Tetrahedron 64 (2008) 6461–6474

Contents lists available at ScienceDirect

Tetrahedron

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

Synthesis of pyrrolo[3,4-*b*]pyrroles and perhydrothiazolo-[3′,4′-2,3]pyrrolo[4,5-*c*]pyrroles

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ARTICLE INFO

Article history:
Received 19 January 2008
Received in revised form 16 April 2008
Accepted 17 April 2008
Available online 20 April 2008

Keywords:
Pyrrolidine
Pyrrolo[3,4-*b*]pyrrole
Cycloaddition
Heterotricycle
Perhydrothiazolo[3′,4′-2,3]pyrrolo-[4,5-*c*]pyrrole
Stereoselective
Azomethine ylide
Alkenyl aldehyde

ABSTRACT

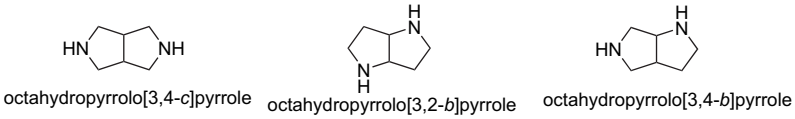
The 1,3-dipolar cycloaddition reactions of various *N*-tethered alkenyl aldehydes with some cyclic and acyclic amino acids have been studied. Some key sulfonamides having strategically positioned aldehyde and olefinic tether have been synthesized and effectively subjected to intramolecular azomethine ylide cycloaddition reaction resulting in a series of pyrrolo[3,4-*b*]pyrrole and its N-1–C-2 derivatives, and a series of novel heterotricyclic compounds, perhydrothiazolo[3′,4′-2,3]pyrrolo[4,5-*c*]pyrroles, in good yields. The intramolecular cycloaddition reaction was found to be highly stereoselective to form only cis-fused cycloadducts in all cases.

1. Introduction

The molecules built on pyrrolidine skeleton are among the important class of architectures that form the basic units for many naturally occurring materials.[1] The synthesis of pyrrolidine-based heterocycles is ever fascinating since they promise a wide spectrum of pharmacological activities like preventing and treating rheumatoid arthritis, asthma, allergies, rhinitis, and related diseases as they inhibit the production of prostaglandin E2 and intracellular phospholipase A2.[2] Due to the ease of substitution and modifications at several positions, many derivatives of pyrrolidines and pyrroles have been synthesized with varying properties.[3] It has been well established that the fused bis-pyrrolidines are the basic units of adenosine kinase inhibiting scaffolds for controlling neurodegeneration, seizures, ischemia, inflammation, and pain.[4] The pyrrolo[3,4-*b*]pyrrole derivatives found to serve as useful intermediates in the synthesis of uracil based antibacterials.[5] The importance of pyrrolo[3,4-*b*]pyrrole derivatives has been further vindicated since they have been proved to be h5-HT_{1D} receptor agonists.[6]

Several inhibitors of human cytomegalovirus (HCMV) protease have been designed, based on the pyrrolo[3,2-*b*]pyrrole ring system.[7] Pyrrolo[1,2-*a*]pyrrole compounds are used as anti-inflammatory and analgesic agents,[8] and certain pyrrolo[3,4-*c*]pyrroles act as potent and selective orphanin FQ/nociceptin (N/OFQ) receptor (NOP) agonists.[9]

The novelty of the octahydropyrrolopyrrole ring system has been well documented since C-7 position of quinolone and



octahydropyrrolo[3,4-*c*]pyrrole octahydropyrrolo[3,2-*b*]pyrrole octahydropyrrolo[3,4-*b*]pyrrole

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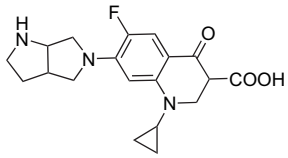
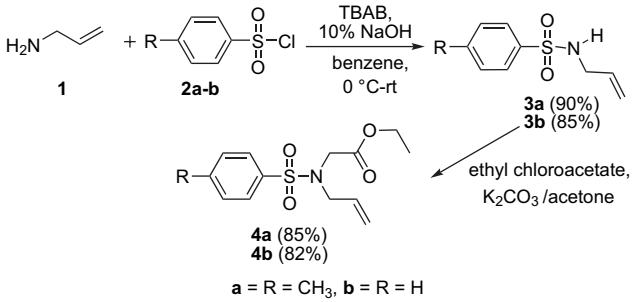
doi:10.1016/j.tet.2008.04.063

pyridone ring systems has been found to be the most effective to alter the bioactivities by altering the substituents. Many structure–activity relationship (SAR) studies lead to the conclusion that a cyclic system containing a secondary or tertiary amine moiety is one of the best substituent at C-7 of quinalone and pyridone antibactetials.[10]



Octahydropyrrolo[3,4-*b*]pyrrole attached at C-7 position of Quinolone - A potent antibacterial agent

The five-membered nitrogen containing heterocycles can be constructed in a facile manner by the application of 1,3-dipoalar cycloaddition methodology.[11] An 'azomethine ylide', a class of allenyl type dipole containing a nitrogen atom flanked by two methylene carbons can be prepared by several methods from easily available starting material and undergoes cycloaddition to dipolarophiles in a facile manner to yield five-membered heterocycle directly. Of the many routes available for the generation of azomethine ylide the 'decarboxylation route' offers a general method in which an aldehyde or a ketone is reacted with α-amino acids.[12] Though the in situ generated azomethine ylides can be cyclized either by inter- or intramolecularly to yield pyrrolidine scaffolds,[13] the latter mode of azomethine ylide cycloaddition has gained much interest recently since it resulted in elegant syntheses of stereochemically defined heterocycles.[14,15] The very advantage lies in the fact that even an unactivated internal olefin can be annulated to a proline moiety with high regio- and stereocontrol, which do not react intermolecularly.[16] This novel methodology has been extensively applied for the synthesis of complex optically pure heterocycles with removable and fixed chiral auxiliaries.[17,18] Since we have been involved in the synthesis of polycyclic heterocycles[19] and in continuation of our earlier communication on the synthesis of fused pyrrolidines,[20] we report herein a detailed synthetic studies on pyrrolo[3,4-*b*]pyrroles and their N-1–C-2 fused analogues, and perhydrothiazolo[3′,4′-2,3]pyrrolo[4,5-*c*]pyrroles.



Scheme 1.

2. Results and discussion

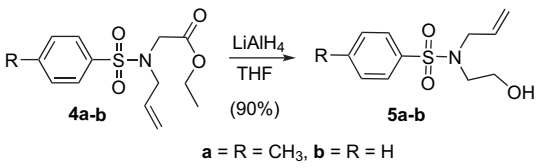
2.1. Synthesis of precursor alkenyl aldehydes

Our synthetic study started with envisaging substrates **6a**,**b**, which consist both an aldehyde component and an olefin tethered by a nitrogen atom. Firstly, for the synthesis of **6a**,**b** allyl amine **1** was chosen as a platform on which various synthetic transformations were performed out to reach the target. Firstly, N-tosylation of allyl amine was performed by reacting equimolar quantities of allyl amine **1** and *p*-toluenesulfonyl chloride **2a** or benzenesulfonyl chloride **2b** in benzene with 25% sodium hydroxide solution in the presence of the phase transfer catalyst, tetrabutylammonium bromide (TBAB). During the addition of *p*-toluenesulfonyl chloride the temperature of the reaction mixture was maintained at 0 °C and was increased to room temperature slowly. After stirring for 8 h, partitioning the reaction mixture and evaporation of organic layer yielded crude *N*-tosyl-*N*-allyl amine, which was purified through column chromatography to give **3a**,**b** in 90% yield (Scheme 1).

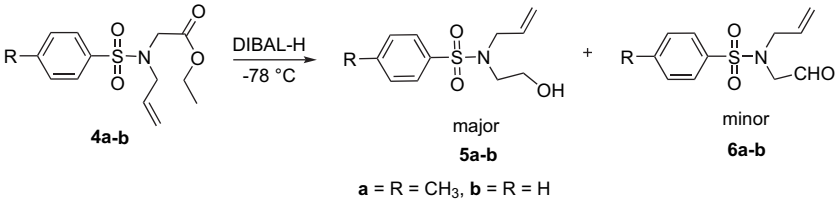
The *N*-tosylated allyl amine **3a** was then subjected to N-alkylation with ethyl bromoacetate to obtain the ester *N*-allyl-*N*-(ethoxycarbonylmethyl)-toluene sulfonamide **4a** in 85% yield. Treating **3a** and ethyl bromoacetate in dry acetone in presence of excess potassium carbonate effected the alkylation. Though the chemical yield of the alkylated product was superior to ethyl chloroacetate, the latter was preferred in bulk synthesis since it is cheap and less lachrymatory than ethyl bromoacetate (Scheme 1).

Having synthesized the ester **4a** in good yield, the next task was to convert the ester into an aldehyde. Although the direct conversion of the ester group to the aldehyde was attempted by reduction of the ester with DIBAL-H, we ended up in getting the alcohol **5a** as a major product along with the desired aldehyde **6a** in very low yield[21] (Scheme 2). Hence a two-step sequence involving reduction of an ester to an alcohol and its subsequent oxidation was adopted.

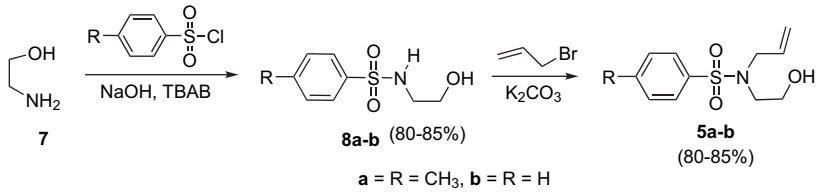
Thus, 1 equiv of the ester dissolved in dry tetrahydrofuran was added dropwise to a stirred suspension of 1.5 equiv of LAH in dry tetrahydrofuran under nitrogen atmosphere. After the addition was complete the temperature of the reaction mixture was raised to 65 °C. After 4 h of effective stirring at this temperature, the reaction was quenched by the dropwise addition of 10% NaOH solution under cold conditions. The mixture was filtered and the solvent was evaporated. Column chromatographic separation of the residue afforded the pure alcohol **5a** in 90% yield (Scheme 3).



Scheme 3.



Scheme 2.



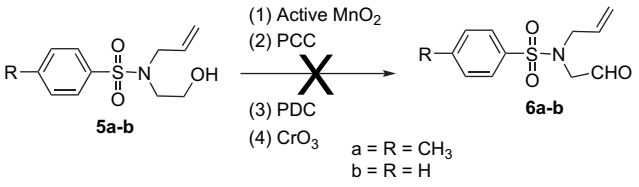
Scheme 4.

Alternatively, the synthesis of the alkenyl alcohols **5a**,**b** can also be accomplished from ethanolamine. Thus, *N*-tosylethanolamines **8a**,**b** were obtained by the reaction of *p*-toluenesulfonyl chloride on ethanolamine **7** under standard PTC conditions, which on treatment with equimolar amount of allylbromide and anhydrous potassium carbonate in dry acetone solvent afforded the alcohols **5a**,**b** (Scheme 4).

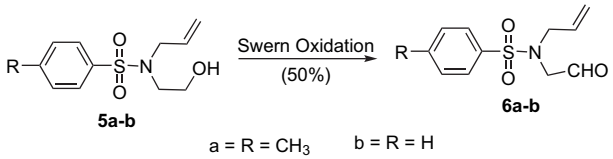
Attempts were made to oxidize the alcohols **5a**,**b** to the corresponding aldehydes **6a**,**b**. Oxidation with PCC in dichloromethane was not fruitful since this method gave a mixture of inseparable products. Carrying out the reaction in a neutral medium by the addition of sodium acetate was also fruitless in minimizing the number of side products. The oxidation with other routine oxidizing agents like PDC, active MnO_2, and CrO_3 under different reaction conditions did not give the expected results (Scheme 5a).

Though Swern oxidation[22] converted the alcohols **5a**,**b** to aldehydes **6a**,**b** in 50% yield (Scheme 5b), an unwanted stench byproduct (dimethyl sulfide) obtained along with the aldehyde led to go for a most effective oxidation protocol. Finally, the oxidation was pleasingly accomplished almost in quantitative yield by iodoxybenzoic acid (IBX) in DMSO solvent.[23] One equivalent of alcohol in DMSO was effectively oxidized to the alkenyl aldehyde **6a**,**b** by 1.5 equiv of iodoxybenzoic acid (IBX) in excellent yield as a pale yellowish viscous liquid, which turned to brown on storage (Scheme 5c).

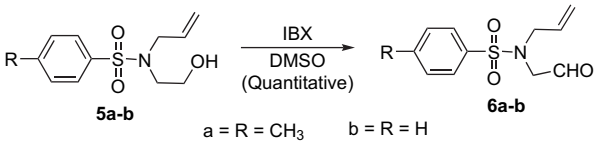
A similar reaction protocol was extended for the synthesis of alkenyl aldehyde **6b** by replacing benzenesulfonyl chloride with *p*-toluenesulfonyl chloride. It is noteworthy to mention that though the formation of alkenyl aldehyde **6a** has been observed as a side product by Suritami et al., [24] the present reaction protocol is a straightforward and affords the strategic alkenyl aldehydes **6a**,**b** in excellent yield.



Scheme 5a.



Scheme 5b.



Scheme 5c.

2.2. Synthesis of pyrrolo[3,4-*b*]pyrroles

2.2.1. Synthesis of 1-methyl-5-tosyl/benzenesulfonyl-octahydropyrrolo[3,4-b]pyrroles

With aldehydes **6a** and **6b** in hand the cycloaddition reactions were carried out with the formation of unstabilized azomethine ylides generated by decarboxylative condensation with various secondary amino acids. Condensation of **6a** and **6b** with sarcosine **9** in refluxing toluene under Dean–Stark reaction conditions, generated the azomethine ylide, which cyclized to yield the cis adducts, 1-methyl-5-tosyl/benzenesulfonyloctahydropyrrolo[3–4-*b*]pyrrole **10a**,**b** as brownish oils in 78 and 72% yields, respectively (Scheme 6).

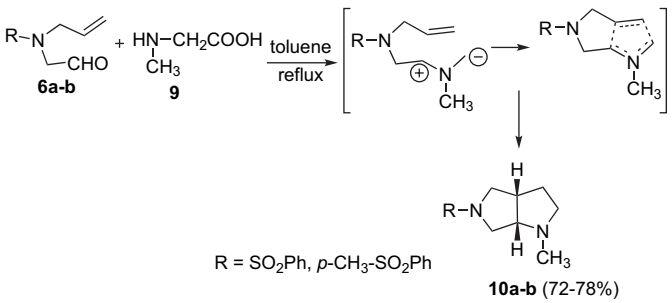
The cycloadduct formation was established by spectroscopic data. For instance, the IR spectrum of **10a** showed two absorption bands at 1346 and 1161 cm^{-1} confirming the presence of sulfonyl group. The ^1H NMR spectrum of **10a** exhibited two singlets at δ 2.26 and 2.38 corresponding to *N*-methyl and aryl-methyl groups, respectively. Apart from a cluster of multiplets for the *N*-methylene and *C*-methylene protons in the corresponding regions, a peak in the range of δ 3.25–3.28 with doublet of triplet splitting pattern was observed for the *N*–CH proton. The coupling constant of 2.4 and 6.8 Hz suggested a cis fusion at the ring junction.

The presence of *N*-methyl and aromatic methyl groups were confirmed by the two signals at δ 21.90 and 31.11, respectively, in the ^{13}C NMR spectrum of **10a**.

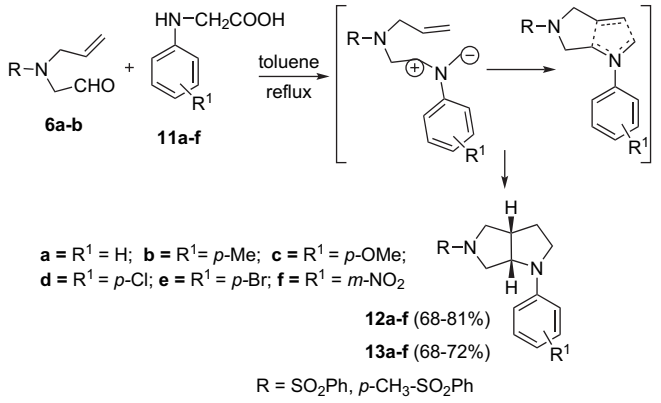
2.2.2. Synthesis of 1-aryl-5-tosyl/benzenesulfonyl-octahydropyrrolo[3,4-b]pyrroles

The same reaction was carried out with various *N*-aryl glycines **11a**–**f** to obtain cis-fused cycloadducts **12a**–**f** and **13a**–**f** in good yields (Scheme 7).

A spectral pattern similar to the cycloadduct **10a** was obtained for 1-*N*-arylpyrrolo[3,4-*b*]pyrroles. The structure of the cycloadduct was deduced on the basis of 2D NMR experiments. In a typical



Scheme 6.



Scheme 7.

^{1}H NMR spectrum of **12e**, a singlet at δ 2.35 confirmed the presence of aromatic methyl group. The characteristic *N*-methine proton at ring junction was observed in the range δ 3.92–3.94 (dt, J=2.4 and 6.8 Hz) in the proton NMR spectrum of the compound. The small coupling constant value, which was in analogy with similar systems,[25] reiterated the cis fusion at the ring junctions. The methyl carbon on the aryl sulfonyl group exhibited a signal at δ 21.54 and the *N*-methine carbon exhibited a signal at δ 62.57. Further the structures of the cycloadducts were corroborated by the single crystal X-ray diffraction analyses of the cycloadducts **12e**[26] (Fig. 1) and **12f**[27] (Fig. 2). In the molecular structure of **12f**, the fused pyrrolidine rings adopt envelope conformations. The molecular packing is stabilized by weak intermolecular C–H···O interactions and van der Waals forces. The pyrrolidine rings of **12f** adopt a half-chair conformation, while the other is in an envelope conformation.

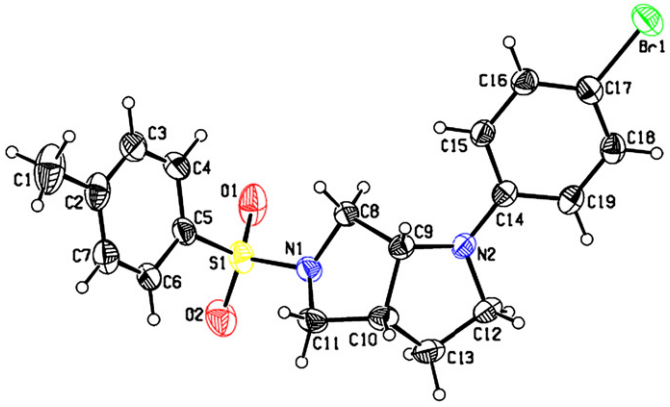


Figure 1. X-ray crystal structure of compound **12e**.

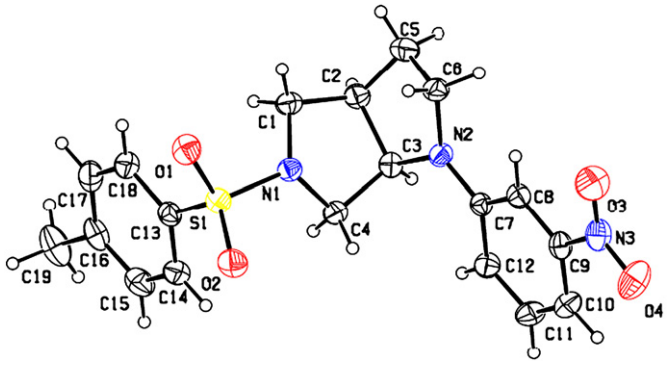
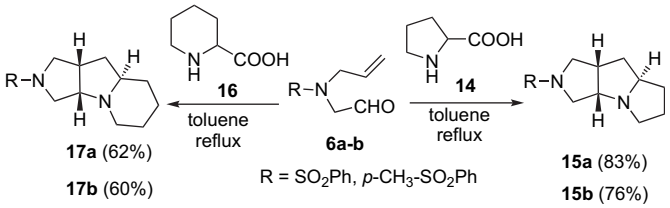


Figure 2. X-ray crystal structure of compound **12f**.

2.2.3. *Synthesis of 2-tosyl/benzenesulfonyldecahydropyrrolo[3,4-b]pyrrolizines and 2-tosyl/benzenesulfonyldecahydro-1H-pyrrolo[3,4-b]indolozines*

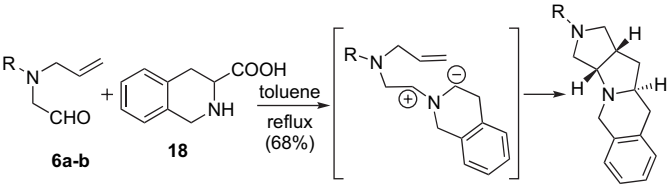
In order to extend the scope of the intramolecular azomethine ylide cycloaddition reaction for the synthesis of N-1–C-2 fused derivatives of pyrrolo[3,4-*b*]pyrroles, the alkenyl aldehydes **6a**,**b** were treated with proline **14** and pipecolinic acid **16** to afford the tricyclic compounds **15a**,**b** and **17a**,**b** in good yields (Scheme 8). The angular hydrogen atom next to the nitrogen atom is in trans position to the hydrogen atoms at the ring junction was confirmed by the NOESY studies. The observed stereochemistry in the cycloadducts can be explained by selective addition of the dipole to the alkene through an *exo* approach.[28]



Scheme 8.

2.2.4. *cis-1-Tosyl/benzenesulfonyloctahydropyrrolo[3,4-b]isoquinolino[2,3-a]pyrrole*

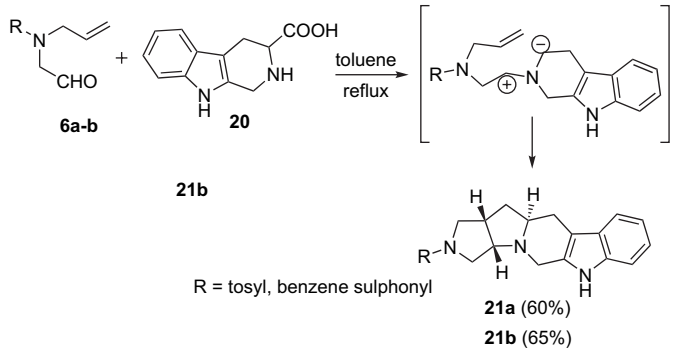
The biological significance of isoquinoline-based scaffolds[29] prompted us to synthesize pyrrolo[3,4-*b*]pyrroles fused with isoquinoline at N-1–C-2 positions. Thus a stereoselective intramolecular cycloaddition reaction of isoquinoline-2-carboxylic acid **18** with the alkenyl aldehydes **6a** and **6b** yielded the tetracyclic products **19a**,**b** in good yields. The hydrogens at the ring junction were found to be cis to each other from the spectroscopic data (Scheme 9). Similarly with Scheme 8, the angular hydrogen is trans to the hydrogens at ring junctions. This may be attributed to the pi-facial selectivity of the dipole toward the tethered alkene.



Scheme 9.

2.2.5. *cis-1-Tosyl/benzenesulfonyloctahydropyrrolo[3,4-b]pyridoindolo[2,3-a]pyrrole*

Pyrido[3,4-*b*]indoles have been proved to be depressants of the central nervous system[30] and potent antiulcer agents.[31] In anticipation of enhanced bioactivity, pyrrolo[3,4-*b*]pyrroles incorporated with tetrahydro pyridoindole unit **21a**,**b** were synthesized by the intramolecular 1,3-dipolar cycloaddition reaction of **6a**,**b** with 1,2,3,4-tetrahydro-β-carboline-3-carboxylic acid **20**[32] (Scheme 10). In all cases the cycloaddition took place to give a cis-fused product through decarboxylation route. The coupling constants of hydrogen atoms on the ring junctions corresponded closely to those of **12e** reported earlier. The angular hydrogen next to nitrogen is stereochemically in trans position to the hydrogens at the ring junctions.



Scheme 10.

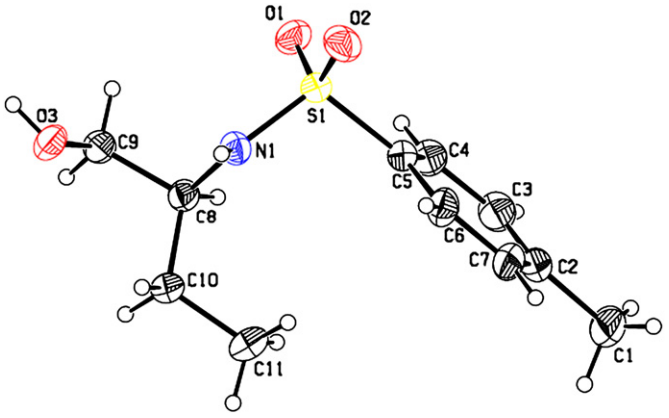
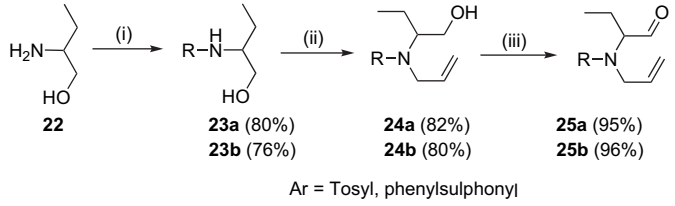


Figure 3. ORTEP diagram of **23a**.

2.3. Synthesis of 2-ethyl-substituted alkenyl aldehydes

Structural modifications on any synthetic precursor will lead to the synthesis of a library of potent synthetic molecules from which best and effective candidates could be selected for the construction of bioactive molecules. In order to synthesize structurally modified pyrrolo[3,4-*b*]pyrrole framework, ethyl substituted alkenyl aldehyde precursors **25a**,**b** were envisaged. These alkenyl aldehydes were synthesized in good yields from 2-aminobutan-1-ol **22** instead of 2-aminoethanol **7** in analogies to the Schemes 4 and 5. Thus, aminobutan-1-ol **22** was *N*-sulfonylated by *p*-toluenesulfonyl chloride and benzenesulfonyl chloride under standard PTC conditions to afford *N*-sulfonylated-aminobutan-1-ol **23a**,**b** in good yields.

The *N*-sulfonylated alcohols were then subjected to N-allylation using allylbromide with anhydrous potassium carbonate in dry acetone solvent to obtain the alcohols **24a**,**b**, which were oxidized to their corresponding aldehydes **25a**,**b** quantitatively by IBX in DMSO solvent (Scheme 11).

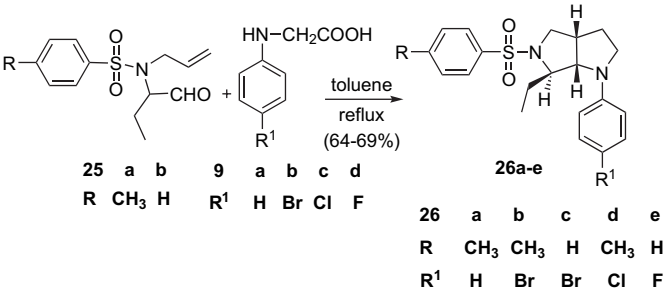


Scheme 11. Reagents and conditions: (i) $ArSO_2Cl$, TBAB, 10% NaOH, 0 °C–rt; (ii) allylbromide, K_2CO_3–acetone; (iii) IBX, DMSO.

The compound **23a** has been confirmed by single crystal X-ray diffraction analysis (Fig. 3).[33] The crystal packing of the compound **23a** is stabilized by the O–H···O and N–H···O hydrogen bonds and intermolecular π–π interactions.

2.4. Synthesis of 6-ethyl-5-tosyl/benzenesulfonyl-octahydropyrrolo[3,4-*b*]pyrroles

A series of 6-ethyl substituted cis-fused octahydropyrrolo[3,4-*b*]pyrrole derivatives were obtained in moderate to good yields by the intramolecular azomethine ylide cycloaddition reaction of **25a**,**b** with various amino acids **9a**–**f** (Scheme 12). Spectral patterns obtained for the cycloadducts are in analogy with the spectral patterns of cycloadducts obtained in Scheme 7. The stereochemistry of the hydrogen atom at C-6 was found to be trans to the hydrogens at the ring junctions and was confirmed by single crystal X-ray diffraction analysis of the cycloadducts **26b**,[34] **26c**,[35] and **26e**[36] (Figs. 4–6). In the compounds **26b** and **26e**, one of the fused



Scheme 12.

pyrrolidine rings adopts an envelope conformation, while the other is in a twist conformation. The molecules are primarily related by π–π interactions into a chain. In compound **26c**, both pyrrolidine rings adopt twist conformations and are stabilized by intermolecular C–H···O hydrogen bonds and π–π interactions.

2.5. Synthesis of thiazolo[3′,4′-2,3]pyrrolo[4,5-*c*]pyrroles

Having fascinated by the structural and therapeutic diversities of thiazolidine ring such as anti-oxidant, anti-amoebic, anti-

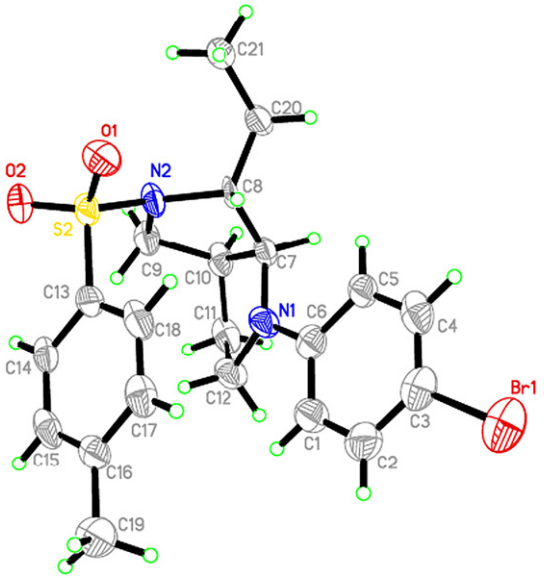


Figure 4. X-ray crystal structure of compound **26b**.

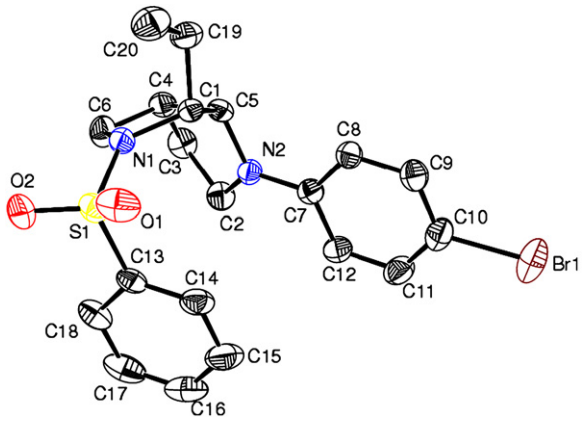


Figure 5. X-ray crystal structure of compound **26c**.

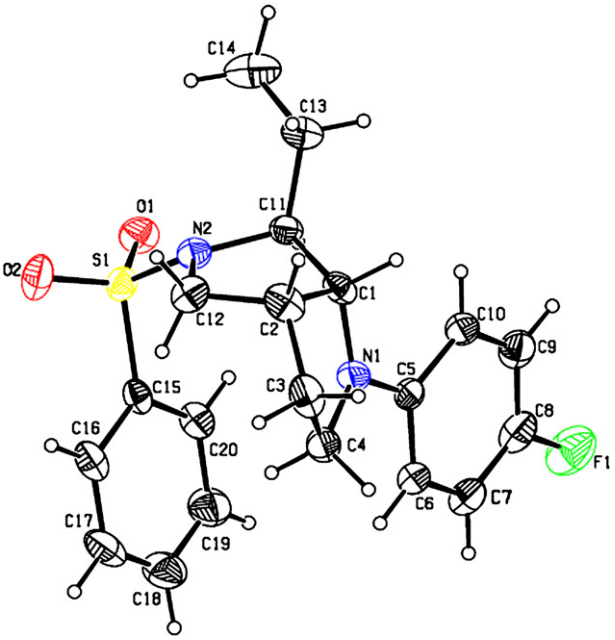
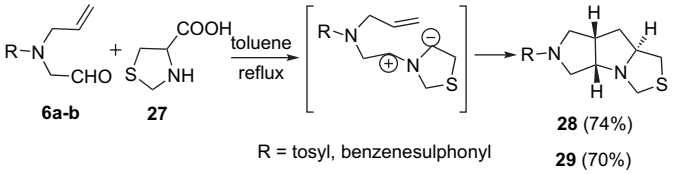


Figure 6. X-ray crystal structure of compound **26e**.

diabetic, and anti-inflammatory activities,[37] pyrrolo[3,4-*b*]pyrroles fused with thiazolidine ring was conceived as targets on the design and synthesis of new heterocycles. Cyclic α-amino acids such as 1,3-thiazolidine-4-carboxylic acids can be used for the generation of non-stabilized azomethine ylides by decarboxylative condensation with carbonyl compounds. The reaction with aldehydes is reported to involve the highly stereoselective formation of *anti*-dipole.[38]

2.5.1. cis-5-Tosyl/benzenesulfonylperhydrothiazolo[3′,4′-2,3]pyrrolo[4,5-c]pyrroles

In order to synthesize thiazolo[3′,4′-2,3]pyrrolo[4,5-*c*]pyrroles, the alkenyl aldehydes **6a**,**b** were condensed with L-thiazolidine-4-carboxylic acid **27** in refluxing toluene under Dean–Stark reaction conditions to generate the azomethine ylide. The in situ generated non-stabilized cyclic ylides were efficiently annulated by the olefinic tether of the aldehyde moiety to afford a novel heterotricyclic compounds *cis*-perhydrothiazolo[3′,4′-2,3]pyrrolo[4,5-*c*]pyrroles **28** and **29** in good yields (Scheme 13). As the cyclic dipole approach the alkene in pi-facial selective manner the angular hydrogen and the hydrogens at the ring junctions are in trans geometry. The structure was corroborated unambiguously by single crystal X-ray



Scheme 13.

diffraction analysis of the cycloadduct **29**[39] (Fig. 7). All the five-membered rings of the tricyclic molecule adopt envelope conformations. Intermolecular C–H–O hydrogen bonds link the molecules into a two-dimensional network parallel to the 'ab' plane.

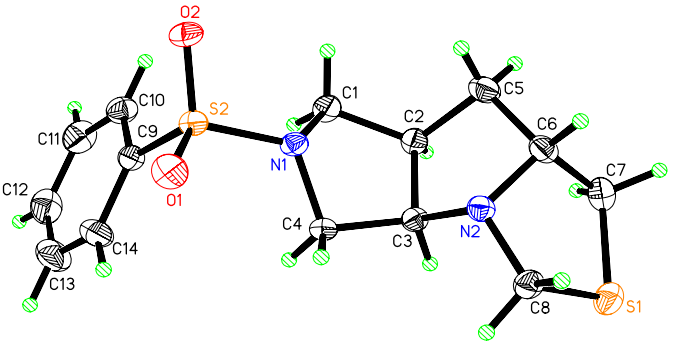


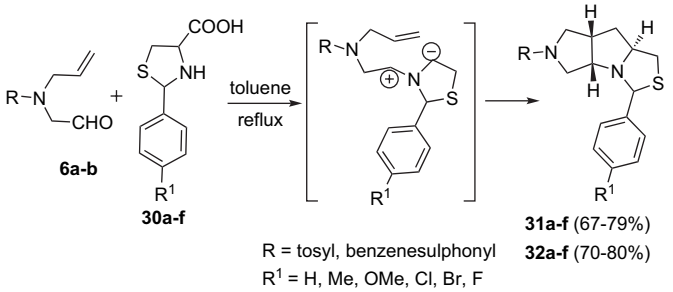
Figure 7. ORTEP diagram of **29**.

2.5.2. cis-2-Aryl-5-tosyl/benzenesulfonylperhydrothiazolo[3′,4′-2,3]pyrrolo[4,5-c]pyrroles

Similarly, when 2-aryl-thiazolidine-4-carboxylic acids **30a**–**f** were treated with **6a**,**b**, a series of 2-aryl substituted heterotricyclic compounds *cis*-2-aryl-5-tosyl/benzenesulfonylperhydrothiazolo-[3′,4′-2,3]pyrrolo[4,5-*c*]pyrroles **31a**–**f** and **32a**–**f** were obtained in good yields (Scheme 14).

The structures of the compounds were established on the basis of their spectroscopic data and single crystal X-ray diffraction analysis of some cycloadducts[40–44] (Figs. 8–12). As the dipole–dipolarophile interaction happens to be similar to the Scheme 13 the angular hydrogen is trans to the hydrogens at the ring junction. In compound **31e**, the two pyrrolidine rings adopt envelope conformations and the thiazolidine ring adopts a twisted conformation. The adjacent inverted molecules are related by C–H-π interactions in the crystal packing (Table 1).

In compound **32d**, both the thiazolidine ring and the two pyrrolidine rings adopt twisted conformations. In the molecule, **32b** the two pyrrolidine rings adopt twisted conformations, while the thiazolidine ring is in an envelope conformation with the N atom at the flap position. Adjacent chains are interconnected via π–π and



Scheme 14.

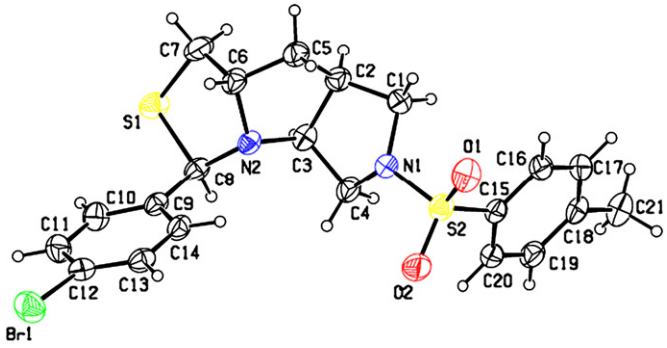


Figure 8. ORTEP diagram of **31e**.

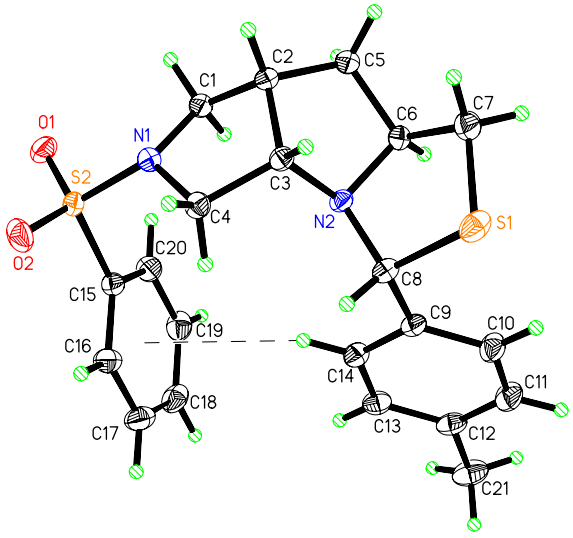


Figure 9. ORTEP diagram of **32b**.

C–H-π interactions to form sheets parallel to the 'ab' plane. In the compound **32f**, the thiazolidine ring is disordered and both conformers adopt envelope conformations. One of the pyrrolidine rings adopts an envelope conformation, while the other is in a twist conformation.

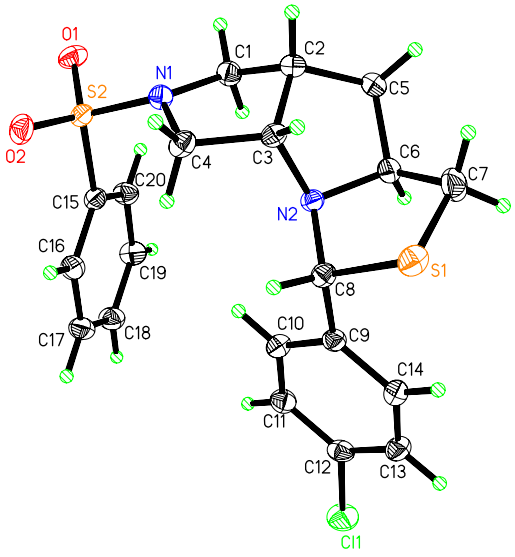


Figure 10. ORTEP diagram of **32d**.

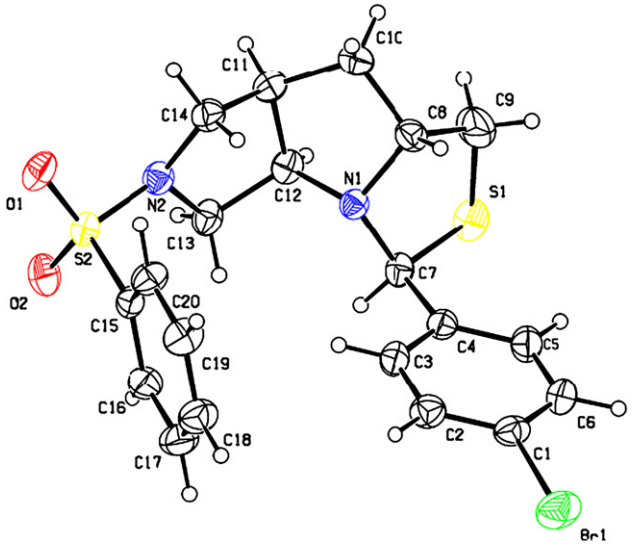


Figure 11. ORTEP diagram of **32e**.

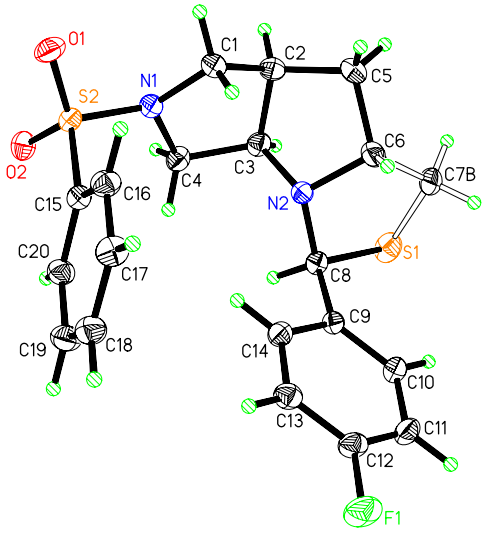


Figure 12. ORTEP diagram of **32f**.

Table 1
Intramolecular azomethine ylide cycloadditions of compounds **6a**,**b** with secondary amino acids **30a–f**

Entry	Amino acid+**6a**,**b**	Time (h)	Product	Yield (%)
1	**30a**+**6a**	3	**31a**	70
2	**30b**+**6a**	4	**31b**	68
3	**30c**+**6a**	3	**31c**	67
4	**30d**+**6a**	2.5	**31d**	73
5	**30e**+**6a**	2.5	**31e**	70
6	**30f**+**6a**	3.5	**31f**	79
7	**30a**+**6b**	3	**32a**	70
8	**30b**+**6b**	3	**32b**	73
9	**30c**+**6b**	3	**32c**	71
10	**30d**+**6b**	2.5	**32d**	75
11	**30e**+**6b**	2	**32e**	80
12	**30f**+**6b**	4.5	**32f**	77

3. Conclusion

In conclusion, synthetically useful *N*-tethered alkenyl aldehydes were synthesized in good yields and were successfully subjected to intramolecular azomethine ylide cycloaddition reactions by

treating with glycine derivatives to form variety of structurally important pyrrolo[3,4-*b*]pyrroles and with various cyclic secondary amino acids to form some N-1–C-2 fused derivatives of pyrrolo[3,4-*b*]pyrroles. Further the precursor alkenyl aldehydes were reacted with various thiazolidine-4-carboxylic acids to afford a series of unprecedented heterotricyclic systems, *cis*-perhydrothiazolo[3′,4′-2,3]pyrrolo[4,5-*c*]pyrroles. Absolute stereoselectivity was observed in the cycloaddition reaction of all cases studied.

4. Experimental

4.1. General considerations

All melting points are uncorrected. IR spectra were recorded on a SHIMADZU IR-8300 series FT-IR spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on JEOL 300, JEOL 400 MHz, and JEOL 500 MHz instruments in $CDCl_3$ solvent with TMS as a standard. Mass spectra were recorded on JEOL-DX303 HF mass spectrophotometer. Elemental analyses were carried out using Perkin–Elmer CHNS 2400 and Carlo Erba 1106 instruments. Single crystal X-ray diffraction analyses were performed on Bruker SMART APEX CCD area-detector diffractometer and Bruker SMART APEXII CCD area-detector diffractometer.

Column chromatography was performed on silica gel (ACME, 100–200 mesh). Routine monitoring of the reaction was made using thin layer chromatography developed on glass plates coated with silica gel-G (ACME) of 25 mm thickness and visualized with iodine.

4.2. Tosylation/benzenesulfonylation of allyl amine

To a solution of 5.7 g (0.1 mol) of allyl amine in 50 ml benzene at 0 °C was added one portion of 0.1 mol of *p*-toluenesulfonyl chloride/benzenesulfonyl chloride. The reaction mixture was stirred vigorously. After 10 min, 30 mL of benzene was added and then the remaining portion of *p*-toluenesulfonyl chloride/benzenesulfonyl chloride was added slowly. Then, a catalytic amount (500 mg) of the phase transfer catalyst, tetrabutylammonium bromide (TBAB), was added. To this stirred mixture, 25% solution of sodium hydroxide (0.1 mol) was added in drops by an additional funnel resulting in a thick flocculation. The temperature of the reaction mixture was raised to room temperature once the addition of sodium hydroxide was complete. After 8–10 h, the reaction mixture was diluted with 100 mL of water. It was then extracted with 50 mL of benzene and washed with brine solution. The organic layer was then dried over anhydrous sodium sulfate and concentrated in vacuum to yield crude *N*-sulfonylated allyl amines. Pure products were obtained by column chromatography using 9:1 mixture of hexane–ethylacetate.

4.2.1. *N-Tosyl prop-2-en-1-amine* ***3a***

Colorless solid, 90% (19.00 g); mp: 57–59 °C; IR (KBr): 1338, 1161 and 3120 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.41 (s, 3H, Ar–CH_3), 3.56 (d, 2H, *N*–CH_2), 5.04–5.17 (m, 2H, CH_2), 5.29 (br s, 1H, NH), 5.67–5.73 (m, 1H, CH), 7.29 (d, 2H, *J*=7.6 Hz, Ar–H), 7.77 (d, 2H, *J*=8.4 Hz, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.4, 45.6, 117.4, 127.1, 129.6, 133.0, 136.8, and 143.4. Mass spectrum (EI, 70 eV): *m*/*z*, 211.29 (M^+). Anal. Calcd for $C_{10}H_{13}NO_2S$: C, 56.85; H, 6.20; N, 6.63%. Found: C, 56.92; H, 6.28; N, 6.67%.

4.2.2. *N-Benzenesulfonylprop-2-en-1-amine* ***3b***

Colorless liquid, 85% (16.76 g); IR (KBr): 1337, 1163, and 3124 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.65 (d, 2H, *N*–CH_2), 5.08–5.20 (m, 2H, CH_2), 5.25 (br s, 1H, NH), 5.68–5.90 (m, 1H, CH), 7.20–7.80 (m, 5H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 45.80, 117.2, 126.8, 129.6, 133.2, 135.9, and 143.4. Mass spectrum (EI, 70 eV): *m*/*z*, 197.27 (M^+). Anal. Calcd for $C_{10}H_{11}NO_2S$: C, 54.79; H, 5.62; N, 7.10%. Found: C, 54.70; H, 5.57; N, 7.18%.

4.3. Synthesis of *N*-allyl-*N*-(ethoxycarbonylmethyl)toluene/benzenesulfonamide

To a solution of 0.05 mol of *N*-aryl sulfonylated allyl amine in 50 mL of dry acetone under nitrogen atmosphere was added 0.15 mol of potassium carbonate. To this stirred solution, 0.075 mol of chloro ethylacetate in 20 mL of dry acetone was added. The stirring was continued for 8–10 h. After completion of the reaction, the mixture was filtered, the residue was washed several times with acetone, the filtrate was concentrated in vacuum, and extracted with dichloromethane (40 mL) and water (40 mL). The organic extract was washed with brine solution and concentrated under reduced pressure. The crude product was subjected to column chromatography with hexane–ethylacetate mixture (9:1) to obtain pure *N*-alkylated sulfonamides.

4.3.1. *N-Allyl-N-(ethoxycarbonylmethyl)toluene-4-sulfonamide* ***4a***

Colorless liquid, 85% (12.62 g); IR (KBr): 1337, 1160, 1744, and 1600 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.19 (t, 3H, CH_3), 2.42 (s, 3H, Ar–CH_3), 3.90 (d, 2H, *N*–CH_2–, *J*=6.5 Hz), 4.00 (s, 2H, *N*–CH_2–CO), 4.09 (q, 2H, O–CH_2), 5.15–5.20 (m, 2H, CH_2), 5.62–5.73 (m, 1H, CH), 7.29 (d, 2H, Ar–H, *J*=8.28 Hz), 7.73 (d, 2H, Ar–H, *J*=8.28 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 13.8, 21.3, 46.8, 50.5, 61.0, 119.6, 127.2, 128.1, 129.4, 132.6, 136.6, 143.3, and 168.7. Mass spectrum (EI, 70 eV): *m*/*z*, 297.08 (M^+). Anal. Calcd for $C_{14}H_{19}NO_4S$: C, 56.55; H, 6.44; N, 4.71%. Found: C, 56.62; H, 6.38; N, 4.78%.

4.3.2. *N-Allyl-N-(ethoxycarbonylmethyl)benzenesulfonamide* ***4b***

Colorless liquid, 82% (11.60 g); IR (KBr): 1335, 1160, 1744, and 1601 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.18 (t, 3H, –CH_3), 3.87 (d, 2H, *N*–CH_2–, *J*=6.54 Hz), 4.11 (s, 2H, *N*–CH_2–CO), 4.09 (q, 2H, O–CH_2), 5.15–5.20 (m, 2H, CH_2), 5.60–5.72 (m, 1H, CH), 7.29–7.73 (m, 5H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.8, 46.8, 50.3, 61.1, 119.4, 127.0, 128.5, 129.5, 132.4, 136.0, 142.9, and 168.9. Mass spectrum (EI, 70 eV): *m*/*z*, 283.09 (M^+). Anal. Calcd for $C_{13}H_{17}NO_4S$: C, 55.11; H, 6.05; N, 4.94%. Found: C, 55.19; H, 6.12; N, 4.88%.

4.4. Reduction of *N*-allyl sulfonamide esters by LAH

One equivalent (0.05 mol) of the ester dissolved in dry tetrahydrofuran (60 mL) was added dropwise to a stirred suspension of 1.5 equiv of LAH (0.075 mol) in dry tetrahydrofuran (100 mL) under nitrogen atmosphere. After the addition was complete the temperature of the reaction mixture was raised to 65 °C. After 4 h of effective stirring at this temperature, the reaction was quenched by the dropwise addition of 10% NaOH solution under cold condition. The mixture was filtered and the solid was washed several times with tetrahydrofuran. The combined filtrate was evaporated under reduced pressure and the residue was extracted with dichloromethane and water. The organic layer was washed with brine and was dried over anhydrous sodium sulfate. The solvent was evaporated in vacuum and the residue was column chromatographed using ethylacetate–hexane mixtures (1:9) to obtain the alcohol.

4.4.1. *2-(N-Allyl-N-tosylamino)ethanol* ***5a***

Pale yellow liquid, 90% (11.39 g); IR (KBr): 1337, 1160, 1600, and 3450 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.04 (br s, 1H, OH), 2.43 (s, 3H, Ar–CH_3), 3.24 (t, 2H, C–CH_2–O, *J*=5.4 Hz), 3.73 (s, 2H, *N*–CH_2–C, *J*=5.4 Hz), 3.85 (d, 2H, N–CH_2–allyl), 5.15–5.21 (m, 2H, CH_2), 5.60–5.71 (m, 1H, CH), 7.32 (d, 2H, Ar–H, *J*=8.2 Hz), 7.71 (d, 2H, Ar–H, *J*=8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.4, 49.5, 52.0, 60.8, 119.3, 127.1, 129.7, 132.8, 136.0, and 143.5. Mass spectrum (EI, 70 eV): *m*/*z*,

255.33 (M^+). Anal. Calcd for $C_{12}H_{17}NO_3S$: C, 56.45; H, 6.71; N, 5.49%. Found: C, 56.53; H, 6.79; N, 5.40%.

4.4.2. 2-(N-Allyl-N-benzenesulfonylamino)ethanol ***5b***

Pale yellow liquid, 84% (10.13 g); IR (KBr): 1335, 1161, 1600, 3452 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.52–2.58 (br s, 1H, OH), 3.27 (t, 2H, C–CH_2–O, J=5.6 Hz), 3.73 (s, 2H, N–CH_2–C, J=5.5 Hz), 3.87 (d, 2H, N–CH_2–allyl, J=6.3 Hz), 5.14–5.21 (m, 2H, CH_2), 5.58–5.72 (m, 1H, CH), 7.50–7.85 (m, 5H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 49.5, 51.9, 60.7, 119.3, 127.0, 129.1, 132.7, and 139.0. Mass spectrum (EI, 70 eV): m/z, 241.31 (M^+). Anal. Calcd for $C_{11}H_{15}NO_3S$: C, 54.75; H, 6.27; N, 5.80%. Found: C, 54.82; H, 6.20; N, 5.70%.

4.5. Synthesis of *N*-allyl-*N*-(2-oxo-ethyl)toluene-4-sulfonamide

Method A: Diisobutylaluminium hydride (DIBAL-H) (10 mmol in hexane, 55.4 mL) was added dropwise with a syringe to a solution of **4a** (10 mmol, 2.97 g) in 80 mL of dry toluene at −78 °C toluene under nitrogen atmosphere. The reaction mixture was stirred for 1 h until TLC analysis showed the absence of **4a** and was then quenched with 20 mL of MeOH. The mixture was then poured over 5% aqueous hydrochloric acid and then extracted with diethyl ether. The ethereal layer was washed with brine solution and was then concentrated under reduced pressure.

Method B: 2.94 g (0.01 mol) of 2-iodobenzoic acid (IBX) was dissolved in dimethyl sulfoxide, DMSO (10 mL), by stirring the mixture for 15 min. To this solution was added 1.674 g (0.006 mol) of 2-(*N*-Allyl-*N*-tosylamino)ethanol, **5a**. After 2 h of vigorous stirring, the reaction mixture was diluted with water and the precipitate formed was filtered and washed with ethylacetate (20 mL). The filtrate was then extracted with ethylacetate (2×20 mL). The organic layer was dried over anhydrous sodium sulfate and the solvent was distilled off at reduced pressure to get a brown colored crude aldehyde in quantitative yield. It was subjected to column chromatography (silica gel, 100–200 mesh) using hexane–ethylacetate mixture (9:1) to obtain pure 2(*N*-allyl-*N*-tosylamino)butanal, **6a**.

The same procedure was adopted for the synthesis of **6b**.

4.5.1. N-Allyl-N-(2-oxo-ethyl)toluene-4-sulfonamide ***6a***

Pale yellow viscous liquid, 98% (1.52 g); IR (KBr): 1336, 1163, and 1735 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.38 (s, 3H, Ar–CH_3), 3.74–3.77 (m, 4H, N–CH_2), 5.10–5.16 (m, 2H, CH_2), 5.57–5.65 (m, 1H, CH–), 7.28 (d, 2H, J=8.1 Hz, Ar–H), 7.67 (d, 2H, J=8.5 Hz, Ar–H), 9.53 (s, 1H, CHO); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.3, 52.1, 55.8, 120.5, 127.2, 129.7, 131.8, 135.5, 143.9, and 197.9. Mass spectrum (EI, 70 eV): m/z, 253.08 (M^+). Anal. Calcd for $C_{12}H_{15}NO_3S$: C, 56.90; H, 5.97; N, 5.53%. Found: C, 56.97; H, 5.91; N, 5.46%.

4.5.2. N-Allyl-N-(2-oxo-ethyl)benzenesulfonamide ***6b***

Pale yellow viscous liquid, 96% (1.38 g); IR (KBr): 1335, 1163, 1734 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 3.79–3.84 (m, 4H, N–CH_2), 5.15–5.30 (m, 2H, CH_2), 5.31–5.71 (m, 1H, CH–), 7.53–7.83 (m, 5H, Ar–H), 9.58 (s, 1H, CHO); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 52.1, 55.8, 120.8, 127.2, 129.3, 131.7, 133.1, 138.4, and 198.0. Mass spectrum (EI, 70 eV): m/z, 239.40 (M^+). Anal. Calcd for $C_{11}H_{13}NO_3S$: C, 55.21; H, 5.48; N, 5.85%. Found: C, 55.29; H, 5.40; N, 5.81%.

4.6. General procedure for the synthesis of cycloadducts

A mixture of 1.0 mmol of alkenyl aldehyde and 1.5 mmol of secondary amino acid in 30 mL of dry toluene was refluxed under Dean–Stark conditions till the completion of the reaction. The reaction mixture was then concentrated under reduced pressure. The residue was then extracted with dichloromethane (2×20 mL) and water (2×20 mL). The organic layer was washed with brine solution (2×20 mL), dried over anhydrous sodium sulfate, and concentrated in vacuum. The residue was then subjected to column chromatography (silica gel, 100–200 mesh) with hexane–ethylacetate (8:2) to obtain the cycloadducts (R_f=0.4–0.6).

4.6.1. cis-1-Methyl-5-tosyl-octahydropyrrolo[3,4-b]pyrrole ***10a***

Brown colored viscous liquid, 78% (0.218 g); IR (KBr): 1346 and 1161 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.58–1.62 (m, 1H), 1.94–1.98 (m, 1H), 2.26 (s, 3H, N–Me), 2.38 (s, 3H, Ar–CH_3), 2.63–2.67 (m, 1H), 2.29–2.84 (m, 3H), 2.91–3.07 (m, 3H), 3.25–3.28 (dt, 1H, J_1=2.4 Hz, J_2=6.8 Hz), 7.26–7.65 (m, 4H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.9, 31.1, 40.8, 42.6, 52.8, 54.7, 57.5, 69.8, 128.4, 129.9, 132.6, and 143.9. Mass spectrum (EI, 70 eV): m/z, 280.29 (M^+). Anal. Calcd for $C_{14}H_{20}N_2O_2S$: C, 59.97; H, 7.19; N, 9.99%. Found: C, 59.90; H, 7.24; N, 9.93%.

4.6.2. cis-1-Methyl-5-benzenesulfonyloctahydropyrrolo-[3,4-b]pyrrole ***10b***

Brown colored viscous liquid, 70% (0.186 g); IR (KBr): 1335 and 1165 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.56–1.60 (m, 1H), 1.94–2.00 (m, 1H), 2.24 (s, 3H, N–Me), 2.66–2.68 (m, 1H), 2.27–2.83 (m, 3H), 2.90–3.07 (m, 3H), 3.23–3.27 (dt, 1H, J_1=2.4 Hz, J_2=6.8 Hz), 7.20–7.66 (m, 5H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 31.1, 40.8, 42.2, 52.8, 54.5, 57.5, 69.7, 128.2, 128.4, 128.9, 129.9, and 143.8. Mass spectrum (EI, 70 eV): m/z, 266.40 (M^+). Anal. Calcd for $C_{13}H_{18}N_2O_2S$: C, 58.62; H, 6.81; N, 10.52%. Found: C, 58.50; H, 6.87; N, 10.48%.

4.6.3. cis-1-Phenyl-5-p-tosyloctahydropyrrolo[3,4-b]pyrrole ***12a***

White solid, 76% (0.260 g); mp: 110–111 °C; IR (KBr): 1336 and 1165 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.90–1.96 (m, 1H), 2.13–2.18 (m, 1H), 2.44 (s, 3H), 2.93–2.98 (m, 1H), 3.20–3.50 (m, 6H), 3.97–4.10 (dt, 1H, J_1=2.4 Hz, J_2=6.8 Hz), 6.46–6.48 (d, 2H, J=7.8 Hz), 6.73–7.68 (m, 7H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.5, 29.51, 41.9, 48.1, 52.9, 53.9, 62.0, 113.8, 119.2, 121.0, 127.8, 128.3, 129.2, 132.9, 143.0, and 144.0. Mass spectrum (EI, 70 eV): m/z, 342.70 (M^+). Anal. Calcd for $C_{19}H_{22}N_2O_2S$: C, 66.64; H, 6.48; N, 8.18%. Found: C, 66.58; H, 6.57; N, 8.25%.

4.6.4. cis-1-(4-Methyl)-phenyl-5-p-tosyloctahydropyrrolo-[3,4-b]pyrrole ***12b***

White fluffy solid, 79% (0.281 g); mp: 157–151 °C; IR (KBr): 1336 and 1165 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.86–1.89 (m, 1H), 2.00–2.12 (m, 1H), 2.25 (s, 3H), 2.42 (s, 3H), 2.90–2.92 (m, 1H), 3.13–3.42 (m, 6H), 4.00–4.03 (dt, 1H, J_1=2.4 Hz, J_2=9.4 Hz), 6.38–7.75 (m, 8H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.0, 21.9, 29.1, 41.0, 48.1, 52.1, 54.1, 62.4, 113.1, 119.0, 121.9, 127.1, 128.0, 129.9, 132.2, 143.7, and 144.8. Mass spectrum (EI, 70 eV): m/z, 356.50 (M^+). Anal. Calcd for $C_{20}H_{24}N_2O_2S$: C, 67.38; H, 6.79; N, 7.86%. Found: C, 67.30; H, 6.86; N, 7.80%.

4.6.5. cis-1-(4-Methoxy)-phenyl-5-p-tosyloctahydropyrrolo-[3,4-b]pyrrole ***12c***

White fluffy solid, 81% (0.301 g); mp: 159–161 °C; IR (KBr): 1336 and 1165 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.86–1.91 (1H, m), 2.03–2.20 (m, 1H), 2.42 (s, 3H, Ar–CH_3), 2.93–2.98 (m, 1H), 3.11–3.38 (m, 6H), 3.75 (s, 3H, OMe), 4.00–4.02 (dt, 1H, J_1=2.4 Hz, J_2=6.4 Hz), 6.46–7.45 (m, 8H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.2, 21.5, 29.7, 42.2, 49.0, 52.7, 53.3, 55.8, 63.3, 113.8, 114.9, 127.8, 129.5, 132.1, and 143.6. Mass spectrum (EI, 70 eV): m/z, 371.79 (M^+). Anal. Calcd for $C_{20}H_{24}N_2O_3S$: C, 64.49; H, 6.49; N, 7.52%. Found: C, 64.38; H, 6.58; N, 7.43%.

4.6.6. cis-1-(4-Chloro)-phenyl-5-p-tosyloctahydropyrrolo-[3,4-b]pyrrole ***12d***

White fluffy solid, 79% (0.297 g); mp: 164–166 °C; IR (KBr): 1335 and 1161 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.80–1.87 (m, 1H), 2.00–2.08 (m, 1H), 2.38 (s, 3H), 2.80–2.91 (m, 1H), 3.06–3.29 (m, 6H),

3.93–3.99 (dt, 1H, J_1=2.4 Hz, J_2=6.7 Hz), 6.24–7.57 (m, 8H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.5, 29.5, 42.3, 48.3, 52.3, 53.1, 62.5, 113.4, 121.6, 127.8, 128.9, 129.6, 132.1, 143.7, and 144.9. Mass spectrum (EI, 70 eV): *m*/*z*, 376.50 (M^+). Anal. Calcd for $C_{19}H_{21}N_2O_2SCl$: C, 60.55; H, 5.62; N, 7.43%. Found: C, 60.48; H, 5.73; N, 7.38%.

4.6.7. cis-1-(4-Bromo)-phenyl-5-p-tosyloctahydropyrrolo-[3,4-b]pyrrole ***12e***

White powder, 79% (0.33 g); mp: 210–211 °C; IR (KBr): 1338 and 1161 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.83–1.86 (m, 1H), 2.05–2.07 (m, 1H), 2.35 (s, 3H), 2.85–2.89 (m, 1H), 3.06–3.13 (m, 4H), 3.20–3.29 (m, 2H), 3.92–3.94 (dt, 1H, J_1=2.4 Hz, J_2=6.8 Hz), 6.21–7.57 (m, 8H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 21.5, 29.5, 42.3, 48.3, 52.4, 53.1, 62.5, 108.9, 114.1, 127.8, 129.6, 131.8, 132.2, 143.7, and 145.2. Mass spectrum (EI, 70 eV): *m*/*z*, 421.60 (M^+). Anal. Calcd for $C_{19}H_{21}N_2O_2SBr$: C, 54.16; H, 5.02; N, 6.64%. Found: C, 54.28; H, 5.12; N, 6.54%.

4.6.8. cis-1-(3-Nitro)-phenyl-5-p-tosyloctahydropyrrolo-[3,4-b]pyrrole ***12f***

Yellow solid, 68% (0.263 g); mp: 176–178 °C; IR (KBr): 1336, 1165, 1550, and 1352 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.96–2.01 (1H, m), 2.15–2.21 (m, 1H), 2.43 (s, 3H, Ar–CH_3), 3.01–3.48 (m, 7H), 4.01–4.14 (dt, 1H, J_1=2.4 Hz, J_2=6.4 Hz), 6.69–7.66 (m, 8H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.5, 29.5, 42.3, 48.3, 52.4, 53.8, 62.4, 106.5, 111.3, 118.0, 127.8, 129.8, 132.0, 143.9, 146.8, and 149.2. Mass spectrum (EI, 70 eV): *m*/*z*, 371.79 (M^+). Anal. Calcd for $C_{19}H_{21}N_3O_4S$: C, 58.90; H, 5.46; N, 10.85%. Found: C, 58.99; H, 5.38; N, 10.74%.

4.6.9. cis-1-Phenyl-5-benzenesulfonyloctahydropyrrolo-[3,4-b]pyrrole ***13a***

White solid, 68% (0.223 g); mp: 99–101 °C; IR (KBr): 1337 and 1165 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.81–1.89 (m, 1H), 2.05–2.14 (m, 1H), 2.88–2.92 (m, 1H), 3.12–3.37 (m, 6H), 4.02–4.04 (dt, 1H, J_1=2.4 Hz, J_2=6.8 Hz), 6.41–7.76 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 29.4, 42.2, 48.1, 52.3, 53.4, 62.4, 112.4, 116.7, 127.7, 129.0, 129.2, 132.8, 135.3, and 146.4. Mass spectrum (EI, 70 eV): *m*/*z*, 328.12 (M^+). Anal. Calcd for $C_{18}H_{20}N_2O_2S$: C, 65.83; H, 6.14; N, 8.53%. Found: C, 65.72; H, 6.23; N, 8.48%.

4.6.10. cis-1-(4-Methyl)-phenyl-5-benzenesulfonyloctahydropyrrolo[3,4-b]pyrrole ***13b***

White fluffy solid, 70% (0.239 g); mp: 149–151 °C; IR (KBr): 1336 and 1169 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.84–1.89 (m, 1H), 2.09–2.16 (m, 1H), 2.24 (s, 3H), 2.91–2.93 (m, 1H), 3.13–3.33 (m, 6H), 4.01–4.04 (dt, 1H, J_1=2.4 Hz, J_2=9.4 Hz), 6.38–7.75 (m, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.9, 29.1, 41.0, 48.1, 52.1, 54.1, 62.4, 113.1, 119.0, 121.9, 127.1, 128.0, 129.9, 132.2, 143.7, and 144.8. Mass spectrum (EI, 70 eV): *m*/*z*, 342.14 (M^+). Anal. Calcd for $C_{19}H_{22}N_2O_2S$: C, 66.64; H, 6.48; N, 8.18%. Found: C, 66.59; H, 6.50; N, 8.07%.

4.6.11. cis-1-(4-Methoxy)-phenyl-5-benzenesulfonyloctahydropyrrolo[3,4-b]pyrrole ***13c***

White fluffy solid, 71% (0.254 g); mp: 147–149 °C; IR (KBr): 1338 and 1166 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.86–1.91 (1H, m), 2.03–2.20 (m, 1H), 2.42, 2.93–2.98 (m, 1H), 3.11–3.38 (m, 6H), 3.74 (s, 3H, OMe), 4.00–4.02 (dt, 1H, J_1=2.4 Hz, J_2=6.4 Hz), 6.46–7.45 (m, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.4, 29.7, 42.2, 49.0, 52.7, 53.3, 55.8, 63.3, 113.8, 114.9, 127.8, 129.5, 132.1, and 143.6; Mass spectrum (EI, 70 eV): *m*/*z*, 358.14 (M^+). Anal. Calcd for $C_{19}H_{22}N_2O_3S$: C, 63.66; H, 6.19; N, 7.82%. Found: C, 63.54; H, 6.07; N, 7.90%.

4.6.12. cis-1-(4-Chloro)-phenyl-5-benzenesulfonyloctahydropyrrolo[3,4-b]pyrrole ***13d***

White fluffy solid, 69% (0.249 g); mp: 158–160 °C; IR (KBr): 1335 and 1166 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.89–1.92 (m, 1H), 2.12–2.16 (m, 1H), 2.91–2.97 (m, 1H), 3.15–3.34 (m, 6H), 3.99–3.02 (dt, 1H, J_1=2.4 Hz, J_2=6.7 Hz), 6.32–7.77 (m, 9H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 29.5, 30.9, 42.3, 48.3, 52.3, 53.2, 62.5, 113.5, 121.7, 127.7, 129.0, 132.9, 135.3, and 144.9. Mass spectrum (EI, 70 eV): *m*/*z*, 362.09 (M^+). Anal. Calcd for $C_{18}H_{19}N_2O_2SCl$: C, 59.58; H, 5.28; N, 7.72%. Found: C, 59.49; H, 5.34; N, 7.78%.

4.6.13. cis-1-(4-Bromo)-phenyl-5-benzenesulfonyloctahydropyrrolo[3,4-b]pyrrole ***13e***

White powder, 72% (0.293 g); mp: 201–203 °C; IR (KBr): 1337 and 1164 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.85–1.94 (m, 1H), 2.08–2.17 (m, 1H), 2.91–2.99 (m, 1H), 3.14 (m, 6H), 3.92–3.96 (dt, 1H, J_1=2.4 Hz, J_2=6.8 Hz), 6.24–7.52 (m, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 29.5, 42.3, 48.2, 52.3, 53.1, 62.4, 108.7, 114.0, 127.7, 129.0, 131.8, 132.8, 135.2, and 145.2. Mass spectrum (EI, 70 eV): *m*/*z*, 407.32 (M^+). Anal. Calcd for $C_{18}H_{19}N_2O_2SBr$: C, 53.08; H, 4.70; N, 6.88%. Found: C, 53.01; H, 4.79; N, 6.80%.

4.6.14. cis-1-(3-Nitro)-phenyl-5-benzenesulfonyloctahydropyrrolo[3,4-b]pyrrole ***13f***

Yellow solid, 67% (0.249 g); mp: 155–157 °C; IR (KBr): 1335, 1166, 1151, and 1350 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.90–2.00 (1H, m), 2.14–2.21 (m, 1H), 3.01–3.45 (m, 7H), 4.01–4.14 (dt, 1H, J_1=2.4 Hz, J_2=6.4 Hz), 6.69–7.66 (m, 9H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 29.5, 42.3, 48.3, 52.4, 53.8, 62.4, 106.5, 111.3, 118.0, 127.8, 129.8, 132.0, 143.9, 146.2, and 149.6. Mass spectrum (EI, 70 eV): *m*/*z*, 373.11 (M^+). Anal. Calcd for $C_{18}H_{19}N_3O_4S$: C, 57.89; H, 5.13; N, 11.25%. Found: C, 57.95; H, 5.04; N, 11.32%.

4.7. Synthesis of N-1–C-2 cycloalkane fused octahydro-[3,4-*b*]pyrroles

A mixture of 1.0 mmol of alkenyl aldehyde and 1.5 mmol of proline or pipecolinic acid in 30 mL of dry toluene was refluxed under Dean–Stark conditions till the completion of the reactions (7–8 h). The reaction mixture was then concentrated under reduced pressure. The residue was extracted with dichloromethane (2×20 mL) and water (2×20 mL). The organic layer was washed with brine solution (2×20 mL), dried over anhydrous sodium sulfate, and concentrated in vacuum. The residue was then subjected to column chromatography (silica gel, 100–200 mesh) with hexane–ethylacetate (8:2) to obtain the cycloadducts (R_f=0.2–0.4).

4.7.1. cis-2-p-Tosyldecahydropyrrolo[3,4-b]pyrrolizine ***15a***

Brown colored viscous liquid, 83% (0.254 g); IR (KBr): 1338 and 1161 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.32–1.43 (2H, m), 1.53–1.60 (2H, m), 1.63–1.93 (2H, m), 2.36 (s, 3H, Ar–Me), 2.78–2.80 (1H, m), 2.87–2.92 (1H, m), 2.95–3.03 (1H, m), 3.10–3.15 (1H, m), 3.22–3.28 (2H, m), 3.39–3.53 (3H, m), 7.21–7.63 (4H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.9, 25.5, 31.3, 36.7, 43.5, 53.3, 54.6, 65.3, 70.2, 128.2, 129.9, 133.1, and 143.9. Mass spectrum (EI, 70 eV): *m*/*z*, 306.63 (M^+). Anal. Calcd for $C_{16}H_{22}N_2O_2S$: C, 62.71; H, 7.24; N, 9.14%. Found: C, 62.79; H, 7.16; N, 9.06%.

4.7.2. cis-2-Benzenesulfonyldecahydropyrrolo[3,4-b]-pyrrolizine ***15b***

Brown colored viscous liquid, 76% (0.222 g); IR (KBr): 1339 and 1161 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.30–1.40 (2H, m), 1.52–1.60 (2H, m), 1.64–1.95 (2H, m), 2.79–2.81 (1H, m), 2.87–2.92 (1H, m), 2.93–3.05 (1H, m), 3.12–3.15 (1H, m), 3.23–3.28 (2H, m), 3.36–3.55 (2H, m), 7.19–7.48 (5H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 25.5, 31.2, 36.1, 43.4, 53.0, 54.6, 65.9, 70.0, 128.3, 129.9, 133.1, and 143.3. Mass spectrum (EI, 70 eV): *m*/*z*, 292.40 (M^+). Anal. Calcd for $C_{15}H_{20}N_2O_2S$: C, 61.62; H, 6.89; N, 9.58%. Found: C, 61.70; H, 6.79; N, 9.47%.

4.7.3. cis-2-p-Tosyldecahydro-1H-pyrrolo[3,4-b]indolizine ***17a***

Brown colored viscous liquid, 62% (0.198 g); IR (KBr): 1340 and 1170 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.02–1.05 (1H, m), 1.05–1.20 (1H, m), 1.24–1.47 (1H, m), 1.60–1.97 (m, 6H), 2.43 (s, 3H, Ar–Me), 2.47–3.11 (m, 6H), 3.45–3.47 (m, 1H), 3.80–3.82 (dt, 1H, J_1=2.4 Hz, J_2=10.2 Hz), 7.28–8.01 (4H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.5, 23.9, 24.8, 31.1, 31.4, 39.1, 39.3, 54.8, 59.3, 65.7, 128.1, 129.5, 143.7, and 162.5. Mass spectrum (EI, 70 eV): *m*/*z*, 320.16 (M^+). Anal. Calcd for $C_{17}H_{24}N_2O_2S$: C, 63.72; H, 7.55; N, 8.74%. Found: C, 63.63; H, 7.47; N, 8.83%.

4.7.4. cis-2-Benzenesulfonyldecahydro-1H-pyrrolo[3,4-b]-indolizine ***17b***

Brown colored viscous liquid, 60% (0.183 g); IR (KBr): 1341 and 1168 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.00–1.04 (1H, m), 1.05–1.21 (1H, m), 1.24–1.44 (1H, m), 1.59–1.96 (m, 6H), 2.46–3.13 (m, 6H), 3.44–3.47 (m, 1H), 3.84–3.86 (dt, 1H, J_1=2.4 Hz, J_2=10.2 Hz), 7.11–7.98 (5H, m, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 23.5, 24.3, 31.1, 31.2, 39.7, 39.8, 54.2, 59.6, 65.1, 128.1, 129.8, 143.1, and 162.5. Mass spectrum (EI, 70 eV): *m*/*z*, 306.42 (M^+). Anal. Calcd for $C_{16}H_{22}N_2O_2S$: C, 62.71; H, 7.24; N, 9.14%. Found: C, 62.62; H, 7.33; N, 9.08%.

4.7.5. cis-11-p-Tosyldecahydropyrrolo[3,4-b]pyrrolo-[1,2-b]isoquinoline ***19a***

White solid, 68% (0.250 g); mp: 170–172 °C; IR (KBr): 1343 and 1170 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.81–1.93 (m, 2H), 2.42 (s, 3H, Ar–CH_3), 2.55–2.64 (m, 1H), 2.69–2.75 (m, 1H), 2.85–2.89 (m, 2H), 3.00–3.11 (m, 3H), 3.45–3.54 (m, 1H), 3.85–4.00 (m, 3H), 7.06–7.69 (m, 8H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.52, 34.5, 38.8, 40.0, 48.4, 49.4, 54.3, 56.4, 65.4, 125.8, 126.3, 126.6, 128.0, 128.8, 129.5, 131.2, 133.4, 133.6, and 143.8. Mass spectrum (EI, 70 eV): *m*/*z*, 368.49 (M^+). Anal. Calcd for $C_{21}H_{24}N_2O_2S$: C, 68.45; H, 6.56; N, 7.60%. Found: C, 68.51; H, 6.49; N, 7.52%.

4.7.6. cis-11-Benzenesulfonylpyrrolo[3,4-b]pyrrolo-[1,2-b]isoquinoline ***19b***

White solid, 68% (0.250 g); mp: 141–143 °C; IR (KBr): 1332 and 1168 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.77–1.92 (m, 2H), 2.53–2.60 (m, 1H), 2.74–2.76 (m, 1H), 2.83–2.87 (m, 2H), 3.05–3.14 (m, 3H), 3.53–3.56 (m, 1H), 3.84–3.97 (m, 3H), 7.06–7.81 (m, 9H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 34.6, 38.8, 40.1, 48.5, 49.4, 54.3, 56.3, 65.4, 125.8, 126.3, 126.6, 127.9, 128.8, 128.9, 132.8, 133.7, 133.8, and 134.7. Mass spectrum (EI, 70 eV): *m*/*z*, 354.14 (M^+). Anal. Calcd for $C_{20}H_{22}N_2O_2S$: C, 67.77; H, 6.26; N, 7.90%. Found: C, 67.70; H, 6.18; N, 8.00%.

4.7.7. cis-1-Tosyloctahydropyrrolo[3,4-b]pyridoindolo-[2,3-a]pyrrole ***21a***

Brown colored solid, 65% (0.265 g); mp: 226–228 °C; IR (KBr): 3338, 1338, and 1168 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 1.19–1.14 (m, 2H), 1.77–1.86 (m, 2H), 2.32 (s, 3H, Ar–CH_3), 2.55–2.87 (m, 3H), 2.99–3.01 (dd, 1H, J_1=2.3 Hz, J_2=9.4 Hz), 3.01–3.06 (m, 1H), 3.32–3.35 (dd, 1H, J_1=2.3 Hz, J_2=10.3 Hz), 3.62–3.65 (dt, 1H, J_1=2.5 Hz, J_2=6.9 Hz), 3.78 (d, 1H, J=15.4 Hz), 3.91 (d, 1H, J=15.4 Hz), 6.85–7.53 (m, 8H, Ar–H), 10.10 (s, 1H, NH); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 21.2, 25.8, 38.1, 43.9, 49.6, 54.3, 56.8, 106.4, 110.7, 117.2, 118.3, 120.4, 126.6, 127.7, 129.4, 130.9, 131.3, 136.3, and 143.6. Mass spectrum (EI, 70 eV): *m*/*z*, 407.76 (M^+). Anal. Calcd for $C_{23}H_{25}N_3O_2S$: C, 67.79; H, 6.18; N, 10.31%. Found: C, 67.70; H, 6.27; N, 10.25%.

4.7.8. cis-1-Benzenesulfonyloctahydropyrrolo-[3,4-b]pyridoindolo[2,3-a]pyrrole ***21b***

Brown colored solid, 60% (0.235 g); mp: 207–209 °C; IR (KBr): 3336, 1338, and 1169 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.18–1.20 (m, 2H), 1.80–1.86 (m, 2H), 2.55–2.87 (m, 3H), 2.86–2.92 (m, 1H), 3.01–3.06 (m, 1H), 3.30–3.34 (m, 1H), 3.62–3.65 (dt, 1H, J_1=2.4 Hz, J_2=6.8 Hz), 3.81 (d, 1H, J=15.2 Hz), 4.01 (d, 1H, J=15.2 Hz), 6.67–7.81 (m, 9H, Ar–H), 8.85 (s, 1H, NH); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 25.5, 37.6, 40.2, 44.1, 49.1, 54.5, 58.5, 64.6, 107.2, 111.1, 117.8, 119.3, 119.5, 121.6, 127.1, 128.1, 128.9, 132.0, 132.4, 133.2, 136.6, and 140.1. Mass spectrum (EI, 70 eV): *m*/*z*, 393.17 (M^+). Anal. Calcd for $C_{22}H_{23}N_3O_2S$: C, 67.15; H, 5.89; N, 10.68%. Found: C, 67.07; H, 5.93; N, 10.59%.

4.8. Synthesis of ethyl substituted analogues of 5a,b

The *N*-sulfonylated amino alcohols **23a**,**b** were synthesized in good yields from 2-amino butanol as described in Section 4.2. The N-allylation reactions were performed as follows.

To a stirring solution of 0.05 mol of *N*-sulfonylated amino alcohol **23a**,**b** in 100 ml of dry acetone was added 0.15 mol of potassium carbonate followed by 0.05 mol of allylbromide in 20 mL of dry acetone under nitrogen atmosphere. The stirring was continued for 8–10 h. After completion of the reaction, the mixture was filtered and the residue was washed several times with acetone. The filtrate was concentrated in vacuum and extracted with dichloromethane (40 mL) and water (40 mL). The organic extract was washed with brine solution and concentrated under reduced pressure. The crude product was subjected to column chromatography with hexane–ethylacetate mixture (9:1) to obtain pure *N*-allyl, *N*-sulfonylated amino alcohols **24a**,**b**.

4.8.1. 2-(Tosylamino)butan-1-ol ***23a***

Colorless crystals, 80% (9.72 g); mp: 62–64 °C; IR (KBr): 1336, 1170, 3120, and 3540 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 0.71 (t, 3H, CH_3), 1.34–1.50 (m, 2H, CH_2), 2.41 (s, 3H, Ar–CH_3), 2.80 (br s, 1H, OH), 3.10–3.14 (m, 1H), 3.47–3.58 (m, 2H), 5.49 (s, 1H, NH), 7.29–7.78 (m, 4H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 10.1, 21.5, 24.6, 57.1, 64.2, 127.0, 129.6, 137.7, and 143.4. Mass spectrum (EI, 70 eV): *m*/*z*, 243.09 (M^+). Anal. Calcd for $C_{11}H_{17}NO_3S$: C, 54.30; H, 7.04; N, 5.76%. Found: C, 54.15; H, 7.18; N, 5.66%.

4.8.2. 2-(Benzenesulfonylamino)butan-1-ol ***23b***

Colorless oil, 76% (8.70 g); IR (KBr): 1334, 1168, 3122, and 3540 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 0.69 (t, 3H, CH_3), 1.32–1.51 (m, 2H, CH_2), 2.87 (br s, 1H, OH), 3.13–3.16 (m, 1H), 3.45–3.58 (m, 2H), 5.44 (s, 1H, NH), 7.32–7.69 (m, 5H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 10.1, 24.6, 57.7, 64.0, 127.0, 129.7, 137.8, and 140.0. Mass spectrum (EI, 70 eV): *m*/*z*, 229.08 (M^+). Anal. Calcd for $C_{10}H_{15}NO_3S$: C, 52.38; H, 6.59; N, 6.11%. Found: C, 52.22; H, 6.69; N, 6.01%.

4.8.3. 2-(N-Allyl-N-tosylamino)butan-1-ol ***24a***

Pale yellow liquid, 82% (11.61 g); IR (KBr): 1330, 1170, and 3541 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 0.69 (t, 3H, CH_3), 1.32–1.51 (m, 2H, CH_2), 2.37 (br s, 1H, OH), 2.41 (s, 3H, Ar–CH_3), 3.56 (d, 2H, C–CH_2–O, J=6.4 Hz), 3.70–3.77 (m, 2H, *N*–CH_2), 3.92–3.98 (m, 1H, *N*CH), 5.10–5.24 (m, 2H, CH_2), 5.84–5.91 (m, 1H, CH), 7.32–7.71 (m, 4H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 11.0, 21.5, 22.1, 29.2, 46.4, 53.7, 61.9, 63.3, 117.6, 127.2, 129.5, 135.9, 137.9, and 143.3. Mass spectrum (EI, 70 eV): *m*/*z*, 283.40 (M^+). Anal. Calcd for $C_{14}H_{21}NO_3S$: C, 59.33; H, 7.47; N, 4.94%. Found: C, 59.41; H, 7.39; N, 4.85%.

4.8.4. 2-(N-Allyl-N-benzenesulfonylamino)butan-1-ol ***24b***

Pale yellow liquid, 80% (10.77 g); IR (KBr): 1333, 1168, and 3541 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 0.67 (t, 3H, CH_3), 1.24–1.52 (m, 2H, CH_2), 2.37 (br s, 1H, OH), 3.57 (d, 2H, C–CH_2–O, J=6.4 Hz), 3.70–3.80 (m, 2H, *N*–CH_2), 3.96–3.98 (m, 1H, NCH), 5.10–5.24 (m, 2H, CH_2), 5.85–5.87 (m, 1H, CH), 7.29–7.86 (m, 5H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 10.8, 22.0, 46.3, 61.8, 63.1, 117.5, 127.0, 128.8, 128.9, 132.4, 135.6, and 140.7. Mass spectrum (EI, 70 eV): *m*/*z*,

269.40 (M^+). Anal. Calcd for $C_{13}H_{19}NO_3S$: C, 57.96; H, 7.10; N, 5.20%. Found: C, 57.80; H, 7.21; N, 5.28%.

4.9. Synthesis of ethyl substituted alkenyl aldehydes, 25a,b

The alcohols **24a**,**b** (0.05 mol) were converted to the corresponding aldehydes by the experimental procedure described in Section 4.5 (Method B).

*4.9.1. 2-(N-Allyl-N-tosylamino)butanal **25a***

Pale yellow liquid, 95% (13.36 g); IR (KBr): 1330, 1170, and 1735 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 0.82 (t, 3H, CH_3), 1.44–1.52 (m, 1H, CH_2), 1.96–1.99 (m, 1H, CH_2), 2.43 (s, 3H, Ar–CH_3), 3.73–79 (dd, 1H, *N*–CH_2, J_1=7.3 Hz, J_2=15.6 Hz), 3.88–3.93 (dd, 1H, *N*–CH_2, J_1=5.8 Hz, J_2=15.8 Hz), 4.09–4.13 (dd, 1H, NCH, J_1=5.8 Hz, J_2=9.0 Hz), 5.14–5.19 (m, 2H, CH_2), 5.73–5.79 (m, 1H, –CH), 7.28–7.74 (m, 4H, Ar–H), 9.56 (s, 1H, CHO); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 10.6, 19.9, 21.4, 48.4, 67.4, 119.6, 127.0, 129.6, 133.6, 137.3, 143.6, and 199.8. Mass spectrum (EI, 70 eV): *m*/*z*, 281.38 (M^+). Anal. Calcd for $C_{14}H_{19}NO_3S$: C, 59.75; H, 6.80; N, 4.97%. Found: C, 59.84; H, 6.67; N, 5.06%.

*4.9.2. 2-(N-Allyl-N-benzenesulfonylamino)butanal **25b***

Pale yellow liquid, 96% (12.83 g); IR (KBr): 1332, 1169, and 1735 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 0.80 (t, 3H, CH_3), 1.42–1.52 (m, 1H, CH_2), 2.02–2.04 (m, 1H, CH_2), 3.73–3.80 (dd, 1H, *N*–CH_2, J_1=6.4 Hz, J_2=15.8 Hz), 3.89–3.95 (dd, 1H, *N*–CH_2, J_1=6.4 Hz, J_2=15.8 Hz), 4.09–4.12 (dd, 1H, *N*CH, J_1=5.4 Hz, J_2=1.28 Hz), 5.14–5.19 (m, 2H, CH_2), 5.71–5.81 (m, 1H, CH), 7.50–7.86 (m, 5H, Ar–H), 9.56 (s, 1H, CHO); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 10.7, 20.0, 48.6, 67.6, 119.8, 127.1, 129.2, 132.9, 133.7, 140.3, and 199.8. Mass spectrum (EI, 70 eV): *m*/*z*, 267.35 (M^+). Anal. Calcd for $C_{13}H_{17}NO_3S$: C, 58.40; H, 6.40; N, 5.24%. Found: C, 58.29; H, 6.49; N, 5.36%.

4.10. Synthesis of *cis*-6-ethyl-5-arylsulfonyloctahydropyrrolo[3,4-*b*]pyrroles 26a–e

*4.10.1. cis-1-Phenyl-5-tosyl-6-ethyloctahydropyrrolo[3,4-b]-pyrrole **26a***

Pale yellow crystals, 68% (0.251 g); mp: 128–130 °C; IR (KBr): 1336 and 1167 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.15 (t, 3H, CH_3), 1.62–1.66 (m, 1H), 1.75–1.79 (m, 3H), 2.35 (s, 3H, Ar–CH_3), 2.48–2.55 (m, 1H), 2.88–3.09 (m, 3H), 3.73–3.78 (m, 2H), 3.94–3.97 (t, 1H, J=6.6 Hz), 6.13–7.41 (m, 9H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 10.4, 21.4, 27.8, 28.3, 42.1, 46.8, 51.8, 65.1, 67.1, 112.6, 116.3, 127.2, 128.7, 129.3, 134.4, 142.6, and 145.7. Mass spectrum (EI, 70 eV): *m*/*z*, 370.17 (M^+). Anal. Calcd for $C_{21}H_{26}N_2O_2S$: C, 68.08; H, 7.07; N, 7.56%. Found: C, 68.19; H, 6.96; N, 7.49%.

*4.10.2. cis-1-(4-Bromophenyl)-5-tosyl-6-ethyl-octahydropyrrolo-[3,4-b]pyrrole **26b***

Pale yellow crystals, 69% (0.310 g); mp: 162–164 °C; IR (KBr): 1336 and 1167 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.13 (t, 3H, CH_3), 1.67–1.69 (m, 1H), 1.73–1.76 (m, 3H), 2.36 (s, 3H, Ar–CH_3), 2.51–2.53 (m, 1H), 2.89–3.10 (m, 3H), 3.69–3.78 (m, 2H), 3.87–3.90 (t, 1H, J=5.8 Hz), 6.00–7.42 (m, 8H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 10.4, 21.4, 27.9, 28.2, 42.2, 46.9, 51.8, 64.6, 67.2, 108.3, 114.1, 127.2, 129.3, 131.4, 134.5, 142.8, and 144.6. Mass spectrum (EI, 70 eV): *m*/*z*, 450.40 (M^+). Anal. Calcd for $C_{21}H_{25}N_2O_2SBr$: C, 56.12; H, 5.61; N, 6.23%. Found: C, 56.27; H, 5.53; N, 6.17%.

*4.10.3. cis-1-(4-Bromophenyl)-5-benzenesulfonyl-6-ethyl-octahydropyrrolo[3,4-b]pyrrole **26c***

Pale yellow crystals, 67% (0.292 g); mp: 147–149 °C; IR (KBr): 1335 and 1169 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.15 (t, 3H, CH_3), 1.67–1.70 (m, 1H), 1.71–1.76 (m, 3H), 2.51–2.55 (m, 1H), 2.81–3.03 (m, 3H), 3.66–3.78 (m, 2H), 3.80–3.91 (t, 1H, J=6.0 Hz), 6.12–7.43 (m, 9H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 10.4, 27.7, 28.3, 42.8, 46.6, 51.4, 64.1, 67.8, 108.3, 114.6, 127.8, 129.0, 131.0, 134.7, 142.8, and 143.6. Mass spectrum (EI, 70 eV): *m*/*z*, 436.06 (M^+). Anal. Calcd for $C_{20}H_{23}N_2O_2SBr$: C, 55.17; H, 5.32; N, 6.43%. Found: C, 55.09; H, 5.44; N, 6.31%.

*4.10.4. cis-1-(4-Chlorophenyl)-5-tosyl-6-ethyl-octahydropyrrolo[3,4-b]pyrrole **26d***

Pale yellow crystals, 64% (0.259 g); mp: 145–147 °C; IR (KBr): 1336 and 1166 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.12 (t, 3H, CH_3), 1.64–1.67 (m, 1H), 1.74–1.77 (m, 3H), 2.34 (s, 3H, Ar–CH_3), 2.51–2.54 (m, 1H), 2.87–3.10 (m, 3H), 3.68–3.77 (m, 2H), 3.87–3.90 (t, 1H, J=6.2 Hz), 6.04–7.47 (m, 8H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 10.4, 21.4, 27.9, 28.3, 42.2, 46.9, 51.8, 64.6, 67.3, 108.5, 114.1, 127.2, 129.3, 131.4, 134.5, 142.8, and 143.9. Mass spectrum (EI, 70 eV): *m*/*z*, 404.93 (M^+). Anal. Calcd for $C_{21}H_{25}N_2O_2SCl$: C, 62.28; H, 6.22; N, 6.92%. Found: C, 62.17; H, 6.33; N, 6.81%.

*4.10.5. cis-1-(4-Fluorophenyl)-5-benzenesulfonyl-6-ethyl-octahydropyrrolo[3,4-b]pyrrole **26e***

Pale yellow crystals, 66% (0.246 g); mp: 113–115 °C; IR (KBr): 1335 and 1170 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.14 (t, 3H, CH_3), 1.67–1.71 (m, 1H), 1.72–1.76 (m, 3H), 2.53–2.56 (m, 1H), 2.85–3.03 (m, 3H), 3.69–3.78 (m, 2H), 3.87–3.94 (t, 1H, J=6.2 Hz), 6.17–7.40 (m, 9H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 10.4, 27.8, 28.5, 42.9, 46.7, 51.7, 64.1, 67.8, 108.4, 114.8, 127.6, 129.5, 131.4, 134.7, 142.8, and 141.1. Mass spectrum (EI, 70 eV): *m*/*z*, 374.15 (M^+). Anal. Calcd for $C_{20}H_{23}N_2O_2SF$: C, 64.15; H, 6.19; N, 7.48%. Found: C, 64.27; H, 6.08; N, 7.40%.

4.11. Synthesis of *cis*-perhydrothiazolo[3′,4′-2,3]pyrrolo-[4,5-*c*]pyrrole derivatives

A mixture of 2-(*N*-allyl-*N*-tosylamino)butanal **6a** (1.0 mmol) and thiazolidine-4-carboxylic acid **27** (1.5 mmol) in 30 mL of dry toluene was refluxed under Dean–Stark conditions till the completion of the reaction (2–5 h). The reaction mixture was then concentrated under reduced pressure. The residue was extracted with dichloromethane (2×20 mL) and water (2×20 mL). The organic layer was washed with brine solution (2×20 mL), dried over anhydrous sodium sulfate, and concentrated in vacuum. The residue was then subjected to column chromatography (silica gel, 100–200 mesh) with hexane–ethylacetate (8:2) to obtain the cycloadducts **28** and **29** (R_f=0.4–0.6).

*4.11.1. cis-6-N-p-Tosylperhydrothiazolo[3′,4′-2,3]pyrrolo-[4,5-c]pyrrole **28***

Colorless solid, 74% (0.240 g); mp: 127–129 °C; IR (KBr): 1338 and 1166 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.08–2.10 (m, 2H), 2.43 (s, 3H, Ar–CH_3), 2.37–2.49 (m, 1H), 2.80–3.02 (m, 4H), 3.16–3.20 (dd, 1H, J_1=3.5 Hz, J_2=9.3 Hz), 3.25–3.28 (m, 1H), 3.38–3.40 (m, 1H), 3.57–3.62 (dt, 1H, J_1=2.7 Hz, J_2=9.2 Hz), 4.01 (d, 1H, J=9.8 Hz), 4.21 (d, 1H, J=9.8 Hz), 7.34–7.69 (m, 4H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.5, 35.5, 36.6, 40.9, 53.9, 54.7, 59.1, 65.5, 71.3, 127.9, 129.5, 129.6, 132.3, and 143.5. Mass spectrum (EI, 70 eV): *m*/*z*, 324.80 (M^+). Anal. Calcd for $C_{15}H_{20}N_2O_2S_2$: C, 55.53; H, 6.21; N, 8.63%. Found: C, 55.44; H, 6.29; N, 8.58%.

*4.11.2. cis-6-N-Benzenesulfonylperhydrothiazolo-[3′,4′-2,3]pyrrolo[4,5-c]pyrrole **29***

Colorless solid, 70% (0.217 g); mp: 116–119 °C; IR (KBr): 1337 and 1168 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.07–2.10 (m, 2H), 2.37–2.42 (m, 1H), 2.80–3.05 (m, 4H), 3.18–3.19 (dd, 1H, J_1=3.6 Hz, J_2=9.8 Hz), 3.25–3.28 (m, 1H), 3.40–3.43 (m, 1H), 3.52–3.57 (m, 1H), 4.00 (d, 1H, J=9.8 Hz), 4.19 (d, 1H, J=9.8 Hz), 7.52–7.88 (m, 5H,

Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 35.4, 36.6, 45.6, 53.8, 54.6, 58.9, 65.4, 71.1, 126.9, 127.7, 128.8, 128.9, 132.7, and 135.2. Mass spectrum (EI, 70 eV): *m*/*z*, 310.08 (M^+). Anal. Calcd for $C_{14}H_{18}N_2O_2S_2$: C, 54.17; H, 5.84; N, 9.02%. Found: C, 54.10; H, 5.89; N, 8.85%.

4.12. Synthesis of *cis*-(2-aryl)-perhydrothiazolo[3′,4′-2,3]-pyrrolo[4,5-*c*]pyrrole derivatives 31a–f and 32a–f

Syntheses of the title compounds were accomplished in good yields by adopting the procedure described in Section 4.11 by replacing various 2-aryl-thiazolidine-4-carboxylic acids **30a–f** with thiazolidine-4-carboxylic acid (R_f=0.5–0.7).

4.12.1. cis-2-Phenyl-6-N-p-tosylperhydrothiazolo[3′,4′-2,3]-pyrrolo[4,5-c]pyrrole ***31a***

Brown colored viscous liquid, 70% (0.280 g); IR (KBr): 1340, 1170 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.01–2.11 (m, 2H), 2.43 (s, 3H, Ar–CH_3), 2.57–2.60 (m, 1H), 2.85–2.99 (m, 4H), 3.08–3.23 (m, 3H), 3.39–3.67 (dt, 1H, J_1=2.5 Hz, J_2=9.0 Hz), 5.35 (s, 1H), 7.15–7.70 (m, 9H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.3, 34.0, 37.0, 41.0, 52.0, 54.6, 67.3, 68.9, 120.3, 127.1, 128.4, 129.0, 131.3, 131.9, and 142.9. Mass spectrum (EI, 70 eV): *m*/*z*, 400.56 (M^+). Anal. Calcd for $C_{21}H_{24}N_2O_2S_2$: C, 62.97; H, 6.04; N, 6.99%. Found: C, 62.90; H, 6.11; N, 6.90%.

4.12.2. cis-2-(p-Methyl)-phenyl-6-N-p-tosylperhydrothiazolo-[3′,4′-2,3]pyrrolo[4,5-c]pyrrole ***31b***

Colorless solid, 68% (0.281 g); mp: 112–115 °C; IR (KBr): 1339 and 1165 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.01–2.10 (m, 2H), 2.32 (s, 3H, Ar–CH_3), 2.44 (s, 3H, Ar–CH_3), 2.56–2.61 (m, 1H), 2.84–2.88 (m, 1H), 2.96–3.01 (m, 1H), 3.10–3.24 (m, 3H), 3.39–3.50 (m, 2H), 3.71–3.73 (dt, 1H, J_1=2.4 Hz, J_2=9.4 Hz), 5.43 (s, 1H), 7.04–7.71 (m, 8H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.0, 21.5, 34.9, 38.7, 41.0, 53.6, 54.7, 67.3, 69.1, 126.5, 127.8, 128.7, 129.6, 132.7, 136.8, 140.1, and 143.0. Mass spectrum (EI, 70 eV): *m*/*z*, 414.58 (M^+). Anal. Calcd for $C_{22}H_{26}N_2O_2S_2$: C, 63.74; H, 6.32; N, 6.76%. Found: C, 63.82; H, 6.25; N, 6.67%.

4.12.3. cis-2-(p-Methoxy)-phenyl-6-N-p-tosylperhydrothiazolo-[3′,4′-2,3]pyrrolo[4,5-c]pyrrole ***31c***

Colorless solid, 67% (0.288 g); mp: 117–119 °C; IR (KBr): 1340 and 1170 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.99–2.06 (m, 2H), 2.43 (s, 3H, Ar–Me), 2.54–2.63 (m, 1H), 2.80–2.87 (m, 1H), 2.94–3.00 (m, 1H), 3.11–3.28 (m, 3H), 3.41–3.50 (m, 2H), 3.67–3.71 (dt, 1H, J_1=2.5 Hz, J_2=9.3 Hz), 3.73 (s, 3H, Ar–OCH_3), 5.44 (s, 1H), 7.00–7.69 (m, 8H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.3, 34.7, 37.2, 38.2, 41.8, 53.0, 54.5, 67.4, 69.0, 126.9, 127.9, 127.4, 128.4, 128.2, 132.4, 135.9, 136.7, and 143.1. Mass spectrum (EI, 70 eV): *m*/*z*, 430.14 (M^+). Anal. Calcd for $C_{22}H_{26}N_2O_3S_2$: C, 61.37; H, 6.09; N, 6.51%. Found: C, 61.30; H, 6.15; N, 6.60%.

4.12.4. cis-2-(p-Chloro)-phenyl-6-N-p-tosylperhydrothiazolo-[3′,4′-2,3]pyrrolo[4,5-c]pyrrole ***31d***

Colorless solid, 73% (0.318 g); mp: 127–130 °C; IR (KBr): 1339 and 1168 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.02–2.16 (m, 2H), 2.42 (s, 3H, Ar–CH_3), 2.57–2.62 (m, 1H), 2.87–3.00 (m, 4H), 3.07–3.48 (m, 3H), 3.67 (dt, 1H, J_1=2.3 Hz, J_2=9.2 Hz), 5.39 (s, 1H), 7.18–7.70 (m, 8H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 30.9, 34.9, 38.8, 41.1, 53.6, 54.6, 67.3, 69.1, 117.6, 127.1, 127.8, 128.1, 128.1, 129.6, 132.7, 141.7, and 143.5. Mass spectrum (EI, 70 eV): *m*/*z*, 436.21 (M^+). Anal. Calcd for $C_{21}H_{23}N_2O_2S_2Cl$: C, 57.98; H, 5.33; N, 6.44%. Found: C, 58.06; H, 5.42; N, 6.38%.

4.12.5. cis-2-(p-Bromo)-phenyl-6-N-p-tosylperhydrothiazolo-[3′,4′-2,3]pyrrolo[4,5-c]pyrrole ***31e***

Colorless solid, 70% (0.336 g); mp: 159–161 °C; IR (KBr): 1338 and 1161 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.02–2.10 (m, 2H), 2.45 (s, 3H, Ar–CH_3), 2.57–2.61 (m, 1H), 2.87–2.99 (m, 4H), 3.08–3.22 (m, 3H), 3.37–3.69 (dt, 1H, J_1=2.4 Hz, J_2=9.2 Hz), 5.37 (s, 1H), 7.15–7.70 (m, 8H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 34.8, 38.8, 41.1, 53.6, 54.6, 67.3, 69.0, 120.9, 127.8, 128.4, 129.6, 131.1, 132.7, 142.2, and 143.5. Mass spectrum (EI, 70 eV): *m*/*z*, 480.87 (M^+). Anal. Calcd for $C_{21}H_{23}N_2O_2S_2Br$: C, 52.61; H, 4.84; N, 5.84%. Found: C, 52.69; H, 4.77; N, 5.77%.

4.12.6. cis-2-(p-Fluoro)-phenyl-6-N-p-tosylperhydrothiazolo-[3′,4′-2,3]pyrrolo[4,5-c]pyrrole ***31f***

Pale brown solid, 70% (0.292 g); mp: 138–140 °C; IR (KBr): 1340 and 1170 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.02–2.11 (m, 2H), 2.43 (s, 3H, Ar–CH_3), 2.55–2.61 (m, 1H), 2.87–3.00 (m, 4H), 3.07–3.22 (m, 3H), 3.38–3.69 (dt, 1H, J_1=2.4 Hz, J_2=9.2 Hz), 5.40 (s, 1H), 7.08–7.69 (m, 8H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.4, 34.9, 38.7, 41.0, 45.7, 53.6, 54.6, 67.2, 69.0, 114.8, 117.6, 127.1, 127.8, 128.3, 129.6, 129.7, 132.9, 138.8, 143.5, 160.5, and 163.0. Mass spectrum (EI, 70 eV): *m*/*z*, 418.55 (M^+). Anal. Calcd for $C_{21}H_{23}N_2O_2S_2F$: C, 60.26; H, 5.54; N, 6.69%. Found: C, 60.34; H, 5.48; N, 6.77%.

4.12.7. cis-2-Phenyl-6-N-benzenesulfonylperhydrothiazolo-[3′,4′-2,3]pyrrolo[4,5-c]pyrrole ***32a***

Brown colored viscous liquid, 68% (0.262 g); IR (KBr): 1344 and 1169 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.00–2.11 (m, 2H), 2.57–2.60 (m, 2H), 2.85–2.97 (m, 4H), 3.08–3.23 (m, 4H), 3.39–3.67 (dt, 1H, J_1=2.5 Hz, J_2=9.0 Hz), 5.35 (s, 1H), 7.05–7.70 (m, 10H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.5, 34.3, 37.0, 41.9, 52.4, 54.6, 67.7, 68.2, 120.5, 127.5, 128.4, 129.0, 130.6, 131.3, and 131.9. Mass spectrum (EI, 70 eV): *m*/*z*, 386.53 (M^+). Anal. Calcd for $C_{20}H_{22}N_2O_2S_2$: C, 62.15; H, 5.74; N, 7.25%. Found: C, 62.22; H, 5.80; N, 7.18%.

4.12.8. cis-2-(p-Methyl)-phenyl-6-N-benzenesulfonylper-hydrothiazolo[3′,4′-2,3]pyrrolo[4,5-c]pyrrole ***32b***

Colorless solid, 71% (0.284 g); mp: 130–140 °C; IR (KBr): 1338 and 1161 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.99–2.07 (m, 2H), 2.32 (s, 3H, Ar–CH_3), 2.55–2.60 (m, 1H), 2.80–2.87 (m, 1H), 2.95–2.99 (m, 1H), 3.13–3.27 (m, 3H), 3.41–3.50 (m, 2H), 3.69–3.71 (dt, 1H, J_1=2.5 Hz, J_2=9.4 Hz), 5.47 (s, 1H), 7.03–7.82 (m, 9H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.0, 34.9, 38.6, 41.1, 53.6, 54.7, 67.4, 69.0, 126.5, 127.0, 127.7, 128.7, 128.9, 132.7, 135.8, 136.8, and 140.1. Mass spectrum (EI, 70 eV): *m*/*z*, 400.16 (M^+). Anal. Calcd for $C_{21}H_{24}N_2O_2S_2$: C, 62.97; H, 6.04; N, 6.99%. Found: C, 62.89; H, 6.11; N, 6.90%.

4.12.9. cis-2-(p-Methoxy)-phenyl-6-N-benzenesulfonylper-hydrothiazolo[3′,4′-2,3]pyrrolo[4,5-c]pyrrole ***32c***

Colorless solid, 69% (0.287 g); mp: 141–143 °C; IR (KBr): 1339 and 1167 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.97–2.06 (m, 2H), 2.55–2.63 (m, 1H), 2.81–2.87 (m, 1H), 2.94–3.00 (m, 1H), 3.12–3.28 (m, 3H), 3.40–3.50 (m, 2H), 3.68–3.71 (dt, 1H, J_1=2.5 Hz, J_2=9.3 Hz), 3.73 (s, 3H, Ar–OCH_3), 5.45 (s, 1H), 7.03–7.82 (m, 9H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 34.9, 37.0, 38.1, 41.0, 53.5, 54.5, 67.0, 69.0, 126.7, 127.7, 127.2, 128.8, 128.8, 132.1, 135.9, 136.7, and 142.1. Mass spectrum (EI, 70 eV): *m*/*z*, 416.13 (M^+). Anal. Calcd for $C_{21}H_{24}N_2O_3S_2$: C, 60.55; H, 5.81; N, 6.72%. Found: C, 60.64; H, 5.90; N, 6.65%.

4.12.10. cis-2-(p-Chloro)-phenyl-6-N-benzenesulfonylper-hydrothiazolo[3′,4′-2,3]pyrrolo[4,5-c]pyrrole ***32d***

Colorless solid, 71% (0.299 g); mp: 118–120 °C; IR (KBr): 1339 and 1167 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.99–2.07 (m, 2H), 2.56–2.61 (m, 1H), 2.85–2.87 (m, 1H), 2.94–2.98 (m, 1H), 3.12–3.24 (m, 3H), 3.40–3.48 (m, 2H), 3.67–3.69 (dt, 1H, J_1=2.4 Hz, J_2=9.5 Hz), 5.39 (s, 1H), 7.20–7.82 (m, 9H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 34.9, 38.7, 41.1, 53.6, 54.7, 67.4, 69.0, 72.6, 127.7, 127.8, 128.1, 128.6, 128.9, 129.0, 130.7, 132.7, 135.7, and 141.6. Mass spectrum (EI,

70 eV): *m*/*z*, 424.30 (M^+). Anal. Calcd for $C_{20}H_{21}N_2O_2S_2Cl$: C, 57.06; H, 5.03; N, 6.65%. Found: C, 57.14; H, 5.10; N, 6.58%.

4.12.11. cis-2-(p-Bromo)-phenyl-6-N-benzenesulfonylperhydrothiazolo[3′,4′-2,3]pyrrolo[4,5-c]pyrrole ***32e***

Colorless solid, 69% (0.323 g); mp: 129–131 °C; IR (KBr): 1338 and 1166 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.00–2.13 (m, 2H), 2.54–2.63 (m, 1H), 2.85–2.99 (m, 4H), 3.08–3.23 (m, 3H), 3.41–3.70 (dt, 1H, J_1=2.5 Hz, J_2=9.3 Hz), 5.39 (s, 1H), 7.16–7.71 (m, 9H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 34.8, 38.5, 41.4, 53.4, 54.9, 67.3, 69.0, 120.9, 127.7, 128.3, 129.6, 131.1, 132.7, 142.2, and 143.5. Mass spectrum (EI, 70 eV): *m*/*z*, 468.12 (M^+). Anal. Calcd for $C_{20}H_{21}N_2O_2S_2Br$: C, 51.61; H, 4.55; N, 6.02%. Found: C, 51.57; H, 4.61; N, 5.93%.

4.12.12. cis-2-(p-Fluoro)-phenyl-6-N-benzenesulfonylperhydrothiazolo[3′,4′-2,3]pyrrolo[4,5-c]pyrrole ***32f***

Pale brown solid, 72% (0.291 g); mp: 135–137 °C; IR (KBr): 1340 and 1166 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.99–2.12 (m, 2H), 2.57–2.61 (m, 1H), 2.86–2.88 (m, 1H), 2.95–2.99 (m, 1H), 3.10–3.26 (m, 3H), 3.41–3.50 (m, 2H), 3.67–3.69 (dt, 1H, J_1=2.5 Hz, J_2=9.4 Hz), 5.40 (s, 1H), 6.89–7.83 (m, 9H, Ar–H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 30.9, 34.9, 38.7, 41.1, 53.6, 54.7, 67.3, 68.9, 114.7, 114.9, 127.7, 128.3, 128.3, 129.0, 132.7, 135.7, 138.8, 160.6, and 163.0. Mass spectrum (EI, 70 eV): *m*/*z*, 404.52 (M^+). Anal. Calcd for $C_{20}H_{21}N_2O_2S_2F$: C, 59.38; H, 5.23; N, 6.93%. Found: C, 59.30; H, 5.32; N, 6.84%.

Acknowledgements

The authors thank Department of Science and Technology (DST), New Delhi, India for financial support. One of the authors M.P. thanks Council of Scientific and Industrial Research (CSIR), New Delhi, for the financial support as the award of Senior Research Fellowship (SRF).

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