View metadata, citation and similar papers at core.ac.uk

brought to you by CORE

provided by CiteSeerX

Tetrahedron 66 (2010) 6293–6299

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Synthesis of highly functionalized 2,5-disubstituted pyrrolidines via an aza-Morita–Baylis–Hillman-type reaction

James E. Kitulagoda, Anders Palmelund, Varinder K. Aggarwal *

School of Chemistry, University of Bristol, Cantock's Close, Bristol BS8 1TS, UK

ARTICLE INFO

Article history:
Received 8 March 2010
Received in revised form 5 May 2010
Accepted 13 May 2010
Available online 20 May 2010

This paper is dedicated with admiration to Professor Steven Ley on the award of the Tetrahedron Prize for creativity in organic chemistry. Many congratulations!

ABSTRACT

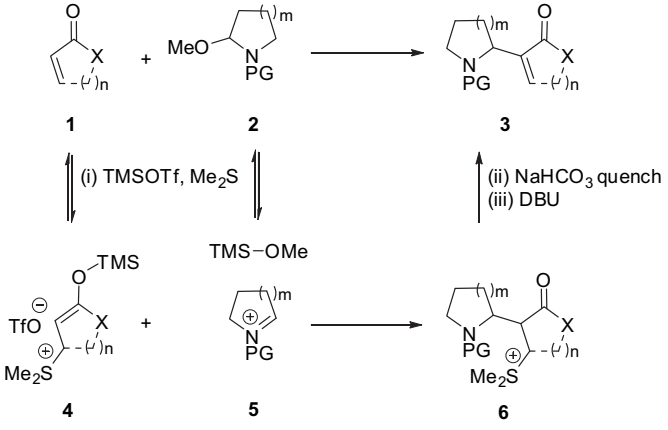
An aza-Morita–Baylis–Hillman-type reaction of Michael acceptors with 5-substituted cyclic *N*,*O*-acetals derived from pyrrolidines has been investigated. It has been found that the combination of Me_2S and TMSOTf work well with unhindered and reactive enals and enones whilst the use of quinuclidine and TMSOTf is superior for more hindered Michael acceptors. The reactions lead to 2,5-*trans*-disubstituted pyrrolidines with good to excellent diastereoselectivity. The origin of the selectivity is discussed.

© 2010 Elsevier Ltd. All rights reserved.

1. Introduction

2,5-Disubstituted pyrrolidines are common motifs found in many natural products, as well as molecules with potential pharmaceutical applications. In addition they have been used as chiral auxiliaries,[1] chiral ligands[2] and as organocatalysts for asymmetric synthesis.[3] A common strategy towards their synthesis involves nucleophilic addition to 5-substituted *N*,*O*-acetals. A broad range of nucleophiles have been reported, including organosilanes,[4] allylstannanes,[5] organocuprates,[6] cyanides[7] and thiols,[8] but the diastereoselectivity of the addition reactions has been found to be highly substrate- and nucleophile-dependent.

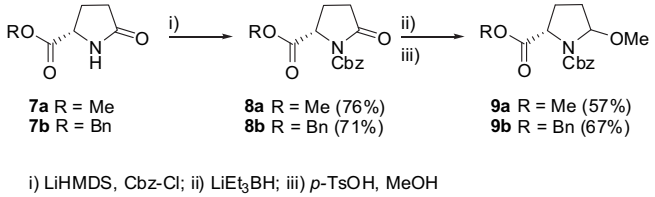
Recently, we reported a novel protocol for the synthesis of β′-amido-α,β-unsaturated carbonyl compounds **3** through a mechanism akin to the aza-Morita–Baylis–Hillman reaction (aza-MBHR) (Scheme 1).[9] In this protocol, the combination of TMSOTf, Me_2S and Michael acceptor gave an intermediate β-sulfonium silyl enol ether **4**, which reacted with an iminium ion **5** to give the Mannich adduct **6**. Following base treatment the aza-MBH adduct **3** was generated. In this paper we report an extension of this general protocol to 5-substituted pyrrolidine-derived *N*,*O*-acetals to give highly functionalized 2,5-disubstituted pyrrolidines with good-high trans-diastereoselectivity.



Scheme 1. Aza-Morita–Baylis–Hillman-type reaction of *N*,*O*-acetals.

2. Results and discussion

The required *N*,*O*-acetal substrates were prepared following the general procedure shown in Scheme 2.[10]



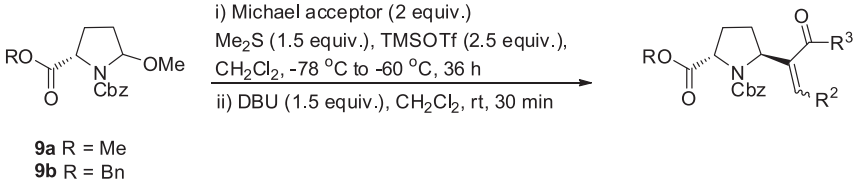
Scheme 2. Synthesis of *N*,*O*-acetals.

* Corresponding author. Tel.: +44 117 954 6315; fax: +44 117 929 8611; e-mail address: v.aggarwal@bristol.ac.uk (V.K. Aggarwal).

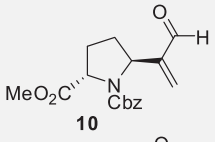
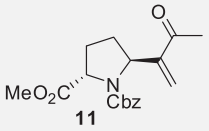
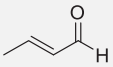
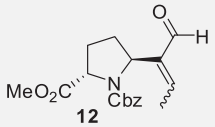
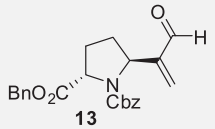
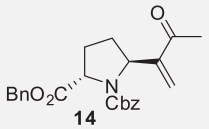
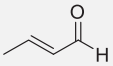
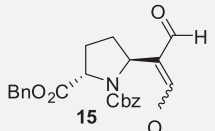
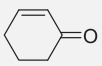
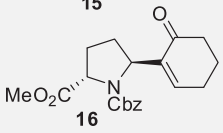
0040-4020/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2010.05.047

Application of our previously reported reaction conditions to a series of Michael acceptors and *N*,*O*-acetals, but extending the reaction time from 3 h to 36 h, gave the aza-MBH adducts in moderate-good yield and with moderate-high trans-selectivity (Table 1). repeating the experiment in entry 7 at −50 °C failed to afford any of the desired product. Variable temperature NMR experiments of the reaction of cyclohexenone, TBDMSOTf and Me_2S performed by Lee and Iwasawa demonstrated that the β-sulfonium silyl enol ether was

Table 1
Aza-Morita–Baylis–Hillman-type reactions of aminals using Me_2S as Lewis base



9a R = Me
9b R = Bn

Entry	*N*,*O*-Acetal	Michael Acceptor	Product	Yield[a] (%)	trans/cis[b]
1	**9a**		 **10**	61	>95:5
2	**9a**		 **11**	75	80:20
3	**9a**		 **12**	72	84:16[c]
4	**9b**		 **13**	57	>95:5
5	**9b**		 **14**	62	>95:5
6	**9b**		 **15**	71	70:30[d]
7	**9a**		 **16**	25	87:13

[a] Yield of isolated product.
[b] Determined by ^1H NMR of the crude product.
[c] trans-Diastereoisomer isolated as a 1:4 (*Z*/*E*) mixture of diastereoisomers.
[d] trans-Diastereoisomer isolated as a 1:3 (*Z*/*E*) mixture of diastereoisomer.

Acrolein gave very high trans-selectivity with both *N*,*O*-acetals (entries 1 and 4) whilst MVK gave higher selectivity with the more hindered *N*,*O*-acetal **9b** (entries 2 and 5). Crotonaldehyde gave a mixture of *E*- and *Z*-enals with moderate diastereoselectivity (entries 3 and 6). However, cyclohexenone only gave the aza-MBH adduct in low yield and the corresponding reaction with cyclopentenone only gave traces of the desired product. The low yield obtained with cyclohexenone and cyclopentenone prompted us to study this reaction further.

We reasoned that the β-sulfonium silyl enol ether of this more hindered and less reactive substrate might require higher reaction temperatures to undergo addition to the iminium ion. However,

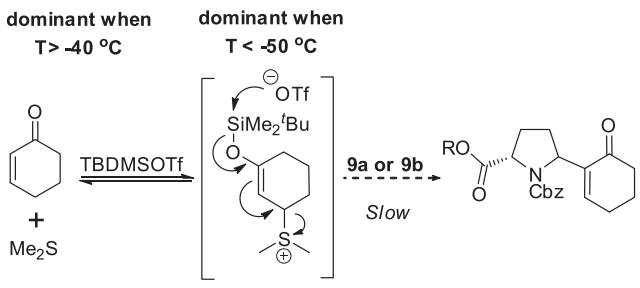
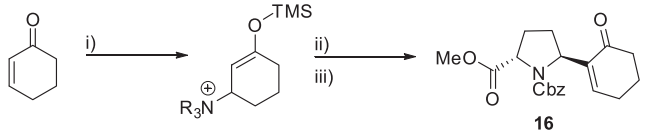


Figure 1. Stability of sulfonium silyl enol ether triflate as a function of temperature.

Table 2
Aza-Morita–Baylis–Hillman-type reactions of aminals using amines as Lewis bases



i) NR_3 (1 equiv.), TMSOTf (1.5 equiv.), CH_2Cl_2, -78 °C to rt, 1 h;
ii) **9a** (0.5 equiv.), -40 °C, 3 h;
iii) DBU (1.5 equiv.), CH_2Cl_2, rt, 30 min

Entry	Tertiary amines	Yield[a] (%)	trans/cis[b]
1	Pyridine	69	75:25
2	4-*tert*-Butyl pyridine	85	76:24
3	5,6,7,8-Tetrahydroquinoline	90	82:18
4	Quinoline	<5	87:13
5	DMAP	45	72:28
6	DABCO	0	—
7	Quinuclidine	80	92:8

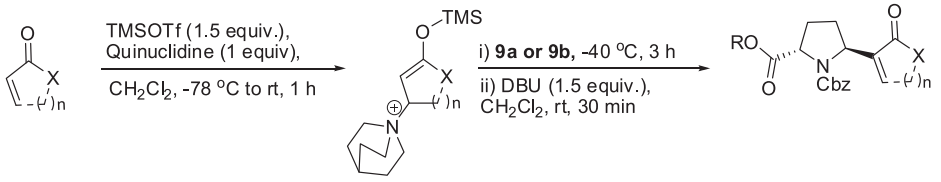
[a] Yield of isolated product.
[b] Determined by ^{1}H NMR of the crude product.

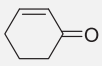
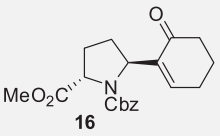
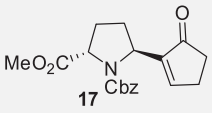
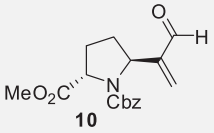
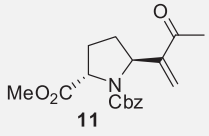
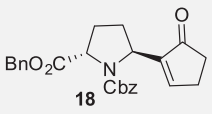
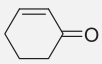
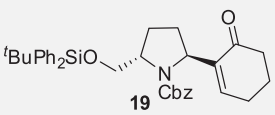
in a dynamic equilibrium with the starting materials.[11] At low temperature ($T < -50$ °C), the β-sulfonium silyl enol ether was the dominant species but at higher temperatures ($T > -45$ °C) the starting materials were favoured (Fig. 1). We presumed therefore that at the higher temperatures required for Mannich addition (i.e., $T > -50$ °C) the concentration of the β-sulfonium silyl enol ether was considerably lower, which could account for the poor conversion (Fig. 1).

Minor changes in the silyl reagent/Lewis acid or reaction conditions did not offer any significant improvements.[12] We therefore considered alternative Lewis bases, particularly as Kim had reported that β-ammonium silyl enol ether triflates were stable even at room temperature.[13] A range of amine bases were therefore tested in place of Me_2S. As an illustration of the protocol, pyridine and TMSOTf were added to cyclohexenone at −78 °C and allowed to warm to room temperature. The reaction mixture was re-cooled to −40 °C and the *N,O*-acetal **9a** added. After 3 h at −40 °C, the reaction was quenched with aqueous $NaHCO_3$, and subjected to DBU treatment, affording the product **16** in a 69% yield and a 25:75 (cis/trans) diastereomeric ratio (Table 1, entry 1). Of the bases tested (Table 2), quinuclidine proved optimum giving the aza-MBH adduct in high yield and high trans-selectivity (entry 7).

Extension of the amine-based protocol to other Michael acceptors and *N,O*-acetals was also effective (Table 3). Whilst

Table 3
Aza-Morita–Baylis–Hillman-type of *N,O-acetals* using quinuclidine as a Lewis base



Entry	*N,O*-Acetal	Michael acceptor	Product	Yield[a] (%)	trans/cis[b]
1	**9a**		 **16**	80	92:8
2	**9a**		 **17**	66	61:31
3	**9a**		 **10**	43	>95:5
4	**9a**		 **11**	0	—
5	**9b**		 **18**	86	68:32
6	**9c**		 **19**	41	<95:5

[a] Yield of isolated product.
[b] Determined by ^{1}H NMR of the crude product.

cyclopentenone gave lower diastereoselectivity (entries 2 and 5) acrolein gave very high trans-selectivity albeit in lower yield than what we had achieved with the sulfide protocol (entry 3). Unexpectedly, MVK failed to give the aza-MBH adduct under these conditions. Hemi-aminal **9c**[14] also performed well giving the adduct in moderate yield but very high dr with cyclohexenone (entry 6).

Rationalisation of the stereochemical outcome of the reactions involving pyroglutamic acid derivatives is challenging since these systems are influenced by a balance between steric and electronic factors.[15] The carbamate moiety will force the C_5-substituent into an axial position to minimize $A_{1,3}$ strain.[4a,16] The C_5-substituent will then block one face and result in preferential formation of the trans-isomer [Fig. 2 (Eq. 1)]. However, electronic effects are also operative. It has been suggested that attractive interactions between the ester side chain and silyl-based nucleophiles can be involved [Fig. 2 (Eq. 2)],[4a] which account for the cis-selectivity observed in allyl silane[4a–c,17] or silyl enol ether additions[4c] to such iminium ions. Representative results from Izawa are shown in Scheme 3.

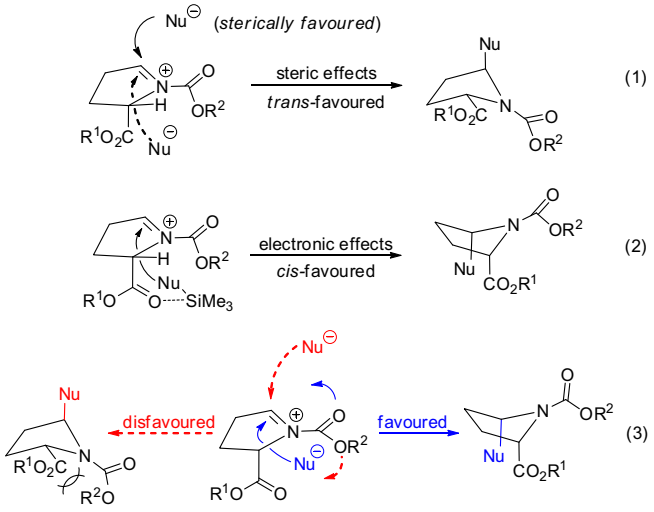
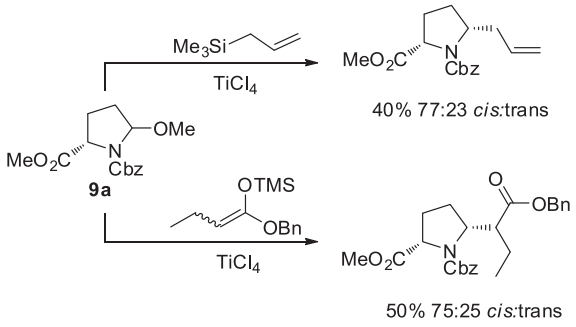


Figure 2. Electronic and steric effects on the addition of nucleophiles to pyroglutamic acid-derived iminium ions.



Scheme 3. Representative results by Izawa on addition of allyl silanes and silyl enol ethers to pyroglutamic acid-derived iminium ions.

Furthermore, it has also been suggested that trans-addition of a nucleophile pushes the *N*-carbamate group towards the C_5-substituent (due to changes in the dihedral angle) during the TS thereby incurring an energetic penalty. Conversely, cis-approach pushes the *N*-carbamate group away from the ester substituent and so will be favoured electronically (Fig. 2, Eq. 3).[4a,18]

In our case, the steric bulk of the silyl enol ether seems to dominate the stereochemical outcome of the reactions thus favoring the trans-isomer. The lower diastereoselectivity observed in certain cases may result from either competing attractive interactions between the silyl enol ether nucleophile and ester moiety or the change in dihedral angle in the TS both of which would favor the cis-isomer. Interestingly, replacement of the ester substituent for a substituent that cannot provide attractive interactions ($CH_2OSiPh_2{}^tBu$) led to complete trans-selectivity suggesting the importance of the former electronic effect (Fig. 3).

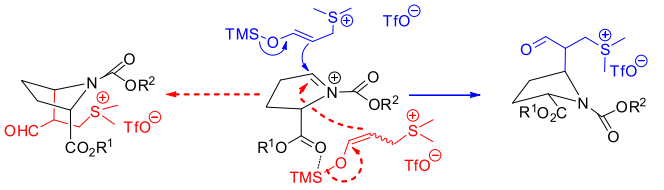


Figure 3. Origin of trans-selectivity in addition of silyl enol ethers to pyroglutamic acid-derived iminium ions.

3. Conclusions

In conclusion, we have developed two sets of reaction conditions for effecting the aza-MBH-type reaction of 5-substituted cyclic aminals: a protocol employing Me_2S and TMSOTf, which works well with unhindered and reactive enals and enones; or the use of quinuclidine and TMSOTf, which is better for more hindered Michael acceptors. The reactions lead to 2,5-*trans*-disubstituted pyrrolidines with good-high diastereoselectivity. The selectivity appears to be dominated by steric effects where a bulky silyl enol ether approaches the iminium ion from the face opposite to the C_5-substituent. In certain cases, the degree of trans-selectivity is reduced, presumably because of attractive electronic interactions between the ester substituent and the silyl enol ether.

4. Experimental

4.1. General procedure for the synthesis of aza-MBH adducts using TMSOTf/Me_2S protocol

A solution of *N*,*O*-acetals (0.34 mmol), olefin substrate (0.68 mmol) and dimethyl sulfide (39 μl, 0.51 mmol) in CH_2Cl_2 (1.6 ml) was cooled to −78 °C, to which TMSOTf (154 μl, 0.85 mmol) was added drop-wise. The reaction mixture was allowed to warm to −60 °C and stirred overnight (ca. 16 h). The reaction was quenched with saturated aqueous $NaHCO_3$ (2.5 ml), allowed to warm to room temperature. Water (20 ml) was added and the reaction mixture extracted with CH_2Cl_2 (2×20 ml). The organic phases were combined, dried ($MgSO_4$) and the solvent removed. The residue was re-dissolved in CH_2Cl_2 (1.6 ml) and DBU (76 μl, 0.51 mmol) added. The reaction mixture was allowed to stir at room temperature for 30 min before being diluted with CH_2Cl_2 (20 ml) and saturated aqueous NH_4Cl (20 ml) added. The layers were separated and the organic layer further washed with saturated aqueous NH_4Cl (20 ml). The aqueous layers were combined and extracted with CH_2Cl_2 (20 ml). The organic phases were combined, dried ($MgSO_4$) and the solvent removed. The resultant oil was purified by flash column chromatography.

*4.1.1. (2S,5S)-1-Benzyl 2-methyl 5-(3-oxoprop-1-en-2-yl)pyrrolidine-1,2-dicarboxylate (**10**).* Purification by column chromatography (1:2 EtOAc/petrol) gave **10** (66 mg, 61%) as a colourless oil.

R_f (2:3 EtOAc/petrol) 0.19; $[\alpha]_D^{25}$ −68.5 (*c* 1.3, $CHCl_3$); ν_{max} ($CDCl_3$)/cm^{-1} 1691, 1745; ^1H NMR δ_H (400 MHz, $CDCl_3$, rotamers) 1.54–1.68 (1H, m), 1.84–1.95 (1H, m), 1.96–2.15 (1H, m), 2.17–2.35

(1H, m), 3.48, 3.67 (3H, 2×s), 4.42, 4.46 (1H, 2×dd, *J*=8.9, 1.1 Hz), 4.91–4.98 (2H, m), 5.08, 5.12 (1H, 2×d, *J*=12.2 Hz), 5.93, 6.01 (1H, 2×br s), 6.00, 6.08 (1H, 2×d, *J*=1.5 Hz), 7.13–7.29 (5H, m), 9.50, 9.55 (1H, 2×s); ^{13}C NMR δ_C (101 MHz, $CDCl_3$, rotamers) 26.9, 28.1, 28.9, 29.8, 52.1, 52.3, 55.8, 56.6, 59.7, 59.8, 67.2, 127.6, 127.9, 127.9, 128.0, 128.3, 128.4, 132.6, 132.8, 136.2, 149.1, 150.1, 153.8, 154.5, 172.4, 172.7, 193.1, 193.3; HRMS (ESI) calcd for $C_{17}H_{20}O_5N$ [M+H$^+$] 318.1336, found 318.1344; calcd for $C_{17}H_{19}O_5NNa$ [M+Na$^+$] 340.1155, found 340.1163.

*4.1.2. (2S)-1-Benzyl 2-methyl 5-(3-oxobut-1-en-2-yl)pyrrolidine-1,2-dicarboxylate (**11**).* Purification by column chromatography (1:2 EtOAc/petrol) gave **11** (85 mg, 75%) as a 79:21 (trans/cis) mixture of diastereoisomers, separable by column chromatography. Both diastereoisomers were afforded as colourless oils.

*cis-**11***: R_f (1:2 EtOAc/petrol) 0.18; $[\alpha]_D^{25}$ −55.5 (*c* 2.0, $CHCl_3$); ν_{max} ($CDCl_3$)/cm^{-1} 1672, 1705, 1746; ^{1}H NMR δ_H (400 MHz, $CDCl_3$, rotamers) 1.59–1.86 (2H, m), 2.06–2.27 (2H, m), 2.24, 2.31 (3H, 2×s), 3.54, 3.72 (3H, 2×s), 4.25–4.33 (1H, m), 4.85–4.87 (1H, m), 4.96–5.09 (2H, m), 6.11, 6.16 (1H, 2×s), 6.61, 6.65 (1H, 2×s), 7.15–7.29 (5H, m); ^{13}C NMR δ_C (101 MHz, $CDCl_3$, rotamers) 26.1, 26.2, 28.0, 28.9, 31.4, 32.3, 52.0, 52.3, 57.6, 58.5, 60.3, 60.6, 67.1, 67.4, 126.3, 126.6, 127.6, 127.8, 128.0, 128.4, 136.3, 136.4, 147.4, 148.4, 154.0, 154.9, 173.2, 173.4, 199.2; MS (ESI) 332.15 [M+H$^+$], 354.13 [M+Na$^+$], 370.11 [M+K$^+$]; HRMS (ESI) calcd for $C_{18}H_{21}O_5NNa$ [M+Na$^+$] 354.1312, found 354.1312.

*trans-**11***: R_f (1:2 EtOAc/petrol) 0.14; $[\alpha]_D^{25}$ −6.6 (*c* 0.3, $CHCl_3$); ν_{max} ($CDCl_3$)/cm^{-1} 1673, 1705, 1744; ^{1}H NMR δ_H (400 MHz, DMSO-d_6, rotamers) 1.43–1.55 (1H, m), 1.81–1.93 (1H, m), 2.02–2.17 (2H, m), 2.28, 2.33 (3H, 2×s), 3.55, 3.65 (3H, 2×s), 4.53, 4.57 (1H, 2×d, *J*=8.0 Hz), 4.81, 4.86 (1H, 2×d, *J*=8.1 Hz), 4.91–5.10 (2H, m), 5.77, 5.79 (1H, 2×d, *J*=1.2 Hz), 6.23, 6.24 (1H, 2×s), 7.18–7.23 (1H, m), 7.23–7.41 (4H, m); ^{13}C NMR δ_C (101 MHz, DMSO-d_6, rotamers) 26.3, 26.4, 27.4, 29.0, 30.0, 52.0, 56.5, 57.1, 59.0, 59.4, 66.0, 66.2, 124.8, 124.8, 127.1, 127.3, 127.7, 127.8, 128.3, 128.3, 136.5, 136.7, 147.2, 148.1, 153.0, 153.5, 172.4, 172.7, 198.9, 199.0; MS (ESI) 332.15 [M+H$^+$], 354.13 [M+Na$^+$], 370.11 [M+K$^+$]; HRMS (ESI) calcd for $C_{18}H_{21}O_5NNa$ [M+Na$^+$] 354.1312, found 354.1301.

*4.1.3. (2S,5S)-1-Benzyl 2-methyl 5-(1-oxobut-2-en-2-yl)pyrrolidine-1,2-dicarboxylate (**12**).* Purification by column chromatography (1:2 EtOAc/petrol), gave **12** (81 mg, 72%) as a 84:16 (trans/cis) mixture of diastereoisomers. The diastereoisomers could be partially separated, with the trans-product (colourless oil) obtained as a 20:80 (*Z*/*E*) mixture of double bond isomers.

R_f (1:2 EtOAc/petrol) 0.18; ν_{max} ($CDCl_3$)/cm^{-1} 1701, 1744; ^{1}H NMR δ_H (400 MHz, $CDCl_3$, rotamers) 1.59–1.66 (0.2H), 1.72–1.80 (1.6H), 1.93–2.19 (3.4H), 2.27–2.67 (1.8H), 3.53, 3.73, 3.75 (3H, 3×s), 4.46, 4.49 (0.2H, 2×d), 4.55, 4.57 (0.8H, 2×t, *J*=2.5 Hz), 4.91–5.22 (3H, m), 6.32 (0.1H, q, *J*=7.5 Hz), 6.38–6.45 (0.4H, m), 6.64 (0.5H, m), 7.21–7.35 (5H, m), 9.22, 9.32 (0.8H, 2×s), 10.11, 10.17 (0.2H, 2×s); ^{13}C NMR δ_C (101 MHz, $CDCl_3$, rotamers) 12.5, 12.7, 14.2, 14.5, 26.9, 28.1, 28.7, 29.5, 29.7, 29.7, 30.3, 30.8, 51.9, 52.0, 52.15, 52.2, 53.6, 54.3, 56.6, 57.7, 59.8, 59.9, 60.4, 60.8, 66.8, 66.9, 67.1, 67.2, 127.6, 127.7, 127.8, 127.8, 127.9, 128.0, 128.0, 128.1, 128.3, 128.3, 128.3, 128.3, 136.2, 136.3, 136.3, 136.5, 139.3, 140.1, 142.0, 142.1, 143.1, 143.8, 151.2, 152.1, 153.7, 154.3, 172.5, 172.8, 173.2, 173.5, 189.6, 189.8, 193.7, 193.9; HRMS (ESI) 332.15 [M+H$^+$], 354.13 [M+Na$^+$], 371.13 [M+K$^+$]; MS (ESI) calcd for $C_{18}H_{21}O_5NNa$ [M+Na$^+$] 354.1312, found 354.1319.

*4.1.4. (2S,5S)-Dibenzyl 5-(3-oxoprop-1-en-2-yl)pyrrolidine-1,2-dicarboxylate (**13**).* Purification by column chromatography (2:1 EtOAc/petrol) gave **13** (61 mg, 57%) as a colourless oil.

R_f (1:2 EtOAc/petrol) 0.34; $[\alpha]_D^{25}$ −62.5 (*c* 1.2, $CHCl_3$); ν_{max} ($CDCl_3$)/cm^{-1} 1692, 1745; ^{1}H NMR δ_H (400 MHz, $CDCl_3$, rotamers) 1.56–1.62 (1H, m), 1.85–1.92 (1H, m), 1.96–2.13 (1H, m), 2.18–2.30 (1H, m), 4.45, 4.51 (1H, 2×d, *J*=7.6 Hz), 4.88–4.98 (3.5H, m), 5.05–5.15 (1.5H, m), 5.91, 5.99 (1H, 2×s), 6.00, 6.06 (1H, 2×d, *J*=1.2 Hz), 7.13–7.28 (10H, m), 9.49, 9.53 (1H, 2×s); ^{13}C NMR δ_C (101 MHz, $CDCl_3$, rotamers) 26.8, 28.1, 28.9, 29.8, 55.8, 56.7, 59.8, 60.0, 66.8, 66.9, 67.1, 67.1, 127.6, 127.9, 128.0, 128.1, 128.2, 128.3, 128.3, 128.4, 128.5, 132.6, 132.7, 135.3, 135.5, 136.1, 136.2, 149.1, 150.1, 153.7, 154.5, 171.7, 172.0, 193.1, 193.2; MS (ESI) 394.17 [M+H$^+$], 416.15 [M+Na$^+$], 432.12 [M+K$^+$]; HRMS (ESI) calcd for $C_{23}H_{23}O_5NNa$ [M+Na$^+$] 416.1468, found 416.1474.

*4.1.5. (2S,5S)-Dibenzyl 5-(3-oxobut-1-en-2-yl)pyrrolidine-1,2-dicarboxylate (**14**).* Purification by column chromatography (2:1 EtOAc/petrol) gave **14** (70 mg, 62%) as a colourless oil.

R_f (1:2 EtOAc/petrol) 0.19; $[\alpha]_D^{24}$ −51.0 (*c* 0.95, $CHCl_3$); ν_{max} ($CDCl_3$)/cm^{-1} 1677, 1702, 1745; ^{1}H NMR δ_H (400 MHz, DMSO-d_6, rotamers) 1.42–1.54 (1H, m, C^{9}H$_2$), 1.80–1.93 (1H, m), 2.02–2.19 (2H, m), 2.28, 2.32 (3H, 2×s), 4.59 and 4.63 (1H, 2×d, *J*=7.8 Hz), 4.82 and 4.86 (1H, d, *J*=8.0 Hz), 5.14–4.92 (4H, m), 5.76, 5.78 (1H, 2×d, *J*=1.1 Hz), 6.23, 6.24 (1H, 2×s), 7.19–7.40 (10H, m); ^{13}C NMR δ_C (101 MHz, DMSO-d_6, rotamers) 26.3, 26.4, 26.4, 27.4, 29.0, 30.0, 56.5, 57.1, 59.2, 59.6, 66.1, 66.1, 66.3, 66.3, 124.9, 124.9, 127.1, 127.3, 127.8, 127.8, 127.9, 127.9, 128.1, 128.2, 128.3, 128.4, 128.5, 135.7, 135.9, 136.5, 136.7, 147.2, 148.1, 153.0, 153.7, 171.8, 172.1, 199.1; MS (ESI) 408.18 [M+H$^+$], 430.16 [M+Na$^+$], 446.14 [M+K$^+$]; HRMS (ESI) calcd for $C_{24}H_{26}O_5N$ [M+H$^+$] 408.1805, found 408.1803; calcd for $C_{24}H_{25}O_5NNa$ [M+Na$^+$] 430.1625, found 430.1622.

*4.1.6. (2S)-Dibenzyl 5-(1-oxobut-2-en-2-yl)pyrrolidine-1,2-dicarboxylate (**15**).* Purification by column chromatography (1:2 EtOAc/petrol), gave the product (95 mg, 69%) as a 70:30 (trans/cis) mixture of diastereoisomers. The diastereoisomers could be partially separated, with the cis-product obtained as a single isomer.

*cis-**15*** isolated as a >95:5 (*Z*/*E*) mixture of double bond isomers: R_f (1:2 EtOAc/petrol) 0.31; $[\alpha]_D^{25}$ −17.1 (*c* 0.23, $CHCl_3$); ν_{max} (film)/cm^{-1} 1669, 1702, 1743; ^{1}H NMR δ_H (400 MHz, $CDCl_3$, rotamers) 1.57–1.68 (1H, m), 1.72–1.86 (1H, m), 1.90, 1.99 (3H, 2×d, *J*=7.3 Hz), 2.06–2.21 (2H, m), 4.30, 4.36 (1H, 2×t, *J*=7.8 Hz), 4.79 (1H, br s), 4.92–5.13 (4H, m), 7.14–7.28 (11H, m), 10.0, 10.1 (1H, 2×s); ^{13}C NMR δ_C (101 MHz, $CDCl_3$, rotamers) 12.6, 12.7, 28.1, 29.0, 31.4, 32.2, 57.0, 57.9, 60.5, 60.8, 67.0, 67.3, 127.7, 127.9, 128.1, 128.2, 128.2, 128.4, 128.6, 135.2, 135.5, 136.2, 136.4, 139.0, 139.8, 144.5, 145.0, 154.0, 154.9, 172.4, 172.7, 190, 190.1; MS (ESI) 408.18 [M+H$^+$], 430.16 [M+Na$^+$], 446.16 [M+K$^+$]; MS (ESI) calcd for $C_{24}H_{25}O_5NNa$ [M+Na] 430.1625, found 430.1630.

*trans-**15*** isolated as a 25:75 (*Z*/*E*) mixture of double bond isomers: R_f (1:2 EtOAc/petrol) 0.20; ν_{max} (film)/cm^{-1} 1702, 1743; ^{1}H NMR δ_H (400 MHz, $CDCl_3$, rotamers) 1.56–1.65 (0.5H, m), 1.69–1.79 (1.5H, m), 1.88–2.20 (3H, m), 2.22–2.37 (1H, m), 2.45–2.67 (1H, m), 4.42, 4.47 (0.23H, 2×d, *J*=8.8 Hz), 4.54 (0.77H, app. dt, *J*=7.9, 2.7 Hz), 4.89–5.31 (5H, m), 6.34 (0.12H, q, *J*=7.6 Hz), 6.38–6.46 (0.43H, m), 6.64 (0.45H, q, *J*=7.2 Hz), 7.18–7.40 (10H, m), 9.23, 9.33 (0.77H, 2×s), 10.12, 10.17 (0.23H, 2×s); ^{13}C NMR δ_C (101 MHz, $CDCl_3$, rotamers) 12.6, 12.8, 14.2, 14.6, 27.0, 28.2, 28.8, 29.6, 29.8, 30.4, 30.9, 53.8, 54.5, 56.8, 57.8, 66.7, 66.8, 66.8, 66.9, 67.1, 67.3, 127.7, 127.9, 128.1, 128.2, 128.3, 128.3, 128.4, 128.4, 128.4, 128.5, 128.5, 128.6, 135.4, 135.5, 135.6, 135.7, 136.3, 136.4, 136.5, 139.4, 140.2, 142.1, 142.2, 143.2, 143.9, 151.2, 152.2, 153.8, 153.8, 154.4, 154.6, 171.9, 172.2, 172.6, 172.9, 189.7, 189.8, 193.8, 194.0; MS (ESI) 408.18 [M+H$^+$], 430.16 [M+Na$^+$], 446.16 [M+K$^+$]; MS (ESI) calcd for $C_{24}H_{25}O_5NNa$ [M+Na] 430.1625, found 430.1632.

4.2. General procedure for the synthesis of aza-MBH adducts using TMSOTf/quinuclidine protocol

A solution of olefin substrate (0.68 mmol) and quinuclidine (76 mg, 0.68 mmol) in CH_2Cl_2 (1 ml) was cooled to −78 °C, to which TMSOTf (185 μl, 1.02 mmol) was added drop-wise. The cooling bath

was removed and the reaction mixture allowed to warm to room temperature. After 1 h, the reaction mixture was re-cooled to −40 °C and a solution of *N,O*-acetal (0.34 mmol) in CH_2Cl_2 (0.6 ml) added drop-wise. The reaction mixture was stirred at −40 °C for 3 h before being quenched with saturated aqueous $NaHCO_3$ (2.5 ml). Water (20 ml) was added and the reaction mixture extracted with CH_2Cl_2 (2×20 ml). The organic phases were combined, dried ($MgSO_4$) and the solvent removed. The residue was re-dissolved in CH_2Cl_2 (1.6 ml) and DBU (76 μl, 0.51 mmol) added. The reaction mixture was allowed to stir at room temperature for 30 min before being diluted with CH_2Cl_2 (20 ml) and 1 M $HCl_{(aqueous)}$ (20 ml) added. The layers were separated and the organic layer further washed with 1 M $HCl_{(aqueous)}$ (20 ml). The aqueous layers were combined and extracted with CH_2Cl_2 (20 ml). The organic phases were combined, dried ($MgSO_4$) and the solvent removed. The resultant oil was purified by flash column chromatography.

*4.2.1. (2S)-1-Benzyl 2-methyl 5-(6-oxocyclohex-1-enyl)pyrrolidine-1,2-dicarboxylate (**16**).* Purification by column chromatography (20%→33% EtOAc/petrol) gave **16** as a colourless oil (97 mg, 80%) in a 92:8 (trans/cis) mixture of diastereoisomers, separable by column chromatography.

*cis-**16***: R_f (1:2 EtOAc/petrol) 0.20; $[\alpha]_D^{25}$ +18.3 (*c* 0.6, $CHCl_3$); ν_{max} ($CDCl_3$)/cm^{-1} 1670, 1705, 1744; ^1H NMR δ_H (400 MHz, $CDCl_3$, rotamers) 1.64–2.54 (10H, m), 3.61, 3.78 (3H, 2×s), 4.31, 4.37 (1H, 2×t, *J*=7.3 Hz), 4.91 (1H, br t, *J*=10.3 Hz), 4.99, 5.04, 5.12, 5.18 (2H, 4×d, *J*=12.5 Hz), 7.23–7.35 (5H, m), 7.50 (1H, app. br q, *J*=3.6 Hz); ^{13}C NMR δ_C (101 MHz, $CDCl_3$, rotamers) 22.8, 25.7, 28.2, 28.9, 31.4, 32.3, 38.5, 38.5, 52.0, 52.2, 56.7, 57.8, 60.2, 60.4, 67.0, 67.3, 127.6, 127.8, 127.9, 128.0, 128.4, 136.3, 136.5, 138.1, 139.0, 145.5, 145.9, 154.0, 154.9, 173.3, 173.5, 198.9; MS (ESI) 358.17 [M+H^+], 380.15 [M+Na^+]; HRMS (ESI) calcd for $C_{20}H_{23}O_5NNa$ [M+Na^+] 380.1468, found 380.1475.

*trans-**16***: R_f (1:2 EtOAc/petrol) 0.14; $[\alpha]_D^{25}$ −79.1 (*c* 0.37, $CHCl_3$); ν_{max} ($CDCl_3$)/cm^{-1} 1672, 1700, 1741; ^1H NMR δ_H (400 MHz, $CDCl_3$, rotamers) 1.59–1.67 (1H, m), 1.84–2.49 (9H, m), 3.54 and 3.74 (3H, 2×s), 4.45, 4.50 (1H, 2×dd, *J*=8.9, 1.1 Hz), 4.92, 4.98, 5.19, 5.27 (2H, 4×d, *J*=12.4 Hz), 5.00–5.04 (1H, m), 6.46, 6.58 (1H, 2×dt, *J*=4.2, 1.1 Hz), 7.22–7.37 (5H, m); ^{13}C NMR δ_C (101 MHz, $CDCl_3$, rotamers) 22.6, 22.6, 25.4, 25.5, 26.9, 28.1, 29.5, 30.3, 38.4, 38.5, 52.0, 52.2, 56.3, 57.4, 59.8, 59.9, 66.7, 67.0, 127.7, 127.8, 127.9, 127.9, 128.3, 128.3, 136.3, 136.6, 138.3, 139.2, 143.2, 14.3, 153.7, 154.5, 172.5, 172.8, 198.4; MS (ESI) 358.17 [M+H^+], 380.15 [M+Na^+], 396.12 [M+K^+]; HRMS (ESI) calcd for $C_{20}H_{23}O_5NNa$ [M+Na^+] 380.1468, found 380.1475.

*4.2.2. (2S)-1-Benzyl 2-methyl 5-(5-oxocyclopent-1-en-1-yl)pyrrolidine-1,2-dicarboxylate (**17**).* A portion of the crude material (116 mg of 130 mg) was purified by column chromatography (1:2 EtOAc/petrol), affording the product as a 69:31 (trans/cis) mixture of diastereoisomers, partially separable by column chromatography. Both diastereoisomers were afforded as colourless oils (71 mg, 66% scaled yield).

*cis-**17***: R_f (1:2 EtOAc/petrol) 0.11; $[\alpha]_D^{24}$ +27.3 (*c* 0.22, $CHCl_3$); ν_{max} (film)/cm^{-1} 1636, 1696, 1747; ^1H NMR δ_H (400 MHz, $CDCl_3$, rotamers) 1.81–1.94 (2H, m), 2.20–2.27 (2H, m), 2.31–2.70 (4H, m), 3.62, 3.79 (3H, 2×s), 4.34, 4.39 (1H, 2×t, *J*=7.5 Hz), 4.74, 4.80 (1H, 2×t, *J*=7.3 Hz), 5.05, 5.14, 5.15 (2H, 3×d, *J*=12.5 Hz), 7.23–7.36 (5H, m), 7.94 (1H, br s), ^{13}C NMR δ_C (101 MHz, $CDCl_3$, rotamers) 26.5, 28.4, 29.2, 30.1, 31.2, 35.3, 35.5, 52.1, 52.3, 54.8, 55.8, 59.9, 60.1, 67.1, 67.4, 127.8, 128.0, 128.4, 136.3, 136.4, 145.6, 146.5, 153.9, 154.6, 159.9, 160.1, 173.3, 173.4, 208.6, MS (ESI) 344.15 [M+H^+], 366.13 [M+Na^+], 382.11 [M+K^+]; HRMS (ESI) calcd for $C_{19}H_{22}O_5N$ [M+H^+] 344.1492, found 344.1503.

*trans-**17***: R_f (1:2 EtOAc/petrol) 0.07; $[\alpha]_D^{24}$ +25 (*c* 0.36, $CHCl_3$); ν_{max} (film)/cm^{-1} 1636, 1696, 1747; ^1H NMR δ_H (400 MHz, $CDCl_3$, rotamers) 1.76–1.84 (1H, m), 1.93–2.02 (1H, m), 2.09–2.66 (6H, m), 3.55, 3.74 (3H, 2×s), 4.48 (0.5H, d, *J*=7.8 Hz), 4.52 (0.5H, d, *J*=8.8 Hz), 4.87 (0.5H, d, *J*=8.8 Hz), 4.90 (0.5H, d, *J*=7.6 Hz), 4.97 (1H, app. t, *J*=12.7 Hz), 5.19, 5.25 (1H, 2×d, *J*=12.2 Hz), 7.07 (0.5H, br s), 7.22–7.37 (5.5H, m); ^{13}C NMR δ_C (101 MHz, $CDCl_3$, rotamers) 26.1, 26.2, 27.5, 28.4, 28.6, 29.4, 35.3, 35.5, 52.0, 52.3, 54.4, 55.3, 59.5, 59.6, 66.9, 67.1, 127.8, 127.9, 128.0, 128.3, 128.4, 136.3, 136.5, 145.8, 146.7, 153.9, 154.5, 157.6, 158.1, 172.5, 172.9, 207.7, 207.9; MS (ESI) 344.15 [M+H^+], 366.13 [M+Na^+]; HRMS (ESI) calcd for $C_{19}H_{22}O_5N$ [M+H^+] 344.1492, found 344.1506.

*4.2.3. (2S)-Dibenzyl 5-(5-oxocyclopent-1-en-1-yl)pyrrolidine-1,2-dicarboxylate (**18**). cis-**18***: R_f (1:2 EtOAc/petrol) 0.22; $[\alpha]_D^{23}$ +29.2 (*c* 0.48, $CHCl_3$); ν_{max} (film)/cm^{-1} 1636, 1693, 1743; ^1H NMR δ_H (400 MHz, $CDCl_3$, rotamers) 1.70–1.89 (2H, m), 2.02–2.58 (6H, m), 4.31, 4.38 (1H, 2×t, *J*=7.6 Hz), 4.66, 4.71 (1H, 2×d, *J*=7.2 Hz), 4.92–5.14 (4H, m), 7.13–7.30 (10H, m), 7.74 (1H, br s); ^{13}C NMR δ_C (101 MHz, $CDCl_3$, rotamers) 23.9, 25.8, 26.7, 27.5, 28.6, 32.7, 32.9, 52.2, 53.3, 57.5, 57.8, 64.4, 64.8, 125.2, 125.3, 125.4, 125.5, 125.6, 125.7, 125.8, 125.8, 125.9, 125.9, 126.0, 132.7, 132.9, 133.7, 133.8, 142.9, 143.8, 151.4, 152.0, 157.4, 157.6, 169.9, 170.1, 205.9, 206.0; MS (ESI) 420.18 [M+H^+], 442.16 [M+Na^+], 458.14 [M+K^+]; MS (ESI) calcd for $C_{25}H_{26}O_5N$ [M+H^+] 420.1805, found 420.1817.

*trans-**18***: R_f (1:2 EtOAc/petrol) 0.15; $[\alpha]_D^{23}$ −73.6 (*c* 1.21, $CHCl_3$); ν_{max} (film)/cm^{-1} 1635, 1693, 1742; ^1H NMR δ_H (400 MHz, $CDCl_3$, rotamers) 1.74–1.81 (1H, m), 1.94–1.99 (1H, m), 2.09–2.66 (6H, m), 4.52 (0.5H, d, *J*=8.1 Hz), 4.58 (0.5H, d, *J*=8.6 Hz), 4.86 (0.5H, d, *J*=7.3 Hz), 4.91 (0.5H, d, *J*=8.6 Hz), 4.94–5.05 (2.5H, m), 5.14–5.28 (1.5H, m), 7.08 (0.5H, br s), 7.21–7.38 (10.5H, m); ^{13}C NMR δ_C (101 MHz, $CDCl_3$, rotamers) 26.1, 26.2, 27.4, 28.4, 28.6, 29.4, 35.3, 35.5, 54.4, 55.3, 59.7, 59.8, 66.8, 66.9, 67.0, 127.8, 127.8, 127.9, 127.9, 128.0, 128.1, 128.2, 128.3, 128.3, 128.5, 135.3, 135.5, 136.2, 136.4, 145.8, 146.7, 153.9, 154.5, 157.6, 158.1, 171.9, 172.2, 207.7, 207.9; MS (ESI) 420.18 [M+H^+], 442.16 [M+Na^+]; MS (ESI) calcd for $C_{25}H_{26}O_5N$ [M+H^+] 420.1805, found 420.1818.

*4.2.4. (2S)-Benzyl 2-(((tert-butyldiphenylsilyl)oxy)methyl)-5-(6-oxocyclohex-1-en-1-yl)pyrrolidine-1-carboxylate (**19**).* Purification by column chromatography (1:4 EtOAc/petrol) gave **19** (79 mg, 41%) as a colourless oil.

R_f (1:4 EtOAc/petrol) 0.29; $[\alpha]_D^{25}$ −65.6 (*c* 0.9, $CHCl_3$); ν_{max} (film)/cm^{-1} 1697, 1671; ^1H NMR δ_H (400 MHz, DMSO-d_6, rotamers) 0.98, 1.00 (9H, 2×s), 1.37 (1H, app. ddd, *J*=12.7, 12.7, 5.1 Hz), 1.66–1.97 (4H, m), 2.04–2.37 (5H, m), 3.60 (0.4H, dd, *J*=9.8, 7.1 Hz), 3.72–3.81 (1.6H, m), 4.01–4.10 (1H, m), 4.69, 4.75 (1H, 2×d, *J*=8.3 Hz), 4.78 (0.6H, d, *J*=12.6 Hz), 4.89 (0.8H, m), 5.16 (0.6H, d, *J*=12.6 Hz), 6.45, 6.48 (1H, 2×t, *J*=4.0 Hz), 7.07–7.12 (0.8H, m), 7.18–7.35 (4.2H, m), 7.37–7.50 (6H, m), 7.54–7.65 (4H, m); ^{13}C NMR δ_C (101 MHz, DMSO-d_6, rotamers) 18.7, 18.8, 22.3, 22.4, 24.4, 24.9, 25.3, 26.5, 28.8, 30.3, 38.0, 37.9, 55.7, 56.2, 58.4, 59.0, 63.1, 63.9, 65.5, 65.9, 127.4, 127.6, 127.6, 127.7, 127.8, 1278, 127.9, 128.2, 128.2, 129.8, 132.8, 132.9, 132.9, 135.0, 136.6, 137.0, 138.0, 139.2, 142.5, 142.9, 152.7, 153.2, 197.8, 198.0; MS (ESI) 568.29 [M+H^+], 590.27 [M+Na^+]; HRMS (ESI) calcd for $C_{35}H_{42}O_4NSi$ [M+H^+] 568.2878, found 568.2903; calcd for $C_{35}H_{41}O_4NNaSi$ [M+Na^+] 590.2697, found 590.2722.

Acknowledgements

We would like to thank the EPSRC for support of this work. We are grateful to Dr. Craig Butts for assistance with NMR analysis.

Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.05.047. This data include MOL file and InChIKey of the most important compounds described in this article.

References and notes

1. Whitesell, J. K.; Felman, S. W. *J. Org. Chem.* **1977**, *42*, 1663–1664; (b) Yamazaki, T.; Welch, J. T.; Plummer, J. S.; Gimi, R. *Tetrahedron Lett.* **1991**, *32*, 4267–4270; (c) Genicot, C.; Ghosez, L. *Tetrahedron Lett.* **1992**, *33*, 7357–7360; (d) Zhang, Q.; Mohan, R. M.; Cook, L.; Kazanis, S.; Peisach, D.; Foxman, B. M.; Snider, B. B. *J. Org. Chem.* **1993**, *58*, 7640–7651; (e) He, S.; Kozmin, S. A.; Rawal, V. H. *J. Am. Chem. Soc.* **2000**, *122*, 190–191; (f) Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1985**, *26*, 5807–5810; (g) Kawanami, Y.; Ito, Y.; Kitagawa, T.; Taniguchi, Y. *Tetrahedron Lett.* **1984**, *25*, 857–860; (h) Taber, D. F.; Gorski, G. J.; Liable-Sands, L. M.; Rheingold, A. L. *Tetrahedron Lett.* **1997**, *38*, 6317–6318; (i) Kim, B. H.; Lee, H. B.; Hwang, J. K.; Kim, Y. G. *Tetrahedron: Asymmetry* **2005**, *16*, 1215–1220.
2. (a) Chen, H.; Sweet, J. A.; Lam, K.-C.; Rheingold, A. L.; McGrath, D. V. *Tetrahedron: Asymmetry* **2009**, *20*, 1672–1682; (b) Hoen, R.; van denBerg, M.; Bernsmann, H.; Minnaard, A. J.; de Vries, J. G.; Feringa, B. L. *Org. Lett.* **2004**, *6*, 1433–1436; (c) Stranne, R.; Moberg, C. *Eur. J. Org. Chem.* **2001**, 2191–2195.
3. Halland, N.; Braunton, A.; Bachmann, S.; Marigo, M.; Jorgensen, K. A. *J. Am. Chem. Soc.* **2004**, *126*, 4790–4791.
4. (a) Shono, T.; Fujita, T.; Matsumura, Y. *Chem. Lett.* **1991**, 81–84; (b) Aggarwal, V. K.; Astle, C. J.; Iding, H.; Wirz, B.; Rogers-Evans, M. *Tetrahedron Lett.* **2005**, *46*, 945–947; (c) Asada, S.; Kato, M.; Asai, K.; Ineyama, T.; Nishi, S.; Izawa, K.; Shono, T. *J. Chem. Soc., Chem. Commun.* **1989**, 486–488; (d) Pilli, R. A.; Dias, L. C.; Maldaner, A. O. *J. Org. Chem.* **1995**, *60*, 717–722; (e) Martin, S. F.; Barr, K. J.; Smith, D. W.; Bur, S. K. *J. Am. Chem. Soc.* **1999**, *111*, 6990–6997.
5. Chiesa, M. V.; Manzoni, L.; Scolastico, C. *Synlett* **1996**, 441–443.
6. (a) Wistrand, L.-G.; Skrinjar, M. *Tetrahedron* **1991**, *47*, 573–582; (b) Collado, I.; Ezquerra, J.; Pedregal, C. *J. Org. Chem.* **1995**, *60*, 5011–5015.
7. (a) Corey, E. J.; Francis, P.-W. Y.; Hannon, F. J.; Wierda, D. A. *J. Org. Chem.* **1990**, *55*, 784–786; (b) Sunilkumar, G.; Nagamani, D.; Argade, N. P.; Ganesh, K. N. *Synthesis* **2003**, 2304–2306; (c) Ahman, J.; Somfai, P. *Tetrahedron* **1992**, *48*, 9537–9544; (d) Katoh, T.; Nagata, Y.; Kobayashi, Y.; Arai, K.; Minami, J.; Terashima, S. *Tetrahedron* **1990**, *50*, 6221–6238; (e) Langlois, N.; Rojas. *Tetrahedron* **1993**, *49*, 77–82; (f) Langlois, N.; Rojas-Rousseau, A.; Decavallas, O. *Tetrahedron: Asymmetry* **1996**, *7*, 1095–1100; (g) Katoh, T.; Nagata, Y.; Kobayashi, Y.; Arai, K.; Minami, J.; Terashima, S. *Tetrahedron Lett.* **1993**, *34*, 5743–5746.
8. Matsumara, Y.; Kinoshita, T.; Yanagihara, Y.; Kanemoto, N.; Watanabe, M. *Tetrahedron Lett.* **1996**, *37*, 8395–8398.
9. (a) Myers, E. L.; de Vries, J. G.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2007**, *46*, 1893–1896; (b) Killen, J. C.; Leonard, J.; Aggarwal, V. K. *Synlett* **2010**, 579–582.
10. These conditions have been applied to the analogous Boc *N*,*O*-acetals, see Ref. 4b.
11. Lee, K.; Kim, H.; Miura, T.; Kiyota, K.; Kusama, H.; Kim, S.; Iwasawa, N.; Lee, P. H. *J. Am. Chem. Soc.* **2003**, *125*, 9682–9688 See Ref. 9 for a related VT NMR study..
12. TBDMSOTf, TIPSOTf, $TiCl_4$, $BF_3{\cdot}OEt_2$ and $BF_3{\cdot}OEt_2$/TMSOTf were screened with temperatures ranging from −60 °C to room temperature
13. Kim, S.; Kim, Y. G.; Park, J. H. *Tetrahedron Lett.* **1991**, *32*, 2043–2044; β-Phosphino silyl enol ethers are also known to be stable at room temperature, see: Evans, D. A.; Hurst, K. M.; Takacs, J. M. *J. Am. Chem. Soc.* **1978**, *100*, 3467–3477.
14. See Supplementary data for the preparation of hemi-aminal **9c** from which pyrrolidine **19** is derived.
15. For a discussion of the factors affecting diastereoselectivity in reactions of cyclic oxocarbenium ions see: Smith, D. M.; Woerpel, K. A. *Org. Biomol. Chem.* **2006**, *4*, 1195–1201.
16. (a) Oba, M.; Koguchi, S.; Nishiyama, K.; Kaneno, D.; Tomoda, S. *Angew. Chem., Int. Ed.* **2004**, *43*, 2412–2415; (b) Barrett, A. G. M.; Pilipauskas, D. *J. Org. Chem.* **1991**, *56*, 2787–2800.
17. Mulzer, J.; Schülzchen, F.; Bats, J.-W. *Tetrahedron* **2000**, *56*, 4289–4298.
18. Dhimane, H.; Vanucci-Bacque, C.; Hamon, L.; Lhommet, G. *Eur. J. Org. Chem.* **1998**, 1955–1963.