

The ISHC Bulletin

Recent Publications of ISHC Members

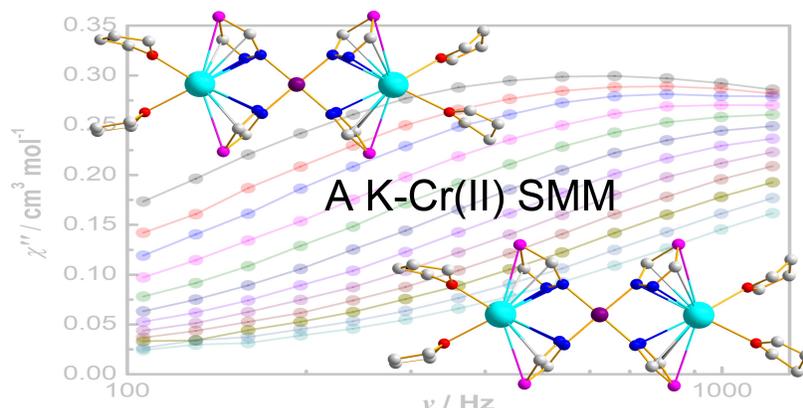
Issue 45; June/July 2020; PART II

1,2-Diaza-4-phospholide Complexes of Chromium(II): Dipotassium Organochromates Behaving as Single-Molecule Magnets

Jing Su, Lei Yin, Zhongwen Ouyang, Zhenxing Wang,* and Wenjun Zheng* (zxwang@hust.edu.cn or wjzheng_sxnu@qq.com)

Dalton Trans. **2020**, 49, 6945–6949.

DOI: 10.1039/d0dt00878h



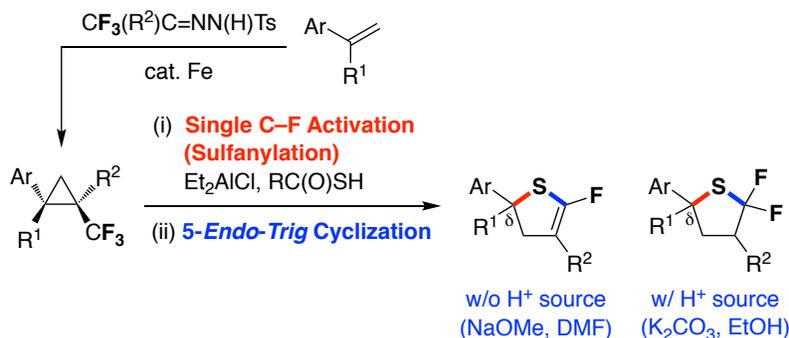
Abstract: The 1,2-diaza-4-phospholide (dp-) dipotassium ate complexes of chromium(II) $\{[(\eta^1\text{-}N\text{-}3,5\text{-}t\text{Bu}_2\text{dp})_4\text{Cr}][(\eta^5\text{-}(N,N,C,C,P)\text{-}K(\eta^2\text{-}(O,O\text{-}THF)_2)_2)]\}$ (**5**) and $\{[(\eta^1\text{-}N\text{-}3,5\text{-}Ph_2dp)_4\text{Cr}](\eta^5\text{-}(N,N,C,C,P)\text{-}K(\eta^2\text{-}(O,O\text{-}THF)_2)_2)\}_\infty$ (**6**) were synthesized and characterized by the X-ray single crystal structure analysis. Complex **5** with a near-square planar geometry at the chromium(II) ion was unambiguously characterized by the high field electron paramagnetic resonance (HF-EPR) technique and magnetic measurements, revealing that it was a field-induced single-molecule magnet (SMM).

Synthesis of Ring-Fluorinated Thiophene Derivatives Based on Single C–F Bond Activation of CF₃-Cyclopropanes: Sulfanylation and 5-endo-trig Cyclization

Kohei Fuchibe, Tatsuki Fushihara, and Junji Ichikawa* (junji@chem.tsukuba.ac.jp)

Org. Lett. **2020**, 22, 2201–2205.

DOI: 10.1021/acs.orglett.0c00385

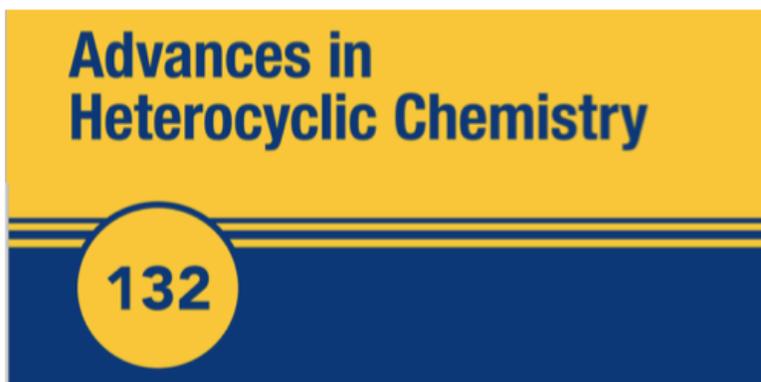


Abstract: Treatment of CF₃-bearing cyclopropanes with Et₂AlCl generated stabilized difluorocarocations, which underwent a nucleophilic addition of thiocarboxylic acids or thiols. The sulfur functionality was introduced at the position δ to the fluorine substituents in a regioselective manner (single activation of CF₃-cyclopropanes). The formed 1,1-difluoro-1-alkenes underwent successive deesterification/5-endo-trig cyclization. Intramolecular vinylic substitution proceeded in an aprotic solvent, whereas intramolecular addition proceeded in a protic solvent to afford pharmaceutically and agrochemically promising 2-fluoro-4,5-dihydrothiophene and 2,2-difluoro-4,5-dihydrothiophene scaffolds, respectively.

Synthesis and Reactivity of Fluorinated Heterocycles

Frederick A. Luzzio* (faluzz01@louisville.edu)

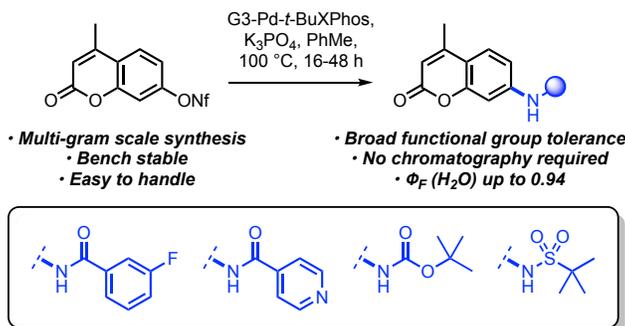
Advances in Heterocyclic Chemistry Vol. 132; ISBN: HC: 9780128211687; eB: 9780128211724
 Scriven, E. F. V.; Ramsden, C. A., Eds. Elsevier, 2020, Chapter 1, pp 1–84.



Abstract: The synthesis of heterocycles and their fluorinated analogues is a central focus within the development of medicinal compounds, agrochemicals and advanced materials. New synthetic strategies are constantly contrived for the incorporation of fluorine into heterocycles and their further utilization as viable synthetic intermediates. In biomolecules the replacement of hydrogen with fluorine offers substantial diversity and latitude in terms of conformation, stability, transport, or metabolism. This chapter addresses developments reported throughout the past 25 years which involve both the preparation and reactions of fluorinated heterocycles. While the bulk of the coverage is in the 25-year window, some earlier work is included in order to provide perspective. The chapter begins with coverage of the smallest ring systems and progresses to polycyclic heterocyclic systems, and within each ring system, its chemical preparation and derivatization is detailed and is followed by the specific reactions that each system undergoes. The preparation and reactions of heterocyclic compounds having fluorine directly on the ring is detailed, compounds having fluorinated alkyl group side chains (e.g., difluoromethyl, trifluoromethyl, and pentafluoroethyl) are not included in the coverage.

Cross-Coupling of Amide and Amide Derivatives to Umbelliferone Nonaflates: Synthesis of Coumarin Derivatives and Fluorescent Materials

Shane M. Hickey, Samuel O. Nitschke, Martin J. Sweetman, Christopher J. Sumbly, Douglas A. Brooks, Sally E Plush, and Trent D. Ashton* (ashton.t@wehi.edu.au)
J. Org. Chem. **2020**, *85*, 7986–7999. DOI: 10.1021/acs.joc.0c00813



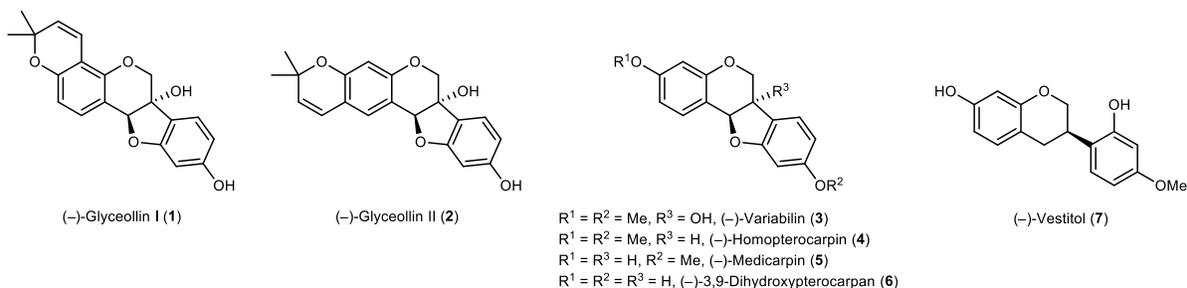
Abstract: The Buchwald–Hartwig cross-coupling reaction between 4-methylumbelliferone-derived nonaflates with amides, carbamates, and sulfonamides is described. A wide variety of *N*-substituted 7-amino coumarin analogues was prepared in good to excellent yields. The photophysical properties of aqueous-soluble derivatives were determined, and they displayed auxochrome-based variations. Gram-scale synthesis provided an acrylamide analogue, which was used to fabricate a fluorescent poly(2-hydroxyethyl methacrylate) (pHEMA) hydrogel that was resistant to leaching in ultrapure H₂O. We envisage that our reported protocol to access 7-amino-4-methylcoumarin derivatives will find use toward the development of new fluorescent coumarin-based probes by researchers in the field.

Asymmetric One-Pot Transformation of Isoflavones to Pterocarpan and its Application in Phytoalexin Synthesis

Philipp Ciesielski and Peter Metz* (peter.metz@chemie.tu-dresden.de)

Nat. Commun. **2020**, *11*, 3091 (1–8).

DOI: 10.1038/s41467-020-16933-y



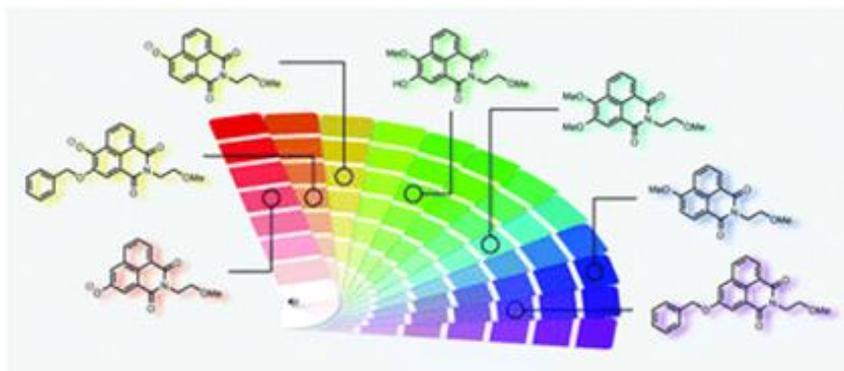
Abstract: Phytoalexins have attracted much attention due to their health-promoting effects and their vital role in plant health during the last years. Especially the 6a-hydroxypterotharpan glyceollin I and glyceollin II, which may be isolated from stressed soy plants, possess a broad spectrum of bioactivities such as anticancer activity and beneficial contributions against western diseases by anti-oxidative and anti-cholesterolemic effects. Aiming for a catalytic asymmetric access to these natural products, we establish the asymmetric syntheses of the natural isoflavonoids (-)-variabilin, (-)-homopterotharpin, (-)-medicarpin, (-)-3,9-dihydroxypterotharpan, and (-)-vestitol by means of an asymmetric transfer hydrogenation (ATH) reaction. We successfully adapt this pathway to the first catalytic asymmetric total synthesis of (-)-glyceollin I and (-)-glyceollin II. This eight-step synthesis features an efficient one-pot transformation of a 2^h-hydroxyl-substituted isoflavone to a virtually enantiopure pterocarpan by means of an ATH and a regioselective benzylic oxidation under aerobic conditions to afford the susceptible 6a-hydroxypterotharpan skeleton.

Mixed Alkoxy/Hydroxy 1,8-Naphthalimides: Expanded Fluorescence Colour Palette and *in vitro* Bioactivity

Elley E. Rudebeck, Rosalind P. Cox, Toby D. M. Bell, Rameshwor Acharya, Zikai Feng, Nuri Gueven, Trent D. Ashton,* and Frederick M. Pfeffer* (ashton.t@wehi.edu.au or fred.pfeffer@deakin.edu.au)

Chem. Commun. **2020**, *56*, 6866–6869.

DOI: 10.1039/d0cc01251c



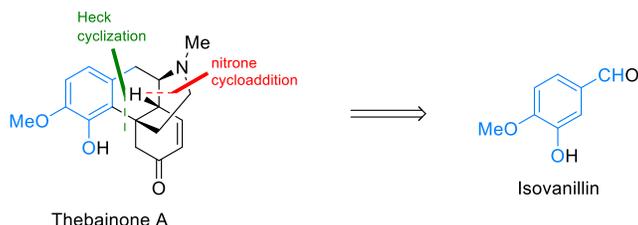
Abstract: An efficient and functional group tolerant route to access hydroxy 1,8-naphthalimides has been used to synthesize a range of mono- and disubstituted hydroxy-1,8-naphthalimides with fluorescence emissions covering the visible spectrum. The dialkoxy substituted compounds prepared possess high quantum yields (up to 0.95) and long fluorescent lifetimes (up to 14 ns). The method has been used to generate scriptaid analogues that successfully inhibit HDAC6 *in vitro* with tubulin acetylation assays confirming that these compounds are more effective than tubastatin.

Total Synthesis of (±)-Thebainone A by Intramolecular Nitronc Cycloaddition

Yuzhou Wang, André Hennig, Thomas Küttler, Christian Hahn, Anne Jäger, and Peter Metz*
(peter.metz@chemie.tu-dresden.de)

Org. Lett. **2020**, *22*, 3145–3148.

DOI: 10.1021/acs.orglett.0c00905



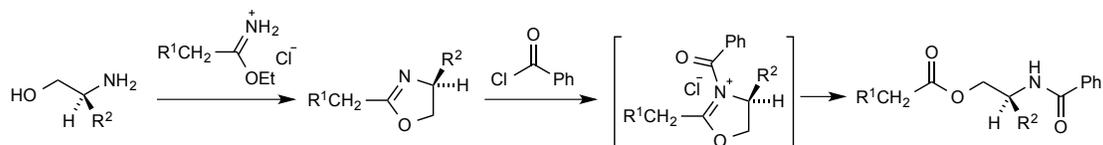
Abstract: Using an intramolecular nitronc cycloaddition and a Heck cyclization as the crucial transformations, a total synthesis of the racemic morphine alkaloid thebainone A was accomplished in 22 steps commencing with isovanillin.

Generation and Hydrolysis of *N*-Acylloxazolinium Salts Allowing Regiospecific Acylation of Chiral Amino Alcohols

R. Alan Aitken,* Alexandra M. Z. Slawin, and Andrew Wilson (raa@st-and.ac.uk)

Chem. Heterocycl. Comp. **2020**, *56*, 611–614.

DOI: 10.1007/s10593-020-02707-3



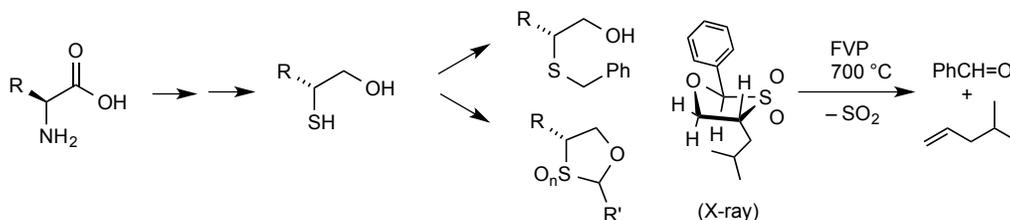
Abstract: In an attempt to form 2-alkylidene-1,3-oxazolidines, chiral 2-oxazolines have been *N*-alkylated and *N*-acylated. Two new *N*-methyloxazolinium salts have been prepared and characterised but base treatment resulted in their decomposition. In contrast, attempts to isolate three *N*-benzyloxazolinium salts gave the products of their ring hydrolysis: unsymmetrically diacylated amino alcohols whose structure was confirmed by X-ray diffraction in one case. Overall the method allows stepwise regiospecific *N,O*-diacylation of 1,2-amino alcohols.

Synthesis, Structure and Reactivity of Some Chiral Benzylthio Alcohols, 1,3-Oxathiolanes and their *S*-Oxides

R. Alan Aitken,* Philip Lightfoot, and Andrew W. Thomas (raa@st-and.ac.uk)

J. Sulfur Chem. **2020**, *41*, 369–387.

DOI: 10.1080/17415993.2020.1754418



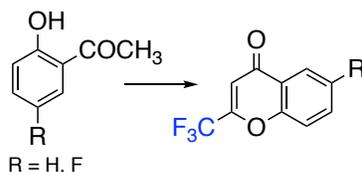
Abstract: A series of amino acid-derived chiral benzylthio alcohols have been prepared and characterized. A chiral mercapto alcohol derived from *S*-leucine has been used to form three chiral 2,4-disubstituted 1,3-oxathiolanes. One of these has been oxidized to the *S*-oxide and another to the *S,S*-dioxide. The *cis* and *trans* isomers have been characterized by ¹H NMR in each case and it appears that thermal epimerisation at C-2 is possible at the sulfoxide oxidation state. The X-ray structure of major *trans* diastereomer of 2-phenyl-4-isobutyl-1,3-oxathiolane *S,S*-dioxide shows an envelope conformation with oxygen at the flap and an internal angle at sulfur of just 93.8°. This compound fragments upon flash vacuum pyrolysis at 700 °C to give SO₂, benzaldehyde and 4-methylpent-1-ene.

Cyclodehydration and Baker-Venkataraman Rearrangement Methodologies for the Preparation of Fluorinated 4*H*-Chromones

Chloe Fernandes, Sang H. Park, Joseph Sloop,* and Karla Wilmott (jsloop@ggc.edu)

Chemical Methodologies **2020**, *4*, 554–564.

DOI: 10.33945/SAMI/CHEMM.2020.5.2



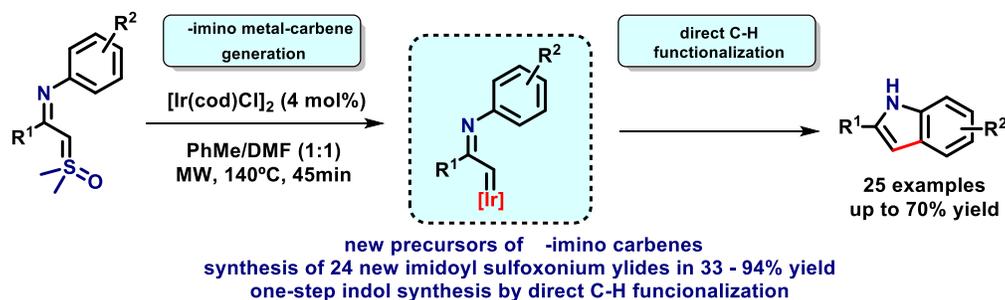
Abstract: Trifluoromethylated and ring-fluorinated 4*H*-chromones have been prepared via cyclodehydration and via the Baker–Venkataraman rearrangement. The cyclodehydration of 4,4,4-trifluoro-1-(1-naphthol-2-yl)-1,3-butanedione was performed under a variety of base promoted and acid catalyzed processes enroute to 2-trifluoromethyl-β-naphthochromone. Using microwave irradiative, sonication and conventional processes, selected *o*-hydroxyaromatic ketones underwent single-pot, base promoted Baker–Venkataraman rearrangements with trifluoroacetic anhydride to give trifluoromethylated 4*H*-chromones in yields ranging from 50–82%. Microwave irradiation conditions allowed for yields ranging from 50–80%, which compare favorably to yields achieved via conventional methods (60–82%) as well as reducing reaction times by 55% compared to conventional refluxing conditions.

α-Imino Iridium Carbenes from Imidoyl Sulfoxonium Ylides: Application in the One-Step Synthesis of Indoles

Clarice A. D. Caiuby, Matheus P. de Jesus, and Antonio C. B. Burtoloso* (antonio@iqsc.usp.br)

J. Org. Chem. **2020**, *85*, 7433–7445.

DOI: 10.1021/acs.joc.0c00833



Abstract: Imidoyl sulfoxonium ylides are presented for the first time as potential precursors to generate α-imino metal-carbene intermediates and applied in direct C–H functionalization reactions catalyzed by [Ir(cod)Cl]₂ (4 mol %) to provide 2-substituted indoles (up to 70% yield) in just one step. This class of sulfur ylide is successfully obtained from imidoyl chloride and dimethylsulfoxonium methylide (23 new examples in 45–85% yield) or by imino group formation from the corresponding β-keto sulfoxonium ylides and anilines in the presence of TiCl₄ as a Lewis acid (9 examples in 33–94% yield).