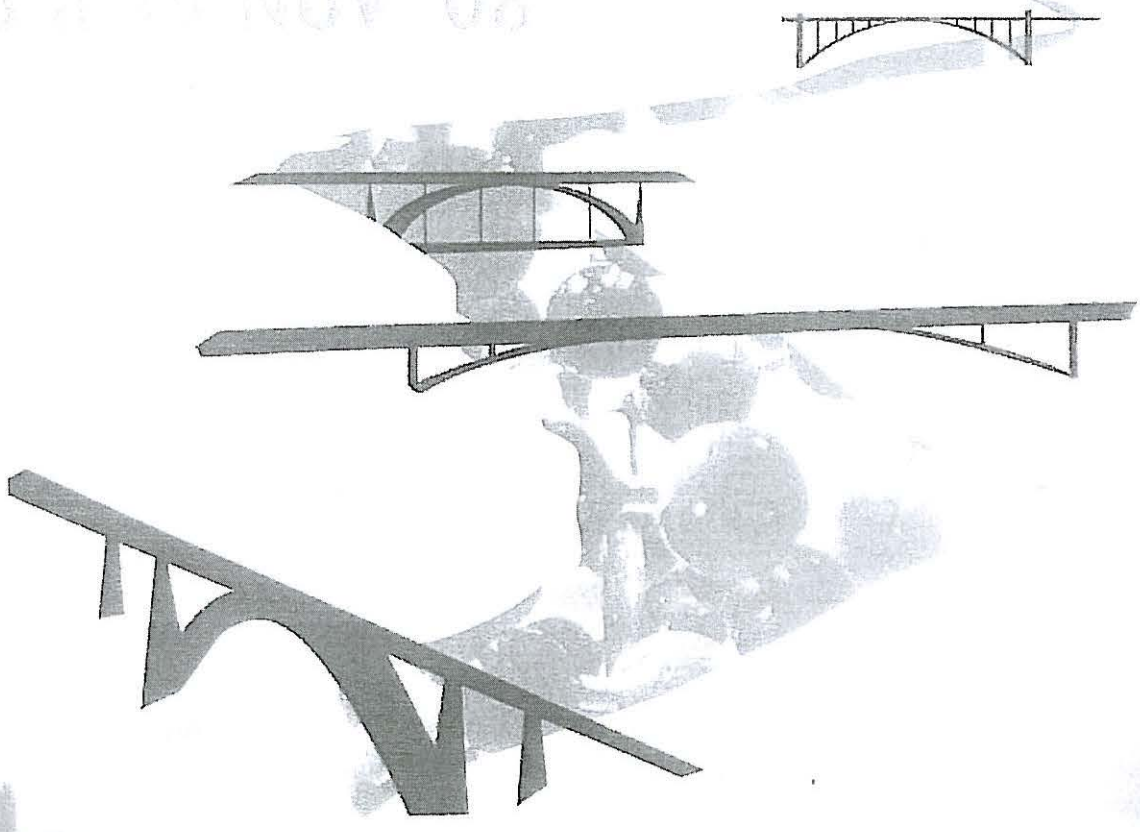
1º Encontro Nacional de Química Terapêutica

13 A 15 NOV '08



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LIVRO DE RESUMOS
BOOK OF ABSTRACTS

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P-117

NEW METHOXYLATED DI(HETERO)ARYLAMINES DERIVATIVES OF A THIENOPYRIDINE: SYNTHESIS AND EVALUATION OF ANTIOXIDANT ACTIVITY USING DIFFERENT METHODS

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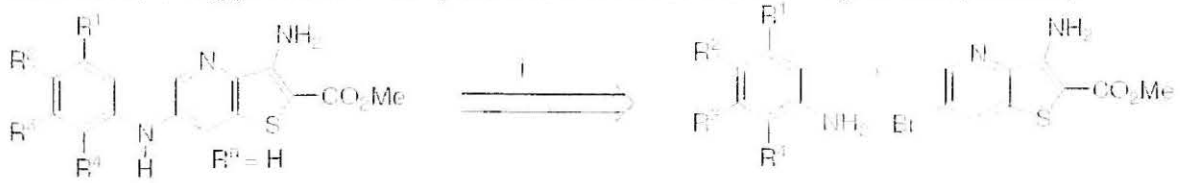
Abstract

Thienopyridines derivatives have attracted much attention because of their potential biological activity. Recently 7-(aryl)aminothieno[3,2-*b*]pyridines have been identified as potent inhibitors of VEGR-2 kinase (Vascular-Endothelial Growth Factor Receptor-2) which has been identified as a key component of the signalling patway responsible for the sprouting and maturation of new blood vessels from the tumor leading to tumor growth and metastasis [1].

Here we present the synthesis of new 6-(aryl)aminothieno[3,2-*b*]pyridines **1a-d** by palladiumcatalyzed Buchwald-Hartwig C-N coupling [2] of the methyl 6-bromo-3-minothieno[3,2-*b*]pyridine-2-carboxylate with anisidines or dimethoxyanilines (Scheme).



1a R^2 = OMe, 21h, 50%
1b R^2 = R^3 = OMe, 4h, 60%
1c R^2 = R^4 = OMe, 6h, 60%
1d R^1 = R^3 = OMe, 27h, 40%

i) $Pd(OAc)_2$ (16 mol%), *rac*-BINAP (18 mol%), Cs_2CO_3 (1.8 equiv.), toluene, 100 °C, under Ar

Scheme

For some years now we have been interested in the antioxidant activity of di(hetero)arylamines [3]. Antioxidant assays as free radical scavenging activity on DPPH radicals, reducing power and lipid peroxidation inhibition using the beta-carotene linoleate system and the thiobarbituric acid reactive substances (TBARS) assay, were performed on the new diarylamines **1a-d**, using alphatocopherol and ascorbic acid as standards. The results will be discussed in terms of EC_{50}. The best compound in all the methods studied is **1c** with two methoxy groups, one in the *meta* and the other in the *para* positions. For the TBARS assay the EC_{50} results for compounds **1a-c** are even better than for alpha-tocopherol (0.011 ± 0.001 mM). It was thus possible to establish some structure-antioxidant activity relationships depending on the number and position of the methoxy groups.

References

[1] M.J. Munchhof *et al. Bioorg. Med. Chem. Lett.*, 2004, *14*, 21-24.

[2] I.C.F. R. Ferreira, M.-J.R.P. Queiroz, G. Kirsch *Tetrahedron*, 2003, *59*, 975-981, and references cited.

[3] M.-J.R.P. Queiroz, I.C.F. R. Ferreira, R.C. Calhelha, L.M. Estevinho, *Bioorg. Med. Chem.*, 2007, *15*, 1788-1794.

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P-030

ALMOND (*PRUNUS DULCIS*) AS A GOOD SOURCE OF HEALTH BENEFICIAL FATTY ACIDS

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Abstract

With the demographic imperative of an aging population worldwide, there is an understandable emphasis in the food industry to manufacture products that can be labeled with claims for health promotion and the prevention of chronic disease. Furthermore, growers of natural foods rich in a specific ingredient now seek to associate that constituent with health benefits (*1*). Almond (*Prunus dulcis*) is an example of these foods. This study focused on fatty acids (FA) composition of some selected regional and commercial almond cultivars. FA were determined by gas-liquid chromatography with flame ionization detection. The analyzed samples contained, in average, 9.48±0.77% saturated fatty acids (SFA), 66.79±7.26% monounsaturated fatty acids (MUFA) and 23.63±6.69% polyunsaturated fatty acids (PUFA). The obtained results presented enlighten that almond kernel oil is mainly constituted by three FA: oleic (C18:1ω9 = 66.14±7.27%), linoleic (C18:2ω6 = 23.55±6.69%) and palmitic (C16:0 = 7.08±0.46%) accounting for more than 96% of the total FA content. Besides these three main FA, 14 more were identified and quantified. Some of these FA (*cis*-10-heptadecenoic acid and *cis*-11,14-eicosadienoic acid) hadn't yet been detected in previous works, and, as far as we know, this is the first study that elucidates the different proportions of the C18:1 (C18:1ω9*t*, C18:1ω9 and C18:1ω7), C18:2 (C18:2ω6*tt*, C18:2ω6, C18:2ω6*ct* and C18:2ω6*tc*) and C18:3 (C18:3ω6 and C18:3ω3) isomers, with *cis*-9-octadecenoic acid (C18:1ω9) and *cis*-9,12-octadecadienoic acid (C18:2ω6) as the major compounds. Although almonds present high fat content, 90% or more is unsaturated fat, mainly oleic and linoleic acid, presenting a profile that might be cardio-protective, promote the development of the brain and retina of infants or improve the inflammatory response. These premises had already been confirmed by epidemiological studies (*2, 3*). In addition, it is widely recognized that the type of fat in the diet influences plasma cholesterol levels to a greater extent than total fat intake (*4*).

References

(1) Chen, C.-Y.; Lapsley, K.; Blumberg, J. A nutrition and health perspective on almonds. *J. Sci. Food. Agric.* 2006, *86*, 2245-2250.

(2) Rajaram, S.; Burke, K.; Connell, B.; Myint, T.; Sabate, J. A monounsaturated fatty acidrich pecan-enriched diet favourably alters the serum lipid profile of healthy men and women. *J. Nutr.* **2001**, *131*, 2275-2279.

(3) Kelley, D. S. Modulation of human immune and inflammatory responses by dietary fatty acids. Nutrition, **2001**, *17*, 669-673.

(4) Albert, C. M.; Gaziano, J. M.; Willett, W. C.; Manson, J. E. Nut consumption and decreased risk of sudden cardiac death in the Physicians' Health Study. *Arch. Intern. Med.* **2002**, *162*, 1382-1387.

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P-070

A CONVENIENT HIGH PERFORMANCE COMPUTING (HPC) METHODOLOGY FOR VIRTUAL SCREENING USING AUTODOCK 4

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Abstract

Introduction: The main goal of protein-ligand docking is to predict how small molecules, such as substrates or potential drugs, bind to a protein of known 3D structure. Protein-ligand docking can be used to perform virtual screening of up to millions of compounds in a reasonable time, and is an increasingly important tool in drug discovery, as it can reduce significantly the number of possible compounds to be further investigated. However this technique requires a lot of computer processing power, and to meet this challenge, it is necessary to use high performance computing (HPC) platforms and techniques.

Methodology: In this work we describe a HPC method for assembling a computer "cluster" that can be used to screen large quantities of compounds using the protein-ligand docking software Autodock 4.0 [1] and a HPC platform based on ParallelKnoppix (linux) operating system [2].

We used a cluster of 8 Intel Dual-Core 2.8 GHz computers. One computer was used as "master" and was CD-booted using a ParallelKnoppix distribution previously compiled by us with Autodock 4.0. The 7 remaining computers were also CD-booted and used as "nodes". We developed a small script that automated the preparation and distribution of the studied compounds to the different computer "nodes". It's important to note that, because we used Dual-Core computers, the script was optimized to allow the simultaneous use of both processors essentially multiplying by two the processing power used. The script finally copied the results to a USB flash drive for convenient storage and latter analysis. As a test protein target we selected the Human Progesterone Receptor Protein [3], recognized as a potential target for the discovery of new anti-cancer drugs, and the compounds used were part of the Anti-cancer agent mechanism NCI database, composed of 122 compounds with known anticancer activity.

Results and conclusions: We were able to perform all 122 virtual docking experiments in approximately 9 hours in our "cluster". The same work takes 144 hours of computer processing on a single computer. The cluster remained stable during the experiment and showed that the addition to the "cluster" of more "nodes" should probably be simple. That main advantage of this methodology is that it can be used in any type of computers available, without the need for expensive dedicated "clusters". Also, as we used a CD-booted operating system, the original operating systems installed on the computers were not used, so cannot be corrupted.

References

[1] G.M. Morris, D.S. Goodsell, R.S. Halliday, R. Huey, W.E. Hart, R.K. Belew, A.J. Olson *J. Computational Chemistry*, 1998, *19*, 1639-1662.

[2] M. Creel "ParallelKnoppix", Grecs Computer Code 003.05, Research Group in Computation and Simulations (GRECS), 2005.

[3] S.P. Williams, P.B. Sigler *Nature*, 1998, *393*, 392-6.

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