Tetrahedron 64 (2008) 9396–9400

Contents lists available at ScienceDirect

Tetrahedron

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

α-Amido sulfones: novel substrates for the practical and efficient aza-Morita–Baylis–Hillman reaction under neat conditions☆

Biswanath Das *, Kongara Damodar, Nikhil Chowdhury, Darshanala Saritha, Bommena Ravikanth, Maddeboina Krishnaiah

Organic Chemistry Division-I, Indian Institute of Chemical Technology, Uppal Road Hyderabad-500007, Andhra Pradesh, India

ARTICLE INFO

Article history:
Received 2 April 2008
Received in revised form 21 July 2008
Accepted 23 July 2008
Available online 26 July 2008

Keywords:
α-Amido sulfones
aza-Morita–Baylis–Hillman reaction
α-Methylene β-amino esters
Elimination–addition reaction
DABCO–alkyl acrylate couple

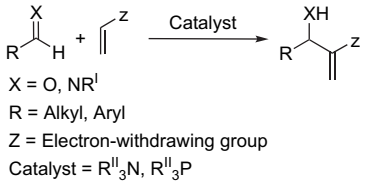
ABSTRACT

α-Amido sulfones undergo aza-Morita–Baylis–Hillman reaction efficiently with alkyl acrylates under neat conditions in the presence of DABCO at room temperature. These sulfones generate aryl imines in the presence of DABCO and form the corresponding adducts in high yields (85–94%) within 9–12 h.

1. Introduction

The Morita–Baylis–Hillman reaction involves the coupling of an activated vinylic system with an electrophile in the presence of a catalyst, generally a phosphine or a tertiary amine, leading to the formation of multifunctional molecule, known as adduct.[1] The reaction can also be catalyzed by a Lewis acid, such as $TiCl_4$ without direct use of a Lewis base.[2] The original process uses an aldehyde as an electrophile and appears as a useful carbon–carbon bond-forming method. If the aldehyde is replaced by an imine the reaction is known as the aza-Morita–Baylis–Hillman reaction[3] (Scheme 1). This reaction results in the formation of an α-methylene β-amino carbonyl compound and in particular, of an α-methylene β-amino ester when an acrylate is employed as a Michael acceptor.

The α-methylene β-amino esters are highly useful in the synthesis of various valuable compounds such as cinnamic acid derivatives, amino acid analogues, peptides, β-lactams and other nitrogen heterocycles.[4,5] The aza-Morita–Baylis–Hillman reaction is thus an important method for the preparation of the starting materials for the synthesis of these compounds.



Scheme 1. Morita–Baylis–Hillman reaction and its aza-version.

The reactions between sulfonylimines and activated olefins in the presence of DABCO as a catalyst required high temperatures and long reaction times.[3a–c] Moreover, imines, in general, tend to be unstable during purification process. Therefore, alternative methods involving the in situ generation of imines from amines and aldehydes are more attractive.[6] However, still the harsh reaction conditions, complex experimental procedures, long reaction period and unsatisfactory yields are the drawbacks in many of these methods.

An alternative access to α-methylene β-amino carbonyl compounds has been discovered starting from Morita–Baylis–Hillman adducts by converting them to the corresponding allyl bromides, acetates or related derivatives followed by treatment with amines.[7] However, such conversions require multistep transformations and in several cases the overall times are long, yields are low and regioisomers are formed. Here, we wish to report a convenient and efficient method for the preparation of α-methylene β-amino esters

☆ Part 167 in the series, 'Studies on Novel Synthetic Methodologies'.

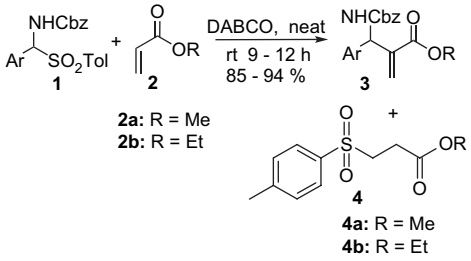
* Corresponding author. Tel./fax: +91 40 27160512.
E-mail address: biswanathdas@yahoo.com (B. Das).

0040-4020/$ – see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2008.07.093

involving α-amido sulfones. The α-amido sulfones can be conveniently prepared[8] from aldehydes, sodium salt of *p*-toluene sulfinic acid and benzylcarbamate. Most of the α-amido sulfones are stable solids and can be stored for prolonged times. A variety of nucleophilic reagents[9] can be used for reactions with these α-amido sulfones including organometallic reagents, stable carbanions, heteronucleophiles and reducing agents. Earlier, we have utilized these compounds in Sakurai reactions for the synthesis of homoallylic amines.[10] The α-amido sulfones have been employed now for the synthesis of α-methylene β-amino esters.

2. Results and discussions

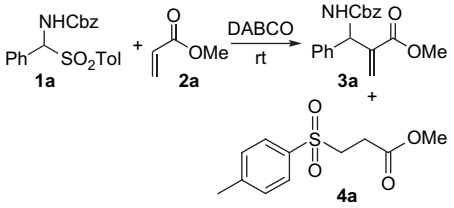
In continuation of our work[11] on the Morita–Baylis–Hillman reaction we have observed that α-amido sulfones are novel substrates for the aza-version of this reaction (Scheme 2). The reaction was conducted in the presence of DABCO at room temperature. The corresponding α-methylene β-amino esters were formed in high yields (85–94%) within 9–12 h.



Scheme 2. aza-Morita–Baylis–Hillman reaction of α-amido sulfones.

Initially the effects of solvents (Table 1) and catalysts (Table 2) on the above reaction were carefully studied. The α-amido sulfone

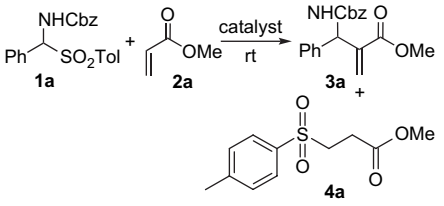
Table 1
Effect of solvent on the aza-Morita–Baylis–Hillman reaction of α-amido sulfones[a]



Entry	Solvent	Methyl acrylate (*x* mmol)	Time (h)	Yield[b] (%)
1	CH_2Cl_2	5	24	10
2	CH_2Cl_2	10	24	20
3	$CHCl_3$	5	24	10
4	$CHCl_3$	10	24	15
5	THF	5	24	40
6	THF	10	24	55
7	1,4-Dioxane	5	24	45
8	1,4-Dioxane	10	24	60
9	EtOAc	5	24	Trace
10	EtOAc	10	24	10
11	MeOH	5	24	Trace
12	MeOH	10	24	<10
13	Neat	5	24	10
14	Neat	10	24	20
15	Neat	15	24	35
16	Neat	20	11	60
17	Neat	20	24	80
18	Neat	25	11	90
19	Neat	25	24	92

[a] Reaction conditions: **1a** (1 mmol), **2a** (*x* mmol) and DABCO (1 mmol) in solvent (5 mL) at RT.
[b] Yields of isolated, pure compounds after column chromatography.

Table 2
Effect of catalyst on the aza-Morita–Baylis–Hillman reaction of α-amido sulfones[a]



Entry	Catalyst	Catalyst loading (mmol)	Time (h)	Yield[b] (%)
1	DABCO	0.25	24	35
2	DABCO	0.50	24	50
3	DABCO	0.75	11	60
4	DABCO	0.75	24	75
5	DABCO	1.00	11	90
6	DBU	1.00	24	55
7	PPh_3	1.00	11	65
8	PPh_3	1.00	24	85
9	DMAP	1.00	24	35

[a] Reaction conditions: **1a** (1 mmol) and **2a** (25 mmol) at RT.
[b] Yields of isolated, pure compounds after column chromatography.

1a (Ar=Ph) was treated with methyl acrylate in the presence of DABCO (a general catalyst for Morita–Baylis–Hillman reaction) at room temperature in various solvents as well as under neat conditions.

The yield of the product **3a** (Ar=Ph) was found to be the best (91%) when no solvent was used. Different other catalysts such as DBU, PPh_3 and DMAP were also used for the above reaction. However, DABCO was found to be the most effective to carry out the reaction. These results thus guided us to use DABCO under neat conditions for the subsequent reactions. Recently, some aza-Morita–Baylis–Hillman reactions have also been carried out under neat conditions.[12]

A series of adducts, α-methylene β-amino esters have been prepared from various α-amido sulfones by treatment with methyl acrylate (Table 3). The amine group in these α-amido sulfones was protected by Cbz (benzyloxycarbonyl) group, which can more easily be deprotected in the products compared to the tosyl group.[13] The α-amido sulfones derived from aromatic aldehydes containing both electron–donating and electron–withdrawing groups underwent the conversion smoothly. Different heterocyclic aldehydes were also used to prepare these adducts. However, in the case of aliphatic α-amido sulfones enecarbamates was only formed and this finding is in agreement with the earlier observation.[14] Instead of methyl acrylate

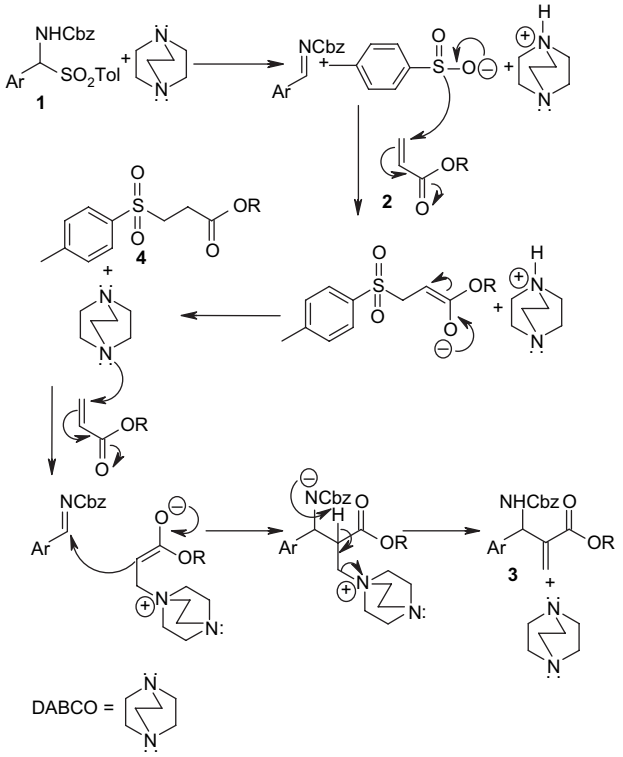
Table 3
The aza-Morita–Baylis–Hillman reaction of α-amido sulfones with alkyl acrylate (Scheme 2)[a]

Entry	α-Amido sulfone	Alkyl acrylate	Product **3**[b]	Time (h)	Yield[c] (%)
1	C_6H_5	**2a**	**3a**	11	90
2	C_6H_5	**2b**	**3b**	11	89
3	4-Cl–C_6H_4	**2a**	**3c**	10	92
4	4-MeO–C_6H_4	**2a**	**3d**	9	93
5	3,4-$(MeO)_2$–C_6H_3	**2a**	**3e**	10	92
6	3,4,5-$(MeO)_3$–C_6H_2	**2a**	**3f**	10	90
7	Vanilyl	**2a**	**3g**	10	91
8	4-NO_2–C_6H_4	**2a**	**3h**	12	85
9	3-NO_2–C_6H_4	**2a**	**3i**	12	88
10	4-Tolyl	**2a**	**3j**	10	91
11	4-Isopropylphenyl	**2a**	**3k**	10	90
12	2-Napthyl	**2a**	**3l**	11	88
13	Furan-2-yl	**2a**	**3m**	10	93
14	Thiophene-2-yl	**2a**	**3n**	10	94

[a] Reaction conditions: **1** (1 mmol), **2** (25 mmol) and DABCO (1 mmol) at RT.
[b] Structures of these compounds were determined from their NMR (^1H and ^{13}C), MS and IR data.
[c] Yields of isolated, pure compounds after column chromatography.

when ethyl acrylate was used the conversion showed almost similar results. For example, the reaction of **1a** (Ar=Ph) with methyl and ethyl acrylates afforded the corresponding aza-adducts in the yields of 91 and 89%, respectively, in 11 h (Table 3; entries 1 and 2).

The plausible mechanism of the conversion is discussed as follows. The reaction of α-amido sulfones (**1**) with DABCO produces the Cbz-protected aryl imines along with *p*-toluenesulfinate ion.[14] The latter undergoes the oxa-Michael addition with alkyl acrylate to form the by-product, alkyl-3-(*p*-tolylsulfinyloxy) propanoate (**4**). The Cbz-protected aryl imines, on the other hand, react with alkyl acrylate in the presence of DABCO following the general mechanism of the Morita–Baylis–Hillman reaction[15] to form the adducts, α-methylene β-amino esters (**3**) (Scheme 3). The whole process can be considered as tandem elimination–addition reaction that can be carried out using DABCO–alkyl acrylate couple.



Scheme 3. Proposed reaction mechanism.

In the present reaction if the sulfone **1** and the acrylate **2** were used in 1:1 mole ratio, only thia-Michael addition product **4** was formed.

3. Conclusions

In conclusion, we have developed a novel and efficient method for the preparation of α-methylene β-amino esters through the aza-Morita–Baylis–Hillman reaction involving α-amido sulfones and alkyl acrylates in the presence of DABCO at room temperature. The mild reaction conditions, solvent-free procedure, high yields, short reaction times and the formation of single regioisomer are the advantages of the method.

4. Experimental

4.1. General methods

Melting points were measured on a Buchi-510 apparatus and are uncorrected. The spectra were recorded with the following instruments; IR: Perkin–Elmer RX1 FTIR spectrophotometer; NMR: Varian Gemini 200 MHz (^{1}H) and 50 MHz (^{13}C) spectrometer; FABMS: VG-Autospec micromass and HRMS: QSTAR XL, Hybrid MS system (Applied Biosystems). Column chromatography was performed with silica gel (BDH 100–200 mesh) and TLC with silica gel GF_{254} pre-coated plates. Visualization was accomplished with UV lamp or I_2 stains. All chemicals were used as commercially available. α-Amido sulfones **1** have been prepared by reported method.[8] Organic extracts were dried over anhydrous Na_2SO_4.

4.2. General experimental procedure

To a mixture of α-amido sulfone **1** (1 mmol) and alkyl acrylate (2.15 g of methyl acrylate or 2.5 g of ethyl acrylate, 25 mmol) DABCO (112 mg, 1 mmol) was added and the mixture was stirred at room temperature. The reaction was monitored by TLC. After completion 5% aqueous HCl (10 mL) was added and the mixture was extracted with EtOAc (3×10 mL). The extract was dried over anhydrous Na_2SO_4 and concentrated. The residue was subjected to column chromatography over silica gel (EtOAc/hexane; 15:85 to 25:75) to obtain the adduct **3** and the by-product **4**.

4.3. Typical experimental procedure

*4.3.1. Methyl 3-benzyloxycarbonylamino-3-phenyl-2-methylene propanoate (**3a**)*

Following Section 4.2, α-amido sulfone **1a** (395 mg, 1 mmol), methyl acrylate **2a** (2.15 g, 25 mmol) and DABCO (112 mg, 1 mmol) gave, after purification by column chromatography (15% EtOAc/hexane), the aza-Morita–Baylis–Hillman adduct **3a** (292.5 mg, 90%) as a colourless liquid; R_f (30% EtOAc/hexane) 0.42; IR (neat): 3338, 1722, 1500, 1447, 1230 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.39–7.21 (10H, m, Ar–H), 6.32 (1H, s, H_2C=C), 5.91 (1H, s, H_2C=C), 5.78 (1H, d, *J* 8.8 Hz, –NH–), 5.69 (1H, d, *J* 8.8 Hz, –C*H*–NH–), 5.10 (2H, s, –O*CH*$_2$–Ph), 3.66 (3H, s, –OCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 166.2, 156.4, 139.7, 136.5, 128.8, 128.7, 128.3, 127.8, 127.2, 126.6, 67.2, 56.9, 52.1; FABMS: *m*/*z* 326 $[MH]^+$, 348 $[MNa]^+$; HRMS (ESI): $[MNa]^+$, found 348.1211. $C_{19}H_{19}NO_4Na$ requires 348.1211.

*4.3.2. Ethyl 3-benzyloxycarbonylamino-3-phenyl-2-methylene propanoate (**3b**)*

Following Section 4.2, α-amido sulfone **1b** (395 mg, 1 mmol), ethyl acrylate **2b** (2.5 g, 25 mmol) and DABCO (112 mg, 1 mmol) gave, after purification by column chromatography (15% EtOAc/hexane), the aza-Morita–Baylis–Hillman adduct **3b** (301.7 mg, 89%) as a colourless liquid; R_f (30% EtOAc/hexane) 0.46; IR (neat): 3344, 1718, 1500, 1232 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.40–7.18 (10H, m, Ar–H), 6.34 (1H, s, H_2C=C), 5.89 (1H, s, H_2C=C), 5.75 (1H, d, *J* 8.7 Hz, –NH–), 5.70 (1H, d, *J* 8.7 Hz, C*H*–NH–), 5.10 (2H, s, –O*CH*$_2$–Ph), 4.11 (2H, q, *J* 7.0 Hz, –O*CH*$_2$CH$_3$), 1.18 (3H, t, *J* 7.0 Hz, –OCH_2*CH*$_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 165.8, 155.8, 140.2, 139.9, 136.6, 128.8, 128.7, 128.4, 127.8, 126.9, 126.7, 67.2, 61.1, 56.9, 14.2; FABMS: *m*/*z* 340 $[MH]^+$, 362 $[MNa]^+$; HRMS (ESI): $[MNa]^+$, found 362.1377. $C_{20}H_{21}NO_4Na$ requires 362.1368.

*4.3.3. Methyl 3-benzyloxycarbonylamino-3-(4-chlorophenyl)-2-methylene propanoate (**3c**)*

Following Section 4.2, α-amido sulfone **1c** (429.5 mg, 1 mmol), methyl acrylate **2a** (2.15 g, 25 mmol) and DABCO (112 mg, 1 mmol) gave, after purification by column chromatography (20% EtOAc/hexane), the aza-Morita–Baylis–Hillman adduct **3c** (330.7 mg, 92%) as a pale yellow colour solid; R_f (35% EtOAc/hexane) 0.52; mp: 61–63 °C; IR (KBr): 3440, 1719, 1688, 1528, 1285 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.38–7.13 (9H, m, Ar–H), 6.32 (1H, s, H_2C=C), 5.91 (1H, s, H_2C=C), 5.80 (1H, d, *J* 8.9 Hz, –NH–), 5.65 (1H, d, *J* 8.9 Hz, C*H*–NH–), 5.11 (1H, d, *J* 12.0 Hz, –O*CH*$_2$–Ph), 5.04 (1H, d, *J*

12.0 Hz, –OC*H*$_2$–Ph), 3.68 (3H, s, –OCH$_3$); ^{13}C NMR (50 MHz, CDCl$_3$): δ 166.0, 155.7, 139.4, 138.3, 136.3, 133.6, 128.9, 128.7, 128.4, 128.1, 127.9, 127.7, 67.3, 56.5, 52.2; FABMS: *m*/*z* 360, 362 [MH]$^+$, 382, 384 [MNa]$^+$; HRMS (ESI): [MNa]$^+$, found 382.0831. $C_{19}H_{18}ClNO_4Na$ requires 382.0822.

4.3.4. Methyl 3-benzyloxycarbonylamino-3-(4-methoxyphenyl)-2-methylene propanoate (*3d*)

Following Section 4.2, α-amido sulfone **1d** (425 mg, 1 mmol), methyl acrylate **2a** (2.15 g, 25 mmol) and DABCO (112 mg, 1 mmol) gave, after purification by column chromatography (20% EtOAc/hexane), the aza-Morita–Baylis–Hillman adduct **3d** (330.2 mg, 93%) as a white colour solid; R_f (35% EtOAc/hexane) 0.46; mp: 66–68 °C; IR (KBr): 3344, 1720, 1509, 1245 cm^{-1}; ^{1}H NMR (200 MHz, CDCl$_3$): δ 7.38–7.23 (5H, m, Ar–H), 7.14 (2H, d, *J* 8.0 Hz, Ar–H), 6.79 (2H, d, *J* 8.0 Hz, Ar–H), 6.32 (1H, s, H$_2$C=C), 5.88 (1H, s, H$_2$C=C), 5.63 (2H, br s, –NH– and C*H*–NH–), 5.08 (2H, s, –OC*H*$_2$–Ph), 3.75 (3H, s, –OCH$_3$), 3.67 (3H, s, –OCH$_3$); ^{13}C NMR (50 MHz, CDCl$_3$): δ 166.0, 158.9, 155.4, 139.9, 136.3, 131.5, 128.4, 128.1, 127.7, 126.3, 113.9, 66.9, 56.0, 55.1, 51.9; FABMS: *m*/*z* 356 [MH]$^+$, 378 [MNa]$^+$; HRMS (ESI): [MNa]$^+$, found 378.1322. $C_{20}H_{21}NO_5Na$ requires 378.1317.

4.3.5. Methyl 3-benzyloxycarbonylamino-3-(3,4-dimethoxyphenyl)-2-methylene propanoate (*3e*)

Following Section 4.2, α-amido sulfone **1e** (455 mg, 1 mmol), methyl acrylate **2a** (2.15 g, 25 mmol) and DABCO (112 mg, 1 mmol) gave, after purification by column chromatography (20% EtOAc/hexane), the aza-Morita–Baylis–Hillman adduct **3e** (354.2 mg, 92%) as a white colour solid; R_f (35% EtOAc/hexane) 0.39; mp: 76–78 °C; IR (KBr): 3351, 1722, 1513, 1459, 1258 cm^{-1}; ^{1}H NMR (200 MHz, CDCl$_3$): δ 7.41–7.24 (5H, m, Ar–H), 6.76 (3H, br s, Ar–H), 6.31 (1H, s, H$_2$C=C), 5.89 (1H, s, H$_2$C=C), 5.63 (2H, br s, –NH– and C*H*–NH–), 5.10 (1H, d, *J* 12.0 Hz, –OC*H*$_2$–Ph), 5.04 (1H, d, *J* 12.0 Hz, –OC*H*$_2$–Ph), 3.85 (3H, s, –OCH$_3$), 3.82 (3H, s, –OCH$_3$), 3.69 (3H, s, –OCH$_3$); ^{13}C NMR (50 MHz, CDCl$_3$): δ 166.1, 155.5, 149.1, 148.6, 140.0, 136.4, 132.2, 128.5, 128.2, 126.4, 118.7, 111.2, 110.2, 67.0, 56.4, 55.9, 51.9; FABMS: *m*/*z* 408 [MNa]$^+$; HRMS (ESI): [MNa]$^+$, found 408.1429. $C_{21}H_{23}NO_6Na$ requires 408.1423.

4.3.6. Methyl 3-benzyloxycarbonylamino-3-(3,4,5-trimethoxyphenyl)-2-methylene propanoate (*3f*)

Following Section 4.2, α-amido sulfone **1f** (485 mg, 1 mmol), methyl acrylate **2a** (2.15 g, 25 mmol) and DABCO (112 mg, 1 mmol) gave, after purification by column chromatography (25% EtOAc/hexane), the aza-Morita–Baylis–Hillman adduct **3f** (373.5 mg, 90%) as a white colour solid; R_f (45% EtOAc/hexane) 0.57; mp: 79–82 °C; IR (KBr): 3350, 1721, 1592, 1502, 1234 cm^{-1}; ^{1}H NMR (200 MHz, CDCl$_3$): δ 7.40–7.22 (5H, m, Ar–H), 6.45 (2H, s, Ar–H), 6.31 (1H, s, H$_2$C=C), 5.88 (1H, s, H$_2$C=C), 5.73 (1H, d, *J* 8.8 Hz, –NH–), 5.61 (1H, d, *J* 8.8 Hz, C*H*–NH–), 5.12 (1H, d, *J* 12.0 Hz, –OC*H*$_2$–Ph), 5.05 (1H, d, *J* 12.0 Hz, –OC*H*$_2$–Ph), 3.78 (6H, s, 2×–OCH$_3$), 3.74 (3H, s, –OCH$_3$), 3.70 (3H, s, –OCH$_3$); ^{13}C NMR (50 MHz, CDCl$_3$): δ 166.1, 155.5, 153.3, 139.8, 137.5, 136.4, 135.2, 130.0, 128.5, 128.1, 126.7, 103.8, 66.9, 60.7, 56.7, 56.1, 52.0; FABMS: *m*/*z* 438 [MNa]$^+$; HRMS (ESI): [MNa]$^+$, found 438.1539. $C_{22}H_{25}NO_7Na$ requires 438.1528.

4.3.7. Methyl 3-benzyloxycarbonylamino-3-(4-hydroxy-3-methoxyphenyl)-2-methylene propanoate (*3g*)

Following Section 4.2, α-amido sulfone **1g** (441 mg, 1 mmol), methyl acrylate **2a** (2.15 g, 25 mmol) and DABCO (112 mg, 1 mmol) gave, after purification by column chromatography (25% EtOAc/hexane), the aza-Morita–Baylis–Hillman adduct **3g** (337.6 mg, 91%) as a pale yellow colour liquid; R_f (50% EtOAc/hexane) 0.44; IR (neat): 3360, 1718, 1514, 1276 cm^{-1}; ^{1}H NMR (200 MHz, CDCl$_3$): δ 7.35–7.23 (5H, m, Ar–H), 6.80–6.18 (3H, m, Ar–H), 6.30 (1H, s, H$_2$C=C), 5.87 (1H, s, H$_2$C=C), 5.62 (1H, d, *J* 8.9 Hz, –NH–), 5.61 (1H, d, *J* 8.9 Hz, C*H*–NH–), 5.49 (1H, br s, –OH), 5.11 (1H, d, *J* 12.0 Hz, –OC*H*$_2$–Ph), 5.06 (1H, d, *J* 12.0 Hz, –OC*H*$_2$–Ph), 3.83 (3H, s, –OCH$_3$), 3.69 (3H, s, –OCH$_3$); ^{13}C NMR (50 MHz, CDCl$_3$): δ 166.2, 155.5, 146.7, 145.3, 140.0, 136.4, 131.5, 128.5, 128.2, 126.3, 119.3, 114.5, 109.6, 67.0, 56.5, 55.9, 52.0; FABMS: *m*/*z* 394 [MNa]$^+$; HRMS (ESI): [MNa]$^+$, found 394.1276. $C_{20}H_{21}NO_6Na$ requires 394.1266.

4.3.8. Methyl 3-benzyloxycarbonylamino-3-(4-nitrophenyl)-2-methylene propanoate (*3h*)

Following Section 4.2, α-amido sulfone **1h** (440 mg, 1 mmol), methyl acrylate **2a** (2.15 g, 25 mmol) and DABCO (112 mg, 1 mmol) gave, after purification by column chromatography (25% EtOAc/hexane), the aza-Morita–Baylis–Hillman adduct **3h** (314.5 mg, 85%) as a pale yellow colour solid; R_f (45% EtOAc/hexane) 0.50; mp: 72–74 °C; IR (KBr): 3346, 1722, 1521, 1348, 1236 cm^{-1}; ^{1}H NMR (200 MHz, CDCl$_3$): δ 8.17 (2H, d, *J* 8.0 Hz, Ar–H), 7.45 (2H, d, *J* 8.0 Hz, Ar–H), 7.40–7.22 (5H, m, Ar–H), 6.39 (1H, s, H$_2$C=C), 6.02 (1H, s, H$_2$C=C), 5.98 (1H, d, *J* 8.8 Hz, –NH–), 5.73 (1H, d, *J* 8.8 Hz, C*H*–NH–), 5.12 (1H, d, *J* 12.0 Hz, –OC*H*$_2$–Ph), 5.09 (1H, d, *J* 12.0 Hz, –OC*H*$_2$–Ph), 3.70 (3H, s, –OCH$_3$); ^{13}C NMR (50 MHz, CDCl$_3$): δ 165.8, 155.9, 147.5, 147.3, 138.2, 136.2, 129.2, 128.8, 128.6, 128.5, 127.3, 124.0, 67.6, 57.0, 52.5; FABMS: *m*/*z* 371 [MH]$^+$, 393 [MNa]$^+$; HRMS (ESI): [MNa]$^+$, found 393.1055. $C_{19}H_{18}N_2O_6Na$ requires 393.1062.

4.3.9. Methyl 3-benzyloxycarbonylamino-3-(3-nitrophenyl)-2-methylene propanoate (*3i*)

Following Section 4.2, α-amido sulfone **1i** (440 mg, 1 mmol), methyl acrylate **2a** (2.15 g, 25 mmol) and DABCO (112 mg, 1 mmol) gave, after purification by column chromatography (25% EtOAc/hexane), the aza-Morita–Baylis–Hillman adduct **3i** (325.6 mg, 88%) as a pale yellow colour solid; R_f (45% EtOAc/hexane) 0.55; mp: 69–72 °C; IR (KB): 3338, 1721, 1530, 1349, 1232 cm^{-1}; ^{1}H NMR (200 MHz, CDCl$_3$): δ 8.18–8.09 (2H, m, Ar–H), 7.62 (1H, d, *J* 8.0 Hz, Ar–H), 7.50 (1H, t, *J* 8.0 Hz, Ar–H), 7.40–7.24 (5H, m, Ar–H), 6.42 (1H, s, H$_2$C=C), 6.02 (1H, s, H$_2$C=C), 6.01 (1H, d, *J* 8.7 Hz, –NH–), 5.79 (1H, d, *J* 8.7 Hz, C*H*–NH–), 5.15 (1H, d, *J* 12.0 Hz, –OC*H*$_2$–Ph), 5.09 (1H, d, *J* 12.0 Hz, –OC*H*$_2$–Ph), 3.71 (3H, s, –OCH$_3$); ^{13}C NMR (50 MHz, CDCl$_3$): δ 165.6, 155.5, 148.5, 145.1, 142.1, 138.4, 136.0, 135.6, 132.4, 130.0, 129.6, 128.6, 128.4, 128.2, 67.4, 56.6, 52.3; FABMS: *m*/*z* 371 [MH]$^+$, 393 [MNa]$^+$; HRMS (ESI): [MNa]$^+$, found 393.1081. $C_{19}H_{18}N_2O_6Na$ requires 393.1062.

4.3.10. Methyl 3-benzyloxycarbonylamino-3-(4-methylphenyl)-2-methylene propanoate (*3j*)

Following Section 4.2, α-amido sulfone **1j** (409 mg, 1 mmol), methyl acrylate **2a** (2.15 g, 25 mmol) and DABCO (112 mg, 1 mmol) gave, after purification by column chromatography (20% EtOAc/hexane), the aza-Morita–Baylis–Hillman adduct **3j** (308.5 mg, 91%) as a white colour solid; R_f (35% EtOAc/hexane) 0.52; mp: 62–64 °C; IR (KBr): 3338, 1723, 1508, 1442, 1282, 1230 cm^{-1}; ^{1}H NMR (200 MHz, CDCl$_3$): δ 7.39–7.22 (5H, m, Ar–H), 7.12 (2H, d, *J* 8.0 Hz, Ar–H), 7.04 (2H, d, *J* 8.0 Hz, Ar–H), 6.30 (1H, s, H$_2$C=C), 5.87 (1H, s, H$_2$C=C), 5.73 (1H, d, *J* 8.8 Hz, –NH–), 5.61 (1H, d, *J* 8.8 Hz, C*H*–NH–), 5.05 (2H, s, –OC*H*$_2$–Ph), 3.62 (3H, s, –OCH$_3$), 2.29 (3H, s, Ar–C*H*$_3$); ^{13}C NMR (50 MHz, CDCl$_3$): δ 165.9, 155.4, 139.8, 137.1, 136.5, 136.3, 129.2, 128.4, 128.0, 126.3, 66.8, 56.3, 51.7, 20.9; FABMS: *m*/*z* 340 [MH]$^+$; HRMS (ESI): [MNa]$^+$, found 362.1373. $C_{20}H_{21}NO_4Na$ requires 362.1368.

4.3.11. Methyl 3-benzyloxycarbonylamino-3-(4-isopropylphenyl)-2-methylene propanoate (*3k*)

Following Section 4.2, α-amido sulfone **1k** (437 mg, 1 mmol), methyl acrylate **2a** (2.15 g, 25 mmol) and DABCO (112 mg, 1 mmol) gave, after purification by column chromatography (20% EtOAc/hexane), the aza-Morita–Baylis–Hillman adduct **3k** (330.3 mg, 90%) as a colourless liquid; R_f (35% EtOAc/hexane) 0.46; IR (neat): 3341,

1723, 1506, 1228 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.40–7.22 (5H, m, Ar–H), 7.18 (2H, d, *J* 8.0 Hz, Ar–H), 7.11 (2H, d, *J* 8.0 Hz, Ar–H), 6.31 (1H, s, H_2C=C), 5.88 (1H, s, H_2C=C), 5.79 (1H, d, *J* 8.9 Hz, –NH–), 5.65 (1H, d, *J* 8.9 Hz, C*H*–NH–), 5.06 (2H, s, –OCH_2–Ph), 3.63 (3H, s, –OCH_3), 2.84 (1H, m, –Ar–C*H*$(CH_3)_2$), 1.22 (6H, d, *J* 7.0 Hz, Ar–CH(CH_3)$_2$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 166.1, 155.6, 148.2, 139.9, 136.9, 136.4, 128.5, 128.2, 126.7, 126.5, 67.0, 56.5, 52.0, 33.7, 24.0; FABMS: *m*/*z* 368 $[MH]^+$, 390 $[MNa]^+$; HRMS (ESI): $[MNa]^+$, found 390.1697. $C_{22}H_{25}NO_4Na$ requires 390.1681.

4.3.12. Methyl 3-benzyloxycarbonylamino-3-(2-naphthyl)-2-methylene propanoate (**3l**)

Following Section 4.2, α-amido sulfone **1l** (445 mg, 1 mmol), methyl acrylate **2a** (2.15 g, 25 mmol) and DABCO (112 mg, 1 mmol) gave, after purification by column chromatography (20% EtOAc/hexane), the aza-Morita–Baylis–Hillman adduct **3l** (330.0 mg, 88%) as a white colour solid; R_f (40% EtOAc/hexane) 0.49; mp: 99–101 °C; IR (KBr): 3426, 1720, 1502, 1225 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.85–7.68 (5H, m, Ar–H), 7.50–7.22 (7H, m, Ar–H), 6.40 (1H, s, H_2C=C), 5.98 (1H, s, H_2C=C), 5.83 (2H, br s, –NH– and C*H*–NH–), 5.12 (2H, s, –OCH_2–Ph), 3.64 (3H, s, –OCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 166.1, 155.7, 139.8, 137.1, 136.4, 133.3, 132.9, 128.6, 128.2, 128.1, 127.7, 127.2, 126.3, 125.2, 124.8, 67.1, 56.8, 52.0; FABMS: *m*/*z* 376 $[MH]^+$, 398 $[MNa]^+$; HRMS (ESI): $[MNa]^+$, found 398.1351. $C_{23}H_{21}NO_4Na$ requires 398.1368.

4.3.13. Methyl 3-benzyloxycarbonylamino-3-(furan-2-yl)-2-methylene propanoate (**3m**)

Following Section 4.2, α-amido sulfone **1m** (385 mg, 1 mmol), methyl acrylate **2a** (2.15 g, 25 mmol) and DABCO (112 mg, 1 mmol) gave, after purification by column chromatography (20% EtOAc/hexane), the aza-Morita–Baylis–Hillman adduct **3m** (293.0 mg, 93%) as a pale yellow colour solid; R_f (35% EtOAc/hexane) 0.47; mp: 76–78 °C; IR (KBr): 3338, 1723, 1504, 1231 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.37–7.25 (6H, m, Ar–H and furan–H), 6.33 (1H, s, H_2C=C), 6.28 (1H, m, furan–H), 6.13 (1H, d, *J* 2.0 Hz, furan–H), 5.91 (1H, s, H_2C=C), 5.74 (2H, br s, –NH– and C*H*–NH–), 5.11 (2H, s, –OCH_2–Ph), 3.72 (3H, s, –OCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 165.8, 155.4, 152.3, 142.2, 137.8, 136.3, 128.5, 128.2, 127.5, 110.5, 106.8, 67.1, 52.0, 51.3; FABMS: *m*/*z* 316 $[MH]^+$, 338 $[MNa]^+$; HRMS (ESI): $[MNa]^+$, found 338.0997. $C_{17}H_{17}NO_5Na$ requires 338.1004.

4.3.14. Methyl 3-benzyloxycarbonylamino-3-(thiophene-2-yl)-2-methylene propanoate (**3n**)

Following Section 4.2, α-amido sulfone **1n** (401 mg, 1 mmol), methyl acrylate **2a** (2.15 g, 25 mmol) and DABCO (112 mg, 1 mmol) gave, after purification by column chromatography (20% EtOAc/hexane), the aza-Morita–Baylis–Hillman adduct **3n** (311.1 mg, 94%) as a pale yellow colour liquid; R_f (35% EtOAc/hexane) 0.53; IR (neat): 3336, 1720, 1500, 1223 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.35–7.22 (5H, m, Ar–H), 7.13 (1H, d, *J* 4.0 Hz, thiophene–H), 6.91–6.80 (2H, m, thiophene–H), 6.32 (s, 1H, H_2C=C), 5.97 (1H, d, *J* 8.8 Hz, –NH–), 5.91 (1H, s, H_2C=C), 5.85 (1H, d, *J* 8.8 Hz, C*H*–NH–), 5.12 (1H, d, *J* 12.0 Hz, –OCH_2–Ph), 5.04 (1H, d, *J* 12.0 Hz, –OCH_2–Ph), 3.68 (3H, s, –OCH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 166.0, 155.5, 144.0, 139.4, 136.4, 128.7, 128.4, 127.4, 127.2, 125.2, 124.9, 67.3, 53.4, 52.2; FABMS: *m*/*z* 354 $[MNa]^+$; HRMS (ESI): $[MNa]^+$, found 354.0789. $C_{17}H_{17}NO_4SNa$ requires 354.0775.

4.3.15. Methyl-3-(p-tolylsufinyloxy) propanoate (**4a**)

Colourless solid; mp: 66–69 °C; IR (KBr): 1737, 1597, 1411, 1285 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.79 (2H, d, *J* 8.0 Hz, Ar–H), 7.34 (2H, d, *J* 8.0 Hz, Ar–H), 3.66 (3H, s, –OCH_3), 3.32 (2H, t, *J* 7.0 Hz, –OCH_2CH_2–), 2.71 (2H, t, *J* 7.0 Hz, –OCH_2CH_2–), 2.47 (3H, s, Ar–CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 170.5, 145.1, 135.5, 130.0, 128.2, 52.3, 51.5, 27.7, 21.7; FABMS: *m*/*z* 243 $[MH]^+$; HRMS (ESI): $[MNa]^+$, found 265.0509. $C_{11}H_{14}O_4SNa$ requires 265.0510.

4.3.16. Ethyl-3-(p-tolylsufinyloxy) propanoate (**4b**)

Colourless solid; mp: 68–71 °C; IR (KBr): 1735, 1597, 1316, 1148 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.77 (2H, d, *J* 8.0 Hz, Ar–H), 7.34 (2H, d, *J* 8.0 Hz, Ar–H), 4.05 (2H, q, *J* 7.0 Hz, –OCH_2CH_3), 3.31 (2H, t, *J* 7.0 Hz, –OCH_2CH_2–), 2.64 (2H, t, *J* 7.0 Hz, OCH_2CH_2–), 2.42 (3H, s, Ar–CH_3), 1.21 (3H, t, *J* 7.0 Hz, –OCH_2CH_3); FABMS: *m*/*z* 279 $[MNa]^+$; HRMS (ESI): $[MNa]^+$, found 279.0678. $C_{12}H_{16}O_4SNa$ requires 279.0667.

Acknowledgements

The authors thank CSIR and UGC, New Delhi for financial assistance. They are also thankful to NMR, Mass and IR divisions of IICT for spectral recording.

Supplementary data

Copies of ^1H NMR spectra for all compounds, copies of ^{13}C NMR spectra for compounds **3a**–**3n** and **4a** and copies of HRMS spectra for all compounds. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.07.093.

References and notes

1. (a) Morita, K.; Suzuki, Z.; Hirose, H. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 2815; (b) Baylis, A. B.; Hillman, M. E. D. German patent 2155113, 1972; *Chem. Abstr.* **1972**, *77*, 34174q; (c) Basavaiah, D.; Rao, A. J.; Satyanarayana, T. *Chem. Rev.* **2003**, *103*, 811; (d) Basavaiah, D.; Rao, K. V.; Reddy, R. J. *Chem. Soc. Rev.* **2007**, *36*, 1581.
2. Li, G.; Wei, H.-X.; Gao, J. J.; Caputo, T. D. *Tetrahedron Lett.* **2000**, *41*, 1.
3. (a) Perlmutter, P.; Teo, C. C. *Tetrahedron Lett.* **1984**, *25*, 5951; (b) Balan, D.; Adolfsson, H. *Tetrahedron Lett.* **2003**, *44*, 2521; (c) Matsui, K.; Takizawa, S.; Sasai, H. *Synlett* **2006**, 761; (d) Li, Q.; Shi, M.; Lyte, J. M.; Li, G. *Tetrahedron Lett.* **2006**, *47*, 7699.
4. (a) Shi, Y.-L.; Shi, M. *Eur. J. Org. Chem.* **2007**, 2905; (b) Masson, G.; Housseman, C.; Zhu, J. *Angew. Chem., Int. Ed.* **2007**, *46*, 4614; (c) Kamimura, A.; Okawa, H.; Morisaki, Y.; Ishikawa, S.; Uno, H. *J. Org. Chem.* **2007**, *72*, 3569.
5. (a) Lee, H. J.; Seong, M. R.; Kim, J. N. *Tetrahedron Lett.* **1998**, *39*, 6223; (b) Lee, H. J.; Kim, H. S.; Kim, J. N. *Tetrahedron Lett.* **1998**, *40*, 4363; (c) Kundig, E. P.; Xu, L.-H.; Romanens, P. *Tetrahedron Lett.* **1995**, *36*, 4047; (d) Sergeeva, N. N.; Golubev, A. S.; Burger, K. *Synthesis* **2001**, 281; (e) Dunn, P. J.; Hughes, M. L.; Searle, P. M.; Wood, A. S. *Org. Process Res. Dev.* **2003**, *7*, 244; (f) Buchholz, R.; Hoffmann, H. M. R. *Helv. Chim. Acta* **1991**, *74*, 1213; (g) Lee, H. S.; Kim, J. M.; Kim, J. N. *Tetrahedron Lett.* **2007**, *48*, 4119.
6. (a) Bertenshaw, S.; Kahn, M. *Tetrahedron Lett.* **1989**, *30*, 2731; (b) Richter, H.; Jung, G. *Tetrahedron Lett.* **1998**, *39*, 2729; (c) Ribiere, P.; Enjalbal, C.; Aubagnac, J.-L.; Yadav-Bhatgnagar, N.; Martinez, J.; Lamaty, F. *J. Comb. Chem.* **2004**, *6*, 464; (d) Ribiere, P.; Declerck, V.; Martinez, J.; Lamaty, F. *Chem. Rev.* **2006**, *106*, 2249.
7. (a) Brown, J. M.; James, A. P.; Prior, L. M. *Tetrahedron Lett.* **1987**, *28*, 2179; (b) Kim, J. N.; Lee, H. J.; Lee, K. Y.; Gong, J. H. *Synlett* **2002**, 173; (c) Rajesh, S.; Banerjee, B.; Iqbal, J. *J. Org. Chem.* **2002**, *67*, 7852; (d) Galeazzi, R.; Mortelli, G.; Mobbili, G.; Orena, M.; Rinaldi, S. *Org. Lett.* **2004**, *6*, 2571; (e) Chen, H.-Y.; Patkar, L. N.; Ueng, S.-H.; Lin, C.-C.; Lee, A. S.-Y. *Synlett* **2005**, 2035.
8. (a) Pearson, W. H.; Lindbeck, A. C.; Kampf, J. W. *J. Am. Chem. Soc.* **1993**, *115*, 2622; (b) Mecozzi, T.; Petrini, M. *J. Org. Chem.* **1999**, *64*, 8970.
9. (a) Petrini, M. *Chem. Rev.* **2005**, *105*, 3949; (b) Petrini, M.; Torregiani, E. *Synthesis* **2007**, 159 and references cited therein.
10. Das, B.; Damodar, K.; Saritha, D.; Chowdhury, N.; Krishnaiah, M. *Tetrahedron Lett.* **2007**, *48*, 7930.
11. (a) Das, B.; Banerjee, J.; Mahender, G.; Majhi, A. *Org. Lett.* **2004**, *6*, 3349; (b) Das, B.; Majhi, A.; Banerjee, J.; Chowdhury, N.; Venkateswarlu, K. *Tetrahedron Lett.* **2005**, *46*, 5713; (c) Das, B.; Chowdhury, N.; Banerjee, J.; Majhi, A.; Mahender, G. *Chem. Lett.* **2006**, *35*, 358; (d) Das, B.; Chowdhury, N.; Damodar, K. *Helv. Chim. Acta* **2007**, *90*, 2037.
12. (a) Aggarwal, V. K.; Castro, A. M. M.; Mereu, A.; Adams, H. *Tetrahedron Lett.* **2002**, *43*, 1577; (b) Wu, Z.; Zhou, G.; Zhou, J.; Guo, W. *Synth. Commun.* **2006**, *36*, 2491.
13. (a) Felix, M. *J. Org. Chem.* **1974**, *39*, 1427; (b) Meienhofer, J.; Kuromizu, K. *Tetrahedron Lett.* **1974**, 3259; (c) Lott, R. S.; Chauhan, V. S.; Stammer, C. H. *Chem. Commun.* **1979**, 495; (d) Sakaitani, M.; Ohfune, Y. *J. Org. Chem.* **1990**, *55*, 870; (e) Beecher, J. E.; Tirrell, D. A. *Tetrahedron Lett.* **1998**, *39*, 3927.
14. (a) Mecozzi, T.; Petrini, M. *Synlett* **2000**, 73; (b) Chemla, F.; Hebbe, V.; Normant, J.-F. *Synthesis* **2000**, 75.
15. Yu, C.; Liu, B.; Hu, L. *J. Org. Chem.* **2001**, *66*, 5413.