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Short Communication

Selenium Carotenoids III:* First Synthesis of Optically Active Carotenoid Phosphates

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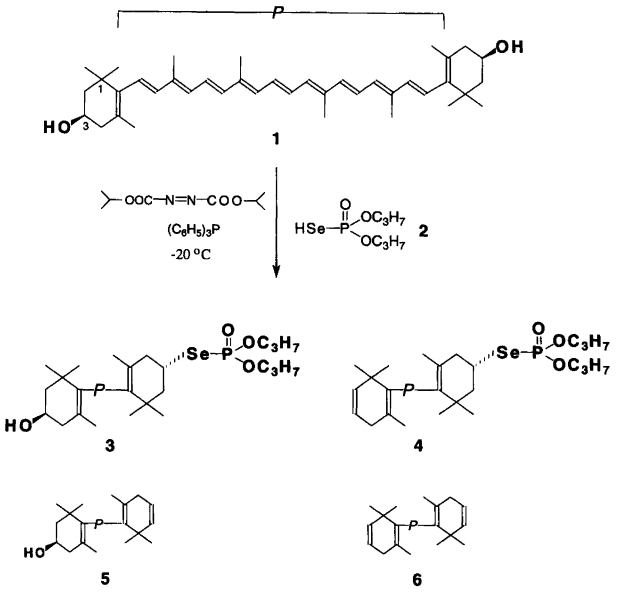
The optical activity of β-ring carotenoids orginates predominantly from an intrinsically chiral 'out of polyene plane' deviation of the ring double bond (C5–C6). This conformation is stabilized by substituents at the C-atoms (mainly C3) of the cyclohexene ring.[3] We have observed that the conformational blocking effect of O, N and S substituents attached to the asymmetric C-3 atom are similar. Thus (3*R*,3′*S*)-3′-mercapto-β,β-caroten-3-ol and (3*R*,3′*S*)-3′-amino-β,β-caroten-3-ol did not show electronical optical activity due to a *pseudo meso* situation.[4,5] However, (3*R*,3′*S*)-3′-phenylseleno-β,β-caroten-3-ol exhibited a CD-effect.[1] The optical activity of this compound can be explained by different conformational properties of the O and Se substituted cyclohexene ring. In order to verify the influence of Se substituents on the conformationally dependent optical activity of β-ring carotenoids, we combined the search for a new (3*R*,3′*S*)-selenium–carotenol derivative with the synthesis of the first carotenoid phosphates.[6]

When (3*R*,3′*R*)-zeaxanthin (**1**) was reacted in a Mitsunobu reaction[7] with di-*O*,*O*-propyl *Se*-hydrogen phosphate (**2**)[8] concurrent elimination reactions were favoured,[1,4,5] decreasing the yield of Se-carotenoids to 1%, Scheme 1. The mass spectra of the products **3** and **4** indicated the presence of Se by a characteristic carotenoid–Se isotopic pattern of the molecular ion. A fragmentation peak $M-122$ with an Se isotopic pattern was compatible with an –Se–P=O structure.[8,9] The weak Cotton effect of the hydroxy selenophosphate **3** (Fig. 1) further supports the selenol structure. A selonoxo isomer –O–P=Se would probably behave as a *pseudo meso* compound.[4,5] The Cotton effects of the selenophosphate **4** were opposite and of comparable intensities to that of the hydroxy compound **5**, Fig. 1. The extrema of compound **3** are the same as for **5** (Fig. 2), but inverted relative to product **4**. The optical activity of **3** corroborates the adoption of different conformational properties for *O*- and *Se*-substituted cyclohexene end-rings as was assumed for phenylseleno carotenoids.[1] Weak n→s* and other possible transitions of the Se atom[10,11] are mostly submerged in the intense bands caused by the twisted, inherently chiral C(5)=C(6)–C(7)=C(8) s-*cis* diene chromophore.[3]

The carotenoid selenophosphates **3** and **4** seem to be as stable as zeaxanthin. Carotenoid phosphates have not yet been detected in Nature, although the biosynthesis of carotenoids is based on phosphate precursors.[12] The



Scheme 1. Sliwka cartonoid phosphates.

* Parts 1 and 2: Refs. 1, 2.

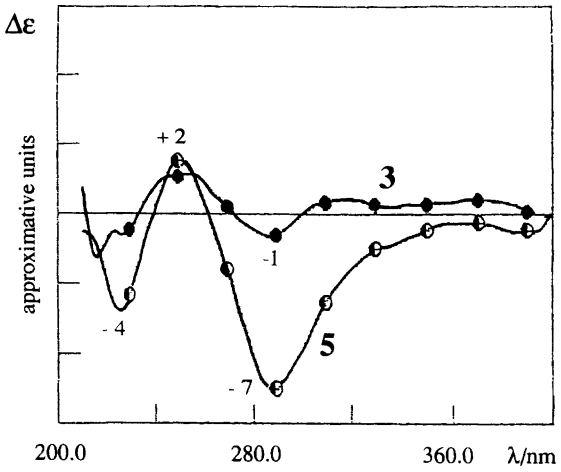


Fig. 1. CD spectra of *Se*-[(3*R*,3′*S*)-3-hydroxy-β,β-caroten-3′-yl] di-*O*,*O*-propyl selenophosphate (**3**) ● and (3*R*)-2′,3′-didehydro-β,β-caroten-3-ol (**5**) ◐.

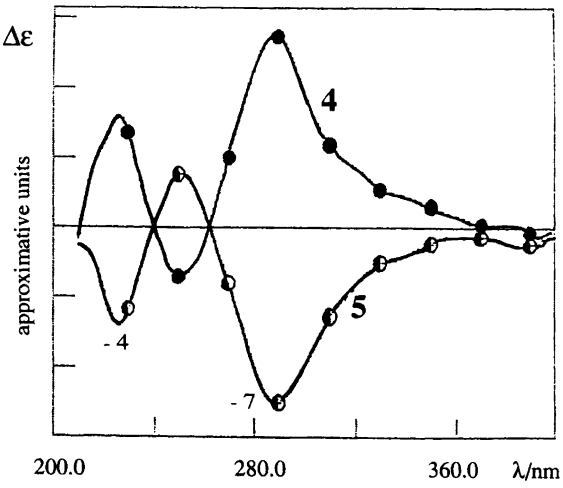


Fig. 2. CD spectra of *Se*-[(3*S*)-2′,3′-didehydro-β,β-caroten-3-yl] di-*O*,*O*-propyl selenophosphate (**4**) ● and (3*R*)-2′,3′-didehydro-β,β-caroten-3-ol (**5**) ◐.

carotenoid selenophosphates **3** and **4** might combine the antioxidant properties of carotenoids and selenium.[1]

Experimental

General methods. General precautions for work with Se-carotenoids were taken.[1]

Di-O,O-propyl Se-*hydrogen phosphate* (**2**). Sodium di-*O,O*-propyl selenophosphate[8] (110 mg, 0.41 mmol) was suspended in benzene (2 ml) and sulfuric acid (10%, 1 ml) was added. After 15 min, the organic phase was separated and dried over Na_2SO_4.

Reaction of zeaxanthin (**1**) *with di*-O,O-*propyl* Se-*hydrogen phosphate* (**2**). Triphenylphosphine (104.8 mg, 0.4 mmol) and diisopropyl azodicarboxylate (79 ml, 0.4 mmol) were stirred in THF (2.5 ml) at 0 °C. After formation of the white precipitate,[7] (3*R*,3′*R*)-zeaxanthin (**1**) (56.8 mg, 0.1 mmol), dissolved in THF (5 ml), was added dropwise at 0 °C. The solution was cooled to −20 °C after which the above benzene solution of **2** was added with a syringe. Stirring overnight between −20 °C and +10 °C provided, after chromatic work-up, unreacted **1** (38.8 mg), elimination products **5** and **6**, and the Se-compounds **3** and **4** (0.26 mg, 1%). The products **3**,**4**,**5**,**6** were isolated in a ratio of 1.4:1:36:4.5.

Se-*[(3R,3′S)-3′-Hydroxy-β,β-caroten-3′-yl] di*-O,O-*propyl selenophosphate* (**3**). Available: 0.15 mg; R_F 0.33 (**1** R_F 0.23); VIS λ_{max}: 446, 473 nm, as for **1**; MS (*m/z*): 796 (*M*, Se-isotopic pattern), 778 (Se-isotopic pattern, $M-H_2O$), 674 (Se-isotopic pattern, $M-C_3H_7PO_3$), 550 [674 − $HSeC_3H_7$ and $M-HSeP(O)(OC_3H_7)_2$], 532 (550 − H_2O), 458 (550 − toluene), 444 (550 − xylene), 392 (550–158); CD: Fig. 1; ^{1}H NMR (400 MHz, $CDCl_3$): Se substituted β-ring: δ 1.0, 1.10 (6 H, 2 × CH_3 C-1), 1.31, 1.68 (2 H, C-2), 2.89 (H, C-3), 2.08, 2.32 (2 H, C-4), 1.72 (3 H, CH_3, C-5), 1.97 (12 H, 4 CH_3 in chain), *O*-propyl: 1.0 (6 H, 2 × CH_3), 1.4 (4 H, 2 × CH_2), 4.2 (4 H, 2 × CH_2O); the data for the 3-hydroxy β-ring were in agreement with reference data.[13]

Se-*(3S)-2′,3′-Didehydro-β,β-caroten-3yl] di*-O,O-*propyl selenophosphate* (**4**). Available: 0.11 mg; R_F 0.42; VIS λ_{max}: as for **3**; MS (*m/z*): 778 (*M*, Se-isotopic pattern), 656 (Se-isotopic pattern, $M-C_3H_7PO_3$), 532 [656 − $HSeC_3H_7$ and $M-HSeP(O)(OC_3H_7)_2$], 440 (532 − toluene), 426 (532 − xylene), 374 (532–158); CD: Fig. 2; ^{1}H NMR: for the Se substituted β-ring as for **3**, the data for the dihydro β-ring were in agreement with reference data.[13]

(3R)-2′,3′-Didehydro-β,β-caroten-3-ol (**5**). Available: 3.98 mg; R_F 0.36; VIS λ_{max}: 448, 474 nm; MS and co-chromatography were identical with the product described elsewhere.[1,4]

Tetradehydro-β,β-carotene (**6**).[1,4] Available: 0.5 mg; R_F 0.73; VIS λ_{max}: 446 (472) nm.

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