

## Enantioselective Organo-SOMO Catalysis: The $\alpha$ -Vinylolation of Aldehydes

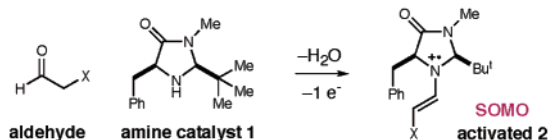
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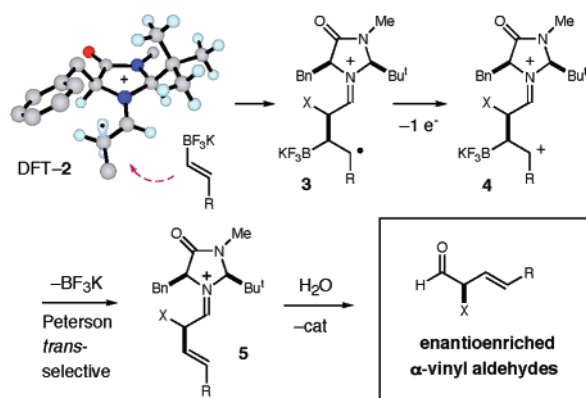
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The catalytic union of nascent enolates with aryl or vinyl coupling partners has become a mainstay transformation in organic synthesis, primarily driven by advances in transition metal chemistry.<sup>1</sup> In particular, the seminal work of Buchwald and Hartwig has provided a number of enantioselective enolate  $\alpha$ -arylations that enable quaternary carbon formation directly adjacent to both ketone and lactone moieties.<sup>2</sup> Surprisingly, however, the asymmetric  $\alpha$ -vinylation of enolates has been slow to develop and thus far is restricted to the production of stereogenicity that cannot epimerize or be destroyed via olefin isomerization to an  $\alpha,\beta$ -unsaturated product.<sup>3</sup> Recently, our laboratory introduced a new mode of organocatalytic activation, termed SOMO catalysis, that is founded upon the mechanistic hypothesis that one-electron oxidation of a transient enamine intermediate (derived from aldehydes and chiral amine catalyst **1**) will render a  $3\pi$ -electron SOMO-activated species **2** that can readily participate in a range of unique asymmetric bond constructions (eq 1).<sup>4</sup> In this communication, we demonstrate that organo-SOMO catalysis has been successfully exploited to achieve the first asymmetric  $\alpha$ -vinylation of aldehydes using vinyl trifluoroborate salts and a commercial amine catalyst. Notably, these mild catalytic conditions allow the production of  $\alpha$ -formyl,  $\alpha$ -vinyl, methine stereogenic centers without olefin transposition or subsequent erosion in enantiopurity.

### SOMO Catalysis: A Novel Mode of Organocatalytic Activation (eq 1)



### Enantioselective $\alpha$ -Vinylolation of Aldehydes via SOMO Catalysis (eq 2)



**Design Plan.** In our previous reports,<sup>4</sup> we advocated that the aldehyde-derived radical cation DFT-2<sup>5</sup> should function as a generic platform of induction and reactivity for a variety of unprecedented transformations. Continuing this theme, we hypothesized that vinyl potassium trifluoroborate salts<sup>6</sup> should readily participate in enantio-

**Table 1.** Organocatalytic Vinylolation: Scope of Aldehyde Substrate

| entry | product <sup>a,b</sup> | yield, <sup>c</sup> ee <sup>d</sup> | entry | product <sup>a,b</sup> | yield, <sup>c</sup> ee <sup>d</sup> |
|-------|------------------------|-------------------------------------|-------|------------------------|-------------------------------------|
| 1     |                        | 72% yield<br>94% ee                 | 4     |                        | 79% yield<br>93% ee                 |
| 2     |                        | 78% yield<br>95% ee                 | 5     |                        | 78% yield<br>93% ee                 |
| 3     |                        | 82% yield<br>96% ee                 | 6     |                        | 76% yield<br>96% ee                 |

<sup>a</sup> Stereochemistry assigned by chemical correlation or by analogy. <sup>b</sup> Only (*E*)-olefin isomer observed by <sup>1</sup>H NMR (400 MHz). <sup>c</sup> Isolated yield of the corresponding alcohols. <sup>d</sup> Enantiomeric excess determined by chiral SFC analysis.

and regioselective carbon–carbon bond formation with DFT-2 to form a  $\beta$ -borato-stabilized radical **3** (eq 2), which in the presence of a suitable oxidant will undergo rapid electron transfer to render the  $\beta$ -cation **4**. Subsequent Peterson elimination<sup>7,8</sup> of the trifluoroborate group with *trans*-selectivity followed by iminium hydrolysis would then reveal an optically enriched  $\alpha$ -(*E*)-vinyl aldehyde. Central to this design plan, we anticipated that our imidazolidinone catalyst would be inert to enamine formation with the  $\alpha$ -vinyl aldehyde product, an essential criterion if we hoped to preclude product epimerization, olefin conjugation, and bisvinylation pathways. In terms of enantiocontrol, we presumed that the activated radical DFT-2 would position the  $3\pi$ -electron system away from the bulky *tert*-butyl group, while adopting an (*E*)-configuration to minimize nonbonding interactions. In this topography, the benzyl group on the imidazolidinone framework effectively shields the *Re* face leaving the *Si* face exposed toward asymmetric bond formation.

Our organocatalytic SOMO vinylolation was first evaluated using potassium styryltrifluoroborate, imidazolidinone catalyst **1**, and a series of  $\alpha$ -substituted aldehydes (Table 1, eq 3).<sup>9</sup> Initial optimization experiments revealed that high levels of enantiocontrol, *trans*-olefin selectivity, and reaction efficiency are possible when the reaction is performed in DME using 2.5 equiv of oxidant (ceric ammonium nitrate (CAN)), 4.0 equiv of H<sub>2</sub>O, and 2.0 equiv of sodium bicarbonate (NaHCO<sub>3</sub>). As summarized in Table 1, these mild oxidative conditions are tolerated by a wide range of functional groups including aromatic rings, olefins, benzyl ethers, and carbamates (entries 2, 4–6, 76–79% yield, 93–96% ee). Moreover, the steric demands of the aldehyde substrate have little influence

**Table 2.** Scope of the Vinyl Potassium Trifluoroborate Salt

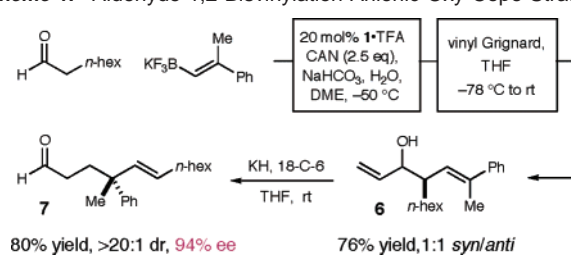
|       |                                     | (4)            |                        |                      |                   |
|-------|-------------------------------------|----------------|------------------------|----------------------|-------------------|
| entry | R                                   | R <sub>1</sub> | product <sup>b,c</sup> | % yield <sup>d</sup> | % ee <sup>e</sup> |
| 1     | C <sub>6</sub> H <sub>5</sub>       | H              |                        | 81                   | 94                |
| 2     | 4-F-C <sub>6</sub> H <sub>4</sub>   | H              |                        | 63                   | 93                |
| 3     | 4-Cl-C <sub>6</sub> H <sub>4</sub>  | H              |                        | 77                   | 95                |
| 4     | 4-Me-C <sub>6</sub> H <sub>4</sub>  | H              |                        | 76                   | 92                |
| 5     | 4-MeO-C <sub>6</sub> H <sub>4</sub> | H              |                        | 61                   | 95                |
| 6     | C <sub>6</sub> H <sub>5</sub>       | Me             |                        | 93                   | 94                |
| 7     | C <sub>8</sub> H <sub>17</sub>      | H              |                        | 82                   | 89                |
| 8     | Bn                                  | H              |                        | 71                   | 91                |
| 9     | c-hex                               | H              |                        | 84                   | 90                |
| 10    | c-hexene                            | H              |                        | 73                   | 93                |

<sup>a</sup> Solvent: entries 1–6 = DME; entries 7–10 = acetone. <sup>b</sup> Stereochemistry assigned by chemical correlation or by analogy. <sup>c</sup> Only (*E*)-olefin isomer observed by <sup>1</sup>H NMR (400 MHz). <sup>d</sup> Isolated yields of the corresponding alcohols. <sup>e</sup> Enantiomeric excess determined by chiral SFC analysis.

on yield or enantiocontrol (X = *c*-hexyl, 4-piperidinyl, entries 3 and 6, 76–82% yield, 96% ee).

As revealed in Table 2, an extensive range of trifluoroborate coupling partners are suitable for this enantioselective vinylation protocol (eq 4).<sup>9</sup> For example, *para*-substituted styryl systems that incorporate electron-donating, -withdrawing, or -neutral groups undergo addition with near identical selectivities (entries 1–5, 61–81% yield, 92–95% ee). Furthermore, trisubstituted olefins can be successfully utilized with stereoselective formation of the *trans*-geometrical isomer (entry 6, 93% yield, 94% ee). Perhaps most important, this technology can produce  $\gamma$ -alkyl-substituted  $\beta,\gamma$ -unsaturated aldehydes without olefin isomerization to the  $\alpha,\beta$ -conjugated adduct, a true testament to the mild reaction conditions that are operable in this organocatalytic process (entries 7–9, 71–84% yield, 89–91% ee).

A demonstration of the utility of this organocatalytic vinylation and the accompanying products is presented in the two-stage (three-

**Scheme 1.** Aldehyde-1,2-Bisvinylation Anionic Oxy-Cope Strategy

step) conversion of simple aldehydes to enantioenriched oxy-Cope products.<sup>10</sup> As highlighted in Scheme 1, exposure of octanal to our asymmetric olefin coupling followed by *in situ* vinyl Grignard addition provided the corresponding 1,5-dienyl alcohol in good yield but with no diastereocontrol (**6**, *anti*/*syn* 1:1). Subsequent exposure of this isomeric mixture to Evans' anionic oxy-Cope protocol, however, allows rapid and stereoconvergent [3,3]-rearrangement to provide the quaternary carbon-bearing aldehyde **7** with complete enantioselectivity (94% ee) and as a single diastereomer.<sup>11</sup> Given that oxy-Cope substrates are typically produced via the allylation of  $\alpha,\beta$ -unsaturated aldehydes, we present this new operationally simple aldehyde 1,2-bisvinylation sequence as an alternative oxy-Cope retron.

Last, the sense of enantioinduction for all cases presented is in complete accord with our calculated model DFT-2. To our knowledge, this is (i) the first enantioselective catalytic  $\alpha$ -vinylation of aldehydes and (ii) the first use of boron salts as coupling reagents for radical-based processes. Full details of this organo-SOMO catalysis technology will be forthcoming.

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**Supporting Information Available:** Experimental procedures and spectral data are provided. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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