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Report

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Synthesis of 2*H*-benzo[*g*]furo/thieno/pyrrolo[2,3-*e*]indazoles *via* Intramolecular Dehydrogenation Photocyclization

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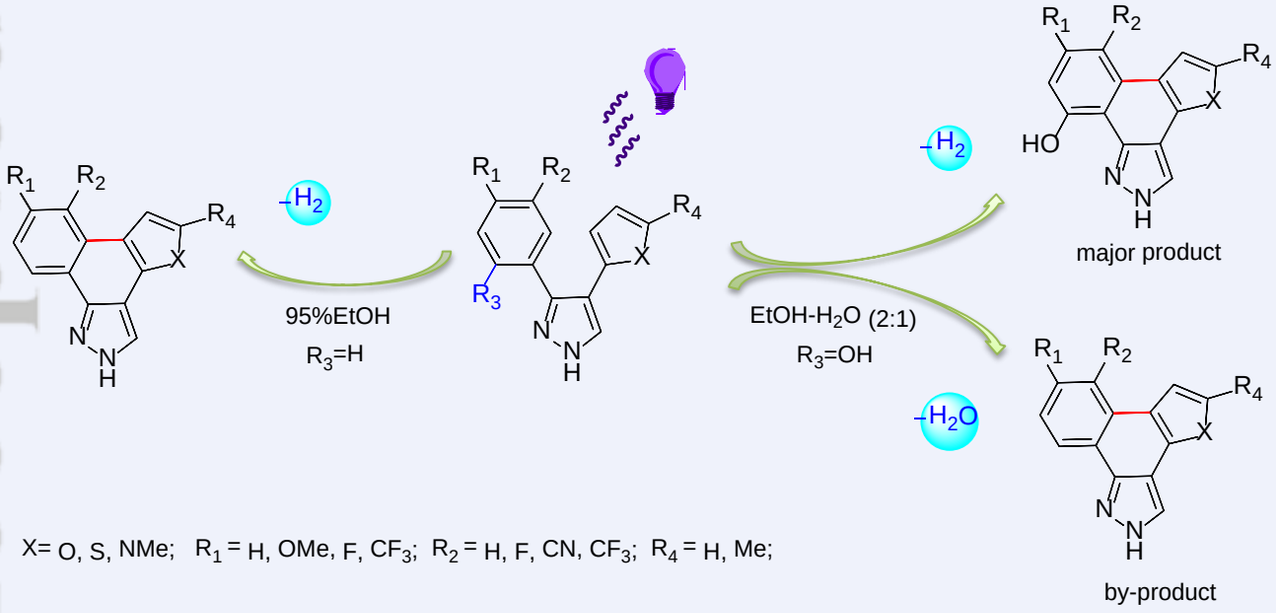
Keywords

2H-benzo[g]furo[2,3-e]indazoles | 6π-electroncyclization | Photocyclization | Dehydrogenative annulation | Chemo-selectivity

Main observation and conclusion

A catalyst-, acid- and base-free, environmental-friendly method for the synthesis of 2*H*-benzo[*g*]furo[2,3-*e*]indazoles, 2*H*-benzo[*g*]thieno[2,3-*e*]indazoles and 2*H*-benzo[*g*]pyrrolo[2,3-*e*]indazoles via a UV light irradiation of 3-phenyl-4-(2-heteroaryl)pyrazoles (aryl=furanyl, thiophenyl and N-methylpyrrolyl) in EtOH/H_2O at room temperature under argon atmosphere was described. Irradiation of 3-(2-hydroxyphenyl)-4-(2-heteroaryl)pyrazoles showed a high chemo-selectivity to obtain dehydrogenation product 2*H*-benzo[*g*]furo/thieno/pyrrolo[2,3-*e*]indazols-10-ol. The mechanism of photocyclization was expound that through the process of 6π-electroncyclization, [1,5]-hydrogen shift, pyrazole tautomerism, 1,3-eneamine tautomerism and evolution H_2.

Comprehensive Graphic Content



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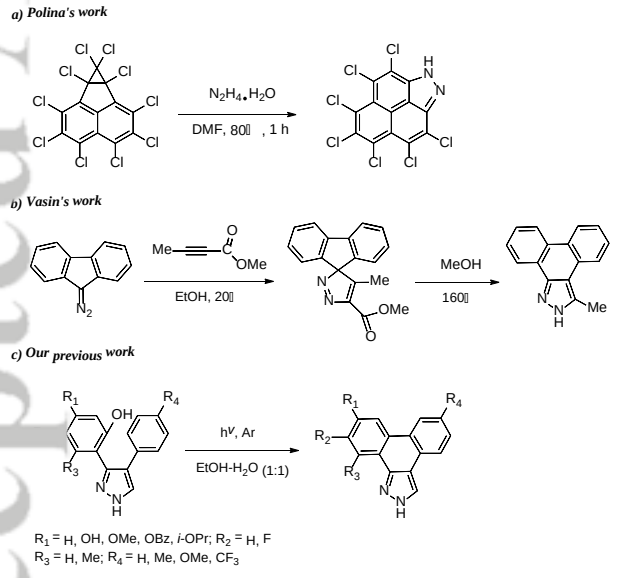
Background and Originality Content

Indazole derivatives have been recognized as important pharmacophores in the development of antitumor, antimicrobial, anti-inflammatory agents, and anti-HIV.[1-4] The structurally diverse indazole moiety has a variety of biological properties, especially in benzoindazoles. Biological evaluation of those pharmacophores was revealed that benzo-indazoles was an effective CK2 inhibitors.[5] Moreover, furo-indazole derivatives were used as 5-HT2C agonists,[6] which was a promising treatment of CNS-related diseases. Although a number of methods for the preparation of indazoles were known,[7] only few reports on the synthesis of dibenzoindazoles was disclosed. For example, treating perchloro-7*H*-cyclopropano[*a*]acenaphthylene with hydrazine hydrate in DMF at 80 °C, 3,4,5,6,7,8,9-heptachlorophenaleno [1,9-*bc*]pyrazole was obtained (Scheme 1a),[8] and it was the first example of a phenalene fused pyrazole. Also, the mixture of diazofluoren and methyl 2-butynoate were heated at 160 °C for 20 min to give 1,3-dipolar cycloaddition products of 2*H*-dibenzo[*e,g*]indazoles (Scheme 1b).[9] In our previous work, 2*H*-phenanthro[9,10-*c*]pyrazoles was achieved by the photocyclization dehydration of 3-(2-hydroxyphenyl)-4-(2-phenyl)-1*H*-pyrazoles in the EtOH–H_2O (1/1, v/v) solution (Scheme 1c).[10]

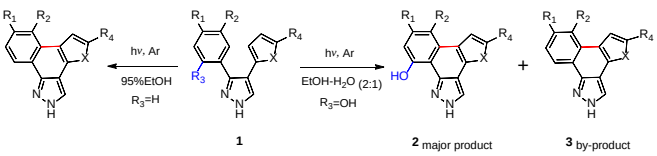
Scheme 1 Previous Reports on the Synthesis of Dibenzoindazoles.



Photoinduced organic reactions have been playing significant roles in synthesis of medicinal drugs, preparation of fine chemicals, especially in the construction of polycyclic aromatic compounds.[11] As well-known, cyclization is one of the key steps for the synthesis of fused heterocyclic compounds, which includes Scholl reaction,[12] photocyclization[13-14] etc. Synthesis of polycyclic aromatic hydrocarbons or fused heterocyclic aromatic ring via photochemical cyclization reaction can be divided into three categories: oxidation photocyclization,[15] elimination photocyclization and transition metal catalyzed photocyclization. Oxidants O_2[16] or I_2,[17] were necessary for the intramolecular oxidation photocyclization. Elimination photocyclization usually requires a leaving group at a certain location, such as halogen and hydroxyl, etc.[18] There are few examples of transition-metal catalyzed dehydrogenation photocyclizations for synthesis fused heterocyclic aromatic hydrocarbons as well.[19, 20]

Based on our previous work,[10, 21, 22] we planned to synthesize 2*H*-benzo[*g*]aryl[2,3-*e*]indazoles **3** by the photocyclization dehydration of 3-(2-hydroxyphenyl)-4-(2-heteroaryl)pyrazoles (aryl=furanyl, thiophenyl and *N*-methylpyrrolyl). Surprisingly, dehydration products **3** as a by-product, dehydrogenation products **2** were obtained (Scheme 2). Given our interest in development of strategy to synthesis ploybenzne fused heterocyclic aromatic compounds *via* photoinduced annulation as well as the existence of limited literature reports on intramolecular dehydrogenative annulation.[23] In this paper, we would like to report the syntheses of 2*H*-benzo[*g*]furo/thieno [2,3-*e*]indazoles and 2*H*-benzo[*g*]furo/thieno/pyrrolo [2,3-*e*]indazols-10-ol *via* the intramolecular dehydrogenation photocyclization of 3-phenyl-4-(2-hetero-aryl)pyrazoles and 3-(2-hydroxyphenyl)-4-(2-hetero-aryl)pyrazoles in solution of EtOH/H_2O. Irradiation of 3-(2-hydroxyphenyl)-4-(2-hetero-aryl) pyrazoles to obtain 2*H*-benzo[*g*]furo/thieno/pyrrole [2,3-*e*]indazols-10-ol is a high chemical selectivity. Using EtOH/H_2O as solvent, catalyst-, acid- and base-free, transition-metal-free and intramolecular dehydrogenation photocyclization to synthesis 2*H*-benzo[*g*]furo/thieno[2,3-*e*] indazoles is a friendly environment strategy. Most of the photoinduced cross-dehydrogenative coupling (CDC) reactions were needed oxidants or transition metals.[24, 25] Photochemical organic synthesis in the absence of photocatalysts, oxidant, base and acid has received great attention due to their economic and synthetic value.[26]

Scheme 2 Synthesis of 2*H*-Benzo[*g*]furo/thieno/pyrrolo[2,3-*e*]indazoles and 2*H*-Benzo[*g*]furo/thieno/pyrrolo[2,3-*e*]indazols-10-ol via Intramolecular Dehydrogenation Photocyclization.



X= O, S, NMe; R_1 = H, OMe, F, CF_3; R_2 = H, F, CN, CF_3; R_3=H, OH; R_4 = H, Me.

Results and Discussion

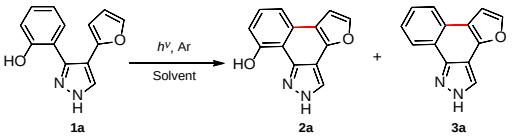
The substrate 2-(4-(fur-2-yl)-1*H*-pyrazol-3-yl)phenol **1a** was synthesized following the literature report.[27, 28] The UV absorption spectroscopy (SI Figure S3) of starting substrate **1a** was determined.

The solution of **1a** (0.25 mmol) in EtOH (50 mL) was irradiated with a high-pressure mercury lamp (500 W) at 25 °C under argon atmosphere for 6 hours to give dehydrogenation product **2a** (32%, Table 1, entry 1) and dehydrated product **3a** (12%, Table 1, entry 1). Compared to other polar and nonpolar aprotic solvent, polar protic solvents MeOH and t-BuOH were screened but no improvement was observed (entries 2–3). Reaction was almost not carried out in the use of nonpolar aprotic solvent DCM (entry 4) and solvent ACE gave only 20% dehydrogenation product and trace amount of dehydrated product (entry 5). Better results were obtained using EtOH–H_2O mixed solvents (entries 6–9). The best results were given when the solvent was EtOH–H_2O (v/v, 2/1) (entry 8). The concentration of the reaction solution was screened (entries 10-11). It was important to note that formation of dehydrogenation product was completely inhibited with the presence of external oxidant, whereas, formation of dehydration product was slightly boosted (entries 12–13). Thus, the optimal condition was determined as below: irradiation of **1a** (5.0×10^{-3} mol/L) in EtOH–H_2O (v/v, 2/1) under UV irradiation for 6 h at ambient temperature under an Ar atmosphere.

Compared with **1a**, the absence of hydroxyl group 4-(furan-2-yl)-3-phenyl-1*H*-pyrazole **1k** was preparation according to literature reports.[29, 30] (UV spectroscopy in SI Figure S3). By a

similar optimization process as **1a**, irradiation of **1k** (0.25 mmol) in EtOH/H_2O (v/v, 95/5) with a high pressure mercury lamp (500 W) at room temperature under Ar atmosphere **3a** as the sole product was obtained and it's yield was 61%.

Table 1 Optimization of the Photocyclization Reaction Conditions [a]



1a **2a** **3a**

Entry	Solvent	Concn(N)	Time(h) [c]	Yield(%) **2a** [b]	Yield(%) **3a** [b]
1	EtOH	10^{-3}	6	32	12
2	MeOH	10^{-3}	6	28	10
3	t-BuOH	10^{-3}	12	Trace	Trace
4	DCM	10^{-3}	12	Trace	Trace
5	ACE	10^{-3}	8	20	Trace
6	EtOH-H_2O(1:2)	10^{-3}	8	35	11
7	EtOH-H_2O(1:1)	10^{-3}	7	36	14
8	EtOH-H_2O(2:1)	10^{-3}	6	45	15
9	EtOH-H_2O(3:1)	10^{-3}	6	38	11
10	EtOH-H_2O(2:1)	10^{-2}	8	21	9
11	EtOH-H_2O(2:1)	10^{-4}	5	37	11
12	EtOH-H_2O(2:1) [d]	10^{-3}	6	/	35
13	EtOH-H_2O(2:1) [e]	10^{-3}	6	/	29

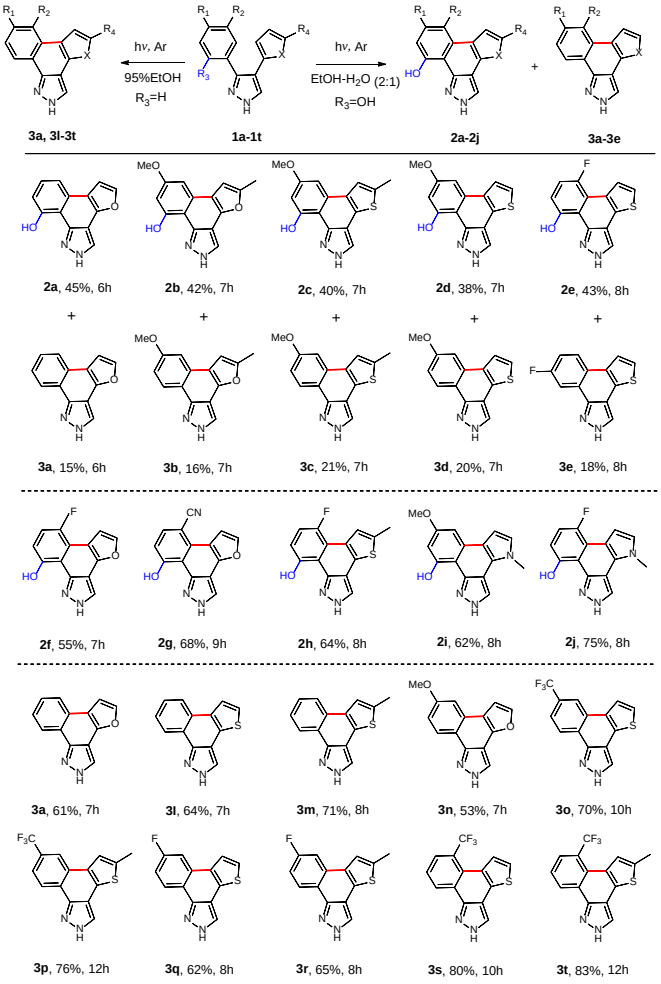
[a] Irradiation of **1a** in various solvents (50 ml) with a high pressure mercury lamp (500 W) at room temperature. [b] Isolated yields. [c] Reaction time was determined by the complete consumption of **1a** as indicated by the thin-layer chromatography (TLC). [d] Adding catalyst amount iodine. [e] In the open air.

With the optimized condition in hand, a array of **2a**-**2j** and **3a**-**3e**, **3l**-**3t** have been synthesized and shown in Scheme 3. Photocyclization of **1a**-**1j** and **1k**-**1t** in EtOH–H_2O (v/v, 2/1) and EtOH-H_2O (v/v, 95/5) under UV irradiation gave corresponding dehydrogenation products **2a**-**2j**, **3a**, **3l**-**3t** and dehydrated products **3a**-**3e**. And all of the isolated products were characterized by FT-IR, ^{1}H NMR, ^{13}C NMR and HRMS. Moreover, the absolute structure of **2i** was determined by X-ray diffraction and the data and molecular structure are displayed in Supporting Information Table S1 and Figure S1.

In the process of annulation **1a-1j** via light irradiation, shown that at a high chemo-selectivity to obtain dehydrogenation product 2*H*-benzo[*g*]furo/thieno/pyrrolo[2,3-*e*]indazols-10-ol **2**, and dehydrated **3** as a byproduct. It was important to note that irradiation of **1a-1e** gave dehydrogenation products **2a-2e** as the major isomers (38–45%) along with dehydrated products **3a-3e** as the minor isomers (15–21%). Interestingly, photocyclization of **1f-1j** only yielded dehydrogenation products **2f-2j** in 55–75% without observation of dehydration products. When the heteroaromatic of **2** was 1-N-methylpyrrole and R_2 was electron withdraw group such as CN and F, the irradiation reaction of 3-(2-hydroxy-phenyl)-4-(2-aryl)pyrazoles have a high chemo- selectivity to obtain dehydrogenation product 2*H*-benzo[*g*]furo/thieno/pyrrolo [2,3-*e*]indazols-10-ol.

Similarly, irradiation of **1k-1t** with UV light, dehydrogenation products **3a**, **1l-1t** was also afforded. The aromatic heterocyclic of **2** was thiophene gave products in better yields than furan. The yield of **3l** was 64% and **3a**, **3n** were 61%, 53%. As same as **1a-1j** of dehydrogenation photocyclization, when R_1 and R_2 of substrates **1k-1t** was electron withdraw group CF_3, F, 2*H*-benzo[*g*]furo/thieno[2,3-*e*]indazoles **3** gave in higher yields than the substrates bearing an electron donor group (Me, OMe). For instance, substrates **1o**, **1p**, **1s**, **1t** containing a CF_3 group, the yields of **3o**, **3p**, **3s** and **3t** were 70%, 76%, 80% and 83% and higher than others. For the intramolecular dehydrogenation photocyclization, the substrates of **1** tolerated Me, OMe, F, CN, CF_3 groups.

Scheme 3 Synthesis of 2H-benzo[g]furo/thieno/pyrrolo[2,3-e]indazoles and 2H-benzo[g]furo/thieno/pyrrolo [2,3-e] indazols-10-ol. [a b c]

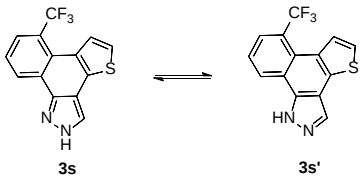


[a] Irradiation of **1a-1j** (0.25 mmol) in EtOH/H_2O (50 ml, 5 mM, v/v, 2/1) with a high pressure mercury lamp (500 W) at room temperature under Ar atmosphere for 6-9 h. [b] Irradiation of **1k-1t** (0.25 mmol) in EtOH/H_2O (50 ml, 5 mM, v/v, 95/5) with a high pressure mercury lamp (500 W) at room temperature under Ar atmosphere for 7–12 h. [c] Reaction time was determined by the complete consumption of substrate as indicated by the thin-layer chromatography (TLC).

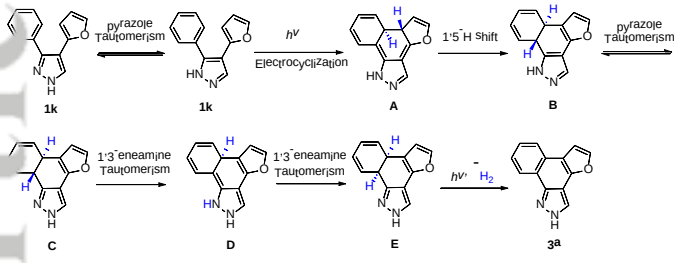
Since the dehydrogenation and dehydration cyclization products are derivatives of pyrazoles,[31] both **2** and **3** could exist in tautomeric forms (Scheme 4). In the ^{1}H NMR (DMSO-d_6) of **3s**, a major proton peak at 14.31 ppm accompanied by a minor peak at 14.16 ppm were observed along with some other small peaks in the aromatic region. However, the peaks at 14.31 ppm and 14.16 ppm were disappeared with the presence of D_2O and the spectra was simplified by the deuterium (^{2}D)-exchange experiments, which indicated the presence of two tautomeric isomers for 7-(trifluoromethyl)-2*H*-benzo[*g*]thieno[2,3-*e*]indazole. Moreover,

the ratio of two isomers (4.35:1) was determined on the basis of the integration of two active NH peaks. Similar ratio (5:1) was also observed for **3p**.

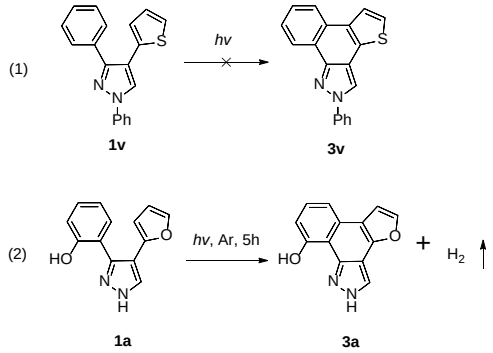
Scheme 4 Tautomeric Isomers of **3s**.



Scheme 5 Plausible Reaction Mechanism.



Scheme 6 Mechanism Research Experiments.



On the basis of experimental results and previous work,[23, e] a plausible mechanism for the formation of **3a** is proposed and presented in Scheme 5. Irradiation of **1k** with a high-pressure mercury lamp give *trans*-6*a*,6*b*-dihydro-1*H*-benzo[*g*]furo[2,3-*e*] indazole **A** via an intramolecular 6π-electron cyclization.[32] Followed by the thermal suprafacial [1,5]-H shift[33] and the recovery of the aromatic furan ring lead to the formation of intermediate *trans*-3*b*,6*a*-dihydro-1*H*-benzo[*g*]furo[2,3-*e*]indazole **B**. Proceeding the pyrazole tautomerism, *trans*-3*b*,6*a*-dihydro-2*H*-benzo [*g*]furo[2,3-*e*]indazole **C** is produced. By the 1,3-eneamine tautomerization, **C** is tautomerized *trans*-2,3-dihydro-1*H*-benzo[*g*] furo[2,3-*e*]indazole **D** and by the 1,3-eneamine tautomerization of **D**, *cis*-3*b*,6*a*-dihydro-2*H*-benzo[*g*]furo[2,3-*e*]indazole **E** is generated. Finally, **E** releases H_2 to obtain **3a** via the irradiation. This is similar to our previous work annulation of *o*-Phenylfuranylpyridines via photo-induced hydrogen evolution.[23, e]

To validate the mechanism described above, a series of experiments was designed and performed (Scheme 6). Subjection of 1,3-diphenyl-4-(thiophen-2-yl)-1*H*-pyrazole **1v** to the optimal condition failed to provide dehydrogenative product **3v** (Scheme 6, Eq. 1), which indicated the presence of active hydrogen on nitrogen and its tautomerism in the pyrazole ring **1v** was critical. H_2 was successfully detected by Gas Chromatography (GC) during the cyclization of 2-(4-(furan-2-yl)-1*H*-pyrazol-3-yl)phenol **1a**. The retention time of blank sample and standard H_2 sample was 2.471 min and 3.151 min, and the retention time of gas in the quartz tube was 2.441 min. It showed that there was generated H_2 in the process of photoinduced **1a**. (Scheme 6, Eq. 2, Results are displayed in Supporting Information Figure S2). It is given an evidence for the proposed mechanism of intramolecular dehydrogenation photocyclization.

Conclusions

In summary, an efficient, mild, and transition-metal, acid- and base-free method for the synthesis of (2*H*-benzo[*g*]furo/thieno/pyrrolo[2,3-*e*]indazols-10-ol and 2*H*-benzo[*g*]furo/thieno[2,3-*e*] indazoles) in the EtOH/H_2O with a high-pressure mercury lamp at room temperature under argon atmosphere was developed. Compared to the annulation 3-(2-hydroxyphenyl)-4-(2-phenyl) -1*H*-pyrazoles, 2-(6-phenyl-[1,2,4]triazolo[4,3-*a*]pyrimidin-7-yl) phenol and 2-(5-(naphthalen-1-yl)pyrimidin-4-yl)phenol to synthese 2*H*-phenanthro[9,10-*c*]Pyrazoles,[10] dibenzo[*f*,*h*][1,2,4] triazolo[3,4-*b*]quinazolines,[21] and polybenzoquinazolines[22] via the photocyclization dehydration, irradition of 3-(2-hydroxyphenyl)-4-(2-aryl)pyrazoles shows a high chemoselectivity to afford dehydrogenation product 2*H*-benzo[*g*] furo/thieno/pyrrolo[2,3-*e*]indazols-10-ol. The mechanism of dehydrogenation photocyclization was the process of 6π-electroncyclization, [1,5]-hydrogen shift, pyrazole tautomerism, 1,3-eneamine tautomerism and release H_2. A green-friendly method for synthesis of fused indazoles containing heterocyclic rings was provided.

Experimental

General Information. Unless otherwise noted, all reagents were purchased from commercial suppliers and used without purification. Thin-layer chromatography (TLC) analysis was performed using precoated glass plates. Silica gel was used for column chromatography. ^{1}H NMR spectra were recorded on 400 or 600 MHz spectrometer. Spectra were referenced internally to the residual proton resonance in $CDCl_3$ (δ 7.26 ppm) or DMSO-d_6 (δ 2.50 ppm). Chemical shifts (δ) were reported as part per million (ppm) in δ scale downfield from TMS. ^{13}C NMR spectra were recorded on 100 or 150 MHz spectrometer and the spectra were referenced to $CDCl_3$ (δ 77.16 ppm, the middle peak) or DMSO-d_6 (δ 39.5 ppm, the middle peak). Coupling constants (J) are reported in hertz (Hz). High-resolution mass spectrometry (HRMS) was recorded with a HRMS-ESI-Q-TOF. Melting points were measured with a micro-melting point apparatus and uncorrected. IR spectra were recorded with a FT-IR spectrophotometer with KBr pellets. Hydrogen was detected by GC.

General Procedure A for the Synthesis of 3-Phenyl-4-(2-heteroaryl)pyrazoles (aryl=furanyl, thiophenyl and *N*-methylpyrrolyl) 1a-1j.[27,28,34] Refer to the methods in the relevant literatures: the mixture of *o*-hydroxyacetophenones (10 mmol) and DMF-DMA (2 eq, 20 mmol) was dissolved in DMF (60 mL). The reaction mixture was allowed to stir at 120 °C and refluxed for 2 – 4 h. the resulting mixture was poured into saturated salt solution and then precipitate the solid. After filtration and evaporation of the solvent. The rough solid (6 mmol) undergo cyclization reaction with iodine (2 eq, 1.4 mmol) in trichloromethane solution (50 mmol). The products were purified via column chromatography on silica gel (ethyl acetate/petroleum ether, 1:60) and obtained 3-iodiochromones in good yields (85–95%) (**6**) [SI Scheme S1 1)].

The mixture of 3-iodiochromones **6** (3 mmol), arylboronic acid (3 eq, 9 mmol), $Pd(PPh_3)_4$ (5% mmol) and Cs_2CO_3 (5 eq, 15 mmol) was dissolved in a mixed solvent composed of dioxane : H_2O = 4:1 (20 ml : 5 ml). The reaction mixture was allowed to stir at 85 °C for 6 – 12 h under Ar. Then, the crude reaction mixture was poured

into water (30 mL) and extracted with EtOAc (3 × 20 mL). The volatiles were removed under reduced pressure and the residue was purified on silica gel column chromatography (ethyl acetate / petroleum ether, 1:40) to give 3-heteroarylchromones (**7**) [SI Scheme S1 2)].

A mixture of 3-iodiochromones **6** (2 mmol), pyrrole (8eq, 16 mmol), and 80mL CH_3CN was placed in a 50-mL quartz tube, and then the tube was irradiated for 5 h with a high-pressure mercury lamp (500 W). The tube was cooled to room temperature with tap water by means of an internal cold finger. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel (ethyl acetate / petroleum ether, 1:30) to give the corresponding product (**8**) [SI Scheme S1 3)].

The mixture of 3-heteroarylchromones **7, 8** (1.4 mmol) and hydrazine hydrate (2 eq, 2.8 mmol) was dissolved in EtOH (40 mL). The reaction mixture was allowed to stir at 80 °C and refluxed for 2 – 4 h. All reactions were monitored by TLC until the 3-heteroarylchromones was fully consumed. After that the mixture was poured into ice water (100 mL) and was adjusted to pH 6 – 7 with 10% HCl. The white formed precipitate was filtered and purified via column chromatography on silica gel gave product **1a-1j** in 70% – 95% [SI Scheme S2].

General Procedure B for the Synthesis of 3-Phenyl-4-(2-furanyl/thiophenyl)pyrazoles 1k-1u.[29, 30] The synthesized 3-phenylpyrazoles (5 mmol) and N-halosuccinimide (1.2 eq, 6 mmol) were dissolved in anhydrous dichloromethane (30 mL), the mixture was stirred at room temperature for 15 min to give 4-iodo-3-phenyl-1H-pyrazoles. After extraction and evaporation of the solvent, the rough solid (20 mmol) was dissolved in 30 mL THF and cooled to 0 °C under an argon atmosphere. NaH (1.5 eq, 30 mmol) was added slowly at 0 °C and the resulting mixture was allowed to stir for 30 minutes, or until hydrogen evolution was complete. SEMCl (1.05 eq, 21 mmol, 3.7 mL) was added slowly and the reaction allowed to warm to room temperature and stirred for an additional 12 hours. The reaction was quenched with 5 mL deionized water, extracted with ether, washed with brine, dried with $MgSO_4$ and the solvent removed. After workup, the resulting crude mixture was separated via column chromatography on silica gel gave product 4-iodo-3-phenyl-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrazole **9** [SI Scheme S3].

The mixture of 4-iodo-3-phenyl-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrazole **9** (1.4 mmol), arylboronic acid (3 eq, 4.2 mmol), $Pd(PPh_3)_4$ (5% mmol) and Cs_2CO_3 (5 eq, 7 mmol) was dissolved in a mixed solvent composed of dioxane : H_2O = 4 : 1 (20 ml : 5 ml). The reaction mixture was allowed to stir at 85 °C for 6 – 12 h under Ar. Then, the mixture was poured into the water and extracted with ethyl acetate (30 mL × 3). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was dissolved in 95% ethanol (15 mL) and 3 N HCl (2 mL) was added refluxing for 3 hours. To quench, 10% aqueous (byweight) NaOH (6 mL) solution was added until the mixture was neutralized as measured with pH paper, and deionized water (5 mL) and ethyl acetate (30 mL) was added. The organic layer were removed under reduced pressure, and the residue was purified by column chromatography (ethyl acetate / petroleum ether, 1:25) to get 3-phenyl-4-(2-furanyl/thiophenyl) pyrazoles **1k-1u** [SI Scheme S4].

General Procedure C for the Synthesis of 2*H*-Benzo[*g*]furo/thieno/pyrrolo[2,3-*e*]indazoles and 2*H*-Benzo[*g*]furo/thieno/pyrrolo[2,3-*e*]indazols-10-ol. 2a-2j, 3a-3t. 3-(2-Hydroxyphenyl)-4-(2-heteroaryl) pyrazoles (aryl=furanyl, thiophenyl and N-methylpyrrolyl) **1a-1j** (0.25 mmol) was added to EtOH/H_2O (v/v=2/1) (50 mL, 5 mM) and 3-phenyl-4-(2-aryl) pyrazoles **1k-1t** (0.25 mmol) was added to EtOH/H_2O (v/v=95/5) (50 mL, 5 mM). The solution was contained in a 100 mL quartz tube, degassed (ultrasound) for 30 min, deaerated by bubbling argon for 30 min and the quartz tube was sealed by parafilm; it was irradiated in a BL-GHX-V photo-chemical reactor at room temperature until reactant was consumed completely as indicated by thin-layer chromatography (TLC). The solvent was removed under reduced pressure, and the residue was purified by column chromatography (ethyl acetate/petroleum ether = 1:30 ~ 1:5) to get 2H-benzo[g]furo/thieno/pyrrolo[2,3-e]indazols-10-ol **2** and 2H-benzo[g]furo/thieno/pyrrolo[2,3-e] indazoles **3**.

Synthesis of 3s in 1 mmol Scale. 4-(Thiophen-2-yl)-3-(3-(trifluoromethyl)phenyl)-1*H*-pyrazole **1s** (294 mg, 1 mmol) was added to EtOH/H_2O (v/v=95/5) (200 mL, 5 mM). The solution was contained in 200 mL quartz tube, degassed (ultrasound) for 30 min, deaerated by bubbling argon for 30 min three times and the quartz tube was sealed by parafilm, and irradiated in a BL-GHX-V photo-chemical reactor at room temperature for 2 h, until **1s** was consumed completely as indicated by thin-layer chromatography (TLC). The solvent was removed under reduced pressure, and the residue was purified by column chromatography (ethyl acetate / petroleum ether, 1:15) to get 9-(trifluoromethyl)-2*H*-benzo[*g*]thieno[2,3-*e*]indazole **3s** (75%, 219 mg).

H_2 Detection by GC.

Gas Chromatography Conditions

With nitrogen as carrier gas, thermal conductivity detector (TCD temperature at 150 °C) and stainless steel column (column length 2 m, column temperature at 40 °C, Tam TDS-01 60~80 mesh) were used for gas chromatography analysis. Under conditions of gas velocity of 0.06 Mpa and the flow rate of 70 mL/min, gas was analyzed at room temperature with injection of 50 μL.

Experiment of Photoinduced dehydrogenative annulation of 1a

Solvent chromatographic ethanol (100 mL) and distilled water (100 mL) were both degassed for 1 h to remove most of the dissolved oxygen by ultrasonic method. Then, sodium sulfite (16 g) was added and the mixture was refluxed for 1 h under nitrogen atmosphere for solvent deoxidization. To sample quartz tube, 57 mg (0.25 mmol) **1a** and a magneton were added, and 50 mL deoxidized EtOH/H_2O (v/v=2/1) was injected into the quartz tube under nitrogen atmosphere. The blank quartz tube was treated as the same condition without **1a**. The sample quartz tube and blank quartz tube were irradiated at λ ≥ 300 nm with a high-pressure mercury lamp (500 W) for 7 h. Gas in the tubes was detected though Gas Chromatography.

Supporting Information

The supporting information for this article is available on the WWW under https://doi.org/10.1002/cjoc.2021xxxxx.

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Entry for the Table of Contents

Synthesis of 2*H*-benzo[*g*]furo/thieno/pyrrolo[2,3-*e*]indazoles *via* Intramolecular Dehydrogenation Photocyclization

Wei Zhang, Ping Wang, Xi Zhang, Rui Wang, Tao Wang, Zhicun Liu,* Zunting Zhang*

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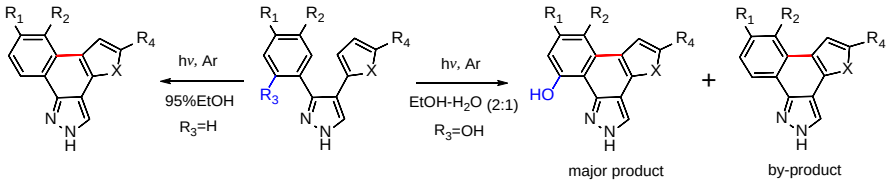

X= O, S, NMe; R_1 = H, OMe, F, CF_3; R_2 = H, F, CN, CF_3; R_3=H, OH; R_4 = H, Me.

• catalyst-, acid- and base-free; • environmental-friendly method; • high chemo-selectivity.

A catalyst-, acid- and base-free, environmental-friendly method for the synthesis of 2H-benzo[g]furo/thieno/pyrrolo[2,3-e]indazoles derivatives via irradiation of 3-phenyl-4-(2-heteroaryl)pyrazoles in EtOH/H_2O with UV light at room temperature under argon atmosphere was described. Irradiation of 3-(2-hydroxyphenyl)-4-(2-heteroaryl)pyrazoles showed a high chemo-selectivity to obtain dehydrogenation product 2H-benzo[g]furo/thieno/pyrrolo[2,3-e]indazols-10-ol.

