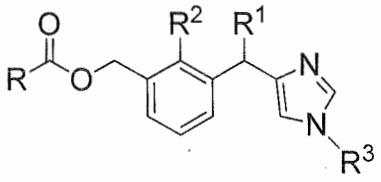
What is claimed is:

1. A compound for use in the manufacture of a medicament for the treatment of skin diseases and skin conditions in a subject in need of such treatment wherein the compound is of Formula I, its individual enantiomers, its individual diastereoisomers, its hydrates, its solvates, its crystal forms, its individual isomers, its individual tautomers or a pharmaceutically acceptable salt thereof,



Formula I

wherein

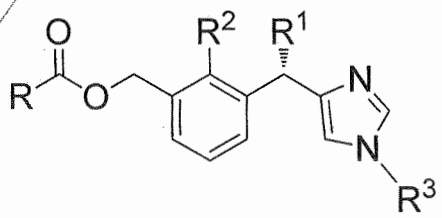
R^1 is H or C_{1-3} alkyl;

R^2 is H or C_{1-3} alkyl;

R^3 is H, C_{1-10} alkyl, heterocycle or aryl; and

R is C_{1-10} alkyl, heterocycle or aryl.

2. A use according to claim 1 wherein the compound is of Formula II, its individual diastereoisomers, its hydrates, its solvates, its crystal forms, its individual isomers, its individual tautomers or a pharmaceutically acceptable salt thereof,



Formula II

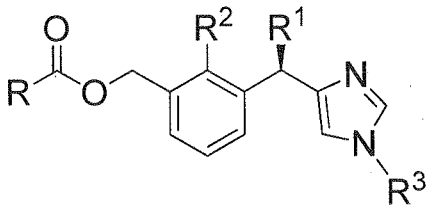
wherein

R^1 is H or C_{1-3} alkyl;

R^2 is H or C_{1-3} alkyl;

R^3 is H, C_{1-10} alkyl, heterocycle or aryl; and
R is C_{1-10} alkyl, heterocycle or aryl.

3. A use according to claim 1 wherein the compound is of Formula III, its individual diastereoisomers, its hydrates, its solvates, its crystal forms, its individual isomers, its individual tautomers or a pharmaceutically acceptable salt thereof,



Formula III

wherein
R^1 is H or C_{1-3} alkyl;
R^2 is H or C_{1-3} alkyl;
R^3 is H, C_{1-10} alkyl, heterocycle or aryl; and
R is C_{1-10} alkyl, heterocycle or aryl.

4. A use according to claim 2, wherein R^1 is C_{1-3} alkyl, R^2 is C_{1-3} alkyl R^3 is H and R is C_{1-10} alkyl.

5. A use according to claim 2, wherein R^1 is methyl, R^2 is methyl, R^3 is H and R is C_{1-4} alkyl.

6. A use according to claim 2, wherein the compound is selected from:
iso-Butyric acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;
2,2-Dimethyl-propionic acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;
Acetic acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;
Benzoic acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;
3-Methyl-butyric acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

3-Phenyl-propionic acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

2-Amino-3-methyl-butyric acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

2-(2-Amino-3-methyl-butyrylamino)-3-methyl-butyric acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

2-(2-Amino-acetylamino)-3-methyl-butyric acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester; and

2-Amino-3-phenyl-propionic acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester.

7. A use according to claim 2, wherein the compound is selected from:

iso-Butyric acid 3-[(*S*)-1-(1-*iso*-butyryl-1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

2,2-Dimethyl-propionic acid 3-{(*S*)-1-[1-(2,2-dimethyl-propionyl)-1*H*-imidazol-4-yl]-ethyl}-2-methyl-benzyl ester;

Acetic acid 3-[(*S*)-1-(1-acetyl-1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

Benzoic acid 3-[(*S*)-1-(1-benzoyl-1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

3-Methyl-butyric acid 2-methyl-3-{(*S*)-1-[1-(3-methyl-butyryl)-1*H*-imidazol-4-yl]-ethyl}-benzyl ester;

Phenyl-propionic acid 2-methyl-3-{(*S*)-1-[1-(3-phenyl-propionyl)-1*H*-imidazol-4-yl]-ethyl}-benzyl ester;

2-*tert*-Butoxycarbonylamino-3-methyl-butyric acid 3-{(*S*)-1-[1-(2-*tert*-butoxy carbonylamino-3-methyl-butyryl)-1*H*-imidazol-4-yl]-ethyl}-2-methyl-benzyl ester;

2-*tert*-Butoxycarbonylamino-3-methyl-butyric acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

2-(2-*tert*-Butoxycarbonylamino-3-methyl-butyrylamino)-3-methyl-butyric acid 3-{(*S*)-1-[1-(2-*tert*-butoxycarbonylamino-3-methyl-butyryl)-1*H*-imidazol-4-yl]-ethyl}-2-methyl-benzyl ester;

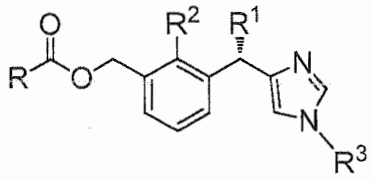
2-(2-*tert*-Butoxycarbonylamino-3-methyl-butyrylamino)-3-methyl-butyric acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

2-(2-*tert*-Butoxycarbonylamino-acetylamino)-3-methyl-butyric acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester; and

2-*tert*-Butoxycarbonylamino-3-phenyl-propionic acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester.

8. A use according to claim 1 wherein the disease is selected from: rosacea, sunburn, chronic sun damage, discreet erythemas, psoriasis, atopic dermatitis, menopause-associated hot flashes, hot flashes resulting from orchiectomyatopic dermatitis, photoaging, seborrheic dermatitis, acne, allergic dermatitis, irritant dermatitis, telangiectasia (dilations of previously existing small blood vessels) of the face, rhinophyma (hypertrophy of the nose with follicular dilation), red bulbous nose, acne-like skin eruptions (may ooze or crust), burning or stinging sensation of the face, irritated and bloodshot and watery eyes, cutaneous hyperactivity with dilation of blood vessels of the skin, Lyell's syndrome, Stevens-Johnson syndrome, erythema multiforme minor, erythema multiforme major and other inflammatory skin diseases. Skin conditions which result in rosacea can be induced by intake of spicy food, of alcohol, of chocolate, of hot or alcoholic drinks, temperature variations, heat, exposure to ultraviolet or infrared radiation, exposure to low relative humidity, exposure of the skin to strong winds or currents of air, exposure of the skin to surfactants, irritants, irritant dermatological topical agents, and cosmetics.

9. An article of manufacture comprising packaging material and a pharmaceutical agent contained within said packaging material, wherein the pharmaceutical agent is therapeutically effective for treating skin diseases and skin conditions and wherein the packaging material comprises a label which indicates the pharmaceutical agent can be used for treating skin diseases and skin conditions and wherein said pharmaceutical agent comprises an effective amount of compound is of Formula II, its individual diastereoisomers, its hydrates, its solvates, its crystal forms, its individual isomers, its individual tautomers or a pharmaceutically acceptable salt thereof,



Formula II

wherein

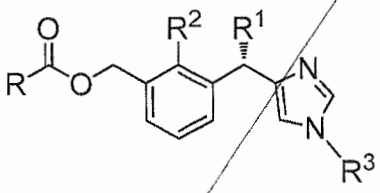
R^1 is H or C $_{1-3}$ alkyl;

R^2 is H or C $_{1-3}$ alkyl;

R^3 is H, C $_{1-10}$ alkyl, heterocycle or aryl; and

R is C $_{1-10}$ alkyl, heterocycle or aryl.

10. A pharmaceutical composition for treating skin diseases and skin conditions in a subject comprising a compound having a structure



Formula II

wherein

R^1 is H or C $_{1-3}$ alkyl;

R^2 is H or C $_{1-3}$ alkyl;

R^3 is H, C $_{1-10}$ alkyl, heterocycle or aryl; and

R is C $_{1-10}$ alkyl, heterocycle or aryl.

11. The pharmaceutical composition of claim 10 wherein the compound is selected from:

iso-Butyric acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

2,2-Dimethyl-propionic acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

Acetic acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

Benzoic acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

3-Methyl-butyric acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

3-Phenyl-propionic acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

2-Amino-3-methyl-butyric acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

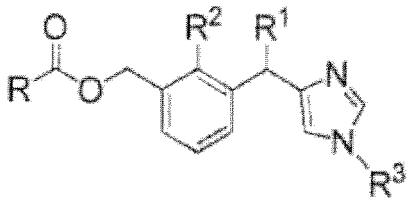
2-(2-Amino-3-methyl-butyrylamino)-3-methyl-butyric acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

2-(2-Amino-acetylamino)-3-methyl-butyric acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester; and

2-Amino-3-phenyl-propionic acid 3-[(*S*)-1-(1*H*-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester.

Claims

1. Use of a composition comprising a compound according to Formula **1,** its individual enantiomers, its individual diastereoisomers, its hydrates, its solvates, its crystal forms, its individual tautomers or a pharmaceutically acceptable salt thereof,



Formula I

wherein

R^1 is H or C_{1-3} alkyl;

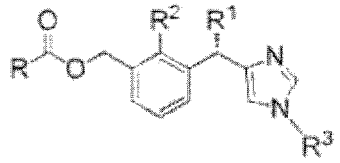
R^2 is H or C_{1-3} alkyl;

R^3 is H; C_{1-10} alkyl; an aromatic or non-aromatic 5- to 10-membered monocyclic or bicyclic heterocycle containing at least one heteroatom selected from 0 or N or S or combinations thereof; or a C6-1O monocyclic or bicyclic aryl group; and

R is a C_{1-10} alkyl group optionally substituted by amino groups, aryl groups and halogen atoms, wherein one methylene group of the alkyl chain can be replaced by carbonyl, -NH-, carboxyl, amide, -S- or -0-; an aromatic or non-aromatic 5 to 10 membered monocyclic or bicyclic heterocycle containing at least one heteroatom selected from 0 or N or S or combinations thereof, wherein the heterocycle is optionally substituted by C_{1-6} alkyl, amino, halogen, -O(C_{1-6} alkyl), -OC(O)(C_{1-6} alkyl), -C(O)O(C_{1-6} alkyl), -NHC(O)(C_{1-6} alkyl), -C(O)NH(C_{1-6} alkyl), -S(C_{1-6} alkyl) groups; or a C_{6-10} monocyclic or bicyclic aryl group optionally substituted by C_{1-6} alkyl, amino, halogen, -O(C_{1-6} alkyl), -OC(O)(C_{1-6} alkyl), -C(O)O(C_{1-6} alkyl), -NHC(O)(C_{1-6} alkyl), -C(O)NH(C_{1-6} alkyl) or -S(C_{1-6} alkyl) groups in the manufacture of a medicament for treating skin diseases and skin conditions in a subject;

wherein said skin diseases and skin conditions are selected from: rosacea, sunburn, chronic sun damage, discreet erythemas, psoriasis, atopic dermatitis, menopause-associated hot flashes, hot flashes resulting from orchiectomy, atopic dermatitis, photoaging, seborrheic dermatitis, acne, allergic dermatitis, and irritant dermatitis; and wherein the medicament is to be administered by topical dermatological applicantion.

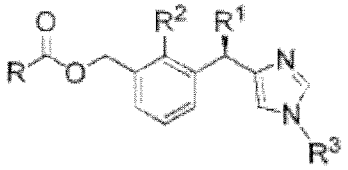
2. The use according to Claim 1 wherein the compound is as defined by Formula II, its individual diastereoisomers, its hydrates, its solvates, its crystal forms, its individual tautomers or a pharmaceutically acceptable salt thereof,



Formula II

wherein R^1, R^2, R^3 and R are as defined above.

3. The use according to Claim 1 wherein the compound is as defined by Formula III, its individual diastereoisomers, its hydrates, its solvates, its crystal forms, its individual tautomers or a pharmaceutically acceptable salt thereof,



Formula III

wherein R^1, R^2, R^3 and R are as defined above.

4. The use according to Claim 2, wherein R^1 is C_{1-3} alkyl, R^2 is C_{1-3} alkyl, R^3 is H and R is C_{1-10} alkyl.

5. The use according to Claim 2, wherein R^1 is methyl, R^2 is methyl, R3 is H and R is C_{1-4} alkyl.

6. The use according to Claim 2, wherein the compound is selected from:

iso-Butyric acid 3-[(S)-1-(lH-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

2,2-Dimethyl-propionic acid 3-[(S)-1-(1H-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

Acetic acid 3-[(S)-1-(1H-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

Benzoic acid 3-[(S)-I-(1H-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

3-Methyl-butyric acid 3-[(S)-1-(1H-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

3-Phenyl-propionic acid 3-[(S)-1-(1H-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

2-Amino-3-methyl-butyric acid 3-[(S)-1-(lH-imidazol-4-yl)-ethyl]-2-methylbenzyl ester;

2-(2-Amino-3-methyl-butyrylamino)-3-methyl-butyric acid 3-[(S)-1-(1H-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

2-(2-Amino-acetylamino)-3-methyl-butyric acid 3-[(S)-1-(lH-imidazol-4-yl)ethyl]-2-methyl-benzyl ester; and

2-Amino-3-phenyl-propionic acid 3-[(S)-1-(1H-imidazol-4-yl)-ethyl]-2-methylbenzyl ester.

7. The use according to Claim 2, wherein the compound is selected from:

iso-Butyric acid 3-[(S)-l-(l-iso-butyryl-lH -imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

2,2-Dimethyl-propionic acid 3-{(S)-1-[1-(2,2-dimetbyl-propionyl)-1H-imidazol-4-yl]-ethyl}-2-methyl-benzyl ester;

Acetic acid 3-[(S)-1-(l-acetyl-1H-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

Benzoic acid 3-[(S)-1-(l-benzoyl-1H-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

3-Methyl-butyric acid 2-methyl-3-{(S)-l-[1-(3-methyl-butyryl)-1H-imidazol-4-yl]-ethyl}-benzyl ester;

Phenyl-propionic acid 2-methyl-3-{(S)-1-[1-(3-phenyl-propionyl)-1H-imidazol-4-yl]-ethyl}-benzyl ester;

2-tert-Butoxycarbonylamino-3-methyl-butyric acid 3-{(S)-1-[1-(2-tert-butoxy carbonylamino-3-methyl-butyryl)-1H -imidazol-4-yl]-ethyl}-2-methyl-benzyl ester;

2-tert-Butoxycarbonylamino-3-methyl-butyric acid 3-[(S)-1-(1H-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

2-(2-tert-Butoxycarbonylamino-3-methyl-butyrylamino)-3-methyl-butyric acid 3-{(S)-l-[1-(2-tert-butoxycarbonylamino-3-methyl-butyryl)-1H-imidazol-4-yl]-ethyl}-2-methyl-benzyl ester;

2-(2-tert-Butoxycarbonylamino-3-methyl-butyrylamino)-3-methyl-butyric acid 3-[(S)-1-(1H-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester;

2-(2-tert-Butoxycarbonylamino-acetylamino)-3-methyl-butyric acid 3-[(S)-1-(1H-imidazol-4-yl)-ethyl]-2-methyl-benzyl ester; and

2-tert-Butoxycarbonylamino-3-phenyl-propionic acid 3-[(S)-1-(1H-imidazol-4-yl)ethyl]-2-methyl-benzyl ester.