

Other Activities

1. Preparation of 1-phenyl-1,4 dihydro[1,8]naphthyridin-4-one-3-carboxamide derivatives as PDE4 inhibitors for treatment of psychiatric disorders

Edward, S. M.

Merck Co., USA

PCT Int. Appl. WO 2004, 45, 508 (Cl. A61k), 3 Jun 2004, US Appl. PV426, 529, 15 Nov. 2002; 40 pp; C.A. 141(2): 23432m

Abstract: This is an attempt to develop PDE4 inhibitors. Synthesis of 1-phenyl-1,4 dihydro[1,8]naphthyridin-4-one-3-carboxamide derivatives was carried out.

Activity: These compounds have exhibited potency to treat psychiatric disorders alone or in combination with psychotherapy. These are also useful for specific phobias, panic disorders, anxiety disorders including post-traumatic stress disorders etc.

Origin: Synthetic

2. Preparation of 4-hydroxypiperidine derivatives for treatment of respiratory diseases

Yasushige, A. and Kazuyuki, M.

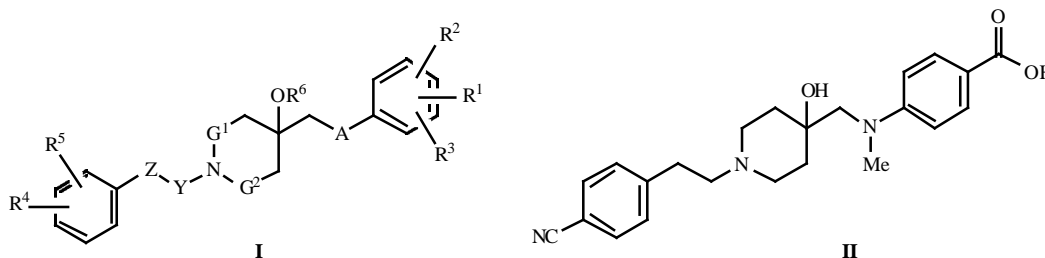
Mochida Pharmaceutical Co., Ltd., Japan

PTC Int. Appl. WO 2004, 48, 236 (Cl. C07D205/04), 10 Jun 2004, JP Appl. 2002/41, 251, 25 Nov. 2002; 125 pp; C.A. 141(2): 23429r

Abstract: This patent mainly deals with the preparation, formulations and biological studies of compound **I** [wherein A = L-W; L = a bond or CH₂; W = O, SO, SO₂, NH, or -N-alkylene; G¹ and G² = independently none, CH₂, CH₂CH₂, etc.; Y = alkylene or (un)substituted benzylidene; Z = a bond, O, etc.; R¹ = NO₂, alkoxy, (un) substituted carbamoyl, OH, CO₂H, etc.; R² and R³ = independently H, halo, NO₂, (un)substituted alkyl, or alkoxy; R⁴ and R⁵ = independently H, halo, CN, alkyl-SO₂, (un)substituted alkyl, or alkoxy; R⁶ = H or alkyl; with provisos], their salts and solvates.

Activity and bioassay: Compound **II**. HCl, salt of compound **I**, prepared during this research work, was found to exhibit 59% inhibition of cough induced by citric acid in 1 h, when tested in guinea pig at the amount of 30 mg/kg. These compounds displayed potent biological activities against respiratory diseases, such as lung cancer, common cold syndrome, pulmonary tuberculosis, pneumonia, acute bronchitis etc.

Origin: Synthetic



Web URL: www.chimia.ch

3. Synthesis and herbicidal activity of phenylpyridines- A new lead

Peter, S., Gerhard, H., Michael, P., Karl-Otto, W. and Cyrill, Z.

BASF Aktiengesellschaft, D-67056 Ludwigshafen, Germany

Chimia 2003, **57**(11), 715-719; *C.A.* **141**(2): 23397y

Abstract: Syntheses of novel phenylpyridines, based on molecular modeling studies and their structure-activity relationships, are described.

Activity and bioassay: These compounds possessed strong biological activity against broad leaf and grass weed species under pre- and post-emergent conditions and inhibited protoporphyrinogen-IX-oxidase.

Origin: Synthetic

4. Preparation of piperidinyl prostaglandin E analogs as ocular hypotensives

David, O. W. and Thang, D. D.

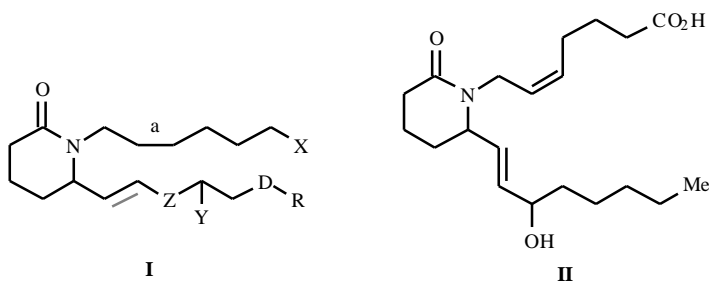
Allergan, Inc., USA

U.S. 6,747, 037 (Cl. 514-277; A61k31/435), 8 Jun 2004, Appl. 456, 275,6 Jun 2003; 16 pp; *C.A.* **141**(2): 23343h

Abstract: Studies on preparation of synthetic analogues of piperidinyl prostaglandine E **I** [D = bond, CH₂, O, S, NH; X = (substituted) CO₂H, CONH₂, CHOH, etc.; Y = oxo, (substituted) OH; Z = CH₂, bond; R = Ph, isopropyl; bond a = single, double or triple bond], formulation alongwith their biological activities were carried out.

Activity and bioassay: These compounds are useful for the treatment of ocular hypertension. Compound **II** was found to display EC₅₀ = 46 nM when tested against hEP4.

Origin: Synthetic



5. Use of diamide derivative for inhibiting chronic tissue transplant rejection

John, W. M.

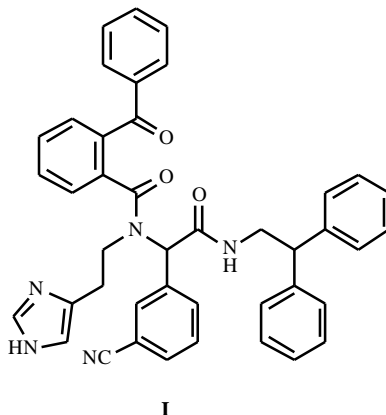
Genzyme Corporation, USA

PTC Int. Appl. WO 47.825 (Cl. A61K31/16), 10 Jun 2004, US Appl. PV. 428,332 21 Nov. 2002; 36 pp; *C.A.* **141**(2): 17602a

Abstract: A diamide compound **I** is found to inhibit acute and chronic tissue transplant rejection.

Activity: This compound is reported to inhibit chronic tissue transplant rejection.

Origin: Synthetic



6. Effects of polysaccharide ginsan from *Panax ginseng* on liver function

Jie-Young, S., Medea, A., Alexander, P., Hyung-Doo, K., In-Sung, J., Young-Soo, H. and Yeon-Sook, Y.

Laboratory of Immunology, Kaeri, Korea Instituted of Radiological and Medical Sciences, Seol, 139-706 S. Korea

Archives of Pharmacol. Research 2004, **27**(5), 531-538; *C.A.* **141**(2): 17190q

Abstract: A potent immunomodulator, ginsan, was analyzed for some immune function by i.p. injection. Detailed biological data is provided in the manuscript.

Activity and bioassay: 100 mg/kg of dose of ginsan significantly decreased heme oxygenase (HO) activity 1.7~2 fold 20-34% hepatic cytochrome P 450 (CYP450), 65-70%, prolongation of oxazolamine-induced paralysis time. This treatment did not cause any hepatic injury. Ginsan treatment did not change total bilirubin and albumin, and did not effect sine serum aminotransferase (AST), Ala aminotransferase (ALT), alk. phosphatase (ALP), ALR, ALP, along with ALP activities and levels.

Origin: Natural product

7. Preparation of sinomenine compounds for the treatment of cognitive disorders

Guo-Wei, Q., Xi-Can, T., Rui, W., Tian-Xi, Z., Pierre, L., Daniel-Henri, C. and Pierre, R.

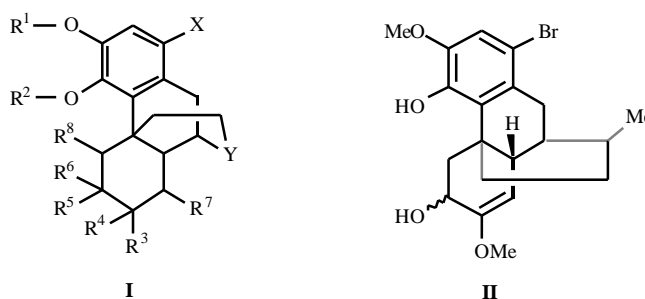
Shangai Institute of Mareria Medica, Chinese Academy of Sciences; Les Laboratoires Servier, Peop. Rep. China

PTC Int. Appl. WO 2004, 48, 340 (Cl. CO7D221/28), 10, Jun 2004, CN Appl. 2,002, 153, 819 28 Nov. 2002; 35 pp; *C.A.* **141**(2): 23767z

Abstract: Synthesis of sinomenine, its pharmaceutical composition and its derivatives **I** [Y = (substituted) N, (substituted) N-oxide, disubstituted N+ halide; X= halo; R¹ = alkyl; R² = H, acyl; R³ = OH, alkoxy; R⁴, R⁷ = H; R⁴R⁷ = bond; R³R⁴ = oxo, (substituted) N; R⁵, R⁸ = H, R⁵R⁸ = bond; R⁶ = OH, acyl, etc.] are described.

Activity and bioassay: A difference of -36 s was displayed by compound **II** at a dose of 20 mg/kg in social recognition in the Wistar rat.

Origin: Synthetic



Web URL: <http://sciencedirect.com>

8. Stereoselective synthesis and moulting activity of 2,3-diepi-20-hydroxyecdysone and 2,3-diepi-5-20-hydroxyecdysone

Sureepron, H., Aporn, C., Nitirat, C. and Apichart, S.

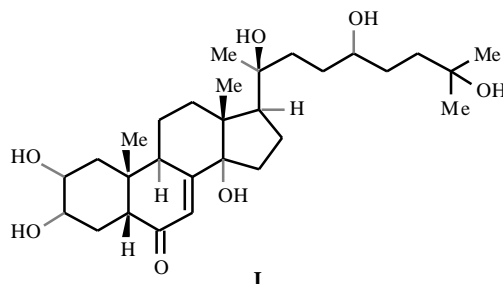
Faculty of Science, Department of Chemistry, Ramkhamhaeng University, Huamrk, Bangkok, Bangkok Thailand 10240

Tetrahedron 2004, **60**(15), 3433-3438; *C.A.* **141**(2): 2376b

Abstract: Synthesis of 2,3-diepi-20-hydroxyecdysone (**I**) and 2,3-diepi-5-20-hydroxyecdysone and their biological activities are described.

Activity and bioassay: 20-Hydroxyecdysone was more active than 2,3-diepi-5-analog and was found to display 1.5 fold less activity than its 5-analog in *Musca* bioassay.

Origin: Synthetic



9. Preparation of isothiazoles and pesticides containing them for controlling plant diseases

Yoshinori, K., Micheal, O., Haruko, S., Takuma, S. and Lutz, A.

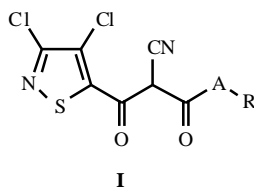
Bayer A-G., Germany

Jpn. Kokai Tokkyo Koho JP 2004, 161, 712 (Cl. Co7D5/02), 10 Jun 2004, Appl. 2002/331,736, 15 Nov. 2002; 17pp; *C.A.* **141**(3): 38602r

Abstract: Preparations of isothiazole compounds of formula **I** [A = (cycloalkyl-substituted alkylene, cycloalkylidene; R = Ph (substituted with halo, alkyl, alkenyl, alkoxy, Ph NO₂, etc.)] are described.

Activity and bioassay: Compound **I** (AR =4-CH₂C₆H₄Cl) displayed 80 antifungal activity against *Pyricularia oryzae* 8 kg/ha when it was used on rice paddy.

Origin: Synthetic



10. Preparation of benzoyl compounds and herbicides containing them for rice paddy

Mineyuko, K., Yoriyoshi, T. and Kazuyoshi, K.

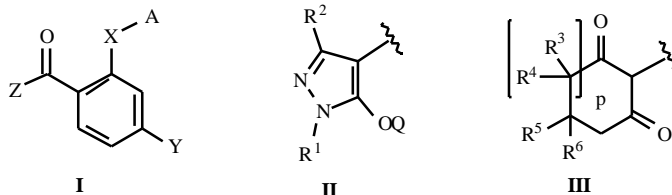
Idemitsu Kosan Co., Ltd., Japan

Jpn. Kokai Tokkyo Koho JP 2004, 168, 682 (Cl. C07C49/84), 17 Jun 2004, Appl. 2002/334,006, 18 Nov. 2002; 62 pp; C.A. **141**(3): 38609y

Abstract: Preparation of benzoyl compounds of formula **I** [$X = 0, SO_1 NR^{11}$; $1 = 0-2$; $R^{11} = H, C_{1-4}$ alkyl; $Y = SO_n R^7, R^8$; $R^7 = C_{1-4}$ alkyl; $n = 0-2$; $R^8 = C_{1-4}$ fluoroalkyl; $Z = \text{II, III}$; $R^1, R^2 = H, C_{1-4}$ alkyl, C_{3-6} cycloalkyl; $R^3-R^6 = H, C_{1-4}$ alkyl; $p = o, 1$; $Q = H, C_{1-8}$ alkylsulfonyl, $R^{12} C CCHR^{13}$; $R^{12}, R^{13} = H, C_{1-4}$ alkyl; $A = (\text{un})\text{substituted Ph, } (\text{un})\text{substituted 5- or 6-membered heterocyclyl}$] is described.

Activity and bioassay: Compound **I** ($XA = \text{OPh}$, $Y = \text{SO}_2\text{Me}$, $Z = 1\text{-ethyl-5-hydroxypyrazol-4-yl}$) displayed herbicidal activity at 300 g/ha 100% against *Echinochloa crus-galli*, but was harmless to rice crops.

Origin: Synthetic



11. A dolabellane diterpene from the Brazilian brown alga *Dictyota pfaffii*

Pinheiro, B. J., Laneuville, T. V., Roberto, V., Cresop, P. R., Lourenco, A. J. and Palmer de Paixao, F. I. C.

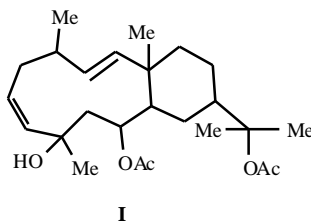
Institutode Quimica, Pos-Graduacao em Quimica Organica, Universidade Federal Fluminense (UFF), CEP 24020-150 Nteroi, Brazil

Biochemical Systematics and Ecology 2003, **31**(12), 1451-1453; C.A. **141**(3): 36019g

Abstract: Dolabellane-1 (**I**) was isolated from the extracts of Brazilian brown alga *Dictyota pfaffii*. This plant defends itself from other aquatic life forms.

Activity and bioassay: Compound **I** exhibited defensive properties related to *D. pfaffii* against herbivores.

Origin: Natural product



12. Preparation of 2-aryl-1,2,4-triazine-3,5-di(thi)ones as herbicides

Karl-Heinz, L., Roland, A., Dorothee, H., Hans-Georg, S., Joachim, K., Wilhelm, D. M., Peter, D., Dieter, F. and Rolf, P.

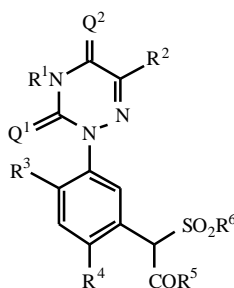
Bayer Cropscience A.-G., Germany

Ger. Offen. De 10, 255, 416 (Cl. C07D253/075), 9 Jun 2004, Appl. 10, 255, 416, 28 Nov. 2002; 30 pp; *C.A. 141*(2): 23556e

Abstract: Preparation of 2-aryl-1,2,4-triazine-3,5-di(thi)ones [**I**; Q¹, Q² = O, S; R¹ = H, cyano, amino, (substituted) alkyl, alkoxy, alkylamino, dialkylamino, etc.; R² = H, halo, NO₂, carboxy, cyano, thiocarbamoyl, (substituted) alkyl, alkoxy, alkylthio, alkylamino, etc.; R³ = H, cyano, halo; R⁴ = halo; R⁵ = H, alkoxycarbonyl, etc.; R⁶ = amino, OH, etc.] was carried out.

Activity and bioassay: 2-[5-(*N*-2,4-difluorophenylpropionyl-*N*-ethylsulfonylamino)-4-bromo-2-fluorophenyl]-4-methyl-1,2,4-triazine-3,5-(2*H*,4*H*)-dione displayed excellent pre- and post-emergent herbicidal activity without crop damage.

Origin: Synthetic



I

13. 1,2,4-Thiadiazole compounds, their preparation their use as pesticides, and arthropod-controlling compositions containing them

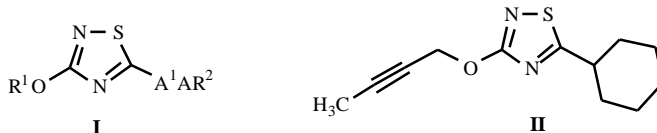
Hideki, I. and Daisuke, T.

Sumitomo Chemical Company Limited, Japan

PCT Int. Appl. WO 2004, 46, 125 (Cl. C07D285/08), 3 Jun 2004, JP Appl. 2002/337, 884, 21 Nov. 2002; 47 pp; *C.A. 141*(2): 23538a

Abstract: Synthesis of 1,2,4-thiadiazole compounds **I** [wherein; R¹ = C₃₋₇ alkynyl that may be substituted with halo; R² = C₃₋₈ cycloalkyl which may be substituted with C₁₋₄ alkyl, halo, CF₃, or the like; A¹ = bond, C₁₋₂ alkylene, or C₂₋₃ alkylidene], 5-cyclohexyl-3-(2-butynyloxy)-1,2,4-thiadiazole (**II**), their formulation including biological activities are described in this patent.

Activity and bioassay: The compounds were found to be useful as pesticides having strong potency for arthropod-controlling activity control for arthropod pests such as insects, acaroids, and related species.



I

II

14. Preparation of 8,8-dimethyl7,8-dihydronaphthalenes as antagonists of RARs receptors and their use in human or veterinary medicine and in cosmetics for treating skin diseases and irritations

Philippe, D., Catherine, R. and Thibaud, B.

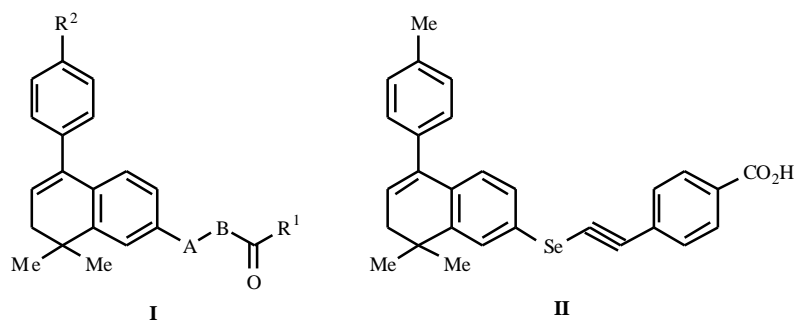
Galdarma Research & Development, S.N.C., France

PCT Int. Appl. WO 2004, 46, 096 (Cl.C07C39/102), 3 Jun 2004, US Appl. PV430, 640 4 Dec. 2002; 88 pp; C.A. 141(2): 23308a

Abstract: Derivatives of **I** [wherein A = CH₂, CHOH, C:O, C:NOH, S or Se; B = -CH:CH₂H₄-, -CH:CHAr-, -(C:O)NHAr-, etc.; Ar = C₅H₃N, (un)substituted phenylene; R¹ = OH and derives., monoalkyl/amino; R² = H, F, Cl, Br, alkyl, CF₃, OH and derives., NH₂ and derivatives, 2-, 3-, or 4-pyridinyl, 2-thiophenyl, CH₂NH₂ and derivatives, (un)substituted Ph, etc.; their optical isomers, and pharmaceutical acceptable salts with certain exception], and **II**, their syntheses, pharmaceutical compositions, formulation and medicinal uses are described in the current patent.

Activity and bioassay: Some of the compounds **I** exhibited a K_{d app} value of 100 nM and inhibited RAR receptors in a transactivation test with an IC₅₀ value of 25 nM. These are useful in skin diseases and irritations.

Origin: Synthetic



15. Preparation of anthranilic acid amides and their derivatives as cosmetic and pharmaceutical active substances

Gerhard, S., Holger, J., Martina, H., Christopher, S.-L. and Tobias, V.

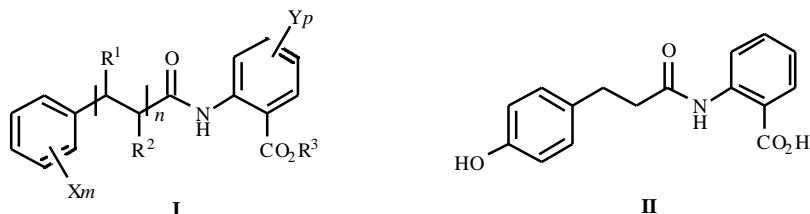
Symrise GmbH and Co. Kg, Germany

Ger. Offen. DE 10, 254, 872 (Cl. C07C235/42), 3 Jun 2004, Appl. 10.254,872, 25 Nov. 2002; 40 pp; C.A. 141(2): 23300s

Abstract: The synthesis of compounds **I** [m = 0 - 3; p = 0 - 2; n = 0 - 2, (with the proviso that when n = 1, 2, p + m > 0); R¹ = R² = H; R¹R² = bond; Y = OH, O-alkyl, O-acyl; R³ = H, alkyl; Y = OH, O-alkyl, O-acyl] dihydrocinnamic acid amide (**II**), their mixture, including their pharmaceutical significance is reported.

Activity and bioassay: The compounds showed the inhibition of the substance P induced release of histamine from mast cells. At 0.5 ppm compound **II** displayed inhibition of the substance P at 5.0 ppm: 26% inhibition, at 50 ppm: 40% inhibition.

Origin: Synthetic



Web URL: <http://sciencedirect.com>

16. Lamotrigine: a depression mood stabiliser

Erik, H.

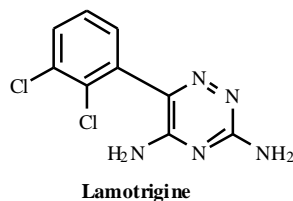
Psychiatric Office, Psychiatric Clinic, Charles University, Prague, Praha, Czech. Rep. 160 00

European Neuropsychopharmacology 2004, **14**(Suppl.2) S89-S93; *C.A.* **141**(1): 222d

Abstract: This study provides real-world evidence of lamotrigine as a mood stabilizer for patients with bipolar disorder. It is an anticonvulsant, and its frequent effectiveness for patient who failed to respond to antidepressants or mood stabilisers proved it to have more antidepressant potency. Patients who could not tolerate any other antidepressant drug because of switches to mania or increased speed, or intensity of cycling or development of mixed states, were able to tolerate therapeutic doses in presence of lamotrigine. Trial studies showed that without mood destabilising, this compound is effective for the prevention of bipolar depression (bipolar-I). Its treatment can also be extended to treat patients with bipolar-II disorders.

Activity: Anti-depression and mood stabilizer

Origin: Synthetic



Web URL: <http://www.cab.publishing.org>

17. Milbemycin oxime in a new formulation, combined with praziquantel, does not reduce the efficacy of praziquantel against *Echinococcus multilocularis* in cats

Jenkins, D.J. and Romig, T.

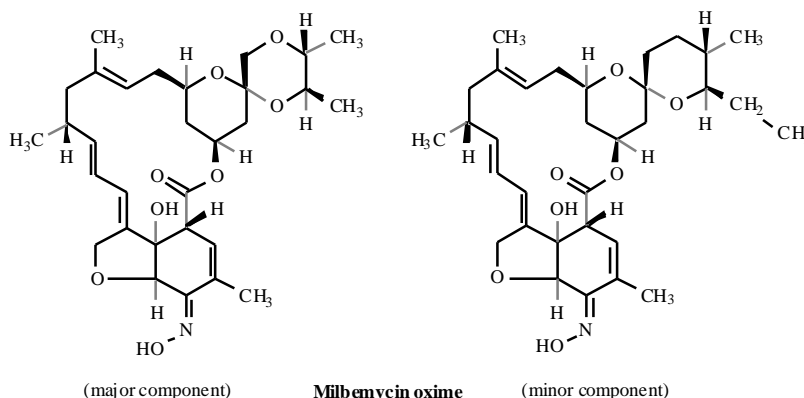
Australian Hydatid Control and Epidemiology Program. Fyshwick ACT, 2609 Australia

Journal of Helminthology 2003, **77**(4), 367-370; *C.A.* **141**(1): 451c

Abstract: Praziquantel is an anti-helminthic or anti-worm medication, prevents worms from growing and is used to treat their infections. Milbemycin oxime on combination with praziquantel was used to treat cats infected with 15,000 protozoocoles of *Echinococcus multilocularis*

Activity and bioassay: Infected cats treated with and without this combined drug were tested, and found that untreated cats were infected with *E. multilocularis* with worm burdens ranging from 235 to 1920 worms per cat, whereas treated cats showed absence of *E. multilocularis*.

Origin: Synthetic



18. Mixed kappa/mu opioids and uses thereof

John, N. L. and Ao, Z.

The Mclean Hospital Corporation, USA

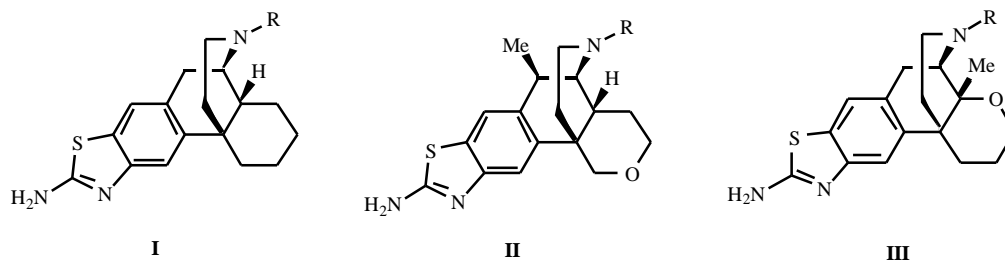
PCT Int. Appl. WO 45, 562 (Cl. A61k), 3 Jun 2004, US Appl. Pv 461, 157, 8 Apr 2003; 56 pp; C.A. **141**(1): 7330w

Abstract: Synthesis of a number of kappa and mu opioids compounds incorporating the general formula **I**, **II**, and **III** (R = H, C₁₋₇ alkyl, C₂₋₇ alkenyl, C₂₋₇ alkynyl, C₂₋₆ heterocyclyl, C₆₋₁₂ aryl, C₇₋₁ alkaryl, C₃₋₁₀ alkheterocyclyl, and C₁₋₇ heteroalkyl) and their medicinal uses are given.

Activity and bioassay: K_i of 130 nM for the μ receptor and a K_i of 29 nM for the kappa opioid receptor was exhibited by aminothiazole **Ia** (R = Me). These analogs are used for therapeutic conditions in pain or on dopamine dysregulation diseases, such as schizophrenia, attention deficit hyperactivity disorder (ADHD), attention deficit hyperactivity disorder (ADD), Parkinson's disease, hyperprolactinemia, depression and addiction.

Activity: Anti inflammatory, Parkinson's diseases

Origin: Synthetic



19. Staminane- and isopimarane-type diterpenes from *Orthosiphon stamineus* of Taiwan and their nitric oxide inhibitory activity

Thi, N.M.T., Suresh, A., Yasuhiro, T., Chien-Hsiung, C., Shigetoshi, K.

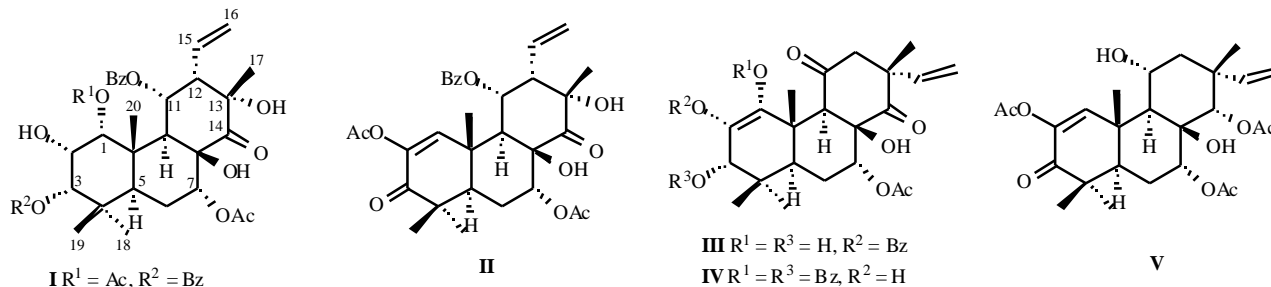
Institute of Natural Medicine, Toyama Medical and Pharmaceutical University, Toyama, Japan 930-0194

Journal of Natural Products 2004, **67**(4), 654-658; C.A. **141**(1): 4136b

Abstract: Two new staminane-type diterpenes staminols C (**I**) and D (**II**), three new isopimarane-type diterpenes orthosiphonone C (**III**) and D (**IV**) and 14-deoxo-14-*O*-acetylorthosiphol Y (**V**) were isolated along with 16 known diterpenes, orthosiphols A, B, D, K, M, N, O, X and Y nororthosiphonolide A, neoorthosiphol B, orthosiphonone A, secoorthosiphols B and C, 3-*O*-deacetylorthosiphol I, and 2-*O*-deacetylorthosiphol from the MeOH extract of Taiwanese *Orthosiphon stamineus*.

Activity and bioassay: NO production in lipopolysaccharide (LPS)-activated macrophage-like J744.1 cells. All compounds showed remarkable dose-dependent inhibition. **IV** showed the highest activity with an IC₅₀ = 35.0 μM. The diterpenoid constituents of this plant exhibited significant inhibition of NO production showing its anti-inflammatory effect.

Origin: Natural product



Web URL: <http://cpb.pharm.or.jp>

20. **Microbial transformation of terreusinone, an ultraviolet-A(UV-A) protecting dipyrroloquinone, by *Streptomyces* sp.**

Li, Xifeng; Lee, sang Mi; choi Hong Dae; Kang, Jung sook; son, Byeng Wha

Department of Chemistry, Pukyong National University, Pusan, 608-737 S. Korea

Chemistry & Pharmaceutical Bulletin 2003, **51**(12), 1458-1459 (Eng) *C.A.* **141**(2): 20197c

Abstract: Biotransformation study was conducted on the marine dipyrroloquinone terreusinone (**I**) isolated from the marine-derived fungus *Aspergillus terreus*. Preparative-scale fermentation of terreusinone with *Streptomyces* species has resulted in the isolation of a new oxidized metabolite, terreusinal (**II**). The structure of **II** was elucidated as 2-[(1*R*)-1-hydroxyisobutyl]-6-[(1*R*)-1,2-dihydroxyisobutyl]-1*H*,5*H*-pyrrolo[2,3-*b*]indole-4,8-dione on the basis of physicochemical evidence. **II** showed an UV-A (320-390nm) protecting activity with ED₅₀ values of 150 μM, which is more active than oxybenzone (ED₅₀, 350μM) currently being used as sunscreen.

