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Selenolate Anion as an Organocatalyst: Reactions and Mechanistic Studies

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Abstract. A new organocatalyst, the selenolate anion $[RSe]^-$, generated from bench-stable and commercially available diphenyl diselenide or from phenyl benzyl selenide (10 mol%) is introduced. Benchmarking is performed in the conversion of benzylic chlorides into *trans*-stilbenes selectively at room temperature. Mechanistic studies support the intermediacy of the selenolate anion and of 1,2-diphenylethyl phenyl selenide.

Keywords: Organocatalyst; Selenolate anion; Screening; Substrate; Selenium

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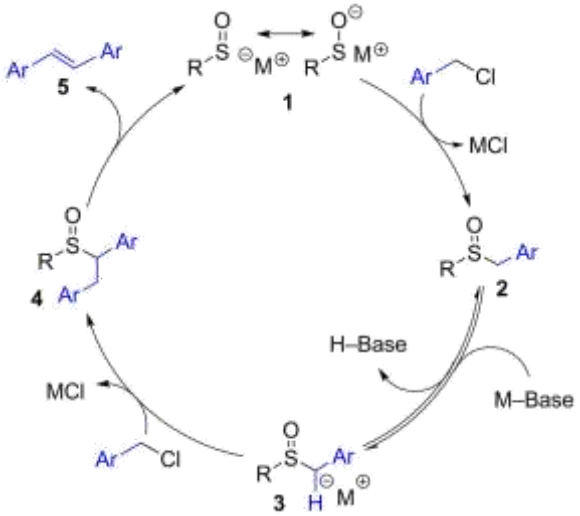
Introduction

The advent of modern organocatalysis has fundamentally changed the landscape of organic chemistry and asymmetric catalysis by introducing new modes of reactivity.[1,2] In turn, this has led to the development of novel bond-formations and invention of new reactions.[1a-c,2] Key to the success of the field of organocatalysis is the diversity of catalyst classes that have been reported, which often exhibit unique patterns of reactivity. As such, the search for new types of organocatalysts represents a clear pathway to discovery of new chemical transformations.

In this regard, we recently introduced a new class of organocatalysts, sulfenate anions.[1] Sulfenate anions, $[RSO]^-$, and their conjugate acids, sulfenic acids, RSOH, are known to be reactive intermediates in organic and biological chemistry, but had not been previously used as catalysts. We were attracted to these species based on their ability to behave as both nucleophiles and leaving groups in metal catalyzed reactions,[1e-g] and we hypothesized that they could act as organocatalysts. In probing this hypothesis, we demonstrated that sulfenate anions could behave as organocatalysts in the context of the dehydrocoupling of benzyl chlorides in the presence of base, as shown in Scheme 1. The sulfenate anion **1** reacts with benzyl chloride via an S_N2 to give sulfoxide **2**. Reversible deprotonation of sulfoxide **2** with base leads to the anion **3**, which gets trapped with a second equivalent of benzyl chloride to yield **4**. Finally, E2 elimination of **4** extrudes stilbene **5** to close the catalytic cycle. It was determined that the sulfenate anions can catalyze reactions using as little as 2.5 mol% catalyst while affording yields as high as 99%.[1a]

In an effort to develop related catalysts that can show enhanced reactivity, we focused our attention on selenium compounds.[2] Although sulfur and selenium have almost identical electronegativities, selenium is more polarizable and, therefore, can act as a better nucleophile. Herein, we disclose the generation of selenolate organocatalysts for the dehydrocoupling of benzyl halides to olefins, demonstrate the substrate scope of these catalysts, and also probe the reaction mechanism for this transformation.

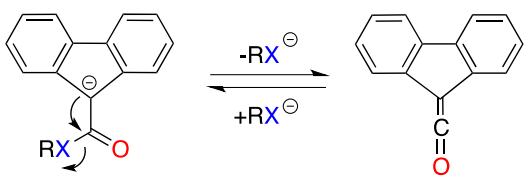


Scheme 1. Proposed mechanism of the sulfenate anion catalyzed generation of *trans*-stilbenes.

Results and Discussion

Reaction Development and Optimization. In our search for new organocatalysts, we use the dehydrocoupling of benzyl halides to form *trans*-stilbenes as our test reaction. We were inspired to explore systems that could promote such catalytic processes *at room temperature*. Preliminary studies using benzyl phenyl sulfoxide, $PhS(O)CH_2Ph$ (Scheme 1),[1a] and $ArCH_2Cl$ as the substrate (Ar = substituted aryl but not Ph) in the presence of base, resulted in formation of an unsymmetrical stilbene (PhCH=CHAr) in the first turnover. To circumvent the formation of unsymmetrical stilbene a "traceless" precatalyst PhS(O)*t*Bu, which under basic conditions eliminates isobutylene concurrent with the sulfenate anion, was developed. This catalyst allows the sulfenate anion **1** to enter the catalytic cycle, therefore avoiding contamination of the product with an unsymmetrical stilbene that is usually difficult to separate from the desired symmetric *trans*-stilbene, ArCH=CHAr.[1b]

Selenolates are expected to be better leaving groups because of their greater polarizability.[3] For example, the selenol ester (X = Se) decomposes to ketene 180 times faster than its thiol ester analogue (X = S) as shown in Scheme 2.[4]



Scheme 2. Decomposition of selenol and sulfanol ester to ketene (the rate of expulsion (k_{el}) of $[PhSe]^-$ is 20 s^{-1} and of $[PhS]^-$ is 36 $\times 10^2$ s^{-1} at 25 °C).

Selenolate anions have been isolated and characterized by single crystal X-ray diffraction studies. In general, the selenium of (RSe)M is bound to the metal in a terminal fashion.[5-6] As a source of selenolate anion, we decided to use commercially available benzyl phenyl selenide and diphenyl diselenide.[7] To establish proof-of-concept that such selenides could behave as organocatalysts, we set out to developed the base-promoted conversion of benzyl halides into *trans*-stilbenes.

We initiated a search for conditions for the selenolate-anion-catalyzed synthesis of *trans*-stilbene from benzyl chloride by screening eight different bases (LiO*t*Bu, NaO*t*Bu, KO*t*Bu, $LiN(SiMe_3)_2$, $NaN(SiMe_3)_2$, $KN(SiMe_3)_2$, KH and NaO*t*Pent) in the presence of benzyl phenyl selenide (10 mol %) in twelve different solvents [THF, DME (1,2-dimethoxyethane), 1,4-dioxane, CPME (cyclopentyl methyl ether), Et_2O, 2-Me-THF, DMSO, DMF, ACN (acetonitrile), DCE (1,2-dichloroethane), hexanes, and nBu_2O] for 10 h at room temperature and in microscale quantities. The results are illustrated graphically in Figure 1 (for screening details see Supporting Information, pages S19-S22).

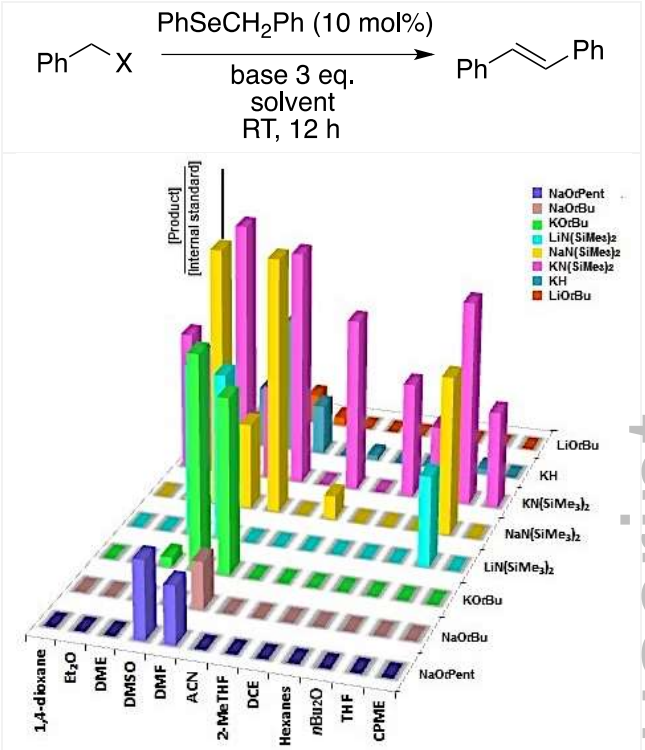


Figure 1. Optimization of the formation of stilbene from benzyl chloride using benzyl phenyl selenide (10 mol%) as catalyst.

Table 1. Lab scale optimization of the formation of stilbene from benzyl chloride with benzyl phenyl selenide as catalyst.

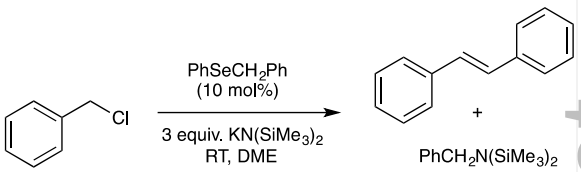
Entry[a)]	Solvent	Base	Catalyst mol %	Equiv. base	T,°C	Stilbene[b)] AY (%)
1	CPME	$KN(SiMe_3)_2$	5	3	RT	38
2	CPME	$KN(SiMe_3)_2$	10	3	RT	51
3	CPME	$KN(SiMe_3)_2$	10	3	80	39
4	DME	$KN(SiMe_3)_2$	5	3	RT	56
5	DME	$KN(SiMe_3)_2$	10	3	RT	72
6	DME	$NaN(SiMe_3)_2$	10	3	RT	69
7	DME	$KN(SiMe_3)_2$[c]	10	2	RT	90
8	DME	$KN(SiMe_3)_2$[c]	10	3	RT	92
9	DME	KO*t*Bu	10	3	RT	34
10	DME	$KN(SiMe_3)_2$	10	3	60	59
11	DMF	$KN(SiMe_3)_2$	5	3	RT	40
12	DMF	$NaN(SiMe_3)_2$	5	3	RT	21
13	THF	$KN(SiMe_3)_2$	5	3	RT	53
14	THF	$KN(SiMe_3)_2$	10	3	RT	60
15	Toluene	$KN(SiMe_3)_2$	5	3	RT	32

[a)] Reactions conditions: (0.2 mmol benzyl chloride, 1.0 equiv), 12 h, solvent 1 mL. [b)] AY (assay yields) determined by ^1H NMR spectroscopy using CH_2Br_2 as an internal standard. [c]Slow addition of benzyl chloride solution over 1 h.

As illustrated in Figure 1, strong bases such as $NaN(SiMe_3)_2$ and especially $KN(SiMe_3)_2$ gave the most promising results in polar solvents such as DMF and DME. Screening also showed that the $KN(SiMe_3)_2$/DME base-solvent system was the most effective for conversion (Supporting Information, pages S17-S20, Figure 1). Surprisingly, KH and KO*t*Bu did not provide good results, despite being very effective in the sulfenate anion catalyzed dehydrocoupling of benzyl chlorides.[1a] In more polar solvents, such as DMSO and DMF, stilbene formation was observed with almost all the bases used. Expanding these results to a preparatory scale employing these solvents, however, resulted in multiple products with lower yields of stilbene (vide infra).

Further optimization of the reaction conditions were performed on laboratory scale (0.2 mmol $PhCH_2Cl$) employing the most promising base and solvent combinations from the high-throughput screening illustrated in Figure 1. The results are listed in Table 1, where the assay yields (AY) were determined by ^{1}H NMR spectroscopy analysis of crude reaction mixtures. Employing CPME as solvent with 5 mol% of catalyst and 3 equiv of $KN(SiMe_3)_2$ resulted in the formation of *trans*-stilbene in 38% AY, entry 1. Under the same conditions with 10 mol% catalyst loading, the AY of *trans*-stilbene increased to 51% (entry 2). Raising the reaction temperature to 80 °C did not improve the reaction AY (entry 3). When DME was used as the solvent at 5 mol% catalyst loading 56% AY of *trans*-stilbene was obtained (entry 4) and with 10 mol% of catalyst the AY increased to 72% (entry 5). Changing the alkali metal in the form of $KN(SiMe_3)_2$ to $NaN(SiMe_3)_2$ did not significantly affect the yields (69% AY, entry 6).

During the course of the optimization it was found that a byproduct formed, namely *N*-benzyl-*N*,*N*-bis-(trimethylsilyl)amine [$PhCH_2N(SiMe_3)_2$][7] (Scheme 3). Amine $PhCH_2N(SiMe_3)_2$ is presumably generated via a background S_N2 reaction between $KN(SiMe_3)_2$ and the benzyl chloride. We hypothesized that slow catalyst turnover and its low concentration in solution provided ample time for the $KN(SiMe_3)_2$ and benzyl chloride to react to form the undesired amine byproduct. If this hypothesis is correct, decreasing the concentration of the benzyl chloride should reduce the formation of the amine byproduct. To our delight, the slow addition of benzyl chloride substrate over 1 h suppressed such background reaction leading to higher yields of product (entries 7–8, Table 1). Changing the rate of addition of $NaN(SiMe_3)_2$ did not improve the yield overall when compared to $KN(SiMe_3)_2$. Neither changing the base to KO*t*Bu nor increasing the reaction temperature to 60 °C improved the AY (entries 9–10). Finally, reactions in DMF with $KN(SiMe_3)_2$ or $NaN(SiMe_3)_2$ bases (entries 11 and 12) gave 40 and 21% AY of *trans*-stilbene, respectively, along with multiple impurities based on ^{1}H NMR spectroscopy. Using THF and $KN(SiMe_3)_2$ with 5 and 10 mol% catalyst afforded 53 and 60% AY of *trans*-stilbene, respectively (entries 13–14), while the use of toluene with 5 mol% of catalyst reduced the formation of product to 32% AY (entry 15).



Scheme 3. Stilbene and silylamine formation from benzyl chloride, catalyst and $KN(SiMe_3)_2$.

Based on the laboratory scale experiments in Table 1, the best reaction conditions for the benzyl phenyl selenide catalyzed dehydrocoupling of benzyl chloride to *trans*-stilbene was 10 mol% $PhSeCH_2Ph$ with 3.0 equiv of $KN(SiMe_3)_2$ in DME at room temperature and with slow addition of benzyl chloride using a syringe pump (see Supporting Information for details, page S4). We next examined the catalyst loading and how this affected AY (Table 2, entries 1–3). It was found that decreasing the amount of benzyl phenyl selenide catalyst from 10 to 5 and 2.5 mol% resulted in a decrease in yield from 88 to 73 and 51%, respectively (Table 2, entries 1–3). A control experiment employing the same conditions, but without benzyl phenyl selenide catalyst, resulted in formation of $PhCH_2N(SiMe_3)_2$ (98% yield, Table 2, entry 4) with no stilbene being produced.

We were motivated to find an alternative and more convenient entry to the $PhSe^-$ catalyst. As mentioned in the Introduction, starting with benzyl phenyl selenide ($PhSeCH_2Ph$), the benzyl group from the catalyst is incorporated into the stilbene product in the first turnover of the catalytic cycle (Scheme 4). This can be problematic when substrates other than the parent benzyl halides are employed, because the mol% of catalyst would ultimately yield the same % of unsymmetrical stilbene as an impurity (Scheme 4). We speculated that commercially available diphenyl diselenide might prove to be a good precatalyst if it could react with $KN(SiMe_3)_2$ to generate the catalyst $[PhSe]^-$ and $PhSeN(SiMe_3)_2$, the former which would serve as a catalyst. Despite half the precatalyst being lost in the reaction through $PhSeN(SiMe_3)_2$, this process would represent a more direct route to $[PhSe]^-$.

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Table 2. Formation of stilbene and *N*-benzyl-*N*,*N* bis(trimethylsilyl) amine from benzyl chloride with benzyl phenyl selenide as catalyst (entries 1–3) and diphenyl diselenide as precatalyst (entries 5–7)

Entry[a)]	Catalyst mol %	Catalyst	Stilbene (AY, %)[b)]	$PhCH_2N(SiMe_3)_2$ (AY, %)	Time (min)
1	10	$PhSeCH_2Ph$	88[c)]	19	300
2	5	$PhSeCH_2Ph$	73	22	300
3	2.5	$PhSeCH_2Ph$	51	49	300
4	0	-	<1	98	300
5	10	Ph_2Se_2	92	3	300
6	5	Ph_2Se_2	83	12	300
7	2.5	Ph_2Se_2	58	39	300

a) Reaction conditions: (0.2 mmol benzyl chloride, 1.0 equiv, in 1.5 mL of DME), base (3.0 equiv), RT, addition rate 5 µL/min. b) AY (assay yields) determined by ^1H NMR spectroscopy using CH_2Br_2 as an internal standard. Solvent: DME (total 2 mL, in syringe: 1.5 mL: in vial 0.5 mL). c) Total yield greater than 100% because of stilbene formation from 10 mol% of catalyst employed.

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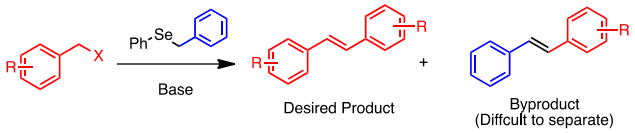

Scheme 4. Undesired byproduct formation with use of benzyl phenyl selenide as precatalyst.

Thus, using the optimized reaction conditions for the coupling process with precatalyst $PhSeCH_2Ph$, we employed Ph_2Se_2 instead (10 mol%). We were pleased to discover that stilbene formed in 92% AY (Table 2, entry 5). Despite only 50% of the precatalyst being converted to the active catalyst (see discussion below), the AY under these conditions rivals reactions using 10 mol% $PhSeCH_2Ph$. Reducing the loading of Ph_2Se_2 from 10 to 5 and 2.5 mol%, however, resulted in a decrease in the AY from 92 to 88 and 51% (Table 2, entries 5–7). However, the percentage of *N*-benzyl-*N*,*N*-bis(trimethylsilyl)amine side product is lower when precatalyst Ph_2Se_2 was used compared to $PhSeCH_2Ph$ (Table 2, entries 5–7).

Substrate Scope of the Coupling of Benzyl Halides. With the optimized conditions in hand for the reactions promoted by precatalyst Ph_2Se_2 (Table 2, entry 5) and $PhSeCH_2Ph$ (Table 2, entry 1), the substrate scope for the electrophiles was next examined (Table 3). Because Ph_2Se_2 afforded better results, and is commercially available, isolated yields were only obtained using this precatalyst. For comparison purposes between the two catalyst systems, ^1H NMR spectroscopic assay yields (AY) have been measured [Ph_2Se_2 (**A**) and $PhSeCH_2Ph$ (**B**)] as indicated in Table 3.

As anticipated, benzyl chlorides were more suitable substrates than benzyl bromides, because the latter readily undergo S_N2 reactions with the base to generate $ArCH_2N(SiMe_3)_2$. Consequently, with diphenyl diselenide employed as catalyst, benzyl bromide was dehydrocoupled to the stilbene in 65% yield whereas benzyl chloride was dehydrocoupled with yields as high as 93% (entries 1–2, Table 3). Methyl benzyl chlorides gave the corresponding products in reasonable to very good yields (70–84%, Table 3, entries 3–5). More sterically hindered di-*ortho*-substituted benzyl chloride derivatives such as 1-chloro-2-(chloromethyl)-3-fluorobenzene and 1,3-dichloro-2-(chloromethyl)benzene also gave good yields (70 and 67%, respectively, Table 3, entries 6–7). For benzyl chlorides bearing a fluoro atom at the 2, 3, and 4 positions relative to the chloromethyl group (Table 3, entries 8–10), the yields where in the 72–86% range. The substrate bearing a 4-chloro substituent was dehydro coupled in 85% yield (Table 3, entry 11) whereas 4-CF_3-benzyl chloride resulted in only 36% yield (Table 3, entry 12), possibly due to elimination of F^- upon deprotonation at the benzylic position. 1-(Chloromethyl)-naphthalene proved to be a fine substrate, being dehydrocoupled to the respective olefin product in 71% yield (Table 3, entry 13). Unfortunately, benzyl chlorides bearing strong electron donating groups, such as 4-OMe, gave very low yields, possibly due to the decreased acidity of the benzylic protons. When yields for Ph_2Se_2 (**A**) where compared to $PhSeCH_2Ph$ (**B**), similar trends were observed (Table 3, entries 1–13, column B). In the case of $PhSeCH_2Ph$ however, AY's are slightly lower, most likely due to the formation of unsymmetrical stilbene byproducts previously discussed in Scheme 4 (vide supra).[1a-1b]

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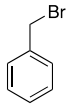
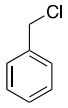
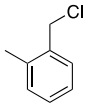
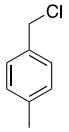
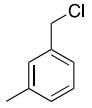
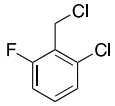
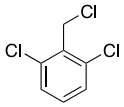
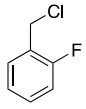
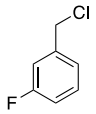
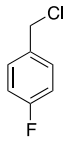
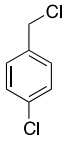
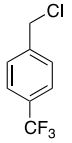
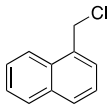
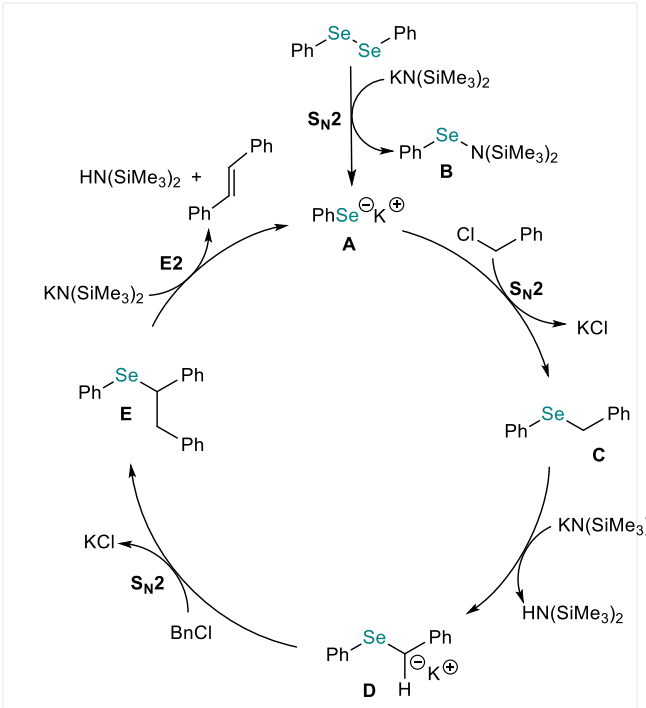
Table 3. Substrate scope of the selenolate-anion-catalyzed dehydrocoupling of benzyl halides.

Entry[a]	Equivalents of base [b]	Substrate	Stilbene IY (AY)[c]		$PhCH_2N(SiMe_3)_2$, AY(%)	
			A	B	A	B
1	3		65 (62)	74 (69)	20	28*
2	3		93 (92)	(88)	3	19*
3	3		70 (77)	(79)	n.d.	20
4	3		82 (86)	-	9	-
5	3		84 (86)	(74)	9	26
6	3		70 (71)	(64)	n.d.	n.d.
7	3		67 (69)	(72)	n.d.	n.d.
8	1.5		85(99)	(76)	n.d.	n.d.
9	1.5		72 (85)	(75)	n.d.	n.d.
10	1.5		86 (94)	(77)	5	23
11	1.5		85 (97)	(90)	n.d.	n.d.
12	1.5		36 (27)	-	n.d.	-
13	3		71 (81)	(82)	n.d.	n.d.

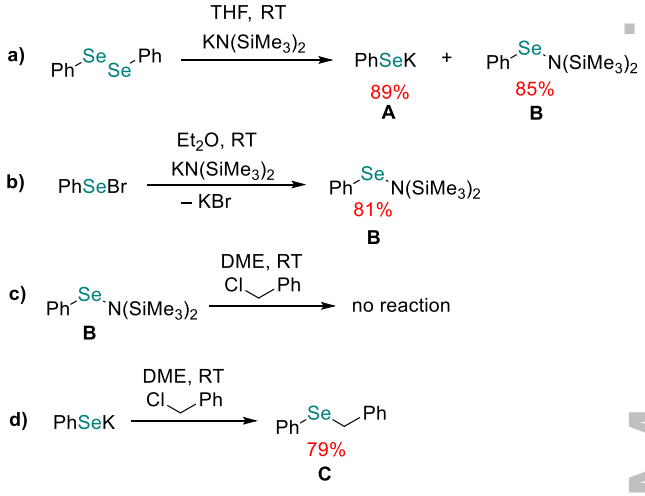
*Total yield more than 100% because of stilbene formation from 10% of catalyst compound
a) Catalyst Ph_2Se_2 (**A**), $PhCH_2SePh$ (**B**). Reactions conditions: (0.2 mmol aryl chloride, 1.0 equiv), RT. b) $KN(SiMe_3)_2$ (3.0 equiv for entries 1-7 and 13, 1.5 equiv for entries 8-12). c) AY (assay yields) determined by ^1H NMR spectroscopy using CH_2Br_2 as an internal standard. IY (isolated yields). Solvent: DME (total 2 mL, in syringe: 1.5 mL: in vial 0.5 mL, addition rate 5 µL/ min, 0.1 M for entries 1-7 and 13. For entries 8-12: total volume 1 mL, in syringe: 0.5 mL: in vial 0.5 mL, 0.2 M, addition rate 30 µL/ min.

Characterization of Reaction Intermediates. We hypothesized that Ph_2Se_2 reacts with $KN(SiMe_3)_2$ to form PhSeK (**A**) and $PhSeN(SiMe_3)_2$ (**B**) as shown in Scheme 5. The generated **A** is a strong nucleophile and therefore should rapidly react with benzyl chloride to form $PhSeCH_2Ph$ (**C**). In the presence of $KN(SiMe_3)_2$, **C** is most likely in equilibrium with its conjugate base [PhSeCHPh][K] (**D** Scheme 5). The resulting carbanion **D** then reacts with benzyl chloride to generate 1,2-diphenylethyl phenyl selenide (**E**). Deprotonation of **E** at the β-position is speculated to promote E2 elimination generating *trans*-stilbene with concurrent expulsion of the potassium selenolate catalyst (**A**).



Scheme 5. Proposed mechanism of the selenolate-anion-catalyzed coupling of benzyl halides to form symmetric stilbenes using precatalyst Ph_2Se_2.

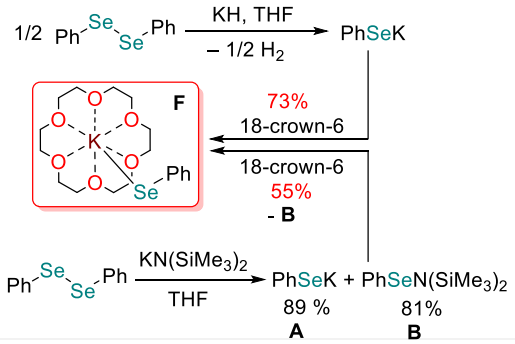
To probe the reaction mechanism, we independently synthesize key proposed reaction intermediates. We began our investigation with the reaction of Ph_2Se_2 with one equiv of $KN(SiMe_3)_2$, which we proposed should form potassium selenolate **A** and side product **B** (Scheme 6a). Thus, treatment of $KN(SiMe_3)_2$ with Ph_2Se_2 in THF at RT resulted in formation of a white precipitate that was recovered by filtration and presumed to be **A**. The volatile materials were removed from the filtrate leaving behind a yellow oil. The identity of the oil was assigned as $PhSeN(SiMe_3)_2$ based on NMR spectroscopic characterization (^1H, $^{13}C\{^1H\}$ and ^{77}Se NMR spectroscopy) as well as mass spectrometry (see Supporting Information, page S17). Compound **B** was also independently synthesized by the reaction of PhSeBr with $KN(SiMe_3)_2$[9] in Et_2O (Scheme 6b). It should be noted that isolated **B** is highly moisture sensitive and samples of this reagent did not react with benzyl chloride (Scheme 6c).



Scheme 6. Synthesis of catalytic intermediates.

The white insoluble solid, presumed to be **A** formed from the reaction shown in Scheme 6a, was dried under reduced pressure and then treated with one equiv of benzyl chloride in DME at RT. This reaction furnished benzyl phenyl selenide in 79% yield, which was also confirmed by ^1H NMR spectroscopy (Scheme 6d). We further characterized the selenolate salt **A** by an independent route and derivatization. Accordingly, reaction of ½ Ph_2Se_2 with KH (Scheme 7, top) followed by the addition of 18-crown-6 yielded the derivative **F**, namely [PhSeK(18-crown-6)] in 73% yield (Scheme 7 and Supporting Information, page S23). The resulting white solid is partially soluble in DME and THF thus allowing us to characterize and identify this species in solution (^{77}Se NMR: 149 ppm). To determine if the solid formed after reaction of Ph_2Se_2 with $KN(SiMe_3)_2$ is the same as that formed in the reaction of ½ Ph_2Se_2 with KH, compound **F** was independently synthesized from the reaction of Ph_2Se_2 with $KN(SiMe_3)_2$, followed by addition of 18-crown-6 (Scheme 7, bottom). The solid formed from this reaction was identical spectroscopically to that observed for the same material [PhSeK(18-crown-6)] (**F**) prepared from KH and crown-ether addition to

Ph_2Se_2. Notably, compound **F** was subsequently crystallized from THF, and single crystal X-ray diffraction analysis confirmed its identity and connectivity. As shown in Figure 2 the solid state structure of **F** reveals a monomeric system with a partially encapsulated potassium cation by the crown, since the Se center still coordinates to the counter cation.



Scheme 7. Synthetic routes for [PhSeK(18-crown-6)] (**F**).

The Se–K bond distance of 3.3068(9) Å in [PhSeK(18-crown-6)] lie in a range of reported terminal Se–K bond lengths (3.17–3.47 Å) and the encapsulated K^+ is oriented almost orthogonal to the plane of the arene (K–Se–C_{ipso} angle is 99.01(11)°).[5a, 10]

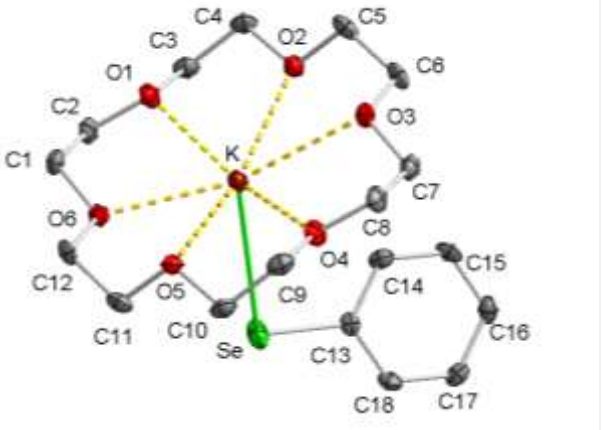
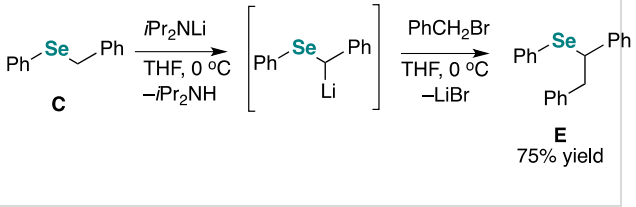


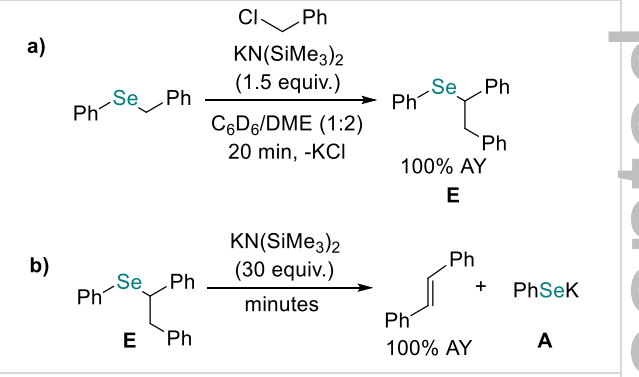
Figure 2. Crystal structure of [PhSeK(18-crown-6)] with 50% thermal ellipsoids (hydrogens have been omitted for clarity). Selected bond lengths (Å) and angle (deg): Se-C13 1.900(4); O1-K-Se 111.20(6); O1-K-O2 59.81(8); O4-K-Se 86.18(6).

To probe the reactivity of the proposed carbanion **D** (Scheme 5), we combined $PhSeCH_2Ph$ with $KN(SiMe_3)_2$ and benzyl chloride and monitored the reaction by ^1H NMR spectroscopy to observe 1,2-diphenylethyl phenyl selenide (Ph_2Se_2)[11] (**E**, Scheme 5). To confirm the identity of **E**, such species was independently synthesized by addition of benzyl phenyl selenide to 2 equiv LDA (iPr_2NLi) with subsequent dropwise addition of benzyl bromide. This resulted in the formation of **E** in 75% isolated yield (Scheme 8).[11]



Scheme 8. Independent synthesis of 1,2-diphenylethyl phenyl selenide.

In the proposed mechanism shown in Scheme 5 species **E** undergoes a concerted base promoted elimination (E2) to generate *trans*-stilbene and PhSeK (**A**). To probe this step we performed the reaction between benzyl chloride, $KN(SiMe_3)_2$ and $PhSeCH_2Ph$ (**C**) in a J. Young tube using an internal standard (capillary using a known concentration of dibromomethane). After 20 min at RT compound **E** was formed quantitatively (Scheme 9a). Next, combination of the latter species with excess $KN(SiMe_3)_2$ (30 equiv, which is a similar amount used under catalytic conditions) afforded *trans*-stilbene in 100% AY, Scheme 9 (see Supporting Information, pages S13-S14).



Scheme 9. Stoichiometric steps to form intermediate **E** and its conversion to *trans*-stilbene and **A**.

Conclusion

In summary, we hypothesized that selenolate anions would be efficient organocatalysts because of the enhanced polarizibility of Se relative to S. This feature renders the $PhSe^-$ anion a better leaving group in comparison to the sulfur analogue. The benchmark reaction supporting this conjecture was the dehydrocoupling of benzylic chlorides into *trans*-stilbenes. It was shown that commercially available

Ph_2Se_2 reacts cleanly with $KN(SiMe_3)_2$ to provide easy access to the selenolate anion $PhSe^-$, without the necessity of isolation nor purification, and which also catalyzes the conversion of benzyl halides into *trans*-stilbenes. Reactivity studies in combination with control experiments and independent syntheses provided strong evidence for the intermediacy of species such as PhSeK (**A**), $PhSeCH_2Ph$ (**B**), and $PhSeCHPhCH_2Ph$ (**E**). Based on these studies, we conjecture that selenolate anions have significant potential in organocatalysis by taking advantage of their ability to stabilize carbanions and also promote C=C formation via an E2 mechanism. Other related reactions that are catalyzed by this novel class of catalysts are currently under investigation in our laboratories.

Experimental Section

General Procedure for Catalysis with Diphenyl Diselenide: To an oven-dried microwave vial equipped with a stir bar was added diphenyl diselenide and $KN(SiMe_3)_2$ (3.0 equiv for entries 1-7 and 13 (Table 3), or 1.5 equiv for entries 8-12 (Table 3)), under nitrogen atmosphere followed by 1.5 mL (entries 1-7 and 13, Table 3) or 0.5 mL (entries 8-12, Table 3) dry DME at 21 °C. The microwave vial was sealed with a cap containing a septum. Benzyl chloride (23 µL, 0.20 mmol) in dry DME was added by syringe pump (5 µL/ min, 0.1 M) to a solution of the diphenyl diselenide with $KN(SiMe_3)_2$ for entries 1-7 and 13, (30 µL/ min, 0.2 M, for entries 8-12. After the reaction was complete (defined by screening of the reaction mixture by ^{1}H NMR spectroscopy and TLC), the sealed vial was opened to air, and the reaction mixture was passed through a short pad of silica gel. The pad was then rinsed with 10 mL of ethyl acetate and the solvent was removed under reduced pressure. The crude product was purified by dissolving in hexanes, filtering through a short pad of silica gel, and solvent removed under reduced pressure. The residue was washed with 3-5 mL cold pentane or flash chromatography on silica gel (eluted with hexanes). For further details of the synthesis and characterization, see the Supporting Information.

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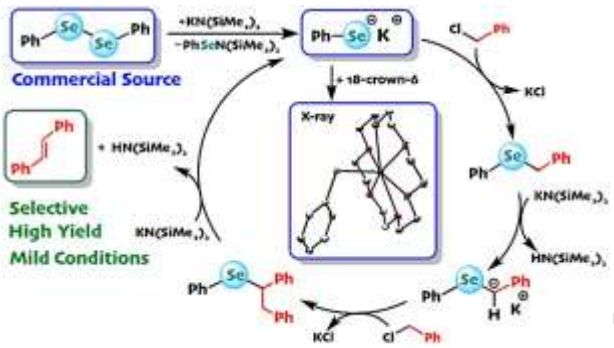
FULL PAPER

Selenolate Anion as an Organocatalyst: Reactions and Mechanistic Studies



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