CHAPTER 2

Microwave Irradiated Ugi four-component reaction (Ugi-4CR): Expedited synthesis of Steroid-Amino Acid Conjugates-A Novel Class of Peptidomimetic Hybrid Compounds based on Seco-Steroids (A, B & D Ring Cleavage)
2.1: Introduction

Steroids on account of their enhanced and varied biological properties, the medicinal chemistry demands a promising challenge in their chemical transformations. In recent times the development of soft corticosteroids\textsuperscript{1, 2} applying retro-metabolic drug design concept has gained considerable importance in steroid drug industry to minimise the severe side effects associated with corticosteroids including percutaneous absorption and cutaneous atrophy. Besides these, synthetic works towards the development of the modified steroid molecules and a number of molecular hybrids as combinations of parts of different steroid molecules with other building blocks are also emerging as areas of interest because of their diverse biological properties.\textsuperscript{3, 4}

Hence among the modern organic chemists, one of the most fascinating challenges is to design new synthetic strategies that could provide structurally diverse and complex molecules with novel physical, chemical and biological properties\textsuperscript{5} in order to develop newer and potential steroid based drug molecules. It has been found that macrocyclic skeletons due to their several preorganised structural architectural features are considered to be an especial class of target hosts, as they can combine with conformational flexibility and biological stability.\textsuperscript{6} Steroids due to their rigid framework with significant biological properties, numerous therapeutic effects,\textsuperscript{7} having ability to penetrate the cell membrane and specific in nature towards hormonal receptors have therefore considered as target host for many hybrid systems. Attachment of many synthetic biomolecule to the naturally occurring saponins\textsuperscript{7} demonstrated a promising
approach to obtain structurally diverse chemical substances for pharmacological testing. For example sugars attached to the steroid A and D-rings hydroxyl groups\(^8\) have shown to possess novel amphiphilicity on phospholipid membranes. Similarly, steroid-peptide conjugates have been found to exhibit potent biological activity. They are recognized to be used as artificial proteolytic enzymes, \(^9\) employed in the construction of anion receptors and cationic antibiotics, \(^10\) and as synthetic receptors for oligopeptides. \(^11\) The steroid skeletons are transformed into spiroketal moiety, which results in the reversal of multidrug resistance in hippurin-1, \(^12\) and subnanomolar anticancer activity in cephalostatins and ritterazine M. \(^13\) Squalamine like novel aminosterols are synthesised, which provide strong antiproliferative properties indicating a promising challenge in cancer chemotherapy. \(^14\) Thus chemical transformations of steroids towards the formation of a chemically stable linkages between steroids and other building blocks find a remarkable application in designing novel steroid drugs. Recently, Benerjee et al \(^15\) have reported the synthesis of some triple hybrids of steroids, spiroketals and oligopeptides as new bimolecular chimeras, some of them showing potent integrin antagonistic effect.

In continuation of our work on steroid transformations, \(^2, 16-24\) and our long-term interest on synthesis of biologically important steroidal derivatives, we initiated some work on the synthesis of some new peptidomimetic steroid- amino acid conjugates starting from easily available 20-oxopregnanes \(^24\) and some other steroid molecules applying Ugi-4CR \(^25\) on key intermediates, \(viz., \) seco-steroidal hydroxyl

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acids. Earlier Rivera et al.\textsuperscript{26} reported the synthesis of peptidomimetic spirostane hybrids and macrocyclic hybrid structures with chiral host molecules successfully utilising the reaction. However, a general conjugation process of biomolecules to steroids utilizing this approach is still very new and needs further exploration. Several methods for the synthesis of steroid peptide conjugates using Ugi-4CR have been reported in the literature,\textsuperscript{27-30} although application of MW energy in synthesizing such hybrid systems has not been reported so far.

**Ugi-four Component Reaction (Ugi-4CR):**

Multicomponent reactions (MCRs) offer a great route to generate efficient libraries of complex molecules with high degree of diversity.\textsuperscript{31} The Ugi-four component reaction (Ugi-4CR) is one of the cornerstone MCRs, first reported by Ivar Ugi in 1959.\textsuperscript{32} Along with the Passerini reaction, it is classified as an isocyanide-based multicomponent reaction.\textsuperscript{33} Ugi-4CR is the one-pot condensation of a primary amine, an oxo component, a carboxylic acid, and an isocyanide to afford an N-substituted dipeptide backbone (Scheme 2.1).\textsuperscript{34} The reaction is usually conducted in a polar protic solvent such as methanol with some success in water has also recently been shown.\textsuperscript{35}
Since the discovery, Ugi-4CR has not been explored elaborately because of the limited availability of isocyanides. However major advances in the scope of the Ugi- reaction have occurred during the last two decades and presently Ugi- 4CR has become as one of the great reactions in diversity-oriented approaches toward drug discovery. In order to further increase its versatility and the complexity-generating power, a variety of reactions have been done in association with Ugi-4CRs for the synthesis of medicinally relevant heterocycles.

A straightforward strategy (Schemes 2.2a-b) towards very large steroid–peptide hybrid macro cycle compound (7) through a one-pot multiple Ugi-4CR of steroidal bifunctional building blocks was described by Wessjohann et al. (Schemes 2.2a) represents the synthesis of the steroidal bifunctional building blocks (5) and (6) from lithocholic acid (4) first reduction by a double Mitsunobu reaction followed by azide displacement, reduction and subsequent isonitrile formation. Scheme 2.2b describes the multiple macrolization step by Ugi-4CR carried out under pseudo-dilution

Scheme 2.1

\[
R_2-\text{NH}_2 + R_1 \text{H} + \text{HC}R_2 + \text{C}=\text{N}R_4 \rightarrow R_2\text{N}R_1 \text{O}R_3 \text{R}_4
\]
condition by adding the diisonitrile (6) to the mixture of other components, viz.,
diamino compound (5), carboxylic acid and alcohol resulted to form the large Steroid-
Peptide-hybrid macrocycle compound (7).

Scheme 2.2a Reagents and Conditions: i) LiAlH₄, THF; ii) DIAD, PPh₃, MeSO₃H; iii) NaN₃, DMPU; iv) H₂, PtO₂ v) HCO₂Et, Δ; vi) POCl₃, i-Pr₂NEt.

Scheme 2.2b Double Ugi-4CR macrocyclisation of steroidal bifunctional building blocks.

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Synthesis of a library of non-racemic, non-repetitive peptoid-containing steroid biaryl ether hybrid macro cycles were again described by Wessjohann et al\textsuperscript{28} utilizing the multiple Ugi-4CR macrocyclization including bifunctional building blocks (MiB). They demonstrated the possibilities of side chain and skeletal variation and the diversity that can be achieved by the combination of just two types of bifunctional building blocks: steroidal dicarboxylic acid (8) and biaryl ether diisocyanide (9) (Scheme 2.3) to synthesize macrocyclic steroid-peptide hybrid molecule like compound (10). Cholic acid derivatives with concave oriented hydrogen binders are found to be important building blocks in supramolecular and pharmaceutical chemistry and hence considered as the dicarboxylic acid component. The diacid/diisocyanide combined peptoid core may serve as a unique binding motif towards the synthesis of macrocyclic receptors due to its fully endocyclic core with dual hydrogen-bond donor/-acceptor capabilities.

![Scheme 2.3](image-url)
Rivera and co-workers\textsuperscript{29} reported the synthesis of peptidomimetic-spirostane hybrid (14) utilizing Ugi-4CR under classical heating method (Scheme 2.4). They synthesized different novel steroid-peptide conjugates introducing oligopeptides either by their C-terminus or by N-terminus at varied positions of steroid nucleus and hence by functionalizing steroids with carboxy or amino groups. A number of commercially available isocyanides were used for the reaction. In Scheme 2.4, oxidation of 5-hydroxy-6-oxo sapogenin (11) produced seco-steroid acid (12) which upon reduction followed by BV oxidation furnished followed seco-steroidal acid derivative with an A-ring lactone moiety (13) with proper functionalization for the Ugi-4CR. The carboxy functionality at C-6 of the compound was employed to achieve the desired conjugate by using ε-N-Cbz-L-lysine methyl ester as the amino acid component and methyl isocyanate as the isocyanide component to get the desired peptidomimetic-steroid spirostane hybrid (14).
Scheme 2.4: Reagents and Conditions: i) Ac₂O, Py; ii) Jones reagent; iii) H₂, Pd-C; iv) m-CPBA, CH₂Cl₂; v) Ugi-4CR: paraformaldehyde, ε-N-Cbz-L-lysine methyl ester, methyl isocyanate.

Thus from the above discussion it is noteworthy to mention that steroid macrocycles constitute as an interesting host compound for molecular and ion–pair recognition studies. Different types of steroid-based macrocycles are been reported to be useful for the design of artificial ion channel, ³⁹ drug targeting, ⁴⁰ and as scaffold for the assembly of combinatorial libraries. ⁴¹ On the other hand, diversity oriented synthesis in a single pot with novel physicochemical and biological properties are one of the greatest
challenges among modern organic chemists. Definitely like all other multicomponent reactions, Ugi-4CR reaction is also able to fulfil a lot of this growing demand of versatile synthesis of complex structural scaffolds.

2.2 Results and Discussion

The present chapter describes a microwave-prompted synthesis of Steroid-Amino Acid Conjugates from easily available steroid molecules utilizing Ugi-4CR as the coupling reaction with various amino acid residues. So far no report on synthesis of this class of potential biologically active steroid hybrid molecules through the application of MW Energy Ugi-4CR has been reported in the literature. We introduced the peptide sequences at different positions particularly at A, B and D ring sites of the steroid nucleus by their C-terminus. Steroid molecules, viz., 16-dehydropregnenolone acetate and its relatives, cholesterol, 5α-androstan-20-one and estrone were used as the starting materials to obtain various A, B and D-ring cleavage seco-steroidal acids to introduce peptide bonds through MW promoted Ugi-4CR. Besides commercially available steroidal acids are considered as the starting molecules for synthesizing this important class of steroid hybrid molecules. Further an Ansa-Seco-Steroid, obtained through Diels-Alder-retro-Diels-Alder reaction of ergosteryl acetate with an acetylenic dienophile viz., methyl propiolate was also used to get an ansa-seco-steroid based amino acid conjugate through MW-assisted Ugi-4CR.

Microwave Irradiated Ugi four-component reaction (Ugi-4CR): Expedited synthesis of Steroid-Amino acid Conjugates - A Novel Class of Peptidomimetic Hybrid Compounds based on Seco-Steroids (A, B & D Ring Cleavage).
In order to introduce Ugi functionality in the A and D rings of steroid molecules, the key step was the Baeyer-Villiger (BV) oxidation of the 3-keto (for ring A cleavage) and 17-keto (for D-ring cleavage) steroids to convert into the corresponding lactones. Subsequent ring opening of the lactones under basic hydrolysis resulted the corresponding hydroxy acid derivatives which were directly subjected to Ugi-4CR with L-alanine methyl ester or L-valine methyl ester in presence of benzyl isocyanide, paraformaldehyde and triethylamine to get the desired Steroid- Amino Acid Conjugates. Varying the carboxy acid component derived from different steroid nuclei, synthesis of three different steroid-peptide conjugate molecules have been synthesized through the manipulation of ring A to obtain A-ring cleavage Steroid-Amino Acid Conjugates. In the same way, D-ring cleavage Steroid Amino Acid Conjugates are synthesized through the Baeyer-Villiger (BV) oxidation followed by ring opening reaction of 17-keto steroids under basic hydrolysis which resulted the corresponding hydroxy acid derivatives which were directly subjected to Ugi-4CR as described above in case of synthesizing A-ring cleavage Steroid-Amino Acid Conjugates. B-ring cleavage Steroid- Amino Acid Conjugate were synthesized through i) Jones oxidation of 5α,6α-epoxy steroid to generate its B-ring cleavage seco-steroid acid derivatives followed by Ugi-4CR as described above and ii) oxidation of Δ^5, 7-oxo-steroid derivative, to generate its B-ring cleavage seco-steroid acid derivative followed by Ugi-4CR as above to get the desired B-ring cleavage Steroid-Amino-Acid Conjugates. Commericially available steroidal acids, viz., Cholic acid and hyodeoxycholic acids were directly subjected to MW- irradiated Ugi-4CR with L-alanine methyl ester or L-valine methyl ester in
presence of benzylisocyanide, paraformaldehyde and triethylamine to get their respective Steroid-Amino-Acid Conjugates. Further *Ansa-Seco*-Steroid prepared as above was converted to its carboxylic acid derivative for its eventual conjugation through MW-promoted Ugi-4CR using L-Lysine methyl ester to furnish its Steroid-Amino-Acid Conjugate.

All the Steroid-Amino Acid Conjugates described as above were purified by modern separation technique like flash chromatography and were fully characterised by their IR, NMR, mass spectral and elemental analyses.

During the investigation it has been found that, in each case the various *seco-* steroidal acid derivatives through MW irradiated Ugi-4CR with L-alanine methyl ester and L-valine methyl ester, paraformaldehyde, benzylisocyanide and \((\text{C}_2\text{H}_5)_3\text{N}\) resulted in high yield formation of Steroid-Amino Acid Conjugates with different amino acid residues in a very fast and clean reaction with no side products as listed in Table 1. In all cases, Ugi-4CR under classical conditions furnished the respective Steroid-Amino Acid Conjugates in 17-35% yield only. The Table 2 shows the advantages of this expedited Ugi-4CR under MW irradiation over the classical Ugi-4CR in synthesizing various Steroid-Amino Acid Conjugates as listed in Table 1.

### 2.3: Synthesis of Steroid-Amino Acid Conjugate through the cleavage of ring A

#### 2.3: Steroid-Amino Acid Conjugate (21a) & (21b)
The Scheme 2.5 describe the synthesis of Steroid-Amino Acid Conjugates (21a) & (21b) starting from 16-dehydropregnenolone acetate (16-DPA) (15), which is available in the laboratory. The compound (15) was hydrogenated by 10% Pd-C (on charcoal as catalyst) to form 3β-acetoxy-5α-pregnan-20-one (16) as the major product and was subjected to hydrolysis by using 3% KOH in MeOH-H$_2$O to give 3β-hydroxy-5α-pregnan-20-one (17) in quantitative yield. PCC oxidation of the compound (17) produced 5α-pregnan-3, 20-dione (18) in almost quantitative yield. The compound (16), (17), and (18) were directly compared with the authentic materials. BV oxidation of the compound (18) under MW irradiation at 350 W, in chloroform furnished the regioisomeric mixture of 3-oxa-4-oxo-4a-homolactone (19a) (60%) and 3-oxo-4-oxa-4a-homolactone (19b) (40%) in a very clean and fast reaction with an overall yield of 65%. The compound (19a) and (19b) were directly compared with the authentic materials. Opening of the lactone ring of the major lactone (19a) under basic hydrolysis furnished seco-steroid-dihydroxy acid derivative (20) in 45% yield. In its IR spectrum, the band at 1700 cm$^{-1}$ confirmed the formation of a carboxylic acid group. Seco-steroid acid derivative (20) was then subjected to the conjugation process first with L-alanine methyl ester in presence of benzyl isocyanide, paraformaldehyde and triethylamine under MW assisted Ugi-4CR to form (21a) in 85% yield. Replacing L-alanine methyl ester with L-valine methyl ester the other A-ring cleavage Steroid-Amino Acid Conjugate (21b) was obtained in 86% yield. In the IR spectra of (21a) & (21b), the carbonyl frequency observed near 1704 cm$^{-1}$ for (20) was replaced by an ester band near 1736 cm$^{-1}$. In their $^1$H NMR spectra, methyl ester group appeared as singlet at
δ 3.7 ppm while five aromatic protons appeared in the region δ 7.32-7.39 ppm. In their 
\(^{13}\)C NMR spectra, peaks near δ 169.1, 172.3, 176.5 ppm confirmed the presence of three 
different carbonyl functionalities in the molecule as expected as per structures 
represented by (21a) & (21b).
Scheme 2.6: Reagents and Conditions: i) H₂, Pd-C, EtOH; ii) 3% KOH, MeOH-H₂O; iii) PCC, DCM; iv) m-CPBA, CHCl₃, MW, 3-5 mins; v) 5% KOH, MeOH-H₂O, reflux; via) Ugi-4CR: L-alanine methyl ester, paraformaldehyde, L-valine methyl ester, benzylisocyanide, (C₂H₅)₃N, 400W, 100°C, 15 bar, 10 min; vib) Ugi-4CR: L-valine methyl ester, paraformaldehyde, L-valine methyl ester, benzylisocyanide, (C₂H₅)₃N, 400W, 100°C, 15 bar, 10 min.

2.3.2: Steroid–Amino Acid Conjugates (27a) & (27b)

The scheme 2.7 was conceived to synthesis of A-ring cleavage Steroid-Amino Acid Conjugates (27a) & (27b) starting from cholesterol (22).
Scheme 2.7: Reagents and Conditions: i) H₂, Pd-C; ii) PCC, DCM; iii) m-CPBA, CHCl₃, MW, 3-5 mins; iv) 5% KOH, MeOH-H₂O, reflux; via) L-alanine methyl ester, paraformaldehyde, benzylisocyanide, (C₂H₅)₃N, 400W, 100°C, 15 bar; vib) Ugi-4CR: paraformaldehyde, L-valine methyl ester, benzylisocyanide, (C₂H₅)₃N, 400W, 100°C, 15 bar, 10 min.

Cholesterol (22) was subjected to hydrogenation with 10% Pd/C to furnish 5α, 6β-dihydrocholesterol (23) as the sole product in 98% yield. Oxidation of the compound (23) with PCC in DCM produced 5α-cholestan-3-one (24) in a very good yield.⁴⁵ Both
the compounds (23) and (24) were directly compared with the authentic materials.\textsuperscript{45} MW assisted BV oxidation of the compound (24) as discussed earlier furnished both the 3-oxa-4-oxo-4a-homo lactone (25a) and 3-oxo-4-oxa-4a-homo lactone (25b) almost in 3: 2 ratio with an overall yield of 67%. The IR spectrum of both the lactones showed absorption bands near 1736 cm\(^{-1}\), indicating the presence of the 7-membered lactone rings. In \(^{13}\)C NMR, the two lactones showed two signals at \(\delta\) 176.3 and 176.4 ppm respectively indicating the replacement of the normal CO function by –OCO function. In the \(^1\)H NMR spectrum, signals at \(\delta\) 3.88 (d, \(J = 13.2\) Hz) ppm and \(\delta\) 4.61 - 4.68 (m) ppm were accounted for the H-2\(\alpha\) and H-2\(\beta\) of lactone (25a) and the signals at \(\delta\) 4.0-4.1 (m) ppm and \(\delta\) 4.20-4.25 (m) ppm were assigned for the H-4a\(\alpha\) and H-4a\(\beta\) of the lactone (25b) respectively. Thus spectral observations supported that the lactone (25a) is 3-oxa-4-oxo-4a-homo lactone and lactone (25b) is 3-oxo-4-oxa-4a-homo lactone. The lactones (25a) and (25b) were directly compared with the authentic materials.\textsuperscript{43} Base hydrolysis of the major lactone (25a) furnished the desired A-ring cleavage seco-steroid hydroxyl acid derivative (26) in 75% yield. Its IR spectrum exhibited the carbonyl frequency at 1700 cm\(^{-1}\) and hydroxyl band at 3400 cm\(^{-1}\). Seco-steroid hydroxy acid compound (26) thus obtained was then subjected to Ugi-4CR under MW irradiation as earlier first with L-alanine methyl ester to furnish the desired A-ring cleavage Steroid- Amino Acid Conjugate (27a) in 80% yield. Replacing L-alanine methyl ester with L-valine methyl ester, the other A-ring cleavage Steroid-Amino Acid Conjugate (27b) was obtained in 82% yield. In their \(^1\)H NMR spectra, newly introduced five aromatic protons appeared as multiplates in the region \(\delta\) 7.36-7.40 ppm while the methyl ester group appeared as a
sharp singlet near δ 3.5 ppm. In their $^{13}$C NMR spectra peaks near δ 169.1, 172.3, 176.5 ppm confirmed the presence of three different carbonyl functionalities in the molecules as expected as per structures represented by $(27a)$ & $(27b)$.

### 2.3.3: Steroid -Amino Acid Conjugate 30a & 30b

Scheme 2.8 describes the synthesis of other A-ring cleavage Steroid-Amino Acid Conjugates viz., $(30a)$ & $(30b)$ starting from cholesterol $(22)$ via its oxidation to induce carboxy group in the ring A. Thus oxidation of cholesterol with PCC furnished $\Delta^4$-cholestanone in 61% yield\(^45\) which was directly compared with the authentic compound\(^46\). The compound $(28)$ upon oxidation with KMnO$_4$-NaIO$_4$ in refluxing isopropanol furnished the A-ring cleavage seco-steroidal acid $(29)$ in 89% yield\(^47\). The compound $(29)$ was directly compared with the authentic compound\(^47\). In its IR spectrum, the band for α,β-unsaturated carbonyl frequency at 1675 cm$^{-1}$ appearing for the compound $(28)$ was replaced with a double strength carbonyl frequency at 1700cm$^{-1}$ for the hexanone system and the carboxylic acid group. In its $^{13}$C NMR spectrum, peaks at 179 and 215 ppm appeared for two carbonyl functionalities present in the molecule.
Scheme 2.8 Reagents and Conditions: i) PCC, DCM; ii) KMnO₄, Na₂CO₃, NaIO₄, isopropanol, reflux; iii) Ugi-4CR: L-alanine methyl ester, paraformaldehyde, benzylisocyanide, (C₂H₅)₃N, 400W, 100°C, 15 bar; iiib) Ugi-4CR: L-valine methyl ester, paraformaldehyde, benzylisocyanide, (C₂H₅)₃N, 400W, 100°C, 15 bar, 10 min.

A ring cleavage seco-steroid hydroxy acid (29) thus obtained was then subjected to Ugi-4CR under MW irradiation as per general procedure with two different amino acid residues, viz., L-alanine methyl ester, and L-valine methyl ester as discussed already furnished the corresponding Steroid-Amino Acid Conjugates (30a) and (30b) respectively in 75% and 78% yields. In their ¹H NMR spectra, methyl ester protons appeared as a sharp singlet at δ 3.6 ppm while another singlet at δ 6.1 ppm integrating to
one proton was assigned for the NH-proton. The five aromatic protons of the conjugate (30a) & (30b) appeared as multiplets in the region δ 7.33-7.39 ppm. In their $^{13}$C NMR spectra, the four carbonyl groups appeared as four separate signals in the region δ 171.2- 216 ppm as desired. All these data suggested the formation of desired A-ring cleavage Steroid–Amino Acid Conjugates viz. (30a) & (30b).

2.4: Steroid-Amino Acid Conjugate through the cleavage of Ring B  

2.4.1: Steroid-Amino Acid Conjugates (37a), (37b) & (38a), (38b)

The Scheme 2.9 was conceived to synthesize Ring-B cleavage Steroid-Amino Acid Conjugates starting from pregnenolone acetate (31) which is easily obtainable from 16-DPA. The compound (31) on epoxidation with mCPBA furnished 5α,6α-epoxy-pregnenolone acetate (32) in 80% yield. The compound (32) was directly compared with the authentic compound. The epoxide (32) was subjected to chromic acid oxidation with Jones reagent at 50°C as per literature procedure to furnish four oxidized products, viz., 33-36. They were separated by column chromatography using hexane and ethyl acetate [EA::P.E:1:10]. The major product (50%) obtained as white solid was confirmed to be as 5α-hydroxy-6-oxo-pregnenolone acetate (33). The compound exhibited IR bands at 3300, 1710 (double strength) and 1730 cm$^{-1}$ corresponding to a hydroxyl, two carbonyl groups and one acetate group respectively. Its $^{13}$C NMR exhibited a peak at 212.3 ppm for an additional carbonyl group. The structure was further securely confirmed through its Single Crystal X-Ray crystallography [Fig.2.1] showing stereochemistry at C-5 as α-OH. The next major
product isolated was a B-ring cleavage seco-steroidal acid (34) (27mg, 30%) with an α, β-unsaturated carbonyl group. IR spectrum of the compound exhibited the presence of an α, β-unsaturated carbonyl group at 1675 cm\(^{-1}\) while the normal C=O group and carboxylic acid group appeared as a double strength band at 1700 cm\(^{-1}\). In \(^{13}\)C NMR spectrum exhibited three peaks at 178.4, 202.1, 209.5 ppm corresponding to three carbonyl functionalities. The next major product isolated was another B-ring cleavage seco-steroidal acid (35) (16.2mg, 15%) with a 3β-acetoxy group. In its IR spectrum, a triple strength band at 1710 cm\(^{-1}\) was attributed to carboxylic acid group, hexanone system and C-20 carboxyl group while acetate group appeared at 1735 cm\(^{-1}\). The stereochemistry of the group containing the COOH moiety has been shown to be as \(\alpha\)-orientation.\(^{26a}\) The minor product isolated was \(\Delta^4\)6-oxo derivative (36) (4.9mg, 5%) which is the dehydrated product of the compound (33). Its IR spectrum exhibited at 1675 cm\(^{-1}\) for the α,β-unsaturated carbonyl group while a double strength peak at 1710 cm\(^{-1}\) for the C-20 carbonyl and the carboxylic acid groups. It is pertinent to note that the major compound (33) could be again converted to the desired B-ring cleavage seco-steroidal hydroxyl acids (34) and (35) by oxidation with Jones reagent as discussed above to get more of these products for their eventual conjugation with amino acids get B-ring cleavage Steroid-Amino-Acid Conjugates. The stereochemistry of the oxidized products (34) & (35) were assigned on the basis of the earlier reports.\(^{26a, 49}\) The seco-steroid hydroxyl acids (34) was then subjected to MW assisted Ugi-4CR first with B-ring cleavage Steroid-Amino Acid Conjugate with L-Alanine methyl ester as per general procedure to isolate the desired Steroid-Amino Acid conjugate (37a) in 72%
yield. Replacing, L-Alanine methyl ester with L-lysine methyl ester we synthesized the other B-ring cleavage Steroid-Amino Acid Conjugate (37b) in 71% yield. In the same way, compound (35) furnished B-ring cleavage Steroid-Amino Acid conjugate (38a) (87%) and (38b) (85%) with L-alanine methyl ester and L-lysine methyl ester respectively. All these B-ring cleavage Steroid-Amino Acid Conjugates (37a, b)-(38a, b) exhibited the methyl ester band at 1736 cm$^{-1}$ and N-H bending absorption frequency near 1650 cm$^{-1}$. In their $^1$H NMR spectra, newly introduced five aromatic protons appeared as multiplets in the region 7.36-7.40 ppm while the methyl ester protons appeared as sharp singlet near 3.5 ppm. In their $^{13}$C NMR, four different carbonyl functionalities appeared in the region $\delta$ 169-177 ppm. All these data are in quite conformity with their structures as proposed.

![ORTEP representation of 5α-hydroxy-6-oxo-pregnenolone acetate (33) with the ellipsoids of C, O atoms.](image)

Fig.2.1: ORTEP representation of 5α-hydroxy-6-oxo-pregnenolone acetate (33) with the ellipsoids of C, O atoms.
Scheme 2.9: Reagent and condition: i) m-CPBA, CHCl₃, rt; ii) Jones reagent, acetone, 50°C, 3hr; iii) Ugi-4CR: L-alanine methyl ester, paraformaldehyde, benzylisocyanide, (C₂H₅)₃N, 400W, 100°C, 15 bar; iv) Ugi-4CR: L-lysine methyl ester, paraformaldehyde, benzylisocyanide, (C₂H₅)₃N, 400W, 100°C, 15 bar.
Scheme 2.9: Reagent and condition: i) m-CPBA, CHCl₃, rt; ii) Jones reagent, acetone, 50 °C, 3h; iii) Ugi-4CR: L-alanine methyl ester, paraformaldehyde, benzylisocyanide, (C₂H₅)₃N, 400W, 100°C, 15 bar; iiib) Ugi-4CR: L-lysine methyl ester, paraformaldehyde, benzylisocyanide, (C₂H₅)₃N, 400W, 100 °C, 15 bar.

2.4.2 Steroid-Amino Acid Conjugates (41a) & (41b)

Scheme 2.10 was conceived to get some more of B-ring cleavage Steroid-Amino Acid conjugates viz., (41a) & (41b) starting from Cholesteryl acetate (39). The compound (39) was oxidized with PCC as per literature procedure ⁴⁶ to get 7-oxo-cholesteryl acetate (40) in 70% yield. The compound (40) was directly compared with authentic compound.⁴⁶ The α,β-unsaturated carbonyl system in the compound (40) facilitated to get the B-ring cleavage seco-steroidal acid derivative (41). This was
achieved by oxidizing the compound (40) with KMnO$_4$ in presence of NaIO$_4$ in refluxing isopropanol to furnish the B-ring cleavage seco-steroid acid derivative (41) in 89\% yield.$^{26a, 47}$ Its IR, NMR, and mass spectral data were compared with those of the literature values$^{47}$ to confirm its structure as (41). The B-ring cleavage seco-steroidal acid derivative (41) thus obtained was subjected to MW assisted Ugi-4CR with L-alanine methyl ester and L-valine methyl ester as described in earlier to furnish the desired B-ring cleavage Steroid-Amino Acid Conjugates, viz., (41a) and (41b) respectively. Their IR, NMR and elemental analysis are in quite conformity with the proposed structures.
Scheme 2.10: Reagents and Conditions: i) PCC, CH₂Cl₂, rt; ii) KMnO₄, Na₂CO₃, NaIO₄, iso-propanol, reflux; iii) L-alanine methyl ester, paraformaldehyde, benzylisocyanide, (C₂H₅)₃N, 400W, 100°C, 15 bar; iiia) L-valine methyl ester, paraformaldehyde, benzylisocyanide, (C₂H₅)₃N, 400W, 100°C, 15 bar.

2.5: Synthesis of Steroid-Amino Acid Conjugate through the cleavage of D-ring
This section comprises the synthesis of Steroid-Peptide Conjugates through the cleavage of ring D of steroid nucleus. In order to introduce Ugi-functionality in the D ring of steroid molecules, the key step was the Baeyer-Villiger (BV) Oxidation of the 17-keto steroid to furnish the corresponding lactone. Subsequent ring opening of the lactone ring produced the desired D-ring cleavage Seco-Steroid hydroxyl acid for its eventual subjecting to MW irradiated Ugi-4CR using different amino acid residues to get the desired D-ring cleavage Steroid-Amino Acid Conjugates. It is pertinent to note that so far no reports on D-ring cleavage Steroid-Amino Acid Conjugates are reported in literature.

2.5.1: Steroid-Amino Acid Conjugates (47a) & (47b)

The scheme 2.11, was formulated to synthesize D-ring cleavage Steroid-Amino-Acid Conjugates (47a) & (47b) starting from a 20-oxo-steroid (42) which was obtained during long time (6h) hydrogenation of 16-DPA with 10% Pd/C in 10% yield. The hydrogenolysis product (42) of 16- DPA was characterized through its IR, NMR, and Mass spectral data. The compound (42) was subjected to MW assisted BV oxidation to furnish the 17-acetoxy compound (43). In its IR spectrum, the carbonyl frequency at 1710 cm\(^{-1}\) in (42) was replaced with an acetoxy band at 1735 cm\(^{-1}\). Alkaline hydrolysis of the compound (43) followed by oxidation with PCC furnished 17-keto steroid (44). Its IR spectrum displayed the cyclopentanone band at 1750 cm\(^{-1}\). The compound (44) was subjected to MW assisted BV oxidation with m-CPBA to furnish the steroid lactone (45) in 65% yield. The compound (45) was directly compared with the authentic material. In its IR spectrum the six member lactone displayed the band at 1741 cm\(^{-1}\).
The compound (45) was then easily converted to D-ring cleavage seco-steroidal hydroxyl acid derivative (46) through ring opening with a base. IR spectrum of the compound (46) exhibited bands at 1700 and 3400 cm\(^{-1}\) for the carboxylic acid and hydroxyl group respectively. Its \(^{13}\)C NMR displayed a new peak at 178.5 ppm for the carboxylic acid carbon atom.

\[ \text{Scheme 2.11: Reagents and Conditions: i) m-CPBA, CHCl}_3, \text{ MW, 3-5mins; ii. a) 3\% KOH, MeOH-H}_2\text{O; b) PCC, DCM; iii) m-CPBA, CHCl}_3, \text{ MW, 3-5mins; iv) 5\% KOH, MeOH-H}_2\text{O, reflux; va)Ugi-4CR: L-alanine methyl ester, paraformaldehyde,} \]
benzylisocyanide, \((\text{C}_2\text{H}_5)_3\text{N}\), 400W, 100°C, 15 bar; vb) Ugi-4CR: L-valine methyl ester, paraformaldehyde, benzylisocyanide, \((\text{C}_2\text{H}_5)_3\text{N}\), 400W, 100°C, 15 bar.

D-ring cleavage seco-steroidal hydroxyl acid (46) was then subjected to MW assisted Ugi-4CR with amino acid residues, viz., L-alanine methyl ester and L-valine methyl ester as in earlier cases to furnish the desired D-ring cleavage Steroid-Amino Acid Conjugates (47a) and (47b) respectively. A sharp singlet near \(\delta\ 3.8\) ppm integrating to three protons corresponds to the \(\text{CH}_3\) protons of \(-\text{COOCH}_3\). The five aromatic protons of steroid-peptide conjugates (47a) & (47b) appeared as multiplets in the region \(\delta\ 7.31-7.37\) ppm. The three carbonyl groups appeared as three separate signals in the region \(\delta\ 171-174\) ppm for three carbonyl functionalities. All these data suggested the formation of the desired D-ring cleavage Steroid-Amino Acid Conjugates (47a) and (47b).

2.6: Synthesis of Steroid-Amino Acid Conjugates starting from Cholic acid and Hyodeoxycholic acid

2.6.1: Steroid-Amino Acid Conjugates (49a), (49b), (51a) and (51b)

Synthesis of Steroid-Amino Acid Conjugates based on two commercially available steroidal acids, viz., Cholic acid (48) and hyodeoxycholic acid (50) were carried out. Both these steroidal acids were procured from Aldrich-Sigma.

Thus when cholic acid (48) was subjected to Ugi-4CR under MW irradiation using L-alanine methyl ester as per general procedure, the desired Steroid-Amino Acid...
Conjugate (49a) was obtained in 86% yield. The reaction was repeated with L-valine methyl ester to furnish the other Steroid-Amino Acid Conjugate (49b) in 84% yield. In their IR spectra, presence of an absorption peak near 1735 cm\(^{-1}\) indicated the presence of the ester function and N-H bending displayed absorption frequency near 1650 cm\(^{-1}\). In their \(^1\)H NMR spectra a singlet at 3.5 ppm integrating to three protons corresponded to the CH\(_3\) protons of –COOCH\(_3\) group. The five aromatic protons appeared as multiplets in the region δ 7.31-7.37 ppm. In their \(^{13}\)C NMR spectra, the three carbonyl groups appeared as three separate peaks in the region δ 171-174 ppm. All these data suggested the formation of the Steroid-Amino Acid Conjugates (49a) and (49b).

Scheme 2.12 Reagents and Conditions: ia) L-alanine methyl ester, paraformaldehyde, benzylisocyanide, (C\(_2\)H\(_5\))\(_3\)N, 400W, 100°C, 15 bar, ib) L-valine methyl ester, paraformaldehyde, benzylisocyanide, (C\(_2\)H\(_5\))\(_3\)N, 400W, 100°C, 15 bar.
In the same way, hyodeoxycholic acid (50) furnished Steroid-Amino Acid Conjugates (51a) and (51b) with L-alanine methyl ester and L-valine methyl ester in 82% and 79% yields respectively under the MW prompted expedite Ugi-4CR. Their spectral data are in quite conformity with proposed structures as represented by (51a) and (51b) as illustrated in Scheme 2.13.

Scheme 2.13 Reagents and Conditions: ia) L-alanine methyl ester, paraformaldehyde, benzylisocyanide, (C$_2$H$_5$)$_3$N, 400W, 100°C, 15 bar; ib) L-valine methyl ester, paraformaldehyde, benzylisocyanide, (C$_2$H$_5$)$_3$N, 400W, 100°C, 15 bar.

2.7: Synthesis of a Steroid-Amino-Acid Conjugate based on an Ansa-Seco-Steroid

2.7.1: Ansa-Seco Steroid-Amino Acid Conjugate (57)
Considering the importance of Ansa-Seco-Steroids,\textsuperscript{50} we synthesized another novel class of Steroid-Peptide Conjugates incorporating a peptide bond into the ansa-steroid backbone. The compound (55) which is the requisite precursor for an Ansa-Seco-steroidal acid derivative (56), for the synthesis of Steroid-Peptide-Conjugate (57) was prepared by the Diels-Alder-retro-Diels-Alder reaction sequences of ergosteryl acetate (52) with an acetylenic dienophile, viz., methyl propiolate (53) as per literature procedure\textsuperscript{50} as depicted in Scheme 2.14. The spectral data of the compound (55) was compared with those of the authentic Ansa-Seco-Steroid\textsuperscript{50} to confirm its structure. Methyl ester group present in the aromatic ring of the compound (55) was hydrolysed refluxing with an aqueous methanolic alkaline solution to get the desired Ansa-Seco-Steroidal acid (56) in high yield with simultaneous hydrolysis of the 3β-acetoxyl group as well. The compound (56) was then subjected to MW irradiated Ugi-4CR using L-lysine methyl ester to furnish Ansa-Seco-Steroid-Amino Acid Conjugate (57) in 73\% yield. IR spectrum of the compound displayed the ester band at 1737 cm\textsuperscript{-1} and the peak for N-H bending appeared at 1684 cm\textsuperscript{-1}. Its \textsuperscript{1}H NMR spectrum displayed a singlet at 3.93 ppm for the ester protons and the eight aromatic protons appeared as multiplets in the region 7.17-7.8 ppm.
Scheme 2.14: Reagents and Conditions: i) 3% KOH, MeOH-H$_2$O; ii) Ugi-4CR: L-lysine methyl ester, paraformaldehyde, benzylisocyanide, (C$_2$H$_5$)$_3$N, 400W, 100°C, 15 bar.

Table 1: MW assisted Ugi-4CR in synthesizing Steroid-Amino Acid Conjugates in expedited way
<table>
<thead>
<tr>
<th>Substrate</th>
<th>Amino acid residue</th>
<th>Steroid-Amino acid Conjugate^a</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Substrate Image" /></td>
<td>L-Alanine methyl ester</td>
<td><img src="image2.png" alt="Conjugate Image" /></td>
</tr>
<tr>
<td><img src="image3.png" alt="Substrate Image" /></td>
<td>L-Valine methyl ester</td>
<td><img src="image4.png" alt="Conjugate Image" /></td>
</tr>
<tr>
<td><img src="image5.png" alt="Substrate Image" /></td>
<td>L-Alanine methyl ester</td>
<td><img src="image6.png" alt="Conjugate Image" /></td>
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<tr>
<td><img src="image7.png" alt="Substrate Image" /></td>
<td>L-Valine methyl ester</td>
<td><img src="image8.png" alt="Conjugate Image" /></td>
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</table>

Contd..
<table>
<thead>
<tr>
<th>Substrate</th>
<th>Amino acid residue</th>
<th>Steroid-Amino acid Conjugate$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="" /></td>
<td>L-Alanine methyl ester</td>
<td><img src="image2" alt="" /></td>
</tr>
<tr>
<td><img src="image3" alt="" /></td>
<td>L-Valine methyl ester</td>
<td><img src="image4" alt="" /></td>
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<tr>
<td><img src="image5" alt="" /></td>
<td>L-Alanine methyl ester</td>
<td><img src="image6" alt="" /></td>
</tr>
<tr>
<td><img src="image7" alt="" /></td>
<td>L-Lysine methyl ester</td>
<td><img src="image8" alt="" /></td>
</tr>
</tbody>
</table>

Contd..
| Substrate | Aminic acid residue | Steroid-Aminic acid Conjugate
|
|-----------|---------------------|-----------------------------|
| ![Substrate 35](image1.png) | L-Alanine methyl ester | ![Steroid Conjugate 38a](image2.png) |
| ![Substrate 41](image3.png) | L-Lysine methyl ester | ![Steroid Conjugate 38b](image4.png) |
| ![Substrate 35](image1.png) | L-Alanine methyl ester | ![Steroid Conjugate 41a](image5.png) |
| ![Substrate 41](image3.png) | L-Lysine methyl ester | ![Steroid Conjugate 41b](image6.png) |

Contd..
<table>
<thead>
<tr>
<th>Substrate</th>
<th>Amino acid residue</th>
<th>Steroid-Amino acid Conjugate(^a)</th>
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<tbody>
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<td><img src="image2" alt="47a" /></td>
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<tr>
<td><img src="image3" alt="L-Lysine methy ester" /></td>
<td><img src="image4" alt="47b" /></td>
<td><img src="image4" alt="47b" /></td>
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<tr>
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<tr>
<td><img src="image7" alt="L-Valine methy ester" /></td>
<td><img src="image8" alt="49b" /></td>
<td><img src="image8" alt="49b" /></td>
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</table>

Contd..

*Microwave Irradiated Ugi four-component reaction (Ugi-4CR): Expedited synthesis of Steroid-Amino acid Conjugates- A Novel Class of Peptidomimetic Hybrid Compounds based on Seco-Steroids (A, B & D Ring Cleavage).*
All the products were fully characterised by their IR, NMR, Mass & Microanalyses

*a* Microwave Irradiated Ugi four-component reaction (Ugi-4CR): Expedited synthesis of Steroid-Amino acid Conjugates- A Novel Class of Peptidomimetic Hybrid Compounds based on Seco-Steroids (A, B & D Ring Cleavage).
Table 2: Comparison between MW assisted and Classical Ugi-4CR in synthesizing Steroid-Amino Acid Conjugates

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Steroid-Amino-acid Conjugate</th>
<th>MW assisted reaction</th>
<th>Classical reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Yield (%)</td>
<td>Time reqd. (min)</td>
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<tr>
<td>20</td>
<td>21a</td>
<td>80</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>21b</td>
<td>82</td>
<td>15</td>
</tr>
<tr>
<td>26</td>
<td>27a</td>
<td>95</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>27b</td>
<td>96</td>
<td>15</td>
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<tr>
<td>29</td>
<td>30a</td>
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</tr>
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<td>30b</td>
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<td>37a</td>
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<td>41</td>
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<td>41b</td>
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<td>46</td>
<td>47a</td>
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<td>48</td>
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<td>51b</td>
<td>79</td>
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</tr>
<tr>
<td>55</td>
<td>66a</td>
<td>73</td>
<td>15</td>
</tr>
</tbody>
</table>

a Yields refer to the isolated product which are fully characterized by spectral and micro analysis
2.7: Conclusion

In conclusion, the work involves a first hand report of a Microwave (MW) promoted Ugi-4CR to synthesize a number of Steroid-Amino Acid Conjugates- a class of novel peptidomimetic steroid hybrids based on A, B and D-ring as well as of normal steroidal acids incorporating a peptide bond with different amino acid residues. The method would undoubtedly find a significant place in organic synthesis as steroid-peptide conjugates are currently gaining considerable importance because of their diverse biological properties. MW prompted Ugi-4CR may also be helpful in promoting green technology in organic synthesis. The reaction proceeds smoothly requiring very short duration of time giving very high yield of Ugi- 4C coupling products in desired way.

2.8: Experimental and Spectral Data

2.9: Typical procedure for the Ugi-4CR

2.9.1: Under MW irradiation

A mixture of steroid precursor, viz., seco-steroid acid (1.0mmol), L-alanine methyl ester (139mg, 1.0mmol)/ L-valine methyl ester (167mg, 1mmol)/ L-lysine methyl ester (233mg, 1mmol), paraformaldehyde (30mg, 1.0mmol), triethylamine (0.14mL, 1.0mmol) and benzylisocyanide (0.12mL, 1.0mmol) in MeOH (60mL) was irradiated in a closed vessel in a Synthos 3000 Microwave Reactor at 400 W, 100ºC and 15 bar for 10 min. The reaction mixture was then allowed to cool to room temperature. The solution was concentrated under reduced pressure and then poured into water and
extracted with CHCl₃ (3x100mL). The organic extract was dried over anhyd. Na₂SO₄ and evaporated under reduced pressure to get a residue which was purified by preparative TLC or column chromatography using combination of ethyl acetate and petroleum ether as eluent.

2.9.2: By classical

A solution of L-alanine methyl ester (139mg, 1.0mmol)/ L-Valine methyl ester (167mg, 1mmol)/ L-Lysine methyl ester (233mg, 1mmol), paraformaldehyde (30mg, 1.0mmol) and triethylamine (0.14mL, 1.0mmol) in MeOH (60mL) were stirred at room temperature for 1 hr to accomplish the formation of the corresponding imine. Steroid precursor, viz., seco-steroid acid (1.0 mmol) and benzylisocyanide (0.12mL, 1.0mmol) were then added and the reaction mixture was stirred for 48 h at rt. The solution was concentrated under reduced pressure and then poured into water and extracted with CHCl₃ (3x100mL). The organic extract was dried over anhyd. Na₂SO₄ and evaporated under reduced pressure to get a residue which was purified by preparative TLC or column chromatography using combination of ethyl acetate and petroleum ether as the eluent.

2.9.3: 3β-Acetoxy-5α-pregnane (16)

2 gms of 16-DPA (15) in 100mL of ethanol was subjected to hydrogenation at 45 psi pressure using 500mg of 10% Pd/C for a period of 5-6h. The reaction mixture was filtered and alcohol was distilled off under reduced pressure to obtained the crude hydrogenated product which was then purified by column chromatography over silica
gel using EtOAc:PE::1:15 as the eluent to furnish 3β-acetoxy-5α-pregnane (16) in pure form as white solid (1.2g, 94%).

\[
\begin{align*}
\text{AcO} & \quad \hat{\text{O}} \\
\text{H} & \\
\text{H} & \\
\end{align*}
\]

mp 172°C; IR (CHCl₃): 1735, 1704, 1450, 1200 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 0.9 (s, 3H, Me), 1.1 (s, 3H, Me), 0.9–1.8 (m, 23H, –CH and –CH₂), 2.0 (s, 3H, OAc), 2.2 (s, 3H, COMe), 4.3 (m, 1H, acetate proton); ¹³C NMR (75 MHz, CDCl₃): 15.2, 16.7, 20.9, 22.9, 25.7, 28.1, 29.0, 32.0, 34.2, 34.7, 35.3, 35.8, 39.5, 39.5, 39.5, 40.5, 41.9, 46.2, 55.4, 69.5, 78.6, 172.9, 212.5, MS (ESI): m/z 360 (M⁺). Anal. Calcd. for C₂₃H₃₆O₃: C, 76.66; H, 10.00; Found: C, 76.62; H, 10.06.

2.9.4: 3β-Hydroxy-5α-pregn-20-one (17)

1gm of 3β-Acetoxy-5α-pregnane (16) (2.7mmol) was dissolved in 30mL of 3% solution of KOH in MeOH-H₂O (85-15mL). The reaction mixture was stirred at rt for 3h. After completion of the reaction, the mixture was concentrated under reduced pressure and poured into cold water and acidified by using aq. citric acid solution. It was then extracted with DCM (3x100mL). The organic extract was dried over anhyd. Na₂SO₄ and evaporated under reduced pressure to get a residue which was purified by column chromatography by using EtOAc:PE::1:8 as eluent to get pure hydrolysed product (17) as white solid (750mg, 85%).
mp 151°C; IR (CHCl₃): 3400, 1710, 1450, 1200 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 0.9 (s, 3H, Me), 1.0 (s, 3H, Me), 0.9–1.9 (m, 25H, –CH and –CH₂), 2.2 (s, 3H, COMe); ¹³C NMR (75 MHz, CDCl₃): 15.2, 16.7, 20.9, 21.3, 22.9, 28.1, 29.0, 32.1, 34.2, 34.7, 35.1, 35.4, 39.5, 40.5, 41.9, 46.0, 55.4, 69.5, 75.6, 212.5, MS (ESI): m/z 318 (M⁺); Anal. Calcd. for C₂₁H₃₄O₂: C, 79.24; H, 10.69; Found: C, 79.19; H, 10.71.

2.9.5: 5α-pregn-3, 20-dione (18)

500mg (1.5mmol) of the compound (17) was subjected to oxidation with PCC, stirring in DCM (30mL) at room temperature for 1h by adding 100mg of PCC. The reaction mixture was diluted with 5 volumes of anhyd. ether and then passed through a pad of active alumina. The organic extract was dried over anhyd. Na₂SO₄ and was evaporated under reduced pressure to get a residue which was purified by column chromatography by using EtOAc: PE:: 1:20 as eluent to get pure oxidised product (18) as white solid (367 mg, 74%).

Microwave Irradiated Ugi four- component reaction (Ugi-4CR): Expedited synthesis of Steroid-Amino acid Conjugates- A Novel Class of Peptidomimetic Hybrid Compounds based on Seco-Steroids (A, B & D Ring Cleavage).
mp 160°C; IR(CHCl₃): 1710, 1445, 1200 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): 0.9 (s, 3H, Me), 1.1 (s, 3H, Me), 0.9–1.9 (m, 19H, –CH and –CH₂), 2.01 (s, 3H, COMe), 2.11-2.14 (m, 4H); ¹³C NMR (75 MHz, CDCl₃): δ 15.2, 16.7, 20.9, 21.3, 22.9, 28.1, 29.0, 32.0, 34.2, 34.7, 35.1, 35.4, 39.5, 39.5, 40.5, 42.9, 46.2, 55.4, 69.5, 209.6, 212.5; MS (ESI): m/z 316 (M⁺); Anal. Calcd. for C₂₁H₃₂O₂: C, 79.74; H, 10.12; Found: C, 79.10; H, 10.19.

2.9.6: 17β-Acetoxy-3-oxa-A-homo-5α-androstan-4-one (19a) and 17β-acetoxy-4-oxa-A-homo-5α-androstan-3-one (19b)

A mixture of m-CPBA (66mg, 3.9mmol) and 5α-pregnan-3,17-dione (474mg, 1.5mmol) in CHCl₃ (10mL) were irradiated in a closed vessel in a Synthon 3000 microwave reactor at 350 W, 105°C and 7.1 bar for 5 min. The reaction mixture was then allowed to cool to rt and washed subsequently with 10% Na₂SO₃ (2 x 100mL) and aq.10% NaHCO₃ (2x100mL). The organic phase was dried over anhyd. Na₂SO₄ and evaporated under reduced pressure to get a residue which was purified by column chromatography over silica gel using EA:PE::1:10 as the eluent to furnish the pure lactones 17β-acetoxy-3-oxa-A-homo-5α-androstan-4-one (19a) (313mg, 60%) and 17β-acetoxy-4-oxa-A-homo-5α-androstan-3-one (19b) in 40% yield.

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*Microwave Irradiated Ugi four- component reaction (Ugi-4CR): Expedited synthesis of Steroid-Amino acid Conjugates- A Novel Class of Peptidomimetic Hybrid Compounds based on Seco-Steroids (A, B & D Ring Cleavage).*
IR(CHCl₃): 1740, 1400, 1250, 950 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 0.66 (s, 3H, Me), 0.89 (d, 3H, J = 8.4 Hz), 1.1 (s, 3H, Me), (0.7–1.1, m, 12H), 2.01 (s, 3H, OAc), 3.68 (d, 1H, J = 12.9 Hz, H-2a), 4.15–4.17 (m, 1H, H-4αa), 4.25–4.29 (overlapping signal, m, 2H, H-4ab and H-17), 4.61 (m, 1H, H-2b); ¹³C NMR (75 MHz, CDCl₃): δ 20.9, 24.4, 25.7, 26.9, 27.4, 29.8, 30.7, 34.5, 35.6, 36.2, 36.8, 37.8, 40.5, 41.4, 42.6, 51.4, 63.3, 79.8, 171.9, 176.4; MS (ESI): m/z 348 (M⁺); Anal. Calcd. for C₂₁H₃₂O₄: C, 72.41; H, 9.19; Found: C, 72.38; H, 9.26.

17β-acetoxy-4-oxa-A-homo-5a-androstan-3-one (19b)

IR(CHCl₃): 1735, 1400, 1250, 950 cm⁻¹; ¹H NMR (300 MHz,CDCl₃): 0.66 (s, 3H, Me), 0.89 (d, 3H, J = 8.4 Hz), 1.3 (s, 3H, Me), (0.7–1.1, m, 12H), 2.01 (s, 3H, OAc), 4.15–4.17 (m, 1H, H-4αa), 4.25–4.29 (overlapping signal, m 2H, H-4ab and H-17), 4.56 (m, 1H, H-2b). ¹³C NMR (75 MHz, CDCl₃): δ 20.9, 24.4, 25.7, 26.9, 27.4, 29.8, 30.7, 34.5, 35.6, 36.2, 36.8, 37.8, 40.5, 41.4, 42.6, 51.4, 63.3, 79.8, 171.9, 176.3; MS (ESI): m/z 348 (M⁺); Anal. Calcd. for C₂₁H₃₂O₄: C, 72.41; H, 9.19; Found: C, 72.38; H, 9.26.

2.9.8: 2, 3-seco-2, 17-dihydroxy-3- carboxy-5α-pregnane (20)

The major lactone (19a) (300mg, 0.086mmol) was dissolved in 30mL of a 5% solution of KOH in MeOH-H₂O (85-15mL). The reaction mixture was refluxed for 3h.
After completion of the reaction, the mixture was concentrated under reduced pressure and poured into cold water and acidified by using an aq. solution of citric acid. The reaction mixture was then extracted with DCM (3x100mL). The organic extract was dried over anhyd. Na$_2$SO$_4$ and evaporated under reduced pressure to get a crude residue. The crude product was purified by column chromatography by using EtOAc:PE::1:4 as eluent to get pure 2,3-seco-2,17-dihydroxy-3-carboxy-5α-pregnane (20) as gum (125mg, 45%).

IR (CHCl$_3$): 3400, 1705, 1400, 1253, 950 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$): 0.9 (s, 3H, Me), 1.2 (s, 3H, Me), 0.9–1.9 (m, 23H, –CH and –CH$_2$), 3.54 (m, 3H, H-2 & H-17); $^{13}$C NMR (75 MHz, CDCl$_3$): δ 15.2, 16.7, 20.9, 22.9, 28.1, 29.0, 29.5, 32.0, 34.2, 34.7, 35.4, 39.5, 40.5, 41.9, 46.2, 55.4, 59.1, 76.5, 175.5; MS (ESI): m/z 324 (M$^+$); Anal. Calcd. for C$_{19}$H$_{32}$O$_4$: C, 70.33; H, 9.87; Found: C, 70.33; H, 9.94.

### 2.9.8: Steroid-Amino Acid Conjugate (21a)

**Ugi-4CR: MW**

324mg (1.0mmol) of the seco-steroidal acid (20) furnished A-ring cleavage Steroid-Amino Acid Conjugate (21a) (449mg, 80%) using L-alanine methyl ester as amino acid residue as per general procedure.
Ugi-4CR: Classical:

324mg (1.0mmol) of the seco-steroidal acid (20) furnished A-ring cleavage Steroid-Amino Acid Conjugate (21a) (195mg 34%) using L-alanine methyl ester as amino acid residue as per general procedure.

\[
\text{HO} \quad \text{O} \\
\text{N} \quad \text{CO}_2 \text{Me} \\
\text{O} \quad \text{N} \quad \text{H} \\
\text{OH}
\]

mp 231°C; \([\alpha]_D: (-)134.43^\circ\ (c1, \text{CHCl}_3)\); IR (CHCl\(_3\)): 3400, 1735, 1660, 1400, 1250, 950 cm\(^{-1}\); \(^1\)H NMR(CHCl\(_3\)): 0.9 (s, 3H, Me), 1.0 (s, 3H, Me), 0.9–1.9 (m, 26H, \(-\text{CH and } \text{CH}_2\)), 3.9 (s, 3H, OCH\(_3\)), 4.06-4.09 (m, 2H, NCH), 4.21-4.24 (m, 2H, CH\(_2\)), 4.72-4.74 (m, 2H, CH\(_2\)), 7.17-7.21 (m, 5H, Ph), 8.6 (m, 1H, NH); \(^{13}\)C NMR: δ 15.2, 16.7, 20.9, 22.9, 28.1, 29.0, 31.5, 32.0, 34.2, 34.7, 35.4, 39.5, 40.5, 41.9, 46.2, 47.9, 48.2, 49.2, 51.4, 55.4, 59.1, 76.5, 127.2, 127.9, 129.1, 138.9, 171.2, 172.0, 173.2; MS (ESI): \(m/z\) 556 (M\(^+\)); Anal. Calcd. for C\(_{32}\)H\(_{48}\)N\(_2\)O\(_6\): C, 69.06; H, 8.6; N, 5.03; Found: C, 69.04; H, 8.69; N, 5.03.

2.9.9: Steroid-Amino Acid Conjugate (21b)

Ugi-4CR: MW

324mg (1.0mmol) of the seco-Steroidal acid (20) furnished A-ring cleavage Steroid-Amino Acid Conjugate 21b (455mg, 82%) using L-valine methyl ester as amino acid residue as per general procedure.
Ugi-4CR: Classical:

324mg (1.0mmol) of the seco-steroidal acid (20) furnished A-ring cleavage Steroid-Amino Acid Conjugate 21b (172.3mg, 35%) using L-valine methyl ester as amino acid residue as per general procedure.

mp 236°C; [α]D\textsuperscript{25} (c1, CHCl\textsubscript{3}): 113.67\textdegree; IR (CHCl\textsubscript{3}): 3400, 1735, 1660, 1400, 1250, 950 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (CDCl\textsubscript{3}): δ 0.9 (s, 3H, Me), 1.0 (s, 3H, Me), 1.1-1.3 (bs, 6H, methyl groups), 0.9–1.9 (m, 26H, –CH and –CH\textsubscript{2}), 3.9 (s, 3H, OCH\textsubscript{3}), 4.06-4.09 (m, 2H, NCH), 4.21-4.24 (m, 2H, CH\textsubscript{2}), 4.72-4.74 (m, 2H, CH\textsubscript{2}), 7.17-7.21 (m, 5H, Ph), 8.6 (m 1H, -NH); \textsuperscript{13}C NMR: δ 15.2, 16.7, 16.8, 20.9, 22.9, 24.8, 28.1, 29.0, 31.5, 32.0, 34.2, 34.7, 35.4, 39.5, 40.5, 41.9, 46.2, 47.9, 48.2, 49.2, 51.4, 55.4, 59.1, 76.5, 127.2, 127.9, 129.1, 138.9, 171.2, 172.0, 173.2; MS (ESI): m/z 584 (M\textsuperscript{+}); Anal. Calcd. for C\textsubscript{34}H\textsubscript{52}N\textsubscript{2}O\textsubscript{6}: C, 69.86; H, 8.9; N, 4.7; Found: C, 69.83; H, 8.96; N, 4.79.

2.9.10: 5a, 6-dihydrocholesterol (23)

Cholesterol (22) (2gm, 5.17mmol) was dissolved in 90mL of ethyl alcohol taken in hydrogenation bottle and 0.65g 10% palladium on charcoal (0.6mmol) was added to the solution. The mixture was allowed to shake under H\textsubscript{2} gas at a pressure of 45 Psi for 8 hours in the hydrogenation apparatus. Then the reaction mixture was filtered through
celite to remove the solid materials. Removal of the solvent of the filtrate under reduced pressure furnished 5α, 6-dihydrocholesterol as white flakes (1.97gm, 98%).

\[
\text{mp 136-138°C; IR (CHCl}_3\text{): 3400, 1445, 1200 cm}^{-1}; \text{ }^{1}\text{H NMR (CDCl}_3\text{): }\delta\text{ 0.9 (s, 3H, Me), 1.0 (s, 3H, Me), 0.9–1.9 (m, 38H, –CH and –CH}_2\text{), 2.1 (s, 3H, COMe), 3.4 (m, 1H, C-3). }^{13}\text{C NMR (75 MHz, CDCl}_3\text{): }\delta\text{ 15.2, 16.7, 21.3, 20.9, 21.5, 22.6, 22.8, 22.9, 24.6, 28.1, 28.3, 29.0, 32.0, 34.2, 34.7, 35.1, 35.4, 35.7, 39.5, 39.7, 40.5, 41.9, 46.2, 55.4, 69.5, 72.6; MS (ESI): m/z 388 (M^+); Anal. Calcd. for C}_{27}\text{H}_{48}\text{O: C, 83.5; H, 12.37; Found: C, 83.44; H, 12.45.}
\]

2.9.11: 5α-cholest-3-one (24)

5,6-dihydrocholesterol (23) (1gm, 2.57mmol) was dissolved in 100mL of toluene and stirred to obtain a clear solution. To this stirring solution, PCC (8.5g) on alumina (8.16mmol) was added in small portions and the whole amount was added within 3 hours. After completion of the reaction (TLC), the reaction mixture was diluted with 5 volumes of anhydrous ether and then passed through a pad of active alumina. The organic extract thus obtained was dried over anhyd. Na₂SO₄. It was then evaporated under reduced pressure to get a residue which was purified by column chromatography.
by using EtOAc: PE:: 1:9 as eluent to get pure 5α-cholest-3-one (24) as white solid (0.88 gm, 88.5%).

mp 120-122°C; IR (cm$^{-1}$): 1710, 1445, 1200; $^1$H NMR (300 MHz, CDCl$_3$): 0.9 (s, 3H, Me), 1.1 (s, 3H, Me), 0.9–1.9 (m, 37H, –CH and –CH$_2$), 2.2 (s, 3H, COMe); $^{13}$C NMR (75 MHz, CDCl$_3$): δ 15.2, 16.7, 20.9, 21.3, 21.5, 22.6, 22.8, 22.9, 24.6, 28.1, 28.3, 29.0, 32.0, 34.2, 34.7, 35.1, 35.4, 35.5, 39.5, 39.7, 39.5, 40.5, 41.9, 46.2, 55.4, 69.5, 212.6; MS (ESI): m/z 386 (M$^+$); Anal. Calcd. for C$_{27}$H$_{46}$O: C, 83.93; H,11.91; Found: C, 83.87; H, 11.99.

2.9.12: 3-oxa-A-homo-5α-cholest-4-one (25a) and 4-oxa-A-homo-5α-cholest-3-one (25b)

A mixture of m-CPBA (0.66g, 3.9mmol) and 5α-cholestan-3-one (24) (600mg, 1.5mmol) in CHCl$_3$ (10mL) was irradiated in a closed vessel in a Synthon 3000 microwave reactor at 350 W, 105°C and 7.1 bar for 5 min. The reaction mixture was then allowed to cool to rt and washed subsequently with 10% Na$_2$SO$_3$ (2 x 100mL) and aq. 10% NaHCO$_3$ (2x100mL). The organic phase thus obtained was dried over anhyd. Na$_2$SO$_4$. It was then evaporated under reduced pressure which was further purified by column chromatography over silica gel using EtOAc:PE::1:10 as the eluent to furnish
the pure lactones 3-Oxa-A-homo-5α-cholest-4-one (25a) (418mg, 67%) and 4-Oxa-A-
homo-5α-cholest-3-one (25b) (193mg, 33%).

IR (CHCl₃): 1740, 1400, 1250, 950 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 0.66 (s, 3H,
Me), 0.89 (d, 3H, J = 8.4 Hz), 1.2 (s, 3H, Me), 0.7–2.1 (m, 35-H), 3.88 (d, 1H, J = 13.2
Hz, H-2a), 4.0–4.1 (m, 1H, H-4aa), 4.2–4.25 (m, 1H, H-4ab), 4.68 (m, 1H, H-2b), ¹³C
NMR (75 MHz, CDCl₃): δ 15.4, 15.4, 15.8, 18.7, 20.9, 22.6, 22.8, 24.4, 24.6, 25.7, 26.9,
28.3, 29.8, 34.5, 35.7, 36.2, 36.8, 37.8, 39.1, 39.7, 40.5, 42.6, 43.9, 51.8, 63.3, 176.3,
176.4; MS (ESI) m/z: 402 (M⁺); Anal. Calcd. for C₂₇H₄₆O₂: C, 80.39; H, 11.41; Found:
C, 80.54; H, 11.52.

4-oxa-A-homo-5α-cholest-3-one (25b)

IR (CHCl₃): 1740, 1400, 1250, 950 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): 0.66 (s, 3H,
Me); 0.89 (d, 3H, J = 8.4 Hz); 1.3 (s, 3H, Me); 0.7–2.1 (m, 35-H); 4.0–4.1 (m, 1H, H-
4aa); 4.2–4.25 (m, 1H, H-4ab); 4.61 (m, 1H, H-2b); ¹³C NMR (75 MHz, CDCl₃): δ
15.4, 15.4, 15.8, 18.7, 20.9, 22.6, 22.8, 24.4, 24.6, 25.7, 26.9, 28.3, 29.8, 34.5, 35.7,
36.2, 36.8, 37.8, 39.1, 39.7, 40.5, 42.6, 43.9, 51.8, 63.3, 176.3, 176.4; MS (ESI) m/z:
402 (M⁺); Anal. Calcd. for C₂₇H₄₆O₂: C, 80.39; H, 11.41; Found: C, 80.54; H, 11.52.
4.9.13: 2, 3-seco-2-hydroxy-3-carboxy-5α-cholestan (26)

Steroid lactone (25a) (400mg, 0.99mmol) was dissolved in a 5% solution of KOH in MeOH-H$_2$O (85-15mL). The reaction mixture was refluxed for 3h. After completion of the reaction, the mixture was poured into cold water and acidified by adding aq. solution of citric acid. It was then extracted with DCM (3x100mL). The organic extract was dried over anhyd. Na$_2$SO$_4$ and evaporated under reduced pressure to get a residue. The crude product was purified by column chromatography by using EtOAc: PE:: 1:7 as eluent to get the pure 2, 3-seco-2-hydroxy-3-carboxy-5α-cholestan (26) as a gum (195 mg, 47%).

IR (CHCl$_3$): 3400, 1705, 1400, 1250, 950 cm$^{-1}$; $^1$H NMR (CDCl$_3$): 0.9 (s, 3H, Me), 1.0 (s, 3H, Me), 0.9–1.9 (m, 36H, –CH and –CH$_2$), 3.54 (m, 2H, H-2); $^{13}$C NMR: δ 15.2, 15.8, 16.7, 20.9, 22.6, 22.8, 22.9, 24.6, 28.1, 28.3, 29.0, 29.3, 32.0, 34.2, 34.7, 35.4,
35.7, 39.5, 39.5, 39.7, 40.5, 41.9, 46.2, 59.1, 55.4, 76.5, 214.6; MS (ESI) m/z: 420 (M⁺);
Anal. Calcd. for C_{27}H_{48}O_{3}: C, 77.14; H, 11.42; Found: C, 77.09; H, 11.50.

2.9.14: Steroid-Amino Acid Conjugate (27a)

Ugi-4CR: MW

420mg (1.0mmol) of the seco-steroidal acid (26) furnished A-ring cleavage Steroid-Amino Acid Conjugate (27a) (554.2mg, 85%) using L-alanine methyl ester as amino acid residue by Ugi-4CR as per general procedure.

Ugi-4CR: Classical

420mg (1.0mmol) of the seco-steroidal acid (26) furnished A-ring cleavage Steroid-Amino Acid Conjugate (27a) (198mg, 30%) using L-alanine methyl ester as amino acid residue by Ugi-4CR as per general procedure.

mp 242°C; [α]_D^{25}: (-) 210.45° (c1, CHCl₃); IR (CHCl₃): 3400, 1735, 1400, 1250, 950 cm⁻¹; $^1$H NMR(CDCl₃): δ 0.9 (s, 3H, Me), 1.0 (s, 3H, Me), 0.9–1.9 (m, 42H, –CH and –CH₂), 3.9 (s, 3H, OCH₃), 4.06-4.09 (m, 2H, NCH), 4.21-4.24 (m, 2H, CH₂), 4.72-4.74 (m, 2H, CH₂), 7.17-7.21(m, 5H, Ph); $^{13}$C NMR: δ 15.2, 16.7, 16.7, 20.9, 22.6, 22.6, 22.9, 24.6, 28.1, 29.0, 29.7, 30.2, 31.5, 32.3, 32.0, 34.2, 34.7, 35.4, 35.7, 39.5, 40.5, 41.9, 46.2, 47.9, 48.2, 49.2, 51.4, 55.4, 59.1, 76.5, 127.2, 127.9, 129.1, 138.9, 171.2,
2.9.15: Steroid-Amino Acid Conjugate (27b)

**Ugi-4CR: MW**

420 mg (1.0mmol) of the seco-steroidal acid (26) furnished A-ring cleavage Steroid-Amino Acid Conjugate (27b) (585mg, 86%) using L-valine methyl ester as amino acid residue by Ugi-4CR as per general procedure.

**Ugi-4CR: Classical**

420 mg (1.0mmol) of the seco-steroidal acid (26) furnished A-ring cleavage Steroid-Amino Acid Conjugate (27b) (70mg, 25%) using L-valine methyl ester as amino acid residue by Ugi-4CR as per general procedure.

mp 241°C; [α]D²⁵ : (-) 192.76° (c1, CHCl₃); IR (CHCl₃): 3400, 1735, 1400, 1250, 950 cm⁻¹; ¹H NMR (CDCl₃): δ 0.9 (s, 3H, Me), 1.0 (s, 3H, Me), 1.2-1.3 (br s, 6H, methyl groups), 0.9–1.9 (m, 42H, –CH and –CH₂), 3.9 (s, 3H, OCH₃), 4.06-4.09 (m, 2H, NCH), 4.21-4.24 (m, 2H, CH₂), 4.72-4.74 (m, 2H, CH₂), 7.17-7.21 (m, 5H, Ph); ¹³C NMR: δ 15.2, 16.6, 16.6, 16.7, 16.7, 20.9, 22.6, 22.6, 22.9, 24.7, 24.6, 28.1, 29.0, 29.7, 30.2, 31.5, 32.0, 32.3, 34.2, 34.7, 35.4, 35.7, 39.5, 40.5, 41.9, 46.2, 47.9, 48.2, 49.2, 51.4, 55.4, 59.1, 76.5, 127.3, 127.9, 129.1, 138.9, 171.2, 172.0, 173.2, MS (ESI) m/z: 680 (M⁺); Anal. Calcd. for C₂₇H₄₈O: C, 71.32; H, 10.00; N, 4.11; Found: C, 74.08; H, 10.06; N, 4.11.
2.9.16: Cholest-4-en-3-one (28)

500mg of the cholesterol (1.3mol) was dissolved in 50mL of DCM. To the stirring solution was added 100mg of PCC and was allowed to stir at room temperature for a period of 48h. Then the reaction mixture was diluted with 5 volumes of anhydrous ether and then passed through a pad of active alumina. The organic extract thus obtained was dried over anhyd. Na$_2$SO$_4$ and evaporated under reduced pressure to get a crude residue. The pure product of cholest-4-en-3-one (28) was obtained by crystallisation from alcohol as white solid (287 mg, 61%).

mp 135-137$^\circ$C; IR (CDCl$_3$): 1675, 1445, 1200 cm$^{-1}$; $^1$H NMR (CDCl$_3$): $\delta$ 0.9 (s, 3H, Me), 1.1 (s, 3H, Me), 1.0–1.9 (m, 34H, –CH and –CH$_2$), 6.2 (s, 1H); $^{13}$C NMR: $\delta$ 15.2, 16.7, 20.9, 21.3, 21.5, 22.6, 22.8, 22.9, 24.6, 28.1, 28.3, 29.0, 32.0, 34.2, 34.7, 35.1, 35.4, 35.7, 39.5, 39.7, 40.5, 46.2, 55.4, 69.5, 122.3, 162.4, 202.6; MS (ESI) $m/z$: 384 (M$^+$); Anal. Calcd. for C$_{27}$H$_{44}$O: C, 84.3; H,11.45; Found: C, 84.31; H, 11.53.
2.9.17: 5-Oxo-A-nor-3, 5-seco-cholest-3-oic acid (29)

To a solution of cholest-4-en-3-one (28) (3gm, 7.8mmol) in isopropanol (40mL) was added solution of Na$_2$CO$_3$ (1.2gm, 11.8mmol) in water (20mL). The mixture was brought to reflux and to it was added NaIO$_4$ (12gm, 56mmol) and KMnO$_4$ (0.09gm, 0.5mmol) and was kept at 75ºC for a period of 1h. The reaction was cooled to 30ºC and after 15 min the solid was removed by filtration. The aq. residue was cooled and acidified with concentrated HCl solution and extracted with DCM (3x100mL). The organic extract thus obtained was dried over anhyd. Na$_2$SO$_4$. Removal of the solvent under reduced pressure afforded the crude product which was purified by column chromatography by using EtOAc: PE:: 1:4 as eluent to get pure 5-oxo-A-nor-3,5-seco-cholest-3-oic acid (29) as white solid (2.8gm, 89%).

mp 137-138ºC; IR (CHCl$_3$): 1707, 1466, 1312, 1220, 772 cm$^{-1}$; $^1$H NMR (CDCl$_3$): δ 0.9 (s, 3H, Me), 1.0 (s, 3H, Me), 0.9–1.9 (m, 34H, –CH and –CH$_2$), 2.1 (m, 4H, H-2 & H-6); $^{13}$C NMR: δ 15.2, 16.7, 20.9, 21.3, 21.5, 22.6, 22.9, 24.6, 28.1, 28.3, 29.0, 32.0, 34.2, 34.7, 35.1, 35.4, 35.7, 39.7, 39.5, 40.5, 46.2, 55.4, 69.5, 177.6, 215.3; MS (ESI) m/z: 404 (M$^+$); Anal. Calcd. for C$_{26}$H$_{44}$O$_3$: C, 77.22; H, 10.89; Found: C, 77.18; H, 10.96.
2.9.18: Steroid-Amino Acid Conjugate (30a)

Ugi-4CR: MW

404mg (1.0mmol) of the seco-steroidal acid (29) furnished A-ring cleavage Steroid-Amino Acid Conjugate (30a) (477mg, 75%) using L-alanine methyl ester as amino acid residue by Ugi-4CR as per general procedure.

Ugi-4CR: Classical

404mg (1.0mmol) of the seco-steroidal acid (29) furnished A-ring cleavage Steroid-Amino Acid Conjugate (30a) (159mg, 25%). using L-alanine methyl ester as amino acid residue by Ugi-4CR as per general procedure.

\[
\begin{align*}
\text{mp } 231^\circ C; \quad [\alpha]_{D}^{25}: (-) 183.86^\circ (c 1, CHCl_3); \quad \text{IR} (CHCl_3): 3400, 1735, 1400, 1250, 950 cm^{-1}; \quad ^1H \text{ NMR} (CDCl}_3): \delta 0.9 (s, 3H, Me), 1.0 (s, 3H, Me), 0.9–1.9 (m, 40H, –CH and –CH}_2), 3.9 (s, 3H, OCH}_3), 4.06-4.09 (m, 2H, NCH), 4.21-4.24 (m, 2H, CH}_2), 4.72-4.74 (m, 2H, CH}_2), 7.17-7.21 (m, 5H, Ph); \quad ^13C \text{ NMR}: \delta 34.2, 59.1, 31.5, 28.1, 29.0, 46.2, 35.4, 20.9, 40.5, 43.8, 34.7, 22.9, 26.5, 16.7, 15.2, 49.2, 51.4, 171.2, 172.0, 173.2, 215.6, 127.2, 127.9, 129.1, 138.9, 47.9, 48.2, 30.2, 32.3, 35.7, 24.6, 29.7, 30.1, 22.6,
\end{align*}
\]
22.6, MS (ESI) \( m/z: 636 (M^+) \); Anal. Calcd. for C\(_{39}\)H\(_{60}\)N\(_2\)O\(_5\): C, 73.55; H, 9.50; N, 4.40.

Found: C, 73.52; H, 9.48; N, 4.47.

2.9.19: Steroid-Amino Acid Conjugate (30b)

**Ugi-4CR: MW**

404mg (1.0mmol) of the Seco-Steroidal acid (29) furnished A-ring cleavage Steroid-Amino Acid Conjugate (30b) (517mg, 78%) using L-valine methyl ester as amino acid residue by Ugi-4CR as per general procedure.

**Ugi-4CR: Classical**

404mg (1.0mmol) of the seco-steroidal acid (29) furnished A-ring cleavage Steroid-Amino Acid Conjugate (30b) (132mg, 20%) using L-valine methyl ester as amino acid residue by Ugi-4CR as per general procedure.

mp 240°C; \([\alpha]_D^{25}\): (-) 164.67° (c1, CHCl\(_3\)); IR (CHCl\(_3\)): 3400, 1735, 1400, 1250, 950 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)): \( \delta \) 0.9 (s, 3H, Me), 1.0 (s, 3H, Me), 1.1-1.3 (br s, 6H, methyl groups), 0.9–1.9 (m, 40H, –CH and –CH\(_2\)), 3.9 (s, 3H, OCH\(_3\)), 4.06-4.09 (m, 2H, NCH), 4.21-4.24 (m, 2H, CH\(_2\)), 4.72-4.74 (m, 2H, CH\(_2\)), 7.17-7.21 (m, 5H, Ph); \(^{13}\)C NMR: \( \delta \) 15.2, 16.6, 16.6, 16.7, 16.7, 20.9, 22.6, 22.6, 22.9, 24.6, 24.7, 28.1, 29.0, 29.7, 30.2,
31.5, 32.0, 32.3, 34.2, 34.7, 35.4, 35.7, 39.5, 40.5, 41.9, 46.2, 47.9, 48.7, 49.2, 51.4, 55.4, 59.1, 76.5, 127.2, 127.9, 129.1, 132.7, 171.2, 172.0, 173.2, 215.6; MS (ESI) m/z: 664 (M⁺); Anal. Calcd. for C₄₁H₆₄N₂O₅: C, 74.06; H, 9.70; N, 4.21. Found: C, 74.04; H, 9.63; N, 4.21.

2.9.20: 5α, 6α-epoxy-3β-acetoxy-pregnenolone (32)

To a (200mg, 0.557mmol) solution of 3β-acetoxy-pregn-5-ene (31) in 8mL chloroform was added (100mg, 0.6mmol) of m-CPBA. The reaction mixture was kept overnight at room temperature. After completion of the reaction, the reaction mixture was then poured into cold water and was extracted with DCM. The organic extract was washed first with an aq. solution of sodium-meta bisulphite and then with a 5% NaOH solution. The organic extract thus obtained was drying over anhyd. Na₂SO₄. It was then distilled under reduced pressure to furnish a crude residue which was purified by column chromatography (EtOAc:PE::1:6) to get pure 5α,6α-epoxy-3β-acetoxy-pregnenolone (32) as a white solid (188mg, 90%) as the major product.

\[
\text{mp } 140.7°C; \text{ IR (CHCl₃): } 1735, 1704, 1450, 1243\text{cm}^{-1}; \text{ } ^{1}H \text{ NMR (CDCl₃): } \delta \text{ } 0.59 \text{ (s, 3H, Me), 1.07 (s, 3H, Me), 1.96 (s, 3H, OCH₃), 2.47 (t, 1H, 17H), 2.91 (t, 1H, 6H), 4.91-5.00 (m, 1H, OCOCH₃), 7.17-7.21 (m, 5H, Ph); } ^{13}C \text{ NMR: } \delta \text{ 13.1, 18.2, 20.1, 21.0, 23.1.}
\]
22.8, 23.4, 27.3, 30.2, 30.8, 31.1, 31.5, 33.6, 34.2, 35.1, 36.1, 38.1, 43.3, 44.5, 55.1, 
59.1, 61.3, 63.4, 69.3, 72.8, 170.1, 209.4, MS (ESI): \( m/z \) 374 (M⁺); Anal. Caled. for 
\( \text{C}_{23}\text{H}_{34}\text{O}_4 \): C, 73.76; H, 9.15; Found: C, 73.79; H, 9.09.

**2.9.21: Oxidation of 5α, 6α-epoxy-3β-acetoxy-pregnenolone (32)**

To a solution of 1 gm of 5α, 6α-epoxy-3β-acetoxy-pregnenolone (32) in 50mL 
of dry acetone was added freshly prepared Jones reagent (3mL) dropwise and was 
refluxed at 50°C for a period of 12h. The reaction was followed on TLC. After 
completion of the reaction, the reaction mixture is poured into cold water (200mL) and 
quenched with methanol (5mL) to destroy excess oxidants. The reaction mixture was 
then extracted with DCM. The organic layer thus obtained was drying over anhyd. 
\( \text{Na}_2\text{SO}_4 \). It was then distilled under reduced pressure to furnish a residue which was 
purified by column chromatography (EtOAc:PE::1:4) to get the four pure products as 
white solids, \textit{viz.}, 5α-hydroxy-6-keto-3β-acetoxy-20-oxo-pregnane (33) (0.521mg, 
50%), 5, 20-dione-5, 7-seco-pregn-4-ene (34) (27mg, 30%), 3β-acetoxy-7-carboxy-5, 7-
seco-pregn-5, 20-dione (35) (16.2mg, 15%), 3β-acetoxy-6, 20-dione-pregn-4-ene (36) 
(4.9mg, 5%).

**2.9.21.1: 5α-hydroxy-6-keto-3β-acetoxy-20-oxo-pregnane (33)**
mp 148.6°C; IR (CHCl₃): 3450, 1735, 1710 (double strength), 1243, 900 cm⁻¹; ¹H NMR (CDCl₃): 0.80 (s, 3H, Me), 1.15 (s, 3H, Me), 2.0 (s, 3H, OCH₃), 2.1 (s, 3H, methyl ketone), 5.07 (m, 1H, 3-H); ¹³C NMR: δ 13.3, 13.9, 21.3, 21.3, 22.7, 24.0, 26.2, 29.5, 31.4, 32.3, 37.0, 38.5, 41.4, 42.4, 44.1, 44.5, 56.3, 63.4, 70.5, 80.1, 170.1, 209.4, 212, MS (ESI): m/z 390 (M⁺); Anal. Calcd. for C_{23}H_{34}O_{5}: C, 70.74; H, 8.78; Found: C, 70.76; H, 8.71.

Crystal data of the compound (33) C_{23}H_{34}O_{5}, (M⁺) 390, tetragonal, space group P2₁, a = 10.3595(9), b = 10.3595(9), c = 40.397(5) Å, V = 4335.4(9) Å³, Z = 8, Dcalc (g cm⁻³) = 1.246, θmax = 26.080, F(000) = 396.0, μ (mm⁻¹) = 0.086, No of reflections 4299 [2588], multi-scan absorption correction, Tmin = 0.975, Tmax = 0.986, number of parameters = 291, wR2 = 0.1782.

2.9.21.2: 5, 20-dione-5, 7-Secopregn-4-ene (34)

mp 134.8°C IR(CHCl₃): 1710 (double strength), 1676, 1310, 1150, 800 cm⁻¹; ¹H NMR (CDCl₃): δ 1.1 (s, 3H, Me), 1.2 (s, 3H, Me), 2.1 (s, 3H, methyl ketone), 5.88 (d, J=9.6, 4-H), 6.8 (m, 1H, 3-H); ¹³C NMR: δ 12.9, 18.1, 20.5, 22.6, 24.8, 24.0, 28.1, 29.6, 31.4, 34.6, 34.80, 35.1, 38.7, 41.6, 43.1, 47.5, 54.3, 63.4, 128.6, 147.0, 177.6, 209.1, 209.3, MS (ESI) m/z: 346 (M⁺); Anal. Calcd for C_{21}H_{30}O_{4}: C, 72.80; H, 8.73; Found: C, 72.83; H, 8.67.
2.9.21.3: 3β-acetoxy-7-carboxy-5, 7-Seco-pregn-5, 20-dione (35)

mp 267.4°C; IR (CHCl₃): 1732, 1703, 1453, 1243 cm⁻¹; ¹H NMR (CDCl₃): 0.65 (s, 3H, Me), 1.1 (s, 3H, Me), 2.0 (s, 3H, methyl ketone), 2.2 (s, 1H, COCH₃), 3.19 (dd, J=6, CH₂), 3.23 (dd, J=6, CH₂) 4.5 (m, 1H, acetate proton); ¹³C NMR: δ 13.0, 17.1, 21.2, 22.6, 23.0, 24.6, 25.2, 31.4, 35.4, 38.7, 41.1, 43.1, 43.9, 52.3, 54.0, 63.3, 73.3, 170.3, 177.0, 209.1, 210.3, MS (ESI): m/z 406 (M⁺); Anal. Calcd for C₂₃H₃₄O₆: C, 67.96; H, 8.43; Found: C, 67.98; H, 8.37.

2.9.21.4: 3β-acetoxy-6, 20-dione-pregn-4-ene (36)

mp 132°C; IR (CHCl₃): 1735, 1703, 1676, 1453, 1243, 1150, 850 cm⁻¹; ¹H NMR (CDCl₃): 0.84 (s, 3H, Me), 1.1 (s, 3H, Me), 2.0 (s, 3H, OCH₃), 2.1 (s, 3H, methyl ketone), 4.2 (m, 1H, 3-H); 5.9 (d, J=9, 4-H), 6.8 (dd, 7-H); ¹³C NMR: δ 13.3, 13.9, 21.3, 21.3, 22.7, 24.0, 26.2, 29.5, 31.4, 32.3, 37.0, 38.5, 41.4, 42.4, 44.1, 44.5, 56.3, 63.4, 70.5, 80.1, 170.1, 178.7, 209.4, 212, MS (ESI) m/z: 372 (M⁺); Anal. Calcd. for C₂₃H₃₂O₄: C, 70.74; H, 8.78; Found: C, 70.76; H, 8.71.
2.9.22: Steroid-Amino Acid Conjugate (37a)

Ugi-4CR: MW

346mg (1.0mmol) of the seco-steroidal acid (34) furnished B-ring cleavage Steroid-Amino Acid Conjugate (37a) (502mg, 87%) using L-alanine methyl ester as amino acid residue using Ugi-4CR as per general procedure.

Ugi-4CR: Classical

346mg (1.0mmol) of the seco-steroidal acid (34) furnished Steroid-Amino Acid Conjugate (37a) (15mg, 20%) using L-alanine methyl ester as amino acid residue using Ugi-4CR as per general procedure.

mp 203°C; [α]D: (+) 209.66° (c2, CHCl₃); IR (CHCl₃): 3400, 1741, 1698, 1430, 1215 cm⁻¹; ¹H NMR: 0.64 (s, 3H, Me), 1.01 (s, 3H, Me), 2.0 (bs, 6H, methyl groups), 3.5 (s,
3H, OCH$_3$), 3.68-3.82 (m, 2H, NCH), 4.1-4.6 (m, 2H, CH$_2$), 6.1 (d, 1H), 6.7 (d, 1H),
7.2-7.5 (m, 5H, Ph); 8.3 (NH Proton); $^{13}$C NMR: δ 16.8, 19.8, 21.0, 22.4, 23.4, 24.3,
24.6, 27.1, 27.3, 30.4, 31.1, 32.2, 34.4, 35.7, 36.1, 42.1, 42.3, 44.8, 48.1, 50.1, 53.3,
57.4, 57.9, 126.7, 127.1, 127.2, 128.1, 128.1, 128.3, 142.7, 145.4, 168.2, 172.1, 171.3,
209.1; MS (ESI) m/z: 578 (M$^+$); Anal. Calcd. for C$_{34}$H$_{46}$N$_2$O$_6$: C, 70.56; H, 8.01; N,
4.84. Found: C, 70.49; H, 7.94; N, 4.83.

2.9.23: Steroid-Amino Acid Conjugate (37b)

Ugi-4CR: MW

346mg (1.0mmol) of the seco-steroidal acid (34) furnished B-ring cleavage Steroid-
Amino Acid Conjugate (37b) (551mg, 85%) using L-lysine methyl ester as per general
procedure.

Ugi-4CR: Classical

346mg (1.0mmol) of the seco-steroidal acid (34) furnished B-ring cleavage Steroid-
Amino Acid Conjugate (37b) (162mg, 25%) using L-lysine methyl ester as amino acid
residue using Ugi-4CR as per general procedure.

![Steroid-Amino Acid Conjugate (37b) diagram]
mp 210°C; [α]D: (+) 146.23° (c1, CHCl₃); IR (CHCl₃): 3400, 1741, 1698, 1665, 1430, 1218 cm⁻¹; ¹H NMR: δ 1.2 (s, 3H, Me), 1.3 (s, 3H, Me), 3.8 (s, 3H, OCH₃), 2.68-2.82 (m, 2H, NCH), 4.1-4.6 (m, 2H, CH₂), 6.1(d, 1H), 6.7 (d, 1H), 7.2-7.5 (m, 5H, Ph), 8.3 (NH Proton); ¹³C NMR: δ 16.8, 19.8, 21.0, 22.4, 23.4, 23.6, 24.6, 24.3, 24.6, 27.1, 27.3, 29.7, 30.4, 31.1, 32.2, 34.4, 35.7, 36.1, 42.1, 42.3, 44.8, 48.1, 50.1, 53.3, 57.4, 57.9, 126.7,127.1, 128.1, 128.1, 128.3, 142.7, 145.4, 173.3, 171.3, 172.2, 203.3, 211.1, MS (ESI) m/z: 649 (M⁺); Anal Calcd. for C₃₈H₅₅N₃O₆: C, 70.23; H, 8.53; N, 6.47. Found: C, 70.26; H, 8.47; N, 8.01.

2.9.24: Steroid-Amino Acid Conjugate (38a):

Ugi-4CR: MW

390mg (1.0mmol) of the seco-steroidal acid (35) furnished B-ring cleavage Steroid-Amino Acid Conjugate (38a) (459mg, 72%) using L-alanine methyl ester as the amino acid residue using Ugi-4CR as per general procedure.

Ugi-4CR: Classical

390mg (1.0mmol) of the seco-steroidal acid (35) furnished B-ring cleavage Steroid-Amino Acid Conjugate (38a) (133mg, 21%) using L-alanine methyl ester as the amino acid residue using Ugi-4CR as per general procedure.
mp 223°C; $[\alpha]_D$: (+) 119.28° (c1, CHCl₃); IR (CHCl₃): 3400, 1735, 1705, 1400, 1250, 950 cm⁻¹; ¹H NMR(CDCl₃): 0.9 (s, 3H, Me), 1.0 (s, 3H, Me), 1.2-1.3 (br s, 6H, methyl groups), 0.9–1.9 (m, 42H, –CH and –CH₂), 3.9 (s, 3H, OCH₃), 4.06–4.09 (m, 2H, NCH), 4.21–4.24 (m, 2H, CH₂), 4.72–4.74 (m, 2H, CH₂), 7.17–7.21 (m, 5H, Ph); ¹³C NMR: δ 15.2, 16.7, 20.9, 22.9, 24.6, 28.1, 29.0, 29.7, 30.2, 31.5, 32.0, 32.3, 34.2, 34.7, 35.4, 35.7, 39.5, 41.9, 40.5, 46.2, 47.9, 48.2, 49.2, 51.4, 55.4, 59.1, 76.5, 171.2, 172.0, 173.2, 215.6, 127.2, 127.9, 129.1, 138.9; MS (ESI) m/z: 638 (M⁺). Anal. Calcd. for C₃₆H₅₀N₂O₈: C, 67.69; H, 7.89; N, 4.39. Found: C, 67.62; H, 7.82; N, 4.38.

2.9.25: Steroid-Amino Acid Conjugate (37b)

Ugi-4CR: MW

390mg (1.0mmol) of the seco-steroidal acid (35) furnished B-ring cleavage Steroid-Amino Acid Conjugate (38b) (514mg, 71%) using L-lysine methyl ester as the amino acid residue using Ugi-4CR as per general procedure.

Ugi-4CR: Classical
390mg (1.0mmol) of the seco-stereoidal acid (35) furnished B-ring cleavage Steroid-Amino Acid Conjugate (38b) (144mg, 20%) using L-lysine methyl ester as the amino acid residue using Ugi-4CR as per general procedure.

mp 223°C; [α]D: (+) 113.72° (c1, CHCl₃); IR (CHCl₃): 3400, 1735, 1705, 1250 cm⁻¹; ¹H NMR(CDCl₃): 0.9 (s, 3H, Me), 1.0 (s, 3H, Me), 1.2-1.3 (bs, 6H, methyl groups), 0.9–1.9 (m, 42H, –CH and –CH₂), 3.9 (s, 3H, OCH₃), 4.06–4.09 (m, 2H, NCH), 4.21–4.24 (m, 2H, CH₂), 4.72–4.74 (m, 2H, CH₂), 7.17–7.21 (m, 5H, Ph); ¹³CNMR: δ 34.2, 59.1, 31.5, 41.9, 32.0, 29.0, 46.2, 35.4, 20.9, 39.5, 40.5, 55.4, 34.7, 22.9, 76.5, 16.7, 15.2, 49.2, 51.4, 171.2, 172.0, 173.2, 215.6, 127.2, 127.9, 129.1, 138.9, 47.9, 48.2, 16.7, 30.2, 32.3, 35.7, 24.6, 29.7, 22.6, 22.6, MS (ESI) m/z: 724 (M⁺). Anal. Calcd. for C₄₁H₆₂N₃O₈: C, 68.00; H, 8.56; N, 5.80 Found: C, 67.7; H, 8.38; N, 5.96.

2.9.26: 3β-Acetoxy-7-oxo-cholest-5-ene (40)

Pyridine (16.2mL, 200mmol) was added to a solution of chromium trioxide (10.61g, 106mmol) in dry DCM (100mL). The solution was stirred at rt under nitrogen atmosphere for 2h. After that cholesteryl acetate (39) (5g, 12mmol) was added and the mixture was stirred for 12h. The solution was filtered, washed with 0.1 N HCl (100mL),...
5% NaHCO$_3$ (100mL) and finally with water 100mL) and extracted with DCM. The organic layer was dried over anhyd. Na$_2$SO$_4$ and evaporated under reduced pressure to give crude product, which was purified by chromatography on silica gel column (EtOAc: PE::1:8) to afford pure 3β-Acetoxy-7-oxo-cholest-5-ene (40) as solid (3.3 g, 62%).

```
AcO

mp 149-151°C IR (CHCl$_3$): 1735, 1673, 1400, 1250, 950 cm$^{-1}$; $^1$H NMR (CDCl$_3$): 0.9 (s, 3H, Me), 1.0 (s, 3H, Me), 0.9–1.9 (m, 38H, –CH and –CH$_2$), 2.1 (s, 3H, acetate proton), 3.9 (m, 1H, H-3), 6.2 (d, 1H, H-6); $^{13}$C NMR: δ 34.2, 35.1, 173.6, 39.5, 153.4, 128.1, 213.2, 29.0, 46.2, 35.4, 20.9, 39.5, 40.5, 55.4, 34.7, 22.9, 69.5, 16.7, 15.2, 21.5, 21.3, 35.7, 24.6, 39.7, 28.3, 22.6, 22.8; MS (ESI) m/z: 442 (M$^+$). Anal. Calcd. for C$_{29}$H$_{46}$O$_3$: C, 78.68; H, 10.47. Found: C, 78.65; H, 10.45.

2.9.27: 3β-Acetoxy- 5-oxo-B-nor- 5,6-seco-cholest-6-oic acid (41)

To a solution of the compound (40) (3g, 0.0065mmol) in isopropanol (40mL) was added solution of Na$_2$CO$_3$ (1.2gm, 11.8mmol) in water (6mL). The mixture was brought to reflux and a solution of NaIO$_4$ (12gm, 56mmol) and KMnO$_4$ (0.09gm, 0.5mmol) in warm water (75°C) was added. The reaction was cooled to 30°C and after 15 min the solid was removed by filtration. The solid was washed with water (50mL)

*Microwave Irradiated Ugi four-component reaction (Ugi-4CR)*: Expedited synthesis of Steroid-Amino acid Conjugates- *A Novel Class of Peptidomimetic Hybrid Compounds based on Seco-Steroids (A, B & D Ring Cleavage).*
and the aq. residue was cooled and acidified with concentrated HCl solution. The product was extracted with DCM (3x100mL) and dried over anhyd. Na₂SO₄. Removal of the solvent afforded the crude which purified by column chromatography by using EtOAc: PE::1:4 as eluent to get pure 3β-Acetoxy- 5-oxo-B-nor- 5,6-seco-cholest-6-oic acid (41) (1.42 gm, 45%) as a solid.

\[
\text{mp 127-129}^\circ\text{C; IR (CHCl}_3\text{: 1735,1705, 1400, 1250, 950 cm}^{-1}; \text{ }^1\text{H NMR (CDCl}_3\text{): 0.9 (s, 3H, Me), 1.0 (s, 3H, Me), 0.9–1.9 (m, 39H, –CH and –CH}_2\text{), 3.9 (m, 1H, H-3); }^{13}\text{C NMR: } \delta \text{ 34.2, 35.1, 173.6, 39.5, 215.4, 202.1, 29.0, 46.2, 35.4, 20.9, 39.5, 40.5, 55.4, 34.7, 22.9, 69.5, 16.7, 15.2, 21.5, 21.3, 35.7, 24.6, 39.7, 28.3, 22.6, 22.8; MS (ESI) m/z: 462 (M}^+\text{); Anal. Calcd. for C}_{28}\text{H}_{46}\text{O}_5\text{: C, 72.69; H, 10.02. Found: C, 72.67; H, 10.01.}
\]

2.9.28: Steroid-Amino Acid Conjugate (41a)

Ugi-4CR: MW

462mg (1.0mmol) of the seco-steroidal acid (41) furnished B-ring cleavage Steroid-Amino Acid Conjugate (41a) (520mg, 75%) using L-alanine methyl ester as the amino acid residue using Ugi-4CR as per general procedure.

Ugi-4CR: Classical
462mg (1.0mmol) of the seco-steroidal acid (41) furnished B-ring cleavage Steroid-Amino Acid Conjugate (41a) (138mg, 20%) using L-alanine methyl ester as the amino acid residue using Ugi-4CR as per general procedure.

\[
\text{mp } 221{}^\circ\text{C; } [\alpha]_D^{25}: (+) 196.45^\circ \text{ (c2, CHCl}_3); \text{ IR (CHCl}_3): 3400, 1735, 1705, 1400, 1250, 950 \text{ cm}^{-1}; \text{ } ^1\text{H NMR (CDCl}_3): 0.9 \text{ (s, 3H, Me), 1.0 \text{ (s, 3H, Me), 0.9–1.9 \text{ (m, 42H, –CH} \\
\text{and –CH}_2, 3.9 \text{ (s, 3H, OCH}_3, 4.06-4.09 \text{ (m, 2H, NCH), 4.21-4.24 \text{ (m, 2H, CH}_2, 4.72-4.74 \text{ (m, 2H, CH}_2, 7.17-7.21 \text{ (m, 5H, Ph); } ^{13}\text{CNMR: } \delta 15.2, 16.7, 16.7, 20.9, 22.6, 22.6; \text{ } 22.9, 24.6, 28.1, 29.0, 29.7, 30.2, 31.5, 32.0, 32.3, 34.2, 34.7, 35.4, 35.7, 39.5, 40.5, 41.9, 46.2, 47.9, 48.2, 49.2, 51.4, 55.4, 59.1, 76.5, 127.2, 127.9, 129.1, 138.9, 171.2, 172.0, 173.2, 215.6; \text{ MS (ESI) m/z: 694 (M}^+); \text{ Anal. Calcd. for C}_{39}\text{H}_{60}\text{N}_{2}\text{O}_5: C, 73.55; \text{ H,9.50; N, 4.40. Found: C, 73.52; H, 9.48; N, 4.47.}
\]

**2.9.29: Steroid-Amino Acid Conjugate (41b):**

**Ugi-4CR: MW**

462mg (1.0mmol) of the seco-steroidal acid (41) furnished B-ring cleavage Steroid-Amino Acid Conjugate (41b) (534mg, 74%) using L-valine methyl ester as the amino acid residue using Ugi-4CR as per general procedure.
Ugi-4CR: Classical

462mg (1.0mmol) of the seco-steroidal acid (41) furnished B-ring cleavage Steroid-Amino Acid Conjugate (41b) (166mg, 23%) using L-valine methyl ester as the amino acid residue using Ugi-4CR as per general procedure.

$\text{mp } 231^\circ\text{C}; \left[\alpha\right]_D^{25}: (+) 163.72^\circ (c2, \text{CHCl}_3); \text{IR (CHCl}_3): 3400, 1735, 1705, 1400, 1250, 950 \text{ cm}^{-1}; \text{^1H NMR (CDCl}_3): 0.9 \text{ (s, 3H, Me)}, 1.0 \text{ (s, 3H, Me)}, 1.2-1.3 \text{ (br s, 6H, methyl groups)}, 0.9–1.9 \text{ (m, 42H, –CH and –CH}_2), 2.1 \text{ (s, 3H, acetate proton)}, 3.9 \text{ (s, 3H, OCH}_3), 4.06-4.09 \text{ (m, 2H, NCH), 4.21-4.24 \text{ (m, 2H, CH}_2), 4.72-4.74 \text{ (m, 2H, CH}_2), 7.17-7.21 \text{ (m, 5H, Ph)}; \text{^13C NMR: } \delta 15.2, 16.7, 16.7, 20.9, 22.6, 22.6, 22.9, 24.6, 28.1, 29.0, 29.7, 32.0, 30.2, 31.5, 32.3, 34.2, 34.7, 35.4, 35.7, 39.5, 40.5, 41.9, 46.2, 47.9, 48.2, 49.2, 51.4, 55.4, 59.1, 76.5, 127.2, 127.9, 129.1, 138.9, 172.0, 171.2, 173.2, 215.6; \text{MS (ESI) } m/z: 722 \text{ (M')}; \text{Anal. Calcd. for } C_{43}H_{66}N_2O_7: \text{C, 71.40; H, 9.14; N, 3.87. Found: C, 71.41; H, 9.13; N, 3.89.}

2.9.30: 17β-acetate-5α-androstane (43)

A mixture of m-CPBA (0.66g, 3.9mmol) and 5α-androst-20-one (42) (453mg, 1.5mmol) in CHCl\(_3\) (10mL) was irradiated in a closed vessel in a Synthon 3000
microwave reactor at 350 W, 105°C and 7.1 bar for 5 min. The reaction mixture was then allowed to cool to room temperature and washed subsequently with 10% Na$_2$SO$_3$ (2x100mL) and aq. 10% NaHCO$_3$ (2x100mL). More water was added and was extracted with DCM. The organic phase was dried over anhyd. Na$_2$SO$_4$ and evaporated under reduced pressure to get the crude product which was purified by column chromatography over silica gel using EtOAc:P.E::1:10 as the eluent to furnish the pure 17β-acetate-5α-androstane (43) (372mg, 78%).

mp 78-80°C; IR (CHCl$_3$): 1735, 1400, 1250, 950 cm$^{-1}$; $^1$H NMR (CDCl$_3$): 0.9 (s, 3H, Me), 1.0 (s, 3H, Me), 0.9–1.9 (m, 24H, –CH and –CH$_2$), 2.0 (s, 3H, acetate proton); $^{13}$C NMR: δ 15.2, 16.7, 19.8, 20.9, 22.9, 25.1, 27.6, 28.1, 28.7, 29.0, 29.5, 34.2, 39.5, 40.5, 46.2, 53.4, 55.4, 69.5, 82.9, 177.6; MS (ESI): m/z 318 (M$^+$); Anal. Calcd. for C$_{21}$H$_{34}$O$_2$: C, 79.19; H, 10.76. Found: C, 79.17; H, 10.75.

2.9.31: 5α-androst-17-one (44)

17β-acetate-5α-androstane (43) (318mg, 1mmol) was treated with 10mL of 3% solution of KOH in MeOH-H$_2$O (85-15mL). The reaction mixture was stirred at rt for 3h. After completion of the reaction the mixture was poured into cold water and acidified with an aq. citric acid solution. It was then extracted with DCM (3x100mL). The organic extract was dried over anhyd. Na$_2$SO$_4$ and evaporated under reduced pressure to get the crude product which was purified by column chromatography over silica gel using EtOAc:P.E::1:10 as the eluent to furnish the pure 5α-androst-17-one (44) (341mg, 71%).

mp 112-114°C; IR (CHCl$_3$): 3300, 1735, 1400, 1250, 1100 cm$^{-1}$; $^1$H NMR (CDCl$_3$): 0.9–1.9 (m, 24H, –CH and –CH$_2$), 2.0 (s, 3H, acetate proton); $^{13}$C NMR: δ 15.2, 16.7, 19.8, 20.9, 22.9, 25.1, 27.6, 28.1, 28.7, 29.0, 29.5, 34.2, 39.5, 40.5, 46.2, 53.4, 55.4, 69.5, 82.9, 177.6; MS (ESI): m/z 318 (M$^+$); Anal. Calcd. for C$_{21}$H$_{34}$O: C, 80.80; H, 11.81. Found: C, 80.79; H, 11.78.
pressure to get a residue. The crude hydrolysed product thus obtained was dissolved in 20mL of DCM and to it was added 100mg of PCC and stirred for 1h at room temp. On completion of the reaction (TLC), the reaction mixture was diluted with 5 volumes of anhyd. ether and then passed through a pad of active alumina. The organic extract was dried over anhyd. Na$_2$SO$_4$ and evaporated under reduced pressure to get the crude product which was purified by preparative TLC using EtOAc:PE::1:10 as the eluent to get pure 5α-androst-17-one (44) (257mg, 81%).

![Image](image_url)

mp 96-98°C; IR (CHCl$_3$): 1750, 1400, 1250, 950 cm$^{-1}$; $^1$H NMR(CDCl$_3$): 0.9 (s, 3H, Me), 1.0 (s, 3H, Me), 0.9–1.9 (m, 24H, –CH and –CH$_2$), 2.2 (m, 1H, H-17); $^{13}$C NMR: δ 15.2, 16.7, 20.9, 22.9, 29.0, 25.1, 27.6, 28.1, 29.5, 32.0, 34.7, 39.5, 40.5, 46.2, 53.4, 55.4, 177.6; MS (ESI) m/z: 318 (M$^+$); Anal. Calcd. For C$_{19}$H$_{30}$O: C, 83.15; H, 11.02. Found: C, 83.13; H, 10.99.

2.9.32: 17-oxa-5α-androst-17-one (45)

A mixture of m-CPBA (0.66g, 3.9mmol) and 5α-androst-17-one (44) (411mg, 1.5mmol) in CHCl$_3$ (10mL) was irradiated in a closed vessel in a Synthon 3000 microwave reactor at 350 W, 105°C and 7.1 bar for 5 min. The reaction mixture was then allowed to cool to room temperature and washed subsequently with 10% Na$_2$SO$_3$ (2 x 100mL) and aq. 10% NaHCO$_3$ (2x100mL). More water was added and was
extracted with DCM. The organic phase was dried over anhyd. Na$_2$SO$_4$ and evaporated under reduced pressure to get a residue which was purified by column chromatography over silica gel using EtOAc:PE::1:10 as the eluent to furnish the pure 17-oxa-5α-androst-17-one (45) as solid (313mg, 72%).

mp 109–111$^\circ$C; IR (CHCl$_3$): 1741, 1400, 1250, 950 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$): 0.9 (s, 3H, Me), 1.1 (s, 3H, Me), 0.9–1.9 (m, 22H, CH & CH$_2$), 2.2 (m, 2H); $^{13}$C NMR (CDCl$_3$): δ 34.2, 28.2, 22.9, 33.1, 40.9, 27.2, 31.7, 37.1, 56.9, 36.5, 19.8, 38.2, 74.3, 53.5, 35.9, 43.1, 172.2, 16.7, 15.2; MS (ESI) m/z: 290 (M$^+$); Anal. Calcd. For C$_{19}$H$_{30}$O$_2$: C, 78.57; H, 10.41. Found: C, 78.54; H, 10.39.

2.9.33: 13, 17-seco-13-hydroxy-17-carboxy-5α-androstane (46)

Steroidal lactone (45) (290mg, 1mmol) was treated with 40mL of 5% solution of KOH in MeOH-H$_2$O (85-15mL). The reaction mixture was refluxed for 3h. After completion of the reaction, the mixture was poured into cold water (200mL) and acidified with an aq. citric acid solution. The reaction mixture was then extracted with DCM (3x100mL). The organic extract was dried over anhyd. Na$_2$SO$_4$ and evaporated under reduced pressure to get a crude residue. The crude product was purified by preparative TLC by using EtOAc:PE::1:7 as eluent to get the pure 13,17-seco-13-hydroxy-17-carboxy-5α-androstane (46) as gum (156 mg, 54%).
IR (CHCl₃): 3400, 1707, 1400, 1250, 950 cm⁻¹; ¹H NMR (CDCl₃): δ 0.9 (s, 3H, Me), 1.0 (s, 3H, Me), 0.9–1.9 (m, 24H, –CH and –CH₂), 2.1 (m, 2H); ¹³C NMR (CDCl₃): δ 15.2, 16.7, 19.8, 22.9, 27.2, 28.2, 31.7, 33.1, 34.2, 35.9, 36.5, 37.1, 38.2, 40.9, 43.1, 53.5, 56.9, 75.3, 176.2; MS (ESI) m/z: 308 (M⁺); Anal. Calcd. For C₁₉H₃₀O₂: C, 73.98; H, 10.46. Found: C, 73.96; H, 10.45.

2.9.34: Steroid-Amino Acid Conjugate (47a)

Ugi-4CR: MW

308mg (1.0mmol) of the seco-steroidal acid (46) furnished D-ring cleavage Steroid-Amino Acid Conjugate (47a) (437mg, 81%) using L-alanine methyl ester as amino acid residue using Ugi-4CR as per general procedure.

Ugi-4CR: Classical

308mg (1.0mmol) of the seco-steroidal acid (46) furnished D-ring cleavage Steroid-Amino Acid Conjugate (47a) (172mg, 32%) using L-alanine methyl ester as amino acid residue using Ugi-4CR as per general procedure.
mp 211 °C; [α]D^{25}: (-) 123.57° (c1, CHCl₃); IR (CHCl₃): 3400, 1735, 1400, 1250, 950 cm⁻¹; ¹H NMR (CDCl₃): δ 0.9 (s, 3H, Me), 1.0 (s, 3H, Me), 0.9–1.9 (m, 28H, –CH and –CH₂), 3.9 (s, 3H, OCH₃), 4.06-4.09 (m, 2H, NCH), 4.21-4.24 (m, 2H, CH₂), 4.72-4.74 (m, 2H, CH₂), 7.17-7.21 (m, 5H, Ph); ¹³C NMR: δ 15.2, 16.7, 16.7, 22.6, 22.9, 28.9, 29.0, 29.1, 30.2, 31.4, 31.5, 32.0, 34.2, 34.7, 35.4, 38.1, 39.2, 40.9, 43.6, 46.2, 47.9, 48.2, 76.5, 127.2, 127.9, 128.6, 128.6, 129.1, 138.9, 171.2, 172.0, 173.2; MS (ESI) m/z: 540 (M⁺); Anal. Calcd. for C₃₂H₄₈N₂O₅: C, 71.08; H, 8.95; N, 5.18. Found: C, 71.05; H, 8.93; N, 5.16.

2.9.35: Steroid-Amino Acid Conjugate (47b)

**Ugi-4CR: MW**

308mg (1.0mmol) of the seco-steroidal acid (46) furnished D-ring cleavage Steroid-Amino Acid Conjugate (47b) (454mg, 80%) using L-valine methyl ester as amino acid residue using Ugi-4CR as per general procedure.

**Ugi-4CR: Classical**

308mg (1.0mmol) of the seco-steroidal acid (46) furnished D-ring cleavage Steroid-Amino Acid Conjugate (47b) (142mg, 25%) using L-valine methyl ester as amino acid residue using Ugi-4CR as per general procedure.
mp 217°C; [α]_D$^{25}$: (-) 107.85° (c1, CHCl$_3$); IR (CHCl$_3$): 3400, 1735, 1400, 1250, 950 cm$^{-1}$; $^1$H NMR (CDCl$_3$): δ 0.9 (s, 3H, Me), 1.0 (s, 3H, Me), 1.1-1.3 (bs, 6H, methyl groups), 0.9–1.9 (m, 28H, –CH and –CH$_2$), 3.9 (s, 3H, OCH$_3$), 4.06-4.09 (m, 2H, NCH), 4.21-4.24 (m, 2H, CH$_2$), 4.72-4.74 (m, 2H, CH$_2$), 7.17-7.21 (m, 5H, Ph); $^{13}$C NMR: δ 15.2, 16.6, 16.6, 16.7, 16.7, 22.6, 22.9, 24.7, 28.9, 29.0, 29.1, 30.2, 31.4, 31.5, 32.0, 34.2, 34.7, 35.4, 38.1, 39.2, 40.9, 43.6, 46.2, 47.9, 48.2, 76.5, 127.2, 127.9, 129.1, 138.9, 171.2, 172.0, 173.2, MS (ESI) m/z: 568 (M$^+$); Anal. Caled. for C$_{34}$H$_{52}$N$_2$O$_5$: C, 71.8; H, 9.29; N, 4.93. Found: C, 71.73; H, 9.14; N, 4.92.

2.9.36: Steroid-Amino Acid Conjugate (49a)

Ugi-4CR: MW

408mg (1.0mmol) of the cholic acid (48) furnished the Steroid-Amino Acid Conjugate (49a) (536mg, 86%) using L-alanine methyl ester as amino acid residue using Ugi-4CR as per general procedure.

Ugi-4CR: Classical

408mg (1.0mmol) of the cholic acid (48) furnished the Steroid-Amino Acid Conjugate (49a) (162mg, 26%) using L-alanine methyl ester as amino acid residue using Ugi-4CR as per general procedure.
mp 240°C; [α]D25: (-) 277.78° (c1, CHCl3); IR (CHCl3): 3400, 1736, 1653, 1454, 1216, 980 cm⁻¹; ¹H NMR: 0.65 (s, 3H, Me), 0.96 (s, 3H, Me), 3.6 (s, 3H, OCH₃), 3.84-4.13 (m, 2H, NCH), 4.21-4.48 (m, 2H, CH₂), 4.9 (m, 2H, CH₂); 7.2-7.3 (m, 5H, Ph); 8.7 (NH Proton); ¹³C NMR: δ 12.4, 12.8, 13.2, 13.7, 17.2, 26.1, 28.4, 29.1, 30.1, 30.3, 32.1, 33.1, 36.2, 37.1, 38.2, 42.3, 43.1, 44.5, 48.1, 48.2, 50.1, 50.3, 52.7, 52.9, 57.2, 68.9, 71.9, 72.1, 83.1, 127.4, 127.8, 128.1, 128.4, 143.1, 173.5, 169.0, 174.4; MS (ESI) m/z: 640 (M⁺); Anal Calcd. for C₃₇H₅₆N₂O₇: C, 69.34; H, 8.82; N, 4.37. Found: C, 69.28; H, 8.73; N, 4.36.

2.9.37: Steroid-Amino Acid Conjugate (49b)

**Ugi-4CR: MW**

408mg (1.0mmol) of the cholic acid (48) furnished the Steroid-Amino Acid Conjugate (49b) (547mg, 84%) using L-valine methyl ester as amino acid residue using Ugi-4CR as per general procedure.

**Ugi-4CR: Classical**

408mg (1.0mmol) of the cholic acid (48) furnished the Steroid-Amino Acid Conjugate (49b) (163mg, 25%) using L-valine methyl ester as amino acid residue using Ugi-4CR as per general procedure.
mp 247°C; $\{\alpha\}^{25}_D$: (-)239.47°(c1, CHCl₃); IR (CHCl₃): 3400, 1736, 1653, 1454, 1216, 980 cm⁻¹; ¹H NMR: δ 0.65 (s, 3H, Me), 0.96 (s, 3H, Me), 1.01 (s, 3H, CH₃), 1.12 (s, 3H, CH₃); 3.6 (s, 3H, OCH₃), 3.84-4.13 (m, 2H, NCH), 4.21-4.48 (m, 2H, CH₂), 4.9 (m, 2H, CH₂), 7.2-7.3 (m, 5H, Ph); 8.7 (NH Proton); ¹³C NMR: δ 12.8, 13.2, 16.9, 16.9; 17.2, 26.1, 28.4, 29.1, 30.1, 30.3, 32.1, 33.1; 36.2, 37.1, 38.2, 42.1, 43.1, 44.5, 48.1, 48.2, 50.1, 50.3, 52.9, 57.2, 68.9, 72.1, 83.1, 127.1, 127.2, 128.1, 128.4, 143.1, 171.1, 171.1, 172, 172, 173.1, 173.1; MS (ESI) m/z: 668(M⁺); Anal Calcd. for C₃₀H₆₀N₂O₇: C, 70.03; H, 9.04; N, 4.19. Found: C, 69.9; H, 8.96; N, 4.18.

2.9.38: Steroid-Amino Acid Conjugate (51a)

Ugi-4CR: MW

392mg (1.0mmol) of the hyodeoxycholic acid (50) furnished the Steroid-Amino Acid Conjugate (51a) (511mg, 82%) using L-Alanine methyl as amino acid residue using Ugi-4CR ester as per general procedure.

Ugi-4CR: Classical

392mg (1.0mmol) of the hyodeoxycholic acid (50) furnished the Steroid-Amino Acid Conjugate (51a) (156mg, 25%) using L-alanine methyl ester as amino acid residue using Ugi-4CR as per general procedure.

*Microwave Irradiated Ugi four-component reaction (Ugi-4CR): Expedited synthesis of Steroid-Amino acid Conjugates- A Novel Class of Peptidomimetic Hybrid Compounds based on Seco-Steroids (A, B & D Ring Cleavage).*
mp 174.3°C;  [α]D° 25: (-) 209.99° (c1, CHCl₃); IR (CHCl₃): 3400, 1739, 1645, 1454, 1216, 980 cm⁻¹; ¹H NMR: δ 0.65 (s, 3H, Me), 0.96 (s, 3H, Me), 3.6 (s, 3H, OCH₃), 3.84-4.13 (m, 2H, NCH), 4.21-4.48 (m, H, CH), 4.9 (m, 2H, CH₂), 7.2-7.3 (m, 5H, Ph); 8.7 (NH Proton); ¹³C NMR: δ 12.8, 13.2, 17.2, 26.1, 28.4, 29.1, 30.1, 30.3, 32.1, 33.1, 36.2, 37.1, 38.2, 42.1, 43.1, 44.5, 48.1, 48.2, 50.1, 50.3, 52.9, 57.2, 68.9, 72.1, 83.1, 127.1, 128.1, 127.2, 128.4, 143.1, 172, 173.1, 171.1, 171.1, 172.0, 173.1; MS (ESI) m/z: 624 (M⁺), Anal Calcd. for C₃₇H₅₆N₂O₆: C, 71.12; H, 9.03; N, 4.48; Found: C, 71.12 H, 8.96; N, 4.48.

2.9.39: Steroid-Amino Acid Conjugate (51b)

**Ugi-4CR: MW**

392mg (1.0mmol) of the hyodeoxycholic acid (50) furnished the Steroid-Amino Acid Conjugate (51b) (515mg, 79%) using L-valine methyl ester as amino acid residue using Ugi-4CR as per general procedure.

**Ugi-4CR: Classical**

392mg (1.0mmol) of the hyodeoxycholic acid (50) furnished the Steroid-Amino Acid Conjugate (51b) (143mg, 22%) using L-valine methyl ester as amino acid residue using Ugi-4CR as per general procedure.

*Microwave Irradiated Ugi four- component reaction (Ugi-4CR): Expedited synthesis of Steroid-Amino acid Conjugates- A Novel Class of Peptidomimetic Hybrid Compounds based on Seco-Steroids (A, B & D Ring Cleavage).*
mp 227ºC; [α]D 25: (-) 187.76º (c1, CHCl3); IR (CHCl3): 3400, 1739, 1650, 1450, 1220 cm⁻¹; ¹H NMR: 0.65 (s, 3H, Me), 0.96 (s, 3H, Me), 1.03 (s, 3H, CH₃), 1.12 (s, 3H, CH₃); 3.6 (s, 3H, OCH₃), 3.84-4.13 (m, 2H, NCH), 4.21-4.48 (m, H, CH), 4.9 (m, 2H, CH₂, 7.2-7.3 (m, 5H, Ph); 8.7(NH Proton); ¹³CNMR: δ 12.8, 13.2, 16.7, 16.7, 17.2, 26.1, 28.4, 29.1, 30.1, 30.3, 32.1, 33.1, 36.2, 37.1, 38.2, 42.1, 43.1, 44.5, 48.1, 48.2, 50.1, 50.3, 52.9, 57.2, 68.9, 72.1, 83.1, 173.1, 127.1, 127.2, 128.1, 128.4, 143.1, 171.1, 172, 171.1, 172, 173.1; MS (ESI) m/z: 652(M⁺); Anal Calcd. for C₃₀H₆₀N₂O₆: C, 71.74; H, 9.26; N, 4.29. Found: C, 71.68; H, 9.18; N, 4.28.

2.9.40: **Ansa-seco-steroid (55)**

396 mg (1mmol) of ergosteryl (52) was dissolved in 10mL of dry toluene and heated to boil. To the boiling solution was added 420mg (5mmol) of methyl propiolate (53) slowly. The reaction mixture was refluxed continuously for a period of 96 h when about a 60-75% conversion due to Diels-Alder-retro-Diels-Alder reaction sequences to a mixture of products was observed in the ratio of 4:1. The reaction mixture was poured into cold water and extracted with DCM (3x 100mL). The organic extract after drying over anhyd. Na₂SO₄ was evaporated under reduced pressure to get a residue which showed two spots on TLC, indicating two products which were separated by preparative
TLC (EtOAc: PE::1: 8). The major and more polar product was *ansa-seco*-steroid (55) was obtained as white solid (154.44 mg, 32%).

![Image](image_url)

mp 120°C; IR (CHCl₃): 1730, 1460, 1260, 1100 cm⁻¹; ¹H NMR (300MHz, CDCl₃): δ 0.8-1.1 (m, 12 H), 1.3 (s, 3H), 1.4-1.9 ( m, 14H), 2.0 (s, 3H, acetate proton), 2.6 (dd, J= 14, 6, 1H), 3.2 (dd, J=14, 6, 1H), 3.40-3.80 (m, 4H), 3.9 (s, 3H), 4.0 (m, 1H), 5.2 (m, 1H), 7.3 (s, 2H), 7.55 (bs, 1H); ¹³C NMR (300 MHz, CDCl₃): 15.8, 16.3, 16.9, 18.1, 18.9, 21.2, 23.9, 24.3, 26.1, 29.8, 31.7, 32.5, 34.2, 35.1, 39.2, 39.5, 40.1, 42.5, 49.3, 51.5, 78.6, 129.2, 128.3, 124.9, 132.1, 132.9, 133.9, 136.1, 141.2, 143.1, 150.1, 168.3, 171.2; MS (ESI): m/z 522 (M⁺); Anal. Calcd. for C₃₄H₅₀O₄: C,78.16; H, 9.57; found: C,78.12; H, 9.14

### 2.9.41: *Ansaseco*-steroid (56)

*ansa-seco*-steroid (55) (480mg, 1mmol) was treated with 15mL of 5% solution of KOH in MeOH-H₂O (85-15mL). The reaction mixture was refluxed for 2h. After completion of the reaction, the mixture was poured into cold water and acidified with aq. citric acid solution. It was then extracted with DCM (3x100mL). The organic extract was dried over anhyd. Na₂SO₄ and evaporated under reduced pressure to get the crude product. The crude hydrolysed product was purified by column chromatography by

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*Microwave Irradiated Ugi four-component reaction (Ugi-4CR): Expedited synthesis of Steroid-Amino acid Conjugates- A Novel Class of Peptidomimetic Hybrid Compounds based on Seco-Steroïds (A, B & D Ring Cleavage).*
using EtOAc: PE::1:7 as eluent to get the pure \textit{ansa-seco}-steroid (56) as a white solid (195 mg, 47%).

\begin{center}
\includegraphics[width=0.5\textwidth]{ansa-seco-steroid.png}
\end{center}

mp 178\textdegree C; IR(CHCl\textsubscript{3}): 3400, 1695, 1460, 1260, 1100 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (300MHz, CDCl\textsubscript{3}): \(\delta\) 0.8-1.1 (m, 12 H), 1.3 (s, 3H), 1.4-1.9 (m, 15H), 2.6 (dd, J= 14, 6, 1H), 3.2 (dd, J=14, 6, 1H), 3.40-3.80 (m, 4H), 4.0 (m, 1H), 5.2 (m, 1H), 7.4 (s, 2H), 7.8 (bs, 1H);
\textsuperscript{13}C NMR (300 MHz, CDCl\textsubscript{3}): \(\delta\) 15.8, 16.3, 16.9, 18.1, 18.1, 21.2, 23.9, 26.1, 31.7, 32.5, 34.2, 35.1, 39.2, 39.2, 39.5, 40.1, 42.5, 49.3, 50.1, 78.6, 124.3, 129.2, 128.3, 124.9, 136.1, 132.1, 132.9, 133.9, 141.2, 143.1, 173.2; MS (ESI): \(m/z\) 466 (M\textsuperscript{+}); Anal. Calcd. for C\textsubscript{31}H\textsubscript{46}O\textsubscript{3}: C, 79.78; H, 10.28; found: C, 79.75; H, 10.25.

\textbf{2.9.42: Ansa-Steroid Amino Acid Conjugate (57)}

\textbf{Ugi-4CR: MW}

466mg (1.0mmol) of the \textit{ansa-seco}-steroid (56) furnished the Steroid-Amino Acid Conjugate (57) (541mg, 73%) using L-lysine methyl ester as amino acid residue using Ugi-4CR as per general procedure.

\textbf{Ugi-4CR: Classical}

466mg (1.0mmol) of the \textit{ansa-seco}-steroid (56) furnished the Steroid-Amino Acid Conjugate (57) (126mg, 17%) using L-lysine methyl ester as per general procedure.
mp 252\(^\circ\)C; \([\alpha]_D^{25}\) (-)0.286\(^\circ\) (c2, CHCl\(_3\)); IR (CHCl\(_3\)): 3345, 1737, 1684; 1435, 1200, 971 cm\(^{-1}\); \(^1\)H NMR: \(\delta\) 0.8-1.1 (m, 12H), 1.3 (s, 3H), 1.4-1.9 (m, 16H), 2.6 (dd, \(j=14, 6, 1H\)), 3.2 (dd, \(J=14, 6, 1H\)), 3.4-3.8 (m, 4H), 3.93 (s, 3H, OCH\(_3\)) 4.06-4.09 (m, 2H, NCH), 4.21-4.24 (m, 2H, CH\(_2\)), 4.72-4.74 (m, 2H, CH\(_2\)), 4.0 (m, 1H), 5.2 (m, 1H); 7.17-7.21 (m, 5H), 7.4 (s, 2H), 7.8 (bs, 1H); \(^{13}\)C NMR: \(\delta\) 16.3, 16.4, 19.0, 20.8, 20.8, 23.0, 25.1, 28.0, 29.6, 32.4, 33.2, 34.0, 34.5, 38.9, 40.2, 42.1, 43.4, 45.0, 47.9, 51.3, 54.3, 56.5, 69.3, 74.4, 126.0, 126.1, 126.1, 127.0, 127.1, 127.5, 128.3, 128.5, 131.0, 132.3, 132.0, 132.4, 134.4, 135.7, 135.5, 171.1, 169.3, 171.0; MS (ESI) \(m/z\): 742(M\(^+\)); Anal Calcd. for C\(_{46}\)H\(_{67}\)N\(_3\)O\(_5\): C, 74.40; H, 9.02; N, 5.66. Found: C, 74.43; H, 9.07; N, 5.70.

2.10: References


18. Borah, P.; Chowdhury, P.; *Ind. Pat. No.* **184893**.


47. Borthakur, M., Boruah, R. C; *Steroids, 2008*, *7*, 637.


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Microwave Irradiated Ugi four-component reaction (Ugi-4CR): Expedited synthesis of Steroid-Amino acid Conjugates- A Novel Class of Peptidomimetic Hybrid Compounds based on Seco-Steroids (A, B & D Ring Cleavage).