml) containing the adduct (**4c**) (1 mmol), at room temperature without any precautions to exclude moisture, until the solution was saturated. The solution was diluted with ether to afford 14β-hydroxyaminocodeinone (**17**) hydrochloride (90%), identified by spectroscopic comparison with a reference sample.[4]

Cleavage of the Cycloadduct (**4d**) *with Base.*—The adduct (**4d**) (0.1 mmol) was treated with 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) (0.1 mol) in benzene at room temperature. After 1 h, DBN (0.2 mmol) was added and after a further 30 min the solution was evaporated. The residue was chromatographed on silica plates, developed with chloroform–methanol (95:5), to give thebaine (**3**) (39%) and an unstable oil (56%) identified spectroscopically as the epoxyimino derivative (**18**); δ 3.41 (s, NMe), 3.54 (s, 6-OMe), 3.81 (s, 3-OMe), 6.60 (s, 5-H), 5.90 and 6.06 (ABq, *J* 9 Hz, 8- and 7-H), and 6.59 and 6.63 (ABq, 1- and 2-H). Attempts to crystallise this product led to its conversion into thebaine (**3**). The foregoing cleavage of (**4d**) was repeated and the reaction mixture, in benzene, was stirred with 10% hydrochloric acid (2 ml) for 15 min. The mixture was treated with an excess of sodium hydrogen carbonate and water (15 ml) and then extracted with dichloromethane. The extract was evaporated and the residue treated with methanolic hydrogen chloride and ether, as before, to give 14β-hydroxyaminocodeinone (**17**) hydrochloride[4] (71%).

Cleavage of the Cycloadduct (**8b**) *with Zinc.*—The adduct (**8b**) (161 mg) was treated in acetic acid (5 ml) with zinc powder (130 mg) for 2 h at room temperature. The organic products were isolated in the usual way and chromatographed on silica plates to give ergosteryl acetate (**7**) (81%).

Thermal Transfer of Benzyl Nitrosoformate from (**10a**) *to Thebaine.*—The adduct (**10a**) (0.28 mmol) and thebaine (**3**) (0.33 mmol) were heated in benzene (5 ml) under reflux for 5 h under nitrogen. Chromatography of the mixture on silica plates developed with chloroform gave the adduct (**4a**) of thebaine (100%). Kinetic measurements were conducted as before[1b,c] in benzene at 60 °C, the release of 9,10-dimethylanthracene being monitored spectrometrically (absorption at 385 nm). Essentially the same value for the rate constant, $k = 4.3 \times 10^{-4}$ s^{-1}, was obtained using the adduct (**10a**) with 1 or 2 mol equiv. of thebaine.

Thermal Transfer of Trichloroethyl Nitrosoformate from (**6b**) *to Ergosteryl Acetate* (**7**) *and the Bicyclohexenyl* (**15**).—The adduct (**6b**) (0.2 mmol) and ergosteryl acetate (**7**) (0.2 mmol) were heated under reflux in benzene (10 ml). Benzene was allowed to distil out slowly and was replenished from time to time. The reaction was complete (t.l.c. control) in 8 h. Evaporation of the mixture gave the crystalline adduct (**8b**) (96%) directly. Similarly, (**6b**) (0.33 mmol) and the bicyclohexenyl (**15**) (0.33 mmol) gave, after 4 days heating, the adduct (**16b**) as a brown oil. Crystallisation from ethyl acetate–pentane gave pure material (49%). Repetition of this experiment, using toluene in place of benzene and a slow stream of nitrogen to assist removal of cyclopentadiene, gave (**16b**) (60%).

Thermolysis of Benzyl Azidoformate in Dimethyl Sulphoxide.—Benzyl azidoformate[9] (**19a**) (1.0 g) was heated in dimethyl sulphoxide (10 ml) at 130 °C for 2 h. The mixture was diluted with water (100 ml) and extracted with chloroform (2 × 50 ml). The combined extracts were dried (Na_2SO_4) and evaporated. Crystallisation of the residue afforded N-*benzyloxycarbonyl*-S,S-*dimethylsulphoximide* (**20a**) (50—60% yield from several experiments) as flakes, m.p. 100—101 °C (from ethyl acetate–light petroleum) (Found C, 53.0; H, 5.7; N, 5.8. $C_{10}H_{13}NO_3S$ requires, C, 52.9; H, 5.7; N, 6.1%); $\nu_{max.}$ 1 655 cm^{-1}; δ 3.30 (s, 2 × Me), 5.15 (s, CH_2), and 7.37 (s, Ph); *m/z* 227. In a separate experiment, the products were extracted with dichloromethane. The extracts were dried and the solvent was distilled off through a short fractionating column. The residue was shown to contain benzaldehyde by g.l.c. (15% yield) and by formation of the corresponding 2,4-dinitrophenylhydrazone (14%). The azidoformate (**19a**) (1.8 mmol) and thebaine (**3**) (0.32 mmol) were heated in dimethyl sulphoxide (6 ml) at 130 °C for 5 h. The products were isolated as before and separated on silica plates to give the adduct (**4a**) (66%) of thebaine together with the sulphoximide (**20a**) and benzaldehyde.

Thermolysis of t-Butyl Azidoformate (**19c**) *in Dimethyl Sulphoxide.*—The azidoformate (**19c**) (3.5 mmol) was heated in dimethyl sulphoxide (2 ml) at 115 °C for 2 h. The dark-red mixture was diluted with water (200 ml) and extracted with dichloromethane (4 × 25 ml). The combined extracts were washed with water (5 × 200 ml), dried ($MgSO_4$), and evaporated. The residual oil was chromatographed on silica plates to give N-*t-butoxycarbonyl*-S,S-*dimethylsulphoximide* (**20c**) (58%), m.p. 72—74 °C (from benzene–light petroleum) (Found: C, 43.7; H, 7.9; N, 7.2; S, 16.3. $C_7H_{15}NO_3S$ requires C, 43.5; H, 7.8; N, 7.25; S, 16.7%); $\nu_{max.}$ 1 660 cm^{-1}; δ 1.44 (s, Bu^t) and 3.24 (s, 2 × Me); *m/z* 193. The azidoformate (**19c**) (0.25 mmol) and thebaine (**3**) (0.5 mmol) were heated in dimethyl sulphoxide (2 ml) as before. Chromatography of the products gave the thebaine adduct (**4c**) [25% yield based on (**19c**)], the sulphoximide (**20c**) [40% based on (**19c**)], and thebaine (**3**) (73%). Again, heating (**19c**) (2.5 mmol) and (**3**) (0.5 mmol) in dimethyl sulphoxide gave (**4c**) [84% based on (**3**)], (**20c**) [51% based on (**19c**)], and no detectable amounts of thebaine.

Deoxygenation of Benzyl Nitrosoformate with Triphenylphosphine.—The adduct (**10a**) (0.4 mmol) and triphenylphosphine (0.4 mmol) were heated under reflux in dry benzene (5 ml) for 2 h under nitrogen. The products were chromatographed on silica plates developed with benzene to give, along with triphenylphosphine oxide and 9,10-dimethylanthracene, N-*benzyloxycarbonylazepine* (**24a**) (22—32% in several experiments) as an unstable, yellow oil (Found: *m/z* 227.0944. $C_{14}H_{13}NO_2$ requires M^+, 227.0946); $\nu_{max.}$ (liquid film) 1 715 cm^{-1}; δ 5.22 (s, CH_2), 5.51 (br m, 3- and 6-H), 5.88 (dm, *J* 7 Hz, 2- and 7-H), 6.08 (tm, *J* 3 Hz, 4- and 5-H), and 7.36 (s, Ph). The azepine (**24a**) was also obtained (28—30%) by heating benzyl

azidoformate in benzene in an evacuated, sealed tube at 120 °C for 3 h. Heating (**10a**) (0.4 mmol) with triphenylphosphine (0.8 mmol), as before, gave (**24a**) (25%). The reaction of (**10a**) with triphenylphosphine (1 and 2 mol equiv.) proceeded at essentially the same rate ($k = 4.2 \times 10^{-4}$ s^{-1}) at 60 °C in benzene as did that of (**10a**) with thebaine (**3**). Similarly, the cyclopentadiene adduct (**6a**) (2.19 mmol) and triphenylphosphine (2.41 mmol) were heated under reflux in benzene (100 ml) for 1.75 h. The solution was evaporated and the brown residue chromatographed on a short, silica column. Elution with hexane–ethyl acetate (9:1) gave triphenylphosphine (0.27 mmol) and then a yellow fraction which was rechromatographed to afford the azepine (**24a**) (19%). The adduct (**6a**) (0.66 mmol) and triphenylphosphine (1.32 mmol) were heated in dichloromethane (5 ml) in a sealed tube at 80 °C for 1 h to give a complex mixture of products. Repeated layer chromatography gave the phosphine imide (**25**) (5 mg) which was identified by comparison with a sample prepared as follows. Benzyl azidoformate (**19c**) (1 mmol) in light petroleum (5 ml) was added slowly to triphenylphosphine (1 mmol) in light petroleum (5 ml). After 30 min at room temperature the solution was evaporated to give *triphenylphosphine benzyloxycarbonylimide* (**25**) (100%), m.p. 108—109 °C (Found: C, 75.6; H, 5.3; N, 3.4. $C_{26}H_{22}NO_2P$ requires C, 75.9; H, 5.35; N, 3.4%); $\nu_{max.}$ 1 642 cm^{-1}; δ 5.05 (s, CH_2), 7.25 (s, Ph), and 7.30—7.90 (m, Ph_3P); *m/z* 411.

Deoxygenation of t-Butyl Nitrosoformate with Triphenylphosphine.—The adduct (**6c**) (1 mmol) and triphenylphosphine (1 mmol) were heated in benzene (50 ml) under reflux for 1.5 h. The mixture was concentrated and diluted with ether to precipitate triphenylphosphine oxide (58%), which was filtered off. The filtrate was evaporated and the residue chromatographed on Florisil (t.l.c. grade). Elution with chloroform containing increasing amounts of ethyl acetate gave, successively, *N*-t-butoxycarbonylazepine[11] (**24c**) (6.6%) as a yellow oil (Found: *m/z* 193.1104. Calc. for $C_{11}H_{15}NO_2$: M^+, 193.1103); δ 1.45 (s, Bu^t), 5.43 (br m, 3- and 6-H), 5.80 (dm, *J* 8 Hz, 2- and 7-H), and 5.99 (tm, *J* 3 Hz, 4- and 5-H), 5,5-dimethyloxazolidin-2-one (**26**) (4%), m.p. 75—80 °C (lit.,[12] 80 °C); δ 1.46 (s, 2 × Me), 3.34 (s, CH_2), and 6.14 (br s, NH, exch. with D_2O) (lit., 1.45, 3.35, and 6.87); *m/z* 115, and triphenylphosphine oxide (19%). The adduct (**6c**) (2 mmol) and triphenylphosphine (2.2 mmol) were heated in a sealed tube in dichloromethane (6 ml) at 82 °C for 1 h. Triphenylphosphine oxide was precipitated as before and the residue chromatographed on silica plates developed with ether. The component with R_f *ca.* 0.1 was rechromatographed to give the oxazolidinone (**26**) (2%).

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