Organic &
Biomolecular Chemistry

ROYAL SOCIETY
OF CHEMISTRY

REVIEW

View Article Online
View Journal | View Issue

Check for updates

Cite this: *Org. Biomol. Chem.*, 2024, **22**, 3109

Phenyliodine bis(trifluoroacetate) as a sustainable reagent: exploring its significance in organic synthesis

Sumit Kumar,†[a] Aditi Arora,†[a] Sunil K. Singh, *[b] Rajesh Kumar,[c]
Bhawani Shankar [d] and Brajendra K. Singh *[a]

Received 3rd December 2023,
Accepted 15th March 2024

DOI: 10.1039/d3ob01964k

rsc.li/obc

Iodine-containing molecules, especially hypervalent iodine compounds, have gained significant attention in organic synthesis. They are valuable and sustainable reagents, leading to a remarkable surge in their use for chemical transformations. One such hypervalent iodine compound, phenyliodine bis(trifluoroacetate)/bis(trifluoroacetoxy)iodobenzene, commonly referred to as PIFA, has emerged as a prominent candidate due to its attributes of facile manipulation, moderate reactivity, low toxicity, and ready availability. PIFA presents an auspicious prospect as a substitute for costly organometallic catalysts and environmentally hazardous oxidants containing heavy metals. PIFA exhibits remarkable catalytic activity, facilitating an array of consequential organic reactions, including sulfenylation, alkylarylation, oxidative coupling, cascade reactions, amination, amidation, ring-rearrangement, carboxylation, and numerous others. Over the past decade, the application of PIFA in synthetic chemistry has witnessed substantial growth, necessitating an updated exploration of this field. In this discourse, we present a concise overview of PIFA's applications as a 'green' reagent in the domain of synthetic organic chemistry. A primary objective of this article is to bring to the forefront the scientific community's awareness of the merits associated with adopting PIFA as an environmentally conscientious alternative to heavy metals.

1. Introduction

Iodine, the heaviest element in the Periodic Table, is typically classified as a non-metal and is one of the most massive elements found on Earth. Due to its substantial size, the bonding behavior of iodine-containing compounds differs significantly from its lighter counterparts in the same group. The term 'hypervalent iodine compounds' refers to iodine compounds in higher oxidation states. Iodine, being the most polarizable and least electronegative halogen, exhibits unique reactivity. Various oxidation states of iodine, including I(III), I(V), and I(VII), can form hyper-coordinate compounds. In hyper-coordinate iodine(III) compounds, a linear 3-center-4-electron (**3c–4ē**) bonding arrangement results, with electronegative ligands occupying the axial positions and giving these compounds a T-shaped geometry.[1]

Hypervalent iodine compounds exhibit structural and reactivity characteristics akin to transition metal elements. Notably, their reaction mechanisms often align with those attributed to transition metals, encompassing phenomena like ligand coupling, oxidative addition, ligand exchange, and reductive elimination. Iodine, as an element, offers economic feasibility, with bulk prices ranging from \$20 to \$100 per kilogram over the past decade, and it boasts environmental safety credentials, unlike heavy metals. Consequently, the employment of hypervalent iodine compounds for effecting synthetic organic transformations has experienced rapid proliferation.[2–4] Over the past two decades, the functionalization of a wide array of organic molecules, within the broader context of organic synthesis, has witnessed significant utilization of organic hypervalent iodine compounds as environmentally friendly and potential oxidizing agents.[5–12] These hypervalent compounds serve as environmentally conscious alternatives to heavy metal oxidants like Pb(IV), Hg(II), and Tl(III). Their attributes, including ready availability, mild reactivity, enhanced efficiency, moisture stability, minimal toxicity, and ease of handling, contribute to their green chemistry appeal.

(Bis(trifluoroacetoxy)iodo)benzene/phenyliodine bis(trifluoroacetate), commonly referred to as PIFA, stands out as a

---

[a] *Bioorganic Laboratory, Department of Chemistry, University of Delhi, Delhi-110007, India. E-mail: singhbk@chemistry.du.ac.in*
[b] *Department of Chemistry, Kirori Mal College, University of Delhi, Delhi-110007, India. E-mail: chem.sunil@kmc.du.ac.in*
[c] *Department of Chemistry, R.D.S College, B.R.A. Bihar University, Muzaffarpur-842002, India*
[d] *Department of Chemistry, Deshbandhu College, University of Delhi, Delhi-110019, India*

† Authors have equal contribution.

prominent example of a hypervalent iodine compound extensively employed in synthetic chemistry. PIFA's versatility extends to its successful application as a viable replacement for hazardous organometallic catalysts and heavy metal oxidants, among other roles.[13] Commercially, PIFA is acquired as a light-sensitive, colorless solid that maintains stability at room temperature.

PIFA catalyzes a wide range of organic transformations, including ring-rearrangements, amidations, sulfenylations, carboxylations, and various others.[14,15] These reactions result in the synthesis of *N*-arylated and *N*-alkylated heterocyclic compounds,[16] oxidative deprotection reactions,[17] and the formation of pyrrolidinone and lactone frameworks,[18] alongside various other transformations.[19,20] Additionally, under acidic conditions, PIFA can facilitate the Hofmann rearrangement.[21] Notably, in 1990, Kikugawa *et al.*[22] elucidated a synthetic pathway for *N*-acylated nitrenium ions through PIFA-mediated amide oxidation. Substituted nitrenium ions, as consequential intermediates, serve as versatile precursors for constructing N–N, N–C, and N–S bond connections.[23,24]

PIFA demonstrates versatility in catalyzing various coupling reactions, leveraging its highly electrophilic iodine core.[25,26] Among these reactions, intramolecular phenolic coupling processes mediated by PIFA serve as effective biomimetic methodologies for the synthesis of fused and spirocyclic molecules.[27,28] PIFA also participates in ligand-exchange reactions with diverse nucleophiles, followed by reductive elimination.[29,30] Furthermore, PIFA has been established as a catalyst for the cyclo-isomerization of propargylamides,[31] oxidative amidation reactions of alkynes,[32] and carboxylation processes.[33] In these reactions, PIFA activates the triple bond, enabling cyclization.

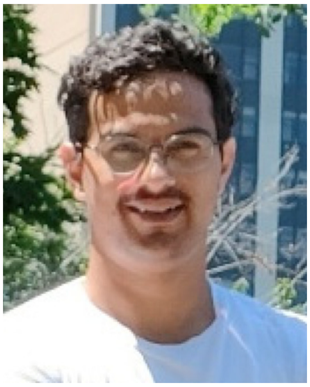
Owing to the potent electron-withdrawing attributes of the fluorine atom, PIFA exhibits higher reactivity in comparison with its counterpart, phenyliodine diacetate (PIDA). In the presence of basic olefin substrates, PIFA-mediated alkene functionalization facilitates the swift introduction of diverse functional groups into organic molecules, thereby enabling efficient and expedited molecular complexity enhancement.[34,35] PIFA frequently acts as an electrophilic species in metal-free reactions, generating an intermediate iodonium ion. This intermediate subsequently undergoes transformation into a leaving group, facilitating nucleophilic attack.[36] Recently, the field of alkene functionalization reactions has experienced renewed vigor through the synergistic combination of transition metal catalysts with iodine-based reagents.[37]

An update in this field is warranted, considering PIFA's significant diversification in organic chemistry in the past decade. This report offers a concise overview of PIFA's role as a green reagent in synthetic organic chemistry, with the aim of highlighting its potential as an eco-friendly substitute for heavy metals to the scientific community.

2. Synthesis

Various methodologies exist for the synthesis of PIFA. Herein, we outline some commonly employed procedures as shown in Fig. 1:

- Reaction of benzene with tris(trifluoroacetoxy)iodine[38]
- Oxidation of iodobenzene with xenon bis(trifluoroacetate)[39]
- Oxidation of iodobenzene with sodium percarbonate/$(CF_3CO)_2O/CH_2Cl_2$ [40]



Sumit Kumar

Sumit Kumar obtained his Master's Degree in Organic Chemistry from the Department of Chemistry, University of Delhi, in 2020 and Honours Degree from Kirori mal College, University of Delhi, in 2018. Currently, he is pursuing a Ph.D. from the Department of Chemistry, University of Delhi, under the supervision of Prof. Brajendra K. Singh. His research interests include design and synthesis of sugar-modified heterocyclic motifs of therapeutic importance. He visited Medgar Evers College, City University of New York (CUNY) in the Chemistry and Environmental Science Department as a Research Scholar. He has published several research articles in various reputable journals such as European Journal of Polymer Chemistry, New Journal of Chemistry, Beilstein Journal of Organic Chemistry, Synthesis, Organic and Biomolecular Chemistry *and others.*

Aditi Arora

Aditi Arora obtained her Honours Degree from Miranda House, University of Delhi, in 2018. She completed her Master's in Organic Chemistry from the Department of Chemistry, University of Delhi, in 2020. She was a Gold Medalist during her Master's. At present, she is pursuing a Ph.D. from the Department of Chemistry, University of Delhi. Her research interests include design and synthesis of carbohydrate and coumarin-modified molecules. She has published several research articles in various reputable journals.

- Oxidation of iodobenzene with using a $K_2S_2O_8/CF_3COOH/CH_2Cl_2$ system[41]
- Oxidation of iodobenzene with trifluoroperoxyacetic acid[42]
- Oxidation of iodobenzene with $HNO_3/(CF_3CO)_2O$[43]
- Reaction of iodosylbenzene with $Me_3Si(OCOCF_3)$[44]
- Reaction of (dichloroiodo)benzene with $AgOCOCF_3$ [45]

3. PIFA in organic synthesis

3.1. Amidation reaction

The amide functionality constitutes a substantial structural element in a majority of natural products and pharmaceutical compounds, playing a pivotal role in biologically and pharmaceutically relevant molecules.[46] Notably, approximately 25% of medicinal compounds feature amide groups.[47] Beyond their pharmaceutical significance, amides find diverse applications in organic chemistry as dyes, polymers, and agrochemicals. Amides also serve as crucial functionalities in peptides and proteins, with the *N*-formyl group being readily removable without affecting the peptide linkage.[48] Moreover, fatty acid amides hold promise for their potential anti-inflammatory, anti-bacterial, anti-tubercular, and antiproliferative properties.[49] Fundamentally, amides serve as a central scaffold for synthesizing a vast spectrum of organic compounds. Due to the paramount importance of the amide functionality, numerous synthetic strategies have evolved over time.

Kamble *et al.*[50] presented an effective, mild, metal-free procedure for catalyzing the transamidation reaction using PIFA (Scheme 1). High yields of amide analogs **3** were achieved by employing various aromatic amines **1**, predominantly those featuring fluoro substituents. In this synthetic protocol, DMF/DMAc **2** underwent transamidation with amines. PIFA was involved in the reaction *via* an ionic pathway, actively participating in the process through its contribution to the ionic mechanism.

The intramolecular insertion of a nitrogen atom represents an efficacious approach for the synthesis of nitrogen-containing heterocyclic compounds. Alkyne hydroamination stands as an attractive synthetic route for accessing both linear and cyclic amines/imine functionalities through intra/intermolecular reactions.[51] Serna *et al.*[52] reported a simple intramolecular amidation reaction for the synthesis of 5-substituted pyrrolidinone analogues **7a–n** catalyzed by PIFA with overall yields of 58–84% (Scheme 2). Firstly, the β-alkynylamide precursors **6a–n** were obtained by following a two-step procedure as described in Scheme 2. Treatment of *p*-anisidine with 4-pentynoic acid **4** in the presence of EDC·HCl/HOBt[53] resulted in the formation of amide **5**. Finally, a Sonogashira cross-coupling reaction[54] was employed to substitute the terminal alkyne functionality[55] of amide **5** in 32–81% yields. The desired compounds **7a–n** were further obtained by treatment of precursors **6a–n** with PIFA in acidic media at 0 °C. PIFA engaged in the reaction by following the ionic pathway.

Quinolino and pyrazino analogs of quinoxalin-6(5*H*)-ones represent intriguing heterocyclic structures with notable applications.[56] A swift, metal-free, and effective intramolecular reaction was described by Hu *et al.*[57] for the synthesis of quinoline-quinoxalinones **9** in satisfactory yields using readily accessible starting materials **8**. The ring-closure C–H amidation was conducted at ambient temperature with PIFA serving as the catalyst (Scheme 3). PIFA engaged in the reaction by following the ionic pathway, actively participating in the process through its involvement in ionic mechanisms.

Serna *et al.*[58] reported PIFA-mediated reaction on aromatic substrates to yield isoindolinones as well as isoquinolin-2-

---

Sunil K. Singh

Dr Sunil K Singh is an Associate Professor at the Department of Chemistry, Kirori Mal College, University of Delhi. He received his Ph.D. from the Department of Chemistry, University of Delhi, India, in the area of synthesis of modified nucleosides and biocatalytic organic transformations. He has published 32 articles in the journals of international repute. He has also published three book chapters.

Rajesh Kumar

Dr Rajesh Kumar received his Master of Science degree in Chemistry from the University of Delhi in 2010. He joined the same Department for a Ph.D. and completed his Ph.D. in 2017, and during his Ph.D. Dr Kumar visited the University of Southern Denmark as a Research Assistant from December 2014 to August 2015. After completion of his Ph.D., he joined as Assistant Professor in Chemistry at B.R.A. Bihar University, India. He has published more than 30 research papers in reputable national and international journals such as Journal of Organic Chemistry, Theranostics, European Polymer Journal, etc. *His research interest lies in Metal Complexes, Biotransformations, Catalysis, Green Chemistry, Nucleoside and Heterocyclic Chemistry.*

ones. Isoindolinone **11** was obtained in 23% yield from amide **10a** on treatment with PIFA/$BF_3·OEt_2$ in DCM at −20 °C (Scheme 4a). In contrast, isoquinolinone **12** was produced in 28% yield by employing TFA rather than $BF_3·OEt_2$ through a less preferred 6-*endo*-trigcyclization mechanism. They hypothesized that the enhanced nucleophilicity of the styrene fragment would enable nitrogen atom to readily undergo cyclization, leading to improved results. To achieve this, a low-temperature condition was maintained for the treatment of amide **10b** with PIFA/CF_3CH_2OH in the absence of an activating agent (Scheme 4b). As expected, the 5-*exo-trig* cyclization went without a hitch, resulting in a 95% yield of the isoindolinone **13a**. For a complete structural identification, this molecule was later acetylated to produce derivative **13b**. The behavior of amides **14a–b** was then examined in order to increase the viability of the intended synthesis (Scheme 4c and d). A 6-*exo-trig* cyclization occurred on treating CF_3CH_2OH solution of amide **14a** with PIFA, producing isoquinolinone **15a** in 72% yield. Similarly, amide **14b** resulted in the formation of isoquinolinone **16a** at room temperature in excellent yield. Furthermore, these motifs were acetylated to yield compound **15b** and **16b**, respectively, in order to obtain a complete structural identification. PIFA was involved in the reaction *via* an ionic pathway. Future research in the area of heterocyclic chemistry will benefit from the introduction of this subsidiary hydroxyl functionality which will enable the synthesis of advanced heterocycles.

In addition to serving as a pivotal functionality in tryptophan-containing compounds, indole and indoline scaffolds constitute integral components of biologically significant natural products.[59] Due to their compelling therapeutic applications, substantial research efforts have been dedicated to the development of innovative and efficacious synthetic methodologies for these heterocyclic structures.

Correa *et al.*[60] introduced an innovative synthetic strategy for the synthesis of indoline derivatives. Their work demonstrates that the PIFA-mediated amidohydroxylation reaction represents a rapid and efficient route to access indoline derivatives. Notably, compared with other metal-based approaches, this method allows for the dual functionalization of the alkene moiety, leading to the incorporation of both a hydroxyl group and a C–N linkage in the final product. This capability enables the synthesis of complex heterocycles through subsequent transformations. The critical cyclization step involves the PIFA-catalyzed generation of *N*-acylated nitrenium ions, followed by their intramolecular trapping with olefins. PIFA contributed to the reaction by engaging in the ionic pathway, playing a role in the process through its involvement. Optimization of reaction conditions revealed that treating substrate **17** with PIFA in trifluoroethanol for 3 hours at room temperature yields superior results in the amidation process. The broad applicability of this reaction was demonstrated by preparing a diverse set of indoline derivatives **18a–f** (Scheme 5).

Tellitu *et al.*[61] conducted an intramolecular electrophilic cyclization reaction catalyzed by PIFA using readily available alkynyl-amides **19a–i** and alkynyl carboxylic acids **19j–m** as substrates. This process led to the formation of pyrrolidinones **20a–i** and lactone derivatives **20j–m**, respectively. Specifically, amides **19a–i**, when dissolved in CF_3CH_2OH and subjected to the reaction at 0 °C, yielded the corresponding pyrrolidinones **20a–i** in a brief reaction time (Scheme 6). Similarly, the reaction of carboxylic acids **19j–m** with PIFA in the presence of

Bhawni Shankar

Dr Bhawani Shankar is an Associate Professor at the Department of Chemistry, Deshbandhu College, University of Delhi. He obtained his Ph.D. in Chemistry from the Department of Chemistry, University of Delhi, in 2022 under the supervision of the late Professor Ashok K. Prasad. His area of research includes synthesis of modified sugars, nucleosides, heterocyclic compounds and hydroxamic acids for different applications.

Brajendra K. Singh

Professor Brajendra K. Singh currently holds the position of Professor in the Department of Chemistry, University of Delhi, Delhi, India. He visited the Department of Chemistry, University of Leuven, Leuven, Belgium, as International Scholar for the period November 2005–April 2007 and then as post-doctoral fellow until November 2009. His key interest areas are the study and investigation of bio-catalysis and metal-catalysis, C–H activation, specifically in the design, synthesis and evaluation of bioactive compounds and LED-mediated synthesis. He has published more than 85 research articles in internationally reputable journals. He has delivered around 30 Invited Lectures in various National and International Conferences at different Universities and Institutes. He has served and is serving in different capacities in administration at Delhi University.

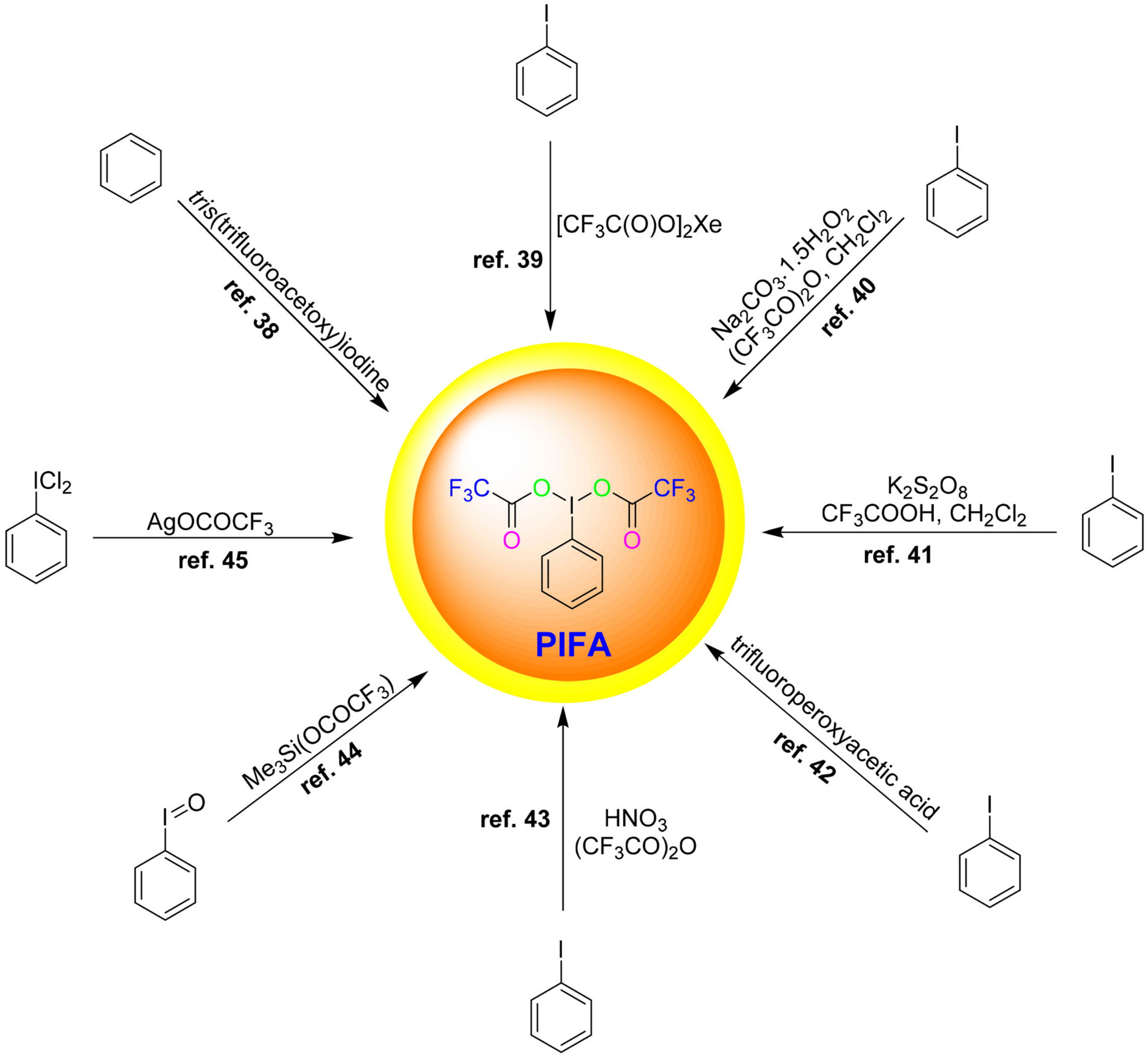


Fig. 1 Synthesis of PIFA.

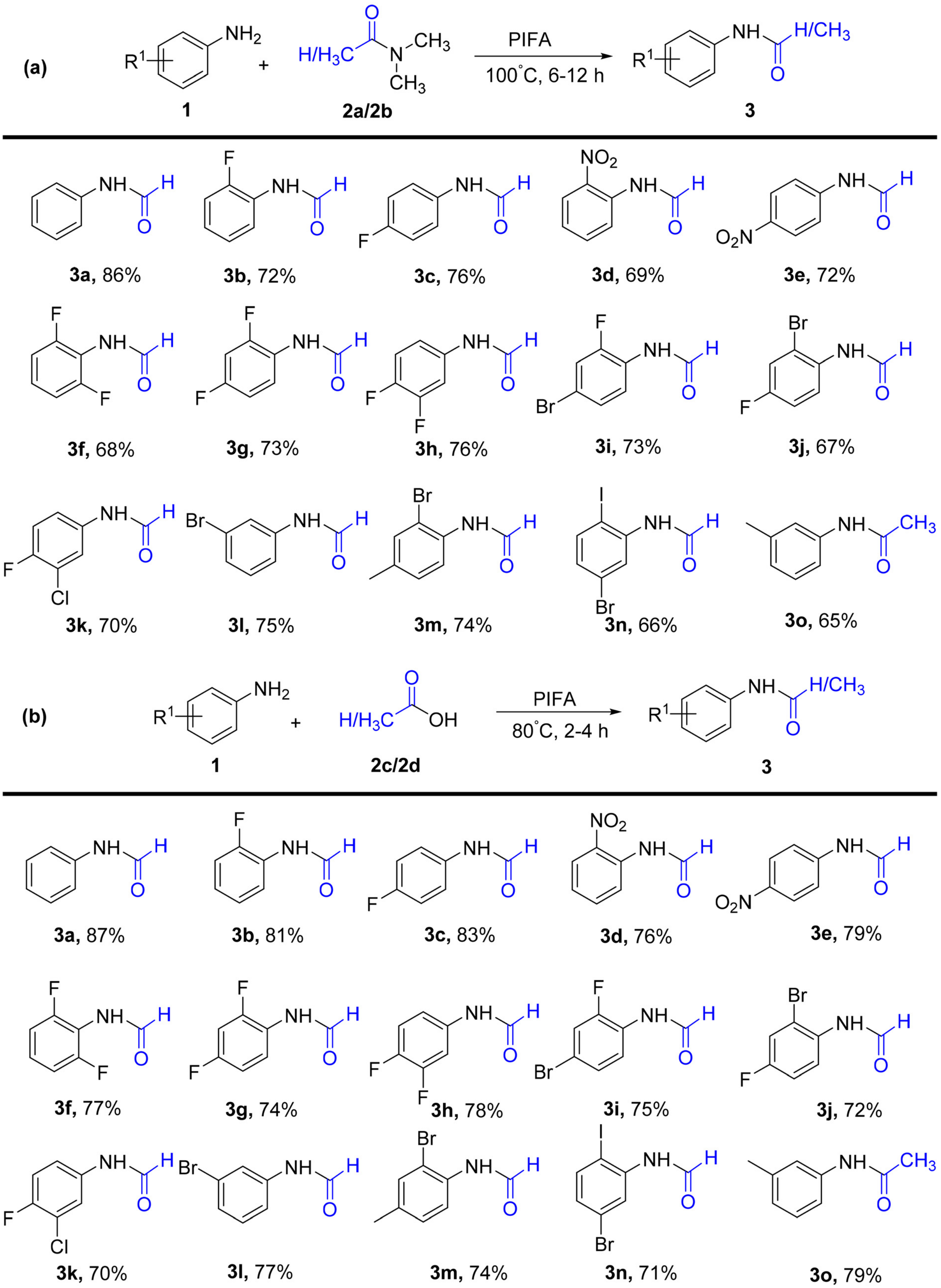
CF_3CH_2OH at 0 °C resulted in the formation of the predicted furanones **20j–m** in excellent yields (Scheme 6). PIFA was involved in the reaction *via* an ionic pathway.

3.2. Amination reaction

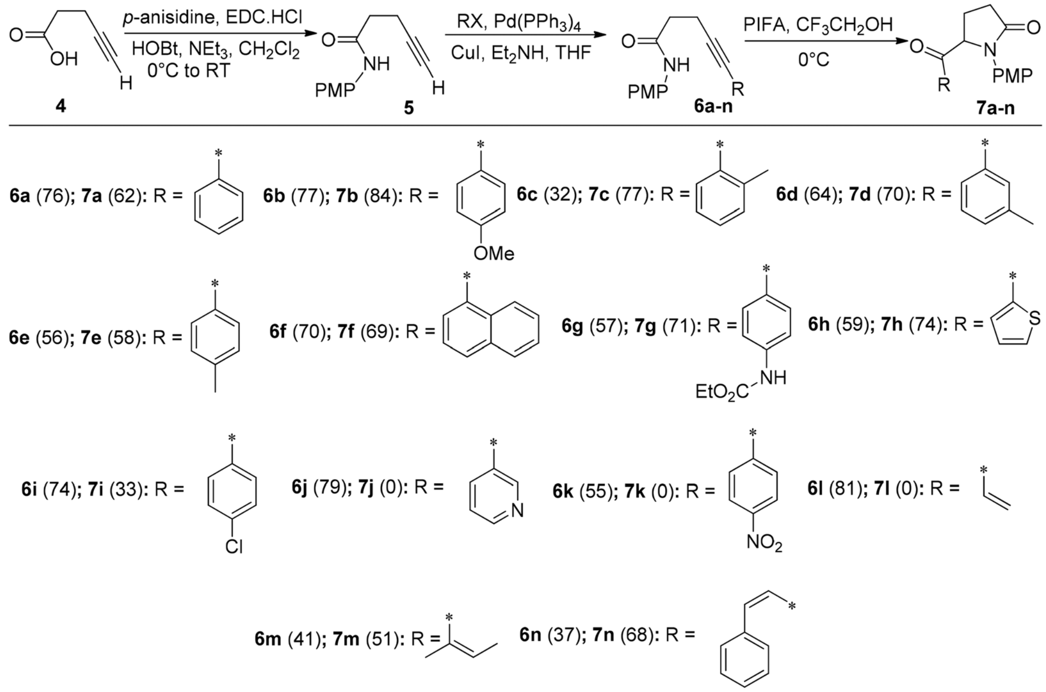
Azides serve as efficient amino sources for catalyzing amination reactions on aromatic C–H bonds with transition metals. Their effectiveness is attributed to their ready availability, diverse structural versatility, and the environmentally friendly production of N_2 gas as a byproduct of the reaction.[62] The selective functionalization of double bonds has become increasingly important as a versatile method for synthesizing complex molecules using a minimal number of steps.[63–65]

Paveliev *et al.*[66] synthesized analogs of 2-(hydroxyamino) ethanols **23a–n** *via* a PIFA-catalyzed reaction between azides **21a–n** and NHPI **22** (Scheme 7). PIFA actively engaged in the reaction by following a free radical pathway, specifically through hydrogen abstraction. The mild reaction conditions offer a broad substrate scope for vinyl azides. The reaction mechanism initiates with the formation of an *N*-oxyl radical through an oxidative pathway. Subsequently, it reacts with the vinyl azide. Finally, another *N*-oxyl radical molecule captures the resulting iminyl radical.

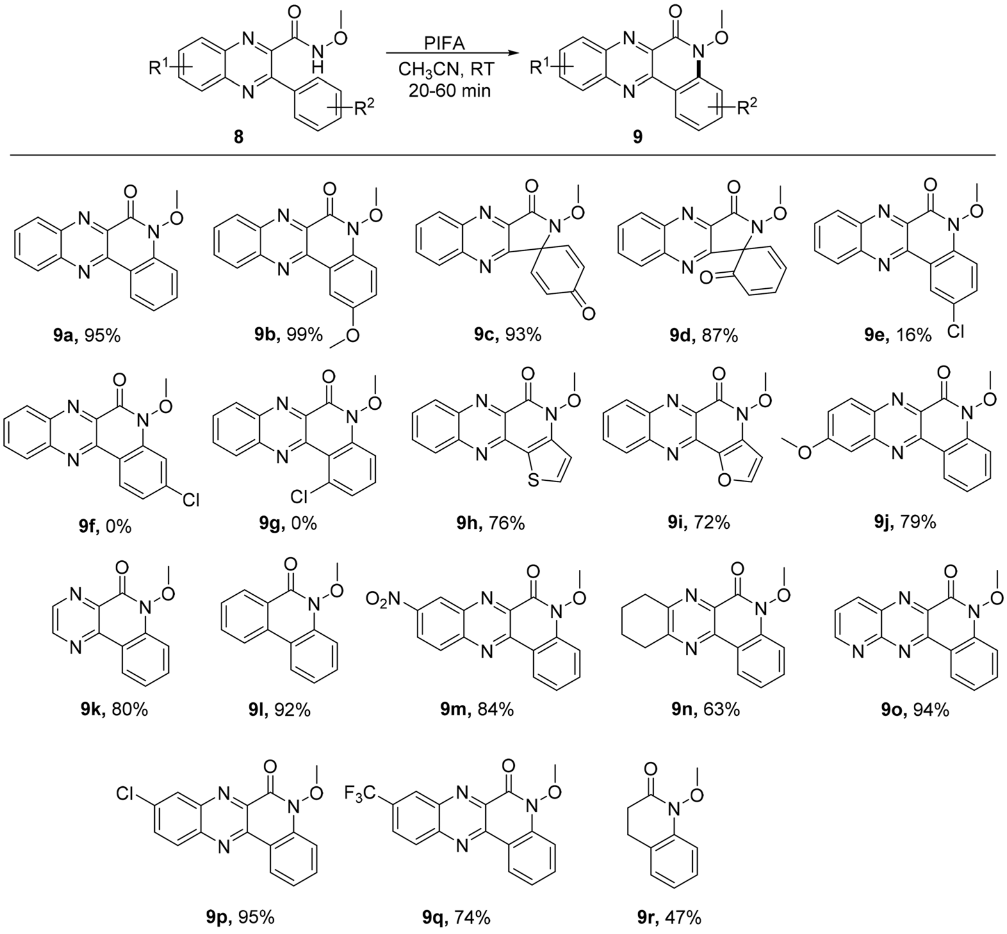
1*H*-Indazole scaffolds hold great importance as key components in biologically active compounds, synthetic medicines, and potential drug candidates.[67,68] Zhang *et al.*[69] reported a method for synthesizing substituted heterocycles **25** through a PIFA-mediated C–N coupling reaction, using readily available substrates **24** without the need for any metal catalyst (Scheme 8). PIFA was involved in the reaction *via* an ionic pathway. In addition, the cyclization of starting materials **24y** bearing a tosyl group at the nitrogen atom and **24z** did not



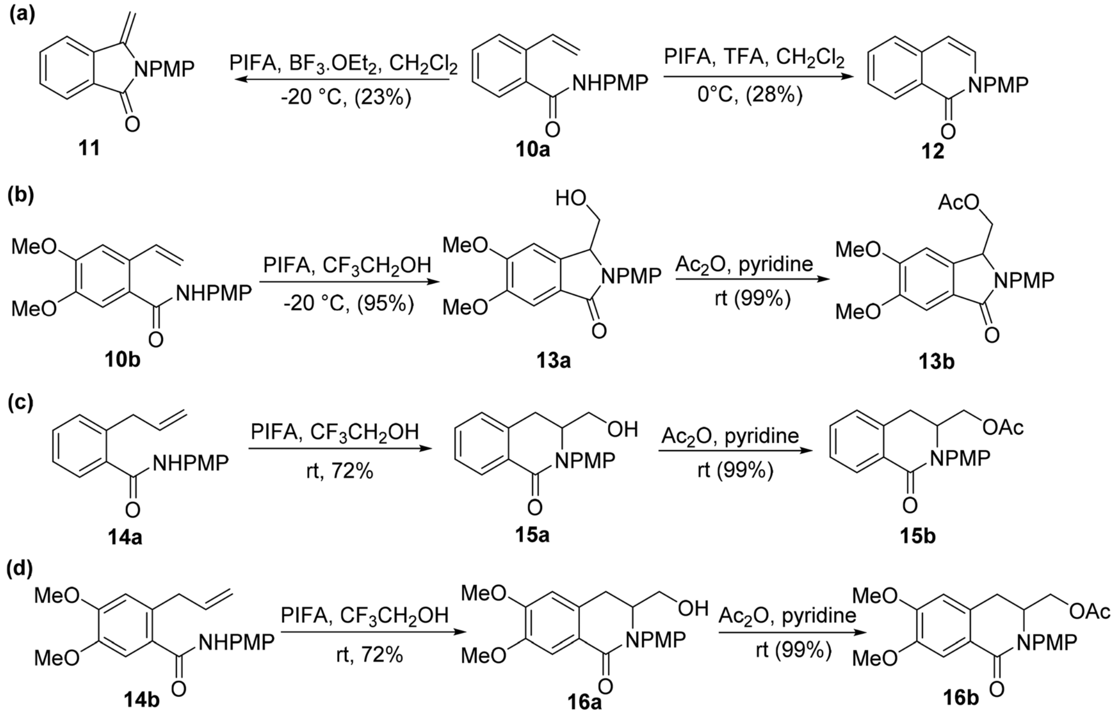
Scheme 1 a) Synthetic scheme for amides using DMF and DMAc. (b) Synthesis of amides using carboxylic acids.



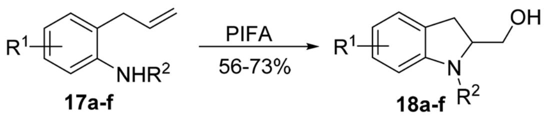
Scheme 2 Aminohydroxylation of alkyne catalyzed by PIFA.



Scheme 3 Synthesis of quinolino[3,4-*b*]quinoxalin-6(5*H*)-ones **9a–r**.



Scheme 4 Synthesis of isoindolinones as well as isoquinolin-2-ones from suitably modified aromatic substrates.



Compound (a-f)	17/18	Compound (a-f)	17/18
a	R^1 = H, R^2 = Ts	d	R^1 = 4-Et, R^2 = Ts
b	R^1 = H, R^2 = Bz	e	R^1 = 4-Br, R^2 = Bz
c	R^1 = 4-OMe, R^2 = Bz	f	R^1 = 6-Et, R^2 = Bz

Scheme 5 Synthesis of indoline derivatives **18a–f**.

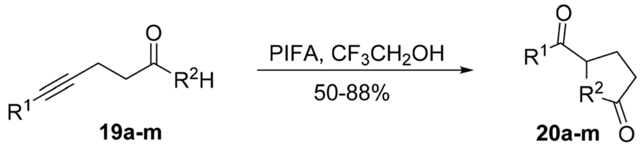
react under the current optimal conditions. This reaction demonstrates excellent tolerance for various functional groups and substrates.

3.3. C–H functionalization

In modern synthetic organic chemistry, the functionalization of sp^3 C-atoms through C–H bonds is a significant methodology for accessing C–C, C–O, and C–N linkages.[70]

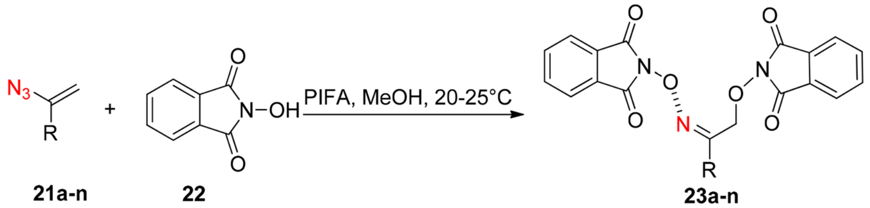
Lu *et al.*[71] employed visible light-enabled photocatalysis in the presence of 4CzIPN and PIFA to perform a radical cascade oxidation of *N*-aryl/benzoyl acrylamides **26**/**28**/**30**, yielding both oxindole **27**/**29** and isoquinolinedione **31** analogs in good yields. This reaction exhibited several noteworthy features, including a broad substrate scope, mild reaction conditions, and excellent tolerance for diverse functional groups (Scheme 9). PIFA actively engaged in the reaction by following a free radical pathway, specifically through single-electron oxidation. To expand the applicability of this photocatalytic pathway, the researchers investigated various substrates by modifying substituents at the R_2/R_3 positions, resulting in the facile synthesis of desired products **29a–l** with high to excellent yields (Scheme 10). In addition, they delved into the synthesis of cyano-functionalized isoquinolinedione **31** (Scheme 11), a pivotal structural motif commonly encountered in pharmaceuticals and agrochemicals.[72]

Organochalcogenides have consistently demonstrated substantial potential as prospective candidates for therapeutic applications, attributable to their inherent versatility as molecular scaffolds capable of accommodating an extensive array of functional groups.[73] Furthermore, they find broader utility



Compound (a-m)	19/20	Compound (a-m)	19/20
a	R^1 = Ph, R^2 = NPMP	**h**	R^1 = 2-thienyl, R^2 = NBn
b	R^1 = Ph, R^2 = NMe	**i**	R^1 = Ph, R^2 = N-*o*-BrC_6H_4
c	R^1 = Ph, R^2 = NAllyl	**j**	R^1 = Ph, R^2 = O
d	R^1 = Ph, R^2 = NBn	**k**	R^1 = *p*-$MeOC_6H_4$, R^2 = O
e	R^1 = Ph, R^2 = N*c*Hex	**l**	R^1 = 1-naphthyl, R^2 = O
f	R^1 = *p*-$MeOC_6H_4$, R^2 = NBn	**m**	R^1 = 2-thienyl, R^2 = O
g	R^1 = 1-naphthyl, R^2 = NBn		

Scheme 6 Synthetic scheme for pyrrolidinone as well as lactone derivatives.



Compound (a-n)	21/22	Compound (a-n)	21/22
a	R = Ph, 70%	**h**	R = 2-FC_6H_4, 68%
b	R = 4-MeC_6H_4, 52%	**i**	R = 3-ClC_6H_4, 79%
c	R = 3-MeC_6H_4, 69%	**j**	R = 2-ClC_6H_4, 67%
d	R = 4-$ButC_6H_4$, 51%	**k**	R = 4-BrC_6H_4, 72%
e	R = 4-$MeOC_6H_4$, 40%	**l**	R = 3-BrC_6H_4, 62%
f	R = 4-$AcOC_6H_4$, 68%	**m**	R = 1-benzimidazolyl, 50%
g	R = 4-FC_6H_4, 79%	**n**	R = CO_2Me, 51%

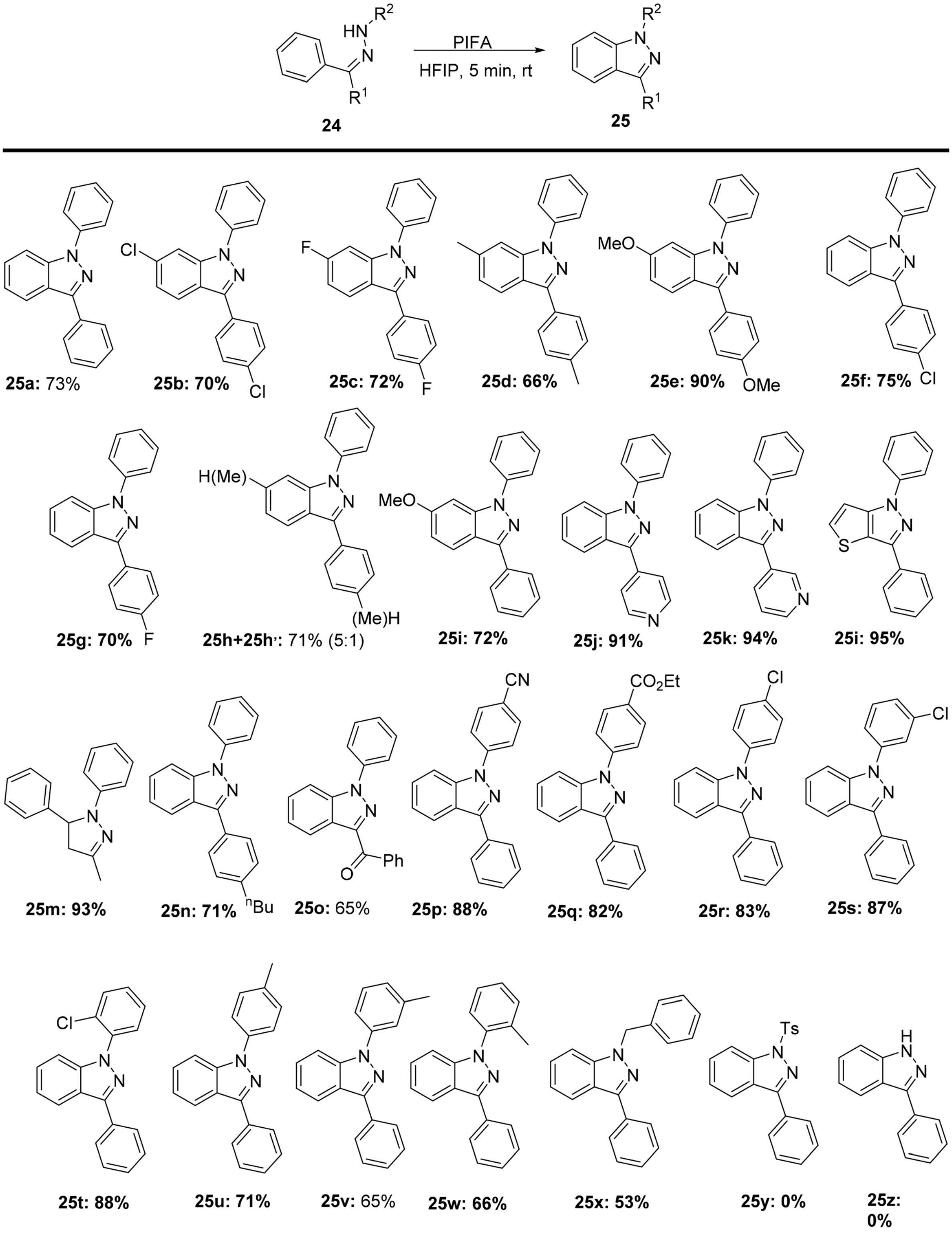
Scheme 7 Synthesis of analogues of 2-(hydroxyimino)ethanols.

across diverse domains, including agrochemistry, catalysis, materials science, and organic synthesis.[74]

Ghosh *et al.*[75] presented a more environmentally friendly approach employing PIFA ($PhI(OCOCF_3)_2$) for the C–H functionalization of pyrimidine-4-one **32**, enabling the direct selenylation process to afford the desired products **33a–s** in high yields, as depicted in Scheme 12. PIFA actively engaged in the reaction by following a free radical pathway, specifically through hydrogen abstraction, contributing to the process through this mechanism. Notably, this reaction exhibited remarkable tolerance towards a wide array of functional groups and structural variations, consistently delivering excellent yields of the target compounds. Furthermore, the applicability of the reaction scheme was extended to encompass various diaryl diselenides, as illustrated in Scheme 13.

The structural components of benzothiazoles serve as essential constituents of various naturally occurring molecules, agricultural chemicals, synthetic compounds as well as pharmaceuticals.[76] *C*-2-Arylacylated benzothiazole derivatives are such compounds that have drawn considerable attention because of their therapeutic importance.

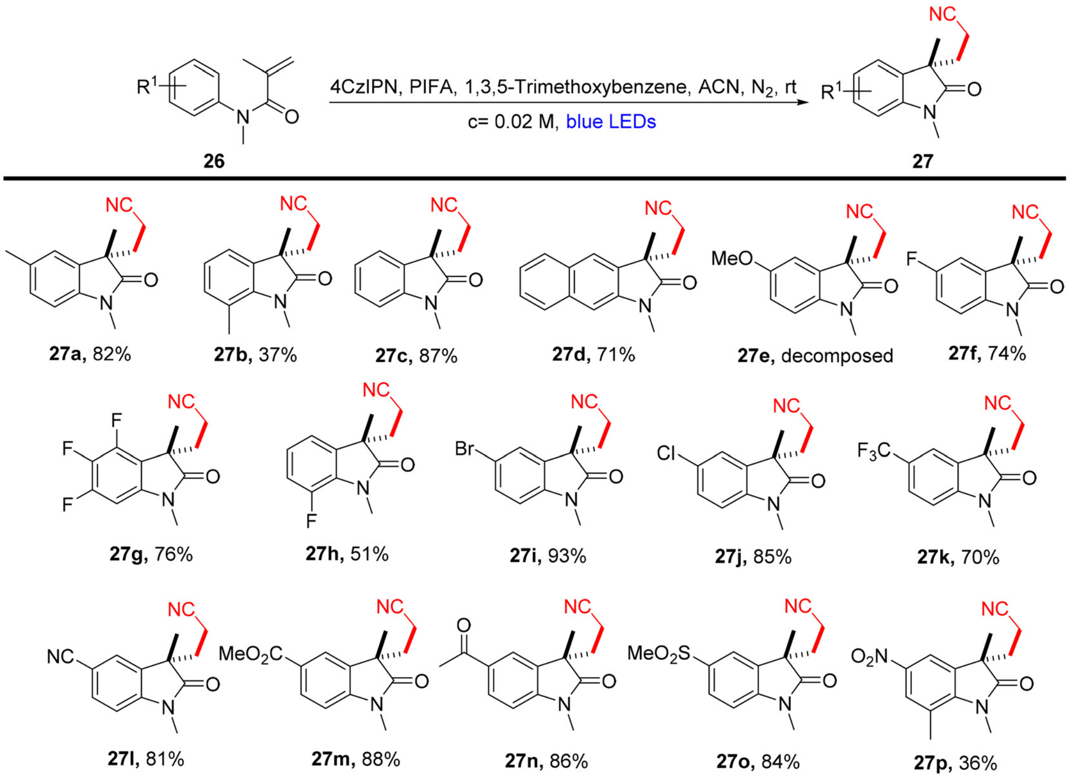
Sun *et al.*[77] developed an efficient method using PIFA as a mediator to synthesize distinct *C*-2-arylacylated benzothiazoles **37** with yields ranging from 70% to 95%. These compounds show promise as potential therapeutic scaffolds and are obtained through a ring-opening reaction of 2*H*-benzothiazoles **35** (Scheme 14). PIFA actively engaged in the reaction through a free radical pathway, involving hydrogen abstraction as a mechanism for its participation in the process. This protocol is versatile, accommodating various substrates under favor-



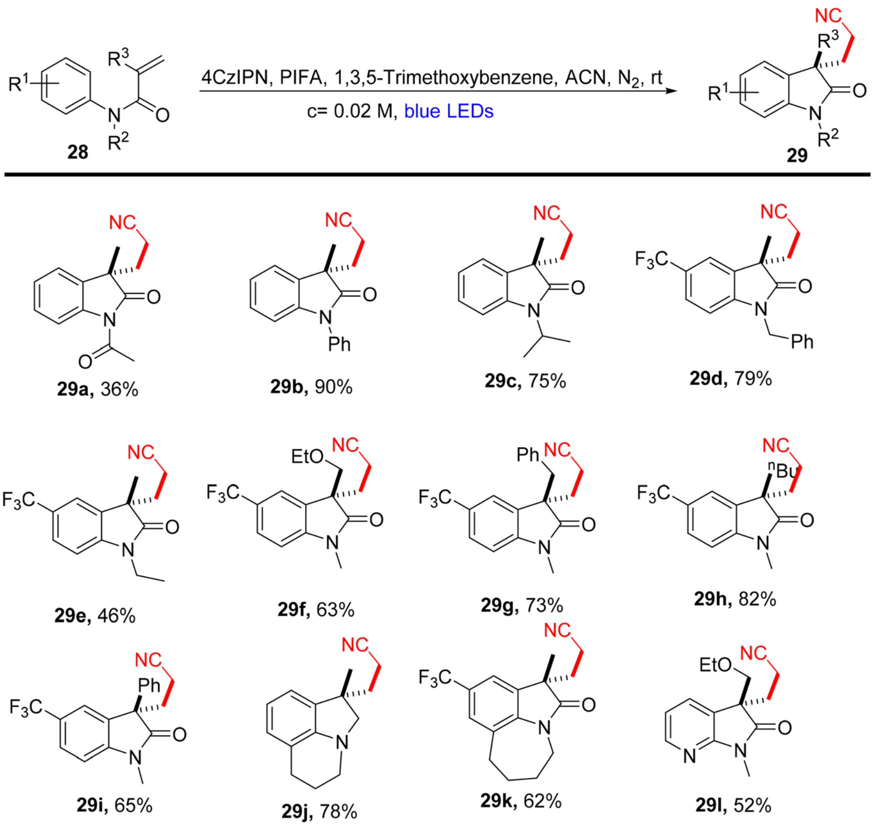
Scheme 8 Synthetic pathway for construction of 1*H*-indazole analogues.

able conditions, offering a faster and simpler route compared with prior methods for producing *C*-2-arylacylated benzothiazoles **37**.

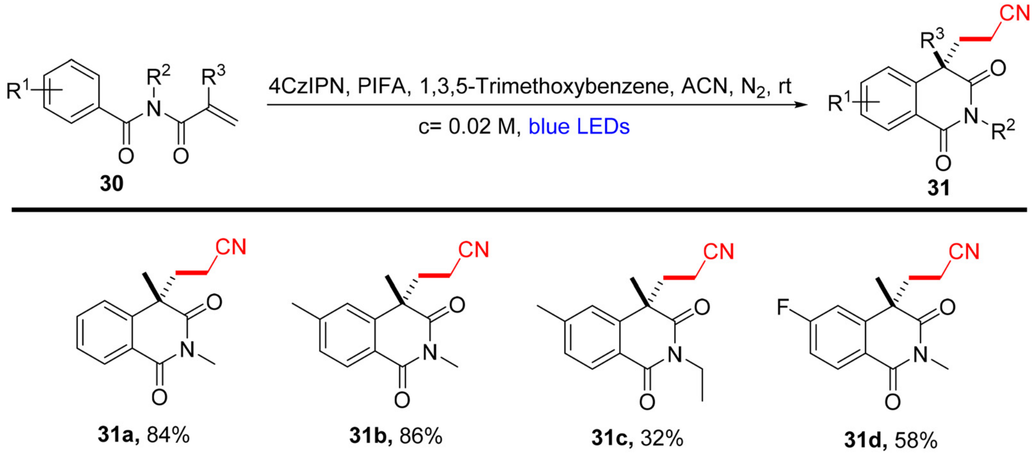
Numerous methodologies have been documented for converting alkylbenzenes into their respective benzyl esters. However, a significant portion of the recently reported esterifi-



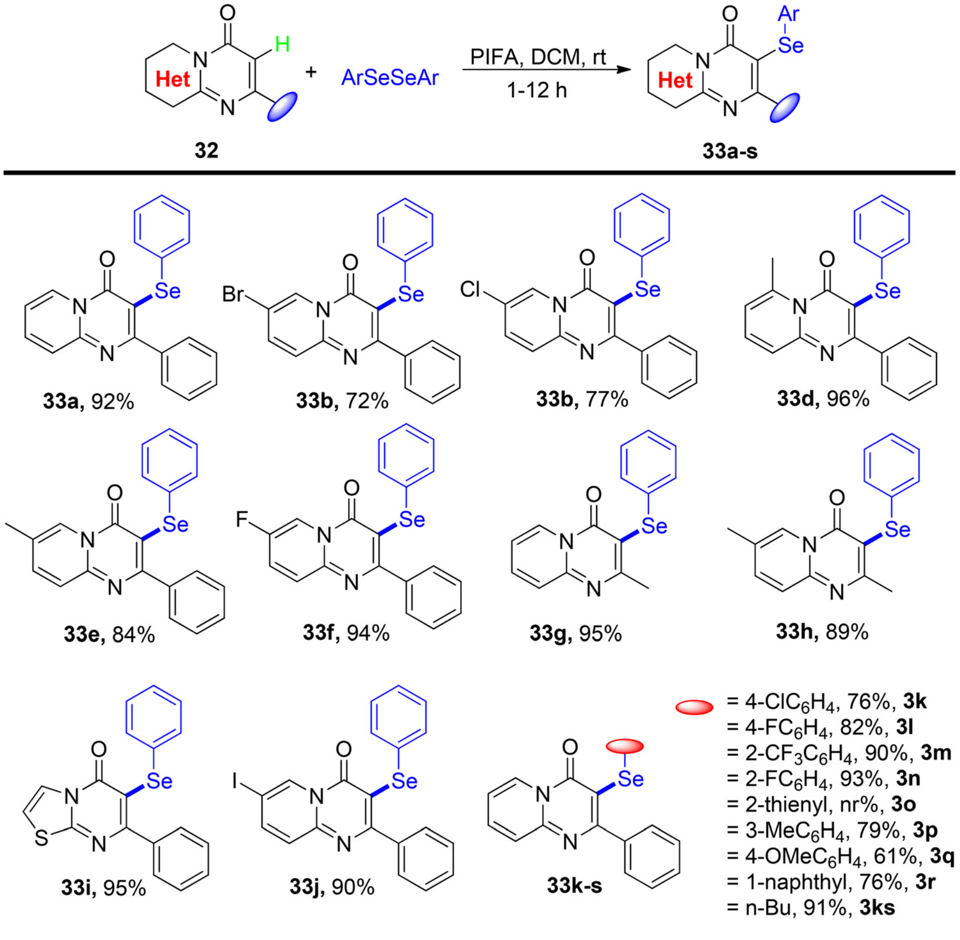
Scheme 9 Synthesis of functionalized oxindoles **27a–p**.



Scheme 10 Synthesis of functionalized oxindoles **29a–l**.



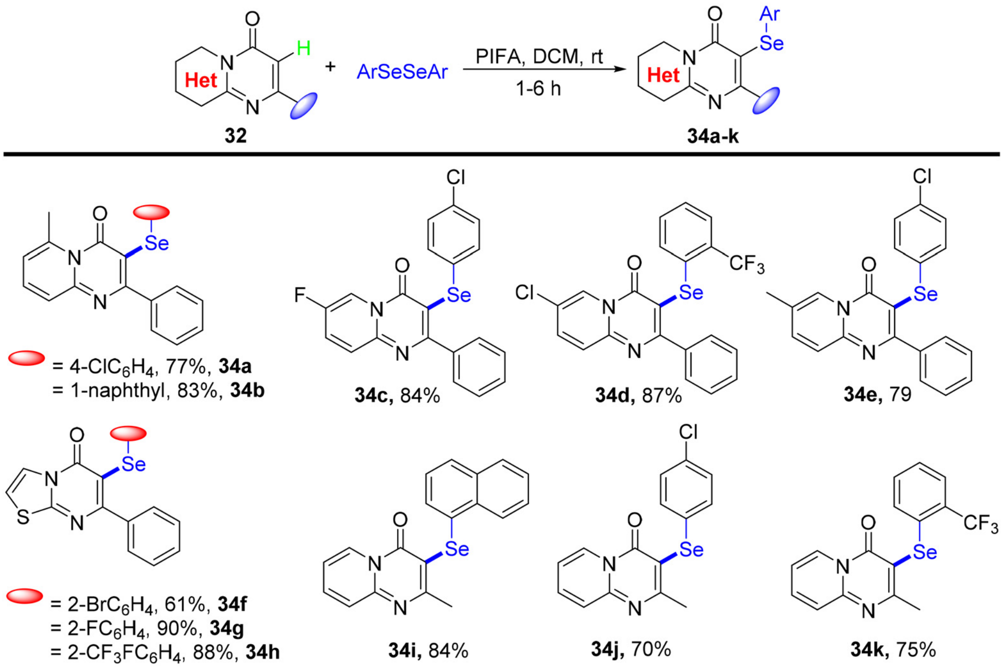
Scheme 11 Synthesis of isoquinolinediones **31a–d**.



Scheme 12 Synthesis of selenylated-pyrimidin-4-ones **33a–s**.

cation processes involving benzylic C–H bonds necessitate the use of excessive acid or elevated temperatures (>60 °C).[78]

Sakamoto *et al.*[79] accomplished the esterification of alkylbenzenes through a combination of PIFA catalysis and visible light irradiation. This methodology yielded favorable results, providing high yields of desired benzyl ester derivatives **39** from various alkylbenzenes **38** (Scheme 15). PIFA actively engaged in the reaction through a free radical pathway, invol-



Scheme 13 Synthetic of selenylated-pyrimidin-4-ones **34a–k**.

ving hydrogen abstraction as a mechanism for its participation in the process. The versatility of this approach was demonstrated through an exploration of its substrate scope, as illustrated in Schemes 15 and 16a. Furthermore, the acyclic analogue **42** underwent a straightforward reaction, resulting in the production of α-hydroxy carbonyl compound **43** with a yield of 54% (Scheme 16b).

As reported by Couto *et al.*,[80] the fused lactone was synthesized *via* a metal-free C–H activation reaction. Subsequently, the adducts **44a–j** underwent a transformation into the corresponding pyrimidinones **45a–j** through an intramolecular reaction mediated by PIFA (Scheme 17). PIFA was involved in the reaction *via* an ionic pathway, actively participating in the process through its contribution to the ionic mechanism.

Mudithanapelli *et al.*[81] introduced a PIFA-catalyzed, metal-free/NaCN reaction capable of effecting oxygenation, cyanation, and nitration through sp^3 and sp^2 C–H activation processes, respectively. This versatile methodology was successfully applied to a range of amine derivatives **46**, as outlined in Scheme 18. Under the influence of CH_3NO_2/H_2O (9 : 1), all conversions were efficiently catalyzed by PIFA/NaCN (Scheme 18). Notably, in cyanation complete conversion of substrates **46a–o** to the desired products **50a–o** was achieved (Scheme 19). The oxidized compounds **51a–p** were readily obtained from cyclic amines **46a–p** in yields ranging from 73% to 91% (Scheme 20). However, it is worth noting that none of the oxygenation products **51a–f** were obtained when 6-membered amines were employed as substrates. This methodology stands out due to the cost-effectiveness and compatibility of PIFA as an oxidant. Remarkably, a single catalytic system, namely PIFA/NaCN, proved highly effective in facilitating three distinct types of functionalizations. PIFA was involved in the reaction *via* an ionic pathway.

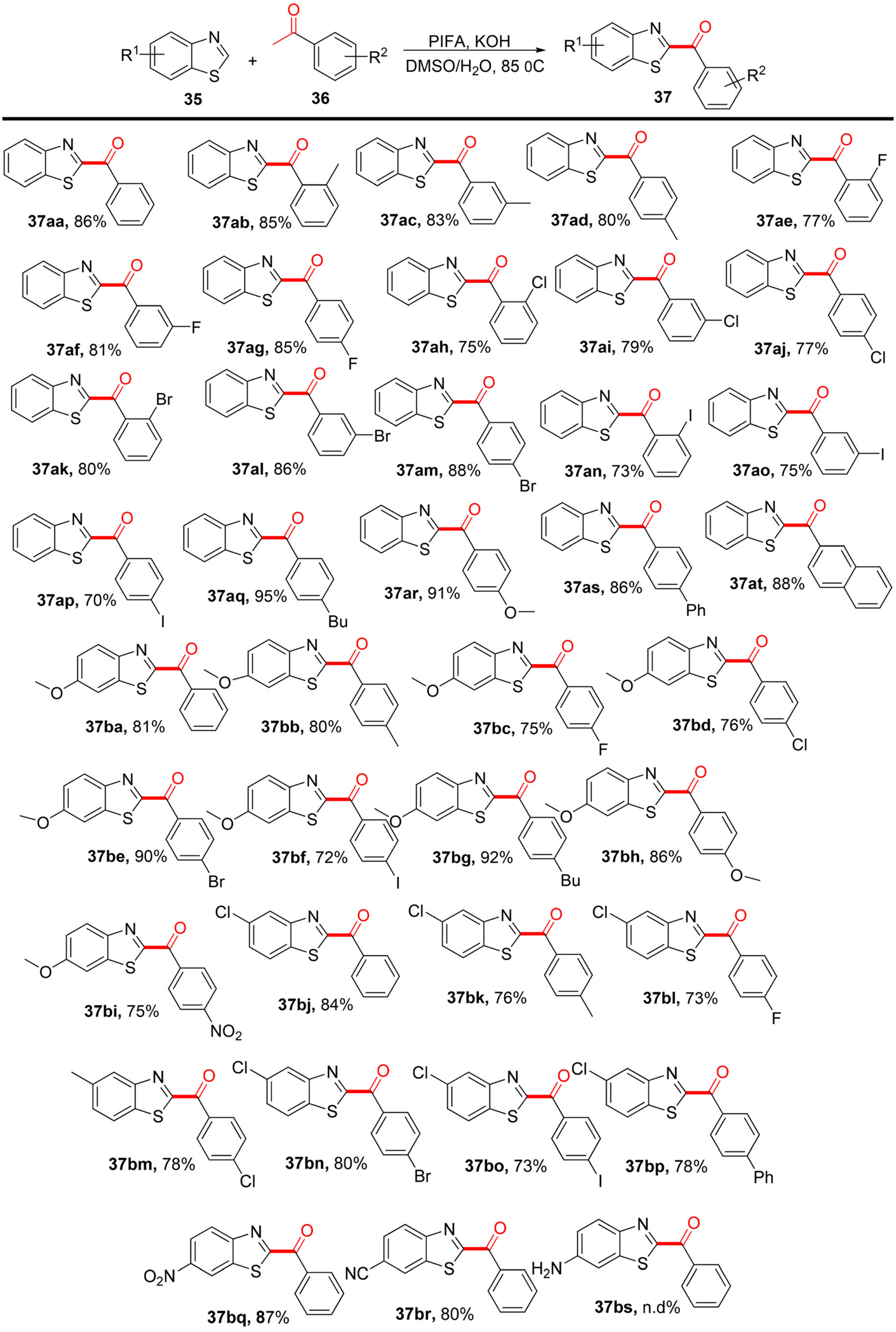
3.4. Coupling reaction

Owing to their myriad applications in sensors, photosynthetic systems, and nonlinear optical (NLO) devices, porphyrin and chlorin derivatives have garnered significant scientific attention.[82]

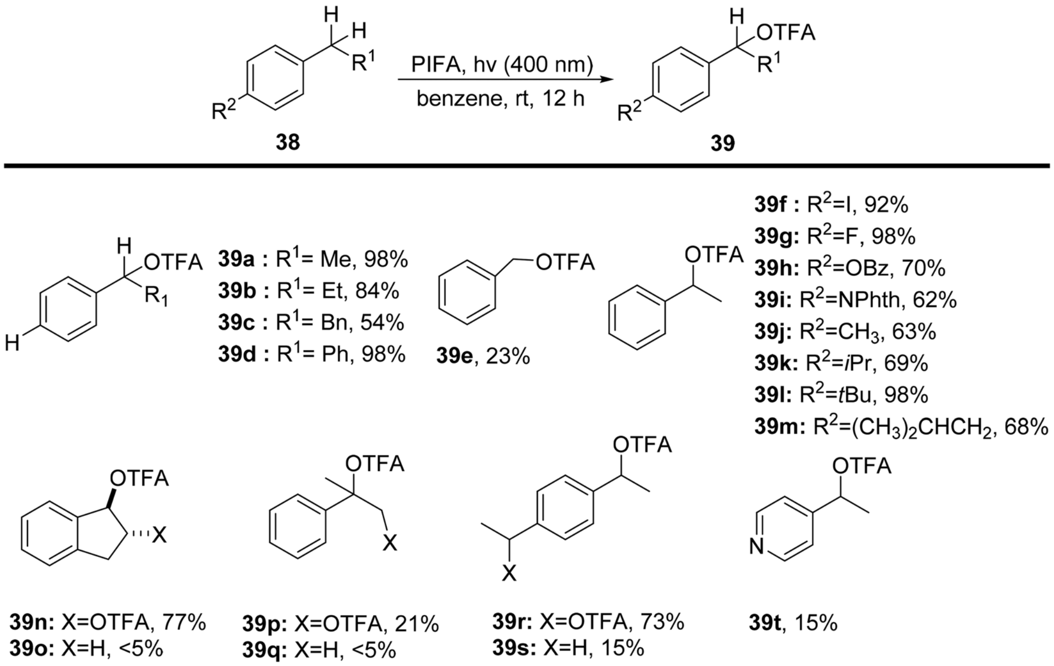
Cheng *et al.*[83] used different oxidants to study the interactions between anilines **53** and chlorins **52**. Aminated compounds were obtained by performing the oxidation reaction of anilines as well as chlorins in presence of PIFA. $NaAuCl_4·2H_2O$ was used to successfully carry out the amination reaction (Scheme 21). It is interesting to note that when monomeric Zn (II) chlorin was treated with *p*-toluidine in the presence of $NaAuCl_4·2H_2O$ and PIFA as the catalyst, diaminated chlorin dimers **54** were obtained (Scheme 21). Moreover, the inactive 10th position also undergoes amination reaction. Further, these chlorin analogues can be developed to function as photosensitizers.

Nitriles represent a notable class of functional groups in organic synthesis, typically serving as precursors for the conversion into various other functional groups, including amines, amides, carboxylic analogs, heterocyclic compounds, and aldehydic moieties.[84]

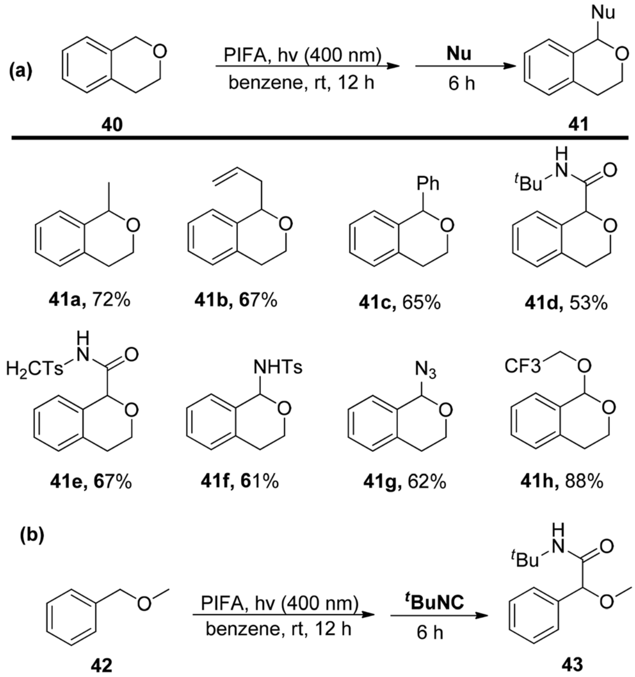
Yan *et al.*[85] effectively converted nitriles **59** into their respective *N*-phenyl amides **60** through a PIFA-catalyzed intermolecular cross-coupling mechanism conducted in the absence of any solvent. PIFA actively engaged in the reaction by following a free radical pathway, specifically through single-electron oxidation, contributing to the process through this



Scheme 14 Synthesis of *C*-2-arylacylated benzothiazoles **37**.



Scheme 15 C–H functionalization of alkylbenzenes in mild conditions using PIFA.



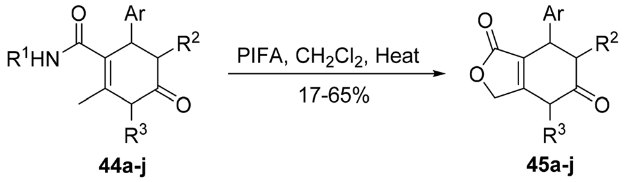
Scheme 16 C–H functionalization of alkylbenzenes in mild conditions using PIFA.

mechanism. This method represents a mild oxidative reaction scheme for achieving high yields of *N*-phenyl amides **60**. It encompasses the cleavage of sp^2 C–N linkages concomitant with the formation of new C–N bonds, as illustrated in Scheme 22.

By C–H functionalization of electron-rich aromatic hydrocarbons in water and further coupling with an equal stoichiometry of allyl sulphides, Feng *et al.*[86] described a methodology to obtain aryl sulphides **64**. The Lipshutz surfactant, TPGS-750-M, which utilizes water as the recyclable reaction media, facilitates this arylthiolation. Varied allyl aryl sulphides were useful cross-coupling partners for *m*-dimethoxybenzene or 1,3,5-trimethoxybenzene **62** in the case of allyl sulphides (Scheme 23). Allyl phenyl sulphide **63** was successfully coupled with diverse electron-rich arenes **62**. The fact that this reaction took place in an aqueous medium rather than an organic one and allowed for the recycling of water, surfactant and catalyst is perhaps its most notable feature. PIFA actively engaged in the reaction by following a radical pathway, specifically through single-electron oxidation.

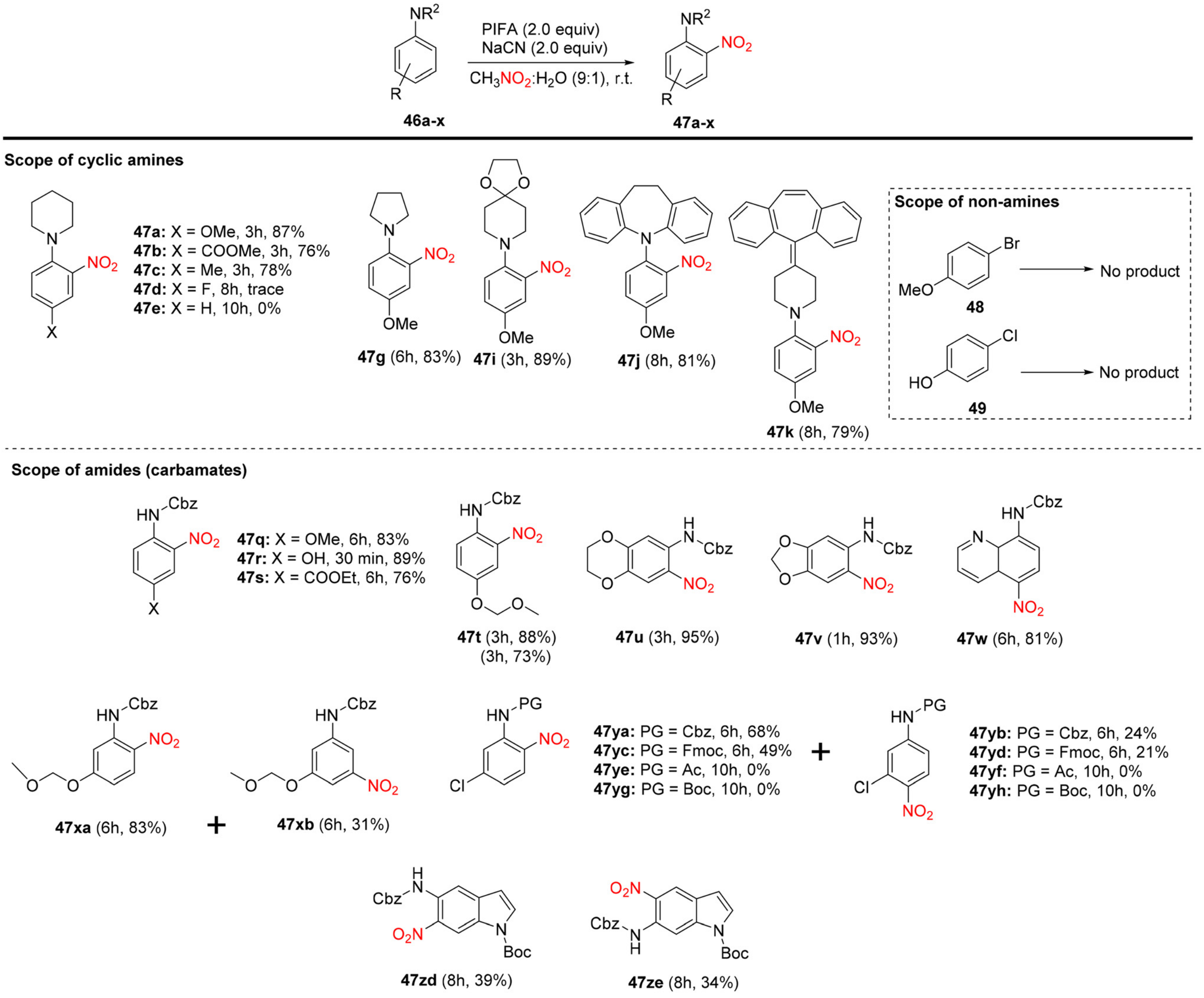
Bodipy-based dyes hold significant importance due to their exceptional optical properties, enhanced solubility, outstanding photochemical stability, high absorption coefficients, and ease of functionalization.[87] While Bodipy dimers possess intriguing characteristics related to charge delocalization, their potential utility as fluorescent or redox probes has not been a primary area of research focus.

Rihn *et al.*[88] reported the coupling reaction of monomeric Bodipy **65**, mediated by both a Lewis acid and PIFA, leads to the formation of a mixture of various oligomers. The formation of dimers is favored when one of the positions is occupied by either an iodine(I) or phenyl (Ph) substituent, as shown in Scheme 24. PIFA actively participated in the reaction by employing a free radical pathway, particularly through single-electron oxidation. These dimers exhibit two consecutive oxidative and reductive waves, with an approximate separ-

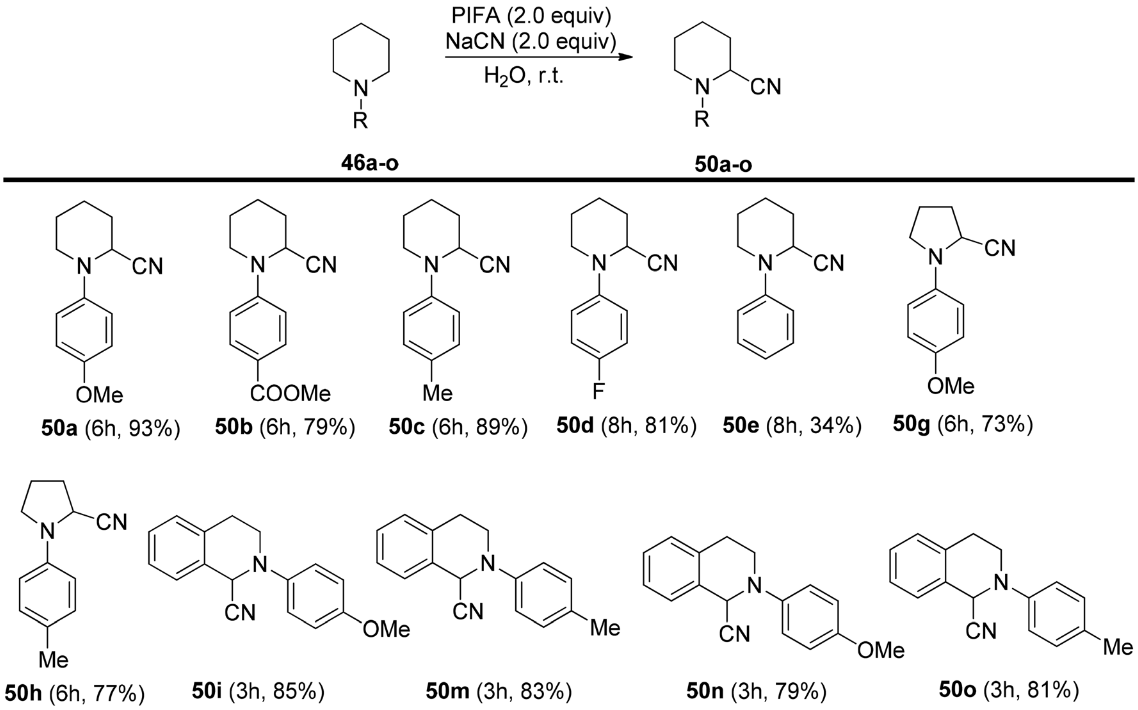


	44/45		44/45
a	R^1 = Ph, R^2 = H, R^3 = H, Ar = *m*-$MeOC_6H_4$	**f**	R^1 = Ph, R^2 = Et, R^3 = Et, Ar = *m*-$MeOC_6H_4$
b	R^1 = Ph, R^2 = H, R^3 = Me, Ar = *m*-$MeOC_6H_4$	**g**	R^1 = 2,4-$Me_2C_6H_3$, R^2 = Me, R^3 = Me, Ar = P
c	R^1 = Ph, R^2 = Me, R^3 = Me, Ar = *m*-$MeOC_6H_4$	**h**	R^1 = H, R^2 = Me, R^3 = Me, Ar = Ph
d	R^1 = Ph, R^2 = Me, R^3 = Me, Ar = Ph	**i**	R^1 = Ph, R^2 = Me, R^3 = Me, Ar = 2-thienyl
e	R^1 = *p*-$NO_2C_6H_4$, R^2 = Me, R^3 = Me, Ar = Ph	**j**	R^1 = Ph, R^2 = Me, R^3 = Me, Ar = *o*-$NO_2C_6H_4$

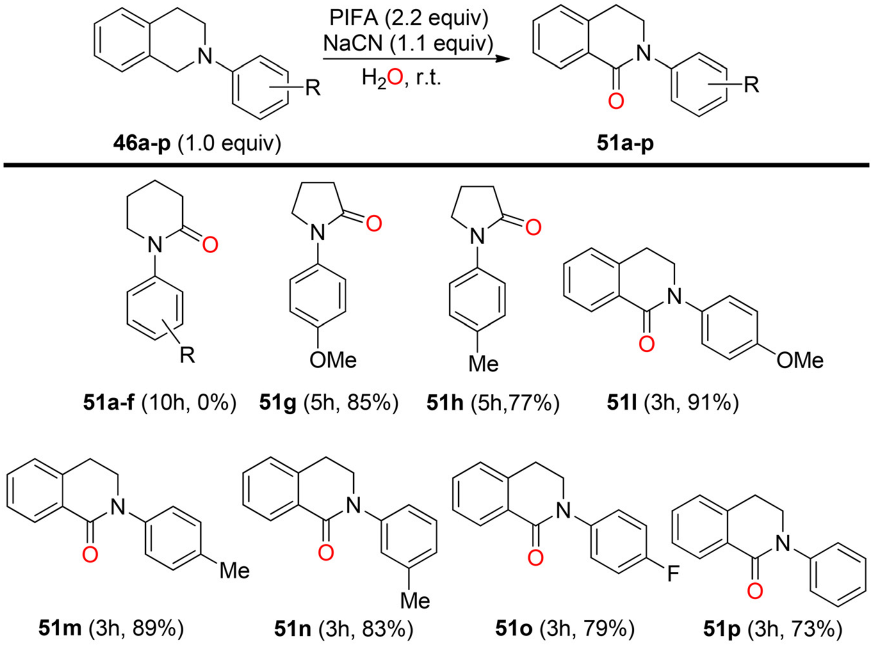
Scheme 17 Synthetic scheme for pyrimidine-2,5-dione analogues **45a–j**.



Scheme 18 Variation of substrates in nitration reaction.



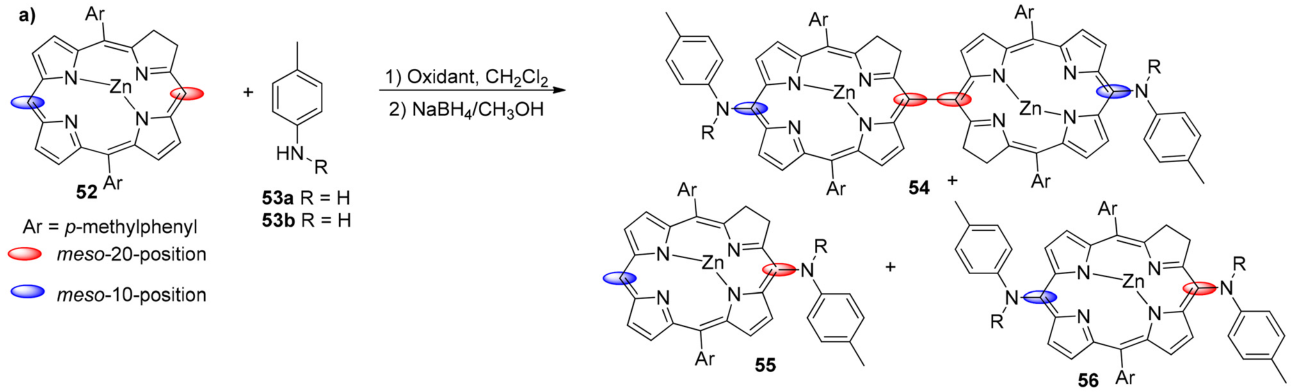
Scheme 19 Scope of cyanation reaction.



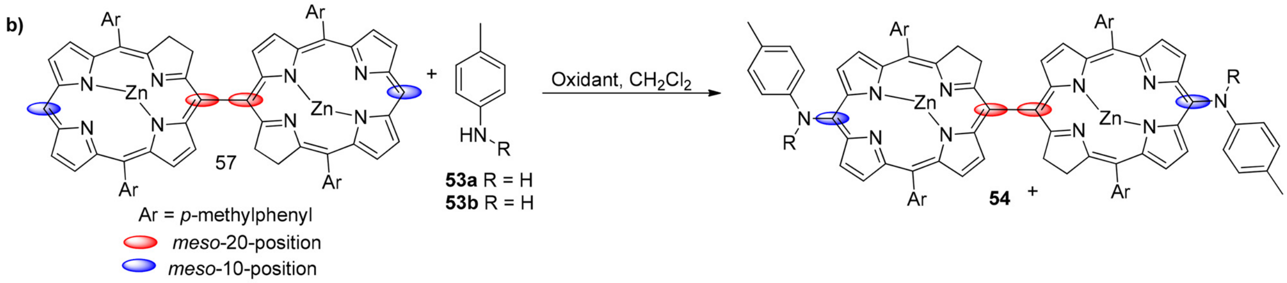
Scheme 20 Oxygenation reaction with varied substrates.

ation of 260 mV and 130 mV, respectively. Interestingly, the three dimers, namely **66a**, **66b**, and **66c**, were found to display near identical stability and reactivity compared with Bodipy monomer units.

Porphyrin and chlorin dimers hold considerable significance due to their applications in nonlinear optical (NLO) devices, sensors, and photosynthetic systems.[89] Ouyang *et al.*[90] provided the inaugural account of synthesizing dimeric zinc chlorin by efficiently oxidizing zinc chlorin monomers **67** using PIFA, as outlined in Scheme 25. This process yielded a 74% yield, demonstrating a selective formation of dichlorin **68**. Importantly, the reaction exhibited regioselectivity at the



Entry	Oxidant (equiv)	R	Time	Yield (%)
1.	$NaAuCl_4.2H_2O$ (1.5)	H	1 min	**54a,** 68; **55a,** <5
2.	PIFA (1)	H	1 min	**55a,** 40
3.	PIFA (0.25)	H	1 min	**55a,** 15
4.	PIFA (1.5)	H	1 min	**55a,** 65
5.	PIFA (3)	H	1 min	decomposition
6.	$NaAuCl_4.2H_2O$ (1.5)	CH_3	1 min	**54b,** < 5; **56a,** 60
7.	PIFA (1.5)	CH_3	1 min	**54b,** 61; **56a,** 17

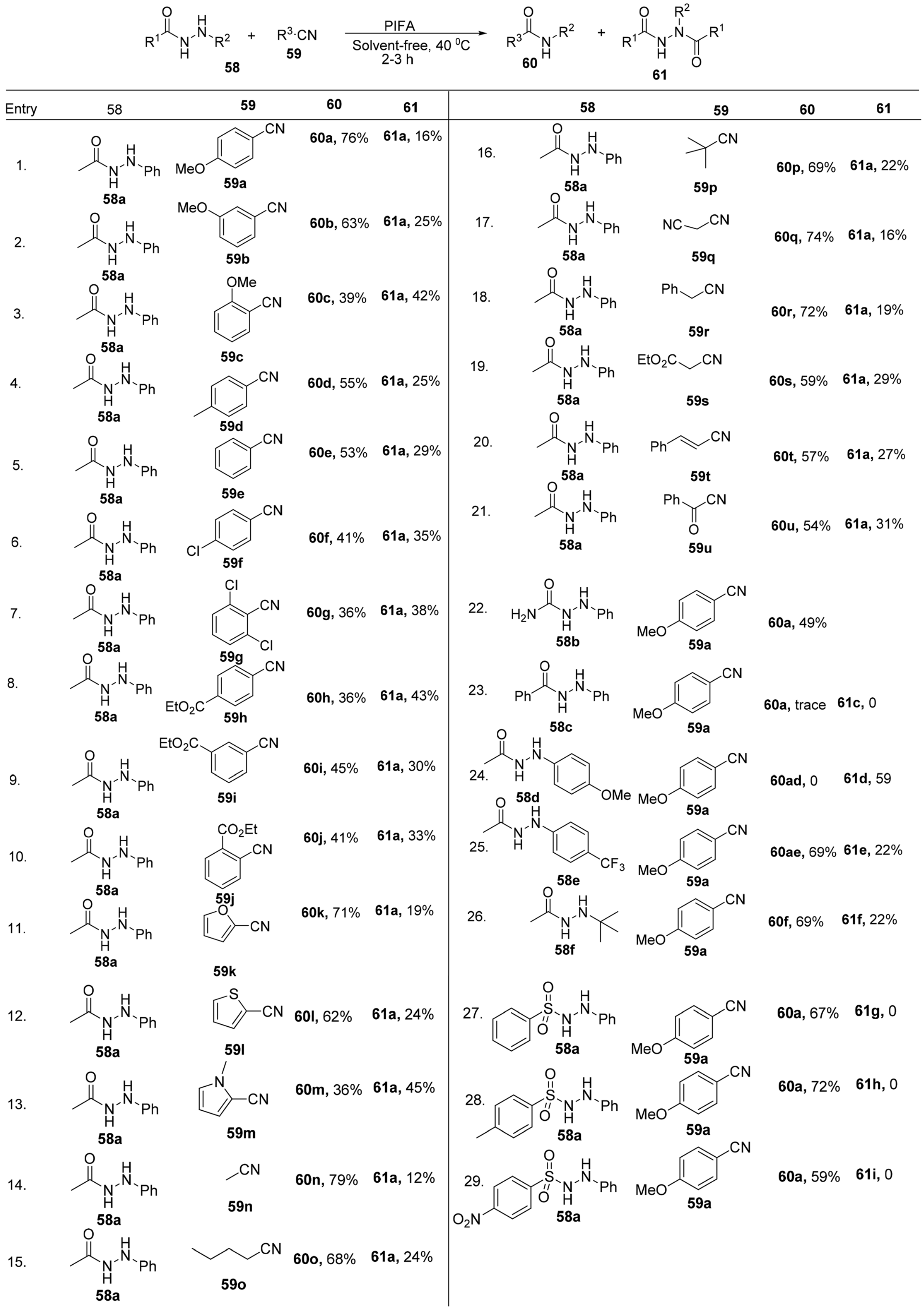


Entry	Oxidant (equiv)	R	Time	Yield (%)
1.	$NaAuCl_4.2H_2O$ (1.5)	H	1 min	**54a,** 70
2.	PIFA (1.5)	H	1 min	**54a,** 49
3.	$NaAuCl_4.2H_2O$ (1.5)	CH_3	1 min	**54b,** 67
4.	PIFA (1.5)	CH_3	1 min	**54b,** 79

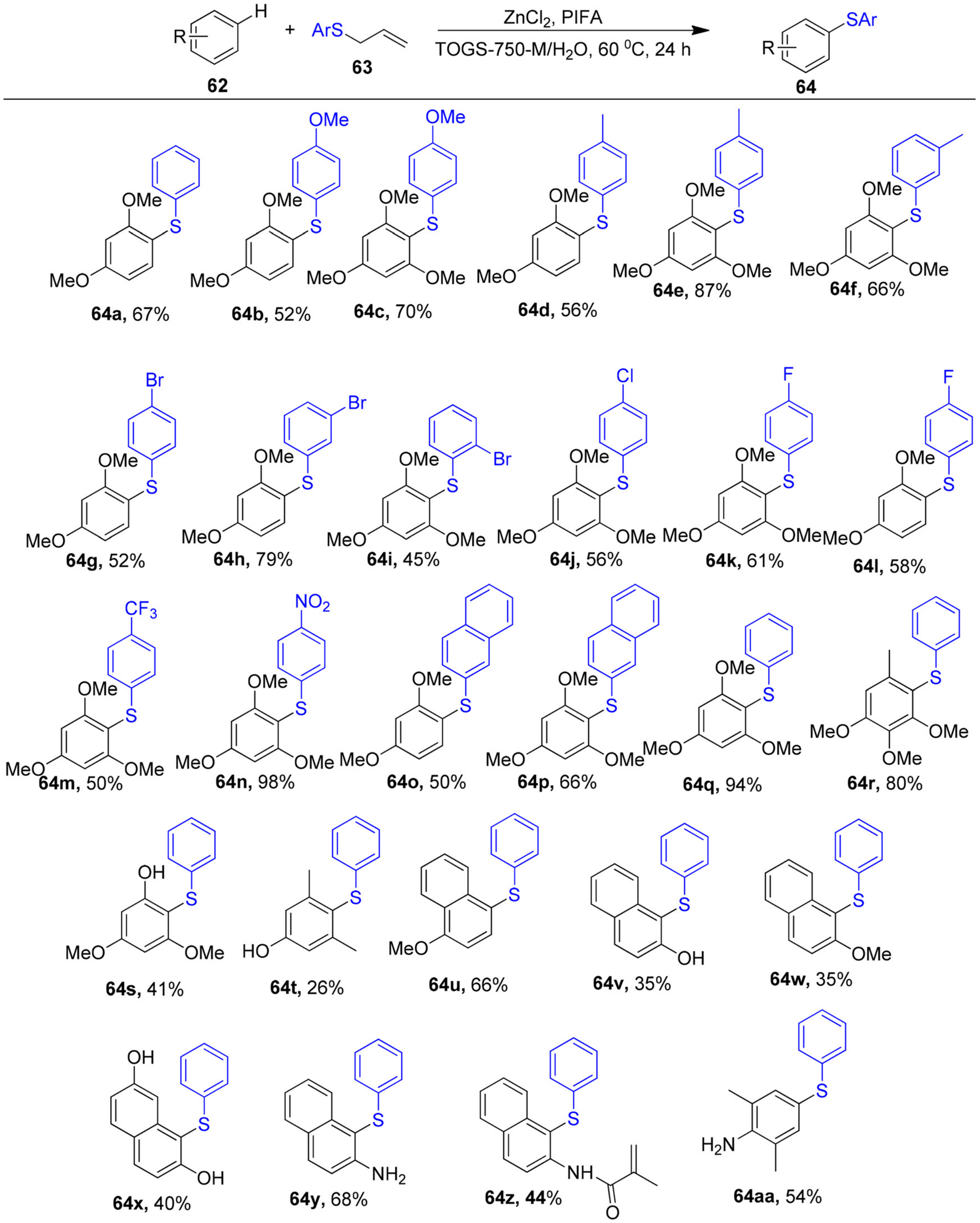
Scheme 21 Amination reaction of chlorins as well as *N*-unsubstituted anilines.

20th position of the pyrrole ring. PIFA actively participated in the reaction by employing a free radical pathway, particularly through single-electron oxidation.

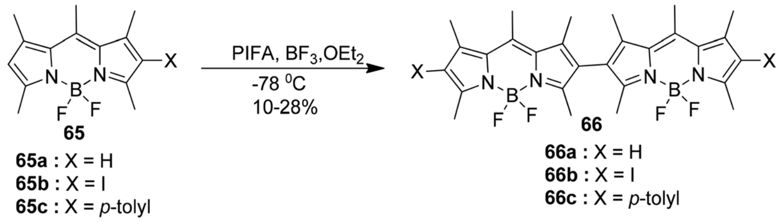
Spirooxindoles serve as essential intermediates for the synthesis of biologically significant molecules.[91] PIFA functions as an effective catalyst for the synthesis of diversely functiona-



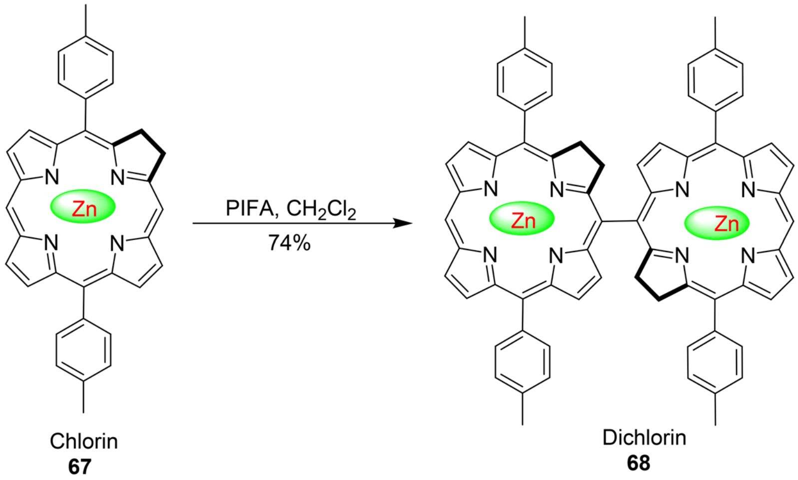
Scheme 22 Synthesis of *N*-phenyl amides.



Scheme 23 Synthesis of aryl sulfides.



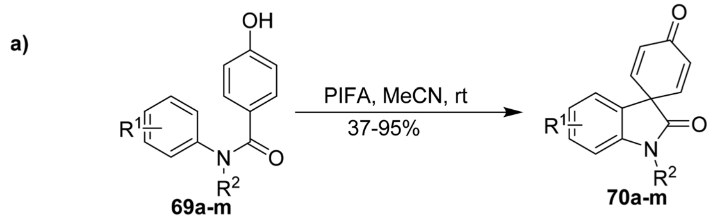
Scheme 24 Synthesis of bodipy dimers.



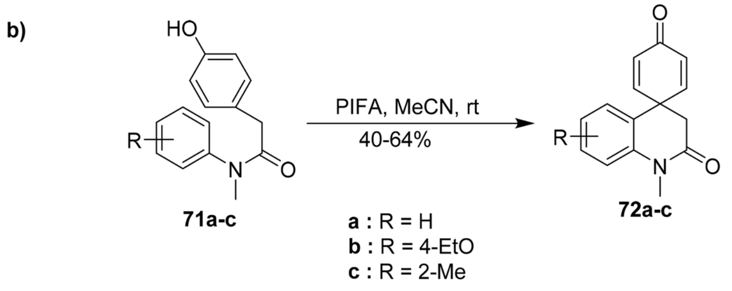
Scheme 25 Synthesis of zinc chlorin dimer.

lized *N*-phenylbenzamides by oxidative coupling. Yu *et al.*[92] described an effective methodology for synthesizing such molecules **70a–m** in moderate yields from **69a–m** as demonstrated in Scheme 26a. This approach can further be utilized to obtain functionalized spirooxindole analogues. Also, the spirooxindoles **72a–c** were synthesized from the *N*-acetamides **71a–c** (Scheme 26b). PIFA was involved in the reaction *via* an ionic pathway.

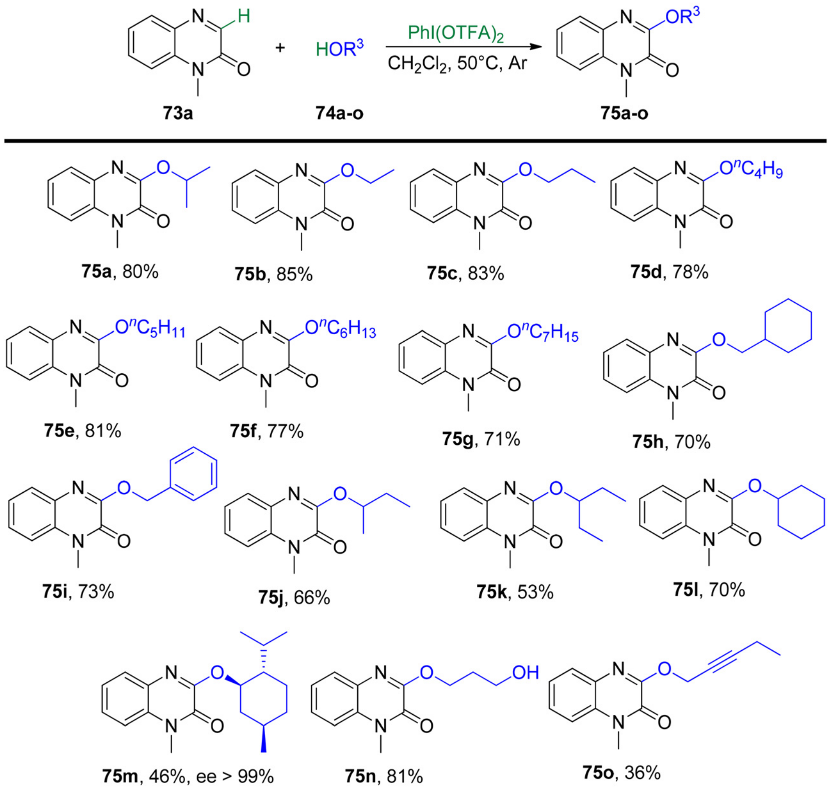
Yang *et al.*[93] have unveiled a straightforward and effective alkoxylation method for quinoxalin-2(1*H*)-ones **73** using primary or secondary alcohols **74** (Schemes 27 and 28). This process operates under catalyst-free conditions and involves cross-dehydrogenative coupling. By employing PIFA as an oxidant, this technique offers a convenient means to access 3-alkoxylquinoxalin-2(1*H*)-ones **75** in good to excellent yields. PIFA actively engaged in the reaction by following a free radical



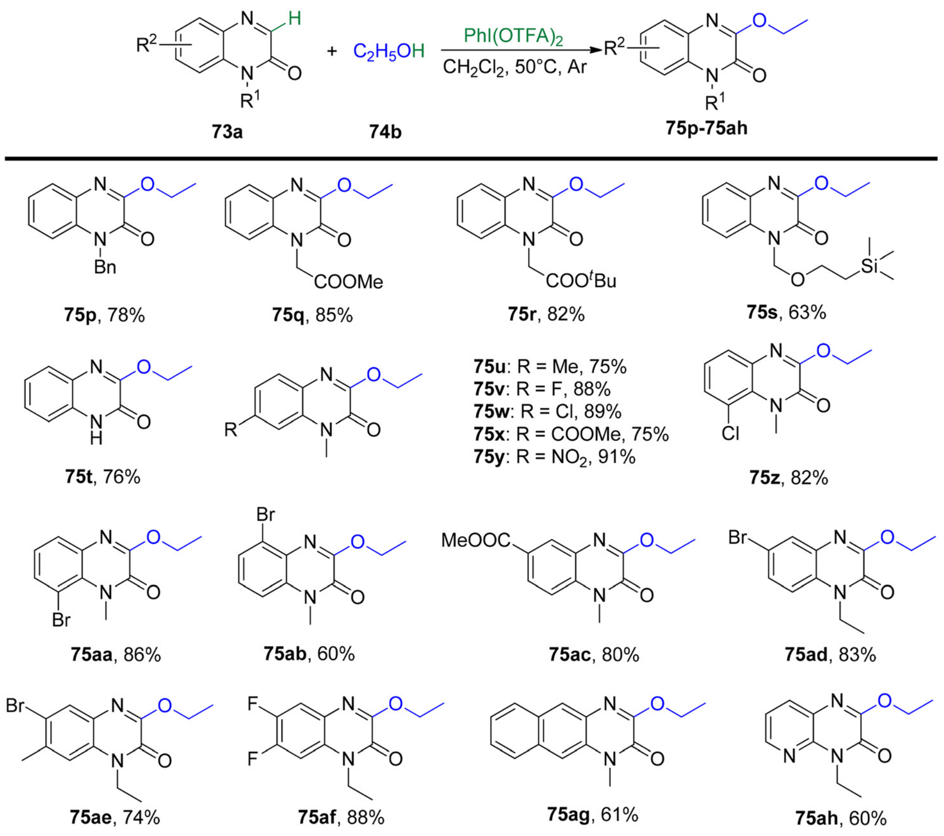
Compound (a-m)	69/70	Compound (a-m)	69/70
a	R^1 = H, R^2 = Me	h	R^1 = 3-Cl, R^2 = Me
b	R^1 = 4-EtO, R^2 = Me	i	R^1 = H, R^2 = Bn
c	R^1 = 4-Me, R^2 = Me	j	R^1 = 4-EtO, R^2 = Bn
d	R^1 = 2-MeO, R^2 = Me	k	R^1 = 4-Me, R^2 = Bn
e	R^1 = 2-Me, R^2 = Me	l	R^1 = 2-MeO, R^2 = Bn
f	R^1 = 4-Cl, R^2 = Me	m	R^1 = 2-Cl, R^2 = Bn
g	R^1 = 2-Cl, R^2 = Me		



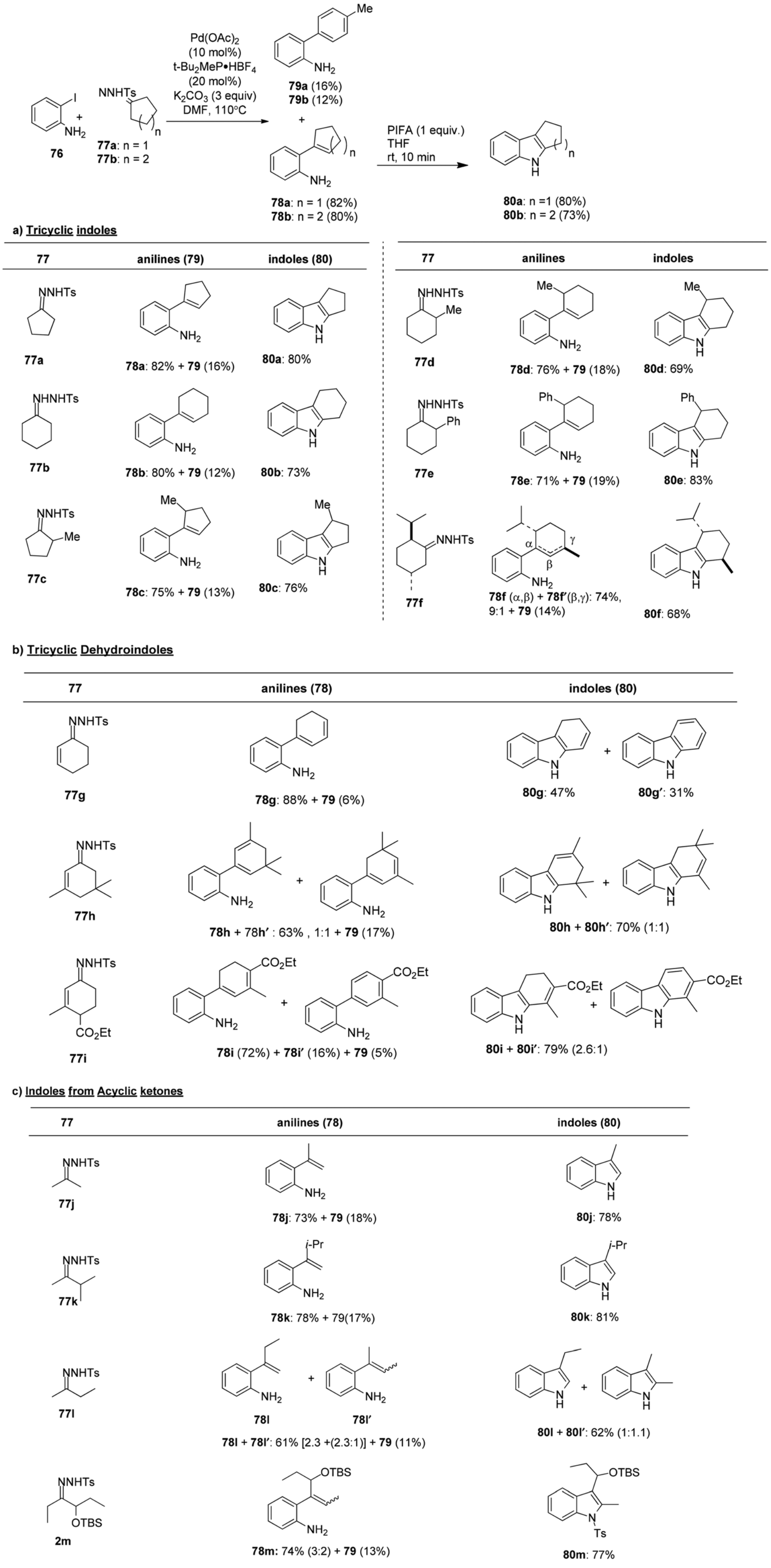
Scheme 26 Synthesis of zinc chlorin dimer.



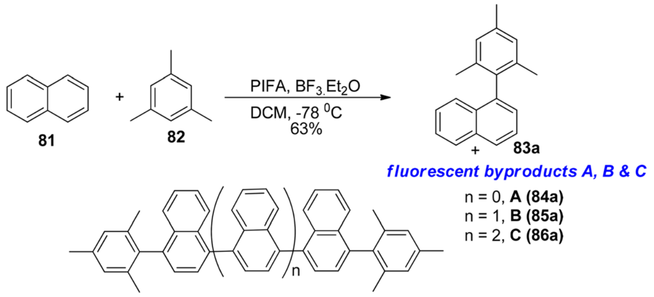
Scheme 27 Synthesis of 3-alkoxylquinoxalin-2(1*H*)-ones.



Scheme 28 Synthesis of 3-alkoxylquinoxalin-2(1*H*)-ones.



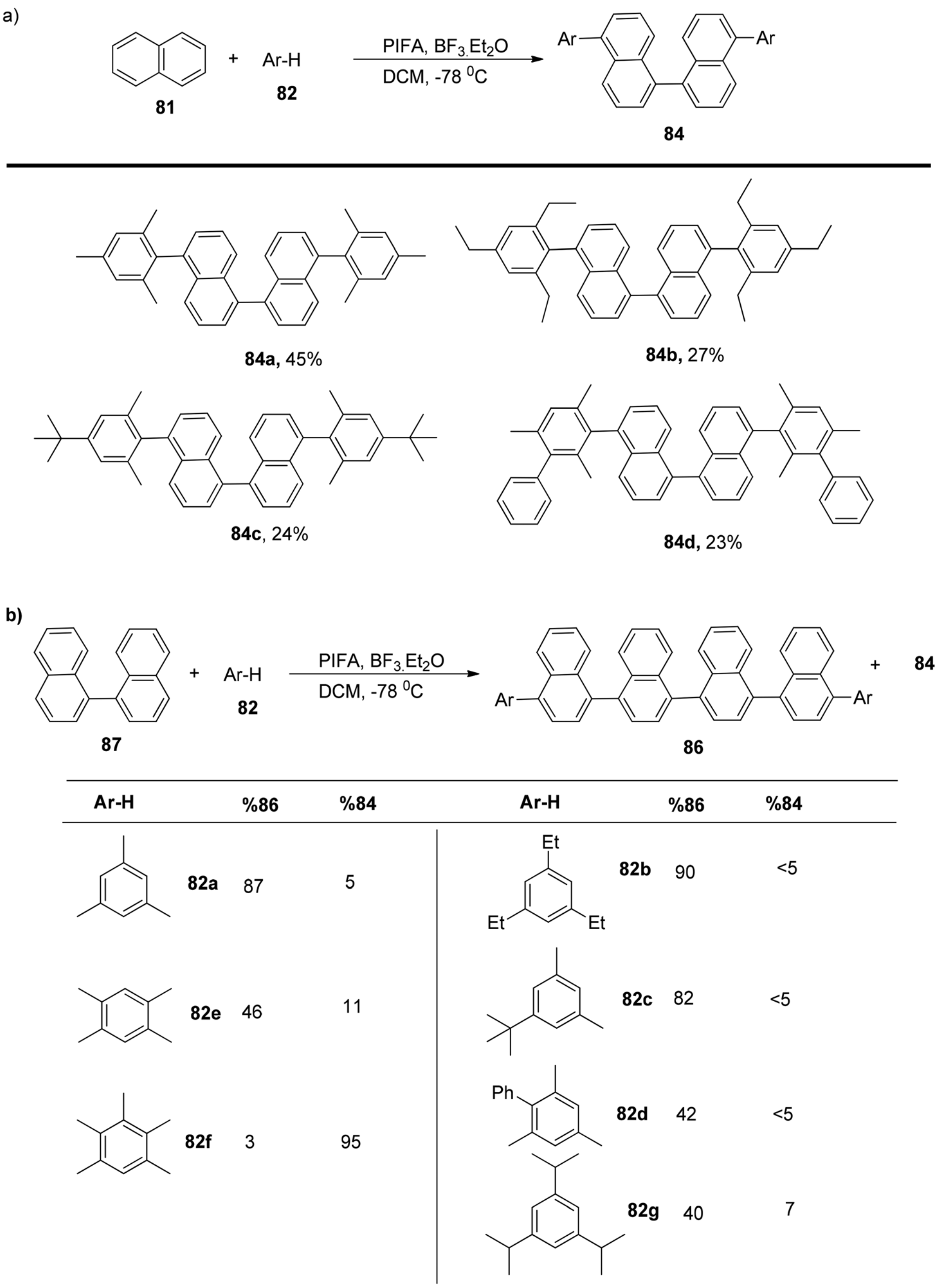
Scheme 29 An efficient method for synthesizing indoles **80**.



Scheme 30 Kita-type coupling reaction between naphthalene **81** and substituted benzenes.

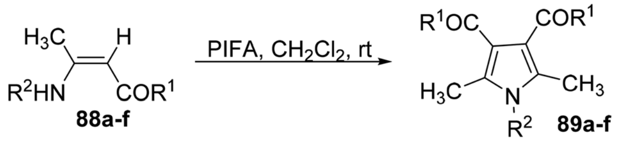
pathway, specifically through hydrogen abstraction. The method is characterized by its user-friendliness, simplicity of the reaction system, and a broad tolerance for various functional groups. Consequently, it provides a pathway to effortlessly produce a range of potential drug molecules containing 3-alkoxylquinoxalinone frameworks in excellent yields.

Chebieb *et al.*[94] have introduced an efficient method for synthesizing indoles **80** by orchestrating a two-step process that involves the cross-coupling reaction of *o*-haloanilines **76** and the PIFA oxidation of the resulting 2-alkenylanilines **78.** A notable feature of this sequential approach is its modular strategy, which is applicable to both acyclic and cyclic starting



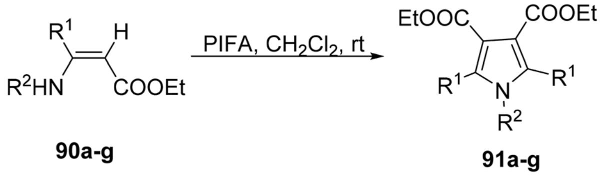
Scheme 31 Oxidative four-component Kita-type coupling reaction.

materials. The regiochemistry of this method complements the Fischer indole synthesis and related approaches. Another advantage of this method is that it enables the direct preparation of N–H indoles without the need for N-protecting groups. The scope of this indole synthesis was further explored using tosylhydrazones derived from cyclopentanone and cyclohexanone, with a specific focus on achieving the regioselective formation of indole products **80a–f** (Scheme 29). The formation of dehydroindoles (dihydrocarbazoles) was also investigated, starting with cyclohexenone-derived tosylhydrazones and proceeding to the oxidative cyclization of 1,3-dienyanilines **78g–i** (Scheme 29). Finally, the versatility of the method was



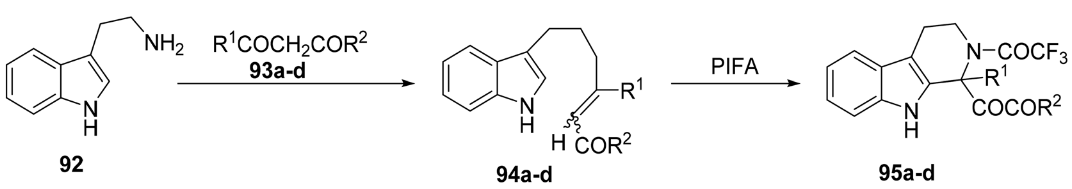
Compound (a-f)	88/89	Compound (a-f)	88/89
a	R^1 = Ph, R^2 = Bn	**d**	R^1 = CH_3, R^2 = CH_3
b	R^1 = CH_3, R^2 = Bn	**e**	R^1 = Ph, R^2 = *p*-Cl-C_6H_4
c	R^1 = Ph, R^2 = CH_3	**f**	R^1 = CH_3, R^2 = *p*-Cl-C_6H_4

Scheme 32 Synthesis of substituted pyrroles **89a–f**.



Compound (a-g)	90/91	Compound (a-g)	90/91
a	R^1 = CH_3, R^2 = CH_3	**e**	R^1 = Ph, R^2 = Bz
b	R^1 = CH_3, R^2 = Bz	**f**	R^1 = Ph, R^2 = CH_3
c	R^1 = Ph, R^2 = *p*-ClC_6H_4	**g**	R^1 = Ph, R^2 = Pr
d	R^1 = CH_3, R^2 = *p*-ClC_6H_4		

Scheme 33 Synthesis of substituted pyrroles **91a–f**.

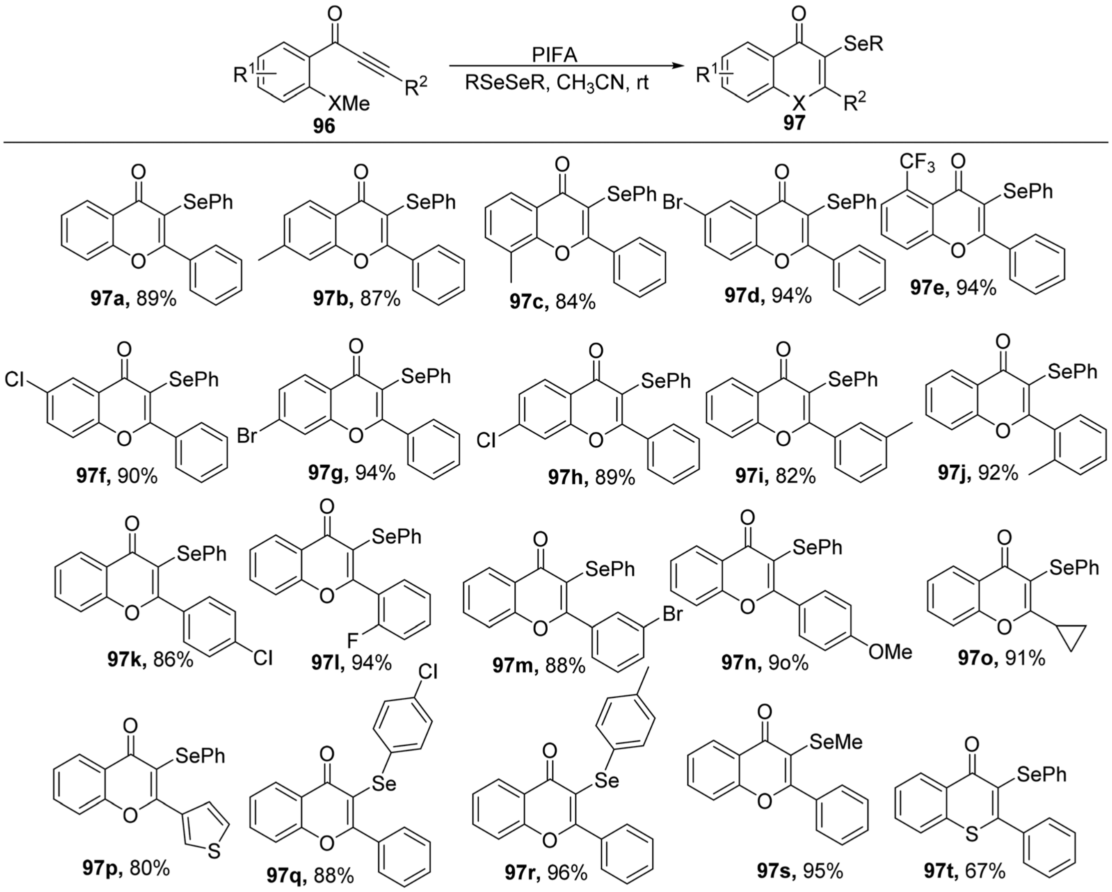


Compound (a-d)	93/94/95	Compound (a-d)	93/94/95
a	R^1 = Me, R^2 = OEt	**c**	R^1 = Ph, R^2 = Me
b	R^1 = Me, R^2 = Me	**d**	R^1 = Pr, R^2 = OEt

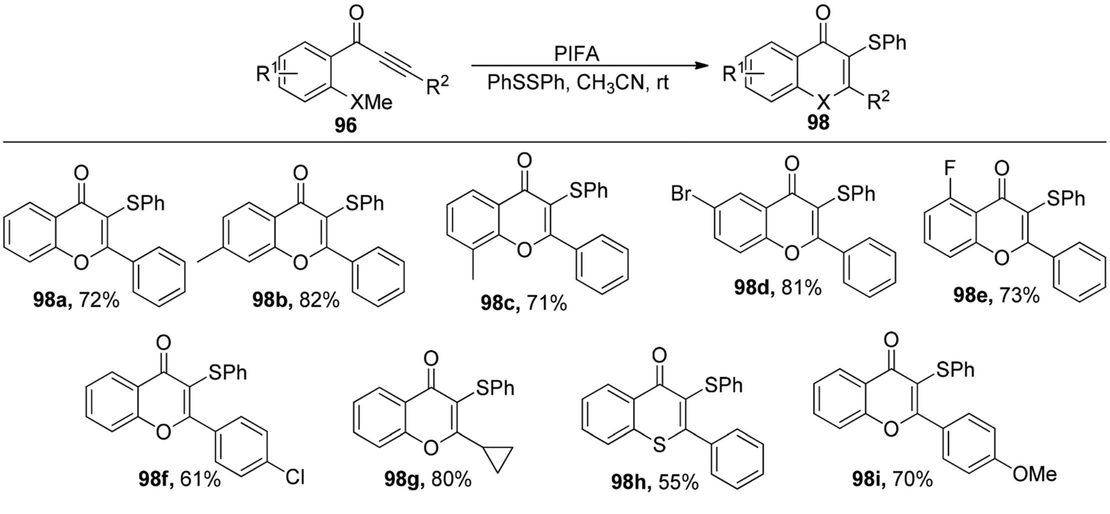
Scheme 34 Synthetic methodology for carboline analogues **95a–d**.

demonstrated by synthesizing indoles **80j–m** from acyclic substrates, showcasing a broad substrate scope (Scheme 29).

A direct oxidative Kita-type coupling reaction was observed between naphthalene **81** and substituted benzenes reported by Faggi *et al.*,[95] resulting in the formation of a linear tetraarene with a binaphthalene core, **83a**, in a 63% yield after 3 hours at −78 °C when using PIFA/BF_3·Et_2O as a catalyst (Scheme 30). The ratio of **83a** to potential overoxidation products like **84a**,



Scheme 35 Reaction scheme for synthesizing 3-Se chromones/thiochromones.



Scheme 36 Reaction scheme for synthesizing 3-S chromones/thiochromones.

85a, and **86a** seemed to be influenced by the quantity of PIFA oxidant utilized.

To explore this, an excess of PIFA was employed, allowing the extension of the method to various electron-rich arenes, yielding tetraaryl products **84a–d** in the range of 45–23% yields (Scheme 31a). This methodology could also be applied to the coupling of unfunctionalized 1,1′-binaphthalene **87** with mesitylene **82**, resulting in the selective formation of a linear hexaarene product with an impressive 87% yield (Scheme 31b).

3.5. Substituted pyrroles

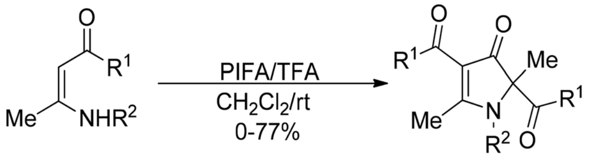
Owing to their paramount importance as the principal structural constituents within various alkaloids and pharmacologically active compounds, highly substituted pyrrole derivatives have been the focal point of considerable scientific interest in recent years.[96] Oxidative dimerization emerges as a pivotal synthetic route for the acquisition of symmetric compounds.

Zhang *et al.*[97] elucidated a tandem dimerization–cyclocondensation strategy for the synthesis of highly substituted pyrrole analogues utilizing enaminones in the presence of PIFA. This method demonstrates efficiency and offers multiple advantages, including readily available starting materials, non-toxic reagents, and mild reaction conditions. PIFA was involved in the reaction *via* an ionic pathway, actively participating in the process through its contribution to the ionic mechanism. To assess the scope of this reaction, several enaminones **88a–f** were subjected to experimentation, as outlined in Scheme 32. Product characterization involved a comprehensive array of analytical techniques, including melting point analysis, infrared spectroscopy, nuclear magnetic resonance (NMR) spectroscopy, and mass spectrometry (MS), leading to the characterization of products **89a–f**.

Furthermore, within the same year, Zhang *et al.*[98] explored the applicability of this reaction to various enamine-esters (Scheme 33). Utilizing PIFA as a catalyst, the transformation of enamine-esters **90a–g** into pyrrole derivatives **91a–g** was achieved with ease. PIFA was involved in the reaction *via* an ionic pathway. Subsequently, the compounds underwent comprehensive structural characterization, encompassing analyses such as melting point determination, MS, infrared spectroscopy, as well as NMR spectroscopic investigations.

3.6. Cyclization

The Pictet–Spengler methodology is a recognized synthetic approach for the construction of both indole and isoquinoline alkaloids. Papadopoulou *et al.*[99] demonstrated its application in the derivatization of tryptophan and tryptamine derivatives to yield 1,2,3,4-tetrahydro-β-carbolines **95a–d** (Scheme 34). The straightforward combination of tryptamine **92** with β-dicarbonyl compounds **93a–d** leads to the formation of car-



99a-t **100a-t**

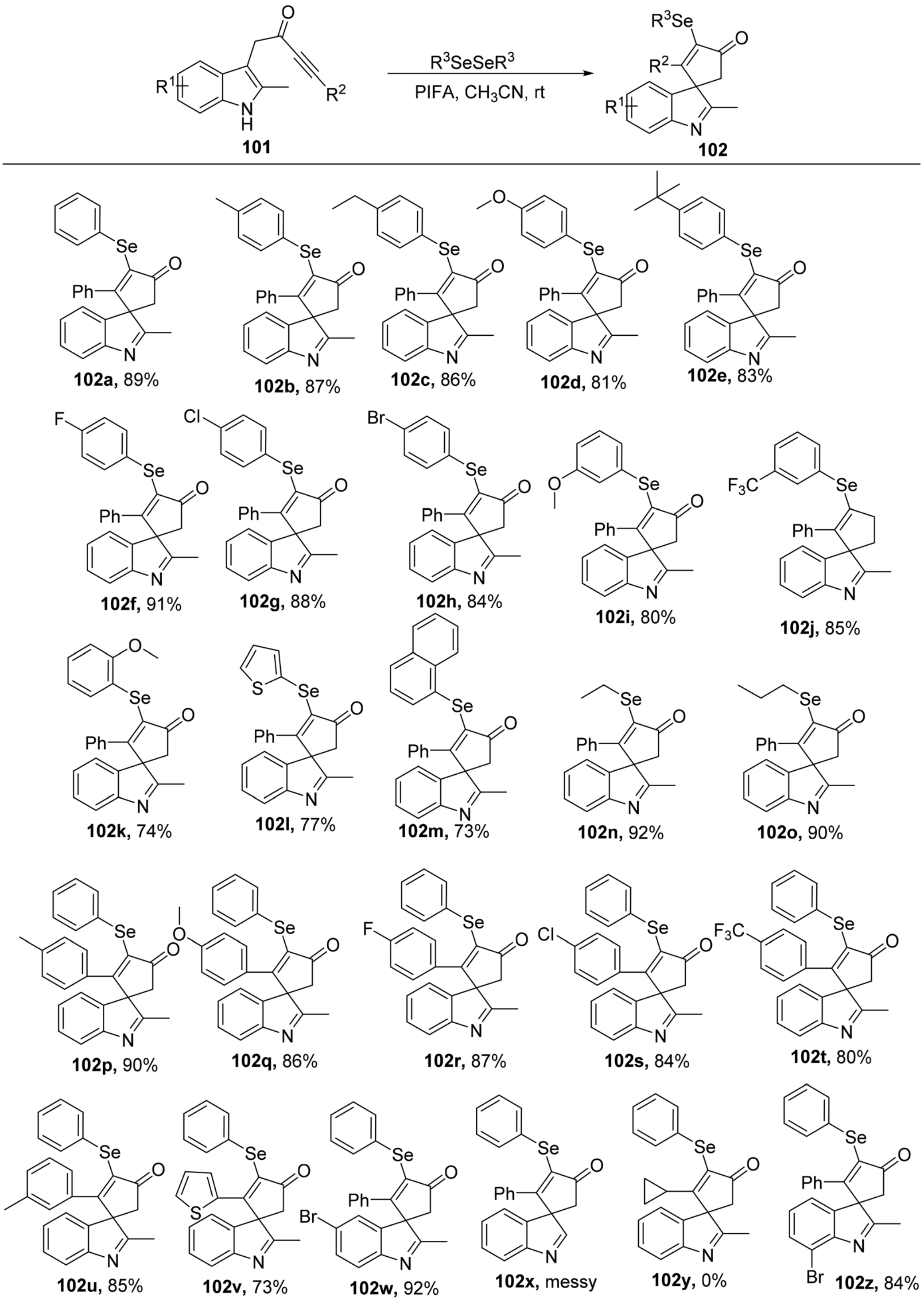
Compound (a-t)	99/100	Compound (a-t)	99/100
a	R^1 = PhNH, R^2 = Bn	**k**	R^1 = 4-ClPhNH, R^2 = Me
b	R^1 = 4-MePhNH, R^2 = Bn	**l**	R^1 = 2-MePhNH, R^2 = Me
c	R^1 = 4-MeOPhNH, R^2 = Bn	**m**	R^1 = CH_3, R^2 = *p*-Cl-C_6H_4
d	R^1 = 4-ClPhNH, R^2 = Bn	**n**	R^1 = 2-MeOPhNH, R^2 = Me
e	R^1 = 2-MePhNH, R^2 = Bn	**o**	R^1 = 4-ClPhNH, R^2 = Me
f	R^1 = 2-MeOPhNH, R^2 = Bn	**p**	R^1 = PhNH, R^2 = Ph
g	R^1 = 2-ClPhNH, R^2 = Bn	**q**	R^1 = 2-MePhNH, R^2 = Ph
h	R^1 = PhNH, R^2 = Me	**r**	R^1 = OEt, R^2 = Me
i	R^1 = 4-MePhNH, R^2 = Me	**s**	R^1 = Me, R^2 = Bn
j	R^1 = 2-MeOPhNH, R^2 = Me	**t**	R^1 = Me, R^2 = Me

Scheme 37 Synthesis of pyrrolin-4-one derivatives **85a–t**.

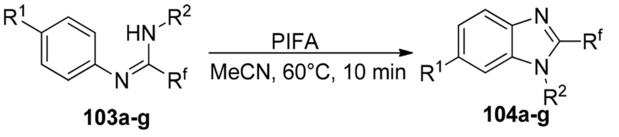
bonyl compounds of the type **94a–d**.[100] Under controlled reaction conditions ranging from 0 °C to room temperature, the synthesis of carboline analogues **95a–d** was achieved in the presence of PIFA, serving as the cyclization agent.

Chromones, characterized by their unique heterocyclic framework, are commonly encountered in both pharmaceuticals and natural compounds.[101] The introduction of sulfur or selenium functionalities into the chromone structure imparts intriguing biological properties to the resultant molecules, thereby attracting significant scientific interest over recent decades.[102]

Ai *et al.*[103] accomplished the synthesis of 3-selenyl/sulfenyl chromones/thiochromones **97**/**98** through the reaction of



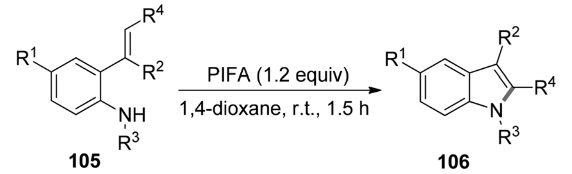
Scheme 38 Synthesis of selenated spiro[cyclopentenone-1,3′-indoles].



103a-g **104a-g**

Entry	R^1	R^2	R^f	Yield of 104 (%)
1	H	Ph	CF_2Br	**104a** (62)
2	H	Bn	CF_3	**104b** (68)
3	OMe	Bn	CF_3	**104c** (75)
4	Cl	Bn	CF_3	**104d** (58)
5	H	Bn	CF_2Br	**104e** (65)
6	H	Bu	CF_2Br	**104f** (48)
7	CF_3	Bn	CF_2Br	**104g** (45)

Scheme 39 Synthetic scheme for development of *N*-alkyl-2-fluoromethylbenzimidazoles.

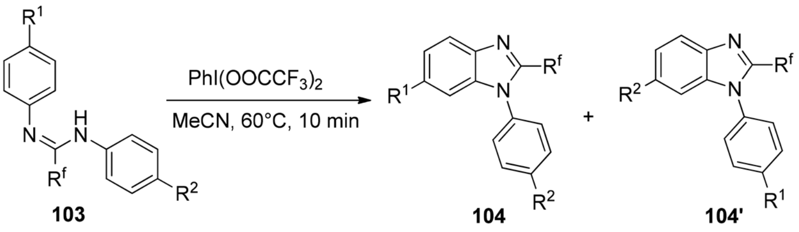


105 **106**

Entry	R^1	R^2	R^3	R^4	Yield (%)
1	H	Ph	H	H	78 (**106a**)
2	Me	Ph	H	H	64 (**106b**)
3	*i*-Pr	Ph	H	H	63 (**106c**)
4	*t*-Bu	Ph	H	H	71 (**106d**)
5	F	Ph	H	H	56 (**106e**)
6	H	4-Me-C_6H_4	H	H	73 (**106f**)
7	H	Ph	Me	H	68 (**106g**)
8	Br	4-F-C_6H_4	H	H	63 (**106h**)
9	Cl	4-Cl-C_6H_4	H	H	57 (**106i**)
10	H	H	H	Ph	- (**106j**)
11	H	Ph	H	Me	trace (**106k**)

Scheme 41 Synthesis of indole derivatives **106** with 2-vinylanilines **105** and PIFA.

alkynyl aryl ketonic substrates **96** with diselenides/disulfides, employing PIFA as the catalytic agent (Scheme 35). Furthermore, the synthesis of sulfenylated chromone derivatives was explored using PIFA/PhSSPh (Scheme 36). PIFA was involved in the reaction *via* an ionic pathway. Notably, this methodology is distinguished by its metal-free nature, wide substrate applicability, mild reaction conditions, and the production of high-yielding products.



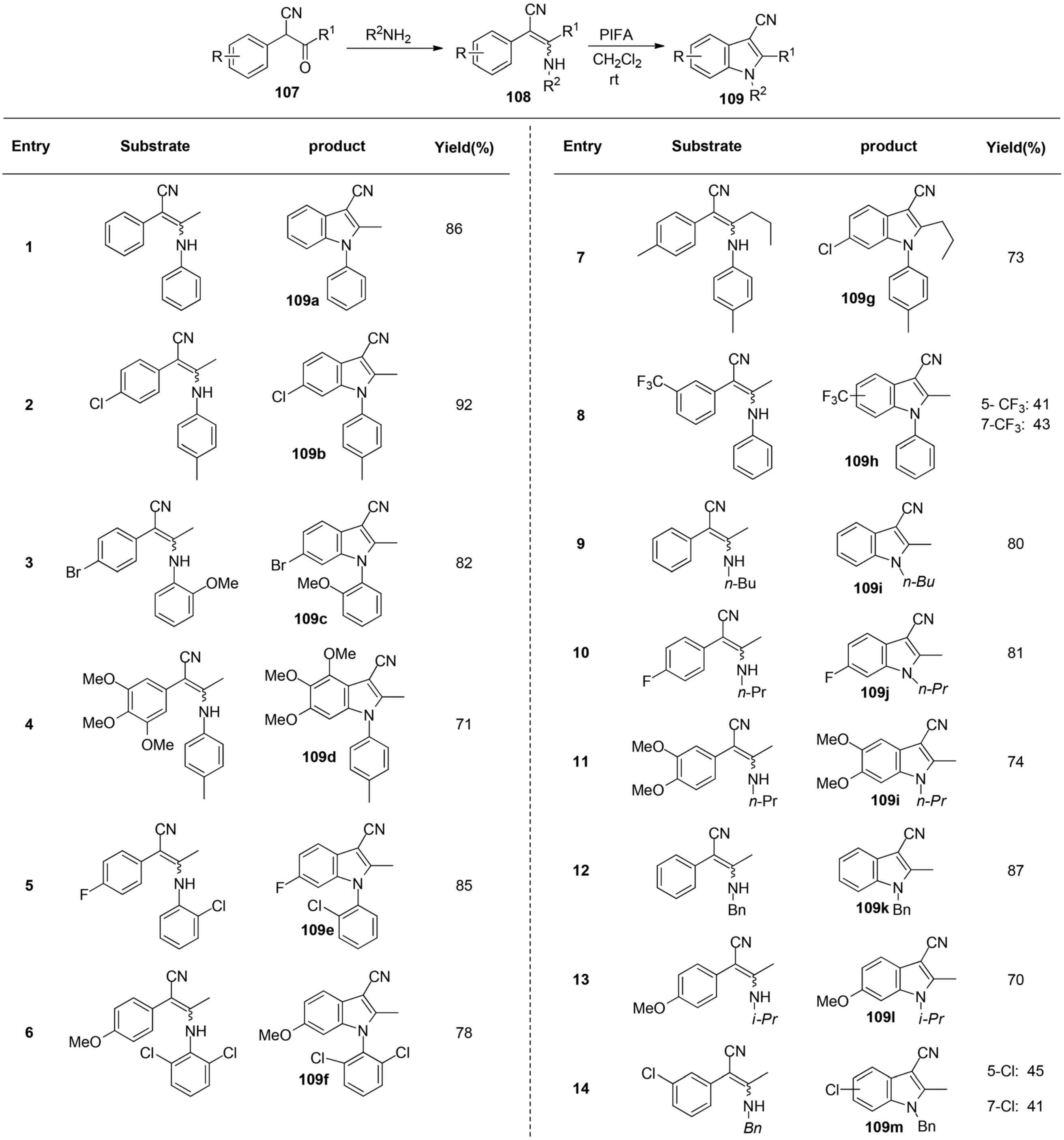
103 **104** **104'**

Entry	R^1	R^2	R^f	Yield of 104 (%)	104/104'
1	Me	Me	CF_3	**104h** (82)	
2	H	H	CF_3	**104i** (83)	
3	Cl	Cl	CF_3	**104j** (90)	
4	NO_2	NO_2	CF_3	-	
5	H	H	CF_2Br	**104a** (62)	
6	H	OMe	CF_2Br	**104k** (54)	<1:99
7	H	Me	CF_2Br	**104l** (73)	1:6.7
8	H	F	CF_2Br	**104m** (65)	1:3.3
9	H	Cl	CF_2Br	**104n** (69)	1.44:1
10	H	Br	CF_2Br	**104o** (63)	1.27:1
11	H	I	CF_2Br	**104p** (83)	1:1.2
12	H	COOEt	CF_2Br	**104q** (83)	>99:1
13	H	CN	CF_2Br	**104r** (77)	>99:1
14	H	CF_3	CF_2Br	**104s** (81)	>99:1
15	H	NO_2	CF_2Br	**104t** (87)	>99:1
16	H	Ac	CF_2Br	**104u** (78)	>99:1
17	H	*t*-Bu	CF_2Br	**104v** (70)	1:6.7
18	OMe	OMe	CF_2Br	**104w** (71)	
19	*t*-Bu	*t*-Bu	CF_2Br	**104x** (71)	

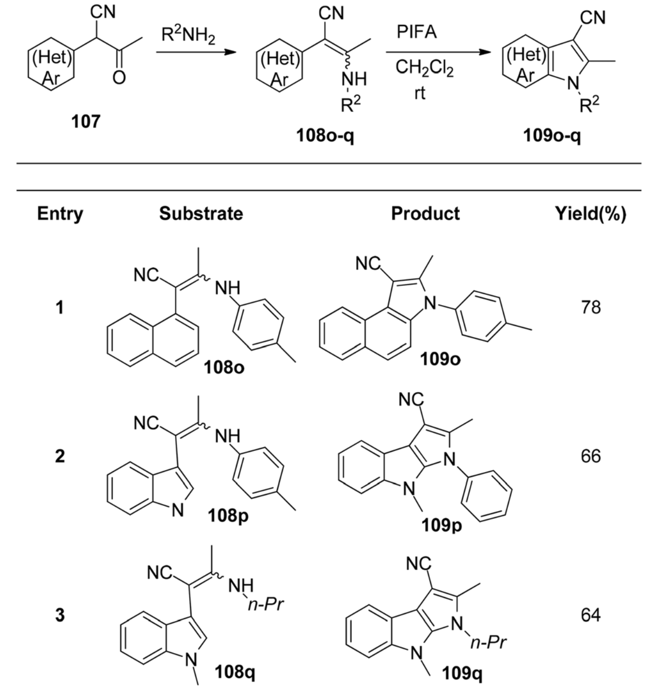
Scheme 40 Synthesis of *N*-aryl-2-fluorobenzimidazoles.

Enaminones, arising from the union of nucleophilic enamines and electrophilic enones, represent pivotal synthetic intermediates due to their auspicious structural attributes.[104] Pyrrolin-4-one analogues, nitrogen-containing heterocycles, find extensive utility as fundamental building blocks in the design and synthesis of anti-cancer, anti-thrombotic, and antibacterial pharmaceutical agents.[105]

The readily accessible enaminones **99a–t** underwent PIFA-mediated cyclization reactions to yield highly substituted pyrrolin-4-ones **100a–t**, as reported by Huang *et al.*[106] This rearrangement reaction entails concurrent cleavage and formation of C–N and C–C bonds (Scheme 37). PIFA engaged in reactions *via* the ionic pathway. Noteworthy advantages of this process include its mild reaction conditions, wide substrate



Scheme 42 Synthesis of a range of *N*-arylated and *N*-alkylated indole derivatives **109**.

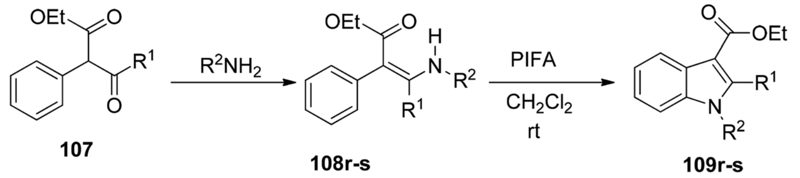


Scheme 43 Synthesis of novel pyrrole-fused aromatic compounds **109o–q**.

versatility, accessibility of starting materials, and the attainment of excellent product yields.

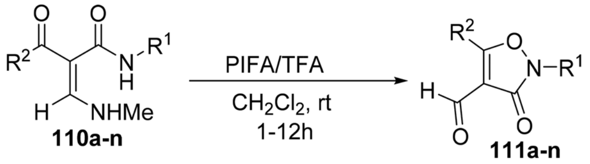
Spirocycles are integral components of pharmaceuticals, natural products, and valuable materials.[107] Among these spirocycles, spiroindolenines have garnered significant attention among organic chemists due to their diverse array of biological properties.[108] The key class of bioactive chemicals known as organoselenides, on the other hand, are widely present in physiologically active substances and medications.[109] Organo-selenide synthesis has been the subject of extensive research up to this point.[110] Chen *et al.*[111] described a rapid, mild selenylative spirocyclization of indolyl ynones **101** *via* the use of PIFA that involved an ionic route and an electrophilic cyclization to obtain selenated spiroindolenines **102a–z**. Indolyl ynones undergo an electrophilic dearomative cascade cyclization catalyzed by PIFA leading to the *in situ* generation of $RSeOCOCF_3$ from diselenides. PIFA engaged in reactions *via* the ionic pathway. This approach offers a rapid and effective pathway to develop selenated spiro[cyclopentenone-1,3′-indoles] with diverse functional group tolerance (Scheme 38).

Fluorine exhibits distinct properties, and consequently, organofluorine compounds, particularly those containing fluorine heterocyclic motifs, hold significant importance in



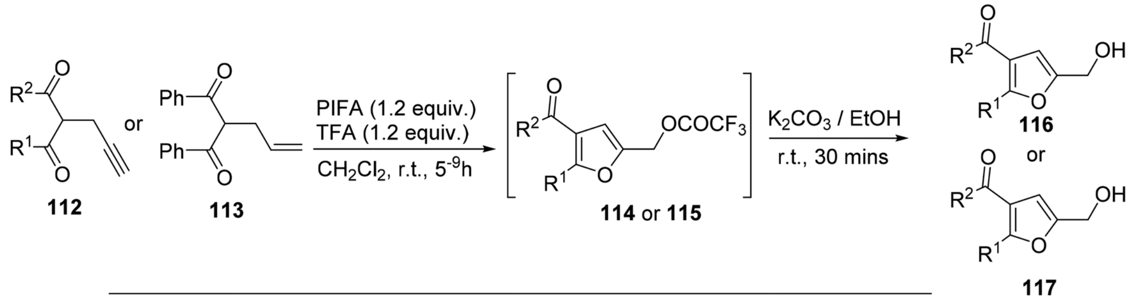
109r $R^1 = CH_3$, $R^2 = Ph$ (75%)
109s $R^1 = Bn$, $R^2 = n\text{-}Pr$ (68%)

Scheme 44 Synthesis of *N*-arylated and *N*-alkylated indole derivatives **109r–s**.



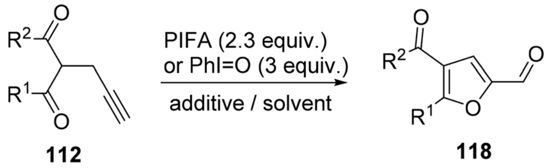
Compound (a-n)	110/111	Compound (a-n)	110/111
a	$R^1 = 4\text{-}ClC_6H_4$, $R^2 = CH_3$	h	$R^1 = 4\text{-}ClC_6H_4$, $R^2 = n\text{-}Pr$
b	$R^1 = Ph$, $R^2 = CH_3$	i	$R^1 = 4\text{-}ClC_6H_4$, $R^2 = Ph$
c	$R^1 = 4\text{-}MeC_6H_4$, $R^2 = CH_3$	j	$R^1 = Ph$, $R^2 = Ph$
d	$R^1 = 4\text{-}BrC_6H_4$, $R^2 = CH_3$	k	$R^1 = Ph$, $R^2 = 4\text{-}MeC_6H_4$
e	$R^1 = 2\text{-}ClC_6H_4$, $R^2 = CH_3$	l	$R^1 = Ph$, $R^2 = 4\text{-}ClC_6H_4$
f	$R^1 = 3\text{-}ClC_6H_4$, $R^2 = CH_3$	m	$R^1 = 2\text{-}Cl$, $R^2 = Bn$
g	$R^1 = 4\text{-}NO_2C_6H_4$, $R^2 = CH_3$	n	$R^1 = Ph$, $R^2 = 4\text{-}MeOC_6H_4$

Scheme 45 Reaction scheme for isoxazol-3(2*H*)-ones **111a–n** synthesis.



Entry	Substrate	R^1	R^2	Product	% Yield
1	**112a**	Ph	Ph	**116a**	70
2	**112b**	Ph	OEt	**116b**	60
3	**112c**	Me	OEt	**116c**	68
4	**112d**	Me	Me	**116d**	41
5	**112e**	Et	Et	**116e**	64
6	**112f**	*i*Pr	*i*Pr	**116f**	71
7	**112g**	*t*Bu	*t*Bu	**116g**	78
8	**113**	-	-	**117**	65

Scheme 46 The oxidative cyclo-isomerization of propargylated/allylated-1,3-diketones **112**/**113** to obtain analogues of furfuryl alcohols **116**/**117**.



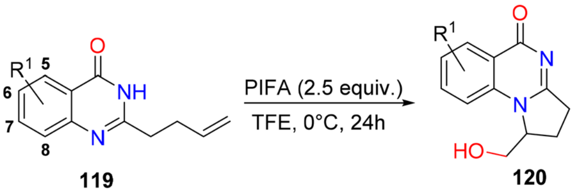
Entry	Substrate	Method A			Method B			Method C or D		
		(°C)	(h)	**118 (%)**	(°C)	(h)	**118 (%)**	(°C)	(h)	**118 (%)**
1	**11a**	rt	2	78	rt	19	51	60	23	33
2	**11b**	rt	3	60	60	4	53	60	19	31
3	**11c**	rt	17	48	60	19	53	60	19	59
4	**11d**	rt	5	30	rt	19	26	60	22	68
5	**11e**	rt	9	38	rt	19	41	60	22	45
6	**11f**	rt	21	24	rt	22	41	60	22	15
7	**11g**	rt	17	35	rt	21	72	60	20	0

Method A: PIFA (entries 1,2 and 7: 2 equiv., entries 3-6: 3 equiv.), $BF_3.OEt_2$ (1 equiv.)/CH_2Cl_2,
Method B: PIFA (entries 1-6: 3 equiv., entry 7: 2 equiv.)/HFIP,
Method C: (entries 1-3): PhI=O (3 equiv.)/DCE-HFIP (3:1),
Method D: (entries 4-7): PhI=O (3 equiv.), silica gel/DCE.

Scheme 47 The oxidative cyclo-isomerization of different propargylated-1,3-diketones **112** to obtain analogues of furfurals **118**.

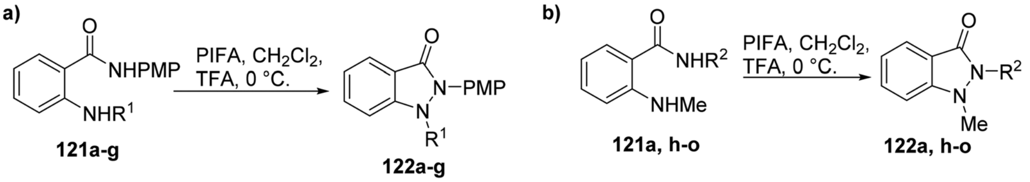
the fields of medicine, agriculture, and materials chemistry.[112] Notably, 2-fluoroalkylbenzimidazoles are recognized for their potency as insecticides and herbicides.[113]

The interaction of PIFA with *N*,*N*-disubstituted fluoroethanimidamides **103** to produce *N*-substituted 2-fluoromethylbenzimidazoles was disclosed by Zhu *et al.*[114] as a novel methodology for the synthesis of these compounds. The group investigated the range and limitations of this transformation after determining the ideal conditions. As a result of the initial testing of a number of *N*-aryl-*N*′-alkylfluoroethanimidamides **103**, fluoromethylbenzimidazoles **104b–g** were obtained in moderate yields (Scheme 39). Furthermore, *N*,*N*′-diarylfluoroethanimidamides were utilized, either symmetrically or asymmetrically, and the outcomes are compiled in Scheme 40. PIFA engaged in reactions *via* the ionic pathway.



Entry	Substrate	R^1	Product	% Yield
1	**119a**	H	**120a**	80
2	**119b**	5-NO$_2$	**120b**	82
3	**119c**	5-F	**120c**	83
4	**119d**	6-Me	**120d**	79
5	**119e**	6-OMe	**120e**	75
6	**119f**	6-Cl	**120f**	81
7	**119g**	6-NO$_2$	**120g**	75
8	**119h**	6,7-(OMe)$_2$	**120h**	76
9	**119i**	7-Cl	**120i**	80
10	**119j**	8-Me	**120j**	81
11	**119k**	8-Br	**120k**	76
12	**119l**	8-F	**120l**	82

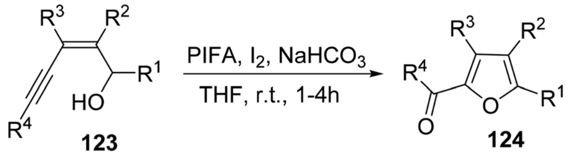
Scheme 48 Synthetic scheme for analogues of dihydropyrroloquinazolinones **120a–l**.



Entry	R^1	122 (%)
1	Me	**122a** (68)
2	allyl	**122b** (62)
3	PhCH$_2$	**122c** (67)
4	Ph	**122d** (61)
5	H	**122e** (0)
6	COOEt	**122f** (0)
7	TolSO$_2$	**122g** (0)

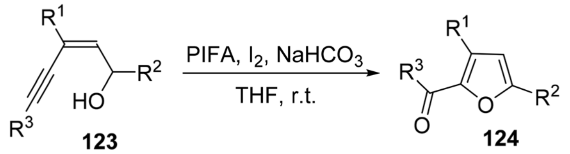
Entry	R^2	122 (%)
1	*p*-OMePh	**122a** (68)
2	Ph	**122h** (60)
3	1-Naph	**122i** (61)
4	*p*-EtPh	**122j** (60)
5	*p*-BrPh	**122k** (45)
6	H	**122l** (0)
7	PhCH$_2$	**122m** (0)
8	allyl	**122n** (0)
9	OMe	**122o** (0)

Scheme 49 a) Synthesis of indazolones **122a–g**. (b) Synthesis of indazolones **122a,h–o**.



Entry	Enynol	R^1	R^2	R^3	R^4	Product	% Yield
1	**123a**	Ph	H	H	Ph	**124a**	83
2	**123b**	4-ClC$_6$H$_4$	H	H	4-MeOC$_6$H$_4$	**124b**	79
3	**123c**	Et	H	H	Ph	-	-
4	**123d**	Ph	Et	H	Bu	**124d**	54
5	**123e**	4-ClC$_6$H$_4$	Et	H	Ph	**124e**	90
6	**123f**	4-MeC$_6$H$_4$	Et	H	Ph	**124f**	78
7	**123g**	Ph	CH(OTBS)Ph	H	Ph	**124g**	92
8	**123h**	Et	Et	H	Bu	-	-
9	**123i**	Ph	Et	Et	4-MeOC$_6$H$_4$	**124i**	81
10	**123j**	4-MeC$_6$H$_4$	Bu	Bu	Ph	**124j**	69
11	**123k**	Ph	Ph	Ph—≡	Ph	**124k**	47

Scheme 50 Synthetic pathway for 2-acyl furan analogues **124a–k** in presence of PIFA/I$_2$.



Entry	Enynol	R^1	R^2	R^3	Time (h)	Product	% Yield
1	**123l**	Bu	Ph	Ph	2	**124l**	63
2	**123m**	TMS	Ph	Ph	2	**124m**	82
3	**123n**	Bu	Ph	Bu	2	**124n**	83
4	**123o**	Ph	Ph	Ph	2	**-**	-
5	**123p**	Ph	Ph	H	2	**124p**	53
6	**123q**	Ph	4-ClC$_6$H$_4$	H	2	**124q**	64
7	**123r**	CH$_2$OTBS	Ph	Bu	1	**124r**	59
8	**123s**	COOEt	Ph	Bu	2	**124s**	31
9	**123t**	Bu	Ph	CH$_2$OTBS	2	**124t**	76
10	**123u**	COOEt	Ph	CH$_2$OTBS	1.5	**124u**	42

Scheme 51 Synthetic methodology for 2-acyl furans **124l–u** catalyzed by PIFA/I$_2$.

Wu *et al.*[115] introduced a method for synthesizing different indoles **106** *via* cyclization reactions involving 2-vinylanilines **105** in the presence of PIFA, all conducted under mild reaction conditions. This strategy exhibits notable versatility and works well with a diverse array of substituents, both electron-withdrawing and electron-donating groups on the aromatic ring and the nitrogen atom of 2-vinylanilines **105**, resulting in the desired products with moderate to good yields (Scheme 41). PIFA engaged in reactions *via* the ionic pathway.

Du *et al.*[116] have developed a method for the synthesis of a range of *N*-arylated and *N*-alkylated indole derivatives **109** through a PIFA-mediated intramolecular cyclization (Scheme 42). This innovative approach enables the formation of an indole framework by linking the N-atom in the side chain to the benzene ring **108** in the final step of synthesis. Furthermore, this method can also be employed to produce novel pyrrole-fused aromatic compounds **109o–q** (Scheme 43) and *N*-substituted indole-3-carboxylic acid ester **109r–s** (Scheme 44). PIFA actively engaged in the reaction by following a free radical pathway, specifically through single-electron oxidation. The creation of substituted indole frameworks has garnered significant interest over the years, as the indole unit has found increasingly diverse applications in both natural products and designed medicinal agents.[117] This method stands out for its accessible starting materials, mild reaction conditions, and straightforward workup process.

3.7. Oxidative cyclization

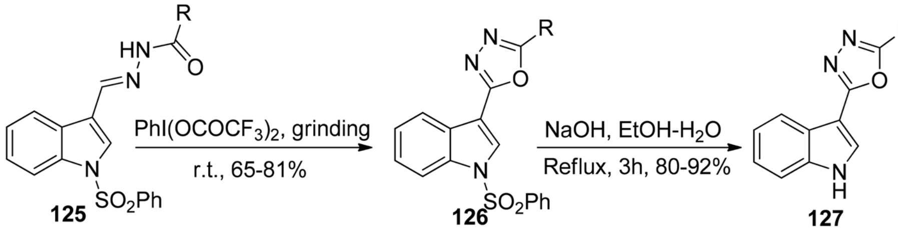
Some compounds, both naturally occurring and synthetic, feature isoxazolones and their heterocyclic counterparts as central structural motifs. These compounds also encompass a diverse array of bio-, physio-, and pharmacological properties.[118,119] Analogues of isoxazol-3(2*H*)-ones are commonly utilized in agrochemistry, materials chemistry, and organic chemistry.[120]

Using PIFA/TFA as the catalytic system, Yuan *et al.*[121] observed that α-acyl acrylamides **110a–n** underwent intramolecular cyclization at room temperature (Scheme 45). This chemoselective and mild oxidative transformation, free of metal catalysts, provides an alternative methodology to create O–N linkages, ultimately resulting in the formation of isoxazolone analogues **111a–n**. PIFA engaged in the reaction by following the ionic pathway.

Saito *et al.*[122] employed PIFA in the oxidative cycloisomerization of propargylated/allylated β-keto esters **112**/**113**, leading to the formation of furfuryl alcohol analogues **116**/**117** (Scheme 46) as well as furfurals **118** (Scheme 47). The direct synthesis of furfurals **118** from 2-propargyl 1,3-dicarbonyl compounds was accomplished by PIFA in hexafluoroisopropanol (HFIP) or PIFA–BF_3–OEt_2 in CH_2Cl_2.

To cultivate novel motifs with enhanced potential for generating potent lead compounds featuring advantageous physicochemical attributes, structural modifications of naturally occurring compounds represent a fundamental design approach in contemporary drug discovery.[123] This approach facilitates the synthesis of analogues based on natural compounds, a critical endeavor for synthetic chemists.

Vaskevych *et al.*[124] detailed an oxidative and regioselective PIFA-mediated synthetic methodology for the synthesis of dihydropyrroloquinazolinones **120a–l**, structural analogues of vasicinone alkaloids, derived from quinazolinones **119a–l**. All quinazolones **119a–l** underwent 5-*exo-trig* cyclization, resulting in the desired products **120a–l** obtained with



125 **126** **127**

127a: R = C_6H_5
127b: R = $CH_2C_6H_5$
127c: R = 4-pyridiyl
127d: R = 3-pyridyl
127e: R = 4-$CH_3OC_6H_4$
127f: R = 4-Cl-C_6H_4
127g: R = 3,4-di-$CH_3OC_6H_3$
127h: R = 2,3,4-tri-$CH_3OC_6H_2$
127i: R = 4-BnO-3-$CH_3OC_6H_3$
127j: NH = NCH_3; R = 4-BnO-3-$CH_3OC_6H_3$
127k: R = 4-HO-3-$CH_3OC_6H_3$
127l: R = CH_3
127m: R = CF_3

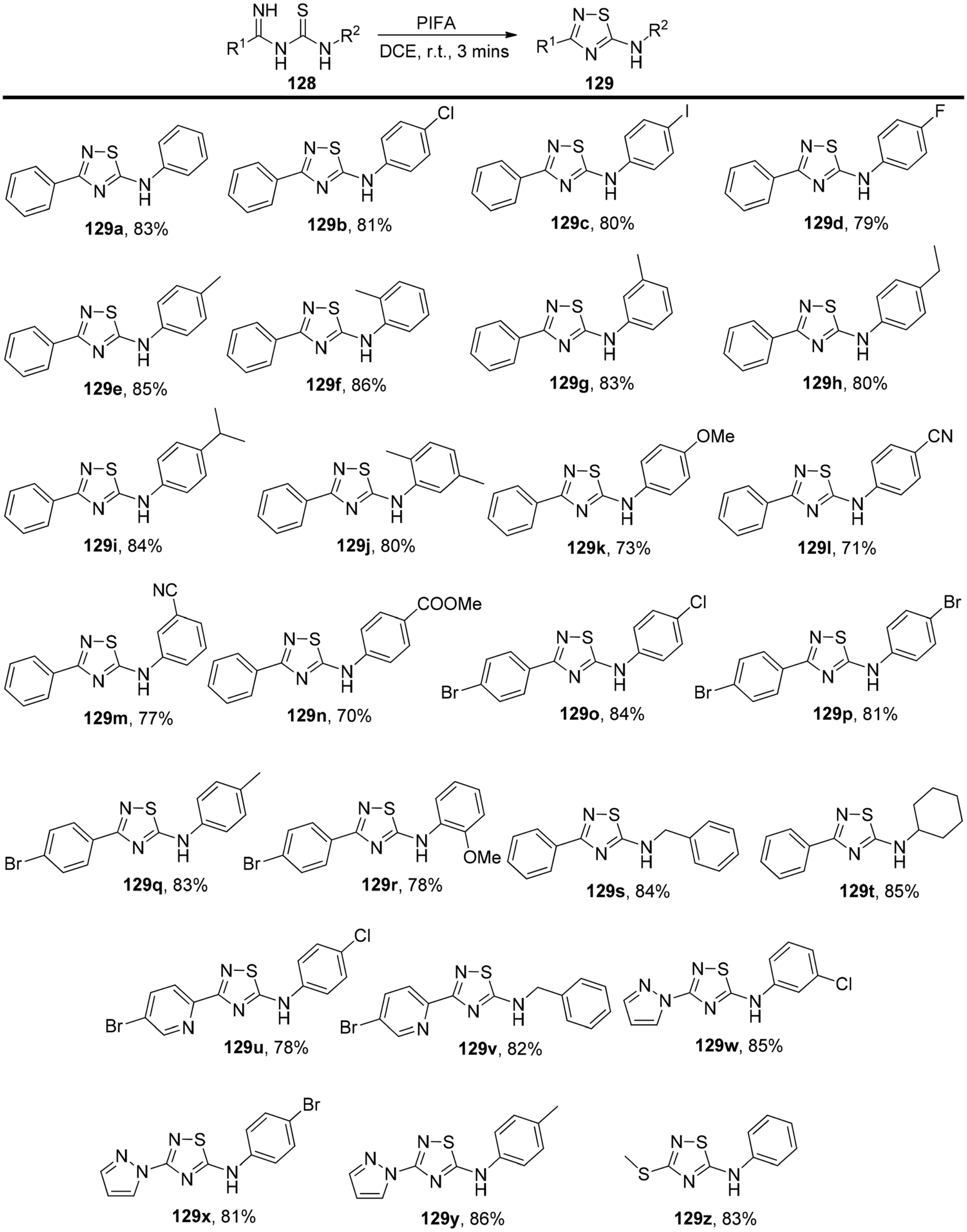
CH_3I, KOH, DMSO
Stirring, r.t.m 80%

Scheme 52 Synthetic scheme for indolyl-1,3,4-oxadiazoles **126** as well as 5-(3′-indolyl)-1,3,4-oxadiazole analogues **127a–m**.

yields ranging from 75–83% (Scheme 48). PIFA engaged in the reaction by following the ionic pathway.

Various domains within the field of chemistry have significantly contributed to the advancement of organic synthesis over the years, with a major emphasis on identifying efficient methodologies to facilitate complex transformations.[125]

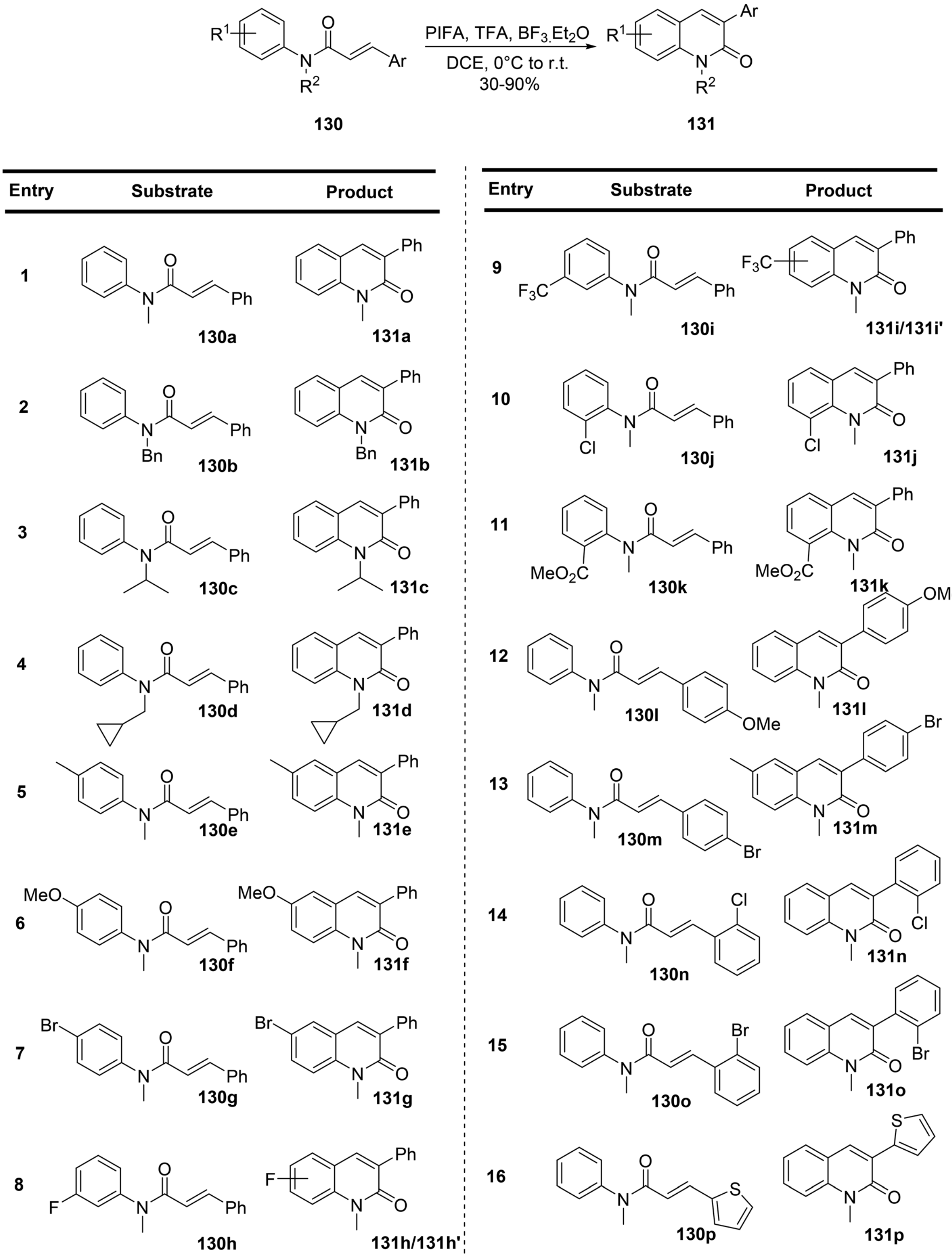
Correa *et al.*[126] effectively harnessed the potential of cost-effective, easy-to-handle PIFA to synthesize functionalized



Scheme 53 Synthesis of compounds **129a–z**.

indazolones **122** (Scheme 49). The use of PIFA on amide derivatives **121** led to the generation of *N*-acylated nitrenium ions, representing the pioneering instance of successful intramolecular trapping of these ions by the amine group. This breakthrough allowed for the synthesis of N-heterocycles through N–N bond formation.

To achieve the synthesis of 2-acyl furans at room temperature, Du *et al.*[127] employed an oxidative cycloisomerization



Scheme 54 Synthesis of 4-unsubstituted 3-arylquinol-2-one **131** *via* PIFA-mediated C–C bond formation and 1,2-aryl shift.

approach using *cis*-enynols in the presence of PIFA/molecular iodine. These reactions demonstrate efficacy with a diverse range of substrates, making them valuable for the synthesis of furan analogues. The proposition is that trifluoroacetylhypoiodite, generated *in situ*, serves as the activator for alkyne **123** in these reactions. Employing this methodology, C-1/C-5 functionalized *cis*-enynols have been processed, yielding 2-acyl furan analogues **124** in notably high yields (Schemes 50 and 51). PIFA engaged in the reaction by following the ionic pathway.

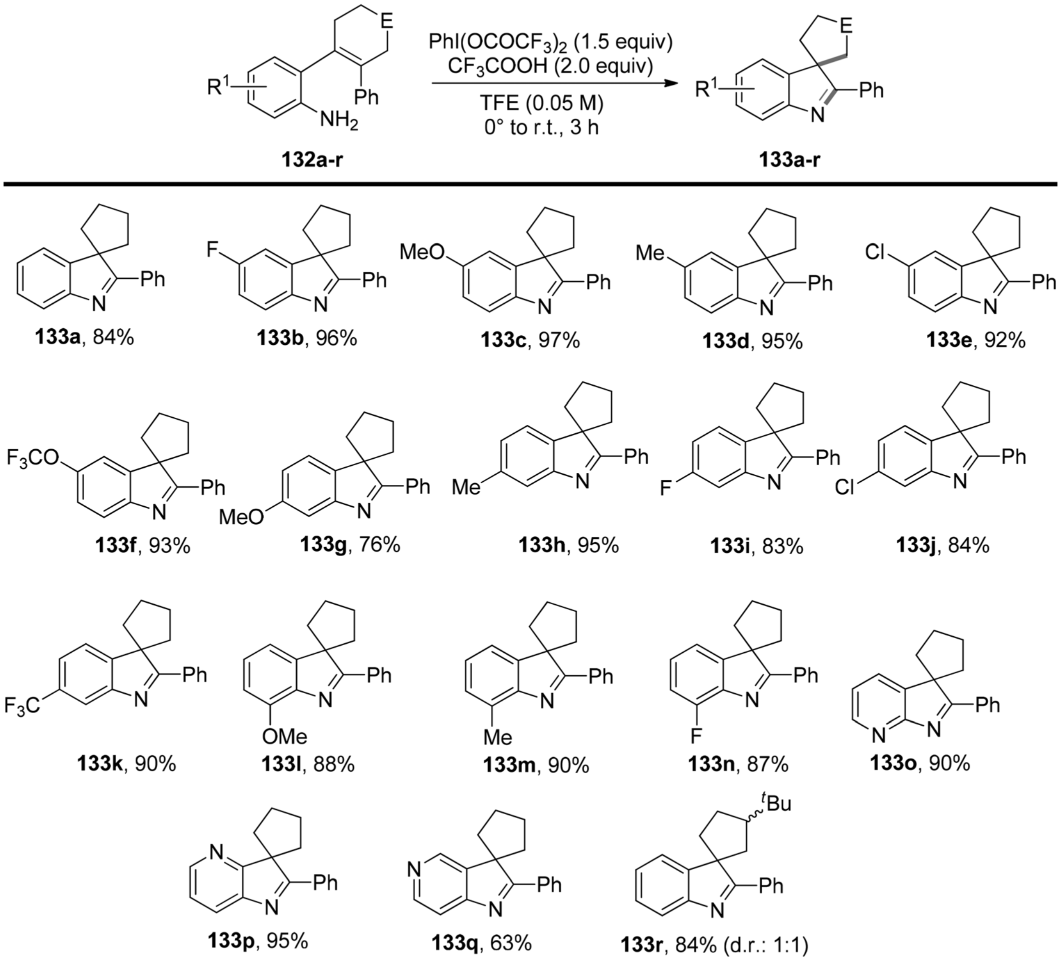
This method surpasses the IBX synthetic pathway, showcasing superior attributes such as mild reaction conditions and shortened reaction durations.

1,3,4-Oxadiazole analogues constitute prominent heterocyclic motifs with diverse therapeutic properties,[128,129] serving as crucial intermediates in the synthesis of organic compounds.[130]

In a solvent-free environment, Kumar *et al.*[131] presented a PIFA-mediated synthetic methodology for obtaining analogues of 1,3,4-oxadiazoles **127** (Scheme 52). The key step in this approach involved PIFA-mediated solvent-free cyclization of *N*-acylated hydrazones **125**. The *in vitro* anti-cancer activity of the synthesized 1,3,4-oxadiazoles **127a–m** was assessed for their potential against various cancer cell lines (PC3, LnCaP, DU145, PaCa2, MD-MDA231, and MCF7).

Mariappan *et al.*[132] have introduced an exceptionally efficient method for producing 3-substituted-5-arylamino-1,2,4-thiadiazoles **129**. This innovative process involves the intramolecular oxidative formation of S–N bonds within imidoyl thioureas **128**, with PIFA acting as the catalyst. PIFA engaged in the reaction by following the ionic pathway. This method stands out due to its metal-free character, broad applicability across different substrates, rapid reaction kinetics, and its capacity to deliver good to excellent yields, all while using readily available starting materials. It represents a convenient and gentle approach for synthesizing 3-substituted 5-arylamino-1,2,4-thiadiazoles **129** in a remarkably short timeframe at room temperature, as showcased in Scheme 53.

Liu *et al.*[133] have introduced a novel and versatile method for synthesizing a range of 3-arylquinolin-2-one compounds **131**. This method involves the reaction of readily available *N*-methyl-*N*-phenylcinnamamides **130** with PIFA in the presence of Lewis acids (Scheme 54). PIFA engaged in the reaction

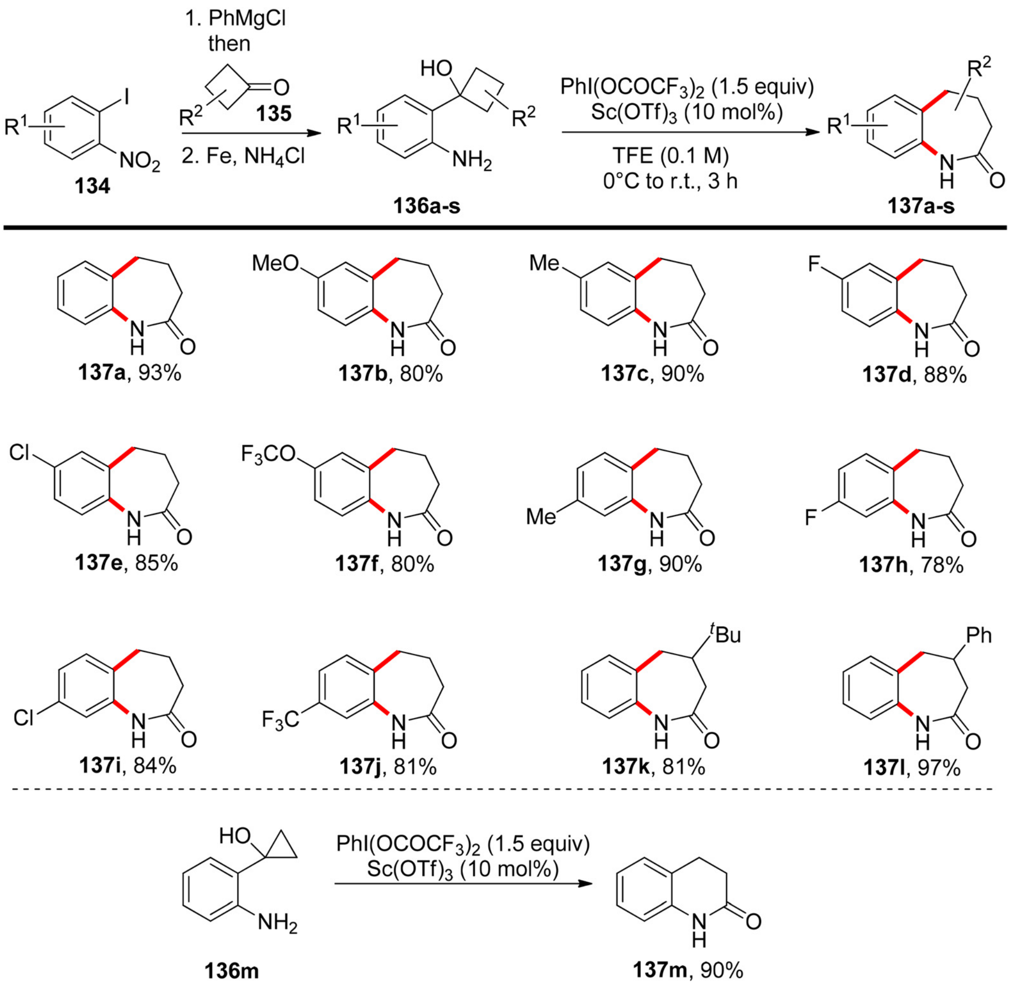


Scheme 55 Investigation of the scope and limitations of the oxidative generation of *N*-aryl nitrenes.

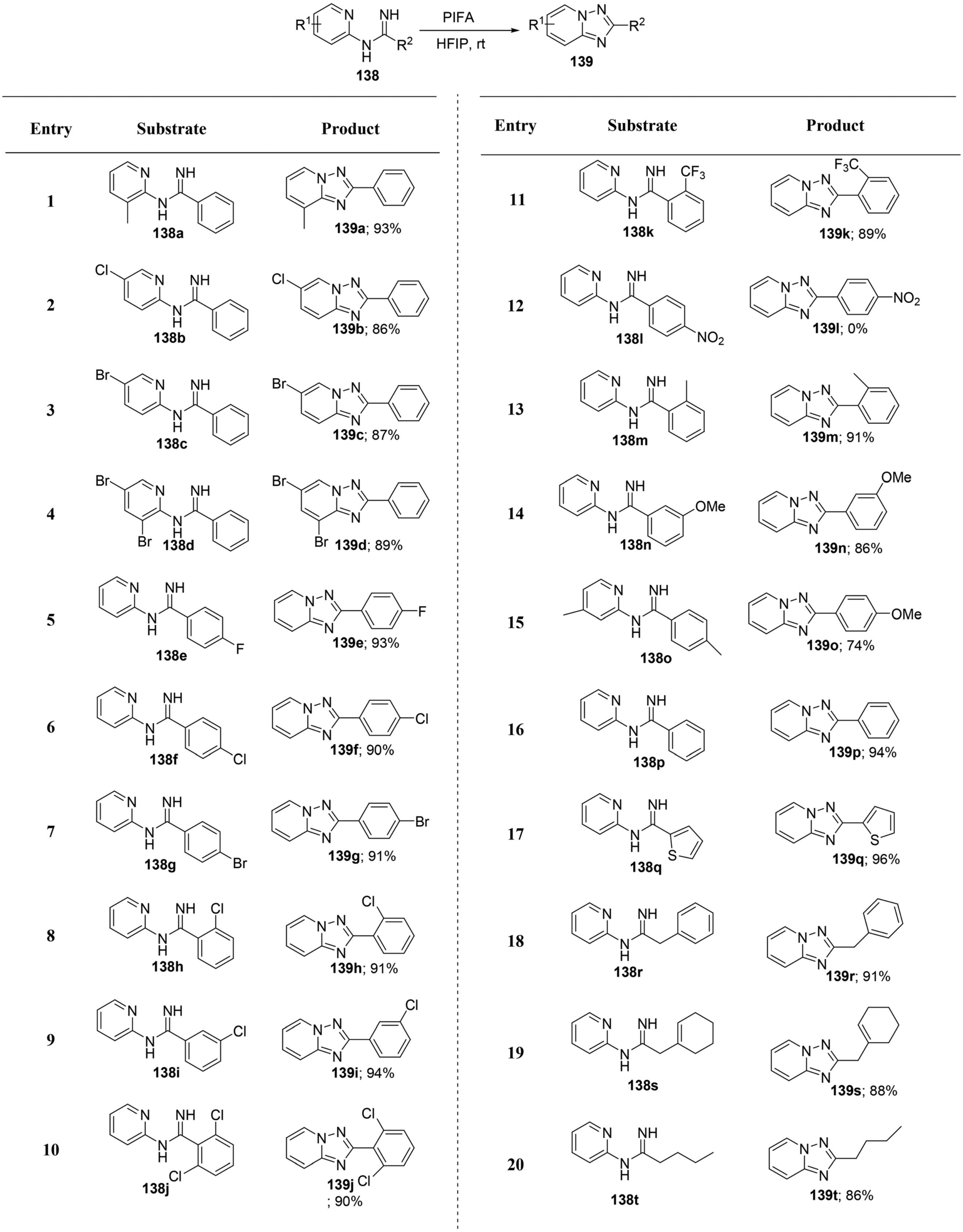
by following the ionic pathway. What sets this approach apart is its ability to facilitate metal-free oxidative C(sp^2)–C(sp^2) bond formation and a distinctive 1,2-aryl migration.

Deng *et al.*[134] have introduced a method for oxidizing 2-substituted anilines **132** at low temperatures without the need for protecting groups. This process generates an electrophilic *N*-aryl nitrenoid intermediate capable of participating in the formation of C–NAr bonds, enabling the construction of functionalized N-heterocycles **133** (Scheme 55). When 2-substituted anilines are exposed to PIFA and trifluoroacetic acid, or 10 mol% Sc(OTf)$_3$, it triggers the formation of the nitrenoid intermediate. Subsequently, this leads to the selective and efficient formation of C–NAr and C–C bonds, resulting in the creation of spirocyclic or bicyclic 3*H*-indoles or benzazepinones **133** or **137**. PIFA engaged in the reaction by following the ionic pathway. The generation of 3*H*-indoles occurs as the *N*-aryl nitrogen reactive intermediate is captured by the *ortho*-alkenyl substituent, triggering a 1,2 shift. The direction of this shift is controlled by the stabilization of the partial positive charge and the reduction of interactions between the aryl C–H and hydrogen atoms on the contracting ring. By altering the identity of the *ortho* substituent on a cyclobutanol **136**, access to benzazepinones **137** is achieved through a selective and stereospecific ring-expansion reaction (Scheme 56).

Zheng *et al.*[135] have introduced an efficient method for synthesizing biologically significant 1,2,4-triazolo[1,5-*a*]pyridines **139** from *N*-(pyridin-2-yl)benzimidamides **138**, utilizing PIFA-mediated intramolecular annulation (Scheme 57). This innovative approach enables the convenient construction of the 1,2,4-triazolo[1,5-*a*]pyridine framework through direct metal-free oxidative N–N bond formation. The method stands out for its brief reaction time and high yields, representing a novel pattern of N–N bond formation mediated by PIFA. PIFA engaged in reactions *via* the ionic pathway, contributing to the process through its involvement in the ionic mechanisms. Remarkably, this method accommodates a broad range of substrates, offers mild reaction conditions, and delivers high yields, rendering it exceptionally efficient for click chemistry applications.

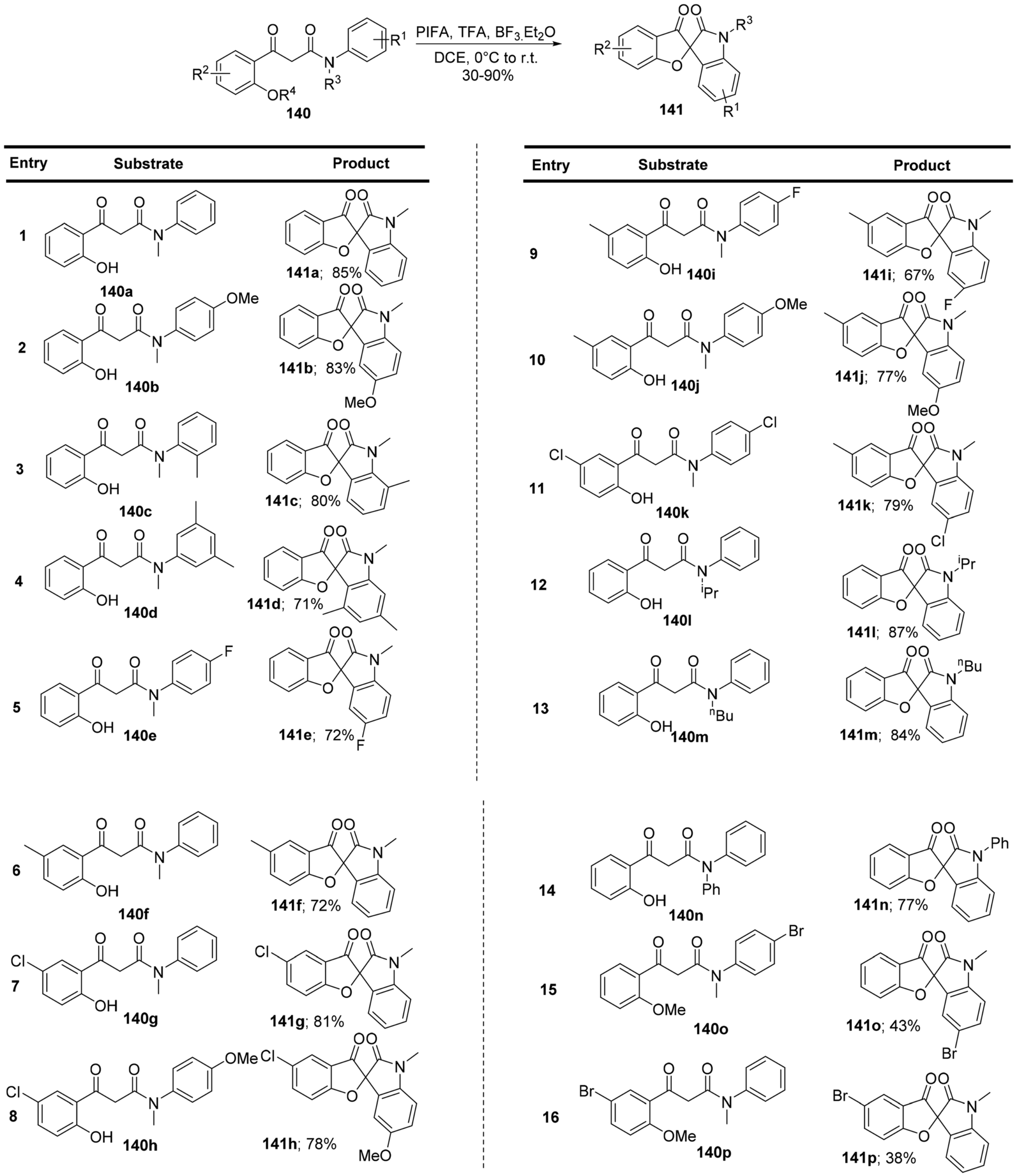


Scheme 56 Construction of benzazepinones **137** from 2-cyclobutanol-substituted anilines **136**.



Scheme 57 Synthesis of 1,2,4-triazolo[1,5-*a*]pyridines **139**.

Sun *et al.*[136] have successfully developed an innovative method for synthesizing a novel class of spirofurooxindole molecules **141**. This process, mediated by hypervalent iodine, involves a cascade of C–O and C–C bond formations under metal-free and mild reaction conditions. They achieved this by conveniently converting 3-(2-hydroxyphenyl)-3-oxo-*N*-phenyl propanamides **140** and their derivatives into previously undocumented spirofurooxindoles **141**



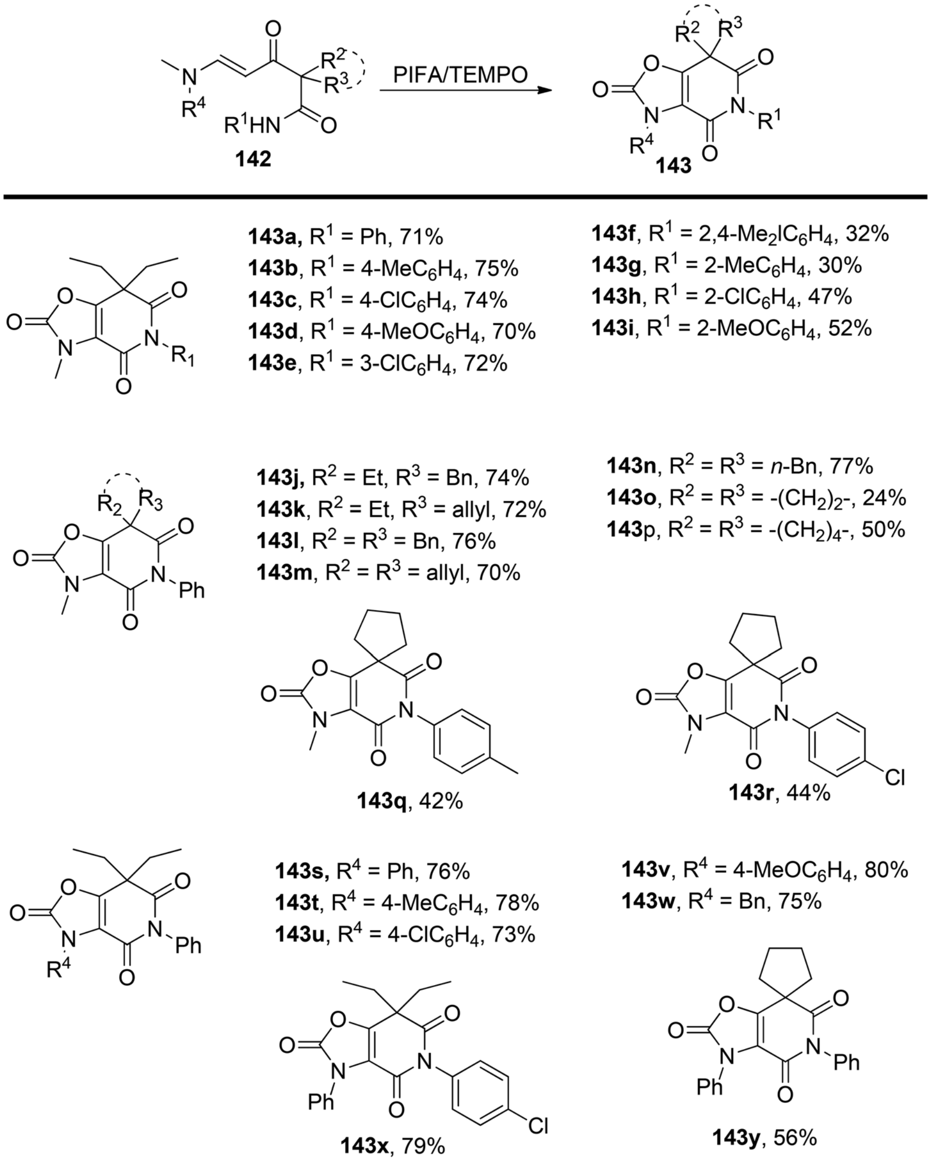
Scheme 58 Synthesis of spirofurooxindole molecules **141**.

(Scheme 58). PIFA engaged in reactions *via* the ionic pathway. Control experiments substantiated that this spirocyclization process unfolds as a sequence of oxidative reactions, with the formation of a C–O bond preceding the formation of a C–C bond.

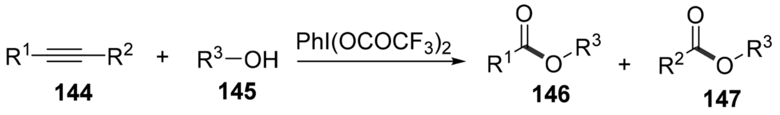
Yuan *et al.*[137] have introduced an innovative oxidative cascade cyclization process involving α-[(β-dimethylamino)propenoyl]-alkyl amides **142**, under the mediation of PIFA and TEMPO. This transformation comprises a radical-induced aziridination, ring-opening reaction, and intramolecular *O*-alkylation sequence (Scheme 59). PIFA actively engaged in the reaction by following a free radical pathway, specifically through hydrogen abstraction. The noteworthy features of this reaction are its mild reaction conditions, straightforward execution, and its capacity to yield good results while maintaining high levels of chemoselectivity and regioselectivity. As a result, it offers an efficient and convenient approach for synthesizing polysubstituted 3,7-dihydro-oxazolo[4,5-*c*]pyridine-2,4,6-(5*H*)-triones **143**.

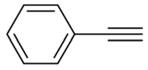
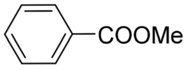
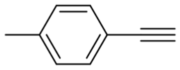
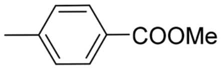
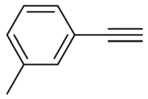
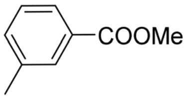
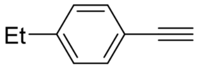
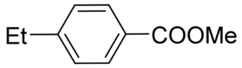
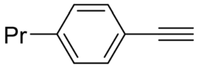
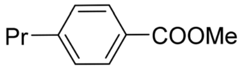
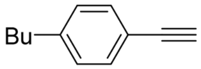
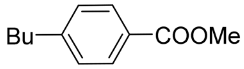
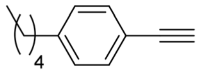
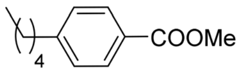
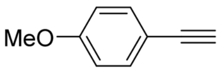
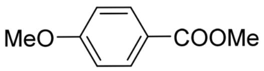
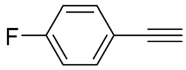
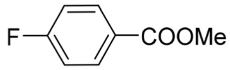
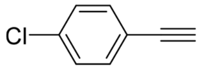
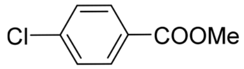
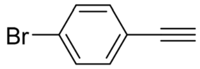
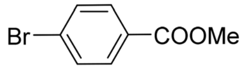
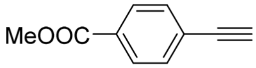
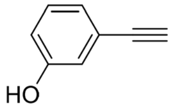
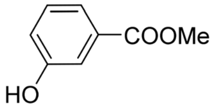
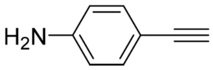
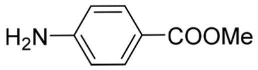
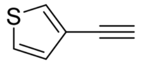
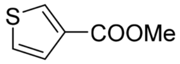
3.8. Oxidative reaction

Jiang *et al.*[138] elucidated a mild, PIFA-mediated practical synthetic pathway for the conversion of alkyne **144** or alcohol **145** into carboxylic ester **146** or **147**. The reaction exhibited tolerance to a wide array of substrates with diverse functionalities, resulting in the synthesis of carboxylic esters in high yields (Scheme 60). PIFA actively engaged in the reaction by following an ionic pathway. Mechanistic inquiries disclosed that the transformation proceeds through intermediates such as hydroxyethanones and ethanediones.

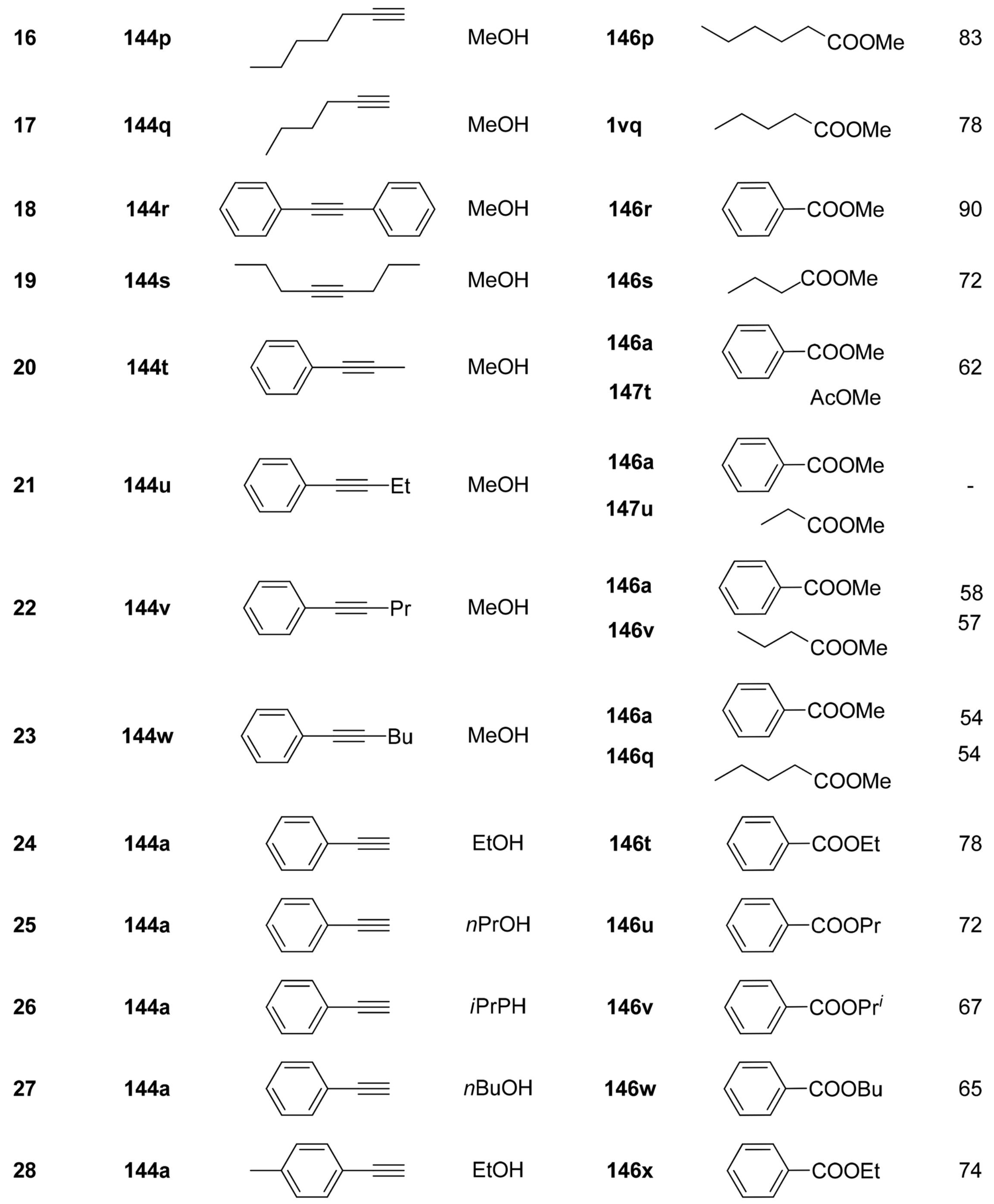


Scheme 59 Synthesis of polysubstituted 3,7-dihydro-oxazolo[4,5-*c*]pyridine-2,4,6-(5*H*)-triones **143**.



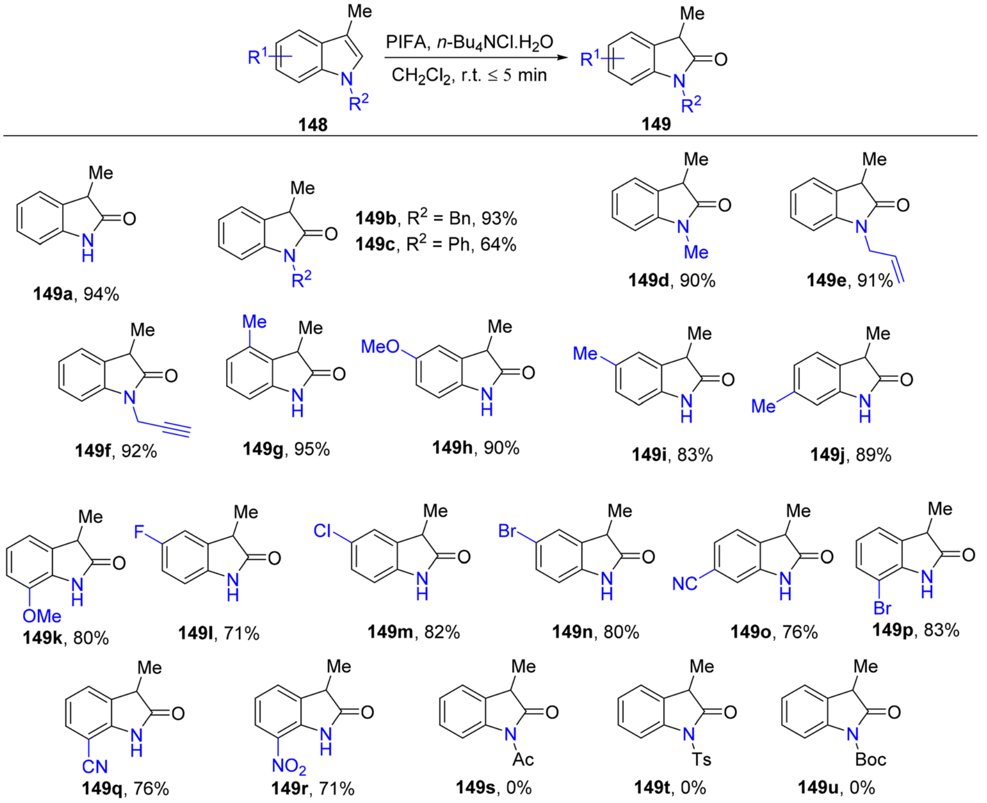
Entry	Compound	Alkyne	R^3–OH	Compound	Product	% Yield
1	**108a**		MeOH	**146a**		82
2	**144b**		MeOH	**146b**		78
3	**144c**		MeOH	**146c**		74
4	**144d**		MeOH	**146d**		68
5	**144e**		MeOH	**146e**		67
6	**144f**		MeOH	**146f**		62
7	**144g**		MeOH	**146g**		64
8	**144h**		MeOH	**146h**		86
9	**144i**		MeOH	**146i**		65
10	**144j**		MeOH	**146j**		73
11	**144k**		MeOH	**146k**		76
12	**144l**		MeOH	**146l**		63
13	**144m**		MeOH	**146m**		0
14	**144n**		MeOH	**146n**		0
15	**144o**		MeOH	**146o**		63

Scheme 60 Synthetic pathway for oxidative esterification with varied substrates.

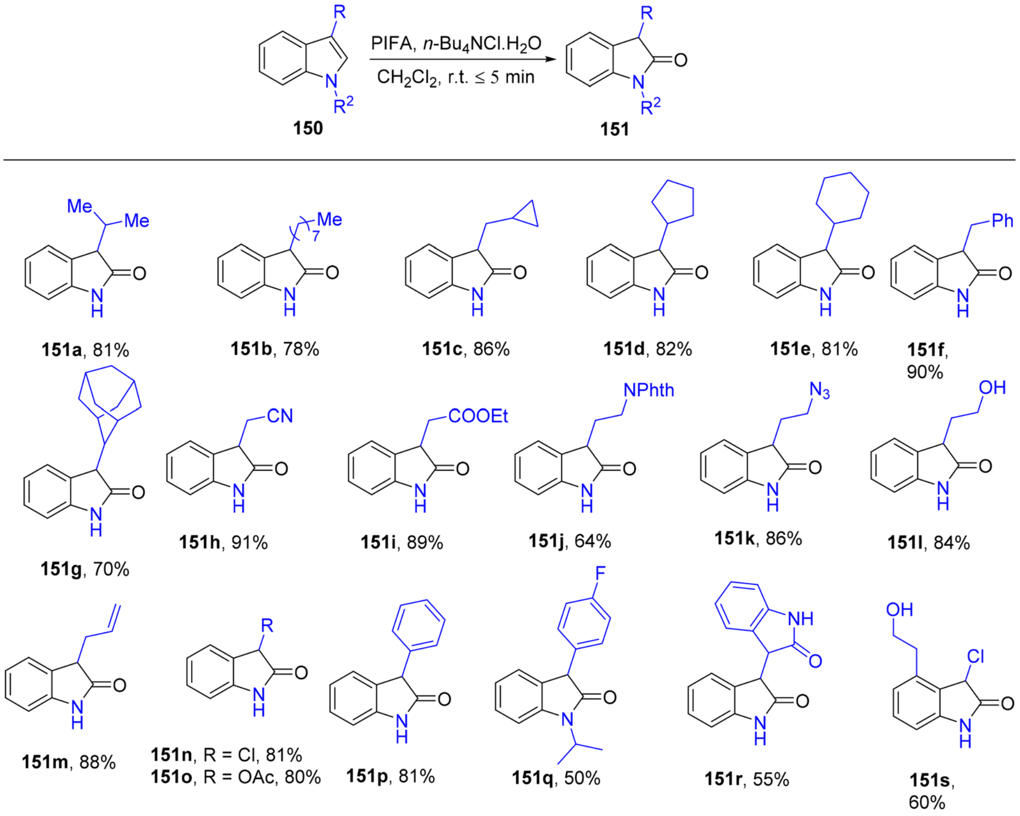


Scheme 60 *(Contd)*.

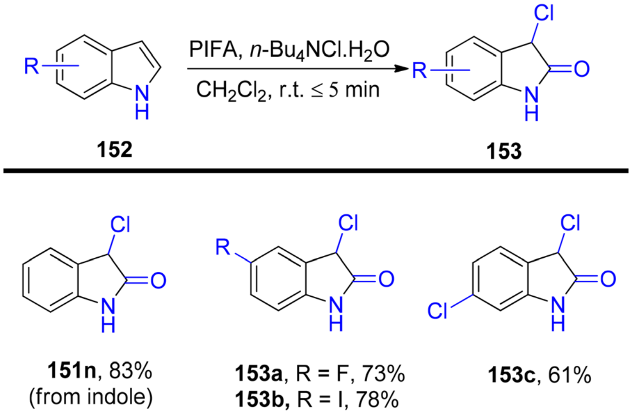
3-Substituted 2-oxindole moiety is a versatile structure employed in the synthesis of biologically relevant indole compounds.[139] Liang *et al.*[140] established an efficient methodology catalyzed by PIFA/*n*-$Bu_4NCl \cdot H_2O$ for the rapid *in situ* transformation of indoles into their respective 2-oxindoles. The reaction exhibited broad functional group tolerance and could furnish 2-oxindoles **149**/**150** in yields of up to 95% within just 5 minutes. Notably, this methodology was applied successfully in the synthesis of (−)-folicanthine and demonstrated gram-scale preparation capability. The findings of their investigation involving substituted indole derivatives **148** are summarized in Scheme 61. To extend the applicability of these transformations, reports on 3-substituted indoles **150** were also presented (Scheme 62). Moreover, the synthetic methodology was utilized to convert indole derivatives **152** into oxindole analogues **153** with



Scheme 61 Synthetic scheme with substituted indole derivatives **148**.



Scheme 62 Synthesis from 3-substituted indole derivatives **150**.



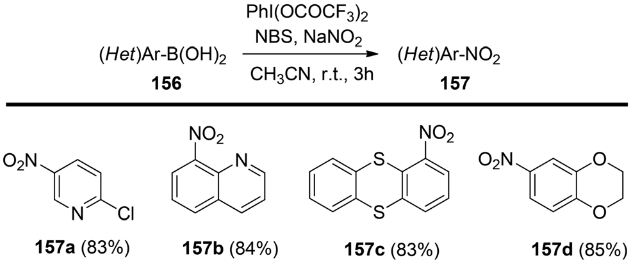
Scheme 63 Transformation of indole derivatives **152** into oxindole analogues **153**.

moderate yields (Scheme 63). PIFA actively engaged in the reaction by following an ionic pathway. This reaction sequence boasts advantages such as minimal reaction times (<5 minutes), high functional group tolerance, and excellent yields.

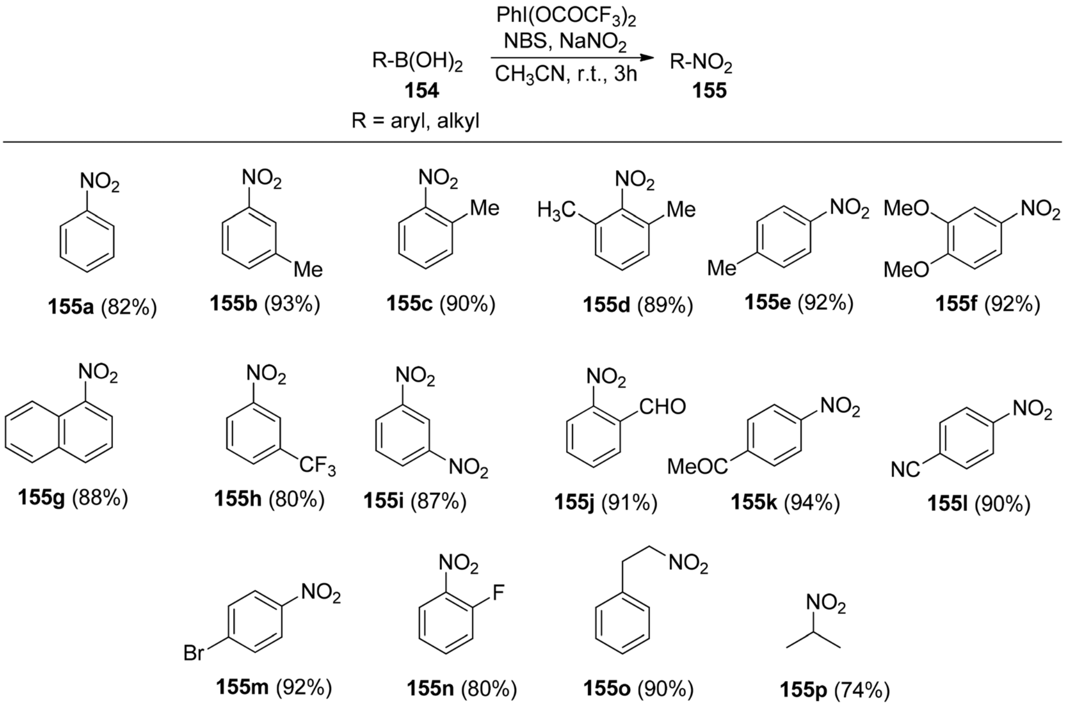
Given the extensive range of applications in which nitroarenes have been employed over the past century, including insecticides, dyes, agrochemicals, and medications, they are recognized as significant structural motifs.[141]

Chatterjee *et al.*[142] introduced a metal-free synthetic methodology based on PIFA/NBS to functionalize organoboronic acids **154** with a –NO_2 group **155** at room temperature. The envisioned reaction involved the generation of NO_2 as well as organoboronic acid radicals, which subsequently combine to establish the O–N linkage. Following this, the –NO_2 group experiences a 1,3-aryl migration, ultimately becoming incorporated into the aryl moiety. This approach is distinguished by its simplicity, utilization of readily accessible substrates, and exceptional efficiency. Nitration was successfully demonstrated with a diverse array of starting materials (Scheme 64). PIFA actively engaged in the reaction by following a free radical pathway. Additionally, the typically challenging task of nitration for hetero-arylboronic acids **156** was achieved conveniently through this methodology, yielding highly favorable results (Scheme 65).

Kinugawa *et al.*[143] reported the convenient synthesis of the indoloquinone anti-tumor agent EO 9 (**163**)[144] on a large scale. The aminoindole **159** was obtained from **158** upon treatment

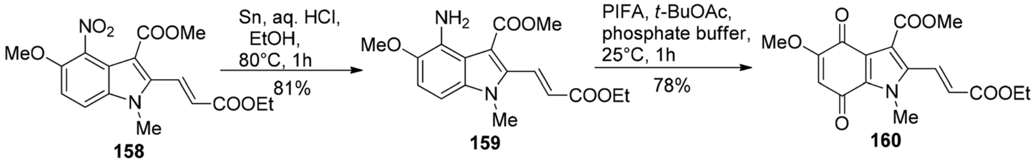


Scheme 65 PIFA-mediated *ipso* nitration of heteroarylboronic acids.

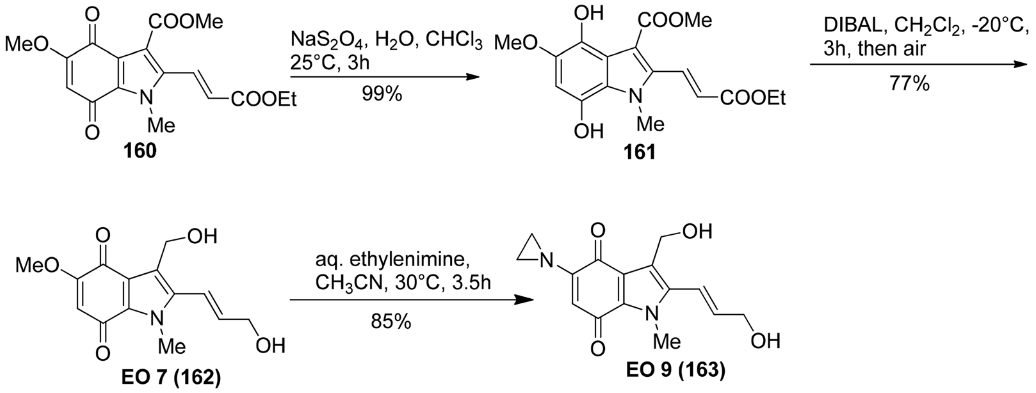


Scheme 64 PIFA-catalyzed nitration reaction of aryl- and alkylboronic acids.

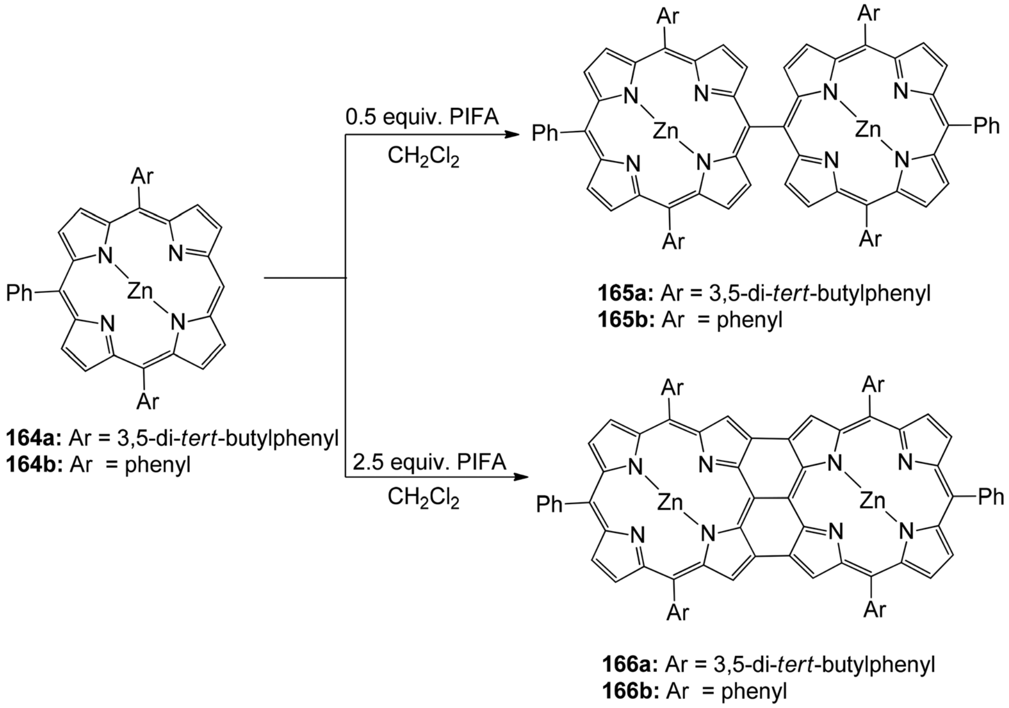
with tin and HCl in 81% yield. 4-Aminoindole **159** then underwent oxidation in the presence of PIFA to result in the formation of the corresponding indoloquinone **160** (Scheme 66). EO 7 (**162**) was derived from **160** by reduction, followed by diisobutylaluminium hydride reduction and then finally air oxidation (Scheme 67). In the final step, substitution of methoxy group with ethylenimine results in the incorporation of aziridinyl group to give indoloquinone **163** (Scheme 67).



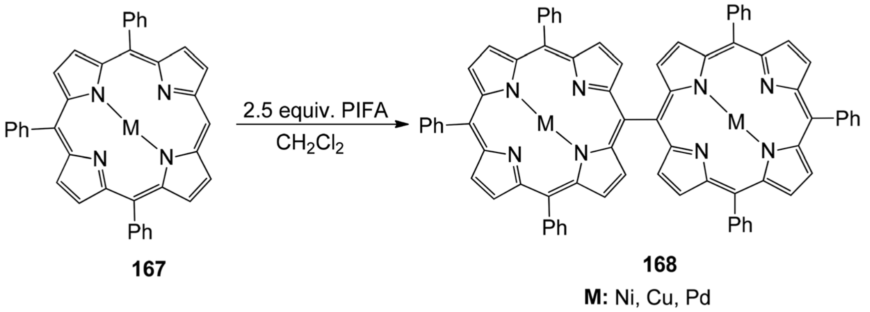
Scheme 66 Synthesis of indoloquinone **160**.



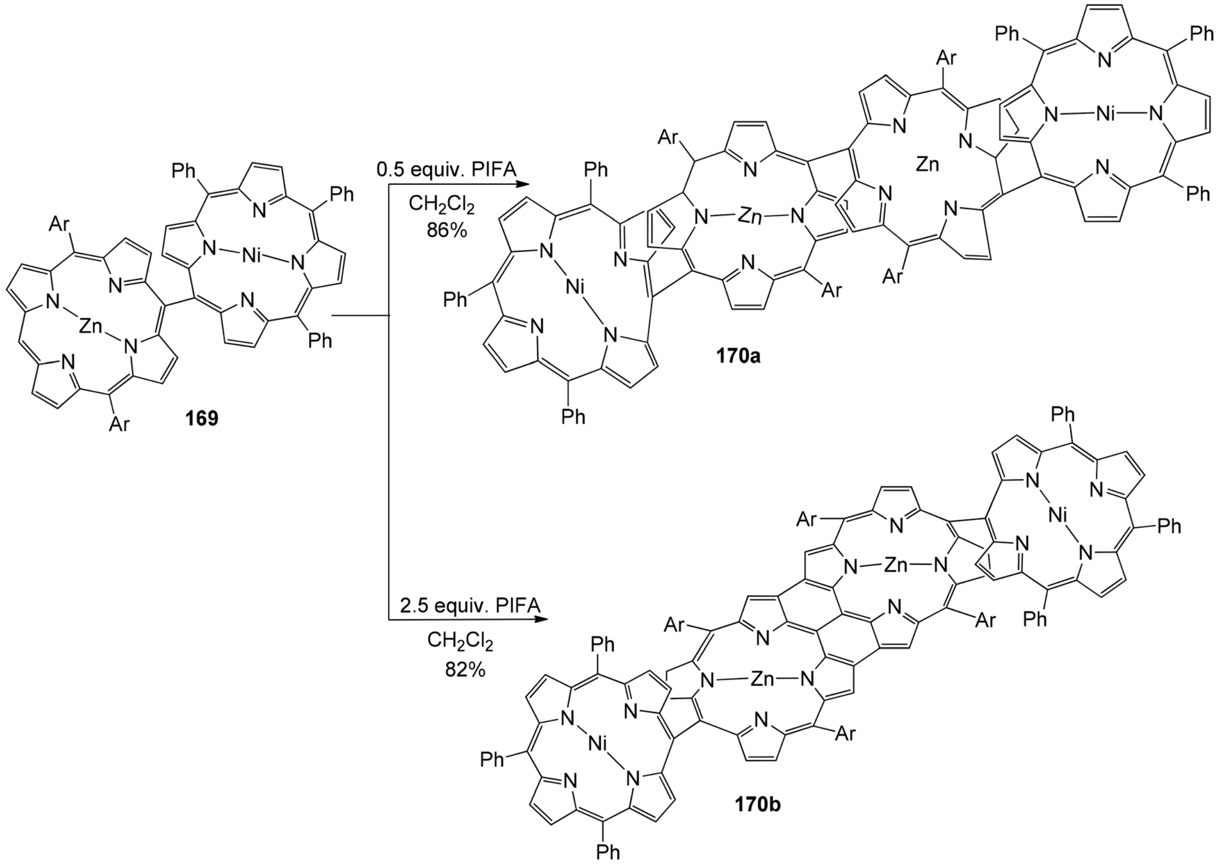
Scheme 67 Synthetic scheme for hydroquinone **161**, indoloquinone EO 7 (**162**) and indoloquinone antitumor agent EO 9 (**163**).



Scheme 68 Synthesis of diporphyrins **165** and **166**.



Scheme 69 Reaction pathway for Cu(II), Ni(II) and Pd(II) porphyrin coupling.



Scheme 70 PIFA-mediated coupling of hybdrid diphorphyrin.

Covalently linked multiporphyrin arrays represent important functionalities due to their wide range of applications, including nonlinear optical (NLO) devices, molecular wires, photosynthetic systems, and sensors.[145]

Ouyang *et al.*[146] described an effective methodology utilizing PIFA to obtain diporphyrins **165**, **166** and **168** in the absence of a metal. The porphyrin array exhibited strong selectivity for Zn(II) porphyrins **164** (Scheme 68). The reaction was also performed with Cu(II), Pd(II) as well as Ni(II) porphyrins **167** (Scheme 69). The diporphyrin precursor **169** was chosen because of its straightforward synthetic methodology with a 91% yield.[147,148] Singly linked tetraporphyrin **170a** was

$$\underset{\mathbf{171}}{PhCH_2OR} \xrightarrow{\text{PIFA}} \underset{\mathbf{172}}{PhCHO} + \underset{\mathbf{173}}{CF_3COOR}$$

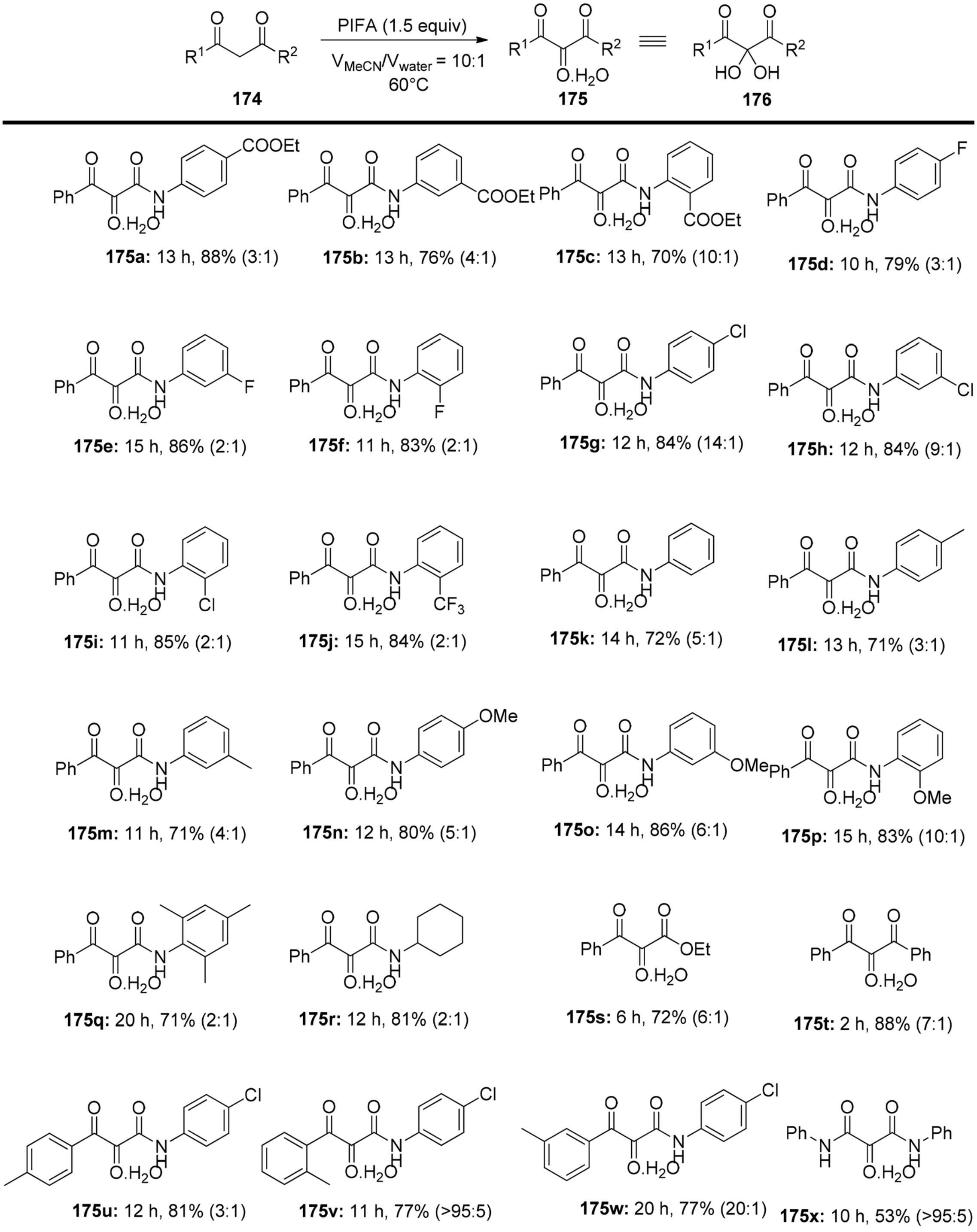
Ether	Products
$(PhCH_2)_2O$ **171a**	$PhCHO$ **172a** + CF_3COOCH_2Ph **173a**
$PhCH_2OEt$ **171b**	$PhCHO$ **172a** + CF_3COOEt **173b**
$PhCH_2OC_8H_{17}$ **171c**	$PhCHO$ **172a** + $CF_3COOC_8H_{17}$ **173c**

Scheme 71 Oxidation of benzyl ethers **171**.

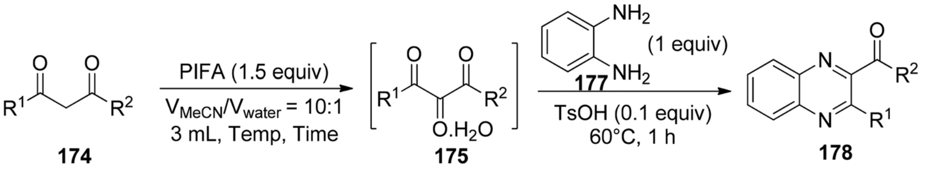
obtained with an 86% yield by the addition of 0.5 equiv. of PIFA. On increasing the equivalents of PIFA to 2.5, the porphyrin array **170b** was produced in 82% yield. It consisted of one triple linkage and two single linkages (Scheme 70).

Spyroudis *et al.*[149] reported the oxidation of benzyl ethers **171** to their respective carbonyls **172** and benzyl trifluoroacetates **173** using PIFA (Scheme 71). PIFA actively engaged in the reaction by following an ionic pathway.

Liu *et al.*[150] have introduced a simple and direct oxidative method for producing vicinal tricarbonyl amides **175**, yielding from moderate to excellent results, in the range of 53% to 88%. This process commences with the use of readily accessi-

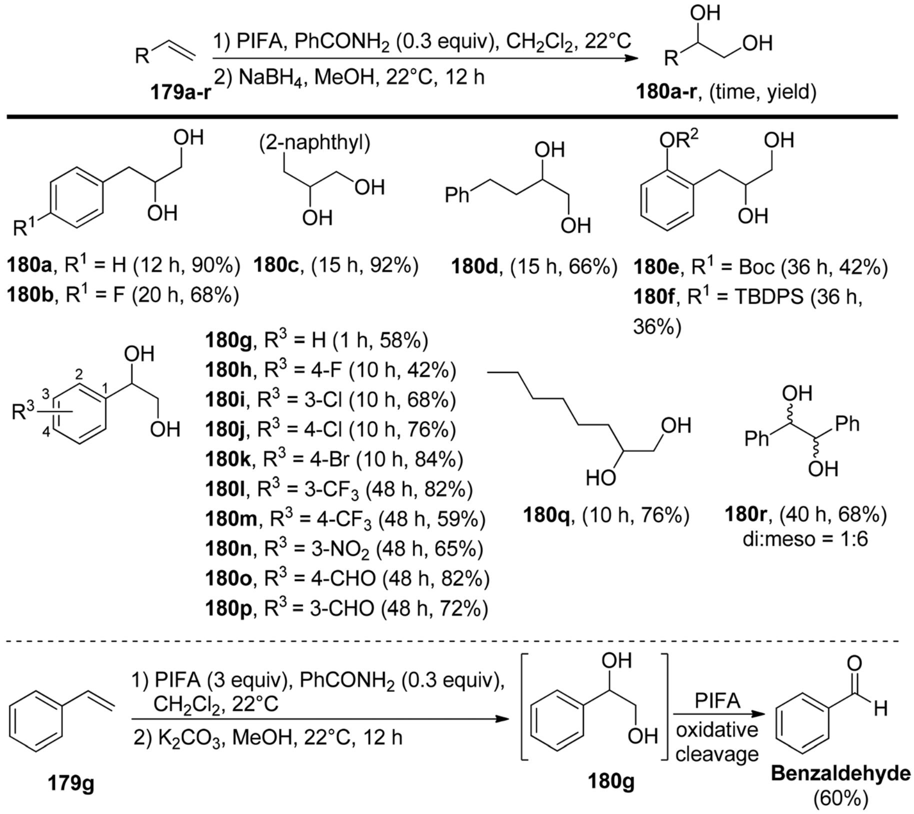


Scheme 72 Synthesis of vicinal tricarbonyl amides **175**.

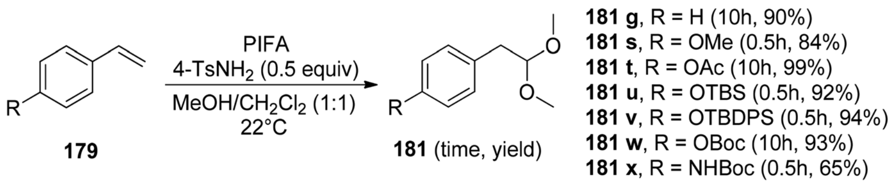


Entry	R^1	R^2	Temp (°C)	Time	Yield of 4 (%)
1	Me	NHPh	40	4 h	**178y**, 70
2	Me	NH_2	rt	15 min	**178z**, 41
3	Me	$N(Me)_2$	40	4 h	**178a'**, 83
4	^{t}Bu	NHPh	60	8 h	**178b'**, 85
5	^{n}Bu	NHPh	60	5 h	**178c'**, 87
6	^{n}Bu	OMe	60	5 h	**178d'**, 75

Scheme 73 One-pot synthesis of quinoxaline derivative **178**.



Scheme 74 One-pot synthesis of vicinal diols **180a–r**.



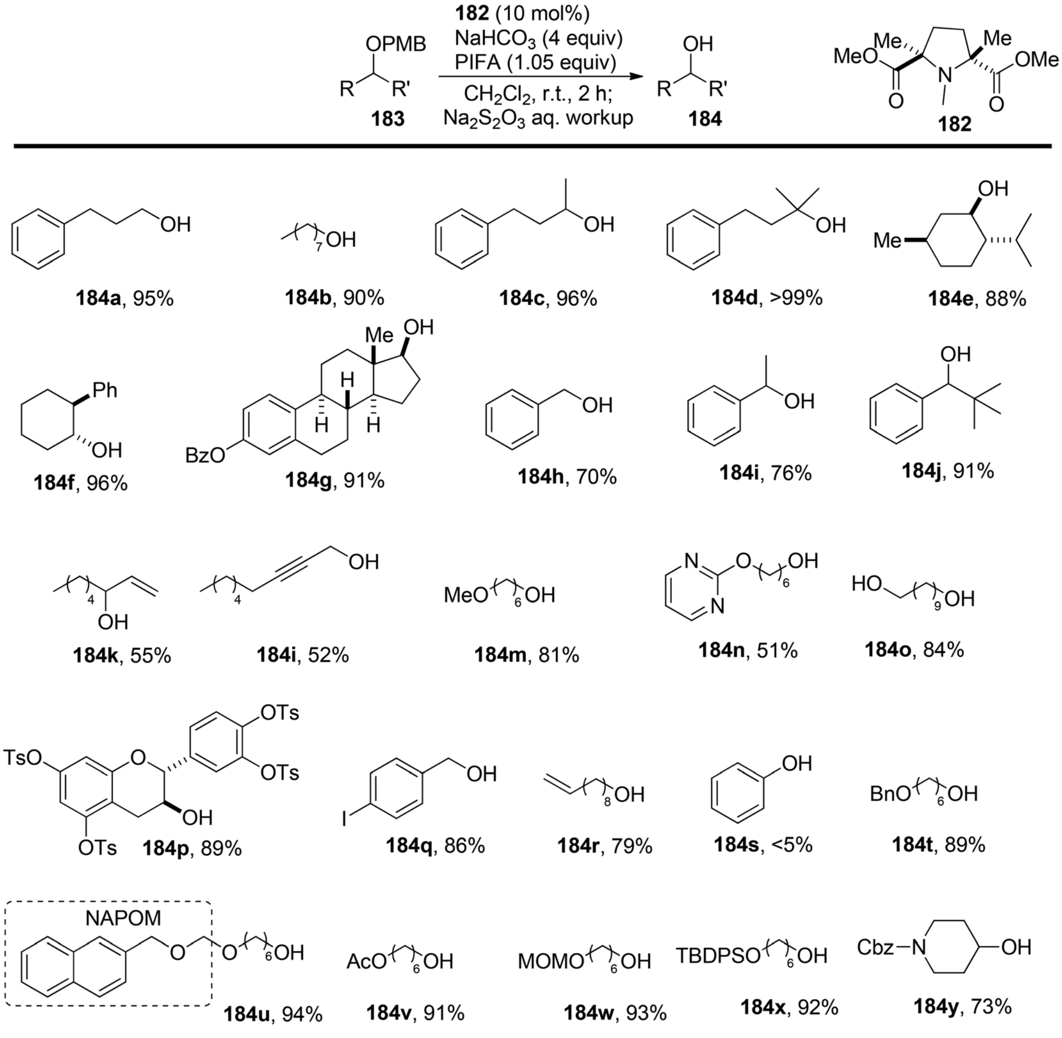
Scheme 75 Synthesis of anti-Markovnikov methyl acetals from styrene derivatives using Lewis base-activated HIR.

ble β-ketoamides **174** in the presence of PIFA, as outlined in Scheme 72. The advantages of this approach encompass the accessibility of starting materials, the attainment of high yields, the flexibility to introduce various substitutions, and the substantial synthetic potential of the resultant products. To further expand the versatility of this method, subsequent modifications were executed using benzene-1,2-diamine **177** in conjunction with 4-methylbenzenesulfonic acid at 60 °C in a one-pot reaction. Encouragingly, this approach proved effective for a range of aliphatic β-ketoamides, spanning from **174z** to **174c′**, and even extended to aliphatic β-keto ester **174d′**, yielding their respective derivatives **178z** to **178d′** with cumulative yields spanning from 41% to 87% (Scheme 73).

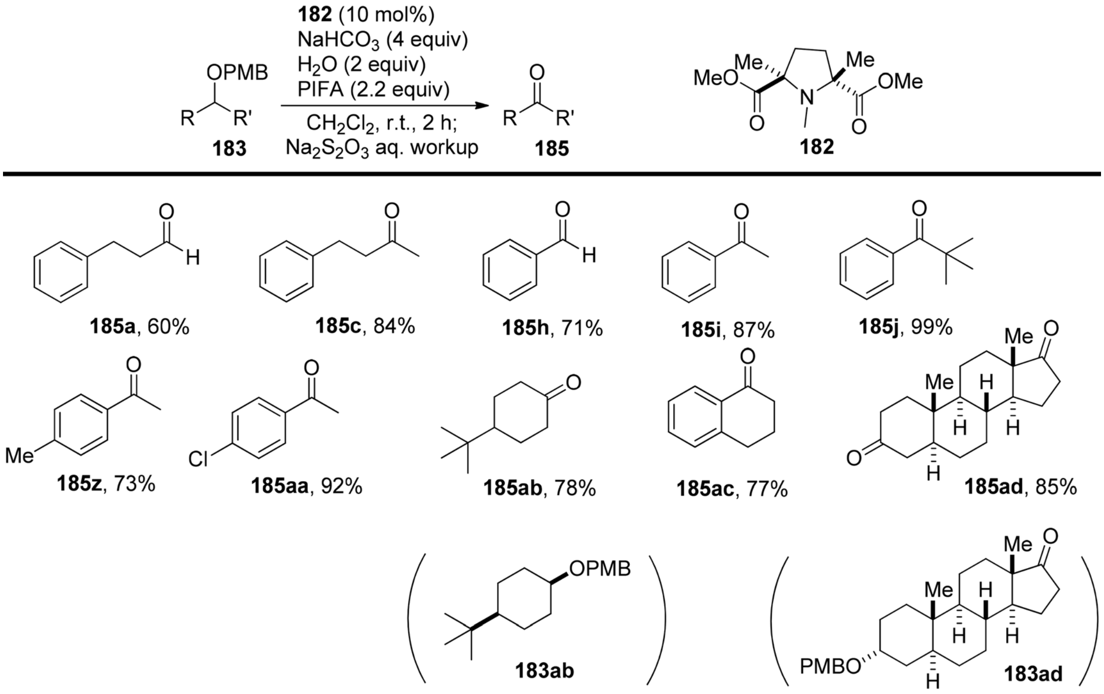
1,2-Diols play a crucial role in the synthesis of pharmaceuticals and natural compounds. The direct addition of oxygen atoms to adjacent positions (vicinal dioxygenation) of olefins is a simple and widely employed approach for the preparation of 1,2-diols. Numerous effective methods have been developed and are extensively utilized in contemporary chemistry.[151]

Pan *et al.*[152] have introduced a catalytic method for accomplishing the vicinal dioxygenation of olefins **179** (Scheme 74). They employed hypervalent iodine reagents with Lewis bases as catalysts. These reaction conditions are gentle and versatile, making them suitable for a wide array of functional groups. After fine-tuning the reaction conditions, they investigated the practicality of this dioxygenation process in a one-step approach, leading to the synthesis of the corresponding diols **180**. Significantly, the authors were pleased to discover that styrenes **179** carrying diverse substituents, such as ethers, esters, silyl ethers, OBoc, and NHBoc, were well tolerated, yielding the desired products **181** with robust yields and exceptional selectivity, as illustrated in Scheme 75. PIFA actively engaged in the reaction by following an ionic pathway. Crucially, this method is compatible with compounds that are sensitive to both acids and oxidants.

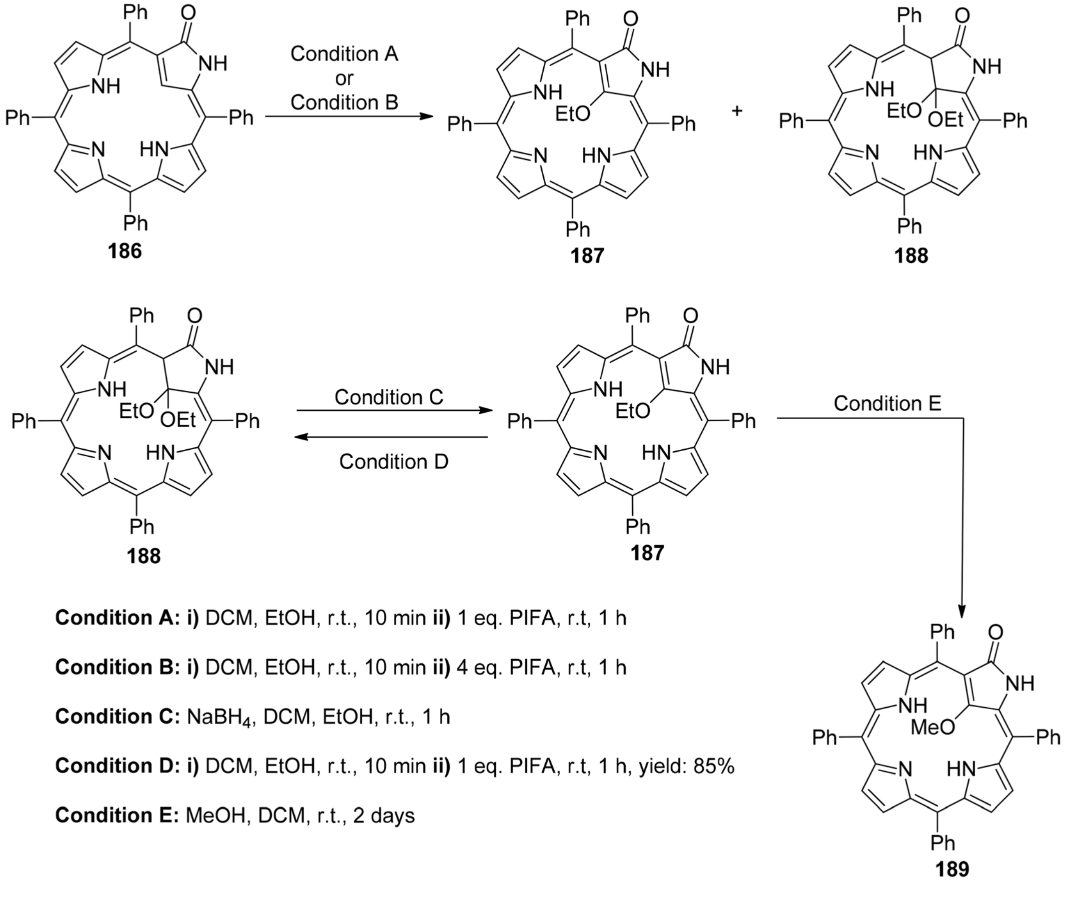
Hamada *et al.*[153] achieved the oxidation of *p*-methoxy benzyl (PMB) ethers **183** using a nitroxyl radical catalyst labeled as catalyst **182**. This catalyst features electron-with-



Scheme 76 Oxidative deprotection of PMB groups by I/PIFA.



Scheme 77 Direct synthesis of ketones and aldehydes from PMB-protected alcohols by I/PIFA.



Condition A: **i)** DCM, EtOH, r.t., 10 min **ii)** 1 eq. PIFA, r.t, 1 h

Condition B: **i)** DCM, EtOH, r.t., 10 min **ii)** 4 eq. PIFA, r.t, 1 h

Condition C: $NaBH_4$, DCM, EtOH, r.t., 1 h

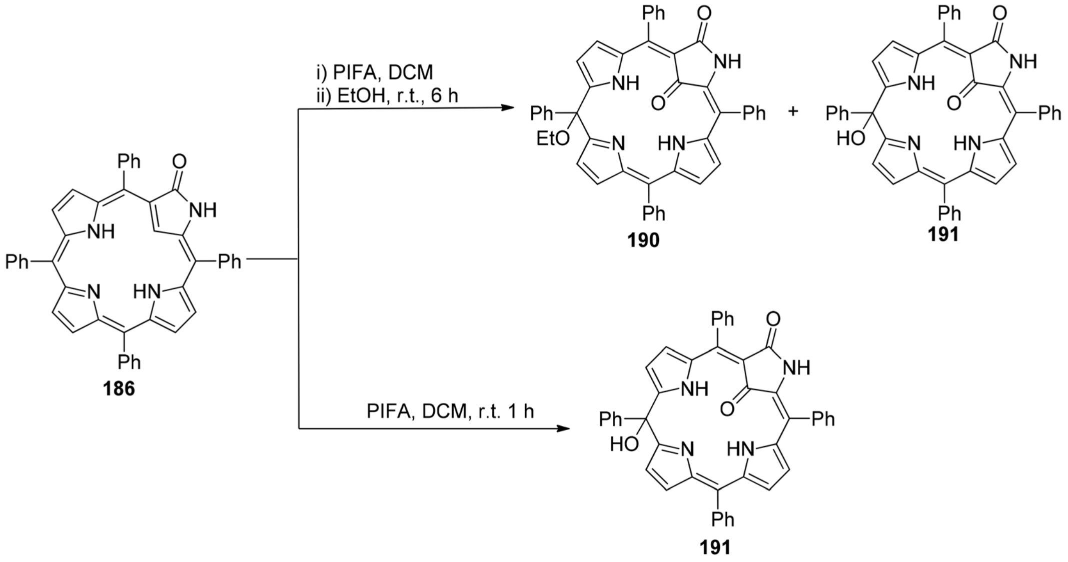
Condition D: **i)** DCM, EtOH, r.t., 10 min **ii)** 1 eq. PIFA, r.t, 1 h, yield: 85%

Condition E: MeOH, DCM, r.t., 2 days

Scheme 78 Synthesis of **187**, **188** & **189**.

drawing ester groups positioned in close proximity to the nitroxyl group. The removal of PMB protective groups from hydroxyl compounds occurred through oxidative deprotection when catalyst **182** was treated with an equivalent of the co-oxidant PIFA (Scheme 76). This system displayed remarkable selectivity in deprotecting PMB ethers, even in the presence of a diverse range of functional groups, some of which are susceptible to oxidation. The desired carbonyl compounds **185** were obtained by reacting the PMB-protected alcohols **183** with catalyst **182** and an excess of PIFA, as illustrated in Scheme 77. PIFA actively engaged in the reaction by following a free radical pathway, specifically through single-electron oxidation.

Zhang *et al.*[154] have reported the synthesis of 21-ethoxy- and 21,21-diethoxy-ONCPs **187** and **188** through a sequence involving the conjugate addition of ethanol followed by oxidation with PIFA. This process enabled the inner ethoxylation of 3-oxo-*N*-confused tetraphenylporphyrin **186** (ONCP) (Scheme 78). The initial step involved the oxidation of ONCP with PIFA, followed by treatment with ethanol, resulting in the generation of two additional *N*-confused phlorin derivatives, denoted as **190** and **191** (Scheme 79). The transformation from **186** to **187**, **188**, **189**, **190** and **191** has been well established through the use of PIFA and ethanol. This signifies the versatility of the conjugated lactam structural feature for making modifications at both the C21 (inner core) and the C10 (outer *meso*-position) of these molecules. The formation of phlorins **190** and **191** highlights that ONCPs serve as an intriguing platform for *meso* modifications. N-Confused porphyrins (NCPs),



Scheme 79 Synthesis of *N*-confused phlorins derivatives, denoted as **190** and **191**.

$$\underset{\textbf{192a-s}}{RCONH_2} \xrightarrow[\substack{\text{2. NaOH}\\ \text{55-92\%}}]{\text{1. PIFA, HCl}} \underset{\textbf{193a-s}}{RNH_2}$$

Comp. (a-q)	192/193	Comp. (a-q)	192/193
a	R = CH_3CH_2	**k**	R = cycloheptyl
b	R = $CH_3(CH_2)_4$	**l**	R = 1-adamantyl
c	R = $(CH_3)_3C$	**m**	R = 3-cyclohexenyl
d	R = $C_6H_5CH(CH_3)$	**n**	R = 1-napthyl-CH_2
e	R = *p*-$CH_3OC_6H_4CH_2$	**o**	R = $EtO_2CCH_2CH_2$
f	R = $NO_2C_6H_4CH_2$	**p**	R = $HO_2CCH_2CH_2$
g	R = cyclobutyl	**q**	R = $Et_2NCOCH(NHAc)CH_2CH_2$
h	R = cyclopentyl	**r**	R = Ac-HN−CH$^-$ $CH_2C_6H_5$
i	R = Ac-Ala-HN−CH-CO-Ala-Gly $CH_2CH_2^-$	**s**	R = Ac-HN−CH$^-$ $CH_2(CH_3)_2$
j	R = cyclohexyl		

Scheme 80 Synthesis of pyridoquinazolin-6-ones **193a–s**.

Amide $RCONH_2$ Product $RNH_3^+Cl^-$ R =	% Yield	Amide $RCONH_2$ Product $RNH_3^+Cl^-$ R =	% Yield
CH_3CH_2	85	3-cylcohexenyl	75
$CH_3(CH_2)_4$	92	1-naphthyl-CH_2	85
$(CH_3)_3C$	92	$EtO_2CCH_2CH_2$	86
$C_6H_5CH(CH_3)$	84	$HO_2CCH_2CH_2$	81
p-$CH_3OC_6H_4CH_2$	70	$EtNCOCH(NHAc)CH_2CH_2$	55
$NO_2C_6H_4CH_2$	85	Ac-Ala-NH-CH-CO-Ala-Gly CH_2CH_2–	79
Cylcopentyl	91		
Cylcohexyl	90	AcNHCH- $CH_2C_6H_5$	79
Cylcoheptyl	85		
1-adamantyl	85	AcNHCH- $CH(CH_3)_2$	75

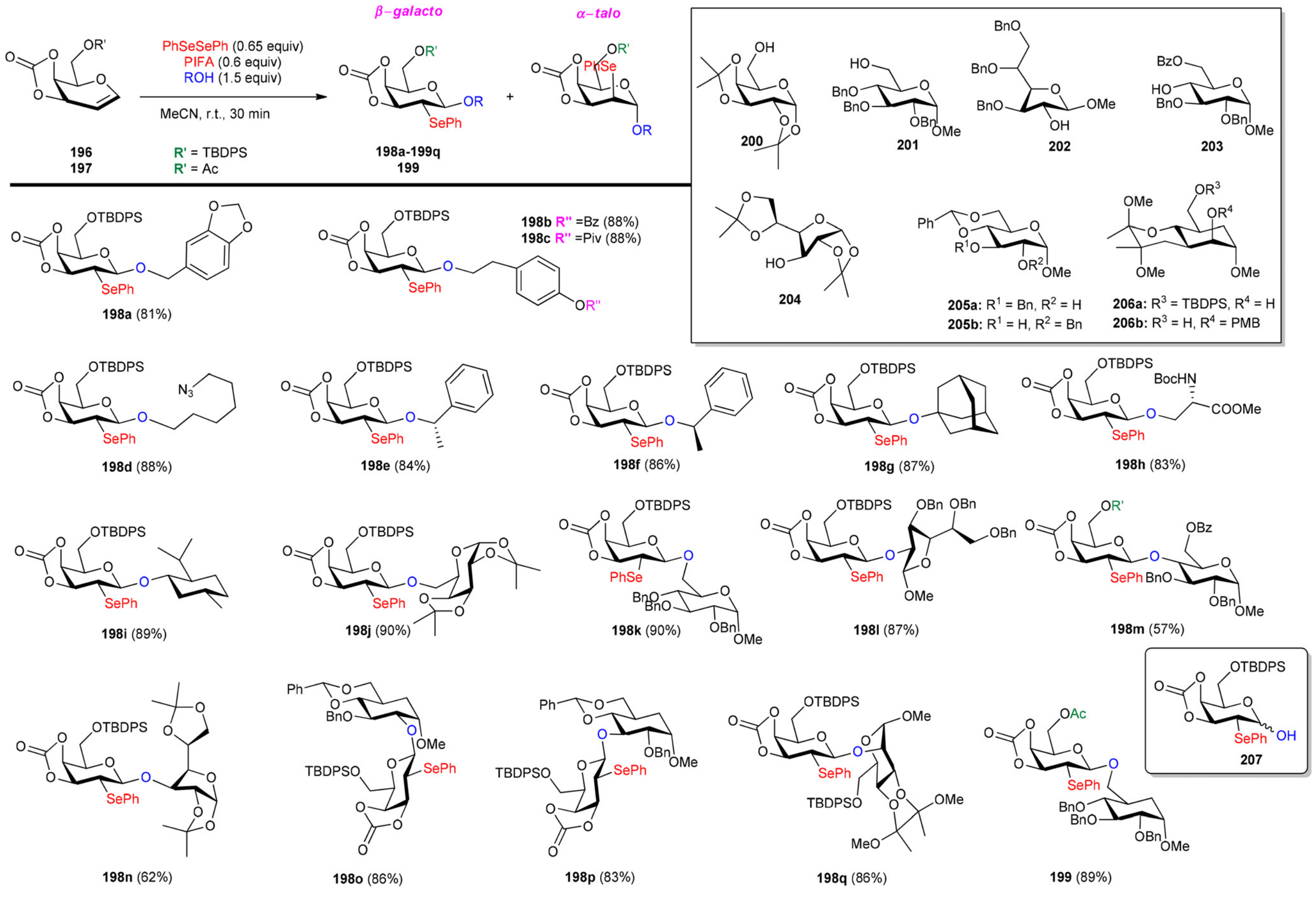
Scheme 81 Transformation of 1° amides to amines by PIFA-mediated rearrangement reaction.

introduced by the Furuta and Latos-Grażyński groups,[155,156] exhibit fascinating properties distinct from regular porphyrins due to the presence of a unique pyrrole arrangement.

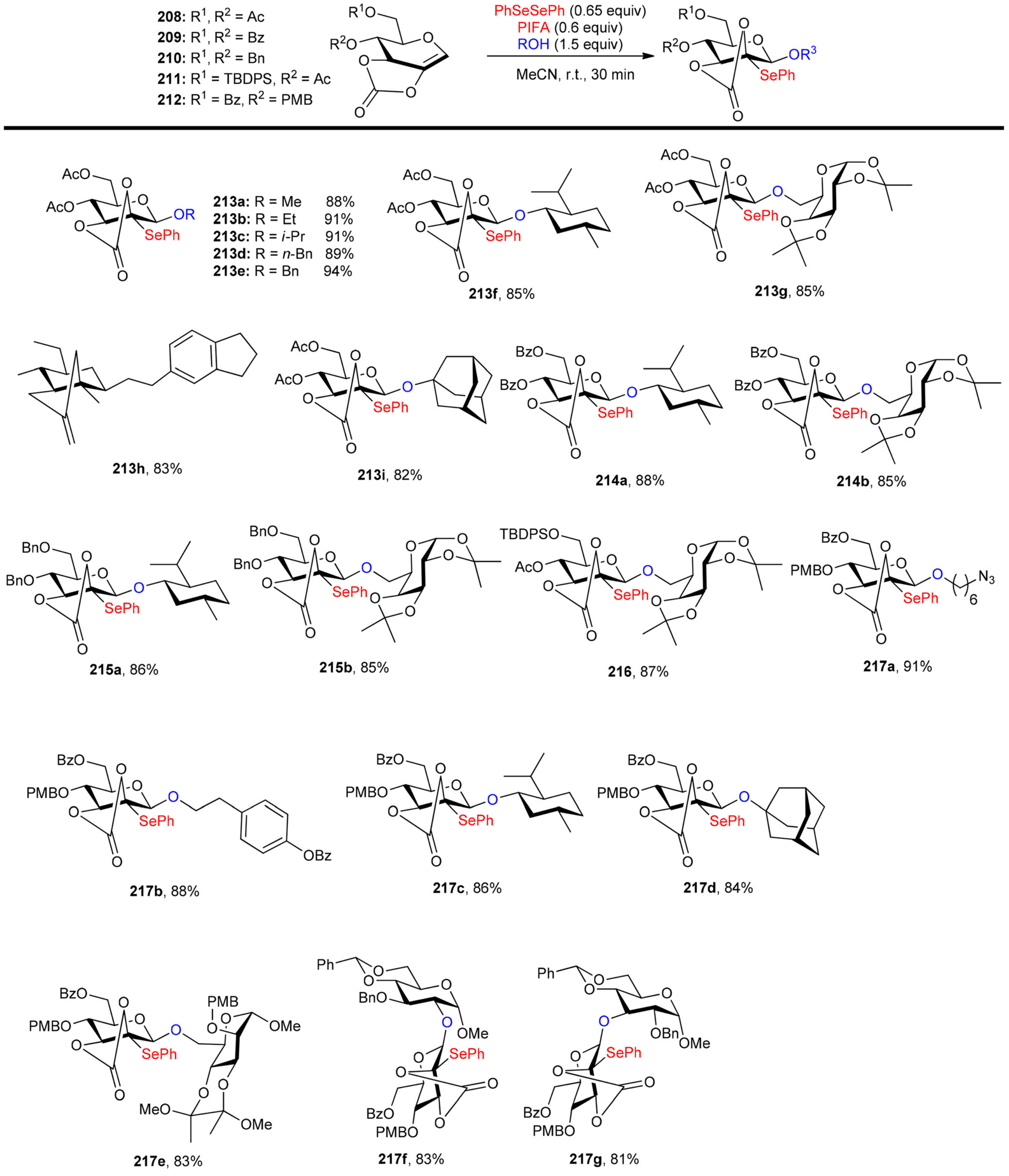
3.9. Hoffmann reaction

Organic fluorescent molecules are significant molecules in varied scientific domains, including chemical biology, photocatalytic chemistry and materials research owing to their specificity, easy accessibility, and stability as well as sensitivity.[157] Gao *et al.*[158] reported an effective and simple methodology to construct pyrido-quinazolin-6-ones **193** by subjecting readily accessible carboxamide derivatives **192** to Hofmann rearrangement. The PIFA-catalyzed reaction was performed at room temperature for 1 hour to obtain the pyridoquinazzolin-6-ones **193a–s** in 55–92% yields (Scheme 80). PIFA engaged in reactions *via* the ionic pathway. This straightforward methodology allows the development of excellent yields of fluorophores chemoselectively under mild conditions. The reaction also tolerates a range of functional groups.

Loudon *et al.*[159] employed PIFA under mild acidic conditions to catalyze the rearrangement of aliphatic amides **194**, yielding amines **195**. The reaction, known as the "acidic Hofmann rearrangement", proceeds with complete retention of configuration for the migrating group. Although the reac-



Scheme 82 Synthetic scheme for stereoselective formation of 2-phenylseleno-2-deoxy-β-galactosides.



Scheme 83 Phenylselenoglycosylation reaction of 2,3-*O*-carbonate-2-hydroxyglucals.

tion involves isocyanates as intermediate species, under mildly acidic conditions, they rapidly degrade to yield amines. The resultant amines **195** are protected from urea formation due to the degradation of isocyanate intermediates in an acidic environment. The addition of pyridine to maintain a pH of approximately 3 expedites the reaction. Scheme 81 provides additional visual representations of the reaction. PIFA engaged in reactions *via* the ionic pathway.

3.10. PIFA in carbohydrate chemistry

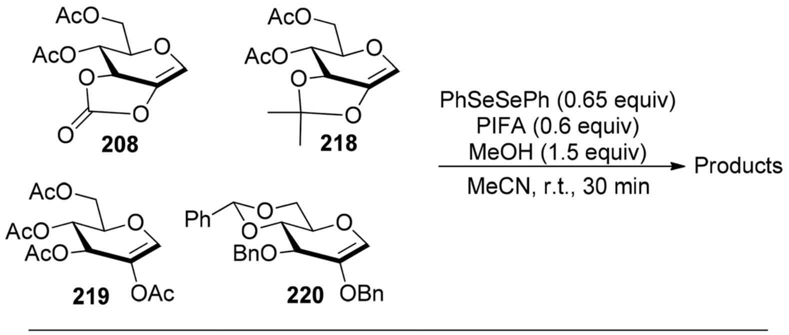
Glycoconjugates and oligosaccharides are crucial components for numerous biological processes.[160,161] Meng *et al.*[162] described a PIFA-mediated phenylselenoglycosylation of glycol analogues under benign conditions. By attachment of fused carbonate to the glycols, stereo-selective glycosylation was accomplished. Galactal **196** resulted in the formation of 2-phenylseleno-2-deoxy-β-galactosides in all of these noncarbohydrate acceptor processes in excellent yields (Scheme 82). Additionally, they reported the glycosylation of compound **196** with various acceptors derived from sugars **200–206**. The majority of primary alcohols and several secondary alcohols exhibited efficient reactivity with **196**, yielding the corresponding β-linked disaccharides in yields ranging from 83% to 90%. When coupling with sugars **203** and **204**, disaccharides **198m** and **198n** were obtained with yields of 57% and 62%, respectively, and lactol **207** was isolated in yields of 36% and 30%, respectively (Scheme 82). The glycosylation of **197** with acceptor **201** under the optimal condition provided β-linked disaccharide **200** in 89% yield. The phenylselenoglycosylation process was applied to a variety of 2,3-*O*-carbonate-2-hydroxyglucal **208–212** donors to produce the 2-phenylseleno-2,3-*O*-carbonate-mannosides **213–217** in yields of 81–94% (Scheme 83). For comparison, donors protected by 2,3-*O*-carbonate **208**, 4,6-*O*-benzylidene **220**, 2,3-*O*-isopropylidene **218** and peracetylation **219** with structural flexibility were also synthesised. The best conditions were utilized to glycosylate these four donors in methanolic media (Scheme 84). The majority of donor **219** was retrieved after 24 hours, likely due to its limited reactivity attributed to the electron-withdrawing impact of 2-*O*-Ac. Conversely, the electron-rich olefins in **218** and **220** could be overly responsive to electrophilic species, possibly causing them to react directly with PIFA, leading to the formation of intricate byproducts. Intriguingly, only the reaction involving donor **208** yielded promising results, with the identification of product **213a** as a β-glycoside. PIFA engaged in reactions *via* the ionic pathway.

The complex oligosaccharides located on the cell surface play crucial roles in various biological processes, particularly in cell-to-cell adhesions, as evidenced by advancements in the field of glycosciences. Drugs containing glycoside linkages are now commonly employed in the treatment of diabetes, influenza virus, and cardiovascular ailments.[163]

Substituted analogues of D-glucopyranoside as well as D-galactopyranoside were utilized as the glycosyl donors in the study by Kajimoto *et al.*[164] The reaction gave good yields with cholestanol, 1-,2-adamantanols as well as (−)-menthol acceptor molecules. Thioglycosides **221**, and **222** and a range of alkanols **223–230** were glycosylated by activating PIFA with TfOH (Scheme 85). Additionally, utilizing this reaction scheme, disaccharides with a D-glucosamine/galactosamine **231j–k** functionality at the non-reducing end can also be synthesized (Scheme 86).

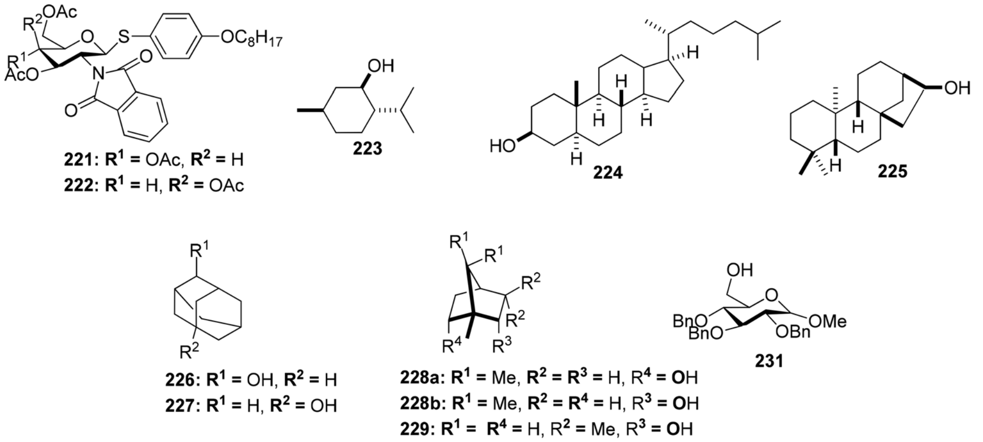
3.11. One-pot reaction

Tetrazoles, known for their high lipophilicity, serve as important heterocyclic motifs and bioisosteres of carboxylic acids and amides.[165] Imai *et al.*[166] achieved the direct synthesis of various 5-aryl-2-methyltetrazoles and 5-aryl-2-benzyltetrazoles. The researchers prepared a library of arylated tetrazoles through a two-step process starting from substituted aromatic aldehydes **232**. In the initial step, the aldehydic substrates were reacted with hydrazones **A** and **B**. This was followed by a reaction with DBAD/PIFA, resulting in the desired tetrazoles **233** (Scheme 87).



Entry	Donar	Result
1	208	93%, **213a**
2	218	decomposed
3	219	no reaction
4	220	decomposed

Scheme 84 Glycosylation of 2-hydroxyglucals **208**, **218–220**.



221: **R^1** = OAc, **R^2** = H
222: **R^1** = H, **R^2** = OAc

223

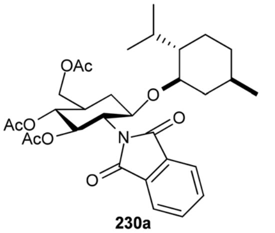
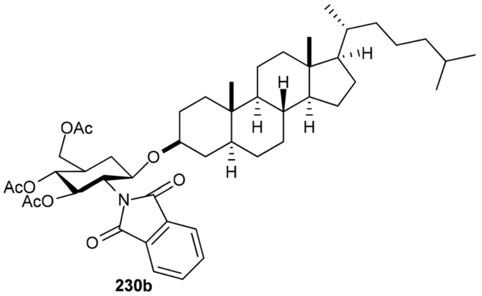
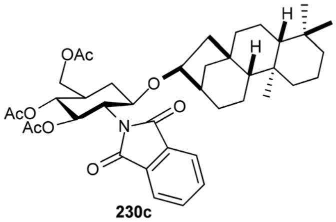
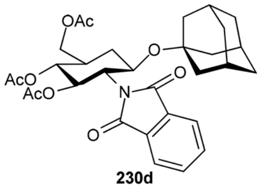
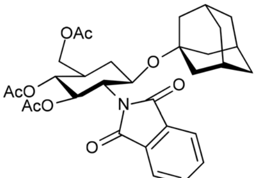
224

225

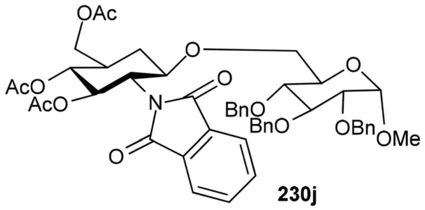
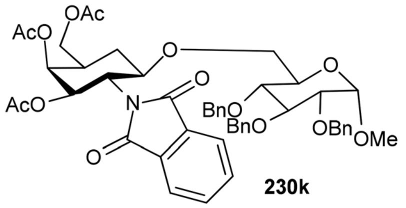
226: **R^1** = OH, **R^2** = H
227: **R^1** = H, **R^2** = OH

228a: **R^1** = Me, **R^2** = **R^3** = H, R^4 = **O**H
228b: **R^1** = Me, **R^2** = **R^4** = H, R^3 = **O**H
229: **R^1** = **R^4** = H, R^2 = Me, R^3 = **O**H

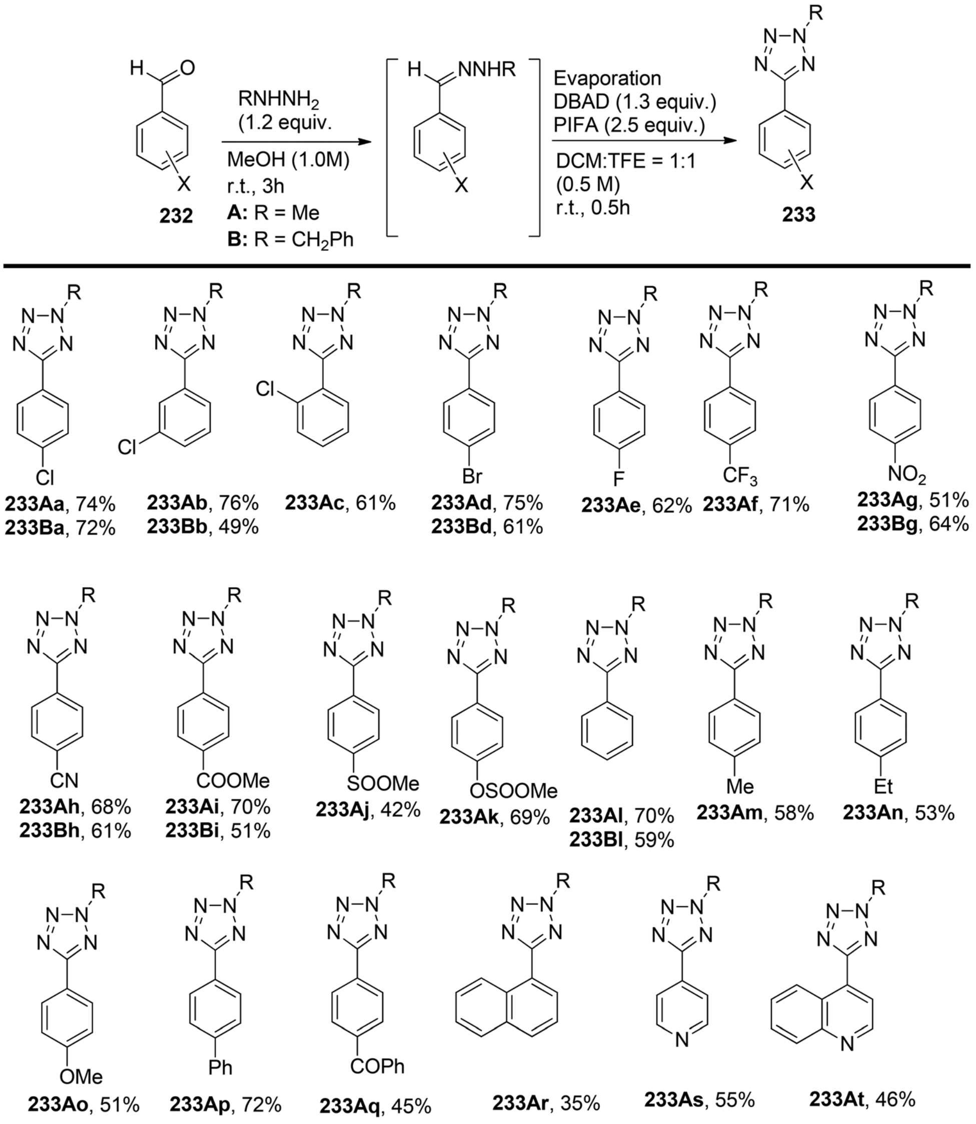
231

Entry	Donar	Acceptor	Product	% Yield
1	**221**	**223**	 **230a**	68
2	**221**	**224**	 **230b**	76
3	**221**	**225**	 **230c**	83
4	**221**	**226**	 **230d**	70
5	**221**	**227**	 **230e**	71

Scheme 85 PIFA/TfOH catalyzed glycosylation reaction of thioglycosides as well as various alkanols.

Entry	Donar	Acceptor	Product	% Yield
1	**221**	**231**	 **230j**	87
2	**222**	**231**	 **230k**	63

Scheme 86 Disaccharide synthetic methodology *via* thioglycosylation in presence of PIFA/TfOH.



Scheme 87 Synthetic scheme for transforming aromatic aldehydes to 2-alkyl-5-aryltetrazoles.

$$\underset{\mathbf{234}}{RSO_2Na} + \underset{\mathbf{235}}{ArSeSeAr} \xrightarrow[CH_2Cl_2]{PhI(OCOCF_3)_2} \underset{\mathbf{236}}{RSO_2SeAr}$$

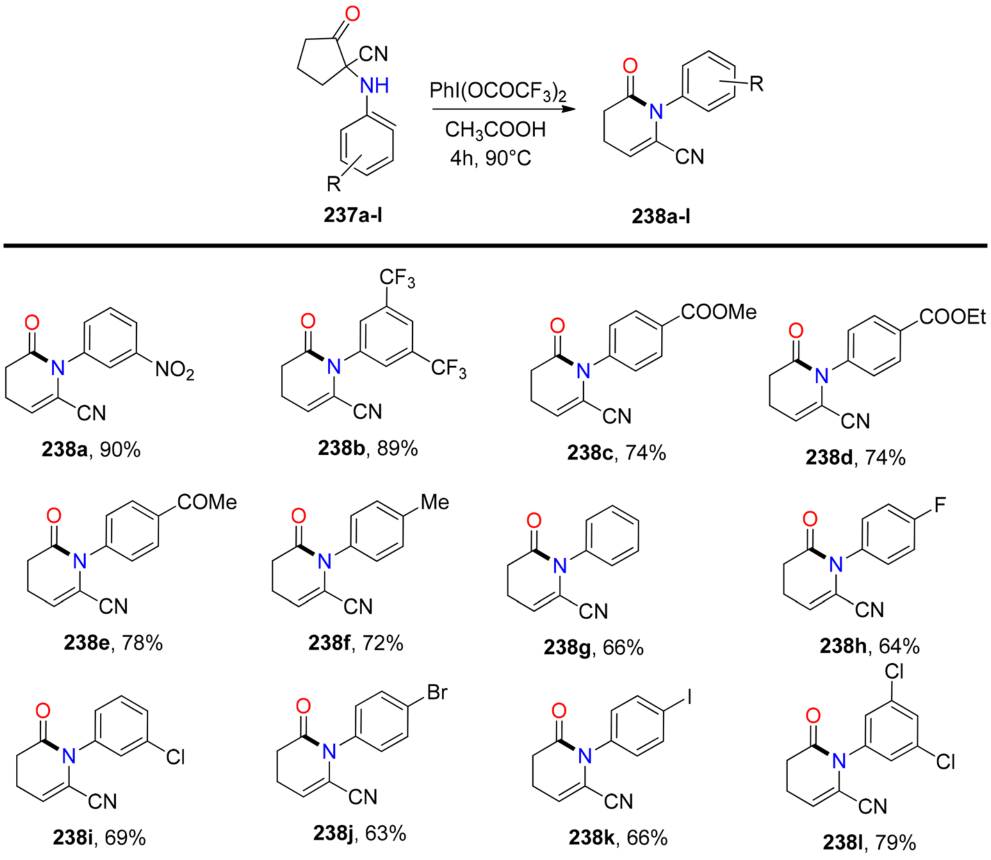
Entry	R of Sodium Sulfinate	Ar of Diaryl Diselenide	% Yield of RSO_2SeAr
1	*p*-$CH_3C_6H_4$	Ph	81
2	*p*-$CH_3C_6H_4$	*p*-$CH_3C_6H_4$	74
3	*p*-$CH_3C_6H_4$	*p*-ClC_6H_4	75
4	Ph	Ph	81
5	Ph	*p*-$CH_3C_6H_4$	80
6	Ph	*p*-ClC_6H_4	76
7	*p*-ClC_6H_4	Ph	83
8	*p*-ClC_6H_4	*p*-$CH_3C_6H_4$	81
9	*p*-ClC_6H_4	*p*-ClC_6H_4	68

Scheme 88 Preparation of selenosulfonates **236**.

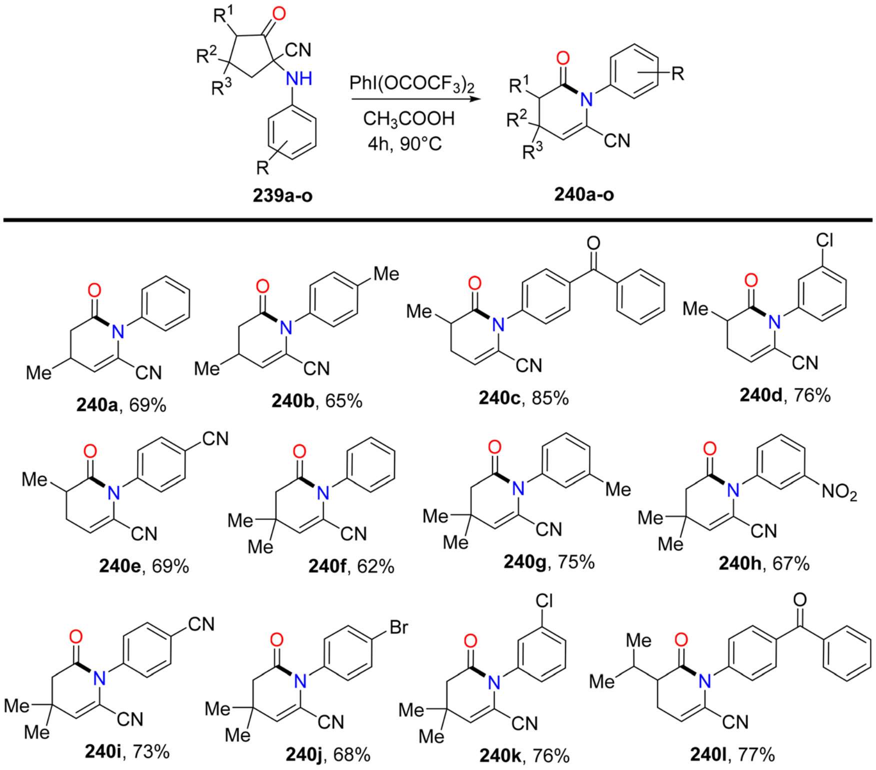
Recently, selenosulfonates have garnered significant attention in chemical synthesis. These compounds undergo selenosulfonations with diazomethane, olefins, acetylenes, and allenes through electrophilic and free radical reactions. Chen *et al.*[167] introduced an innovative one-pot methodology for synthesizing selenosulfonates **236** using diaryl diselenides **235**, sodium sulfinates **234**, and PIFA (Scheme 88).

3.12. Miscellaneous

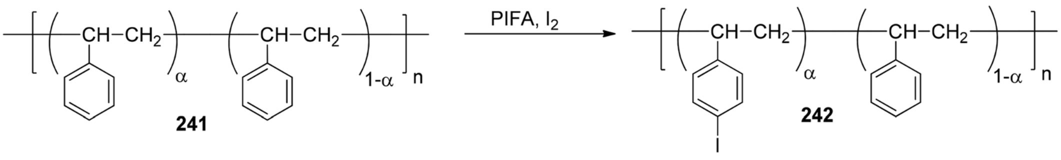
Bhattacherjee *et al.*[168] reported the first synthetic methodology for regioselective formation of *N*-aryl-valerolactams **238a–l** *via* PIFA-catalyzed rearrangement of carbonitriles **237a–l.** The reaction involves the rearrangement of the C–N bond, elimination of the C–5H atom, and opening of the C1–C2 linkage. Structural integrity of the lactam was further confirmed through single-crystal XRD measurements. PIFA actively participated in the reaction by employing an ionic pathway. The reaction conditions exhibited tolerance to various functionalities, yielding lactams in good to exceptional yields. Remarkably, electron-deficient cyclopentanones resulted in outstanding product yields due to stabilized positive charge (Scheme 89). Subsequently, the reaction was explored with variably substituted cyclopentanone derivatives **239** (Scheme 90). This reaction scheme also provides a novel



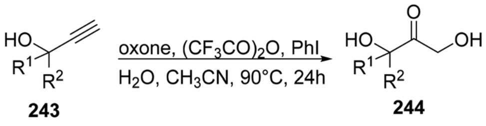
Scheme 89 Synthesis of *N*-aryl-valerolactams **238a–l** *via* PIFA-catalyzed rearrangement of carbonitriles **237a–l**.

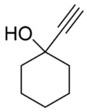


Scheme 90 Examination of the lactamization reaction with variably substituted substrates.



Scheme 91 Iodination of polystyrene (PS) **241**.



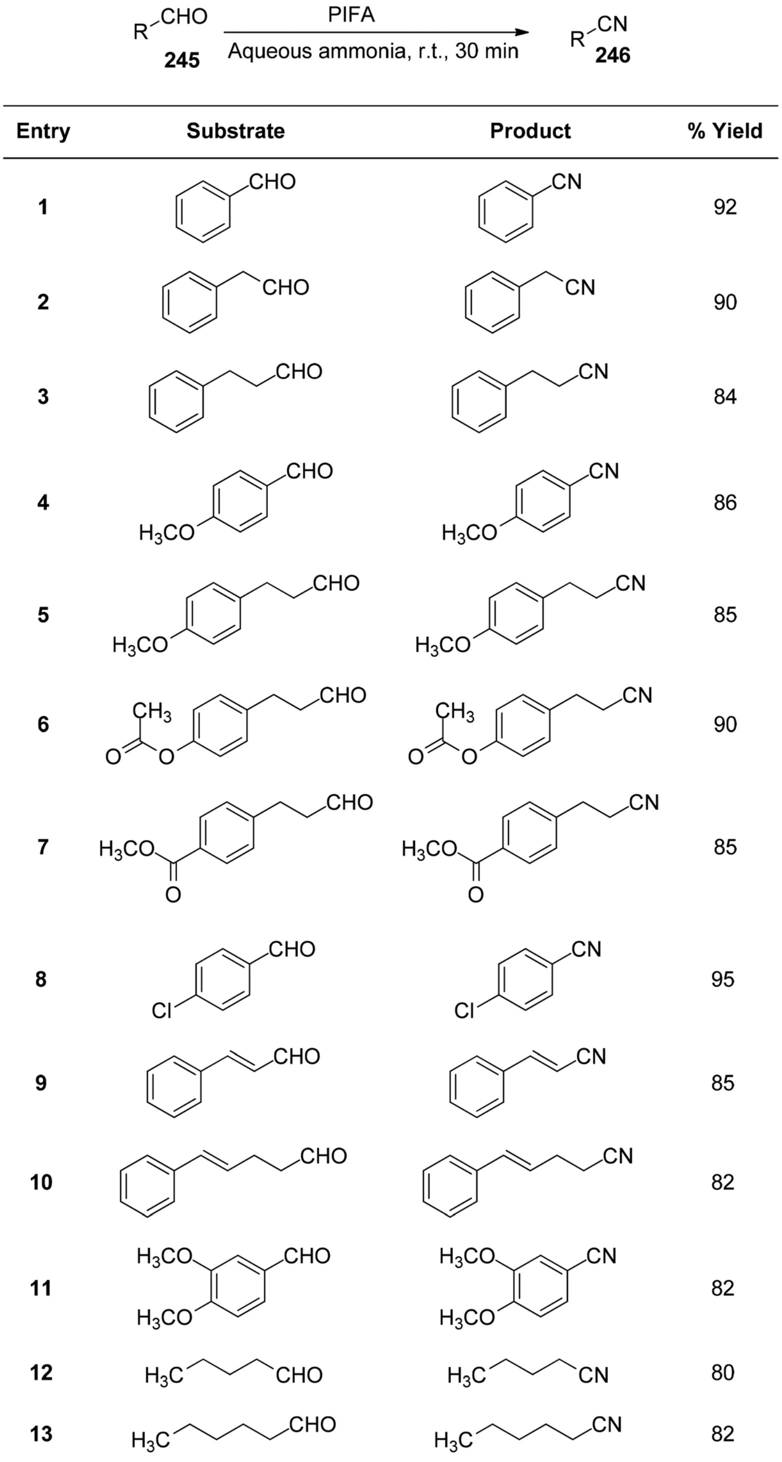
Entry	R^1	R^2	% Yield
1	Ph	Me	76
2	4-MePh	Me	75
3	4-ClPh	Me	72
4	4-BrPh	Me	82
5	4-IPh	Me	80
6	4-MeOPh	Me	86
7	4-NO_2Ph	Me	58
8	3-MePh	Me	73
9	3-BrPh	Me	81
10	Ph	Ph	86
11	4-MePh	4-MePh	62
12	4-ClPh	4-ClPh	85
13	Ph	Bn	81
14			63
15	Me	Me	71
16	Me	Et	74

Scheme 92 Reaction scheme for converting ethynyl carbinols to α,α′-dihydroxy ketones in the presence of oxone/$(CF_3CO)_2O$ system.

pathway for obtaining biologically significant nitrile-functionalized lactams.

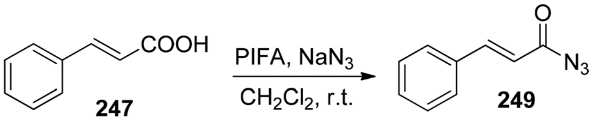
Yudina *et al.*[169] investigated the room temperature PIFA-mediated direct iodination of polystyrene **241** (PS) (Scheme 91). The resulting poly(*p*-iodostyrene) **242** exhibited a molecular weight distribution (MWD) quite similar to that of the original PS. Varying the substrate to reagent ratio resulted in the production of iodinated PS samples with a degree of substitution ranging from 0.5 to 1.

The α,α′-dihydroxy ketone **243** moiety is a significant component of many naturally occurring molecules such as betamethasone and pirarubicin. Thus, its synthetic protocol is of

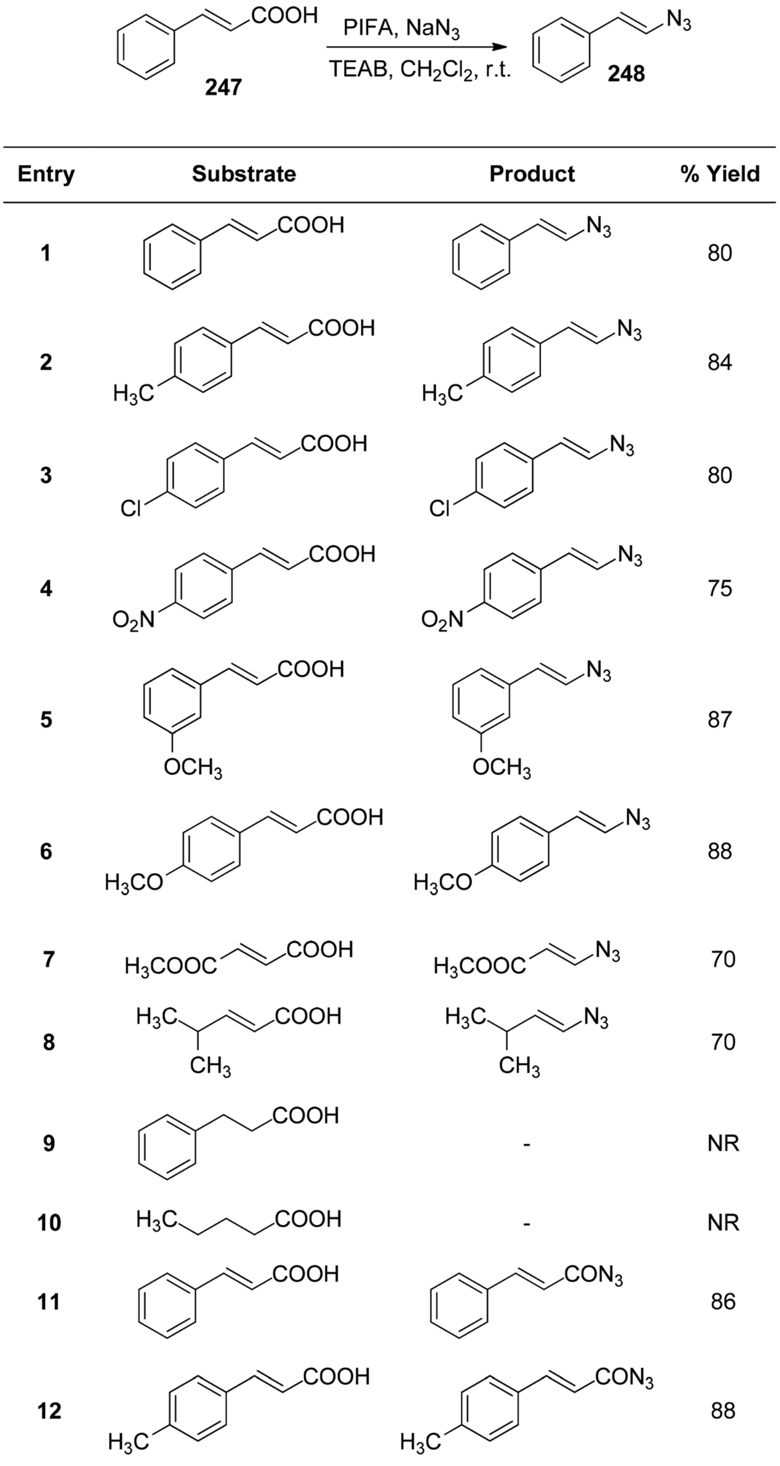


Scheme 93 Preparation of nitriles **246** from aldehydes **245**.

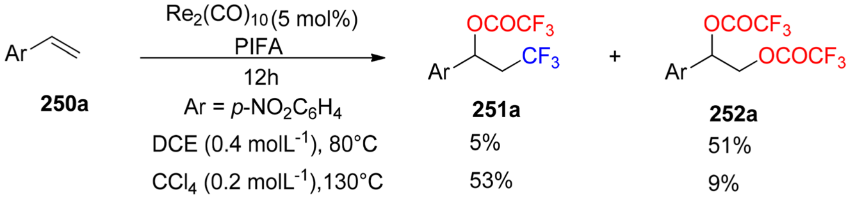
great interest.[170] Chen *et al.*[171] utilized a PIFA/oxone/($CF_3CO)_2O$ system to obtain a series of α,α′-dihydroxy ketones **244** (Scheme 92). PIFA actively participated in the reaction by employing an ionic pathway. This methodology is easy to handle and does not utilize stoichiometric ratios of PIFA.



Scheme 95 Cinnamic acid converted into acyl azide using PIFA and sodium azide.



Scheme 94 Carboxylic acid reaction with PIFA and NaN_3.



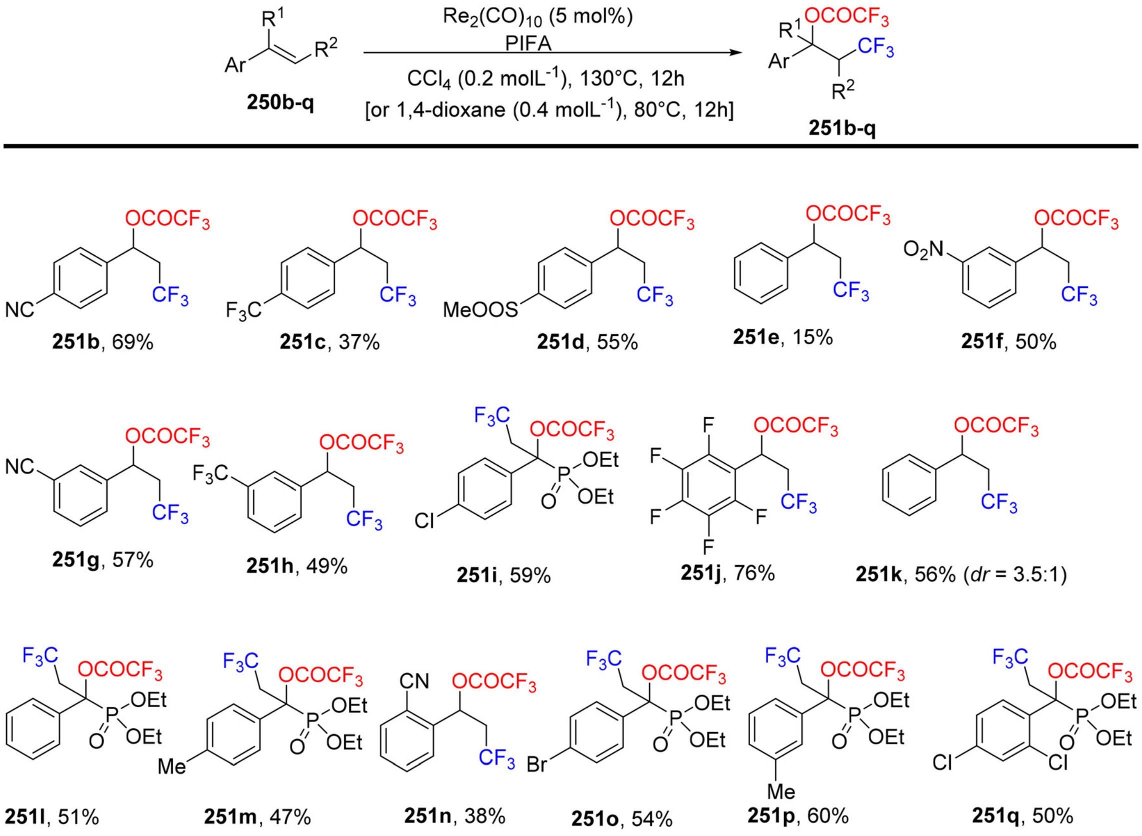
Scheme 96 Re-catalyzed decarboxylative oxytrifluoromethylation of styrene using PIFA.

Telvekar *et al.*[172] presented a straightforward and mild process to convert aldehydes **245** with various substitutions into nitriles **246** at room temperature, utilizing aqueous ammonia and PIFA. This system demonstrated rapid reaction times, a simple setup, and yielded nitriles in average to good yields. Both aliphatic and aromatic substrates showed successful formation of nitriles using this methodology, with yields ranging from good to outstanding (Scheme 93).

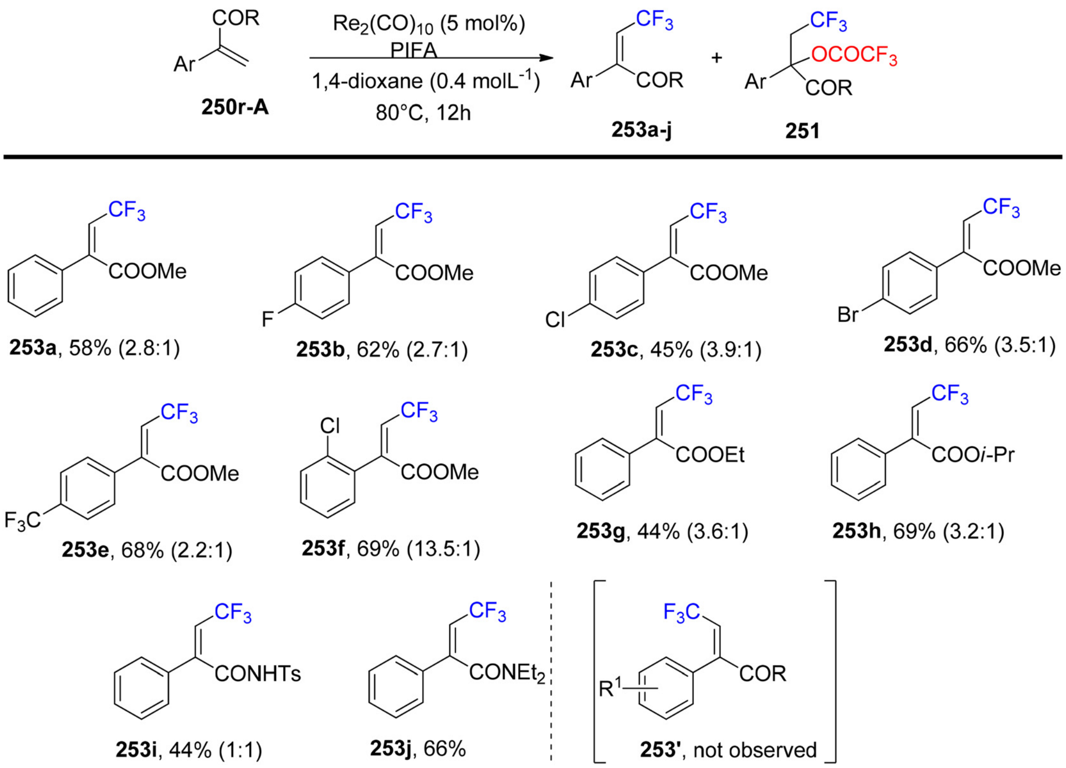
Telvekar *et al.*[173] employed PIFA/TEAB in the presence of sodium azide to synthesize vinyl azides **248** from α,β-unsaturated carboxylic acids **247** with various substitutions. This mild reaction exhibited broad substrate tolerance, consistently yielding excellent yields of vinyl azides. Diverse α,β-unsaturated carboxylic acids **247** were successfully transformed into vinyl azides **248**, obtaining yields ranging from 70–88% (Scheme 94).

Shorter reaction times as well as the use of non-toxic substrate are the associated advantages for this synthetic scheme. Furthermore, it can also be used to obtain the acyl azides **249** (Scheme 95).

Wang *et al.*[174] employed PIFA to achieve the inaugural oxytrifluoromethylation of styrenes **250a** utilizing rhenium as the catalyst (Scheme 96). Following optimization, they investigated the reactivity of different alkenes **250b–q** with PIFA as their reaction counterpart (Scheme 97). Notably, when they subjected α,β-unsaturated esters and amides **250r-A** to the reaction conditions, the primary product formed was the Heck-type trifluoromethylation product **253a–j,** while the concurrent generation of the oxytrifluoromethylation product **251** occurred but in a relatively minor quantity (Scheme 98). PIFA actively participated in the reaction by employing a free radical pathway, particularly through hydrogen abstraction.



Scheme 97 Oxytrifluoromethylation of styrenes.



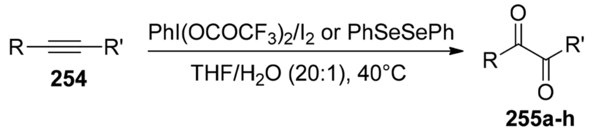
Scheme 98 Trifluoromethylation reaction of α,β-unsaturated esters as well as amides stereoselectively.

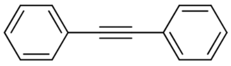
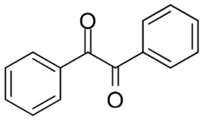
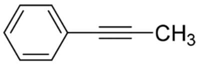
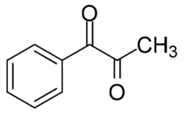
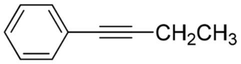
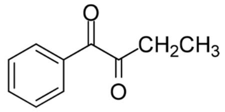
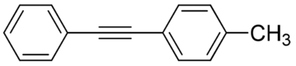
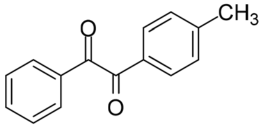
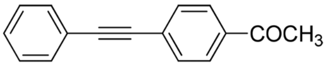
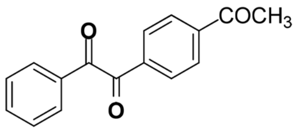
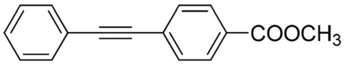
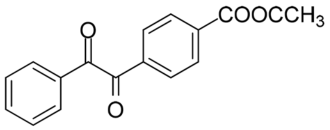
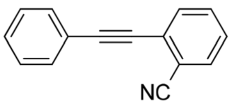
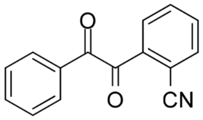
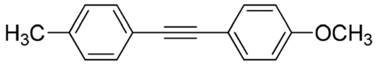
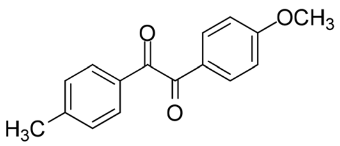
In order to synthesize 1,2-dicarbonyls **255** from variably substituted alkynes **254**, Tingoli *et al.*[175] investigated the usage of *in situ*-produced iodonium and selenium species (Scheme 99). PIFA enables the synthesis of 1,2-diketones **255**, utilizing diphenyl diselenides as well as elemental iodine, from internal alkynes **254**. Unfortunately, initial reactions with iodine resulted in incomplete conversion. Diphenyl diselenide, on the other hand, was more effective and resulted in the formation of the desired product in excellent yields. Furthermore, in order to synthesize quinoxaline derivatives, a second condensation procedure was utilized, thus validating the dicarbonyls as vicinal.

Catir *et al.*[176] utilized a PIFA/H_2O_2 system and singlet oxygen acceptor molecules to generate singlet oxygen products.[177] PIFA was used to study the breakdown of hydrogen peroxide **256**. PIFA actively participated in the reaction by employing a free radical pathway. The outcomes of the study exhibited that hydrogen peroxide treatment on a PIFA molecule results in generation of $^1O_2$ (Scheme 100a). Furthermore, the production of $^1O_2$ was confirmed by chemiluminescence detection at 1270 nm as well as trapping experiments. There is strong evidence to support the idea that the hydroperoxyl radical, formed when hydrogen peroxide and PIFA combine, decomposes into singlet molecular oxygen through a tetraoxidane intermediate. The decomposition of the experiment has been also reported with optically pure (1*S*)-1-phenylethyl hydroperoxide **261** instead of hydrogen peroxide **256** (Scheme 100b).

Kita *et al.*[178] conducted innovative and direct nucleophilic reactions using PIFA for sulfenylation (Schemes 101 and 102) and thiocyanation (Scheme 103) of phenol ethers and related compounds **267**. This study successfully synthesized numerous unsymmetrical diaryl sulfides **268** and aryl thiocyanates **273** in high yields, which can serve as synthons for sulfur aromatics. Unlike other solvents such as CH_3CN and CH_2Cl_2, which produced only minimal sulfenylation products, $(CF_3)_2$–CHOH, a polar, protic, and weakly nucleophilic solvent, facilitated the reaction effectively. Additionally, variably substituted thiophenols were employed as sulfur nucleophiles. Under similar conditions, arylthiol molecules **269** and **270** were obtained by treating **267b** with thiophenols, achieving excellent yields. However, substrates with electron-releasing substituents like OMe/Me resulted in reduced yields of the sulfenylated products **271** and **272.** PIFA actively participated in the reaction by employing a free radical pathway, particularly through single-electron oxidation, contributing to the process through this mechanism. Moreover, this methodology proved useful for the synthesis of diverse sulfur-containing aromatic molecules.

Wu *et al.*[179] have introduced a novel metal-free approach for the synthesis of olefins **275** through microwave-assisted direct decarboxylative elimination of arylacetic acids **274**, as illustrated in Scheme 104. This method, employing commercially available PIFA, demonstrates a high level of efficiency in generating a variety of aryl/diphenylvinyl compounds **275** with yields ranging from moderate to good. PIFA actively engaged in the reaction by following a radical pathway, specifically



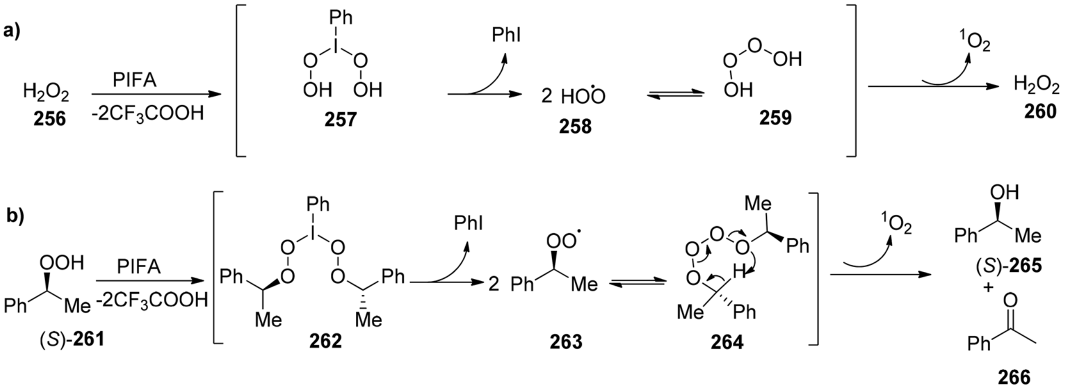
Entry	Alkyne	1,2-Diketone		% Yield	
				A	B
1			a	52	87
2			b	56	75
3			c	45	62
4			d	54	67
5			e	40	75
6			f	45	85
7			g	48	65
8			h	52	78

Scheme 99 Synthetic scheme for 1,2-diketones from alkynes in presence of (**A**) $PhI(OCOCF_3)_2$ or (**B**) PhSeSePh.

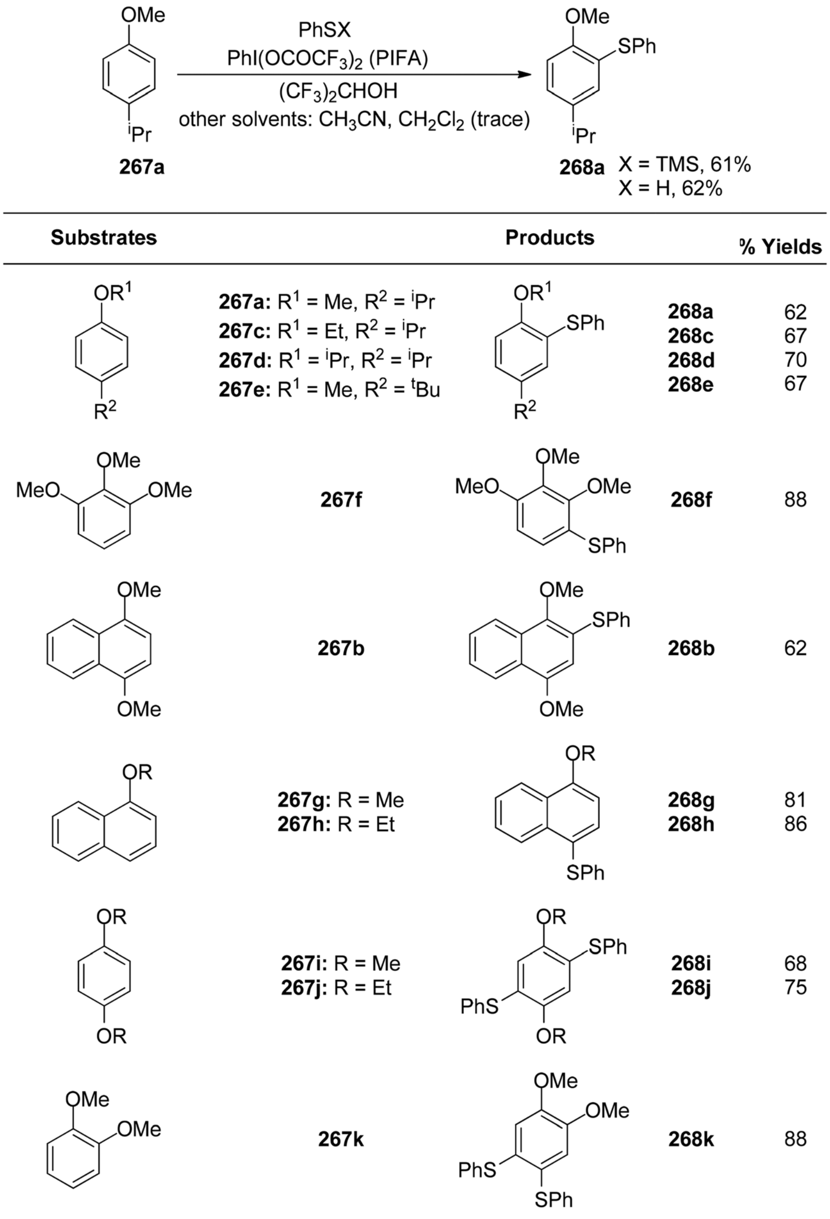
through hydrogen abstraction. It is noteworthy that this decarboxylation process exclusively produces E-olefins, which could potentially be the thermodynamically favored products. Preliminary mechanistic inquiries suggest the involvement of a radical process in the decarboxylative elimination reaction.

Kitamura *et al.*[180] have introduced an efficient and practical method for synthesizing 2,2-difluoroethylarenes **277** through the use of a hypervalent iodine-mediated fluorination reaction involving various styrene derivatives **276**. They conducted a systematic exploration of different styrene derivatives **276** to investigate the scope of substrates, as outlined in Scheme 105.

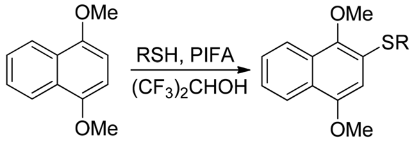
Chatterjee *et al.*[181] have introduced an effective, metal-free, and base-free approach for the precise synthesis of primary amines **279** derived from boronic acids **278**, encompassing various types such as aryl, heteroaryl, and alkyl. This reaction takes place at room temperature and relies on the combined



Scheme 100 Decomposition of **256** and (*S*)-**261** with PIFA.



Scheme 101 Synthesis of direct sulfenylation compound **267**.



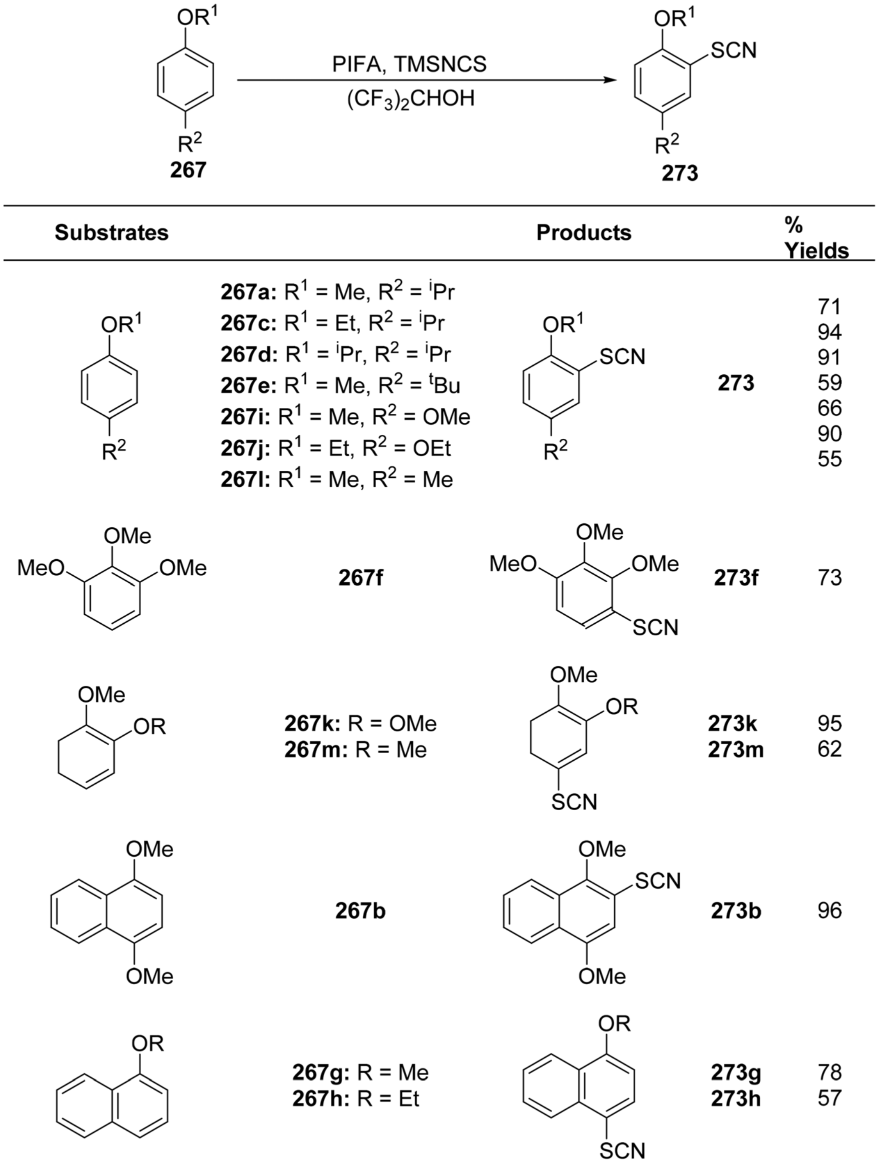
267b **268-272**

Substrate	R	Product	% Yield
267b	4-nitrophenyl	**269**	87
	2,3,5,6-tetrafluorophenyl	**270**	72
	phenyl	**268b**	62
	4-methoxyphenyl	**271**	37
	4-methylphenyl	**272**	40

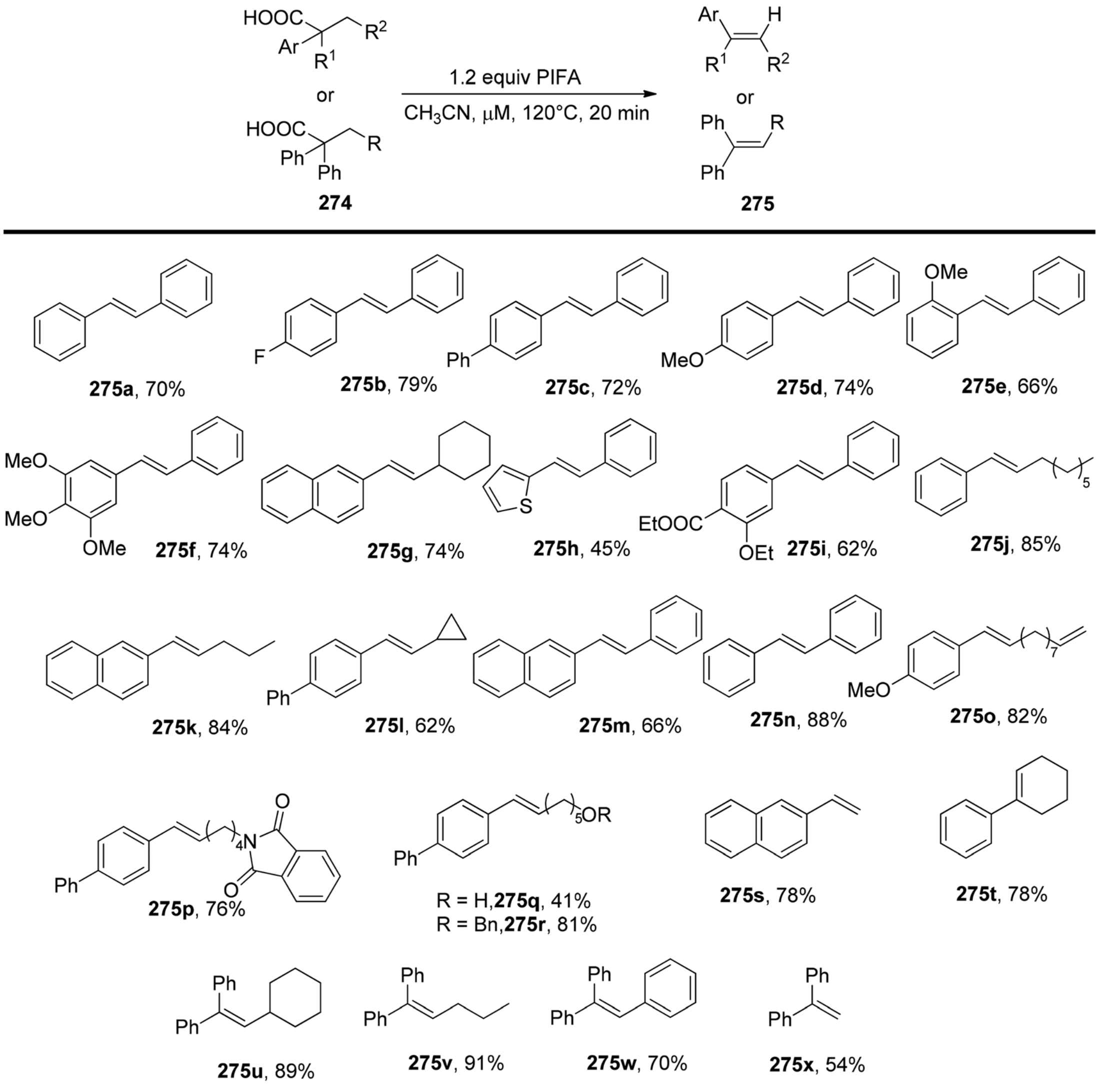
Scheme 102 Sulfenylation of **267b** by various thiophenols.

action of PIFA and NBS, employing cyanamidyl/arylcyanamidyl radicals as pivotal intermediates for the amination process. PIFA actively engaged in the reaction by following a radical pathway. It is noteworthy that these reactions are remarkably fast, typically completing within just one hour. Furthermore, to gain a deeper insight into the underlying reaction mechanism, the researchers conducted computational studies using DFT. These quantum chemical calculations, combined with experimental observations, validate that the *ipso* amination of substituted boronic acids **278** involves the generation of cyanamidyl/arylcyanamidyl radicals, followed by their regiospecific interaction with the boron atom of the boronic acids. This specific interaction leads to the selective formation of primary amines **279**, as exemplified in Schemes 106 and 107.

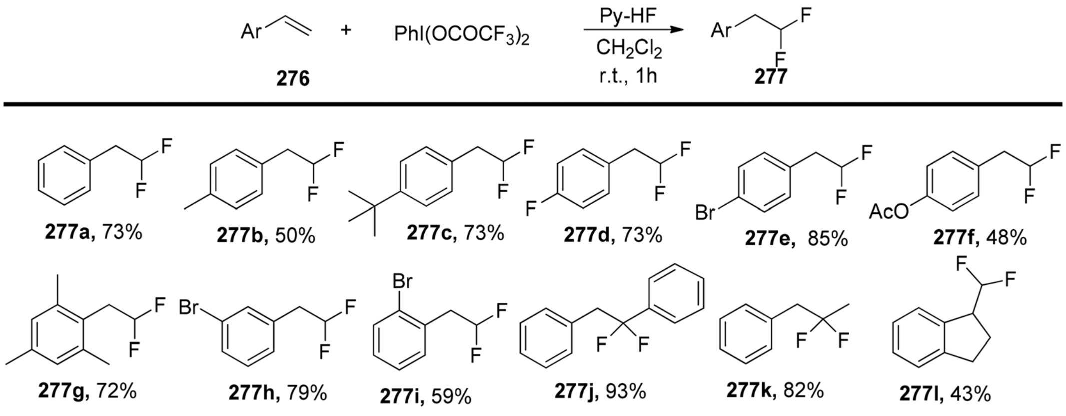
Gondo *et al.*[182] have introduced a method for desilylative acetoxylation of (trimethylsilyl)-arenes **282**, effectively convert-



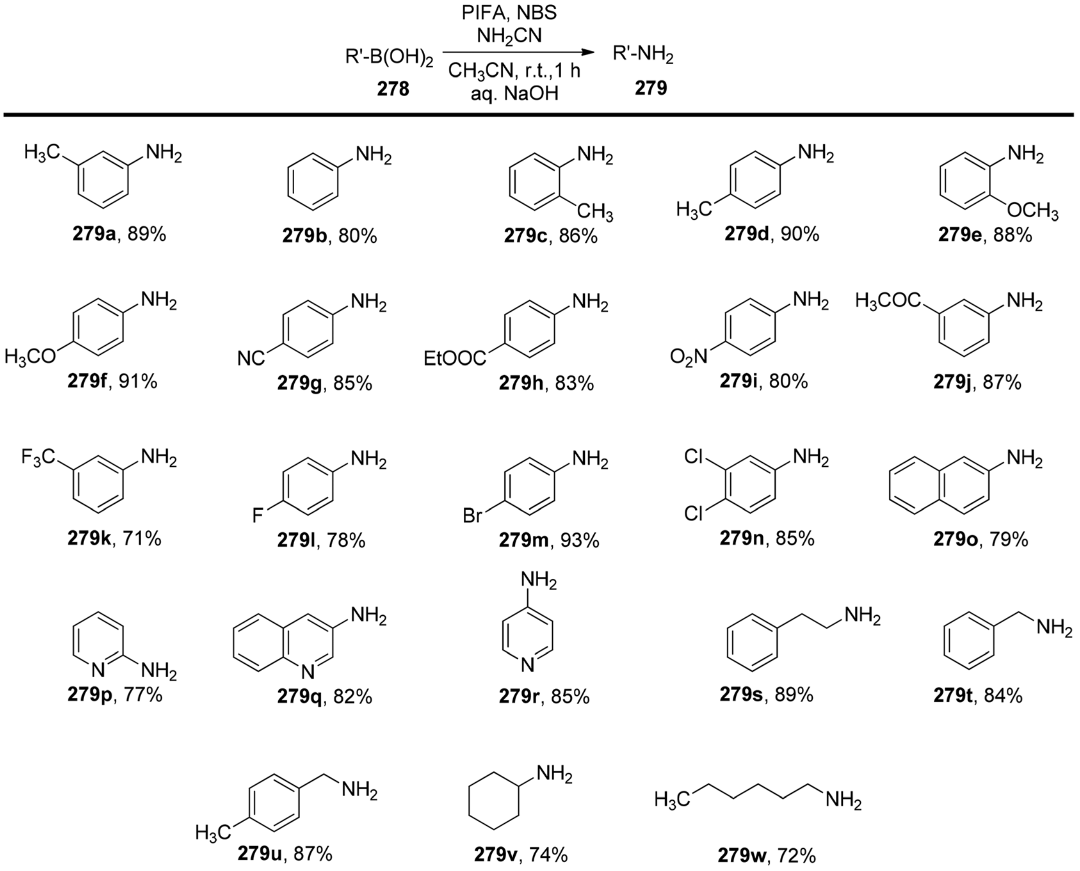
Scheme 103 Thiocyanation of phenol ethers and alkoxynaphthalenes.



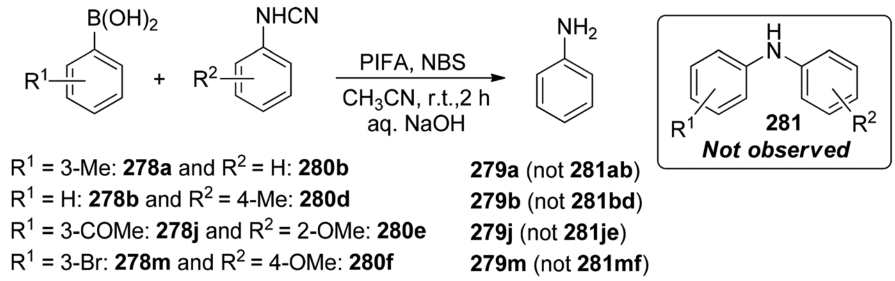
Scheme 104 Substrate scope of aryl/diphenylacetic acids **274**.



Scheme 105 Synthesis of 2,2-difluoroethylarenes **277**.



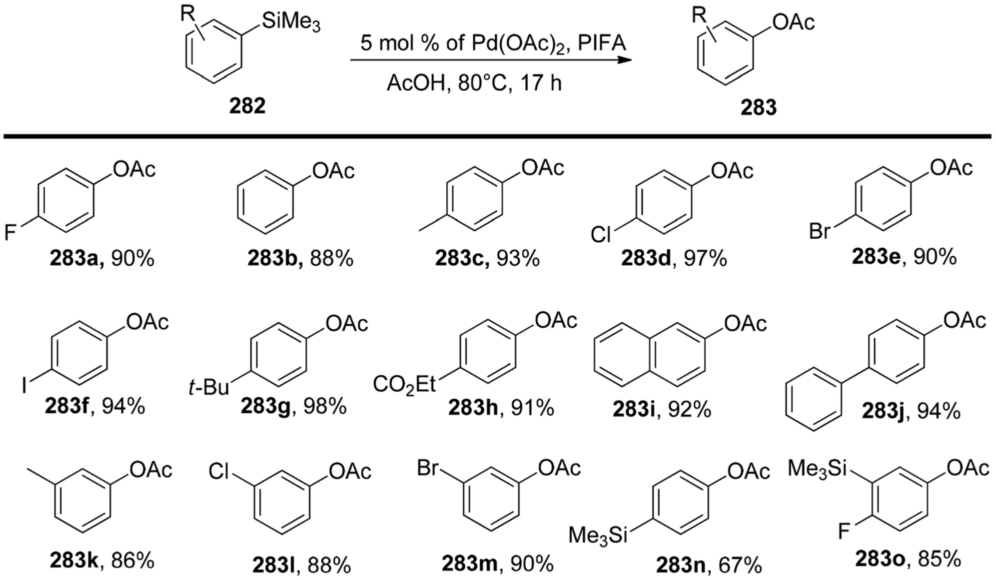
Scheme 106 PIFA–NBS–NH_2CN mediated *ipso*-amination of different boronic acids **278**.



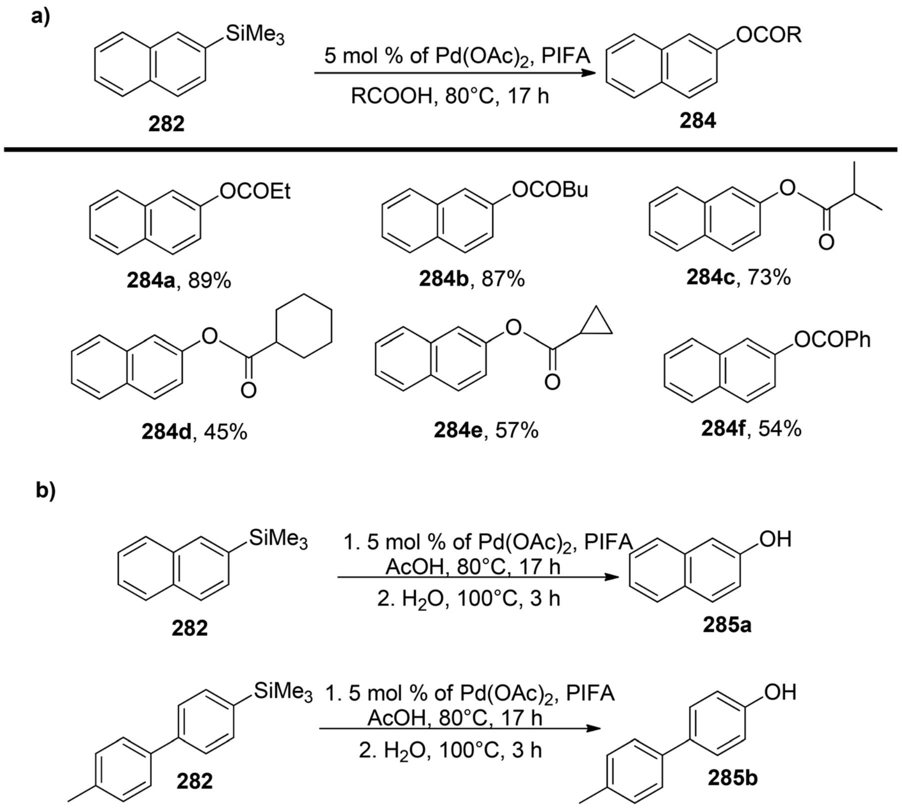
Scheme 107 Reaction with arylcyanamides **280** and arylboronic acids **278** mediated by PIFA–NBS.

ing them into acetoxyarenes **283** (Scheme 108). The direct acetoxylation is achieved by employing 5 mol% of $Pd(OAc)_2$ and 1.5 equiv. of PIFA in AcOH at 80 °C for 17 hours, resulting in the formation of acetoxyarenes **283** in good to high yields (ranging from 67% to 98%). The practicality of this approach is demonstrated through a one-pot transformation of (trimethylsilyl)arenes **282** into phenols **284** by carrying out successive acetoxylation and hydrolysis (Scheme 109a). Furthermore, the desilylative acyloxylation of 2-(trimethylsilyl)-naphthalene **282** is achieved using various carboxylic acids (Scheme 109b). The utilization of "non-activated" (trimethylsilyl)arenes for acetoxylation or acyloxylation offers an efficient and practical means of synthesizing phenol derivatives.

Pan *et al.*[183] have developed a mechanochemical and solvent/catalyst-free method for functionalizing olefins **286** using PIFA reagents, facilitating the synthesis of 1,3-dioxygenated compounds **287** (Scheme 110) and 1,4-iodoalcohols **289** (Scheme 111). The process, challenging with conventional methods, involves an intermolecular cascade triggered by the active monomeric form of PIFA through an ionic pathway, as revealed by mechanistic studies. The synthetic efficiency of the described method is exemplified by the facile two-step syn-



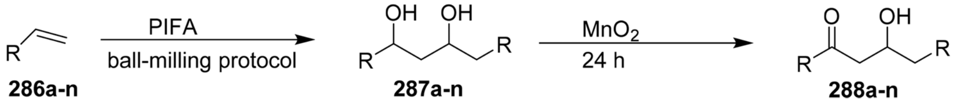
Scheme 108 Desilylative acetoxylation of (trimethylsilyl)-arenes **282**.



Scheme 109 a) One-pot transformation of (trimethylsilyl)arenes **282** into phenols **284**. (b) Desilylative acyloxylation of 2-(trimethylsilyl)-naphthalene **282** using various carboxylic acids.

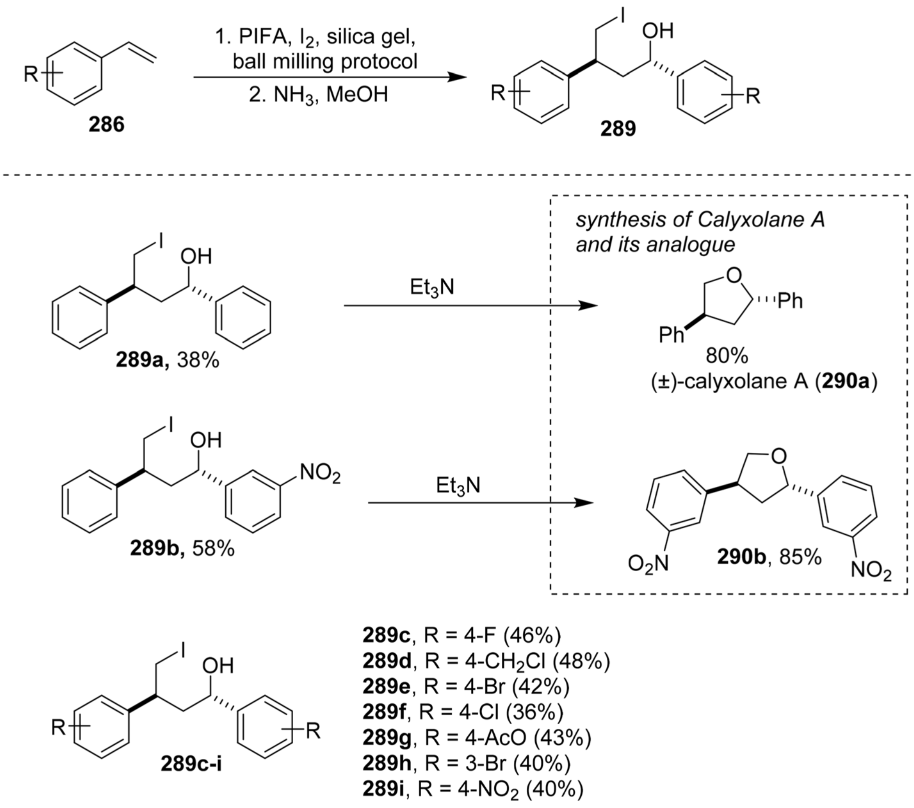
thesis of the natural product (±)-calyxolane A (**290a**)[184,185] from styrene (**286a**). Additionally, the calyxolane A analogue **290b** (85%) was obtained from 3-nitrostyrene (**286b**), showcasing the advantages of the ball-milling protocol over traditional multi-step syntheses,[186] yielding **290a** in just two steps with a 30% overall yield.

Berthelot *et al.*[187] have detailed the synthesis and characterization of zinc(II) *meso*-pyridin-2-ylthio-porphyrins **296–298**



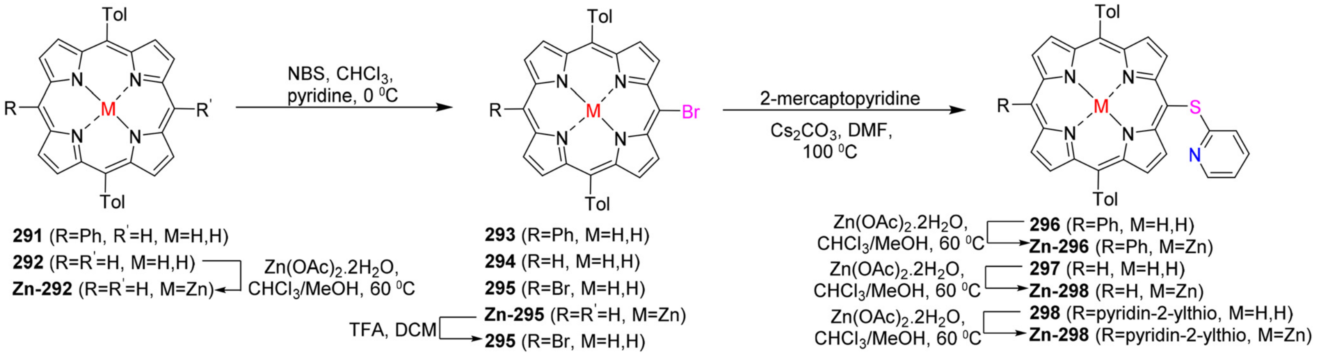
Entry	Substrate, R	**287**, yield	**288**, yield
1.	**286a**, Ph	**287a**, 64%	**288a**, 68%
2.	**286b**, 2-Me-C_6H_4	**287b**, 65%	**288b**, 49%
3.	**286c**, 3-Me-C_6H_4	**287c**, 72%	**288c**, 63%
4.	**286d**, 4-Me-C_6H_4	**287d**, 60%	**288d**, 60%
5.	**286e**, 4-*t*Bu-C_6H_4	**287e**, 63%	**288e**, 54%
6.	**286f**, 4-$ClCH_2$-C_6H_4	**287f**, 35%	**288f**, 59%
7.	**286g**, 4-MeO-C_6H_4	**287g**, 58%	**288g**, 70%
8.	**286h**, 4-*t*BuO-C_6H_4	**287h**, 37%	**288h**, 62%
9.	**286i**, 4-TBSO-C_6H_4	**287i**, 64%	**288i**, 68%
10.	**286j**, 4-AcO-C_6H_4	**287j**, 51%	**288j**, 60%
11.	**286k**, 3-F-C_6H_4	**287k**, 60%	**288k**, 73%
12.	**286l**, 3-Cl-C_6H_4	**287l**, 73%	**288l**, 60%
13.	**286m**, 3-Br-C_6H_4	**287m**, 48%	**288m**, 66%
14.	**286n**, 4-Br-C_6H_4	**287n**, 46%	**288n**, 42%

Scheme 110 Synthesis of 1,3-dioxygenated compounds.

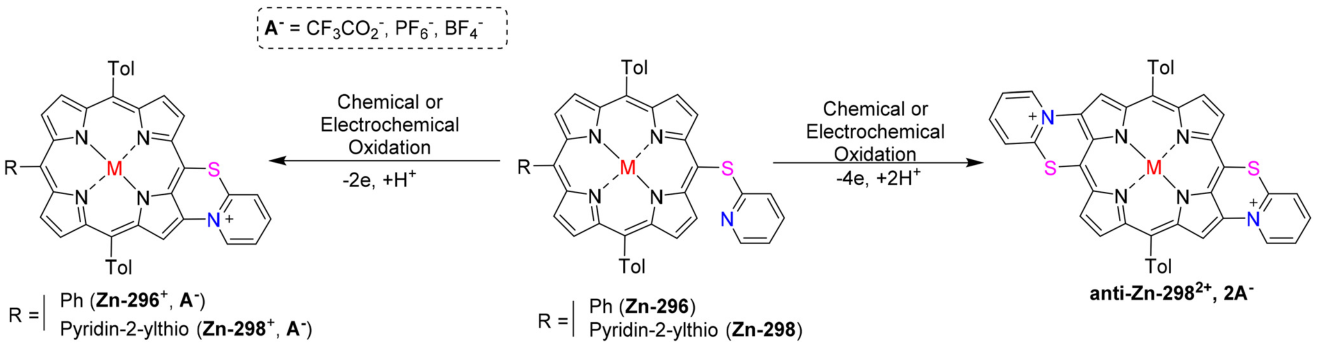


Scheme 111 Synthesis of 1,4-iodoalcohols **289** and (±)-calyxolane A.

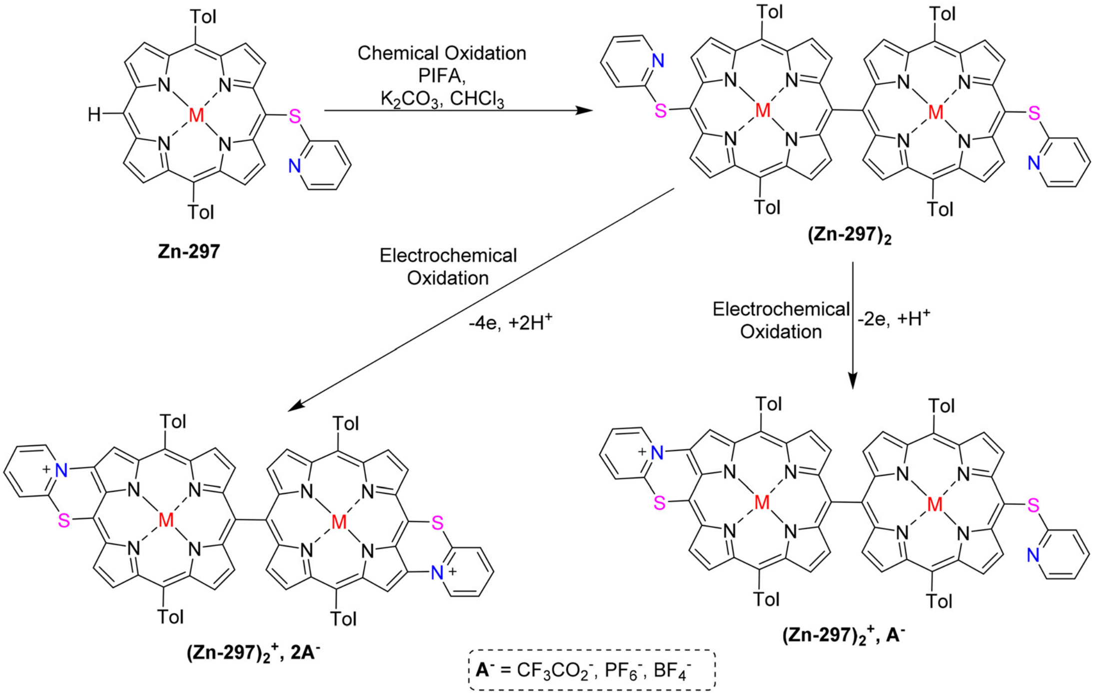
(Scheme 112). The electrochemical oxidation of zinc(II) porphyrins, specifically [5-(pyridin-2-ylthio)-10,20-bis(*p*-tolyl)-15-phenylporphyrinato] zinc(II) **Zn-296** or [5,15-bis(pyridin-2-ylthio)-10,20 bis(*p*-tolyl)porphyrinato] zinc(II) **Zn-298,** results in the intriguing formation of one or two C–N bonds (Scheme 113). This transformation occurs through an intramolecular nucleophilic attack of the peripheral thiopyridinyl fragments on the adjacent β-pyrrolic positions, leading to a C–N fusion reaction. Moreover, the oxidation of [5-(pyridin-2-ylthio)-10,20-bis(*p*-tolyl)-porphyrinato] zinc(II) **Zn-297**, which



Scheme 112 Synthesis of porphyrins **Zn-296**, **Zn-297**, and **Zn-298**.



Scheme 113 Intramolecular C–N oxidative coupling.



Scheme 114 Oxidative behaviour of **Zn-297**.

possesses a vacant *meso* position, predominantly yields the *meso*,*meso*-dimer (**Zn-297**)$_2$. Sequential electrochemical oxidation steps then result in the selective formation of both mono and bis C–N fused *meso*,*meso*-dimer products (Scheme 114). The planarization of the molecules and the generation of positive charges during the C–N fusion reaction lead to significant electronic alterations. These changes manifest in observable shifts in the UV–vis absorption spectra, including a bathochromic shift of the Soret and Q bands, as well as the splitting of the Soret bands. Additionally, the cyclic voltammograms demonstrate modifications such as the reduction of the pyridinium moiety-(ies) occurring between −0.5 and −1.0 V.

4. Conclusion

Iodine, characterized as the most polarizable, least electronegative, and largest halogen, exhibits unique reactivity. Iodine manifests itself in various oxidation states, forming hypercoordinate compounds such as I(III), I(V), and I(VII). Over time, hypercoordinate iodine compounds have gained significance as reagents in synthesis due to their low toxicity, cost-effectiveness, environmental friendliness, and transition metal-like reactivity under mild conditions. Hypervalent iodine reagents, recognized for their low toxicity, accessibility, ease of handling, efficiency, stability to air and moisture, and safe substitution for toxic heavy metal reagents like lead(IV), thallium(III), and mercury(II), have been widely embraced as green oxidants in organic synthesis. Among them, [bis(trifluoroacetoxy)iodo]arenes (PIFA) stand as pivotal compounds extensively employed as chemoselective oxidants in contemporary organic synthesis. The pronounced electron-withdrawing nature of the fluorine atom renders PIFA more reactive than its counterpart, phenyliodine diacetate (PIDA). PIFA is known to facilitate reactions that may not proceed efficiently with PIDA. Moreover, PIFA is recognized as a potent and attractive catalyst for numerous crucial chemical processes, encompassing amination, sulfenylation, oxidative coupling, amidation, carboxylation, ring-rearrangement, cascade reactions, alkylarylation, and more. It also finds application in simple oxidation of nitrogen compounds, phenolic oxidation, oxidation of alkynes, ketones, sulfur compounds, and oxidative biaryl coupling, among other processes.

The utilization of PIFA reagents in chemical synthesis is continuously evolving. This review comprehensively summarizes synthetic methodologies and various PIFA-catalyzed oxidative reactions for the production and functionalization of heterocyclic compounds, providing illustrative examples. The diverse applications of PIFA in organic synthesis, including amidation, amination, C–H functionalization, coupling, cyclization, oxidative and Hoffmann reactions, as well as in carbohydrate chemistry, one-pot reactions, and more, are systematically presented. We anticipate that researchers in synthetic organic chemistry and related fields will find this compilation to be a valuable addition.

Abbreviations

PIFA	(Bis(trifluoroacetoxy)iodo)benzene
PIDA	(Diacetoxyiodo)benzene
Kg	Kilogram
DMF	Dimethylformamide
DMAc	Dimethylacetamide
HOBt	Hydroxybenzotriazole
EDC·HCl	(3-Dimethylamino-propyl)-ethyl-carbodiimide·hydrochloride
TFA	2,2,2-Trifluoroacetic acid
NHPI	*N*-Hydroxyphthalimide
4CzIPN	1,2,3,5-Tetrakis(carbazol-9-yl)-4,6-dicyanobenzene
KOH	Potassium hydroxide
NLO	Non-linear optical
mV	Millivolt
IR	Infra-red
NMR	Nuclear magnetic resonance
MS	Mass spectrum
m.p.	Melting point
HFIP	Hexafluoroisopropanol
DCE	Dichloroethane
TFE	Tetrafluoroethylene
IBX	2-Iodoxybenzoic acid
THF	Tetrahydrofuran
SAR	Structure–activity relationship
IC_{50}	Half maximal inhibitory concentration
μM	Micromolar
EtOH	Ethanol
HOCl	Hypochlorous acid
CH_2Cl_2	Dichloromethane
NBS	*n*-Bromo succinimide
PS	Polystyrene
DIBAL	Diisobutylaluminium hydride
TfOH	Triflic acid
NaOH	Sodium hydroxide
DBAD	Di-*tert*-butyl azodicarboxylate
TFE	Tetrafluoroethylene
XRD	X-ray diffraction
MWD	Molecular weight distributions
TEAB	Tetraethylammonium bromide

Author contributions

SK, AA, and SKS conceived and gathered the data. The initial manuscript was composed by SK, AA, and SKS, and later revised by RK and BS. SKS and BKS provided critical reviews of the manuscript and played a pivotal role in its finalization. The final version of the manuscript received approval from all authors.

Conflicts of interest

Authors declare no potential conflict of interest.

Acknowledgements

We thank the Institute of Eminence at the University of Delhi for contributing funds to promote research and development. A Senior Research Fellowship (SRF) was awarded to Sumit Kumar (File No.: 09/045(1798)/2020-EMR-I) and Aditi Arora (File No.: 09/0045(11270)/2021-EMR-I) by the Council of Scientific and Industrial Research (CSIR), New Delhi, India.

References

1 T. Wirth, *Angew. Chem., Int. Ed.*, 2005, **44**, 3656–3665.
2 T. Dohi and Y. Kita, *Chem. Commun.*, 2009, **16**, 2073–2085.
3 V. V. Zhdankin and P. J. Stang, *Chem. Rev.*, 2008, **108**, 5299–5358.
4 A. Yoshimura and V. V. Zhdankin, *Chem. Rev.*, 2016, **116**, 3328–3435.
5 L. Long, J. Wang, L. Gu, S. Yang, L. Qiao, G. Luo and Z. Chen, *J. Org. Chem.*, 2021, **86**, 12084–12092.
6 J. P. Brand and J. Waser, *Chem. Soc. Rev.*, 2012, **41**, 4165–4179.
7 M. Arisawa, S. Utsumi, M. Nakajima, N. G. Ramesh, H. Tohma and Y. Kita, *Chem. Commun.*, 1999, **5**, 469–471.
8 M. T. Alam, S. Maiti and P. Mal, *Beilstein J. Org. Chem.*, 2018, **14**, 2396–2403.
9 A. Bal, S. Maiti and P. Mal, *Chem. – Asian J.*, 2020, **15**, 624–635.
10 K. Choudhuri, S. Maiti and P. Mal, *Adv. Synth. Catal.*, 2019, **361**, 1092–1101.
11 T. Kumar Achar and P. Mal, *Adv. Synth. Catal.*, 2015, **357**, 3977–3985.
12 S. Maiti and P. Mal, *Adv. Synth. Catal.*, 2015, **357**, 1416–1424.
13 R. D. Richardson and T. Wirth, *Angew. Chem., Int. Ed.*, 2006, **45**, 4402–4404.
14 V. V. Zhdankin, *ARKIVOC*, 2009, **1**, 1–62.
15 T. Wirth, M. Ochiai, V. V. Zhdankin, G. F. Koser, H. Tohma and Y. Kita, *Top. Curr. Chem.*, 2003, **224**, 99–136.
16 Y. Du, R. Liu, G. Linn and K. Zhao, *Org. Lett.*, 2006, **8**, 5919.
17 F. Fleming, L. Funk, R. Altundas and Y. Tu, *J. Org. Chem.*, 2001, **66**, 6502.
18 I. Tellitu, S. Serna, M. T. Herrero, I. Moreno, E. Domínguez and R. SanMartin, *J. Org. Chem.*, 2007, **72**, 1526.
19 R. M. Moriarty, B. A. Berylund and R. Penmasta, *Tetrahedron Lett.*, 1992, **33**, 6065.
20 O. Karam, J. C. Jacquesy and M. P. Jouannetand, *Tetrahedron Lett.*, 1994, **35**, 2541.
21 J. Aubé, C. Fehl, R. Liu, M. C. McLeod and H. F. Motiwala, *Heteroatom Manipulations. Comprehensive Organic Synthesis II*, 1993, vol. 6, pp. 598–635.
22 Y. Kikugawa and M. Kawase, *Chem. Lett.*, 1990, **19**, 581–582.
23 D. J. Wardrop and W. Zhang, *Org. Lett.*, 2001, **3**, 2353.
24 N. Itoh, T. Sakamoto, E. Miyazawa and Y. Kikugawa, *J. Org. Chem.*, 2002, **67**, 7424.
25 T. Dohi, M. Ito, M. Iwata and Y. Kita, *Angew. Chem., Int. Ed.*, 2008, **47**, 1301.
26 A. Kar, N. Mangu, H. M. Kaiser, M. Beller and M. K. Tse, *Chem. Commun.*, 2008, **3**, 386.
27 Y. Kita, T. Tanaka, M. Gyoten, H. Tohma, M. H. Zenk and J. Eichhorn, *J. Org. Chem.*, 1996, **61**, 5857.
28 T. Honda and H. Shigehisa, *Org. Lett.*, 2006, **8**, 657.
29 P. J. Stang and V. V. Zhdankin, *Chem. Rev.*, 1996, **96**, 1123.
30 V. V. Zhdankin and P. J. Stang, *Chem. Rev.*, 2002, **102**, 2523.
31 A. Saito, A. Matsumoto and Y. Hanzawa, *Tetrahedron Lett.*, 2010, **51**, 2247.
32 S. Serna, I. Tellitu, E. Domínguez, I. Moreno and R. SanMartin, *Org. Lett.*, 2005, **7**, 3073.
33 I. Tellitu, S. Serna, M. T. Herrero, I. Moreno, E. Domínguez and R. SanMartin, *J. Org. Chem.*, 2007, **72**, 1526.
34 A. Minatti and K. Muñiz, *Chem. Soc. Rev.*, 2007, **36**, 1142–1152.
35 S. R. Chemler and P. H. Fuller, *Chem. Soc. Rev.*, 2007, **36**, 1153–1160.
36 H. M. Lovick and F. E. Michael, *J. Am. Chem. Soc.*, 2010, **132**, 1249–1251.
37 J. Streuff, C. H. Hövelmann, M. Nieger and K. Muñiz, *J. Am. Chem. Soc.*, 2005, **127**, 14586–14587.
38 I. I. Maletina, V. V. Orda and L. M. Yagupolskii, *J. Org. Chem. USSR*, 1974, **10**, 294.
39 T. M. Kasumov, V. K. Brel, Y. K. Grishin, N. S. Zefirov and P. J. Stang, *Tetrahedron*, 1997, **53**, 1145.
40 P. Kazmierczak and L. Skulski, *Molecules*, 2002, **7**, 810.
41 M. D. Hossain, *et al.*, *Bull. Chem. Soc. Jpn.*, 2006, **79**, 1.
42 V. V. Zhdankin, M. C. Scheuller and P. J. Stang, *Tetrahedron Lett.*, 1993, **34**, 6853.
43 L. M. Yagupolskii, I. I. Maletina, N. V. Kondratenko and V. V. Orda, *Synthesis*, 1977, 574.
44 N. S. Zefirov, S. O. Safronov, A. A. Kaznacheev and V. V. Zhdankin, *J. Org. Chem. USSR*, 1989, **25**, 1807.
45 N. W. Alcock and T. C. Waddington, *J. Chem. Soc.*, 1963, 4103.
46 B. Alcaide, P. Almendros and C. Aragoncillo, *Chem. Rev.*, 2007, **107**, 4437–4492.
47 J. Carey, D. Laffan, C. Thomson and T. Mike, *Org. Biomol. Chem.*, 2006, **4**, 2337.
48 T. Cupido, J. Tulla-Puche, J. Spengler and A. Fernando, *Curr. Opin. Drug Discovery Dev.*, 2007, **10**, 768–783.
49 J. Kothandapani, A. Ganesan and S. S. Ganesan, *Synthesis*, 2017, 685–692.
50 O. S. Kamble, R. Chatterjee and R. Dandela, *ARKIVOC*, 2022, **5**, 270–281.
51 F. Pohlki and S. Doye, *Chem. Soc. Rev.*, 2003, **32**, 104.
52 S. Serna, I. Tellitu, E. Domínguez, I. Moreno and R. SanMartín, *Org. Lett.*, 2005, **7**, 3073–3076.
53 N. Sukekatsu, *Chem. Lett.*, 1997, **26**, 1.

54 K. J. Sonogashira, *Organomet. Chem.*, 2002, **653**, 46.
55 Y. Tamura, T. Yakura, J.-I. Haruta and Y. Kita, *Tetrahedron Lett.*, 1985, **26**, 3837.
56 F. Palluotto, A. Sosic, O. Pinato, *et al.*, *Eur. J. Med. Chem.*, 2016, **123**, 704–717.
57 C. Hu, Z. Zhang, W. Gao, G. Zhang, T. Liu and Q. Liu, *Tetrahedron*, 2018, **74**, 665–671.
58 S. Serna, I. Tellitu, E. Domínguez, I. Moreno and R. SanMartín, *Tetrahedron Lett.*, 2003, **44**, 3483–3486.
59 D. A. Horton, G. T. Bourne and M. L. Smythe, *Chem. Rev.*, 2003, **103**, 893–930.
60 A. Correa, I. Tellitu, E. Domínguez and R. SanMartin, *J. Org. Chem.*, 2006, **71**, 8316–8319.
61 I. Tellitu, S. Serna, M. T. Herrero, I. Moreno, E. Domínguez and R. SanMartin, *J. Org. Chem.*, 2007, **72**, 1526–1529.
62 D.-G. Yu, M. Suri and F. Glorius, *J. Am. Chem. Soc.*, 2013, **135**, 8802.
63 T. Koike and M. Akita, *Org. Chem. Front.*, 2016, **3**, 1345.
64 G. Yin, X. Mu and G. Liu, *Acc. Chem. Res.*, 2016, **49**, 2413.
65 L. Lin, Q. Liang, X. Kong, Q. Chen and B. Xu, *J. Org. Chem.*, 2020, **85**, 15708.
66 S. A. Paveliev, O. O. Segida, U. V. Fedorova, O. M. Mulina and A. O. Terent'ev, *Mendeleev Commun.*, 2022, **32**, 167–169.
67 M. J. Haddadin, W. E. Conrad and M. J. Kurth, *Mini-Rev. Med. Chem.*, 2012, **12**, 1293.
68 N. A. S. Ali, B. A. Dar, V. Pradhan and M. Farooqui, *Mini-Rev. Med. Chem.*, 2013, **13**, 1792.
69 Z. Zhang, Y. Huang, G. Huang, G. Zhang and Q. Liu, *J. Heterocycl. Chem.*, 2017, **54**, 2426–2433.
70 R. G. Bergman, *Nature*, 2007, **446**, 391.
71 S. Cai, M. Lu, T. Zhang, D. Tan, C. Chen, Y. Zhang and M. Huang, *Adv. Synth. Catal.*, 2019, **361**, 4237–4242.
72 S. Tang, Y.-L. Deng, J. Li, W. Wang, Y. Wang, Z.-Z. Li, L. Yuan, S.-L. Chen and R.-L. Sheng, *Chem. Commun.*, 2016, **52**, 4470.
73 I. L. Martins, C. Charneira, V. J. L. Ferreira da Silva, G. C. Justino, J. P. Telo, A. J. S. C. Vieira, C. Marzano and A. M. M. Antunes, *J. Med. Chem.*, 2015, **58**, 4250–4265.
74 F. Frankel, M. Priven, E. Richard, C. Schweinshault, O. Tongo, A. Webster, E. Barth, K. Slejzer and S. Edelstein, *Int. J. Food Prop.*, 2016, **19**, 537–548.
75 P. Ghosh, G. Chhetri, E. Perl and S. Das, *Adv. Synth. Catal.*, 2021, **363**, 2148–2156.
76 Sumit, A. Kumar and A. K. Mishra, *Mini-Rev. Med. Chem.*, 2021, **21**, 314–335.
77 X.-T. Sun, Z.-G. Hu, Z. Huang, L.-L. Zhou and J.-Q. Weng, *Molecules*, 2022, **27**, 726.
78 G. Majji, S. Guin, A. Gogoi, S. K. Rout and B. K. Patel, *Chem. Commun.*, 2013, **49**, 3031.
79 R. Sakamoto, T. Inada, S. Selvakumar, S. A. Moteki and K. Maruoka, *Chem. Commun.*, 2016, **52**, 3758–3761.
80 I. Couto, I. Tellitu and E. Domínguez, *J. Org. Chem.*, 2010, **75**, 7954–7957.
81 C. Mudithanapelli, L. P. Dhorma and M. Kim, *Org. Lett.*, 2019, **21**, 3098–3102.
82 Y. Ding, W.-H. Zhu and Y. Xie, *Chem. Rev.*, 2017, **117**, 2203.
83 Q. Cheng, Y.-H. Qiu, S.-L. Luo, L. Shuai, Y. Yuan, Y.-C. Chen and Q. Ouyang, *Org. Lett.*, 2017, **19**, 3871–3874.
84 S. F. Rach and F. E. Kühn, *Chem. Rev.*, 2009, **109**, 2061.
85 Y. Yan, Z. Zhang, Y. Wan, G. Zhang, N. Ma and Q. Liu, *J. Org. Chem.*, 2017, **82**, 7957–7963.
86 Q. Feng, D. Chen, M. Hong, F. Wang and S. Huang, *J. Org. Chem.*, 2018, **83**, 7553–7558.
87 A. Loudet and K. Burgess, *Chem. Rev.*, 2007, **31**, 496.
88 S. Rihn, M. Erdem, A. De Nicola, P. Retailleau and R. Ziessel, *Org. Lett.*, 2011, **13**, 1916–1919.
89 P. F. H. Schwab, M. D. Levin and J. Michl, *Chem. Rev.*, 1999, **99**, 1863.
90 Q. Ouyang, K.-Q. Yan, Y.-Z. Zhu, C.-H. Zhang, J.-Z. Liu, C. Chen and J.-Y. Zheng, *Org. Lett.*, 2012, **14**, 2746–2749.
91 C. V. Galliford and K. A. Scheidt, *Angew. Chem., Int. Ed.*, 2007, **46**, 8748.
92 W. Yu, Z. Yu, X. Ju and J. Wang, *Synthesis*, 2011, 860–866.
93 Q. Yang, X. Han, J. Zhao, H. Y. Zhang and Y. Zhang, *J. Org. Chem.*, 2019, **84**, 11417–11424.
94 A. Chebieb, Y. G. Kim and J. K. Cha, *J. Org. Chem.*, 2023, **88**, 10164–10170.
95 E. Faggi, R. M. Sebastián, R. Pleixats, A. Vallribera, A. Shafir, A. Rodríguez-Gimeno and C. Ramirez de Arellano, *J. Am. Chem. Soc.*, 2010, **132**, 17980–17982.
96 R. A. Jones and G. P. Bean, *The Chemistry of Pyrroles*, Academic, London, 1977, vol. 9, pp. 525.
97 P. F. Zhang and Z. C. Chen, *J. Chem. Res.*, 2001, **2001**, 150–152.
98 P.-F. Zhang and Z.-C. Chen, *Synth. Commun.*, 2001, **31**, 1619–1624.
99 D. Papadopoulou, I. Papoutsis, S. Spyroudis and A. Varvoglis, *Tetrahedron Lett.*, 1998, **39**, 2865–2866.
100 M. A. Sucari and J. M. Vernon, *Tetrahedron*, 1983, **39**, 793.
101 K. Zhou, F. Zhao, Z. Liu, Y. Zhuang, L. Chen and F. Qiu, *J. Nat. Prod.*, 2009, **72**, 1563.
102 C. W. Nogueira, G. Zeni and J. B. T. Rocha, *Chem. Rev.*, 2004, **104**, 6255.
103 Z. Ai, J. Xiao, Y. Li, B. Guo, Y. Du and K. Zhao, *Org. Chem. Front.*, 2020, **7**, 3935–3940.
104 B. Stanovnik and J. Svete, *Chem. Rev.*, 2004, **104**, 2433–2480.
105 M. N. S. Saudi, M. M. A. El Semary and G. El Sawaf, *Pharmazie*, 2002, **57**, 519–522.
106 J. Huang, Y. Liang, W. Pan, Yang and D. Dong, *Org. Lett.*, 2007, **9**, 5345–5348.
107 W.-T. Wu, L. Zhang and S.-L. You, *Chem. Soc. Rev.*, 2016, **45**, 1570.
108 J. Bariwal, L. G. Voskressensky and E. V. Van der Eycken, *Chem. Soc. Rev.*, 2018, **47**, 3831.
109 B. Banerjee and M. Koketsu, *Coord. Chem. Rev.*, 2017, **339**, 104.

110 S. Wu, J. Shi and C.-P. Zhang, *Org. Biomol. Chem.*, 2019, **17**, 7468.

111 Z. Chen, J. Li, W. Weng, X. Xie and J. Lei, *RSC Adv.*, 2022, **12**, 28800–28803.

112 K. Uneyama, H. Amii, T. Katagirl, T. Kobayashi and T. Hosokawa, *J. Fluorine Chem.*, 2005, **126**, 165.

113 K. C. Joshi, R. Jain, A. Dandia and K. Sharma, *J. Fluorine Chem.*, 1992, **56**, 1.

114 Y. Wu, J. Zhu, H. Xie, Z. Chen and S. Li, *Synlett*, 2009, **2009**, 3299–3302.

115 M. Wu and R. Yan, *Synlett*, 2017, **28**, 729–733.

116 Y. Du, R. Liu, G. Linn and K. Zhao, *Org. Lett.*, 2006, **8**, 5919–5922.

117 B. P. Smart, R. C. Oslund, L. A. Walsh and M. H. Gelb, *J. Med. Chem.*, 2006, **49**, 2858–2860.

118 A. A. Jensen, N. Plath, M. H. F. Pedersen, V. Isberg, J. Krall, P. Wellendorph, T. B. Stensbol, D. E. Gloriam, P. Krogsgaard-Larsen and B. Frolund, *J. Med. Chem.*, 2013, **56**, 1211.

119 L. Cheng, D. Pettersen, B. Ohlsson, P. Schell, M. Karle, E. Evertsson, S. Pahlén, M. Jonforsen, A. T. Plowright, J. Boström, T. Fex, A. Thelin, C. Hilgendorf, Y. Xue, G. Wahlund, W. Lindberg, L.-O. Larsson and D. Gustafsson, *ACS Med. Chem. Lett.*, 2014, **5**, 538.

120 M. D. Cullen, T. Sarkar, E. Hamel, T. L. Hartman, K. M. Watson, R. W. Buckheit Jr., C. Pannecouque, E. De Clercqd and M. Cushman, *Bioorg. Med. Chem. Lett.*, 2008, **18**, 469.

121 R. Zhang, D. Dong, J. Yuan, C. Rao, Q. Zhang, Y. Liang and N. Zhang, *Synthesis*, 2018, 1875–1882.

122 A. Saito, T. Anzai, A. Matsumoto and Y. Hanzawa, *Tetrahedron Lett.*, 2011, **52**, 4658–4661.

123 O. O. Grygorenko, D. M. Volochnyuk, S. V. Ryabukhin and D. B. Judd, *Chem. – Eur. J.*, 2020, **26**, 1196–1237.

124 A. I. Vaskevych, N. O. Savinchuk, R. I. Vaskevych, E. B. Rusanov and O. O. Grygorenko, *Beilstein J. Org. Chem.*, 2021, **17**, 2787–2794.

125 *Classics in Total Synthesis*, ed. K. C. Nicolaou and E. J. Sorensen, VCH Publishers, New York, 1995.

126 A. Correa, I. Tellitu, E. Domínguez and R. SanMartin, *J. Org. Chem.*, 2006, **71**, 3501–3505.

127 Y. Liu, X. Du, H. Chen, Y. Chen and J. Chen, *Synlett*, 2011, 1010–1101.

128 M. T. Khan, M. I. Choudhary, K. M. Khan, M. Rani and A. U. Rahman, *Bioorg. Med. Chem.*, 2005, **13**, 3385.

129 A. S. Aboraia, H. M. Abdel-Rahman, N. M. Mahfouz and M. A. Gendy, *Bioorg. Med. Chem. Lett.*, 2006, **14**, 1236.

130 R. N. Warrener, *Eur. J. Org. Chem.*, 2000, 3363.

131 D. Kumar, S. Sundaree, E. O. Johnson and K. Shah, *Bioorg. Med. Chem. Lett.*, 2009, **19**, 4492–4494.

132 A. Mariappan, K. Rajaguru, N. Merukan Chola, S. Muthusubramanian and N. Bhuvanesh, *J. Org. Chem.*, 2016, **81**, 6573–6579.

133 L. Liu, H. Lu, H. Wang, C. Yang, X. Zhang, D. Zhang-Negrerie, Y. Du and K. Zhao, *Org. Lett.*, 2013, **15**, 2906–2909.

134 T. Deng, W. Mazumdar, R. L. Ford, N. Jana, R. Izar, D. J. Wink and T. G. Driver, *J. Am. Chem. Soc.*, 2020, **142**, 4456–4463.

135 Z. Zheng, S. Ma, L. Tang, D. Zhang-Negrerie, Y. Du and K. Zhao, *J. Org. Chem.*, 2014, **79**, 4687–4693.

136 D. Sun, X. Zhao, B. Zhang, Y. Cong, X. Wan, M. Bao, X. Zhao, B. Li, D. Zhang-Negrerie and Y. Du, *Adv. Synth. Catal.*, 2018, **360**, 1634–1638.

137 J. Yuan, B. Deng, Y. Liang, C. B. Rao, R. Zhang, Y. Zhao and D. Dong, *Adv. Synth. Catal.*, 2019, **361**, 4324–4333.

138 Q. Jiang, A. Zhao, B. Xu, J. Jia, X. Liu and C. Guo, *J. Org. Chem.*, 2014, **79**, 2709–2715.

139 A. P. Sakla, P. Kansal and N. Shankaraiah, *Eur. J. Org. Chem.*, 2021, 757–772.

140 P. Liang, H. Zhao, T. Zhou, K. Zeng, W. Jiao, Y. Pan and H. Shao, *Adv. Synth. Catal.*, 2021, **363**, 3532–3538.

141 K. S. Ju and R. E. Parales, *Microbiol. Mol. Biol. Rev.*, 2010, **74**, 250–272.

142 N. Chatterjee, D. Bhatt and A. Goswami, *Org. Biomol. Chem.*, 2015, **13**, 4828–4832.

143 M. Kinugawa, Y. Masuda, H. Arai, H. Nishikawa, T. Ogasa, S. Tomioka and M. Kasai, *Synthesis*, 1996, 633–636.

144 E. A. Oostveen and W. N. Speckamp, *Tetrahedron*, 1987, **43**, 255.

145 J.-H. Chou, M. E. Kosal, H. S. Nalwa, N. A. Rakow and K. S. Suslick, in *The Porphyrin Handbook*, ed. K. M. Kadish, K. M. Smith and R. Guilard, Academic Press, San Diego, CA, 2000, vol. 6, pp. 43–131.

146 Q. Ouyang, Y.-Z. Zhu, C.-H. Zhang, K.-Q. Yan, Y.-C. Li and J.-Y. Zheng, *Org. Lett.*, 2009, **11**, 5266–5269.

147 M. A. Miller, R. K. Lammi, S. Prathapan, D. Holten and J. S. Lindsey, *J. Org. Chem.*, 2000, **65**, 6634.

148 N. Aratani and A. Osuka, *Org. Lett.*, 2001, **3**, 4213.

149 S. Spyroudis and A. Varvoglis, *J. Chem. Soc., Chem. Commun.*, 1979, **14**, 615–616.

150 Y. Liu, Z. Zhang, Y. Wan, G. Zhang, Z. Li, J. Bi, N. Ma, T. Liu and Q. Liu, *J. Org. Chem.*, 2017, **82**, 3901–3907.

151 C. J. R. Bataille and T. J. Donohoe, *Chem. Soc. Rev.*, 2011, **40**, 114–128.

152 L. Pan, Z. Ke and Y. Y. Yeung, *Org. Lett.*, 2021, **23**, 8174–8178.

153 S. Hamada, K. Sugimoto, E. E. Elboray, T. Kawabata and T. Furuta, *Org. Lett.*, 2020, **22**, 5486–5490.

154 Y. Zhang, H. Liu, H. He, B. Zou, Z. Zhai, T. Yu, A. Osuka and H. W. Jiang, *Eur. J. Org. Chem.*, 2023, e202300666.

155 H. Furuta, T. Asano and T. Ogawa, *J. Am. Chem. Soc.*, 1994, **116**, 767–768.

156 P. J. Chmielewski, L. Latos-Grażyński, K. Rachlewicz and T. Glowiak, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 779–781.

157 X. Lang, X. Chen and J. Zhao, *Chem. Soc. Rev.*, 2014, **43**, 473.

158 W. Gao, Y. Wan, Z. Zhang, H. Wu, T. Liu and G. Zhang, *Green Chem.*, 2020, **22**, 7955–7961.

159 G. M. Loudon, A. S. Radhakrishna, M. R. Almond, J. K. Blodgett and R. H. Boutin, *J. Org. Chem.*, 1984, **49**, 4272–4276.

160 A. Varki, *Glycobiology*, 2017, **27**, 3.

161 C. R. Bertozzi and L. L. Kiessling, *Science*, 2001, **291**, 2357.

162 S. Meng, W. Zhong, W. Yao and Z. Li, *Org. Lett.*, 2020, **22**, 2981–2986.

163 T. Kajimoto and M. Node, *Curr. Top. Med. Chem.*, 2009, **9**, 13–33.

164 T. Kajimoto, K. Morimoto, R. Ogawa, T. Dohi and Y. Kita, *Eur. J. Org. Chem.*, 2015, 2138–2142.

165 J. Roh, K. Vavrova and A. Hrabalek, *Eur. J. Org. Chem.*, 2012, 6101.

166 T. Imai, R. Harigae, K. Moriyama and H. Togo, *J. Org. Chem.*, 2016, **81**, 3975–3980.

167 D. W. Chen and Z. C. Chen, *Tetrahedron Lett.*, 1994, **35**, 7637–7638.

168 D. Bhattacherjee, S. Kang, A. Kumar, A. Sharma, R. Purohit and P. Das, *Org. Biomol. Chem.*, 2020, **18**, 745.

169 N. D. Yudina, V. S. Raida, O. L. Vasil'eva, V. V. Deniskin, M. P. Stepanets and A. S. Sitnikov, *Polym. Sci. USSR*, 1989, **31**, 1318–1323.

170 M. E. Smith, B. H. Chen, E. G. Hibbert, U. Kaulmann, K. Smithies, J. L. Galman, F. Baganz, P. A. Dalby, H. C. Hailes, G. J. Lye, J. M. Ward, J. M. Woodley and M. Micheletti, *Org. Process Res. Dev.*, 2010, **14**, 99.

171 C. Chen, M. You and H. Chen, *Synth. Commun.*, 2015, **46**, 73–78.

172 V. N. Telvekar, R. A. Rane and T. V. Namjoshi, *Synth. Commun.*, 2010, **40**, 494–497.

173 V. N. Telvekar, B. S. Takale and H. M. Bachhav, *Tetrahedron Lett.*, 2009, **50**, 5056–5058.

174 Y. Wang, Y. Yang and C. Wang, *Chin. J. Chem.*, 2019, **37**, 1229–1233.

175 M. Tingoli, M. Mazzella, B. Panunzi and A. Tuzi, *Eur. J. Org. Chem.*, 2011, 399–404.

176 M. Catir, H. Kilic, V. Nardello-Rataj, J.-M. Aubry and C. Kazaz, *J. Org. Chem.*, 2009, **74**, 4560–4564.

177 M. Catir and H. Kilic, *Synlett*, 2004, **12**, 2151–2154.

178 Y. Kita, T. Takada, S. Mihara, B. A. Whelan and H. Tohma, *J. Org. Chem.*, 1995, **60**, 7144–7148.

179 S. W. Wu, J. L. Liu and F. Liu, *Org. Lett.*, 2016, **18**, 1–3.

180 T. Kitamura, K. Muta and J. Oyamada, *J. Org. Chem.*, 2015, **80**, 10431–10436.

181 N. Chatterjee, M. Arfeen, P. V. Bharatam and A. Goswami, *J. Org. Chem.*, 2016, **81**, 5120–5127.

182 K. Gondo, J. Oyamada and T. Kitamura, *Org. Lett.*, 2015, **17**, 4778–4781.

183 L. Pan, L. Zheng, Y. Chen, Z. Ke and Y. Y. Yeung, *Angew. Chem., Int. Ed.*, 2022, **61**, e202207926.

184 A. D. Rodríguez, O. M. Cóbar and O. L. Padilla, *J. Nat. Prod.*, 1997, **60**, 915–919.

185 A. M. Bernard, A. Frongia, P. P. Piras, F. Secci and M. Spiga, *Org. Lett.*, 2005, **7**, 4565–4568.

186 S. J. Gharpure, D. S. Vishwakarma and S. K. Nanda, *Org. Lett.*, 2017, **19**, 6534–6653.

187 M. Berthelot, F. Akhssas, A. K. Dimé, A. Bousfiha, J. Echaubard, G. Souissi, H. Cattey, D. Lucas, P. Fleurat-Lessard and C. H. Devillers, *Inorg. Chem.*, 2022, **61**, 7387–7405.