Stereocontrol in the intramolecular Buchner reaction of diazoamides and diazoesters

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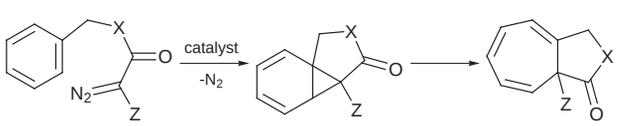
Received (in Cambridge) 30th September 1998, Accepted 28th October 1998

Dirhodium(II) catalysed decomposition of diazoamide **5** resulted in formation of β-lactams **6/7** by intramolecular C–H insertion, the intramolecular Buchner reaction being disfavoured for conformational reasons. The diazoamide **8**, however, gave products resulting from both the intramolecular Buchner reaction and C–H insertion. Chiral diazoesters **14**–**16** derived from α-substituted benzyl alcohols gave cycloheptatrienes in a highly diastereoselective manner; the norcaradiene isomer of the cycloheptatrienes was readily intercepted in a Diels–Alder reaction with 4-phenyl-1,2,4-triazoline-3,5-dione to give adducts **19**–**21**.

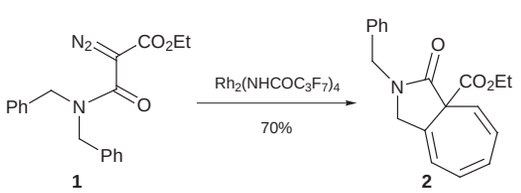
Introduction

The reaction of ethyl diazoacetate with aromatic hydrocarbons is one of the oldest known reactions of diazocarbonyl compounds, being first investigated by Buchner in the 1880s. Subsequently, the reaction has been widely studied, but it is only relatively recently with the introduction of dirhodium(II) catalysts that the intramolecular version of the reaction (Scheme 1) has become well known.[1,2] Examples of the intramolecular reaction starting from diazoketones (Scheme 1, X = CH_2),[1–3] diazoamides (X = NBu^t or CH_2NBu^t),[4] or diazoesters (X = O)[5] have all been described. The reaction involves initial formation of a norcaradiene intermediate which can ring open to give the cycloheptatriene; evidence for the involvement of norcaradienes comes from their interception in Diels–Alder cycloaddition reactions with 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD),[6] and from direct spectroscopic characterisation.[7]



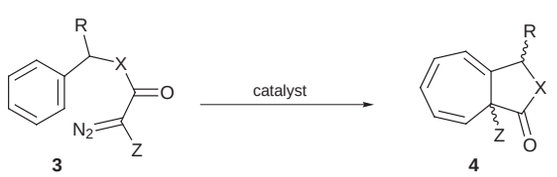
Scheme 1

Our interest in the intramolecular Buchner (IMB) reaction stemmed from our work on dirhodium(II) catalysed reactions of diazoamides, and the effect of the metal ligands on such reactions.[8,9] For example, dirhodium(II) perfluorobutyramide catalysed reaction of the *N*,*N*-dibenzyl diazomalonamide derivative **1** resulted in the formation of the cycloheptapyrrolone **2** (70%) by the IMB reaction (Scheme 2), together with small amounts (12%) of a β-lactam formed by intramolecular C–H insertion into the benzylic CH_2-group.[9]



Scheme 2

Since the trienes formed in such cyclisations contain a new chiral centre at the ring junction, we decided to investigate the possibility of diastereocontrol in the IMB reaction using substrates containing an existing stereocentre as illustrated in general in Scheme 3. At the outset of our work there were conflicting reports in the literature on the stereochemical outcome of the IMB reaction. In early work using copper catalysis, Julia and co-workers reported that diazoester **3** (R = Me, X = O, Z = CO_2Me) gave a 1:1 mixture of cycloheptatrienes **4** in poor yield.[10,11] Subsequently Doyle and co-workers studied a related reaction **3** (R = Ph, X = O, Z = H) using a range of dirhodium(II) catalysts, although they did not comment on the stereochemistry of the resulting cycloheptatriene.[12] The dirhodium(II) catalysed IMB reaction of diazoketone **3** (R = Me, X = CH_2CH_2, Z = H) was reported to proceed with complete lack of diastereoselectivity,[13] whereas a related α-phenoxy-α-methyl diazoketone, *i.e.* a substrate similar to the diazocarbonyl compound **3** in which the CHR and X (= O) groups reversed, gave a single cycloheptafuranone with the substituents *cis*.[14] During the course of our studies, three further reports appeared. Zaragoza described the dirhodium(II) acetate catalysed decomposition of a diazoamide **3** (R = 2-tolyl, X = NCH-(CO_2Me)CH_2Ph, Z = Ac) which resulted in formation of a mixture of diastereomeric cycloheptapyrrolones in a ratio of 87:13 (de 74%), with the isomer with the R and Z groups *trans* to each other predominating.[15] The preference for *trans*-diastereoselectivity in the IMB reaction of a series of diazoketones **3** (R = Me, Pr, i-Pr, Bu, Bu^t, X = CH_2, Z = Me) was unambiguously confirmed by Maguire and co-workers; in all cases the diastereocontrol was excellent.[16] The details of this work are described in the following paper.[17] Finally, very recent work by a Japanese group has established that suitably substituted



Scheme 3

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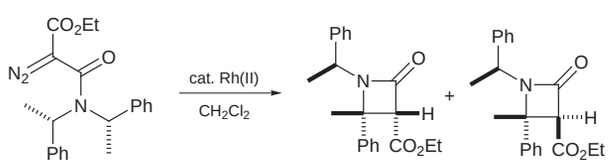
diazoesters also undergo IMB reaction with *trans*-diastereoselectivity.[18]

Results and discussion

Chiral diazoamides as substrates for the intramolecular Buchner reaction

A series of homochiral diazoamide substrates was prepared and the dirhodium(II) catalysed decomposition chemistry was investigated. The first substrate, as a direct analogy to dibenzyldiazoamide **1**, was the homochiral C_2 symmetric bis(α-methylbenzyl)diazomalonamide ester **5** which was readily prepared in 47% yield from commercially available (−)-bis[(*S*)-1-phenylethyl]amine and ethyl diazomalonyl chloride,[19] the moderate yield reflecting the steric crowding around the nucleophilic amine nitrogen. The diazoamide **5** with two identical phenyl rings appropriately tethered to the diazo moiety augured well for a good yield of IMB reaction products by analogy with the similar achiral diazoamide **1**. Moreover, potential for diastereoselection in the transformation was envisaged, with control being effected by the chiral centre close to the reacting aromatic ring. In the event, the catalyst of choice for effecting carbenoid additions to aromatic rings,[8,9] dirhodium(II) perfluorobutyramide, led to the formation of only trace amounts (by NMR) of the desired triene(s), and the actual isolated products were a mixture of the β-lactam **6** along with its epimer **7** (Scheme 4) in



5 **6** **7**

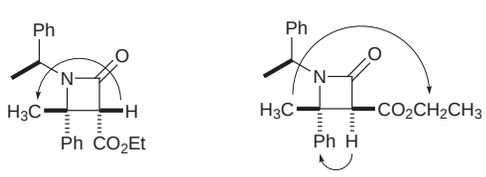
catalyst	yield **6** (%)	yield **7** (%)
$Rh_2(NHCOC_3F_7)_4$	41	27
$Rh_2(OAc)_4$	47	29

Scheme 4

an overall yield of about 70%. Dirhodium(II) acetate catalysed decomposition of **5** gave a very similar result (Scheme 4), illustrating that unlike the reaction of diazoamide **1**, there are no significant ligand effects.[9] The formation of β-lactams by intramolecular C–H insertion reactions of rhodium carbenoids is well known.[1,2]

The assignment of relative stereochemistry in the product β-lactams **6** and **7** was made from NMR studies. In particular, NOE experiments showed clearly the relative stereochemistry in the lactam ring (Fig. 1). The absolute stereochemistry of the lactam rings was assigned on the assumption that the intramolecular C–H insertion reaction, which affords the β-lactam products, proceeds with retention of stereochemistry at the reacting chiral centre. Retention of configuration at the reacting C–H bond during dirhodium(II) mediated intramolecular C–H insertion reactions is precedented in the literature, for example in Taber's total synthesis of (+)-α-cuparenone,[20] and in the synthesis of (+)-grandisol reported by Monteiro and Zukerman-Schpector.[21]

The change in chemoselectivity from the IMB reaction in the



6 **7**

Fig. 1 Selected NOE correlations for the lactams **6** and **7**.

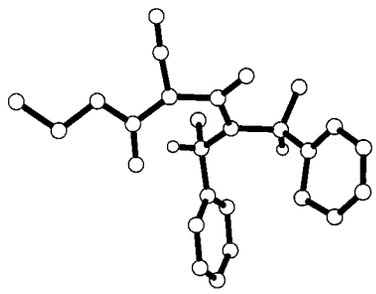


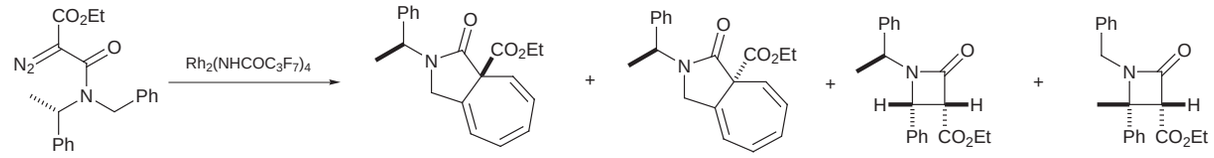
Fig. 2 Unrefined X-ray crystal structure of C_2 symmetric diazoamide **5**.

dirhodium(II) catalysed decomposition of achiral dibenzyldiazoamide **1** to C–H insertion with the chiral diazoamide **5** was disappointing, but we believe that the explanation lies in the conformation of the starting diazoamide **5**. Although we do not know the exact nature of the intermediate metal carbenoid, the conformation of the starting diazoamide **5** was readily obtained by a single crystal X-ray analysis (Fig. 2), although the small size of the crystals precluded full anisotropic refinement of the structure. However, enough information was obtained to confirm that the two phenyl rings are in a position remote to the diazo (and supposedly the carbenoid) centre, and are in a favourable edge-to-face orientation. On the other hand, the actual sites of attack in the carbenoid reaction (the benzylic methines) were shown to be in close proximity to the diazo carbon. It is interesting that in Doyle's study of the IMB reaction of *N*-benzyl-*N*-(3,4-dimethoxybenzyl)diazoacetamide, the observed, but unexpected, addition to the less electron rich aromatic ring was also explained on the grounds of a preferred conformation of the metal carbenoid intermediate.[4a]

In an attempt to remove some of the conformational constraint that appeared to be preventing the IMB reaction of diazoamide **5**, the less hindered substrate **8** was prepared by diazoacylation of commercially available (*S*)-(−)-*N*-benzyl-1-phenylethylamine. Under dirhodium(II) perfluorobutyramide catalysis there was a significant amount of trienic material formed. However, the isolated yield of the diastereomeric pair of cycloheptatrienes **9** and **10** amounted to only 35% after flash silica gel column chromatography, the remainder being an equal mixture of the β-lactams **11** and **12** which were isolated in 40% combined yield (Scheme 5). These two pairs were further separated by preparative HPLC, and subsequent NMR and analytical HPLC analysis showed that the trienes **9** and **10** were formed in a ratio of 56:44, that is, with only 12% de, although it is not known which of **9/10** is the major diastereomer. The diastereocontrol afforded by the chiral α-methylbenzyl group is clearly limited due to its remoteness from the reacting centres. It is noteworthy that, again, there was no detected attack on the phenyl ring of the α-methylbenzyl moiety. Dirhodium(II) acetate and dirhodium(II) trifluoroacetate catalysed decomposition of **8** gave broadly similar results.

The final diazoamide investigated was **13** derived from the commercially available amine and ethyl diazomalonyl chloride in 93% yield. However, no IMB reaction products could be isolated from its dirhodium(II) perfluorobutyramide catalysed decomposition, and the only product identified in the complex reaction mixture appeared to be a *trans* β-lactam arising from intramolecular C–H insertion into the *N*-methyl group, although the material could never be characterised. The X-ray crystallographic analysis of a single crystal of diazoamide **13** showed a conformation in which the diazo carbon was found to be in close proximity to the *N*-methyl group which is apparently attacked in its rhodium catalysed reaction (Fig. 3), although again the small size of the crystals precluded full anisotropic refinement of the structure.

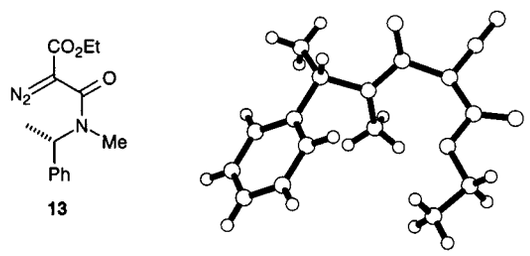
Hence it is clear that steric and conformational effects inherent in the above diazoamides override the chemoselective attack on aromatic rings normally favoured by dirhodium(II)



8 **9** **10** **11** (20%) **12** (20%)

combined yield of **9** and **10** = 35%; de = 12%

Scheme 5



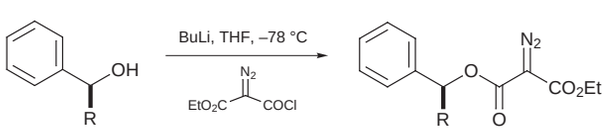
13

Fig. 3 Unrefined X-ray crystal structure of diazoamide **13**.

perfluorobutyramide catalysed decomposition of diazoamides. Therefore alternative diazocarbonyl substrates were considered.

Chiral diazomalonates as substrates for the intramolecular Buchner reaction

In pursuit of diastereoselection in the IMB reaction, attention was turned to the reactions of chiral diazoesters, the most readily available substrates being chiral diazomalonates derived in one step from commercially available homochiral α-alkylbenzyl alcohols. Initial efforts to prepare the chiral diazomalonate **14**, from commercial α-methylbenzyl alcohol and ethyl diazomalonyl chloride using amine bases were low yielding. After some experimentation it was found that treatment of the alcohol with *n*-butyllithium in tetrahydrofuran at about −78 °C, followed by addition of a slight excess of the diazo acid chloride gave the best results. Using the *n*-butyllithium method the homologous series of chiral diazomalonates **14**–**16** was prepared in high yield from their respective, commercially available chiral alcohol precursors (Scheme 6). In order to prove that optical purity was not compromised

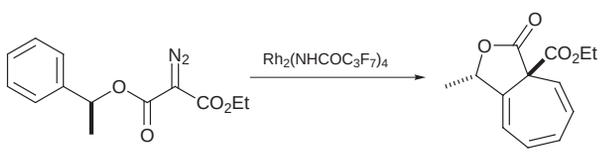


14 R = Me (76%)
15 R = Et (86%)
16 R = Pr (75%)

Scheme 6

by the strong base, the racemate of **14** was prepared using the same method and the product was isolated in an excellent 94% yield. This racemic diazo compound proved to be an excellent substrate for analysis by chiral shift NMR spectroscopy. Thus, addition of 0.2 equivalents of $Eu(hfc)_3$ split the three proton doublet at 1.60 ppm into two equal doublets at 1.65 and 1.78 ppm, proving the racemic nature of this compound. The same conditions with the product **14**, derived from homochiral (*S*)-phenylethyl alcohol, did not result in any splitting of the peak, and thus it was concluded that the diazoester **14** had completely retained chirality within the limits of observation inherent in such an NMR experiment.

Homochiral diazomalonate **14** was found to decompose fairly rapidly at room temperature under dirhodium(II) perfluorobutyramide catalysis in dichloromethane solution. Analysis of the ^{1}H NMR spectrum of the crude mixture revealed a disappointingly complex mixture but it was clear that trienic material formed a significant component. After flash silica gel column chromatography the desired cycloheptafuranone **17** was isolated in about 27% yield as an oil (Scheme 7). The yield could not be improved by changing the reaction



14 **17** (27%)

Scheme 7

conditions. Close inspection of the ^{1}H NMR spectrum of the crude mixture demonstrated that the attack of the carbenoid had indeed been completely diastereoselective, attacking the aromatic ring from one face only. Attack was assumed to be from the less hindered face, that opposite to the methyl group and giving rise to a triene with the methyl group *trans* or anti to the ethyl ester group. This mode of attack also passes the transient carbenoid through a conformation which minimises $A^{1,3}$ strain.[16] However, attempts to confirm this relative stereochemistry by NOE studies were unsuccessful. It is interesting that no β-lactones, derived by intramolecular insertion into the benzylic C–H bond, were detected in the above reaction, although this is a known process in the dirhodium(II) catalysed decomposition of diazomalonates.[22]

Since cycloheptatrienes have been shown to exist in dynamic equilibrium with their norcaradiene isomers, and such dienes can be intercepted in [4 + 2]-cycloadditions with reactive dienophiles such as PTAD,[6] the triene **17** was treated with PTAD to give quantitative conversion to a single product which was fully characterised as **19**, the cycloadduct of a putative norcaradiene **18** (Scheme 8). More importantly adduct **19** gave crystals suitable for X-ray analysis (Fig. 4), and although the small size of the crystals precluded full anisotropic refinement of the structure, enough information to confirm the relative stereochemistry was obtained. This established that the stereochemical outcome of the reaction was as postulated, giving rise to a product in which the R (alkyl) group is disposed *anti* to the ester moiety.

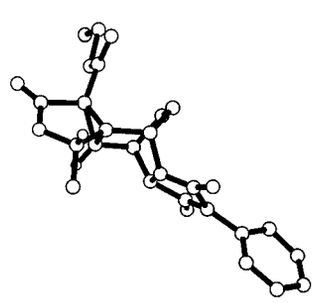
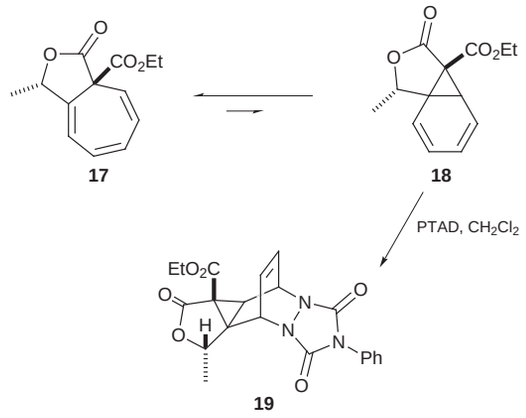


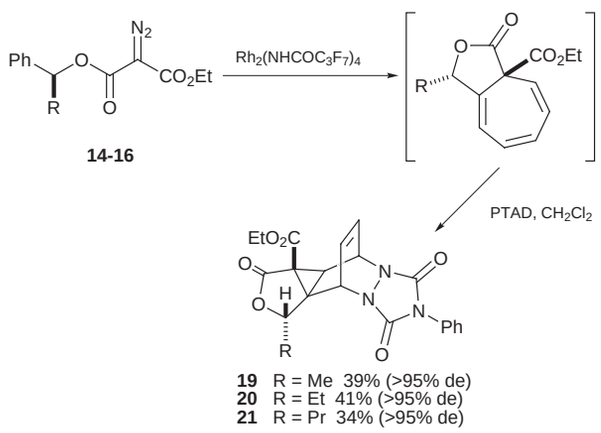
Fig. 4 Unrefined X-ray structure of the cycloadduct **19**.

Since the starting diazomalonate **14** was homochiral, it would be expected that the single diastereomeric triene **17** should also be a single enantiomer. The first evidence of this was that the material significantly rotated the plane of polarised light ($[\alpha]_D^{25}$ −127°, $c = 0.09$ in $CHCl_3$). To confirm the optical



Scheme 8

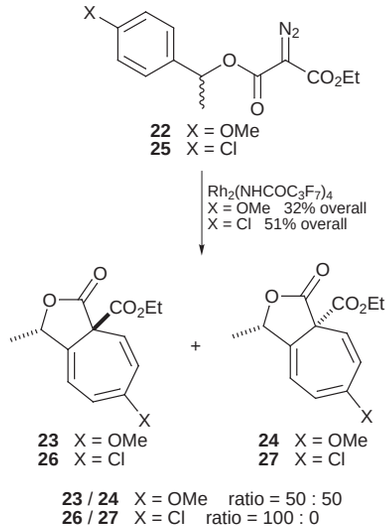
purity of triene **17**, racemic diazomalonate (±)-**14** was decomposed under dirhodium(II) perfluorobutyramide catalysis in dichloromethane; purification of the crude product by flash silica gel column chromatography afforded the racemic cycloheptafuranone (±)-**17** as a single diastereoisomer in about 20% yield. Chiral shift NMR using $Eu(hfc)_3$ did not give any useful splitting of peaks, and therefore chiral HPLC separation of the racemate was attempted. Suitable conditions, as described in the Experimental section, were readily found and this allowed comparison with the product **17** from decomposition of homochiral **14**. It was thus conclusively demonstrated that, within experimental limits, the result was a single enantiomer (>97% ee) arising from a highly stereoselective IMB reaction.



Scheme 9

The two steps of the IMB reaction followed by the [4 + 2]-cycloaddition with PTAD could be performed sequentially in one pot without isolation of the triene intermediate **17**. Thus the diazomalonate **14** was heated under reflux in dichloromethane in the presence of dirhodium(II) perfluorobutyramide for 30 min, then the mixture was cooled to 0 °C before addition of PTAD (1 equivalent) and purification by flash silica gel column chromatography to give the polycyclic cycloadduct **19** in 39% yield (from **14**) as a crystalline solid. This yield is higher than the isolated yield of the triene **17** (28%), and since the [4 + 2]-cycloaddition was shown to be essentially quantitative, it would appear that the triene is partly lost during flash silica gel column chromatography. The diazomalonates **15** and **16** were similarly converted by the one-pot protocol to their respective cycloaddition products **20** and **21** in moderate overall yields, but in excellent diastereoselectivity (Scheme 9).

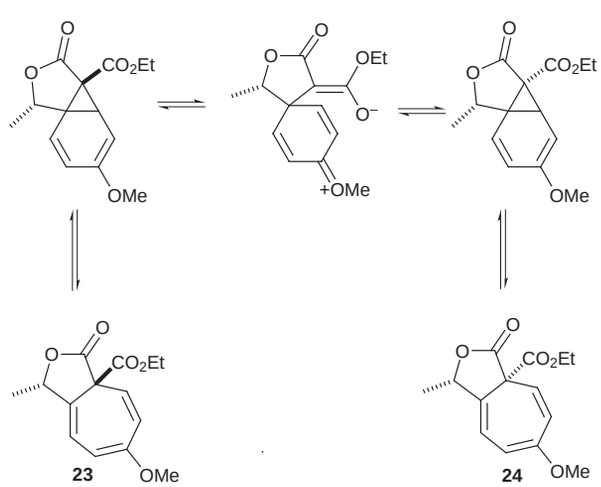
In an attempt to improve the yield of the IMB reaction, racemic diazomalonate **22**, which has a methoxy substituted aryl ring, was prepared and decomposed with dirhodium(II)



Scheme 10

perfluorobutyramide in the standard fashion (Scheme 10). Remarkably, the result was a 1:1 mixture of *anti*- and *syn*-diastereomers **23** and **24**, recovered in a disappointing yield of only 32% after flash silica gel column chromatography.

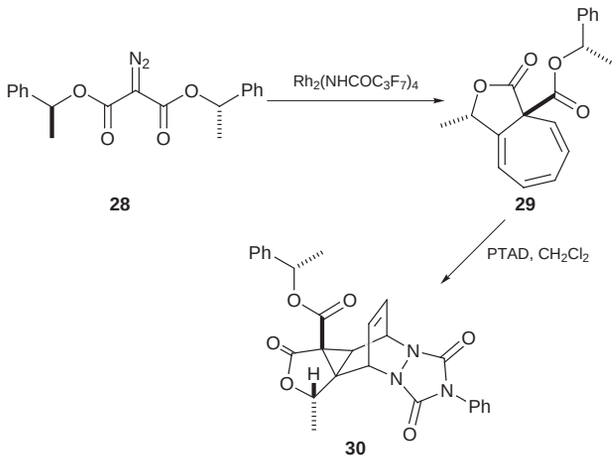
It is believed that the apparent complete lack of diastereoselection was a result of epimerisation of the newly formed chiral centre in an intermediate norcaradiene initially formed as a single *anti*-diastereomer. This epimerisation is promoted by the methoxy substituent in the original aromatic ring which assists the cleavage of one of the newly formed C–C bonds, leading to equilibration of norcaradienes as shown in Scheme 11. Evidence in support of this equilibration involving the



Scheme 11

methoxy group came from the racemic 4-chlorophenyl diazomalonate **25**, dirhodium(II) perfluorobutyramide catalysed decomposition of which gave, as expected, the chloro-substituted cycloheptafuranone **26** in moderate yield (51%) as a single *anti*-diastereomer (Scheme 10). No trace of the isomeric triene **27** was detected.

Finally the C_2 symmetric diazomalonate **28** was investigated. This substrate was readily prepared by diazo transfer onto the active methylene of the corresponding C_2 symmetric malonate, which itself was available by standard dicyclohexylcarbodiimide (DCC) mediated condensation of two equivalents of (*S*)-(−)-1-phenylethanol with malonic acid. Dirhodium(II) perfluorobutyramide catalysed decomposition of diazoester **28** gave the chiral cycloheptafuranone **29** as a single *anti*-diastereomer, and this was isolated as its PTAD cycloadduct **30** in 47% yield (from **28**) (Scheme 12).



Scheme 12

In conclusion, although the chiral diazoamides investigated are apparently prevented from undergoing an efficient IMB reaction by conformational constraints, we have shown that chiral diazoesters do indeed undergo the IMB reaction with complete *anti*-diastereoselectivity. These excellent levels of diastereocontrol are also found in the IMB reactions of diazoketones as described in the following paper.[17]

Experimental

For general experimental details, see ref. 8. Coupling constants (*J*) are given in Hz. GGATR refers to IR spectra obtained by golden-gate attenuated total internal reflection. Light petroleum refers to the fraction with bp 40–60 °C.

General procedure for the preparation of chiral diazoamides

A stirred solution of the appropriate amine (1.0 equiv.) in dry dichloromethane (10 ml per mmol alcohol) was treated with triethylamine (2.0 equiv.), and ethyl diazomalonyl chloride (1.0 equiv.) was added and the resulting mixture stirred for a further 3–18 h. The mixture was washed with dilute HCl (2 M), brine, then dried (Na_2SO_4), filtered and concentrated under reduced pressure to give the crude product. Flash silica gel column chromatography gave the diazoamides as oils or solids (recrystallised as indicated below).

Ethyl 2-diazo-3-{bis[(1*S*)-1-phenylethyl]amino}-3-oxopropanoate 5. Prepared from (−)-bis[(*S*)-1-phenylethyl]amine hydrochloride salt (47%); mp 52–53 °C (light petroleum) (Found: C, 69.0; H, 6.45; N, 11.4. $C_{21}H_{23}N_3O_3$ requires C, 69.0; H, 6.3; N, 11.5%); $[a]_D^{21}$ −85.4 ($c = 0.192$, $CHCl_3$); ν_{max}(GGATR)/cm^{-1} 2983, 2127, 1715, 1615, 1417, 1323, 1283, and 1099; δ_H (300 MHz; $CDCl_3$) 1.30 (3H, t, *J* 7.1), 1.77 (6H, d, *J* 7.0), 4.26 (2H, q, *J* 7.1), 4.91 (2H, q, *J* 7.0), and 7.10–7.25 (10H, m); δ_C (75.5 MHz; $CDCl_3$) 14.4 (CH_3), 18.6 (CH_3), 55.9 (NCH), 61.4 (OCH_2), 127.2 (CH), 127.7 (CH), 128.0 (CH), 140.4 (C), 160.3 (C=O), and 163.2 (C=O); diazo C unobserved; *m*/*z* 337 (M − N_2^+, 2%), 264 (M − N_2 − CO_2Et^+, 6), 222 (14), 208 (8), 190 (24), 105 (100), and 77 (31).

Rhodium catalysed decomposition of diazoamide 5. A solution of diazoamide **5** (0.100 g, 0.274 mmol) in dry dichloromethane (5.5 ml) was treated with dirhodium(II) perfluorobutyramide (0.006 g) and the mixture stirred at room temperature until the starting material was consumed (TLC; about 21 h). The mixture was preadsorbed onto silica and subjected to flash silica gel column chromatography to afford a mixure of **6** and **7**.

Ethyl (2R,3R)-2-methyl-4-oxo-2-phenyl-1-[(1S)-1-phenylethyl]azetidine-3-carboxylate **6** (41%) (Found: M^+, 337.1669. $C_{21}H_{23}NO_3$ requires 337.1678); ν_{max}(film)/cm^{-1} 3064, 2981, 2935, 1760, 1732, 1448, 1316, 1262, 1029, 913, 731, and 699; δ_H (300 MHz; $CDCl_3$) 0.76 (3H, t, *J* 7.1), 1.72 (3H, d, *J* 7.1), 1.91 (3H, s), 3.64 (2H, m), 3.96 (1H, s), 4.40 (1H, q, *J* 7.1), 7.17 (5H, m), 7.26–7.40 (3H, m), and 7.46 (2H, m); δ_C (75.5 MHz; $CDCl_3$) 13.5 (CH_3), 21.7 (CH_3), 25.0 (CH_3), 54.9 (CH), 60.9 (OCH_2), 64.9 (C), 66.9 (CH), 126.7 (CH), 127.4 (CH), 127.5 (CH), 127.9 (CH), 128.0 (CH), 128.7 (CH), 138.5 (C), 141.9 (C), 160.7 (C=O), and 166.1 (C=O); *m*/*z* 337 (M^+, 2%), 322 (2), 264 (M − CO_2Et^+, 6), 190 (98), 160 (23), 145 (72), 132 (25), 115 (34), 105 (100), and 77 (38).

Ethyl (2R,3S)-2-methyl-4-oxo-2-phenyl-1-[(1S)-1-phenylethyl]azetidine-3-carboxylate **7** (27%) (Found: M^+, 337.1672. $C_{21}H_{23}NO_3$ requires 337.1678); ν_{max}(film)/cm^{-1} 2978, 1755, 1725, 1679, 1447, 1307, 1256, and 1179; δ_H (300 MHz; $CDCl_3$) 1.29 (3H, t, *J* 7.1), 1.62 (3H, d, *J* 7.2), 1.72 (3H, s), 3.93 (1H, s), 4.25 (2H, m), 4.51 (1H, q, *J* 7.2), and 7.20–7.40 (10H, m); δ_C (75.5 MHz; $CDCl_3$) 14.3 (CH_3), 19.6 (CH_3), 20.7 (CH_3), 54.8 (NCH), 61.4 (OCH_2), 62.9 (C), 66.5 (CH), 125.5 (CH), 127.3 (CH), 127.6 (CH), 128.0 (CH), 128.5 (CH), 128.6 (CH), 141.5 (C), 142.1 (C), 162.7 (C=O), and 166.7 (C=O); *m*/*z* 337 (M^+, 1%), 322 (1), 264 (M − CO_2Et^+, 8), 190 (76), 145 (65), 132 (24), 115 (26), 105 (100), 91 (12), and 77 (38).

Dirhodium(II) acetate catalysed decomposition of diazoamide **5** at room temperature in dichloromethane for 71 h gave a mixture of **6** and **7** (47 and 29% isolated yields respectively).

Ethyl 3-{benzyl[(1*S*)-1-phenylethyl]amino}-2-diazo-3-oxopropanoate 8. Prepared from (*S*)-(−)-*N*-benzyl-1-phenylethylamine (75%) (Found: MH^+, 352.1661. $C_{20}H_{22}N_3O_3$ requires 352.1661); $[a]_D^{22}$ −74.0 ($c = 0.164$, $CHCl_3$); ν_{max}(GGATR)/cm^{-1} 3029, 2125, 1706, 1621, 1411, 1280, 1107, and 747; δ_H (300 MHz; $CDCl_3$) 1.29 (3H, t, *J* 7.1), 1.62 (3H, d, *J* 7.0), 4.03 (1H, AB, *J* 16.1), 4.26 (2H, q, *J* 7.1), 4.66 (1H, AB, *J* 16.1), 5.47 (1H, q, *J* 7.0), and 7.09–7.40 (10H, m); δ_C (75.5 MHz; $CDCl_3$) 14.4 (CH_3), 17.3 (CH_3), 47.6 (NCH_2), 56.5 (NCH), 61.4 (OCH_2), 67.2 (C=N_2), 126.7 (CH), 127.0 (CH), 127.2 (CH), 127.6 (CH), 128.4 (CH), 128.6 (CH), 138.2 (C), 140.4 (C), 162.5 (C=O), and 162.6 (C=O); *m*/*z* 352 (MH^+, 18%), 341 ([MNH_4 − N_2]$^+$, 12), 326 (22), 210 (100), 134 (24), and 120 (14).

Rhodium catalysed decomposition of diazoamide 8. A solution of diazoamide **8** (0.140 g, 0.40 mmol) in dry dichloromethane (8 ml) was treated with dirhodium(II) perfluorobutyramide (catalytic amount) and the mixture stirred at room temperature until the starting material was consumed (TLC; about 48 h). The mixture was preadsorbed onto silica and subjected to flash silica gel column chromatography to afford a mixure of diastereomers **9** and **10** (56:44 ratio by analytical HPLC; 12% de; 0.045 g, 35%) along with a mixture of **11** and **12** (0.051 g, 40%). The two mixtures were separated by preparative HPLC (Dynamax column; eluent 10:90 and 2:98 ethyl acetate–hexane for the two mixtures respectively; flow rate 15 ml min^{-1}; UV detection at 260 nm) to give each component as a colourless oil: *ethyl (3aS)-3-oxo-2-[(1S)-1-phenylethyl]-1,2,3,3a-tetrahydrocyclohepta[c]pyrrole-3a-carboxylate* and *ethyl (3aR)-3-oxo-2-[(1S)-1-phenylethyl]-1,2,3,3a-tetrahydrocyclohepta[c]-pyrrole-3a-carboxylate* **9**/**10**.

Diastereomer 1 (Found: M^+, 323.1515. $C_{20}H_{21}NO_3$ requires 323.1521); ν_{max}(film)/cm^{-1} 2925, 2853, 1740, 1706, 1497, 1455, 1388, 1224, 1028, 735, and 700; δ_H (250 MHz; $CDCl_3$) 1.11 (3H, t, *J* 7.1), 1.59 (3H, d, *J* 7.1), 3.95–4.25 (4H, m), 5.60–5.65 (2H, m), 6.25 (1H, m), 6.40–6.52 (3H, m), and 7.25–7.50 (5H, m); δ_C (75.5 MHz; $CDCl_3$) 14.0 (CH_3), 16.2 (CH_3), 46.2 (NCH_2), 49.5 (NCH), 61.7 (OCH_2), 120.5 (CH), 122.5 (CH), 127.1 (CH), 127.7 (CH), 128.2 (CH), 128.3 (CH), 128.6 (CH), 129.9 (CH), 130.7 (C), 139.3 (C), 168.0 (C=O), and 171.1 (C=O); *m*/*z* 323 (M^+, 2%), 250 (74), 176 (8), 146 (12), 128 (14), 105 (100), 91 (38), and 77 (20).

Diastereomer 2 (Found: M^+, 323.1515. $C_{20}H_{21}NO_3$ requires 323.1521); ν_{max}(film)/cm^{-1} 2981, 2928, 1734, 1702, 1654, 1457,

1363, 1223, 1028, and 700; δ_H (250 MHz; $CDCl_3$) 1.17 (3H, t, *J* 7.1), 1.63 (3H, d, *J* 7.1), 3.72 and 4.33 (2 × 1H, AB, *J* 15.0), 4.00–4.25 (2H, m), 5.60 (1H, q, *J* 7.1), 5.64 (1H, m), 6.22 (1H, m), 6.39–6.46 (3H, m), and 7.25–7.45 (5H, m); δ_C (75.5 MHz; $CDCl_3$) 14.1 (CH_3), 15.9 (CH_3), 46.3 (NCH_2), 49.8 (NCH), 61.7 (OCH_2), 120.6 (CH), 122.4 (CH), 127.0 (CH), 127.8 (CH), 128.0 (CH), 128.4 (CH), 128.7 (CH), 129.8 (CH), 130.9 (C), 139.2 (C), 167.8 (C=O), and 170.6 (C=O); *m*/*z* 323 (M^+, 2%), 250 (63), 176 (10), 146 (13), 128 (15), 105 (100), 91 (8), and 77 (18).

Ethyl (3R,4R)-2-oxo-4-phenyl-1-[(1S)-1-phenylethyl]-azetidine-3-carboxylate **11** (Found: M^+, 323.1524. $C_{20}H_{21}NO_3$ requires 323.1521); ν_{max}(film)/cm^{-1} 2980, 1761, 1720, 1496, 1456, 1371, 1299, 1185, 1018, and 769; δ_H (300 MHz; $CDCl_3$) 0.81 (3H, t, *J* 7.1), 1.44 (3H, d, *J* 7.2), 3.76 (2H, q, *J* 7.1), 4.19 (1H, d, *J* 6.3), 4.59 (1H, d, *J* 6.3), 5.06 (1H, q, *J* 7.2), and 7.20–7.40 (10H, m); δ_C (75.5 MHz; $CDCl_3$) 13.6 (CH_3), 19.3 (CH_3), 53.0 (CH), 52.1 (CH), 60.0 (CH), 61.1 (CH_2), 127.3 (CH), 127.5 (CH), 128.0 (CH), 128.3 (CH), 128.8 (CH), 128.9 (CH), 135.5 (C), 139.4 (C), 163.1 (C=O), and 165.8 (C=O); *m*/*z* 323 (M^+, 2%), 250 (1), 194 (8), 176 (86), 148 (19), 131 (83), 105 (100), and 77 (36).

Ethyl (2R,3R)-1-benzyl-2-methyl-4-oxo-2-phenylazetidine-3-carboxylate **12** (Found: M^+, 323.1527. $C_{20}H_{21}NO_3$ requires 323.1521); ν_{max}(film)/cm^{-1} 3023, 1768, 1723, 1217, and 749; δ_H (300 MHz; $CDCl_3$) 0.80 (3H, t, *J* 7.1), 1.66 (3H, s), 3.67 (2H, q, *J* 7.1), 3.99 (1H, s), 4.07 and 4.84 (2 × 1H, AB, *J* 15.0), and 7.25–7.40 (10H, m); δ_C (75.5 MHz; $CDCl_3$) 13.6 (CH_3), 25.2 (CH_3), 44.6 (NCH_2), 61.0 (OCH_2), 64.8 (C), 67.5 (CH), 126.5 (CH), 127.0 (CH), 128.2 (CH), 128.4 (CH), 128.7 (CH), 128.8 (CH), 136.3 (C), 137.8 (C), 162.7 (C=O), and 165.8 (C=O); *m*/*z* 323 (M^+, 1%), 250 (17), 208 (15), 190 (50), 161 (12), 145 (44), 115 (17), 91 (100), and 77 (14).

Diazomalonate **8** (0.052 g, 0.148 mmol) in dichloromethane (3 ml) was decomposed under $Rh_2(OAc)_4$ catalysis at room temperature. The reaction was followed by ^1H NMR and took about 5 days to go to completion. NMR analysis of the mixture showed a mixture of **9**, **10**, **11**, and **12** in a ratio of approximately 10 : 10 : 15 : 65.

Diazomalonate **8** (0.051 g, 0.145 mmol) in dichloromethane (2.9 ml) was decomposed under $Rh_2(O_2CCF_3)_4$ catalysis at room temperature. The reaction was followed by ^1H NMR and took about 5 days to go to completion, including one day at reflux and addition of more catalyst. NMR analysis of the mixture showed a mixture of **9**, **10**, **11**, and **12** in a ratio of approximately 16 : 16 : 33 : 33.

Ethyl 3-{methyl[(1*S*)-1-phenylethyl]amino}-2-diazo-3-oxopropanoate 13. Prepared from (*S*)-(−)-*N*,α-dimethylbenzylamine (93%); mp 30–31 °C (pentane) (Found: C, 61.1; H, 6.45; N, 15.1. $C_{14}H_{17}N_3O_3$ requires C, 61.1; H, 6.2; N, 15.3%) (Found: M^+, 275.1271. $C_{14}H_{17}N_3O_3$ requires 275.1270); $[\alpha]_D^{21}$ −163.0 (*c* = 0.378, $CHCl_3$); ν_{max}(CH_2Cl_2)/cm^{-1} 2948, 2940, 2133, 1710, 1618, 1400, 1288, 1267, 1076, and 896; δ_H (250 MHz; $CDCl_3$) 1.29 (3H, t, *J* 7.1), 1.60 (3H, d, *J* 7.0), 2.69 (3H, s), 4.25 (2H, q, *J* 7.1), 5.65 (1H, q, *J* 7.0), and 7.22–7.40 (5H, m); δ_C (100.6 MHz; $CDCl_3$) 14.4 (CH_3), 15.9 (CH_3), 31.0 (NCH_3), 53.7 (NCH), 61.4 (OCH_2), 66.6 ($C=N_2$), 127.2 (CH), 127.4 (CH), 128.5 (CH), 139.9 (C), 162.0 (C=O), and 162.4 (C=O); *m*/*z* 276 (MH^+, 78%), 275 (<1), 248 (66), 190 (52), 174 (85), 134 (83), 118 (72), and 105 (100).

General procedure for the preparation of chiral diazomalonates

A solution of the appropriate homochiral alcohol (1.0 equiv.) in dry THF (10 ml per mmol alcohol) was cooled to −78 °C and treated with *n*-BuLi (1.6 M solution in hexanes; 1.2 equiv.). After stirring for 1 h, ethyl diazomalonyl chloride (1.3 equiv.) was added and the resulting mixture stirred for a further 2 h whilst allowing the temperature to rise to ambient level. The reaction was quenched with saturated NH_4Cl, diluted with water and extracted with EtOAc (×3). The combined extracts were washed with water and saturated brine, then dried (Na_2SO_4), filtered and concentrated under reduced pressure to give the crude product. Flash silica gel column chromatography (eluting with 9 : 1 light petroleum–EtOAc) afforded the desired product as a pale yellow oil.

Ethyl [(1*S*)-1-phenylethyl] 2-diazomalonate 14. (76%), oil (Found: M + NH_4^+, 280.1297. $C_{13}H_{18}N_3O_4$ requires 280.1297); $[\alpha]_D^{25}$ +29.0 (*c* = 0.276, $CHCl_3$); ν_{max}(GGATR)/cm^{-1} 3023, 2983, 2938, 2144, 1748, 1728, 1689, 1369, 1339, 1310, 1271, 1081, and 750; δ_H (300 MHz; $CDCl_3$) 1.32 (3H, t, *J* 7.1), 1.60 (3H, d, *J* 6.6), 4.30 (2H, q, *J* 7.1), 6.04 (1H, q, *J* 6.6), and 7.39–7.26 (5H, m); Chiral Shift NMR: δ_H (250 MHz; $CDCl_3$), $Eu(hfc)_3$ (0.2 equiv.) CH_3 doublet does not split (*cf*. racemate); δ_C (75.5 MHz; $CDCl_3$) 14.3 (CH_3), 22.4 (CH_3), 61.7 (CH_2), 73.8 (CH), 126.0 (CH), 128.1 (CH), 128.6 (CH), 141.0 (C), 160.5 (C=O), and 161.0 (C=O); diazo C unobserved; *m*/*z* (CI) 280 (M + NH_4^+, 14%), 254 (20), 176 (100), 138 (75), 122 (95), and 105 (39).

Ethyl [(1*S*)-1-phenylpropyl] 2-diazomalonate 15. (86%), oil (Found: M + NH_4^+, 294.1454. $C_{14}H_{20}N_3O_4$ requires 294.1454); $[\alpha]_D^{23}$ +6.8 (*c* = 0.35, $CHCl_3$); ν_{max}(film)/cm^{-1} 2974, 2879, 2142, 1762, 1734, 1685, 1373, 1323, 1269, and 1096; δ_H (300 MHz; $CDCl_3$) 0.90 (3H, t, *J* 7.3), 1.31 (3H, t, *J* 7.2), 1.80–2.00 (2H, m), 4.29 (2H, q, *J* 7.2), 5.81 (1H, t, *J* 6.8), and 7.39–7.25 (5H, m); δ_C (75.5 MHz; $CDCl_3$) 9.8 (CH_3), 14.4 (CH_3), 29.4 (CH_2), 61.6 (CH_2), 65.4 ($C=N_2$), 78.7 (CH), 126.5 (CH), 128.1 (CH), 128.5 (CH), 139.8 (C), 160.6 (C=O), and 161.0 (C=O); *m*/*z* (CI) 294 (M + NH_4^+, 34%), 268 (21), 176 (100), 152 (80), 149 (35), 135 (34), and 105 (42).

Ethyl [(1*S*)-1-phenylbutyl] 2-diazomalonate 16. (75%), oil (Found: M + NH_4^+, 308.1610. $C_{15}H_{22}N_3O_4$ requires 308.1610); $[\alpha]_D^{24}$ +11.8 (*c* = 0.44; $CHCl_3$); ν_{max}(GGATR)/cm^{-1} 2967, 2150, 1761, 1735, 1692, 1371, 1309, 1273, and 1077; δ_H (300 MHz; $CDCl_3$) 0.91 (3H, t, *J* 7.3), 1.20–1.44 (2H, m), 1.31 (3H, t, *J* 7.1), 1.59–1.90 (1H, m), 1.90–2.05 (1H, m), 4.29 (2H, q, *J* 7.1), 5.89 (1H, t, *J* 6.9), and 7.20–7.50 (5H, m); δ_C (75.5 MHz; $CDCl_3$) 13.8 (CH_3), 14.3 (CH_3), 18.7 (CH_2), 38.4 (CH_2), 61.4 (OCH_2), 77.3 (OCH), 126.5 (CH), 128.1 (CH), 128.5 (CH), 140.2 (C), 160.6 (C=O), and 161.1 (C=O); diazo C unobserved; *m*/*z* (CI) 308 (M + NH_4^+, 11%), 282 (17), 176 (83), 166 (100), 150 (45), 149 (83), 132 (14), and 105 (21).

General procedure for dirhodium perfluorobutyramide catalysed decomposition of diazomalonates

A solution of the diazomalonate in CH_2Cl_2 (20 ml per mmol) was heated under reflux and immediately treated with a catalytic amount (1–2 mol%) of $Rh_2(NHCOC_3F_7)_4$. Reflux was maintained for 30 min, and then the mixture was allowed to cool to ambient temperature, filtered through Celite and the solvent removed under reduced pressure to give crude triene. Analysis of the NMR spectrum of the crude mixture showed a single diastereoisomer (R = Me, Et, Pr). Flash silica gel column chromatography (eluting with 9 : 1 light petroleum–EtOAc) for R = Me at this stage yielded the triene **17** as a colourless oil.

Ethyl (1*S*,3a*S*)-1-methyl-3-oxo-3,3a-dihydro-1*H*-cyclohepta-[*c*]furan-3a-carboxylate 17. (28%), oil (Found: M − CO_2Et^+, 161.0593. $C_{10}H_9O_2$ requires 161.0603); $[\alpha]_D^{25}$ −126.7 (*c* = 0.086, $CHCl_3$); ν_{max}(GGATR)/cm^{-1} 2924, 2846, 1778, 1735, 1454, 1215, 1028, and 757; δ_H (300 MHz; $CDCl_3$) 1.16 (3H, t, *J* 7.1), 1.50 (3H, d, *J* 6.5), 4.08 (2H, q, *J* 7.1), 5.51 (1H, dq, *J* 6.5 and 2.1), 5.57 (1H, m), 6.25 (1H, m), and 6.43–6.52 (3H, m); δ_C (75.5 MHz; $CDCl_3$) 13.9 (CH_3), 22.1 (CH_3), 58.3 (C), 62.4

(CH_2), 78.7 (CH), 119.5 (CH), 121.3 (CH), 128.4 (CH), 128.8 (CH), 130.3 (CH), 138.2 (C), 165.8 (C=O), and 173.0 (C=O); *m*/*z* 234 (M^+, 3%), 206 (3), 161 (100), 117 (75), 105 (60), 91 (40), and 77 (45). Chiral HPLC: Chiracel OD column (25 × 0.46 cm diameter), eluent: 99 : 1 hexane–isopropyl alcohol; flow rate: 0.75 ml min^{-1}; UV detection at 254 nm; retention time: 20.28 min.

General procedure for [4 + 2]-cycloaddition trapping of norcaradienes with PTAD

Fresh CH_2Cl_2 (5 ml) was added to the crude triene–norcaradiene. The solution was cooled in an ice bath and treated with PTAD (1.0 equiv.). After stirring for 15–30 min the mixture was preadsorbed onto silica and purified by column chromatography (gradient elution: 25–50% EtOAc in light petroleum) to afford the cycloadduct as a colourless solid which could be made analytically pure by recrystallisation.

Ethyl (3*S*,6*R*,7*R*)-3-methyl-5,10,12-trioxo-11-phenyl-4-oxa-9,11,13-triazapentacyclo[6.5.2.$0^{2,6}$.$0^{2,7}$.$0^{9,13}$]pentadec-14-ene-6-carboxylate 19. (39%), mp 166–167 °C (Found: C, 61.5; H, 4.9; N, 10.1. $C_{21}H_{19}N_3O_6$ requires C, 61.6; H, 4.7; N, 10.3%) (Found: M^+, 409.1283. $C_{21}H_{19}N_3O_6$ requires 409.1274); $[\alpha]_D^{25}$ −52.9 (*c* = 0.140, $CHCl_3$); ν_{max}(GGATR)/cm^{-1} 2981, 1778, 1718, 1502, 1408, 1251, 1073, and 766; δ_H (300 MHz; $CDCl_3$) 1.29 (3H, t, *J* 7.2), 1.53 (3H, d, *J* 6.1), 2.18 (1H, d, 4.6), 4.19 (2H, m), 5.08 (1H, q, *J* 6.1), 5.31 (1H, d, *J* 5.8), 5.52 (1H, t, *J* 4.6), 6.10 (1H, m), 6.29 (1H, m), and 7.30–7.50 (5H, m); δ_C (75.5 MHz; $CDCl_3$) 14.0 (CH_3), 16.6 (CH), 20.4 (CH_3), 38.3 (C), 42.7 (C), 52.2 (CH), 52.2 (CH), 62.6 (CH_2), 77.0 (CH), 125.4 (CH), 126.8 (CH), 127.4 (CH), 128.7 (CH), 129.3 (CH), 130.8 (C), 156.7 (C=O), 156.7 (C=O), 163.4 (C=O), and 168.6 (C=O); *m*/*z* 409 (M^+, 1%), 336 (M − CO_2Et^+, 13), 177 (10), 161 (43), 115 (34), 105 (13), 91 (25), and 77 (17).

Ethyl (3*S*,6*R*,7*R*)-3-ethyl-5,10,12-trioxo-11-phenyl-4-oxa-9,11,13-triazapentacyclo[6.5.2.$0^{2,6}$.$0^{2,7}$.$0^{9,13}$]pentadec-14-ene-6-carboxylate 20. (41%), mp 190 °C (light petroleum–EtOAc–EtOH) (Found: C, 62.5; H, 5.2; N, 9.8. $C_{22}H_{21}N_3O_6$ requires C, 62.4; H, 5.0; N, 9.9%) (Found: M^+, 423.1430. $C_{22}H_{21}N_3O_6$ requires 423.1430); $[\alpha]_D^{23}$ −96.4 (*c* = 0.278, $CHCl_3$); ν_{max}($CHCl_3$)/cm^{-1} 1774, 1720, 1601, 1503, 1407, 1315 and 1012; δ_H (250 MHz; $CDCl_3$) 1.13 (3H, t, *J* 7.2), 1.28 (3H, t, *J* 7.2), 1.60 (1H, m), 2.10 (1H, m), 2.22 (1H, d, *J* 4.6), 4.18 (2H, m), 4.86 (1H, dd, *J* 9.9 and 2.6), 5.32 (1H, dd, *J* 5.8 and 1.5), 5.52 (1H, t, *J* 5.0), 6.10 (1H, m), 6.29 (1H, m), and 7.30–7.50 (5H, m); δ_C (100.6 MHz; $CDCl_3$) 10.5 (CH_3), 13.9 (CH_3), 20.8 (CH), 24.8 (CH_2), 37.7 (C), 42.5 (C), 52.3 (CH), 52.4 (CH), 62.5 (CH_2), 82.4 (CH), 125.4 (CH), 126.8 (CH), 127.4 (CH), 128.7 (CH), 129.2 (CH), 130.9 (C), 156.7 (2 × C=O), 163.4 (C=O), and 168.6 (C=O); *m*/*z* 423 (M^+, 1%), 378 (M − OEt^+, 2), 350 (M − CO_2Et^+, 19), 175 ($PTAD^+$, 100), 131 (38), 119 (43), 91 (85), and 77 (25).

Ethyl (3*S*,6*R*,7*R*)-3-propyl-5,10,12-trioxo-11-phenyl-4-oxa-9,11,13-triazapentacyclo[6.5.2.$0^{2,6}$.$0^{2,7}$.$0^{9,13}$]pentadec-14-ene-6-carboxylate 21. (34%), mp 112–115 °C (light petroleum–EtOAc) (Found: C, 63.2; H, 5.7; N, 9.4. $C_{23}H_{23}N_3O_6$ requires C, 63.15; H, 5.3; N, 9.6%) (Found: M + NH_4^+, 455.1931. $C_{23}H_{23}N_3O_6$ requires 455.1931); $[\alpha]_D^{25}$ −83.25 (*c* = 0.386, $CHCl_3$); ν_{max}($CHCl_3$)/cm^{-1}1774, 1720, 1601, 1503, 1407, 1314, 1141, and 1012; δ_H (300 MHz; $CDCl_3$) 1.00 (3H, t, *J* 7.0) 1.29 (3H, t, *J* 7.0), 1.20–1.45 (2H, m), 1.46–1.84 (1H, m), 1.95–2.05 (1H, m), 2.20 (1H, d, *J* 4.7), 4.18 (2H, dq, *J* 7.0 and 2.5), 4.92 (1H, m), 5.31 (1H, dd, *J* 5.9 and 1.4), 5.51 (1H, m), 6.09 (1H, m), 6.28 (1H, m), and 7.25–7.60 (5H, m); δ_C (100.6 MHz; $CDCl_3$) 14.2 (CH_3), 14.4 (CH_3), 21.2 (CH), 33.7 (CH_2), 38.2 (C), 42.8 (C), 52.7 (CH), 52.7 (CH), 63.0 (CH_2), 81.3 (CH), 125.8 (CH), 127.2 (CH), 127.8 (CH), 129.1 (CH), 129.6 (CH), 131.2 (C), 157.1 (C=O), 157.1 (C=O), 163.8 (C=O), and 169.1 (C=O); *m*/*z* (CI) 455 (M + NH_4^+, 6%), 280 (59), 219 (84), 154 (44), 137 (34), 119 (15), and 94 (100).

Preparation of racemic diazomalonates

Procedures described above for the preparation of chiral diazomalonates **14**–**16** were adopted for the preparation of the racemic diazomalonates (±)-**14**, **22**, and **25** through the condensation of the appropriate commercially available racemic alcohol and ethyl diazomalonyl chloride. These diazomalonates were isolated as light yellow oils after flash silica gel column chromatography.

Ethyl (1-phenylethyl) 2-diazomalonate (±)-14. (94%) (Found: MH^+, 263.1036. $C_{13}H_{15}N_2O_4$ requires 263.1032); ν_{max}(film)/cm^{-1} 2984, 2938, 2141, 1760, 1732, 1691, 1372, 1310, 1268, 1093, 760 and 700; δ_H (250 MHz; $CDCl_3$) 1.32 (3H, t, *J* 7.1), 1.60 (3H, d, *J* 6.6), 4.30 (2H, q, *J* 7.1), 6.04 (1H, q, *J* 6.6), and 7.39–7.26 (5H, m); Chiral Shift NMR: δ_H (250 MHz; $CDCl_3$) Eu(hfc)$_3$ (0.2 equiv.) CH_3 doublet splits into two doublets (1.66 and 1.79 ppm) of ratio 1 : 1; δ_C (100.6 MHz; $CDCl_3$) 14.3 (CH_3), 22.4 (CH_3), 61.6 (CH_2), 73.7 (CH), 126.0 (CH), 128.1 (CH), 128.6 (CH), 141.0 (C), 160.4 (C=O), and 161.0 (C=O); diazo C unobserved; *m*/*z* 263 (MH^+, 18%), 215 (24), 159 (76), 121 (26), 105 (100), and 77 (18).

Ethyl [1-(4-methoxyphenyl)ethyl] 2-diazomalonate 22. (69%) (Found: M^+, 292.1059. $C_{14}H_{16}N_2O_5$ requires 292.1059); ν_{max}(film)/cm^{-1} 2938, 2839, 2141, 1756, 1732, 1694, 1516, 1372, 1311, 1246, 1077, 1034, and 833; δ_H (250 MHz; $CDCl_3$) 1.31 (3H, t, *J* 7.1), 1.58 (3H, d, *J* 6.5), 3.80 (3H, s, OMe), 4.29 (2H, q, *J* 7.1), 6.01 (1H, q, *J* 6.5), 6.88 (2H, AA′BB′) and 7.31 (2H, AA′BB′); δ_C (100.6 MHz; $CDCl_3$) 14.7 (CH_3), 22.5 (CH_3), 55.7 (OCH_3), 62.0 (CH_2), 73.9 (OCH), 114.3 (CH), 128.0 (CH), 133.5 (C), 159.9 (C), 160.7 (C=O), and 161.5 (C=O); diazo C unobserved; *m*/*z* 292 (M^+, 2%), 191 (10), 151 (20), and 135 (100).

Ethyl [1-(4-chlorophenyl)ethyl] 2-diazomalonate 25. (75%) (Found: M^+, 296.0559. $C_{13}H_{13}ClN_2O_4$ requires 296.0564); ν_{max}(film)/cm^{-1} 2985, 2141, 1759, 1732, 1693, 1372, 1313, 1269, 1093, and 1015; δ_H (250 MHz; $CDCl_3$) 1.32 (3H, t, *J* 7.1), 1.58 (3H, d, *J* 6.6), 4.30 (2H, q, *J* 7.1), 5.99 (1H, q, *J* 6.6), and 7.27–7.33 (4H, m); δ_C (100.6 MHz; $CDCl_3$) 14.3 (CH_3), 22.3 (CH_3), 61.7 (CH_2), 65.9 (C=N_2), 73.0 (OCH), 127.5 (CH), 128.8 (CH), 133.9 (C), 139.5 (C), 160.4 (C=O), and 161.0 (C=O); *m*/*z* 297 (MH^+, 2%), 296 (M^+, <1%), 224 (9), 159 (41), 139 (100), 103 (53), and 77 (28).

Dirhodium(II) perfluorobutyramide catalysed decomposition of racemic diazomalonates

Decomposition of the racemic diazomalonates under standard conditions of dirhodium(II) perfluorobutyramide catalysis in refluxing dichloromethane afforded the respective racemic cycloheptafuranone(s) and these were isolated after chromatography as oils.

Ethyl 1-methyl-3-oxo-3,3a-dihydro-1*H*-cyclohepta[*c*]furan-3a-carboxylate (±)-17. (20%) (Found: MH^+, 235.0970. $C_{13}H_{15}O_4$ requires 235.0970); ν_{max}(film)/cm^{-1} 2984, 1780, 1744, 1449, 1322, 1197, 1167, 1054, 1028, 762, and 711; δ_H (250 MHz; $CDCl_3$) 1.17 (3H, t, *J* 7.1), 1.51 (3H, d, *J* 6.5), 4.09 (2H, q, *J* 7.1), 5.52 (1H, dq, *J* 6.5 and 2.1), 5.57 (1H, m), 6.25 (1H, m), and 6.43–6.52 (3H, m); δ_C (100.6 MHz; $CDCl_3$) 13.9 (CH_3), 22.1 (CH_3), 58.3 (C), 62.3 (CH_2), 78.6 (CH), 119.4 (CH), 121.3 (CH), 128.4 (CH), 128.8 (CH), 130.3 (CH), 138.2 (C), 165.7 (C=O), and 172.9 (C=O); *m*/*z* (CI) 252 (M + NH_4^+, 65%), 235 (MH^+, 17), 191 (100), 180 (28), and 122 (13).

Chiral HPLC: Chiracel OD column, eluent: 99:1 hexane–isopropyl alcohol; flow rate: 0.75 ml min^{-1}; UV detection at 254 nm; retention time: 19.20 min (1*S*, 3a*R* enantiomer), 26.56 min (1*R*, 3a*S* enantiomer).

Ethyl 6-methoxy-1-methyl-3-oxo-3,3a-dihydro-1*H*-cyclohepta[*c*]furan-3a-carboxylate 23/24. (Racemic mixture of inseparable diastereomers [1:1 ratio]; isolated yield 32%) (Found: M^+, 264.0994. $C_{14}H_{16}O_5$ requires 264.0998); ν_{max}(film)/cm^{-1} 2938, 1779, 1739, 1672, 1635, 1514, 1371, 1321, 1238, 1165, 1065, 1038, 965, and 862; δ_H (250 MHz; $CDCl_3$) 1.178 and 1.184 (2 × 3H, t, *J* 7.1), 1.49 and 1.71 (2 × 3H, d, *J* 6.4), 3.62 (2 × 3H, s), 4.00–4.20 (2 × 2H, m), 5.24 (1H, q, *J* 6.4), 5.48 (1H, q, *J* 6.4), 5.60–5.75 (2 × 2H, m), 6.14 (2 × 1H, m), and 6.25–6.40 (2 × 1H, m); δ_C (100.6 MHz; $CDCl_3$) 13.7 and 13.8 (CH_3), 21.8 and 21.9 (CH_3), 54.9 (2 × CH_3), 57.9 (2 × C), 62.3 and 62.4 (OCH_2), 78.7 and 79.0 (OCH), 101.2 and 101.6 (CH), 118.1 and 118.0 (CH), 122.6 and 122.7 (CH), 127.0 and 127.2 (CH), 128.9 and 129.0 (C), 159.3 and 159.4 (C), 166.0 and 166.1 (C=O), and 173.0 and 173.4 (C=O); *m*/*z* 264 (M^+, 9%), 221 (9), 206 (23), 191 (100), 178 (56), 135 (38), 105 (40), 91 (34), and 77 (34).

Ethyl 6-chloro-1-methyl-3-oxo-3,3a-dihydro-1*H*-cyclohepta-[*c*]furan-3a-carboxylate 26. (51%) (Found: $M - CO_2Et^+$, 195.0213. $C_{10}H_8ClO_4$ requires 195.0213); ν_{max}(film)/cm^{-1} 2984, 2936, 1841, 1781, 1748, 1328, 1229, 1201, 1167, 1064, 836, and 771; δ_H (250 MHz; $CDCl_3$) 1.20 (3H, t, *J* 7.1), 1.51 (3H, d, *J* 6.5), 4.05–4.25 (2H, m), 5.50 (1H, dq, *J* 6.5 and 1.1), 5.62 (1H, d, *J* 10.3), 6.17 (1H, dd, *J* 6.9 and 2.3), 6.46 (1H, dd, *J* 10.3 and 1.1), and 6.67 (1H, d, *J* 6.9); δ_C (100.6 MHz; $CDCl_3$) 13.8 (CH_3), 22.0 (CH_3), 58.1 (C), 62.8 (CH_2), 78.6 (CH), 118.0 (CH), 122.6 (CH), 126.9 (CH), 130.8 (CH), 135.6 (C), 165.3 (C=O), and 172.1 (C=O); 1 quaternary C unobserved; *m*/*z* 268 (M^+, 10%), 225 (45), 195 ($M - CO_2Et^+$, 100), 115 (45), 116 (81), 89 (41), 43 (35), and 29 (48).

Preparation and dirhodium(II) perfluorobutyramide catalysed decomposition of diazomalonate 28

Bis[(1*S*)-1-phenylethyl] malonate. A solution of malonic acid (0.104 g, 1.0 mmol) in acetonitrile (5 ml) was treated with (*S*)-α-methylbenzyl alcohol (0.244 g, 2.0 mmol), and then dicyclohexylcarbodiimide (0.412 g, 2.0 mmol). An exothermic reaction ensued immediately, and after stirring at room temperature for 2 h, the precipitated dicyclohexylurea was filtered off and washed with ethyl acetate. Solvent was then stripped under reduced pressure and the residue taken up in ethyl acetate (20 ml), washed with water (2 × 20 ml) and then saturated brine (20 ml). The resulting solution was dried (Na_2SO_4) and then subjected to flash silica gel column chromatography (9:1 light petroleum–ethyl acetate) to furnish *bis[(1S)-1-phenylethyl] malonate* (0.246 g, 79%) as a colourless oily solid (Found: $M + NH_4^+$, 330.1705. $C_{19}H_{20}NO_4$ requires 330.1705); ν_{max}(film)/cm^{-1} 3036, 2984, 2935, 1732, 1496, 1456, 1268, 1152, and 1063; δ_H (250 MHz; $CDCl_3$) 1.56 (6H, d, *J* 6.5), 3.41 (2H, s), 5.93 (2H, q, *J* 6.5), and 7.25–7.36 (10H, m); δ_C (60.5 MHz; $CDCl_3$) 21.9 (CH_3), 42.1 (CH_2), 73.5 (OCH), 126.0 (CH), 127.9 (CH), 128.4 (CH), 140.8 (C), and 165.6 (C=O); *m*/*z* 330 ($M + NH_4^+$, 72%), 225 (100), 122 (100), and 100 (41).

Bis[(1*S*)-1-phenylethyl]-2-diazomalonate 28. A solution of the above malonate (0.069 g, 0.221 mmol) in dry THF (1.9 ml) was treated with caesium carbonate (0.072 g, 0.221 mmol) and then a solution of toluene-*p*-sulfonyl azide (0.44 g, 0.221 mmol) in THF (0.5 ml) was added. After stirring at room temperature for about 4 hours the mixture was filtered through a pad of Celite and stripped of solvent to give an oily residue. Toluene-*p*-sulfonamide was triturated out with ether and filtered off. The filtrate was preadsorbed onto silica and subjected to flash silica gel column chromatography (14:1 light petroleum–ethyl acetate) to afford *bis[(1S)-1-phenylethyl] 2-diazomalonate* **28** (0.065 g, 87%) as a pale yellow oil (Found: $M + NH_4^+$, 356.1610. $C_{19}H_{22}N_3O_4$ requires 356.1610); ν_{max} (film)/cm^{-1} 3065, 3035, 2983, 2934, 2143, 1757, 1729, 1690, 1366, 1342, 1304, 1268, 1092, 1061, 1029, 759, and 699; δ_H (250 MHz; $CDCl_3$) 1.59 (6H, d, *J* 6.6), 6.05 (2H, q, *J* 6.6), and 7.26–7.40 (10H, m); δ_C (60.5 MHz; $CDCl_3$) 22.4 (CH_3), 73.7 (OCH), 126.0 (CH), 128.0 (CH), 128.5 (CH), 140.9 (C), and 160.3 (C=O); diazo C not observed; *m*/*z* 356 ($M + NH_4^+$, 10%), 330 (36), 252 (31), 226 (18), 180 (12), 138 (23), and 122 (100).

(1*S*)-1-Phenylethyl (3*S*,6*R*,7*R*)-3-methyl-5,10,12-trioxo-11-phenyl-4-oxa-9,11,13-triazapentacyclo[6.5.2.$0^{2,6}$.$0^{2,7}$.$0^{9,13}$]pentadec-14-ene-6-carboxylate 30. Diazomalonate **28** (0.064 g, 0.189 mmol) was decomposed with dirhodium(II) perfluorobutyramide under the standard conditions described above and the crude reaction mixture treated with PTAD to give crude cycloadduct. Flash silica gel column chromatography gave pure *cycloadduct* **30** (0.043 g, 47%) as a colourless solid; mp 191.5–192.5 °C (light petroleum–EtOAc) (Found: C, 66.6; H, 4.8; N, 8.3. $C_{27}H_{23}N_3O_6$ requires C, 66.8; H, 4.8; N, 8.7%); $[\alpha]_D^{21}$ −122.0 (*c* = 0.282, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 1776, 1722, 1503, 1407, 1306, 1204, 1140, 1071, 1029, and 1008; δ_H (250 MHz; $CDCl_3$) 1.52 (3H, d, *J* 6.3), 1.60 (3H, d, *J* 6.7), 2.16 (1H, d, *J* 4.6), 5.07 (1H, q, *J* 6.3), 5.18 (1H, dd, *J* 5.9 and 1.4), 5.46 (1H, t, *J* 5.0), 5.55 (1H, m), 5.81 (1H, t, *J* 6.7), 5.95 (1H, q, *J* 6.7), and 7.26–7.52 (10H, m); δ_C (60.5 MHz; $CDCl_3$) 16.5 (CH_3), 20.3 (CH_3), 20.7 (CH), 38.4 (C), 42.8 (C), 52.0 (NCH), 52.1 (NCH), 74.7 (OCH), 76.7 (OCH), 125.3 (CH), 126.8 (CH), 127.1 (CH), 128.5 (CH), 128.6 (2 × CH), 128.7 (CH), 129.1 (CH), 130.7 (C), 139.4 (C), 156.5 (C=O), 156.6 (C=O), 162.5 (C=O), and 168.5 (C=O); *m*/*z* (CI) 503 ($M + NH_4^+$, 7%), 328 ([MNH_4 − PTAD]$^+$, 24), 180 (98), and 122 (100).

Acknowledgements

We thank the EPSRC and AgrEvo for a CASE Award (to S. M.), and the EPSRC Mass Spectrometry Service at Swansea for mass spectra.

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