

Brønsted Acid Catalyzed PhSe Transfer versus Radical Aryl Transfer: Linear Codimerization of Styrenes and Internal Olefins

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Supporting Information

ABSTRACT: Brønsted acid *p*-TsOH·H₂O-catalyzed hydrovinylation of styrenes with internal olefins α -oxo ketene dithioacetals was efficiently achieved in the presence of *N*-phenylselenophthalimide (*N*-PSP), regioselectively affording Markovnikov phenylselenative hydrovinylation products through PhSe transfer of the phenylseleno ketene dithioacetal intermediates. Radical reduction of the resultant PhSe-alkyl-substituted ketene dithioacetals with AIBN/*n*-Bu₃SnH gave the corresponding anti-Markovnikov hydrovinylation products formally from the linear codimerization of styrenes and the internal olefins.

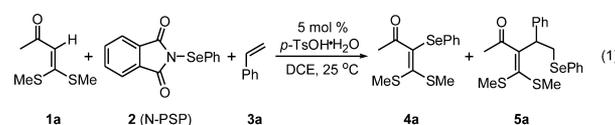


Highly selective carbon–carbon bond formation has been one of the most important tasks in organic chemistry. Metal-catalyzed hydrovinylation, that is, the addition of a vinyl group and a hydrogen (donor) across an olefin (acceptor), has been paid considerable attention for C–C bond construction since its first report in 1965.¹ Transition-metal-catalyzed hydrovinylation,^{2,3} in particular, codimerization of styrene and other vinylarenes with ethylene gas, has been extensively investigated because the resultant 3-aryl-1-butenes are important intermediates for the synthesis of 2-arylpropionic acids that are widely used as anti-inflammatory drugs.⁴ However, side reactions are always encountered in transition-metal-catalyzed hydrovinylation, including dimerization of either styrene⁵ or ethylene,⁶ isomerization of the 3-aryl-1-butene to the more stable 3-aryl-2-butenes, and olefin oligomerization.² Lewis acids were seldom reported as the sole catalysts for hydrovinylation of vinylarenes.⁷ Although hydrovinylation has been known for about half a century and shown promising potential in organic synthesis, it is still an underused reaction due to the above-mentioned side reactions occurring in the overall catalytic cycle. In order to overcome the reaction limitations, continuous efforts have been directed toward tuning the transition-metal catalyst systems to reach good selectivity for the target products. In general, transition-metal or Lewis acid catalyzed hydrovinylation reactions usually afford branched alkyl-substituted olefin products from the head-to-tail (Markovnikov type) codimerization of two olefins, while head-to-head (anti-Markovnikov type) linear codimerization between olefins has only been rarely reported.⁸ Both Markovnikov and anti-Markovnikov functionalizations of olefins are of extraordinary importance for the selective synthesis of many organic compounds.⁹ Brønsted and Lewis acids have been well-known to promote hydro(hetero)-arylation of olefins to furnish Markovnikov-type branched alkylarenes, and transition-metal catalysts may alter the regioselectivity of a hydro(hetero)arylation process to form

anti-Markovnikov-type linear alkylarenes or facilitate dominant formation of the linear products by means of directing groups or using specific heteroarene substrates.¹⁰ Unfortunately, Brønsted acids have not yet been reported to catalyze a hydrovinylation reaction of two olefins to date.

Internal olefin α -oxo ketene dithioacetals are versatile building blocks in organic synthesis,¹¹ and we recently found that they could be used as alkenylating reagents under Brønsted acid or transition-metal catalysis.¹² Thus, we reasonably envisioned Brønsted acid catalyzed hydrovinylation of styrene and α -oxo ketene dithioacetals. However, tentative treatment of styrene with an α -oxo ketene dithioacetal in the presence of *p*-TsOH·H₂O (*p*-toluenesulfonic acid monohydrate) at ambient temperature did not result in any detectable product. To our delight, *N*-phenylselenophthalimide (*N*-PSP) was found to facilitate such a reaction as we previously reported.¹³ Herein, we report *p*-TsOH·H₂O-catalyzed phenylselenative hydrovinylation between styrene and other vinylarenes with α -oxo ketene dithioacetals as well as the radical reductive aryl transfer of the resultant Markovnikov-type codimerization products (Scheme 1).

Initially, the reaction of α -oxo ketene dithioacetal **1a**, *N*-PSP (**2**), and styrene (**3a**) in a 1:1.1:3 molar ratio was conducted in the presence of 5 mol % of *p*-TsOH·H₂O in 1,2-dichloroethane (DCE) at ambient temperature (eq 1). Over a period of

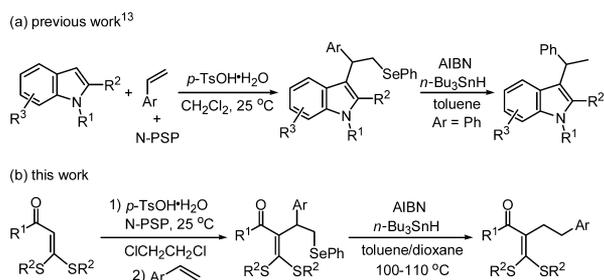


5 h, most of the starting **1a** was consumed to form a mixture of phenylseleno-substituted olefin **4a** and the branched

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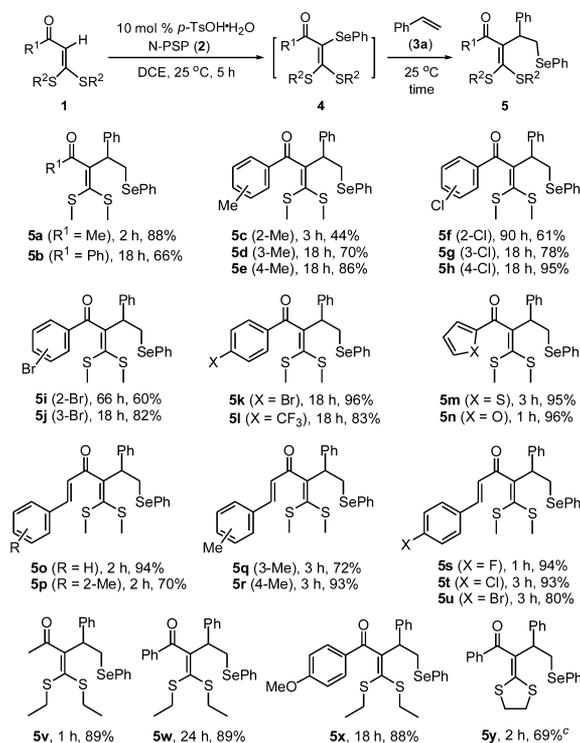
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Scheme 1. PhSe-Assisted Hydroheteroarylation and Hydrovinylation



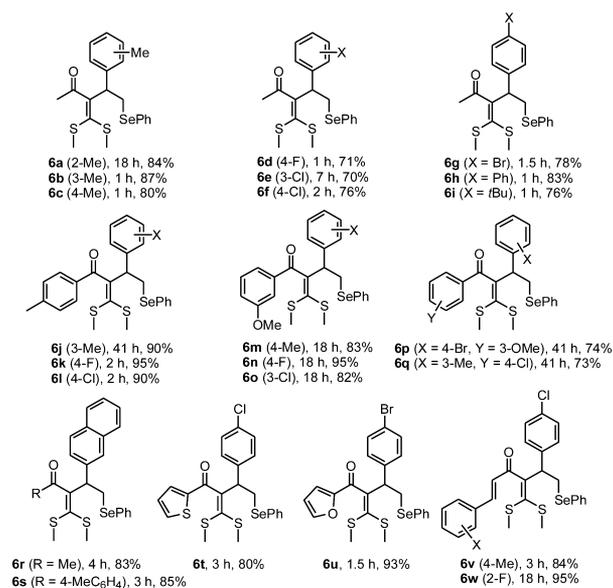
phenylselenative hydrovinylation product **5a**, from which **4a** and **5a** were difficult to separate by silica gel column chromatography. As the reaction proceeded, **4a** was gradually converted to **5a**, and at the end of 17 h **4a** disappeared to form **5a** as the only product in 79% isolated yield. It is noteworthy that **1a** did not react with styrene (**3a**) in the absence of *N*-PSP, and **4a** could be prepared in 96% yield from the reaction of **1a** with **2** (see the Supporting Information). *N*-PSP played a key role in initiating and directing such a Markovnikov-type hydrovinylation reaction.¹³ In order to ease separation of the target product **5a**, a one-pot, two-step procedure was developed under the following conditions: (1) The first step, phenylselenation of **1a** with **2** (1:1.1 molar ratio), was conducted with 10 mol % of *p*-TsOH·H₂O as the catalyst in DCE at ambient temperature for 5 h, completely converting **1a** to intermediate species **4a**. (2) At the end of the first step, 3 equiv of styrene was added and the reaction was continued for 2 h until **4a** was completely consumed by TLC monitoring. Under the optimal conditions, **5a** was obtained in 88% isolated yield. Lewis acid TiCl₄-mediated or radical-driven PhSe transfer has been reported to functionalize organic compounds,¹⁴ but our case unambiguously featured a Brønsted acid catalysis pathway.

Next, the protocol generality was explored under the optimized conditions by varying the second-step reaction time (Scheme 2). A variety of α -oxo ketene dithioacetals (**1**) were treated with *N*-PSP (**2**) to form phenylselenation compounds **4** in situ, which were directly used to react with styrene (**3a**) for the phenylselenative codimerization of the two olefins via Brønsted acid catalyzed PhSe transfer. α -Acetyl-, aroyl-, and cinnamoyl-functionalized ketene dithioacetals reacted to give the target products **5** in 44–96% yields. The substituted aroyl-functionalized substrates usually exhibited a reactivity higher than their unsubstituted analogue **1b**, and the 2-substituents in **1c**, **1f**, and **1i** showed an obvious steric effect on the yields of **5c**, **5f**, and **5i** (44–61%). In the cases of using *para*-substituted substrates such as **1e**, **1h**, and **1k**, the corresponding products **5e** (86%), **5h** (95%), and **5k** (96%) were efficiently produced. Methyl, chloro, bromo, fluoro, trifluoromethyl, and methoxy were tolerated in substrates **1**. 2-Furoyl- and thienoylketene dithioacetals underwent the reactions efficiently to give **5m** (95%) and **5n** (96%), respectively. Although α -cinnamoyl ketene dithioacetals have two reactive C–H sites α -adjacent to the carbonyl moiety, the first step, phenylselenation, regioselectively occurred at the C–H site of the dithioacetene moiety, which is attributed to the push–pull effect of the two thioalkyls and the α -oxo moiety on the internal C–H bond activation.^{11b} The dithioethyl substrates **1v–x** also efficiently underwent the reactions to afford **5v–x** (88–89%), while cyclic substrate **1y** exhibited a rather low reactivity to form **5y** (69%).

Scheme 2. Brønsted Acid-Catalyzed Codimerization of α -Oxo Ketene Dithioacetals (**1**) with Styrene (**3a**)^{a,b}

^aConditions: **1** (0.5 mmol), **2** (0.55 mmol), **3a** (1.5 mmol), *p*-TsOH·H₂O (10 mg, 0.05 mmol), DCE (5 mL), 25 °C. ^bIsolated yields based on **1**. ^cUsing 20 mol % *p*-TsOH·H₂O.

The substrate scope was then extended to other vinylarenes by using the same one-pot, two-step procedure as shown in Scheme 2 (Scheme 3). The reactions of internal olefins **1** with **2**, followed

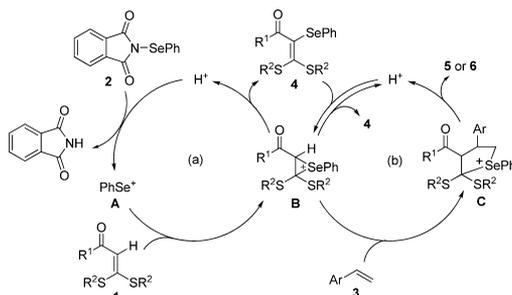
Scheme 3. Brønsted Acid Catalyzed Codimerization of **1** with Vinylarenes (**3**)^{a,b}

^aConditions: **1** (0.5 mmol), **2** (0.55 mmol), **3** (1.5 mmol), *p*-TsOH·H₂O (10 mg, 0.05 mmol), DCE (5 mL), 25 °C. ^bIsolated yields based on **1**.

by treating with terminal vinylarenes **3**, proceeded smoothly to afford the target products **6** in 70–95% yields. Substituents such as methyl, fluoro, chloro, bromo, phenyl, and *tert*-butyl were tolerated on the aryl moieties of the vinylarene substrates. 2-Vinylnaphthalene also reacted to form **6r** (83%) and **6s** (85%), respectively. It is noted that vinylarenes bearing a strong electron-withdrawing group (EWG = NO₂, AcO, or CN) on the aryl moiety could not undergo the second-step reactions in the overall one-pot, two-step reaction sequence. Internal olefins *trans*- β -methylstyrene and cyclohexene, terminal olefins α -methylstyrene, phenyl vinyl sulfone, and allylbenzene did not participate in the second-step reactions either. 2-Vinylpyridine did not react due to its easy protonation by the acid catalyst.

Compounds **5** and **6** are the Markovnikov-type phenylselenative hydrovinylation products of styrene and other vinylarenes **3** with internal olefins **1** under Brønsted acid catalysis. Incorporation of a phenylseleno functionality into the products led to absolute control of the regioselectivity for the Markovnikov hydrovinylation of the two olefins, which is differentiated from those transition metal catalyzed-hydrovinylation reactions accompanied by the above-mentioned side reactions. The formation pathway of **5** and **6** is depicted in Scheme 4. The

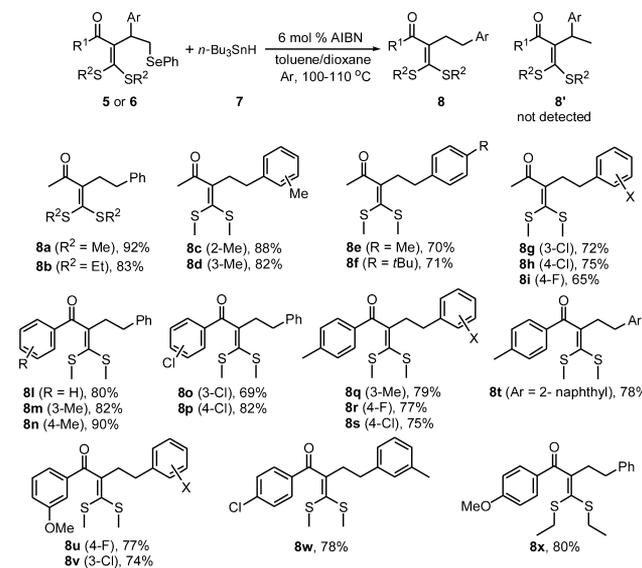
Scheme 4. Proposed Mechanism for Brønsted Acid Catalyzed Branched Phenylselenative Hydrovinylation



Brønsted acid initiates the in situ generation of cation PhSe⁺ (A) from *N*-PSP (**2**), which attacks the electron-rich vinylic carbon of α -oxo ketene dithioacetal **1**, forming episelenonium ion **B**.^{13,15} Proton release from species **B** affords the phenylselenative intermediate **4** (path a). Upon addition of styrene or a vinylarene **3** to the reaction system at the end of step one reaction, the equilibrated species **B** interacts with **3** to generate cation **C** via regioselective insertion of the vinylic C=C bond of **3** into the C–Se bond of **B**. Regeneration of the catalyst gives the target product **5** or **6** (path b).

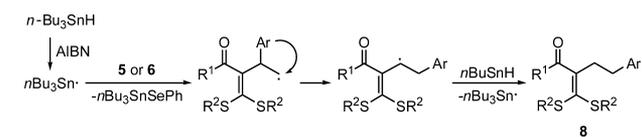
In order to obtain the dephenylselenative products, radical reduction was tentatively applied to compound **5a** by means of AIBN (2,2'-azobis(isobutyronitrile))/*n*-Bu₃SnH. Surprisingly, the desired Markovnikov-type dephenylselenative product of type **8'** was not obtained, whereas the linear alkylated olefin **8a**, formally formed from the *anti*-Markovnikov linear codimerization of styrene and α -oxo ketene dithioacetal **1a** was unambiguously formed (Scheme 5). The AIBN/*n*-Bu₃SnH system has been known to promote radical aryl migration from silicon to carbon.¹⁶ In our case, unusual radical aryl transfer from carbon to carbon was thus achieved, demonstrating a rare example of regioselectivity inversion in carbon–carbon bond formation (Scheme 6). Under heating **5** and **6** underwent the radical reductive dephenylselenation/aryl transfer to form the *anti*-Markovnikov-type linear alkylated olefin products **8a–i** in 65–92% yields (Scheme 5). The electron-withdrawing substituents

Scheme 5. Radical Dephenylselenative Aryl Transfer of **5 and **6** To Form Linear Hydrovinylation Products **8^{a,i}****

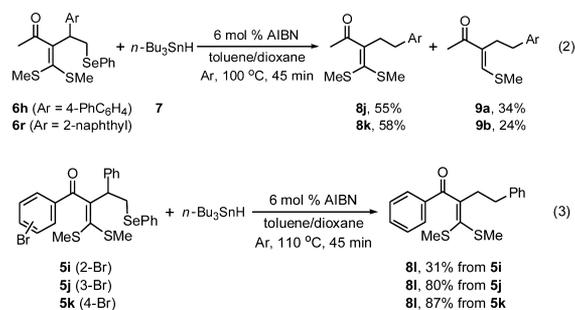


^aConditions: **5** or **6** (0.3 mmol), **7** (1.8 mmol, added in three portions), AIBN (6 mol %), toluene/dioxane (3 mL, v/v = 1:1), argon, 100 °C for **8a–k**, 110 °C for **8l–x**, 45 min. ^bIsolated yields.

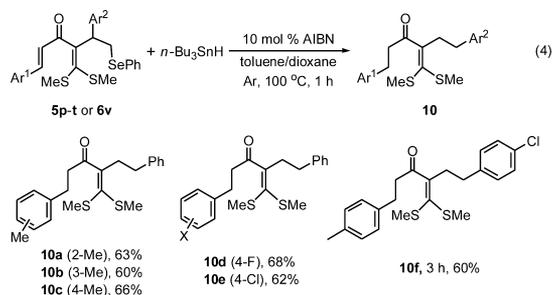
Scheme 6. Radical Reductive Aryl Transfer of **5 and **6****



such as chloro and fluoro on the aryl moiety of the starting vinylarenes lessened the product yields to some extent. In the cases of using the substrates bearing a bulky aryl group such as 4-PhC₆H₄ or 2-naphthyl, i.e., **6h** and **6r**, the reactions produced the target products **8j** (55%) and **8k** (58%) as well as monodesulfurative products **9a** (34%) and **9b** (24%) (eq 2),



respectively. Treatment of α -aroyl-bearing substrates **5** and **6** under the same conditions also gave linear alkylated olefins, that is, **8l–x**, in good to excellent yields (69–90%), and the chloro and fluoro substituents exhibited a negative impact on the product yields (Scheme 5). However, with bromoaroyl-functionalized substrates **5i–k** double reduction (reductive dephenylselenation–aryl transfer/hydrodebromination) occurred to form linear α -benzoyl- α -(2-phenylethyl) ketene dithioacetal **8l** as the product (31–87%), and the 2-Br substituent exhibited an obvious steric effect (eq 3). Double reduction also happened to cinnamoyl-bearing compounds **5p–t** and **6v** (eq 4). It is interesting that the fully functionalized C=C bond of the dithio ketene moiety



withstood the reaction conditions, while the less substituted C=C bond of the cinnamoyl was reduced to an alkyl. Compounds **10a–f** were thus obtained in 60–68% isolated yields. It should be noted that in all the reduction reactions the tributyltin moiety was transformed to *n*-Bu₃SnSePh,¹⁷ and the molecular structures of **5k** and **8u** were structurally confirmed by X-ray crystallographic determinations (see the Supporting Information).

In conclusion, PhSe-assisted, Brønsted acid *p*-TsOH·H₂O-catalyzed hydrovinylation of styrene and vinylarenes with α -oxo ketene dithioacetals efficiently afforded the branched phenylselenative codimerization products. Radical reductive aryl transfer occurred to transform the resultant Markovnikov-type olefins to the corresponding linear codimerization products formally from the anti-Markovnikov hydrovinylation of the two olefins. The present protocol provides a novel route to regioselectivity-tunable hydrovinylation of olefins.

■ ASSOCIATED CONTENT

Supporting Information

Complete experimental procedures and characterization data for the prepared compounds, X-ray crystallographic data for **5k** and **8u**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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