

Two polymorphs of 20-desmethyl- β -caroteneMadeleine Helliwell,^{a*} Synnøve Liaaen-Jensen^b and James Wilkinson^a^aDepartment of Chemistry, University of Manchester, Manchester M13 9PL, England, and ^bDepartment of Chemistry, Norwegian University of Science and Technology, Trondheim, Norway

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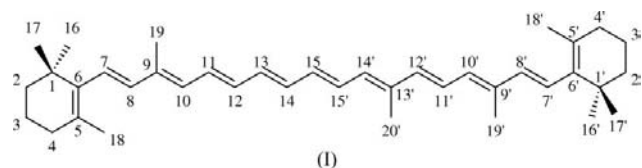
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Two polymorphs of 20-desmethyl- β -carotene (systematic name: 20-nor- β , β -carotene), C₃₉H₅₄, in monoclinic and triclinic space groups, were formed in the same vial by recrystallization from pyridine and water. Each polymorph crystallizes with the complete molecule as the asymmetric unit, and the two polymorphs show differing patterns of disorder. The β end rings of both polymorphs have the 6-*s-cis* conformation, and are twisted out of the plane of the polyene chain by angles of -53.2 (8) and 47.3 (8) $^\circ$ for the monoclinic polymorph, and -43.6 (3) and 56.1 (3) $^\circ$ for the triclinic polymorph. The cyclohexene end groups are in the half-chair conformation, but the triclinic polymorph shows disorder of one ring. Overlay of the molecules shows that they differ in the degree of nonplanarity of the polyene chains and the angles of twist of the end rings. The packing arrangements of the two polymorphs are quite different, with the monoclinic polymorph showing short intermolecular contacts of the disordered methyl groups with adjacent polyene chain atoms, and the triclinic polymorph showing π - π stacking interactions of the almost parallel polyene chains. The determination of the crystal structures of the two title polymorphs of 20-desmethyl- β -carotene allows information to be gained regarding the structural effects on the polyene chain, as well as on the end groups, *versus* that of the parent compound β -carotene. The absence of the methyl group is known to have an impact on various functions of the title compound.

Comment

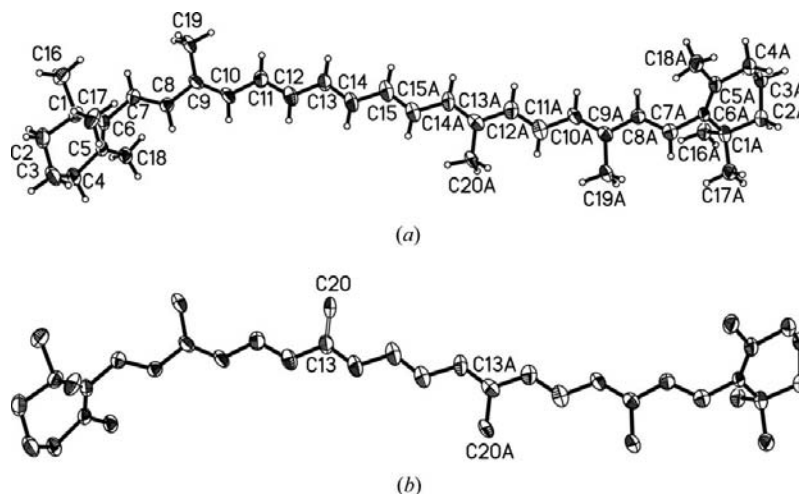
The isoprenoid structure with methyl groups in positions 19, 20, 19' and 20' of the polyene chain in carotenoids is a consequence of the biosynthetic pathway (Britton, 1998). These methyl groups cause a bathochromic shift of the absorption spectrum in visible light relative to unsubstituted aryl polyenes (Zechmeister, 1963). The in-chain methyl substituents facilitate NMR assignments of the polyene chain (Englert, 1995). Norcarotenoids lacking lateral methyl groups

have been prepared as models by total synthesis (Britton *et al.*, 1997; Weesie *et al.*, 1999; Martin *et al.*, 1999; Wirtz *et al.*, 2001), and are particularly useful for assessing the specificity of the C20 cleavage enzyme (Wirtz *et al.*, 2001), Raman spectroscopic studies (Weesie *et al.*, 1999) and antioxidant properties (Martin *et al.*, 1999), and for carotenoprotein binding (Britton *et al.*, 1997). It has been demonstrated that the 20-methyl group is essential for recombination of the colourless apo-crustacyanin with carotenoids to provide blue carotenoproteins (Britton *et al.*, 1997), and recent X-ray studies of β -crustacyanin provide a three-dimensional structural basis to rationalize the previous findings (Cianci *et al.*, 2002). We report here the crystal structures of two polymorphs of 20-desmethyl- β -carotene, (I), formed in the same recrystallization vial, which crystallize in the monoclinic space group $P2_1$ and the triclinic space group $P\bar{1}$, and which we thus refer to as (I)- $P2_1$ and (I)- $P\bar{1}$, respectively.

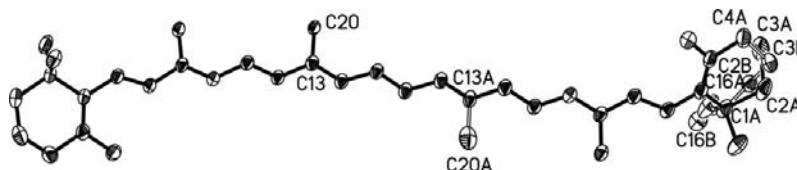


In the scheme of 20-desmethyl- β -carotene, the numbering of the C atoms is indicated according to IUPAC nomenclature rules (IUPAC-IUB, 1974). However, in the crystal structures, primed positions are denoted with the suffix *A* for clarity, e.g. C13' = C13A. The structures of the two polymorphs are shown in Figs. 1 and 2, respectively, with disordered atoms omitted in Fig. 1(a). Each crystal structure shows disorder of the C13 and C20 sites with those on the other half of the molecule, *viz.* C13A and C20A (Figs. 1b and 2). The proportions of the disordered components are quite different. For (I)- $P2_1$ the value is 1:1, but for (I)- $P\bar{1}$ the highest occupancy fraction refines to a value of 0.821 (4). The (I)- $P\bar{1}$ polymorph shows additional disorder of atoms C2A, C3A and C16A of one cyclohexene ring, with the refined occupancy of the major component being 0.542 (9) (Fig. 2).

In common with β -carotene and other all-*trans* C₄₀ carotenoids (Mo, 1995; Bartalucci *et al.*, 2007), in each polymorph of (I) the polyene chain methyl groups of each half of the molecule are arranged on opposite sides of the chain and there is a pronounced S shape of the polyene chain to minimize steric hindrance (Figs. 1 and 2). Overall, the conformations of the two polymorphs are fairly similar to one another and to that of β -carotene [Senge *et al.*, 1992; Cambridge Structural Database (CSD; Allen, 2002) refcode CARTEN01], with end groups in the 6-*s-cis* conformation (Mo, 1995; Bartalucci *et al.*, 2008). These are twisted out of the plane of the polyene chain by angles defined by the C5–C6–C7–C8 and C5A–C6A–C7A–C8A torsion angles, which describe the nonplanarity between the best planes through the double-bond systems of the ring and the polyene chain (Sundaralingam & Beddell, 1972; Mo, 1995; Bartalucci *et al.*, 2008); these angles are -53.2 (8) and 47.3 (8) $^\circ$ for (I)- $P2_1$ and -43.6 (3) and 56.1 (3) $^\circ$ for (I)- $P\bar{1}$ (Table 1), compared with a value of ± 41.6 (6) $^\circ$ for the centrosymmetric β -carotene mol-

**Figure 1**

(a) The molecular structure of (I)- $P2_1$, showing the atom-numbering scheme adopted for both polymorphs. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii. Disordered atoms have been omitted for clarity. (b) The disorder of atoms C20 and C20A, which each have an occupancy of 0.5; the second component is shown with an open bond. H atoms have been omitted for clarity.

**Figure 2**

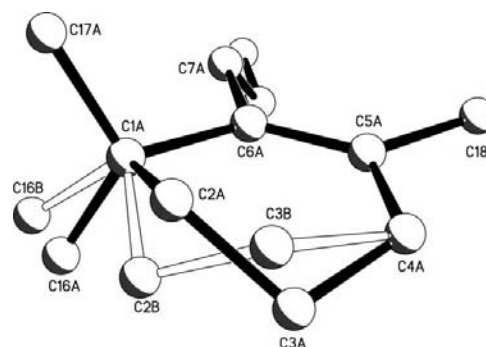
The molecular structure of (I)- $P\bar{1}$, with displacement ellipsoids drawn at the 50% probability level, showing the disorder of atoms C20 and C20A, and atoms C2A/C3A/C16A and C2B/C3B/C16B. The major and minor components are represented with solid and open bonds, respectively. H atoms have been omitted for clarity.

ecule (Senge *et al.*, 1992; CSD refcode CARTEN01). These values are in reasonable agreement with the calculated value for β -carotene of 48.0° (Hashimoto *et al.*, 2002), since such a twist of the end ring minimizes steric hindrance between the H atoms bonded to atoms C7 and C8 and those of the end ring methyl H atoms, and therefore is the most stable conformer.

The cyclohexene end rings are all in the usual half-chair conformation and are well ordered except for one ring of (I)- $P\bar{1}$. This ring shows disorder of atoms C2A, C3A and C16A (Fig. 3) similar to that shown by, for example, β -carotene and canthaxanthin (Senge *et al.*, 1992; Bartalucci *et al.*, 2007), indicating that both possible half-chair conformations are present. In the half-chair conformation, atoms C1 and C4–C6 (C1A and C4A–C6A) are approximately coplanar, with atoms C2 and C3 (C2A and C3A) lying above and below this plane. For (I)- $P2_1$, the distances of atoms C2 and C3 (C2A and C3A) from the C1/C4–C6 (C1A/C4A–C6A) plane are 0.370 (5) and -0.409 (6) Å [-0.231 (5) and 0.516 (5) Å], respectively, and the angle between the C1/C4–C6 and C1A/C4A–C6A planes is 24.3 (3) $^\circ$. For (I)- $P\bar{1}$, the distances from the corresponding planes are 0.343 (2) and -0.412 (3) Å [-0.466 (8) and 0.347 (7) Å for atoms C2A and C3A, and -0.300 (8) Å for atoms C2B and C3B from the C1A/C4A–C6A plane], respectively, and the angle between the end ring planes is 22.8 (1) $^\circ$. The torsion angles about the end rings of each polymorph (Table 1) display the normal features expected for a half-chair conformation. In particular, the largest torsion angle is about the C2–C3 bond, with values in

the range 61.8 (5)– 66.5 (8) $^\circ$. The smallest values are expected to be about the C5=C6 double bond, which they are to within experimental error, in the range 2.3 (9)– 8.3 (3) $^\circ$.

The polyene chains in both polymorphs are significantly nonplanar, shown by the torsion angles along the polyene chains, as is normally the case (Mo, 1995; Bartalucci *et al.*, 2008). The largest deviations from 180° are C11–C12–C13–C14 = -172.6 (5) $^\circ$ for (I)- $P2_1$ and C8A–C9A–C10A–C11A = -173.3 (2) $^\circ$ for (I)- $P\bar{1}$, and the torsion angles for both polymorphs show less deviation from 180° towards the centre of the molecule, and for one half of the molecule *versus* the other. The latter trend is also reflected in the methyl group torsion angles along the polyene chains, with largest values of

**Figure 3**

The disordered end ring of (I)- $P\bar{1}$. The refined occupancy of the A component, shown with solid bonds, is 0.542 (9).

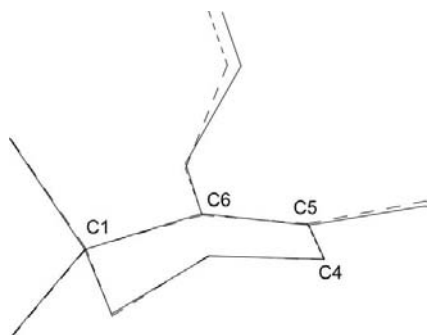


Figure 4
 Overlay of atoms C1/C4–C6 of the C1–C6 end rings of the two polymorphs, showing their similarity; the (I)- $P2_1$ polymorph is represented with dashed lines.

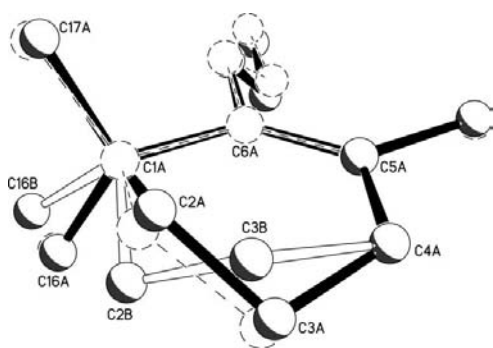


Figure 5
 Overlay of atoms C1A/C4A–C6A of the C1A–C6A end rings of the two polymorphs. The A component of the disordered (I)- $P\bar{1}$ polymorph is represented with shaded atoms and solid bonds, and the B component with shaded atoms and open bonds. The (I)- $P2_1$ polymorph is represented with dashed atoms and bonds.

$C11-C12-C13-C20 = -13.5(10)^\circ$ for (I)- $P2_1$ and $C20A-C13A-C14A-C15A = 12.0(6)^\circ$ for (I)- $P\bar{1}$. The greatest deviations of the methyl groups from the plane of the polyene chain are $-0.735(6)$ Å for atom C19 in (I)- $P2_1$ and $0.363(2)$ Å for atom C19A in (I)- $P\bar{1}$.

A detailed comparison of the two polymorphs has been carried out by overlaying the structures using the program *OFIT* from the *SHELXTL* package (Bruker, 2001). Firstly, an overlay of atoms C1 and C4–C6 of the C1–C6 end rings of (I)- $P2_1$ and (I)- $P\bar{1}$ clearly shows that these rings are very similar and in the same half-chair conformation (with the selected absolute configuration) (Fig. 4). A similar overlay of atoms C1A and C4A–C6A of the C1A–C6A end rings shows that the A component of the disordered end ring of (I)- $P\bar{1}$ fits reasonably closely, illustrating that the B component has the alternative half-chair conformation (Fig. 5). An overlay of the polyene chain atoms of each polymorph shows that they are reasonably similar, with an r.m.s. deviation of 0.22 Å. Looking down on the plane of the polyene chain, the chains appear to fit very well (Fig. 6a), but the differences leading to the r.m.s. deviation of 0.22 Å are much more apparent when the overlay is viewed down the plane of the polyene chain of (I)- $P\bar{1}$, reflecting the differences in torsion angles along the polyene chain for the two polymorphs (Fig. 6b). When the end ring atoms are included in the fit (excluding atoms C2B and C3B

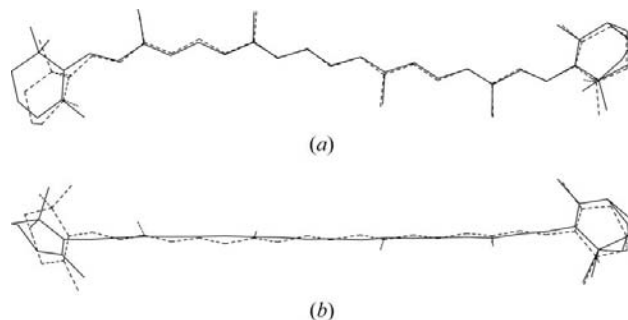


Figure 6
 Overlays of the polyene chains of the two polymorphs, viewed (a) face on to the plane of the polyene chain and (b) down the plane of the polyene chain of (I)- $P\bar{1}$. The (I)- $P2_1$ polymorph is represented with dashed lines.

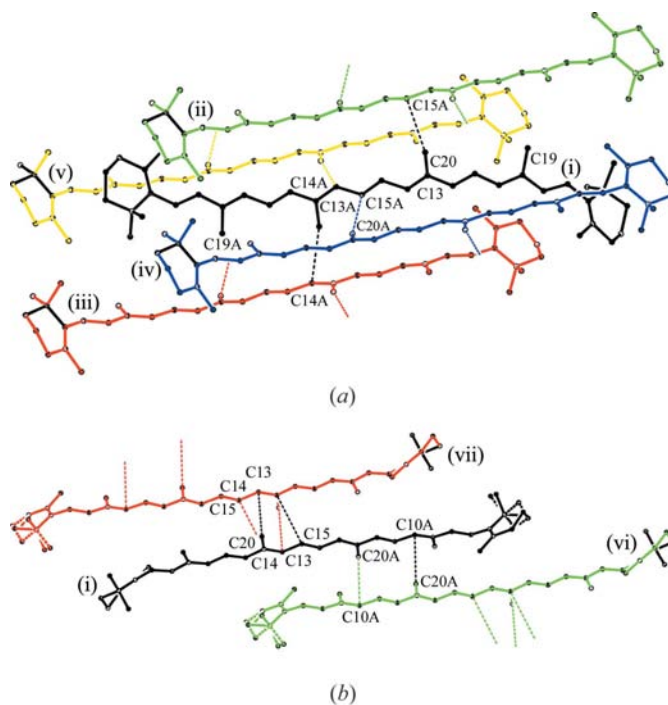


Figure 7
 Intermolecular interactions for (a) polymorph (I)- $P2_1$ [symmetry codes: (i) x, y, z ; (ii) $1-x, -\frac{1}{2}+y, -z$; (iii) $-x, \frac{1}{2}+y, -z$; (iv) $1-x, \frac{1}{2}+y, -z$; (v) $-x, -\frac{1}{2}+y, 1-z$] and (b) polymorph (I)- $P\bar{1}$ [symmetry codes: (i) x, y, z ; (vi) $1-x, 2-y, 2-z$; (vii) $-x, 1-y, -z$].

and the methyl groups), the r.m.s. deviation doubles to 0.44 Å, due to both the differing tilt angles of the end rings and the differing deviations from planarity of the polyene chains (Fig. 6).

In the (I)- $P2_1$ polymorph, there is no indication of the π -stacking interactions between polyene chains which have been seen in a number of related carotenoids (Bartalucci *et al.*, 2007, 2008). However, there are some short contacts between the half-occupancy atoms C20 and C20A and atoms of adjacent polyene chains. The shortest contacts are $C20 \cdots C15A(1-x, -\frac{1}{2}+y, -z)$ and $C20A \cdots C14A(-x, \frac{1}{2}+y, -z)$ of $3.01(1)$ and $3.07(2)$ Å, respectively (Fig. 7a). For (I)- $P\bar{1}$, the shortest contacts again involve the partially occupied atoms C20 and C20A [occupancies $0.821(4)$ and $0.179(4)$], with distances of $3.444(3)$ and $3.34(1)$ Å for $C20 \cdots C14(-x, -y+1,$

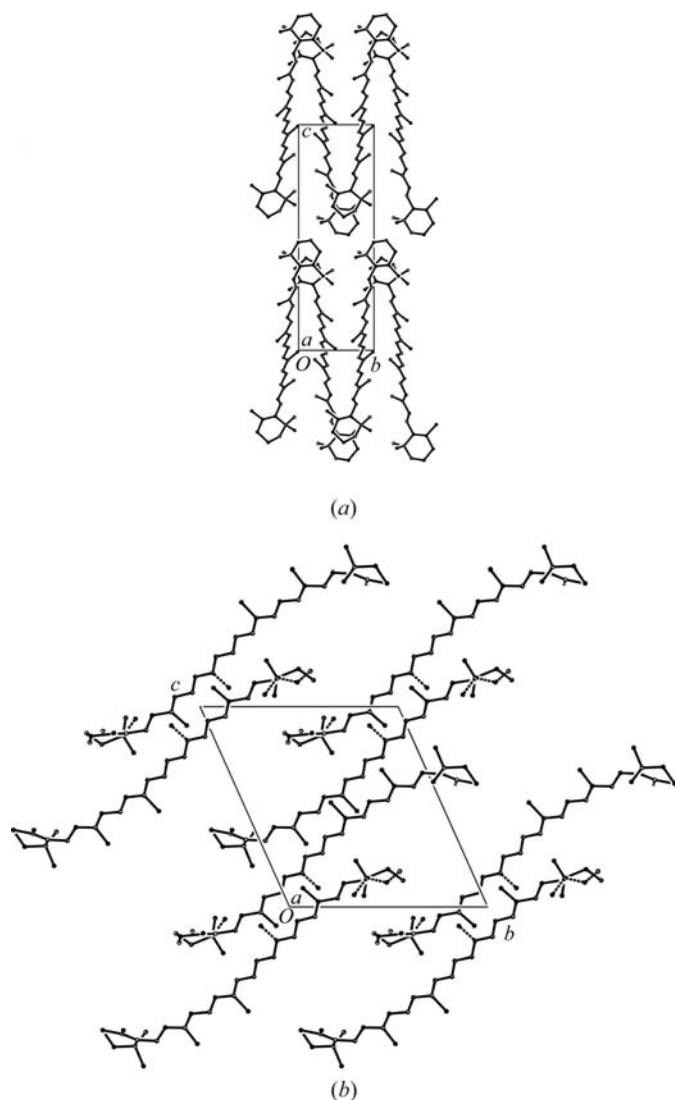


Figure 8
Packing diagrams for (a) (I)- $P2_1$ and (b) (I)- $P\bar{1}$, viewed in each case down the a axis.

$-z + 1$) and $C20A \cdots C10A(-x + 1, -y + 2, -z + 2)$, respectively (Fig. 7b). The polyene chains lie one above the other with possible π - π stacking interactions of the almost parallel polyene chains, with a minimum distance for $C13 \cdots C15(-x, -y + 1, -z + 1)$ of $3.687(3)$ Å. Overall, the packing arrangements of the two polymorphs are of course quite different, by virtue of the different space group symmetries (Fig. 8).

In summary, the two polymorphs of 20-desmethyl- β -carotene, (I), show differences in their patterns of disorder and conformations, as well as having quite different packing arrangements.

Experimental

For the present work, synthetic 20-desmethyl- β -carotene, (I) (Wirtz *et al.*, 2001), was available and thus offered information on the structural effect on the polyene chain for an intact 20-norcarotene. The two different polymorphs of (I) were crystallized in the same vial

using a vapour diffusion technique with water diffused into a solution of (I) in pyridine, with the solvents in an arbitrary ratio.

Polymorph (I)- $P2_1$

Crystal data

$C_{39}H_{54}$	$V = 1673.3(6)$ Å ³
$M_r = 522.82$	$Z = 2$
Monoclinic, $P2_1$	Mo $K\alpha$ radiation
$a = 9.442(2)$ Å	$\mu = 0.06$ mm ⁻¹
$b = 7.6914(16)$ Å	$T = 100(2)$ K
$c = 23.090(5)$ Å	$0.40 \times 0.22 \times 0.05$ mm
$\beta = 93.733(3)^\circ$	

Data collection

Bruker SMART CCD area-detector diffractometer	3196 independent reflections
8554 measured reflections	1530 reflections with $I > 2\sigma(I)$
	$R_{int} = 0.085$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.058$	1 restraint
$wR(F^2) = 0.112$	H-atom parameters constrained
$S = 0.85$	$\Delta\rho_{max} = 0.15$ e Å ⁻³
3195 reflections	$\Delta\rho_{min} = -0.15$ e Å ⁻³
373 parameters	

Polymorph (I)- $P\bar{1}$

Crystal data

$C_{39}H_{54}$	$\gamma = 99.084(3)^\circ$
$M_r = 522.82$	$V = 1681.1(4)$ Å ³
Triclinic, $P\bar{1}$	$Z = 2$
$a = 8.5717(13)$ Å	Mo $K\alpha$ radiation
$b = 14.089(2)$ Å	$\mu = 0.06$ mm ⁻¹
$c = 15.638(2)$ Å	$T = 100(2)$ K
$\alpha = 111.776(2)^\circ$	$0.90 \times 0.10 \times 0.10$ mm
$\beta = 99.304(3)^\circ$	

Data collection

Bruker SMART CCD area-detector diffractometer	8651 measured reflections
Absorption correction: multi-scan (SADABS; Bruker, 2001)	5808 independent reflections
$T_{min} = 0.868$, $T_{max} = 1.000$	3869 reflections with $I > 2\sigma(I)$
(expected range = 0.863–0.994)	$R_{int} = 0.021$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.052$	4 restraints
$wR(F^2) = 0.142$	H-atom parameters constrained
$S = 1.02$	$\Delta\rho_{max} = 0.25$ e Å ⁻³
5808 reflections	$\Delta\rho_{min} = -0.20$ e Å ⁻³
401 parameters	

Table 1

Torsion angles ($^\circ$) about the cyclohexene ring bonds of (I)- $P2_1$ and (I)- $P\bar{1}$.

ϕ_{x-y} are the torsion angles about the C_x-C_y bonds and 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.

	(I)- $P2_1$	(I)- $P2_1A$	(I)- $P\bar{1}$	(I)- $P\bar{1}A$	(I)- $P\bar{1}B$
ϕ_{1-2}	45.9(6)	-40.2(6)	43.2(3)	-50.3(6)	50.0(7)
ϕ_{2-3}	-64.0(6)	61.8(5)	-62.5(3)	66.5(8)	-63.6(8)
ϕ_{3-4}	46.0(6)	-49.9(6)	44.3(3)	-46.3(7)	45.6(8)
ϕ_{4-5}	-13.2(8)	19.5(8)	-10.7(3)	13.9(5)	-13.4(4)
ϕ_{5-6}	-5.0(9)	2.3(9)	-8.3(3)	2.6(3)	
ϕ_{6-1}	-11.2(7)	7.7(7)	-7.9(3)	15.4(4)	
$C5-C6-C7-C8$	-53.2(8)	47.3(8)	-41.4(2)	56.1(3)	

Polymorphs (I)- $P2_1$ and (I)- $P\bar{1}$ both show disorder between the two halves of the molecule, arising from the absence of the 20-methyl group bonded to C13 (or C13A). In (I)- $P2_1$, the occupancy of C20 refined to a value of 0.498 (8) and so the C20/C20A components were fixed at 0.5 for the final rounds of refinement. For (I)- $P\bar{1}$, the final refined occupancy of C20 (*versus* C20A) was 0.821 (4). (I)- $P\bar{1}$ showed additional disorder of atoms C2A, C3A and C16A arising from the presence of both half-chair conformations of the cyclohexene ring. The final refined occupancy of the major component was 0.542 (9). Some restraints were applied to the geometry of the disordered atoms of (I)- $P\bar{1}$: in the disordered end ring, equivalent bond distances of the two components were restrained to be the same using the SAME command (*SHELXL97*; Sheldrick, 2008), and the C13A–C20A distance was restrained to be 1.5 Å. In both structures, H atoms were included in calculated positions, with C–H distances varying from 0.95 to 0.99 Å and with U_{iso} values of 1.2 or 1.5 times U_{eq} of the parent C atom. 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.

For both polymorphs, data collection: *SMART* (Bruker, 2001); cell refinement: *SMART*. Data reduction: *SMART* for (I)- $P2_1$; *SAINTE* (Bruker, 2002) for (I)- $P\bar{1}$. For both compounds, program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *SHELXTL* (Bruker, 2001), *PLATON* (Spek, 2003), *WinGX* (Farrugia, 1999) and *PARST* (Nardelli, 1995); software used to prepare material for publication: *SHELXTL*.

Synthetic 20-desmethyl- β -carotene was a gift from Hoffmann–La Roche, Basel (Drs A. Giger, R. K. Müller and H. Schneider).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: JZ3128). Services for accessing these data are described at the back of the journal.

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