THE CHEMISTRY OF ORGANO-SELENIUM REAGENTS

a thesis presented by

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ABSTRACT

Cholestan-3-one p-nitrophenylhydrazone may be converted into cholesta-1,4-dien-3-one p-nitrophenylhydrazone and cholesta-1,4,6-trien-3-one in 80% and 61% yields respectively by treatment with a suitable base (potassium t-butoxide) and oxidant (p-nitrobenzoic acid). The conditions for the reaction have been extensively examined and optimised.

Cholesta-1,4-dien-3-one is regenerated from cholesta-1,4-dien-3-one p-nitrophenylhydrazone in 73% yield using benzeneseleninic anhydride. The regeneration reaction was further shown to be general, thus phenylhydrazones, p-nitrophenylhydrazones, tosylhydrazones, oximes and semicarbazone derivatives of ketones afforded the parent ketone after treatment with benzeneseleninic anhydride. For example, benzophenone phenylhydrazone afforded benzophenone in 89% yield, cholest-4-en-3-one tosylhydrazone afforded cholest-4-en-3-one in 86% yield. In the case of oximes and tosylhydrazones, the reaction is further extended to aldehyde derivatives. Phenylhydrazone and p-nitrophenylhydrazone derivatives of aldehydes were shown not to regenerate the parent aldehyde but instead give a high yield of carbonyl-azo compounds; for example, benzaldehyde phenylhydrazone afforded benzoyl azobenzene in 67% yield.

Cholestan-3-one reacts at elevated temperature (95-132^{o}C) with benzeneseleninic anhydride to afford cholesta-1,4-dien-3-one in 63% yield. The reaction is general for A and C ring ketones. Thus, lanostan-3-one afforded lanost-1-en-3-one in 67% yield, hecogenin acetate afforded 9,(11)-dehydro-hecogenin acetate in 91% yield. A byproduct from the reaction was shown to be the A-nor ketone. Thus, 4,4-dimethylcholest-5-en-

-3-one after treatment with excess anhydride afforded in addition to 4,4-dimethylcholest-1,5-dien-3-one, A-nor-4,4-dimethylcholest-5-en-3-one in 28% yield.

It was shown possible to generate benzeneseleninic anhydride *in situ* for use in the dehydrogenation reaction from diphenyldislenide and *t*-butylhydroperoxide. The reaction is possible on a catalytic scale. Thus, lanost-1-en-3-one has been prepared in 69% employing *t*-butylhydroperoxide and only 1/5 eqv. diphenyl diselenide.

Carbon-hydrogen oxidation reactions using benzeneseleninic anhydride at elevated temperature (95-132^{o}C) have been shown to be general. Thus, xylene is converted into tolualdehyde, 2-picoline is converted into picoline-2-aldehyde and anthracene is converted into anthraquinone in good yield. Acenaphthalene has been converted into acenaphthaquinone in excellent yield under milder (64^{o}C) conditions. Benzyl alcohol and cynnamyl alcohol are both converted quantitatively into the aldehyde on treatment with benzeneseleninic anhydride. No further oxidation to the respective acids has been observed.

Finally, nitrogen-hydrogen oxidations have been carried out with the anhydride. Several examples have been chosen, in all cases reaction takes place smoothly at room temperature. For example, hydrazobenzene is converted into azobenzene, furanoyl hydrazobenzene is converted into furanoyl azobenzene, and *t*-butylhydroxylamine is converted into nitroso-*t*-butane, all in good yield. *p*-Nitrophenylhydrazine, on treatment with benzeneseleninic anhydride, affords both phenylseleno-*p*-nitrobenzene and nitrobenzene in 63% and 27% yields respectively.

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SECTION 1

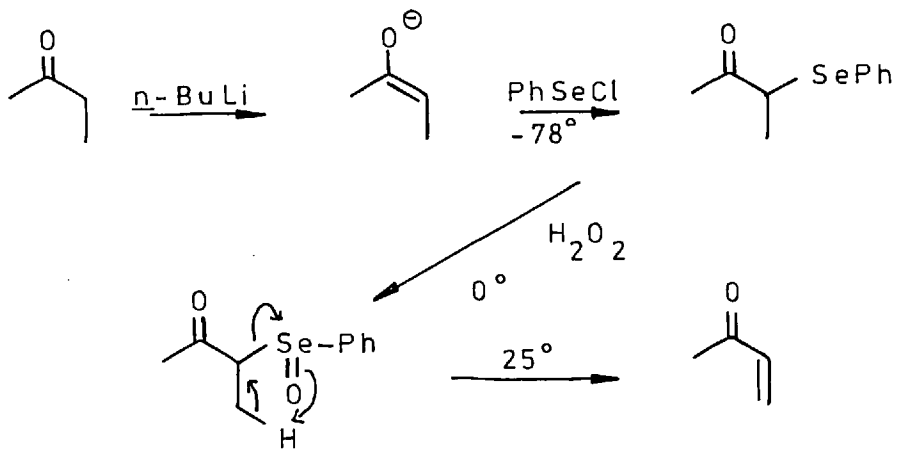
NEW ORGANO-SELENIUM OXIDISING REACTIONS

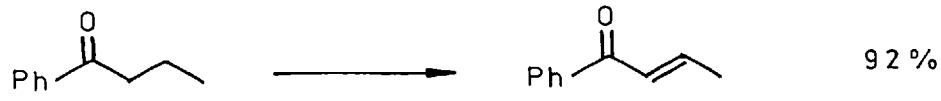
Introduction

Organo-selenium reagents are becoming increasingly popular and important synthetic reagents for organic chemists. Their wide application to many fields permits synthetic transformations previously unknown by conventional methodology. It is beyond the scope of any short review to cover the vast applications of organo-selenium reagents known up to date. This review simply outlines some of the most recent important applications of organo-selenium reagents to organic chemistry.

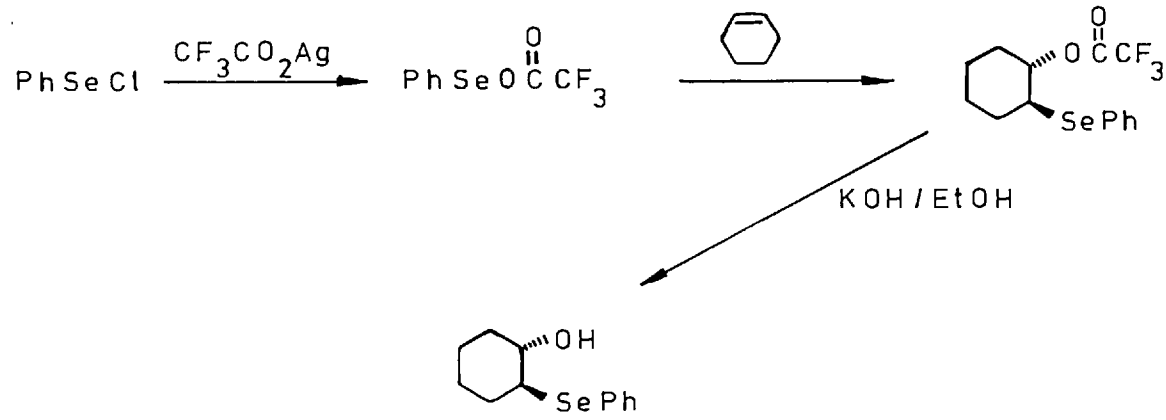
Preparation and Synthetic use of Selenoxides

A recent review[1] extensively covers the preparation of organic selenoxides from divalent selenium containing species followed by oxidation using either hydrogen peroxide, sodium periodate or ozone, and the range of compounds obtained after elimination of selenenic acid. For example, lithium enolates prepared from ketones react at low temperature (-78°C) with phenylselenenyl chloride to give α-seleno species in high yield. Oxidation at 0°C by either hydrogen peroxide or sodium periodate affords the selenoxide which, on warming to room temperature, looses phenylselenenic acid generating an α,β-unsaturated ketone in 35-80% yield[2].

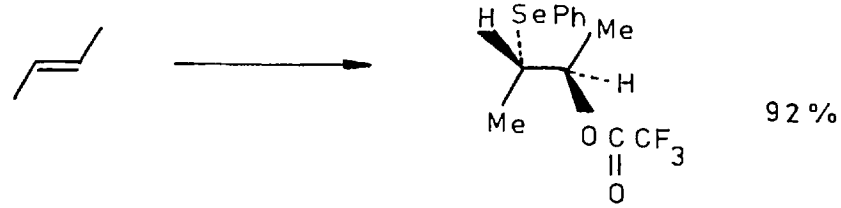


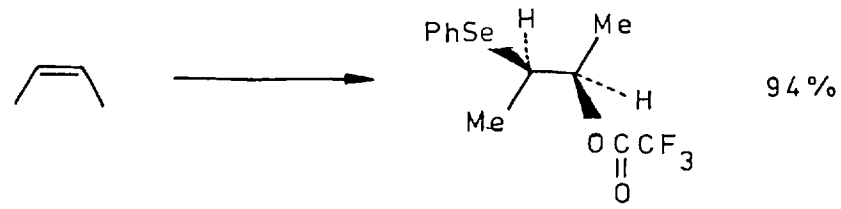


Phenylselenyl chloride reacts with silver acetate in benzene to afford phenylselenotrifluoroacetate as a yellow orange solution. On addition to unactivated double bonds, it gives the trans-phenylselenotrifluoroaceto compound. Treatment with alcoholic potassium hydroxide affords 2-selenophenyl alcohols in high yield[3].

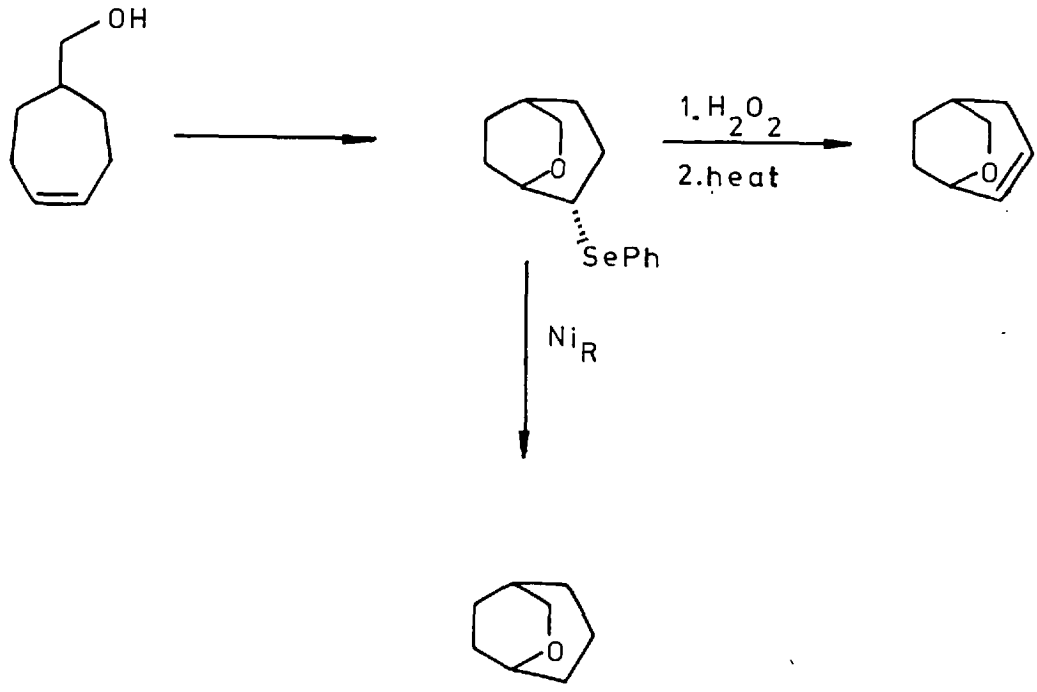


Although the reaction is not regiospecific for highly substituted olefins, it is highly stereospecific. This high stereospecificity is observed in the reactions with cis and trans but-2-enes to afford different adducts.





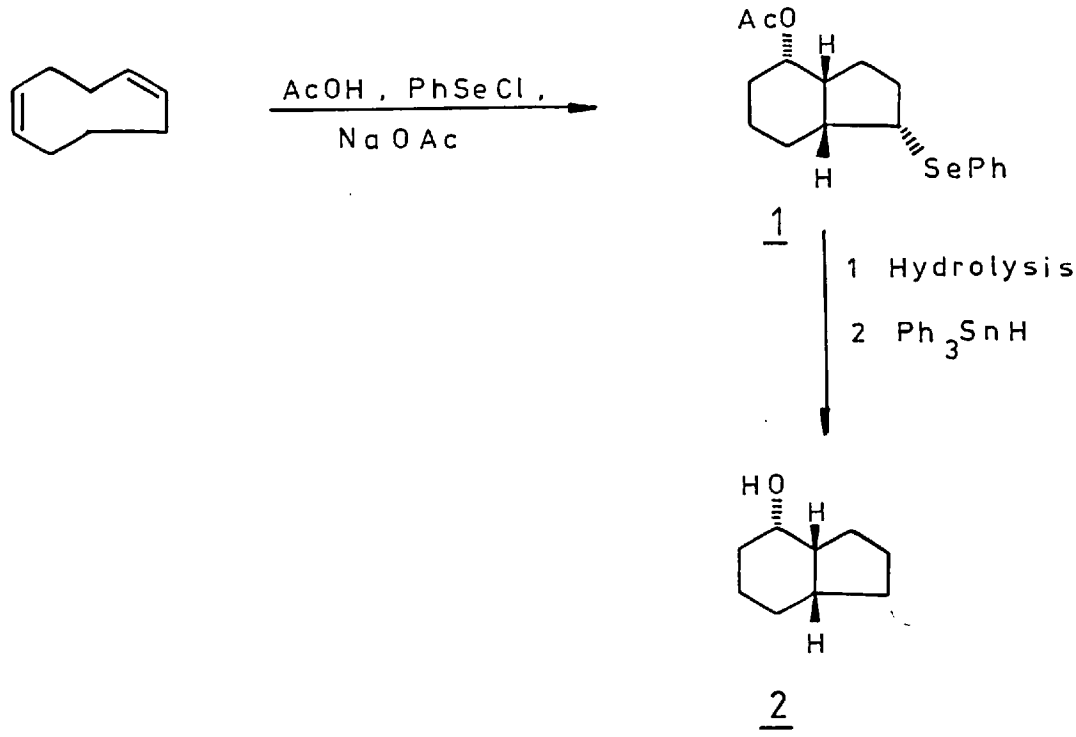
Cyclic ethers have been prepared by a new cyclofunctionalization procedure involving intramolecular trapping of episelenonium ions by a hydroxy group[4]. Treatment of the phenylseleno derivative with Raney nickel affords a saturated cyclic ether; alternatively, oxidation with hydrogen peroxide at $0^{o}C$ followed by warming to room temperature produces the unsaturated cyclic ether in excellent yield.



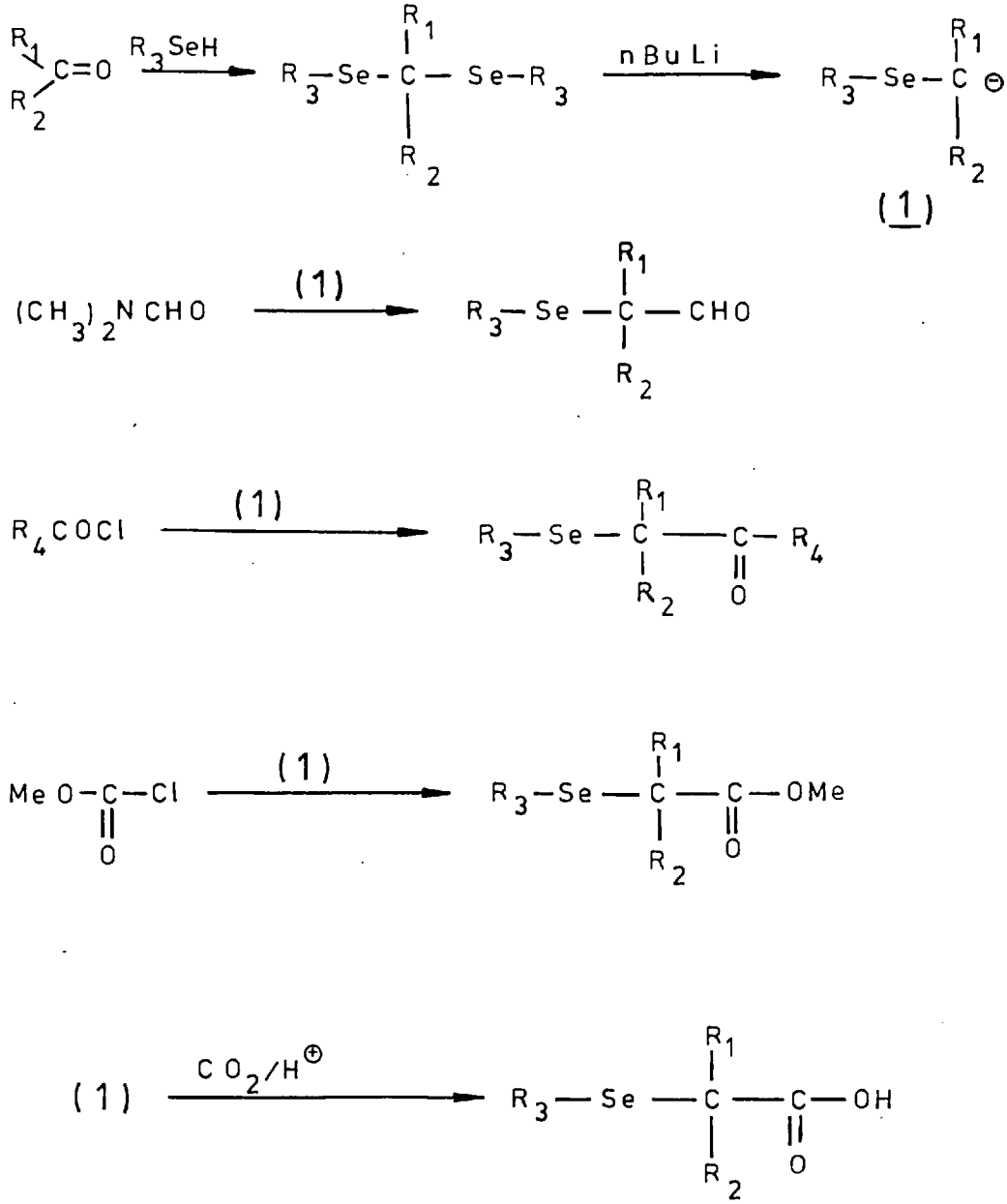
This type of reaction has been shown to be fairly general and, in a recent paper by Nicolaou[5], he gives many examples including the formation of phenylseleno lactones in over 90% yield.

Recently[6], a transannular example of cyclofunctionalisation using benzeneselenyl chloride has been reported. Cyclonona-1,5-diene affords the hydrindanyl acetate (1) after treatment with benzeneselenenyl chloride in acetic acid containing sodium acetate. Hydrolysis followed by treatment with triphenyltin hydride, under reflux in benzene, affords the alcohol (2) in good yield (43%). The stereochemistry of the alcohol (2) was confirmed by n.m.r. spectroscopy and shows clearly the trans

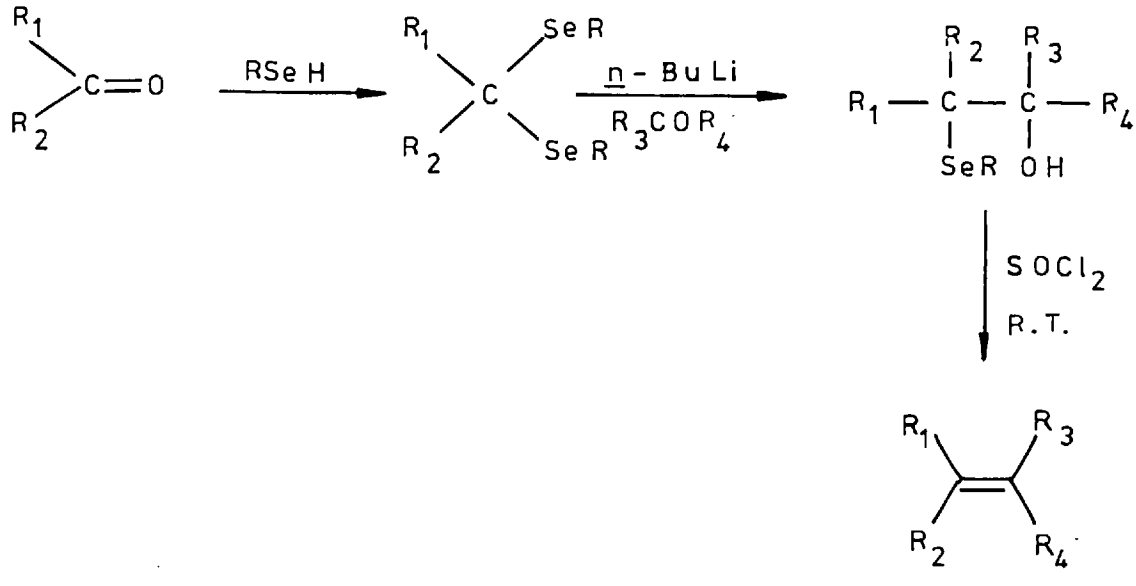
addition of benzeneselenenyl chloride to double bonds.

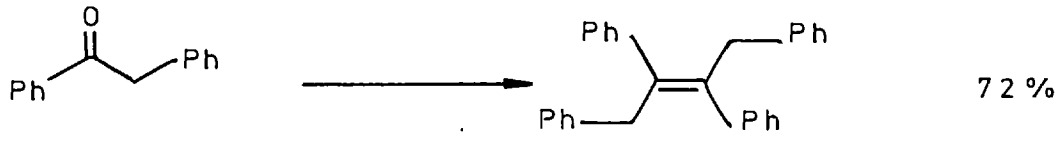


Carbonyl compounds react rapidly with selenols affording ortho-seleno esters in high yield. Treatment of the ortho-seleno ester with n-butyl lithium generates the carbanion, with the loss of one seleno alkyl group, offering an excellent synthesis of α-seleno aldehydes, ketones, esters and acids [7].

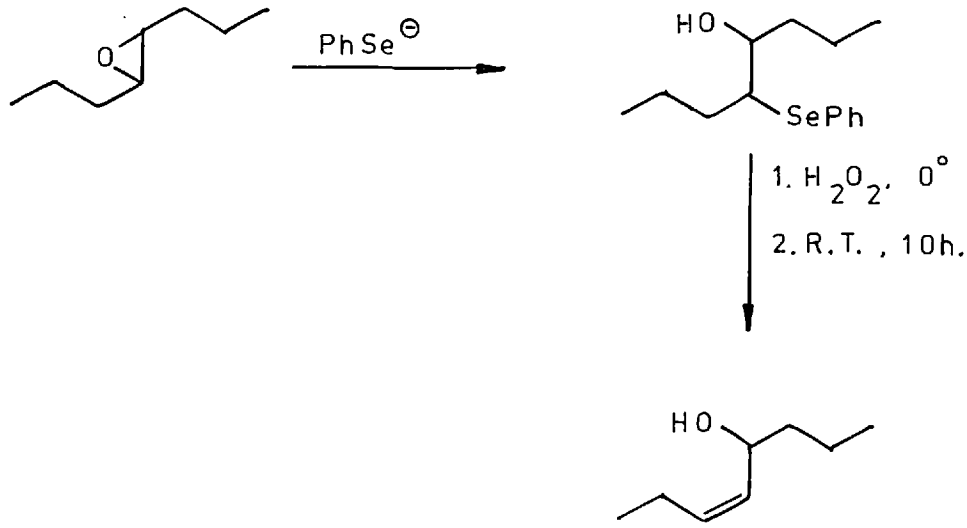


Reaction of the anion with a ketone affords an α-hydroxy selenide in excellent yield. When further treated with thionyl chloride or thionyl chloride/triethylamine at room temperature, an olefin is produced in excellent yield[8]. The method is superior to the Wittig reaction and allows highly substituted olefins to be prepared easily. No rearranged products have so far been observed during the course of the reaction.

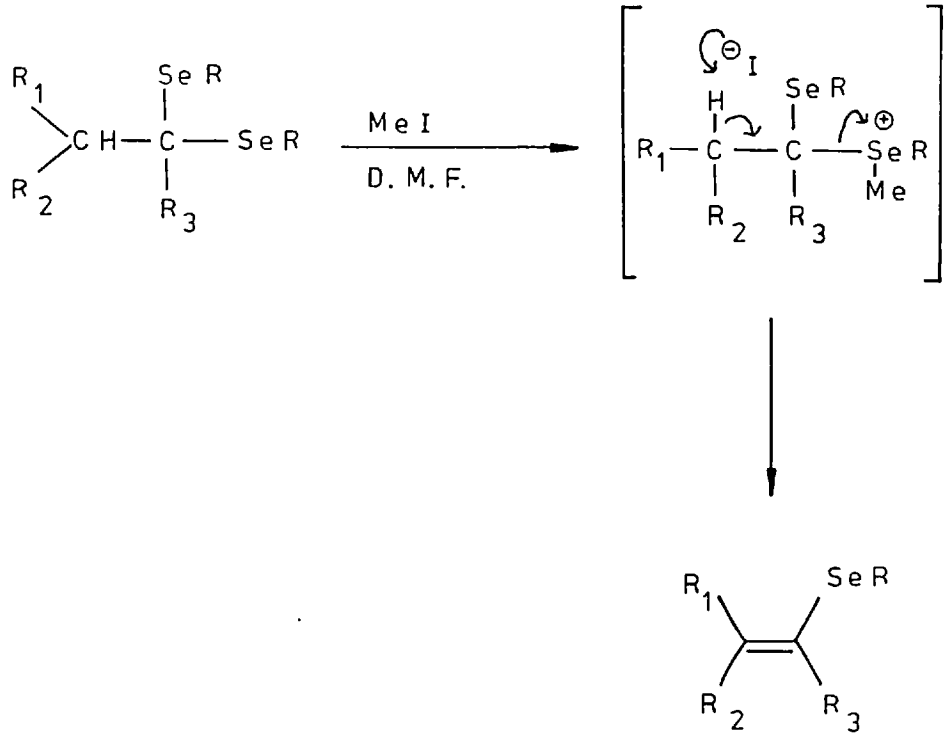




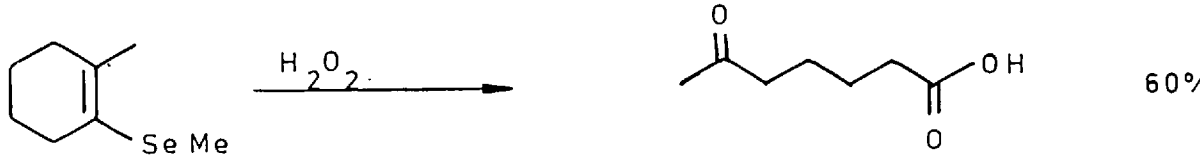
α-Hydroxy-selenides may also be prepared by reaction of the phenyl-selenide anion with an epoxide[9]. After oxidation with hydrogen peroxide, elimination of phenylselenenic acid always occurs away from the hydroxyl group to afford α,β-unsaturated alcohols.



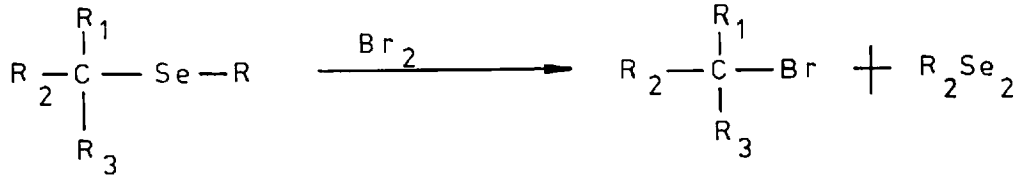
Vinyl selenides may be prepared in excellent yields from ortho selenides containing an α-hydrogen atom by treatment with methyl iodide in DMF. The more substituted olefin results in cases where two elimination pathways are possible[10].

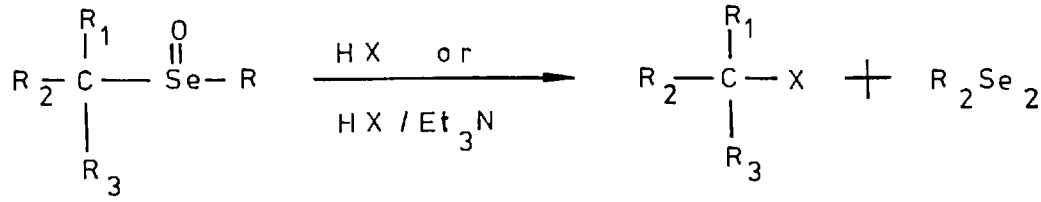


Vinyl selenides are excellent synthetic building blocks, showing many general reactions. Of particular interest is the reaction with hydrogen peroxide which leads to the ketoacid[10].



Alkyl halides may be obtained from selenides[11] or selenoxides[12] by treatment with either bromine or hydrogen chloride, bromide or iodide respectively.





Diphenyl selenoxide as an Oxidant

Diphenyl selenoxide has been known since 1893[13]. It is most readily prepared from diphenylselenide by treatment with bromine followed by

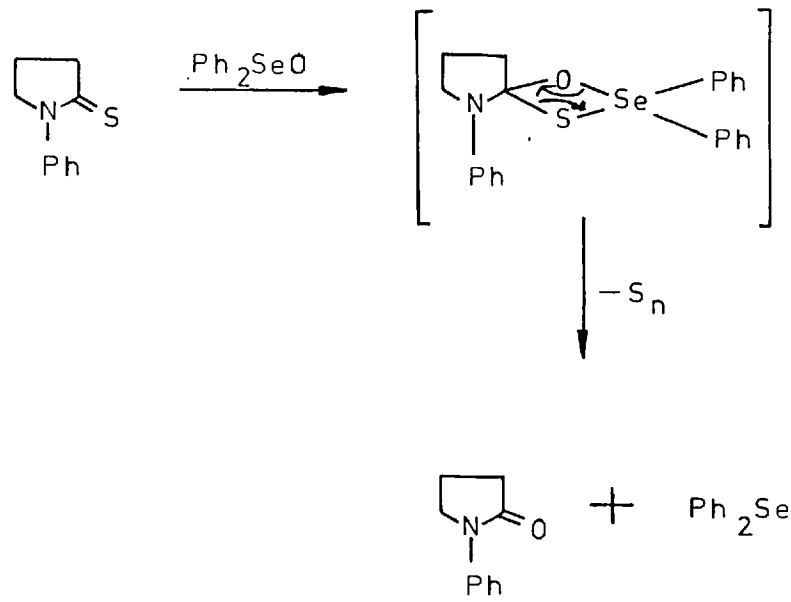
subsequent hydrolysis of the resulting dibromide with aqueous sodium hydroxide to give a colourless crystalline stable solid. However, it is only recently that it has been explored as an oxidising agent in organic systems. The following examples serve to illustrate some of its more recent applications.

Hydrazines, after treatment with diphenyl selenoxide are converted into symmetrical hydrazides in quantitative yield[14]. The reaction is much more selective and generally affords higher yields than the corresponding preparations by reduction of the azide.

$$PhCONHNH_2 \xrightarrow{Ph_2SeO} PhCONHNHCOPh \qquad 100\%$$

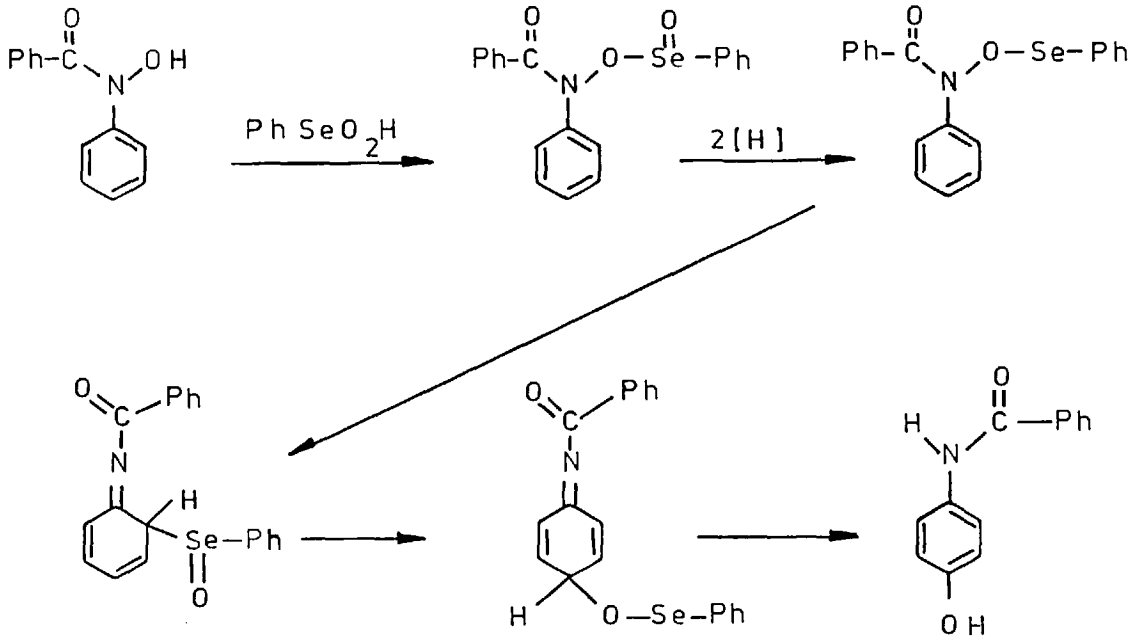
Diphenyl selenoxide has also been used in the preparation of N-oxides. Thus, treatment of strychnine, brucine, nicotinamide, trimethylamine, and triethylamine with diphenyl selenoxide produces the corresponding N-oxides in excellent yield[15].

The ease with which selenoxides exchange oxygen from sulphur has been demonstrated by treating, for example, N-phenylpyrrolidine-2-thione with diphenyl selenoxide which gives N -phenylpyrroline-2-one in 83% yield[16]. The unstable thioselenoxide intermediate breaks down precipitating elemental sulphur. The mechanism of the reaction has been postulated as occurring via a 4-centred transition state in which the selenoxide adds directly accross the thione.

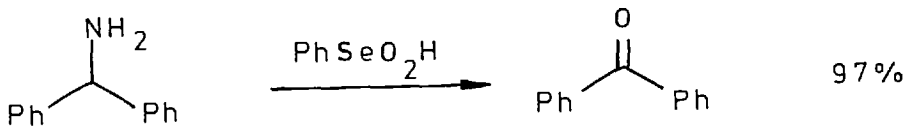


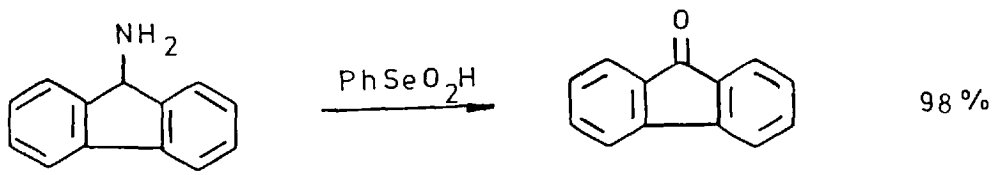
Benzeneseleninic Acid as an Oxidant

Benzeneseleninic acid is increasingly being examined as a selective organic oxidant. N-arylbenzohydramic acids have been shown to rearrange to p-hydroxybenzanilides in 30-70% yield in the presence of a catalytic quantity of benzeneseleninic acid[17]. The reaction has been shown to be inhibited by traces of hydrogen peroxide and is thus believed to be occurring by some reduction of an intermediate selenoxide. The nature of the reductants is not obvious.



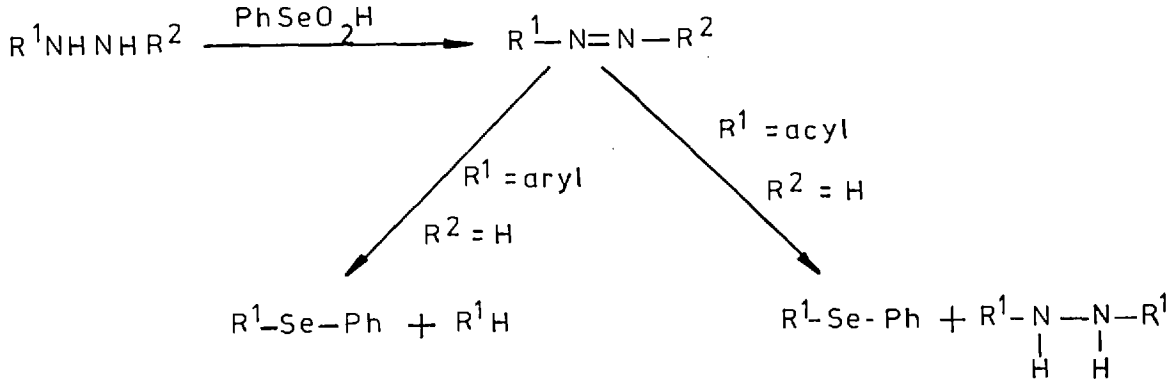
Amines react with benzeneseleninic acid to afford ketones in excellent yields[18]. The reaction is not general as amines capable of forming enamines (e.g. cyclohexylamine, indole) afford a complex reaction mixture from which some Pummerer like decomposition products have been characterised. The addition of base did not improve the reaction[19].



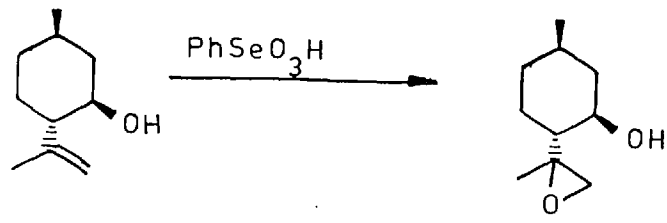


Benzylamine gave only a poor yield of benzaldehyde (isolated as benzoic acid) when treated with only one equivalent of benzeneseleninic acid. With two equivalents, a high yield (96%) of benzonitrile was observed.

Hydrazine is converted into di-imide on treatment with benzeneseleninic acid. Di-imide, generated <u>in situ</u> from hydrazine hydrate and benzeneseleninic acid quantitatively reduces azo-benzene to hydrazobenzene, and cinnamic acid to hydrocinnamic acid. Substituted hydrazines afford substituted azides which may further spontaneously decompose to generate phenylseleno species[20].



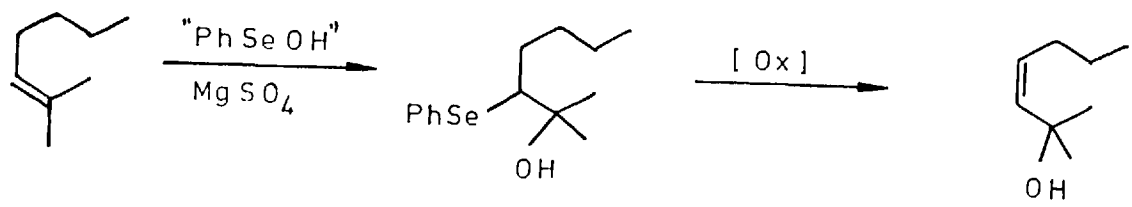
Benzeneseleninic acid, on treatment with hydrogen peroxide is converted into the peracid which is a useful epoxidising reagent when used in conjunction with a phosphate buffer at pH 7[21].



Benzeneseleninic acid is thought to react with diphenyldiselenide and water to produce the unstable benzeneselenenic acid *in situ*[22].

$$PhSeO_2H + Ph_2Se_2 + H_2O \rightleftharpoons 3\ PhSeOH$$

Olefins, after treatment with benzeneseleninic acid generated *in situ* as above, afford high yields of 2-selenophenyl alcohols. Oxidation followed by elimination affords allylic alcohols in excellent yield. The reaction offers high regioselectivity with unique addition in the Markownikoff sense, particularly in the presence of magnesium sulphate.

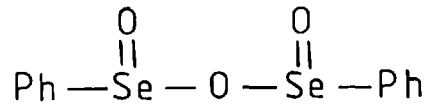


100 %

Benzeneseleninic Anhydride

Benzeneseleninic anhydride has been known since 1909[23], but it was not until 1962[24] that an efficient synthesis by ozonolysis from diphenyl diselenide was devised. The large scale preparation of benzeneseleninic anhydride is most conveniently achieved by the nitric acid oxidation of diphenyl diselenide. The resulting seleninic acid hydronitrate may be converted quantitatively to the anhydride by heating at 130°C *in vacuo* for several hours[25].

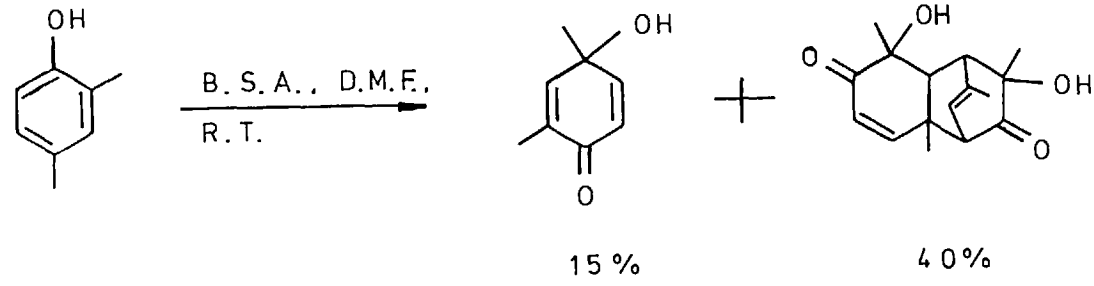
N.m.r.[26], infra-red and raman spectroscopy[27] have shown, contrary to the sulphur analogue[28], that benzeneseleninic anhydride is a true anhydride having a symmetrical structure.



Benzeneseleninic anhydride is a white powder m.p. 164°C. It is hydrolysed by moist air giving benzeneseleninic acid, but this process is slow and no special precautions are necessary when handling the reagent. It reacts rapidly with ethanol and methanol to form selenoesters at room temperature, consequently, solvents such as T.H.F., benzene, chlorobenzene have been employed. The reagent is only slightly soluble in most solvents. The anhydride is most commonly used as a suspension, hence vigorous stirring during reactions is required.

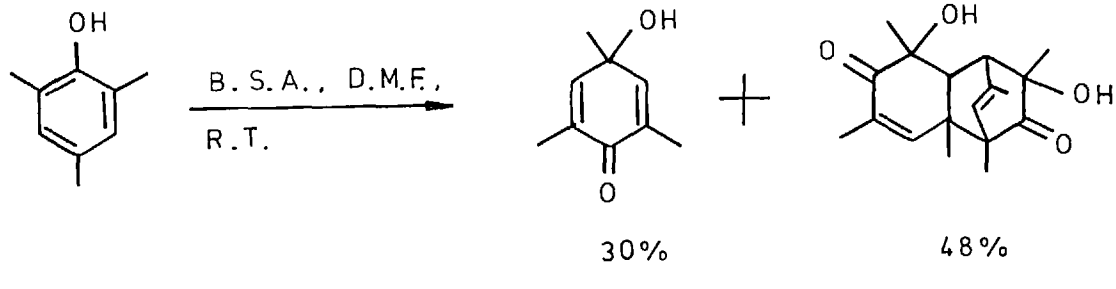
Benzeneseleninic anhydride has successfully been used to carry out *O*-hydroxylation of phenols. Thus, 2,4-xylenol afforded the *p*-hydroxydienone and *O*-hydroxydienone in 15% and 40% yields respectively. When treated with anhydride, mesitol similarly treated afforded the

p-hydroxydienone and o-hydroxydienone in 30% and 48% yields respectively. The reaction is important to the Imperial College approach to tetracycline[29].



15 %

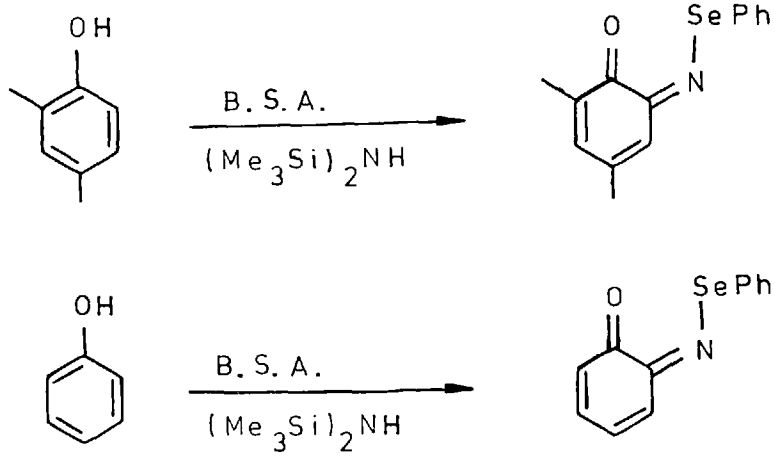
40 %



30%

48%

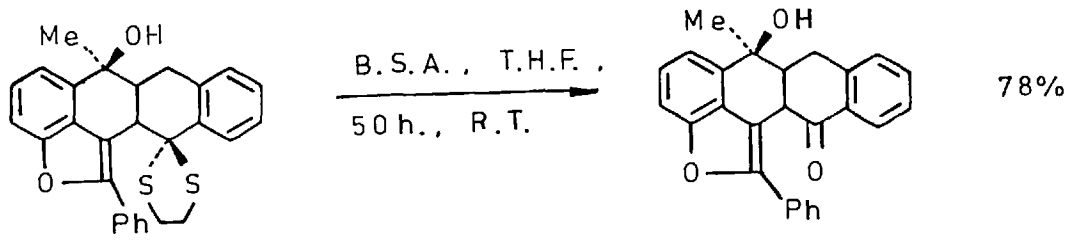
Phenylselenoimines have been generated in good (45-85%) yield by treatment of phenols with benzeneseleninic anhydride in the presence of hexamethyldisilazane. This new class of compounds was readily reduced in high yield to aminophenols. The reaction shows marked ortho selectivity for the formation of o-phenylselenoimines[30].



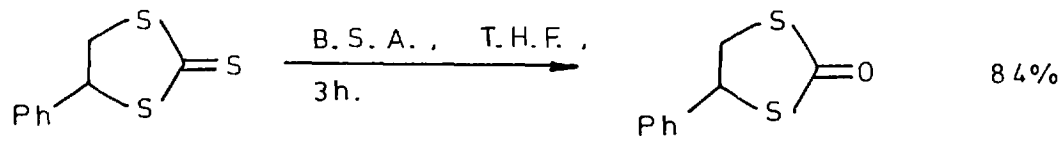
65 %

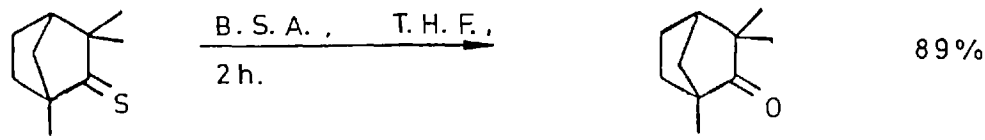
45 %

Benzeneseleninic anhydride has also been used to regenerate ketones and aldehydes from 1,3-dithiolans in cases where all other common methods have failed[31].



A large number of thiocarbonyl compounds have recently been shown to react with benzeneseleninic anhydride in T.H.F. at room temperature to afford the oxo derivatives in high yield[32].





Increasingly, organic chemists are using selenium containing reagents to efficiently perform difficult synthetic transformations, particularly in the field of natural products chemistry. Many significant developments have taken place over the past 3 years and, undoubtedly, organoselenium chemistry will prove to be a viable area of organic research for years to come.

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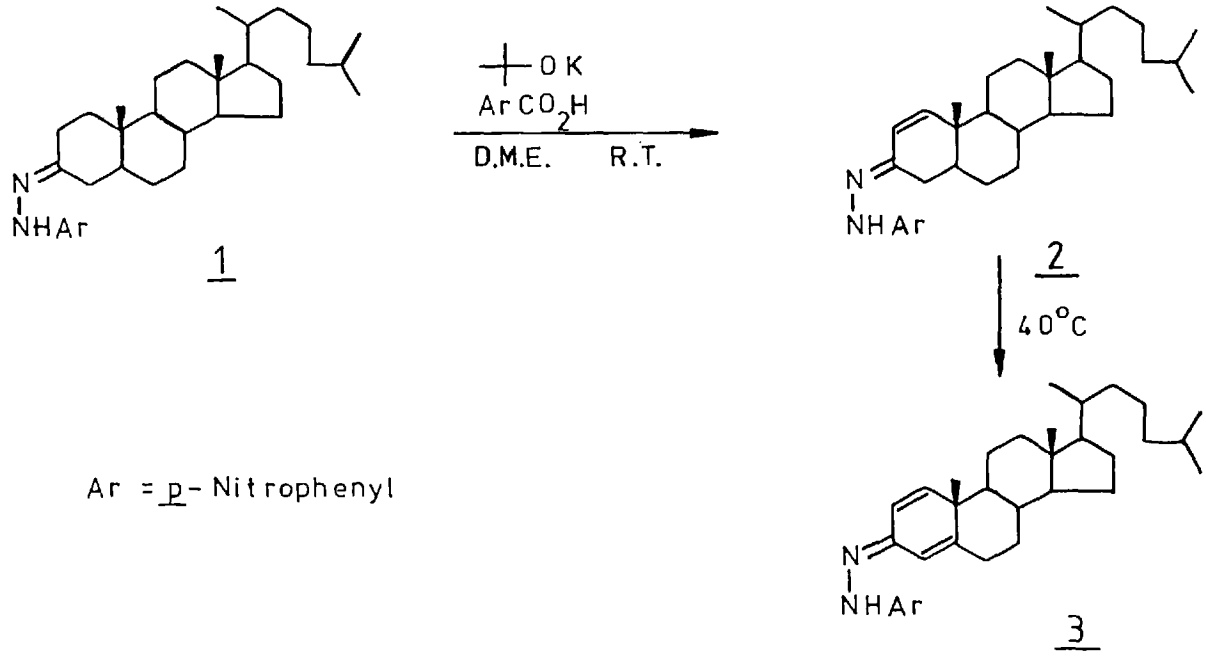
SECTION 2

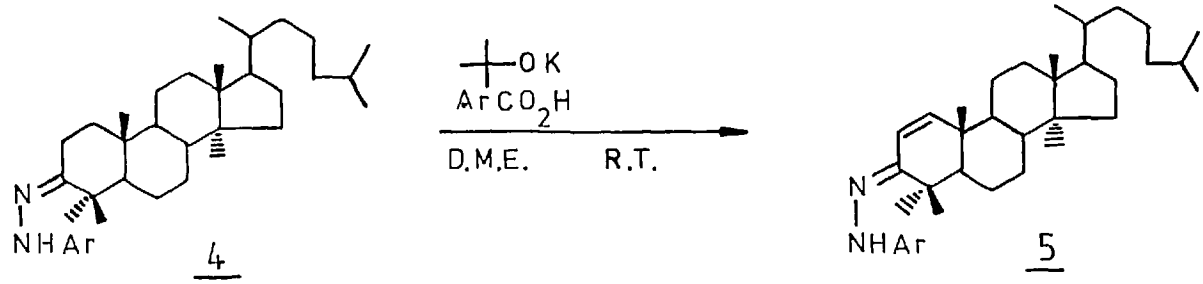
(a) DEHYDROGENATION OF STEROIDAL HYDRAZONES

Recently, cholestan-3-one p-nitrophenylhydrazone (1) has been shown to be converted cleanly to its enone (2) and dienone (3) p-nitrophenylhydrazones, in excellent yield, by treating with an excess of potassium t-butoxide and p-nitrobenzoic acid at room temperature in glyme[1].



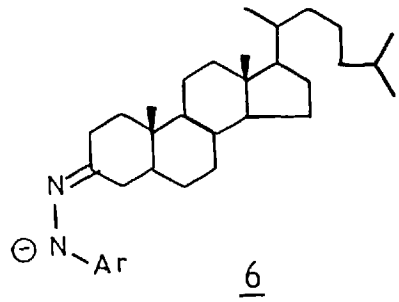
Ar = p-Nitrophenyl

Similarly, lanostan-3-one p-nitrophenylhydrazone (4) was converted to lanost-1-en-3-one p-nitrophenylhydrazone (5).



Ar = p-Nitrophenyl

Since the reaction uses a large excess of expensive reagents, for it to be of industrial use, it was necessary to try to develop cheaper reaction conditions. For high yields, the reaction has to be performed under rigorous exclusion of moisture and with carefully purified reagents. Typically resublimed potassium t-butoxide (>35 equivalents) is added to a stirred solution of the hydrazone and p-nitrobenzoic acid in dry glyme. The initial red colour can be attributed to the anion (6) which is rapidly converted to a red/purple colour of the anion (7).



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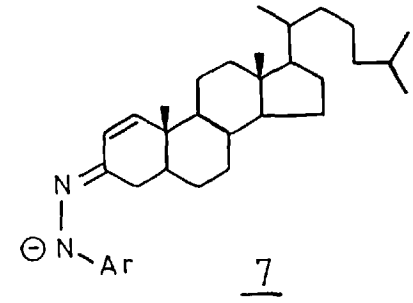

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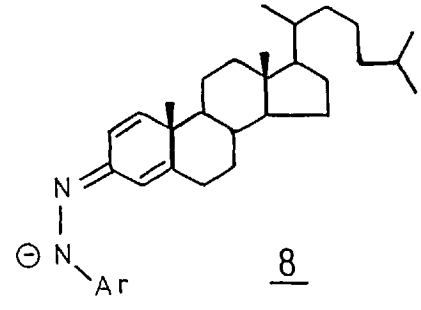
Ar = p- Nitrophenyl

At room temperature, little further reaction is observed but on warming to 40°C smooth conversion to the dienone hydrazone (3) takes place via formation of an intense purple colour thought to be the anion (8).



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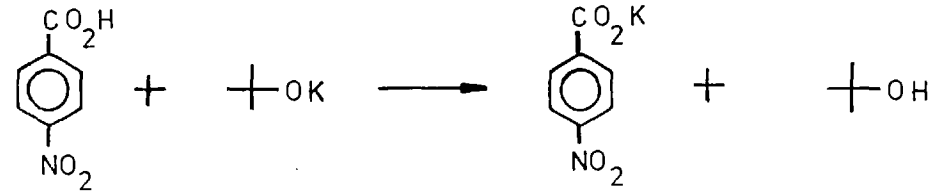
Ar = p- Nitrophenyl

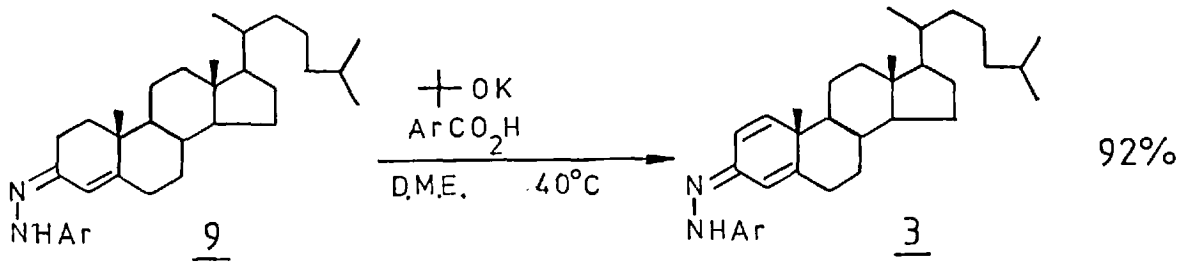
If the quantity of base is reduced to 15 equivalents or less, then the reaction stops at the enone hydrazone (2) stage and it is not possible to form the dienone hydrazone (3). The replacement of nitrobenzoic acid by nitrobenzene does allow the quantity of base to be reduced to 15 equivalents, although it is much more difficult to remove after completion of the reaction. Chromatography on a small scale is effective for removing the nitrobenzene but would not be convenient on a larger scale. Also, in larger scale work, the longer reaction times involved could lead to serious decomposition of the nitrobenzene. p-Nitrobenzoic acid offers many advantages as oxidant since it is readily removed by washing with sodium bicarbonate solution, leaving the product as an easily isolated solid, requiring only purification by recrystallisation. Other oxidants examined include nitromesitylene and nitromethane. Although nitromesitylene was stable to the bases used, it appeared too hindered to carry out the oxidation reaction. After 18 h at 40°C, the p—nitrophenylhydrazone (I) could be recovered almost quantitatively. Nitromethane, although more reactive, was not useful since it readily reacts with the base to form an insoluble anion $CH_2^-NO_2$. Ethanolic sodium ethoxide, or sodium hydroxide rather than t-butoxide/glyme were used without success. In each case, the red anion is formed but serious decomposition, with blackening of the reaction mixture, results. Sodium hydride prevents decomposition after the formation of the red anion (6) but after 2 days at 50°C no oxidation had taken place.

As a large excess of both base and p-nitrobenzoic acid are used in the oxidation reaction, it was thought that t-butanol, formed by reaction of the acid with the base, was necessary for a clean reaction to take place.



However, on treatment of the hydrazone (1) with excess (15 equivalents) nitrobenzene, t-butanol (15 equivalents) and sodium hydride (1.1 equivalents) in glyme at 50°C for 3 days, no reaction was observed. It is unlikely, therefore, that the alcohol is playing an important role in the reaction.

The dehydrogenation reaction leading to the dienone hydrazone was improved using cholest-4-en-3-one p-nitrophenylhydrazone (9) which is readily prepared from cholesterol as the starting material. Thus, cholest-4-en-3-one p-nitrophenylhydrazone (9) was converted cleanly into the dienone hydrazone (III) in 92% yield using the standard conditions.



Ar = p-Nitrophenyl

The synthesis of the dienone hydrazone (III) from cholesterol is much more convenient than using cholestan-3-one as the initial starting material.

Although potassium t-butoxide is an expensive reagent, a hindered base is necessary for good reaction. Owing to the lower relative cost of sodium hydride and t-butanol, a method of generating the t-butoxide *in situ* was developed. The method has two main advantages. Firstly, cheaper reagents are used and secondly, it is much easier to purify the alcohol than to purify potassium t-butoxide by sublimation. Typically, 30 equivalents of t-butanol and sodium hydride were employed with an excess of 15 equivalents of p-nitrobenzoic acid in glyme. Yields of up to 90% of the dienone hydrazone (3) were obtained.

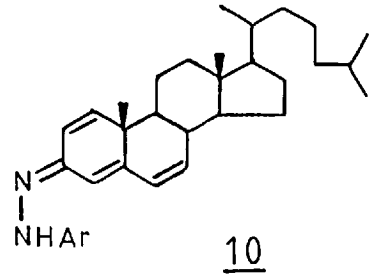
Since toluene is a more practical solvent for larger scale work than glyme, experiments using this as solvent were investigated. The reaction failed initially due to insolubility of sodium t-butoxide in toluene, however, sodium t-amylate, generated *in situ* from sodium hydride and t-amyl alcohol, proved to be a better base. Although, in toluene alone, poor yields of the dienone hydrazone (3) were obtained, if a mixture of glyme and toluene was employed, the yields could be improved. For example, a 15% solution of glyme in toluene gave a 77% yield of the dienone hydrazone (3) after chromatography. These conditions appear to be the best compromise between solvent cost and yield of reaction.

The reaction has so far been scaled up to 5 g using 10% glyme in toluene as solvent. Nitrobenzene was used as oxidant because p-nitrobenzoic acid was only sparingly soluble under the reaction conditions. However, only a low yield of the dienone hydrazone (III) could be obtained owing to degradation of products under prolonged reaction times.

By comparison, reaction in glyme and using p-nitrobenzoic acid with sodium t-butoxide generated *in situ*, gave the dienone p-nitrophenylhydrazone (3) in excellent yield (92%) which crystallised directly from

the reaction mixture.

On carrying out the oxidation at 60°C, another product was observed on t.l.c. along with many polar decomposition products on t.l.c. The deep red product obtained in 61% yield exhibited a λ_{max}^{EtOH} at 434 nm (ε 33500) and molecular ion at 515, suggesting the compound is cholesta-1,4,6-trien-3-one p-nitrophenylhydrazone (10).



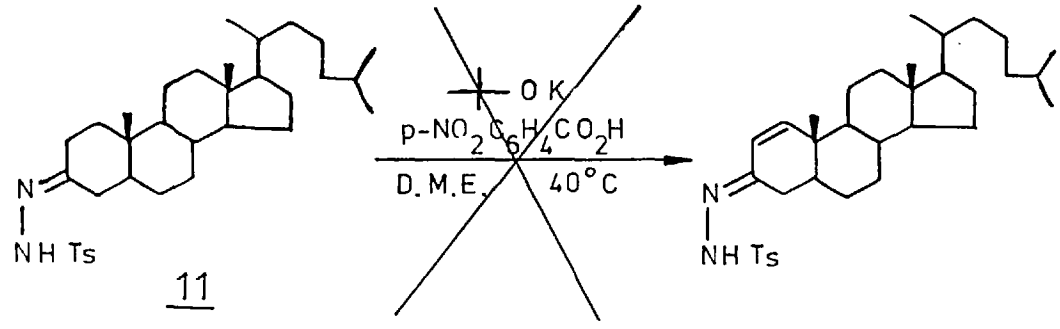
10

Ar = p-Nitrophenyl

The n.m.r. spectrum is consistent with this structure δ, 8.2-7.2 (4H, q, aromatic H) and 6.8-6.0 (5H, m, H-1, H-2, H-4, H-6, H-7). The compound gave satisfactory analytical data and, on removal of the hydrazone moiety, gave cholesta-1,4,6-trien-3-one (see later). The p-nitrophenylhydrazone (10) was also identical to an authentic sample prepared by DDQ oxidation of cholesterol followed by preparation of the hydrazone by standard methods. The preparation has been carried out on a large scale in glyme. However, it is not possible to obtain the pure trienone (10) directly by crystallisation from the reaction mixture due to the presence of contaminating decomposition products. Chromatography affords the pure trienone hydrazone (10) in 46% yield. This method does not compare too well with existing literature preparations of cholesta-1,4,6-tien-3-one from cholesterol or cholest-5-en-3-one using DDQ in which yields of up to 49% and 71% respectively have been reported.[2]

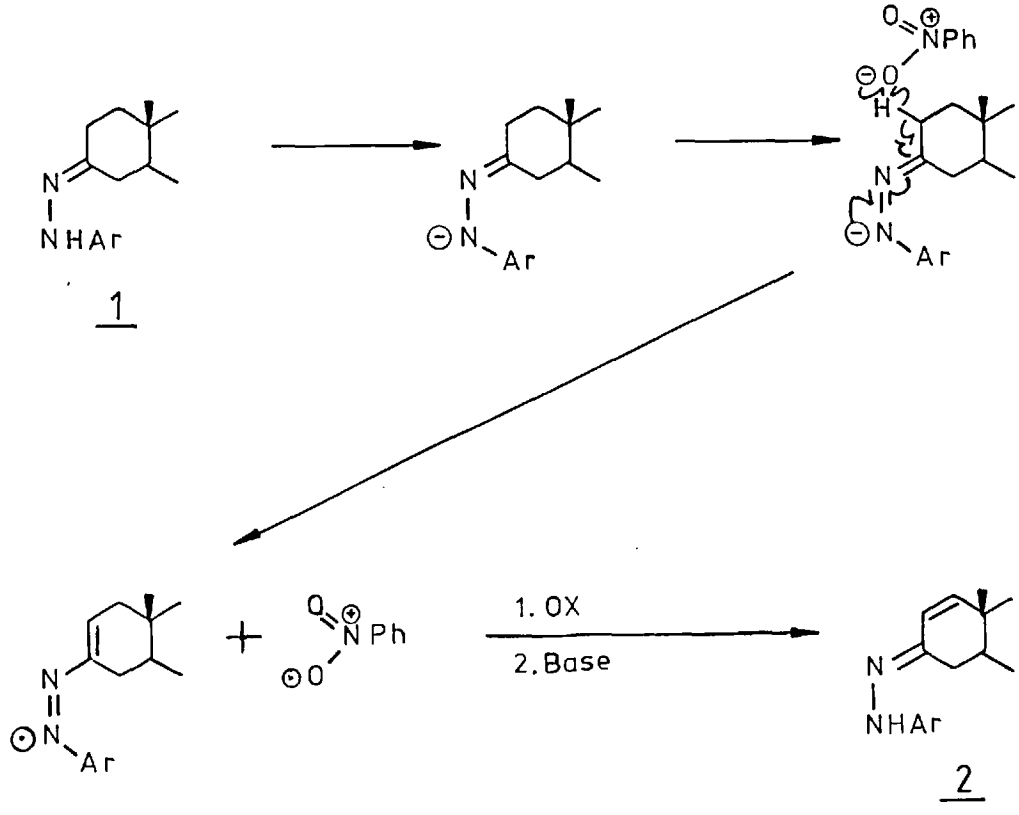
In view of the ease with which carbonyl compounds are regenerated from tosyl hydrazones, the tosylhydrazone of cholestan-3-one (11) was

examined in the dehydrogenation reaction. Dehydrogenation could not be achieved, possibly due to the increases stability of the tosylate anion.



11

The mechanism of the reaction is unknown. Clearly, a large excess of both base and oxidant are necessary for clean reaction. The reaction is probably occurring via two one-electron transfers from the anion of the nitrogroup of the p-nitrobenzoic acid coupled with proton loss (Scheme 1). The dependence on a large excess of base for satisfactory



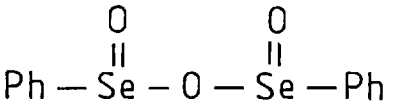
Scheme 1

reaction is in agreement with this and further suggests that the base is playing a more important part in mechanism than just initial anion formation. It is even conceivable that the t-butoxide is behaving as a radical transfer agent. Trimesityl boron, easily prepared by the action of mesityl magnesium bromide on boron trifluoride etherate[3], has been used as a good radical transfer species[4]. On addition of trimesityl boron to any of the dehydrogenation reactions, no improvement of yield was observed. Either the t-butoxide is already acting as an efficient transfer species as proposed, or the reaction is not occurring via a radical transfer pathway. The reaction is clearly very sensitive requiring large excess of expensive reagents before good yield can be obtained. Later work in this thesis shows the use of benzeneseleninic anhydride as an improved method for the dehydrogenation of steroidal ketones.

(B) REGENERATION OF FREE KETONES FROM STEROIDAL p-NITROPHENYLHYDRAZONES

The regeneration of ketones from their hydrazones has been extensively examined in the literature. Methods for removal of the hydrazone are often fairly vigorous and include titanium trichloride[5], molecular oxygen[6] in the presence of triphenyl phosphine, nitrosonium salts[7], sodium peroxide[8], molybdenum oxychloride[9], and cupric acetate catalysed cleavage at pH 5[10]. When applied to cholesta-1,4-dien-3-one p-nitrophenylhydrazone, all the existing literature reactions failed to regenerate the ketone in good yield.

Benzeneseleninic anhydride[11] (12), on the other hand, was found to react smoothly with cholesta-1,4-dien-3-one p-nitrophenylhydrazone, regenerating the ketone in up to 86% yield. Typically, the anhydride was added to a solution of the dienone p-nitrophenylhydrazone (100 mg) in THF and the suspension heated to reflux. The anhydride slowly dissolved



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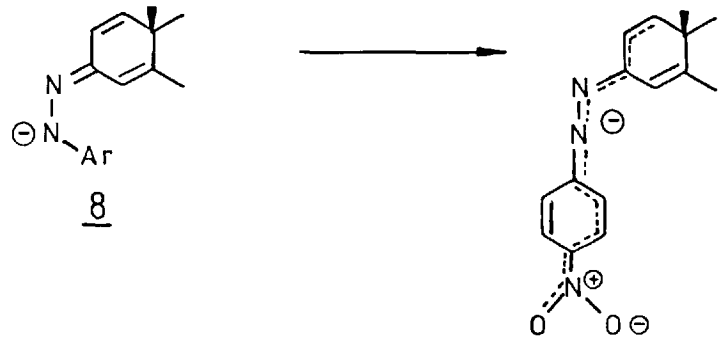
over a period of 3 h and the reaction could easily be followed by t.l.c. A complete molar equivalent of the anhydride was necessary for complete reaction. The reaction was found to go to completion on heating at 64°C for 3 h or stirring at 40°C overnight. From reaction of one mole of anhydride with one mole of hydrazone, diphenyl diselenide ($\frac{1}{2}$ mole), the ketone (86%), nitrobenzene (1 mole) and, benzeneseleninic acid ($\frac{1}{2}$ mole by titration) were obtained. If the anion (8) of the hydrazone (3) was initially formed by reaction with sodium hydride, little reaction took

place with the anhydride.

Mechanistically, it is thought that initial attack by the nitrogen on the anhydride seems likely (see later). It is possible that the anion (8) once formed is too stable to react with the anhydride, the charge being dispersed over much of the molecule (Scheme 2). After initial nitrogen attack, the intermediate (8) rearranges via a 2,3-sigmatropic shift to afford intermediate (14). The breakdown of



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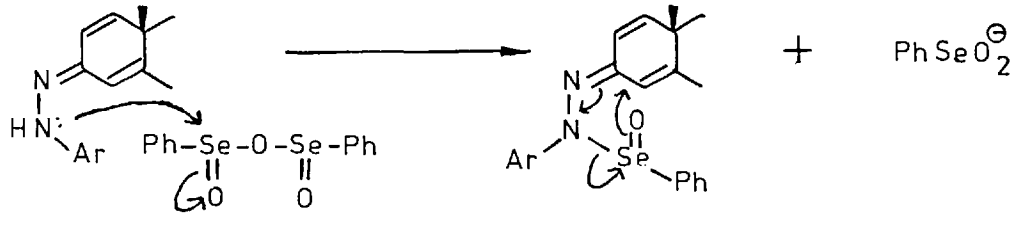
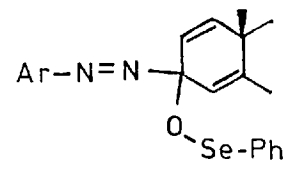
Scheme 2



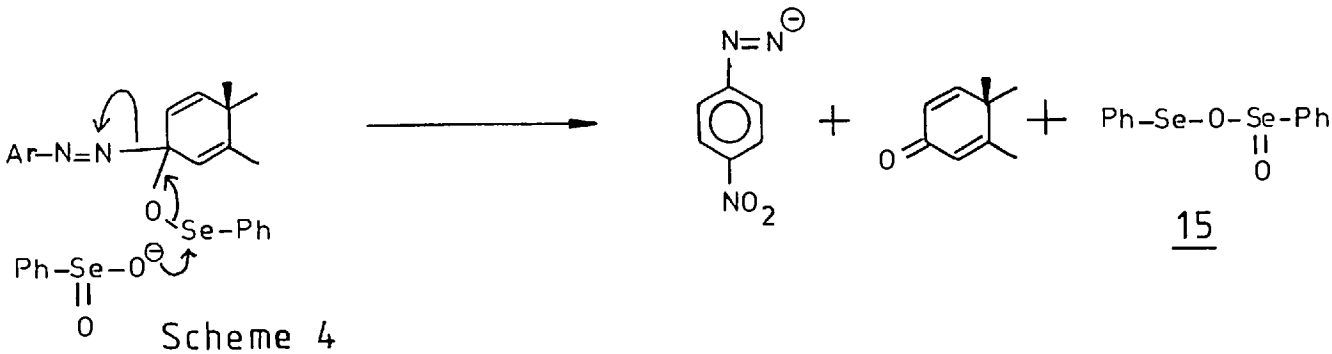
intermediate 13

Scheme 3

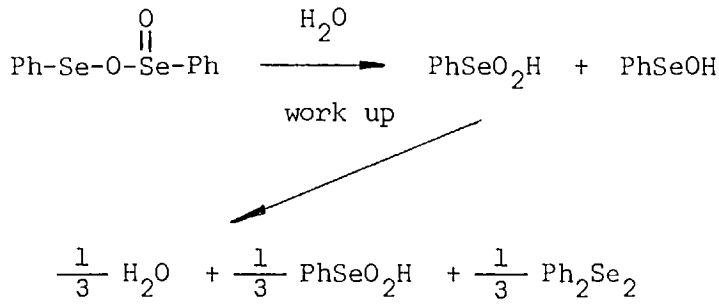


intermediate 14

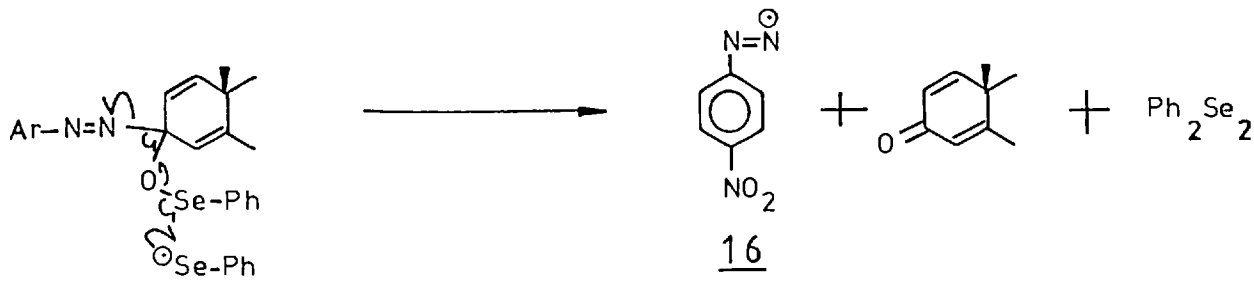
intermediate (14) may either occur via reaction of the benzeneseleninate anion being used as a nucleophile (Scheme 4) or via a radical pathway (Scheme V). The radical pathway is favoured.



Scheme 4



i.e. $Ph_2Se_2O_3 \longrightarrow \frac{1}{3} Ph_2Se_2 + \frac{4}{3} PhSeO_2H$



Scheme 5

The mechanism outlined in Scheme 4 gives the mixed anhydride (15) which on work up will disproportionate giving 1/3 mole diphenyl diselenide and 4/3 mole benzeneseleninic acid. This is not observed in practice.

If the radical mechanism is proposed, then the products are diphenyldiselenide (1/2 mole) and benzeneseleninic acid (1 mole) as observed experimentally. Furthermore, benzeneseleno radicals are known to be present in the anhydride under the influence of ambient laboratory light[12]. Unfortunately, the reaction takes place in the dark, and is not influenced by the presence of oxygen. The reaction produces nitrobenzene in high yield even when oxygen is bubbled through the reaction mixture. The ease with which oxygen quenches radicals makes it unlikely that they are present in the reaction. Alternatively, the radicals formed are trapped much quicker by the intermediate (14) than by molecular oxygen.

The reaction has been carried out on a preparative scale (5 g) but it did not prove possible to crystallise the cholesta-1,4-dien-3-one directly from the reaction mixture. Chromatography afforded the pure ketone in 73% yield. All the selenium could be recovered either as diphenyl deselenide or as benzeneseleninic acid. Thus, although benzeneseleninic anhydride is an expensive reagent, diphenyldiselenide may be recovered after the reaction and reoxidised to the anhydride by treatment with nitric acid followed by heating at 130°C *in vacuo* for several hours. Cholesta-1,4,6-trien-3-one, when prepared from its *p*-nitrophenylhydrazone was always obtained as an oil. Treatment with alkaline hydrogen peroxide in methanol afforded the crystalline 1α,2α-epoxide which could be more readily characterised.

SECTION 3

REGENERATION OF KETONES FROM HYDRAZONES, OXIMES AND SEMICARBAZONES

The encouraging observation that benzeneseleninic anhydride could be successfully used to regenerate cholesta-1,4-dien-3-one from its p-nitrophenylhydrazone prompted an investigation of other ketone derivatives with the anhydride. For the first of these ketones, benzophenone was converted to its phenylhydrazone p-nitrophenylhydrazone, 2,4-dinitrophenylhydrazone, tosyl hydrazone, oxime, and semicarbazone derivatives. The phenylhydrazone reacted readily with the anhydride to give benzophenone smoothly in 90% yield but, surprisingly, the p-nitrophenylhydrazone reacted sluggishly and only gave a poor yield of benzophenone (50%) after 3 days. The 2,4-dinitrophenylhydrazone failed to react under comparable conditions. The slow reaction of the p-nitrophenylhydrazone and the complete lack of reactivity of the 2,4-dinitrophenylhydrazones has been attributed to the strong electron withdrawing effect of the nitro group decreasing the nucleophilicity of the nitrogen atom towards the anhydride.

Tosylhydrazone and oximes react particularly readily with the anhydride affording the ketone in 95% and 89% yield respectively. N,N-Dimethylhydrazones or O-methyloximes failed to react with the anhydride thus providing selectivity in the deprotection reaction, should it be required in a synthetic scheme. Many other carbonyl derivatives have been prepared and the carbonyl compound regenerated by treatment with benzeneseleninic anhydride. The yields are summarised in Table I[11].

For comparison, the ketone derivatives were also treated with selenium dioxide and in most cases only gave low yields of regenerated carbonyl compound thus showing benzeneseleninic anhydride to be the more superior reagent. Other procedures were not investigated as these

are well documented in the literature.

TABLE 1. REGENERATION USING BENZENESELENINIC ANHYDRIDE

Derivative	Benzophenone	Cholestan-3-one	Cholest-4-en-3-one	2-furfural	2-Naphthaldehyde
Phenylhydrazone	90	64	57	87	70
p-Nitrophenylhydrazone	56	95	57	70	90
Tosylhydrazone	95	97	86	88	99
Oxime	89	83	96	36	94
Semicarbazone	89	83	85	2	5

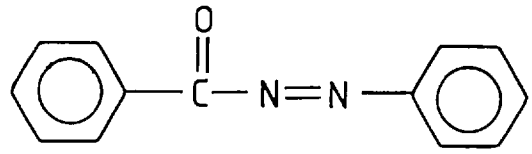
TABLE 2*. REGENERATION USING SELENIUM DIOXIDE

Derivative	Benzophenone	Cholestan-3-one	Cholest-4-en-3-one	2-furfural	2-Naphthaldehyde
Phenylhydrazone	49	14	44	19(8h)	1 (8h)
p-Nitrophenylhydrazone	35	5	-	37(8h)	2 (8h)
Tosylhydrazone	73	35	20	trace after 8 h	50(10h)
Oxime	13	16	80		35(10h)
Semicarbazone	2	45	trace		trace

* The times of reaction are shown in brackets where different from the benzeneseleninic anhydride reaction. Underlined yields refer to Carbonylazo species.

Aldehydic derivatives behaved similar to the ketones except for the phenylhydrazone and p-nitrophenylhydrazone. After adding the anhydride

to a solution of benzaldehyde phenylhydrazone in THF, the mixture aquired a deep red colour. Isolation afforded a low melting (28-29°C) red solid which exhibited a ν_{max} 1705 cm^{-1} and molecular ion at 212 (M^+ +2). The n.m.r. spectrum showed two groups of aromatic protons δ 5.6-6.2 (5H,m) and 7.6-8.2 (5H, m). The data are consistent with benzoyl azobenzene (17).



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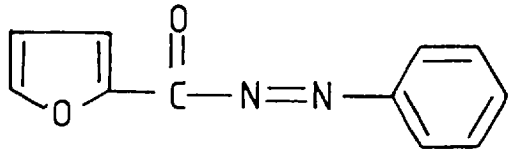
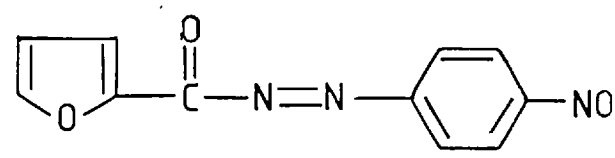
Benzoyl azobenzene has been prepared previously by Boch et al. by oxidation of the hydrazo compound with NBS[13], prepared by reaction of the acid chloride with the hydrazine. The new method of preparation, although similar in yield to the literature route, is possibly quicker to use as the starting material is the readily available aldehyde rather than the acid chloride of the Boch route. Several previously unknown carbonyl-azo compounds (18)-(21) have been prepared by this method. All compounds gave satisfactory spectral and microanalytical data[13].



18

Furanoyl azobenzene



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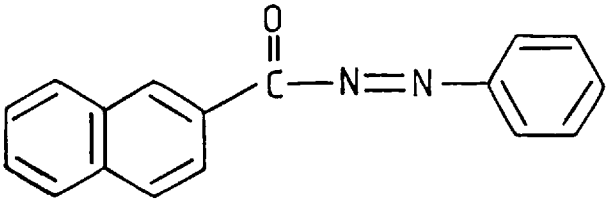
Furanoyl azo-p-nitrobenzene



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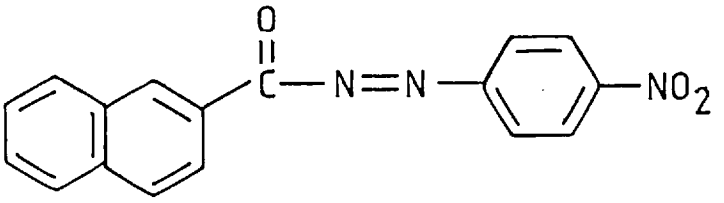
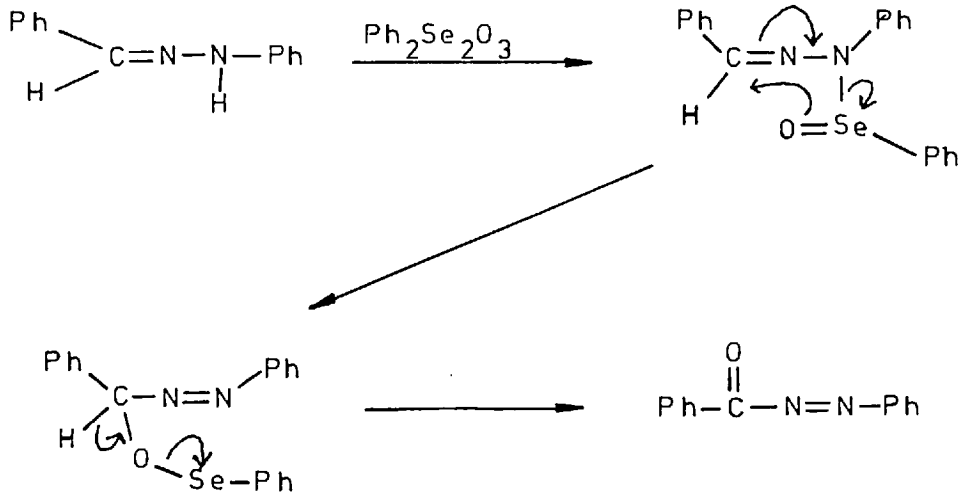
Naphthoyl azobenzene



21

Naphthoyl azo-p-nitrobenzene

The isolation of the carbonyl-azo derivative is further strong evidence in favour of the proposed mechanism in which the anhydride attacks at nitrogen followed by a 2,3-sigmatropic rearrangement (Scheme 6).



Scheme 6

Loss of benzeneselenol affords benzoyl azobenzene.

The regeneration reaction has been carried out in many dry solvents. The results are tabulated in Tables (7) and (8). All solvents examined were suitable for the reaction. THF is often the solvent of choice since the anhydride is most soluble in this solvent in the cold and leads to shorter reaction times.

A fair amount of work has been carried out on the mechanism of the reaction, but the exact course of the reaction is still far from certain. Benzeneseleninic acid is an oxidising agent and as such liberates iodine from potassium iodide. From the half equations:

$$Ph_2Se_2O_3 \xrightarrow{H_2O} 2PhSeO_2H$$

$$2PhSeO_2H + 6H^+ + 6e \longrightarrow Ph_2Se_2 + 4H_2O$$

$$2I^- \longrightarrow I_2 + 2e$$

$$I_2 + 2S_2O_3^{2-} \longrightarrow S_4O_6^{2-} + 2I^-$$

it can be seen that $1/3\ Ph_2Se_2O_3 \equiv 2Na_2S_2O_3$.

Benzeneseleninic anhydride may readily be titrated[14] against standard thiosulphate in the usual way after the addition of a little ethanol to the mixture to solublise the diphenyldiselenide formed. In the absence of ethanol, low titration figures result.

Titration of the oxidising power offers an excellent method for determining the rate of the reaction. Several identical reactions have been carried out and quenched after varying times. Since the anhydride is not readily soluble in the reaction solvent, care has to be taken to

powder the anhydride carefully. Variable reaction times have been attributed to the particle size of the anhydride used.

The reaction of the anhydride with benzophenone phenylhydrazone has been examined in the most detail, a plot of residual oxidising power against time is shown in Figure 1.

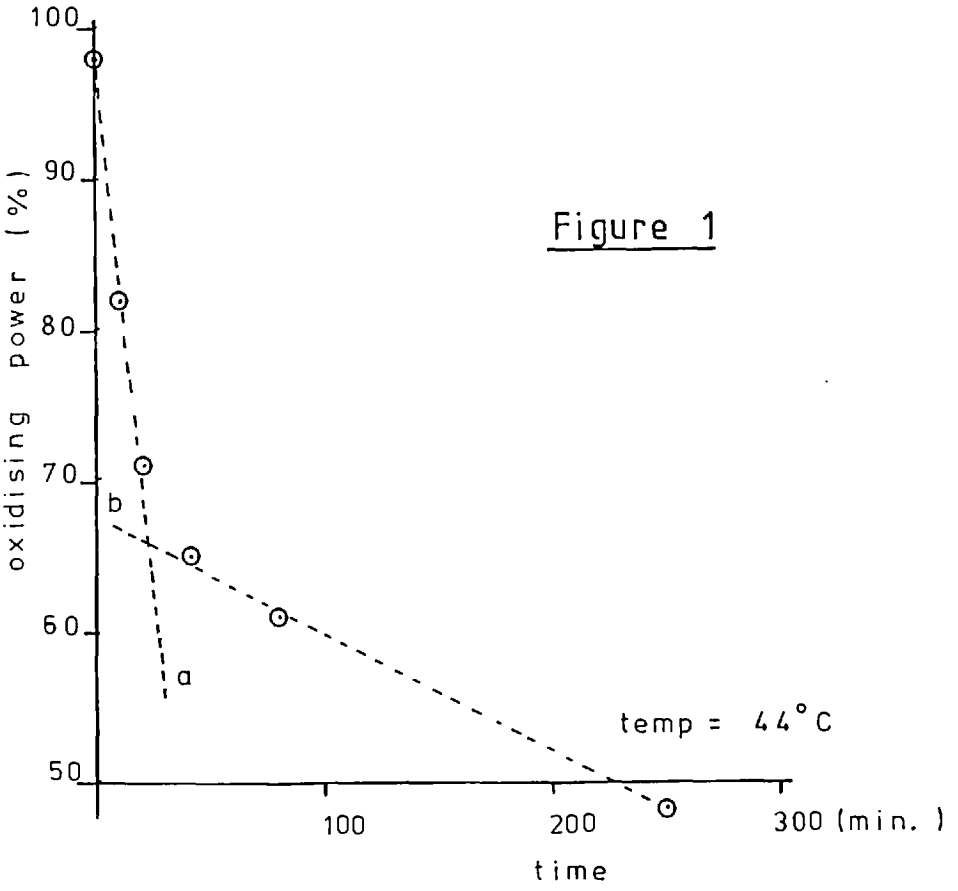
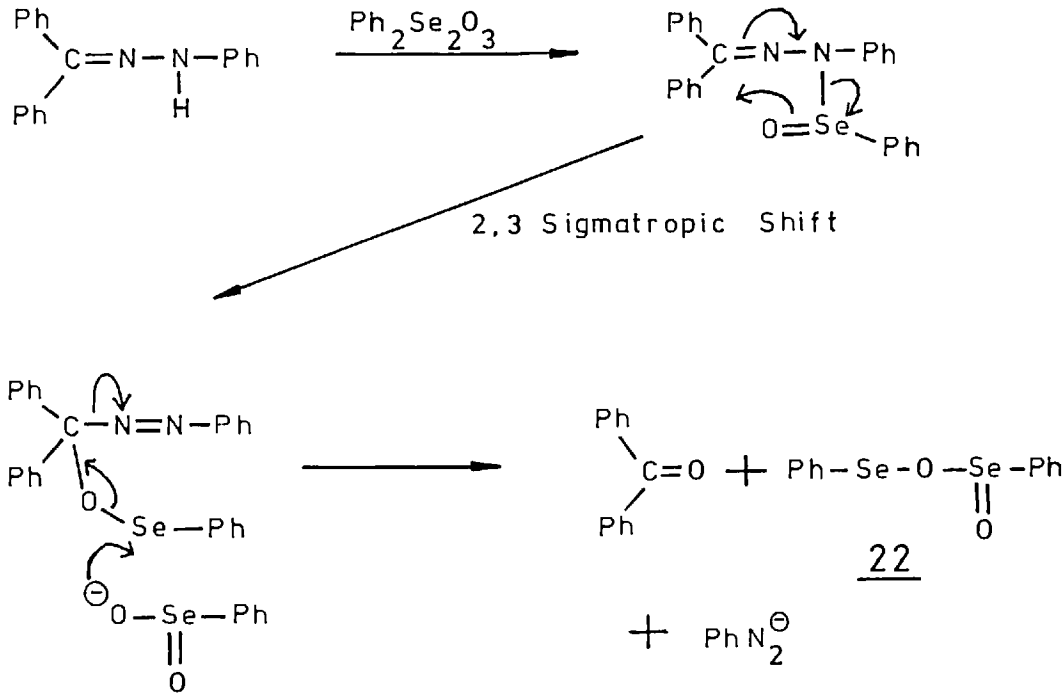


Figure 1

The graph shows an initial rapid fall in reaction rate followed by a slow tailing off to a final value of 50%. The shape of this graph is typical of many anhydride reactions and suggests a change in rate. Two almost straight lines (a, b) may be drawn through the point suggesting a change in mechanism.

For the mechanism proposed in Scheme 7,



Scheme 7

A partially reduced form of the anhydride (22) is generated, itself an oxidising agent. It is likely that it is reaction of this species that is observed during the latter half of the reaction time. The mechanism requires the oxidising power to fall only to 66%, not 50% (See Scheme 4). The 16% error is not accounted for by experimental error which is estimated at 5-8%. The figure is reproducible for many systems, suggesting that the figure is reliable. Furthermore, when the reaction is repeated with concurrent recovery of the diphenyl diselenide product, a perfect mass balance is obtained. For reaction of benzophenone phenylhydrazone (0.131 mmol) with benzeneseleninic anhydride (0.125 mmol), diphenyl diselenide (55%) was produced together with a residual oxidising power of 45%. All the experimental data are consistent with itself but is not fully accounted for by the mechanism.

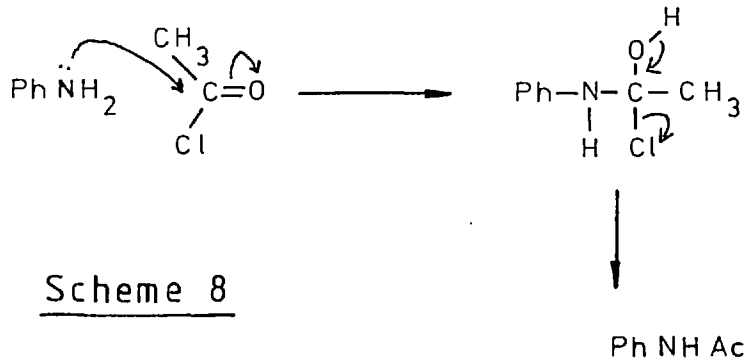
Reaction of excess benzophenone phenylhydrazone (5 molar equv.) with benzeneseleninic anhydride has shown that the anhydride is capable of reacting with exactly two equivalents of the hydrazone. The reaction was carried out in benzene using a method to account for all material. The benzophenone phenylhydrazone (5 eqv.) was treated with the anhydride (1 eqv.) for 18 h to ensure complete reaction. Base extraction extracted any residual benzeneseleninic acid. Titration showed there to be negligible (1.3%) oxidising power remaining. P.l.c. afforded diphenyl diselenide in quantitative yield, benzophenone (46%), and recovered starting material (54%). The results are consistent within experimental error with one equivalent of anhydride completely reacting with two equivalents of hydrazone. The results suggest that the mixed anhydride (22), if formed, is capable of further reacting with hydrazone to generate ketone. When benzophenone phenylhydrazone was treated with benzeneseleninic acid, little reaction was observed, further suggesting that if the acid was the product of the deprotection reaction, then further reaction to generate ketone would not be possible. Most evidence is in favour of the proposed mechanistic scheme (7) although it fails to completely account for the oxidising power of the reaction.

Much evidence has been collected favouring initial nitrogen attack. Benzophenone N,N-dimethylhydrazone has been prepared and shown to be completely inert to the anhydride under the usual reaction conditions. Further, O-methylbenzophenone oxime has been prepared by treatment of benzophenone oxime with sodium hydride and methyl iodide in glyme. The prepared compound exhibited a sharp resonance in the n.m.r. spectrum δ, 3.9 (3 H, s) and gave satisfactory analytical data. When treated with benzeneselninic anhydride under normal conditions, O-methyl-benzophenone oxime was found to be completely inert.

2,6-Dimethylphenylhydrazine was prepared by the improved method

of Carlin and Carlson[15]. Attempts to prepare 2,6-dimethyl-4-nitrophenyl hydrazine by conventional methods, however, failed. Benzophenone 2,6-dimethylphenylhydrazone was readily prepared and gave satisfactory spectral and analytical data. On treatment with the anhydride, the hydrazone afforded a high yield of benzophenone. This was not expected since the methyl groups were expected to cause sufficient steric hindrance to the nitrogen atom so as to block initial attack by the anhydride. A reaction rate determination was carried out by titrating the residual oxidising power during the course of the reaction, and compared with the rate of reaction of benzophenone phenylhydrazone under identical conditions. The half life for benzophenone phenylhydrazone was determined as 16 minutes and that for 2,6-dimethylphenylhydrazone was determined as 156 minutes thus the reaction of the more hindered compound is some ten times slower than benzophenone phenylhydrazone.

Acetylation of amines is known to occur <u>via</u> initial nitrogen attack (Scheme 8)

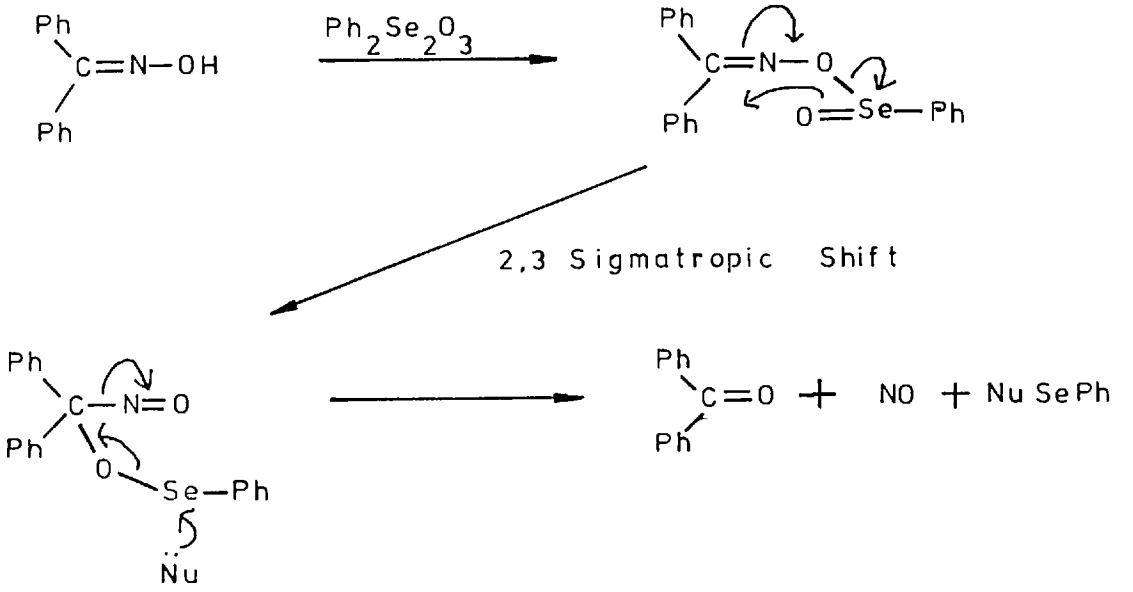


Scheme 8

A competitive rate study of acetylation of the two amines was readily carried out,using n.m.r. spectrometry,which showed that aniline reacted 4 times faster than 2,6-dimethylaniline. The relative reaction

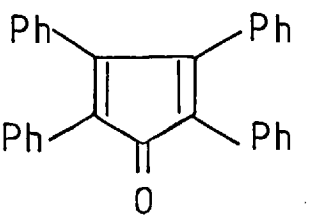
rate is of the same order as the relative rates of reaction of benzophenone phenylhydrazone and benzophenone 2,6-dimethylphenylhydrazone with benzeneseleninic anhydride, again evidence for initial attack by the anhydride on nitrogen.

In the case of oximes, if a similar reaction mechanism operates then the following intermediates may be proposed: Scheme 9.



Scheme 9

Attack by some nucleophile or even radical on intermediate (23) leads to the final product. Tetracyclone (24), an excellent trap for nitroso derivatives[16], on addition to the reaction mixture, failed to trap



24

any reaction intermediate such as (23).

Attempted conversion of benzophenone phenylhydrazone, benzophenone p-nitrophenylhydrazone, benzophenone tosylhydrazone, furfural semicarbazone, and benzophenone oxime to the corresponding carbonyl compound using benzeneseleninic acid at 50° for 3 h failed.

Finally, as aldehydes are most conveniently regenerated from their tosylhydrazone derivative without further oxidation to the acid it was of interest to compare both alkyl and aryl derivatives. Thus, a number of tosylhydrozones of aldehydes were treated with the anhydride and in all cases the yields of aldehyde were excellent, (Table 3). It is important, however, to rigorously exclude oxygen during the reaction so that no further oxidation to acid occurs.

TABLE 3

Tosylhydrazone	Yield of regenerated aldehyde (%)
iso-buteraldehyde	71
valeraldehyde	92
n-heptaldehyde	89
crotonaldehyde	68
cinnamaldehyde	91

SECTION 4

(a) DEHYDROGENATION OF STEROIDAL KETONES WITH BENZENESELENINIC ANHYDRIDE

The dehydrogenation reaction of steroidal ketones is an extremely important area of study, particularly in the drug industry. Methods for carrying out this dehydrogenation reaction include bromination/dehydrobromination[17], treatment with selenium dioxide[18], and with dichlorodicyanoquinone, D.D.Q.[18]. All of these methods have practical drawbacks and an improved method would certainly be useful. Precedence from other selenium chemistry suggested that benzeneseleninic anhydride would be a suitable reagent for this dehydrogenation.

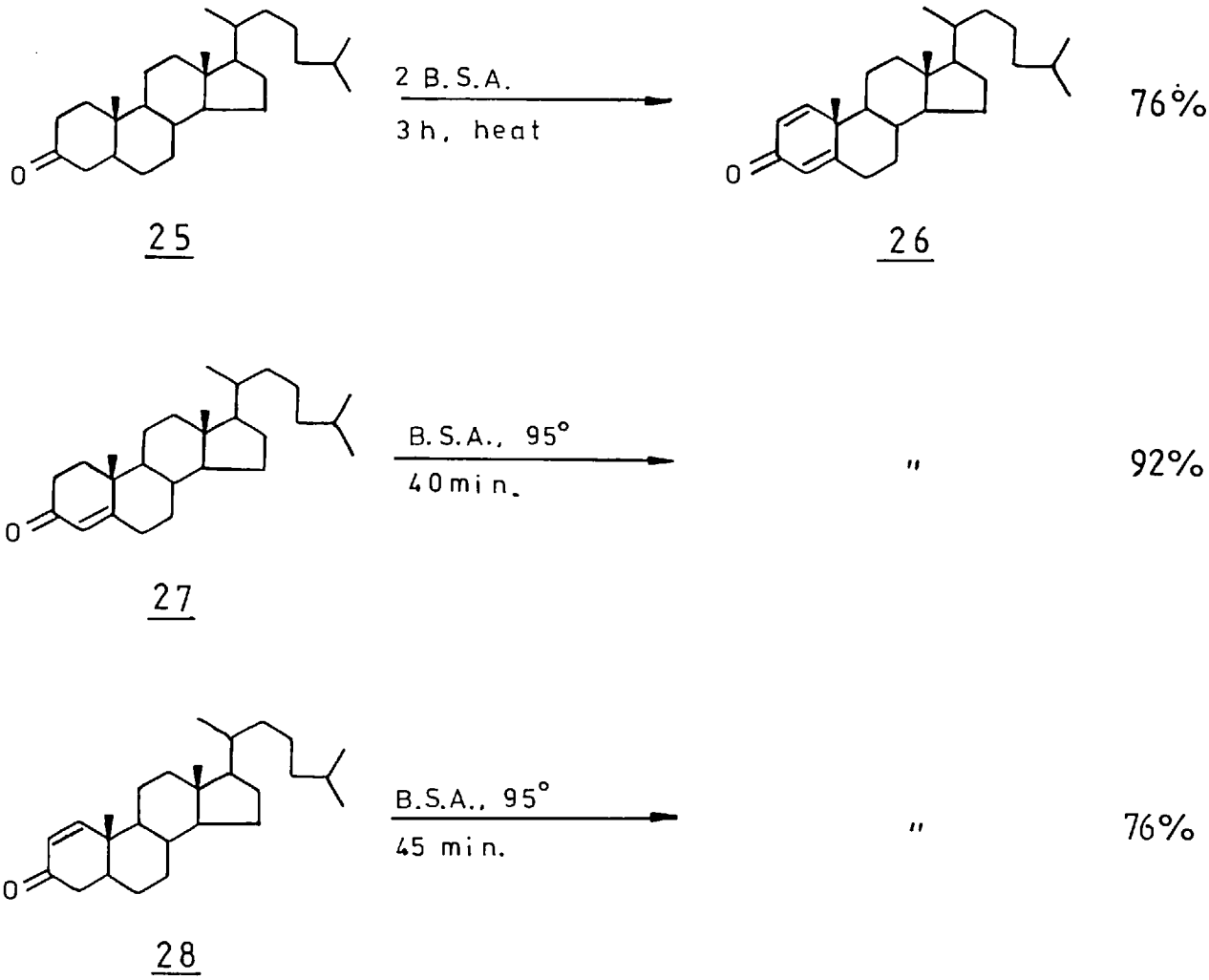
Thus, treatment of steroidal ring A or C ketones with benzeneseleninic anhydride in chlorobenzene at temperatures in excess of 95°C leads to the formation of the dehydro derivatives in good yield.[19] Diphenyl diselenide produced as a byproduct in the reaction is readily removed from the product by chromatography or recrystallization.

Cholestan-3-one (25) when treated with benzeneseleninic anhydride (2 eqv.) in chlorobenzene under reflux for 3 h afforded after chromatography cholesta-1,4-dien-3-one (26) in 76% yield. It was not possible to crystallise the product directly. For small scale work, chlorobenzene was readily removed after reaction by washing down a short silica column, followed by releasing the reaction products with methanol and subjecting them to p.l.c. If the quantity of anhydride was reduced to only one equivalent, then the yield of cholestadienone (26) was reduced to only 50%. Prolonged reaction times with excess anhydride did not afford cholesta-1,4,6-trien-3-one.

Treatment of cholestanone with limited anhydride did not afford the 1-enone cleanly. Mixtures of 1-enone, 4-enone and 1,4-dienone were produced which were impossible to separate without extremely careful chromatography. The reaction is best carried out with excess benzene-

seleninic anhydride to ensure a clean production of cholesta-1,4-dien-3-one.

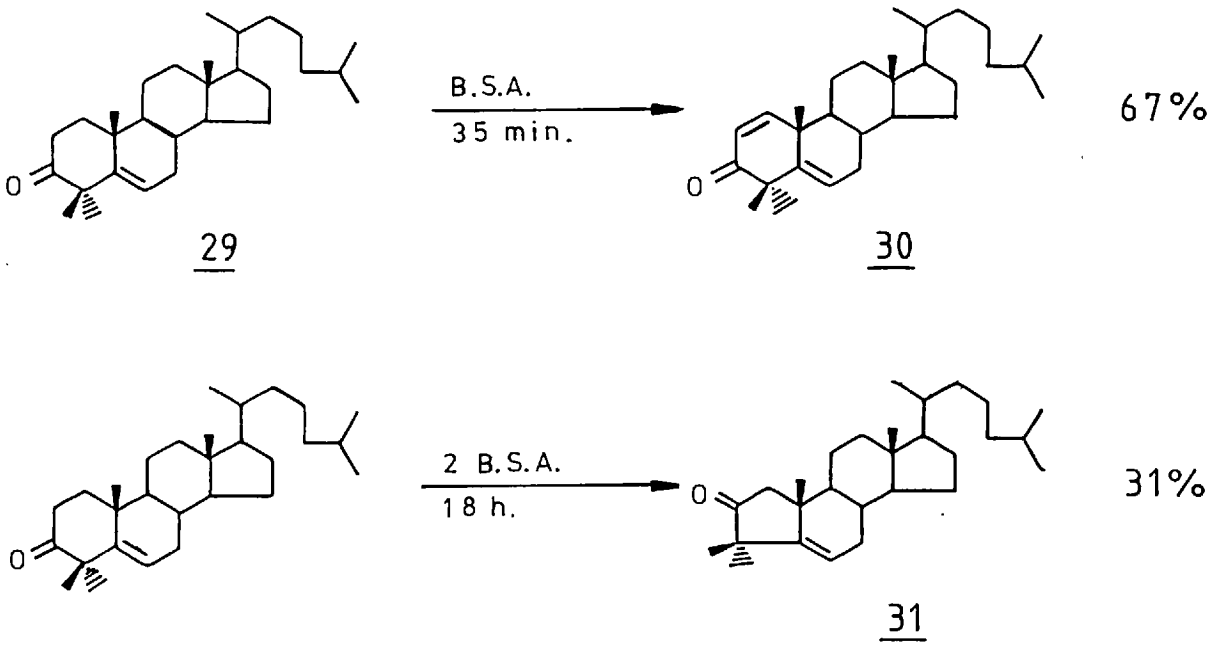
Treatment of cholest-4-en-3-one (27) and cholest-1-en-3-one (28) both afforded cholestdienone (26) in excellent yield on treatment with the anhydride (Scheme 10).



Scheme 10

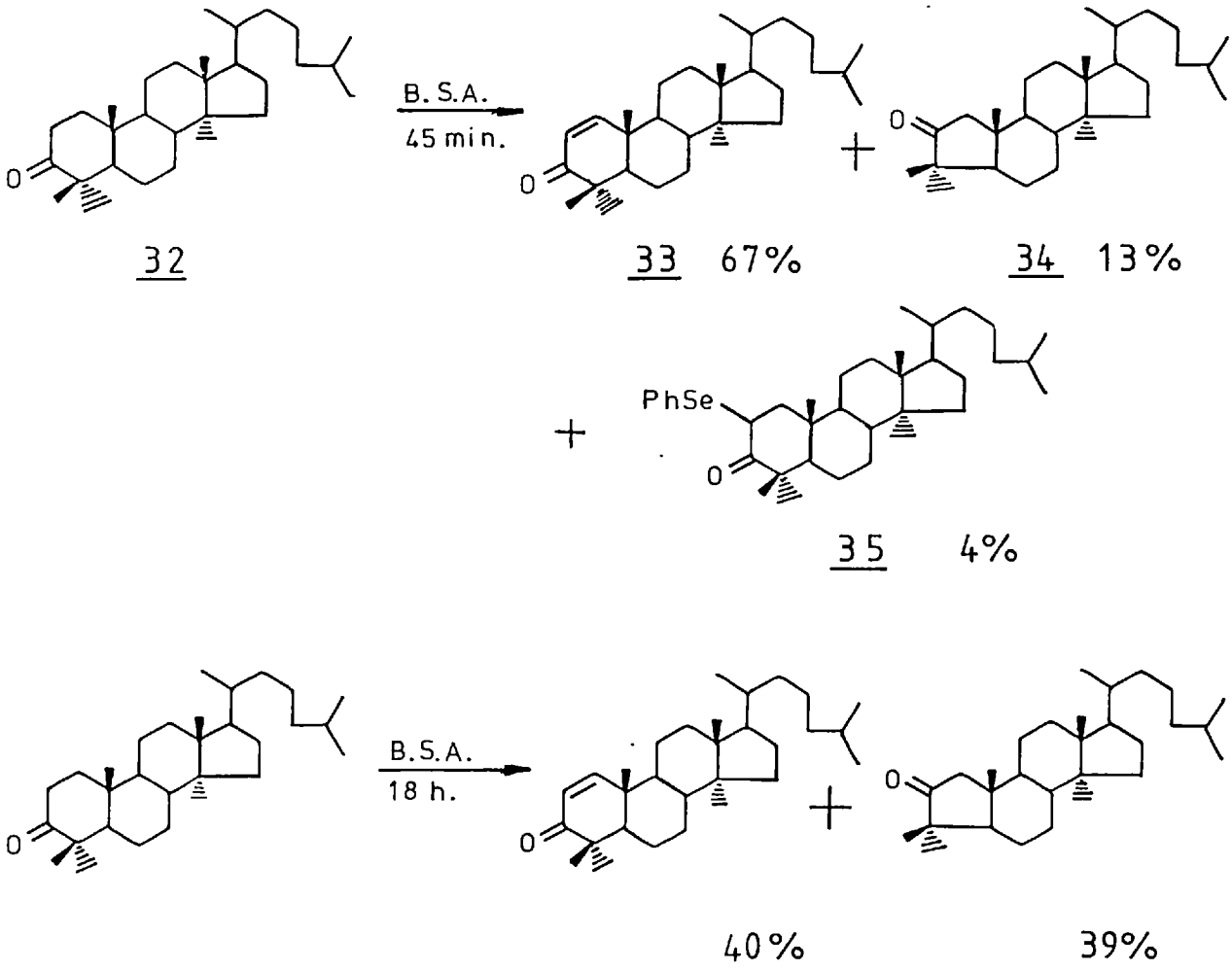
4,4-Dimethylcholest-5-en-3-one (29) afforded the 1-enone (30) in 67% yield together with a small quantity (ca. 10%) of a non u.v. active compound. If the reaction was repeated with excess anhydride

(2 eqv.) with an extended reaction time (18 h) then the yield of this compound was increased to 28%. The compound exhibited a high carbonyl stretching frequency at 1745 cm^{-1} characteristic of a 5-ring ketone, the n.m.r. spectrum showed the olefinic proton δ, 5.6 (1H, m)to be still present. The compound was characterised as the A-nor compound (31) and found to be identical to A-nor-4,4-dimethylcholest-5-en-3-one described in the literature[20] (Scheme 11).



Scheme 11

Lanostanone (32) when similarly treated with 1 eqv. anhydride afforded lanost-1-en-3-one (33) (67%) and the A-nor compound (34) characterised by its high carbonyl absorption in the infrared and also a very high rotation $|\alpha|_D^{22}$ + 206°. The compound gave satisfactory spectral and analytical data (Scheme 12).



32

33 67%

34 13%

35 4%

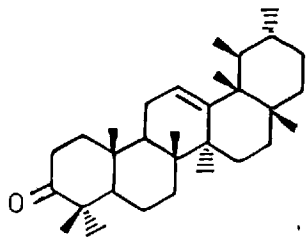
40%

39%

Scheme 12

A further u.v. active compound was isolated in low (4%) yield and shown to be identical to 2-phenylselenolanostanone prepared by treatment of the enolate of lanostanone with phenylselenenyl chloride.

α-Amyrone (36) and β-amyrone (37) both reacted smoothly with the anhydride to afford the 1-enones and A-nor compounds in a similar way. The anhydride was completely without effect on the 12 double bond in contrast to selenium dioxide which oxidises to the ketone at position 11. All compounds compared well with literature samples.



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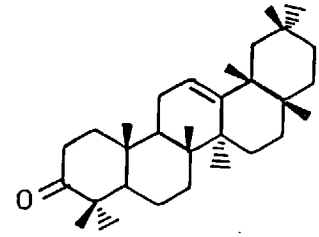

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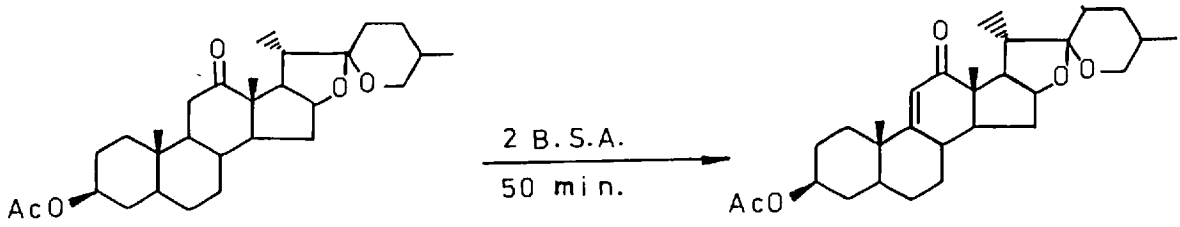
Ketones in ring C similarly react smoothly with benzeneseleninic anhydride. Thus, treatment of hecogenin acetate (38) with 2 equivalents of the anhydride afforded the 9(11)dehydro (39) compound in 91% yield. To prevent contamination of the enone (39) with starting material, it was found necessary to use excess anhydride and to carefully follow the reaction by I.R. spectroscopy. The dehydrocompound compared well with literature compounds.

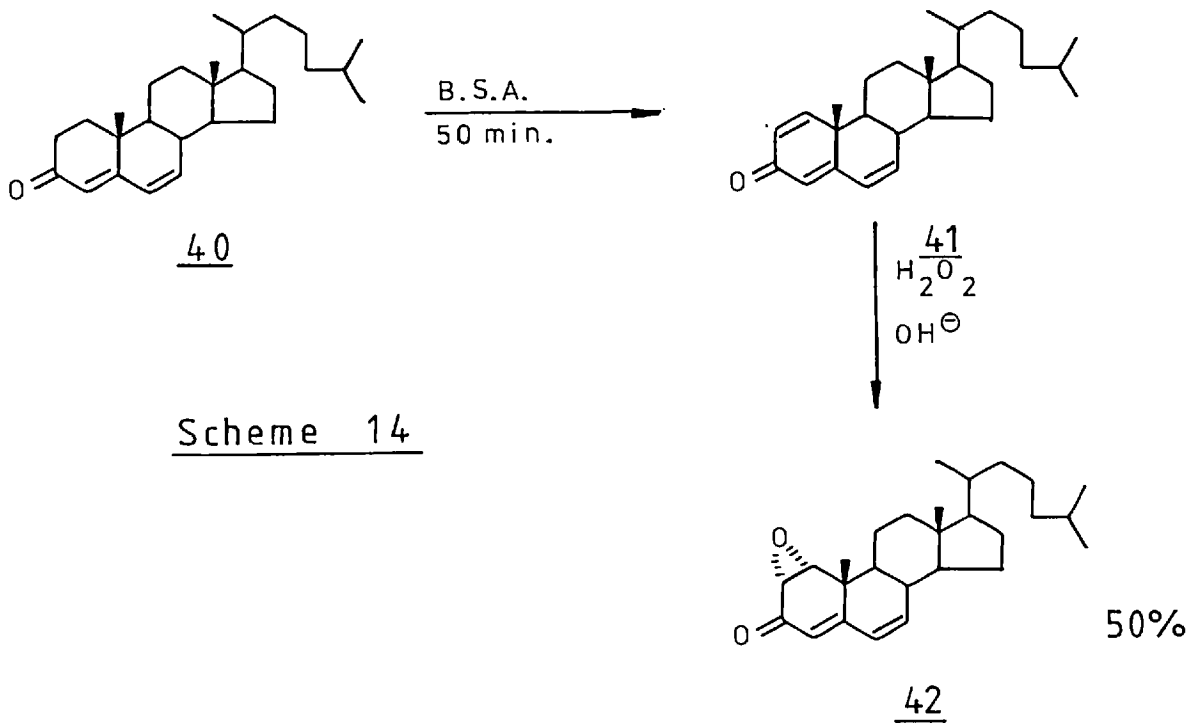


38 39

Scheme 13

Cholesta-1,4,6-trien-3-one (41) is an important intermediate for the synthesis of 1,α-hydroxycholesterol[21]. However, it was not possible to dehydrogenate cholestan-3-one directly to the trienone. Cholesta-4,6-dien-3-one (40) can be readily prepared from cholesterol by the

method of Nickon and Bagli[22] which on treatment with the anhydride does give the trienone (41) in high yield. The reaction has been used on a larger scale (up to 10 g) for the preparation of 1α,2α-epoxycholesta-4,6-dien-3-one (42) in an overall 50% yield (Scheme 14).

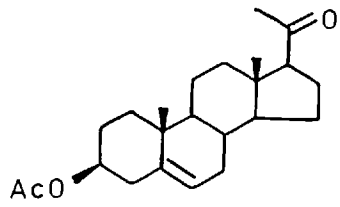


40 42

Scheme 14

Pregnenolone acetate (43) when treated with the anhydride fails to afford any 17-dehydro compound or any other characterisable product. Hydrogenation afforded prenenolone acetate (44), which also produced products with the anhydride. Progesterone (45) and andosterone acetate (46) all gave complex mixtures of products when treated with the anhydride, therefore, it is not suitable for dehydrogenation of 5-membered rings.

A summary of some failed reactions is given in Table 9.



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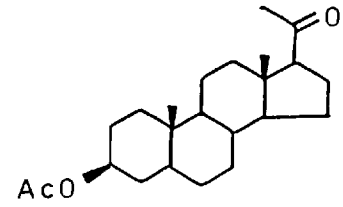

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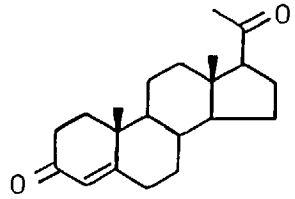

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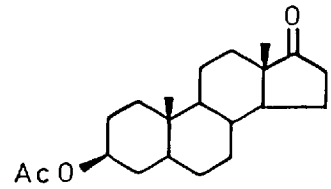

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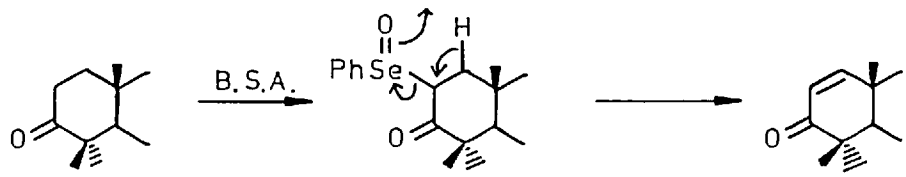
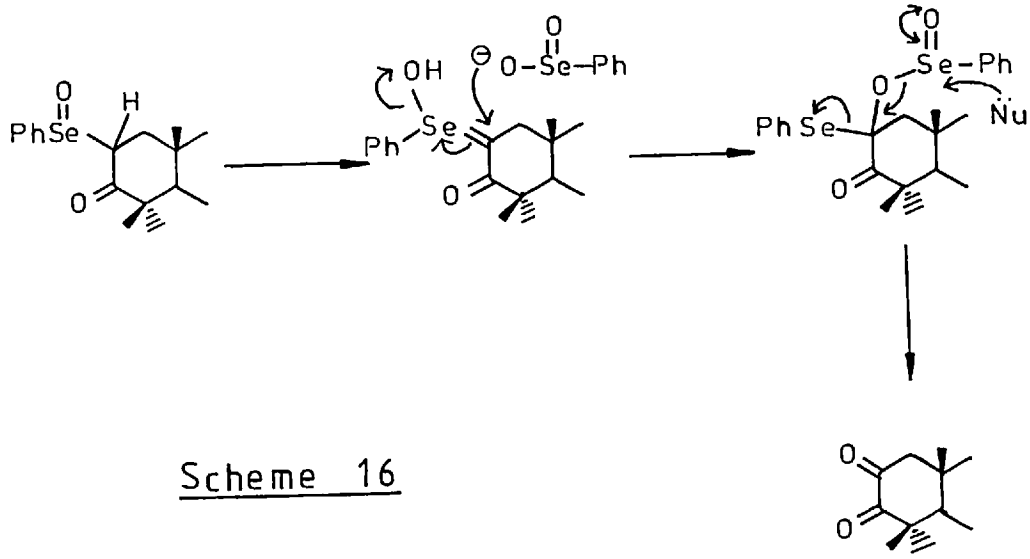
The mechanism of the dehydrogenation reaction is believed to go via a 2-phenylselenoxy intermediate[23]. Attack of the anhydride at carbon affords the 2-phenylselenoxy intermediate (48) which rapidly syn eliminates to afford the enone (Scheme 15).



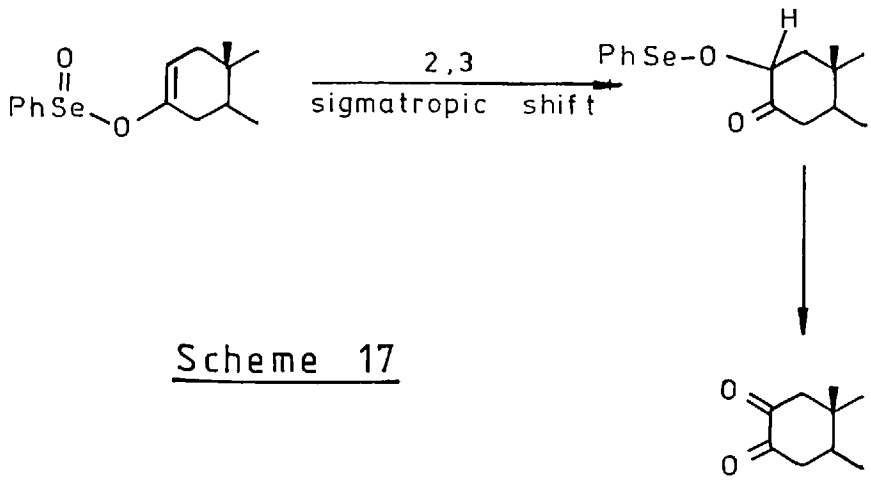
Scheme 15

Alternatively, the 2-phenylselenoxy species may undergo a Pummerer type reaction to give the 2,3-dione which further reacts to afford the 5-ring ketone via a benzilic acid type rearrangement (Scheme 16).



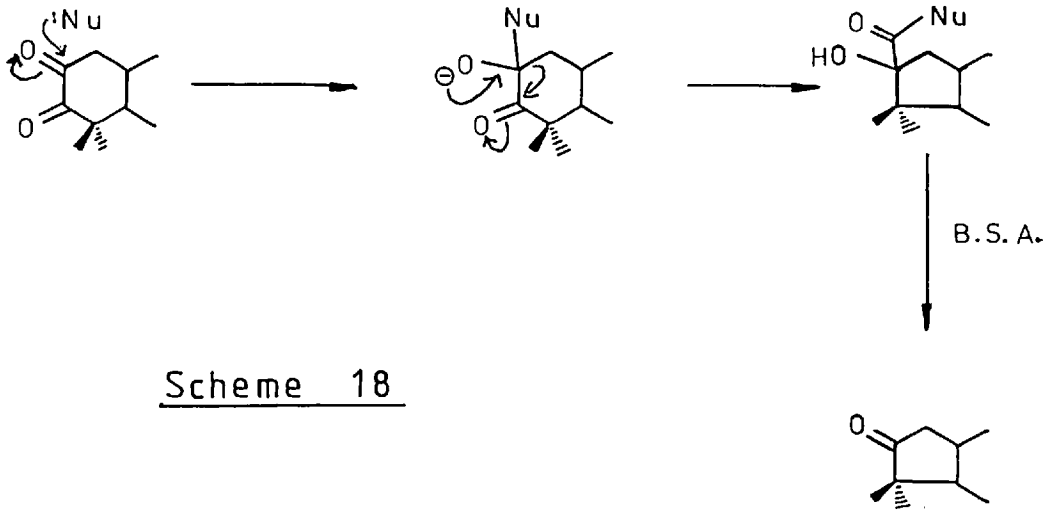
Scheme 16

It is possible that the 2,3-dione is arising by initial attack of the anhydride on the oxygen atom of the enolate. A 2,3-sigmatropic shift followed by loss of benzeneselenenic acid affords the 2,3-diketone (Scheme 17). This route is less likely since selenium, being a soft-centre, would prefer attack at the softer carbon centre to the harder oxygen centre.



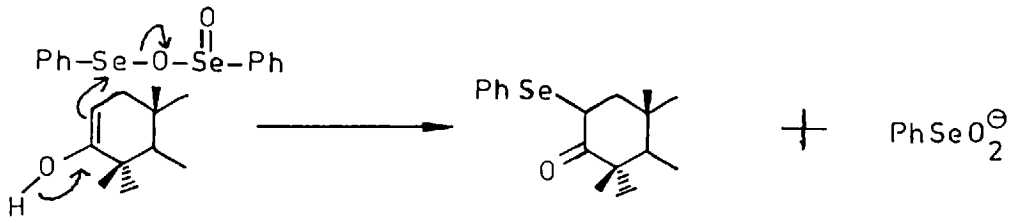
Scheme 17

Reaction of the 2,3-diketone with some nucleophile, typically the benzeneseleninate anion affords the A-nor compound. The proposal is supported by the fact that on treatment of benzilic acid with the anhydride under reflux in chlorobenzene, benzophenone may be isolated in 95% yield (Scheme 18).



Scheme 18

The appearance of 2-phenylselenated material suggests the presence of some phenylselenating species, possibly Ph-Se-O-Se(O)Ph generated by partial reduction of the anhydride (Scheme 19).



Scheme 19

If benzeneseleninic acid is used for the dehydrogenation reaction, then the dehydrocompounds and A-nor compounds are obtained in virtually identical yields to when the anhydride itself is employed. Under the conditions of the reaction it is conceivable that the acid is firstly converted into the anhydride.

$$2PhSeO_2H \longrightarrow Ph_2Se_2O_3 + H_2O$$

At low temperatures, benzeneseleninic acid exists essentially as the free acid, but on heating dehydration takes place with a resulting increased concentration of anhydride.

(b) REGENERATION OF BENZENESELENINIC ANHYDRIDE IN SITU: Catalytic Reactions

Benzeneseleninic anhydride is a relatively expensive reagent, however, after reaction, all the diphenyl diselenide produced may be re-oxidised to benzeneseleninic acid and recycled. The possibility of using diphenyl diselenide catalytically was examined. In theory, it is possible to use a cheap oxidant to which both reactants and product are stable, but which readily converts diphenyldiselenide to the anhydride.

N-Oxides have been examined but found of little value to this aim.

Benzoyl peroxide has been used successfully to convert diphenyl diselenide into benzeneseleninic acid. Treatment of diphenyl diselenide with benzoyl peroxide under reflux in dichloromethane gives benzeneseleninic acid after isolation in almost quantitative yield.

Unfortunately, the short half life of benzoyl peroxide at elevated (130°C) temperatures does not allow the oxidant to be used for dehydrogenation of steroids.

Diphenyldiselenide, after reaction with benzoylperoxide under reflux in chloroform afforded, on further reaction with 2-naphthol, both 1-phenylseleno-2-naphthol and 1,2-naphthoquinone in 34% and 22% yield respectively. The results compare favourably with reports of reactions of benzeneseleninic anhydride with 2-naphthol from which 1-phenylseleno-2-naphthol and 1,2-naphthoquinone have been isolated in 28% and 35% yields respectively[24]. Since the diselenide is consumed during the course of the reaction, it was not possible to use diphenyl diselenide in less than a molar quantity.

In a search for a more stable peroxide, t-butyl peroxide was examined. At 130° overnight, the diphenyldiselenide appeared unchanged. t-Butyl hydroperoxide has been used in the literature for the preparation of many seleninic anhydrides. It proved to be a useful reagent for the catalytic dehydrogenation of model ketones. Cholestanone, when treated with excess t-butylhydroperoxide and diphenyldiselenide (1/5 equivalent) at 95°C, afforded both cholest-1-en-3-one (43%) and an impure sample of cholesta-1,4-dien-3-one (28%). Although the reactants and products were stable in control reactions, the reaction mixture darkened considerably in colour. Lanostanone, when similarly treated, afforded lanost-1-en-3-one (69%) slightly contaminated with starting material although, in this case, the reaction mixture was much cleaner.

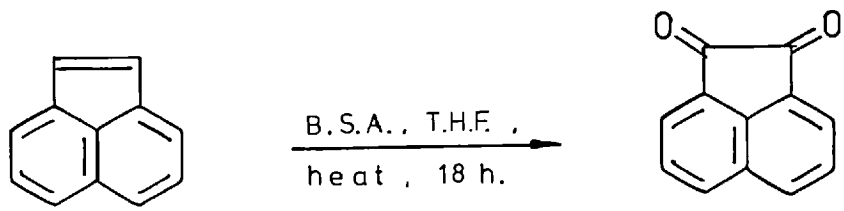
The reaction offers the prospects of an excellent industrial process. t-Butylhydroperoxide has shown much promise. A better oxidant will undoubtedly solve the problem and afford dehydrosteroids in excellent yields.

SECTION 5

CARBON-HYDROGEN AND ALCOHOL OXIDATIONS USING BENZENESELENINIC ANHYDRIDE

The reactions of benzeneseleninic anhydride often closely resemble those of selenium dioxide. For this reason, we have also studied hydrocarbon oxidations using the anhydride.

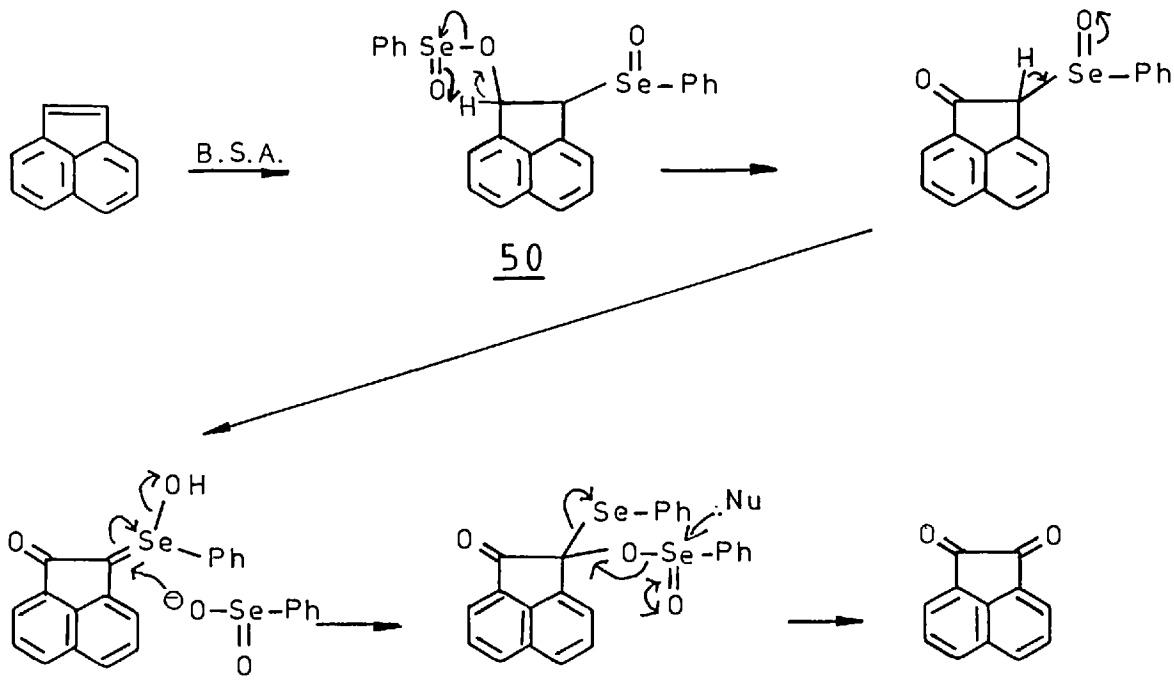
On treatment of anthracene, a fairly reactive hydrocarbon, with the anhydride under reflux in T.H.F. for several days, the anthracene could be recovered virtually unchanged. However, acenaphthalene (48) with the anhydride under reflux in T.H.F. for 18 h, an excellent yield (90%) of acenaphthaquinone (49) was obtained (Scheme 20)



48 49

Scheme 20

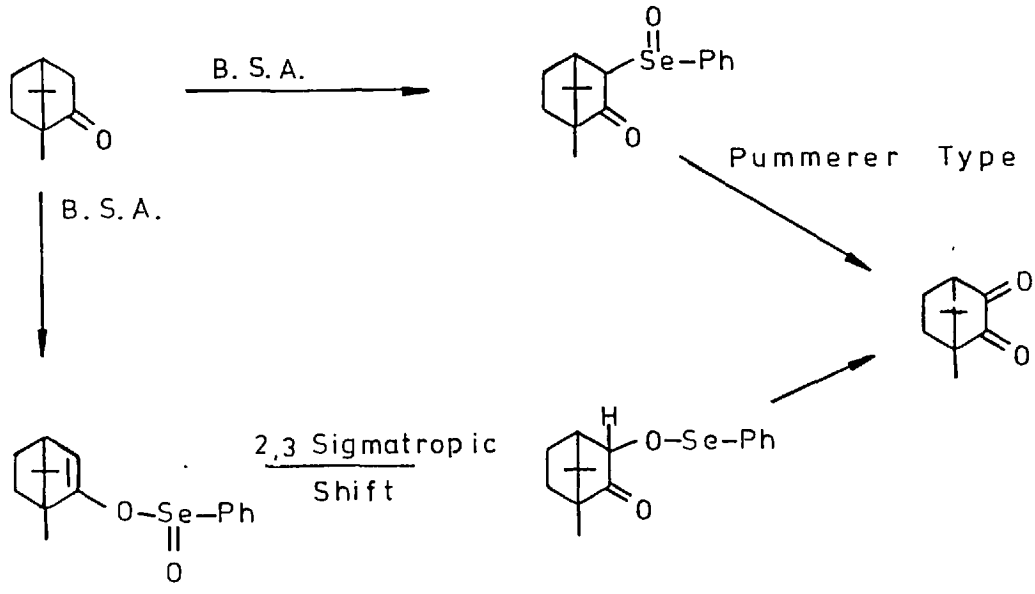
The reaction is believed to be occurring by addition of the anhydride accross the activated double bond to afford the di-selenoxy intermediate (50). A Pummerer type rearrangement leads to the formation of acenaphthaquinone (49), (Scheme 21). Additions of selenium reagents to double bonds have been examined by Reich[25] who postulates benzeneselenenic acid as the species reacting directly with the double bond.



Scheme 21

Anthracene, although unreactive towards the anhydride at reflux in T.H.F, at higher temperatures in chlorobenzene, affords anthraquinone in good (81%) yield. The reaction is easily carried out since the product may be readily crystallised from the reaction mixture on cooling. trans-Stilbene affords (96%) benzil on treatment with the anhydride under equivalent conditions.

Camphor affords camphorquinone in good (74%) yield when treated with the anhydride under reflux in chlorobenzene. Two reaction mechanisms are possible, either initial attack on oxygen or carbon, as shown in Scheme 22.



Scheme 22

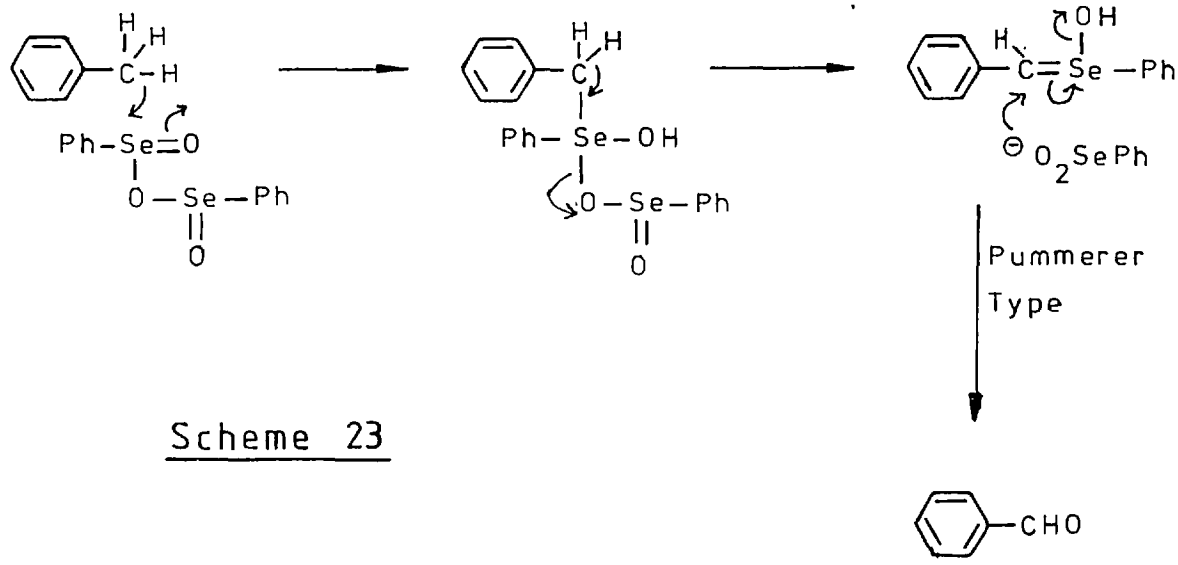
Attempts to use toluene as reaction solvent always failed, the anhydride being quickly converted into diphenyl diselenide with no apparent reaction on the substrate. Closer examination showed that, in fact, the toluene was being converted into benzaldehyde in high yield.

o-Xylene could be converted into the di-aldehyde by treatment with 2 equivalents of the anhydride. When carried out in the minimum quantity of chlorobenzene, reaction took 10 h. The use of excess solvent reduced the rate of reaction to almost nil. The aldehyde was best isolated and characterised as its 2,4-dinitrophenylhydrazone to minimise any atmospheric oxidation. Similarly, m- and p-xylenes were converted into their dialdehydes.

A comparative rate study by g.l.c. on the relative rates of reaction of toluene, p-nitrotoluene and p-methoxytoluene showed that

p-nitrotoluene was virtually inert to the anhydride while p-methoxytoluene reacted about three times faster than toluene itself. Equimolar mixtures of toluene and either p-nitrotoluene or p-methoxytoluene were prepared and treated with limited ($\frac{1}{2}$ equivalent) benzeneseleninic anhydride. G.l.c. analysis gave the ratio of products hence a quick estimate of the relative rates of reaction.

Initial attack of the anhydride is believed to occur at the polarised C-H bond. Loss of the elements of benzeneseleninic acid affords a typical Pummerer type intermediate, which may react with a nucleophile (in this case the phenylseleninate anion) to afford the aldehyde.



Scheme 23

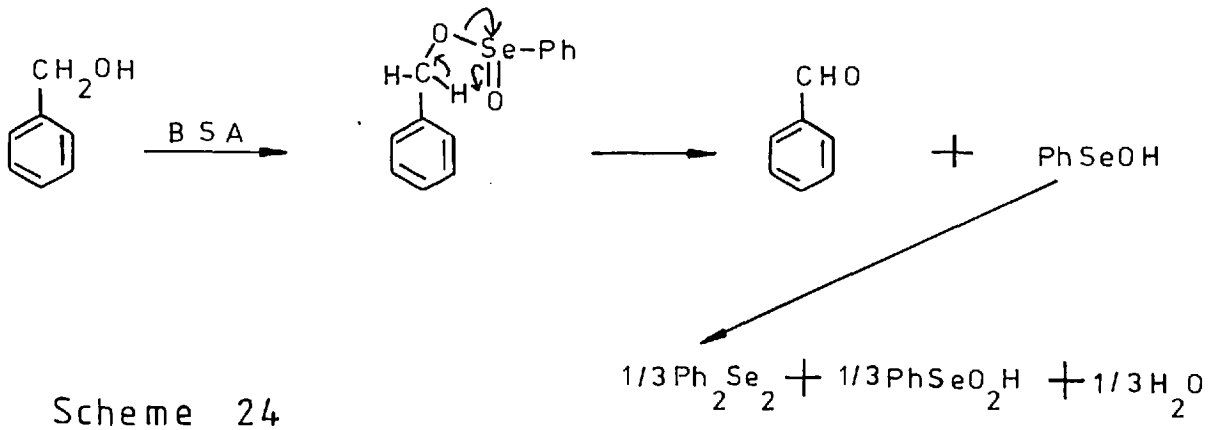
The reaction of aromatic methyl groups with the anhydride appears to be fairly general. 2-Quinaldine has been successfully converted into quinaldehyde. The aldehyde was isolated as both its 2,4-dinitrophenylhydrazone and the free aldehyde. The yield of free aldehyde was some 15% less than that of the 2,4-dinitrophenylhydrazone. This is attributed to the difficulty of isolating aldehydes, particularly on a small scale. Atmospheric oxidation to the acid often occurs with a resulting diminishing yield. 2-Picoline has been converted into pyridine 2-aldehyde in 41% isolated yield.

Aromatic alcohols also react smoothly with the anhydride at room temperature. Benzyl alcohol on treatment with the anhydride affords benzaldehyde in poor yield. The poor yield has been attributed to the difficulty of completely excluding oxygen on a small scale for the prolonged 26 h reaction time necessary to observe complete reaction of all starting material. If the reaction is carried out under reflux, then the reaction time is reduced to only 10 minutes and the aldehyde may be isolated as its 2,4-dinitrophenylhydrazone in quantitative yield. The aldehyde produced is completely stable to the anhydride. Prolonged reflux (3h) in benzene with excess anhydride still afforded the aldehyde in quantitative yield. No benzoic acid could be isolated from the reaction. Benzyl alcohol requires only 1/3 molar equivalent of the anhydride for complete reaction under reflux in benzene. All the selenium may be recovered as diphenyl diselenide.

Allylic alcohols (e.g. cinnamyl alcohol) failed to react with the anhydride at room temperature and even on reflux in benzene. However, on reflux in chlorobenzene, cinnamayl alcohol was smoothly converted into cinnamaldehyde (10 h) which was isolated in 53% as its 2,4-dinitrophenylhydrazone.

Lanostanol has been treated with benzeneseleninic anhydride (1 equivalent) at 95° in chlorobenzene. Lanost-1-enone was obtained in 73% yield. The reaction is believed to be occurring *via* initial oxidation to the ketone. The scope of the reaction is thus increased offering a single step reaction for the conversion of steroidal alcohols to enones.

The reaction mechanism for the oxidation of alcohols is believed to go *via* initial attack at oxygen, followed by *syn* elimination of the α-proton to afford the aldehyde.



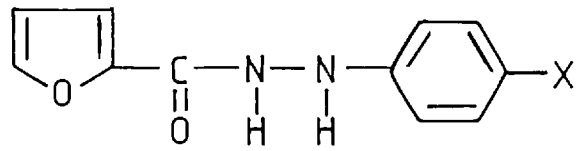
Scheme 24

SECTION 6

NITROGEN-HYDROGEN OXIDATION REACTIONS USING BENZENESELENINIC ANHYDRIDE

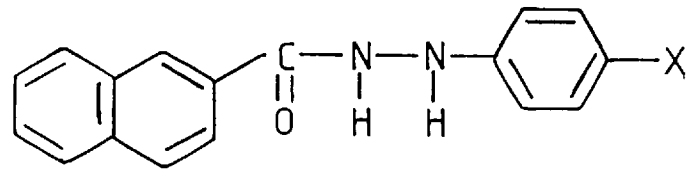
The versatility of benzeneseleninic anhydride as an oxidising agent has been further extended by the study of oxidation of N-H containing compounds and other related species.

Hydrazocompounds for example may conveniently be prepared by reaction of an acid chloride with a hydrazine in the presence of pyridine. Thus, 2-furanoyl chloride, prepared by treatment of 2-furanoic acid with excess (3 eqv.) thionyl chloride in the presence of aluminium chloride reacted smoothly with phenylhydrazine and p-nitrophenyl-hydrazine to afford furanoyl hydrazobenzene (51) and furanoyl hydrazo-p-nitrobenzene (52) respectively. Naphthoyl chloride similarly afforded naphthoyl hydrazobenzene (53) and naphthoyl hydrazo-p-nitrobenzene (54). All new compounds gave satisfactory spectral and microanalytical data.



51, X = H

52, X = NO_2



53, X = H

54, X = NO_2

The hydrazo compounds afforded the azo compounds in good yield when treated with the anhydride (1 eqv.) for 5-10 minutes at room temperature. Although theoretically only 1/3 equivalent of the anhydride is required, much better yields of the azo compounds were obtained if a complete equivalent of anhydride was employed. The reaction generally offered slightly better yields than the reaction of the anhydride with an aldehydic hydrazone[13], or by oxidation of the hydrazo compound with N-bromosuccinimide (see earlier). A summary of the yields is given in Table 4.

TABLE 4

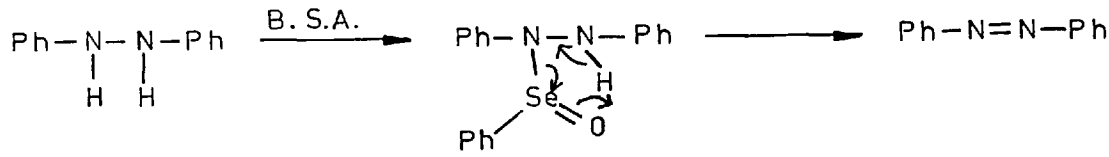
Compound	BSA(%)	NBS(%)	from hydrazone
Furanoyl hydrazobenzene	92	65	87(82)
Furanoyl hydrazo-p-nitro-benzene	95(86)	78(64)	70(64)
Naphthoyl hydrazobenzene	72	47	70(49)
Naphthoyl hydrazo-p-nitro-benzene	89(80)	70(57)	90(89)
Benzoyl hydrazobenzene	85	80	73(67)
Benzoyl hydrazo-p-nitro-benzene	99	79	76(72)

In view of the availability of hydrazones over hydrazocompounds, preparation of the azo-compounds from hydrazones is, however, preferred.

Hydrazobenzene, reacted smoothly with the anhydride at room temperature to afford azobenzene in excellent (94%) yield. Phenyl hydroxylamine afforded nitrosobenzene on reaction with the anhydride in 91% yield. Further oxidation to nitrobenzene was not observed.

All the prepared compounds compared well with authentic samples.

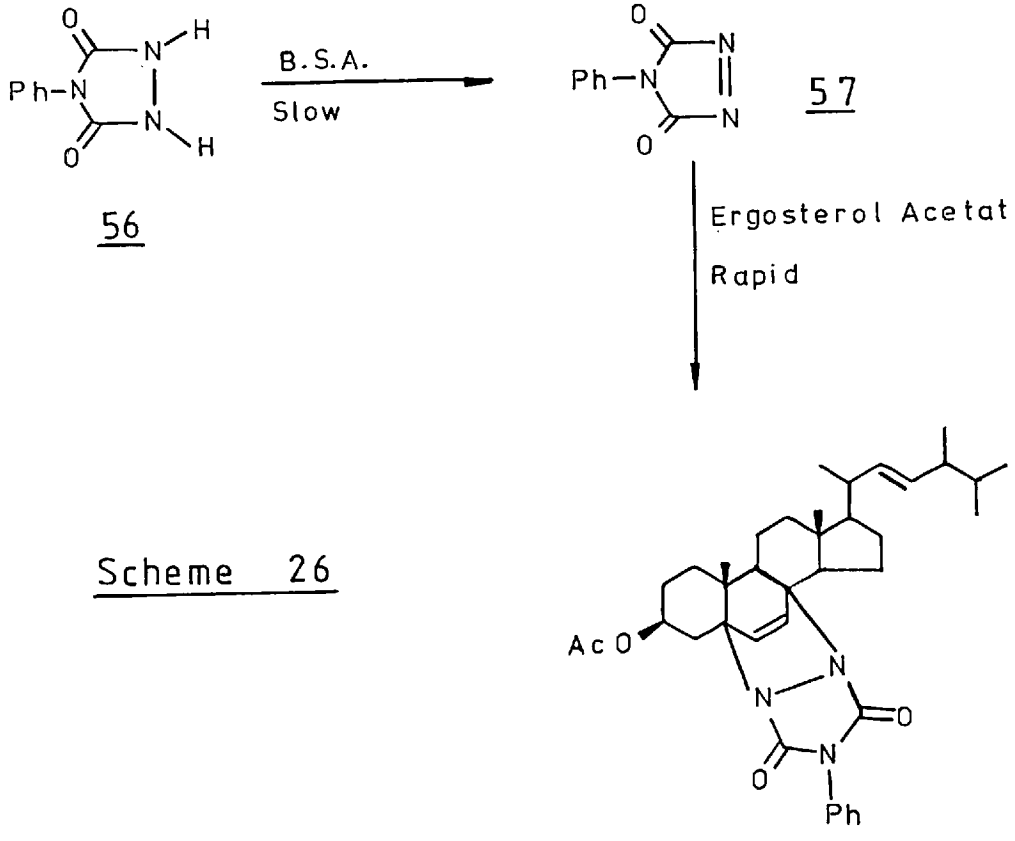
The mechanism of the reaction is believed to follow a simple elimination pathway (Scheme 25).



Scheme 25

t-Butyl hydroxylamine, as an aliphatic example, reacts almost instantaneously to afford the blue nitroso compound. The compound was so volatile that all attempts to isolate the pure monomer failed. Distillation of the solution always resulted in co-distillation of t-butylhydroxylamine. The yield of nitroso-t-butane was thus estimated from a careful measurement of the u.v. extinction coefficient and comparison with literature values[26]. The absorption of the diphenyl-diselenide was observed not to interfer with the determination.

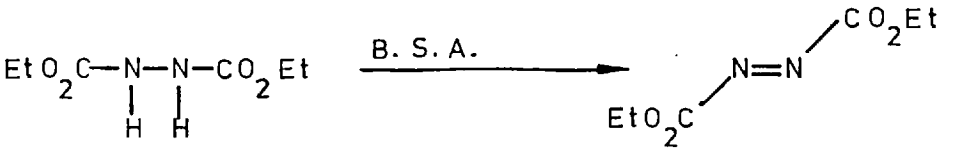
4-Phenyl-1,2,4-triazoline-3,5-dione (55)has been used for protection of the diene of ergosterol acetate. Benzeneseleninic anhydride offers a convenient method for the oxidation of 4-phenyl-1,2,4-triazolidine-3,5-dione (56) to 4-phenyl-1,2,4-triazoline-3,5-dione and reaction with ergosterol acetate in situ. The method avoids a somewhat difficult, if not even dangerous isolation of 4-phenyl-1,2,4-triazoline-3,5-dione by sublimation. The reaction takes place smoothly in T.H.F. at room temperature, taking some 3-4 minutes to reach completion. By employing a slight excess of the reagent, the reaction is self indicating, the reaction mixture aquiring a deep red colour after complete reaction. It is necessary to work up the reaction mixture soon after the reaction is complete, since the product is not stable to any excess anhydride over long (2-3 h) periods of time (Scheme 26).



56 57

Scheme 26

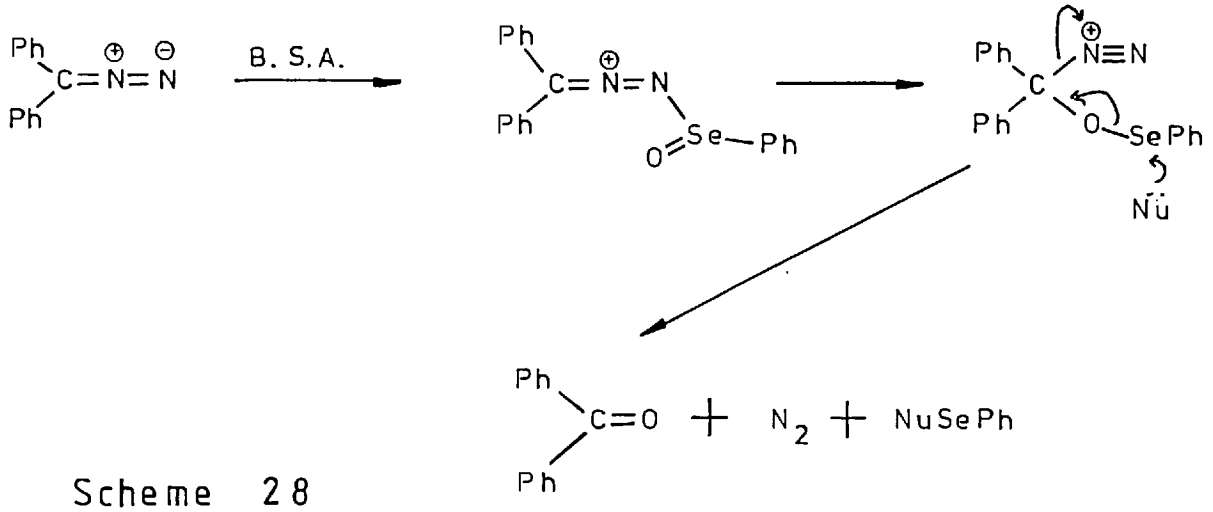
N,N'-Dicarbethoxyhydrazine (57) affords N,N'-dicarbethoxyazide (58) on reaction with the anhydride under reflux in benzene for 5 minutes. The reaction does not take place at room temperature, presumably due to the increased stability caused by the carbethoxy groups. Surprisingly, when 2,3-dimethylbuta-1,4-diene or anthracene were added to the reaction mixture, then no adduct was formed. This has been attributed to the formation of the hydrazide in a trans configuration, which is much less reactive to dienes than its cis isomer. N,N'-dicarbethoxyazide is obtained as a pale yellow liquid, double distillation was required to completely free the compound of diphenyldiselenide (Scheme 27).



57 58

Scheme 27

Diphenyldiazomethane is conveniently prepared by treating benzophenone hydrazone with mercuric oxide. Diphenyldiazomethane is obtained in excellent yield as a deep purple, low melting solid. Reaction of diphenyldiazomethane with benzeneseleninic anhydride proceeds smoothly at room temperature, the purple colour slowly being discharged over a period of 50 minutes to afford benzophenone in high yield. The mechanism is believed to follow a similar pathway as observed in previous reactions, outlined in Scheme 28.

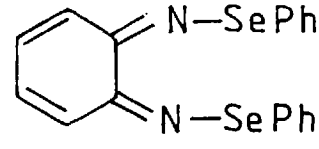


Scheme 28

Enamines do not react cleanly with benzeneseleninic anhydride. The reaction of cyclohexanone morpholine enamine with the anhydride at room temperature is very rapid affording many polar decomposition products on t.l.c. Carrying out the reaction at $0^{\circ}C$ results in a much

cleaner reaction. P.l.c. afforded 2-selenophenylcyclohexanone as the major product (38%). The compound had a carbonyl absorption frequency of 1700 cm^{-1}, consistent with a substituted 6-ring ketone, had only aromatic signals δ, 7.8-7.2 (5H, m) and aliphatic signals δ, 3.9 (H, m, α hydrogen), and δ 2.4-2.8 (8H, m) in the n.m.r. spectrum, exhibited a molecular ion at 224 and gave analytical data all consistent with the proposed structure. The reaction is of little synthetic value, since α-selenoketones are best prepared by the method of Sharpless by treatment of the enolate prepared from lithium diisopropylamine with phenylselenenyl chloride[26].

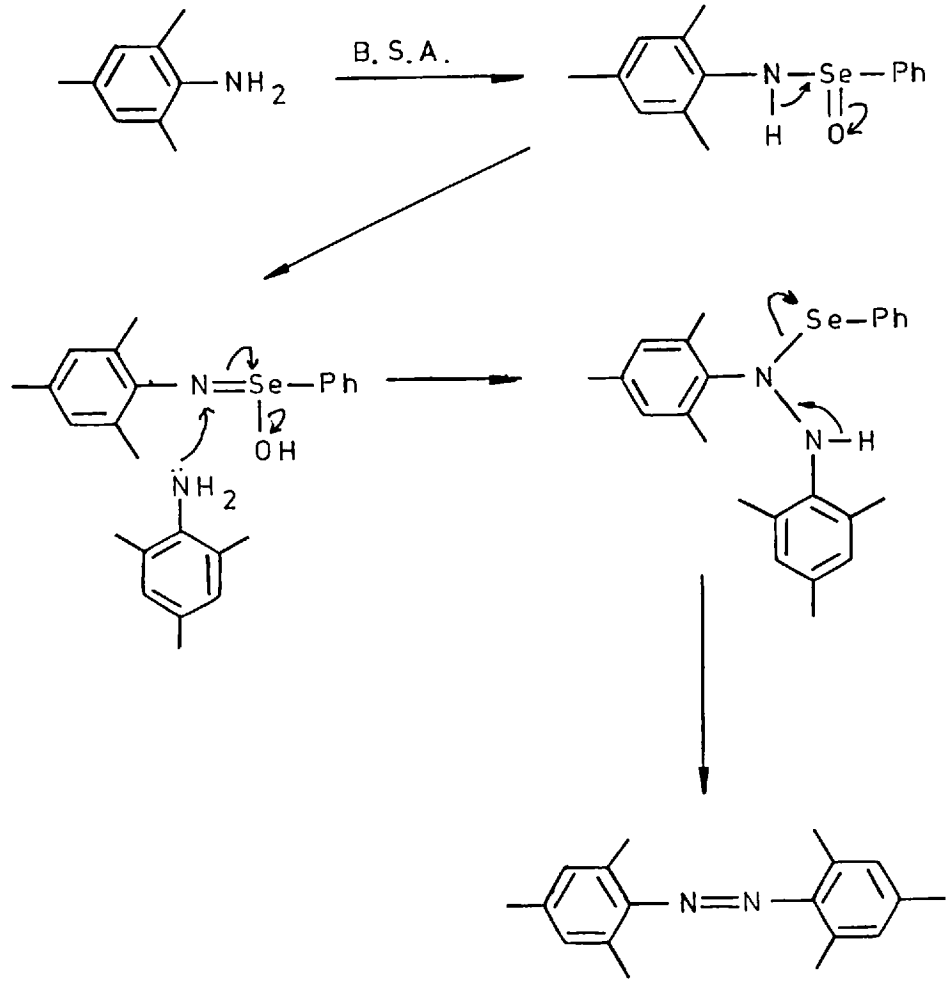
Treatment of o-phenylenediamine with the anhydride at room temperature rapidly affords a deep red colour. The reaction is best performed at -17°C for 30 min, when a much cleaner reaction takes place. The mechanism of the reaction is not known - the red product is believed to be N,N'-selenophenyldehydro-o-phenylenediamine (59). It has no characteristic absorbances in the infra-red spectrum and shows only signals in the region δ 6.7-8.1. The compound does not show a molecular ion in the mass spectrum - the parent ion shows the loss of one phenylseleno group. The compound gave microanalytical data in agreement with the proposed structure.



59

Anilines, in general, give rise to very complicated mixtures of products with the anhydride, even at low temperatures. 2,4,6-Trimethyl-

aniline reacts smoothly with the anhydride at room temperature to afford azomesitylene in moderate (52%) yield. Hydrazomesitylene is possibly an intermediate in the reaction, which on further reaction affords azomesitylene, (Scheme 29).



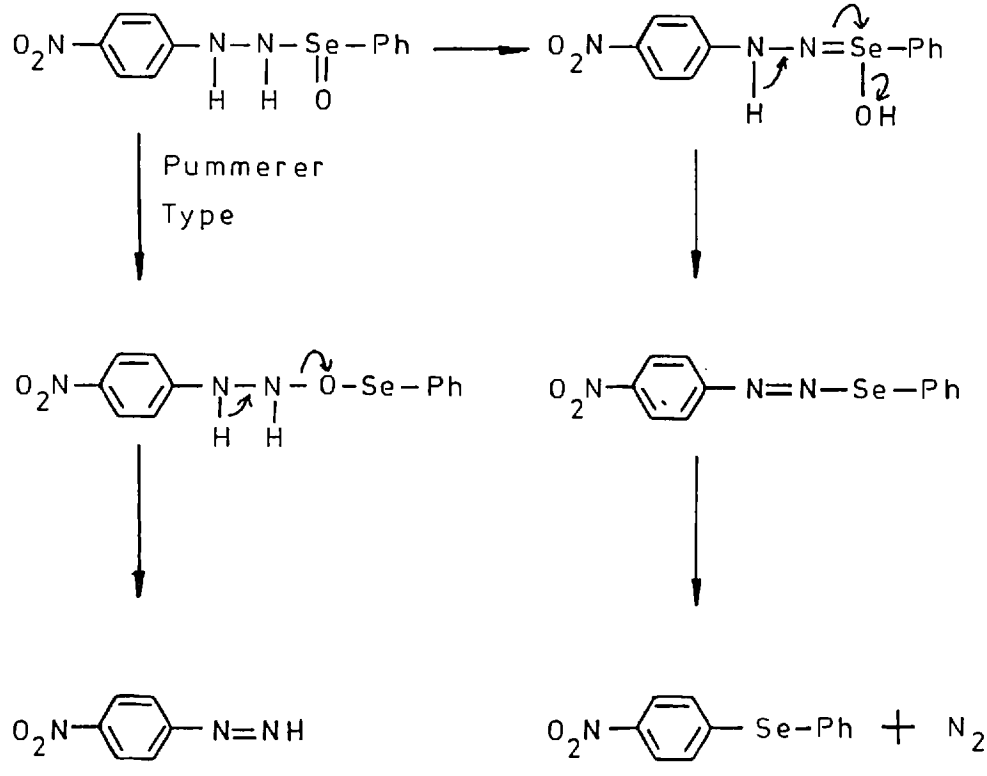
Scheme 29

The success of the reaction is accounted for by the methyl groups blocking any possible rearrangement products and consequently affording complex mixtures of products.

p-Nitrophenylhydrazine has been shown to react rapidly with benzeneseleninic anhydride at room temperature, liberating nitrogen and

and affording a complex mixture of products. At $0^{o}C$, a cleaner reaction takes place. Isolation by p.l.c. using a multiple elution technique by affords nitrobenzene (27%), shown to be pure by measurement of its u.v. extinction coefficient and p-selenophenylnitrobenzene (63%). Interestingly, if excess anhydride was employed, the hydrazine solution being slowly added to the anhydride solution, then the product ratio was inverted and nitrobenzene became the major (72%) product. If excess lithium benzeneselenate was added, then the yield of nitrobenzene was diminished and p-selenophenylnitrobenzene became the major (43%) product of reaction.

Several mechanistic schemes have been considered, none of which completely account for the observed changes in product ratio. It is possible that the reaction is occurring via a radical mechanism, or via an imine intermediate (Scheme 30).



Scheme 30

SECTION 7

EXPERIMENTAL

Melting points were determined on a Kofler hot stage and are uncorrected. Infra-red spectra were recorded on a Unicam SP 200 or Perkin Elmer 257 spectrophotometer. Ultra-violet spectra were recorded in ethanol, unless otherwise stated, on a Unicam SP 800 spectrophotometer. N.m.r. spectra were recorded in deuteriochloroform or carbon tetrachloride with tetramethylsilane as an internal reference on a Varian EM 360 instrument. Mass spectra were recorded on an A.E.I.M.S. 9 spectrometer. Microanalyses were carried out within the Department of Imperial College.

Thin-layer chromatography, both preparative and analytical, was carried out using GF_{254} silica plates.

Solvents were purified and dried according to standard techniques. Petrol refers to the fraction with b.p. 40-60°.

Organic solutions were dried using either sodium or magnesium sulphate.

The following abbreviations are used:

THF : tetrahydrofuran
DMF : dimethylformamide
DMA : dimethylacetamide
DME : dimethoxyethane

Preparation of Cholesta-1,4-dien-3-one p-Nitrophenylhydrazone from Cholestan-3-one p-Nitrophenylhydrazone

To a solution of cholestan-3-one p-nitrophenylhydrazone (1.0 g, 1.93 mmol) in dry D.M.E. (100 ml) under nitrogen was added p-nitrobenzoic acid (3.5 g, 21 mmol) and potassium t-butoxide (7.0 g, 94.6 mmol) with stirring at 40°C. After 2 h, acetic acid (5% aqueous, 200 ml) was added with cooling to precipitate cholesta-1,4-dien-3-one p-nitrophenylhydrazone (1.0 g, 100%) as an orange solid. Chromatography (alumina, type H, 100 g; methylene chloride as eluent) afforded cholesta-1,4-dien-3-one p-nitrophenylhydrazone (0.8 g, 80%), m.p. 179-181° (from nitromethane), (lit.[28], 178-180°), ν_{max} 3320, 1600, 1520, 1500, 1320, 1270, and 1110 cm^{-1}, λ_{max} 420 nm (ε 29500), (lit.[28], λ_{max} 420 nm (ε 30000), δ 8.2-7.1 (4H, q), and 6.8-6.1 (3H, m), (lit.[28], δ 8.13-7.19 (4H, q) and 6.55-6.1 (3H, m)), m/e 517 (M^+, 100%).

Preparation of Cholesta-1,4-dien-3-one p-Nitrophenylhydrazone from Cholest-4-en-3-one p-Nitrophenylhydrazone

To a solution of cholest-4-en-3-one p-nitrophenylhydrazone (100 mg, 0.19 mmol) in dry D.M.E. (10 mg), under nitrogen, was added p-nitrobenzoic acid (350 mg, 2.87 mmol) and potassium t-butoxide (700 mg, 6.25 mmol) with stirring at 40°C for 15 min. Acetic acid (5% aqueous, 20 ml) was added with cooling to precipitate cholesta-1,4-dien-3-one p-nitrophenylhydrazone. P.l.c. afforded cholesta-1,4-dien-3-one p-nitrophenylhydrazone (92 mg, 92%), m.p. 179-181° (from nitromethane, 84 mg, 84%), (lit.[28], 178-180°), identical with previous samples.

Preparation of Cholesta-1,4-dien-3-one p-Nitrophenylhydrazone from cholestan-3-one p-Nitrophenylhydrazone with in situ generation of Sodium t-butoxide

To a stirred suspension of sodium hydride (22 mg, 0.73 mmol) in dry D.M.E. (1.0 ml) was added t-butanol (45 mg, 0.61 mmol) and the suspension stirred at 50° under nitrogen until the formation of sodium t-butoxide was complete (15 min). Nitrobenzene (71 mg, 0.58 mmol) and a solution of cholestan-3-one p-nitrophenylhydrazone (20 mg, 0.038 mmol) in dry D.M.E. (1 ml) were added and the mixture stirred at 50° under nitrogen. Acetic acid (10% aqueous, 10 ml) was added and the mixture extracted with methylene chloride (2 x 10 ml). P.l.c. afforded cholesta-1,4-dien-3-one as summarised in Table 5.

TABLE 5

Solvent	Base	Yield(%)	Comments
D.M.E.	$NaOAm^t$	71	Slower reaction than with $NaOBu^t$.
D.M.E.	$NaOBu^t$	51	Only 5 eqv. nitrobenzene added.
D.M.E./15% toluene	$NaOBu^t$	20.5	
"	$NaOAm^t$	61	Mixture darkened in colour after adding oxidant.
"	$NaOBu^t$	44	Cholest-4-en-3-one p-nitrophenylhydrazone as substrate.

/continued...

TABLE 5/continued...

Solvent	Base	Yield(%)	Comments
D.M.E./15% toluene	$NaOAm^t$	77	Cholest-4-en-3-one p-nitrophenylhydrazone as substrate.
D.M.E./5% toluene	"	62	"
toluene	"	27%	"

Effects of Changing Base, Solvent and Oxidant in the Oxidation of Cholestan-3-one p-Nitrophenylhydrazone

To a solution of cholestan-3-one p-nitrophenylhydrazone (10 mg, 0.019 mmol) in dry D.M.E. (1 ml) was added either p-nitrobenzoic acid (35 mg, 0.29 mmol) or nitrobenzene (36 mg, 0.29 mmol) as oxidant and a base (0.63 mmol) with stirring at 60°C. Acetic acid (10% aqueous, 5 ml) was added and the mixture extracted into methylene chloride. P.l.c. afforded cholesta-1,4-dien-3-one p-nitrophenylhydrazone as summarised in Table 6.

TABLE 6

Solvent	Base	Oxidant	Time Temp.	Comments
D.M.E.	NaOH	$ArCO_2H$	18 h, 60°C	Red anion formed but Na salt pptd. Only decomposition observed on t.l.c.
D.M.E.	NaOH	ArH	4 h, 60°C	Red anion formed followed by decomp.
D.M.E.	NaOEt	ArH	15 min, 60°C	Red anion formed followed by rapid decomposition.
D.M.E.	$KOBu^t$	ArH	15 min, 60°C	92% dienone
EtOH/MePh 1 : 4	NaOH	ArH	3 h, 60°C	7.5% enone isolated, much decomposition.
EtOH/MePh	NaOH	$ArCO_2H$	3 h, 60°C	Oxidant not completely soluble. Mainly decomposition.
PhMe	NaOH	ArH	3 h, 60°C	Red anion formed very slowly due to poor solubility of base.
Nitrobenzene	NaOH	ArH	3 h, 60°C	As above but base slightly more soluble.
Et_3N	$KOBu^t$	ArH	- 50°C	Substrate not sufficiently soluble.
PhMe/5% D.M.E.	NaH 2 eqv.	ArH	3 days, 60°C	Red anion formed. No further reaction.

Preparation of Cholesta-1,4,6-trien-3-one p-Nitrophenylhydrazone from Cholestan-3-one p-Nitrophenylhydrazone

To a solution of cholestanone p-nitrophenylhydrazone (100 mg, 0.19 mmol) in dry D.M.E. (10 ml), were added p-nitrobenzoic acid (recrystallised, 350 mg) and potassium t-butoxide (700 mg), with stirring at 60°C. After 5 h, acetic acid (5%, aqueous, 20 ml) was added with cooling to precipitate cholesta-1,4,6-trien-3-one p-nitrophenylhydrazone (100 mg, 100%) as a red solid. P.l.c. afforded cholesta-1,4,6-trien-3-one p-nitrophenylhydrazone (61 mg, 61%), m.p. 156-160° (from nitromethane) mixed m.p. 154-160°, ν_{max} 3320, 1600, 1460, 1330, 1270,1110, 840, and 750 cm^{-1}, λ_{max} 434 nm (ε 33500), δ 8.2-7.2 (4H, q) and 6.8-6.0 (5H, m), M^+, 515, 500, and 379, $|\alpha|_D^{22}$ -5.2° (C 0.500) (Found: C, 76.8; H, 8.5; N, 7.9%. $C_{33}H_{45}N_3O_2$ requires C, 76.9; H, 8.7; N, 8.1%).

Large Scale Preparation of Cholesta-1,4,6-trien-3-one p-Nitrophenylhydrazone

Glyme (500 ml) was distilled under dry argon into a three necked flask equipped with a mechanical stirrer and rubber septum, containing sodium hydride (80%, 11.0 g, 0.37 mol). During the distillation, t-butanol (27 g, 34.5 ml, 0.36 mol) was slowly introduced whilst stirring the mixture. After the formation of sodium t-butoxide (1 h) solid p-nitrobenzoic acid (17.5 g, 0.1 mmol) was added followed by cholestan-3-one p-nitrophenylhydrazone (5.0 g, 0.01 mmol) and the solution stirred at 55-60°C for 10 h. The reaction was followed by u.v. control. Dilute acetic acid (5%, 1 l) was carefully added to the cooled mixture to precipitate the product as a red solid (4.8 g). Column chromatography (alumina, methylene chloride) afforded cholesta-

1,4,6 trien-3-one p-nitrophenylhydrazone (2.3 g, 46%) m.p. 156-160°, identical with previous samples.

Preparation of Cholesta-1,4-dien-3-one from Cholesta-1,4-dien-3-one p-Nitrophenylhydrazone

To a solution of cholesta-1,4-dien-3-one (3.5 g, 6.77 mmol) in dry T.H.F. (25 ml) was added benzeneseleninic anhydride (2.45 g, 6.8 mmol) and the suspension heated to 40°C with stirring in the dark for 18 h. Chromatography (silica, petrol/methylene chloride, 2:1) afforded diphenyl diselenide (1.0 g, 47%) and cholesta-1,4-dien-3-one (2.1 g, 81%), m.p. 83-97° (from methanol). P.l.c. (alumina, benzene:ethyl acetate, 90:10) afforded cholesta-1,4-dien-3-one (1.79 g, 73%) m.p. 109-111° (from methanol), (lit.[29], 112°), λ_{max} 241 nm (ε 14400) (lit.[29], λ_{max} 242 nm (ε 15000)), ν_{max} 1670, 1625, 1605, 1290, 1240, 895, and 810 cm^{-1}, $|\alpha|_D^{23}$ + 26.9° (C 1.0), (lit.[29], $|\alpha|_D$ + 28°).

Preparation of 1α,2α-Epoxycholesta-1,4,6-trien-3-one from 1α,2α-Epoxycholesta-1,4,6-trien-3-one p-Nitrophenylhydrazone

To a solution of 1α,2α-epoxycholesta-1,4,6-trien-3-one p-nitrophenylhydrazone (100 mg, 0.19 mmol) in dry T.H.F. (10 ml) was added benzeneseleninic anhydride (70 mg, 0.19 mmol) and the solution stirred at 40°C in the dark for 18 h. P.l.c. afforded a brown oil (84 mg) Rf 0.04-0.30 which was subjected to further chromatography (alumina, benzene:ethyl acetate, 95:5) to afford an orange oil (71.3 mg) which crystallised on standing in methanol at 0° for 2 days to afford cholesta-1,4,6-trien-3-one (51.3 mg, 74%) m.p. 60-9°, (lit.,[30] 82-3°),

λ_{max} 226 (ε 12700), 256 (9700), and 302 nm (7350), (lit.[31], λ_{max} 244 (ε 10700), 258 (9640) and 300 nm (12900)). Cholesta-1,4,6-trien-3-one was dissolved in methanol (2.8 ml) and treated with methanolic sodium hydroxide (10%, 0.019 ml) and hydrogen peroxide (30%, 0.13 ml) and the solution allowed to stand at room temperature overnight. Cooling to -40°C afforded a brown solid (50 mg, 68%), m.p. 85-97°. P.l.c. (benzene:ethyl acetate, 95:5) afforded 1α,2α-epoxycholesta-1,4,6-trien-3-one (31.1 mg, 43%), m.p. 104-106° (from methanol/acetone), (lit.[32], 106-108°), λ_{max}, 291 nm (ε 18500), (lit.[32], λ_{max} 292 nm (ε 1900)), $|\alpha|_D^{22}$ + 195.9° (C 0.40), (lit.[32], $|\alpha|_D$ + 200°).

Regeneration of Benzophenone from Benzophenone phenylhydrazone

(a) To a solution of benzophenone phenylhydrazone (50 mg, 0.18 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (66 mg, 0.18 mmol) and the suspension stirred at 50°C for 3 h when t.l.c. showed complete reaction. P.l.c. afforded benzophenone (29.8 mg, 89.5%), m.p. 47-48° (from ethanol, 27.0 mg, 81%) (lit.,[33] 49°) identical with an authentic sample.

(b) The above reaction was repeated in different dry solvents. The results are summarised in Table 7.

TABLE 7

Solvent	Reaction Time (h)	Yield of Benzophenone
D.M.A.	4	28.6mg, 86%
D.M.F.	4	30.6 mg, 92%
Benzene	3	29.6 mg, 89%

/continued...

TABLE 7/continued...

Solvent	Reaction Time (h)	Yield of Benzophenone
Toluene	3	28.6 mg, 86%
D.M.F.	2	29.6 mg, 89%
T.H.F.	3	29.8 mg, 89.5%

Regeneration of Benzophenone from Benzophenone p-Nitrophenylhydrazone

To a solution of benzophenone p-nitrophenylhydrazone (50 mg, 0.16 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (57 mg, 0.16 mmol) and the suspension stirred at 50°C for 3 days. P.l.c. afforded benzophenone (16.1, 56%), m.p. 45-47° (lit.,[33] 49°).

Regeneration of Benzophenone from Benzophenone Tosylhydrazone

(a) To a solution of benzophenone tosylhydrazone (50 mg, 0.14 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (51.5 mg, 0.14 mmol) and the suspension stirred at 50°C for 20 min. when t.l.c. showed complete reaction. P.l.c. afforded benzophenone (24.7 mg, 95%), m.p. 47-48° (from ethanol, 23.1 mg, 89%) (lit.[33], 49°).

(b) The above reaction was repeated in different dry solvents. The results are summarised in Table 8.

TABLE 8

Solvent	Reaction Time (h)	Yield of Benzophenone
D.M.A.	1	25.0 mg, 96%
D.M.F.	1	25.7 mg, 99%
Benzene	2	16.1 mg, 62%
Toluene	2	16.4 mg, 63%
Glyme	15 min	25.7 mg, 99%
T.H.F.	20 min	24.7 mg, 95%

Regeneration of Benzophenone from Benzophenone Oxime

To a solution of benzophenone oxime (50 mg, 0.25 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (92 mg, 0.25 mmol) and the suspension stirred at 50°C for 3 h. P.l.c. afforded benzophenone (41.0 mg, 89%), m.p. 47-48° (from ethanol, 35.0 mg, 76%) (lit.[33], 49°).

Regeneration of Benzophenone from Benzophenone Semicarbazone

To a solution of benzophenone semicarbazone (50 mg, 0.21 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (75 mg, 0.21 mmol) and the suspension stirred at 50°C for 2 h. P.l.c. afforded benzophenone (34 mg, 89%), m.p. 47-48° (from ethanol, 27.1 mg, 71%) (lit,[33] 49°).

Regeneration of Cholestan-3-one from Cholestan-3-one Phenylhydrazone

To a solution of cholestanone phenylhydrazone (50 mg, 0.105 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (37.8 mg, 0.105 mmol) and the suspension stirred at 50°C for 10 h. P.l.c. afforded cholestanone (25.9 mg, 64%), m.p. 127-9° (from ethanol, 21.1 mg, 52%) (lit.[34], 128-129°).

Regeneration of Cholestan-3-one from Cholestan-3-one p-Nitrophenylhydrazone

To a solution of cholestanone p-nitrophenylhydrazone (50 mg, 0.096 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (34.5 mg, 0.096 mmol) and the suspension stirred at 50°C for 10 h. P.l.c. afforded cholestanone (35.2 mg, 95%), m.p. 128-30° (from ethanol, 30.8 mg, 83%) (lit.[34] 128-129°).

Regeneration of Cholestan-3-one from Cholestan-3-one Tosylhydrazone

To a solution of cholestanone tosylhydrazone (50 mg, 0.090 mmol) in T.H.F. (5 ml) was added benzeneseleninic anhydride (32 mg, 0.090 mmol) and the suspension stirred at 50°C for 20 min. P.l.c. afforded cholestanone (33.7 mg, 97%), m.p. 129-30° (from ethanol 30.2 mg, 87%) (lit.[34], 128-129°).

Regeneration of Cholestan-3-one from Cholestan-3-one Oxime

To a solution of cholestanone oxime (50 mg, 0.125 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (45 mg, 0.125 mmol) and the suspension stirred at 50°C for 50 min. P.l.c. afforded cholestanone (40 mg, 83%), m.p. 129-30° (from ethanol, 30 mg, 60%) (lit.[34], 128-129°).

Regeneration of Cholestan-3-one from Cholestan-3-one Semicarbazone

To a solution of cholestanone semicarbazone (50 mg, 0.11 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (39.6 mg, 0.11 mmol) and the suspension stirred at 50°C for 4 h. P.l.c. afforded cholestanone (34.5 mg, 83%), m.p. 127-9° (from ethanol 27.9 mg, 67%) (lit.[34], 128-129°).

Regeneration of Cholest-4-en-3-one from Cholest-4-en-3-one Phenylhydrazone

To a solution of cholest-4-en-3-one phenylhydrazone (50 mg, 0.105 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (37.8 mg, 0.105 mmol) and the suspension stirred at 50°C for 10 h. P.l.c. afforded cholest-4-en-3-one (23.0 mg, 57%), m.p. 77-79°, (from ethanol 16.1 mg, 40%) (lit.[35], m.p. 80°).

Regeneration of Cholest-4-en-3-one from Cholest-4-en-3-one p-Nitrophenylhydrazone

To a solution of cholest-4-en-3-one p-nitrophenylhydrazone (50 mg, 0.096 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride

(34.5 mg, 0.096 mmol) and the suspension stirred at 50°C for 10 h. P.l.c. afforded cholest-4-en-3-one (20.8 mg, 56.5%), m.p. 77-79° (from ethanol 14.4 mg, 41%) (lit.[35], m.p. 80°).

Regeneration of Cholest-4-en-3-one from Cholest-4-en-3-one Tosylhydrazone

To a solution of cholest-4-en-3-one tosylhydrazone (50 mg, 0.091 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (33 mg, 0.091 mmol) and the suspension stirred at 50°C for 20 min. P.l.c. afforded cholest-4-en-3-one (30.1 mg, 86%), m.p. 79-80° (from ethanol, 25.9 mg, 74%), (lit.[35], 80°).

Regeneration of Cholest-4-en-3-one from Cholest-4-en-3-one Oxime

To a solution of cholest-4-en-3-one oxime (50 mg, 0.125 mmol) in T.H.F. (5 ml) was added benzeneseleninic anhydride (45 mg, 0.125 mmol) and the suspension stirred at 50°C for 50 min. P.l.c. afforded cholest-4-en-3-one (46.1 mg, 96%), m.p. 79-80° (from ethanol, 38.4 mg, 80%) (lit.[35], 80).

Regeneration of Cholest-4-en-3-one from Cholest-4-en-3-one Semicarbazone

To a solution of cholest-4-en-3-one semicarbazone (50 mg, 0.11 mmol) in T.H.F. (5 ml) was added benzeneselninic anhydride (41 mg, 0.11 mmol) and the suspension stirred at 50°C for 4 h. P.l.c. afforded cholest-4-en-3-one (36.7 mg, 85%), m.p. 77-79°, (from ethanol 30.8 mg, 71%), (lit.[35], 80°).

Regeneration of Furfural from Furfural Tosylhydrazone

To a solution of furfural tosylhydrazone (50 mg, 0.19 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (69 mg, 0.19 mmol) and the suspension stirred at 50°C for 2 h. P.l.c. afforded furfural (16.0 mg, 88%), identical by I.R. to an authentic sample.

Regeneration of Furfural from Furfural Oxime

To a solution of furfural oxime (50 mg, 0.45 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (162 mg, 0.45 mmol) and the suspension stirred at 50° for 6 h. P.l.c. afforded furfural (15.6 mg, 36%) identical by I.R. to an authentic sample.

Regeneration of Furfural from Furfural Semicarbazone

To a solution of furfural semicarbazone (50 mg, 0.33 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (119 mg, 0.33 mmol) and the suspension stirred at 50°C for 1 h. P.l.c. afforded furfural (0.63 mg, 2%) characterised by mass spectrum.

Regeneration of 2-Naphthaldehyde from 2-Naphthaldehyde Tosylhydrazone

To a solution of 2-naphthaldehyde tosylhydrazone (50 mg, 0.15 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (52 mg, 0.14 mmol) and the suspension stirred at 50°C for 30 min. P.l.c. afforded

2-naphthaldehyde (24.0 mg, 99%), m.p. 58-60° (from ethanol 22.6 mg, 87%) (lit.[36], 59°).

Regeneration of 2-Naphthaldehyde from 2-Naphthaldehyde Oxime

To a solution of 2-naphthaldehyde oxime (50 mg, 0.29 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (105 mg, 0.29 mmol) and the suspension stirred at 50°C for 20 min. P.l.c. afforded 2-naphthaldehyde (42.8 mg, 94%), m.p. 59-60° (from ethanol 36.8 mg, 81%) (lit.[36], 59°).

Regeneration of 2-Naphthaldehyde from 2-Naphthaldehyde Semicarbazone

To a solution of 2-naphthaldehyde semicarbazone (50 mg, 0.23 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (86 mg, 0.23 mmol) and the suspension stirred at 50°C for 1 h. P.l.c. afforded 2-naphthaldehyde (1.8 mg, 5%), m.p. 57-59° (lit.[36], 59°).

Reaction of Benzeneseleninic Anhydride with Benzaldehyde Phenylhydrazone

To a solution of benzaldehyde phenylhydrazone (50 mg, 0.25, 0.25 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (91 mg, 0.25 mmol) and the suspension stirred at 50°C for 1 h. P.l.c. afforded benzoyl azobenzene (39.0 mg, 73%), m.p. 28-29° (from ethanol at -78°, 35.7 mg, 67%), ν_{max} 3100, 1705, 1605, 1590, 1500, 1450, 1250, 1000, 765, 730, and 700 cm^{-1}, λ_{max}^{EtOH} 441 (ε 120) and 286 nm (10900), δ, 5.6-6.2 (5H, m), and 7.6-8.2 (5H, m), M^+, 212 ($M^+ + 2$), (lit.[37],

m.p. 30°, λ_{max}^{EtOH} 443 (ε 121) and 288 (13400).

Reaction of Benzeneseleninic Anhydride with Benzaldehyde p-Nitrophenylhydrazone

To a solution of benzaldenyde p-nitrophenylhydrazone (50 mg, 0.21 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (78 mg, 0.21 mmol) and the suspension stirred at 50°C for 1 h. P.l.c. afforded benzoyl azo-p-nitrobenzene (40.2 mg, 76%), m.p. 99-100° (from ethanol, 38.1 mg, 72%), ν_{max} 3100, 1705, 1605 , 1580, 1530, 1505, 1350, 1260, 1180, 1110, 1000, 880, 860, 760, 720, and 700 cm^{-1}, $\lambda_{max}^{CHCl_3}$ 460 (ε 153) and 286 (23800), δ 7.2-7.6 (4H, m) and 7.8-8.5 (5H, m), M^+, 257 (M^+ + 2) (lit.[37], m.p. 99-100°, λ_{max} 458 (ε 141) and 284 nm (24500)) (Found: C, 61.1; H, 3.6; N, 16.55. $C_{13}H_9N_3O_3$ requires C, 61.2; H, 3.55; N, 16.45%).

Reaction of Benzeneseleninic Anhydride with 2-Naphthaldehyde Phenylhydrazone

To a solution of 2-naphthaldehyde phenylhydrazone (50 mg, 0.20 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (73 mg, 0.20 mmol) and the suspension stirred at 50°C for 30 min. P.l.c. afforded 2-naphthoylazobenzene (36.5 mg, 69%), m.p. 53-56° (from ethanol at -78°, 25.5 mg, 49%), ν_{max} 3050, 1700, 1620, 1600, 1500, 1180, 1040, 830, and 700 cm^{-1}, $\lambda_{max}^{CHCl_3}$ 492 (ε 86) and 288 nm (17800), δ 7.2-8.6 (12H, m), m/e 260 (M^+ + 2).

Reaction of Benzeneseleninic Anhydride with 2-Naphthaldehyde p-Nitrophenylhydrazone

To a solution of 2-naphthaldehyde p-nitrophenylhydrazone (50 mg, 0.17 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (62 mg, 0.17 mmol) and the suspension stirred at 50° C for 20 min. P.l.c. afforded 2-naphthoylazo-p-nitrobenzene (47.2 mg, 90%), m.p. 141-142° (from ethanol, 46.7 mg, 89%), ν_{max} 3050, 1700, 1630, 1505, 1520, 1350, 1260, 1180, 1010, 870, 780, and 700 cm^{-1}, $\lambda_{max}^{CHCl_3}$ 498 (ε 160) and 286 nm (25500), δ 7.2-8.4 (11 H, m), M^+, 307 (M^+ + 2) (Found: C, 66.9; H, 3.65; N, 13.7. $C_{17}H_{11}N_3O_3$ requires C, 66.9; H, 3.65; N, 13.75%).

Reaction of Benzeneseleninic Anhydride with 2-Furfural Phenylhydrazone

To a solution of 2-furfural phenylhydrazone (50 mg, 0.27 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (97 mg, 0.27 mmol) and the suspension stirred at 50°C for 45 min. P.l.c. afforded 2-furanoyl azobenzene (46.8 mg, 87%) as deep red oil, ν_{max} 3100, 1700, 1570, 1510, 1460, 1400, 1300, 1150, 1040, 780, and 700 cm^{-1}, $\lambda_{max}^{CHCl_3}$ 494 (ε 134) and 301 nm (11800), δ 7.2-7.5 (3H, m) and 7.5-8.2 (5H, m), M^+, 202 (M^+ +2) (Found: C, 66.05; H, 4.0; N, 13.85. $C_{11}H_8N_2O_3$ requires C, 66.0; H, 4.05; N, 14.0%).

Reaction of Benzeneseleninic Anhydride with 2-Furfural p-Nitrophenylhydrazone

To a solution of 2-furfural p-nitrophenylhydrazone (50 mg, 0.22 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (78 mg,

0.22 mmol) and the suspension stirred at 50°C for 35 min. P.l.c. afforded 2-furanoylazo-p-nitrobenzene (37.0 mg, 70%), m.p. 187-9° (from ethanol, 33.8 mg, 64%), ν_{max} 3100, 1700, 1610, 1570, 1400, 1310, 1110, 1050, 1010, 870, 780, and 700 cm^{-1}, $\lambda_{max}^{CHCl_3}$ 466 (ε 190) and 287 nm (23500), δ 4.5 (1H, dd, J 5,3 Hz), 5.2-5.7 (2H, m) and 5.8-6.4 (4H, m), M^+ 245, $(M^+ + 2)$ (Found: C, 53.75; H, 3.0; N, 17.05. $C_{11}H_7N_3O_4$ requires : C, 53.9; H, 2.9; N, 17.15%).

General method for Titration of Change in Oxidising Power during Regeneration of Benzophenone from its Phenylhydrazone Using Benzeneseleninic Anhydride

To a solution of benzophenone phenylhydrazone (32.5 mg, 0.125 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (45.0 mg, 0.125 mmol) and the mixture stirred at 44°C for a time t. The reaction was quenched by pouring quantitatively into a mixture of potassium iodide solution (10%, 10 ml), dilute sulphuric acid (2M, 10 ml), and ethanol (10 ml) previously titrated against M/100 thiosulphate so that no iodine was present. The liberated iodine was titrated against M/10 thiosulphate solution. 45 mg Benzeneseleninic anhydride ≡ 7.5 ml M/10 thiosulphate.

Time (t, min)	Titre (ml)
0	7.40
10	6.20
20	5.40
40	4.90
80	4.60
250	3.60

Titration of Change in Oxidising Power with Concurrent Recovery of Diphenyl diselenide Produced

To a solution of benzophenone phenylhydrazone (34.0 mg, 0.131 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (45.0 mg, 0.125 mmol) and the stirred solution heated at 60°C for 3 h. The reaction was quenched by pouring into dilute sulphuric acid (2M, 5ml) and the solution extracted with ether (2 x 5 ml). The etherial layer was evaporated under reduced pressure to yield an oil. P.l.c. afforded diphenyl diselenide (21.5 mg, 55%), m.p. 61-63° (lit.[38], 63°). The aqueous layer was quantitatively transferred to a flask containing aqueous potassium iodide solution (10%, 10 ml), dilute sulphuric acid (2M, 5ml) and ethanol (15 ml) previously titrated against M/100 thiosulphate so no iodine was present. The liberated iodine was titrated against M/10 thiosulphate. Titre - 3.4 ml, 45% remaining oxidising power.

Reaction of Excess Benzophenone Phenylhydrazone with Benzeneseleninic Anhydride

To a solution of benzophenone phenylhydrazone (340 mg, 1.25 mmol) in benzene (15 ml) was added benzeneseleninic anhydride (90 mg, 0.25 mmol) and the suspension heated to reflux under argon for 18 h. The cooled solution was extracted with 10% aqueous sodium bicarbonate solution (2 x 10 ml) and the base extract tritated against standard sodium thiosulphate in the usual way. Titre = 0.2 ml, 0.1 M thiosulphate, 1.3% residual oxidising power. The organic layer was subjected to p.l.c. which afforded diphenyl diselenide (78.0 mg, 100%),

m.p. 59-61° (lit.[38], 63°), benzophenone (104.2 mg, 46%), m.p. 47-8° (lit.[33], 49°), and recovered starting material (184.8 mg, 54%).

The results of several similar experiments are tabulated in Table 9.

TABLE 9

Solvent	Anhydride (mmol)	Hydrazone (mmol)	Recovered Hydrazone (%)	Yield benzophenone (%)	Residual oxidising power (%)
T.H.F.	0.2	0.50	0	96	18
T.H.F.	0.25	0.75	34	68	8
PhH	0.25	1.25	54	46	1
PhH	0.25	0	0	0	97

Preparation of O-Methylbenzophenone Oxime

To a solution of benzophenone oxime (1.5 g, 7.6 mmol) in dry D.M.E. (5 ml) was added sodium hydride (50%, 7.8 mmol) and the mixture stirred for 5 min at room temperature to complete the formation of the anion. Methyl iodide (1.0 ml, 16.0 mmol) was added and stirring continued for a further 10 min. On pouring into 20% aqueous acetic acid (100 ml) O-methylbenzophenone oxime separated as a colourless solid. Recrystallisation from ethanol afforded colourless needles (1.2 g, 69%), m.p. 58-9°, ν_{max} 1590, 1560, 1460, 1320, 1300, 1160, 1060, 990, 890, 780, and 705 cm^{-1}, δ 7.3 (10 H, m) and 3.9 (3H, s) (Found: C, 79.65; H, 6.2; N, 6.6. $C_{14}H_{13}ON$ requires C, 79.6; H, 6.2; N, 6.65%).

Reaction of O-Methylbenzophenone Oxime with Benzeneseleninic Anhydride

To a solution of O-methylbenzophenone oxime (50 mg, 0.32 mmol) in T.H.F. (5 ml) was added benzeneseleninic anhydride (85 mg, 0.31 mmol) and the suspension stirred at 50° under nitrogen for 10 h. P.l.c. afforded O-methylbenzophenone (44.9 mg, 98%) identical to the starting material (m.p., i.r., n.m.r.).

Preparation of 2,6-Dimethylphenylhydrazine Hydrochloride

2,6-Xylidine (6.45 g, 0.053 mol) was added with stirring to a solution of concentrated hydrochloric acid (13.4 ml) in water (6 ml). The solution was cooled to -5°C and diazotised in the usual way using a solution of sodium nitrite (4.9 g, 0.58 mol) in water (6 ml). The resulting diazo solution was stirred at 0°C for 15 min before adding a solution of stannous chloride (27 g) in dilute hydrochloric acid (36 ml, 50% by volume) to the stirred solution. The solution was allowed to warm to room temperature over a period of 4 h and stirring was continued overnight. A solution of sodium hydroxide (34 g) in water (45 ml) was carefully added with cooling and the solution extracted with ether (3 x 40 ml). The etherial solution was dried diluted to 200 ml with ether and saturated with hydrogen chloride. 2,6-Dimethylphenylhydrazine hydrochloride separated as a white solid (5.9 g, 64%) recrystallisation from ethanol gave needles, m.p. 201-2° (lit.[39], 202°), ν_{max} 3300, 2700, 1520, 840, and 790 cm^{-1}.

Preparation of Benzophenone 2,6-Dimethylphenylhydrazone

To a solution of 2,6-dimethylphenylhydrazine hydrochloride (0.5 g, 3.2 mmol) and potassium acetate (0.3 g) in methanol (5 ml)

containing water (1.8 ml) was added benzophenone (0.54 g, 0.30 mmol) and the mixture heated to reflux for 1 h under nitrogen. Benzophenone 2,6-dimethylphenylhydrazone (0.7 g, 79%) separated on cooling and was recrystallised from methanol as colourless needles, m.p. 113-4.5° ν_{max} 3300, 1580, 1550, 1480, 1320, 1270, 1230, 1120, 1070, 1030, 920, 780, and 720 cm^{-1}, δ 7.7-6.8 (13 H, m) and 2.3 (6H, s) (Found: C, 83.65; H, 6.8; N, 9.3. $C_{21}H_{20}N_2$ requires C, 83.95; H, 6.7; N, 9.35%).

Reaction of Benzophenone 2,6-Dimethylphenylhydrazone with Benzeneseleninic Anhydride

To a solution of benzophenone 2,6-dimethylphenylhydrazone (50 mg, 0.18 mmol) in dry T.H.F. (15 ml) was added benzeneseleninic anhydride (60 mg, 0.17 mmol) and the solution stirred at 50°C for 18 h under argon. Evaporation of the solvent under reduced pressure followed by p.l.c. afforded diphenyl diselenide (28.8 mg, 61%), recovered starting material (5 mg, 10%) and benzophenone (29.6 mg, 97%). All products were identical (m.p.) with authentic samples.

Regeneration of iso-Butyraldehyde from iso-Butyraldehyde Tosylhydrazone

To a solution of iso-butyraldehyde tosylhydrazone (0.5 g, 2.2 mmol) in dry diglyme (5 ml) was added benzeneseleninic anhydride (0.75 g, 2.1 mmol) at room temperature and dry nitrogen bubbled through the solution. The volatile products were condensed in a tube cooled to -78°C using carbon dioxide/acetone. The reaction was complete after 15 min. Isobutyraldehyde (101.4 mg, 71%), n_D^{23} 1.3716, (authentic

material n_D^{22} 1.3721) was obtained as a colourless liquid, identical by n.m.r. to an authentic sample.

Regeneration of Cinnamaldehyde from Cinnamaldehyde Tosyl Hydrazone

To a solution of cinnamaldehyde tosylhydrazone (100 mg, 0.33 mmol) in dry T.H.F. (1 ml) was added benzeneseleninic anhydride (120 mg, 0.33 mmol) and the suspension stirred at room temperature for 15 min. P.l.c. (petrol:methylene chloride, 50:50) afforded cinnamaldehyde (40 mg, 91%) having identical n.m.r. and i.r. spectra to authentic material.

Regeneration of Crotonaldehyde from Crotonaldehyde Tosyl Hydrazone

To a solution of crotonaldehyde tosylhydrazone (100 mg, 0.44 mmol) in T.H.F. (1 ml) was added benzeneseleninic anhydride (160 mg, 0.44 mmol) and the suspension stirred at room temperature for 15 min. P.l.c. (petrol:methylene chloride, 50:50) afforded crotonaldehyde (16.5 mg, 68%), identical by n.m.r. to authentic material.

Regeneration of Heptaldehyde from Heptaldehyde Tosyl Hydrazone

To a solution of heptaldehyde tosylhydrazone (100 mg, 0.35 mmol) in T.H.F. (1 ml) was added benzeneseleninic anhydride (126 mg, 0.35 mmol) and the suspension stirred at room temperature for 15 min. P.l.c. (petrol:methylene chloride, 50:50) afforded heptaldehyde (35.5 mg, 89%), identical by i.r. and n.m.r. to authentic material.

Regeneration of Valeraldehyde from Valeraldehyde Tosylhydrazone

To a solution of valeraldehyde tosylhydrazone (100 mg, 0.39 mmol) in T.H.F. (1 ml) was added benzeneseleninic anhydride (140 mg, 0.39 mmol) and the solution stirred at room temperature for 15 min. P.l.c. (petrol:methylene chloride, 50:50) afforded valeraldehyde (31.6 mg, 92%), identical by n.m.r. to authentic material.

Reaction of Cholestan-3-one with Benzeneseleninic Anhydride

To a solution of cholestan-3-one (100 mg 0.26 mmol) in chlorobenzene (5 ml) was added benzeneseleninic anhydride (188 mg, 0.52 mmol) and the mixture heated to reflux under nitrogen in the dark for 3 h. The reaction mixture was washed down a short silica column with petrol containing 10% methylene chloride and the crude products released from the column by eluting with methanol. P.l.c. afforded cholesta-1,4-dien-3-one (63.3 mg, 63%), m.p. 110-112° (from methanol), λ_{max} 242 nm (ε 14500), (lit.[29], λ_{max} 242 nm (ε 15000)), ν_{max} 1660, 1620, 1600, 1290, 1240, 885, and 810 cm^{-1}, $|\alpha|^{22}$ + 28° (lit.[29], + 28°), m/e 382 (M^+, 100%), 269, 261, 247.

The results of several runs are tabulated in Table 10.

TABLE 10

Anhydride (mmol)	Time (h)	Yield of cholesta-1,4-dien-3-one (%)
0.26	3	50
0.52	3	76
0.78	18	69*

* No cholesta-1,4,6-trien-3-one was detected.

Reaction of Cholest-4-en-3-one with Benzeneseleninic Anhydride

To a solution of cholest-4-en-3-one (100 mg, 0.26 mmol) in dry chlorobenzene (0.5 ml) was added benzeneseleninic anhydride (94 mg, 0.26 mmol) and the mixture heated to reflux under nitrogen for 40 min. P.l.c. (methylene chloride:methanol, 97:3) afforded cholesta-1,4-dien-3-one (92 mg, 92%), m.p. 110-112° (from methanol) (lit.[29], 112°) identical with authentic material.

Reaction of Cholest-1-en-3-one with Benzeneseleninic Anhydride

To a solution of cholest-1-en-3-one (40 mg, 0.10 mmol) in dry chlorobenzene (0.7 ml) was added benzeneseleninic anhydride (38mg, 0.11 mmol) and the suspension heated to 95°C with stirring for 45 min. P.l.c. afforded cholesta-1,4-dien-3-one (30.4 mg, 76%), m.p. 109-111° (from ethanol), (lit.[29], 112°) identical with previous samples.

Reaction of 4,4-Dimethylcholest-5-en-3-one with Benzeneseleninic Anhydride

To a solution of 4,4-dimethylcholest-5-en-3-one (100 mg, 0.24 mmol) in chlorobenzene (0.7 ml) was added benzeneseleninic anhydride (87 mg, 0.24 mmol) and the suspension heated to 95°C with stirring under nitrogen for 35 min. P.l.c. afforded (a) diphenyl diselenide (47.7 mg, 63%), m.p. 61-63° (lit.[38], 63°), (b) A-nor-4,4-dimethyl-cholest-5-en-3-one, not isolated and (c) 4,4-dimethylcholest-1,5-dien-3-one (67 mg, 67%), m.p. 75-76° (from ethanol/water), (lit.[40], 77-78°),

ν_{max} 1685 cm^{-1}, λ_{max}, 230 nm (ε 7200), (lit.[40], λ_{max} 227 nm, (ε 9350)), δ 6.6 (1H, d), 5.9 (1H, d), and 5.6 (1H, m), $|\alpha|_D^{22}$ + 54.9° (C 1.00) (lit.[40], $|\alpha|_D$ + 53° (C 1.00), m/e 410.

Reaction of 4,4-Dimethylcholest-5-en-3-one with Excess Benzeneseleninic Anhydride

To a solution of 4,4-dimethylcholest-5-en-3-one (100 mg, 0.24 mmol) in chlorobenzene (0.5 ml) was added benzeneseleninic anhydride (174 mg, 0.48 mmol) and the suspension heated to 95°C with stirring for 17 h. P.l.c. afforded (a) diphenyl diselenide (100 mg, 133% based on steroid) m.p. 61-63° (lit.[38], 63°), (b) A-nor-4,4-dimethylcholest-5-en-3-one (26.7 mg, 28%), m.p. 127-128° (from ethanol/water) (lit.[41], 129-130°), ν_{max} 1745 cm^{-1}, $\lambda_{max}^{CHCl_3}$ 304 nm (ε 70), (lit., $\lambda_{max}^{CHCl_3}$ 300 nm (ε 94)), δ 2.1 (2H, m) and 5.6 (1H) (lit.[41], δ 2.15 (2H, m) and 5.4 (1H, m)), $|\alpha|^{22}$ + 53° (C 1.00) (lit.[41], $|\alpha|_D$ + 54.5° (C 0.26)) and 4,4-dimethylcholest-1,5-dien-3-one (30.7 mg, 31%), m.p. 75-77° (from ethanol) identical with previous samples.

Reaction of Lanostan-3-one with Benzeneseleninic Anhydride

To a solution of lanostanone (100 mg, 0.23 mmol) in chlorobenzene (0.7 ml) was added benzeneseleninic anhydride (85 mg, 0.24 mmol) and the mixture heated to 95°C with stirring under nitrogen for 45 min. The reaction was followed by both t.l.c. and i.r. spectroscopy. P.l.c. afforded 2- phenylselenolanostan -3-one (4.0 mg, 3%) identical with a prepared authentic sample, A-nor-lanostan-3-one (12.3 mg, 13%) m.p. 98-100° (from ethanol/water), and lanost-1-en-3-one (67.0 mg, 67%) m.p. 119-120° (from ethanol) (lit.[42], m.p. 118-120°), ν_{max} 1670 cm^{-1},

λ_{max} 232 nm (ε 9200) (lit.[42], λ_{max} 229 nm (ε 9000)), $|\alpha|_D^{22}$ + 48.4° (C 1.00), (lit.[42], $|\alpha|_D$ + 47° (C 0.53)), m/e 426. The results from several similar experiments are tabulated in Table 11.

TABLE 11

BSA	1-enone	A-nor	2-PhSe	time	comments
1	63	NI	NI	20 m	contaminated with A-nor compound.
2/3	84	NI	NI	20 m	contaminated with both A-nor compound and starting material. Not possible to purify by crystallisation.
2/3	74	NI	8	25 m	Phenylselenated band resolvable into two components on active t.l.c. plates.
2	66	17	NI	105 m	
1	71	17	NI	1 h	
2	40	39	0	18 h	Several polar bands not isolated.
11	67	13	4	45 m	1-Enone pure and completely free of all above contaminants. Other more polar products observed on p.l.c. but not isolated.

Reaction of Lanostan-3-one with Excess Benzeneseleninic Anhydride

To a solution of lanostan-3-one (100 mg, 0.23 mmol) in chlorobenzene (0.7 ml) was added benzeneseleninic anhydride (170 mg, 0.48 mmol) and the suspension heated to 95°C for 18 h with stirring. P.l.c. afforded lanost-1-en-3-one (40 mg, 40%) m.p. 119-120° (from ethanol/water)(lit.[42], m.p. 118-120°), identical with previous samples and A-nor-lanostan-3-one (40.3 mg, 39%), m.p. 98-100°, ν_{max} 1745 cm^{-1}, δ 1.6-0.7 (complex multiplet), $|\alpha|_D^{24}$ + 206° (C 0.50) (Found: C, 83.85; H, 12.15. $C_{29}H_{50}O$ requires C, 84.0; H, 12.15%).

Preparation of Authentic 2-Phenylselenolanostan-3-one

To a solution of dry diisopropylamine (47 mg, 0.47 mmol) in dry T.H.F. (2 ml) at -78° was added n-butyl lithium (1.66 M, 0.76 ml) with stirring under nitrogen. After stirring for a further 5 min at -78°C, a solution of lanostan-3-one (200 mg, 0.47 mmol) in T.H.F. (2 ml) was added and stirring continued at -78°C for 10 min. A solution of benzeneselenenyl chloride (87.5 mg, 0.46 mmol) in dry T.H.F. (2 ml) was added dropwise to the solution with stirring at -78°C and then the mixture was allowed to attain room temperature over a period of 15 min. The complete reaction mixture was poured into dilute sulphuric acid (M, 10 ml) and extracted with methylene chloride (2 x 5 ml). Drying, evaporation of the solvent and recrystallisation from ethanol/water gave 2-phenylselenolanostan-3-one (170 mg, 62%) m.p. 150-152°, ν_{max} 1705, 1580, 745, and 700 cm^{-1}, m/e 584 (Found: C, 73.9; H, 9.65. $C_{36}H_{56}OSe$ requires C, 73.95; H, 9.6%).

Reaction of α-Amyr-3-one with Benzeneseleninic Anhydride

To a solution of α-amyrone (100 mg, 0.23 mmol) in chlorobenzene (0.7 ml) was added benzeneseleninic anhydride (85 mg, 0.24 mmol) and the suspension heated to 95°C with stirring under nitrogen for 25 min. P.l.c. afforded diphenyl diselenide (54.9 mg, 75%) m.p. 61-63° (lit.[38], 63°) and α-amyr-1-en-3-one (74.0 mg, 74%), m.p. 156-8°, ν_{max} 1665 cm^{-1}, λ_{max} 229 nm (ε 8800), $|\alpha|_D^{22}$ + 136.4° (C 1.00), m/e 422. (Found: C, 85.1; H, 11.0. $C_{30}H_{44}O$ requires C, 85.25; H, 11.0%).

Reaction of α-Amyr-3-one with Excess Benzeneseleninic Anhydride

To a solution of α-amyrone (100 mg, 0.23 mmol) in chlorobenzene (0.5 ml) was added benzeneseleninic anhydride (170 mg, 0.47 mmol) and the mixture heated to 95°C with stirring under nitrogen for 17 h. P.l.c. afforded (1) diphenyl diselenide (104 mg, 140% based on steroid), m.p. 61-63° (lit.[38], 63°), (2) α-Amyr-1-en-3-one (38.8 mg, 39%), m.p. 156-158°, identical with previous samples and (3) A-nor-α-amyr-3-one (46.3 mg), m.p. 189-191° (from ethanol, 37 mg, 39%), ν_{max} 1745 cm^{-1}, $|\alpha|_D^{22}$ + 440° (C 1.00).

Reaction of β-Amyr-3-one with Benzeneseleninic Anhydride

To a solution of β-amyrone (100 mg, 0.23 mmol) in chlorobenzene (0.7 ml) was added benzeneseleninic anhydride (85mg, 0.24 mmol) and the suspension heated to 95°C with stirring under nitrogen for 25 min. P.l.c. afforded (1) diphenyl diselenide (56.3 mg, 76%), m.p. 61-63° (lit. m.p. 63°), (2) A-nor-β-amyr-3-one (7.3 mg, 9%), m.p. 168-170°, identical with characterised sample, and (3) β-amyr-1-en-3-one

(54.0 mg, 54%), m.p. 174-175° (from ethanol) (lit.[43] 174-175°), ν_{max} 1665 cm^{-1}, λ_{max} 230 nm (ε 8000), (lit.[43], λ_{max} 230 nm (ε 9700)), $|\alpha|_D^{22}$ + 140° (C 0.50), (lit.[43], $|\alpha|_D^{22}$ + 141° (C 1.5)), m/e 422.

Reaction of β-Amyrone with excess Benzeneseleninic Anhydride

To a solution of β-amyrone (100 mg, 0.23 mmol) in chlorobenzene (0.5 ml) was added benzeneseleninic anhydride (170 mg, 0.47 mmol) and the mixture heated to 95°C with stirring under nitrogen for 17 h. P.l.c. afforded (1) diphenyl diselenide (130.7 mg, 178% based on steroid), m.p. 61-63° (lit.[38], 63°), m.p. 174-175° (from ethanol) (lit.[43], 174-175°), and (3) A-nor-β-amyrone (35 mg, 36%), m.p. 168-170° (from ethanol/water), ν_{max} 1745 cm^{-1}, $|\alpha|_D^{22}$ + 236° (C 0.50).

Reaction of Hecogenin Acetate with Benzeneseleninic Anhydride

To a solution of hecogenin acetate (100 mg, 0.21 mmol) in chlorobenzene (1 ml) was added benzeneseleninic anhydride (152 mg, 0.42 mmol) and the suspension heated to 95°C with stirring under nitrogen for 50 min. The reaction was followed carefully by both t.l.c. and i.r. spectroscopy. The reaction mixture was washed through a short silica column with petrol containing 10% methylene chloride and the crude products released from the column by eluting with methanol. The residue on evaporation of the methanol (166.7 mg) was subjected to p.l.c. (methylene chloride: methanol, 93:7) which afforded 9(11)-dehydrohecogenin acetate (90.3 mg, 91%), m.p. 217-220° (from methanol), (lit.[44], 218-220°), ν_{max} 1730 and 1670 cm^{-1}, λ_{max} 237 nm (ε 1900), (lit.[44], λ_{max} 238 nm (ε 1500)), $|\alpha|_D^{22}$ - 7.6° (C 1.00), (lit.[44], $|\alpha|_D^{22}$ - 8.7°).

Preparation of 1α,2α-Epoxycholesta-1,4,6-trien-3-one from Cholesta-4,6-dien-3-one

To a solution of cholesta-4,6-dien-3-one (10.0 g, 0.028 mol) in dry chlorobenzene (80 ml), heated to 95°C with stirring in the dark was added benzeneseleninic anhydride (10.0 g, 0.027 mol) in portions over a period of 1 h. The solution was allowed to crystallised at 0°C and the benzeneseleninic acid (4.6 g) filtered at the pump and washed with a little cold chlorobenzene. The filtrate was distilled under reduced pressure to yield a yellow oil. The oil was dissolved in methanol (250 ml) at room temperature and treated with methanolic sodium hydroxide (10%, 2.6 ml) and hydrogen peroxide (30%, 18 ml) and allowed to stand at room temperature overnight. Cooling to -30°C afforded crude 1α,2α-epoxycholesta-1,4,6-trien-3-one (6.0 g, 54%) m.p. 96-98° (from methanol, 5.5 g, 50%). Further recrystallisation from methanol/acetone afforded pure 1α,2α-epoxycholesta-1,4,6-trien-3-one m.p. 104-106° (lit.[32], 106-108°), λ_{max} 291 nm (ε 18500) (lit.[32], λ_{max} 292 nm (ε 19000)), $|\alpha|_D^{22}$ + 192° (C 1.00) (lit.[32], $|\alpha|_D$ + 200°).

TABLE 12 : SUMMARY OF FAILED DEHYDROGENATION REACTIONS OF STEROIDS

Substrate	BSA moles	Time	Comments
Pregnenolone acetate	1	15 min	26% starting material as the only characterisable product.
Pregnenolone acetate	1	25 min	38% starting material plus selenium containing mixture (mass spectrum)
Pregnanone acetate	1	2 h	Many products on t.l.c.

/continued...

TABLE 12/continued...

Substrate	BSA moles	Time	Comments
Progesterone	2	1 h	82% mixture - dehydro and many phenylselenated products.
Progesterone	1.2	2 h	Followed carefully by i.r. but mass spectrum shows product (88%) of compounds.
Progesterone	2	1 h	Mixture. Several i.r. absorptions 1600-1700 cm^{-1}. Major component (43%) unresolved mixture.
Cholesterol	1	1 h	Mixture rapidly blackened. Many products.
Cholesteryl acetate	1	1 h	Slower than cholesterol but similar messy reaction
Andosterone acetate	1	1 h	Many products on t.l.c.
3β-acetoxy-16α-methyl-5-pregnan-20-one	1	$2\frac{1}{2}$ h	I.r. showed no 1-enone. T.l.c. very many products.

Reaction of Benzilic Acid with Benzeneseleninic Anhydride

To a solution of benzilic acid (114 mg, 0.5 mmol) in chlorobenzene (0.6 ml) was added benzeneseleninic anhydride (180 mg, 0.5 mmol) and the suspension heated to reflux with stirring for 20 h. P.l.c. afforded benzophenone (86.5 mg, 95%), m.p. 57-58° (from ethanol) (lit.[33], 57-58°) identical with authentic samples.

Reaction of Lanostanone with Phenylseleninic Acid

To a solution of lanostanone (100 mg, 0.23 mmol) in dry chlorobenzene (0.7 ml) was added phenylseleninic acid (85 mg, 0.45 mmol) and the mixture heated to 100°C with stirring for 150 min. P.l.c. afforded lanost-1-en-3-one (63.5 mg, 64%), m.p. 119-120° (from methanol), (lit.[42], m.p. 118-120°), identical to previous samples and A-norlanostan-3-one (9.4 mg, 10%), m.p. 98-100° (frome ethanol/water), identical with previous samples.

Reaction of Hecogenin Acetate with Phenylseleninic Acid

To a solution of hecogening acetate (100 mg, 0.21 mmol) in chlorobenzene (0.8 ml) was added benzeneseleninic acid (77 mg, 0.41 mmol) and the mixture heated to 100°C with stirring for 160 min. P.l.c. afforded 9(11)-dehydrohecogenin acetate (80.8 mg, 81%), m.p. 217-220° (from methanol), (lit.[44], 218-220°), identical with previous samples.

Reaction of Benzoyl Peroxide with Diphenyl diselenide

To a solution of diphenyl diselenide (156 mg, 0.5 mmol) in dry methylene chloride (5 ml) was added benzoyl peroxide (339 mg, 1.5 mmol) and the solution heated to reflux overnight. P.l.c. afforded (1) unreacted diphenyl diselenide (11.5 mg, 7%), m.p. 61-63° (lit.[38], m.p. 63°), (2) benzoic acid (273 mg), m.p. 120-121° (from water), (lit.[45], m.p. 122°), and (3) a mixture of benzoic acid and benzeneseleninic acid (196 mg) shown to contain benzeneseleninic acid (158 mg, 100% based on recovered diphenyl diselenide).

Reaction of Diphenyl Diselenide with Benzoyl Peroxide and 2-Naphthol

To a solution of diphenyl diselenide (156 mg, 0.5 mmol) in dry T.H.F. was added benzoyl peroxide (242 mg, 1.0 mmol) and the solution heated to reflux for 1 h. 2-Naphthol (74 mg, 0.5 mmol) was added and heating continued for a further 10 min. P.l.c. afforded 1-selenophenyl-2-naphthol (54.2 mg, 34%) m.p. 76-78° (lit.[24], m.p. 77-78°) and 1,2-naphthoquinone (24 mg, 22%), m.p. 144-146° (from benzene), (lit.[24], m.p. 145-146°).

Reaction ot t-Butylhydroperoxide with Cholestan-3-one with Diphenyl Diselenide as catalyst

To a solution of cholestan-3-one (50 mg, 0.14 mmol) in dry chlorobenzene (1 ml) was added diphenyl diselenide (7 mg, 0.02 mmol) and t-butylhydroperoxide (35 mg, 0.39 mmol) and the solution heated to 95°C with stirring under nitrogen for 4h. P.l.c. afforded cholest-1-en-3-one (21.4 mg, 43%), m.p. 90-92° (from methanol) (lit.[46], 43%) m.p. 90-92° (from methanol) (lit.[46], m.p. 92°), λ_{max} 232 nm (ε 10000) (lit.[47], λ_{max} 232 nm (ε 10500)) and cholesta-1,4-dien-3-one (14.2 mg, 28%) as an oil, λ_{max} 242 nm (ε 9000), (lit.[29], λ_{max} 242 nm (ε 15000)).

Catalytic Dehydrogenation of Lanostan-3-one using t-Butylhydroperoxide and Diphenyl Diselenide

To a solution of lanostan-3-one (100 mg, 0.23 mmol) in chlorobenzene (1 ml) was added diphenyl diselenide (15 mg, 0.048 mmol) and t-butylhydroperoxide (110 mg, 1.22 mmol) and the solution heated to 100°C with stirring under nitrogen for 25 min. P.l.c. afforded lanost-

-1-en-3-one (68.5 mg, 69%), m.p. 107-113° (from methanol), (lit.[42], m.p. 118-120°), ν_{max} 1710 cm^{-1} (contaminant approx. 20%) and 1670 cm^{-1}, λ_{max} 232 nm (ε 6400) (lit.[42], λ_{max} 229 nm (ε 9000)).

Reaction of Acenaphthalene with Benzeneseleninic Anhydride

To a solution of acenaphthalene (50 mg, 0.33 mmol) in dry T.H.F. (5 ml) was added benzeneseleninic anhydride (118 mg, 0.33 mmol) and the mixture heated to reflux for 18 h. P.l.c. afforded diphenyl diselenide (87.8 mg, 85%), m.p. 61-63° (lit.[38], 63°) and acenaphthaquinone (55.3 mg, 92%) m.p. 259-260° (from ethanol, 54.1 mg, 90%), (lit.[48], 260°), ν_{max} 1710, 1600, 1280, 1210, 1010, 900, 840, and 780 cm^{-1}.

Oxidation of Anthracene using Benzeneseleninic Anhydride

To a solution of anthracene (89 mg, 0.5 mmol) in hot, dry chlorobenzene (3 ml) was added benzeneseleninic anhydride (180 mg, 0.5 mmol) and the solution heated to reflux with stirring for 15 min. T.l.c. showed complete conversion into the quinone. On cooling, a colourless solid separated which was washed free of benzeneseleninic acid using saturated sodium bicarbonate solution and dried under vacuum to give 9, 10-anthraquinone (84.5 mg, 81%), m.p. 285-287° (lit.[49], 286° sub.), identical with authentic material.

Oxidation of trans – stilbene with Benzeneseleninic Anhydride

To a solution of trans-stilbene (100 mg, 0.56 mmol) in dry chlorobenzene (5 ml) was added benzeneseleninic anhydride (300 mg,

0.83 mmol) and the suspension heated to reflux with stirring for 12 h. The reaction mixture was filtered through a short silica column and washed with petrol containing 10% methylene chloride. The column was subseuqently eluted with methanol and the residue on evaporation of solvent was subjected to p.l.c. to afford benzil (111 mg, 96%) m.p. 95-96° (from ethanol) (lit.[50], 95-96°), ν_{max} 3010, 1660, 1600, 1450, 1230, 1300, 1215, 1180, 1000, 880, 800, and 730 cm^{-1}.

Oxidation of Camphor with Benzeneseleninic Anhydride

To a solution of camphor (100 mg, 0.66 mmol) in chlorobenzene (3 ml) was added benzeneseleninic anhydride (236 mg, 0.66 mmol) and the suspension heated to reflux with stirring for 12 h. T.l.c. showed almost complete reaction. The reaction mixture was filtered down a short silica column and washed with petrol containing 10% methylene chloride to remove the chlorobenzene and most of the diphenyl diselenide. The column was washed with methanol and the methanolic solution subjected to p.l.c. (methylene chloride, 2% methanol) which afforded camphorquinone (81.1 mg, 74%) m.p. 198-199° (lit.[51], 199°) $\nu_{max.}$ 1770, 1750, 1320, 1360, 1050, 1000, 970 and 900 cm^{-1}.

Reaction of o-Xylene with Benzeneseleninic Anhydride

Benzeneseleninic anhydride (200 mg, 0.56 mmol) was added to dry o-xylene (2 ml, 1.66 mmol) and the mixture heated to reflux under nitrogen with stirring for 10 h. A solution of 2,4-dinitrophenylhydrazine (200 mg, 1.01 mmol) in methanol (2 ml) containing sulphuric

acid (0.2 ml) was added to the cooled reaction mixture. An orange solid separated which after filtration afforded o-tolualdehyde 2,4-dinitrophenylhydrazone (106.2 mg, 33%), m.p. 195-7° (from ethanol) (lit.[52], 194°). The filtrate, after evaporation, was subjected to column chromatography (silica gel, petrol) to afford diphenyl diselenide (171 mg, 93%) m.p. 61-63°, (lit.[38], 63°).

Reaction of m-Xylene with Benzeneseleninic Anhydride

Benzeneseleninic anhydride (200 mg, 0.56 mmol) was added to dry m-xylene (2 ml, 1.63 mmol) and the mixture heated to reflux with stirring under nitrogen for 10 h. A solution of 2,4-dinitrophenylhydrazine (200 mg, 1.01 mmol) in methanol (2 ml) containing sulphuric acid (0.2 ml) was added to the cooled reaction mixture. An orange solid separated which after filtration afforded m-tolualdehyde 2,4-dinitrophenylhydrazone (156.8 mg, 49%) m.p. 201-203° (from ethanol), (lit.[53] 194°). The filtrate, after evaporation was subjected to column chromatography (silica gel, petrol) to afford diphenyl diselenide (123 mg, 71%), m.p. 61-63° (lit.[38], 63°).

Reaction of p-Xylene with Benzeneseleninic Anhydride

Benzeneseleninic anhydride (200 mg, 0.56 mmol) was added to dry p-xylene (2 ml, 1.62 mmol) and the mixture heated to reflux with stirring under nitrogen for 10 h. A solution of 2,4-dinitrophenylhydrazine (200 mg, 1.01 mmol) in methanol (2 ml) containing sulphuric acid (0.2 ml) was added to the cooled reaction mixture. An orange solid separated which after filtration afforded p-tolualdehyde

2,4-dinitrophenylhydrazone (166 mg, 52%), m.p. 234-6° (from ethanol), (lit.[54], 234°). The filtrate, after evaporation was subjected to column chromatography (silica gel, petrol) to afford diphenyl diselenide (163.3 mg, 93%) m.p. 61-63° (lit.[38], 63°).

Oxidation of 2-Quinaldine with Benzeneseleninic Anhydride

(a) Isolation of 2-quinaldehyde as its 2,4-D.N.P.

To a solution of 2-quinaldine (72 mg, 0.50 mmol) in chlorobenzene (5 ml) was added benzeneseleninic anhydride (180 mg, 0.50 mmol) and the stirred suspension heated to reflux under nitrogen for 15 min. The solution was allowed to cool to 70°C before adding a solution of 2,4-dinitrophenylhydrazine (200 mg, 1 mmol) in methanol (2 ml), containing sulphuric acid (0.2 ml). A bright yellow solid separated which was recrystallised from pyridine to afford 2-quinaldehyde 2,4-dinitrophenylhydrazone (94.8 mg, 59%), m.p. 249-252° (lit.[55], 253°).

(b) Isolation as free 2-quinaldehyde

To a solution of 2-quinaldine (143 mg, 1 mmol) in chlorobenzene (5 ml) was added benzeneseleninic anhydride (120 mg, 0.30 mmol) and the suspension heated to reflux with stirring under nitrogen for 2h. P.l.c. afforded diphenyl diselenide (88.9 mg, 89%), m.p. 62-63° (lit.[38], 63°) 2-quinaldine (46.3 mg, 37%) and 2-quinaldehyde (68.0 mg, 43%), m.p. 65-8° (lit.[56], 71°).

Oxidation of 2-Picoline with Benzeneseleninic Anhydride

To a solution of 2-picoline (93 mg, 1 mmol) in dry chlorobenzene (5 ml) was added benzeneseleninic anhydride (120 mg, 0.33 mmol) and the stirred suspension heated to reflux under nitrogen for 2 h. A solution of 2,4-dinitrophenylhydrazine (200 mg, 1 mmol) in methanol (2 ml) containing sulphuric acid (0.2 ml) was added to the cooled solution. A yellow solid separated which was recrystallised from pyridine to afford 2-picoline 2,4-dinitrophenylhydrazone (112.9 mg 41%), m.p. 235-236° (from pyridine) (lit.[57], m.p. 235°).

Reaction of Benzyl Alcohol with excess Benzeneseleninic Anhydride

To a solution of benzyl alcohol (50 mg, 0.46 mmol) in dry benzene (5 ml) was added benzeneseleninic anhydride (333mg, 0.93 mmol) and the suspension heated to reflux under nitrogen for 3 h. After 20 min, t.l.c. showed no further change. The cooled mixture was extracted with aqueous sodium hydroxide (5%, 2 x 5 ml) and the base extract acidified with concentrated hydrochloric acid. Sodium metabisulphite solution (15%, 5 ml) was added and the solution extracted with ether (3 x 7 ml) The etherial extract after drying and evaporating under reduced pressure afforded diphenyl diselenide (209.7 mg, 0.672 mmol), m.p. 61-63° (lit.[38], 63°). The organic layer was treated with a solution of 2,4-dinitrophenylhydrazine (200 mg, 1.01 mmol) in methanol (2 ml) containing sulphuric acid (0.2 ml). A red solid separated which after filtration and washing with ice cold methanol afforded benzaldehyde 2,4-dinitrophenylhydrazone (133.5 mg, 99.5%), m.p. 236-237° (lit.[58], 237°). The filtrate was subjected to column chromatography (silica gel, petrol) to afford diphenyl diselenide (51.7 mg, 0.116 mmol).

Oxidation of Cinnamyl Alcohol with Benzeneseleninic Anhydride

To a solution of cinnamyl alcohol (120 mg, 0.90 mmol) in chlorobenzene (2 ml) was added benzeneseleninic anhydride (120 mg, 0.30 mmol) and the suspension heated to reflux with stirring under nitrogen for 10 h. The solution was allowed to cool to 70°C before adding a solution of 2,4-dinitrophenylhydrazine (200 mg, 1 mmol) in methanol (2 ml) containing sulphuric acid (0.2 ml). Cinnamaldehyde 2,4-dinitrophenylhydrazone (154.4 mg, 53%) separated on cooling, m.p. 250-251° (from ethanol) (lit.[59], 251-253°), identical with authentic material (i.r. mixed m.p.). The mother liquor after chromatography down a short silica column yielded diphenyl diselenide (102 mg, 100%), m.p. 62-63° (lit.[38] 53°).

Reaction of Lanostanol with Benzeneseleninic Anhydride

To a solution of lanostanol (100 mg, 0.23 mmol) in dry chlorobenzene (0.7 ml) was added benzeneseleninic anhydride (84 mg, 0.23 mmol) and the stirred suspension heated at 100° for 90 min. P.l.c. afforded lanost-1-en-3-one (72.5 mg, 73%), m.p. 116-118° (from ethanol, 58 mg, 58%) (lit.[42], m.p. 119-120°), identical with previous samples.

Preparation of Furanoyl Hydrazobenzene

To a solution of phenylhydrazine (216 mg, 2 mmol) in ethanol (4 ml) containing pyridine (0.2 ml) was added furfuroyl chloride (260 mg, 2 mmol) and the solution heated to its boiling point. Water (2 ml) was added and the mixture allowed to crystallise to give furanoyl hydrazobenzene (350 mg, 86%), m.p. 142-145° (from ethanol/

water), ν_{max} 3240 and 1630 cm^{-1} (Found: C, 65.05; H, 4.95; N, 13.7. $C_{11}H_{10}N_2O_2$ requires C, 65.35; H, 5.0; N, 13.85%).

Preparation of Furanoyl Hydrazo-p-nitrobenzene

To a solution of p-nitrophenylhydrazine (153 mg, 1 mmol) in hot ethanol (2 ml) containing pyridine (0.1 ml) was added furanoyl chloride (130 mg, 1 mmol). The reaction mixture was allowed to stand for 5 min at 50-60°C then water (0.5 ml) was added to give, on cooling furanoyl hydrazo-p-nitrobenzene (170 mg, 69%), m.p. 179-180°C (from ethanol/water), ν_{max} 3230 and 1650 cm^{-1}. (Found: C, 53.55; H, 3.7; N, 17.0. $C_{11}H_9N_3O_4$ requires C, 53.45; H, 3.65; N, 17.0%).

Preparation of 2-Naphthoyl Hydrazobenzene

To a solution of phenylhydrazine (216 mg, 2 mmol) in ethanol (4 ml) containing pyridine (0.2 ml) was added 2-naphthoyl chloride (380 mg, 2 mmol) and the solution heated to reflux for 5 minutes. Water (0.5 ml) was added and the mixture allowed to crystallise to give 2-naphthoyl hydrazobenzene (347 mg, 62%), m.p. 185-186°, ν_{max} 3200 and 1650 cm^{-1} (Found: C, 77.85; H, 5.4; N, 10.65. $C_{17}H_{14}N_2O$ requires C, 77.85; H, 5.4; N, 10.7%).

Preparation of 2-Naphthoyl Hydrazo-p-Nitrobenzene

To a solution of p-nitrophenylhydrazine (153 mg, 1 mmol) in hot ethanol (2 ml) containing pyridine (0.1 ml) was added 2-naphthoyl

chloride (190 mg, 1 mmol) and the solution heated to reflux for 5 min. Water (0.5 ml) was added and the mixture allowed to crystallise to give 2-naphthoyl hydrazo-p-nitrobenzene (234 mg, 72%), m.p. 246-248° (from ethanol/water), ν_{max} 3200 and 1630 cm^{-1}. (Found: C, 65.9; H, 4.2 N, 13.5. $C_{17}H_{13}N_3O_3$ requires C, 66.45; H, 4.25; N, 13.65%).

Reaction of Benzoyl Hydrazobenzene with Benzeneseleninic Anhydride

To a solution of benzoyl hydrazobenzene (50 mg, 0.25 mmol) in T.H.F. (1.5 ml) was added benzeneseleninic anhydride (90 mg, 0.25 mmol) and the suspension stirred at room temperature for 10 minutes. P.l.c. afforded benzoyl azobenzene (42.5 mg, 85%) as an oil, identical (i.r. m.s., n.m.r.) with previous samples.

Reaction of Benzoyl Hydrazo-p-nitrobenzene with Benzeneseleninic Anhydride

To a solution of benzoyl hydrazo-p-nitrobenzene (50 mg, 0.20 mmol) in T.H.F. (2 ml) was added benzeneseleninic anhydride (73 mg, 0.20 mmol) and the suspension stirred at room temperature for 10 minutes. P.l.c. afforded benzoyl azo-p-nitrobenzene (49.5 mg, 99%) m.p. 98-99° (from ethanol), identical with previously prepared samples.

Reaction of Furanoyl Hydrazobenzene with Benzeneseleninic Anhydride

To a solution of furanoyl hydrazobenzene (50 mg, 0.25 mmol) in T.H.F. (1.5 ml) was added benzeneseleninic anhydride (90 mg, 0.25 mmol) and the suspension stirred at room temperature for 10 minutes.

P.l.c. afforded furanoyl azobenzene (46 mg, 92%) as an oil with identical i.r. , n.m.r. and m.s. to previously prepared samples.

Reaction of 2-Furanoyl Hydrazo-p-nitrobenzene with Benzeneseleninic Anhydride

To a solution of furanoyl hydrazo-p-nitrobenzene (50 mg, 0.20 mmol) in dry T.H.F. (1.5 ml) was added benzeneseleninic anhydride (73 mg, 0.20 mmol) and the suspension stirred at room temperature for 10 min. P.l.c. afforded 2-furanoyl azo-p-nitrobenzene (47.4 mg, 95%) m.p. 187-189° (from methanol, 43.0 mg, 86%) identical to other previously prepared samples and diphenyl diselenide (17.4 mg, 27%), m.p. 61-63° (lit.[38], 63°).

Reaction of Naphthoyl Hydrazobenzene with Benzeneseleninic Anhydride

To a solution of naphthoyl hydrazobenzene (50 mg, 0.20 mmol) in T.H.F. (2 ml) was added benzeneseleninic anhydride (76 mg, 0.21 mmol) and the suspension stirred at room temperature for 10 min. P.l.c. afforded naphthoyl azobenzene (36 mg, 72%) as an oil, with identical i.r., n.m.r. , and m.s. to previously prepared samples.

Reaction of Naphthoyl Hydrazo-p-nitrobenzene with Benzaneseleninic Anhydride

To a solution of naphthoyl hydrazo-p-nitrobenzene (50 mg, 0.16 mmol) in T.H.F. (2 ml) was added benzeneseleninic anhydride (64 mg, 0.18 mmol) and the suspension stirred at room temperature for 10 min. P.l.c.

afforded naphthoyl azo-p-nitrobenzene (44.5 mg, 89%), m.p. 141-142° (from ethanol, 40 mg, 80%), identical to previously prepared samples.

Control Reaction of Furanoyl Hydrazo-p-nitrobenzene with N-Bromosuccinimide

To a solution of furanoyl hydrazo-p-nitrobenzene (50 mg, 0.20 mmol) in methylene chloride (5 ml) containing pyridine (0.2 ml) was added N-bromosuccinimide (72 mg, 0.40 mmol) and the solution stirred at room temperature for 2 min. The mixture was extracted with dilute sulphuric acid (2M, 1 x 3 ml) and subjected to p.l.c. which afforded furnaoyl azo-p-nitrobenzene (39 mg, 78%) m.p. 187-189° (from methanol, 31.9 mg, 64%), identical with previously prepared samples.

The results of several similar experiments are summarised in Table 4 (see Discussion).

Reaction of Hydrazobenzene with Benzeneseleninic Anhydride

To a solution of hydrazobenzene (92 mg, 0.50 mmol) in dry T.H.F. (2 ml) was added benzeneseleninic anhydride (180 mg, 0.50 mmol) and the suspension stirred at room temperature for 5 min. P.l.c. (petrol) afforded azobenzene (91 mg, 99%), m.p. 65-67° (from ethanol/water, 87mg, 94%), (lit.[60], 67-68°), λ_{max} 315 (ε 4300) and 435 nm (940), (lit.[61], λ_{max} 313 (ε 5100) and 430 nm (890)).

Reaction of Phenylhydroxylamine with Benzeneseleninic Anhydride

To a solution of phenylhydroxylamine (109 mg, 1 mmol) in T.H.F. (5 ml) was added benzeneseleninic anhydride (360 mg, 1 mmol) and the suspension stirred at room temperature for 3 min. P.l.c. (petrol, under nitrogen) afforded diphenyl diselenide (85.9 mg, 28%) m.p. 61-63° (lit.[38] 63°) and nitrosobenzene (98.1 mg, 91%), m.p. 65-67° (lit.[62], 68°).

Reaction of t-Butylhydroxylamine with Benzeneseleninic Anhydride

To a solution of t-butylhydroxylamine (38.4 mg, 0.431 mmol) in T.H.F. (1 ml) was added a solution of benzeneseleninic anhydride (200 mg, 0.556 mmol) in T.H.F. (7 ml) and the mixture made up to exactly 10.0 ml with T.H.F. The transmission of the solution at 685 nm was measured and the yield of nitroso-t-butane (96%) estimated from the calculated extinction coefficient[26].

Preparation of 4-phenyl-1,2,4-triazoline-3,5-dione and Trapping with Ergosterol Acetate

To a solution of 4-phenyl-1,2,4-triazolidine-3,5-dione (50 mg, 0.28 mmol) in T.H.F. (2 ml) containing ergosterol acetate (112 mg, 0.25 mmol) was added benzeneseleninic anhydride (180 mg, 0.5 mmol) and the suspension stirred at room temperature until a deep red colour developed (3-4 min). P.l.c. (methylenechloride:petrol, 50:50) afforded the adduct (120.1 mg, 78%) m.p. 172-174° (from ethanol, 111 mg, 72%)

(lit.[63], 173-175°), $|\alpha|_D^{22}$ - 114° (C 1.0) (lit.[63], $|\alpha|_D$ - 118° (C 0.98)), δ, 7.25 (5H, m), 6.2 (2H, m), and 5.1 (2H, m).

Reaction of N,N'-Dicarbethoxyhydrazide with Benzeneseleninic Anhydride

To a solution of N,N-dicarbethoxyhydrazide (100 mg, 0.57 mmol) in dry benzene (3 ml) was added benzeneseleninic anhydride (100 mg, 0.28 mmol) and the suspension heated to reflux with stirring for 5 min. The cooled solution was extracted with saturated sodium bicarbonate solution (2 x 3 ml) and the combined bicarbonate extracts extracted with methylene chloride (2 x 3 ml). The combined organic extracts after drying resulted in an oil which was distilled twice under vacuum (0.1 mm) to afford N,N-dicarbethoxyazide (77.2 mg, 44%), ν_{max} 1780, 1370, 1240, 1020, 860, and 810 cm^{-1}, λ_{max} 404 nm (ε 229) (lit.[64], λ_{max} 405 nm (ε 240)), δ 1.5 (2H, t), and 4.5 (3H, q).

Reaction of Diphenyldiazomethane with Benzeneseleninic Anhydride

To a solution of diphenyldiazomethane (97 mg, 0.5 mmol) in T.H.F. (1 ml) was added benzeneseleninic anhydride (180 mg, 0.5 mmol) and the suspension stirred at room temperature for 50 min. P.l.c. afforded benzophenone (81.3 mg, 89%), m.p. 47-48° (lit.[33], 49°) identical to authentic material.

Reaction of Cyclohexanone-Morpholine Enamine with Benzeneseleninic Anhydride

To a solution of cyclohexanone-morpholine enamine (167 mg, 1 mmol)

in T.H.F. (3 ml) cooled to 0°C was added benzeneseleninic anhydride (360 mg, 1 mmol) and the suspension stirred at 0°C for 1 h. Dilute sulphuric acid (2M, 5 ml) was added and the mixture allowed to warm up to room temperature. The mixture was extracted with methylene chloride (3 x 5 ml) and the dried extract evaporated to yield an oil. P.l.c. (petrol:methylene chloride; 70:30) afforded diphenyl diselenide (179.6 mg, 58%), m.p. 61-63°, (lit.[38] 63°), and 2-selenophenylcyclohexanone (93.1 mg, 38%) m.p. 54-55° (from petrol), ν_{max} 1700, 1580, 1120, 1000, and 920 cm^{-1}, δ 7.8-7.2 (5H, m), 3.9 (1H, m) and 2.4-2.8 (8H, m), m/e 244. (Found: C, 56.7; H, 5.4. $C_{12}H_{14}OSe$ requires C, 56.45; H, 5.55%).

Reaction of o-Phenylenediamine with Benzeneseleninic Anhydride

To a solution of o-phenylenediamine (108 mg, 1 mmol) in T.H.F. (2 ml), cooled to -17°C in a salt/ice bath was added benzeneseleninic anhydride (360 mg, 1 mmol) and the suspension stirred for 30 min. P.l.c. (petrol) afforded a red, non-polar band (180 mg) and no diphenyl diselenide. Further p.l.c. followed by recrystallisation from petrol at -78°C afforded N,N'-selenophenyldehydro-o-phenylenediamine (55.2 mg, 13%), m.p. 49-50°, ν_{max} 1570, 1470, 1440, 1400, 1020, 750, and 700 cm^{-1}, λ_{max} 236 (ε 21700), 440 (8000), and 494 nm (12350), δ 6.7-8.1 (4H, m). No molecular ion at 418 m/e 261 (M^+ - PhSe) (Found: C, 51.6; H, 3.35; N, 6.55. $C_{18}H_{14}N_2Se_2$ requires C, 51.7; H, 3.35; N, 6.7%).

Reaction of 2,4,6-Trimethylaniline with Benzeneseleninic Anhydride

To a solution of 2,4,6-trimethylaniline (135 mg, 1 mmol) in T.H.F. (2 ml) was added benzeneseleninic anhydride (360 mg, 1 mmol) and the suspension stirred at room temperature for 10 min. P.l.c. (petrol:

methylene chloride, 70:30) afforded azomesitylene (70 mg, 52%), m.p. 73-4° (from petrol), (lit.[65], 75°), λ_{max} 240 (ε 1000), 329 (8500), and 464 nm (800) (lit.[65] λ_{max} 241 (ε 7900), 332 (1300), and 462 nm (950)), δ 6.8 (2H, s), 2.4 (6H, s), and 2.3 (3H, s), m/e 266.

Reaction of p-Nitrophenylhydrazine with Benzeneseleninic Anhydride

To a solution of p-nitrophenylhydrazine (153 mg, 1 mmol) in T.H.F. (5 ml) at 0°C was added benzeneseleninic anhydride (360 mg, 1 mmol) and the suspension stirred with cooling for 20 min. P.l.c. (petrol, multiple elution) afforded (1) diphenyl diselenide (90.1 mg, 32%), m.p. 61-63° (lit.[38], 63°, (2) nitrobenzene (32.8 mg, 27%), identical by i.r. and u.v. to authentic material, and (3) p-selenophenylnitrobenzene (112 mg, 63%), m.p. 57-58.5° (from methylene chloride/petrol), (lit.[66], 58°), λ_{max} (ε 3800) and 346 nm (100) (lit.[67] $\lambda_{max.}$ 275 (ε 3980) and 340 nm (ε 1000), δ 8.1-7.1 (m), m/e 279.

Reaction of p-Nitrophenylhydrazine with excess Benzeneseleninic Anhydride

A solution of p-nitrophenylhydrazine (76 mg, 0.50 mmol) in T.H.F. (5 ml) was added to a stirred suspension of benzeneseleninic anhydride (360 mg, 1 mmol) in T.H.F. (2 ml) at room temperature over a period of 40 min. P.l.c. (petrol, multiple elution) afforded (1) diphenyl diselenide (69.5 mg, 22%), m.p. 61-63° (lit.[38] 63°), (2) nitrobenzene (44.7 mg, 72%), $\lambda_{max.}$ 260 nm (ε 8000) (lit.[69] $\lambda_{max.}$ 260 nm (ε 8100))

and (3) p-nitroselenophenylbenzene (22.5 mg, 16%) m.p. 57-58.5° (from methylene/chloride/petrol), (lit.[67] 58°), identical with previously prepared samples.

Reaction of p-Nitrophenylhydrazine with Benzeneseleninic Anhydride in the presence of Lithium Phenylselenate

To a solution of p-nitrophenylhydrazine (77 mg, 0.5 mmol) in T.H.F. (3 ml) was added lithium phenylselenate (196 mg, 1 mmol) and benzeneseleninic anhydride (180 mg, 0.5 mmol). The solution was stirred at room temperature for 45 min. P.l.c. (petrol, multiple elution) afforded p-selenophenylnitrobenzene (60.3 mg, 43%), m.p. 57-59° (from methylene chloride/petrol) (lit.,[66] m.p. 58°) and nitrobenzene (4.2 mg, 7%), λ_{max} 260 nm (ε 8000), (lit.[68], λ_{max} 260 nm (ε 8100)).

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