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HIGHLY EFFICIENT STEREOSELECTIVE SYNTHESIS OF β-AMINO ACIDS BY ASYMMETRIC METHOD

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ABSTRACT

β-amino acids are the important building blocks for the production of medicines, a precursor for β lactams and building blocks for oligomers. The present study illustrates, novel and efficient asymmetric method for the synthesis of β amino acids has been described. So, the present work deals with the transformation of chiral aspartic acid to β, γ-aziridine carboxylic acid ester, a key precursor followed by regio-and stereoselective ring opening would produce a large number of β-amino acids. This discovery could provide a scope for the large-scale preparation of β-amino acids and their derivatives

Keywords: β-amino acids, Synthesis, Asymmetric, Stereoselective

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INTRODUCTION

In recent years the development of β-amino acids has played a significant role in medicinal chemistry particularly biopeptides containing β-amino acids have numerous biological functions and its novel synthetic accessibility are needed[1]. β-amino acids are the precursors of β-lactams and also building blocks for oligomers "foldamers"[2]. Seebach[3] and Gellman[4] have reported the oligomers of β-amino acids are similar to α-peptides and exhibit characteristics of peptidomimetics[5]. Different strategies have reported for the asymmetric synthesis of β-amino acids by using various catalyst[6]. From the literature, it is evident that the asymmetric synthesis of β-amino acids carried out by using $Ru(O_2CCH_3)_2$ as catalyst[7]. Yang *et al.,* has reported the synthesis of β-amino acids and its derivatives by oxidative cleavage of chiral dihydro pyridinones[8]. β-amino acid esters are synthesized by using Vilsmeir-Haack reaction using different nucleophiles[9]. Liu has reported the novel chemical method for resolution of β-amino acids and the procedure is highly suitable for the synthesis antiviral drug moraviroc[10]. Synthesis of β-amino acids are reported by using various chiral auxiliaries viz., pseudoephedrine[11], hexahydrobenzoxazolidinone[2], (4S)-4-benzyl-1,3-oxazolidin-2-one[13].

β-amino acids have numerous pharmacological properties as antidiabetic, antifungal, anthelmintic, and antimicrobial peptides[14-16]. Some of the important bioactive compounds containing β-amino acids are taurine, TGF-β, Amyloid-β-peptide, β-defensins, β-amino amides, Fascins, β-thromboglobulins, β-alanine, carnosine, β-Lactam. Peptides containing b-amino acids have gained significant attention in the field of drug design[17]. The presentation describes the synthesis of regio- and stereoselective synthesis of β-amino acids by asymmetric acids with the opening of the aziridine ring by employing different catalyst as shown in Scheme-1

EXPERIMENTAL

Material and Methods

All the chemicals and reagents were purchased from Aldrich Chemicals, USA. The characterization was done by ^{1}H-NMR on Bruker-NMR spectrophotometer at 400MHz.

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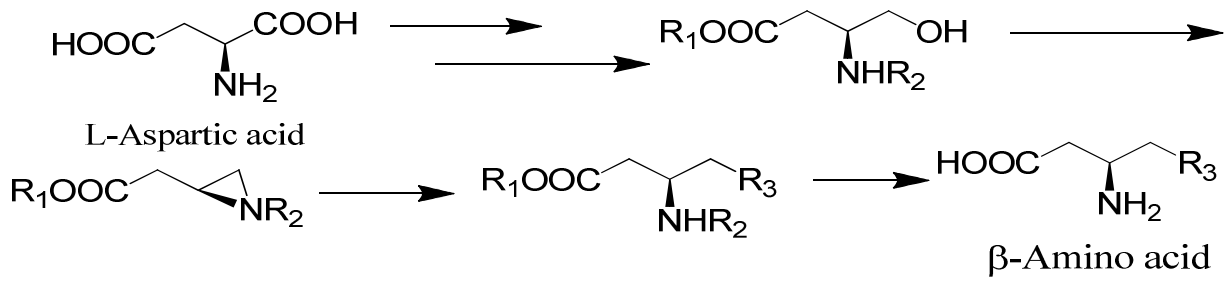
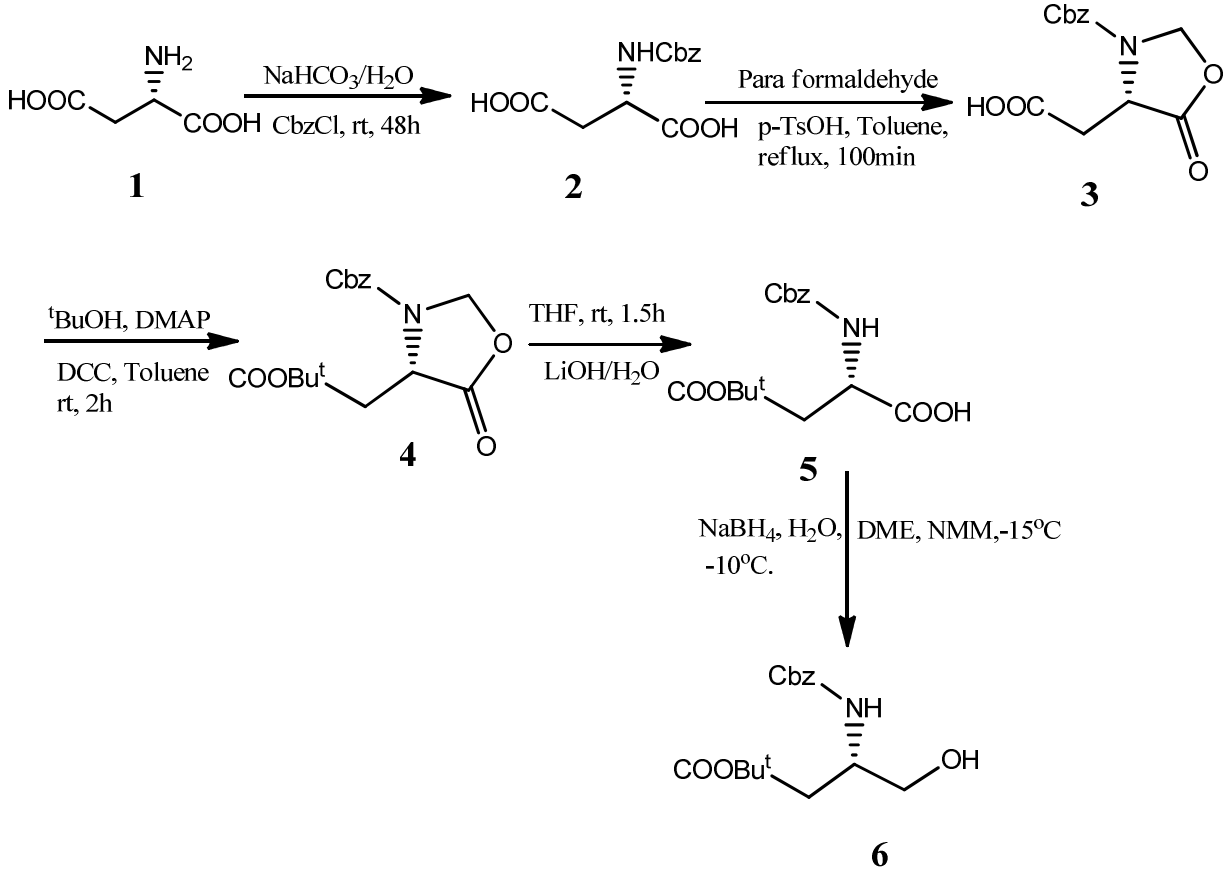


Scheme-1: Overall Reaction



Scheme-2: Synthesis of Intermediate Compound 6

General Procedure

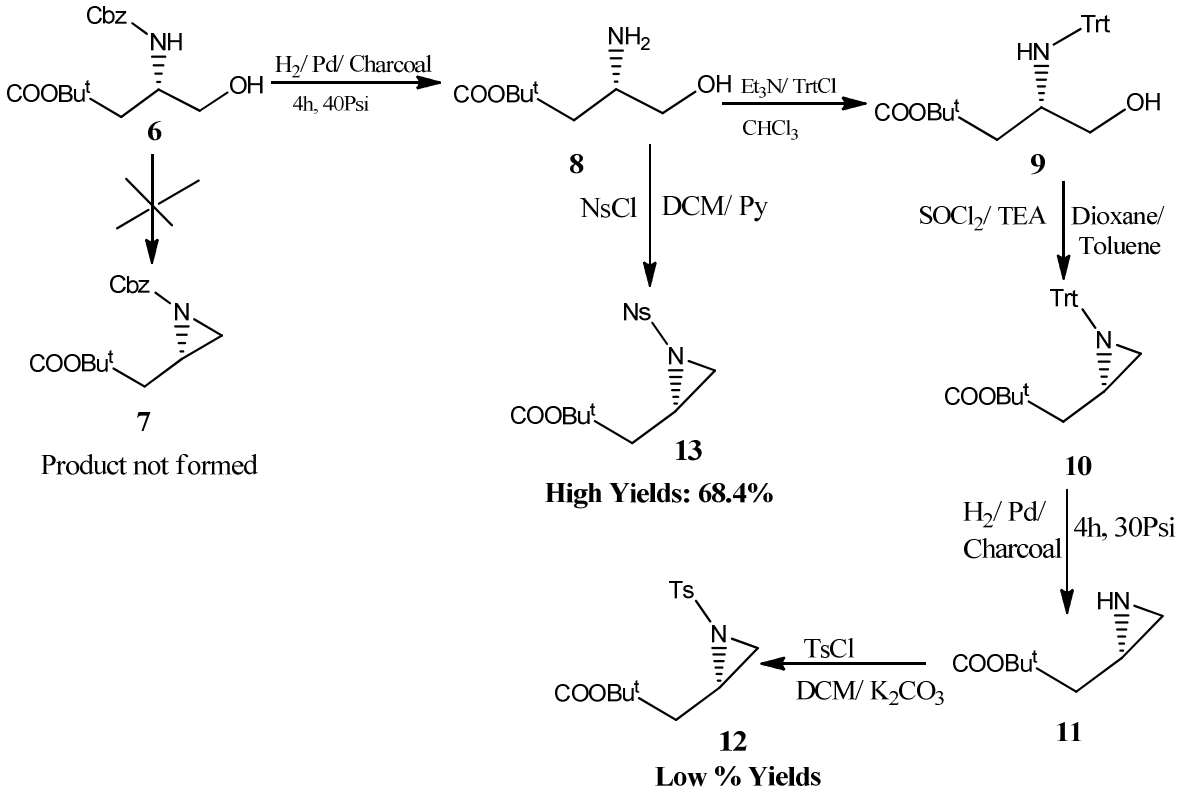
Synthesis of L-N-benzyloxycarbonyl-aspartic acid (2)

A solution of $NaHCO_3$ (18g, 210mmoles) in 258mL of bidistilled H_2O is added with L-aspartic acid (**1**)(10g, 75mmoles). The solution is cooled to 0°C, and then added with 1.7eq of benzyl chloroformate (18.2mL, 127.5mmoles) using magnetic stirring. The solution stirred at room temperature for 48h and the resulting mixture was ether washed and the aqueous phase is treated with 6N HCl and subsequently extracted with Ethyl acetate and dried over dry Na_2SO_4. R_f=0.6 (*n*-BuOH: Glacial AcOH: Water (3:1:1) Yield: 59.73%. ^{1}H NMR-400MHz in$CDCl_3$; δ=7.2997-7.3661 (m, 6H), 5.2883(s, 1H), 5.1110 (s, 2H), 3.1030 (s, 1H), 2.8778 (d, *J*=17.44Hz, 1H).

Synthesis of 2-(3-(benzyloxycarbonyl)-5-oxooxazolidin-4-yl)acetic acid(3)

N-C*bz*-L-aspartic acid (**2**) (1.9g, 7.17mmoles) was suspended in 108mL toluene and paraformaldehyde (1.34g, 44.88mmoles) and p-toluenesulphonicacid (136mg, 0.717mmoles) were added. The above mixture was refluxed for 2hrs in Dean-stark apparatus. R_f= 0.3by 2:8 EtOAc: Hexane as mobile phase.

Yield 5.5g (87.73%) of oil. The resultant product was confirmed by LC-MS $[M-H^+]^+$ 278 and ^1H NMR-400MHz in $CDCl_3$; δ=7.3562 (d, *J*=4.88, 5H), 5.5038 (s, 2H), 5.1377-5.2252 (m, 2H), 4.3620 (s, 1H), 3.6038 (d, *J*=17.8Hz, 2H).



Scheme-3: Synthesis of Aziridine

Synthesis of Benzyl-4-(2-tert-butoxy-2-oxoethyl)-5-oxooxazolidine-3-carboxylate (4)

To compound (**3**) (850mg, 2.972mmoles), 6mL toluene, DMAP (36.3mg, 0.2972mmoles), ^{t}BuOH (330mg, 4.458mmoles) were added under nitrogen atmosphere at 0°C, to it DCC (920mg, 4.458mmoles) was added and then stirred at rt for 2h. To it 50mL EtOAc was added, stirred for 16h.TLC at R_f=0.75 in 3:7 EtOAc: Hexane. Yield 56.5%. The product was confirmed by ^{1}HNMR-400MHz in $CDCl_3$; δ=7.3507 (s, 5H), 5.5047 (s, 1H), 5.3309 (s, 1H), 4.2821 (s, 1H), 2.9331 (d, *J*=16.48Hz, 2H), 1.4124 (s, 9H).

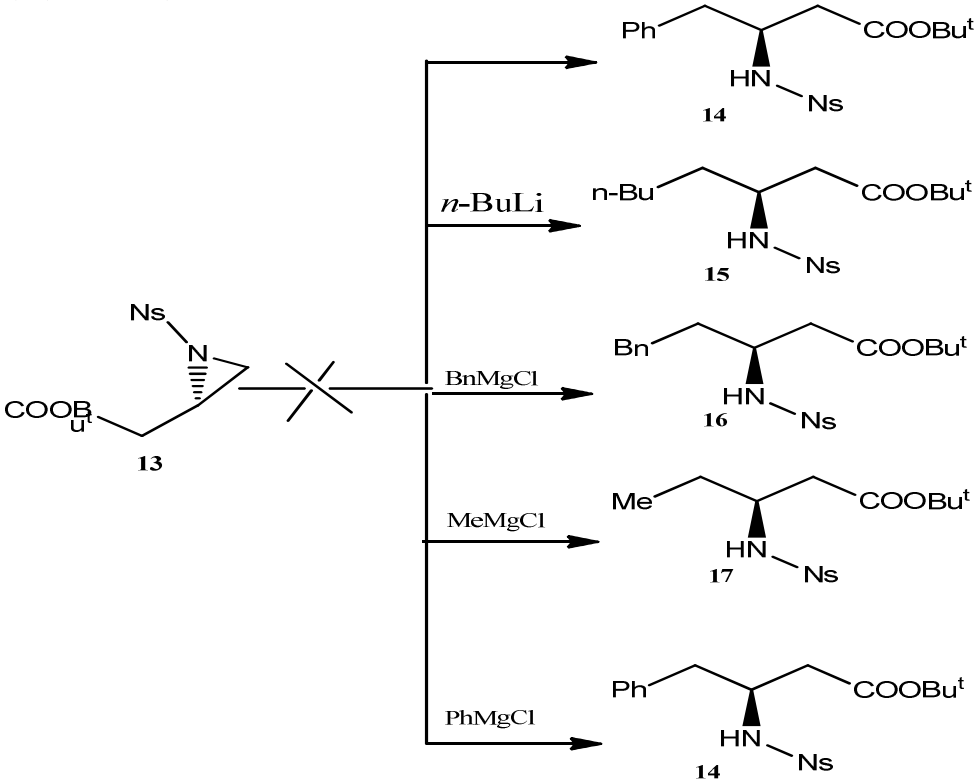
Synthesis of 2-(benzyloxycarbonyl)-4-tert-butoxy-4-oxobutanoic acid(5)

LiOH (6.3mg, 0.149mmoles) was dissolved in 0.5mL water and stirred for 5 min with a magnetic stirrer. To it compound (**4**) (50mg, 0.149mmoles) dissolved in 0.8mL THF was added and at rt for 1.5h is stirred. The solvent was evaporated, to this 2mL of$H_2O$and EtOAc was added. 8mL EtOAc was added and it was acidified with 2N HCl under ice-cold condition. Then extracted and dried over anhydrous Na_2SO_4 and evaporated *in vaccuo.* R_f=0.3 in 1:9 MeOH: DCM. Yield 86.4%. LC-MS $[M+H^+]^+$ 324.4 , $[M-H^+]^+$ 322.4 and by ^{1}H NMR-400MHz in [D_6]DMSO; δ=12.8237 (s, 1H), 7.5947 (d, *J*=8.44Hz, 1H), 7.3436 (s, 5H), 5.0382 (s, 2H), 4.3446 (dd, *J*=7.92, 8.28Hz, 1H), 2.6847 (dd, *J*=5.52, 4.92Hz, 1H), 2.5199 (d, *J*=16.52Hz, 1H), 1.3699 (s, 9H).

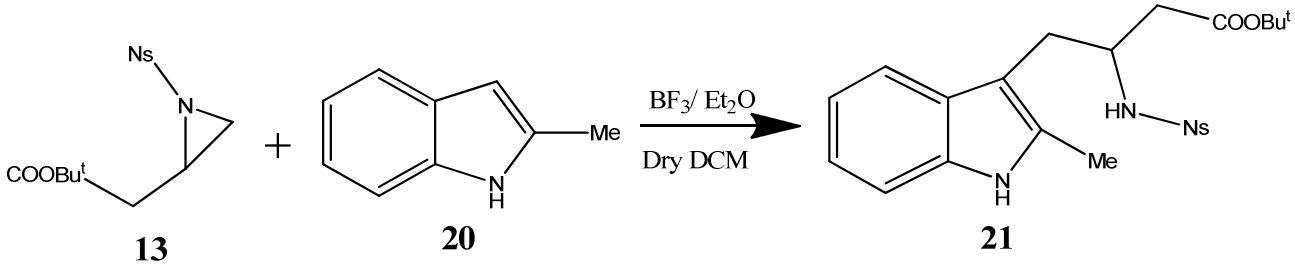
Synthesis of tert-butyl 3-(benzyloxycarbonyl)-4-hydroxybutanoate (6)

To a solution of compound **(5)** (1g, 3.095mmoles) in 25mL DME was added NMM (360µL, 3.249mmoles). The reaction was stirred for 10 min and cooled at -30oC. Isobutyl chloroformate(420µL, 3.249moles) was added drop wise. After stirring for 5min at this temperature, in $NaBH_4$solution (360mg,

9.285moles) was added with gas evolution. After stirring for 1.5h, 25mL water was added and the alcohol was extracted with EtOAc. R_f=0.6 (1:1 EtOAc: Hexane), the yield is 68%, as a yellow liquid. The product was confirmed by LC-MS $[M+H^+]^+$ 310.2 and by ^{1}H NMR-400MHz in $CDCl_3$; δ=7.3043-7.342 (m, 5H), 5.4525 (s, 1H), 5.099 (s, 2H), 4.071 (dd, *J*=6.92, 6.96Hz, 1H), 3.7144 (s, 2H), 2.5324-2.6007 (m, 2H), 1.4267 (s, 9H). (Scheme-2)



Scheme-4: Opening of Aziridine Ring with Gilman Reagent



Scheme-5: Optimized Reaction for the opening of Aziridine Ring

Synthesis of benzyl-2-(2-tert-butoxy-2-oxoethyl)aziridine-1-carboxylate (7)

To the solution of Ph_3P (102mg, 0.03878mmoles) in 1mL THF, cooled and added DIBAD (140mg, 0.684mmoles) over 30min under argon atmosphere. A solution of compound (**6**) (60mg, 0.1939mmoles) in 0.5mL THF was added drop wise over 15 min at the same temperature. After 1h at 0ºC, and stirred at rt for 48h. The reaction was monitored by using TLC with 1:1 EtOAc: Hexane. It was observed that starting material was not consumed, but two new spots with R_f=0.6 and 0.3 were separated by using 2:8 EtOAc: Hexane and 3:7 EtOAc: Hexane as mobile phases respectively. From LC-MS and data it was confirmed that desired product was not formed in the reaction.

Synthesis of tert-butyl 3-amino-4-hydroxybutanoate (8)

Hydrogenation of compound (**6**) (200mg, 0.646mmoles) was performed using palladium on charcoal (14mg) under a hydrogen atmosphere in abs EtOH(20mL) for 4h under the pressure of 40Psi. The reaction was determined by the consumption of starting material and formation of ninhydrin spot in TLC

(3:7 EtOAc: Hexane) and (3:1:1 *n*-BuOH: AcOH: H_2O). Evaporation of the solvent furnished the amino alcohol (**8**).Crude yield: 130mg.

Synthesis of tert-butyl 4-hydroxy-3-(tritylamino)butanoate (9)

To compound (**8**) (120mg, 0.6848mmoles) was dissolved in chloroform (2mL/mmol), triethylamine (0.2mL, 1.369mmoles) was added under argon gas. Then it is cooled at 0°C &tritylchloride (210mg, 0.753mmoles) was added and stirred for 4h. Further it is diluted with DCM and washed with $NaHCO_3$ (2 times) and brine.

^{1}H NMR-400MHz in $CDCl_3$; δ=3.4075 (dd, *J*=3.6, 3.44Hz, 1H), 3.129 (dd, *J*=5.8, 5.88Hz, 1H), 2.9752 (s, 1H), 1.7792-1.8767 (m, 2H), 1.3909 (s, 9H).

Synthesis of tert-butyl 2-(1-tritylaziridin-2-yl)acetate (10)

To compound (**9**) (70mg, 0.1678mmoles) was dissolved in dry toluene(3mL) and triethylamine (51mg, 0.503mmoles) was added under argon atmosphere. Then it is cooled to -50°C and drop by drop $SOCl_2$ (27.2mg, 0.20mmoles) was added. It is warmed at rt keeping the solution at basic.

^{1}H NMR 400 MHz in $CDCl_3$; δ=7.4699-7.5392(m, 6H), 7.2655-7.2860 (2H), 7.2282-7.2508 (m, 4H), 7.1652-7.2013 (m, 3H), 2.6679 (m, *J*=5.6, 5.56Hz, 1H), 2.4594 (m, *J*=6.36, 5.8Hz, 1H), 1.7016 (d, *J*=3.08Hz,1H), 1.5122-1.5617 (m, 1H), 1.3827 (s, 9H), 1.1280 (d, *J*=6.24Hz, 1H).

Synthesis of tert-butyl 2-(aziridin-2-yl)acetate (11)

Hydrogenation of compound (**10**) (150mg, 0.375mmoles) was performed using palladium on charcoal (8mg) under a hydrogen atmosphere in MeOH(20mL) for 4h under the pressure of 30Psi. The reaction was determined by the consumption of starting material and formation of ninhydrin spot in TLC (3:7 EtOAc: Hexane) (3:1:1 *n*-BuOH: AcOH: H_2O). Evaporation of the solvent furnished the amino alcohol (**11**) as oil.Yield: 60mg.

Synthesis of tert-butyl 2-(1-tosylaziridin-2-yl)acetate (12)

The synthesis has been carried out as reported earlier in the literature.

^{1}H NMR 400MHz $CDCl_3$; δ=7.8225 (d, *J*=7.92Hz, 2H), 7.3195 (d, *J*=7.88Hz, 2H), 3.0572 (dd, *J*=5.56, 5.96Hz, 1H), 2.4241 (s, 3H), 2.3455 (dd, *J*=6.08, 6.2Hz, 2H), 1.5593 (s, 1H), 1.381 (s, 9H), 1.2432 (s, 1H).

Synthesis of tert-butyl 2-(1-(4-nitrophenyl sulfonyl)aziridine-2-yl)acetate (13)

NsCl (3.477g, 15.69mmoles) was added to amino alcohols (**8**) (1.1g, 6.277mmoles) in dry 2:1 DCM/pyridine (1mL/mmole, 4.35 equivalents) at 0ºC and the stirred at rt for 2-4h. It was diluted with 190mL EtOAc and washed with 2M citric acid (3 x 11mL), which was subsequently extracted with EtOAc. The organic layer was combined, extracted with 2M KOH (6 x 21mL) and the aqu portions were subsequently extracted with EtOAc. The organic portions were combined and dried over anhydrous Na_2SO_4 and the solvent was removed to afford compound (**13**). The yield was 53.4%. LC-MS ($[M+H^+]^+$ 343.3 and by ^{1}H NMR-400MHz in $CDCl_3$; δ=8.3659 (d, *J*=8.24Hz , 2H), 8.1717 (d, *J*=8.28Hz, 2H), 3.1886 (s, 1H), 2.8270 (d, *J*=7Hz, 2H), 2.5081 (m, *J*=4.8, 4.64Hz, 1H), 2.2923 (m, *J*=7.44, 7.52Hz, 1H), 2.2212 (d, *J*=4.28Hz, 1H), 1.3405 (s, 9H).

Synthesis of tert-butyl 3-(4-nitrophenylsulfonamido)-4-phenylbutanoate(14)

PhLi (1.8M in Bu_2O, 0.152mL, 0.3045mmoles) was added to a suspension of CuCN (11mg, 0.1232mmoles) in 1mL THF argon at -78ºC. Then stirred for 10 min and then allowed to warm to rt. After 30min the cuprate was cooled to -78ºC and a solution of compound (**13**) (40mg, 0.116mmoles) in 1mL THF was added. The reaction was left for 3h at -78ºC, allow to warm at room temperature and stirred for 18h under argon. Water was added and the aqueous mixture was extracted with EtOAc (3 x 6mL). The combined organic fractions were dried over anhydrous Na_2SO_4 and the solvent was removed *in vacuo*.

Synthesis of tert-butyl 3-(4-nitrophenylsulfonamido)octanoate (15)
n-BuLi (0.49mL, 0.487mmoles) was added to a suspension of CuCN (30mg, 0.310mmoles) in 1mL THF at -78ºC using argon. The reaction was left at -78ºC for 30min and brought at rt. The mixture was cooled to -78ºC and a solution of compound (**13**) (50mg, 0.146mmoles) in 1mL THF was added and stirred for 15h. Then water is added and the filtrate is acidified to P^H 4
^{1}H NMR-400MHz in $CDCl_3$; δ=8.3651 (d, *J*=8.48Hz, 2H), 8.0482 (d, *J*=8.96Hz, 2H), 6.5709-6.6363 (m, 1H), 5.8147 (d, *J*=15.6Hz, 1H), 3.8289 (s, 2H), 1.4304 (s, 9H).

Synthesis of tert-butyl 3-(4-nitrophenylsulfonamido)-5-phenylpentanoate(16)
BnMgCl (3M in THF, 0.56mL, 0.438mmoles) and CuCN (19.6mg, 0.219mmoles) was added to a solution of compound (**13**) (5mg, 0.146mmoles) in 1.5mL THF under argon at -78ºC and stirred for 10min. Then water is added and the filtrate is acidified to P^H 4. From LC-MS data it was confirmed that the desired product was not formed in the reaction.

Synthesis of tert-butyl 3-(4-nitrophenylsulfonamido)pentanoate (17)
MeMgCl (3M in THF, 0.15mL, 0.438mmoles) and CuCN (19.6mg, 0.219mmoles) was added to a solution of compound (**13**) (5mg, 0.146mmoles) in 1.5mL THF under argon at -78ºC. The reaction was stirred at -78ºC for 10min and warmed at rt for 3h. 10mL Then water is added and the filtrate is acidified to P^H 4. From LC-MS data it was confirmed that the desired product was not formed in the reaction.

Synthesis of tert-butyl 3-(4-nitrophenylsulfonamido)-4-phenylbutanoate (14)
PhMgBr (3M in THF, 0.45mL, 0.438mmoles) was added to compound (**13**) (50mg, 0.146mmoles) in 1.5mL THF at -78ºC and stirred for 10min, warmed to rt and stirred for 3h. From TLC in 2:8 EtOAc: Hexane it was confirmed that starting material was not consumed.

Synthesis of tert-butyl 4-(2,3-dimethoxyphenyl)-3-(4-nitrophenylsulfonamido)butanoate (19)
A mixture of compound(**13**) (50mg, 0.146mmoles), compound(**18**) (24.17mg, 0.1752mmoles), $Cu(OTf)_2$ (5.28mg, 0.0146mmoles) in 2mL dry DCM were placed in a tightly capped test tube, and stirred for 48h at rt. It is diluted with 5mL water and extracted with EtOAc. The extract was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*.From LC-MS data it was confirmed that the desired product was not formed.

Synthesis of tert-butyl 4-(2-methyl-1H-indol-3-yl)-3-(4-nitrophenylsulfonamido)butanoate (21)
Method A
A mixture of compound(**13**) (50mg, 0.146mmoles), compound(**20**) (22.98mg, 0.175mmoles), $Cu(OTf)_2$ (5.28mg, 0.0146mmoles) in 2mL dry DCM were placed in test tube, and stirred for 48h at rt and diluted with 5mL water and extracted with EtOAc. From LC-MS data it was confirmed that the desired product was not formed.

Method B
A mixture of compound(**13**) (50mg, 0.146mmoles), compound(**20**) (35mg, 0.263mmoles), $Cu(OTf)_2$ (105mg, 0.292mmoles) in 2mL $CHCl_3$ were placed in a tightly capped test tube, and stirred for 24h at 78ºC. From the TLC it was observed that starting material was fully consumed. The reaction mixture was diluted with 5mL water and extracted with EtOAc and washed with brine. The extract was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (100-200G) with 2:8 EtOAc as the mobile phase. From LC-MS data it was confirmed that the desired product was not formed.

Method C
A mixture of compound(**13**) (50mg, 0.146mmoles), compound(**20**) (35mg, 0.263mmoles), $FeCl_3$ (5.6mg, 0.0146mmoles) in 2mL dry DCM were placed in a test tube, and stirred for 48h at rt and diluted with 5mL water. From LC-MS data it was confirmed that the desired product was not formed.

Method D

A mixture of compound (**13**) (50mg, 0.146mmoles), compound (**20**) (35mg, 0.263mmoles), $InCl_3$ (7.2mg, 0.0146mmoles) in 2mL dry DCM were placed in a tightly capped test tube, and stirred for 48h at rt. The TLC of this reaction was matched with a new spot formed with $FeCl_3$catalysed aziridine ring opening reaction.

Method E

A mixture of compound (**13**) (50mg, 0.146mmoles), compound (**20**) (39mg, 0.292mmoles) held at 0ºC under Nitrogen was added 0.7mL of BF_3etherate. After 45min, 3mL EtOAc is added. The resultant mixture was washed with 3mL saturated aqu Na_2CO_3 solution and with water (3 x 3mL). The organic phase was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Then purified by flash-chromatography on silica gel (100-200G) at R_f=0.3 by using 5% MeOH: DCM as the mobile phase. From the ^{1}H NMR data, it was confirmed that the desired product was formed. ^{1}H NMR-400MHz in [D_6]DMSO; δ=8.6874 (s, 1H), 4.3479 (dd, *J*=6.36, 6.08Hz, 1H), 4.0950 (s, 1H), 4.0220-4.0455 (m, 1H), 2.6693-2.7654 (m, 1H), 2.2471 (dd, *J*=4.32, 4.36Hz, 1H) and ^{1}H NMR-400MHz in D_2O exchange; δ=8.4202 (d, *J*=8.28Hz, 2H), 8.0619 (d, *J*=8.4Hz, 2H), 7.2692-7.3802 (m, 4H), 1.2868 (s, 3H), 1.2100 (s, 6H).

RESULTS AND DISCUSSION

The present study, the practical synthetic route for the asymmetric synthesis of β-amino acids have described. In the first step, the procedure involves the N-C*bz* protection of readily available, enantiopure L-Aspartic acid with of benzyl chloroformate, $NaHCO_3$ and H_2O to afford **2**. Cyclisation of N-C*bz*-L-aspartic acid **2** was done with the addition of toluene, paraformaldehyde &*p*-toluene sulphonic acid to afford **3.** Esterification of **3** was done with ^{t}BuOH, DMAP and DCC to afford **4**. Hydrolysis of **4** was done with LiOH, water and THF to afford **5**. Then reduction of **5** was done with DME, NMM, Isobutyl chloroformate and $NaBH_4$- H_2O to afford **6.** Nosylation of compound **6** was done by using Nosylchloride, dry 2:1 DCM/pyridine to afford **13**. This reaction was done successfully. Compound **13** was treated with different Grignard reagents, but the reaction was not successful. Then compound **13** was treated with 2-methyl indole with different catalysts like Cu(O*Tf*)$_2$, $FeCl_3$, $InCl_3$ in dry DCM. But the desired product was not formed. And finally compound **13** was treated with 2-methyl indole, Cu(O*Tf*)$_2$, BF3-etherate to afford compound **21**. From ^{1}H NMR it was confirmed that opening of aziridine ring was done successfully to give β-amino acids (Scheme-1).

Synthesis of Aziridine

Trial 1

Compound **6** was subjected to mitsunobu reaction with DEAD, Ph_3P and THF to afford **7**. But this reaction was not successful. This mitsunobu reaction was repeated with DIAD, DIBAD by changing the parameters. Starting material was not consumed in TLC but numerous new spots were formed and no product mass was found in LC-MS (Scheme-2).

Trial 2

C*bz* deprotection of compound **6** was done by hydrogenation using H_2/Pd/charcoal at a pressure of 40 Psi to afford **8**. This crude was used for N-Trt protection by using triethylamine, tritylchloride and chloroform to afford **9**.

Then compound **9** was treated with dry toluene, triethylamine and $SOCl_2$ to afford **10**. But this compound 10 was not stable and not favoring the stereospecific ring opening. So detritylation of trityl aziridine **10** was done by hydrogenation using H_2/Pd/charcoal at a pressure of 30 Psi to afford **11**. Then tosylation of compound **11** was done by using tosylchloride, activated Potassium carbonate and DCM to afford compound **12**. But here the yield was very poor.

Trial 3

Nosylation of compound **6** was done by using Nosylchloride, dry 2:1 DCM/pyridine to afford **13**. This reaction was done successfully.

The Opening of Aziridine Ring with Gilman Reagent

The compound **13** was treated with PhLi and CuCN in 2:1 ratio (Gilman reagent) to afford **14**. But the desired product was not formed. Then tried with *n*-BuLi and CuCN in 2:1 ratio to afford 15. But an alkene, probably *tert*-butyl 3-(4-nitro phenyl sulfonamido) but-3- enoate (Scheme-3).

The Opening of Aziridine Ring with a Grignard Reagent

Compound **13** was treated with different Grignard reagents, but the reaction was not successful. The opening of Aziridine ring using different catalysts and reagents are shown in Table-1.

Table-1: Opening of Aziridine ring using Different Catalysts

Reagent	Catalyst (CuCN)	Starting Material	Product
BnMgCl	No	Present in TLC but not in LC-MS	No of peaks in LC-MS CR900-3459-27
BnMgCl (3eq.)	1.5eq.	Present	CR900-3459-28
MeMgCl	1.5eq.	Consumed	No product CR900-3459-29A
PhMgCl	No	Present	Neither product nor new spot

Compound **13** was treated with dimethyl catechol, Cu(O*Tf*)$_2$ and dry DCM to afford compound **19**. But the reaction was failed. Then compound **13** was treated with 2-methyl indole with different catalysts like Cu(O*Tf*)$_2$, $FeCl_3$, $InCl_3$ in dry DCM. But the desired product was not formed. And finally compound **13** was treated with 2-methyl indole, Cu(O*Tf*)$_2$, BF3-etherate to afford compound **21**. From ^{1}H NMR it was confirmed that opening of aziridine ring was done successfully to give β-amino acids.

Optimized Reaction Conditions

The optimized reaction conditions as presented in the Scheme-4 are shown in Table-2. The desired product has formed by the Lewis catalyzed condensation of indole derivatives activated aziridine carboxylate the C-3 position of indole has invariably been found to attack the C-3 position of the aziridine.

Table-2: Optimized Reaction Conditions

S. No.	Catalyst	Solvent	Product (21)
1	$Cu(OTf)_2$	Dry DCM	Not Formed
2	$Cu(OTf)_2$	$CHCl_3$	Not Formed
3	$FeCl_3$	Dry DCM	Not Formed
4	$InCl_3$	Dry DCM	Mixture
5	BF_3/Et_2O	Dry DCM	Product Formed

CONCLUSION

Development of a versatile and efficient method for the synthesis of a variety of β-aminoacids from a common precursor is highly desirable. So present work deals with the transformation of chiral aspartic acid to β, γ-aziridine carboxylic acid ester, a key precursor followed by regio- and stereoselective aziridine ring opening by Gilman reagents would produce a large number of β-aminoacids. Moreover, both enantiomers of β-aminoacids can be synthesized by using commercially available both enantiomers of aspartic acid.

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