

Bis[2-(2-pyridyl)phenyl] diselenide, a more effective catalyst for oxidation of alcohols to carbonyl compounds

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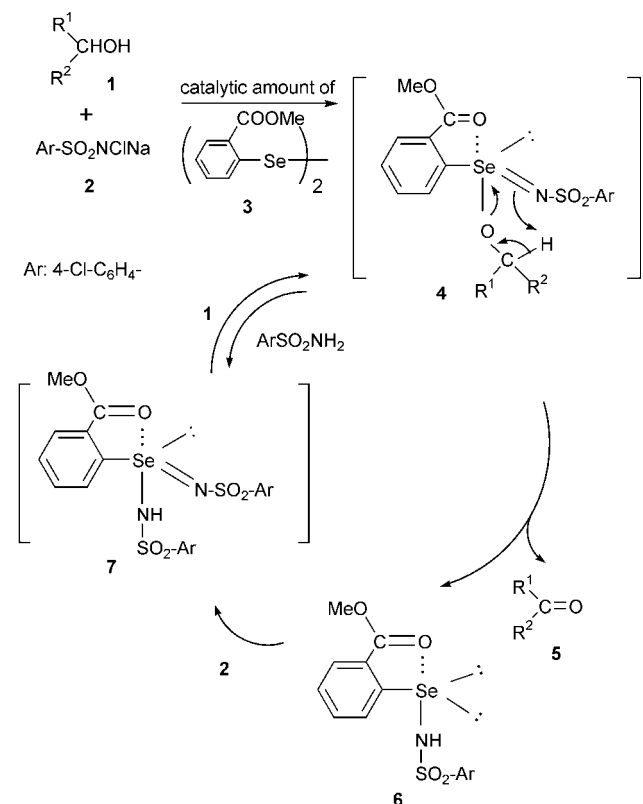
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Bis[2-(2-pyridyl)phenyl] diselenide was found to be a more effective catalyst than any of the diselenides reported earlier by us for the oxidation of alcohols; secondary alcohols and a β,γ -unsaturated primary alcohol were oxidized to carbonyl compounds in high yields by using 0.002–0.01 mol equiv. (0.2–1 mol%) of the new diselenide and a stoichiometric amount of *N*-chloro-4-chlorobenzenesulfonamide sodium salt as oxidant. The reason why the new catalyst is more efficient has been discussed.

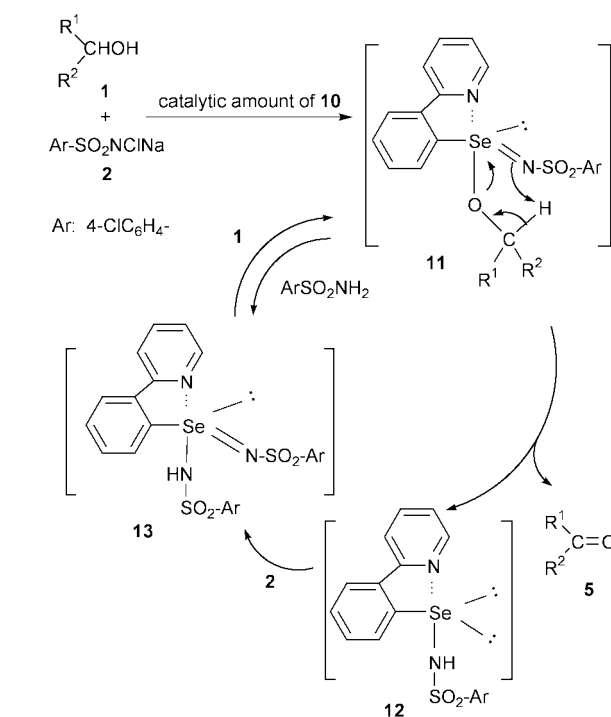
We have reported¹ the oxidation of alcohols to carbonyl compounds using a catalytic amount of diaryl diselenide **3** and a stoichiometric amount of *N*-chloro-4-chlorobenzenesulfonamide sodium salt (**2**) as oxidant, and proposed the reaction mechanism to be as shown in Scheme 1. The catalytic oxidation

nitrogen atom was expected to coordinate more strongly to the selenium atom, and bis[2-(2-pyridyl)phenyl] diselenide (**10**) was successfully obtained. Upon being oxidized with *N*-chloro-4-chlorobenzenesulfonamide sodium salt (**2**), the nitrogen atom of the pyridine ring in this new diselenide is expected to hyper-coordinate strongly to the selenium atom as depicted in the structures of intermediates **11**, **12**, or **13** (Scheme 2). In this



Scheme 1 Selenium-catalyzed oxidation of alcohols.¹

reported is a rare case which depends on the presence of a main group element (Se) to act as a redox catalytic center, and we have also suggested that *ortho* substituents on the benzene ring, which can hypercoordinate² to the selenium atom in the manner shown in **4**, accelerate the oxidation rate. Therefore, we tried to prepare another diaryl diselenide with nitrogen-containing substituents at the *ortho* position of the benzene rings in the hope of getting a more effective catalyst since the



Scheme 2 Selenium-catalyzed oxidation of alcohols using diselenide **10**.

report, we would like to describe the preparation of the new catalyst (**10**) and its superiority over diselenide **3**, which has previously been known to be the most efficient catalyst.¹

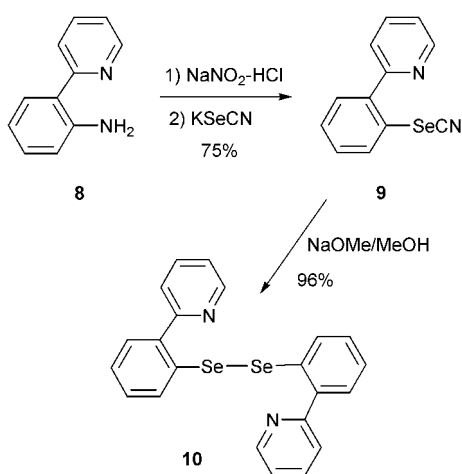
Results and discussion

Diselenide **10** was prepared from 2-(2-pyridyl)aniline (**8**) as shown in Scheme 3, while the starting compound **8** was derived

Table 1 Oxidation of alcohols by using 4-ClC₆H₄SO₂NCINa (**2**) and a catalytic amount of diaryl diselenide^a

Entry	Alcohol	Catalyst/mol equiv.	Time ^b /h	Product	Yield ^b (%)
1	Octan-2-ol	10 (0.01)	7	Octan-2-one	99
2	Octan-2-ol	3 (0.01)	36	Octan-2-one	98
3	Octan-2-ol	3 (0.02)	7	Octan-2-one	99
4	1-Phenylethanol	10 (0.002)	3	Acetophenone	99
5	1-Phenylethanol	3 (0.002)	16	Acetophenone	99
6	1-Phenylethanol	3 (0.005)	3	Acetophenone	99
7	Geraniol	10 (0.005)	7	Geranial	92 ^c
8	Geraniol	3 (0.005)	36	Geranial	74 ^{c,d}
9	Geraniol	3 (0.015)	7	Geranial	92 ^{c,e}
10	Decan-1-ol	10 (0.02)	2	Decan-1-al	44 ^f
11	Decan-1-ol	3 (0.02)	2	Decan-1-al	24 ^g

^a A mixture of alcohol (0.5 mmol), anhydrous 4-ClC₆H₄SO₂NCINa (0.6 mmol), and diaryl diselenide (0.001–0.01 mmol) in dry 1,2-dichloroethane (3 ml) was vigorously stirred at 80 °C. ^b The progress of the reactions was monitored by GC, and yields were determined by GC relative to internal standards. ^c The yield decreased gradually after this. ^d A small amount (3.3%) of the unreacted alcohol was recovered. ^e A small amount (1.6%) of the unreacted alcohol was recovered. ^f The reaction ceased at 71% conversion. ^g The reaction ceased at 63% conversion.

**Scheme 3**

from commercially available 2-nitroaniline according to the literature method.³ Using this new diselenide as catalyst, four kinds of typical alcohols were oxidized to carbonyl compounds in the presence of a stoichiometric amount of the oxidant **2**, and the results were compared with those of the reactions using diselenide **3**, which has previously been known to be the most efficient catalyst.¹

As can be seen in Table 1, a saturated secondary alcohol (entry 1), a β,γ -unsaturated secondary alcohol (entry 4), and a β,γ -unsaturated primary alcohol (entry 7) were oxidized to carbonyl compounds in high yields by using 0.002–0.01 mol equiv. (0.2–1 mol%) of diselenide **10**. In all these cases, the amounts of the diselenide were reduced to between one third and one half, whilst 2–3 times as much diselenide **3** compared to **10** is required to get the same results in respect of reaction times and yields (entries 3, 7 and 9). In the oxidation of a saturated primary alcohol (entries 10 and 11), the yield of the corresponding aldehyde increased to 44% by using 0.02 mol equiv. of diselenide **10** instead of the same amount of **3**. However, the yield is still poor, and the reaction ceased at 71% conversion.

Use of the same amount of diselenide **3** as that of **10** did not result in a decrease in the yields of carbonyl compounds in the cases of octan-2-ol and 1-phenylethanol, but the reaction time required to ensure complete oxidation of the alcohols was about 5 times that for **10** (entries 2 and 5). In the case of geraniol, however, the yield decreased markedly when using **3**, and the reaction failed to reach completion even after 36 h (entry 8).

In order to examine whether the decomposition of ester **11** (Scheme 2) is a rate-determining step, oxidation rates of 1-phenylethanol and 1-phenylethanol-1-*d* were measured; 1-phenylethanol was found to be oxidized 3.2 times faster than

1-phenylethanol-1-*d* at 60 °C when the catalyst **10** was used.† A similar rate ratio ($k_H/k_D = 3.1$ ‡) was observed when diselenide **3** was used as catalyst. Such isotope effects indicate that the proton-transfer step in the decomposition of the esters is rate-determining.§

Although the reason why diselenide **10** is more active than diselenide **3** is not clear, stronger coordination of the nitrogen atom to the central selenium atom in the manner shown in intermediate **11** (Scheme 2) may cause formation of a fractional negative charge on the nitrogen atom of the Se=N moiety. This would result in a more basic nitrogen atom which abstracts an α -hydrogen from the alkoxy group more readily. This would lead to the more facile decomposition of intermediate **11** to the divalent selenium compound **12**, yielding ketone **5**.

We suggested previously that *ortho* substituents on the benzene ring which can hypercoordinate to the selenium atom in the manner shown in the intermediate **4** (Scheme 1) could be essential for a rapid catalytic reaction.^{1,6} Such a speculation clearly receives further support from these new studies with the *ortho*-2-pyridyl substituent.

Experimental

Melting points were determined on a capillary tube melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Perkin-Elmer Spectrum One infrared spectrometer and nuclear magnetic resonance (¹H NMR and ¹³C NMR) spectra were recorded on a JEOL JNM-EX270 spectrometer. Tetramethylsilane (TMS) was used as internal standard; chemical shifts are denoted in ppm downfield to TMS. Gas chromatographic (GC) analyses were performed on a Hewlett Packard 5890 gas chromatograph with flame ionization detectors. Gas chromatography–mass spectra (GC-MS) were recorded on a Hitachi M-80B mass spectrometer system. 1,2-Dichloroethane was dried and stored over molecular sieves 3 Å.

Preparation of 2-(2-pyridyl)phenyl selenocyanate (**9**)

2-(2-Pyridyl)aniline³ (1.380 g, 8.11 mmol) was dissolved in 37 ml of 2.7% hydrochloric acid. After cooling the solution to

† The calculated rate ratio (k_H/k_D) is 5.1 if the proton (deuteron) transfer step (**11**→**12**) is fully rate-determining. The calculation was made on the basis of observed IR stretching frequencies of C(1)–H bond (2878 cm⁻¹) in 1-phenylethanol and C(1)–D bond (2128 cm⁻¹) in 1-phenylethanol-1-*d*. See ref. 4.

‡ The rate ratio of 5.2 was reported previously,¹ but this time the reaction was reinvestigated using the more reliable method (see the Experimental section).

§ The ratio of more than 2 suggests that the proton transfer occurs in the transition state of the rate-determining step. See ref. 5.

2 °C, a chilled solution of sodium nitrite (98.5% pure, 597 mg, 8.52 mmol) in 4.5 ml of water was added dropwise maintaining the temperature at 2–4 °C. Stirring was then continued for 5 min at 4–5 °C. Urea (*ca.* 90 mg) was added and the reaction was checked with starch–iodide paper. To this reaction mixture, sodium acetate (*ca.* 2.2 g) was added until pH paper indicated a pH of about 5. A solution of potassium selenocyanate (98.5% pure, 1.353 g, 8.92 mmol) in 4.6 ml of water was added dropwise to the reaction mixture at 4–5 °C, and the resulting mixture was allowed to warm to room temperature. After making the mixture basic (pH 9) with sodium carbonate, a precipitated solid was collected, washed with water and dried to give 2.042 g of brown powder. In order to remove minor polar impurities, the crude product was passed through a short plug of silica gel (10 g) using benzene as eluent. Evaporation of the benzene afforded 1.611 g of crystals, which were washed with 1:1 ethanol–hexane to give the title compound **9** (1.566 g, 75%) as needles. An analytical sample was obtained by recrystallization from ethanol: mp 114.6–115.4 °C (Found: C, 55.58; H, 3.35; N, 10.50. C₁₂H₈N₂Se requires C, 55.61; H, 3.11; N, 10.80%); $\nu_{\max}(\text{KBr})/\text{cm}^{-1}$ 2136w (CN), 1595, 1438, 1019, 749, 730; $\delta_{\text{H}}(270 \text{ MHz}; \text{CDCl}_3; \text{Me}_4\text{Si})$ 7.33 (1H, ddd, $J = 7.6, 5.3, 1.3$ Hz), 7.42–7.49 (2H, m), 7.89 (1H, ddd, $J = 8.3, 7.3, 1.7$ Hz), 7.97–8.05 (2H, m), 8.24 (1H, m), 8.65 (1H, ddd, $J = 5.3, 1.7, 1.0$ Hz, 6-pyridyl proton); $\delta_{\text{C}}(67.8 \text{ MHz}; \text{CDCl}_3; \text{Me}_4\text{Si})$ 111.2 (–SeCN), 119.4, 122.7, 126.7, 127.4, 128.4, 130.7, 131.4, 134.0, 137.9, 144.6, 153.5.

Preparation of bis[2-(2-pyridyl)phenyl] diselenide (**10**)

To a suspension of 2-(2-pyridyl)phenyl selenocyanate (1.037 g, 4.0 mmol) in 25 ml of methanol was added a 28% solution of sodium methoxide in methanol (1.63 ml, 8.0 mmol). The resulting mixture was stirred for 6 h at 25 °C. After addition of water (8 ml), the precipitated crystals were collected by filtration, washed with water, and dried to give 0.924 g of the title compound **10**. Recrystallization from ethyl acetate (20 ml) gave 0.841 g of pure bis[2-(2-pyridyl)phenyl] diselenide. Concentration of the mother liquor to *ca.* 1 ml afforded a second crop of 56 mg of crystals. Therefore, the total yield of **10** was 0.897 g (96%); mp 142.8–143.7 °C (Found: C, 56.46; H, 3.58; N, 5.89. C₂₂H₁₆N₂Se₂ requires C, 56.66; H, 3.46; N, 6.01%); $\nu_{\max}(\text{KBr})/\text{cm}^{-1}$ 1589, 1574, 1481, 1464, 1435, 1423, 1017, 745; $\delta_{\text{H}}(270 \text{ MHz}; \text{CDCl}_3; \text{Me}_4\text{Si})$ 7.19–7.32 (6H, m), 7.69 (2H, dd, $J = 7.6, 2.0$ Hz), 7.76–7.86 (4H, m), 8.02 (2H, dd, $J = 7.9, 1.3$ Hz), 8.74 (2H, m, 2-pyridyl protons); $\delta_{\text{C}}(67.8 \text{ MHz}; \text{CDCl}_3; \text{Me}_4\text{Si})$ 121.6, 122.1, 126.2, 127.9, 129.5, 131.8, 132.2, 136.8, 138.3, 147.2, 157.5.

General procedure used for the determination of yields in the catalytic oxidation of alcohols

To a mixture of alcohol (0.50 mmol, listed in Table 1), diaryl diselenide (0.001–0.01 mmol, listed in Table 1) and a suitably chosen straight chain hydrocarbon (internal standard for GC analysis) in 3.0 ml of 1,2-dichloroethane was added 0.6 mmol of anhydrous *N*-chloro-4-chlorobenzenesulfonamide sodium salt⁷ (dried at 80 °C *in vacuo*), and the mixture was magnetically stirred at 80 °C under a nitrogen atmosphere. Samples of *ca.* 30 μl were withdrawn periodically, diluted with 1.5 ml of 1:1 diethyl ether–benzene, washed with an aqueous solution made up of two parts 1 M NaOH and one part saturated NaCl, and were dried (Na₂SO₄) and analyzed by GC (15 m DB-1 or DB-17, 0.53 mm id, 3.0 μm).

Rate comparisons

To a mixture of 1-phenylethanol (64.9 mg, 0.532 mmol) and 1-phenylethanol-1-*d*¹ (57.6 mg, 0.468 mmol) in 5.2 ml of 1,2-dichloroethane, was added a solution of bis[2-(2-pyridyl)phenyl] diselenide (3.73 mg, 8.0 μmol) in 0.80 ml of 1,2-dichloroethane under nitrogen atmosphere. After addition of anhydrous *N*-chloro-4-chlorobenzenesulfonamide sodium salt (304 mg, 1.24 mmol), the mixture was stirred magnetically at 60 \pm 0.2 °C using a temperature-controlled bath. Samples of 10 μl were withdrawn periodically, diluted with 1.0 ml of 1:1 diethyl ether–benzene, washed with an aqueous solution made up of two parts 1 M NaOH and one part saturated NaCl, and were dried (Na₂SO₄) and analyzed by both GC (15 m DB-17, 0.53 mm id, 3.0 μm , 70–150 °C) and GC-MS (GC: 15 m DB-1, 0.53 mm id, 3.0 μm , 60 °C; MS: 20 eV). Ratios of 1-phenylethanol to 1-phenylethanol-1-*d* in the reaction mixture were determined by integration of GC-MS peaks at *m/z* 122 and 123.

The amounts of the alcohols (1-phenylethanol and 1-phenylethanol-1-*d*) oxidized were plotted against reaction times and each reaction rate of the oxidations of 1-phenylethanol and 1-phenylethanol-1-*d* was determined by the differentiation of fitted equations of the third degree in reaction time.⁸ The observed reaction rates ($d[\text{ketone}]/dt$) after 31.6 min (at this point, [1-phenylethanol] = [1-phenylethanol-1-*d*]) for 1-phenylethanol and 1-phenylethanol-1-*d* were 2.69×10^{-3} and $8.40 \times 10^{-4} \text{ M min}^{-1}$, respectively, which gave $k_{\text{H}}/k_{\text{D}} = 3.2$.

The rate measurement using dimethyl 2,2'-diselenodibenzate (5.0 μmol) as catalyst was similarly carried out. A mixture of 1-phenylethanol (0.516 mmol) and 1-phenylethanol-1-*d* (0.484 mmol) was used. The observed reaction rates ($d[\text{ketone}]/dt$) after 70.2 min (at this point, [1-phenylethanol] = [1-phenylethanol-1-*d*]) for 1-phenylethanol and 1-phenylethanol-1-*d* were 1.26×10^{-4} and $4.12 \times 10^{-5} \text{ M min}^{-1}$, respectively, which gave $k_{\text{H}}/k_{\text{D}} = 3.1$.

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