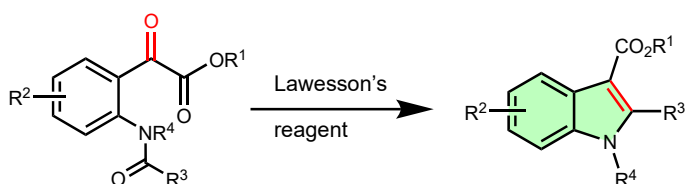


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Synthesis of Indoles through C2–C3 Bond Formation Using Lawesson's Reagent

Yao Cheng, Tom Yu, Mohan Bhadbhade, David StC Black, Naresh Kumar
J Org Chem. **2025**, 90, 3290-3300. DOI: 10.1021/acs.joc.4c02922

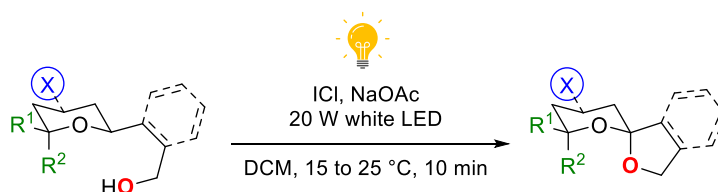


- 48 Examples
- Metal free
- Mild condition
- Good functional group tolerance
- Environmentally friendly

An efficient synthetic route for the construction of functionalized indoles has been developed through C2–C3 bond formation between amidophenylglyoxylic esters, mediated by Lawesson's reagent. This metal-free transformation facilitates the intramolecular annulation of two carbonyl functionalities—an amide and a keto ester—via a sulfur-mediated process. The method exhibits broad substrate tolerance, accommodating a diverse array of esters and amides, as well as various substituents on the benzene ring, while affording a wide range of 2,3-disubstituted indoles in moderate to good yields. Mechanistic investigations, including radical inhibition and by-product analysis, support a carbene-mediated pathway, as evidenced by the formation of elemental sulfur as a byproduct. The reaction also tolerates electronic variations on both the aromatic ring and the nitrogen substituent, underscoring its synthetic versatility. Furthermore, the process is scalable to gram quantities and readily facilitates downstream modifications of the indole core, including conversion to 2-substituted derivatives.

Oxidative Photochemical Cyclisations to Access Spiroketal

Jonathan Trevorrow, Nhlanhla Sibanda, Anne O'Kearney-McMullan, Lucie Miller Potucka, and Adrian P. Dobbs*
Adv. Synth. Catal. **2024**, 366, 4694 – 4701 DOI: <https://doi.org/10.1002/adsc.202400393>



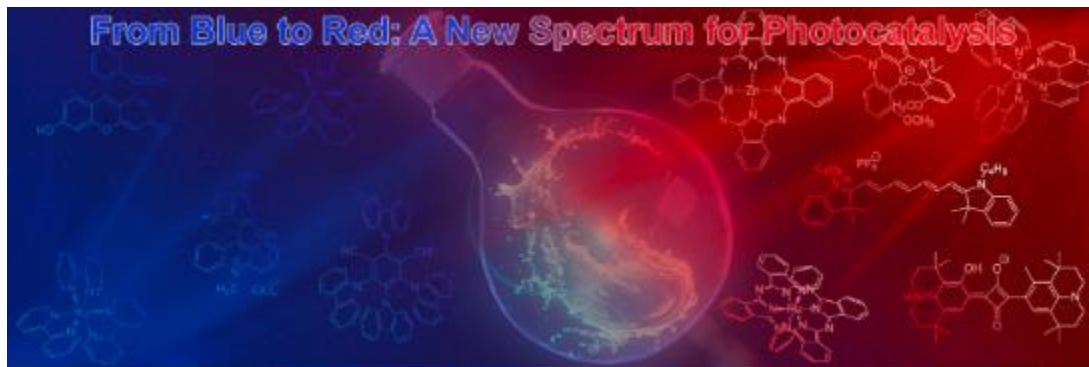
The spiroketal moiety is an important substructure within many biological natural products. One method to access them is *via* the oxidative cyclisation of a pendant hydroxyl group on to a pre-formed pyran. However applications of this methodology have been severely limited by requiring the use of toxic and powerful oxidants, such as lead (IV) tetraacetate or mercuric oxide. Herein we report a novel and high yielding photochemical route to prepare complex spiroketals using a photochemical oxidative approach with mild and non-toxic reagents and demonstrate the methodology to the synthesis of a number of insect pheromones.

Red light excitation: illuminating photocatalysis in a new spectrum

Lucas Fortier, Corentin Lefebvre, N. Hoffmann

Beilstein J. Org. Chem. **2025**, *21*, 296-326.

DOI: <https://doi.org/10.3762/bjoc.21.22>



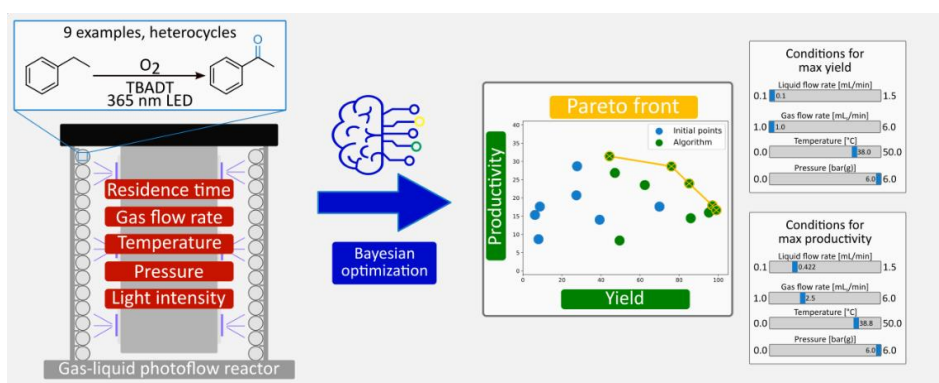
Red-light-activated photocatalysis has become a powerful approach for achieving sustainable chemical transformations, combining high efficiency with energy-saving, mild conditions. By harnessing the deeper penetration and selectivity of red and near-infrared light, this method minimizes the side reactions typical of higher-energy sources, making it particularly suited for large-scale applications. Recent advances highlight the unique advantages of both metal-based and metal-free catalysts under red-light irradiation, broadening the range of possible reactions, from selective oxidations to complex polymerizations. In biological contexts, red-light photocatalysis enables innovative applications in phototherapy and controlled drug release, exploiting its tissue penetration and low cytotoxicity. Together, these developments underscore the versatility and impact of red-light photocatalysis, positioning it as a cornerstone of green organic chemistry with significant potential in synthetic and biomedical fields.

Efficient multi-objective Bayesian optimization of gas-liquid photochemical reactions using an automated flow platform

Stefan Desimpel¹, Jan Dijkmans², Koen P.L. Kuijpers², Matthieu Dorbec^{2,*}, Kevin M. Van Geem³, Christian V. Stevens^{1*}

Chemical Engineering Journal, **2024**, *501*, 157685

DOI: 10.1016/j.cej.2024.157685

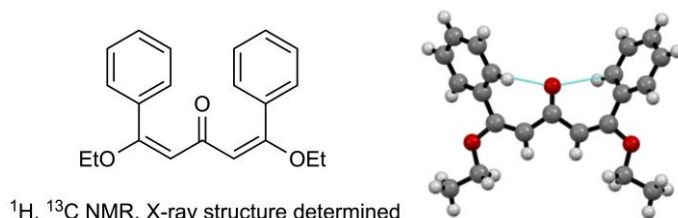


We developed an automated platform capable of performing photochemical gas-liquid reactions. The platform was augmented with a state-of-the-art Bayesian optimization algorithm and was tested on the decatungstate-catalyzed aerobic oxidation of ethyl benzene, to optimize both yield and productivity, and identify the Pareto front of these objectives. Although photochemical gas-liquid systems are highly complex due to numerous interactions between the parameters, including effects on mass-transfer, gas solubility and light absorption, the algorithm demonstrated impressive speed to navigate the parameter space towards optimal conditions. Furthermore, this approach also proved highly flexible, allowing for modification of objectives and parameter ranges on the fly. The identified conditions were then tested on a select scope of substrates, to better understand the generality of these conditions, especially on molecules where selectivity comes into play. The results show the platform to be a useful tool for reaction optimization and process intensification.

(*E,E*)-1,5-Diethoxy-1,5-diphenylpenta-1,4-dien-3-one

R. Alan Aitken, David B. Cordes, Verity Kennett and Aidan P. McKay
Molbank **2025**, 2025, M1986 (1–5).

DOI: 10.3390/M1986

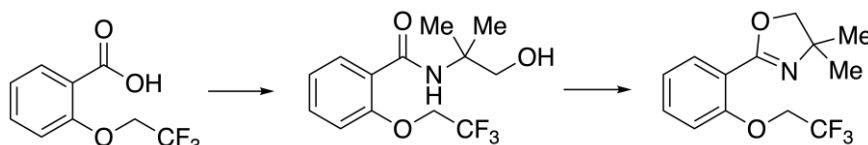


The title compound has been fully characterised for the first time. Fully assigned ¹H and ¹³C NMR spectra and the X-ray structure are presented.

Synthesis of a 2-(2-Trifluoroethoxyphenyl)oxazoline

R. Alan Aitken and Andrew D. Harper
Molbank **2025**, 2025, M1989 (1–5).

DOI: 10.3390/M1989

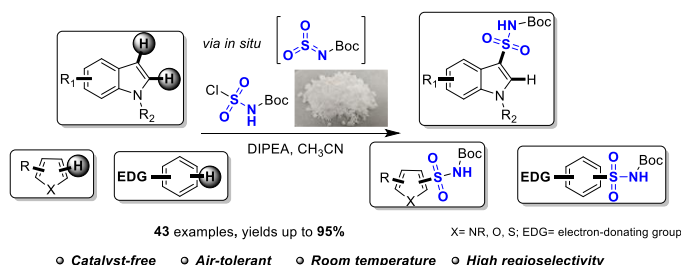


Full spectroscopic characterisation

The title compound has been prepared in four steps starting from ethyl 2-fluorobenzoate. The final product as well as the intermediates are fully characterised by spectroscopic methods with the ¹H and ¹³C NMR spectra, featuring coupling to ¹⁹F being particularly informative.

Direct Aminosulfonylation of Electron-rich (hetero)Arenes Utilizing tert-Butyl Chlorosulfonyl carbamate with Diisopropylethylamine.

Xiaofei Zhang, Jiangtao Tan, Yuancheng Zhong, Zhen Zhuang, Qian He, Min Jiang* and Chunhao Yang.*
Org. Chem. Front. **2025**, 12, 670–677. DOI: 10.1039/D4QO01731E



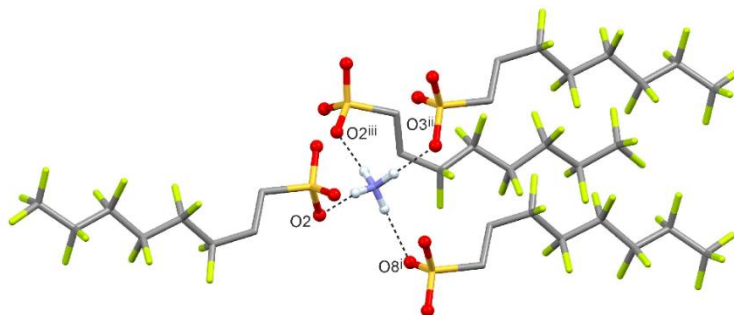
Sulfonamides, especially primary aryl sulfonamides, are very important scaffolds not only because of their wide applications as pharmacophores in drugs, but also their derivatization into other sulfonamides and different sulfur-containing compounds. Among aryl sulfonamides, most syntheses of electron-rich (hetero)aryl sulfonamides are still severely limited by the classic chlorosulfonation or oxidative chlorination reactions with significant drawbacks. In this work, using the proposed and unique tert-butyl sulfonylcarbamate intermediate generated in situ from easily accessible tert-butyl chlorosulfonylcarbamate and diisopropylethylamine, a catalyst-free, mild and very practical aminosulfonylation protocol for a wide range of electron-rich (hetero)arene substrates with good to excellent yields was reported.

Ammonium 6:2 fluorotelomer sulfonate: crystal structure, thermal analysis and use as internal standard in PFAS analysis

Johanna Freilinger,^{*} Thomas Gelbrich, Doris E. Braun, Ulrich J. Griesser, Rania Bakry, Volker Kahlenberg, Thomas Müller, Christoph Kreutz, Sven Nerdinger, Lukas Fliri, Herwig Schottenberger

Journal of Molecular Structure **2025**, 1327, 141232.

DOI: <https://doi.org/10.1016/j.molstruc.2024.141232>



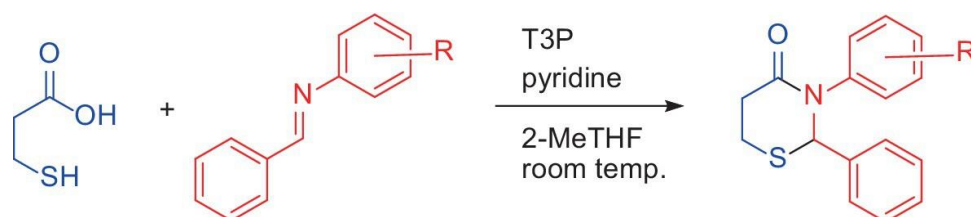
Alkali salts of the common fluorosurfactant 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-1-octanesulfonic acid (**6:2 FTSA**) exhibit a remarkably low solubility in water, which enables the precipitation of these salts from water. The same applies for the corresponding ammonium salt **6:2 FTS NH₄** which can be obtained in crystalline form by slowly adding aqueous ammonia to an aqueous solution of **FTSA**. To understand the cause of this behavior on a molecular basis, an X-ray single crystal structure determination of **6:2 FTS NH₄** was performed, allowing to further examine the molecular interactions in the solid state responsible for its low solubility. A hydrogen-bonded layer structure results from four distinct N—H···O interactions, that involve all four NH groups, the given ammonium ion and sulfonate-O atoms belonging to four different anion units. Columns of parallel aligned fluoroalkyl chains dominate the packing of molecules in the crystal. The characterization was accompanied by thermal as well as spectroscopic analysis. The lack of hygroscopicity and its high thermal stability make **6:2 FTS NH₄** a suitable gravimetric standard substance for analytical applications. HPLC MS/MS measurements showed that **6:2 FTS NH₄** can adequately substitute commercial ¹³C labelled compounds at least for routine analysis of common perfluorinated contaminants using standard internal calibration.

T3P-Promoted Synthesis of a Series of Novel 3-Aryl-2-phenyl-2,3,5,6-tetrahydro-4H-1,3-thiazin-4-ones

Lee J. Silverberg, Tapas Mal, Anthony Lagalante, Mark Olsen, Michael Fleming, Tracy Garcia, Aloura Gavalis, Kyanna Gonzalez, Casey Gregory, Laine Hackenberg, Madeline Lawler, Eddie Li, Evelyn Louca, Shaheem Mack, Kristen Perhonitch, Kelsey Shaffer, Carter Thompson, Sarah Tran, Evan Vidal, Ryan Vidal

J. Heterocycl. Chem. **2025**, 62, 338-344.

DOI: 10.1002/jhet.4938



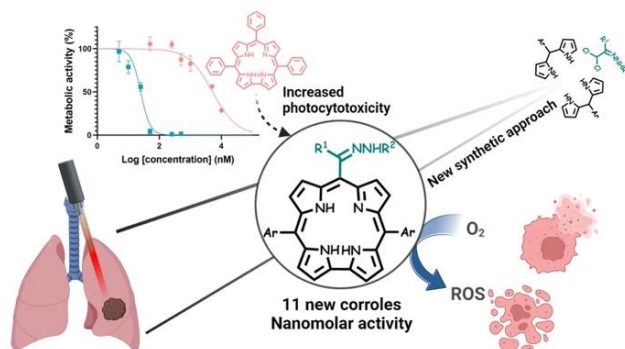
A series of 12 novel 3-aryl-2-phenyl-2,3,5,6-tetrahydro-4H-1,3-thiazin-4-ones was prepared at room temperature by T3P-mediated cyclization of C-phenyl-N-aryl imines with 3-mercaptopropionic acid. Both electron-withdrawing and electron-donating substituents were used. All substituents were successful, including *p*-nitro. Some reactions were run as 3-component reactions, forming the imine in situ. The reactions were operationally simple and gave yields as high as 79%. An example was also done where a *p*-nitro group was on both the C-aryl and the N-aryl. This provides ready access to N-aryl compounds in this family, which have been generally difficult to prepare.

Hydrazone-functionalized *trans*-A₂B-Corroles: Effective Synergy in Photodynamic Therapy of Lung Cancer

Bruna D. P. Costa, João C. S. Simões, Susana M. M. Lopes, Mafalda Laranjo, Ana Clara B. Rodrigues, Ana Cristina Gonçalves, J. Sérgio Seixas de Melo, M. Filomena Botelho, Marta Pineiro, Teresa M. V. D. Pinho e Melo*

J. Med. Chem. **2024**, 67, 21934-21951.

<https://doi.org/10.1021/acs.jmedchem.4c01824>



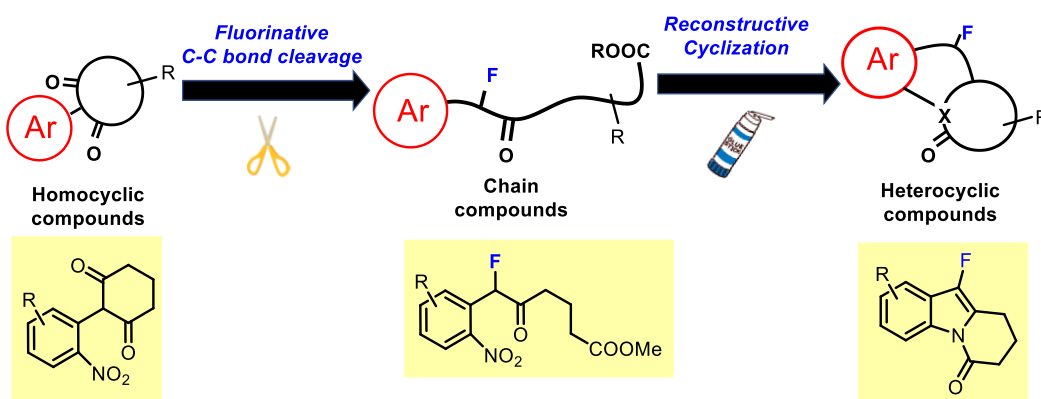
A synthetic route to *trans*-A₂B-corroles combining the macrocyclic core with a hydrazone moiety, based on the reactivity of azoalkenes toward dipyrromethanes, has been established with the aim of developing a new class of photosensitizers for photodynamic therapy of lung cancer. The study of the photophysical properties of the novel macrocycles allowed the identification of photosensitizers with absorption within the phototherapeutic window and high singlet oxygen quantum yield. Relevant structure–photodynamic activity correlations were established by studying the new corroles-based photodynamic therapy (PDT) in human lung cancer cell lines (A549 and H1299). The methyl-hydrazone corroles were more active than phenylhydrazone corroles, with the N-Boc and N-Ts groups being key structural features to ensure high activity. The lead photosensitizers, with IC₅₀ values below 100 nM and no cytotoxicity per se, were significantly more active than 5,10,15-triphenylcorrole, showing that the presence of the hydrazone functional group has a strong influence on PDT activity.

Reconstructive Synthesis of Fluorinated [1,2-*a*]dihydropyridoindolones by a Cyclohexadione Cut-to-Fuse Strategy

Hideyasu China,* Yuusuke Yoto, Hirotaka Sasa, Kotaro Kikushima, Toshifumi Dohi*

Adv. Synth. Catal. **2025**, 367, e202401037.

DOI: <https://doi.org/10.1002/adsc.202401037>



We describe a fluorinative ring-cleavage reaction that breaks C–C bonds in cyclic β-diketones bearing aryl moiety using *N*-fluorobenzenesulfonimide (NFSI) in the presence of inorganic carbonates (Cs₂CO₃ or K₂CO₃) in methanol at room temperature within one hour. Generated fluorinated keto acid esters bearing ortho-nitro aryl groups were transformed into fluorinated dihydropyrido[1,2-*a*]indolones (DHPis) via reductive cyclization using B₂(OH)₄ followed by amidation in the presence of K₂CO₃. This "cut-to-fuse" strategy enables the reconstructive synthesis of valuable fused heterocycles from relatively simple cyclohexadione.

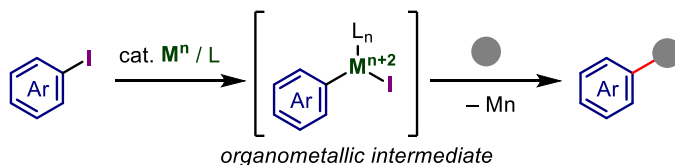
Iodoarene Activation: Take a Leap Forward Toward Green and Sustainable Transformations

Toshifumi Dohi,* Elghareeb E. Elboray, Kotaro Kikushima, Koji Morimoto, Yasuyuki Kita*

Chem. Rev. 2025, 125, 3440-3550.

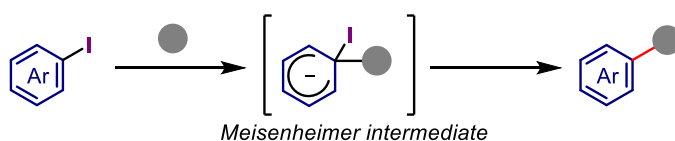
DOI: <https://doi.org/10.1021/acs.chemrev.4c00808>

a) Transition metal-catalyzed cross-coupling (M = metal, L = ligand)



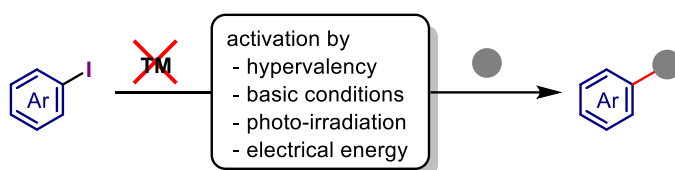
- requiring expensive and rare metal complex
- generating metal wastes - unsustainable chemistry

b) Direct nucleophilic aromatic substitution (S_NAr)



- limitation of substrates and nucleophiles - harsh conditions

c) Transition-metal-free activation of iodoarene



- transition metal-free process - less toxicity
- mild and cost-effective conditions - sustainable chemistry

Constructing chemical bonds under green sustainable conditions has drawn attention from environmental and economic perspectives. The dissociation of (hetero)aryl–halide bonds is a crucial step of most arylations affording (hetero)arene derivatives. Herein, we summarize the (hetero)aryl halides activation enabling the direct (hetero)arylation of trapping reagents and construction of highly functionalized (hetero)arenes under benign conditions. The strategies for the activation of aryl iodides are classified into (i) hypervalent iodoarene activation followed by functionalization under thermal/photochemical conditions, (ii) aryl–I bond dissociation in the presence of bases with/without organic catalysts and promoters, (iii) photoinduced aryl–I bond dissociation in the presence/absence of organophotocatalysts, (iv) electrochemical activation of aryl iodides by direct/indirect electrolysis mediated by organocatalysts and mediators acting as electron shuttles, and (v) electrophotochemical activation of aryl iodides mediated by redox-active organocatalysts. These activation modes result in aryl iodides exhibiting diverse reactivity as formal aryl cations/radicals/anions and aryne precursors. The coupling of these reactive intermediates with trapping reagents leads to the facile and selective formation of C–C and C–heteroatom bonds. These ecofriendly, inexpensive, and functional group-tolerant activation strategies offer green alternatives to transition metal-based catalysis.