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13-*cis*-β,β-Carotene and 15-*cis*-β,β-carotene

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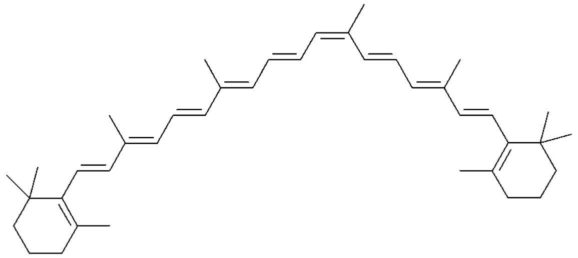
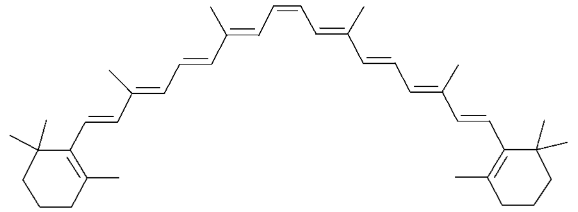
13-*cis*-β,β-Carotene, $C_{40}H_{56}$, crystallizes with a complete molecule in the asymmetric unit, whereas 15-*cis*-β,β-carotene, also $C_{40}H_{56}$, has twofold symmetry about an axis through the central bond of the polyene chain. The polyene methyl groups are arranged on one side of the polyene chains for each molecule and the 6-*s*-*cis* β end groups, with the cyclohexene rings in half-chair conformations, are twisted out of the planes of the polyene chains by angles ranging from 41.37 (17) to 52.2 (4)°. The molecules in each structure pack so that the arms of one occupy the cleft of the next, and there is significant π–π stacking of the almost-parallel polyene chains of the 15-*cis* isomer, which approach at distances of 3.319 (1)–3.591 (1) Å.

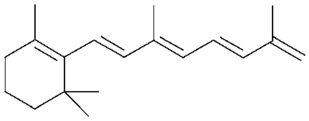
Comment

Carotenes have the general formula $C_{40}H_{56}$ and are the chromophores responsible for the orange colour in carrots and many other fruits and vegetables. The structure of all-*trans*-β,β-carotene has been determined a number of times [Sterling, 1964; Senge *et al.*, 1992; Hursthouse *et al.*, 2004; Cambridge Structural Database (CSD; Allen, 2002) refcodes CARTEN, CARTEN01 and CARTEN02, respectively], but none of the *cis* isomers has been characterized crystallographically. Carotenoids readily undergo *trans*–*cis* (*E*/*Z*) isomerization in organic solvents (Zechmeister, 1962) and the *cis* isomers are the most abundant artefacts formed during isolation procedures (Liaaen-Jensen, 1997). Kinetic and thermodynamic data for the thermal interconversion of all-*trans*-β-carotene and the 13-*cis*-, (I), and 15-*cis*-, (II), isomers have been published (von Doering *et al.*, 1995). The 13-*cis* isomer, (I), is formed readily in a kinetically controlled process, whereas the 9-*cis* isomer is the dominant *cis* isomer in iodine-catalyzed equilibrium mixtures (Zechmeister, 1962; Molnár & Szabolcs, 1993), assumed to represent the thermodynamic equilibrium (Refvem *et al.*, 1999). The 15-*cis* isomer, (II), is formed only in minor quantities under equilibrium conditions (Zechmeister, 1962; Molnár & Szabolcs, 1993; Schirle *et al.*, 1995). Nevertheless, the natural occurrence of the 15-*cis* isomer, (II), is well demonstrated in photosynthetic systems, where it serves an important function (Koyama & Mubai, 1993). The kinetically favoured 13-*cis* isomer, (I), has been reported, *e.g.* from human tissues, including serum (Stahl *et al.*, 1992). The 9-*cis* isomer is a dominant isomer of β-carotene in the green alga *Dunaliella* spp. grown under stressed conditions (Ben-Amotz *et al.*, 1988). We report here the structures of 13-*cis*-β,β-carotene, (I), and 15-*cis*-β,β-carotene, (II).


(I)


(II)

The structures of (I) and (II) are shown in Figs. 1 and 2, respectively. In the scheme above, the 13-*cis* isomer, (I), is drawn as the identical 13′-*cis* isomer for direct comparison with Fig. 1. For (I), the asymmetric unit consists of the whole molecule, due to the asymmetry of the polyene chain. The methyl groups along the polyene chain are all on the outside of the bent chain, presumably to minimize steric crowding of the methyl groups. The end groups have the 6-*s*-*cis* conformation, where 6-*s*-*cis* (6-single-*cis*) defines the conformation of the single bond at the 6-position, connecting the substituted cyclohexene ring and the polyene chain. The other alternative is 6-*s*-*trans*, which is shown in the second scheme shown below. The end rings are twisted out of the plane of the polyene chain by angles defined by the C5—C6—C7—C8 and C5*A*—C6*A*—C7*A*—C8*A* torsion angles of 47.6 (4) and 52.2 (4)°, respectively. Although the end rings are nonplanar, the C5—C6—C7—C8 torsion angle is normally used to define the angle of twist, since it describes the nonplanarity between the best planes through the double-bond systems of the ring and the polyene chain (Sundaralingam & Beddell, 1972; Mo, 1995). In (II), the asymmetric unit contains half the molecule, and the entire molecule is generated by means of a twofold axis at the centre of the C15—C15*A* bond. As for (I), the methyl groups along the bent polyene chain are all on the outside, and the


6-*s*-*trans*

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crystallographically equivalent end rings are in the 6-*s-cis* conformation at an angle to the plane of the polyene chain of −41.37 (17)°.

In both structures, the cyclohexene end rings are in the half-chair conformation, as is generally found for carotenoids with *β* end rings (Sundaralingam & Beddell, 1972; Mo, 1995). In the half-chair conformation, which is the most stable conformation for cyclohexene rings, four atoms are approximately coplanar and the fifth and sixth atoms, opposite the double bond, lie above and below this plane. For (I), atoms C2 and C3 are displaced from the best plane through atoms C1/C4–C6 by −0.334 (3) and 0.422 (3) Å, respectively, and atoms C2*A* and C3*A* are displaced from the plane defined by atoms C1*A*/C4–C6 by 0.325 (3) and −0.434 (3) Å, respectively. Similarly, atoms C2 and C3 in (II) are displaced from the corresponding plane by 0.402 (1) and −0.342 (1) Å, respectively. Within the cyclohexene ring, the largest torsion angle is about the C2—C3 bond (Clayden *et al.*, 2000; Sundaralingam & Beddell, 1972; Mo, 1995; Table 1) and takes values of 62.9 (3) and 62.7 (3)° for the two end rings of (I), and −61.70 (12)° for (II) (where the two end rings are crystallographically equivalent). The smallest torsion angle is about the C5=C6 double bond (Table 1).

The structures of (I) and (II) can be compared with that of all-*trans*-*β*,*β*-carotene, which is centrosymmetric, with the four polyene chain methyl groups arranged in pairs along each side of the polyene chain and a pronounced S-shape of the chain, arising from steric crowding of the methyl groups. Again, the *β* end rings are in the 6-*s-cis* conformation and the C5—C6—C7—C8 torsion angle is −41.6 (6)° (Senge *et al.*, 1992; CSD refcode CARTEN01). The end rings are in the half-chair conformation, but disorder in a 0.5:0.5 ratio of atoms C2 and C3 was seen, indicating that both possible half-chair conformations are present in the crystal structure. This is in contrast with the structures of (I) and (II), where no such disorder is observed. The fact that, in all three structures, the end rings are found to be in the 6-*s-cis* conformation and twisted out of the plane of the polyene chain by about 40–50° is in keeping

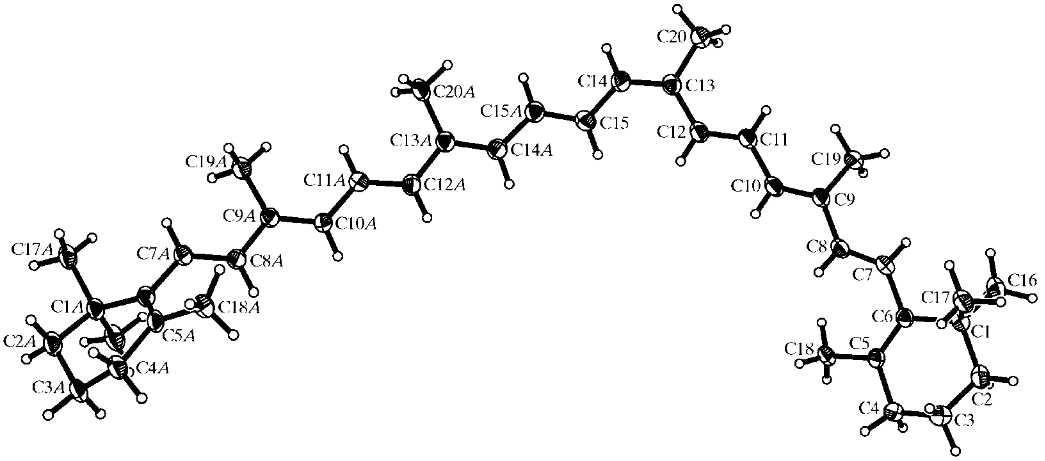

Figure 1
A view of 13-*cis*-*β*,*β*-carotene, (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

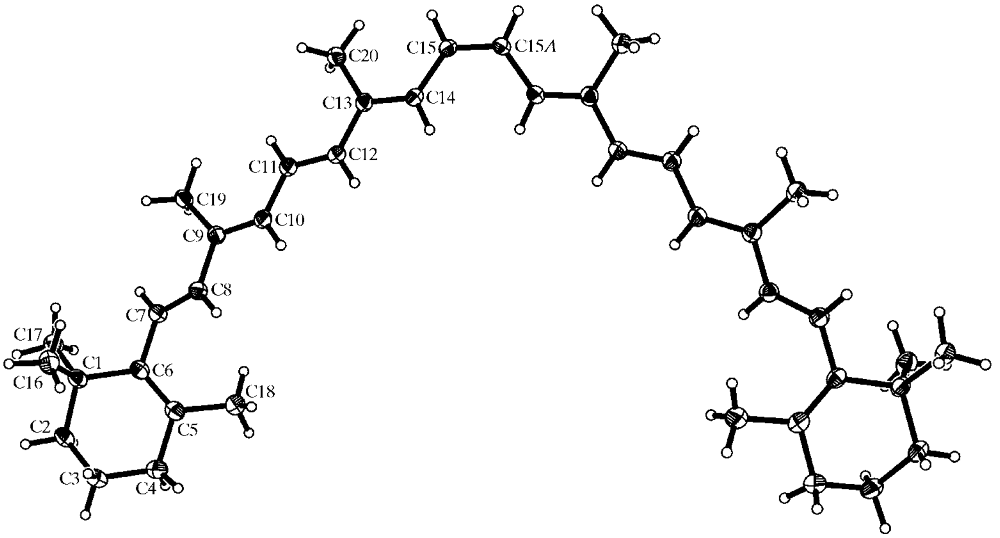

Figure 2
A view of 15-*cis*-*β*,*β*-carotene, (II), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

with most of the other carotenoids and xanthophyll structures with β end rings (Mo, 1995), and these twist angles agree with calculated values of between 40 and 50° for a number of such molecules (Hashimoto *et al.*, 2002). It is assumed that this preferred conformation arises from steric crowding between the end-ring methyl groups and the H atoms bonded to atoms C7 and C8. There are some exceptions, including, for example, (3*R*,3*S*′, *meso*)-zeaxanthin, with 6-*s-cis* end rings and a C5—C6—C7—C8 torsion angle of ±74.9 (3)° (Bartalucci *et al.*, 2007), zeaxanthin-3,3′-diyl bis[(−)-(1*R*)-2-methyl-5-(1-methylethyl)cyclohexyl carbonate] (Linden *et al.*, 2004), which has one β end ring in the *s-trans* conformation and the other in the *s-cis* conformation, with C5—C6—C7—C8 torsion angles of 144.5 (6) and 48.5 (8)°, respectively, and β-8′-β-apocarotenal (Drikos *et al.*, 1988), with an *s-trans* β end ring and a C5—C6—C7—C8 torsion angle of −158.4 (8)°; these deviations from the expected values may arise from packing forces in the crystal structures (Mo, 1995).

The polyene chains in (I), (II) and all-*trans*-β,β-carotene are significantly nonplanar, as shown by the torsion angles along the polyene chains, which deviate by up to about 8° from 180° for (I), 9° for (II) and 5° for all-*trans*-β,β-carotene. The methyl groups deviate likewise from the plane of the polyene chain.

Fig. 3 shows the packing of (I), illustrating how the short arm of one molecule fits into the cleft made by the next molecule. There is often a high degree of π–π stacking between the polyene chains of carotenoid molecules aligned above one other (Bartalucci *et al.*, 2007). In this case, there is a close approach of the molecules of 3.465 (4) Å between atoms C10 and C14*A*(1 + *x*, *y*, *z*), but away from this point of minimum distance the polyene chains become further and further apart (Fig. 4). In addition, atom C12 shows a short contact to the C20*A*(1 + *x*, *y*, *z*) methyl group of 3.415 (4) Å, and the C12 and C13 distances to H20*F*(1 + *x*, *y*, *z*) are 2.711 (3) and 2.797 (3) Å, respectively (Fig. 4). Other contacts are van der Waals interactions, with the shortest contact between adjacent molecules being 3.374 (4) Å between methyl groups C19*A* and C19*A*(−*x* − 1, −*y* + 1, −*z*) (Fig. 4).

The packing of (II) is shown in Fig. 5 and again the molecules fit together so that the arms of one molecule fit into the

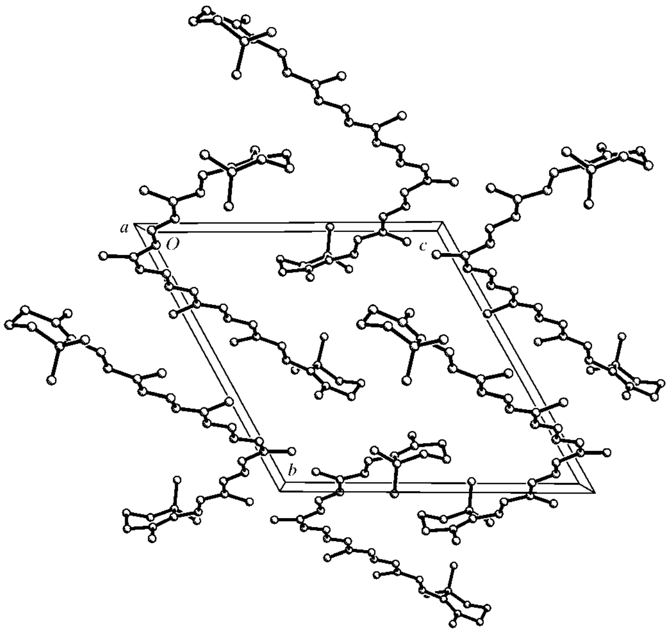

Figure 3
A packing diagram for 13-*cis*-β,β-carotene, (I), viewed down *a*, showing the arms of each molecule fitting into the cleft of the next. H atoms have been omitted for clarity.

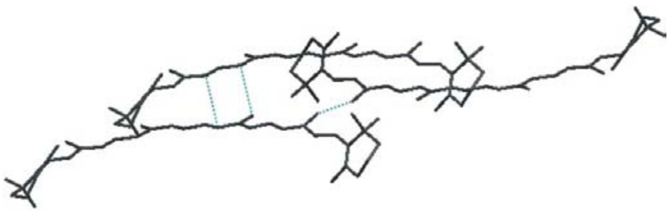

Figure 4
A plot of the short intermolecular C10···C14*A*(1 + *x*, *y*, *z*), C12···C20*A*(1 + *x*, *y*, *z*) and C19*A*···C19*A*(−*x* − 1, −*y* + 1, −*z*) contacts in 13-*cis*-β,β-carotene, (I) (dashed lines). H atoms have been omitted for clarity.

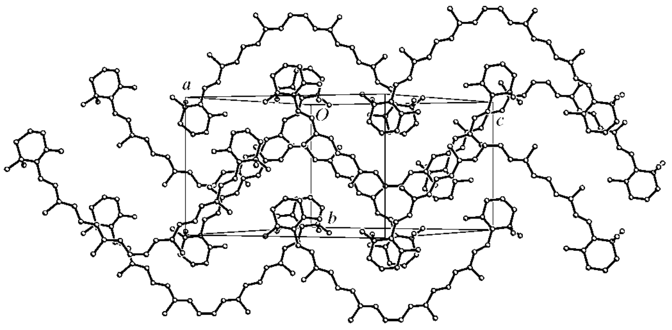

Figure 5
A packing diagram for 15-*cis*-β,β-carotene, (II), showing the arms of each molecule fitting into the cleft of the next. The π–π stacking of the polyene chains can also be seen. H atoms have been omitted for clarity.

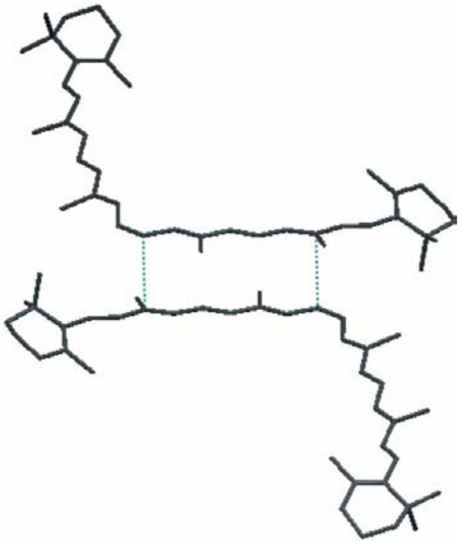

Figure 6
A plot showing the π–π stacking interactions of 15-*cis*-β,β-carotene, (II) (dashed lines). H atoms have been omitted for clarity.

cleft of the next. This time, however, there is significant π–π stacking between adjacent polyene chains which are arranged almost parallel above one other, with intermolecular distances ranging from 3.319 (1) to 3.591 (1) Å between atom pairs C9 and C15($1 - x, 1 - y, 2 - z$), and C13 and C10($1 - x, 1 - y, 2 - z$) (Fig. 6). Other contacts are normal van der Waals interactions.

Experimental

The 13-*cis*, (I), and 15-*cis*, (II), isomers of β,β-carotene used here were samples prepared by total synthesis (Bernhard & Mayer, 1991) and kindly provided by Hoffmann–La Roche, Basel. Both isomers were recrystallized from solutions in pyridine by vapour diffusion with water in an arbitrary ratio.

Compound (I)

Crystal data

$C_{40}H_{56}$
$M_r = 536.85$
Triclinic, $P\overline{1}$
$a = 8.076$ (3) Å
$b = 15.482$ (5) Å
$c = 15.636$ (5) Å
$\alpha = 60.751$ (6)°
$\beta = 84.929$ (6)°
$\gamma = 83.967$ (6)°
$V = 1694.6$ (10) Å^3
$Z = 2$
Mo $K\alpha$ radiation
$\mu = 0.06$ mm^{-1}
$T = 100$ (2) K
0.60 × 0.40 × 0.10 mm

Data collection

Bruker SMART CCD area-detector diffractometer
8509 measured reflections
5860 independent reflections
2959 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.067$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.049$
$wR(F^2) = 0.113$
$S = 0.83$
5860 reflections
371 parameters
H-atom parameters constrained
$\Delta\rho_{\rm max} = 0.22$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.15$ e Å^{-3}

Compound (II)

Crystal data

$C_{40}H_{56}$
$M_r = 536.85$
Monoclinic, $C2/c$
$a = 17.6168$ (13) Å
$b = 11.5544$ (9) Å
$c = 17.4124$ (13) Å
$\beta = 108.0840$ (10)°
$V = 3369.2$ (4) Å^3
$Z = 4$
Mo $K\alpha$ radiation
$\mu = 0.06$ mm^{-1}
$T = 100$ (2) K
0.5 × 0.3 × 0.3 mm

Data collection

Bruker SMART CCD area-detector diffractometer
9559 measured reflections
3451 independent reflections
2981 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.029$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.039$
$wR(F^2) = 0.111$
$S = 1.07$
3451 reflections
186 parameters
H-atom parameters constrained
$\Delta\rho_{\rm max} = 0.29$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.17$ e Å^{-3}

H atoms were included in calculated positions, with C—H distances varying in the range 0.95–0.99 Å and with $U_{\rm iso}$(H) = 1.2 or 1.5$U_{\rm eq}$(C). Methyl H atoms were defined using the AFIX 137 command (*SHELXL97*; Sheldrick, 2008), which varies the torsion angle to maximize the electron density at the three H-atom positions.

Table 1
Torsion angles (°) about the cyclohexene ring bonds of (I) and (II).

The C5—C6—C7—C8 torsion angle gives a measure of the angle of twist of the end rings from the plane of the polyene chain.

	φ1–2	φ2–3	φ3–4	φ4–5	φ5–6	C5—C6—C7—C8
(I)	−43.5 (3)	62.9 (3)	−46.0 (3)	13.3 (3)	5.7 (4)	47.6 (4)
(I*A*)	−43.7 (3)	62.7 (3)	−46.6 (3)	15.0 (3)	4.1 (4)	52.2 (4)
(II)	46.4 (1)	−61.7 (1)	42.7 (1)	−11.6 (2)	−3.3 (3)	−41.4 (2)

For both compounds, data collection: *SMART* (Bruker, 2001); cell refinement: *SMART*; data reduction: *SAINT* (Bruker, 2002); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *SHELXTL* (Bruker, 2001); software used to prepare material for publication: *SHELXTL*, *PLATON* (Spek 2003), *WinGX* (Farrugia, 1999) and *PARST* (Nardelli, 1995).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: JZ3117). Services for accessing these data are described at the back of the journal.

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