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Insights

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SNAPSHOTS OF SOME TOPICS OF INTEREST OF RECENT NOTABLE ADVANCES IN CHEMISTRY

- 2,2,2-Trichloroethoxycarbonyl azide as efficient aminating agent for carbonyl-directed, Iridium-catalyzed C-H amination
- Isolation of n-type semiconductor with high electron mobility
- Stereoselective synthesis of *cis*-α,α-difluorocyclopropanes: 4 ⟶ 3 fluorinative ring contraction
- Synthesis of cyclohepta[*b*]indoles and cyclohepta[*b*]pyrroles

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Snapshots of some topics of interest of recent notable advances in chemistry

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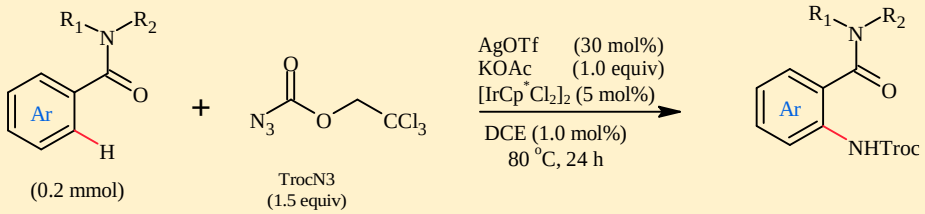
2,2,2-Trichloroethoxycarbonyl Azide as Efficient Aminating Agent for Carbonyl-Directed, Iridium-Catalyzed C-H Amination

The snapshot describes an iridium-mediated, carbonyl-directed C-H mono amination of arenes using 2,2,2-trichloroethoxycarbonyl azide ($TrocN_3$) as an aminating agent.

KEYWORDS: C-H amination, Aminating reagents, Organic azides, TM Catalysis.

Ortho-amino arylketones are valuable intermediates in medicinal chemistry. The available synthetic pathways of these compounds are still limited. In fact, the use of ketone, a weakly coordinating group, as a functional group-directed amination of an *ortho*-C-H bond of arenes in a catalytic reaction is difficult due to the enolization and minimal Lewis basicity of ketone, which is a burden on the catalytic process to generate a durable metallocyclic intermediate. However, a limited range of ketone-directed C-H amination of arenes has been developed, in which the nitrogen atom of aminating sources is attached to a strongly electron-withdrawing groups, such as sulfonyl, carbonyl phosphoryl, or azide group, leading to enhancement of the reactivity of aminating agents as well as to reduce the coordinative ability of amination products.

In this context, Lu and co-workers reported a synthetic procedure based on organic azides, taking advantage of the unique properties of these functional groups in catalytic C-H amination reactions such as synthetic simplicity, mild reaction condition, green byproduct, and compatibility with other functional groups. The approach is based on an iridium-catalyzed, carbonyl-directed C-H mono amination of arenes using $[Cp^*Ir(III)Cl_2]_2$ as a catalyst and 2,2,2-trichloroethoxycarbonyl azide ($TrocN_3$) as an aminating agent (Scheme 1). The choice of using $TrocN_3$ is related to the strong electron-withdrawing property of Troc group, which can enhance the reactivity of $TrocN_3$. In addition, the resulting aminated products with sequentially attached Troc groups are easily removed by deprotection and can provide an opportunity for subsequent transformations.



Scheme 1. Amination of arylcarbonyl compound using iridium as a catalyst, $TrocN_3$ as an aminating source and KOAc as an additive.

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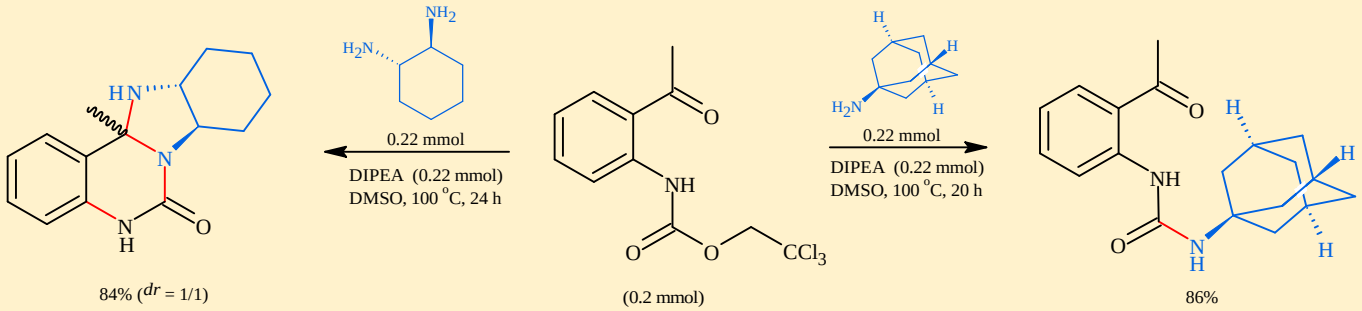
The amination proceeds smoothly with a wide range of substrates, including alkyl and vinyl arylketones, secondary and tertiary aryl amides, and acetyl indoles. The reaction exhibits excellent functional group tolerance.

In the post-transformation processes, the obtained aminated products contain two electrophilic carbonyl groups, namely Troc and ketone functionalities, which the selective deprotection of the Troc group by a single nucleophile was achieved, generating different arylamines, whereas the dinucleophilic reagent was simultaneously coupled with two electrophilic sites of the Troc-NH amination products, providing fused N-heterocyclic compounds (Scheme 2). The functional group conversion conditions are simple and compatible with a variety of single and dual nucleophilic reactants.



Scheme 2. Synthetic transformations of aminated products to arylamines and fused N-heterocyclic compounds.

This C−H bond amination procedure will expand the synthetic utility of directing group in the synthesis of complex molecules.

Review

X. Dong, M. Shang, S. Chen, T. Zhang, H. B. Jalani, H. Lu, *J. Org. Chem.*, **2022**, *87*, 13990-14004.

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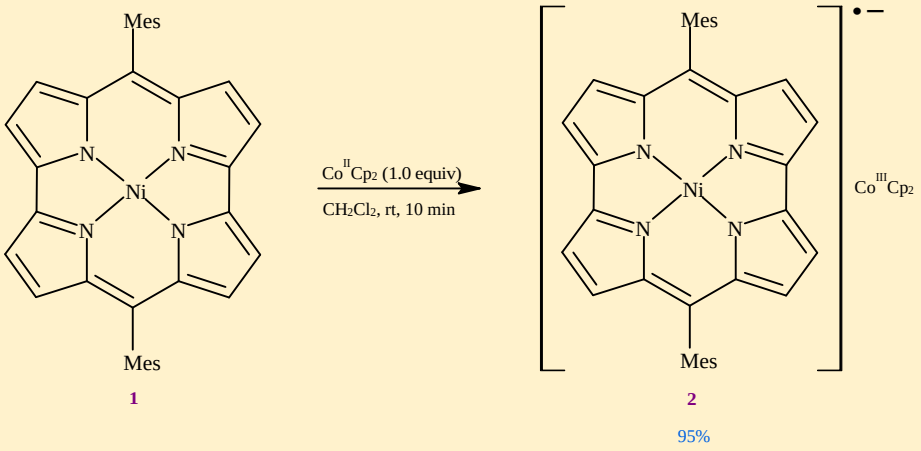
Isolation of n-type Semiconductor with High Electron Mobility

Isolation of Ni(II) *meso*-dimesitylnorcorrole radical anion *via* one-electron reduction of the corresponding neutral norcorrole is described.

KEYWORDS: Radical anion, Norcorrole, Antiaromatic.

In a general sense, the strategy for designing a π-conjugated compound with high carrier mobility is to impose small reorganization energies through suppressing structural changes upon electron injection. Based on this approach, Shinokubo and co-workers reported the preparation of a radical anion of Ni(II) *meso*-dimesityl-norcorrole **2** *via* one-electron reduction of the corresponding neutral molecule **1** by cobaltocene ($Co^{II}Cp_2$) (Scheme 1). The antiaromatic compound **1** with a 16 π-electronic system is characterized by its multi-redox abilities due to their narrow HOMO-LUMO energy gap.



1 2

95%

Scheme 1. Chemical reduction of **1** to yield radical anion **2**.

Radical anion **2** exhibited high stability under degassed solution conditions. Whereas X-ray structure analysis of **2** indicated that the structural change by one-electron reduction is small. Moreover, it showed good electron-affinity as seen in its reduction potential of – 0.92 V vs a ferrocene/ferrocenium couple (Fc/Fc^+).

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This study highlights appealing features of norcorrole, which should assist in the further architecture of n-type semiconductors.

Review

S. Ukai, N. Fukui, T. Ikeue, H. Shinokubo, *Chem. Lett.*, **2022**, *51*, 182-184.

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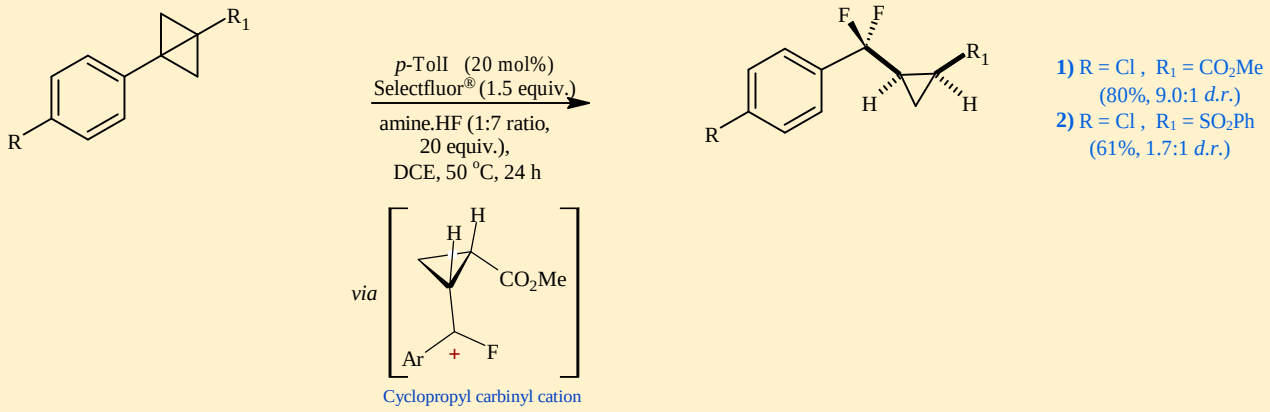
Stereoselective Synthesis of *cis*-α,α-Difluorocyclopropanes: 4→3 Fluorinative Ring Contraction

A facile synthetic pathway of *cis*-α,α-difluorocyclopropanes is highlighted, in which a skeletal rearrangement of disubstituted bicyclobutanes was achieved via I(I)/I(III)-catalysis in the presence of HF source.

KEYWORDS: Cyclopropanes, Fluorination, Isosteres, Hypervalent iodine.

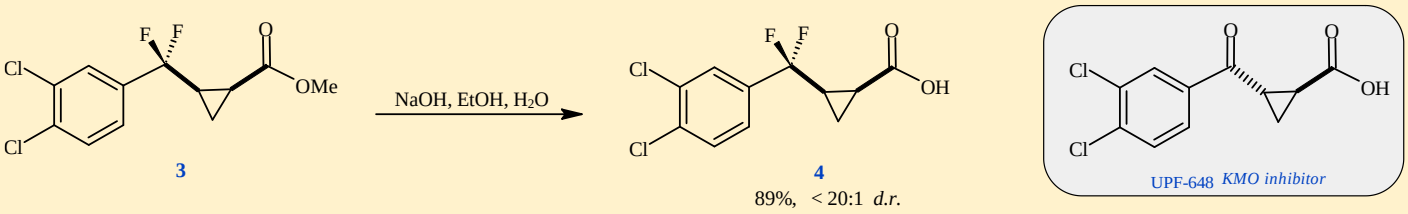
The combination of cyclopropyl isosteres with fluorine plays an important role in the drug discovery. Moreover, the conformationally restricted isosteres of 1,4-dicarbonyl groups are ubiquitous in biology, which can be generated from the *cis*-configured derivatives.
Gilmour and his team reported a synthetic route for *cis*-α,α-difluorocyclopropanes based on the fluorinated skeletal rearrangement of disubstituted bicyclobutanes **1** that uses *p*-TolI as catalyst, Selectfluor as a terminal oxidant, amine.HF complexes as a fluoride source, and DCE as the reaction medium (Scheme 1). The Brønsted acidity of the HF serves to unmask **1** and reveal a cyclobutene, this then engages with *in situ* generated *p*-TolIF$_2$. A fluorination/ stereospecific ring contraction/fluorination sequence provides the *cis* product with high levels of selectivity (up to >20:1 *cis*/*trans*) and up to 88% yield.



Scheme 1. Synthesis of *cis*-α,α-difluorocyclopropanes by I(I)/I(III) catalysis. Note: exposing cyclobutene directly to the reaction conditions led to rapid decomposition. Whereas, exposure of bicyclobutane *p*-F-Ph to these conditions resulted in an inversion of diastereoselectivity to favor the *trans* product.

Mechanistic studies revealed that this unprecedented 4 → 3 rearrangement proceeds via a cation in which all three substituents confer a stabilizing effect. Furthermore, to being benzylic, this cation is stabilized by the cyclopropyl Walsh orbitals and the proximal fluorine atom.

The synthetic utility of the difluorocyclopropyl motif facilitates access to structural isosteres of I,4-dicarbonyl compounds. Compound **4** is a fluorinated analogue of the UPF-648, which has a range of clinical applications in translational neurology (Scheme 2).



Scheme 2. Preparation of a fluorinated analogue of the API, UPF-648.

The authors anticipated that this study will stimulate interest in the activation of strained-ring systems by hypervalent iodine catalysis.

Review

K. Livingstone, K. Siebold, S. Meyer, V. Martín-Heras, C. G. Daniliuc, R. Gilmour, *ACS Catal*., **2022**, *12*, 14507−14516.

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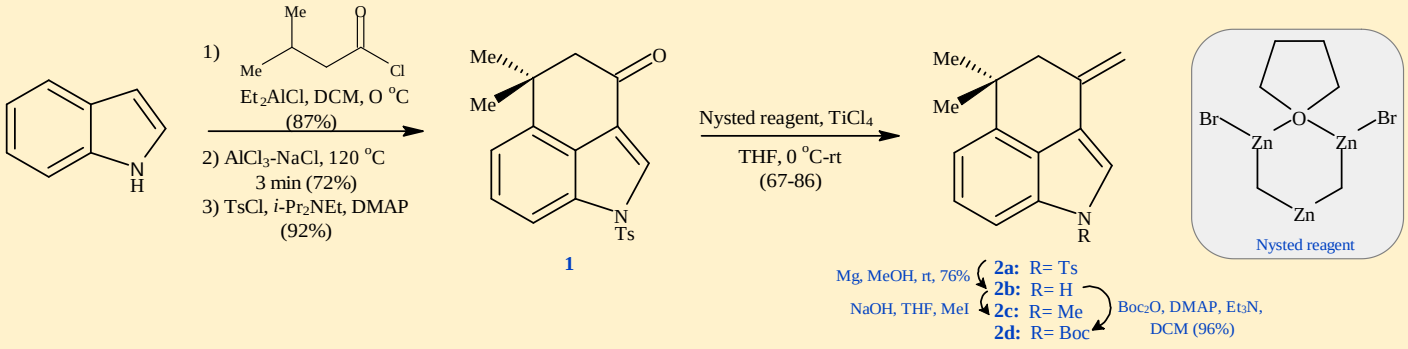
Synthesis of Cyclohepta[*b*]indoles and Cyclohepta[*b*]pyrroles

A one-step synthetic procedure of cyclohepta[*b*]indoles and cyclohepta[*b*]pyrroles is outlined based on the dearomative (4+3) cycloaddition reactions of 3-alkenylindoles and 3-alkenylpyrroles with *in situ*-generated oxyallyl cations.

KEYWORDS: Heterocycles, Dearomative (4+3) cycloaddition, Oxyallyl cations.

Indoles and pyrroles and their derivatives are important units in the skeletons of a range of bioactive natural products. Considerable efforts have been devoted to designing robust synthetic routes for natural products containing these scaffolds embedded in their complex architectures. Further stimulation of these efforts, Taenzler *et al.* described a synthetic procedure for cyclohepta[*b*]indoles and cyclohepta[*b*]pyrroles based on dearomative (4+3) cycloaddition of alkenylindoles and alkenylpyrroles with oxyallyl cations.

The substrate tricyclic *N*-tosyl-3-alkenylindole **2a** was prepared from ketone **1** using Nysted reagent (Scheme 1), whereas silyl enol ether acetal **3** was employed as a oxyallyl cation precursor. The cyclohepta[*b*]indole **4** was obtained in high yields and diastereoselectivities from the (4+3) cycloaddition of substrate **2a** with acetal **3** in the presence of Lewis acid-promoted the reaction, TMSOTf, and THF as an optimal solvent that exhibits the ability to stabilize the *in situ*-generated oxyallyl cation (Scheme 2).



Scheme 1. Synthesis of the 3-Alkenyindole Compound.

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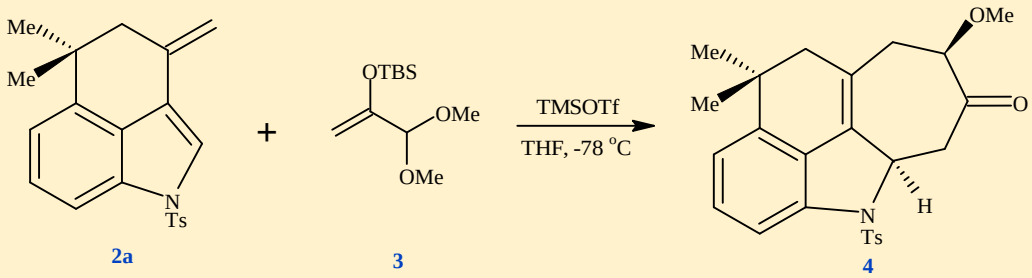
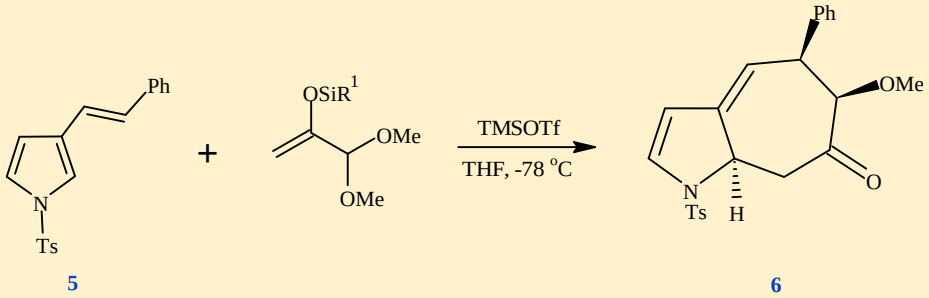


Scheme 2. Dearomative (4 + 3) Cycloadditions between alkenylindoles and dimethyl Acetal.

The 3-alkenylpyrrole substrates **5** underwent the dearomative (4+3) cycloaddition reaction yielding the corresponding cycloadducts **6** in good yield (Scheme 3).



Scheme 3. Dearomative (4 + 3) Cycloadditions between alkenylpyrroles and TBS enol ether dimethyl Acetal.

This synthetic procedure enables the one-step construction of the structurally complex core skeletons existed in a wide range of bioactive natural products.

Review

F. Taenzler, J. Xu, S. Athe, V. H. Rawal, *Org. Lett*., **2022**, *24*, 8109−8114.