

Reactions involving inorganic compounds*

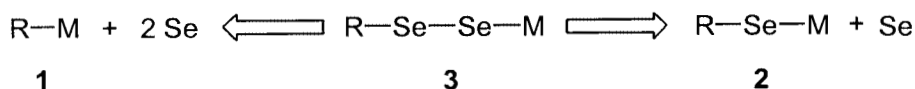
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Abstract: Selenium chemistry became, over the last 30 years, particularly useful for synthetic organic chemistry [1]. Inorganic as well as organic selenium compounds allow transformation which otherwise cannot be done or require much more drastic conditions to proceed. We have over the last 25 years explored the reactivity of elemental selenium as well as its inorganic and organic derivatives. We report here our recent finding concerning (i) organic diselenols and -diselenolates and (ii) the role of selenoxides in the enantioselective dihydroxylation of C,C double bonds using catalytic amounts of osmium tetroxide.

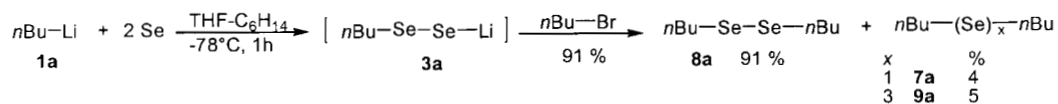
SYNTHESIS OF ORGANIC DISELENOLS OR THEIR SALTS

Organic diselenols (RSeSeH **4**) or their salts (RSeSeM **3**), the selenium analogs of hydroperoxides or their salts (ROOM) [2], are at present unknown. It was therefore of interest to know if these species could exist and what kind of reactivity they possess. The synthetic approaches planned were straightforward and implied selective insertion of (i) two selenium atoms into the carbon-metal bonds of organometallics **1** or of (ii) one selenium atom into selenolates **2** (Scheme 1).



Scheme 1

The reaction of elemental selenium with organometallics of various kinds is one of the most valuable method to synthesize organic selenolates **2** [3]. It is nevertheless poorly described and up to now, no effort has been made to elucidate its mechanism. We decided to investigate the reaction between *n*-butyllithium **1a** (1.6N in hexane) and two equivalents of elemental selenium in tetrahydrofuran (THF) and were delighted to find [4] that all the selenium disappeared quite rapidly already at -78°C , producing a dark-red clear solution (Stage A). Subsequent addition of a solution of *n*-butyl bromide led to the disappearance of *n*-butyl bromide after one hour at -78°C and the formation, in almost quantitative yield, of di-*n*-butyl diselenide **8a** contaminated with small amounts (< 5% each) of di-*n*-butyl selenide **7a** and di-*n*-butyl triselenide **9a** (Scheme 2).



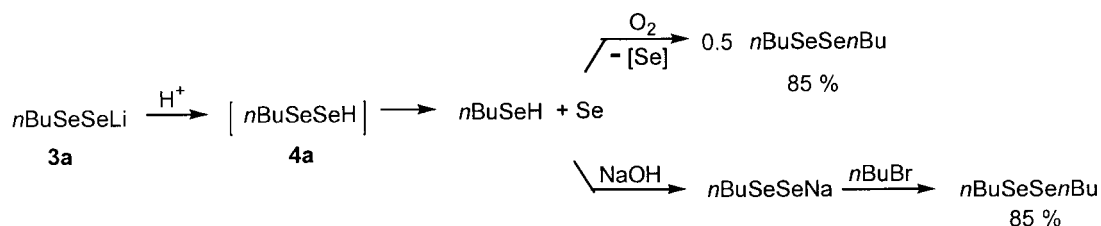
Scheme 2

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Successful alkylation of *n*-butyl diselenolate **3a** has been also achieved [4] with *sec*-butyl bromide (80% yield), but this reaction affords a statistical mixture of the expected *n*-butyl *sec*-butyl diselenide **8b** as well as *di*-*n*-butyl diselenide **8a** and *disec*-butyl diselenide **8c** resulting from the diselenide **8b** probably under the influence of the basic medium (**8b/8a/8c** : 50/25/25) [5].

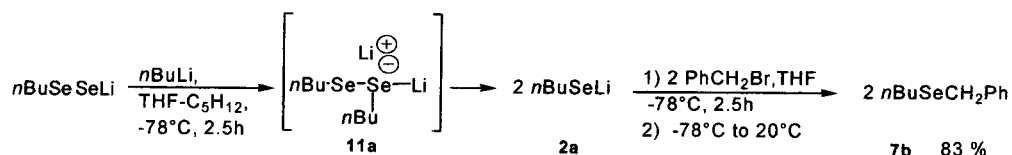
Having in hand an efficient synthesis of *n*-butyl diselenolates we planned to transform it to the yet unknown *n*-butyl diselenol (*n*-BuSeSeH) **4a** by acidification of the medium (Stage A), but all our attempts have been unsuccessful. In fact, addition of hydrochloric acid (1N aq. solution) resulted in the release of elemental selenium (0.5 h, 95% recovery after centrifugation). ^{77}Se NMR of the remaining solution clearly shows the presence of *n*-butylselenol which is then quantitatively oxidized to *di*-*n*-butyl diselenide **8a** on reaction with oxygen (Scheme 3) [4].



Scheme 3

We have also found that *n*-butyl diselenolate can be regenerated (85% yield) if oxygen is omitted and sodium hydroxide instead added to the medium. As a correlate to that observation we have observed [4] that *n*-butyl diselenolates **3** can be directly produced on reaction at room temperature, in THF or dimethylformamide (DMF) of lithium *n*-butyl selenolate **2a** with gray metallic elemental selenium. Related results were observed from magnesium-, sodium- and potassium *n*-butyl selenolates.

We have shown, in separate experiments, that lithium *n*-butyl diselenolate **3a**, prepared from butyllithium and selenium in THF (i) is quite stable under argon even when heated at reflux for 1 h and (ii) reacts with *n*-butyllithium to produce two equivalents of lithium *n*-butyl selenolate **2a** (Scheme 4). This may be explained by assuming that *n*-butyllithium selectively reacts with the selenium atom bearing the lithium counter ion.



Scheme 4

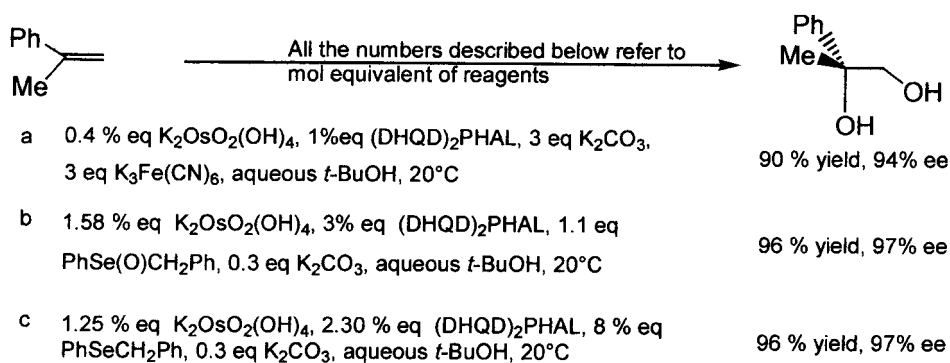
The reactions disclosed here are not limited to *n*-butyllithium. Other organolithium compounds such as *sec*-butyllithium and *tert*-butyllithium also produce the corresponding diselenolates under similar conditions.

In conclusion we have presented some evidence that *n*-butyl diselenolates **3** exist and that they are very easily prepared from readily available starting material.

ENANTIOSELECTIVE DIHYDROXYLATION OF C,C DOUBLE BONDS USING CATALYTIC AMOUNTS OF OSMIUM TETROXIDE SELENIDES AND AIR

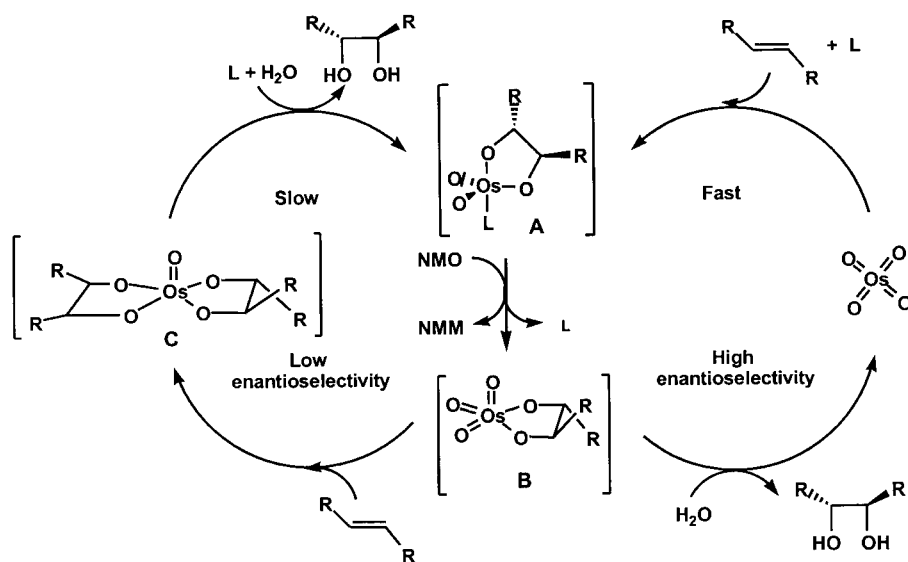
In the course of a work directed toward the synthesis of the active principle of cheddar cheese [6], we decided to use the catalytic enantioselective dihydroxylation reaction of olefins (Scheme 5) described by Sharpless [7a] to an alkylidene cyclopropane. We knew that this reaction required catalytic amounts

[% in weight] of (i) potassium osmate dihydrate [0.104%, the pre-oxidant] and of (ii) one of the phthalazine linked to two chincona alkaloid ligands [(DHQD)₂PHAL or (DHQ)₂PHAL, 0.552%, the chiral inductor], but we were rather surprised by the large amount of reagent (1.4 g of a premix, AD-mix) needed to perform this reaction, mainly due to potassium ferricyanide [K₃Fe(CN)₆, 69.96%, the co-oxidant] and potassium carbonate [29.39 %, the base] (Scheme 5) [7a].



Scheme 5

Several oxidants, such as N-methyl morpholine N-oxide (NMO) [7a], sodium peroxodisulphate (Na₂S₂O₈) [7a] and iodine (I₂) [7b] have been tested in place of the ferricyanide (which accounts for the larger amount of matter in the premix), but none of them have been able to supplant it. NMO which proved to be particularly useful in the catalytic, non-enantioselective, dihydroxylation of olefins give constantly lower ees, and all the efforts, including slow addition of the co-oxidant to the medium [7a], do not lead to substantial improvements. The lower ees observed with NMO were attributed [7a] to the presence of a second cycle of “poor enantioselectivity” involving a trioxoglycolate complex which competes with the usual “high enantioselectivity” cycle in which liganded osmium tetroxide is operative (Scheme 6).



Scheme 6

We thought that selenoxides could be more efficient oxidants than aminoxides and that they could advantageously replace both potassium ferricyanide or NMO, allowing less of the former and the low weight amount of the latter. Other expected advantages will be the absence of large quantities of metal salt in the waste and the easy recycling of the resulting selenides to selenoxides.

We have effectively found [8] that selenoxides are efficient stoichiometric co-oxidants in the asymmetric dihydroxylation of olefins. The reaction (SeOAD reaction) [8] is best achieved in aqueous *t*-butanol, using (i) the same catalyst, (ii) amounts of catalyst and osmium tetroxide similar to those used in AD-mix and (iii) benzyl phenylselenoxide. We also used potassium carbonate, but we only needed one tenth of the amount present in AD-mix. The reaction has been first carried out on α -methylstyrene leading to the corresponding diol in yield (93%) and ee (97%) almost identical to those described by Sharpless using the AD-mix method (Scheme 5, entry b, compare to entry a) [7a].

Results similar to those published by Sharpless using AD-mix [7a] method have been also obtained using SeOAD reaction from styrene (Yield %, ee %, time h: 93,97,12), stilbene (84,99,72), 1-phenyl-1-propene (92,99,20), 1-phenyl cyclohexene (95,99,96), 4-decene (60,97,3), and 2-methyl-2-heptene (85,99,20). As general trends, the reaction is highly pH dependant and is usually substantially faster if carried with aryl selenoxides bearing an electron withdrawing group on the phenyl group.

The same reactions can be achieved with catalytic amount of selenides (SeAD reaction). In such case, the selenide should be constantly oxidized *in situ* to the corresponding selenoxide until all the olefin present is transformed to the corresponding diol. Singlet oxygen which we used for that purpose long ago [9], was selected. Under the conditions described above, but using (i) 8% of benzyl phenylselenide instead of 110% benzyl phenylselenoxide, (ii) trace amount of rose bengale (RB, the sensitizer for $^3\text{O}_2$ to $^1\text{O}_2$ activation, 0.3%), (iii) under a slight pressure of dioxygen (the co-oxidant, from 3.8 to 2.7 mmHg) and (iv) light (2×500 watts Osram 64702 R7s, 500 W-230 V, bought in a supermarket for 10 Euro each), the dihydroxylation of α -methylstyrene was achieved [8] after 24 h in yield (93%) and ee (97%) almost identical to those reported in the stoichiometric version (Scheme 5, compare entry c to entry b). Similar results were obtained using air instead of oxygen (87% yield, 93% ee).

We finally found the AD reaction can be efficiently carried out with NMO [7a] under the conditions we developed for the SeOAD reaction using NMO in place of benzyl phenylselenoxide. Both the yield and the ee of this reaction proved to be highly pH dependant, but whereas the best yield is observed around pH 8.54, the best ee was found when the reaction is performed at pH 10.4.

In conclusion, we have demonstrated that selenides are able, in the presence of light, to promote the efficient dihydroxylation of α -methylstyrene. This new version of the AD reaction not only uses a simpler, more available, and more ecological co-oxidant, but it also requires much less matter: 87 mg of matter is required to oxidize the same olefin in the SeAD reaction instead of 1400 mg when AD-mix is used. *Three* cycles have to work in concert for that purpose, and this is apparently the case [10].

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10. The following amount of reagents (in mg) has been used to oxidize 1 mmol of α -methylstyrene in aqueous *t*-BuOH by the original Sharpless AD reaction using AD-mix or our SeAD reaction. (AD/SeAD) : $\text{K}_2\text{OsO}_2(\text{OH})_4$ (1.45/4.6); $(\text{DHQD})_2\text{PHAL}$ (7.7/17.9); K_2CO_3 (411/41); $\text{K}_3\text{Fe}(\text{CN})_6$ (979/-); PhSeCH_2Ph (-/20) rose bengale (-/3); overall (1400/87).