



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification ⁶ : C07H 15/04, 3/04</p>	<p>A3</p>	<p>(11) International Publication Number: WO 96/03413 (43) International Publication Date: 8 February 1996 (08.02.96)</p>
<p>(21) International Application Number: PCT/EP95/03034 (22) International Filing Date: 27 July 1995 (27.07.95) (30) Priority Data: 9415169.3 27 July 1994 (27.07.94) GB 9422304.7 4 November 1994 (04.11.94) GB (71) Applicant (for all designated States except US): GENZYME LIMITED [GB/GB]; 37 Hollands Road, Haverhill, Suffolk CB9 8PU (GB). (72) Inventors; and (75) Inventors/Applicants (for US only): FLITSCH, Sabine [DE/GB]; St Hilda's College, Oxford OX4 1DY (GB). GUILBERT, Benedicte [FR/GB]; The Dyson Perrins Laboratory, University of Oxford, South Parks Road, Oxford OX1 3QY (GB). (74) Agents: FROUD, Clive et al.; Elkington and Fife, Prospect House, 8 Pembroke Road, Sevenoaks, Kent TN13 1XR (GB).</p>	<p>(81) Designated States: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA, US, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD, SZ, UG). Published <i>With international search report.</i> (88) Date of publication of the international search report: 18 July 1996 (18.07.96)</p>	
<p>(54) Title: REGIOSELECTIVE SULFATION</p>		
<p>(57) Abstract <i>Inter alia</i>, a direct method for the regioselective sulfation of an organic molecule having optionally derivatized hydroxyl groups at least on two adjacent carbon atoms characterised in that it comprises the treatment of a di-(optionally substituted alkyl and/or aryl) stannylene acetal derivative thereof with an electrophilic sulfating agent is disclosed.</p>		

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 95/03034

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07H15/04 C07H3/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07H

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	J. ORG. CHEM., vol. 51, 1986 pages 1525-9, K.W. PANKIEWICZ ET AL. '(Trifluormethyl)sulfonyl (Triflyl) Migration' see abstract ---	1-7
P,X	HELV. CHIM. ACTA, vol. 77, no. 8, 1 August 1994 pages 2341-53, S. LANGSTON ET AL. 'Temporary Protection and Activation in the Regioselective Synthesis of Saccharide Sulfates' see the whole document --- -/--	1-10

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

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- *&* document member of the same patent family

Date of the actual completion of the international search

1 April 1996

Date of mailing of the international search report

19.04.96

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 95/03034

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	TETRAHDRON LETT., vol. 35, no. 47, 21 November 1994 pages 8795-6, A. LUBINEAU ET AL. 'Regioselective Sulfation of Galactose Derivatives through the Stannylene Procedure' see the whole document ---	1-10
P,X	TETRAHEDR. LETT., vol. 35, no. 35, 29 August 1994 pages 6563-6, B. GUILBERT ET AL. 'Regioselective Sulfation of Disaccharides Using Dibutylstannylene Acetals' see the whole document ---	1-10
Y	CHEM. PHARM. BULL., vol. 39, 1991 pages 2883-7, Y. TSUDA ET AL. 'Regioselective Monotosylation of Non-protected and Partially Protected Glycosides by the Dibutyltin Oxide Method' reaction 21 -> 22 see page 2883 ---	1-7
P,A	CHEMICAL ABSTRACTS, vol. 122, no. 15, 10 April 1995 Columbus, Ohio, US; abstract no. 187916, T.V. ZEMLYANUKHINA ET AL. 'Receptors for Selectins' page 1095; see abstract ---	1-7
X A	& BIOORG. KHIM., vol. 20, no. 5, 1994 pages 556-9, ---	10 1-7
P,X	TETRAHEDRON: ASYMMETRIE, vol. 5, no. 11, 11 November 1994 pages 2163-78, B. GUILBERT ET AL. 'Dibutylstannylene Acetals: Useful Intermediates for the Regioselective Sulfation of Glycosides' see the whole document ---	1-10
Y	TETRAHEDRON LETT., vol. 33, 1992 pages 5519-20, K. FUJITA ET AL. 'Selective Preparation of Hexakis(6-0-arenesulfonyl)-alpha-cyclodext rin' see the whole document ---	1-7
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INTERNATIONAL SEARCH REPORT

Inter national Application No
PCT/EP 95/03034

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP,A,0 410 953 (MONSANTO COMPANY) 30 January 1991 see the whole document ---	1-7
A	CARBOHYDR. RES., vol. 214, 1991 pages 245-56, K.G. LUDWIG-BAXTER ET AL. 'Regioselectivity in the Sulfation of Dermatan Sulfate and Methyl 4,6-O-benzylidene-alpha-D-idopyranoside' see page 251 ---	1-7
X	CAN. J. CHEM., vol. 68, 1990 pages 1122-27, A. RASHID ET AL. 'Novel Synthesis of Monosulfated Methyl-alpha-D-Galactopyranosides' see page 1123 ---	8
X	BIOSCI., BIOTECH., BIOCHEM., vol. 56, 1992 pages 1413-16, S. HARA ET AL. 'Regioselectivity in Sulfation of Galactosides by Sulfuric Acid and Dicyclohexylcarbodiimide' 'Fraction B1' see page 1415, right column ---	8
X	J. CHEM. SOC. PERKIN TRANS. 1, 1994 pages 359-68, N.J. DAVIES AND S.L. FLITSCH 'Chemical Synthesis of Disaccharides which are Partial Structures of the Glycosaminoglycan Heparan Sulfate' cited in the application see page 360, 361 'compounds 5, 6, 35, 36' ---	8
X	WO,A,94 00596 (HEALTH RESEARCH INC) 6 January 1994 see the whole document ---	8,9
X	J. BIOL. CHEM., vol. 269, no. 3, 21 January 1994 pages 1595-8, T. FEIZI ET AL. 'Sulfated Blood Group Lewis a' cited in the application see the whole document ---	10
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INTERNATIONAL SEARCH REPORT

International Application No

PC1/EP 95/03034

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHEMICAL ABSTRACTS, vol. 120, no. 1, 3 January 1994 Columbus, Ohio, US; abstract no. 8924, Y. MORIKAWA ET AL. 'Preparation of acidic glycolipids for pharmaceutical microparticle carriers such as liposomes' page 985; see 'formula II' & JP,A,05 186 491 (DEI DEI ESU KENKYUSHO) 27 July 1993 -----	10

INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP 95/ 03034

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. Claims: 1-7 Regioselective preparation of organic sulfates of 1,2-diols using a stannylene acetal intermediate
2. Claims: 8-10 Monosulfate derivatives of specific organic diol compounds.

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 95/03034

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A-410953	30-01-91	US-A- 5025021 US-A- 5026713 AT-T- 129997 CA-A- 2022061 DE-D- 69023408 JP-A- 3058969 US-A- 5175168 US-A- 5130320 US-A- 5218121	18-06-91 25-06-91 15-11-95 28-01-91 14-12-95 14-03-91 29-12-92 14-07-92 08-06-93

WO-A-9400596	06-01-94	AU-B- 4652093 CA-A- 2137008 EP-A- 0648279 JP-T- 7508730 NO-A- 945062	24-01-94 06-01-94 19-04-95 28-09-95 23-02-95
