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Bioorganic & Medicinal Chemistry Letters Volume 21, Issue 7, 2011

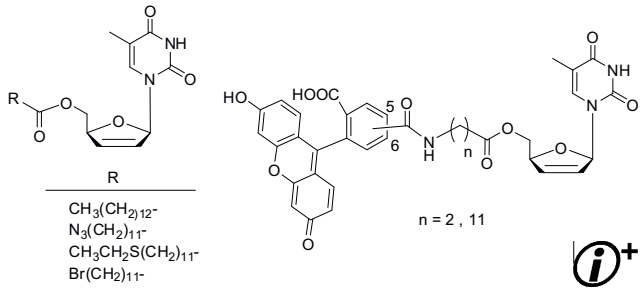
Contents

ARTICLES

Synthesis and biological evaluation of fatty acyl ester derivatives of 2′,3′-didehydro-2′,3′-dideoxythymidine **pp 1917–1921**

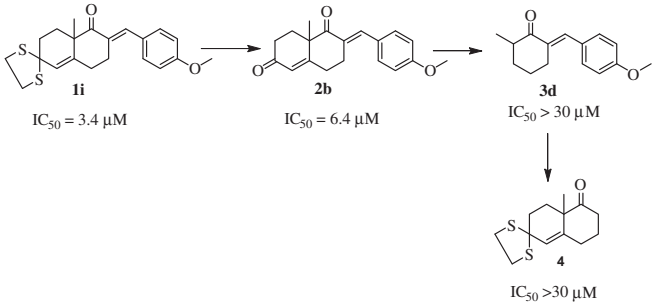
Hitesh K. Agarwal, Kelly Loethan, Deendayal Mandal, Gustavo F. Doncel*, Keykavous Parang*

The synthesis, anti-HIV activities against cell-free and cell-associated virus, cellular cytotoxicity, and cellular uptake studies of 5′-*O*-fatty acyl derivatives of 2′,3′-didehydro-2′,3′-dideoxythymidine (stavudine, d4T) are reported.



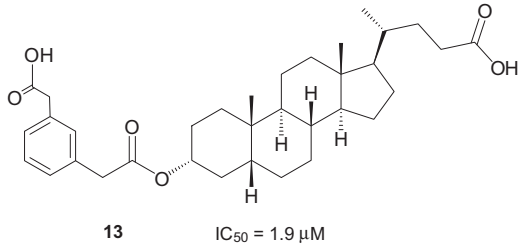
Structural requirements of (*E*)-6-benzylidene-4a-methyl-4,4a,5,6,7,8-hexahydronaphthalen-2(3*H*)-one derivatives as novel melanogenesis inhibitors **pp 1922–1925**

Pillaiyar Thanigaimalai, Ki-Cheul Lee, Vinay K. Sharma, Eeda Vekateswara Rao, Eunmiri Roh, Youngsoo Kim, Sang-Hun Jung*

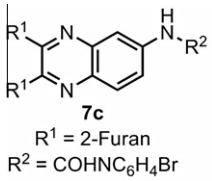


Synthesis and proteasome inhibition of lithocholic acid derivatives **pp 1926–1928**

Zhao Dang, Andrew Lin, Phong Ho, Dominique Soroka, Kuo-Hsiung Lee, Li Huang*, Chin-Ho Chen*

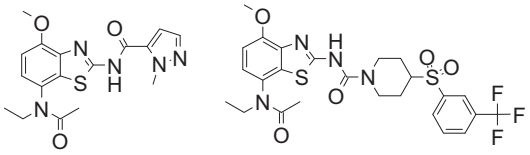


2,3-Substituted quinoxalin-6-amine analogs as antiproliferatives: A structure–activity relationship study **pp 1929–1932**
Qianyi Chen, Vashti C. Bryant, Hernando Lopez, David L. Kelly, Xu Luo, Amarnath Natarajan*



Cell line	$GI_{50}(\mu M)$
A549	6.4
AsPC1	17.3
HT29	12.1
MDAMB231	8.4
PC3	5.9
SKOV3	16.8
U2OS	10.8

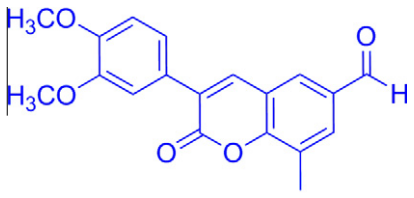
Discovery of benzothiazole-based adenosine A_{2B} receptor antagonists with improved A_{2A} selectivity **pp 1933–1936**
Fariborz Firooznia, Adrian Wai-Hing Cheung, John Brinkman, Joseph Grimsby, Mary Lou Gubler, Rachid Hamid, Nicholas Marcopulos, Gwendolyn Ramsey, Jenny Tan, Yang Wen, Ramakanth Sarabu*



2 **30**

The highly potent but modestly selective *N*-(2-amino-4-methoxy-benzothiazol-7-yl)-*N*-ethyl-acetamide derivative **2** was selected as the starting point for the design of novel selective A_{2B} antagonists, due to its excellent potency, and good drug-like properties. A series of compounds containing nonaromatic amides or ureas of five- or six-membered rings, and also bearing an *m*-trifluoromethyl-phenyl group (shown to impart superior potency) were prepared and evaluated for their selectivity against the A_{2A} and A_1 receptors. This work resulted in the identification of compound **30**, with excellent potency and high selectivity against both A_{2A} and A_1 receptors.

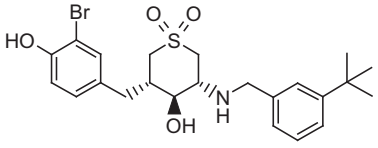
Discovery and synthesis of novel 3-phenylcoumarin derivatives as antidepressant agents **pp 1937–1941**
Koneni V. Sashidhara*, Abdhesh Kumar, Manavi Chatterjee, K. Bhaskara Rao, Seema Singh, Anil Kumar Verma, Gautam Palit



6

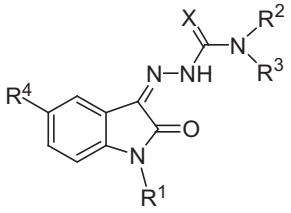
A series of novel 3-phenylcoumarin derivatives have been synthesized and evaluated for their in vivo antidepressant activities. The most active compound **6** was selected as lead compound for further antidepressant research.

Structure based design, synthesis and SAR of cyclic hydroxyethylamine (HEA) BACE-1 inhibitors **pp 1942–1947**
Heinrich Rueeger*, Jean-Michel Rondeau, Clive McCarthy, Henrik Möbitz, Marina Tintelnot-Blomley, Ulf Neumann, Sandrine Desrayaud



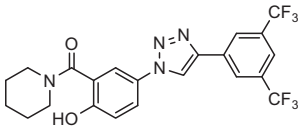
22c IC_{50} **55 nM**

Isatin-β-thiosemicarbazones as potent herpes simplex virus inhibitors **pp 1948–1952**
Iou-Jiun Kang, Li-Wen Wang, Tsu-An Hsu, Andrew Yueh, Chung-Chi Lee, Yen-Chun Lee, Ching-Yin Lee, Yu-Sheng Chao, Shin-Ru Shih*, Jyh-Haur Chern*



The synthesis and SAR of herpes simplex virus inhibitors based on an isatin-β-thiosemicarbazone scaffold are described.

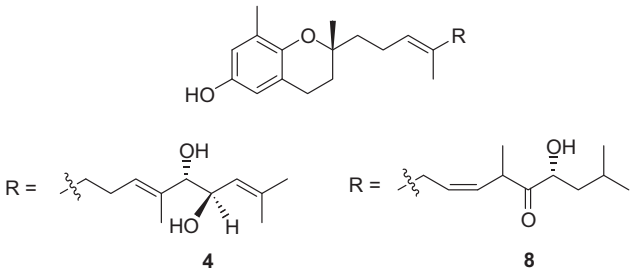
Syntheses of 1,2,3-triazolyl salicylamides with inhibitory activity on lipopolysaccharide-induced nitric oxide production **pp 1953–1957**
Jieun Yoon, Lan Cho, Sang Kook Lee*, Jae-Sang Ryu*



28-membered salicylamide library
29g (IC_{50} = 12.8 μM)

A 28-membered 1,2,3-triazolyl salicylamide library was synthesized via a click chemistry. Compound **29g** inhibited NO production in LPS-activated RAW264.7 macrophage cells with the IC_{50} value of 12.8 μM.

Sargachromanols as inhibitors of Na^+/K^+ ATPase and isocitrate lyase **pp 1958–1961**
Soon-Chun Chung, Kyoung Hwa Jang, Jiyoung Park, Chan-Hong Ahn, Jongheon Shin*, Ki-Bong Oh*

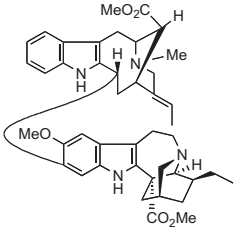


4 **8**

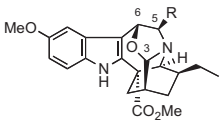
Sargachromanol D (**4**) and H (**8**) were found to be strong Na^+/K^+ ATPase inhibitors, with IC_{50} values of 3.6 and 4.6 μM, respectively.

Discovery of indole alkaloids with cannabinoid CB1 receptor antagonistic activity **pp 1962–1964**
Mariko Kitajima, Masumi Iwai, Ruri Kikura-Hanajiri, Yukihiro Goda, Mitsuru Iida, Hisatoshi Yabushita, Hiromitsu Takayama*

CB1 Receptor Antagonists from *Voacanga africana*

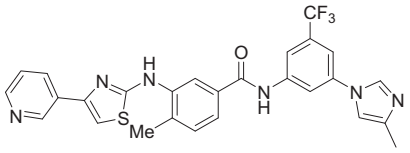


Voacamine (**1**)

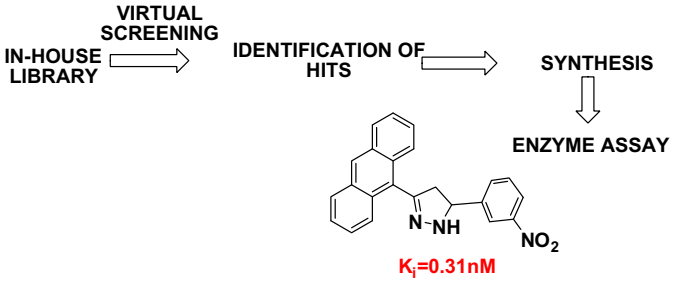


R=H : 3,6-Oxidovoacangine (**2**)
R=OH : 5-Hydroxy-3,6-oxidovoacangine (**3**)

Hybrid compounds as new Bcr/Abl inhibitors **pp 1965–1968**
Deping Wang, Zhang Zhang, Xiaoyun Lu, Yubing Feng, Kun Luo, Jirong Gan, Liu Yingxue, Junting Wan, Xiang Li, Fengxiang Zhang, Zhengchao Tu, Qian Cai, Xiaomei Ren, Ke Ding*

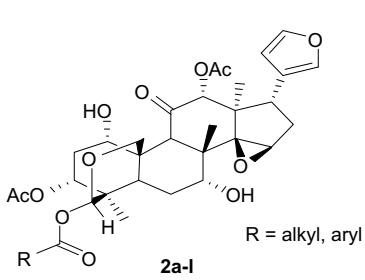


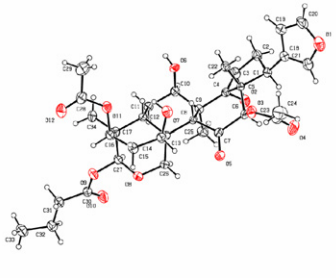
Development of selective and reversible pyrazoline based MAO-B inhibitors: Virtual screening, synthesis and biological evaluation **pp 1969–1973**
Nibha Mishra*, D. Sasmal



The workflow for the current work.

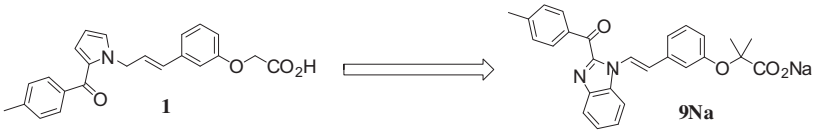
Natural products-based insecticidal agents 9. Design, semisynthesis and insecticidal activity of 28-acyloxy derivatives of toosendanin against *Mythimna separata* Walker in vivo **pp 1974–1977**
Hui Xu*, Jun-Liang Zhang





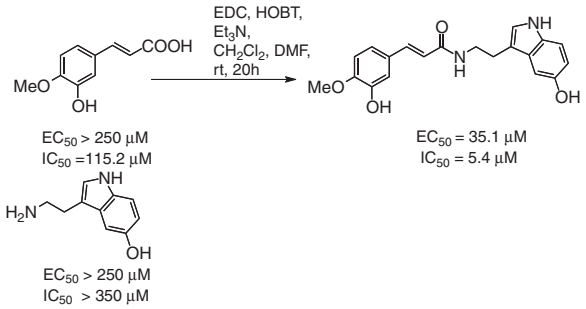
It indicated that the butanoyloxy or phenylacryloyloxy moiety at the 28-position of toosendanin was important for the insecticidal activity.

Synthesis and pharmacological evaluation of novel benzoylazole-based PPAR α/γ activators **pp 1978–1982**
Kantaro Ushiroda*, Katsunori Maruta, Takeshi Takazawa, Tomokazu Nagano, Mutsuo Taiji, Tetsuya Kohno, Yasuhiro Sato, Shinji Horai, Kazunori Yanagi, Ryu Nagata*

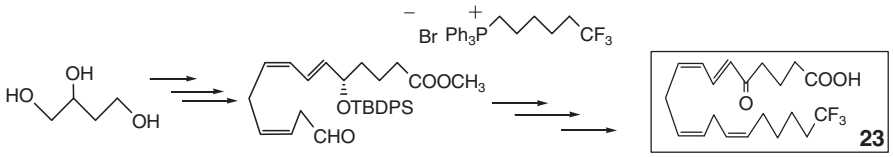


We explored the structure–activity relationships of a series of benzoylazole-based carboxylic acids starting from compound **1** found by our group. The anti-diabetic and lipid-lowering effects of the selected compound **9Na** were superior to those of pioglitazone in rodent models of type 2 diabetes with no serious body weight gain.

Synthesis and structure–activity relationships of phenylpropanoid amides of serotonin on tyrosinase inhibition pp 1983–1986
Toshiyuki Takahashi, Mitsuo Miyazawa*



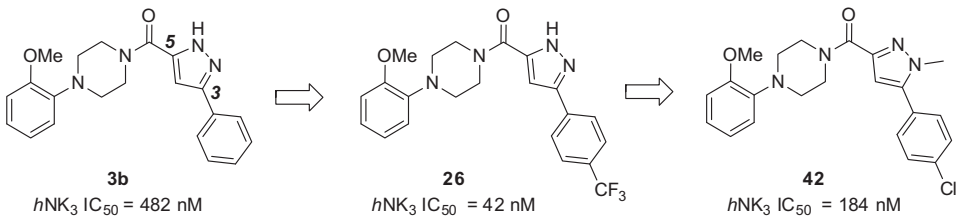
C_{20}-trifluoro-5-oxo-ETE: A metabolically stable 5-oxo-ETE derivative pp 1987–1990
Pranav Patel, Vivek Gore, William S. Powell, Joshua Rokach*



The total synthesis of C_{20}-trifluoro-6(*E*),8(*Z*),11(*Z*),14(*Z*) 5-oxo-ETE is reported. This compound was designed as an ω-oxidation-resistant analog of 5-oxo-ETE that would be resistant to metabolism. The trifluoro derivative of 5-oxo-ETE stimulated calcium mobilization in neutrophils and desensitized these cells to subsequent exposure to 5-oxo-ETE.

Discovery of 3-aryl-5-acylpiperazinyl-pyrazoles as antagonists to the NK_3 receptor pp 1991–1996
Hamid R. Hoveyda*, Marie-Odile Roy, Sebastien Blanc, Sophie Noël, Joseph M. Salvino, Mark A. Ator, Graeme Fraser

A series of 3-aryl-5-acylpiperazine-pyrazoles (e.g., **3b**) were identified through a high-throughput screening campaign as novel, potent small molecule antagonists of the *h*NK^3 receptor. This series displayed a tractable SAR. Issues of plasma and metabolic stability in rodents proved optimizable. Improved potency and pharmacokinetic profile was possible through such analogs as **26** and **42**.



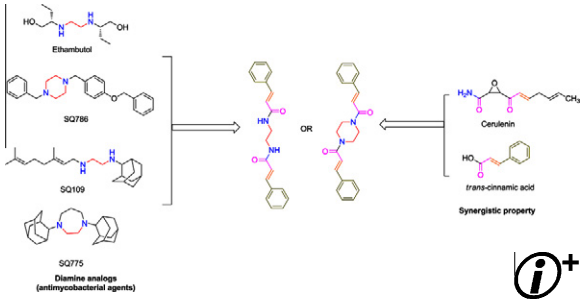
3b
hNK_3 IC_{50} = 482 nM
RLM $T_{1/2}$ = 5 min
unstable in rat plasma

26
hNK_3 IC_{50} = 42 nM
RLM $T_{1/2}$ = 5 min
55% intact after 1 h in rat plasma

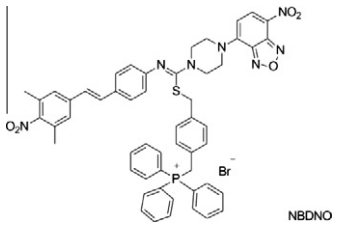
42
hNK_3 IC_{50} = 184 nM
RLM $T_{1/2}$ = 40 min
%*F* = 53
BrP at 10 min = 0.64

Design, synthesis and antimycobacterial activity of cinnamide derivatives: A molecular hybridization approach pp 1997–1999
Manoj D. Kakwani, Prashant Suryavanshi, Muktikant Ray, M. G. R. Rajan, Sharmila Majee, Abdul Samad, Padma Devarajan, Mariam S. Degani*

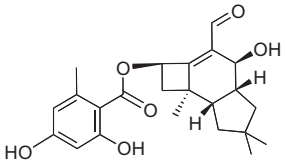
A series of cinnamide derivatives was designed as potential antimycobacterial agents using molecular hybridization approach. The synthesized molecules showed good to moderate activity with MIC in the range of 5–150 μM and good safety profile. Additionally, the most potent compound exhibited synergy with rifampicin.



A novel mitochondria-localizing nitrobenzene derivative as a donor for photo-uncaging of nitric oxide **pp 2000–2002**
Taeko Horinouchi, Hidehiko Nakagawa*, Takayoshi Suzuki, Kiyoshi Fukuhara, Naoki Miyata*

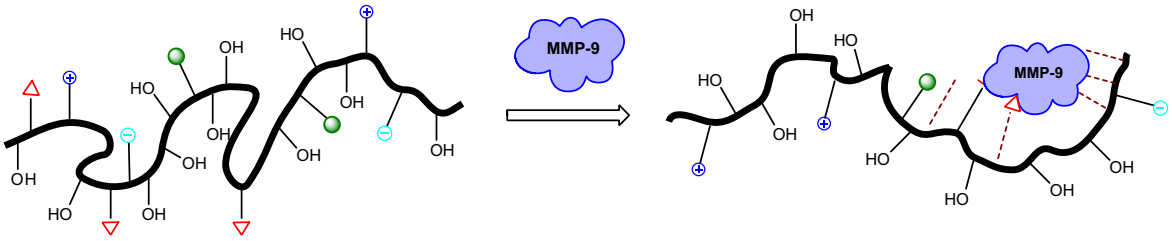


In vitro cytotoxicity of melleolide antibiotics: Structural and mechanistic aspects **pp 2003–2006**
Markus Bohnert, Sebastian Miethbauer, Hans-Martin Dahse, Johannes Ziemen, Markus Nett, Dirk Hoffmeister*

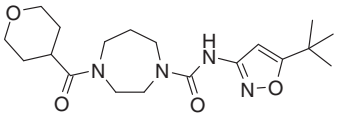


9
IC_{50} = 5.0 μM

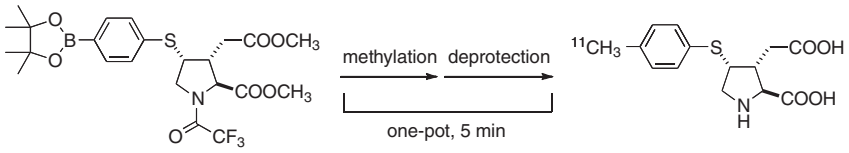
Fluorescent water soluble polymers for isozyme-selective interactions with matrix metalloproteinase-9 **pp 2007–2010**
Rinku Dutta, Michael D. Scott, Manas K. Haldar, Bratati Ganguly, D. K. Srivastava, Daniel L. Friesner, Sanku Mallik*



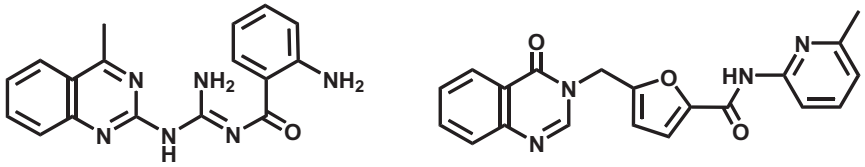
1,4-Diazepane compounds as potent and selective CB2 agonists: Optimization of metabolic stability **pp 2011–2016**
Doris Riether*, Lifen Wu, Pier F. Cirillo, Angela Berry, Edward R. Walker, Monika Ermann, Beatriz Noya-Marino, James E. Jenkins, Dan Albaugh, Claudia Albrecht, Michael Fisher, Mark J. Gemkow, Heather Grbic, Sabine Löbbe, Clemens Möller, Kathy O'Shea, Achim Sauer, Daw-Tsun Shih, David S. Thomson



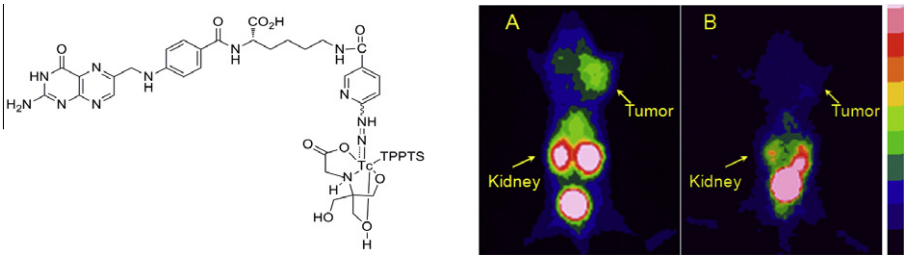
Synthesis of an acromelic acid A analog-based ^{11}C-labeled PET tracer for exploration of the site of action of acromelic acid A in allodynia induction pp 2017–2020
Masakatsu Kanazawa, Kyoji Furuta*, Hisashi Doi, Tomoko Mori, Toshiaki Minami, Seiji Ito, Masaaki Suzuki*



Structure-based virtual screening approach to the discovery of phosphoinositide 3-kinase alpha inhibitors pp 2021–2024
Hwangseo Park*, Hwanho Choi, Seunghee Hong, Donghee Kim, Dal-Seok Oh, Sungwoo Hong*

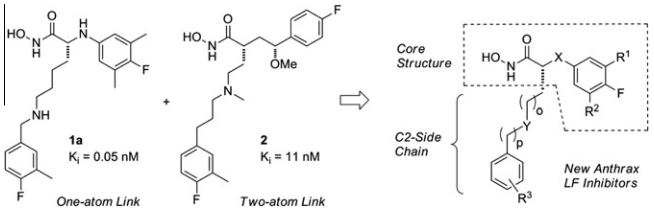


The synthesis of pteroyl-lys conjugates and its application as Technetium-99m labeled radiotracer for folate receptor-positive tumor targeting pp 2025–2029
Hongjuan Guo, Fang Xie, Meilin Zhu, Yan Li, Zhi Yang, Xuebin Wang, Jie Lu*



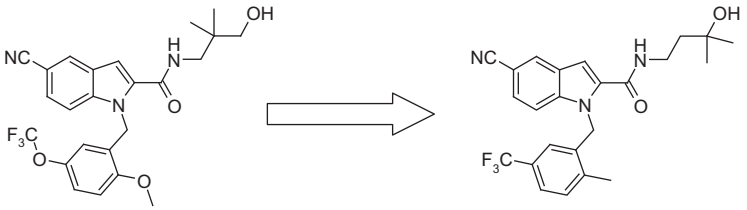
The novel complex ^{99m}Tc(HYNIC-lys-pteroyl)(tricine/TPPTS) was able to specifically target the FR-positive tumor cells and tissues both in vitro and in vivo, highlighting its potential as an effective folate receptor targeted agent for tumor imaging.

Antidotes to anthrax lethal factor intoxication. Part 2: Structural modifications leading to improved in vivo efficacy pp 2030–2033
Seongjin Kim, Guan-Sheng Jiao, Mahtab Moayeri, Devorah Crown, Lynne Cregar-Hernandez, Linda McKasson, Stephen A. Margosiak, Stephen H. Leppla, Alan T. Johnson*



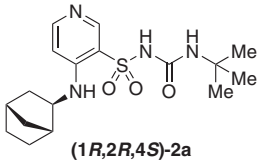
New anthrax lethal factor inhibitors (LFIs) were designed based upon previously identified potent inhibitors **1a** and **2**. Combining the new core structures with modifications to the C2-side chain yielded analogs with improved efficacy in the rat lethal toxin model.

Pharmacokinetic optimisation of novel indole-2-carboxamide cannabinoid CB_1 antagonists **pp 2034–2039**
Phillip M. Cowley*, James Baker, Kirsteen I. Buchanan, Ian Carlyle, John K. Clark, Thomas R. Clarkson, Maureen Deehan, Darren Edwards, Yasuko Kiyoi, Iain Martin, Dawn Osbourn, Glenn Walker, Nick Ward, Grant Wishart



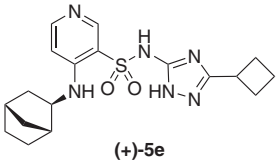
CB_1 pIC_{50}	8.9	8.3
In vivo ID_{50}	0.88 μmol/kg	1.16 μmol/kg
Predicted human F	4%	65%

Pyridinesulfonylureas and pyridinesulfonamides as selective bombesin receptor subtype-3 (BRS-3) agonists **pp 2040–2043**
Michael M.-C. Lo*, Harry R. Chobanian, Oksana Palyha, Yanqing Kan, Theresa M. Kelly, Xiao-Ming Guan, Marc L. Reitman, Jasminka Dragovic, Kathryn A. Lyons, Ravi P. Nargund, Linus S. Lin



(1*R*,2*R*,4*S*)-2a

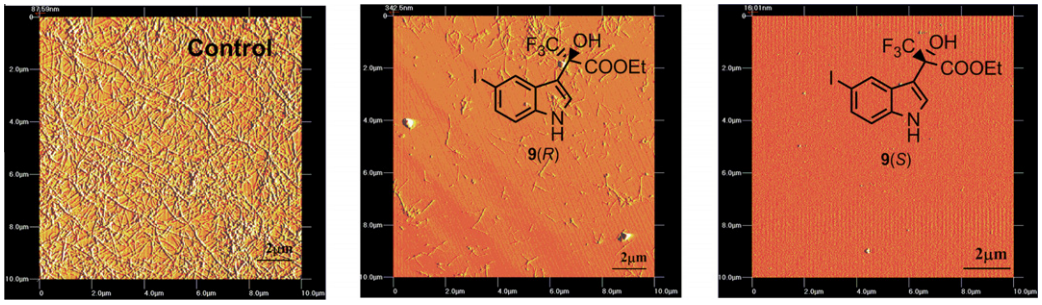
*h*BRS-3 EC_{50} 55 nM (100%act.)
*m*BRS-3 EC_{50} 21 nM (100%act.)



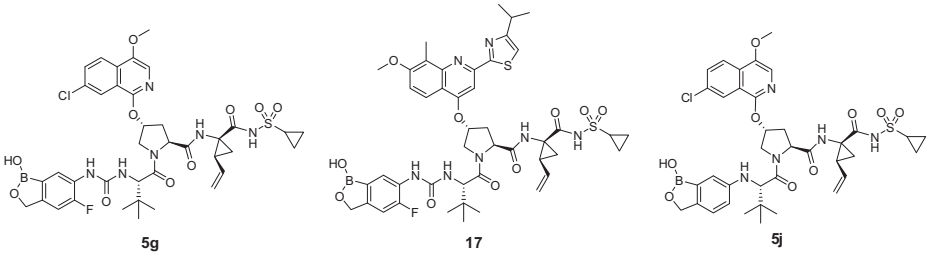
(+)-5e

*h*BRS-3 EC_{50} 380 nM (62%act.)
*m*BRS-3 EC_{50} 51 nM (87%act.)

Disassembly of preformed amyloid beta fibrils by small organofluorine molecules **pp 2044–2047**
Abha Sood, Mohammed Abid, Catharine Sauer, Samson Hailemichael, Michelle Foster, Béla Török, Marianna Török*

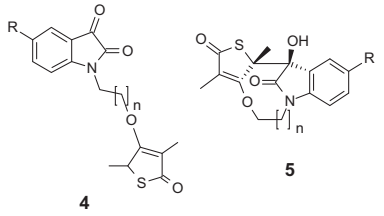


Synthesis and SAR of acyclic HCV NS3 protease inhibitors with novel P4-benzoxaborole moieties **pp 2048–2054**
Xianfeng Li*, Suoming Zhang, Yong-Kang Zhang, Yang Liu, Charles Z. Ding, Yasheen Zhou, Jacob J. Plattner, Stephen J. Baker, Wei Bu, Liang Liu, Wieslaw M. Kazmierski*, Maosheng Duan, Richard M. Grimes, Lois L. Wright, Gary K. Smith, Richard L. Jarvest, Jing-Jing Ji, Joel P. Cooper, Matthew D. Tallant, Renae M. Crosby, Katrina Creech, Zhi-Jie Ni, Wuxin Zou, Jon Wright



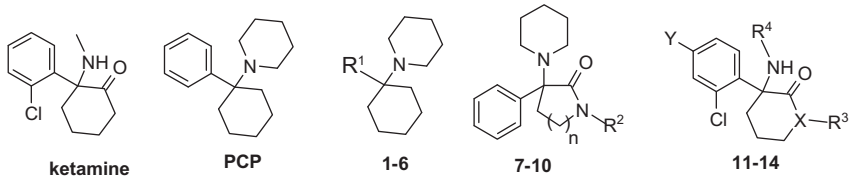
5g 17 5j

Novel thiolactone–isatin hybrids as potential antimalarial and antitubercular agents **pp 2055–2058**
Renate H. Hans, Ian J. F. Wiid, Paul D. van Helden, Baojie Wan, Scott G. Franzblau, Jiri Gut, Philip J. Rosenthal, Kelly Chibale*



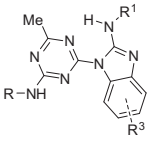
The biological evaluation of novel thiolactone–isatin hybrids are described. Structure–activity relationships are explored and the activity profile of these derivatives revealed.

Novel analogues of ketamine and phencyclidine as NMDA receptor antagonists **pp 2059–2063**
Paola Zarantonello*, Ezio Bettini, Alfredo Paio, Chiara Simoncelli, Silvia Terreni, Francesco Cardullo*

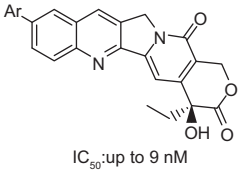


The identification of structurally novel analogues of ketamine and phencyclidine (PCP), as NMDA receptor antagonists, with low to moderate potency at GluN2A and GluN2B receptors is discussed. In particular, some examples, such as compounds **6** and **10**, show decreased calculated lipophilicity, when compared to PCP, while retaining moderate activity. Moreover, the germinal aryl amino substituted lactam ring, as exemplified in compounds **7**–**10** and **11**–**13**, constitutes a novel scaffold with potential application in the design of biologically active compounds.

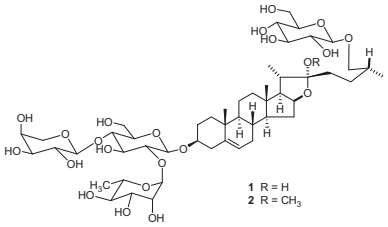
Discovery of triazine-benzimidazoles as selective inhibitors of mTOR **pp 2064–2070**
Emily A. Peterson*, Paul S. Andrews, Xuhai Be, Alessandro A. Boezio, Tammy L. Bush, Alan C. Cheng, James R. Coats, Adria E. Colletti, Katrina W. Copeland, Michelle DuPont, Russell Graceffa, Barbara Grubinska, Jean-Christophe Harmange, Joseph L. Kim, Erin L. Mullady, Philip Olivieri, Laurie B. Schenkel, Mary K. Stanton, Yohannes Teffera, Douglas A. Whittington, Ti Cai, Daniel S. La*



Synthesis and antitumor activity of 10-arylcamptothecin derivatives **pp 2071–2074**
Yu Jiao, Hongchun Liu, Meiyu Geng*, Wenhu Duan*

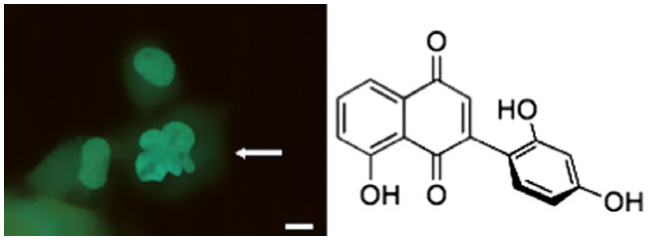


Furostanol saponins from the rhizomes of *Dioscorea japonica* and their effects on NGF induction **pp 2075–2078**
Ki Hyun Kim, Min Ah Kim, Eunjung Moon, Sun Yeou Kim, Sang Zin Choi, Mi Won Son, Kang Ro Lee*



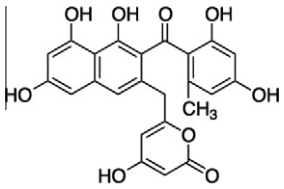
Two new furostanol saponins, coreajaponins A (**1**) and B (**2**), together with 10 known compounds (**3**–**12**) were isolated from the rhizomes of *Dioscorea japonica*. Coreajaponin B (**2**) upregulated NGF content without significant cell toxicity.

8-Hydroxynaphthalene-1,4-dione derivative as novel compound for glioma treatment **pp 2079–2082**
Giuseppe Zagotto*, Marco Redaelli, Riccardo Pasquale, Domenico D'Avella, Giorgio Cozza, Luca Denaro, Francesca Pizzato, Carla Mucignat-Caretta



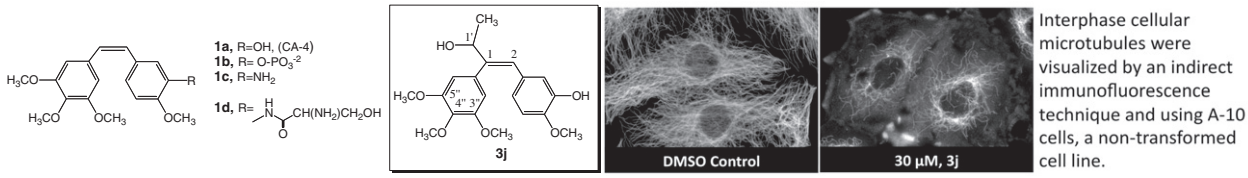
A new juglone derivative showed very promising activity, in terms of apoptotic versus necrotic cell death, compared to the reference drug temozolomide in glioma cells.

Enzymatic formation of an aromatic dodecaketide by engineered plant polyketide synthase **pp 2083–2086**
Kiyofumi Wanibuchi, Hiroyuki Morita, Hiroshi Noguchi, Ikuro Abe*



The enzymatic formation of TW95a by a structure-based mutant is reported.

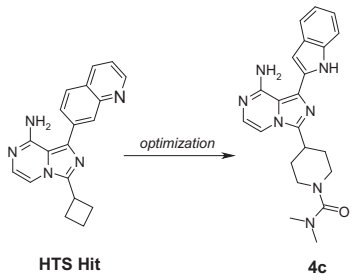
Design and synthesis of novel enhanced water soluble hydroxyethyl analogs of combretastatin A-4 **pp 2087–2091**
Megan Lee, Olivia Brockway, Armaan Dandavati, Samuel Tzou, Robert Sjoholm, Alexis Nickols, Balaji Babu, Sameer Chavda, Vijay Satam, Rachel M. Hartley, Cara Westbrook, Susan L. Mooberry, Gregory Fraley, Moses Lee*



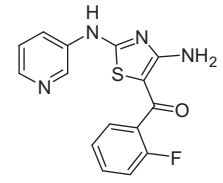
Interphase cellular microtubules were visualized by an indirect immunofluorescence technique and using A-10 cells, a non-transformed cell line.

Imidazo[1,5-*a*]pyrazines: Orally efficacious inhibitors of mTORC1 and mTORC2 **pp 2092–2097**
Andrew P. Crew*, Shripad V. Bhagwat, Hanqing Dong, Mark A. Bittner, Anna Chan, Xin Chen, Heather Coate, Andrew Cooke, Prafulla C. Gokhale, Ayako Honda, Meizhong Jin, Jennifer Kahler, Christine Mantis, Mark J. Mulvihill, Paula A. Tavares-Greco, Brian Volk, Jing Wang, Douglas S. Werner, Lee D. Arnold, Jonathan A. Pachter, Robert Wild, Neil W. Gibson

The discovery of a selective and orally efficacious imidazo[1,5-*a*]pyrazine mTOR inhibitor (**4c**) via optimization of an HTS hit is described.

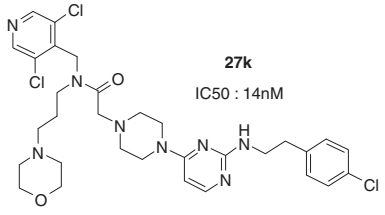


Structure–activity relationship study of 2,4-diaminothiazoles as Cdk5/p25 kinase inhibitors **pp 2098–2101**
Joydev K. Laha, Xuemei Zhang, Lixin Qiao, Min Liu, Snigdha Chatterjee, Shaughnessy Robinson, Kenneth S. Kosik, Gregory D. Cuny*

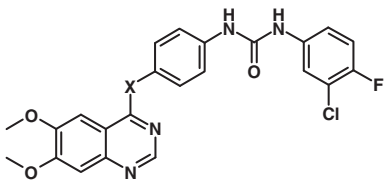


LDN-193594 (**26**)
Cdk5/p25 IC_{50} = 0.030 μM

Development of 2,4-diaminopyrimidine derivatives as novel SNSR4 antagonists **pp 2102–2105**
Malken Bayrakdarian, Joanne Butterworth, Yun-Jin Hu, Vijayaratnam Santhakumar*, Mirosław J. Tomaszewski



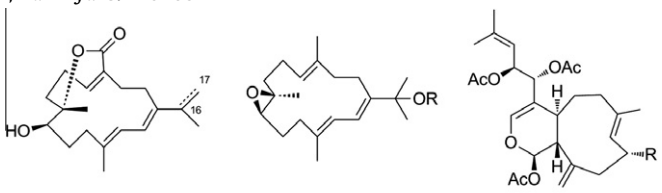
Impact of aryloxy-linked quinazolines: A novel series of selective VEGFR-2 receptor tyrosine kinase inhibitors **pp 2106–2112**
Antonio Garofalo, Laurence Goossens*, Perrine Six, Amélie Lemoine, Séverine Ravez, Amaury Farce, Patrick Depreux



23 : X = NH IC_{50} = 4300 nM (VEGFR-2)
24 : X = N-CH_3 IC_{50} = > 10000 nM (VEGFR-2)
17 : X = O IC_{50} = 40 nM (VEGFR-2)

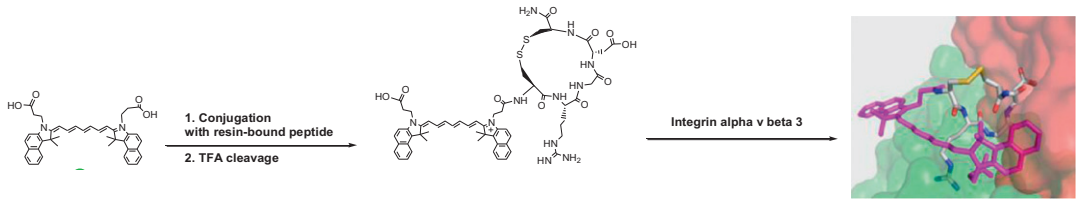
Three series of 6,7-dimethoxyquinazoline derivatives substituted in the 4-position by aniline, *N*-methylaniline and aryloxy entities, targeting EGFR and VEGFR-2 tyrosine kinases, were designed and synthesized. In vitro activities of these compounds have been evaluated for their enzymatic inhibition of VEGFR-2 and EGFR and for their antiproliferative activities on various cancer cell lines. We have studied the impact of the variation in the 4-position substitution of the quinazoline core. Substitution by aryloxy groups led to new compounds which are selective inhibitors of VEGFR-2 enzyme with IC_{50} values in the nanomolar range in vitro.

Identification and evaluation of soft coral diterpenes as inhibitors of HIF-2α induced gene expression **pp 2113–2115**
Tanja Grkovic, Emily L. Whitson, Daniel C. Rabe, Roberta S. Gardella, Donald P. Bottaro, W. Marston Linehan, James B. McMahon, Kirk R. Gustafson, Tawnya C. McKee*

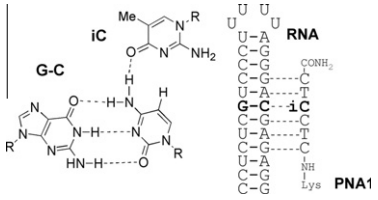


Two new cembrane diterpenes, (4*Z*,8*S**,9*R**,12*E*,14*E*)-9-hydroxy-1-(prop-1-en-2-yl)-8,12-dimethyl-oxabicyclo[9.3.2]-hexadeca-4,12,14-trien-18-one (**1**), and (1*E*,3*E*,7*R**,8*R**,11*E*)-1-(2-methoxypropan-2-yl)-4,8,12-trimethyl-oxabicyclo[12.1.0]-pentadeca-1,3,11-triene (**7**), as well as eight known compounds, **2**–**6** and **8**–**10** were isolated.

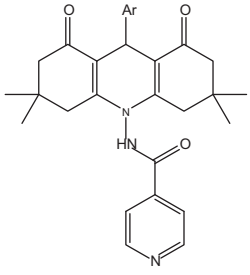
Exploring new near-infrared fluorescent disulfide-based cyclic RGD peptide analogs for potential integrin-targeted optical imaging **pp 2116–2120**
Yunpeng Ye, Baogang Xu, Gregory V. Nikiforovich, Sharon Bloch, Samuel Achilefu*



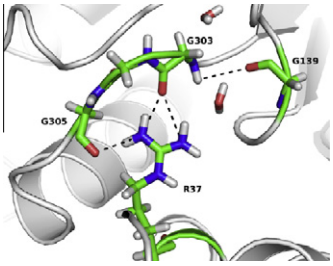
PNA containing isocytidine nucleobase: Synthesis and recognition of double helical RNA **pp 2121–2124**
Thomas Zengeya, Ming Li, Eriks Rozners*



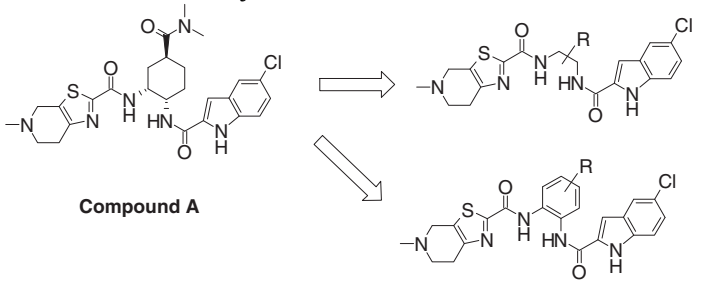
Microwave assisted one-pot synthesis of highly potent novel isoniazid analogues **pp 2125–2128**
Thimmappa H. Manjashetty, Perumal Yogeeswari, Dharmarajan Sriram*



On the function of the internal cavity of histone deacetylase protein 8: R37 is a crucial residue for catalysis **pp 2129–2132**
Shozeb Haider, Caleb G. Joseph, Stephen Neidle, Carol A. Fierke, Matthew J. Fuchter*

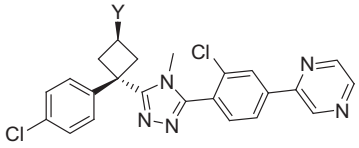


Design, synthesis and SAR of novel ethylenediamine and phenylenediamine derivatives as factor Xa inhibitors **pp 2133–2140**
Kenji Yoshikawa*, Toshiharu Yoshino, Yoshihiro Yokomizo, Kouichi Uoto, Hiroyuki Naito, Katsuhiro Kawakami, Akiyoshi Mochizuki, Tsutomu Nagata, Makoto Suzuki, Hideyuki Kanno, Makoto Takemura, Toshiharu Ohta



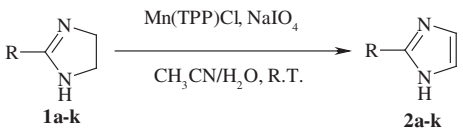
A series of ethylenediamine and phenylenediamine derivatives were synthesized as factor Xa (fXa) inhibitors.

Substituted phenyl triazoles as selective inhibitors of 11β-Hydroxysteroid Dehydrogenase Type 1 **pp 2141–2145**
Wanying Sun*, Milana Maletic, Steven S. Mundt, Kashmira Shah, Hratch Zokian, Kathy Lyons, Sherman T. Waddell, James Balkovec



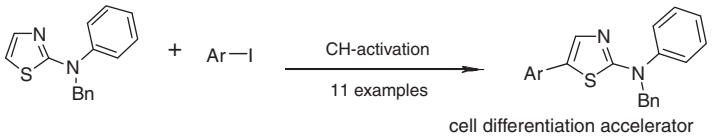
The synthesis and biological activity of selective inhibitors of 11β-Hydroxysteroid Dehydrogenase Type 1 are reported.

Dehydrogenation of 2-imidazolines with sodium periodate catalyzed by manganese(III) tetraphenylporphyrin **pp 2146–2148**
Hadi Kargar*, Majid Moghadam, Valiollah Mirkhani, Shahram Tangestaninejad, Iraj Mohammadpoor-Baltork, Iman Nameni



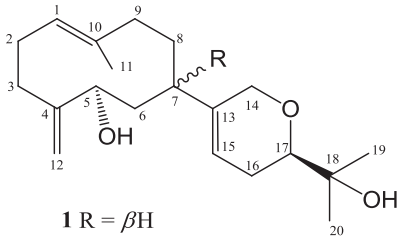
Dehydrogenation of 2-substituted imidazolines with sodium periodate in the presence of Mn(TPP)Cl, is reported. A wide variety of 2-imidazolines efficiently converted to their corresponding imidazoles by Mn(TPP)Cl/$NaIO_4$ catalytic system at room temperature. The effect of reaction parameters such as kind of solvent and catalyst amount was also investigated.

Synthesis of 5-arylated *N*-arylthiazole-2-amines as potential skeletal muscle cell differentiation promoters **pp 2149–2154**
Michael Schnürch*, Birgit Waldner, Karlheinz Hilber, Marko D. Mihovilovic*



An efficient synthetic strategy towards arylated aminothiazoles was developed based on CH-activation as key step. The obtained compounds displayed high activity to accelerate cell-differentiation of progenitor cells towards muscle cells.

Cytotoxic and antioxidant activities of diterpenes and sterols from the Vietnamese soft coral *Lobophytum compactum* **pp 2155–2159**
Chau Van Minh*, Phan Van Kiem, Nguyen Xuan Nhiem, Nguyen Xuan Cuong, Nguyen Phuong Thao, Nguyen Hoai Nam, Hoang Le Tuan Anh, Do Cong Thung, Dinh Thi Thu Thuy, Hee-Kyoung Kang, Hae-Dong Jang, Young Ho Kim*



1 R = βH
2 R = αH

Two new diterpenes, lobocompactols A (**1**) and B (**2**), and five known compounds (**3**–**7**) were isolated from the methanol extract of the soft coral *Lobophytum compactum* using combined chromatographic methods and identified based on NMR and MS data. Each compound was evaluated for cytotoxic activity against A549 (lung) and HL-60 (acute promyelocytic leukemia) human cancer cell lines. Among them, compound **5** exhibited strong cytotoxic activity against the A549 cell line with an IC_{50} of 4.97 ± 0.06 μM. All compounds exhibited moderate cytotoxicity against the HL-60 cell line, with IC_{50} values ranging from 17.80 ± 1.43 to 59.06 ± 2.31 μM. Antioxidant activity was also observed, with compounds **1** and **2** exhibiting moderate peroxyl radical scavenging activity of 1.4 and 1.3 μM Trolox equivalents, respectively, at a concentration of 5 μM.

*Corresponding author
Supplementary data available via ScienceDirect

COVER

Botulinum neurotoxins are the most deadly toxins known to man, approximately 10 million times more deadly than cyanide. Botulinum neurotoxins are classified by the US Centers for Disease Control (CDC) as bioterrorism agents. The etiological agent responsible for botulinum intoxication is a metalloprotease; as such this is a key therapeutic target. Currently, there are no approved pharmacological treatments for botulinum intoxication. Discovering molecules that could be used as a path forward for therapeutic development as botulinum protease inhibitors is tantamount. A benzylidene cyclopentenedione-based inhibitor was found to be the first affinity reagent to covalently modify the active site of botulinum neurotoxin A light chain metalloprotease. Its kinetic parameters are reported and such an approach for inhibition of this deadly neurotoxin. [Capková, K.; Hixon, M. S.; Pellett, S.; Barbieri, J. T.; Johnson, E. A.; Janda, K. D. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 206.]

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