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# Access to 1*a*,6*b*-Dihydro-1*H*-benzofuro[2,3-*b*]azirines and Benzofuran-2-amines via Visible Light Triggered Decomposition of *α*-Azidochalcones

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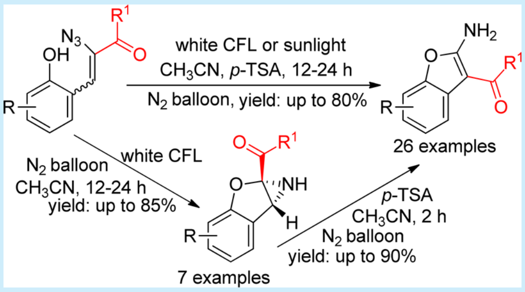
Supporting Information

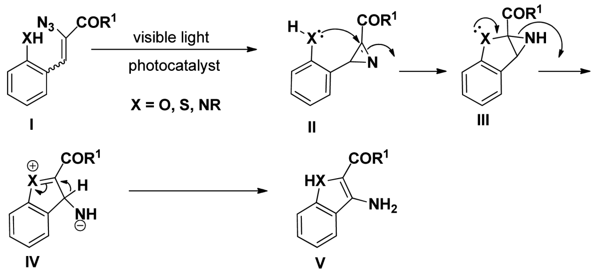
**ABSTRACT:** A novel, efficient, organic process that involves a photocatalyst-free visible light triggered decomposition of *α*-azidochalcones, followed by intramolecular cyclization, 1,2-acyl migration, and isomerization to construct benzofuran based molecular architectures, is described. The scope and limitation of the synthetic strategy were studied by synthesizing over 30 structurally diverse benzofurans in high yields.



Developing innovative solutions that access heterocyclic scaffolds through tuning the novel reactivity of reaction intermediates is a continuous enterprise in academia and industry.[1] Light is considered a traceless and nonpolluting reagent in organic chemistry that can be readily obtained from renewable sources.[2] Early development of photochemical reactions largely utilized high energy ultraviolet (UV) radiation. However, in recent years, visible light driven organic transformations have become more popular due to the selectivity, ease of handling, safety, and economics perspectives.[2−7] Most of the visible light driven synthetic methodologies reported to date require an organic,[4] metal[5] or semiconductor[6] based photocatalyst for their success. Examples of visible light driven organic transformations without using photocatalysts are very few.[7] It is largely because most of the organic compounds are transparent in the visible range of the electromagnetic radiation. This manuscript describes an efficient photochemical process that harvests visible light energy without using any external photocatalyst to construct exigent benzofuran scaffolds.

*α*-Azidochalcones are among the highly reactive azido species that have been widely utilized as a pivotal three-atom synthon for the formation of numerous fine chemicals and pharmaceuticals.[8,9] Our recent investigations on visible light driven coupling of *α*-keto vinyl azides with several substrates have established the generation of highly electrophilic 2*H*-azirines in a photosensitized manner.[9] During the course of our study, we were curious if the 2*H*-azirines could be trapped intramolecularly to construct remarkable aziridine scaffolds. In particular, we wondered if the lone pair of the heteroatom (X) could trigger the release of the strain embedded in the aziridine system **III** to generate another intermediate such as **IV**, which could be further rearranged (Scheme 1). If successful, this unprecented ring opening and rearrangement, in principle, might access 3-amino substituted benzofurans, benzothiophenes, and indoles. Presented in this manuscript are the results of a visible light triggered decomposition of 2-azido-3-(2-hydroxyphenyl)-1-phenylprop-2-en-1-ones to access substituted benzofurans.

**Scheme 1. Proposed Photodecomposition of *α*-Azidochalcones into 2*H*-Azirines and Its Intramolecular Trapping**



To test our hypothesis, 2-azido-3-(2-hydroxyphenyl)-1-phenylprop-2-en-1-one **1a** (0.1 M in $CH_3CN$) was illuminated with a 17 W white compact fluorescent lamp (CFL) in the presence of 0.1 mol % of $Ru(bpy)_3(PF_6)_2$ (Scheme 2). The reaction gave a clean new spot on TLC, and after workup and purification using column chromatography, a yellow solid (60%) was isolated which was characterized as (2-aminobenzofuran-3-yl)(phenyl)methanone **2a** rather than ((3-aminobenzofuran-2-yl)(phenyl)methanone **2a′**. Structural assignment of the product **2a** was done by comparing its $^1H/^{13}C$ NMR/IR spectra and

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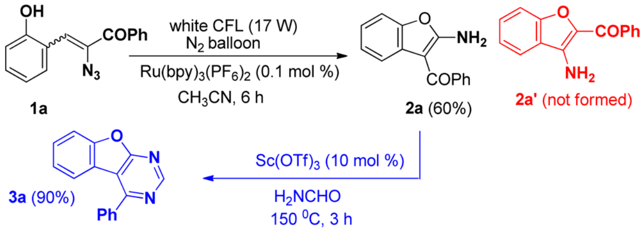
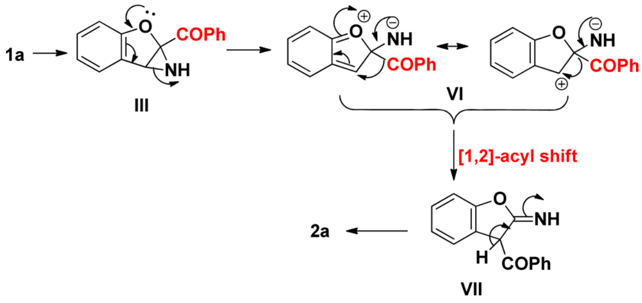
**Scheme 2. Formation of the 2-Aminobenzofuran 2a from $\alpha$-Azidochalcone 1a, and Its Conversion to 3a**



melting point with those reported in literature.[10] Though its spectral data were in good agreement with the reported values, the melting point of our product (132–133 °C) was lower by 7 °C compared to the literature report (138.9–140.3 °C). We, therefore, synthesized a known derivative of our product **3a** by reacting it with formamide in the presence of $Sc(OTf)_3$. All the spectral data including the melting point of the compound **3a** matched well with the literature reports.[10b]

Formation of **2a** can be rationalized by considering the ring opening of the initially formed aziridine **III** via generation of a benzylic carbocation **VI** followed by 1,2-acyl migration (Scheme 3). Preferential formation of **VI** over **IV** can be accounted for by considering the higher stability of the benzylic carbocation over the other alternative. Synthesis of 2-aminobenzofurans is challenging as they are considered unstable compounds, unless there is some substitution at the nitrogen atom or 3-position of the ring.[10a] This unprecendented reaction utilizes a unique reaction cascade (photodecomposition of $\alpha$-azidochalcone into 2*H*-azirine, its intramolecular trapping by neighboring OH group, 1,2-acyl migration, and isomerization) to yield 2-aminobenzofurans. A careful survey of the literature revealed that 1,2-acyl migration is well explored though its application in the synthesis of heterocylic scaffolds is rather limited.[11] This prompted us to investigate in detail the scope and limitation of the method for synthesizing this important class of heterocycle which is challenging to construct with the existing methodologies.

**Scheme 3. Mechanistic Rationalization for the Formation of the 2-Aminobenzofuran 2a from $\alpha$-Azidochalcone 1a**



An attempt to synthesize **2a** through refluxing a solution of **1a** (0.1 M in $CH_3CN$) for 6 h in the absence of light and catalyst failed, as it produced multiple spots on TLC which could not be purified. While working with compound **1a**, we found it to be light sensitive. Indeed, the UV–visible spectrum of compound **1d** (*wide infra*) showed a strong absorption of light in the 430–300 nm range with the absorption maxima at 378 nm. It showed that these compounds absorb light in the long UV to visible (violet-blue) range of the electromagnetic radiation. Therefore, we illuminated a solution of **1a** (0.1 M $CH_3CN$) in the absence of the photocatalyst with the same light source and noticed the complete decomposition of **1a** in a period of 24 h. After purification of the crude reaction product, we obtained 2-aminobenzofuran **2a** in 40% yield along with some uncharacterized products. As the yield of **2a** was better (60% vs 40%) and the reaction time was shorter (6 h vs 24 h) in the presence of the photocatalyst, a few other $\alpha$-azidochalcones **1b–n** were photodecomposed in the presence of the same photocatalyst (Figure 1).

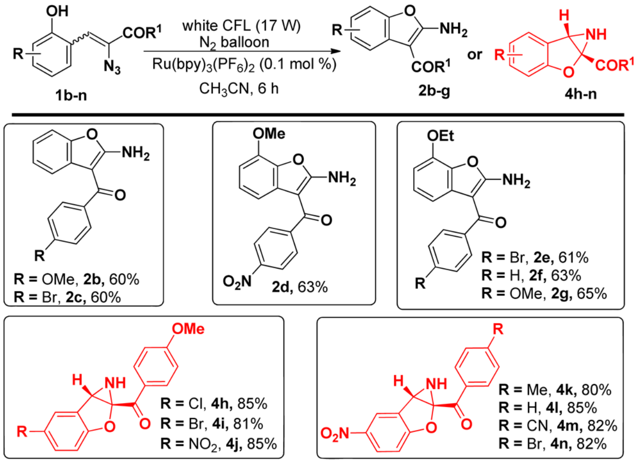


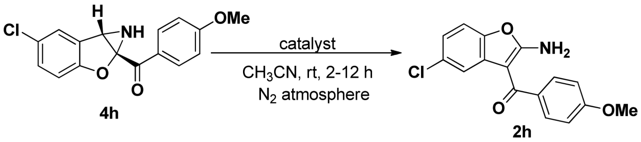
**Figure 1.** Visible light photodecomposition of $\alpha$-azidochalcones **1** to synthesize benzofurans.

The 2-aminobenzofurans **2b** (60%), **2c** (60%), **2d** (63%), **2e** (61%), **2f** (63%), and **2g** (65%) were easily synthesized using the same method in moderate yields. It is worth noting here that, in all these examples **2a–g**, the substituent R of the hydroxyphenyl ring of the substrate **1** is either H or an electron-donating (OEt and OMe) group. When the substituent R is an electron-withdrawing group such as $NO_2$ or halogen (Cl, Br), the reaction exclusively yielded the aziridine product **4h–n** in high yields (80–85%). The chemical structures of these aziridines were tentatively assigned as depicted in Figure 1 based on expected intramolecular trapping of the initially generated 2*H*-azirine **II** and were supported by their $^1H/^{13}C$ NMR, IR, and HRMS spectra. The corresponding aziridine products for the substrates **1a–g** were never isolated in any case.

Aziridines are highly strained molecules which readily undergo ring opening.[12] However, in the examples **4h–n**, it appears that the electron-withdrawing substituents ($NO_2$, Cl, Br) deactivate the ring toward the generation of *o*-quinone methides **VI** and thereby prevent further rearrangements (1,2-acyl migration and isomerization). It led us to reoptimize the reaction conditions for the formation of 2-aminobenzofurans. We wondered if a Bronsted or Lewis acid would ease the ring opening of the aziridines **4h–n** via its interaction with the lone pair of electrons of the nitrogen atom. The aziridine substrate **4h** when treated with AcOH (20 mol %), $InCl_3$ (20 mol %), $Yb(OTf)_3$ (20 mol %), and *p*-toluenesulfonic acid (*p*-TSA) (20 mol %) in acetonitrile gave 2-aminobenzofuran **2h** in 0% (no conversion), 77%, 70%, and 90% yields, respectively (Scheme 4).

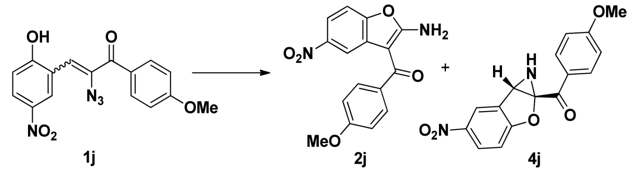
As the addition of *p*-TSA led to a very clean formation of 2-aminobenzofuran **2h** from the corresponding aziridine **4h** (Scheme 4), we thought of investigating the photodecomposition of another $\alpha$-azidochalcone **1j** in its presence (Table 1). Illuminating $\alpha$-azidochalcone **1j** with 17 W CFL for 24 h led to its

### Scheme 4. Ring Opening of the Aziridine 4h To Yield 2-Aminobenzofuran 2h



| catalyst : | p-TSA | InCl$_3$ | Yb(OTf)$_3$ | AcOH |
|---|---|---|---|---|
| catalyst loading: | 20 mol % | 20 mol % | 20 mol % | 20 mol % |
| yield of 2h : | 90% | 77% | 70% | no conversion |

### Table 1. Decomposition of $\alpha$-Azidochalcone 1j To Yield 2-Aminobenzofuran 2j and Aziridine 4j[a]



| entry | light/heating | catalyst/additives | time (h) | yield of 2j (%) | yield of 4j (%) |
|---|---|---|---|---|---|
| 1 | 17 W CFL | none | 24 | 0 | 80 |
| 2 | heating at 60 °C in dark | 20 mol % *p*-TSA | 12 | 60 | 0 |
| 3 | 17 W CFL | 20 mol % *p*-TSA | 24 | 75 | 0 |
| 4 | 17 W CFL | 20 mol % *p*-TSA and 0.1 mol % Ru(bpy)$_3$(PF$_6$)$_2$ | 6 | 75 | 0 |
| 5 | sunlight | 20 mol % *p*-TSA | 24 | 73 | 0 |
| 6 | 17 W CFL | 10 mol % *p*-TSA | 24 | 55 | 0 |
| 7 | 17 W CFL | 5 mol % *p*-TSA | 24 | 40 | 0 |
| 8 | 17 W LED | 20 mol % *p*-TSA | 48 | ND | ND |
| 9 | 17 W LED | 20 mol % *p*-TSA and 0.1 mol % Ru(bpy)$_3$(PF$_6$)$_2$ | 12 | 72 | 0 |

[a] Reaction condition: **1j** (0.1 M in CH$_3$CN), catalyst/additive, stir, ambient temperature, N$_2$ atmosphere. Yields refer to isolated yields after column chromatography. ND = Not determined.

complete decomposition yielding **4j** (80%), exclusively (Table 1, entry 1). In the presence of *p*-TSA, illuminating and heating the solution of **1j** independently gave **2j** in 75% and 60% yields, respectively (Table 1, entries 2–3). It is noteworthy that *p*-TSA guided the formation **2j** in both the thermal and photochemical conditions. It was also observed that the addition of the photocatalyst along with *p*-TSA did not affect the yield of **2j**, though the reaction time was significantly decreased from 24 to 6 h (Table 1, entry 4). A high yield of **2j** (73%) was achieved when the solution of **1j** containing *p*-TSA (20 mol %) was exposed to sunlight (Table 1, entry 5). Decreasing the amount of *p*-TSA from 20 to 5 mol % decreased the yield of **2j** (Table 1, entries 6–7). The aziridine **4j** was never detected in the reaction mixture when *p*-TSA was used (Table 1). The decomposition of **1j** was incomplete even after 48 h when the light source was changed from CFL to white LED (17 W) (Table 1, entry 8). However, **2j** was isolated in 72% yield in the presence of catalytic Ru(bpy)$_3$(PF$_6$)$_2$ and the LED light (Table 1, entry 9). As the UV–visible absorption maxima of the $\alpha$-azidochalcones lies at 378 nm, their photocatalyst-free decomposition by CFL or sunlight might be attributed to the long UV radiation associated with these light sources. In the presence of LED and photocatalyst, the reaction follows photosensitized decomposition of the $\alpha$-azidochalcones[9] (Figure 1).

As the addition of *p*-TSA significantly increased the yields of 2-aminobenzofurans, we next performed the photodecomposition of a number of $\alpha$-azidochalcones using the same method (Figure 2). A series of $\alpha$-azidochalcones (**1a–z**, **1aa–bb**) were photodecomposed in the presence of *p*-TSA to give 2-aminobenzofurans (**2a–z**, **2aa-bb**) in decent yields (up to 80%). Two $\alpha$-azidochalcones (**1aa** and **1bb**) were photodecomposed under natural sunlight, yielding the corresponding 2-aminobenzofurans in 70–75% yields. The $\alpha$-azidochalcones bearing electron-donating, electron-withdrawing, and halogen groups in the hydroxyphenyl ring yielded 2-aminobenzofurans in good yields. The corresponding aziridine products were never obtained in any case. The electron-withdrawing as well as electron-donating functional groups in the aroyl group were well tolerated by this method. The substrate **1** where the substituent R$^1$ of the COR$^1$ fragment is H or aliphatic chain was not accessible; therefore, the 1,2-acyl migration with such substrates could not be attempted.

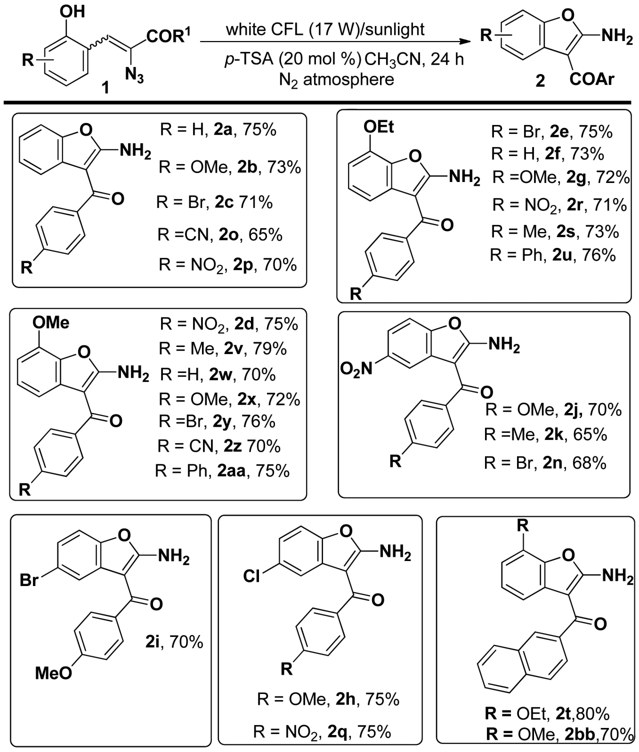
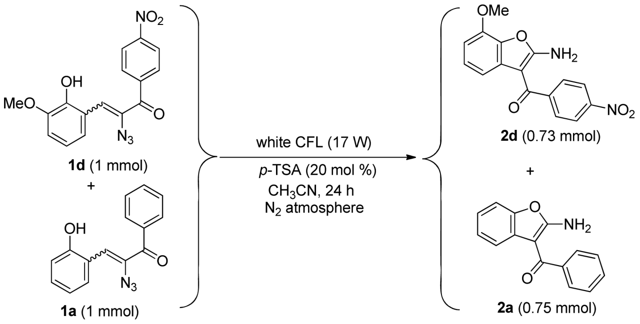


**Figure 2.** Visible light photodecomposition of $\alpha$-azidochalcones **1** to synthesize 2-aminobenzofurans **2** in the presence of *p*-TSA.

In order to test whether the 1,2-acyl migration is intermolecular or intramolecular, a crossover experiment was performed with the $\alpha$-azidochalcones **1a** and **1d** (Scheme 5). After workup, the reaction mixture yielded 2-aminobenzofurans **2a** and **2d** in 75% and 73% yields, respectively. As no crossover product was detected, the 1,2-acyl migration was suggested to be intramolecular.

In conclusion, we have developed a visible light driven, high yielding, proficient, synthetic strategy to access 2-aminobenzofurans. The striking features of the method include harvesting visible light energy without any external photocatalyst, and the use of natural sunlight to access complex benzofurans in high yields. It involves visible light triggered decomposition of $\alpha$-azidochalcones into 2*H*-azirines that undergo intramolecular trapping with the neighboring hydroxyl group. In the presence of

**Scheme 5. Crossover Experiment: Photodecomposition of the $\alpha$-Azidochalcones 1a and 1d in the Presence of *p*-TSA**



catalytic *p*-TSA, the aziridines underwent efficient ring opening, 1,2-acyl migration, and isomerization to yield 2-aminobenzofurans. The generality of the synthetic strategy was demonstrated by synthesizing 26 2-aminobenzofurans in high yields (65−80%). The intermediate fused aziridines were stable enough for isolation and characterization especially in the case of $\alpha$-azidochalcones containing a halogen- or electron-withdrawing group in the hydroxyphenyl ring. Seven such fused aziridines were isolated in 80−85% yields. Further exploration of this method over $\alpha$-azidochalcones containing thiol and amino groups (instead of hydroxyl group) to build benzothiophenes and indoles is under investigation, and the results will be communicated in due course.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.7b02643.

Experimental procedures, characterization data, $^{1}H/^{13}C$ NMR spectra of all the products (PDF)

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### Notes

The authors declare no competing financial interest.

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