

Intermediates in the Autoxidation of a Non-conjugated Cyclic Diene

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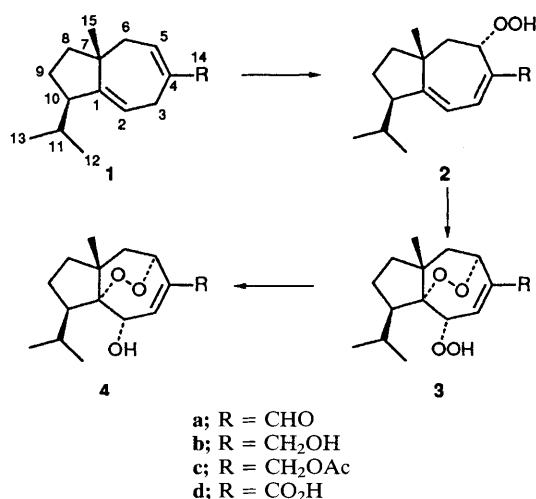
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The isolation of a 5-hydroperoxide which has been postulated as an initial intermediate in oxidative transformation of carota-1,4-dienes into 1,5-epidioxy derivatives was facilitated by using 14-acetoxycarota-1,4-diene **1c**; the present results allowed us to substantiate the aspects for the autoxidation pathway in non-conjugated 1,4-diene systems.

Carotane sesquiterpenes, carota-1,4-dien-14-al **1a** and rugosal A (1,5-epidioxy-2-hydroxycarot-3-en-14-al) **4a** have been isolated from the *Rosa rugosa* leaves,^{1,2} and an autoxidative conversion scheme from **1a** to **4a** has been proposed.^{1,3} However, the detection of the 5-hydroperoxy intermediate **2a** on TLC was unsuccessful owing to consecutive cyclization to yield **3a** and **4a**. In a photosensitized autoxidation of guaia-6,9-diene (having a 1,4-diene system) into the corresponding epidioxy derivative hanalpinol reported by Morita *et al.*, isolation of the intermediary hydroperoxide was also unsuccessful; however, the intermediate was confirmed as the alcohol derivative obtained by reduction of the photosensitized autoxidation product with triphenylphosphine.⁴

In the present study, carota-1,4-dien-14-ol **1b**[†] and 14-acetoxycarota-1,4-diene **1c**[†] were used as substrates for the autoxidation, because the 1,3-diene conjugation system may give a clear indication of their 5-hydroperoxy intermediates (**2b**, **2c**). A thin film of compound **1c** on a glass wall heated at 60 °C for 30 min in the dark yielded a product showing a UV quenching spot on silica gel 60 F₂₅₄ plates and a positive

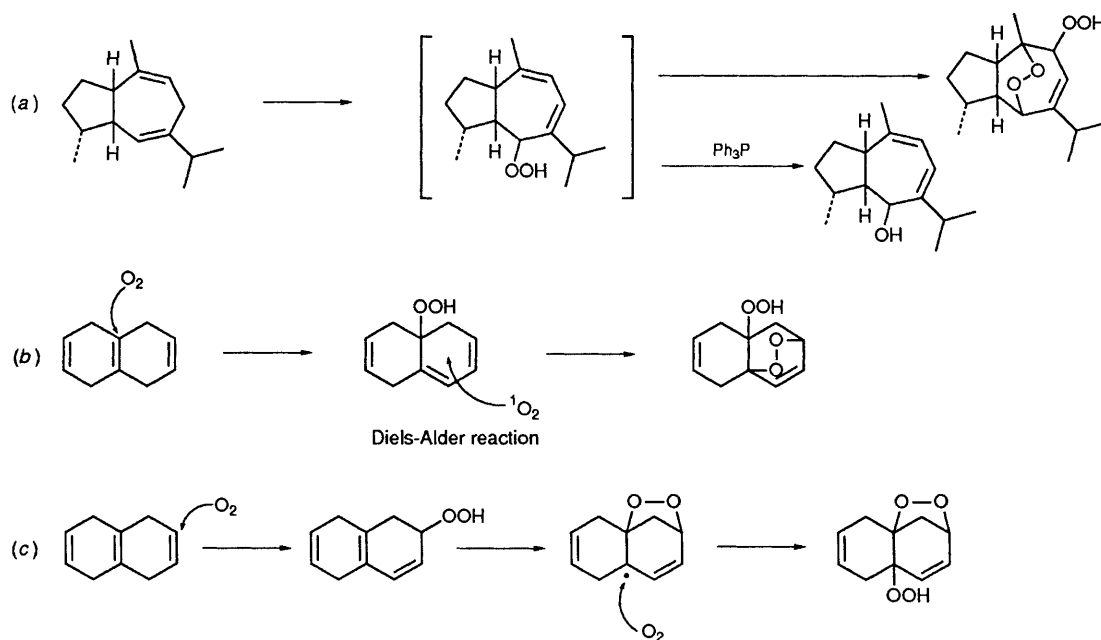
response to a peroxide reagent (*N,N*-dimethyl-*p*-phenylenediamine sulphate⁵). The expected 14-acetoxy-5-hydroperoxycarota-1,3-diene **2c** (0.9 mg of a colourless syrup from 3.0 mg of **1c**) could be isolated by preparative TLC.[†] The yields



[†] Compound **1a** in EtOH was treated with an excess of NaBH₄ at room temperature, and the product **1b** (79%) was obtained by preparative TLC; *R_f* 0.48 (n-hexane-EtOAc, 4:1); *m/z* 220 (M⁺, 100%). Compound **1b** was acetylated in Ac₂O-pyridine at 60 °C to give **1c** (85%); *R_f* 0.65 (n-hexane-EtOAc, 20:1); *m/z* 262 (M⁺, 100%).

14-Acetoxy-5-hydroperoxycarota-1,3-diene **2c** had *R_f* 0.54 (n-hexane-EtOAc, 3:1; cf. **1c**, *R_f* 0.94).

Scheme 1 Peroxidation pathway of carotane-1,4-dienes into carotane 1,5-hydroperoxy derivatives. In the actual autoxidation process, the hydroperoxide intermediates **2** and **3** are considered to be formed as exoperoxy radicals. (**2a** and **2d** were not identified).



Scheme 2 Examples of formation of epidioxy linkages on cyclized 1,4-dienes: (a) photooxidation of a guaiane sesquiterpene;⁴ (b) peroxidation of a cyclized 1,4-diene;⁸ (c) peroxidation pathway (this work)

depended not on the amount of substrate but on the surface area of the thin film. The UV maximum of **2c** in methanol (262 nm) was attributable to the 1,3-diene chromophore in the seven-membered ring.⁶ The molecular ion at m/z 294 (M^+ , 100%) was detected by both FDMS and FIMS, and the latter spectrum associated with the dehydration peak [m/z 276 (52%)]. FIHRMS confirmed the molecular formula to be $C_{17}H_{26}O_4$ (found 294.184; calc. 294.183). Two =CH protons [δ_H 5.34 (dd, J 8 and 2 Hz) and 5.97 (d, J 8 Hz)] and a methine proton [δ_H 4.59 (br. ddd, J 12, 6 and 2 Hz)] in the 1H NMR spectrum implied a 1,3-diene 5-hydroperoxide structure. The C-5 hydroperoxy proton observed as an exchangeable singlet at δ_H 8.20 was characteristic of a non-hydrogen-bonding -OOH signal.^{4,7} The IR absorption of the free hydroperoxy group (CCl_4 , ca. 0.3 mmol dm^{-3}) appeared at 3552 cm^{-1} , which is reasonable for such a group.⁷ The carbon signals assignable to the two double bonds were at δ_C 162.1, 114.2 and 134.0, and the remaining signal overlapped with the solvent peaks; an oxygenated sp^3 carbon (δ_C 82.4) substantiated the structure **2c** in Scheme 1. Compound **2c** on treatment with triphenylphosphine⁴ yielded 14-acetoxy-5-hydroxycarota-1,3-diene.

In the autoxidation, compound **1c** also yielded 14-acetoxy-1,5-epidioxy-2-hydroperoxycarot-3-en-14-ol **3c** and 1,5-epidioxy-2-hydroxycarot-3-en-14-ol **4c**. Furthermore, compound **2c** was spontaneously converted into **3c**, **4c** and by-products including a 5-oxocarotane and a norcarotane derivative.³ Identification of **2c** therefore provided conclusive proof for the assumed autoxidation pathway of **1a** into **4a**. Compound **1b** also yielded the 5-hydroperoxide intermediate **2b**, showing physicochemical properties which were similar to those of **2c** [e.g. positive peroxide test, UV λ_{max} (MeOH) 264 nm, and two =CH protons at δ_H 6.09 and 5.89 (each J 11 Hz) and a methine proton at δ_H 4.59 (in $CDCl_3$)]; however, the intermediate was unstable and easily decomposed during column chromatography or prolonged NMR scanning (several hours). The allylic hydroxy group of **1b** was considered to be responsible for the lability of **2b** and **1b** themselves.

It is believed that introduction of an epidioxy group in photooxidation of some cyclic 1,4-dienes is due to Diels-Alder-type addition of 1O_2 to the hydroperoxy-1,3-diene

intermediates [e.g. pathway (b) in Scheme 2].^{8,9} However, our results and those of Morita's group⁴ in which the formation of an epidioxy linkage on cyclic dienes occurred through a cyclization of an initially formed exoperoxy radical provide an alternative reaction pathway to that proposed by Gollnick and Schenck [(c) in Scheme 2].

In conversion of 1,4-diene compounds into a non-Diels-Alder-type of epidioxy derivative, the introduction of the exoperoxy radical is expected to be an initial step in the peroxidation. Isolation of intermediate **2c** which clearly verified the peroxidation pathway of carota-1,4-dienes **1a-d** into 1,5-epidioxy carotanes **4a-d** is evidence in favour of a mechanism involving peroxidation and successive cyclization for 1,4-diene compounds including polyunsaturated fatty acids.

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References

- Y. Hashidoko, S. Tahara and J. Mizutani, *Phytochemistry*, 1989, **28**, 425.
- Y. Hashidoko, S. Tahara and J. Mizutani, *Phytochemistry*, 1990, **29**, 867.
- Y. Hashidoko, S. Tahara and J. Mizutani, *J. Chem. Soc., Perkin Trans. 1*, 1991, 211.
- H. Morita, N. Tomioka, Y. Iitaka and H. Itokawa, *Chem. Pharm. Bull.*, 1988, **36**, 2984.
- E. Knappe and D. Peteri, *Z. Anal. Chem.*, 1962, **190**, 386.
- R. M. Silverstein, G. C. Bassler and T. C. Morrill, *Spectroscopic Identification of Organic Compounds*, 4th edn., Wiley, New York, 1981, p. 274.
- W. H. Richardson, in *The Chemistry of Functional Groups, Peroxides*, ed. S. Patai, Wiley, Chichester, 1983, p. 129.
- K. Gollnick and G. O. Schenck, in *1,4-Cycloaddition Reactions*, ed. J. Harner, Academic Press, New York, 1967, p. 276.
- G. O. Schenck, *Angew. Chem.*, 1967, **64**, 12.