

Cluster Preface: Organic Chemistry in Thailand

Sumrit Wacharasindhu*

Department of Chemistry, Faculty of Science, Chulalongkorn University, Bangkok 10330, Thailand
sumrit.w@chula.ac.th

Published as part of the Cluster *Organic Chemistry in Thailand*



Received: 03.08.2022
Accepted after revision: 03.08.2022
Published online: 18.08.2022
DOI: 10.1055/s-0041-1738688; Art ID: st-2022-u8888-c

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.¹ 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. Kuhakarn² and Ngernmeesri³ developed straightforward methods to prepare quinoline and 2-arylindole derivatives via cyclization between *o*-alkynylisocyanobenzenes/*N*-acetyl-2-methyl-3-nitroaniline and active methylene compounds/2-fluorobenzaldehydes, respectively, under basic conditions using Cs₂CO₃. Meanwhile, Meesin⁴ demonstrated the dimerization of 3-chlorooxindoles to prepare a series of isoindigos using potassium ethylxanthate, whilst Phakhodee⁵ has described the use of Ph₃P/I₂ as a dehydrating agent to prepare benzimidazol-2-ones from hydroxamic acids. In addition,

Sumrit Wacharasindhu is a professor at Chulalongkorn University, Bangkok, Thailand. He received his Ph.D. in 2005 from the University of Missouri-Columbia under guidance of Prof. Michael Harmata, then undertook an industrial postdoctoral research post with Dr. Tarek Mansour at Wyeth Research (now Pfizer) in New York. In 2010, he started an independent career at Chulalongkorn University. His initial research focus was medicinal chemistry. In 2013, he began to explore chemical synthesis under the guidance of green chemistry principles, initially focusing on the use of carbide as a sustainable starting material for acetylenic compound synthesis. Subsequently, he expanded his research program to include the development of sustainable chemical processes such as flow chemistry, on and in water reaction, visible light mediated reaction and electro-oxidation processes.

Luanphaisarnnont⁶ demonstrated an efficient method to prepare coumarin derivatives via the cyclization between salicylaldehydes and alkynolic esters 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 et al.^{7,8} reported two different methods to functionalize alkynes leading to the preparation of 1,4-enedione derivatives, dihaloketones and dihalolactols. These authors performed (i) an oxidative coupling of 1,3-keto esters with terminal alkynes leading to the preparation of 1,4-enediones using ceric ammonium nitrate (CAN), and (ii) halogenation of internal alkynes and alkynols by using the in situ generation of Cl₂ or CIBr from aqueous HCl and NCS or NBS to provide 2,2-dihaloketone and *gem*-dihalolactol analogues, respectively. Moreover, Padungros⁹ has described the use of bromodiethyl 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, Kaeobamrungs¹⁰ and Thasana¹¹ 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 enaminone 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(I) 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, Ajavakom¹² 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 tetrahydroindeno[1,2-*a*]indenes was reported by Ploypradith¹³ via a key acid-mediated transannular cyclization step between 1,3,5-trimethoxybenzene and benzannulated cyclooctenes containing tertiary alcohols. Akkarasamiyo¹⁴ utilized nickel triflate in combination with triphenylphosphine to perform the stereoinvertive deoxygenation of *trans*-3-aryl glycidates to prepare a panel of (*Z*)-cinnamate esters. The reaction showed broad functional group tolerance with high stereoselectivity. Interestingly, Soorukram¹⁵ demonstrated the use of an AgNO₃/K₂S₂O₈ combination to perform the decarboxylation of paraconic acids leading to the preparation of β-nitro- and β-hydroxy-γ-butyrolactones in good combined yields and moderate selectivities. Meanwhile, Somsook¹⁶ 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. Vilaivan¹⁷ discovered a highly selective asymmetric acylation of *dl*-hydrobenzoin using copper(II) with a chiral thiophene-derived amino alcohol ligand. Meanwhile, Thongpanchang¹⁸ 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, Sirion¹⁹ 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, Pattarawarapan²⁰ has demonstrated an efficient method to prepare oxadiazoles via condensation between *N*-acylbenzotriazoles and acylhydrazides me-

diated by PPh₃ and TCCA as a dehydrating agent. Moreover, Acharasatian²¹ has performed the amination of squaric acid to provide squaramides by utilizing recyclable [bmim]Cl as the solvent. Remarkably, a reusable solid acid catalyst, silica-supported H₂SO₄, was utilized by Jaratjaroonphong²² to perform a transindolylolation 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. Chuanopparat²³ successfully performed asymmetric formal syntheses of (–)-swainsonine from two different starting materials, D-mannose or D-arabinose, in 19 steps (3.8% yield) and 17 steps (3.2% yield), respectively, while Kuntiyong²⁴ used L-asparagine 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, Tadpetch²⁵ successfully performed the convergent synthesis of 7-*O*-methylnigrosporolide and pestalotioprolide 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 Rashatasakhon²⁶ and Promarak²⁷ respectively. Colorimetric sensors based on tetracyanobutadienes were used to detect hydrogen sulfide,²⁶ while fluorescent dendrimers based on chrysenes were utilized as highly deep-blue emitters for OLED applications.²⁷ Moreover, Bunchuay²⁸ 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.

Sumrit Wacharasindhu
July 2022

Conflict of Interest

The authors declare no conflict of interest.

References

- (1) For examples of natural product research, see: (a) Shienghong, D.; Verasarn, A.; NaNonggai-Suwanrath, P.; Warnhoff, F. W. *Tetrahedron* **1965**, *21*, 917. (b) Shienghong, D.; Kokpol, U.; Karntiang, P.; Massy-Westropp, R. A. *Tetrahedron* **1974**, *30*, 2211. (c) Mongkolsuk, S.; Dean, F. M. *J. Chem. Soc.* **1964**, 4654. (d) Ollis, W. D.; Ramsay, M. V. J.; Sutherland, I. O.; Mongkolsuk, S. *Tetrahedron* **1965**, *21*, 1453.
- (2) La-ongthong, K.; Sawekteeratana, N.; Klaysuk, J.; Soorukram, D.; Leowanawat, P.; Reutrakul, V.; Krobthong, S.; Wongtrakoongate, P.; Kuhakarn, C. *Synlett* **2022**, *33*, DOI: 10.1055/a-1784-2513.
- (3) Kraikruan, P.; Rakchaya, I.; Sang-aroon, P.; Chuanopparat, N.; Ngermmeesri, P. *Synlett* **2022**, *33*, DOI: 10.1055/a-1796-9647.
- (4) Meesin, J.; Chotsaeng, N.; Kuhakarn, C. *Synlett* **2022**, *33*, DOI: 10.1055/a-1784-2304.
- (5) Wiriya, N.; Yamano, D.; Hongsibsong, S.; Pattarawarapan, M.; Phakhodee, W. *Synlett* **2022**, *33*, DOI: 10.1055/s-0040-1719897.
- (6) Saejong, P.; Somprasong, S.; Rujirasereesakul, C.; Luanphaisarnnont, T. *Synlett* **2022**, *33*, DOI: 10.1055/a-1797-0386.
- (7) Ruengsangtongkul, S.; Kuribara, T.; Chaisan, N.; Tummatorn, J.; Thongsornkleeb, C.; Ruchirawat, S. *Synlett* **2022**, *33*, DOI: 10.1055/a-1774-6966.
- (8) Chaisan, N.; Ruengsangtongkul, S.; Thongsornkleeb, C.; Tummatorn, J.; Ruchirawat, S. *Synlett* **2022**, *33*, DOI: 10.1055/a-1774-7077.
- (9) Chooppawa, T.; Janprasert, P.; Padungros, P. *Synlett* **2022**, *33*, DOI: 10.1055/a-1852-6889.
- (10) Saebang, Y.; Kaebamrung, J.; Rukachaisirikul, V. *Synlett* **2022**, *33*, DOI: 10.1055/a-1793-1321.
- (11) Worayuthakarn, R.; Suddee, N.; Nealmongkol, P.; Ruchirawat, S.; Thasana, N. *Synlett* **2022**, *33*, DOI: 10.1055/a-1784-1973.
- (12) Ajavakom, V.; Pandokrak, P.; Salim, S. S.; Moustafa, G. A. I.; Bellingham, R. K.; Hill-Cousins, J. T.; Ajavakom, A.; Brown, R. C. *Synlett* **2022**, *33*, DOI: 10.1055/a-1845-4195.
- (13) Songthammawat, P.; Phumjan, T.; Ruchirawat, S.; Ploypradith, P. *Synlett* **2022**, *33*, DOI: 10.1055/a-1778-8143.
- (14) Akkarasamiyo, S.; Chitsomkhuan, S.; Buakaew, S.; Samec, J. S. M.; Chuawong, P.; Kuntiyong, P. *Synlett* **2022**, *33*, DOI: 10.1055/s-0040-1719911.
- (15) Phae-nok, S.; Kuhakarn, C.; Leowanawat, P.; Reutrakul, V.; Soorukram, D. *Synlett* **2022**, *33*, DOI: 10.1055/a-1792-7169.
- (16) Chumkao, P.; Poonsawat, T.; Yunita, I.; Temnuch, N.; Meechai, T.; Kumpan, N.; Khamthip, A.; Chuaitammakit, L. C.; Chairam, S.; Somsook, E. *Synlett* **2022**, *33*, DOI: 10.1055/a-1817-1038.
- (17) Mansawat, W.; Yukhet, P.; Bhanthumnavin, W.; Reiser, O.; Vilaivan, T. *Synlett* **2022**, *33*, DOI: 10.1055/a-1815-7091.
- (18) Dolophon, K.; Soponpong, J.; Kornsakulkarn, J.; Thongpanchang, C.; Thongpanchang, T. *Synlett* **2022**, *33*, DOI: 10.1055/s-0041-1737992.
- (19) Rinkam, S.; Senapak, W.; Watchasit, S.; Saeeng, R.; Sirion, U. *Synlett* **2022**, *33*, DOI: 10.1055/a-1809-7768.
- (20) Yamano, D.; Wiriya, N.; Phakhodee, W.; Wet-osot, S.; Pattarawarapan, M. *Synlett* **2022**, *33*, DOI: 10.1055/s-0040-1719867.
- (21) Soonthonhut, S.; Acharasatian, P. *Synlett* **2022**, *33*, DOI: 10.1055/a-1795-8322.
- (22) Yimyaem, J.; Chantana, C.; Boonmee, S.; Jaratjaroonphong, J. *Synlett* **2022**, *33*, DOI: 10.1055/s-0040-1719915.
- (23) Lamor, A.; Uipanit, S.; Yakhampom, S.; Ngermmeesri, P.; Kongkathip, N.; Kongkathip, B.; Chuanopparat, N. *Synlett* **2022**, *33*, DOI: 10.1055/s-0041-1737335.
- (24) Kuntiyong, P.; Inprung, N.; Attanonchai, S.; Kheakwanwong, W.; Bunrod, P.; Akkarasamiyo, S. *Synlett* **2022**, *33*, DOI: 10.1055/a-1806-6089.
- (25) Thiraporn, A.; Iawsipo, P.; Tadpetch, K. *Synlett* **2022**, *33*, DOI: 10.1055/a-1792-8402.
- (26) Pham, Q. N. N.; Silpcharu, K.; Vchirawongkwin, V.; Sukwattanasinitt, M.; Rashatasakhon, P. *Synlett* **2022**, *33*, DOI: 10.1055/a-1806-6258.
- (27) Chatsirisupachai, J.; Sudyoadsuk, T.; Namuangrak, S.; Promarak, V. *Synlett* **2022**, *33*, DOI: 10.1055/a-1771-9389.
- (28) Khanthong, A.; Khamphaijun, K.; Ruengsuk, A.; Docker, A.; Limpanuparb, T.; Tantirungrotechai, J.; Bunchuay, T. *Synlett* **2022**, *33*, DOI: 10.1055/a-1806-5999.