Cluster Preface: Organic Chemistry in Thailand

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Abstract This SYNLETT cluster highlights research work conducted in universities across Thailand. As a country rich in biodiversity, chemical research in Thailand was originally founded on the study of natural products. The discovery and development of novel, biologically active agents has contributed to drug discovery and advanced the development of novel compounds. Since the 1990s, the growth of petrochemical industries in Southeast Asia has spurred chemical research on synthetic methodologies, the creation of high-value compounds from petroleum-based starting materials and polymer sciences. The results have led to significant economic and strategic advantages that have enabled the competitiveness of local petrochemical industries. Moving into the new era, Thailand and the region faces global sustainability challenges. Green chemistry has also become a key theme for driving chemical research, which is expected to help in generating new ideas and innovations to deliver a more sustainable society. This cluster contains 27 articles that have been submitted from 12 different Thai universities. The articles are organized into 3 main themes, as outlined below.

(1) Synthetic Methodology

Several research groups have reported new synthetic methods to access various aromatic heterocyclic compounds via metal-free approaches. Kuhakarn and Ngernmeesri developed straightforward methods to prepare quinoline and 2-arylindole derivatives via cyclization between o-alkynylsilycyanobenzenes/N-acetyl-2-methyl-3-nitroaniline and active methylene compounds/2-fluorobenzaldehydes, respectively, under basic conditions using Cs₂CO₃. Meanwhile, Meesin demonstrated the dimerization of 3-chlorooxindoles to prepare a series of isoindigos using potassium ethylxanthate, whilst Phakhodee has described the use of Ph₃P/I₂ as a dehydrating agent to prepare benzimidazol-2-ones from hydroxamic acids. In addition, Luanphaisarnmont demonstrated an efficient method to prepare coumarin derivatives via the cyclization between salicylaldehydes and alkynoates using p-toluenesulfonic acid monohydrate and piperidine as a dual organocatalyst. Besides heterocyclic compounds, several groups have reported the synthesis of other important organic precursors via metal-free processes. For example, Thongsornkleeb reported two different methods to functionalize alkenes leading to the preparation of 1,4-enedione derivatives, dihaloketones and dihaloolactols. These authors performed (i) an oxidative coupling of 1,3-keto esters with terminal alkenes leading to the preparation of 1,4-enediones using ceric ammonium nitrate (CAN), and (ii) halogenation of internal alkenes and alkynols by using the in situ generation of Cl₂ or ClBr from aqueous HCl and NCS or NBS to provide 2,2-dihaloketone and gem-dihalolactol analogues, respectively. Moreover, Padungros has described the use of bromodihethyl sulfonium bromopentachloroantimonate (BDSB) as a mild oxidizing agent to perform a one-pot synthesis of glycosyl chlorides from the corresponding thioglycosides.

In contrast to these metal-free approaches, Kaeobamrung and Thasana utilized copper as a catalyst to prepare quinazolinones and coumarins/indoles, respectively.
The straightforward synthesis of quinazolinones containing an N-fused medium-sized cyclic urea was successfully developed by employing copper to catalyze a domino reaction of a cyclic enammine to generate the core quinazolinone followed by urea ring formation. Meanwhile, three different derivatives, including 3-amidocoumarin, 3-amidoazacoumarin and N-benzoylindol-2-carboxamide, were successfully prepared via selective C–O bond formation (in a six-membered ring) and C–N bond formation (in a five-membered ring), respectively, from azlactones using a Cu(II) catalyst. In addition to aromatic heterocycles, many synthetic methods have utilized either metal or organometallic reagents to prepare other valuable organic building blocks. For instance, Ajavakom demonstrated an unprecedented ring-closing metathesis of vinyl bromides to prepare several carbocyclic and heterocyclic seven-membered bromo-olefins without the need of a protecting group on the olefin by using Grubbs II catalyst. Moreover, an efficient and selective approach to access tetrahydroindenol[1,2-a]quinolines was reported by Ploypradith via a key acid-mediated transannular cyclization step between 1,3,5-trimethoxybenzene and benzannulated cyclooctenes containing tertiary alcohols. Akkarasamiyo utilized nickel triflate in combination with triphenylphosphine to perform the stereoinvertive deoxygenation of trans-3-arylglycldates to prepare a panel of (Z)-cinnaminate esters. The reaction showed broad functional group tolerance with high stereoselectivity. Interestingly, Soorukram demonstrated the use of an AgNO₃/K₂S₂O₈ combination to perform the decarboxylation of paraconic acids leading to the preparation of β-nitro- and β-hydroxyγ-butyrolactones in good combined yields and moderate selectivities. Meanwhile, Somsook has prepared ferrocenium-doped manganese(IV) oxide and used it as a catalyst for the selective aerobic oxidation of alcohols to the corresponding aldehydes.

On the other hand, several research groups have focused on asymmetric synthesis and its applications. Vilaivan discovered a highly selective asymmetric acylation of dl-hydrobenzoins using copper(II) with a chiral thiophene-derived amino alcohol ligand. Meanwhile, Thongpanchang developed a very reliable method to determine the absolute configuration of chiral diols by using a chiral derivatizing agent namely, THENA (tetrahydro-1,4-epoxynaphthalene-1-carboxylic acid).

In addition, bearing in mind the concept of green chemistry, several synthetic methods aimed at replacing the use of conventional organic solvents are reported in this cluster. By employing solvent-free conditions, Sirion reported a multicomponent coupling reaction between various aldehydes, N,N-dialkylanilines and indoles to prepare a panel of unsymmetrical triarylmethanes by using a Brønsted acidic ionic liquid as the catalyst. Interestingly, under mechanochemical conditions, Pattarawarapan has demonstrated an efficient method to prepare oxadiazoles via condensation between N-acylbenzotriazoles and acylhydrazides mediated by PPh₃ and TCCA as a dehydrating agent. Moreover, Acharasatian has performed the amination of squaric acid to provide squaramides by utilizing recyclable [bmim]Cl as the solvent. Remarkably, a reusable solid acid catalyst, silico-supported H₂SO₄, was utilized by Jaratjaroonphong to perform a transindolylation between symmetrical bis(indolyl)methanes (BIMs) and indoles in order to access unsymmetrical BIMs.

(2) Total Synthesis of Natural Products

Two research groups have utilized natural chiral building blocks to prepare natural products. Chuannopparat successfully performed asymmetric formal syntheses of (−)-swainsosine from two different starting materials, D-mannose or D-arabinose, in 19 steps (3.8% yield) and 17 steps (3.2% yield), respectively, while Kuntyong used L-asparagin to prepare a chiral dibenzylaminosuccinimide key intermediate, which was then successfully converted into a range of 8-aminoindolizidine analogues. On the other hand, starting from commercially available (S)-propylene oxide, Tadpatch successfully performed the convergent synthesis of 7-O-methylingiroporoside and pestaliotiporoside D. These natural products were obtained via 17 and 22 steps, with 1.7% and 2.6% overall yields, respectively, and exhibited cytotoxicity against six human cancer cell lines.

(3) Organic Material Chemistry

The synthesis and application of chromic and emissive organic compounds has been demonstrated by the groups of Rashatasakhon and Promarak, respectively. Colorimetric sensors based on tetracyanobutadienes were used to detect hydrogen sulfide, while fluorescent dendrimers based on chrysenes were utilized as highly deep-blue emitters for OLED applications. Moreover, Bunchua prepared a new class of pillararene supramolecules by incorporating sulfur atoms via thionation using Lawesson’s reagent. These compounds also showed interesting host–guest binding properties with electron-deficient molecules such as 1,4-dicyanobutane and 1,4-dibromobutane.

In summary, chemical research in Thailand is diverse in terms of research areas, themes, and applications. Scientific research is well supported by the Government of Thailand and international collaboration is highly promoted. The local organic chemistry research groups hope to make a significant contribution to the international community, especially in solving global sustainability challenges.

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Conflict of Interest

The authors declare no conflict of interest.

References


