Intramolecular 'Ene' Reactions of Transient, Allylic, and Homoallylic *C*-Nitrosoformate Esters

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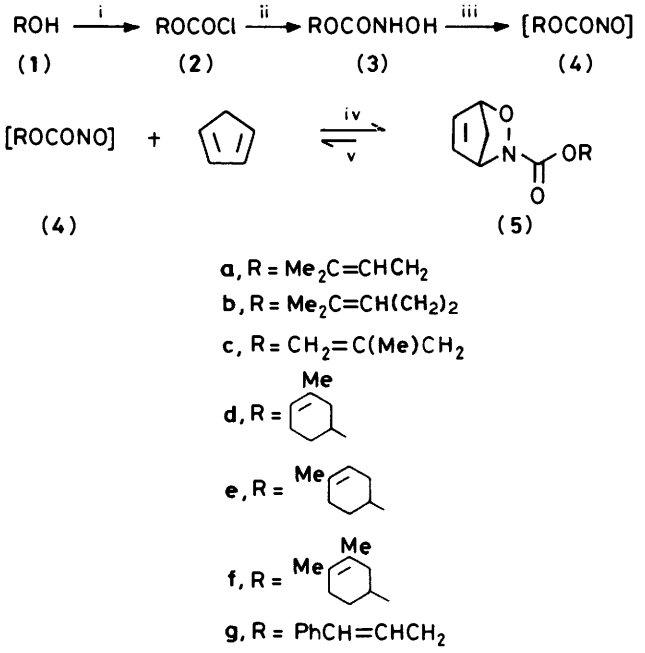
Various allylic and homoallylic alcohols have been treated successively with phosgene and hydroxylamine to form the corresponding *N*-hydroxycarbamic esters (**3**). Oxidation of these hydroxamic acid derivatives with sodium or tetraethylammonium periodate in the presence of cyclopentadiene gave the cycloadducts (**5**) derived from transient allylic and homoallylic *C*-nitrosoformate esters (**4**) and cyclopentadiene. When the cycloadducts were heated in benzene at 80 °C, or toluene at 111 °C, they dissociated and the *C*-nitrosoformate esters underwent intramolecular 'ene' reactions to give hydroxamic acid derivatives having newly formed, five- six- or seven-membered heterocyclic rings.

In earlier papers we presented evidence that oxidation of the hydroxamic acids, RCONHOH[1,2] and ROCONHOH,[3] produces transient nitrosocarbonyl compounds, RCONO and ROCONO, which may be trapped efficiently *in situ* as their cycloadducts with conjugated dienes. Similarly, oxidation of *N*-hydroxyureas[4,5] in the presence of conjugated dienes gives *N*-carbamoyl-3,6-dihydro-2*H*-1,2-oxazines derived, apparently, from transient *C*-nitrosoformamides, R^1R^2NCONO. It was appreciated from the outset[4] that studies on the 'ene' reactions of nitrosocarbonyl compounds with mono-olefins would require a different experimental approach. The 'ene' reaction products are themselves hydroxamic acids sensitive to the oxidising conditions used to form the nitrosocarbonyl compounds. However, nitrosocarbonyl compounds may also be generated under mild conditions by thermal dissociation of their cycloadducts with 9,10-dimethylanthracene. The first examples[2,4] of the intermolecular 'ene' reactions of *C*-nitrosocarbonyl compounds, RCONO, were observed in this way. Keck *et al.*[6] later exploited the same device in a wider investigation of the inter- and intra-molecular 'ene' reactions of *C*-nitrosocarbonyl compounds. We now report the first study of the intramolecular 'ene' reactions of nitrosoformate esters, ROCONO, derived from allylic and homoallylic alcohols.

Although cycloadducts of 9,10-dimethylanthracene are excellent auxiliary sources of reactive nitroso compounds,[4,7] 9,10-dimethylanthracene is not readily available and generally must be separated chromatographically from the other, desired thermolysis products. More recently, we showed that the cycloadducts of both *C*-nitrosocarbonyl compounds[2] and nitrosoformate esters[3] with cyclopentadiene are also satisfactory sources of the transient nitroso compounds. Since cyclopentadiene is readily available and volatile it was chosen in preference to 9,10-dimethylanthracene for the present study. The general procedure for the synthesis of cyclopentadiene adducts is illustrated in Scheme 1. Scheme 2 lists the observed products of the intramolecular, 'ene' reactions; the alphabetical designation given therein to each allyl and homoallyl group is used through this paper.

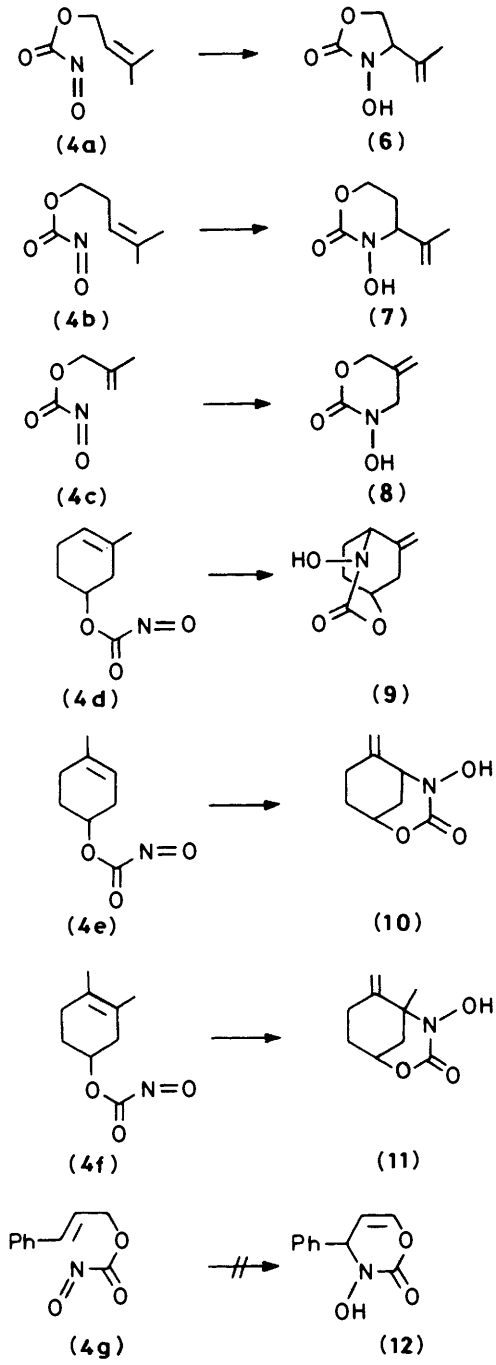
3-Methylbut-2-en-1-ol (**1a**) was treated at −40 °C with phosgene in toluene to give a solution containing the chloroformate (**2a**). This was shaken with aqueous hydroxylamine to give the *N*-hydroxycarbamate (**3a**), obtained as an oil after chromatography on Florisil. Oxidation of (**3a**) with sodium periodate in the presence of cyclopentadiene gave the oily cycloadduct (**5a**), which was purified chromatographically. The decomposition of the adduct (**5a**) in benzene at 80 °C was monitored by t.l.c. and judged to be complete in 3 h; evaporation of the solution then gave directly the crystalline *N*-hydroxyoxazolidinone (**6**). The ^1H and ^{13}C n.m.r. spectra of the



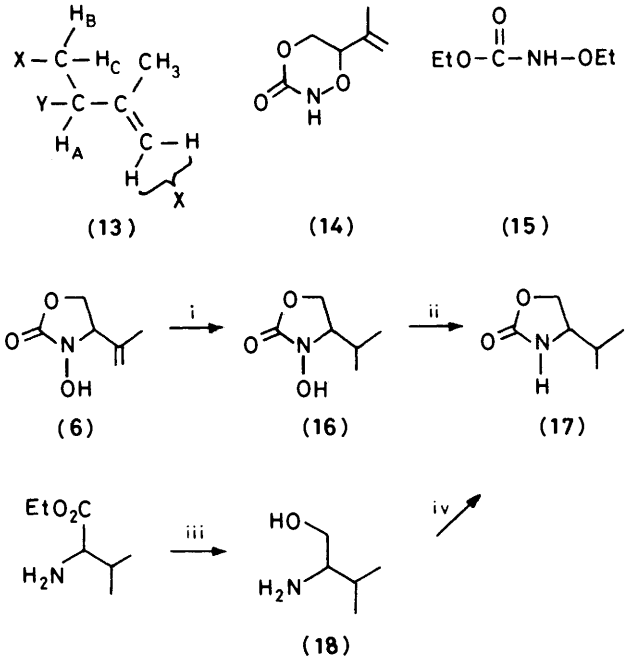
Scheme 1. *Reagents:* i, $COCl_2$ in PhMe; ii, NH_2OH in H_2O; iii, $NaIO_4$ or Et_4NIO_4; iv, 0 °C; v, 80 or 111 °C

product established the part structure (**13**), the heterocyclic protons giving an ABC system, analysed using a spin simulation programme, with additional, fine coupling between H_A and an olefinic proton, H_X. Two alternative structures, (**6**) and (**14**), were therefore considered for the product. An unambiguous distinction could not be made by i.r. spectroscopy. The product gave a high frequency carbonyl band, $\nu_{max.}$ 1 775 cm^{-1}, consistent with a five-membered ring, but the amide (**15**), prepared as a model for the structure (**14**), gave a band at 1 765 cm^{-1} and it was conceivable that a somewhat higher frequency might pertain for a six-membered ring. Normally, a decision between structures (**6**) and (**14**) would be made using the characteristic ferric chloride test for hydroxamic acids. However, the compound (**6**), unlike all the other 'ene' reaction products listed in Scheme 2, gave only a transient blue colour with ethanolic ferric chloride, and then only when a freshly neutralised solution was used. The structure (**6**) was therefore confirmed, as shown in Scheme 3, by chemical correlation with a derivative (**17**) of (±)-valinol (**18**).

Reductive cleavage of the N–O bond in hydroxamic acids had



Scheme 2.



Scheme 3. *Reagents:* i, H_2, Pd-C; ii, SO_2, pyridine; iii, $LiAlH_4$; iv, $(EtO)_2CO$

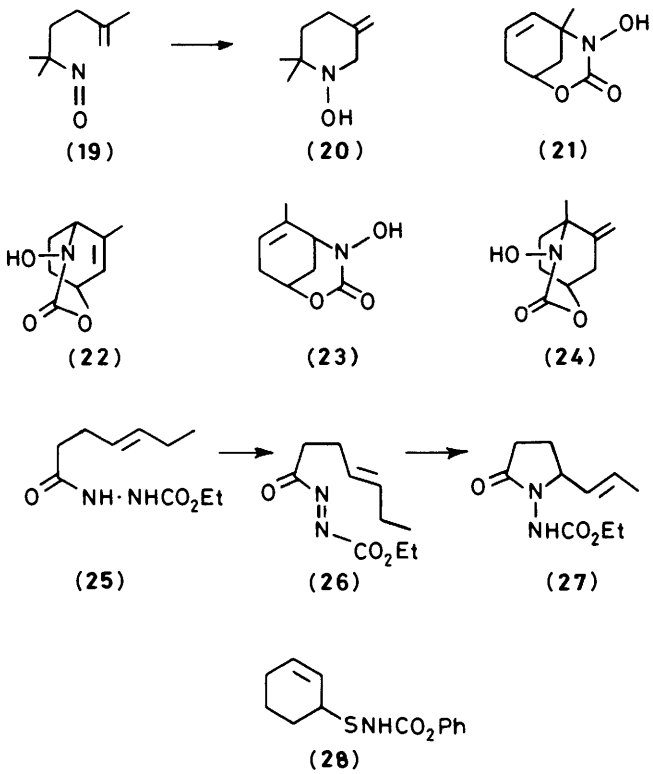
been accomplished by Keck and Webb[8] who treated the corresponding *O*-acetyl derivatives with sodium amalgam. However, in our hands, this method failed to cleave the *O*-acetyl derivatives of either of the hydroxamic acids (**6**) and (**16**). Keck *et al.* later reported[6] similar difficulties with their procedure, the outcome of which is apparently highly dependent on the batch of sodium amalgam employed. They recommended instead reductive cleavage of hydroxamic acids with titanium trichloride.[9] We had found, in a separate study,[10] that the ethylene acetals of 14β-(*N*-acyl-hydroxyamino)codeinones could be reductively cleaved to give the corresponding amides using sulphur dioxide in refluxing pyridine. Under these conditions, the hydroxamic acid (**16**) was converted into the amide (**17**), which was identical with material prepared (Scheme 3) from (±)-valine ethyl ester.

The adduct (**5b**), prepared by the standard procedure (Scheme 1) from the homoallylic alcohol (**1b**), decomposed cleanly in benzene at 80 °C, though somewhat more slowly than did the adduct (**5a**), to give the oily hydroxamic acid (**7**). The structure (**7**) was deduced from the ^1H and ^{13}C n.m.r. spectra, taking into account a positive ferric chloride test ($\lambda_{max.}$ 525 nm) for a hydroxamic acid. Thus, the allylic (**4a**) and homoallylic (**4b**) nitrosoformate esters both cyclise by a Type I mechanism, as defined by Oppolzer and Snieckus.[11] In both cases, the transition states for concerted cyclisation are relatively strain free, being fused, rather than bridged, bicyclic in character.

The cycloadduct (**5c**) was selected next for study since cyclisation of the derived nitrosoformate (**4c**), to give hydroxamic acid (**8**), would exemplify the less common, Type II mechanism, requiring in this case a bicyclo[3.3.1] transition state. Moreover, the first reported example of an intramolecular 'ene' reaction of any *C*-nitroso-compound was of this type; Motherwell and Roberts[12] found that the nitroso-olefin (**19**) cyclised readily at room temperature to give the hydroxylamine (**20**). When the cycloadduct (**5c**) was heated in benzene at 80 °C, decomposition occurred very slowly and was judged, by ^1H n.m.r. spectroscopy, to be only 50% complete in 21 h. However, decomposition was complete in 9 h in toluene at 111 °C. Chromatography of the dark brown reaction mixture gave the hydroxamic acid (**8**) as the only identifiable product. Thus, nitrosoformate esters can undergo the Type II intramolecular 'ene' reaction but clearly this process is less favourable than the Type I; indeed, the adduct (**5c**) decomposed much more slowly than any others, apart from (**5g**), in the present series. However, it does not follow from this observation that the cyclisation (**4c**)→(**8**) is necessarily slower than the cyclisation (**19**)→(**20**). The transient nitrosoformate (**4c**) may either cyclise, or combine with cyclopentadiene to regenerate the adduct (**5c**). The latter reaction must be faster than the former, at least when substantial amounts of cyclopentadiene are present, since otherwise the adduct could not be prepared according to

Scheme 1. Nevertheless, we have at present no method for measuring separately the rates of these two competing reactions of the transient species (**4c**).

A series of cyclic, homoallylic nitrosoformates (**4d**—**f**) was chosen to elucidate further the selectivity of intramolecular, 'ene' cyclisations. The required alcohols were readily obtained from the appropriate phenols *via* Birch reduction of the derived methyl ethers. Thermolysis of the cycloadduct (**5d**) in benzene gave the bridged hydroxamic acid (**9**) as the sole identifiable product. In contrast, the adduct (**5e**) gave a product (**10**) having a newly formed, six-membered ring. Clearly, cyclisation of the nitrosoformates (**4d**) and (**4e**) is not controlled simply by the size of the new heterocyclic ring. Thus, (**4d**) gives the oxazepinone (**9**) rather than the oxazinone (**21**) even though the transition



states for concerted cyclisation appear, from molecular models, in both cases to be free from any severe angle strain or non-bonded interactions. It is possible that electronic effects play a role in controlling cyclisation of the nitrosoformate (**4d**). If C–N bond formation precedes hydrogen abstraction[6] then, in the polarised transition state, the electrophilic nitroso group would carry a partial negative and the olefinic group a partial positive charge. Attack at the less substituted end of the olefinic double bond would then be favoured. In principle, this could lead to either of the oxazepinones (**9**) or (**22**). However, molecular models indicate that the transition state leading to (**22**) would be significantly strained. The observed cyclisation of the nitrosoformate (**4e**) to give the exocyclic olefin (**10**) rather than the endocyclic olefin (**23**) may reflect the more extended, and therefore less congested, transition state leading to the former product.

Finally, cyclisation of the nitrosoformate (**4f**), generated from the adduct (**5f**) in benzene at 80 °C, gave the oxazinone (**11**) rather than the oxazepinone (**24**); in this case, the mode of cyclisation is presumably controlled by the size of the newly formed ring. The structure of the product (**11**) was deduced from the i.r. carbonyl absorption at 1 686 cm^{-1}, which resembled that of the oxazinone (**10**), at 1 680 cm^{-1}, rather than of the oxazepinone (**9**), 1 640 cm^{-1}. Reduction of the oxazinone (**11**) with sulphur dioxide in pyridine gave the corresponding amide (**11**; OH = H).

Cyclisation of (*E*)-cinnamyl nitrosoformate (**4g**) to give the hydroxamic acid (**12**) would represent an example of the rare, Type III 'ene' reaction, in that the enophilic nitroso group is attached to the allylic terminus of the 'ene' component. However, the corresponding adduct (**5g**) was stable to prolonged heating in benzene at 80 °C and decomposed in toluene at 111 °C to give a complex, intractable mixture of products. Clearly, the cyclisation (**4g**)→(**12**), if it occurs at all, must proceed more slowly than any of the preceding examples.

It was noted on several occasions that the cycloadducts (**5**) decomposed thermally at rates, monitored by t.l.c. or ^1H n.m.r. spectroscopy, dependent upon their initial concentrations in benzene. Generally, decomposition was faster for more dilute solutions. This phenomenon was not studied quantitatively but, qualitatively, it is the expected outcome of the reversible dissociation of the adducts (**5**). Although the 'ene' reaction products are formed by two, consecutive, first-order processes, the overall reaction is retarded by a fast, second-order capture of the nitrosoformate (**4**) by cyclopentadiene to regenerate the adduct (**5**) (Scheme 1). As the reaction proceeds, the concentration of cyclopentadiene increases with a resulting marked decrease in the overall rate. Furthermore, the effect of this second-order retardation is greater for more concentrated solutions. The present studies were carried out conveniently on a small scale with dilute solutions. For larger scale preparations, removal of the cyclopentadiene by distillation and replenishment of the solvent should be beneficial.[3]

The intramolecular 'ene' reaction of nitrosocarbonyl compounds is analogous to that of acylazocarboxylates. For example, Vedejs and Meier[13] showed that oxidation of the hydrazide (**25**) with manganese dioxide gave an unstable azo-compound (**26**), which cyclised at room temperature to form the lactam (**27**). Recently, Meth-Cohn and van Vuuren[14] have shown that thionitroso compounds, formed as reactive intermediates by thermolysis of S,N-ylides, readily undergo intermolecular 'ene' reactions with mono-olefins and even conjugated dienes. For example, phenyl thionitrosoformate, PhOCONS, reacts with cyclohexene to give the adduct (**28**). Unlike nitrosoformate esters, phenyl thionitrosoformate reacts with olefins to form a C–S rather than a C–N bond: a study of the intramolecular 'ene' reactions of thionitrosoformates should therefore be of particular interest.

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 ^1H 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. Hydroxamic acids were revealed as purple spots on thin-layer chromatograms by spraying with 5% ethanolic ferric chloride; the cycloadducts (**5**) also gave purple spots with ferric chloride but only after some delay.

Formation of 3-Hydroxy-4-isopropenyloxazolidin-2-one (**6**) *by Thermolysis of the Cycloadduct* (**5a**).—3-Methylbut-2-en-1-ol (**1a**) (1.1 ml, 10 mmol) was added dropwise with stirring to phosgene (20 mmol) in toluene (17.5 ml) at −40 °C. The mixture was stirred for 3 h at −40 °C and then slowly added with shaking to an ice-cold solution of hydroxylamine hydrochloride (3.5 g, 50 mmol) and sodium hydroxide (2.8 g, 70

mmol) in water (50 ml). The mixture was shaken at room temperature for 1 h and then acidified with hydrochloric acid and extracted with ether. The extracts were washed with brine, dried ($MgSO_4$), and evaporated to give a yellow oil, which was purified by chromatography on Florisil. Elution with chloroform–methanol (95:5) gave the *N*-hydroxycarbamate (**3a**) (650 mg, 45%) as an oil. This carbamate (**3a**) (290 mg, 2 mmol) in ethyl acetate (5 ml) was added during 10 min, with vigorous stirring at 0 °C, to freshly distilled cyclopentadiene (0.33 ml, 4 mmol) in ethyl acetate (70 ml), and sodium periodate (428 mg, 2 mmol) in aqueous 0.5M-sodium acetate (35 ml) previously adjusted to pH 6 with hydrochloric acid. After 1 h at 0 °C, the ethyl acetate layer was washed with brine, dried ($MgSO_4$), and evaporated. Chromatography of the residue on silica plates gave the cycloadduct (**5a**) (350 mg, 83%) as an oil; $\nu_{max.}(CCl_4)$ 1 750 and 1 705 cm^{-1}; δ_H 1.68 (br s, Me), 1.72 (br s, Me), 1.99 (1 H, dm, *J* 9 Hz, bridge-methylene-H), 4.62 (br d, *J* 8 Hz, OCH_2), 5.04 and 5.24 (2 × m, NCH and OCH), 5.35 (br t, *J* 8 Hz, $CH_2CH{=}CMe_2$), and 6.41 (2 H, br s, $CH{=}CH$). This cycloadduct (**5a**) (50 mg, 0.24 mmol) was heated under reflux in anhydrous benzene (40 ml) under nitrogen for 3 h. Evaporation of the solution gave an oily residue of the oxazolidinone (**6**) (33 mg, 97%), judged by ^1H n.m.r. spectroscopy to be substantially pure. *3-Hydroxy-4-isopropenyloxazolidin-2-one* (**6**) had m.p. 74.5—75 °C (from hexane) (Found: C, 50.4; H, 6.3; N, 9.7. $C_6H_9NO_3$ requires C, 50.35; H, 6.3; N, 9.8%); $\nu_{max.}(CCl_4)$ 3 250 and 1 775 cm^{-1}; δ_H 1.77 (br s, Me), 3.88—4.55 (3 H, m, 4- and 5-H), 5.05—5.20 (2 H, m, vinyl-H), and 8.45 (br s, OH, exch. with D_2O); δ_C 29.7 (Me), 64.8 (4-C), 65.8 (5-C), 117.0 ($CH_2{=}CMe$), 139.1 ($CH_2{=}CMe$), and 161.1 (2-C); *m/z* 143 (M^+), 127, and 112. The protons attached to the heterocyclic ring gave an ABC n.m.r. pattern with additional, fine coupling to an olefinic proton, H_X [see structure (**13**)]. Approximate δ and *J* values were obtained from the 360 MHz spectrum; refined values were obtained from the 100 MHz spectrum using a spin simulation programme;[15] δ 4.43 (H_A), 4.41 (H_B), 4.02 (H_C), and 5.14 (H_X); J_{AB} +8.5, J_{AC} + 8.6, J_{BC} −8.7, and $|J_{AX}|$ 0.5 Hz.

3-Acetoxy-4-isopropenyloxazolidin-2-one.—The foregoing *N*-hydroxyoxazolidinone (**6**) was treated with an excess of acetic anhydride in pyridine at room temperature overnight. The solution was evaporated and the residue crystallised from light petroleum to give *3-acetoxy-4-isopropenyloxazolidin-2-one*, m.p. 37.5 °C (Found: C, 51.8, H, 6.3; N, 7.8. $C_8H_{11}NO_4$ requires C, 51.9; H, 6.0; N, 7.6%); $\nu_{max.}(CCl_4)$ 1 782 cm^{-1}; δ_H 1.79 (br s, vinyl-Me), 2.13 (s, Ac), 3.88—4.60 (3 H, m, 4- and 5-H), and 4.99—5.15 (2 H, m, vinyl-H); *m/z* 185 (M^+). Analysis of the ABCX spin system [see structure (**13**)], as for compound (**6**), gave: δ 4.56 (H_A), 4.49 (H_B), 4.13 (H_C), and 5.06 (H_X); J_{AB} +8.5, J_{AC} +8.6, J_{BC} −8.7, and $|J_{AX}|$ 0.5 Hz.

Conversion of the N-*Hydroxyoxazolidinone* (**6**) *into* 4-*Isopropyloxazolidin-2-one* (**17**).—The *N*-hydroxyoxazolidinone (**6**) (438 mg) was hydrogenated in ethanol (10 ml) at ambient temperature and pressure using 10% Pd-C catalyst (104 mg) for 44 h. The product was chromatographed in chloroform on Florisil to give *3-hydroxy-4-isopropyloxazolidin-2-one* (**16**) (282 mg) as an oil (Found: *m/z* 145.0738. $C_6H_{11}NO_3$ requires *M*, 145.0738); $\nu_{max.}(CCl_4)$ 3 250 and 1 772 cm^{-1}; δ_H 0.93 and 0.98 (2 × d, *J* 7 Hz, 2 × Me), 1.90—2.34 (m, Me_2CH), 3.64—4.47 (3 H, m, 4- and 5-H), and 7.72 (br s, OH, exch. with D_2O). Sulphur dioxide was passed into a solution of the *N*-hydroxy-compound (**16**) (127 mg) in dry pyridine (10 ml).[10] The solution became hot and turned yellow. The mixture was heated under reflux for 1.5 h, with occasional introduction of more sulphur dioxide, and then was evaporated to give a partly crystalline, acidic residue. This was treated with aqueous sodium hydrogen carbonate and extracted with ether. The extracts were evaporated and the residue was freed from pyridine by addition and evaporation of toluene. The residue was dissolved in the minimum amount of tetrachloromethane and the solution was diluted with light petroleum. 4-Isopropyloxazolidin-2-one (**17**) (55 mg), m.p. and mixed m.p. 75 °C, crystallised from the mixture and had spectroscopic properties identical with those of material prepared, as follows, from (±)-valinol.

Preparation of 4-*Isopropyloxazolidin-2-one* (**17**) *from* (±)-*Valinol* (**18**).—(±)-Valinol[16] (230 mg) was heated in redistilled diethyl carbonate[17] (10 ml) and a small quantity of the solvent was distilled out to remove any traces of water. Sodium methoxide (*ca.* 0.04 mol equiv.) in methanol (*ca.* 0.25 ml) was added to the cooled mixture which was heated under reflux for 30 min and then evaporated. The residue was dissolved in ether and washed successively with dilute hydrochloric acid and water, dried (Na_2SO_4), and evaporated to give *4-isopropyloxazolidin-2-one* (169 mg), m.p. 75 °C (from tetrachloromethane–light petroleum) (Found: C, 55.7; H, 8.6; N, 10.7. $C_6H_{11}NO_2$ requires C, 55.8; H, 8.5; N, 10.85%); $\nu_{max.}$ 3 248 and 1 745 cm^{-1}; δ_H 0.89 and 0.95 (2 × d, *J* 7 Hz, 2 × Me), 1.50—1.95 (m, Me_2CH), 3.63 (distorted q, *J* 8 Hz, 4-H), 4.00—4.60 (2 H, m, 5-H), and 6.93 (br s, NH, exch. with D_2O); *m/z* 129 (M^+).

Formation of 3-*Hydroxy-4-isopropenyltetrahydro*-1,3-*oxazin-2-one* (**7**) *by Thermolysis of the Cycloadduct* (**5b**).—4-Methylpent-3-en-1-ol[18] (**1b**) was treated with an excess of phosgene in toluene, as described before for (**1a**) but at 0 °C for 3 h, to form the chloroformate (**2b**). This was converted, as before, into the *N*-hydroxycarbamate (**3b**) (42%), which was obtained as an oil after chromatography on Florisil. Oxidation of the *N*-hydroxycarbamate (**3b**) in the presence of cyclopentadiene, as before, and chromatography of the product on Florisil gave the cycloadduct (**5b**) (59%) as an oil; $\nu_{max.}$(liquid film) 1 745 and 1 705 cm^{-1}; δ_H 1.61 (s, Me), 1.69 (s, Me), 1.99 (1 H, dm, *J* 9 Hz, bridge-methylene-H), 2.33 (2 H, br q, *J* 8 Hz, $CH_2CH{=}CMe_2$), 4.09 (t, *J* 8 Hz, OCH_2), 5.04 (br s, NCH or OCH), 5.09 (m, $CH_2CH{=}CMe_2$), 5.24 (br s, NCH or OCH), and 6.42 (2 H, br s, $CH{=}CH$). The cycloadduct (**5b**) (90 mg) was heated under reflux in benzene (60 ml) under nitrogen. The thermolysis was monitored by ^1H n.m.r. spectroscopy and judged to be 55% complete after 3 h and 90% complete after 7 h. The mixture was evaporated and the brown, oily residue chromatographed on Florisil. Elution with chloroform–methanol (95:5) gave the *oxazinone* (**7**) (46 mg, 72%) as an undistillable oil (Found: *m/z* 157.0733 and 141.0786. $C_7H_{11}NO_3$ requires *M*, 157.0739 and *M* − O, 141.0790); $\nu_{max.}(CCl_4)$ 3 210 and 1 705 cm^{-1}; δ_H 1.74 (s, Me), 2.06 [m, collapsing to an ABq (δ 1.95 and 2.20, *J* 14 Hz) upon irradiation at δ 4.17, 5-CH_2], 4.20 (3 H, m, 6-CH_2 and 4-H), 5.08 (2 H, br s, $CH_2{=}CMe$), and 5.30 (br s, OH, exch. with D_2O); δ_C 18.4 (Me), 26.9 (5-C), 63.7 (4-C), 63.7 (6-C), 114.0 ($CH_2{=}CMe$), 141.2 ($CH_2{=}CMe$), and 155.5 (2-C). This oxazinone (**7**) gave a purple colour ($\lambda_{max.}$ 525 nm) with ethanolic ferric chloride.

Formation of 3-*Hydroxy-5-methylenetetrahydro*-1,3-*oxazin-2-one* (**8**) *by Thermolysis of the Cycloadduct* (**5c**).—2-Methylprop-2-en-1-ol (**1c**) was treated for 3 h at 0 °C in toluene with an excess of phosgene, as before, to give the chloroformate (**2c**), which was converted, as before, into the *N*-hydroxycarbamate (**3c**). This was obtained (49%) as an oil after chromatography on silica gel. The *N*-hydroxycarbamate (**3c**) was oxidised in the presence of cyclopentadiene, as before, to give *3-(2-methylallyloxycarbonyl)-2-oxa-3-azabicyclo*[2.2.1]*hept-5-ene* (**5c**) (74%), b.p. 110 °C (Kugelrohr distillation, 0.015 mmHg) (Found: *m/z* 195.0900. $C_{10}H_{13}NO_3$ requires 195.0895); $\nu_{max.}(CCl_4)$ 1 755 and 1 705 cm^{-1}; δ_H 1.72 (s, Me), 1.76 (1 H, br d, *J* 9 Hz, 7-H), 1.98 (1 H, dm, *J* 9 Hz, 7-H), 4.52 (s, OCH_2), 4.95 (br s, $CH_2{=}CMe$),

5.05 (br s, NCH or OCH), 5.25 (br s, NCH or OCH), and 6.42 (br s, 5- and 6-H). This adduct (**5c**) (50 mg) was heated under reflux in benzene (40 ml), under nitrogen, for 21 h. The ^{1}H n.m.r. spectrum of the resulting mixture indicated that the thermolysis was *ca.* 50% complete. However, when the adduct (**5c**) (280 mg) was heated under reflux in toluene (60 ml), under nitrogen, for 9 h, the thermolysis was complete (n.m.r. control). The mixture was evaporated to give a brown oil, which was chromatographed on silica plates developed with chloroform–methanol (90 : 10) to give the *oxazinone* (**8**) (66 mg, 36%), m.p. 68—69 °C (from di-isopropyl ether) (Found: C, 46.5; H, 5.5; N, 10.55. $C_5H_7NO_3$ requires C, 46.5; H, 5.4; N, 10.85%); $\nu_{max.}$(CCl_4) 3 220 and 1 705 cm^{-1}; δ_H 4.31 (br s, 4-CH_2), 4.61 (br s, 6-CH_2), 5.24 (2 H, br s, vinyl-H), and 7.45 (br s, OH, exch. with D_2O): δ_C 54.0 (4-C), 70.1 (6-C), 114.4 [*C*H_2=C(5)], 133.3 (5-C), and 156.3 (2-C); *m/z* 129 (M^+), 113, and 95. This oxazinone (**8**) gave a purple colour ($\lambda_{max.}$ 525 nm) with ethanolic ferric chloride.

Formation of 4-*Hydroxy*-6-*methylene*-2-*oxa*-4-*azabicyclo*[3.2.2]*nonan*-3-*one* (**9**) *by Thermolysis of the Cycloadduct* (**5d**).—3-Methylcyclohex-3-en-1-ol[19,20] (**1d**) was treated for 3 h at 0 °C in toluene with an excess of phosgene, as before, to give the chloroformate (**2d**), which was converted, as before, into 3-*methylcyclohex*-3-*enyl* N-*hydroxycarbamate* (**3d**) (58%), m.p. 92—94 °C (from benzene–light petroleum) (Found: C, 56.3; H, 7.4; N, 8.0. $C_8H_{13}NO_3$ requires C, 56.1; H, 7.6; N, 8.2%); $\nu_{max.}$ 3 320 and 1 680 cm^{-1}; δ_H 1.62 (br s, Me), 1.5—2.0 (m, 6-CH_2), 1.8—2.4 (m, 2- and 5-CH_2), 4.8—5.2 (m, 1-H), 5.39 (br s, 4-H), and 7.50 (br s, NH and OH, exch. with D_2O); *m/z* 171 (M^+). Oxidation of the *N*-hydroxycarbamate (**3d**) in the presence of cyclopentadiene, as before, and chromatography of the product on Florisil gave 3-(3-*methylcyclohex*-3-*enyloxycarbonyl*)-2-*oxa*-3-*azabicyclo*[2.2.1]*hept*-5-*ene* (**5d**) (66%) as an oil (Found: *m/z* 235.1216. $C_{13}H_{17}NO_3$ requires 235.1208); $\nu_{max.}$(liquid film) 1 740 and 1 695 cm^{-1}; δ_H 1.62 (br s, Me), 1.4—2.4 (8 H, m, 4 × CH_2), 4.99 (m, OCH), 5.04 (br s, NCH or OCH), 5.24 (br s, NCH or OCH), 5.39 (br s, cyclohex-3-en-4-yl-H), and 6.40 (2 H, m, C*H*=C*H*). The cycloadduct (**5d**) (60 mg) was heated under reflux in benzene (40 ml) under nitrogen for 6 h. The mixture was evaporated and the residue was shown by ^{1}H n.m.r. spectroscopy to contain the cycloadduct (**5d**) (*ca.* 40%) and the 'ene' reaction product (**9**) (*ca.* 60%). The mixture was redissolved in benzene (40 ml) and heated under reflux for 10 h. Evaporation of the solution and crystallisation of the residue from hexane gave the *oxazepinone* (**9**) (25 mg, 58%), m.p. 98—99 °C (Found: C, 56.5; H, 6.5; N, 8.0. $C_8H_{11}NO_3$ requires C, 56.8; H, 6.5; N, 8.3%); $\nu_{max.}$ 3 200 and 1 640 cm^{-1}; δ_H 1.5—2.5 (4 H, m, 8- and 9-H), 2.55 and 2.97 (2 H, ABq with fine splitting, *J* 18 Hz, 7-CH_2), 4.15 (m, 5-H), 4.60 (m, 1-H), 4.98 and 5.18 (2 × br s, vinyl-H), and 8.85 (br s, OH, exch. with D_2O); δ_C 25.4 (8- or 9-C), 25.8 (8- or 9-C), 34.6 (7-C), 64.1 (5-C), 75.8 (1-C), 113.8 [*C*H_2=C(6)], 140.4 (6-C), and 156.6 (3-C); *m/z* 169 (M^+) and 152. The oxazepinone (**9**) gave a purple colour ($\lambda_{max.}$ 575 nm) with ethanolic ferric chloride. When the cycloadduct (**5d**) (180 mg) was heated under reflux in benzene (50 ml) for 18 h the reaction mixture was shown by ^{1}H n.m.r. spectroscopy to contain the cycloadduct (**5d**) (*ca.* 30%) and the oxazepinone (**9**) (*ca.* 70%).

Formation of 4-*Hydroxy*-6-*methylene*-2-*oxa*-4-*azabicyclo*[3.3.1]*nonan*-3-*one* (**10**) *by Thermolysis of the Cycloadduct* (**5e**).—4-Methylcyclohex-3-en-1-ol[19,21] (**1e**) was converted, as described for the 3-methyl isomer, into 4-*methylcyclohex*-3-*enyl* N-*hydroxycarbamate* (**3e**) (72%), m.p. 129—131 °C (from ethyl acetate–light petroleum) (Found: C, 56.0; H, 7.8; N, 8.0. $C_8H_{13}NO_3$ requires C, 56.1; H, 7.6; N, 8.2%); $\nu_{max.}$ 3 330 and 1 680 cm^{-1}; δ_H 1.63 (br s, Me), 1.4—2.5 (6 H, m, 3 × CH_2), 4.8—5.2 (m, 1-H), 5.30 (br s, 3-H), and 7.20 (br s, NH and OH, exch. with D_2O). This carbamate (**3e**) was converted, as before, into 3-(4-*methylcyclohex*-3-*enyloxycarbonyl*)-2-*oxa*-3-*azabicyclo*[2.2.1]*hept*-5-*ene* (**5e**) (71%), m.p. 61—62 °C (from ether-light petroleum) (Found: C, 66.2; H, 7.5; N, 5.9. $C_{13}H_{17}NO_3$ requires C, 66.4; H, 7.2; N, 6.0%); $\nu_{max.}$ 1 750 cm^{-1}; δ_H 1.63 (br s, Me), 1.5—2.4 (8 H, m, 4 × CH_2), 4.90 (m, OCH), 4.97 (br s, NCH or OCH), 5.20 (2 H, br s, NCH or OCH and cyclohex-3-en-3-yl-H), and 6.35 (2 H, m, C*H*=C*H*); *m/z* 235 (M^+). The cycloadduct (**5e**) (60 mg) was heated under reflux in benzene (40 ml) under nitrogen for 6 h. The mixture was evaporated and the residue was shown by ^{1}H n.m.r. spectroscopy to contain the cycloadduct (**5e**) (*ca.* 33%) and the 'ene' reaction product (**10**) (*ca.* 67%). The mixture was redissolved in benzene (40 ml), heated under reflux for 6 h, then evaporated. The *oxazinone* (**10**) crystallised from chloroform–light petroleum as platelets (30 mg), m.p. 190—192 °C (Found: C, 56.55; H, 6.5; N, 8.1. $C_8H_{11}NO_3$ requires C, 56.8; H, 6.5; N, 8.3%); $\nu_{max.}$ 3 180 and 1 680 cm^{-1}; δ_H 1.5—2.3 (6 H, m, 7-, 8-, and 9-H), 4.09 (m, 5-H), 4.55 (m, 1-H), 4.82 (2 H, br s, vinyl-H), and 7.50 (br s, OH, exch. with D_2O); δ_C(CD_3OD) 25.9, 33.5 and 33.5 (8-, 7- and 9-C, not necessarily in this order), 63.6 (5-C), 75.3 (1-C), 112.3 [*C*H_2=C(6)], 145.7 (6-C), and 157.0 (3-C); *m/z* 169 (M^+), 153 and 125. The oxazinone (**10**) gave a purple colour ($\lambda_{max.}$ 550 nm) with ethanolic ferric chloride.

Formation of 4-*Hydroxy*-5-*methyl*-6-*methylene*-2-*oxa*-4-*aza*[3.3.1]*nonan*-3-*one* (**11**) *by Thermolysis of the Cycloadduct* (**5f**).—3,4-Dimethylcyclohex-3-en-1-ol[19,22] (**1f**) was converted, as described for the 3-methyl-derivative (**1d**), into 3,4-*dimethylcyclohex*-3-*enyl* N-*hydroxycarbamate* (**3f**) (33%), m.p. 108—110 °C (decomp.) (from ethyl acetate–light petroleum) (Found: C, 58.5; H, 8.0; N, 7.5. $C_9H_{15}NO_3$ requires C, 58.4; H, 8.2; N, 7.6%); $\nu_{max.}$ 3 330 and 1 684 cm^{-1}; δ_H 1.59 (6 H, s, 2 × Me), 1.3—2.6 (6 H, m, 3 × CH_2), 4.8—5.2 (m, 1-H), and 6.5 and 7.2 (2 × br s, NH and OH, exch. with D_2O). This carbamate (**3f**) was converted, as before, into 3-(3,4-dimethylcyclohex-3-enyloxycarbonyl)-2-oxa-3-azabicyclo[2.2.1]hept-5-ene (**5f**), which was obtained (79%) as an oil after chromatography on silica plates; $\nu_{max.}$($CHCl_3$) 1 730 cm^{-1}; δ_H 1.58 (s, 2 × Me), 1.5—2.6 (8 H, m, 4 × CH_2), 4.90 (m, cyclohex-1-yl-H), 5.02 and 5.24 (2 × br s, OCH and NCH), and 6.40 (2 H, m, C*H*=C*H*); δ_C (multiplicities in parenthesis were obtained by off-resonance decoupling) 18.6 (q), 19.9 (q), 28.1 (t), 29.6 (t), 36.7 (t), 48.1 (t), 65.0 (d), 72.7 (d), 83.6 (d), 122.3 (s), 125.2 (s), 132.9 (d), 134.3 (d), and 159.3 (s). The cycloadduct (**5f**) (200 mg) was heated under reflux in benzene (180 ml) under nitrogen for 18.5 h. The mixture was evaporated and the residue chromatographed on silica plates, developed with chloroform–methanol (9:1), to give the *oxazinone* (**11**) (39%), m.p. 174 °C (from benzene) (Found: C, 59.2; H, 7.2; N, 7.5. $C_9H_{13}NO_3$ requires C, 59.0; H, 7.15; N, 7.65%); $\nu_{max.}$ 3 190 and 1 686 cm^{-1}; δ_H 1.53 (s, Me), 1.5—2.5 (m, 3 × CH_2), 4.5—4.7 (m, 1-H), 4.98 and 5.04 (2 × br s, vinyl-H), and 8.25 (br s, OH, exch. with D_2O); δ_C 21.3 (Me), 27.0, 32.5, and 39.6 (8-, 7-, and 9-C, not necessarily in this order), 61.0 (5-C), 73.3 (1-C), 110.8 [*C*H_2=C(6)], 147.0 (6-C), and 156.4 (3-C); *m/z* 183 (M^+). The oxazinone (**11**) gave a purple colour with ethanolic ferric chloride. Reduction of (**11**) (30 mg) was effected, as described for the *N*-hydroxy-compound (**16**), with an excess of sulphur dioxide in pyridine, with heating under reflux for 8 h, to give 5-*methyl*-6-*methylene*-2-*oxa*-4-*azabicyclo*[3.3.1]*nonan*-3-*one* (12 mg), m.p. 148 °C (from ethyl acetate–light petroleum) (Found: C, 64.6; H, 7.6; N, 8.1. $C_9H_{13}NO_2$ requires C, 64.65; H, 7.8; N, 8.4%); $\nu_{max.}$ 3 220, 3 100, and 1 698 cm^{-1}; $\nu_{max.}$($CHCl_3$) 3 440 and 1 697 cm^{-1}; δ_H 1.41 (s, Me), 1.4—2.9 (6 H, m, 3 × CH_2), 4.72 (m, 1-H), 4.83 (2 H, br s, vinyl-H), and 5.83 (br s, NH, exch. with D_2O); *m/z* 167 (M^+). This product gave no colour with ethanolic ferric chloride.

Preparation of (E)-*Cinnamyl* N-*Hydroxycarbamate* (**3g**) *and*

the Cycloadduct (**5g**).—(*E*)-Cinnamyl alcohol (**1g**) was treated with an excess of phosgene in toluene, as before, at −78 °C for 3 h, and the resulting chloroformate (**2g**) was converted, as before, into the *N*-hydroxycarbamate (**3g**). This was chromatographed on Florisil to give (E)-*cinnamyl* N-*hydroxycarbamate* (**3g**) (44%), m.p. 92—94 °C (from benzene–hexane) (Found: C, 62.2; H, 5.5; N, 7.3. $C_{10}H_{11}NO_3$ requires C, 62.2; H, 5.7; N, 7.25%); $\nu_{max.}$ 3 320 and 1 695 cm^{-1}; δ_H 4.77 (d, *J* 7 Hz, OCH_2), 6.25 (dt, *J* 15 and 7 Hz, CH=C*H*CH_2), 6.64 (d, *J* 15 Hz, C*H*=$CHCH_2$), 7.32 (br s, Ph), and 7.65 (br s, NH and OH, exch. with D_2O); *m/z* 193 (M^+). The *N*-hydroxycarbamate (**3g**) (410 mg) in chloroform (10 ml) was added with stirring to cyclopentadiene (0.33 ml) and tetraethylammonium periodate (642 mg) in chloroform (40 ml) at 0 °C. After 1 h, the mixture was washed successively with aqueous sodium thiosulphate and brine, and was dried ($MgSO_4$) and evaporated. The residue was eluted through a short silica column in chloroform–methanol (95:5) to give 3-[(E)-*cinnamyloxycarbonyl*]-2-*oxa*-3-*azabicyclo*-[2.2.1]*hept*-5-*ene* (**5g**) (64%), m.p. 60.5—62 °C (from ethyl acetate–light petroleum) (Found: C, 70.1; H, 5.6; N, 5.4. $C_{15}H_{15}NO_3$ requires C, 70.0; H, 5.8; N, 5.45%); $\nu_{max.}$ 1 705 cm^{-1}; δ_H 1.72 (1 H, br d, *J* 8 Hz, 7-H), 1.98 (1 H, dm, *J* 8 Hz, 7-H), 4.78 (d, *J* 7 Hz, OCH_2), 5.09 and 5.22 (2 × br s, 1- and 4-H), 6.25 (dt, *J* 15 and 7 Hz, CH=C*H*CH_2), 6.42 (br s, 5- and 6-H), 6.65 (d, *J* 15 Hz, PhC*H*=CH), and 7.32 (br s, Ph); *m/z* 257 (M^+) and 241. The cycloadduct (**5g**) was stable to heating in benzene under reflux for 10 h; after heating in toluene under reflux for 16 h it had decomposed to give a dark, oily multicomponent (t.l.c.) mixture.

Ethyl N-*Ethoxycarbamate* [**15**].—Ethyl chloroformate (2.71 g, 25 mmol) was added dropwise with stirring to ethoxyammonium chloride (2.43 g, 25 mmol) and sodium hydroxide (2 g, 50 mmol) in water (50 ml). The mixture was shaken for 1 h and then worked-up in the usual way to give ethyl *N*-ethoxycarbamate[23] (**15**); $\nu_{max.}$ (liquid film) 3 400, 1 765 and 1 730 cm^{-1}; δ_H 1.19 (t, *J* 7 Hz, Me), 1.24 (t, *J* 7 Hz, Me), 3.90 (q, *J* 7 Hz, $NOCH_2$), 4.18 (q, *J* 7 Hz, OCH_2), and 7.72 (br s, NH, exch. with D_2O).

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