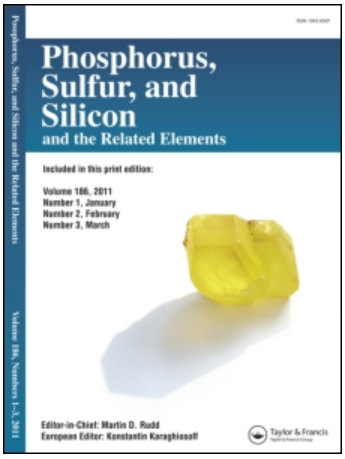

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Diaryl Diselenides and Related Compounds as Oxygen-Transfer Agents

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Diaryl Diselenides and Related Compounds as Oxygen-Transfer Agents

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The progress in application of diaryl diselenides and related compounds as transfer agents is presented. The review is limited to the diaryl diselenides having electron-withdrawing substituents, such as nitro, trifluoromethyl, carbamoylphenyl, and polymeric diselenides PADS and PPDS. The methods of their synthesis are described. These compounds are used as effective catalyst for a simple and multi-electron hydroperoxide oxidation of different organic compounds. Transformation of functional groups, cycloalkanones ring contraction, cyclocondensation and degradation of electron–rich arenes is described. Mechanisms of the reactions involved Se(II) and Se(IV) intermediates are discussed.

Keywords Antibiotic; arene; carboxylic acid; catalysis; diselenide; lactone; oxidation; quinone

INTRODUCTION

Discovery of *syn* selenoxide elimination started a broad interest in the application of organoselenium compounds in organic synthesis.[1] Barton, Back, and Ley have popularized their role as stoichiometric oxidants.[2,3] During the last three decades, diaryl diselenides and related compounds have been extensively studied as oxidation catalysts of practical importance.[4,5] Several works have been recently done in our laboratory and are presented briefly in this review. Our research interest has been focused on diaryl diselenides **1** and related compounds, as oxygen-transfer agents useful in organic synthesis. In these reactions, the diselenides are oxidized by hydroperoxides to the corresponding areneseleninic acids **2**, which are the proper catalysts. They act via corresponding peroxyseleninic acids **3**[5] and selenoxyradicals **4**,[6] as highly electrophilic oxidants and electron acceptors, (Scheme 1).

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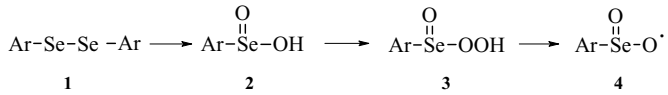


SCHEME 1 Active forms of diaryl diselenides oxygen–transfer catalysts.

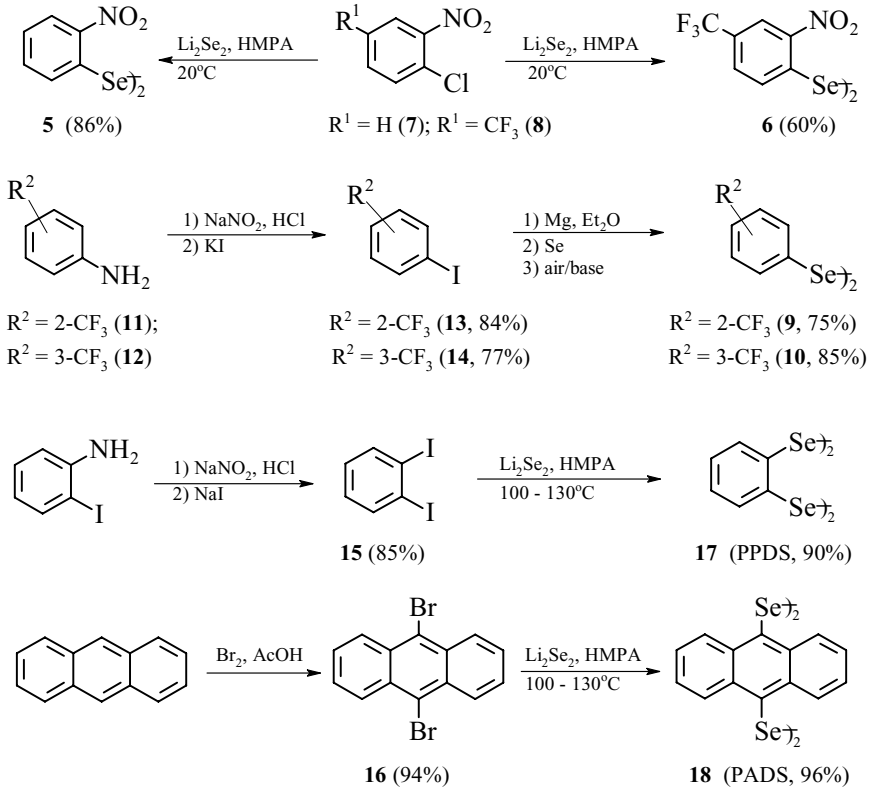
The use of hydrogen peroxide and *tert*-butylhydroperoxide as the stoichiometric oxidants is in accord with modern trends in organic synthesis since both of those reagents are cheap and environmentally friendly, and are used on both laboratory and industrial scales.[7] Nevertheless, both of them are low or only moderately active toward the most of the organic substrates, and suitable activators must be used.[5] It has been found that some organoselenium compounds are very efficient activators of those convenient oxidants. The compounds having selenium bonded to aromatic moieties are used almost exclusively as the catalysts, because bond between selenium and sp^3 carbon is rather weak. Generally, functionalization of the aromatic ring with electron-withdrawing nitro, carbamoylphenyl, and trifluoromethyl substituents make the catalysts more efficient and selective.[5] Recently we have successfully employed poly(bis-9,10-anthracenyl)[8] and poly(bis-1,2-phenylene) diselenide,[9] and silica-supported selenenamides.[10] These compounds are easy to prepare in laboratory from cheap, commercially available arene halides or substituted anilines and elemental selenium.

The above described catalysts were used for functional group transformations, ring rearrangement of cycloalkanones, oxidative degradation of naphthalene ring and electron-rich benzene ring, using 30% aqueous hydrogen peroxide or 80% *tert*-butyl hydroperoxide (TBHP) as stoichiometric oxidants.

PREPARATION OF DIARYL DISELENIDES AND RELATED COMPOUNDS

2,2′-Dinitrodiphenyl diselenide **5** and its 4,4′-ditrifluoromethyl derivative **6** were obtained by treating of 2-nitrochlorobenzenes **7** or **8**, with dilithium diselenide at ambient temperature.[11,12] 2,2′- And 3,3′-ditrifluoromethylphenyl diselenides **9** and **10** were prepared by Reich and Renda procedure starting from trifluoromethylanilines **11** and **12** via trifluoromethyliodobenzenes **13** and **14** by insertion of elemental selenium into Grignard reagents.[12,13] Treatment of 1,2-diiodobenzene **15** or 9,10-dibromoantracene **16** with dilithium diselenide, at 110–130°C, gave polymeric 1,2-diphenylene diselenide **17** (PPDS) and polymeric 9,10-dianthracenyldiselenides **18** (PADS), respectively.[8,9] The

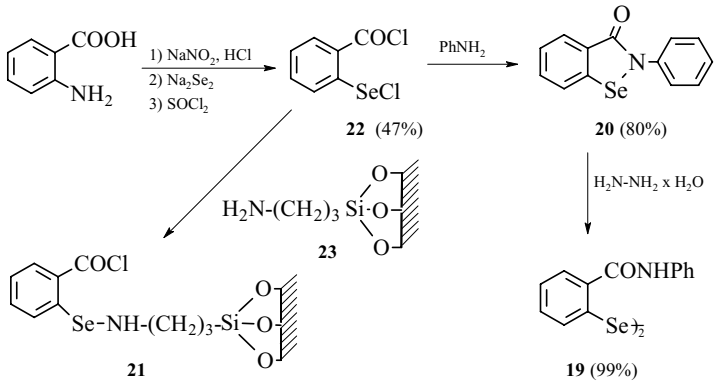
dihaloarenes were obtained from 2-iodoaniline or anthracene, respectively, (Scheme 2).[12,14]



SCHEME 2 Preparation of diaryl diselenides.

2,2′-Dicarbamoylphenyldiphenyl diselenide **19** and related selenenamide **20** and **21** were prepared from anthranilic acid via 2-(chloroseleno)benzoyl chloride (**22**). The reaction of chloride **22** and aniline resulted in heterocyclic of 2-phenylbenzisoselenazol-3(2*H*)-one (**20**) known as ebselen. When chloride **22** reacted with aminopropylsilicate **23**, selenenylation of the primary amino group takes place exclusively, and recoverable heterogenous silica-supported selenenamide **21** was produced. Ebselen treated with hydrazine hydrate underwent ring opening to diselenide form **19**, (Scheme 3).[10,15]

Because lithium diselenide is a very convenient and versatile reagent for the introduction of selenium to organic substrates, and it can be used to prepare inorganic selenium compounds, we describe our proven procedure of its preparation in the Experimental section.

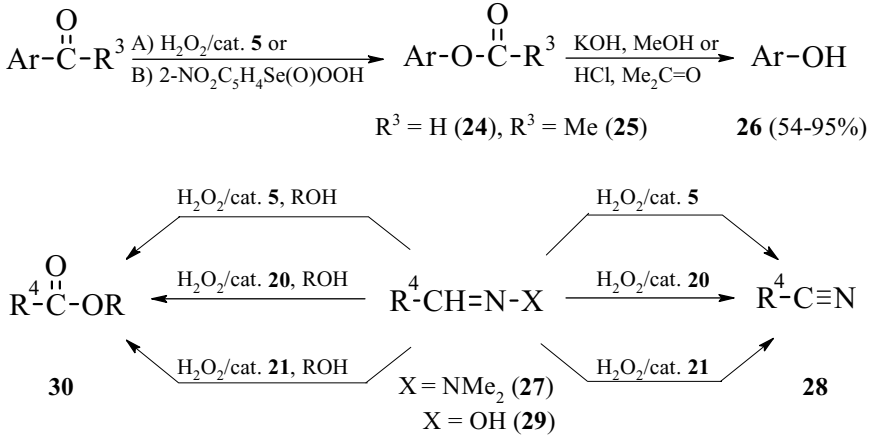


SCHEME 3 Preparation of selenenamides **20** and **21**, and 2,2′-dicarbamoyldiphenyl diselenide **19**.

FUNCTIONAL GROUP TRANSFORMATIONS

2,2′-Dinitrodiphenyl diselenide (**5**) has been applied as a catalysts for Baeyer–Villiger oxidation of aldehydes and aryl methyl ketones into phenols formates **24** or acetates **25**, which in one-pot procedures subsequently were hydrolyzed to phenols **26**. That is a convenient method for the synthesis of phenols with electron-donating substituents or polycondensed ring systems.[16] Oxidation of carbonyl compounds with 2-nitrobenzeneperoxyseleninic acid, used as a stoichiometric oxidant, gave similar results.[17] The above results present a new methodology in hydroperoxide oxidation of organic substrates. The same reagent, H_2O_2/cat. **5**, has been used for oxidative transformation of azomethine derivatives of carbonyl compounds. 1,1-Dimethyl hydrazones **27** were converted into nitriles **28**, whereas aldoximes **29** in the presence of primary or secondary alcohols produced carboxy esters **30**.[18] Recently, similar results we have observed, while ebselen (**20**) or silica-supported selenenamide **21** have been applied, (Scheme 4).[10,19,20]

Catalytic activity of silica-supported selenenamide **21** was demonstrated in *tert*-butylhydroperoxide oxidations of benzaldehydes to benzoic acids, and benzylamines to benzonitriles. Moreover, this catalyst was employed for hydrogen peroxide oxidation of tosylhydrazones and oximes to parent carbonyl compounds and arenecarboxylic acids depending on the substrate used and the reaction conditions. The catalysts **21** was simply recovered by filtration and could be reused.[10]Another polymeric catalyst, 1,2-diphenylene and 9,10-dianthracenyl diselenides **17** and **18** were used for preparative hydrogen peroxide oxidation of aldazines, aldoximes and tosylhydrazones in THF



R = primary or secondary alkyl; R^4 = alkyl, aryl, furyl, cinnamyl

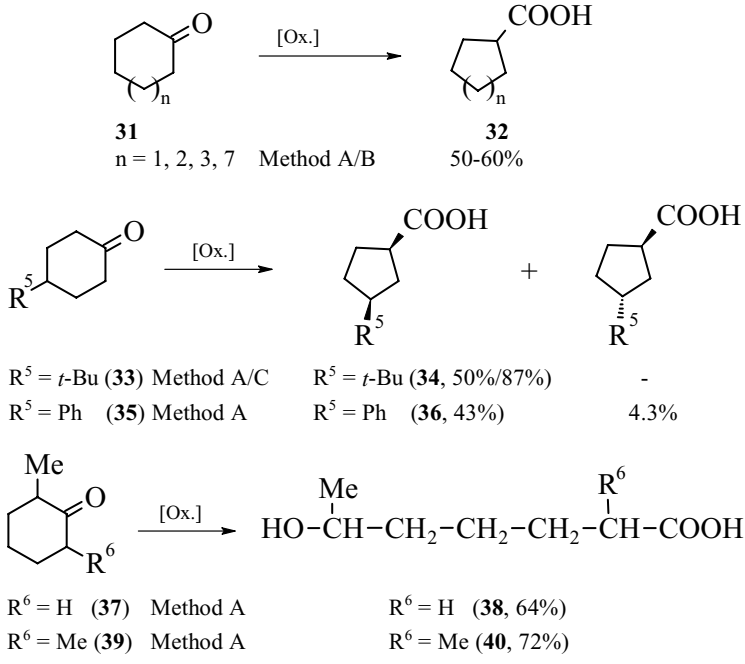
SCHEME 4 Transformations of carbonyl compounds and its imine derivatives.

to arenecarboxylic acids,[9] and 1,1-dimethylhydrazones in *tert*-butanol to unsaturated and aromatic nitriles, in excellent preparative yields.[21]

RING REARANGEMENT OF CYCLOALKANONES

The 9,10-dianthracenyl diselenide (**18**) used in 0.6 mol % catalyzed conversion of cyclohexanones and cycloheptanone **31** and **33** by hydrogen peroxide into medium ring cycloalkanecarboxylic acids **32** and **34** with good yields.[8] Scarcely enolizable ketones, such cyclooctanone and cyclododecanones **31** require higher concentration of the catalyst (6 mol %) and prolonged reaction time, 1 to 4 days, respectively, and the cycloheptane and cycloundecanecarboxylic acids **32** have been obtained in good yields.[22] Compounds with five- to seven-membered rings are important substrates in the synthesis of natural products and pharmaceuticals. They cannot be obtained via the Favorski reaction in many instances. The presented route is more environmentally friendly than the use of stoichiometric amounts of thallium(III) salts.[23] The oxidative rearrangement of ketones promoted either by thallium(III) or by H_2O_2/cat. **18** occurs with similar diastereoselectivity, as ring contraction of bulky substituted cyclohexanone **33** to *cis*-3-*tert*-butylcyclopentanecarboxylic acid (**34**), because both oxidants react through an electrophilic addition to the enol form of the ketones.[24,25] The ring contraction of 4-phenylcyclohexanone (**35**) promoted by hypervalent iodine(III) compounds such iodobenzenediacetate has been

used for the synthesis of 1-piperidinobenzobicyclo[2.2.1]heptane.[26,27] In this example, the relative configuration of formed methyl ester of 3-phenylcyclopentanecarboxylic acid was not assigned. Oxidation of **35** with H_2O_2/cat. **18** system resulted in *cis*-3-phenylcyclopentanecarboxylic acid (**36**) in moderate 43% yield, and *trans* isomer is also formed.[8] If cyclohexanone substituted with methyl at 2-positions **37** and **39** have been used as substrates, only Baeyer–Villiger rearrangement takes place, and lactone open chain 6-hydroxyheptanecarboxylic acids **38** and **40** were the final products, (see Experimental, and Scheme 5).[22]

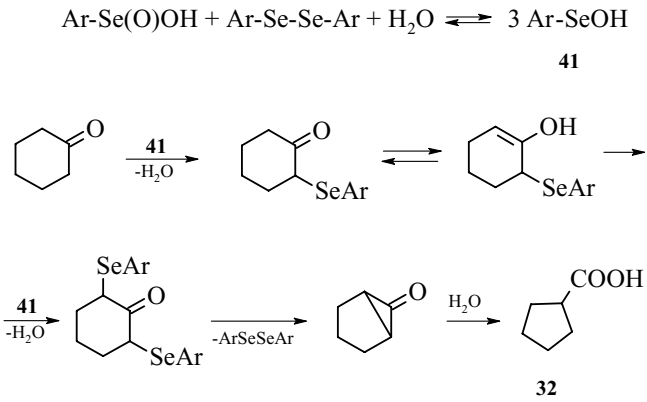


[Ox.]: Method A - H_2O_2/cat. **18** (0.6 mol %), *t*-BuOH, reflux, 5-60 h;
Method B - H_2O_2/cat. **18** (6 mol %), *t*-BuOH, reflux, 1-4 days;
Method C - TTN, CH_2Cl_2, 20°C

SCHEME 5 Cycloalkanones ring contraction.

It has been proposed that a Se(VI) species is responsible for oxidative ring contraction.[23] We propose that a Se(II) intermediate **41** is responsible for the oxidative ring contraction, whereas a Se(IV) intermediate catalyzes conventional Baeyer–Villiger ketone rearrangement, (Scheme 5).[22] In the contraction reaction, the key intermediate is the

cyclopropanone formed as a result of electron-rich 9,10-dianthracenyl diselenide elimination (Scheme 6).[22]

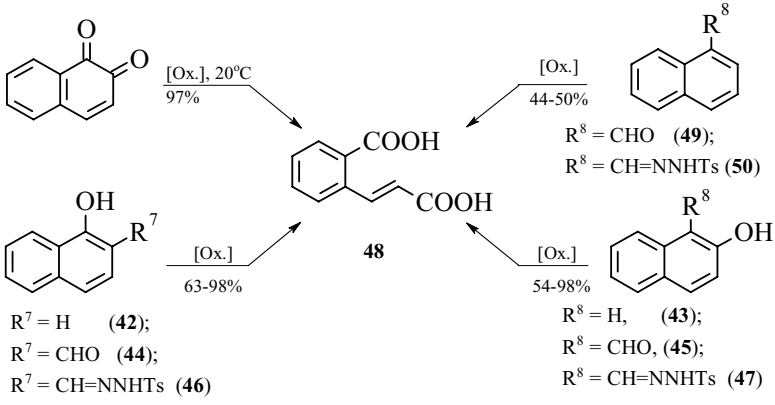


SCHEME 6 Mechanism of cyclohexanone ring contraction.

OXIDATIVE DEGRADATION OF NAPHTHALENE RING

Six-electron oxiadation of both hydroxynaphthalenes **42** and **43**, *ortho* substituted formyl **44** and **45** and its tosylhydrazone derivatives **46** and **47** with 30% hydrogen peroxide in THF in the presence of poly(bis-1,2-diphenylene) diselenide (**17**, PPDS) is a convenient way to obtain *trans*-2-carboxycinnamic acid **48**. The results are similar for both of the substrates, since the reaction proceeds via intermediate 1,2-naphthoquinone. None of hydroxylated 1-formylnaphthalene (**49**) and its imine derivatives, such as oxime, azine, and tosylhydrazone **50** produce carboxycinnamic acid **48** with yield up to 50%, instead isomeric (1-oxo-1,3-dihydroisobenzofuran-1-yl)acetic acid and 1-naphthoic acid is formed (Scheme 7).[9,28]

30% Hydrogen peroxide in *tert*-butanol in the presence of bis-(2-nitrophenyl)diselenides **5** and **6** at mild reaction conditions (55°C, 6 h) led to complete conversion of 2-naphthol to 2-carboxycinnamic acid **48**. The **6**, having two electron-withdrawing substituents (nitro and trifluoromethyl groups), was a better one catalyst, because it gave the colorless product **48**.[12] The reagent, H_2O_2/cat. **6** was successfully applied for oxidative degradation of 6- or 7- substituted 2-hydroxynaphthalenes to cinnamic acids **51** with substituent on benzene remote ring carbon atom, (Scheme 7).[29] The ring substituted cinnamic acids could find synthetic application, similarly to industrially produced *trans*-cinnamic acid.[32]

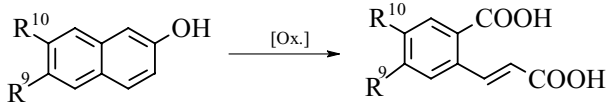


R^8 = CHO (**49**);
R^8 = CH=NNHTs (**50**)

R^7 = H (**42**);
R^7 = CHO (**44**);
R^7 = CH=NNHTs (**46**)

R^8 = H, (**43**);
R^8 = CHO, (**45**);
R^8 = CH=NNHTs (**47**)

[Ox.]: 30% H_2O_2/cat. **17** (5 mol %), THF, reflux, 20 h.



$R^9 = R^{10}$ = H (**43**)	Method A	**48** (100%)
R^9 and/or R^{10} = X	Method B	**51** (60-90%)

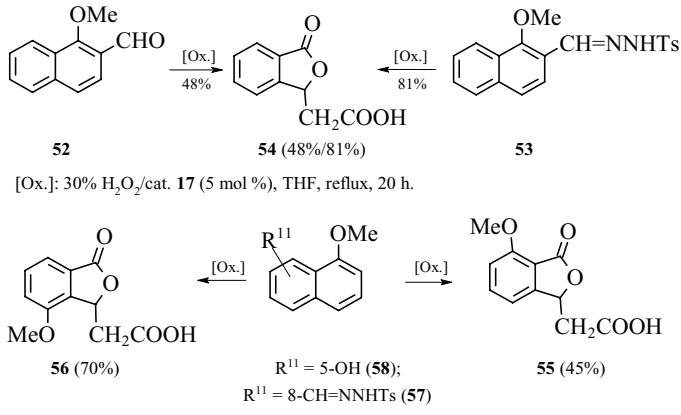
X = H, OH, OMe, COOH, COOMe

[Ox.]: Method A - 30% H_2O_2/cat. **5** or **6** (5 mol %), *t*-BuOH, 55°C, 6 h;
Method B - 30% H_2O_2/cat. **6** (5 mol %), *t*-BuOH, reflux, 60 h

SCHEME 7 Oxidative domino transformation of 1- and/or 2-substituted naphthalenes.

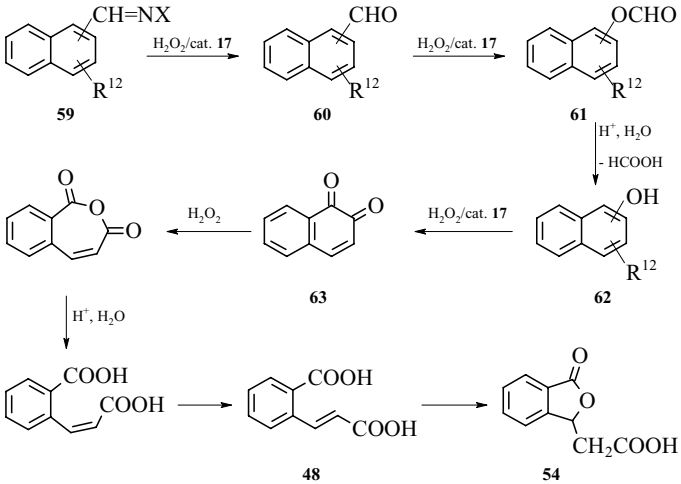
Interestingly, 2-formyl-1-methoxynaphthalene (**52**) and its derivative **53** is good benzofuranone **54** precursors.[28] Its 4 and 7 methoxy derivatives **55** and **56** were formed from corresponding methoxynaphthalenes **57** and **58**, (Scheme 8).[29] Phthalides are a core part of the structure of several alkaloids, and isoochracinic acid, a toxic metabolite from a parasite responsible for black spot disease of Japanese pears, our compounds could be eligible intermediates for their synthesis.[31]

These results are in accordance with our previous experiments on functional groups transformations. Naphthaldehyde imine derivatives **59** underwent oxidative regeneration of the parent carbonyl compounds **60**.[9] The electron-rich carbonyl compounds underwent Baeyer–Villiger rearrangement to naphthol formate **61**, which was directly hydrolyzed to hydroxynaphthalene **62**.[16] If hydroxy or methoxy group at *ortho* position is absent, *ortho*-hydroxylation takes place, similarly as Barton proposed in benzeneseleninic(IV) acid and its anhydride



SCHEME 8 Oxidative domino naphthalene ring transformation.

oxidation of both naphthols to *ortho*-naphthoquinone (**63**).[32] Baeyer–Villiger oxidation of intermediate **63**, consecutive ring opening of *cis*-2-carboxycinnamic acid anhydride and isomerization, give finally the stable *trans*-2-carboxycinnamic acid (**48**). The labile formyl and tosylhydrazone groups were source of acids which catalyze intramolecular Michael addition of cinnamic acid **48** to phthalide form **54**, (Scheme 9).

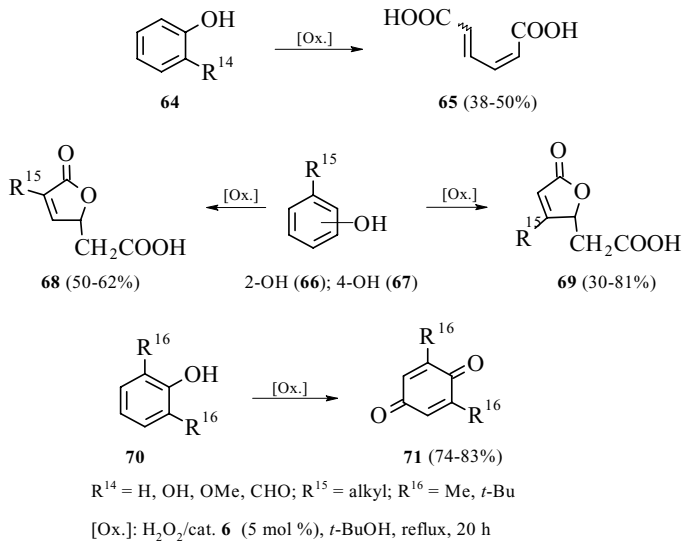


SCHEME 9 Oxidation of naphthalene ring.

OXIDATIVE DEGRADATION OF ELECTRON-RICH BENZENE RING

Oxidative degradation of electron-rich benzene rings with formation of quinone and ring cleaved products, such as carboxylic acids and lactones expand the utility of benzenoid synthons in organic synthesis. Unfortunately, aromatic hydrocarbons and its more oxidized derivatives as catechols and *ortho*-quinones require strong oxidizing agents or activated hydroperoxides, and mixture of many different compounds are produced in low yield, and this is a reason of a little synthetic value of this methodology.[33]

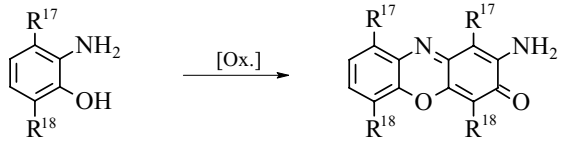
We elaborated the practical hydroperoxide oxidation of phenol and its derivatives. Unsubstituted phenol, its *ortho* hydroxy, methoxy and formyl derivatives **64** with H_2O_2/cat. **6** system rearranged to 2,4-hexadienedioic acids named muconic acid (**65**).[34] Other 2- and 4-alkyl substituted phenols **66** and **67** underwent ring rearrangement to 2- and 3-substituted muconolactones **68** and **69**. If both *ortho* positions are substituted by alkyl group in phenols **70**, 1,4-benzoquinones **71** were formed in good yield, (Scheme 10).[35] A similar oxidation pattern of catechol or hydroquinone ether by peracetic acid and TBHP/cat. **17** system was observed.[6,36]



SCHEME 10 Oxidative degradation of benzene ring.

Phenol having amino group in *ortho* position **72** is a good substrate for enzymatic and biomimetic oxidative cyclocondensation to the

2-amino-3*H*-phenoxazin-3-one known as questiomycin A (**73**).[37,38] The naturally occurred questiomycin A prevents the proliferation of some microorganisms, such mycobacteria.[39,40] The cyclocondensation of *ortho*-aminophenol, with the aid of dioxygen or hydroperoxides alone, did not proceed, or questiomycin A was formed in low yield.[41–43] More satisfactory results were found in the presence of selenium catalysts, particularly 2- and 3-di-trifluoromethyldiphenyl diselenides (**9** and **10**) for TBHP oxidation, and 2,2′-dicarbamoylphenyldiphenyl diselenide (**19**) and related ebselen (**20**) for H_2O_2 oxidation.[43] Since the 2-amino-3*H*-phenoxazin-3-one ring system is a basic part of the skeleton of actinomycin D[44], the anticancer antibiotic extensively used in recent years in chemotherapy of cancer,[45] we applied the above methodology for the practical synthesis of the questiomycin A derivatives.[46] 2-Amino-3-methylphenol (**74**) was oxidized to the dimethyl derivative of questiomycin A **75** smoothly because the methyl group in the vicinity of the amino group strongly activates the substrate molecule. In contrast, an electron-withdrawing carboxy substituent present at the same position in **76** prevents the reaction and cinnabarinic acid (**77**) was not formed. The electron donating methyl group in the vicinity to the hydroxyl group of 2-amino-3-carboxy-6-methylphenol (**78**) made the substrate susceptible to cyclocondensation, and actinocin (**79**) was formed as the sole product (Scheme 11).[45]



72	Method A-D	**73** (80-92%)
74	Method A/C	**75** (92%/64%)
76	Method A/C	**77** (- / -)
78	Method A	**79** (81%)

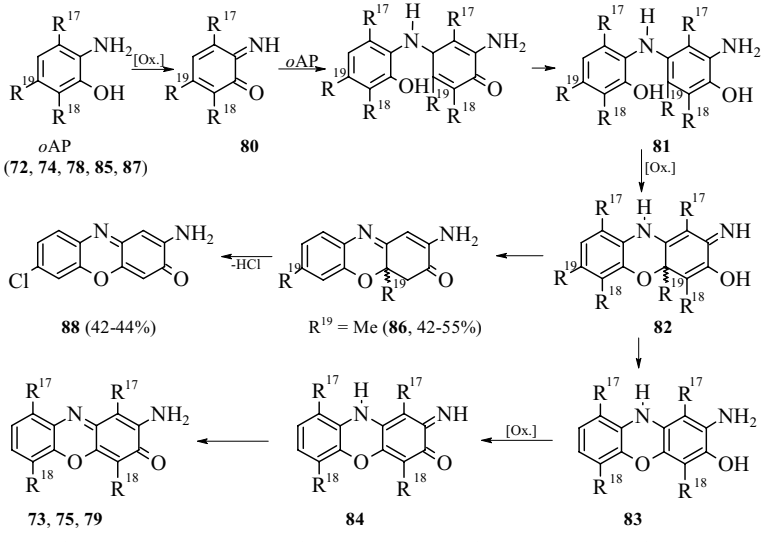
$R^{17} = R^{18} = H$ (**72**, **73** - *questiomycin A*);
$R^{17} = Me$, $R^{18} = H$ (**74**, **75**);
$R^{17} = COOH$, $R^{18} = H$ (**76**, **77** - *cinnabarinic acid*);
$R^{17} = COOH$, $R^{18} = Me$ (**78**, **79** - *actinocin*)

[Ox.]: Method A - H_2O_2/cat. **20** (5 mol %), *t*-BuOH, 20°C, 20 h;
Method B - H_2O_2/cat. **19** (5 mol %), *t*-BuOH, 20°C, 20 h;
Method C - TBHP/cat. **10** (5 mol %), *t*-BuOH, 55°C, 20 h;
Method D - TBHP/cat. **9** (5 mol %), *t*-BuOH, 55°C, 20 h

SCHEME 11 Oxidative cyclocondensation of *ortho*-aminophenols.

In the first step of the oxidative cascade, the aminophenol **72** and its derivatives having substituents in the *ortho* positions towards

the amino and/or hydroxyl groups **74** and **78** (*o*AP) are oxidized to the highly electrophilic quinone imine **80**. The amino group of other molecule of aminophenol (*o*AP), then adds to the quinone imine **80**, resulting in unstable intermediate, which tautomerizes to more stable *ortho*-aminophenol aromatic **81**. This oxidation-addition-tautomerization sequence is repeated in the subsequent steps of the reactions via intermediate **82** and **83**. The final oxidation of **83** and tautomerization of azaquinone **84** gives the aminophenoxazinone chromophore **73**, **75**, and **79**. *Ortho*-aminophenol with methyl group substituted at *para* position to the amino group in **85** was converted to the 2-amino-4α,7-dimethyl-4,4α-dihydro-3*H*-phenoxazin-3-one (**86**), and analogously substituted chloroaminophenol **87** gave 2-amino-7-chloro-3*H*-phenoxazin-3-one (**88**) with one molecule of hydrochloride elimination, (Schemes 11 and 12).[43,46]



SCHEME 12 Mechanism of *ortho*-aminophenols cyclocondensation.

Catalyzed by organoselenium compounds hydroperoxide oxidation of electron-rich benzene ring of hydroquinone ether and *ortho*-aminophenol gave results similar to those, when one-electron oxidants such as, cerium(IV), silver(II), or manganese(III) were the reagents.[6,43] Moreover, formation of aminophenoxy radicals by oxidation of *ortho*-aminophenol by above reagents are crucial steps in their conversion to 2-aminophenoxazin-3-one, most probably by action of selenoxyradical **4** intermediates, a strong electron acceptors.[43] Our

findings are also in accordance with well-known mechanisms of oxidation of phenolic substrates by laccase and peroxidase.[46]

EXPERIMENTAL

Preparation of Dilithium Diselenide in 50 mmol Scale

A clean chunk of lithium (0.73–0.75 g) is weighted in kerosene. To an oven dried 100 ml round bottom flask with a long neck, fitted with a stopcock adapter, is placed 50 ml purified THF.[47] From the above chunk of lithium 0.10–0.20 g pieces are cut, dried with filter paper and hammered to a thin foil on a greased with paraffin oil anvil. The foil is folded and hammered again. This operation is repeated several times. The wound foil of lithium is cut with scissors in such a way that the small pieces of lithium fall directly into the flask containing THF. 4,4′-Di-*tert*-butylbiphenyl (0.10 g)[48] is then added. The flask is fitted with the stopcock adapter[49] and connected to vacuum (water aspirator). Some amount of THF is removed during its boiling. The connection with vacuum is cut off by means of the stopcock and the flask is put into an ultrasonic bath. During the sonication permanent green coloration should appear after less than 15 min.[50] The flask is removed from the bath, the stopcock adapter dismounted and selenium (8.0 g) in the form of powder is added. The adapter is put at its place and the mixture is degassed as above. The closed flask is sonicated until all lithium is consumed (about 4 h). During the sonication temperature of the bath can raise to 40–50°C. If lithium is not completely consumed during the 4 h period of sonication a magnetic stirring bar is placed in the flask, the reaction mixture is degassed, as above, and stirred overnight at ambient temperature.[52] The prepared dilithium diselenide can be allowed to stand in the reaction flask, under vacuum for months, it is quite stable but its solubility in THF is limited. As prepared dilithium diselenide is soluble in hexamethyl phosphoramide (HMPA) (20 ml) or DMF. The Li_2Se_2 complex with HMPA (deep green) is only moderately susceptible towards the air.

Preparation of 6-Hydroxyheptanecarboxylic Acids 38 and 40 in 50 mmol Scale[22]

To a stirred solution of 2-methylcyclohexanone (**37**) or 2,6-dimethylcyclohexanone (**39**) (50 mmol) in *tert*-butanol (15 ml) heated to 65°C with a catalyst **18** (PADS, 100 mg, 0.30 mmol, 0.60 mol %), 30% aqueous hydrogen peroxide (10 ml, 0.10 mol) was added dropwise for 45 min, and the mixture was refluxed for 3 or 21 h, respectively. The solvent was distilled off and cold residue was extracted with chloroform

(10 ml and 2 × 5 ml). The extract was treated with a pinch of Pt/C, dried with anhydrous Na_2SO_4 and solvent was removed. Acids (**38**, **40**) were purified on silica gel (70–230 mesh, 100 g) using diethyl ether as an eluent.

DATA

6-Hydroxyheptanecarboxylic Acid (38)

Colorless oil, (4.69 g, 64%). ^{1}H NMR (300 MHz, DMSO-d_6); 11.50 (s, 1H, COOH), 4.30 (s, 1H, OH), 3.45–3.55 (m, 1H), 2.15 (t, $J = 7.3$ Hz, 2H), 1.40–1.50 (m, 2H), 1.20–1.30 (m, 4H), 0.98 (d, $J = 6.1$ Hz, 3H, Me). IR (Film); 3370 cm^{-1} (OH), 2200–3600 cm^{-1} (COOH), 1711 cm^{-1} (C = O), 1150–1250 cm^{-1} (out of plane, C–O).

6-Hydroxy-2-methylheptanecarboxylic Acid (40)

Colorless oil, (5.74 g, 72%). ^{1}H NMR (300 MHz, $CDCl_3$); 6.23 (s, 2H, OH and COOH), 3.75–3.85 (m, 1H), 2.40–2.53 (m, 1H), 1.60–1.75 (m, 1H), 1.35–1.55 (m, 5H), 1.19 (d, $J = 6.0$ Hz, 3H, Me), 1.18 (d, $J = 6.8$ Hz, 3H, Me). ^{13}C NMR (75 MHz, $CDCl_3$); 181.5 (C=O), 39.2, 67.8 (CH), 38.7, 33.4, 23.2 (CH_2), 23.0, 16.8 (CH_3). IR (Film); 3380 cm^{-1} (OH), 2200–3600 cm^{-1} (COOH), 1708 cm^{-1} (C=O), 1150–1250 cm^{-1} (out of plane, C–O).

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[47] To the preliminary purified THF [51] in round bottom flask with a long neck, several pieces of clean sodium or potassium or both and benzophenone are added. The flask is closed and put into an ultrasonic bath, and sonicated until deep blue, permanent coloration appears. Next THF is distilled using a Vigroux column. The contact of THF with ambient atmosphere should be avoided. Such a purified THF should be used on the same day.
[48] Diphenyl acetylene can be used instead.[11]
[49] The stopcock adapter should be vacuum proof, silicone grease is used to tighten its connections.
[50] If there is no deep permanent green coloration during 30 min, something is wrong and the experiment should be discontinued.
[51] THF distilled from $LiAlH_4$ is appropriate for the further purification.
[52] The period necessary for the completion of the reaction depends on purity of selenium used. Selenium of lower purity grade reacts faster. The technical grade selenium was found quite satisfactory.