

## **Combretastatin A-4 and Its Analogues as Antineoplastic Agents**

**by K. Dzierzbicka and A.M. Kołodziejczyk**

*Department of Organic Chemistry, Gdańsk University of Technology,  
11/12 G. Narutowicza Street, 80-952 Gdańsk, Poland*

*(Received October 1st, 2003; revised manuscript November 11th, 2003)*

Combretastatin A-4 is a potent antineoplastic and antiangiogenesis natural substance isolated from the South African tree *Combretum caffrum*. This article concerns synthesis and biological activity of combretastatin A-4 and its analogues which are considered as prodrugs.

**Synthesis, Crystal Structure and Magnetic Properties  
of  $[\text{Mn}(\text{L})_2(\text{N}(\text{CN})_2)_2]$ , a One-Dimensional Systems with  
End to End Single Dicyanamide Bridges  
( $\text{L} = 4\text{-Cyanopyridine N-Oxide}$ )**

by **Q.-H. Zhao<sup>1</sup>, Y.-Q. Liu<sup>1,2</sup> and R.-B. Fang<sup>2</sup>**

<sup>1</sup>*Department of Chemistry, Yunnan University, Kunming 650091, P. R. China*

<sup>2</sup>*School of Pharmacy, Yunnan University, Kunming 650091, P. R. China*

*(Received November 3rd, 2003)*

A new 1-D polymeric coordination compound  $[\text{Mn}(\text{L})_2(\text{N}(\text{CN})_2)_2]$  ( $\text{L} = 4\text{-cyanopyridine N-oxide}$ ) has been synthesized and characterized. The crystal structure of this compound was determined by X-ray diffraction analysis. In the crystal structure, the  $[\text{Mn}(\text{L})_2]^{2+}$  units are linked by  $[\text{N}(\text{CN})_2]^-$   $\mu$ -bridging ligands to form one dimensional structure. The manganese ions display four coordination, with two terminal N atoms of different  $[\text{N}(\text{CN})_2]^-$  ligands and two O atoms of different 4-cyanopyridine N-oxide ligands. Analysis of variable temperature magnetic susceptibility (2–300 K) indicates that the polymer shows weak antiferromagnetic interaction.

## **Formation of Copper Sulfide Layers on the Surface of Polyethylene Films of Various Density by the Use of Polythionic Acids**

by **I. Ancutienė<sup>1</sup>**, **V. Janickis<sup>1</sup>** and **R. Giesa<sup>2</sup>**

<sup>1</sup>*Faculty of Chemical Technology, Kaunas University of Technology,  
Radvilėnų str. 19, LT-3028 Kaunas, Lithuania*

<sup>2</sup>*Macromolecular Chemistry I, Polymer Processing, University of Bayreuth, D-95440 Bayreuth, Germany*

*(Received July 22nd, 2003; revised manuscript October 27th, 2003)*

The kinetic study of sulfur adsorption-diffusion processes from higher polythionic acid,  $\text{H}_2\text{S}_{33}\text{O}_6$ , solution into polyethylene films of high, medium and low density showed that the sulfur concentration in polyethylene of various density and thickness increases with increasing temperature of the solution and the duration of treatment. Sulfur concentration in the film is related to the film density and thickness. An increase in the negative apparent adsorption heat of sulfur adsorption was observed with an increase of polyethylene films density. The estimated apparent sulfur diffusion coefficients in polyethylene increase with increasing temperature of the polythionic acid solution but decrease with growing crystallinity in the films. The concentration of sulfur in the film is limited by the stage of the acid decomposition, because the apparent activation energy of sulfur diffusion in polyethylene is nine to seventeen times lower than the energy needed for the polythionic acid decomposition. By treating polyethylene film sulfured in  $\text{H}_2\text{S}_{33}\text{O}_6$  solution with copper(I–II) salt solution, copper sulfide ( $\text{Cu}_x\text{S}$ ) layers are formed in the surface matrix of a polymer. The amount of copper in these layers is related to the density and thickness of the polyethylene film and the sulfuration conditions. The amount of copper increases with a decrease in the density of the polyethylene film and with an increase in the temperature of  $\text{H}_2\text{S}_{33}\text{O}_6$  solution used and the duration of the treatment. Initially, dielectric polyethylene films after formation of copper sulfide layers in their surface matrix become electrical conductors. Samples of low density polyethylene with the layers of  $\text{Cu}_x\text{S}$  were the most conductive.

## Synthesis of Naphtho[2,1-*b*]furanylum Cation and Its Reaction with Alcohols and Trialkyl Phosphites

by I. Yavari, M. Anary-Abbasinejad and Z. Hossaini

*Department of Chemistry, University of Tarbiat Modarres, PO Box 14115-175, Tehran, Iran*

*(Received November 17th, 2003)*

The reaction between dibenzoylacetylene and 2-naphthol in the presence of a catalytic amount of pyridine leads to 2-hydroxy-1-(2-oxo-2-phenylethylidene)-2-phenyl-1,2-dihydro-naphtho[2,1-*b*]furan in nearly quantitative yield. Treatment of this heterocyclic system with trimethyl chlorosilane in chloroform leads quantitatively to 1-(2-oxo-2-phenylethylidene)-2-phenyl-1*H*-naphtho[2,1-*b*]furanylum chloride. Addition of nucleophiles such as alcohols or trialkyl phosphites to this salt produces functionalized 1,2-dihydronaphthofuran derivatives in excellent yields.

## Syntheses and *In Vitro* Antitumor Activity of 3-Amino-*N*-(4-chlorobenzenesulfonyl)guanidine Derivatives Containing *N'*-Arylidene Moiety

by J. Sławiński<sup>1</sup>, P. Bednarski<sup>2</sup> and P. Reszka<sup>2</sup>

<sup>1</sup>Department of Chemical Technology of Drugs, Medical University of Gdańsk,  
Al. Gen. J. Hallera 107, 80-416 Gdańsk, Poland

<sup>2</sup>Department of Pharmaceutical and Medicinal Chemistry, Institute of Pharmacy,  
University of Greifswald, L.-John Str. 17, D-17487 Greifswald, Germany

(Received November 18th, 2003)

The syntheses of new 3-arylideneamino-1-(2-alkylthio-4-chloro-5-methylbenzenesulfonyl)guanidines **2–8** and 1-arylidene-2-(2-alkylthio-4-chloro-5-R<sup>3</sup>-benzenesulfonyl)-3-methylaminoguanidines **9–16** are described. The *in vitro* antitumor screening of compounds **2**, **3**, **9** and **10** was evaluated at the Institute of Pharmacy, University of Greifswald. The remaining compounds **5**, **11–14** and **16** were screened at the National Cancer Institute (NCI) for their activities against a panel of 55 human tumor cell lines, and relationships between structure and anticancer activity *in vitro* are discussed. The highest anticancer activity was found for 2-(2-benzylthio-4-chloro-5-methylbenzenesulfonyl)-3-methylamino-1-(5-nitrothienylidene)guanidine (**12**) (GI<sub>50</sub> in the range 0.3–0.6 μM), while other compounds exhibit reasonable (**16**) or moderate (**9**, **13**) anticancer activities.

## **Mild Conditions Synthesis of Mixed Organic Peroxides from Alkyl Halides and Organic Hydroperoxides**

by **S. Baj, T. Krawczyk, A. Siewniak and A. Rączkowska**

*Department of Organic Chemical Technology and Petrochemistry, Silesian University of Technology,  
ul. Krzywoustego 4, 44-100 Gliwice, Poland*

*Fax: 048 32 2371032; E-mail: baj@polsl.gliwice.pl*

*(Received October 6th, 2003; revised manuscript November 24th, 2003)*

The synthesis of mixed organic peroxides by reaction of alkyl halides with tertiary hydroperoxides under basic phase-transfer catalysis conditions was described.

## **Efficient Synthesis of 3,4-Dihydropyrimidin-2(1*H*)-ones by Aluminum Hydrogensulfate**

by **M.M. Khodaei<sup>1</sup>, P. Salehi<sup>2\*</sup>, M.A. Zolfigol<sup>3</sup> and S. Sirouszadeh<sup>3</sup>**

<sup>1</sup>*Department of Chemistry, Faculty of Science, Razi University, Kermanshah, Iran*

<sup>2</sup>*Department of Phytochemistry, Medicinal Plants Research Institute, Shahid Beheshti University, Evin, Tehran 19835-389, Iran, E-mail: p-salehi@cc.sbu.ac.ir, Fax: +98-21-2418679*

<sup>3</sup>*Department of Chemistry, Faculty of Science, Bu-Ali Sina University, Hamadan, Iran*

*(Received August 13th, 2003; revised manuscript November 24th, 2003)*

3,4-Dihydropyrimidin-2(1*H*)-ones are synthesized by the three-component condensation of aromatic aldehydes,  $\beta$ -ketoesters and urea or thiourea in methanol or under solvent-free conditions, using aluminum hydrogensulfate as the catalyst

**X-ray,  $^1\text{H}/^{13}\text{C}$  2D and 3D NMR Studies of the Structures of Davallene and Adipedatol, Two Triterpenes Isolated from American *Adiantum capillus-veneris***

by **C.K. Jankowski<sup>1</sup>**, **A. Aumelas<sup>1</sup>**, **P. Thuéry<sup>2</sup>**, **R. Reyes-Chilpa<sup>3</sup>**,  
**M. Jimenez-Estrada<sup>3</sup>**, **H. Barrios<sup>3</sup>** and **E. Diaz<sup>3</sup>**

<sup>1</sup>*Département de Chimie et Biochimie, Université de Moncton, Moncton, Nouveau-Brunswick, Canada, E1A 3E9*

<sup>2</sup>*CEA/Saclay, DSM/DRECAM/SCM (URA 331), Bât. 125, 91191 Gif-sur-Yvette, France*

<sup>3</sup>*Instituto de Química, Universidad Nacional Autónoma de México, Circuito Exterior, Ciudad Universitaria, Coyoacán 04510 México D.F., México*

*(Received November 25th, 2003)*

Two triterpenic compounds, Davallene **1** and Adipedatol **2** were isolated from the roots of Mexican *Adiantum capillus-veneris* L. (*Adiantaceae*). The structures of both compounds are discussed on the basis of new 2D and 3D NMR spectroscopic and single crystal X-ray diffraction data.

**Synthesis of Conjugates of Muramyl Dipeptide and  
nor-Muramyl Dipeptide with Retro-Tuftsins  
(Arg-Pro-Lys-ThrOMe) as Potential Immunostimulants**

**by K. Dzierzbicka**

*Department of Organic Chemistry, Gdansk University of Technology,  
11/12 G. Narutowicza Street, 80-952 Gdansk, Poland*

*(Received October 22nd, 2003; revised manuscript November 28th, 2003)*

The synthesis of retro-tuftsins analogue of sequence Arg-Pro-Lys-ThrOMe (Scheme 1) and its conjugates containing MDP (muramyl dipeptide) or nor-MDP (nor-muramyl dipeptide) (Scheme 2) are described.

## Synthesis of 4,5-Dicyanoimidazoles

by M. Bukowska\*, J. Prejzner and P. Szczeciński

*Warsaw University of Technology, Faculty of Chemistry, Noakowskiego 3, 00-664 Warszawa, Poland*

*(Received September 22nd, 2003; revised manuscript December 15th, 2003)*

The effective procedure of preparation of 2-trifluoromethyl-4,5-dicyanoimidazole (**3a**) from diaminomaleonitrile (**1**) and trifluoroacetic anhydride has been elaborated. The syntheses of five other 2-substituted imidazoles from appropriate acyl derivatives of **1** have been attempted. Out of them only 4,5-dicyanoimidazole (**3b**) could be obtained in good yield.

## **Proctolin Analogues Modified at Position 4 of the Peptide Chain. Synthesis and Myotropic Effects in Insects**

by **I. Woźnica**<sup>1</sup>, **G. Rosiński**<sup>2</sup> and **D. Konopińska**<sup>1</sup>

<sup>1</sup>*Faculty of Chemistry, University of Wrocław, PL 50-383 Wrocław, ul. F. Joliot-Curie 14, Poland  
e-mail: dk@wchuwr.chem.uni.wroc.pl*

<sup>2</sup>*Department of Animal Physiology, A. Mickiewicz University, 60-225 Poznań, Poland*

*(Received October 27th, 2003; revised manuscript December 1st, 2003)*

The object of these investigations was synthesis and biological evaluation of new analogues of proctolin (H-Arg-Tyr-Leu-Pro-Thr-OH) modified at position 4 of the peptide chain by natural or non-natural amino acid residues, such as: Phe (**1**), D-Phe (**2**), Phg (**3**), D-Phg (**4**), N-Me-Ala (**5**), N-Me-Val (**6**), N-Me-Leu (**7**), Tyr (**8**), Arg (**9**), Lys (**10**), Nva (**11**), Acp (**12**), Ser (**13**),  $\gamma$ -Abu (**14**), and  $\Delta^{3,4}$ -Pro (**15**). Synthesis was performed by classical solid-phase method. Myotropic activity of proctolin analogues was assayed *in vitro* on the semi-isolated heart of the yellow mealworm *Tenebrio molitor*. Analogues **1**, **9**, and **14** retained about 50% of proctolin activity. Other analogues showed about 20% activity or were inactive. The importance of the hydrophobic amino acid residues at position 4 for the myotropic activity of proctolin was inferred.

## **Determination of Enantiomeric Excess of Cyclophosphamide by X-Ray Powder Diffraction (XRPD)**

by **E.J. Tadeusiak<sup>1</sup>**, **R. Kruszyński<sup>2</sup>** and **K. Misiura<sup>3</sup>**

<sup>1</sup>*Department of Structural Studies, Centre of Molecular and Macromolecular Studies,  
Polish Academy of Sciences, Sienkiewicza 112, 90-363 Łódź, Poland  
E-mail: elatad@bilbo.cbmm.lodz.pl*

<sup>2</sup>*X-ray Crystallography and Crystal Chemistry Group, Institute of General and Ecological Chemistry,  
Technical University of Łódź, Żeromskiego 116, 90-924 Łódź, Poland*

<sup>3</sup>*Department of Bioorganic Chemistry, Centre of Molecular and Macromolecular Studies,  
Polish Academy of Sciences, Sienkiewicza 112, 90-363 Łódź, Poland*

*(Received October 10th, 2003; revised manuscript December 3rd, 2003)*

The anticancer agent: cyclophosphamide **1** was studied by X-ray powder diffraction. The linear correlations between intensity/spectra from X-ray powder diffraction/and enantiomeric excess was observed.

## **Kinetics and Mechanism of Perborate Oxidation of Aromatic Aldehydes**

by **H.A.A. Medien**

*Department of Chemistry, Faculty of Science, Ain Shams University, Cairo, Egypt*

*(Received May 26th, 2003; revised manuscript December 8th, 2003)*

The kinetics of oxidation of benzaldehyde by sodium perborate in an acetic acid medium have been studied. The reaction is first order with respect to both oxidant concentration and to the substrate. Hydrogen ion accelerates the rate of reaction. A mechanism involving the formation of an unstable perborate ester, which decomposes to the reaction products, has been suggested. The activation parameters associated with the rate-determining step have been calculated. The effects of various functional groups on the ring at the *meta*, and *para* positions of benzaldehyde have also been examined.

**Studies on the Controllable Luminescence Properties  
from Red to Green of Rare Earth Complexes**

by **ZH.H. Cai<sup>1</sup>**, **Y. Tang<sup>2</sup>** and **M.Y. Tan<sup>2</sup>**

<sup>1</sup>*School of Pharmacy, Southwest Jiaotong University, Emei 614202, P. R. China*

<sup>2</sup>*College of Chemistry and Chemical Engineering, Lanzhou University, Lanzhou 730000, P. R. China*

*(Received October 20th, 2003)*

**Syntheses and Characterization of Transition  
Metal Doped Molybdovanadophosphoric  
Heteropoly Compounds**

**by S.-B. Jing, Z.-J. Jin, W.-C. Zhu, Z.-L. Wang and G.-J. Wang**

*College of Chemistry, Jilin University, Changchun 130023, P.R. China*

*(Received June 10th, 2003; revised manuscript December 8th, 2003)*

**Kinetics of Nitrito-O Substitution in a Macrocyclic  
Chromium(III) Complex in Alkaline Media**

by **A. Katafias, E. Madej, O. Impert, B. Cywińska and P. Kita**

*Faculty of Chemistry, N. Copernicus University, 87-100 Toruń, Poland*

*(Received September 22nd, 2003; revised manuscript December 8th, 2003)*