~~ether (O) linkage~~; and

R^4 is methyl or R^4 and R^1 together form C_{2-6} alkylene;

provided that R^1 and R^2 are not both H; and
provided that alkoxyalkyl or hydroxyalkoxyalkyl is other than alkoxymethyl or hydroxyalkoxymethyl

~~provided that where R^2 is carbalkoxyalkyl or $(R^3)_3Si$, X and Y are not both O~~.

2. Compounds according to claim 1 selected from the following:

1. 40-O-Benzyl-rapamycin
2. 40-O-(4'-Hydroxymethyl)benzyl-rapamycin
3. 40-O-[4'-(1,2-Dihydroxyethyl)]benzyl-rapamycin
4. 40-O-Allyl-rapamycin
5. 40-O-[3'-(2,2-Dimethyl-1,3-dioxolan-4(S)-yl)-prop-2'-en-1'-yl]-rapamycin
6. (2'E, 4'S)-40-O-(4',5'-Dihydroxypent-2'-en-1'-yl)-rapamycin
7. 40-O-(2-Hydroxy)ethoxycarbonylmethyl-rapamycin
8. 40-O-(2-Hydroxy)ethyl-rapamycin
9. 40-O-(3-Hydroxy)propyl-rapamycin
10. 40-O-(6-Hydroxy)hexyl-rapamycin
11. 40-O-[2-(2-Hydroxy)ethoxy]ethyl-rapamycin
12. 40-O-[(3S)-2,2-Dimethyldioxolan-3-yl]methyl-rapamycin
13. 40-O-[(2S)-2,3-Dihydroxyprop-1-yl]-rapamycin
14. 40-O-(2-Acetoxy)ethyl-rapamycin
15. 40-O-(2-Nicotinoyloxy)ethyl-rapamycin
16. 40-O-[2-(N-Morpholino)acetoxy]ethyl-rapamycin
17. 40-O-(2-N-Imidazolylacetoxy)ethyl-rapamycin
18. 40-O-[2-(N-Methyl-N'-piperazinyl)acetoxy]ethyl-rapamycin
19. 39-O-Desmethyl-39,40-O,O-ethylene-rapamycin
20. (26R)-26-Dihydro-40-O-(2-hydroxy)ethyl-rapamycin
21. 28-O-Methyl-rapamycin
22. 40-O-(2-Aminoethyl)-rapamycin

AMENDED SHEET

23. 40-O-(2-Acetaminoethyl)-rapamycin
24. 40-O-(2-Nicotinamidoethyl)-rapamycin
25. 40-O-(2-(N-Methyl-imidazo-2'-ylcarbethoxamido)ethyl)-rapamycin
26. 40-O-(2-Ethoxycarbonylaminoethyl)-rapamycin
27. 40-O-(2-Tolylsulfonamidoethyl)-rapamycin
28. 40-O-[2-(4',5'-Dicarboethoxy-1',2',3'-triazol-1'-yl)-ethyl]-rapamycin

3. Compounds according to claim 1 where X and Y are both O, R^2 is H, R^4 is methyl, and R^1 is other than H.

4. The compound according to claim 1 which is 40-O-(2-Hydroxy)ethyl-rapamycin.

5. A process for making compounds according to any one of claims 1 through 4 comprising the steps of ~~obtained or obtainable by~~ (i) reacting a rapamycin, deoxorapamycin, or dihydrorapamycin (optionally in O-protected form) with an organic radical (R^1 or R^2 as defined in claim 1, optionally in protected form) attached to a leaving group (X) ~~under suitable acidic or neutral reaction conditions~~, such that

(a) X is $CCl_3(NH)O$- and the reaction takes place in the presence of an acid; or
(b) X is CF_3SO_3- and the reaction takes place in the presence of a base;

and (ii) optionally reducing and/or (where necessary) deprotecting the product.

6. A compound according to any one of claims 1-5 for use as a pharmaceutical.

7. A pharmaceutical composition comprising a compound according to any one of claims 1-5 together with a pharmaceutically acceptable diluent or carrier.

8. Use of a compound according to claims 1-5 in the manufacture of a medicament for treating or preventing any of the following conditions:

(i) autoimmune disease,
(ii) allograft rejection,

(iii) graft vs. host disease,

(iv) asthma,

(v) multidrug resistance,

(vi) tumors or hyperproliferative disorders, or

(vii) fungal infections.

(viii) inflammation,

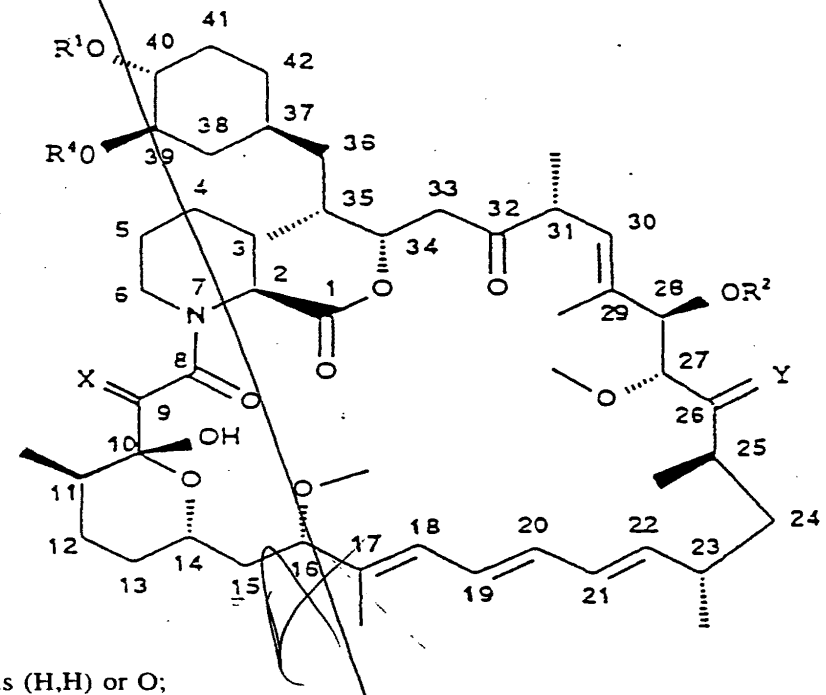
(ix) infection by pathogens having Mip or Mip-like factors, or

(x) overdose of macrophilin-binding immunosuppressants.

~~9. Novel products, processes, and utilities substantially as described herein.~~

(Amended) CLAIMS

1. A compound of Formula I



(I)

wherein

X is (H,H) or O;

Y is (H,OH) or O;

R^1 and R^2 are independently selected from

H, alkyl, ~~thioalkyl,~~ arylalkyl, hydroxyalkyl, dihydroxyalkyl, hydroxyalkylarylalkyl, dihydroxyalkylarylalkyl, alkoxyalkyl, acyloxyalkyl, aminoalkyl, alkylaminoalkyl, alkoxycarbonylaminoalkyl, acylaminoalkyl, arylsulfonamidoalkyl, allyl, dihydroxyalkylallyl, dioxolanylallyl, and hydroxyalkoxyalkyl ~~-caralkoxyalkyl, and $(R^3)_3Si$ where each R^3 is independently selected from H, methyl, ethyl, isopropyl, t-butyl, and phenyl~~; wherein "alk-" or "alkyl" refers to C_{1-6} alkyl, branched or linear, preferably C_{1-3} alkyl~~, in which the carbon chain may be optionally interrupted by an~~

~~ether (O) linkage~~; and

R^4 is methyl or R^4 and R^1 together form C_{2-6} alkylene;

provided that R^1 and R^2 are not both H; and
provided that alkoxyalkyl or hydroxyalkoxyalkyl is other than alkoxymethyl or hydroxyalkoxymethyl

~~provided that where R^1 is carbalkoxyalkyl or $(R^3)_3Si$, X and Y are not both O~~.

2. Compounds according to claim 1 selected from the following:

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8. 40-O-(2-Hydroxy)ethyl-rapamycin
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22. 40-O-(2-Aminoethyl)-rapamycin

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