บทความวิชาการ

การประยุกต์ใช้ไฮเปอร์วาเลนซ์ไอโอดีน(III) รีเอเจนต์เพื่อการสังเคราะห์สารประกอบไบเอริล

รัชนก ปิ่นแก้ว*

บทคัดย่อ

ในช่วง 2-3 ทศวรรษที่ผ่านมา ปัญหามลภาวะทางสิ่งแวดล้อมได้รับความสนใจเป็นอย่างมาก ดังนั้นจึงได้มีการพัฒนาสารประกอบไฮเปอร์วาเลนซ์ซึ่งมีคุณสมบัติที่ดี คือ สามารถเกิดปฏิกิริยาได้ในสภาวะที่ไม่รุนแรง มีความเฉพาะเจาะจง อีกทั้งยังเป็นมิตรต่อสิ่งแวดล้อม รีเอเจนต์นี้มีบทบาทสำคัญต่อการนำมาใช้ประโยชน์ในการสังเคราะห์สารได้หลากหลายชนิด ทั้งที่เป็นและไม่เป็นสารผลิตภัณฑ์ธรรมชาติโดยใช้ปฏิกิริยาออกซิเดทีฟคับปลิง ขอบเขตของบทความนี้กล่าวถึงปฏิกิริยาออกซิเดทีฟคับปลิงของสารไบเอริล เอริล-เฮเทอโรเอริล และ บิส-เฮเทอโรเอริล

คำสำคัญ: ไฮเปอร์วาเลนซ์ไอโอดีน ไบเอริล

ภาควิชาเคมี คณะวิทยาศาสตร์ มหาวิทยาลัยศรีนครินทรวิโรฒ

* ผู้นิพนธ์ประสานงาน, e-mail: ratchanok@swu.ac.th

Hypervalent Iodine(III) Reagent: Application for the Synthesis of Biaryl Compounds

Ratchanok Pingaew*

ABSTRACT

In the last few decades, environmental pollution has been concerned and received considerable attentions. Therefore, hypervalent iodine(III) reagent with promising properties; exceptionally mild, selective and environmentally friendly had been developed. Such reagent plays an important role in synthetic utilities for a wide range of natural and unnatural compounds through oxidative coupling. The scopes of this review include biaryl, aryl-heteroaryl and bis-heteroaryl oxidative coupling.

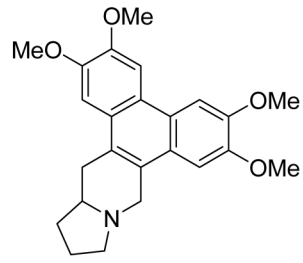
Keywords: hypervalent iodine, biaryl

Department of Chemistry, Faculty of Science, Srinakharinwirot University

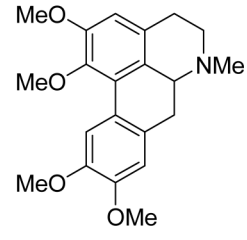
*Corresponding author, e-mail: ratchanok@swu.ac.th

Introduction

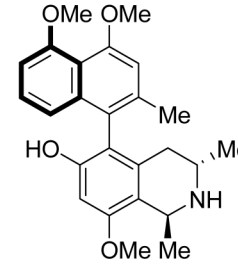
There are a large number of bioactive natural products possessing a biaryl motif, such as tylophorine **1** [1, 2], glaucine **2** [3, 4], (-)-ancistrocladine **3** [5-7], calphostins **4** [8], (-)-gossypol **5** [9, 10], and mastigophorenes **6** [11].



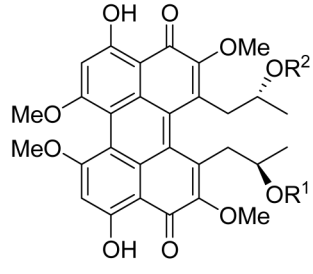
tylophorine 1

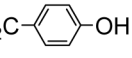


glaucine 2

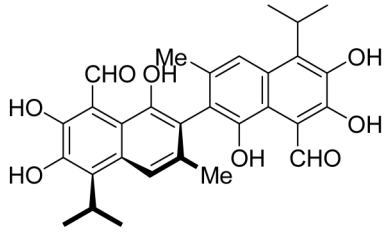


(-)-ancistrocladine 3

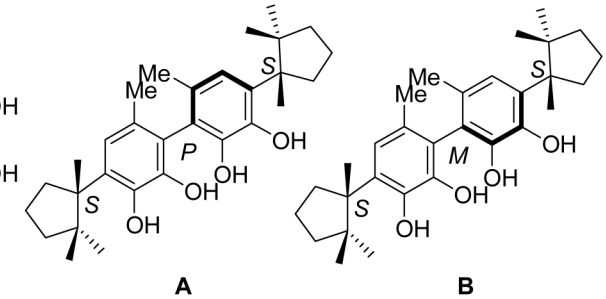


A : R^1 = Bz, R^2 = Bz
B : R^1 = Bz, R^2 = H
C : R^1 = Bz, R^2 = O_2C–  –OH
D : R^1 = H, R^2 =H

calphostins 4



(-)-gossypol 5



A **B**

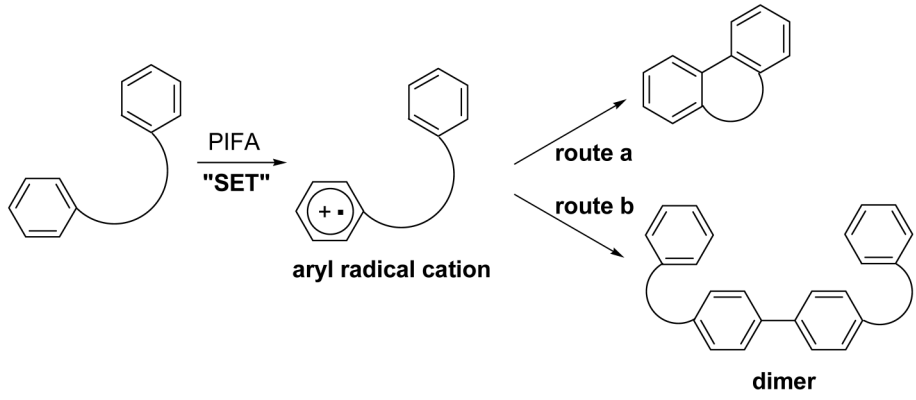
magtigophorenes 6

Owing to their interesting features not only as bioactive targets but also as chiral ligands in asymmetric reactions [12, 13], thus, natural and unnatural biaryls have received considerable attraction. Various methodologies have been developed for the construction of these biaryls [14]. Among existing approaches, the biomimetic oxidative coupling reaction is one of the most commonly used methods, because no additional functionalization on the coupling position is required [15, 16]. In the last two decades, hypervalent iodine reagents

with exceptionally mild, selective and environmentally friendly properties, have been recognized as powerful oxidizing reagents alternative to heavy metal reagents in organic synthesis [17-21]. So there are many synthetic utilities of these reagents have been reported including oxidative biaryl coupling reaction strategy [20, 21].

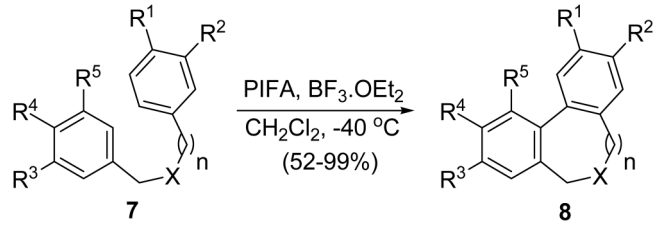
General Aspects for Biaryl Bond Formation

In 1994, Kita *et al.* demonstrated that phenyliodine(III) bis(trifluoroacetate) ($PhI(OCOCF_3)_2$; PIFA) has been used to produce aryl radical cations generated by a single electron transfer (SET) mechanism [22]. By this strategy, the PIFA reagent was successfully utilized to promote inter- and intramolecular oxidative biaryl coupling reactions. The success of the intramolecular cyclization (route a) would probably rely firstly on the ease of formation of the radical cation intermediate located on one of the rings, and secondly on the high nucleophilic character of the other ring to facilitate ring closure. But, when the latter isn't fulfilled, dimerization processes are observed (route b) (Scheme 1) [23, 24]. In this context, some synthetic applications of the PIFA reagent, especially, for oxidative cyclization including biaryl, aryl-heteroaryl and bis-heteroaryl oxidative couplings have been reviewed.



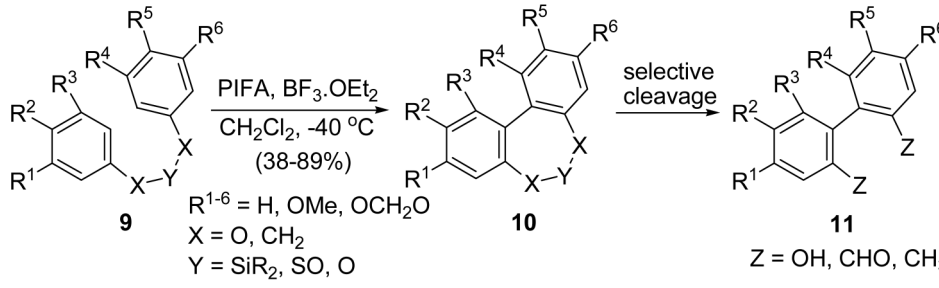
Scheme 1

In 1996, an application of intramolecular biaryl coupling reaction of phenol ether derivatives was investigated to synthesize various dibenzoheterocyclic compounds. These nonphenolic derivatives **7** reacted with PIFA in the presence of $BF_3{\cdot}Et_2O$ in CH_2Cl_2 to give the coupling products **8** in moderate to good yield (Scheme 2) [25]. As illustrated previously, electron donation substrates were required in order to accomplish the expected coupling products. The cyclization regiospecifically occurred at the *para* position with respect to one of the alkoxy substituents (Scheme 2).



Scheme 2

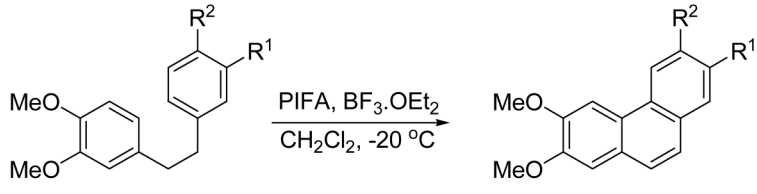
Under the similar strategy, the synthesis of oxygen and sulfur-containing dibenzoheterocyclic compounds **10** had been demonstrated (Scheme 3) [26]. The cleavage of side chain moiety of the coupling products **10** led to both symmetrical and unsymmetrical biphenyl compounds **11** in which the latter couldn't be easily access by intermolecular biaryl coupling process.



Scheme 3

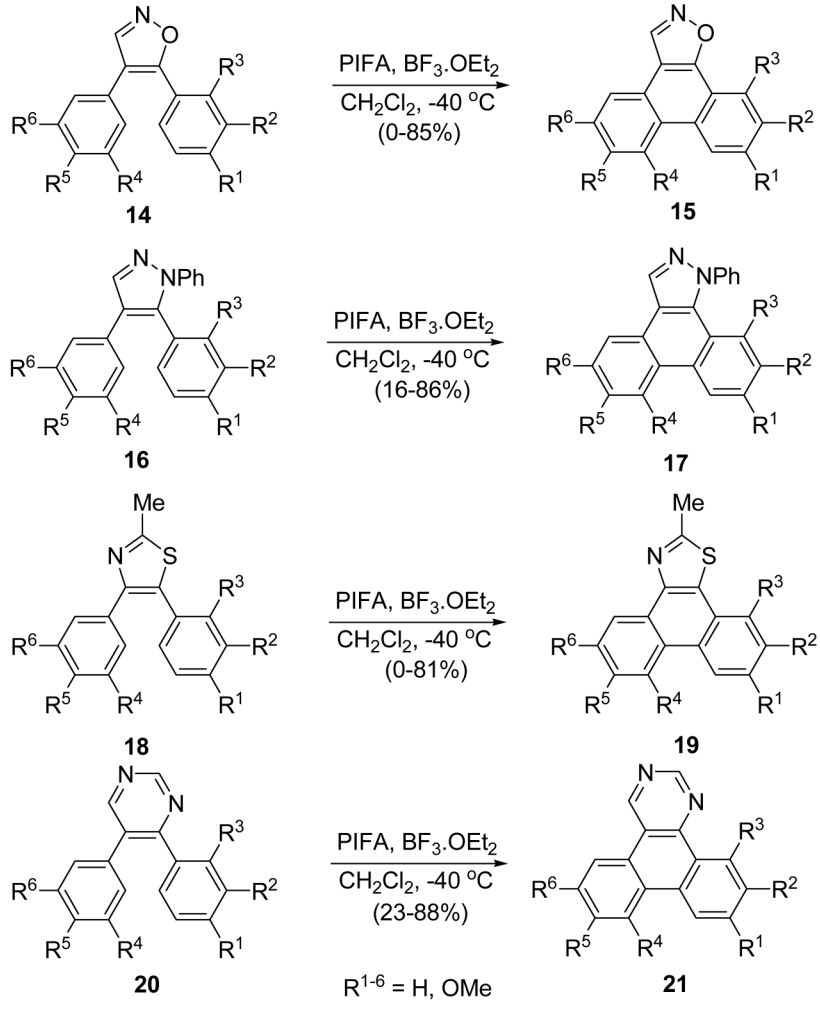
Synthesis of Phenanthrenes and Phenanthridines

Based on the application of the coupling procedure, when 1,2-diarylethane **12a** was subjected to PIFA- $BF_3{\cdot}Et_2O$ combination, the desired phenanthrene **13a** was afforded in 91% yield. However, when the less activated substrate **12b** was exposed to the same reaction conditions, the expected phenanthrene **13b** could not be accomplished [24]. These results supported the electronic requirement of the reaction (Scheme 4).



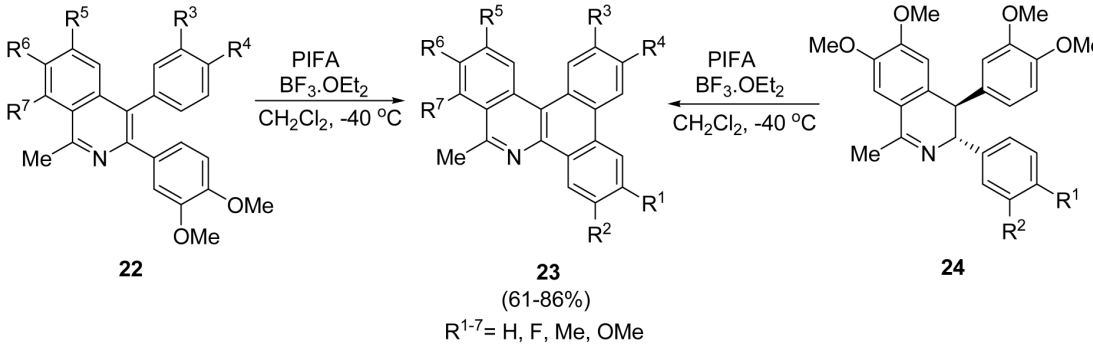
Scheme 4

In an attempt to extend the scope of the PIFA-mediated oxidative coupling approach, the protocol had been utilized for conversions of diaryl azoles **(14, 16, 18)** and pyrimidines **20** to phenanthro-fused isoxazoles **15**, pyrazoles **17**, thiazoles **19** and pyrimidines **21**, respectively [27-29] as shown in scheme 5. For substrate in which the two aryl rings were tethered by a heteroaromatic ring, an activation with electron donating groups in only one of the rings was enough for the reaction to proceed with good yields.



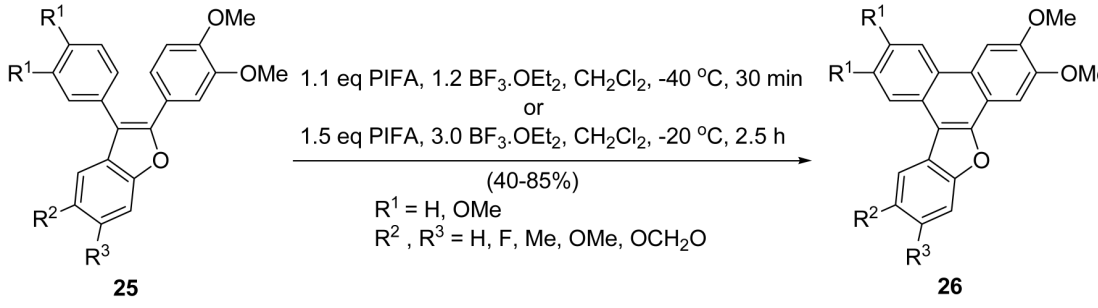
Scheme 5

Utilization of the oxidative coupling reaction, dibenzo[*a,c*]phenanthridines **23** were prepared in moderate to good yield [30]. The failure in the coupling of weakly activated substrates would probably rely on the difficulty of formation of the charge-transfer complex either because of the lack of electron-donating groups or steric reasons (Scheme 6).

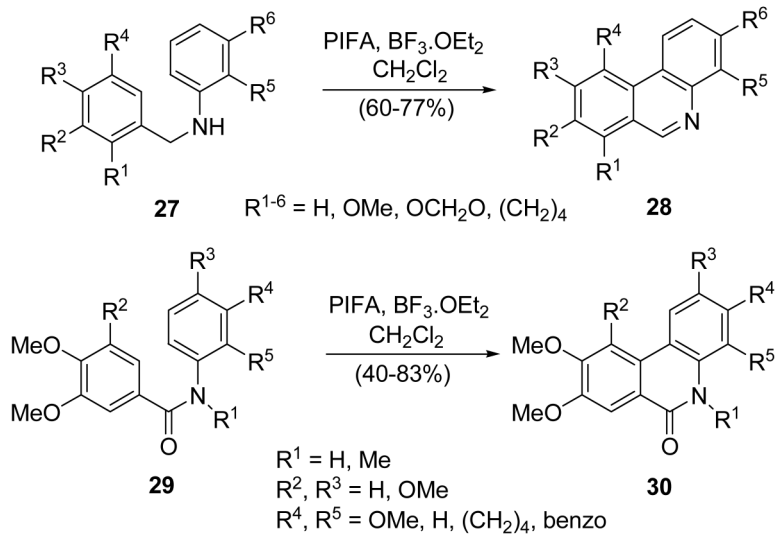


Scheme 6

The application of PIFA was utilized for the construction of benzo[*b*]phenanthro [9,10-*d*]furans **26** [31] (Scheme 7). It was found that the reaction conditions depended on the electronic nature of substrates.



Scheme 7

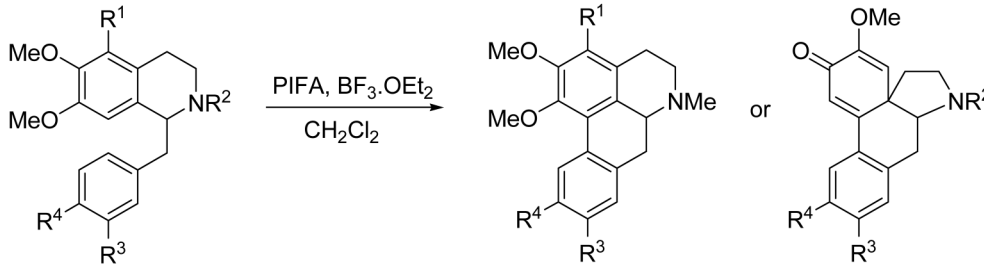


Scheme 8

The PIFA/BF_3·Et_2O combination (Scheme 8) was also useful for conversions of methoxy-substituted arylbenzylamines **27** to the phenanthridines **28**, and of methoxy-substituted *N*-arylbenzamides **29** to the phenanthridones **30** [23]. To generate the proper amide configuration for intramolecular coupling over dimerization process, a *N*-methyl substitution or a higher reaction temperature was necessary in some cases of the amide cyclization.

Synthesis of Aporphines, Neospirinedienones and Morphinandienones

Intramolecular oxidative coupling reaction of *N*-protected-1-benzyltetrahydroisoquinolines **31** using the hypervalent iodine reagent has been reported by our group [32] and others [33-36]. The oxidation of *N*-methyl- and *N*-acyl-1-benzyltetrahydroisoquinolines using PIFA-BF_3·Et_2O under dry condition afforded aporphine **32** and neospirinedienone **33** alkaloids, respectively [32-36] (Scheme 9).



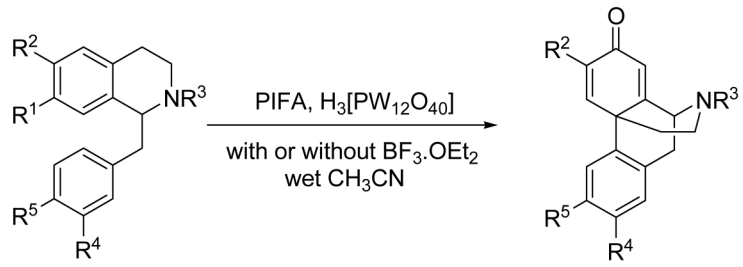
1-benzylisoquinoline : 31
R^1 = H, OMe
R^2 = Me, CHO, CH_3CO, CF_3CO
R^3, R^4 = OMe, OCH_2O

aporphine : 32
R^1 = H, OMe
R^3, R^4 = OMe, OCH_2O

neospirinedienone : 33
R^2 = CHO, CH_3CO, CF_3CO
R^3, R^4 = OMe, OCH_2O

Scheme 9

On the other hand, morphinandienone alkaloids **35** (Scheme 10) could be obtained from *N*-protected-1-benzyltetrahydroisoquinolines **34** by employing the combination of PIFA and heteropoly acid (HPA) in wet acetronitrile [35-36].



1-benzylisoquinoline : 34 **morphinandienone : 35**

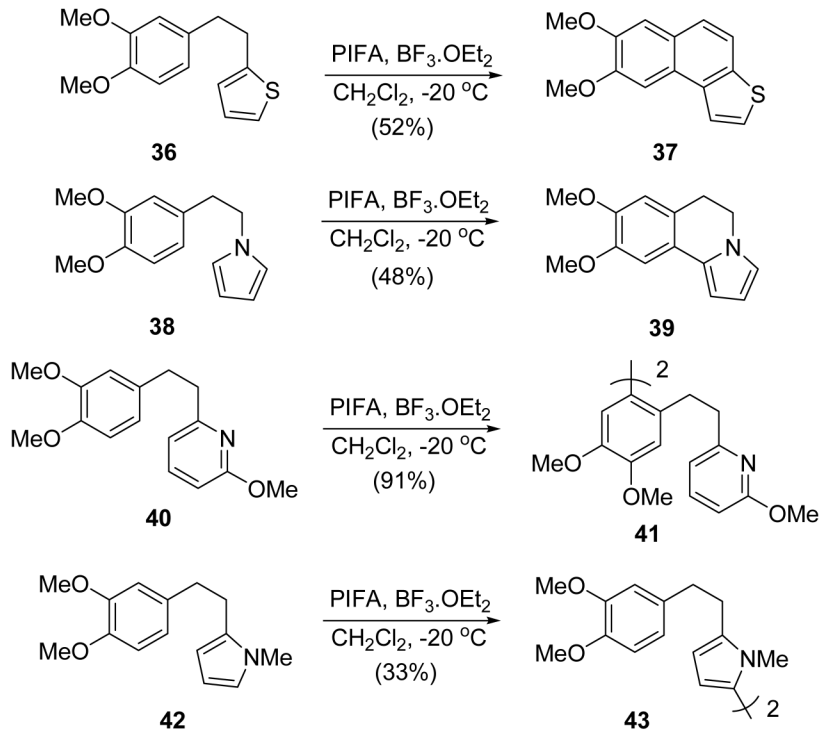
R^1,R^2, R^4, R^5 = OMe, OBn, OCH_2O
R^3 = Me, CF_3CO

Scheme 10

As illustrated, It could be concluded that the reaction mechanism of biaryl coupling took place via *p-p* coupling involving six-membered transition state in the initial step followed by further reactions depending on the methoxylation pattern on the aromatic ring and the nature of the substituents on the nitrogen.

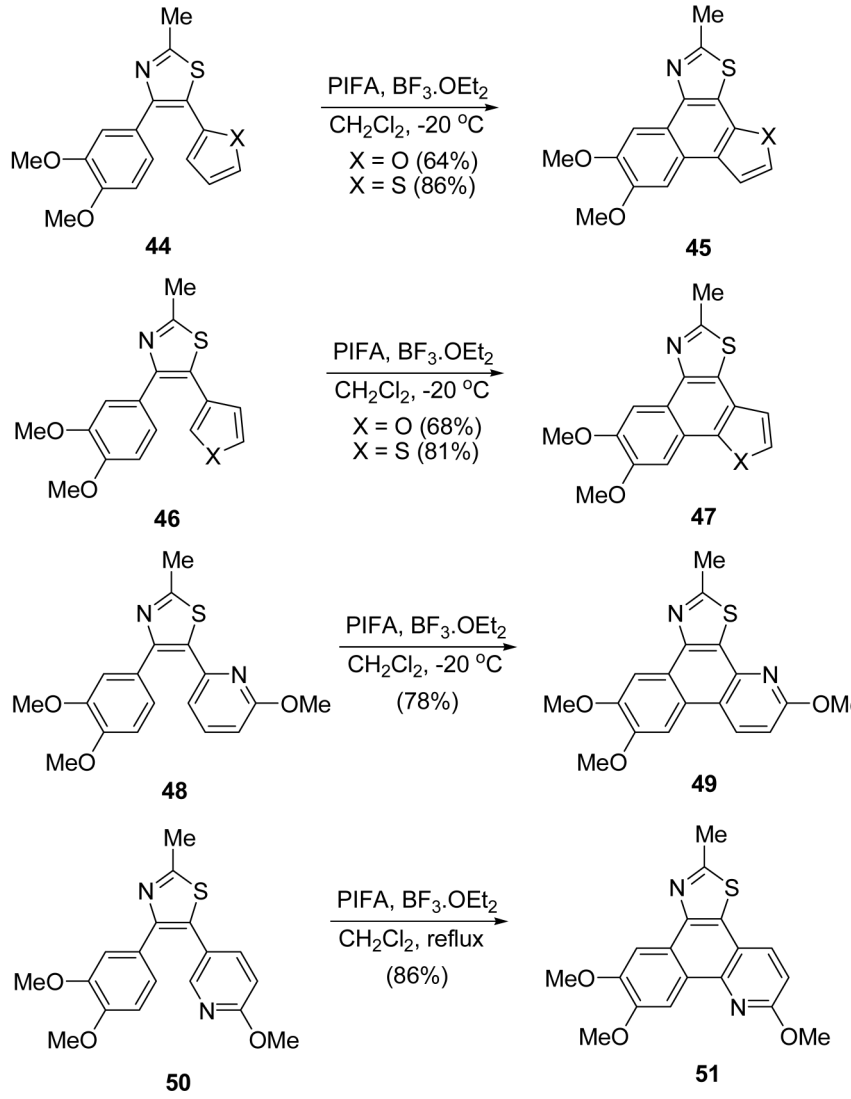
Aryl-Heteroaryl Bond Formation

In order to evaluate a series of arylheteroaryl-substituted ethanes under oxidative coupling conditions, Domínguez *et al.* succeeded in the synthesis of naphthothiophene **37** and pyrroloisoquinoline **39** [24, 37]. In other cases, dimerization processes to yield dimers **41** and **43** from pyridine **40** and pyrrole **42**, respectively, could be observed (Scheme 11).



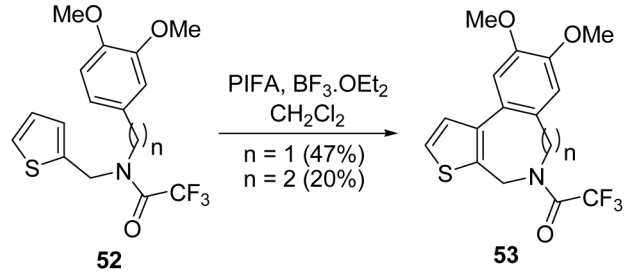
Scheme 11

Furthermore, phenanthroid-fused thiazoles possessing thiophene, furan and methoxypyridine rings were regioselectively accessed by the application of hypervalent iodine [24, 37]. However, the cyclization on non-activated pyridine ring could not be accomplished (Scheme 12).



Scheme 12

In addition, oxidative cyclization of trifluoroacetamides **52** was noted leading to thienobenzazepine (n=1) and thienobenzoazocene (n=2) derivatives **53**. However, formation of the expected thienoquinolinone (n=0) was not observed under these conditions [38] (Scheme 13).



52 **53**

Scheme 13

Bis-Heteroaryl Bond Formation

Faul *et al.* had explored the use of PIFA for oxidation of bisindolylmaleimides **54** (Scheme 14). It was found that the maleimides **54** could be converted to the corresponding indolo[2,3-a]carbazoles **55** in 15-56%. However, under the same condition the bisindolylmaleimide (R^1, R^2, R^3 = H) and maleimides possessing one *N*-methylindolyl group and one *p*-anisyl or α-naphthyl group could not yield the corresponding carbazoles [39].

54 **55**

Scheme 14

Conclusions and Future Prospects

Hypervalent iodine(III) reagent shows a promising property in replacing highly toxic heavy metal oxidants as well as providing a useful tool for the preparation of a wide range of synthetic and naturally occurring products containing biaryl or heteroaryl structures. From the structure and reactivity point of view, it is challenge to apply such reagent for the design and synthesis of novel biaryl compounds. Author hopes that this article will give insight into further development, not only oxidative biaryl coupling strategy, but also other chemical transformations involving hypervalent iodine compounds.

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ได้รับบทความวันที่ 4 ธันวาคม 2551
ยอมรับตีพิมพ์วันที่ 18 กุมภาพันธ์ 2552