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COMMUNICATION

N-Heterocyclic Carbene/Photo-Cocatalyzed Oxidative Smiles Rearrangement: Synthesis of Aryl Salicylates from *O*-Aryl Salicylaldehydes

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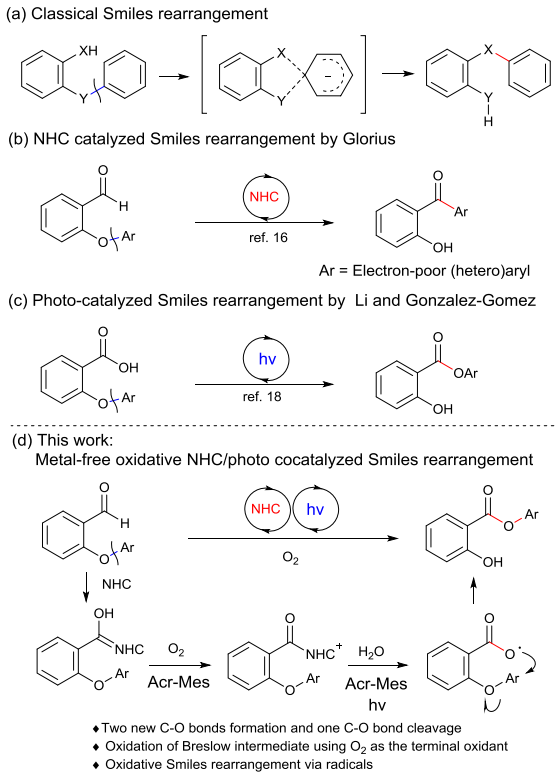
The N-heterocyclic carbene/photo-cocatalyzed oxidative Smiles rearrangement of *O*-aryl salicylaldehydes was developed. Both electron-deficient and electron-rich aryls worked well as the migrating group, giving the corresponding aryl salicylates in good yields. This reaction features two new C-O bonds formation and one C-O bond cleavage via metal-free oxidation of Breslow intermediate using oxygen as the terminal oxidant and following Smiles rearrangement under photocatalysis.

Classically, the catalytic generation of Breslow intermediate from aldehyde is the key step in N-heterocyclic carbene (NHC) catalysis[1] for various reactions, such as benzoin reaction,[2] aza-benzoin[2] and Stetter reaction.[3] The NHC-catalyzed generation of homoenolate intermediate had been independently reported by Bode et al.[4] and Glorius et al.[5] In recent years, the oxidation of Breslow and homoenolate intermediates to the corresponding azolium intermediates have been widely used in NHC organocatalysis. Typical oxidative NHC catalysis requires stoichiometric oxidants, such as MnO_2,[6] phenazine,[7] quinones,[8] TEMPO,[9] polyhalides[10] and phenyliodine(III) diacetate.[11] In 2006, Chen et al. reported the NHC-catalyzed ring-opening of aziridines with aldehydes under aerobic conditions.[12] The oxidative NHC catalysis using oxygen as the terminal oxidant has also been established in the presence of transition metals.[13]

Smiles rearrangement,[14] the migration of aryl ring via intramolecular nucleophilic aromatic *ipso*-substitution, has been used for synthesis of various arenes and heteroarenes in medicine and natural products (Scheme 1, reaction a).[15] Recently, Glorius et al. reported an NHC-catalyzed Smiles rearrangement for the synthesis of diarylketones (Scheme 1, reaction b).[16] Meanwhile, visible light mediated photoredox catalysis is of great interest due to its unique redox and green properties.[17] The visible light catalyzed Smiles rearrangement for the formation of ester was independently reported by Li et al. and Gonzalez-Gomez et al (Scheme 1, reaction c).[18] In 2012, the NHC/photoredox catalysis was pioneered by Rovis et al for the α-acylaiton of tertiary amines.[19] In 2016, Sun et al. reported one example of NHC/photo-cocatalyzed γ-dichloromethylation of enals.[20] The esterification of enals under NHC/photocatalysis was also established.[21] Very recently, we reported the NHC/photo-cocatalyzed γ- and ε-alkylation via radicals.[22] In this paper, we report an N-heterocyclic carbene/photo cocatalyzed oxidative Smiles rearrangement for the synthesis of aryl salicylates from *O*-aryl



Scheme 1. Reported Smiles rearrangement and reaction design

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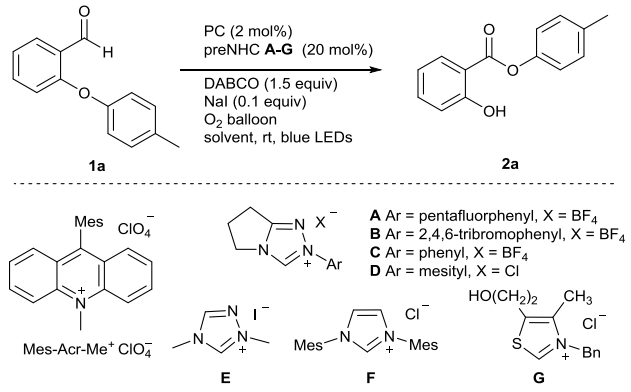
Table 1. Optimization of reaction conditions.[a]

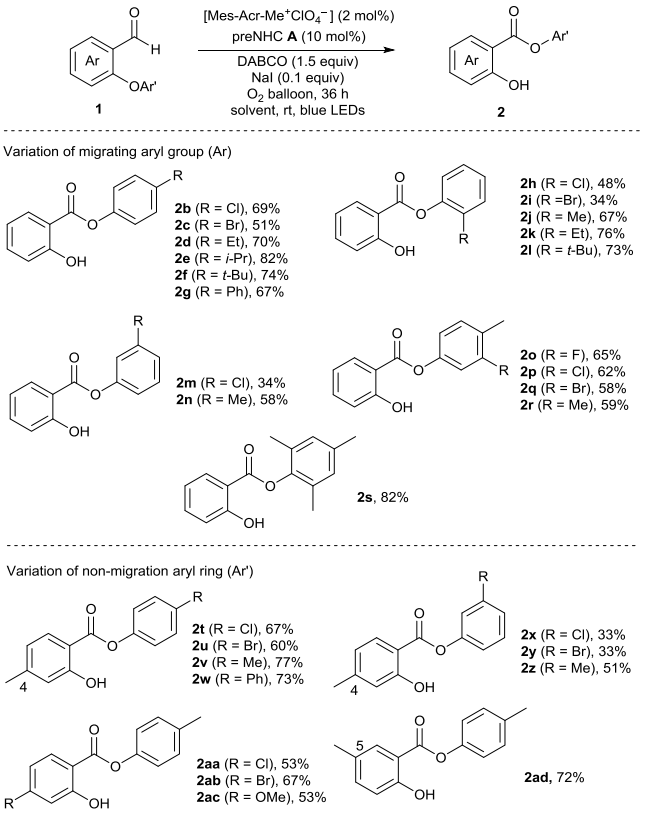


entry	preNHC	solvent, t	PC	yield[b] (%)
1[c]	**A**	DCM, 13h	Mes-Acr-Me$^+$ClO$_4^-$	39
2	**A**	DCM, 13h	Mes-Acr-Me$^+$ClO$_4^-$	57
3	**B**	DCM, 13h	Mes-Acr-Me$^+$ClO$_4^-$	34
4	**C-G**	DCM, 13h	Mes-Acr-Me$^+$ClO$_4^-$	trace/NR
5	**A**	1,4-dioxane, 13h	Mes-Acr-Me$^+$ClO$_4^-$	23
6	**A**	MeCN, 13h	Mes-Acr-Me$^+$ClO$_4^-$	29
7	**A**	DMF, 13h	Mes-Acr-Me$^+$ClO$_4^-$	trace
8	**A**	DMSO, 13h	Mes-Acr-Me$^+$ClO$_4^-$	trace
9	**A**	DCM, 13h	Ir(ppy)$_3$	NR
10	**A**	DCM, 13h	Ru(bpy)$_3$Cl$_2$	NR
11	**A**	DCM, 13h	PDI	50%
12	**A**	DCM, 13h	Eosin Y	NR
13	**A**	DCM, 13h	4CZIPN	NR
14	**A**	DCM, 36h	Mes-Acr-Me$^+$ClO$_4^-$	79
15[d]	**A**	DCM, 36h	Mes-Acr-Me$^+$ClO$_4^-$	79
16[e]	**A**	DCM, 36h	Mes-Acr-Me$^+$ClO$_4^-$	73

[a] General conditions: **1a** (0.3 mmol), PC (2 mol%), preNHC **A-G** (20 mmol%), DABCO (0.45 mmol) and solvent (3 mL); irradiation by 18 W blue LEDs at room temperature for 13 h under an oxygen atmosphere. [b] Isolated yields. [c] No NaI was added. [d] preNHC (10 mol%). [e] preNHC (5 mol%). PC = photocatalyst; DABCO = 1,4-Diazabicyclo[2.2.2]octane; NR = no reaction.

salicylic aldehydes (Scheme 1, reaction d). This reaction features two new C-O bonds formation and one C-O bond cleavage via metal-free oxidation of Breslow intermediate using oxygen as the terminal oxidant and following Smiles rearrangement under photocatalysis**.**

The reaction of *O*-tolyl salicylaldehyde **1a** was carried out under oxidative NHC/photo catalysis using oxygen as the terminal oxidant (Table 1). We were encouraged to find the desired oxidative Smiles rearrangement product **2a** was isolated in reasonable yields for the reaction in the presence of 20 mol% *N*-pentafluorophenyl preNHC **A** and 2 mol% 9-mesityl-10-methylacridin-10-ium perchlorate (Mes-Acr-Me$^+$ClO$_4^-$)[23] as the photocatalyst under blue LEDs irradiation (Table 1, entries 1). Inspired by Li[24] and Fu's[25] works, 10 mol% NaI was added as additives to facilitate the electron transfer, which led to an increased yield (Table 1, entry 2). The reaction using *N*-2,4,6-tribromophenyl triazolium preNHC **B** gave the product 34% (entry 3), while the triazolium preNHC **C**-**E**, imidazolium preNHC **F** and thioazolium preNHC **G** with *N*-phenyl or electron-donating groups failed to catalyze the reaction (entries 4, see SI for detail). Screening of solvents revealed that the reaction went in dichoromethane, 1,4-dioxane and acetonitrile but not in DMF or DMSO (entries 5-8). Interestingly, Ir(ppy)$_3$ and Ru(bpy)$_3$Cl$_2$ did not work as acridinium phtocatalyst, possibly due to their low oxidative potential[17a, 26] (entries 9 & 10). While the reaction using PDI as the photocatalyst gave 2a in 50% (entry 11), other organic dyes such as Eosin Y and 4CZIPN did not work (entries 12-13). Further improvement of the yield was realized when the reaction time was prolonged to 36 hours (entry 14). The good yield was kept when the loading of preNHC **A** was decreased to 10 mol% (entry 15), while a slight loss of yield was observed with 5 mol% of preNHC **A** (entry 16).



Scheme 2. Substrate scope.

With the optimized reaction conditions in hand, a variety of *O*-aryl salicylaldehydes were tested for the reaction (Scheme 2). The migrating *O*-aryl with electron-withdrawing groups in the *para* position (Ar' = 4-ClC$_6$H$_4$, 4-BrC$_6$H$_4$) resulted in some decrease of the yields (**2b**-**2d**). It is worthy to note that electron-rich group, which fails to migrate in classical Smiles rearrangement, worked in our oxidative reaction. It was found that migration of aryl groups with electron-donating substituent (Ar' = 4-EtC$_6$H$_4$, 4-*i*-PrC$_6$H$_4$, 4-*t*-BuC$_6$H$_4$) led to better yields (**2d**-**2f**). The reaction of *O*-4-phenylphenyl alicylaldehyde gave product **2g** in 67% yield. The aryls with *ortho*- (**2h**-**2l**) and *meta*-substituents (**2m**-**2n**) are tolerated, but low yields were observed for those with electron-withdrawing group. The migration of aryl group with two or three electron-withdrawing or electron-donating substituents

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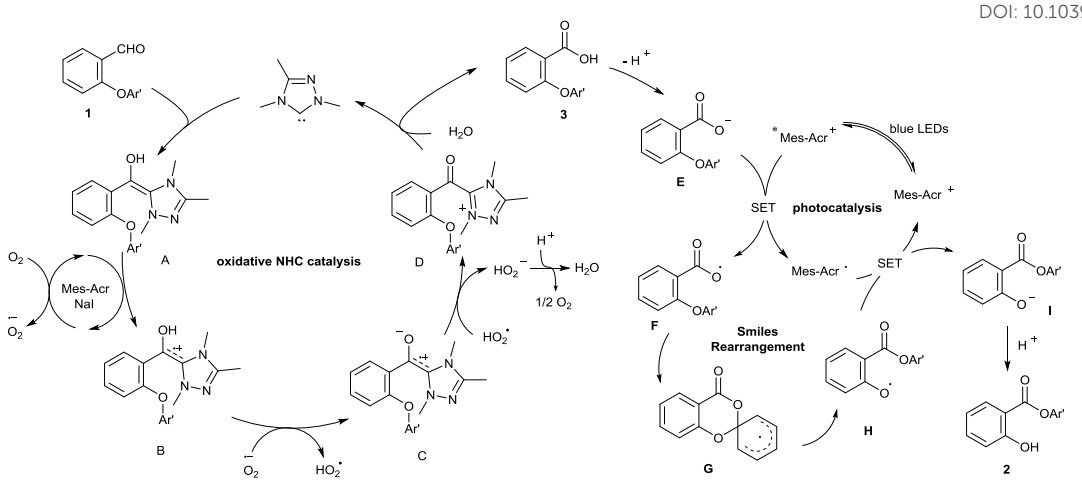
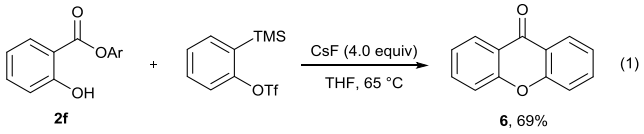


Scheme 3. Plausible catalytic cycles.

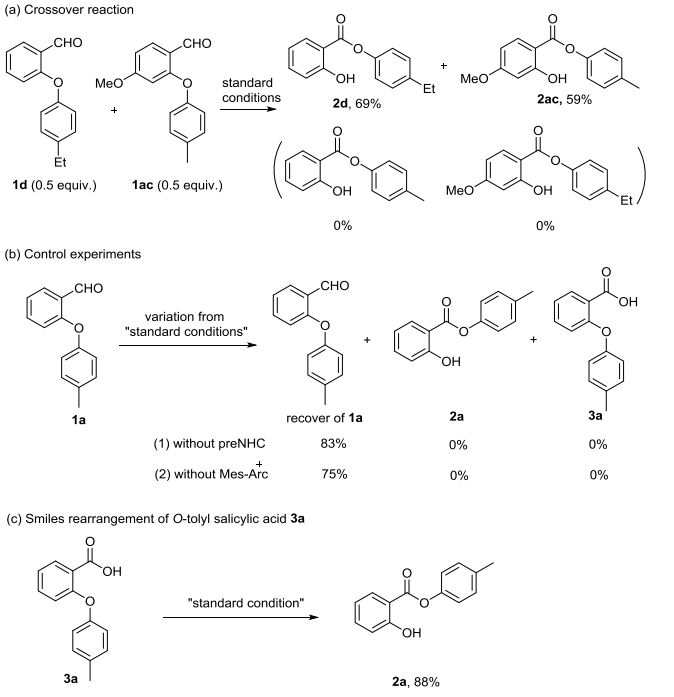
gave the corresponding products (**2o-2s**) in good to high yields. The salicylaldhydes with substituent(s) on the parental non-migration aryl ring was then investigated. All the *O*-aryl-4-methylsalicylaldhydes worked well, giving the oxidative Smiles rearrangement products (**2t**-**2z**) in moderate to good yields. Other *O*-tolyl-4-substituted-salicylaldhydes (4-Cl, 4-Br, 4-MeO) and *O*-tolyl-5-methylsalicylaldhyde showed similar reactivity (**2aa**-**2ad**).

A further chemical transformation of compound **2f** was demonstrated by its [4+2] annulation with the in situ generated benzyne, giving xanthone **6** in 69% yield (eq. 1).



(1)

A series of experiments was carried out to elucidate the reaction mechanism (Scheme 4). The crossover experiment of two *O*-aryl salicylaldehydes **1d** and **1ac** gave only two intramolecular oxidative Smiles rearrangement products **2d** and **2ac** without the observation of any crossover products (Scheme 4a). Control experiments revealed the reaction did not occur in the absence of preNHC with the recovery of most salicyladehyde (Scheme 4b, reaction 1). The NHC-catalyzed aerobic oxidation of aldehydes to carboxylic acids was reported recently.[27] Our control experiment revealed that no oxidation and Smiles rearrangement occurred in the absence of acridinium in our system (Scheme 4b, reaction 2). Further experiment revealed that the Smiles rearrangement of *O*-tolyl salicylic acid **3a** went well under the "standard condition" to give corresponding product in 88% yield (Scheme 4c). Other control experiments to trap the acylazolium intermediate by MeOH and the radical intermediate by TEMPO were also successful (See SI for detail).



Scheme 4. Investigation on mechanism.

Based on the above investigation, a plausible mechanism is depicted as in Scheme 3. The addition of NHC to aldehyde **1** gives Breslow intermediate **A**, which is oxidized by oxygen in the presence of acridinium and NaI as the (co)catalyst via single electron transfer (SET) to afford the radical cation **B**. Deprotonation of intermediate **B** gives zwitterionic radical species **C**, which was further oxidized by the *in situ* generated hydroperoxide radical to furnish acyl azolium **D**. The *O*-aryl salicylic acid **3** is generated from acycl azolium **D** via hydrolysis which closes the oxidative NHC catalysis cycle. The anion **E** of the salicylic acid is oxidized by the excited-state Acr-Mes$^+$ to

furnish the carboxyl radical **F**,[18] followed by a radical Smiles rearrangement via spirocyclic intermediate **G** to give radical **H**. The second SET between the two radicals of Acr-Mes radical and **H** regenerates the photocatalyst and affords the anion **I**, which is protonated to furnish the final salicylate **2**.

Conclusions

In summary, the oxidative Smiles rearrangement of *O*-aryl salicylaldehydes using oxygen as the terminal oxidatnt was developed under N-heterocyclic carbene and visible light catalysis. Both electron-deficient and electron-rich aryls worked well as the migrating group, giving the corresponding aryl salicylates in good yields. Control experiments support oxidation of the Breslow intermediate by oxygen in the presence of acridium and NaI as the (co)catalyst, which provides a new strategy for oxidative NHC catalysis under mild conditions. In this reaction, one C-O bond is cleavaged with two new C-O bonds formation. Further investigations on dual N-heterocyclic carbene/photoredox catalysis and detailed mechanistic studies are currently underway in our laboratory.

Acknowledgements

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Conflicts of interest

There are no conflicts to declare.

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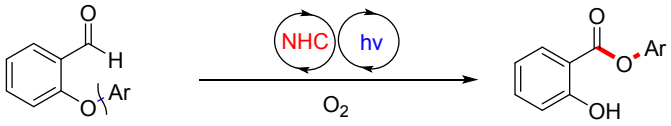

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