Azidohydroperoxidation of pinenes: stereoselectivity pattern and the first X-ray structure of a 2-azidohydroperoxide

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The photoinduced electron transfer of azide anions in the presence of an excited organic dyestuff, oxygen, and α- or β-pinene, respectively, gave 2-azidohydroperoxides in excellent regio- and good diastereoselectivity.

Photooxygenation in the presence of azide anions leads to difunctionalized products which can derive either from an azide trapping reaction of cyclic peroxidic intermediates or from an oxygen trapping reaction of intermediary α-azido carbon radicals.[1–3] The resulting 2-azidohydroperoxides have seldom been isolated and are usually reduced to the corresponding azido- or aminoalcohols.[4] Recent investigation by Workentin *et al.* showed that azidyl radicals are produced under photoinduced electron transfer (PET) conditions and these highly reactive azidyl radicals readily add to nucleophilic alkenes.[5]

In order to evaluate the facial selectivity of the azidyl radical addition in combination with simple diastereoselectivity originating from the secondary attack of molecular oxygen, we investigated the enantiomerically pure α- and β-pinene as substrates. The trisubstituted α-pinene (**1**) was among the most reactive alkenes when irradiated with visible light in the presence of azide anions, oxygen and an organic dye (Scheme 1). The crude reaction mixture consisted of a mixture of diastereoisomeric azidohydroperoxides **2a**–**c** (d.r. 90 : 8 : 2) and the corresponding azidoalcohols **3** which could be separated chromatographically (total yield 58%). The hydroperoxide–alcohol ratio could be altered by use of different PET-sensitizers and variation of the water content and was optimal (79 : 21) for rhodamine B in a 95 : 5 MeOH–H_2O mixture. Stern–Volmer analysis of the fluorescence quenching gave a rate constant for PET from N_3^- to rhodamine B of $k_{ET} = 1.6 \times 10^9$ M^{-1} s^{-1} (Fig. 1) comparable with the rate constants determined for 9,10-dicyanoanthracene[6] and thioxanthone.[7]

The configuration of the major diastereoisomer **2a** was determined by NOE-spectroscopy and by comparison of the aminoalcohol **4a** which resulted from the LAH-reduction of **2a** with the literature-known compound.[8] The relative configuration of the two minor components were determined from the $^3J_{HH}$ coupling constants of the hydrogen proximal to the azido group. Thus, the primary attack of the azidyl radical proceeds with a 11 : 1 *endo*-selectivity and the subsequent oxygen attack with a 49 : 1 *endo*-selectivity.

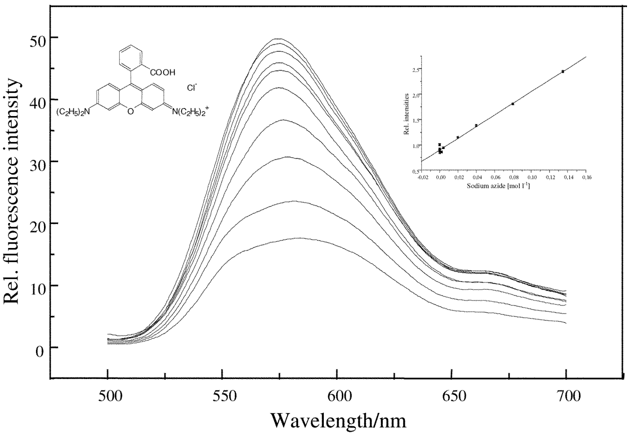
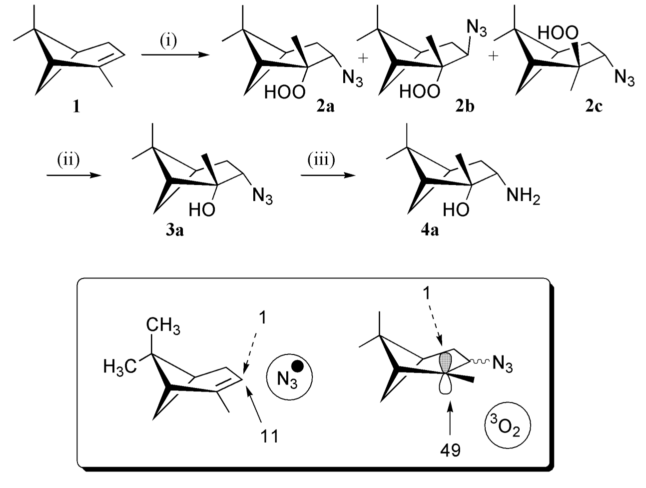


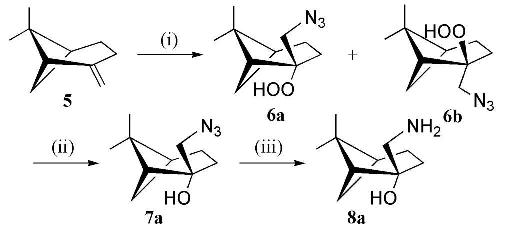
Fig. 1 Fluorescence quenching of rhodamine B by azide anions.



Scheme 1 *Reagents and conditions*: (i) NaN_3, O_2, Rh-B, *hν*, MeOH–H_2O, (ii) $NaBH_4$, MeOH, (iii) $LiAlH_4$, Et_2O.

Unexpectedly, β-pinene (**5**) also showed noticeable reactivity under standard reaction conditions (Scheme 2): the azidohydroperoxides **6a**,**b**† (Fig. 2) were formed with a dr of 76 : 24 (72% based on converted **5b**). The addition of molecular oxygen was again directed by the shielding effect of the dimethylmethylene bridge in **5**. From both the azidohydroperoxides **6a**,**b** as well as the azidoalcohol **7a** the aminoalcohol **8a**, was generated by LAH-reduction. Crystallization from hexane–ethyl acetate gave single crystals of the azidohydroperoxide **6a**. X-Ray structure analysis of **6a** revealed that the molecules are connected by intermolecular hydrogen bonds between the OOH group and the internal nitrogen of the azido function.

Thus, this procedure serves as a simple synthetic approach to aminoalcohols from unsaturated substrates from the ‘chiral pool’. Additionally, the pinene skeleton offered the opportunity to study the rate of oxygen addition due to the highly reactive cyclobutylcarbenium radicals (radical clocks) formed after azidyl radical addition. The corresponding ring-opening processes have been studied in free radical additions to α- and β-



Scheme 2 *Reagents and conditions*: (i) NaN_3, O_2, Rh-B, *hν*, MeOH–H_2O, (ii) $NaBH_4$, MeOH, (iii) $LiAlH_4$, Et_2O.

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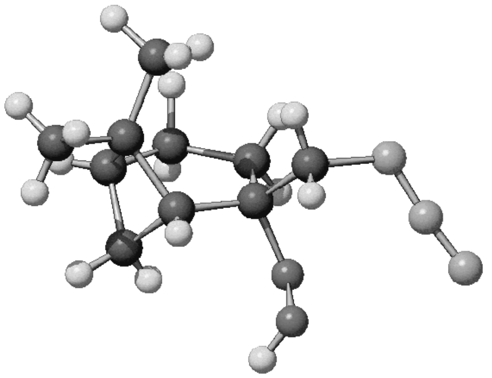

Fig. 2 Structure of the azidohydroperoxide **6a** in the crystal (SCHAKAL).

pinene and rate constants of 8×10^5 s^{-1} were determined.[9] In our hands, less than 5% of ring-opening products (from **2** and **5**) were detected in the crude NMR-spectra. From this data, a bimolecular rate constant for the oxygen addition step of $> 5 \times 10^9$ l M^{-1} s^{-1} resulted. This value is in good agreement with the rate constants determined for the reaction of triplet oxygen with benzylic radicals (1.6–4.9×10^9 l M^{-1} s^{-1}).[10] Decreasing the oxygen concentration, *e.g.* by use of air instead of a pure oxygen gas flow gave a number of products. These could not be identified.

The azidohydroperoxidation reaction was also applied for the allylic hydroperoxide **9** (available *via* photooxyenation of α-pinene **1**) and proceeded smoothly to give the corresponding azido *bis*-hydroperoxide which was reduced *in situ* to the azidodiol **10** (Scheme 3).

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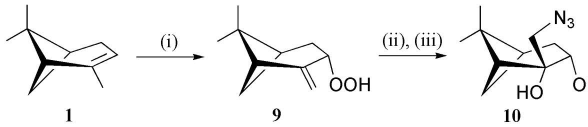

Scheme 3 *Reagents and conditions*: (i) $^1O_2$, MeOH, (ii) NaN_3, O_2, Rh-B, $h\nu$, MeOH–H_2O, (iii) $NaBH_4$, MeOH.

Notes and references

† *Crystal data*: $C_{10}H_{17}N_3O_2$ (from hexane–ethyl acetate 3:1) **6a**: M = 211.27, monoclinic, a = 10.070(1), b = 11.071(1), c = 10.418(1) Å, β = 91.180(1)°, space group $P2_1$, Mo-K$_\alpha$, 9958 reflections measured, 4376 reflections with $I > 2\sigma(I)$ R_1 = 0.0367, wR_2 = 0.0870. CCDC 182/1810. See http://www.rsc.org/suppdata/cc/b0/b005834n/ for crystal data in tabular format.

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