





solithromycin synthesis



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### **Solithromycin** inhibition of protein **synthesis** and ribosome biogenesis in *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Haemophilus influenzae*

W Rodgers, AD Frazier... - *Antimicrobial agents and ...*, 2013 - *Am Soc Microbiol*

ABSTRACT The continuing increase in antibiotic-resistant microorganisms is driving the search for new antibiotic targets and improved antimicrobial agents. Ketolides are semisynthetic derivatives of macrolide antibiotics, which are effective against certain ...

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### **Synthesis** and antibacterial activity of desosamine-modified macrolide derivatives

N LeTourneau, P Vimal, D Klepacki, A Mankin... - *Bioorganic & medicinal ...*, 2012 - Elsevier

... Structural factors behind erm macrolide resistance were studied through **synthesis** of new macrolide ... **Synthesized** compounds with 2'-deoxy and 3'-desmethyl desosamine rings demonstrated decreased ... such as telithromycin 3 2d, cethromycin 4 2e, and **solithromycin** 5 2f ...

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### In vitro and in vivo activity of **solithromycin** (CEM-101) against *Plasmodium* species

S Wittlin, E Ekland, JC Craft, J Lotharius... - *Antimicrobial agents ...*, 2012 - *Am Soc Microbiol*

... RESULTS. **Solithromycin** demonstrates potent antimalarial activity in vitro. Like other prokaryotic protein **synthesis** inhibitors, **solithromycin** induced a delayed-death effect in *Plasmodium* parasites. **Solithromycin** was much more ...

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### [\[PDF\]](#) Pikromycin Derivative of **Solithromycin**: Discussion of Activity

D Pereira, J Li, P Fernandes, S Matsa - [cempra.com](#)

... Therefore, the pikromycin- CEM-101 (4) was **synthesized** and MICs determined.

Pikromycin-CEM-101 (4) is structurally similar to **solithromycin** with the exception of the absence of the 6-methoxy and the C-10 methyl groups. The **synthesis** of pikromycin-CEM-101 starting ...

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Author Name

- Fernandes, P. (2)
- Andrade, R.B. (1)
- Arenz, S. (1)
- Beckmann, R. (1)
- Berninghausen, O. (1)

Subject Area

- Pharmacology, Toxicology and Pharmaceutics (10)
- Medicine (8)
- Biochemistry, Genetics and Molecular Biology (4)
- Chemistry (2)

Ribosome-Templated Azide-Alkyne Cycloadditions: Synthesis of Potent Macrolide Antibiotics by in Situ Click Chemistry 1 Glassford, I., Teijaro, C.N., Daher, S.S., (...), Cooperman, B.S., Andrade, R.B. 2016 Journal of the American Chemical Society

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Endless resistance. Endless antibiotics? 2 Fisher, J.F., Mobashery, S. 2016 MedChemComm

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Molecular basis for erythromycin-dependent ribosome stalling during translation of the ErmBL leader peptide 3 Arenz, S., Ramu, H., Gupta, P., (...), Mankin, A.S., Wilson, D.N. 2014 Nature Communications

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Antimicrobial activity of solithromycin against clinical isolates of Legionella pneumophila serogroup 1 4 Mallegol, J., Fernandes, P., Melano, R.G., Guyarda, C. 2014 Antimicrobial Agents and Chemotherapy

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Progress in the discovery of treatments for C. difficile infection: A clinical and medicinal chemistry review 5 Tsutsumi, L.S., Owusu, Y.B., Hurdle, J.G., Sun, D. 2014 Current Topics in Medicinal Chemistry

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Are we facing a post-antibiotic future in surgery? 6 Cerwenka, H., Krause, R. 2014 European Surgery - Acta Chirurgica Austriaca



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1. Seiple IB, Zhang Z, Jakubec P, Langlois-Mercier A, Wright PM, Hog DT, Yabu K, Allu SR, Fukuzaki T, Carlsen PN, Kitamura Y, Zhou X, Condakes ML, Szczypiński FT, Green WD, Myers AG. *Nature*. 2016 May 18;533(7603):338-45. doi: 10.1038/nature17967. PMID: 27193679  
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[In vitro activity of solithromycin and its metabolites, CEM-214 and N-acetyl-CEM-101, against 100 clinical \*Ureaplasma\* spp. isolates compared with azithromycin.](#)

3. Furfaro LL, Spiller OB, Keelan JA, Payne MS. *Int J Antimicrob Agents*. 2015 Sep;46(3):319-24. doi: 10.1016/j.ijantimicag.2015.04.015. Epub 2015 Jun 19. PMID: 26141231  
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1. **A platform for the discovery of new macrolide antibiotics**

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By Seiple, Ian B.; Zhang, Ziyang; Jakubec, Pavol; Langlois-Mercier, Audrey; Wright, Peter M.; Hog, Daniel T.; Yabu, Kazuo; Allu, Senkara Rao; Fukuzaki, Takehiro; Carlsen, Peter N.; et al

From Nature (London, United Kingdom) (2016), 533(7603), 338-345. | Language: English, Database: CAPLUS

The chem. modification of structurally complex fermn. products, a process known as semisynthesis, has been an important tool in the discovery and manuf. of antibiotics for the treatment of various infectious diseases. However, many of the therapeutics obtained in this way are no longer effective, because bacterial resistance to these compds. has developed. Here we present a practical, fully **synthetic** route to macrolide antibiotics by the convergent assembly of simple chem. building blocks, enabling the **synthesis** of diverse structures not accessible by traditional semisynthetic approaches. M...

2. **Process for preparation of Solithromycin intermediates**

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By Zheng, Fei; Xu, Hui; Zhang, Tao; Huang, Yue

From Faming Zhuanli Shenqing (2016), CN 105503976 A 20160420. | Language: Chinese, Database: CAPLUS

The invention discloses a method for **prepg. Solithromycin** and intermediates I [wherein R<sup>2</sup> = NH<sub>2</sub>, protected amino group, or NO<sub>2</sub>]. The process effectively reduces side reactions, avoids dangerous and toxic operation, and increases reaction conversion ratio.

3. **Preparation of 14-membered ketolide macrolide aminoglycosides via coupling and macrocyclization reactions as antibacterial and antiinflammatory agents**

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By Myers, Andrew G.; Seiple, Ian Bass; Zhang, Ziyang

From PCT Int. Appl. (2016), WO 2016057798 A1 20160414. | Language: English, Database: CAPLUS



14-Membered ketolides I, wherein Z is ketone, alkoxyalkyl; L<sup>3</sup> is alkoxyalkyl, alkyl, alkenyl; R<sup>3</sup> is H, halogen, carbonyl, alkyl, alkenyl, alkynyl, carbocycdyl, heterocycdyl, aryl, heteroaryl; R<sup>4</sup> is H, OR<sup>2</sup>; R<sup>2</sup> is H, alkyl, alkenyl, alkynyl, carbocycdyl, heterocycdyl, aryl, heteroaryl, oxygen protecting group; each of R<sup>5a</sup> and R<sup>5b</sup> is independently H, halogen, silyl, alkyl, carbocycdyl, heterocycdyl; R<sup>5</sup> is H, alkyl, alkenyl, alkynyl, carbocycdyl, heterocycdyl, aryl, aralkyl, heteroaryl, heteroalkyl, hydroxyl, substituted hydroxyl, thiol, substituted thiol, amino, substituted amino, carbonyl, sil...

4. **Process for preparation of Solithromycin from Clarithromycin**

[Quick View](#) [PATENTPAK](#)

By Xu, Hui; Zheng, Fei; Zhang, Tao; Huang, Yue

From Faming Zhuanli Shenqing (2016), CN 105348341 A 20160224. | Language: Chinese, Database: CAPLUS

The present invention discloses a method for **prepg. Solithromycin** from from Clarithromycin comprising sulfonation, azidation, fluorination, cyclization, and deprotection. The process effectively reduces the occurrence of side effects, avoid dangerous and poisonous operation steps, improve the reaction conversion ratio, thus reduce prodn. cost.

5. **Ribosome-Templated Azide-Alkyne Cycloadditions: Synthesis of Potent Macrolide Antibiotics by In Situ Click Chemistry**

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By Glassford, Ian; Tejjaro, Christiana N.; Daher, Samer S.; Weil, Amy; Small, Meagan C.; Redhu, Shiv K.; Colussi, Dennis J.; Jacobson, Marlene A.; Childers, Wayne E.; Buttarro, Bettina; et al

From Journal of the American Chemical Society (2016), 138(9), 3136-3144. | Language: English, Database: CAPLUS



Over half of all antibiotics target the bacterial ribosome-nature's complex, 2.5 MDa nanomachine responsible for decoding mRNA and **synthesizing** proteins. Macrolide antibiotics, exemplified by erythromycin, bind the 50S subunit with nM affinity and inhibit protein **synthesis** by blocking the

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- *Wiley*
- *Elsevier, Cell Press*
- *(MDPI)*
- *(Beilstein Institute)*

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- **>20 wow! Ma di solito molto generico (Nature...)**
- **>10 wow! (Angew. Chem, JACS)**
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- **<3... poco influente...**

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<input type="checkbox"/>	102	Trends in Environmental Analytical Chemistry	173	4.462	0.00100
<input type="checkbox"/>	103	Science China-Chemistry	4,228	4.448	0.00800
<input type="checkbox"/>	104	APPLIED SURFACE SCIENCE	76,301	4.439	0.09700
<input type="checkbox"/>	105	JOURNAL OF MOLECULAR CATALYSIS A-CHEMICAL	21,041	4.397	0.01600
<input type="checkbox"/>	106	PARTICLE & PARTICLE SYSTEMS CHARACTERIZATION	2,826	4.384	0.00600
<input type="checkbox"/>	107	Marine Drugs	8,753	4.379	0.01600
<input type="checkbox"/>	108	ACS Infectious Diseases	749	4.325	0.00300
<input type="checkbox"/>	109	TALANTA	37,747	4.244	0.04400
<input type="checkbox"/>	110	INTERNATIONAL JOURNAL OF HYDROGEN ENERGY	75,123	4.229	0.08100

<input type="checkbox"/>	111	<b>SEPARATION AND PURIFICATION REVIEWS</b>	675	4.212	0.00100
<input type="checkbox"/>	112	<b>ACS Chemical Neuroscience</b>	4,336	4.211	0.01300
<input type="checkbox"/>	113	<b>Frontiers in Chemistry</b>	1,183	4.155	0.00400
<input type="checkbox"/>	114	<b>DALTON TRANSACTIONS</b>	67,778	4.099	0.10400
<input type="checkbox"/>	115	<b>Liquid Crystals Reviews</b>	133	4.091	0.00100
<input type="checkbox"/>	116	<b>Journal of Ginseng Research</b>	1,364	4.053	0.00200
<input type="checkbox"/>	117	<b>ORGANOMETALLICS</b>	40,867	4.051	0.04600
<input type="checkbox"/>	118	<b>COLLOIDS AND SURFACES B-BIOINTERFACES</b>	25,844	3.997	0.03500
<input type="checkbox"/>	119	<b>RUSSIAN CHEMICAL REVIEWS</b>	4,119	3.991	0.00300
<input type="checkbox"/>	120	<b>CRYSTAL GROWTH &amp; DESIGN</b>	28,165	3.972	0.04000
<input type="checkbox"/>	121	<b>Future Medicinal Chemistry</b>	3,456	3.969	0.00900

		Full Journal Title	Total Cites	Journal Impact Factor 	Eigenfactor Score
<input type="checkbox"/>	121	Structural Dynamics	540	3.969	0.00300
<input type="checkbox"/>	123	FUEL PROCESSING TECHNOLOGY	17,840	3.956	0.02300
<input type="checkbox"/>	124	Reviews in Computational Chemistry	506	3.933	0.00000
<input type="checkbox"/>	125	BIOORGANIC CHEMISTRY	2,123	3.929	0.00300
<input type="checkbox"/>	126	INTERNATIONAL JOURNAL OF BIOLOGICAL MACROMOLECULES	20,621	3.909	0.03000
<input type="checkbox"/>	127	PHYSICAL CHEMISTRY CHEMICAL PHYSICS	95,774	3.906	0.20600
<input type="checkbox"/>	128	Journal of Cheminformatics	2,117	3.893	0.00600
<input type="checkbox"/>	129	Journal of Energy Chemistry	1,871	3.886	0.00400

		Full Journal Title	Total Cites	Journal Impact Factor 	Eigenfactor Score
<input type="checkbox"/>	130	JOURNAL OF NATURAL PRODUCTS	24,905	3.885	0.02300
<input type="checkbox"/>	131	ANALYST	28,767	3.864	0.04700
<input type="checkbox"/>	132	Topics in Organometallic Chemistry	1,642	3.833	0.00400
<input type="checkbox"/>	133	Journal of Chemical Information and Modeling	14,366	3.804	0.02000
<input type="checkbox"/>	134	ACS Medicinal Chemistry Letters	4,851	3.794	0.01500
<input type="checkbox"/>	135	LANGMUIR	118,255	3.789	0.11900
<input type="checkbox"/>	136	JOURNAL OF ALLOYS AND COMPOUNDS	84,802	3.779	0.10600
<input type="checkbox"/>	137	DYES AND PIGMENTS	14,560	3.767	0.01500
<input type="checkbox"/>	138	JOURNAL OF CHROMATOGRAPHY A	61,361	3.716	0.05100


		Full Journal Title	Total Cites	Journal Impact Factor ▼	Eigenfactor Score
		CHROMATOGRAPHY A			
<input type="checkbox"/>	139	Soft Matter	35,376	3.709	0.08400
<input type="checkbox"/>	140	Chemistry-An Asian Journal	10,936	3.692	0.02200
<input type="checkbox"/>	141	INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES	37,071	3.687	0.09300
<input type="checkbox"/>	142	MICROPOROUS AND MESOPOROUS MATERIALS	22,438	3.649	0.02600
<input type="checkbox"/>	143	APPLIED CLAY SCIENCE	13,193	3.641	0.01300
<input type="checkbox"/>	144	JOURNAL OF ENZYME INHIBITION AND MEDICINAL CHEMISTRY	4,162	3.638	0.00600
<input type="checkbox"/>	145	PHYTOMEDICINE	8,972	3.610	0.00900

<input type="checkbox"/>	146	JOURNAL OF ANALYTICAL ATOMIC SPECTROMETRY	9,217	3.608	0.01100
<input type="checkbox"/>	147	ORGANIC PROCESS RESEARCH & DEVELOPMENT	6,475	3.584	0.01000
<input type="checkbox"/>	148	APPLIED ORGANOMETALLIC CHEMISTRY	3,891	3.581	0.00300
<input type="checkbox"/>	149	ACTA PHARMACOLOGICA SINICA	8,041	3.562	0.01000
<input type="checkbox"/>	150	BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN	10,941	3.526	0.00600
<input type="checkbox"/>	151	CHINESE JOURNAL OF CATALYSIS	4,608	3.525	0.00700
<input type="checkbox"/>	152	JOURNAL OF PHYSICAL AND CHEMICAL REFERENCE DATA	7,434	3.510	0.00200
<input type="checkbox"/>	153	ACS Combinatorial Science	1,668	3.500	0.00400
<input type="checkbox"/>	154	CURRENT MEDICINAL CHEMISTRY	15,405	3.469	0.01800



<input type="checkbox"/>	155	<b>JOURNAL OF ANALYTICAL AND APPLIED PYROLYSIS</b>	11,759	3.468	0.01300
<input type="checkbox"/>	156	<b>Catalysts</b>	1,995	3.465	0.00400
<input type="checkbox"/>	157	<b>CATALYSIS COMMUNICATIONS</b>	14,174	3.463	0.01500
<input type="checkbox"/>	158	<b>CHEMICAL RESEARCH IN TOXICOLOGY</b>	12,692	3.432	0.01300
<input type="checkbox"/>	159	<b>Advances in Carbohydrate Chemistry and Biochemistry</b>	621	3.429	0.00000

		Full Journal Title	Total Cites	Journal Impact Factor ▼	Eigenfactor Score
<input type="checkbox"/>	160	FARADAY DISCUSSIONS	9,070	3.427	0.01900
<input type="checkbox"/>	161	ORGANIC & BIOMOLECULAR CHEMISTRY	30,329	3.423	0.05800
<input type="checkbox"/>	162	JOURNAL OF APPLIED CRYSTALLOGRAPHY	25,526	3.422	0.02000
<input type="checkbox"/>	163	INTERMETALLICS	8,988	3.420	0.01100
<input type="checkbox"/>	164	JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY	103,329	3.412	0.07400
<input type="checkbox"/>	165	CURRENT TOPICS IN MEDICINAL CHEMISTRY	6,432	3.374	0.01000
<input type="checkbox"/>	166	Green Chemistry Letters and Reviews	658	3.364	0.00100
<input type="checkbox"/>	167	PHYTOTHERAPY RESEARCH	12,203	3.349	0.01000
<input type="checkbox"/>	168	MARINE CHEMISTRY	9,014	3.337	0.00800

		Full Journal Title	Total Cites	Journal Impact Factor 	Eigenfactor Score
<input type="checkbox"/>	169	PHARMACEUTICAL RESEARCH	21,071	3.335	0.01400
<input type="checkbox"/>	170	ANALYTICAL AND BIOANALYTICAL CHEMISTRY	28,970	3.307	0.04200
<input type="checkbox"/>	171	CRYSTENGGCOMM	27,544	3.304	0.04900
<input type="checkbox"/>	172	JOURNAL OF ELECTROANALYTICAL CHEMISTRY	25,100	3.235	0.01500
<input type="checkbox"/>	173	CRITICAL REVIEWS IN ANALYTICAL CHEMISTRY	1,131	3.231	0.00100
<input type="checkbox"/>	174	JOURNAL OF COMPUTATIONAL CHEMISTRY	34,677	3.221	0.02200
<input type="checkbox"/>	175	ChemPlusChem	2,692	3.205	0.00700
<input type="checkbox"/>	176	NEW JOURNAL OF CHEMISTRY	20,421	3.201	0.03100
<input type="checkbox"/>	177	ChemNanoMat	761	3.173	0.00200

<input type="checkbox"/>	178	JOURNAL OF PHYSICAL CHEMISTRY B	113,923	3.146	0.09500
<input type="checkbox"/>	179	Environmental Chemistry Letters	2,039	3.125	0.00200
<input type="checkbox"/>	180	JOURNAL OF SUPERCRITICAL FLUIDS	9,309	3.122	0.01000
<input type="checkbox"/>	181	JOURNAL OF ETHNOPHARMACOLOGY	32,891	3.115	0.02900
<input type="checkbox"/>	182	MOLECULES	31,047	3.098	0.05600
<input type="checkbox"/>	183	CATALYSIS SURVEYS FROM ASIA	725	3.081	0.00100
<input type="checkbox"/>	184	JOURNAL OF PHARMACEUTICAL SCIENCES	23,383	3.075	0.01800
<input type="checkbox"/>	185	Advances in Heterocyclic Chemistry	916	3.071	0.00100

<input type="checkbox"/>	185	<b>Advances in Heterocyclic Chemistry</b>	916	3.071	0.00100
<input type="checkbox"/>	186	<b>JOURNAL OF INORGANIC BIOCHEMISTRY</b>	11,223	3.063	0.01000
<input type="checkbox"/>	187	<b>ChemMedChem</b>	5,940	3.009	0.01200
<input type="checkbox"/>	188	<b>Drug Testing and Analysis</b>	2,606	2.993	0.00500
<input type="checkbox"/>	188	<b>Journal of Biobased Materials and Bioenergy</b>	953	2.993	0.00100
<input type="checkbox"/>	190	<b>REACTIVE &amp; FUNCTIONAL POLYMERS</b>	5,944	2.975	0.00600
<input type="checkbox"/>	191	<b>Arabian Journal of Chemistry</b>	4,266	2.969	0.00600
<input type="checkbox"/>	192	<b>JOURNAL OF FOOD COMPOSITION AND</b>	6,398	2.956	0.00600