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(54) Title: SULFUR-HETEROCYCLE EXCHANGE CHEMISTRY AND USES THEREOF

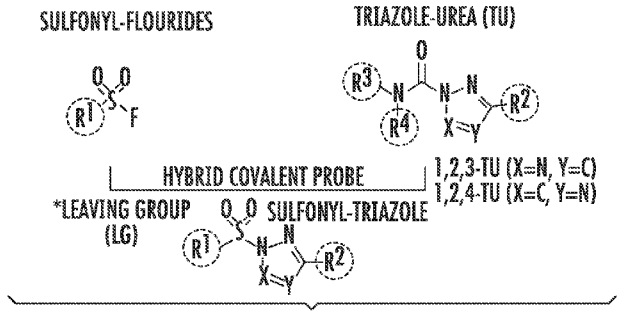

FIG. 1A

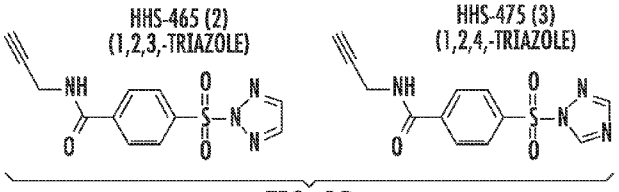

FIG. 1B

(57) Abstract: Sulfonyl-triazole compounds and related sulfonyl-heterocycle compounds are described. The compounds can be used to identify reactive nucleophilic amino acid residues, such as reactive tyrosines and reactive lysines, in proteins and to modify the activity of proteins with reactive nuclophilic amino acid residues via the formation of protein adducts comprising a fragment of the compounds. Methods are also described for screening the compounds to identify ligands of proteins comprising a reactive lysine or a reactive tyrosine.

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[Continued on next page]

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 20/24286

A. CLASSIFICATION OF SUBJECT MATTER

IPC - C07D 401/12; C07D 401/14; C07D 405/14 (2020.01)

CPC - A61P 13/12; A61P 43/00; A61P 9/00; A61P 9/04; A61P 9/10

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)
See Search History document

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PubChem-CID-11045411, Create Date: 26 October 2006 (26.10.2006), pg 2, Fig.	33-36
A	NARAYANAN et al. "Sulfonyl fluorides as privileged warheads in chemical biology", Chem. Sci., 2015. Vol. 6, pp 2650-2659, entire document, especially: pg 2654, col 1, para 2-3; pg 2656, Fig. 7a, formula DAS1; Fig. 3, formula, FSBA.	1-8,21-30,51-52
A	LIU et al. "Aryl vinyl sulfonates and sulfones as active site-directed and mechanism-based probes for protein tyrosine phosphatases", J Am Chem Soc. 2008. Vol. 130(26), pp 8251-8260, entire document, especially: abstract; pg 4, para 2; pg 7, para 1; pg 13, Figure 1.	1-8,21-30,51-52
A	PubChem-CID-69947416, Create Date: 1 December 2012 (01.12.2012), pg 2, Fig.	1-8,21-30,51-52
A	PubChem-CID-71376695, Create Date: 22 May 2013 (22.05.2013), pg 2, Fig.	33-36
A	PubChem-CID-12585520, Create Date: 8 February 2007 (08.02.2007), pg 2, Fig.	1-8,21-30,33-36,51-52
P/X	HAHM et al. "Global targeting of functional tyrosines using sulfur triazole exchange chemistry", Nat Chem Biol. 25 November 2019 (25.11.2019), Vol. 16(2), pp 150-159, entire document.	1-8,21-30,33-36,51-52

☐ Further documents are listed in the continuation of Box C. ☐ 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
"D" document cited by the applicant in the international application
"E" earlier application or patent but published on or after the international filing date
"I." 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)
"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
"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
"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
"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
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
1 November 2020	22 JAN 2021
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Lee Young Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 20/24286

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 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.: 9-20 and 37-38
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
--see attached extra 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 additional fees, this Authority did not invite payment of additional fees.

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.:
1-8, 21-30, 33-36 and 51-52

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/US 20/24286

--BOX III - LACK OF UNITY--

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 searched, the appropriate additional search fees must be paid.

Group I: Claims 1-8, 21-32 and 51-52 directed to a method of identifying a reactive tyrosine or lysine of a protein, the method comprising: (a) providing a protein sample comprising isolated proteins, living cells, or a cell lysate; (b) contacting the protein sample with a probe compound of Formula (I) for a period of time sufficient for the probe compound to react with at least one reactive tyrosine (or lysine) in a protein in the protein sample, thereby forming at least one modified reactive tyrosine (or lysine) residue; and (c) analyzing proteins in the protein sample to identify at least one modified tyrosine (or lysine) residue, thereby identifying at least one reactive tyrosine (or lysine) of a protein; wherein the probe compound has a structure of Formula (I).

Group II: Claims 33-36 and 39-50, directed to a modified tyrosine-containing protein comprising a modified tyrosine residue wherein the modified tyrosine residue is formed by the reaction of a tyrosine residue with a non-naturally occurring tyrosine-reactive compound having a structure of Formula (III).

Special Technical Features

The inventions listed as Groups I and II 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 requires a compound of Formula (I), which is not required by Group II.

Group II requires a compound of Formula (III), which is not required by Group I.

Shared Common Features

The only feature shared by Groups I and II that would otherwise unify the groups is a compound having the structure of a sulfonyl with a five-membered nitrogen containing heteroaryl on one side and a carbon atom containing group on the other side. However, this shared technical feature does not represent a contribution over prior art, because the shared technical feature is anticipated by the document entitled PubChem-CID-12585520 (hereinafter 'PubChem-520').

PubChem-520 discloses a sulfonyl with a five-membered nitrogen containing heteroaryl on one side and a carbon atom containing group on the other side (pg 2, Fig).

As the technical features were known in the art at the time of the invention, this cannot be considered a special technical feature that would otherwise unify the groups. Groups I and II therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.

Note reg. item 4: Claims 9-20 and 37-38 are unsearchable because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Note: Claim 31 lacks clarity with respect to Formula (II). Claim 31 refers to a modified tyrosine-containing protein, but Formula (II) in claim 31 shows only a toluene modified with a sulfonyl. Claim 1 also refers to a modified tyrosine-containing residue of Formula (II), but claim 1 indicates that the substructure indicated is further connected to another group with a wavy line. For the purposes of the opinion, it was assumed that claim 31 should also be interpreted to include the same wavy line found for Formula (II) in claim 1.

Note: Claims 31-32 were incorrectly listed under Group I, and claims 33-36 were incorrectly listed under Group II. Claims 31-32 are directed to the invention of Group II and claims 33-36 are directed ot the invention of Group I. Therefore for the purposes of the opinion, the claim grouping was: Clams 1-8, 21-30, 33-36, 51-52 for Group I and claims 31-32 and 39-50 for Group II.