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X = Y - ZH Systems as Potential 1,3-Dipoles Part 35. Generation of Nitrones from Oximes. Class 3 Processes. Tandem Intramolecular Michael Addition (1,3-Azaprotio Cyclotransfer) - Intermolecular 1,3-Dipolar Cycloaddition Reactions.[1,2]

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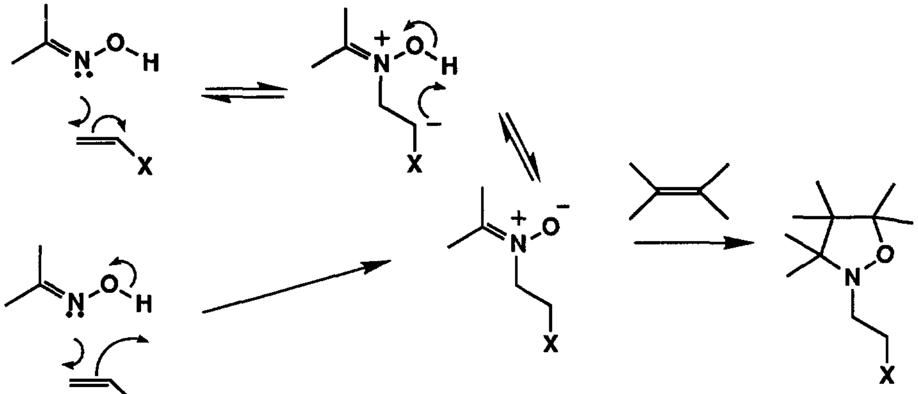
Abstract: *Aldoximes and ketoximes possessing γ- or δ-alkenyl substituents undergo thermal conversion to 5- and 6- membered cyclic nitrones via a 1,3-azaprotio cyclotransfer, a 2n + 2σ + 2π concerted process, rather than a Michael addition. The reactions can be performed as a tandem nitrone formation-cycloaddition sequence or, if required, the intermediate nitrones can be isolated. The cycloadditions usually proceed via an exo-transition state and show both regio- and diastereofacial-specificity. Preliminary attempts at chiral induction via a menthyl auxiliary are reported.*

We have established that the four atom X = Y - ZH systems in which the central Y- atom possesses a lone pair of electrons are sources of 1,3-dipoles via a formal 1,2- prototropy of the ZH proton. The new, general prototropic equilibrium of the neutral (1) and the dipolar (2) species depends on the basicity of the central Y-atom and the acidity of the ZH proton. Although the equilibrium concentration of the dipoles (2) is small they can be readily trapped by suitable dipolarophiles to give five-membered heterocycles in a simple, one pot 2-step sequence. Typical X = Y - ZH systems include imines, oximes and hydrazones.[3,4] We have further exploited the nucleophilicity/basicity of oximes to create a range of tandem nitrone formation - cycloaddition processes[5] in addition to the tandem 1,2-prototropy - cycloaddition sequence.

When oximes react with electronegative alkenes they invariably prefer to undergo a formal Michael addition reaction via the nitrogen lone pair to generate nitrones followed by cycloaddition reactions with a second molecule of alkene (Scheme 1).[2,6] In general, 1,2-prototropy in oximes is a higher energy process compared to the formal Michael addition reaction to an alkene bearing an electronegative substituent. However, we have reported one example where prototropy, in the 2-mono oximes of 1,2,3-triketones, takes precedence over the formal Michael addition to such an alkene (N-methylmaleimide). Here we postulated that the formal 1,2-prototropy is achieved via an intramolecular 1,5-H shift[3].

$$X=\ddot{Y}-ZH \rightleftharpoons X=\underset{H}{\overset{+}{Y}}-\overset{-}{Z}$$

(1) (2)



Scheme 1

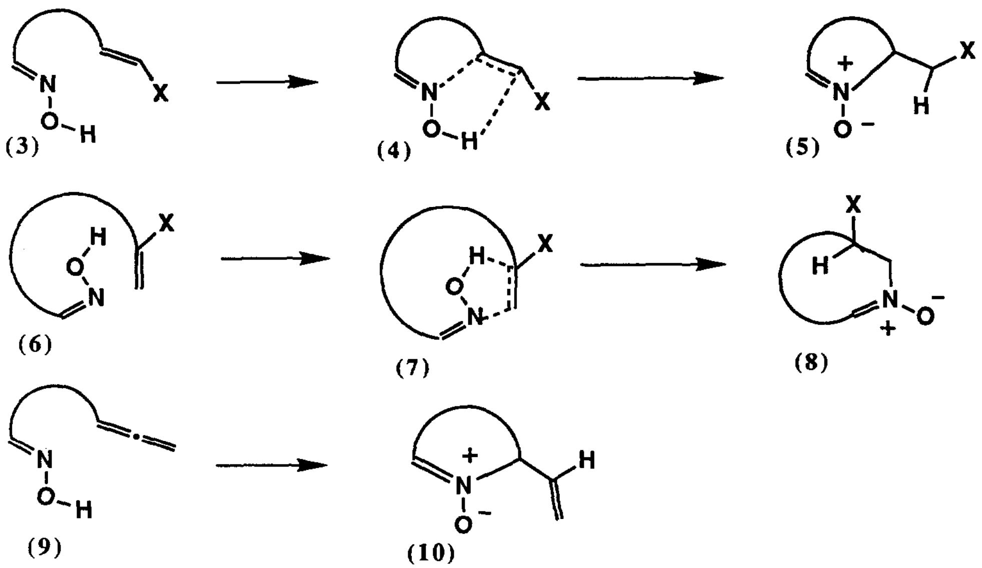
The tandem oxime Michael addition(1,3-azaprotio cyclotransfer) - cycloaddition sequence has four broad synthetic variants (Table)

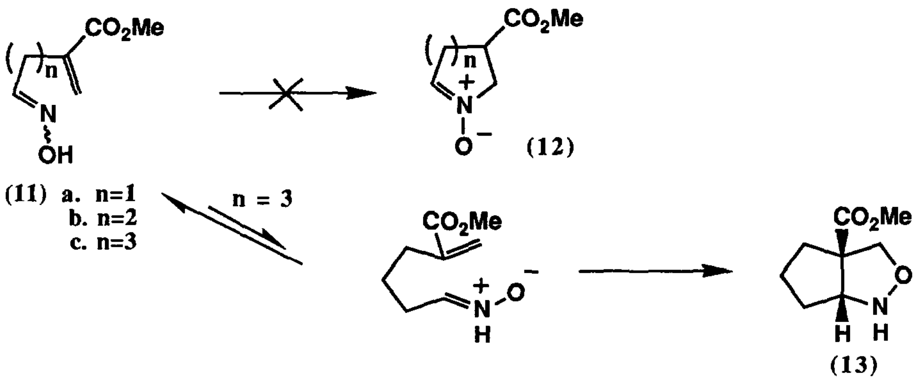
Table Synthetic Variants of the Michael Addition (1,3-azaprotio cyclotransfer) - Cycloaddition Sequence

Class	Nitrone Formation	Cycloaddition
1	intermolecular	intermolecular
2	intermolecular	intramolecular
3	intramolecular	intermolecular
4	intramolecular	intramolecular

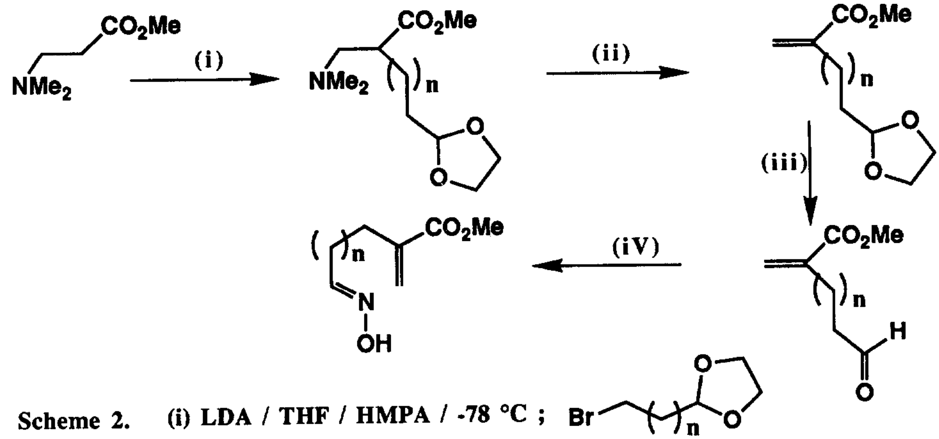
In the preceding papers of this series we have discussed the Class 1[7] and Class 2[1,8] synthetic variants and drawn attention to the fact that the nitrone forming step could involve a Michael addition or an ene like process (Scheme 1). Japanese workers have recently applied our Class 1 methodology to the preparation of sugar derivatives[9]. In this paper we consider Class 3 processes and present evidence in favour of the concerted ene-like mechanism which we designate a 1,3-azaprotio cyclotransfer reaction (see below).

Exo- versus Endo- Trig Cyclisation Processes. The Class 3 process provides a facile new route to cyclic nitrones that can conceptually be achieved either via an exo-trig (or exo-dig) cyclisation (3) → (5) or an endo-trig (or endo-dig) cyclisation (6) → (8). To date we have only explored exo- and endo-trig cyclisations. In addition to our work, Gallagher has reported extensive studies of silver catalysed allenic oxime cyclisations (9) → (10) which also furnish cyclic nitrones.[10]





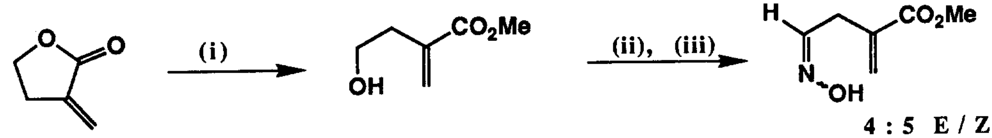
The potential endo-trig cyclisation substrates (11a-c) all failed to cyclise to the corresponding nitrones (12a-c). However (11c) furnished (13) in boiling acetonitrile via the tandem 1,2-prototropy-cycloaddition route in 80% yield (60% conversion)[4]. The alkenyl oximes (11a-c) were prepared according to Schemes 2 and 3.



Scheme 2. (i) LDA / THF / HMPA / -78 °C ; Br

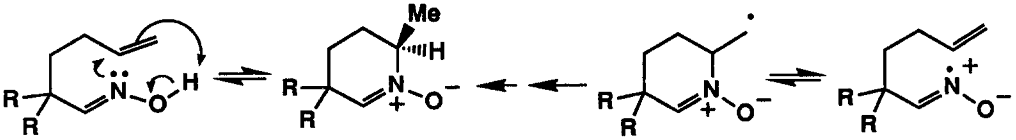
(ii) MeI / MeOH / 25 °C; then DBN / benzene / 80 °C / 2.3h 100 °C

(iii) 1N HCl / 100 °C (iv) NH_2OH



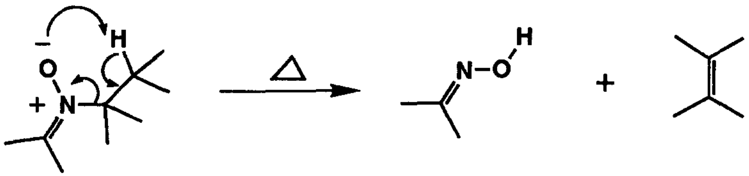
Scheme 3. (i) MeOH / H^+ / 68 °C; (ii) PCC / CH_2Cl_2 / r.t; (iii) NH_2OH

Our initial classification of the nitrone forming step, in the reaction of oximes with electronegative olefins, as a Michael addition process[6] was called into question when we[11] and others[12] observed analogous intramolecular processes, forming 6-membered cyclic nitrones, involving non-activated olefins. We considered two mechanisms for these latter processes one of which is the ene-like process depicted in Scheme 1. The other mechanism involved a radical process. These are summarised in Scheme 4.

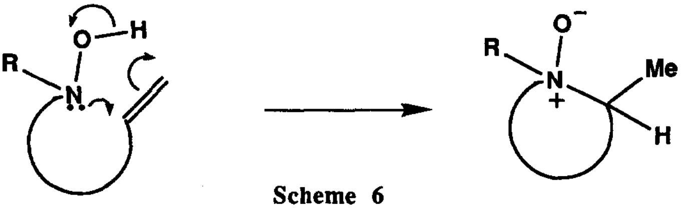


Scheme 4

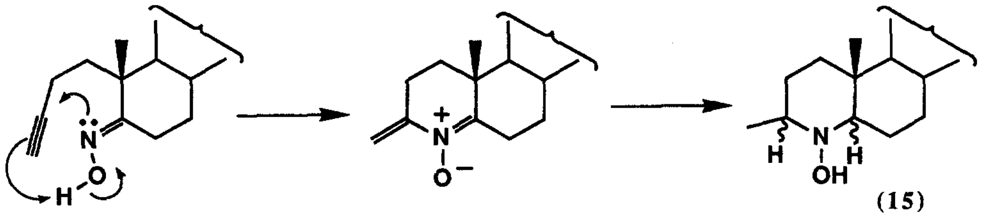
The possibility of a radical cyclisation process was considered because of reports of the cyclisation of δ-alkenyl hydroxylamines to N-hydroxypryrrolidines via a radical chain involving an intermediate nitroxide radical.[13] However, we observed little effect of peroxides or hydroquinone on our cyclisations.[11] Moreover, the acyclic cases of the reverse of the nitrone forming cyclisation, the thermal fragmentation of N-alkyl nitrones (Scheme 5) is known, and in most cases proceeds via a concerted mechanism.[14] Subsequently both Ciganek[15] and Holmes[16] reinvestigated the hydroxylamine-alkene reactions and concluded these were concerted ene-like processes (Scheme 6) and Holmes provided an example of an analogous hydroxylamine-alkyne process. An analogous intramolecular oxime-alkyne ene-like process has been suggested to occur in the borohydride reduction of the secosteroid oxime (14) to a stereoisomeric mixture of hydroxylamines (15)[17]. Earlier work by Padwa on the reaction of hydroxylamines with alkynes can now be reinterpreted in terms of the ene-like process.[18] The acyclic reverse process of Scheme 6 is the well known Cope elimination reaction.[19]



Scheme 5



Scheme 6

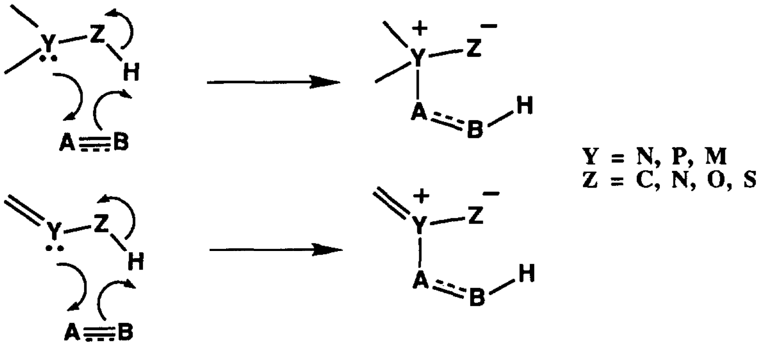


(14)

(15)

Our failure to achieve the endo-trig cyclisations of (11a-c) to the corresponding cyclic nitrones is understandable if an ene-like process is involved. The transition states (4) for the observed exo-trig processes resemble a fused ring system with a C-N double bond at the ring junction whilst the corresponding transition states for the endo-trig processes(7) resemble a highly strained anti-Bredt [n.2.1] system with a bridgehead double bond.

The Ene[20] and Imino - ene[21] reactions differ from the ene-like process in Scheme 1 in that they are $2\pi + 2\sigma + 2\pi$ electron processes proceeding via a 6-membered transition state whereas the novel hydroxylamine and oxime ene-like processes are $2n + 2\sigma + 2\pi$ electron processes (n = lone pair electrons) proceeding via cyclic 5-membered transition states. Thus the topologies and geometrical requirements of the $2\pi + 2\sigma + 2\pi$ and the 2n + 2σ + 2π electron processes are different and observations on the 2π + 2σ + 2π processes are not necessarily relevant to the 2n + 2σ + 2π processes. The new processes can be generalised as shown in Scheme 7 and it is proposed that these processes be called **1,3-Azaprotio Cyclotransfer Reactions** for the case where Y = N.



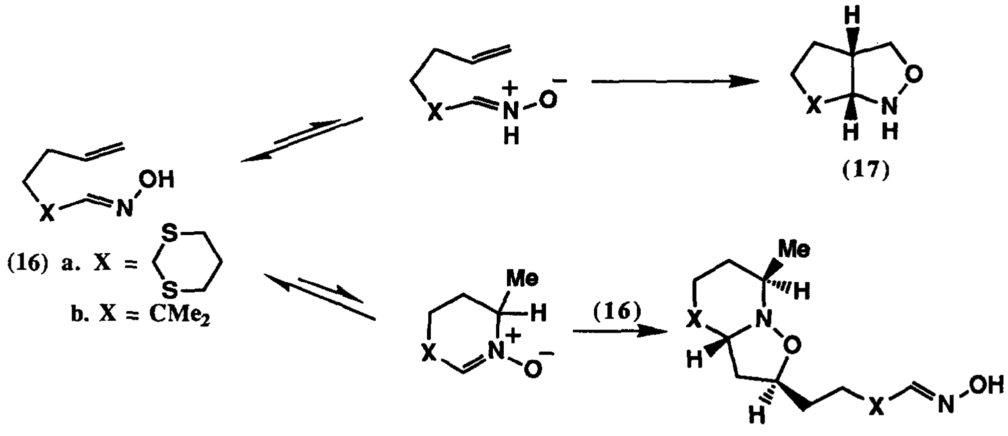
Scheme 7

Conceptually the 2n + 2σ + 2π process can encompass other Y and Z atoms including cases where Y is a metal centre capable of undergoing a 2e redox process. The 1,3-azaprotio cyclotransfer reaction may be in competition with other processes and some examples of this type are considered next.

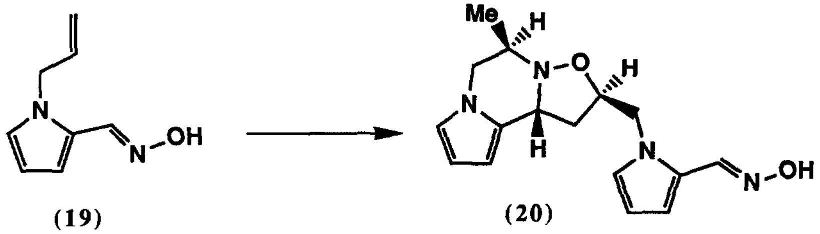
Exo-trig Processes Involving Non-activated Alkenes.

Substrates of this type exhibit two types of nitrone forming processes: 1,2-prototropy and 1,3-azaprotio cyclotransfer. The energetics of the two processes are sensitive to substitution and geometry (below) as shown by the action of heat (xylene, 140°C) on (16a) which gives a 2.8:1 mixture (87%) of (17a) and (18a) (Scheme 8).[4] The dimer (18a) arises from regiospecific cycloaddition of the nitrone to the terminal alkene moiety of (16a) via an exo-transition state. Facial selectivity is controlled by the methyl substituent in the intermediate nitrone with the dipolarophile adding to the least hindered face of the nitrone.

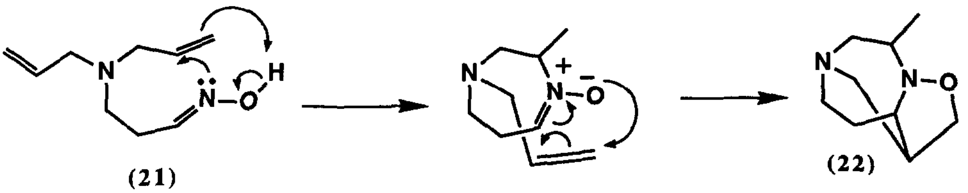
Further study identified other δ-alkenyl oximes that react solely by the 1,3-azaprotio cyclotransfer route and which exhibit the same regio- and stereo- chemical specificity. Thus oxime (16b) reacts (xylene, 140°, 16h) to give (18b) (74%) with no detectable amount of (17b), and (19), under identical conditions, gives a 2:1 mixture (52%) of the syn- and anti- oximes of dimer (20) as the sole product. Thus operation of the Thorpe-Ingold effect and other structural factors which assist attainment of the required transition state geometry promote the 1,3-azaprotio cyclotransfer reaction. A related intramolecular 1,3-azaprotio cyclotransfer-intramolecular cycloaddition[11] will be discussed in a later paper in this series. The cyclisation reaction of the ω-alkenyl oxime (21) previously interpreted as a conventional ene reaction appears to be a further example of a 1,3-azaprotio cyclotransfer.[22], and reinterpretation in this way requires the product be reformulated as (22).

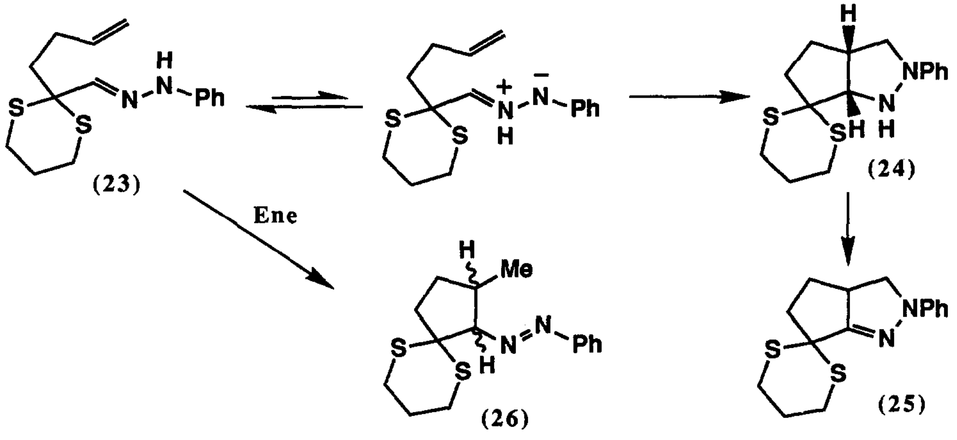


Scheme 8



In contrast to oxime (16a), the corresponding hydrazone (23) on heating in boiling xylene gave a mixture of (24) (20%)[23] and the conventional ene product (26) (38%), together with a trace amount of the pyrazoline (25). The azo-product (26) was obtained as a 2.4:1 mixture of trans- and cis- isomers. No product arising from a 1,3- azaprotio cyclotransfer was observed in this case.

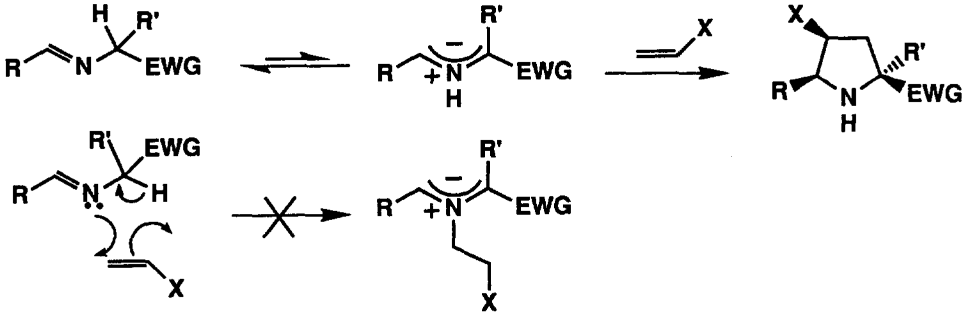




Scheme 9

Our extensive experience of cycloaddition reactions of imines activated by electron withdrawing groups (Scheme 10) has shown these react exclusively by the 1,2-prototropy route, and not by the 1,3-azaprotio cyclotransfer reaction, in all cases studied thus far.[3]

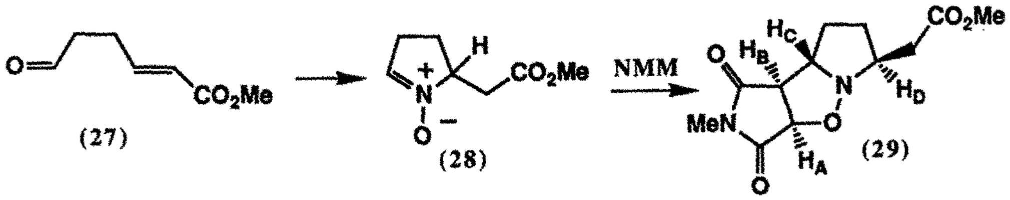
These results call into question the generality of Scheme 7 but we are currently studying the influence of the Thorpe-Ingold effect and acidity of the ZH proton on these latter two classes.



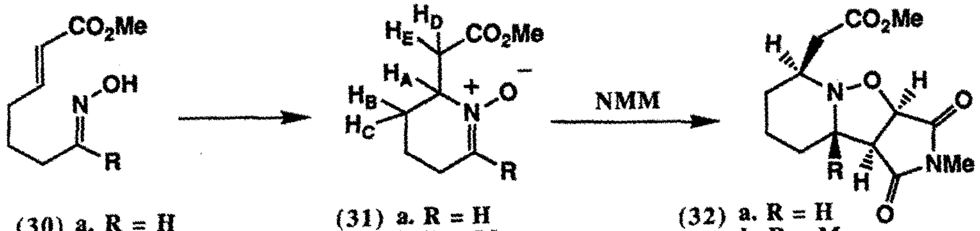
Scheme 10

Exo-trig Processes Involving Activated Alkenes. These processes can be carried out stepwise with isolation of the intermediate nitrone or as a tandem one-pot procedure.

Only one example of a 5-membered cyclic nitrone has been studied. Reaction of aldehyde (27) with hydroxylamine in water at room temperature for 4 h afforded the pyrroline-N-oxide (28)(51%)[24]. Treatment of the nitrone with N-methylmaleimide (NMM) afforded the cycloadduct (29) in 50% yield. Traces of two other isomers were apparent in the p.m.r. spectrum of the crude product but these were not isolated.



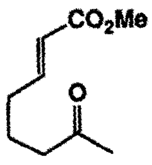
(27) (28) (29)



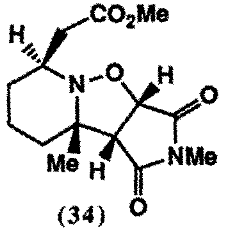
(30) a. R = H
b. R = Me

(31) a. R = H
b. R = Me

(32) a. R = H
b. R = Me



(33)

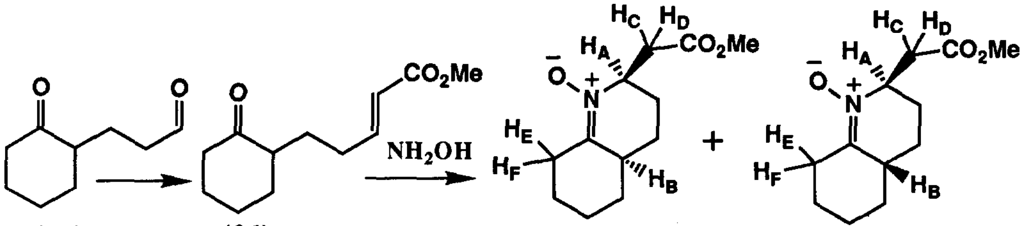


(34)

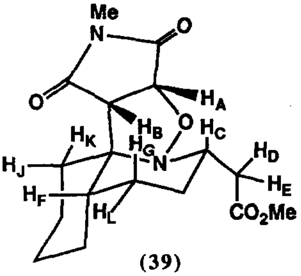
The stereochemistry of (29) was established using n.O.e difference spectroscopy. Thus irradiation ($CDCl_3$) of the signal for H_B caused enhancements of H_A (8%),H_C(3%) and H_D (1%), whilst irradiation of H_A resulted in enhancements of H_B (6%) and H_D (3%). Irradiation of H_D (d_8 -toluene) caused an enhancement of H_A (2%). This assignment is further supported by the coupling constants J_{AB} 7.3 H_Z (H_A/H_B - cis) compared to J_{BC} 1.6 H_Z (H_B/H_C - trans). Thus (29) is derived via an exo-addition of the dipolarophile to the face of the ring opposite to the CH_2CO_2Me group (28).

Oxime (30a) on heating in boiling toluene in the presence of N-phenylmaleimide (NPM) furnishes the cycloadduct (32a) as a single stereoisomer in 70% yield. The product arises via a diastereofacially specific exo-addition of NPM to the intermediate nitrone (31a) on the face trans to the CH_2CO_2Me group. The stereochemistry of (32a) is assigned on the basis of n.O.e. data and decoupling experiments.

The methyl ketone (33) reacts with hydroxylamine in water to give nitrone (31b)[24] in 72% yield. Nitrone (31b) reacts with NMM in chloroform at room temperature to give a 3:1 mixture (100%) of endo-(32b)- and exo- (34)- cycloadducts with the expected diastereofacial specificity. When the cycloaddition is conducted in boiling toluene the product is predominantly (>90%) (32b). Proton H_A gives rise to a multiplet in the p.m.r. spectrum of (31b) due to coupling with adjacent methylene protons H_B and H_C with $J_{AB} + J_{AC}$ ca. $14H_Z$ showing that H_A is pseudo-axial.



(35) (36) (37) (38)



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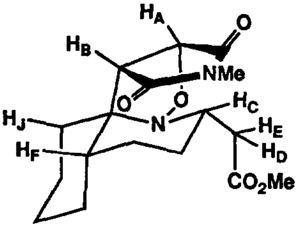

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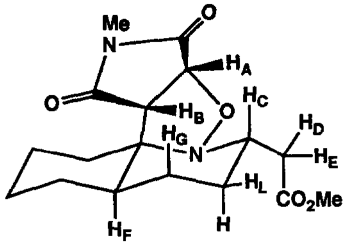
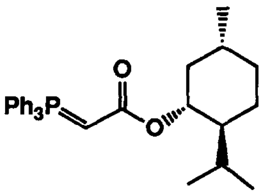


(41)

The keto-ester (36), prepared from the known keto-aldehyde (35) by Wittig olefination, similarly reacts with hydroxylamine to give a 3.3:1 mixture (89%) of nitrones (37) and (38). This mixture of nitrones on treatment with N-methylmaleimide in boiling chloroform gives a 4:3:2 mixture (100%) of (39) - (41) via a diastereofacially specific cycloaddition. The isomers were separated by fractional crystallisation and their stereochemistries were assigned on the basis of n.O.e. data. In the major isomer (39) a multiplet at δ 2.24 in the p.m.r. spectrum is assigned to H_F, since irradiation of this signal did not result in any large geminal proton n.O.e. enhancements and decoupling experiments support this assignment. The stereochemistry of cycloadduct (39) shows it has arisen via an exo-addition of the dipolarophile to the less hindered face of the major cis-nitrone (37). The n.O.e. data of (40) is consistent with the stereochemistry shown although the ring junction proton H_F could not be assigned with certainty due to overlapping signals. Examination of molecular models indicates that the CH_2CO_2Me group should be in an equatorial position to avoid 1,3-diaxial non-bonded interactions. Isomer (40) arises via endo-addition of the dipolarophile from the less hindered face of the nitrone (37). From the n.O.e. data, the minor isomer is assigned structure (41) and is derived from exo-addition of the dipolarophile to the less hindered face of the trans-nitrone (38). Heating the isomeric cycloadducts separately in deuteriochloroform over 36h showed no interconversion of the isomers but some decomposition producing

N-methylmaleimide occurred. When the cycloaddition was carried out under more forcing conditions (d_8-toluene, 110°C, 25h) a 16:4:3 mixture of (39) - (41) was obtained together with trace amounts of another two isomers.



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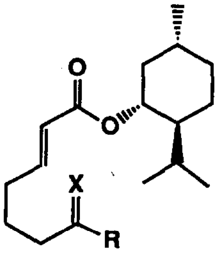
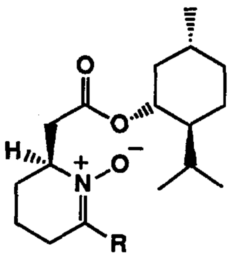
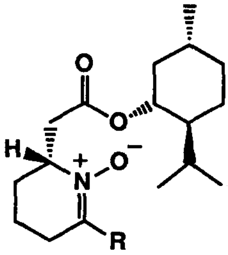


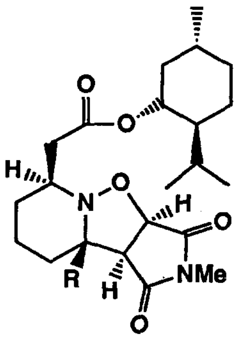
(43) a. R = H, X = O
b. R = H, X = NOH
c. R = Me, X = O



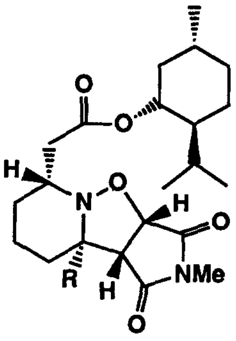
(44) a. R = H
b. R = Me



(45) a. R = H
b. R = Me



(46) a. R = H
b. R = Me



(47) a. R = H
b. R = Me

Attempted Asymmetric Induction. The effect of a chiral auxiliary on the Class 3 processes has been briefly explored. The chiral Wittig reagent (42) was reacted with glutaraldehyde to give (43a). Conversion to the oxime (43b) followed by heating in boiling toluene afforded a 1:1 mixture of diastereomeric nitrones (44a) and (45a). Despite the total lack of induction the cycloaddition of (43b) with NMM in boiling toluene was performed to yield a 1:1 mixture (61%) of diasteromeric cycloadducts (46a) and (47a). One of the cycloadducts was isolated in the pure form by column chromatography followed by fractional crystallisation from ether, m.p. 124-126°C, $\alpha]_D$-22.8°($CHCl_3$). A similar sequence was performed on ketoester (43c) derived from Wittig mono-olefination of the corresponding ketoaldehyde using Wittig reagent (42). Treatment of ketoester (43c) with hydroxylamine in aqueous acetonitrile at room temperature afforded a 13:12 mixture of two diastereomeric nitrones (44b) and (45b)[25]. The nitrone mixture readily decomposes and the individual diastereomers could not be separated. When the nitrone mixture was treated with NMM in boiling toluene it afforded a ca. 1:1 mixture of cycloadducts (46b) and (47b) together with a small amount of an unidentified third isomer. Again only one of the major diastereomeric cycloadducts was isolated in the pure form. The mixture of diastereomeric nitrones (44b) and (45b) reacted with NMM in chloroform at room temperature to produce the same mixture of cycloadducts.

Experimental Melting points were determined on a Koffler hot-stage apparatus and are uncorrected. Infrared spectra were recorded on Perkin-Elmer Model 598 and 983 G instruments and refer to potassium bromide discs unless otherwise noted. Mass spectral data were obtained from VG 7070 and Autospec instruments operating at 70 eV. Nuclear magnetic resonance spectra were recorded on Bruker WM250, QE300 and Bruker AM400 instruments operating at 250, 300 and 400 MHz respectively. Unless otherwise specified deuteriochloroform was used as solvent. Microanalyses were obtained using a Carbo Erba MOD 11016 instrument. Preparative t.l.c. plates were prepared using silica gel 60 PF(Merck 7748). Column chromatography was performed with silica gel 60(Merck 9385). Petroleum ether refers to the fraction with b.p. 40-60°C. 5-Carbomethoxy-4-pentenal[26], 3-(2^1-oxocyclohexyl) propanal,[27] and methyl hept-2-enoate-7-al[28] were prepared by the literature methods.

Aldehydes and Ketones.

2-(4'-N-N-Dimethyl-3'-carbomethoxybutyl)-1,3-dioxolane. Methyl 3-N,N-dimethyl aminopropionate (10g, 76 mmol) was added to a stirred solution of lithium diisopropylamide (83.9 mmol) [from 1.6M n-BuLi (57.25ml) and Pr^i_2 NH (8.4g)] in dry THF (150 ml) at
-78°C under an atmosphere of nitrogen. After 30 min a solution of 2-(2^1-bromoethyl)-1,3-dioxolane (14.5g, 80 mmol) in HMPA (16ml) was added dropwise over 15 min. The resulting mixture was stirred and allowed to warm to room temperature over 1 hr., quenched with saturated ammonium chloride solution (50ml) and partitioned between ether and water.

The aqueous layer was further extracted with ether and the combined ether extract washed with brine and then with water, dried ($MgSO_4$) and the solvent removed under reduced pressure. The residual oil was purified by chromatography (SiO_2, ether) and distilled to afford the product as a colourless oil (4.4g, 25%), b.p. 100°C/0.7mm Hg. (Found: C, 56.95; H, 9.4; N, 6.2. $C_{11}H_{21}O_4N$ requires C, 57.1; H, 9.15; N, 6.05%); δ 4.85 (brs, 1H, OCHO) 3.9 (m, 4H, 2xCH_2O), 3.71(s, 3H,OMe). 2.6(m, 2H, CH_2N), 2.25 (m, 1H, $C\underline{H}CO_2Me$), 2.2 (s, 2x3H, 2xNMe) and 1.6 (brs, 4H, 2xCH_2); $^m/_z$(%) 231(M^+,4), 73(39) and 58(100).

2-(3'-Carbomethoxybut-3'-enyl)-1,3-dioxolane. A solution of 2-(4'-N,N-dimethyl-3'-carbomethoxybutyl)-1,3-dioxolane (3.7g, 16mmol) and methyliodide (34.2g, 240mmol) in methanol (40ml) was kept at room temperature in the dark for 18 h. The solvent and excess methyliodide were then removed under reduced pressure, the residue suspended in a solution of diazabicyclononane (5.9g, 478 mmol) in benzene (50ml) and the mixture boiled under reflux for 2.5 h. The cooled solution was then washed with 1M hydrochloric acid and water, dried ($MgSO_4$) and the solvent removed under reduced pressure. The residual oil was distilled to afford the product (1.7g, 57%) b.p. 60-63°C/0.5mm Hg. (Found: C, 57.8; H, 7.6. $C_9H_{14}O_4$ requires, C, 58.05; H, 7.55%); δ 6.18 and 5.55 (2xs, 2x1H, CH_2 =), 4.84 (t, 1H, J 1.5H_Z, OCHO), 3.9 (m, 4H, 2x$CH_2$0), 3.68(s, 3H, OMe), 2.35 (m, 2H, CH_2), and 1.6 (m, 2H, CH_2); ${}^m/_z$ (%) 186 (M^+,2) and 73 (100).

4-Carbomethoxy-pent-4-enal 2-(3'-Carbomethoxybut-3'-enyl)-1,3-dioxolane (1.4g) was dissolved in a mixture of THF (30ml) and 1M hydrochloric acid (40ml) and the solution boiled under reflux for 4.5h. Work-up in the usual way followed by molecular distillation afforded the product (0.8g, 75%) as a colourless oil, b.p. 28-30°C/0.05mm Hg (furnace temp.). (Found; C, 59.0; H, 6.85. $C_7H_{10}O_3$ requires C, 59.1 and H, 7.1%); δ 9.8 (br s, 1H, CHO), 6.2 (s, 1H,CH =), 5.6 (s, 1H, CH =), 3.8 (s, 3H, OMe), 2.6(m, 2H, CH_2 CHO), 1.9 (m, 1H) and 1.7 (m, 1H).

2-(5'-N,N-Dimethyl-4'-Carbomethoxypentyl)-1,3-dioxolane. Methyl 3-N,N-dimethylaminopropionate (3.8g, 29mmol) was added to a stirred solution of lithium diisopropylamide (32mmol) [from 1.6M n-BuLi (19.9ml) and isopropylamine (3.22g)] in dry THF (100ml) at -78°C under an atmosphere of nitrogen. After 30 min. a solution of 2-(3'-bromopropyl)-1,3-dioxolane (5.9g, 30 mmol) in HMPA (5.6ml) was added dropwise over 15 min. The resulting mixture was stirred and allowed to warm to room temperature over 1h, quenched with saturated aqueous ammonium chloride (30ml) and partitioned between ether and water. The aqueous layer was further extracted with ether and the combined ether extract washed with brine and then with water, dried ($MgSO_4$), and the solvent removed under reduced pressure. The residual oil was purified by flash chromatography (SiO_2, ether) to afford the product as a colourless oil (2g,28%), b.p. (mole still, furnace temp.) 67-70°C/0.1mm Hg. (Found: C, 58.45; H, 9.75; N, 5.55. $C_{12}H_{23}O_4$ requires C, 58.75; H, 9.45; and N, 5.75%); δ 4.83 (t, 1H, OCHO), 3.88 (m, 4H, 2xCH_2O), 3.69 (s, 3H, OMe), 2.64(m, 2H, CH_2N), 2.22 (m, 1H, CH CO_2Me), 2.20 (s, 6H, NMe_2) and 1.38-1.68(m, 6H, 3xCH_2); ${}^m/_z$(%) 245 (M^+,3).

2-(4'-Carbomethoxypent-4'-enyl)-1,3-dioxolane. A solution of 2-(5'-N,N-dimethyl-4'-carbomethoxypentyl)-1,3-dioxolane (2.7g, 11 mmol) and methyliodide (18.8g, 132 mmol) in methanol (30ml) was kept at room temperature in the dark for 18 h. The solvent and excess methyl iodide were then removed under reduced pressure, the residue suspended in a solution of diazabicyclononane (2g, 16.2 mol) in benzene (30ml) and the mixture boiled under reflux for 2.5h. The cooled solution was then washed with 1M hydrochloric acid and water, dried ($MgSO_4$), and the solvent removed under reduced pressure. The residual oil was purified by molecular distillation to afford the product (1.3g, 60%) as a colourless oil, b.p. 32°C (furnace temp.)/0.2 mm Hg. (Found: C, 59.75; H, 8.1. $C_{10}H_{16}O_4$ requires C, 60.0; H, 8.05%); δ 5.55 and 6.15 (2xs, 2X1H, = CH_2), 4.87 (t, 1H, J 4.6Hz, OCHO), 3.9 (m, 4H, 2xCH_2O) 3.75 (s, 3H, OMe), 2.35(m, 2H, = CCH_2) and 1.66 (m, 4H, 2xCH_2); ${}^m/_z$(%) 200 (M^+, 2), 139 (60) and 73 (100).

5-Carbomethoxyhex-5-ene-1-al. 2-(4'-Carbomethoxyhex-4'-enyl)-1,3-dioxolane (1.3g) was dissolved in a mixture of THF (30ml) and in 1N hydrochloric acid (40ml) and the solution boiled under reflux for 4.5h. Work up in the usual way followed by molecular distillation afforded the product (0.79g, 80%) as a colourless oil, b.p 30-32°C (furnace temp.)/0.2 mm Hg. (Found: c, 61.7; H, 7.5. $C_8H_{12}O_3$ requires C, 61.5; H, 7.75%); δ 9.8 (t, 1H, J 1.5 Hz, CHO), 6.2 and 5.6 (d and m, 2x1H, = CH_2), 3.7 (s, 3H, OMe), 2.5 (m, 2H, CH_2 CHO), 2.3 (t, 2H, J 7.5Hz, = CCH_2), and 1.85 (m, 2H, CH_2).

3-Carbomethoxybut-3-enal Pyridinium chlorochromate (2.48g, 11.5mmol) in dry methylene chloride (30ml) was stirred magnetically and a solution of 3-carbomethoxy-but-3-enol (1g, 7.6 mol) [obtained by opening

(MeOH/H^+) of the known lactone (Scheme 3)] in methylene chloride (15ml) was added in one portion. The mixture was stirred for 2h. at room temperature and then dry ether (50ml) was added. The solution was decanted off and the residue washed with ether (2x20ml). The combined organic phase was then filtered through florisil and the solvent removed under reduced pressure. The residual oil was molecularly distilled to give 3-carbomethoxybut-3-enal as a colourless oil (0.54g, 55%). b.p 50-54°C/0.6mm Hg. (Found: C, 56.3; H, 6.3. $C_5H_8O_3$ requires C, 56.25; H, 6.3%); δ 9.7(s, 1H, CHO), 6.42 and 5.75 (2xS, 2x1H, CH_2 =), 3.78 (s, 3H, OMe) and 3.43 (s, 2H, $C\underline{H}_2$ CHO); $^{m}/_{z}$(%) 128 (M^+,50), 99 (100) and 97 (39).

Methyl trans-7-oxo-2-octenoate(33). Prepared in four steps from ethyl acetoacetate.

(i) 1-[2'-(1',3'-Dioxolanyl]-3-carboethoxypentan-4-one.

To a solution of the sodio ethyl acetoacetate [prepared from ethylacetoacetate (26g, 0.2 mol) and sodium (4.6g, 0.2 mol)] in boiling ethanol (150ml) was added 2-(2-bromoethyl)-1,3-dioxolane (36.2g, 0.2 mol) with stirring over a 1h. period. The solution was boiled under reflux for a further 10h. The solvent was then removed and the residue extracted with ether, washed with water dried (anhy Na_2SO_4) and the solvent removed. Distillation of the residual oil under reduced pressure afforded the product, b.p 106-115°C/0.05 mm Hg, as a colourless liquid (23g, 50%) (Found : C, 57.35; H, 7.7. $C_{11}H_{18}O_5$ requires, C, 57.4; H, 7.9%). υmax (film) 2980, 2890, 1740, 1710 and 1145 cm^{-1}; δ 4.75 (t, 1H, acetal CH, J 4.5 Hz), 4.09 (q, 2H, $OC\underline{H}_2Me$), 3.79 (m, 4H, acetal CH_2CH_2), 3.42 (t, 1H, $C\underline{H}$, J 7.4 Hz), 2.13 (s, 3H, Me), 1.86 (m, 2H, CH_2), 1.56 (m, 2H, CH_2), and 1.16 (t, 3H, OCH_2Me); $^{m}/_{z}$(%) 230 (M^+,11), 100(11), 99(17) and 73(100).

(ii) 1-[2'-(1',3'-Dioxolanyl)]-pentan-4-one. A mixture of the foregoing acetal ester (20.7g, 0.09mol), and 5% aqueous sodium hydroxide solution (216ml, 0.27 mol) was boiled and stirred under reflux for 16h. After cooling the reaction mixture was extracted with ether (4x100ml). The organic phase was dried (Na_2SO_4) and evaporated to afford the crude keto-acetal (12.5g, 88%). Distillation gave the product b.p 99-101°C/35mm Hg. (lit^{29}., b.p 124-125°C/18 mm Hg) as a colourless liquid. δ 4.85 (t, 1H, J 4.2Hz, acetal CH), 3.91 (m, 4H, acetal CH_2CH_2), 2.50 (t, 2H, CH_2CO), 2.14 (s, 3H, Me) and 1.68 (m, 4H, $2xCH_2$).

(iii) 5-Oxo-hexanal. To a cooled solution of the keto-acetal (7.9g, 50 mmol) in tetrahydrofuran (100ml) was added, dropwise with stirring 1M hydrochloric acid (150ml, 150 mmol). The solution was allowed to warm to room temperature and then stirred for 22h. After neutralisation with $NaHCO_3$ (15.9g, 150mmol) the product was extracted with methylene chloride. The organic phase was dried (Na_2SO_4), evaporated and the residue distilled to afford 5-oxo-hexanal (3.2g, 56%), b.p 76-78°C (5mm Hg) (lit^{30}., b.p 65°C/0.1mm Hg) as a colourless liquid. δ 9.76 (t, 1H, CHO), 2.51, (q, 4H, CH_2CH_2), 2.15 (s, 3H, Me) and 1.88 (m, 2H, CH_2).

(iv) Methyl trans-7-oxo-2-octenoate. A solution of carbomethoxymethylene-triphenylphosphorane (8.35g, 25 mmol) in methylene chloride (25ml) was added dropwise with stirring to a solution of 5-oxo-hexanal (2.85g, 25mmol). The reaction mixture was allowed to stir overnight at room temperature. After removal of the solvent the residue was triturated repeatedly with ether to remove the bulk of the triphenylphosphine oxide. Distillation of the residual oil afforded the product (3g, 71%) as a colourless liquid, b.p 84-90°C/0.7mm Hg. (Found: C, 63.4; H, 8.4. $C_9H_{14}O_3$ requires C, 63.5; H, 8.3%); υ_{max} (film). 2950, 1720, 1655, 1445, 1275, 1200-1150 (3 bands), 1045 and 985 cm^{-1}; δ 6.93 (d of t, 1H, J 6.9 and 15.7Hz, $CH_2C\underline{H}$=C), 5.84 (d of t, 1H, J 1.5 and 15.6Hz, $C\underline{H}CO_2Me$), 3.73 (s, 3H, Me), 2.48 (t, 2H, CH_2CO), 2.22 (m, 2H, allylic CH_2), 2.15 (s, 3H, Me) and 1.75 (m, 2H, CH_2); $^{m}/_{z}$(%) 170 (M^+,1), 138 (53), 113(48), 100(30), 81(34) and 43(100). Only a trace of the cis-product was detected.

Methyl trans-5(2'-oxocyclohexyl)-2-pentenoate (36). A solution of Carbomethoxymethylene-triphenyl phosphorane (10.02g, 0.03 mol) in methylene chloride (30ml) was added dropwise with stirring to a solution of 3-(2'-oxocyclohexyl)-propanal (4.62g, 0.03mol) in methylene chloride (30ml). The reaction mixture was stirred overnight at room temperature. The solvent was removed and the residue triturated with ether to remove the bulk of the triphenylphosphine oxide. This process was repeated several times after which the ether was removed. The residual oil was distilled to afford the pure keto-ester (36) (4.3g, 68%) as a colourless liquid. b.p 120-125°C/0.05mm Hg. (Found: C, 68.35; H, 8.75. $C_{12}H_{18}O_3$ requires C, 68.55; H, 8.65%); δ 6.95 (d of t, 1H, J 6.9 and 15.6Hz, CH=$CHCO_2Me$), 5.83 (d of t, 1H, J 1.5 and 15.7Hz, = $CHCO_2Me$), 3.73 (S, 3H, OMe) and 2.38- 1.25(m, 13H, $6xCH_2$, methine CH). A small amount, ca. 5% of cis-product was also detected which exhibited the following p.m.r. signals: δ 6.2 and 5.8 (2xd of t, 2x1H, olefinic) and 3.70 (S, 3H, OMe).

(L)-Carbomenthyloxymethylene triphenylphosphorane (42). L-Menthyl bromoacetate[31] was reacted with triphenyl phosphine in benzene using the procedure for the corresponding methyl ester. Basification of the salt with 1N sodium hydroxide afforded the product (62%) which crystallised as colourless prisms from ether, m.p. 156-158°C (Found: C, 78.55; H, 7.85. $C_{30}H_{35}O_2P$ requires C, 78.55; H, 7.7%); δ7.42-7.69 (m, 15H, 3xPh), 4.55 (br t, 1H, CH=P), 2.84 (brs, 1H, CHO), 1.91 (brs, 1H), 1.39-1.59 (br m, 3H), 0.60-0.97 (m, 14H); $^m/_z$ (%) 458 (M^+, 31), 414(16), 321(40), 320(100), 318(50), 302(89), 274(56), 261(19), 195(14), 182(48), 164(28) and 94(16).

(L)-Menthyl trans-hept-2-enoate-7-al (43a). (L)-Carbomenthoxymethylene triphenylphosphorane (8.5g, 0.0186 mol) in dry methylene chloride (50ml) was added dropwise to glutaraldehyde (6.0g, 0.06 mole) in dry methylene chloride (50ml). The solution was stirred under nitrogen at room temperature for 18 hrs. and the solvent removed under reduced pressure. The residue was triturated several times with diethyl ether to remove the crystalline triphenyl-phosphine oxide and further purified by flash-chromatography (ether) to give a colourless liquid (4.40g, 85%). The product was distilled using a short path distillation apparatus to give a colourless oil (b.p 155-165°C at 0.1mm Hg). (Found: C, 72.55; H, 10.2. $C_{17}H_{28}O_3$ requires C, 72.8; H, 10.05%); δ 9.78 (S, 1H, CHO), 6.90 (dt, 1H, J 6.9 and 15.6Hz, CH_2CH=CH), 5.83 (dt, 1H, J 1.3 and 15.6Hz, CH_2CH=CH), 4.74 (ddd, 1H, J 4.4Hz, CH-O), 2.51 (t, 2H, J 7.2Hz), 2.25 (m, 2H), 0.93 - 2.03 (m, 11H), 0.90 (q, 6H, 2xMe), 0.76 (d, 3H, J 6.95Hz, Me); $^m/_z$(%) 279(M-H, 21), 278(76), 277(100), 201(36), 199(31), 183(29), 167(7), 152(18), 138(81), 125(55), 95(77) and 81(86).

(L)-Menthyl trans-7-oxo-2-octenoate (43c). To a stirred solution of 5-oxo-hexanal (1.0g, 8.77mmol) in dry methylene chloride (35ml) was added dropwise (L-)-Carbomenthyloxymethylenetriphenylphosphorane (4.0g, 8.77 mmol) in dry methylene chloride (20ml) under a nitrogen atmosphere. The solution was stirred at room temperature for 16 hrs. and the solvent removed under reduced pressure. The residue was triturated several times with ether to remove the crystalline triphenylphosphine oxide and purified by flash chromatography (ether, silica gel) to give a colourless oil. (2.26g; 88%). (Found: C, 73.35; H, 10.4. $C_{18}H_{30}O_3$ requires C, 73.5 and H, 10.3%); δ 6.90 (dt, 1H, J 6.9 and 15.6 Hz, = $CHCH_2$), 5.82 (dd, 1H, J 1.4 and 15.6Hz, CHCO), 4.74 (ddd, 1H, J 4.4 Hz, CHO), 2.47(t, 2H, J 7.3 Hz, CH_2CO), 2.21 (m, 2H, CH_2), 2.15 (s, 3H, CH_3CO), 2.04 - 0.86 (m, 11H), 0.90 (2xd, 6H, J. 2.6 and 3.1 Hz, 2xMe), 0.76 (d, 3H, J 6.95 Hz, Me); $^m/_z$(%) 294 (M^+, 0.5), 278(7), 277(16), 235(6), 156(33), 139(45), 138(100), 123(23), 111(39), 110(10), 97(19) and 83(63).

Oximes and Hydrazones

3-Carbomethoxybut-3-enyl oxime (11a). Prepared in the usual way in aqueous acetonitrile. The product (85%) was a colourless oil, which comprised a 4:5 mixture of E- and Z- isomers. (Found: C,50.1; H, 6.35; N, 9.85. $C_6H_9O_3N$ requires C, 50.35, H, 6.35 and N, 9.8%); δ 8.5 (brs, 1H, NOH), 7.5 (t, 1H, J 6Hz, E- CH = N), 6.8 (t, 1H, J 5.3 Hz, Z- CH = N), 6.28 and 6.3 (2xs, 2x1H, E- and Z- CHH =), 5.67 and 5.72 (2xs, 2x1H, E- and Z- CHH =), 3.78 (s,3H, OMe), 3.4 (d, 1H, J 5.1 Hz, CHHCH = NOH) and 3.22 (d, 1H, J 5.8Hz, CHHCH = NOH); $^m/_z$(%) 143 (M^+,6), 59(40) and 31(100).

4-Carbomethoxy-pent-4-enyloxime (11b). Prepared from the corresponding aldehyde in the usual manner in aqueous acetonitrile. The product (83%) was a colourless liquid which comprised a 7:5 mixture of E- and Z-isomers. (Found: C, 53.5; H, 7.6. $C_7H_{11}NO_3$ requires, C, 53.6; H, 7.35%); δ 8.1 and 8.6 (2xbrs, 2x1H, 2xNOH), 7.42 (t, 1H, J 5.6Hz, E- CH=N), 6.7 (brs, 1H, Z-CH=N), 6.2 and 5.6 (2xs, 2x1H, $C\underline{H}_2$=), 3.76 (s, 3H, OMe), and 2.4-2.6(m, 4H, 2xCH_2); $^{m}/_{z}$ (%) 157 (M^+,3) and 98 (30).

5-(Carbomethoxy)-5-hexenyl oxime (11c). A solution of the corresponding aldehyde (500 mg, 3.2 mmol) in acetonitrile (15ml) was added to a solution of hydroxylamine hydrochloride (250mg, 3.5mmol) and sodium acetate (320mg, 3.8mmol) in water (5ml). The resulting solution was stirred at ambient temperature for 3h and then extracted with chloroform 2x20ml). The combined organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The product (410mg, 81%) was a colourless liquid which comprised a 3:2 mixture of E- and Z- isomers. (Found: C, 55.9; H, 7.65; N, 7.65. $C_8H_{13}NO_3$ requires C, 56.15; H, 7.65 and N, 8.2%); δ 7.4 (t, 1H, E- CH=N), 6.8 (brs, 1H, Z- CH=N), 5.5 and 6.2 (2xm, 2x2H, C=CH_2), 3.76 and 3.75 (2xs, 2x3H, E- and Z- CO_2Me), 2.3 (t, 2x2H, J 7.6Hz, 2x$C\underline{H}_2C$=CH_2), 2.2 (q, 2x2H, J 6.9Hz, 2x$C\underline{H}_2$CH=N) and 1.69 (m,2x2H, 2xCH_2).

2,2-Dimethyl-5-hexenal oxime (16b). A mixture of 2,2-dimethyl-5-hexenal (1.68g, 0.013mol)[32], hydroxylamine hydrochloride (1.11g, 0.016 mol) and sodium acetate (1.64g, 0.02mol) was stirred at room temperature in water (5ml) and acetonitrile (20ml) for 3 hrs. The solvent was removed and the residue extracted with methylene chloride. The methylene chloride extract was evaporated and the residual oil distilled to afford the Z- oxime as a colourless liquid (1.65g, 88%), b.p 38-40°C/0.03mmHg. (Found: C, 67.85; H, 10.95; N, 10.15. $C_8H_{15}NO$ requires C, 68.05; H, 10.7 and N, 9.9%); δ 9.05 (brs, 1H, OH), 7.32 (s, 1H, CH=N), 5.79 (m, 1H, CH=), 4.98 (m, 2H, CH_2=), 2.02 (m, 2H, CH_2C=), 1.49 (m, 2H, CH_2CMe_2) and 1.10 (s,6H, 2xMe); $^{m}/_{z}$(%) 141 (M^+,3), 126(27), 124(33), 100(13), 98(10), 87(100) and 83(15).

2-(But-3'-enyl)-2-formyl-1,3-dithianyl phenylhydrazone (23) A solution containing 2- (but-3'-enyl)-2-formyl-1,3-dithiane (2.0g, 9.90 mmol) and phenylhydrazine (1.1ml, 11.18mmol) was stirred at room temperature in dry ethanol (40ml) for 16 hrs. The solvent was removed under reduced pressure to give a yellowish solid, which was crystallised from ether - pet ether (40-60°C) to give the product (2.2g; 76%) as colourless prisms, m.p 103°C. [Found: C, 61.55; H, 6.8; N, 9.45; S, 21.95. $C_{15}H_{20}N_2S_2$ requires C, 61.6; H, 6.9; N, 9.55 and S, 21.95%]; δ 7.45 (s, 1H, NH), 7.26 (t, 2H, ArH), 7.02 (d, 2H, ArH), 6.95 (s, 1H, CH=N), 6.86 (t, 1H, ArH), 5.81 (m, 1H, CH=), 5.02 (m, 2H, =CH_2), 3.21 (m, 2H), 2.72 (m,2H), 2.30 (m, 2H), and 1.88 - 2.12 (m, 4H); $^{m}/_{z}$(%) 292 (M^+,87), 237(20), 218(34), 217(73), 200(12), 187(13), 185(12), 177(10), 160(10), 145(25), 126(34) and 93(100).

Methyl hept-2-enoate-7-al oxime (30a) To a stirred solution of methyl hept-2-enoate-7-al(1.0g, 6.41mmol)[28] in acetonitrile (10ml) was added a solution of hydroxylamine hydrochloride (0.54g, 7.77mmol) and sodium acetate (0.79g, 9.63mmol) in water (5ml). The solution was stirred at room temperature for 3 hrs. The usual work up followed by crystallisation from ether afforded the product (0.78g, 72%) as a colourless prisms which comprised a 1:3 mixture of E- and Z- isomers, m.p. 85-87°C (Found: C, 56.25; H, 7.7; N, 8.25. $C_8H_{13}NO_3$ requires C, 56.15; H, 7.65 and N, 8.20%); υ_{max} 3200, 1715, 1642, 1435, 1330, 1200, 932 and 720 cm^{-1}; δ (mixture) 8.9 and 8.5 (brs, 2xOH), 7.43 (t, 1H, J 6.0Hz, E-CH=N), 6.96 (m, 2x1H, $C\underline{H}$=$CHCO_2Me$), 6.73 (t, 1H, J 5.5Hz, Z- CH=N), 5.86 (dt, 2x1H, J 2.6 and 15.9Hz, $C\underline{H}CO_2Me$), 3.74 (s, 2x3H, OMe), 2.43 (m, 2x2H), 2.28 and 1.68 (2xm, 8H, 4x2H).

(L)-Menthyl trans-hept-2-enoate-7-al oxime (43b). (L)-Menthyl trans-hept-2-enoate-7-al (2.82g, 0.0096mol) in acetonitrile (25ml) was added to the stirred solution of hydroxylamine hydrochloride (0.84g, 0.012mol) and sodium acetate (1.25g, 0.015mole) in water (10ml). The solution was stirred at room temperature for 5 hrs. and worked-up as usual by extraction into methylene chloride. The product was purified by flash chromatography (1:1v/v ether-pet ether) to give a colourless oil (2.36g, 79%), whose p.m.r. spectrum indicated it comprised a 1:1 mixture of two isomers, (Found: C, 69.35; H, 10.1; N, 5.1. $C_{17}H_{29}NO_3$ requires, C, 69.1; H, 9.9 and N, 4.75%); δ (mixed isomers): 9.25 and 8.82 (br,2x1H, OH), 7.43 and 6.72 (t, 2x1H, J 5.9 and 5.1 Hz resp, CH=NOH), 6.93 (m, 1H, CH=CHCO), 5.84 (d, 1H, J 8.25Hz, CHCO), 4.73 (m, 1H, CH-O), 2.42 (q, 1H, J 7.4Hz, CH), 2.23 (m, 3H), 1.76-2.04 (m, 2H), 1.70 (q,4H, J 7.3Hz), 1.36-1.60(m,3H), 1.05 (m,2H), 0.90 (q, 6H, J 3.2Hz, 2xMe), 0.76 (d,3H, J6.9Hz,Me); $^m/_z$(%) 295 (M^+,72), 280(96), 255(25), 237(27), 158(74), 140(79), 139(100), 123(43), 95(98) and 81(95).

General Procedure for the Synthesis of Nitrones

A mixture of the keto- or aldehyde-ester (5mmol), hydroxylamine hydrochloride (7.5mmol) and sodium carbonate (3.75mmol) [or sodium acetate (7.5mmol)] in water (10ml) was stirred at room temperature for 2.5-6h. The product was then extracted into methylene chloride (2x10ml) and the methylene chloride extract washed with water (2x10ml) (or 5% sodium carbonate solution (2x10ml). After drying (Na_2SO_4 or $MgSO_4$) the solvent was removed to afford the nitrone as a colourless oil which was used without further purification.

5-Carbomethoxymethylpyrroline-1-oxide (28) Prepared from 5-carbomethoxy-4-pentenal (27) according to the general procedure. Obtained (48mg, 51%) as a colourless oil. The nitrone (28) was characterised only by its p.m.r. spectrum: δ 6.89 (dd, 1H, J 2.5 and 4.5Hz, CH=N), 4.32 (m, 1H, CHN), 3.65(s,3H, OMe). 3.19 (dd, 1H, J 4.2 and 16.6Hz, $CHCO_2Me$), 2.67-2.31 (m, 4H, 3 ring-H's and $CHCO_2Me$) and 1.95 (m, 1H, ring-H).

2-Carbomenthyloxymethyl-6-methyl-2,3,4,5-tetrahydropyridine-1-oxide (44b) and (45b) To a solution of hydroxylamine hydrochloride (0.55g, 7.91 mmol) and sodium acetate (0.82g, 10.0mmol) in water (10ml) was added (L)-menthyl trans-7-oxo-2-octenoate (1.95g, 6.63mmol) in acetonitrile (5ml). The solution was stirred at room temperature for 16 hrs. and then the solvent was removed under reduced pressure. After usual work up the product was obtained as a colourless viscous liquid (1.6g, 78%). P.m.r. spectrum in C_6D_6 indicated the presence of a 13:12 mixture of two nitrones. All attempts to separate the two nitrones were unsuccessful due to their instability. (Found: N, 4.2, $C_{18}H_{31}NO_3$ requires N, 4.5%); δ(nitrone mixture) 4.71 (m, 2x1H, CHO), 4.23 (brs, 2x1H, CHN), 3.42 (dd, 1H, J 4.1 and 9.7Hz, CHCO), 3.37 (dd, 1H, J 4.6 and 10.3Hz, CHCO), 2.46-2.64 (m, 2x2H), 2.12(s, 2x3H, CH_3 C=N), 0.93-2.09 (m, 2x14H), 0.90 (m, 2x6H, 2xMe) and 0.76 (d, 2x3H,Me); $^m/_z$(%) 309(15), 293(9), 186(22), 172(82), 153(68), 138(34), 123(24), 110(40), 95(62) and 83(100).

2-Methoxycarbonylmethyl-6-methyl-2,3,4,5,-tetrahydropyridine-1-oxide (31b). Prepared according to the general procedure. The product (0.80g, 72%) was a colourless oil (Found: N, 7.3. $C_9H_{15}NO_3$ requires N, 7.55%); δ 4.27 (m, 1H, H_A), 3.73 (s, 3H, OMe), 3.24 (dd, 1H, J 5.5 and 16.1Hz, H_D), 2.60 (dd, 1H J 7.6 and 16.1Hz, H_E), 2.50 (brt, 2H, CH_2), 2.16 (m, 1H, CH), 2.11 (d, 3H, J 1.3Hz, Me) and 1.95 - 1.43 (m, 3H, CH_2 + CH); $^m/_z$(%) 185 (M^+,100), 154(59), 153(89), 126(10) and 112(50).

Nitrones (37) and (38) Prepared from (36) using the general procedure and obtained (89%) as a colourless oil whose p.m.r. spectrum indicated the presence of two isomers in the ratio 3.3:1 [Found (isomers): N, 6.15. $C_{12}H_{19}NO_3$ required N, 6.2%]; ν_{max} (isomers) 2930, 2860, 1735, 1575, 1440 and 1200 cm^{-1}; $^m/_z$(isomers) 225 (M^+,56), 209(23), 194(43), 193(69), 165(31) and 152(100).

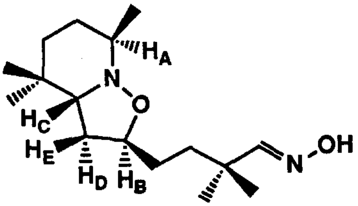
Major isomer (37)

δ 4.28 (brm, 1H, H_A), 3.72 (s, 3H, OMe), 3.7 (m, 1H, H_E), 3.09 (dd, 1H, J 6.9 and 16.0Hz, Hc), 2.55 (dd, 1H, J 5.8 and 16.0Hz, H_D), 2.43 (brm, 1H, H_B), 2.19 - 1.21 (m, 11H, $5xCH_2$ and H_F).

The minor isomer (38) exhibited the following p.m.r. signals: δ 3.29 (dd, 1H, J 4.6 and 16.0Hz, H_C) and 2.64 (dd, 1H, J 9.3 and 16.0Hz, H_D).

Cycloadducts

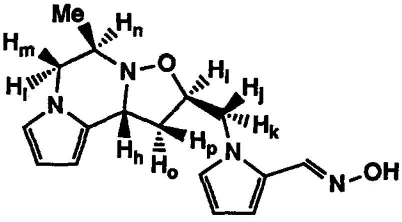
Dimer (18b) from 2,2-dimethyl-5-hexenal oxime A solution of 2,2-dimethyl-5-hexenal oxime (500mg) in xylene (10ml) was boiled under reflux for 16 hrs. The solvent was removed under reduced pressure and the residue purified by flash chromatography (1:1^{v}/v ether-pet ether) and the resulting solid crystallised from ether-pet ether (40-60°C) to give the product (0.36g, 72%) as colourless prisms, m.p 78°C. (Found: C, 67.85; H, 10.65; N, 9.7. $C_{16}H_{30}N_2O_2$ requires C, 68.05; H, 10.7 and N, 9.9%); δ 8.62 (brs, 1H, OH), 7.26 (s, 1H, CH=N), 4.17 (m, 1H, CHO), 3.11 (dd, 1H, J 7.1 and 11.9Hz, CHN), 2.54 (m, 1H, MeCHN), 2.19 (ddd, 1H, J 9.55Hz), 1.28-1.60 (m, 8H), 1.22 (m,1H), 1.15(s, 3H, Me), 1.11 (d, 3H, J 5.9Hz, MeCH), 1.05 (s, 6H, 2xMe), 0.90 (s, 3H, Me); $^{m}/_{z}$(%) 282 (M^+,16), 267(32), 265(M^+-OH,100), 249(10), 247(21), 154(11), 142(41), 126(14) and 124(19). The stereochemistry was assigned on the basis of n.O.e. data (Table).



Irradiated	n.O.e. (%)				
Proton	H_A	H_B	H_C	H_D	H_E
H_A	-	7.3	-12.7	4.0	-
H_B	7.1	-	-	4.5	-
H_C	-	-	-	-	6.3
H_D	5.2	5.8	-	-	19.1

Dimer (20) from N-allylpyrrole-2-carboxyaldehyde oxime. A solution containing mainly the Z- isomer of N-allylpyrrole-2-carboxyaldehyde oxime (0.5g, 3.33mmol)[8,33] was boiled under reflux in xylene (10ml) for 16 hrs. The solvent was removed from the dark reaction mixture and the residue which contains mainly a 2:1 mixture of E- and Z- oxime dimers (20) (by ^{1}H NMR), was subjected to flash chromatography (1:19$^{v}/_{v}$ ethyl acetate -ether). T.L.C. monitoring of the crude reaction mixture indicated the presence of trace amounts of an unidentified product.

Major isomer (syn-oxime). This was the less polar isomer and was obtained (0.175g, 35%) as colourless prisms which became pale brown on standing, m.p. 127-128°C (from MeOH) (Found: C, 63.95; H, 6.9; N, 18.7. $C_{16}H_{20}N_4O_2$ requires C, 64.0; H, 6.7; N, 18.65%).



δ 8.07 (s, 1H, CH=N), 8.01 (s, 1H, OH), 6.12 and 6.91 (2xt, 2x1H, pyrrole H), 5.86, 6.14, 6.39 and 6.47 (4xdd, 4x1H, pyrrole H), 4.49 (m, 2H, Hh and Hi), 4.43 (d, 1H, J 5.9Hz, Hj), 4.36 (dd, 1H, J 3.7 and 13.8Hz, Hk), 3.96 (dd, 1H, J 3.6 and 12.3Hz, Hl), 3.64 (dd, 1H, J 8.5 and 12.3Hz, Hm), 3.34 (m, 1H, Hn), 2.33 (m, 2x1H, Ho and Hp) and 1.27 (d, 3H, J 6.3Hz, CH_3); 2D - COSY, decoupling experiments and n.O.e. data were used to assign the stereo chemistry; $^{m}/_{z}$(%) 300 (M^+, 0.5), 283 (M-OH, 14), 249(11), 177(100), 153(19), 150(45), 135(24), 133(26), 118(24).

Minor isomer (anti-oxime) This was the more polar isomer and was obtained (87mg, 17%) as pale orange tiny prisms (from Et_2O), m.p. 76-78°C. δ 7.51 (s, 1H, CH=N), 7.33 and 6.26 (dd, 2x1H, pyrrole-H), 6.85, 6.47 and 6.12 (3xt, 3x1H, pyrrole-H), 5.88 (d, 1H, pyrrole-H), 4.50 (t, 1H, J 7.3Hz, Hh), 4.42 (m, 1H, Hi), 4.25 (dd,1H, J 6.7 and 14.9Hz, Hj), 4.08 (dd, 1H, J 4.0 and 14.9Hz, Hk), 3.99 (dd, 1H, J 3.7 and 12.2Hz, Hl), 3.61 (dd, 1H, J 7.4 and 12.2Hz, Hm), 3.40 (m, 1H, Hn), 2.38 (m, 2H, Ho and Hp) and 1.25 (d, 3H, J 6.4 Hz, CH_3); see also the n.O.e. data below. $^{m}/_{z}$(%) 300 (M^+,1), 282 (M- H_2O, 29), 227(14), 177(62), 150(88), 146(24), 135(38), 132(46), 118(41), and 110(56).

Proton		n.O.e.(%)				
irradiated	Hn	Ho	Hp	Hi	Hh	CH_3
Hh			7.0			2.0
Hn		2.0		2.9		6.4
Ho	3.2		6.3	6.3		
Hp					7.7	

Cycloaddition (24) and ene (26) products from 2-(but-3'-enyl)-2-formyl-1,3-dithianyl phenylhydrazone. A solution of 2-(but-3'-enyl)-2-formyl-1,3-dithianyl phenylhydrazone (0.5g, 1.71 mmol) in dry degassed xylene (15ml) was stirred and boiled under reflux for 56 hrs. The reaction was monitored by p.m.r. and small amounts of unreacted starting material remained even after 56 hrs. The solvent was removed under reduced pressure and TLC of the residue indicated the presence of two major products, identified as ene-adduct and the 1,2-prototropy cycloadduct. Trace amounts of a third product believed to be the pyrazoline (25) were detected but not isolated. The mixture was separated by flash chromatography eluting with 1:9$^{v}/_{v}$ ether-pet.ether.

Cycloadduct (24). Obtained (0.098g; 20%), as off-white prisms from ether, which become pale brown on standing, m.p. 107-108°C. (Found: C, 61.4; H, 6.95; N, 9.55; S, 22.2. $C_{15}H_{20}N_2S_2$ requires C, 61.6; H, 6.9; N, 9.55 and S, 21.9%); δ 7.23 and 7.08 (dd, 2x2H, ArH), 6.84 (t, 1H, ArH), 4.04 (d, 1H, J 7.4Hz, $C\underline{H}NH$), 3.95 (brm, 1H, NH), 3.78 (dd, 1H, J 5.3 and 7.8Hz, CHN), 2.76 - 3.14 (m, 6H), 2.00 - 2.16 (m, 5H) and 1.65 (m, 1H); $^{m}/_{z}$(%) 292 (M^+,100), 290(11), 217(14), 186(12), 185(27), 157(36) and 121(30).

Ene-adduct (26). Obtained (0.19g, 38%) as yellow prisms from ether, m.p. 91-92°C. The product comprised a 2.4:1 mixture of cis- and trans-isomers. (Found: C, 61.35; H, 6.7; N, 9.4; S, 22.0. $C_{15}H_{20}N_2S_2$ requires C, 61.60; H, 6.90; N, 9.6 and S, 21.90%). δ (mixture): 7.73 (m, 2x2H, ArH), 7.45 (m, 2x3H, ArH), 4.19 (d, 1H, J 4.9Hz, CHN), 3.88 (d, 1H, J 7.5Hz, CHN), 1.68-3.10 (m, 2x11H), 1.04 (d, 3H, J 6.9Hz, CH_3), and 0.84 (d, 3H, J 7.1Hz, CH_3). $^m/_z$(%): 292 (M^+,31), 188(12), 187(100), 147(11), 145(93), 113(14), 107(40), 81(46) and 77(48).

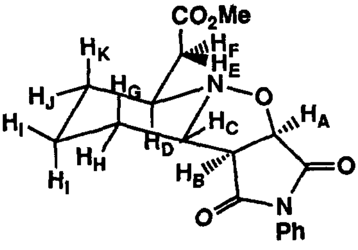
Cycloadduct (29). A solution of 5-carbomethoxymethylpyrroline-1-oxide (48mg, 0.3mmol) and N-methylmaleimide (34mg, 0.3mmol) in d_8-toluene (1.0ml) was heated in an n.m.r. tube at 110°C for 15h. After this time the p.m.r. spectrum indicated the presence of predominantly one isoxazolidine (29) together with trace amounts of another two isomers. Evaporation of the solvent gave a brown gum. Column chromatography (silica gel-ether) afforded a pure sample of the above mixture as a colourless gum (40mg, 50%). The stereochemistry was established using NOEDSY experiments (see discussion). [Found (mixed isomers): C, 53.65; H, 6.2; N, 10.25, $C_{12}H_{16}N_2O_5$ requires C, 53.7; H, 6.0 and N, 10.45%]; $^m/_z$(%) (mixed isomers) 268 (M^+,25), 237(12), 196(12) and 195(100).

(29) δ 4.87 (d, 1H, J 7.3Hz, H_A), 3.87 (m, 2H, H_C and H_D), 3.70 (s, 3H, OMe), 3.53 (dd, 1H, J 1.6 and 7.2Hz, H_B), 3.05 (s, 3H, NMe), 2.63 (dd, 1H, J 5.7 and 15.7Hz, H_E), 2.34 (m, 1H, ring-H), 2.29 (dd, 1H, J 9.1 and 15.7Hz, H_F), 2.17, 1.80 and 1.56 (m, 3H, ring -H).

The presence of another two isomers was inferred from the following signals in the p.m.r. spectrum (250MHz, d_8-toluene) of the crude product. δ 4.33 (d, 1H) and 4.16 (d, 1H) corresponding to H_A in each isomer.

Cycloadduct (32a) (with Dr.P. Armstrong). Methyl trans-hept-2-enoate-7-al oxime (0.25g, 1.46mmol), and N-phenylmaleimide (0.25g, 1.45mmol) were heated in boiling toluene for 3h.

under argon. The toluene was removed under vacuo to leave a pale yellow oil which comprised the product (32a) in 90% yield. Flash chromatography (silica gel, Et_2O) afforded pure (32a) (70%) as colourless prisms from ether, m.p. 157-158°C. (Found: C, 62.6; H, 5.95; N, 8.15. $C_{18}H_{20}N_2O_5$ requires C, 62.8; H, 5.85; N, 8.15%); υ_{max} 2940, 1720, 1495, 1395, 1390, 801, 750 and 697cm^{-1}; δ 7.41-7.22 (m, 5H, ArH), 4.94 (d, 1H, J_{AB} 7.8Hz, H_A), 3.66 (m, 1H, H_C), 3.60 (s, 3H, OMe), 3.40 (t, 1H, J 7.7Hz, H_B), 3.12 (m, 1H, H_D), 2.74 (dd, 1H, J_{ED} 6.6 and J_{EF} 15.4Hz, H_E), 2.26 (dd, 1H, J_{FD} 6.3Hz, H_F), 2.00 (m, 1H, H_G), 1.86 (m, 1H, H_H), 1.74 (m, 1H, H_J), 1.41 (m, 2H, H_I) and 1.26 (m, 1H, H_K).

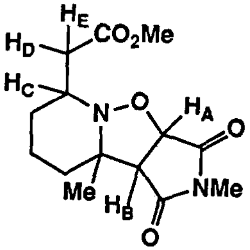


These assignments were supported by decoupling experiments on H_C,H_D,H_B and H_A. $^m/_z$(%) 344(M^+,14), 271(70), 173(100), 139(23), 98(15), 81(16), 77(9), 68(14), 59(19) and 54(27).

Cycloadducts (32b) and (34). A solution of the nitrone (31b) (0.71g, 3.8mmol) and N-methylmaleimide (0.42g, 3.8mmol) in chloroform (15ml) was stirred at room temperature for 50 h. Removal of the solvent afforded the crude product whose p.m.r. spectrum indicated it comprised (100%) a 3:1 mixture of isoxazolidines (32b) and (34). The major isomer (32b) was obtained (0.23g, 21%) by fractional crystallisation from ether at 0°C. Flash chromatography (silica gel-ether) of the residue afforded a fraction as a colourless gum which was enriched (70%) in the minor isomer. Stereochemical assignments of both isomers are based on NOEDSY spectra.

Major cycloadduct (32b). Obtained as colourless rods from ether, m.p. 79-81°C.

(Found: C, 59.6; H, 6.85; N, 9.35.$C_{14}H_{20}N_2O_5$ requires C, 56.75; H, 6.8; N, 9.45%). δ 5.15 (d, 1H, J 8.4Hz, H_A), 3.72 (d, 1H, H_B), 3.71 (s, 3H, OMe), 3.11 (m, 1H, H_C), 3.00 (s, 3H, NMe), 2.84 (dd, 1H, J 5.8 and 15.7Hz, H_D), 2.30 (dd, 1H, J 6.2 and 15.7Hz, H_E), 2.24 and 1.87-1.22 (m, 1H and m, 5H, 3xring- CH_2) and 1.19 (s, 3H, C(Me)); $^m/_z$(%) 296 (M^+,16), 281(18) and 223(100). ^1H NOEDSY (%): irradiation of the signal for H_A results in enhancements of the signal for H_B (7%) and H_C (6%) but there was no effect on the C(Me) signal. Irradiation of H_C caused an enhancement of H_A (9%) but also had no effect on the C(Me) signal. Finally, irradiation of the signal for the C(Me) group had no effect on the signals for H_A, H_B or H_C.



Minor cycloadduct (34). δ 4.84 (d, 1H, J 8.0Hz, H_A), 3.66 (s, 3H, OMe), 3.27 (d, 1H, J 8.0 Hz, H_B), 3.01 (s, 3H, NMe), 2.97 (dd, 1H, H_D), 2.67 (m, 2H, H_C and 1 ring- H), 2.27 (dd, 1H, J 8.5 and 15.7Hz, H_E), 1.86-1.54 (m, 4H, 2x ring- CH_2), 1.35 (s, 3H, C(Me)) and 1.21 (m, 1H, ring- H). ^1H NOEDS (%): irradiation of the signal for H_A caused enhancements of H_B (10%) and C(Me) (1%) but had no effect on H_C, whereas irradiation of C(Me) caused enhancements of H_A (2%) and H_B (5%) but had no effect on H_C.

Cycloadducts (39) - (41). A solution of the 3:1 mixture of isomeric nitrones (37) and (38) (0.65g, 2.9mmol) in chloroform (20ml) was stirred and boiled under reflux with N-methylmaleimide (0.32g, 2.9mmol) for 36 h. The reaction was monitored by p.m.r. spectroscopy and was complete at this time. Removal of the solvent under reduced pressure left a pale brown gum whose p.m.r. spectrum showed it to comprise a 4:3:2 mixture of (39), (40) and (41) in essentially quantitative yield. The isomers were separated by fractional crystallisation from ether. [Found (mixed isomers): C, 60.75; H, 7.3; N, 8.35. $C_{17}H_{24}N_2O_5$ requires C, 60.7; H, 7.2; N, 8.35%]; $^m/_z$(%) (mixed isomers) 336 (M^+,47), 293(72), 263(100) and 225(41).

(39). Obtained (0.125g, 13%) as colourless rods, m.p. 127-129°C; δ 5.08 (d, 1H, J_{AB} 8.5Hz, H_A), 3.84 (d, 1H, J_{BA} 8.5Hz, H_B), 3.69 (s, 3H, OMe), 3.17 (m, 1H, H_C), 2.98 (s, 3H, NMe), 2.85 (dd, 1H, J 5.4 and 15.7 Hz, H_D), 2.33 (dd, 1H, J 6.5 and 15.7Hz, H_E), 2.23 (m, 1H, H_F), 1.88 (m, 1H, H_G), 1.77 (m, 1H, H_K), 1.74-1.22 (m, 9H, H_I and $4xCH_2$), and 1.03 (m, 1H, H_J). The stereochemistry of this isomer was assigned with the aid of NOEDSY (below) and 2D-COSY spectra.

N.O.e. data for cycloadduct (39)

Signal	Enhancement(%)								
irradiated	H_A	H_B	H_C	H_D	H_E	H_F	H_G	H_J	H_K
H_A	-	4	5	0	0	0	0	0	0
H_B	5	-	5	0	0	3	8	0	0
H_C	8	6	-	0	2	0	2	0	0
H_D	0	0	0	-	10	0	0	0	0
H_F	0	2	0	0	0	-	0	2	0
H_J	0	0	0	0	0	5	0	-	23

(40). Obtained (0.1g, 10%) as colourless prisms, m.p. 122-124°C; δ 4.74 (d, 1H, J_{AB} 8.1Hz, H_A), 3.67 (d, 1H, J_{BA} 8.1Hz, H_B), 3.60 (s, 3H, OMe), 2.96 (s, 3H, NMe), 2.92 (dd, 1H, J 3.5 and 15.8Hz, H_D), 2.73 (m, 1H, H_C), 2.20 (dd, 1H, J 8.6 and 15.8Hz, H_E), 2.05 (m, 1H, H_J) and 1.87-1.17 (m, 12H, remaining ring protons including H_F). The stereochemistry of this isomer was assigned using NOEDSY and 2D-COSY experiments (see Table below).

N.O.e data for cycloadduct (40)

Signal	Enhancement(%)						
irradiated	H_A	H_B	H_C	H_D	H_E	H_J	N-Me
H_A	-	6	0	0	0	0	0
H_B	3	-	0	0	0	2	0
H_C	0	0	-	0	2	0	4
H_E	0	0	4	5	-	0	8
H_J	0	0	0	0	0	-	0

(41). Obtained (0.06g, 6%) as colourless needles, m.p. 154-156°C; δ 5.22 (d, 1H, J_{AB} 8.5Hz, H_A), 3.75 (d, 1H, J_{BA} 8.5Hz, H_B), 3.68 (s, 2H, OMe), 3.15 (m, 1H, H_C), 3.01 (s, 3H, NMe), 2.82 (dd, 1H, J 5.6 and 15.7Hz, H_D), 2.26 (dd, 1H, J 6.2 and 15.7Hz, H_E), 1.96 (m, 2H, ring H's), 1.84 (m, 2H, ring- H, including H_L), 1.70 (m, 2H, ring-H) and 1.58-1.15 (m, 8H, ring-H including H_G @ ca.1.45). The stereochemistry of this isomer was assigned using NOEDSY and 2D-COSY experiments (see Table below).

N.O.e. data for cycloadduct (41)

Signal	Enhancement(%)						
irradiated	H_A	H_B	H_C	H_D	H_E	H_G	H_L
H_A	-	2	4	0	0	0	0
H_B	6	-	6	0	0	6	0
H_C	7	7	-	2	2	2	2

When the above experiment was performed in d_8-toluene (110°,25h) a 16:4:3 mixture of (39), (40) and (41) was obtained together with traces of another two isomers.

Cycloadducts (46a) and (47a). The isomeric mixture of oximes (43b) (0.50g, 1.69mmol) and N-methylmaleimide (0.19g, 1.71mmol) were boiled under reflux in dry toluene (15ml) for 5 hrs. The solvent was then removed from the cooled reaction mixture under reduced pressure. The p.m.r. spectrum of the residue indicated the presence of two isomers in the ratio of 1:1. The mixture was purified by flash chromatography eluting with 3:2 $^{v}/_{v}$ ether-pet ether, to give a colourless solid (0.42g, 61%) [Found (mixed isomers): C, 65.25; H, 8.4; N, 7.15. $C_{22}H_{34}N_2O_5$ requires C, 65.0; H, 8.4 and N, 6.90%].

One of the diastereoisomer was isolated by fractional crystallisation of the mixture from ether. m.p. 124-126°C, colourless prisms from ether. $[\alpha]_D$ - 22.8° ($CHCl_3$); δ 5.06 (d, 1H, J 7.1Hz, CHON), 4.69 (ddd, 1H, J 4.3Hz, CHO), 3.56 (m, 2H, CHN and CHCON), 3.17 (m, 1H, CHN), 3.00 (s, 3H, NMe), 2.80 (dd, 1H, J 5.7 and 15.9Hz, CHCO), 2.29 (dd, 1H, J 6.6 and 15.7H$_Z$, CHCO), 0.97-2.18 (m, 15H), 0.92 (m, 6H, 2xMe) and 0.79 (d, 3H, Me); $^{m}/_{z}$(%) 406 (M$^+$,47), 377(6), 347(7), 321(16), 295(11), 279(69), 269(100), 251(13), 209(47), 193(9), 158(11), 142(35), 95(41) and 82(43).

Cycloadducts (46b) and (47b). The 13.12 mixture of nitrones (44b) and (45b) (0.515g, 1.67mmol) and N-methylmaleimide (0.185g, 1.67mmol) were stirred and boiled in toluene (15ml) under nitrogen for 5 hrs. The solvent was then removed under reduced pressure and the p.m.r. spectrum of the residue indicated the presence of two major isomers and a minor isomer in the ratio 4.2: 4.2:1. The minor isomer was presumably an endo-adduct. Only one isomer (0.13g, 19%) was isolated in pure form by flash chromatography eluting with 19:1$^{v}/_{v}$ ether-ethylacetate. It formed colourless prisms, m.p. 156-157°C from ether-pet ether. (Found: C, 65.5; H, 8.7; N, 6.75. $C_{23}H_{36}N_2O_5$ requires C, 65.7; H, 8.65 and N, 6.65%); δ 5.18 (d, 1H, J 8.4Hz, OCHCO), 4.71 (m, 1H, CHO), 3.72 (d, 1H, J 8.4Hz, CCHCO), 3.11 (m, 1H, CHN), 3.00 (s, 3H, NMe), 2.88 (dd, 1H, J 5.1 and 16.0Hz, COCH), 2.26 (dd, 1H, J 6.9 and 16.0Hz, COCH), 2.24 (m, 1H), 1.19 (s, 3H, Me), 0.91 (d, 6H, J 6.8Hz, (Me)$_2$CH), 0.79 (d, 3H, J 6.9Hz, CHMe) and 0.74-2.00 (m, 14H); $^{m}/_{z}$(%) 420(M$^+$,4), 405(4), 309(4), 292(12), 283(19), 267(16), 224(22), 223(100), 172(46), 171(42), 154(66), 138(12), 112(15) and 95(30).

Other major isomer. δ 5.16 (d, 1H, J 8.4Hz, OCHCO), 4.69 (m, 1H, CHO), 3.74 (d, 1H, J 8.4Hz, CCHCO), 3.08 (m, 1H, CHN), 2.99 (s, 3H, NMe), 2.77 (dd, 1H, J 6.1 and 15.5Hz, COCH), 2.26 (m, 2H), 1.19 (s, 3H, Me), 0.91 (d, 6H, J 6.7Hz, (Me)$_2$CH), 0.75 (d, 3H, J 7.0Hz, CHMe) and 0.74-2.11 (m, 14H).

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REFERENCES

1. Part 34. Grigg, R.; Dorrity, M.J., Heaney, F., Malone, J.F., Rajviroongit, S., Sridharan, V., and Surendrakumar, S., *Tetrahedron*, 1991, **47**, 8297-8322.
2. Preliminary publication: Armstrong, P., Grigg, R., Surendrakumar, S., and Warnock, W.J., *J.Chem.Soc., Chem.Commun.*, 1987, 1327-1328.
3. **Imines:** Grigg, R.; Gunaratne, H.Q.N., and Kemp, J., *J.Chem.Soc.,Perkin Trans.1*, 1984, 41-46; Grigg, R.; Donegan, G., Gunaratne, H.Q.N., Kennedy, D., Malone, J.F., Sridharan, V. and Thianpatanagul, S., *Tetrahedron*, 1989, **45**, 1723-1746;

   Oximes: Grigg, R.; Thianpatanagul, S., *J.Chem.Soc.,Perkin Trans.1*, 1984, 653-656;

   Hydrazones: Grigg, R.; Dowling, M., Jordan, M.W., and Sridharan, V., *Tetrahedron*, 1987, **43**, 5873-5886.
4. Grigg, R.; Heaney, F., Markandu, J., Surendrakumar, S., Thornton-Pett, M., and Warnock, W.J., *Tetrahedron*, 1991, **47**, 4007-4030.
5. Grigg, R.; Markandu, J., *Tetrahedron Lett.*, 1989, **30**, 5489-5492; Grigg, R.; Markandu, J., and Surendrakumar, S., *ibid*, 1990 **31**, 1191-1194; Grigg, R.; Markandu, J., *ibid*, 1991, **32**, 279-282.
6. Grigg, R.; Jordan, M., Tangthongkum, A., Einstein, F.W.B. and Jones, T., *J.Chem.Soc.Perkin Trans.1*, 1984, 47-57; Armstrong, P.; Grigg, R., and Warnock, W.J., *J.Chem.Soc.,Chem.Commun.*, 1987, 1325-1327.
7. Grigg, R.; Heaney F., Surendrakumar, S., and Warnock, W.J., *Tetrahedron*, 1991, **47**, 4477-4494.
8. Armstrong, P.; Grigg, R., Heaney, F., Surendrakumar, S., and Warnock, W.J., *Tetrahedron*, 1991, **47**, 4495-4518.
9. Yokoyama, M.; Sujino, K., Irie, M., Yamazaki, N., Hijama, T., Yamada, N., and Togo, H., *J.Chem.Soc.,Perkin Trans.1*, 1991, 2801-2809.

10. Kinsman, R.; Lathbury, D., Vernon, P. and Gallagher, T., *J.Chem.Soc.,Chem.Commun.*, 1987, 243-244; Vernon, P. and Gallagher, T., *J.Chem.Soc.,Chem.Commun.*, 1987, 245-246. Lathbury, D.C., Shaw, R.W., Bates, P.A., Hursthouse, M.B and Gallagher, T., *J.Chem Soc.,Perkin Trans 1.*, 1989, 2415-2424.
11. Grigg, R.; Markandu, J., Perrior, T., Surendrakumar, S., and Warnock, W.J., *Tetrahedron Lett.*, 1990, **31**, 559-562.
12. Bishop, R.; Brooks, P.R., and Hawkins, S.C., *Synthesis*, 1988, 997-999.
13. House, H.O.; Manning, D.T., Melillo, D.G., Lee L.F., Haynes O.R., and Wilkes, B.E., *J.Org. Chem.*, 1976, **41**, 855-863. House, H.O.; Lee L.F., *ibid*, 1976, **41**, 863-869.
14. Boyd, D.R.; Neill, D.C., *J.Chem.Soc.,Perkin Trans.1*, 1977, 1308-1313; Boyd, D.R.; Neill, D.C., Stubbs, M.E., *J.Chem.Soc.,Perkin Trans.2*, 1978, 30-34; Goodrow, M.H.; Villarreal, J.A., Grubbs, E.J., *J.Org.Chem.*, 1974, **39**, 3447-3449; Sommermeyer, K.; Seiffert, W., and Wilker, W., *Tetrahedron Lett.*, 1974, **20**, 1821-1824.
15. Ciganek, E., *J.Org.Chem.*, 1990, **55**, 3007-3009, and references therein.
16. Homes, A.B.; Smith, A.L., Williams, S.F., Hughes, L.R., Lidert, Z., and Swithenbank, C., *J.Org.Chem.*, 991, **56**, 1393-1405.
17. Pradhan, S.K.; Akamanchi, K.G., Divakaran, P.P., and Pradhan, P.M., *Heterocycles*, 1989, **28**, 813-839.
18. Padwa, A.; and Wong, G.S.K., *J.Org.Chem.* 1986, **51**, 3125-3133.
19. Cope, A.C.; Trumbull, E.R., *Org.React.*, 1960, **11**, 317-493.
20. B.B. Snider in Comprehensive Organic Synthesis, Ed.B.M. Trost, Pergamon Press, 1991, Vol.5, p.p. 127.
21. Tschaen, D.M.; Turos, E., Weinreb, S.M., *J.Org.Chem.*, 1984, **49**, 5058-5064; Braxmeier, H.; Kresze, G., *Synthesis*, 1985, 683-684; Lin, J.-M.; Koch, K., and Fowler, F.W., *J.Org.Chem.*, 1986, **51**, 167-174; for a related acyl iminium ion process see: Marson, C.M.; Grabowska, U., Walsgrove, T., Eggleston, D.S., and Baures, P.W., *J.Org.Chem.*, 1991, **56**, 2603-2605.
22. Hassner, A., Maurya, R., *Tetrahedron Lett.*, 1989, **30**, 2289-2292.
23. For a fuller discussion of 1,2-prototropy in hydrazones see: Grigg, R.; Dowling, M., Jordan, M.W., and Sridharan, V., *Tetrahedron*, 1987, **43**, 5873-5886.
24. The nitrone could have arisen via a facile 1,3-azaprotio cyclotransfer or via Michael addition of the hydroxylamine to the acrylate moiety followed by condensation with the aldehyde.
25. It is not known which isomer predominates.
26. House, H.O.; Cronin, T.H., *J.Org.Chem.* 1965, **30**, 1061-1070.
27. Allan, R.D., Cordiner, B.G., and Wells, R.J., *Tetrahedron Lett.*, 1968, **58**, 6055-6056.
28. Eiter, K.; *Liebigs Ann.Chem.*, 1962, **658**, 91-99.
29. Gen, A.; Wiedhaup, K., Swoboda, J.J., Dunathan, H.C., and Johnson, W.S., *J.Am.Chem.Soc.*, 1973, **95**, 2656-2663.
30. Garnick, R.L. and LeQuesne, P.W., *J.Chem.Soc.*, 1978, **100**, 4213-4219.
31. Whitesell, J.K.; Lawrence, R.M., and Chen, H.-H., *J.Org.Chem.*, 1986, **51**, 4779-4784; Jurczak, J.; Zamajski, A., *Roczniki Chemii*, 1970, **44**, 2257-2259.
32. Beckwith, A.L.J.; Lawrence, T., *J.Chem.Soc.,Perkin Trans II*, 1979, 1535-1539; Ashby, E.C.; Argyropoulos, J.N., *J.Org.chem.*, 1985, **50**, 3274-3283.
33. N-Allypyrrole-2-carboxaldehyde oxime as prepared (crude) comprises a ca. 3:2 mixture of E- and Z-isomers. After distillation (b:p. 86-92°C/0.5mmHg) the oxime is essentially pure Z- isomer and solidifes.