

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
21 August 2003 (21.08.2003)

PCT

(10) International Publication Number  
**WO 03/068913 A3**

- (51) International Patent Classification<sup>7</sup>: C07C 321/12, 321/16, 319/14, 69/02, A61K 51/04
- (21) International Application Number: PCT/US03/03525
- (22) International Filing Date: 6 February 2003 (06.02.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
10/074,669 13 February 2002 (13.02.2002) US
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- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:**  
— with international search report
- (88) Date of publication of the international search report:  
24 December 2003
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*



WO 03/068913 A3

(54) Title: SYNTHESIS OF <sup>2</sup>H- AND <sup>13</sup>C- SUBSTITUTED DITHIANES

(57) Abstract: The present invention is directed to labeled compounds, [2-<sup>13</sup>C]dithiane wherein the <sup>13</sup>C atom is directly bonded to one or two deuterium atoms. The present invention is also directed to processes of preparing [2-<sup>13</sup>C]dithiane wherein the <sup>13</sup>C atom is directly bonded to one or two deuterium atoms. The present invention is also directed to labeled compounds, e.g., [<sup>2</sup>H<sub>1-2</sub>, <sup>13</sup>C]methanol (arythio)-, acetates wherein the <sup>13</sup>C atom is directly bonded to exactly one or two deuterium atoms.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/03525

<b>A. CLASSIFICATION OF SUBJECT MATTER</b>		
IPC(7) : C07C 321/12, 321/16, 319/14, 69.02; A61K 51/04		
US CL : 568/38, 39, 57; 569/1, 129, 231		
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b>		
Minimum documentation searched (classification system followed by classification symbols) U.S. : 568/38, 39, 57; 560/1, 129, 231; 424/1.65, 1.81		
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 practicable, search terms used) Please See Continuation Sheet		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A -	Database CAPLUS on STN Chem. Abstracts( Columbus, OHIO USA) No. 92:21897. LAMBERT et al. 'Protonic and conformational equilibriums of 1,3-dithiaalkanes and their congeners in highly acidic media' abs of Journal of Organic Chemistry 44(25) pages 4689-95, 1979.	1-4
A -	Database CAPLUS on STN Chem. Abstracts (Columbus OHIO, USA) No. 93:90890. BATTERSBY et al. 'Studies of enzyme-mediated reactions. Part 12. Stereochemical course of decarboxylation of (2-S)-tyrosine to tyramine by microbial, mammalian, and plant systems' abs of J. Chem Soc. Perkin Trans. 1 : Organic and BioOrganic Chemistry (1) pages 31-42, 1980.	1-4
A -	Database CAPLUS on STN Chem. Abstracts (Columbus OHIO USA) No. 100:102632. ASHER et al. 'Carbon-13 NMR spectra of carbanions derived from 2-substituted 1,3-dithianes, 9-substituted fluorenes, and biphenylmethanes as related to structure and charge density' abs Journal of the American Chem. Soc. 106(5) pages 1432-40, 1984.	1-4
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
* Special categories of cited documents:		
"A"	document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E"	earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means	
"P"	document published prior to the international filing date but later than the priority date claimed	"&" document member of the same patent family
Date of the actual completion of the international search		Date of mailing of the international search report
22 June 2003 (22.06.2003)		07 AUG 2003
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230		Authorized officer Jean F. Vollano Telephone No. 703-308-1235

## INTERNATIONAL SEARCH REPORT

## C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Database STN on CAPLUS Chem. Abstracts (Columbus OHIO USA) No. 89:128836. FURUKAWA et al. 'Pummerer-type reaction of sulfilimines with acetic anhydride' abs of Phosphorus and Sulfur and the Related Elements 3(3) pages 277-80, 1977.	5-9
A	Database CAPLUS on STN Chem. Abstracts (Columbus OHIO USA) No. 99:194546. PAVLOVA et al. 'Synthesis and disproportionation of monothioacetals' abs of Sint. Metody Osn. Elementoorg. Soedin pages 85-93, 1982	5-7

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/03525

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

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

1.  Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claim 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.  Claim 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:  
Please See Continuation Sheet

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.

**BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-4, drawn to a deuterio labels dithiane and a method of preparing the dithiane.

Group II, claim(s) claims 5-7 ( in part), drawn to a compound of the formula Ar S CD<sub>2</sub>-xHxOR wherein x is 0 or 1 and R is alkyl. This would be an alcohol thio compound.

Group III, claim(s) 5-7 (in part ) and 8-9( in full ) , drawn to an aryl thio ester.

The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Group I is drawn to a deuterated dithiane and a method of making that dithiane. This Group is drawn to a compound and a method of making the compound and in itself has unity of invention and has been kept together in one group. Group II is drawn to a deuterated arylthio alcohol which is a structural unit different from the ester in Group III and the dithiane in Group I. The only thing that links the ester the alcohol and the dithiane ( sulfur ring system) is the fact that they are all deuterated. This may be a technical feature but it is the same technical feature share by thousands of compounds . It is not a special technical feature. Group I has within itself a special technical feature and that is the compound and the method of making the compound. As such that invention has been grouped together. Group II nor Group III can use the method of preparation found in Group I and there is no structural special technical feature uniting the groups. There is no special technical feature uniting the groups and there is no unity of invention since the groups are all different compounds and the method of making in Group I is not applicable to Groups II and III.

**Continuation of B. FIELDS SEARCHED Item 3:**  
CAS ONLINE , EAST

search terms: structure drawings, deuterio, carbon-13, 13C, 1,3-dithiane, thio acetate, thiomethanol