Tetrahedron Vol. 41, No. 17, pp. 3547 to 3558, 1985
Printed in Great Britain.

0040–4020/85 $3.00 + .00
Pergamon Press Ltd.

X=Y—ZH SYSTEMS AS POTENTIAL 1,3-DIPOLES—5[1]

INTRAMOLECULAR CYCLOADDITIONS OF IMINES OF α-AMINO ACID ESTERS

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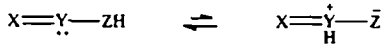
(*Received in Switzerland* 17 *December* 1984)

Abstract—Azomethine ylides are readily generated from imines of α-amino acid esters by a formal 1,2-H shift. A suitably positioned unactivated double or triple bond in either of the two precursors of the imines (aldehyde or α-amino ester) leads to an intramolecular cycloaddition generating fused ring systems in good yield. *Cis* stereochemistry is assigned to the newly created ring junction of the cycloadducts based on NOE difference spectroscopy and, in the case of **8a**, by a single crystal X-ray structure. Equilibration of the kinetically formed dipole leads to mixtures of epimeric cycloadducts for imines of phenylglycine methyl ester but equilibration is not observed for other imines. Reasons for this are discussed. The intramolecular cycloaddition is sensitive to ring size with 6/5 and 5/5 *cis*-fused systems being most easily formed depending in which moiety (aldehyde or amino acid) the dipolarophile is located. Intramolecular trapping of the azomethine ylide by an alkyne is accompanied by variable amounts of aromatized pyrrolic products.

The well-known versatility of 1,3-dipolar cycloaddition reactions for the construction of 5-membered heterocyclic rings dates from Huisgen's recognition of the general concept and scope of these processes.[2] The regio- and stereoselectivity of 1,3-dipolar cycloadditions have resulted in many elegant applications of intramolecular 1,3-dipolar cycloaddition reactions to the synthesis of natural products.[3,4] In this context it was of interest to see if our novel prototropic generation (**1** ⇌ **2**) of 1,3-dipoles from X=Y—ZH systems[5] could be extended to the intramolecular case and, in particular, to substrates where the dipolarophile was an unactivated alkene. In general, the corresponding intermolecular cycloaddition of X=Y—ZH systems to unactivated alkenes does not occur, apart from one or two exceptions such as acenaphthalene. The importance of the concept of a formal 1,2-H shift (**1** ⇌ **2**) and its synthetic realization is two-fold. Firstly it introduces a new and mechanistically important general prototropic process and secondly the readily generated dipoles provide a facile entry into a wide range of heterocycles.[5–7]



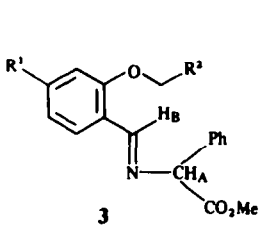
1 **2**

The ease of generation of 1,3-dipoles from X=Y—ZH systems by prototropy (**1** ⇌ **2**) depends on the basicity of Y and the pK_a of the ZH proton.[5] We have described our results on intramolecular cycloadditions of 1,3-dipoles generated from oximes in a full paper[6] and preliminary accounts of intramolecular cycloadditions of 1,3-dipoles generated from imines and hydrazones have appeared.[7] Dipole generation from oximes is difficult to achieve by (**1** ⇌ **2**) and normally proceeds by a different route.[5] This paper describes in detail our results with dipoles generated by prototropy from imines of α-amino acid esters (type II X=Y—ZH systems).[5]

In intramolecular cycloadditions of imines of α-amino acid esters the dipolarophile can be incorporated into either of the two imine precursors, the aldehyde or the amino acid ester. Examples of both types have been studied and successful cycloadditions achieved in both cases.

A. *Cycloadditions of aryl imines of phenylglycine methyl ester*

(1) *Intramolecular cycloaddition to non-activated terminal alkenes.* Our initial studies involved imines of alkenyl and alkynyl ethers of salicaldehyde (**3a–h**) and the corresponding 1-formyl-2-naphthol (**4a,b**). The aryl alkenyl and aryl alkynyl ethers were prepared by conventional methods and converted into the corresponding imines, usually in quantitative yield, by condensation with phenylglycine methyl ester in methanol at room temperature.



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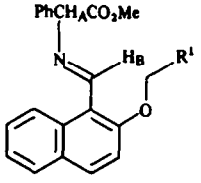

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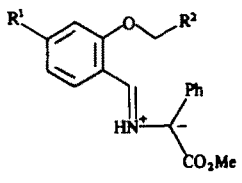
a. R^1 = H, R^2 = CH=CH_2
b. R^1 = H, R^2 = C≡CH
c. R^1 = H, R^2 = CH_2CH=CH_2
d. R^1 = OEt, R^2 = CH=CH_2
e. R^1 = H, R^2 = CH=$CHCO_2Me$
f. R^1 = H, R^2 = C(Cl)=CH_2
g. R^1 = H, R^2 = C(Me)=CH_2
h. R^1 = H, R^2 = CH=CHMe

a. R^1 = CH=CH_2
b. R^1 = C≡CH

When the Schiff's base (**3a**) was heated in boiling xylene for 24 hr it was converted via, we believe, the intermediate azomethine ylide (**5**) into a 3 : 2 mixture of **6a** and **7a**. The major isomer (**6a**) was readily separated by crystallization but a pure sample of **7a** was not obtained. The corresponding naphthalene imine (**4a**) reacted in an analogous way to give a 53 : 47 mixture of **8a** and **8b** which was readily separated by crystallization.



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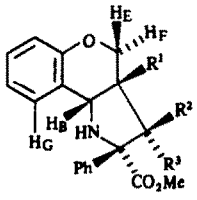

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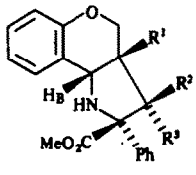
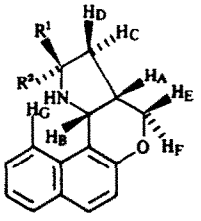


7

a. $R^1 = H_A$, $R^2 = H_C$, $R^3 = H_D$
b. $R^1 = Cl$, $R^2 = H_C$, $R^3 = H_D$
c. $R^1 = H_A$, $R^2 = H_C$, $R^3 = CO_2Me$



8

a. $R^1 = Ph$, $R^2 = CO_2Me$
b. $R^1 = CO_2Me$, $R^2 = Ph$

The assignment of *cis*-stereochemistry to the ring junction of cycloadducts (**6–8**) was initially made by analogy with the stereochemistry observed for conventional 1,3-dipolar cycloadditions in similar systems[8] and, more tenuously, on the basis of the observed coupling constants of the ring junction protons ($J_{AB} = 6$–7 Hz). The chemical shift of the protons H_C and H_D is a distinguishing feature of the PMR spectra ($CDCl_3$) of **6a**, **7a**, **8a** and **8b**. In **6a** and **8a** these proton signals occur together as part of a multiplet centered at δ 2.62 and 2.70, respectively, whilst in **7a** (δ 1.69 and 3.22) and **8b** (δ 1.79 and 3.37) the signals for H_C and H_D are well separated. The stereochemistry of **8a** was subsequently established by an X-ray crystal structure analysis and, more recently, NOE difference spectra have supported the original assignments. The cycloadducts **8a** and **8b** are configurationally stable under the reaction conditions showing that the epimers are formed concurrently and that one is not the precursor of the other.

Crystal data for **8a**: $C_{23}H_{21}NO_3$. M = 359.4. Monoclinic, space group $P2_1/n$. $a = 15.12(1)$, $b = 10.88(1)$, $c = 11.24(1)$ Å, $\beta = 104.9(1)°$, $U = 1786.5$ Å^3. $Z = 4$. $D_x = 1.34$ g cm^{-3}. 3026 independent diffraction intensities were recorded on an Enraf-Nonius CAD3 automatic diffractometer, using CuKα radiation. After correcting for Lorentz and polarization effects the 2257 data with $I > 3\sigma(I)$ were used in the subsequent analysis and refinement. The structure was solved by the direct phasing procedures of MULTAN and refined by least squares, allowing anisotropic vibrations for C, N and O atoms, using SHELX76 and with inclusion of all hydrogen atoms with isotropic temperature factors. A projection of the molecule is shown in Fig. 1.†

The NOE difference spectra ($CDCl_3$) of **8a** correlated well with the known stereochemistry established by the X-ray crystal structure. Thus irradiation of H_B resulted in enhancement of the signals for H_G (19%), H_A (11%) and the ortho protons of the C(2)-phenyl substituent (5%). Irradiation of H_E resulted in enhancement of the signals for H_F (36%), H_A (10%) and H_D (3%) whilst irradiation of H_F caused enhancement of the signals of H_E (31%), H_A (5%) and H_C (2%). The NOE difference spectra of **8b** are also in accord with the assigned stereochemistry. Thus irradiation of H_B causes enhancement of the signals of H_G (17%) and H_A (10%) whilst irradiation of H_A results in enhancement of the signals of H_B (10%), H_D (11%) and H_E (7%).

(2) *Effect of increased chain length on intramolecular cycloaddition.* When the chain length between the incipient dipole and dipolarophile was increased in **3c** the rate of cycloaddition slowed considerably and was accompanied by substantial decomposition. Thus after 3 d in boiling xylene only **9a** (20%) could be isolated although the NMR spectrum of the crude mixture suggested it comprised of a 1:1 mixture of **9a** and **b** together with uncharacterized resinous material.

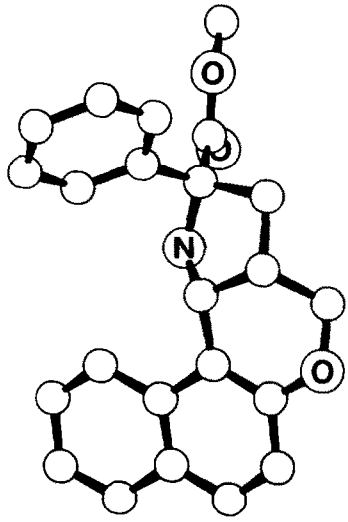
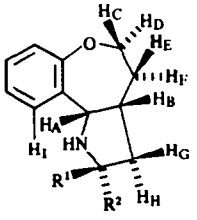


Fig. 1. A crystallographic projection of molecule **8a**.

† Atomic coordinates, temperature factors, derived results and supporting data have been deposited with the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, U.K.

Assignment of stereochemistry to **9a** is based in part on the observation of two PMR signals ($CDCl_3$) for carbomethoxy groups at δ 3.69 and 3.73 in the crude mixture. The isolated isomer **9a** showed the signal at δ 3.69 in its PMR spectrum and work with the previous isomer mixtures (**6**, **7** and **8a,b**) showed the lower δ value in these isomeric pairs arose from **6a** and **8a** due to shielding of the carbomethoxy group by the *cis*-arylether ring. The NOE difference spectra (C_6D_6) were in accord with the assigned stereochemistry for **9a**. Thus irradiation of H_A produced enhancements in the signals for H_B (5%), H_E (3%), H_I (9%) and the ortho protons of the C(2)-phenyl substituent (8%), whilst irradiation of the ortho protons of the C(2)-phenyl substituent produced enhancements in the signals for H_A (2%), H_B (2%) and H_G (2%).



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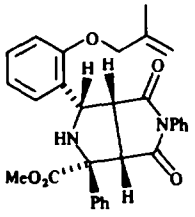


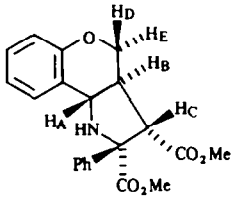
10

a. R^1 = Ph, R^2 = CO_2Me
b. R^1 = CO_2Me_2, R^2 = Ph

Attempted intramolecular cycloadditions of **3g** and **3h** in boiling xylene were unsuccessful and resulted in decomposition of the imines. The lack of reactivity in these cases is attributed to a combination of an unfavourable dipole HOMO–dipolarophile LUMO energy gap[9,10] and steric interactions in the cycloaddition transition state. Oppolzer and Keller reported the successful intramolecular cycloaddition of the N-methyl nitrone corresponding to **3g** and assigned *cis*-stereochemistry to the resulting cycloadduct.[11] Clear evidence that the lack of intramolecular cycloaddition, in the case of **3g** and **h**, was not due to inhibition of dipole formation was readily obtained by heating **3g** with N-phenylmaleimide in boiling xylene (18 hr) under argon when adduct **10** (90%) was obtained. The stereochemistry of **10** is assigned on the basis of our previous work.

(3) *Intramolecular cycloaddition to activated terminal alkenes.* The vinyl chloride moiety proved sufficiently reactive for the cycloaddition process to proceed and **3f** in boiling xylene over 2 d gave a 1 : 1 mixture of two stereoisomers from which **6b**, m.p. 145–147°, was isolated by fractional crystallization. The PMR spectrum (250 MHz, $CDCl_3$) of **6b** showed, *inter alia*, a signal for H_B at δ 4.27 which exhibited long range W coupling to H_E (J_{BE} = 1.1 Hz). Both methylene groups showed geminal coupling constants of the expected order of magnitude [δ 3.0 (H_C), 3.29 (H_D), J = 14.7 Hz; δ 4.17 (H_E), 3.97 (H_F), J = 11.8 Hz]. The ring junction stereochemistry was assigned as *cis* on the basis that all the intramolecular cycloadditions we have studied result solely, or in greater than 85%, in a *cis*-ring junction and related intramolecular cycloadditions of a vinyl bromide result in the creation of a *cis*-ring junction.[11]

The more activated dipolarophile in **3e** resulted in a cleaner intramolecular cycloaddition. Thus **3e** (boiling xylene, 2 d) gave a 5 : 1 mixture (38%) of the major isomer (**11** or **12**), and the minor isomer (**6c**), which was separated by preparative HPLC. Assignment of stereochemistry to the major isomer posed some problems. Previous studies of the prototropic generation of 1,3-dipoles from aryl imines of phenyl glycine methyl ester (**13a**) showed that **14a** was the kinetically generated dipole and that an endo-transition state for the cycloaddition is energetically preferred.[5]



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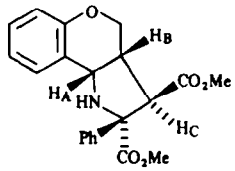

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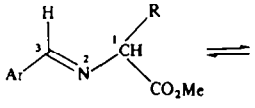

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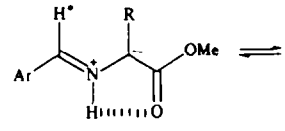

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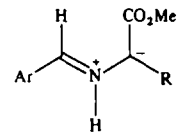


15

a. R = Ph
b. R = Me, alkyl

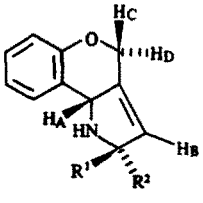
However, in the case of **3e**, this sequence of events would lead to **11** which has the thermodynamically less favoured *trans*-ring junction. Alternatively, if secondary orbital interaction were less important, or the reaction conditions were severe enough to permit equilibration, then stereoisomer **12** could be produced. It is, of course, well known that kinetically controlled intramolecular cycloadditions, such as the Diels–Alder reaction, can be used to produce the thermodynamically unfavourable *trans*-6/5 ring fusion geometry.[12] Moreover, we have previously demonstrated the lack of

reversibility of our intramolecular 1,3-dipolar cycloadditions in boiling xylene (above). Further PMR evidence in favour of **11** was provided by the unusually low chemical shift of H_A ($CDCl_3$, $\delta \sim 3.5$, obscured by CO_2Me signal) compared to the normal value of δ 4.5 in the *cis*-fused adducts (**6–8a,b** and **9a**). Inspection of Dreiding models of **11** and **12** shows the 2-phenyl substituent to be significantly closer to H_A in **11** compared to **12**. Thus shielding of H_A by the π-cloud of the 2-phenyl substituent in **11** would account for the unusually low δ value observed for this proton. NOE difference spectroscopy studies on **11** were not very informative due to overlap of signals. However, irradiation of H_C produced a 22% enhancement in the signals for the ortho-protons of the C(2)-phenyl substituent confirming their *cis*-relationship. The stereochemistry of minor isomer **6c** arises via an endo-transition state. NOE difference spectra ($CDCl_3$) of **6c** support the assigned stereochemistry.† Thus irradiation of H_B effects enhancements in the signals of H_A (12%), H_C (5%), H_G (4%), and the ortho-protons of the C(2)-phenyl substituent (1%), whilst irradiation of H_C effects enhancement of H_A (3%), $H_{E,F}$ (3%) and the orthoprotons of the C(2)-phenyl substituent (3%).

(4) *Factors affecting dipole stereomutation.* The formation of mixtures of intramolecular cycloadducts epimeric at C(2), such as **6** and **7**, **8a,b**, etc., reflects the stereomutation of the kinetically formed dipole **14a** into **15a**. This stereomutation is observed when the reactivity of the dipolarophile is low. This results in a change of the rate determining step from dipole formation to the cycloaddition step.[15,24] This phenomena is easily demonstrated. Thus addition of intermolecular cycloaddition of **3a** to N-phenylmaleimide (dipole formation rate determining). We have previously demonstrated that both Lewis and Bronsted acids catalyse the formation of 1,3-dipoles from imines of α-amino acid esters.[25]

The presence of the phenyl substituent in **14a** is thought to facilitate the stereomutation in two ways: (a) by partial delocalization of the charge into the phenyl ring with concomitant reduction of the C(1)—N(2) bond order in **14a** and resultant lowering of the barrier to rotation about the C(1)—N(2) bond, and (b) by steric interaction of the R group in **14** with the imine hydrogen atom H*, this latter effect being substantially greater in **14a** than in **14b**. Stereomutation of **14b** has not, thus far, been observed but studies with **13** (R = i-Pr and t-Bu) are in hand. The product ratio **6a** : **7a** and **8a** : **8b** suggests the energies of the **14a** and **15a** are very similar, i.e. that the positive effects of H-bonding in **14a** are negated by the steric repulsion between the imine H atom (H*) and the R(=Ph) substituent.

(5) *Intramolecular cycloadditions to terminal alkynes.* The imines of alkynyl ethers (**3b** and **4b**) reacted, under similar conditions to **3a** and **4a**, in boiling xylene under argon to give a 4 : 1 mixture (75%) of **16a** and **b** and a 3 : 1 mixture (90%) of **17a** and **b**, respectively. In both cases a small amount (*ca* 3%) of aromatized rearranged product, **18** and **19**, respectively, was obtained. In addition to these products **3b** also afforded **20** (7.5%). The increased proportion of products (**16a** and **17a**), arising from the kinetically formed dipole **14** suggests the lower LUMO energies of alkynes compared to alkenes promotes trapping of the dipole and hence reduces dipole stereomutation.



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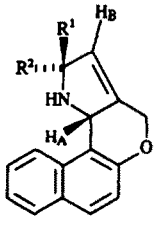

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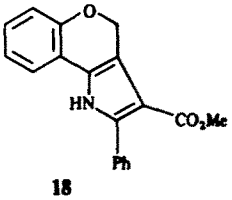
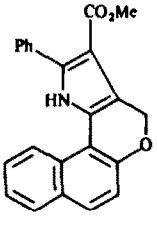


18

a. R^1 = Ph, R^2 = CO_2Me
b. R^1 = CO_2Me, R^2 = Ph



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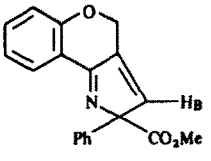

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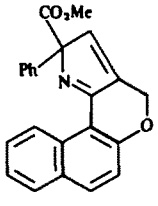

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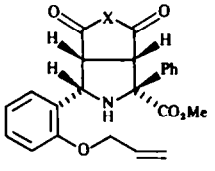
acetic acid has no accelerating effect on the rate of intramolecular cycloaddition (cycloaddition rate determining) of **3a** but substantially accelerates the

The stereochemical assignments are based on the chemical shifts of the H_A proton in the PMR spectra using the criterion that a *cis*-C(2)-phenyl substituent shields the H_A proton, e.g. [**16a**, $\delta(H_A)$ 4.90] and [**16b**, $\delta(H_A)$ 5.27], and [**17a**, $\delta(H_A)$ 5.24] and [**17b**, $\delta(H_A)$ 5.69]. Subsequent to our original work Japanese workers reported identical cycloadditions but failed to detect the minor isomer **16b**.[13]

† It is believed that this isomer arises from a small amount of methyl *cis*-4-bromocrotonate present in the methyl *trans*-4-bromocrontonate used to prepare **3e**.

The nature of the reaction products implicates **20** as a precursor of **18** and suggests the analogous naphthylpyrrolenine **21** is a precursor of **19**. Indeed, when **20** was heated in xylene at 140° it rearranged quantitatively to **18** via a thermally allowed 1,5-sigmatropic shift of the ester group. The structures of **18** and **19** were initially assigned on the basis of the established order of migratory aptitudes in sigmatropic processes CHO > H > CO_2R > Ph ≫ alkyl[14] and our own work on sigmatropic rearrangement of pyrrolenines which shows that ester groups migrate approximately 6–7 times as fast as phenyl groups.[15] Japanese workers subsequently reported the preparation of the alternative (phenyl migration) isomer by direct intramolecular cycloaddition[13] confirming our assignment for **18**. Increased yields of **18** were obtained when the imine **3b** was heated in boiling xylene in contact with air and under similar conditions **4b** gave **21** (10%). As expected, **21** was smoothly converted to **19** by heating in xylene at 140° for 15 min.

One example of a substituted salicylaldehyde imine **3d** has been studied. The *p*-ethoxy derivative was chosen because, in simple aryl imines, this substituent promotes 1,3-dipole formation by enhancing the basicity of the imine N atom.[5] However, all attempts to effect intramolecular cyclization of **3d** failed and on prolonged heating in boiling xylene decomposition occurred. Once again it was possible to demonstrate that the 1,3-dipole was being generated and intermolecular cycloadducts (**22a** and **b**) were obtained with N-phenylmaleimide and maleic anhydride, respectively. A competitive study of the intermolecular cycloaddition of **3a** and **d** with N-phenylmaleimide showed that **3d** → **22a** occurred approximately seven times slower than **3a** → **22c**. The precise reason for the rate retardation in the case of **3d** remains to be ascertained.



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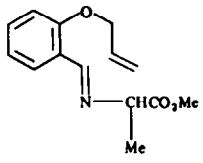
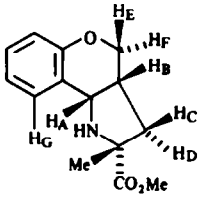
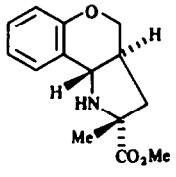


23

a. R = EtO, X = NPh
b. R = EtO, X = O
c. R = H, X = NPh



24



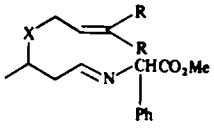
25

Intramolecular cycloadditions of aryl imines of alanine methyl ester

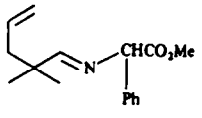
All the imines discussed so far are imines of phenyl glycine methyl ester. The alanine imine (**23**) has also been studied and found to undergo quantitative intramolecular cycloaddition in boiling xylene over 24 hr to give a 19:2 mixture of stereoisomers. The stereochemistry of the major isomer (**24**) is assigned on the basis of NOE difference spectroscopy (C_6D_6). Thus irradiation of H_A resulted in enhancement of the signals of H_B (8%), H_C (3%), H_G (8%) and the C—Me group (9%), whilst irradiation of H_B effects enhancements in the signals for H_A (18%) and H_E (10%). Irradiation of H_E caused enhancements of the signals of H_B (8%) and H_F (17%). The minor isomer (**25**) was not isolated and assignment of stereochemistry is tentative and rests on the general lack of isomerization of kinetically formed dipoles of type **14b**, and the observation of minor amounts of adducts arising via exo-transition states in intermolecular cycloadditions of such dipoles.[24] Trace amounts of a possible third isomer (< 5%) were detected but thus far it has not proved possible to isolate this product.

C. *Aliphatic imines of phenylglycine methyl ester*

A second series of imines incorporating the dipolarophile into an aliphatic aldehyde precursor **26a,b** and **27** was briefly studied.



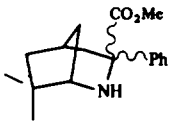
26



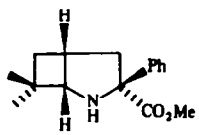
27

a. X = CH_2, R = Me
b. X = O, R = H

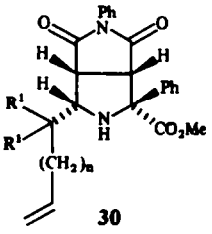
Imines **26a** and **b** were not particularly stable at room temperature, neither afforded an intramolecular cycloadduct on heating in boiling xylene, decomposition occurring instead. The instability of **26a** and **b** is due to the presence of labile protons adjacent to the imine double bond as shown by the stability of **27** which was stable to prolonged heating in boiling xylene. However intramolecular cycloaddition of **27** to give either **28** or **29** failed to occur, presumably due to unfavourable orbital overlap in the case of **28** and the strained transition state necessary for the formation of **29**. Dipole formation from **27** was readily demonstrated by trapping with N-phenylmaleimide (boiling xylene, 19 hr) to give **30a** (95%).



28

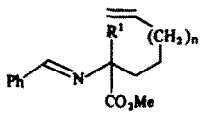


29

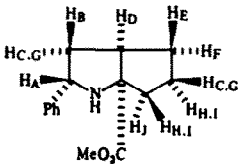


30

a. R^1 = Me, n = 1
b. R^1 = H, n = 2
c. R^1 = H, n = 3

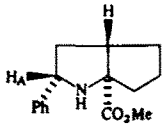


31



32

a. n = 1, R^1 = H
b. n = 2, R^1 = H
c. n = 2, R^1 = —$(CH_2)_2CH{=}CH_2$



33

D. *Intramolecular cycloaddition of aryl imines of alkenyl amino acid esters*

Incorporation of the dipolarophile into the amino-acid moiety proved more successful. The pentenyl glycine imine **31a** was prepared from the imine of glycine methyl ester by alkylation with 5-bromopent-1-ene in THF at −63° using LDA as base. Heating **31a** in boiling xylene afforded an 87:13 mixture (81%) of a cycloadduct formulated as **32** (major) and **33** (minor). The assignment of stereochemistry to **32** is based on the assumption that cycloaddition involves the kinetically preferred dipole and on NOE difference spectra ($CDCl_3$). In the NMR spectrum of **32** the signals for H_C and H_G and for H_H and H_I were superimposed. Nevertheless the NOE difference spectra provide clear support for **32**. Thus irradiation of H_A caused enhancement of the signals for H_E (4%), $H_{H,I}$ (2%) and NH (2%), whilst irradiation of H_D effected an enhancement of the signals for $H_{C,G}$ (7%), H_F (4%), $H_{H,I}$ (3%), H_J (2%) and NH (−13%). Irradiation of H_E resulted in the enhancement of the signals for H_A (4%), H_B (2%) and H_F (17%) and irradiation of H_J produced enhancements of the signals for H_D (3%) and $H_{H,I}$ (20%). The minor isomer **33** is characterized by signals in the NMR spectrum ($CDCl_3$, isomer mixture) at δ 4.01 (dd, H_A) and 3.67 (s, OMe).

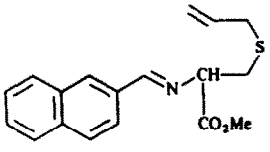
The hexenyl glycine imine **31b** was prepared in an analogous manner to **31a**, although in this case a 4:1 mixture of mono-**31b**- and di-**31c**-alkylated products was obtained which was separated by fractional distillation. Surprisingly, **31b** failed to undergo intramolecular cycloaddition on heating in xylene at 145° (NMR experiment) over 24 hr and further heating caused decomposition. Both **31a** and **b** gave good yields of the expected intermolecular cycloadducts **30b** and **c** with N-phenylmaleimide.

The intramolecular cycloaddition of the cysteine thioether **34** has also been investigated. Imine **34** undergoes cycloaddition in boiling xylene over 24 hr to give a 92:8 mixture of **35** and **36** in quantitative yield. The major isomer **35** was readily separated and its stereochemistry assigned on the basis of its NMR spectrum and NOE difference spectroscopy (below). Assignment of stereochemistry to the minor isomer is tentative and rests on the general lack of isomerization of kinetically formed dipoles of type **14b** even when trapped with less reactive dipolarophiles and the observation of minor amounts of adducts arising via exo-transition states in intermolecular cycloadditions of such dipoles.[24] The NOE difference spectra (xylene-d_{10}) of **35** were readily interpretable apart from the coincidence of the H_B methylene protons. Thus irradiation of H_A caused enhancement of the signals for H_B (5%), H_D (3%), H_F (2%) and the naphthyl proton multiplet (9%), whilst irradiation of H_C resulted in clear enhancement of the signal for H_B (7%) only. The chemical shift of H_E, H_G and H_C are very close and it did not prove possible to measure accurate enhancements for H_E and H_G in this case. Irradiation of the signal for H_E effected an enhancement of the signals of H_C (6%) and H_D (24%) whilst irradiation of H_D caused enhancement of the signals of H_A (5%), H_E (26%) and H_B (3%). The minor isomer **36** is characterized by signals in the NMR spectrum ($CDCl_3$) of the mixture at δ 4.28 (dd, H_A) and 3.81 (s, OMe).

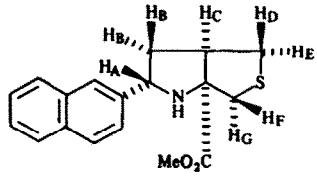
EXPERIMENTAL

General details were as noted previously.[5] All NMR spectra are determined for solns in $CDCl_3$ unless otherwise noted. All the alkenyl and alkynyl ethers of salicylaldehyde and related naphthols, apart from two, were prepared by lit procedures.[16–23] Details of the two new ethers are given below.

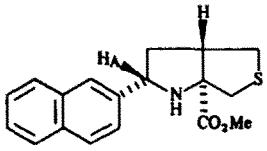
General procedure for the synthesis of alkenyl and alkynyl ethers of salicylaldehydes. A soln of the appropriate 2-



34



35



36

Table 1. Imines prepared by the general procedure

Compd.	Yield† (%)	b.p./mmHg or m.p. (°)	m/z (%)	Formula	Found (requires) C	H	N
3a	100	57–62°/0.05‡	309 (M^+, 4), 279 (7), 251 (19), 250 (100), 209 (37), 208 (14), 181 (11), 180 (21), 160 (48), 145 (18), 144 (19), 132 (16),	$C_{19}H_{19}NO_3$	73.9 (73.75	6.2 6.2	4.85 4.55)
3b	91	260–305°/0.1	307 (M^+, 1), 249 (19), 248 (100), 209 (18), 158 (11), 106 (21), 77 (11)	$C_{19}H_{17}NO_3$	M^+ 307.1211 (307.120835)		
3c	100	75–80°/0.05‡	323 (M^+, 4), 278 (10), 265 (20), 264 (100), 210 (19), 174 (11), 159 (14), 131 (16), 106 (28), 91 (19), 77 (12)	$C_{20}H_{21}NO_3$	74.0 (74.3	6.65 6.55	4.25 4.35)
3d	65	71–72°	353 (M^+, 23), 295 (15), 294 (100), 238 (11), 209 (5), 137 (5), 91 (3), 77 (3)	$C_{21}H_{23}NO_4$	71.35 (71.35	6.45 6.55	4.0 3.95)
3e	85	not distilled	367 (M^+, 1), 309 (16), 308 (71), 202 (13), 171 (15), 107 (18), 106 (100), 104 (15), 79 (43), 77 (28)	$C_{21}H_{21}NO_5$	M^+ 367.14187 (367.14196)		
3f	100	not distilled	343 (M^+, 1), 286 (34), 285 (19), 284 (100), 209 (34), 194 (20), 180 (13), 106 (22), 90 (15), 77 (14)	$C_{19}H_{18}NO_3Cl$	M^+ 343.09752 (343.09752)		
3g	88	72–76°/0.1‡	323 (M^+, 8), 265 (21), 264 (100), 209 (25), 208 (14), 174 (68), 159 (28), 158 (17), 106 (37), 91 (19)	$C_{20}H_{21}NO_3$	74.3 (74.3	6.6 6.55	4.4 4.35)
3h	100	65–72°/0.001‡	323 (M^+, 2), 278 (22), 269 (13), 264 (41), 211 (16), 210 (100), 174 (70), 122 (35), 121 (30), 106 (40), 55 (49)	$C_{20}H_{21}NO_3$	74.1 (74.3	6.65 6.55	4.45 4.35)
4a	100	69–71°	359 (M^+, 53), 301 (23), 300 (94), 260 (16), 259, (59), 258 (59), 231 (16), 230 (35), 210 (100), 195 (53), 182 (29), 128 (53)	$C_{23}H_{21}NO_3$	77.1 (76.85	5.95 5.9	4.15 3.9)
4b	100	91–93°	357 (M^+, 30), 318 (5), 299 (30), 298 (100), 259 (26), 258 (25), 230 (13), 208 (41), 193 (25), 128 (20), 127 (16), 121 (22), 106 (41), 77 (22)	$C_{23}H_{19}NO_3$	77.1 (77.3	5.4 5.35	3.8 3.9)
26a	98	134–138°/0.1	301 (M^+, 8), 258 (11), 243 (20), 242 (100), 219 (20), 218 (34), 191 (24), 160 (14), 149 (11), 132, (74), 121 (18), 106 (90), 91 (20)	$C_{19}H_{27}NO_2$	75.4 (75.7	9.0 9.05	4.6 4.65)
26b	95	unstable oil	276 (M + 1, 4), 234 (36), 216 (29), 160 (20), 159 (17), 158 (93), 149 (27), 132 (62), 121 (66), 106 (47), 104 (64), 91 (55), 41 (100)				
27	80	106–107°/0.1	259 (M^+, 56), 258 (28), 244 (59), 201 (16), 200 (100), 186 (15), 158 (41), 149 (27), 131 (48), 121 (28), 106 (38), 91 (33)	$C_{16}H_{21}NO_2$	74.15 (74.1	8.3 8.15	5.55 5.4)

† Yield of crude product.
‡ Kugelrohr distillation.

Table 2. PMR ($CDCl_3$) and IR (film) data of imines (**3a–h**), (**4a,b**) and (**26, 27**)

Compd.	ν_{max} (cm^{-1}) C=N	C=O	δ	CO_2CH_3	H_A†	H_B†
3a	1635,	1745	7.5 (m, 9H, ArH), 6.0 (m, 1H, C<u>H</u>=CH_2), 5.4 (m, 2H, CH=C<u>H_2</u>), 4.6 (m, 2H, OCH_2)	3.70	5.25	8.83
3b	1640,	1740	7.58 (m, 9H, ArH), 4.73 (d, 2H, OCH_2, J = 2 Hz), 2.53 (t, 1H)	3.75	5.27	8.9
3c	1630,	1730	7.5 (m, 9H, ArH), 5.80 (m, 1H, C<u>H</u>=CH_2), 5.05 (m, 2H, CH=C<u>H_2</u>), 3.95 (t, 2H, OCH_2, J = 6 Hz), 2.48 (q, 2H, CH_2)	3.65	5.20	8.75
3d	1635,	1745	7.21 (m, 8H, ArH), 6.07 (m, 1H, C<u>H</u>=CH_2), 5.35 (m, 2H, CH=C<u>H_2</u>), 4.64 (dt, 2H, OCH_2, J = 5 Hz, J = 1.5 Hz), 4.17 (q, 2H, <u>CH_2</u>Me), 1.47 (t, 3H, CH_2<u>Me</u>)	3.74	5.18	8.22
3e	1630,	1735	7.56 (m, 10H, ArH; C<u>H</u>=C<u>H</u>-CO_2Me, J = 16 Hz, J = 2 Hz), 4.77 (dd, 2H, OCH_2, J = 4 Hz, J = 2 Hz), 3.67 (m, 3H, OMe)	3.67	5.3	8.9
3f	1630,	1740	7.35 (m, 9H, ArH), 5.40 (m, 2H, C=CH_2), 4.55 (s, 2H, OCH_2)	3.65	5.2	8.85
3g	1635,	1750	7.48 (m, 9H, ArH), 5.03 (m, 2H, C=CH_2), 4.43 (s, 2H, OCH_2), 1.80 (s, 3H, Me)	3.70	5.27	8.88
3h	1625,	1730	7.5 (m, 9H, ArH), 5.80 (m, 2H, CH=CH), 4.5 (m, 2H, OCH_2), 1.80 (d, 3H, <u>Me</u>CH)	3.70	5.2	8.80
4a	1650,‡	1745‡	9.56 and 7.3 (d, m, 11H, ArH), 5.90 (m, 1H, C<u>H</u>=CH_2), 5.23 (m, 2H, CH=C<u>H_2</u>), 4.46 (dt, 2H, OCH_2)	3.67	5.23	9.11
4b	1645,‡	1745‡	9.52 and 7.45 (2 × m, 11H, ArH), 4.67 (d, 2H, OCH_2, J = 2.4 Hz), 2.44 (t, 1H, C≡CH)	3.69	5.23	9.08
26a	1660,	1750	7.39 (m, 5H, ArH), 5.07 (m, 1H, Me_2C=C<u>H</u>), 2.5–1.08 (m, 7H, CH_2 and MeC<u>H</u>), 1.67 and 1.60 (s, 6H, Me_2C), 0.95 (dd, 3H, <u>Me</u>CH)	3.72	4.97	7.77 (t)
26b	1650,	1740	7.3 (m, 5H, ArH), 5.9 (m, 1H, C<u>H</u>=CH_2), 5.25 (m, 2H, CH=C<u>H_2</u>), 4.0 (m, 3H, OCH_2 and CH), 2.55 (t, 2H, C<u>H_2</u>CH=N), 1.2 (d, 3H, Me)	3.8	4.95	7.8 (t)
27	1660,	1745	7.32 (m, 5H, ArH), 6.68 (m, 1H, C<u>H</u>=CH_2), 5.0 (m, 2H, CH=C<u>H_2</u>), 2.18 (d, 2H, CH_2), 1.05 (s, 6H, Me_2)	3.65	4.92	7.55

† Singlets unless otherwise noted.
‡ KBr disc.

hydroxy-1-arylaldehyde (1 mol) in dry EtOH was refluxed with stirring (6–48 hr) with the appropriate allyl halide (1.1 mol) and anhyd K_2CO_3 (1 mol). Work up involved either pouring the mixture into cold water followed by ether extraction or filtration followed by evaporation of the solvent. The resulting crude product was then distilled to afford the desired aldehyde.

2 - [(2 - *Chloro* - 2 - *propenyl*)*oxy*] - *benzaldehyde*. Obtained (49%) as a colourless oil, b.p. 110–115°/0.2 mmHg. (Found: C, 61.4; H, 4.55. $C_{10}H_9ClO_2$ requires C, 61.1; H, 4.6%); *m/z* (%) 196 (M^+, 17), 161 (26), 133 (10), 122 (23), 121 (69), 120 (100), 105 (15) and 75 (20); ν_{max} (film) 2750, 1680, 1595, 1480 and 1450 cm^{-1}; δ 10.45 (s, 1H, CHO), 7.33 (m, 4H, ArH), 5.5 (d, 2H, C=C<u>H_2</u>, J_{gem} = 8 Hz) and 4.62 (s, 2H, OCH_2).

4 - *Ethoxy* - 2 - (2 - *propenyloxy*) - *benzaldehyde*. Obtained (82%) as a pale yellow liquid, b.p. 123–127°/0.01 mmHg. (Found: C, 70.1; H, 7.0. $C_{12}H_{14}O_3$ requires C, 69.9; H, 6.85%); *m/z* (%) 206 (M^+, 80), 165 (17), 149 (9), 138 (11), 137 (100), 109 (31), 81 (17) and 79 (7); ν_{max} (film) 1695, 1600, 1515, 1440, 1270 and 1135 cm^{-1}; δ 9.83 (s, 1H, CHO), 7.2 (m, 3H, ArH), 6.09 (m, 1H, C<u>H</u>=CH_2), 5.38 (m, 2H, CH=C<u>H_2</u>), 4.69 (m, 2H, OCH_2), 4.18 (q, 2H, C<u>H_2</u>Me) and 1.48 (t, 3H, CH_2<u>Me</u>).

General procedure for the preparation of imines. Phenylglycine methyl ester hydrochloride (26.25 mmol) was treated with a soln of NaOMe (from 26.25 mmol of Na metal) in 30 ml of dry MeOH, followed by addition of a soln of the appropriate aldehyde (25 mmol). The resulting mixture was stirred at 25° for 24 hr, the solvent evaporated *in vacuo*, the residue dissolved in CH_2Cl_2 and washed with water and dried (Na_2SO_4). The dried solvent was then concentrated to afford the crude imine, small amounts of which were purified for analysis by crystallization or distillation as appropriate. The

crude imines were used directly in most cases for the intramolecular cycloadditions, as distillation often resulted in cyclization and/or decomposition. Imine **26b** was especially unstable and no attempts were made to purify this compound. For compounds **3b** and **e**, $NaHCO_3$ aq was employed instead of methanolic NaOMe. The physical data of **3a–h** and **4a,b** are summarized in Tables 1 and 2.

Methyl N - [2 - (2 - *propenyloxy*)*benzylidene*]*alanine* (**23**). A mixture of alanine methyl ester hydrochloride (5 g, 36 mmol), anhyd $MgSO_4$ (5 g) and Et_3N (3.6 g, 40 mmol) in dry CH_2Cl_2 (100 ml) was stirred for 10 min and then a soln of 2-(2-propenyloxy)benzaldehyde (5.51 g, 34 mmol) in dry CH_2Cl_2 (20 ml) added. The resulting mixture was stirred at ambient temp for 16 hr, filtered, and the filtrate washed with water (100 ml), dried ($MgSO_4$) and evaporated to leave a yellow oil. The oil was distilled to afford **23** (6.21 g, 73%) as a pale yellow oil, b.p. 115–120°/0.05 mmHg. (Found: C, 68.0; H, 7.2; N, 5.6. $C_{14}H_{17}NO_3$ requires: C, 68.0; H, 6.95; N, 5.55%); ν_{max} 1730, 1628, 991 and 925 cm^{-1}; *m/z* (%) 247 (M^+, 6), 188 (100), 160 (43), 146 (27), 145 (38), 132 (84) and 82 (27); δ 8.79 (s, 1H, CH=N), 8.05–6.87 (m, 4H, ArH), 6.06 (m, 1H, C<u>H</u>=CH_2), 5.37 (m, 2H, CH=C<u>H</u>$_2$), 4.57 (m, 2H, OCH_2), 4.17 (q, 1H, C<u>H</u>Me, J = 6.8 Hz), 3.73 (s, 3H, OMe) and 1.52 (d, 3H, Me).

S-(2-Propenyl)-L-cysteine methyl ester hydrochloride. Thionyl chloride (7.14 g, 4.35 ml) was added over 5 min to dry MeOH (25 ml) cooled to −10° and the soln stirred for a further 5 min when *S*-(2-propenyl)-L-cysteine (3.22 g)[26] was added. The amino acid dissolved over *ca* 5 min and the resulting soln was stirred for 2 hr at −10° and then kept at room temp for a further 16 hr. The soln was then poured into ether 600 ml and refrigerated for 2 hr. The product (3.25 g, 77%) separated as colourless needles, m.p. 117° and was removed by filtration. (Found: C, 39.25; H, 6.6; N, 6.55. $C_7H_{14}NO_2SCl$ requires: C, 39.7; H, 6.6; N, 6.65%); ν_{max} 3300–2500 (br), 1733, 1632 and 990 cm^{-1}; *m/z* (%) 175 (M − HCl, 4), 116 (17), 103 (21), 88 (100) and 74 (43); δ (D_2O) 5.75 (m, 1H, C<u>H</u>=CH_2), 5.14 (m, 2H, CH=C<u>H</u>$_2$), 4.29 (dd, 1H, C<u>H</u>CO_2Me), 3.79 (s, 3H, OMe) and 3.02 (m, 4H, 2 × CH_2).

Methyl N-*naphthylidene S-allylcysteine* (**34**). *S*-Allylcysteine methyl ester hydrochloride (1 g) was converted to the imine in an analogous manner to the foregoing experiment. The crude imine (1.35 g, 91%) was crystallized from 40–60° petroleum ether–ether to yield **34** (0.82 g, 55%) as colourless needles, m.p. 63°. (Found: C, 68.9; H, 6.3; N, 4.7. $C_{18}H_{19}NO_2S$ requires: C, 69.0; H, 6.1; N, 4.45%); ν_{max} 1725, 1627, 993 and 912 cm^{-1}; *m/z* (%) 313 (M^+, 38), 254 (7), 241 (45), 313 (38), 241 (45), 182 (100), 167 (56), 166 (49), 155 (37) and 154 (30); δ 8.47 (s, 1H, CH=N), 8.10–7.46 (m, 7H, ArH), 5.77 (m, 1H, C<u>H</u>=CH_2), 5.13 (m, 2H, CH=C<u>H</u>$_2$), 4.19 (dd, 1H, C<u>H</u>CO_2Me), 3.78 (s, 3H, CO_2Me) and 3.06 (m, 4H, 2 × CH_2S).

Methyl benzylidene pent-4-enylglycine (**31a**). A stirred mixture of diisopropylamine (6.3 g, 62 mmol) and dry THF (40 ml) was cooled to −63° and n-BuLi (40 ml of a 1.6 M soln in hexane) added followed by hexamethylphosphoramide (115 ml). Methyl benzylidene glycine (11 g, 62 mmol) in dry THF was then added followed by dropwise addition of 5-bromopent-1-ene (9.25 g, 62 mmol) in dry THF (20 ml) to the stirred mixture. After the addition was complete the mixture was stirred for a further 10 min at −63° and then allowed to warm to room temp over 4 hr. Work up with ice-cold NH_4Cl aq–ether, followed by distillation of the dried organic layer afforded the product (8.8 g, 58%) as a colourless oil, b.p. 116–120°/0.05 mmHg. (Found: C, 73.45; H, 7.8; N, 5.7. $C_{15}H_{19}NO_2$ requires: C, 73.45; H, 7.9; N, 5.55%); *m/z* (%) 245 (M^+, 7), 244 (21), 190 (9), 187 (14), 186 (100), 132 (12), 119 (13), 117 (16), 106 (22), 104 (26), and 91 (23); ν_{max} 1635 and 1730 cm^{-1}; δ 8.27 (s, 1H, CH=N), 7.55 (m, 5H, ArH), 5.77 (m, 1H, C<u>H</u>=CH_2), 5.0 (m, 2H, CH=C<u>H</u>$_2$), 4.0 (dd, 1H, CH), 3.73 (s, 3H, OMe) and 2.31–1.13 [m, 6H, $(CH_2)_3$].

Methyl benzylidene hex-5-enylglycine (**31b**) *and methyl benzylidene bis(hex-5-enyl)glycine* (**31c**). Methyl benzylidene glycine (11 g) was alkylated with 6-bromohex-1-ene (10.11 g) in an analogous manner to the previous experiment. Work up in the usual way gave a red–brown oil (12.86 g) whose PMR spectrum showed it to comprise a 4:1 mixture of **30b** and **c**. Fractional distillation afforded pure samples of **30b** (4.05 g, 25%), b.p. 116–125°/0.001 mmHg, and **30c** (0.5 g, 2.3%), b.p. 130–136°/0.001 mmHg, together with a middle fraction (4.5 g) which was an approximately 1:1 mixture of **30b** and **30c**. **30b** (Found: C, 73.9; H, 8.2; N, 5.1. $C_{16}H_{21}NO_2$ requires: C, 74.1; H, 8.15; N, 5.4%); *m/z* (%) 259 (M^+, 5), 218 (26), 200 (100), 106 (30), 105 (45), 91 (49) and 41 (25); ν_{max} (film) 1730, 1634, 910 and 990 cm^{-1}; δ 8.01 (s, 1H, CH=N), 7.73 and 7.08 (2 × m, 5H, ArH), 5.7 (m, 1H, C<u>H</u>=CH_2), 4.96 (m, 2H, CH=C<u>H</u>$_2$), 3.84 (dd, 1H, CH), 3.36 (s, 3H, OMe), 2.17 and 1.28 [2 × m, 2 × 4H, $(CH_2)_4$]. **30c** (Found: C, 77.25; H, 9.35; N, 4.35. $C_{22}H_{31}NO_2$ requires: C, 77.35; H, 9.15; N, 4.1%); *m/z* (%) 341 (M^+, 3), 283 (25), 282 (100), 200 (27), 91 (34) and 41 (35); ν_{max} (film) 1723, 1633, 910 and 990 cm^{-1}; δ 8.47 (s, 1H, CH=N), 7.8 and 7.15 (2 × m, 5H, ArH), 5.74 (m, 2H, 2 × C<u>H</u>=CH_2), 4.99 (m, 4H, 2 × CH=C<u>H</u>$_2$), 3.41 (s, 3H, OMe), 2.03 and 1.38 [2 × m, 2 × 8H, 2 × $(CH_2)_4$].

Intramolecular cycloadditions

2 - *Methoxycarbonyl* - 2 - *phenyl* - 4H - 2,3,3a,9b - *tetrahydropyrro*[2,3 - d]*benzo*[b]*pyran* (*cycloadducts* **6a** *and* **7a**). A soln of **3a** (7.2 g, 23 mmol) in xylene (40 ml) was boiled under reflux under argon for 1 d. Removal of the solvent *in vacuo* gave a yellow viscous oil (7.2 g) whose NMR indicated the absence of imine and quantitative formation of **6a** and **7a** (ratio *ca* 3:2). The crude oil was dissolved in MeOH and stored at 0° for 3 d. During this time crystallization occurred yielding large colourless prisms. These were filtered and recrystallized from MeOH to give pure **6a** (1.0 g, 14%), m.p. 95–97°. (Found: C, 73.75; H, 6.2; N, 4.55. $C_{19}H_{19}NO_3$ requires: C, 73.65; H, 6.25; N, 4.65%); ν_{max} 3340, 1730, 1600, 1580, 1485 and 1445 cm^{-1}; *m/z* (%) 309 (M^+, 100), 307 (4), 294 (3), 156 (3), 145 (4), 144 (4), 132 (3), 131 (9), 125 (9), 115 (4), 107 (10), 104 (7), 103 (3), 91 (6) and 77 (9); δ ($CDCl_3/D_2O$) 7.72–6.82 (m, 9H, ArH), 4.18 (d, 1H, H_B, J_{AB} = 6.25 Hz), 4.07 (dd, 1H, H_E, J_{EF} = 11 Hz, J_{AE} = 4 Hz), 3.72 (dd, 1H, H_F, J_{AF} = 9 Hz), 3.53 (s, 3H, OMe), 2.62 (m, 2H, H_CH_D) and 2.56 (m, 1H, H_A). **7a** δ ($CDCl_3/D_2O$) 4.11 (d, 1H, H_B, J_{AB} = 6.6 Hz), 3.73 (s, 3H, OMe), 3.22 (dd, 1H, H_D, J_{CD} = 13.6 Hz, J_{AD} = 8.5 Hz), 2.48 (m, 1H, H_A) and 1.69 (dd, 1H, H_C, J_{AC} = 5 Hz).

2 - *Methoxycarbonyl* - 2 - *phenyl* - 4H - 2,3,3a,11c - *tetrahydropyrro*[2,3 - d]*naphtho*[2,1 - b]*pyran* (*cycloadducts* **8a** *and* **8b**). A soln of **4a** was boiled under reflux under argon for 1 d. Removal of the solvent *in vacuo* gave a dark red–orange oil (8.8 g) which essentially contained only **8a** and **b** (ratio *ca* 53:47). The crude oil was dissolved in MeOH and stored at 0° for several days. During this time crystallization occurred yielding an off-white solid (6.3 g) which was a mixture of **8a** and **b**. Fractional crystallization from MeOH afforded **8a** as colourless prisms m.p. 107–108° and **8b** as colourless needles m.p. 142–143°.

Cycloadduct **8a**. (Found: C, 76.8; H, 6.0; N, 4.0. $C_{23}H_{21}NO_3$ requires: C, 76.85; H, 5.9; N, 3.9%); ν_{max} 3300, 1720, 1625, 1600 and 1260 cm^{-1}; *m/z* (%) 359 (M^+, 1), 301 (23), 300 (100), 181 (7), 157 (13) and 150 (10); δ 8.43–7.0 (m, 11H, ArH), 4.58 (d, 1H, H_B, J_{AB} = 5.75 Hz), 4.15 (dd, 1H, H_E, J_{EF} = 11.5 Hz, J_{AE} = 4.4 Hz), 3.79 (dd, 1H, H_F, J_{AF} = 9.5 Hz), 3.50 (s, 3H, OMe), 3.28 (brs, 1H, NH, exchanges with D_2O), 2.70 (m, 2H, H_C, H_D), 2.61 (m, 1H, H_A).

Cycloadduct **8b**. (Found: C, 76.75; H, 6.0; N, 3.8. $C_{23}H_{21}NO_3$ requires: C, 76.85; H, 5.9; N, 3.9%); ν_{max} 3340, 1720, 1625, 1600 and 1230 cm^{-1}. *m/z* (%) 359 (M^+, 1), 301 (23), 300 (100), 181 (7), 157 (14) and 150 (10); δ 8.13–7.04 (m, 11H, ArH), 4.51 (d, 1H, H_B, J_{AB} = 5.75 Hz), 4.13 (m, 1H, H_E), 3.88 (s, 3H, OMe), 3.83 (m, 1H, H_F), 3.37 (dd, 1H, H_D, J_{CD} = 13.9 Hz, J_{AD} = 8.5 Hz), 2.61 (m, 1H, H_A) and 1.79 (dd, 1H, H_C, J_{AC} = 3.2 Hz).

2 - *Methoxycarbonyl* - 2 - *phenyl* - 4H,5H - 2,3,3a,10b - *tetrahydropyrro*[2,3 - d]*benzo*[b]*oxepan* (*cycloadducts* **9a** *and* **9b**). A soln of **3c** (3.5 g, 10.8 mmol) in xylene (40 ml) was refluxed under argon for 3 d. Removal of the solvent *in vacuo* gave a viscous orange oil (3.5 g) whose NMR indicated the presence of the desired **165** and **166** (ratio *ca* 50:50), together with

uncharacterized polymeric material and unreacted starting material (10%). The crude oil was triturated with MeOH and the resulting colourless solid (0.75 g; 20%) crystallized from MeOH affording **9a** as colourless needles m.p. 167–169°. Analysis ($CDCl_3$) of the crude remaining oil indicated the presence of the other stereoisomer **9b** (OMe signal at δ 3.73, cf. δ 3.69 for cycloadduct **9a**), but this isomer was not isolated pure.

Cycloadduct **9a**. (Found: C, 73.9; H, 6.9; N, 4.3. $C_{20}H_{21}NO_3$ requires: C, 74.3; H, 6.55; N, 4.35%); ν_{max} 3370, 1710, 1595, 1485, 1440, 1420, 1235 and 1220 cm^{-1}; *m/z* (%) 324 (M + 1, 1), 265 (22), 264 (100), 235 (9), 156 (5), 145 (8), 131 (12), 128 (14), 115 (20), 104 (39), 91 (27) and 77 (24); δ (C_6D_6) 7.53 (m, 1H, H_I), 7.32 (m, 2H, C(2)Ph, ortho-H), 6.93–6.71 (m, 6H, ArH), 3.98 (d, 1H, H_A, J_{AB} = 9 Hz), 3.79 (m, 1H, H_C), 2.94 (m, 1H, H_D), 2.95 (s, 3H, OMe), 2.83 (m, 1H, H_G), 1.42 (m, 2H, H_B and H_F or H_H) and 1.12 (m, 2H, H_E and H_F or H_H).

2 - *Methoxycarbonyl* - 2 - *phenyl* - 3a - *chloro* - 4H - 2,3,9b - *trihydropyro*[2,3 - d]*benzo*[b]*pyran* (*cycloadducts* **6b** *and* **7b**). A soln of **3f** (6.4 g, 18.6 mmol) in xylene (40 ml) was refluxed under argon for 2 d. Removal of the solvent *in vacuo* gave a viscous orange oil. NMR analysis of the crude oil indicated it comprised an approximately 1:1 mixture of **6b** and **7b**. Trituration of the crude oil with MeOH resulted in almost complete solidification of the oil. The off-white solid was filtered and crystallized from MeOH to afford **6b** (2.3 g, 36%) as long colourless needles, m.p. 145–147°. (Found: C, 66.35; H, 5.3; N, 3.9; Cl, 10.35. $C_{19}H_{18}ClNO_3$ requires: C, 66.4; H, 5.3; N, 4.05; Cl, 10.3%); ν_{max} 3340, 1715, 1580, 1485, 1425, 1305 and 1260 cm^{-1}; *m/z* (%) 344 (M^+, 0.5), 286 (33), 285 (19), 284 (100), 248 (12), 104 (10) and 77 (10); δ 7.73–6.91 (m, 9H, ArH), 4.27 (s, 1H, H_B), 4.17 (d, 1H, H_E, J_{EF} = 11.8 Hz, J_{BE} = 1.1 Hz), 3.97 (d, 1H, H_F, 3.55 (s, 3H, OMe), 3.29 (d, 1H, H_C, J_{CD} = 14.7 Hz), 3.00 (d, 1H, H_D), 1.60 (br s, 1H, NH, exchanges with D_2O).

2,3 - *Di*(*methoxycarbonyl*) - 2 - *phenyl* - 4H - 2,3,3a,9b - *trihydropyrro*[2,3 - d]*benzo*[b]*pyran* (*cycloadducts* **11** *and* **6c**). A soln of methyl N-[2-(3-carbomethoxy-2-propenyl)oxy]-benzylidene phenylglycine (11.35 g, 31 mmol) in xylene (40 ml) was refluxed under argon for 2 d. Removal of the solvent *in vacuo* gave a dark oil together with some solid material. The crude oil was dissolved in MeOH and stored at 0° for several days. This resulted in the precipitation of a pale brown amorphous powder (4.3 g, 38%). A small quantity (500 mg) of this crude material was subjected to preparative HPLC [Lichroprep. Si60 (25–40 μm), $CHCl_3$, 254 nm] and resulted in the separation of **11** (256 mg), colourless rods from EtOH, m.p. 146–147°, and **6c** (46 mg), colourless rods from EtOH, m.p. 167–169°.

Cycloadduct **11**. (Found: C, 68.9; H, 5.9; N, 3.7. $C_{21}H_{21}NO_5$ requires: C, 68.85; H, 5.75; N, 3.8%); ν_{max} 3290, 1740, 1610 and 1580 cm^{-1}; *m/z* (%) 367 (M^+, 8), 366 (16), 309 (78), 308 (100), 306 (15), 276 (21), 249 (19), 248 (36), 203 (17), 131 (23), 104 (19) and 77 (25); δ (^{13}C) 49.5 (d), 52.5 (q), 53.3 (q), 58.8 (d), 60.6 (d), 68.9 (t) and 77.8 (s); δ (^1H; d^5-pyridine/D_2O) 8.26–6.96 (m, 9H, ArH), 4.65 (dd, 1H, H_E, J_{DE} = 10.3 Hz, J_{BE} = 4.0 Hz), 4.20 (dd, 1H, H_D, J_{BD} = 11.0 Hz), 3.90 (s, 3H, C(3) CO_2Me), 3.83 (d, 1H, H_A, J_{AB} = 11.4 Hz), 3.64 (s, 3H, C(2) CO_2Me), 3.53 (d, 1H, H_C, J_{BC} = 11.4 Hz), 2.78 (m, 1H, H_B).

Cycloadduct **6c**. (Found: C, 68.6; H, 5.9; N, 3.7. $C_{21}H_{21}NO_5$ requires: C, 68.65; H, 5.75; N, 3.8%); ν_{max} 3360, 1720, 1610 and 1585 cm^{-1}; *m/z* (%) 309 (21), 308 (100), 248 (8), 131 (9), 115 (7), 104 (9), 77 (12) and 59 (11); δ 7.56–6.86 (m, 9H, ArH), 4.80 (d, 1H, H_B, J_{AB} = 7.2 Hz), 4.34 (d, 1H, H_C, J_{AC} = 7.2 Hz), 4.11 (m, 2H, H_E, H_F), 3.30 (s, 3H, C(2) CO_2Me), 3.26 (m, 1H, H_A), 3.16 (s, 3H, C(3) CO_2Me).

Intramolecular cycloaddition of methyl N - [2 - (2 - *propynyloxy*)*benzylidene*] *phenylglycine* (**3b**). A soln of **3b** (8.15 g, 26.5 mmol) in xylene (40 ml) was refluxed under argon for 1 d. Removal of the solvent *in vacuo* gave an orange oil (**8g**) which solidified on keeping and comprised a 4:1 mixture of **16a** and **b** (NMR). Crystallization from MeOH afforded **16a** (3.9 g, 48%) as pale yellow prisms m.p. 93–94°. TLC of a portion of the gummy residue from the mother liquors (320 mg) (silica gel, ether/40–60° light petroleum) afforded **16b** (R_f 0.32; 74 mg) slightly contaminated with the oxidized form **20** plus very small quantities of **18** (R_f 0.24; 20 mg) and **20** (R_f 0.14; 24 mg).

Cycloadduct **16a**. (Found: C, 74.5; H, 5.8; N, 4.55. $C_{19}H_{17}NO_3$ requires: C, 74.25; H, 5.6; N, 4.55%); ν_{max} 3300 and 1730 cm^{-1}; *m/z* (%) 307 (M^+, 0.5), 249 (31), 248 (100), 247 (6), 246 (12) and 115 (5); δ 7.63–6.75 (m, 9H, ArH), 6.28 (m, 1H, H_B), 4.9–4.7 (m, 3H, H_A, H_C, H_D), 3.65 (s, 3H, OMe) and 3.24 (br s, 1H, NH, exchanges with D_2O).

Cycloadduct **16b**. δ 7.69–6.78 (m, 9H, ArH), 6.07 (m, 1H, H_B), 5.27 (br s, 1H, H_A), 4.88 (br s, 2H, H_C, H_D), 3.78 (s, 3H, OMe) and 3.24 (br s, 1H, NH, exchanges with D_2O).

Oxidized cycloadduct **20**. m.p. 88–90° (Found: C, 74.25; H, 4.7, N, 4.65. $C_{19}H_{15}NO_3$ requires: C, 74.75; H, 4.9; N, 4.6%); ν_{max} 1740, 1655 and 1620 cm^{-1}; *m/z* (%), 305 (M^+, 82), 304 (22), 291 (21), 290 (100), 272 (29), 246 (19), 245 (12) and 137 (23); δ 8.29–6.93 (m, 10H, ArH and H_B), 5.13 (t, 2H, OCH_2) and 3.74 (s, 3H, OMe).

Rearranged cycloadduct **18**. m.p. 210–212°, colourless prisms from methanol. (Found: C, 74.85; H, 5.2; N, 4.7. $C_{19}H_{15}NO_3$ requires: C, 74.75; H, 4.9; N, 4.6%); ν_{max} 3320, 1675, 1610, 1450 and 1270 cm^{-1}; *m/z* (%) 305 (M^+, 90), 304 (22), 291 (20), 290 (100), 272 (24), 246 (6) and 245 (9); δ 7.68–6.77 (m, 9H, ArH), 5.57 (s, 2H, OCH_2), 3.72 (s, 3H, OMe) and 1.64 (br s, 1H, NH, exchanges with D_2O).

When the intramolecular cycloaddition was carried out in boiling xylene over 3 d in the presence of air an increased yield of **18** (29.5%) was obtained.

Thermal rearrangement of 2 - *methoxycarbonyl* - 2 - *phenyl* - 2H - *pyrro*[2,3 - d]*benzo*[b]*pyran* (**20**). **20** (30 mg) was dissolved in xylene-d_{10} (0.5 ml) and the soln sealed in an NMR tube and heated in an oil bath (150°) for 3 hr. NMR monitoring demonstrated clean and quantitative rearrangement to **18** had occurred.

Intramolecular cycloaddition of methyl N - [2 - (2 - *propynyloxy*)*naphthylidene*]*phenylglycine* (**4b**). A soln of **4b** (9.2 g, 25.8 mmol) in xylene (40 ml) was refluxed under argon for 1 d. Removal of the solvent *in vacuo* gave a viscous red–brown oil. Trituration of this oil with MeOH gave a pale brown solid (8.6 g, 93%) whose NMR indicated that it comprised a 3:1 mixture of **17a** and **b** together with a very small amount of **19**. TLC [silica gel, ether (40%)/40–60° light petroleum (60%)] of a portion of the crude material (300 mg) afforded **17a** (R_f 0.42; 218 mg, 72% recovery) as pale yellow platelets (MeOH) m.p. 65–68°; cycloadduct **17b** (R_f 0.34; 50 mg, 16% recovery) as pale yellow platelets (MeOH) m.p. 53–56°; and oxidized adduct **21** (R_f 0.30; 30 mg, 10% recovery) as pale yellow prisms (MeOH) m.p. 169–171°.

Cycloadduct **17a**. (Found: C, 76.95; H, 5.4; N, 3.9. $C_{23}H_{19}NO_3$ requires: C, 77.3; H, 5.35; N, 3.9%); ν_{max} 3300 and 1735 cm^{-1}; *m/z* (%) 357 (M^+, 2), 355 (4), 299 (24), 298 (100), 296 (10) and 149 (8); δ 8.61–7.0 (m, 11H, ArH), 6.5 (m, 1H, H_B), 5.24 (d, 1H, H_A, J = 2.4 Hz), 4.95 and 4.61 (2 × d, 2 × 1H, H_C, H_D, J_{CD} = 12 Hz), 3.64 (s, 3H, OMe) and 3.27 (br s, 1H, NH, exchanges with D_2O).

Cycloadduct **17b**. (Found: C, 77.0; H, 5.2; N, 3.73. $C_{23}H_{19}NO_3$ requires: C, 77.3; H, 5.35; N, 3.9%); ν_{max} 3400 and 1740 cm^{-1}; *m/z* (%) 357 (M^+, 5), 355 (4), 299 (24), 298 (100), 296 (15), 280 (6), 210 (5), 149 (34), 105 (10), 97 (12), 85 (12), 83 (12), 81 (7) and 77 (8); δ 8.24–7.0 (m, 11H, ArH), 6.28 (m, 1H, H_B), 5.69 (d, 1H, H_A, J = 2.4 Hz), 4.95 and 4.66 (2 × d, 2 × 1H, H_C, H_D, J_{CD} = 12 Hz), 3.82 (s, 3H, OMe) and 2.15 (br s, 1H, NH, exchanges with D_2O).

2 - *Methoxycarbonyl* - 2 - *phenyl* - 2H - *pyrro*[2,3 - d]*naphthopyran* (**21**). (Found: C, 77.5; H, 4.8; N, 3.8. $C_{23}H_{17}NO_3$ requires: C, 77.75; H, 4.8; N, 3.95%); ν_{max} 1725, 1640, 1610, 1590, 1240 and 1230 cm^{-1}; *m/z* (%) 355 (M^+, 100), 340 (27), 322 (13), 297 (21), 296 (88) and 162 (17); δ 9.82 (d, 1H, ArH), 7.9–7.1 (m, 11H, ArH and H_B), 5.26 and 5.14 (2 × dd, 2 × 1H, H_C, H_D; J_{CD} = 15.1 Hz, J_{BC}, J_{BD} = 1.84 Hz), and 3.75 (s, 3H, OMe).

2 - *Phenyl* - 3 - *methoxycarbonylpyrro*[2,3 - d]*naphthopyran* (**19**). Compound **21** (30 mg) was dissolved in xylene-d_{10} (0.5 ml) sealed in an NMR tube and heated in an oil bath (150°) for 1 min. On cooling the product (25 mg, 83%) crystallized as pale

yellow needles, m.p. 235–237°. ν_{max} 3230, 1680, 1450, 1370, 1285 and 1125 cm^{-1}; *m/z* (%) M^+ 355.1208 ($C_{23}H_{17}NO_3$ requires 355.12084); δ 8.3–7.0 (m, 11H, ArH), 5.58 (s, 2H, OCH_2) and 3.78 (s, 3H, OMe).

2 - *Methoxycarbonyl* - 2 - *methyl* - 4H - 2,3,3a,9b - *tetrahydropyrro*[2,3 - d]*benzo*[b]*pyran* (**24**). A soln of methyl N-[2-(2-propenyloxy)benzylidene] alanine (2 g, 8.1 mmol) in xylene (30 ml) was boiled under reflux for 24 hr. The xylene was then removed under reduced pressure to leave a thick yellow oil (2 g), which rapidly solidified. The NMR spectrum ($CDCl_3$) of the crude product shows it to comprise a 19 : 2 : 1 mixture of isomers. The solid was triturated with 40–60° petroleum ether and filtered to yield an off-white solid (1.38 g, 69%). Crystallization of the crude product from 40–60° petroleum ether–ether yielded the pure major **24** (0.48 g, 24%) as colourless prisms, m.p. 86–87°. (Found: C, 68.0; H, 6.95; N, 5.55. $C_{14}H_{17}NO_3$ requires: C, 68.0; H, 6.95; N, 5.65%); ν_{max} 3290 and 1720 cm^{-1}; *m/z* (%) 247 (M^+, 2), 188 (100), 131 (6), 107 (7) and 94 (8); δ (C_6D_6) 7.81–7.21 (m, 4H, ArH), 4.4 (d, 1H, H_A, J_{AB} = 6 Hz), 4.11 (dd, 1H, H_E), 3.93 (t, 1H, H_F), 3.61 (s, 3H, OMe), 3.02 (br s, NH, exchanges with D_2O), 2.51 (m, 1H, H_B), 2.22 (dd, 1H, H_C), 2.06 (dd, 1H, H_D) and 1.81 (s, 3H, Me).

Methyl - 3 - *phenyl* - 2 - *azabicyclo*[3.3.0]*octane* - 1 - *carboxylate* (**32**). A soln of **30a** (8.8 g, 36 mmol) in xylene (40 ml) was boiled under reflux under an argon atmosphere for 48 hr. Removal of the solvent and distillation of the residue afforded an 87 : 13 mixture of **32** and **33** (glc, 2.5% SGR, 180°; 7.1 g, 81%), b.p. 120–123°/0.05 mmHg as a clear colourless liquid. (Found: C, 73.15; H, 7.85; N, 5.85. $C_{15}H_{19}NO_2$ requires: C, 73.45; H, 7.8; N, 5.7%); ν_{max} 3340 and 1725 cm^{-1}; *m/z* (%) 245 (M^+, 3), 187 (14), 186 (100), 184 (6), 119 (8) and 91 (8); δ (major isomer) 7.4–7.16 (m, 5H, ArH), 4.23 (dd, 1H, H_A), 3.67 (s, 3H, OMe), 2.84 (br q, 1H, H_D), 2.64 (br s, 1H, NH), 2.28 (m, 1H, H_J), 2.02 (m, 1H, H_F), 1.91 (m, 1H, H_B), 1.82 (m, 2H, H_C, H_G), 1.72 (m, 2H, H_H, H_I) and 1.47 (m, 1H, H_J).

Methyl 3 - (2 - *naphthyl*) - 2 - *aza* - 7 - *thiabicyclo*[3.3.0]*octane* - 1 - *carboxylate* (**35**). A soln of **34** (0.65 g, 2.08 mmol) in xylene (10 ml) was boiled under reflux under argon for 24 hr. Removal of the solvent left a thick oil (0.65 g) whose NMR spectrum showed it to comprise a 92:8 mixture of two isomeric cycloadducts. Trituration with 40–60° petroleum ether–ether followed keeping it at 0° for 16 hr affording pure **35** (0.41 g, 63%) as colourless solid. An analytical sample was crystallized from MeOH–ether to afford colourless prisms, m.p. 51°. (Found: C, 68.75; H, 6.3; N, 4.4. $C_{18}H_{19}NO_2S$ requires: C, 69.0; H, 6.1; N, 4.45%); ν_{max} 3325 and 1721 cm^{-1}; *m/z* (%) 313 (M^+, 17), 254 (20), 169 (100) and 154 (12); δ (xylene-d_{10}) 8.14–7.71 (m, 7H, ArH), 4.93 (dd, 1H, H_A), 3.87 (s, 3H, OMe), 3.75 (d, 1H, H_F), 3.53 (m, 1H, H_C), 3.33 (dd, 1H, H_E), 3.11 (d, 1H, H_F), 2.81 (dd, 1H, H_D), 2.65 (br s, NH, exchanges with D_2O) and 2.33 (m, 2H, 2 × H_B).

Intermolecular cycloadditions

General procedure. A soln of equimolar amounts of the appropriate imine and N-phenylmaleimide in xylene was boiled under reflux under argon for 1–20 hr. The xylene was then removed and the crude cycloadduct crystallized from the appropriate solvent.

Methyl c - 4 - [2 - (2 - *methylprop* - 2 - *enyl*)*oxyphenyl*] - 2,7 - *diphenyl* - 6,8 - *dioxo* - 3,7 - *diazabicyclo*[3.3.0]*octane* - r - 2 - *carboxylate* (**10**). Obtained (90%) as colourless prisms from MeOH, m.p. 190–191°. (Found: C, 72.6; H, 5.7; N, 5.5. $C_{30}H_{28}N_2O_5$ requires: C, 72.55; H, 5.7; N, 5.65%); ν_{max} 3340, 1780, 1725 and 1710 cm^{-1}; *m/z* (%) 496 (M^+, 2), 438 (16), 437 (49), 324 (23), 323 (100), 269 (15), 268 (62), 209 (12), 208 (25) and 91 (14); δ ($CDCl_3/D_2O$) 7.72–6.78 (m, 14H, ArH), 4.95 (dt, 2H, C=CH_2), 4.63 (d, 1H), 4.44 (s, 2H, OCH_2), 4.22 (d, 1H), 3.69 (dd, 1H), 3.78 (s, 3H, OMe) and 1.72 (s, 3H, Me).

Methyl c - 4 - [2 - (*prop* - 2 - *enyloxy*) - 4 - *ethoxyphenyl*] - 2,7 - *diphenyl* - 6,8 - *dioxo* - 3,7 - *diazabicyclo*[3.3.0]*octane* - r - 2 - *carboxylate* (**22a**). Obtained (95%) as colourless needles from MeOH, m.p. 178–180°. (Found: C, 70.65; H, 5.85; N, 5.05. $C_{31}H_{30}N_2O_6$ requires: C, 70.7; H, 5.75; N, 5.3%); ν_{max} 3340, 1780, 1740 and 1710 cm^{-1}; *m/z* (%) 526 (M^+, 6), 467 (13), 354 (24), 353 (100), 313 (10), 312 (17), 293 (23) and 252 (17); δ ($CDCl_3/D_2O$) 7.67–6.67 (m, 13H, ArH), 6.05 (m, 1H, C<u>H</u>=CH_2), 5.33 (m, 2H, CH=C<u>H</u>$_2$), 4.57 (d, 2H, OCH_2), 4.30 (d, 1H), 4.21 (d, 1H), 3.95 (m, 2H, O<u>CH</u>$_2$Me), 3.78 (s, 3H, OMe), 3.45 (dd, 1H), and 1.35 (t, 3H, CH_2<u>Me</u>).

Methyl c - 4 - [2 - (*prop* - 2 - *enyloxy*) - 4 - *ethoxyphenyl*] - 2 - *phenyl* - 6,8 - *dioxo* - 3 - *aza* - 7 - *oxabicyclo*[3.3.0]*octane* - r - 2 - *carboxylate* (**22b**). Obtained (91%) as a colourless amorphous solid from xylene, m.p. 152–155°. (Found: C, 66.15; H, 5.6; N, 3.0. $C_{25}H_{25}NO_7$ requires: C, 66.5; H, 5.6; N, 3.1%); ν_{max} 3340, 1860, 1785 and 1745 cm^{-1}; *m/z* (%) 451 (M^+, 12), 392 (10), 354 (23), 353 (100), 320 (16), 313 (14), 312 (23), 306 (24), 294 (10), 293 (33), 253 (14) and 252 (17); δ ($CDCl_3/D_2O$) 7.45 (s, 5H, ArH), 6.85 (m, 3H, ArH), 6.06 (m, 1H, C<u>H</u>=CH_2), 5.31 (m, 2H, CH=C<u>H</u>$_2$), 4.57 (dt, 2H, OCH_2), 4.33 (d, 1H), 4.24 (d, 1H), 4.06 (q, 2H, O<u>CH</u>$_2$Me), 3.79 (s, 3H, OMe), 3.52 (dd, 1H) and 1.41 (t, 3H, OCH_2<u>Me</u>).

Methyl c - 4 - [2 - (*prop* - 2 - *enyloxy*)*phenyl*] - 2,7 - *diphenyl* - 6,8 - *dioxo* - 3,7 - *diazabicyclo*[3.3.0]*octane* - r - 2 - *carboxylate* (**22c**). The product (93%) crystallized from MeOH as colourless needles, m.p. 196–197°. (Found: C, 71.9; H, 5.65; N, 5.65. $C_{29}H_{26}N_2O_5$ requires: C, 72.2; H, 5.45; N, 5.8%); ν_{max} 3310, 1780, 1730 and 1710 cm^{-1}; *m/z* (%) 482 (M^+, 1), 424 (12), 423 (27), 310 (12), 309 (49), 268 (21), 208 (12), 116 (75), 114 (18) and 98 (100); δ ($CDCl_3/D_2O$) 7.66–6.8 (m, 14H, ArH), 5.96 (m, 1H, C<u>H</u>=CH_2), 5.22 (m, 2H, CH=C<u>H</u>$_2$), 4.56 (m, 3H, CH and OCH_2), 4.22 (d, 1H), 3.78 (s, 3H, OMe) and 3.68 (dd, 1H).

Methyl c - 4 - (2,2 - *dimethylbut* - 3 - *enyl*) - 2,7 - *diphenyl* - 6,8 - *dioxo* - 3,7 - *diazabicyclo*[3.3.0]*octane* - r - 2 - *carboxylate* (**30a**). The product (95%) crystallized from MeOH as colourless needles, m.p. 153–155°. (Found: C, 72.15; H, 6.35; N, 6.6. $C_{26}H_{28}N_2O_4$ requires: C, 72.2; H, 6.55; N, 6.5%); ν_{max} 3300, 3320, 1770 and 1710 cm^{-1}; *m/z* (%) 432 (M^+, 2), 374 (18), 373 (71), 350 (21), 349 (100), 290 (13), 289 (61), 218 (14), 170 (43), 158 (14), 143 (18) and 142 (28); δ ($CDCl_3/D_2O$) 7.77–7.18 (m, 10H, ArH), 5.79 (m, 1H, C<u>H</u>=CH_2), 5.05 (m, 2H, CH=C<u>H</u>$_2$), 4.16 (d, 1H), 3.7 (s, 3H, OMe), 3.33 (dd, 1H), 2.95 (d, 1H), 2.36 (d, 2H, CH_2) and 1.15 and 1.1 (2 × s, 2 × 3H, 2 × Me).

Methyl c - 4 - (*pent* - 4 - *enyl*) - 2,7 - *diphenyl* - 6,8 - *dioxo* - 3,7 - *diazabicyclo*[3.3.0]*octane* - r - 2 - *carboxylate* (**30b**). The product (79%) crystallized from MeOH–EtOAc as colourless prisms, m.p. 149°. (Found: C, 71.5; H, 6.35; N, 6.6 $C_{25}H_{26}N_2O_4$ requires: C, 71.75; H, 6.25; N, 6.7%); ν_{max} 3340, 1739 and 1705 cm^{-1}; *m/z* (%) 418 (M^+, 26), 360 (25), 359 (100), 349 (31) and 186 (51); δ 7.47–7.28 (m, 8H, ArH), 7.05 (m, 2H, ArH), 5.77 (m, 1H, C<u>H</u>=CH_2), 5.04 (m, 2H, CH=C<u>H</u>$_2$), 4.74 (d, 1H), 3.88 (s, 3H, OMe), 3.64 (dd, 1H), 3.44 (d, 1H), 2.7 (br s, NH, exchanges with D_2O), and 2.16–1.26 [m, 6H, $(CH_2)_3$].

Methyl c - 4 - (*hex* - 5 - *enyl*) - 2,7 - *diphenyl* - 6,8 - *dioxo* - 3,7 - *diazabicyclo*[3.3.0]*octane* - r - 2 - *carboxylate* (**30c**). The product (88%) crystallized from MeOH–EtOAc as colourless prisms, m.p. 177–178°. (Found: C, 72.3; H, 6.6; N, 6.35. $C_{26}H_{28}N_2O_4$ requires: C, 72.2; H, 6.55; N, 6.5%); ν_{max} 3338, 1745 and 1710 cm^{-1}; *m/z* (%) 432 (M^+, 27), 374 (31), 373 (100), 349 (42) and 200 (53); δ 7.47–7.27 (m, 8H, ArH), 7.05 (m, 2H, ArH), 5.78 (m, 1H, C<u>H</u>=CH_2), 4.99 (m, 2H, CH=C<u>H</u>$_2$), 4.73 (br d, 1H), 3.87 (s, 3H, OMe), 3.64 (dd, 1H), 3.44 (d, 1H), 2.75 (br s, NH, exchanges in D_2O) and 2.17–1.17 [m, 8H, $(CH_2)_4$].

Acknowledgements—We thank SERC, DENI, MRC and Queen's University for support for this work.

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