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[54] **4-AMINO SUBSTITUTED-2-SUBSTITUTED-1, 2,3,4-TETRAHYDROQUINOLINES**

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Related U.S. Application Data

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[51] **Int. Cl.**[7] **A61K 31/47**; C07D 215/38

[52] **U.S. Cl.** **514/313**; 546/159

[58] **Field of Search** 546/159; 514/313

[56] **References Cited**

U.S. PATENT DOCUMENTS

5,231,101	7/1993	Honda et al.	514/290
5,231,102	7/1993	Baker et al. .	
5,288,725	2/1994	Witherup et al. .	

FOREIGN PATENT DOCUMENTS

0818448	1/1998	European Pat. Off. .

OTHER PUBLICATIONS

Gordon DJ, et al., Circulation. 79(1):8–15, Jan. 1989, "High–density lipoprotein cholesterol and cardiovascular disease. Four prospective American studies".

Chemical Abstracts vol. 116, 1992, 116:151569g.

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[57] **ABSTRACT**

Cholesteryl ester transfer protein inhibitors, pharmaceutical compositions containing such inhibitors and the use of such inhibitors to elevate certain plasma lipid levels, including high density lipoprotein-cholesterol and to lower certain other plasma lipid levels, such as LDL-cholesterol and triglycerides and accordingly to treat diseases which are exacerbated by low levels of HDL cholesterol and/or high levels of LDL-cholesterol and triglycerides, such as atherosclerosis and cardiovascular diseases in some mammals, including humans.

44 Claims, No Drawings

4-AMINO SUBSTITUTED-2-SUBSTITUTED-1, 2,3,4-TETRAHYDROQUINOLINES

This application claims priority from provisional application U.S. Ser. No. 60/100,927 filed Sep. 17, 1998, the benefit of which is hereby claimed under 37 C.F.R. §1.78 (a)(3).

BACKGROUND OF INVENTION

This invention relates to cholesteryl ester transfer protein (CETP) inhibitors, pharmaceutical compositions containing such inhibitors and the use of such inhibitors to elevate certain plasma lipid levels, including high density lipoprotein (HDL)-cholesterol and to lower certain other plasma lipid levels, such as low density lipoprotein (LDL)-cholesterol and triglycerides and accordingly to treat diseases which are affected by low levels of HDL cholesterol and/or high levels of LDL-cholesterol and triglycerides, such as atherosclerosis and cardiovascular diseases in certain mammals (i.e., those which have CETP in their plasma), including humans.

Atherosclerosis and its associated coronary artery disease (CAD) is the leading cause of mortality in the industrialized world. Despite attempts to modify secondary risk factors (smoking, obesity, lack of exercise) and treatment of dyslipidemia with dietary modification and drug therapy, coronary heart disease (CHD) remains the most common cause of death in the U.S., where cardiovascular disease accounts for 44% of all deaths, with 53% of these associated with atherosclerotic coronary heart disease.

Risk for development of this condition has been shown to be strongly correlated with certain plasma lipid levels. While elevated LDL-C may be the most recognized form of dyslipidemia, it is by no means the only significant lipid associated contributor to CHD. Low HDL-C is also a known risk factor for CHD (Gordon, D. J., et al.,: "High-density Lipoprotein Cholesterol and Cardiovascular Disease", Circulation, (1989), 79: 8–15).

High LDL-cholesterol and triglyceride levels are positively correlated, while high levels of HDL-cholesterol are negatively correlated with the risk for developing cardiovascular diseases. Thus, dyslipidemia is not a unitary risk profile for CHD but may be comprised of one or more lipid aberrations.

Among the many factors controlling plasma levels of these disease dependent principles, cholesteryl ester transfer protein (CETP) activity affects all three. The role of this 70,000 dalton plasma glycoprotein found in a number of animal species, including humans, is to transfer cholesteryl ester and triglyceride between lipoprotein particles, including high density lipoproteins (HDL), low density lipoproteins (LDL), very low density lipoproteins (VLDL), and chylomicrons. The net result of CETP activity is a lowering of HDL cholesterol and an increase in LDL cholesterol. This effect on lipoprotein profile is believed to be pro-atherogenic, especially in subjects whose lipid profile constitutes an increased risk for CHD.

No wholly satisfactory HDL-elevating therapies exist. Niacin can significantly increase HDL, but has serious toleration issues which reduce compliance. Fibrates and the HMG CoA reductase inhibitors raise HDL-C only modestly (~10–12%). As a result, there is a significant unmet medical need for a well-tolerated agent which can significantly elevate plasma HDL levels, thereby reversing or slowing the progression of atherosclerosis.

Thus, although there are a variety of anti-atherosclerosis therapies, there is a continuing need and a continuing search in this field of art for alternative therapies.

EP0818448 (970624) discloses the preparation of certain 5,6,7,8 substituted tetrahydroquinolines and analogs as cholesteryl ester transfer protein inhibitors.

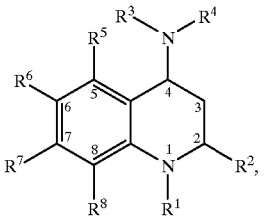
U.S. Pat. No. 5,231,102 discloses a class of 4-substituted 1,2,3,4-tetrahydroquinolines that possess an acidic group (or group convertible thereto in vivo) at the 2-position that are specific antagonists of N-methyl-D-aspartate (NMDA) receptors and are therefore useful in the treatment and/or prevention of neurodegenerative disorders.

U.S. Pat. No. 5,288,725 discloses pyrroloquinoline bradykinin antagonists.

SUMMARY OF THE INVENTION

This invention is directed to compounds of Formula I

Formula I



prodrugs thereof, and pharmaceutically acceptable salts of said compounds and of said prodrugs;

wherein R^1 is Y, W-X or W-Y;

wherein W is a carbonyl, thiocarbonyl, sulfinyl or sulfonyl;

X is —O-Y, —S-Y, —N(H)-Y or —N-(Y);

wherein Y for each occurrence is independently Z or a fully saturated, partially unsaturated or fully unsaturated one to ten membered straight or branched carbon chain wherein the carbons, other than the connecting carbon, may optionally be replaced with one or two heteroatoms selected independently from oxygen, sulfur and nitrogen and said carbon is optionally mono-, di- or tri-substituted independently with halo, said carbon is optionally mono-substituted with hydroxy, said carbon is optionally mono-substituted with oxo, said sulfur is optionally mono- or di-substituted with oxo, said nitrogen is optionally mono-, or di-substituted with oxo, and said carbon chain is optionally mono-substituted with Z;

wherein Z is a partially saturated, fully saturated or fully unsaturated three to eight membered ring optionally having one to four heteroatoms selected independently from oxygen, sulfur and nitrogen, or a bicyclic ring consisting of two fused partially saturated, fully saturated or fully unsaturated three to six membered rings, taken independently, optionally having one to four heteroatoms selected independently from nitrogen, sulfur and oxygen;

wherein said Z substituent is optionally mono-, di- or tri-substituted independently with halo, (C_2–C_6) alkenyl, (C_1–C_6) alkyl, hydroxy, (C_1–C_6)alkoxy, (C_1–C_4)alkylthio, amino, nitro, cyano, oxo, carboxy, (C_1–C_6)alkyloxycarbonyl, mono-N- or di-N,N-(C_1–C_6)alkylamino wherein said (C_1–C_6) alkyl substituent is optionally mono-, di- or tri-substituted independently with halo, hydroxy, (C_1–C_6)alkoxy, (C_1–C_4)alkylthio, amino, nitro, cyano, oxo, carboxy, (C_1–C_6)alkyloxycarbonyl, mono-N- or di-N,N-(C_1–C_6)alkylamino, said

(C_1–C_6)alkyl substituent is also optionally substituted with from one to nine fluorines;

R^2 is a partially saturated, fully saturated or fully unsaturated one to six membered straight or branched carbon chain wherein the carbons, other than the connecting carbon, may optionally be replaced with one or two heteroatoms selected independently from oxygen, sulfur and nitrogen wherein said carbon atoms are optionally mono-, di- or tri-substituted independently with halo, said carbon is optionally mono-substituted with oxo, said carbon is optionally mono-substituted with hydroxy, said sulfur is optionally mono- or di-substituted with oxo, said nitrogen is optionally mono- or di-substituted with oxo; or said R^2 is a partially saturated, fully saturated or fully unsaturated three to seven membered ring optionally having one to two heteroatoms selected independently from oxygen, sulfur and nitrogen, wherein said R^2 ring is optionally attached through (C_1–C_4)alkyl;

wherein said R^2 ring is optionally mono-, di- or tri-substituted independently with halo, (C_2–C_6) alkenyl, (C_1–C_6) alkyl, hydroxy, (C_1–C_6)alkoxy, (C_1–C_4)alkylthio, amino, nitro, cyano, oxo, carboxy, (C_1–C_6)alkyloxycarbonyl, mono-N- or di-N,N-(C_1–C_6)alkylamino wherein said (C_1–C_6)alkyl substituent is optionally mono-, di- or tri-substituted independently with halo, hydroxy, (C_1–C_6)alkoxy, (C_1–C_4)alkylthio, oxo or (C_1–C_6)alkyloxycarbonyl;

R^3 is hydrogen or Q;

wherein Q is a fully saturated, partially unsaturated or fully unsaturated one to six membered straight or branched carbon chain wherein the carbons, other than the connecting carbon, may optionally be replaced with one heteroatom selected from oxygen, sulfur and nitrogen and said carbon is optionally mono-, di- or tri-substituted independently with halo, said carbon is optionally mono-substituted with hydroxy, said carbon is optionally mono-substituted with oxo, said sulfur is optionally mono- or di-substituted with oxo, said nitrogen is optionally mono-, or di-substituted with oxo, and said carbon chain is optionally mono-substituted with V;

wherein V is a partially saturated, fully saturated or fully unsaturated three to eight membered ring optionally having one to four heteroatoms selected independently from oxygen, sulfur and nitrogen, or a bicyclic ring consisting of two fused partially saturated, fully saturated or fully unsaturated three to six membered rings, taken independently, optionally having one to four heteroatoms selected independently from nitrogen, sulfur and oxygen;

wherein said V substituent is optionally mono-, di-, tri-, or tetra-substituted independently with halo, (C_1–C_6)alkyl, (C_2–C_6)alkenyl, hydroxy, (C_1–C_6) alkoxy, (C_1–C_4)alkylthio, amino, nitro, cyano, oxo, carboxamoyl, mono-N- or di-N,N-(C_1–C_6) alkylcarboxamoyl, carboxy, (C_1–C_6) alkyloxycarbonyl, mono-N- or di-N,N-(C_1–C_6) alkylamino wherein said (C_1–C_6)alkyl or (C_2–C_6) alkenyl substituent is optionally mono-, di- or tri-substituted independently with hydroxy, (C_1–C_6)alkoxy, (C_1–C_4)alkylthio, amino, nitro, cyano, oxo, carboxy, (C_1–C_6)alkyloxycarbonyl, mono-N- or di-N,N-(C_1–C_6)alkylamino, said (C_1–C_6)alkyl or (C_2–C_6)alkenyl substituents are also optionally substituted with from one to nine fluorines;

R^4 is cyano, formyl, W^1Q^1, W^1V^1, (C_1–C_4)alkyleneV^1 or V^2;

wherein W^1 is carbonyl, thiocarbonyl, SO or SO_2,

wherein Q^1 a fully saturated, partially unsaturated or fully unsaturated one to six membered straight or branched carbon chain wherein the carbons, may optionally be replaced with one heteroatom selected from oxygen, sulfur and nitrogen and said carbon is optionally mono-, di- or tri-substituted independently with halo, said carbon is optionally mono-substituted with hydroxy, said carbon is optionally mono-substituted with oxo, said sulfur is optionally mono- or di-substituted with oxo, said nitrogen is optionally mono-, or di-substituted with oxo, and said carbon chain is optionally mono-substituted with V^1;

wherein V^1 is a partially saturated, fully saturated or fully unsaturated three to six membered ring optionally having one to two heteroatoms selected independently from oxygen, sulfur and nitrogen, or a bicyclic ring consisting of two fused partially saturated, fully saturated or fully unsaturated three to six membered rings, taken independently, optionally having one to four heteroatoms selected independently from nitrogen, sulfur and oxygen;

wherein said V^1 substituent is optionally mono-, di-, tri-, or tetra-substituted independently with halo, (C_1–C_6)alkyl, (C_1–C_6)alkoxy, hydroxy, oxo, amino, nitro, cyano, (C_1–C_6)alkyloxycarbonyl, mono-N- or di-N,N-(C_1–C_6)alkylamino wherein said (C_1–C_6) alkyl substituent is optionally mono-substituted with oxo, said (C_1–C_6)alkyl substituent is also optionally substituted with from one to nine fluorines;

wherein V^2 is a partially saturated, fully saturated or fully unsaturated five to seven membered ring containing one to four heteroatoms selected independently from oxygen, sulfur and nitrogen;

wherein said V^2 substituent is optionally mono-, di- or tri-substituted independently with halo, (C_1–C_2) alkyl, (C_1–C_2)alkoxy, hydroxy, or oxo wherein said (C_1–C_2)alkyl optionally has from one to five fluorines;

wherein R^4 does not include oxycarbonyl linked directly to the C^4 nitrogen;

wherein either R^3 must contain V or R^4 must contain V^1; and

R^5, R^6, R^7 and R^8 are independently hydrogen, a bond, nitro or halo wherein said bond is substituted with T or a partially saturated, fully saturated or fully unsaturated (C_1–C_{12}) straight or branched carbon chain wherein carbon may optionally be replaced with one or two heteroatoms selected independently from oxygen, sulfur and nitrogen, wherein said carbon atoms are optionally mono-, di- or tri-substituted independently with halo, said carbon is optionally mono-substituted with hydroxy, said carbon is optionally mono-substituted with oxo, said sulfur is optionally mono- or di-substituted with oxo, said nitrogen is optionally mono- or di-substituted with oxo, and said carbon chain is optionally mono-substituted with T;

wherein T is a partially saturated, fully saturated or fully unsaturated three to twelve membered ring optionally having one to four heteroatoms selected independently from oxygen, sulfur and nitrogen, or a bicyclic ring consisting of two fused partially saturated, fully saturated or fully unsaturated three to six membered rings, taken independently, optionally

having one to four heteroatoms selected independently from nitrogen, sulfur and oxygen;

wherein said T substituent is optionally mono-, di- or tri-substituted independently with halo, (C_1–C_6)alkyl, (C_2–C_6)alkenyl, hydroxy, (C_1–C_6)alkoxy, (C_1–C_4)alkylthio, amino, nitro, cyano, oxo, carboxy, (C_1–C_6)alkyloxycarbonyl, mono-N- or di-N,N-(C_1–C_6)alkylamino wherein said (C_1–C_6)alkyl substituent is optionally mono-, di- or tri-substituted independently with hydroxy, (C_1–C_6)alkoxy, (C_1–C_4)alkylthio, amino, nitro, cyano, oxo, carboxy, (C_1–C_6)alkyloxycarbonyl, mono-N- or di-N,N-(C_1–C_6)alkylamino, said (C_1–C_6)alkyl substituent also optionally has from one to nine fluorines;

wherein R^5 and R^6, or R^8 and R^7, and/or R^7 and R^8 may also be taken together and can form at least one ring that is a partially saturated or fully unsaturated four to eight membered ring optionally having one to three heteroatoms independently selected from nitrogen, sulfur and oxygen;

wherein said rings formed by R^5 and R^6, or R^6 and R^7, and/or R^7 and R^8 are optionally mono-, di- or tri-substituted independently with halo, (C_1–C_6)alkyl, (C_1–C_4)alkylsulfonyl, (C_2–C_6)alkenyl, hydroxy, (C_1–C_6)alkoxy, (C_1–C_4)alkylthio, amino, nitro, cyano, oxo, carboxy, (C_1–C_6)alkyloxycarbonyl, mono-N- or di-N,N-(C_1–C_6)alkylamino wherein said (C_1–C_6)alkyl substituent is optionally mono-, di- or tri-substituted independently with hydroxy, (C_1–C_6)alkoxy, (C_1–C_4)alkylthio, amino, nitro, cyano, oxo, carboxy, (C_1–C_6)alkyloxycarbonyl, mono-N- or di-N,N-(C_1–C_6)alkylamino, said (C_1–C_6)alkyl substituent also optionally has from one to nine fluorines.

A preferred group of compounds, designated the A Group, contains those compounds having the Formula I as shown above wherein

the C^2 substituent is beta;

the C^4 nitrogen is beta;

R^1 is W-X;

W is carbonyl, thiocarbonyl or sulfonyl;

X is —O-Y-, S-Y-, N(H)-Y- or —N-$(Y)_2$-;

Y for each occurrence independently is (C_1–C_4)alkyl, said (C_1–C_4)alkyl optionally having hydroxy or from one to nine fluorines or said (C_1–C_4)alkyl optionally mono-substituted with Z;

wherein Z is a partially saturated, fully saturated or fully unsaturated three to six membered ring optionally having one to two heteroatoms selected independently from oxygen, sulfur and nitrogen;

wherein said Z substituent is optionally mono-, di- or tri-substituted independently with halo, (C_1–C_4)alkyl, (C_1–C_4)alkoxy, (C_1–C_4)alkylthio, nitro, cyano, oxo, or (C_1–C_6)alkyloxycarbonyl, said (C_1–C_4)alkyl optionally substituted with from one to nine fluorines;

R^2 is a partially saturated, fully saturated or fully unsaturated (C_1–C_4) straight or branched carbon chain wherein the carbons, other than the connecting carbon, may optionally be replaced with one heteroatom selected independently from oxygen, sulfur and nitrogen wherein said carbon atoms are optionally mono-, di- or tri-substituted independently with halo, said carbon is optionally mono-substituted with oxo or hydroxy, said sulfur is optionally mono- or di-substituted with oxo, said nitrogen is optionally mono- or di-substituted with oxo; or said R^2 is a partially saturated, fully saturated or fully unsaturated three to five membered ring optionally having one heteroatom selected independently from oxygen, sulfur and nitrogen;

wherein said R^2 ring is optionally mono-, di- or tri-substituted independently with halo, hydroxy, (C_1–C_6)alkoxy, amino, nitro, (C_1–C_4) alkyloxycarbonyl or carboxy;

R^3 is Q-V wherein Q is (C_1–C_4)alkyl and V is a five or six membered partially saturated, fully saturated or fully unsaturated ring optionally having one to three heteroatoms selected independently from oxygen, sulfur and nitrogen;

wherein said V ring is optionally mono-, di-, tri- or tetra-substituted independently with halo, (C_1–C_6) alkyl, hydroxy, (C_1–C_6)alkoxy, (C_1–C_6) alkoxycarbonyl, nitro, cyano or oxo, wherein said (C_1–C_6)alkyl substituent optionally has from one to nine fluorines;

R^4 is carbonyl or carbamoyl wherein said carbonyl moiety is optionally mono-substituted with V^1 or (C_1–C_2)alkyl and said carbamoyl moiety is optionally mono- or di-substituted independently with V^1 or (C_1–C_2)alkyl, in either instance said (C_1–C_2)alkyl optionally mono-substituted with V^1 or said (C_1–C_2)alkyl optionally having one to five fluorines;

wherein V^1 is a partially saturated, fully saturated or fully unsaturated three to six membered ring optionally having one to two heteroatoms selected independently from oxygen, sulfur and nitrogen;

wherein said V^1 substituent is optionally mono-, di- or tri-substituted independently with halo, nitro or (C_1–C_2)alkyl, said (C_1–C_2)alkyl optionally having from one to five fluorines;

R^6 and R^7 are each independently hydrogen, halo, T, (C_1–C_6)alkoxy or (C_1–C_6)alkyl, said (C_1–C_6)alkoxy or (C_1–C_6)alkyl substituent optionally having from one to nine fluorines or said (C_1–C_6)alkoxy or (C_1–C_6)alkyl substituent optionally mono-substituted with T;

wherein T is a partially saturated, fully saturated or fully unsaturated five to six membered ring optionally having one to two heteroatoms selected independently from oxygen, sulfur and nitrogen;

wherein said T substituent is optionally mono-, di- or tri-substituted independently with halo, (C_1–C_6) alkyl, hydroxy, (C_1–C_6)alkoxy, (C_1–C_4)alkylthio, amino, oxo, carboxy, (C_1–C_6)alkyloxycarbonyl, mono-N- or di-N,N-(C_1–C_6)alkylamino wherein said (C_1–C_6)alkyl substituent optionally has from one to nine fluorines; or

wherein R^6 and R^7 are taken together and form one ring that is a partially saturated or fully unsaturated five or six membered ring optionally having one to two heteroatoms independently selected from nitrogen, sulfur and oxygen;

R^5 and R^8 are H; and

pharmaceutically acceptable salts thereof.

A group of compounds which is preferred among the A Group of compounds, designated the B Group, contains those compounds wherein

W is carbonyl;

X is O-Y wherein Y is (C_1–C_4)alkyl, wherein said (C_1–C_4)alkyl substituent optionally has hydroxy or from one to nine fluorines;

R^2 is (C_1–C_4)alkyl, (C_1–C_2)alkyloxymethylene or (C_3–C_5)cycloalkyl;

Q is (C_1–C_4)alkyl and V is phenyl, pyridinyl, or pyrimidinyl;

wherein said V ring is optionally mono-, di- or tri-substituted independently with halo, (C_1–C_6)alkyl, hydroxy, (C_1–C_6)alkoxy, nitro, cyano or oxo wherein said (C_1–C_6)alkyl substituent optionally has from one to nine fluorines;

R^4 is carbonyl or carbamoyl wherein said carbonyl or carbamoyl is optionally mono-substituted with hydrogen or (C_1–C_2)alkyl;

R^6 and R^7 are each independently hydrogen, (C_1–C_3) alkoxy or (C_1–C_6)alkyl, said (C_1–C_3)alkoxy optionally having from one to seven fluorines, said (C_1–C_6)alkyl optionally having from one to nine fluorines; and

pharmaceutically acceptable salts thereof.

A group of compounds which is preferred among the B Group of compounds, designated the C Group, contains those compounds wherein

Q is methyl and V is phenyl or pyridinyl;

wherein said V ring is optionally mono-, di- or tri-substituted independently with halo, nitro or (C_1–C_2) alkyl, wherein said (C_1–C_2)alkyl optionally has from one to five fluorines; and pharmaceutically acceptable salts thereof.

Especially preferred compounds of Formula I are the compounds:

[2S,4S]4-[(3,5-bis-trifluoromethyl-benzyl)-formyl-amino]-2-cyclopropyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid isopropyl ester;

[2S,4S]4-[(3,5-bis-trifluoromethyl-benzyl)-formyl-amino]-2-cyclopropyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid propyl ester;

[2S,4S]4-[acetyl-(3,5-bis-trifluoromethyl-benzyl)-amino]-2-cyclopropyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid tert-butyl ester;

[2R,4S]4-[acetyl-(3,5-bis-trifluoromethyl-benzyl)-amino]-2-ethyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid isopropyl ester;

[2R,4S]4-[acetyl-(3,5-bis-trifluoromethyl-benzyl)-amino]-2-methyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid ethyl ester;

and pharmaceutically acceptable salts of said compounds.

Other especially preferred compounds of Formula I are the compounds:

[2S,4S]4-[1-(3,5-bis-trifluoromethyl-benzyl)-ureido]-2-cyclopropyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid isopropyl ester;

[2R,4S]4-[acetyl-(3,5-bis-trifluoromethyl-benzyl)-amino]-2-ethyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid ethyl ester;

[2S,4S]4-[acetyl-(3,5-bis-trifluoromethyl-benzyl)-amino]-2-methoxymethyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid isopropyl ester;

[2S,4S) 4-[acetyl-(3,5-bis-trifluoromethyl-benzyl)-amino]-2-cyclopropyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid propyl ester;

[2S,4S]4-[acetyl-(3,5-bis-trifluoromethyl-benzyl)-amino]-2-cyclopropyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid ethyl ester;

[2R,4S]4-[(3,5-bis-trifluoromethyl-benzyl)-formyl-amino]-2-ethyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid isopropyl ester;

and pharmaceutically acceptable salts of said compounds.

Other especially preferred compounds of Formula I are the compounds:

[2R,4S]4-[(3,5-bis-trifluoromethyl-benzyl)-formyl-amino]-2-methyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid ethyl ester;

[2S,4S]4-[acetyl-(3,5-bis-trifluoromethyl-benzyl)-amino]-2-cyclopropyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid isopropyl ester;

[2R,4S]4-[(3,5-bis-trifluoromethyl-benzyl)-formyl-amino]-2-ethyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid ethyl ester;

[2S,4S]4-[(3,5-bis-trifluoromethyl-benzyl)-formyl-amino]-2-cyclopropyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid ethyl ester;

[2R,4S]4-[(3,5-bis-trifluoromethyl-benzyl)-formyl-amino]-2-methyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid isopropyl ester;

[2R,4S]4-[acetyl-(3,5-bis-trifluoromethyl-benzyl)-amino]-2-methyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid isopropyl ester;

and pharmaceutically acceptable salts of said compounds.

Especially preferred compounds within the C Group of compounds are compounds wherein

a.
Y is isopropyl;
R^2 is cyclopropyl;
R^3 is 3,5-bis-trifluoromethylphenylmethyl;
R^4 is formyl;
R^6 is trifluoromethyl; and
R^7 is H;

b.
Y is n-propyl;
R^2 is cyclopropyl;
R^3 is 3,5-bis-trifluoromethylphenylmethyl;
R^4 is formyl;
R^6 is trifluoromethyl; and
R^7 is H;

c.
Y is tert-butyl;
R^2 is cyclopropyl;
R^3 is 3,5-bis-trifluoromethylphenylmethyl;
R^4 is acetyl;
R^6 is trifluoromethyl; and
R^7 is H;

d.
Y is isopropyl;
R^2 is ethyl;
R^3 is 3,5-bis-trifluoromethylphenylmethyl;
R^4 is acetyl;
R^6 is trifluoromethyl; and
$R^7$is H;

e.
Y is ethyl;
R^2 is methyl;
R^3 is 3,5-bis-trifluoromethylphenylmethyl;
R^4 is acetyl;
R^6 is trifluoromethyl; and
R^7 is H;

f.
Y is isopropyl;
R^2 is cyclopropyl;
R^3 is 3,5-bis-trifluoromethylphenylmethyl;
R^4 is carbamoyl;
R^6 is trifluoromethyl; and
R^7 is H;

g.
Y is ethyl;
R^2 is ethyl;
$R^3$is 3,5-bis-trifluoromethylphenylmethyl;
R^4 is acetyl;
R^6 is trifluoromethyl; and

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