

ether (-O-) linkage; and

R⁴ is methyl or R⁴ and R¹ together form C₂₋₆ alkylene;

provided that R¹ and R² are not both H; and

provided that alkoxyalkyl or hydroxyalkoxyalkyl is other than alkoxymethyl or hydroxyalkoxymethyl

~~provided that where R² is carbalkoxyalkyl or (R²)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

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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, R² is H, R⁴ is methyl, and R¹ 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 (R¹ or R² 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 CCl₃(NH)O- and the reaction takes place in the presence of an acid; or
 - (b) X is CF₃SO₃- 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,

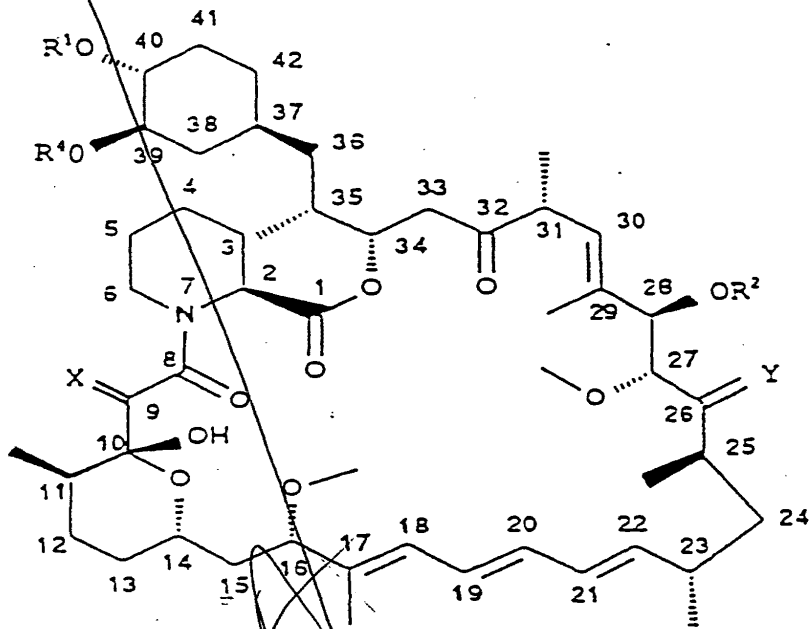
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- (iii) graft vs. host disease,
- (iv) asthma,
- (v) multidrug resistance,
- (vi) tumors or hyperproliferative disorders, or
- (vii) fungal infections,
- (viii) inflammation,
- (ix) infection by pathogens having Mip or Mip-like factors, or
- (x) overdose 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;

R¹ and R² are independently selected from

H, alkyl, ~~thioalkyl~~, arylalkyl, hydroxyalkyl, dihydroxyalkyl, hydroxyalkylarylalkyl, dihydroxyalkylarylalkyl, alkoxyalkyl, acyloxyalkyl, aminoalkyl, alkylaminoalkyl, alkoxycarbonylaminoalkyl, acylaminoalkyl, arylsulfonamidoalkyl, allyl, dihydroxyalkylallyl, dioxolanylallyl, and hydroxyalkoxyalkyl ~~or alkoxyalkyl, and (R³)₃Si where each R³ is independently selected from H, methyl, ethyl, isopropyl, t-butyl, and phenyl;~~ wherein "alk-" or "alkyl" refers to C₁₋₆ alkyl, branched or linear, preferably C₁₋₃ alkyl, in which the carbon chain may be optionally interrupted by an

ether (-O-) linkage; and

R⁴ is methyl or R⁴ and R¹ together form C₂₋₆ alkylene;

provided that R¹ and R² are not both H; and

provided that alkoxyalkyl or hydroxyalkoxyalkyl is other than alkoxymethyl or hydroxyalkoxymethyl

~~provided that where R⁴ is carbalkoxyalkyl or (R²)₃Si, X and Y are not both O.~~

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

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7. 40-O-(2-Hydroxy)ethoxycarbonylmethyl-rapamycin
8. 40-O-(2-Hydroxy)ethyl-rapamycin
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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

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