Unexpected formation of β-(phenylseleno)alkyl nitrates by the reaction of alkenes with the diselenide–nitrogen dioxide couple

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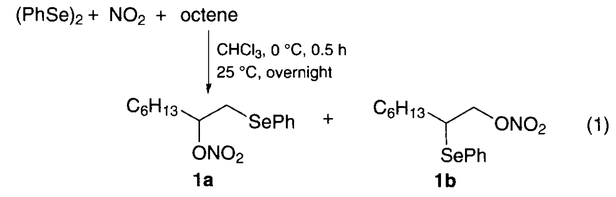
Alkenes react with NO_2 and $(PhSe)_2$ with the evolution of NO to afford high yields of β-(phenylseleno)alkyl nitrates which are easily hydrolysed to the corresponding β-hydroxyalkyl selenides.

The chemistry of nitrogen oxides and organoselenium compounds has attracted increasing interest in view of their wide applications in organic synthesis,[1] their unique biological activity[2] and/or their environmental impact.[3] However, synthetic reactions based on the combination of NO_2 and $(RSe)_2$ are unknown. This is not surprising in view of their well known reactivities; the diselenides are easily oxidized and NO_2 is highly oxidizing. Accordingly any other reactions except the oxidation of $(RSe)_2$ by NO_2 do not appear to proceed cleanly.[4] We have, however, found that β-(phenylseleno)alkyl nitrates **1** are formed in high yields when alkenes are treated with $(PhSe)_2$ and NO_2.

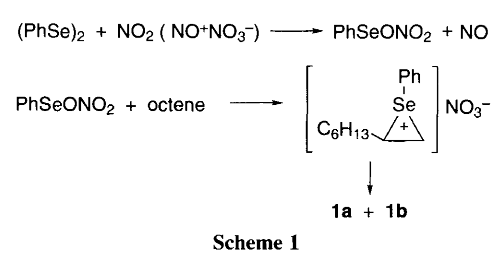
When NO_2 in CCl_4 (0.5 ml, 1 mmol) was slowly added to a solution of $(PhSe)_2$ (0.25 mmol) and octene (0.5 mmol) in $CHCl_3$ (2 ml) at 0 °C, a transparent green colour immediately developed with the vigorous evolution of a gas.[†] After the solution was kept at 0 °C for a further 0.5 h, the ice bath was removed and the solution slowly warmed to 25 °C. Stirring the solution overnight followed by preparative HPLC afforded 157 mg (95% yield) of a mixture of **1a** and **1b**[‡] (**1a**/**b** > 97/3) as a pale yellow oil [eqn. (1)].

Experiments to determine the stoichiometry of the reaction indicated that the use of 4 equiv. of NO_2 relative to $(PhSe)_2$ was necessary for the completion of the reaction. When 2 equiv. of NO_2 were employed, for example, yields of the adducts dropped to about 50% and half of the $(PhSe)_2$ was recovered unreacted. In addition to $CHCl_3$, THF and CCl_4 could also be used as solvents without significant change in the product yield.

The regioselectivity of the reaction shown in eqn. (1) seems to have resulted from the isomerization of **1b** to its thermodynamically more favourable isomer **1a**. This could indeed be confirmed by monitoring the reaction by ^1H NMR spectroscopy. Thus, when the CCl_4 solution of NO_2 was added at 0 °C, octene disappeared completely within 0.5 h to result in a quantitative formation of the adducts in a ratio of **1a**/**1b** = 64/36. This ratio of the products gradually changed on standing at 25 °C, and became 81/19 and 98/2, respectively, after 2 and 16 h. Note that this regioselectivity is quite similar to that reported for the electrophilic addition of selenenyl halids (RSeX) to alkenes which is proposed to proceed through a seleniranium ion intermediate.[5] Combining this similarity together with the stoichiometry of the reaction, we propose that the present reaction proceeds through an electrophilic addition of a selenic electrophile such as $PhSeONO_2$ to the alkene (Scheme 1). The seleniranium ion formed by the electrophilic addition of the selenenic species to the double bond undergoes ring opening upon an attack of NO_3^-. The attack at the primary carbon gives the *anti*-Markovnikov adduct **1b** whereas the attack at the more hindered but more positively charged secondary carbon forms the Markovnikov product **1a**. An attempted isolation of $PhSeONO_2$ failed.[†] However, the Se–Se bond of diselenides is easily cleaved by halogen *etc.* to form selenenic electrophiles.[5] In addition, NO_2 is known to afford $NO^+NO_3^-$ in solution.[6] Accordingly, it is quite reasonable to assume the *in situ* generation of $PhSeONO_2$ under the reaction conditions. The stereochemistry of the products is also in good agreement with the proposed mechanism involving the seleniranium ion being attacked by NO_3^- from the *anti*-side; the reaction of cyclohexene gave only the *trans*-adduct **1c**[‡] in 93% yield, and *trans*- and *cis*-oct-4-enes gave *erythro*- and *threo*-isomers respectively (*vide infra*).

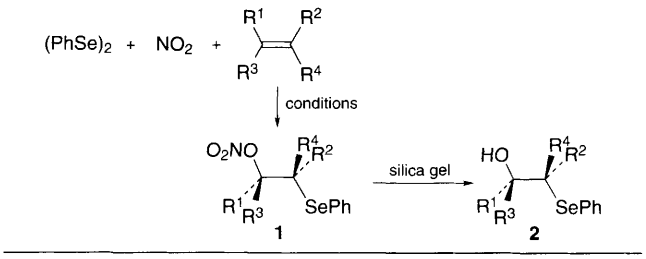


1a **1b**



Scheme 1

Table 1 Synthesis of β-hydroxyalkyl selenides by the reaction of alkenes with the $(PhSe)_2$–NO_2 couple



Alkene	Conditions	Yield of **2** (%)[a]
octene	0 °C, 0.5 h; 25 °C, 12 h	69[b]
cyclohexene	0 °C, 0.5 h	71[c]
trans-oct-4-ene	0 °C, 0.5 h	57[d]
cis-oct-4-ene	0 °C, 0.5 h	62[e]
styrene	−30 °C, 0.5 h[f]	77[g]

[a] Isolated yield. [b] **2a** ($R^1 = R^2 = R^4 = H$; $R^3 = C_6H_{13}$)/**2b** ($R^1 = R^3 = R^4 = H$; $R^2 = C_6H_{13}$) = 92/8 by ^1H NMR. [c] *Trans*-adduct. [d] *Erythro*-isomer. [e] *Threo*-isomer. [f] A messy mixture resulted when the reaction was run at 0 °C. [g] $R^1 = R^2 = R^4 = H$; $R^3 = Ph$.

The application of the reaction to organic synthesis could be readily exemplified by the easy transformation of the β-(phenylseleno)alkyl nitrates **1** to the corresponding β-hydroxyalkyl selenides **2**, a useful class of synthetic intermediates which, for example, can be readily converted into allylic alcohols, alkenes, epoxides and alkenyl selenides.[7] Their synthetic methods have been extensively studied, including those by the reaction of selenium anions with epoxides,[7] by the addition of selenium-stabilized anions to ketones or aldehydes,[7] and the simple but powerful hydroxyselenation of carbon–carbon double bonds *via* electrophilic addition of either *in situ* generated selenenic acids or more generally the incorporation of water in the addition of reactions of a number of selenenic electrophiles to alkenes.[7,8] Our present method offers another novel preparation of β-hydroxyalkyl selenides *via* the hydroxyselenation methodology. As demonstrated by Table 1, simply passing the crude reaction mixture through a short silica gel column afforded the corresponding β-hydroxyalkyl selenides in moderate to good yields.[§] In addition, only one stereoisomer was obtained from symmetrical internal alkenes, *i.e. trans*-adduct from cyclohexene, *erythro*- and *threo*-adducts from *trans*- and *cis*-oct-4-enes, respectively. As regards regioselectivity, octene formed **2a** as a major product along with a small quantity of another isomer **2b**, but styrene gave only one regioisomer.

We thank the Research Development Corporation of Japan for awarding a postdoctoral fellowship to L. B. H.

Footnotes

[†] The gas immediately turned to reddish brown upon exposure to air, indicative of NO. Evolution of the gas and the green colour were also observed in an attempted experiment to isolate PhSeONO$_2$; NO$_2$ was added to the solution of (PhSe)$_2$ at −78 °C in the absence of the alkene. As the mixture was warmed, it slowly became transparent green with evolution of a gas at about −30 °C. However, the colour faded away rather rapidly even at that temperature and a white precipitate of benzeneseleninic anhydride formed. Neither **1a** nor **1b** could be obtained when octene was added after the green colour had disappeared.

[‡] *^{1}H NMR spectral data* (CDCl$_3$, 300 MHz) for **1a** δ 7.53–7.57 (m, 2 H), 7.26–7.31 (m, 3 H), 5.10 (m, 1 H), 3.15 (dd, 1 H, *J* 5.5 and 13.1 Hz), 3.03 (dd, 1 H, *J* 5.5 and 13.1 Hz), 1.72–1.83 (m, 2 H), 1.24–1.36 (m, 8 H) and 0.88 (t, 3 H, *J* 6.4 Hz). For **1b** δ 7.24–7.62 (m, 5 H), 4.65 (dd, 1 H, *J* 5.4 and 11.8 Hz), 4.46 (dd, 1 H, *J* 9.7 and 11.3 Hz), 3.32 (m, 1 H), 1.25–1.85 (m, 10 H) and 0.80 (t, 3 H, *J* 7.0 Hz). For **1c** δ 7.57–7.61 (m, 2 H), 7.26–7.34 (m, 3 H), 5.02 (dt, 1 H, *J* 4.1 and 8.2 Hz), 3.25 (dt, 1 H, *J* 4.1 and 8.6 Hz), 2.19–2.24 (m, 2 H), 1.61–1.69 (m, 4 H) and 1.38–1.42 (m, 2 H).

[§] *General experimental procedure:* A CCl$_4$ (1 ml) solution of NO$_2$ (2 mmol) was added to a mixture of (PhSe)$_2$ (0.5 mmol) and an alkene (1 mmol) in CHCl$_3$ (3 ml) and the resulting solution was stirred under the conditions shown in Table 1. After the reaction was complete, the solution was degased twice and then a saturated aq. NaHCO$_3$ solution added. Extraction with Et$_2$O, drying (MgSO$_4$) and concentration afforded crude **1** as a yellow oil which was subsequently passed through a short silica gel column (ethyl acetate–hexane = 1 : 30) to give crude **2**. Purification by preparative TLC (silica gel, ethyl acetate–hexane = 1 : 15) gave pure **2** as a pale yellow oil.

References

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Received, 11th October 1995; Com. 5/06729D