Ritter reactions. Part 11.[1] The diverse reactivity of 5,10-(azenometheno)-5*H*-dibenzo[*a*,*d*]cyclohepten-11-yl amides with dimethyl acetylenedicarboxylate

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Each of the 5,10-(azenometheno)-5*H*-dibenzo[*a*,*d*]cyclohepten-11-yl amide derivatives 8a–c reacts with dimethyl acetylenedicarboxylate (DMAD) through its imine group to yield novel and unexpected heterocyclic products. Imine 8a undergoes 1:1 addition to give the conjugated enamine 10, or 1:2 addition yielding the cyclobutyl tetraester 11, depending on the conditions employed. In contrast, imine 8b undergoes addition of both DMAD and methanol affording the orthoester 12, while imine 8c is converted into the unsaturated lactam 14. Tentative mechanistic explanations for these diverse and unpredictable reactions are provided. These are supported by X-ray crystal structures of compounds 8c, 11, 12 and 14. Tetraester 11 was isolated as its inclusion compound (11)·$(C_6H_6)_{0.5}$ and the host–guest interactions involved therein are analysed in crystal engineering terms.

Introduction

For appropriate substrates the Ritter reaction[2,3] may be employed as an intramolecular process[4] affording a wide range of fused heterocyclic ring systems.[5,6] In contrast, relatively few *bridged* products have been obtained using this approach. So far all of these have involved intramolecular reaction of an olefinic group with the initial nitrilium ion intermediate to produce a 1-azacyclohexene ring and a carbenium ion. The latter then undergoes a stereoselective but otherwise conventional Ritter reaction yielding an amide functionality on work-up of the reaction.

This one-flask synthetic process is typified by the reactions of 2,6-bis(methylene)bicyclo[3.3.1]nonane **1** with nitriles **2a–c** to form the derivatives of 3-azatricyclo[5.3.1.$0^{4,9}$]undec-2-ene **3a–c** respectively.[7] The ready availability of these cyclic imines led us to react these with dimethyl acetylenedicarboxylate (DMAD) with a view to rapid construction of non-natural alkaloid-like products from simple precursors. These hopes were realised through formation of the disparate products **4–6** (Scheme 1) but were tempered by the complete lack of structure predictability for the products of these three reactions.[8,9]

We now present the results of a subsequent investigation into the reactivity of a further set of bridged imines with DMAD and we attempt to rationalise the unusual chemistry observed. Because of the unpredictability of these reactions, and the diversity of structural types encountered, we have used X-ray crystallography wherever possible to obtain unambiguous structures for these products.

Results

Preparation and structure of the imine precursors 8a–c

Ritter reactions carried out using sulfuric acid, the nitriles **2a–c** and 5*H*-dibenzo[*a*,*d*]cyclohepten-5-ol (dibenzosuberenol) **7** yielded the 5,10-(azenometheno)-5*H*-dibenzo[*a*,*d*]cyclohepten-11-yl amides **8a–c** (Scheme 2) through the series of steps that we have described previously for **8a**.[10] Formation of these bridged imines took place in one-flask processes in comparable yields to those found earlier for **3a–c**. As for the case of **3c**,[7] it is noteworthy that use of the reagent benzyl cyanide **2c** led to isolation of the product **8c** in which oxidation of the side group R^2 has taken place.

The sense of addition of nitrile reagents **2** across the ring of 5*H*-dibenzo[*a*,*d*]cycloheptene derivatives was first considered by Lamanec *et al.*[11] who concluded through NMR arguments that the nitrogen became attached at position C-5 (rather than C-10) of the cycloheptatrienyl cation intermediate. Subsequently we have confirmed this by X-ray structural studies of two such 5,10-(azenometheno)-5*H*-dibenzo[*a*,*d*]cyclohepten-11-yl amide products.[1,10]

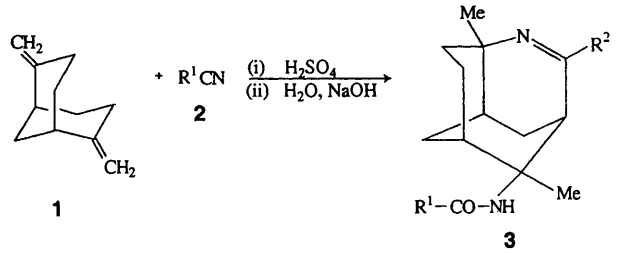
To explain the isolation of the unexpected oxidation product **3c** (R^2 = Bz rather than Bn) we proposed[7] that this arose through autoxidation of the highly reactive benzylic-allylic methylene group of the initially formed Ritter product. A rather similar outcome in the tetrahydrobenz[*f*]indole series provided good supporting evidence for this suggestion.[12] However, it was conceivable that some alternative process was involved in generating the products which had been assigned the structures **3c** and **8c** on the basis of spectral evidence.

In light of the unusual reactivity of the latter imine with DMAD (described later) we decided to confirm its structure by X-ray methods and rule out any possibility of the Ritter product being **9** or some other isomeric structure formed through rearrangement. The confirmed molecular structure **8c** is presented in Fig. 1, while numerical details of the solution and refinement of this and subsequent X-ray structures are shown in Table 1.

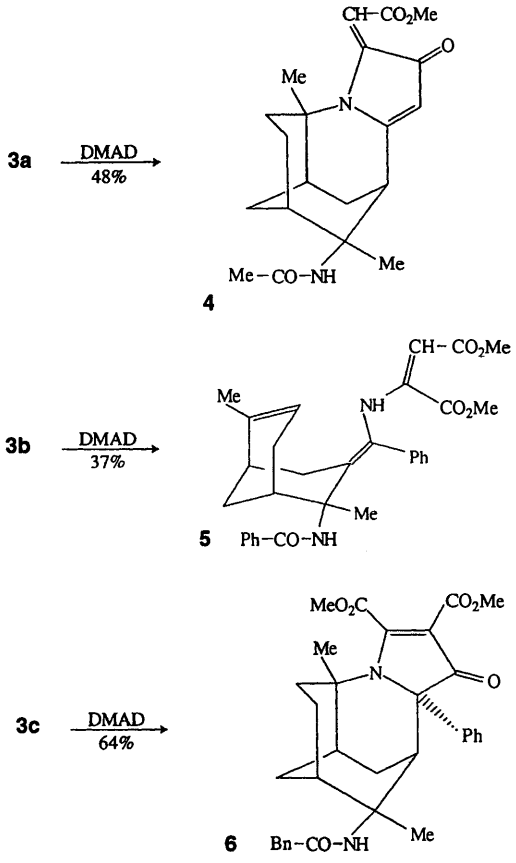
Reactivity of imine 8a with DMAD

Imine **8a** and DMAD were refluxed overnight in chloroform solution. Solvent was evaporated and then the crude material was recrystallised from benzene to give a 44% yield of a single product. Microanalysis gave the formula $C_{25}H_{24}N_2O_5$ revealing addition of one equivalent of DMAD, while both the ^1H and ^{13}C NMR spectra indicated that the basic ring system remained intact but also clearly showed the presence of an olefinic methylene group (at δ 5.95 and 97.2 respectively). Hence this material was assigned the unsaturated enamine structure **10** on the basis of its measured characteristics; for example the carbon atom β- to nitrogen in 6-membered ring enamines is observed in the range δ 94–100.[13]

In an alternative reaction **8a** and DMAD were refluxed overnight in methanol, solvent was then evaporated, and the crude product recrystallised from benzene to give a 35% yield of a different and more complex material. The combustion analysis indicated that this substance was an inclusion compound of composition $(C_{31}H_{30}N_2O_9)\cdot(C_6H_6)_{0.5}$. Mass spectral data confirmed both the presence of benzene (*m*/*z* 78) and the formula $C_{31}H_{30}N_2O_9$ (M^+ = 574). These results



	R^1	R^2	Yield
a	Me	Me	63%
b	Ph	Ph	47%
c	Bn	Bz	33%



Scheme 1 Preparation of the imines **3a–c** and their reaction products with DMAD

indicated addition of two equivalents of DMAD to the starting imine. Single crystal X-ray structural analysis (Table 1) revealed that this product was the complex cyclobutyl tetraester **11** depicted in Fig. 2.

Reactivity of imine 8b with DMAD

Reaction of imine **8b** with DMAD in refluxing benzene, followed by recrystallisation of the crude product from methanol, resulted in isolation of a low yield (14%) of a product with formula $C_{36}H_{32}N_2O_6$, from addition of one equivalent each of DMAD and methanol. The ^1H and ^{13}C NMR spectra clearly showed the presence of an olefinic methine and three methoxy groups in this product. Single crystal X-ray structural analysis (Table 1) revealed that this compound was the orthoester **12** depicted in Fig. 3.

Reactivity of imine 8c with DMAD

In contrast to the previous two imines, compound **8c** proved reluctant to react with DMAD except under more forcing conditions. After 2 weeks in refluxing chloroform, a small

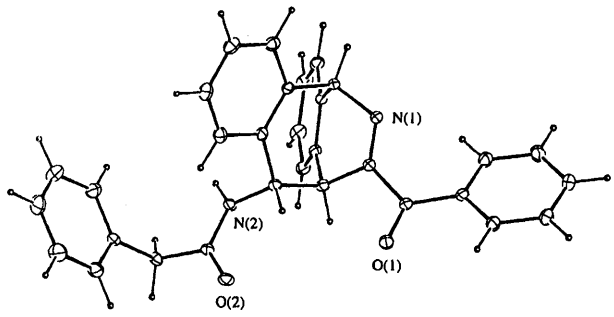


Fig. 1 Molecular structure of imine **8c** determined by X-ray crystallography. Only non-C/H atoms are labelled in this, and subsequent, figures.

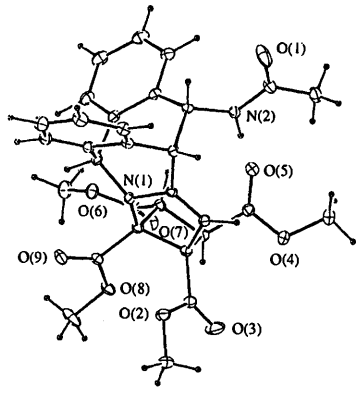
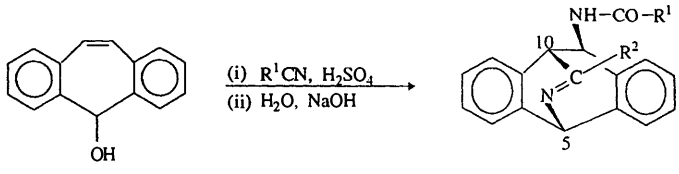
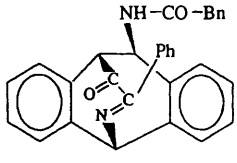


Fig. 2 Molecular structure of the tetraester **11** determined by X-ray crystallography



	R^1	R^2	Yield
a	Me	Me	64%
b	Ph	Ph	39%
c	Bn	Bz	30%



Scheme 2 Preparation of the imines **8a–c** *via* Ritter reaction

quantity of a pure product was obtained after recrystallisation of the crude residues from methanol. This material proved to be the unsaturated lactam **14** when its X-ray crystal structure was solved (Table 1 and Fig. 4).

Discussion

First it should be noted that the three bridged imines **8a–c** reacted entirely differently with DMAD and gave quite different product structures. Many prior examples of similar diversity and complexity in the reactions of DMAD with other imines are documented.[14–17] However, in addition, all four products obtained in this present work were *also* quite

Table 1 Numerical details of the solution and refinement of the four structures **8c**, **(11)**·$(C_6H_6)_{0.5}$, **12** and **14** determined by X-ray crystallography

Compound number	**8c**	**(11)**·$(C_6H_6)_{0.5}$	**12**	**14**
Formula	$C_{31}H_{24}N_2O_2$	$(C_{31}H_{30}N_2O_9)\cdot(C_6H_6)_{0.5}$	$C_{36}H_{32}N_2O_6$	$C_{37}H_{30}N_2O_6$
Formula mass	456.5	613.6	588.7	598.7
Crystal description	{100} {010} {12−1} (0−2−1) (021) (0−21)	(0−10) (−11−1) (31−1) (111) (−311) {100} {001}	{012} {001} {10−3} (110) (−1−10)	{100} {010} {001}
Space group	$P2_1/c$	$C2/c$	$P2_1/c$	$P\bar{1}$
a/Å	10.160(2)	39.832(2)	11.8119(9)	10.586(1)
b/Å	24.829(2)	11.0716(3)	9.6624(4)	11.527(2)
c/Å	9.983(1)	14.8792(7)	25.832(2)	14.003(2)
α/°	90	90	90	100.964(7)
β/°	105.082(7)	109.646(2)	90.211(4)	105.907(6)
γ/°	90	90	90	101.899(7)
V/Å^3	2431.7(5)	6179.7(5)	2948.2(4)	1551.7(3)
Z	4	8	4	2
D_{calc}/g cm^{-3}	1.25	1.32	1.33	1.28
μ/cm^{-1}	5.83	7.57	6.97	6.73
Crystal dimensions/mm	0.16 × 0.18 × 0.28	0.15 × 0.35 × 0.22	0.30 × 0.30 × 0.12	0.20 × 0.04 × 0.09
$2\theta_{max}$/°	140	140	120	120
ω Scan angle	0.6 + 0.15 tan θ	0.5 + 0.15 tan θ	0.5 + 0.15 tan θ	0.5 + 0.15 tan θ
Max., min. transmission coefficients	0.92, 0.85	0.90, 0.81	0.93, 0.79	0.97, 0.91
R_{int} for (no.) multiple measurements	0.016 (366)	0.014 (366)	0.007 (106)	—
Largest peak in final diff. map/e Å^{-3}	0.20	0.39	0.35	0.40
No. of intensity measurements	4993	6430	4786	4595
No. of independent obsd. reflections	3115	4163	3322	2404
No. of reflections (m) and variables (n) in final refinement	3115, 316	4163, 406	3322, 397	2404, 401
$R = \Sigma^m\|\Delta F\|/\Sigma^m\|F_o\|$	0.044	0.049	0.045	0.055
$R_w = [\Sigma^m w\|\Delta F\|^2/\Sigma^m w\|F_o\|^2]^{\frac{1}{2}}$	0.059	0.068	0.062	0.068
$s = [\Sigma^m w\|\Delta F\|^2/(m-n)]^{\frac{1}{2}}$	2.02	2.44	2.28	2.10
Crystal decay	None	None	None	1 to 0.95

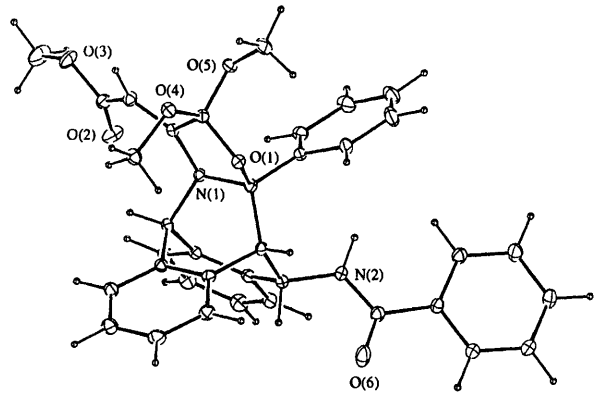


Fig. 3 Molecular structure of the orthoester **12** determined by X-ray crystallography

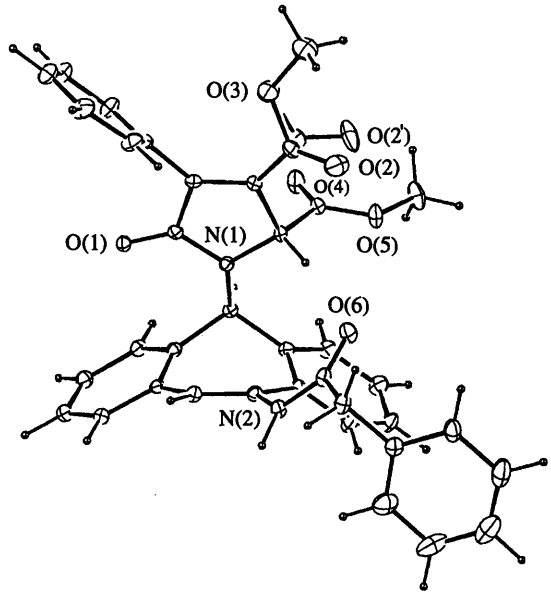


Fig. 4 Molecular structure of the lactam **14** determined by X-ray crystallography. Both components of the disordered ester carbonyl group are shown and are distinguished by the labels O(2) and O(2'). Their occupancies are 0.526(5) and 0.474 respectively.

dissimilar to those found in the previous reactions between DMAD and the bridged imines **3a–c**. This is considerably more surprising given that the imine substitution pattern in each of the **a–c** pairs (*e.g.* **3b**/**8b**) was identical.

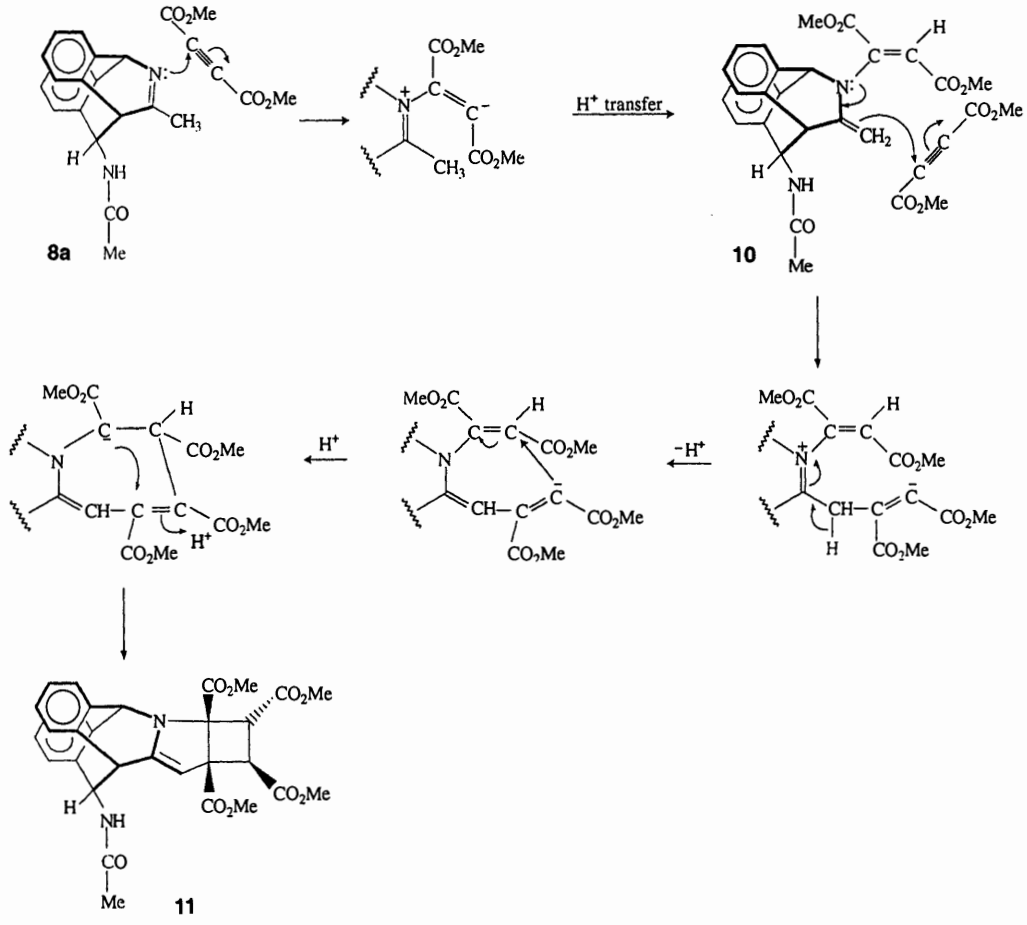
Reaction of imine 8a with DMAD to yield 10 and 11

Methyl imines such as **3a** and **8a** have ambident nucleophilic reactivity, since potentially they are capable of reacting through the nitrogen atom of the imine form, or through the carbon atom of the enamine tautomer. Evidence for the presence of such an equilibrium in the case of **3a** has been demonstrated through exchange of the methyl group hydrogens using deuterium oxide at room temperature. This was clearly revealed by both ^{1}H and ^{13}C NMR spectroscopy.[7,18]

Formation of **10** must involve nucleophilic attack by nitrogen on a molecule of DMAD followed by proton transfer (Scheme 3). Isolation of a stable conjugated enamine such as this has precedent in the work of Huisgen[19] and in our isolation of **5** from the reaction of **3b** with DMAD.[8]

Precise details of the generation of tetraester **11** must be considered more problematical. However, a reasonable proposal is outlined in Scheme 3. This commences with attack on a second molecule of DMAD by the nucleophilic carbon of enamine **10**. Stepwise cycloadditions of electron rich and electron poor alkenes to yield cyclobutane derivatives are well-known to proceed through either radical[20] or ionic pathways.[21] Here, reaction could proceed through the carbanionic intermediates indicated. Geometrical constraints of intramolecular ring formation would require the second DMAD-derived group to react as the *cisoid* carbanion. Together with the *trans*-nature of the first DMAD-derived group, this is reflected in formation of the resulting cyclobutane product **11**, which has three *cis*-carbomethoxy substituents.

The environment of the benzene guest molecule in **(11)**·$(C_6H_6)_{0.5}$ is shown in Fig. 5. Four neighbouring molecules



Scheme 3 Proposed mechanistic pathway for the conversion of imine **8a** and DMAD into the conjugated enamine **10** and the tetraester **11**

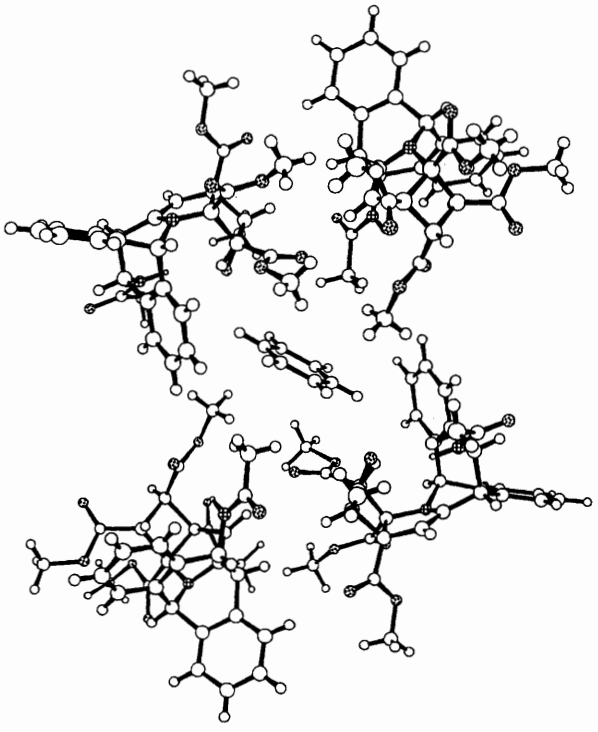


Fig. 5 The packing structure in (**11**)·$(C_6H_6)_{0.5}$ showing the benzene guest occupying the cavity produced by four neighbouring tetraester **11** host molecules

of tetraester **11** form the cavity in which the benzene lies. There is a centre of symmetry at the centre of the benzene molecule, so the four tetraester molecules comprise two symmetry-related pairs. The following description of host–guest behaviour therefore relates to only one half of the benzene ring and to only two of the four host molecules surrounding the cavity.

Three different types of host–guest interactions stabilise this inclusion compound. First, there is an edge-face aromatic interaction[22] between the benzene and a host benzo group (in the sense guest Ar–H · · · host Ar ring). The shortest C · · · C distance is 3.7 Å.

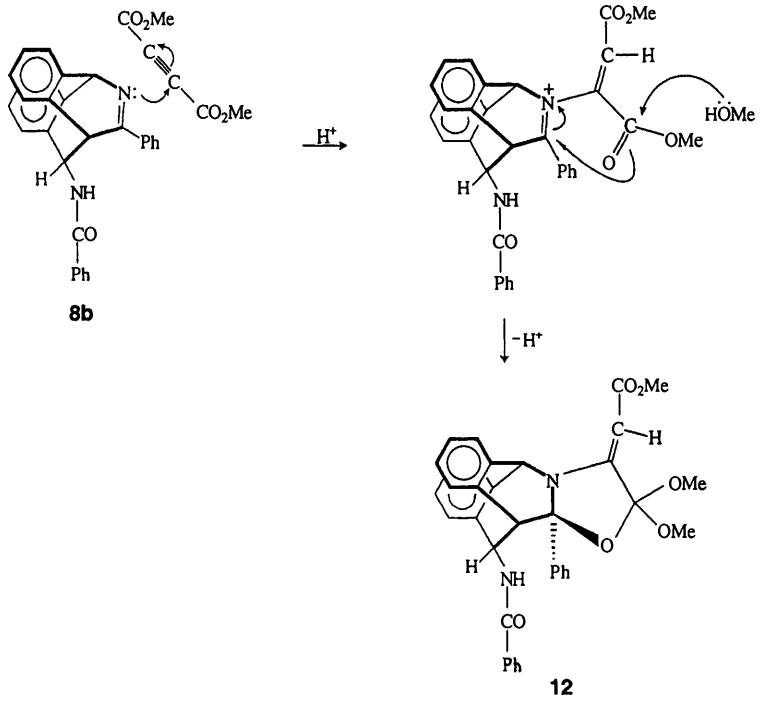
Secondly, there are interactions between the benzene molecule and two different neighbouring methyl groups of one host. Both have the methyl carbon within 3.5 Å of a benzene carbon atom. Methyl · · · aromatic ring interactions are not uncommon. A search of the Cambridge Structural Database (CSD)[23] for methyl · · · benzene contacts < 3.6 Å gave 88 instances.[24] This type of interaction was found to be as short as 3.2 Å in some cases.

The third type of stabilising interaction is a face–face interaction between the benzene ring and one of the ester groups defined by the labels O(6) and O(7) in Fig. 2. The shortest C · · · C distance is 3.7 Å and the angle between the normals to the plane of the benzene and ester groups is 20.7°. A search of the CSD revealed that this type of interaction is prevalent also. Methyl ester groups were found within 4.0 Å of aryl groups in 155 cases (the average being about 3.7 Å).[25] Often the aromatic and ester groups are close to coplanar. In 109 out of these 155 cases the angle between the normals to the planes was < 20°.

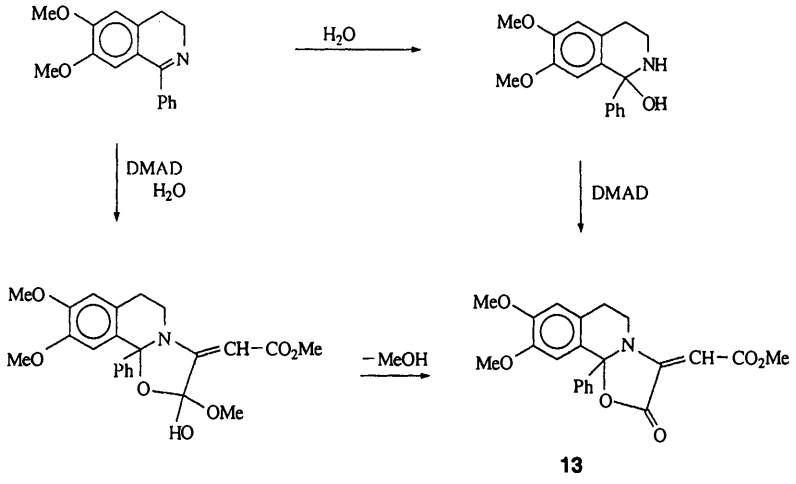
Reaction of imine 8b with DMAD to yield orthoester 12

A mechanistic explanation accounting for the formation of **12** is shown in Scheme 4. Initial nucleophilic attack by the imine nitrogen atom on DMAD produces an intermediate which readily cyclises to the observed product through attack initiated by the methanol solvent.

Some precedent for this behaviour is available from the reaction of 1-phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline



Scheme 4 Proposed mechanistic pathway for the conversion of imine **8b** and DMAD into the orthoester **12**



Scheme 5 Alternative possible pathways for formation of the lactone **13**

with DMAD in methanol[26] which afforded the cyclic lactone **13** shown in Scheme 5, since hypothetical conversion of the lactone carbonyl group into its dimethoxy acetal would give an orthoester structure analogous to our compound **12**. This conversion was rationalised by initial addition of water (from the wet solvent) to the imine group followed by (unspecified) addition, cyclisation and dehydration steps to yield the lactone. In light of our observation that bridged imines of this type are not especially reactive with water, for example **3a** forms a stable hydrate,[7] a more probable pathway would be for the reaction to proceed through a route similar to Scheme 4 but with the cyclisation step being initiated by water rather than methanol. Loss of methanol from the resulting intermediate would then yield the isolated product **13**.

Reaction of imine 8c with DMAD to yield lactam 14

In common with the earlier case of imine **3c**, reaction of **8c** with DMAD resulted in formation of a novel rearrangement product. As noted earlier the structure of both the starting material **8c** and product **14** were determined unambiguously by means of X-ray crystallography. The latter proved to be a five-membered ring unsaturated lactam, and during its formation the azenometheno bridge had become cleaved. This latter type of behaviour had earlier been observed for conversion of **3b** to **5**,[8] but for none of the other cases studied.

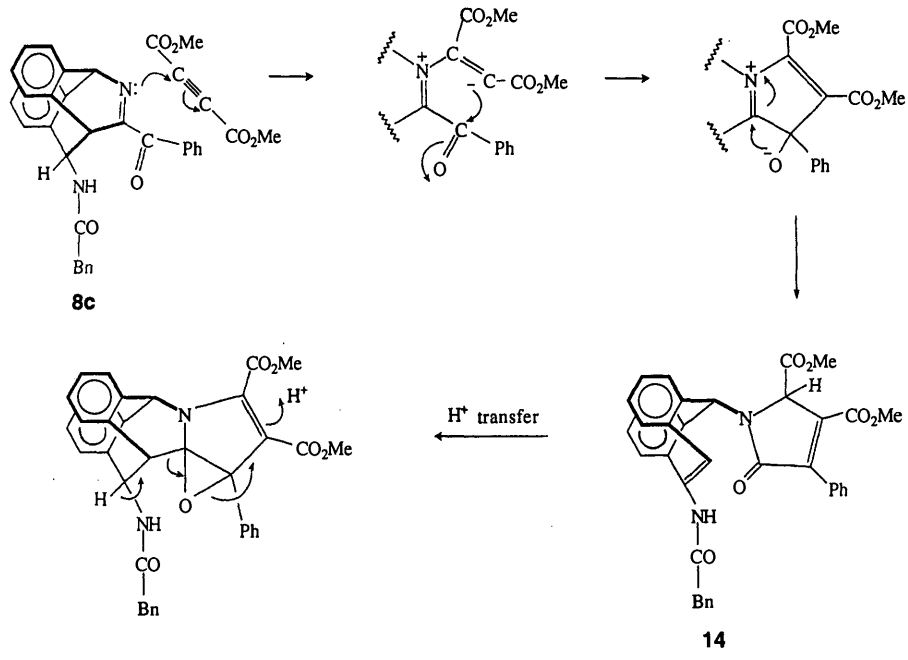
A possible mechanistic explanation for this reaction is outlined in Scheme 6. Nucleophilic attack by the imine nitrogen atom on a molecule of DMAD is followed by ring formation *via* the carbonyl group. The resulting zwitterion can achieve neutrality by means of epoxide formation. Finally, a proton transfer sequence generates the dibenzocycloheptenyl ring, breaks the former azenometheno bridge and affords product **14**.

Conclusions

This investigation has demonstrated that the reaction of imines with DMAD remains a fertile source of new and thoroughly unexpected chemistry. It appears that little in the way of general prediction can be made and the wide range of product types likely to be encountered in such reactions requires special caution when making structural assignments.

Experimental

^{1}H (300 MHz) and ^{13}C (75.3 MHz) NMR spectra were recorded on a Bruker ACF300 instrument and are reported as



Scheme 6 Possible mechanistic pathway for conversion of the imine **8c** and DMAD into the lactam **14**

chemical shifts (δ) relative to $SiMe_4$. The substitution of carbon atoms was determined by the DEPT procedure and coupling constants (J) measured in hertz (Hz). Melting points were determined with a Kofler instrument and are uncorrected. Mass spectra were recorded using a VG QUATTRO Triple Quadrupole instrument employing electron impact (EI) or electrospray (water–acetonitrile solvent system) methods. The IR spectra were recorded on a Perkin-Elmer 298 infrared spectrophotometer. Elemental analyses were carried out at the University of New South Wales by Dr H. P. Pham.

(5*R*,10*S*,11*S*)-*N*-{10,11-Dihydro-12-methyl-5,10-(azeno-metheno)-5*H*-dibenzo[*a*,*d*]cyclohepten-11-yl}acetamide 8a

5*H*-Dibenzo[*a*,*d*]cycloheptene-5-ol (dibenzosuberenol) **7**[10,27] and acetonitrile **2a** were reacted to yield **8a** as described previously by us.[1]

(5*R*,10*S*,11*S*)-*N*-{10,11-Dihydro-12-phenyl-5,10-(azeno-metheno)-5*H*-dibenzo[*a*,*d*]cyclohepten-11-yl}benzamide 8b

Concentrated sulfuric acid (98%; 0.8 cm^3) was cooled to 0 °C in a round-bottomed flask fitted with a condenser and drying tube. Alcohol **7** (0.42 g, 2 mmol) was dissolved in benzonitrile **2b** (5 cm^3), then added dropwise to the flask *via* the condenser. The reaction mixture was stirred at 0 °C for 30 min, then overnight at room temperature (r.t.). Water (10 cm^3) was added and after stirring for 30 min, the material was transferred to a separating funnel containing sodium hydroxide (1 mol dm^{-3}; 30 cm^3). The organic material was extracted several times with chloroform, the combined extracts were washed with water (4 × 25 cm^3) and dried (Na_2SO_4). Evaporation of solvent from the filtrate gave a suspension of solid in unreacted benzonitrile. Trituration with light petroleum (50 cm^3) gave more solid which was filtered to yield **8b** (0.32 g, 39%), mp 275–277 °C (from benzene) (Found: C, 84.1; H, 5.55; N, 6.8. $C_{29}H_{22}N_2O$ requires C, 84.0; H, 5.35; N, 6.8%); ν_{max}(paraffin mull)/cm^{-1} 3220s, 1630s, 1615m, 1575w, 1540m, 1000w, 800w, 780w, 760s, 700m, 685m; $\delta_H(CDCl_3)$ 8.02 (2 H, d, J 7.0), 7.63–7.13 (16 H, m), 6.14 (1 H, d, J 8.1), 6.09 (1 H, s), 5.54 (1 H, dd, J 8.1 and 4.4), 5.39 (1 H, d, J 4.4); $\delta_C(CDCl_3)$ 170.7 (C), 167.2 (C), 143.0 (C), 139.6 (C), 137.5 (C), 134.6 (C), 133.9 (C), 132.8 (C), 132.0 (CH), 131.7 (CH), 130.9 (CH), 128.8 (CH), 128.6 (CH), 128.5 (CH), 128.2 (CH), 127.5 (CH), 127.4 (CH), 127.2 (CH), 126.8 (CH), 124.1 (CH), 69.2 (CH), 50.4 (CH), 45.7 (CH) (two additional Ar-H peaks were obscured and not observed); m/z (electrospray) 415 [$(M + 1)^+$, 11%], 294 [$\{(M + 1) - 121\}^+$, loss of benzamide, 100].

(5*R*,10*S*,11*S*)-*N*-{10,11-Dihydro-12-benzoyl-5,10-(azeno-metheno)-5*H*-dibenzo[*a*,*d*]cyclohepten-11-yl}phenylacetamide 8c

Concentrated sulfuric acid (98%; 0.8 cm^3) was cooled to 0 °C in a round-bottomed flask fitted with a condenser and drying tube. The alcohol **7** (0.42 g, 2 mmol) was dissolved in benzyl cyanide **2c** (5 cm^3) then added dropwise to the flask *via* the condenser. The reaction mixture was stirred at 0 °C for 30 min then for 3 d at r.t. Water (10 cm^3) was added and after stirring for 30 min the material was transferred to a separating funnel containing sodium hydroxide (1 mol dm^{-3}; 30 cm^3). The aqueous solution was extracted several times with chloroform, the combined extracts washed with water (4 × 25 cm^3) and dried (Na_2SO_4). Evaporation of solvent from the filtrate gave a slurry of white solid (phenylacetamide) suspended in a pale yellow oil. This crude mixture was eluted through a column of activated alumina commencing with light petroleum (bp 60–80 °C) and using increasing amounts of chloroform. Initial fractions comprised unreacted benzyl cyanide containing about one-third of the total amount of **8c**. After 3 d at room temperature some solid **8c** had precipitated from these fractions and was filtered. Passage of the bulk of **8c** down the column could be monitored as a pale yellow band which was eluted using light petroleum–chloroform (2:3). This oil from the column solidified on standing. The total yield of **8c** was 0.27 g (30%), mp 240–241 °C (from benzene) (Found: C, 81.7; H, 5.9; N, 6.1. $C_{31}H_{24}N_2O_2$ requires C, 81.6; H, 5.3; N, 6.1%); ν_{max}(paraffin mull)/cm^{-1} 3310s, 3040w, 1675s, 1655s, 1605w, 1580w, 1260m, 1150m, 1010w, 990w, 935m, 885m, 830w, 775m, 765m, 740m, 735m, 690m; $\delta_H(CDCl_3)$ 7.97 (2 H, d, J 7.4), 7.55–7.05 (15 H, m), 6.71 (1 H, d, J 7.3), 6.06 (1 H, s), 5.66 (1 H, dd, J 9.3 and 4.2), 5.46 (1 H, d, J 9.3), 4.76 (1 H, d, J 4.2), 3.69 and 3.64 (1 H, H_{AB}, J 15.4), 3.54 and 3.48 (1 H, H_{AB}, J 15.4); $\delta_C(CDCl_3)$ 191.2 (C), 170.2 (C), 170.0 (C), 141.8 (C), 137.7 (C), 135.4 (C), 134.73 (C), 134.65 (C), 133.4 (CH), 132.3 (CH), 130.8 (CH), 129.4 (CH), 129.1 (CH), 129.0 (CH), 128.3 (CH), 128.2 (CH), 128.0 (CH), 127.6 (CH), 127.44 (CH), 127.41 (CH), 124.6 (CH), 69.9 (CH), 45.8 (CH) 45.5 (CH), 44.0 (CH_2), one Ar quaternary and one Ar-H signal were obscured and not

observed; *m/z* (EI, > 20% plus significant peaks) 456 (M^+, 7%), 351 [$(M - 105)^+$, loss of C_6H_5CO, 9], 337 (16), 322 (44), 321 [$(M - 135)^+$, loss of benzyl cyanide, 95], 293 (51), 292 (100), 291 (27), 217 (24), 216 (50), 206 (27), 191 (47), 189 (31), 178 (38), 128 (23), 105 [$(C_6H_5CO)^+$, 86], 91 [$(C_7H_7)^+$, 94], 77 [$(C_6H_5)^+$, 81]. The structure of this product was confirmed by means of X-ray crystallography.

(5*R*,10*S*,11*S*)-*N*-{13-[(*E*)-1,2-Bis(methoxycarbonyl)ethenyl]-10,11-dihydro-12-methylidene-5,10-(azenometheno)-5*H*-dibenzo[*a*,*d*]cyclohepten-11-yl}acetamide 10

The imine **8a** (0.60 g, 2 mmol) was dissolved in chloroform (50 cm^3) in a round-bottomed flask fitted with a condenser and drying tube. DMAD (0.60 g) was added to the stirred solution which was then refluxed vigorously for not less than 16 h. The reaction was evaporated to dryness to give viscous red–brown material. This material was heated in boiling benzene (10 cm^3), filtered while hot, and the filtrate allowed to stand at r.t. for 3 d. Filtration of the yellow solid yielded **10** (0.40 g, 43.8%), mp 227–229 °C (from benzene) (Found: C, 69.7; H, 5.8; N, 6.3. $C_{25}H_{24}N_2O_5$ requires C, 69.4; H, 5.6; N, 6.5%); ν_{max}(paraffin mull)/cm^{-1} 3390m, 1740m, 1715m, 1675s, 1650m, 1590s, 1525m, 1405m, 1165s, 1045w, 1000w, 930w, 875m, 825m, 765m, 750m, 635m; δ_H[$(CD_3)_2SO$] 7.76 (1 H, d, *J* 8.79, NH), 7.48–7.19 (8 H, m), 5.95 (2 H, s, $=CH_2$), 5.20 (1 H, dd, *J* 8.79 and 4.43), 4.49 (1 H, s), 4.42 (1 H, s), 3.97 (1 H, d, *J* 4.43), 3.74 (3 H, s, OCH_3), 3.59 (3 H, s, OCH_3), 1.95 (3 H, s, CH_3); δ_C[$(CD_3)_2SO$] 169.0 (C), 166.6 (C), 166.0 (C), 148.6 (C), 143.2 (C), 140.4 (C), 139.1 (C), 135.8 (C), 135.5 (C), 132.2 (CH), 129.0 (CH), 128.7 (CH), 127.7 (CH), 127.6 (CH), 127.0 (CH), 124.7 (CH), 99.9 (CH), 97.2 (CH_2), 64.6 (CH), 53.0 (CH_3), 52.8 (CH), 51.4 (CH_3), 50.4 (CH), 23.0 (CH_3), one Ar-H was obscured and not observed; *m/z* (EI; > 20% plus significant peaks) 432 (M^+, 1%), 431 [$(M - 1)^+$, 2], 373 [$(M - 59)^+$, loss of acetamide or CO_2CH_3, 6], 314 [$(M - 2 \times 59)^+$, 100], 254 (22), 231 (26), 78 (43), 43 (32). The same product was also obtained if benzene was employed as the solvent (yield 0.36 g, 39.5%).

(5*R*,10*S*,11*S*,13a*R*,14*R*,15*R*,15a*R*)-*N*-{13a,14,15,15a-Tetrakis(methoxycarbonyl)-10,11,13a,14,15,15a-hexahydro-5*H*-5,10-[1,2]cyclobuta[*b*]pyrrolodibenzo[*a*,*d*]cyclohepten-11-yl}-acetamide 11

The imine **8a** (0.60 g, 2 mmol) was dissolved in methanol (50 cm^3) then transferred to a round-bottomed flask fitted with a condenser and drying tube. Dimethyl acetylenedicarboxylate (DMAD) (0.60 g) was added to the stirred solution, which was then refluxed vigorously for not less than 16 h. The reaction was evaporated to dryness to give viscous red–brown material. This was dissolved in benzene (10 cm^3) and the solution allowed to stand at r.t. for 3 d. Filtration then yielded the tetraester **11** (0.40 g, 35%), mp (from benzene) indistinct over 212–240 °C with decomposition and colour change (yellow to orange) [Found: C, 66.6; H, 5.5; N, 4.55. $(C_{31}H_{30}N_2O_9)\cdot(C_6H_6)_{0.5}$ requires C, 66.55; H, 5.4; N, 4.6%]; ν_{max}(paraffin mull)/cm^{-1} 3380m, 3085w, 1760s, 1740s, 1710m, 1675s, 1640m, 1505m, 1295m, 1270m, 1215m, 1195m, 1145m, 1045w, 1025m, 1000w, 930w, 890w, 865w, 820w, 765s, 745w, 710w, 685s, 625m; δ_H[$(CD_3)_2SO$] 7.42–7.21 (9 H, m, Ar-H and NH), 5.32 (1 H, s), 5.19 (1 H, dd, *J* 9.42 and 3.80), 4.58 (1 H, s), 3.90 (1 H, d, *J* 3.80), 3.85 (1 H, d, *J* 9.50), 3.73 (3 H, s, OCH_3), 3.69 (3 H, s, OCH_3), 3.59 (3 H, s, OCH_3), 3.56 (3 H, s, OCH_3), 3.16 (1 H, d, *J* 9.50), 2.06 (3 H, s, CH_3CO); δ_C[$(CD_3)_2SO$] 171.8 (C), 170.1 (C), 169.9 (C), 168.9 (C), 168.7 (C), 151.3 (C), 142.7 (C), 138.2 (C), 135.7 (C), 133.3 (C), 131.7 (CH), 129.2 (CH), 128.8 (CH), 128.1 (CH), 127.7 (CH), 127.63 (CH), 127.57 (CH), 124.2 (CH), 92.9 (CH), 74.1 (C), 62.5 (C), 60.6 (CH), 52.9 (CH_3), 52.7 (CH_3), 52.33 (CH), 52.33 (CH_3), 52.27 (CH_3), 48.2 (CH), 43.9 (CH), 42.9 (CH), 23.2 (CH_3), plus guest benzene Ar-H at 128.6; *m/z* (EI; > 10% plus significant peaks) 575 [$(M + 1)^+$, 0.5%], 574 [M^+, 0.6], 430 [$(M - 144)^+$, loss of $CH_3CO_2CH{=}CHCO_2CH_3$), 25], 371 [$(430 - 59)^+$, loss of acetamide or CO_2CH_3, 19], 313 (25), 312 [$(371 - 59)^+$, 100], 79 (13), 78 [(included benzene)$^+$, 99], 77 (33), 74 (14). The structure of this product was confirmed by means of X-ray crystallography.

(5*R*,10*S*,11*S*,12*R*)-*N*-{15,15-Dimethoxy-14-methoxycarbonylmethylidene-12-phenyl-10,11,12,13,14,15-hexahydro-5*H*-5,10-[3,2]oxazolodibenzo[*a*,*d*]cyclohepten-11-yl}benzamide 12

The imine **8b** (0.60 g, 2 mmol) was dissolved in boiling benzene (100 cm^3) in a round-bottomed flask fitted with a condenser and drying tube. DMAD (0.60 g) was added to the stirred solution which was then refluxed vigorously for not less than 16 h. The reaction was evaporated to dryness to give viscous brown material. This was dissolved in methanol (50 cm^3) and allowed to stand at r.t. for a week. Filtration then yielded **12** (0.12 g, 13.6%), mp 259–261 °C (from methanol) (Found: C, 73.4; H, 5.4; N, 5.0. $C_{36}H_{32}N_2O_6$ requires C, 73.45; H, 5.5; N, 4.8%); ν_{max}(paraffin mull)/cm^{-1} 3460m, 1715s, 1660s, 1590m, 1510s, 1285s, 1215s, 1165s, 1140w, 1120s, 1070w, 1060s, 980s, 960m, 900m, 880m, 830s, 770s, 715s, 620s; δ_H($CDCl_3$) 7.98 (1 H, d, *J* 7.92), 7.64–6.94 (17 H, m), 6.64 (1 H, s, =CH), 5.61 (1 H, d, *J* 9.22), 5.06 (1 H, s), 5.03 (1 H, d, partly obscured by peak at 5.06), 4.19 (1 H, d, *J* 2.46), 3.82 (3 H, s, OCH_3), 2.96 (3 H, s, OCH_3), 2.34 (3 H, s, OCH_3); δ_C($CDCl_3$) 167.4 (C), 166.3 (C), 156.4 (C), 143.2 (C), 141.5 (C), 136.6 (C), 136.4 (C), 136.2 (C), 133.5 (C), 132.0 (CH), 130.3 (CH), 129.4 (CH), 129.1 (CH), 129.0 (CH), 128.9 (CH), 128.84 (CH), 128.77 (CH), 128.5 (CH), 127.8 (CH), 127.7 (CH), 127.2 (CH), 127.1 (CH), 124.8 (CH), 119.9 (C), 99.3 (C), 89.8 (CH), 66.0 (CH), 53.3 (CH), 52.9 (CH), 51.5 (CH_3), 51.4 (CH_3), 50.1 (CH_3); *m/z* (electrospray) 589 [$(M + 1)^+$, 15%], 557 [$(M - OCH_3)^+$, 100]. The structure of this product was confirmed by means of X-ray crystallography.

(5*R*)-*N*-{5-[4,5-Bis(methoxycarbonyl)-2-oxo-3-phenyl-2,5-dihydropyrrolyl]-5*H*-dibenzo[*a*,*d*]cyclohepten-10-yl}-phenylacetamide 14

The imine **8c** (0.60 g, 2 mmol) was dissolved in boiling chloroform (40 cm^3) in a round-bottomed flask fitted with a condenser and drying tube. DMAD (0.80 g) was added to the stirred solution which was then refluxed vigorously for 14 d. The reaction mixture was evaporated to dryness to give viscous brown material. This was boiled with methanol (10 cm^3), filtered while hot, and the filtrate allowed to stand at r.t. for 3 d. Filtration then yielded **14** (*ca.* 0.07 g, 10%), mp 253–255 °C (from methanol) (Found: C, 73.7; H, 5.3; N, 4.6. $C_{37}H_{30}N_2O_6$ requires C, 74.2; H, 5.05; N, 4.7%); *m/z* (EI; M^+ and > 10%) 598 (M^+, 6%), 421 (30), 325 (26), 324 (100), 232 (38), 216 (15), 207 (22), 206 (63), 179 (17), 178 (54), 129 (17), 91 (98). This material was insufficiently soluble in $(CD_3)_2SO$ for adequate NMR data to be obtained, and consequently the structure of this product was determined by means of X-ray crystallography.

Determination of the four crystal structures

Reflection data were measured at 21 °C with an Enraf-Nonius CAD-4 diffractometer in $\theta/2\theta$ scan mode using nickel filtered copper radiation (λ 1.5418 Å). Data were corrected for absorption using the method of de Meulenaer and Tompa.[28] Reflections with $I > 3\sigma(I)$ were considered observed. The structures were determined by direct phasing and Fourier methods. Hydrogen atoms were included in calculated positions and were assigned thermal parameters equal to those of the atom to which they were bonded. Positional and anisotropic thermal parameters for the non-hydrogen atoms were refined using full-matrix least-squares. Reflection weights used were $1/\sigma^2(F_o)$, with $\sigma(F_o)$ being derived from $\sigma(I_o) = [\sigma^2(I_o) + (0.04I_o)^2]^{\frac{1}{2}}$. The weighted residual is defined as $R_w = (\Sigma w\Delta^2/\Sigma wF_o^2)^{\frac{1}{2}}$. Atomic scattering factors and anomalous dispersion parameters were from International Tables for X-Ray Crystallography.[29] Structure solution was by MULTAN80[30]

and refinement used BLOCKLS, a local version of ORFLS.[31] ORTEP-II[32] running on a Macintosh IIcx was used for the structural diagrams (Figs. 1–4), and a DEC Alpha-AXP workstation was used for calculations.

In structure **14**, the carbonyl oxygen atom O(2) exhibited very high thermal motion. A disordered model of this ester group was therefore introduced in which the methoxy group remained common to both, but the carbonyl group occupied two alternative positions of approximately equal occupancy. Refinement was performed using RAELS,[33] a program capable of constrained refinement. The thermal motion of all atoms of the disordered ester group was described by a single *TL* group (where *T* is the translational tensor, and *L* is the librational tensor).

Atomic coordinates, thermal parameters and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Soc., Perkin Trans. 1*, 1996, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 207/28.

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