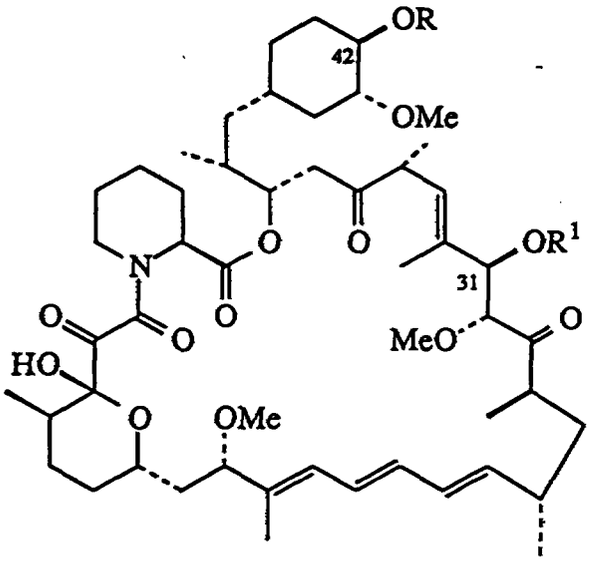
CLAIMS

CLAIMS:

~~What is claimed is:~~

1. A compound of the structure



I

wherein R and R^1 are each, independently, $-\overset{O}{\overset{\|}{C}}-(CH_2)_nR^2$ or hydrogen;

R^2 is a heterocyclic radical of 5-12 ~~carbon~~ ring atoms having at least one N, O, or S, which may be optionally mono-, di-, or tri- substituted with a group selected from alkyl of 1-6 carbon atoms, arylalkyl in which the alkyl portion contains 1-6 carbon atoms, alkoxy of 1-6 carbon atoms, cyano, halo, hydroxy, nitro, carbalkoxy of 2-7 carbon atoms, trifluoromethyl, trifluoromethoxy, amino, dialkylamino of 1-6 carbon atoms per alkyl group, dialkylaminoalkyl of 3-12 carbon atoms, hydroxyalkyl of 1-6 carbon atoms, alkoxyalkyl of 2-12 carbon atoms, alkylthio of 1-6 carbon atoms, $-SO_3H$, $-PO_3H$, and $-CO_2H$;

n = 0-6;

with the proviso that R and R^1 are both not hydrogen, or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1 wherein R^1 is hydrogen or a pharmaceutically acceptable salt thereof.

3. The compound of claim 2 wherein R^1 is hydrogen and n = 0 or a pharmaceutically acceptable salt thereof.

4. The compound of claim 3 wherein R^2 is pyridinyl, pyrazinyl, triazinyl, pyrimidinyl, pyridazinyl, imidazolyl, pyrazolyl, quinolinyl, tetrahydroquinolinyl, or isoquinolinyl, or a pharmaceutically acceptable salt thereof.

5. ~~The~~ A compound of claim 1 which ~~is~~ is one of the following rapamycin 42-ester with 2-methylnicotinic ~~acid or a pharmaceutically acceptable salt thereof.~~

~~6. The compound of claim 1 which is~~ rapamycin 42-ester with nicotinic ~~acid or a pharmaceutically acceptable salt thereof.~~

~~7. The compound of claim 1 which~~ is rapamycin 42-ester with 6-methylpyridine-3-carboxylic acid ~~or a pharmaceutically acceptable salt thereof.~~

~~8. The compound of claim 1 which~~ is rapamycin 42-ester with 5-methylpyrazine-2-carboxylic acid ~~or a pharmaceutically acceptable salt thereof.~~

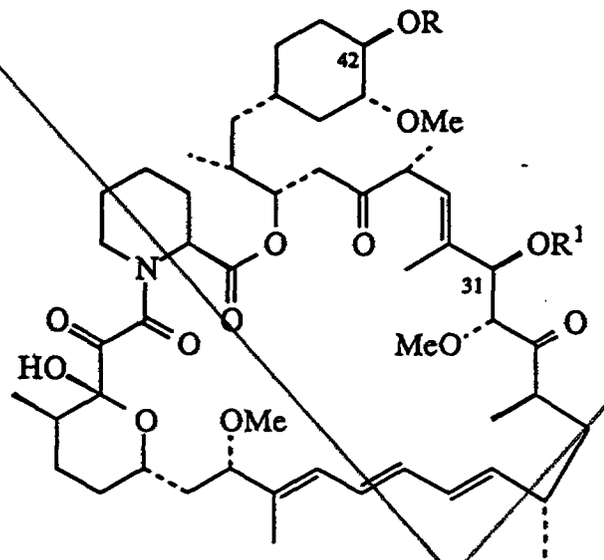
~~9. The compound of claim 1 which~~ rapamycin 42-ester with quinoline 6-carboxylic acid ~~is or a pharmaceutically acceptable salt thereof.~~

~~10. The compound of claim 1 which is~~ rapamycin 42-ester with quinoline-8-carboxylic acid ~~or a pharmaceutically acceptable salt thereof.~~ or

~~11. The compound of claim 1 which is~~ rapamycin 42-ester with 1-methyl-1,2,3,4-tetrahydroquinoline-6-carboxylic acid, or a pharmaceutically acceptable salt thereof.

6. Use of a compound ~~20~~ as claimed in claim 1 in the preparation of a medicament for

~~19. A method of~~ inducing immunosuppression in a mammal ~~in need thereof, which comprises administering an immunosuppressive effective amount of a compound of the structure~~



I

wherein R and R^1 are each, independently, $-\overset{O}{\overset{\|}{C}}-(CH_2)_nR^2$ or hydrogen;

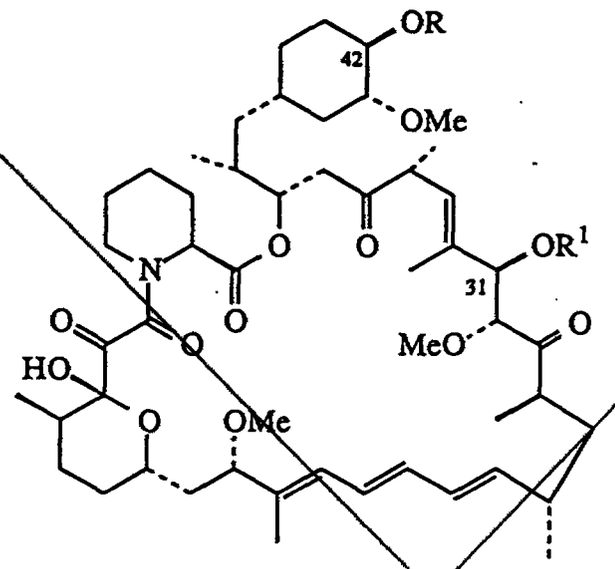
R^2 is a heterocyclic radical of 5-12 carbon atoms having at least one N, O, or S, which may be optionally mono-, di-, or tri- substituted with a group selected from alkyl of 1-6 carbon atoms, arylalkyl in which the alkyl portion contains 1-6 carbon atoms, alkoxy of 1-6 carbon atoms, cyano, halo, hydroxy, nitro, carbalkoxy of 2-7 carbon atoms, trifluoromethyl, trifluoromethoxy, amino, dialkylamino of 1-6 carbon atoms per alkyl group, dialkylaminoalkyl of 3-12 carbon atoms, hydroxyalkyl of 1-6 carbon atoms, alkoxyalkyl of 2-12 carbon atoms, alkylthio of 1-6 carbon atoms, $-SO_3H$, $-PO_3H$, and $-CO_2H$;

n = 0-6;

with the proviso that R and R^1 are both not hydrogen, or a pharmaceutically acceptable salt thereof.

7. Use of a compound as claimed in claim 1 in the preparation of a medicament for

~~13.~~ ~~A method of~~ treating transplantation rejection or graft vs. host disease in a mammal ~~in need thereof which comprises administering an antirejection effective amount of a compound of the structure~~



I

wherein R and R^1 are each, independently, $-\overset{O}{\overset{\|}{C}}-(CH_2)_nR^2$ or hydrogen;

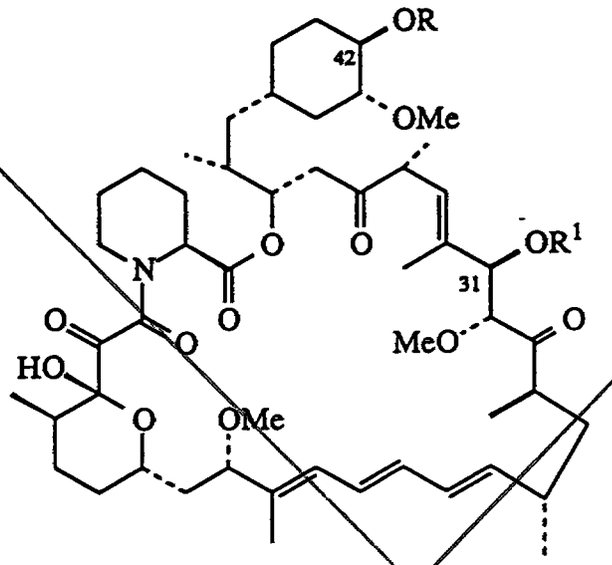
R^2 is a heterocyclic radical of 5-12 carbon atoms having at least one N, O, or S, which may be optionally mono-, di-, or tri- substituted with a group selected from alkyl of 1-6 carbon atoms, arylalkyl in which the alkyl portion contains 1-6 carbon atoms, alkoxy of 1-6 carbon atoms, cyano, halo, hydroxy, nitro, carbalkoxy of 2-7 carbon atoms, trifluoromethyl, trifluoromethoxy, amino, dialkylamino of 1-6 carbon atoms per alkyl group, dialkylaminoalkyl of 3-12 carbon atoms, hydroxyalkyl of 1-6 carbon atoms, alkoxyalkyl of 2-12 carbon atoms, alkylthio of 1-6 carbon atoms, $-SO_3H$, $-PO_3H$, and $-CO_2H$;

n = 0-6;

with the proviso that R and R^1 are both not hydrogen, or a pharmaceutically acceptable salt thereof.

8. Use of a compound as claimed in claim 1 in the preparation of a medicament for

~~14.~~ ~~A method of~~ treating rheumatoid arthritis in mammal in need thereof ~~which comprises administering an antiarthritis effective amount of a compound of the structure~~



I

wherein R and R^1 are each, independently, $-C-(CH_2)_nR^2$ or hydrogen;

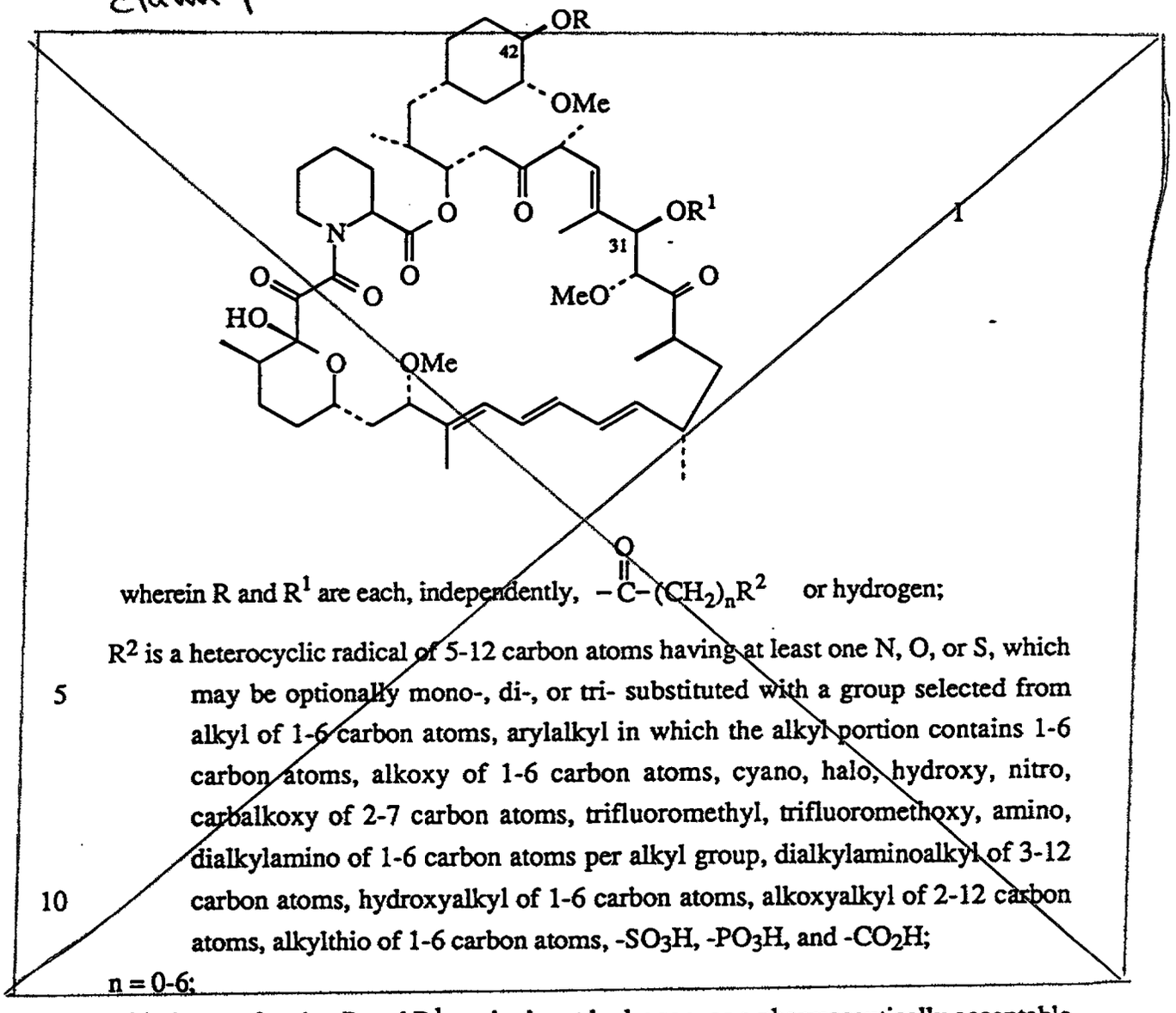
R^2 is a heterocyclic radical of 5-12 carbon atoms having at least one N, O, or S, which may be optionally mono-, di-, or tri- substituted with a group selected from alkyl of 1-6 carbon atoms, arylalkyl in which the alkyl portion contains 1-6 carbon atoms, alkoxy of 1-6 carbon atoms, cyano, halo, hydroxy, nitro, carbalkoxy of 2-7 carbon atoms, trifluoromethyl, trifluoromethoxy, amino, dialkylamino of 1-6 carbon atoms per alkyl group, dialkylaminoalkyl of 3-12 carbon atoms, hydroxyalkyl of 1-6 carbon atoms, alkoxyalkyl of 2-12 carbon atoms, alkylthio of 1-6 carbon atoms, $-SO_3H$, $-PO_3H$, and $-CO_2H$;

n = 0-6;

with the proviso that R and R^1 are both not hydrogen, or a pharmaceutically acceptable salt thereof.

as claimed in claim 1

~~15.~~ 9. A pharmaceutical composition which comprises a compound ~~of the structure~~



1

wherein R and R^1 are each, independently, $-C-(CH_2)_nR^2$ or hydrogen;

R^2 is a heterocyclic radical of 5-12 carbon atoms having at least one N, O, or S, which may be optionally mono-, di-, or tri- substituted with a group selected from alkyl of 1-6 carbon atoms, arylalkyl in which the alkyl portion contains 1-6 carbon atoms, alkoxy of 1-6 carbon atoms, cyano, halo, hydroxy, nitro, carbalkoxy of 2-7 carbon atoms, trifluoromethyl, trifluoromethoxy, amino, dialkylamino of 1-6 carbon atoms per alkyl group, dialkylaminoalkyl of 3-12 carbon atoms, hydroxyalkyl of 1-6 carbon atoms, alkoxyalkyl of 2-12 carbon atoms, alkylthio of 1-6 carbon atoms, $-SO_3H$, $-PO_3H$, and $-CO_2H$;

n = 0-6;

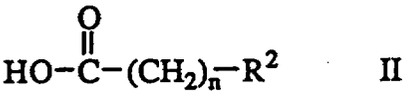
~~with the proviso that R and R^1 are both not hydrogen,~~ or a pharmaceutically acceptable salt thereof, and a pharmaceutical carrier.

10. A process for preparing a compound of Claim 1 which comprises:

a) acylating rapamycin or a functional derivative thereof with an acylating agent, or

b) sequentially acylating rapamycin or a functional derivative thereof with two acylating agents.

said acylating agents selected from acids of formula



II

wherein n and R^2 are as defined in Claim 1, or a reactive derivative thereof, if desired protecting the 42-position of rapamycin with an appropriate protecting group and removing same as required.