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# *gem*-Dimethylcyclopropanation of dibenzylideneacetone using triisopropyl sulfoxonium tetrafluoroborate

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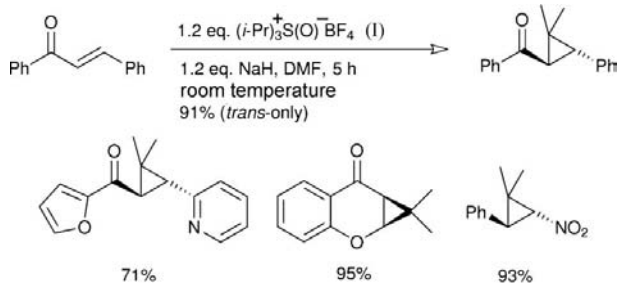
The reaction between dibenzylideneacetone (dba) and triisopropyl sulfoxonium tetrafluoroborate has been reinvestigated. The stereochemistry of the major diasteromeric bis(*gem*-dimethylcyclopropane) adduct has now been assigned as [(1*RS*,3*RS*)-2,2-dimethyl-3-phenylcyclopropyl][(1*SR*,3*SR*)-2,2-dimethyl-3-phenylcyclopropyl]methanone, $C_{23}H_{26}O$, by X-ray crystallographic studies on a twinned crystal. The asymmetric unit contains two molecules of the adduct, the conformations of which differ in the orientation of the phenyl ring relative to the adjacent cyclopropanated double bond. The carbonyl groups of each adduct are aligned approximately along the *a* axis and in opposite directions to each other. The molecules pack to give a sinusoidal pattern along the *b* axis. This is the first acyclic bis(dimethylcyclopropyl) ketone for which an X-ray crystal structure determination has been reported, and is also the first bis-cyclopropanated dba analogue. The knowledge that the major diastereomer has the *meso* structure (and therefore the confirmation that the minor isomer is the racemate) will prove invaluable in future studies to utilize bis(dimethylcyclopropyl) ketones as reagents, in rearrangement processes, and as potential ligands and ligand precursors in organometallic chemistry.

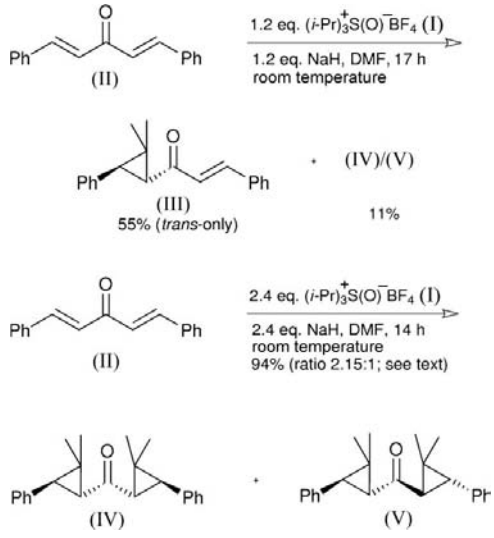
## Comment

We recently reported the preparation of triisopropyl sulfoxonium tetrafluoroborate, (I), and its use as an isopropylidene transfer reagent for the *gem*-dimethylcyclopropanation of a range of electron-deficient alkenes (Edwards *et al.*, 2008). Good to excellent yields were obtained with a range of cyclic and acyclic $\alpha,\beta$-unsaturated ketones and related systems (see first scheme).

The dimethylcyclopropanation of dienones was also studied. Interestingly, dibenzylideneacetone, (II), gave a mixture of the expected dimethylcyclopropane derivative, (III), together with two inseparable diastereomers of the bis-cyclopropyl adducts, (IV) and (V) (see top part of second scheme). With excess sulfoxonium salt, the bis-adducts (IV) and (V) were formed in 94% yield as an inseparable mixture of diastereomers (2.15:1), but we were unable to assign the structure of the major diastereoisomer.




We have now repeated the bis(dimethylcyclopropanation) of dibenzylideneacetone in order to clarify the stereochemical outcome of this reaction (see bottom part of second scheme). Repeated recrystallization (ten times) of the (IV)/(V) mixture from ethanol–water, and analysis by $^1$H NMR spectroscopy, produced a pure sample of the major diastereomeric product. X-ray crystallographic analysis then confirmed that the major product was the title *meso* isomer, (IV) (Fig. 1).




The asymmetric unit contains two molecules of the adduct (IV) with differing conformations. The carbonyl groups of each adduct are aligned approximately along the *a* axis and in opposite directions to each other. The conformation of the individual molecules is such that there is almost a mirror plane of symmetry along the carbonyl axis, perpendicular to the C8/C9/C10/O1 plane (this is also true for the plane perpendicular to C31/C32/C33/O2, although the correspondence is less good).

The differences between the two conformations are significant, with the r.m.s. best fit for overlap of the heavy atoms being 0.252 Å. Closer inspection reveals that the major difference is in the orientation of the phenyl ring relative to the adjacent cyclopropanated double bond. For one adduct, both rings are twisted with approximately equivalent angles of −15.6 (10) and 16.5 (10)°. In the other, one phenyl ring and bond are almost coplanar, the angles being 2.8 (11) and

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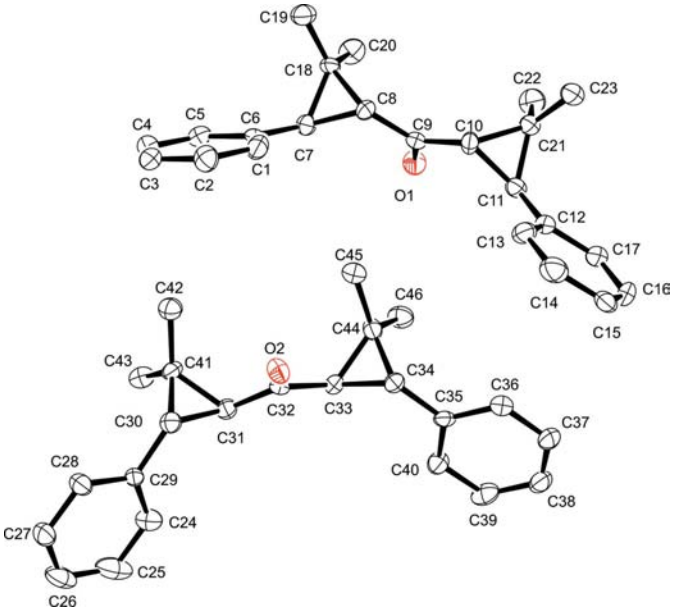


**Figure 1**
A view of the asymmetric unit of compound (IV), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms have been omitted for clarity.

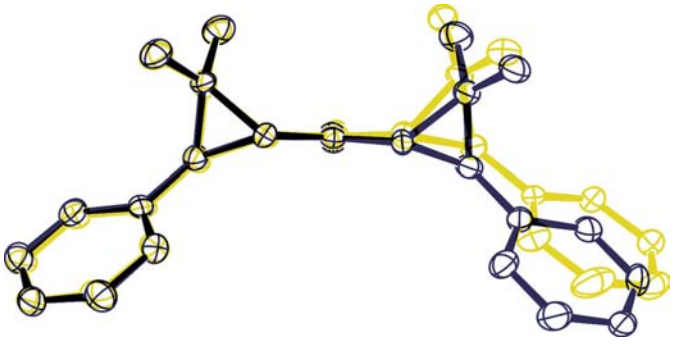

**Figure 2**
Overlaid crystal structures of the two independent molecules of (IV) (H atoms omitted), highlighting the significant conformational differences of one half of each molecule. [In the electronic version of the paper, molecule 1 (atoms C1–C23/O1) is coloured blue, dark here, and molecule 2 (atoms C24–C46/O2) is coloured yellow, light here.]

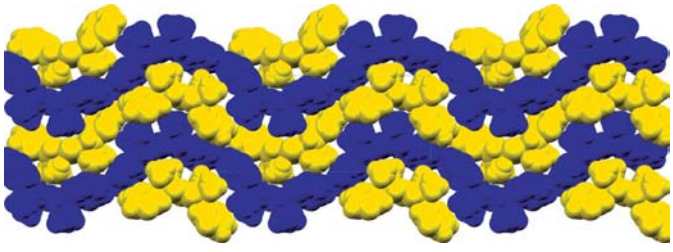

**Figure 3**
A packing diagram for (IV), viewed along the *a* axis. The different colours denote the two different molecular conformations (*cf.* Fig. 2).

−13.5 (10)°. This difference is also reflected in the angle between the planes for each pair of cyclopropane and phenyl groups; the angles are 58.8 (6) and 59.2 (6)° for the first adduct, and 61.5 (5) and 65.9 (6)° for the second. It is notable that for the second conformer, half of the molecule has an orientation closely similar to that of the first conformer, whilst the remainder is significantly different. This is clearly illustrated in Fig. 2.

The packing of the molecules within the crystal structure also shows some interesting behaviour. Each conformer is arranged to form a sinusoidal pattern orientated along the *b* axis (Fig. 3). Analysis of the packing shows that there are no intermolecular $\pi$–$\pi$ interactions (neither face-to-face nor edge-to-face) as there are no pairs of atoms which are significantly closer (0.2 Å) than the sum of their van der Waals radii.

A search of the Cambridge Structural Database (Version 5.29, with August 2008 update; Allen, 2002) reveals that only 29 crystal structures have been reported previously which contain the cyclopropyl–carbonyl–cyclopropyl (CyP–CO–CyP) sequence. All but three of these have the (CyP–CO–CyP) moiety as part of a cyclic structure, with the majority being derived from 1,4-benzoquinone. Only two structures are reported which have two dimethylcyclopropyl groups, one being derived from benzoquinone (Edwards *et al.*, 2008) and the other based on tropone (Cetinkaya *et al.*, 1982). Thus, the crystal structure of (IV), with the dimethylcyclopropyl groups and carbonyl group in an acyclic arrangement, appears to be the first of its type to be reported.

## Experimental

[(1*RS*,3*RS*)-2,2-Dimethyl-3-phenylcyclopropyl][(1*SR*,3*SR*)-2,2-dimethyl-3-phenylcyclopropyl]methanone, (IV), and [(1*RS*,3*RS*)-2,2-dimethyl-3-phenylcyclopropyl][(1*RS*,3*RS*)-2,2-dimethyl-3-phenylcyclopropyl]methanone, (V), were prepared as follows.

A 25 ml round-bottomed flask equipped with a stirrer bar was charged with sodium hydride (60% dispersion in mineral oil, 111 mg, 2.78 mmol, 2.4 equivalents), sealed with a rubber septum and purged with argon. The flask was maintained under argon and anhydrous *N*,*N*-dimethylformamide (10 ml) was added. The stirred suspension was cooled to 273 K (ice bath), the septum briefly removed and triisopropyl sulfoxonium tetrafluoroborate (735 mg, 2.78 mmol, 2.4 equivalents) added in a single portion. The mixture was stirred for 5 min before the addition of a solution of dibenzylideneacetone (272 mg, 1.16 mmol, 1.0 equivalents) in *N*,*N*-dimethylformamide (5 ml) dropwise by cannula. The cooling bath was removed and the yellow solution stirred at room temperature until the reaction was shown to be complete by thin-layer chromatographic analysis (14 h). The reaction was quenched by the addition of saturated aqueous $NH_4Cl$ (15 ml), diluted with water (60 ml) and extracted with $Et_2O$ (3 × 50 ml). The combined organic extracts were dried ($Na_2SO_4$) and the solvent removed *in vacuo*. The residue was purified by column chromatography (petrol/$Et_2O$, 19:1 *v*/*v*) to afford 350 mg (94%) of a colourless solid, a chromatographically inseparable mixture of diastereoisomers (IV) and (V) (2.15:1) (m.p. 331–333 K). Analysis: $R_F$ = 0.63 (petrol–EtOAc, 3:1 *v*/*v*; no separation); IR (NaCl, $\nu$, cm$^{-1}$): 3027, 2972, 2950, 2919, 2871, 2361, 2338, 1666, 1602, 1579, 1497, 1443, 1422, 1375, 1278, 1103, 1070, 770; MS (ESI): *m*/*z* = 341 $[M + Na]^+$; HRMS–ESI: *m*/*z* $[M + Na]^+$ calculated for $C_{23}H_{26}NaO$: 341.1876; found: 341.1882 (1.82 p.p.m. error). Repeated recrystallization (ten times) from EtOH–$H_2O$ (EtOH with *ca.* 5–10% $H_2O$ added dropwise) gave a single diastereomer; X-ray analysis identified this as (IV)

(m.p. 336–338 K). Analysis: $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 1.03 (*s*, 6H, $CH_3$), 1.29 (*s*, 6H, $CH_3$), 2.54 (*d*, $J$ = 6.1 Hz, 2H, CH), 2.93 (*d*, $J$ = 6.1 Hz, 2H, CH), 7.17–7.32 (*m*, 10H, ArH); $^{13}$C NMR (125 MHz, $CDCl_3$): $\delta$ 20.6 ($CH_3$), 22.6 ($CH_3$), 33.7 (C), 38.6 (CH), 42.0 (CH), 126.3 (ArH), 128.1 (ArH), 128.9 (ArH), 138.0 (Ar), 205.2 (C=O).

*Crystal data*

$C_{23}H_{26}O$
$M_r$ = 318.44
Monoclinic, $P2_1$
$a$ = 5.7287 (7) Å
$b$ = 27.517 (4) Å
$c$ = 11.9206 (17) Å
$\beta$ = 91.881 (8)°
$V$ = 1878.1 (4) Å$^3$
$Z$ = 4
Mo $K\alpha$ radiation
$\mu$ = 0.07 mm$^{-1}$
$T$ = 120 (2) K
0.28 × 0.24 × 0.02 mm

*Data collection*

Bruker–Nonius APEXII CCD diffractometer on $\kappa$-goniostat
Absorption correction: multi-scan (*TWINABS*; Sheldrick, 2007)
$T_{min}$ = 0.454, $T_{max}$ = 0.999
6207 measured reflections
4341 independent reflections
3685 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.072

*Refinement*

$R[F^2 > 2\sigma(F^2)]$ = 0.087
$wR(F^2)$ = 0.186
$S$ = 1.24
4341 reflections
442 parameters
1 restraint
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.38 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.36 e Å$^{-3}$

The crystal was discovered to be nonmerohedrally twinned by a 180° rotation about the [$\bar{1}$00] direction. The orientation matrix for each twin component was determined using *DIRAX* (Duisenberg, 1992), allowing a HKLF 5 file (*SHELXL97*; Sheldrick, 2008) to be prepared. The twin fraction refined to 0.470 (3). H atoms were placed using a riding model, with C—H = 0.98 ($CH_3$), 0.95 (aromatic CH) or 1.00 Å (aliphatic CH). They were refined isotropically with $U_{iso}$(H) = 1.2$U_{eq}$(C) or 1.5$U_{eq}$($C_{methyl}$).

Data collection: *COLLECT* (Nonius, 1998); cell refinement: *DENZO* (Otwinowski & Minor, 1997) and *COLLECT*; data reduction: *DIRAX* (Duisenberg, 1992), *DENZO*, *COLLECT* and *EVALCCD* (Duisenberg *et al.*, 2003); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3 for Windows* (Version 2.02; Farrugia, 1997) and *Mercury* (Version 1.4.2; Macrae *et al.*, 2008); software used to prepare material for publication: *PLATON* (Spek, 2003).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: BM3069). Services for accessing these data are described at the back of the journal.

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