

Optical Induction in Chiral Crystals.

IV.* The Correlation between the Absolute *Conformation* of 4,4'-Dimethylchalcone and the Absolute Configuration of Its Dibromide

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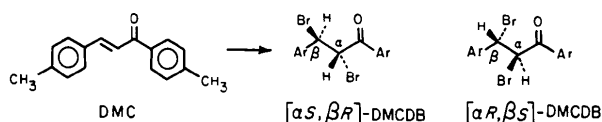
Abstract

The structure and absolute configuration of the enantiomer of 4,4'-dimethylchalcone dibromide ($C_{17}H_{16}Br_2O$) formed in excess in a gas/solid bromination reaction of a single crystal of 4,4'-dimethylchalcone have been determined at 85 K. The crystals are orthorhombic, space group $P2_12_12_1$, with $a = 35.167(4)$, $b = 5.544(1)$, $c = 7.915(1)$ Å, $Z = 4$. Refinement of the two possible enantiomers gave $R = 0.0489, 0.0618$; $R_w = 0.0323, 0.0436$ for a total of 1806 observed reflections. The successful determination of the chirality of the conformation of the reactant (the absolute *conformation*) made it possible, for the first time, to correlate the absolute configuration and optical rotation of the product and the conformation of the achiral, optically inactive, olefinic reactant in a chiral crystal. This correlation supports the proposed reaction mechanism involving a bromonium ion intermediate. The striking similarity of the packing arrangements of the product and reactant may explain the exclusive crystallization of crystals of one-handedness in excess, when minute quantities of the former are added to solutions of the latter.

Introduction

In part I of this series (Rabinovich & Shakked, 1974) we have discussed the different behaviour of 4,4'-dimethylchalcone (DMC) and 4-methoxychalcone (MC) in gas/single-crystal bromination reactions (Penzien & Schmidt, 1969). The formation of an excess of one of the two possible enantiomers of the dibromide in DMC (scheme I) and the apparent absence of optical induction in MC were interpreted in terms of the different molecular conformations in the crystal. We

have argued that the marked non-planar conformation of DMC results in different front–rear topologies of the C=C double bond which lead to preferential formation of a bridged bromonium ion on one side of the bond. The nearly planar environmental topology of the C=C double bond in MC explains the absence of any optical induction.



Scheme (I)

The determination of the structure and absolute configuration of 4,4'-dimethylchalcone dibromide (DMCDB) described here, and the successful determination of the absolute *conformation* of DMC (Rabinovich & Hope, 1980) were performed to enable a critical examination of the foregoing hypothesis by correlating the geometries of the reactant and the product.

Experimental

A sample of dextrorotatory DMCDB, prepared by the reaction of Br_2 vapour on a large crushed single crystal of DMC grown from the melt, was crystallized from benzene:hexane, 1:1. The first two crystallizations afforded colourless crystals with no remaining traces of DMC; after four more crystallizations a batch of crystals having $[\alpha]_D^{CHCl_3} = 159^\circ$ ($c = 2.0$ g dm^{-3}) was obtained. A small crystal ($0.08 \times 0.08 \times 0.10$ mm) from this batch was used for the X-ray analysis. Crystal data are given in Table 1.

Intensities ($\theta < 27^\circ$, one octant of the reciprocal sphere, 1883 reflections) were collected at liquid-nitrogen temperature (85 K) on a Picker automatic four-circle diffractometer with graphite-monochro-

* Part III: Shakked (1979).

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Table 1. *Crystal data*

4,4'-Dimethylchalcone dibromide, C ₁₇ H ₁₆ Br ₂ O, m.p. 449 K	
Orthorhombic, P2 ₁ 2 ₁ 2 ₁	$M_r = 396.1$, $U = 1543.2 \text{ \AA}^3$
$a = 35.167(4) \text{ \AA}$	$D_x = 1.70 \text{ Mg m}^{-3}$ for $Z = 4$
$b = 5.544(1) \text{ \AA}$	$D_m = 1.71$
$c = 7.915(1) \text{ \AA}$	$\mu(\text{Mo K}\alpha) = 5.12 \text{ mm}^{-1}$

mated Mo K α radiation. The intensities were measured by the ω -scan technique followed by two point-background counts at each end of the scan. The intensity of a standard reflection was monitored every 100 reflections and no significant variations were observed. The data were corrected for Lorentz and polarization effects but not for absorption. The random error of an observation was estimated to comprise 1% of the net intensity ($I - B$) in addition to the statistical counting error.

Structure determination and refinement

The structure was solved by Patterson and heavy-atom techniques. The structure was first refined isotropically by least squares. Next, all H atoms except for those of the methyl groups were introduced geometrically and the structure was refined anisotropically for the Br and isotropically for the rest of the atoms. A subsequent difference synthesis located the methyl H atoms. The final refinement was with *SHELX 76* (Sheldrick, 1976) in the following manner: the non-hydrogen atoms were refined anisotropically, the phenyl H were riding on the corresponding C atoms with fixed bond length (1.0 Å) and with one common adjustable isotropic temperature factor. H(22) and H(23), Fig. 1, were riding on C(7) and C(8). The methyl H atoms were refined as rigid groups, retaining their threefold symmetry, again with one common isotropic temperature factor. While these constraints had a negligible effect on R , they resulted in much more sensible H atom parameters in the presence of the two heavy Br scatterers. Refinements of both possible enantiomorphous structures were carried out to establish the absolute configuration. The final $R = \sum |F_o - k|F_c| / \sum F_o = 0.0489$, 0.0618 , and $R_w = [\sum w(F_o - k|F_c|)^2 / \sum wF_o^2]^{1/2} = 0.0323$, 0.0436 , where $w = 1/\sigma^2(F_o)$, for 190 refined parameters and 1806 re-

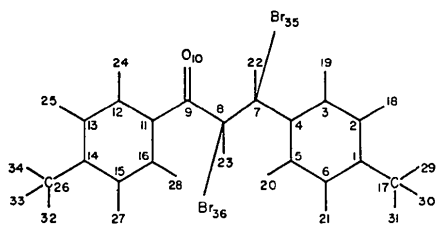


Fig. 1. 4,4'-Dimethylchalcone dibromide (DMCDB). Chemical formula and numbering of atoms.

Table 2. *Atom coordinates* ($\times 10^5$ for Br, $\times 10^4$ for C and O) and *equivalent isotropic thermal parameters* ($\times 10^4$ for Br, $\times 10^3$ for C and O)

	x	y	z	$U_{eq} (\text{\AA}^2)^*$
C(1)	2562 (2)	-3540 (14)	393 (9)	16 (4)
C(2)	2578 (2)	-1357 (13)	1268 (8)	18 (4)
C(3)	2256 (2)	-56 (13)	1575 (7)	16 (4)
C(4)	1902 (2)	-849 (13)	1045 (8)	16 (4)
C(5)	1880 (2)	-3047 (13)	178 (9)	19 (4)
C(6)	2207 (2)	-4353 (13)	-151 (8)	18 (4)
C(7)	1558 (2)	618 (13)	1440 (8)	17 (4)
C(8)	1200 (2)	359 (13)	318 (8)	19 (4)
C(9)	901 (2)	2223 (15)	667 (9)	20 (4)
O(10)	996 (1)	4236 (9)	1163 (6)	23 (3)
C(11)	501 (2)	1594 (12)	346 (8)	15 (4)
C(12)	218 (2)	3191 (13)	879 (8)	16 (4)
C(13)	-162 (2)	2721 (13)	569 (9)	19 (4)
C(14)	-274 (2)	634 (13)	-283 (8)	19 (4)
C(15)	10 (2)	-953 (13)	-797 (8)	16 (4)
C(16)	389 (2)	-524 (13)	-490 (8)	18 (4)
C(17)	2916 (2)	-4990 (13)	59 (9)	20 (4)
C(26)	-687 (2)	132 (16)	-626 (10)	27 (5)
Br(35)	13493 (2)	-2890 (13)	37185 (8)	229 (4)
Br(36)	13617 (2)	10291 (14)	-20431 (8)	258 (4)

$$* U_{eq} = \frac{1}{3} \text{trace } \bar{U}.$$

flections with $(I - B) > 0$.^{*} The coordinates and thermal parameters of the two structures agree within 2σ . Scattering factors and anomalous-dispersion terms were taken from *International Tables for X-ray Crystallography* (1974).

Use of Hamilton's (1965) test indicates that the difference between the two refined enantiomorphs as implied by the R_w values is highly significant and the handedness given by the parameters of the first enantiomorph (Table 2) with a right-handed coordinate system is the correct one. Hence, the absolute

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35617 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

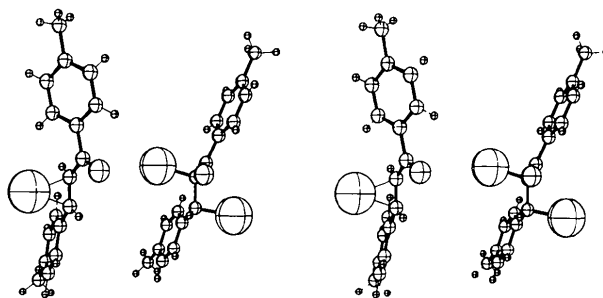


Fig. 2. Stereoscopic view of the absolute geometries of 4,4'-dimethylchalcone and its related (-)-[α , S , β , R] dibromide. Also shown is the proposed bridged bromonium ion.

Table 3. H atom coordinates ($\times 10^4$) and isotropic temperature factors ($\text{\AA}^2 \times 10^3$)

	x	y	z	U
H(18)	2829 (2)	-741 (13)	1673 (8)	10 (6)
H(19)	2276 (2)	1510 (13)	2195 (7)	10 (6)
H(20)	1626 (2)	-3665 (13)	-194 (9)	10 (6)
H(21)	2187 (2)	-5896 (13)	-799 (8)	10 (6)
H(22)	1661 (2)	2287 (13)	1310 (8)	37 (16)
H(23)	1101 (2)	-1304 (13)	531 (8)	37 (16)
H(24)	291 (2)	4690 (13)	1502 (8)	10 (6)
H(25)	-361 (2)	3895 (13)	940 (9)	10 (6)
H(27)	-66 (2)	-2449 (13)	-1418 (8)	10 (6)
H(28)	586 (2)	-1717 (13)	-852 (8)	10 (6)
H(29)	2863 (2)	-5975 (13)	-973 (9)	60 (12)
H(30)	2984 (2)	-6083 (13)	1017 (9)	60 (12)
H(31)	3131 (2)	-3861 (13)	-170 (9)	60 (12)
H(32)	-822 (2)	1718 (16)	-619 (10)	60 (12)
H(33)	-784 (2)	-894 (16)	319 (10)	60 (12)
H(34)	-733 (2)	-702 (16)	-1727 (10)	60 (12)

Table 4. Bond lengths (\AA)

C(2)-C(1)	1.396 (9)	C(6)-C(1)	1.397 (9)
C(17)-C(1)	1.504 (8)	C(3)-C(2)	1.365 (8)
C(4)-C(3)	1.385 (8)	C(5)-C(4)	1.400 (9)
C(7)-C(4)	1.491 (9)	C(6)-C(5)	1.383 (9)
C(8)-C(7)	1.545 (8)	Br(35)-C(7)	2.010 (6)
C(9)-C(8)	1.502 (9)	Br(36)-C(8)	1.988 (6)
O(10)-C(9)	1.230 (8)	C(11)-C(9)	1.472 (8)
C(12)-C(11)	1.396 (8)	C(16)-C(11)	1.404 (9)
C(13)-C(12)	1.382 (8)	C(14)-C(13)	1.396 (9)
C(15)-C(14)	1.390 (9)	C(26)-C(14)	1.505 (8)
C(16)-C(15)	1.375 (8)		

Table 5. Bond angles ($^\circ$)

C(6)-C(1)-C(2)	117.9 (7)	C(17)-C(1)-C(2)	121.2 (6)
C(17)-C(1)-C(6)	120.9 (7)	C(3)-C(2)-C(1)	120.9 (7)
C(4)-C(3)-C(2)	121.6 (7)	C(5)-C(4)-C(3)	118.2 (6)
C(7)-C(4)-C(3)	119.5 (6)	C(7)-C(4)-C(5)	122.2 (6)
C(6)-C(5)-C(4)	120.2 (6)	C(5)-C(6)-C(1)	121.1 (7)
C(8)-C(7)-C(4)	119.2 (5)	Br(35)-C(7)-C(4)	110.3 (4)
Br(35)-C(7)-C(8)	101.3 (4)	C(9)-C(8)-C(7)	113.7 (5)
Br(36)-C(8)-C(7)	106.9 (4)	Br(36)-C(8)-C(9)	104.1 (5)
C(10)-C(9)-C(8)	119.4 (6)	C(11)-C(9)-C(8)	118.5 (6)
C(11)-C(9)-O(10)	122.1 (7)	C(12)-C(11)-C(9)	118.6 (6)
C(16)-C(11)-C(9)	123.2 (6)	C(16)-C(11)-C(12)	118.2 (6)
C(13)-C(12)-C(11)	121.0 (7)	C(14)-C(13)-C(12)	121.0 (7)
C(15)-C(14)-C(13)	117.6 (6)	C(26)-C(14)-C(13)	120.9 (7)
C(26)-C(14)-C(15)	121.5 (7)	C(16)-C(15)-C(14)	122.2 (7)
C(15)-C(16)-C(11)	120.0 (6)		

Table 6. Torsion angles ($^\circ$)

C(5)-C(4)-C(7)-C(8)	-25.8 (9)
C(4)-C(7)-C(8)-C(9)	189.9 (6)
C(7)-C(8)-C(9)-O(10)	30.4 (9)
O(10)-C(9)-C(11)-C(12)	-10.1 (10)
Br(35)-C(7)-C(8)-Br(36)	183.0 (3)

configuration of the analysed crystal of (+)-DMCDB is ($\alpha R, \beta S$).

A view of the molecule is displayed in Fig. 2. Note, however, that (-)-DMCDB ($\alpha S, \beta R$) is shown; this inversion was performed so as to relate properly the configuration of DMCDB to that in part I (Rabinovich & Shakked, 1974).

Tables 2 to 6 list the atomic coordinates, bond lengths, bond angles and some relevant torsion angles.

Data collection, structure solution and the first refinement stages were carried out at the University of California, Davis, during the sabbatical leave of one of us (DR).

Discussion

The correlation of the absolute geometries of DMC and DMCDB

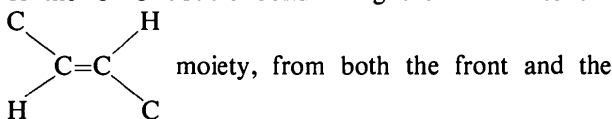
A detailed account of the determination of the absolute *conformation* of DMC is given in a separate paper (Rabinovich & Hope, 1980); a brief description, relevant to the present discussion, is outlined below. Essentially, the determination rests on the anomalous scattering of the single O atom (Cu $K\alpha$ radiation) in DMC, which manifests itself by small, yet detectable, intensity differences in a number of enantiomer-sensitive Bijvoet pairs. The intensities were painstakingly measured from two carefully prepared spherical samples of DMC grown from the melt. Two of the results of this study, namely (1) that boules (I) and (II) are enantiomers, and (2) that the absolute *conformation* of boule (I) corresponds to that published in part I, are of importance in our context.

It must be emphasized that, unlike DMCDB, the absolute *conformation* of the olefinic DMC is not a molecular property *per se* and thus is of little significance unless it is associated with a macroscopic attribute of the chiral crystal. Such an attribute, in the present case, is the formation of an excess of one of the two possible enantiomeric dibromides by gas/solid bromination of single crystals of DMC (Penzien & Schmidt, 1969; part I). Bromination of samples from boule (I) yields laevorotatory (-)-DMCDB while samples from (II) afford (+)-DMCDB. Not only are these results consistent with the X-ray analysis, but they allow for the first time a correlation between the absolute *conformation* of a species whose chirality is meaningful only in the solid with the molecular absolute configuration of a stable reaction product; *i.e.* we can state that molecules of DMC [boule (I)] having the absolute *conformation* of Fig. 2 yield the (-)-DMCDB enantiomer in excess. This correlation is crucial to the elucidation of the stereochemical course of the reaction.

Front-rear topology and the stereocourse of the reaction

In part I the different conformations of DMC and 4-methoxychalcone (MC) in the crystalline state were invoked in order to interpret the observed formation of an excess of one enantiomeric dibromide in DMC and the absence of optical induction in MC in gas/solid bromination reactions. The dissimilar front-rear environmental topologies of the C=C double bond were presented there in terms of the difference in the degree of molecular non-planarity as expressed by the relevant torsion angles.

The distinction between the topologies in the two molecules is brought here into sharper focus by calculating the differences in the energy of interaction, $\Delta E = E_{\text{rear}} - E_{\text{front}}$, as a Br atom approaches the centre of the C=C double bond along the normal to the



rear sides. A Lennard-Jones potential (6-12) was used in the calculations; non-bonded Br...C, Br...H and Br...O parameters were taken from Kawaguchi, Takashina, Tanaka & Watanabe (1972) and from Scott & Scheraga (1966). The results of these calculations (Fig. 3) display clearly the difference in the front-rear environment in DMC and MC, *i.e.* the increase in ΔE as a function of R is conspicuously steeper in DMC and is large enough to ensure preferential front-side attack (left-side attack in Fig. 2) of the Br atom; the almost flat curve in MC accounts for the lack of any apparent optical yield.

The preferred side of the Br attack dictates the stereochemistry of the bridged bromonium ion and the configuration of the dibromide formed in excess. Attack from the left in Fig. 2 leads to the formation of a bridged bromonium ion on the left, retention of configuration at C(8), and inversion of configuration at C(7), thus leading to the formation of the ($\alpha S, \beta R$) configuration of DMCDB.

A critical examination of the chemical implications of the foregoing results will be published elsewhere.

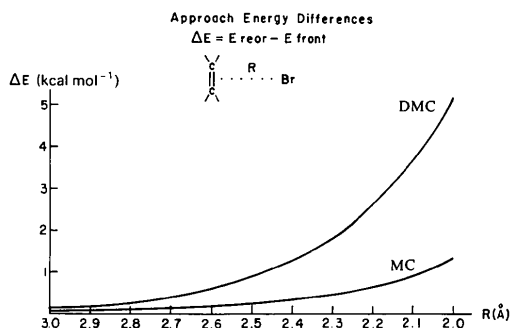


Fig. 3. Approach-energy curves of 4,4'-dimethylchalcone (DMC) and 4-methoxychalcone (MC). [$1 \text{ kcal mol}^{-1} \equiv 4.2 \text{ kJ mol}^{-1}$.]

The similarity of the packing arrangements of DMCDB and DMC

Fig. 4(a) shows a view of the packing of DMCDB down the short b axis. Fig. 4(a) shows a striking resemblance to the corresponding view ($b = 5.91 \text{ \AA}$) of DMC (Fig. 4b). In both, the molecules are arranged in nearly equidistant layers parallel to (001). The average interlayer distance is $c/2 = 3.95$ and $c/4 = 3.65 \text{ \AA}$ in DMCDB and DMC respectively. The former is slightly wider, due to the presence of the two Br atoms which fill the voids between the methyl groups of adjacent molecules along the a axis, pushing the molecules somewhat apart in the vertical direction compared to DMC; this effect results in a vertical repeat in DMCDB of 35.17 \AA , longer than $2a = 30.49 \text{ \AA}$ in DMC.

The arrangement of the molecules in the layers is, nevertheless, different in the two structures, due to the dissimilar distribution of the symmetry operations with respect to the molecules. In DMCDB the screw axes along [100] lie nearly on the molecular best planes resulting in layers in which the molecules are alternately oriented up and down. In DMC the corresponding screw operations are situated half-way between the molecular layers, which are constructed of identically oriented translationally related molecules.

The Br...Br intramolecular vector is nearly parallel to [001], resulting in a short intermolecular Br...Br contact of 3.43 \AA with a roughly linear C-Br...Br-C geometry between adjacent molecules along this axis (C-Br...Br angles of 151.1 and 145.2°). Similar

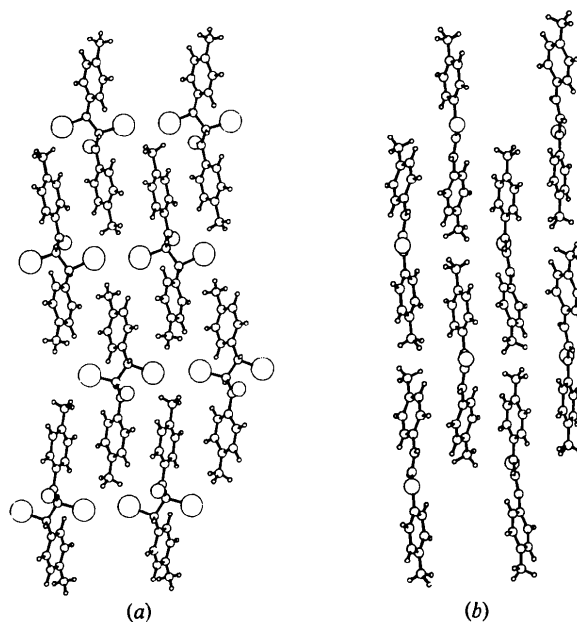


Fig. 4. (a) DMCDB: view of the packing arrangement along [010]. a is vertical and c horizontal. The contents of the origin and the 0,0,1 unit cells are depicted. (b) DMC: view of the packing arrangement along [010]. a is vertical and c horizontal. The contents of the origin and the 1,0,0 unit cells are depicted.

Br...Br interactions are discussed by Rabinovich & Shakked (1977).

Directed crystal chirality of DMC by DMCDDB

When solutions of DMC are allowed to crystallize, the formation of an excess of right- or left-handed crystals is equally probable. However, in the presence of small amounts of (+)-DMCDDB crystallization leads to one enantiomorph in excess; the presence of (–)-DMCDDB causes preferential crystallization of the second enantiomorph (Green & Heller, 1974). The correlation of the absolute geometries of DMC and DMCDDB now allows one to state that the presence of (+)-DMCDDB leads to an excess of DMC having the absolute *conformation* of Fig. 2.

The striking resemblance of the packing arrangements of the two compounds may afford an explanation of the directed crystallization of DMC with one chirality in excess by small amounts of DMCDDB: the molecules of the latter stabilize pre-nuclei aggregates of one-handedness of the former.

Molecular geometry

Tables 4 and 5 list the bond lengths and angles uncorrected for curvilinear thermal motion. The r.m.s. values of the e.s.d. in bond lengths and angles are $\langle\sigma(r)\rangle = 0.0085 \text{ \AA}$ and $\langle\sigma(\alpha)\rangle = 0.60^\circ$ respectively. The former may be compared to the sample $\{\hat{\sigma} = [\sum (r_i - \bar{r})^2 / (n - 1)]^{1/2} = 0.0103 \text{ \AA}\}$ of the 12 aromatic bonds which have a mean $r = 1.390 \text{ \AA}$. The small discrepancy between the two error estimates may be accounted for by a slight, but distinct, quinoid character of the aromatic rings (Leser & Rabinovich, 1978). Indeed, when the 12 bonds are classified into two samples of long and short bonds according to the *p*-quinone arrangement, the mean bond lengths are $\bar{r}_8 = 1.396$, $\bar{r}_4 = 1.376$ with $\hat{\sigma}_8 = 0.0058$ and $\hat{\sigma}_4 = 0.0083 \text{ \AA}$ respectively. The difference $\bar{r}_8 - \bar{r}_4 = 0.020 \text{ \AA}$ is highly significant.

Small values of the aromatic bond angles at the substituted atoms have been observed in DMC and in other related compounds. Discussion of this effect is given in part I.

The geometry of the dibromoethane moiety can be compared, for example, with that of five recently published β,β -dibromoadipic acid derivatives (Rabinovich & Shakked, 1977). The C(7)–C(8) bond (1.545 Å), though longer than the average value quoted there, is still within 2σ of the two long ones (1.530, 1.528 Å). The two C–Br bonds in DMCDDB (1.988, 2.010 Å) are probably the longest observed in such compounds; the average given for the dibromoadipic acid derivatives is 1.974 Å. Also outstanding are the two Br–C(7)–C(8) and Br–C(8)–C(9) angles, 101.3 and 104.1°, which are appreciably smaller than the values accepted for tetrahedral angles which are observed quite consistently in the dibromoadipic acid derivatives (107.2–109.0°).

The DMCDDB molecule (excluding the Br atoms) is nearly planar, as can be seen from Table 6, Figs. 2 and 4(a) and from the very small angle between the phenyl rings [3.0 (2)°]. This is in contrast to the heavily twisted DMC in the crystal. It seems plausible that the C–C–Br...Br–C–C–Br... backbone which links the molecular layers together allows enough free space for the phenyl rings to adopt their isolated-molecule conformation.

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