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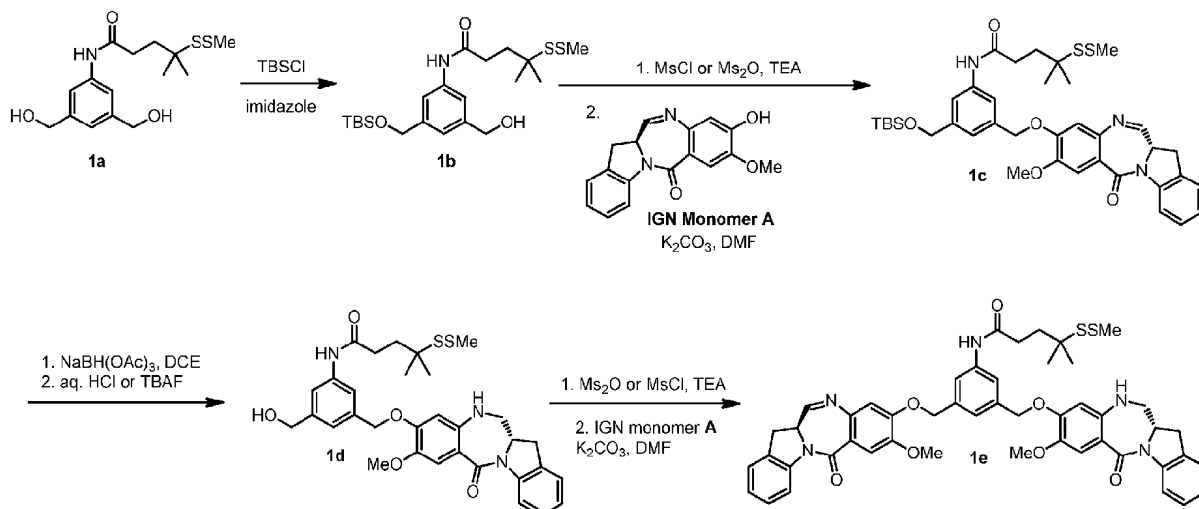
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(62) Document number(s) of the earlier application(s) in  
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**20181645.1 / 3 778 602**  
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(54) **METHODS OF PREPARING CYTOTOXIC BENZODIAZEPINE DERIVATIVES**

(57) The invention relates to novel methods for preparing indolinobenzodiazepine dimer compounds and their synthetic precursors.



**FIG. 1**



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DOCUMENTS CONSIDERED TO BE RELEVANT

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Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
A	WO 2010/091150 A1 (IMMUNOGEN INC [US]; LI WEI [US] ET AL.) 12 August 2010 (2010-08-12) * claim 1 *	1-15	INV. C07D487/04 C07C303/28
A	WO 2011/064141 A1 (HOFFMANN LA ROCHE [CH]; ANDERSON KEVIN WILLIAM [US] ET AL.) 3 June 2011 (2011-06-03) * page 118; example 35 *	1-15	
A	CARSTEN BEHRENS ET AL: "Synthesis of Achiral Linker Reagents for Direct Labelling of Oligonucleotides On Solid Supports", NUCLEOSIDES AND NUCLEOTIDES, vol. 18, no. 2, 1 February 1999 (1999-02-01), pages 291-305, XP055299325, US ISSN: 0732-8311, DOI: 10.1080/15257779908043075 * the whole document *	1-15	TECHNICAL FIELDS SEARCHED (IPC)  C07D
A	US 2011/159481 A1 (LIU DAVID J [US] ET AL) 30 June 2011 (2011-06-30) * figure 11; compound 1 *	1-15	
A,D	WO 2012/128868 A1 (IMMUNOGEN INC [US]; LI WEI [US] ET AL.) 27 September 2012 (2012-09-27) * claim 1 *	1-15	

The present search report has been drawn up for all claims

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Place of search <b>Munich</b>	Date of completion of the search <b>2 January 2024</b>	Examiner <b>Gettins, Marc</b>
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ON EUROPEAN PATENT APPLICATION NO.

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02-01-2024

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2010091150 A1	12-08-2010	AU 2010210646 A1	11-08-2011
		BR PI1008749 A2	25-08-2015
		CA 2750519 A1	12-08-2010
		CA 3014224 A1	12-08-2010
		CN 102365021 A	29-02-2012
		CN 105175434 A	23-12-2015
		CN 105198908 A	30-12-2015
		CN 108727407 A	02-11-2018
		EP 2393362 A1	14-12-2011
		EP 3100745 A1	07-12-2016
		EP 3360879 A1	15-08-2018
		ES 2604668 T3	08-03-2017
		IL 214475 A	29-10-2015
		IL 271761 A	27-02-2020
		IL 295601 A	01-10-2022
		JP 5977522 B2	24-08-2016
		JP 6204294 B2	27-09-2017
		JP 6581630 B2	25-09-2019
		JP 2012516896 A	26-07-2012
		JP 2015017095 A	29-01-2015
		JP 2015187144 A	29-10-2015
		JP 2018021056 A	08-02-2018
		KR 20110120308 A	03-11-2011
		KR 20180027613 A	14-03-2018
		KR 20190060009 A	31-05-2019
		MX 368362 B	30-09-2019
		NZ 594177 A	28-02-2014
		NZ 620649 A	25-09-2015
		RU 2011136686 A	20-03-2013
		RU 2015103852 A	10-11-2015
		RU 2019108153 A	22-09-2020
		SG 173152 A1	29-08-2011
		SG 2014009138 A	28-03-2014
		SG 10201706294V A	28-09-2017
		US 2010203007 A1	12-08-2010
		US 2013266596 A1	10-10-2013
		US 2013302357 A1	14-11-2013
		US 2015030616 A1	29-01-2015
		US 2016222013 A1	04-08-2016
		US 2017183419 A1	29-06-2017
		US 2018079823 A1	22-03-2018
		US 2018355055 A1	13-12-2018
		US 2019276552 A1	12-09-2019
		US 2021238301 A1	05-08-2021
		WO 2010091150 A1	12-08-2010
		ZA 201105352 B	25-09-2014

EPC FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

ANNEX TO THE EUROPEAN SEARCH REPORT  
ON EUROPEAN PATENT APPLICATION NO.

EP 23 18 3947

5 This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.  
The members are as contained in the European Patent Office EDP file on  
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

02-01-2024

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2011064141 A1	03-06-2011	BR 112012012333 A2	20-10-2020
		CA 2779089 A1	03-06-2011
		CN 102753538 A	24-10-2012
		EP 2504324 A1	03-10-2012
		ES 2536210 T3	21-05-2015
		HK 1175181 A1	28-06-2013
		JP 5559346 B2	23-07-2014
		JP 2013511492 A	04-04-2013
		KR 20120085334 A	31-07-2012
		RU 2012125843 A	27-12-2013
		US 2011124686 A1	26-05-2011
WO 2011064141 A1	03-06-2011		
US 2011159481 A1	30-06-2011	NONE	
WO 2012128868 A1	27-09-2012	AU 2012217719 A1	18-04-2013
		AU 2012231640 A1	02-05-2013
		AU 2016200752 A1	25-02-2016
		AU 2017268554 A1	21-12-2017
		AU 2019264595 A1	05-12-2019
		BR 112013019913 A2	17-10-2017
		BR 112013020540 A2	21-03-2017
		CA 2824864 A1	27-09-2012
		CA 2825919 A1	23-08-2012
		CA 3034596 A1	27-09-2012
		CA 3110544 A1	27-09-2012
		CN 103687623 A	26-03-2014
		CN 103702686 A	02-04-2014
		CN 107050468 A	18-08-2017
		CN 107335061 A	10-11-2017
		CN 113896731 A	07-01-2022
		CY 1117340 T1	26-04-2017
		CY 1121532 T1	29-05-2020
		DK 2675479 T3	11-04-2016
		DK 2675480 T3	15-04-2019
		EP 2675479 A1	25-12-2013
		EP 2675480 A1	25-12-2013
		EP 2675481 A1	25-12-2013
EP 3053600 A1	10-08-2016		
EP 3498303 A1	19-06-2019		
EP 3666289 A1	17-06-2020		
ES 2567418 T3	22-04-2016		
ES 2717657 T3	24-06-2019		
HK 1186686 A1	21-03-2014		
HR P20160164 T1	11-03-2016		

EPC FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

55

ANNEX TO THE EUROPEAN SEARCH REPORT  
ON EUROPEAN PATENT APPLICATION NO.

EP 23 18 3947

5 This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.  
The members are as contained in the European Patent Office EDP file on  
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

02-01-2024

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		HR P20190576 T1	17-05-2019
		HU E028736 T2	30-01-2017
		HU E043976 T2	30-09-2019
		IL 227963 A	31-08-2017
		IL 227964 A	28-09-2017
		IL 279304 A	31-01-2021
		IL 293365 A	01-07-2022
		JP 5826863 B2	02-12-2015
		JP 6049642 B2	21-12-2016
		JP 6216356 B2	18-10-2017
		JP 6526138 B2	05-06-2019
		JP 6703632 B2	03-06-2020
		JP 2014506892 A	20-03-2014
		JP 2014521591 A	28-08-2014
		JP 2016040298 A	24-03-2016
		JP 2018027966 A	22-02-2018
		JP 2019142928 A	29-08-2019
		JP 2020143102 A	10-09-2020
		JP 2022009073 A	14-01-2022
		KR 20140010067 A	23-01-2014
		KR 20140010076 A	23-01-2014
		KR 20190051081 A	14-05-2019
		KR 20190089048 A	29-07-2019
		KR 20200140939 A	16-12-2020
		KR 20200141534 A	18-12-2020
		LT 2675480 T	10-04-2019
		ME 02381 B	20-06-2016
		MX 343337 B	01-11-2016
		MX 346635 B	27-03-2017
		MY 169448 A	11-04-2019
		MY 183977 A	17-03-2021
		NZ 613121 A	29-05-2015
		NZ 613162 A	30-10-2015
		PL 2675479 T3	30-09-2016
		PL 2675480 T3	31-07-2019
		PT 2675480 T	15-04-2019
		RU 2013141829 A	27-03-2015
		RU 2013142179 A	27-03-2015
		RU 2017117634 A	01-11-2018
		RU 2017131902 A	06-02-2019
		SG 191955 A1	30-08-2013
		SG 191965 A1	30-08-2013
		SG 10201601046Q A	30-03-2016
		SG 10202007640V A	29-09-2020
		SI 2675479 T1	29-04-2016
		SI 2675480 T1	31-05-2019

EPC FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

55

ANNEX TO THE EUROPEAN SEARCH REPORT  
ON EUROPEAN PATENT APPLICATION NO.

EP 23 18 3947

5 This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.  
The members are as contained in the European Patent Office EDP file on  
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

02-01-2024

10	Patent document cited in search report	Publication date	Patent family member(s)	Publication date
			SM T201600099 B	29-04-2016
			TW 201309674 A	01-03-2013
			UA 120696 C2	27-01-2020
15			US 2012238731 A1	20-09-2012
			US 2012244171 A1	27-09-2012
			US 2013302359 A1	14-11-2013
			US 2014088089 A1	27-03-2014
			US 2015099874 A1	09-04-2015
			US 2016108129 A1	21-04-2016
20			US 2016324980 A1	10-11-2016
			US 2017044266 A1	16-02-2017
			US 2018002440 A1	04-01-2018
			US 2018037659 A1	08-02-2018
			US 2019263924 A1	29-08-2019
25			WO 2012112687 A1	23-08-2012
			WO 2012112708 A1	23-08-2012
			WO 2012128868 A1	27-09-2012
			ZA 201305386 B	25-11-2015
			ZA 201704808 B	25-11-2020
30	-----			
35				
40				
45				
50				

EPC FORM P0459

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

55