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## Structure and Conformation of Substituted Cycloheptatrienes.

### I. 2,5-Dimethyl-3,4-diphenyl-1,3,5-cycloheptatriene

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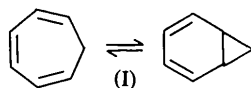
(Received 26 March 1979; accepted 21 May 1979)

#### Abstract

$C_{21}H_{20}$  is monoclinic, space group  $P2_1/c$ , with  $a = 11.312(5)$ ,  $b = 8.503(5)$ ,  $c = 16.91(1)$  Å,  $\beta = 98.04(1)^\circ$ ,  $Z = 4$ . The structure was refined to  $R = 0.044$  for 1119 counter reflections. The seven-membered ring is boat-shaped with structure angles  $\alpha = 52.6^\circ$  and  $\beta = 34.3^\circ$ . Empirical force-field calculations of the isolated molecule predict  $\alpha = 51.0^\circ$  and  $\beta = 27.5^\circ$ , while  $\alpha = 51.9^\circ$  and  $\beta = 31.9^\circ$  were calculated considering packing effects. The enthalpy of the inversion barrier between the two boat forms has been calculated to be  $59 \text{ kJ mol}^{-1}$ .

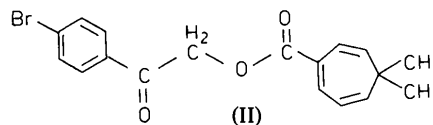
#### Introduction

Structures and conformations of seven-membered ring systems have been of interest for many years (for a review see Tochtermann, 1970). Cycloheptatriene displays a flexible boat-shaped structure, which can be influenced by substituents over a wide range, up to the valence isomer norcaradiene [(I); Berson, Hartter, Klinger & Grubb, 1968].

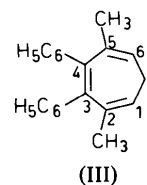


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Conformations of substituted cycloheptatrienes have been investigated mainly by NMR spectroscopy (Lambert, Durham, Lepoutere & Roberts, 1965; Günther, Görlitz & Meisenheimer, 1974; Kessler, 1979) and force-field calculations (Kao & Allinger, 1977; Lindner, 1979). One microwave (Butcher, 1965) and one electron diffraction analysis of cycloheptatriene (Trættemberg, 1964) have been reported and one X-ray analysis of a substituted cycloheptatriene [(II); Davis & Tulinsky, 1966].



In our attempt to clarify the influence of substituents on the conformation of the cycloheptatriene moiety, we determined the crystal structures of a series of its methyl and phenyl derivatives. In this work, we report the structure of 2,5-dimethyl-3,4-diphenyl-1,3,5-cycloheptatriene (III).



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## Experimental

Crystals were prepared by Kessler & Bicker (1976) (see also Bicker, 1977) as long transparent blocks (axis [010]) from  $\text{CDCl}_3$ . Systematic absences  $h0l$  and  $0k0$  for odd indices determined the space group as  $P2_1/c$ . Crystal data are summarized in Table 1. Intensities were collected on a Stoe two-circle diffractometer (Cu  $K\alpha$  radiation) equipped with a graphite monochromator; the crystal was oriented along **b**. 2525 symmetry-independent reflections  $h0l$  to  $h6l$  with  $2.5 \leq \theta \leq 60^\circ$  were measured in the  $\omega$ - $2\theta$  scan mode. The data were corrected for background, Lorentz and polarization factors. 1119 reflections had  $|E| > 3\sigma_E$ .

## Structure analysis and refinement

The structure was determined by direct methods with *SHELX 77* (Sheldrick, 1977). Full-matrix least-squares refinement of the atomic coordinates and anisotropic thermal parameters reduced  $R$  to 0.112; H atoms were located by a difference synthesis. With weights  $w = 1/\sigma(|F|)^2$  and isotropic H-atom thermal parameters, the final  $R$  was 0.044. None of the heavy-atom parameters shifted more than  $0.07\sigma$  in the last cycle. Positional parameters are listed in Table 2.\*

## Results

2,5-Dimethyl-3,4-diphenyl-1,3,5-cycloheptatriene exhibits a boat structure with alternating bond lengths (Fig. 1). The bond angles at the folding lines are about  $120^\circ$ , while they are enlarged at the stern ( $125^\circ$ ) and reduced to a normal  $sp^3$  angle ( $109^\circ$ ) at the bow. Torsion angles are  $65$  and  $40^\circ$  at bow and stern respectively. The double bonds are not twisted (Fig. 2). No effects of conjugation between the phenyl rings and the rear double bond are observed. The connecting bonds show single-bond nature ( $1.50 \text{ \AA}$ ). The planes of the two phenyl rings form an angle of  $58^\circ$  (Table 3).

\* Lists of structure factors and thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 34499 (10 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. Crystal data

Molecular formula  $\text{C}_{21}\text{H}_{20}$ ,  $M_r = 272$ , space group  $P2_1/c$

$a = 11.312(5) \text{ \AA}$	$Z = 4$
$b = 8.503(5)$	$\rho_o = 1.11 \text{ Mg m}^{-3}$ (floatation)
$c = 16.91(1)$	$\rho_c = 1.12$
$\beta = 98.04(1)^\circ$	$\mu = 0.41 \text{ mm}^{-1}$
$V = 1610.5 \text{ \AA}^3$	

Table 2. Positional parameters and their e.s.d.'s

	$x$	$y$	$z$
C(1)	0.6329 (4)	-0.1452 (5)	0.0868 (3)
C(2)	0.7326 (3)	-0.1766 (4)	0.1365 (2)
C(3)	0.7477 (3)	-0.1220 (4)	0.2201 (2)
C(4)	0.7102 (3)	0.0183 (4)	0.2456 (2)
C(5)	0.6523 (3)	0.1412 (5)	0.1930 (2)
C(6)	0.5696 (3)	0.1068 (6)	0.1309 (3)
C(7)	0.5307 (4)	-0.0552 (5)	0.1119 (3)
C(21)	0.8298 (4)	-0.2744 (6)	0.1079 (3)
C(31)	0.8116 (3)	-0.2352 (5)	0.2800 (2)
C(32)	0.9359 (4)	-0.2494 (6)	0.2916 (3)
C(33)	0.9928 (5)	-0.3513 (6)	0.3470 (3)
C(34)	0.9269 (5)	-0.4430 (7)	0.3916 (3)
C(35)	0.8047 (5)	-0.4302 (6)	0.3812 (3)
C(36)	0.7476 (4)	-0.3277 (5)	0.3253 (2)
C(41)	0.7322 (3)	0.0603 (4)	0.3325 (2)
C(42)	0.8428 (4)	0.0911 (4)	0.3726 (3)
C(43)	0.8597 (4)	0.1321 (5)	0.4530 (3)
C(44)	0.7630 (5)	0.1403 (6)	0.4929 (3)
C(45)	0.6516 (5)	0.1102 (5)	0.4543 (3)
C(46)	0.6352 (4)	0.0700 (5)	0.3746 (3)
C(51)	0.6863 (5)	0.3093 (6)	0.2125 (3)
H(C1)	0.633 (4)	-0.201 (4)	0.034 (2)
H(C6)	0.539 (3)	0.206 (4)	0.104 (2)
H(C7)	0.506 (3)	-0.127 (4)	0.156 (2)
H'(C7)	0.461 (3)	-0.067 (4)	0.071 (2)
H(C21)	0.847 (4)	-0.398 (6)	0.142 (3)
H''(C21)	0.907 (3)	-0.214 (4)	0.119 (2)
H''(C21)	0.806 (3)	-0.298 (5)	0.049 (3)
H(C32)	0.978 (3)	-0.177 (4)	0.264 (2)
H(C33)	1.079 (3)	-0.347 (4)	0.355 (2)
H(C34)	0.960 (3)	-0.522 (5)	0.435 (2)
H(C35)	0.758 (3)	-0.507 (5)	0.414 (2)
H(C36)	0.660 (3)	-0.316 (3)	0.318 (2)
H(C42)	0.907 (3)	0.077 (4)	0.348 (2)
H(C43)	0.946 (3)	0.145 (4)	0.480 (2)
H(C44)	0.778 (3)	0.142 (5)	0.546 (3)
H(C45)	0.580 (4)	0.101 (5)	0.484 (3)
H(C46)	0.553 (3)	0.046 (4)	0.345 (2)
H(C51)	0.765 (3)	0.328 (4)	0.221 (2)
H'(C51)	0.663 (4)	0.333 (6)	0.264 (3)
H''(C51)	0.652 (3)	0.387 (4)	0.169 (2)

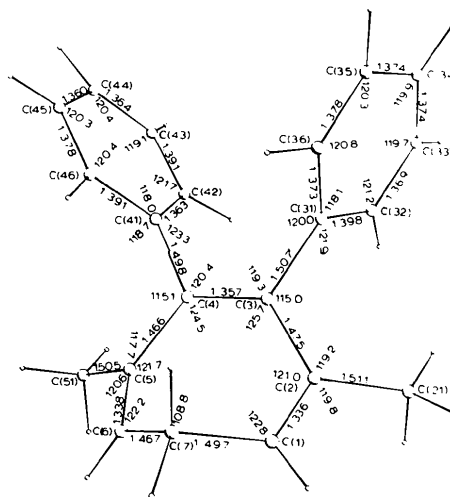


Fig. 1. Bond lengths ( $\text{\AA}$ ) and angles ( $^\circ$ ) of 2,5-dimethyl-3,4-diphenyl-1,3,5-cycloheptatriene ( $\sigma_{\text{CC}} = 0.005 \text{ \AA}$ ,  $\sigma_{\text{CCC}} = 0.2^\circ$ ).

The local  $C_3$  symmetry of the cycloheptatriene ring is disturbed; this can be explained by packing effects (see *Discussion*).

The shortest non-bonded intramolecular distance is between C(1) and C(6) (2.41 Å), which might partly be due to homoconjugation between these two centres (Lindner, 1979; Warner, 1976).

### Packing

The boat axis, formed by C(7) and the centre to the bond between C(3) and C(4), is almost aligned with respect to **a** and tilted in **b**. The molecule forms translational chains along **b** with shortest intermolecular distances between methyl and phenyl groups [C(51)···C(36) 3.64 Å, Table 4] and between two methyl groups [C(51)···C(21) 4.37 Å, Fig. 3]. A second row is formed by the screw axis, the cycloheptatriene rings lying in the holes between the parallel phenyl rings of adjacent molecules in the first row with shortest distances between C(45) and C(7) (3.60 Å).

Table 3. *Least-squares planes with maximum deviations out of the planes, rotation angles and structure angles*

Plane		Maximum deviation (Å) ( $\sigma = 0.005$ Å)
(I) C(6)–C(7)–C(1)		
(II) C(1)–C(2)–C(5)–C(6)	0.003 C(6)	
(III) C(2)–C(3)–C(4)–C(5)	0.010 C(3)	
(IV) C(31)–C(32)–C(33)–C(34)–C(35)–C(36)	0.004 C(34)	
(V) C(41)–C(42)–C(43)–C(44)–C(45)–C(46)	0.003 C(43)	

Rotation angles ( $^\circ$ ) ( $\sigma = 0.4$ $^\circ$ )			
Phenyl (IV)/(III)	79.9	Phenyl (IV)/(II)	97.2
Phenyl (V)/(III)	70.6	Phenyl (V)/(II)	56.8
Phenyl (IV)/phenyl (V)	58.4		

Structure angles ( $^\circ$ ) ( $\sigma = 0.4$ $^\circ$ )			
$\alpha = (I)/(II)$	$= 52.6$	$\beta = (III)/(II)$	$= 34.3$

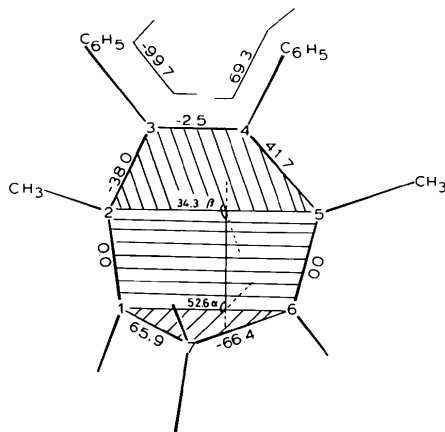


Fig. 2. Dihedral angles ( $^\circ$ ) ( $\sigma_{\text{CCCC}} = 0.4$   $^\circ$ ).

A third row is generated by the inversion centre with the bows of the molecules placed against each other at a distance of 3.87 Å [C(7)···C(7), Fig. 4], and contacts between two phenyl groups [C(34)···C(34), 3.93 Å]. The last row of molecules, interrelated to the first by the inverted screw axis, forms shortest distances to the first row between methyl and phenyl groups [C(21)···C(44) 3.69 Å] and heptatriene and phenyl rings [C(34)···C(6) 4.04 Å].

Table 4. *Shortest intra- and intermolecular distances (Å) ( $\sigma = 0.01$  Å)*

		Symmetry operation on second atom
C(6)···C(1)	2.41	
C(51)···C(36)	3.64	(+x, 1 + y, +z)
C(51)···C(21)	4.37	
C(7)···C(7)	3.87	(1 - x, -y, -z)
C(45)···C(45)	4.38	(1 - x, -y, 1 - z)
C(44)···C(33)	4.01	(2 - x, -y, 1 - z)
C(34)···C(34)	3.93	(2 - x, -1 - y, 1 - z)
C(6)···C(36)	3.80	(1 - x, 0.5 + y, 0.5 - z)
C(45)···C(7)	3.60	
C(3)···C(33)	4.02	(2 - x, 0.5 + y, 0.5 - z)
C(21)···C(34)	3.94	
C(42)···C(21)	3.85	
C(21)···C(35)	4.18	(+x, -0.5 - y, -0.5 + z)
C(21)···C(44)	3.69	
C(34)···C(6)	4.04	(+x, -1.5 - y, -1.5 + z)
C(44)···C(51)	3.95	
C(45)···C(6)	4.04	

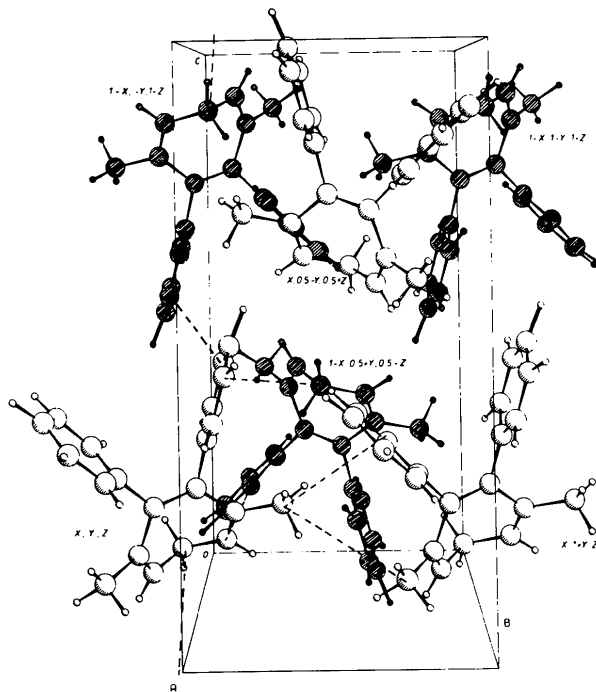


Fig. 3. A view down **a** with **b** horizontal and **c** vertical. Ball and stick model; the unit cell is outlined.



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*Acta Cryst.* (1979). **B35**, 2165–2168

## The Crystal and Molecular Structure of a New Antidepressant, 6-Benzyl-1,2,3,4,5,6,7,8-octahydro-1,3-dimethylpyrimido[4,5-*d*]pyrimidine-2,4-dione

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(Received 10 April 1979; accepted 21 May 1979)

### Abstract

In order to correlate the conformation with the biological activity of a new pyrimido[4,5-*d*]pyrimidine, its crystal structure was determined. The crystal data are  $a = 7.109$  (3),  $b = 12.766$  (3),  $c = 16.110$  (4) Å,  $\beta = 97.52$  (5)°,  $Z = 4$ , space group  $P2_1/c$ . The stereochemistry and the interatomic distances are in accordance with the proposed information relevant to the geometry and properties of the binding sites of the adrenergic  $\alpha$ -receptors.

### Introduction

Because of the widespread use of antidepressants, extensive studies have been carried out to investigate the precise mechanism of their action. It is generally accepted that at least part of the therapeutic action of antidepressants may be a consequence of an increased

availability of norepinephrine (NE) at post-synaptic receptor sites. It has been recently found that antidepressant treatments decrease the sensitivity of the NE  $\alpha$ -receptors (Crews & Smith, 1978). This activity on the receptor mediation explains the feedback inhibition of brain NE neurons (Svensson & Usdin, 1978). We have synthesized (Bernier, Lefebvre, Lespagnol, Navarro & Perio, 1977) a series of pyrimidopyrimidines in which only one compound exhibited antidepressant activity: 6-benzyl-1,2,3,4,5,6,7,8-octahydro-1,3-dimethylpyrimido[4,5-*d*]pyrimidine-2,4-dione (BDPD). It was interesting to study the crystal structure of BDPD in order to correlate its conformation with its biological activity.

### Experimental

Single crystals were transparent parallelepipeds. The data were collected on a Philips diffractometer with