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Graphical Abstract

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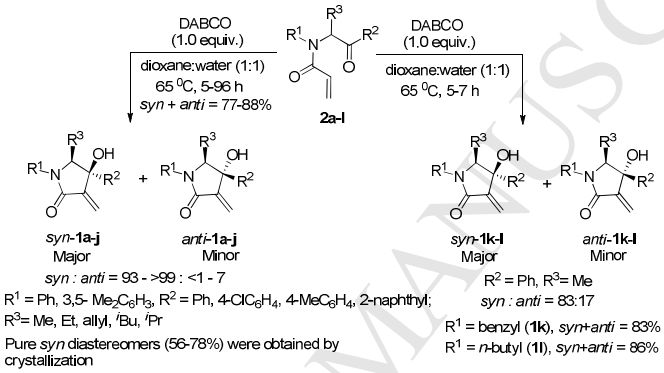

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ABSTRACT

A simple and convenient protocol for highly diastereoselective intramolecular Baylis-Hillman (IBH) reaction of substrates containing less reactive acrylamides as activated alkene and ketones with α-chiral center (racemic) as electrophile components, thus producing α-methylene-γ-lactam frameworks having β-tertiary alcoholic functional group, has been developed.

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1. Introduction

Development of strategies[1] for diastereoselective synthesis of *tertiary* alcohols having α-chiral center has been and continues to be one of the challenging and attractive endeavors in synthetic chemistry because of the presence of such frameworks in number of natural products [2a-c] and bioactive compounds[2a,d-g] (for selected examples see Fig.1). 4-Hydroxy-3,4,5-trisubstituted-pyrrolidin-2-one skeleton[3] is one such unique structural organization (few examples are presented in Figure 2) that has attracted the attention of organic and medicinal chemists in recent years.[1d-f,3a,b]

It has been well documented in the literature that substituent on the chiral carbon α to the keto group plays an important role in directing the attack of nucleophile on keto carbonyl, thus controlling the stereochemistry (diastereo-selectivity of the reaction) at the newly formed chiral center.[1] In continuation of our interest[4] on the Baylis-Hillman (also known as Morita-Baylis-Hillman) reaction[5,6] we herein report a facile and convenient strategy for highly diastereoselective synthesis of *tertiary* alcohols *via* the intramolecular Baylis-Hillman (IBH) reaction of substrates containing less reactive acrylamides as activated alkene and ketones with α-chiral center (racemic) as electrophile components.

Intramolecular Baylis-Hillman (IBH) reaction represents unique branch of BH reaction as it produces useful carbocylic and heterocyclic compounds having several functional groups. [5f,j,7,8]

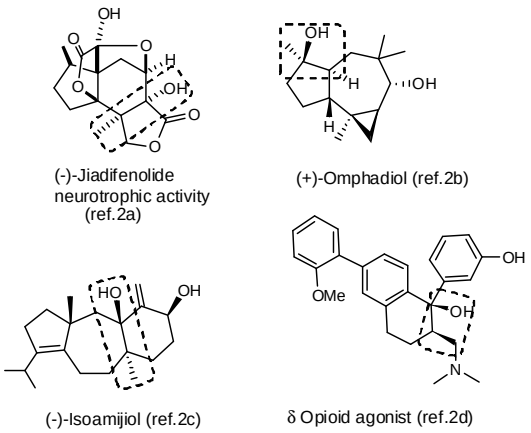
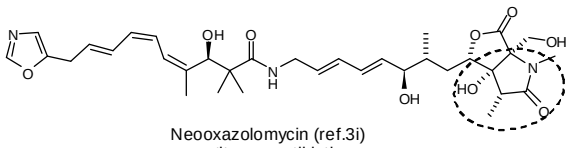


Fig. 1. Representative natural products and bioactive compounds containing *tertiary* alcoholic moiety α- to the chiral center.

The growth of IBH reaction in principle depends on the design and synthesis of substrates containing both activated alkene and electrophile components in a suitable position so that the coupling takes place to yield cyclic compounds. [5f,j,7,8] From the literature it is quite clear that there are few reports on diastereoselective intramolecular Baylis-Hillman reactions producing secondary alcohols[8e,h,i,k] and tertiary alcohols.[8f,g,i,j]



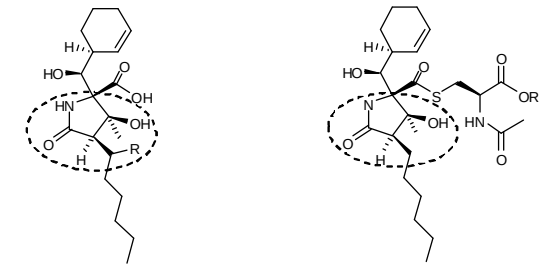
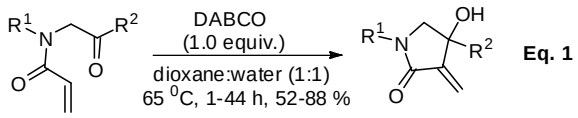


Fig. 2. Representative natural products containing pyrrolidin-2-one framework with *tertiary* alcoholic moiety α- to the chiral center.

2. Results and discussion

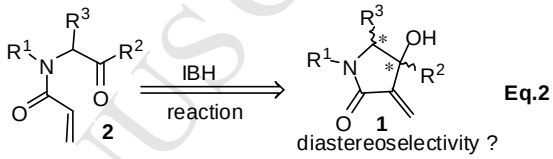
Recently we have reported[8c,d] an interesting intramolecular Baylis-Hillman (IBH) reaction of acrylamide-ketone substrates (less reactive components) under the influence of DABCO, using dioxane:water solvent system at 65 ^{o}C to obtain the resulting IBH-adducts containing *tertiary* alcoholic functional group (Eq.1). Based on this report and also on our long experience in development of the BH reaction, we envisioned that it is possible to achieve high diastereoselectivity in IBH reaction of acrylamide-ketone (AK) substrates **2** containing chiral (racemic) center α to the keto group to produce α-methylene-γ-lactam frameworks **1** according to equation 2.

Our previous work:



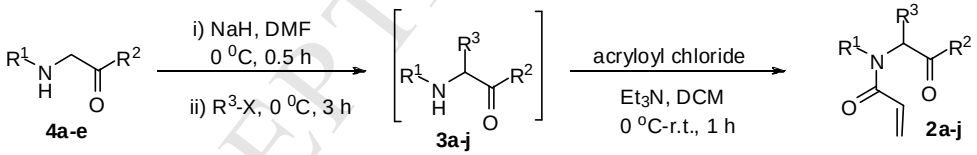
R^1 = aryl; R^2 = aryl, Me

Accordingly we have first selected *N*-(1-oxo-1-phenylpropan-2-yl)-*N*-phenylacrylamide (**2a** R^1= R^2 = phenyl, R^3 = methyl) as a suitable substrate for diastereoselective intramolecular Baylis-Hillman reaction. This compound was conveniently prepared from easily accessible amino-ketone (**4a**, R^1= R^2 = phenyl)[9] following the reaction sequence as shown in Table 1. This reaction sequence involves two steps: i) amino-ketone (**4a**) was methylated (according to the known procedure) [10] with methyl iodide in presence of NaH to provide amino-α-methyl ketone (**3a**), ii) the crude ketone **3a** was used as such (without purification) for treatment with acryloyl chloride in presence of triethylamine to provide *N*-(1-oxo-1-phenylpropan-2-yl)-*N*-phenylacrylamide (**2a**) in 70 % isolated yield over two steps.



Subsequently we have subjected acrylamide-ketone (**2a**) to the IBH reaction. Based on our previous work as shown in Eq.1, we have treated acrylamide-ketone (**2a**) with DABCO (1.0 eq.) in dioxane-water (1:1) solvent system, at 65 °C. We were pleased to notice that the reaction went on very well and is highly diastereoselective thus producing *syn* adduct (***syn*-1a)** as the major product and *anti* adduct ***(anti*-1a)** as a minor product. (***syn*-1a : *anti*-1a** is 93:7) in 86% combined isolated yield after purification through column chromatography (Table 2, entry1) (also see experimental section). Diastereoselectivity was

Table 1: Synthesis of acrylamide-ketones (AK) (**2a-j**)[a]



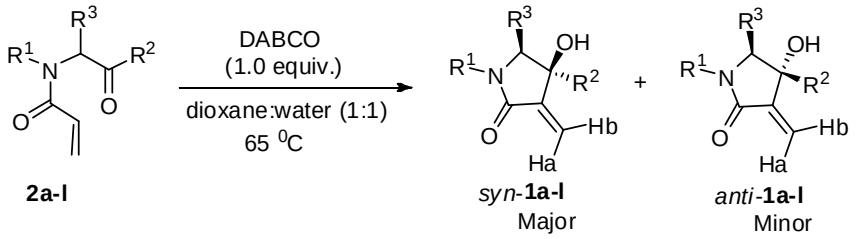
Entry	R^1	R^2	Amino ketone (4)	R^3-X	α-Alkylated amino ketone (3)	Product[b] acrylamide-ketone (2)	Yield[c] (%)
1	C_6H_5	C_6H_5	**4a**	MeI	**3a**	**2a**	70
2	C_6H_5	4-ClC_6H_4	**4b**	MeI	**3b**	**2b**	65
3	C_6H_5	2-naphthyl	**4c**	MeI	**3c**	**2c**	67
4	C_6H_5	C_6H_5	**4a**	EtI	**3d**	**2d**	62
5	C_6H_5	4-ClC_6H_4	**4b**	EtI	**3e**	**2e**	60
6	C_6H_5	C_6H_5	**4a**	allyl bromide	**3f**	**2f**	50
7	3, 5-$Me_2C_6H_3$	C_6H_5	**4d**	allyl bromide	**3g**	**2g**	54
8	C_6H_5	C_6H_5	**4a**	*i*BuI	**3h**	**2h**	55
9	C_6H_5	4-MeC_6H_4	**4e**	*i*BuI	**3i**	**2i**	57
10	C_6H_5	C_6H_5	**4a**	*i*PrI	**3j**	**2j**	48

[a] All the reactions were carried out on a 5.0 mmol scale of amino ketone (**4a-e**) with alkyl halide (6.5 mmol) in the presence of NaH (5.25 mmol) in DMF. The crude product (**3a-j**) thus obtained was treated with acryloyl chloride (6.0 mmol) in the presence of Et_3N (7.0 mmol) in DCM.

[b] These compounds are fully characterized (see experimental section)

[c] Overall two step yield of pure and isolated products

Table 2. Synthesis of 4-hydroxy-3,4,5-trisubstituted-pyrrolidin-2-ones (**1a-l**).[a,b]



2a-l *syn*-**1a-l** Major *anti*-**1a-l** Minor

Entry	AK	R^1	R^2	R^3	Products[c]	*t* (h)	*dr*[d]	Yield[e] (%)
1	**2a**	C_6H_5	C_6H_5	Me	***syn*-1a**[f] + ***anti*-1a**	6	93:7	86 (*60*)[g]
2	**2b**	C_6H_5	4-ClC_6H_4	Me	***syn*-1b**[f] + ***anti*-1b**	5	93:7	79 (*58*)[g]
3	**2c**	C_6H_5	2-naphthyl	Me	***syn*-1c** + ***anti*-1c**	14	94:6	88 (*64*) [g]
4	**2d**	C_6H_5	C_6H_5	Et	***syn*-1d** + ***anti*-1d**	13	95:5	84 (*62*) [g]
5	**2e**	C_6H_5	4-ClC_6H_4	Et	***syn*-1e** + ***anti*-1e**	11	94:6	80 (*63*) [g]
6	**2f**[h]	C_6H_5	C_6H_5	allyl	***syn*-1f** + ***anti*-1f**[i]	13	96:4	81(*78+3*)[g,i]
7	**2g**	3, 5-$Me_2C_6H_3$	C_6H_5	allyl	***syn*-1g** + ***anti*-1g**	60	96:4	77 (*56*)[g]
8	**2h**	C_6H_5	C_6H_5	*i*Bu	***syn*-1h** + ***anti*-1h**	60	96:4	82 (*59*)[g]
9	**2i**	C_6H_5	4-MeC_6H_4	*i*Bu	***syn*-1i** + ***anti*-1i**	96	96:4	81(*56*)[g]
10	**2j**	C_6H_5	C_6H_5	*i*Pr	***syn*-1j** + ***anti*-1j**	84	>99:<1	83[j]
11	**2k**	$CH_2C_6H_5$	C_6H_5	Me	***syn*-1k** + ***anti*-1k**	5	83:17 (97:3)[k]	83 (59)[k]
12	**2l**	*n*-butyl	C_6H_5	Me	***syn*-1l** + ***anti*-1l**	7	83:17	86

AK = acrylamide-ketone, *t* = time, *dr* = diastereomeric ratio

[a] Unless otherwise mentioned, all the reactions were carried out on a 0.5 mmol scale of acrylamide-ketone using DABCO (1.0 equiv.) in dioxane:water (1:1) (1.0 mL) at 65 ^{0}C temperature.

[b] All products were obtained as mixture of *syn* (major) and *anti* (minor) isomers after purification through column chromatography (see experimental section) . Pure *syn* diastereomers were obtained by crystallization [ethyl acetate : hexanes (1:2)] and fully characterized (see experimental section and also SI).

[c] We have assigned *syn*- and *anti* configurations for 4-hydroxy-3,4,5-trisubstituted-pyrrolidin-2-one derivatives (**1a-l**).as in chemical equation shown above (Table 2) [in *syn* diastereomers 'R^3' and 'OH' groups are on the same side and in *anti* isomer 'R^3' and 'OH' groups are on opposite side].

[d] Diastereomeric ratio was determined by integration of the separated olefinic proton (**Ha** and **Hb**) signals of *syn* (major) and *anti* (minor) isomers in the ^{1}H NMR spectra of the crude mixtures (also see the text).

[e] Isolated yields of mixture of *syn* and *anti* diastereomers after purification through column chromatography based on acrylamide-ketones (**2a-l**).

[f] *Syn* stereochemistry of these pure diastereomers was assigned on the basis of single crystal X-ray data analysis.[11] We have assigned the *syn* stereochemistry to all the major isomers of **1c-1l** in analogy with **1a** and **1b**.

[g] yields in parenthesis are isolated yields of pure *syn*- diastereomers (**1a-i**) (obtained after crystallization as mentioned in footnote *b*) based on acrylamide-ketones **2a-j.**

[h] The reaction was carried out on a 4.0 mmol scale of acrylamide-ketone using DABCO (1.0 equiv.) in dioxane:water (1:1)(8.0 mL) at 65 ^{0}C temperature.

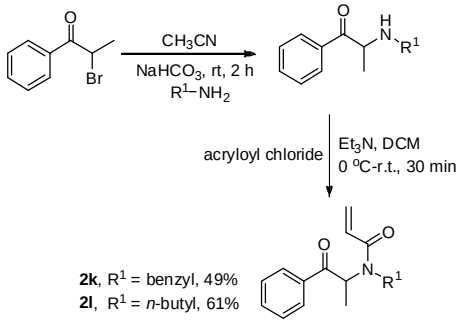
[i] In this case we have separated major and minor diastereomers by column chromatography.

[j] In the case of **1j** pure *syn* isomer (>99:<1) was obtained after purification through column chromatography.

[k] Diastereomeric ratio after crystallization [ethyl acetate : hexanes (1:1)] and yield in parenthesis is the corresponding yield.

determined by the integration of the separated olefinic proton (**Ha** and **Hb**) signals of *syn* (major) and *anti* (minor) isomers in the ^{1}H NMR spectra of the crude mixture [as well as that of the compound (*syn* and *anti*-mixture) after purification by column chromatography]. The major product (***syn*-1a)** was obtained in diastereomerically pure form in 60 % yield by careful crystallization. We have assigned the *syn* stereochemistry to the major product (*syn*-**1a)** on the basis of its single crystal X-ray data analysis.[11] Encouraged by this interesting result, we have prepared representative acrylamide-α-substituted ketones (**2b-j**) and subjected them to IBH reaction under similar conditions. The resulting adducts (**1b-j**) were obtained in 93:7->99:<1(*syn:anti*) diastereomeric ratios and 77-88 % isolated yields (Table 2, entries 2-10). In all the cases (except in the case of **1f**) we were able to obtain pure *syn* diastereomers through careful crystallization as in the case of ***syn*-1a**. Interestingly major and minor diastereomers in the case of **1f** were separated during column chromatography itself.

In all the above examples (**1a-j**) the substitution on nitrogen is an aryl group (R^1= aryl). With a view to understand the effect of substitution on nitrogen we have also prepared two acrylamide-ketones, **2k** (R^1= benzyl) and **2l** (R^1=*n*-butyl), starting from α-

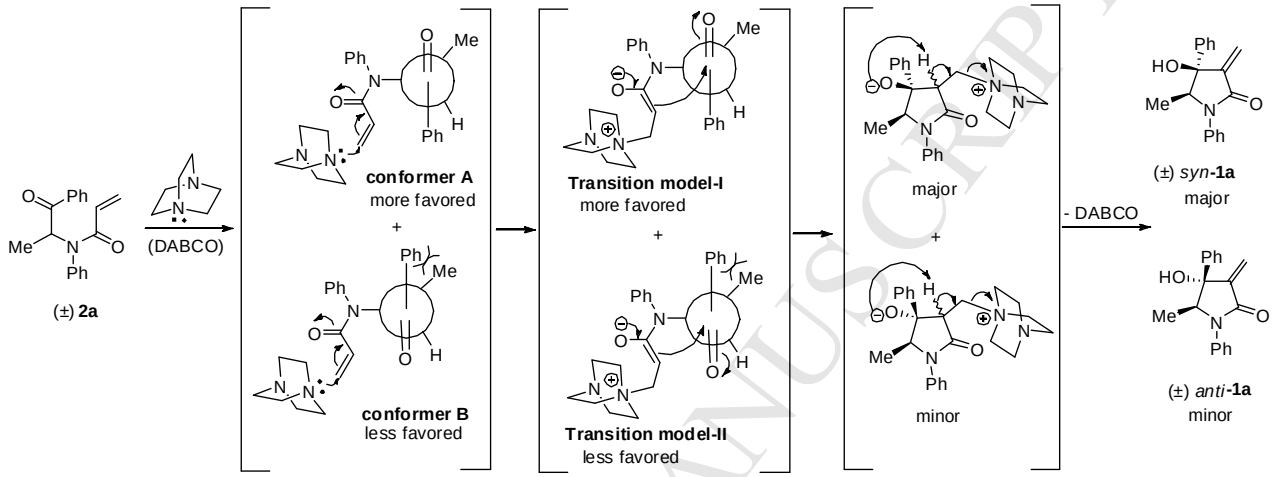


Scheme 1. Synthesis of acrylamide-ketones **2k** and **2l**

bromopropiophenone[13] in a two step process as described in Scheme1. The strategy involves the treatment of α-bromopropiophenone with benzylamine (or butyl amine)[14] followed by the reaction of the *in situ* prepared secondary amine with acryloyl chloride to provide the required acrylamide-ketones (**2k** and **2l**) (Scheme 1). Subsequent intramolecular BH reaction of **2k** and **2l** using DABCO (1.0 equiv.) in dioxane water (1:1) at 65 ^{o}C provided the desired BH adducts, 1-benzyl-4-hydroxy-5-methyl-3-methylene-4-phenylpyrrolidin-2-one (**1k**),

and 1-butyl-4-hydroxy-5-methyl-3-methylene-4-phenyl-pyrrolidin-2-one (**1l**) respectively (Table 2 entries 11 and 12) in 83:17 (*syn*:*anti*) diastereomeric ratio. In the case of **1k**, crystallization [ethyl acetate : hexanes (1:1)] provided the resulting *syn* adduct in 94% diastereomeric excess (*syn*:*anti* is 97:3).

We have determined the diastereoselectivity of the IBH reaction and assigned the stereochemistry of the major (*syn*) and minor (*anti*) products in the case of **1c-1l** by examining the ^{1}HNMR spectra of the crude reaction mixtures in analogy with that of **1a** and **1b**. In the ^{1}H NMR spectra, isomeric olefinic protons



Scheme 2. Plausible mechanism for diastereoselective IBH reaction

Ha and **Hb**) signals of *syn* (major) and *anti* (minor) isomers separate nicely in all the compounds **1a-l**. **Ha** and **Hb** protons in *anti* isomers are deshielded in comparison to that of *syn* isomers. **Ha** protons of *syn* isomer appear at ≈ δ 6.21- 6.42 while that of *anti* isomer appear at ≈ δ 6.32- 6.54. **Hb** Protons in *syn* isomers appear at ≈ δ 5.37-5.60 while that of *anti* isomer appear at ≈ δ 5.49-5.76. Diastereomeric ratios were determined by the integration ratios of diastereomeric olefinic protons (**Ha** as well as **Hb**) of major and minor products in the ^{1}H NMR spectra of the crude mixtures.

Though it is not highly remarkable, we have noticed that, the diastereoselectivity has increased from 86 to 92 % with increasing steric bulk of the substituent at the α-position of keto group in acrylamide-ketones (**2a-i**). It is important to note that the substrate (**2j**), containing i*so*-propyl group at α- to keto group, produced the resulting IBH-adduct (**1j**) in excellent diastereoselectivity (> 99 %) in 83 % isolated yield. From these results it is clear that steric bulk of substituent on carbon α- to keto group plays a key role in directing the stereochemical course of the reaction. From the comparatively low diastereoselectivities obtained in the cases of **1k** and **1l,** it is quite clear that the substrates having aryl groups on nitrogen (R^3 is aryl) offer better diastereoselectivities than substrates having alkyl groups on nitrogen (R^3 is alkyl).

A plausible mechanism for high diastereoselectivities is presented in the Scheme 2 (on basis of well known Felkin-Anh model)[12] by taking the reaction of *N*-(1-oxo-1-phenylpropan-2-yl)-*N*-phenylacrylamide (**2a**) with DABCO, as a model case. Diastereoselectivities are explained on the basis of conformers **A**, **B** and transition states **I** and **II**. The conformer **B** and transition state **II** are disfavored due to the presence of Ph-Me - gauche interactions while the conformer **A** and transition state **I** are favored because of absence of such unfavorable gauche interactions.

3. Conclusion

In conclusion, we have developed a simple methodology for high diastereoselective synthesis of *tertiary* alcohols via DABCO mediated intramolecular Baylis-Hillman cyclization of acrylamide-ketones, containing a chiral (racemic) centre α to ketone functionalty. Our study also demonstrates the high potential of less reactive acrylamides as activated alkene and ketones as electrophile components in IBH reactions.

4. Experimental section

4.1 General remarks

Melting Points were recorded on a MR-Vis+ visual melting point range apparatus of LABINDIA instruments private limited and were uncorrected. Infrared spectra were recorded on a Thermo Scientific Nicolet 380 FT-IR spectrophotometer. All the spectra were calibrated against polystyrene absorption at 1601 cm^{-1}. Solid samples were recorded as KBr wafers. Proton magnetic resonance spectra were recorded on a Bruker-AVANCE-500 and carbon-13 magnetic resonance spectra on a Bruker-AVANCE-400 spectrometer. ^{1}H NMR (500 MHz) spectra for all the samples were measured in chloroform-d, with TMS (δ 0 ppm) as an internal standard. ^{13}C NMR (100 MHz) spectra for all the samples were measured in chloroform-d with middle peak of the triplet (δ 77.10 ppm) of chloroform-d as an internal standard. HRMS spectra were recorded on Bruker maXis ESI-TOF spectrometer. The X-ray diffraction measurement for compound (*syn*-**1a**) was carried out at 298 K on Oxford Diffraction Xcalibur Eos Gemini diffractometer with graphite-monochromated Cu- Kα radiation with wavelength of 1.54184 Å and while for compound (*syn*-**1b**) was carried out at 298 K on Bruker SMART APEX CCD area detector system equipped with a graphite monochromator and a Mo-Kα fine-focus sealed tube (λ = 0.71073 Å).

4.2. Representative procedure for Acrylamide-ketones (2a-j)

*4.2.1. N-(1-Oxo-1-phenylpropan-2-yl)-N-phenylacrylamide (**2a**): This was prepared in two steps:*
Step 1:Preparation of 1-phenyl-2-phenylaminopropanone (methylation of 1-phenyl-2-phenylaminoethanone was performed following the known procedure) [10]

To a stirring suspension of NaH (0.210 g, 5.25 mmol, 60% w/w in mineral oil) in dry DMF (37 mL) at 0 ºC was added 1-phenyl-2-(phenylamino)ethanone (1.055 g, 5.0 mmol). After stirring 30 min at 0 ºC, MeI (0.923 g, 6.5 mmol) was added slowly. Stirring was continued at 0 ºC for 3 h. Then the reaction was carefully poured into ice-cold water and stirred for 10 minutes. Reaction mixture was extracted with EtOAc (2 x 60 mL). Combined organic layer was washed with water (2 x 30 mL) and dried over anhydrous Na_2SO_4. Solvent was removed under reduced pressure and the crude product (1-phenyl-2-phenylaminopropanone) thus obtained, was used as such without purification for the next step.

Step 2: Acrylamide formation

Above obtained crude product 1-phenyl-2-phenylamino-propanone (**3a**) was dissolved in dichloromethane (DCM) (15 mL). To this stirring solution at 0 ºC, Et_3N (0.707 g, 7.0 mmol) was added, followed by a dropwise addition of acryloyl chloride (0.543 g, 6.0 mmol). After stirring for 1h at the same temperature (at 0 ºC), the reaction mixture was diluted with water (30 mL) and extracted with DCM (2 x 30 mL). Combined organic layer was dried over anhydrous Na_2SO_4 and concentrated. The crude product, thus obtained, was purified by column chromatography [silica gel, 20 % ethyl acetate in hexanes] to provide the required product, N-(1-oxo-1-phenylpropan-2-yl)-N-phenylacrylamide (**2a**), in 70 % (0.976 g) yield (over two steps), as a reddish viscous liquid. R_f (20% EtOAc in hexanes): 0.30; IR (neat): ν 1687, 1654, 1616, 1594 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.26 (d, J = 6.0 Hz, 3H), 5.50 (dd, J = 10.5 and 2.0 Hz, 1H), 5.87 (dd, J = 17.0 and 10.5 Hz, 1H), 6.27 (q, J = 7.0 Hz, 1H), 6.37 (dd, J = 17.0 and 2.0 Hz, 1H), 7.12-7.18 (m, 2H), 7.34-7.40 (m, 3H), 7.47-7.52 (m, 2H), 7.57-7.61 (m, 1H) 8.05-8.08 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.31, 55.38, 128.31, 128.41, 128.53, 128.69, 128.84, 129.33, 130.39, 133.30, 135.81, 138.24, 165.65, 198.93; HRMS (ESI): calculated for $C_{18}H_{17}NO_2Na$: 302.1157 $(M+Na)^+$, found: 302.1162 $(M+Na)^+$.

*4.2.2. N-[1-(4-Chlorophenyl)-1-oxopropan-2-yl]-N-phenylacrylamide (**2b**).* Yield: 65 %; R_f (20% EtOAc in hexanes): 0.36; Yellow solid; mp: 113-116 ^0C; IR (KBr): ν 1687, 1649, 1610, 1583 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.25 (d, J = 7.5 Hz, 3H), 5.51 (dd, J = 10.5 and 2.0 Hz, 1H), 5.86 (dd, J = 17.0 and 10.5 Hz, 1H), 6.20 (q, J = 7.5 Hz, 1H), 6.37 (dd, J = 17.0 and 2.0 Hz, 1H), 7.10-7.15 (m, 2H), 7.35-7.40 (m, 3H), 7.45-7.49 (m, 2H), 8.00-8.03 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.20, 55.27, 128.24, 128.54, 128.79, 129.16, 129.40, 129.95, 130.28, 134.15, 138.05, 139.70, 165.65, 197.76; HRMS (ESI): calculated for $C_{18}H_{16}ClNO_2Na$: 336.0767 $(M+Na)^+$, found: 336.0769 $(M+Na)^+$.

*4.2.3. N-[1-(Naphthalen-2-yl)-1-oxopropan-2-yl]-N-phenylacrylamide (**2c**).* Yield: 67 %; R_f (20% EtOAc in hexanes): 0.32; Yellow viscous liquid; IR (neat): ν 1687, 1654, 1618, 1594 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.32 (d, J = 7.0 Hz, 3H), 5.49 (dd, J = 10.5 and 2.0 Hz, 1H), 5.87 (dd, J = 17.0 and 10.5 Hz, 1H), 6.38 (dd, J = 17.0 and 2.0 Hz, 1H), 6.43 (q, J = 7.0 Hz, 1H), 7.13-7.20 (m, 2H), 7.33-7.40 (m, 3H), 7.48-7.58 (m, 1H), 7.59-7.63 (m, 1H), 7.89 (d, J = 7.0 Hz, 1H), 7.93 (d, J = 9.0 Hz, 1H), 8.00 (d, J = 8.0 Hz, 1H), 8.06 (dd, J = 8.5 and 1.5 Hz, 1H), 8.67 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.44, 55.51, 124.38, 126.80, 127.82, 128.31, 128.51, 128.58, 128.72, 129.37, 129.89, 130.19, 130.45 132.74, 133.15, 135.80, 138.35, 165.73, 198.91; HRMS (ESI): calculated for $C_{22}H_{19}NO_2Na$: 352.1313 $(M+Na)^+$, found: 352.1317 $(M+Na)^+$.

*4.2.4. N-(1-Oxo-1-phenylbutan-2-yl)-N-phenylacrylamide(**2d**).* Yield: 62 %; R_f (20% EtOAc in hexanes): 0.38; Yellow viscous liquid; IR (neat): ν 1693, 1654, 1616, 1594 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 0.97 (t, J = 7.5 Hz, 3H), 1.62-1.72 (m, 1H), 1.85-1.95 (m, 1H), 5.50 (dd, J = 10.5 and 2.0 Hz, 1H), 5.84 (dd, J = 16.5 and 10.5 Hz, 1H), 6.27 (t, J = 7.5 Hz, 1H), 6.39 (dd, J = 16.5 and 2.0 Hz, 1H), 6.99 (bs, 2H), 7.28-7.38 (m, 3H), 7.47-7.52 (m, 2H), 7.57-7.62 (m, 1H); 8.07-8.11 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 11.03, 22.49, 60.25, 128.42, 128.60, 128.72, 128.91, 129.31, 130.02, 133.43, 136.40, 138.06, 165.90, 198.19; HRMS (ESI): calculated for $C_{19}H_{19}NO_2Na$: 316.1313 $(M+Na)^+$, found: 316.1313 $(M+Na)^+$.

*4.2.5. N-[1-(4-Chlorophenyl)-1-oxobutan-2-yl]-N-phenylacrylamide (**2e**).* Yield: 60 %; R_f (20% EtOAc in hexanes): 0.40; Yellow viscous liquid (neat): ν 1687, 1649, 1616, 1589 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 0.97 (t, J = 7.5 Hz, 3H), 1.62-1.72 (m, 1H), 1.82-1.92 (m, 1H), 5.52 (dd, J = 10.5 and 2.0 Hz, 1H), 5.83 (dd, J = 17.0 and 10.5 Hz, 1H), 6.20 (t, J = 7.5 Hz, 1H), 6.39 (dd, J = 16.5 and 2.0 Hz, 1H), 6.97 (bs, 2H), 7.29-7.38 (m, 3H), 7.45-7.49 (m, 2H), 8.03-8.07 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.96, 22.48, 60.12, 128.26, 128.69, 128.85, 129.25, 129.40, 129.95, 130.05, 134.75, 137.89, 139.90, 165.93, 197.10; HRMS (ESI): calculated for $C_{19}H_{18}ClNO_2Na$: 350.0924 $(M+Na)^+$, found: 350.0929 $(M+Na)^+$.

*4.2.6. N-(1-Oxo-1-phenylpent-4-en-2-yl)-N-phenylacrylamide (**2f**).* Yield: 50 %; R_f (20% EtOAc in hexanes): 0.38; Yellow viscous liquid; IR (neat): ν 1687, 1654, 1610, 1594 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 2.39-2.48 (m, 1H), 2.60-2.68 (m, 1H), 5.06-5.11 (m, 1H), 5.12-5.17 (m, 1H), 5.50 (dd, J = 10.0 and 2.0 Hz, 1H), 5.76-5.86 (m, 2H), 6.39 (dd, J = 17.0 and 2.0 Hz, 1H), 6.48 (dd, J = 8.5 and 6.5 Hz, 1H), 6.99 (bs, 2H), 7.28-7.37 (m, 3H), 7.47-7.52 (m, 2H), 7.57-7.62 (m, 1H), 8.06-8.10 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 33.39, 58.31, 118.15, 128.33, 128.57, 128.64, 128.84, 128.94, 129.33, 130.12, 133.54, 134.04, 136.04, 137.90, 165.84, 197.47; HRMS (ESI): calculated for $C_{20}H_{19}NO_2Na$: 328.1313 $(M+Na)^+$, found: 328.1312 $(M+Na)^+$.

*4.2.7. N-(3,5-Dimethylphenyl)-N-(1-oxo-1-phenylpent-4-en-2-yl)-acrylamide (**2g**).* Yield: 54 %; R_f (20% EtOAc in hexanes): 0.46; Yellow viscous liquid; IR (neat): ν 1687, 1649, 1616, 1594 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 2.22 (bs, 6 H), 2.40-2.49 (m, 1H), 2.61-2.69 (m, 1H), 5.06-5.11 (m, 1H), 5.12-5.18 (m, 1H), 5.49 (dd, J = 10.0 and 2.0 Hz, 1H), 5.77-5.89 (m, 2H),* 6.34-6.65 (m, 4H), # 7.46-7.52 (m, 2H), 7.56-7.61 (m, 2H), 8.03-8.08 (m, 2 H). *It contains a dd (J = 16.5 and 10.0 Hz). # It contains a dd (J = 16.5 and 2.0 Hz) and it also contains another dd (J = 8.0 and 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.16, 33.49, 58.36, 118.03, 127.66, 128.26, 128.45, 128.59, 128.88, 130.44, 133.41, 134.28, 136.31, 137.59, 138.99, 165.77, 197.60; HRMS (ESI): calculated for $C_{22}H_{23}NO_2Na$: 356.1626 $(M+Na)^+$, found: 356.1624 $(M+Na)^+$.

*4.2.8. N-(4-Methyl-1-oxo-1-phenylpentan-2-yl)-N-phenylacrylamide (**2h**).* Yield: 55 %; R_f (20% EtOAc in hexanes): 0.46; Yellow viscous liquid; IR (neat): ν 1693, 1660, 1610, 1594 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 0.89 (d, J= 6.5 Hz, 3 H), 1.01 (d, J= 6.5 Hz, 3 H), 1.49-1.56 (m, 1H), 1.57-1.66 (m, 1H),* 1.67-1.73 (m, 1H), 5.50 (dd, J=10.0 and 2.0 Hz, 1H), 5.83 (dd, J = 17.0 and 10.0 Hz, 1H), 6.39 (dd, J = 17.0 and 2.0 Hz, 1H), 6.46 (dd, J = 8.0 and 6.0 Hz, 1H), 6.98 (bs, 2H), 7.28-7.38 (m, 3 H), 7.48-7.53 (m, 2H), 7.57-7.62 (m, 1H), 8.09-8.13 (m, 2 H). * It contains moisture peak; ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.58, 22.78, 24.83, 37.82, 56.92, 128.23, 128.38, 128.51, 128.58, 128.80, 129.17, 129.99, 133.31, 136.15, 137.93, 165.66, 198.10; HRMS (ESI): calculated for $C_{21}H_{23}NO_2Na$: 344.1626 $(M+Na)^+$, found: 344.1632 $(M+Na)^+$.

*4.2.9. N-(4-Methyl-1-oxo-1-(4-methylphenyl)pentan-2-yl)-N-phenylacrylamide (**2i**).* Yield: 57 %; R_f (20% EtOAc in hexanes):

0.48; Yellow solid; mp: 109-112 ^{0}C; IR (KBr): *v* 1676, 1654, 1611, 1605 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.90 (d, *J*=6.5 Hz, 3 H), 1.01 (d, *J*= 6.5 Hz, 3 H), 1.48-1.55 (m, 1H), 1.56-1.65 (m, 1H),* 1.66-1.73 (m, 1H), 2.43 (s, 3H), 5.49 (dd, *J* = 10.0 and 2.0 Hz, 1H), 5.82 (dd, *J* = 16.5 and 10.0 Hz, 1H), 6.39 (dd, *J* = 16.5 and 2.0 Hz, 1H), 6.45 (dd, *J* = 8.0 and 6.0 Hz, 1H), 6.97 (bs, 2H), 7.27-7.36 (m, 5H), 8.00 (d, *J* = 8.0 Hz, 2H). * It contains moisture peak; ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.73, 22.70, 22.87, 24.91, 37.93, 56.79, 128.22, 128.53, 128.63, 128.74, 129.22, 129.59, 130.10, 133.73, 138.04, 144.24, 165.71, 197.70; HRMS (ESI): calculated for $C_{22}H_{25}NO_2Na$: 358.1783 $(M+Na)^+$, found: 358.1784 $(M+Na)^+$.

*4.2.10. N-(3-Methyl-1-oxo-1-phenylbutan-2-yl)-N-phenylacrylamide (**2j**).* Yield: 48 %; R_f (20% EtOAc in hexanes): 0.46; Yellow solid; mp: 140-142 ^{0}C; IR (KBr): *v* 1692, 1644, 1611, 1590 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.94 (d, *J* = 6.5 Hz, 3 H), 1.19 (d, *J* = 6.5 Hz, 3 H), 2.30-2.45 (m, 1H), 5.51 (dd, *J* = 10.0 and 2.0 Hz, 1H), 5.83 (dd, *J* = 16.5 and 10.0 Hz, 1H), 6.23 (d, *J* = 10.5 Hz, 1 H), 6.41 (dd, *J* = 16.5 and 2.0 Hz, 1H), 6.60-7.38 (m, 5H),* 7.45-7.54 (m, 2H), 7.56-7.65 (m, 1H), 8.06-8.12 (m, 2H). * It contains $CHCl_3$ peak; ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.25, 19.82, 27.32, 63.06, 128.26, 128.45, 128.48, 128.56, 128.79, 129.12, 133.42, 136.47, 137.97, 165.80, 196.47; HRMS (ESI): calculated for $C_{20}H_{21}NO_2H$: 308.1651 $(M+H)^+$, found: 308.1650 $(M+H)^+$ and calculated for $C_{20}H_{21}NO_2Na$: 330.1470 $(M+Na)^+$, found: 330.1473 $(M+Na)^+$

4.3. Representative procedure

*4.3.1. (4S,5S)/(4R,5R)[15]-4-Hydroxy-5-methyl-3-methylene-1,4-diphenylpyrrolidin-2-one (**syn-1a**).* DABCO (0.056 g, 0.5 mmol) was added to a solution of *N*-(1-oxo-1-phenylpropan-2-yl)-*N*-phenylacrylamide (0.139 g, 0.5 mmol) (**2a**) in dioxane : H_2O (1:1) (0.5 mL :0.5 mL) solvent system. Resulting reaction mixture was heated at 65 °C, for 6 h (reaction monitored by TLC) with stirring. The reaction mixture was diluted with water (2 mL) and extracted with DCM (2 x 15 mL). Combined organic layer was washed with water (10 mL) and dried over anhydrous Na_2SO_4. Solvent was removed under reduced pressure. The crude product thus obtained (in 93:7 diastereomeric ratio) was subjected to column chromatography [silica gel, EtOAc:Hexanes (30:70);] to provide the required Baylis-Hillman adduct **1a** as 93:7 diastereomeric mixture (***syn*-1a: *anti*-1a**) in 86 % (0.120 g) isolated yield.

The major diastereomer (***syn*-1a**) was obtained by crystallization [ethyl acetate : hexanes (1:2)] of diastereomeric mixture (***syn*-1a**+***anti*-1a**) (obtained through silicagel column chromatography) in 60 % (0.083 g) yield as a colorless solid. R_f (30% EtOAc in hexanes): 0.36.; mp: 184-186 ^{0}C; IR (KBr): *v* 3227, 1687, 1650, 1594 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.24 (d, *J* = 6.5 Hz, 3H), 2.32 (s, 1H), 4.34 (q, *J* = 6.5 Hz, 1H), 5.55 (s, 1H), 6.38 (s, 1H), 7.22-7.27 (m, 1H), 7.32-7.37 (m, 1H), 7.38-7.43 (m, 6H), 7.52-7.55 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.56, 65.78, 76.71, 120.90, 124.23, 126.14, 126.29, 127.86, 128.42, 129.00, 137.04, 143.12, 148.17, 165.68; HRMS (ESI): calculated for $C_{18}H_{17}NO_2H$: 280.1338 $(M+H)^+$, found: 280.1332 $(M+H)^+$ and calculated for $C_{18}H_{17}NO_2Na$: 302.1157 $(M+Na)^+$, found: 302.1152 $(M+Na)^+$.

*4.3.1.1. Crystal data for **syn-1a**.* empirical formula: $C_{18}H_{17}NO_2$; formula weight: 279.32; crystal color: colorless; block; crystal dimensions: 0.36 X 0.24 X 0.12mm^3; crystal system: tetragonal; unit cell parameters: *a* = 20.2021(5) Å, *b* = 20.2021(5) Å, *c* = 14.6232(6) Å, α = 90.00, β = 90.00, γ = 90.00; *V* = 5968.1(3) Å^3; space group: *I 41/a*; *Z* = 16; *D* calcd = 1.243 g / cm^3; *F000* = 2368; λ(Cu-Kα) = 1.54184 Å; *R (I* ≥ 2σ*1)* = 0.0520; wR^2 = 0.1417. Detailed X-ray crystallographic data is available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (for compound ***syn-1a*:** CCDC # 1491071).

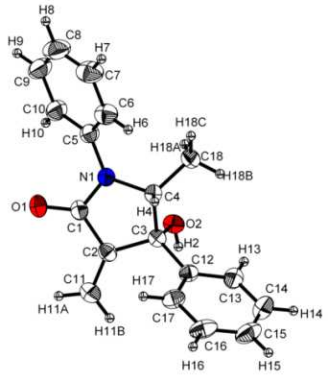


Fig. 1. ORTEP diagram of compound ***syn-1a***.

*4.3.2. (4S,5S)/(4R,5R)-4-(4-Chlorophenyl)-4-hydroxy-5-methyl-3-methylene-1-phenylpyrrolidin-2-one (**syn-1b**).* Reaction time: 5 h; Yield of diastereomeric mixture (***syn*-1b**+***anti*-1b**) **(**after column purification): 79 %; diastereomeric ratio: 93:7; Yield of ***syn*-1b (**after crystallization): 58 %; colorless solid; mp: 188-190 ^{0}C; R_f (30% EtOAc in hexanes): 0.36, IR (KBr): *v* 3326, 1676, 1649, 1589 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.21 (d, *J* = 6.5 Hz, 3H), 2.45 (s, 1H), 4.28 (q, *J* = 6.5 Hz, 1H), 5.53 (s, 1H), 6.38 (s, 1H), 7.23-7.28 (m, 1H)*, 7.35-7.43 (m, 6H), 7.48 (d, 2H, *J*=8.0 Hz), * It contains $CHCl_3$ peak; ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.38, 65.85, 76.36, 121.18, 124.38, 126.53, 127.74, 128.54, 129.05, 133.79, 136.79, 141.57, 147.84, 165.64; HRMS (ESI): calculated for $C_{18}H_{16}ClNO_2Na$: 336.0767 $(M+Na)^+$, found: 336.0770 $(M+Na)^+$.

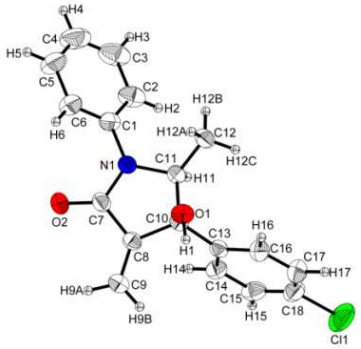


Fig. 2. ORTEP diagram of compound ***syn*-1b**.

*4.3.2.1. Crystal data for **syn-1b**.* empirical formula: $C_{18}H_{16}ClNO_2$; formula weight: 313.77; crystal color: colorless; block; crystal dimensions: 0.36 X 0.24 X 0.12 mm^3; crystal system: tetragonal; unit cell parameters: *a* = 19.9759(18) Å, *b* = 19.9759(18) Å, *c* = 16.065(3) Å, α = 90.00, β = 90.00, γ = 90.00; *V* = 6410.6(14) Å^3; space group: *I 41/a*; *Z* = 16; *D* calcd = 1.300 g / cm^3; *F000* = 2624; λ(Mo-Kα) = 0.71073 Å; *R (I* ≥ 2σ*1)* = 0.0569; wR^2 = 0.1411. Detailed X-ray crystallographic data is available from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK (for compound ***syn*-1b:** CCDC # 1491072).

*4.3.3. (4S,5S)/(4R,5R)-4-Hydroxy-5-methyl-3-methylene-4-(naphth-2-yl)-1-phenylpyrrolidin-2-one (**syn-1c**).* Reaction time: 14 h; Yield of ***syn*-1c**+***anti*-1c (**after column purification): 88 %;; diastereomeric ratio: 94:6; Yield of ***syn*-1c (**after crystallization): 64 %; white solid; mp: 195-197 ^{0}C; R_f (30% EtOAc in hexanes): 0.38; IR (KBr): *v* 3265, 1682, 1650, 1594 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.26 (d, *J* = 6.5 Hz, 3H), 2.64 (s, 1H), 4.45 (q, *J*

= 6.5 Hz, 1H), 5.55 (s, 1H), 6.42 (s, 1H), 7.22-7.27 (m, 1H)*, 7.37-7.43 (m, 4H), 7.49-7.55 (m, 3H), 7.84-7.89 (m, 3H), 8.09 (d, *J* = 1.5 Hz, 1H), * It contains $CHCl_3$ peak; ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.56, 65.56, 76.89, 121.20, 124.15, 124.33, 125.35, 126.37, 126.46, 126.54, 127.63, 128.33, 128.39, 129.02, 132.84, 132.96, 137.00, 140.19, 148.15, 165.75; HRMS (ESI): calculated for $C_{22}H_{19}NO_2Na$: 352.1313 $(M+Na)^+$, found: 352.1310 $(M+Na)^+$.

*4.3.4. (4S,5S)/(4R,5R)-5-Ethyl-4-hydroxy-3-methylene-1,4-diphenylpyrrolidin-2-one (**syn-1d**).* Reaction time: 13 h; Yield of ***syn*-1d**+***anti*-1d** (after column purification): 84 %; diastereomeric ratio: 95:5; Yield of ***syn*-1d** (after crystallization): 62 %; white solid; mp: 124-126 ^{0}C; R_f (30% EtOAc in hexanes): 0.40; IR (KBr): ν 3210, 1682, 1660, 1594 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.81 (t, *J* = 7.5 Hz, 3H), 1.73-1.91 (m, 2H), 2.54 (s, 1H), 4.29 (dd, *J* = 8.5 and 3.5 Hz, 1H), 5.50 (s, 1H), 6.34 (s, 1H), 7.21-7.25 (m, 1H), 7.29-7.34 (m, 1H), 7.35-7.45 (m, 6H), 7.49-7.54 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.49, 21.87, 70.88, 76.74*, 120.34, 124.07, 125.70, 126.32, 127.77, 128.50, 129.08, 137.51, 145.02, 149.07, 165.50, * It almost merges with one of $CDCl_3$ peak; HRMS (ESI): calculated for $C_{19}H_{19}NO_2H$: 294.1494 $(M+H)^+$, found: 294.1495 $(M+H)^+$.

*4.3.5. (4S,5S)/(4R,5R)-4-(4-Chlorophenyl)-5-ethyl-4-hydroxy-3-methylene-1-phenylpyrrolidin-2-one (**syn-1e**).* Reaction time: 11 h; Yield of ***syn*-1e**+***anti*-1e** (after column purification): 80 %; diastereomeric ratio: 94:6; Yield of ***syn*-1e** (after crystallization): 63 %; white solid; mp: 148-152 ^{0}C; R_f (30% EtOAc in hexanes): 0.37; IR (KBr): ν 3205, 1682, 1654, 1594 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.78 (t, *J* = 7.5 Hz, 3H), 1.70-1.89 (m, 2H), 2.66 (s, 1H), 4.21 (dd, *J* = 8.5 and 3.5 Hz, 1H), 5.47 (s, 1H), 6.33 (s, 1H), 7.23-7.27 (m, 1H)*, 7.31-7.35 (m, 2H), 7.40 (d, *J* = 4.0 Hz, 4H), 7.44-7.48 (m, 2H), * It contains $CHCl_3$ peak; ^{13}C NMR (100 MHz, $CDCl_3$): δ 10.51, 21.77, 70.96, 76.35, 120.68, 124.27, 126.56, 127.31, 128.60, 129.14, 133.65, 137.30, 143.50, 148.87, 165.37; HRMS (ESI): calculated for $C_{19}H_{18}ClNO_2Na$: 350.0924 $(M+Na)^+$, found: 350.0928 $(M+Na)^+$.

*4.3.6. (4S,5S)/(4R,5R)-5-Allyl-4-hydroxy-3-methylene-1,4-diphenylpyrrolidin-2-one (**syn-1f**).* Reaction time: 13h; diastereomeric ratio: 96:4; Yield of ***syn*-1f**: 78 %; white solid; mp: 130-133 ^{0}C; R_f (30% EtOAc in hexanes): 0.45; IR (KBr): ν 3227, 1687, 1654, 1594 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.40-2.80 (m, 3H), 4.45 (dd, *J* = 7.0 and 3.5 Hz, 1H), 5.02 (d, *J*= 10.0Hz, 1H,), 5.04-5.10 (m, 1H), 5.58 (s, 1H), 5.71-5.81 (m, 1H), 6.36 (s, 1H), 7.21-7.25 (m, 1H), 7.30-7.34 (m, 1H), 7.35-7.42 (m, 4H), 7.46-7.51 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 33.22, 69.31, 76.84, 118.32, 120.55, 123.86, 125.41, 126.29, 127.77, 128.50, 129.06, 134.04, 137.24, 145.08, 148.34, 165.48; HRMS (ESI): calculated for $C_{20}H_{19}NO_2H$: 306.1494 $(M+H)^+$, found: 306.1496 $(M+H)^+$.

*4.3.7. (4R,5S)/(4S,5R)-5-Allyl-4-hydroxy-3-methylene-1,4-diphenylpyrrolidin-2-one (**anti-1f**).* Yield of ***anti*-1f**: 3 %; white solid; mp: 147-150 ^{0}C; R_f (30% EtOAc in hexanes): 0.36; IR (KBr): ν 3353, 1676, 1649, 1594 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.89-1.96 (m, 1H), 1.98-2.06 (m, 1H), 2.90 (s, 1H), 4.34 (dd, *J* = 8.5 and 4.0 Hz, 1H), 4.49-4.56 (m, 1H), 4.61-4.66 (m, 1H), 4.91-5.01 (m, 1H), 5.63 (s, 1H), 6.45 (s, 1H), 7.20-7.25 (m, 1H), 7.33-7.42 (m, 5H), 7.53-7.61 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 35.45, 70.61, 78.17, 117.67, 121.67, 123.74, 126.16, 127.81, 128.14, 128.33, 129.12, 132.51, 137.66, 139.43, 147.28, 165.43; HRMS (ESI): calculated for $C_{20}H_{19}NO_2Na$: 328.1313 $(M+Na)^+$, found: 328.1317 $(M+Na)^+$.

*4.3.8. (4S,5S)/(4R,5R)-5-Allyl-1-(3,5-dimethylphenyl)-4-hydroxy-3-methylene-4-phenylpyrrolidin-2-one (**syn-1g**).* Reaction time: 60 h; Yield of ***syn*-1g**+***anti*-1g** (after column purification): 77 %; diastereomeric ratio: 96:4; Yield of ***syn*-1g** (after crystallization): 56 %; white solid; mp: 170-172 ^{0}C; R_f (30% EtOAc in hexanes): 0.46; IR (KBr): ν 3260, 1676, 1649, 1600 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.31 (s, 6H), 2.53-2.63 (m, 2H), 2.66 (s, 1H), 4.39 (dd, *J* = 7.0 and 3.5 Hz, 1H), 5.00-5.05 (m, 1H), 5.06-5.12 (m, 1H), 5.55 (s, 1H), 5.71-5.81 (m, 1H), 6.34 (s, 1H), 6.85-6.89 (m, 1H), 7.07 (s, 2H), 7.29-7.34 (m, 1H), 7.35-7.40 (m, 2H), 7.47-7.50 (m, 2H) ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.43, 33.29, 69.35, 77.00, 118.40, 120.27, 121.72, 125.35, 127.80, 128.24, 128.57, 134.27, 137.07, 138.82, 145.20, 148.67, 165.34; HRMS (ESI): calculated for $C_{22}H_{23}NO_2H$: 334.1807 $(M+H)^+$, found: 334.1810 $(M+H)^+$.

*4.3.9. (4S,5S)/(4R,5R)-4-Hydroxy-5-iso-butyl-3-methylene-1,4-diphenylpyrrolidin-2-one (**syn-1h**).* Reaction time: 60 h; Yield of ***syn*-1h**+***anti*-1h** (after column purification): 82 %; diastereomeric ratio: 96:4; Yield of ***syn*-1h** (after crystallization): 59 %; white solid; mp: 160-162 ^{0}C; R_f (30% EtOAc in hexanes): 0.32; IR (KBr): ν 3232, 1682, 1650, 1594 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.61 (d, *J* = 6.5 Hz, 3H), 0.73 (d, *J* = 6.5 Hz, 3H), 1.32-1.40 (m, 1H), 1.55-1.66 (m, 1H)*, 1.78-1.85 (m, 1H), 2.39 (s, 1H), 4.39 (dd, *J* = 9.5 and 4.0 Hz, 1H), 5.47 (s, 1H), 6.34 (s, 1H), 7.23-7.27 (m, 1H)@, 7.30-7.35 (m, 1H), 7.36-7.43 (m, 6H), 7.49-7.54 (m, 2H), * It contains moisture peak, @ It contains $CHCl_3$ peak; ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.44, 23.56, 24.67, 37.83, 67.88, 76.84&, 120.79, 124.73, 125.93, 126.50, 127.68, 128.39, 129.02, 137.29, 144.38, 149.18, 165.57, & It almost merges with one of $CDCl_3$ peak; HRMS (ESI): calculated for $C_{21}H_{23}NO_2H$: 322.1807 $(M+H)^+$, found: 322.1805 $(M+H)^+$.

*4.3.10. (4S,5S)/(4R,5R)-4-Hydroxy-5-iso-butyl-3-methylene-1-phenyl-4-(4-methylphenyl)pyrrolidin-2-one (**syn-1i**).* Reaction time: 96 h; Yield of ***syn*-1i**+***anti*-1i** (after column purification): 81 %; diastereomeric ratio: 96:4; Yield of ***syn*-1i** (after crystallization): 56 %; white solid; mp: 190-192 ^{0}C; R_f (30% EtOAc in hexanes): 0.36; IR (KBr): ν 3265, 1682, 1650, 1589 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.63 (d, *J* = 6.5 Hz, 3H), 0.73 (d, *J* = 6.5 Hz, 3H), 1.31-1.38 (m, 1H), 1.57-1.67 (m, 1H)*, 1.77-1.84 (m, 1H), 2.36 (s, 3H), 2.45 (s, 1H), 4.37 (dd, *J* = 9.5 and 4.0 Hz, 1H), 5.47 (s, 1H), 6.32 (s, 1H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.22-7.27 (m, 1H)@, 7.36-7.41 (m, 6H); *It contains moisture peak, @ It contains $CHCl_3$ peak; ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.10, 21.55, 23.54, 24.70, 37.95, 67.80, 76.84, 120.54, 124.60, 125.79, 126.39, 128.98, 129.08, 137.37, 141.49, 149.19, 165.56; HRMS (ESI): calculated for $C_{22}H_{25}NO_2Na$: 358.1783 $(M+Na)^+$, found: 358.1783 $(M+Na)^+$.

*4.3.11. (4S,5S)/(4R,5R)-4-Hydroxy-5-isopropyl-3-methylene-1,4-diphenylpyrrolidin-2-one (**syn-1j**).* Reaction time: 84 h; Yield of ***syn*-1j**+***anti*-1j** (after column purification): 83 %; diastereomeric ratio: >99:<1; colorless solid; mp: 160-162 ^{0}C; R_f (30% EtOAc in hexanes): 0.42; IR (KBr): ν 3292, 1676, 1649, 1595 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.83 (d, *J* = 7.5 Hz, 3H), 1.04 (d, *J* = 7.0 Hz, 3H), 2.30-2.55 (m, 2H), 4.32 (d, *J* = 2.5 Hz, 1H), 5.60 (s, 1H), 6.37 (s, 1H), 7.17-7.22 (m, 1H), 7.30-7.40 (m, 7H), 7.46-7.51 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.73, 19.98, 30.12, 74.60, 77.78, 118.65, 124.10, 124.99, 126.19, 127.88, 128.70, 128.87, 138.34, 146.77, 148.56, 165.58; HRMS (ESI): calculated for $C_{20}H_{21}NO_2H$: 308.1651 $(M+H)^+$, found: 308.1647 $(M+H)^+$.

*4.3.12. N-Benzyl-N-(1-oxo-1-phenylpropan-2-yl)acrylamide (**2k**)*: To a stirring mixture of 2-bromo-1-phenylpropan-1-one (2.13 g, 10.0 mmol) and benzylamine (2.14 g, 20.0 mmol) in acetonitrile (10 mL), $NaHCO_3$ (1.26 g, 15 mmol) was added. After stirring at rt for 2 h (reaction monitored by TLC), the solvent was evaporated and the reaction mixture was diluted with DCM (15

mL). The resulting organic layer was washed with water (2x15 mL), and dried over anhydrous sodium sulphate and concentrated under reduced pressure. The crude thus obtained was used as such for the next step without any purification.

The crude, thus obtained, was dissolved in DCM (15 mL) and the resulting solution was cooled at 0 ºC. To this stirring solution, Et_3N (1.11g, 11.0 mmol) was added followed by the dropwise addition of acryloyl chloride (0.99 g, 11.0 mmol) at 0 ºC. After stirring for 30 min at same temperature, the reaction mixture was diluted with water (30 mL) and extracted with DCM (2 x 30 mL). Combined organic layer was dried over anhydrous Na_2SO_4 and concentrated. The residue thus obtained was purified by column chromatography [silica gel, 20 % ethyl acetate in hexanes] to afford the desired product **2k** in 49% (1.44 g) yield (over two steps), as a yellow viscous liquid. R_f (30% EtOAc in hexanes): 0.48; IR (neat): ν 1686, 1644, 1613 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.36 (d, *J* = 7.2 Hz, 3H), 4.60 & 4.72 (AB q, *J* = 18.0 Hz, 2H), 5.65 (dd, *J* = 10.0 and 2.4 Hz, 1H), 6.29 (q, *J* = 7.2 Hz, 1H), 6.35 (dd, *J* = 16.4 and 10.0 Hz, 1H), 6.45 (dd, *J* = 16.4 and 2.4 Hz, 1H), 7.09 (d, *J* = 6.8 Hz, 2H), 7.18-7.29 (m, 3H)*, 7.43 (t, *J* = 7.6 Hz, 2H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.91-8.02 (m, 2H), * It contains $CHCl_3$ peak; ^{13}C NMR (125 MHz, $CDCl_3$): δ 14.60, 47.91, 53.72, 126.08, 127.33, 127.76, 128.51, 128.69, 128.74, 129.68, 133.37, 135.51, 137.77, 167.27, 199.49; HRMS (ESI): calculated for $C_{19}H_{19}NO_2H$: 294.1494 $(M+H)^+$, found: 294.1487$(M+H)^+$.

4.3.13. N-Butyl-N-(1-oxo-1-phenylpropan-2-yl)acrylamide (***2l***): Yield: 61 %; R_f (30% EtOAc in hexanes): 0.46;Yellow viscous liquid; IR (neat): ν 1686, 1644, 1608 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 0.86 (t, *J* = 7.5 Hz, 3H), 1.18-1.48 (m, 7H), 3.10-3.30 (m, 2H), 5.73 (dd, *J* = 9.0 and 3.5 Hz, 1H), 6.19 (q, *J* = 7.0 Hz, 1H), 6.40-6.53 (m, 2H)*, 7.40-7.48 (m, 2H), 7.52-7.58 (m, 1H), 7.96-8.03 (m, 2H) * it contains one dd at δ 6.43 (*J* = 16.5 and 3.5 Hz) and one dd at δ 6.49 (*J* = 16.5 and 9.0 Hz), one of the peaks of dd at δ 6.43 with high chemical shift value merges with one of the peaks of dd at δ 6.49 with lower chemical shift value; ^{13}C NMR (125 MHz, $CDCl_3$): δ 13.53, 14.40, 20.15, 33.44, 44.29, 53.26, 127.40, 128.38, 128.68, 128.97, 133.32, 135.40, 165.92, 199.22; HRMS (ESI): calculated for $C_{16}H_{21}NO_2H$: 260.1651 $(M+H)^+$, found: 260.1652$(M+H)^+$.

*4.3.14. 1-Benzyl-4-hydroxy-5-methyl-3-methylene-4-phenyl-pyrrolidin-2-one (**1k**):* Reaction time: 5 h; Yield of ***syn***+***anti*** (after column purification): 83 %; ***syn***:***anti*** diastereomeric ratio: 83:17; white solid; Crystallization [from ethyl acetate : hexanes (1:1)] of this mixture provided the BH adduct in 59 % yield : in diastereomeric ratio: 97:3(***syn***:***anti);*** white solid; mp: 160-161 ^0C; IR (KBr): *ν* 3297, 1680, 1644 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): *δ* 0.66 & 1.19 (2d, *J* = 6.5 Hz, 3H), 3.00 (bs, 1H), 3.58 & 3.63 (2q, *J* = 6.5 Hz, 1H), 4.07 (d, *J* = 15.0 Hz, 1H), 5.17 (d, *J* = 15.0 Hz, 1H), 5.43 & 5.56 (2s, 1H), 6.28 & 6.39 (2s, 1H), 7.18-7.40 (m, 10H), * It contains $CHCl_3$ peak; ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 11.58, 44.32, 63.54, 76.62, 120.38, 126.21, 127.51, 127.64, 128.00, 128.11, 128.73, 136.05, 142.90, 148.13, 166.85 ppm. HRMS (ESI): calculated for $C_{19}H_{19}NO_2H$: 294.1494 $(M+H)^+$, found: 294.1496 $(M+H)^+$. The underlined chemical shift values with low intensity arise due to the minor isomer. The ratio is determined by the integration of isomeric olefinic proton signals at δ 6.39 & 6.28.

*4.3.15. 1-Butyl-4-hydroxy-5-methyl-3-methylene-4-phenylpyrro-lidin-2-one (**1l**):*. Reaction time: 7 h; Yield of ***syn***+***anti*** (after purification by column chromatography): 86 %; ***syn***:***anti*** diastereomeric ratio: 83:17; white solid; mp (mixture): 101-102 ^oC, R_f (30% EtOAc in hexanes): 0.22; IR (KBr): *ν* 3282, 1682,1644 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 0.71 & 1.24 (2d, *J* = 6.5 Hz, 3H), 0.91 & 0.95 (2t, *J* = 7.5 Hz, 3H), 1.26-1.55 (m, 4H), 2.54 (bs, 1H), 2.95-3.09 (m, 1H), 3.70-3.87 (m, 2H), 5.37 & 5.49 (2s, 1H), 6.21 & 6.32 (2s, 1H), 7.29-7.34 (m, 1H), 7.34-7.39 (m, 2H), 7.41-7.48 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 11.76, 13.82, 13.86, 16.75, 20.17, 20.20, 29.43, 29.46, 40.15, 40.40, 64.04, 64.45, 76.65, 78.83, 119.69, 119.88, 126.21, 127.22, 127.59, 127.83, 127.99, 128.21, 140.77, 143.20, 147.73, 148.37, 166.34, 166.48; HRMS (ESI): calculated for $C_{16}H_{21}NO_2H$: 260.1651 $(M+H)^+$, found: 260.1649$(M+H)^+$. The underlined chemical shift values with low intensity arise due to the minor isomer. The ratio is determined by the integration of isomeric olefinic proton signals at δ 6.32 & 6.21.

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