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SELECTIVE CATECHOL OXIDATIONS WITH DIPHENYL SELENOXIDE. APPLICATIONS TO PHENOLIC COUPLING.[1]

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Summary

Diphenyl selenoxide was used as a mild and selective oxidant in the synthesis of aporphines and homoaporphines. An intramolecular coupling between a phenol and a catechol is believed to proceed via catechol selenurane intermediates.

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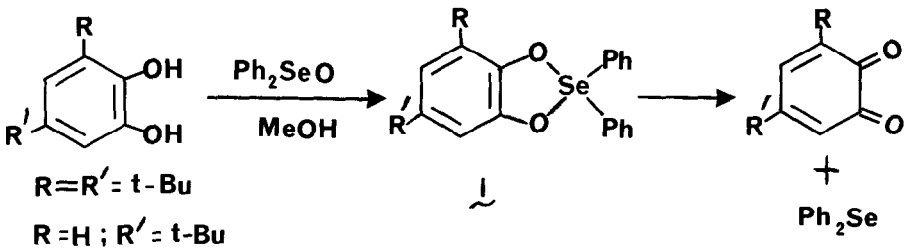
While the chemistry of organoselenium compounds is growing at a rapid rate, the use of selenoxides as oxidants for organic synthesis has received little attention.[3] Unlike its sulfur counterpart, diphenyl selenoxide can function as a mild oxidant for hydrazides,[4] amines,[5] and catechols.[6] Balenovic has reported that diphenyl selenoxide can oxidize catechols in acetic acid, and furthermore, the resulting o-quinones can be trapped by an amine nitrogen. Except for the oxidation of adrenaline to adrenochrome,[7] it has not been established that diphenyl selenoxide offers distinct advantages over alternate oxidative methods. In this report, we wish to describe some practical applications of diphenyl selenoxide oxidations in the area of benzylisoquinolines.

Our interest in selenoxide oxidations stems from a desire to develop selective oxidants for phenolic compounds which are non-metallic, and which proceed via a two-electron oxidation process. We previously reported[8] the use of N-succinimido-S,S-dimethylsulfonium salts for the mild oxidation of substituted catechols. This reagent does, however, react with simple phenols[9] and thus is not selective for catechols. In contrast to the succinimide sulfonium salts and in accordance with Balenovic's work, we have found that diphenyl selenoxide selectively oxidizes catechols and hydroquinones and has no effect on simple phenols.

Diphenyl selenoxide is readily available from the hydrolysis of diphenylselenium dibromide[10] with sodium hydroxide or the oxidation of diphenylselenide with sodium metaperiodate.[11] As an oxidant, diphenyl

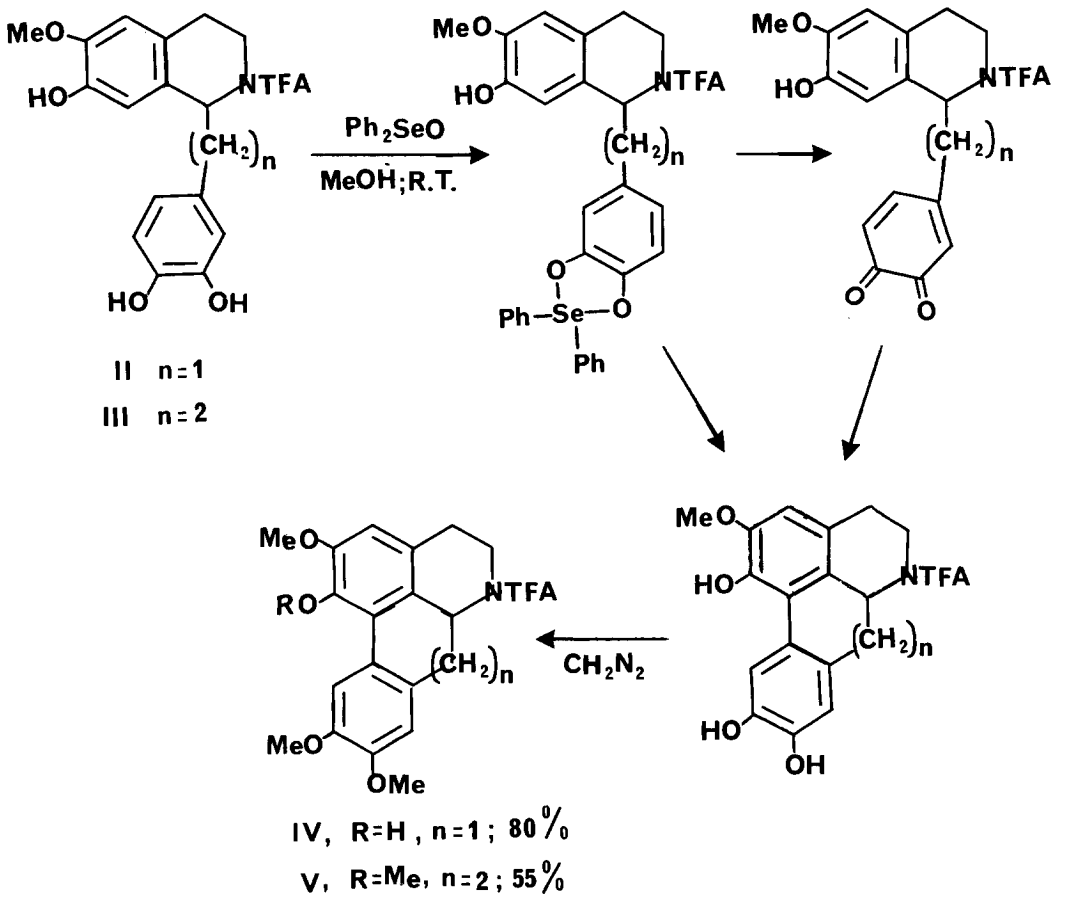
selenoxide can be used in stoichiometric amounts in several organic solvents (DME, CH_2Cl_2, methanol). In contrast to Balenovic's acidic reaction conditions, we found that one equivalent of this reagent oxidizes the 3,5-t-butylcatechols in quantitative yield in 30 minutes in anhydrous methanol (0°C or room temperature).

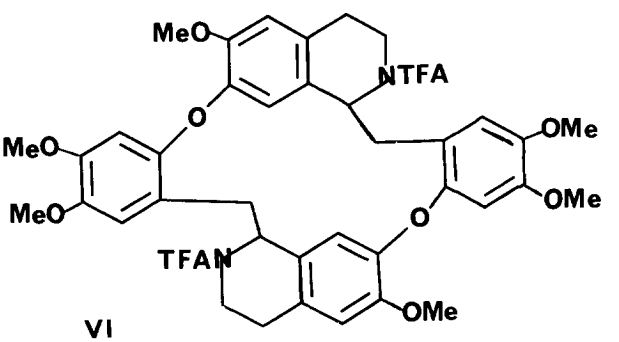


An attractive but not compulsory intermediate[12] for this oxidation is the cyclic catechol selenurane I. Diphenyl selenoxide is also very effective for the oxidation of hydroquinone (>95%) to p-benzoquinone. Since the by-product of oxidation is diphenyl selenide, no over-oxidation can occur and the selenide can be recycled after removal by chromatography. Most important from a selectivity standpoint, substituted monohydric phenols were recovered unchanged after 24 hrs at reflux in DME with diphenyl selenoxide.

Given this selectivity for diphenyl selenoxide in the oxidation of catechols, we proceeded to test the possibility of generating an o-quinone in a molecule which also contained an additional phenolic group. In particular, we were interested in affecting an intramolecular phenolic coupling between a catechol ring and a phenolic ring. When the benzylisoquinoline system II and the phenethylisoquinoline compound III were each treated with one equivalent of diphenyl selenoxide at room temperature in methanol, intramolecular coupling to the aporphine and homoaporphine skeletons occurred in good yield. Subsequent treatment of these reaction mixtures with ethereal diazomethane yielded an 80% yield of N-trifluoroacetyl Wilsonirine[13] IV and a 55% yield of the methylated homoaporphine V.[14]

Both of these couplings occurred regiospecifically to yield the Corytuberine type of aporphine alkaloids. The efficiency and advantages of diphenyl selenoxide were further reinforced when treatment of III with o-chloranil, a common catechol oxidant, yielded less than 10% of compound IV. This last control experiment may suggest that there is something unique about a selenurane intermediate in the oxidative coupling process. At the present time, we cannot distinguish between the o-quinone and the selenurane as the species undergoing the cyclization. Further efforts will deal with the isolation of catechol selenuranes and their reactions with various nucleophiles.


MeO
HO
NTFA
(CH2)n
HO
OH
Ph2SeO
MeOH;R.T.
O
Ph–Se–O
Ph
O
O
II n=1
III n=2
MeO
RO
NTFA
(CH2)n
MeO
OMe
CH2N2
MeO
HO
NTFA
(CH2)n
HO
OH
IV, R=H, n=1; 80%
V, R=Me, n=2; 55%


MeO
NTFA
O
MeO
MeO
OMe
OMe
O
TFAN
OMe
VI

All of the aforementioned oxidations involved the addition of the catechol to a methanol solution of diphenyl selenoxide. When a methanol solution of the oxidant was slowly dropped into a solution of catechol II, the major product isolated by column chromatography was a dimer. Methylation of this dimer with diazomethane yielded a compound which was assigned structure VI on the basis of its mass spectral fragmentation pattern.[15] The symmetrical dimer most likely arises from the coupling of a catechol selenurane intermediate. We are presently investigating the use of this oxidation system in the synthesis of unsymmetrical dimeric alkaloids which contain a catechol ring.

Acknowledgments

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References and Footnotes

1. Presented in part at the 174th ACS National Meeting, Chicago, Illinois, September 2, 1977, ORGN 189.
2. Taken in part from the Ph.D. Thesis, 1979, of Alan Schwartz, College of Pharmacy, University of Michigan.
3. For a review of selenoxides as oxidizing agents see: H. J. Reich, Chapt. 1 of Oxidations in Organic Chemistry, Part C, W. S. Trahanovsky, Ed., Academic Press, New York, N.Y., 1978.
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14. Spectral data compared well with trimethyl analog reported in ref. 13; (mp V, 114-116°C from methylene chloride-ether).
15. Characteristic benzylic cleavage: m/e 848; 424 (80%).

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