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Ortho-substitution groups promoted photo-induced E (trans) → Z (cis) isomerization

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ABSTRACT

The past decades have witnessed the fast growth of *ortho*-directing group assisted in C—H activation and olefination. Herein we addressed these olefination products' photo-induced $E \rightarrow Z$ isomerization in term of various *ortho*-substitution groups. Initially, we discovered ortho benzoxazolyl aryl acrylates effectively undertook $E \rightarrow Z$ isomerization (up to 88% yields) under 365 nm direct irradiation. Furthermore, scoping other five directing groups in C—H activation and olefination revealed that acetylamino group also present to be good *ortho*-substituted groups that enhancing $E \rightarrow Z$ isomerization. Controlled experiment shows the substitution position is vital for photo-induced isomerization or [2 + 2] cycloaddition. Lastly, prevalent interesting fluorescent quenching/change phenomenon were always in accompany with the isomerization. X-ray single crystallography disclose the isomerization process undertook significant conjugated distortion of the aryl acrylates fragment, we proposed such change could contribute to fluorescent and absorbent decrease.

Introduction

The alkene with two different substituents on different carbons owns two kind isomers, stereo specially *E*-, *Z*- isomers. *E*- isomer configuration, the two substituents are dispersed in most extent, is thermodynamic favored configuration. However, methodologies normally access to *E*-isomer were much more than *Z*-isomer, [1] including the traditional olefin methods [2] as well as transition-metal-catalyzed C—H oxidative olefination. [3] To fabricate thermodynamically disfavored *Z*-alkenes, special reaction reagents or catalysts are required [4] With the photochemistry development in recent years, much attentions have focused on the photochemically driving alkene *E*/*Z* isomerization by energy uphill catalyst/photosensitizer. For example, Weaver took use of cyclometalated iridium(III) photo-sensitizer complex as photocatalyst in the *trans*-to-*cis* isomerization of aryl allylamine. [5] Gilmour developed a bio-inspired organic photo-sensitizer which especially effective for *β*-substituted acrylates with electron-withdrawing groups, like cyano, ester, carboxylic acid, more recently, energy transfer strategy was also applied in aryl or alkyl acrylates double bonds *E*/*Z* isomerization [6]. Arthur E. Bragg reported a higher conjugated alkene molecule (1,2-dithienyl-1,2-dicyanoethene), which could undergo reversible quantitative isomerization under triplet or singlet electron manifold relaxation. [7] Moreover, acrylate naphthalenyl [8] or anthracenyl [9] had undertaken the $E \rightarrow Z$ isomerization by direct ultraviolet excitation without energy transfer catalyst.

Additionally, *ortho* C—H activation for olefination have developed in full blossom with various directing groups and transition metal catalyzed C—H activation. Up to now, directing groups that could furnish C—H olefination with alkyl acrylate mainly comes from oxygen-containing groups or nitrogen-containing groups with weak coordination ability [10], for example, oxazoline [11], ketone [12], ester [13], acetylamide [14], *N*-sulfonyl imine [15], hydroxyl [16]. It is proved that the olefination of C—H bond usually affords the *E*-olefins, since the key step involves thermal stable favored *β*-H elimination during the conversion. Considering the *E*/*Z*-isomers difference in structure and physical property, it is necessary to develop feasible method for converting *E*-olefins to the corresponding *Z*-isomers.

In recent years, our group have focused on the 2-aryl benzoxazoles backbone construction and application in C—H activation, organometallic catalyst [17]. In the C—H olefination study[17a], we observed an interesting phenomenon. The fluorescent light spot of compound ***E*-1** (see Table 1) on the TLC plate was slowly changed from sky blue to yellow when irradiated by UV-365 nm (0.4 mW/cm^2). For understanding the process deeply, *in-situ* NMR experiment was conducted that exposure ***E*-1** solution to 365 nm irradiation. To our surprised, after 8 h, the typical signal

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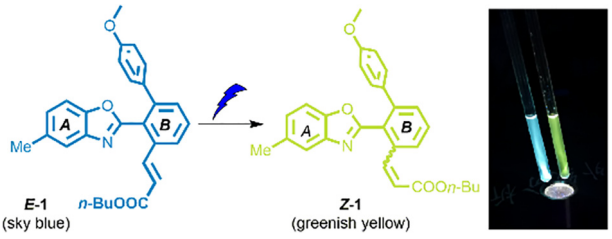
Table 1
The initial discovery of *ortho*-benzoxazoyl aryl acrylate UV-induced *E*/*Z* isomerization [a].

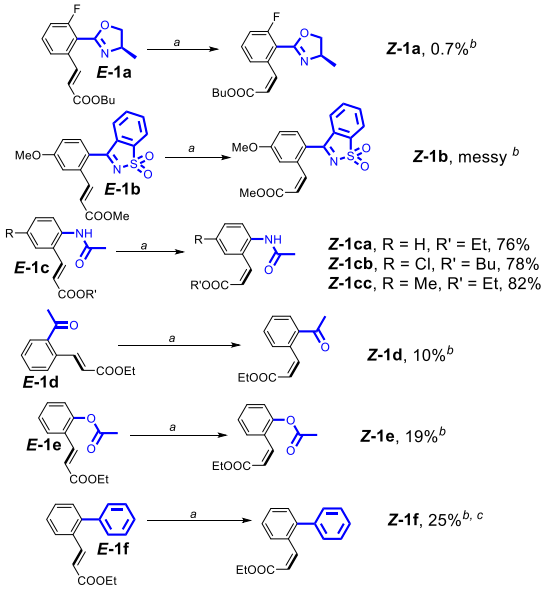


[a] $CDCl_3$ (0.5 mL, 0.1 M), 0.4 mW/cm^2 365 nm, room temperature (r.t.), 3 days, isolated yield 73%, *in-situ* NMR yield 88%. The right picture shows the $CDCl_3$ solutions of ***E*-1** (sky blue) and ***Z*-1** (greenish yellow) when exposed to 365 nm.

(J = 16 Hz) of *trans*-olefin decreased, generated a new set signal (J = 12 Hz), which demonstrated alkene take place *E*-*Z* isomerization (For detailed H NMR spectra of time-course UV-365 nm, see **Fig. S1** in Supporting Information). Additionally, elongation of the exposure time to 3 days, the new set signal constituted up to 88%, and after silica gel chromatography, affording ***Z*-1** with 73% isolated yield. For improving conversion efficiency, we tested a more powerful UV light source (365 nm laser, 4 mW/cm^2). Surprised, after two hours irradiation, 64% *Z*-isomer ^{1}H NMR yield was observed, however, irradiation another 2 h heated the reaction solution up to 40 ^{0}C and messed up the reaction. So, to acquire high yield of *Z*-isomer, we chose 0.4 mW/cm^2 365 nm light for the optimal condition. In Addition, we have screened different solvents, only slight influence was observed on this *E*/*Z* isomerization (**Table S1**). Herein, we tried to disclose a feasible complement to *Z*-alkenes of *ortho*-substitution aryl acrylates with resort to $E \rightarrow Z$ isomerization in the absence of energy transfer catalyst.

With the initial discovery of the benzoxazolyl containing aryl acrylate *E*/*Z* isomerization, we proposed that it's the benzoxazolyl fragment that play the vital role for light sensitizer and fluorescent property. To demonstrate our proposal, we test other directing groups that ever utilized in C—H activation (Table 2).

Table 2
Scope of other *ortho*-directing groups for UV-induced *E*/*Z* isomerization [a].



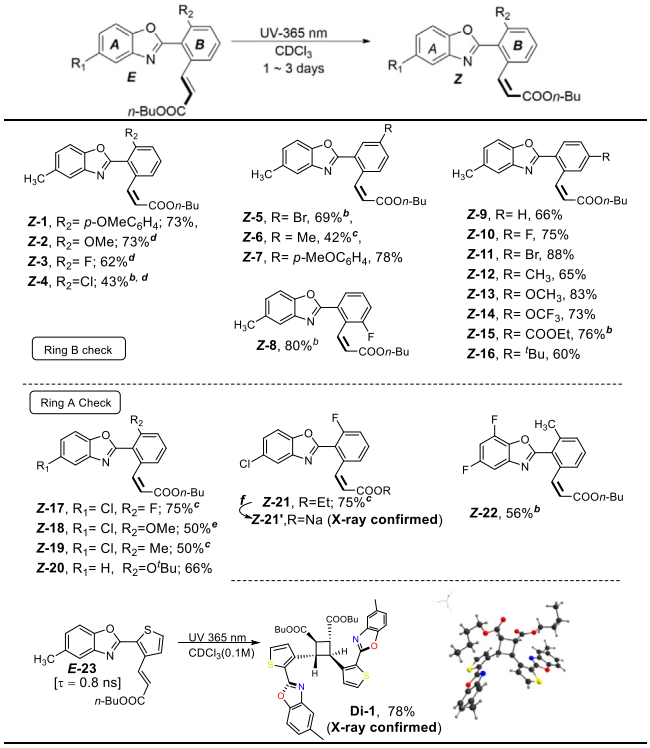
[a] Without other notes: $CDCl_3$ (0.5 mL, 0.1 M), 0.4 mW/cm^2 365 nm, r.t., 3 days, isolated Yield; [b] *in-situ* NMR yields; [c] 7 days.

Initially, we tested non-conjugated oxazolinyl containing ***E*-1a**, only 0.7% *Z*-isomer was observed (*in-situ* H NMR) when exposed to 365 nm for 3 days. This result indicates the conjugated benzoxazolyl fragment is crucial for the ***E*/*Z*** isomerization. Then, ***E*-1b** was applied under the standard condition, the reaction present messy to observe the apparent ***Z***-isomer by *in situ* ^{1}H NMR, which may result from side reactions between the methyl acrylate with amine bond (-C=N-) site [18]. After exploring the benzoxazolyl analogous directing groups, we checked other important and simple directing group, acetylamino (-NHAc), which was the first one utilized as the *ortho* C—H activation and olefination [19]. To our delight, we found ***E*-1ca** showed good *E*-*Z* isomerization under 365 nm irradiation, more importantly, its *Z*-isomer could easily be isolated from *E*-isomer due to large R_f differential existed. Additionally, ***E*-1cb** with electron-withdrawing group chloro, ***E*-1cc** with electron-donating group methyl also showed high $E \rightarrow Z$ isomerization to give ***Z*-1cb** (78%), ***Z*-1cc** (82%). Furthermore, low conjugated directing groups, acetyl (***Z*-1d**), OAc (***Z*-1e**) and phenyl (***Z*-33**), their low *E*/*Z* isomerization demonstrated the importance of *ortho*-benzoxazolyl and acetylamino groups.

After the initial discovery and substitution scope, benzoxazolyl and acetylamino groups are both special and efficient chromophore that could enhance the $E \rightarrow Z$ isomerization. In this paper, benzoxazolyl containing molecules will be further discussed in terms of functional groups tolerance, the relative position between benzoxazolyl and acrylate fragment for this reaction. We scope various benzoxazolyl containing aryl acrylates. Firstly, electronic effect and steric effect from 2-aryl benzoxazoles were scoped. Considering the 2-aryl benzoxazoles containing two aryl fragments, we denoted two aryl rings of the molecule backbone as ring **A** and **B** respectively for convenient discussion (Table 3).

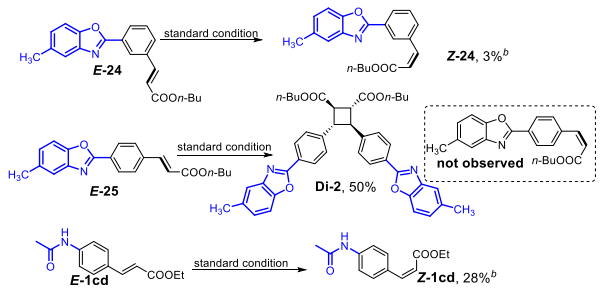
When ring **A** was substituted by methyl, ring **B** was substituted with electron-withdrawing group (EWG) fluoro, or electron-donating group (EDG) methoxy, totally showed moderate to good isolated yield of *Z* isomers (***Z*-2**, 73%, ***Z*-3**, 62%). However, the chloro substituted showed comparatively lower conversion (***Z*-4**, 43%). Then, we turned the substitution of ring **B** to *meta* position, bromo, *p*-$MeOC_6H_4$ all undertook good $E \rightarrow Z$ isomerization (***Z*-5**, ***Z*-7**), which demonstrated that the pseudo-heavy atom could accelerate this conversion, while methyl shows moderate conversion (***Z*-6**). More interesting, when butyl acrylate fragment was anchored between fluoro and benzoxazolyl groups, it could also isomerize (***Z*-8**, 80%). In our previous work, it was proved that olefinic hydrogen have hydrogen bond effect with nitrogen and fluoro atom in compound ***E*-8**,[17a] which means no negative effect result from hydrogen bond interaction. Lastly, *para* substitution substrates show good tolerance to this conversion, albeit with moderate to good isolated yields (***Z*-9** ~ ***Z*-16**). Worthy to note, EWG substituted substrates bear high *E*-*Z* isomerization under optimized condition. Furthermore, electronic effect for this conversion was also checked in regard of substitution on ring **A**. When ring **A** was forged with chloro or hydrogen substrates, ***Z*-17** ~ ***Z*-21** could be obtained in moderate to good yield (50% ~ 75%). The isomerization efficiency decreases dramatically as for difluoro anchored substrate (***Z*-22**, 56%, 3 days) with comparison to ***Z*-2** (73%, 50 h), ***Z*-18** (50%, 10 h). Apart from *E*-*Z* isomerization, we observed some substrates undertook chemo-selectively alkene [2 + 2] dimerization to give *anti*-head-to-head cyclobutanyl derivatives, for example, ***E*-23** forged **Di-1** (78%) [20]. Its solid structure was disclosed by X-ray single crystallography, and adopt thermodynamically stable configuration, *anti-head-to-head*. (see **Table S2, S3** for details) Furthermore, we addressed the relative position between benzoxazolyl fragment and aryl acrylate. To our surprise, ***E*-24**, whose acrylate fragment located *meta* to the benzoxazolyl fragment, failed to

Table 3
The scope of *ortho*-benzoxazolyl substituted aryl acrylates under 365 nm irradiation [a].



[a] Without other notes: $CDCl_3$(0.5 mL, 0.1 M), 0.4 mW/cm^2, r.t., isolated yield, exposure to 365 nm, 3 days; [b] *in-situ* NMR yields; [c] 2 days; [d] 1.5 days; [e] 0.5 days; [f] **Z-21** hydrolysis by 2.0 eq NaOH in THF/H_2O (1 mL/0.2 mL), r.t., 6 h.

Table 4
The comparison of *meta*, *para to ortho*-benzoxazolyl aryl acrylates on the UV-induced *E*/*Z* isomerization [a].



[a] $CDCl_3$ (0.1 M, 0.5 mL), 0.4 mW/cm^2 365 nm, r.t., 3 days, isolated Yield; [b] *in-situ* observed NMR yields.

observe effective conversion. In contrast, ***E*-25** was exclusively converted [2 + 2] to dimer product (**Di-2**) in 50% NMR yield without detectable *Z*-isomer. Hence benzoxazolyl fragment substituted position was vital to determine aryl acrylates behaviors under direct 365 nm irradiation. Similar relative position effect was also observed in *ortho* (Table 2, ***E*-1ca** ~ **1cc**)/*para* (Table 4, ***E*-1cd**)-acetyl amide differential: the former afforded at least 76% yield, while the later undertook only 28% isomerization, outline the vital role of substituted special chromophore for direct *E*/*Z* isomerization.

To disclose the ***E*/*Z*** isomers spatial distribution, several attempts were focused on the molecules with relatively high polar functional groups, like ester, halogen, methoxy group. Several careful attempts for *Z*-isomer suitable single crystal failed. Strategy of increasing molecular polarity, either shortening the flexible alkyl linkage (***Z*-21**) or direct hydrolysis acrylate ester into acrylate acid (***Z*-21′**) both successfully forged *Z*-isomer single crystals. Meanwhile, we are lucky to get a single crystal of ***E*-17**, which has the same molecular skeleton as ***E*-21**, only the ester group is slightly different. The X-ray diffraction showed that ***Z*-21** and ***E*-17** possessed structural characteristics of olefins trans /cis isomerism (Fig. 1) and disclosed *cis*-configuration ***Z*-21** and ***Z*-21′** owns 58°and 40° torsion angle respectively between acrylate fragment and Ring **B** (**Table S5, S6**), and the acrylate fragment adopted the *cis*-configuration as expected [21].

Interesting, exclusively significant fluorescent change was accompanied by these efficient *ortho* chromophores assisted *E* → *Z* isomerization (benzoxazolyl containing substrates). For example, Fig. 2 showed ***E*-21** bore apparent 365 nm fluorescent emission property, presenting strong fluorescent quantum yield ($\Phi_{E\text{-}21}$ = 0.61), however, after *E* → *Z* isomerization, the fluorescent intensity of ***Z*-21** decreased 32-folds ($\Phi_{Z\text{-}21}$ = 0.02), which may result from aryl acrylate co-plane distortion (*vide supra*).

The excited triplet lifetimes of some typical *E*-isomers were tested. Preliminary results showed that the *ortho* effect will elongate the excited triplet lifetime (τ) (Table 5 and **Figs. S2-S5**), nearly three times as long as lifetimes of *ortho* ***E*-9** in comparison to *meta* ***E*-24** and *para* ***E*-25**. Meanwhile the short lifetime of ***E*-23** (0.8 ns) may result from thiophene's sulfur heavy atom spin–orbit effect and not be facilitate *E*/*Z* isomerization.

In summary, we discovered *ortho*-benzoxazolyl/ acetylamino substituted aryl acrylate could undertake *E* → *Z* isomerization without uphilled or energy transfer catalyst. This approach makes

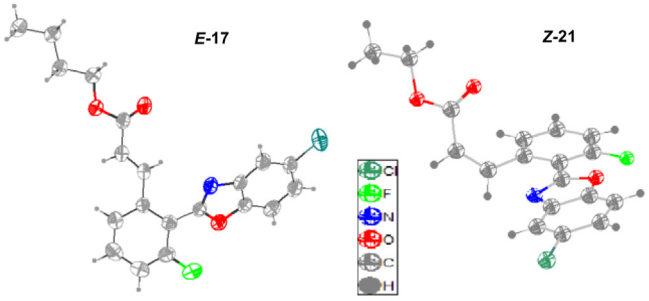


Fig. 1. The structures of *E*-17 (left) and *Z*-21(right).

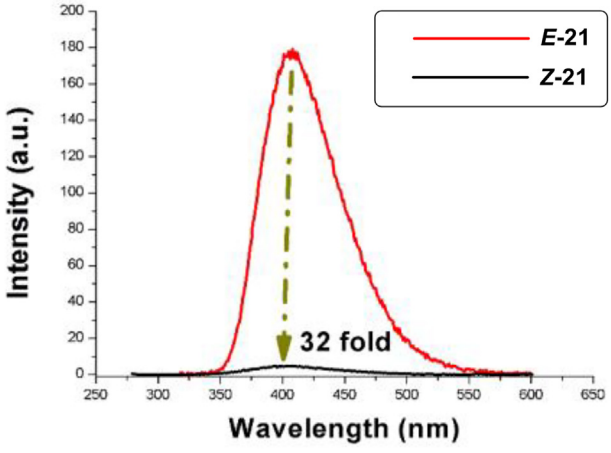
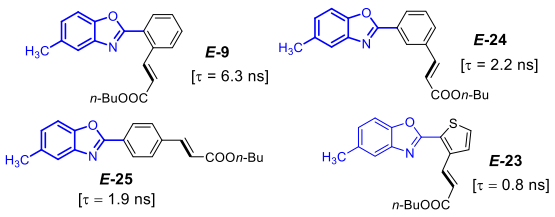


Fig. 2. Emission spectra of *E*/*Z*-21 at in dichloromethane (10^{-4} M) at 298 K.

Table 5
The excited triplet lifetimes of some *E*-isomers.



one good complement to directing group assisted C—H olefination, which dominantly afforded *E*-alkenes. Substrates scope demonstrated the broad functional groups tolerance for the photo-induced *E* → Z isomerization. The X-ray diffraction disclosed the configuration of *trans* and *cis*-isomers and the isomerization process undertake significant conjugated distortion of the aryl acrylates fragment. Furthermore, controlled substrates experiment demonstrated that the relative position between the benzoxazolyl/acetyl amido groups and acrylate fragment: only the *ortho* position will facilitate the *efficient E-Z* isomerization while the *meta or para* will either decrease the isomerization efficiency or forge [2 + 2] dimer. Furthermore, the excited triplet lifetime of the *E*-isomer with the *ortho* position is longer than the *meta or para* one. Lastly, significant fluorescent decreases as well as spatial distortion was accompanied by the special acrylates *E/Z* isomerization according to fluorescent chromatography and X-ray single crystallography.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

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Appendix A. Supplementary data

Supplementary material that may be helpful in the review process should be prepared and provided as a separate electronic file. That file can then be transformed into PDF format and submitted along with the manuscript and graphic files to the appropriate editorial office. Supplementary data to this article can be found online at https://doi.org/10.1016/j.tetlet.2020.152396.

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[21] Crystal of E-17, Z-21, Z-21' and Di-1 have deposited in The Cambridge Crystallographic Data Centre, their deposit codes are 2016770, 1978544, 2016771, 1858990 respectively.