C-Nitrosoformamides, a New Class of Transient Dienophiles Formed by Oxidation of *N*-Hydroxyureas

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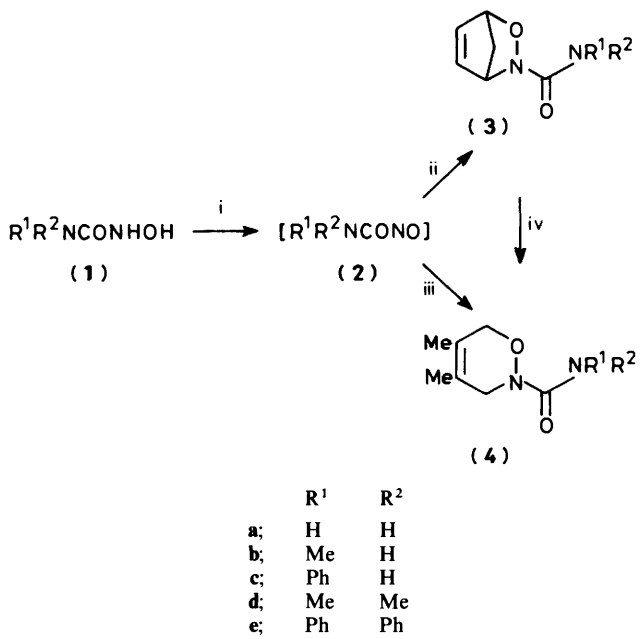
Oxidation of hydroxyurea with sodium or tetraethylammonium periodate in the presence of cyclopentadiene gave a cycloadduct (**3a**) formed, apparently, by capture of the transient dienophile, *C*-nitrosoformamide. *N*-Methyl-, *N*-phenyl-, *N,N*-dimethyl-, and *N,N*-diphenyl-*C*-nitrosoformamide were likewise trapped as their cycloadducts with cyclopentadiene. Cycloadducts of 2,3-dimethylbuta-1,3-diene, thebaine, ergosteryl acetate, and 9,10-dimethylanthracene (DMA) were prepared similarly. The cyclopentadiene adducts (**3**) dissociated at 80 °C in the presence of 2,3-dimethylbuta-1,3-diene to give the corresponding adducts (**4**) of the nitrosoformamides and dimethylbutadiene. Unexpectedly, the 1,4-adducts (**4**) were accompanied by substantial amounts of hydroxamic acids (**5**) arising from 'ene' reactions of the nitrosoformamides and dimethylbutadiene. The cyclopentadiene adducts of *N,N*-dimethyl- and *N,N*-diphenyl-*C*-nitrosoformamide, when heated alone, decomposed to give the corresponding carbamic anhydrides. The cycloadduct (**15**) of DMA and *C*-nitrosoformamide dissociated at 40 °C in the presence of thebaine (**11**) to give the thebaine adduct (**12**; R = H) and DMA.

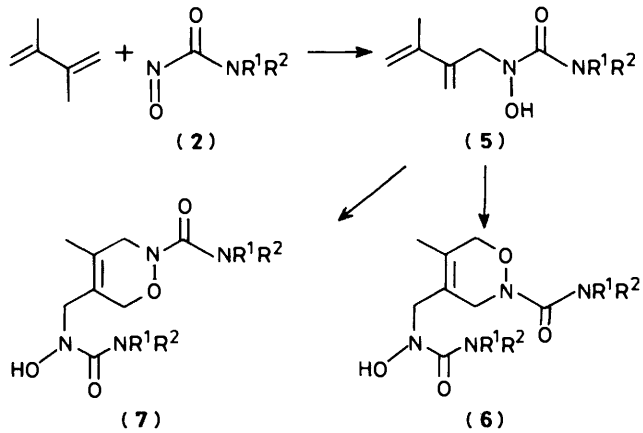
We have presented evidence that oxidation of the hydroxamic acids RCONHOH[1] and ROCONHOH[2] produces transient nitrosocarbonyl compounds, RCONO and ROCONO, which may be trapped *in situ* as their cycloadducts with conjugated dienes. Further, we reported[3] preliminary experiments indicating that oxidation of *N*-hydroxyureas (**1**) similarly forms transient *C*-nitrosoformamides (**2**). We describe here a wider study of this new class of reactive nitrosocarbonyl compounds.

Hydroxyurea (**1a**), the mono- and di-methyl derivatives (**1b**) and (**1d**), and the mono- and di-phenyl derivatives (**1c**) and (**1e**), were each oxidised in the presence of cyclopentadiene to give the corresponding cycloadducts (**3**) (Scheme 1). Similarly, oxidation of the *N*-hydroxyureas in the presence of 2,3-dimethylbuta-1,3-diene gave the set of cycloadducts (**4**). As usual, the oxidations were carried out at 0 °C using sodium or tetraethylammonium periodate. Minor variations on the standard conditions were made to take account of the different solubilities of the *N*-hydroxyureas. The structures of the products were readily established spectroscopically by comparison with the corresponding cycloadducts of *C*-nitrosocarbonyl compounds[1] and nitrosoformate esters.[2]



Scheme 1. *Reagents:* i, $NaIO_4$ or Et_4NIO_4, 0 °C; ii, cyclopentadiene; iii, 2,3-dimethylbuta-1,3-diene; iv, an excess of 2,3-dimethylbuta-1,3-diene, 80 °C.

The cycloadducts of cyclopentadiene with *C*-nitrosocarbonyl compounds, RCONO,[1c] and nitrosoformate esters, ROCONO,[2] dissociate at 80 °C, thereby serving as convenient auxiliary sources of the transient nitroso compounds. The cycloadducts (**3**) behaved similarly (Scheme 1). Each adduct (**3**) was heated under reflux in benzene or ethyl acetate with an excess of 2,3-dimethylbuta-1,3-diene to give the corresponding dihydrooxazine (**4**). However, in every case the expected, major product (**4**) was accompanied by a hydroxamic acid (**5**), arising (Scheme 2) from an 'ene' reaction of the diene and the nitrosoformamide.



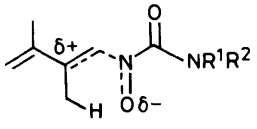
Scheme 2.

For example, the monomethyl adduct (**3b**) and dimethylbutadiene (10 mol equiv.) reacted at 80 °C during 2 h to give the

dihydro-oxazine (**4b**) (71%) and the 'ene' reaction product (**5b**) (22%). Similarly, the monophenyl adduct (**3c**) gave the corresponding dihydro-oxazine (**4c**) (75%) and the 'ene' reaction product (**5c**) (20%). When the cyclopentadiene adducts (**3**) were heated with equimolar amounts of dimethylbutadiene, the reaction mixtures were more complex. In several experiments, a third product was isolated and judged spectroscopically to have structure (**6**) or (**7**) arising, as expected, from 1,4-cycloaddition of the nitrosoformamide (**2**) with the newly-formed diene (**5**). Very likely, the 'ene' reaction products (**5**) are also produced when the hydroxyureas (**1**) are oxidised in the presence of dimethylbutadiene. However, since the products (**5**) are hydroxamic acids, they also would be oxidised and therefore not survive the reaction conditions.

It was clear from our earlier studies, and from those by Keck *et al.*,[4] that nitrosocarbonyl compounds react much more rapidly with conjugated dienes, to give 1,4-adducts, than with mono-olefins, to give 'ene' reaction products. The foregoing reactions of the nitrosoformamides (**2**) with dimethylbutadiene were therefore surprising in that 1,4-cycloaddition occurred only 3—4 times faster than the 'ene' reaction. However, it is possible that dimethylbutadiene is more reactive in the 'ene' reaction than a typical mono-olefin, especially in response to attack by a highly electrophilic heterodienophile. If the transition state for a concerted 'ene' reaction is polarised as shown in structure (**8**), with C–N bond formation leading hydrogen transfer,[4] then the positive charge developing on the 'ene' component will be stabilised by the other double bond, and the 'ene' reaction will be correspondingly favoured. Meth-Cohn and van Vuuren have recently reported[5] that thionitroso carbonyl compounds show even less periselectivity in their reactions with 2,3-dimethylbuta-1,3-diene. For example, phenyl thionitrosoformate, PhOCONS, gave approximately equal amounts of a 1,4-adduct and an 'ene' reaction product, although in this case the 'ene' reaction occurred with C–S rather than C–N bond formation. It is not possible to measure directly the rates of pericyclic reactions of any of these transient species, but competition experiments using 2,3-dimethylbuta-1,3-diene and for example, 2-methylbut-1-ene or 2-phenylpropene, should be informative.

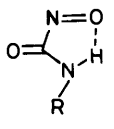
The various cyclopentadiene adducts (**3**) reacted with dimethylbutadiene at qualitatively similar rates. However, when heated alone, the adducts showed markedly different stabilities dependent upon the degree of substitution on nitrogen. The *N*,*N*-dimethyl derivative (**3d**) was the least stable



(**8**)

$(R^1R^2NCO)_2O$

(**9**)

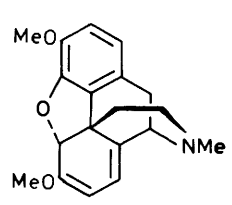


(**10**)

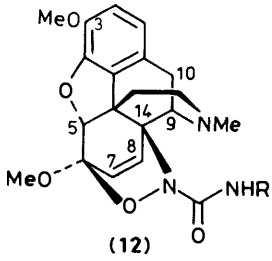
of the series; indeed, partial decomposition was observed upon prolonged storage at room temperature. Decomposition was complete within 2 h in benzene at 80 °C, giving the carbamic anhydride (**9d**), which was identified by comparison with material prepared from *N*,*N*-dimethylcarbamoyl chloride. Similarly, the *N*,*N*-diphenyl derivative (**3e**) decomposed to give the corresponding anhydride (**9e**). The formation of anhydrides supports the view that the cycloadducts (**3**) dissociate to release the transient nitrosoformamides (**2**), since we had earlier found that the cycloadduct of nitrosocarbonylbenzene and 9,10-dimethylanthracene decomposed thermally to give benzoic anhydride.[1c] In contrast, the unsubstituted cycloadduct (**3a**) was stable to heating under reflux in ethyl acetate for 2 h, conditions adequate to effect complete transfer of *C*-nitroso-formamide (**2a**) from the adduct (**3a**) to dimethylbutadiene. Even after 5 h of heating, very little decomposition was observed. The mono-substituted cycloadducts (**3b**) and (**3c**) were likewise stable at 80 °C for 2 h.

That the cycloadducts (**3**) react with dimethylbutadiene at qualitatively similar rates suggests, not unexpectedly, that their rates of dissociation are little influenced by the nature or number of substituents on nitrogen. If this is so, then the markedly different behaviour of the adducts when heated alone indicates that the derived nitrosoformamides (**2**) must differ significantly in either their rates of decomposition, or of reaction with cyclopentadiene, or both. For example, if the parent nitrosoformamide (**2a**) decomposes more slowly, or recombines with cyclopentadiene more rapidly, than the *N*,*N*-dimethyl derivative (**2d**), then the adduct (**3a**) will be more stable to heating than (**3d**), as observed. Intramolecular hydrogen-bonding, as shown in structure (**10**), in the nitrosoformamides (**2a—c**) might result in an increased stability relative to that of the disubstituted derivatives (**2d—e**), and thus account for the greater stability of the cycloadducts (**3a—c**). Alternatively, hydrogen-bonding might increase the dienophilic character of the nitroso compounds, just as Lewis acids increase that of carbonyl compounds, and thereby accelerate recombination with cyclopentadiene. For these reasons, the synthesis of nitrosocarbonyl compounds able to form six-membered, cyclic hydrogen-bonds, for example using chiral α-hydroxy- or α-amino-acids, should be profitable.

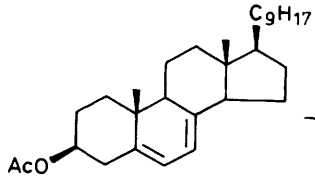
Two unsymmetrical dienes, thebaine (**11**) and ergosteryl acetate (**13**), were chosen to compare the regioselectivity of the



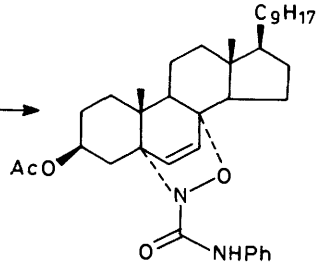
(**11**)



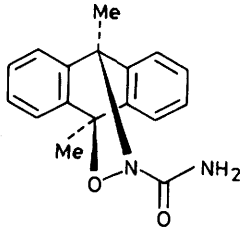
(**12**)



(**13**)



(**14**)



(**15**)

C-nitrosoformamides with that of other *C*-nitroso compounds. Oxidation of hydroxyurea (**1a**) in the presence of thebaine gave, in good yield, a single cycloadduct, which was assigned the structure (**12**; R = H) by spectroscopic comparison with material prepared earlier[6] by hydrolysis of the cycloadduct of thebaine and nitrosyl cyanide. Similarly, thebaine and *N*-phenyl-*C*-nitrosoformamide (**2c**) gave the corresponding adduct (**12**; R = Ph). The reactions of thebaine with the other nitrosoformamides were not examined, but it appears clear that these reactive intermediates behave like other classes of *C*-nitroso-compounds[1,2,6,7] in adding to thebaine with attachment of nitrogen at C(14). In contrast, ergosteryl acetate (**13**) forms two well-characterised series of 1,4-adducts with *C*-nitroso-compounds.[1d,8b] However, oxidation of *N*-hydroxy-*N'*-phenylurea (**1c**) in the presence of ergosteryl acetate gave only one detectable adduct. The structure (**14**) was assigned on the basis of a characteristically low-field signal, δ 3.50 (dd, *J* 14 and 5 Hz), in its ^{1}H n.m.r. spectrum, attributable[1d] to 4α-H. In this respect, *N*-phenyl-*C*-nitrosoformamide (**2c**) behaves like nitrosoformate esters[2] and nitrosocarbonylmethane.[1d]

We had earlier demonstrated[1,2,8] the value of cycloadducts of 9,10-dimethylanthracene [as (**15**)] in studies on the chemistry of labile *C*-nitroso-compounds. The corresponding adduct (**15**) of *C*-nitrosoformamide was prepared, in the usual way, and found to be stable to the normal operations of chromatography and crystallisation. However, it was less stable than the corresponding adduct (**3a**) of cyclopentadiene and underwent complete decomposition in benzene at 80 °C during 15 min. When the adduct (**15**) was heated in benzene in the presence of thebaine (**11**), transfer of *C*-nitrosoformamide occurred to give the adduct (**12**; R = H) of thebaine together with 9,10-dimethylanthracene (DMA). This reaction was studied kinetically, as described before for other adducts of DMA. First-order kinetics, $k = 9.1 \times 10^{-5}$ s^{-1} at 40 °C, were observed for the release of DMA (absorption at 378 nm), consistent with slow dissociation of the adduct (**15**) followed by rapid capture of *C*-nitrosoformamide by thebaine. Thus, the adduct (**15**) dissociates more rapidly at 40 °C than does the corresponding adduct of nitrosocarbonylmethane (MeCONO)[1a] at 60 °C, $k = 4.7 \times 10^{-5}$ s^{-1}. It appears therefore that cycloadducts of DMA will serve as convenient, 'clean' precursors of *C*-nitrosoformamide and, presumably, its *N*-substituted derivatives, under exceptionally mild conditions.

The value of *C*-nitrosocarbonyl compounds and nitrosoformate esters in the synthesis of complex, nitrogen-containing, natural products has been demonstrated by several research groups.[4,9] The present survey of the chemistry of *C*-nitrosoformamides indicates that these reactive intermediates also should find applications in synthesis. Hydroxyureas generally are readily prepared from primary and secondary amines *via* the corresponding carbamoyl chlorides; the nitrosoformamides derived from unsaturated amines should provide, *via* intramolecular diene and 'ene'[10] reactions, routes to a variety of heterocyclic products.

Experimental

M.p.s were determined with a Kofler hot-stage apparatus. Except where otherwise stated, i.r. spectra were recorded for KBr discs, and n.m.r. spectra for deuteriochloroform solutions, with tetramethylsilane as internal standard, at 90 MHz for ^{1}H and 25.2 MHz for ^{13}C. Mass spectra were obtained by electron impact with an ionising voltage of 70 eV. Light petroleum refers to the fraction b.p. 40—60 °C.

Synthesis of Cycloadducts of the C-*Nitrosoformamides* (**2**): *General Methods.*—The hydroxyureas (**1**) were oxidised with either sodium or tetraethylammonium periodate in the presence of the appropriate diene. The preparation of only one cycloadduct of each diene is described in detail, as follows, to illustrate typical procedures and the range of solvents which may be employed.

Cycloadducts (**3**) *of Cyclopentadiene.*—*N*-Hydroxy-*N'*-phenylurea[11] (**1c**) (254 mg, 1.67 mmol) in ethanol (12.5 ml) was added dropwise with stirring to cyclopentadiene (1.52 ml, 1.84 mmol) in ethanol (62.5 ml) containing tetraethylammonium periodate (590 mg, 1.84 mmol) during 10 min at 0 °C. After a further 30 min, the mixture was evaporated and the residue was dissolved in dichloromethane (50 ml) and washed with aqueous sodium thiosulphate and then with water. The solution was dried (Na_2SO_4) and evaporated, and the residue was chromatographed on a short, silica column. Elution with chloroform gave 3-(N-*phenylcarbamoyl*)-2-*oxa*-3-*azabicyclo*-[2.2.1]*hept*-5-*ene* (**3c**) (67%), m.p. 103 °C (from ethyl acetate–light petroleum) (Found: C, 66.7; H, 5.45; N, 13.05. $C_{12}H_{12}N_2O_2$ requires C, 66.65; H, 5.6; N, 12.95%); $\nu_{max.}$ 3 368 and 1 663 cm^{-1}; δ_H 1.79 and 2.00 (ABq, *J* 9 Hz, with fine splitting, 7-CH_2), 5.23 (br s, 1- and 4-H), 6.39 and 6.48 (2 × m, 5-and 6-H), and 6.9—7.6 (m, Ph); *m/z* 216 (M^+). The other cycloadducts (**3**) were characterised as follows: 3-*carbamoyl*-2-*oxa*-3-*azabicyclo*-[2.2.1]*hept*-5-*ene* (**3a**), m.p. 137 °C (decomp.) (from ethyl acetate) (Found: C, 51.2; H, 5.9; N, 20.0. $C_6H_8N_2O_2$ requires C, 51.4; H, 5.75; N, 20.0%); $\nu_{max.}$ 3 435, 3 295, 3 250, 3 182, 1 660, and 1 625 cm^{-1}; δ_H 1.80 and 2.00 (ABq, *J* 9 Hz, with fine splitting, 7-CH_2), 5.20 (m, 1- and 4-H), 5.50 (br s, NH_2, exch. with D_2O), and 6.38 and 6.42 (2 × m, 5- and 6-H); *m/z* 140 (M^+); 3-(N-*methylcarbamoyl*)-2-*oxa*-3-*azabicyclo*[2.2.1]*hept*-5-*ene* (**3b**), m.p. 83 °C (decomp.) (from ethyl acetate–light petroleum) (Found: C, 54.3; H, 6.6; N, 18.2. $C_7H_{10}N_2O_2$ requires C, 54.5; H, 6.5; N, 18.2%); $\nu_{max.}$ 3 375 and 1 658 cm^{-1}; δ_H 1.73 and 1.95 (ABq, *J* 9 Hz, with fine splitting, 7-CH_2), 2.71 (d, *J* 6 Hz, NMe), 5.16 (br s, 1-and 4-H), 5.62 (br s, NH, exch. with D_2O), and 6.36 (m, 5- and 6-H); *m/z* 154 (M^+); 3-(N,N-*dimethylcarbamoyl*)-2-*oxa*-3-*azabicyclo*[2.2.1]*hept*-5-*ene* (**3d**), m.p. *ca.* 30 °C (decomposing upon attempted recrystallisation) (Found: *m/z* 168.0904. $C_8H_{12}N_2O_2$ requires *M*, 168.0898); $\nu_{max.}$(CHCl$_3$) 1 650 cm^{-1}; δ_H 1.74 and 1.94 (ABq, *J* 9 Hz, with fine splitting, 7-CH_2), 2.93 (s, NMe_2), 4.93 and 5.08 (2 × br s, 1-and 4-H), and 6.38 and 6.52 (2 × m, 5-and 6-H): 3-(N,N-*diphenylcarbamoyl*)-2-*oxa*-3-*azabicyclo*[2.2.1]*hept*-5-*ene* (**3e**), m.p. 126—134 °C (decomp.) (from ethyl acetate) (Found: C, 73.7; H, 5.3; N, 9.5. $C_{18}H_{16}N_2O_2$ requires C, 74.0; H, 5.5; N, 9.6%); $\nu_{max.}$ 1 664 cm^{-1}; δ_H1.58 and 1.79 (ABq, *J* 9 Hz, with fine splitting, 7-CH_2), 4.82 and 5.00 (2 × br s, 1- and 4-H), 6.40 and 6.55 (2 × m, 5- and 6-H), and 6.97—7.47 (m, NPh_2); *m/z* 292 (M^+).

Cycloadducts (**4**) *of* 2,3-*Dimethylbuta*-1,3-*diene.*—*N*-Hydroxy-*N'*,*N'*-dimethylurea (**1d**)[12] (4 mmol) suspended in dichloromethane (60 ml) was added with stirring to 2,3-dimethylbuta-1,3-diene (20 mmol) in dichloromethane (20 ml) containing tetraethylammonium periodate (8 mmol) during 30 min at 0 °C. After a further 45 min the mixture was washed successively with aqueous sodium thiosulphate and brine, and was dried (Na_2SO_4) and evaporated. Chromatography of the residue on silica plates gave 3,6-*dihydro*-4,5-*dimethyl*-2-(N,N-*dimethylcarbamoyl*)-2H-1,2-*oxazine* (**4d**) (60%), b.p. 110 °C (0.04 mbar, Kügelrohr distillation) (Found: C, 58.5; H, 9.0; N, 15.2%; *m/z* 184.1210. $C_9H_{16}N_2O_2$ requires C, 58.7; H, 8.8; N, 15.2%; 184.1212); $\nu_{max.}$(CHCl$_3$) 1 654 cm^{-1}; δ_H 1.59 and 1.67 (2 × br s, 2 × Me), 2.95 (s, NMe_2), and 3.71 and 4.15 (2 × br s, 2 × CH_2). The other cycloadducts (**4**) were characterised as follows: 2-*carbamoyl*-3,6-*dihydro*-4,5-*dimethyl*-2H-1,2-*oxazine* (**4a**), m.p. 106 °C (from ethyl acetate) (Found: C, 53.7; H, 7.8; N, 18.0. $C_7H_{12}N_2O_2$ requires C, 53.8; H, 7.75; N, 17.9%); $\nu_{max.}$ 3 410, 3 285, 3 210, and 1 654 cm^{-1}; δ_H 1.59 and 1.70 (2 × br s,

2 × Me), 3.94 and 4.23 (2 × br s, 2 × CH_2), and 5.67 (br s, NH, exch. with D_2O); *m/z* 156 (M^+); 3,6-*dihydro*-4,5-*dimethyl*-2-(N-*methylcarbamoyl*)-2H-1,2-*oxazine* (**4b**), m.p. 71 °C (from ethyl acetate–light petroleum) (Found: C, 56.4; H, 8.45; N, 16.35. $C_8H_{14}N_2O_2$ requires C, 56.5; H, 8.3; N, 16.5%); $\nu_{max.}$ 3 358 and 1 658 cm^{-1}; δ_H 1.57 and 1.66 (2 × br s, 2 × Me), 2.83 (d, *J* 6 Hz, NMe), 3.86 and 4.18 (2 × br s, 2 × CH_2), and 5.84 (br s, NH, exch. with D_2O); *m/z* 170 (M^+); 3,6-*dihydro*-4,5-*dimethyl*-2-(N-*phenylcarbamoyl*)-2H-1,2-*oxazine* (**4c**), m.p. 101.5 °C (from ethyl acetate) (Found: C, 67.4; H, 7.2; N, 11.9. $C_{13}H_{16}N_2O_2$ requires C, 67.2; H, 6.9; N, 12.0%); $\nu_{max.}$ 3 280 and 1 652 cm^{-1}; δ_H 1.58 and 1.68 (2 × br s, 2 × Me), 3.98 and 4.30 (2 × br s, 2 × CH_2), 6.90—7.60 (m, Ph), and 7.65 (br s, NH, exch. with D_2O); *m/z* 232 (M^+); 3,6-*dihydro*-4,5-*dimethyl*-2-(N,N-*diphenylcarbamoyl*)-2H-1,2-*oxazine* (**4e**), m.p. 134 °C (from acetone–light petroleum) (Found: C, 74.05; H, 6.5; N, 9.05. $C_{19}H_{20}N_2O_2$ requires C, 74.1; H, 6.5; N, 9.1%); $\nu_{max.}$ 1 668 cm^{-1}; δ_H 1.44 and 1.63 (2 × br s, 2 × Me), 3.43 and 3.85 (2 × br s, 2 × CH_2), and 7.00—7.45 (m, NPh_2); *m/z* 308 (M^+).

Cycloadducts (**12**) *and* (**14**) *of Thebaine and Ergosteryl Acetate.*—Hydroxyurea (**1a**) (114 mg, 1.5 mmol) was added slowly in portions with vigorous stirring to thebaine (**11**) (311 mg, 1.0 mmol) in ethyl acetate (12 ml), and sodium periodate (321 mg, 1.5 mmol) in aqueous 0.5 M-sodium acetate (10 ml) previously adjusted to pH 7 with hydrochloric acid, at 0 °C. Stirring was continued for 0.5 h and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 10 ml) and the extracts were combined with the ethyl acetate layer and washed with a little water, dried ($MgSO_4$), and evaporated. The residue (329 mg) was judged by ^1H n.m.r. spectroscopy to consist largely of the adduct (**12**; R = H) and to be free from thebaine. Crystallisation from ethanol gave 6β,14β-(*N*-carbamoylepoxyimino)-6,14-dihydrothebaine (**12**; R = H) (304 mg, 79%), m.p. 177—178 °C (decomp.) (lit.,[6] 177 °C), which had spectroscopic properties in good agreement with those reported[6] earlier for material prepared from the cycloadduct of thebaine and nitrosyl cyanide. Similarly, oxidation of *N*-hydroxy-*N'*-phenylurea (**1c**) with tetraethylammonium periodate in the presence of thebaine gave 6,14-*dihydro*-6β,14β-(N-*phenylcarbamoylepoxyimino*)*thebaine* (**12**; R = Ph), m.p. 185—188 °C (decomp.) (from ethanol) (Found: C, 67.7; H, 5.8; N, 9.2. $C_{26}H_{27}N_3O_5$ requires C, 67.7; H, 5.9; N, 9.1%); $\nu_{max.}$ 3 420 and 1 695 cm^{-1}; δ_H (60 MHz) 2.54 (s, NMe), 3.40 (d, *J* 19 Hz, 10β-H), 3.70 (s, 3-OMe), 3.83 (s, 6-OMe), 4.70 (s, 5-H), 4.85 (d, *J* 7 Hz, 9-H), 6.12 (s, 7- and 8-H), 6.66 (br s, 1-and 2-H), 7.0—7.5 (m, Ph), and 7.74 (br s, NH, exch. with D_2O); *m/z* 461 (M^+). Ergosteryl acetate (**13**) was converted similarly into 5,8-*dihydro*-8α,5α-(N-*phenylcarbamoylepoxyimino*)*ergosteryl acetate* (**14**), m.p. 146—148 °C (from methanol) (Found: C, 74.9; H, 9.0; N, 4.8. $C_{37}H_{52}N_2O_4$ requires C, 75.5; H, 8.8; N, 4.8%); $\nu_{max.}$ 3 390, 1 735, and 1 695 cm^{-1}; δ_H (60 MHz) 2.02 (s, Ac), 3.50 (dd, *J* 14 and 5 Hz, 4α-H), 5.24 (m, 22- and 23-H), 5.37 (m, 3-H), 6.28 (br s, 6- and 7-H), 7.0—7.5 (m, Ph), and 7.92 (br s, NH, exch. with D_2O); *m/z* 438 (M − PhNHCONO).

Cycloadduct (**15**) *of* 9,10-*Dimethylanthracene.*—Hydroxyurea (**1a**) (152 mg, 2 mmol) in water (1 ml) and methanol (2 ml) was added dropwise with stirring during 10 min to 9,10-dimethylanthracene (206 mg, 1 mmol) in dichloromethane (10 ml) and methanol (5 ml) containing tetraethylammonium periodate (642 mg, 2 mmol) at 0 °C. After a further 15 min, the mixture was diluted with dichloromethane (10 ml) and water (5 ml). Aqueous sodium thiosulphate was added to discharge the colour of iodine and the layers were separated. The aqueous layer was extracted with dichloromethane (2 × 5 ml) and the extracts were combined with the dichloromethane layer then dried ($MgSO_4$) and evaporated. The residue (209 mg) was judged by ^1H n.m.r. spectroscopy to contain the cycloadduct (**15**) and 9,10-dimethylanthracene in the ratio 10:1. The mixture was chromatographed on silica. Elution with chloroform gave 9,10-dimethylanthracene and with chloroform–methanol (19:1) gave 9,10-(N-*carbamoylepoxyimino*)-9,10-*dihydro*-9,10-*dimethylanthracene* (**15**) (151 mg, 54%), m.p. 182—183 °C (decomp.) (from benzene–hexane) (Found: C, 72.3; H, 5.55; N, 9.9. $C_{17}H_{16}N_2O_2$ requires C, 72.8; H, 5.75; N, 10.0%; $\nu_{max.}$ 3 528, 3 400, 1 706, and 1 680 cm^{-1}; δ_H 2.22 (s, Me), 2.66 (s, Me), 5.12 (br s, NH_2, exch. with D_2O), and 7.15—7.65 (m, aryl-H); *m/z* 206 (M − H_2NCONO).

Thermolysis of the Cyclopentadiene Adducts (**3**).—The cycloadduct (**3d**) (40 mg) was heated under reflux in benzene (40 ml) for 2 h. The mixture was evaporated and the residue chromatographed on silica plates to give the cycloadduct (**3d**) (10 mg) and *N,N*-dimethylcarbamic anhydride (**9d**) (10 mg), which was identified by spectroscopic comparison with material prepared[13] from *N,N*-dimethylcarbamoyl chloride; $\nu_{max.}$ 1 735 and 1 706 cm^{-1}; $\delta_H(CDCl_3)$ 2.98 (s, 4 × Me); $\delta_H[CDCl_3$–C_6D_6 (1:1)] 2.60 (s, 2 × Me), and 2.70 (s, 2 × Me); $\delta_C(CDCl_3)$ 36.5 (2 × Me), 36.7 (2 × Me), and 151.0 (2 × CO). Similarly, the cycloadduct (**3e**) was heated in benzene, until decomposition was complete (t.l.c. control), to give *N,N*-diphenylcarbamic anhydride (**9e**) (70%), m.p. 132 °C (from ethyl acetate–light petroleum) (lit.,[14] 128.5—132 °C) (Found: C, 76.3; H, 4.9; N, 6.7. Calc. for $C_{26}H_{20}N_2O_3$: C, 76.45; H, 4.9; N, 6.9%); $\nu_{max.}$ 1 758 and 1 727 cm^{-1}; δ_H 6.9—7.6 (m, Ph); *m/z* 408 (M^+).

Thermolysis of the Cyclopentadiene Adducts (**3**) *in the Presence of* 2,3-*Dimethylbuta*-1,3-*diene: Formation of the 'Ene' Reaction Products* (**5**).—The cyclopentadiene adduct (**3b**) (63 mg, 0.41 mmol) and 2,3-dimethylbuta-1,3-diene (0.47 ml, 4.1 mmol) were heated in ethyl acetate (10.3 ml) for 2 h. The mixture was evaporated and the residue was chromatographed on a silica column and then on silica plates to give the dimethylbutadiene adduct (**4b**) (71%) and N-*hydroxy*-N'-*methyl*-N-(3-*methyl*-2-*methylenebut*-3-*enyl*)*urea* (**5b**) (22%), m.p. 105 °C (from ethyl acetate) (Found: C, 56.2; H, 8.2; N, 16.2%; *m/z* 170.1056. $C_8H_{14}N_2O_2$ requires C, 56.5; H, 8.3; N, 16.5%; *M*, 170.1055); $\nu_{max.}$ 3 365, 3 160, 1 625, and 1 650 cm^{-1}; $\lambda_{max.}$(EtOH) 239 nm (ε 4 390); δ_H 1.89 (s, vinyl-Me), 2.76 (d, *J* 6 Hz, NMe), 4.31 (s, NCH_2), 4.97, 5.13, 5.17, and 5.23 (4 × br s, 4 × vinyl-H), 5.92 (br s, NH, exch. with D_2O), and 7.15 (br s, OH, exch. with D_2O). Similarly, the cycloadduct (**3c**) (0.4 mmol) and dimethylbutadiene (4 mmol) were heated under reflux in benzene (10 ml) for 3 h to give the dimethylbutadiene adduct (**4c**) (75%) and N-*hydroxy*-N-(3-*methyl*-2-*methylenebut*-3-*enyl*)-N'-*phenylurea* (**5c**) (20%), m.p. 133 °C (from ethyl acetate–light petroleum) (Found: *m/z* 232.1204. $C_{13}H_{16}N_2O_2$ requires *M*, 232.1211); $\delta_H[(CD_3)_2CO]$ 1.89 (s, vinyl-Me), 4.41 (s, NCH_2), 5.01 (br s, vinyl-H), 5.28 (br s, 3 × vinyl-H), 6.85—7.45 (3 H, m, *m*- and *p*-phenyl-H), 7.55—7.75 (2 H, m, *o*-phenyl-H), 8.53 (br s, NH, exch. with D_2O), and 8.73 (br s, OH, exch. with D_2O). Similarly, the cycloadduct (**3e**) and dimethylbutadiene (10 mol equiv.) gave the dimethylbutadiene adduct (**4e**) (56%), N-*hydroxy*-N-(3-*methyl*-2-*methylenebut*-3-*enyl*)-N',N'-*diphenylurea* (**5e**) (14%), m.p. 101 °C (from ethyl acetate–light petroleum) (Found: C, 74.1; H, 6.5; N, 9.1. $C_{19}H_{20}N_2O_2$ requires C, 74.0; H, 6.5; N, 9.1%); $\nu_{max.}$ 3 100, 1 616, 1 590, and 1 577 cm^{-1}; δ_H 1.89 (s, vinyl-Me), 4.31 (s, NCH_2), 5.03 (br s, 2 × vinyl-H), 5.15 and 5.24 (2 × br s, 2 × vinyl-H), 5.66 (br s, OH, exch. with D_2O), and 7.00—7.55 (m, NPh_2); *m/z* 308 (M^+), and the cycloadduct (**6e**) or (**7e**) (11%); δ_H 1.64 (br s, Me), 3.43, 3.86, and 3.93 (3 × br s, 3 × CH_2), and 6.90—7.60 (m, 2 × NPh_2); this last product was not characterised further. Similarly, heating the cycloadduct (**3a**) with an excess of dimethylbutadiene gave (**4a**) (50%) and the 'ene' reaction

product (**5a**) (12%), which was not fully characterised. The cycloadduct (**3d**) with an equimolar amount of dimethylbutadiene gave (**4d**) (35%), the anhydride (**9d**) (26%), and the 'ene' reaction product (**5d**) (8%), which was not fully characterised. In contrast, (**3d**) with an excess of dimethylbutadiene gave (**4d**) (66%), (**5d**) (19%), and the adduct (**6d**) or (**7d**) (19%), which was not fully characterised.

Thermolysis of the Cycloadduct (**15**) *in the Presence of Thebaine*.—The cycloadduct (**15**) (70 mg, 0.25 mmol) and thebaine (78 mg, 0.25 mmol) were heated in benzene (5 ml) under reflux for 10 min. The mixture was evaporated and the residue was chromatographed on a short column of neutral alumina. Elution with chloroform gave 9,10-dimethylanthracene (DMA), and with chloroform–methanol (19:1) gave the cycloadduct (**12**; R = H) (90 mg). Crystallisation of the latter from ethanol gave material (55 mg, 57%), m.p. 176—178 °C (decomp.), having spectroscopic properties identical with those of a sample prepared from thebaine and hydroxyurea. The cycloadduct (**15**) (11.2 mg, 0.04 mmol) and thebaine (12.4 mg, 0.04 mmol) were dissolved in dichloromethane (0.5 ml) and the solution was diluted with benzene (9.5 ml) and kept at 40 °C. Aliquots (0.5 ml) were removed periodically and diluted with hexane–ethanol (1:1) (9.5 ml). The release of DMA was monitored during 4.5 h by the absorption at 378 nm. An 'infinity' reading, taken after 24 h, corresponded closely with that obtained using pure DMA (0.04 mmol). First-order kinetics, $k = 9.1 \times 10^{-5} s^{-1}$, were observed.

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References

1 (*a*) G. W. Kirby and J. G. Sweeny, *J. Chem. Soc., Perkin Trans. 1*, 1981, 3250; (*b*) J. E. T. Corrie, G. W. Kirby, and R. P. Sharma, *ibid.*, 1982, 1571; (*c*) J. E. T. Corrie, G. W. Kirby, and J. W. M. Mackinnon, *ibid.*, 1985, 883; (*d*) G. W. Kirby and J. W. M. Mackinnon, *ibid.*, 1985, 887.
2 G. W. Kirby, H. McGuigan, J. W. M. Mackinnon, D. McLean, and R. P. Sharma, *J. Chem. Soc., Perkin Trans. 1*, 1985, 1437.
3 G. W. Kirby, *Chem. Soc. Rev.*, 1977, **6**, 1.
4 G. E. Keck, R. R. Webb, and J. B. Yates, *Tetrahedron*, 1981, **37**, 4007 and references cited therein.
5 O. Meth-Cohn and G. van Vuuren, *J. Chem. Soc., Chem. Commun.*, 1984, 1144.
6 P. Horsewood and G. W. Kirby, *J. Chem. Soc., Perkin Trans. 1*, 1980, 1587.
7 G. W. Kirby, K. W. Bentley, P. Horsewood, and Serjinder Singh, *J. Chem. Soc., Perkin Trans. 1*, 1979, 3064.
8 (a) J. E. T. Corrie, G. W. Kirby, A. E. Laird, L. W. Mackinnon, and J. K. Tyler, *J. Chem. Soc., Chem. Commun.*, 1978, 275; (*b*) P. Horsewood, G. W. Kirby, R. P. Sharma, and J. G. Sweeny, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1802.
9 J. E. Baldwin, P. D. Bailey, G. Gallacher, K. A. Singleton, and P. M. Wallace, *J. Chem. Soc., Chem. Commun.*, 1983, 1049; G. W. Kirby and D. McLean, *J. Chem. Soc., Perkin Trans. 1*, 1985, 1443.
10 G. W. Kirby, H. McGuigan, and D. McLean, *J. Chem. Soc., Perkin Trans. 1*, 1985, 1961.
11 C. D. Hurd, *J. Am. Chem. Soc.*, 1923, **45**, 1472.
12 G. Zinner and G. Isensee, *Arch. Pharm. (Weinheim, Ger.)*, 1974, **307**, 7.
13 E. G. Wallace, U.S.P. 4,117,153/1978 (*Chem. Abstr.*, 1979, **90**, 71782a).
14 W. A. Schroder and P. E. Wilcox, *J. Am. Chem. Soc.*, 1950, **72**, 3814.

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