Pot-economic synthesis of diarylpyrazoles and pyrimidines involving Pd-catalyzed cross-coupling of 3-trifloxychromone and triarylbi-muth

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Abstract. The present study reveals the formation of 3,4-diarylpyrazole and 4,5-diarylpyrimidine in one-pot operation starting from 3-trifloxychromone and triarylbi-muth. The complete process encompasses two steps in the one-pot operation. The first step leads to the formation of isoflavone via cross-coupling reaction of 3-trifloxychromone and triarylbi-muth as a threefold arylating reagent. These isoflavones were further converted into 3,4-diarylpyrazole and 4,5-diarylpyrimidine using hydrazine hydrate and guanidinium chloride in the successive step in the same pot. Interestingly the formation of 3,4-diarylpyrazole was achieved in the shortest reaction time i.e., 30 min that too at room temperature. Overall the developed methodology provides easy access to the medicinally important diarylpyrazole and pyrimidine moiety in one-pot operation and in short reaction time.

Keywords. Cross-coupling; triarylbi-muth; isoflavones; diarylpyrazoles; diarylpyrimidines; pot-economy.

1. Introduction

Pyrazoles and pyrimidines are significant scaffolds present in several biologically active molecules as well as in drug molecules.^{1–10} These are known to exhibit a vast range of biological activities such as anti-tumour,^{3,4} anti-inflammatory,⁵ anti-depressant⁶ and so on. In particular, diaryl pyrazoles and pyrimidines are present as core moieties in a number of drugs and agrochemicals. Figure 1 shows example of few drugs with arylated pyrazole or pyrimidines as core scaffold which are being prescribed to treat various physiological disorders. For example, Celecoxib (Figure 1a),⁷ is an example of non-steroidal anti-inflammatory drug (NSAID) and is known to be COX-2 (cyclooxygenase-2) inhibitors.¹ Rosuvastatin (Figure 1b) is a drug for cardiovascular disorders.⁸ Importantly, phenol substituted pyrazoles and pyrimidines have exhibited appealing biological properties. For example, 3,4-diarylpyrazole (Figure 1c) has been studied as heat shock protein inhibitors and with

anti-cancer activities.^{4,9} Likewise pyrimidine-based compounds are known for various biological applications including as tubulin polymerization inhibitors (Figure 1d).^{10,11} Phenol-substituted pyrazoles can easily be converted to phenanthropyrazoles.¹² Apart from that, pyrazole derivatives are also known to serve as insecticides,¹³ fungicides¹⁴ and as versatile ligands.^{15,16}

There have been a few synthetic methods for the preparation of aryl substituted pyrazoles^{17–23} and pyrimidines.^{10,24,25} Among those, the phenol substituted pyrazoles and pyrimidines have been obtained using isoflavones as a precursor. The vast therapeutic value associated with these phenol substituted 3,4-diarylpyrazoles and 4,5-diaryl-2-aminopyrimidines prompted us to develop a pot-economic protocol for their synthesis involving *in situ* formation of isoflavones using triarylbi-muths under Pd-catalyzed condition.²⁶ Utilization of triarylbi-muths with sub-stoichiometric loadings in cross-coupling reactions is practically useful in organic synthesis.^{27–33} It was envisaged that the isoflavones obtained from cross-coupling reaction using triarylbi-muth could further be converted to

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3,4-diarylpyrazoles and pyrimidines in one-pot operation. For the cross-coupling step, it was decided to employ 3-trifloxychromone as electrophilic coupling partner as the reactivity of this substrate has not been investigated so far in couplings with triarylbi-muth reagents. Overall, our aim was to develop efficient pot-economic methods for the synthesis of phenol-substituted diarylpyrazoles and pyrimidines by clubbing cross-coupling step for the formation of isoflavone as well as their transformation to diarylpyrazoles and pyrimidines.

2. Experimental

2.1 General

For structural characterization, NMR spectra were recorded on JEOL-400 MHz (JNM ECS-400) spectrometer. WATERS-Q-ToF Premier-HAB213, in addition to WATERS GCT Premier-CAB155 instrument, were used for HRMS measurements. The Bruker Vector 22 FTIR spectrometer was used in IR measurements. Standard drying methods were followed for the distillation of solvents prior to use. All the coupling reactions were performed using oven-dried Schlenk tubes under inert atmosphere conditions. The 3-trifloxychromones (1a–1e) required for coupling reactions were obtained following the literature procedures.^{34–36a} The triarylbi-muth compounds were prepared by adopting the known procedures.^{36b–c} All the products were isolated using column chromatography with silica gel (100–200 mesh) and GF-254 silica gel (Merck) for thin layer chromatography.

2.2 Representative procedures for the preparation of 3-trifloxychromones (Scheme 1)

(A) Representative procedure for the preparation of 2-aryl-3-hydroxyflavones:³⁴

Step 1: Preparation of (E)-1-(2-hydroxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one (1A): To an oven dried round bottom flask, 2'-hydroxyacetophenone (5.0 g, 36.72 mmol) and *p*-anisaldehyde (4.5 mL, 36.72 mmol) were charged in ethanol. To this, sodium hydroxide (6.3 g, 157.8 mmol) was added at 0 °C and the reaction mixture

was allowed to stir at rt for 18 h. After complete consumption of starting materials, acetic acid (30% v/v) was added to neutralize the reaction mixture. The precipitate obtained was filtered and washed with water. It was further purified through crystallization from ethanol to obtain compound 1A as yellow solid in 80% yield (7.4 g).

Step 2: Preparation of 3-hydroxy-2-(4-methoxyphenyl)-4H-chromen-4-one (2A): To an oven dried round bottom flask, compound 1A (5.0 g, 19.6 mmol) was taken in ethanol. To this, sodium hydroxide (1.5 g, 39.3 mmol) was added at ice-bath temperature. The mixture was stirred for 10 min and was added H₂O₂ (30% w/v, 5.0 mL, 43.2 mmol). It was allowed to stir at rt for 18 h. It was acidified with dil HCl and the yellow precipitate obtained was filtered and dried under vacuum. It was further purified by crystallization in ethanol to obtain 2A in 73% yield (3.8 g).

(B) Representative procedures for the preparation of 3-hydroxychromones:³⁵

Step 1: Preparation of (E)-3-(dimethylamino)-1-(2-hydroxyphenyl)prop-2-en-1-one (1B): To an oven dried round bottom flask, 2-hydroxyacetophenone (10.0 mL, 83.0 mmol) and *N,N*-dimethylformamide dimethyl acetal (10.0 mL, 83.0 mmol) were charged. It was refluxed for 1 h. The reaction mixture was cooled to rt. The red precipitate was filtered and washed with petroleum ether to get enamide, (E)-3-(dimethylamino)-1-(2-hydroxyphenyl)prop-2-en-1-one in 94% yield (19.8 g). It was used in the next step without further purification.

Step 2: Preparation of 4H-chromen-4-one (2B): To an oven dried round bottom flask, (E)-3-(dimethylamino)-1-(2-hydroxyphenyl)prop-2-en-1-one (10.0 g, 53.0 mmol) was dissolved in dichloromethane (50.0 mL). To this, conc. HCl (50 mL) was added and the mixture was refluxed for 1 h. It was cooled to rt and poured into cold water. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2 × 30 mL). The combined organic extract was washed with water and brine and dried over anhydrous MgSO₄. The solvent was evaporated and dried under vacuum to obtain 4H-chromen-4-one as red solid in 90% yield (6.8 g).

Step 3: Preparation of 3-hydroxychromone (3B): To an oven dried round bottom flask 4H-chromen-4-one (5.0 g,

Figure 1. Pyrazole and pyrimidine-based biological scaffolds and drugs.

Scheme 1. Synthesis of functionalized 3-trifloxychromones.

34.2 mmol) was dissolved in dichloromethane (50 mL). Sodium hydroxide (2.0 g, 51.3 mmol) was added to it. Reaction mixture was cooled to 0 °C and H₂O₂ (30% w/v, 13.5 mL, 119.7 mmol) was slowly added at the same temperature. After complete addition, the mixture was stirred at 0–15 °C. After complete disappearance of chromone as monitored by TLC, it was quenched with water and extracted with dichloromethane (3 × 20 mL). The combined organic extract was washed with water and brine, dried over anhydrous MgSO₄ and evaporated using rotatory evaporator. In the second step, conc. HCl (50 mL) was added to the crude reaction mixture and was stirred at 70 °C for 1 h. After that, it was cooled to rt and poured into water. The solid precipitate obtained was filtered and washed with water and dried under vacuum to obtain a white solid as 3-hydroxychromone in 64% yield (3.54 g).

*(C) Representative procedure for the preparation of triflate derivatives:*³⁶

To a two-neck round bottom flask 3-hydroxychromone (5.0 g, 18.5 mmol) was charged in dry dichloromethane (50 mL). The mixture was cooled to 0 °C and triethylamine (3.0 mL, 22.2 mmol) was added with continuous stirring for 10 min followed by triflic anhydride (4.6 mL, 27.7 mmol) and the resultant mixture was allowed to stir at rt for 10 h. After that, it was quenched with water and extracted with dichloromethane (3 × 20 mL) and dried over anhydrous MgSO₄ and concentrated. It was purified by silica gel column chromatography (5% EtOAc/petroleum ether) to obtain 1c as white solid (3.9 g, 72%).

2.3 Representative procedure for cross-coupling reaction

Representative cross-coupling procedure for Tables 1 and 2: A hot-oven dried Schlenk tube was charged with 1a (0.164 g, 0.412 mmol), tri(p-anisyl)Bi (0.066 g, 0.125 mmol), Pd(PPh₃)₄ (0.012 g, 0.011 mmol), K₃PO₄ (0.053 g, 0.25 mmol), and DMF (3 mL) under N₂ atmosphere. The reaction mixture was stirred in an oil bath at 90 °C for 4 h. At the end of the reaction time, the contents were brought to rt, quenched with water (10 mL) and extracted with ethyl acetate. The organic extract was treated with brine, dried using MgSO₄ and was concentrated under reduced pressure. The crude product was subjected to silica gel column chromatography using 10% EtOAc/petroleum ether as eluent to obtain product 2.1 as white solid (0.109 g, 81%). For the yield calculation, 0.375 mmol of the product was considered as 100% yield.

2.4 Pot-economic synthesis of 2-(4-phenyl-1H-pyrazol-3-yl)phenol (3.1, Table 3)

A hot-oven dried Schlenk tube was charged with 1c (0.121 g, 0.412 mmol), BiPh₃ (0.055 g, 0.125 mmol), Pd(PPh₃)₄ (0.012 g, 0.011 mmol), K₃PO₄ (0.053 g, 0.25 mmol), and DMF (3 mL) under N₂ atmosphere. The reaction mixture was stirred in an oil bath at 90 °C for 4 h. At the end of the reaction time, the contents were brought to rt and hydrazine hydrate (0.03 mL, 0.625 mmol) was added to the reaction mixture. It was further stirred at rt for 30 min. After it was quenched with water (10 mL) and extracted with ethyl acetate.

Table 1. Screening for 3-trifloxychromone coupling.^{a–e}

Entry	Catalyst	Base (equiv.)	Temp. (°C)	Solvent	Yield 2.1 (%)
1	PdCl ₂ (PPh ₃) ₂	K ₃ PO ₄ (6)	90	DME	46
2	Pd(PPh ₃) ₄	K ₃ PO ₄ (1)	90	DMF	58
3	Pd(PPh ₃) ₄	K ₃ PO ₄ (2)	90	DMF	81
4	Pd(PPh ₃) ₄	K ₃ PO ₄ (3)	90	DMF	76
5	Pd(PPh ₃) ₄	K ₃ PO ₄ (2)	90	DMA	77
6	Pd(PPh ₃) ₄	K ₃ PO ₄ (2)	90	NMP	65
7	Pd(PPh ₃) ₄	Cs ₂ CO ₃ (2)	90	DMF	54
8	Pd(PPh ₃) ₄	K ₂ CO ₃ (2)	90	DMF	60
9	Pd(PPh ₃) ₄	K ₃ PO ₄ (2)	60	DMF	48
10	Pd(PPh ₃) ₄	K ₃ PO ₄ (2)	100	DMF	77
11	Pd(PPh ₃) ₄	K ₃ PO ₄ (2)	90	DMF	72 ^c
12	Pd(PPh ₃) ₄	K ₃ PO ₄ (2)	90	DMF	80 ^d
13	Pd(PPh ₃) ₄	K ₃ PO ₄ (2)	90	DMF	52 ^e
14	Pd(PPh ₃) ₄	None	90	DMF	30
15	None	K ₃ PO ₄ (2)	90	DMF	None

^aReaction conditions: 1a (0.412 mmol, 3.3 equiv.), Bi(*p*-anisyl)₃ (0.125 mmol, 1 equiv.) Pd(PPh₃)₄ (0.011 mmol, 0.09 equiv.) K₃PO₄ (0.25 mmol, 2 equiv.), DMF (3 mL), 4 h, 90 °C. ^bIsolated yields based on three aryl couplings from BiAr₃ reagents

^cWith 3 h. ^dWith 5 h. ^eWith 0.05 equiv. catalyst.

The organic extract was treated with brine, dried using MgSO₄ and the solvent was concentrated under reduced pressure. The crude product was subjected to silica gel column chromatography using 15% EtOAc/petroleum ether as eluent to obtain 3.1 as white solid (0.067 g, 76%).

2.5 Pot-economic synthesis of

2-(2-amino-5-phenylpyrimidin-4-yl)phenol (4.1, Table 5)

The cross-coupling reaction with 1c was carried according to the procedure given in 2.3. After that, guanidinium chloride (0.048 g, 0.5 mmol) and NaOH (0.050 g, 1.25 mmol) were added to the reaction mixture. It was further stirred at 90 °C for 10 h. The product mixture was quenched with water (10 mL) and neutralized with dil. HCl. It was further extracted with ethyl acetate. The organic extract was treated with brine, dried using MgSO₄ and concentrated under reduced pressure. The crude product was subjected to silica gel column chromatography using 10% EtOAc/dichloromethane as eluent to obtain product 4.1 as yellow solid (0.078 g, 79%).

3. Results and Discussion

The required 3-trifloxychromones (1a–1e) for this investigation were accessed through literature procedures

in good yields following method A and B as given in Scheme 1.^{34–36} Next, the cross-coupling reactivity of 3-trifloxychromones with triarylbismuth reagent was explored. It was investigated to establish an optimized protocol under Pd-catalyzed conditions (Table 1). It was done initially using 2-(*p*-methoxyphenyl)-3-trifloxychromone (1a) and tri(*p*-anisyl)bismuth using catalytic PdCl₂(PPh₃)₂ conditions and K₃PO₄ base in DME at 90 °C (entry 1, Table 1).²⁶ This catalytic protocol furnished the desired isoflavone 2.1 in 46% yield (entry 1, Table 1). Another attempt using catalytic Pd(PPh₃)₄ afforded 2.1 in 58% yield (entry 2, Table 1). However, it was dramatically improved to 81% yield when the reaction was performed with 2 equiv. of base (entry 3, Table 1). Further improvement was not seen with 3 equiv. of the base (entry 4, Table 1). At this stage, more investigations were carried out in different solvents using *N,N*-dimethylacetamide (DMA) and *N*-methyl-2-pyrrolidone (NMP).

In these cases, we did not witness any further improvement in the cross-coupling yield (entries 5 and 6, Table 1). The impact of Cs₂CO₃ and K₂CO₃ base condition proved to be ineffective (entries 7 and 8, Table 1). The cross-couplings performed at 60 and 100 °C conditions found to be low yielding (entries 9 and 10, Table 1). Additional check with different time durations proved to

Table 2. Cross-couplings of functionalized 3-trifloxychromones.^{a–c}

Entry	3-Trifloxychromone	Product	Yield (%)
1			81
2			65
3			68
4			67
5			78
6			75
7			79
8			77
9			82
10			79
11			65
12			71
13			75
14			82
15			82
16			73
17			62
18			64
19			64

^aReaction conditions: 3-Trifloxychromone, 1a–1e (0.412 mmol, 3.3 equiv.) BiAr_3 (0.125 mmol, 1 equiv.) $\text{Pd(PPh}_3)_4$ (0.011 mmol, 0.09 equiv.) K_3PO_4 (0.25 mmol, 2 equiv.) DMF (3 mL), 90 °C, 4 h. ^bIsolated yields based on threefold coupling from triarylbiaryl reagents and 0.375 mmol corresponds to a 100% yield. ^cHomo-coupled biaryls formed 10–15% amounts.

Table 3. Pot-economic synthesis of 3,4-diaryl-1*H*-pyrazoles.^{a–c}

Entry	3-Trifloxychromone	3,4-Diarylpyrazole	Yield (%)
1			76
2			72
3			80
4			67
5			71
6			74
7			60
8			78
9			78
10			74
11			66
12			75
13			55
14			62

^aReaction conditions: for step 1: 3-Trifloxychromone, 1c–1e (0.412 mmol, 3.3 equiv.) BiAr₃ (0.125 mmol, 1 equiv.) Pd(PPh₃)₄ (0.011 mmol, 0.09 equiv.) K₃PO₄ (0.25 mmol, 2 equiv.) DMF (3 mL), 90 °C, 4 h for Step 2: hydrazine hydrate (0.625 mmol, 5 equiv.) rt, 0.5 h. ^bIsolated yields based on threefold coupling from triarylbismuth reagents and 0.375 mmol of 3,4-diarylpyrazole corresponds to a 100% yield. ^cHomo-coupled biaryls formed 10–15% amounts.

Figure 2. X-ray structural analysis for 3.10 (CCDC No. 1412753).³⁹

be less effective (entries 11 and 12, Table 1). To optimize the catalyst loading, a coupling reaction was performed with 0.05 equiv. of catalyst and this gave 52% yield (entry 13, Table 1). The absence of either base or catalyst proved to be ineffective as they were crucial for an effective coupling process (entries 14 and 15, Table 1).

With this study, it was realized that the protocol involving $\text{Pd}(\text{PPh}_3)_4$ (0.09 equiv.) and K_3PO_4 (2 equiv.) in DMF at 90 °C for 4 h as promising for the effective cross-coupling of 3-trifloxychromone with triarylbismuth reagent (entry 3, Table 1). With this optimized protocol, the cross-coupling reactivity of various functionalized 3-trifloxychromones was further investigated (Table 2). The coupling reaction of 1a was first evaluated against different triarylbismuth reagents. This study delivered a facile cross-coupling performance with the formation of differently functionalized isoflavones in good to high yields (entries 1–19, Table 2). Further, this also revealed the possibility for chemo-selective couplings when the reactive bromo group in 1b and 1e got survived during the coupling course under the optimized conditions (entries 3–5 and 17–19, Table 2). Other studies with electronically variant triphenylbismuth reagents also demonstrated viable reactivity under our optimized conditions (entries 6–12, Table 2). Even the vinyl group was intact when coupling was performed with vinyl substituted triphenylbismuth reagent (entry 6, Table 2). This amply reflected the overall efficacy of the established palladium protocol conditions to deliver a library of isoflavones in high yields. Encouraged by this, it was further decided to explore a pot-economic protocol by combining the cross-coupled synthesis of isoflavones and their *in situ* conversion to either 3,4-diarylpyrazoles or 4,5-diarylpyrimidines. For example, a brief literature search revealed that such transformation of isoflavone to pyrazole was performed with the direct reaction of isoflavones with hydrazine or after the

Table 4. Screening for pyrimidine formation.^{a–b}

Entry	Temp. (°C)	Time (h)	Yield (%)
1	rt	34	74
2	70	13	77
3	90	10	79
4	90	7	56

^aReaction conditions: for Step 1, 1c (0.412 mmol, 3.3 equiv.), BiAr_3 (0.125 mmol, 1 equiv.), $\text{Pd}(\text{PPh}_3)_4$ (0.011 mmol, 0.09 equiv.), K_3PO_4 (0.25 mmol, 2 equiv.), DMF (3 mL), 90 °C, 4 h for Step 2, guanidinium chloride (0.5 mmol, 4 equiv.), NaOH (1.25 mmol, 10 equiv.), temp., time. ^bIsolated yields.

cross-coupling process.^{22,23} This search also revealed that not many pot-economic protocols were readily available with a possibility to combine two or more reactions in a one-pot operation. Further, the known protocol in this regard requires longer reaction time for access 3,4-diarylpyrazoles in a one-pot operation and this encouraged us to further explore any further improvement. Hence additional efforts were made with a view to developing a pot-economic combined protocol for the synthesis of 3,4-diarylpyrazoles using our rapid protocol conditions. To start with, it was done with the addition of hydrazine hydrate to the reaction mixture obtained after the cross-coupling step. Quantitative formation of 3,4-diarylpyrazole was observed at rt in just 0.5 h conditions.

As reported, this transformation with an organoboron reagent such as arylboronic acid under the Suzuki coupling conditions requires longer reaction time.²² Hence it was of interest to further expand the scope for the development of a viable method for rapid access of pyrazoles in a one-pot operation. This resulted in the preparation of a library of 3,4-diarylpyrazoles and these results are as given in Table 3. This pot-economic protocol involving cross-couplings with triarylbismuths followed by reaction with hydrazine afforded a variety of 3,4-diarylpyrazoles in a facile manner.

In general, the fast formation of 3,4-diarylpyrazoles was achieved when differently functionalized isoflavones were smoothly transformed under our pot-economic protocol conditions. We also obtained single crystal X-ray analysis of 3.10 (Figure 2) and this unequivocally established the formation of 3,4-diarylpyrazole.

It further encouraged us to establish a pot-economic protocol for the synthesis of various 4,5-diarylpyrimidines. It was done through the initial generation of

Table 5. Pot-economic synthesis of 4,5-diaryl 2-amino-pyrimidines.^{a–c}

Entry	3-Trifloxychromone	4,5-diaryl 2-aminopyrimidines	Yield (%)
1			79
2			74
3			68
4			79
5			61
6			68
7			72

^aReaction conditions: for step 1, **1c** (0.412 mmol, 3.3 equiv.), BiAr₃ (0.125 mmol, 1 equiv.), Pd(PPh₃)₄ (0.011 mmol, 0.09 equiv.), K₃PO₄ (0.25 mmol, 2 equiv.), DMF (3 mL), 90 °C, 4 h. For step 2, guanidinium chloride (0.5 mmol, 4 equiv.), NaOH (1.25 mmol, 10 equiv.), 90 °C, 10 h. ^bIsolated yields based on threefold coupling from triarylbismuth reagents and 0.375 mmol of pyrimidine corresponds to a 100% yield. ^cHomo-coupled biaryls formed 10–15% amounts.

isoflavone followed by its reaction with guanidinium chloride in a one-pot operation. A trial reaction was initially carried out with guanidinium chloride after the cross-coupling step at room temperature. It delivered 74% of 4,5-diaryl-pyrimidine (**4.1**) in 34 h reaction time (entry 1, Table 4). In order to reduce the reaction time, the reaction condition was investigated by optimizing the reaction temperature (entries 2 and 3, Table 4). At 90 °C, quantitative conversion of isoflavone to 4,5-diarylpyrimidine was achieved in 10 h (entry 3, Table 4). On decreasing the reaction time at the same temperature, the yield of 4,5-diarylpyrimidine decreased to 56% (entry 4, Table 4).

Reaction attempted without the addition of base in the second step did not provide desired 4,5-diarylpyrimidine (**4.1**). Hence further study for the conversion

Figure 3. X-ray structural analysis of **4.4** (CCDC No. 1412754).³⁹

of isoflavone to 4,5-diarylpyrimidine was continued with 90 °C and 10 h condition in presence of an additional base in a second step. This optimized reaction

Figure 4. Proposed mechanism for the formation of diarylpyrazole and pyrimidine.

condition was applied in the synthesis of various functionalized 4,5-diarylpyrimidines (Table 5). The cross-coupling of 1c was carried out with different triarylbiuth reagents followed by the reaction of guanidinium chloride. This pot-economic protocol thus gave 4,5-diarylpyrimidines (4.1–4.7) in good to high yields. It is notable that this pot-economic protocol for the preparation of 4,5-diarylpyrimidines is synthetically more viable as it involves triarylbiuth reagents in substoichiometric loading with faster reactivity and overall high yields. Our efforts thus unequivocally established the compatibility of triarylbiuth cross-coupling conditions in further developing pot-economic combined protocols for rapid access of 3,4-diarylpyrazoles and 4,5-diarylpyrimidines in high yields.

Further, the crystal structure obtained for 2-(2-amino-5-arylpyrimidin-4-yl) phenol (4.4) is given in Figure 3. Overall, an easy accessibility of isoflavones through cross-couplings under catalytic palladium conditions and their subsequent cyclocondensation to give 3,4-diarylpyrazoles under pot-economic protocol conditions is expected to have a definitive advantage in organic synthesis.²⁴ And this advantage also applies to the transformation of isoflavones with guanidine to rapid access to 4,5-diarylpyrimidines under pot-economic protocol conditions.

3.1 Mechanism

As shown in Figure 4, the formation of 3,4-diarylpyrazoles and 4,5-diarylpyrimidines involves the initial

formation of isoflavones (A) through Pd-catalyzed cross-coupling reaction.²⁶

In the second step, it was expected to undergo cyclocondensation with hydrazine involving nucleophilic attack of hydrazine (B), ring opening (C) followed by cyclocondensation to give 3,4-diarylpyrazole (D).¹² Whereas the formation of 4,5-diarylpyrimidines is expected to begin with the base-mediated ring opening of isoflavone^{37,38} leading to F which undergoes condensation with guanidine to give 4,5-diarylpyrimidine (G).

4. Conclusions

We have disclosed an efficient method for the synthesis of 3,4-diarylpyrazoles and 4,5-diarylpyrimidines starting with triarylbiuth as threefold arylating reagent and 3-trifloxychromones. These pot-economic protocols provide the rapid access to medicinally important 3,4-diarylpyrazoles and 4,5-diarylpyrimidines in high yields. It is important to highlight that 3,4-diarylpyrazoles can be obtained at room temperature and within 30 min reaction time, the shortest time reported so far.

Supplementary Information (SI)

Characterization data and spectra (¹H, ¹³C NMR, Mass) of the compounds included in Tables 2, 3, 5 are given in the supplementary information which is available at www.ias.ac.in/chemsci.

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39. CCDC-1412753 and CCDC-1412754 contains all crystallographic details for compounds **3.10** and **4.4** respectively. It is available free of charge at www.ccdc.cam.ac.uk/conts/-retrieving.html or can be ordered from the following address: Cambridge Crystallographic Data Centre, 12 Union Road, GB-Cambridge CB21EZ Fax: (+44)1223-336-033 or deposit@ccdc.cam.ac.uk