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Synthesis of *cis*/*trans*-dihydrochromenones *via* a photoinduced rearrangement of 4-phenyl-3-aryl/cyclohexenylcoumarins†

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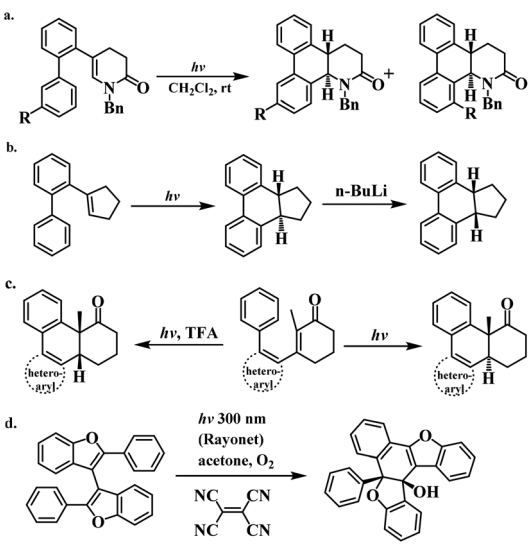
A concise and environmentally friendly protocol has been developed for the synthesis of *cis*-dihydrochromenones and *trans*-dihydrochromenones in EtOH at room temperature. Irradiation of 4-phenyl-3-arylcoumarins in EtOH with 313 nm UV light under an argon atmosphere at room temperature gave *cis*-4b,15c-dihydro-16*H*-benzofuro[3′,2′:7,8]phenanthro[9,10-*c*]chromen-16-ones and *cis*-8c,14b-dihydro-9*H*-benzo[11,12]chryseno[5,6-*c*]chromen-9-ones in good yields. And an analogous treatment of 4-phenyl-3-alkenylcoumarins as 4-phenyl-3-arylcoumarins provided *trans*-1,2,3,4,4a,14b-hexahydro-5*H*-phenanthro[9,10-*c*]chromen-5-ones. The described photorearrangement proceeded smoothly without the addition of any transition metals and additives. The photorearrangement of 4-phenyl-3-arylcoumarins is believed to proceed *via* 6π-electrocyclization, a [1,3]-hydrogen shift and keto–enol isomerization.

Introduction

According to the number of electrons involved in a given π system, electrocyclic reactions can be summarized mainly into 4, 6 and 8π-electron electrocyclization reactions.[1] They are effective and predictable methods with excellent regio- and stereocontrol explained by Woodward–Hoffmann's rules.[2] In recent years, 6π-electrocyclization reactions have been playing significant roles in the synthesis of complex target molecules,[3] especially in the synthesis of polyheterocyclic compounds and stereochemical compounds.[4] This reaction offers a diastereo selective method for the synthesis of fused polyheterocyclic compounds.[5] Irradiation of stilbene analogues through 6π-electrocyclization is one of the good strategies to synthesize *trans*-polyheterocyclic compounds.[6] For example, irradiation of biphenyldihydropyridones in CH_2Cl_2 at room temperature with a 350 nm UV light gave *trans*-dihydrophenanthrenes (Scheme 1a).[7] Photoinduced cyclization of 2-vinylbiphenyls gave *trans*-2,3,3a,11b-tetrahydro-1*H*-cyclopenta[*l*]phenanthrenes. Subsequent treatment of *trans*-2,3,3a,11b-tetrahydro-1*H*-cyclopenta[*l*]phenanthrenes with *n*-BuLi yielded *cis*-2,3,3a,11b-tetrahydro-1*H*-cyclopenta[*l*]phenanthrenes in 75% yield (Scheme 1b).[8] Photochemical syntheses of a few other *cis*-polyheterocyclic compounds have been reported. In 2020, Jon D. Rainier reported *cis*-fused dihydrophenanthrenes *via* irradiation of trisubstituted cyclopentenones in the presence of TFA with a 350 nm UV lamp in $CHCl_3$ and *trans*-fused dihydrophenanthrenes were also obtained without TFA (Scheme 1c).[9]



Scheme 1 Synthesis of *cis*/*trans* compounds *via* 6π-electrocyclization.

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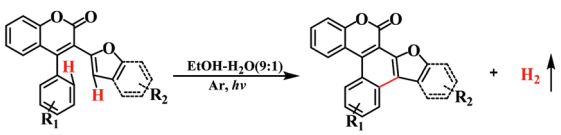
Irradiation of 2,2′-diphenyl-3,3′-bibenzofurans with 300 nm UV light under an oxygen atmosphere in the presence of tetracyanoethylene (TCNE) yielded *cis*-phenyl[1-*b*]-hydroxy[2-*b*]-naphthalenylidene-[1,2-*b*:4,3-*b*′]bisbenzofuran in 32% yield (Scheme 1d).[10]

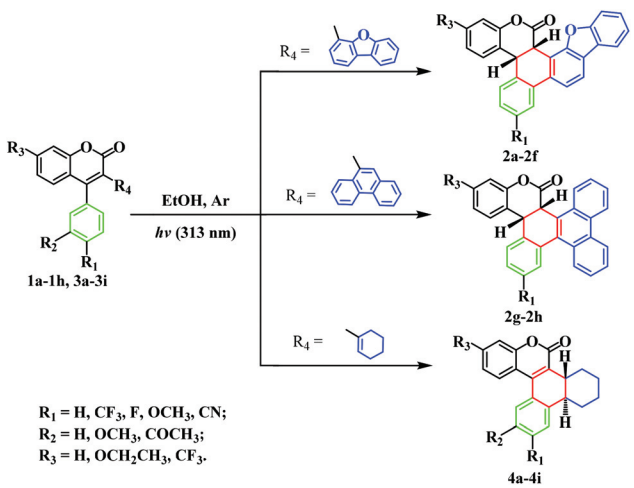
Our group has been focussing on the synthesis of aromatic fused heterocyclic compounds *via* the photocyclic dehydrogenation reaction without any oxidants or additives,[11] such as synthesizing polycyclic heteroaromatic coumarin derivatives *via* the photoinduced dehydrogenative annulation of 4-phenyl-3-heteroarylcoumarins (Scheme 2).[11g] Encouraged by our previous work, 3-(dibenzo[*b*,*d*]-furan-4-yl)-4-phenyl-2*H*-chromen-2-ones (**1**) were irradiated in EtOH with UV light (313 nm) at room temperature under an argon atmosphere. To our surprise, *cis*-4b,15c-dihydro-16*H*-benzofuro[3′,2′:7,8]phenanthro[9,10-*c*]chromen-16-ones (**2**) were obtained. In this paper, we would like to report a strategy for the synthesis of *cis*/*trans*-dihydrochromenones *via* irradiation of 4-phenyl-3-aryl/cyclohexenylcoumarins in EtOH with UV light (313 nm) at room temperature under an argon atmosphere (Scheme 3).

Results and discussion

3-(Dibenzo[*b*,*d*]furan-4-yl)-4-phenyl-2*H*-chromen-2-one **1a** was chosen as the substrate to optimize reaction conditions, and the selected reaction conditions are summarized in Table 1. Initially, irradiation of **1a** (0.25 mmol) in CH_3CN (50 mL) with a lamp (313 nm) at room temperature for 5 h gave the photo-

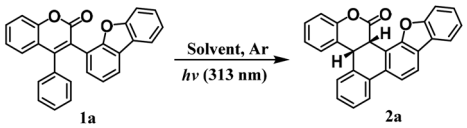


Scheme 2 Photoinduced dehydrogenative annulation of 4-phenyl-3-heteroarylcoumarins.



Scheme 3 Synthesis of *cis*/*trans*-dihydrochromenones **2** and **4**.

Table 1 Optimization of reaction conditions[a]



Entry	Solvent (v/v)	*C* (mol L^{-1})	Time[b] (h)	Yield[c] (%)
1	Acetonitrile	0.005	5	35
2	Dichloromethane	0.005	5	38
3	Acetone	0.005	4.5	43
4	*N*,*N*-Dimethylformamide	0.005	6	28
5	Toluene	0.005	6	27
6	Methanol	0.005	4	49
7	Ethanol	0.005	4	58
8	95% ethanol	0.005	5	55
9	Ethanol	0.020	6	43
10	Ethanol	0.010	5	45
11	Ethanol	0.004	4	48
12	Ethanol	0.002	4	46
13[d]	Ethanol	0.005	4	32

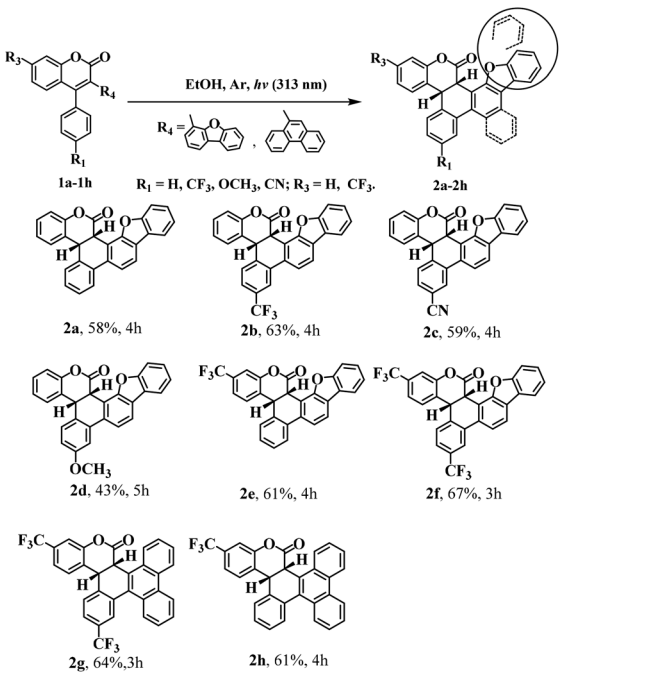
[a] Substrate **1a** (0.25 m mol) was dissolved in various solvents (50 mL, 5 mM) and irradiated with a lamp (64 W, 313 nm) at room temperature under Ar. [b] Reaction time was determined by the complete consumption of **1a** as indicated by thin layer chromatography (TLC). [c] Isolated yields were based on **1a**. [d] Performed under an open air atmosphere.

rearrangement product **2a** in 35% yield (Table 1, entry 1). Higher yields of **2a** were obtained in DCM or ACE (38–43%, entries 2 and 3) compared with those in DMF and toluene (27–28%, entries 4 and 5). Since the aprotic solvents did not give acceptable results, polar protic solvents were further examined. To our delight, the yields of **2a** were significantly elevated in MeOH and EtOH (49% and 58%, entries 6 and 7). A slightly worse result was obtained in 95% EtOH (55%, entry 8), which indicated that the presence of water might inhibit the reactivity of the radical intermediate. Furthermore, various substrate concentrations were explored. It was disappointing to observe that either higher or lower substrate concentration led to worse yields (entries 9–12). The worst yield of **2a** was observed when the reaction was performed in the open air (32%, entry 13). As a result, irradiation of **1a** (5 mM) in EtOH at room temperature under an Ar atmosphere was determined to be the optimal conditions for the synthesis of **2a**.

With the optimized conditions in hand, the scope of 3-aryl-4-phenyl-2*H*-chromen-2-ones **1** was explored and the results are listed in Table 2. Generally, substrates **1** with electron-withdrawing groups (CN or CF_3) at the R_1 or R_3 position gave photoinduced rearrangement products **2** in higher yields compared to the substrates bearing an electron-donating group (OMe). It could be further proved that substrates with two electron-withdrawing groups (CF_3) led to even higher yields of **2f** and **2g** (67%, 64%). It is worth noting that when a phenyl group is present at the 3-position (R_4 = Ph) of **1**, only a trace amount of the corresponding intramolecular rearranged product was detected by ^{1}H NMR.

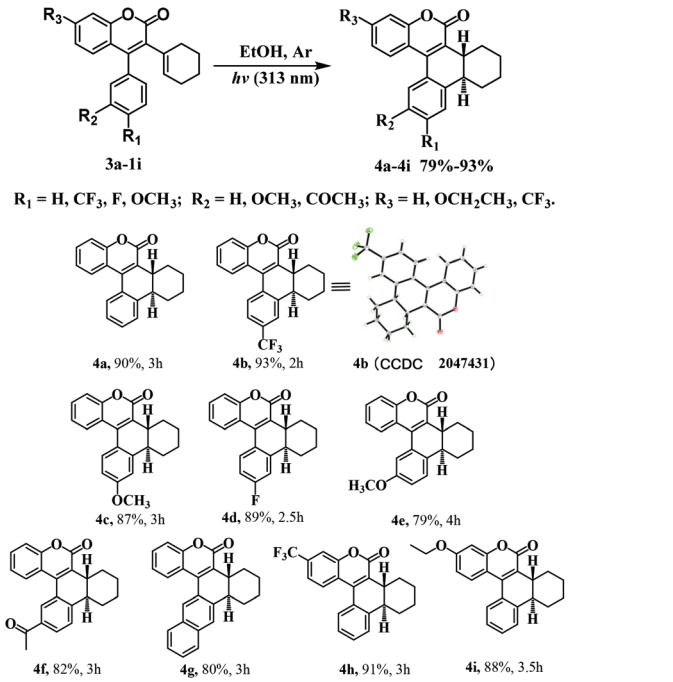
It is surprising to find out that the treatment of 3-(cyclohex-1-en-1-yl)-4-phenyl-2*H*-chromen-2-ones **3** under the optimized

Table 2 Synthesis of *cis*-dihydrochromenones **2** *via* irradiation of **1**[a,b]



[a] Irradiation of **1** (5 mM) in EtOH (50 mL) with a lamp (313 nm, 64 W) at room temperature under an argon atmosphere. [b] Reaction time was determined by the complete consumption of **1** as indicated by TLC. Isolated yield.

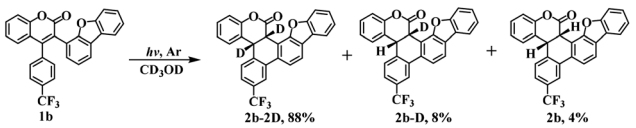
Table 3 Synthesis of *trans*-dihydrochromenones **4** *via* irradiation of **3**[a,b]



[a] Irradiation of **3** (5 mM) in EtOH (50 mL) with a lamp (313 nm) at room temperature under an argon atmosphere. [b] Reaction time was determined by the complete consumption of **3** as indicated by TLC. Isolated yield.

conditions yielded *trans*-1,2,3,4,4a,14b-hexahydro-5*H*-phenanthro[9,10-*c*]chromen-5-ones **4** in good yields (79%–93%) (Table 3). Substrates **3** with electron-withdrawing groups (Ac, F or CF_3) at the R_1, R_2 or R_3 positions gave photoinduced rearrangement products **4** in higher yields compared to the substrates bearing an electron-donating group (OMe or OEt). It is important to note that only the *trans*-dihydro isomer was obtained for 3-(cyclohex-1-en-1-yl)-4-phenyl-2*H*-chromen-2-one **3**, whereas, the sole *cis*-dihydro isomer was isolated for 3-aryl-4-phenyl-2*H*-chromen-2-one substrates **1**. The crystal structure of **4b** was characterized by single crystal X-ray diffraction, and detailed information is provided in the ESI. As illustrated in Fig. S2,† the molecule of **4b** includes two benzene rings [A (C9, C10, C11, C15, C21, C22) and D (C1, C3, C5, C12, C14, C17)], one 2*H*-pyran-2-one ring B (C4, O1, C6, C7, C9, C10), one cyclohexa-1,3-diene ring C (C1, C2, C4, C5, C7, C8), and one cyclohexane ring E (C2, O8, C16, C18, C19, C20). In the chair conformation of cyclohexane, the two dihedral angles are P1[C(8), C(16), C(20), C(18)]/P2 [C(8), C(2), C(18)] 128.61° and P1[C(8), C(16), C(20), C(18)]/P3 [C(16), C(19), C(20)] −129.93°. The twisted chair configuration of the formed cyclohexane and steric hindrance might be responsible for the *trans*-configuration.

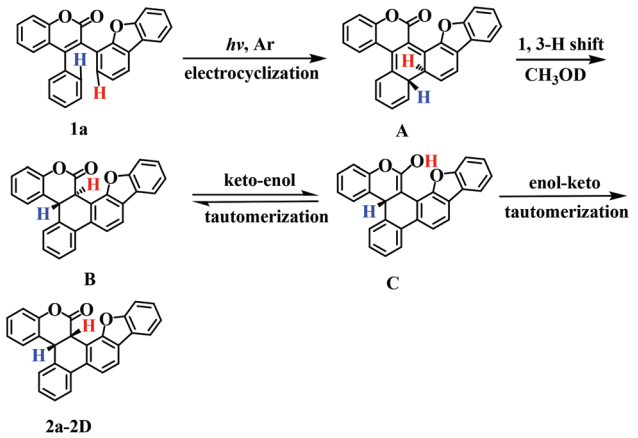
In order to further examine and validate the mechanism for the formation of **2**, irradiation of **1b** in CD_3OD with a lamp (313 nm) at room temperature under an Ar atmosphere led to the formation of 4b,15c-dideuterium of **2b** (**2b-2D**, 88%), 15c-deuterium of **2b** (**2b-D**, 8%) and **2b** (**2b**, 4%), separately (Scheme 4).



Scheme 4 Irradiation of **1b** in CD_3OD. The yields of **2b-2D**, **2b-D**, and **2b** were determined by ^1H NMR.

On the basis of literature reports[12] and experimental evidence, a plausible mechanism for the formation of **2a** is proposed and illustrated in Scheme 5. Irradiation of **1a** generates intermediate **A** *via* an intramolecular 6π-electrocyclization.[12] Second, intermediate **B** is formed *via* a suprafacial [1,3]-H shift of intermediate **A** occurring twice. It is apparent that polar protic solvent is beneficial for the process of [1,3]-H shift and keto–enol isomerization; this accounts for the irradiation of **1b** in CD_3OD, and **2b-2D** and **2b-D** were obtained. Third, the keto–enol tautomerization of **B** led to the formation of intermediate **C**, and **C** was converted to the more stable **2a**. The theoretical calculations results indicated that the energy of *trans*-4b,15c-dihydro-16*H*-benzofuro[3′,2′:7,8]phenanthro[9,10-*c*]chrom-en-16-one (**2a′**) is higher than that of **2a** (Fig. 1), which explains why *trans* **2a′** is easily converted to *cis* **2a**.

A plausible mechanism for the formation of **4a** is also proposed and illustrated in Scheme 6. Irradiation of **3a** with a 313 nm lamp led to the formation of intermediate **D**, and this



Scheme 5 Proposed possible mechanism for the formation of **2a**.

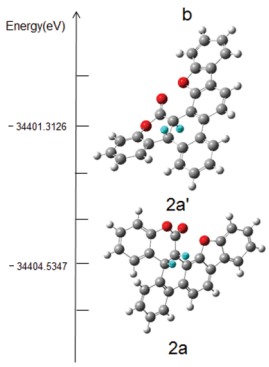
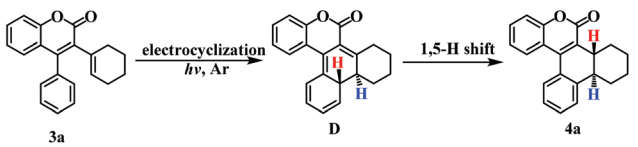


Fig. 1 The energy of **2a** and **2a'**: B3LYP/6-31G(d,p).



Scheme 6 Proposed mechanism for the formation of **4a**.

is a typical well-known intramolecular 6π-electrocyclization.[12] Intermediate **D** undergoes a [1,5]-H shift and gives product **4a**. The rearomatization of the benzene ring is the force driving this [1,5]-H shift.

Conclusions

In conclusion, we have successfully demonstrated an approach for the synthesis of *cis*-4b,15c-dihydro-16*H*-benzofuro[3′,2′:7,8] phenanthro[9,10-*c*]chromen-16-ones, *cis*-8c,14b-dihydro-9*H*-benzo[11,12] chryseno[5,6-*c*]chromen-9-ones, and *trans*-1,2,3,4,4a,14b-hexahydro-5*H*-phenanthro[9,10-*c*]chromen-5-ones by the irradiation of 4-phenyl-3-aryl/cyclohexenyl coumarin in EtOH with a lamp (64 W, 313 nm) at room temperature under an argon atmosphere. The described method proceeded under mild conditions with high atom efficiency without any additives. The mechanism for the photo- rearrangement of 4-phenyl-3-arylcoumarin to *cis*-dihydrochromenones involves 6π-electrocyclization, a [1,3]-hydrogen shift occurring twice and keto–enol isomerization.

Experimental

General procedure for the preparation of 2 and 4

Substrate 3-(cyclohex-1-en-1-yl)-4-phenyl-2*H*-chromen-2-one (**3a**) (150 mg, 0.5 mmol) was dissolved in EtOH (100 mL) at ambient temperature in a quartz tube (100 mL). The solution was degassed (ultrasound) for 30 min, deaerated by bubbling argon for 30 min, irradiated with a lamp (30 W, 313 nm) at room temperature until the reactant was consumed completely as indicated by thin-layer chromatography (TLC). Then, the volatiles were removed under reduced pressure, and the residue was purified by column chromatography (ethyl acetate/petroleum ether, 1 : 70) to give **4a** (135 mg, 90%). Analogously, compounds **2** were synthesized using the same methodology described above, with 33–93% yields.

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgements

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