1. Analysis of an old controversy: The compensation temperature for micellization of surfactants

By Vazquez-Tato, M. Pilar; Mejide, Francisco; Seijas, Julio A.; Fraga, Francisco; Vazquez Tato, Jose
From Advances in Colloid and Interface Science (2018), Ahead of Print. Language: English, Database: CAPLUS, DOI:10.1016/j.cis.2018.03.003

The actual significance of the so-called compensation temp. $T_c$ for micellization of surfactants is reviewed. It is demonstrated that it is possible to obtain as many $T_c$ values as the no. of temp. intervals in which the dependencies of enthalpy and entropy changes with temp. are analyzed. The value of each $T_c$ will be the central value $T_o$ of each temp. interval. These two facts suggest that $T_c$ is simply such exptl. $T_o$. Thus any phys. interpretation derived from $T_c$ is unfounded.

~0 Citings

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2. Ionic liquid-catalyzed green protocol for multi-component synthesis of dihydropyrano[2,3-c]pyrazoles as potential anticancer scaffolds

By Nimbalkar, Urja D.; Seijas, Julio A.; Vazquez-Tato, Maria Pilar; Damale, Manoj G.; Sangshetti, Jaiprakash N.; Nikalje, Anna Pratima G.
From Molecules (2017), 22(10), 1628/1-1628/17. Language: English, Database: CAPLUS, DOI:10.3390/molecules22101628

A series of 6-amino-4-substituted-3-methyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitriles I ($Ar =$ 4-hydroxyphenyl, thiophen-2-yl, 3,4-dimethoxyphenyl, etc.) was synthesized via one-pot, four-component condensation reactions of aryl aldehydes ArCHO, propanedinitrile, hydrazine hydrate and Et acetoacetate under solvent-free conditions. The use of the Bronsted acid ionic liqu. (BAIL) triethylammonium hydrogen sulfate [Et$_3$NH][HSO$_4$] as catalyst for this multi-component synthesis has been reported. Compared with the available reaction methodol., this new method has consistent advantages, including excellent yields, a short reaction time, mild reaction conditions and catalyst reusability. Selected synthesized derivs. were evaluated for in vitro anticancer activity against four human cancer cell lines viz. melanoma cancer cell line (SK-MEL-2), breast cancer cell line(MDA-MB-231), leukemia cancer cell line (K-562) and cervical cancer cell line (HeLa). Compds. I ($Ar =$ 4-chlorophenyl, 4-methoxyphenyl, 3,4-dimethoxyphenyl, 3-nitrophenyl, 4-benzyloxyphenyl) exhibited promising anticancer activity against all selected human cancer cell lines, except HeLa. Mol. docking studies also confirmed I ($Ar =$ 4-chlorophehnyl and 4-methoxyphenyl) as good lead mols. An in silico ADMET study of the synthesized anticancer agents indicated good oral drug-like behavior and non-toxic nature.

~0 Citings

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3. Facile synthesis of novel coumarin derivatives, antimicrobial analysis, enzyme assay, docking study, ADMET prediction and toxicity study

By Tiwari, Shailee V.; Seijas, Julio A.; Vazquez-Tato, Maria Pilar; Sarkate, Aniket P.; Karnik, Kshipra S.; Nikalje, Anna Pratima G.
From Molecules (2017), 22(7), 1172/1-1172/18. Language: English, Database: CAPLUS, DOI:10.3390/molecules22071172
The synthesis of fifteen novel 3-((dicyclohexylamino)(substituted phenyl/heteryl)methyl)-4-hydroxy-2H-chromen-2-one derivs. I (R = Ph, 4-MeOC₆H₄, 2-thienyl, etc.) as potential antimicrobial agents was reported under solvent-free condition using the ionic liq. [Et₃NH][HSO₄] as a catalyst. All the synthesized compds. were evaluated for their in vitro antifungal and antibacterial activity. The compd. I [R = 4-OH-3-MeOC₆H₃ (II)] was found to be the most active antifungal agent and compd. I (R = 2,4-F₂C₆H₃) was found to be the most active antibacterial agent. The mode of action of the most promising antifungal compd. II was established by an ergosterol extn. and quantitation assay and it was found that it acts by inhibition of ergosterol biosynthesis in C. albicans. Mol. docking studies revealed a highly spontaneous binding ability of the tested compds. to the active site of lanosterol 14α-demethylase, which suggests that the tested compds. inhibit the synthesis of this enzyme. The synthesized compds. were analyzed for in silico ADMET properties to establish oral drug like behavior and showed satisfactory results. To establish the antimicrobial selectivity and safety, the most active compds. were further tested for cytotoxicity against human cancer cell line HeLa and were found to be non-cytotoxic in nature. An in vivo acute oral toxicity study was also performed for the most active compds. and results indicated that the compds. are non-toxic.

4. Microwave-assisted facile synthesis, anticaner evaluation and docking study of N-((5-(substituted methylene amino)-1,3,4-thiadiazol-2-yl)methyl) benzamide derivatives

By Tiwari, Shailee V.; Siddiqui, Sumaiya; Seijas, Julio A.; Vazquez-Tato, M. Pilar; Sarkate, Aniket P.; Lokwani, Deepak K.; Nikalje, Anna Pratima G.


In the present work, 12 novel Schiff's bases contg. a thiadiazole scaffold and benzamide groups coupled through appropriate pharmacophore were synthesized. These moieties are assocd. with important biol. properties. A facile, solvent-free synthesis of a series of novel 7(a-l) N-((5-(substituted methylene amino)-1,3,4-thiadiazol-2-yl)methyl) benzamide was carried out under microwave irradn. Structures of the synthesized compds. were confirmed by IR, NMR, mass spectral study and elemental anal. All the synthesized hybrids were evaluated for their in vitro anticaner activity against a panel of four human cancer cell lines, viz. SK-MEL-2 (melanoma), HL-60 (leukemia), HeLa (cervical cancer), MCF-7 (breast cancer) and normal breast epithelial cell (MCF-10A) using 3-(4,5-dimethythiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay method. Most of the synthesized compds. exhibited promising anticaner activity, showed comparable GI50 values comparable to that of the std. drug Adriamycin. The compds. 7k, 7l, 7b, and 7a were found to be the most promising anticaner agents in this study. A mol. docking study was performed to predict the probable mechanism of action and computational study of the synthesized compds. 7(a-l) was performed to predict absorption, distribution, metab., excretion and toxicity (ADMET) properties, by using QikProp v3.5 (Schrodinger LLC). The results showed the good oral drug-like behavior of the synthesized compds. 7(a-l).

5. Ultrasound mediated one-pot, three component synthesis, docking and ADME prediction of novel 5-amino-2-(4-chlorophenyl)-7-substituted phenyl-8,8a-dihydro-7H-(1,3,4)thiadiazolo(3,2-α)pyrimidine-6-carbonitrile derivatives as anticaner agents

By Tiwari, Shailee V.; Seijas, Julio A.; Vazquez-Tato, M. Pilar; Sarkate, Aniket P.; Lokwani, Deepak K.; Nikalje, Anna Pratima G.

From Molecules (2016), 21(8), 894/1-894/13. Language: English, Database: CAPLUS, DOI:10.3390/molecules21080894
Herein, an environmentally friendly, rapid, and convenient one-pot ultrasound-promoted synthesis of 5-amino-2-(4-chlorophenyl)-7-substituted phenyl-8,8a-dihydro-7H-(1,3,4)thiadiazolo(3,2-α)pyrimidine-6-carbonitrile derivs. I (R = 4-CIC₆H₄, 4-MeOC₆H₄, Ph, etc.) is reported. The in-vitro anticancer activities of these compds. were evaluated against four human tumor cell lines. Among all the synthesized derivs., compd. which has substituent 3-hydroxy-4-methoxyphenyl I (R = 3-HO-4-MeOC₆H₄) is found to have the highest GI₅₀ value of 32.7 µM, 55.3 µM, 34.3 µM, 28.9 µM for MCF-7, K562, HeLa and PC-3 cancer cell lines resp. A docking study of the newly synthesized compds. were performed, and the results showed good binding mode in the active site of thymidylate synthase enzyme. ADME properties of synthesized compds. were also studied and showed good drug like properties.

6. Nonlinear absorption in ionic liquids with transition metallic atoms in the anion

By Novoa-Lopez, Jose A.; Lopez Lago, Elena; Seijas, Julio A.; Pilar Vazquez-Tato, M.; Troncoso, Jacobo; de la Fuente, Raul; Salgueiro, Jose R.; Michinel, Humberto
From Optical Materials (Amsterdam, Netherlands) (2016), 52, 144-149. Language: English, Database: CAPLUS, DOI:10.1016/j.optmat.2015.12.024

Nonlinear absorption has been investigated by open aperture Z-scan in ionic liqs. obtained by combination of 1-butyl-3-methyl-imidazolium cations with anions contg. a transition metal (Co, Zn, Cu or Ni) and thiocyanate groups. The laser source was a Ti:Sapphire oscillator (80-fs pulses, λ = 810 nm, repetition rate of 80.75 MHz). All liqs. present quite low heat capacities that favor the development of strong thermal effects. Thermal effects and nonlinear absorption make them potential materials for optical limiting purposes.

7. A rapid and sensitive determination of hypoxic radiosensitizer agent nimorazole in rat plasma by LC-MS/MS and its application to a pharmacokinetic study

By Das, Soumyajit; Dubey, Ramkumar; Roychowdhury, Subhradip; Ghosh, Manik; Sinha, Barij Nayan; Kumar Pradhan, Kishanta; Bal, Trishna; Muthukrishnan, Venkateswari; Seijas, Julio A.; Pujarid, Abhijit

A highly sensitive, accurate and robust LC-MS/MS method was developed and validated for detn. of nimorazole (NMZ) in rat plasma using metronidazole (MNZ) as internal std. (IS). The analyte and IS were extd. from plasma by pptg. protein with acetonitrile and were chromatographed using an Agilent Poroshell 120, EC-C₁₈ column. The mobile phase was composed of a mixt. of acetonitrile and 0.1 % formic acid (85:15 vol./vol.). The total run time was 1.5 min and injection vol. was 5 µL. Multiple reaction monitoring mode using the transitions of m/z 227.1 → m/z 114.0 for MNZ and m/z 172.10 → m/z 128.1 for IS were monitored on a triple quadrupole mass spectrometer, operating in pos. ion mode. The calibration curve was linear in the range of 0.25-200 ng/mL (r² > 0.9996) and the lower limit of quantification was 0.25 ng/mL in the rat plasma samples. Recoveries of NMZ ranged between 88.05 and 95.25%. The precision (intra-day and inter-day) and accuracy of the quality control samples were 1.25-8.20% and -2.50-3.10, resp. The analyte and IS were found to be stable during all sample storage and anal. procedures. The LC-MS/MS method described here was validated and successfully applied to pharmacokinetic study in rats. Copyright © 2015 John Wiley & Sons, Ltd.

8. Novel microwave-assisted synthesis of the immunomodulator organotellurium compound ammonium trichloro(dioxoethylene-O,O')tellurate (AS101)
Ammonium trichloro(1,2-ethanediolato-O,O')-tellurate (AS101) is the most important synthetic Te compd. from the standpoint of its biol. activity. It is a potent immunomodulator with a variety of potential therapeutic applications and antitumoral action in several preclin. and clin. studies. An exptl. design has been used to develop and optimize a novel microwave-assisted synthesis (MAOS) of the AS101. In comparison to the results obsd. in the literature, refluxing Te(IV) chloride and ethylene glycol in acetonitrile (Method A), or by refluxing Te(IV) chloride and ammonium chloride in ethylene glycol (Method B), it was found that the developed methods in the present work are an effective alternative, because although performance slightly decreases compared to conventional procedures (75% vs. 79% by Method A, and 45% vs. 51% by Method B), reaction times decreased from 4 h to 30 min and from 4 h to 10 min, by Methods A and B resp. MAOS is proving to be of value in the rapid synthesis of compds. with new and improved biol. activities, specially based on the benefit of its shorter reaction times.

~0 Citings

9. Microwave assisted synthesis, crystal structure and modeling of cytotoxic dehydroacetic acid enamine: a natural alkaloid from Fusarium incarnatum (HKI0504)

By Seijas, Julio A.; Crecente-Campo, Jose; Feas, Xesus; Vazquez-Tato, M. Pilar

A novel, fast and efficient method for the synthesis of (3E)-3-(1-aminoethylidene)-6-methyl-3,4-dihydro-2H-pyran-2,4-dione (I), a natural antiproliferative and cytotoxic product isolated from Fusarium incarnatum (HKI0504), was developed from dehydroacetic acid and urea under solvent-free microwave irradn. The anal. of the co-crystal structure revealed an asym. unit formed by a pair of mols. Each mol. is joined by two different hydrogen bonds to another two mols., ordered as four-unit clusters linked by π-stacking, assembled in a brick like layered structure in a set of parallel walls. Besides, the preferred tautomer for crystal structure is the enamine form. This is corroborated by computational NBO anal., outlining the contribution of enamine resonance and modeling the non-covalent interactions involved by means of Hirshfeld surfaces and G09 counterpoise calcns.

~1 Citing

10. Structure elucidation and HPLC-MS/MS determination of a potential biomarker for estradiol administration in cattle

By Regal, Patricia; Seijas, Julio A.; Cepeda, Alberto; Fente, Cristina

Administration of hormonal compds. as growth promoters in livestock farming was banned by Council Directive 96/22/EC. However, this kind of substances is sometimes reported within the framework of European monitoring residue plans. Various anal. methods have been previously developed to screen for their misuse, and they are now esp. efficient for monitoring the illegal administration of synthetic and semisynthetic hormones. Nevertheless, proving an exogenous administration of hormones from natural origin (i.e., estradiol-17β or progesterone) still remains a challenge for European authorities. These target compds. are indeed always present in the animal matrix, and the establishment of ref. thresholds appears very difficult because of the extreme variability existing among animals. In 2011, a metabolomics study was performed on serum samples obtained from cows treated with estradiol-17β (or its ester estradiol benzoate) and from control animals using a high-performance liq. chromatog. (HPLC)-LTQ-Orbitrap system. After appropriate data processing and multivariate statistical anal. (orthogonal partial least squares discriminant anal.), it was possible to highlight one potential biomarker candidate of estradiol treatments in bovine animals. Now, this biomarker has been structurally elucidated as a dipeptide, and its usefulness has been tested through a targeted HPLC-MS/MS method. Its presence in the previous samples has been confirmed and also in addnl. samples from estradiol-treated animals.
11. Triacylglyceride, antioxidant and antimicrobial features of virgin Camellia oleifera, C. reticulata and C. sasanqua oils

By Feas, Xesus; Estevinho, Leticia M.; Salinero, Carmen; Vela, Pilar; Sainz, Maria J.; Vazquez-Tato, Mara Pilar; Seijas, Julio A.
From Molecules (2013), 18, 4573-4587. Language: English, Database: CAPLUS, DOI:10.3390/molecules18044573

Virgin oils obtained from seeds of Camellia oleifera (CO), Camellia reticulata (CR) and Camellia sasanqua (CS) were studied for their triacylglyceride compn., antioxidant and antimicrobial activities. Levels of fatty acids detd. by 1H-NMR anal. were similar to those reported for olive oils (82.30%-84.47%; 5.69%-7.78%; 0.26%-0.41% and 8.04%-11.2%, for oleic, linoleic, linolenic and satd. acids, resp.). The CR oil showed the best antioxidant potential in the three in vitro models tested. With regard to EC_{50} values (µg/mL), the order in DPPH radical-scavenging was CR (33.48) < CO (35.20) < CS (54.87). Effectiveness in reducing power was CR (2.81) < CO (3.09) < CS (5.32). IC_{50} for LPO inhibition were 0.37, 0.52 and 0.75 µg/mL for CR, CO and CS, resp. All the oils showed antimicrobial activity and exhibited different selectivity and MICs for each microorganism tested (E. coli, B. cereus and C. albicans). B. cereus was the less sensitive species (MIC: 52.083 ± 18.042 for CO; 41.667 ± 18.042 for CR; 104.167 ± 36.084 for CS mg/mL) and the E. coli was the most sensitive to camellia oil's effect. The std. gentamicin presented higher MIC for E. coli (4.2) than the CR (MIC = 2.6) and CO (MIC = 3.9) oils.

12. Palynological, physicochemical, and microbiological attributes of organic lavender (Lavandula stoechas) honey from Portugal

By Estevinho, M. L.; Vazquez-Tato, M. P.; Seijas, J. A.; Feas, X.

At the present time, the quality, integrity, sanitation, and nutritional value of honeys receive attention on an international level due to the increasing content of chems. in the aforementioned matrix. The present study aims to characterize org. honey (n=73) from Northeast Portugal, with respect to floral nectar origin, physicochem. parameters, microbial safety, and com. quality. All org. honey samples can be classified as monofloral lavender (Lavandula stoechas L.), exceed in quality the international physicochem. stds., and show low microbiol. counts (yeast, molds, and aerobic mesophiles), with neg. results in respect to faecal coliforms, Salmonella, and sulphite-reducing clostridia. Correlating the palynol., physicochem., and microbiol. results is necessary in order to check the authenticity, quality, and sanitation of honey.

13. Comprehensive study of honey with Protected Denomination of Origin and contribution to the enhancement of legal specifications

By Iglesias, Antonio; Feas, Xesus; Rodrigues, Sandra; Seijas, Julio A.; Vazquez-Tato, M. Pilar; Dias, Luis G.; Estevinho, Leticia M.
From Molecules (2012), 17, 8561-8577. Language: English, Database: CAPLUS, DOI:10.3390/molecules17078561

In this study the characterization of a total of 60 honey samples with Protected Denomination of Origin (PDO) collected over three harvests (2009-2011, inclusive), from the Northeast of Portugal was carried out based on the presence of pollen, physicochem. and microbiol. characteristics. All samples were found to meet the European Legislation, but some didn't meet the requirements of the PDO specifications. Concerning the floral origin of honey, our results showed the prevalence of rosemary (Lavandula pedunculata) pollen. The microbiol. quality of all the analyzed samples was satisfactory, since fecal coliforms, sulfite-reducing clostridia and Salmonella were absent, and molds and yeasts were detected in low counts. Significant differences between the results were studied using one-way anal. of variance (ANOVA), followed by Tukey's HSD test. The samples were submitted to discriminant function anal., in order to det. which variables differentiate between two or more naturally occurring groups (Forward Stepwise Anal.). The variables selected were in this order: diastase activity, pH, reducing sugars, free acidity and HMF. The pollen spectrum has perfect discriminatory power. This is the first study in which a honey with PDO was tested, in order to assess its compliance with the PDO book of specifications.
14. Organic bee pollen: botanical origin, nutritional value, bioactive compounds, antioxidant activity and microbiological quality

By Feas, Xesus; Vazquez-Tato, M. Pilar; Estevinho, Leticia; Seijas, Julio A.; Iglesias, Antonio
From Molecules (2012), 17, 8359-8377. Language: English, Database: CAPLUS, DOI:10.3390/molecules17078359

Org. bee pollen (BP, n = 22) harvested from the Douro International Natural Park (DINP, Portugal) was studied. Nine botanical families were found in the mixt. of the samples. The water activity and pH ranged 0.21-0.37 and 4.3-5.2, resp. The BP analyses averaged 67.7% carbohydrates, 21.8% crude protein, 5.2% crude fat and 2.9% ash. The energy ranged from 396.4 to 411.1 kcal/100 g. The principal fatty acid found was linolenic, followed by linoleic acid, palmitic acid and oleic acid. The phenolic and flavonoid contents varied from 12.9 to 19.8 mg of gallic acid equiv./g of ext. and from 4.5 to 7.1 mg of catechin equiv./g of ext., resp. The scavenger activity and β-carotene bleaching assays values (EC50) were 3.0 ± 0.7 mg/mL and 4.6 mg/mL ± 0.9 mg/mL, resp. E. coli, sulphite-reducing Clostridia, Salmonella and S. aureus were not found. Since there are studies indicating appreciable differences among BPs from different regions, the full characterization of BP from diverse origins still appears to be a sound research priority in order to obtain reliable data about this beehive product.

~19 Citings

15. 1H-nuclear magnetic resonance analysis of the triacylglyceride composition of cold-pressed oil from Camellia japonica

By Salinero, Carmen; Feas, Xesus; Mansilla, J. Pedro; Seijas, Julio A.; Vazquez-Tato, M. Pilar; Vela, Pilar; Sainz, Maria J.
From Molecules (2012), 17, 6716-6727. Language: English, Database: CAPLUS, DOI:10.3390/molecules17066716

Camellia japonica (CJ) has oil-rich seeds, but the study of these oils has received little attention and has mainly focused only on their health properties. In the present work the relative compn. of the fatty acid (FA) components of the triglycerides in cold-pressed oil from CJ is studied by 1H-NMR. The results obtained were: 75.75%, 6.0%, 0.17% and 18.67%, for oleic, linoleic, linolenic and satd. FA resp. Levels of C18 unsatd. FA found in CJ oil were similar to those reported for olive oils. We also checked the possibility of using 13C-NMR spectroscopy; however, the results confirmed the drawback of 13C over 1H-NMR for the study of FA components of CJ triglycerides due to its low gyromagnetic ratio and its very low natural abundance.

~7 Citings

16. Organic honey from Tras-Os-Montes region (Portugal): Chemical, palynological, microbiological and bioactive compounds characterization

By Estevinho, Leticia M.; Feas, Xesus; Seijas, Julio A.; Pilar Vazquez-Tato, M.

At the present time, the quality, integrity, sanitation and nutritional value of honeys receive attention on an international level due to the increasing content of chems. in the aforementioned matrix. This work was conducted to evaluate the quality of 75 org. honey samples from the Tras-Os-Montes region (Portugal). Mean values obtained for physico-chem. parameters were: pH 3.7; 15.6% moisture; 0.26 mS/cm elec. cond.; 0.25% ash; 1.1 mg/kg HMF; 15.3 Gothe diastase activity; 40.3 meq/kg free acidity; 67.8% invert sugars and 2.7% apparent sucrose. All honey samples can be classified as monofloral Erica sp., as showed by pollen features. The amts. of phenols and flavonoids in the samples were also detd. In respect to sanitary quality (fecal coliforms) and safety (sulfite-reducing clostridia and Salmonella), all org. honey samples were neg. Furthermore, yeast and molds were detected in low counts, with mean values obtained of 5.5 cfu/g and the value of total aerobic mesophiles obtained from honeys was established in 1.3 x 102 cfu/g ± 7.4 x 101 cfu/g. The levels of flavonoids had a stronger impact on both mesophiles (p = 0.0004) and molds (p = 0.0138) than the sucrose concn. (p = 0.001 and 0.0278; resp.). The results reported in this study should be introduced in the org. honey label, and may help beekeepers, the industry, researchers and consumers better understand honey properties.

~15 Citings

17. Efficient synthesis of heterophosphole-2-sulfides by solvent-free microwave reaction

By Seijas, Julio A.; Vazquez-Tato, M. Pilar; Crecente-Campo, Jose
Microwave irradn. of a stoichiometric amt. of Lawesson’s reagent in the presence of o-aminophenols, o-aminothiophenols, o-phenylenediamines, or catechols leads to benzoazaphosphole-, benzothiazaphosphole-, benzodiazaphosphole-, and benzodioxaphosphole-2-sulfides, resp., in good yields in a fast and direct way under solventless conditions. The procedure requires short reaction times and is similar for all reagents; thus it may be used in parallel synthesis.

~7 Citings

18. Microwave-Promoted, One-Pot, Solvent-Free Synthesis of 4-Arylcoumarins from 2-Hydroxybenzophenones


4-Arylcoumarins are synthesized in very good yields through solvent-free microwave irradn. of 2-hydroxybenzophenones and alkyl malonate in the presence of DBU. The one-pot synthesis is carried out with Knoevenagel condensation, intramol. lactonization, and decarboxylation reactions. The method can be applied to a broad scope of neoflavonoids, e.g., I (R = H, MeO, EtO, OH).

~9 Citings

19. Direct syntheses of 4-aryl-1,2,3,4-tetrahydroisoquinolines and 1-aryl-2,3,4,5-tetrahydro-3-benzazepines via hydroamination of enol carbamates

By Crecente-Campo, Jose; Vazquez-Tato, M. Pilar; Seijas, Julio A.; From Tetrahedron (2009), 65(13), 2655-2659. Language: English, Database: CAPLUS, DOI:10.1016/j.tet.2009.01.098

An efficient and simple procedure for the syntheses of 4-aryl-1,2,3,4-tetrahydroisoquinolines and 1-aryl-2,3,4,5-tetrahydro-3-benzazepines has been developed. The approach uses easily available starting materials and requires just three steps. The hydroamination of an enol carbamate is the key step. This general and direct method has been applied to the total synthesis of the natural alkaloid cherylline and to biol. active 3-benzazepines as well.

~16 Citings

20. Use of acrylic acid in the synthesis of molecularly imprinted polymers for the analysis of cyproheptadine

The synthesis and comparative characterization of molecularly imprinted polymers (MIPs) with cyproheptadine (CYP), using two different monomers, acrylic acid (AA) and methacrylic acid (MAA), are described. Polyacids (PA) [poly(methacrylic acid) (PMAA) and poly(acrylic acid) (PAA)] were obtained by the radical polymerization of MAA and AA, respectively, in dichloromethane as the porogen solvent-imprinted medium. The non-covalent imprinting process was performed via thermal decomposition of an azo-initiator at 60°C, using ethylene glycol dimethacrylate as the cross-linker and 2,2'-azobis(2-methylpropionitrile) as the initiator. The selectivities of MIPs and NIPs particles were evaluated in binding experiments of the four synthesized polymeric materials (MIP_{aa}, MIP_{maa}, NIP_{maa}, and NIP_{aa}) with CYP. The effects of monomers on: (a) the surface morphology, (b) the binding capacity and (c) the swelling properties of imprinted and non-imprinted polymers were studied and are presented here. Polymer material morphology was assessed with SEM. This revealed differences in monomer function, depending on which one was employed, as well as differences in function when polymerization occurred in the presence of template or without it. Non-specific retention of the template to NIPs was higher for NIPs-PAA polymers than for NIPs-PMAA materials. In terms of specific binding (ΔQ = Q_{MIP} - Q_{NIP}), MIP_{maa} showed the greatest value (53.47%) in comparison with MIP_{aa} (50.07%).

~15 Citings

21. NMR analysis of a series of substituted pyrazolo[3,4-d]pyrimidines-4-amines
By Rodrigues, Ligia M.; Sivasubramanian, Aravind; Pinto, Elisa M.; Oliveira-Campos, Ana M. F.; Seijas, Julio A.; Vazquez-Tato, M. Pilar
From Magnetic Resonance in Chemistry (2009), 47(1), 84-86. Language: English, Database: CAPLUS, DOI:10.1002/mrc.2329

A series of 21 substituted pyrazolo[3,4-d]pyrimidines-4-amines were studied by 1H and 13C NMR. The application of two-dimensional techniques, HMQC and HMBC, allowed the complete assignment of the spectra for all the compounds.

~1 Citing

22. Syntheses of molecularly imprinted polymers: Molecular recognition of cyproheptadine using original print molecules and azatadine as dummy templates
By Feas, X.; Seijas, J. A.; Vazquez-Tato, M. P.; Regal, P.; Cepeda, A.; Fente, C.

The use of custom-made polymeric materials with high selectivities as target molecules in solid-phase extraction (SPE), known as molecularly imprinted solid-phase extraction (MISPE), is becoming an increasingly important sample preparation technique. However, the potential risk of leakage of the imprinting molecules during the desorption phase has limited application. The use of a mimicking template, called a dummy molecule imprinting polymer (DMIP), that bears the structure of a related molecule and acts as a putative imprinting molecule may provide a useful solution to this problem. In the current study, cyproheptadine (CPH) and azatadine (AZA) were used as templates in the development of an MISPE and DMIP for acrylic acid and methacrylic acid monomers. Our results indicate that DMIPs have equal recognition of CPH, avoiding the problem of leakage of original template during the desorption phase relative to MIPs synthesized in the presence of the print molecule. CPH. Examined the surface structure of the two polymer products by SEM shows appreciable differences in structural morphology and function of the monomers employed. These results are well supplemented by data obtained for swelling ratios and solvent uptake. Molecular modeling of CPH and AZA suggests that both substrates are similar in shape and volume.

~61 Citings

23. Straightforward microwave-assisted synthesis of 2-thiazolines using Lawesson's reagent under solvent-free conditions
By Seijas, Julio A.; Vazquez-Tato, M. Pilar; Crecente-Campo, Jose

2-Thiazolines are synthesized from carboxylic acids and 1,2-amino alcohols in the presence of Lawesson's reagent under solventless conditions. The method is valid for either substituted or unsubstituted amino alcohols, and a wide variety of aromatic, heteroaromatic and aliphatic carboxylic acids; thus it constitutes a general synthetic method for these kinds of compounds. The role of Lawesson's reagent is dual: to transform the 1,2-amino alcohol into 1,2-amino thiol and to activate its reaction with the carboxylic acid leading to the formation of a thiazoline ring, all in one pot.

~26 Citings
24. Substituted pyrazolo[3,4-d]pyrimidines: microwave-assisted, solvent-free synthesis and biological evaluation

By Oliveira-Campos, Ana M. F.; Sivasubramanian, Aravind; Rodrigues, Ligia M.; Seijas, Julio A.; Vazquez-Tato, M. Pilar; Peixoto, Francisco; Abreu, Carlos G.; Cidade, Honorina; Oliveira, Ana Elizabete; Pinto, Madalena

A simple and efficient method has been developed for the synthesis of various pyrazolo[3,4-d]pyrimidines I (R₁ = H, Cl, Br; R₂ = Ph, Bn, 3-CNC₆H₄, 3-pyridyl, 4-pyridyl, 2-thiophenyl, 2-furanyl) by using microwave irradiation under solvent-free conditions. The advantages of applying microwave irradiation compared with the classical method were demonstrated. The structures of all the compounds were confirmed by the usual techniques and, in two cases, by X-ray analysis. The compounds did not display appreciable ability to inhibit xanthine oxidase activity. Screening for antifungal activity showed that some derivs. were active against four fungi, with more significant results for Botrytis.

~12 Citings

25. Microwave-assisted solvent-free synthesis of enol carbamates

By Seijas, Julio A.; Vazquez-Tato, M. Pilar; Crecente-Campo, Jose

An efficient and simple method for the synthesis of enol carbamates by irradiation with microwaves under solvent-free conditions has been developed. The method has been applied to substituted acetophenones, cyclic aryl ketones and α-aryl ketones. Its main advantages are short reaction times, good conversions except for nitro acetophenones, and the environmentally friendly nature of the process. For α-aryl ketones the reaction shows regio-selectivity to afford conjugated products.

~8 Citings

26. Microwaves: a new tool for an ancient element

By Seijas, Julio; Vazquez-Tato, M. Pilar

A review. Microwave assisted solvent-free орг. synthesis in nitrogen acylation, heterocycles synthesis and pericyclic reactions is reviewed, covering only those reactions performed by irradiation of reagents without solvents or any solid support.

~9 Citings
27. Lawesson's reagent and microwaves: a new efficient access to benzoxazoles and benzothiazoles from carboxylic acids under solvent-free conditions

By Seijas, Julio A.; Vazquez-Tato, M. Pilar; Carballido-Reboredo, M. Raquel; Crecente-Campo, Jose; Romar-Lopez, Lucia

Lawesson's reagent acts as an efficient promoter in the solvent-free microwave-assisted synthesis of 2-substituted benzoxazoles from carboxylic acids and 2-aminophenol, and thus, constitutes a general synthetic method for these compds. This new application of Lawesson's reagent is valid also for benzothiazoles with very high efficiency level. A variety of arom., heteroarom., and aliph. carboxylic acids react under the conditions developed with good yields in all cases. Thiobenzoic acid is a good alternative for microwave-assisted synthesis of 2-phenylbenzoxazole and 2-phenylbenzothiazole in the absence of solvents.

~83 Citings

28. Oxazoline as a useful tool in organic synthesis: preparation of 4-aryl-1,2,3,4-tetrahydroisoquinoline alkaloid skeleton

By Seijas, Julio A.; Vazquez-Tato, M. Pilar; Martinez, M. Montserrat; Pizzolatti, Moacir G.

New direct strategy for the synthesis of 4-aryl-1,2,3,4-tetrahydroisoquinolines. The key steps are based on oxazoline chem.: nucleophilic substitution in an (2-methoxyphenyl)oxazoline with a Grignard reagent and a 1,6-conjugate addn. of a lithium amide to [2-(1-phenylethenyl)phenyl]oxazoline.

~14 Citings

29. Solvent-free synthesis of functionalized flavones under microwave irradiation

By Seijas, Julio A.; Vazquez-Tato, M. Pilar; Carballido-Reboredo, Raquel

Eco-friendly direct solvent-free synthesis of flavones, e.g., I, was achieved by microwave irradn. of phloroglucinol and β-keto esters. Heating with microwaves vs. under classical conditions was shown to be higher yielding, cleaner, and faster. The reaction went through a cycloaddn. of an α-oxo ketene intermediate followed by an uncatalyzed thermal Fries rearrangement.

~74 Citings
30. Effect of counterion on thermodynamic micellar properties of tetradecylpyridinium in aqueous solutions

By Galan, J. J.; Gonzalez-Perez, A.; Seijas, J. A.; Uriarte, E.; Rodriguez, J. R.

Electrical cond. of aq. solns. of tetradecylpyridinium bromide and chloride has been measured as a function of surfactant molal concn. and temp. From the molal dependence of cond., the crit. micelle concn. and the micellar ionization degree were estd. The temp. dependence of these parameters has been used for calcg. the thermodn. parameters related with the micellization process by using the classical charged pseudophase sep. model. The effect of the counterion on the conventional thermodn. potentials of micellization such as std. Gibbs free energy, enthalpy and entropy has also been a matter of study. Finally, the occurrence of the enthalpy-entropy compensation phenomenon was verified and the relevant parameters discussed.

~15 Citings

31. Synthesis of anacardic acids by nucleophilic substitution on 2-aryloxazolines

By Seijas, Julio A.; Pilar Vazquez-Tato, M.; Montserrat Martinez, M.; Santiso, Veronica

A new direct synthesis for anacardic acids based on a nucleophilic substitution of a methoxy group in 2-aryloxazolines by long-chained Grignard reagents is reported. Thus, reacting (methoxyphenyl)oxazoline I (R1 = H, R2 = R3 = MeO; R1 = R3 = MeO, R2 = H) with C11H23MgCl gave I (R3 = C11H23).

~7 Citings

32. Thermodynamic interactions of model allelopathic compounds (polyphenols) with α- and β-cyclodextrin

By Mejide, Francisco; Perez, Jose; Cabrera, Pedro Ramos; Seijas, Julio; Ulloa, Haydee; Fraga, Francisco; Tato, Jose Vazquez

The present thermodn. study is an initial attempt to check the possible efficiency of cyclodextrins in trapping allelopathic substances and therefore to reduce their phytotoxic effect. As a first choice, phenols have been chosen as models for complexation study. The equil. consts. for the complexation of the polyphenols with α- and β-cyclodextrins have been detd. In many occasions the stoichiometry of the complex formed can also be obtained.

~0 Citings

33. Microwave enhanced synthesis of acridines. A new aspect in the Bernthsen reaction

By Seijas, Julio A.; Vazquez-Tato, M. Pilar; Martinez, M. Montserrat; Rodriguez-Parga, Jacobo
The Bernthsen reaction is studied using microwaves as the heat source. This leads to acridines with arom. and aliph. substituents in position 9, shortening reaction times and increasing yields, with a redn. in Lewis acid catalyst (ZnCl₂), allowing a more environmentally friendly reaction.

~29 Citings

34. Microwave promoted synthesis of a rehabilitated drug: Thalidomide
By Seijas, Julio A.; Vazquez-Tato, M. Pilar; Gonzalez-Bande, Cristobal; Martinez, M. Montserrat; Pacios-Lopez, Beatriz
A new direct synthesis of thalidomide in high yield by microwave irradn. of N-phthaloyl-L-glutamic in the presence of thiourea is described. Thalidomide was also obtained in good yield from L-glutamic acid, phthalic anhydride and thiourea in a one-pot procedure.
~25 Citings

35. β-Phenylethylamines, indolines and isoquinolones via hydroamination of styrenes by microwave irradiation
By Seijas, Julio A.; Vazquez-Tato, M. Pilar; Martinez, M. Montserrat
Microwave irradn. promotes hydroamination of styrenes. This method can be used as a direct way of producing different kinds of bioactive compds.: open chain compds. like β-phenylethylamines or cyclized products like indolines or isoquinolones.
~16 Citings

36. Microwave-enhanced synthesis of 4-aminoquinazolines
By Seijas, Julio A.; Vazquez-Tato, M. Pilar; Martinez, M. Montserrat
Arom. nitriles react with anthranilonitrile in a domestic microwave oven to afford good yields of the corresponding 4-aminoquinazolines, e.g. I, in a very short irradn. time.

~89 Citings

37. Direct synthesis of imides from dicarboxylic acids using microwaves
By Seijas, Julio A.; Vazquez-Tato, M. Pilar; Martinez, M. Montserrat; Nunez-Corredoira, Gonzalo
1,4- and 1,5-dicarboxylic acids, when treated with amines in a domestic microwave oven, afford good yields of the corresponding imides. For example, the reaction of butanedioic acid with aniline gave 1-phenyl-2,5-pyrrolidinedione. The reaction of 2-carboxybenzeneacetic acid with aniline gave 2-phenyl-1,3(2H,4H)-isoquinolinedione.

~43 Citings

38. Complexation of Sodium Cholate and Sodium Deoxycholate by β-Cyclodextrin and Derivatives

By Ramos Cabrer, P.; Alvarez-Parrilla, E.; Meijide, F.; Seijas, J. A.; Rodriguez Nunez, E.; Vazquez Tato, J.

The complexation behavior of two bile salts-sodium cholate (NaC) and sodium deoxycholate (NaDC)-with β-cyclodextrin (β-CD), 6-deoxy-6-amino-β-cyclodextrin (β-CDNH₂), and dimer I (N,N'-bis(6-deoxy-β-cyclodextrin)pyromellic acid diamide) was studied by NMR techniques. Complexes formed between β-CD and β-CDNH₂ with NaC and NaDC have 1:1 and 2:1 (host:guest) stoichiometries, resp. Complexes with β-CDNH₂ show higher equil. consts. than those with β-CD because of the electrostatic effect of the protonated amine group. Dimer I showed 1:2 and n:n stoichiometries with NaC and NaDC, resp. ROESY spectra indicated that bile salts enter first with their 5-C ring toward the inner cavity by the side of the secondary hydroxyl groups of cyclodextrins. In the complexes formed with β-CDNH₂, the steroid body of the bile salt enters deeper into the cavity, while the carboxylated side chain is extended toward the protonated amine group at C-6, allowing an electrostatic interaction between both groups. In complexes with 2:1 stoichiometry, the second cyclodextrin complexes with ring A of the steroid body.

~27 Citings

39. Synthesis of β-phenylethylamines from styrene derivatives

By Seijas, Julio A.; Vazquez-Tato, M. Pilar; Entenza, Cesar; Martinez, M. Montserrat; Onega, M. Gabriela; Veiga, Susana

β-Phenylethylamines are prepd. from the styrene derivs., such as 4,4-dimethyl-2-(2-vinylphenyl)-2-oxazoline, 2-(3-methoxy-2-vinylphenyl)-4,4-dimethyl-2-oxazoline, 2-vinylbenzoic acid, styrene, β-methylstyrene, and α-methylstyrene. For example, the addn. of diethylamine to 2-(2-vinylphenyl)-4,5-dihydro-4,4-dimethyl-2-oxazolyl)benzeneethanamine.

~36 Citings

40. Synthesis of β-phenylethylamines from styrene derivatives

By Seijas, Julio A.; Vazquez-Tato, M. Pilar; Entenza, Cesar; Martinez, M. Montserrat; Onega, M. Gabriela; Veiga, Susana

β-Phenylethylamines are prepd. from the styrene derivs., such as 4,4-dimethyl-2-(2-vinylphenyl)-2-oxazoline, 2-(3-methoxy-2-vinylphenyl)-4,4-dimethyl-2-oxazoline, 2-vinylbenzoic acid, styrene, β-methylstyrene, and α-methylstyrene. For example, the addn. of diethylamine to 2-(2-vinylphenyl)-4,5-dihydro-4,4-dimethyl-2-oxazolyl)benzeneethanamine.

~36 Citings

41. 1,6-Conjugate addition to o-vinylphenyloxazolines. Syntheses of chuangxinol and 3-n-butylphthalide

By Martinez, M. Montserrat; Onega, M. Gabriela; Fe Tellado, M.; Seijas, Julio A.; Vazquez-Tato, M. Pilar

Phtalhides are prepd. from o-vinylphenyloxazolines in one pot reaction by 1,6-conjugate addn. of alkylithium and trapping of the benzylc anion with MoOPH, followed by hydrolysis with aq. oxalic acid. This method was applied to the syntheses of two natural products: chuangxinol and 3-n-butylphthalide.

~9 Citings
42. Synthesis, affinity at 5-HT2A, 5-HT2B and 5-HT2C serotonin receptors and structure-activity relationships of a series of cyproheptadine analogs

By Honrubia, Maria Angeles; Rodriguez, Jesus; Dominguez, Rosa; Lozoya, Estrella; Manaut, Francesc; Seijas, Julio A.; Villaverde, Maria Carmen; Calleja, Jose M.; Cadavid, Maria Isabel; et al.

Cyproheptadine (Cyp) is a drug that shows high affinity for type 2 (5-HT2) receptors. The authors studied a series of compounds obtained by modification of the tricyclic system of Cyp (dibenzocycloheptadiene ring) to make the thioxanthene, xanthene, dihydrodibenzocycloheptadiene, di-Ph, fluorene, and phenylmethyl analogs. Their activities at the rat cerebral cortex 5-HT2A receptor were (pK[i]): 8.80 (Cyp), 8.60 (thioxanthene analog), 8.40 (xanthene analog), 8.05 (dihydrodibenzocycloheptadiene analog), 7.87 (di-Ph analog), and undetectable (fluorene analog, phenylmethyl analog); and those at the rat stomach fundus 5-HT2B receptor (pA2) were: 9.14 (Cyp), 8.49 (thioxanthene analog), 7.58 (xanthene analog), 7.02 (dihydrodibenzocycloheptadiene analog), 6.07 (di-Ph analog), and undetectable (fluorene analog, phenylmethyl analog); and those at the pig choroidal plexus 5-HT2C receptor (pKi) were: 8.71 (Cyp), 8.68 (thioxanthene analog), 8.58 (xanthene analog), 7.95 (dihydrodibenzocycloheptadiene analog), 7.57 (di-Ph analog), 6.98 (fluorene analog) and 6.63 (phenylmethyl analog). The slopes did not differ significantly from unity. The compounds exhibited the same order of activities at every type of receptor, and the most active molecules presented certain steric (butterfly conformation of the tricyclic system) and electrostatic (proton affinity on the top of the central rings) patterns. It is concluded that the activity of cyproheptadine derivs. at 5-HT2 receptors is related to these mol. features, which make feasible a common disposition to interact with all three 5-HT2 subtypes.

~9 Citings

43. Antiemetic activity of ondansetron in acute gastroenteritis

By Cubeddu, L. X.; Trujillo, L. M.; Talmaciu, I.; Gonzalez, V.; Guariaguata, J.; Seijas, J.; Miller, I. A.; Paska, W.

The mechanism of nausea and vomiting associated with gastroenteritis is unknown. The role of 5-HT3 receptors in emesis associated with gastroenteritis was investigated in pediatric patients. A randomized, double-blind, placebo-controlled, parallel-group study was conducted in three groups of 12 patients each, receiving either a single i.v. dose of ondansetron (0.3 mg/kg), metoclopramide (0.3 mg/kg) or placebo (sterile saline). Food was restricted and oral rehydration was administered for 4 h. During 0-24 h, the no. of emetic episodes experienced was significantly greater (P = 0.048) with placebo (mean = 5) than ondansetron (mean = 2) and the proportion of patients experiencing no emesis was significantly greater (P = 0.039) with ondansetron (58%) than placebo (17%). A numerical difference, in favor of ondansetron, was observed between ondansetron and metoclopramide groups for both of the above parameters. Fewer treatment failures were observed with ondansetron (17%) than placebo (33%) and metoclopramide (42%). More diarrheal episodes were observed in the groups receiving anti-emetic treatment. All three treatments were well tolerated. Ondansetron, a 5HT3 receptor antagonist, was significantly superior to placebo in preventing emesis associated with acute gastroenteritis, in pediatric patients. Therefore, serotonin, acting through 5HT3 receptors, may play a role in this form of emesis.

~14 Citings

44. Synthesis of (3S,5S)-quinuclidine-3,5-diol and of [3S-(3α,3aα,7aα)]-octahydro-2-furo[2,3-c]pyridinol from D-arabinose

By Vazquez-Tato, M. Pilar; Seijas, Julio A.; Fleet, George W. J.; Mathews, Christopher J.; Hemmings, Philippa R.; Brown, David

The synthesis of (3S,5S)-quinuclidine-3,5-diol is achieved by an introduction of a 2 carbon chain at C-3 of D-arabinose, followed by joining the terminus of the chain extension to C-1 and C-5 of the sugar; the synthesis of [3S-(3α,3aα,7aα)]-octahydro-2-furo[2,3-c]pyridinol, a potential muscarine mimic, is described.

~21 Citings
45. Synthesis of pyrrolizidines via copper(I) catalyzed radical atom transfer cyclization. [Erratum to document cited in CA116(25):255857r]

By Seijas, Julio A.; Vazquez-Tato, M. Pilar; Castedo, Luis; Estevez, Ramon J.; Onega, M. Gabriela; Ruiz, Maria
From Tetrahedron (1992), 48(35), 7057. Language: English, Database: CAPLUS, DOI:10.1016/S0040-4020(01)88722-6

Errors in the \(^1\)H NMR spectrum of (1R,8S)-1-chloromethyl-2-dichloro-3-oxo-hexahydropyrrolizidine have been cor. The errors were not reflected in the abstr. or the index entries.

~0 Citings

46. Reactivity of o-styryloxazolines with nucleophiles

By Seijas, Julio A.; Vazquez-Tato, M. Pilar; Castedo, Luis; Estevez, Ramon J.; Ruiz, Maria

The o-styryloxazolines I (R = MeO, H) react with organolithium reagents affording, as a result of conjugate addn. to the exocyclic double bond, substituted benzenes II (R = MeO, R\(^1\) = Bu, Me\(_3\)C, Me, H, Ph, R\(^2\) = Me, H; R = H, R\(^1\) = Bu, Me\(_3\)C, Me, R\(^2\) = Me) in good yields. The presence of a methoxy substituent in position 3 of the benzene ring enhances reactivity. I (R = MeO) reacts with aryl- and alkyllithium reagents, while I (R = H) (no MeO in the ring) reacts only with alkyllithium reagents.

~14 Citings

47. Synthesis of pyrrolizidines via copper(I) catalyzed radical atom transfer cyclization

By Seijas, Julio A.; Vazquez-Tato, M. Pilar; Castedo, Luis; Estevez, Ramon J.; Onega, M. Gabriela; Ruiz, Maria
From Tetrahedron (1992), 48(9), 1637-42. Language: English, Database: CAPLUS, DOI:10.1016/S0040-4020(01)88722-6

Trachelanthamidine (I, R = CH\(_2\)OH) and pseudoheliotridane (I, R = Me) were synthesized from (2S)-N-trichloroacetyl-2-vinylpyrrolidine (II) by a 5-exo-trig radical cyclization. The intermediate radical is generated heating II in a sealed tube (CH\(_3\)CN/160°C) using CuCl as catalyst and the cyclization occurs in very good yield (93%). Cyclized product III is transformed either into (-)-trachelanthamidine (55% yield from II) or into (-)-pseudoheliotridane (42% yield from II).
48. A new synthesis of azaphenanthrenes

By Castedo, Luis; Cid, M. Magdalena; Seijas, Julio A.; Villaverde, M. Carmen

A new synthesis of azaphenanthrenes I and II starting from aryloxazoline III (R = OMe) is reported. Lithiation of 3-bromopyridine, followed by coupling with III (R = OMe) gave III (R = 3-pyridinyl) (IV). Hydrolysis of IV, followed by esterification, LiAlH₄ redn, and Swern oxidn., and Wittig reaction gave styrenes V (R = H, Br). V were then irradiated to give I and II.

49. Total synthesis of oxoaporphines

By Castedo, L.; Estevez, J. C.; Estevez, R. J.; Seijas, J. A.; Vazquez Tato, M. P.; Villaverde, M. C.
From Anales de Quimica (1990), 86(7), 805-7. Language: Spanish, Database: CAPLUS

The total synthesis of oxoaporphine deriv. I from benzyltetrahydroisoquinolone II (R = H) was investigated by two routes. Pschorr cyclization of II (R = NH₂) did not lead to I and photolysis of II (R = iodo) gave norponteverdrine. The synthesis of II (R = H) is described.
50. Synthesis of the necine base platynecine from glucose
By Fleet, George W. J.; Seijas, Julio A.; Vazquez-Tato, M. Pilar
A synthesis of platynecine (I) from an intermediate II is described which has previously been used for the synthesis of the enantiomers of retronecine; the stereochem. of the necine base is detd. by the formation of a tricyclic amide intermediate.

51. N-Methylsecoglaucine, a new phenanthrene alkaloid from fumariaceae
By Blanco, Olga; Castedo, Luis; Cid, Magdalena; Seijas, Julio A.; Villaverde, Carmen
From Heterocycles (1990), 31(6), 1077-80. Language: English, Database: CAPLUS
The isolation and its total synthesis of the new phenanthrene alkaloid N-methylsecoglaucine (I) from Platycapnos spicata are reported.
52. Reactivity of heteroaromatic aldehydes with low valent titanium

By Castedo, Luis; Cid, M. Magdalena; Dominguez, Rosa; Seijas, Julio A.; Villaverde, M. Carmen
From Heterocycles (1990), 31(7), 1271-4. Language: English, Database: CAPLUS, DOI:10.3987/COM-90-5357

Ti-catalyzed coupling reaction of arom. heterocycles was studied. Coupling of 4-pyridinecarboxaldehyde gave exclusively the reduced product, i.e., 1,2-bis(4-pyridyl)ethane, while 3-pyridinecarboxaldehyde gave both 1,2-bis(3-pyridyl)ethene and 1,2-dihydroxy-1,2-bis(3-pyridyl)ethane. Coupling of 3-bromo-4-pyridine-, 2- and 3-thiophene-, 3-furan-, and N-acyl-2-pyrrolecarboxaldehydes gave the corresponding bis(heteroaryl)ethenes, and 1-methyl-2-imidazolecarboxaldehyde gave the -ethane. Thus, compds. with low electron d. at the benzylic position gave reduced products.

~2 Citings

53. New total synthesis of phenanthrene alkaloids

By Estevez, Juan C.; Villaverde, M. Carmen; Estevez, Ramon J.; Seijas, Julio A.; Castedo, Luis
From Canadian Journal of Chemistry (1990), 68(6), 964-8. Language: English, Database: CAPLUS, DOI:10.1139/v90-151

A new synthesis of phenanthrene alkaloids I (R = H, OMe; R¹ = H, Me) is based on the photocyclization of stilbene II (R² = OMe, NH₂) prepd. by Friedel-Crafts reaction of 3,4-(MeO)₂C₆H₃CH₂CO₂Me with 3,4-R₂C₆H₃COCl, redn., and dehydration.

~10 Citings
54. A new simple route to styryl amides

By Estevez, J. C.; Villaverde, M. C.; Estevez, R. J.; Seijas, J. A.; Castedo, L.
From Synthetic Communications (1990), 20(4), 503-7. Language: English, Database: CAPLUS, DOI:10.1080/00397919008244897

Treatment of BzNHCH₂CH₂C₆H₃RR₁-3,4 (R = R₁ = H, OMe; R = H, R₁ = OMe) with DDQ and AcOH gave BzNHCH₂CH(OAc)C₆H₃RR₁-3,4 quant. Thermolysis of the latter at 250° gave 3:1 E-Z mixts. of BzNH:CH:C₆H₃RR₁-3,4.

~8 Citings

55. Complex quinuclidines (1-azabicyclo[2.2.2]octanes) from sugars: synthesis of (1α,3α,4α,5α)-quinuclidine-3,5-diol from D-glucose

By Fleet, George W. J.; Mathews, Christopher J.; Seijas, Julio A.; Vazquez Tato, M. P.; Brown, David

The synthesis of (1α,3α,4α,5α)-quinuclidine-3,5-diol (I) from D-glucose by 2 alternative ring closures is described. Azido alc. II is a key intermediate.

~3 Citings

56. Chiral quinuclidines (1-azabicyclo[2.2.2]octanes) from sugars: synthesis of (3S,5S)-quinuclidine-3,5-diol from D-arabinose

By Fleet, George W. J.; Mathews, Christopher J.; Seijas, Julio A.; Vazquez Tato, M. P.; Brown, David J.

The synthesis of (3S,5S)-quinuclidine-3,5-diol (I) from D-arabinose by 2 alternative ring closures is described. Protected lyxo-furanose II is the key intermediate.

~4 Citings

57. New total synthesis of patulin

By Seijas, Julio A.; Vazquez Tato, M. Pilar; Estevez, Ramon; Castedo, Luis; Riguera, Ricardo
Patulin (I) was prep'd. in 23% overall yield from L-arabinose via Wittig reaction of pentopyranosidulose II.

58. Oxidation with Fremy's salt of aryl oximes and benzylamine to carbonyl compounds

By Vazquez Tato, M. P.; Seijas, J. A.; Castedo, L.; Riguera, R.
From Anales de Quimica, Serie C: Quimica Organica y Bioquimica (1988), 84(3), 374-5. Language: Spanish, Database: CAPLUS

The oxidn. of aryl oximes ArCR: NOH (Ar = aryl, R = H, Me) and benzylamines with Fremy's salt, (KO\(_2\))\(_2\)NO, afforded carbonyl compds. in good yields. The reaction proceeds via a benzylic radical. Aliph. oximes and amines do not react under these conditions.

59. New synthesis of cyproheptadine and related compounds using low valent titanium

By Cid, M. M.; Seijas, J. A.; Villaverde, M. C.; Castedo, L.

A simple method is described for the prepn. of biphenylmethylene-epiperidine (I), cyproheptadine (II) and related compds. based on asym. dicarbonyl coupling of two suitable ketones with low valent titanium. Thus, Ph\(_2\)CO and N-ethoxycarbonyl-4-piperidone gave I after redn. of the cross-coupling product.

60. Synthesis of cis- and trans-1-amino-3-(hydroxymethyl)cyclobutane-1-carboxylic acids
The stereospecific synthesis of the title compds. I and II from bicyclo compd III is described.

61. A direct conversion of phenanthrenes to aporphinoids

By Seijas, Julio A.; Rodriguez de Lera, Angel; Villaverde, Carmen; Castedo, Luis
From Heterocycles (1985), 23(12), 3079-84. Language: English, Database: CAPLUS

The (aminoethyl)phenanthrenediones I (R = H, COCF₃), prepd. by oxidn. of the corresponding 9,10-unsatd. derivs., were cyclized by treatment with Na₂CO₃ to give aporphinoids II and III.

~5 Citings
62. Reductive dicarbonyl coupling with low-valent titanium reagents: a new entry to phenanthrene alkaloids

By Seijas, Julio A.; De Lera, Angel R.; Villaverde, M. Carmen; Castedo, Luis

Phenanthrene alkaloids were prepd. using a low-valent Ti reagent which is compatible with ethoxycarbonyl as the N-protecting group. E.g., atherosperminine was prepd. in 5 steps from 6,7-dimethoxy-3,4-dihydroisoquinoline. The key step was the mixed reductive coupling of 6,4,3-HCO(MeO)\(_2\)C\(_6\)H\(_2\)(CH\(_2\))\(_2\)NMeCO\(_2\)Et with PhCHO in the presence of TiCl\(_3\) and Li in refluxing (MeOCH\(_2\))\(_2\) to give 55% (E)-6,4,3-PhCH:CH(MeO)\(_2\)C\(_6\)H\(_2\)(CH\(_2\))\(_2\)NMeCO\(_2\)Et.

~5 Citings

63. 4,5-O-Substituted phenanthrenes from cyclophanes. The total synthesis of cannithrene II

By Ben, Ines; Castedo, Luis; Saa, Jose M.; Seijas, Julio A.; Suau, Rafael; Tojo, Gabriel

A new procedure for the synthesis of phenathrenes I (R = OMe, R\(^1\) = R\(^2\) = H, R\(^3\) = H, OMe; R = R\(^1\) = H, R\(^2\) = R\(^3\) = H, OMe; R = R\(^2\) = R\(^3\) = H, R\(^1\) = Me) is based on the regioselective cyclization of the conformationally rigid cis-stilbene moiety of a cyclophane II. II were obtained by the intramol. reductive carbonyl coupling of dicarbonyl compds. III by active Ti. This new approach was successfully applied to obtain cannithrene II (IV).

~27 Citings

64. Ionic Liquid-Promoted Synthesis of Novel Chromone-Pyrimidine Coupled Derivatives, Antimicrobial Analysis, Enzyme Assay, Docking Study and Toxicity Study
Herein, we report an environmentally friendly, rapid, and convenient ionic liquid ([Et$_3$NH][HSO$_4$])-promoted facile synthesis of ethyl 4-(6-substituted-4-oxo-4H-chromen-3-yl)-6-methyl-2-thioxo/oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate derivatives 4(a-f) and 4-(6-substituted-4-oxo-4H-chromen-3-yl)-6-methyl-2-thioxo/oxo-1,2,3,4-tetrahydropyrimidine-5-carbohydrazide derivatives 6(a-f). All the synthesized derivatives 4(a-f) and 6(a-f) were evaluated for their in vitro antifungal and antibacterial activity, by method recommended by National Committee for Clinical Laboratory Standards (NCCLS). The compound 6c bearing a fluoro group on the chromone ring and oxygen and a hydrazino group (-NHNH$_2$) on the pyrimidine ring, was found to be the most potent antibacterial compound amongst the synthesized derivatives. The compound 6f bearing a methoxy group (-OCH$_3$) on the chromone ring and sulphur group on the pyrimidine ring, was found to exhibit equipotent antifungal activity when compared with the standard drug miconazole. A D-alanine-D-alanine ligase (DdlB) enzyme assay study and an ergosterol extraction and quantitation assay study were performed to predict the mode of action of the synthesized compounds. A molecular docking study was performed to predict the binding interactions with receptors and mode of action of the synthesized derivatives. Further, analysis of the ADMET parameters for the synthesized compounds has shown that these compounds have good oral drug-like properties and can be developed as oral drug candidates. To establish the antimicrobial selectivity and safety, the most active compounds 6c and 6f were further tested for cytotoxicity against the human cancer cell line HeLa and were found to be non-cytotoxic in nature. An in vivo acute oral toxicity study was also performed for the most active compounds 6c and 6f and the results indicated that the compounds are non-toxic in nature.
The work reports the synthesis under solvent-free condition using the ionic liquid [Et3NH][HSO4] as a catalyst of fifteen novel 3-((dicyclohexylamino)(substituted phenyl/heteryl)-methyl)-4-hydroxy-2H-chromen-2-onederivatives 4a-o as potential antimicrobial agents. The structures of the synthesized compounds were confirmed by IR, 1H-NMR, (13)C-NMR, mass spectral studies and elemental analyses. All the synthesized compounds were evaluated for their in vitro antifungal and antibacterial activity. The compound 4k bearing 4-hydroxy-3-ethoxy group on the phenyl ring was found to be the most active antifungal agent. The compound 4e bearing a 2,4-difluoro group on the phenyl ring was found to be the most active antibacterial agent. The mode of action of the most promising antifungal compound 4k was established by an ergosterol extraction and quantitation assay. From the assay it was found that 4k acts by inhibition of ergosterol biosynthesis in C. albicans. Molecular docking studies revealed a highly spontaneous binding ability of the tested compounds to the active site of lanosterol 14α-demethylase, which suggests that the tested compounds inhibit the synthesis of this enzyme. The synthesized compounds were analyzed for in silico ADMET properties to establish oral drug like behavior and showed satisfactory results. To establish the antimicrobial selectivity and safety, the most active compounds 4e and 4k were further tested for cytotoxicity against human cancer cell line HeLa and were found to be non-cytotoxic in nature. An in vivo acute oral toxicity study was also performed for the most active compounds 4e and 4k and results indicated that the compounds are non-toxic.

~0 Citings

67. Microwave-Assisted Facile Synthesis, Anticancer Evaluation and Docking Study of N-((5-(Substituted methylene amino)-1,3,4-thiadiazol-2-yl)methyl) Benzamide Derivatives

By Tiwari Shailee V; Siddiqui Sumaiya; Lokwani Deepak K; Nikalje Anna Pratima G; Seijas Julio A; Vazquez-Tato M Pilar; Sarkate Aniket P
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In the present work, 12 novel Schiff’s bases containing a thiadiazole scaffold and benzamide groups coupled through appropriate pharmacophore were synthesized. These moieties are associated with important biological properties. A facile, solvent-free synthesis of a series of novel 7(a-l) N-((5-(substituted methylene amino)-1,3,4-thiadiazol-2-yl)methyl) benzamide was carried out under microwave irradiation. Structures of the synthesized compounds were confirmed by IR, NMR, mass spectral study and elemental analysis. All the synthesized hybrids were evaluated for their in vitro anticancer activity against a panel of four human cancer cell lines, viz. SK-MEL-2 (melanoma), HL-60 (leukemia), HeLa (cervical cancer), MCF-7 (breast cancer) and normal breast epithelial cell (MCF-10A) using 3-(4,5-dimethythiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay method. Most of the synthesized compounds exhibited promising anticancer activity, showed comparable GI50 values comparable to that of the standard drug Adriamycin. The compounds 7k, 7l, 7b, and 7a were found to be the most promising anticancer agents in this study. A molecular docking study was performed to predict the probable mechanism of action and computational study of the synthesized compounds 7(a-l) was performed to predict absorption, distribution, metabolism, excretion and toxicity (ADMET) properties, by using QikProp v3.5 (Schrodinger LLC). The results showed the good oral drug-like behavior of the synthesized compounds 7(a-l).

~2 Citings

68. Ultrasound Mediated One-Pot, Three Component Synthesis, Docking and ADME Prediction of Novel 5-Amino-2-(4-chlorophenyl)-7-Substituted Phenyl-8,8a-dihydro-7H-(1,3,4)thiadiazolo(3,2-α)pyrimidine-6-carbonitrile Derivatives as Anticancer Agents

By Tiwari Shailee V; Nikalje Anna Pratima G; Seijas Julio A; Vazquez-Tato M Pilar; Sarkate Aniket P; Lokwani Deepak K
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Herein, we report an environmentally friendly, rapid, and convenient one-pot ultrasound-promoted synthesis of 5-amino-2-(4-chlorophenyl)-7-substituted phenyl-8,8a-dihydro-7H-(1,3,4)thiadiazolo(3,2-α)pyrimidine-6-carbonitrile derivatives. The in-vitro anticancer activities of these compounds were evaluated against four human tumor cell lines. Among all the synthesized derivatives, compound 4i, which has substituent 3-hydroxy-4-methoxyphenyl is found to have the highest GI50 value of 32.7 µM, 55.3 µM, 34.3 µM, 28.9 µM for MCF-7, K562, HeLa and PC-3 cancer cell lines respectively. A docking study of the newly synthesized compounds were performed, and the results showed good binding mode in the active site of thymidylate synthase enzyme. ADME properties of synthesized compounds were also studied and showed good drug like properties.

~0 Citings