Oxidative Free-radical Additions of α-Nitro Ketones and α-Nitro Amides to Alkenes and Alkynes Mediated by Electrochemically Regenerable Manganese(III) Acetate

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Manganese(III) acetate mediated oxidative additions of the α-aryl α-nitro ketones **1** and **9** to simple alkenes forms the isoxazoline *N*-oxides **3** and **10** as the main products in 13–62% yield. Depending upon the structure of the unsaturated system used, the α-allylated α-nitro ketones **4**, the tricyclic product **5** or the aromatised isoxazole **7** were also obtained. The oxidative addition of α-methyl α-nitro ketones **11** to hex-1-ene has been shown to yield the γ-acetoxylated α-nitro ketones **12**. Based upon the influence of substituents in both the α-nitro ketone and the alkene, the outcome of the reaction mechanism is discussed. The oxidative addition of α-nitro amides **13** to hex-1-ene furnished the cyclic nitronates **14** together with the isoxazolines **15**, which have been shown to be formed independently during the course of the reaction. Representative oxidative radical additions were performed using anodically *in situ* generated manganese(III) acetate from catalytical amounts of manganese(II) acetate. In these cases, yields as high, or even slightly higher, were obtained compared to those reactions employing 2 molar equiv. of the transition metal oxidant.

Inter- and intra-molecular oxidative additions of highly enolisable carbonyl- and related compounds to unsaturated systems mediated by the one-electron oxidant manganese(III) acetate have become increasingly attractive in organic synthesis over the last decade and have recently been comprehensively reviewed.[1] Despite the broad applicability of these reactions to different classes of CH-acidic compounds, the synthetically interesting aliphatic nitro compounds[2] have rarely been used in the intermolecular addition to alkenes using manganese(III) salts as the oxidant. The oxidation of aliphatic nitro compounds to the highly electrophilic α-nitroalkyl radicals with manganese(III) acetate and their subsequent addition to olefins has been shown to yield radical adducts, but only in low yield.[3] With manganese(III) pyridine-2-carboxylate, the oxidative addition of *aci*-silylnitronates to electron rich alkenes was shown to proceed effectively.[4]

As expected from related reactions of enolisable 1,3-dicarbonyl compounds,[1,5] the presence of a second activating carbonyl group, as present in α-nitro carbonyl compounds, should greatly enhance the overall rate of oxidative addition of nitro compounds to unsaturated systems. We therefore examined the oxidative additions of some α-nitro carbonyl compounds to unsaturated systems.

The overall manganese(III) acetate mediated addition of CH-acidic compounds to unsaturated systems requires 2 mol equiv. of the transition metal oxidant per mol equiv. of the CH-acidic compound. Therefore, we were also interested in conducting the oxidative addition of α-nitro carbonyl compounds to unsaturated systems in the presence of catalytic amounts of the metal salt, by electrochemically regenerating the manganese(III) consumed in the reaction. The Mn^{2+}/Mn^{3+} couple thus should act as a mediator[6] for the oxidative addition.

Since oxidative additions of α-nitro carbonyl compounds to unsaturated systems mediated by manganese(III) acetate have not been previously described, we first looked for suitable substrates for such reactions by employing equimolar amounts of manganese(III) acetate. After optimising the reaction conditions, representative reactions were performed with electrochemical regeneration of the oxidant in an *in-cell* process. The result of these reactions are described in this paper.

Table 1 Oxidative additions of nitroacetophenone **1** to various unsaturated systems mediated by manganese(III) acetate[a]

Entry	Unsaturated component	Reaction time (min)	Product(s) [yield (%)][b]
1	**2a**	45	**3a** [62]
2	**2a**[c]	45	**3a** [52] **4a** [11]
3	**2b**	45	**3b** [38]
4	**2c**	15	**3c** [18]
5	**2d**	5	**4b** [34]
6	**2e**	15	**3d** [22]
7	**2f**	180[d]	**3e** [17][e]
8	**2g**	60	**3f** [30][f] **5** [30]
9	**2h**	50[g]	**4c** [13] **3g** [3]
10	**6**	30	**7** [34]

[a] The reactions were carried out in glacial acetic acid using 2 molar equiv. of manganese(III) acetate and of the unsaturated compound under an argon atmosphere. Heating was performed at 60 °C until decolouration occurred. [b] Isolated yield based on **1**. [c] In the presence of 1 molar equiv. of $Cu(OAc)_2 \cdot H_2O$. [d] Heating at 110 °C was necessary to achieve reaction. [e] *cis*:*trans* = 2.3:1. [f] Only *trans*-isomer formed. [g] Reaction performed using 6 molar equiv. of **2h**.

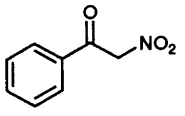
Results and Discussion

Oxidative Addition of Nitroacetophenone to various Unsaturated Compounds.—As a first example, nitroacetophenone **1** was treated with hex-1-ene **2a** in the presence of 2 mol equiv. of manganese(III) acetate dihydrate in glacial acetic acid at 60 °C (see Table 1, entry 1). The reaction took place within 45 min as indicated by the colour change from dark brown to pale yellow. After work-up and purification, the *N*-oxide **3a** was obtained in 62% yield. Surprisingly, the nitro group participated in the reaction to form an isoxazoline ring. A similar product had already been observed for the oxidative addition of *aci*-silylnitroalkanes to electron-rich double bonds, mediated by manganese(III) pyridine-2-carboxylate.[4]

The influence of the reaction conditions upon the reaction of the nitro compound **1** with hex-1-ene was further investigated. However, the product yield was unaltered when either

anhydrous manganese(III) acetate was used or when the reaction was conducted at a higher temperature. In the latter case, the reaction time could be shortened to 10 min (100 °C), although a significant amount of benzoic acid was formed as by-product, resulting from a retro-Claisen-like cleavage of the nitro ketone. Lowering the reaction temperature to < 60 °C, however, gave no addition products, even after an extended period of stirring. A number of manganese(III)-mediated oxidative additions have also been conducted under milder reaction conditions in DMF or ethanol as the solvent at ambient temperature.[4,5] However, in DMF, the addition of the nitro compound **1** to hex-1-ene only occurred at 120 °C to yield the product **3a**, whilst the reaction in ethanol at 75 °C caused the cleavage of compound **1** and ethyl benzoate was isolated.

Snider has shown that the addition of 1 mol equiv. of copper(II) acetate to the reaction mixture in the oxidative addition of 1,3-dicarbonyl compounds to unsaturated systems can drastically alter the product distribution.[5] In our case, the addition of 1 mol equiv. of copper(II) acetate to the reaction mixture gave rise to a second product **4a**, together with the *N*-oxide **3a** (entry 2). The total yield did not change significantly in comparison to the reaction performed without addition of the co-oxidant. Whilst the formation of compound **3a** was considered surprising, the formation of the unsaturated nitro compound **4a** has precedent in the known reactions of closely related 1,3-dicarbonyl compounds.[1]



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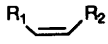
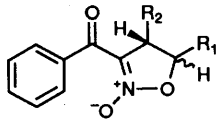
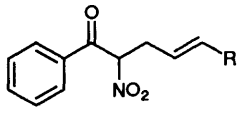


2 a R^1 = Bu, R^2 = H
b R^1 = CH_2OAc, R^2 = H
c R^1 = CH_2SiMe_3, R^2 = H
d R^1 = CH_2SnPh_3, R^2 = H
e R^1 = $CH_2CH_2CO_2H$, R^2 = H
f R^1, R^2 = -$[CH_2]_6$-
g R^1, R^2 = -CH_2CH_2CH=$CHCH_2CH_2$-
h R^1 = cyclo-C_3H_5, R^2 = H





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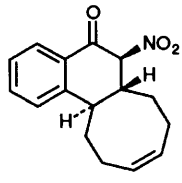
4a R = Pr
b R = H
c R = Et

The addition of the methyl ester of *aci*-nitroacetophenone is known to proceed in benzene as solvent, in the presence of catalytic amounts of toluene-*p*-sulfonic acid to yield the corresponding isoxazoline *via* a [1,3]-dipolar cycloaddition.[7] To exclude a cycloaddition or an acid-catalysed reaction pathway, control experiments were performed in the absence of the transition metal oxidant as well as in the presence of a catalytic amount of manganese(II) acetate. In both cases, no addition product was formed even after extended warming in acetic acid (110 °C, 3 h), as judged by GLC–MS analysis of the reaction mixtures.

Manganese(III) mediated oxidative additions of 1,3-dicarbonyl compounds to alkenes, proceeding *via* a highly electrophilic α,α'-dioxo alkyl radical, are inhibited when halide ions are present in the reaction mixture. In this case, 2-halogenated 1,3-dicarbonyl compounds are obtained.[8,9] When the addition of compound **1** to hex-1-ene was conducted in the presence of potassium bromide, no oxidative addition took place. Instead, α-bromo-α-nitroacetophenone was formed quantitatively.

These control experiments led to the conclusion that the addition of compound **1** to hex-1-ene indeed proceeds *via* an oxidative pathway, probably similar to the already known radical-based reactions of 1,3-dicarbonyl compounds. To distinguish between the two possibilities of either a radical or a cation radical based C–C-coupling reaction, oxidative additions of compound **1** to several unsaturated systems were performed. The conditions for the successful addition of compound **1** to hex-1-ene, in the presence of manganese(III) acetate as the only oxidant, were adapted for most of the additions to unsaturated systems. The results are summarised in Table 1.

The oxidative addition of compound **1** to allyltributylstannane **2d** gave rise to the allylated product **4b** (entry 5). In contrast, the *N*-oxides **3b** and **3c** were obtained upon addition of compound **1** to allyl acetate **2b** and allyltrimethylsilane **2c**, respectively (entries 3, 4). Addition of compound **1** to pent-4-enoic acid **2e** (entry 6) proceeded equally well to give the adduct **3d**, with the carboxy group apparently not interfering in the formation of the heterocyclic ring. The oxidative addition of nitroacetophenone to cyclooctene **2f** and cycloocta-1,5-diene **2g** was very informative (entries 7 and 8). The addition of compound **1** to the octene **2f** required relatively drastic reaction conditions (110 °C, 3 h) to yield the expected *N*-oxide **3e**. In contrast, reaction of compound **1** with the octadiene **2g** proceeded smoothly (60 °C, 30 min) to give the corresponding isoxazoline *N*-oxide **3f**, together with the tricyclic compound **5**. No ring contraction by an intramolecular 5-*exo*-cyclisation, as observed for the closely related reactions using either cyano acetoacetate or ethyl acetoacetate as the CH-acidic compound,[10] was observed. Both the product distribution and yield of compounds **3f** and **5** remained unchanged upon the addition of a 1 mol equiv. of copper(II) acetate to the reaction mixture (see Discussion). The structural assignment of compound **5** was made on the basis of a ^1H–^1H-COSY NMR experiment. The $^3J_{HH}$-coupling constants of the bridgehead protons and the proton in the α-position to the nitro group were both in the range of 10–12 Hz, which clearly supports the *trans-trans* relationship of these three protons as shown in the structure of **5** (Fig. 1).



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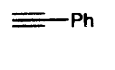

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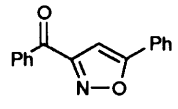

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Fig. 1

Since the above results do not completely exclude a cationic addition mechanism, the reaction of compound **1** with vinylcyclopropane **2h** as a free radical clock was examined. Two products were formed in this reaction: the isoxazoline *N*-oxide **3g** was isolated as a by-product, whereas the main product was the rearranged open-chain product **4c**.

The oxidative addition of an intermediate α-nitro α-oxoalkyl radical to a triple bond would give an intermediate vinyl radical. The fate of this radical might be different from the related additions to a double bond. When compound **1** was oxidatively added to phenylacetylene **6**, the aromatised isoxazole **7** was isolated in 34% yield (entry 10).

Oxidative Additions of other α-Nitro Ketones to Hex-1-ene.— The oxidative addition of the nitro ketone **1** to several

Table 2 Oxidative additions of α-nitro ketones to hex-1-ene **2a** mediated by manganese(III) acetate[a]

Entry	α-Nitro ketone	Reaction time (min)	Product [yield (%)]
11	**9a**	60	**10a** [18]
12	**1**	45	**3a** [62]
13	**9b**	30	**10a** [67]
14	**9c**	30	**10c** [83]
15	**9d**	15	**10d** [21][b]
16	**11a**	20	**12a** [81]
17	**11b**	20	**12b** [73]

[a] Reactions were carried out as indicated in Table 1. For better comparison, the reaction of **1** with hex-1-ene was included (Entry 12, see Table 1, Entry 1). [b] Yield over two steps. Since nitro ketone **9d** is instable, **10d** was prepared without purification of **9d** directly from pyridine-2-carboxylic acid (see Experimental section).

unsaturated systems has been shown to proceed smoothly to yield the corresponding isoxazoline *N*-oxide as the main product, depending upon the structure of the unsaturated compound used. In order to extend this reaction principle to other α-nitro ketones, oxidative addition of a series of α-unsubstituted α-nitro ketones **8a–d** to hex-1-ene as the model substrate were attempted, under the standard reaction conditions. However, no formation of the addition products was observed, although the formal introduction of a methyl group at the α-position of ketone **8b** to give the nitro ketone **11b**, enabled the oxidative addition to proceed smoothly (Table 2, entry 17) to yield the expected addition product **12b**, containing an acetoxy group, in 73% yield. An analogous adduct **12a** was isolated in 81% yield when the α-nitro α-methyl ketone **11a** was oxidatively added to hex-1-ene (entry 16). As observed with the previous reactions, the outcome was unchanged by the addition of copper(II) acetate to the reaction mixture. It therefore appears that the introduction of an α-substituent greatly facilitates the reaction of α-nitro ketones.

The influence of electron-donating and electron-withdrawing substituents on the aromatic ring of α′-aryl α-nitro ketones **9a–d** was then examined. As expected, the overall yield of the

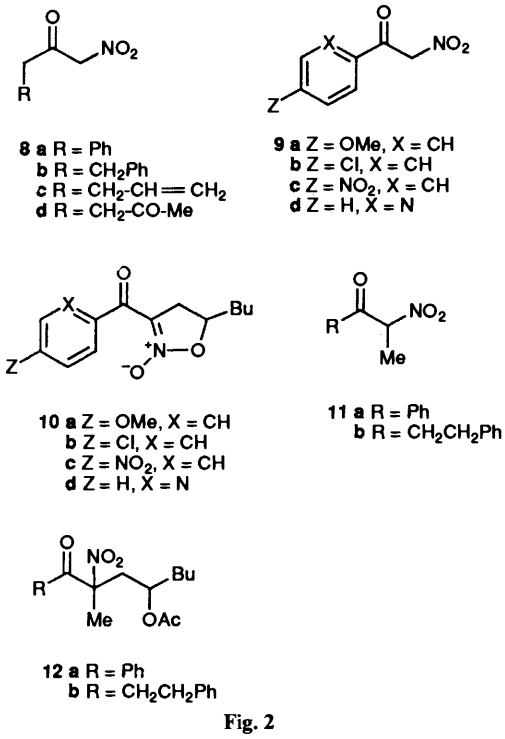
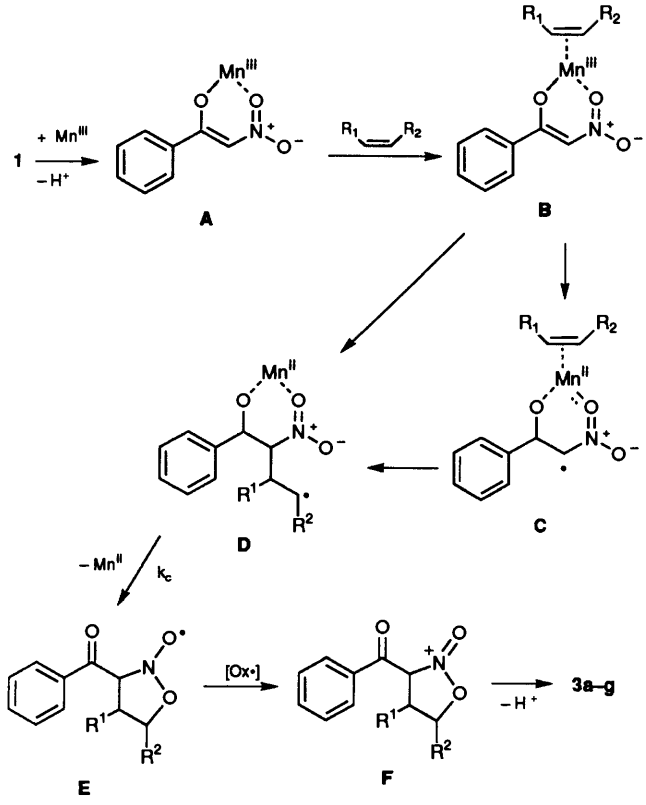


Fig. 2

oxidative addition of the nitro ketones **9a–d** to hex-1-ene was also enhanced by increasing the electron-withdrawing character of the aromatic ring. This decreases the electron density at the carbonyl group, thus enhancing the acidity of the α-CH protons. As shown in Table 2, the overall yield of the isoxazoline *N*-oxides **10a–d** is roughly correlated with the electron-withdrawing character of the substituent on the aromatic ring. The highly enolisable and unstable pyridyl-substituted α-nitro ketone **9d** was prepared from pyridine-2-carboxylic acid and immediately reacted in the oxidative addition to hex-1-ene without prior isolation (see Experimental section). The yield of 21% represents the overall two-step yield, starting from the carboxylic acid.

Mechanism of the Oxidative Addition of α-Nitro Ketones to Unsaturated Systems Mediated by Manganese(III) Acetate.— Scheme 1 shows the most likely reaction mechanism for the formation of the cyclic nitronates **3a–g** and **10a–d** based upon the reactions described above and upon the already known manganese(III) mediated reactions. The formation of the different adducts such as compounds **4a–c** and **5** can also be readily rationalised by the proposed mechanism.



Scheme 1

It is well known from manganese(III) mediated reactions of 1,3-dicarbonyl- and related compounds that they proceed *via* a manganese(III) enolate.[8] The formation of an analogous complex **A** in the first step of the reaction can be deduced from the colour change from light to dark brown when the α-nitro ketones were added to a solution of manganese(III) acetate in acetic acid. Although a manganese(II) complex of the nitroacetophenone has been described,[11] showing that the nitro group is as good a ligand as the keto group, we were unable to crystallise a similar manganese(III) complex. Further evidence in support of the assumption that complex **A** is formed during the first step, is that in no case do reactions occur at temperatures < 60 °C. Mn^{III}/Mn^{II} Complexes need elevated temperatures in order to undergo facile ligand exchange,[12] and

even the preparation of the known complex between Mn^{II} and compound **1** from manganese(II) acetate requires temperatures > 50 °C.[11]

As already proposed for manganese(III)-based reactions of β-keto esters[8,13] and *aci*-silylnitroalkanes,[4] the unsaturated acceptor compound must also be complexed to the Mn^{III} to form a Mn^{III}•**1**• alkene complex **B**. The formation of this complex is clearly demonstrated by comparison of the reactions of the nitro ketone **1** with cyclooctene **2f** and cycloocta-1,5-diene **2g**. Since cycloocta-1,5-diene is known to act as a labile bidentate ligand in transition-metal complexes, the formation of complex **B** should be more likely using compound **2g** rather than compound **2f**. Indeed, the change from the alkene **2f** to **2g** not only allowed a lower reaction temperature for the addition, but also dramatically increased the total yield of addition products from 17% **3e** to 60% **3f** + **5** (Table 1). This clearly supports the formation of complexes of type **B**.

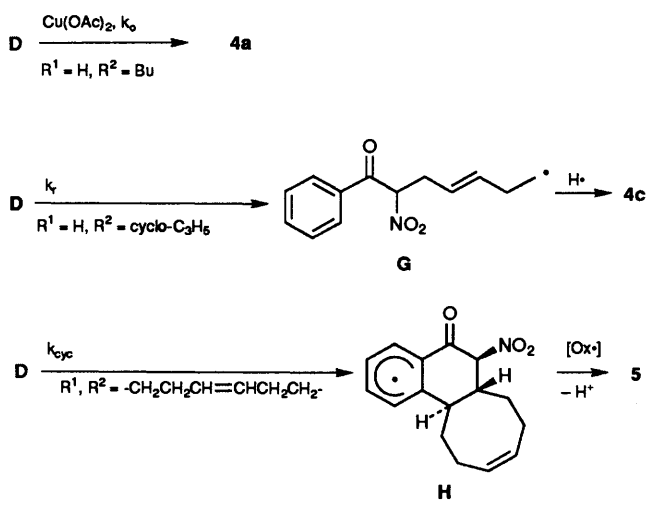
The main C–C-coupling reaction from complex **B** to form the addition products must proceed *via* a free radical intermediate. This has been proved by the formation of the rearranged open-chain adduct **4c** upon addition of the nitro ketone **1** to vinylcyclopropane **2h**. Formation of the allylated species **4b** in the reaction of compound **1** with the allylstannane **2d** also accounts for a free-radical step, but does not completely exclude a cationic mechanism. Whether the secondary alkyl radical **D** is formed directly from the complex **B** or *via* the α-nitro α-keto radical **C** (complexed to Mn^{II}), cannot, as yet, be determined. Again, in the intermolecular additions of β-keto esters to alkenes, it has been shown by Snider[8] that species comparable to **C** are not involved when the CH-acidic compound has no α-substituent. Instead, the radical adducts are formed directly from complexes of type **B** without the intermediacy of **C**.

The formation of the isoxazoline *N*-oxides **3a–g** from the adduct radicals **D** can be easily explained by assuming the formation of a nitroxyl radical **E** in the following step of the reaction. An analogous intermediate has already been proposed in the intramolecular oxidative radical cyclisation of ω-alkenyl nitronate anions.[14] Nitroxyls are relatively stable free radicals and **E** should be readily oxidised to the nitrosonium ion **F**. Since **F** still has an α-hydrogen atom, it is finally deprotonated to give the *N*-oxides **3a–g**.

Formation of products other than the *N*-oxides **3** in reactions of compound **1** with certain unsaturated systems can also be explained with this mechanism. First, the formation of the allylated product **4b** in the reaction of compound **1** with allyltriphenylstannane also accounts for a free-radical pathway of the reaction *via* **D**. The presence of any long-lived cationic intermediate can also be excluded by examining the reaction of compound **1** with pent-4-enoic acid **2e**. In this case, the corresponding *N*-oxide **3d** was isolated as the only product, while a reaction *via* a cationic species would at least additionally have led to a lactone-type product by an intramolecular attack at the carboxy group.

The final proof that a free-radical species **D** is involved in the reaction mechanism is from formation of the rearranged open-chain product **4c** in the reaction of compound **1** with vinylcyclopropane **2h**. Free methylcyclopropyl radicals rearrange to the corresponding allyl radicals **G** (Scheme 2) at a reaction rate of *ca.* $k_r \approx 1 \times 10^8\ s^{-1}$ (37 °C).[15] Since the main product in the addition of nitroacetophenone to vinylcyclopropane is the rearranged compound **4c**, the intramolecular interaction of the nitro group with the secondary radical centre to give the nitroxyl radicals of type **E** must occur with a rate constant k_c which is comparable, or slightly lower, than the rate constant for the rearrangement k_r, to give the primary radical **G**. The latter intermediate **G** will readily abstract a hydrogen atom, *e.g.* from the solvent, to yield the final product **4c**.

As shown in Table 1, entry 2, an additional open-chain



Scheme 2

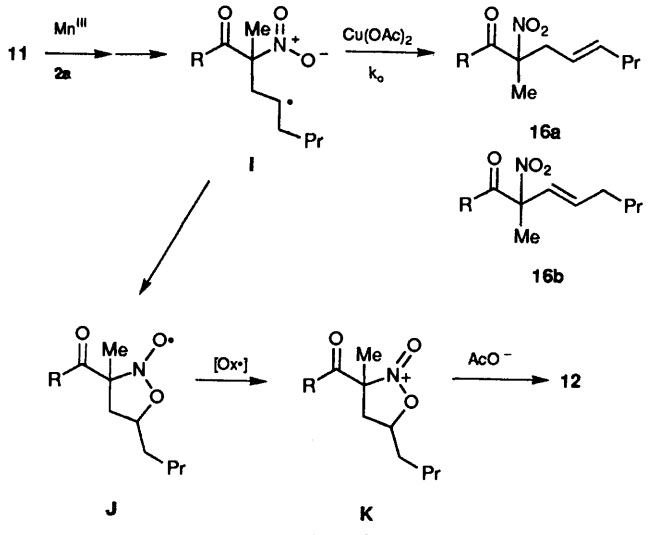
product **4a** is also formed in the reaction of compound **1** with hex-1-ene when copper(II) acetate is present as the cooxidant. Copper(II) acetate oxidises secondary alkyl radicals to the corresponding unsaturated compounds *ca.* 350 times faster than does manganese(III).[16] The rate constant of the Cu^{II}-oxidation has been determined to be $k_o = 7.6 \times 10^7\ dm^3\ mol^{-1}\ s^{-1}$ (57 °C, AcOH).[17] Thus, the formation of the unsaturated open-chain product **4a** in the reaction of compound **1** with hex-1-ene in the presence of copper(II) acetate can again be rationalised by the proposed reaction mechanism leading to the adduct radical **D** (Scheme 2). Apparently, the oxidation of this secondary alkyl radical must occur with a rate constant slightly lower than the rate constant k_c for the formation of the nitroxyl radical **E**. Assuming that the product ratio of **3a** : **4a** represents the ratio of $k_c : k_o$, one can estimate that $k_c \approx 4.7 \times k_o \approx 3.6 \times 10^8\ s^{-1}$. This value is quite similar to the known rate constant of the rearrangement of cyclopropylmethyl radicals, as described above.

While the comparable oxidative addition of acetophenone to alkenes has been shown to furnish 1-tetralones in 40–53% yield by intramolecular cyclisation,[18] the oxidative addition of nitroacetophenone to alkenes **2** normally gives the *N*-oxides **3**. This difference can also be explained on the basis of kinetic data. As determined by Heiba and Dessau,[18] internal cyclisation of secondary δ-oxo-δ-phenyl butyl radicals to the corresponding cyclohexadienyl radicals occurs with a rate constant of $k_{cyc} = 3 \times 10^5\ s^{-1}$. This rate constant is some three orders of magnitude lower than the rate constant k_c for the internal cyclisation of radical **D** to the nitroxyl radical **E** estimated above. Therefore, internal cyclisation to the tetralone system does not normally occur upon oxidative additions of compound **1** to simple olefins. The only case in which a tetralone system was formed was the oxidative addition of compound **1** to cyclohexa-1,5-diene (Table 1, entry 6). This reaction again supports the assumption that the unsaturated compound also serves as a ligand for the manganese ion involved. Thus, the cyclooctadienyl residue in the intermediate **D** will still be complexed to the Mn^{II} ion, thereby enhancing the cyclisation rate to the aromatic ring to give the cyclohexadienyl radical **H** which is then easily further oxidised to the final product **5** (Scheme 2). The product ratio of **3f** : **5** (30 : 30) in this reaction clearly shows that the rate constant k_{cyc} to furnish cyclohexadienyl radical **H** must at least be comparable to the rate constant of the internal cyclisation k_c to give the nitroxyl radical **E**. The cyclisation is thus accelerated by a factor of *ca.* 1000 by complexation of the cycloocta-1,5-diene residue to Mn^{III}/Mn^{II} as compared with the reactions of acetophenone.

This mechanism also explains why the product ratio is not changed upon addition of copper(II) acetate as co-oxidant. In both cases, the final formation of compounds **3f** from **E** and **5** from **H** does not involve an oxidation step which is likely to be dependent on the oxidising agent.

The proposed reaction mechanism cannot completely explain the formation of the aromatised isoxazole **7** upon oxidative addition of compound **1** to phenylacetylene. Although it remains unclear at which stage of the reaction the isoxazole-nitrogen is deoxygenated, it is known that phenyl-substituted isoxazoline *N*-oxides easily aromatise to the corresponding isoxazoles upon treatment with acetic acid anhydride or bases,[19] conditions which closely resemble the present reaction conditions. Recently, a somewhat related deoxygenation of *N*-hydroxy-2-azetidinones by manganese(III) acetate has also been reported.[20] It should be stated that the *N*-oxides **3** proved to be stable under the reaction conditions employed in the oxidative additions described above.

The proposed mechanism also clearly holds for the oxidative additions of the α-methyl-α-nitro ketones **11** to hex-1-ene leading to the adduct radical **I**. In compounds **11**, no α-hydrogen atom is present. Consequently, an intermediate nitrosonium ion of type **K** is opened by acetate ions to give the γ-acetoxylated products **12** (Scheme 3). In aqueous media, a



Scheme 3

similar γ-hydroxylated nitro compound has already been isolated by Bowman in the intramolecular oxidative radical cyclisation of an unsaturated nitronate.[14] In the present case, the addition of $Cu(OAc)_2$ left the product distribution unchanged. This can also be explained by the participation of the nitro group in the radical reaction since the oxidation of nitroxyl radicals of type **J** should be independent of the type of oxidant employed. Apparently, the formation of the nitroxyl radical **J** and its subsequent oxidation to the nitrosonium **K** in this case is faster than the oxidation of the nitroxyl radical **J** by Cu^{II} to unsaturated derivatives **16**. A possible explanation for this fact might be an increased stabilisation of the intermediate **K** through the electron-donating effect of the methyl group, thus favouring the formation of the radical **J** in comparison to the oxidation to **16**.

The reason for the failure of α-unsubstituted α'-alkyl α-nitro ketones **8** to react in manganese(III) based reactions can be rationalised when the reactions of the α'-aryl-α-nitro ketones **9** are considered. Apparently, an electron-withdrawing substituent in the α'-position of α-unsubstituted α-nitro ketones is a prerequisite for the addition to proceed. This can readily be explained by the reaction mechanism depicted in Scheme 1, which first involves the formation of a manganese(III) enolate **A** from the α-nitro ketone. The formation of this enolate is greatly favoured when an electron-withdrawing α'-substituent, increasing the CH-acidity of the α-nitro ketone, is present.

For the α-methyl-α-nitro ketones **11**, the arguments just stated for the α-unsubstituted derivatives do not hold. In ketones **11**, the α-methyl substituent is electron-donating and thus decreases the acidity of the α-proton. This behaviour again closely resembles the properties and reactions of acetoacetates investigated by Snider.[8] Analogously to α-unsubstituted and α-methyl acetoacetates,[21] an α-methyl substituent in α-nitro ketones should facilitate the oxidation of the enolate to the corresponding radical. Therefore, the reason for the reaction to proceed in the case of α-substituted α-nitro ketones is the stabilisation of the radical produced from the magnanese(III) enolate by the methyl group. This is also demonstrated by the reaction of compound **11a** which is formally derived from compound **1** by the introduction of a α-methyl group. This structural change consequently increased the total yield for the oxidative addition to hex-1-ene from 62% **3a** to 81% **12a**.

Oxidative Additions of α-Nitro Amides to Hex-1-ene.— Manganese(III) based oxidative radical additions of suitably substituted amides have rarely been reported until now.[22] Parallel to the work described above, we decided to incorporate the hitherto unused α-nitro amides **13** in our study (see Fig. 3).

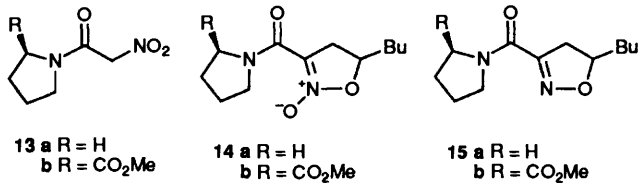


Fig. 3

Chiral α-nitro amides can readily be prepared from chiral amines[23] and their oxidation with manganese(III) acetate would result in the formation of chiral substituted α-nitro-α-amido radicals. Since amide substituted radicals have recently been shown to add to alkenes with high diastereoselectivity,[24] we expected to achieve similar results in the manganese(III) mediated oxidative radical additions of α-nitro amides. If, on the other hand, the oxidative addition of α-nitro amides to alkenes led to isoxazoline *N*-oxides **14**, the resulting heterocycles would be of special synthetic interest because 3-amidoisoxazolines cannot be obtained by other synthetic methods.

Oxidative additions of α-nitro amides to alkenes mediated by metal salts have not been described in the literature. Therefore, we first chose the readily available α-nitro amide **13a** as a model substrate. Under the standard conditions of the oxidative addition, **13a** reacted with hex-1-ene within 30 min to furnish two products **14a** (43%) and the *N*-deoxygenated isoxazoline **15a** (12%). Similarly, the chiral α-nitro amide **13b**, derived from L-proline, furnished the isoxazoline *N*-oxide **14b** (14%) and the isoxazoline **15b** (10%), both as 1 : 1 mixture of diastereoisomers as shown by GLC measurements. The low total yield in the reaction of compound **13b** can undoubtedly be attributed to the very low solubility of the α-nitro amide in acetic acid. Attempted oxidative additions of closely related α-nitro amides to hex-1-ene failed completely for the same reason.

The successful reaction of the α-nitro amides **13** was surprising considering the results of the additions of α-nitro ketones to alkenes. The formation of the *N*-deoxygenated adducts **15** was also unexpected. Therefore, we conducted control experiments to exclude the formation of compound **15** from **14** during the reaction course. However, compound **14a**

Table 3 Oxidative additions of α-nitro carbonyl compounds to unsaturated systems mediated by electrochemically regenerated manganese(III) acetate[a]

Entry	α-Nitro carbonyl compound	Alkene or alkyne	Current density (mA cm^{-2})	Charge consumption (F mol^{-1})[b]	Product [yield (%)]
18	**1**	**2a**	0.5	2	**3a** [59]
19	**1**	**2b**	0.3[c]	2	**3b** [37]
20	**1**	**6**	0.3[c]	2	**7** [49]
21	**11a**	**2a**	0.2[c]	5	**12a** [54][d]
22	**13a**	**2a**	0.12	3	**14a** [48]

[a] The electrolyses were performed under galvanostatic conditions in a beaker-type thermostatable electrolysis cell under an argon atmosphere at 60 °C. 1 Mmol of the α-nitro carbonyl compound and 2 mmol alkene or alkyne in 50 cm^3 0.05 mol dm^{-3} Bu_4NBF_4 were allowed to react using 0.1 mmol manganese(II) acetate tetrahydrate as the mediator. Anode: Sigraflex graphite foil; cathode: Pt-wire, separated from the anode compartment by a G5 glass sinter frit. [b] Charge consumption until the α-nitro carbonyl compound was totally consumed as judged by GLC analysis. [c] 0.1 mol dm^{-3} Et_3N–AcOH used as electrolyte. [d] Significant amounts of benzoic acid were formed during the prolonged electrolysis time.

could not be converted into compound **15a** either by heating with manganese(II) acetate in acetic acid or in the presence of hex-1-ene. Heating compound **14a** in the presence of manganese(III) acetate in acetic acid led to the complete destruction of the starting material with no identifiable products. Therefore, the two different products **14** and **15** must be formed *via* different pathways during the oxidative addition. Although some explanations for the different outcome of the oxidative addition of α-nitro amides **13** to hex-1-ene in comparison to the reactions of α-nitro ketones appear to be possible, a full mechanistic interpretation of these results would be speculative at the present stage.

Oxidative Additions Mediated by Electrochemically in-situ *Regenerated Manganese*(III) *Acetate*.—It has previously been shown by several groups that manganese(III)-based oxidative additions of CH-acidic compounds to alkenes can be conducted in the presence of catalytic amounts of Mn^{II} salt, when the oxidant is regenerated electrochemically.[10,25] After a series of α-nitro carbonyl compounds were successfully added to alkenes and alkynes using 2 molar equiv. of the transition metal oxidant manganese(III) acetate, we performed representative reactions using electrochemically *in-situ* produced manganese(III) acetate. Table 3 shows the results of these electrolyses. Using 10 mole percent of manganese(II) acetate as mediator, the products of the oxidative addition of α-nitro carbonyl compounds **1**, **12a** and **14a** were obtained in yields which are as high or even slightly higher than in reactions using equimolar amounts of the transition metal oxidant.

The reaction of compound **1** with phenylacetylene (entry 20) furnished the aromatic addition product in a yield 15% higher than in the addition using equimolar amounts manganese(III) acetate (Table 1, entry 10). Furthermore, for the reaction of compound **14a**, the only addition product found in the reaction conducted electrochemically was the *N*-oxide **15a**. The by-product **16a**, found in the oxidative addition using an equimolar amount of manganese(III) acetate, was not produced. Apparently, the reason for this behaviour must be seen in the low concentration of the oxidant during the addition course.

In general, the current densities applied were rather low (see Table 3). Increasing the current densities in all cases gave rise to side products which could not be isolated. This can readily be explained upon the basis of the reaction mechanism of the oxidative addition. Chemical regeneration of Mn^{II} from the intermediate **D** proceeds relatively slowly (30–60 min) as compared with its electrochemical reoxidation to Mn^{III} at the anode. Therefore, at high current densities, all Mn^{II} ions present in the solution will be oxidised to Mn^{III}. Then, direct electrochemical oxidation of the organic substances present or the solvent will occur, leading to the side products observed. To exclude the possibility of a direct oxidation of the α-nitro carbonyl compounds at the anode, we conducted electrolyses without adding any manganese(II) acetate. However, only trace amounts of the addition products could be detected by GLC–MS analysis of the electrolysis mixture in all cases. Examination of the electrochemical properties of the α-nitro carbonyl compounds by performing cyclic voltammetry under the acidic conditions used in the electrolyses was also performed. However, in 0.05 mol dm^{-3} Bu_4NBF_4–AcOH, oxidation of the solvent at about +2.0 V *vs.* SCE occurred and no oxidation potentials of α-nitro carbonyls were detectable at lower potentials. Changing the solvent to 0.05 mol dm^{-3} Bu_4NBF_4–CF_3CO_2H containing 1% $(CF_3CO)_2O$ made the detection of irreversible oxidation peaks at 1950–2490 mV *vs.* SCE possible. Based upon the fact that α-nitro carbonyl compounds in protic media mainly exist in the keto nitro form and not in the corresponding enol form[26] and upon literature data for the oxidation potentials of different functional groups,[27] we attributed the detected oxidation peaks to the unsaturated groups or the amide moieties and not to the electrochemical oxidation of the α-nitro carbonyl compounds to the cation radicals. Moreover, compounds **8**, which failed to react in manganese(III) acetate mediated reactions, showed similar electrochemical properties as compared with the compounds being used successfully. We therefore concluded that the indirect electrochemical addition of α-nitro carbonyl compounds shown in Table 3 indeed proceeds *via* the manganese(III) based inner-sphere electron transfer and not *via* outer-sphere electron transfer.

Conclusions.—α'-Aryl α-nitro ketones **1** and **10** can be added to unsaturated systems with manganese(III) acetate as oxidant, furnishing the heterocyclic *N*-oxides **3** as normal products in good to modest yield. Depending upon the structure of the unsaturated compound, other or additional products such as **4**, **5** and **7** are obtained. In contrast, α'-alkyl α-unsubstituted α-nitro ketones **8** do not react under the conditions of the oxidative addition. The introduction of a α-substituent in α-nitro ketones **11** causes the addition to hex-1-ene to proceed effectively to give the γ-acetoxylated adducts **12** in good yield. Oxidative addition of α-nitro amides **13** to hex-1-ene gives the isoxazoline *N*-oxides **14** and the isoxazolines **15** as products in modest overall yields. The use of 2 molar equiv. manganese(III) acetate can be readily substituted by regeneration of the oxidant in an electrochemical *in-cell* process using the Mn^{II}/Mn^{III} redox couple as a mediator for the oxidative radical addition.

Experimental

General.—All reactions were performed under an argon atmosphere. Analytical thin layer chromatography (TLC) was performed on Merck silica gel F_{254} precoated aluminium plates. Analytical gas chromatography was performed on a HP-5890 instrument equipped with a HP-1 fused silica capillary column, 12.5 m, 0.20 mm internal diam., coupled to a mass selective detector HP 5970 using helium as a carrier gas or on a Carlo Erba Series 4100 instrument equipped with a fused silica capillary column, 15 m, 0.53 internal diam. and a flame ionisation detector (FID) using nitrogen as a carrier gas. For electrolyses, a beaker-type 50 cm^3 glass cell with a cylindrical Sigraflex anode (4 cm diameter × 6.5 cm height) and a platinum wire cathode, separated from the anode compartment by a G5 glass frit, was used. A FUG Model NTN 700 M-200 current supply modified as a potentiostat was used as power source and the charge flow was measured with a home-made DC integrator.

Measurements.—The ^1H and ^{13}C spectra were recorded using either a Bruker WH 90 (90 MHz for ^1H and 22.5 MHz for ^{13}C), AC 200 (200 MHz for ^1H and 50.32 MHz for ^{13}C), WH 250 (250 MHz) or an AC 400 (400 MHz) spectrometer, with the solvent $CDCl_3$ being used as the internal standard. Chemical shifts are reported as δ values and J values are given in Hz. Assignments of ^{13}C signals were made by spin echo or DEPT experiments. The IR spectra were measured on a Perkin-Elmer FT–IR 1600 Series spectrometer and the values are expressed in cm^{-1}. Mass spectra were measured on an AEI MS 50 instrument.

Due to very easy fragmentation under the conditions of electron ionisation mass spectroscopy, high-resolution mass spectra could not be obtained for all compounds. In these cases, either fast atom bombardment mass spectroscopy (FAB) on a Kratos Concept 1H instrument using *m*-nitrobenzyl alcohol (*m*NBA) as the matrix with argon as the reactant gas, or chemical ionisation mass spectroscopy (CI) using methane as the reactant gas on a Hewlett Packard HP 5989A MS Engine GLC–MS system, were performed. However, the purity of all products was confirmed by GLC measurements.

Materials.—All solvents for chromatography were distilled before use. Petroleum refers to the fraction with the boiling range 40–60 °C. Acetic acid (99.8%, Riedel-de-Haën) was used as purchased. Manganese(III) acetate dihydrate was prepared according to a method described in the literature.[28] α-Nitro ketones were prepared by a modification of a method described in the literature[29] from the corresponding carboxylic acids, by alkylation of the imidazolide with the dianion of the appropriate nitroalkyl compound. α-Nitro amides were prepared *via* the corresponding ketene N,S-acetals as described in the literature.[23] Unsaturated compounds were purchased (Merck or Aldrich). Liquids were distilled before use whereas solid compounds were used as purchased. Vinylcyclopropane **2h** was prepared by methylenation of cyclopropanecarbaldehyde with 'instant ylide' (Fluka), using mesitylene as solvent.

General Procedure for the Oxidative Addition of α-Nitro Ketones and α-Nitro Amides to Unsaturated Systems using Equimolar Amounts of Manganese(III) Acetate.—Manganese(III) acetate (2 mmol) and the appropriate α-nitro carbonyl compound (1 mmol) were dissolved in glacial acetic acid (50 cm^3) and the unsaturated component (2 mmol) was added *via* a syringe. Solid compounds were predissolved in acetic acid (5 cm^3) before addition. The reaction mixture was stirred at 60 °C until decolouration of the deep brown solution occurred. After cooling to room temp., the reaction mixture was diluted with water and extracted twice with methylene dichloride. The combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated. The residue was purified as indicated below.

General Procedure for the Oxidative Addition of α-Nitro Ketones and α-Nitro Amides to Unsaturated Systems using Electrochemically Regenerated Manganese(III) Acetate.—Manganese(II) acetate tetrahydrate (25 mg, 0.1 mmol) and the α-nitro carbonyl compound (1 mmol) were dissolved in Bu_4NBF_4–AcOH (50 cm^3, 0.05 mol dm^{-3}) or in Et_3N–AcOH (50 cm^3; 1%) in the electrochemical cell. The solution was thermostatted to 60 °C and the unsaturated component (2 mmol) was added while a continuous flow of argon was maintained above the electrolyte. The electrolysis was performed at the current density indicated in Table 3 until the charge listed in Table 3 was consumed. The reaction mixture was stirred at 60 °C for a further 1 h to assure completion of the reaction and then worked up as described above to yield the addition products. Yields are listed in Table 3.

3-*Benzoyl*-5-*butyl*-4,5-*dihydroisoxazole* 2-*Oxide* **3a**.—Yellow oil after flash chromatography with petroleum–diethyl ether (3:1) (Found: M^+, 247.1211. Calc. for $C_{14}H_{17}NO_3$: *M*, 247.1208); ν_{max}(NaCl, film)/cm^{-1} 1740, 1600, 1460, 1280 and 715; δ_H(200 MHz, $CDCl_3$) 8.19 (2 H, ddd, *J* 7.7, 2.6 and 1.3, 2′-H and 6′-H), 7.59 (1 H, tt, *J* 7.7 and 1.3, 4′-H), 7.45 (2 H, ddd, *J* 7.7, 2.6 and 1.3, 3′-H and 5′-H), 4.78 (1 H, dddd, *J* 10.3, 9, 6.4 and 2.6, 5-H), 3.40 (1 H, dd, *J* 16.8 and 10.3, 4-H), 3.0 (1 H, dd, *J* 16.8 and 9, 4-H), 1.55–1.85 (2 H, m, 1″-CH_2), 1.42 (4 H, m, 2″-CH_2 and 3″-CH_2) and 0.95 (3 H, t, *J* 7.6, Me); δ_C(50.32 MHz, $CDCl_3$) 185.37 (C=O), 135.46 (>C=), 132.84 (=CH–), 128.50 (=CH–), 127.98 (=CH–), 115.52 (>C=N), 76.64 (>CH–O), 36.63 (>CH_2), 33.90 (>CH_2), 26.62 (>CH_2), 22.06 (>CH_2) and 13.63 (–Me); *m*/*z* (70 eV) 247 (M^+, 0.13%), 231 (9), 174 (18), 126 (28), 105 (100) and 84 (10).

5-(*Acetoxymethyl*)-3-*benzoyl*-4,5-*dihydroisoxazole* 2-*Oxide* **3b**.—After standard work-up, the product was purified by flash chromatography with petroleum–diethyl ether (3:1) to give a yellow oil (Found: M^+, 263.0785. Calc. for $C_{13}H_{13}NO_5$: *M*, 263.0793); ν_{max}(NaCl, film)/cm^{-1} 1765, 1675, 1380, 1260 and 720; δ_H(200 MHz, $CDCl_3$) 8.19 (2 H, ddd, *J* 8.3, 3.5 and 1.2, 2′-H and 6′-H), 7.6 (1 H, tt, *J* 7.2 and 1.2, 4′-H), 7.46 (2 H, ddd, *J* 8.3, 7.2 and 1.2, 3′-H and 5′-H), 5.25 (1 H, dddd, *J* 10.7, 8.3, 6 and 3.6, 5-H), 4.3 (1 H, dd, *J* 11.9 and 3.6, 1″-H), 4.19 (1 H, dd, *J* 11.9 and 6, 1″-H), 3.47 (1 H, dd, *J* 17.9 and 10.7, 4-H), 3.18 (1 H, dd, *J* 17.9 and 8.3, 4-H), 2.1 (3 H, s, –Me); δ_C(50.32 MHz, $CDCl_3$) 185.87 (COMe), 170.55 (C=O), 157.44 (>C=N), 135.49 (>C=), 133.67 (=CH–), 130.22 (=CH–), 128.35 (=CH–), 79.76 (>CH–), 64.48 (>CH_2), 36.11 (>CH_2), 20.61 (–Me); *m*/*z* (70 eV) 263 (M^+, 0.9%), 203 (5), 187 (52), 174 (61) and 105 (100).

3-*Benzoyl*-5-(*trimethylsilylmethyl*)-4,5-*dihydroisoxazole* 2-*Oxide* **3c**.—Colourless crystals after flash chromatography using petroleum–diethyl ether (20:1 v/v); m.p. 85 °C (Found: M^+, 277.1143. Calc. for $C_{14}H_{19}NO_3Si$: *M*, 277.1134); ν_{max}(KBr)/ cm^{-1} 1700, 1590, 1580, 1370, 1260 and 700; δ_H(200 MHz, $CDCl_3$) 7.75 (2 H, ddd, *J* 8.3, 1.5 and 1.5, 2′-H and 6′-H), 7.55 (1 H, tt, *J* 6.9 and 1.4, 4′-H), 7.45 (2 H, ddd, *J* 8.3, 6.9 and 1.5, 3′-H and 5′-H), 4.96 (1 H, dddd, *J* 9.7, 9.6, 8.3 and 5.6, 5-H), 3.55 (1 H, dd, *J* 16.7 and 8.3, 4-H), 3.19 (1 H, dd, *J* 16.7 and 9.7, 4-H), 1.35 (1 H, dd, *J* 13.9 and 5.6, 1″-H), 1.15 (1 H, dd, *J* 13.9 and 9.2, 1″-H) and 0.12 (9 H, s, $SiMe_3$); δ_C(50.32 MHz, $CDCl_3$) 185.91 (C=O), 135.65 (>C=), 133.18 (=CH–), 128.84 (=CH–), 128.26 (=CH–), 116.47 (>C=N), 76.69 (>CH–O), 39.39 (>CH_2), 23.23 (>CH_2), and −1.00 (Si-(Me)$_3$); *m*/*z* (35

eV) 277 (M^+, 1.94%), 260 (1), 247 (2), 179 (12), 105 (100) and 73 (98).

3-*Benzoyl*-5-(2-*carboxyethyl*)-4,5-*dihydroisoxazole* 2-*Oxide* **3d**.—Flash chromatography with diethyl ether–petroleum (5:1) yielded a pale yellow oil which was inseparable from traces of higher fatty acids produced in the reaction (Found: M^+, 247.0850. Calc. for $C_{13}H_{13}NO_4$: M − O, 247.0845); ν_{max}(NaCl, film)/cm^{-1} 1720, 1645, 1280, 1190, 720 and 510; δ_H(250 MHz, $CDCl_3$) 8.17 (2 H, d, J 9.3, 2′-H and 6′-H), 7.55 (1 H, t, J 9.3, 4′-H), 7.49 (2 H, dd, J 9.3 and 9.3, 3′-H and 5′-H), 4.88 (1 H, br, 5-H), 3.45 (1 H, br, 4-H), 3.05 (1 H, br, 4-H), 2.6 (2 H, br, 1″-CH_2), 2.05 (2 H, br, 2″-CH_2); m/z (35 eV) 247 (0.89%), 229 (0.5), 216 (0.5), 201 (1), 187 (5), 174 (100), 142 (61), 124 (81) and 105 (87).

rel-(3aR,9aS)-3-*Benzoyl*-3a,4,5,6,7,8,9,9a-*octahydrocyclo-octa*[1,2-d]*isoxazole* 2-*Oxide* (cis-**3e**) *and* rel-(3aR,9ar)-3-*Benzoyl*-3a,4,5,6,7,8,9,9a-*octahydrocycloocta*[1,2-d]-*isoxazole* 2-*Oxide* (trans-**3e**) (2.3:1 *Mixture of Isomers*).—Purification of the crude product by chromatography using petroleum–diethyl ether (3:1), followed by recrystallisation from diethyl ether–pentane (1:1 v/v) gave white crystals: m.p. 143 °C (Found: M^+, 273.1367. Calc. for $C_{16}H_{19}NO_3$: M, 273.1365); ν_{max}(KBr)/cm^{-1} 1705, 1655, 1595, 1375, 1275 and 695; δ_H(200 MHz, $CDCl_3$) 7.75 (2 H, m, 2′-H and 6′-H), 7.55 (1 H, m, 4′-H), 7.42 (2 H, m, 3′-H and 5′-H), [4.83 (ddd, J 10.8, 9.6 and 2.8) and 4.78 (ddd, J 12, 10.7 and 4.3) (1 H, 9a-H)], [3.92 (ddd, J 12, 6 and 3.4) and 3.73 (1H, ddd, J 9.6, 8.4 and 1.2) (1 H, 3a-H)], 1.2–2.3 (12 H, m); δ_C(22.5 MHz, $CDCl_3$) 186.24 (C=O), 135.98 and 135.69 (>C=), 133.68 and 133.29 (=CH–), 129.12 and 128.82 (=CH–), 128.50 and 128.37 (=CH–), 120.60 and 120.10 (>C=N), 82.70 and 81.96 (>CH–O), 48.81 and 47.87 (>CH–), 33.24 and 31.59 (>CH_2), 29.39 (>CH_2), 26.77 and 26.64 (>CH_2), 25.44 and 25.31 (>CH_2), 25.02 and 24.50 (>CH_2), 23.43 and 21.91 (>CH_2); m/z (70 eV) 273 (M^+, 5.9%), 256 (5), 174 (1), 168 (2), 122 (50) and 105 (100).

rel-(3aR,9aR)-3-*Benzoyl*-3a,4,5,8,9,9a-*hexahydrocycloocta*-[1,2-d]*isoxazole* 2-*Oxide* **3f**.—Purification by flash chromatography with petroleum–diethyl ether (3:1 v/v), followed by recrystallisation from diethyl ether yielded white crystals: m.p. 136 °C (Found: C, 70.6, H, 6.3, N, 5.0. Calc. for $C_{16}H_{17}NO_3$: C, 70.83, H, 6.32, N, 5.16%) (Found: M^+, 271.1209. Calc. for $C_{16}H_{17}NO_3$: M, 271.1208); ν_{max}(KBr)/cm^{-1} 1610, 1470, 1400, 1275, 750, 710 and 670; δ_H(400 MHz, $CDCl_3$) 7.78 (2 H, ddd, J 8.4, 3.6 and 1.2, 2′-H and 6′-H), 7.58 (1 H, tt, J 7.2 and 1.2, 4′-H), 7.45 (2 H, ddd, J 8.4, 7.2 and 1.2, 3′-H and 5′-H), 5.75 (1 H, ddd, J 21.5, 11.9 and 7.2, 6-H or 7-H), 5.70 (1 H, ddd, J 21.5, 11.9 and 6.7, 6-H or 7-H), 4.72 (1 H, ddd, J 12, 10.9 and 4.3, 9a-H), 3.99 (1 H, ddd, J 12, 10.7 and 4.3, 3a-H), 2.26 (6 H, m, 4-H, 5-CH_2, 8-CH_2 and 9-H), 1.74 (1 H, m, 19-H), 1.51 (1 H, m, 4-H); δ_C(50.32 MHz, $CDCl_3$) 186.23 (C=O), 135.51 (>C=), 133.58 (–CH=), 129.65 (–CH=), 129.44 (–CH=), 129.00 (=CH–), 128.41 (=CH–), 119.28 (>C=N), 82.39 (>CH–O), 48.55 (>CH–), 31.12 (>CH_2), 27.70 (>CH_2), 23.08 (>CH_2) and 21.13 (>CH_2); m/z (70 eV) 271 (M^+, 1.17%), 254 (1.3), 243 (4.3) and 105 (100).

3-*Benzoyl*-5-*cyclopropyl*-4,5-*dihydroisoxazole* 2-*Oxide* **3g**.—Flash chromatography using ethyl acetate–heptane (1:10 v/v) gave a colourless oil; ν_{max}(NaCl, film)/cm^{-1} 1700, 1655, 1555, 1255 and 700; δ_H(200 MHz, $CDCl_3$) 8.18 (2 H, ddd, J 8, 1.5 and 1.5, 2′-H and 6′-H), 7.60 (1 H, td, J 7.5 and 1.5, 4′-H), 7.48 (2 H, ddd, J 8, 7.5 and 1.5, 3′-H and 5′-H), 4.32 (1 H, ddd, J 11.3, 8.9 and 7.5, 5-H), 3.42 (1 H, dd, J 17.9 and 11.3, 4-H), 3.16 (1 H, dd, J 17.9 and 8.9, 4-H) and 1.05–1.15 (1 H, m, 1″-H) and 0.3–0.6 (4 H, m); m/z (35 eV) 215 (10%), 199 (2), 186 (2) and 105 (100).

2-*Nitro*-1-*phenyloct*-4-*ene*-1-*one* **4a**.—Yellow oil after flash chromatography with petroleum–diethyl ether (3:1 v/v) (Found: M^+, 247.1210. Calc. for $C_{14}H_{17}NO_3$: M, 247.1208); ν_{max}(NaCl, film)/cm^{-1} 1700, 1580, 1270, 1230 and 690; δ_H(200 MHz, $CDCl_3$) 7.75 (2 H, ddd, J 8.3, 2.8 and 1.4, 2′-H and 6′-H), 7.65 (1 H, tt, J 6.9 and 1.4, 4′-H), 7.5 (2 H, ddd, J 8.3, 6.9 and 1.4, 3′-H and 5′-H), 6.07 (1 H, dd, J 9.5 and 5.6, 2-H), 5.6 (1 H, dddt, J 16.7, 6.9, 6.9 and 1.4, 4-H), 5.37 (1 H, dddt, J 16.7, 6.9, 6.9 and 1.6, 5-H), 2.7–3.1 (2 H, m, 3-CH_2), 1.95 (2 H, m, 6-CH_2), 1.32 (2 H, m, 7-CH_2) and 0.83 (3 H, t, J 7.6, –Me); δ_C(50.32 MHz, $CDCl_3$) 188.68 (C=O), 136.77 (=CH–), 134.75 (=CH–), 134.05 (>C=), 129.25 (=CH–) 128.87 (=CH–), 121.94 (=CH–), 89.62 (>CH–NO_2), 34.53 (>CH_2), 33.80 (>CH_2), 22.17 (>CH_2) and 13.57 (–Me); m/z (70 eV) 247 (M^+, 0.2%), 201 (21), 157 (60) and 105 (100).

2-*Nitro*-1-*phenylpent*-4-*ene*-1-*one* **4b**.—The crude product was dissolved in diethyl ether and filtered through a short pad of silica gel to remove most of the stannane-containing by-products. The ethereal solution was evaporated to dryness and the residue was purified by flash chromatography (diethyl ether–petroleum 2:1) to give a yellow oil (Found: M^+, 189.0789. Calc. for $C_{11}H_{11}NO_2$: M − O, 189.0790); ν_{max}(NaCl, film)/cm^{-1} 1695, 1560, 1330, 1260 and 690; δ_H(200 MHz, $CDCl_3$) 7.96 (2 H, ddd, J 8.3, 1.4 and 1.4, 2′-H and 6′-H), 7.68 (1 H, tt, J 6.9 and 1.4, 4′-H), 7.53 (2 H, ddd, J 8.3, 6.9 and 1.4, 3′-H and 5′-H), 6.11 (1 H, dd, J 8.6 and 5.6, 2-H), 5.80 (1 H, dddd, J 16.7, 9.7, 6.9 and 5.5, 4-H), 5.22 (1 H, ddd, J 16.7, 2.7 and 1.4, 5-H_{trans}), 5.19 (1 H, ddd, J 9.7, 2.7 and 1.4, 5-H_{cis}), 3.11 (1 H, dddd, J 8.6, 6.9, 2.7 and 1.4, 3-H) and 2.94 (1 H, dddd, J 5.6, 5.5, 2.7 and 1.4, 3-H); δ_C(50.32 MHz, $CDCl_3$) 188.37 (C=O), 134.88 (=CH–), 133.89 (>C=), 130.64 (=CH–), 129.32 (=CH–), 128.90 (=CH–), 120.32 (=CH_2), 88.95 (>CH–NO_2) and 34.59 (>CH_2); m/z (CI) 206 [(M + H)$^+$, 2%], 189 (2), 174 (4), 159 (8), 105 (87) and 68 (100); m/z (40 eV) 189 [0.01%, (M − O)$^+$], 175 (1), 127 (5) and 105 (100).

2-*Nitro*-1-*phenylhex*-4-*ene*-1-*one* **4c**.—The reaction was performed at 50 °C in a sublimation apparatus by cooling the top of the flask to −10 °C with a methanol-filled cooling bath to minimise loss of the highly volatile vinylcyclopropane. The crude reaction product was purified by flash chromatography using ethyl acetate–heptane (1:10 v/v) to give a pale yellow oil; ν_{max}(NaCl, film)/cm^{-1} 1720, 1550, 1260, 1250 and 710; δ_H(200 MHz, $CDCl_3$) 7.95 (2 H, ddd, J 7.5, 1.5 and 1.5, 2′-H and 6′-H), 7.67 (1 H, tt, J 8.9 and 1.5, 4′-H), 7.51 (2 H, ddd, J 8.9, 7.5 and 1.5, 3′-H and 5′-H), 6.07 (1 H, dd, J 11.9 and 6, 2-H), 5.54 (1 H, dddt, J 14.9, 14.9, 8.9 and 1.5, 4-H), 5.37 (1 H, dddt, J 14.9, 8.9, 7.5 and 1.5, 5-H), 2.75–3.1 (1 H, m, 3-CH_2), 2.0 (2 H, ddqd, J 8.9, 7.5, 7.5 and 1.5, 6-CH_2) and 0.9 (3 H, t, J 7.5, –Me); δ_C(50.32 MHz, $CDCl_3$) 188.72 (C=O), 138.37 (=CH–), 134.75 (=CH–), 134.06 (>C=), 129.25 (=CH–), 128.87 (=CH–), 120.86 (=CH–), 89.64 (>CH–NO_2), 33.73 (>CH_2), 25.53 (>CH_2) and 13.36 (–Me); m/z (FAB) 234 [(M + H)$^+$, 6%], 215 (3), 187 (5), 154 (46), 136 (38) and 105 (100); m/z (70 eV) 203 (1%), 187 (21), 157 (30) and 105 (100).

rel-(6S,6aR,12aR)-6-*Nitro*-6a,7,8,11,12,12a-*hexahydroocta*-[2]*naphthalen*-5(H)-*one* **5**.—Yellow oil after flash chromatography using petroleum–diethyl ether (3:1 v/v) (Found: M^+, 271.1211. Calc. for $C_{16}H_{17}NO_3$: M, 271.1208); ν_{max}(NaCl, film)/cm^{-1} 1705, 1555, 1370, 1305, 770 and 750; δ_H(400 MHz, $CDCl_3$) 7.77 (1 H, ddd, J 7.6, 1.6 and 0.4, 4-H), 7.59 (1 H, ddd, J 7.6, 6.4 and 1.2, 3-H), 7.32 (1 H, dddd, J 8, 6.4, 1.6 and 0.4, 2-H), 7.24 (1 H, dddd, J 8, 2.4, 1.2 and 0.6, 1-H), 5.83 (1 H, ddd, J 10.2, 7.8 and 6.8, 9-H or 10-H), 5.76 (1 H, dddd, J 10.2, 8.8, 6.4 and

0.8, 9-H or 10-H), 5.27 (1 H, d, *J* 12.8, 6-H), 3.20 (1 H, dddd, *J* 10.8, 6, 3.6 and 0.6, 12a-H), 2.95 (1 H, dddd, *J* 12.8, 10.8, 5.8 and 2.6, 6a-H), 2.42 (2 H, m, 8-H and 11-H), 2.30 (2 H, m, 8-H and 11-H), 1.91 (1 H, dddd, *J* 14, 10.8, 4.4 and 3.6, 12-H), 1.74 (1 H, dddd, *J* 13.2, 8, 3.8 and 2.6, 7-H) and 1.56 (2 H, m, 12-H and 7-H); δ_C(50.32 MHz, $CDCl_3$) 188.14 (C=O), 146.73 (>C=), 135.04 (–CH=), 129.95 (>C=), 129.84 (–CH=), 129.05 (–CH=), 126.97 (–CH=), 126.73 (–CH=), 96.06 (>CH–), 41.39 (>CH–), 41.02 (>CH–), 39.35 (>CH_2), 33.95 (>CH_2), 24.97 (>CH_2) and 24.72 (>CH_2); *m/z* (70 eV) 271 (M^+, 3.7%), 254 (15), 243 (8), 225 (72), 196 (100), 157 (92), 145 (25), 141 (28), 131 (40), 128 (53), 115 (47), 105 (70), 103 (22) and 91 (25).

3-*Benzoyl*-5-*phenylisoxazole* **7**.—Filtration of the crude product over SiO_2 using petroleum–diethyl ether (3:1 v/v) gave a white solid: m.p. 78–79 °C (Found: M^+, 249.0782. Calc. for $C_{16}H_{11}NO_2$: *M*, 249.090); ν_{max}(KBr)/cm^{-1} 1620, 1480, 1450, 1430, 1320, 820 and 700; δ_H(200 MHz, $CDCl_3$) 8.34 (2 H, m), 7.85 (2 H, m), 7.67 (1 H, dt, *J* 11.1), 7.53 (5 H, m), 7.04 (1 H, s); δ_C(50.32 MHz, $CDCl_3$) 185.78 (C=O), 170.82 (>C=N), 162.54 (=C<), 135.83 (=C<), 134.17 (=CH–), 130.83 (–CH=), 129.26 (–CH=), 128.71 (–CH=), 126.77 (=C<), 126.08 (–CH=) and 100.41 (=CH–); *m/z* (70 eV) 249 (M^+, 15%), 143 (3) and 105 (100).

5-*Butyl*-3-(4′-*methoxybenzoyl*)-4,5-*dihydroisoxazole* 2-*Oxide* **10a**.—Purification by flash-chromatography using petroleum–diethyl ether (10:1 v/v) as eluent gave a yellow oil (Found: M^+, 277.1314. Calc. for $C_{15}H_{19}NO_4$: *M*, 277.1314); ν_{max}(NaCl, film)/cm^{-1} 1640, 1600, 1585, 1365, 1260 and 755; δ_H(250 MHz, $CDCl_3$) 9.23 (2 H, dd, *J* 8.3 and 1.6, 2′-H and 6′-H), 6.93 (2 H, dd, *J* 8.3 and 1.6, 3′-H and 5′-H), 4.75 (1 H, dddd, *J* 10, 8.3, 6 and 3.3, 5-H), 3.88 (3 H, s, O-Me), 3.37 (1 H, dd, *J* 16.7 and 10, 4-H), 2.98 (1 H, dd, *J* 16.7 and 8.3, 4-H), 1.75 (1 H, m, 1″-H), 1.65 (1 H, m, 1″-H), 1.3–1.5 (4 H, m, 2″-CH_2 and 3″-CH_2) and 0.9 (3 H, t, *J* 7.3, –Me); δ_C(50.32 MHz, $CDCl_3$) 184.65 (C=O), 163.97 (=C<), 132.72 (>C=N), 128.69 (>C=), 113.59 (=CH–), 83.05 (>CH–O), 55.44 (–O–Me), 39.10 (>CH_2), 34.82 (>CH_2), 27.34 (>CH_2), 22.43 (>CH_2), 13.93 (–Me): *m/z* (70 eV) 277 (M^+, 2.85%), 261 (43), 204 (12), 152 (18) and 135 (100).

5-*Butyl*-3-(4-*chlorobenzoyl*)-4,5-*dihydroisoxazole* 2-*Oxide* **10b**.—Pale yellow crystals after crystallisation from chloroform: m.p. 55 °C (Found: M^+, 281.0819. Calc. for $C_{14}H_{16}NO_3Cl$: *M*, 281.0819); ν_{max}(NaCl, film)/cm^{-1} 1720, 1590, 1460, 1275, 1175 and 805; δ_H(200 MHz, $CDCl_3$) 7.70 (2 H, dd, *J* 9 and 2.1, 2′-H and 6′-H), 7.42 (2 H, dd, *J* 9 and 2.1, 3′-H and 5′-H), 4.81 (1 H, dddd, *J* 12.9, 7.7, 5.1 and 3.9, 5-H), 3.57 (1 H, dd, *J* 16.7 and 12.9, 4-H), 3.22 (1 H, dd, *J* 16.7 and 7.7, 4-H), 1.7–2.0 (2 H, m, 1″-CH_2), 1.3–1.5 (4 H, m, 2″-CH_2 and 3″-CH_2) and 0.9 (3 H, t, *J* 7.5, –Me); δ_C(50.32 MHz, $CDCl_3$) 184.33 (C=O), 139.29 (>C=), 133.74 (>C=), 130.23 (=CH–), 128.42 (=CH–), 115.86 (>C=N), 76.97 (>CH–O), 36.61 (>CH_2), 34.08 (>CH_2), 26.77 (>CH_2), 22.21 (>CH_2), 13.76 (–Me); *m/z* (40 eV) 281 (M^+, 6%), 264 (2), 224 (1), 139 (100) and 111 (27).

5-*Butyl*-3-(4-*nitrobenzoyl*)-4,5-*dihydroisoxazole* 2-*Oxide* **10c**.—Purification of the crude product by flash chromatography using petroleum–diethyl ether (5:1 v/v) gave a yellow oil which solidified slowly with time (Found: M^+, 292.1058. Calc. for $C_{14}H_{16}N_2O_5$: *M*, 292.1059); ν_{max}(NaCl, film)/cm^{-1} 1700, 1590, 1520, 1350, 1270 and 720; δ_H(250 MHz, $CDCl_3$) 8.27 (2 H, dd, *J* 8.3 and 1.6, 3′-H and 5′-H), 7.82 (2 H, dd, *J* 8.3, 2′-H and 6′-H), 4.84 (1 H, dddd, *J* 10, 8.3, 8.3 and 5, 5-H), 3.58 (1 H, dd, *J* 16.7 and 10, 4-H), 3.24 (1 H, dd, *J* 16.7 and 8.3, 4-H), 1.83 (2 H, m, 1″-CH_2), 1.4 (4 H, m, 2″-CH_2 and 3″-CH_2) and 0.93 (3 H, t, *J* 7.3, –Me). δ_C(22.5 MHz, $CDCl_3$) 184.43 (C=O), 150.06 (>C=), 140.99 (>C=), 129.70 (=CH–), 123.52 (=CH–), 116.49 (>C=N), 77.62 (>CH–O), 36.19 (>CH_2), 34.34 (>CH_2), 26.90 (>CH_2), 22.37 (>CH_2), 13.89 (–Me); *m/z* (35 eV) 292 (M^+, 16%), 275 (13), 162 (4), 244 (2), 235 (9), 219 (5), 206 (21), 134 (42), 120 (52), 111 (50) and 104 (100).

5-*Butyl*-3-(2-*pyridylcarbonyl*)-4,5-*dihydroisoxazole* 2-*Oxide* **10d**.—In an adaptation of the literature method,[29] 2-nitro-1-(2-pyridyl)ethanone **9d** was prepared from pyridine-2-carboxylic acid and nitromethane. The crude nitro ketone **9d** was not purified but was directly treated with hex-1-ene **2a** in the presence of manganese(III) acetate as described under method A. Purification by flash chromatography using petroleum–diethyl ether (3:1 v/v) as eluent gave a dark yellow oil (Found: M^+, 248.1160. Calc. for $C_{13}H_{16}N_2O_3$: *M*, 248.1161); ν_{max}(NaCl, film)/cm^{-1} 1735, 1670, 1570, 1370, 1240, 745 and 690; δ_H(250 MHz, $CDCl_3$) 8.77 (1 H, dd, *J* 5.3 and 1.8, 3′-H), 8.08 (1 H, d, *J* 5.5, 6′-H), 7.84 (1 H, ddd, *J* 8.6, 8.6 and 1.8, 5′-H), 7.46 (1 H, dd, *J* 8.6 and 1.8, 4′-H), 4.78 (1 H, dddd, *J* 11, 8.7, 8.6 and 6.9, 5-H), 3.42 (1 H, dd, *J* 17.3 and 11, 4-H), 3.03 (1 H, dd, *J* 17.3 and 8.7, 4-H), 1.7–1.85 (1 H, m, 1″-H), 1.55–1.7 (1 H, m, 1″-H), 1.2–1.5 (4 H, m, 2″-CH_2 and 3″-CH_2) and 0.9 (3 H, t, *J* 6.9, –Me); δ_C(50.32 MHz, $CDCl_3$) 185.95 (C=O), 157.21 (>C=), 152.86 (>C=), 149.40 (=CH–), 136.76 (=CH–), 126.81 (=CH–), 124.87 (=CH–), 83.88 (>CH–O), 38.41 (>CH_2), 34.62 (>CH_2), 27.15 (>CH_2), 22.23 (>CH_2) and 13.76 (–Me); *m/z* (35 eV) 248 (M^+, 2%), 231 (0.3), 215 (1), 175 (100), 106 (78) and 78 (95).

rel-(2S,4R)-4-*Acetoxy*-2-*methyl*-2-*nitro*-1-*phenyloctan*-1-*one and* rel-(2S,4S)-4-*Acetoxy*-2-*methyl*-2-*nitro*-1-*phenyloctan*-1-*one* **12a**.—Purification of the crude product by filtration through a short column of Florisil using methylene dichloride as eluent yielded a yellow oil: ν_{max}(NaCl, film)/cm^{-1} 1705, 1605, 1560, 1320, 1275 and 710; δ_H(200 MHz, $CDCl_3$) 7.35–7.6 (3 H, m, 3′-H, 4′-H and 5′-H), 7.75 (2 H, m, 2′-H and 6′-H), [5.18 (ddd, *J* 12.3, 6.5 and 6.5) and 4.96 (dddd, *J* 10.3, 5.7, 5.3 and 2.6) (1 H, 4-H)], [1.95 and 1.92 (3 H, s, –COMe)], [1.89 and 1.75 (3 H, s, 2-Me)], 1.2–1.4 (8 H, m, 3-, 5-, 6- and 7-CH_2) and 0.85 (3 H, t, *J* 7.2, 8-Me); δ_C(50.32 MHz, $CDCl_3$) [191.77 and 190.60 (*C*OMe)] [170.65 and 170.05 (C=O)], [133.79 and 133.61 (>C=)], [130.62 and 129.76 (=CH–)], [128.92 and 128.85 (=CH–)], [128.52 and 128.30 (=CH–)], [94.16 and 94.10 (>C<)], [69.68 and 69.00 (>CH–)], [41.48 and 40.19 (>CH_2)], [35.10 and 35.05 (>CH_2)], [27.34 and 27.00 (>CH_2)], [26.96 and 26.55 (>CH_2)], [23.89 and 22.51 (–Me)], [20.67 and 20.51 (–Me)] and 13.94 (–Me); *m/z* (35 eV) 215 (3%), 170 (8), 147 (8), 105 (100) and 43 (22); *m/z* (FAB-MS, no matrix) 322 [$(M + H)^+$, 2%], 306 (1), 289 (2), 262 (12), 216 (24) and 105 (100).

rel-(4S,6R)-6-*Acetoxy*-4-*methyl*-4-*nitro*-1-*phenyldecan*-3-*one and* rel-(4S,6S)-6-*Acetoxy*-4-*methyl*-4-*nitro*-1-*phenyldecan*-3-*one* **12b**.—The crude product was purified by filtration over Florisil using methylene dichloride as eluent to yield a yellow oil: ν_{max}(NaCl, film)/cm^{-1} 1635, 1545, 1455, 1375, 1235 and 750; δ_H(250 MHz, $CDCl_3$) 7.1–7.35 (5 H, m, –Ph), [5.05 (ddd, *J* 11, 6.3, 3.2) and 4.90 (ddd, *J* 12.6, 6.3, 4.7) (1 H, 6-H)], 2.5–3.0 (4 H, m, 1-CH_2 and 2-CH_2), [2.1 and 1.92 (3 H, s, COMe)], [1.63 and 1.50 (3 H, s, 4-Me)], 1.4–1.15 (8 H, m) and 0.9 (3 H, t, *J* 7.3, 10-Me); δ_C(22.5 MHz, $CDCl_3$) [200.62 and 199.84 (>C=O)], [170.64 and 170.13 (>C=O)], [140.22 and 140.02 (>C=)], 128.69 (=CH–), 128.40 (=CH–), [126.59 and 126.53 (=CH–)], [95.91 and 95.74 (>C<)], [69.75 and 69.11 (>CH–)], [39.26 and 39.20 (>CH_2)], [38.58 and 38.19 (>CH_2)], [35.02 and 34.92 (>CH_2)], [30.07 and 29.88 (>CH_2)], [27.00 and 26.93 (>CH_2)], [22.72 and 22.50 (>CH_2)], [20.62 and 20.46 (–Me)], 18.64 (-Me) and 13.92 (–Me); *m/z* (FAB-MS, matrix: *m*-NBA) 350 [$(M + H)^+$, 4%], 334 (2), 325 (3), 244 (77), 193 (21), 158 (52), 127 (31) and 105 (100).

5-Butyl-3-(pyrrolidin-1-ylcarbonyl)-4,5-dihydroisoxazole 2-Oxide **14a**.—Yellow oil after purification by flash-chromatography with cyclohexane–ethyl acetate (1:1 v/v) as eluent (Found: M^+, 240.1483. Calc. for $C_{12}H_{20}N_2O_3$: *M*, 240.1474); ν_{max}(NaCl, film)/cm^{-1} 1650, 1460, 1350, 1310 and 740; δ_H(400 MHz, $CDCl_3$) 4.63 (1 H, dddd, *J* 10, 8, 6 and 4, 5-H), 3.78 (2 H, dd, *J* 8 and 6, 2′-H and 5′-H), 3.56 (2 H, dd, *J* 8 and 6, 2′-H and 5′-H), 3.32 (1 H, dd, *J* 18 and 10, 4-H), 2.95 (1 H, dd, *J* 18 and 8, 4-H), 1.9 (4 H, m, 3′-CH_2 and 4′-CH_2), 1.73 (1 H, m, 1″-H), 1.57 (1 H, m, 1″-H), 1.37 (4 H, m, 2″-CH_2 and 3″-CH_2) and 0.91 (3 H, t, *J* 7.2, 4″-Me); δ_C(22.5 MHz, $CDCl_3$) 159.31 (>C=O), 154.91 (>C=N), 81.99 (>CH–O), 48.75 (>CH_2), 46.97 (>CH_2), 40.59 (>CH_2), 34.76 (>CH_2), 27.42 (>CH_2–), 26.25 (>CH_2–), 23.79 (>CH_2–), 22.43 (>CH_2) and 13.92 (–Me); *m*/*z* (70 eV) 240 (M^+, 0.34%), 223 (100), 183 (1), 170 (2), 154 (66) and 98 (77).

(2′R,5RS)-5-*Butyl*-3-[2′-(*methoxycarbonyl*)*pyrrolidin*-1-*ylcarbonyl*]-4,5-*dihydroisoxazole* 2-*Oxide* **14b** (*1:1 Mixture of Diastereoisomers*).—The crude product was purified by flash-chromatography using ethyl acetate–heptane (1:1, v/v) as eluent to give a pale yellow oil (Found: M^+, 298.1534. Calc. for $C_{14}H_{22}N_2O_5$: *M*, 298.1529); ν_{max}(NaCl, film)/cm^{-1} 1750, 1630, 1450, 1200 and 730; δ_H(400 MHz, $CDCl_3$) [4.99 (ddd, *J* 8.5, 6 and 3) and 4.46–4.72 (m) (2 H, 5-CH and 2′-CH, rotamers)], [3.85–4.0 (m) and 3.6–3.8 (m) (2 H, 5′-CH_2, rotamers)], [3.72 and 3.69 (3 H, s, –CO_2Me, rotamers], [3.29 (ddd, *J* 17.3, 8.7 and 7.3), 3.27 (ddd, *J* 16.9, 10.8 and 6.6), 2.88 (ddd, *J* 17.8, 8.5 and 7.8) and 2.89 (ddd, *J* 10, 8.4 and 7) (2 H, 4-CH_2, rotamers)], 2.1–2.3 (2 H, m), 1.8–2.1 (2 H, m), 1.6–1.75 (1 H, m), 1.45–1.6 (1 H, m), 1.2–1.4 (4 H, m) and [0.88 and 0.90 (3 H, t, *J* 7, Me)]; δ_C(50.32 MHz, $CDCl_3$) [172.72, 172.27 and 172.25 (–*C*O_2Me)], [159.98, 159.84 and 159.57 (>C=O)], [154.72, 154.65, 154.51 and 154.41 (>C=N)], [82.35 and 82.20 (>CH–O)], [60.62 and 59.91 (>CH–)], [52.42 and 52.29 (–CO_2*Me*)], [47.61 and 47.51 [>CH_2)], [40.22 and 40.14 (>CH_2)], [25.02 and 24.98 (>CH_2)], [27.42, 27.35 and 27.29 (>CH_2)], 28.68 (>CH_2–), [34.69 and 31.32 (>CH_2)], [22.41, 22.31, 22.07 and 22.00 (>CH_2)] and 13.91 (–Me). *m*/*z* (70 eV) 298 (M^+, 0.52%), 281 (19), 239 (21), 223 (12), 221 (13), 170 (12), 154 (38), 128 (88) and 70 (100).

5-Butyl-3-(pyrrolidin-1-ylcarbonyl)-4,5-dihydroisoxazole **15a**.—Yellow oil after purification of the crude product by flash chromatography using cyclohexane–ethyl acetate (1:1 v/v) as eluent (Found: M^+, 224.1531. Calc. for $C_{12}H_{20}N_2O_2$: *M*, 224.1525); ν_{max}(NaCl, film)/cm^{-1} 1715, 1630, 1585, 1450, 1170 and 730; δ_H(200 MHz, $CDCl_3$) 4.71 (1 H, dddd, *J* 9.1, 8.4, 5.6 and 2.8, 5-H), 3.45–3.65 (4 H, m, 2′-CH_2 and 5′-CH_2), 3.42 (1 H, dd, *J* 16.7 and 9.1, 4-H), 3.08 (1 H, dd, *J* 16.7 and 8.4, 4-H), 1.85–2.0 (4 H, m), 1.6–1.85 (2 H, m), 1.25–1.45 (4 H, m) and 0.7 (3 H, t, *J* 7, 4″-Me); δ_C(22.5 MHz, $CDCl_3$) 157.92 (>C=O), 112.38 (>C=N), 77.04 (>CH–O), [46.48 and 46.22 (>CH_2, rotamers)], 37.26 (>CH_2), 34.34 (>CH_2), 26.96 (>CH_2), 25.80 (>CH_2–), 23.95 (>CH_2), 22.37 (>CH_2) and 13.89 (–Me); *m*/*z* (70 eV) 224 (M^+, 4.3%), 223 (47), 154 (30) and 98 (100).

(2′R,5RS)-5-*Butyl*-3-[(2-*methoxycarbonyl*)*pyrrolidin*-1-*ylcarbonyl*]-4,5-*dihydroisoxazole* **15b** (*1:1 Mixture of Diastereoisomers*).—Purification by flash chromatography as described for the oxide **14b** led to a pale yellow oil (Found: M^+, 282.1581. Calc. for $C_{14}H_{22}N_2O_4$: *M*, 282.1580); ν_{max}(NaCl, film)/cm^{-1} 1720, 1700, 1560, 1260, 1230 and 690; δ_H(400 MHz, $CDCl_3$) [4.98 (dd, *J* 8.4 and 3.6), 4.65–4.75 (m), 4.54–4.49 (m) and 4.45–4.51 (m) (2 H, 5-H and 1′-H)], 3.6–3.9 (2 H, m, 4′-CH_2), 3.72 (3 H, s, –CO_2Me), [3.48 (dd, *J* 16.9 and 9.3), 3.37 (dd, *J* 16.7 and 8.9), 3.20 (dd, *J* 9 and 4.1), 3.14 (dd, *J* 16.7 and 8.9), 3.05 (dd, *J* 16.9 and 7.6) and 2.84 (dd, *J* 17 and 6.6) (2 H, 4-CH_2)], 2.3–2.4 (1 H, m), 2.15–2.25 (1 H, m), 1.9–2.1 (2 H, m), 1.8–1.9 (1 H, m), 1.6–1.7 (1 H, m), 1.25–1.45 (4 H, m) and 0.9 (3 H, t, *J* 7, Me); δ_C(50.32 MHz, $CDCl_3$) [172.80, 171.89 and 171.83 (–*C*O_2Me)], [158.52 and 158.28 (>C=O)], [114.10, 113.50, 112.14 and 111.76 (>C=N)], [77.53, 77.27, 77.09 and 76.99 (>CH–O)], [59.47 and 58.27 (>CH–)], [52.73, 52.67 and 52.40 (–CO_2-Me)], [47.09, 46.70 and 46.60 (>CH_2)], [37.22, 37.06, 36.99 and 36.77 (>CH_2)], [34.47, 34.40, 34.14 and 34.06 (>CH_2)], [30.79, 30.73, 28.91 and 27.59 (>CH_2)], [26.92 and 26.81 (>CH_2)], [24.57 and 24.45 (>CH_2)], [22.58, 22.40 and 22.34 (>CH_2)] and [14.03 and 13.87 (–Me)]; *m*/*z* (70 eV) 282 (M^+, 6.2%), 223 (100), 154 (85) and 128 (86).

Acknowledgements

Technical assistance by Mr. Lars Berger as well as financial support by the Bundesministerium für Wirtschaft through the Arbeitsgemeinschaft industrieller Forschungsvereinigungen (AIF-Nr. 8463) the Fonds der Chemischen Industrie, and BASF Aktiengesellschaft is gratefully acknowledged.

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Paper 4/00178H
Received 12*th January* 1994
Accepted 10*th March* 1994