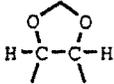
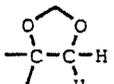


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5	147	PhCH ₂ CH ₂ -		PhCH ₂ CH ₂ -
10	148	BocNH Ph-CH-CH ₂ -	-CH(OH)-	CH ₃ C(O)NH Ph-CH-CH ₂ -
15	149B	PhCH ₂ CH ₂ -	-CH(OH)CH(OH)-	PhCH ₂ CH ₂ -
20	150	PhCH ₂ CH ₂ -		PhCH ₂ CH ₂ -
25	151	PhCH ₂ CH ₂ -		PhCH ₂ CH ₂ -
30	152	PhCH ₂ CH ₂ -	-C(OCH ₃) ₂ -	PhCH ₂ CH ₂ -
35	153	R ₃₄₅ -Leu-NH Ph-CH-CH ₂ - (R ₃₄₅ = H ₂ NC(CH ₃) ₂ CH ₂ C(O)-)	-CH(OH)-	BocNH Ph-CH-CH ₂ -
40	154	Cbz-Leu-Asn-NH Ph-CH-CH ₂ -	-CH(OH)-	Cbz-Leu-Asn-NH Ph-CH-CH ₂ -
45	155B	BocNH Ph-CH-CH ₂ -	-CH ₂ S(O) ₂ CH ₂ -	BocNH Ph-CH-CH ₂ -
50	156B	PhOC(O) Ph-CH-CH ₂ -	-CH ₂ S(O) ₂ CH ₂ -	PhOC(O) Ph-CH-CH ₂ -

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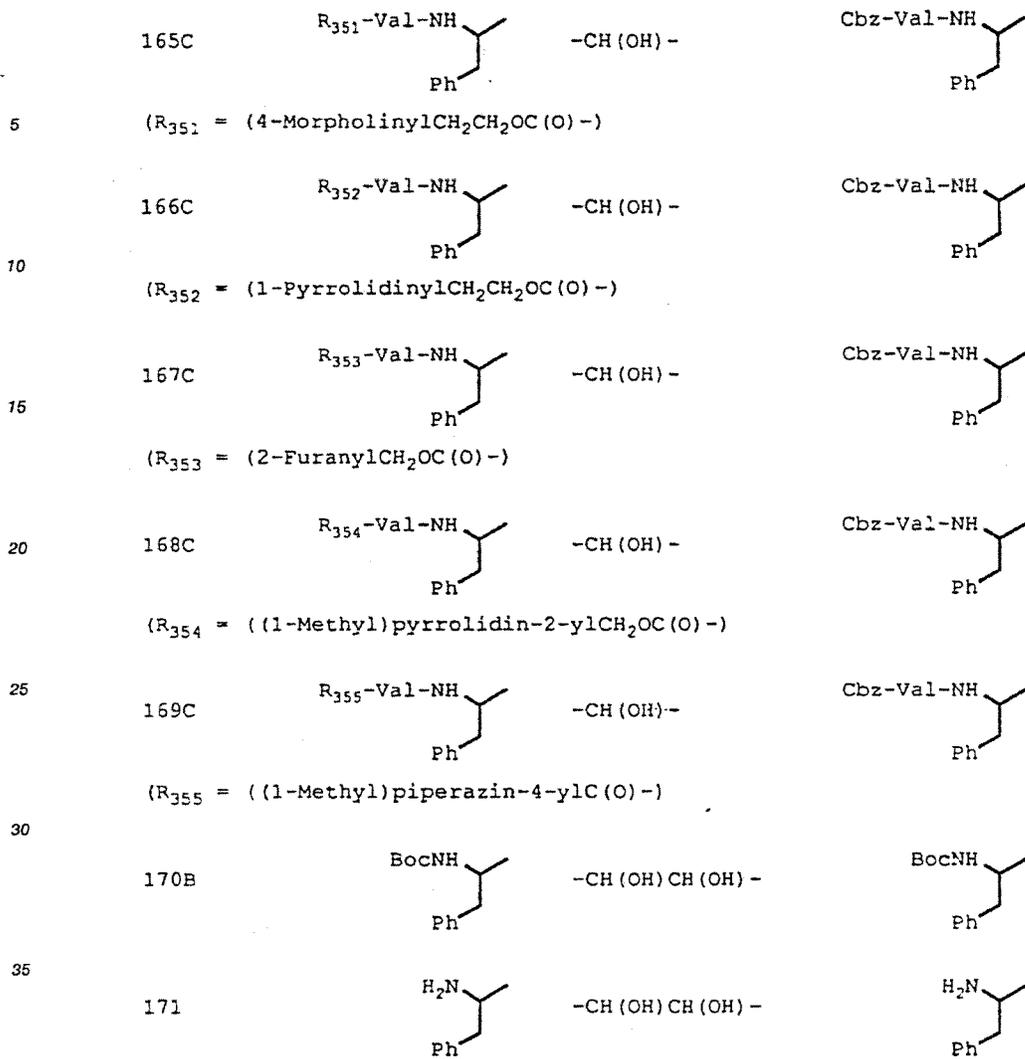
5	157		-CH ₂ S(O)CH ₂ -	
	158		-CH ₂ S(O)CH ₂ -	
10	159B		-CH ₂ N(OH)CH ₂ -	
15	160D		-CH(OH)-	
		(R ₃₄₆ = (4-PyridylCH ₂ OC(O)-)		
20	161C		-CH(OH)-	
		(R ₃₄₇ = (3-PyridylCH ₂ OC(O)-)		
25	162C		-CH(OH)-	
		(R ₃₄₈ = (2-PyridylCH ₂ OC(O)-)		
30	163C		-CH(OH)-	
35		(R ₃₄₉ = (3-Pyridyl-C(O)-)		
40	164C		-CH(OH)-	
		(R ₃₅₀ = (4-Pyridyl-C(O)-)		

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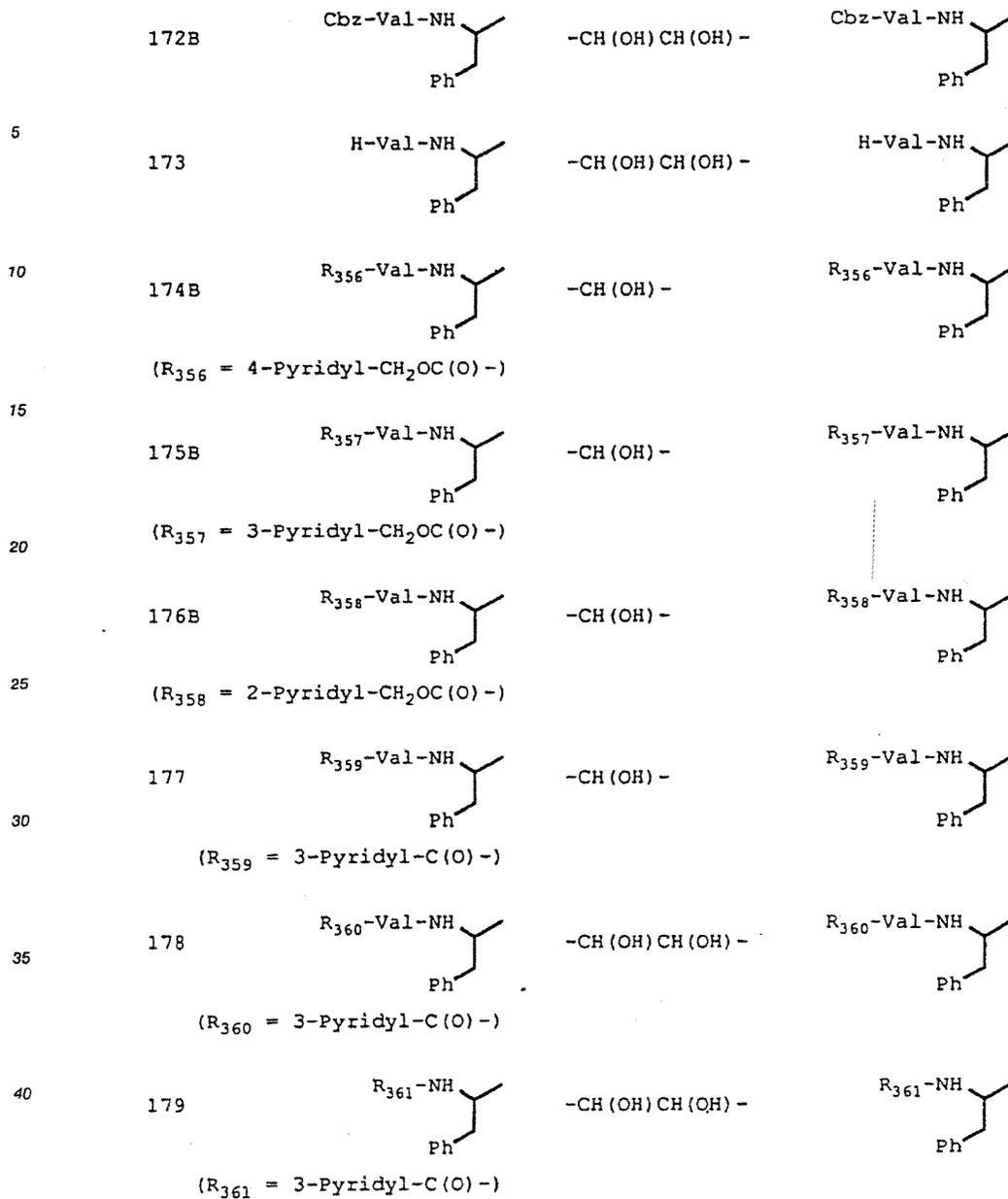
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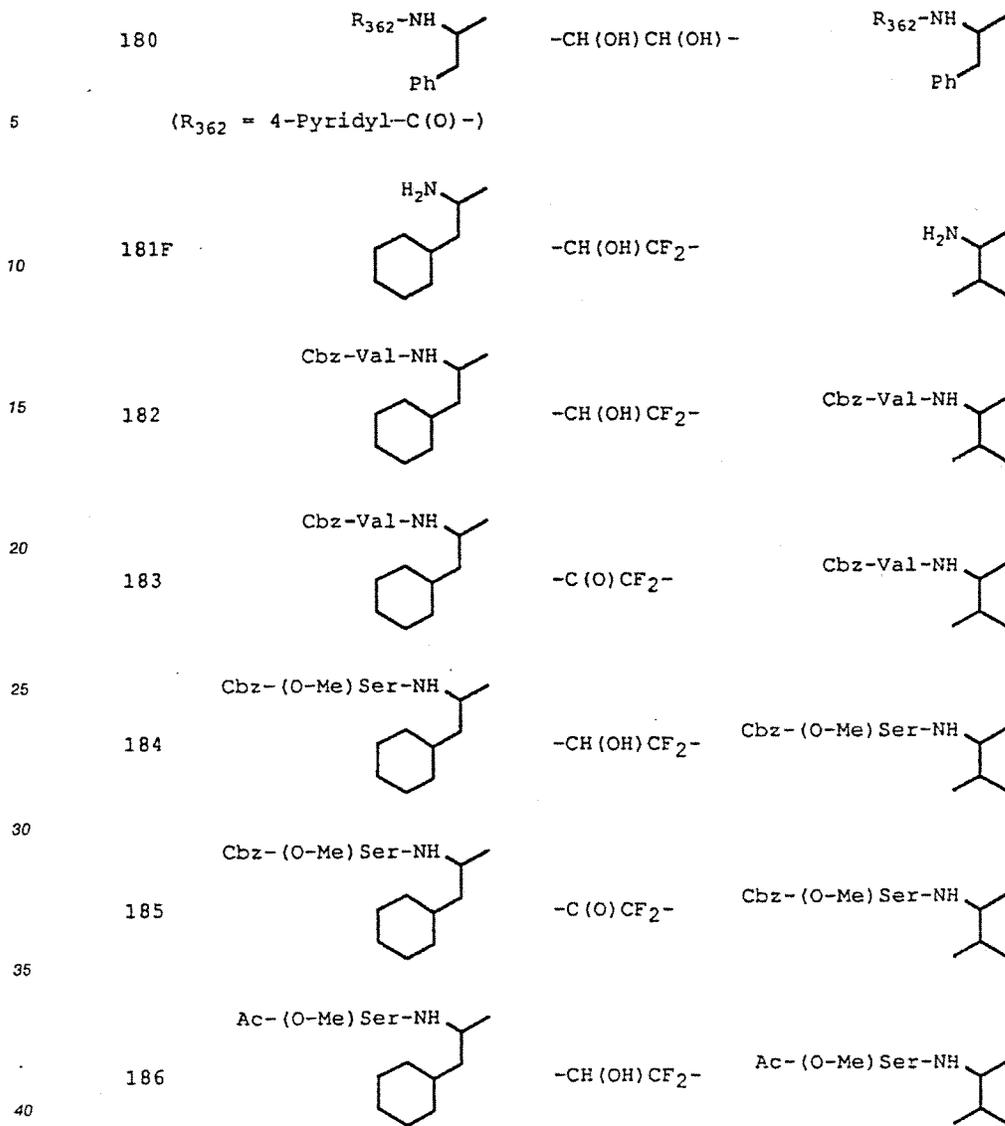


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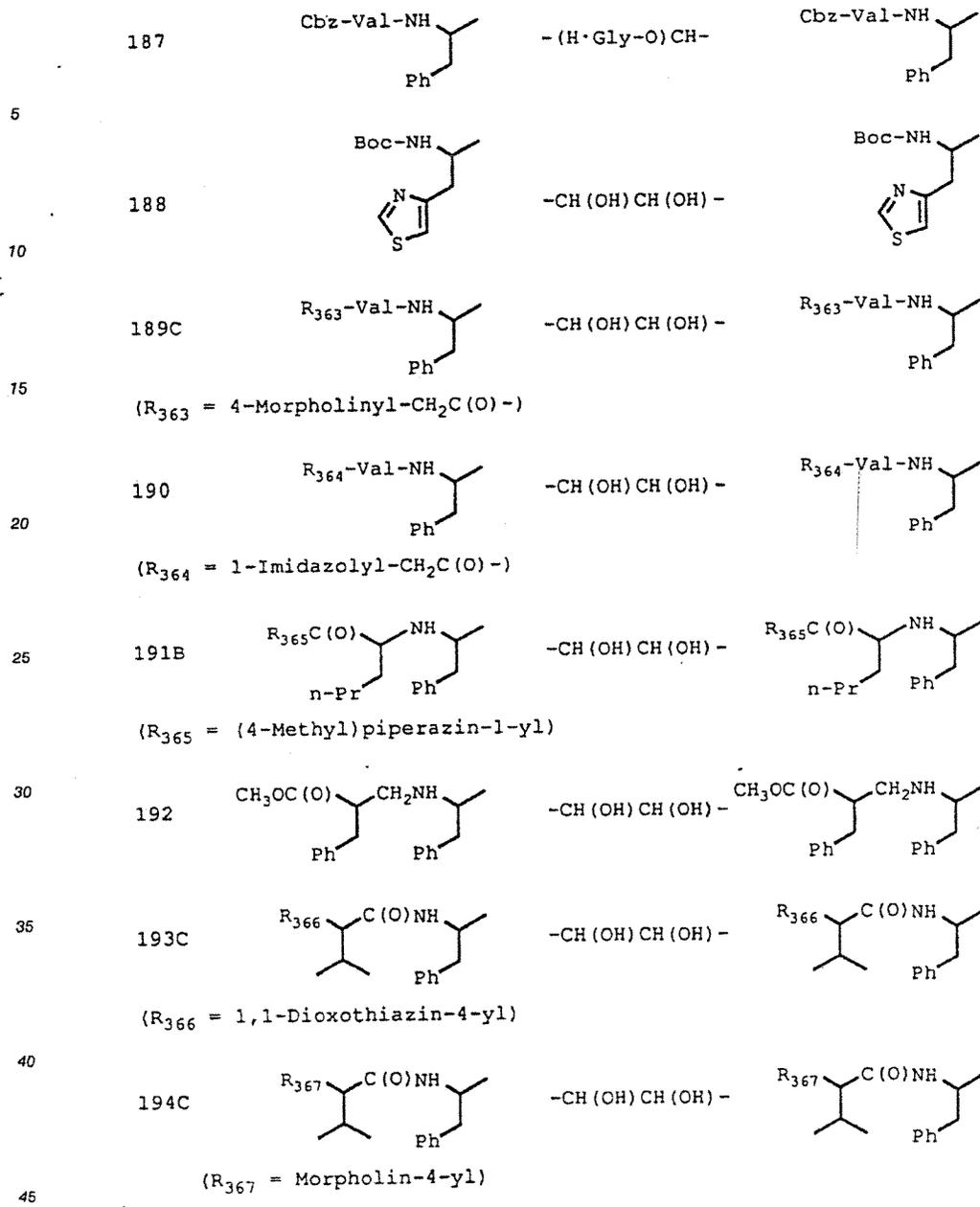
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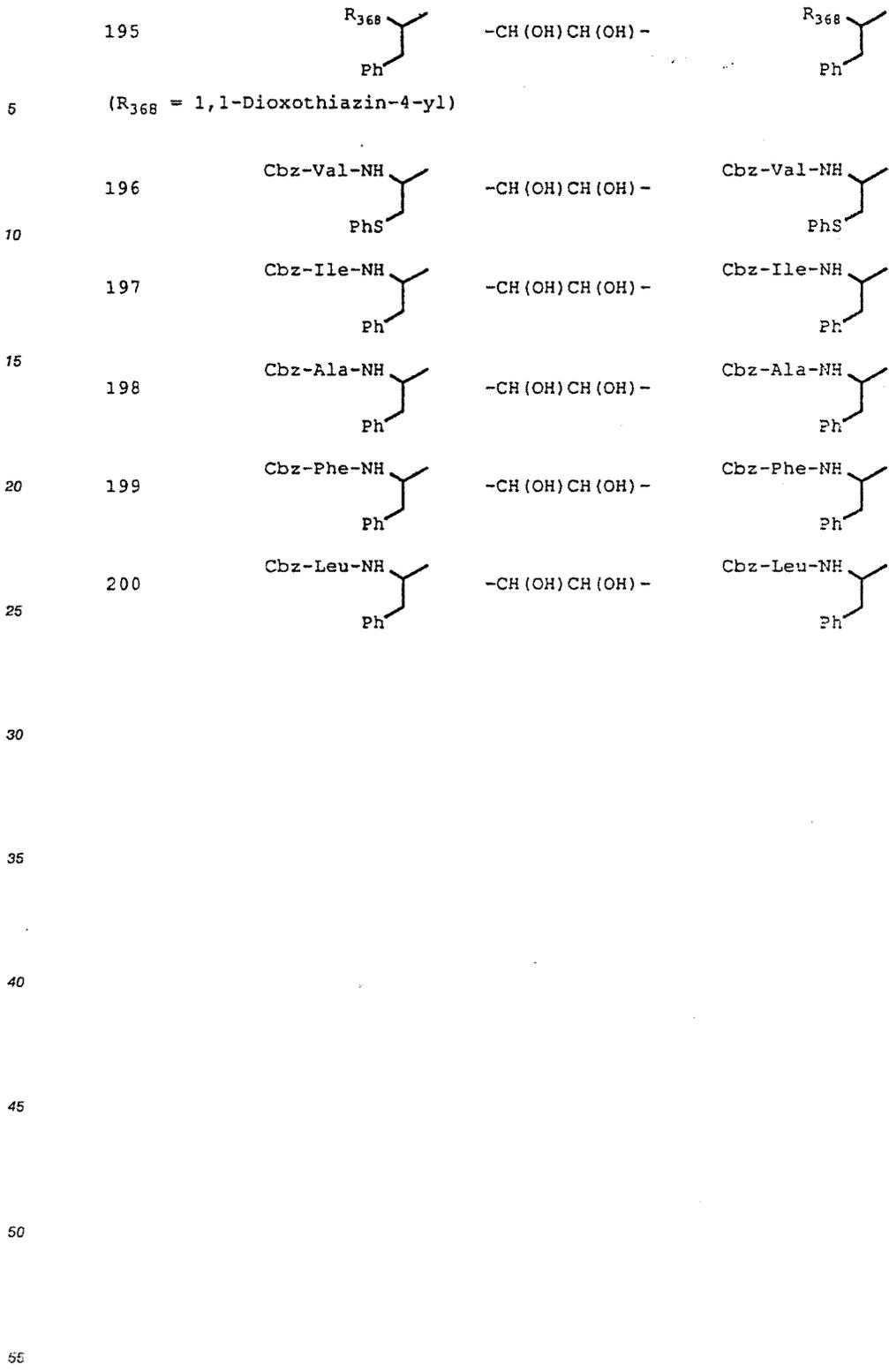
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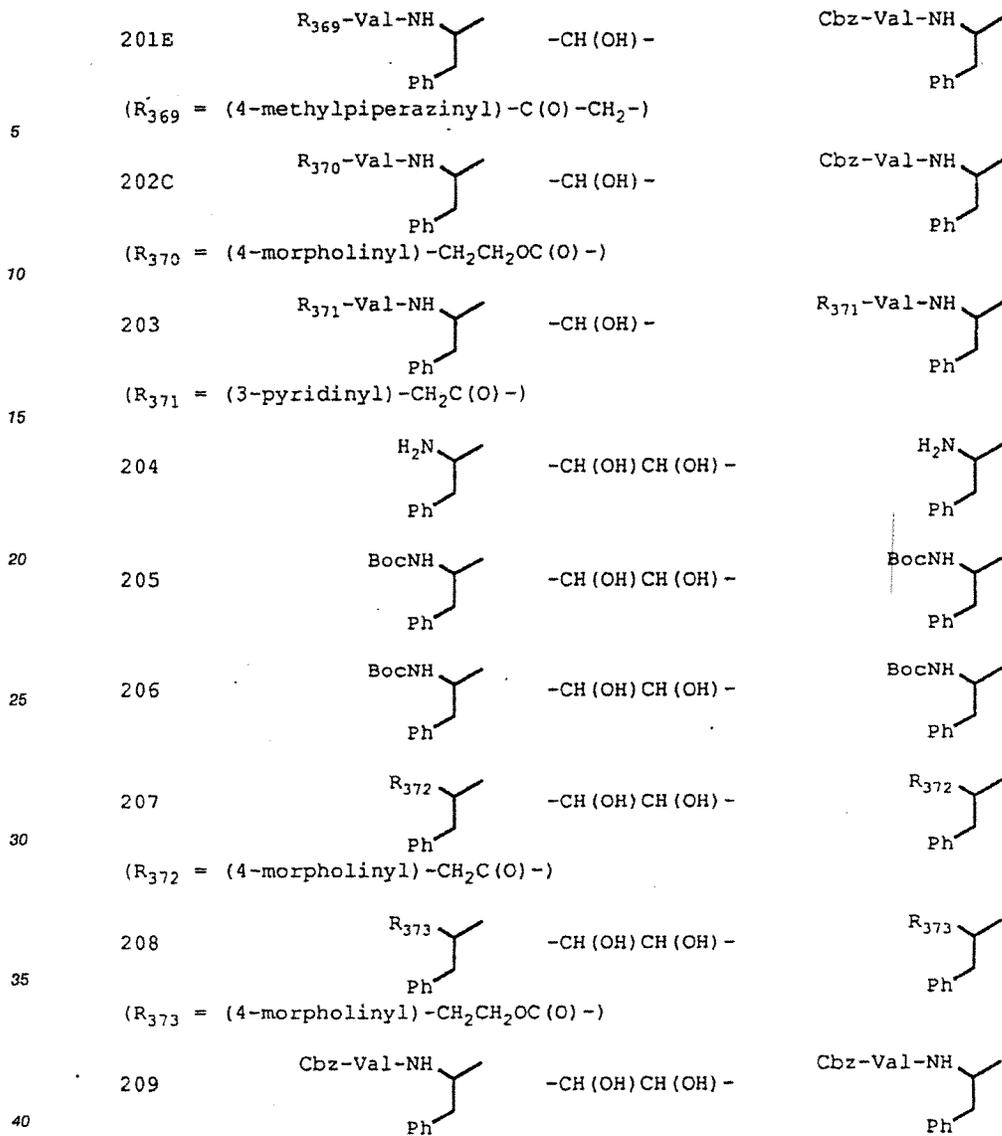
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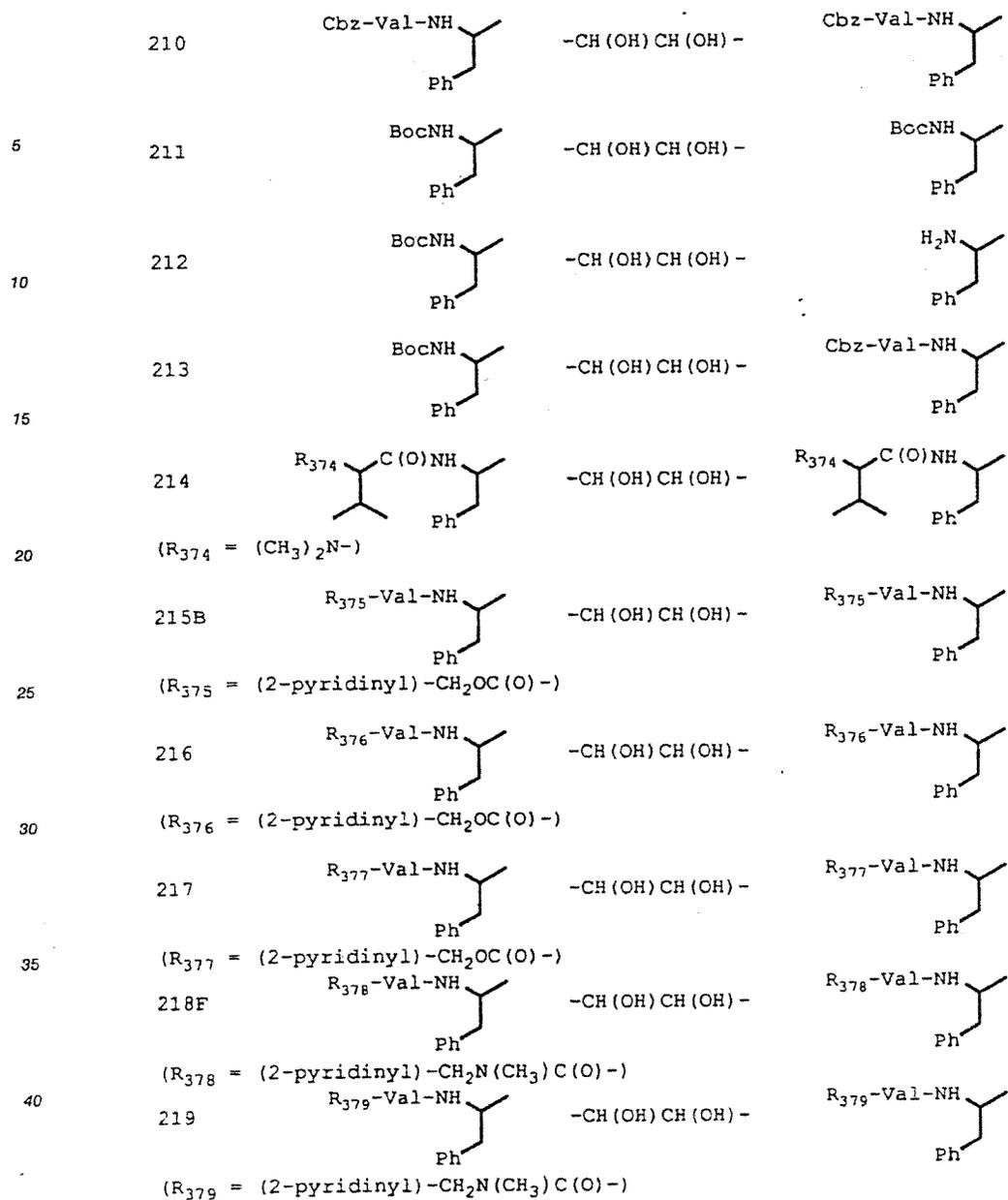


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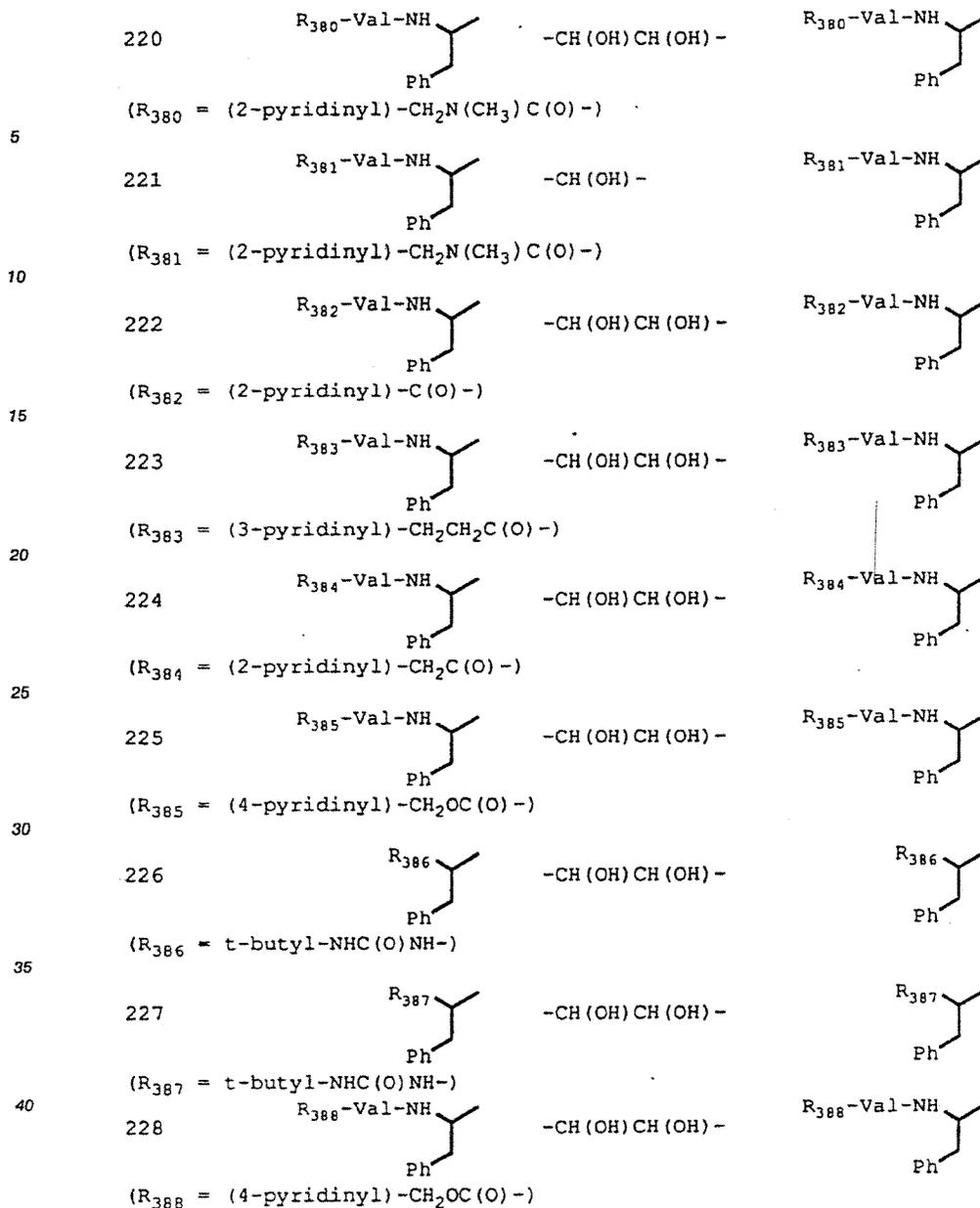
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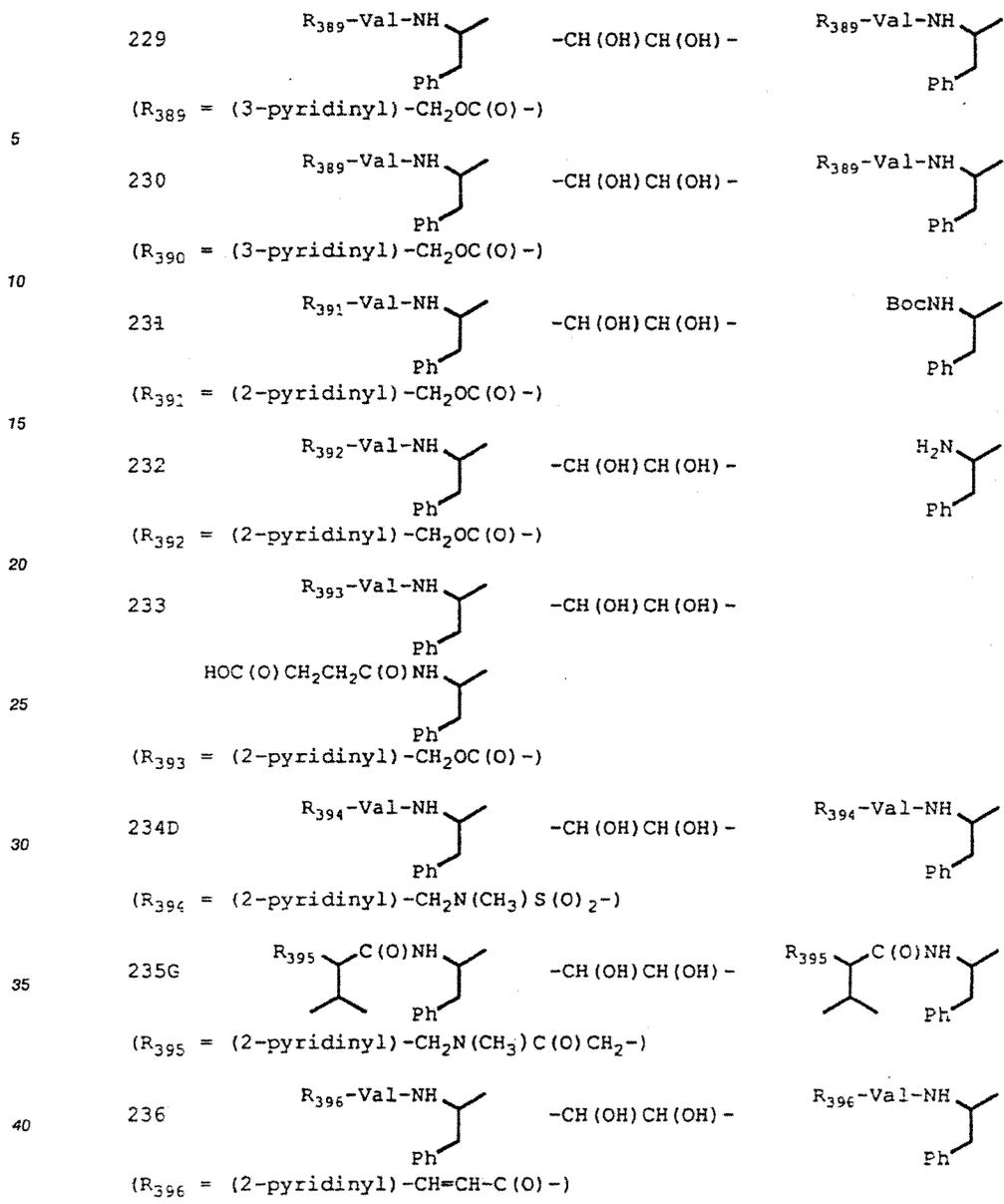
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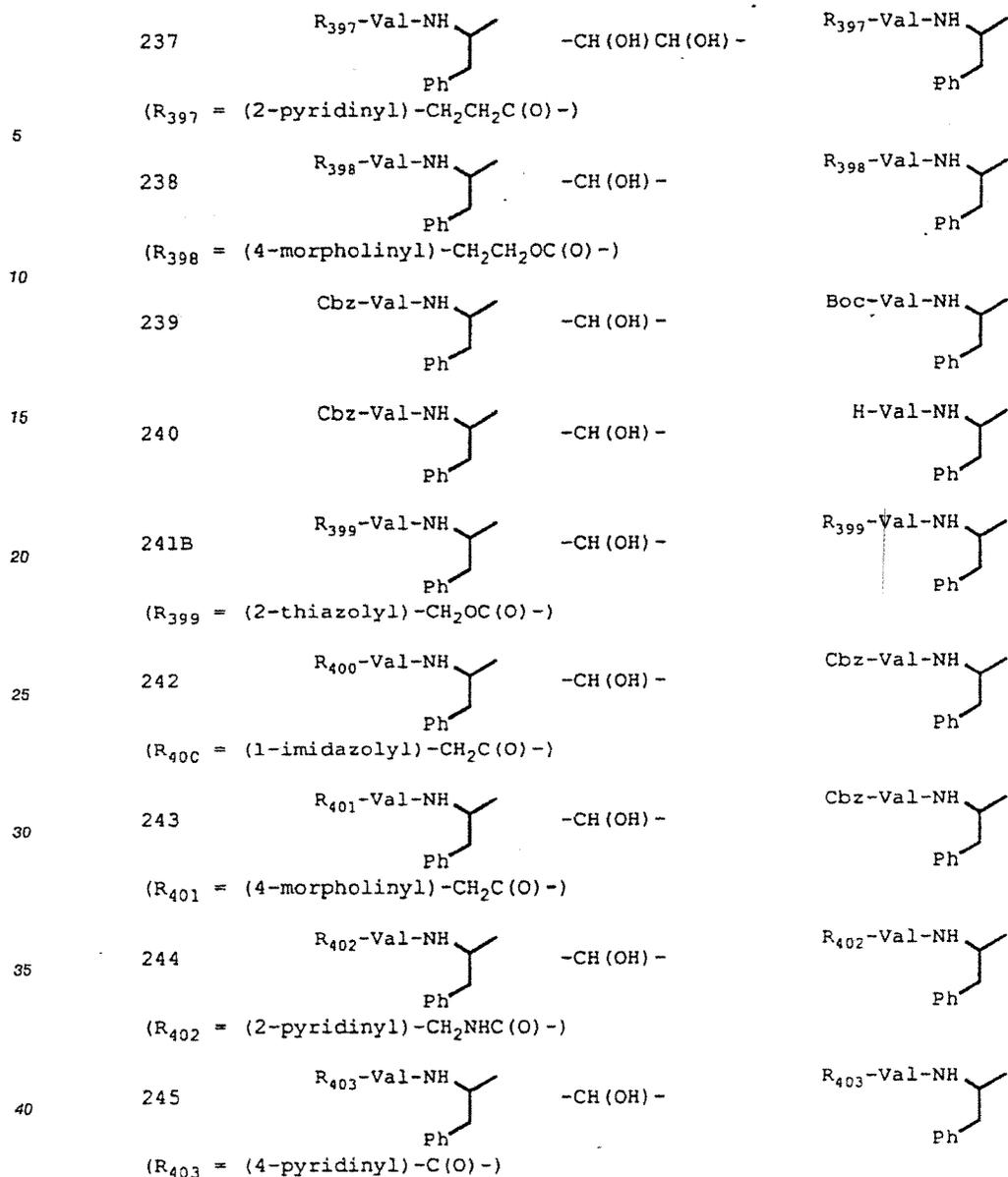


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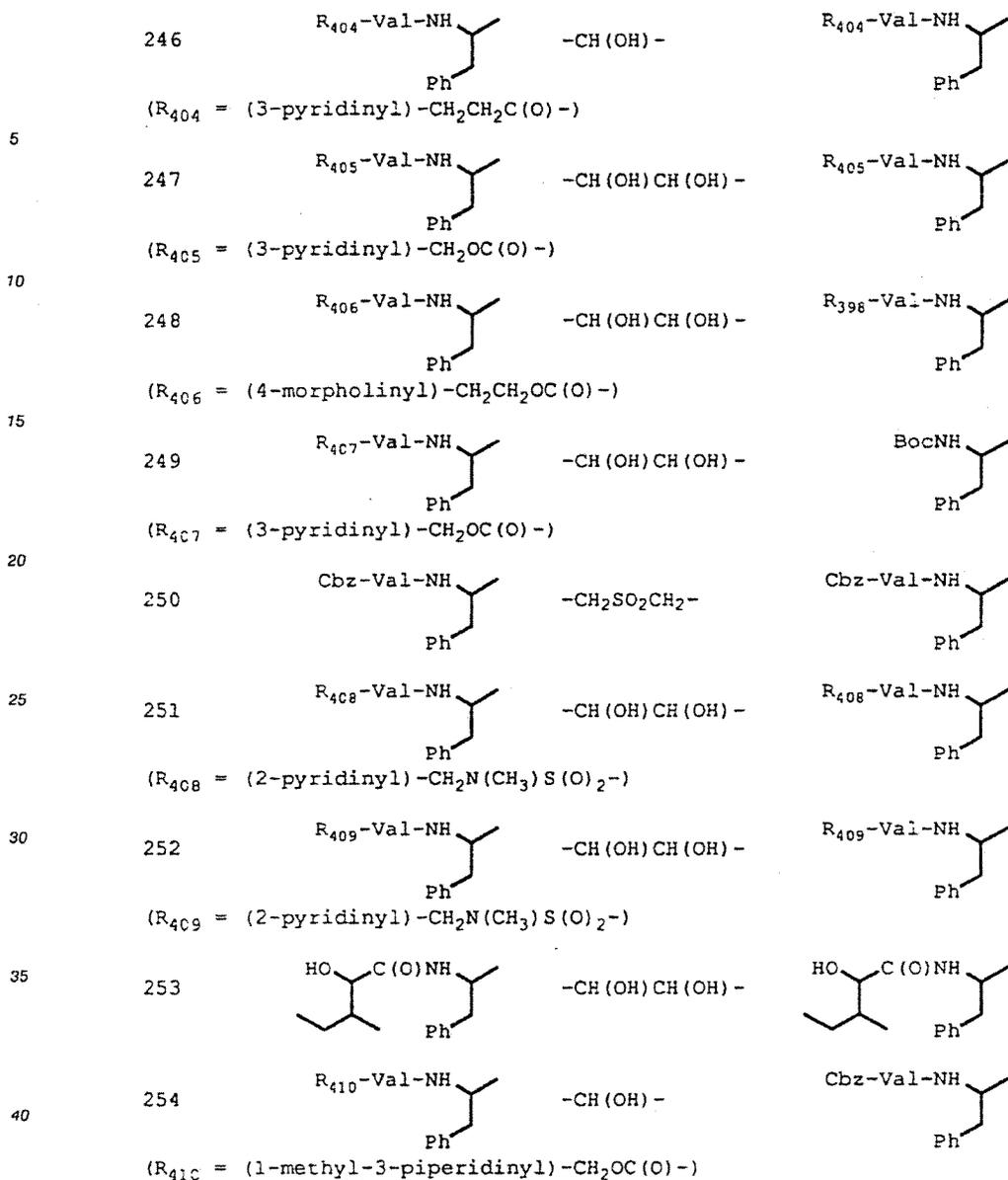


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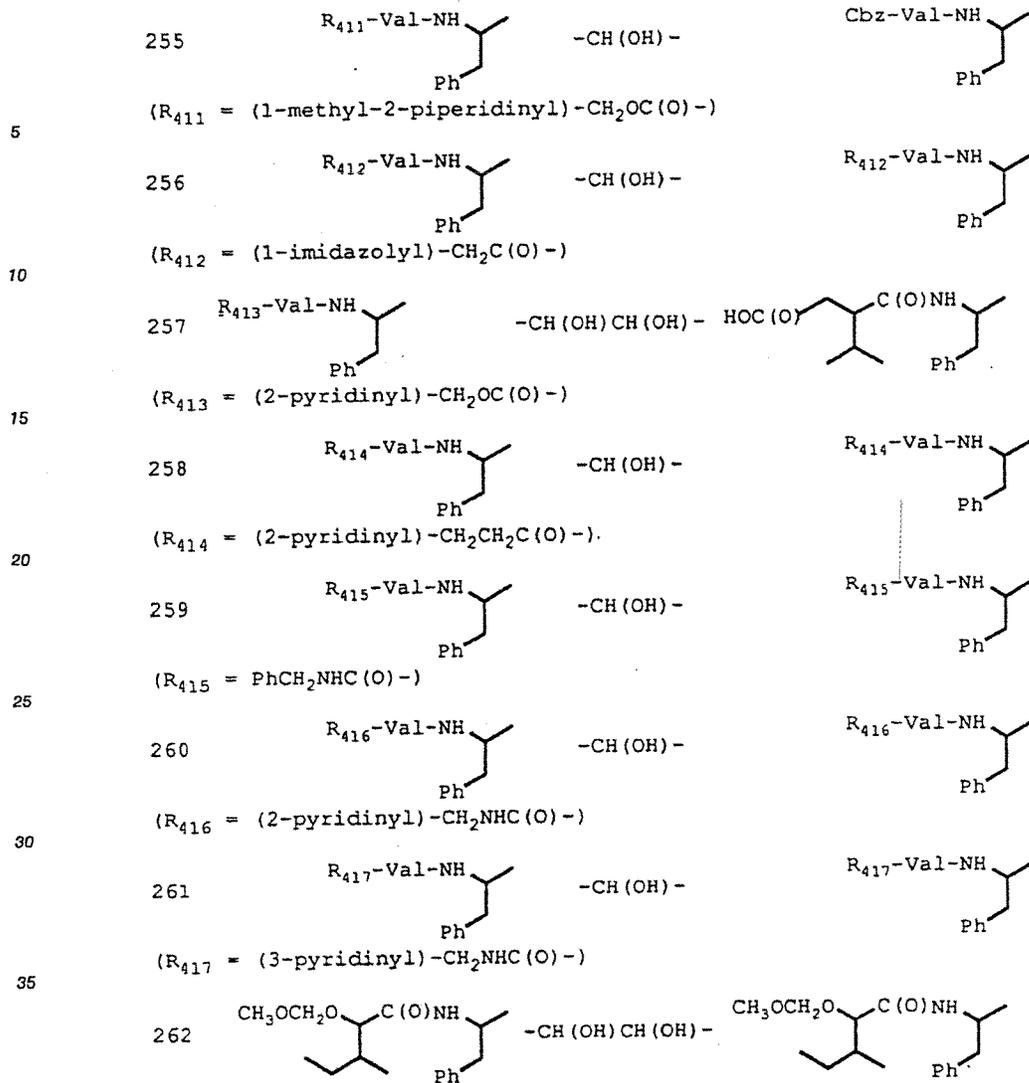


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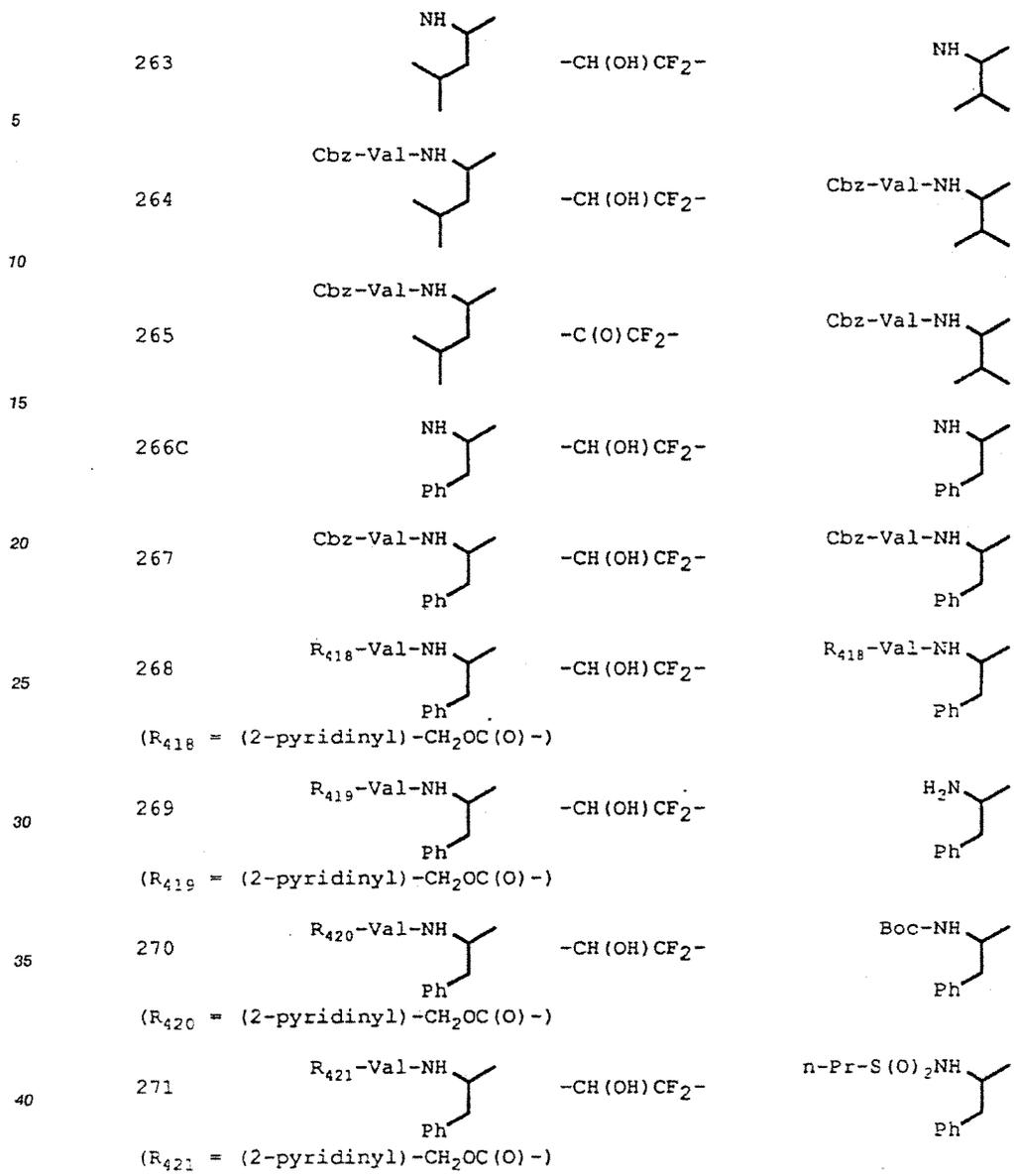
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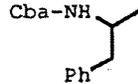
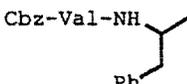
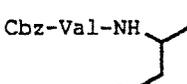
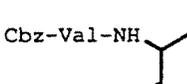
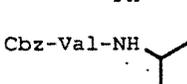
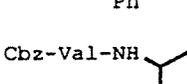
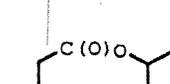
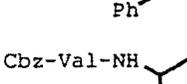
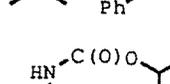
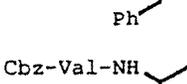
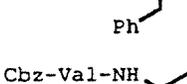
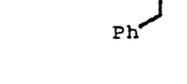
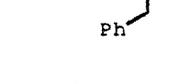
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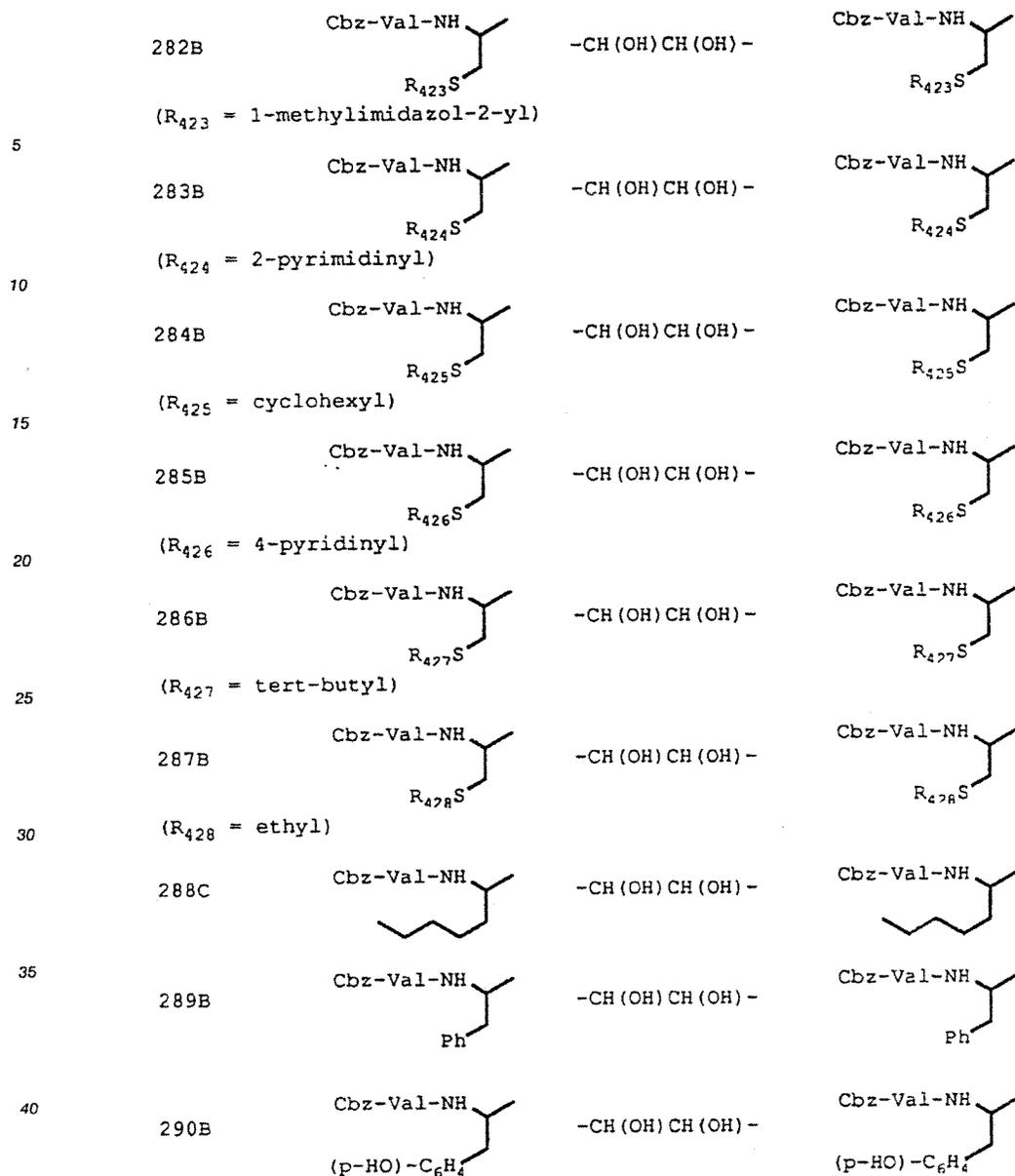


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5	272B		-CH(OH)CF ₂ -	
10	273		-CH(OH)CF ₂ -	
15	274		-CH(OH)CF ₂ -	
20	275D		-CH(OH)CF ₂ -	PhCH ₂ CH ₂ -
25	276		-C(O)CF ₂ -	PhCH ₂ CH ₂ -
30	277		-CH(OH)CF ₂ -	
35	278		-CH(OH)CF ₂ -	
40	279		-CH(OH)CF ₂ -	
45	280		-C(O)CF ₂ -	
50	281B		-CH(OH)CH(OH)-	
55	(R ₄₂₂ = 2-pyridinyl)			

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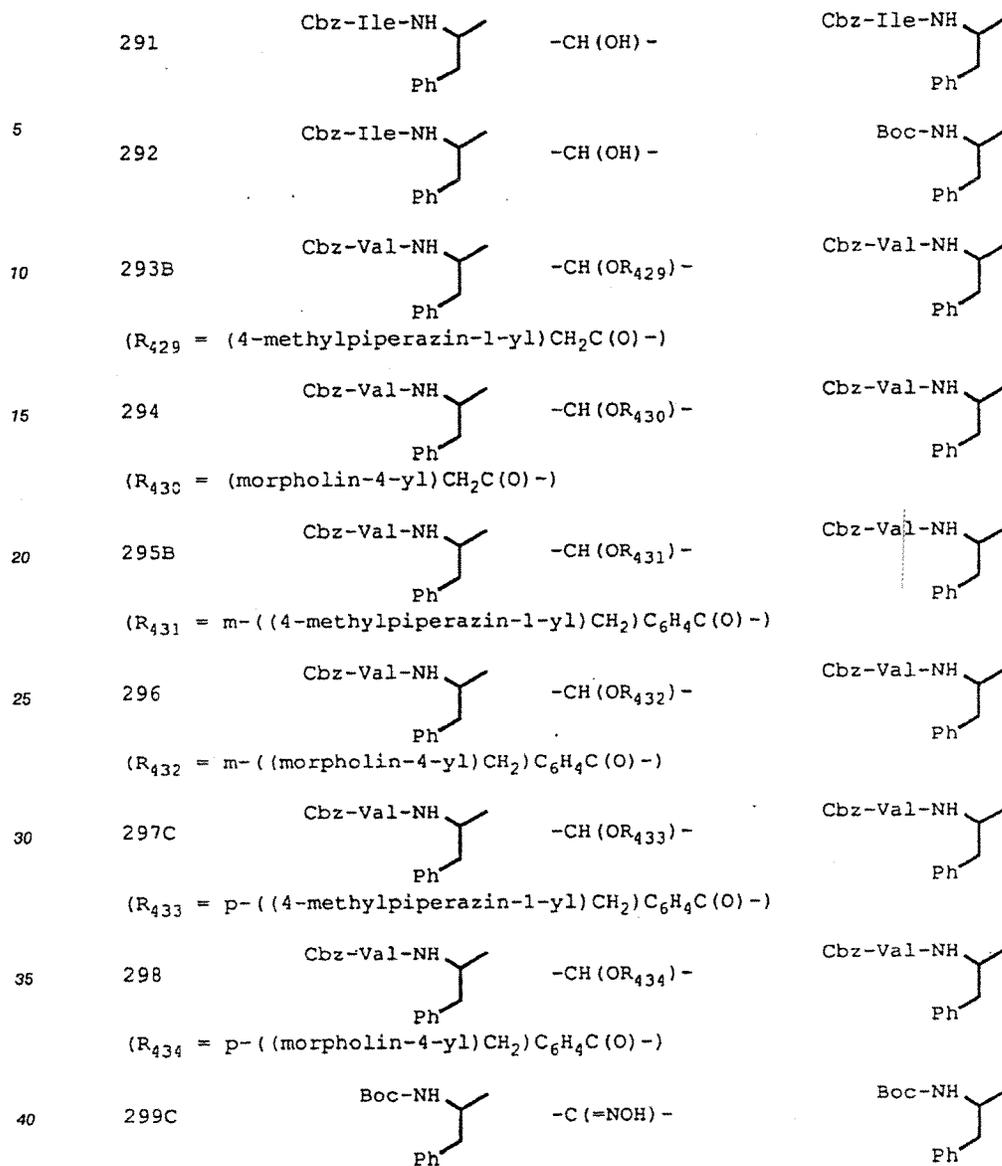


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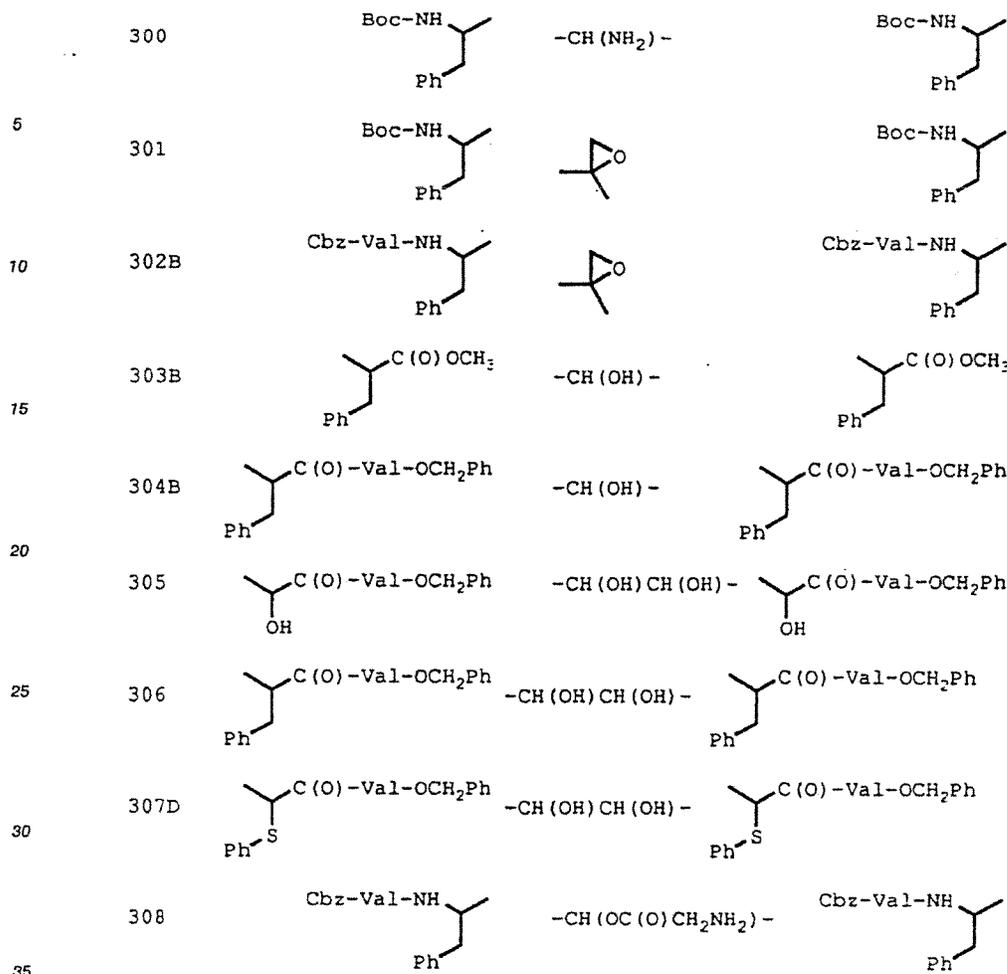


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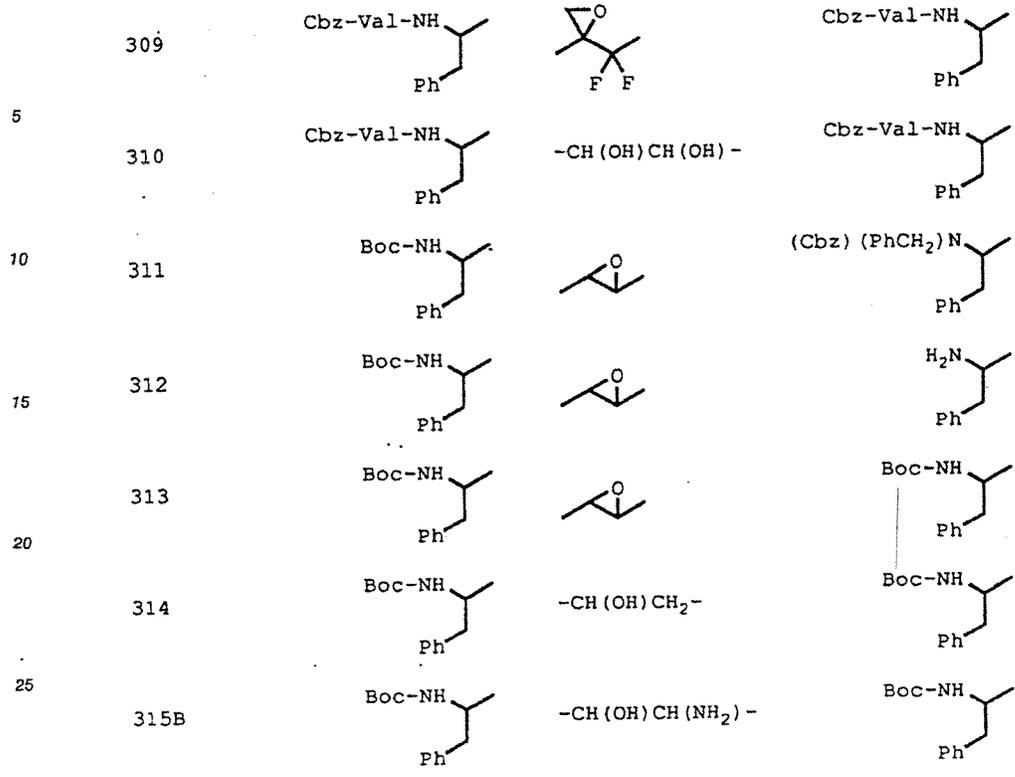
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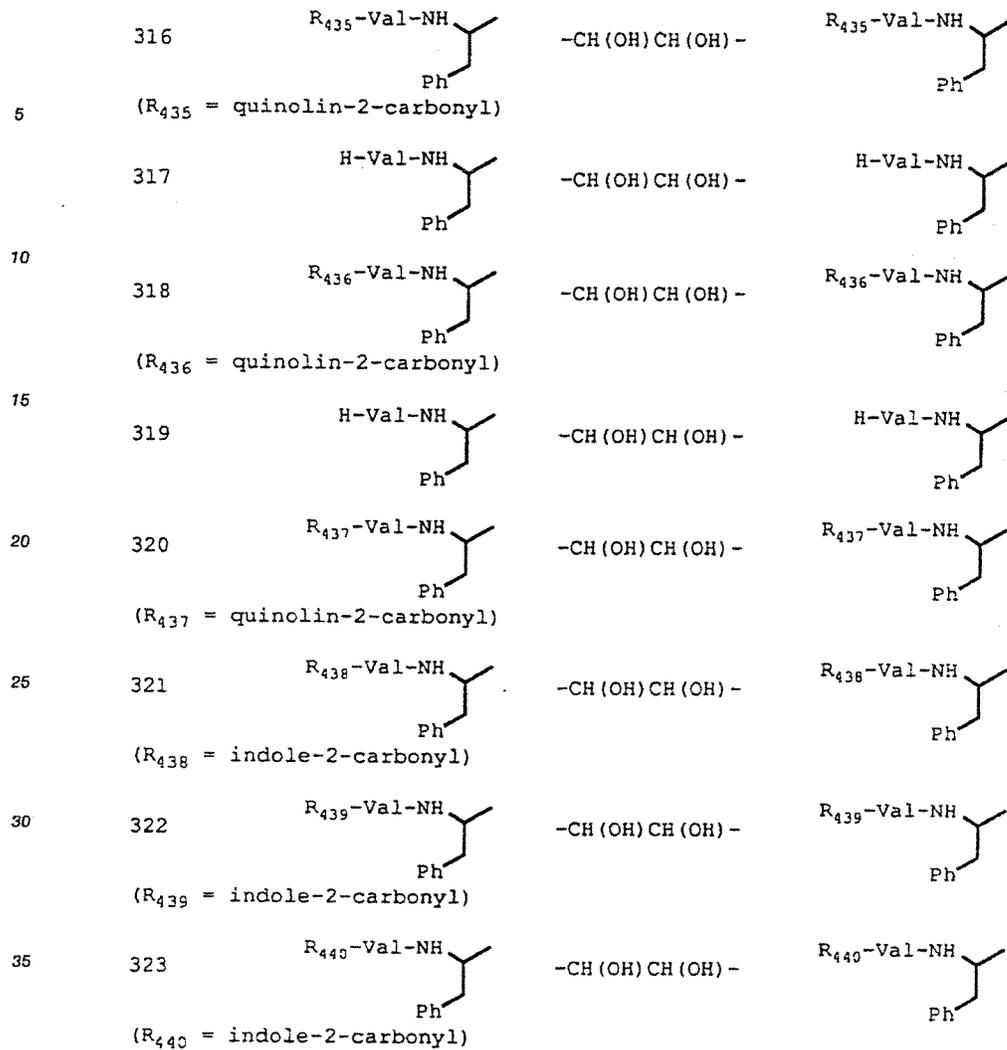


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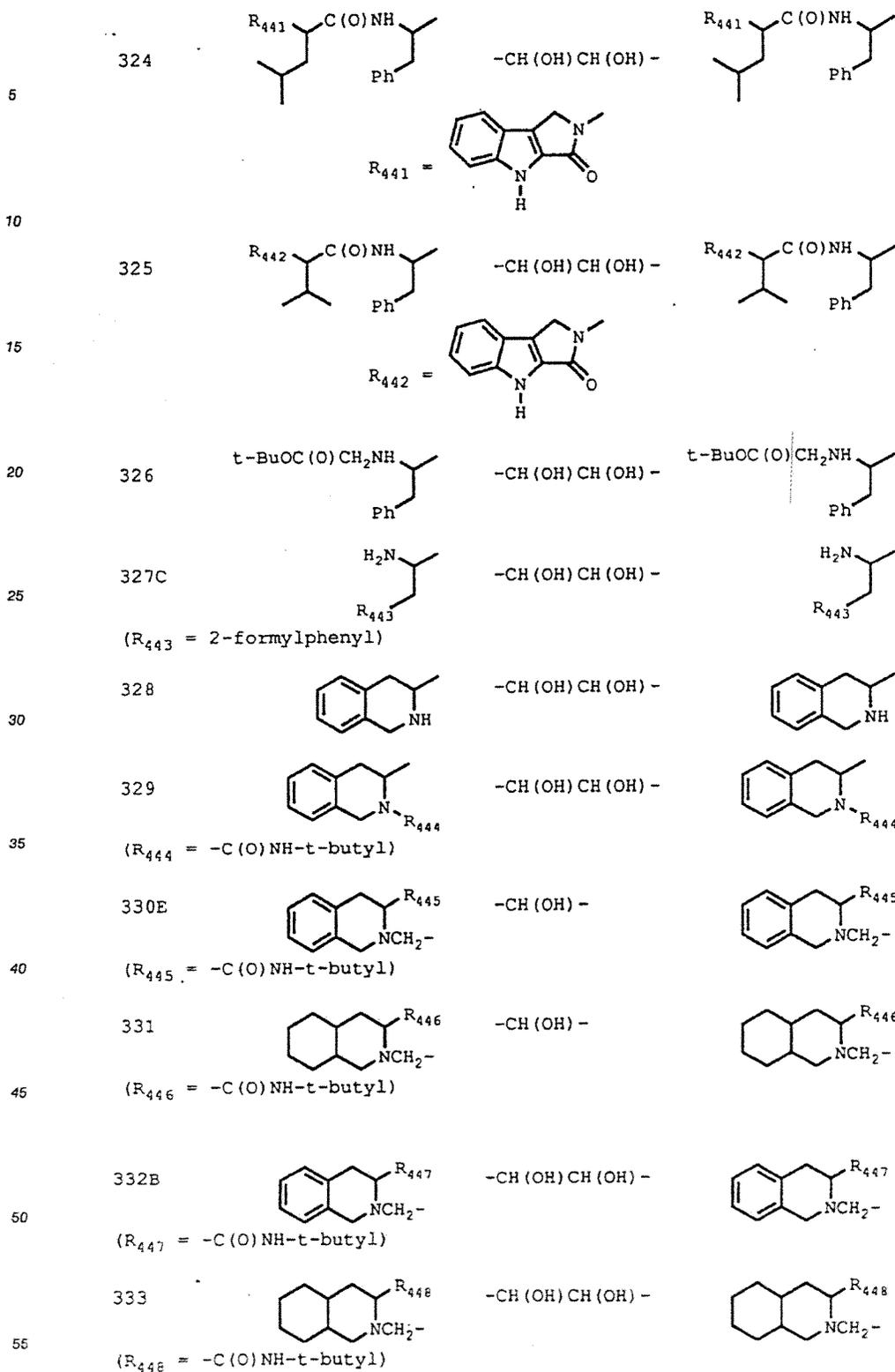
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The compounds of the invention can be prepared as shown in Schemes 1-13. The syntheses of segments (II), (III), (IV), and (V) are described in the Examples. The process shown in Scheme 1 discloses the condensation of carboxylic or sulfonic acid G - OH to segments (II) and (III) in the presence of a coupling reagent to give (VI) and (VII), respectively. The process shown in Scheme 1 also discloses the condensation of segments (IV) and (V) to NR₁₅R₁₆ in the presence of a coupling reagent to give (VIII) and (IX), respectively. Coupling reagents known in the art which can be used include, but are not limited to, dicyclohexylcarbodiimide (DCC), 3-ethyl-3'-(dimethylamino)propylcarbodiimide (EDC), bis(2-oxo-3-oxazolidinyl)-phosphinic chloride (BOP-Cl), diphenylphosphoryl azide (DPPA) and the like.

In addition to the use of the carboxylic acids or sulfonic acids shown in the scheme, acid halide and other activated ester derivatives of the carboxylic acid or sulfonic acid are useful for the coupling reactions with (II), (III), and HNR₁₅R₁₆. Acid halide derivatives include the acid chloride. Activated ester derivatives include activated esters commonly used by those skilled in the art for activating carboxylic acid groups for coupling with an amine to form an amide bond or for coupling with an alcohol to form an ester bond including, but not limited to, formic and acetic acid derived anhydrides, anhydrides derived from alkoxy-carbonyl halides such as isobutyloxycarbonylchloride and the like, N-hydroxysuccinimide derived esters, N-hydroxyphthalimide derived esters, N-hydroxybenzotriazole derived esters, N-hydroxy-5-norbornene-2,3-dicarboxamide derived esters, 2,4,5-trichlorophenol derived esters and the like.

The compounds of the invention having a fluorinated X group can be prepared as shown in the synthetic Scheme 2. The process shown in the synthetic scheme shows the preparation of the key intermediate XV. The synthesis starts with a protected amino alcohol X, which was oxidized by Swern oxidation to the corresponding aldehyde XI. Reformatsky reaction with ethyl bromodifluoroacetate provided XII. Deprotection of XII, followed by treatment with phosgene gave XIII which upon hydrolysis of the ester and treatment with an organometallic such as an alkyl lithium or alkyl Grignard provided compound XIV. Oxime formation from XIV and hydrogenation, followed by basic hydrolysis of the oxazolidinone ring gave the key intermediate XV. Coupling of protected amino acid, or amino acid derivatives or peptidyl fragments J to the intermediate XV provides the compounds of the invention XVI. Oxidation of XVI provided the compounds of the invention XVII.

Compounds of the invention wherein X is -CH(OR₂₀₁)- can be prepared as shown in Scheme 3. The process shown in Scheme 3 discloses the reduction and subsequent addition of vinylmagnesium bromide to protected aminoester XVIII. The resulting allylic alcohol XIX is mesylated to provide XX, which is treated with a Grignard reagent and catalytic CuCN to provide olefin XXI. Epoxidation of XXI leads to XXII which is regioselectively opened with azide anion to provide XXIII. Reduction of the azide gives XXIV and deprotection provides XXV, both of which can be coupled according to Scheme 1 to provide compounds of the invention.

Compounds of the invention wherein X is -CH(OR₂₀₁)-CH(OR₂₀₂)- can be prepared as shown in Scheme 4. The process shown in Scheme 4 discloses the oxidation of XXVI to protected aminoaldehyde XXVII. Reductive dimerization of XXVII provides the doubly protected diaminodiol XXVIII, which is deprotected to give diaminodiol XXIX. Coupling of XXIX according to Scheme 1 provides compounds of the invention.

Compounds of the invention of the type XXXII, in which d=0 or 1 and R₃ and R₅₀₀ are as defined above, may be prepared as outlined in Scheme 5. Thus the known aziridine XXX (Y. L. Merrer, et al *Heterocycles*, 1987, 25, 541-548) is acylated (e.g. with G=Cbz-valine), sulfonated (e.g. with G=p-toluene sulfonic acid), or phosphorylated (e.g. with G=diphenylphosphinic acid), to provide compounds of the formula XXXI. These compounds are in turn treated with various nucleophiles, such as thiols, alcohols, amines, or organometallic reagents, which serve to open the aziridine ring. The acetonide can be removed by acid hydrolysis. When G is a sulfonic acid residue, e.g. p-toluenesulfonyl, this group may be removed reductively, for example, with sodium in liquid ammonia or with sodium naphthalenide, to provide compounds of the formula XXXII wherein G is hydrogen. These compounds, in turn, can be N-acylated with protected amino acids, e.g. Cbz-valine, to provide additional compounds of the formula XXXII.

As outlined in Scheme 6, compounds of the invention of the formula XXXVI and XXXVII may be prepared by acylation of XXXIII with bromoacetyl bromide, followed by displacement of the bromide with various amine nucleophiles. R₈₀₀ and R₈₀₁ may be selected independently from hydrogen and alkyl, or may constitute a heterocyclic ring incorporating the nitrogen to which they are appended, e.g., rings such as morpholine, piperidine, and piperazine. Compounds of the invention of formula XL and XLI may be prepared by acylation of XXXIII with (chloromethyl)benzoyl chloride, followed by displacement of the benzylic chloride group with various amine nucleophiles.

As outlined in Scheme 7, compounds of the invention of formula XLV and XLVI, and L and LI, are prepared in analogous fashion from compounds XLII and XLVII.

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As outlined in Scheme 8, compounds of the invention of the formula LIII are prepared from compounds of the formula LII by treatment with diazomethane. Compounds of the formula LIV may be oxidized to ketones of the formula LV by treatment with the oxalyl chloride/DMSO reagent followed by treatment with triethylamine. Ketones of the formula LV may be converted to epoxides of the formula LVI by treatment with diazomethane.

As outlined in Scheme 9, the compound of the formula LVII (C. H. Chen, et al, *J. Org. Chem.*, 1981, 46, 2752-2757) is converted to the compound of the formula LVIII by hydrogenation, reduction with sodium borohydride, followed by saponification of the ester to provide the diacid. This compound is in turn, coupled with various amino acid esters or amides to provide compounds of the formula LIX, wherein R_{803} may be NH or O, and R_3 is as defined above.

As outlined in Scheme 10, compounds of the formula LX (W.N. Haworth, et al, *J. Chem. Soc.*, 1944, 217.) are treated with amino acid esters or amides, followed by acetone with an acid catalyst, followed by triflic anhydride to provide compounds of the formula LXI, wherein R_{803} may be NH or O, and R_3 is as defined above. These compounds are in turn treated with various alcohol, thiol, or amine nucleophiles, followed by acid catalyzed hydrolysis of the acetone, to provide compounds of the formula LXII, wherein R_{803} may be NH or O, and R_3 and R_{500} are as defined above.

As outlined in Scheme 11, the diepoxide LXIII (R.S. Tipson, et al, *Carbohydrate Research*, 1968, 7, 232-243.) is converted to the diester of the formula LXIV by oxidation, first with the DMSO/oxalyl chloride/triethylamine reagent (Swern reagent) to the dialdehyde, and then with bromine in methanol/aqueous sodium bicarbonate. This compound is in turn treated with various alcohol, thiol, or amine nucleophiles, or with organometallic nucleophiles, followed by protection of the alcohols with a protecting group P' , to provide compounds of the formula LXV, wherein $d = 0$ or 1 , and R_{500} and R_3 are as defined above. Saponification of LXV followed by coupling with various amino acid esters or amides and deprotection of the alcohol protecting groups provides compounds of the formula LXVI, wherein R_{803} may be NH or O, $d = 0$ or 1 , and R_{500} and R_3 are as defined above.

As outlined in Scheme 12, the compound of the formula LXIII may be oxidized with the Swern reagent in a solvent like THF, and without isolation, treated with an organometallic reagent, such as a Grignard reagent, to provide compounds of the formula LXVII. These compounds, may in turn, be converted to the carbamates LXVIII with an isocyanate, wherein R_{804} is hydrogen or benzyl or substituted benzyl. These carbamates may then be treated with a strong base such as potassium t-butoxide or sodium hydride in a suitable solvent such as THF, and the resulting cyclic carbamates treated with hydrogen over a palladium catalyst to provide compounds of the formula LXIX.

As outlined in Scheme 13, compounds of the formula LV may be converted to the oxime LXX with hydroxylamine hydrochloride in the presence of pyridine. These compounds may then be reduced with hydrogen over a catalyst to provide compounds of the formula LXXI.

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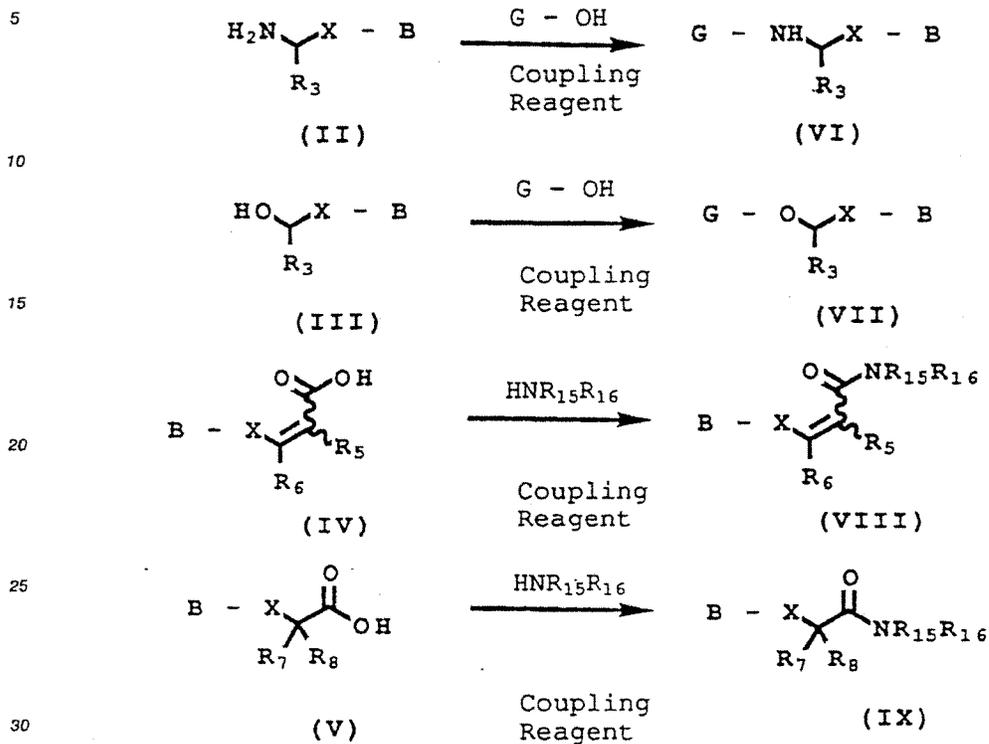
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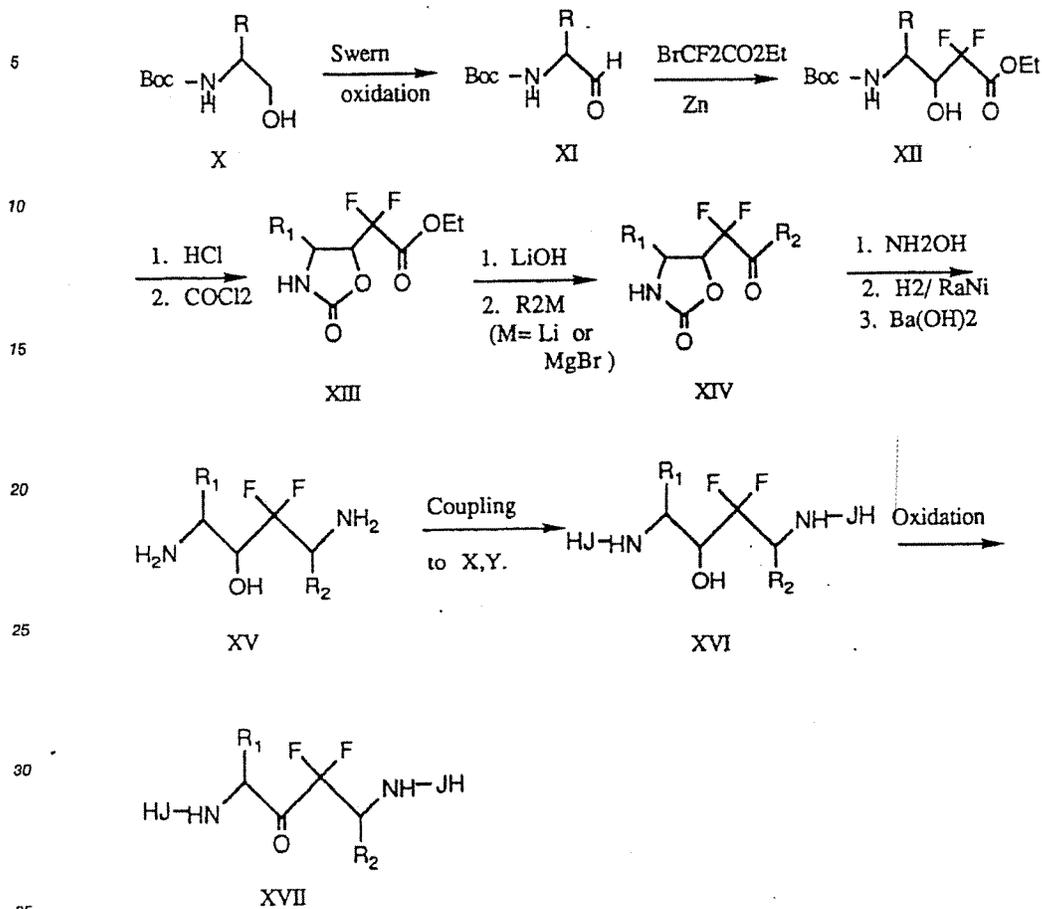
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Scheme 1



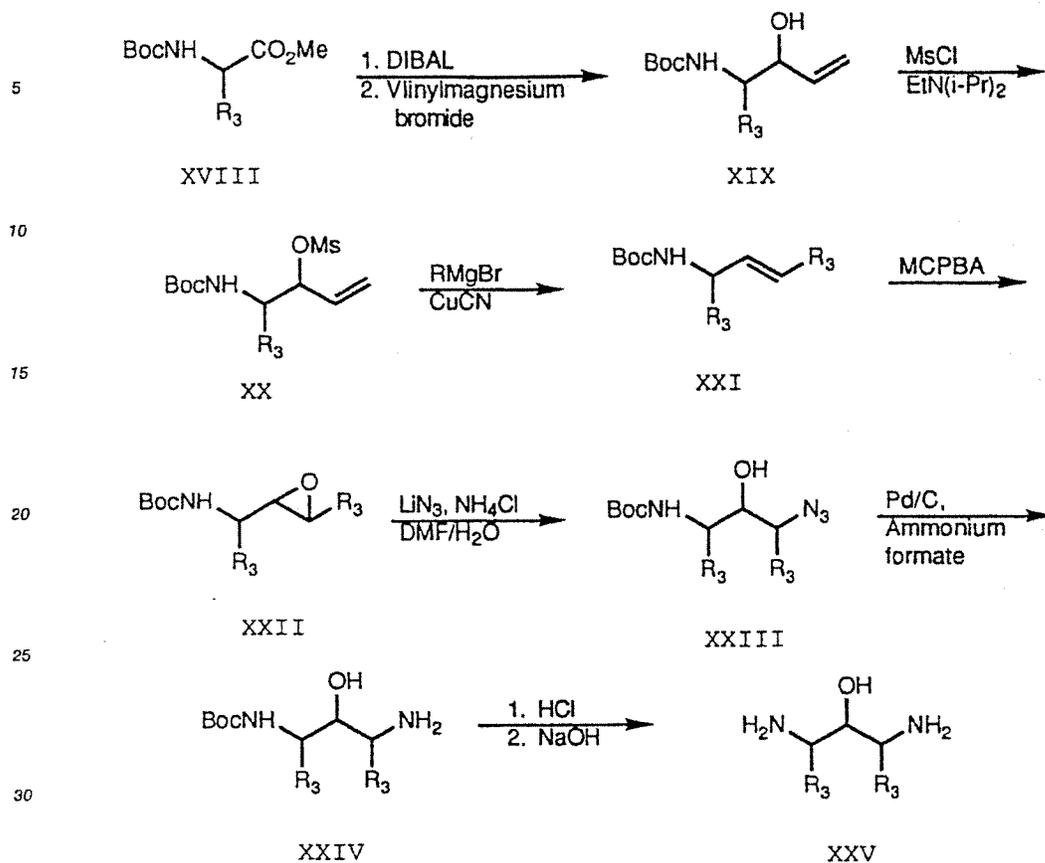
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Scheme 2



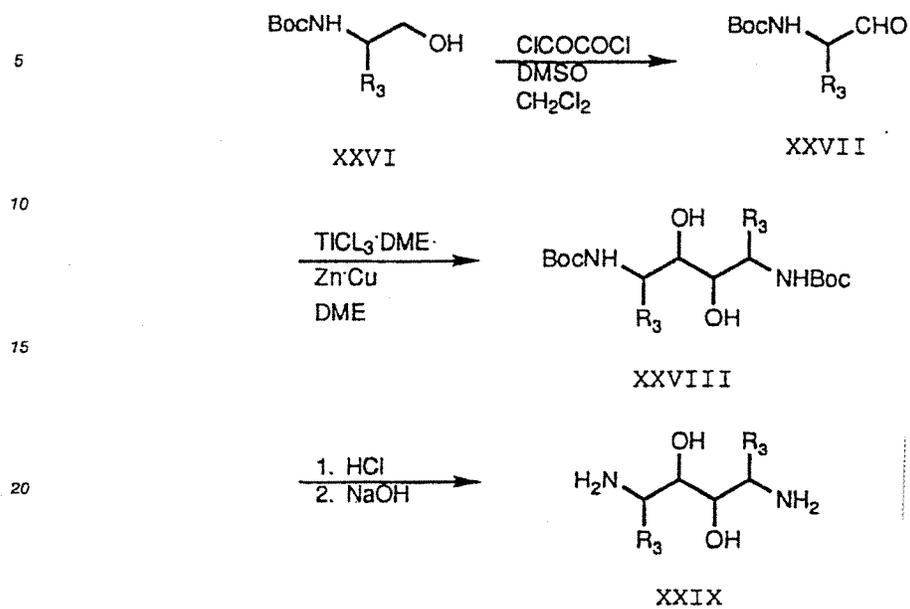
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Scheme 3

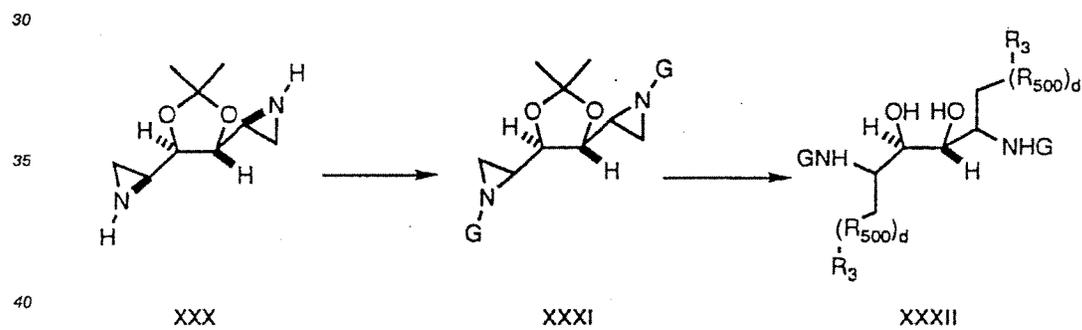


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Scheme 4

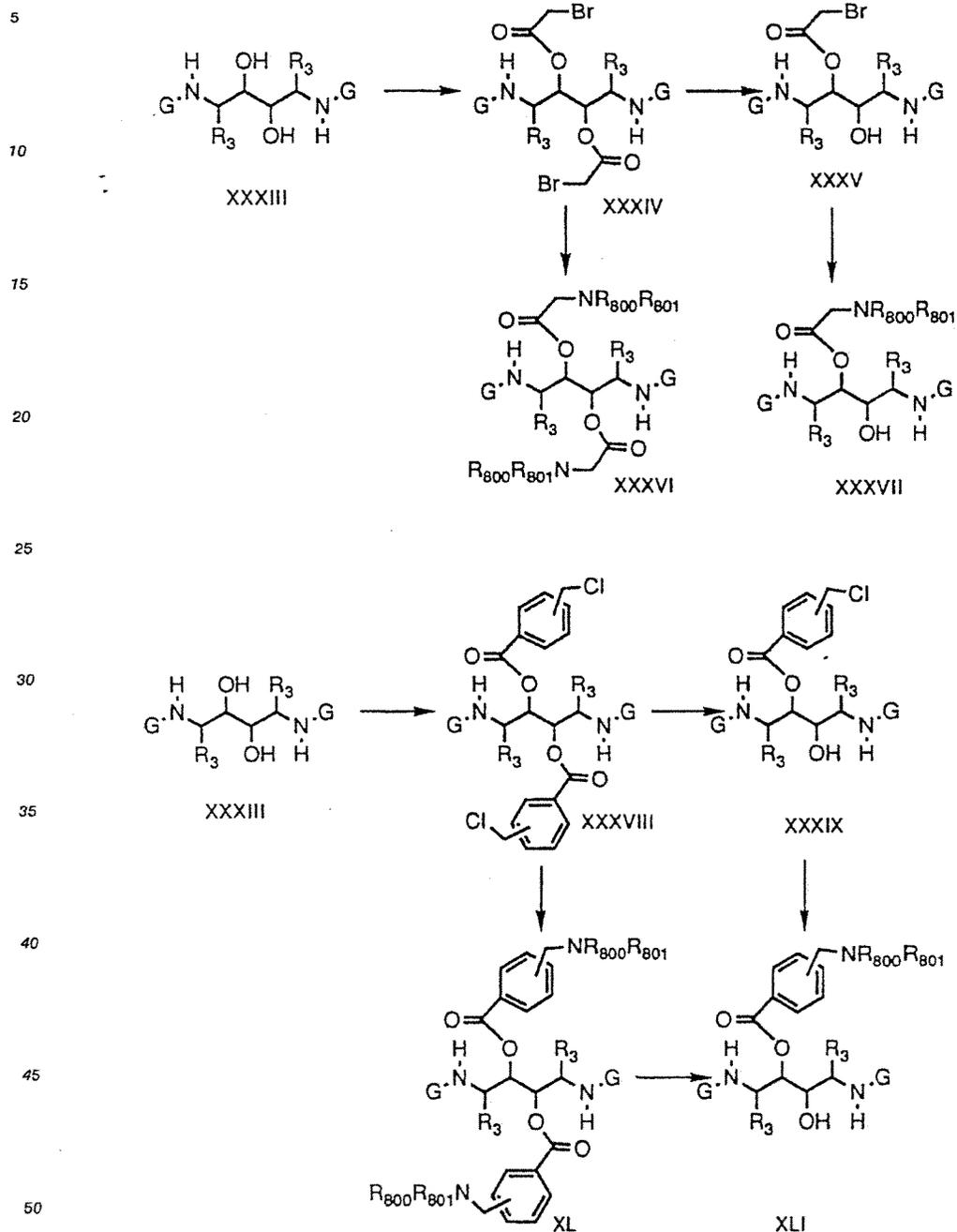


SCHEME 5



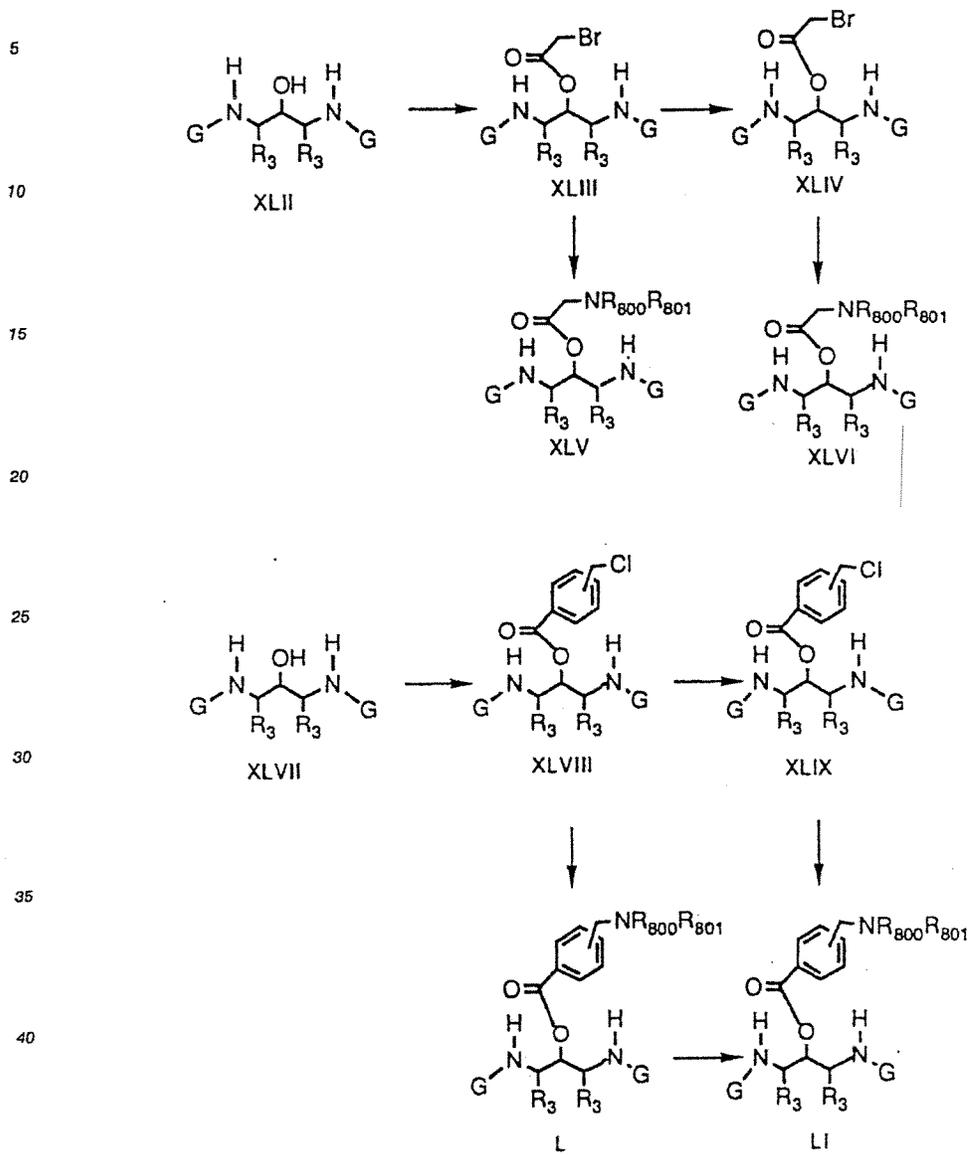
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SCHEME 6



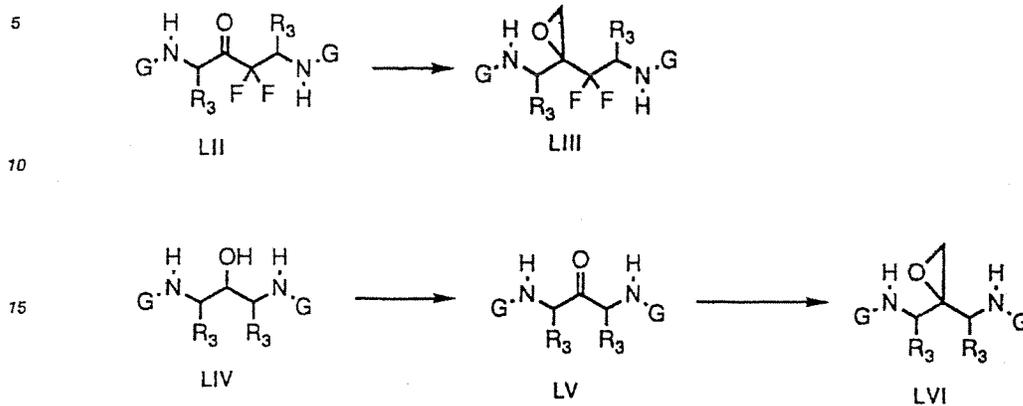
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SCHEME 7



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SCHEME 8



SCHEME 9

