Communication

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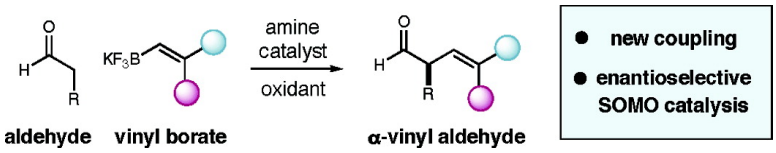

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Enantioselective Organo-SOMO Catalysis: The α-Vinylation of Aldehydes

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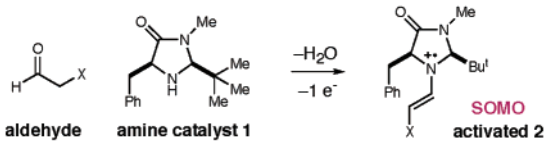
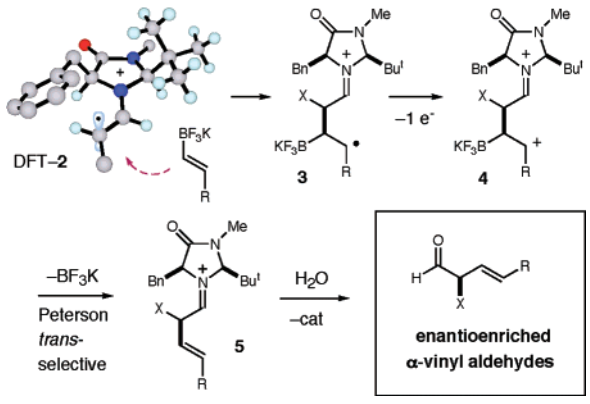
The catalytic union of nascent enolates with aryl or vinyl coupling partners has become a mainstay transformation in organic synthesis, primarily driven by advances in transition metal chemistry.[1] In particular, the seminal work of Buchwald and Hartwig has provided a number of enantioselective enolate α-arylations that enable quaternary carbon formation directly adjacent to both ketone and lactone moieties.[2] Surprisingly, however, the asymmetric α-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 α,β-unsaturated product.[3] 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 3π-electron SOMO-activated species **2** that can readily participate in a range of unique asymmetric bond constructions (eq 1).[4] In this communication, we demonstrate that organo-SOMO catalysis has been successfully exploited to achieve the first asymmetric α-vinylation of aldehydes using vinyl trifluoroborate salts and a commercial amine catalyst. Notably, these mild catalytic conditions allow the production of α-formyl, α-vinyl, methine stereogenic centers without olefin transposition or subsequent erosion in enantiopurity.

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

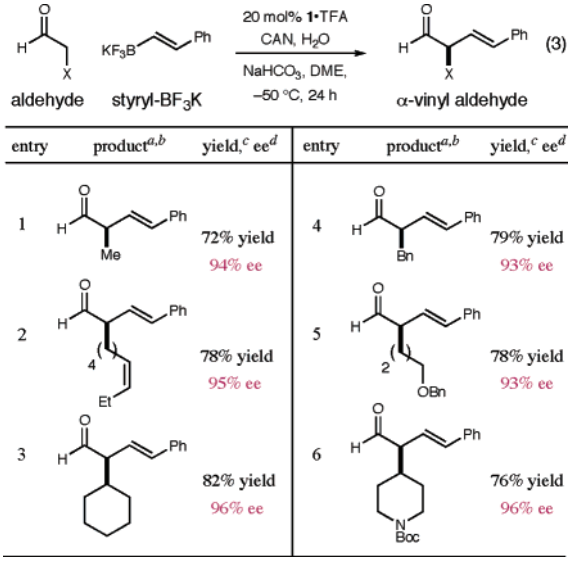


Enantioselective α-Vinylation of Aldehydes via SOMO Catalysis (eq 2)



Design Plan. In our previous reports,[4] we advocated that the aldehyde-derived radical cation DFT-**2**[5] 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[6] should readily participate in enantio- and regioselective carbon−carbon bond formation with DFT-**2** to form a β-borato-stabilized radical **3** (eq 2), which in the presence of a suitable oxidant will undergo rapid electron transfer to render the β-cation **4**. Subsequent Peterson elimination[7,8] of the trifluoroborate group with *trans*-selectivity followed by iminium hydrolysis would then reveal an optically enriched α-(*E*)-vinyl aldehyde. Central to this design plan, we anticipated that our imidazolidinone catalyst would be inert to enamine formation with the α-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 3π-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.

Table 1. Organocatalytic Vinylation: Scope of Aldehyde Substrate

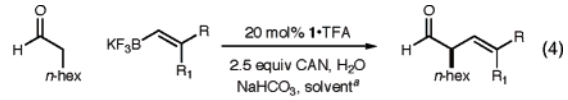


[a] Stereochemistry assigned by chemical correlation or by analogy. [b] Only (*E*)-olefin isomer observed by ^{1}H NMR (400 MHz). [c] Isolated yield of the corresponding alcohols. [d] Enantiomeric excess determined by chiral SFC analysis.

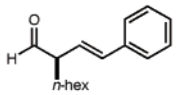
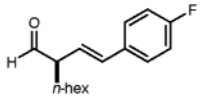
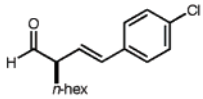
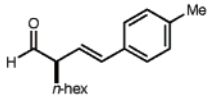
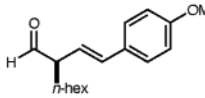
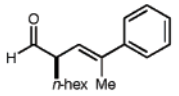
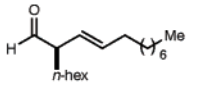
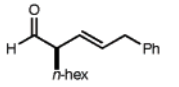
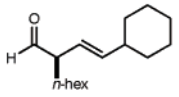
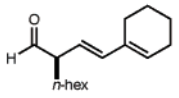
Our organocatalytic SOMO vinylation was first evaluated using potassium styryltrifluoroborate, imidazolidinone catalyst **1**, and a series of α-substituted aldehydes (Table 1, eq 3).[9] Initial optimization experiments revealed that high levels of enantiocontrol, *trans*-olefin selectivity, and reaction 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_2O, and 2.0 equiv of sodium bicarbonate ($NaHCO_3$). 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

10.1021/ja077212h CCC: $40.75

Table 2. Scope of the Vinyl Potassium Trifluoroborate Salt



octanal | vinyl-BF_3K | α-vinyl aldehyde

entry	R	R_1	product[b,c]	% yield[d]	% ee[e]
1	C_6H_5	H		81	94
2	4-F-C_6H_4	H		63	93
3	4-Cl-C_6H_4	H		77	95
4	4-Me-C_6H_4	H		76	92
5	4-MeO-C_6H_4	H		61	95
6	C_6H_5	Me		93	94
7	C_8H_{17}	H		82	89
8	Bn	H		71	91
9	*c*-hex	H		84	90
10	*c*-hexene	H		73	93

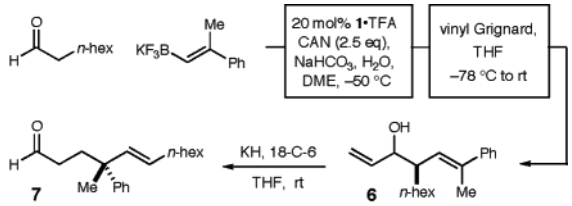
[a] Solvent: entries 1−6 = DME; entries 7−10 = acetone. [b] Stereochemistry assigned by chemical correlation or by analogy. [c] Only (*E*)-olefin isomer observed by ^{1}H NMR (400 MHz). [d] Isolated yields of the corresponding alcohols. [e] Enantiomeric excess determined by chiral SFC analysis.

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).[9] 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 γ-alkyl-substituted β,γ-unsaturated aldehydes without olefin isomerization to the α,β-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-step) conversion of simple aldehydes to enantioenriched oxy-Cope products.[10] 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 enantioretention (94% ee) and as a single diastereomer.[11] Given that oxy-Cope substrates are typically produced via the allylation of α,β-unsaturated aldehydes, we present this new operationally simple aldehyde 1,2-bisvinylation sequence as an alternative oxy-Cope retron.

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



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 α-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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