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# The first target specific, highly diastereoselective synthesis, design and characterization of pyranoquinolinyl acrylic acid diastereomers as potential α-glucosidase inhibitors

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ABSTRACT

In the present investigation we report the first target specific, highly diastereoselective synthesis of new class of pyranoquinolinyl/furoquinolinyl-acrylic acid diastereomers and evaluation of their *invitro* α-glucosidase inhibitory activity. All the products were thoroughly characterized by $^{1}$H NMR, $^{13}$C NMR, FT-IR, Mass spectral and CHN analysis. A highly diastereoselective target specific route of synthesis for the biologically active diastereomers were developed by usingchiral catalyst Europium tris[3-heptafluoropropylhydroxyl methylene]-(−)-camphorate (A) or Europiumtris[3-(trifluoromethyl)hydroxylmethylene]-(+)-camphorate (B). It was found that among a set of 4 diastereomeric products obtained, exodiasteromers of pyranoquinolinyl acrylic acid adducts exhibited relatively high α-glucosidase inhibitory activity. The newly synthesized compounds exhibited $IC_{50}$ values in the range of (0.40 ± 0.02–30.3 ± 0.84 μM) as compared to standard acarbose ($IC_{50}$ = 0.65 ± 0.02 μM). It was found that compounds **11a, 11c, 11d** and **12d** were found to be more active than standard acarbose. It was also found that unsubstituted compound (**11a**) or compounds with chlorine or methoxy substituent (**11c, 11d, 12d**) showed potential α-glucosidase inhibitory activity. However a reversal in activity was observed with Nitro substituent (**11b, 13b**) wherein the endodiastereomers were found to be more active than exodiastereomers. Molecular docking studies were used for design of the compound and understand the mode of binding between the compound and target enzyme. A plausible mechanism for the diastereoselective synthesis was also proposed.

## 1. Introduction

Diabetes describes a group of metabolic diseases in which the person has high blood sugar either because of inadequate insulin production (or) because the body's cells do not respond properly to insulin (or) both [1,2]. In 2013, it was estimated that over 382 million people throughout the world had diabetes [3,4]. Different types of drugs such as biguanidus, sulfonylureas, thiazolidinedones and α-glucosidase inhibitors are used for the control and mitigation of diabetes [5,6]. α-glucosidase enzyme exists in the brush border surface of the intestinal cells wherein they slow down the absorption of monosaccharide's in the intestine and hence reduce the glucose level in the blood stream [7]. α-glucosidase inhibitors like acarbose, voglibose, miglitol, nojirimycin are used effectively as a therapeutic drugs for the last two decenniums [8,9]. During the last two decades, various α-glucosidase inhibitors have been reported [10–19]. However many of these commercial α-glucosidase inhibitors are associated with side effects such as flatulence, obesity, hepatic disorders, gastrointestinal diseases, diarrhea, improper absorption and elimination [20–23]. Christian Bommer et al. [24] reported the economic burden of diabetes, including its diagnosis treatment costs and hence loss of productivity to be around 1.8% of the global gross domestic product. As a result of its direct impact on the global economy and on the individual quality of life, the development of new, potential antidiabetic compounds with minimal or no side effects is desired. In the present investigation we report the design, synthesis and characterization of new class of pyranoquinolinyl/furoquinolinyl acrylic acid diastereomers as potential α-glucosidase inhibitors. We have also established the diastereoselectivity-α-glucosidase inhibitory activity relationship. To the best of our knowledge there are no reports in literature on the relationship between diastereoselectivity and α-glucosidase inhibitory activity of novel pyranoquinolinyl/furoquinolinyl acrylic acid diastereomers.

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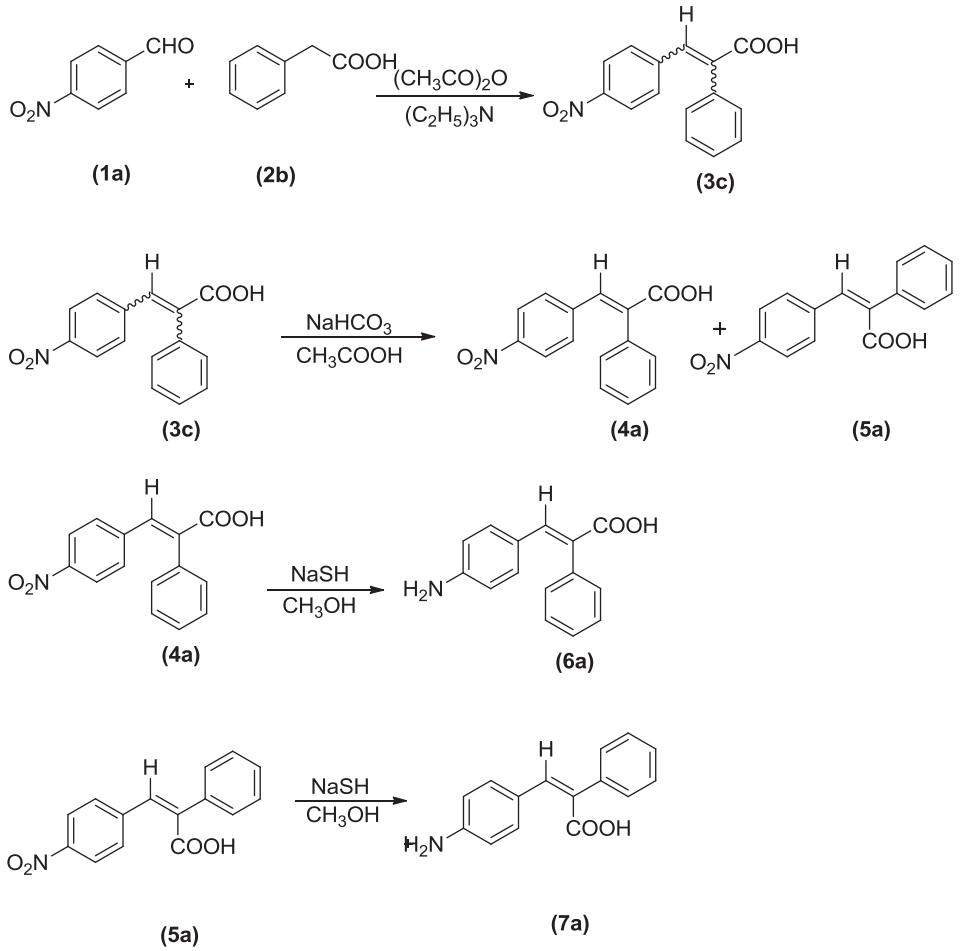
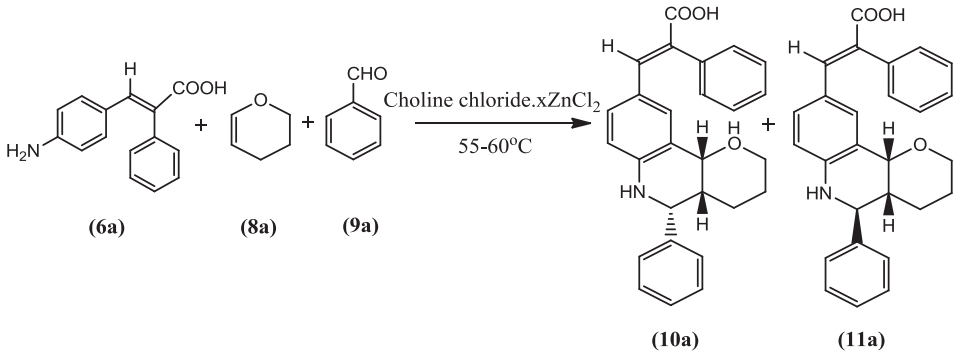


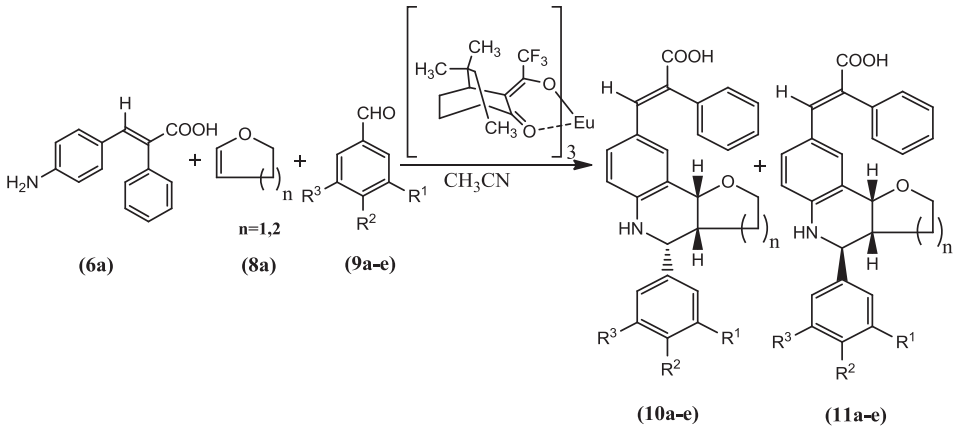

**Scheme 1.** Synthesis of 3-(4-aminophenyl)-2-Phenylprop-2-enoic acid.




**Scheme 2.** Choline chloride/$ZnCl_2$ ionic liquid mediated synthesis of Pyranoquinolinyl acrylic acid adducts.

## 2. Chemistry

The target compound was synthesized by a series of steps given in Scheme 1. The first step involves the Perkin condensation reaction between p-nitro benzaldehyde and phenyl acetic acid in the presence of triethyl amine at 95–100 °C to yield a mixture of (2*E*)-3-(4-nitrophenyl)-2-phenylprop-2-enoic acid and (2*Z*)-3-(4-nitrophenyl)-2-phenylprop-2-enoic acid as reported in literature. The mixture of (2*E*)-3-(4-nitrophenyl)-2-phenylprop-2-enoic acid and (2*Z*)-3-(4-nitrophenyl)-2-phenylprop-2-enoic was separated into their constituent isomers by using a modified procedure reported by Roger Ketcham [25]. The mixture of cis and trans 3-(4-nitrophenyl)-2-phenylprop-2-enoic acid **(3a)** was dissolved in saturated $NaHCO_3$ and filtered through Whatmann (40) filter paper. The filterate was acidified to pH 4.5 by using glacial acetic acid. The precipitated product (2*E*)-3-(4-nitrophenyl)-2-phenylprop-2-enoic acid was filtered and dried **(4a)**. The filtrate was further acidified with concentrated hydrochloric acid to pH 2.0–2.5 and the precipitated (2*Z*)-3-(4-nitrophenyl)-2-phenylprop-2-enoic acid was filtered and dried **(5a).** The purity of the samples was further established by melting point as reported by Roger Ketcham [25] and high performance liquid chromatography. The nitro group present in 3-(4-nitrophenyl)-2-phenylprop-2-enoic acid was further reduced to amine by using NaSH/$CH_3OH$ at 95–100 °C yielding the corresponding (2Z)-3-(4-aminophenyl)-2-phenylprop-2-enoic acid **(6a)** and (2*E*)-3-(4-aminophenyl)-2-phenylprop-2-enoic acid **(7a)** in good yields. The one-pot reaction of 2,3 dihydropyran, (2Z)-3-(4-aminophenyl)-2-phenylprop-2-enoic acid **(6a)** and benzaldehyde in the presence of choline chloride/Zinc chloride ionic liquid as catalyst and medium at 55–60 °C via

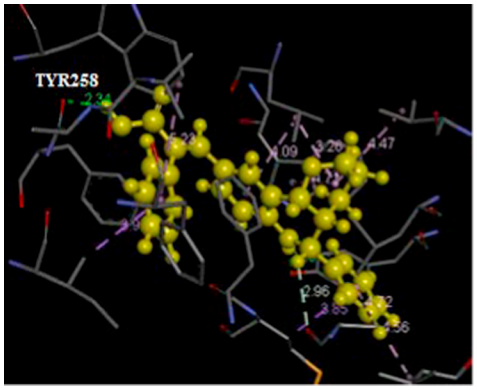



**Scheme 3.** [Eu(tfc)$_3$] catalysed diastereoselective synthesis of Pyranoquinolinyl/furanoquinolinyl acrylic acid adducts.

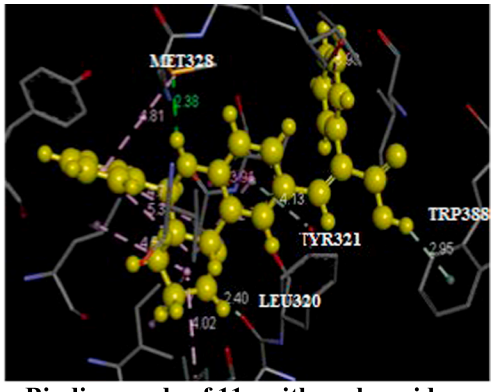
inverse electron demand Diels Alder reaction (IED) afforded thepyranoquinolinyl acrylic acid adducts (**10a and 11a**) in 80% yield in the ratio of 49:51 (see Scheme 2).

However when a mixture of diastereomers in the ratio of 49:51obtained from the above reaction **(10a and 11a)** was evaluated for α-glucosidase inhibitory activity, diminished activity was found even at higher concentrations as is evident in Table 4. Hence the mixture was separated into their component diastereomers by flash column (200–400 Mesh) and evaluated for their inhibitory activity. Out of the two diastereomers**10a** and **11a**, the exodiastereomer **(11a)** exhibited relatively good α-glucosidase inhibitory activity ($IC_{50}$ = 0.62 ± 0.02 μM) whereas the endodiastereomer (**10a**) exhibited relatively diminished activity ($IC_{50}$ = 4.2 ± 0.52 μM) as compared to standard acarbose ($IC_{50}$ = 0.65 ± 0.02 μM) which is evident in Table 4.

diastereomers was that the carboxylic acid group of diastereomer **10a** formed one hydrogen bond with TYR258 residue (bond length -2.3406 A) whereas the other diastereomer **11a** formed three hydrogen bonds (−COOH, −NH, −CH−) with the aminoacid residues of target enzyme MET328 (bond length −2.3802 A), LEU320 (bond length −2.4001 A), TRP388 (bond length −2.9510 A). Hence better anchorage of the diastereomer **11a** results in improved α-glucosidase inhibitory activity than diastereomer **10a**. Moreover the estimated binding energies were −9.56 kcal/mol for pyranoquinolinyl acrylic acid adduct **10a** whereas −15.43 kcal/mol for diasteromer **11a** respectively. *Invitro*α-glucosidase inhibitory activity studies reported in Table 4 revealed an $IC_{50}$ value of4.2 ± 0.52 μM for diastereomer**10a** and 0.62 ± 0.02 μM for diastereomer**11a** which is consistent with the results of the docking studies.




**Binding mode of 10a with α-glucosidase**




**Binding mode of 11a with α-glucosidase**

## 3. Results and discussion

### 3.1. Molecular docking

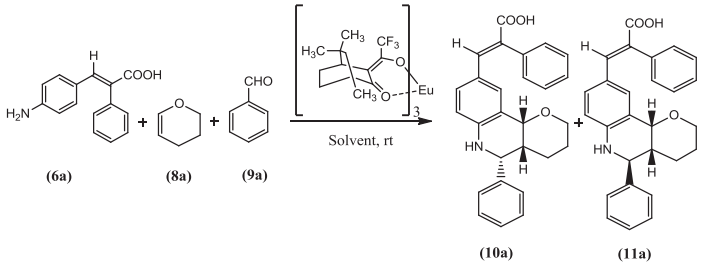
Docking studies were carried out to find which of the diastereomers **10a or 11a** exhibited relatively better α-glucosidase inhibitory activity and also to identify the binding modes of the compounds. Docking was performed by using GOLD *suite* program using genetic algorithm parameters with interactive docking set-up via Hermes. The active site of the crystal structure of α-glucosidase was obtained from the PDBsum protein data bank and the c-terminal domain of human intestinal α-glucosidase (PDB ID: IU33) was used as a molecular target for target-specific binding studies. The docking results revealed that both the diastereomers are well accommodated in the binding pockets of α-glucosidase. However the main difference between the binding of two

Hence in order to avoid the formation of less active isomer **(10a)**, avoid the inhibition of active diastereomer **(11a)** by **(10a)** and circumvent the cumbersome separation of diastereomers by flash chromatography, we have developed a highly diastereoselective, target specific synthesis of active diastereomer **(11a)** by reacting 2,3 dihydropyran, (2Z)-3-(4-aminophenyl)-2-phenylprop-2-enoic acid **(6a)** and benzaldehyde in the presence of Europium tris[3-(trifluoromethyl)hydroxylmethylene]-(+)-camphorate] (B) as catalyst at 20 mol% at room temperature affording the pyranoquinolinyl acrylic acid adducts in the ratio of 2:98 and 78% yields (Scheme 3).

### 3.2. Effect of solvent on the IED synthesis of pyranoquinolinyl acrylic acid diastereomers

Inorder to improve the yield and diastereoselectivity of the reaction,

**Table 1**
Effect of solvent on the diastereoselective synthesis.




| S No | Solvent | Temperature (°C) | Time (h) | Yield (%) | Endo : Exo ratio |
|---|---|---|---|---|---|
| 1 | $CH_2Cl_2$ | 27 | 8.0 | 30.0 | 22:88 |
| 2 | $C_6H_5CH_3$ | 110 | 8.0 | 20.0 | 10:90 |
| 3 | $C_2H_5OH$ | 80 | 7.0 | 65.0 | 7:93 |
| 4 | THF | 65 | 8.0 | 60.0 | 9:91 |
| 5 | $CH_3CN$ | 27 | 5.0 | 78.0 | 2:98 |

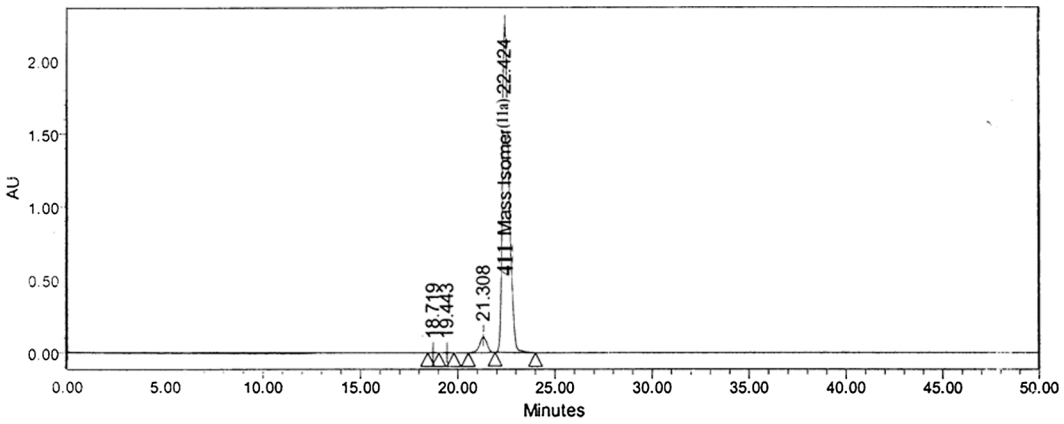
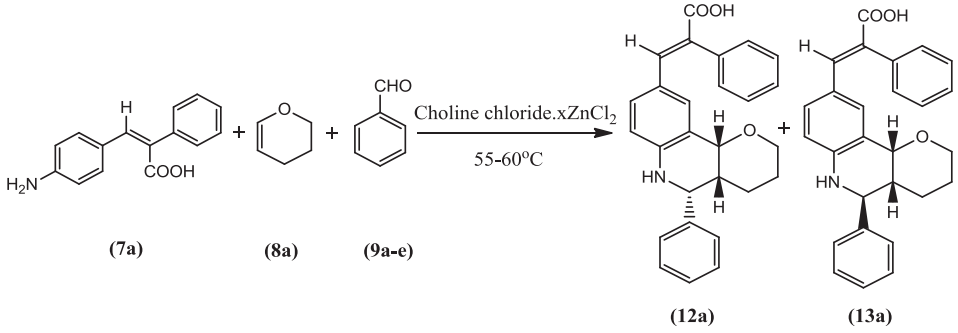



**Fig. 1.** HPLC chromatogram of pyranoquinolinyl acrylic acid adducts **(10a:11a)**.



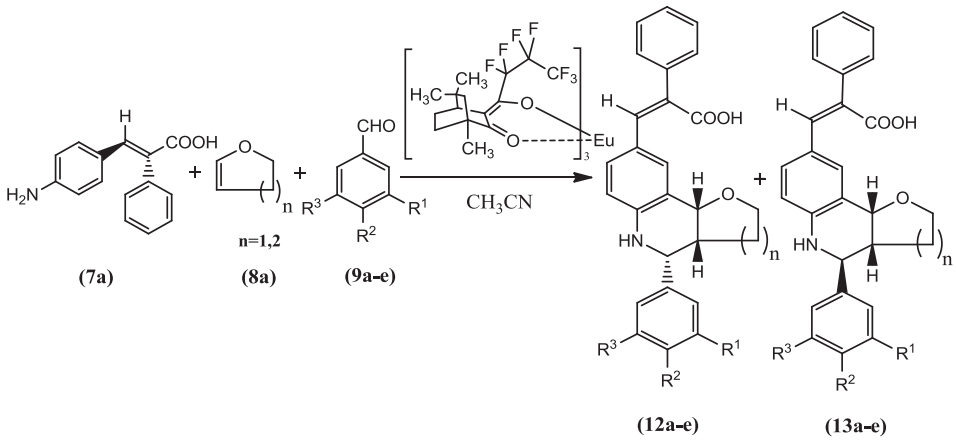

**Scheme 4.** Choline chloride/$ZnCl_2$ ionic liquid mediated synthesis of Pyranoquinolinyl acrylic acid adducts.

the reaction of 2,3 dihydropyran, (2Z)-3-(4-aminophenyl)-2-phenyl-prop-2-enoic acid **(6a)** and benzaldehyde in the presence of Europium tris[3-(trifluoromethyl)hydroxylmethylene]-(+)-camphorate (B) as catalyst at 20 mol% was chosen as a model for comparison of solvents. The results of the reaction are given in Table 1. Among the solvents examined, acetonitrile proved to be the most effective solvent for Europiumtris[3-(trifluoromethyl)hydroxylmethylene]-(+)-camphorate, catalysed IED reaction offering high yields (78%) at room temperature over a period of 5.0 h with highest diastereoselectivity of 2:98 (%). The reaction also proceeded to completion within 7.0 h in ethanol medium, however the reaction offered comparatively less yields in ethanol medium at 80 °C whereas in all other solvents the desired reaction proceeded slowly giving poor yields and less diastereoselectivity.

The ratio of diastereomers (**10a:11a**) were further established based on HPLC (Xterra RP-18 reverse phase columns with acetonitrile/methanol/water as solvent, 0.02 M ammonium acetate with UV detector and a flow rate of 1.0 ml/min) and column chromatographic yields. The yields of the products were established after column chromatography (see Fig. 1).

| Name | RT | % Area |
|---|---|---|
| | 18.719 | 0.03 |
| | 19.443 | 0.05 |
| Diastereomer (**10a**), 411($M^+$) | 21.308 | 2.01 |
| Diastereomer (**11a**), 411($M^+$) | 22.424 | 97.91 |

The stereochemistry of the products was assigned based on the scalar coupling constant values between the protons C—H **(4a)** and C—H **(5)**. In the isomer **10a**, the coupling constant value for the doublet obtained




**Scheme 5.** [Eu(hfc)$_3$] catalysed diastereoselective synthesis of Pyranoquinolinyl/furanoquinolinyl acrylic acid adducts.

around 5.10 δ is J (4a-5) = 5.3 Hz which is smaller and typical for a gauche conformation, wherein the pyran ring and phenyl group are present in cis orientation. However in the diastereomer **11a** the coupling constant value for the doublet obtained at 4.93 δ is J (4a-5) = 16.0 Hz indicating anti-reciprocal orientation of C—H **(4a)** and C—H **(5)**. This orientation is possible only when the pyran ring and phenyl group are present in trans orientation with respect to quinoline ring of **11a.**

However when an imino Diels Alder reaction was carried out by reacting the (2*E*)-3-(4-aminophenyl)-2-phenylprop-2-enoic acid **(7a)** with 2,3 dihydropyran and benzaldehyde in the presence of choline chloride/zinc chloride ionic liquid as catalyst and medium at 55–60 °C, a mixture of diastereomers **12a** and **13a** was obtained in the ratio of 65:35 in 73% yield. The mixture was resolved into their component diastereomers by flash chromatography and subjected to α-glucosidase inhibitory activity studies it was found that the endo isomer **12a** exhibited relatively good activity ($IC_{50}$ = 1.63 ± 0.37 μM) than exo isomer **13a** ($IC_{50}$ = 3.12 ± 0.31 μM) as is shown in Table 4 (Scheme 4).

Hence to synthesize the active diastereomer **12a**, we have developed a highly target specific synthesis of active diastereomer **12a** by reacting 2,3dihydropyran, 2E)-3-(4-aminophenyl)-2-phenylprop-2-enoic acid **(7a)** and benzaldehyde in the presence of Europium tris[3-heptafluoropropylhydroxylmethylene]-(−)-camphorate (A) as catalyst at 20 mol% by using acetonitrile as solvent at room temperature affording the pyranoquinolinyl acrylic acid adducts in the ratio of 98:2 and 80% yields (Scheme 5).

In order to demonstrate the efficiency of this protocol to obtain the target specific active diastereomer by employing chiral catalyst (A) and (B), we explored the generality of our methodology by reacting various other aldehydes with 2,3 dihydropyran and (2Z)-3-(4-aminophenyl)-2-phenylprop-2-enoic acid **(6a)** or (2*E*)-3-(4-aminophenyl)-2-phenylprop-2-enoic acid **(7a)** in the presence of Europiumtris[3-heptafluoro propylhydroxylmethylene]-(−) camphorate (A) and Europiumtris[3-(trifluoromethyl)hydroxylmethylene]-(+)-camphorate (B) as catalyst at 20 mol% by using acetonitrile as solvent. The reaction progresses well with both electron donating and electron withdrawing groups/substituents affording the products in good yields. The results of the reaction are given in Table 2.

The oxygen atom on the pyranoquinolinyl acrylic acid diastereomer ring is essential for potential α-glucosidase inhibitory activity which is evident in the *invitro* alpha glucosidase inhibitory studies. On replacing the oxygen atom of the quinoline moiety with carbon atom by employing cyclopentadiene as dienophile, the α-glucosidase inhibitory activity reduced considerably ($IC_{50}$ = 10.7 ± 0.31–24.4 ± 0.20 μM) as shown in Table 4. Synthesis of tetrahydro-3H-cyclopenta[c]quinolin-8-yl)acrylic acid adducts was accomplished by reacting cyclopenta-1,3-diene, (2Z)-3-(4-aminophenyl)-2-phenylprop-2-enoic acid **(6a)** and benzaldehyde in the presence of choline chloride/Zinc chloride ionic liquid as catalyst and medium at 55–60 °C via inverse electron demand Diels Alder reaction (IED) to afford the cyclopentaquinolinyl acrylic acid adduct (**14a**) in 68.0% yield. The results of the reaction are summarized in Table 3 (Scheme 6).

### 3.3. α-glucosidase inhibitory activity

α-glucosidase inhibitory activity studies were carried out to establish the diastereoselectivity–activity relationship by comparing activities of **31** diastereomericpyranoquinolinyl/furoquinolinylacyrilic acid compounds. When a mixture of diastereomers **(10a and 11a)** or **(12a**

**Table 2**
Effect of substituent's on the Pyranoquinolinyl/furoquinolinyl acrylic acid synthesis.

| Sl. No | Amine (6a/7a) | Aldehyde (R1/R2/R3) | Dienophile (n = 1,2) | Chiral Catalyst (A/B) | Time (h) | Yield (%)[a] | Product No | Endo:Exo Ratio[b] |
|---|---|---|---|---|---|---|---|---|
| 1 | 6a | $R_1$, $R_2$, $R_3$ = H | 2 | B | 5.00 | 78.0 | 10a:11a | 2:98 |
| 2 | 6a | $R_1$, $R_3$ = H, $R_2$ = $NO_2$ | 2 | B | 7.00 | 80.0 | 10b:11b | 2:98 |
| 3 | 6a | $R_1$, $R_3$ = H, $R_2$ = Cl | 2 | B | 5.50 | 81.0 | 10c:11c | 1:99 |
| 4 | 6a | $R_1$, $R_2$, $R_3$ = $OCH_3$ | 2 | B | 6.00 | 61.8 | 10d:11d | 3:97 |
| 5 | 6a | $R_1$, $R_2$, $R_3$ = H | 1 | B | 6.00 | 83.0 | 10e:11e | 1:99 |
| 6 | 6a | $R_1$, $R_2$ = Cl, $R_3$ = H | 1 | B | 6.00 | 63.0 | 10f:11f | 2:98 |
| 7 | 7a | $R_1$, $R_2$, $R_3$ = H | 2 | A | 5.50 | 80.0 | 12a:13a | 98:2 |
| 8 | 7a | $R_1$, $R_3$ = H, $R_2$ = $NO_2$ | 2 | A | 7.00 | 78.1 | 12b:13b | 96:4 |
| 9 | 7a | $R_1$, $R_3$ = H, $R_2$ = Cl | 2 | A | 5.30 | 79.3 | 12c:13c | 97:3 |
| 10 | 7a | $R_1$, $R_2$, $R_3$ = $OCH_3$ | 2 | A | 8.25 | 60.0 | 12d:13d | 97:3 |
| 11 | 7a | $R_1$, $R_2$, $R_3$ = H | 1 | A | 5.30 | 65.8 | 12e:13e | 98:2 |
| 12 | 7a | $R_1$, $R_2$ = Cl, $R_3$ = H | 1 | A | 5.45 | 69.1 | 12f:13f | 98:2 |

[a] The yield is based on isolation by column chromatography.
[b] Theendo:exo ratio is based on column chromatographic yield and HPLC.

**Table 3**
Synthesis of Tetrahydro-3H-cyclopenta[*c*]quinolin-8-yl) acrylic acid adducts.

| Sl. No | Amine (6a/7a) | Aldehyde ($R_1$) | Time (h) | Yield (%) | Product |
|---|---|---|---|---|---|
| 1 | 6a | H | 5.0 | 68.0 | 14a |
| 2 | 6a | $NO_2$ | 5.5 | 52.63 | 14b |
| 3 | 7a | $NO_2$ | 4.0 | 55.5 | 14c |
| 4 | 7a | Cl | 2.0 | 62.5 | 14d |

**and 13a)** were subjected to α-glucosidase inhibitory activity studies, these diastereomeric mixtures exhibited very $IC_{50}$ values in the range of ($IC_{50}$ = 28.4 ± 0.21–30.3 ± 0.84 μM) inhibitions even at high concentrations. However among pyranoquinolinyl acrylic acid diastereomers **(10a, 11a, 12a and 13a)**, the diastereomer **11a** exhibited relatively good α-glucosidase inhibitory values ($IC_{50}$ = 0.62 ± 0.02 μM) when compared to standard acarbose ($IC_{50}$ = 0.65 ± 0.02 μM). All the other diastereomers **(10a, 12a, 13a)** exhibited $IC_{50}$ values in the range of 1.63 ± 0.37–4.2 ± 0.52 μM. On exploring the role of substituents on the pyranoquinolinyl acrylic acid diastereomers, it was found that a trimethoxy substituted pyranoquinolinyl acrylic acids exhibited relatively excellent activity followed by chloro substituted pyranoquinolinyl acrylic acid diastereomers. Of all the diastereomers screened, (E)-2-phenyl-3-((4aR,5S,10bR)-5-(3,4,5-trimethoxyphenyl)-3,4,4a,5,6,10b-hexahydro-2H pyrano[3,2-*c*]quinolin-9yl)acrylic acid **(11d)** exhibited excellent $IC_{50}$ values of 0.40 ± 0.02 μM. Generally, the exo-isomers **(11a-e)** obtained by reaction of 2Z)-3-(4-aminophenyl)-2-phenylprop-2-enoic acid **(6a)** (Cis), with pyran and aromatic aldehyde exhibited relatively better α-glucosidase inhibitory activity than the endo isomers. However in the case of pyranoquinolinyl acrylic acid diastereomers obtained by reacting (2E)-3-(4-aminophenyl)-2-phenylprop-2-enoic acid **(7a)** (Trans), with pyran and aromatic aldehyde, it was found that the endo-diastereomers **(13a-e)** exhibited relatively better α-glucosidase inhibitory activity than the exo-diastereomers **(12a-e)**. However a reversal in activity was observed for nitro substituted pyranoquinolinyl acrylic acid diastereomers wherein the endodiastereomers exhibited relatively better activity than the exo-diastereomers. It is evident from the studies that oxygen atom of the pyranoquinolinyl ring is essential for α-glucosidase inhibition because upon replacement of the oxygen atom with carbon as Tetrahydro-3H-cyclopenta[*c*]quinolin-8-yl) acrylic acid adducts **(14a-d)** there was considerable decrease in α-glucosidase inhibitory activity.

### 3.4. Mechanism

Although the mechanistic details are still under investigation, a plausible mechanism for the Europium tris[3-(trifluoromethyl)hydroxylmethylene]-(+)-camphorate (B) mediated inverse electron demand Diels Alder reaction is proposed in Scheme 7 wherein a more basic substrate, such as the 2-azadiene binds to the europium metal centre leading to the formation of an intermediate hepta-coordinate schiff base – Europium complex. This highly hindered intermediate might be the plausible reason for the high diastereoselectivity of the IED- Diels Alder reaction. A plausible mechanism for the diastereoselective synthesis of pyranoquinolinyl acrylic acid adducts is given in Scheme 7.

All the products were evaluated for Lipinski's rule of five (RO5) and it was found that all the products were in compliance with Lipinski rule with one or no violations indicating good oral bioavailability. The results of Lipinski evaluation are given in Table 5.

## 4. Conclusion

In conclusion, this work reports the first target specific, design and highly diastereoselective synthesis of new class of pyranoquinolinyl/furoquinolinyl acrylic acid diastereomers. This is the first report wherein diastereoselectivity- has been established among a set of 4 diastereomers for the same molecule. A highly diastereoselective α-glucosidase inhibitory activity relationship target specific route of synthesis for the active diastereomer was developed by using chiral catalyst Europiumtris[3-heptafluoropropylhydroxylmethylene]-(−)-camphorate (A) and Europium tris [3-(trifluoromethyl)hydroxylmethylene]-(+)-camphorate (B). The methodology avoids the formation of less active isomer, overcomes competitive inhibition of active diastereomer and circumvents the cumbersome separation of diastereomers by flash chromatography. The newly synthesized compounds exhibited $IC_{50}$ values in the range of (0.40 ± 0.02–30.3 ± 0.84 μM) as compared to standard acarbose ($IC_{50}$ = 0.65 ± 0.02 μM). Molecular docking studies were used for design of the compound and understand the mode of binding between the compound and target enzyme.

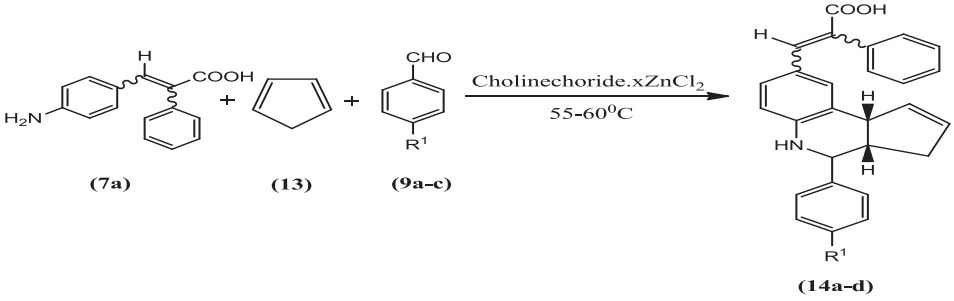
## 5. Experimental

### 5.1. Typical experimental procedure for the synthesis of pyranoquinolinyl/furoquinolinyl adducts

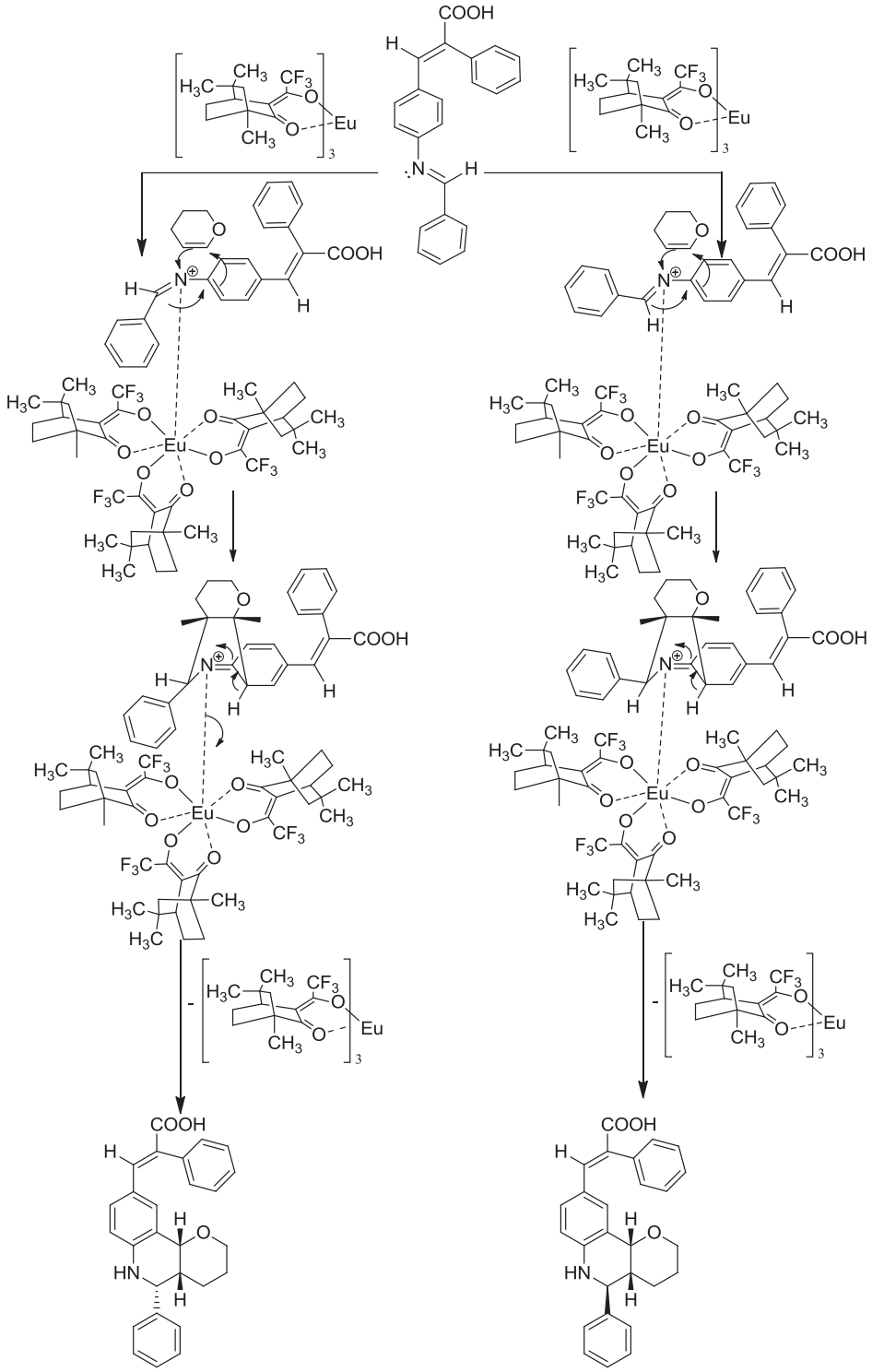
A mixture of 3-(4-aminophenyl)-2-phenylprop-2-enoic acid (0.0011 mol), aromatic aldehyde **(9a)** (0.0064 mol), 2,3-dihydropyran **(8a)** (0.0064 mol) or 2,3 dihydrofuran (0.0064 mol) and acetonitrile (10 ml) was added into the round bottom flask containingchiral catalyst Europiumtris[3-heptafluoropropylhydroxylmethylene]-(−)-camphorate (A) (20 mol%). The reaction mixture was stirred at room temperature for an appropriate time (Table 2). After complete conversion, as indicated by TLC, the solvent was removed by using high vacuum. Ethylacetate (30 ml) and water (20 ml) was added to the reaction mixture, sturred for 5 min and the reaction mixture was transferred to separating funnel. The organic layer was separated and concentrated under vacuum. The crude product was purified by column chromatography on silica gel (Merck, 200–400 mesh, ethylacetate/petroleum ether, 1:4) to give the product (10a) in78%yield.

#### 5.1.1. (E)-2-phenyl-3-((4aR,5R,10bR)-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-9-yl)acrylic acid (10a)

**FT-IR (KBr)**$\nu_{max}$ $cm^{-1}$: 3380, 3325, 2940, 1603, 1484, 1074; **$^1$H NMR** (400 MHz, $CDCl_3$)δ : 9.60 (s, 1H), 8.12 (t, 3H), 7.86 (d, 2H), 7.62 (d, 1H), 7.51–7.41 (m, 5H), 7.40–7.23 (m, 3H), 4.92 (s, 1H), 4.60–4.59




**Scheme 6.** Choline chloride/$ZnCl_2$ ionic liquid mediated synthesis of cyclopentaquinolinyl acrylic acid adducts.



**Scheme 7.** Plausible mechanism for [Eu(tfc)$_3$] mediated synthesis of Pyranoquinolinyl acrylic acid adducts.

(d, 1H, $J$ = 4.00 Hz), 4.46 (brs, 1H, NH), 3.54–3.41 (m, 2H), 2.42 (t, 1H), 2.17 (s, 1H), 1.72 (t, 2H), 1.28 (d, 1H); **$^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 175.09, 171.76, 146.54, 143.22, 140.00, 136.53, 131.69, 130.40, 130.3, 129.70, 128.63, 127.94, 127.34, 126.01, 122.99, 118.02, 90.18, 73.44, 63.6, 54.27, 38.72, 24.07, 21.7; **MS** *m/z*: 411 ($M^+$); **Anal. Calcd. for** $C_{27}H_{25}NO_3$: C, 78.81; H, 6.12; N, 3.40; **Found**: C, 78.80; H, 6.10; N, 3.38.

*5.1.2. (E)-2-phenyl-3-((4aR,5S,10bR)-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-9-yl)acrylic acid (**11a**)*

**FT-IR (KBr)**$\nu_{max}$ cm$^{-1}$: 3323, 2916, 1697, 1589, 1440, 1020; **$^1$H NMR** (400 MHz, $CDCl_3$)δ : 9.59 (s, 1H), 8.10 (s, 2H), 7.84 (d, 2H), 7.59 (s, 1H), 7.51–7.43 (m, 6H), 7.31–7.25 (m, 3H), 4.92 (s, 1H), 4.46 (d, 1H, $J$ = 12.0 Hz), 4.01 (brs, 1H, NH), 3.78–3.63 (m, 2H), 2.17 (s, 2H), 1.54 (t, 2H), 1.28 (m, 1H); **$^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 172.9, 159.4, 142.5, 140.3, 138.1, 132.7, 132.9, 131.2, 130.7, 129.3, 129.2, 129.0, 128.1, 119.6, 117.4, 117.3, 99.2, 68.5, 64.9, 38.2, 27.8, 23.8, 22.8; **MS** *m/z*: 411 ($M^+$); **Anal. Calcd. for** $C_{27}H_{25}NO_3$: C, 78.81; H, 6.12; N, 3.40,

**Table 4**
α-glucosidase inhibitory activity studies.

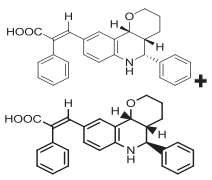
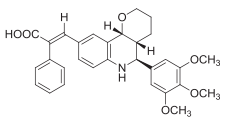
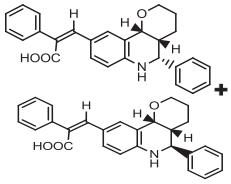
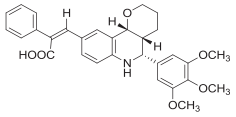
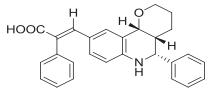
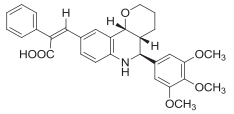
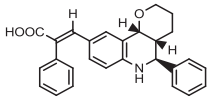
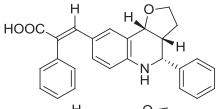
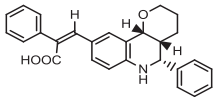
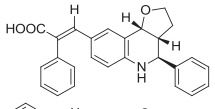
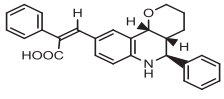
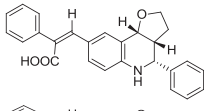
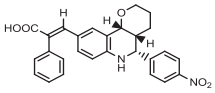
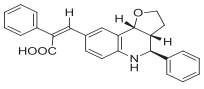
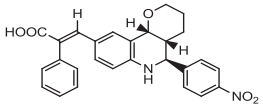
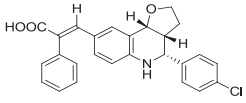
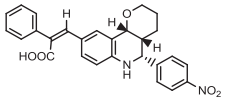
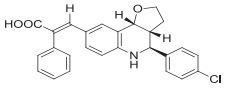
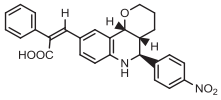
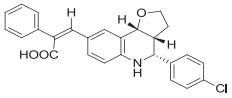
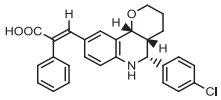
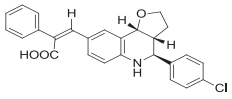
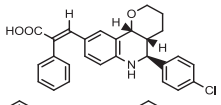
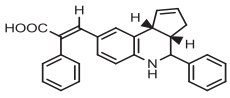
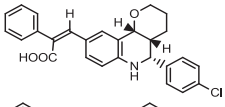
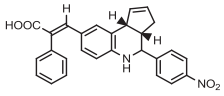
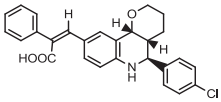
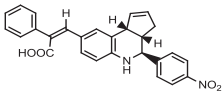
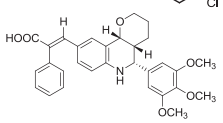
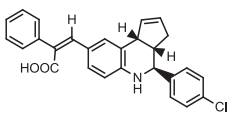
| Product Number | Diastereomer | $IC_{50}$ ± SEM (μM) | Product Number | Diastereomer | $IC_{50}$ ± SEM (μM) |
|---|---|---|---|---|---|
| **10a + 11a (1:1)** |  | 30.3 ± 0.84 | **11d** |  | 0.40 ± 0.02 |
| **12a + 13a (1:1)** |  | 28.4 ± 0.21 | **12d** |  | 0.58 ± 0.07 |
| **10a** |  | 4.2 ± 0.52 | **13d** |  | 3.18 ± 0.92 |
| **11a** |  | 0.62 ± 0.02 | **10e** |  | 4.98 ± 0.25 |
| **12a** |  | 1.63 ± 0.37 | **11e** |  | 0.97 ± 0.21 |
| **13a** |  | 3.1 ± 0.31 | **12e** |  | 3.80 ± 0.89 |
| **10b** |  | 6.5 ± 0.39 | **13e** |  | 6.50 ± 0.08 |
| **11b** |  | 2.8 ± 0.21 | **10f** |  | 7.84 ± 0.02 |
| **12b** |  | 8.4 ± 0.38 | **11f** |  | 3.04 ± 0.15 |
| **13b** |  | 3.0 ± 0.27 | **12f** |  | 3.8 ± 0.95 |
| **10c** |  | 8.3 ± 0.86 | **13f** |  | 7.13 ± 0.01 |
| **11c** |  | 0.58 ± 0.06 | **14a** |  | 14.3 ± 0.17 |
| **12c** |  | 3.59 ± 0.67 | **14b** |  | 10.7 ± 0.31 |
| **13c** |  | 6.98 ± 0.08 | **14c** |  | 12.3 ± 0.91 |
| **10d** |  | 0.69 ± 0.04 | **14d** |  | 24.4 ± 0.20 |
| **15** | **Std. Acarbose** | **0.65 ± 0.02** | | | |

**Table 5**
Lipinski evaluation for the synthesized products.

| Product No | MW | LIPINSKI's evaluation | | | | | |
|---|---|---|---|---|---|---|---|
| | | cLogP | TPSA | nAON | nDOHNH | MR ($cm^3$/mol) | No of Violations |
| **10a** | 411 | 2.04505 | 58.56 | 4 | 2 | 122.10 | 0 |
| **11a** | 411 | 2.04505 | 58.56 | 4 | 2 | 122.10 | 0 |
| **12a** | 411 | 2.04505 | 58.56 | 4 | 2 | 122.10 | 0 |
| **13a** | 411 | 2.04505 | 58.56 | 4 | 2 | 122.10 | 0 |
| **10b** | 456 | 1.78805 | 104.38 | 7 | 2 | 128.49 | 0 |
| **11b** | 456 | 1.78805 | 104.38 | 7 | 2 | 128.49 | 0 |
| **12b** | 456 | 1.78805 | 104.38 | 7 | 2 | 128.49 | 0 |
| **13b** | 456 | 1.78805 | 104.38 | 7 | 2 | 128.49 | 0 |
| **10c** | 445 | 2.75805 | 58.56 | 4 | 2 | 126.70 | 0 |
| **11c** | 445 | 2.75805 | 58.56 | 4 | 2 | 126.70 | 0 |
| **12c** | 445 | 2.75805 | 58.56 | 4 | 2 | 126.70 | 0 |
| **13c** | 445 | 2.75805 | 58.56 | 4 | 2 | 126.70 | 0 |
| **10d** | 501 | 1.34515 | 86.25 | 7 | 2 | 143.58 | 1 |
| **11d** | 501 | 1.34515 | 86.25 | 7 | 2 | 143.58 | 1 |
| **12d** | 501 | 1.34515 | 86.25 | 7 | 2 | 143.58 | 1 |
| **13d** | 501 | 1.34515 | 86.25 | 7 | 2 | 143.58 | 1 |
| **10e** | 397 | 1.61605 | 58.56 | 4 | 2 | 117.50 | 0 |
| **11e** | 397 | 1.61605 | 58.56 | 4 | 2 | 117.50 | 0 |
| **12e** | 397 | 1.61605 | 58.56 | 4 | 2 | 117.50 | 0 |
| **13e** | 397 | 1.61605 | 58.56 | 4 | 2 | 117.50 | 0 |
| **10f** | 431 | 2.32905 | 58.56 | 4 | 2 | 122.10 | 0 |
| **11f** | 431 | 2.32905 | 58.56 | 4 | 2 | 122.10 | 0 |
| **12f** | 431 | 2.32905 | 58.56 | 4 | 2 | 122.10 | 0 |
| **13f** | 431 | 2.32905 | 58.56 | 4 | 2 | 122.10 | 0 |
| **14a** | 397 | 2.6475 | 49.33 | 3 | 2 | 121.82 | 0 |
| **14b** | 438 | 2.3905 | 101.14 | 6 | 2 | 126.48 | 0 |
| **14c** | 438 | 2.3905 | 101.14 | 6 | 2 | 126.48 | 0 |
| **14d** | 428 | 3.3605 | 49.33 | 3 | 2 | 126.43 | 0 |

**Found**: C, 78.79; H, 6.09; N, 3.42.

*5.1.3. (Z)-2-phenyl-3-((4aR,5R,10bR)-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-9-yl)acrylic acid (**12a**)*

**FT-IR (KBr)**$\nu_{max}$ $cm^{-1}$: 3329, 2926, 1699, 1599, 1460, 1040; **$^1$H NMR** (400 MHz, $CDCl_3$)δ : 9.80 (s, 1H), 7.96 (s, 1H), 7.80 (m, 1H), 7.48 (t, 1H), 7.33–7.22 (m, 5H), 7.21 (m, 4H), 6.98 (m, 2H), 5.29 (brs, 1H, NH), 5.01 (s, 1H), 4.63–4.61 (d, 1H, *J* = 8.00 Hz), 4.04–4.01 (m, 2H), 1.97 (t, 2H), 1.36 (d, 1H), 0.81 (m, 2H); $^{13}$C **NMR** (125 MHz, $CDCl_3$)δ: 172.9, 159.4, 142.5, 140.3, 138.1, 132.7, 132.9, 131.2, 130.7, 129.3, 129.2, 129.0, 128.1, 119.6, 117.4, 117.3, 99.2, 68.5, 64.9, 38.2, 27.8, 23.8, 22.8; **MS** *m/z* : 411 ($M^+$); **Anal. Calcd. for** $C_{27}H_{25}NO_3$: C, 78.81; H, 6.12; N, 3.40, **Found:** C, 78.78; H, 6.13; N, 3.39.

*5.1.4. (Z)-2-phenyl-3-((4aR,5S,10bR)-5-phenyl-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-9-yl)acrylic acid (**13a**)*

**FT-IR** (KBr) $\nu_{max}$ $cm^{-1}$: 3408, 2933. 1693, 1597, 1342, 1078; **$^1$H NMR** (400 MHz, $CDCl_3$)δ: 10.08 (s, 1H), 8.14 (d, 1H), 8.05 (d, 1H), 7.99 (d, 1H), 7.93 (t, 1H), 7.70 (m, 1H), 7.54 (s, 1H), 7.33 (t, 2H), 7.31 (s, 1H), 7.30 (m, 3H), 6.99 (m, 2H), 4.79 (s, 1H), 4.44 (d, 1H, *J* = 12.0 Hz), 4.30 (brs, 1H, NH), 4.06–4.00 (m, 2H), 1.97 (t, 2H), 1.20 (t, 1H), 0.81 (m, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 171.1, 167.8, 147.2, 140.8, 139.2, 135.9, 133.9, 130.9, 129.3, 128.6, 123.9, 123.3, 112.3, 90.1, 71.8, 31.6, 29.7, 27.6, 22.7, 19.10; **MS *m/z***: 411 ($M^+$); **Anal. Calcd. for** $C_{27}H_{25}NO_3$: C, 78.81; H, 6.12; N, 3.40; **Found**: C, 78.83; H, 6.11; N, 3.38.

*5.1.5. (E)-3-((4aR,5R,10bR)-5-(4-nitrophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-9-yl)-2-phenylacrylic acid (**10b**)*

**FT-IR** (KBr) $\nu_{max}$ $cm^{-1}$: 3381, 3331, 2940, 1603, 1484, 1074; **$^1$H NMR** (400 MHz, $CDCl_3$) δ : 12.0 (s, 1H), 7.90 (s, 1H), 7.61–7.20 (m, 10H), 6.37 (d, 1H, *J* = 8.4 Hz), 6.01 (d, 1H, *J* = 8.4 Hz), 5.14 (d, 1H, *J* = 5.44 Hz), 5.01 (s, 1H), 3.9 (brs, 1H, −NH), 3.41 (d, 1H), 3.15 (t, 1H), 2.17 (m, 1H), 1.51–1.13 (m, 4H); **$^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 172.4, 170.0, 144.2, 143.5, 141.5, 139.5, 136.2, 135.2, 133.6, 131.2, 129.6, 128.2, 127.2, 126.5, 125.5, 124.6, 123.6, 119.9, 113.3, 73.5, 54.5, 38.1, 27.3, 23. 3, 21.4; **MS *m/z***: 456 ($M^+$); **Anal. Calcd. for**$C_{27}H_{24}N_2O_5$: C, 71.04; H, 5.30; N, 6.14; **Found**: C, 71.0; H, 5.25; N, 6.10

*5.1.6. (E)-3-((4aR,5S,10bR)-5-(4-nitrophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-9-yl)-2-phenylacrylic acid (**11b**)*

**FT-IR** (KBr) $\nu_{max}$ $cm^{-1}$: 3385, 3329, 2953, 1613, 1470, 1053; **$^1$H NMR** (400 MHz, $CDCl_3$)δ :11.4 (s, 1H), 7.81 (s, 1H), 7.35–7.09 (m, 7H), 6.85 (d, 2H, *J* = 7.76 Hz), 6.74 (d, 2H), 6.24 (d, 1H), 4.70 (d, 1H, *J* = 10.48 Hz), 4.2 (s, 1H), 4.03 (brs, 1H, NH), 3.69 (d, 1H), 2.09 (m, 2H), 1.80 (m, 2H), 1.6–1.4 (m, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 172.0, 159.0, 142.0, 140.8, 138.4, 132.9, 132.4, 131.5, 130.9, 129.6, 129.4, 129.2, 128.2, 119.1, 117.7, 117.1, 99.9, 68.5, 64.2, 38.7, 27.6, 23.9, 22.9; **MS *m/z***: 456 ($M^+$); **Anal. Calcd. for**$C_{27}H_{24}N_2O_5$: C, 71.04; H, 5.30; N, 6.14, **Found:** C, 70.99; H, 5.29; N, 6.06.

*5.1.7. (Z)-3-((4aR,5R,10bR)-5-(4-nitrophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-9-yl)-2-phenylacrylic acid (**12b**)*

**FT-IR(KBr)**$\nu_{max}$ $cm^{-1}$: 3379, 3325, 2945, 1613, 1489, 1078; **$^1$H NMR** (400 MHz, $CDCl_3$)δ: 11.0 (s, 1H), 8.24 (d, 2H, *J* = 8.68), 7.89 (s, 1H), 7.55 (d, 2H, *J* = 8.68), 7.37–7.30 (m, 3H), 7.28 (d, 2H, *J* = 9.08 Hz), 6.85 (d, 2H, *J* = 8.48 Hz), 6.42 (d, 1H, *J* = 8.4 Hz), 5.14 (d, 1H, *J* = 5.24 Hz), 4.78 (d, 1H), 4.07 (brs, 1H, NH), 3.40 (d, 1H), 3.16 (t, 1H, *J* = 11.16 Hz), 2.04 (d, 1H), 1.65–1.27 (m, 3H), 1.03 (s, 1H); **$^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 177.3, 166.4, 151.1, 138.3, 132.5, 129.5, 128.8, 127.6, 126.6, 124.5, 123.6, 122.3, 114.9, 112.0, 97.7, 65.5, 60.4, 42.2, 26.6, 24.3, 18.3; **MS** *m/z* : 456 ($M^+$); **Anal. Calcd. for**$C_{27}H_{24}N_2O_5$: C, 71.04; H, 5.30; N, 6.14, **Found:** C, 71.06; H, 5.28; N, 6.13.

*5.1.8. (Z)-3-((4aR,5S,10bR)-5-(4-nitrophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-9-yl)-z2-phenylacrylic acid (**13b**)*

FT-IR (KBr) $\nu_{max}$ $cm^{-1}$: 3368, 3319, 2935, 1600, 1479, 1070; $^1$H NMR (400 MHz, $CDCl_3$)δ : 11.2 (s, 1H), 8.23 (d, 2H, *J* = 8.68), 7.85 (s, 1H), 7.59 (d, 2H, *J* = 14.68 Hz), 7.40–7.35 (m, 4H), 7.26 (s, 1H), 6.75 (d, 2H), 6.30 (d, 1H, *J* = 8.56), 4.81 (d, 1H, *J* = 12.0 Hz), 4.27 (brs, 1H, NH), 4.19 (s, 1H), 3.66 (t, 1H, *J* = 11.48 Hz), 2.10–1.95 (m, 1H), 1.80–1.68 (m, 3H), 1.42–1.35 (m, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 173.10, 171.09, 146.50, 143.50, 140.5, 136.94, 135.9, 129.8, 128.3, 127.3, 125.01, 123.35, 111.34, 100.07, 89.9, 75.1, 60.59, 53.05, 29.36, 24.30, 21.06; **MS** *m/z*: 456 ($M^+$); **Anal. Calcd. for**$C_{27}H_{24}N_2O_5$: C, 71.04; H, 5.30; N, 6.14, **Found:** C, 70.98; H, 5.27; N, 6.07.

*5.1.9. (E)-3-((4aR,5R,10bR)-5-(4-chlorophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano[3,2-c]quinolin-9-yl)-2-phenylacrylic acid (**10c**)*

**FT-IR (KBr)** $\nu_{max}$ $cm^{-1}$: 3375, 3315, 2935, 1609, 1494, 1064; **$^1$H NMR** (400 MHz, $CDCl_3$)δ : 9.98 (s, 1H), 8.04 (d, 2H), 7.71 (s, 1H), 7.53–7.33 (m, 4H), 7.29 (d, 3H), 7.05 (t, 2H), 6.72 (t, 1H), 4.67 (d, 1H, *J* = 8.01 Hz), 4.18 (s, 1H), 4.01 (brs, 1H, NH), 3.66 (t, 2H), 2.38 (s, 1H), 2.28 (t, 1H), 2.13 (s, 1H), 1.33 (t, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 177.19, 172.4, 146.0, 143.5, 141.0, 136.2, 131.2, 130.8, 130.0, 129.9, 128.2, 127.2, 126.9, 122.9, 118.9, 93.5, 74.5, 64.70, 61.12, 38.0, 24.7, 21.4; **MS** *m/z*: 445 **($M^+$); Anal. Calcd. for** $C_{27}H_{24}ClNO_3$: C, 72.72; H, 5.42; N, 3.14; **Found**: C, 72.70; H, 5.39; N, 3.15.

*5.1.10. (E)-3-((4aR,5S,10bR)-5-(4-chlorophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano [3,2-c]quinolin-9-yl)-2-phenylacrylic acid (**11c**)*

**FT-IR (KBr)**$\nu_{max}$ $cm^{-1}$: 3380, 3325, 2940, 1603, 1484, 1074; **$^1$H NMR** (400 MHz, $CDCl_3$)δ : 10.02 (s, 1H), 8.29 (s, 1H), 8.09 (d, 1H), 7.99 (t, 1H), 7.87 (s, 1H), 7.48–7.38 (m, 3H), 7.37 (t, 2H), 7.32 (t, 2H), 7.02 (d, 1H), 6.87 (d, 1H), 4.36 (d, 1H, *J* = 12.0 Hz), 4.22 (s, 1H), 3.96 (brs, 1H, NH), 3.66–3.56 (m, 2H), 2.55 (m, 1H), 2.38 (s, 1H), 2.17 (s, 1H), 1.32 (t, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 177.4, 171.7, 165.1,

162.5, 159.1, 158.5, 141.8, 140.8, 133.5, 131.9, 131.2, 131.2, 129.3, 126.9, 119.3, 118.3, 116.7, 100.1, 98.1, 77.5, 65.07, 55.7, 38.0, 30.7, 29.0; **MS** *m/z*: 445 ($M^+$); **Anal. Calcd. for** $C_{27}H_{24}ClNO_3$: C, 72.72; H, 5.42; N, 3.14; **Found**: C, 72.71; H, 5.40; N, 3.09.

*5.1.11. (Z)-3-((4aR,5R,10bR)-5-(4-chlorophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano [3,2-c] quinolin-9-yl)-2-phenylacrylic acid **(12c)***

**FT-IR (KBr)**$\nu_{max}$ $cm^{-1}$: 3400, 2926, 1681, 1516, 1340, 1085; **$^1$H NMR** (400 MHz, $CDCl_3$)δ : 9.96 (s, 1H), 7.90 (m, 1H), 7.41 (m, 4H), 7.29–7.24 (m, 4H), 7.22–7.15 (m, 4H), 5.12 (d, 1H, *J* = 4.0 Hz), 4.63 (s, 1H), 3.95 (brs, 1H, NH), 3.69 (t, 2H), 2.40 (d, 1H), 1.40 (d, 2H), 1.30 (d, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 178.3, 171.3, 146.4, 141.3, 140.0, 134.5, 132.5, 130.8, 130.1, 129.6, 128.5, 127.2, 127.0, 126.9, 122.4, 118.8, 97.7, 72.7, 60.8, 55.8, 38.7, 24.3, 18.3; **MS** *m/z*: 445 ($M^+$); **Anal. Calcd. for** $C_{27}H_{24}ClNO_3$: C, 72.72; H, 5.42; N, 3.14; **Found**: C, 72.68; H, 5.35; N, 3.12.

*5.1.12. (Z)-3-((4aR,5S,10bR)-5-(4-chlorophenyl)-3,4,4a,5,6,10b-hexahydro-2H-pyrano [3,2-c]quinolin-9-yl)-2-phenylacrylic acid **(13c)***

**FT-IR (KBr)**$\nu_{max}$ $cm^{-1}$: 3310, 2935. 1680, 1514, 1340, 1076; **$^1$H NMR** (400 MHz, $CDCl_3$)δ: 10.16 (s,1H), 8.44 (d, 2H), 8.30 (m, 1H), 8.14 (t, 1H), 7.55 (t, 4H), 7.42 (t, 5H), 5.39 (d, 1H, *J* = 12.0 Hz), 5.17 (s, 1H), 4.89 (brs, 1H, NH), 4.13 (m, 2H), 2.87 (m, 2H), 2.46 (d, 1H), 1.26 (t, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 172.2, 171.3, 147.0, 143.6, 140.9, 136.8, 131.1, 134.3, 130.5, 130.1, 129.9, 128.3, 127.6, 127.2, 127.0, 126.6, 122.8, 117.8, 90.5, 71.9, 66.05, 58.8, 37.6, 24.7, 21.0; **MS** *m/z*: 445 ($M^+$); **Anal. Calcd. for** $C_{27}H_{24}ClNO_3$: C, 72.72; H, 5.42; N, 3.14; **Found**: C, 72.70; H, 5.39; N, 3.05.

*5.1.13. (E)-2-phenyl-3-((4aR,5R,10bR)-5-(3,4,5-trimethoxyphenyl)-3,4,4a,5,6,10b-hexa hydro- 2H-pyrano[3,2-c]quinolin-9-yl)acrylic acid **(10d)***

**FT-IR (KBr)**$\nu_{max}$ $cm^{-1}$: 3377, 3329, 2948, 1605, 1450, 1072; **$^1$H NMR** (400 MHz, $CDCl_3$)δ : 9.80 (s, 1H), 7.78 (s, 2H), 7.35 (d, 4H), 7.10 (s, 3H), 6.83 (d, 2H), 5.66 (d, 1H, *J* = 4.00 Hz), 4.99 (s, 1H), 4.48 (brs, 1H, NH), 3.88 (s, 9H, $OCH_3$), 3.51 (m, 2H), 2.10 (s, 1H), 1.91 (s, 2H), 1.18 (s, 2H);**$^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 178.4, 167.2, 152.1, 139.2, 130.4, 128.3, 127.4, 126.4, 124.1, 123.2, 114.2, 111.7, 98.9, 65.5, 60.4, 60.3, 60.1, 56.6, 42.5, 26.6, 24.2, 20.1; **MS** *m/z*: 501 ($M^+$); **Anal. Calcd. for** $C_{30}H_{31}NO_6$: C, 71.84; H, 6.23; N, 2.79; **Found**: C, 71.86; H, 6.21; N, 2.76.

*5.1.14. (E)-2-phenyl-3-((4aR,5S,10bR)-5-(3,4,5-trimethoxyphenyl)-3,4,4a,5,6,10b-hexa hydro-2H-pyrano[3,2-c]quinolin-9-yl)acrylic acid **(11d)***

**FT-IR (KBr)**$\nu_{max}$ $cm^{-1}$: 3384, 3330, 2950, 1607, 1455, 1080; **$^1$H NMR** (400 MHz, $CDCl_3$)δ: 9.46 (s, 1H), 7.77 (s, 1H), 7.29 (d, 3H), 7.17 (d, 3H), 6.83 (d, 2H), 6.48 (d, 2H), 5.25 (s, 1H), 5.19 (d, 1H, *J* = 12.0 Hz), 4.89 (brs, 1H, NH), 4.01 (s, 9H, $OCH_3$), 3.84 (m, 2H), 1.96 (m, 2H), 1.18 (d, 2H), 0.92 (d, 1H);**$^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 175.3, 164.26, 152.5, 138.2, 130.7, 128.6, 127.9, 123.9, 118.4, 114.5, 97.8, 63.7, 61.4, 60.3, 60.2, 55.8, 41.6, 26.1, 24.7, 20.6; **MS** *m/z*: 501 ($M^+$); **Anal. Calcd. for** $C_{30}H_{31}NO_6$: C, 71.84; H, 6.23; N, 2.79; **Found**: C, 71.76; H, 6.21; N, 2.76.

*5.1.15. (Z)-2-phenyl-3-((4aR,5R,10bR)-5-(3,4,5-trimethoxyphenyl)-3,4,4a,5,6,10b-hexa hydro-2H-pyrano [3,2-c]quinolin-9-yl)acrylic acid **(12d)***

**FT-IR (KBr)**$\nu_{max}$ $cm^{-1}$: 3421, 2981, 1675, 1559, 1456, 1081; **$^1$H NMR** (400 MHz, $CDCl_3$)δ: 9.83 (s, 1H), 7.33 (d, 3H), 7.18 (s, 3H), 7.07 (s, 2H), 6.81 (m, 2H), 6.53 (d, 1H), 5.63 (d, 1H, *J* = 4.01 Hz), 5.10 (s, 1H), 4.79 (brs, 1H, NH), 3.85 (s, 9H, $OCH_3$), 3.68 (t, 2H), 2.09 (s, 1H), 1.22 (d, 2H), 0.94 (t, 1H), 0.81 (t, 1H); **$^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 176.07, 163.80, 150.48, 139.56, 130.24, 128.1, 127.8, 123.61, 115.6, 113.6, 96.73, 65.58, 61.27, 60.91, 60.2, 55.2, 45.63, 29.06, 25.0, 21.2; **MS***m/z*: 501 ($M^+$); **Anal. Calcd. for** $C_{30}H_{31}NO_6$: C, 71.84; H, 6.23; N, 2.79; **Found**: C, 71.81; H, 6.19; N, 2.70.

*5.1.16. (Z)-2-phenyl-3-((4aR,5S,10bR)-5-(3,4,5-trimethoxyphenyl)-3,4,4a,5,6,10b-hexa hydro-2H-pyrano [3,2-c]quinolin-9-yl)acrylic acid **(13d)***

**FT-IR (KBr)**$\nu_{max}$ $cm^{-1}$: 3417, 2933, 1683, 1452, 1350, 1082; **$^1$H NMR** (400 MHz, $CDCl_3$)δ :9.81 (s, 1H), 7.76 (d, 1H), 7.30 (t, 3H), 7.26 (t, 3H), 7.15 (t, 3H), 6.80 (d, 1H), 5.25 (s, 1H), 5.19 (d, 1H, *J* = 12.0 Hz), 4.89 (brs, 1H, NH), 4.03 (s, 9H, $OCH_3$), 3.33–3.24 (m, 2H), 2.01 (s, 1H), 1.27 (d, 3H), 1.00 (d, 1H); **$^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 176.80, 163.65, 150.59, 139.92, 128.25, 127.70, 123.69, 115.54, 113.68, 96.80, 65.51, 61.20, 60.86, 60.15, 55.13, 45.71, 30.21, 25.6, 21.3 ; **MS** *m/z*: 501 ($M^+$); **Anal. Calcd. for** $C_{30}H_{31}NO_6$: C, 71.84; H, 6.23; N, 2.79; **Found:** C, 71.79; H, 6.23; N, 2.76.

*5.1.17. (E)-2-phenyl-3-((3aR,4R,9bR)-4-phenyl-2,3,3a,4,5,9b-hexahydrofuro [3,2-c] quinolin-8-yl)acrylic acid **(10e)***

**FT-IR (KBr)**$\nu_{max}$ $cm^{-1}$:3420, 2925, 1680, 1579, 1450, 1078; **$^1$H NMR** (400 MHz, $CDCl_3$)δ : 10.00 (s, 1H), 8.13 (m, 3H), 7.96 (m, 1H), 7.61 (d, 2H), 7.49 (m, 3H), 7.45 (m, 3H), 7.29 (t, 2H), 5.00 (s, 1H), 4.83 (brs 1H, NH), 4.42 (d, 1H, *J* = 4.0 Hz), 4.04 (m, 1H), 3.84 (m, 1H), 1.80 (m, 2H), 1.23 (s, 1H); **$^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 176.45, 170.79, 165.84, 162.81, 156.90, 152.89, 147.54, 146.85, 133.61, 130.29, 128.98, 128.64, 128.25, 126.60, 123.98, 123.29, 141.31, 106.06, 97.78, 64.89, 57.29, 42.67, 32.36, 19.70; **MS** *m/z*: 397 ($M^+$); **Anal. Calcd. for** $C_{26}H_{23}NO_3$: C, 78.57; H, 5.83; N, 3.52; **Found**: C, 78.54; H, 5.79; N, 3.50.

*5.1.18. (E)-2-phenyl-3-((3aR,4S,9bR)-4-phenyl-2,3,3a,4,5,9b-hexahydrofuro [3,2-c] quinolin-8-yl)acrylic acid **(11e)***

**FT-IR (KBr)**$\nu_{max}$ $cm^{-1}$: 3417, 2900, 1673, 1569, 1468, 1080;**$^1$H NMR** (400 MHz, $CDCl_3$)δ : 9.97 (s, 1H), 7.88–7.77 (m, 2H), 7.60 (d, 2H), 7.48 (d, 2H), 7.37–7.32 (m, 5H), 7.27 (m, 3H), 5.56 (s, 1H), 5.02 (d, 1H, *J* = 20.0 Hz), 4.85 (brs, 1H, NH), 3.78–3.65 (m, 2H), 2.44 (d, 1H), 1.29 (d, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 174.35, 171.68, 163.84, 160.79, 155.90, 153.31, 147.59, 145.03, 133.61, 131.09, 128.94, 128.51, 125.59, 124.28, 123.23, 106.06, 98.32, 63.06, 55.31, 41.04, 32.30, 20.19; **MS** *m/z*: 397 ($M^+$); **Anal. Calcd. for** $C_{26}H_{23}NO_3$: C, 78.57; H, 5.83; N, 3.52; **Found**: C, 78.56; H, 5.85; N, 3.51.

*5.1.19. (Z)-2-phenyl-3-((3aR,4R,9bR)-4-phenyl-2,3,3a,4,5,9b-hexahydrofuro [3,2-c]quinolin-8-yl)acrylic acid **(12e)***

**FT-IR (KBr)**$\nu_{max}$ $cm^{-1}$: 3427, 2935, 1683, 1589, 1458, 1082; **$^1$H NMR** (400 MHz, $CDCl_3$)δ : 9.98 (s, 1H), 7.83 (t, 2H), 7.34–7.28 (m, 5H), 7.19 (d, 3H), 6.87 (d, 2H), 6.58 (d, 1H), 6.37 (d, 1H), 5.23 (s, 1H), 5.18 (d, 1H, *J* = 4.0 Hz), 5.03 (brs, 1H, NH), 3.81–3.73 (m, 2H), 1.97 (d, 1H), 1.19 (t, 2H); **$^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 172.06, 163.11, 159.81, 157.16, 154.52, 152.51, 147.53, 142.56, 135.94, 132.94, 130.30, 128.65, 127.29, 124.26, 113.65, 106.74, 99.43, 89.79, 65.54, 45.61, 34.68, 27.69, 21.07; **MS** *m/z*: 397 ($M^+$); **Anal. Calcd. for** $C_{26}H_{23}NO_3$: C, 78.57; H, 5.83; N, 3.52; **Found**: C, 78.50; H, 5.82; N, 3.49.

*5.1.20. (Z)-2-phenyl-3-((3aR,4S,9bR)-4-phenyl-2,3,3a,4,5,9b-hexahydrofuro [3,2-c] quinolin-8-yl) acrylic acid **(13e)***

**FT-IR (KBr)**$\nu_{max}$ $cm^{-1}$: 3406, 2872, 1691, 1450, 1219, 1016; **$^1$H NMR** (400 MHz, $CDCl_3$)δ : 9.90 (s, 1H), 8.29 (s, 2H), 7.87 (s, 1H), 7.81 (t, 2H), 7.29 (s, 2H), 7.19 (t, 2H), 7.02 (d, 1H), 6.93 (m, 2H), 6.88 (m, 2H), 5.69 (s, 1H), 5.37 (d, 1H, *J* = 12.0 Hz), 5.03 (brs, 1H, NH), 3.92–3.78 (m, 2H), 1.87–1.69 (m, 2H), 1.18 (d, 1H)**;** **$^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 173.34, 172.83, 152.56, 148.06, 147.12, 142.79, 141.66, 140.78, 136.39, 136.34, 135.94, 135.63, 134.51, 132.98,132.71, 129.85, 125.84, 99.0, 67.05, 65.59, 30.88, 29.72, 23.42; **MS** *m/z*: 397 ($M^+$); **Anal. Calcd. for** $C_{26}H_{23}NO_3$: C, 78.57; H, 5.83; N, 3.52; **Found**: C, 78.56; H, 5.80; N, 3.49.

*5.1.21. (E)-3-((3aR,4R,9bR)-4-(4-chlorophenyl-2,3,3a,4,5,9b-hexahydrofuro [3,2-c]quinolin-8-yl)-2-phenyl acrylic acid (**10f**)*

**FT-IR (KBr)**$\nu_{max}$ $cm^{-1}$: 3378, 3320, 2950, 1600, 1490, 1070; **$^1$H NMR** (400 MHz, $CDCl_3$)δ : 10.00 (s, 1H), 8.09 (s, 1H), 8.07 (t, 3H), 7.84 (d, 1H), 7.61 (d, 1H), 7.46–7.34 (m, 5H), 7.28 (d, 2H), 5.51 (d, 1H, *J* = 8.00 Hz), 5.39 (s, 1H), 5.07 (brs, 1H, NH), 3.92–3.72 (m, 2H), 2.63 (m, 1H), 1.59 (m, 1H), 1.26 (s, 1H)**; $^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 171.76, 168.45, 163.45, 159.82, 157.46, 153.86, 147.54, 144.22, 139.53, 131.59, 128.63, 127.94, 119.34, 116.01, 111.02, 108.02, 97.78, 67.89, 66.51, 51.27, 30.72, 25.77; **MS** *m/z*: 431 ($M^+$); **Anal. Calcd. for** $C_{26}H_{22}ClNO_3$: C, 72.30; H, 5.13; N, 3.24; **Found**: C, 72.27; H, 5.10; N, 3.20.

*5.1.22. (E)-3-((3aR,4S,9bR)-4-(4-chlorophenyl-2,3,3a,4,5,9b-hexahydrofuro [3,2-c] quinolin-8-yl)-2-phenyl acrylic acid (**11f**)*

**FT-IR (KBr)**$\nu_{max}$ $cm^{-1}$: 3350, 3315, 2945, 1610, 1480, 1064; **$^1$H NMR** (400 MHz, $CDCl_3$)δ : 9.72 (s, 1H), 8.14 (d, 1H), 8.02–7.93 (m, 1H), 7.60 (d, 1H), 7.51 (s, 1H), 7.44–7.40 (m, 5H), 7.38 (s, 1H), 7.37 (t, 2H), 7.20 (s, 1H), 5.51 (d, 1H, *J* = 12.0 Hz), 5.38 (s, 1H), 5.07 (brs, 1H, NH), 3.87–3.72 (m, 2H), 2.07–1.92 (m, 2H), 1.29 (t, 1H)**; $^{13}$C NMR** (125 MHz, $CDCl_3$) δ : 175.47, 167.49, 162.52, 158.82, 154.17, 146.85, 142.27, 131.29, 128.94, 126.62, 123.67, 123.30, 115.02, 110.05, 107.43, 104.40, 97.77, 56.89, 49.29, 45.01, 35.97, 27.39; **MS** *m/z*: 431 ($M^+$); **Anal. Calcd. for** $C_{26}H_{22}ClNO_3$: C, 72.30; H, 5.13; N, 3.24; **Found** : C, 72.28; H, 5.12; N, 3.19.

*5.1.23. (Z)-3-((3aR,4R,9bR)-4-(4-chlorophenyl-2,3,3a,4,5,9b-hexahydrofuro [3,2-c] quinolin-8-yl)-2-phenyl acrylic acid (**12f**)*

**FT-IR (KBr)**$\nu_{max}$ $cm^{-1}$: 3370, 3310, 2840, 1625, 1454, 1090; **$^1$H NMR** (400 MHz, $CDCl_3$)δ : 10.00 (s, 1H), 8.02 (d, 2H), 7.92–7.53 (m, 1H), 7.51 (d, 1H), 7.42–7.38 (m, 4H), 7.36–7.19 (m, 5H), 5.39 (d, 1H, *J* = 4.0 Hz), 5.17 (brs, 1H, NH), 4.58 (s, 1H), 3.74–3.67 (m, 2H), 2.57–2.46 (m, 1H), 1.57–1.50 (m, 1H), 1.25 (s, 1H)**; $^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 170.68, 147.89, 147.22, 141.58, 140.91, 137.91, 134.54, 131.98, 131.29, 130.96, 130.59, 129.61, 129.33, 127.95, 127.69, 126.60, 125.32, 122.92, 122.33, 106.06, 105.69, 67.53, 57.21, 40.76, 35.78, 25.06; **MS** *m/z*: 431 ($M^+$); **Anal. Calcd. for** $C_{26}H_{22}ClNO_3$: C, 72.30; H, 5.13; N, 3.24; **Found**: C, 72.29; H, 5.09; N, 3.21.

*5.1.24. (Z)-3-((3aR,4S,9bR)-4-(4-chlorophenyl-2,3,3a,4,5,9b-hexahydrofuro [3,2-c] quinolin-8-yl)-2-phenyl acrylic acid (**13f**)*

**FT-IR (KBr)**$\nu_{max}$ $cm^{-1}$: 3345, 3305, 2900, 1660, 1474, 1070; **$^1$H NMR** (400 MHz, $CDCl_3$)δ : 9.99 (s, 1H), 8.20 (d, 2H), 8.10 (d, 1H), 7.92 (s, 1H), 7.62 (d, 1H), 7.48 (d, 2H), 7.40–7.36 (m, 4H), 7.31 (d, 1H), 7.19 (s, 1H), 5.50 (d, 1H, *J* = 12.0 Hz), 5.38 (s, 1H), 5.03 (brs, 1H, NH), 3.82–3.74 (m, 2H), 2.21 (s, 1H), 1.64–1.54 (m, 1H), 1.26 (s, 1H); **$^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 175.76, 170.40, 165.46, 159.80, 154.84, 149.56, 142.57, 134.58, 128.63, 127.66, 123.63, 115.01, 112.68, 107.04, 104.40, 99.43, 67.89, 55.93, 46.66, 30.05, 25.74; **MS** *m/z*: 431 ($M^+$); **Anal. Calcd. for** $C_{26}H_{22}ClNO_3$: C, 72.30; H, 5.13; N, 3.24; **Found**: C, 72.26; H, 5.12; N, 3.22.

*5.1.25. (E)-2-phenyl-3-((3aS,4R,9bR)-4-phenyl-3a,4,5,9b-tetrahydro-3H-cyclopenta[c] quinolin-8-yl)acrylic acid (**14a**)*

**FT-IR (KBr)**$\nu_{max}$ $cm^{-1}$: 3350, 2902, 1654, 1479, 1265, 1080; **$^1$H NMR** (400 MHz, $CDCl_3$)δ : 9.97 (s, 1H), 8.04–7.97 (m, 5H), 7.41 (s, 5H), 7.23 (d, 3H), 6.82 (s, 1H), 6.65 (s, 1H), 6.49 (s, 1H), 5.08 (s, 1H), 4.46 (d, 1H, *J* = 8.0 Hz), 3.85 (brs, 1H, NH), 1.25 (s, 1H), 1.00 (d, 1H), 0.86 (d, 1H)**; $^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 171.77, 171.10, 146.85, 141.22, 140.61, 139.25, 137.89, 135.57, 133.91, 132.93, 131.14, 130.21, 130.97, 129.92, 129.58, 129.53, 128.64, 127.65, 126.61, 124.65, 123.68, 123.30, 29.72, 26.41, 19.40, 19.11; **MS** *m/z*: 393 ($M^+$); **Anal. Calcd. for** $C_{27}H_{23}NO_2$: C, 82.42; H, 5.89; N, 3.56; **Found**: C, 81.36; H, 5.78; N, 3.53.

*5.1.26. (E)-3-((3aS,4R,9bR)-4-(4-nitrophenyl)-3a,4,5,9b-tetrahydro –3H-cyclopenta[c] quinolin-8-yl)-2-phenylacrylic acid (**14b**)*

**FT-IR (KBr)**$\nu_{max}$ $cm^{-1}$: 3354, 2909, 1664, 1489, 1275, 1089; **$^1$H NMR** (400 MHz, $CDCl_3$)δ : **$^1$H NMR** (400 MHz, $CDCl_3$)δ: 10.16 (s, 1H), 8.41 (t, 2H), 8.09–7.96 (m, 6H), 7.41 (d, 3H), 7.40–7.20 (m, 4H), 5.97 (s, 1H), 5.47 (d, 1H, *J* = 8.0 Hz), 4.76 (brs, 1H, NH), 1.29 (t, 2H), 0.82 (t, 1H); **$^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 171.77, 171.10, 146.85, 141.22, 140.61, 139.25, 137.89, 135.57, 133.91, 132.93, 131.14, 130.21, 130.97, 129.92, 129.58, 129.53, 128.64, 127.65, 126.61, 124.65, 123.68, 123.30, 29.72, 26.41, 19.40, 19.11; **MS** *m/z*: 438 ($M^+$); **Anal. Calcd. for** $C_{27}H_{22}N_2O_4$: C, 73.96; H, 5.06; N, 6.39; **Found**: C,73.90; H, 5.01; N, 6.36.

*5.1.27. (Z)-3-((3aS,4S,9bR)-4-(4-nitrophenyl)-3a,4,5,9b-tetrahydro –3H-cyclopenta[c] quinolin-8-yl)-2-phenylacrylic acid (**14c**)*

**FT-IR (KBr)**$\nu_{max}$ $cm^{-1}$: 3365, 2925, 1674, 1499, 1260, 1077; **$^1$H NMR** (400 MHz, $CDCl_3$)δ : 10.01 (s, 1H), 8.26 (d, 3H)), 7.84 (s, 4H), 7.63 (d, 2H), 7.52 (t, 2H), 7.41 (m, 2H), 6.81 (d, 1H), 6.73 (s, 1H), 4.70 (s, 1H), 4.15 (d, 1H, *J* = 8.0 Hz), 3.84 (brs, 1H, NH), 2.48–2.42 (m, 1H), 2.05 (s, 1H), 1.26 (d, 1H); **$^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 172.5, 149.6, 147.3, 146.1, 142.6, 136.4, 133.5, 132.4, 130.2, 129.9, 128.8, 127.8, 127.6, 127.2, 125.7, 125.0, 123.9, 115.6, 57.0, 45.3, 31.2, 21.0; **MS** *m/z*: 438 ($M^+$); **Anal. Calcd. for** $C_{27}H_{22}N_2O_4$: C, 73.96; H, 5.06; N, 6.39; **Found**: C, 73.95; H, 4.99; N, 6.35.

*5.1.28. (Z)-3-((3aS,4S,9bR)-4-chlorophenyl)-3a,4,5,9b-tetrahydro-3H-cyclopenta[c] quinolin-8-yl)-2-phenylacrylic acid (**14d**)*

**FT-IR (KBr)**$\nu_{max}$ $cm^{-1}$: 3379, 2922, 1674, 1489, 1276, 1087; **$^1$H NMR** (400 MHz, $CDCl_3$)δ : 10.02 (s, 1H), 8.04 (t, 2H)), 7.67 (s, 1H), 7.43 (d, 1H), 7.41–7.37 (m, 3H), 7.22–7.29 (m, 4H), 7.29 (s, 1H), 6.91 (d, 1H), 6.77 (t, 1H), 6.42 (d, 1H), 4.62 (d, 1H, *J* = 12.0 Hz), 4.28 (s, 1H), 3.64 (brs, 1H, NH), 1.28 (d, 2H), 0.88 (t, 1H); **$^{13}$C NMR** (125 MHz, $CDCl_3$)δ: 170.3, 148.8, 146.4, 143.0, 140.2, 135.7, 131.5, 130.0, 129.4, 128.4, 128.7, 128.5, 127.2, 125.1, 122.8, 115.4, 56.9, 45.5, 29.2, 19.0; **MS** *m/z*: 428 ($M^+$); **Anal. Calcd. for** $C_{27}H_{22}ClNO_2$: C, 75.78; H, 5.18; N, 3.27; **Found**: C, 75.69; H, 5.17; N, 3.26.

### *5.2. α-glucosidaseinhibiton assay*

Alpha-glucosidase inhibition was analysed by using kinetic end-point assay described by Pistia-Brueggeman. Alpha-glucosidase inhibitory activity was performed by following the modified method of PistiaBrueggeman and Hollingsworth [26]. In a 96-well plate reader, a reaction mixture containing 50 µl of phosphate buffer (50 mM; pH 6.8), 10 µl of alpha-glucosidase (1 U/ml) and 20 µl of the given compound of varying concentrations was pre-incubated for 5 min at 37 °C, and then 20 µl of 1 mM PNPG was added to the mixture as a substrate. After further incubation at 37 °C for 30 min, the reaction was stopped by adding 50 µl of sodium carbonate (0.1 M). All the enzyme, inhibitor and substrate solutions were made using the same buffer. Acarbose was used as a positive control and water as negative control. The yellow colour produced (due to pnitrophenol formation) was quantitated by colorimetric analysis and reading the absorbance at 405 nm. Each experiment was performed in triplicates, along with appropriate blanks. The % inhibition has been obtained using the formula given below. Percentage inhibition = {Absorbance (control) − Absorbance (sample)}/Absorbance (control) × 100. $IC_{50}$ values were calculated from non-linear regression curve of percentage inhibition versus log compound concentration.

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