Tetrahedron Vol. 41, No. 21, pp. 4727 to 4738, 1985
Printed in Great Britain.

0040-4020/85 $3.00 + .00

STUDIES ON THE REACTION OF PRIMARY AND SECONDARY AMINES WITH PHENYLSELENINIC ANHYDRIDE AND WITH PHENYLSELENINIC ACID

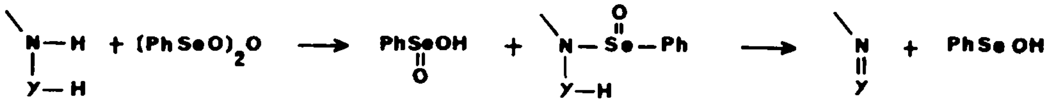
DEREK H.R. BARTON, XAVIER LUSINCHI and PIERRE MILLIET*

Institut de Chimie des Substances Naturelles, C.N.R.S.,
91190 Gif-sur-Yvette, France

(*Received in USA* 16 *November* 1984)

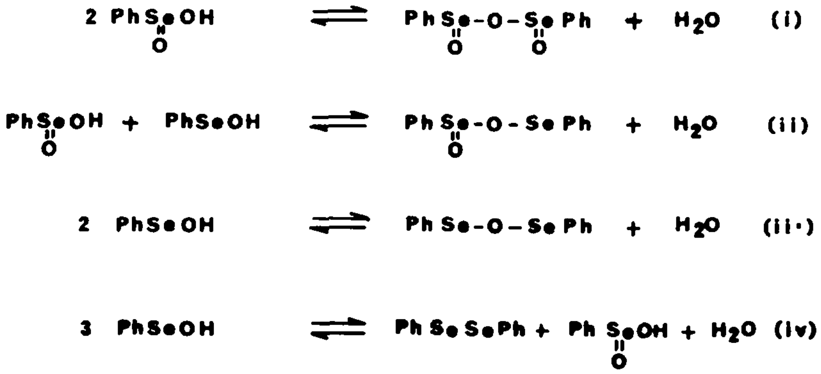
Abstract - The dehydrogenation under mild conditions of indolines with phenylseleninic anhydride or acid affords good yields of indoles or of 3-phenylselenenyl indoles. Tetrahydroquinoline and -isoquinoline show comparable behaviour. The dehydrogenation of primary amines gives more complicated mixtures from which nitriles and bis-2-phenylselenenylaldehydes can be isolated.

In principle, the reaction of phenylseleninic anhydride with a nitrogen function containing an N-H bond leads to an N-selenoxide with concomitant formation of a molecule of phenylseleninic acid. The presence of hydrogen atoms α to the nitrogen allows the subsequent elimination of a molecule of phenylselenenic acid (Scheme 1).



Scheme 1

The phenylselenenic and phenylseleninic acids thus liberated are subject to the various equilibria in Scheme 2.[1]



$$2\ \mathrm{Ph}\underset{\overset{\|}{\mathrm{O}}}{\mathrm{Se}}\mathrm{OH} \rightleftharpoons \mathrm{Ph}\underset{\overset{\|}{\mathrm{O}}}{\mathrm{Se}}\mathrm{{-}O{-}}\underset{\overset{\|}{\mathrm{O}}}{\mathrm{Se}}\mathrm{Ph} + H_2O \qquad \text{(i)}$$

$$\mathrm{Ph}\underset{\overset{\|}{\mathrm{O}}}{\mathrm{Se}}\mathrm{OH} + \mathrm{PhSeOH} \rightleftharpoons \mathrm{Ph}\underset{\overset{\|}{\mathrm{O}}}{\mathrm{Se}}\mathrm{{-}O{-}SePh} + H_2O \qquad \text{(ii)}$$

$$2\ \mathrm{PhSeOH} \rightleftharpoons \mathrm{PhSe{-}O{-}SePh} + H_2O \qquad \text{(iii)}$$

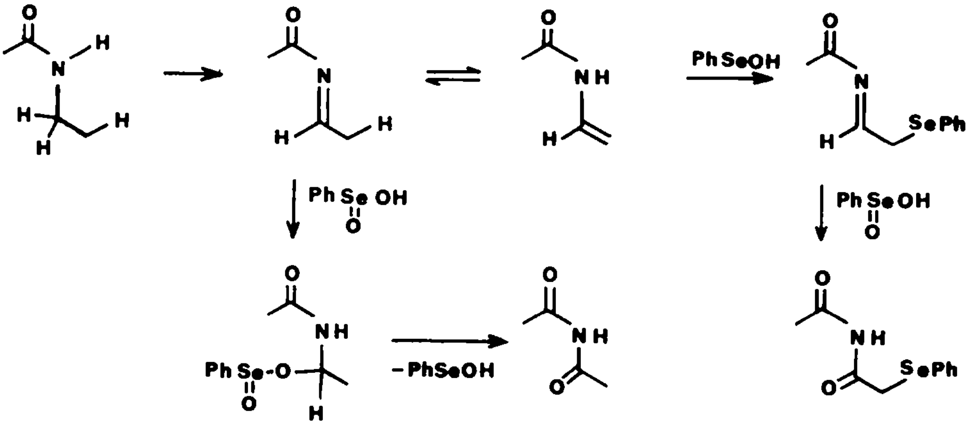
$$3\ \mathrm{PhSeOH} \rightleftharpoons \mathrm{PhSeSePh} + \mathrm{Ph}\underset{\overset{\|}{\mathrm{O}}}{\mathrm{Se}}\mathrm{OH} + H_2O \qquad \text{(iv)}$$

Scheme 2

These equilibria are demonstrative of both the nucleophilic and electrophilic properties of these reagents which, when present in the reaction mixture, can react with either starting materials or products according to Scheme 1.

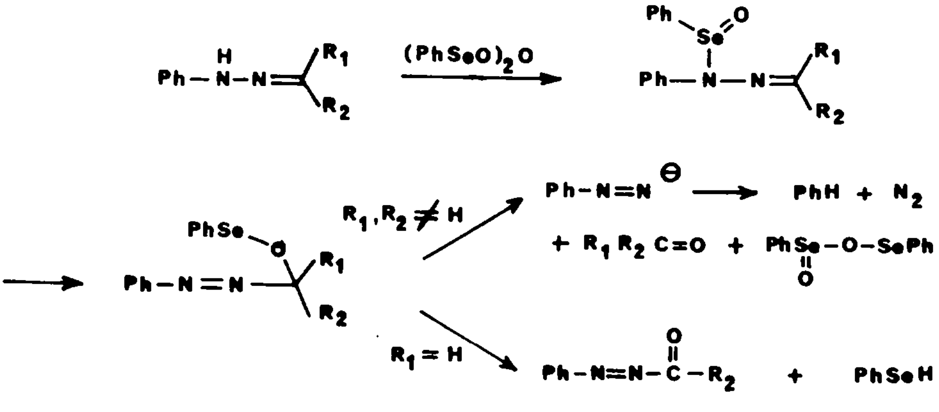
For orbital reasons which are well appreciated for a given element the compounds at a lower valence usually react faster than the corresponding compounds with a higher valence : for example $C^{II} > C^{IV}$, $P^{III} > P^{V}$, $S^{II} > S^{IV} > S^{VI}$. If we suppose that selenium follows the same principle then the establishement of the equilibrium (iii) should be the fastest, followed by (iv), then (ii) and (i) should be the slowest.

Simple dehydrogenations of secondary amines, which have no C-H bonds to the nitrogen, to imines have been observed.[2] Hydrazines and hydrazides give the corresponding azo derivatives[3,4] whilst hydroxylamines are oxidised to nitroso derivatives.[3] Secondary reactions leading to nitriles have been observed with primary amines[2] as well as with amides which react according to scheme 3.[5]



Scheme 3

When there is no hydrogen on the atom α- to the nitrogen the substrate, activated by N-selenoxide formation, follows a different reaction pathway undergoing sigmatropic rearrangement as is shown in Scheme 4 for a phenylhydrazone, but which is equally applicable to semi-carbazones or oximes.[3].



Scheme 4

The dehydrogenation of primary and secondary amines by phenylseleninic anhydride has been limited to a few special cases, the formation of imines and nitriles being observed, only when the isomerisation of the imines to enamines was not possible (no hydrogen on the β-carbon)[2].

In a preliminary communication[6] we demonstrated that the application of such dehydrogenations to indolines leads to indoles in good yield, and under milder conditions than those normally used. We here report fully these results and propose an explaination covering all the observations made.

RESULTS

The reaction of indoline 1 with half a mole of phenylseleninic anhydride, or with one mole of phenylseleninic acid, in THF at room temperature gave, after 1 hour, 2-phenylselenenylindole 6 in 93% yield. When one mole of anhydride was used a similar result was obtained and apart from 6 only a trace of selenoxide 7 was found in the reaction. The following reactions served to confirm the structure of 3-phenylselenenylindole 6. Nickel boride[7] reduction gave indole 5 in 98% yield. The derivative 6 was alternatively synthesised by the action of butyl lithium, then diphenyldiselenide 14 on indole in THF or by deoxygenation with sodium dithionite of selenoxide 7, which could itself be obtained from 6 by treatment with hydrogen peroxide or by reaction of half a mole of phenylseleninic anhydride with indole. In a similar manner 2-methylindoline 2 gave, almost quantitatively, 2-methyl-3-phenyl-selenenylindole 8 which was subsequently reduced to 2-methylindole with nickel boride. Diphenyldiselenide 14 was only formed in trace amounts, observable by t.l.c. in these reactions.

Contrastingly 3-methylindoline did not undergo phenylselenenation at the 3 position but gave 3-methylindole 10 in 54% yield together with unidentified secondary products and a small amount of 3-methyl-2-phenylselenenyl indole 11. Unlike the first two reactions the mass balance was low and furthermore an appreciable quantity of diphenyldiselenide was formed (41% isolated). Analogous results were obtained with methyl-2-(3'-indolinyl)acetate 4 where the indole 12 was formed in 89% together with a trace of the 2-phenylselenenyl derivative and of diphenyldiselenide.

The action of phenylselenenic anhydride on tetrahydroisoquinoline 15 gave only 3,4-dihydroisoquinoline 16 and diphenyldiselenide. 90% yields of dihydroisoquinoline and diphenyldiselenide were obtained when 1.08 mole of anhydride were used for 3 moles of amine.

A different result was observed with tetrahydroquinoline 17, where dehydrogenation to quinoline 18 was accompanied by phenylselenenation of the aromatic ring giving 6-phenylselenenyl tetrahydroquinoline 19, and by phenylselenenation of the heterocyclic nucleus giving the quinoline 20. Structures 19 and 20 are supported by their NMR spectra and by the existence of molecular ions in the mass spectra. Derivative 19 shows signals attributable to the 2,3 and 4 hydrogens and a doublet at δ 6.38 ppm (J = 9Hz) corresponding to an upfield shifted aromatic hydrogen signal. Substitution at 6 by selenium is compatible with the reaction mechanism and seems most likely the upfield signal being due to the aromatic hydrogen at 8. The presence of a singlet at δ 8.9 ppm for the derivative 20 is compatible with a substitution at 3 isolating the hydrogen at 2.

The action of phenylseleninic anhydride on primary amines leads to complex mixtures of products which are difficult to separate.

4-phenylbutylamine 21 in tetrahydrofuran gave 4-phenylbutylronitrile 22 in 45% yield and the diselenenated aldehyde 23 in 10% yield. Slow addition of the anhydride in the same solvent to a solution of the amine enabled isolation of aldehyde 23 in 25% yield. Inverse addition in pyridine increased the yield of nitrile to 65%. The only products isolable from the reaction with 2-phenylethylamine 24 and phenylalanine 26 were, respectively, the diselenenated aldehyde 25 (29%) and the diselenenated nitrile 27 (20%). These unstable products, which slowly lost diphenyldiselenide could only be characterised spectroscopically (M.S., I.R., N.M.R.).

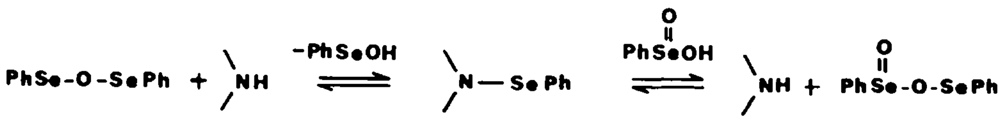
DISCUSSION

The products and stoichiometries found allow several observations to be made on these reactions which take place according to the initial Scheme 1.

The various selenium species participating in the equilibria outlined in Scheme 2 can be divided into two categories : Se^{II} reagents (PhSe-X; X = OSePh, or OH) and Se^{IV} reagents ($\mathrm{Ph\underset{\overset{\|}{O}}{Se}\text{-}X}$; X = $\mathrm{O\text{-}\underset{\overset{\|}{O}}{Se}Ph}$, OSePh or OH) both of which can in principal react at nitrogen.[2,8]

Tetrahydroquinoline was dehydrogenated quantitatively to the imine with a third of a mole of anhydride and with the formation of a stoichiometric amount of diphenyldiselenide. All the equivalents of $\mathrm{Ph\overset{O}{\overset{\|}{Se}}\text{-}X}$, two from the anhydride and one from the disproportionation of phenylselenenic acid according to equation (iv) (Scheme 2), therefore underwent reaction at nitrogen. Seemingly the various PhSe-X species, although capable of reacting with the nitrogen[8] did not do so.

Such a result can be interpreted by assuming the difference in reactivity of the $\mathrm{Ph\underset{\overset{\|}{O}}{Se}\text{-}X}$ and PhSeX species towards nitrogen centres to be so great that the latter had barely reacted at all. In view of the known[8] selenenating properties of selenamides PhSe-N$<$ it is in principle possible that these, too, take part in equilibria (Scheme 5) of the same kind as those described in Scheme 2, but that these reaction rates could be slowler than those of the alternative equilibria (Scheme 2).



Scheme 5

The observed selectivities could be explained, in this case, by the irreversible conversion of the amine to the imine.

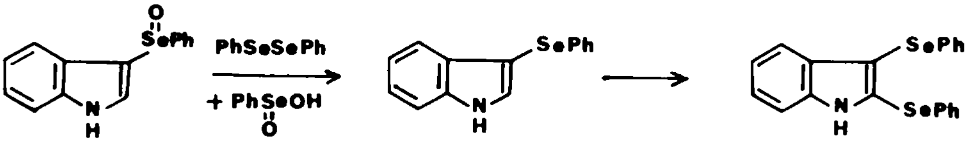
In the case of indoline half a mole of anhydride was consumed and 3-phenylselenenylindole was the product. Unlike isoquinoline the first formed imine isomerised to indole, which is nucleophilic at the 3 position and captures selenenating species (Scheme 6). It is noteworthy that as with isoquinoline the relatively hard $\mathrm{Ph\underset{\overset{\|}{O}}{Se}X}$ species have reacted selectively with the relatively

Scheme 6

hard nitrogen and that the relatively soft PhSeX species have reacted with the relatively soft 3 position. PhSeX reagents therefore react more rapidly than $Ph\underset{\underset{O}{\parallel}}{Se}X$ reagents with carbon nucleophiles. The fact that formation of selenoxide 7 from indole requires several hours whereas selenide 6 is formed in only 30 minutes under the same conditions directly supports this hypothesis.

In contrast to indolines not substituted at position 3, 3-methylindoline 3 and methyl-2-(3'-indolinyl)acetate 4 did not undergo phenylselenenation at 3, but led directly to the corresponding indoles. This is most easily explained by a lowering of nucleophilicity at the 3 position by the increased steric hindrance. It must be pointed out, however, that as the reactions were carried out with half a mole of reagent all the equivalents of $Ph\underset{\underset{O}{\parallel}}{Se}\text{-}X$ must have been consumed by the substrate and that consequently the PhSeX reagents reacted according to Scheme 2 reaction (iv). It was interesting, therefore, to ascertain whether 3-substituted indoles undergo reaction at this position with phenylselenenating reagents.

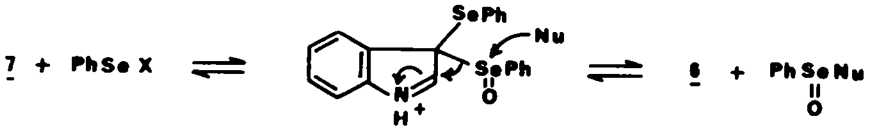
The selenoxide 7 reacted immediately with a mixture of phenylseleninic acid and diphenyldiselenide giving, at first, the 3-phenylselenide 6 which itself was transformed more slowly to the 2,3-di-phenylselenide 13 (Scheme 7).



7 6 13

Scheme 7

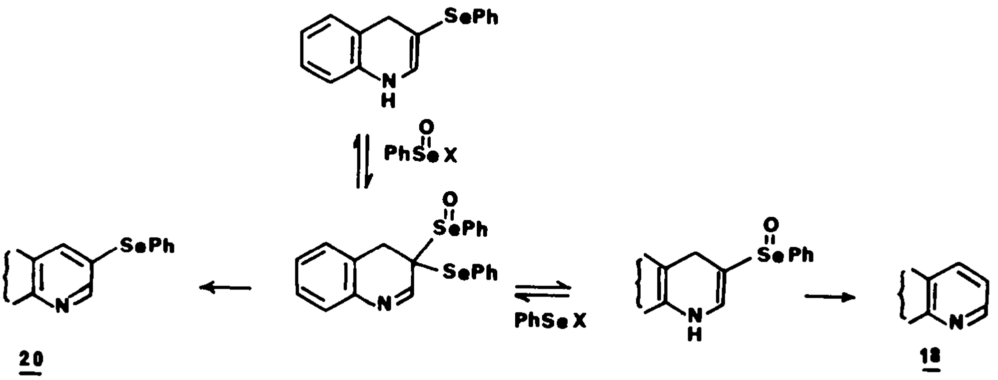
Reaction of equimolar amounts of substrate and reagents gave the di-phenyl selenide 13 in 47% yield after 25 hours, whereas the use of only half a mole of reagents retarded the reaction and allowed isolation of the selenide 6 in 43% yield after 3 days. This result can be explained as in Scheme 8 (Nu = nucleophile), by supposition of the intermediary of an intermediate doubly selenenated at position 3.



Scheme 8

The diselenated intermediate is vinylogous to a selenamide and can consequently react as a seleninating or selenenating reagent. The isolation of 13 effectively demonstrates that 6 is nucleophilic and in order for reaction to occur at position 3 it must react via this centre. Selenide 6 is therefore more stable than selenoxide 7. Furthermore the stability of 6 and 7 is related to the aromaticity of their structures, which is absent from 3,3-disubstituted indoles.

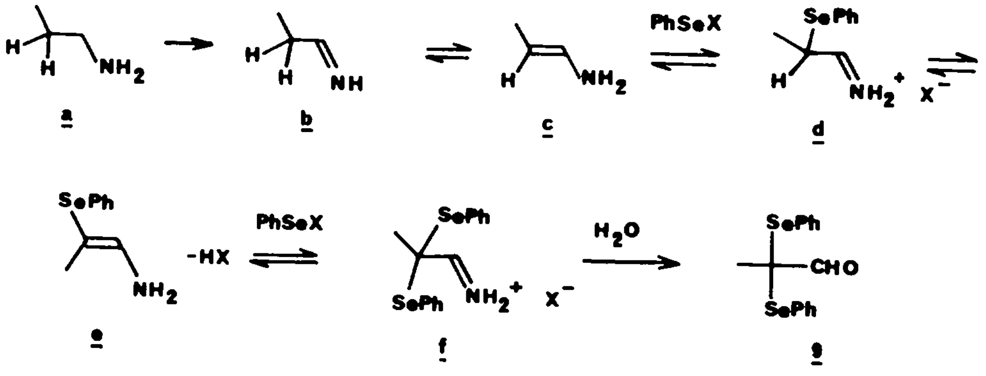
Comparison of the results obtained with tetrahydroquinoline and tetrahydroisoquinoline confirm the previously observed difference in reactivity between amines yielding imines capable of existing in equilibrium with enamines and those unable to do so. Furthermore the isolated products correspond to the intervention of the two kinds of selenating reagents in the reaction, and moreover the formation of quinoline and 3-phenylseleninylquinoline can be interpretated as in Scheme 9.



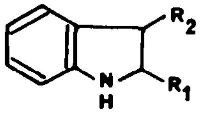
Scheme 9

It is noteworthy that, unlike the indolines, tetrahydroquinoline reacts directly on the aromatic nucleus with selenenating reagents.

The conclusions that can be drawn are limited in the case of primary amines by the low mass balances observed. The first of the two reactions observed with 4-phenylbutylamine 21, formation of nitrile 22, results from two successive reactions of the kind shown in Scheme 3. The second, formation of the doubly selenenated aldehyde 23, can be interpretated as in Scheme 10.



Scheme 10

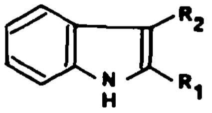


1 $R_1 = R_2 = H$

2 $R_1 = CH_3$, $R_2 = H$

3 $R_1 = H$, $R_2 = CH_3$

4 $R_1 = H$, $R_2 = CH_2CO_2CH_3$



5 $R_1 = R_2 = H$

6 $R_1 = H$, $R_2 = SePh$

7 $R_1 = H$, $R_2 = Se(O)Ph$

8 $R_1 = CH_3$, $R_2 = SePh$

9 $R_1 = CH_3$, $R_2 = H$

10 $R_1 = H$, $R_2 = CH_3$

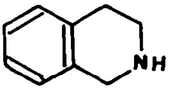
11 $R_1 = SePh$, $R_2 = CH_3$

12 $R_1 = H$, $R_2 = CH_2CO_2CH_3$

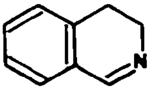
13 $R_1 = R_2 = SePh$

PhSe Se Ph

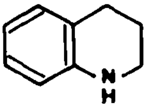
14



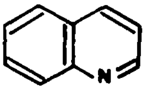
15



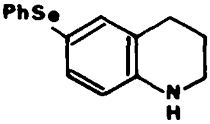
16



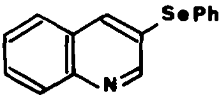
17



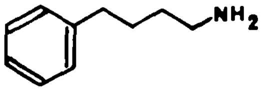
18



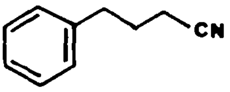
19



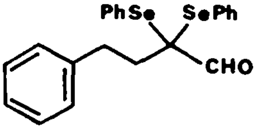
20



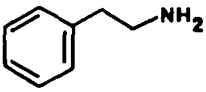
21



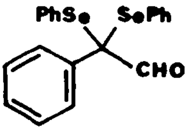
22



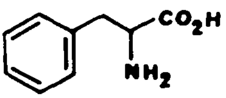
23



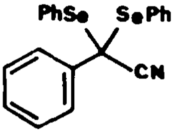
24



25



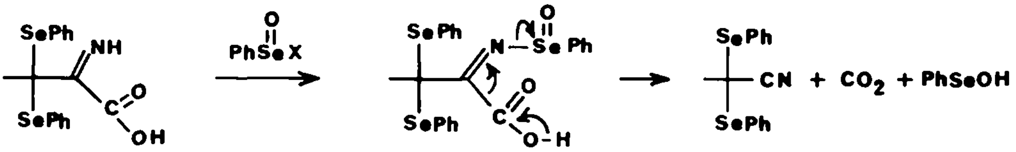
26



27

The aldehyde, therefore, results from the hydrolysis of the immonium ion f, the necessary water being generated in situ. Variation of the conditions enables the reactions to be directed to a certain extent either towards nitrile formation or towards formation of the doubly selenenated aldehyde. Slow addition of the amine to a large excess of reagent favours phenylselenination over phenylselenenation, of the intermediate b and, therefore, eventually nitrile formation. Inverse addition of the anhydride (deficiency of anhydride) ensures that, according to the preceeding conclusions, the $\mathrm{Ph\underset{\underset{O}{\|}}{Se}X}$ reagents react selectively at nitrogen giving the imine b. However equilibrium b $\rightleftharpoons$ c is now attainable, thus allowing subsequent reaction of the phenylselenenating species at carbon. The same arguments as used in the indoline series are therefore applicable here. We note that in the formation of aldehyde 25 one mole more of PhSeX reagent is consumed than is generated by imine formation and that consequently the yield of aldehyde cannot be quantitative. It depends on the amount of nitrile formed.

The formation of the doubly selenenated nitrile 27 from phenylalanine can be explained by a decarboxylative elimination (Scheme 11).



Scheme 11

If this be the case then hydrolysis of intermediate f in Scheme 10 is not the determining factor.

In conclusion, the treatment of a primary or secondary amine with phenylseleninic anhydride or acid yields the imine, which is either isolated as such or after isomerisation to the enamine as in the case of indolines. The enamine form can itself undergo further reaction with the selenium derivatives present in the reaction mixture. The various substrates studied indicate a preference of selenium IV species for nitrogen nucleophiles and of selenium II species for carbon nucleophiles.

The conversion of an indoline into an indole is a reaction frequently employed as a terminal step in the synthesis of ergot alkaloids.[9] It is also a step which often has a low yield. We expect phenylseleninic acid or anhydride to be a useful reagent in the future. Indeed Professor I. Ninomiya has recently informed us[10] that these reagents can be applied advantageously in his elegant synthesis of lysergic acid.[11]

EXPERIMENTAL

Melting points were taken in capillary tubes and are corrected. IR spectra were recorded as nujol mulls. UV spectra are in ethanolic solution and NMR spectra in deuterochloroform with tetramethylsilane as internal standard. Commercial phenylseleninic anhydride was dried under vacuum for 30 minutes at 70°. Indolines 2, 3 and 5 were prepared by literature[12] methods by reduction of the corresponding commercial indoles.

3-Phenylselenenylindole 6

i) From indoline 1.- Indoline (98 mg, 0.82 mmole) was added to a suspension of phenylseleninic anhydride (149 mg, 0.41 mmole) in THF (3 ml). After stirring for 1 h. under nitrogen at 20° the reaction was evaporated to dryness and the residue filtered on silica gel. Elution with dichloromethane gave 6 (220 mg, 98%) as a white crystalline solid mp 143° (ether-hexane), δ 7.05 to 7.80 (10H, aromatic H), 8.38 (1H, m, NH), m/e 273,271 (M^+), 193 (100%, M-Se), ν3400, 1570 cm^{-1}, λ_{max} 250 nm (15,000). (Found C, 61.50; H, 4.19; N, 5.26. Calc. for $C_{14}H_{11}NSe$ C, 61.77; H, 4.07; N, 5.15). Under identical conditions indoline (125 mg, 1.05 mmole) and phenylseleninic acid (208 mg, 1.1 mmole) in THF (10 ml) gave 6 (265 mg, 93%), mp 142°.

To a solution of 6 (142 mg, 0.52 mmole) and nickel chloride hexahydrate (1.185 g, 5 mmole) in 95% ethanol (20 ml) at 0°C was added progressively sodium borohydride (380 mg) in water (3 ml). After stirring at 20° for 18 hrs under nitrogen the black precipitate was filtered off. Ether extraction of the filtrate gave indole (60 mg, 98%) which was homogeneous and identical to an authentic sample by t.l.c.

(ii) From Phenylseleninylindole 7.- Sodium hydrosulphite (5 mg) in water (1 ml) was added to 7 (8 mg) in methanol (2 ml) and the mixture stirred for 30 mins previous to dilution with ether. After washing with water, evaporation of the ether gave 6 (8 mg) homogeneous by t.l.c. and identical to that obtained from indoline.

2-Methyl-3-phenylselenenylindole 8

Phenylseleninic anhydride (180 mg, 0.5 mmole) was added under a nitrogen atmosphere to 2-methylindoline 2 (133 mg, 1 mmole) in THF (5 ml). After 1 h stirring, during which the mixture became homogeneous, the reaction was evaporated to driness, taken up in dichloromethane and filtered on silica gel giving 8 (286 mg, 100%) as a white crystalline solid homogeneous by t.l.c., mp 98° (ether-hexane), δ 2.38 (3H, s, CH_3), 7.0 to 7.8 (9H, aromatic H), 7.89 (1H, m, NH), m/e 287, 285 (M^+), 207 (100%, M-Se), ν3400, 1570 cm^{-1}, λ_{max} 250 nm (14000) (Found C, 62.76; H, 4.61; N, 5.02. Calc. for $C_{15}H_{13}NSe$ C, 62.94; H, 4.60; N, 4.89). Under similar conditions 2 (133 mg, 1 mmole) and phenylseleninic acid (360 mg, 1,9 mmole) gave, after crystallisation from ether-hexane, 8 (199 mg, 70%) mp 98°. Sodium borohydride (380 mg, 10 mmole) was added at 0° with stirring under nitrogen to a solution of 8 (245 mg, 0.86 mmole) and nickel chloride hexahydrate (1.185 g, 5 mmole) in 95% ethanol (20 ml). The reaction was allowed to come to room temperature and then heated to reflux for 4 hrs. After filtration of the black precipitate the reaction was diluted with ether, washed with water and evaporated to driness giving a crude product (145 mg) which after purification by prep. t.l.c. gave 9 (96 mg, 84%) identical by t.l.c. and n.m.r. to an authentic sample.

3-Methylindole 10

A solution of 3-methylindoline 3 (114 mg, 0.84 mmole) in THF (3 ml) under nitrogen was treated with phenylseleninic anhydride (154 mg, 0.43 mmole). After stirring for 1 h. the mixture, diluted with ether, was washed with aqueous sodium bicarbonate, then with water and finally evaporated to dryness. Prep. t.l.c. (eluant ether-hexane 1:4) of the crude product (195 mg) gave 10 (61 mg, 54%) identical to an authentic sample and 3-methyl-2-phenylselenenylindole 11 (28 mg, 11%), δ 2.41 (3H s, CH_3), 7.0 to 7.75 (9H, m, aromatic H), 7.95 (1H, m, NH), m/e 287, 285 (M^+), 207 (100% M-Se) and diphenyldiselenide (55 mg, 41%).

Methyl-2(3'-indolyl)acetate 12

Phenylseleninic anhydride (137 mg, 0.38 mmole) was added under nitrogen to a solution of indoline 4 (145 mg, 0.76 mmole) in THF (5 ml). After stirring for 2 hrs the reaction was diluted with ether, washed with aqueous sodium bicarbonate and water. Evaporation of the solvent followed by prep. t.l.c. (dichloromethane) of the crude product (192 mg) gave diphenyldiselenide (34 mg, 29%) and 12 (128 mg, 89%) identical to an authentic sample.

3-Phenylseleninylindole 7

i) From 3-Phenylselenenylindole 6.- A solution of 6 (52 mg, 0.19 mmole) in THF (5 ml) was treated with 33% hydrogenperoxide (36 μl) for 18 hrs at 20°. After filtration and washing with THF, white crystalline 7 (37 mg, 67%) was obtained, mp 103° dec. (MeOH), δ (CD_3OD) 7.0 to 8.05 (m, aromatic H), ν 1570, 1240, 800, 790 cm^{-1}, λ_{max} 269 nm (11,200). This unstable derivative whose mass spectra, both chemical and electronic ionisation, showed no molecular ion, begins to decompose on standing for several days at room temperature (Found C, 58.26; H, 3.70; N, 4.68; O, 5.31. Calc. for $C_{14}H_{11}NOSe$ C, 58.34; H, 3.85; N, 4.86; O, 5.55).

(ii) From indole 5. - Phenylseleninic anhydride (180 mg, 0.5 mmole) was added under nitrogen to a solution of indole (117 mg, 1 mmole) in THF (3 ml) and dichloromethane (3 ml). After stirring for 18 hrs at 20° the white crystals that were deposited (220 mg, 76%) were filtered off, washed and dried and shown to be identical to 7 obtained as above.

Action of a Mixture of Phenylseleninic Acid and of Diphenyldiselenide on 3-Phenylseleninylindole 7 : 2,3-bis(Phenylselenenyl)indole 13

A solution of 7 (29 mg, 0.1 mmole) in dichloromethane (3 ml) was treated with diphenyldiselenide (31 mg, 0.1 mmole) and phenylseleninic acid (19 mg, 0.1 mmole) under argon. After 25 hrs at room temperature the solution was concentrated and subject to prep. t.l.c. giving 13 (20 mg, 47%) mp 97° (ether), δ 7.0 to 7.9 (14 H, m, aromatic H), 8.50 (1H, m, NH), m/e 429, 427, 425 (M^+) ν 3400, 1580 cm^{-1}. (Found C, 56.13; H, 3.59; N, 3.14. Calc. for $C_{20}H_{15}NSe_2$ C, 56.22; H, 3.54; N, 3.28). T.l.c. analysis of the reaction mixture during the course of the reaction demonstrated the presence of substrate 7 (dichloromethane, 5% methanol, 0.5% ammonia) and of 6 and 13 (ether-hexane 1:3). Under the same conditions, but in the absence of phenylseleninic acid the selenoxide failed to react within 4 hrs. Also under the same conditions and with the following quantities 7 (50 mg, 0.17 mmole), diphenyldiselenide (30 mg, 0.096 mmole) and phenylseleninic acid (17 mg, 0.09 mmole) t.l.c. showed after 3 days the presence of 6 and a small amount of 13 as well as substrate 7. Prep. t.l.c. (hexane-ether 1:3) enabled the isolation of 6 (20 mg, 43%).

3,4-Dihydroisoquinoline 16

Phenylseleninic anhydride (110 mg, 0.3 mmole) was added to 1,2,3,4-tetrahydroisoquinoline 15 (109 mg, 1.08 mmole) in THF (5 ml). After 18 hrs at room temperature the reaction was extracted with 10% aqueous hydrochloric acid. Evaporation of the organic phase gave diphenyldiselenide (76 mg, 90%). The aqueous phase made alkaline, yielded 16 (100 mg, 93%) containing a trace of starting material. Filtration on basic alumina gave 16 (81 mg, 75%) identical to an authentic sample.

Reaction of 1,2,3,4-Tetrahydroquinoline

Phenylseleninic anhydride (144 mg, 0.4 mmole) was added over 1 h. to a solution of 17 (120 mg, 0.9 mmole) in THF (3 ml). After 18 hrs at room temperature, followed by ether extraction, the crude product (225 mg) was subject to prep. t.l.c. (hexane-ether 2:1) giving recovered 17 (14 mg, 12%), quinoline 18 (18 mg, 15.5%) and a mixture of 19 and 20 (130 mg) which after further purification by prep. t.l.c. (dichloromethane-hexane 1:1) gave 19 (93 mg, 36%) mp. 67° (MeOH), δ 1.80 (2H, m, H at 3), 2.73 (2H, m, H at 4), 3.33 (2H, m, H at 2), 3.65 (1H, m, NH), 6.38 (1H, d, J = 9Hz, H at 8), 7.0 to 7.5 (2H, m, aromatic H), m/e 289, 287 (M^+), 209 (M-Se), ν 3350, 1580, 1560, 1020 cm^{-1} (Found C, 62.22; H, 5.19; N, 4.92. Calc. for $C_{15}H_{15}NSe$ C, 62.50; H, 5.25; N, 4.86) and 20 (35 mg, 14%) mp. 91° (MeOH), δ 7.26 to 8 (10H, m, aromatic H), 8.9 (1H, s, H at 2), m/e 285, 283 (M^+), 205 (M-Se), ν 1580, 1020, 950 cm^{-1} (Found C, 63.49; H, 3.74; N, 4.99. Calc. for $C_{15}H_{11}NSe$ C, 63.39; H, 3.90; N, 4.93).

4-Phenylbutyronitrile 22; 4-phenyl-2,2-bis(phenylselenenyl)butanal 23

A solution of 4-phenylbutylamine 21 (94 mg, 0.63 mmole) and phenylseleninic anhydride (152 mg) in THF (4 ml) was stirred under nitrogen at room temperature for 18 hrs. The residue obtained on evaporation to dryness was subject to prep. t.l.c. (ether-hexane 1:4) yielding diphenyldiselenide (72 mg); 23 (28 mg) mp 97.5°, δ 1.90 (2H, m, H at 4), 3.0 (2H, m, H at 3), 6.80 to 7.65 (15H, m, aromatic H), 9.37 (1H, s, CHO), m/e 460, 458, 456 (M^+), 303, 301 (M-PhSe), ν 1690 cm^{-1} (Found C, 57.75; H, 4.42; O, 3.64. Calc. for $C_{22}H_{20}OSe_2$ C, 57.65; H, 4.40; O, 3.49) and 4-phenylbutyronitrile 22 (41 mg), 2.0 (2H, m, H at 3), 2.17 (2H, m, 2H at 4), 3.02 (2H, m, H at 2), 7.20 (5H, m, aromatic H), ν 2230 cm^{-1}. 4-phenylbutylamine (149 mg, 1 mmole) was added over 4 hrs to a solution of phenylseleninic anhydride (360 mg, 1 mmole) in pyridine (3 ml) at 70°. The reaction was kept at 70° for 18 hrs, ether extracted and purified by prep. t.l.c. giving 4-phenylbutyronitrile 22 (96 mg, 65%) and diphenyldiselenide (182 mg). Addition over 4 hrs of phenylseleninic anhydride (142 mg, 0.67 mmole) to a solution of 4-phenylbutylamine (100 mg, 0.62 mmole) in THF (5 ml) at 70°, followed by stirring at 70° for 18 hrs gave, after chromatography on silica gel, diphenyldiselenide (87 mg) and aldehyde 23 (77 mg, 25%). Nitrile 22 was only formed in trace quantities (t.l.c.).

2,2-bis(Phenylselenenyl)-2-phenylacetaldehyde **25**

Phenylseleninic anhydride (283 mg, 0.78 mmole) was added to a solution of 2-phenylethylamine **24** (95 mg, 0.78 mmole) in pyridine (3 ml). After 4 hrs at 80°, under nitrogen, ether extraction and subsequent prep. t.l.c. (hexane-ether 4:1) gave diphenyldiselenide (130 mg) and 2,2-bis(phenylselenenyl)-2-phenylacetaldehyde **25** (50 mg, 14%) as an unstable yellow oil which decomposed with gradual loss of diphenyldiselenide δ 9.41 (1H, s, C$\underline{H}$O), m/e 432, 430, 428 (M^+), 275, 273 (M-PhSe), ν 1690 cm^{-1}.

2,2-bis(Phenylselenenyl)-2-phenylacetonitrile **27**

Phenylalanine (165 mg, 1 mmole) was added to phenylseleninic anhydride (356 mg, 1 mmole) in pyridine (3 ml). After standing for 4 hrs at 80° the reaction was extracted with ether and the crude product purified by prep. t.l.c. (hexane-ether 4:1) yielding 2,2-bis(phenylselenenyl)-2-phenylacetonitrile **27** (98 mg, 20%) as an unstable yellow oil which lost diphenyldiselenide with time. δ 7 to 8.5 (M, aromatic H), m/e 429, 427, 425 (M^+), 272, 270 (M-PhSe), ν 2200 cm^{-1}.

REFERENCES

1 [a]H. Rheinboldt and E. Giesbrecht, Ber., **88**, 666 (1955). [b]H. Rheinboldt and E. Giesbrecht, Ber., **89**, 631 (1956). [c]W. Jenny, Helv. Chim. Acta, **41**, 317 (1958). [d]J.L. Kice, F. McAfee and H. Slebocka-Tilk, Tetrahedron letters., **23**, 3323 (1982), [e]H.J. Reich, W.W. Willis Jr. and S. Wollowitz, Tetrahedron Letters, **23**, 3319 (1982).

2 M.R. Czarny, J. Chem. Soc. Chem. Comm., 81 (1976).

3 D.H.R. Barton, D.J. Lester and S.V. Ley, J. Chem. Soc., Perk. I, 1212 (1980); J. Chem. Soc. Chem. Comm., 445 (1977); 276 (1978).

4 T.G. Back, S. Collins and R.G. Kerr, J. Org. Chem., **46**, 1564 (1981)

5 T.G. Back, J. Org. Chem., **46**, 1442 (1981).

6 D.H.R. Barton, X. Lusinchi and P. Milliet, Tetrahedron Letters, 4949 (1982) and references therein.

7 R.B. Boar, D.W. Hawkins, J.F. McGhie and D.H.R. Barton, J. Chem. Soc. Perk. I, 654 (1973) and references therein.

8 H.J. Reich and J.M. Renga, J. Org. Chem., **40**, 3313 (1975).

9 D.C. Horwell, Tetrahedron, **36**, 3123 (1980); A.P. Kozikowski, Heterocycles, **16**, 267 (1981).

10 Personal Communication, September, 1983.

11 T. Kiguchi, C. Hashimoto, T. Naito and I. Ninomiya, Heterocycles, **19**, 1873 and 2279 (1982).

12 G.W. Gribble and J.H. Hoffman, Synthesis, 859 (1977).