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Visible light photocatalytic one pot synthesis of *Z*-arylvinyl halides from *E*-arylvinyl acids with *N*-halosuccinimide†

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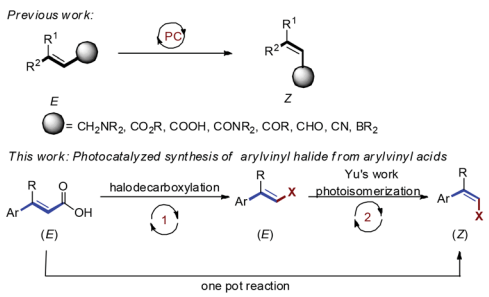
An efficient visible light photocatalytic strategy to synthesize thermodynamically less stable *Z*-arylvinyl halides (with up to >99/1 *Z*/*E* ratio and 86% yield) was developed. The reaction combined base-mediated halodecarboxylation of *E*-arylvinyl acids with *N*-halosuccinimide and visible light Ir-photocatalyzed isomerization of *E*-arylvinyl halides in a one pot sequential catalytic process.

Visible light photocatalysis has received considerable attention in recent years owing to the mild reaction conditions, green and sustainable chemistry features, and high atom-economy.[1] As reported in the literature, two different activation modes are commonly used. Most of the photochemical reactions proceed through a single-electron transfer (SET) process from the excited photosensitizers to the organic substrates or reagents. The other activation mode is an energy transfer (EnT) process in which no charge separation is involved in the whole process. This EnT activation pathway mainly depends on the triplet-state energies of the photosensitizers and the organic substrates. Synthetically useful visible light-induced organic transformation reactions through the EnT process have been successfully developed in the past decades.[1n,2]

The synthesis of multisubstituted alkenes is an important reaction because of their versatile utility as synthetic building blocks for organic synthesis and as structural elements contributing to the significant biological properties of natural products and pharmaceuticals.[3] Unlike *E*-alkenes, the strategies for synthesis of thermodynamically less stable *Z*-alkenes are not readily accessible.[4] Hammond and Arai developed pioneering photochemical $E \rightarrow Z$ isomerisations of stilbenes and styrenes and delineated the reaction mechanisms.[5] Inspired by these mechanistic studies, visible light induced $E \rightarrow Z$ isomerization has attracted great interest. In 2014, Weaver and co-workers reported $Ir(ppy)_3$ catalyzed *E* to *Z* isomerization of allylamines proceeding *via* an EnT mechanism.[6] In 2015, the Gilmour group developed photoisomerization of activated alkenes using (−)-riboflavin as an EnT photocatalyst.[7] Furthermore, Gilmour and co-workers have reported photoisomerization of styrenyl boron species and selective isomerization of β-borylacrylates.[8] In 2020, the same group reported a synthetic procedure for $E \rightarrow Z$ isomerization of β-borylacrylates *via* EnT using thioxanthone as the sensitizer eliminating the need of an aryl unit for alkene isomerization, and the inert aryl rings were replaced by a traceless BPin handle.[9]

Arylvinyl halides are versatile synthetic intermediates for organic synthesis. In particular, transition metal-catalyzed cross couplings of vinyl halides with organometallics, such as, organo boronic and organozinc reagents, are efficient methods for synthesis of multisubstituted alkenes.[10] However, synthesis of the thermodynamically less stable *Z*-isomer still poses a great challenge. In 2019, Yu's group demonstrated a synthetically useful $E \rightarrow Z$ photocatalytic isomerization of styrenyl halides (Scheme 1).[11] On the other hand, decarboxylation of α,β-unsaturated arylvinyl acids accompanied by simultaneous replacement by halogen is a useful reaction for the synthesis of styrenyl halides.[12] Considering the importance of *Z*-vinyl halides in the synthesis of multisubstituted alkenes, we hypothesize that it would be interesting to combine the halodecarboxylation of α,β-unsaturated arylvinyl acids and photoisomerization of *E*-arylvinylhalides in a one pot sequential catalytic process. Herein, we report a novel method to synthesize *Z*-arylvinyl halides by visible



Scheme 1 Photocatalytic synthesis of multisubstituted alkenes.

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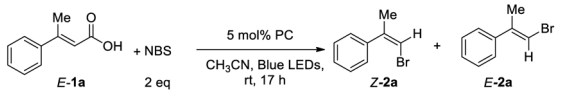
light Ir-photocatalyzed reaction of *E*-arylvinyl acids with *N*-halosuccinimide.

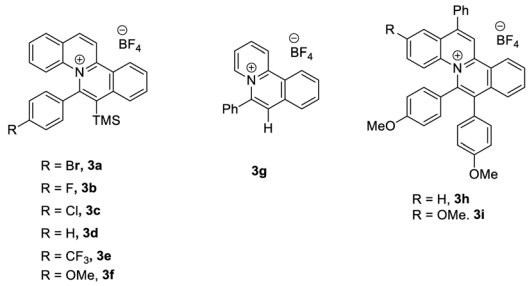
Our group has synthesized a series of new fluorescent quinolizinium compounds from quinolines and alkyne substrates.[13] Due to the high tunability and high excited state reduction potentials of the fluorescent quinolizinium compounds, we proposed that the quinolizinium compounds could be used as photocatalysts for the synthesis of *Z*-arylvinyl halides from α,β-unsaturated arylvinyl acids.

With this idea in mind, we started the initial investigation by treatment of (2*E*)-3-phenyl-2-butenoic acid (**1a**) with 2 equiv. of *N*-bromosuccinimide (NBS) in the presence of 5 mol% of photocatalyst **3a** in CH_3CN at room temperature under 30 W blue LEDs irradiation. 36% NMR yield of the desired product (*Z*/*E*)-(1-bromoprop-1-en-2-yl)benzene (*Z*/*E*-**2a**) was obtained with modest selectivity (*Z*/*E* = 44/56). Next, we optimized the reaction conditions by varying the additives. Adding K_2CO_3 and TBAI, *E*-**2a** was obtained only (entries 2–3, Table 1). Interestingly, adding

Table 1 Optimization of the reaction conditions using quinoliziniums as photocatalyst[a]

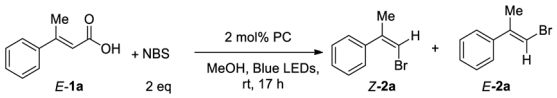


Entry	Photocatalyst (PC)	Additive	Yield[b]	*Z*/*E*[c]
1	**3a**	—	45	44/56
2	**3a**	1 eq. K_2CO_3	88	0/100
3	**3a**	1 eq. TBAI	75	0/100
4	**3a**	1 eq. CH_3CO_2H	43	56/44
5	**3a**	2 eq. CH_3CO_2H	35	77/23
6	**3a**	3 eq. CH_3CO_2H	58	66/34
7	**3a**	2 eq. $PhCO_2H$	21	99/1
8	**3a**	0.3 eq. $PhCO_2H$	32	94/6
9	**3b**	0.3 eq. $PhCO_2H$	29	86/14
10	**3c**	0.3 eq. $PhCO_2H$	22	91/9
11	**3d**	0.3 eq. $PhCO_2H$	38	84/16
12	**3e**	0.3 eq. $PhCO_2H$	24	88/12
13	**3f**	0.3 eq. $PhCO_2H$	33	94/6
14	**3g**	0.3 eq. $PhCO_2H$	35	86/14
15	**3h**	0.3 eq. $PhCO_2H$	49	69/31
16	**3i**	0.3 eq. $PhCO_2H$	63	60/40



[a] Reaction conditions: treatment of *E*-**1a** (0.2 mmol), NBS (0.4 mmol) and photocatalyst (5 mol%) in 2 mL of CH_3CN under N_2 and blue LEDs light for 17 hours at room temperature. [b] Yield was determined by ^1H NMR using dibromomethane as internal standard. [c] The *Z*/*E* ratio was determined by ^1H NMR spectroscopy.

Table 2 Optimization of the reaction conditions[a]



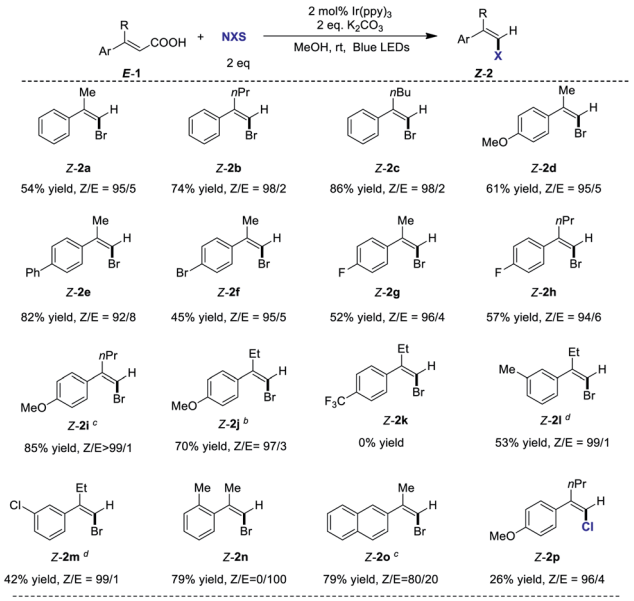
Entry	Photocatalyst (PC)	Additive	Yield[b]	*Z*/*E*[c]
1[d]	$Ir(ppy)_3$	0.3 eq $PhCO_2H$	48	52/48
2	$Ir(ppy)_3$	0.3 eq $PhCO_2H$	0	—
3	$Ir(ppy)_3$	—	0	—
4	$Ir(ppy)_3$	0.3 eq. K_2CO_3	31	61/39
5	$Ir(ppy)_3$	2 eq. K_2CO_3	60	97/3
6	$Ir(ppy)_3$	2.5 eq. K_2CO_3	56	95/5
7	$Ir(ppy)_3$	3 eq. K_2CO_3	49	96/4
8	$Ir(ppy)_3$	2 eq. Na_2CO_3	57	95/5
9	$Ir(ppy)_3$	2 eq. Cs_2CO_3	54	94/6
10	$Ir(ppy)_3$	2 eq. K_3PO_4	64	89/11
11	$Ir(ppy)_3$	2 eq. *t*BuOK	38	92/8
12	$Ir(ppy)_3$	2 eq. DBU	47	94/6
13	$Ir(ppy)_3$	2 eq. Et_3N	9	67/33
14	$Ir(Fppy)_3$	2 eq. K_2CO_3	56	89/11
15	$Ir(diFppy)_3$	2 eq. K_2CO_3	73	79/21
16	Mes-Acr-BF_4	2 eq. K_2CO_3	30	10/90
17	$Ru(bpy)_3(PF_6)_2$	2 eq. K_2CO_3	64	5/95
18	$Ru(bpy)_3Cl_2$	2 eq. K_2CO_3	48	0/100
19[e]	$Ir(ppy)_3$	2 eq. K_2CO_3	74	0/100
20	—	2 eq. K_2CO_3	54	4/96

[a] Reaction conditions: treatment of *E*-**1a** (0.2 mmol), NBS (0.4 mmol) and photocatalyst (2 mol%) in 2 mL of MeOH under N_2 and blue LEDs light for 17 hours at room temperature. [b] Yield was determined by ^1H NMR using dibromomethane as internal standard. [c] The *Z*/*E* ratio was determined by ^1H NMR spectroscopy. [d] The reaction solvent was CH_3CN. [e] No light irradiation.

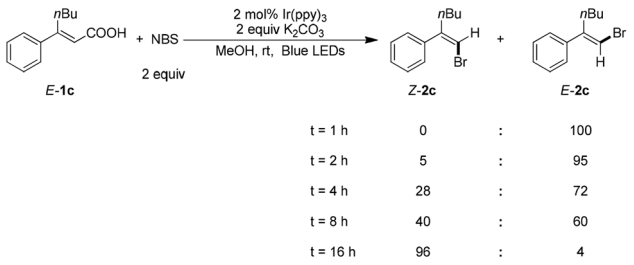
1.0 equiv. of acetic acid as the additive, improvement in the *Z*/*E* ratio of **2a** (56 : 44) was observed (entry 4, Table 1). Then, various acids were examined in this reaction. 0.3 equiv. of benzoic acid was found to be the best additive (entry 8, Table 1). Next, studies were conducted for the photocatalysts. It was found that the reaction could proceed to afford the product **2a** with modest to excellent *Z*/*E* ratios using most of the quinolizinium compounds synthesized by our group (entries 9–16, Table 1). In particular, quinolizinium **3f** was found to be the best photocatalyst giving product (*Z*)-**2a** (*Z*/*E* = 94 : 6) in 33% yield (entry 13, Table 1). With these reaction conditions, we tried to expand the scope of this reaction with different *E*-arylvinylcarboxylic acids. However, no desired product was observed regardless of the substituent on the aryl ring, such as, methyl, electron-donating group (OMe) or electron-withdrawing group (CF_3).

Then, we screened the reaction conditions with metal photocatalyst $Ir(ppy)_3$. Styrenyl hailde **2a** was obtained in 48% NMR yield in a *Z*/*E* ratio (52 : 48) (entry 1, Table 2). When the reaction conditions of 2 mol% $Ir(ppy)_3$ with 0.3 equiv. of K_2CO_3 were used, the reaction proceeded to give the desired product **2a** with 61 : 39 *Z*/*E* ratio. Increasing the base loading from 0.3 equiv. to 2 equiv. improved the NMR yield of **2a** from 31% to 60% and gave a 97 : 3 *Z*/*E* ratio (entry 5, Table 2). When we further increased the loadings of the base, the yield dropped slightly (entries 6

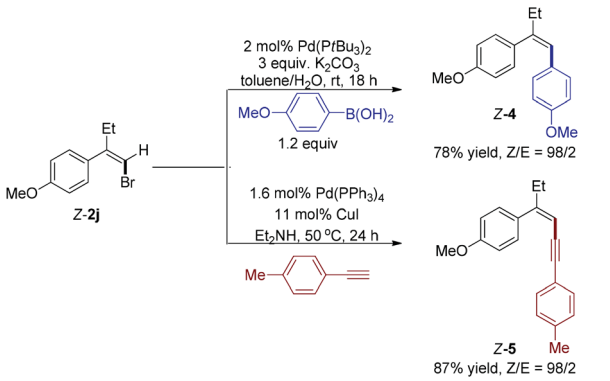
Table 3 Scope of the visible light photocatalytic reactions[a]



[a] Reactions were performed with 0.2 mmol substrate at room temperature in MeOH (2.0 mL) using 2 mol% fac-Ir(ppy)$_3$ under 30 W blue LEDs irradiation. *Z*/*E* ratios were determined by ^{1}H NMR spectroscopy. Isolated yields. [b] 5.0 mmol scale. [c] 5 mol% fac-Ir(ppy)$_3$. [d] 1 mol% fac-Ir(ppy)$_3$.



Scheme 2 Reaction progress monitoring of *E*-**1c**.



Scheme 3 Pd-catalyzed coupling reactions of styrenyl bromide *Z*-**2j**.

and 7, Table 2). Next, various inorganic and organic bases were examined in this reaction, and α,β-unsaturated arylvinyl acid **1a** was found to be successfully converted to **2a** in moderate to good *Z*/*E* ratios (entries 8–13, Table 2). Several other photocatalysts were also screened, such as, Ir(Fppy)$_3$, Ir(diFppy)$_3$, Mes-Acr-BF$_4$, Ru(bpy)$_3$(PF$_6$)$_2$ and Ru(bpy)$_3$Cl$_2$, but none of them gave better yields or *Z*/*E* ratios (entries 14–18, Table 2). Only *E*-**2a** was obtained in the absence of light (entry 19, Table 2), and a trace amount of *Z*-**2a** was observed without photocatalyst (entry 20, Table 2).

After optimizing the reaction conditions, we next sought to explore the scope of the reaction. The results summarized in Table 3 show that this reaction provides a straightforward route to a variety of *Z*-arylvinyl halides **2** directly from *E*-arylvinyl acids **1**. Different alkyl substitutions at the α position (R), such as methyl, ethyl, propyl and butyl were compatible in the reaction, affording the corresponding *Z*-arylvinyl bromides in high stereoselectivities (up to 99/1 *Z*/*E* ratios). The reaction was affected by the electronic effect of the substituents on the aryl ring. Substrates bearing electron-donating group (OMe), phenyl, and halogens gave the desired *Z*-**2** in high *Z*/*E* ratios (up to >99/1) (**2d–2j**, Table 3). However, *E*-arylvinyl acid **1k** with electron-withdrawing group (CF$_3$) did not afford the corresponding bromide **2k**. The efficiency of the reaction was not impeded by *meta*-substituents on the aryl ring (**2l** and **2m**, 53% and 42% yield, respectively, 99/1 *Z*/*E* ratios). In contrast, the *ortho*-substituent hindered the reaction, only providing the halodecarboxylation product *E*-**2n**. In addition, naphthyl ring was also compatible under these mild reaction conditions giving *Z*-**2o** (*Z*/*E* = 80/20) in 79% yield. *N*-Chlorosuccinimide (NCS) can also be used in this halodecarboxylation/isomerization smoothly to afford *Z*-**2p** in 96 : 4 *Z*/*E* ratios. When 1.03 g of **1j** was used, the corresponding styrenyl bromide *Z*-**2j** was obtained without compromising on yield and stereoselectivity, representing the robustness of this reaction.

To gain mechanistic insight on this reaction, the reaction progress was monitored under the optimized reaction conditions (Scheme 2). Complete halodecarboxylation of *E*-**1c** was observed in 1 hour to give *E*-**2c**, which suggests that the isomerisation is the rate-determining step. Some product *Z*-**2c** was obtained after 2 hours. Almost complete $E \rightarrow Z$ isomerization was observed over the course of 16 hours.

At last, we performed two Pd-catalyzed coupling reactions with styrenyl bromide *Z*-**2j** to further illustrate the synthetic utility of this cascade reaction (Scheme 3). When 4-methoxyphenylboronic acid was treated with bromide *Z*-**2j** using Pd(P*t*Bu$_3$)$_2$ as catalyst, Suzuki–Miyaura cross coupling reaction[14] successfully afforded trisubstituted alkene *Z*-**4** (*Z*/*E* = 98/2) in 78% yield. Moreover, Sonogashira coupling reaction[15] with 1-ethynyl-4-methylbenzene gave enyne *Z*-**5** (*Z*/*E* = 98/2) in 87% yield.

Conclusions

In conclusion, we have developed an efficient visible light photocatalytic strategy to synthesize *Z*-arylvinyl halides directly from *E*-arylvinyl acid with *N*-halosuccinimide through a sequential halodecarboxylation/photoisomerization sequence with up to >99/1 *Z*/*E* ratio and 86% yield. A series of *E*-arylvinyl

acids were converted to *Z*-arylvinyl halides with high stereoselectivity under mild reaction conditions.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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