US009408924B2

(12) **United States Patent**
Xu et al.

(10) **Patent No.: US 9,408,924 B2**
(45) **Date of Patent: *Aug. 9, 2016**

(54) **BIOCONJUGATES OF CYANINE DYES**

(71) Applicant: **LI-COR, INC.**, Lincoln, NE (US)

(72) Inventors: **Xinshe Xu**, Lincoln, NE (US); **Daniel R. Draney**, Lincoln, NE (US); **Lael Cheung**, Lincoln, NE (US)

(73) Assignee: **LI-COR, INC.**, Lincoln, NE (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **14/552,396**

(22) Filed: **Nov. 24, 2014**

(65) **Prior Publication Data**

US 2015/0119553 A1 Apr. 30, 2015

Related U.S. Application Data

(63) Continuation of application No. 13/831,345, filed on Mar. 14, 2013, now Pat. No. 8,927,719, which is a continuation of application No. PCT/US2011/057134, filed on Oct. 20, 2011.

(60) Provisional application No. 61/405,161, filed on Oct. 20, 2010, provisional application No. 61/405,158, filed on Oct. 20, 2010.

(51) **Int. Cl.**

C07D 401/06	(2006.01)
C07D 471/04	(2006.01)
A61K 49/00	(2006.01)
C09B 23/01	(2006.01)
C09B 23/08	(2006.01)
C09B 69/00	(2006.01)
G01N 33/574	(2006.01)
G01N 33/58	(2006.01)
C07F 9/6561	(2006.01)
C07K 19/00	(2006.01)
C08B 37/08	(2006.01)

(52) **U.S. Cl.**

CPC ***A61K 49/0058*** (2013.01); ***A61K 49/0032*** (2013.01); ***A61K 49/0052*** (2013.01); ***C07D 471/04*** (2013.01); ***C07F 9/6561*** (2013.01); ***C07K 19/00*** (2013.01); ***C08B 37/0072*** (2013.01); ***C09B 23/0008*** (2013.01); ***C09B 23/0016*** (2013.01); ***C09B 23/0025*** (2013.01); ***C09B 23/0066*** (2013.01); ***C09B 23/083*** (2013.01); ***C09B 23/086*** (2013.01); ***C09B 69/00*** (2013.01); ***G01N 33/574*** (2013.01); ***G01N 33/58*** (2013.01); ***G01N 33/582*** (2013.01)

(58) **Field of Classification Search**

CPC C07D 401/06; C07D 471/04
USPC 546/113
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,723,419	A	3/1973	Mee et al.
3,864,644	A	2/1975	Lincoln et al.
4,011,086	A	3/1977	Simson
4,264,694	A	4/1981	Pu et al.
4,871,656	A	10/1989	Parton et al.

(Continued)

FOREIGN PATENT DOCUMENTS

DE	4445065	A1	6/1996
EP	0 341 958	A2	11/1989

(Continued)

OTHER PUBLICATIONS

Berezin et al., "Ratiometric Analysis of Fluorescence Lifetime for Probing Binding Sites in /albumin with Near-Infrared Fluorescent Molecular Probes," Photochemistry and Photobiology, 2007, vol. 83, pp. 1371-1378.

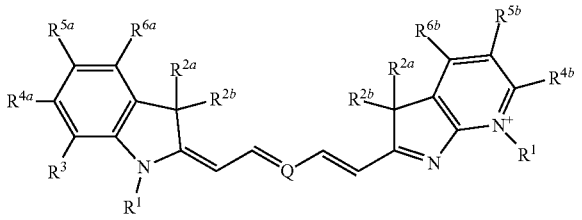
(Continued)

Primary Examiner — Nyeemah A Grazier
(74) *Attorney, Agent, or Firm* — Kilpatrick Townsend & Stockton LLP

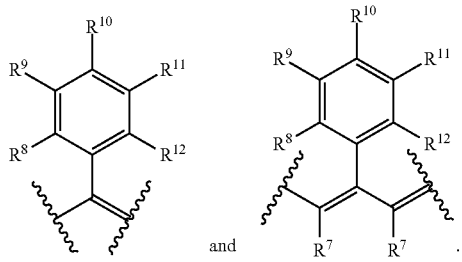
(57) **ABSTRACT**

Compounds are disclosed that are useful for noninvasive imaging in the near-infrared spectral range. Bioconjugate cyanine compounds of Formula II are presented:

II



wherein Q is a portion of a polymethine bridge selected from the group consisting of:



and

.

21 Claims, 31 Drawing Sheets