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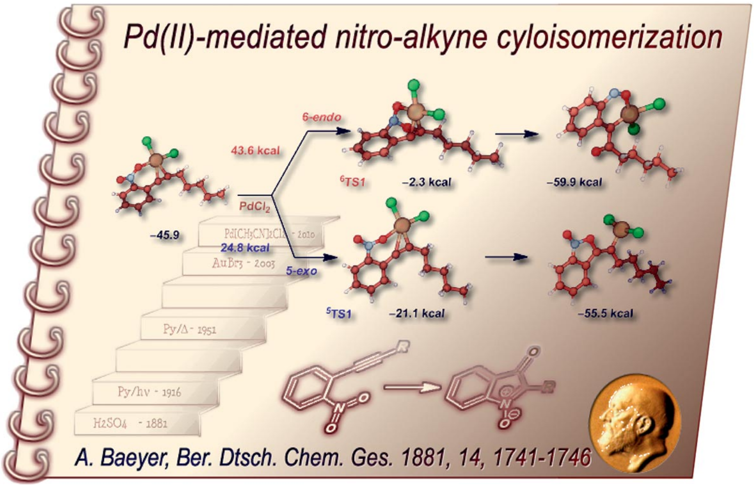
COVER PICTURE

The cover picture shows the historical details of the nitro−alkyne cycloisomerization leading to isatogens. Since the first documentation of this reaction by Baeyer (picture of Baeyer and the corresponding literature citation are shown) in the late 19th century, a mild and general method for the synthesis of isatogens has been sought. The electrophilic Pd^{II} halide complexes are found to bring about this cyclization to provide the desired isatogens and accommodate both aryl and alkyl substituents as well as tolerate commonly employed protecting groups/functional units. Details of the course of the reaction through advanced theoretical studies and the utility of isatogens as new ROS (reactive oxygen species) scavengers are discussed in the article by C. V. Ramana, K. Vanka, A. Degterev et. al. on p. 5955ff.



CONTENTS

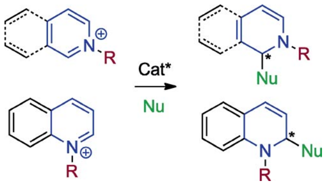
MICROREVIEW

Asymmetric Catalysis

M. Ahamed, M. H. Todd* 5935–5942

Catalytic Asymmetric Additions of Carbon-Centered Nucleophiles to Nitrogen-Containing Aromatic Heterocycles

Keywords: Nitrogen heterocycles / Asymmetric catalysis / Nucleophilic addition / Bifunctional catalysis



In the last decade a small number of highly effective methods have been developed for the catalytic asymmetric addition of carbon-based nucleophiles to aromatic nitrogen heterocycles. The resulting structures are of wide potential utility in synthetic and medicinal chemistry. There is a great deal of room for discovery of new reactions in this class.

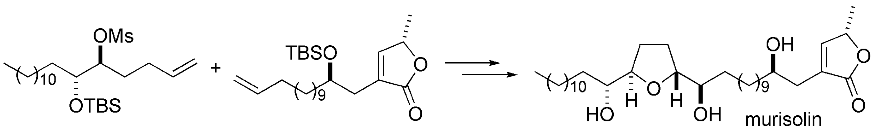
SHORT COMMUNICATIONS

Natural Product Synthesis

K. J. Quinn,* L. Islamaj, S. M. Couvertier,
K. E. Shanley,
B. L. Mackinson 5943–5945

Convergent Total Synthesis of Murisolin

Keywords: Oxygen heterocycles / Total synthesis / Metathesis / Natural products / Polyketides



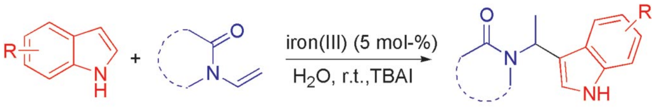
An efficient synthesis of murisolin, employing cross metathesis for assembly of the carbon framework and late-stage tetrahydrofuran formation on the intact backbone, is reported.

Friedel–Crafts Reaction

R. Jiang, X.-J. Wu, X. Zhu, X.-P. Xu,*
S.-J. Ji* 5946–5950

Ferric(III) Nitrate: An Efficient Catalyst for the Regioselective Friedel–Crafts Reactions of Indoles and *tert*-Enamides in Water

Keywords: Iron / Alkylation / Nitrogen heterocycles / Water chemistry / Green chemistry



R = H, Me, Br, BnO, NO_2

31–89% yield

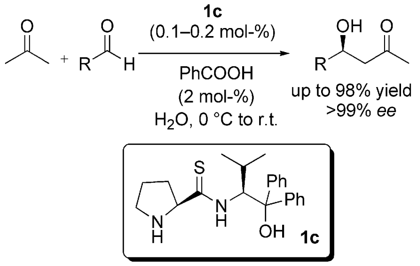
Friedel–Crafts (FC) reactions catalyzed by ferric nitrate in water at room temperature between various indoles and tertiary enamides are described. This atom-economical and environmentally friendly procedure uses an inexpensive catalyst with low loadings and establishes a new example of Lewis acid catalyzed F–C alkylations between indoles with electron-rich olefins.

Aldol Reaction

B. Wang, X.-w. Liu, L.-y. Liu*,
W.-x. Chang, J. Li* 5951–5954

Highly Efficient Direct Asymmetric Aldol Reactions Catalyzed by a Prolinethioamide Derivative in Aqueous Media

Keywords: Aldol reactions / Water chemistry / Asymmetric catalysis / Organocatalysis

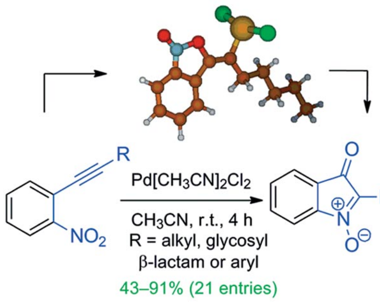


L-Prolinethioamide derivative **1c** was employed in the direct asymmetric aldol reactions of acetone with aromatic aldehydes. A loading of only 0.1–0.2 mol-% afforded excellent enantioselectivities and yields (up to 98% yield, >99%*ee*) in aqueous media.

FULL PAPERS

Synthetic Methodology

Nitro–alkyne cycloisomerization by Pd^{II} halides: Pd^{II} halide complexes were used in cycloisomerizations of *o*-alkynylnitrobenzene derivatives, leading to isatogens. The mechanism of the reaction was investigated by DFT calculations. The 2-alkylisatogens were identified as new candidates for inhibiting necroptosis-mediated cell death through the efficient trapping of reactive oxygen species.



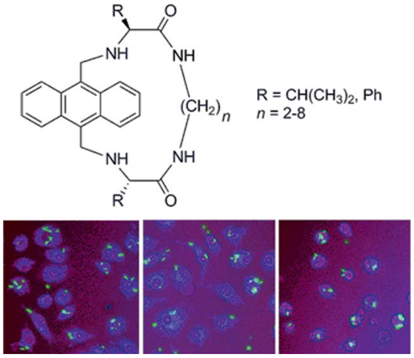
C. V. Ramana,* P. Patel, K. Vanka,*
B. Miao, A. Degterev* 5955–5966

A Combined Experimental and Density Functional Theory Study on the Pd-Mediated Cycloisomerization of *o*-Alkynylnitrobenzenes – Synthesis of Isatogens and Their Evaluation as Modulators of ROS-Mediated Cell Death

Keywords: Nitro–alkyne cycloisomerization / Cyclization / Palladium / Isatogens / Anthranil / Density functional calculations

Fluorescent Probes

A new family of anthracenic macrocycles has been synthesized that can act as fluorescent probes for pH in the range 4.6–6.5. The pK_a values of these compounds can be finely tuned. In flow cytometry experiments, it was found that bacterial killing by human monocytes (U937) occurred with a simultaneous drop in pH, which was monitored by one of the macrocyclic sensors.



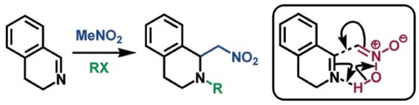
M. I. Burguete, F. Galindo,*
M. A. Izquierdo, J.-E. O'Connor,
G. Herrera, S. V. Luis,*
L. Vigara 5967–5979

Synthesis and Evaluation of Pseudopeptidic Fluorescence pH Probes for Acidic Cellular Organelles: In Vivo Monitoring of Bacterial Phagocytosis by Multiparametric Flow Cytometry

Keywords: Fluorescent probes / Sensors / Acidity / Macrocycles / Peptidomimetics

N-Heterocyclic Chemistry

3,4-Dihydroisoquinoline reacts with nitromethane, likely via a cyclic mechanism employing nitromethane's azinic acid tautomer. The product may be alkylated or acylated. Alternatively a Reissert-like one-pot, three-component coupling may be used to generate a range of β-nitroamines which may be reduced to give new isoquinoline-derived chiral, vicinal diamines.

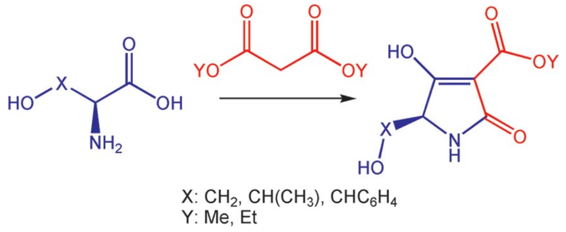


M. Ahamed, T. Thirukkumaran,
W. Y. Leung, P. Jensen, J. Schroers,
M. H. Todd* 5980–5988

Aza-Henry Reactions of 3,4-Dihydroisoquinoline

Keywords: Nitrogen heterocycles / aza-Henry reaction / nitro-Mannich reaction / Nitroalkanes

Five-Membered Nitrogen Heterocycles



An array of functionalized tetramic acids bearing a hydrophilic group on the side arm of the heterocyclic nucleus, as well as their intermediate β-hydroxy-γ-amino acids, were synthesized from suitably protected and activated L-serine, L-tyrosine, and L-threonine in two steps with good-to-excellent enantiomeric purities (up to 95%*ee*) and high yields (up to 92%).

D. Matiadis,
O. Igglessi-Markopoulou* 5989–5995

Design and Synthesis of Optically Active Esters of γ-Amino-β-oxo Acids as Precursors for the Synthesis of Tetramic Acids Derived from L-Serine, L-Tyrosine, and L-Threonine

Keywords: Cyclization / Nitrogen heterocycles / Acylation / Amino acids

CONTENTS

Asymmetric Catalysis

W. J. Fleming, H. Müller-Bunz,
P. J. Guiry* 5996–6004

Synthesis and Post-Resolution Modification of New Axially Chiral Ligands for Asymmetric Catalysis

Keywords: Ligand design / Chiral resolution / Chirality / Atropisomerism / Asymmetric synthesis / Palladium / Hydroboration

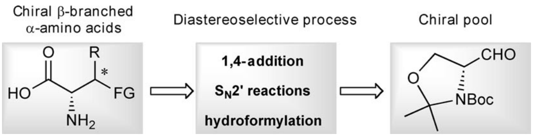
Four new members of the Quinazolinap series of ligands are prepared, three by post-resolution modification. They were applied to the rhodium-catalyzed hydroboration of vinylarenes with regioselectivities of catalyzed allylic of up to >99:1 and *ee* values of up to 68 %. Each of the Quinazolinap ligands prepared were applied to the palladium-catalyzed allylic alkylation of 1,3-diphenylprop-2-enyl acetate in a synthetic and mechanistic study which helped to rationalize the sense of asymmetric induction observed.

β-Amino Acids

T. Spangenberg, A. Schoenfelder,
B. Breit,* A. Mann* 6005–6018

1,2-Diastereoselective C–C Bond-Forming Reactions for the Synthesis of Chiral β-Branched α-Amino Acids

Keywords: Amino acids / Diastereoselectivity / Allylic compounds / Nucleophilic substitution / Hydroformylation



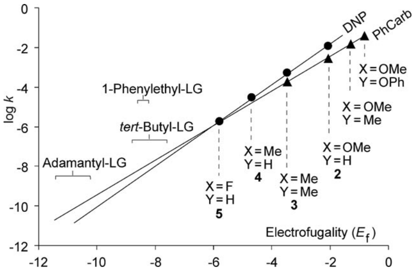
Allylic substitution of (*E*)- or (*Z*)-allylic alcohols derived from Garner's aldehyde with organo-copper nucleophiles deliver *syn* or *anti* β-substituted amino acids with excellent diastereoselectivity. Hydroformylation of an alkene attached to the Garner oxazolidine revealed a strong *syn* preference.

Nucleofugality of Dinitrophenolate

M. Matić, B. Denegri,*
O. Kronja* 6019–6024

Solvolytic Reactivity of 2,4-Dinitrophenolates

Keywords: Reaction mechanisms / Solvent effects / Solvolysis / Nucleofugality scale



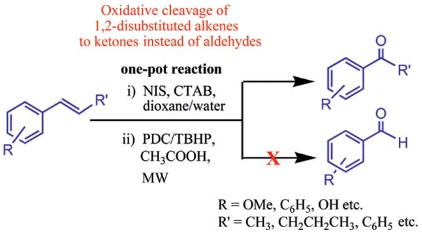
The nucleofuge-specific parameters determined for 2,4-dinitrophenolate (DNP) according to LFER equation $\log k = s_f\,(N_f + E_f)$ indicate that DNPs solvolyze via late TS in which intense charge delocalization occurs. DNPs with weaker electrofuges solvolyze slower than the same substrates with leaving groups of similar reactivity but lower s_f, whereas strong electrofuges solvolyze faster.

Oxidative Cleavage

N. Sharma, A. Sharma, R. Kumar,
A. Shard, A. K. Sinha* 6025–6032

One-Pot Two-Step Oxidative Cleavage of 1,2-Arylalkenes to Aryl Ketones Instead of Arylaldehydes in an Aqueous Medium: A Complementary Approach to Ozonolysis

Keywords: Cleavage reactions / Alkenes / Oxidation / Ketones / Microwave chemistry

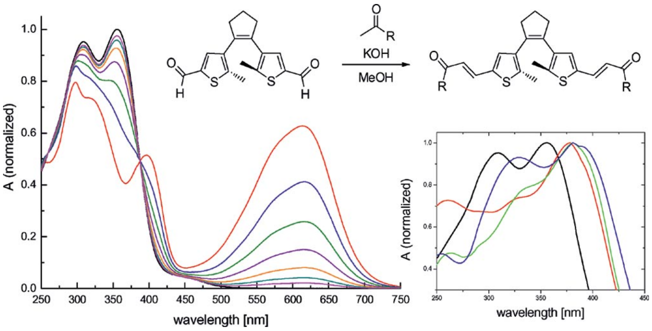


A one-pot, two-step approach has been achieved for the oxidative cleavage of 1,2-disubstituted arylalkenes into the corresponding aryl ketones instead of arylaldehydes (see scheme; NIS = *N*-iodosuccinimide; CTAB = cetyltrimethylammonium bromide; PDC/TBHP = pyridinium dichromate/*tert*-butyl hydroperoxide). The methodology also led to a valuable one-pot oxidative cleavage–condensation reaction that has widespread utility in the total synthesis of natural products.

Visible Light Photoswitches

K. Altenhöner, J.-H. Lamm,
J. Mattay* 6033–6037

Novel Dithienylethenes with Extended π-Systems: Synthesis by Aldol Condensation and Photochromic Properties



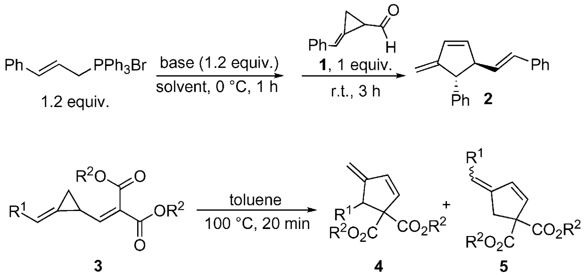
A new synthetic pathway leading to π-extended dithienylethenes is presented. Nine new photoswitches are obtained in a facile and very stereoselective procedure and their photochromic properties are discussed.

Keywords: Photochromism / Photoswitches / Alkenes / Aldol reactions / Dithienylethene

Tandem Reactions

X.-Y. Tang, Y. Wei,*
M. Shi* 6038–6042

Ring-Opening Reaction of Methylenecyclopropanes Derived from Methylenecyclopropyl Aldehydes through Cope Rearrangement



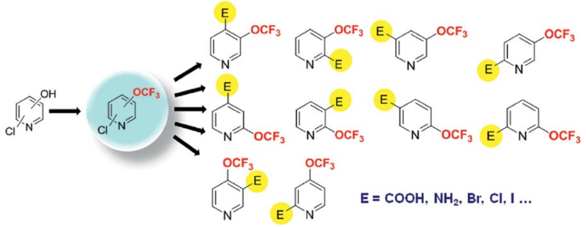
Tandem Wittig reaction/Cope rearrangement of methylenecyclopropyl aldehydes **1** with cinnamyltriphenylphosphonium bromide at room temperature delivered cyclopentenes **2** in moderate yield. Furthermore, treatment of dialkyl 2-[(2-methylenecyclopropyl)methylene]malonates **3** at 100 °C for 20 min afforded cyclopentene derivatives **4** and **5** in good total yields.

Keywords: Cyclization / Rearrangement / Small ring systems / Wittig reactions

Fluorine Chemistry

B. Manteau, P. Genix, L. Brelot,
J.-P. Vors, S. Pazenok,
F. Giornal, C. Leuenberger,
F. R. Leroux* 6043–6066

A General Approach to (Trifluoromethoxy)pyridines: First X-ray Structure Determinations and Quantum Chemistry Studies



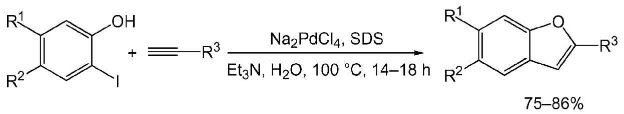
A general and efficient route to (trifluoromethoxy)pyridines is reported. Regioselective functionalization by organometallic methods afforded new and highly important building blocks for life-sciences-oriented research. The first X-ray crystallographic structure determinations of (trifluoromethoxy)pyridines have been performed and supported by in silico studies.

Keywords: Nitrogen heterocycles / Fluorine / Organometallic intermediates / Ab initio calculations

Synthesis of Benzo[*b*]furans in Water

D. Saha, R. Dey,
B. C. Ranu* 6067–6071

A Simple and Efficient One-Pot Synthesis of Substituted Benzo[*b*]furans by Sonogashira Coupling–5-*endo-dig* Cyclization Catalyzed by Palladium Nanoparticles in Water Under Ligand- and Copper-Free Aerobic Conditions



A simple and efficient procedure for the synthesis of 2-substituted benzo[*b*]furan derivatives has been developed by the reaction of 2-iodophenols and arylacetylenes in water catalyzed by palladium nanoparticles generated in situ in open air.

Keywords: Cyclization / Cross-coupling / Palladium / Nanoparticles / Water chemistry

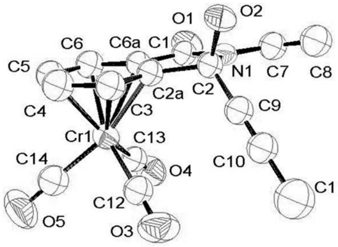
CONTENTS

(Arene)tricarbonylchromium Complexes

O. M. A. Habib, Z. Zhao-Karger, I. A. Abdelhamid, R. Wartchow, H. Butenschön* **6072–6083**

Phthalimide Tricarbonylchromium Complexes: Synthesis, Characterization, Nucleophilic Addition, and Unanticipated *syn* Adduct Formation upon Addition of Propynyllithium

Keywords: Chromium / Carbonyl ligands / Nucleophilic addition / Reaction mechanisms



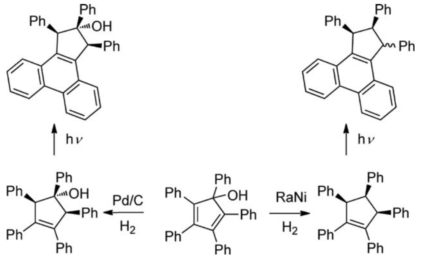
The synthesis of the first phthalimide tricarbonylchromium complexes is reported. Nucleophilic addition to these complexes takes place at one of the imide carbonyl groups from the face opposite the $Cr(CO)_3$ group to give *endo*-hydroxy products. In some cases, however, the unanticipated formation of the *exo*-hydroxy derivatives is observed as a result of isomerization following the original reaction.

Cyclopentadienes

M. Kanthak, E. Muth, G. Dyker* **6084–6091**

💻 Hydrogenation and Dehydrogenation of Pentaphenylcyclopentadienes and Pentaphenylcyclopentenes

Keywords: Carbocycles / Photochemistry / Dehydrogenation / Isomerization / Hydrogenation



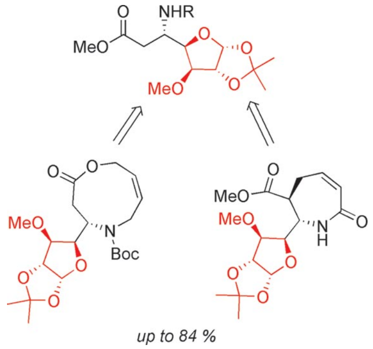
The hydrogenation of pentaphenylcyclopentadienol yields different products depending on the catalyst used. The products obtained, pentaphenylcyclopentene and pentaphenylcyclopentenol, were employed in photochemical dehydrogenation reactions, which were very sensitive to the oxidants and solvents employed.

Cyclic β-Amino Acid Derivatives

B. Sundararaju, T. Sridhar, M. Achard, G. V. M. Sharma, C. Bruneau* **6092–6096**

💻 Preparation of Sugar β-Amino Acid Derivatives with Cyclic Structures by Ring-Closing Metathesis

Keywords: Amino acids / Metathesis / Ruthenium / Carbohydrates



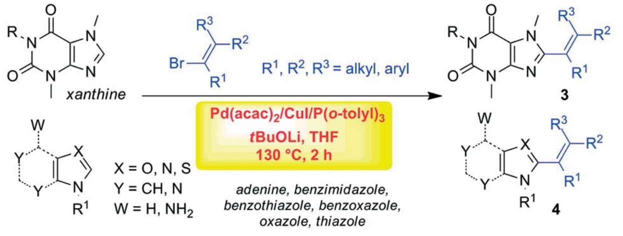
Efficient syntheses of β-amino acid derivatives with cyclic structures were developed. The key steps involve aza-Michael addition and ruthenium-catalyzed allylation for the construction of new acyclic β-amino acid dienes incorporating a sugar fragment, and a ruthenium-catalyzed ring-closing metathesis for the construction of the seven- and nine-membered ring compounds.

C–H Direct Alkenylation

S. Sahnoun, S. Messaoudi, J.-D. Brion, M. Alami* **6097–6102**

💻 Pd/Cu-Catalyzed Direct Alkenylation of Azole Heterocycles with Alkenyl Halides

Keywords: C-H activation / Palladium / Copper / Nitrogen heterocycles / Alkenes



The use of alkenyl bromides as partners in the direct Pd–Cu-catalyzed C–H alkenylation of xanthine allows the preparation of biologically interesting **3** in good yields. Extension of this process to various heterocycles is reported. In addition, the first example of the Pd-catalyzed direct benzylation of caffeine is described.

* Author to whom correspondence should be addressed.

💻 Supporting information on the WWW (see article for access details).