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Mechanistic studies on the formal aza-Diels–Alder reactions of *N*-aryl imines: evidence for the non-concertedness under Lewis-acid catalysed conditions

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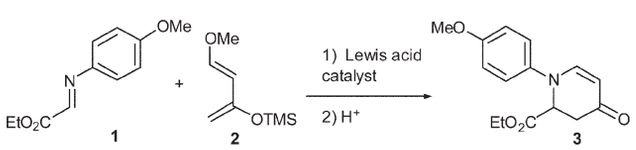
The reaction of a *para*-methoxyaniline, ethyl glyoxalate-derived imine with a series of dienes has resulted in products, which initially suggest the operation of different modes of aza-Diels–Alder reaction. However, a more likely explanation is that a common reaction mechanism is operating, involving a step-wise Lewis-acid catalysed process, which only appears to behave similarly to alternative concerted cycloaddition reactions.

Introduction

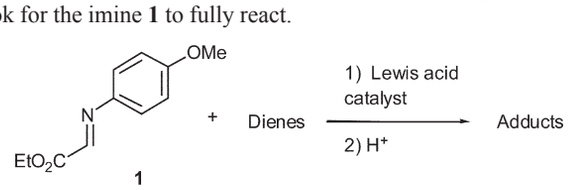
Although the imino-Diels–Alder reaction has been known for some time,[1] it is only in recent years that major advances have been made in developing catalytic asymmetric versions.[2] We have been working towards developing asymmetric aza-Diels–Alder reactions initially using sulfonyl imines as highly electron deficient imines,[3,4] moving on to chiral Lewis acid catalysed asymmetric versions using less electron deficient *N*-aryl imines, such as the example shown in Equation 1.[5] However, such catalytic asymmetric systems can be problematic in terms of reproducible asymmetric induction,[5b] suggesting that a much greater understanding of the mechanism operating in such reactions is required. This has led us to undertake more detailed mechanistic studies, resulting in our recent proposal[6] that in general, aza-Diels–Alder reactions of *N*-aryl imines are unlikely to react in a concerted [4 + 2]-fashion. In this paper we disclose the full details of this work and discuss its implications in a wider context.



(1)

Results and discussion

In order to study the mechanism of reaction of *N*-aryl imine **1** with various dienes, we needed to establish the reactivity of the imine **1** with different dienes, Lewis acids and solvents. These reactions were carried out as detailed in Equation 2, with the corresponding results summarised in Table 1, which shows the length of time it took for the imine **1** to fully react.



(2)

From Table 1, it can be seen that nearly all the reactions failed to proceed in the absence of a catalyst. The lack of an uncatalysed reaction is in contrast to the findings of Ding *et al.*[7] who reported that Danishefsky's diene **2** reacts with benzylidene aniline imine in MeCN at room temperature without either a Lewis or Brønsted acid catalyst (>99%, 2 hours), however, our results show that the uncatalysed reactions are either very slow or do not proceed over a 24 hour period. This screen also shows that the preferred type of Lewis acid for these types of transformations is the soft to medium type [Cu(II) or Yb(III)] and that a more polar solvent (MeCN) is also preferable. In addition, Table 1 shows the expected trend in reactivity: less activated (less electron rich) dienes **4**, **6**, and **10** were slow to react being insufficiently nucleophilic under these reaction conditions; more reactive dienes (cyclopentadiene **5**, Danishefsky's diene **2**, 1-trimethylsilyloxybutadiene **8** and methoxycyclohexadiene **9**) reacted rapidly; acetoxybutadiene **7** showed intermediate reactivity.

After this preliminary screen, scale-up reactions were carried out to isolate the products formed from each of the 'hit' reactions from Table 1, *i.e.* those which resulted in 100% consumption of imine **1**. Since ytterbium(III) triflate seemed to be the preferred catalyst, this Lewis acid was used in dry acetonitrile at ambient temperature to react imine **1** with each of the more reactive dienes. These reactions were complete in 1 to 3 hours, depending on the diene, with the results summarised in Table 2.

Table 2 shows that reactions involving cyclopentadiene **5**, 1-acetoxybutadiene **7** and 1-methoxycyclohexadiene **9** all gave the "inverse-electron-demand" products, *i.e.* tetrahydroquinoline derivatives **10**, **12**, and **14** respectively. Danishefsky's diene **2** on the other hand gave the "normal electron-demand" Diels–Alder adduct **3** as expected, which contrasts with 1-(trimethylsilyloxy)butadiene **8**, which gave an acyclic product **13** (entry 4).

The adducts listed in Table 2 were difficult to purify due to their instability, with the exception of the Danishefsky's diene adduct **3**; the remaining adducts were unstable in air and solutions of the purified compounds darkened rapidly upon standing. It was clear an oxidation process was occurring, resulting in complex mixtures of products in nearly all cases. Having isolated each of the adducts, it was necessary to assign structures for each of the new products, and those shown in Table 2 are the results of analytical data and a series of experiments and findings that are fully documented in this paper.

There are many reports of the use of *N*-aryl imines acting as dienes in Lewis acid catalysed inverse-electron-demand Diels–Alder reactions.[8] However, at the time that these experiments were carried out, it was expected that the imine would react as a dienophile with electron rich dienes, not as a diene. The first evidence of such reversed reactivity came from the isolation of the cyclopentadiene adduct **11**. The structural data obtained was close to that reported

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Table 1 Length of time (hours) for consumption of imine **1** with different dienes and Lewis acid catalysts, according to Equation 2

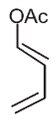
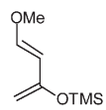
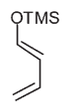
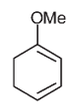
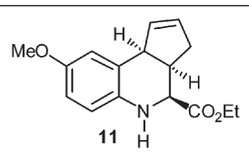
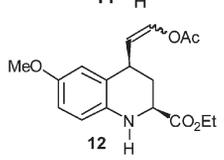
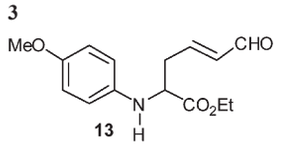
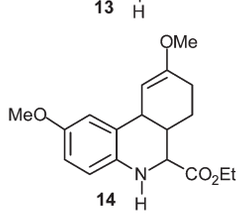
		Reaction time/h							
		Dienes							
									
Solvent	Lewis acid	**4**	**5**	**6**	**7**	**2**	**8**	**9**	**10**
MeCN	None	24	—	—	—	—	—	—	—
	$Cu(OTf)_2$	—	1	—	2	1	1	1	—
	$Yb(OTf)_3$	—	1	—	2	1	1	1	—
	$Co(acac)_3$	—	—	—	—	—	—	—	—
Toluene	None	—	—	—	—	—	—	—	—
	$Cu(OTf)_2$	—	1	—	16	1	1	1	—
	$Yb(OTf)_3$	—	1	—	16	1	1	1	—
	$Co(acac)_3$	—	—	—	—	—	—	—	—

Table 2 Products obtained from the reactions outlined in Equation 1 between imine **1** and various dienes

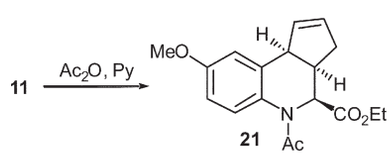
Entry	Diene	Product	Yield (%)
1	**5**	 **11**	81
2	**7**	 **12**	61
3	**2**	**3**	65
4	**8**	 **13**	59
5	**9**	 **14**	57

in related literature compounds,[8e] and the stereochemistry of the adduct **11** was assigned based on literature precedent,[8h,i] and was proven by single crystal X-ray diffraction analysis of the acetamide derivative (*vide infra*). Notably, this product was isolated as a single diastereoisomer according to ^{1}H NMR.

The structure of compound **3** had been confirmed by others,[9] as well as in our own group.[6]

The acyclic product **13** was also straightforward to identify by IR and NMR. It is possible that compound **13** could derive from ring opening of the normal-electron-demand Diels–Alder adduct **15**, *via* the process shown in Scheme 1. This would involve hydrolysis of the trimethylsilyloxy function to give **16**, cleavage of the C–N bond to provide ring-opened product **17**, enolisation (either through proton or Lewis acid assistance) to the thermodynamically favoured *E*,*E*-dienol **18**, final tautomerisation would give the acyclic product **13** with the observed *E*-unsaturated aldehyde geometry. An alternative pathway might involve an intramolecular Michael addition of the amine function of **17** to the unsaturated aldehyde to give **19**, resulting in azetidine **19**. If formed, azetidine **19** would be expected to undergo retro-Michael addition to give the observed product **13**, however, it is worth noting that azetidine-like products were not observed, including aldehyde **20**.

The various adducts produced from the reactions of imine **1** with the different dienes, and ultimately the manner in which the imine reacted, became more readily understood whilst attempting to characterise cyclopentadiene and methoxycyclohexadiene products **11** and **14** respectively. Characterisation of these adducts proved difficult due to their instability and ease of oxidation. By making the corresponding *N*-acetamides, it was expected that stable derivatives would be obtained which would be easier to characterise. Acetylations were carried out in one pot directly after the cycloadditions by treatment with pyridine and acetic anhydride. The acetylation product of the cyclopentadiene adduct **11**, *i.e.* **21**, was isolated in 72% yield as a crystalline solid (Equation 3). Single crystal X-ray diffraction showed that **21** had the structure shown in Fig. 1, *i.e.* with the ethyl ester moiety and the *cis*-fused cyclopentene ring *syn* to each other.† It can also be seen that the acetamide function and aryl ring cause flattening of the tetrahydroquinoline ring.



(3)

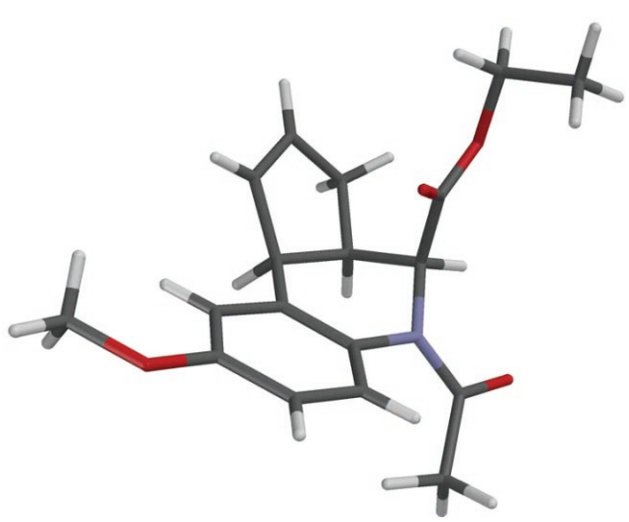
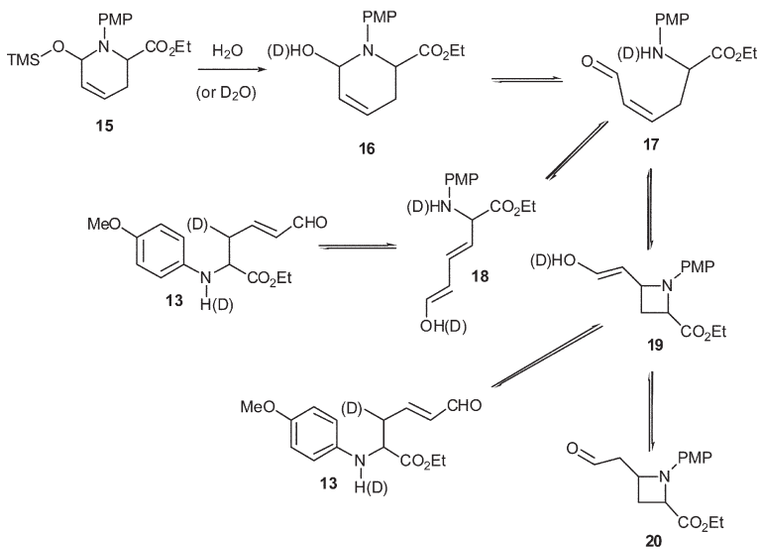


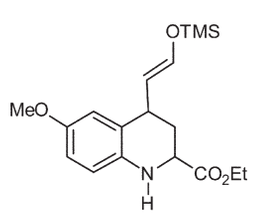
Fig. 1 Molecular structure of compound **21** from X-ray data.

† CCDC reference numbers 237030 and 237039. See http://www.rsc.org/suppdata/ob/b4/b407293f/ for crystallographic data in .cif or other electronic format.

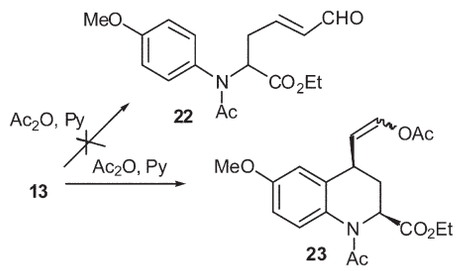


Scheme 1 Possible origin of product **13**, from Diels–Alder adduct **15** and effect of adding deuterium oxide.

The acyclic compound **13** was also exposed to the same acetylation conditions to give an unexpected result; the product contained two new acetyl functions. The expected product, *N*-acetamide **22** (Scheme 2), was clearly not obtained. Indeed, the benzene ring had become tri-substituted according to ^{1}H NMR and the fact that the product from this acetylation was deduced to be tetrahydroquinoline **23** became clear by comparison with the product obtained from partial hydrogenation reaction of acetoxybutadiene adduct **12**, *i.e.*, the crude product from the reaction of acetoxybutadiene with imine **1** was saturated with hydrogen over palladium on carbon. After chromatography, the unexpected compound **24** was isolated in 62% yield; the structure being confirmed by single crystal X-ray crystallography (Fig. 2).† The precursor to structure **24** must therefore have been tetrahydroquinoline **12**, since the hydrogenation had been accompanied by a de-hydrogenation of the ring system to furnish the quinoline (presumably due to incomplete hydrogen saturation of the atmosphere), leaving only the acetoxy-alkene to be reduced. Conclusive evidence was obtained by a PCC oxidation of the same crude reaction mixture derived from acetoxybutadiene and imine **1**, which gave **25** as an approximately 3 : 1 mixture of *E*- and *Z*-isomers, respectively, in 51% overall yield (Scheme 3) (the acetoxybutadiene used was a 1.6 : 1 mixture of *E*- and *Z*-isomers, respectively, according to ^{1}H NMR). The oxidation of adduct **12** to quinoline **25** is particularly facile; certain sources of silica gel used to perform column chromatography caused difficulties in isolating pure adduct **12**, resulting in the isolation of quinoline **25** in 32% yield and as a 6 : 1 ratio of *E*- to *Z*-alkene diastereoisomers. In addition, the crude cycloaddition reaction mixture containing crude **12** could be oxidised cleanly in air by re-dissolving in chloroform and heating to 50 °C for one hour, resulting in isolation of quinoline **25** as an approximately 4 : 1 mixture of *E*- and *Z*-olefin isomers in 83% yield. Similar oxidation also occurs in ethyl acetate, with a half-life of approximately 3 days at room temperature (determined by ^{1}H NMR). To confirm the link between the **24** and **25**, the alkene of **25** could be readily hydrogenated to derive the ethyl acetoxy product **24** as a white crystalline solid in 86% yield (Scheme 3). Following structural elucidation of alkene-isomers **12**, and their derivatives, it was possible to re-analyse the crude product from the reaction of acetoxybutadiene with imine **1**. This revealed the fact that the minor components present were not the result of oxidation and could be assigned tentatively as possessing the *anti*-configuration around the tetrahydroquinoline; in particular, the *E*-alkenyl acetate was present at a level of 17% with respect to the major product (*E*-isomer of **12**). The ring stereochemistry of the major diastereoisomer was assigned according to a similar structure reported in the literature,[10] using the ring methylene and methane coupling constants. It also became clear that the product from the acetylation of trimethylsilyloxybutadiene adduct **13** (Scheme 2) was doubly acetylated to give compound **23**. In addition, the formation of adduct **13** from the reaction of trimethylsilyloxybutadiene with imine **1** required water in the reaction mixture in order to produce aldehyde **13**, as opposed to a complex mixture of products. The reaction was therefore carried out with D_2O, which was, added to anhydrous acetonitrile in order to check for deuterium incorporation into the product **13**. It was anticipated that following either of the mechanisms outlined in Scheme 1, deuterium would be incorporated into the methylene position. However, no deuterium incorporation was observed by ^{1}H NMR, showing that an intermediate Diels–Alder adduct **15** is not involved in the formation of product **13**. Furthermore, triflic acid, derived from hydrolysis of ytterbium(III) triflate, was also not to blame for the formation of **13**. This was demonstrated by using 5 mol% TMS-OTf under the same reaction conditions with trimethylsilyloxybutadiene and imine **1** in MeCN, both with and without water, hence, generating triflic acid under the aqueous conditions. This gave a complex mixture of products by TLC and ^{1}H NMR, which did not include the aldehyde **13**. Hence, ytterbium(III) triflate is the active catalyst required to produce adduct **13**, and the reaction does not proceed through the Diels–Alder adduct **15**. The possible reaction mechanisms operating with the various dienes are: 1) normal-electron-demand imino-dienophile Diels–Alder reaction; 2) inverse-electron-demand Diels–Alder reaction; and 3) a Mannich-like process, whereby the diene adds *via* a nucleophilic addition pathway to a Lewis-acid activated imine. Since the reaction of 1-trimethylsilyloxybutadiene with imine **1** does not occur through a normal electron-demand Diels–Alder reaction, it is extremely unlikely that the inverse-electron-demand product **26** could undergo C–C bond cleavage to give **13**, it became apparent that all the different reaction products (Table 1) could be explained by a single reaction mechanism, *i.e.* the Mannich-like process, involving activation of the imine **1** by ytterbium(III) through imine nitrogen-chelation, followed by addition of the diene to derive intermediates **27** to **31** (Table 3). The fate of each of the intermediates **27** to **31** then depends upon their relative stabilities and ease of cyclisation, to provide either: the "normal-electron-demand Diels–Alder" product in the case of Danishefsky's diene adduct **2**; or the intermediate is unstable and needs to be intercepted by a nucleophile (*i.e.* water), as in the case of 1-trimethylsilyloxybutadiene adduct **28**; or the intermediate has intermediate stability



26



Scheme 2 Cyclisation of adduct **13** under acylation conditions.

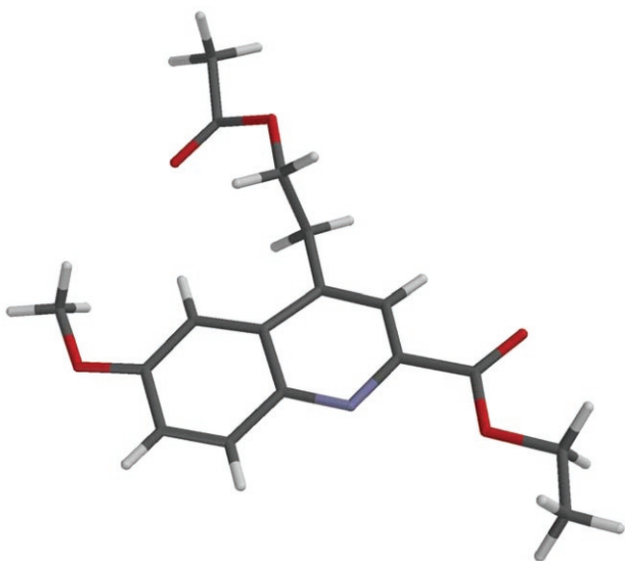
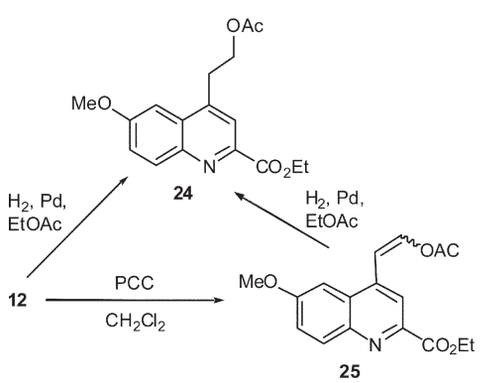


Fig. 2 Molecular structure of compound **24** from X-ray data.



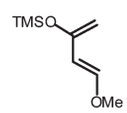
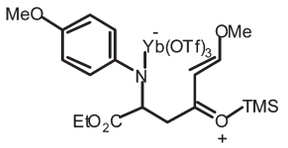
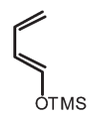
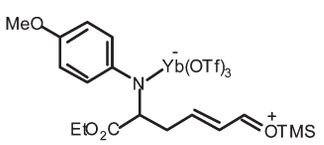
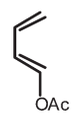
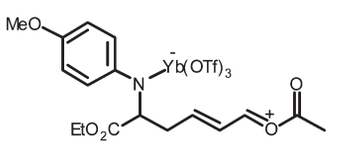
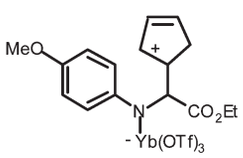
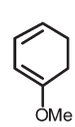
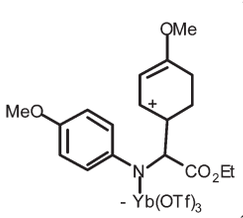
Scheme 3 Interconversion of adduct **12** into derivatives **24** and **25**.

and cyclises to give the "inverse-electron-demand Diels–Alder" product, as in the case of intermediates **29** to **31**.

Examination of the putative intermediates shown in Table 3 shows a strong similarity in structure between intermediates **29** to **31** and **28**, yet intermediate **28** needs to be rapidly quenched by water. The reason for this seems to be the fact that **28** does cyclise to derive the corresponding tetrahydroquinoline if the reaction is carried out in anhydrous conditions. However, this product could not be isolated in a pure form to allow unambiguous characterisation. Comparison of the ^{1}H NMR of the crude 1-trimethylsilyloxybutadiene and imine **1** reaction mixture, executed under dry conditions, and that obtained from the reaction of 1-acetoxybutadiene with imine **1**, shows a distinct correlation in size, shape and chemical shift of certain signals (Fig. 3). This could indicate that some tetrahydroquinoline is produced, but this is even less stable than those systems outlined in Table 1.

The fact that Danishefsky's diene appears to be the only diene to derive the normal-electron-demand Diels–Alder adduct (Table 1), suggests that the 2-trimethylsilyloxy substituent is essential to force cyclisation onto nitrogen *via* intermediate **27**. Hence, we investigated the reaction of 2-trimethylsilyloxy-1,3-

Table 3 Suggested intermediates formed by the ytterbium(III)-catalysed reaction of imine **1** with different dienes

Entry	Diene	Intermediate
1	 **2**	 **27**
2	 **8**	 **28**
3	 **7**	 **29**
4	 **5**	 **30**
5	 **9**	 **31**

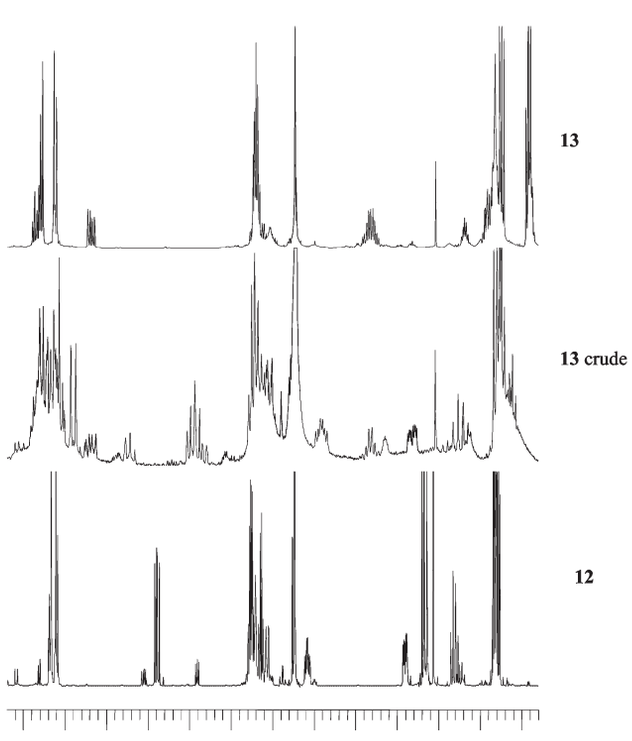
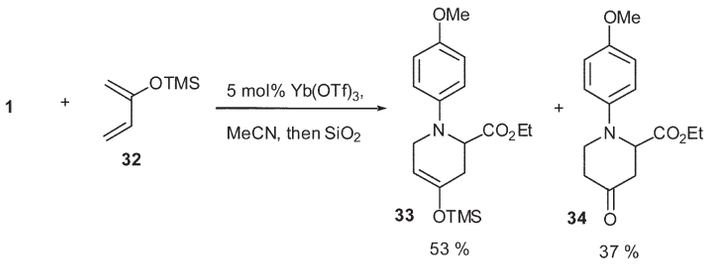


Fig. 3 ^{1}H NMR correlation between acetoxybutadiene adduct and 1-trimethylsilyloxybutadiene.

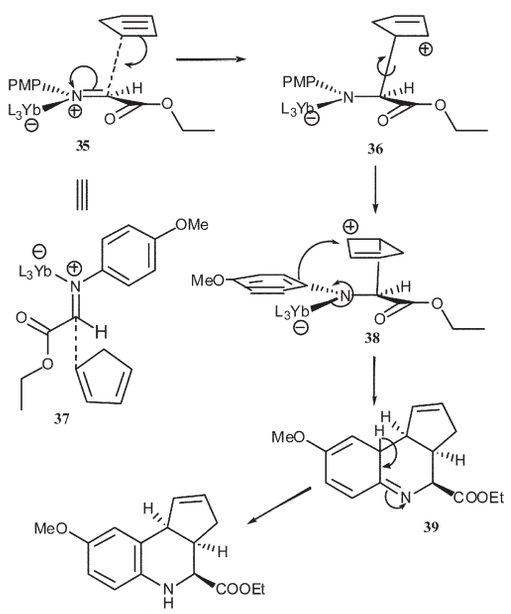


(4)

butadiene **32** with imine **1** (Equation 4) under the usual reaction conditions, *i.e.* with ytterbium(III) triflate in acetonitrile at room temperature, both under anhydrous and aqueous conditions (wet MeCN). The only difference in the results between the anhydrous and aqueous reactions was a reduction in yield when water was present. In each case, two new products were obtained, *i.e.* **33** and **34** (53 and 37% yields respectively from the anhydrous reaction, Equation 4). Importantly, no acyclic product was isolated in either reaction, but the possibility still exists for either **33** or **34** to be produced in a "normal-electron-demand Diels–Alder" reaction. The observed results can also be explained by the stepwise addition-cyclisation mechanism, with the presence of the bulky OTMS group effectively blocking aryl ring-cyclisation, as in the case of the Danishefsky's diene adduct. Product **34** must arise from the hydrolysis of compound **33** on silica gel, although **33** is apparently fairly stable in water and dilute aqueous acid. Nonetheless, it is converted rapidly through to ketone **34** using TBAF.

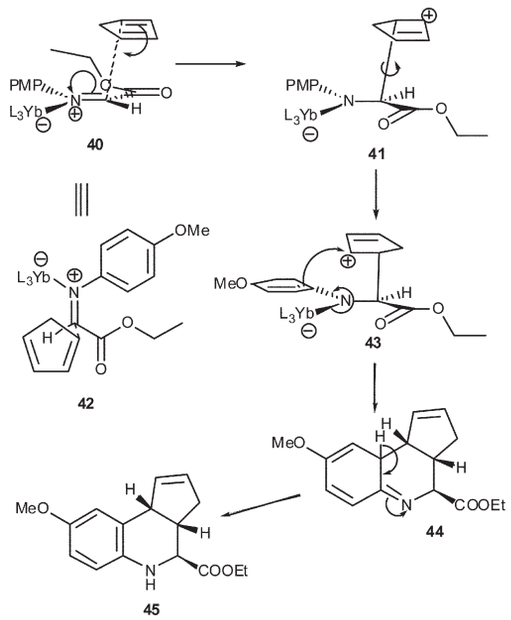
There has been considerable discussion over the mechanism of the imino-Diels–Alder reaction over the years in the chemical literature. In his original paper,[11] Danishefsky deferred any discussion on the mechanism, however, Ojima[12] concluded that the cycloaddition went through a common, acyclic intermediate, although the authors conceded that further mechanistic investigations were needed. The Midland group stated evidence for a pericyclic mechanism in their reactions with Brassard's diene,[13] isolating a cyclic intermediate as a single diastereoisomer which they claimed implicated a normal Diels–Alder reaction as the rationale. In contrast, Kobayashi suggested[14] a stepwise mechanism for the reaction of an *N*-aryl imine with a variety of dienes, corroborated by related reactions with enol ethers. Indeed, in later work on the asymmetric Mannich reaction,[15] Kobayashi *et al.* showed that a catalytic cycle based upon a Mukaiyama aldol reaction explained the observed results, with an alcohol (PrOH) or water being required to free the catalyst. This, together with our own results, certainly indicates that there is a fine balance between the conditions needed to produce either Mannich-type or aza-Diels–Alder-type products and adds more weight to the idea of an essentially similar mechanistic pathway operating. Recently, molecular modelling studies by Domingo and co-workers have added strength to the idea of a stepwise mechanism in related reactions,[16] although based on proton activation rather than Lewis acid activation. They concluded that a reaction between cyclopentadiene and protonated *N*-methylpyridine-2-carboxaldehyde imine proceeded by a stepwise mechanism according to theoretical calculations. Such conclusions are also supported by Sauer *et al.*,[17] who proposed that such aza-Diels–Alder reactions proceeded through transition structures involving allyl cations. A more recent Density Functional Theory (DFT) calculation on an iminium ion reacting with cyclopentadiene[18] also concludes that the reaction "takes place along a highly asynchronous concerted process characterised by the nucleophilic attack of the cyclopentadiene on the ylidene ammonium cation instead of a pericyclic process." However, amidst the number of examples in the relatively recent literature on imino-Diels–Alder reactions (whether they be; imino-dienophiles, 1- or 2-iminodienes, intramolecular or intermolecular reactions), there are still comparatively few that make bold assessments of the mechanism involved in the reactions studied.[19] In fact there are many examples that suggest a concerted (if sometimes asynchronous) mechanism,[20] and equally, there are many that state a stepwise mechanism is the probable mode of operation.[21] Some papers conclude that more than one mechanism is in operation.[22] The problem is certainly complex, however, it is our view that in studies where more than one mechanism is implicated, the likelihood is that a stepwise mechanism is in operation and that two different fates can await a common intermediate.

In light of the computational studies by Domingo *et al.*,[16,18] and the fact that only one diastereoisomer is observed in the reaction between cyclopentadiene and imine **1**, some consideration was given as to how this might arise in a stepwise reaction. In product **11**, the bridgehead protons have to be *syn*. Therefore, the stereochemistry of the chiral centre next to the aromatic ring is predetermined by the manner in which the addition of cyclopentadiene to the imine occurs. Consequently, the stereochemistry of the molecule is set up by the initial nucleophilic attack step. This is diastereoselective, however, with the ethyl ester being *syn* to the cyclopentene ring in the product. Shown in Scheme 4 is our proposed mechanism for the attack of cyclopentadiene on the ytterbium activated imine **1**.

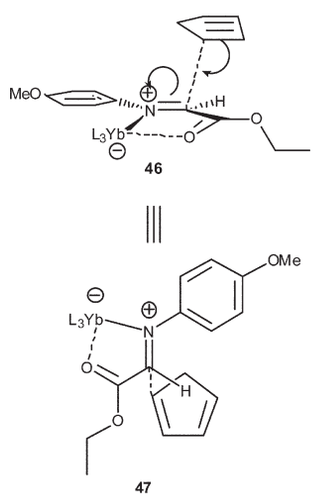


Scheme 4 Proposed mechanism for the formation of adduct **11** from the reaction of cyclopentadiene with imine **1** catalysed by ytterbium(III).

From the Lewis acid-complex **35**, the nucleophile approaches along the least hindered path, as shown by **35** and **37**. The nitrogen end of the imine is blocked by the ytterbium complex and the *p*-methoxyphenyl group, which of course can rotate about the C–N axis. The logical approach of the diene to the activated imine is a Bürgi–Dunitz trajectory, with the major part of the diene orientated away from the ethyl ester, as shown by **37**, producing the intermediate complex **36**. Rotation about the newly formed C–C bond to give **38** then exposes the allylic cation to the aromatic ring, where cyclisation occurs. Re-aromatisation and aqueous work-up subsequently give the cycloadduct **11** with the correct relative configuration. Of course this model relies on the fact that the imine **1** has *E*-stereochemistry; if the imine were to react in an *S-cis*-conformation, the stereochemistry of the product would be incorrect compared to that observed (Scheme 5). In that case, it may be more likely to consider bidentate chelation to ytterbium(III) through the imine nitrogen and the ester carbonyl (see **46** and **47**, Scheme 6), which would essentially lock the imine in the *S-trans*-configuration.



Scheme 5 Alternative mechanism for the reaction of cyclopentadiene with imine **1** catalysed by ytterbium(III).



Scheme 6 Proposed bidentate activation of imine **1** by ytterbium(III) and attack by cyclopentadiene.

It was felt that binding experiments should be undertaken to attempt to understand how binding of the imine **1** to ytterbium(III) might be occurring. To achieve this; ^{13}C NMR experiments were performed with varying catalyst loadings with respect to the imine **1**. It was envisaged that by increasing the catalyst loading, the ^{13}C NMR signals would perhaps shift differentially indicating sites of binding to ytterbium(III).

The ^{13}C NMR spectrum of imine **1** was run on its own in D_3-MeCN and was compared with samples which had been treated with 1, 5, 10, 20, 40, 60, and 100 mol% of $Yb(OTf)_3$, providing chemical shifts which could be correlated with the uncomplexed imine, as outlined in Table 4, using the numbering system in Fig. 4.

At 1 mol%, some observations were noted. Firstly, none of the chemical shifts had changed, except the imine carbon, C_6, by 0.1 ppm to δ 148.3. However, the relative intensities had all diminished somewhat, and as the amount of Yb(III) was increased the most noticeable effect was that observed for the imine carbon C_6. The diminution of the signal intensities continued through 5 and 10 mol% ytterbium(III). At 10 mol%, the aromatic C–H's *ortho* to nitrogen (C_4) showed an appreciable loss in intensity relative to the C_3, signals when compared to lower catalyst loadings. The C_5 peak had completely disappeared from the spectrum at this point. At 20 mol%, most of the peaks had virtually disappeared from the ^{13}C spectrum; in fact, the most interesting data was now extracted from the DEPT spectrum. The ester CH_2 (C_8) and aromatic CH (C_4) had diminished considerably, and the ester CH_3 (C_9) was beginning to lower in intensity relative to methoxy carbon C_1 and aromatic carbons C_3. By 60 mol%, all peaks had disappeared except C_1, C_2, C_3, C_4 and C_9. C_2 and C_9 were barely visible by this point. C_4 had moved to δ 124.0, C_2 had moved to δ 159.7, and C_9 had moved to δ 13.0. This evidence suggests primarily, that the strongest binding interaction exists between ytterbium(III) and the imine nitrogen atom. However, the fact that the ester carbonyl and ethyl units disappear at higher catalyst loadings suggests that binding at the ester carbonyl is also occurring, adding strength to the model proposed by structure **46** (Scheme 6).

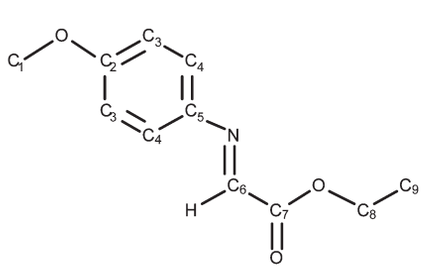
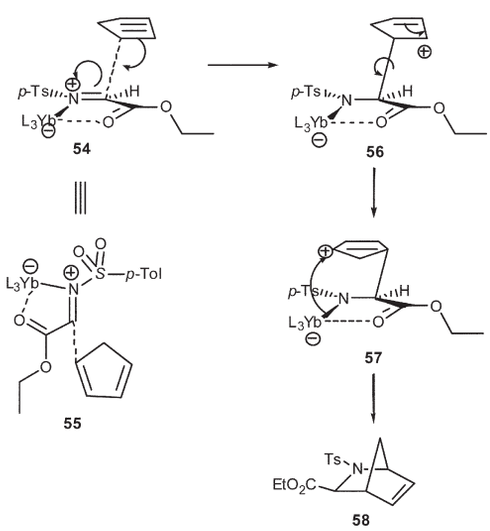


Fig. 4 Numbering scheme for imine **1**.

This seems a plausible argument, and certainly explains the outcome of the various experiments reported herein. Moreover, it may also explain the observed preference for *exo*-products in other imino-Diels–Alder reactions, for example, those reactions involving cyclopentadiene and highly electron deficient imines, such as *N*-sulfonylimines which have been proposed[23] to proceed *via* the reaction of an *E*-imine-*N*-sulfonyl imine and the cyclopentadiene approaching *endo*- relative to the tosyl group, despite the unfavourable *endo*-orientation of *N*-sulfonyl groups in such reactions.[24] However, it can be seen that by invoking a bidentate (metal-substrate) complex, where the metal is bound to the ester carbonyl and the imine nitrogen, the formation of the major *exo*-product **58** can be explained, by a process (Scheme 7) similar to that outlined in Scheme 4 (with imine activation as in Fig. 4) and a stepwise addition reaction.



Scheme 7 Proposed alternative mechanism for the reaction of a sulfonyl imine with cyclopentadiene.

Summary and conclusions

It has long been considered that aza-Diels–Alder reactions can proceed through either an unsymmetric, yet concerted cycloaddition mechanism, or *via* stepwise processes.[1] However, it is very likely that where Lewis acid catalysis is employed (particularly on electron deficient and/or *N*-aryl imines, which seem to behave randomly as either dienes or dienophiles), that these reactions proceed through stepwise addition-cyclisation mechanisms. Indeed, this is a simpler explanation for the observed chemoselectivity, which is controlled by a metal-activation, an acyclic addition reac-

Table 4 Table showing the ^{13}C NMR chemical shift values of the carbon atoms of imine **1** at various loadings of $Yb(OTf)_3$ in a D_3-acetonitrile solvent

	^{13}C Chemical shift (δ)								
$Yb(OTf)_3$ loading(mol%)	C_1	C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_9
0	54.9	160.1	114.2	123.2	141.0	148.2	163.1	61.0	13.2
1	54.9	160.1	114.2	123.2	141.0	148.3	163.1	61.0	13.2
5	54.9	160.1	114.2	123.3	141.0	148.2	163.2	61.0	13.1
10	54.9	160.1	114.3	123.4	[a]	148.1	163.2	61.1	13.1
20	54.9	160.0	114.3	123.5	[a]	148.1	163.2	61.1	13.1
40	54.9	159.9	114.4	123.9	[a]	[a]	[a]	61.3	13.0
60	54.9	159.7	114.5	124.0	[a]	[a]	[a]	[a]	13.0
100	54.7	159.5	114.4	124.0	[a]	[a]	[a]	[a]	[a]

[a] = Peak disappeared.

tion to derive intermediate zwitterionic species, which in certain cases can be intercepted.

Experimental

^1H NMR spectra were recorded on Bruker AC200, AC300 and AC400 instruments and on Varian 200, 300 and 500 model spectrometers at frequencies of 200–500 MHz in d-chloroform unless otherwise stated. ^{13}C NMR spectra were recorded on the same instruments at 75.5, 100 or 125 MHz. Chemical shifts are expressed as parts per million downfield from the internal standard tetramethyl silane. EI (70 eV) and CI mass spectra were performed on Kratos MS25, Micromass Autospec or Finnigan MAT XP 95 spectrometers. ES mass spectra were recorded on Finnigan MAT 900 XLT and Micromass Autospec spectrometers. FAB spectra were recorded on a Kratos MS50 using *meta*-nitrobenzyl alcohol matrix; high resolution spectra were obtained from either Kratos Concept IS, Finnigan MAT 900 XLT or Micromass Autospec spectrometers. IR-spectra were recorded on a Perkin-Elmer 298 spectrometer. Melting points were determined using an Electrothermal melting point apparatus and are uncorrected. HPLC were recorded using a Shimadzu Class VP HPLC system, or a Gilson HPLC system, both with a UV detector set at 254 nm. Column chromatography was performed under medium pressure with Fluka silica gel (pore size 60 Å). TLC was performed on Fluka silica gel aluminium backed plates. Visualisation of TLC plates was effected using UV radiation at 254 nm and 365 nm, and by PMA or Vanillin stain.

All glassware used in anhydrous reactions was first dried with a heat-gun and cooled under a stream of argon. All extracted solvents were first dried with $MgSO_4$. Evaporation was effected at *ca.* 20 mmHg using a Buchi rotary evaporator and water bath, followed by evaporation to dryness under high vacuum.

All solvents used were either distilled over sodium-benzophenone ketyl (THF) or calcium hydride (DCM, petroleum ether, ethyl acetate and toluene) and stored under an argon atmosphere. Acetonitrile was pre-dried over P_2O_5, re-distilled from K_2CO_3 and stored under argon over 4 Å molecular sieves.

2-Trimethylsilyloxy-1,3-butadiene was prepared according to a literature procedure.[25]

All reagents used were purchased from Fluka, Lancaster Synthesis or Aldrich Chemical Co. and used as received. Dicyclopentadiene was cracked using a fractional distillation apparatus to afford the monomer and used immediately. *p*-Anisidine was recrystallised prior to use from distilled water.

X-Ray crystallography†

A crystal of compound **21** was mounted on a Bruker SMART 1 K diffractometer and data were recorded at 120 K using Mo–K(α) (λ = 0.71073 Å) X-radiation using 0.3° ω scans. All measurements were performed on a Rigaku AFC6S diffractometer at room temperature for compound 24 using Cu–K(α) (λ = 1.54178 Å) X-radiation and employing ω-2θ scans. Hydrogen atoms were placed geometrically and not refined for both compounds. The maximum and minimum peaks in the final difference Fourier map were: 0.383 and −0.306 e $Å^{-3}$ respectively for compound **21** and 0.132 and −0.142 e $Å^{-3}$ respectively for compound **24**. Calculations were performed using the crystallographic packages SMART,[26] SAINT[27] (MSC/AFC** for 24) and SHELXTL,[28] absorption correction was applied by the use of SADABS[27] (PSI-SCANS** for 24) The neutral atom scattering factors were taken from The International Tables for Crystallography.[29] In compound **24**, part of the $CH_2CH_2CO_2Me$ group and adjacent region of the pyridine ring were disordered over semi-populated sites and were modelled accordingly. See Table 5 for crystal and structure refinement data for **21** and **24**.

Table 5 Crystal and structure refinement data for **21** and **24**

Molecular compound	Adduct **21**	Quinoline **24**
(*a*) *Crystal data*		
Chemical formula	$C_{18}H_{21}NO_4$	$C_{17}H_{19}NO_5$
F_w	315.36	317.33
Crystal system	Triclinic	Monoclinic
Space group	P-1	P 2_1/n
a (Å)	9.2885(4)	7.959(14)
b (Å)	9.7175(4)	16.440(14)
c (Å)	10.1841(5)	12.342(13)
α (°)	67.610(2)	90
β (°)	83.860(2)	90.01(1)
γ (°)	66.887(2)	90
V ($Å^3$)	780.73(6)	1615(4)
D_{calc} (g cm^{-3})	1.341	1.305
Z	2	4
μ (mm^{-1})	0.095 (Mo–Kα)	0.801 (Cu–Kα)
(*b*) *Data collection, processing and refinement*		
2θ max (°)	60.01	121.5
Data collected (*h*, *k*, *l*)	(−11, −12, −14) to (13, 13, 14)	(−5, −18, −13) to (8, 18, 13)
Total reflections	7014	5069
Unique reflections [R_{int}] (%)	4517 (????)	2397 (0.065)
Observed reflections	4517 [$I > 4\sigma(I)$]	1602 [$I > 2\sigma(I)$]
Absorption corrections	None	psi-scan
Transmission factors		0.8695–0.9599
Number of parameters	209	256
R [$I > 2\sigma(I)$]	0.0490	0.0560
R_w (all reflections)	0.1329	0.1564

General procedure for reaction screens

A solution of imine (20 mg, 0.097 mmol) in dry reaction solvent (1.5 ml) was added to stirred, pre-made solutions of Lewis acid (0.010 mmol) and chiral ligand (0.011 mmol) (each added to all of the reaction vessels as a concentrated solution in an appropriate dry solvent), which had been stirring for approximately 10 minutes at room temperature under argon. After a further 10 minutes, neat diene (0.194 mmol) was added to the reactions and they were monitored by TLC (generally hexane 1 : 1 EtOAC) for consumption of imine. When the imine had been completely consumed

or after 48 hours (whichever was sooner), the reactions were worked-up.

Ethyl 1-(4-methoxyphenyl)-4-oxo-1,2,3,4-tetrahydro-2-pyridinecarboxylate 3

Imine **1** (0.20 g, 0.97 mmol) was added to a stirred solution of $Yb(OTf)_3$ (30 mg, 0.05 mmol) in dry MeCN (5 ml) under argon. Danishefsky's diene **2** (1.45 mmol) was added at room temperature, and stirred for 3 hours. After quenching with brine, extraction with ethyl acetate (3 × 20 ml), and washing with brine (3 × 20 ml), the extract was dried and evaporated to afford crude adduct as a yellow/brown oil. Chromatography [petroleum ether (40–60) : ethyl acetate, 1 : 1 as the eluent] yielded **3** (173 mg, 65%) as a yellow oil whose data agreed with the literature.[11]

Ethyl 8-methoxy-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinoline-4-carboxylate 11

Imine **1** (0.20 g, 0.97 mmol) was added to a stirred solution of $Yb(OTf)_3$ (30 mg, 0.05 mmol) in dry MeCN (5 ml) under argon. Diene **5** (1.45 mmol) was added at room temperature, and stirred for 3 hours. After quenching with brine, extraction with ethyl acetate (3 × 20 ml), and washing with brine (3 × 20 ml), the extract was dried and evaporated to afford crude adduct as a light brown oil. Chromatography [petroleum ether(40–60) : ethyl acetate, 3 : 1 as the eluent] yielded **1** (0.214 g, 81%) as an off white solid; ν_{max} (neat)/cm^{-1} *inter alia* 3330 (NH), 1720 (COOEt); δ_H (300 MHz; $CDCl_3$) 1.35 (3H, t, *J* 7.0, OCH_2CH_3), 2.36 (1H, unsymm. tdd, *J* 2.0, 9.0 and 16.5, HC=CHC*H*H), 2.51 (1H, unsymm. qdd, *J* 2.5, 8.5 and 16.5, HC=CHCH*H*), 3.30–3.39 (1H, m, =$CHCH_2CH$), 3.77 (3H, s, OCH_3), 4.01 (1H, br s, N*H*, *exchanges with D_2O*), 4.06 (1H, d, *J* 3.5, C*H*–N), 4.09 (1H, qd, *J* 1.5 and 9.5, CHC=CHC*H*), 4.21–4.39 (2H, m, OCH_2CH_3), 5.65–5.71 (1H, m, C*H*=CH), 5.72–5.78 (1H, m, CH=C*H*), 6.58–6.64 (3H, m, ArC*H*); δ_C (75.5 MHz; $CDCl_3$) 14.7 (CH_3), 33.0 (HC=CHCH_2), 40.9 (HC=C*H*CH), 47.3 (=$CHCH_2CH$), 56.0 (N*C*H), 57.4 (OCH_3), 61.5 (OCH_2), 112.8 (Ar*C*H), 114.3 (Ar*C*H), 117.1 (Ar*C*H), 127.6 (Ar*C*–CH), 130.4 (HC=*C*HCH_2), 134.3 (H*C*=$CHCH_2$), 138.2 (Ar*C*–N), 153.5 (Ar*C*–O), 172.4 (*C*$OOCH_2$); *m*/*z* (ES^+) 274.1429 (100%, MH^+, $C_{16}H_{20}NO_3$ requires 274.1443), 200 (MH^+–HCO_2Et).

Ethyl 4-[(*E*/*Z*)-2-(acetyloxy)ethenyl]-6-methoxy-1,2,3,4-tetrahydro-2-quinolinecarboxylate 12

Imine **1** (0.20 g, 0.97 mmol) was added to a stirred solution of $Yb(OTf)_3$ (30 mg, 0.05 mmol) in dry MeCN (5 ml) under argon. Diene **7** (1.45 mmol) was added at room temperature, and stirred for 3 hours. After quenching with brine, extraction with ethyl acetate (3 × 20 ml), and washing with brine (3 × 20 ml), the extract was dried and evaporated to afford crude adduct as a light brown oil. Chromatography [petroleum ether (40–60) : ethyl acetate, 3 : 1 as the eluent] yielded a mixture of *cis*- and *trans*-vinyl acetates (approx. 1 : 6 respectively) with a *syn*-arrangement around the tetrahydroquinoline ring, and the *anti*-diastereoisomer with a *trans*-vinyl acetate [approx. 1 : 5 with respect to the major *syn*/*trans*)-diastereoisomer] **12** (0.188 g, 61%) as a yellow oil; (major *E*-diastereoisomer only) ν_{max} (neat)/cm^{-1} *inter alia* 1750 (EtOC=O), 1730 (CH_3C=O), 1620 (C=C); δ_H (300 MHz; $CDCl_3$) 1.33 (3H, t, *J* 7.0, CH_3), 1.81 (1H, td, *J* 11.0 and 12.5, NHCHC*H*H), 2.18 (3H, s, CH_3CO), 2.41 (1H, ddd, *J* 3.5, 5.5 and 12.5, NHCHC*H*H), 3.59 (1H, dt, *J* 5.5 and 10.6, AcOCH=CH*C*H), 3.74 (3H, s, OCH_3), 4.06 (1H, dd, *J* 2.5 and 11.5 C*H*CO_2Et), 4.21 (1H, br s, NH, *Exchanges with D_2O*), 4.26 (2H, q, *J* 7.2, OCH_2CH_3), 5.40 (1H, dd, *J* 10.5 and 12.5 C*H*=CHOAc), 6.57–6.71 (3H, m, ArCH), 7.32 (1H, d, *J* 12.5, CH=C*H*OAc); δ_C (100.6 MHz; $CDCl_3$) 13.2 (OCH_2CH_3), 19.7 (C(O)CH_3), 32.1 (NCHCH_2), 35.4 (HC=CH*C*H), 52.9 (N*C*HCH_2), 54.8 (OCH_3), 60.4 (OCH_2CH_3), 112.7 (Ar*C*H), 113.1 (Ar*C*H), 115.0 (HC=*C*HCH), 116.1 (Ar*C*H), 122.7 (Ar*C*C), 135.9 (Ar*C*N), 136.1 (H*C*=CHCH), 151.3 (Ar*C*O), 167.1 (*C*(O)CH_3), 171.6 (*C*O_2Et); *m*/*z* (ES^+) 320.1507 (100%, MH^+, $C_{17}H_{22}NO_5$ requires 320.1511), 278 ($MH^+ - H_2CCO$).

Ethyl (*E*)-2-(4-methoxyanilino)-6-oxohex-4-enoate 13

Imine **1** (0.20 g, 0.97 mmol) was added to a stirred solution of $Yb(OTf)_3$ (30 mg, 0.05 mmol) in wet MeCN (5 ml) under argon. Diene **8** (1.45 mmol) was added at room temperature, and stirred for 3 hours. After quenching with brine, extraction with ethyl acetate (3 × 20 ml), and washing with brine (3 × 20 ml), the extract was dried and evaporated to afford crude adduct as a red/brown oil. Chromatography [petroleum ether (40–60) : ethyl acetate, 3 : 1 as the eluent] yielded **13** (0.158 g, 59%) as a yellow oil; ν_{max} (neat)/cm^{-1} *inter alia* 3330 (NH), 1730 (COOEt), 1690 (CHO); δ_H (300 MHz; $CDCl_3$) 1.24 (3H, t, *J* 7.2, CH_3), 1.63–1.74 (1H, m, NHC*H*CO), 2.71–2.92 (2H, m, HC=CHCH_2), 3.74 (3H, s, OCH_3), 4.03 (1H, d, *J* 3.8, N*H*, *exchanges with D_2O*), 4.15–4.25 (2H, m, OCH_2CH_3), 6.19 (1H, dd, *J* 7.9 and 15.9, CHOC*H*=CH), 6.62 (2H, d, *J* 9.1, ArCH), 6.78 (2H, d, *J* 9.1, ArCH), 6.85 (1H, td, *J* 7.3 and 15.9, CHOCH=C*H*), 9.51 (1H, d, *J* 7.9, CHO); δ_C (75.5 MHz; $CDCl_3$) 14.6 (CH_3), 36.2 (=CH*C*H_2), 56.2 (OCH_3), 57.1 (NCH), 62.0 (OCH_2), 115.3 (Ar*C*H), 115.8 (Ar*C*H), 135.8 (*C*HCHO), 140.4 (Ar*C*–N), 152.4 (=*C*HCH_2), 153.5 (Ar*C*–O), 173.1 (*C*O_2Et), 193.8 (*C*HO); *m*/*z* (ES^+) 278.1393 (100%, MH^+, $C_{15}H_{20}NO_4$ requires 278.1392), 260 ($MH^+ - H_2O$), 232 (MH^+ − EtOH).

Ethyl 2-methoxy-5,6,6a,7,8,10a-hexahydro-6-phenanthridinecarboxylate 14

Imine **1** (0.20 g, 0.97 mmol) was added to a stirred solution of $Yb(OTf)_3$ (30 mg, 0.05 mmol) in dry MeCN (5 ml) under argon. Diene **9** (1.45 mmol) was added at room temperature, and stirred for 3 hours. After quenching with brine, extraction with ethyl acetate (3 × 20 ml), and washing with brine (3 × 20 ml), the extract was dried and evaporated to afford crude adduct as a light brown oil. Chromatography [petroleum ether (40–60) : ethyl acetate, 3 : 1 as the eluent] yielded **14** (0.175 g, 57%) in approximately 80–90% purity, as a yellow oil; ν_{max} (neat)/cm^{-1} 3380 (NH), 2840 (Ar–OCH_3), 2820 (HC=C–OCH_3), 1710 (COOEt), 1660 (C=C), 1230 (C–O), 1060 (=C–O–CH_3); δ_H (300 MHz; $CDCl_3$) 1.34 (3H, t, *J* 7.2, OCH_2CH_3), 1.40–1.49 (1H, m, CH_2), 1.62 (1H, qd, *J* 6.1 and 12.8, CH), 2.07 (1H, br dd, *J* 5.8 and 15.4, CH_2), 2.19–2.34 (1H, m, CH_2), 2.41–2.49 (1H, m, CH), 3.60 (3H, s, H_3CO–C=CH), 3.75 (3H, s, H_3CO–Ar), 3.70–3.76 (1H, m, CH_2), 4.04–4.25 (1H, br s, NH), 4.15 (1H, d, *J* 2.7, NCH), 4.23–4.36 (2H, m, OCH_2CH_3), 5.14 (1H, br d, *J* 6.1, MeO–C=C*H*), 6.56 (1H, unsymm. d, *J* 8.6, ArC*H*), 6.64 (1H, unsymm. dd, *J* 2.4 and 8.7, ArC*H*), 6.79 (1H, unsymm. d, *J* 2.4, ArC*H*); δ_C (100.6 MHz; $CDCl_3$) 14.7 (OCH_2CH_3), 28.0 (MeO–CCH_2), 35.2 (NCH*C*H), 35.7 (NCHCH*C*H), 54.7 (N*C*H), 56.1 (H_3CO–C=C), 57.8 (H_3CO–Ar), 61.7 (OCH_2CH_3), 95.3 (MeO–C=*C*H), 113.1 (Ar*C*H), 115.1 (Ar*C*H), 116.2 (Ar*C*H), 126.5 (Ar*C*–C), 135.8 (MeO–*C*=CH), 152.9 (Ar*C*–N), 156.3 (Ar*C*–O), 172.6 (*C*$OOCH_2$); *m*/*z* (ES^+) 615 (2M + H^+) 318.174 (100%, MH^+, $C_{18}H_{24}NO_4$ requires 318.1705).

Ethyl 5-acetyl-8-methoxy-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinoline-4-carboxylate 21

Pyridine (1 ml) and acetic anhydride (1 ml) were added to **11** (0.111 g, 0.41 mmol) under argon. After 16 h, the reaction was cooled to 0 °C, quenched with water (5 ml), extracted with EtOAc (2 × 20 ml), washed with 5% HCl (2 × 20 ml), water (2 × 20 ml), dried and evaporated to yield a dark brown oil. Silica gel chromatography [petroleum ether (40–60) : EtOAc, 1 : 1 as eluent] yielded **21** (219 mg, 72%) as a white crystalline solid; mp 109 °C; ν_{max} (neat)/cm^{-1} *inter alia* 1730 (COOEt), 1660 (NC=O), 1650 (C=C); δ_H (300 MHz; $CDCl_3$) 1.12 (3H, t, *J* 7.2, CH_2CH_3), 2.21 (3H, s, $COCH_3$), 2.51–2.69 (2H, m, HC=CHCH_2), 3.2 (1H, ddd, *J* 4.9, 7.3 and 12.4, =$CHCH_2CH$), 3.81 (3H, s, OCH_3), 3.84–3.91 (1H, m, HC=CHC*H*), 3.92–4.02 (2H, m, OCH_2CH_3), 5.52 (1H, d, *J* 7.9, NC*H*), 5.76–5.82 (1H, m, *H*C=CH), 5.85–5.90 (1H, m, HC=C*H*), 6.75–6.81 (2H, m, ArCH), 7.09 (1H, d, *J* 8.3, ArC*H*CN); δ_C (75.5 MHz; $CDCl_3$) 14.4 (CH_3), 22.9 ($COCH_3$), 35.6 (HC=CH*C*H_2), 41.5 (HC=CH*C*H), 46.3 (=$CHCH_2CH$),

54.8 (NCH), 55.8 (OCH$_3$), 61.1 (OCH$_2$), 112.1 (ArCH), 113.4 (ArCH), 126.6 (ArCH), 131.7 (ArC–CH), 131.8 (HC=CHCH$_2$), 132.9 (HC=CHCH$_2$), 134.7 (ArC–N), 157.6 (ArC–O), 170.1 (NCOCH$_3$), 170.3 (COOCH$_2$); *m*/*z* (EI) 316 (100%, MH$^+$), 274 (MH$^+$ − COCH$_2$), 200 (MH$^+$ − CH$_3$CONCHCO$_2$Et). $C_{18}H_{21}NO_4$ requires C, 68.55; H, 6.71; N, 4.44; Found C, 68.44; H, 6.80; N, 4.50%.

4-[2-(Acetyloxy)ethyl]-6-methoxy-2-quinolinyl propionate 24

To a flask charged with 10% palladium on activated carbon (5 mg, 0.005 mmol) and ethyl acetate (15 ml) was added **12** (15 mg, 0.05 mmol). The flask was evacuated and purged with hydrogen three times, then stirred overnight under a positive pressure of hydrogen. Filtration of the reaction mixture through Celite followed by evaporation *in vacuo* gave a crude pale yellow oil which was purified by column chromatography [petroleum ether (40–60) : EtOAc, 3 : 1 as eluent] to give **24** (13 mg, 86%) as a white crystalline solid; mp 110–112 °C; ν_{max} (neat)/cm^{-1} *inter alia* 1730 (H$_3$CC=O), 1710 (EtOC=O); δ_H (300 MHz; CDCl$_3$) 1.50 (3H, t, *J* 7.2, CH$_3$CH$_2$O), 2.08 [3H, s, C(O)CH$_3$], 3.43 (2H, t, *J* 7.4, CH$_2$CH$_2$OAc), 4.03 (3H, s, OCH$_3$), 4.47 (2H, t, *J* 7.4, CH$_2$CH$_2$OAc), 4.55 (2H, q, *J* 7.2, OCH$_2$CH$_3$), 7.43 [1H, s, ArC(5)H], 7.46 [1H, dd, *J* 2.6 and 8.4, ArC(7)H], 8.06 [1H, s, ArC(3)H], 8.22 [1H, dd, *J* 1.1 and 8.4, ArC(8)H]; δ_C (75.5 MHz; CDCl$_3$) 14.8 (OCH$_2$CH$_3$), 21.4 (CH$_3$COO), 32.3 (CH$_2$CH$_2$OAc), 56.2 (OCH$_3$), 62.5 (NCHCH$_2$), 54.3 (NCHCH$_2$), 56.0 (CH$_3$O), 62.5 (OCH$_2$CH$_3$), 63.5 (CH$_2$CH$_2$OAc), 101.5 [ArC(5)–H], 122.3 [ArC(3)H], 123.3 [ArC(7)H], 130.5 [ArC(4)], 133.6 [ArC(8)H], 143.3 [ArC(4a)], 144.3 [ArC(8a)], 145.8 [ArC(2)], 160.1 [ArC(6)], 166.1 (CH$_3$COO), 171.5 (COOCH$_2$); *m*/*z* (ES$^+$) 318.1344 (100%, MH$^+$, $C_{17}H_{20}NO_5$ requires 318.1341), 320 (MH$^+$ − CH$_2$CO), 316 (MH$^+$ − C$_2$H$_5$OH).

4-[(*E*/*Z*)-2-(Acetyloxy)ethenyl]-6-methoxy-2-quinolinyl propionate 25

Imine **1** (0.20 g, 0.97 mmol) was added to a stirred solution of Yb(OTf)$_3$ (30 mg, 0.05 mmol) in dry MeCN (5 ml) under argon. Diene **7** (1.45 mmol) was added at room temperature, and stirred for 3 hours. MeCN was removed *in vacuo*, and the residue re-dissolved in chloroform (10 ml). This was then stirred at room temperature in an air atmosphere for 7 days. Solvent removal was followed by silica gel chromatography (hexane : ethyl acetate gradient) to yield a mixture of *E* and *Z* diastereoisomers (approximately 4 : 1 respectively) of **25** (255 mg, 83%) as a bright yellow powder; mp 124–130 °C; ν_{max} (neat)/cm^{-1} *inter alia* 1760 (H$_3$CC=O), 1710 (EtOC=O), 1645 (C=C–OAc); δ_H (300 MHz; CDCl$_3$) 1.51 (4.11H, t, *J* 7.2, OCH$_3$CH$_2$, both), 2.26 (1.11H, s, CH$_3$COO, minor), 2.30 (3H, s, CH$_3$COO, major), 3.98 (1.11H, s, OCH$_3$, minor), 3.99 (3H, s, OCH$_3$, major), 4.57 (2.74H, q, *J* 7.2, CH$_3$CH$_2$O, both), 6.31 (0.37H, d, *J* 7.3, CH=CH–OAc, minor), 6.98 (1H, d, *J* 12.6, CH=CH–OAc, major), 7.24 [1.37H, unsymm. d, *J* 2.7, ArC(5)H, both], 7.44 [1.37H, dd, *J* 2.7 and 9.4, ArC(7)H, both], 7.69 (0.34H, d, *J* 7.3, CH=CH–OAc, minor), 8.10 (1H, unsymm. d, *J* 12.7, CH=CH–OAc, major), 8.19 [1H, s, ArC(3)H, major], 8.22 [1H, d, *J* 9.4, ArC(8)H, major], 8.23 [0.37H, d, *J* 9.4, ArC(8)H, minor], 8.52 [0.37H, s, ArC(3)H, minor]; δ_C (75.5 MHz; CDCl$_3$) 14.8 (OCH$_2$CH$_3$, both), 21.1 [OC(O)CH$_3$, major], 21.2 [OC(O)CH$_3$, minor], 56.1 (OCH$_3$, both), 62.5 (OCH$_2$CH$_3$, minor), 62.6 (OCH$_2$CH$_3$, major), 101.5 [ArC(5)H, major], 101.7 [ArC(5)H, minor], 106.6 (AcOCH=CH, minor), 110.3 (AcOCH=CH, major), 118.4 [ArC(7)H, major], 122.2 [ArC(7)H, minor], 123.2 [ArC(3)H, minor], 123.4 [ArC(3)H, major], 129.1 [ArC(4a)C, minor], 129.2 [ArC(4a)C, major], 133.4 [ArC(8)H, both], 138.3 (AcOCH=CH, minor), 138.4 [ArC(4)C, minor], 138.6 [ArC(4)C, minor], 139.9 [ArC(4)C, major], 140.8 (AcOCH=CH, major), 144.5 [ArC(2)C, major], 144.6 [ArC(2)C, minor], 145.8 [ArC(8a)N, minor], 145.9 [ArC(8a)N, major], 159.9 [ArC(6)O, both], 166.0 [CH$_3$C(O)O, major], 166.2 [CH$_3$C(O)O, minor], 167.8 (EtO$_2$C, minor), 167.9 (EtO$_2$C, major); *m*/*z* (ES$^+$) 316 (100%, MH$^+$), 255 [MH$^+$ − CH$_3$CO(OH$_2$)]; $C_{17}H_{17}NO_5$ requires C, 64.75; H, 5.43; N, 4.44; Found C, 64.35; H, 5.53; N, 4.55%.

Ethyl 1-acetyl-4-[(*E*/*Z*)-2-(acetyloxy)ethenyl]-6-methoxy-1,2,3,4-tetrahydro-2-quinolinecarboxylate 23

Imine **1** (0.20 g, 0.97 mmol) was added to a stirred solution of Yb(OTf)$_3$ (30 mg, 0.05 mmol) in dry MeCN (5 ml) under argon. Diene **8** (1.45 mmol) was added at room temperature, and stirred for 3 hours. Solvent was evaporated *in vacuo*, and pyridine (2 ml) and acetic anhydride (2 ml) were added at room temperature under an argon atmosphere. The reaction was stirred overnight, after which the reaction was cooled to 0 °C, quenched with water (5 ml), extracted with EtOAc (2 × 30 ml), washed with 5% HCl (2 × 30 ml), saturated sodium bicarbonate (3 × 50 ml), brine (2 × 30 ml), dried (MgSO$_4$) and evaporated to yield a dark brown oil. Silica gel chromatography [petroleum ether (40–60) : EtOAc, 3 : 1 as eluent] yielded **23** (139 mg, 40%) as a light brown oil; ν_{max} (neat)/cm^{-1} *inter alia* 1750 (O=C, AcO and EtO$_2$C), 1660 (C=C and NC=O); δ_H (300 MHz; CDCl$_3$) 1.25 (3H, t, *J* 7.0, CH$_3$CH$_2$O), 1.60 (1H, dt, *J* 10.0 and 12.6 NCHCHH), 2.19 (3H, s, CH$_3$CON), 2.20 (3H, s, CH$_3$COO), 2.64 (1H, ddd, *J* 4.0, 9.5 and 13.1, NCHCHH), 3.23 (1H, ddd, *J* 4.0, 9.0, 13.0 CHCH=CHO), 3.83 (3H, s, OCH$_3$), 4.09–4.21 (2H, m, CH$_3$CH$_2$O), 5.26 (1H, t, *J* 9.5, NCH), 5.55 (1H, dd, *J* 9.5 and 12.5, CHCH=CHO), 6.73 (1H, d, *J* 3.0, ArCH), 6.83 (1H, dd, *J* 3.0 and 8.5, ArCH), 7.16 (1H, d, *J* 8.5, ArCH), 7.34 (1H, d, *J* 12.5, AcOCH=); δ_C (75.5 MHz; CDCl$_3$) 14.5 (OCH$_2$CH$_3$), 21.1 (CH$_3$COO), 22.8 (CH$_3$CON), 35.5 (ArCHCH=), 36.0 (NCHCH$_2$), 54.3 (NCHCH$_2$), 56.0 (CH$_3$O), 61.6 (OCH$_2$CH$_3$), 111.6 (ArCH), 112.0 (ArCH), 113.2 (AcOCH=CH), 126.8 (ArCH), 130.7 (ArC–N), 138.2 (AcOC=CH), 139.0 (ArC–C), 158.0 (ArC–O), 168.3 (CH$_3$COO), 170.6 [NC(O)CH$_3$], 171.9 (COOCH$_2$); *m*/*z* (ES$^+$) 362.1595 (100%, MH$^+$, $C_{19}H_{24}NO_6$ requires 362.1604), 320 (MH$^+$ − CH$_2$CO), 316 (MH$^+$ − C$_2$H$_5$OH).

Ethyl-1-(4-methoxyphenyl)-4-[(trimethylsilyl)oxy]-1,2,3,6-tetrahydro-2-pyridinecarboxylate 33

Imine **1** (0.20 g, 0.97 mmol) was added to a stirred solution of Yb(OTf)$_3$ (30 mg, 0.05 mmol) in dry MeCN (5 ml) under argon. Diene **32** (1.45 mmol) was added at room temperature, and stirred overnight. The reaction mixture was adsorbed onto silica gel and purified by column chromatography (hexane : ethyl acetate gradient) to yield **33** (175 mg, 53%) as a white crystalline solid; mp 69–70 °C; ν_{max} (neat)/cm^{-1} *inter alia* 1735 (COOEt), 1685 (C=C), 1257 (SiMe$_3$); δ_H (200 MHz; CDCl$_3$) 0.00 [9H, s, Si(CH$_3$)$_3$], 0.97 (3H, t, *J* 7.2, OCH$_2$CH$_3$), 2.30 (1H, unsymm. dd, *J* 1.6 and 16.8, NCHCHH), 2.46–2.64 (1H, m, NCHCHH), 3.55 (3H, s, OCH$_3$), 3.58–3.65 (1H, m, NCHH), 3.65–3.72 (1H, q, *J* 2.4, NCHH), 3.78–3.98 (2H, m, OCH$_2$CH$_3$), 4.33–4.39 (1H, dd, *J* 2.2 and 6.6 NCHCHH), 4.71–4.76 (1H, m, CH=COSiMe$_3$), 6.63 (4H, s, ArCH); δ_C (100.6 MHz; CDCl$_3$) 0.0 [Si(CH$_3$)$_3$], 13.9 (OCH$_2$CH$_3$), 32.3 (NCHCH$_2$), 44.4 (NCH$_2$), 55.3 (OCH$_3$), 56.8 (NCHCH$_2$), 60.4 (OCH$_2$CH$_3$), 101.2 (CH=C), 114.2 (ArCH), 116.1 (ArCH), 143.5 (ArC–N), 146.0 (CH=C–OTMS), 152.6 (ArC–O), 171.9 (CO$_2$Et); *m*/*z* (ES$^+$) 721 (2M + Na$^+$), 372 (100%, MNa$^+$). $C_{18}H_{27}NO_4$ requires C, 61.86; H, 7.79; N, 4.01; Found C, 68.89; H, 7.83; N, 3.96%; and **34** (98 mg, 37%) as a yellow oil; ν_{max} (neat)/cm^{-1} *inter alia* 1729 (2 × C=O); δ_H (300 MHz; CDCl$_3$) 1.09 (3H, t, *J* 7.2, OCH$_2$CH$_3$), 2.52–2.61 (2H, m, NCH$_2$CH$_2$), 2.62–2.71 (1H, m, NCHCHH), 2.80 (1H, unsymm. dd, *J* 6.6 and 15.0, NCH$_2$CHH), 3.47–3.56 (1H, unsymm. dd, *J* 5.0 and 11.9, NCHH), 3.58–3.65 (1H, m, NCHH), 3.71 (1H, s, OCH$_3$), 4.04 (2H, q, *J* 7.2, OCH$_2$CH$_3$), 4.46–4.52 (1H, m, NCHCH$_2$), 6.73–6.82 (2H, unsymm. d, *J* 9.0, ArCH), 6.85–6.90 (2H, unsymm. d, *J* 9.0, ArCH); δ_C (100.6 MHz; CDCl$_3$) 13.1 (OCH$_2$CH$_3$), 39.3 (NCH$_2$CH$_2$), 41.4 (NCHCH$_2$), 44.8 (NCH$_2$CH$_2$), 54.6 (OCH$_3$), 60.2 (OCH$_2$CH$_3$), 60.5 (NCHCH$_2$), 113.5 (ArCH), 117.9 (ArCH), 142.3 (ArC–N), 153.3 (ArC–O), 170.1 (CO$_2$Et), 205.3 (C=O); *m*/*z* (ES$^+$) 300.1240 (100%, MNa$^+$, $C_{15}H_{19}NO_4Na$ requires 300.1212).

CCDC deposition numbers for crystal structures: CCDC 237039 for quinoline **24** and CCDC 237030 for adduct **21**.

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