

Isomers of Diformyl[2.2]paracyclophane; X-Ray Structure Determinations of the Pseudo-*ortho* Isomer and Two Polymorphs of the Pseudo-*meta* Isomer

Peter G. Jones^a, Ina Dix^b, Mihaela Negru^c, and Dieter Schollmeyer^c

^a Institute of Inorganic and Analytical Chemistry, Technical University of Braunschweig, PO Box 3329, 38023 Braunschweig, Germany

^b Institute of Organic Chemistry, Technical University of Braunschweig, PO Box 3329, 38023 Braunschweig, Germany

(Current address: Novartis Pharma AG, Forum 1, Novartis Campus, 4056 Basel, Switzerland)

^c Institute of Organic Chemistry, University of Mainz, Duesbergweg 10–14, 55099 Mainz, Germany

Reprint requests to Prof. Dr. P. G. Jones. Fax: +49-531-391-5387. E-mail: p.jones@tu-bs.de

Z. Naturforsch. **2011**, *66b*, 705–710; received May 25, 2011

Pseudo-*ortho*- or 4,16-diformyl[2.2]paracyclophane (**1**) and two polymorphs of pseudo-*meta*- or 4,13-diformyl[2.2]paracyclophane (**2**) all display the usual features of [2.2]paracyclophane strain (lengthened C–C bonds and widened C–C(*sp*³)–C angles in the bridges, narrower *sp*² ring angles at the bridgehead atoms, and flattened boat conformations of the rings). All bulk samples were racemates. Polymorph **2a** crystallizes in space group *P2*₁/*n* with one molecule in a general position, whereas **2b** crystallizes in space group *C2* with two independent molecules, each with crystallographic twofold symmetry. All three molecules of **2** are different rotamers with respect to the formyl groups; in **2a** one is *endo* and one *exo* to the neighbouring bridge, whereas in **2b** both formyls are *exo* in one molecule and *endo* in the other. In all compounds, the packing patterns are preponderantly associated with C–H···O contacts. In **1** the molecules are connected to form tubes parallel to the short *a* axis. **2a** consists of two interconnected layer structures. One is parallel to (100) and involves chains of molecules parallel to [011]; the other is parallel to (001) and involves chains of molecules parallel to the *b* axis. **2b** consists of two hexagonal layers, one for each independent molecule, parallel to (001). One layer contains bifurcated (C–H···)₂O systems, whereas the single H···O interactions in the other are long and markedly bent.

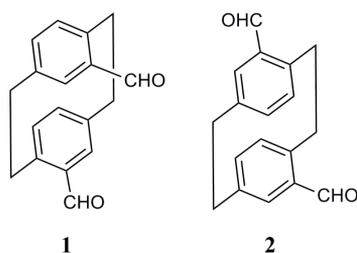
Key words: Paracyclophanes, X-Ray Structures, Secondary Interactions, Polymorphs

Introduction

We are interested in the structural chemistry, and in particular in the molecular packing patterns, of [2.2]paracyclophane derivatives. These are strained molecules in which the strain expresses itself as lengthened C–C bonds and widened C–C(*sp*³)–C angles in the bridges, narrower *sp*² ring angles at the bridgehead atoms, and flattened boat conformations of the rings, whereby the bridgehead atoms are displaced out of the plane of the other four atoms towards the bridges. The packing, especially of simpler (mono- or disubstituted) derivatives that lack classical hydrogen bonds, often involves hexagonal layer substructures with C–H··· π interactions, and these are so similar for a wide variety of small substituents that the cell constants parallel to the layer often display closely similar values of *ca.* 7 and 11 Å; for this reason we refer to the “7,11”-

pattern [1]. For some more recent examples, see *e. g.* refs. [2, 3].

Of particular interest to synthetic chemists, on the other hand, are the diformyl derivatives, of which there are four isomers that bear one substituent on each ring. The preparation, separation and spectroscopic identification of these isomers has recently been described [4], but the crystallographic aspects were omitted. In fact all four isomers were crystallographically characterized [5], but two, the pseudo-*para* and pseudo-*gem* isomers, proved to be severely disordered. The pseudo-*ortho* isomer **1** (Scheme 1) provided an ordered structure, even if this was not very precise because of limited crystal quality; the main features of the molecular packing, however, may be established unambiguously because all hydrogen positions can be geometrically fixed. The structure of the pseudo-*meta* isomer **2a**, which crystallizes in space group *P2*₁/*n*,



Scheme 1.

proved to be ordered and of acceptable quality. We recently determined the structure of a second polymorph **2b** in space group *C2*, for which the structure was initially deposited in the Cambridge Crystallographic Database [6] as a Private Communication with refcode VECRUR01. All three structures are now presented here.

Some comments as to the nomenclature and numbering of [2.2]paracyclophanes are appropriate. The two rings are numbered C3–8 and C11–16, and the first substituent is placed at C4, defining the direction of numbering for this ring. For the second ring, however, the numbering may be in the same or the opposite sense, leading to two possible numbering systems. We have generally adopted the former system, as used in this publication. The description of the isomers as pseudo-*ortho*, *etc.*, based on the relative substituent positions when one ring is projected onto the other, is unambiguous; this isomer is 4,16 in the system used here but would be 4,12 in the alternative system, whereas the pseudo-*meta* isomer is 4,13 (here) or 4,15. The nomenclature of these and other multiply substituted [2.2]paracyclophanes is discussed thoroughly by Vorontsova *et al.* [7].

Discussion

Compound **1** crystallizes with two independent molecules, which are shown in Fig. 1, and display

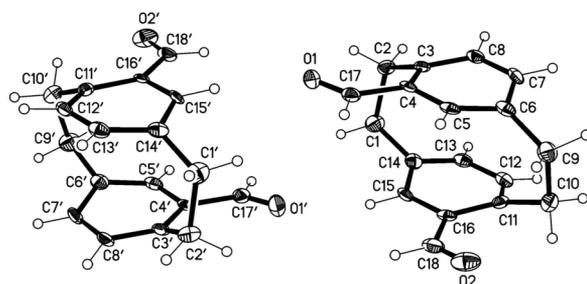


Fig. 1. The two independent molecules of pseudo-*meta* isomer **1**. Ellipsoids represent 30% probability levels. Note the implicit hydrogen bonds H15'...O1 and H15...O1'.

Table 1. Selected geometric parameters (Å, deg) for isomer **1**.

C1–C2	1.604(7)	C1'–C2'	1.583(8)
C9–C10	1.602(7)	C9'–C10'	1.594(8)
C14–C1–C2	112.2(4)	C3'–C2'–C1'	111.8(4)
C8–C3–C4	115.4(5)	C8'–C3'–C4'	116.1(5)
C5–C6–C7	114.7(5)	C5'–C6'–C7'	115.2(5)
C6–C9–C10	112.5(4)	C6'–C9'–C10'	112.3(4)
C12–C11–C16	115.7(5)	C11'–C10'–C9'	112.3(4)
C15–C14–C13	115.2(5)	C12'–C11'–C16'	115.3(5)
C14'–C1'–C2'	112.8(4)	C13'–C14'–C15'	115.7(5)
C14–C1–C2–C3	–20.6(6)	C14'–C1'–C2'–C3'	18.3(7)
C6–C9–C10–C11	–17.8(7)	C6'–C9'–C10'–C11'	18.9(7)
C3–C4–C17–O1	–8.7(8)	C3'–C4'–C17'–O1'	–1.2(8)
C11–C16–C18–O2	3.9(8)	C11'–C16'–C18'–O2'	6.2(8)

Table 2. Hydrogen-bond geometry (Å, deg) for isomer **1**^a.

<i>D</i> –H... <i>A</i>	<i>D</i> –H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> –H... <i>A</i>
C7'–H7'...O1 ⁱ	0.95	2.48	3.430(6)	175
C15'–H15'...O1	0.95	2.44	3.380(6)	173
C5'–H5'...O2 ⁱⁱ	0.95	2.57	3.475(6)	159
C15–H15...O1'	0.95	2.45	3.376(6)	164
C5–H5...O2 ⁱⁱⁱ	0.95	2.49	3.415(6)	164
C12–H12...O2 ^{iv}	0.95	2.55	3.483(7)	168

^a Symmetry codes: ⁱ $-x+1, y-1/2, -z+3/2$; ⁱⁱ $x-1, y, z$; ⁱⁱⁱ $x+1, y, z$; ^{iv} $x+1, -y+3/2, z-1/2$.

the typical features of [2.2]paracyclophane geometry as described above (Table 1); for each ring, the bridgehead atom lies 0.15–0.17 Å out of the plane of the other four ring atoms (details are contained in the Supplementary Information; see note at the end of the paper for availability), and the formyl group is approximately coplanar with the ring and *endo* to its neighbouring bridge (Table 1). Both molecules display approximate twofold symmetry; least-squares fits of the two halves of the same molecule gave r. m. s. deviations of 0.05 Å for the first and 0.08 Å for the second molecule, whereas a fit of the first to the second molecule gave an r. m. s. deviation of 0.07 Å.

The molecular packing involves six interactions of the type C–H...O, all of which are acceptably short (< 2.6 Å) and linear (> 158°) to qualify as weak hydrogen bonds (Table 2); there are no short H... π or π ... π contacts. The molecules are connected to form tubes parallel to the short *a* axis (Fig. 2; one tube shown horizontally, together with some neighbouring molecules). Within the tubes, the molecules are linked by the topologically equivalent contacts H15...O1' / H15'...O1 (within the asymmetric unit) and H5...O2ⁱⁱⁱ / H5'...O2ⁱⁱ (related by *a* axis translation). The topological equivalence of the two molecules no longer applies to the connections to neighbouring tubes, namely H7'...O1ⁱ (*via* the screw

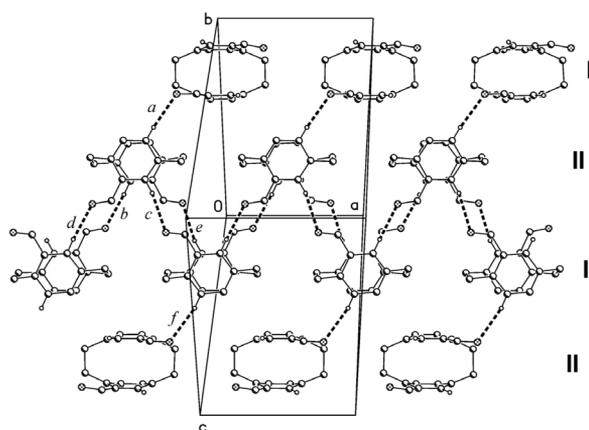


Fig. 2. Packing diagram of isomer **1** showing C–H...O interactions as dashed lines. H atoms not involved in H bonding are omitted. One of each independent interaction type is labelled with italic letters *a–f* according to its order in Table 2. The view direction is perpendicular to (011). Labels **I** and **II** refer to horizontal rows of the first and second independent molecule, respectively.

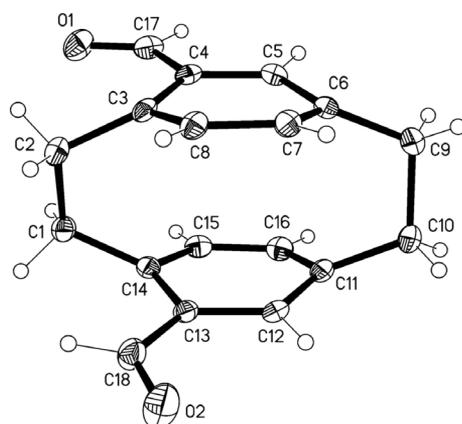


Fig. 3. The molecule of pseudo-*ortho* isomer **2a**. Ellipsoids represent 30% probability levels.

axis) and H12...O2^{iv} (via the glide plane), forming a three-dimensional system.

The molecule of isomer **2a** is shown in Fig. 3. General features (Table 3) are as already noted for **1**, but the formyl groups are differently disposed; C17=O1 is *endo* to the bridge, but C18=O2 is *exo*. The molecular packing is less clear-cut than for isomer **1**; there are four C–H...O contacts, three of which are long (H...O > 2.6 Å), and one C–H... π contact to *Cg*, the centre of gravity of C12, 13, 15, 16 (Table 4). The overall packing is three-dimensional, but can be analyzed as two interconnected layer structures. One of these (Fig. 4), parallel to (100), involves chains of molecules

Table 3. Selected geometric parameters (Å, deg) for isomer **2a**.

C1–C2	1.578(3)	C9–C10	1.586(3)
C14–C1–C2	111.81(15)	C6–C9–C10	111.55(15)
C3–C2–C1	112.22(15)	C11–C10–C9	112.74(15)
C8–C3–C4	116.17(18)	C12–C11–C16	116.32(18)
C5–C6–C7	116.28(18)	C15–C14–C13	116.48(17)
C14–C1–C2–C3	25.6(2)	C3–C4–C17–O1	4.1(3)
C6–C9–C10–C11	17.5(2)	C14–C13–C18–O2	174.3(2)

Table 4. Hydrogen-bond geometry (Å, deg) for isomer **2a**^a.

D–H...A	D–H	H...A	D...A	D–H...A
C8–H8...O1 ⁱ	0.95	2.67	3.589(2)	163
C15–H15...O1 ⁱⁱ	0.95	2.61	3.464(2)	150
C2–H2A...O2 ⁱⁱⁱ	0.99	2.66	3.391(3)	131
C7–H7...O2 ^{iv}	0.95	2.49	3.363(3)	153
C9–H9B...Cg(C12,13,15,16) ^v	0.99	2.89	3.65	160

^a Symmetry codes: ⁱ $-x+3/2, y+1/2, -z+1/2$; ⁱⁱ $-x+1, -y, -z$; ⁱⁱⁱ $-x+3/2, y-1/2, -z+1/2$; ^{iv} $-x+1, -y+1, -z+1$; ^v $-x+1/2, y-1/2, -z+1/2$.

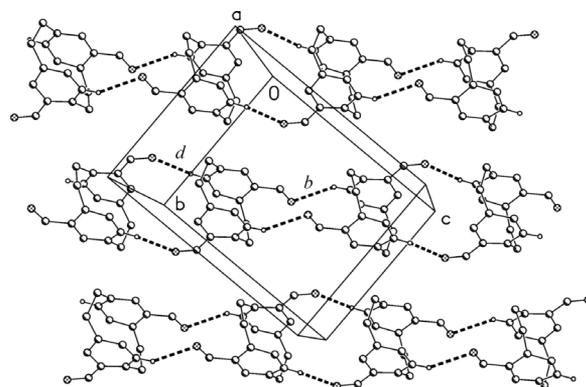


Fig. 4. Packing of isomer **2a**; view direction perpendicular to (100), region $x \approx 0$. H...O interactions are indicated by dashed lines. One of each independent interaction type is labelled with italic letters according to its order in Table 4.

parallel to $[0\bar{1}1]$, linked via the contacts H7...O2^{iv} and H15...O1ⁱⁱ over successive inversion centres. The other (Fig. 5), parallel to (001), involves chains of molecules parallel to the *b* axis, linked by H2A...O2ⁱⁱⁱ and H8...O1ⁱ via the screw axis; the chains are connected by H9B...Cg^v.

Isomer **2b** crystallizes with two independent molecules, each of which displays crystallographic twofold symmetry (Fig. 6). Again, one can make out the typical features of [2.2]paracyclophane geometry as described above (Table 5). The formyl groups are both *endo* to the bridge in the unprimed molecule and *exo* in the primed molecule, so that **2a** and **2b** represent the three possible different rotamers with respect to the formyl groups.

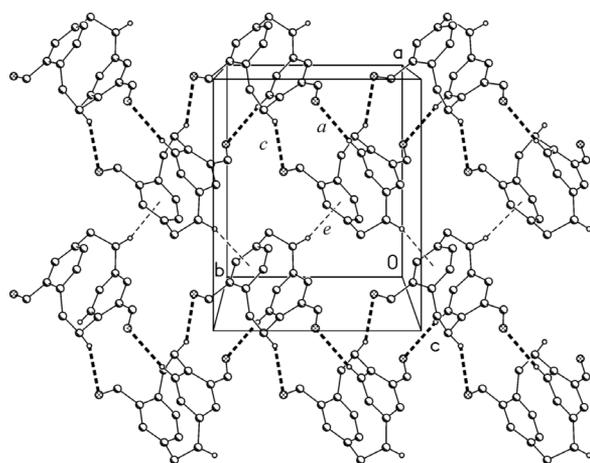


Fig. 5. Packing of isomer **2a**; view direction perpendicular to (001), region $z \approx 1/4$. $\text{H}\cdots\text{O}$ interactions are indicated by thick dashed lines and $\text{H}\cdots\pi$ by thin dashed lines. One of each independent interaction type is labelled with italic letters according to its order in Table 4.

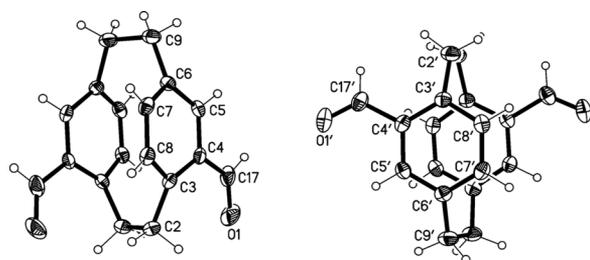


Fig. 6. The two independent molecules of pseudo-*meta* isomer **2b**. Only the asymmetric unit is numbered. The unprimed molecule involves the operator $-x + 1, y, -z$ and the primed molecule $-x, y, -z + 1$. Ellipsoids represent 30% probability levels.

The molecular packing involves layers parallel to (001). The unprimed molecule forms layers at $z \approx 0$ and the primed molecule at $z \approx 1/2$. Within the layers, only long and markedly bent $\text{C}-\text{H}\cdots\text{O}$ interactions can be recognized (Table 6). For the unprimed molecules, this is consistent with the bifurcated nature of the system ($\text{H5}\cdots\text{O1}^{\text{iii}}$, $\text{H7}\cdots\text{O1}^{\text{iv}}$) (Fig. 7). The contacts $\text{H9}'/2\cdots\text{O1}'^{\text{vi}}$ between the primed molecules must be regarded as borderline and are not included in Fig. 8, which shows the linkage of the layers *via* $\text{C2}-\text{H2A}\cdots\text{O1}'^{\text{v}}$. The lack of short secondary interactions may be described as a less efficient packing and is reflected in the somewhat lower density of 1.317 g cm^{-3} , compared to the value of 1.335 for **2a**.

The packing patterns of all three structures thus involve preponderantly $\text{C}-\text{H}\cdots\text{O}$ interactions, albeit many of them rather long and bent, rather than $\text{C}-$

Table 5. Selected geometric parameters (\AA , deg) for isomer **2b**^a.

$\text{C2}-\text{C2}^{\text{i}}$	1.582(4)	$\text{C2}'-\text{C2}'^{\text{ii}}$	1.585(4)
$\text{C9}-\text{C9}^{\text{i}}$	1.573(4)	$\text{C9}'-\text{C9}'^{\text{ii}}$	1.587(4)
$\text{C3}-\text{C2}-\text{C2}^{\text{i}}$	112.18(11)	$\text{C3}'-\text{C2}'-\text{C2}'^{\text{ii}}$	112.71(10)
$\text{C8}-\text{C3}-\text{C4}$	116.23(15)	$\text{C8}'-\text{C3}'-\text{C4}'$	116.64(16)
$\text{C7}-\text{C6}-\text{C5}$	116.45(16)	$\text{C5}'-\text{C6}'-\text{C7}'$	116.96(16)
$\text{C6}-\text{C9}-\text{C9}^{\text{i}}$	113.08(10)	$\text{C6}'-\text{C9}'-\text{C9}'^{\text{ii}}$	112.14(11)
$\text{C3}-\text{C4}-\text{C17}-\text{O1}$	-1.9(3)	$\text{C6}-\text{C9}-\text{C9}^{\text{i}}-\text{C6}^{\text{i}}$	-8.2(4)
$\text{C3}'-\text{C4}'-\text{C17}'-\text{O1}'$	-174.28(18)	$\text{C3}'-\text{C2}'-\text{C2}'^{\text{ii}}-\text{C3}'^{\text{ii}}$	-16.7(4)
$\text{C3}-\text{C2}-\text{C2}^{\text{i}}-\text{C3}^{\text{i}}$	-25.0(3)	$\text{C6}'-\text{C9}'-\text{C9}'^{\text{ii}}-\text{C6}'^{\text{ii}}$	-15.1(4)

^a Symmetry codes: ⁱ $-x + 1, y, -z$; ⁱⁱ $-x, y, -z + 1$.

Table 6. Hydrogen-bond geometry (\AA , deg) for isomer **2b**^a.

$D-\text{H}\cdots A$	$D-\text{H}$	$\text{H}\cdots A$	$D\cdots A$	$D-\text{H}\cdots A$
$\text{C5}-\text{H5}\cdots\text{O1}^{\text{iii}}$	0.95	2.62	3.374(2)	136
$\text{C7}-\text{H7}\cdots\text{O1}^{\text{iv}}$	0.95	2.63	3.334(2)	131
$\text{C2}-\text{H2A}\cdots\text{O1}'^{\text{v}}$	0.99	2.59	3.319(3)	131
$\text{C9}'-\text{H9}'/2\cdots\text{O1}'^{\text{vi}}$	0.99	2.69	3.389(3)	128

^a Symmetry codes: ⁱⁱⁱ $-x + 1/2, y - 1/2, -z$; ^{iv} $x + 1/2, y - 1/2, z$; ^v $x + 1/2, y + 1/2, z$; ^{vi} $-x + 1/2, y + 1/2, -z + 1$.

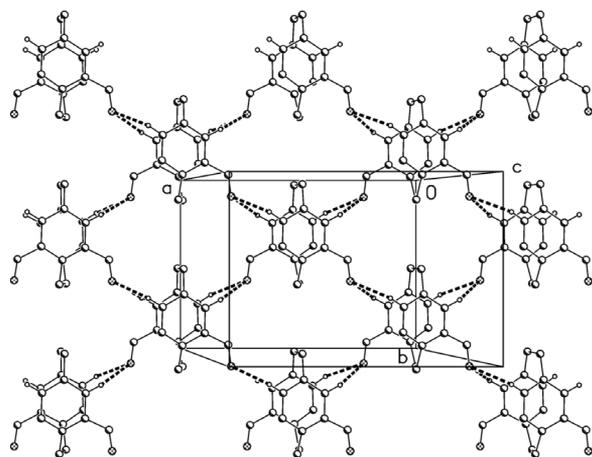


Fig. 7. Packing of isomer **2b**, unprimed molecule; view direction perpendicular to (001), region $z \approx 0$. $\text{H}\cdots\text{O}$ interactions are indicated by dashed lines.

$\text{H}\cdots\pi$. Consistent with this, the “7,11” pattern of cell constants [1] is not observed, despite the presence of layer substructures with hexagonal packing in **2b**.

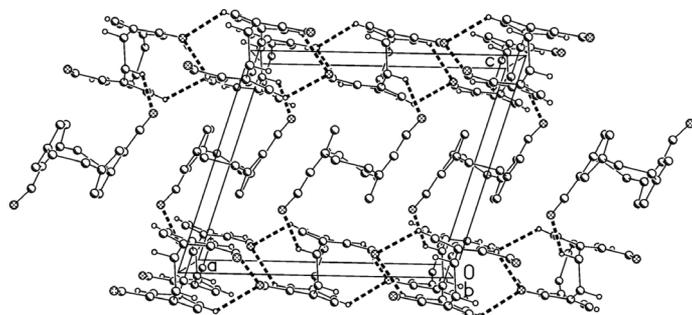
Experimental Section

Isomers **1** and **2a** were prepared as previously described [4,5] and crystallized by evaporation from a solution in chloroform. Isomer **2b** was prepared as previously described [8] and crystallized from a solution in dichloromethane.

X-Ray structure determinations

Crystal data are summarized in Table 7. Data were registered on a Syntex P4 diffractometer using monochromated

Compound	1	2a	2b
Formula	C ₁₈ H ₁₆ O ₂	C ₁₈ H ₁₆ O ₂	C ₁₈ H ₁₆ O ₂
<i>M_r</i>	264.31	264.31	264.31
Crystal size, mm ³	0.50 × 0.45 × 0.40	0.6 × 0.4 × 0.4	0.4 × 0.03 × 0.03
Crystal system	monoclinic	monoclinic	monoclinic
Space group	<i>P</i> 2 ₁ / <i>c</i>	<i>P</i> 2 ₁ / <i>n</i>	<i>C</i> 2
<i>a</i> , Å	9.282(4)	11.665(2)	13.1484(5)
<i>b</i> , Å	16.798(5)	9.5751(12)	9.4383(2)
<i>c</i> , Å	16.931(5)	11.963(2)	11.2313(8)
β , deg	93.54(3)	100.219(16)	106.919(5)
<i>V</i> , Å ³	2634.7(15)	1315.1(4)	1333.46(11)
<i>Z</i>	8	4	4
<i>D_x</i> , Mg m ⁻³	1.33	1.34	1.32
μ , mm ⁻¹	0.1	0.1	0.7
<i>F</i> (000), e	1120	560	560
<i>T</i> , K	173	173	193
λ , Å	0.71073	0.71073	1.54148
2 θ _{max} , deg	50	50	140
Measured / indep. refl. / <i>R</i> _{int}	5131 / 4554 / 0.129	2484 / 2309 / 0.021	2347 / 2347 / –
Ref. parameters	362	181	181
Restraints	368	184	1
<i>R</i> [<i>F</i> ≥ 4 σ (<i>F</i>)]	0.088	0.044	0.038
<i>wR</i> (<i>F</i> ² , all refl.)	0.258	0.108	0.101
<i>S</i>	0.88	0.89	1.06
Max. $\Delta\rho$, e Å ⁻³	0.49	0.20	0.14

Table 7. X-Ray data for compounds **1–3**.Fig. 8. Packing of isomer **2b**, both molecules; view direction parallel to the *b* axis. H···O interactions are indicated by dashed lines. The layers of unprimed molecules at $z \approx 0$ and 1 are linked to the primed molecules at $z \approx 1/2$ by the interaction C2–H2A···O1'^V.

MoK α radiation (**1**, **2a**) or an Enraf-Nonius CAD-4 diffractometer using monochromatized CuK α radiation from a rotating anode (**2b**). Structures were solved using routine Direct Methods and refined using the program SHELXL-97 [9]. The crystal quality was only moderate for **1**. Hydrogen atoms were introduced at calculated positions and refined using a riding model, with C–H 0.95 Å for C(*sp*²)–H and 0.99 Å for C(methylene)–H. The *U*_{iso}(H) values were set equal to 1.2*U*_{eq}(C) of the parent carbons. For structure **2b**, the Flack parameter refined to 0.0(3), giving a weak indication of the absolute structure; however, the compound was a race-

mate and crystallized only by chance in a Sohncke space group.

Supplementary Information

Complete crystallographic data have been deposited at the Cambridge Crystallographic Data Centre under the numbers CCDC 826600–826602 for compounds **1**, **2a**, **2b**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

- [1] K. El Shaieb, V. Narayanan, H. Hopf, I. Dix, A. K. Fischer, P. G. Jones, L. Ernst, K. Ibrom, *Eur. J. Org. Chem.* **2003**, 567–577.
- [2] P. G. Jones, I. Dix, H. Hopf, *Acta Crystallogr.* **2007**, C63, o468–o473.
- [3] K. Broschinski, A. Kannan, P. G. Jones, I. Dix, H. Hopf, *Acta Crystallogr.* **2007**, C63, o711–o713.
- [4] I. Dix, H. Hopf, T. B. N. Satnyarayana, L. Ernst, *Beilstein J. Org. Chem.* **2010**, 6, 932–937.

- [5] I. Dix, Dissertation, Technical University of Braunschweig, Braunschweig (Germany) **2001**.
- [6] F. H. Allen, *Acta Crystallogr.* **2002**, *B58*, 380–388.
- [7] N. V. Vorontsova, V. I. Rozenberg, E. V. Sergeeva, E. V. Vorontsov, Z. A. Starikova, K. A. Lyssenko, H. Hopf, *Chem. Eur. J.* **2008**, *14*, 4600–4617.
- [8] M. Negru, Dissertation, University of Mainz, Mainz (Germany) **2007**.
- [9] G. M. Sheldrick, SHELXL-97, Program for the Refinement of Crystal Structures, University of Göttingen, Göttingen (Germany) **1997**. See also: G. M. Sheldrick, *Acta Crystallogr.* **2008**, *A64*, 112–122.