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ARTICLE

Synthesis of α-(aminoethyl)-α,β-enones via alkyne aza-Prins cyclization and their synthetic application to pyrrolidines

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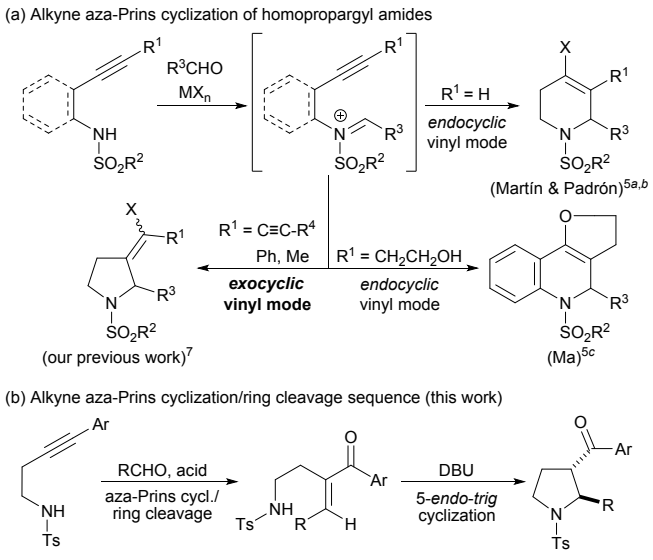
We developed a synthetic method of α-(aminoethyl)-α,β-enones from aryl-substituted homopropargyl sulfonamides and aldehydes, representing the first synthesis of conjugated enones via alkyne aza-Prins cyclization. These products could be converted into pyrrolidines by a formal 5-*endo-trig* cyclization.

Introduction

The intramolecular addition of alkenes to iminium ions, which is known as the aza-Prins cyclization, provides one of the most powerful tools for the synthesis of nitrogen-containing heterocycles.[1a-d] Hence, the aza-Prins cyclization and its variants using alkynes (alkyne aza-Prins cyclization) have been frequently employed in alkaloid synthesis.[1d,e] In the most cases of the alkyne aza-Prins cyclization, alkynes linked with *N*,*O*-acetals[2] or other precursors of iminium intermediates[3] were selected as a substrate. Whereas, the intermolecular reactions of alkynyl amines[4] or amides[5] with carbonyl compounds have been less studied albeit straightforward alternative procedures. Furthermore, although the aza-Prins cyclization using δ-unsubstituted[5a,b] or δ-hydroxyethyl-substituted[5c] homopropargyl sulfonamides were known as the synthetic methods of the 4-functionalized piperidines (R^1 = H or CH_2CH_2OH, Scheme 1a), systematic studies on the reactions of δ-substituted substrates had not been achieved.

Recently, as a part of our studies on efficient syntheses of cyclic compounds by the acid-promoted reactions of alkynes and carbonyls or imines,[6] we reported first synthesis of pyrrolidines with the introduction of functional groups by the aza-Prins cyclization of δ-substituted homopropargyl sulfonamides with aldehydes (R^1 = alkynyl, Ph, Me Scheme 1a).[7,8] Our continuous research on the alkyne aza-Prins cyclization led to finding a highly stereoselective synthesis of α-(aminoethyl)-α,β-enones, which are versatile and useful synthetic intermediates,[9] via alkyne aza-Prins cyclization/ring cleavage sequence (Scheme 1b). To our surprise, although there some reports on one-pot syntheses of cyclic compounds from alkynyl alcohols and aldehydes through the ring cleavage of Prins cyclized intermediates,[5d,6e,10] the synthetic methods of conjugated enones by Prins cyclization and its variants including alkyne aza-Prins cyclization have been unknown. Herein, we report the novel synthesis of conjugated enones from aryl-substituted homopropargyl sulfonamides and aldehydes along with the formation of pyrrolidines by base-mediated cyclization of the enone products in formal 5-*endo-trig* mode, which is prohibited by Baldwin's rules[11] (Scheme 1b).



Scheme 1. Synthesis of heterocycles by alkyne aza-Prins cyclization.

Results and discussion

According to our previous work on the alkyne aza-Prins reaction,[7] unlike alkynyl- or Me-substituted homopropargyl sulfonamides, the Ph-substituted substrate **1a** was treated with benzaldehyde (**2a**, 2 eq.) in the presence of HOTf (Tf = CF_3SO_2, 2 eq.) in DCM (dichloromethane) at room temperature to give enone **3aa** (65%) as a main product (Table 1, entry 1). Therefore, we initially focused our efforts on the screening of acids in the

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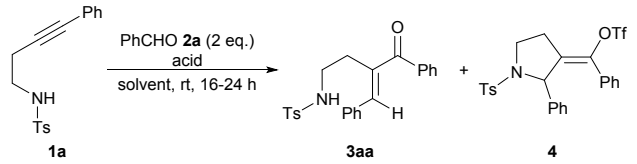
Electronic Supplementary Information (ESI) available: detailed results of screening of acids, experimental procedures, characterisation data for new compounds. See DOI: 10.1039/x0xx00000x

reaction of **1a** with **2a** in DCM (entries 1-5, see ESI for more details). The use of TMSOTf (TMS = trimethylsilyl) instead of HOTf afforded the similar result to entry 1 giving rise to the desired product **3aa** in 60% yield along with aza-Prins cyclized product **4** in 11% yield (entry 2). Unfortunately, $FeCl_3$ (1 eq.), which was used in alkyne Prins cyclization of δ-unsubstituted homopropargyl sulfonamides,[5a] did not show good result (entry 3). In addition, a combination of $MgBr_2$ and TsOH[12] gave a complex mixture that did not include **3aa** (entry 4). Whereas, in the case of BF_3-complexes, the formation of **3aa** depends on the type of complexes (entries 5 and 6) and BF_3·MeCN led to the improved yield of **3aa** up to 79% (entry 6). Also, compared to other solvents (entries 7-9), MeCN was effective on the reaction using TMSOTf or HOTf to produce **3aa** in good yield without the detection of **4** (entry 10 or 11). This is likely because of moderate basicity of MeCN.[13]

Table 1. Screening of acids and solvents.

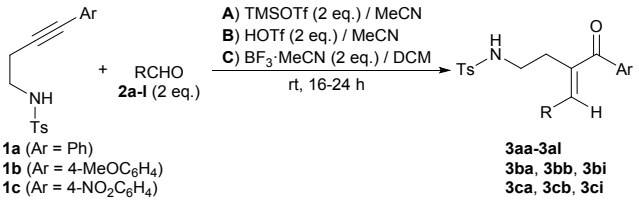


Entry	Acid (eq.)	Solvent	**3aa**[a] (%)	**4**[a] (%)	**1a**[a] (%)
1	HOTf (2)	DCM	65	14[b]	0
2	TMSOTf (2)	DCM	60	11[b]	0
3	$FeCl_3$ (1)	DCE[c]	36	-[d]	0
4	$MgBr_2$-TsOH[e]	DCM	0	-	6
5	BF_3·OEt_2 (2)	DCM	47	-	25
6	BF_3·MeCN (2)	DCM	79	-	0
7	TMSOTf (2)	MeOH	0	0	84
8[f]	TMSOTf (2)	DCM	51	20[g]	0
9	TMSOTf (2)	Et_2O	43	29[h]	0
10	TMSOTf (2)	MeCN	81	0	0
11	HOTf (2)	MeCN	75	0	0

[a] Isolated yields or recovery. [b] Only *E*-isomer of **4** was obtained. [c] Conditions: rt for 2 h and then 80 ºC for 4 h in 1,2-dichloroethane. [d] Chloride analogue of **4** was formed in 8% yield. [e] $MgBr_2$·OEt_2 (2 eq.) and TsOH·H_2O (2 eq.) was used. [f] Additive: MeOH (2 eq.). [g] *Z*-isomer (4%) was included. [h] *Z*-isomer (8%) was included.

Based on the above described results (Table 1, entries 5, 9 and 10), the scope of the formation of enones **3** from aryl-substituted homopropargyl sulfonamides **1a**-**c** and various aldehydes **2a**-**l** was investigated (Table 2). By using TMSOTf in MeCN (method **A**), sulfonamides **1a** successfully reacted with aromatic aldehydes bearing electron-donating groups at *ortho*- or *para*-position to give the corresponding enones **3ab**, **3ac** and **3ae** in 68-79% yields (entries 2, 3 and 5). On the other hand, in the cases of aromatic aldehydes bearing electron-withdrawing groups at *ortho*- or *para*-position, BF_3·MeCN in CH_2Cl_2 (method **C**) led to good yields of **3af**, **3ag** and **3ai** (79-85%, entries 6, 7 and 9). For the reaction with *meta*-substituted aromatic aldehydes, HOTf in MeCN (method **B**) was effective (**3ad**, 84%; **3ah**, 60%; entries 4 and 8). Although all the methods could not be applied to aliphatic aldehydes such as CyCHO (Cy = cyclohexyl) and EtCHO (entries 11 and 12), which gave complex mixtures, ^{t}BuCHO afforded the desired enone **3aj** in 42% yield (method **C**, entry 10). To our delight, in the most cases of the 4-methoxyphenyl-subtituted **1b**, regardless of the kind of aldehydes and the methods **A**-**C**, the enones **3ba**, **3bb** and **3bi** were obtained in excellent yields (method **B** or **C**, 96-98%, entries 13-15). Whereas, although the yields of enones **3ca**, **3cb** and **3ci** derived from 4-nitrophenyl-subtituted **1c** were reduced (entries 14-16), method **B** gave the enones **3ca** and **3cb** in 40% and 63% yields, respectively (entries 16 and 17). Notably, the *E*-enones **3** were obtained as a single stereoisomer in all cases (Table 1 and 2).

Table 2. Scope of alkyne aza-Prins cyclization.



			Yields[a] (%) by Method **A**, **B** or **C**		
entry	**3**	R	**A**	**B**	**C**
1	**3aa**	Ph	81	75	79
2	**3ab**	4-$MeOC_6H_4$	68	61	26[b]
3	**3ac**	2-MeC_6H_4	79	60	68
4	**3ad**	3-MeC_6H_4	66	84	65
5	**3ae**	4-MeC_6H_4	77	76	58
6	**3af**	4-BrC_6H_4	56	33	79
7	**3ag**	2-$NO_2C_6H_4$	6	36	85
8	**3ah**	3-$NO_2C_6H_4$	32	60	12
9	**3ai**	4-$NO_2C_6H_4$	43	51	81
10	**3aj**	^{t}Bu	30	18	42
11	**3ak**	Cy[c]	0	0	0
12	**3al**	Et	0	0	0
13	**3ba**	Ph	92	79	**97**
14	**3bb**	4-$MeOC_6H_4$	95	**98**	95
15	**3bi**	4-$NO_2C_6H_4$	91	91	**96**
16	**3ca**	Ph	30	40	5
17	**3cb**	4-$MeOC_6H_4$	59	63	0
18	**3ci**	4-$NO_2C_6H_4$	0	trace	trace

[a] Isolated yields. [b] Recovery of **1a**: 38%. [c] Cy = cyclohexyl.

The stereochemistries of *E*-enones **3** were confirmed by their NOESY spectra. As shown in Figure 1, NOE correlations between aliphatic protons H^a (2.92 ppm) and H^b (3.22 ppm) of aminoethyl group and *meta*-protons H^d (7.33 ppm) of anisyl group, and between vinylic proton H^c (7.14 ppm) and *ortho*-protons H^e (7.67 ppm) of benzoyl group are observed in spectrum of **3ab**. In spectra of **3aa**, **3ad**, **3ae**, **3ag**, **3ah** and **3aj**, although the observation of NOE correlations between vinylic protons like H^c and *ortho*-protons like H^e of benzoyl group are difficult because those protons are overlapped with other aromatic protons, those of aliphatic protons like H^a and H^b of aminoethyl groups and protons of β-substituents are observed. On the other hand, spectra of other enones **3** show similar NOE

correlations to those of **3ab**. Thus, those products **3** were determined as *E*-isomers.

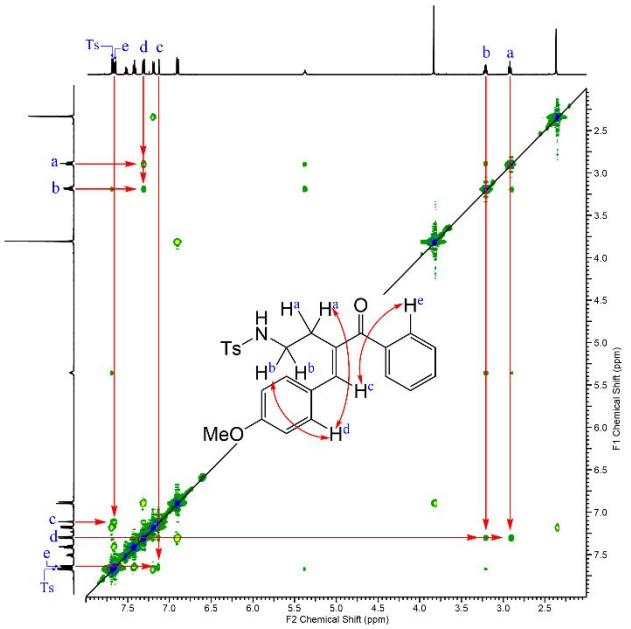
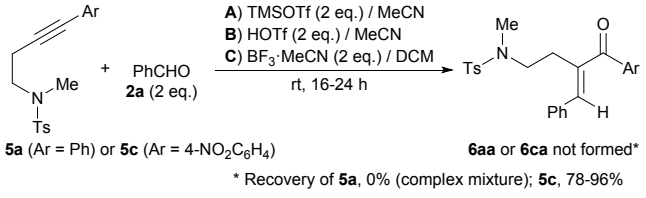


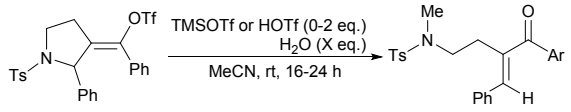
Figure 1. NOESY spectrum of **3ab**.

As an alternative route for the formation of α,β-enones, there is a possibility of metathesis reaction between the alkyne moiety of homopropargyl tosylamides **1** and aldehydes **2**.[6a-d,14] However, *N*-Me-substituted substrate **5a** reacted with aldehyde **2a** using methods **A**-**C** to give a complex mixture and the corresponding enones **6** were not formed (Scheme 2). In cases of **5c**, the substrates **5c** were only recovered in 78-96%. These results suggested that the present synthesis of enones **3** would require the generation of the iminium intermediate from the *N*-unsubstituted **1a**-**1c** and aldehydes **2**.



Scheme 2. Control experiments using *N*-methyl tosylamides **5**.

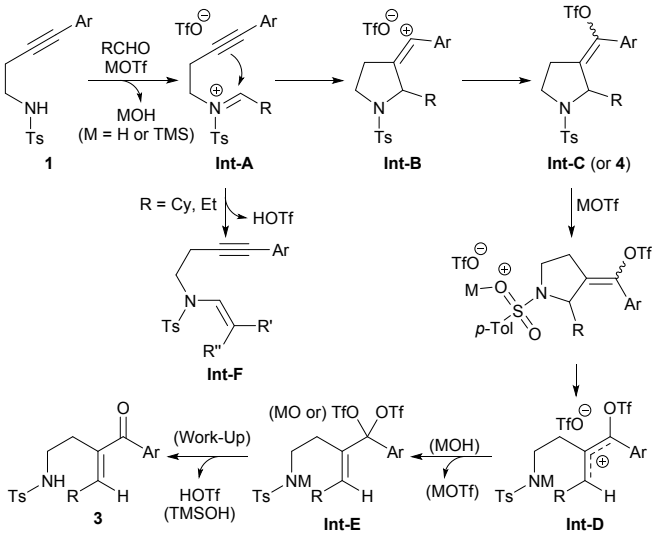
On the other hand, when aza-Prins cyclized product **4** was treated with TMSOTf or HOTf (2 eq.) in MeCN, the corresponding enone **3aa** was obtained in excellent yield (quant. or 96%, Scheme 3). These results would support the involvement of alkyne aza-Prins cyclization in the present synthesis of enones **3**. Furthermore, since the addition of H_2O in the presence or absence of acid resulted in the formation of enone **3aa** (39-43%, recovery of **4**: 22-29%), H_2O would partially participate in the conversion of **4** to **3aa**. Unfortunately, although the sole use of 1 eq. of acid afforded some products, which may be intermediates, along with **3aa** (9-10%, recovery of **4**: 23-39%), these products were converted into **3aa** after the purification using column chromatography and thus these structures cannot be determined. Considering that 2 eq. of acid led to full conversion of **4** to **3aa**, aza-Prins cyclized intermediates would be converted into enones **3** as soon as the formation of **4** (while there is an excess amount of acid) in the present synthesis of enones **3**.



TMSOTf / HOTf (2 eq.), X = 0 quant. (**4**: 0%) / 96% (**4**: 0%)
TMSOTf / HOTf (1 eq.), X = 1 43% (**4**: 29%) / 41% (**4**: 22%)
TMSOTf / HOTf (0 eq.), X = 1 39% (**4**: 22%)
TMSOTf / HOTf (1 eq.), X = 0 9%* (**4**: 39%)* / 10%* (**4**: 23%)*
*Determined by ^{1}H-NMR analysis using an internal standard

Scheme 3. Control experiments using aza-Prins cyclized product **4**.

On the basis of these results and our previous reports of the alkyne aza-Prins cyclization,[7] a proposed mechanism for the present synthesis of α,β-enones **3** using methods **A** and **B** is shown in Scheme 4. In this mechanism, a condensation of tosylamide moiety of **1** with the acid-activated aldehydes lead to iminium ions **Int-A**. And then, **Int-A** undergo an intramolecular addition of alkenes with exocyclic vinyl formation likely due to the the stabilization of vinyl cation in **INT-B** by aryl group followed by the addition of TfO^- to the generated vinyl cation giving rise to aza-Prins cyclized intermediates **Int-C** (**4** in the case of **3aa**). Subsequently, an acid activates the sulfonylamide group of **Int-C** to give allyl cation **Int-D** through the ring cleavage of the pyrrolidine framework. Finally, the addition of TfO^-, H_2O or TMSOH to **Int-D** and then elimination of acid in hemiacetals **Int-E** afford α,β-enones **3**.

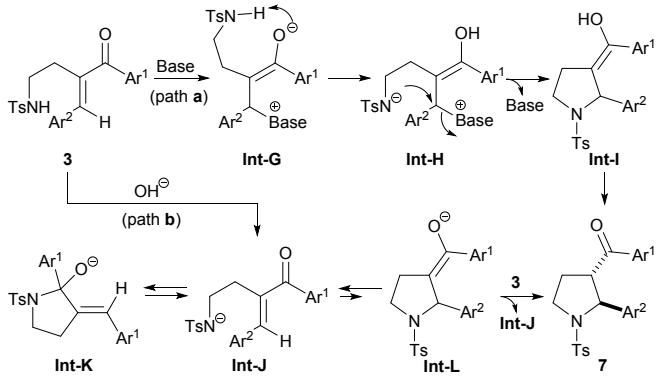


Scheme 4. Proposed mechanism for synthesis of enones **3**.

Since the strong electron donation and cation stabilization effect of 4-methoxyphenyl group of **1b** smoothly promoted the cyclization of **Int-A** as well as ring-opening of **Int-C** to **Int-D**, enones **3ba**, **3bb** and **3bi** were formed in the excellent yields (Table 2, entries 13-15). On the other hand, in cases of CyCHO and EtCHO (Table 2, entries 11 and 12) bearing α-protons, **INT-A** may be converted into enamines **INT-F** to give complex mixtures via side reactions of **INT-F**. Notably, the reaction using method **C** would proceed via the similar mechanism (Scheme 4) mediated by $HOBF_3^-$ instead of TfO^-.

Formal 5-*endo-trig* cyclization of α-(aminoethyl)-α,β-enones

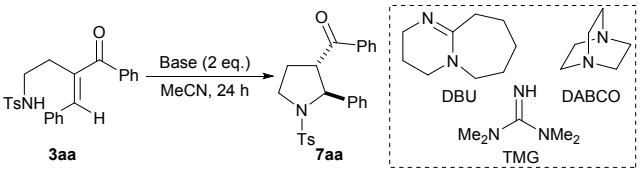
As a synthetic application of α-(aminoethyl)-α,β-enones **3**, organobase-mediated cyclization of enones **3** to pyrrolidines **7** was attempted. Since Michel-type addition of tertiary amines or phosphines to enones has been known to afford the corresponding enolates,[15] we expected the formal 5-*endo-trig* cyclization of **3** via a deprotonation of tosylamides by the generated enolate anions **INT-G** and subsequent intramolecular addition of tosylamide anions to β-carbons of **INT-H** in 5-*exo-tet* mode (Scheme 5, path **a**).



Scheme 5. Proposed mechanism for synthesis of pyrrolidines **7**.

As shown in Table 3, among the attempted amines and phosphines (2 eq.), relatively strong bases such as DBU (1,8-diazabicyclo[5.4.0]undec-7-ene, pK_a = 24.1 in MeCN,[16a] entry 1) and TMG (1,1,3,3-tetramethylguanidine, pK_a = 23.4 in MeCN,[16b] entry 2) promoted the desired cyclization of enones **3aa** in MeCN at room temperature within 24 h. Particularly, by using DBU, the corresponding pyrrolidines **7aa** was obtained in 90% yield (entry 1). Although TBAOH (TBA = tetrabutylammonium) also promoted the similar cyclization of enones **3aa** at room temperature, this reaction would proceed via an alternative route (Scheme 5, path **b**). In the alternative route, OH^- (pK_a = 30.0 in DMSO)[16c] directly absorbs the proton of tosylamide group (pK_a of $PhSO_2NH_2$ = 16.1 in DMSO)[16c] of **3** to afford **INT-J**, which is in equilibrium with the kinetically preferable 5-*exo-trig* cyclized intermediate **INT-K** due to leaving ability of tosylamide anion. Thus, once the unpreferable 5-*endo-trig* cyclization of **INT-J** proceeds, the following protonation of **INT-L** with the tosylamide group of **3** gives rise to pyrrolidines **7**. The similar mechanism was proposed in the inorganic base-promoted 5-*endo-trig* cyclization of α-(aminoethyl)-α,β-enoates.[17] On the other hand, DBU (pK_a = 13.9 in DMSO)[16d] is difficult to absorbs the proton of tosylamide group but the deprotonation by the enolate anions **INT-G** (pK_a of acetophenone = 24.7 in DMSO)[16c] would be possible. Therefore, DBU-mediated cyclization of **3** is considered to proceed via path **a**.

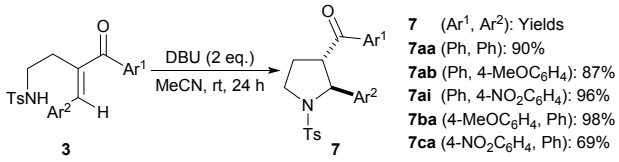
Table 3. Screening of bases.



Entry	Base	pK_{a_MeCN}[a]	Temp.	**7aa**[b] (%)	**3aa**[c] (%)
1	DBU	24.1 (13.9)	rt	90	0
2	TMG	23.4	rt	38	51
3	TMG	above	80 ºC	97	0
4	Et_3N	18.5 (9.0)	rt	0	80
5	DABCO	18.3 (8.9)	rt	0	93
6	DABCO	above	80 ºC	6[c]	85
7[f]	$^nBu_3P$	15.1	rt	0	78
8	Ph_3P	8.8	rt	0	quant.
9	Ph_3P	above	80 ºC	0	91
10	TBAOH	- (32.0)	rt	68	0

[a] Values show pK_a of conjugated acids in MeCN. Values in parentheses show those in DMSO. See ref. 16. [b] Isolated yields. [c] Determined by ^1H NMR analysis using internal standard.

Furthermore, the use of DBU could be applied to the cyclization of the other enones **3** to produce the pyrrolidines **7ab**, **7ai** and **7ba** in excellent yields (87-98%, Scheme 6). Although the yields of **7ca** was reduced possibly due to the inefficient deprotonation of tosylamides by the enolate anions **INT-G**, **7ca** was obtained in 69% yield. Notably, the *trans*-pyrrolidines **7** were obtained as a single stereoisomer in all cases.



Scheme 6. DBU-mediated cyclization of **3**.

The stereochemistries of *trans*-pyrrolidines **7** were confirmed by their NOESY spectra. As shown in Figure 2, NOE correlations between 3-proton H^a (3.86 ppm) of pyrrolidine ring and *meta*-protons H^c (7.29 ppm) of anisyl group, and between 2-proton H^b (5.04 ppm) and *ortho*-protons H^d (7.69 ppm) of benzoyl group are observed in spectrum of **7ab**. In spectra of **7aa** and **7ba**, although the observation of NOE correlations between 3-proton H^a and protons like H^c of phenyl groups are difficult because protons of phenyl groups are overlapped with other aromatic protons, those of 2-protons like H^b and *ortho*-protons like H^d of aryloyl groups are observed. On the other hand,

spectra of other pyrrolidines **7ai** and **7ca** show similar NOE correlations to those of **7ab**. Thus, those products **7** were determined as *trans*-isomers.

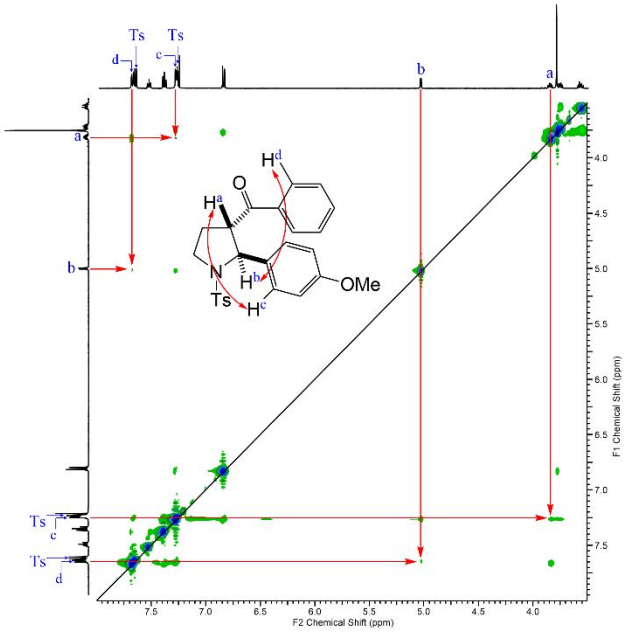


Figure 2. NOESY spectrum of **7ab**.

Conclusions

A synthetic method of α-(aminoethyl)-α,β-enones was developed using the alkyne aza-Prins cyclization of aryl-substituted homopropargyl sulfonamides and aldehydes. These products could be easily converted into pyrrolidines by formal 5-*endo*-*trig* cyclization using DBU, which would proceed via intramolecular addition of Michael adduct intermediates **INT-H** in 5-*exo*-*tet* mode. Although the ring-cleavage of pyrrolidines using alkyl halides and base has been known as the similar synthesis of α-(aminoethyl)-α,β-enones,[9a] our method provides the products with high stereoselectivity. Studies on the domino reaction via alkyne aza-Prins cyclization are underway.

Experimental

Materials and methods.

All reactions were carried out under an argon atmosphere. *N*-(4-Arylhomopropargyl) tosylamides **1a-c**[18] and aza-Prins cyclized product **4**[7] were prepared by the method reported in the literatures. Acids, bases and aldehydes **2a-m** are commercially available. Solvents were purchased as the "anhydrous" and used without further purification. For the TLC analysis, Merck precoated TLC plates (silica gel 60 F254) were used. Column chromatography was performed on silica gel 60N (63-200 µm, neutral, Kanto Kagaku Co., Ltd.). Medium-pressure liquid chromatography (MPLC) was carried out on YAMAZEN W-Prep 2XY. ^{1}H and ^{13}C NMR spectra were measured at 500 (or 300) and 125 (or 75) MHz in $CDCl_3$, and the chemical shifts are given in ppm using $CHCl_3$ (7.26 ppm) in $CDCl_3$ for ^{1}H NMR and $CDCl_3$ (77.0 ppm) for ^{13}C NMR as an internal standard, respectively. Splitting patterns of an apparent multiplet associated with an averaged coupling constant were designed as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broadened). IR spectra were obtained on a JASCO FT/IR-6200. Mass spectra and HRMS were recorded on a JEOL MStation MS700 (double-focusing magnetic sector) by FAB methods or Bruker Daltonics micrOTOF-QII by electrospray ionization (ESI).

General procedure for synthesis of compounds 3.

Method **A** or **B**: To a solution of **1** (**1a**, 119.8 mg; **1b**, 131.8 mg; **1c**, 137.8 mg; 0.4 mmol) and aldehyde **2** (0.8 mmol) in MeCN (2.5 mL) was added TMSOTf (144.5 µL, 0.8 mmol) or HOTf (70.2 µL, 0.8 mmol) at 0 ºC. After being stirred at room temperature for 24 h, the reaction mixture was quenched with sat. $NaHCO_3$ and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated in vacuo to dryness. The residue was purified by MPLC to give **3**.

Method **C**: According to the similar procedure to method **A** or **B** (albeit reaction time is 16 h), BF_3·MeCN (518 µL, 0.8 mmol) and DCM (2.5 mL) were used as an acid and as a solvent, respectively.

Characterization of compounds 3.

(*E*)-*N*-(3-Benzoyl-4-phenylbut-3-en-1-yl)-4-methylbenzenesulfonamide (**3aa**): R_f = 0.20 (hexane: AcOEt = 3:1). **A**, 131.4 mg (81%); **B**, 121.6 mg (75%); **C**, 128.0 mg (79%). Brown solid. MP: 113-115 ˚C. IR (KBr) ν cm^{-1}; 3289, 1644, 1326, 1152. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm; 7.72 (d, *J* = 8.0 Hz, 2H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.46 (dd, *J* = 8.0, 7.5 Hz, 2H), 7.43-7.35 (m, 3H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.20 (s, 1H), 5.15 (t, *J* = 5.7 Hz, 1H), 3.20 (td, *J* = 6.9, 5.7 Hz, 2H), 2.89 (t, *J* = 6.9 Hz, 2H), 2.38 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm; 199.6, 144.9, 143.2, 137.9, 137.5, 136.9, 134.7, 132.2, 129.7, 129.6, 129.14, 192.12, 128.8, 128.3, 127.0, 42.1, 27.7, 21.5. HRMS (ESI): m/z calcd. for $C_{24}H_{23}NNaO_3S$ $[M+Na]^+$ 428.1291; found 428.1285.

(*E*)-*N*-[3-Benzoyl-4-(4-methoxyphenyl)but-3-en-1-yl]-4-methylbenzenesulfonamide (**3ab**): R_f = 0.14 (hexane: AcOEt = 3:1). **A**, 117.8 mg (68%); **B**, 107.0 mg (61%); **C**, 46.0 mg (26%, recovery of **1a**: 38%). Yellow solid. MP: 102-104 ˚C. IR (KBr) ν cm^{-1}; 3265, 1599, 1324, 1260, 1159, 1031. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm; 7.70 (d, *J* = 8.0 Hz, 2H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.44 (dd, *J* = 8.0, 7.5 Hz, 2H), 7.33 (d, *J* = 8.6 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.14 (s, 1H), 6.92 (d, *J* = 8.6 Hz, 2H), 5.39 (t, *J* = 5.7 Hz, 1H), 3.84 (s, 3H), 3.22 (td, *J* = 6.9, 5.7 Hz, 2H), 2.92 (t, *J* = 6.9 Hz, 2H), 2.37 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm; 199.8, 160.5, 145.3, 143.1, 138.3, 136.9, 135.2, 131.8, 131.3, 129.6, 129.5, 128.2, 127.0, 126.9, 114.2, 55.3, 42.0, 27.7, 21.4. HRMS (FAB): m/z calcd. for $C_{25}H_{26}NO_4S$ $[M+H]^+$ 436.1583; found 436.1592.

(*E*)-*N*-[3-Benzoyl-4-(*o*-tolyl)but-3-en-1-yl]-4-methylbenzenesulfonamide (**3ac**): R_f = 0.31 (hexane: AcOEt = 3:1). **A**, 133.2 mg (79%); **B**, 100.6 mg (60%); **C**, 114.6 mg (68%). Yellow solid. MP: 113-115 ˚C. IR (KBr) νcm^{-1}; 3272, 1645, 1332, 1162. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm; 7.78 (d, *J* = 8.0 Hz, 2H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.47 (dd, J = 8.0, 7.5 Hz, 2H), 7.29 (s, 1H), 7.28-7.19 (m, 6H), 4.94 (t, *J* = 6.0 Hz,1H), 3.07 (td, *J* = 6.9, 6.0 Hz, 2H),

2.71 (t, *J* = 6.9 Hz, 2H), 2.38 (s, 3H), 2.19 (s, 3H). ^{13}C NMR (125 MHz) δ ppm; 199.4, 144.5, 143.1, 138.4, 137.9, 136.8, 136.3, 134.3, 132.2, 130.3, 129.6, 128.7, 128.3, 128.0, 127.0, 125.9, 42.2, 27.4, 21.5, 20.1 (note that two carbon peaks overlap with each other). HRMS (ESI): m/z calcd. for $C_{25}H_{25}NNaO_3S$ $[M+Na]^+$ 442.1447; found 442.1422.

(*E*)-*N*-[3-Benzoyl-4-(*m*-tolyl)but-3-en-1-yl]-4-methylbenzenesulfonamide (**3ad**): R_f = 0.29 (hexane: AcOEt = 3:1). **A**, 111.1 mg (66%); **B**, 141.3 mg (84%); **C**, 108.3 mg (65%). Brown solid. MP: 92-94 ˚C. IR (KBr) ν cm^{-1}; 3263, 1634, 1334, 1156. ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm; 7.71 (d, *J* = 8.0 Hz, 2H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.45 (dd, *J* = 8.0, 7.5 Hz, 2H), 7.29 (t, *J* = 8.0 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.19-7.16 (m, 1H), 7.18 (s, 1H), 7.16-7.13 (m, 1H), 7.15 (s, 1H), 5.18 (t, *J* = 6.0 Hz, 1H), 3.19 (td, *J* = 6.9, 6.0 Hz, 2H), 2.89 (t, *J* = 6.9 Hz, 2H), 2.38 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm; 199.7, 145.3, 143.1, 138.5, 138.0, 137.3, 137.0, 134.6, 132.1, 129.94, 129.92, 129.63, 129.58, 128.6, 128.3, 127.0, 126.1, 42.1, 27.8, 21.5, 21.3. HRMS (FAB): m/z calcd. for $C_{25}H_{26}NO_3S$ $[M+H]^+$ 420.1633; found 420.1638.

(*E*)-*N*-[3-Benzoyl-4-(*p*-tolyl)but-3-en-1-yl]-4-methylbenzenesulfonamide (**3ae**): R_f = 0.26 (hexane: AcOEt = 3:1). **A**, 129.6 mg (77%); **B**, 127.0 mg (76%); **C**, 97.5 mg (58%). Yellow solid. MP: 95-97 ˚C. IR (KBr) ν cm^{-1}; 3278, 1643, 1331, 1163.^{1}H NMR (500 MHz) δ ppm; 7.69 (d, *J* = 8.0 Hz, 4H), 7.54 (t, *J* =7.5 Hz, 1H), 7.44 (dd, *J* = 8.0, 7.5 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 4H), 7.17 (s, 1H), 5.36 (t, *J* = 5.7 Hz, 1H), 3.20 (td, J = 6.9, 5.7 Hz, 2H), 2.90 (d, *J* = 6.9 Hz, 2H), 2.37 (s, 6H). ^{13}C NMR (125 MHz) δ ppm; 199.7, 145.3, 143.0, 139.5, 138.0, 136.9, 136.6, 132.0, 131.7, 129.6, 129.5, 129.4, 129.3, 128.2, 127.0, 42.0, 27.7, 21.4, 21.3. HRMS (FAB): m/z calcd. for $C_{25}H_{26}NO_3S$ $[M+H]^+$ 420.1633; found 420.1638.

(*E*)-*N*-[3-Benzoyl-4-(4-bromophenyl)but-3-en-1-yl]-4-methylbenzenesulfonamide (**3af**): R_f = 0.26 (hexane: AcOEt = 3:1). **A**, 108.3 mg (56%); **B**, 63.7 mg (33%); **C**, 152.8 mg (79%). Brown solid. MP: 138-140 ˚C. IR (KBr) ν cm^{-1}; 3276, 1640, 1332, 1162. ^{1}H NMR (500 MHz) δ ppm; 7.72 (d, *J* = 8.0 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.53 (d, *J* = 8.6 Hz, 2H), 7.47 (dd, *J* = 8.0, 7.5 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.21 (d, *J* = 8.6 Hz, 2H), 7.12 (s, 1H), 4.93 (t, *J* = 5.7 Hz, 1H), 3.17 (td, J = 6.9, 5.7 Hz, 2H), 2.86 (t, *J* = 6.9 Hz, 2H), 2.40 (s, 3H). ^{13}C NMR (125 MHz) δ ppm; 199.2, 143.3, 143.2, 138.2, 137.7, 136.8, 133.5, 132.3, 132.0, 130.6, 129.7, 128.4, 127.0, 123.3, 41.9, 27.9, 21.5 (note that two carbon peaks overlap with each other). HRMS (FAB): m/z calcd. for $C_{24}H_{23}BrNO_3S$ $[M+H]^+$ 484.0582; found 484.0576.

(*E*)-*N*-[3-Benzoyl-4-(2-nitrophenyl)but-3-en-1-yl]-4-methylbenzenesulfonamide (**3ag**): R_f = 0.14 (hexane: AcOEt = 3:1). **A**, 11.8 mg (6%); **B**, 64.8 mg (36%); **C**, 153.4 mg (85%). Brown solid. MP: 122-124 ˚C. IR (KBr) ν cm^{-1}; 3268, 1643, 1524, 1348, 1327, 1157. ^{1}H NMR (500 MHz) δ ppm; 8.20 (d, *J* = 7.5 Hz, 1H), 7.85 (d, *J* = 7.5 Hz, 2H), 7.72 (t, *J* = 7.5 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.57 (d, *J* = 7.5 Hz, 2H), 7.50 (s, 1H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.41 (d, *J* = 7.5 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 4.93 (t, *J* = 5.7 Hz, 1H), 3.04 (td, *J* = 6.9, 5.7 Hz, 2H), 2.68 (t, *J* = 6.9 Hz, 2H), 2.38 (s, 3H). ^{13}C NMR (125 MHz) δ ppm; 198.2, 147.2, 143.3, 141.3, 138.4, 137.1, 136.8, 134.0, 132.6, 131.2, 131.0, 129.7, 129.62, 129.57, 128.5, 126.9, 125.2, 41.8, 28.2, 21.5. HRMS (FAB): m/z calcd. for $C_{24}H_{23}N_2O_5S$ $[M+H]^+$ 451.1328; found 451.1306.

(*E*)-*N*-[3-Benzoyl-4-(3-nitrophenyl)but-3-en-1-yl]-4-methylbenzenesulfonamide (**3ah**): R_f = 0.17 (hexane: AcOEt = 3:1). **A**, 57.7 mg (32%); **B**, 108.3 mg (60%); **C**, 21.5 mg (12%). Brown solid. MP: 137-139 ˚C. IR (KBr) ν cm^{-1}; 3272, 1636, 1530, 1335, 1157.^{1}H NMR (500 MHz) δ ppm; 8.20 (d, *J* = 8.0 Hz, 1H), 8.14 (s, 1H), 7.78 (d, *J* = 7.5 Hz, 2H), 7.76 (t, *J* = 8.0 Hz , 1H), 7.66 (d, *J* = 8.0 Hz, 2H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.20 (s, 1H), 5.11 (t, *J* = 5.7 Hz, 1H), 3.16 (td, *J* = 6.9, 5.7 Hz, 2H), 2.88 (t, *J* = 6.9 Hz, 2H), 2.38 (s, 3H). ^{13}C NMR (125 MHz) δ ppm; 198.7, 148.3, 143.4, 140.9, 140.2, 137.2, 136.7, 136.4, 134.6, 132.6, 129.9, 129.7, 129.6, 128.5, 126.9, 123.8, 123.4, 41.8, 28.1, 21.5. HRMS (FAB): m/z calcd. for $C_{24}H_{23}N_2O_5S$ $[M+H]^+$ 451.1328; found 451.1357.

(*E*)-*N*-[3-Benzoyl-4-(4-nitrophenyl)but-3-en-1-yl]-4-methylbenzenesulfonamide (**3ai**): R_f = 0.11 (hexane: AcOEt = 3:1). **A**, 76.8 mg (43%); **B**, 92.0 mg (51%); **C**, 145.7 mg (81%). Yellow solid. MP: 107-109 ˚C. IR (KBr) ν cm^{-1}; 3271, 1643, 1518, 1347, 1333, 1162.^{1}H NMR (500 MHz) δ ppm; 8.23 (d, *J* = 8.6 Hz, 2H), 7.78 (d, *J* = 8.0 Hz, 2H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.52 (d, *J* = 8.6 Hz, 2H), 7.48 (dd, *J* = 8.0, 7.5 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.21 (s, 1H), 5.12 (t, *J* = 5.7 Hz, 1H), 3.16 (td, *J* = 6.9, 5.7 Hz, 2H), 2.87 (t, *J* = 6.9 Hz, 2H), 2.39 (s, 3H). ^{13}C NMR (125 MHz) δ ppm; 198.5, 147.5, 143.5, 141.3, 140.9, 140.6, 137.2, 136.7, 132.7, 129.8, 129.73, 129.71, 128.5, 126.9, 123.9, 41.7, 28.3, 21.5. HRMS (FAB): m/z calcd. for $C_{24}H_{23}N_2O_5S$ $[M+H]^+$ 451.1328; found 451.1307.

(*E*)-*N*-(3-Benzoyl-5,5-dimethylhex-3-en-1-yl)-4-methylbenzenesulfonamide (**3aj**): R_f = 0.31 (hexane: AcOEt = 3:1). **A**, 46.6 mg (30%); **B**, 64.8 mg (42%); **C**, 27.2 mg (18%). Brown solid. MP: 110-112 ˚C. IR (KBr) ν cm^{-1}; 3258, 1633, 1332, 1162. ^{1}H NMR (500 MHz) δ ppm; 7.71 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 8.0 Hz, 2H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.40 (dd, J = 8.0, 7.5 Hz, 2H), 7.23(d, *J* = 8.0 Hz, 2H), 6.28 (s,1H), 5.39 (t, *J* = 5.7 Hz, 1H) 3.08 (td, *J* = 6.9, 5.7 Hz, 2H), 2.76 (t, *J* = 6.9 Hz, 2H), 2.37 (s, 3H), 1.14 (s, 9H). ^{13}C NMR (125 MHz) δ ppm; 200.5, 157.6, 143.1, 138.2, 137.0, 135.5, 131.8, 129.6, 129.5, 128.1, 127.0, 42.8, 34.3, 30.4, 27.2, 21.4. HRMS (ESI): m/z calcd. for $C_{22}H_{27}NNaO_3S$ $[M+Na]^+$ 408.1604; found 408.1599.

(*E*)-*N*-[3-(4-Methoxybenzoyl)-4-phenylbut-3-en-1-yl]-4-methylbenzenesulfonamide (**3ba**): R_f = 0.17 (hexane: AcOEt = 3:1). **A**, 159.6 mg (92%); **B**, 137.3 mg (79%); **C**, 168.4 mg (97%). White solid. MP: 124-126 ˚C. IR (KBr) ν cm^{-1}; 3302, 1595, 1321, 1258, 1159, 1028. ^{1}H NMR (500 MHz) δ ppm; 7.78 (d, *J* = 8.6 Hz, 2H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.43-7.33 (m, 3H), 7.31 (d, *J* = 6.9 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 7.11 (s, 1H), 6.95 (d, *J* = 8.6 Hz, 2H), 5.26 (t, *J* = 5.7 Hz, 1H), 3.88 (s, 3H), 3.16 (td, *J* = 6.9, 5.7 Hz, 2H), 2.86 (t, *J* = 6.9 Hz, 2H), 2.37 (s, 3H). ^{13}C NMR (125 MHz) δ ppm; 198.3, 163.2, 143.1, 142.7, 137.6, 136.9, 134.8, 132.2, 130.1, 129.6, 129.0, 128.9, 128.7, 127.0, 113.6, 55.5, 42.1, 28.0, 21.5. HRMS (ESI): m/z calcd. for $C_{25}H_{25}NNaO_4S$ $[M+Na]^+$ 458.1397; found 458.1384.

(*E*)-*N*-[3-(4-Methoxybenzoyl)-4-(4-methoxyphenyl)but-3-en-1-yl]-4-methylbenzenesulfonamide (**3bb**): R_f = 0.09 (hexane: AcOEt = 3:1). **A**, 176.7 mg (95%); **B**, 181.8 mg (98%); **C**, 164.9 mg (89%). Yellow solid. MP: 197-199 ˚C. IR (KBr) ν cm^{-1}; 3267, 1600, 1324, 1256, 1160, 1028. ^{1}H NMR (500 MHz) δ ppm; 7.73 (d, *J* = 8.6 Hz, 2H), 7.68 (d, *J* = 8.6 Hz, 2H), 7.30 (d, *J* = 9.2 Hz, 2H), 7.20 (d, *J* = 8.6 Hz, 2H), 7.06 (s,

1H), 6.94 (d, *J* = 8.6 Hz, 2H), 6.92 (d, *J* = 9.2 Hz, 2H) , 5.35 (t, *J* = 5.2 Hz, 1H), 3.88 (s, 3H), 3.85 (s, 3H), 3.20 (td, *J* = 6.9, 5.2 Hz, 2H), 2.88 (t, *J* = 6.9 Hz, 2H), 2.37 (s, 3H). ^{13}C NMR (125 MHz) δ ppm; 198.7, 163.0, 160.3, 143.3, 143.1, 137.0, 135.4, 132.1, 131.1, 130.4, 129.6, 127.2, 127.0, 114.2, 113.5, 55.5, 55.4, 42.0, 28.0, 21.5. HRMS (ESI): m/z calcd. for $C_{26}H_{27}NNaO_5S$ $[M+Na]^+$ 488.1502; found 488.1490.

(*E*)-*N*-[3-(4-Methoxybenzoyl)-4-(4-nitrophenyl)but-3-en-1-yl]-4-methylbenzenesulfonamide (**3bi**): R_f = 0.09 (hexane: AcOEt = 3:1). **A**, 175.4 mg (91%); **B**, 175.3 mg (91%); **C**, 184.0 mg (96%). Yellow solid. MP: 70-72 ˚C. IR (KBr) ν cm^{-1}; 3268, 1597, 1519, 1344, 1256, 1159, 1027. ^{1}H NMR (500 MHz) δ ppm; 8.22 (d, *J* = 8.6 Hz, 2H), 7.83 (d, *J* = 8.6 Hz, 2H), 7.66 (d, *J* = 8.0 Hz, 2H), 7.51 (d, *J* = 8.6 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.11 (s, 1H), 6.96 (d, *J* = 8.6 Hz, 2H), 5.18 (t, *J* = 6.0 Hz, 1H), 3.88 (s, 3H) 3.13 (td, *J* = 6.9, 6.0 Hz, 2H), 2.85 (t, *J* = 6.9 Hz, 2H), 2.39 (s, 3H). ^{13}C NMR (125 MHz) δ ppm; 197.2, 163.6, 147.4, 143.4, 141.5, 140.8, 138.6, 136.7, 132.3, 129.71, 129.67, 129.4, 126.9, 123.9, 113.8, 55.5, 41.7, 28.7, 21.5. HRMS (ESI): m/z calcd. for $C_{25}H_{24}N_2NaO_6S$ $[M+Na]^+$ 503.1247; found 503.1239.

(*E*)-4-Methyl-*N*-[3-(4-nitrobenzoyl)-4-phenylbut-3-en-1-yl]benzenesulfonamide (**3ca**): R_f = 0.20 (hexane: AcOEt = 3:1). **A**, 53.8 mg (30%); **B**, 74.6 mg (40%); **C**, 8.9 mg (5%). Yellow solid. MP: 137-139 ˚C. IR (KBr) ν cm^{-1}; 3290, 1650, 1527, 1351, 1321, 1158.^{1}H NMR (500 MHz) δ ppm; 8.29 (d, *J* = 8.6 Hz, 2H), 7.86 (d, *J* = 8.6 Hz, 2H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.45-7.33 (m, 5H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.20 (s, 1H), 5.04 (d, *J* = 6.0 Hz, 1H), 3.21 (td, *J* = 6.9, 6.0 Hz, 2H), 2.93 (t, *J* = 6.9 Hz, 2H), 2.39 (s, 3H). ^{13}C NMR (125 MHz) δ ppm; 197.6, 149.5, 146.9, 143.7, 143.4, 137.5, 136.8, 134.2, 130.3, 129.7, 129.6, 129.3, 128.9, 126.9, 123.5, 41.9, 27.5, 21.5. HRMS (FAB): m/z calcd. for $C_{24}H_{23}N_2O_5S$ $[M+H]^+$ 451.1328; found 451.1358.

(*E*)-*N*-[4-(4-Methoxyphenyl)-3-(4-nitrobenzoyl)but-3-en-1-yl]-4-methylbenzenesulfonamide (**3cb**): R_f = 0.14 (hexane: AcOEt = 3:1). **A**, 118.5 mg (59%); **B**, 121.7 mg (63%); **C**, 0.0 mg (0%). Yellow solid. MP: 118-120 ˚C. IR (KBr) ν cm^{-1}; 3250, 1593, 1513, 1348, 1328, 1264, 1154, 1031.^{1}H NMR (500 MHz) δ ppm; 8.30 (d, *J* = 8.6 Hz, 2H), 7.80 (d, *J* = 8.6 Hz, 2H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.36 (d, *J* = 8.6 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 7.13 (s, 1H), 6.95 (d, *J* = 8.6 Hz, 2H), 4.84 (t, *J* = 6.0 Hz, 1H), 3.87 (s, 3H), 3.25 (td, *J* = 6.9, 6.0 Hz, 2H), 2.97 (t, *J* = 6.9 Hz, 2H), 2.40 (s, 3H). ^{13}C NMR (125 MHz) δ ppm; 197.8, 161.0, 149.3, 147.3, 144.3, 143.4, 136.9, 135.0, 131.7, 130.1, 129.7, 127.0, 126.5, 123.4, 114.4, 55.4, 41.8, 27.5, 21.5. HRMS (FAB): m/z calcd. for $C_{25}H_{25}NO_3S$ $[M+H]^+$ 481.1433; found 481.1408.

General procedure for synthesis of compounds 7.

To a solution of **3** (**3aa**, 162.2 mg; **3ab**, 174.2 mg; **3ai**, 180.2 mg; **3ba**, 174.2 mg; **3ca**, 180.2 mg; 0.4 mmol) in MeCN (2.5 mL) was added DBU (119.6 µL, 0.8 mmol) at room temperature. After being stirred at same temperature for 24 h, the reaction mixture was quenched with NH_4Cl aq. and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated in vacuo to dryness. The residue was purified by MPLC to give **7** (**7aa**, 146.0 mg, 90%; **7ab**, 151.6 mg, 87%; **7ai**, 172.5 mg, 96%; **7ba**, 171.0 mg, 98%; **7ca**, 124.6 mg, 69%).

Characterization of compounds 7.

Phenyl[(2*S,3*S**)-2-phenyl-1-tosylpyrrolidin-3-yl]methanone** (**7aa**): R_f = 0.17 (hexane: AcOEt = 3:1). Yellow solid. MP: 79-81 ˚C. IR (KBr) ν cm^{-1}; 1678, 1342, 1161. ^{1}H NMR (500 MHz) δ ppm; 7.69 (d, *J* = 7.5 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.40 (t, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 8.0 Hz, 2H), 7.31-7.26 (m, 3H), 5.13 (d, *J* = 4.6 Hz, 1H), 3.87 (ddd, *J* = 7.5, 5.7, 4.6 Hz, 1H), 3.78 (ddd, *J* = 10.3, 6.9, 5.7 Hz, 1H), 3.59 (ddd, *J* = 10.3, 7.5, 6.9 Hz, 1H), 2.45 (s, 3H) 2.32-2.23 (m, 1H), 1.95-1.86 (m, 1H). ^{13}C NMR (125 MHz) δ ppm; 197.9, 143.4, 142.5, 135.3, 134.6, 133.5, 129.6, 128.7, 128.5, 127.8, 127.5, 126.2, 65.2, 55.8, 49.0, 28.5, 21.6. HRMS (FAB): m/z calcd. for $C_{24}H_{24}NO_3S$ $[M+H]^+$ 406.1477; found 406.1486.

[(2*S,3*S**)-2-(4-Methoxyphenyl)-1-tosylpyrrolidin-3-yl](phenyl)methanone** (**7ab**): R_f = 0.21 (hexane: AcOEt = 3:1). Yellow solid. MP: 108-110 ˚C. IR (KBr) ν cm^{-1}; 1677, 1335, 1247, 1160, 1036. ^{1}H NMR (500 MHz) δ ppm; 7.69 (d, *J* = 8.0 Hz, 2H), 7.66 (d, *J* = 8.0 Hz, 2H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.40 (dd, *J* = 8.0, 7.5 Hz, 2H), 7.29 (d, *J* = 8.6 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 5.04 (d, *J* = 5.2 Hz, 1H), 3.86 (ddd, *J* = 6.9, 6.0, 5.2 Hz, 1H), 3.79 (s, 3H), 3.76 (ddd, *J* = 10.3, 6.9, 5.7 Hz, 1H), 3.57 (ddd, *J* = 10.3, 7.5, 6.9 Hz, 1H), 2.45 (s, 3H), 2.31-2.22 (m, 1H), 1.95-1.86 (m, 1H). ^{13}C NMR (125 MHz) δ ppm; 198.0, 158.9, 143.3, 135.3, 134.54, 134.48, 133.5, 129.5, 128.6, 128.4, 127.7, 127.4, 114.0, 64.9, 55.8, 55.2, 49.0, 28.4, 21.5. HRMS (ESI): m/z calcd. for $C_{25}H_{25}NNaO_4S$ $[M+Na]^+$ 458.1397; found 458.1387.

[(2*S,3*S**)-2-(4-Nitrophenyl)-1-tosylpyrrolidin-3-yl](phenyl)methanone** (**7ai**): R_f = 0.19 (hexane: AcOEt = 3:1). Yellow solid. MP: 99-101 ˚C. IR (KBr) ν cm^{-1}; 1682, 1518, 1364, 1160. ^{1}H NMR (500 MHz) δ ppm; 8.19 (d, *J* = 8.6 Hz, 2H), 7.73 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.58 (d, *J* = 8.6 Hz, 2H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.42 (dd, *J* = 8.0, 7.5 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 5.27 (d, *J* = 5.7 Hz,1H), 3.82 (ddd, *J* = 7.5, 7.5, 5.7 Hz, 1H), 3.80 (ddd, *J* = 10.3, 6.9, 6.3 Hz, 2H), 3.58 (ddd, *J* = 10.3, 6.9, 6.3 Hz, 1H), 2.47 (s, 3H), 2.35-2.26 (m, 1H), 1.84-1.75 (m, 1H). ^{13}C NMR (125 MHz) δ ppm; 196.9, 150.0, 144.1, 141.8, 135.0, 134.9, 134.0, 129.8, 128.9, 128.4, 127.9, 127.2, 124.0, 64.3, 56.0, 49.2, 29.4, 21.6. HRMS (FAB): m/z calcd. for $C_{24}H_{23}N_2O_5S$ $[M+H]^+$ 451.1328; found 451.1316.

(4-Methoxyphenyl)[(2*S,3*S**)-2-phenyl-1-tosylpyrrolidin-3-yl]methanone** (**7ba**): R_f = 0.16 (hexane: AcOEt = 3:1). White solid. MP: 53-55 ˚C. IR (KBr) ν cm^{-1}; 1672, 1345, 1258, 1160, 1028. ^{1}H NMR (500 MHz) δ ppm; 7.69 (d, *J* = 8.0 Hz, 2H), 7.68 (d, *J* = 9.2 Hz, 2H), 7.40-7.26 (m, 7H), 6.86 (d, *J* = 9.2 Hz, 2H), 5.11 (d, *J* = 5.2 Hz, 1H), 3.84 (s, 3H), 3.82 (ddd, *J* = 6.9, 6.3, 5.2 Hz, 1H), 3.76 (ddd, *J* = 10.3, 6.9, 6.3 Hz, 1H), 3.59 (ddd, *J* = 10.3, 7.5, 6.9 Hz, 1H), 2.45 (s, 3H), 2.28-2.19 (m, 1H), 1.92-1.83 (m, 1H). ^{13}C NMR (75 MHz) δ ppm; 196.5, 163.9, 143.5, 142.7, 134.6, 130.8, 129.6, 128.7, 128.4, 127.8, 127.5, 126.3, 113.8, 65.5, 55.5, 49.1, 28.7, 21.5 (note that two carbon peaks overlap with each other). HRMS (ESI): m/z calcd. for $C_{25}H_{25}NNaO_4S$ $[M+Na]^+$ 458.1397; found 458.1388.

(4-Nitrophenyl)[(2*S,3*S**)-2-phenyl-1-tosylpyrrolidin-3-yl]methanone** (**7ca**): R_f = 0.23 (hexane: AcOEt = 3:1). Yellow solid. MP: 50-52 ˚C. IR (KBr) ν cm^{-1};1690, 1524, 1346, 1160. ^{1}H NMR (500 MHz) δ ppm; 8.23 (d, *J* = 8.6 Hz, 2H), 7.82 (d, *J* = 8.6 Hz, 2H), 7.66 (d, *J* = 8.0 Hz, 2H), 7.34-7.27 (m, 7H), 5.06 (d, *J* = 5.2 Hz, 1H), 3.88 (ddd, *J* = 6.3, 6.3, 5.2 Hz, 1H), 3.79 (ddd, *J* = 10.3, 6.9, 5.7 Hz, 1H),3.62 (ddd,

J = 10.3, 7.5, 6.9, Hz,1H), 2.46 (s, 3H), 2.35-2.26 (m, 1H), 1.99-1.90 (m, 1H). ^{13}C NMR (125 MHz) δ ppm; 196.6, 150.4, 143.6, 141.9, 139.8, 134.4, 129.6, 129.4, 128.7, 127.7, 127.3, 126.2, 123.8, 65.1, 56.3, 48.8, 28.3, 21.6. HRMS (ESI): m/z calcd. for $C_{24}H_{22}N_2NaO_5S$ $[M+Na]^+$ 473.1142; found 473.1138.

Author Contributions

Conceptualization, A.S.; data curation, all; formal analysis, all; funding acquisition, A.S.; investigation, S.A. and S.O., methodology, S.A., S.O. and A.S.; project administration, A.S.; resources, A.S.; supervision, A.S.; visualization, S.A. and A.S.; writing—original draft preparation, A.S.; writing—review and editing, A.T. and A.S.

Conflicts of interest

There are no conflicts to declare.

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