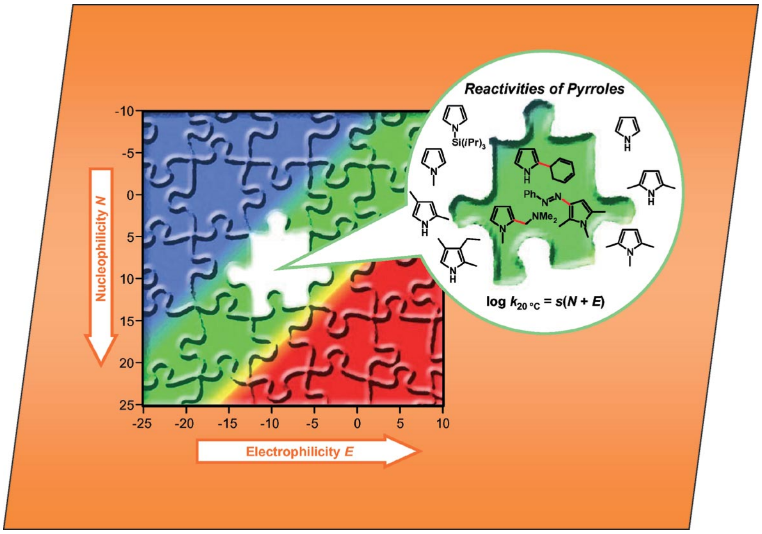
COVER PICTURE

The cover picture is misleading! With the determination of the nucleophilic reactivities of pyrroles, our electrophilicity-nucleophilicity puzzle, where synthetically useful reactions are found in the green corridor (see: R. Lucius, R. Loos, H. Mayr, *Angew. Chem. Int. Ed.* **2002**, *41*, 91–95), is not yet complete. The picture illustrates, however, that the reactions of pyrroles with electrophiles also follow the linear free-energy relationship $\log k_{20^\circ\mathrm{C}} = s(N + E)$, where N and s characterize the reactivities of nucleophiles and E describes the reactivities of electrophiles. Alkyl substitution increases the nucleophilicity of pyrrole by a factor of up to 10 million, and from the nucleophilicity parameters reported in this article by H. Mayr et al. on p. 2369ff, one can derive suitable electrophilic reaction partners for alkyl-substituted pyrroles.



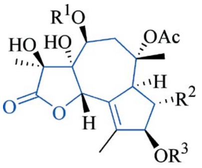
MICROREVIEW

Guaianolides

A. Schall, O. Reiser* 2353–2364

Synthesis of Biologically Active Guaianolides with a *trans*-Annulated Lactone Moiety

Keywords: Total synthesis / Sesquiterpenes / Lactones / Natural products / Asymmetric synthesis



Thapsigargins

Tricyclic guaianolides, for example, thapsigargins, display a broad biological profile, which has prompted the development of diverse synthetic strategies towards them.

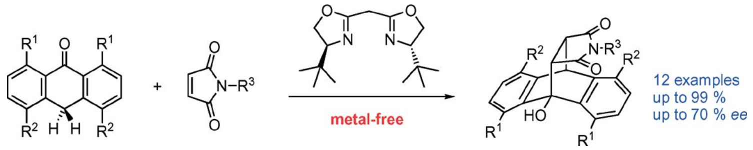
SHORT COMMUNICATION

Metal-Free Catalysis

D. Akalay, G. Dürner,
M. W. Göbel* 2365–2368

A First Case of Asymmetric Catalysis Induced by Metal-Free Bisoxazolines

Keywords: Asymmetric catalysis / Bisoxazolines / Cycloaddition / Enantioselectivity / Organocatalysis



Bisoxazolines catalyze the Diels–Alder reaction between anthrone derivatives and *N*-substituted maleimides leading to products in excellent yields and moderate to good enantioselectivities. This is the first example of their use without any metal in asymmetric catalysis.

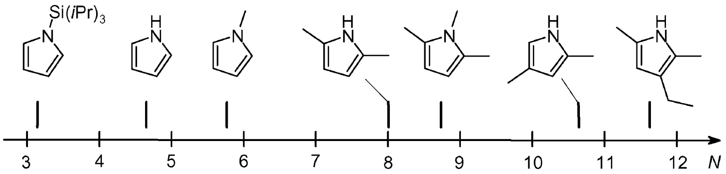
FULL PAPERS

Nucleophilicities of Pyrroles

T. A. Nigst, M. Westermaier, A. R. Ofial,
H. Mayr* 2369–2374

Nucleophilic Reactivities of Pyrroles

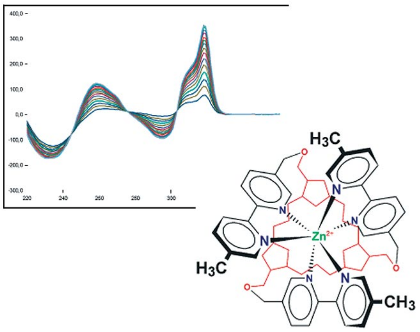
Keywords: Nitrogen heterocycles / Carbocations / Kinetics / Electrophilic substitution / Linear free energy relationships



Kinetics of the reactions of alkyl-substituted pyrroles with benzhydrylium ions were studied photometrically in acetonitrile at 20 °C. According to the linear free energy relationship $\log k_2(20\,°C) = s(N + E)$, the N and s parameters of these pyrroles were determined.

Chirality Transfer

An extended study of the synthesis of macrocyclic oxazole-containing pseudopeptide scaffolds is provided. Coupling of the trialcohol scaffold with 2,2′-bipyridyl sidearms afforded a tripodal ligand which binds transition metals with high diastereoselectivity. Chirality transfer was investigated by CD-titration experiments.



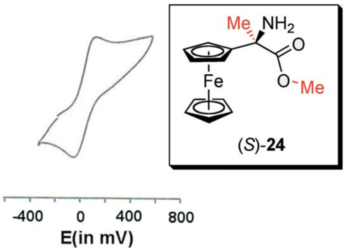
Á. Pintér, G. Haberhauer* **2375–2387**

Oxazole Cyclopeptides for Chirality Transfer in C_3-Symmetric Octahedral Metal Complexes

Keywords: Amino acids / Chirality / Cyclization / Macrocycles / Oxazoles

Ferrocenyl Amino Acids

Are α-ferrocenyl-α-amino esters stable? The answer is yes provided that the α-carbon is tetrasubstituted and that very mild reaction conditions are involved in their generation. Thus, the (*S*) enantiomer of methyl α-ferrocenylalaninate **24**, prepared in around 90% *ee* from 2-ferrocenylpropene, is a stable compound that can be stored for prolonged periods of time without appreciable decomposition.



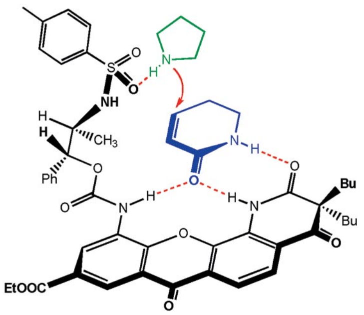
R. M. Moreno, M. Catasús, C. López, A. Moyano* **2388–2396**

Enantiocontrolled Preparation of the First Stable α-Ferrocenylalanine Derivatives

Keywords: Amino acids / Asymmetric synthesis / Bioorganic chemistry / Metallocenes / Transition metals

Supramolecular Catalysis

Oxyanion hole-like structures and novel proton-transfer groups are combined in the design of molecular receptors showing enzyme-like behaviour.

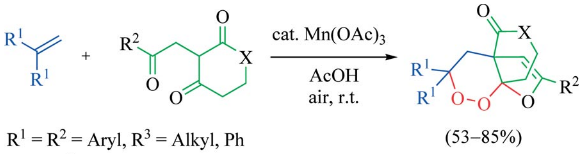


L. Simón, F. M. Muñiz, S. Sáez, C. Raposo, J. R. Morán* **2397–2403**

Enzyme Mimics for Michael Additions with Novel Proton Transport Groups

Keywords: Homogeneous catalysis / Supramolecular chemistry / Hydrogen bonds / Enzyme mimics / Proton slide

Heterocyclic Propellanes



$R^1 = R^2 =$ Aryl, $R^3 =$ Alkyl, Ph
$X = NR^3$, CH_2, CMe_2

3-Oxopropyl-substituted cycloalkane-1,3-diones yield dioxabicyclic propellane precursors that can be converted into the corresponding propellanes by treatment with a Lewis acid. Mn^{III}-mediated aerobic oxidation of mixtures of 2-(2-oxoethyl)-cyclohexane-1,3-dione derivatives and 1,1-diarylethenes produces structurally interesting endoperoxy[4.4.3]propellanes in good yields.

K. Asahi, H. Nishino* **2404–2416**

Facile Endoperoxypropellane Synthesis by Manganese(III) Acetate-Mediated Aerobic Oxidation

Keywords: Nitrogen heterocycles / Peroxides / Radicals / Cyclization / Oxidation

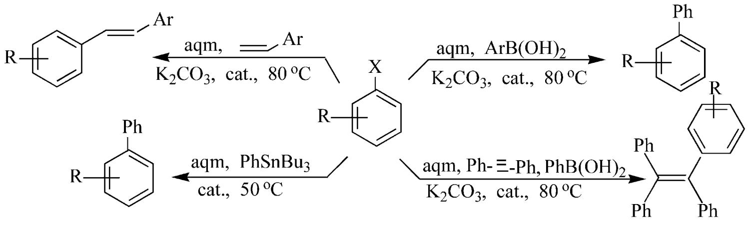
CONTENTS

C–C Coupling

D. Tsvelikhovsky, J. Blum* 2417–2422

Three Phase Microemulsion/Sol–Gel System for Aqueous C–C Coupling of Hydrophobic Substrates

Keywords: C–C coupling / Green chemistry / Sustainable chemistry / Microemulsion / Palladium / Sol–gel processes



aqm = aqeous microemulsion, cat. = $Pd(OAc)_2$@sol-gel, X = Br, I

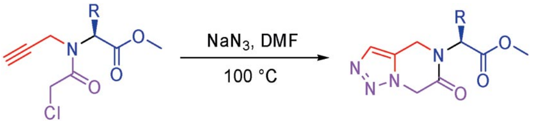
$Pd(OAc)_2$-catalyzed Heck, Stille, Suzuki and three-component coupling reactions with hydrophobic substrates can be performed in an aqueous solution by using a three phase microemulsion/sol–gel transport system. The immobilized catalyst is leach proof and recyclable.

Triazole-Fused Tetrahydropyrazinones

V. Sai Sudhir, R. B. Nasir Baig,
S. Chandrasekaran* 2423–2429

Facile Entry to 4,5,6,7-Tetrahydro[1,2,3]triazolo[1,5-*a*]pyrazin-6-ones from Amines and Amino Acids

Keywords: Triazoles / Alkynes / Cycloaddition / Nitrogen heterocycles / Amino acids



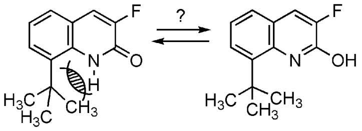
Triazole-fused tetrahydropyrazin-6-ones were synthesized in excellent yield starting from primary amines and amino acids by employing a three-step protocol (i.e. sequential alkylation, acylation, one-pot displacement with azide and cycloaddition). This methodology involves constrained intramolecular cycloaddition as the key step.

Tautomeric Preferences

J.-N. Volle, U. Mävers,
M. Schlosser* 2430–2438

The Tautomeric Persistence of Electronically and Sterically Biased 2-Quinolinones

Keywords: Acidity constants / Amide–hydroxyimine tautomerism / 3-Fluoro-2(1*H*)-quinolinones / Keto–enol tautomerism / Knorr–Effenberger cyclizations



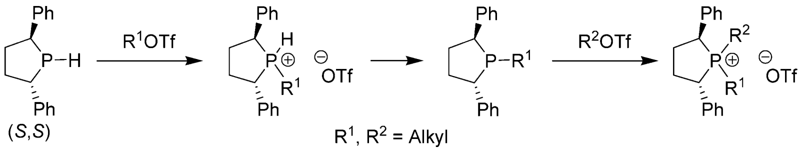
Before calling a spade a spade, one should make sure to have one at all. The tautomeric preferences established for a parent compound may be profoundly altered by substituents. However, in the 2-quinolinone series this does not seem to be the case as the introduction of a fluorine atom and a *tert*-butyl group into the critical 3- and 8-positions, respectively, did not produce detectable amounts of the 2-hydroxyquinoline form.

Phospholane Derivatives

C. Dobrota, A. Duraud, M. Toffano,*
J.-C. Fiaud 2439–2445

Synthesis of Enantiopure 1-*r*-Alkyl-2-*c*,5-*t*-Diphenylphospholanes and Phospholanium Salts through Direct Alkylation of Phospholane

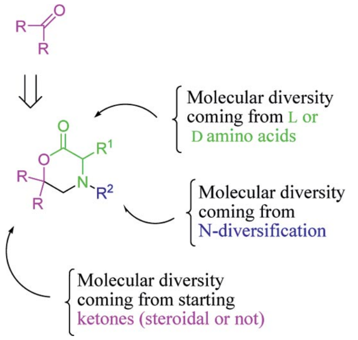
Keywords: Alkylation / Phosphorus heterocycles / P ligands / Phase-transfer catalysis



Chiral enantiopure 1-alkyl-2,5-diphenylphospholanium salts were obtained in one step through alkylation of phospholane with alkyl triflates. The resulting air-stable phosphonium salts are electron-rich trialkylphosphane precursor ligands for transition metals, and they offer a convenient route toward chiral quaternary phosphonium salts as phase-transfer agents.

Steroidal [1,4]Oxazinan-6′-ones

A four-step strategy was developed for the synthesis of different estradiol derivatives bearing a 17-spiro-δ-lactone moiety with a nitrogen atom inserted in the lactone ring. Such [1,4]oxazinan-6′-one derivatives contain two levels of molecular diversity introduced to modulate biological activity.



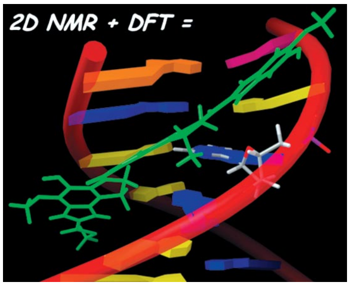
F. Rouillard, J. Roy, D. Poirier* **2446–2453**

Chemical Synthesis of (*S*)-Spiro(estradiol-17,2′-[1,4]oxazinan)-6′-one Derivatives Bearing Two Levels of Molecular Diversity

Keywords: Steroids / Lactones / Amino acids / Estradiol derivatives / Enzyme inhibitors

Ligand–Receptor Interactions

A hybrid approach based on 2D-NMR spectroscopy and quantum mechanical calculations of ^1H chemical shifts at the DFT/MPW1PW91 level was used for the characterization of the covalent complex formed by (+)-yatakemycin and d(GACTAATTGAC)–(GTCAATTAGTC), showing that calculation of NMR parameters can be a useful tool for the structural characterization of ligand–receptor interactions.



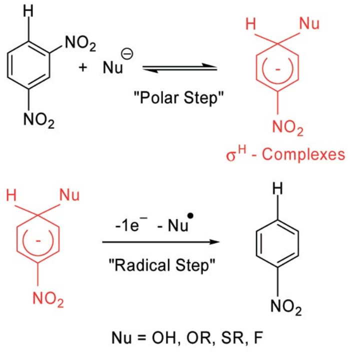
S. Di Micco, D. L. Boger, R. Riccio, G. Bifulco* **2454–2462**

Structural Features of the (+)-Yatakemycin/d(GACTAATTGAC)-(GTCAATTAGTC) Complex – Quantum Mechanical Calculation of NMR Parameters as a Tool for the Characterization of Ligand/DNA Interactions

Keywords: Minor groove binders / NMR spectroscopy / Calculation of NMR parameters

Nucleophilic Aromatic Substitution

Electrochemical oxidation of σ^H complexes by nucleophilic attack of alkoxy, sulfoxy, or fluoride anions has been studied by means of cyclic voltammetry and a mechanism linking the intermediates and products is disclosed. The mechanism for the electrochemical oxidation of the intermediates shows a radical reaction pathway for their decomposition into products.



Nu = OH, OR, SR, F

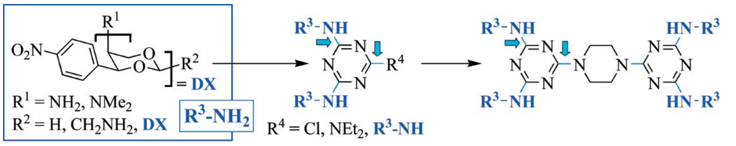
"NASX-type" oxidation process

I. Gallardo,* G. Guirado* **2463–2472**

Thermodynamic Study of σ^H Complexes in Nucleophilic Aromatic Substitution Reactions: Relative Stabilities of Electrochemically Generated Radicals

Keywords: σ^H Complexes / Nucleophilic substitution / Aromatic substitution / Electrochemistry / Oxidation / Reaction mechanisms

Serinol Building Blocks



We report the first iterative synthesis of *N*-substituted melamines by amination of cyanuric chloride with amino-1,3-dioxanes based on the (1*S*,2*S*)-(*p*-nitrophenyl)serinol skeleton. The (pro)diastereomerism in this new class of amino-*s*-triazines, originating from restricted rotation about the C(*s*-triazine)-N< bonds, is described with supporting DNMR and DFT data.

M. Fazekas, M. Pintea, P. Lameiras, A. Lesur, C. Berghian, I. Silaghi-Dumitrescu, N. Plé, M. Darabantu* **2473–2494**

Serinolic Amino-*s*-triazines: Iterative Synthesis of *N*-Substituted Amino-1,3-dioxane Derivatives from *l*-(*p*-Nitrophenyl)serinols and Rotational Stereochemistry Phenomena

Keywords: Amination / Conformation analysis / Molecular modeling / Nitrogen heterocycles / NMR Spectroscopy