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SEMI-SYNTHETIC RHODOMYCINS, A PROCESS FOR THEIR PREPARATION AND THEIR USE AS CYTOSTATICS

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(71) Applicant(s)
BEHRINGEWERKE AKTIENGESELLSCHAFT

(72) Inventor(s)
MANFRED GERKEN; CENEK KOLAR; HANS PETER KRAEMER; DIETER HOFFMANN; PETER HERMENTIN

(74) Attorney or Agent
WATERMARK PATENT & TRADEMARK ATTORNEYS , Locked Bag 5, HAWTHORN ViC 3122

(56) Prior Art Documents
EP 242695
EP 203329
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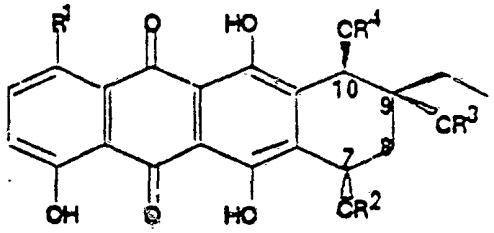
(57) Claim

1. A compound of the formula I or a salt thereof with an inorganic or organic acid

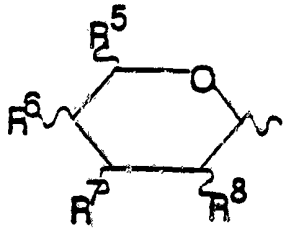


I

in which:

R^1 is hydrogen or a hydroxyl group

R^2 is hydrogen or a structure of the formula II or IV or, together with R^3, of the formula III



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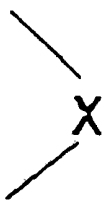

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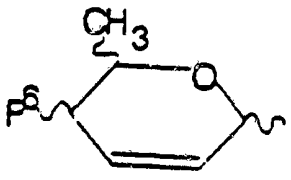

IV

.../2

R^3 is hydrogen or a structure of the formula II or IV or, together with R^2, of the formula III,

R^4 is hydrogen, trimethylsilyl, a protective group which is customary in carbohydrate chemistry, preferably acetyl, trifluoroacetyl, benzoyl or substituted benzoyl, such as para-nitrobenzoyl, a structure of the formula II or a structure of the formula IV,

R^5 is hydrogen, methyl, hydroxymethyl, acyloxymethyl, (C1-C8) or alkoxymethyl (C1-C8),

R^6, R^7 and R^8 independently of one another are hydrogen, hydroxyl, aliphatic acyloxy (C1-C8), benzoyloxy or substituted benzoyloxy, such as para-nitrobenzoyloxy, alkoxy (C1-C8), allyloxy, benzyloxy or substituted benzyloxy or halogen, and R^7 can furthermore be NH_2, NHacyl (C1-C8), $N(alkyl)_2$ (C1-C8), $N(CH_2CN)_2$, $NH(CH_2CN)$ or azido, and

X is a bidentate protective group which is customary in carbohydrate chemistry, preferably alkylboronyl, phenylboronyl, an alkyl ortho-carboxylate, preferably methyl orthoformate or ethyl orthoacetate, or a ketal or acetal, preferably isopropyliden or benzylidene,

the compounds where $R^1=R^2=R^3=R^4=H$, $R^1=OH$ and $R^2=R^3=R^4=H$, $R^1=R^3=R^4=H$ and $R^2=\alpha$-L-daunosaminyl or α-L-rhodosaminyl or 4'-acyl-α-L-rhodosaminyl, $R^1=OH$ or H, $R^3=H$ and $R^2=R^4=\alpha$-L-rhodosaminyl or 4'-acyl-α-L-rhodosaminyl and $R^1=R^2=R^3=H$ and $R^4=\alpha$-L-rhodosaminyl being excluded.

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COMPLETE SPECIFICATION

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Name of Applicant : BEHRINGWERKE AKTIENGESELLSCHAFT

Address of Applicant : D-3550 Marburg, Federal Republic of Germany

Actual Inventor: MANFRED GERKEN, CENEK KOLAR, HANS PETER KRAEMER, DIETER HOFFMANN and PETER HERMENTIN

Address for Service : EDWD. WATERS & SONS,
50 QUEEN STREET, MELBOURNE, AUSTRALIA, 3000.

Complete Specification for the invention entitled:

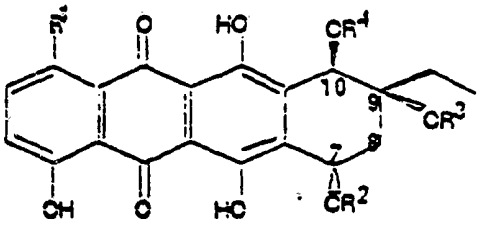
SEMI-SYNTHETIC RHODOMYCINS, A PROCESS FOR THEIR PREPARATION AND THEIR USE AS CYTOSTATICS

The following statement is a full description of this invention, including the best method of performing it known to :- us

BEHRINGWERKE Aktiengesellschaft 87/B 012 - Ma 627
Dr.Ha/Bn

Semi-synthetic rhodomycins, a process for their preparation and their use as cytostatics

The invention relates to compounds of the formula I and their salts with an inorganic or organic acid

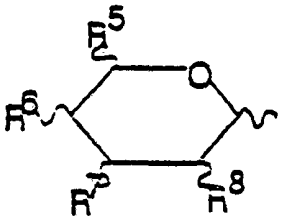


I

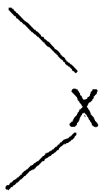
in which:

R^1 is hydrogen or a hydroxyl group

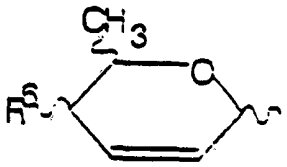
R^2 is hydrogen or a structure of the formula II or IV or, together with R^3, of the formula III



II



III



IV

R^3 is hydrogen or a structure of the formula II or IV or, together with R^2, of the formula III,

R^4 is hydrogen, trimethylsilyl, a protective group which is customary in carbohydrate chemistry, preferably acetyl, trifluoroacetyl, benzoyl or substituted benzoyl, such as para-nitrobenzoyl, a structure of the formula II or a structure of the formula IV,

R^5 is hydrogen, methyl, hydroxymethyl, acyloxymethyl, (C1-C8) or alkoxymethyl (C1-C8),

R^6, R^7 and R^8 independently of one another are hydrogen,

hydroxyl, aliphatic acyloxy (C1-C8), benzoyloxy or substituted benzoyloxy, such as para-nitrobenzoyloxy, alkoxy (C1-C8), allyloxy, benzyloxy or substituted benzyloxy or halogen, and R^7 can furthermore be NH_2, NHacyl (C1-C8), $N(alkyl)_2$ (C1-C8), $N(CH_2CN)_2$, $NH(CH_2CN)$ or azido, and

X is a bidentate protective group which is customary in carbohydrate chemistry, preferably alkylboronyl, phenylboronyl, an alkyl ortho-carboxylate, preferably methyl orthoformate or ethyl orthoacetate, or a ketal or acetal, preferably isopropylidene or benzylidene,

the compounds where $R^1=R^2=R^3=R^4=H$, $R^1=OH$ and $R^2=R^3=R^4=H$, $R^1=R^3=R^4=H$ and $R^2=\alpha$-L-daunosaminyl or α-L-rhodosaminyl or 4'-acyl-α-L-rhodosaminyl, $R^1=OH$ or H, $R^3=H$ and $R^2=R^4=\alpha$-L-rhodosaminyl or 4'-acyl-α-L-rhodosaminyl and $R^1=R^2=R^3=H$ and $R^4=\alpha$-L-rhodosaminyl being excluded.

Numerous anthracyclines exhibit cytostatic activity, and some are used for the therapy of tumors.

Known compounds are β-rhodomycins (structures of the formula I where $R^1=H$) in which position 7 and position 10 are linked α-glycosidically with L-rhodosamine or in which only position 7 is linked α-glycosidically with L-rhodosamine or L-daunosamine, and β-iso-rhodomycins (structures of the formula I where $R^1=OH$) in which position 7 and 10 are each linked with α-L-rhodosamine, and the photolytic mono-demethylation products of these L-rhodosamine glycosides and β-rhodomycinone with oligosaccharide side chains on positions 7 or 10 or on 7 and 10, which are called cytorhodins. The microbial glycosidation of a trisaccharide consisting of L-rhodosamine, L-deoxyfucose and cinerulose A on the 7-position of the β-rhodomycinone is known from Journal of Antibiotics 33, 1331 (1980).

No chemical glycosidation process for β-rhodomycinone or β-iso-rhodomycinone has as yet been described. Because of the many glycosidation possibilities of the three hydroxyl groups in the A ring of the β-rhodomycinone (structure of the formula I where $R^1=R^2=R^3=R^4=H$), selective glycosidations are incomparably more difficult.

Surprisingly, it has been found that β-rhodomycinone and β-iso-rhodomycinone can be glycosidated selectively using certain protective groups on positions 7, 9 and 10 and the glycosides thus obtained, in particular 7-O-α-L-acosaminyl-β-rhodomycinone or 7-O-(3'-N,N-dimethyl-α-L-acosaminyl)-β-rhodomycinone have a cytostatic activity comparable to that of adriamycin.

The present invention is therefore based on the object of preparing, starting from the β-(iso-)rhodomycinones obtainable biologically, novel mono-, bis- and tris-glycosyl-β-(iso-)rhodomycinones which are distinguished by cytostatic activity and are therefore suitable for the treatment of tumors.

This object has been achieved by preparation of compounds of the abovementioned formula I with the definitions given there for R^1 to R^8 and X and the exceptions given.

The invention thus relates to compounds of this formula I with the definitions and exceptions given.

In the following list of compounds of the formula I with the radicals R^1 to R^8 given therein, the group of compounds following a group of compounds is in each case preferable to that group.

1) R^1 to R^8 have the meanings given.
2) R^1 and R^4 have the meanings given, R^2 and R^3 independently of one another are hydrogen or a

structure of the formula II or IV with the meanings given for R^5 to R^8.

3) R^1 is hydrogen and the other definitions are as under 2).

4) R^3 is hydrogen and the other definitions are as under 2).

5) R^1 and R^4 have the meanings given and R^2 and R^3 independently of one another are hydrogen or a structure of the formula II or IV, in which R^5 is methyl, R^6 and R^7 have the meanings given and R^8 is hydrogen or halogen.

6) R^1 is hydrogen and the other definitions are as under 5).

7) R^3 is hydrogen and the other definitions are as under 5).

8) R^1 and R^4 have the meanings given and R^2 and R^3 independently of one another are hydrogen or a structure of the formula II or IV, in which R^5 is methyl, R^6 has the meaning given, R^7 is NH_2, NHacyl (C1-C8), N(alkyl)$_2$ (C1-C8), N($CH_2C_6H_5$)$_2$, NH(CH_2CN) or azido and R^8 is hydrogen or halogen.

9) R^1 is hydrogen and the other definitions are as under 8).

10) R^3 is hydrogen and the other definitions are as under 8).

11) R^1 and R^4 have the meanings given and R^2 and R^3 independently of one another are hydrogen or a structure of the formula II or IV, in which R^5 is methyl, R^6 and R^7 have the meanings given and R^8 is hydrogen or halogen, and the structures of the formula II or IV belong to the L-series of carbohydrates.

12) R^1 is hydrogen and the other definitions are as under 11).

13) R^3 is hydrogen and the other definitions are as under 11).

14) R^1 and R^4 have the meanings given and R^2 and R^3 independently of one another are hydrogen or a structure of the formula II or IV, in which R^5 is

methyl, R^6 has the meaning given, R^7 is NH_2, NHacyl (C1-C8), $N(alkyl)_2$ (C1-C8), $N(CH_2CN)_2$, $NH(CH_2CN)$ or azido and R^8 is hydrogen or halogen, and the structures of the formula II or IV belong to the L-series of carbohydrates.

15) R^1 is hydrogen and the other definitions are as under 14).

16) R^3 is hydrogen and the other definitions are as under 14).

17) R^1 and R^3 are hydrogen and the other definitions are as under 2).

18) R^1 and R^3 are hydrogen and the other definitions are as under 5).

19) R^1 and R^3 are hydrogen and the other definitions are as under 8).

20) R^1 and R^3 are hydrogen and the other definitions are as under 11).

21) R^1 and R^3 are hydrogen and the other definitions are as under 14).

22) R^2 and R^3 are hydrogen and the other definitions are as under 2).

23) R^3 and R^4 are hydrogen and the other definitions are as under 2).

24) R^2 and R^3 are hydrogen and the other definitions are as under 5).

25) R^3 and R^4 are hydrogen and the other definitions are as under 5).

26) R^2 and R^3 are hydrogen and the other definitions are as under 8).

27) R^3 and R^4 are hydrogen and the other definitions are as under 8).

28) R^2 and R^3 are hydrogen and the other definitions are as under 11).

29) R^3 and R^4 are hydrogen and the other definitions are as under 11).

30) R^2 and R^3 are hydrogen and the other definitions are as under 14).

31) R^3 and R^4 are hydrogen and the other definitions

are as under 14).

32) R^1, R^2 and R^3 are hydrogen and R^4 is as under 2).
33) R^1, R^3 and R^4 are hydrogen and R^2 is as under 2).
34) R^1, R^2 and R^3 are hydrogen and R^4 is as under 5).
35) R^1, R^3 and R^4 are hydrogen and R^2 is as under 5).
36) R^1, R^2 and R^3 are hydrogen and R^4 is as under 8).
37) R^1, R^3 and R^4 are hydrogen and R^2 is as under 8).
38) R^1, R^2 and R^3 are hydrogen and R^4 is as under 11).
39) R^1, R^3 and R^4 are hydrogen and R^2 is as under 11).
40) R^1, R^2 and R^3 are hydrogen and R^4 is as under 14).
41) R^1, R^3 and R^4 are hydrogen and R^2 is as under 14).

The invention also relates to a process for the preparation of a compound of the formula I with the definitions given, which comprises first selectively blocking a compound of the formula I in which R^1 has the meaning initially given and R^2 to R^4 are hydrogen by a structure of the formula III on positions 7 and 9 as described below, a compound of the formula I in which R^2 and R^3 together are a structure of the formula III being obtained, and subsequently replacing R^4=H by an acyl protective group, a trimethylsilyl group or a carbohydrate derivative of the structure II or IV and if appropriate deblocking the compound and/or modifying it on the amino function, after which, following selective splitting off of the protective groups on position 7 and 9, either only position 7 or positions 7 and 9 can be glycosidated and the glycosyl radicals can be deblocked and modified, or, after introduction of an acyl group or trimethylsilyl group at position 10 and subsequent selective deblocking at positions 7 and 9, first glycosidating the compound at position 7 or simultaneously at positions 7 and 9, subsequently deblocking the compound completely or partly and if appropriate modifying it on the amino functions, and only then glycosidating position 10 and modifying this glycoside, these steps in detail being carried out by

a) reacting a compound of the formula I in which R^1 has

the meaning initially given and R^2 to R^4 are hydrogen with a boric acid, such as phenylboric acid, or with a ketone, such as acetone, or a ketal, such as 2,2-dimethoxypropane, or an acetal, such as benzaldehyde dimethyl acetal, in a suitable organic solvent, such as toluene or dimethylformamide or mixtures thereof, with a catalyst, such as a mineral, carboxylic or sulfonic acid, at a temperature between 0°C and the boiling point of the solvent, if appropriate with the addition of a dehydrating agent, such as a 4Å molecular sieve, to give a compound of the formula I in which R^1 has the meaning initially given and R^2 together with R^3 form a compound of the formula III, which is isolated by filtration and by removal of the solvent and crystallized out of an organic solvent, such as petroleum ether, after which the hydroxyl group on position 10 is derivatized in a suitable manner,

b) if appropriate acylating with a carboxylic acid anhydride, such as acetic anhydride or trifluoroacetic anhydride, or a phenylcarboxylic acid anhydride or a carboxylic acid halide or by reacting with trimethylsilyl trifluoromethanesulfonate in a suitable organic solvent, such as chloroform, methylene chloride, toluene or mixtures thereof, at a temperature between -40°C and the boiling point of the solvent and in the presence of a base, such as triethylamine or pyridine, to give a compound of the formula I in which
R^1 has the meaning initially given,
R^2 together with R^3 is a structure of the formula III and
R^4 is acyl or trimethylsilyl,

c) or, for example, reacting the compound obtained under a) with 3,4-dihydro-2H-pyran in a suitable organic solvent, such as chloroform, methylene chloride, dimethylformamide or toluene, in the presence of a

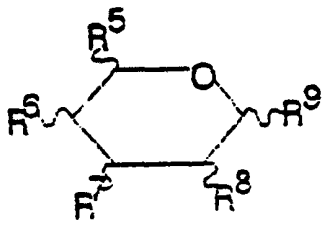
catalyst, such as para-toluenesulfonic acid and a desiccant, such as a 4Å molecular sieve, at a temperature between -30°C and the boiling point of the solvent, to give a compound of the formula I in which

R^1 has the meaning initially given,

R^2 together with R^3 is a structure of the formula III and

R^4 is a structure of the formula II, where R^5 to R^8 are hydrogen,

d) or, for example, reacting the compound obtained under a) with a carbohydrate derivative of the formula V



V

in which

R^5 to R^8, as suitable protective groups, have the meanings initially given and

R^9 is halogen, such as Cl or Br, O-acyl or another leaving group which is customary for glycosidation reactions,

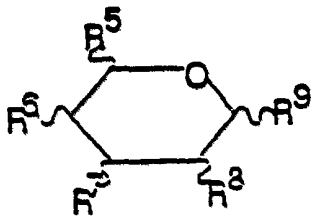
under the conditions customary in carbohydrate chemistry, to give a compound of the formula I in which

R^1 has the meaning initially given,

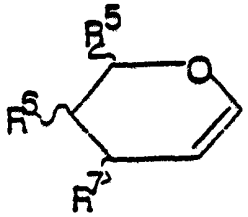
R^2 together with R^3 is a structure of the formula III and

R^4 is a structure of the formula II,

e) or, for example, reacting the compound obtained under a) with a functionalized carbohydrate of the general formula V or VI



V



VI

in which
R^5 to R^8 have the meanings initially given, with the exception of hydroxymethyl, hydroxyl, NH_2, $N(CH_2CN)_2$ and $NH(CH_2CN)$ and
R^9 is acyl which is bonded via oxygen, such as aliphatic acyloxy (C1-C8), such as acetyl, benzoyloxy or substituted benzoyloxy, such as para-nitrobenzoyloxy,

in the presence of an organic solvent, such as chloroform, methylene chloride, toluene, ether, dimethylformamide, acetone, acetonitrile or nitromethane or mixtures thereof, a catalyst, such as para-toluenesulfonic acid or a trialkylsilyl trifluoromethanesulfonate, and if appropriate an acid-trapping agent and a desiccant, such as a molecular sieve, at a reaction temperature of -70°C to +30°C under a protective gas atmosphere, such as nitrogen or argon, to give a compound of the formula I

in which
R^1 has the meaning given,
R^2 together with R^3 is a structure of the formula III and
R^4 is a structure of the formula II or IV, in which
R^5 to R^8 have the meanings initially given, with the exception of hydroxymethyl, hydroxyl, NH_2, $N(CH_2CN)_2$ and $NH(CH_2CN)$,

f) and, if appropriate, possibly deblocking the compound

of stages b) to e) on positions 7 and 9 by reacting this compound in a suitable organic solvent, such as chloroform, methylene chloride, dimethylformamide, toluene or methanol, with a catalyst, such as dilute aqueous solutions of carboxylic acids or para-toluenesulfonic acid, and if appropriate with a diol, such as 2-methyl-2,4-pentanediol, at a temperature between 0°C and the boiling point of the solvent, to give a compound of the general formula I in which
R^1 has the meaning given,
R^2 and R^3 are hydrogen and
R^4 has the meaning given, with the exception of hydrogen,

g) and subsequently, if appropriate, possibly selectively partly or completely deblocking the compound of stage f) in which R^4 is a structure of the formula II or IV with, as radicals R^5 to R^8, one of the protective groups customary in carbohydrate chemistry, in a manner which is known per se on the protected hydroxyl functions and/or on the protected amino functions under the conditions customary in carbohydrate chemistry by means of an inorganic or organic base, such as alkali metal or alkaline earth metal hydroxides, sodium carbonate and triethylamine, in a solvent, such as water, methanol, ethanol or tetrahydrofuran or mixtures thereof, to give a compound of the formula I in which
R^1 is hydrogen or hydroxyl,
R^2 and R^3 are hydrogen and
R^4 is a structure of the formula II or IV, in which
R^5 is hydrogen, methyl, hydroxymethyl or alkoxymethyl,
R^6 is hydrogen, hydroxyl, alkoxy or halogen,
R^7 is NH_2 $N(alkyl)_2$, azido, hydroxyl or alkoxy and
R^8 has the same meaning as R^6 but is independent thereof,

h) and, if appropriate, reacting the compound of stage g) of the formula I, in which

R^1 to R^3 have the meanings given under g) and
R^4 is a structure of the formula II, in which
R^5, R^6 and R^8 have the meanings given under g) and
R^7 is NH_2,

under the conditions which are known per se for reductive amination, to give the corresponding compound of the formula I in which

R^1 to R^3 have the meanings given under g) and
R^4 is a structure of the formula II,

in which

R^5, R^6 and R^8 have the meanings given under g) and
R^7 is $N(alkyl)_2$, or

i) furthermore converting a compound of stage g) of the general formula I in which
R^1 to R^3 have the meanings given under g) and
R^4 is a structure of the formula II in which
R^5, R^6 and R^8 have the meanings given under g) and
R^7 is NH_2,

by reaction with iodoacetonitrile or bromoacetonitrile in a suitable solvent, for example dimethylformamide, in the presence of a suitable base, such as triethylamine, into a compound of the formula I in which R^1 to R^3 have the meanings given under g) and R^4 is a structure of the formula II, in which
R^5, R^6 and R^8 have the meanings given under g) and
R^7 is $N(CH_2CN)_2$ or $NH(CH_2CN)$ and

k) if appropriate glycosidating the compound formed in stage f), h) or i) under the conditions already mentioned in stage e), either only position 7 or simultaneously positions 7 and 9 being glycosidated, depending on the amount of glycosyl donor used, to give

products which correspond to the general formula I in which

R^1 has the meaning given,

R^2 is a structure of the formula II or IV, in which

R^5 to R^8 have the meanings initially given, with the exception of hydroxymethyl, hydroxyl, NH_2, $N(CH_2CN)_2$ and $NH(CH_2CN)$,

R^3 is hydrogen or corresponds to R^2 and

R^4 is acyl, trimethylsilyl or a structure of the general formula II or IV in which

R^5 to R^8 have the meanings initially mentioned, with the exception of hydroxymethyl, hydroxyl and NH_2, and, if appropriate,

l) converting one of the compounds formed in stage f), h) or i) with a glycal of the formula VI, in which R^5 to R^7 have the meanings given in stage e), in the presence of an organic solvent, such as chloroform, methylene chloride, toluene, ether, acetone or acetonitrile or mixtures thereof, with N-iodosuccinimide and if appropriate with a desiccant, such as a molecular sieve, at a temperature from -40°C to +40°C under a protective gas atmosphere, such as nitrogen or argon, into a compound of the formula I in which

R^1 has the meaning given and

R^2 is a structure of the formula II, in which

R^5 is hydrogen, methyl, acyloxymethyl (C1-C8) or alkoxymethyl (C1-C8),

R^6 is acyloxy, alkyloxy, allyloxy or benzyloxy,

R^7 is acyloxy, alkyloxy, allyloxy, benzyloxy, NHacyl, $N(alkyl)_2$ or azido and

R^8 is iodine, and

R^3 and R^4 have the meanings given in stage k), and

m) if appropriate deblocking the compound formed in stage k) or l) in accordance with the conditions of stage g), to give a compound of the formula I in which

R^1 has the meaning given and

R^2 is a structure of the formula II or IV, in which
R^5 is hydrogen, methyl, hydroxymethyl or alkyloxymethyl,
R^6 is hydrogen, hydroxyl, alkyloxy or halogen,
R^7 is NH_2 or $N(alkyl)_2$, azido, hydroxyl or alkoxy and
R^8 has the same meaning as R^6, but is independent thereof,
R^3 is hydrogen or corresponds to R^2 and
R^4 is hydrogen, trimethylsilyl or a structure of the general formula II or IV, in which
R^5 is hydrogen, methyl, hydroxymethyl or alkoxymethyl,
R^6 is hydrogen, hydroxyl, alkoxy or halogen,
R^7 is NH_2, $N(alkyl)_2$, $N(CH_2CN)_2$ or $NH(CH_2CN)$, azido, hydroxyl or alkoxy and
R^8 has the same meaning as R^6, but is independent thereof, or

n) also deblocking the compound formed in stage k) or l) under the conditions of stage g) so that only position 10 is selectively deblocked, to give a compound of the formula I in which
R^1 has the meaning given,
R^2 is a structure of the formula II or IV, in which
R^5 to R^8 have the meanings initially given, with the exception of hydroxymethyl, hydroxyl and NH_2,
R^3 is hydrogen or corresponds to R^2 and
R^4 is hydrogen,

o) and subsequently, if appropriate, converting the compound of stage m), in which R^2 is a structure of the formula II where R^7 is NH_2 and R^3 is hydrogen or R^2, into the corresponding compounds in which R^6 is $N(alkyl)_2$, again in the manner of reductive amination described for stage h), or, if appropriate,

p) converting a compound of stage m) in which R^2 is a structure of the formula II, where R^7 is NH_2 and R^3

is hydrogen or R^2, into the corresponding cyanomethyl derivatives in which
R^7 is $N(CH_2CN)_2$ or $NH(CH_2CN)$ in accordance with the conditions of stage i), and, if appropriate,

q) glycosidating a compound of stage n) under the conditions already given in stage e), either only position 10 or simultaneously positions 9 and 10 being glycosidated, depending on the amount of glycosyl donor used, to give a compound of the formula I in which

R^1 is hydrogen or hydroxyl and
R^2 is a structure of the general formula II or IV, in which
R^5 to R^8 have the meanings initially given, with the exception of hydroxymethyl, hydroxyl and NH_2,
R^3 is hydrogen or R^2 or R^4 and
R^4 is a structure of the general formula II or IV, in which
R^5 to R^8 have the meanings initially given, with the exception of hydroxymethyl, hydroxyl, NH_2, $N(CH_2CN)_2$ or $NH(CH_2CN)$, and, if appropriate,

r) also carrying out the reaction of stages c), d) and l) on a compound of stage n) so as to give a compound of the formula I in which
R^1 has the meaning initially given and
R^2 is a structure of the formula II or IV, in which
R^5 to R^8 have the meanings initially given, with the exception of hydroxymethyl, hydroxyl and NH_2,
R^3 is hydrogen or R^2 or R^4 and
R^4 is a structure of the general formula II or IV in which
R^5 to R^8 have the meanings initially given, with the exception of hydroxymethyl, hydroxyl, NH_2, $N(CH_2CN)_2$ and $NH(CH_2CN)$, and, if appropriate,

s) deblocking this compound of stage q) or r) again as

described in stage g), to give a compound of the formula I in which
R^1 has the meaning initially given and
R^2, R^3 and R^4 independently of one another are hydrogen or a structure of the formula II or IV, in which
R^5 to R^8 have the meanings initially given, with the exception of acyloxymethyl, acyloxy, benzoyloxy or substituted benzoyloxy or NHacyl, and, if appropriate,

t) converting the compound of stage s) into the corresponding derivative in which the radical R^7, which in stage s) was an NH_2 group, is converted into $N(alkyl)_2$, by means of reduction amination in accordance with stage h), or

u) moreover converting a compound of stage s) into the corresponding cyanomethyl derivative in which the radical R^7, which in stage s) was an NH_2 group, into $NH(CH_2CN)$ in accordance with the conditions of stage i),

v) and, if appropriate, reacting a compound of the formula I in which
R^1, R^2 and R^3 have the meanings given and
R^4 is trimethylsilyl,
with tetrabutylammonium fluoride in an organic solvent, such as tetrahydrofuran, diethyl ether, dioxane or mixtures thereof, at temperatures between -40°C and the boiling point of the solvent, to give a compound of the formula I in which
R^1, R^2 and R^3 have the meanings given above and
R^4 is hydroxyl,

w) and, if appropriate, converting compounds of the formula I in which R^1, R^2, R^3 and R^4 have the meanings given and R^7 is NH_2, $N(alkyl)_2$ (C1-C8), $N(CH_2CN)_2$

or $NH(CH_2CN)$ into the salt of an inorganic or organic acid.

The invention also relates to medicaments which contain one or more compounds of the formula I or salts thereof with an inorganic acid, such as HCl, or an organic acid, such as glutamic acid or glucoronic acid, as the active substance.

Such a compound can be processed together with the customary pharmaceutical formulating agents and/or diluents to give a medicament which is used in particular in cancer therapy.

The method of dosage and use essentially correspond here to those for the known anthracyclines, such as adriamycin, daunomycin or aclacinomycin.

The medicaments prepared in this way can also additionally contain other active substances as long as these do not exhibit undesirable side effects together with the compounds according to the invention.

The invention also relates to a composition containing a compound of the formula I, with the definitions and exceptions given, and a carrier substance.

The invention furthermore relates to the use of a compound of the formula I, with the definitions and exceptions given, as a medicament.

The cytostatic activity of the compounds according to the invention has been tested with the aid of L1210 leukemia cells from mice. Colony formation of L1210 leukemia cells on agar plates was used for this. This method is used to demonstrate the influence of the test substances on the growth behavior of the cells following incubation for 1 hour or over several generations. At a cell cycle

time of 10-12 hours, about 14 successive generations are thereby observed over the test period of 7 days. In this test, the cytostatic substances according to the invention effect a reduction of the number of colonies to be observed in comparison with an untreated control sample.

Details of the test method are to be found from the following procedure for the determination of colony formation.

Procedure for determination of colony formation of L1210 leukemia cells in soft agar

500 leukemia cells per plate were incubated with different concentrations of the test substance at 37°C for 1 hour. The cells were then washed twice with McCoy5A medium and finally poured into Petri dishes, after addition of 0.3% agar. Controls were incubated only with fresh medium. Instead of incubation for one hour, in some cases different concentrations and test substances were admixed to the upper agar layer in order thus to achieve continuous exposure of the cells over the entire incubation period. After the agar had solidified, the plates were incubated in an incubating cabinet at 37°C for 7 days (5% by volume of CO_2, 95% relative atmospheric humidity). The number of colonies formed with a diameter of more than 60 µm was then counted. The results were stated as the number of colonies in the treated agar plates as a percentage of the untreated control. The IC_{50} was determined from the resulting dose-effect curve as a measure of the activity of the substance. The results for the compounds described here are summarized in comparison with adriamycin in the following Table 1.

Table 1, Part 1:

Substance No. (Example)	Long-term incubation IC_{50} (µg/ml)	1 hour incubation IC_{50} (µg/ml)
Adriamycin	0.02	0.04
8	>1	>1
9	0.6	>10
10	0.9	6.5
11	>1	>1
12	0.5	>1
13	0.03	>1
14	0.024	>1
15	0.004	0.02
16	0.006	0.02
17	0.004	0.09
18	0.13	>1
19	0.11	>1
21	0.5	>1
24	>1	>1
25	>1	>1
27	>1	>1
28	>1	>1
29	>10	>1
30	0.5	>1

Table 1, Part 2:

Substance No. (Example)	Long-term incubation IC_{50} (µg/ml)	1 hour incubation IC_{50} (µg/ml)
33	>1	>1
34	0.026	0.09
35	>1	>1
37	>1	>1
38	>1	>1
40	0.85	>1
42	0.16	>1
44		>1
45		0.29
46		0.11
48		0.095
49		>1
50	0.1	
51	0.4	0.68
52		0.66
53	0.04	0.05

Examples

The structures of the compounds prepared were determined by means of ^{1}H- and ^{13}C-NMR spectroscopy, incorporating two-dimensional NMR methods and other multi-pulsed techniques, as well as MS and IR spectroscopy. The course of the reaction and the resulting compounds were investigated by thin layer chromatography or by the high performance liquid chromatography technique.

The following examples illustrate the invention in more detail without limiting it:

Example 1:

7,9-O-Phenyl-boronyl-β-rhodomycinone (1)
(Compound of the formula I where R^1=R^4=H and R^2 and R^3=X, where X=phenylboronyl)

A solution of β-rhodomycinone (740 mg = 1.92 mmol) and phenylboric acid (360 mg = 2.95 mmol) in toluene (150 ml) was heated under reflux together with activated 4Å molecular sieve (3 g) for 9 hours, the reaction being monitored by thin layer chromatography (mobile phase: toluene/methanol = 10:1).

After the solution had been cooled, it was filtered and the solvent was stripped off under a high vacuum. The precipitate was dissolved in chloroform and crystallized out with petroleum ether.

Yield: 800 mg (1.7 mmol = 88%)

Example 2:

7,9-O-Isopropylidene-β-rhodomycinone (2)
(Compound of the formula I where R^1=R^4=H and R^2 and R^3=X, where X = isopropylidene)

para-Toluenesulfonic acid (150 mg) was added to a solution of β-rhodomycinone (300 mg = 0.78 mmol) in 30 ml of dry N,N-dimethylformamide (130 ml) and 2,2-dimethoxypropane (36 ml) and the mixture was stirred on a rotary evaporator at 50°C under 320 mbar for 60 hours, further 2,2-dimethoxypropane (35 ml) being added. After the solution had been concentrated, the residue was taken up in methylene chloride, the mixture was extracted by shaking with aqueous sodium bicarbonate solution and the extract was dried and concentrated. Separation by column chromatography (mobile phase: chloroform/acetone/acetic acid/water/triethylamine = 95:5:1:0.25:0.1) gave the product in crystalline form.

Yield: 150 mg (0.35 mmol = 45%)

Example 3:

7-9-O-Benzylidene-β-rhodomycinone (3)
(Compound of the formula I where R^1=R^4=H and R^2 and R^3=X, where X = benzylidene)

para-Toluenesulfonic acid (10 mg) was added to a solution of β-rhodomycinone (30 mg = 0.08 mmol) in dry N,N-dimethylformamide (5 ml) and benzaldehyde dimethyl acetal (2 ml) and the mixture was stirred on a rotary evaporator at 50°C under 50 mbar for one hour. After the solution had been concentrated, the residue was taken up in methylene chloride, the mixture was extracted by shaking with aqueous sodium bicarbonate solution and the extract was dried and concentrated.

Yield: 35 mg (0.07 mmol = 90%)

The two exo/endo-isomers can be separated by chromatography (mobile phase: toluene/methanol = 10:1).

Example 4:

10-O-Trifluoroacetyl-β-rhodomycinone (4)
(Compound of the formula I where $R^1=R^2=R^3=H$ and $R^4=$ trifluoroacetyl)

Trifluoroacetic anhydride (4 ml = 283 mmol) and triethylamine (0.2 ml) were added to a solution of 7,9-O-phenylboronyl-β-rhodomycinone (compound 1) (230 mg = 0.49 mmol) in dry methylene chloride (50 ml) at 0°C and the mixture was stirred at 0°C for 30 minutes.

After the solvent had been stripped off and the residue had been concentrated several times with toluene, the residue was dissolved in methanol and the solution was brought to pH 2.5 with hydrochloric acid, the product precipitating out after stirring for 4 hours. The precipitate was dissolved in methylene chloride, the solution was washed with water and, after drying, the organic phase was concentrated.

Yield: 150 mg (0.31 mmol = 63%)

Example 5:

10-Tetrahydropyranyl-β-rhodomycinone (5)
(Compound of the formula I where $R^1=R^2=R^3=H$ and $R^4=$ structure II where $R^5=R^6=R^7=R^8=H$)

A catalytic amount of para-toluenesulfonic acid (20 mg) was added to a solution of 7,9-O-phenylboronyl-β-rhodomycinone (500 mg = 1.06 mmol) and 3,4-dihydro-2H-pyran (2.5 ml) in dry methylene chloride (125 ml) with 4Å

molecular sieve and the mixture was stirred at room temperature for half an hour. After the molecular sieve had been filtered off, the filtrate was washed with aqueous sodium bicarbonate solution and dried with sodium sulfate and the solvent was distilled off.

This crude product was dried under a high vacuum and then added to a solution of 2-methyl-2,4-pentanediol (5 ml) in dry methylene chloride (40 ml), and the mixture was stirred with a catalytic amount of glacial acetic acid (0.2 ml) at room temperature for 48 hours.

The mixture was then extracted by shaking with aqueous sodium bicarbonate solution and with water and the extract was dried over sodium sulfate. Separation by column chromatography (mobile phase: toluene/methanol = 10:1) gave the pure product.

Yield: 210 mg (0.45 mmol = 42%)

Example 6:

10-O-Trimethylsilyl-β-rhodomycinone (6)
(Compound of the formula I where $R^1=R^2=R^3=H$ and $R^4=$ trimethylsilyl)

Trimethylsilyl trifluoromethanesulfonate (110 µl) was added to a solution of 7,9-O-phenylboronyl-β-rhodomycinone (100 mg = 0.21 mmol) and pyridine (85 µl) in dry methylene chloride and 4Å molecular sieve at -40°C and the mixture was stirred for 1.5 hours.

The reaction mixture was filtered, the filtrate was extracted by shaking with aqueous sodium bicarbonate solution and the extract was dried over sodium sulfate and concentrated.

To split off the boronyl ester, the crude product was

dissolved in dry methylene chloride (10 ml), 2-methyl-2,4-pentanediol (0.55 ml) and glacial acetic acid (0.1 ml) were added and the mixture was stirred at room temperature for 48 hours. The reaction mixture was extracted by shaking with water, the extract was dried over sodium sulfate and concentrated and the residue was separated by column chromatography (mobile phase: methylene chloride/acetic acid/formic acid = 20:1:0.1)
Yield: 57 mg (0.11 mmol = 52%)

Example 7:

10-O-(4-O-Paranitrobenzoyl-3-N-trifluoroacetyl-α-L-acosaminyl)-7,9-O-phenylboronyl-β-rhodomycinone (7)
(Compound of the formula I where R^1=H, R^2 and R^3= phenylboronyl and R^4=structure II = α-L-acosaminyl where R^5=CH_3, R^6=OpNBz, R^7=NHTFA and R^8=H)

A solution of 1,5-anhydro-4-O-paranitrobenzoyl-2,3,6-trideoxy-3-N-trifluoroacetyl-L-arabino-hex-1-enitol (87 mg = 0.23 mmol) in dry methylene chloride (4 ml) was added to a solution of 7,9-O-phenylboronyl-β-rhodomycinone (compound 1) (100 mg = 0.21 mmol) in dry methylene chloride (8 ml) and 4Å molecular sieve, and trimethylsilyl trifluoromethanesulfonate (40 µl = 0.22 mmol) was added under a protective gas atmosphere (argon) at -40°C. After the mixture had been warmed to -20°C, it was stirred at this temperature for a further 4 hours and the reaction was then ended by adding triethylamine (80 µl) to the solution. After filtration, the solution was washed with aqueous sodium bicarbonate solution, dried over sodium sulfonate and concentrated and stripping with toluene was performed several times.

Crude yield: 180 mg (quantitative)

Example 8:

10-O-(4-O-Paranitrobenzoyl-3-N-trifluoro-acetyl-α-L-acosaminyl)-β-rhodomycinone (8)
(Compound of the formula I where R^1=R^2=R^3=H and R^4= structure II= α-L-acosaminyl where R^5=CH_3, R^6=OpNBz, R^7=NHTFA and R^8=H)

A solution of the crude mixture of compound 7 (180 mg = 0.21 mmol) in dry methylene chloride (20 ml) was stirred with 2-methyl-2,4-pentanediol (3.2 ml) and glacial acetic acid (0.2 ml) at room temperature for 24 hours. For working up, stripping with toluene was performed several times and 150 mg of crude product were crystallized out of diethyl ether/petroleum ether and purified by column chromatography (mobile phase: methylene chloride/acetone/formic acid = 20:1:0.2).

Yield: 120 mg (0.16 mmol = 75%)

Example 9:

10-O-(4-O-Paranitrobenzoyl-3-N-trifluoroacetyl-α-L-daunosaminyl)-β-rhodomycinone (9)
(Compound of the formula I where R^1=R^2=R^3=H and R^4= structure II = α-L-daunosaminyl where R^5=CH_3, R^6=OpNBz, R^7=NHTFA and R^8=H)

7,9-O-Phenyl-boronyl-β-rhodomycinone (compound 1) (150 mg = 0.318 mmol) and 1,4-di-O-paranitrobenzoyl-3-N-trifluoroacetyl-L-daunosamine (190 mg = 0.35 mmol) were reacted with trimethylsilyl trifluoromethanesulfonate (0.11 ml = 0.61 mmol) in accordance with the instructions of Example 7.

The crude product thereby formed was deblocked in accordance with the instructions of Example 8 for the purpose of splitting off the boric acid ester.

Yield: 180 mg (0.24 mmol = 75%)

Example 10:

10-O-α-L-Acosaminyl-β-rhodomycinone (10)
(Compound of the formula I where R^1=R^2=R^3=H and R^4= structure II= α-L-acosaminyl where R^5=CH_3, R^6=OH, R^7=NH_2 and R^8=H)

A solution of compound 8 (36 mg = 47 µmol) in methanol (2 ml) and 0.5N sodium hydroxide solution (2 ml) was stirred at room temperature for 30 minutes and the pH was then brought to 2.5 with hydrochloric acid. The mixture was then extracted by shaking with chloroform several times. The aqueous phase was neutralized with sodium bicarbonate solution and extracted by shaking with chloroform several times. This chloroform phase was dried with sodium sulfate and concentrated.

Yield: 17.5 mg (34 µmol = 72%)

Example 11:

10-O-α-L-Daunosaminyl-β-rhodomycinone (11)
(Compound of the formula I where R^1=R^2=R^3=H and R^4= structure II=α-L-daunosaminyl where R^5=CH_3, R^6=OH, R^7=NHz and R^8=H

Compound 9 (53 mg = 70 µmol) was deblocked and the product was worked up in accordance with the conditions described for Example 10.

Yield: 23 mg (45 µmol = 64%)

Example 12:

10-O-(3-N,N-Dimethyl-α-L-acosaminyl)-β-rhodomycinone (12) (Compound of the formula I where R^1=R^2=R^3=H and R^4= structure II=α-L-acosaminyl where R^5=CH_3, R^6=OH, R^7= $N(CH_3)_2$ and R^8=H)

A solution of compound 10 (23 mg = 42 µmol) in methanol (2 ml) is stirred with sodium cyanoborohydride (16 mg = 250 µmol) and formaldehyde (63 µl, 37% strength = 860 µmol) at room temperature for two hours. The mixture is then neutralized with hydrochloric acid and purified by chromatography (mobile phase: chloroform/methanol/acetic acid/water/triethylamine = 80:20:10:4:0.2).

Yield: 15 mg (28 µmol = 67%)

Example 13:

7-O-(4-O-Paranitrobenzoyl-3-N-trifluoroacetyl-α-L-acosaminyl)-10-O-trifluoroacetyl-β-rhodomycinone (13) (Compound of the formula I where R^1=R^3=H, R^4=trifluoroacetyl and R^2=structure II=α-L-acosaminyl where R^5=CH_3, R^6=OpNBz, R^7=NHTFA and R^8=H)

Compound 4 (90 mg = 0.19 mmol) was reacted under the conditions described in Example 7.

Crude yield: 150 mg (0.18 mmol = 95%)

Example 14:

7-O-(4-O-Paranitrobenzoyl-3-N-trifluoroacetyl-α-L-acosaminyl)-β-rhodomycinone (14) (Compound of the formula I where R^1=R^3=R^4=H and R^2= structure II=α-L-acosaminyl where R^5=CH_3, R^6=OpNBz, R^7=NHTFA and R^8=H)

A solution of compound 13 (100 mg = 0.12 mmol) in methanol (5 ml) was brought to pH 10 with 0.1 N sodium hydroxide solution and stirred for 10 minutes.

The reaction mixture was neutralized with diluted hydrochloric acid and the solvent was distilled off. The residue was taken up in methylene chloride and the mixture was washed with water, dried over sodium sulfate and concentrated.

Crude yield: 85 mg (0.11 mmol = 92%)

Example 15:

7-O-α-L-Acosaminyl-β-rhodomycinone (15)
(Compound of the formula I where R^1=R^3=R^4=H and R^2= structure II=α-L-acosaminyl where R^5=CH_3, R^6=OH, R^7= NH_2 and R^8=H)

Compound 14 (27 mg = 35 µmol) was deblocked and the product worked up in accordance with the conditions described for Example 10.

Yield: 15 mg (29 µmol = 83%)

Example 16:

7-O-(3-N,N-Dimethyl-α-L-acosaminyl)-β-rhodomycinone (16)
(Compound of the formula I where R^1=R^3=R^4=H, R^2= structure II=α-L-acosaminyl where R^5=CH_3, R^6=OH, R^7= $N(CH_3)_2$ and R^8=H)

Compound 15 (15 mg = 29 µmol) was reacted under the conditions of Example 12.

Yield: 13 mg (24 µmol = 83%)

Example 17:

7-O-(3-N-Cyanomethyl-α-L-daunosaminyl)-β-rhodomycinone (17)
(Compound of the formula I where R^1=R^3=R^4=H and R^2= structure II=α-L-daunosaminyl where R^5=CH_3, R^6=OH, R^7=$NH(CH_2CN)$ and R^8=H)

7-O-α-L-Daunosaminyl-β-rhodomycinone (200 mg = 0.39 mmol) was dissolved in dry N,N-dimethylformamide (30 ml) and, after addition of triethylamine (0.16 ml) and iodoacetonitrile (0.283 ml), the mixture was stirred at room temperature for 15 hours. The reaction mixture was then evaporated under a high vacuum and the residue was purified by column chromatography over 50 g of silica gel (eluting agent: methylene chloride/acetone/acetic acid = 5:2:1)
Yield: 157 mg (0.28 mmol = 73%)

MS: $M+H^+$ = 555

Example 18:

7-O-(4-O-Paranitrobenzoyl-3-N-trifluoroacetyl-α-L-daunosaminyl)-10-O-trifluoroacetyl-β-rhodomycinone (18)
(Compound of the formula I where R^1=R^3=H, R^4=trifluoroacetyl and R^2=structure II=α-L-daunosaminyl where R^5=CH_3, R^6=OpNBz, R^7=NHTFA and R^8=H)

10-O-Trifluoroacetyl-β-rhodomycinone (500 mg = 1.03 mmol) was dissolved in a mixture of methylene chloride and acetone (1:1; 40 ml). Molecular sieve (4Å, dried powder, 500 mg) and 1,4-di-O-paranitrobenzoyl-3-N-trifluoroacetyl-L-daunosamine (1.1 g = 2.06 mmol) were added to the solution and the mixture was cooled to -30°C, with exclusion of atmospheric humidity. Trimethylsilyl trifluoromethanesulfonate (0.9 ml = 5.15 mmol) was added dropwise to the stirred suspension. After 2 hours, tri-

ethylamine (0.8 ml) was added. The mixture was filtered at room temperature and the filtrate was washed out three times with ice-water. The organic phase was dried over sodium sulfate and evaporated under a waterpump vacuum. The resulting crude product was purified by column chromatography (silica gel 60/35-70, supplied by Amicon, eluting agent: methylene chloride/petroleum ether/acetone = 5:5:1).

Yield: 750 mg (0.88 mmol = 85%)

Example 19:

7-O-(4-O-Paranitrobenzoyl-3-N-trifluoroacetyl-α-L-daunosaminyl)-β-rhodomycinone (19)
(Compound of the formula I where R^1=R^3=R^4=H and R^2= structure II=α-L-daunosaminyl where R^5=CH_3, R^6=OpNBz, R^7=NHTFA and R^8=H)

Compound 18 (660 mg = 0.77 mmol) was dissolved in 30 ml of a mixture of chloroform and methanol 1:1. 0.01 N aqueous sodium hydroxide solution (30 ml) was then added dropwise (pH 7.5). After 3 hours, the solution was neutralized with 0.1 N aqueous hydrochloric acid and evaporated in vacuo. The product, which is uniform according to thin layer chromatography, was purified by column chromatography over 200 g of silica gel 60/35-70 supplied by Amicon (mobile phase: methylene chloride/acetone = 15:1 to 5:1).

Yield: 570 mg (0.75 mmol = 97%)

Example 20:

7-O-(4-O-Paranitrobenzoyl-3-N-trifluoroacetyl-α-L-daunosaminyl)-10-O-tetrahydropyranyl-β-rhodomycinone (20)
(Compound of the formula I where R^1=R^3=H, R^2=structure II=α-L-daunosaminyl where R^5=CH_3, R^6=OpNBz, R^7=NHTFA

and R^8=H; and R^4=structure II where R^5=R^6=R^7=R^8=H)

Compound 19 (150 mg = 0.2 mmol) was dissolved in methylene chloride (20 ml). Paratoluenesulfonic acid (10 mg) and 3,4-dihydro-2H-pyran (2 ml) were added at room temperature, with stirring. After 24 hours, the reaction mixture was washed out three times with a total of 100 ml of ice-water. The organic phase was dried over sodium sulfate and evaporated. The crude product was purified over silica gel (eluting agent: methylene chloride/petroleum ether/acetone = 5:5:1)

Yield: 150 mg (0.178 mmol = 89%)

Example 21:

7-O-α-L-Daunosaminyl-10-O-tetrahydropyranyl-β-rhodomycinone (21)

(Compound of the formula I where R^1=R^3=H, R^2=structure II=α-L-daunosaminyl where R^5=CH_3, R^6=OH, R^7=NH_2, and R^8=H; and R^4=structure II where R^5=R^6=R^7=R^8=H)

Compound 20 (150 mg = 0.17 mmol) was dissolved in chloroform/methanol 1:1 (20 ml) at room temperature and 1 N aqueous NaOH solution (1 ml) was added. After stirring for 1 hour, the solution was neutralized with 1 N hydrochloric acid and evaporated. The residue was further purified by column chromatography (silica gel, eluting agent: methylene chloride/methanol 5:1).

Yield: 87 mg (0.145 mmol = 82%)

Example 22:

7-O-(3-Azido-4-O-paranitrobenzoyl-2,3,6-trideoxy-α-L-arabinohexopyranosyl)-10-O-trifluoroacetyl-β-rhodomycinone (22)

(Compound of the formula I where R^1=R^3=H and R^2= structure II=α-L-2,3,6-trideoxyarabinohexopyranosyl where R^5=CH_3, R^6=OpNBz, R^7=N_3, R^8=H and R^4=trifluoroacetyl)

Compound 4 (100 mg = 0.21 mmol) was dissolved in a mixture of methylene chloride and acetone 5:1 (10 ml), and molecular sieve 4Å (100 mg) was added as a dried powder. After addition of 3-azido-2,3,6-trideoxy-4-O-paranitrobenzoyl-L-arabino-1-hex-1-enitol (127 mg = 0.42 mmol), dissolved in methylene chloride (5 ml), the mixture was cooled to -30°C and trimethylsilyl trifluoromethanesulfonate (46 mg = 0.21 mmol) was added. The reaction temperature was raised to -10°C after 4 hours. Further 3-azido-2,3,6-trideoxy-4-O-paranitrobenzoyl-L-arabino-1-hex-1-enitol (36 mg = 0.21 mmol), dissolved in methylene chloride (25 ml) was then added. After a further 16 hours, the reaction mixture was neutralized with triethylamine, filtered and evaporated. The resulting crude product was purified by column chromatography (silica gel; eluting agent: methylene chloride)

Yield: 127 mg (0.16 mmol = 77%)

Example 23:

7-O-(3-Azido-2,3,6-trideoxy-α-L-arabinohexopyranosyl)-β-rhodomycinone (23)

(Compound of the formula I where R^1=R^3=R^4=H and R^2= structure II=α-L-2,3,6-trideoxy-arabinohexopyranosyl where R^5=CH_3, R^6=OH, R^7=N_3 and R^8=H)

Compound 22 (100 mg = 0.13 mmol) was dissolved in chloroform/methanol 1:1 (10 ml), and 1 N NaOH solution (0.5 ml) is added at room temperature, with stirring. After 1 hour, the reaction batch was neutralized with 1 N HCl. After the solvent had been evaporated off, toluene was added to the product and the mixture was evaporated to

dryness again. The resulting productwas dissolved in chloroform/methanol 3:1 and the insoluble constituents were filtered off. After the filtratehad been concentrated, the crude productwas purified by column chromatography over 50 g of silica gel (methylene chloride/acetone 10:1)

Yield: 53 mg (0.098 mmol = 75%)

Example 24:

7-O-(3,4-Di-O-acetyl-2,6-dideoxy-2-iodo-α-L-talopyranosyl)-10-O-tetrahydropyranyl-β-rhodomycinone (24)
(Compound of the formula I where R^1=R^3=H, R^2=structure II=2,6-dideoxy-α-L-talopyranosyl where R^5=CH_3, R^6=R^7=OAc and R^8=I; and R^4=structure II where R^5=R^6=R^7=R^8=H)

N-Iodosuccinimide (36 mg = 0.16 mmol) was added to a solution of compound 5 (30 mg = 0.06 mmol) and 3,4-di-O-acetyl-1,5-anhydro-2,6-dideoxy-L-lyxo-hex-1-enitol (26 mg = 0.12 mmol) in 3 ml of dry acetonitrile with activated 3 Å molecular sieve at -10°C under a protective gas atmosphere (argon) and the mixture was brought to room temperature during the reaction time of 4 days. After filtration, the filtrate was diluted with methylene chloride and the organic phase was extracted by shaking first with aqueous sodium thiosulfate solution, then with sodium bicarbonate solution and subsequently with water, dried and purified by chromatography (mobile phase: toluene/methanol = 10:1).

Non-optimized yield: 10 mg (0.013 mmol = 20%)

Example 25:

7-O-(3,4-Di-O-acetyl-2,6-dideoxy-2-iodo-α-L-mannopyranosyl)-10-O-tetrahydropyranyl-β-rhodomycinone (25)
(Compound of the formula I where R^1=R^3, R^2=structure II=2,6-dideoxy-α-L-mannopyranosyl where R^5=CH_3, R^6=R^7=OAc and R^8=I; and R^4=structure II where R^5=R^6=R^7=R^8=H)

Compound 5 (70 mg = 0.15 mmol) was reacted with 3,4-di-O-acetyl-1,5-anhydro-2,6-dideoxy-L-arabinohex-1-enitol and the product worked up analogously to Example 24.

Non-optimized yield: 45 mg (0.056 mmol = 37%)

Example 26:

7-O-(3,4-Di-O-acetyl-2,6-dideoxy-2-iodo-α-L-mannopyranosyl)-β-rhodomycinone (26)
(Compound of the formula I where R^1=R^3=R^4=H, R^2=structure II= 2,6-dideoxy-α-L-mannopyranosyl where R^5=CH_3, R^6=R^7=OAc and R^8=I)

Acid ion exchanger (Dowex 50 WXS) was added to a solution of compound 25 (34 mg = 0.04 mmol) in 2 ml of methanol and the mixture was stirred for 24 hours. After the ion exchanger had been filtered, the filtrate was purified by chromatography (mobile phase: methylene chloride/acetone/formic acid = 20:1:0.1).

Non-optimized yield: 13 mg (0.018 mmol = 45%)

Example 27:

7,10-Di-O-(4-O-paranitrobenzoyl-3-N-trifluoroacetyl-α-L-daunosaminyl)-β-rhodomycinone (27)
(Compound of the formula I where R^1=R^3=H and R^2=R^4=structure II=α-L-daunosaminyl where R^5=CH_3, R^6=OpNBz, R^7=NHTFA and R^8=H)

Compound 9 was reacted with 1,4-di-O-paranitrobenzoyl-3-N-trifluoroacetyl-L-daunosamine and trimethylsilyl trifluoromethanesulfonate and the product worked up analogously to Example 7.

Example 28:

7,10-Di-O-(4-O-acetyl-3-N-trifluoroacetyl-α-L-daunosaminyl)-β-rhodomycinone (28)
(Compound of the formula I where R^1=R^3=H and R^2=R^4= structure II=α-L-daunosaminyl where R^5=CH_3, R^6=OAc, R^7=NHTFA and R^8=H)

Compound 1 was reacted with 1,4-di-O-acetyl-3-N-trifluoroacetyl-L-daunosamine and trimethylsilyl trifluoromethanesulfonate analogously to Example 7 and the product was then deblocked at positions 7 and 9 analogously to Example 8 and reacted with 1,4-di-O-acetyl-3-N-trifluoroacetyl-L-daunosamine and trimethylsilyl trifluoromethanesulfonate again analogously to Example 7.

Example 29:

7,10-Di-O-α-L-daunosaminyl-β-rhodomycinone (29)
(Compound of the formula I where R^1=R^3=H and R^2=R^4= structure II=α-L-daunosaminyl where R^5=CH_3, R^6=OH, R^7=NH_2 and R^8=H)

Compound 27 was deblocked and the product worked up in accordance with the conditions described for compound 10.

Compound 30:

7,10-O-Di-(3-N-cyanomethyl-α-L-daunosaminyl)-β-rhodomycinone (30)
(Compound of the formula I where R^1=R^3=H and R^2=R^4= structure II=α-L-daunosaminyl where R^5=CH_3, R^6=OH, R^7=$NH(CH_2CN)$ and R^8=H)

The compound described in the title was prepared analogously starting from compound 29 (132 mg = 0.2 mmol) and iodoacetonitrile (0.15 ml), as already described in Example 17.

Yield: 76.6 mg (0.11 mmol = 53%)

MS: $M+H^+$ = 723

Example 31:

7,10-Di-O-(4-O-paranitrobenzoyl-3-N-trifluoroacetyl-α-L-acosaminyl)-β-rhodomycinone (31)
(Compound of the formula I where R^1=R^3=H and R^2=R^4= structure II=α-L-acosaminyl where R^5=CH_3, R^6=OpNBz, R^7=NHTFA and R^8=H)

Compound 8 was reacted and the product worked up analogously to Example 7.

Example 32:

7,10-Di-O-(4-O-acetyl-3-N-trifluoroacetyl-α-L-acosaminyl)-β-rhodomycinone (32)
(Compound of the formula I where R^1=R^3=H and R^2=R^4= structure II=α-L-acosaminyl where R^5=CH_3, R^6=OAc, R^7=NHTFA and R^8=H)

Compound 1 was reacted with 1,4-di-O-acetyl-3-N-trifluoroacetyl-L-acosamine analogously to Example 28.

Example 33:

7,10-Di-O-α-L-acosaminyl-β-rhodomycinone (33)
(Compound of the formula I where R^1=R^3=H and R^2=R^4= structure II= α-L-acosaminyl where R^5=CH_3, R^6=OH, R^7= NH_2 and R^8=H)

Compound 31 was deblocked and the product worked up analogously to the conditions described for compound 10.

Example 34:

7,10-Di-O-(3-N,N-dimethyl-α-L-acosaminyl)-β-rhodomycinone (34)

(Compound of the formula I where R^1=R^3=H and R^2=R^4= structure II where R^5=CH_3, R^6=OH, R^7=$N(CH_3)_2$ and R^8=H)

Compound 33 was reacted analogously to the conditions of Example 12.

Example 35:

7-O-(4-O-Paranitrobenzoyl-3-N-trifluoroacetyl-α-L-acosaminyl)-10-O-(4-O-paranitrobenzoyl-3-N-trifluoroacetyl-α-L-daunosaminyl)-β-rhodomycinone (35)

(Compound of the formula I where R^1=R^3=H and R^2= structure II=α-L-acosaminyl where R^5=CH_3, R^6=OpNBz, R^7=NHTFA and R^8=H; and R^3=structure II=α-L-daunosaminyl where R^5=CH_3, R^6=OpNBz, R^7=NHTFA and R^8=H)

Compound 9 was reacted and the product worked up analogously to Example 7.

Example 36:

7-O-(4-O-Acetyl-3-N-trifluoroacetyl-α-L-acosaminyl)-10-O-(4-O-paranitrobenzoyl-3-N-trifluoroacetyl-α-L-daunosaminyl)-β-rhodomycinone (36)

(Compound of the formula I where R^1=R^3=H, R^2=structure II=α-L-acosaminyl where R^5=CH_3, R^6=OAc, R^7=NHTFA and R^8=H; and R^4=structure II=α-L-daunosaminyl where R^5=CH_3, R^6=OpNBz, R^7=NHTFA and R^8=H)

Compound 9 was reacted with 1,4-di-O-acetyl-3-N-trifluoroacetyl-L-acosamine and the product worked up analogously

to Example 7.

Example 37:

7-O-α-L-Acosaminyl-10-O-α-L-daunosaminyl-β-rhodomycinone (37)

(Compound of the formula I where R^1=R^3=H, R^2=structure II=α-L-acosaminyl where R^5=CH_3, R^6=OH, R^7=NH_2 and R^8=H; and R^4=structure II=α-L-daunosaminyl where R^5=CH_3, R^6=OH, R^7=NH_2 and R^8=H)

Compound 35 was deblocked and the product worked up in accordance with the conditions described for compound 10.

Example 38:

7-O-(4-O-Benzoyl-α-L-rhodosaminyl)-10-O-(4-O-paranitrobenzoyl-3-N-trifluoroacetyl-α-L-acosaminyl)-β-rhodomycinone (38)

(Compound of the formula I where R^1=R^3=H, R^2=structure II=α-L-rhodosaminyl where R^5=CH_3, R^6=OBz, R^7=$N(CH_3)_2$ and R^8=H and R^4=structure II=α-L-acosaminyl where R^5=CH_3, R^6=OpNBz, R^7=NHTFA and R^8=H)

7-O-(4-O-benzoyl-α-L-rhodosaminyl)-β-rhodomycinone was reacted and the product worked up analogously to Example 7.

Example 39:

10-O-(4-O-Paranitrobenzoyl-3-N-trifluoroacetyl-α-L-acosaminyl)-7-O-α-L-rhodosaminyl-β-rhodomycinone (39)

(Compound of the formula I where R^1=R^3=H and R^2=structure II=α-L-rhodosaminyl where R^5=CH_3, R^6=OH, R^7=$N(CH_3)_2$ and R^8=H; and R^4=structure II=α-L-acosaminyl where R^5=CH_3, R^6=OpNBz, R^7=NHTFA and R^8=H)

7-O-α-L-Rhodosaminyl-β-rhodomycinone was reacted and the product worked up analogously to Example 7.

Example 40:

10-O-α-L-Acosaminyl-7-O-α-L-rhodosaminyl-β-rhodomycinone (40)

(Compound of the formula I where R^1=R^3=H, R^2=structure II=α-L-rhodosaminyl where R^5=CH_3, R^6=OH, R^7=$N(CH_3)_2$ and R^8=H and R^4=structure II=α-L-acosaminyl where R^5=CH_3, R^6=OH, R^7=NH_2 and R^8=H)

Compound 38 was deblocked and the product worked up analogously to the conditions described for compound 10.

Example 41:

10-O-(4-O-Acetyl-2,3,6-trideoxy-α-L-erythro-hex-2-eno-pyranosyl)-7-O-(4-O-paranitrobenzoyl-3-N-trifluoroacetyl-α-L-daunosaminyl)-β-rhodomycinone (41)

(Compound of the formula I where R^1=R^3=H, R^2=structure II=α-L-daunosaminyl where R^5=CH_3, R^6=OpNBz, R^7=NHTFA and R^8=H; and R^4=structure IV=α-L-erythro-hex-2-eno-pyranosyl where R^6=OAc)

Compound 19 (400 mg = 0.52 mmol) was dissolved in methylene chloride/acetone (50 ml). After addition of 3,4-di-O-acetyl-L-rhamnal (225 mg = 1.0 mmol) and molecular sieve 4Å (dried powder) (400 mg), the suspension was cooled to -40°C. Trimethylsilyl trifluoromethanesulfonate was then added dropwise (60 mg = 2.6 mmol). After 2 hours, further 3,4-di-O-acetyl-L-rhamnal (225 mg) was added to the suspension. After 24 hours, the reaction mixture was neutralized with triethylamine and worked up in the customary manner.

Yield: 180 mg (0.2 mmol = 37%)

Example 42:

10-O-(2,3,6-Trideoxy-α-L-erythro-hex-2-enopyranosyl)-7-O-α-L-daunosaminyl-β-rhodomycinone (42)
(Compound of the formula I where R^1=R^3=H, R^2=structure II=α-L-daunosaminyl where R^5=CH_3, R^6OH, R^7=NH_2 and R^8=H; and R^4=structure IV=α-L-erythro-hex-2-eno-pyranosyl where R^6=OH)

Compound 41 (100 mg = 0.13 mmol) was dissolved in methanol (10 ml), and 1 N aqueous NaOH solution (10 ml) was added. The reaction mixture was stirred at room temperature for 24 hours and then neutralized with 1 N hydrochloric acid. After the solvent had been evaporated off, the residue was purified by column chromatography over silica gel (eluting agent: chloroform/methanol 5:1).

Yield: 60 mg (0.096 mmol = 74%)

FAB-MS: m/z 628 = $M+H^+$

Example 43:

7,9,10-Tri-O-(4-O-Paranitrobenzoyl-3-N-trifluoroacetyl-α-L-acosaminyl)-β-rhodomycinone (43)
(Compound of the formula I where R^1=H and R^2=R^3=R^4= structure II=α-L-acosaminyl where R^5=CH_3, R^6=OpNBz, R^7= NHTFA and R^8=H)
Compound 8 was reacted analogously to Example 7 but with twice the equimolar amount of 1,5-anhydro-4-O-paranitro-benzoyl-2,3,6-trideoxy-3-N-trifluoroacetyl-L-arabino-hex-1-enitol at 0°C.

Example 44:

7,9,10-Tri-O-α-L-acosaminyl-β-rhodomycinone (44)
(Compound of the formula I where R^1=H and R^2=R^3=R^4= structure II=α-L-acosaminyl where R^5=CH_3, R^6=OH, R^7=

NH_2 and R^8=H)

Compound 43 was deblocked and the product worked up analogously to the conditions described for compound 10.

Melting point: 225°C

Example 45:

7-O-(3-N-Trifluoroacetyl-α-L-acosaminyl)-β-rhodomycinone (45)
(Compound of the formula I where R^1=R^3=R^4=H and R^2= structure II=α-L-acosaminyl where R^5=CH_3, R^6=OH, R^7= NHTFA and R^8=H)

A solution of compound 13 (27 mg = 32 µmol) in dry methanol (2 ml) and 2 drops of methanolic sodium methanolate solution (33% strength) was stirred at room temperature for one hour, neutralized with acid ion exchanger (Dowex WX8), filtered and concentrated and the residue was purified by chromatography (mobile phase: methylene chloride/methanol/formic acid = 10 : 1 : 0.2).
Yield: 15 mg (25 µmol = 78%)

Example 46:

7-O-α-L-Ristosaminyl-β-rhodomycinone (46)
(Compound of the formula I where R^1=R^3=R^4=H and R^2= structure II = α-L-ristosaminyl where R^5=CH_3, R^6=OH, R^7=NH_2 and R^9=H)

Compound 4 was reacted with 1,5-anhydro-4-O-paranitrobenzoyl-2,3,6-trideoxy-3-N-trifluoroacetyl-L-ribo-hex-1-enitol under the conditions described in Example 7 and the product was deblocked under the conditions described in Example 10.

Melting point: 217°C
MS: $M+H^+$ = 516

MS: $M+H^+$ = 516

Example 47:

7-O-(3-N-Trifluoroacetyl-α-L-ristosaminyl)-β-rhodomycinone (47)
(Compound of the formula I where R^1=R^3=R^4=H and R^2= structure II = α-L-ristosaminyl where R^5=CH_3, R^6=OH, R^7=NHTFA and R^8=H)

Compound 4 was reacted with 1,5-anhydro-4-O-paranitrobenzoyl-2,3,6-trideoxy-3-N-trifluoroacetyl-L-ribo-hex-1-enitol under the conditions described in Example 7 and the product was deblocked under the conditions described in Example 45.

Melting point: 178°C
MS: $M+H^+$ = 612

Example 48:

7-O-(4-O-Benzyl-α-L-acosaminyl)-β-rhodomycinone (48)
(Compound of the formula I where R^1=R^3=R^4=H and R^2= structure II = α-L-acosaminyl where R^5=CH_3, R^6=OBn, R^7= NH_2 and R^8=H)

Compound 4 was reacted with 1,5-anhydro-4-O-benzyl-2,3,6-trideoxy-3-N-trifluoroacetyl-L-arabino-hex-1-enitol under the conditions described in Example 7 and the product was deblocked under the conditions described in Example 10.

MS: $M+H^+$ = 606

Example 49:

7-O-(4-O-Benzyl-3-N-trifluoroacetyl-α-L-acosaminyl)-β-rhodomycinone (49)
(Compound of the formula I where R^1=R^3=R^4=H and R^2= structure II = α-L-acosaminyl where R^5=CH_3, R^6=OBn, R^7= NHTFA and R^8=H)

Compound 4 was reacted with 1,5-anhydro-4-O-benzyl-2,3,6-trideoxy-3-N-trifluoroacetyl-L-arabino-hex-1-enitol under the conditions described in Example 7 and the product was deblocked under the conditions described in Example 45.

Example 50:

7-O-(2,6-Dideoxy-2-iodo-α-L-mannopyranosyl)-β-rhodomycinone (50)
(Compound of the formula I where R^1=R^3=R^4=H and R^2= structure II = 2,6-dideoxy-α-L-mannopyranosyl where R^5= CH_3, R^6=OH, R^7=OH and R^8=I)

Compound 26 was dissolved in dry methanol and two drops of methanolic sodium methanolate solution (33% strength) and the solution was stirred at room temperature for 2 hours, neutralized with acidic ion exchanger (Dowex WX8), filtered and concentrated.

Melting point: 158°C

Example 51:

7,10-Di-O-(4-O-benzyl-α-L-acosaminyl)-β-rhodomycinone (51)
(Compound of the formula I where R^1=R^3=H and R^2=R^4= structure II = α-L-acosaminyl where R^5=CH_3, R^6=OBn, R^7=NH_2 and R^8=H)

Compound 1 was reacted with 1,5-anhydro-4-O-benzyl-2,3,6-trideoxy-3-N-trifluoroacetyl-L-hex-1-enitol analogously

to Example 7, the product was then deblocked on the aglycone analogously to Example 8 and glycosidated again with 1,5-anhydro-4-O-benzyl-2,3,6-trideoxy-3-N-trifluoroacetyl-L-hex-1-enitol analogously to Example 7, and the product was deblocked analogously to Example 10.

MS: $M+H^+$ = 826

Example 52:

7-O-(4-Deoxy-3-N-trifluoroacetyl-α-L-daunosaminyl)-β-rhodomycinone (52)
(Compound of the formula I where $R^1=R^3=H$ and $R^2=R^4=$ structure II = α-L-daunosaminyl where $R^5=CH_3$, $R^6=H$, $R^7=$ NHTFA and $R^8=H$)

Compound 4 was reacted with 1-O-paranitrobenzoyl-4-deoxy-3-N-trifluoroacetyl-L-daunosamine under the conditions described in Example 7 and the product was deblocked under the conditions described in Example 45.

Example 53:

7-O-(4-Deoxy-α-L-daunosaminyl)-β-rhodomycinone (52)
(Compound of the formula I where $R^1=R^3=H$ and $R^2=R^4=$ structure II = α-L-daunosaminyl where $R^5=CH_3$, $R^6=H$, $R^7=$ NH_2 and $R^8=H$)

Compound 4 was reacted with 1-O-paranitrobenzoyl-4-deoxy-3-N-trifluoroacetyl-L-daunosamine under the conditions described in Example 7 and the product was deblocked under the conditions described in Example 10.

The ^{1}N-NMR data of some of the novel compounds 1-53 described above are compiled in the following Tables 2 and 3.

Table 2

^{1}H-NMR data of various compounds of the formula I

The substance numbers in the first lines correspond to the particular example numbers. The chemical shift is stated in ppm, tetramethylsilane being used as the internal standard. Unless indicated otherwise, the spectra are measured in $CDCl_3$ as the solvent.

Abbreviations:
- s: singlet
- d: doublet
- t: triplet
- q: quartet
- m: multiplet
- dd: doublet of a doublet
- ddd: doublet of a doublet of a doublet
- dq: doublet of a quartet

a) measured at 300 MHz
b) B-phenyl 7.4-7.27 m
c) measured at 270 MHz
d) compound 3a and 3b are exo-endo-isomers
e) benzylidene-CH 5.41s, aromatic benzylidene 7.36-7.20m
f) benzylidene-CH 6.13s, aromatic benzylidene 7.36-7.17m
g) tetrahydropyranyl ring H-1 4.91m and 4.99m,
ring protons 4.0-3.1m,
since the substance is present as a diastereomer mixture (R/S on the THP ring C-1), some signals are present in duplicate
h) measured at 400 MHz
i) O-trimethylsilyl 0.13s
k) B-phenyl 7.35-7.17m
l) solvent $CDCl_3$ + CD_3OD
m) solvent $CDCl_3$ + d_6-DMSO
n) $N(CH_3)_2$ 2.086 s
o) tetrahydropyranyl H-1 5.09dd
OAc 2.03s, 2.09s

p) tetrahydropyranyl H-1 5.04dd;
ring protons 4.2-3.0m
OAc 2.03s, 2.01s

q) OAc 2.04s, 2.01s

r) solvent $CDCl_3$ + dioxane

s) measured at 200 MHz

t) benzyl CH_2 4.77d, 4.66d, aromatic benzyl 7.37m

u) benzyl CH_2 4.46d, 4.33d, aromatic benzyl 7.29-7.12m

v) measured at 90 MHz

Table 2, Part 1:

	1[a,b)]	2[c)]	3a[a,de)]	3b[a,d,f)]
H-1	7.907dd	7.821d	7.85dd	7.82dd
H-2	7.698t	7.645t	7.67t	7.64t
H-3	7.774dd	7.262d	7.29dd	7.25dd
H-7	5.672t	5.279t	5.67dd	5.54t
H-8a	2.293dd	2.39dd	2.31dd	2.67dd
H-8b	2.19dd	2.13dd	1.79dd	2.16dd
H-10	4.973d	4.782d	4.94d	4.84d
H-13a	2.22-1.79m	1.95m	1.98-1.71m	1.99-1.89m
H-13b	2.22-1.79m	1.76m	1.98-1.71m	1.99-1.89m
H_3-14	1.256t	1.048t	1.07t	1.11t
H-1'	-	-	-	-
H-2a'	-	-	-	-
H-2e'	-	-	-	-
H-3'	-	-	-	-
H-4'	-	-	-	-
H-5'	-	-	-	-
H_3-6'	-	-	-	-
OH-4	12.145s	12.151s	12.09s	11.96s
OH-6	12.78s	12.683s	12.67s	12.66s
OH-11	13.575s	13.498s	13.70s	13.51s
OH-7	-	-	-	-
OH-9	-	-	-	-
H-10		2.68d	3.18d	2.80d
NHTFA	-	-	-	-
pNBz	-	-	-	-

Table 2, Part 2:

	$_4$[a)]	$_5$[c,g)]	$_6$[h,i)]	$_7$[a,k)]
H-1	7.902dd	7.78d	7.891dd	7.77d
H-2	7.745t	7.64t	7.715t	7.599t
H-3	7.347dd	7.24d	7.312dd	7.70dd
H-7	5.345dt	5.19dd/5.14dd	5.231t	5.680
H-8a	2.408dt	2.30dd	2.228dd	2.45dd
H-8b	2.054ddd	2.05d	2.146dt	2.18d
H-10	6.344d	4.94s/4.81s	4.822d	4.956s
H-13a	1.75m	1.75m	1.718m	1.85m
H-13b	1.56m	1.75m	1.718m	1.85m
H_3-14	1.103t	1.03t	1.075t	1.18t
H-1'	-	-	-	5.64d
H-2a'	-	-	-	1.85m
H-2e'	-	-	-	2.12m
H-3'	-	-	-	4.44m
H-4'	-	-	-	4.786t
H-5'	-	-	-	4.18dq
H_3-6'	-	-	-	1.27d
OH-4	12.010s	11.97s	12.106s	12.032s
OH-6	12.806s	12.81s	12.897s	12.714s
OH-11	13.345d	13.66s/13.6s	13.626s	13.694s
OH-7	3.452d		3.478d	-
OH-9	3.756s		3.148s	
OH-10	-	-	-	
NHTFA	-	6.45d	6.44d	
pNBz	-	8.28-8.08m	8.34-8.15m	

Table 2, Part 3:

	$_{8}$[c)]	$_{9}$[h)]	$_{10}$[a,1)]	$_{11}$[h,m)]
H-1	7.91dd	7.905dd	7.774d	7.812d
H-2	7.75t	7.726t	7.621t	7.653t
H-3	7.34dd	7.344dd	7.209d	7.243d
H-7	5.31d	5.279t	5.087d	5.089d
H-8a	2.36dd	2.308dd	2.154d	2.125dd
H-8b	2.22d	2.195d	2.06d	2.04d
H-10	4.98s	5.020s	4.87s	4.886s
H-13a	1.95-1.72m	1.88-1.38m	1.82m	1.75m
H-13b	1.95-1.72m	1.88-1.38m	1.82m	1.70m
H_3-14	1.16t	1.135t	1.02t	1.018t
H-1'	5.57d	5.659d	5.31d	5.302d
H-2a'	1.8m	2.16-1.89m	1.49m	1.60m
H-2e'	2.09dd	2.16-1.89m	2.09m	2.01m
H-3'	4.48d	4.493m	2.87m	2.9m
H-4'	4.82t	5.409s	2.87m	3.317s
H-5'	4.21dq	4.314q	3.66dq	3.881q
H_3-6'	1.29d	1.228d	1.236d	1.202d
OH-4	12.06s	12.041s		
OH-6	12.89s	12.894s		
OH-11	13.72s	13.735s		
OH-7	3.54d	3.491d		
OH-9	3.34s	3.248s		
OH-10	-	-		
NHTFA	-			-
pNBz	-			-

Table 2, Part 4:

	$12^{h,n)}$	$13^{h)}$	$14^{h)}$	$15^{h,m)}$
H-1	7.821d	7.908d	7.800d	7.78d
H-2	7.644t	7.738t	7.622t	7.64t
H-3	7.245d	7.334d	7.229d	7.21d
H-7	5.167d	5.246t	5.063t	4.995t
H-8a	2.2-2.09m	2.40dd	2.24-1.99m	2.105m
H-8b	2.2-2.09m	2.45d	2.24-1.99m	2.105m
H-10	4.908s	6.414d	4.854d	4.70s
H-13a	1.85-1.66m	1.75m	1.86-1.69m	1.75-1.60m
H-13b	1.85-1.66m	1.75m	1.86-1.69m	1.75-1.60m
H_3-14	1.039t	1.125t	1.073t	0.99t
H-1'	5.417d	5.520d	5.419	5.29d
H-2a'	1.489ddd	1.86ddd	2.24-1.99m	1.49m
H-2e'	2.194ddd	2.01ddd	2.24-1.99m	1.94m
H-3'	2.602ddd	4.3m	4.38m	2.8m
H-4'	3.012t	4.84t	4.891t	2.8m
H-5'	3.699dq	4.3m	4.278dq	3.77dq
H_3-6'	1.268d	1.330d	1.238d	1.23d
OH-4		12.002s	12.023s	
OH-6		12.813s	12.796s	
OH-11		13.380s	13.551s	
OH-7			-	-
OH-9		3.819s	3.575s	
OH-10		-	3.615d	
NHTFA	-	6.47d		-
pNBz	-	8.25-8.9m	8.22-8.09m	-

Table 2, Part 5:

	16[a)]	18[h)]	19[h,l)]	23[h,r)]
H-1	7.79dd	7.74d	7.70d	7.78dd
H-2	7.634t	7.65t	7.62t	7.59t
H-3	7.229dd	7.22d	7.17d	7.21dd
H-7	5.059dd	5.25d	5.06s	4.96dd
H-8a	2.22-2.02m	2.47d	2.13m	2.10m
H-8b	2.22-2.02m	2.08dd	2.13m	2.10m
H-10	4.857d	6.33s	4.78s	4.74s
H-13a	1.90-1.52m	1.77m	1.88m	1.75m
H-13b	1.90-1.52m	1.53m	1.68m	1.65m
H_3-14	1.054t	1.10t	1.05t	1.02t
H-1'	5.472d	5.65s	5.53s	5.23dd
H-2a'	1.90-1.52m		1.90ddd	1.92m
H-2e'	2.22-2.02m		2.13m	2.10m
H-3'	2.578ddd	4.48m	4.34m	4.04m
H-4'	3.101t	5.49s	5.42s	3.45m
H-5'	3.857dq	4.48m	4.44q	3.55dq
H_3-6'	1.320d	1.27d	1.16d	1.25d
OH-4			11.84s	
OH-6		12.68s		
OH-11		13.22s		
OH-7	-	-	-	
OH-9	3.881s	3.85s		
OH-10		-		
NHTFA	-	6.61d		
pNBz	-	8.25m	8.23m	

Table 2, Part 6:

	24[h,o)]	25[h,p)]	26[a,q)]
H-1	7.88d	7.90d	7.83d
H-2	7.69t	7.69t	7.69t
H-3	7.30d	7.31d	7.28d
H-7	5.12t	5.07t	5.02dd
H-8a			2.22d
H-8b			2.11dd
H-10	4.98s	5.04s	4.88s
H-13a			1.91-1.70m
H-13b			1.91-1.70m
H_3-14	1.13t	1.17t	1.10t
H-1'	5.79s	5.37s	5.71d
H-2a'	-	-	-
H-2e'	4.56dd	4.61dd	4.66dd
H-3'	4.27d	4.29dd	4.32dd
H-4'	4.86s	5.16t	5.18t
H-5'	4.08q	4.04dq	4.17dq
H_3-6'	1.21d	1.24d	1.29d
OH-4	12.12s	12.12s	12.04s
OH-6	12.89s	12.90s	12.79s
OH-11	13.78s	13.81s	13.51s
OH-7	-	-	-
OH-9			3.37s
OH-10	-	-	2.80s
NHTFA	-	-	-
pNBz	-	-	-

Table 2, Part 7:

	44[a)]	45[a)]	46[a)]	47[a)]
H-1	7.83dd	7.80d	7.75dd	7.88d
H-2	7.65t	7.69t	7.64t	7.73t
H-3	7.26dd	7.24d	7.15dd	7.32d
H-7	5.22m	5.02t	4.87m	4.96d
H-8a		2.20m	2.08m	
H-8b		2.20m	2.08m	
H-10	5.11s	4.82m	4.60s	4.81s
H-13a		1.72m	1.78m	-
H-13b		1.72m	1.78m	-
H_3-14	0.90t	1.06t	1.04t	1.09t
H-1'		5.35d	5.42d	5.35s
H-2a'		2.20m	2.08m	
H-2e'		2.20m	2.08m	
H-3'		3.80m	3.66m	4.39ddd
H-4'		3.16t	3.52dd	3.50dd
H-5'		3.96dq	4.14dq	4.15dq
H_3-6'		1.32d	1.37d	1.34d
OH-4		12.08s		
OH-6		12.79s		
OH-11		13.59s		
OH-7		-	-	-
OH-9				
OH-10				
NHTFA		7.75d	-	8.01d
pNBz		-	-	-

Table 2, Part 8:

	48[a,t)]	49[h,u)]	50[a)]	52[v)]
H-1	7.88d	7.86d	7.91dd	7.92dd
H-2	7.72t	7.70t	7.76t	7.71t
H-3	7.32d	7.31d	7.35dd	7.28dd
H-7	5.13m	5.24s	5.07d	5.12t
H-8a	2.22d	2.37d		
H-8b	2.16dd	2.10m		
H-10	4.91s	5.09s	4.81d	4.95d
H-13a	1.9-1.5m	1.98m	1.7m	
H-13b	1.9-1.5m	1.98m	1.7m	
H_3-14	1.11t	1.03t	1.08t	1.13t
H-1'	5.43d	5.27d	5.71s	5.52d
H-2a'	2.2-1.5m	2.10m	-	
H-2e'	2.2-1.5m	2.19ddd	4.45dd	
H-3'	3.09ddd	3.93m	3.97dd	4.2m
H-4'	2.91t	3.09t		
H-5'	3.98dq	3.39dq		4.2m
H_3-6'	1.41d	0.98d	1.38d	1.28d
OH-4		12.11s	12.18s	12.14s
OH-6		12.88s	12.93s	12.77s
OH-11		13.65s	13.72s	13.52s
OH-7	-	-	-	-
OH-9				
OH-10				2.68d
NHTFA		6.09d		5.92d
pNBz		-		-

Table 3

^{1}H-NMR data of various compounds of the formula I

The substance numbers of the first line correspond to the particular example numbers. The chemical shift is stated in ppm, tetramethylsilane being used as the internal standard. Unless stated otherwise, the spectra are measured in $CDCl_3$ as the solvent.

Abbreviations:

s:	singlet
d:	doublet
t:	triplet
q:	quartet
m:	multiplet
dd:	doublet of a doublet
ddd:	doublet of a doublet of a doublet
dq:	doublet of a quartet

The carbohydrate protons with a single dash (H-1' etc.) relate to the carbohydrates as R^2, and the carbohydrate protons with a double dash (H-1'' etc.) relate to the carbohydrates as R^4 in the general formula I

a) measured at 270 MHz
b) the values are exchangeable in pairs
c) measured at 300 MHz
d) OAc 2.21s
e) measured at 400 MHz
f) solvent $CDCl_3$ + d_6-DMSO
g) OAc 2.01s, 1.99s
h) solvent D_2O
i) $N(CH_3)_2$ 2.10s, 2.07s
k) OBz 7.72-7.56m;
$N(CH_3)_2$ 2.28s
l) in the case of the protons of the three carbohydrate radicals, the allocation of the carbohydrate ring protons to the individual carbohydrate radicals is

uncertain.

	H-1	5.66d, 5.59d, 5.43d
	H-3	4.74-4.65m, 2 x 4.52-4.35m
	H-4	3 x 4.99-4.76m
5	H-5	2 x 4.20-4.08m, 3.47dq
	H_3-6	1.37d, 1.27d, 0.84d
	NHTFA	2 x 6.67d, 6.45d

Table 3, Part 1:

	27[a)]	28[c,d)]	29[e,f)]
H-1	7.795d	7.905d	7.74d
H-2	7.651t	7.718t	7.59t
H-3	7.241d	7.314d	7.18d
H-7	5.157t	5.138t	4.96t
H-8a	2.24-1.94m		1.69-1.48m
H-8b	2.24-1.94m		1.69-1.48mm
H-10	5.071s	4.873s	4.78s
H-13a	1.85-1.66m		1.69-1.48m
H-13b	1.85-1.66m		1.69-1.48m
H_3-14	1.107t	1.065t	0.92t
H-1'	5.451d[b)]	5.507d[b)]	5.25d[b)]
H-2a'	1.85-1.66m		1.69-1.48m
H-2e'	2.24-1.94m		1.69-1.48m
H-3'	4.47-4.42m	4.53m[b)]	
H-4'	5.595s[b)]	5.14s[b)]	3.29s[b)]
H-5'	4.47-4.42m[b)]	4.34q[b)]	
H_3-6'	1.252d[b)]	1.26d[b)]	1.16d[b)]
H-1''	5.347d[b)]	5.34d[b)]	5.19d[b)]
H-2a''	1.85-1.66m		1.69-1.48m
H-2e''	2.24-1.94m		1.69-1.48m
H-3''	4.47-4.42m	4.53m[b)]	
H-4''	5.589s[b)]	5.14s[b)]	3.26s[b)]
H-5''	4.309q[b)]	4.20q[b)]	3.79q[b)]
H_3-6''	1.147d[b)]	1.21d[b)]	1.12d[b)]
OH-4	11.902s	12.158s	
OH-6	12.804s	12.901s	
OH-11	13.683s	13.674s	
OH-9	3.287s		
NHTFA	6.29d/6.24d	6.54d/6.30d	-
pNBz	8.30-8.18m	-	-

Table 3, Part 2:

	31[c)]	32[e,g)]	33[e,h)]	34[a,f,i)]
H-1	7.85d	7.81dd	7.50d	7.81dd
H-2	7.66t	7.65t	7.35t	7.64t
H-3	7.27d	7.24dd	7.09d	7.24dd
H-7	5.15m	5.07d		5.07t
H-8a	2.29m	2.33-1.92m		1.83-1.39m
H-8b	2.29m	2.33-1.92m		1.83-1.39m
H-10	4.98s	4.95s		4.92s
H-13a	1.93-1.68m	1.82-1.6m		1.83-1.39m
H-13b	1.93-1.68m	1.82-1.6m		1.83-1.39m
H_3-14	1.13t	1.07s	1.03t	1.04t
H-1'	5.45d	5.39d[b)]	5.47d[b)]	5.46d[b)]
H-2a'	1.85ddd	1.82-1.6m		1.83-1.39m
H-2e'	2.35ddd	2.33-1.92m		1.83-1.39m
H-3'	4.28m	4.15m[b)]		2.8-2.5m
H-4'	4.85t	4.55t[b)]		3.09t[b)]
H-5'	4.30dq	4.11dq[b)]		3.85dq[b)]
H_3-6'	1.27d	1.21d[b)]	1.35d[b)]	1.31d[b)]
H-1''	5.50d	5.38d[b)]	5.35d[b)]	5.42d[b)]
H-2a''	1.76ddd	1.82-1.6m		1.83-1.39m
H-2e''	2.02ddd	2.33-1.92m		1.83-1.39m
H-3''	4.34m	4.15m		2.8-2.5m
H-4''	4.74t	4.47t[b)]		3.01t[b)]
H-5''	4.12dq	3.96dq[b)]		3.70dq[b)]
H_3-6''	1.23d	1.17d[b)]	1.33d[b)]	1.27d[b)]
OH-4	12.01s	11.98s		12.07s
OH-6	12.84s	12.78s		12.84s
OH-11	13.71s	13.65s		13.60s
OH-9	3.30s	3.26s		3.53s
NHTFA	6.39d/6.33d	6.62d/6.55d	-	-
pNBz	8.02-8.36m	-	-	-

Table 3, Part 3:

	35[e)]	36[e)]	37[e)]
H-1	7.94dd	7.82dd	7.90dd
H-2	7.76t	7.64t	7.71t
H-3	7.36dd	7.25dd	7.32dd
H-7	5.22t	5.08t	5.10m
H-8a		2.36-1.60m	
H-8b		2.36-1.60m	
H-10	5.12s	4.99s	4.96s
H-13a	2.08-1.79m	2.36-1.60m	
H-13b	2.08-1.79m	2.36-1.60m	
H_3-14	1.21t	1.09t	1.09t
H-1'	5.55d[b)]	5.59d[b)]	5.38s[b)]
H-2a'	2.08-1.79m	2.36-1.60m	
H-2e'	2.08-1.79m	2.36-1.60m	
H-3'	4.55-4.32m	4.12ddd	2.78m
H-4'	4.95t	4.54t	2.92t
H-5'	4.55-4.32m	4.12dq	3.83dq
H_3-6'	1.37d[b)]	1.22d[b)]	1.34d[b)]
H-1''	5.45d[b)]	5.39d[b)]	5.37s[b)]
H-2a''	2.08-1.79m	2.36-1.60m	
H-2e''	2.08-1.79m	2.36-1.60m	
H-3''	4.55-4.32m	4.412ddd	3.04m
H-4''	5.71s	5.34s	3.37s
H-5''	4.55-4.32m	4.24q	3.96q
H_3-6''	1.28d[b)]	1.16d[b)]	1.28d[b)]
OH-4	12.09s	11.97s	
OH-6	12.93s	12.79s	
OH-11	13.83s	13.70s	
OH-9	3.41s	3.29s	
NHTFA	6.54d/6.25d	6.25d/6.13d	
pNBz	8.36-8.2m	8.26-8.09m	

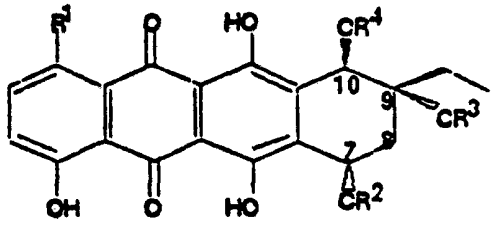
Table 3, Part 4:

	38[e,k)]	39[e)]	40[e)]	43[a,l)]
H-1	7.87d	7.83d	7.89d	7.92d
H-2	7.46t	7.65t	7.71t	7.74t
H-3	7.31d	7.26d	7.32d	7.36d
H-7	5.23s	5.14m	5.13t	5.29t
H-8a	2.05-2.02m		1.9-1.65m	
H-8b	2.05-2.02m		1.9-1.65m	
H-10	4.99s	4.91s	4.95s	5.35s
H-13a	1.93-1.74m		1.9-1.65m	
H-13b	1.93-1.74m		1.9-1.65m	
H_3-14	1.15t	1.14t	1.09t	1.29t
H-1'	5.54s	5.49s[b)]	5.46d[b)]	
H-2a'	1.93-1.74m			
H-2e'	2.21m			
H-3'	2.69ddd	2.23m		
H-4'	5.54s	3.62s	3.67s	
H-5'	4.27q	3.97q	4.02q	
H_3-6'	1.26d	1.34d	1.37d[b)]	
H-1''	5.68d	5.44s[b)]	5.37d[b)]	
H-2a''	1.93-1.74m			
H-2e''	2.21m			
H-3''	4.44ddd	4.37m	2.76m	
H-4''	4.79t	4.73t	2.85t	
H-5''	4.16dq	4.13dq		
H_3-6''	1.21d	1.19d	1.30d[b)]	
OH-4	12.07s	12.08s		12.14s
OH-6	12.88s	12.80s		13.13s
OH-11	13.78s	13.74s		13.92s
OH-9		3.42s		
NHTFA	6.58d	6.28d		
pNBz	8.27-8.08m	8.24-8.08m		8.34-7.96m

PATENTxCLAIMS

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A compound of the formula I or a salt thereof with an inorganic or organic acid

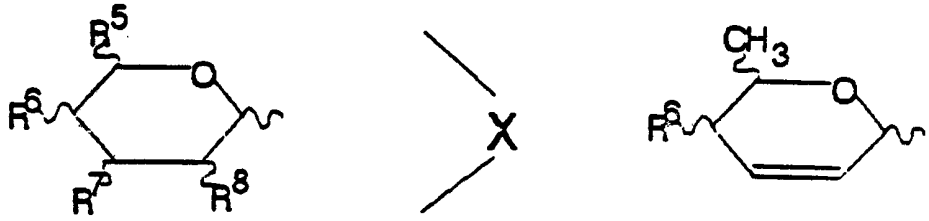


I

in which:

R^1 is hydrogen or a hydroxyl group

R^2 is hydrogen or a structure of the formula II or IV or, together with R^3, of the formula III



II III IV

R^3 is hydrogen or a structure of the formula II or IV or, together with R^2, of the formula III,

R^4 is hydrogen, trimethylsilyl, a protective group which is customary in carbohydrate chemistry, preferably acetyl, trifluoroacetyl, benzoyl or substituted benzoyl, such as para-nitrobenzoyl, a structure of the formula II or a structure of the formula IV,

R^5 is hydrogen, methyl, hydroxymethyl, acyloxymethyl, (C1-C8) or alkoxymethyl (C1-C8),

R^6, R^7 and R^8 independently of one another are hydrogen, hydroxyl, aliphatic acyloxy (C1-C8), benzoyloxy or substituted benzoyloxy, such as para-nitrobenzoyloxy, alkoxy (C1-C8), allyloxy, benzyloxy or substituted benzyloxy or halogen, and R^7 can furthermore be NH_2, NHacyl (C1-C8), N(alkyl)$_2$ (C1-C8),

$N(CH_2CN)_2$, $NH(CH_2CN)$ or azido, and
X is a bidentate protective group which is customary in carbohydrate chemistry, preferably alkylboronyl, phenylboronyl, an alkyl ortho-carboxylate, preferably methyl orthoformate or ethyl orthoacetate, or a ketal or acetal, preferably isopropylidene or benzylidene,
the compounds where $R^1=R^2=R^3=R^4=H$, $R^1=OH$ and $R^2=R^3=R^4=H$, $R^1=R^3=R^4=H$ and $R^2=\alpha$-L-daunosaminyl or α-L-rhodosaminyl or 4'-acyl-α-L-rhodosaminyl, $R^1=OH$ or H, $R^3=H$ and $R^2=R^4=\alpha$-L-rhodosaminyl or 4'-acyl-α-L-rhodosaminyl and $R^1=R^2=R^3=H$ and $R^4=\alpha$-L-rhodosaminyl being excluded.

2. A compound as claimed in claim 1,
wherein
R^2 and R^3 independently of one another are hydrogen or a structure of the formula II or IV with the meanings of R^5 to R^8 given in claim 1.

3. A compound as claimed in claim 1,
wherein
R^2 and R^3 independently of one another are hydrogen or a structure of the formula II or IV in which R^5 is methyl, R^6 and R^7 have the meanings given in claim 1 and R^8 is hydrogen or halogen.

4. A compound as claimed in claim 1,
wherein
R^2 and R^3 independently of one another are hydrogen or a structure of the formula II or IV in which R^5 is methyl, R^6 has the meaning given in claim 1, R^7 is NH_2, NHacyl (C1-C8), $N(alkyl)_2$ (C1-C8), $N(CH_2CN)_2$, $NH(CH_2CN)$ or azido and R^8 is hydrogen or halogen.

5. A compound as claimed in claim 1,
wherein
R^2 and R^3 independently of one another are hydrogen

or a structure of the formula II or IV, in which R^5 is methyl, R^6 and R^7 have the meanings given in claim 1 and R^8 is hydrogen or halogen and the structures of the formula II or IV belong to the L-series of carbohydrates.

6. A compound as claimed in claim 1, wherein R^2 and R^3 independently of one another are hydrogen or a structure of the formula II or IV, in which R^5 is methyl, R^6 has the meaning given in claim 1, R^7 is NH_2, NHacyl (C1-C8), $N(alkyl)_2$ (C1-C8), $N(CH_2CN)_2$, $NH(CH_2CN)$ or azido and R^8 is hydrogen or halogen, and the structures of the formula II or IV belong to the L-series of carbohydrates.

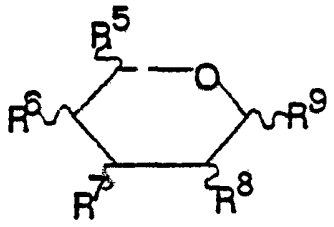
7. A process for the preparation of a compound as claimed in claim 1, which comprises

a) reacting a compound of the formula I in which R^1 has the meaning initially given and R^2 to R^4 are hydrogen with a boric acid, such as phenylboric acid, or with a ketone, such as acetone, or a ketal, such as 2,2-dimethoxypropane, or an acetal, such as benzaldehyde dimethyl acetal, in a suitable organic solvent, such as toluene or dimethylformamide or mixtures thereof, with a catalyst, such as a mineral, carboxylic or sulfonic acid, at a temperature between 0°C and the boiling point of the solvent, if appropriate with the addition of a dehydrating agent, such as 4A molecular sieve, to give a compound of the formula I in which R^1 has the meaning initially given and R^2 together with R^3 form a compound of the formula III, which is isolated by filtration and by removal of the solvent and crystallized out of an organic solvent, such as petroleum ether, after which the hydroxyl group on position 10 is derivatized in a suitable manner,

b) if appropriate acylating with a carboxylic acid anhydride, such as acetic anhydride or trifluoroacetic anhydride, or a phenylcarboxylic acid anhydride or a carboxylic acid halide or by reacting with trimethylsilyl trifluoromethanesulfonate in a suitable organic solvent, such as chloroform, methylene chloride, toluene or mixtures thereof, at a temperature between -40°C and the boiling point of the solvent and in the presence of a base, such as triethylamine or pyridine, to give a compound of the formula I in which
R^1 has the meaning initially given,
R^2 together with R^3 is a structure of the formula III and
R^4 is acyl or trimethylsilyl,

c) or, for example, reacting the compound obtained under a) with 3,4-dihydro-2H-pyran in a suitable organic solvent, such as chloroform, methylene chloride, dimethylformamide or toluene, in the presence of a catalyst, such as para-toluenesulfonic acid and a desiccant, such as 4Å molecular sieve, at a temperature between -30°C and the boiling point of the solvent, to give a compound of the formula I in which
R^1 has the meaning initially given,
R^2 together with R^3 is a structure of the formula III and
R^4 is a structure of the formula II, where R^5 to R^8 is hydrogen,

d) or, for example, reacting the compound obtained under a) with a carbohydrate derivative of the formula V

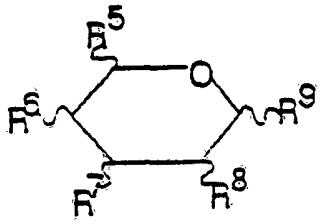


V

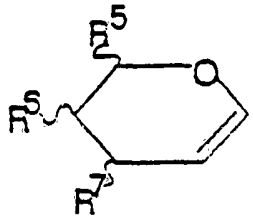
in which
R^5 to R^8, as suitable protective groups, have the meanings initially given and
R^9 is halogen, such as Cl or Br, O-acyl or another leaving group which is customary for glycosidation reactions,

under the conditions customary in carbohydrate chemistry, to give a compound of the formula I in which
R^1 has the meaning initially given,
R^2 together with R^3 is a structure of the formula III and
R^4 is a structure of the formula II,

e) or, for example, reacting the compound obtained under a) with a functionalized carbohydrate of the general formula V or VI



V



VI

in which
R^5 to R^8 have the meanings initially given, with the exception of hydroxymethyl, hydroxyl, NH_2, $N(CH_2CN)_2$ and $NH(CH_2CN)$ and
R^9 is acyl which is bonded via oxygen, such as ali-

phatic acyloxy (C1-C8), such as acetyl, benzoyloxy or substituted benzoyloxy, such as para-nitrobenzoyloxy,

in the presence of an organic solvent, such as chloroform, methylene chloride, toluene, ether, dimethylformamide, acetone, acetonitrile or nitromethane or mixtures thereof, a catalyst, such as para-toluenesulfonic acid or a trialkylsilyl trifluoromethanesulfonate, and if appropriate an acid-trapping agent and a desiccant, such as molecular sieve, at a reaction temperature of -70°C to +30°C under a protective gas atmosphere, such as nitrogen or argon, to give a compound of the formula I

in which
R^1 has the meaning given,
R^2 together with R^3 is a structure of the formula III and
R^4 is a structure of the formula II or IV, in which
R^5 to R^8 have the meanings initially given, with the exception of hydroxymethyl, hydroxyl, NH_2, $N(CH_2CN)_2$ and $NH(CH_2CN)$,

f) and, if appropriate, possibly deblocking the compound of stages b) to e) on positions 7 and 9 by reacting this compound in a suitable organic solvent, such as chloroform, methylene chloride, dimethylformamide, toluene or methanol, with a catalyst, such as dilute aqueous solutions of carboxylic acids or paratoluenesulfonic acid, and if appropriate with a diol, such as 2-methyl-2,4-pentanediol, at a temperature between 0°C and the boiling point of the solvent, to give a compound of the general formula I in which
R^1 has the meaning given,
R^2 and R^3 are hydrogen and
R^4 has the meaning given, with the exception of hydrogen,

g) and subsequently, if appropriate, possibly selectively partly or completely deblocking the compound of stage f) in which R^4 is a structure of the formula II or IV with, as radicals R^5 to R^8, one of the protective groups customary in carbohydrate chemistry, in a manner which is known per se on the protected hydroxyl functions and/or on the protected amino functions under the conditions customary in carbohydrate chemistry by means of an inorganic or organic base, such as alkali metal or alkaline earth metal hydroxides, sodium carbonate and triethylamine, in a solvent, such as water, methanol, ethanol or tetrahydrofuran or mixtures thereof, to give a compound of the formula I in which

R^1 is hydrogen or hydroxyl,
R^2 and R^3 are hydrogen and
R^4 is a structure of the formula II or IV, in which
R^5 is hydrogen, methyl, hydroxymethyl or alkoxymethyl,
R^6 is hydrogen, hydroxyl, alkoxy or halogen,
R^7 is NH_2 $N(alkyl)_2$, azido, hydroxyl or alkoxy and
R^8 has the same meaning as R^6 but is independent thereof,

h) and, if appropriate, reacting the compound of stage g) of the formula I, in which
R^1 to R^3 have the meanings given under g) and
R^4 is a structure of the formula II, in which
R^5, R^6 and R^8 have the meanings given under g) and
R^7 is NH_2,

under the conditions which are known per se for reductive amination, to give the corresponding compound of the formula I in which

R^1 to R^3 have the meanings given under g) and
R^4 is a structure of the formula II,

in which

R^5, R^6 and R^8 have the meanings given under g) and
R^7 is $N(alkyl)_2$, or

i) furthermore converting a compound of stage g) of the general formula I in which
R^1 to R^3 have the meanings given under g) and
R^4 is a structure of the formula II in which
R^5, R^6 and R^8 have the meanings given under g) and
R^7 is NH_2,

by reaction with iodoacetonitrile or bromoacetonitrile in a suitable solvent, for example dimethylformamide, in the presence of a suitable base, such as triethylamine, into a compound of the formula I in which R^1 to R^3 have the meanings given under g) and R^4 is a structure of the formula II, in which
R^5, R^6 and R^8 have the meanings given under g) and
R^7 is $N(CH_2CN)_2$ or $NH(CH_2CN)$ and

k) if appropriate glycosidating the compound formed in stage f), h) or i) under the conditions already mentioned in stage e), either only position 7 or simultaneously positions 7 and 9 being glycosidated, depending on the amount of glycosyl donor used, to give products which correspond to the general formula I in which
R^1 has the meaning given,
R^2 is a structure of the formula II or IV, in which
R^5 to R^8 have the meanings initially given, with the exception of hydroxymethyl, hydroxyl, NH_2, $N(CH_2CN)_2$ and $NH(CH_2CN)$,
R^3 is hydrogen or corresponds to R^2 and
R^4 is acyl, trimethylsilyl or a structure of the general formula II or IV in which
R^5 to R^8 have the meanings initially mentioned, with the exception of hydroxymethyl, hydroxyl and NH_2, and, if appropriate,

l) converting one of the compounds formed in stage f), h) or i) with a glycal of the formula VI, in which R^5 to R^7 have the meanings given in stage e), in the presence of an organic solvent, such as chloroform, methylene chloride, toluene, ether, acetone or acetonitrile or mixtures thereof, with N-iodosuccinimide and if appropriate with a desiccant, such as molecular sieve, at a temperature from -40°C to +40°C under a protective gas atmosphere, such as nitrogen or argon, into a compound of the formula I in which
R^1 has the meaning given and
R^2 is a structure of the formula II, in which
R^5 is hydrogen, methyl, acyloxymethyl (C1-C8) or alkoxymethyl (C1-C8),
R^6 is acyloxy, alkyloxy, allyloxy or benzyloxy,
R^7 is acyloxy, alkyloxy, allyloxy, benzyloxy, NHacyl, $N(alkyl)_2$ or azido and
R^8 is iodine, and
R^3 and R^4 have the meanings given in stage k), and

m) if appropriate deblocking the compound formed in stage k) or l) in accordance with the conditions of stage g), to give a compound of the formula I in which
R^1 has the meaning given and
R^2 is a structure of the formula II or IV, in which
R^5 is hydrogen, methyl, hydroxymethyl or alkyloxymethyl,
R^6 is hydrogen, hydroxyl, alkyloxy or halogen,
R^7 is NH_2 or $N(alkyl)_2$, azido, hydroxyl or alkoxy and
R^8 has the same meaning as R^6, but is independent thereof,
R^3 is hydrogen or corresponds to R^2 and
R^4 is hydrogen, trimethylsilyl or a structure of the general formula II or IV, in which
R^5 is hydrogen, methyl, hydroxymethyl or alkoxymethyl,
R^6 is hydrogen, hydroxyl, alkoxy or halogen,

R^7 is NH_2, $N(alkyl)_2$, $N(CH_2CN)_2$ or $NH(CH_2CN)$, azido, hydroxyl or alkoxy and
R^8 has the same meaning as R^6, but is independent thereof, or

n) also deblocking the compound formed in stage k) or l) under the conditions of stage g) so that only position 10 is selectively deblocked, to give a compound of the formula I in which
R^1 has the meaning given,
R^2 is a structure of the formula II or IV, in which
R^5 to R^8 have the meanings initially given, with the exception of hydroxymethyl, hydroxyl and NH_2,
R^3 is hydrogen or corresponds to R^2 and
R^4 is hydrogen,

o) and subsequently, if appropriate, converting the compound of stage m), in which R^2 is a structure of the formula II where R^7 is NH_2 and R^3 is hydrogen or R^2, into the corresponding compounds in which R^6 is $N(alkyl)_2$, again in the manner of reductive amination described for stage h), or, if appropriate,

p) converting a compound of stage m) in which R^2 is a structure of the formula II, where R^7 is NH_2 and R^3 is hydrogen or R^2, into the corresponding cyanomethyl derivatives in which
R^7 is $N(CH_2CN)_2$ or $NH(CH_2CN)$ in accordance with the conditions of stage i), and, if appropriate,

q) glycosidating a compound of stage n) under the conditions already given in stage e), either only position 10 or simultaneously positions 9 and 10 being glycosidated, depending on the amount of glycosyl donor used, to give a compound of the formula I in which

R^1 is hydrogen or hydroxyl and
R^2 is a structure of the general formula II or IV,

in which
R^5 to R^8 have the meanings initially given, with the exception of hydroxymethyl, hydroxyl and NH_2,
R^3 is hydrogen or R^2 or R^4 and
R^4 is a structure of the general formula II or IV, in which
R^5 to R^8 have the meanings initially given, with the exception of hydroxymethyl, hydroxyl, NH_2, $N(CH_2CN)_2$ or $NH(CH_2CN)$, and, if appropriate,

r) also carrying out the reaction of stages c), d) and l) on a compound of stage n) so as to give a compound of the formula I in which
R^1 has the meaning initially given and
R^2 is a structure of the formula II or IV, in which
R^5 to R^8 have the meanings initially given, with the exception of hydroxymethyl, hydroxyl and NH_2,
R^3 is hydrogen or R^2 or R^4 and
R^4 is a structure of the general formula II or IV in which
R^5 to R^8 have the meanings initially given, with the exception of hydroxymethyl, hydroxyl, NH_2, $N(CH_2CN)_2$ and $NH(CH_2CN)$, and, if appropriate,

s) deblocking this compound of stage q) or r) again as described in stage g), to give a compound of the formula I in which
R^1 has the meaning initially given and
R^2, R^3 and R^4 independently of one another are hydrogen or a structure of the formula II or IV, in which
R^5 to R^8 have the meanings initially given, with the exception of acyloxymethyl, acyloxy, benzoyloxy or substituted benzoyloxy or NHacyl, and, if appropriate,

t) converting the compound of stage s) into the corresponding derivative in which the radical R^7, which in

stage s) was an NH_2 group, is converted into $N(alkyl)_2$, by means of reduction amination in accordance with stage h), or

u) moreover converting a compound of stage s) into the corresponding cyanomethyl derivative in which the radical R^7, which in stage s) was an NH_2 group, into $NH(CH_2CN)$ in accordance with the conditions of stage i),

v) and, if appropriate, reacting a compound of the formula I in which
R^1, R^2 and R^3 have the meanings given and
R^4 is trimethylsilyl,
with tetrabutylammonium fluoride in an organic solvent, such as tetrahydrofuran, diethyl ether, dioxane or mixtures thereof, at temperatures between -40°C and the boiling point of the solvent, to give a compound of the formula I in which
R^1, R^2 and R^3 have the meanings given above and
R^4 is hydroxyl,

w) and, if appropriate, converting compounds of the formula I in which R^1, R^2, R^3 and R^4 have the meanings given and R^7 is NH_2, $N(alkyl)_2$ (C1-C8), $N(CH_2CN)_2$ or $NH(CH_2CN)$ into the salt of an inorganic or organic acid.

8. The process as claimed in claim 7, wherein
a compound of the formula I in which R^1 has the meaning initially given, R^2 together with R^3 forms a structure of the formula III and R^4 is hydrogen, is converted by acylation with a carboxylic acid anhydride, such as acetic anhydride or trifluoroacetic anhydride, or a phenylcarboxylic acid anhydride or a carboxylic acid halide or by reaction with trimethylsilyl trifluoromethanesulfonate in an organic solvent,

such as chloroform, methylene chloride or toluene or mixtures thereof, at a temperature between -40°C and the boiling point of the solvent and in the presence of a base, such as triethylamine or pyridine, into a compound of the formula I in which

R^1 has the meaning initially given,
R^2 together with R^3 is a structure of the formula III and
R^4 is acyl or trimethylsilyl, or

wherein a compound of the formula I in which R^1 has the meaning initially given, R^2 together with R^3 forms a structure of the formula III and R^4 is hydrogen, is converted by reaction with 3,4-dihydro-2H-pyran in a suitable organic solvent, such as chloroform, methylene chloride, dimethylformamide or toluene, in the presence of a catalyst, such as para-toluenesulfonic acid, and a desiccant, such as 4Å molecular sieve, at a temperature between -30°C and the boiling point of the solvent, into a compound of the formula I in which

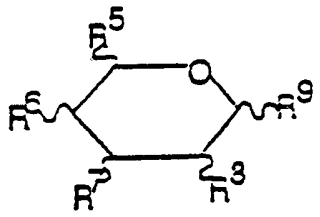
R^1 has the meaning initially given,
R^2 together with R^3 is a structure of the formula III and
R^4 is a structure of the formula II where R^5 to R^8 are hydrogen.

9. The process as claimed in claim 7, wherein a compound of the formula I in which R^1 has the meaning initially given, R^2 together with R^3 forms a structure of the formula III and R^4 has the meaning given, excluding hydrogen, can be deblocked at positions 7 and 9 by reacting this compound in a suitable organic solvent, such as chloroform, methylene chloride, dimethylformamide, toluene or methanol, with a

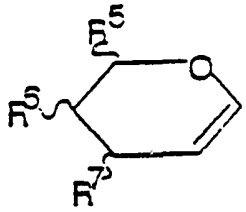
catalyst, such as dilute aqueous solutions of carboxylic acids or para-toluenesulfonic acid, and if appropriate with a diol, such as 2-methyl-2,4-pentanediol, at a temperature between 0°C and the boiling point of the solvent, to give a compound of the general formula I in which

R^1 has the meaning given,
R^2 and R^3 are hydrogen and
R^4 has the meaning given, with the exception of hydrogen.

10. The process as claimed in claim 7,
wherein
a compound of the formula I in which R^1 to R^4 have the meanings given, but R^2 or R^4 must be hydrogen and R^5 to R^8 cannot be hydroxyl, hydroxymethyl or NH_2, is reacted with a functionalized carbohydrate of the general formula V or VI



V



VI

in which
R^5 to R^8 have the meanings initially given, with the exception of hydroxymethyl, hydroxyl, NH_2, $N(CH_2CN)_2$ and $NH(CH_2CN)$ and
R^9 is an acyl protective group bonded via oxygen, such as aliphatic acyloxy (C1-C8), such as acetyl, benzoyloxy or substituted benzoyloxy, such as para-nitrobenzoyloxy,
in the presence of an organic solvent, such as chloroform, methylene chloride, toluene, ether, dimethylformamide, acetone, acetonitrile or nitromethane or mixtures thereof, a catalyst, such as para-toluenesulfonic acid or a trialkylsilyl tri-

fluoromethanesulfonate, and if appropriate an acid-trapping agent and a desiccant, such as molecular sieve, at a reaction temperature of -70°C to +30°C under a protective gas atmosphere, such as nitrogen or argon, to give a compound of the formula I in which

R^1 has the meaning given,
R^2 together with R^3 is a structure of the formula III or R^2, R^3 or R^4 is a structure of the formula II or IV, in which

R^5 to R^8 have the meanings initially given, with the exception of hydroxymethyl, hydroxyl and NH_2, or

wherein a compound of the formula I in which R^1 to R^4 have the meanings given, but R^2 or R^4 must be hydrogen and R^5 to R^8 cannot be hydroxyl, hydroxymethyl or NH_2, is converted in the presence of an organic solvent, such as chloroform, methylene chloride, toluene, ether, acetone or acetonitrile or mixtures thereof, with a glycal of the formula VI, in which R^5 to R^7 have the meanings initially given, with the exception of hydroxymethyl, hydroxyl, NH_2, $N(CH_2CN)_2$ and $NH(CH_2CN)$, with N-iodosuccinimide and if appropriate with a desiccant, such as molecular sieve, at a temperature of -40°C to +40°C under a protective gas atmosphere, such as nitrogen or argon, into a compound of the formula I in which

R^1 has the meaning given,
R^2 together with R^3 is a structure of the formula III or R^2, R^3 or
R^4 is a structure of the formula II or IV, in which
R^5 to R^8 have the meanings initially given, with the exception of hydroxymethyl, hydroxyl, NH_2, $N(CH_2CN)_2$ and $NH(CH_2CN)$.

11. Method of treatment of tumours comprising administering the compound of claim 1 to a patient.

DATED this 25th day of June, 1991.

BEHRINGWERKE AKTIENGESELLSCHAFT

WATERMARK PATENT & TRADEMARK ATTORNEYS,
290 Burwood Road,
HAWTHORN. VIC. 3122
AUSTRALIA

DBM:JMW:JZ