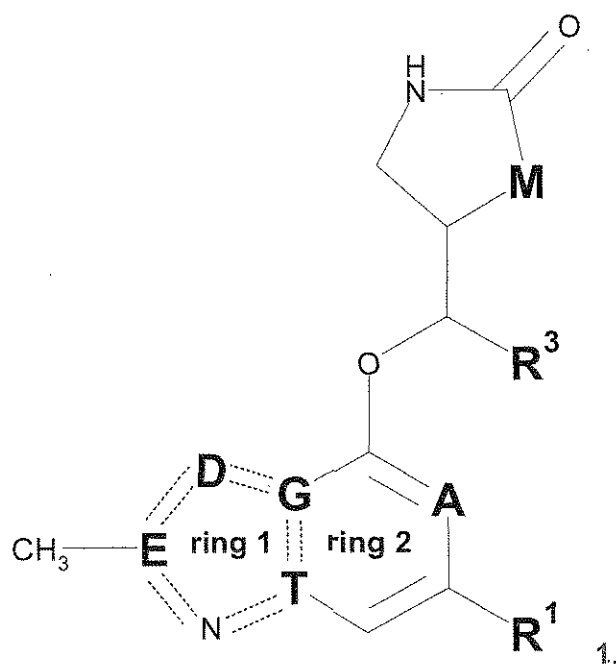


2 DESCRIPTION

2.1 SUMMARY

1. In one aspect, there is provided a compound of formula 1



wherein

A is selected from the group consisting of N and CH

D is CH,

E is selected from the group consisting of C and N,

T is C

G is selected from the group consisting of C and N,

and wherein each of the broken (dotted) double bonds in ring 1 are selected from either a single bond or a double bond under the proviso that all single and double bonds of ring 1 are arranged in such a way that they all form together with ring 2 an aromatic ring system,

and wherein

M is selected from the group consisting of -CH₂-, -O-, -NH- and -N(C₁₋₄-alkyl)-;

R³ is selected from the group consisting of methyl and ethyl;

Het is selected from the group consisting of

a five- to six-membered monocyclic heterocycle with 1, 2, 3 or 4 heteroatoms each independently from one another selected from N, S and O;

and a nine- to eleven-membered bicyclic heterocycle with 1, 2, 3 or 4 heteroatoms each independently from one another selected from N, S and O;

Hetaryl is selected from the group consisting of

a five- to six-membered monocyclic heteroaromate with 1, 2, 3 or 4 heteroatoms each independently from one another selected from N, S and O;

and a nine- to eleven-membered bicyclic heteroaromate with 1, 2, 3 or 4 heteroatoms each independently from one another selected from N, S and O;

and wherein

R¹ is selected from the group consisting of

C₆₋₁₀-aryl, Het and Hetaryl;

which is optionally further substituted by one, two or three substituents Z,

whereby each Z is a substituent selected from the group consisting of

-OH, oxo, -CN, halogen, -C₁₋₆-alkyl, -O-C₁₋₆-alkyl, -C₁₋₆-haloalkyl, three- to seven-membered cycloalkyl, Het, Hetaryl, -CO-N(CH₃)₂, -CO-NHCH₃, -CO-NH₂, -(C₁₋₃-alkylene)-O-(C₁₋₃-alkyl), -O-Het,

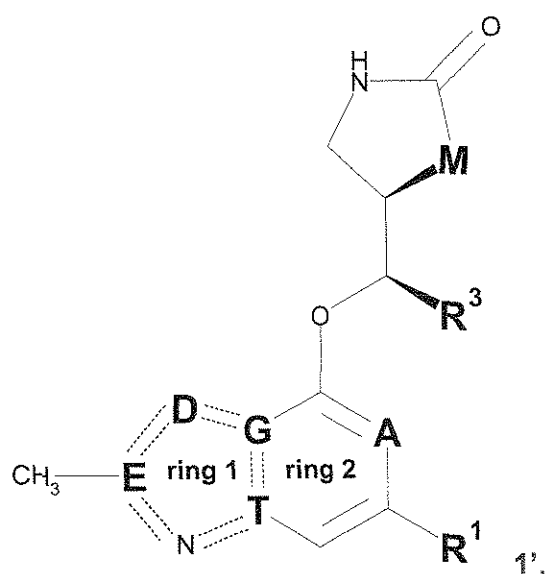
which is optionally further substituted by one, two or three substituents X,

whereby each X is selected from the group consisting of halogen, -OH, oxo, -C₁₋₄-alkyl, -O-C₁₋₄-alkyl, -C₁₋₄-haloalkyl, -O-(C₁₋₄-alkylene)-Het, Het, Hetaryl, -NH₂, -NH(CH₃), -N(CH₃)₂,

whereby substituent X is optionally further substituted by one, two or three substituents of a group selected from oxo, -OH, halogen and C₁₋₃-alkyl,

and the pharmaceutically acceptable salts of the aforementioned compounds.

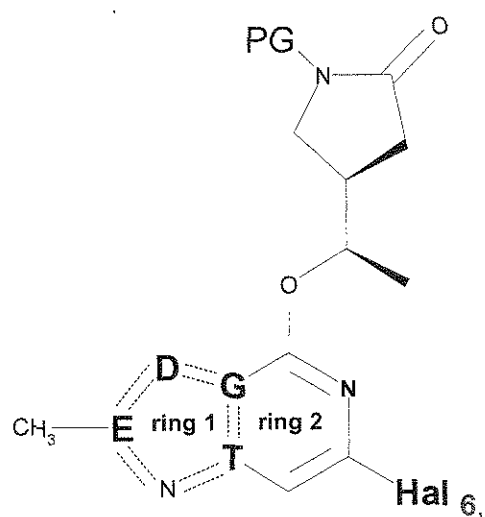
In another aspect, there is provided a compound of formula 1'



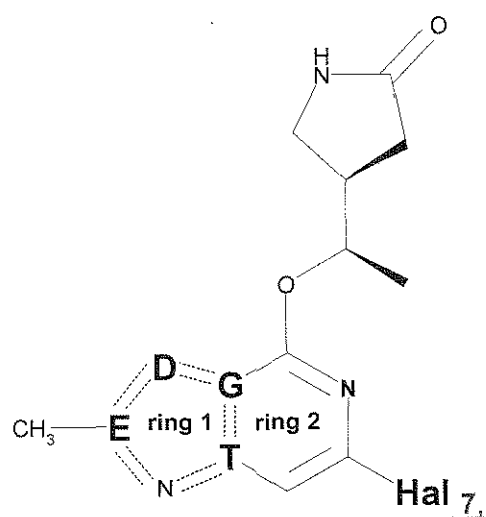
wherein A, D, E, T, G, Het, Hetaryl, R¹ and R³ are defined herein,

and the pharmaceutically acceptable salts of the aforementioned compounds.

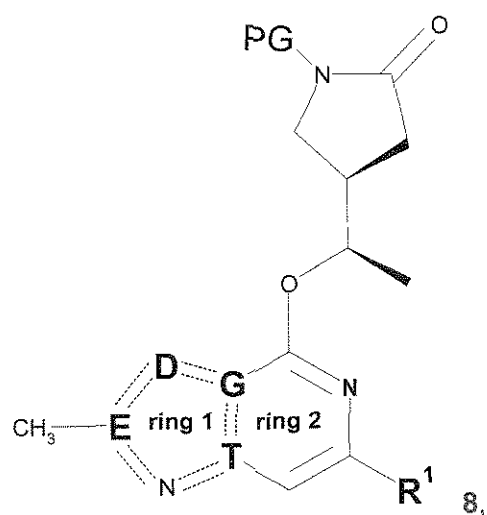
In another aspect, there is provided an intermediate compound selected from the group consisting of formula 6



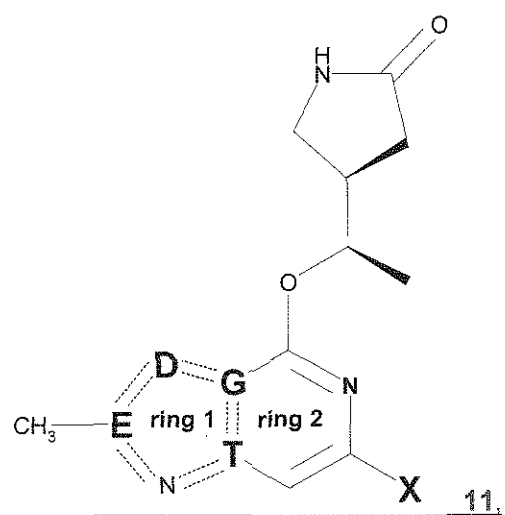
of formula 7



of formula 8



and of formula 11

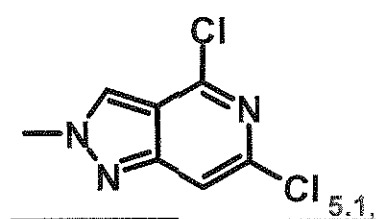


wherein E, D, G, T and R¹ are as defined herein and wherein Hal is Cl or Br

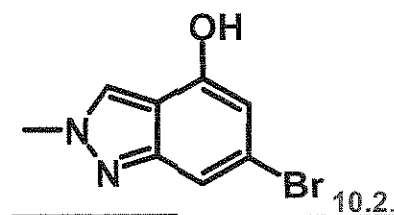
and wherein PG is a protecting group selected from the group consisting of benzyl, 1-phenylethyl, 1-(4-methoxyphenyl)ethyl.

In another aspect, there is provided an intermediate compound selected from the group consisting of

formula 5.1



and of formula 10.2



In another aspect, there is provided the compound as defined herein for the treatment of a disease which can be treated by inhibition of the SYK enzyme.

In another aspect, there is provided the compound as defined herein for the treatment of a disease selected from the group consisting of allergic rhinitis, asthma, COPD, adult respiratory distress syndrome, bronchitis, B-cell lymphoma, dermatitis and contact dermatitis, allergic dermatitis, allergic rhinoconjunctivitis, rheumatoid arthritis, anti-phospholipid syndrome, Berger's disease, Evans's syndrome, ulcerative colitis, allergic antibody-based glomerulonephritis, granulocytopenia, Goodpasture's syndrome, hepatitis, Henoch-Schönlein purpura, hypersensitivity vasculitis, immunohaemolytic anaemia, autoimmune haemolytic anemia, idiopathic thrombocytopenic purpura, Kawasaki syndrome, allergic conjunctivitis, lupus erythematoses, lupus nephritis, capsule cell lymphoma, neutropenia, non-familial lateral sclerosis, arteriosclerosis, Crohn's disease, multiple sclerosis, myasthenia gravis,

osteoporosis, osteolytic diseases, osteopenia, psoriasis, Sjögren's syndrome, sclerodermy, T-cell lymphoma, urticaria / angiooedema, Wegener's granulomatosis and coeliac disease.

In another aspect, there is provided the compound as defined herein for the treatment of a disease selected from the group consisting of asthma, COPD, allergic rhinitis, adult respiratory distress syndrome, bronchitis, allergic dermatitis, contact dermatitis, idiopathic thrombocytopenic purpura, rheumatoid arthritis, lupus erythematoses, lupus nephritis and allergic rhinoconjunctivitis.

In another aspect, there is provided the compound as defined herein for the treatment of a disease selected from the group consisting of asthma, COPD, allergic rhinitis, allergic dermatitis, lupus erythematoses, lupus nephritis and rheumatoid arthritis.

In another aspect, there is provided pharmaceutical formulations, characterised in that they contain one or more compounds as defined herein and a pharmaceutically acceptable excipient.

In another aspect, there is provided pharmaceutical formulations, characterised in that they contain one or more compounds as defined herein in combination with an active substance selected from the group consisting of anticholinergics, betamimetics, corticosteroids, PDE4-inhibitors, EGFR-inhibitors, LTD4-antagonists, CCR3-inhibitors, iNOS-inhibitors, CRTH2-antagonists, HMG-CoA reductase inhibitors and NSAIDs.

In another aspect, there is provided use of the compound as defined herein in the manufacture of a medicament for the treatment of a disease which can be treated by inhibition of the SYK enzyme.

In another aspect, there is provided use of the compound as defined herein in the manufacture of a medicament for the treatment of a disease selected from the group consisting of allergic rhinitis, asthma, COPD, adult respiratory distress syndrome, bronchitis, B-cell lymphoma, dermatitis and contact dermatitis, allergic dermatitis, allergic rhinoconjunctivitis, rheumatoid arthritis, anti-phospholipid syndrome, Berger's disease,

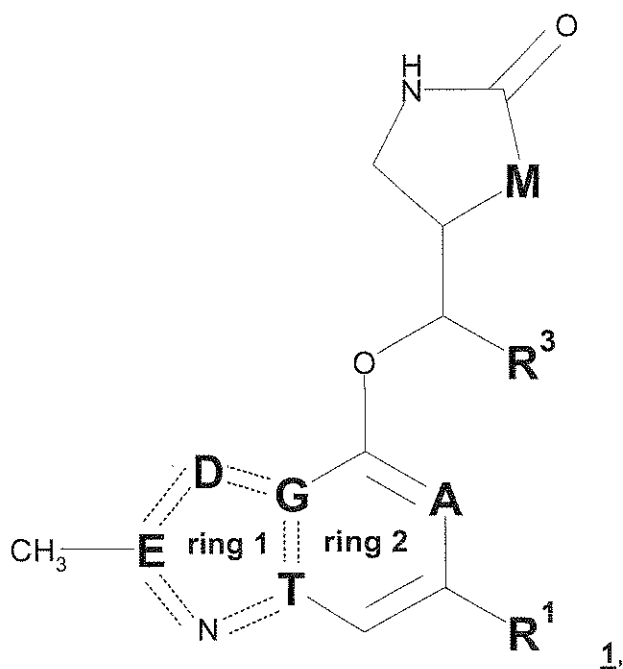
Evans's syndrome, ulcerative colitis, allergic antibody-based glomerulonephritis, granulocytopenia, Goodpasture's syndrome, hepatitis, Henoch-Schönlein purpura, hypersensitivity vasculitis, immunohaemolytic anaemia, autoimmune haemolytic anemia, idiopathic thrombocytopenic purpura, Kawasaki syndrome, allergic conjunctivitis, lupus erythematoses, lupus nephritis, capsule cell lymphoma, neutropenia, non-familial lateral sclerosis, arteriosclerosis, Crohn's disease, multiple sclerosis, myasthenia gravis, osteoporosis, osteolytic diseases, osteopenia, psoriasis, Sjögren's syndrome, sclerodermy, T-cell lymphoma, urticaria / angiooedema, Wegener's granulomatosis and coeliac disease.

In another aspect, there is provided use of the compound as defined herein in the manufacture of a medicament for the treatment of a disease selected from the group consisting of asthma, COPD, allergic rhinitis, adult respiratory distress syndrome, bronchitis, allergic dermatitis, contact dermatitis, idiopathic thrombocytopenic purpura, rheumatoid arthritis, lupus erythematoses, lupus nephritis and allergic rhinoconjunctivitis.

In another aspect, there is provided use of the compound as defined herein in the manufacture of a medicament for the treatment of a disease selected from the group consisting of asthma, COPD, allergic rhinitis, allergic dermatitis, lupus erythematoses, lupus nephritis and rheumatoid arthritis.

2.2 DESCRIPTION OF THE INVENTION

The present invention concerns compounds of formula **1**



wherein

A is selected from the group consisting of N and CH

D is CH

E is selected from the group consisting of C and N,

T is C

G is selected from the group consisting of C and N,

and wherein each of the broken (dotted) double bonds in ring 1 are selected from either a single bond or a double bond under the proviso that all single and double bonds of ring 1 are arranged in such a way that they all form together with ring 2 an aromatic ring system,

and wherein

M is selected from the group consisting of -CH₂-, -O-, -NH- and -N(C₁₋₄-alkyl)-;

R³ is selected from the group consisting of methyl and ethyl;

Het is selected from the group consisting of

osteopenia, psoriasis, Sjögren's syndrome, sclerodermy, T-cell lymphoma, urticaria / angiooedema, Wegener's granulomatosis and coeliac disease.

20. The compound of any of claim 1 to 15 for the treatment of a disease selected from the group consisting of asthma, COPD, allergic rhinitis, adult respiratory distress syndrome, bronchitis, allergic dermatitis, contact dermatitis, idiopathic thrombocytopenic purpura, rheumatoid arthritis, lupus erythematoses, lupus nephritis and allergic rhinoconjunctivitis.
21. The compound of any of claim 1 to 15 for the treatment of a disease selected from the group consisting of asthma, COPD, allergic rhinitis, allergic dermatitis, lupus erythematoses, lupus nephritis and rheumatoid arthritis.
22. Pharmaceutical formulations, characterised in that they contain one or more compounds according to one of claims 1 to 15 and a pharmaceutically acceptable excipient.
23. Pharmaceutical formulations, characterised in that they contain one or more compounds according to one of claims 1 to 15 in combination with an active substance selected from the group consisting of anticholinergics, betamimetics, corticosteroids, PDE4-inhibitors, EGFR-inhibitors, LTD4-antagonists, CCR3-inhibitors, iNOS-inhibitors, CRTH2-antagonists, HMG-CoA reductase inhibitors and NSAIDs.
24. Use of the compound of any of claims 1 to 15 in the manufacture of a medicament for the treatment of a disease which can be treated by inhibition of the SYK enzyme.
25. Use of the compound of any of claim 1 to 15 in the manufacture of a medicament for the treatment of a disease selected from the group consisting of allergic rhinitis, asthma, COPD, adult respiratory distress syndrome, bronchitis, B-cell lymphoma, dermatitis and contact dermatitis, allergic dermatitis, allergic rhinoconjunctivitis, rheumatoid arthritis, anti-phospholipid syndrome, Berger's disease, Evans's syndrome, ulcerative colitis, allergic antibody-based glomerulonephritis, granulocytopenia, Goodpasture's syndrome, hepatitis, Henoch-Schönlein purpura, hypersensitivity vasculitis,

immunohaemolytic anaemia, autoimmune haemolytic anemia, idiopathic thrombocytopenic purpura, Kawasaki syndrome, allergic conjunctivitis, lupus erythematoses, lupus nephritis, capsule cell lymphoma, neutropenia, non-familial lateral sclerosis, arteriosclerosis, Crohn's disease, multiple sclerosis, myasthenia gravis, osteoporosis, osteolytic diseases, osteopenia, psoriasis, Sjögren's syndrome, sclerodermy, T-cell lymphoma, urticaria / angioedema, Wegener's granulomatosis and coeliac disease.

26. Use of the compound of any of claim 1 to 15 in the manufacture of a medicament for the treatment of a disease selected from the group consisting of asthma, COPD, allergic rhinitis, adult respiratory distress syndrome, bronchitis, allergic dermatitis, contact dermatitis, idiopathic thrombocytopenic purpura, rheumatoid arthritis, lupus erythematoses, lupus nephritis and allergic rhinoconjunctivitis.

27. Use of the compound of any of claim 1 to 15 in the manufacture of a medicament for the treatment of a disease selected from the group consisting of asthma, COPD, allergic rhinitis, allergic dermatitis, lupus erythematoses, lupus nephritis and rheumatoid arthritis.