Steric control of reactivity: formation of oximes, benzodiazepinone *N*-oxides and isoxazoloquinolinones

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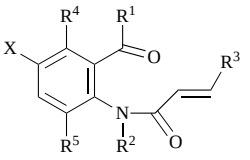
Reaction of the alkenyl carbonyl compounds 1 with hydroxylamine can lead to the formation of the oximes 2, the benzodiazepinone *N*-oxides 3 or the isoxazoloquinolinones 5. The product(s) of reaction are shown to depend on the electronic nature of the terminal olefinic substituent R^3 and the space filling capacity of the substituents R^1, R^2 and R^4. When the olefinic centre is electron poor ($R^3 = CO_2Et$) ketocarbonyls convert exclusively to bicyclic nitrones 3 whereas aldehydes are more sensitive to subtle changes in skeletal structure and give rise to oximes 2, tricycles 5 or mixtures of both. For aldehyde and ketone substrates when the olefinic centre carries an aryl substituent ($R^3 = Ph$) the primary product of reaction is the corresponding oxime which on thermal activation converts to the tricyclic isoxazoloquinolinones.

Introduction

The addition of hydroxylamine to aldehydes and ketones is a well known reaction, indeed the sharp melting points of the highly crystalline oxime derivatives have traditionally been used to characterise the parent carbonyl compounds. With multifunctional alkenyl carbonyl compounds **1** the reaction can be



1

Aldehydes

a. R^1, R^2, R^4, R^5, X = H; $R^3 = CO_2Et$

b. R^1, R^2, R^4, R^5 = H; X = Cl; $R^3 = CO_2Et$

c. R^1, R^2, R^4, R^5, X = H; R^3 = Ph

Ketones–aryl substituted olefin

d. R^1 = Ph; R^2, R^4, R^5 = H; X = H; R^3 = Ph

e. R^1 = Ph; R^2, R^4, R^5 = H; X = Cl; R^3 = Ph

Ketone–ester substituted olefin

f. R^1 = Ph; R^2, R^4, R^5, X = H; $R^3 = CO_2Et$

g. R^1 = Ph; R^2, R^4, R^5 = H; X = Cl; $R^3 = CO_2Et$

h. R^1 = Ph; R^2, R^4, R^5 = H; X = NO_2; $R^3 = CO_2Et$

i. R^1 = Me; R^2, R^4, R^5, X = H; $R^3 = CO_2Et$

Tertiary amide aldehydes

j. R^1, R^4, R^5, X = H; R^2 = Me; $R^3 = CO_2Et$

k. R^1, R^4, R^5, X = H; R^2 = Me; R^3 = Ph

Ring substituted aldehydes

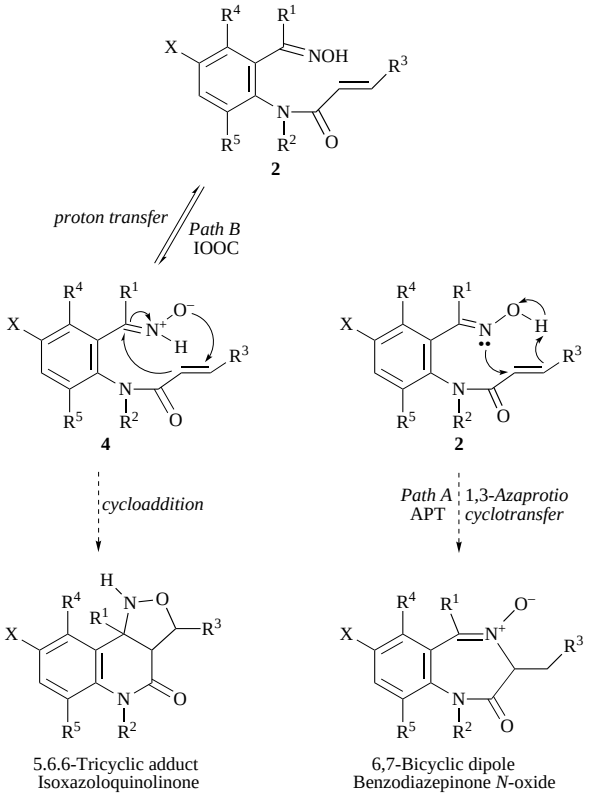
l. R^1, R^2, X = H; R^4, R^5 = Me; $R^3 = CO_2Et$

m. R^1, R^2, R^4, X = H; R^5 = Me, $R^3 = CO_2Et$

n. R^1, R^2, R^5, X = H; R^4 = Me; $R^3 = CO_2Et$

complicated and the primary product may not be that which is isolated; in an earlier communication we have shown that these oximes may react further in one of two ways.[1] (*i*) An intramolecular 1,3-azaprotio cyclotransfer (APT) may take place leading to the formation of a seven-membered cyclic dipole **3** (this is a pseudo 7-*exo trig* process[2]),[3] Scheme 1, *path A*. (*ii*) Oxime–nitrone tautomerisation may be facilitated by the availability of an internal unsaturated moiety which can readily trap the transient dipole in a cycloaddition furnishing the tricyclic adduct **5**,[4] this tandem dipole formation–cycloaddition sequence is also known as an intramolecular oxime olefin cycloaddition reaction, IOOC, Scheme 1, *path B*.

Clearly if reactions of types (*i*) and (*ii*) are to take place then the oxime **2** or the nitrone **4** must be able to adopt the required



2 **4** **2** **5** **3**

Scheme 1

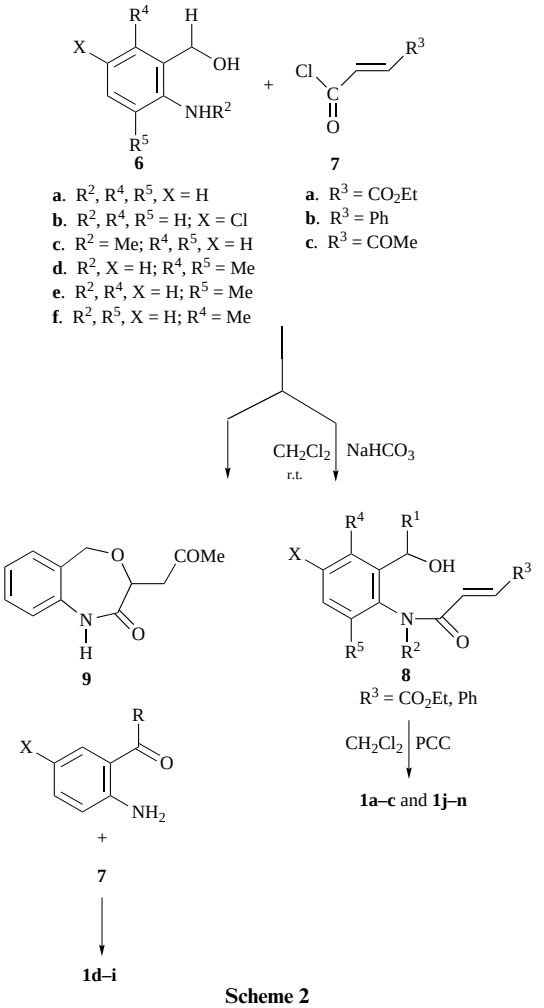
transition state geometry for the cyclisation and cycloaddition reactions. The promotion of cycloadditions is classically driven by employing high pressure or high temperature reaction conditions, the use of a catalyst or a specific solvent or in more recent times by microwave activation.[5] At the most rudimentary level steps taken to increase the rate of encounter of the reacting moieties can be expected to improve the rate of the reaction; therein lies perhaps the most important feature of the intramolecular reaction, the entropic advantage. A higher stratum of control over the participating centres invokes the employment of remote space filling substituents to minimise the spatial disparity between the reactants. In a recent review Sammes and Weller[6a] detail the role of steric factors in promoting or hindering intramolecular reactions. Especially relevant to the current work is a paper on intramolecular cycloadditions where the

reacting dipole and olefin are attached by short handles to an aromatic ring.[6b] Significantly, reactions which do not otherwise take place are shown to proceed well when steric buttresses are incorporated into the *ortho*-position/s of a benzene ring (positions analogous to R^4 and R^5). The article does not cite any examples where bulky substituents, in positions other than *ortho* (*e.g.* R^1 and R^2), are able to act as predictable steric buttresses. Neither are there any illustrated examples of the importance of steric factors in dictating the course of the reaction when the substrate, through its tautomeric form, has the possibility of undergoing more than one type of ring-forming reaction (Scheme 1).

In this paper we will show how the electronic nature of R^3 and the space filling capacity of the substituents, R^1, R^2 and R^4 influence the course of the reaction of **1** with NH_2OH.

Results and discussion

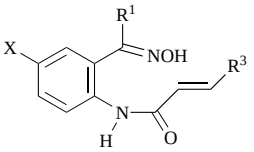
The preparation of the targeted carbonyl substrates **1a**–**c** and **1j**–**n** involves as the key step coupling of the amines **6** with the appropriate acyl halides **7**; oxidation of the resulting *o*-amidobenzyl alcohol **8** furnishes the desired aldehydes (Scheme 2). The ketones **1d**–**i** were prepared by direct condensation of



Scheme 2

the commercially available *o*-aminoacetophenone/benzophenone derivative with the acyl halide **7**. The substrate **7a** was prepared in three steps from maleic anhydride[7] and cinnamoyl chloride **7b** was commercially available. The keto-substituted derivative **7c** was prepared in accordance with the procedure of Scheffold and Dubs[8] and its coupling with the amino alcohol **6a** lead directly to the formation of the 1,4-benzoxazepinone **9**. The formation of this product is considered to be by way of a tandem condensation–intramolecular Michael-type addition and the driving force for the cyclisation reaction is the increased electrophilicity of the olefinic centre in **8**, R^3 = COMe, due to the superior electron withdrawing ability of the ketone substituent with respect to the ester and aryl substituents of the amido alcohols **8**. Benzoxazepines have previously been prepared by a K_2CO_3 promoted cyclisation of amino alcohols like **8**.[9]

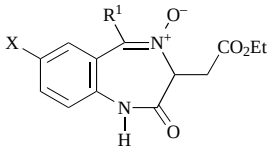
The amido aldehydes **1a**–**c** react with $NH_2OH{\cdot}HCl$ in an ethanolic pyridine solution at room temp. to furnish a single isomer of the corresponding oximes **10a**–**c** (82–85% yield). Dreiding



10

a. R^1, X = H; R^3 = CO_2Et
b. R^1 = H; X = Cl; R^3 = CO_2Et
c. R^1, X = H; R^3 = Ph
d. R^1 = Ph; X = H; R^3 = Ph
e. R^1 = Ph; X = Cl; R^3 = Ph

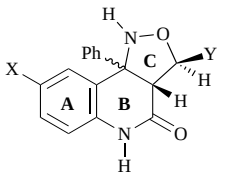
stereomodels of these molecules indicate that the aldoxime functionality enjoys a considerable degree of conformational mobility and therefore under the mild reaction conditions there is no impetus for further reaction (with the pendant olefinic moiety). Oximation of the ketones **1d**,**e** requires more forcing conditions (EtOH, 80 °C) and results in the formation of a ketoxime which has a restricted degree of mobility. It is evident from a study of Dreiding scale models of **10d**,**e** that the planes in which the two aromatic rings lie are at an angle of *ca.* 70° to each other. In this conformation the reacting centres, the oxime moiety or its tautomeric nitrone and the olefinic centre can approach the transition state required for further reaction (formation of the benzodiazepinone *N*-oxides **3** or the isoxazoloquinolinones **5**) (Fig. 1). It is apparent, however, that the



3

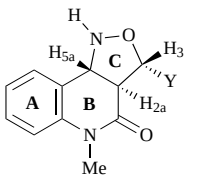
a. R^1, X = H
b. R^1 = H; X = Cl
f. R^1 = Ph; X = H
g. R^1 = Ph; X = Cl
h. R^1 = Ph; X = NO_2
i. R^1 = Me; X = H

activation energy is too high to allow either an APT or an IOOC reaction to take place and so the oximes **10d**,**e** are the sole products of reaction under these conditions.



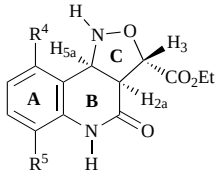
5

d. X = H; Y = Ph
e. X = Cl; Y = Ph
f. X = H; Y = CO_2Et
h. X = NO_2; Y = CO_2Et



5

j. Y = CO_2Et
k. Y = Ph



5

l. R^4, R^5 = Me
m R^4 = H; R^5 = H
n R^4 = Me; R^5 = H

Upon further thermal activation the aldoximes **10a**,**b** (xylene, 140 °C) undergo intramolecular cyclisation (APT) giving the

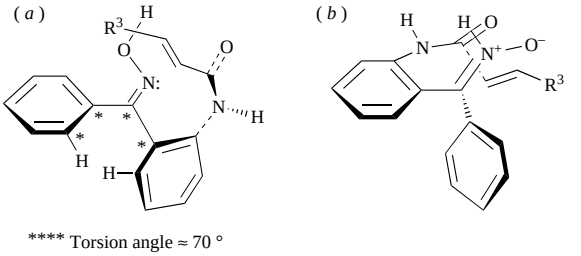
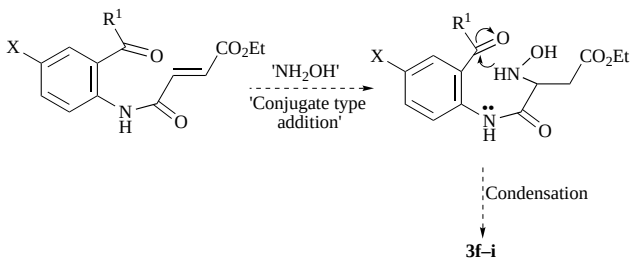


Fig. 1 Model representation of **10d** in the transition state required for (*a*) benzodiazepinone *N*-oxide formation and (*b*) isoxazoloquinolinone formation

benzodiazepinone *N*-oxides **3a**,**b**, in 78 and 62% yield respectively. The analogous aryl substituted aldoxime **10c** fails to cyclise even at this temperature suggesting that the aryl group on the *trans*-disubstituted olefinic bond fails to provide enough electronic activation for the cyclisation reaction. Heating a xylene solution of the conformationally restricted ketoximes **10d**,**e** at reflux temperature effects their conversion, not to the 6,7-bicyclic dipoles, but rather, to the isoxazoloquinolinones **5d**,**e** in 78 and 63% yield, respectively. These observations suggest that the activation energy for the formation of the tricycles, **5d**,**e**, is lower than that required for the alternative intramolecular cyclisation reaction (APT, leading to **3d**,**e**), and that for substrates like **1a**–**e**, even at high reaction temperatures, the olefinic centre needs to be electron deficient for the cyclisation reaction to proceed.

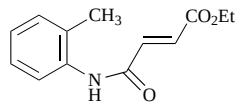
The increased electrophilicity of the unsaturated centre in the ketones **1f**–**i** with respect to **1d**,**e** is expected to influence the course of their reaction with NH_2OH. Therefore it is not surprising that **1f**–**i** react with $NH_2OH{\cdot}HCl$, upon heating at reflux in ethanolic pyridine (24 h), to give the benzodiazepinone *N*-oxides **3f**–**i**. As remarked above, the ketoximes **10d**,**e** have reduced conformational space available to their oxime functionality and the same restricted mobility is expected for the oximes arising from **1f**–**i**. The easy attainment of the transition state for the formation of the 6,7-bicyclic dipole combined with the enhanced electrophilicity of the olefinic moiety in **1f**–**i** promotes the intramolecular APT reaction. The dipoles **3f**–**i** were obtained in 49–64% yield. Surprisingly no conversion of starting material was observed when the reaction was conducted at room temp. The substituent R^1 clearly operates as a steric buttress assisting in the attainment of the transition state required for benzodiazepinone *N*-oxide formation whilst the role of the C-5 aryl ring substituent (**1g**, X = Cl, **1h**, X = NO_2) appears to be restricted to influencing the solubility of the carbonyl parent. In order to maximise the yield of nitrone the continuous extraction technique was employed—even with this precaution **3g**,**h** could only be obtained in 49 and 52% yield, respectively.

That dipole formation (**1f**–**i**→**3f**–**i**) does involve an oxime intermediate (as in Scheme 1, *path A*) rather than proceeding *via* an alternative sequential intermolecular conjugate type addition–intramolecular condensation sequence (Scheme 3) is

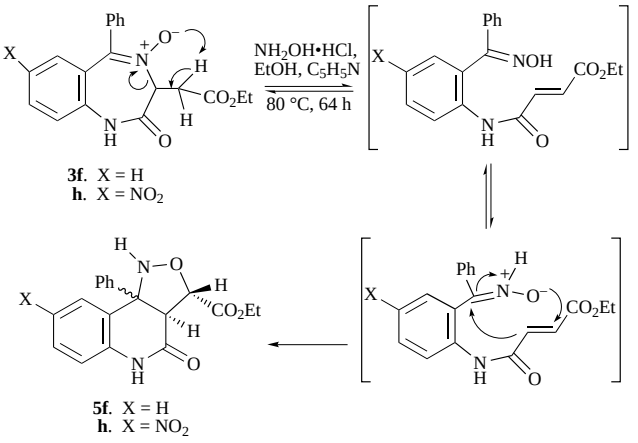


Scheme 3

supported by the failure of **11** to react with NH_2OH, suggesting that attack of the free hydroxylamine at the electron deficient double bond does not occur. Further support for the intermediary oxime in the generation of **3f**–**i** arises from the observation that the isoxazoloquinolinones **5f** (31%) and **5h** (32%), can be isolated on prolonged heating in ethanolic pyridine of the benzodiazepinone *N*-oxides **3f** and **3h**, respectively. The formation of the tricyclic adducts from these dipoles implies that, under these conditions, the bicyclic nitrone exists in equilibrium with the oxime. Thus the tricyclic adducts **5f**,**h** are the thermodynamic products and the dipoles **3f**,**h** the kinetic products of reaction (Scheme 4).

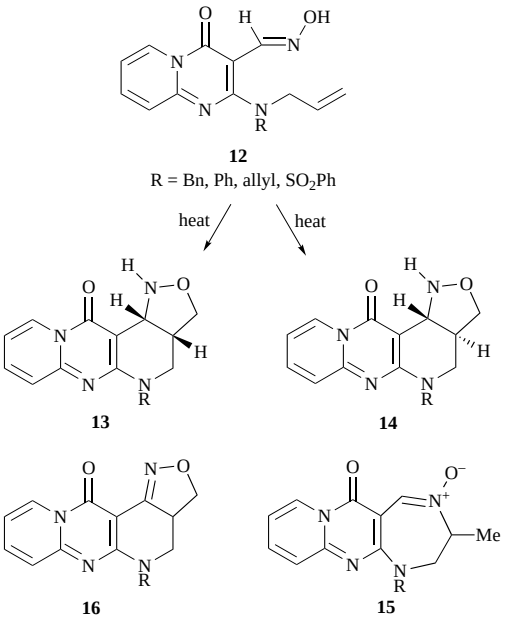


11



Scheme 4

The aldehyde **1j** is a tertiary amide analogue of **1a** and it may be anticipated that the additional substitution on the olefinic tether (R^2 = Me) will influence its reactivity. Reaction with $NH_2OH{\cdot}HCl$ (pyridine, EtOH) at room temp. gives the tricyclic isoxazoloquinolinone **5j** in excellent yield. It may be that the promotion of the IOOC reaction sequence can be ascribed solely to the restricted mobility of the amide tether ensuring that the reacting centres can obtain the required alignment for the cycloaddition step, however in a series of papers on ring formation at the periphery of heterocyclic systems Noguchi and co-workers propose that restriction of the dipole/dipolarophile conformations is only one of two ways in which substitution at the alkenylamide nitrogen atom may influence reactivity of sub-



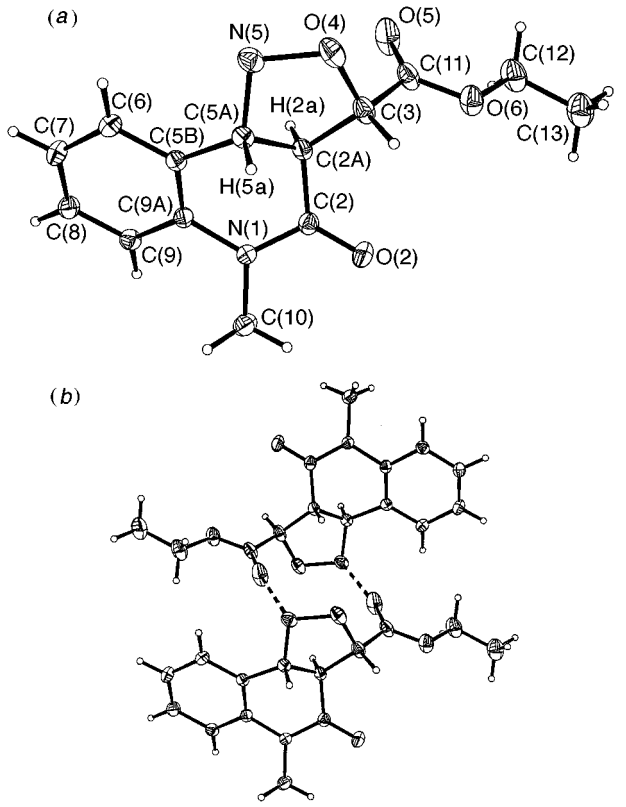
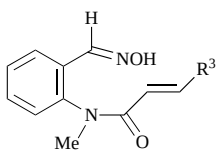


Fig. 2 (*a*) Single crystal X-ray structure of the isoxazoloqinolinone **5j**. (*b*) Dimeric association of **5j** in the unit cell.

strates analogous to **1j**.[10] They postulate that the oxime–NH–nitrone isomerisation cycloaddition sequence in molecules like **12** may be facilitated by either or both the amino nitrogen or the carbonyl group acting as an intramolecular catalyst in the proton transfer step. The pyridopyrimidine **12** reacts upon heating to give the isomeric tetracycles **13** and **14**, their dehydro derivative **16** and the dipole **15**. In the event that such catalysis is an important mechanistic feature then the increased basicity of the amido nitrogen atom in **1j**, with respect to **1a**, may explain the ease of the IOOC reaction sequence leading to the formation of **5j**.

To discover if substitution at the amide *N*-position alone is enough to bring about formation of the tricyclic adduct the amidoaldehyde **1k** was prepared. This substrate carries an *N*-methyl substituent yet its olefinic centre is electron neutral with respect to **1j** and so whether the transient dipole will have sufficient electronic activation to undergo cycloaddition can be examined. On attempting oximation of **1k** at room temp. the corresponding oxime **17k** was isolated. Increasing the reaction



17k. R^3 = Ph
j. R^3 = CO_2Et

temperature to 80 °C failed to promote further reaction, however heating a solution of the oxime in xylene at reflux (140 °C) leads to quantitative conversion to the tricyclic adduct **5k**. Thermal activation is therefore necessary to overcome the poor reactivity of the phenyl substituted internal olefin.

The *trans* stereochemistry at the BC ring junction in **5j**,**k** is suggested on inspection of the magnitude of the vicinal coupling constant, $J_{2a,5a}$ = 13.5 and 13.2 Hz, respectively; structurally related compounds have *trans* coupling constants of *ca.*

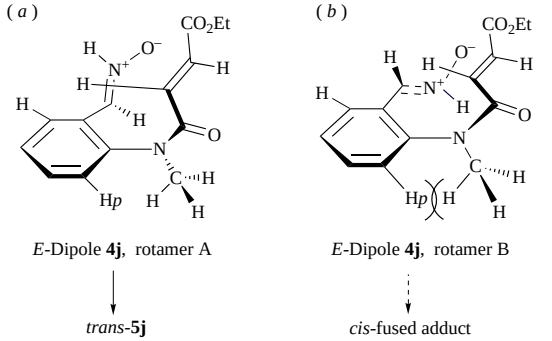


Fig. 3 Model representation of the transition state leading to the isoxazoloquinolinone **5j**

12 Hz.[11] Nuclear Overhauser enhancement difference spectroscopy (NOEDS) results for **5j** failed to lend support to this assignment (irradiation of H-3 causes a 3.3% enhancement on each of H-2a and H-5a) and the relative stereochemistry of this adduct was unambiguously assigned following a single crystal X-ray structure determination. The crystal structure confirms the expected *trans* relationship between H-5a and H-2a as well as between H-2a and H-3 [Fig. 2(*a*)]. It also reveals a dimeric association of **5j**, two molecules make up the unit cell with H-bonding evident between the NH proton of the isoxazolidine ring in one molecule and the carbonyl oxygen atom of the ester side chain at C-3 of a second molecule, the NH···O=C H-bond distance being 3.038 Å [Fig. 2(*b*)].

The observed diastereospecificity in the formation of **5j**,**k** is ascribed to the operation of geometric and steric constraints arising in the transition state leading to the cycloadduct. By studying Dreiding stereomodels of the dipole leading to **5j** it is evident that the approach leading to the formation of the *cis* fused isomer, depicted in Fig. 3(*b*) involves rotamer B of the (*E*)-dipole of **4j** and is severely disadvantaged by a steric clash between the *N*-methyl group (which is only slightly out of the plane of the aromatic ring) and the *peri*-hydrogen H_p. Employing rotamer A of the (*E*)-dipole the approach shown in Fig. 3(*a*) leads to the formation of the *trans*-fused adduct. Attainment of this stereochemically distinct transition state involves displacement of the *N*-methyl group from the plane of the aromatic ring by an angle of *ca.* 50° and consequently it encounters much less steric hindrance than the alternative state, Fig. 3(*b*). Therefore rotamer A is the reactive rotamer and the *trans*-fused adduct **5j** is the only diastereoisomer formed in the reaction.

The effect of space filling substituents on the *ortho*-positions of the aromatic ring in **1** was next investigated. The 3,6-dimethyl derivative **1l** reacts with NH_2OH (EtOH, 80 °C) by the same reaction sequence as **1j**,**k** yet the tricyclic adduct **5l** has opposite stereochemistry at the BC ring junction. In this case product stereochemistry is assigned on the basis of NOEDS results and on the magnitude of the vicinal coupling constant; $J_{2a,5a}$ = 7 Hz which is a typical value for systems of this type which have *cis* fusion of the BC rings of the tricyclic framework.[11] Irradiation of H-5a caused a 10.3% enhancement in H-2a indicating a *cis* relationship between these two protons. Due to the conservation of stereochemistry at the olefinic centre on cycloaddition H-2a and H-3 are expected to be in a *trans* arrangement, this is supported by a 1.2% enhancement on H-2a following irradiation of H-3.

A plausible explanation for the stereochemical course of this reaction, involving geometric and steric factors, arises following inspection of Dreiding scale models of the distinct transition states which can lead to cycloadduct formation. It appears reasonable that the transient dipole **4l** should adopt rotamer B in its preferred conformation [Fig. 4(*a*)]; in the alternative conformation [Fig. 4(*b*)] sizeable steric clashes are evident between the dipole NH hydrogen atom and the adjacent methyl group. Hence the origin of the diastereospecificity of the reaction, the dipole shown in Fig. 4(*a*) is the only low energy conformer

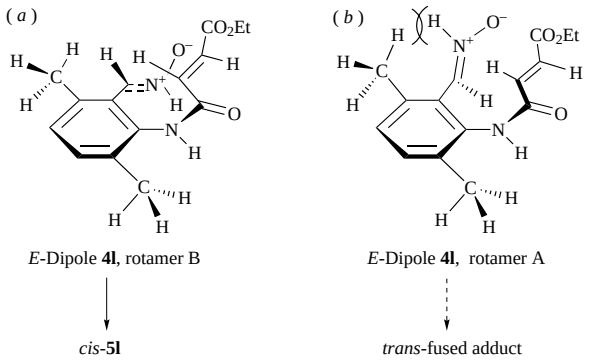
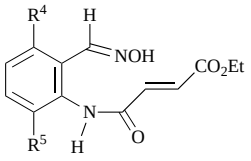


Fig. 4 Model representation of the transition state leading to the isoxazoloquinolinone **5l**

which is able to participate in cycloaddition. Such exquisite discrimination in intramolecular cycloaddition reactions is a well known and attractive feature of this class of pericyclic reaction.

For both nitrones **4j** and **4l** when the dipole has *Z* geometry it is not possible to place the reacting centres (olefinic substituent and dipole) in the same plane and hence this dipolar conformation cannot lead to any cycloaddition product. Nogouchi and co-workers also invoke the *E*-dipole in the intramolecular cycloaddition of the structurally related nitrone arising from **12**.[10]



18l. $R^4 = R^5 = Me$
m. $R^4 = H$, $R^5 = Me$
n. $R^4 = Me$, $R^5 = Me$

That the adducts **5j–l** arise from a domino oximation–tautomerisation–cycloaddition reaction sequence (Scheme 1) is supported by the observation that for each carbonyl parent the reaction can be stopped at the level of the oxime if lower reaction temperatures are employed, −25 °C in the case of **1j** (giving **17j**) and room temp. for **1k** (giving **17k**) or **1l** (giving **18l**); further heating of a solution of the oxime results in formation of the corresponding adducts **5j–l**. Significantly the monomethyl analogue **1m** reacts under standard oximation conditions ($NH_2OH{\cdot}HCl$, EtOH, room temp. or 80 °C) to give only the corresponding oxime (**18m**) in 74% yield. Further heating of the isolated oxime (xylene 140 °C) failed to induce reaction and no trace of the expected tricyclic adduct **5m** was encountered. Since the 3,6-dimethyl substrate **1j** so readily participates in the IOOC reaction sequence and the 3-methyl derivative shows no such reactivity it is apparent that the 6-methyl substituent plays a critical role as a steric buttress encouraging the attainment of the necessary transition state for the cycloaddition reaction of the intermediate nitrone. To investigate if the C-6 substituent is both necessary and sufficient to promote this reaction path the behaviour of the aldehyde **1n** has been studied. Upon heating in ethanolic pyridine (80 °C) with $NH_2OH{\cdot}HCl$ the anticipated tricyclic adduct **5n** was formed in 23% yield together with 61% of the corresponding oxime **18n**. That the BC ring junction in **5n** should be *cis* fused is suggested by comparison with Fig. 4 and this conclusion is sustained by the $J_{2a,5a}$ coupling constant of 8.1 Hz.[11]

Conclusions

The influence of the space filling substituents, R^1, R^2 and R^4 and of the electronic nature of R^3 on the course of the reaction of the carbonyl compounds **1** with NH_2OH, is quite striking. For simple (no *ortho*-ring substituents and secondary amido-alkenyl nitrogen atom) aldehydes and unactivated ketones ($R^3 = Ph$) the reaction produces oximes whilst for simple ketones with $R^3 = CO_2Et$ bicyclic dipoles result. In those cases where a sterically bulky group ($R^4 \neq H$) is positioned *ortho* to the carbonyl functionality tricyclic isoxazolobenzodiazepinones result, this tricyclic system also arises if the amide nitrogen is tertiary ($R^2 \neq H$). In no case is an APT reaction observed when the olefinic moiety is substituted with a phenyl group, one explanation considers that this substituent has no significant influence on the electrophilicity of the pendant olefinic centre and therefore no ability to promote the internal cyclisation reaction. However since intramolecular APT reactions have been observed with terminally unsubstituted olefins[12] the steric bulk of the phenyl group must appreciably increase the activation energy required for the cyclisation reaction. Whilst the details of the mechanism of the IOOC reaction are unclear we have been able to identify certain structural features which effect its promotion; steric buttresses positioned at one of three sites, *ortho* to the oxime group, *i.e.* at R^4, or along the chain connecting either the oxime or the olefin to the benzene ring *i.e.* at R^1 or R^2. That the substituent R^2 may have both a steric and electronic role in facilitating tricycle formation cannot be dismissed.[10] The merit of the steric buttressing effect in the acceleration of intramolecular ring-forming reactions of 'unsaturated oximes', reactions which do not otherwise proceed, has been illustrated. Future studies in this area will be directed toward the incorporation of removable groups at the key positions R^1, R^2 and R^4.

Experimental

Melting points were determined on an Electrothermal melting point apparatus and are uncorrected. Elemental analyses were performed on a Perkin-Elmer model 240 CHN analyser. NMR spectra were recorded using a JEOL EX90 FT NMR and a JEOL EX270 FT NMR spectrometer at probe temperatures with tetramethylsilane as internal reference and deuteriochloroform as solvent; *J* values are given in Hertz. IR spectra were recorded on a Perkin-Elmer 1600 series FTIR spectrophotometer, samples were prepared as nujol mulls. Flash column chromatography was carried out on silica gel (200–400 mesh; Kiesslgel 60, E Merck) with air pump pressure; analytical TLC plates were purchased from Merck. Samples were located by UV illumination using a portable Spectroline Hanovia lamp (λ 254 nm) or by the use of iodine staining. All solvents used were purified by standard procedure and light petroleum refers to that fraction of light petroleum boiling between 40–60 °C.

General procedure for the formation of carbonyl substrates 1

Preparation of the aldehydes 1a–c and 1j–n. *Preparation of the benzyl alcohols* **8**.—The acyl halide **7** (0.057 mol) was added dropwise to a cooled suspension of the amino alcohol **6**[13] (0.057 mol) and sodium hydrogen carbonate (0.067 mol) in anhydrous dichloromethane (50 cm^3). The mixture was stirred for 1 h at room temp. The organic layer was washed, dried and the solvent removed under reduced pressure. The resulting solid was crystallised from diethyl ether–light petroleum to yield the pure alcohols **8**. The yields of the alcohols ranged from 41–84%, all gave satisfactory micro analytical and spectroscopic data, see Table 1(*a*) and (*b*).

Oxidation of the alcohols **8**.—Freshly prepared pyridinium chlorochromate[14] (0.042 mol) was suspended in anhydrous dichloromethane (50 cm^3). The appropriate alcohol **8** (0.028 mol) in dichloromethane (20 cm^3) was added in one portion. After 1.5 h dry diethyl ether was added and the solution was passed through 10 cm of silica gel. The solvent was removed under reduced pressure and the resulting solid was purified by crystallisation from diethyl ether–light petroleum

Table 1(*a*) Analytical data for the alcohols **8**

Entry no.	Compound no.	R^1	R^2	R^3	R^4	R^5	X	Yield (%)	mp/°C	Molecular formula	Found (%) [requires (%)] C	N	H
1	**8a**	H	H	CO_2Et	H	H	H	53	115–116	$C_{13}H_{15}O_4N$	62.63 [62.65]	6.07 [6.02]	5.68 [5.62]
2	**8b**	H	H	CO_2Et	H	H	Cl	46	128–130	$C_{13}H_{14}O_4NCl$	54.99 [55.03]	4.85 [4.93]	4.90 [4.94]
3	**8c**	H	H	Ph	H	H	H	43	118–119	$C_{16}H_{15}O_2N$	75.93 [75.88]	5.89 [5.93]	5.49 [5.53]
4	**8d**	H	Me	CO_2Et	H	H	H	49	70–72	$C_{14}H_{17}O_4N$	63.93 [63.87]	6.41 [6.46]	5.49 [5.32]
5	**8e**	H	Me	Ph	H	H	H	43	93–95	$C_{17}H_{17}O_2N$	76.36 [76.40]	6.39 [6.36]	5.27 [5.24]
6	**8f**	H	H	CO_2Et	Me	Me	H	41	136–137	$C_{15}H_{19}O_4N$	65.02 [64.98]	6.89 [6.86]	5.01 [5.05]
7	**8g**	H	H	CO_2Et	H	Me	H	42	124–125	$C_{14}H_{17}O_4N$	63.82 [63.87]	6.43 [6.46]	5.40 [5.32]
8	**8h**	H	H	CO_2Et	Me	H	H	49	70–72	$C_{14}H_{17}O_4N$	63.89 [63.87]	6.50 [6.46]	5.33 [5.32]

Table 1(*b*) Spectroscopic data for the alcohols **8**

Entry no.	Compound no.	δ_H	δ_C	ν/cm^{-1}
1	**8a**	9.30 (1H, s, NH), 8.02 (1H, d, ArH, *J* 8.02), 7.22 (5H, m, ArH, C*H*=C*H*), 4.65 (2H, s, CH_2OH), 4.24 (2H, q, OCH_2, *J* 7.31), 3.91 (1H, s, CH_2OH), 1.32 (3H, t, CH_2CH_3, *J* 7.31)	165.52 (NHCO), 162.19 (CO_2Et), 136.94 (C-1), 128.79 (C-2), 131.01, 125.15, 122.45 and 123.42 (Ar), 136.63 (*C*H=CHCO$_2$Et), 131.48 (CH=*C*HCO$_2$Et), 63.96 (*C*H$_2$OH), 61.34 (OCH$_2$), 14.09 (CH$_2$*C*H$_3$)	3264.0 (OH), 3121.5 (NH), 1716.6 (CO$_2$Et), 1643.1 (NHCO)
2	**8b**	9.11 (1H, s, NH), 8.14 (1H, d, ArH, *J* 8.12), 7.31 (2H, m, ArH), 7.01 (1H, d, C*H*=CH-CO$_2$Et, *J* 14.57), 6.91 (1H, d, CH=C*H*CO$_2$Et, *J* 14.57), 4.74 (2H, s, CH_2OH), 4.29 (2H, q, OCH$_2$, *J* 7.30), 2.57 (1H, s, OH), 1.35 (3H, t, CH$_2$CH_3, *J* 7.30)	165.12 (*C*O$_2$Et), 162.31 (NH*C*O), 135.21 (C-1), 129.92 (C-2), 121.94 (C-1), 128.47, 128.95 and 123.52 (Ar), 136.52 (*C*H=CHCO$_2$Et), 131.45 (CH=*C*HCO$_2$Et), 64.38 (CH$_2$OH), 61.54 (OCH$_2$), 14.35 (CH$_2$*C*H$_3$)	3275.9 (OH), 3112.0 (NH), 1714.7 (CO$_2$Et), 1643.8 (NHCO)
3	**8c**	8.89 (1H, s, NH), 8.14 (1H, d, ArH, *J* 7.90), 7.78 (1H, d, C*H*=CHPh, *J* 15.80), 7.25 (8H, m, ArH), 6.48 (1H, d, CH=C*H*Ph, *J* 15.80), 4.70 (s, 2H, CH_2OH), 3.42 (1H, br, OH)	163.01 (NH*C*O), 140.56 (Ar), 136.34 (C-1), 129.01 (C-2), 132.92 (*C*H=CHPh), 122.75 (CH=*C*HPh), 128.28, 127.69, 127.49, 126.33, 119.53 and 115.71 (Ar), 66.97 (*C*H$_2$OH)	3256.3 (OH), 3103.6 (NH), 1654.3 (NHCO)
4	**8d**	7.37 (4H, m, ArH), 6.81 (1H, d, C*H*=CH-CO$_2$Et, *J* 15.33), 6.66 (1H, d, CH=C*H*CO$_2$Et, *J* 15.33), 4.57 (2H, s, CH_2OH), 4.12 (2H, q, OCH$_2$, *J* 7.15), 3.36 (3H, s, NCH$_3$), 3.14 (1H, s, CH_2OH), 1.22 (3H, t, CH_2CH_3, *J* 7.15)	165.60 (NCH$_3$*C*O), 165.43 (*C*O$_2$Et), 140.03 (C-1), 129.26 (C-2), 133.38, 131.32, 129.10 and 128.15 (Ar), 138.21 (*C*H=CHCO$_2$Et), 131.40 (CH=*C*HCO$_2$Et), 61.03 (CH$_2$OH), 60.71 (O*C*H$_2$), 37.28 (NCH$_3$), 14.01 (CH$_2$*C*H$_3$)	3258.1 (OH), 1730.4 (CO$_2$Et), 1693.4 (NCH$_3$CO)
5	**8e**	8.21 (1H, d, ArH, *J* 8.02), 7.93 (1H, d, C*H*=CHPh, *J* 15.60), 7.31 (8H, m, ArH), 6.57 (1H, d, CH–C*H*Ph, *J* 15.60), 4.63 (2H, s, OCH$_2$)	166.23 (NCH$_3$CO), 145.41, 142.32, 134.82, 135.89 (*C*H=CHPh), 123.30 (CH=CHPh), 130.45, 128.43, 127.59, 121.09, 118.29, 115.11, 65.34 (*C*H$_2$OH), 36.91 (NCH$_3$)	
6	**8f**	9.60 (1H, br, NH), 7.44 (2H, m, ArH), 7.02 (1H, d, C*H*=CHCO$_2$Et, *J* 14.91), 6.89 (1H, d, CH=C*H*CO$_2$Et, *J* 14.91), 4.65 (2H, s, CH_2OH), 4.21 (2H, q, OCH$_2$, *J* 7.30), 2.23 (3H, s, CH$_3$), 1.98 (3H, s, CH$_3$), 1.21 (3H, t, CH$_2$CH_3, *J* 7.30)	165.79 (NHCO), 162.35 (*C*O$_2$Et), 135.75, 134.41 and 129.30 (Ar), 127.31 (C-6), 121.71 (C-3), 135.52 (*C*H=CHCO$_2$Et), 130.48 (*C*H=CHCO$_2$Et), 67.21 (CH$_2$OH), 61.92 (OCH$_2$), 20.54 (CH$_3$), 18.72 (CH$_3$), 14.91 (t, 3H, CH$_2$*C*H$_3$)	
7	**8g**	9.32 (1H, br, NH), 7.59 (3H, m, ArH), 7.11 (1H, d, C*H*=CHCO$_2$Et, *J* 15.34), 6.92 (1H, d, CH=C*H*CO$_2$Et, *J* 15.34), 4.73 (2H, s, CH_2OH), 4.37 (2H, q, OCH$_2$, *J* 7.30), 2.89 (1H, br s, OH), 1.91 (3H, s, CH$_3$), 1.27 (3H, t, CH$_2$CH_3, *J* 7.30)	165.20 (NHCO), 162.71 (*C*O$_2$Et), 136.47 (C-1), 130.77 (C-2), 127.31 (C-6), 135.90, 133.24 and 127.79 (Ar), 135.45 (*C*H=CHCO$_2$Et), 131.77 (CH=*C*HCO$_2$Et), 65.01 (CH$_2$OH), 61.39 (OCH$_2$), 18.26 (CH$_3$), 14.21 (CH$_2$*C*H$_3$)	3266.2 (OH), 3095.8 (NH), 1716 (CO$_2$Et), 1645.2 (NHCO)
8	**8h**	9.07 (1H, s, NH), 8.01 (1H, d, ArH, *J* 8.04), 7.48 (2H, m, ArH), 7.01 (1H, d, C*H*=CH-CO$_2$Et, *J* 15.38), 6.84 (1H, d, CH=C*H*CO$_2$Et, *J* 15.38), 4.67 (2H, s, CH_2OH), 4.26 (2H, q, OCH$_2$, *J* 7.33), 3.01 (1H, br, OH), 2.33 (3H, s, CH$_3$), 1.34 (3H, t, CH$_2$CH_3, *J* 7.33)	165.50 (*C*O$_2$Et), 161.86 (NH*C*O), 137.01 (C-1), 129.49 (C-2), 122.45 (C-3), 129.73, 134.24 and 122.98 (Ar), 134.81 (*C*H=CHCO$_2$Et), 130.92 (CH=*C*HCO$_2$Et), 64.36 (CH$_2$OH), 61.35 (OCH$_2$), 20.83 (CH$_3$), 14.01 (CH$_2$*C*H$_3$)	3258.1 (OH), 3099.0 (NH), 1730.4 (CO$_2$Et), 1693.4 (NHCO)

yielding the desired aldehydes. The yields of the new compounds ranged from 68–79%; all gave satisfactory micro analytical and spectroscopic data, see Table 2(*a*) and (*b*), entries 1–3 and 10–14.

Preparation of the ketones 1d–i. The acyl halide **7** (0.057 mol) was added dropwise to a cooled suspension of the amino ketone (0.057 mol) and sodium hydrogen carbonate (0.067 mol) in anhydrous dichloromethane (50 cm^3). The mixture was stirred for 1 h at room temp. The organic layer was washed, dried and the solvent removed under reduced pressure. The resulting solid was crystallised from diethyl ether–light petroleum to yield the pure ketones **1d**–**i**. The yields of the ketones ranged from 49–57%; all gave satisfactory micro analytical and spectroscopic data, see Table 2(*a*) and (*b*), entries 4–9.

Table 2(*a*) Analytical data for the carbonyl compounds **1**

Entry no.	Compound no.	R^1	R^2	R^3	R^4	R^5	X	Yield (%)	Molecular formula	mp/°C	Found (%) [requires (%)] C	H	N
1	**1a**	H	H	CO_2Et	H	H	H	73	$C_{13}H_{13}NO_4$	71–73	63.19 [63.16]	5.26 [5.26]	5.69 [5.67]
2	**1b**	H	H	CO_2Et	H	H	Cl	78	$C_{13}H_{12}NO_4Cl$	74–75	55.39 [55.42]	4.29 [4.26]	4.29 [4.26]
3	**1c**	H	H	Ph	H	H	H	68	$C_{16}H_{13}NO_2$	93–95	76.43 [76.49]	5.17 [5.18]	5.57 [5.57]
4	**1d**	Ph	H	Ph	H	H	H	57	$C_{22}H_{17}NO_2$	52–54	80.69 [80.73]	5.17 [5.20]	4.26 [4.28]
5	**1e**	Ph	H	Ph	H	H	Cl	51	$C_{22}H_{16}NO_2Cl$	58–60	72.99 [73.03]	4.47 [4.43]	3.89 [3.87]
6	**1f**	Ph	H	CO_2Et	H	H	H	49	$C_{19}H_{17}NO_4$	62–64	70.61 [70.59]	5.29 [5.26]	4.36 [4.33]
7	**1g**	Ph	H	CO_2Et	H	H	Cl	53	$C_{19}H_{16}NO_4Cl$	98–100	63.72 [63.78]	4.51 [4.48]	3.94 [3.91]
8	**1h**	Ph	H	CO_2Et	H	H	NO_2	53	$C_{19}H_{16}N_2O_6$	112–114	61.98 [61.96]	4.30 [4.35]	7.57 [7.61]
9	**1i**	Me	H	CO_2Et	H	H	H	52	$C_{14}H_{15}NO_4$	73–74	64.39 [64.37]	5.78 [5.75]	5.33 [5.36]
10	**1j**	H	Me	CO_2Et	H	H	H	79	$C_{14}H_{15}NO_4$	81–83	64.39 [64.37]	5.76 [5.75]	5.34 [5.36]
11	**1k**	H	Me	Ph	H	H	H	69	$C_{17}H_{15}NO_2$	102–105	76.95 [76.98]	5.62 [5.66]	5.29 [5.28]
12	**1l**	H	H	CO_2Et	Me	Me	H	68	$C_{15}H_{17}NO_4$	89–90	65.45 [65.40]	6.18 [6.07]	5.09 [5.09]
13	**1m**	H	H	CO_2Et	H	Me	H	65	$C_{14}H_{15}NO_4$	72–75	64.30 [64.37]	5.74 [5.75]	5.39 [5.36]
14	**1n**	H	H	CO_2Et	Me	H	H	72	$C_{14}H_{15}NO_4$	84–86	64.37 [64.37]	5.79 [5.75]	5.30 [5.36]

Preparation of 9; 1,2,3,5-tetrahydro-3-(2-oxopropyl)-4,1-benzoxazepin-2-one

4-Oxopent-2-enoic acid chloride **7c** (0.057 mol) was added dropwise to a cooled suspension of the amino alcohol **6a** (0.057 mol) and sodium hydrogen carbonate (0.067 mol) in anhydrous dichloromethane (50 cm^3). The mixture was stirred for 1 h at room temp. The organic layer was washed, dried and the solvent removed under reduced pressure. The resulting solid was crystallised from diethyl ether–light petroleum to yield the pure benzoxazepinone **9**, yield 84%, mp 98–100 °C; δ_H(270 MHz) 9.32 (1H, s, NH), 7.02–7.75 (4H, m, ArH), 4.72 (1H, d, *J* 11.3, 5-H), 4.59 (1H, d, *J* 11.3, 5-H), 4.32 (1H, dd, *J* 6.0 and 8.1, 3-H), 3.02 (1H, dd, *J* 17.6 and 8.7, CH_2COMe), 2.62 (1H, dd, *J* 17.6 and 6.0, CH_2COMe), 2.24 (3H, s, COMe); δ_C(67.5 MHz) 206.33 ($COCH_3$), 170.43 (NHCO), 130.24, 128.31, 127.11, 125.22, 121.77 and 120.34 (Ar), 70.31 (C-5), 60.08 (C-3), 33.21 (CH_2COMe), 30.21 ($COCH_3$).

General procedure for the formation of the oximes 10a–e

The appropriate carbonyl substrate **1a–e** (0.024 mol), hydroxylamine hydrochloride (0.029 mol) and pyridine (0.029 mol) were stirred at room temp. in anhydrous ethanol (50 cm^3) for 24 h. The ethanol was removed under reduced pressure and the resulting residue was dissolved in dichloromethane and washed with water (4 × 25 cm^3). The organic layer was dried and concentrated to yield the oxime, which was purified by crystallisation from diethyl ether–light petroleum. The yields of the new oximes ranged from 59–85%, all gave satisfactory micro analytical and spectroscopic data, see Table 3(*a*) and (*b*), entries 1–5.

Preparation of the nitrones 3a,b; 3-ethoxycarbonylmethyl-2,3-dihydro-1*H*-1,4-benzodiazepin-2-one *N*-oxides

Aldoximes **10a**,**b** (7.6 mmol) were heated at reflux (110 °C) in toluene (10 cm^3) in the presence of pyridine (8 mmol). The solvent was removed and the resulting white solid crystallised from dichloromethane–light petroleum, yielding the pure nitrone. The yields of the new nitrones ranged from 62–78%, both gave satisfactory micro analytical and spectroscopic data, see Table 4(*a*) and (*b*), entries 1 and 2.

Preparation of the tricycles 5d,e; 3,9b-diphenyl-1,3,3a,4,5,9b-hexahydroisoxazolo[4,3-*c*]quinolin-4-ones

Ketoximes **10d**,**e** (7.6 mmol) were heated at reflux (140 °C) in xylene (10 cm^3). The solvent was removed and the resulting white solid crystallised from diethyl ether–light petroleum, yielding the pure isoxazoloquinolinone. The yields of the new tricycles ranged from 63–78%, both gave satisfactory micro analytical and spectroscopic data, see Table 5(*a*) and (*b*), entries 1 and 2.

General procedure for the formation of the nitrones 3f–i; 3-ethoxycarbonylmethyl-1,3-dihyhdro[1,4]benzodiazepin-2-one *N*-oxides

The appropriate carbonyl substrate **1f–i** (0.024 mol), hydroxylamine hydrochloride (0.029 mol) and pyridine (0.029 mol) were heated at reflux (80 °C) in anhydrous ethanol (50 cm^3) for 16 h. The ethanol was removed under reduced pressure. The resulting residue was dissolved in dichloromethane and washed with water (4 × 25 cm^3). The organic layer was then dried and the dichloromethane removed. Purification was carried out using flash chromatography (SiO_2, diethyl ether) to yield the pure nitrone. The yields of all new nitrones ranged from 49–64%, all gave satisfactory micro analytical and spectroscopic data, see Table 4(*a*) and (*b*), entries 3–6.

Preparation of the tricycles 5f,h: 3-ethoxycarbonyl-9a-phenyl-1,3,3a,4,5,9b-hexahydroisoxazolo[4,3-*c*]quinolin-2-ones

Prolonged heating (72 h) of the above reaction mixture resulted in a decrease in the amount of nitrone present and the

Table 2(*b*) Spectroscopic data for the carbonyl compounds **1**

Entry no.	Compound no.	δ_H	δ_C	ν/cm^{-1}
1	**1a**	11.54 (1H, s, NH), 9.95 (1H, s, CHO), 8.82 (1H, d, ArH, *J* 8.79), 7.65 (2H, m, ArH), 7.30 (1H, t, ArH, *J* 8.79), 7.11 (1H, d, C*H*=CH-CO_2Et, *J* 15.39), 6.93 (1H, d, CH=C*H*CO_2Et, *J* 15.39), 4.29 (2H, q, OCH_2, *J* 7.33), 1.36 (3H, t, CH_2CH_3, *J* 7.33)	195.68 (CHO), 165.13 (NHCO), 162.59 (CO_2Et), 140.27 (C-2), 136.23 (C-1), 136.78, 123.80 and 120.16 (Ar), 135.28 (*C*H=CH CO_2Et), 131.79 (CH=*C*HCO_2Et), 61.28 (O*C*H$_2$), 14.09 (CH_2CH_3)	3125.6 (NH), 1720.6 (CO_2Et), 1688.6 (CHO), 1654.1 (NHCO)
2	**1b**	11.41 (1H, s, NH), 9.90 (1H, s, CHO), 8.82 (1H, d, ArH, *J* 8.58), 7.63 (2H, m, ArH), 7.09 (1H, d, C*H*=CHCO_2Et, *J* 15.37), 6.93 (1H, d, CH=C*H*CO_2Et, *J* 15.37), 4.31 (2H, q, OCH_2, *J* 7.32), 1.35 (3H, t, CH_2CH_3, *J* 7.32)	194.47 (CHO), 164.73 (NHCO), 162.19 (CO_2Et), 138.85 (C-2), 136.06 (C-1), 129.05 (C-4), 122.97, 136.45 and 121.96 (Ar), 135.18 (CH=*C*HCO_2Et), 132.21 (*C*H=CHCO_2Et), 61.47 (OCH_2), 14.20 (CH_2CH_3)	
3	**1c**	11.41 (1H, s, NH), 9.96 (1H, s, CHO), 8.89 (1H, d, ArH, *J* 8.42), 7.68 (1H, d, CH=C*H*Ph, *J* 15.41), 7.46 (8H, m, ArH), 6.63 (1H, d, C*H*=CHPh, *J* 15.41)	195.68 (CHO), 162.18 (NHCO), 142.88 (Ar), 141.30 (C-2), 136.31 (C-1), 134.57, 128.95, 128.24, 121.75, 121.51 and 120.16 (Ar), 131.22 (*C*H=CHPh), 123.01 (CH=*C*HPh)	3110.5 (NH), 1689.1 (CHO), 1643.7 (NHCO)
4	**1d**	10.43 (1H, s, NH), 7.63 (15H, m, ArH, CH=C*H*Ph), 6.75 (1H, d, C*H*=CHPh, *J* 15.81)	192.98 (CO), 162.45 (NHCO), 142.38 (Ar), 140.81 (C-2), 136.73 (C-1), 134.28, 133.92, 133.06, 132.51, 130.88, 130.10, 129.6, 128.93, 128.21, 127.63, 125.90, 125.19 and 121.47 (Ar, *C*H=*C*H)	3121.0 (NH), 1692.3 (CO), 1637.0 (NHCO)
5	**1e**	10.94 (1H, s, NH), 7.42 (14H, m, ArH, CH=C*H*Ph), 6.69 (1H, d, C*H*=CHPh, *J* 15.61)	193.31 (CO), 163.60 (NHCO), 142.89 (Ar), 140.89 (C_2, Ar), 136.51 (C-1), 134.93, 134.41, 132.86, 132.70, 131.28, 129.7, 128.81, 128.25, 127.76, 125.39 and 121.05 (Ar, *C*H=*C*H)	3098.9 (NH), 1695.3 (CO), 1642.1 (NHCO)
6	**1f**	11.37 (1H, s, NH), 8.76 (1H, d, ArH, *J* 8.7), 7.48 (7H, m, ArH), 7.15 (1H, m, ArH), 7.11 (1H, d, C*H*=CHCO_2Et, *J* 15.41), 6.93 (1H, d, CH=C*H*CO_2Et, *J* 15.41), 4.27 (2H, q, OCH_2, *J* 7.32), 1.35 (3H, t, CH_2CH_3, *J* 7.32)	199.91 (CO), 165.24 (NHCO), 162.43 (CO_2Et), 140.12 (C-2), 139.21 (Ar), 137.21 (C-1), 134.36, 133.85, 132.65, 129.93, 128.41, 123.42, 122.97, 121.71 and 101.02 (Ar), 134.48 (C*H*=CH-CO_2Et), 131.45 (CH=C*H*CO_2Et), 61.28 (OCH_2), 14.21 (CH_2CH_3)	3112.0 (NH), 1720.1 (CO_2Et), 1689.2 (CO), 1648.0 (NHCO)
7	**1g**	10.60 (1H, s, NH), 7.62 (8H, m, ArH), 7.05 (1H, d, C*H*=CHCO_2Et, *J* 15.60), 6.56 (1H, d, CH=C*H*CO_2Et, *J* 15.60), 4.25 (2H, q, OCH_2, *J* 7.04), 1.31 (3H, t, CH_2CH_3, *J* 7.04)	193.02 (CO), 166.62 (NHCO), 163.20 (CO_2Et), 140.23 (Ar), 138.35 (C-2), 136.15 (C-1), 132.86, 131.25, 129.60, 129.40, 128.94, 125.35, 128.12 and 125.75 (Ar), 135.06 (*C*H=CHCO_2Et), 130.59 (CH=*C*HCO_2Et), 60.82 (OCH_2), 13.93 (CH_2CH_3)	3115.2 (NH), 1721.2 (CO_2Et), 1687.2 (CO), 1633.3 (NHCO)
8	**1h**	11.12 (1H, s, NH), 8.44 (1H, m, ArH), 7.83 (7H, m, ArH), 7.13 (1H, d, C*H*=CHCO_2Et, *J* 15.61), 6.64 (1H, d, CH=C*H*CO_2Et, *J* 15.61), 4.27 (2H, q, OCH_2, *J* 7.30), 1.32 (3H, t, CH_2CH_3, *J* 7.30)	192.43 (CO), 164.46 (CO_2Et), 161.85 (NHCO), 143.23 (C-2), 140.96 (Ar), 136.28 (C-1), 133.35, 130.95, 129.77, 128.48, 126.74, 125.09 and 124.07 (Ar), 135.95 (*C*H=CHCO_2Et), 130.72 (CH=*C*HCO_2Et), 60.92 (OCH_2), 13.93 (CH_2CH_3)	3120.5 (NH), 1719.5 (CO_2Et), 1690.5 (CO), 1642.9 (NHCO)
9	**1i**	12.20 (1H, s, NH), 8.83 (1H, d, ArH, *J* 8.30), 7.94 (1H, d, ArH, *J* 7.81), 7.59 (1H, t, ArH, *J* 7.32), 7.19 (1H, t, ArH, *J* 7.81), 7.09 (1H, d, C*H*=CHCO_2Et, *J* 15.63), 6.91 (1H, d, CH=C*H*CO_2Et, *J* 15.63), 4.29 (2H, q, OCH_2, *J* 7.33), 2.69 (3H, s, CH_3), 1.35 (3H, t, CH_2CH_3, *J* 7.33)	203.10 (CO), 165.17 (NHCO), 162.45 (CO_2Et), 140.37 (C-2), 137.34 (C-1), 131.13, 123.16, 121.83 and 120.82 (Ar), 135.12 (*C*H=CH-CO_2Et), 131.71 (CH=*C*HCO_2Et), 61.16 (OCH_2), 28.44 (CH_3), 14.08 (CH_2CH_3)	3098.6 (NH), 1718.1 (CO_2Et), 1682 (CO), 1651.3 (NHCO)
10	**1j**	10.05 (1H, s, CHO), 7.99 (1H, d, ArH, *J* 7.33), 7.74 (1H, m, ArH), 7.61 (1H, m, ArH), 7.33 (1H, d, ArH, *J* 7.30), 6.86 (1H, d, C*H*=CH-CO_2Et, *J* 15.39), 6.65 (1H, d, CH=C*H*CO_2Et, *J* 15.39), 4.13 (2H, q, OCH_2, *J* 7.33), 3.40 (3H, s, NCH_3), 1.36 (3H, t, CH_2CH_3, *J* 7.33)	187.87 (CHO), 165.0 (NCH_3CO), 163.94 (CO_2Et), 143.59 (C-2), 132.91 (C-1), 129.27, 132.35 and 131.16 (Ar), 135.60 (*C*H=CH-CO_2Et), 131.87 (CH=*C*HCO_2Et), 60.87 (O*C*H$_2$), 38.23 (NCH_3), 14.09 (CH_2CH_3)	1724 (CO_2Et), 1693.5 (CHO), 1664.3 (NCH_3CO)
11	**1k**	9.98 (1H, s, CHO), 8.73 (1H, d, ArH, *J* 8.02), 7.82 (1H, d, CH=C*H*Ph, *J* 15.41), 7.51 (8H, m, ArH), 6.92 (1H, d, C*H*=CHPh, *J* 15.41), 3.42 (3H, s, NCH_3)	198.72 (CHO), 165.02 (NMe*C*O), 143.29 (Ar), 142.33 (C-2), 137.64 (C-1), 135.87, 129.92, 127.34, 121.68, 121.01 and 120.23 (Ar), 132.98 (*C*H=CHPh), 122.91 (CH=*C*HPh), 37.78 (NCH_3)	1693.3 (CHO), 1648.0 (NMeCO)
12	**1l**	11.49 (1H, br, NH), 9.93 (1H, s, CHO), 7.99 (1H, d, ArH, *J* 8.06), 7.74 (1H, d, ArH, *J* 8.06), 7.34 (1H, d, C*H*=CHCO_2Et, *J* 15.39), 6.92 (1H, d, CH=C*H*CO_2Et, *J* 15.39), 4.27 (2H, q, OCH_2, *J* 7.33), 2.17 (3H, s, CH_3), 1.94 (3H, s, CH_3), 1.28 (3H, t, CH_2CH_3, *J* 7.33)	195.20 (CHO), 166.31 (CO_2Et), 162.67 (NHCO), 146.96 (C-2), 124.23 and 134.29 (Ar), 122.07 (C-5), 118.65 (C-4), 135.75 (*C*H=CH-CO_2Et), 128.19 (CH=*C*HCO_2Et), 61.05 (O*C*H$_2$), 22.45 (s, 3H, CH_3), 19.21 (s, 3H, CH_3), 14.09 (CH_2CH_3)	
13	**1m**	10.98 (1H, br, NH), 9.93 (1H, s, CHO), 7.48 (3H, m, ArH), 7.01 (1H, d, C*H*=CHCO_2Et, *J* 15.34), 6.90 (1H, d, CH=C*H*CO_2Et, *J* 15.34), 4.26 (2H, q, OCH_2, *J* 7.32), 2.16 (3H, s, CH_3), 1.26 (3H, t, CH_2CH_3, *J* 7.32)	193.76 (CHO), 165.74 (CO_2Et), 162.18 (NHCO), 127.75 and 126.49 (Ar), 143.21 (C-2), 137.41 (C-1), 136.06 (*C*H=CHCO_2Et), 132.19 (C-6), 131.79 (CH=*C*HCO_2Et), 61.43 (O*C*H$_2$), 18.45 (s, 3H, CH_3), 14.26 (CH_2CH_3)	
14	**1n**	11.39 (1H, br, NH), 9.87 (1H, s, CHO), 8.60 (1H, d, ArH, *J* 8.06), 7.44 (2H, m, ArH, *J* 8.06), 7.06 (1H, d, C*H*=CHCO_2Et, *J* 15.32), 6.92 (1H, d, CH=C*H*CO_2Et, *J* 15.32), 4.31 (2H, q, OCH_2, *J* 7.33), 2.38 (3H, s, CH_3), 1.33 (3H, t, CH_2CH_3, *J* 7.33)	195.66 (CHO), 165.19 (NHCO), 162.42 (CO_2Et), 137.89 (C-2), 133.61 (C-1), 129.26 (C-3), 121.82 and 120.16 (Ar), 136.30 (CH=*C*HCO_2Et), 131.47 (CH=*C*HCO_2Et), 61.27 (O*C*H$_2$), 20.51 (s, 3H, CH_3), 14.10 (CH_2CH_3)	3214.0 (NH), 1727.1 (CO_2Et), 1694.2 (CHO), 1644.3 (NHCO)

Table 3(*a*) Analytical data for the oximes **10**, **17** and **18**

Entry no.	Compound no.	Substrate no.	Yield (%)	mp/°C	Molecular formula	Found (%) [requires (%)] C	H	N
1	**10a**	**1a**	82	186–187	$C_{13}H_{14}N_2O_4$	59.58 [59.54]	5.38 [5.34]	10.72 [10.69]
2	**10b**	**1b**	83	121–123	$C_{13}H_{13}N_2O_4Cl$	52.58 [52.61]	4.34 [4.38]	9.38 [9.44]
3	**10c**	**1c**	85	121–122	$C_{16}H_{14}N_2O_2$	72.17 [72.18]	5.30 [5.26]	10.54 [10.53]
4	**10d**	**1d**	67	139–141	$C_{22}H_{18}N_2O_2$	77.17 [77.19]	5.30 [5.26]	8.14 [8.18]
5	**10e**	**1e**	59	151–153	$C_{22}H_{17}N_2O_2Cl$	70.19 [70.12]	4.50 [4.52]	7.41 [7.44]
6	**17k**	**1k**	76	102–105	$C_{17}H_{16}N_2O_2$	72.79 [72.86]	5.69 [5.71]	9.95 [10.00]
7	**17j**	**1j**	75	79–80	$C_{14}H_{16}N_2O_4$	60.91 [60.87]	5.83 [5.80]	10.11 [10.14]
8	**18l**	**1l**	69	123–125	$C_{15}H_{18}N_2O_4$	61.98 [62.07]	6.19 [6.21]	9.69 [9.66]
9	**18m**	**1m**	76	79–80	$C_{14}H_{16}N_2O_4$	60.88 [60.87]	5.78 [5.80]	10.09 [10.14]
10	**18n**	**1n**	74	146–147	$C_{14}H_{16}N_2O_4$	60.89 [60.87]	5.83 [5.80]	10.17 [10.14]

Table 3(*b*) Spectroscopic data for the oximes **10**, **17** and **18**

Entry no.	Compound no.	δ_H	δ_C	ν/cm^{-1}
1	**10a**	10.30 (1H, s, NH), 8.47 (1H, d, ArH, *J* 8.63), 7.99 (1H, s, CH=N), 7.49 (2H, m, ArH), 7.29 (1H, m, ArH), 7.14 (1H, d, C*H*=CHCO$_2$Et, *J* 15.31), 6.94 (1H, d, CH=C*H*CO$_2$Et, *J* 15.31), 4.3 (2H, q, OCH$_2$, *J* 7.20), 1.35 (3H, t, CH$_2$C*H*$_3$, *J* 7.20)	165.05 (NHCO), 162.01 (*C*O$_2$Et), 151.03 (CH=N), 139.32 (C-2), 134.36 (C-1), 124.99, 121.77 and 133.03 (Ar), 135.37 (*C*H=CH-CO$_2$Et), 132.59 (CH=*C*HCO$_2$Et), 61.5 (OCH$_2$), 14.21 (CH$_2$*C*H$_3$)	3249.6 (OH), 1719 (CO$_2$Et), 1667.1 (NHCO), 1591.5 (C=N)
2	**10b**	9.24 (1H, s, NH), 8.71 (1H, d, ArH, *J* 8.32), 8.17 (1H, s, CH=N), 7.18 (2H, m, ArH), 7.03 (1H, d, C*H*=CHCO$_2$Et, *J* 15.31), 6.88 (1H, d, CH=C*H*CO$_2$Et, *J* 15.31), 4.26 (2H, q, OCH$_2$, *J* 7.30), 1.33 (3H, t, CH$_2$C*H*$_3$, *J* 7.30)	165.49 (NHCO), 161.89 (*C*O$_2$Et), 151.70 (CH=N), 139.79 (C-2), 135.28 (C-1), 130.75, 121.77 and 120.56 (Ar), 137.77 (*C*H=CH-CO$_2$Et), 131.34 (CH=*C*HCO$_2$Et), 61.48 (OCH$_2$), 14.21 (CH$_2$*C*H$_3$)	3200.2 (OH), 1715.8 (CO$_2$Et), 1644.9 (NHCO), 1578.5 (C=N)
3	**10c**	9.57 (1H, s, NH), 8.78 (1H, d, ArH, *J* 8.43), 8.25 (1H, s, CH=N), 7.65 (1H, d, CH=C*H*Ph, *J* 15.57), 7.34 (3H, m, ArH), 7.16 (5H, m, ArH), 6.47 (1H, d, C*H*=CHPh, *J* 15.57)	165.52 (NHCO), 152.93 (*C*H=N), 142.32 (Ar), 137.89 (C-1), 134.41 (C-2), 132.03, 130.69, 129.98, 128.71, 127.99, 123.57, 121.75, 120.45 and 118.97 (Ar, *C*H=*C*H)	3221.0 (NH), 1665 (NH*CO*)
4	**10d**	9.57 (1H, s, NH), 8.27 (15H, m, ArH, CH=C*H*Ph), 6.57 (1H, d, C*H*=CHPh, *J* 15.57)	164.32 (NHCO), 149.29 (CH=N), 142.32, 133.45, 132.89, 132.55, 132.48, 128.75, 127.43, 124.72, 121.63, 120.15 and 119.12 (Ar, *C*H=*C*H)	
5	**10e**	9.49 (1H, s, NH), 7.92 (14H, m, ArH, CH=C*H*Ph), 6.55 (1H, d, C*H*=CHPh, *J* 15.57)	164.32 (NHCO), 149.29 (CH=N), 142.32, 134.25, 132.89, 132.78, 131.32, 126.92, 125.24, 124.99, 121.22, 119.99 and 118.22 (Ar-C, *C*H=*C*H)	
6	**17k**	8.31 (1H, s, C*H*=N), 7.86 (1H, d, ArH, *J* 8.05), 7.65 (1H, d, CH=C*H*Ph, *J* 15.53), 7.31 (8H, m, ArH), 6.18 (1H, d, C*H*=CHPh, *J* 5.53), 3.45 (s, 3H, NCH$_3$)	171.31 (NMe*C*O), 151.26 (CH=N), 142.31 (Ar), 136.27 (C-2), 135.26 (C-1), 130.21, 129.92, 127.07, 123.78, 121.99 and 117.83 (Ar, *C*H=*C*H), 36.92 (NCH$_3$)	1643.3 (NMeCO)
7	**17j**	8.32 (1H, d, ArH, *J* 8.28), 8.12 (1H, s, CH=N), 7.46 (3H, m, ArH), 6.92 (1H, d, C*H*=CH-CO$_2$Et, *J* 15.31), 6.73 (1H, d, CH=C*H*CO$_2$Et, *J* 15.31), 4.21 (2H, q, OCH$_2$, *J* 7.30), 3.43 (3H, s, NCH$_3$), 1.33 (3H, t, CH$_2$C*H*$_3$, *J* 7.30)	165.32 (NMe*C*O), 163.07 (*C*O$_2$Et), 150.19 (CH=N), 140.26 (C-1), 133.91 (C-2), 132.63, 131.90, 129.16 and 128.17 (Ar), 137.57 (*C*H=CHCO$_2$Et), 131.24 (CH=*C*HCO$_2$Et), 61.36 (OCH$_2$), 37.32 (NCH$_3$), 14.28 (CH$_2$*C*H$_3$)	3325.7 (OH), 1719.1 (CO$_2$Et), 1652.8 (NMeCO), 1586.1 (C=N)
8	**18l**	11.02 (1H, s, NH), 8.92 (1H, s, CH=N), 7.42 (1H, d, ArH, *J* 8.02), 7.28 (1H, d, ArH, *J* 8.02), 7.02 (1H, d, C*H*=CHCO$_2$Et, *J* 15.81), 6.82 (1H, d, CH=C*H*CO$_2$Et, *J* 15.81), 4.26 (2H, q, OCH$_2$, *J* 7.33), 2.36 (3H, s, CH$_3$), 1.91 (3H, s, CH$_3$), 1.33 (3H, t, CH$_2$C*H*$_3$, *J* 7.33)	165.29 (NHCO), 162.71 (*C*O$_2$Et), 150.73 (CH=N), 140.27 (C-2), 136.31 (C-1), 132.03, 127.13, 126.19 and 123.72 (Ar), 136.01 (*C*H=CHCO$_2$Et), 129.61 (CH=*C*HCO$_2$Et), 61.37 (OCH$_2$), 20.26 (CH$_3$), 19.21 (CH$_3$), 14.97 (CH$_2$*C*H$_3$)	3267.2 (OH), 1726.3 (CO$_2$Et), 1649 (NHCO), 1595.3 (C=N)
9	**18m**	8.99 (1H, s, NH), 8.25 (1H, s, CH=N), 7.25 (3H, m, ArH), 7.13 (1H, d, C*H*=CHCO$_2$Et, *J* 15.13), 6.96 (1H, d, CH=C*H*CO$_2$Et, *J* 15.13), 4.28 (2H, q, OCH$_2$, *J* 7.32), 1.74 (3H, s, CH$_3$), 1.34 (3H, t, CH$_2$C*H*$_3$, *J* 7.32)	166.03 (NH*C*O), 161.98 (*C*O$_2$Et), 152.99 (*C*H=N), 137.64 (C-2), 133.51 (C-1), 131.97 (C-6), 131.01, 122.90 and 118.65 (Ar), 134.74 (*C*H=CHCO$_2$Et), 131.71 (CH=*C*HCO$_2$Et), 61.61 (O*C*H$_2$), 18.61 (CH$_3$), 14.13 (CH$_2$*C*H$_3$)	3353.4 (OH), 1715.6 (CO$_2$Et), 1638.8 (NHCO), 1594.3 (C=N)
10	**18n**	11.04 (1H, s, NH), 8.58 (1H, d, ArH, *J* 8.81), 8.18 (1H, s, CH=N), 7.17 (1H, d, ArH, *J* 8.81), 7.04 (2H, m, ArH, C*H*=CHCO$_2$Et), 6.87 (1H, d, CH=C*H*CO$_2$Et, *J* 15.38), 4.23 (2H, q, OC*H*$_2$, *J* 7.33), 2.32 (3H, s, CH$_3$), 1.28 (3H, t, CH$_2$C*H*$_3$, *J* 7.32)	165.90 (NHCO), 162.18 (*C*O$_2$Et), 152.84 (CH=N), 137.88 (C-2), 133.77 (C-1), 132.34 (C-3), 130.45, 120.47 and 118.97 (Ar), 134.80 (*C*H=CHCO$_2$Et), 131.32 (CH=*C*HCO$_2$Et), 61.43 (O*C*H$_2$), 20.59 (CH$_3$), 14.02 (CH$_2$*C*H$_3$)	3244.0 (OH), 1714.7 (CO$_2$Et), 1645.7 (NHCO), 1593.4 (C=N)

Table 4(*a*) Analytical data for the nitrones **3**

Entry no.	Compound no.	Substrate no.	Yield (%)	mp/°C	Molecular formula	Found (%) [requires (%)] C	H	N
1	**3a**	**10a**	78	197–199	$C_{13}H_{14}N_2O_4$	59.57 [59.54]	5.36 [5.34]	10.72 [10.69]
2	**3b**	**10b**	62	212–214	$C_{13}H_{13}N_2O_4Cl$	56.64 [56.62]	4.47 [4.42]	9.39 [9.44]
3	**3f**	**1f**	63	200–204	$C_{19}H_{18}N_2O_4$	67.49 [67.45]	5.37 [5.33]	8.28 [8.28]
4	**3g**	**1g**	49	219–220	$C_{19}H_{17}N_2O_4Cl$	61.23 [61.21]	4.62 [4.55]	7.49 [7.50]
5	**3h**	**1h**	52	219–220	$C_{19}H_{17}N_3O_6$	59.49 [59.53]	4.48 [4.44]	19.93 [10.96]
6	**3i**	**1i**	64	189–190	$C_{14}H_{16}N_2O_4$	60.89 [60.86]	5.87 [5.80]	10.14 [10.14]

Table 4(*b*) Spectroscopic data for the nitrones **3**

Entry no.	Compound no.	δ_H	δ_C	ν/cm^{-1}
1	**3a**	9.49 (1H, s, NH), 8.01 (1H, s, CH=N), 7.33 (4H, m, ArH), 4.64 (1H, d, H-3, *J* 7.30 and 6.15), 4.13 (2H, q, OCH_2, *J* 7.32), 3.56 (1H, dd, $CHCH_2$, *J* 7.30 and 17.81), 3.10 (1H, dd, $CHCH_2$, *J* 6.15 and 17.81), 1.23 (3H, t, CH_3, *J* 7.32)	169.64 (NHCO), 165.91 (CO_2Et), 149.45 (CH=N), 139.47 (C-9a), 128.55 (C-5a), 127.52, 126.89, 123.25 and 121.51 (Ar), 65.48 (C-3), 60.36 (OCH_2), 30.59 ($CHCH_2$), 14.01 (CH_3)	3110.4 (NH), 1715.2 (CO_2Et), 1683.4 (NHCO)
2	**3b**	9.94 (1H, s, NH), 8.06 (1H, 5, CH=N), 7.41 (3H, m, ArH), 4.68 (1H, dd, H-3, *J* 7.10 and 6.12), 4.17 (2H, q, OCH_2, *J* 7.33), 3.61 (1H, dd, $CHCH_2$, *J* 7.10 and 16.94), 3.14 (1H, dd, $CHCH_2$, *J* 6.12 and 16.94), 1.24 (3H, t, CH_3, *J* 7.33)	170.32 (NHCO), 166.12 (CO_2Et), 151.23 (CH=N), 138.71 (C-9a), 129.01 (C-5a), 126.32, 125.11 and 121.13 (Ar), 65.92 (C-3), 61.03 (OCH_2), 30.79 ($CHCH_2$), 14.21 (CH_3)	3121.4 (NH), 1719.3 (CO_2Et), 1691.3 (NHCO)
3	**3f**	10.11 (1H, s, NH), 7.35 (9H, m, ArH), 4.79 (1H, dd, H-3, *J* 8.57 and 5.50), 4.19 (2H, q, OCH_2CH_3, *J* 7.04), 3.74 (1H, dd, $CHCH_2$, *J* 8.57 and 17.80), 3.10 (1H, dd, $CHCH_2$, *J* 5.50 and 17.80), 1.28 (3H, t, CH_3, *J* 7.04)	170.80 (NHCO), 166.63 (CO_2Et), 143.66 (CH=N), 133.47 (C-9a), 125.82 (C-5a), 136.51, 131.58, 130.94, 130.75, 129.67, 127.07, 124.81 and 121.77 (Ar), 66.28 (C-3), 61.03 ($CHCH_2$), 30.66 (OCH_2), 14.15 (OCH_2CH_3)	3217.6 (NH), 1736.2 (C=N), 1702.0 (CO_2Et), 1654.4 (NHCO)
4	**3g**	10.23 (1H, s, NH), 7.55 (2H, m, ArH), 7.31 (4H, m, ArH), 7.16 (1H, d, ArH, *J* 8.79), 7.07 (1H, s, ArH), 4.75 (1H, dd, H-3, *J* 8.29 and 5.37), 4.18 (2H, q, OCH_2CH_3, *J* 7.33), 3.69 (1H, dd, $CHCH_2$, *J* 8.29 and 17.56), 3.06 (1H, dd, $CHCH_2$, *J* 5.37 and 17.56), 1.27 (3H, t, CH_3, *J* 7.33)	170.56 (NHCO), 166.21 (CO_2Et), 142.85 (CH=N), 143.05 (C-7), 132.73 (C-9a), 127.02 (C-5a), 135.02, 130.81, 130.71, 129.98, 129.13, 128.17 and 123.20 (Ar), 66.37 (C-3), 61.11 ($CHCH_2$), 30.53 (OCH_2), 14.08 (CH_2CH_3)	
5	**3h**	10.23 (1H, s, NH), 8.13 (1H, d, ArH, *J*, 9.27), 7.94 (1H, s, ArH), 7.58 (6H, m, ArH), 4.66 (1H, dd, H-3, *J* 8.78 and 5.37), 4.13 (2H, q, OCH_2CH_3, *J* 7.32), 3.59 (1H, dd, $CHCH_2$, *J* 8.78 and 17.56), 3.00 (1H, dd, $CHCH_2$, *J* 5.37 and 17.56), 1.22 (3H, t, CH_3, *J* 7.32)	170.30 (NHCO), 165.56 (CO_2Et), 143.97 (CH=N), 143.05 (C-7), 132.35 (C-9a), 125.18 (C-5a), 140.97, 130.64, 130.58, 128.47, 125.77 and 122.61 (Ar), 66.67 (C-3), 61.30 ($CHCH_2$), 30.50 (OCH_2), 14.11 (OCH_2CH_3)	3218.0 (NH), 1743.2 (C=N), 1709.9 (CO_2Et), 1548.7 (NHCO)
6	**3i**	10.15 (1H, s, NH), 7.46 (2H, m, ArH), 7.29 (2H, m, ArH), 4.66 (1H, dd, H-3, *J* 7.02 and 7.02), 4.12 (2H, q, OCH_2CH_3, *J* 7.13), 3.58 (1H, dd, $CHCH_2$, *J* 7.02 and 17.80), 3.07 (1H, dd, $CHCH_2$, *J* 7.02 and 17.80), 2.57 (3H, s, CH_3), 1.23 (3H, t, CH_3, *J* 7.13)	170.74 (NHCO), 166.31 (CO_2Et), 143.73 (CH=N), 134.99 (C-9a), 125.94 (C-5a), 130.50, 128.60, 125.25 and 122.02 (Ar), 65.08 (C-3), 60.97 ($CHCH_2$), 30.59 (OCH_2), 30.40 (CH_3), 14.02 (OCH_2CH_3)	3321.6 (NH), 1742.0 (C=N), 1724.9 (CO_2Et), 1683.4 (NHCO)

formation of the corresponding isoxazoloquinolinone. The yields of the new tricycles was in the range 31–32%, both gave satisfactory micro analytical and spectroscopic data, see Table 5(*a*) and (*b*), entries 3 and 4. Alternatively the tricyclic adducts **5f**,**h** can be formed on heating the corresponding benzodiazepinone *N*-oxides **3f**,**h** in ethanolic pyridine at 80 °C.

Formation of the tricyclic adduct 5j; 3-ethoxycarbonyl-5-methyl-1,3,3a,4,5,9b-hexahydroisoxazolo[4,3-*c*]quinolin-2-one

The aldehyde **1j** (0.024 mol), hydroxylamine hydrochloride (0.029 mol) and pyridine (0.029 mol) were stirred in anhydrous ethanol (50 cm^3) for 4 h at room temp. The ethanol was removed under reduced pressure and the resulting solid was dissolved in dichloromethane and washed with water (4 × 25 cm^3). The organic layer was dried and the dichloromethane was removed yielding the crude product, which was purified by crystallisation from diethyl ether–light petroleum. The adduct **5j** was obtained in 53% yield, mp 102–105 °C, Table 5(*a*) and (*b*), entry 5.

Preparation of the oxime 17j; ethyl 3-{*N*-[2-(hydroxyiminomethyl)-phenyl]-*N*-methylcarbamoyl}acrylate

The aldehyde **1j** (0.024 mol), hydroxylamine hydrochloride (0.029 mol) and pyridine (0.029 mol) were stirred in anhydrous ethanol (50 cm^3) for 3 h at −25 °C. The ethanol was removed under reduced pressure and the resulting solid was dissolved in dichloromethane and washed with water (4 × 25 cm^3). The organic layer was dried and the dichloromethane removed yielding the crude product, which was purified by crystallis-

Table 5(*a*) Analytical data for the isoxazoloquinolinones **5**

Entry no.	Compound no.	Substrate no.	Yield (%)	mp/°C	Molecular formula	Found (%) [requires (%)] C	H	N
1	**5d**	**10d**	78	98–100	$C_{22}H_{18}N_2O_2$	77.09 [77.16]	5.28 [5.30]	8.21 [8.19]
2	**5e**	**10e**	63	111–113	$C_{22}H_{17}N_2O_2Cl$	70.22 [70.19]	4.59 [4.56]	8.49 [8.51]
3	**5f**	**3f**	31	111–113	$C_{19}H_{18}N_2O_4$	67.41 [67.45]	5.37 [5.33]	8.31 [8.28]
4	**5h**	**3h**	32	102–105	$C_{19}H_{17}N_3O_6$	59.49 [59.53]	4.48 [4.45]	19.93 [10.97]
5	**5j**	**1j**	53	132–133	$C_{14}H_{16}N_2O_4$	60.84 [60.87]	5.80 [5.80]	10.15 [10.14]
6	**5k**	**17k**	84	123–125	$C_{16}H_{16}N_2O_2$	71.68 [71.64]	5.96 [5.97]	10.43 [10.45]
7	**5l**	**1l**	49	143–145	$C_{15}H_{18}N_2O_4$	62.09 [62.07]	6.19 [6.21]	9.65 [9.66]
8	**5n**	**1n**	23	119–121	$C_{14}H_{16}N_2O_4$	60.89 [60.87]	5.84 [5.80]	10.11 [10.14]

Table 5(*b*) Spectroscopic data for the isoxazoloquinolinones **5**

Entry no.	Compound no.	δ_H	δ_C	ν/cm^{-1}
1	**5d**	9.94 (1H, s, NH), 7.31 (9H, m, ArH), 7.04 (5H, m, ArH), 6.51 (1H, d, H-3, *J* 3.24), 4.52 (1H, d, H-2a, *J* 3.24)	165.81 (NHCO), 141.11 (Ar), 131.63 (C-9a), 131.01, 130.23, 129.69, 128.22, 125.11, 123.21, 122.22, 119.23 and 114.93 (Ar), 77.63 (C-3), 60.24, 56.36 (C-2a)	1659.2 (NHCO)
2	**5e**	10.11 (1H, s, NH), 7.63 (5H, m, ArH), 7.31 (4H, m, ArH), 7.11 (4H, m, ArH), 6.43 (1H, d, H-3, *J* 3.12), 4.21 (1H, d, H-2a, *J* 3.12)	168.31 (NHCO), 139.6 (Ar), 131.29, 131.14, 130.66, 129.88, 129.01, 122.94, 123.61, 121.78 and 114.93 (Ar), 77.63 (C-3), 60.24, 56.36 (C-2a)	
3	**5f**	9.77 (1H, s, NH), 7.19 (9H, m, ArH), 6.4 (1H, d, H-3, *J* 3.30), 4.97 (1H, d, H-2a, *J* 3.30), 4.15 (2H, q, OC*H*$_2$, *J* 7.33), 1.22 (3H, t, OCH$_2$C*H*$_3$, *J* 7.33)	170.50 (NHCO), 168.05 (CO$_2$Et), 139.95 (Ar), 135.27 (C-9a), 127.52 (C-5b), 129.73, 128.86, 128.31, 126.33, 124.51 and 116.27 (Ar), 83.15 (C-3), 71.69 (C-5a), 61.90 (OCH$_2$), 59.69 (C-2a), 13.98 (CH$_2$*C*H$_3$)	2193.6 (NH), 1719.3 (CO$_2$Et), 1654.7 (NHCO)
4	**5h**	9.65 (1H, s, NH), 7.39 (7H, m, ArH), 6.93 (1H, d, ArH, *J* 8.06), 6.36 (1H, d, H-3, *J* 3.13), 4.89 (1H, d, H-2a, *J* 3.13), 4.23 (2H, q, OCH$_2$, *J* 7.32), 1.27 (3H, t, CH$_2$C*H*$_3$, *J* 7.32)	171.03 (NHCO), 168.54 (CO$_2$Et), 139.36 (Ar), 135.12 (C-9a), 126.99 (C-5b), 129.54, 128.21, 127.93, 124.87, 121.09 and 116.27 (Ar), 82.95 (C-3), 71.31 (C-5a), 60.74 (OCH$_2$), 59.32 (C-2a), 14.12 (CH$_2$*C*H$_3$)	
5	**5j**	7.37 (1H, m, ArH), 7.12 (3H, m, ArH), 6.11 (1H, d, H-5, *J* 13.74), 4.78 (1H, d, H-3, *J* 8.79), 4.39 (1H, dd, H-5a, *J* 13.74 and 13.50), 4.20 (2H, q, OCH$_2$, *J* 7.32), 3.39 (3H, s, NCH$_3$), 3.23 (1H, dd, H-2a, *J* 8.79 and 13.50), 1.27 (3H, t, CH$_2$C*H*$_3$, *J* 7.32)	170.75 (NCH$_3$*C*O), 166.08 (CO$_2$Et), 140.43 (C-9a), 123.01 (C-5b), 128.95, 123.65 and 115.89 (Ar), 77.10 (C-5a), 62.54 (C-3), 61.90 (OCH$_2$), 57.70 (C-2a), 29.84 (NCH$_3$), 14.31 (CH$_2$*C*H$_3$)	
6	**5k**	7.57 (1H, d, ArH, *J* 7.32), 7.29 (6H, m, ArH), 7.11 (1H, d, ArH, *J* 7.32), 7.07 (1H, d, ArH, *J* 8.80), 5.56 (1H, d, H-3, *J* 3.13), 4.64 (1H, d, H-5a, *J* 13.23), 3.44 (4H, m, NCH$_3$, H-2a)	167.72 (NCH$_3$CO), 140.4, 138.91 (C′), 131.24 (C-9a), 130.21, 128.70, 128.07, 126.09, 123.48 and 114.93 (Ar), 77.57 (C-3), 60.24 (C-5a), 55.96 (C-2a), 29.69 (NCH$_3$)	1654.3 (CONCH$_3$)
7	**5l**	8.20 (1H, s, NH), 7.21 (2H, m, ArH), 5.42 (1H, d, H-3, *J* 2.93), 4.88 (1H, d, H-5a, *J* 7.32), 4.26 (2H, q, OCH$_2$, *J* 7.33), 3.20 (1H, dd, H-2a, *J* 7.32 and 2.93), 2.59 (3H, s, CH$_3$), 2.42 (3H, s, CH$_3$), 1.33 (3H, t, CH$_2$C*H*$_3$, *J* 7.33)	170.11 (NHCO), 167.10 (CO$_2$Et), 137.74, 134.41, 131.64 and 125.39 (Ar), 120.79 (C-6), 113.83 (C-9), 82.72 (C-3), 65.32 (C-6), 58.34 (OCH$_2$), 51.20 (C-2a), 18.84 (CH$_3$), 16.78 (CH$_3$), 14.25 (CH$_2$*C*H$_3$)	3191.6 (NH), 1714.6 (CO$_2$Et), 1643.1 (NHCO)
8	**5n**	8.35 (1H, s, NH), 7.18 (3H, m, ArH), 5.39 (1H, d, H-3, *J* 2.64), 4.89 (1H, d, H-5a, *J* 8.10), 4.14 (2H, q, OCH$_2$, *J* 7.32), 3.18 (1H, dd, H-2a, *J* 8.10 and 2.64), 2.34 (3H, s, CH$_3$), 1.29 (3H, t, CH$_2$C*H*$_3$, *J* 7.32)	170.34 (NHCO), 168.07 (CO$_2$Et), 120.79 (C-6), 136.24 (C-11a), 125.41 (C-5a), 134.22, 130.45 and 123.12 (Ar), 80.43 (C-3), 63.92 (C-6), 59.26 (OCH$_2$), 51.38 (C-2a), 19.23 (CH$_3$), 14.18 (CH$_2$*C*H$_3$)	3213.6 (NH), 1724.8 (CO$_2$Et), 1648.2 (NHCO)

ation from diethyl ether–light petroleum. The adduct **17j** was obtained in 75% yield, mp 79–80 °C, Table 3(*a*) and (*b*), entry 7.

Preparation of the oxime 17k; *N*-[2-(hydroxyiminomethyl)-phenyl]-*N*-methyl-2-phenylacrylamide

The carbonyl substrate **1k** (0.024 mol), hydroxylamine hydrochloride (0.029 mol) and pyridine (0.029 mol) were stirred at room temp. in anhydrous ethanol (50 cm^3) for 24 h. The ethanol was removed under reduced pressure and the resulting residue was dissolved in dichloromethane and washed with water (4 × 25 cm^3). The organic layer was dried and concentrated to yield the oxime, which was purified by crystallisation from diethyl ether–light petroleum. The adduct **17k** was

Table 6 Crystal data and structure refinement for **5j**

Empirical formula	$C_{14}H_{16}N_2O_4$
Formula weight	276.29
T/K	293(2)
λ/Å	0.71069
Crystal system	Triclinic
Space group	$P\bar{1}$
Unit cell dimensions	
a/Å	8.0540(10)
b/Å	8.6674(8)
c/Å	10.8779(7)
α/°	90.349(8)
β/°	104.700(9)
γ/°	111.553(7)
V/Å^3	678.97(11)
Z	2
D calc./Mg m^{-3}	1.351
Absorption coefficent/mm^{-1}	0.100
F(000)	292
Crystal size/mm	0.49 × 0.35 × 0.22
θ range for data collection/°	2.54–27.97
Index ranges	$0 \leq h \leq 9; 0 \leq k \leq 10; -14 \leq l \leq 13$
Reflections collected	1520
Independent reflections	1460 [R(int) = 0.0132]
Reflections observed (>2σ)	1142
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	1460/0/183
Goodness-of-fit on F^2	1.194
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0443$ $wR_2 = 0.1418$
R indices (all data)	$R_1 = 0.0557$ $wR_2 = 0.01497$
Largest diff. peak and hole/e Å^{-3}	0.298 and −0.097

R indices; $R_1 = [\Sigma||F_o| - |F_c||]/\Sigma|F_o|$ (based on F)
$wR_2 = [[\Sigma_w(|F_o^2 - F_c^2|)^2]/[\Sigma_w(F_o^2)^2]]^{\frac{1}{2}}$ (based on F^2)
$w = 1/[(\sigma F_o)^2 + (0.1*P)^2]$
Goodness-of-fit = $[\Sigma_w(F_o^2 - F_c^2)^2/(N_{obs}\text{-}N_{parameters})]^{\frac{1}{2}}$

obtained in 76% yield, mp 102–105 °C, Table 3(*a*) and (*b*), entry 6.

Preparation of the tricyclic adduct 5k; 3-phenyl-5-methyl-1,3,3a,4,5,9b-hexahydroisoxazolo[4,3-*c*]quinolin-2-one

Aldoxime **17k** (7.6 mmol) was heated at reflux (140 °C) in xylene (10 cm^3) for 12 h. The solvent was removed and the resulting white solid crystallised from diethyl ether–light petroleum, yielding the pure isoxazoloquinolinone. The tricyclic adduct **5k** was obtained in 84% yield, mp 123–125 °C, Table 5(*a*) and (*b*), entry 6.

Formation of the tricycle 5l; 3-ethoxycarbonyl-6,9-dimethyl-1,3,3a,4,5,9b-hexahydroisoxazolo[4,3-*c*]quinolin-4-one

The 3,6-dimethyl substituted aldehyde **1l** (0.024 mol), hydroxylamine hydrochloride (0.029 mol) and pyridine (0.029 mol) were heated at reflux (80 °C) in anhydrous ethanol (50 cm^3) for 16 h. The ethanol was removed under reduced pressure and the resulting residue was dissolved in dichloromethane and washed with water (4 × 25 cm^3). The organic layer was dried and the dichloromethane removed. Purification was carried out by flash chromatography (SiO_2, diethyl ether), yielding the pure tricyclic product in 49% yield, see Table 5(*a*) and (*b*), entry 7.

Preparation of the oxime 18l; ethyl 3-[*N*-(2-hydroxyimino-methyl-3,6-dimethylphenyl)carbamoyl]acrylate

The 3,6-dimethyl substituted aldehyde **1l** (0.024 mol), hydroxylamine hydrochloride (0.029 mol) and pyridine (0.029 mol) were stirred at room temp. in anhydrous ethanol (50 cm^3) for 12 h. The ethanol was removed under reduced pressure and the resulting residue was dissolved in dichloromethane and washed with water (4 × 25 cm^3). The organic layer was dried and the dichloromethane removed. Purification was carried out by flash chromatography (SiO_2, diethyl ether). The adduct **18l** was obtained in 69% yield, mp 123–125 °C, see Table 3(*a*) and (*b*), entry 8.

Preparation of the oximes 18m,n; ethyl 3-[*N*-(2-hydroxy-iminomethyl-6-methylphenyl)carbamoyl]acrylate and ethyl 3-[*N*-(2-hydroxyiminomethyl-3-methylphenyl)carbamoyl]-acrylate

The methyl substituted aldehydes **1m**,**n** (0.024 mol), hydroxylamine hydrochloride (0.029 mol) and pyridine (0.029 mol) were stirred at room temp. in anhydrous ethanol (50 cm^3) for 16 h. The ethanol was removed under reduced pressure and the resulting residue was dissolved in dichloromethane and washed with water (4 × 25 cm^3). The organic layer was dried and the dichloromethane removed. Purification was carried out by flash chromatography (SiO_2, diethyl ether). The yields of the new adducts ranged from 74–76%, both gave satisfactory micro analytical and spectroscopic data, see Table 3(*a*) and (*b*), entries 9 and 10.

Formation of tricycle 5n; 3-ethoxycarbonyl-9-methyl-1,3,3a,4,5,9b-hexahydroisoxazolo[4,3-*c*]quinolin-4-one

The methyl substituted aldehyde **1n** (0.024 mol), hydroxylamine hydrochloride (0.029 mol) and pyridine (0.029 mol) were heated at reflux in anhydrous ethanol (50 cm^3) for 12 h. The ethanol was removed under reduced pressure and the resulting residue was dissolved in dichloromethane and washed with water (4 × 25 cm^3). The organic layer was dried and the dichloromethane removed. Purification was carried out by flash chromatography (SiO_2, diethyl ether). The adduct **5n** was obtained in 23% yield, mp 119–121 °C, Table 5(*a*) and (*b*), entry 8.

Crystal structure analysis of 5j (see Table 6)

The structure was solved by direct methods, SHELXS-86,[15] and refined by full-matrix least-squares using SHELXL-93.[16] SHELX operations were rendered paperless using ORTEX which was also used to obtain the drawings.[17] Data were corrected for Lorentz and polarisation effects but not for adsorption. The hydrogen atom on N-5 was not included, all other hydrogen atoms were included in calculated positions with thermal parameters 30% larger than the atom to which they were attached. The non-hydrogen atoms were refined anisotropically. All calculations were performed on a Silicon Graphics R4000 computer.

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