# Direct Conversion of Saturated Hydrocarbons into Phenylseleno Derivatives

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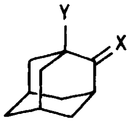
Diphenyl diselenide is an efficient trap for the carbon–iron σ-bonds postulated as intermediates in the Gif system for the substitution of saturated hydrocarbons selectively at secondary positions.

We have described before[1] the Gif system for the selective oxidation of saturated hydrocarbons at secondary positions. In its most convenient form ($\mathrm{Gif}^{\mathrm{IV}}$) this consists of an iron catalyst, oxygen, zinc dust, acetic acid (or other appropriate acid), and pyridine. This process has been adapted as an electrochemical (Gif–Orsay) system with good coulombic efficiency.[2] We now report a study of the effect of diphenyl diselenide on the Gif system.

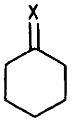
Oxidation of adamantane (**1**) under $\mathrm{Gif}^{\mathrm{IV}}$ conditions affords the oxidation products (**2**)—(**4**), with the ketone (**4**) as major product. Oxidation of (**1**) (using air) in the presence of diphenyl diselenide (Table 1) provoked a decrease in ketone (**4**) formation with the appearance of the phenyl selenides (**5**) and (**6**) (Table 1, entries 1 and 2). The identity of these isomeric phenyl selenides was established by comparison (g.l.c., n.m.r., and mass spectrometry) with authentic specimens prepared by decarboxylative chalcogenation.[3]

From blank experiments relative to the foregoing observations we reached the following conclusions: (i) there is no formation of any of the products (**2**)—(**6**) in the absence of the iron catalyst or in the absence of air; (ii) the small amount of ketone (**4**) (Table 1, entry 2) is not due to further oxidation of (**6**) in the medium, nor is this ketone destroyed in the presence of $(PhSe)_2$ [the ketone (**4**) was recovered largely (75%) unchanged in the presence or absence of $(PhSe)_2$]; (iii) in the absence of adamantane the phenyl selenides (**5**) and (**6**) are largely recovered (60%) after 7 h under the oxidation conditions. Adamantane is definitely more oxidisable than (**5**) and (**6**) under $\mathrm{Gif}^{\mathrm{IV}}$ conditions.

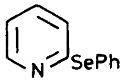
A systematic variation of the parameters of the reaction was next undertaken. Table 1 (entries 2—6) shows that the maximal yield of secondary phenyl selenide (**6**) is obtained using 0.5 mmol of $(PhSe)_2$. Increasing the amount of $(PhSe)_2$ led to an improved yield of tertiary selenide (**5**). It was of note that the amounts of pyridine–hydrocarbon coupled products stayed more or less constant (entries 1, 2, and 4); in other



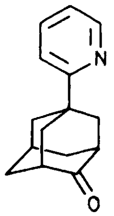
(**1**) X = H2, Y = H
(**2**) X = H2, Y = OH
(**3**) X = H, OH, Y = H
(**4**) X = O, Y = H
(**5**) X = H2, Y = SePh
(**6**) X = H, SePh, Y = H
(**7**) X = H2, Y = 2-pyridyl
(**8**) X = H2, Y = 4-pyridyl



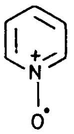
(**10**) X = H2
(**11**) X = H,OH
(**12**) X = O
(**13**) X = H, SePh



(**14**)



(**9**)



(**15**)

**Table 1.** Oxidation of adamantane (**1**) in the presence of $(PhSe)_2$.

$$(\mathbf{1}) + (PhSe)_2 + Zn + [Fe_3O(OAc)_6py_{3.5}](\Delta) + pyH + H_2O + AcOH \xrightarrow[20\,^{\circ}C]{air} (\mathbf{1}) + (\mathbf{2}) + (\mathbf{3}) + (\mathbf{4}) + (\mathbf{5})$$

2 mmol 20 mg atom 28 ml 2.3 ml 40 mmol

| Entry | $(PhSe)_2$ (mmol) | Δ ($10^{-3}$ mmol) | Product yields[a,b] (%) (**2**) | (**3**) | (**4**) | (**5**) | (**6**) | Total (%) | $C^2/C^3$ [c] | (**1**) recovered (%) | Pyridine–hydrocarbon coupled products (**7**)—(**9**) (%)[a] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | | 7 | 0.8 | 1.25 | 17.2 | | | 19.25 | 23 | 45.5 | 16 |
| 2 | 2 | 7 | 0.7 | 2.0 | 3.45 | 3.05 | 11.45 | 20.65 | 4.5 | 53.5 | 14.4 |
| 3 | 0.1 | 7 | 1.2 | 1.25 | 16.9 | — | 2.6 | 21.95 | 17.3 | 60 | |
| 4 | 0.5 | 7 | 1.15 | 1.6 | 11.7 | 1.55 | 10.65 | 26.65 | 8.85 | 51 | 16 |
| 5 | 1.0 | 7 | 0.85 | 2.3 | 6.3 | 1.9 | 10.2 | 21.55 | 3.35 | 66 | |
| 6 | 3.0 | 7 | 0.5 | 2.0 | 2.8 | 4.35 | 11.5 | 21.15 | 3.35 | 56 | |
| 7 | 2 | 0.58 | 0.9 | 2.0 | 3.0 | 1.4 | 12.7 | 20 | 7.7 | 56 | |
| 8 | 2 | 2.3 | 0.8 | 2.55 | 3.5 | 2.0 | 14.8 | 23.65 | 7.4 | 64 | |

[a] Based on substrate. [b] Yields of (**2**)—(**4**) were determined by g.l.c.; yields of (**5**) and (**6**) were determined by g.l.c. after removal of excess of $(PhSe)_2$ by reduction with $NaBH_4$ followed by alkaline work-up. [c] Total oxidised products at secondary position/total oxidised products at tertiary position. A statistical attack would give $C^2/C^3 = 3$.

**Table 2.** Effect of $(PhSe)_2$ on oxidation of cyclohexane (**10**) by the Gif$^{IV}$ system.

$$(\mathbf{10}) + \underset{\text{20 mg atom}}{\mathrm{Zn}} + \underset{\text{40 mmol}}{\mathrm{AcOH}} + \underset{7 \times 10^{-3}\,\text{mmol}}{[\mathrm{Fe_3O(OAc)_6py_{3.5}}]} + (\mathrm{PhSe})_2 \xrightarrow[\text{air, 20 °C, 9 h}]{\text{pyridine (28 ml), } \mathrm{H_2O} \text{ (2.3 ml)}} (\mathbf{11}) + (\mathbf{12}) + (\mathbf{13})$$

| (**10**) (mmol) | $(PhSe)_2$ (mmol) | (**11**) (mmol) | (**12**) (mmol) | (**13**) (mmol) | Total (mmol) | Total (%) |
|---|---|---|---|---|---|---|
| 2 | | 0.02 | 0.5 | | 0.5 | 25 |
| 2 | 1 | 0.05 | 0.15 | 0.15 | 0.35[b] | 17.5 |
| 20 | | 0.1 | 2.35 | | 2.45 | 19.25 |
| 20 | 1 | 0.35 | 1.4 | 0.8 | 2.55 | 12.75 |
| 46 | | 0.45 | 3.6 | | 4.05 | 8.8 |
| 46 | | 1.2 | 1.8 | 0.85 | 3.85 | 8.35 |
| 92[a] | | 0.45 | 3.15 | | 3.6 | 3.9 |
| 92[a] | 1 | 1.0 | 2.3 | 1.45 | 4.75 | 5.15 |

[a] From 92 mmol of (**1**) the reaction mixture is biphasic. [b] 6% [based on $(PhSe)_2$] of 2-pyridyl phenyl selenide was isolated in this experiment.

**Table 3.** Reactions of $(PhSe)_2$ with adamantane (**1**) and cyclohexane (**10**) in the presence of iron powder.

$$\text{Substrate} + (\mathrm{PhSe})_2 + \underset{\text{20 mg atom}}{\mathrm{Fe^0}} + \underset{\text{40 mmol}}{\mathrm{AcOH}} \xrightarrow[\mathrm{H_2O}\text{ (2.3 ml), air, 20—30 °C, 11 h}]{\text{pyridine (28 ml)}} \text{products}$$

| Entry | Substrate (mmol) | $(PhSe)_2$ (mmol) | Product yields[a,b] (%) | Total (%) | $C^2/C^3$ [c] | Starting material recovered (%) |
|---|---|---|---|---|---|---|
| 1 | (**1**) (2) | | (**2**) (3.6), (**3**) (<0.1), (**4**) (6.85) | 10.45 | 1.9 | |
| 2 | (**1**) (2) | 1 | (**5**) (14.8), (**6**) (17.25) | 32.05 | 1.17 | 56 |
| 3 | (**1**) (2) | 2 | (**5**) (16.85), (**6**) (18.45) | 35.35 | 1.09 | 63 |
| 4 | (**10**) (2) | 1 | (**13**) (15.05) | 15.05 | | |
| 5 | (**10**) (2) | 2 | (**13**) (18.15) | 18.15 | | |
| 6[d] | (**1**) (2) | 1 | (**3**) (1.3), (**5**) (13.0), (**6**) (15.05) | 29.35 | 1.26 | 64 |

[a,b,c] See footnotes a—c of Table 1. [d] In this experiment a pyridine–acetone mixture (1 : 1 v/v; 28 ml) was used as solvent.

words, pyridine and diphenyl diselenide do not seem to be in competition for the tertiary position of adamantane.

Because of the relative insolubility of the adamantane in the reaction medium, the effect of a higher concentration of substrate was studied using a different substrate, cyclohexane (**10**) (Table 2). Increasing concentrations of the latter led to higher conversions either in the presence or in the absence of diphenyl diselenide. Interestingly, up to 1.45 mmol of cyclohexyl phenyl selenide (**13**) were formed when 92 mmol of substrate were used, *i.e.* 72.5% of the selenium atoms incorporated in the system were transformed into cyclohexyl phenyl selenide.

In a further mechanistic investigation we compared the oxidations of perdeuteriocyclohexane, $C_6D_{12}$ (iron cluster, zinc, acetic acid, pyridine, air, 9 h, 20 °C) and cyclohexane $C_6H_{12}$ (iron cluster, zinc, AcOD, pyridine, dry air, 9 h, 20 °C) in the presence of diphenyl diselenide. Examination of the cyclohexyl phenyl selenide isolated from these reactions by g.l.c., mass spectrometric, and $^1H$ n.m.r. techniques showed that the C–D (or C–H) bond $\alpha$ to the selenium atom remained unaffected.

In the presence of an oxidant (air) and a reductant (zinc) it was difficult to conclude whether $(PhSe)_2$ or its reduced form was active in the reaction. Separate blank experiments performed under argon showed that zinc powder was a good reductant towards $(PhSe)_2$. As the reaction with hydrocarbons probably occurs with $(PhSe)_2$ and not with its reduced form, we turned to iron powder, a weaker reductant. We had, of course, begun our work on the oxidation of saturated hydrocarbons (Gif systems) using iron powder. Once again the results were dramatic.

The use of iron powder as the source of catalyst and reductant (Table 3) gave impressive results. In a typical experiment aqueous pyridine (30 ml; 6.6% v/v) was added to iron powder (1.12 g, 20 mg atom), diphenyl diselenide (2 mmol), and substrate (2 mmol). Acetic acid (40 mmol) was then added and the mixture stirred in an open-neck conical flask under air for 9 h. Extraction of the neutral products into ether [followed in the case of adamantane (**1**) as substrate by removal of the excess of $(PhSe)_2$ by reduction with $NaBH_4$ and subsequent washing with dilute sodium hydroxide] gave a crude reaction mixture which was analysed by g.l.c.

In the case of adamantane (**1**), a 32% yield of phenyl selenides (**5**) and (**6**) was obtained in the presence of 1 mmol of $(PhSe)_2$, and 56% of the substrate was recovered (Table 3, entry 2). By recycling the neutral extract obtained from this experiment, a 47% yield of phenyl selenides (**5**) and (**6**) was obtained. A slightly higher yield of (**5**) and (**6**) was obtained when 2 mmol of $(PhSe)_2$ were used (entry 3). Under the same conditions, cyclohexane (**10**) gave 18% of cyclohexyl phenyl selenide (**13**) (entry 5). It is noteworthy that half of the pyridine can be replaced by the less expensive acetone with results similar to those obtained in pyridine (Table 3, entry 6). In all the experiments performed with iron powder no oxygenated products (alcohols or ketone) could be detected and no products coupled to pyridine were formed. Again there was no reaction without air (under argon).

In a previous article[4] we have proposed that oxidation in the

Gif system involves the formation of iron–carbon σ-bonds. The present results give strong support to this hypothesis. In the case of adamantane, which is exceptional, the tertiary iron–carbon bond can evolve into radicals which are competitively captured by oxygen or pyridine. No such competition is seen at the secondary positions. The secondary/tertiary ratio for normal oxidation (pyridine coupling) is *ca.* 1.2. This is far from the the value for alkoxyl radical attack (0.15),[5] but similar to that for the new phenylselenation reaction (*ca.* 1.2). We propose that diphenyl diselenide can insert itself very efficiently into the iron–carbon σ-bond.

Recently Geletii, Shilov, and their colleagues[6] have reported on their own studies of the Gif and Gif–Orsay systems. Whilst the experimental facts are in agreement, Geletii and Shilov have proposed an interesting and novel interpretation of the mechanism of oxidation. They suggest that the real oxidant is the radical cation (**15**).

It is difficult for us to imagine that (**15**) would not attack diphenyl diselenide much faster than it attacks a saturated hydrocarbon. Clearly further work will be needed to explain the curious reactivity of saturated hydrocarbons that has now come to light.

Professor J. E. Baldwin, F.R.S. (Oxford) has kindly drawn our attention to his own, independent and prior, proposal[7] that σ-carbon–iron bonds are involved in the biosynthesis of β-lactam antibiotics. We thank Professor Baldwin cordially for this information and for a pre-publication copy of his manuscript.

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