Electrophile-induced Cyclisation–Fragmentation Reactions of Oxime *O*-Allyl and *O*-Benzyl Ethers

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Phenylselenyl bromide-induced cyclisation of γ- and δ-unsaturated aldoxime and ketoxime *O*-allyl and *O*-benzyl ethers is followed by a slow fragmentation furnishing cyclic imines which are readily reduced to pyrrolidines, piperidines or tetrahydroisoquinolines by sodium borohydride; dialkenyl oximes yield quinolizidines by an analogous sequence terminating in a mercury(II)-induced cyclisation.

Recently we have developed a range of electrophile-induced oxime–alkene reactions furnishing nitrones and their salts (Scheme 1) in excellent yield.[1–3] Such processes can be developed into oxime →nitrone→ cycloaddition cascades in appropriate cases. It occurred to us that a similar electrophile-induced cyclisation should occur for oxime ethers generating the salts **1** (Scheme 1) which could, under appropriate conditions, be transformed into nitrones, imines or, by reduction, hydroxylamines. The communication details the formation of imines from γ- and δ-unsaturated aldoximes and ketoximes by a phenylselenyl bromide-induced cyclisation–fragmentation process.†

Aldoxime ether **2** reacts rapidly with phenylselenyl bromide (1 equiv.) in acetonitrile at room temperature to give salt **3**. Keeping the reaction mixture at room temperature for 19 h results in fragmentation **3** → **4**. Reduction (2 equiv. $NaBH_4$, 1 : 1 *v*/*v* MeOH–CH_2Cl_2, 25 °C, 18 h) of **4** gives **5** (79% overall from **2**).‡ A similar sequence starting from **6** affords **7** which upon acetylation (Ac_2O, 25 °C, 1.5 h) affords **8** (60% overall from **6**). In the latter case benzaldehyde is readily detected in the fragmentation step whilst acrolein was not detected in **3** → **4** presumably owing to its instability to acid. Ketoxime ether **9** undergoes a similar sequence to furnish **10** as a 4 : 1 mixture of diastereoisomers.§ Reduction of **10** with sodium borohydride (1 : 1 MeOH–CH_2Cl_2, 25 °C, 19 h) gives **11** (65% overall from **9**) as a 4 : 1 mixture of *trans*- and *cis*-ring junction stereoisomers. The *cis*-relationship between H_A and H_B in both isomers was established from NOE data whilst the ring junction stereochemistry was assigned on the basis of coupling constants and 2-D COSY spectra.¶ (H_C is obscured by the signals of the cyclohexyl protons). The conformation of the major *trans*-isomer is shown in **12**.

The dialkenyl ketoxime ethers **13a,b** were subjected to an analogous sequence of reactions. Both underwent the cyclisation–fragmentation sequence furnishing the salts **14a,b**. Thus **13b** cyclises regiospecifically to the 6-membered imine **14b**. The alternative 7-membered imine was not detected. Sodium borohydride reduction as before afforded a mixture of the piperidines **15a** (63%) and **16a** (9%), and **15b** (60%) and **16b** (7%), respectively.§[4] The potential synthetic utility of dialkenyl oxime ethers is illustrated by the mercury(II) acetate-induced stereospecific cyclisation of **15a** to **17** (81%). The stereochemistry of **17** is based on NOE and decoupling data.¶ Thus irradiation of H_A results in a positive NOE on H_B and H_F, whilst irradiation of H_C results in a positive NOE on H_D/H_E. Additionally the chemical shifts of H_A (δ 2.47) and H_B (δ 2.75) are upfield relative to H_C (δ 3.23) implying that H_A and H_B are *trans* to the nitrogen lone pair and axially orientated whereas H_C is *gauche* to the lone pair and therefore equatorial.

While this work was in progress a report appeared describing the phenylselenyl halide-induced cyclisation of alkenylimines.[5] Further work on these and related electrophile-mediated processes are underway.

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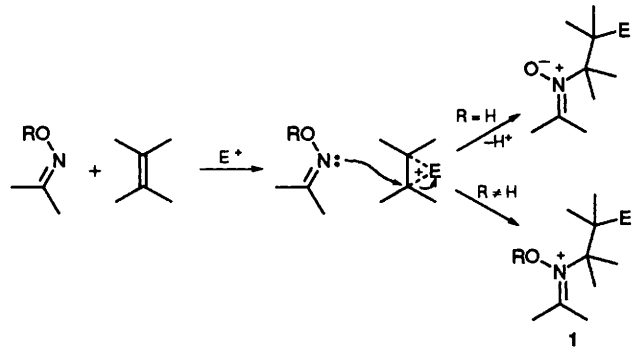
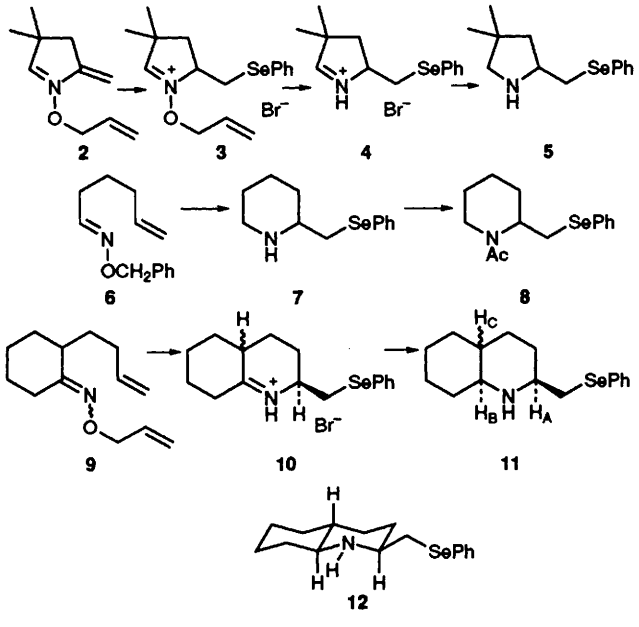
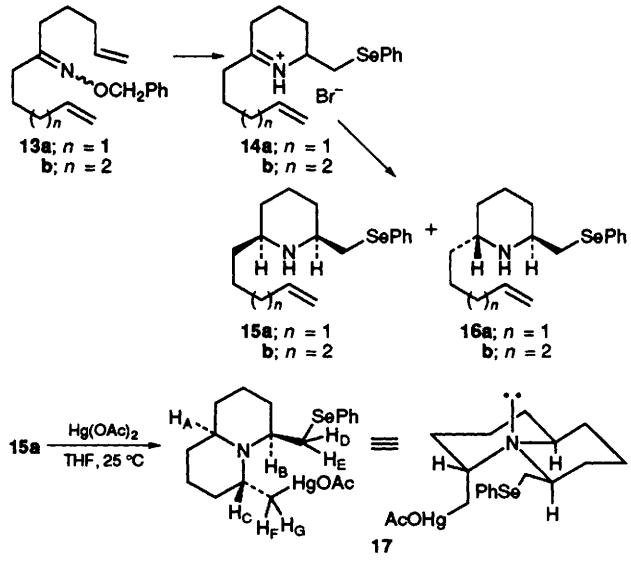


Scheme 1





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Footnotes

† In our original communication on the reaction of oximes with phenylselenyl bromide[2] we erroneously reported, owing to the high stability of nitrone salts, that the reactions proceeded by addition of the reagent to the alkene followed by nucleophilic displacement of the bromide by the oxime. This was corrected subsequently.[3]

‡ All new compounds have been fully characterised (microanalysis, NMR and mass spectra).

§ All diastereoisomer mixtures were readily separated by flash chromatography over silica.

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References

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4 Both *cis*-specific and highly *trans*-selective reductions of pyrrolines can be achieved with the appropriate reagents: D. Bacos, J. P. Celerier, E. Marx, C. Saliou and G. Lhommet, *Tetrahedron Lett.*, 1989, **30**, 1081; *J. Heterocycl. Chem.*, 1990, **27**, 1387.

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