Visible-Light-Mediated Alkenylation, Allylation, and Cyanation of Potassium Alkyltrifluoroborates with Organic Photoredox Catalysts

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Supporting Information

ABSTRACT: Iridium- and ruthenium-free approaches to protected allylic amines and alkyl nitriles under photoredox conditions are reported. An inexpensive organic dye, eosin Y, catalyzes coupling of Boc-protected potassium α-aminomethyltrifluoroborates with a variety of substituted alkenyl sulfones through an α-aminomethyl radical addition–elimination pathway. Allylic and homoallylic amines were formed in moderate yields with high E/Z selectivity. The mechanistic approach was extended using tosyl cyanide as a radical trap, enabling the conversion of alkyltrifluoroborates to nitriles via a Fukuzumi acridinium-catalyzed process.

Visible-light-mediated organic transformations are an area of interest because there is an increased desire to develop sustainable reaction conditions and to access novel radical intermediates and pathways.1 In particular, visible light is increasingly appreciated as an abundant, renewable, and clean energy source for chemical reactions. However, implementing visible light in organic synthesis is limited by the fact that most organic molecules do not absorb visible light and, thus, are unreactive under photochemical conditions. Photoredox catalysis is an attractive approach to activating organic molecules by translating visible light energy via single-electron transfer (SET)2 or energy transfer. Most commonly, ruthenium and iridium photocatalysts are employed because of their advantageous properties, such as relatively long excited state lifetimes and favorable redox potentials. However, ruthenium and iridium are rare and expensive. Environmentally sustainable and inexpensive organic dyes are attractive replacements of traditional photoredox catalysts, although methods employing these organic catalysts are underdeveloped.3 Herein, two methods featuring single-electron oxidation of potassium alkyltrifluoroborates by organic photoredox catalysts are reported.

Alkyl radicals are widely known to add to unsaturated systems, such as acrylates and styrenes, generating α-carbonyl or benzylic radicals, respectively. These stabilized radicals may be captured in polymerization or 1,4 addition reactions. Alternatively, β-leaving groups have been implemented in radical addition–elimination reactions to forge C(sp²)–C(sp³) bonds.4 Recently, designed β-elimination processes were utilized by MacMillan et al. in a photoredox approach to allylic amines via Ir-catalyzed α-alkenylation of α-amino acids.5 Therein, electron-rich α-aminomethyl radicals—generated from single-electron oxidation of cesium carboxylates—reacted with electron-poor alkenyl sulfones through a radical addition–elimination pathway (Scheme 1). Although this method is attractive in its use of readily available α-amino acids, it is limited by the use of an expensive iridium photoredox catalyst. To overcome this limitation, Boc-protected potassium α-aminomethyltrifluoroborates were explored as alternative radical precursors. Potassium alkyltrifluoroborate salts are bench-stable, redox-active solids.6 They have been employed in various radical processes, including 1,4 additions by Akita et al. and dual catalytic cross-couplings by Molander and co-workers.7 Importantly, potassium alkyltrifluoroborates have oxidation potentials lower than those of their corresponding

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cesium carboxylates, enabling the removal of iridium in favor of mild and inexpensive organic dyes, such as eosin Y. Thus, the oxidation potential of potassium \( \alpha \)-pyrrolidinyltrifluoroborate (\( E_{\text{red}}^{1/2} = +0.78 \) V vs SCE) falls within the redox window of eosin Y (\( E_{\text{red}}^{1/2} = +0.83 \) V), whereas cesium \( \alpha \)-pyrrolidinyl carboxylate (\( E_{\text{red}}^{1/2} = +0.95 \) V vs SCE)\(^5\) lies outside of eosin Y’s oxidation window.

Studies began by exploring the reaction of potassium \( \alpha \)-pyrrolidinyltrifluoroborate (1) and phenyl trans-styryl sulfone (2a) in the presence of eosin Y (Scheme 2). After an initial product hit, conditions were optimized to provide the desired product in 73% yield (>98:2 E/Z selectivity). Notably, eosin Y was a more effective catalyst than alternative fluorescein derivatives, including eosin B, rose bengal, and ethyl eosin. Furthermore, the more oxidizing 9-mesityl-10-methylacridinium perchlorate (MesAcr\(^+\)) catalyst (\( E_{\text{red}}^{1/2} = +2.06 \) V vs SCE)\(^8\) results in poor product selectivity. Control reactions were performed to show that photocatalyst and light were essential for reactivity. The addition of 2,6-lutidine, which is a common additive in photoredox reactions of alkyltrifluoroborates,\(^6\) does not significantly alter the yield. Interestingly, switching light sources from 26 W CFL to a green LED (\( \lambda = 530 \) nm) did not influence conversion or selectivity.

With satisfactory conditions in hand, the reaction scope was explored, beginning with the sulfonyl partner. Attractively, aryl-substituted sulfones are stable, crystalline solids. Alkenyl sulfones were readily synthesized by several methods, including iodosulfonation–dehydroiodination of styrene derivatives,\(^8\) olefination of \( \alpha \)-sulfonylphosphonates,\(^7d\) or Heck reaction of phenyl vinyl sulfone with aryl halides.\(^12\) The reaction conditions were not observed owing to the absence of a quenching pathway—either H atom abstraction or reduction–protonation—under the standard conditions. As a result, the reaction conditions provided styrene 3q and acrylate 3r in synthetically useful yields.

| Scheme 2. Control Studies for \( \alpha \)-Alkenylation of Potassium Alkyltrifluoroborate |
|---|
| 1 (1.5 equiv) | 2a (1.0 equiv) |
| BF\(_3\)-Et\(_2\)O | Na\(_2\)Eosin Y (10 mol %) |
| DMF (0.05 M) | 26 W CFL |
| PhO\(_2\)S | or |
| PhO\(_2\)S | Ph |
| Variation from Standard | Yield (%) |
| None | 73% |
| No photocatalyst | 0% |
| No light | 0% |
| 2,6-lutidine | 72% |
| Green LED | 73% |

Unfortunately, the eosin Y-catalyzed alkenylation is largely limited to secondary \( \alpha \)-aminomethyltrifluoroborates. Attempts to extend the method to primary \( \alpha \)-aminomethyl (\( E_{\text{red}}^{1/2} = 0.9 \) V), primary or secondary \( \alpha \)-alkoxy (\( E_{\text{red}}^{1/2} = 0.9 \) V), and benzylic (\( E_{\text{red}}^{1/2} = 1.2 \) V) trifluoroborates provided products in low or trace yield.

Table 1. Scope of Reaction with Alkenyl and Allylic Sulfones\(^a\)

| Reaction | Product | \( E_{\text{red}}^{1/2} \) vs SCE |
|---|---|---|
| 3a | 73%, >98:2 E/Z | 0.73 V |
| 3b | 66%, >98:2 E/Z | 0.66 V |
| 3c | 79%, >98:2 E/Z | 0.79 V |
| 3d | 77%, >98:2 E/Z | 0.77 V |
| 3e | 74%, >98:2 E/Z | 0.74 V |
| 3f | 76%, 97:3 E/Z | 0.76 V |
| 3g | 68%, >98:2 E/Z | 0.68 V |
| 3h | 56%, >98:2 E/Z | 0.56 V |
| 3i | 56%, >98:2 E/Z | 0.56 V |
| 3j | 63%, >98:2 E/Z | 0.63 V |
| 3k | 65%, >98:2 E/Z | 0.65 V |
| 3l | 58% | 0.58 V |

\(^a\)All reactions were conducted on 0.5 mmol scale. Reaction times were 48–72 h. E/Z selectivity determined by \( ^1 \)H NMR.

Scheme 3. Radical Addition and \( \beta \)-Fragmentation of Sulfonyl Leaving Group

Unfortunately, the eosin Y-catalyzed alkenylation is largely limited to secondary \( \alpha \)-aminomethyltrifluoroborates. Attempts to extend the method to primary \( \alpha \)-aminomethyl (\( E_{\text{red}}^{1/2} = 0.9 \) V), primary or secondary \( \alpha \)-alkoxy (\( E_{\text{red}}^{1/2} = 0.9 \) V), and benzylic (\( E_{\text{red}}^{1/2} = 1.2 \) V) trifluoroborates provided products in low or trace yield.

Based on the reactivity of potassium trifluoroborates with alkenyl and allylic sulfones, tosyl cyanide (TsCN) was envisioned as an alternative radical acceptor. Renaud et al. has reported a hyponitrite-mediated deboronative cyanation of boronate esters, generated in situ via hydroboration of alkenes, with TsCN.\(^4\) The reaction required several additions of a

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radical initiator. It was thought that employing TsCN in a photoredox manifold with alkyltrifluoroborates would render the reaction truly catalytic in organic radical initiator and benefit further from utilization of a bench-stable organoboron source. Furthermore, the more oxidizing MesAcrr+ catalyst—which provided inadequate selectivity in alkenylations because of the presence of electron-rich alkene-containing products—could oxidize both stabilized and unstabilized trifluoroborates, providing access to a larger range of alkyl nitriles. The trend in radical stability was anticipated to favor formation of substituted alkyl nitriles that are not easily synthesized via traditional S$_2$2 reactions. When we began our studies, photoredox cyanations were largely limited by substrate scope (e.g., N-aryl tetrahydroisoquinolines) or unfavorable conditions (e.g., iridium/NaCN/AcOH system). However, a deboronative cyanation of potassium alkyltrifluoroborates with TsCN was recently reported. The latter reaction utilized a ruthenium photocatalyst, excess of a hypervalent iodine oxidant, and TFA. Therefore, a precious metal and stoichiometric, oxidant-free photoredox cyanation remained desirable.

Minor optimization to reaction parameters provided suitable conditions for nitrile formation without the addition of external oxidants or acids (Table 2). A series of $\gamma$, $\beta$, and $\alpha$-amino nitriles (6a, 6b, and 6c) were synthesized. This could provide a route to amino acids from simple alkenes via a hydroboration/cyanation/hydrolysis sequence rather than accessing acids from oxidation/reduction manipulation (e.g., oxidation of aldehydes or ketones). Although protection of cyanohydrins is often problematic because deprotonation to the alkoxide results in trigonalization of potassium alkyltrifluoroborates with TsCN, this was recently reported. The latter reaction utilized a ruthenium photocatalyst, excess of a hypervalent iodine oxidant, and TFA. Therefore, a precious metal and stoichiometric, oxidant-free photoredox cyanation remained desirable.

Table 2. Cyanation of Potassium Alkyltrifluoroborates

| $R^1$ | $R^2$ | Ts-CN | MesAcrr+ (3 mol %) | $R^1$ | $R^2$ |
|-------|-------|-------|-------------------|-------|-------|
|       |       |       | DSF (0.10 M) Blue LEDs, 18 h |       |       |
| 4a-f | (1 equiv) | 5 | (2 equiv) | 6a-g |

$^a$All reactions were performed on 0.35 mmol scale.

In summary, inexpensive organic dyes have been employed as sustainable alternatives to iridium photoredox catalysts in potassium alkyltrifluoroborate transformations. Eosin Y is an effective catalyst for $\alpha$-alkenylation of a pyrrolidine-derived trifluoroborate with high stereoselectivity ($E/Z$ selectivity). Furthermore, Fukuzumi’s acridinium catalyst facilitates the formation of alkyl nitriles from various alkyltrifluoroborates, including stabilized $\alpha$-aminomethyl precursors and unactivated primary substrates. These processes largely rely upon the ability of sulfonyl radical traps as leaving groups and oxidants for catalytic turnover.

**Experimental Section**

**General Considerations.** All reactions were carried out under an inert atmosphere of argon. Photoredox reactions were irradiated with a 26 W CFL or a blue LED strip (460–480 nm). Temperatures were controlled using an external fan. Column chromatography was performed by Combiblack using RediSep Rf gold normal-phase silica columns. Melting points (°C) are uncorrected. $^1$H (500 MHz) and $^13$C (126 MHz) NMR chemical shifts are reported relative to internal TMS. Data are presented as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad), coupling constant $J$ (Hz), and integration. Thin-layer chromatography (TLC) was performed on TLC silica gel plates (0.25 mm) precoated with a fluorescent indicator. Visualization of the TLC plates was effected with ultraviolet light. HRMS spectra (ESI-TOF) were recorded in CH$_3$Cl, and acetone.

**General Procedure for Eosin Y-Catalyzed Alkenylation and Allylation.** Sulfone (0.50 mmol, 1.0 equiv), potassium alkyltrifluoroborate (208 mg, 0.75 mmol, 1.5 equiv), and eosin Y disodium salt were subjected to a reaction vial. The vial was placed under argon and enriched with degassed, anhydrous DMSO (10 mL, 0.05 M). The vial was then placed between two 26 W CFLs. Consumption of sulfone was monitored by TLC or HPLC. Upon completion (typically 40–72 h), the reaction was transferred to a separatory funnel with EtOAc (30 mL) and H$_2$O (40 mL). The aqueous layer was washed twice with EtOAc (30 mL). The combined organic layers were washed with brine (40 mL), dried (MgSO$_4$), and photoredox catalyst (PC), either eosin Y or MesAcrr+, to a singlet excited state that may undergo intersystem crossing to a relatively long-lived triplet state (PC*). This excited state may oxidize an appropriate potassium alkyltrifluoroborate, forming an alkyl radical. In the presence of a sulfonyle partner, the carbon-centered radical may undergo radical addition—formation of a new C–C bond and producing an equivalent of a more thermodynamically favored sulfonyl radical. For turnover of the catalytic cycle, the sulfonyl radical ($E_{red}$ = +0.50 V) can accept an electron from the reduced photoredox catalyst (PC*) for eosin Y ($E_{red}$ = −1.14 V) or for MesAcrr* ($E_{red}$ = −0.49 V vs SCE). Thus, the sulfonyl partner acts as a radical acceptor and oxidant.

In summary, inexpensive organic dyes have been employed as sustainable alternatives to iridium photoredox catalysts in potassium alkyltrifluoroborate transformations. Eosin Y is an effective catalyst for $\alpha$-alkenylation of a pyrrolidine-derived trifluoroborate with high stereoselectivity ($E/Z$ selectivity). Furthermore, Fukuzumi’s acridinium catalyst facilitates the formation of alkyl nitriles from various alkyltrifluoroborates, including stabilized $\alpha$-aminomethyl precursors and unactivated primary substrates. These processes largely rely upon the ability of sulfonyl radical traps as leaving groups and oxidants for catalytic turnover.
tert-Butyl (E)-2-(2-(Benzo[d][1,3]dioxol-5-yl)vinyl)pyrrolidine-1-carboxylate (3h).

The general procedure provided the titled compound as a colorless oil (88.8 mg, 56% yield, >98.2 E%): 1H NMR (500 MHz, CDCl₃) δ 7.30 (dd, J = 8.4, 5.4 Hz, 2H), 6.99 (dd, J = 8.7, 6.9 Hz, 2H), 6.35 (d, J = 14.7 Hz, 1H), 6.07–5.93 (br s, 1H), 4.54–4.28 (br m, 1H), 3.51–3.35 (br s, 2H), 2.14–2.01 (br s, 1H), 2.01–1.75 (m, 3H), 1.42 (s, 9H); 13C{1H} NMR (126 MHz, CDCl₃) δ 148.1, 147.1, 131.7, 129.2, 120.9, 108.4, 105.8, 101.1, 79.3, 59.1, 46.4, 32.8, 23.7; IR (neat) ν = 2973, 2875, 1495, 1484, 1449, 1390, 1346, 1248, 1189, 1161, 1099, 1037, 959, 931, 886, 860, 799, 773, 732 cm⁻¹; MS (ESI) m/z calcd for C₁₉H₂₅NO₃Na ([M + Na⁺]⁺) 340.1525, found 340.1518.

tert-Butyl (E)-2-(4-Methoxy)pyrrolidine-1-carboxylate (3i). The general procedure provided the titled compound as a white semisolid (107.0 mg, 61% yield, >98.2 E%): 1H NMR (500 MHz, CDCl₃) δ 7.40 (d, J = 8.1 Hz, 2H), 7.20 (d, J = 8.2 Hz, 2H), 6.32 (d, J = 15.2 Hz, 1H), 6.16–6.00 (br m, 1H), 4.57–4.28 (br m, 1H), 3.52–3.32 (br s, 2H), 2.14–2.01 (br s, 1H), 1.97–1.65 (m, 3H), 1.40 (s, 9H); 13C{1H} NMR (126 MHz, CDCl₃) δ 154.7, 133.3, 128.4, 127.8, 115.6, 79.3, 59.1, 46.4, 32.6, 28.6, 23.3; IR (neat) ν = 2973, 2876, 1687, 1601, 1508, 1457, 1393, 1348, 1332, 1100, 1093, 963, 897, 852, 810, 790, 771, 517 cm⁻¹; MS (ESI) m/z calcd for C₁₉H₂₅NO₃Na ([M + Na⁺]⁺) 314.1544, found 314.1540.

**Note**

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**tert-Butyl 2-(2,2-Diphenylvinyl)pyrrolidine-1-carboxylate (3m).** The general procedure provided the titled compound as a white solid (103.8 mg, 62% yield); mm: mp = 87–90 °C; 1H NMR (500 MHz, CDCl3) δ 7.44–7.07 (m, 10H), 6.02 (d, J = 6.7 Hz, 1H), 4.84 (d, J = 11.6 Hz, 2H), 4.51 (d, J = 11.6 Hz, 2H), 4.14 (t, J = 6.0 Hz, 1H), 2.64 (s, 2H), 1.92–1.82 (m, 4H); 13C{1H} NMR (126 MHz, CDCl3) δ 154.8, 142.5, 140.6, 139.7, 132.3, 130.2, 128.3, 128.2, 127.5, 127.3, 79.3, 56.5, 47.0, 35.0, 28.8, 24.0; IR (neat) ν = 2974, 1687, 1492, 1477, 1444, 1389, 1343, 1250, 1168, 1074, 1030, 910, 877, 860, 762, 731, 698, 645, 626 cm⁻¹; MS (ESI) m/z calcd for C24H22NO (M+) 349.2042, found 349.2040.

**tert-Butyl 2-(Phenylallyl)pyrrolidine-1-carboxylate (3q).** The general procedure provided the titled compound as a colorless oil (83.3 mg, 58% yield); 1H NMR (500 MHz, CDCl3) δ 7.58–7.41 (m, 2H), 7.35–7.27 (m, 3H), 5.35 (s, 1H), 5.07 (s, 1H), 4.00–3.79 (br m, 4H), 3.46–3.03 (br m, 2H), 2.35–2.23 (br m, 1H), 1.89–1.62 (m, 4H), 1.55–1.42 (br m, 4H); 13C{1H} NMR (126 MHz, CDCl3) δ 154.7, 146.1, 128.4, 127.7, 126.4, 115.0, 77.4, 55.8, 46.4, 40.0, 28.8, 20.7, 22.7; IR (neat) ν = 2978, 2869, 1719, 1492, 1477, 1428, 1382, 1290, 1284, 1274, 1193, 1195, 91.5, 940.5. Characterization data matched that reported in the literature.26

**4-Cyanopiperidine-1-carboxylic acid (6a).** Isolated as a colorless oil (42.6 mg, 62% yield); 1H NMR (500 MHz, CDCl3) δ 3.67–3.60 (m, 2H), 3.12–3.04 (m, 1H), 2.60–2.52 (m, 2H), 1.91–1.77 (m, 3H), 1.73–1.64 (br s, 1H), 1.45 (s, 9H); 13C{1H} NMR (126 MHz, CDCl3) δ 154.5, 121.2, 80.2, 41.9, 28.6, 28.5, 26.4. Characterization data matched that reported in the literature.21

**3-Cyanopyrrolidine-1-carboxylic acid (6b).** Isolated as a colorless oil (28.2 mg, 76% yield); 1H NMR (500 MHz, CDCl3) δ 4.60–4.40 (m, 1H), 3.57–3.52 (m, 2H), 2.30–1.93 (m, 4H), 1.51–1.47 (m, 9H); 13C{1H} NMR (126 MHz, CDCl3) δ 153.1, 119.3, 81.6, 47.3, 45.9, 31.8, 28.5, 24.0. Characterization data matched that reported in the literature.21

**2-(Benzyloxyl)-5-phenylpentanenitrile (6e).** Isolated as a colorless oil (64.0 mg, 69% yield); 1H NMR (500 MHz, CDCl3) δ 7.38–7.14 (m, 10H), 4.84 (d, J = 11.6 Hz, 2H), 4.51 (d, J = 11.6 Hz, 2H), 4.14 (t, J = 6.0 Hz, 1H), 2.64 (s, 2H), 1.92–1.82 (m, 4H); 13C{1H} NMR (126 MHz, CDCl3) δ 141.3, 136.0, 128.8, 128.6, 128.5, 128.4, 128.2, 118.4, 72.6, 67.5, 35.2, 33.1, 26.5; FT-IR (neat) ν: 2930, 2927, 2866, 1735, 1603, 1496, 1454, 1334, 1208, 1101, 1028, 911, 747, 698, 495 cm⁻1. HRMS (ESI): m/z calcd for C29H24NO (M+) 425.1647, found 425.1648.

**Phenylpropanenitrile (6f):** Isolated as a colorless oil (29.8 mg, 65% yield); 1H NMR (500 MHz, CDCl3) δ 7.29 (m, 5H), 2.62 (t, J = 6.8 Hz, 2H); 13C{1H} NMR (126 MHz, CDCl3) δ 138.2, 129.0, 128.4, 127.4, 119.3, 31.7, 19.5. Characterization data matched that reported in the literature.

**ASSOCIATED CONTENT**

Supporting Information

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Notes

The authors declare no competing financial interest.

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