Molecular Inclusion in Functionalized Macrocycles Part 10*: Crystal and Molecular Structure of a *p-tert*-Butylcalix[6]arene Hexapodand

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Abstract. Colourless prismatic crystals of (**3**) were obtained from ethanol/CH_2Cl_2 (1 : 1) solution, space group $P2_1/c$, $a = 14.581(5)$, $b = 22.517(8)$, $c = 11.799(5)$ Å, $\beta = 92.13(4)°$. Refinement led to a final conventional R value of 0.074 for 4247 reflections. The conformation of the molecule, which lies on a center of symmetry, is 1,2,3-alternate with one oligoethereal chain pointing inside the molecular cavity.

1. Introduction

We have recently synthesized lipophilic polypodands by introducing short oligoether chains on calixarenes [2]. These macrocycles (**1**) derived from the condensation of phenols and formaldehyde are experiencing new interest as hosts for the inclusion of neutral molecules [1], as potential enzyme models [3] and as stationary phases for chromatographic separations [4].

(**1**) $n = 4\text{-}8$,
$R = H, Bu^t, octyl, Ph, Cl$
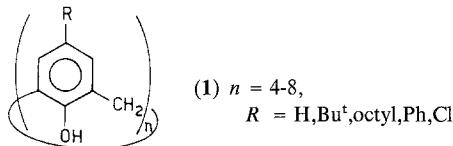
Among the compounds of this type available, *p-tert*-butylcalix[6]arene (**2**) has been utilized to a minor extent, compared with calix[4]- and calix[8]arenes although it can be easily prepared and in high yields through a one step procedure [5].

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* For part 9, see [1]. Results presented in part at the Second International Symposium of Clathrate Compounds and Molecular Inclusion Phenomena, Parma, Italy, 1982.
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(2) R = H
(3) R = CH$_2$CH$_2$OCH$_3$
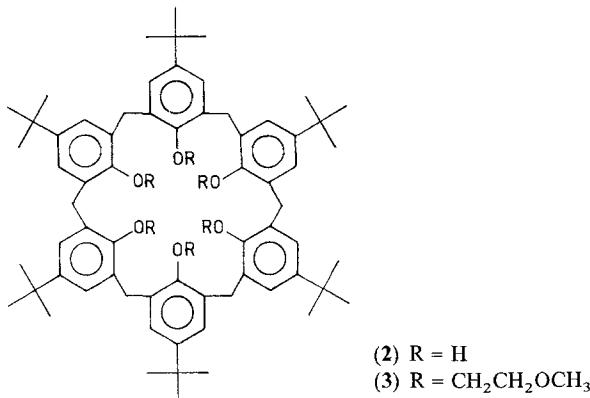
A preliminary inspection of Corey–Pauling–Koltun (CPK) molecular models of (2) showed that the size of the macroring was probably large enough to overcome some conformational problems which were encountered when short polyethereal chains were introduced on the phenolic oxygens of p-*tert*-butylcalix[4]arene (1a) [2]. On the other hand, the ligand (3) and other of the same type built of p-*tert*-butylcalix[6]arene (2) could show less conformational freedom compared with the analogous podands derived from p-*tert*-butylcalix[8]arene (1b) and this should enhance the complexing abilities of these macrocycles toward alkali and ammonium cations [7].

Preliminary extraction data confirmed this hypothesis, since (3) extracted guanidinium, cesium, and ammonium picrates from water to methylene chloride more efficiently than the ligands built on calix[4]- and calix[8]arenes having the same ethereal chain [8].

Therefore it was of interest to study the conformational preference of podands built on p-*tert*-butylcalix[6]arene (1) both in solution and in the solid state. The results obtained in the latter case, through the X-ray single crystal analysis of podand (3) are reported in this paper.

2. Experimental

p-*tert*-Butylcalix[6]arene (2) has been prepared in *ca.* 70% yield using the method reported in the literature [5] with minor modifications.

^{1}H and ^{13}C (at 25.2 MHz) NMR spectra were obtained on a Varian XL 100 instrument, with tetramethylsilane as internal standard. The melting point was determined in a capillary tube sealed *in vacuo* using an Electrothermal (London) melting point apparatus.

Synthesis of 5,11,17,23,29,35-hexa-*tert*-butyl-37,38,39,40,41,42-hexa-(2-methoxyethoxy)calix[6]arene (3) [6]: The general procedure reported in [2] for the synthesis of other calixarene polypodands was followed and product (3) obtained in almost quantitative yield from the calix[6]arene (2).

The crude product (95% purity) was recrystallized from EtOH/CH$_2$Cl$_2$ (1 : 1 v/v) to give colourless elongated prisms. m.p. 282–284°C.

^{1}H NMR (CDCl$_3$), δ: 1.13 [s,54H,4XC(CH$_3$)$_3$]; 2.6–2.8 (bs,42H, CH$_2$CH$_2$OCH$_3$) 3.85 (bs,8H,ArCH$_2$Ar), 7.16 (s,12H,ArH) ^{13}C NMR (CDCl$_3$), δ: 30.37 (Ar,CH_2Ar); 31.38 (C(CH_3)$_3$); 34.16 (C(CH$_3$)$_3$); 58.03 (OCH$_3$); 71.06 (OCH$_2$CH$_2$O); 126.37 (ArC *meta*); 132.66 (ArC *ortho*); 145.35 (ArC *para*); 152.68 (ArC—O).

3. Crystal Data

$C_{84}H_{120}O_{12}$, Formula weight = 1321.86. Monoclinic, $a = 14.581(5)$, $b = 22.517(8)$, $c = 11.799(5)$ Å, $\beta = 92.13(4)°$, $U = 3871.2(2.5)$ Å^3, $Z = 2$, $D_c = 1.13$ g cm^{-3}. Space group $P2_1/c$ (No. 14).

4. Structure Determination

A single, colourless crystal suitable for the X-ray analysis was obtained by slow evaporation of a methylene chloride/ethanol (1 : 1 v/v) solution of (3) at room temperature.

A specimen of $0.3 \times 0.4 \times 0.6$ mm was used for intensity measurements. Lattice parameters were refined by least-squares by use of $29(\theta,\chi,\phi)_{hkl}$ measurements taken on a Siemens AED single crystal diffractometer online to a General Automation Jumbo 220 minicomputer [9]. Intensity data were collected up to θ 70° by using the ω-2θ step scanning mode with nickel-filtered Cu$K\alpha$ radiation. The Lehman–Larsen algorithm [10] was used to analyse the reflection profiles. One standard reflection recorded every hour showed no significant fluctuation in intensity. 4247 Unique significant reflections ($\pm h,k,l$) with $I > 3\sigma(I)$ [$\sigma(I)$ based from profiles analysis] have been retained out of a total of 7939 measured reflections. No corrections were made for absorption.

The structure was solved at the first trial by direct methods using the SHELX system of computer programs [11]. The E map computed with the most consistent set of signs revealed the positions of all non-hydrogen atoms. The approximate atomic parameters were adjusted by several cycles of full-matrix least-squares calculations first with isotropic and then with anisotropic temperature factors. The final R value was 0.074 (unit weights). The hydrogen atoms have been refined with the geometric constraint C—H = 1.08 Å. The final difference electron-density map showed the highest residual peaks of *ca.* 0.4 eÅ^{-3}. Plots of $|\Delta F|$ as a function of scattering angle, magnitude of $|F_o|$ and Miller indices revealed almost a linear trend.

Calculations were carried out on the CDC Cyber 76 Computer of CINECA, Casalecchio, Bologna. Atomic coordinates are given in Table I, bond lengths, bond angles and selected torsion angles are reported in Table II. Thermal parameters and observed and calculated structure factors are in Supplementary Publication No. 82011 deposited at the British Library.

5. Discussion of Results

In Figure 1 is given a projection of the molecule on the mean plane of the bridging methylene groups. The macrocycle possess a center of symmetry which coincides with a crystallographic center of symmetry. Three adjacent phenolic units point their ethereal chains above the mean molecular plane, which practically coincides with that found by the bridging methylene groups and has been taken as a reference plane, whereas the corresponding *tert*-butyl groups are directed below this plane.

The opposite situation is observed for the three remaining phenolic units which point the *tert*-butyl groups above and the polyethereal chains below the reference plane. Two groups (the unprimed and primed ones) of each set of three adjacent nuclei are almost perpendicular to the reference plane (the dihedral angles they form are 73.0(1) and 104.1(1)°, respectively).

The third phenolic unit is tilted by 42.9(1)° with respect to the reference plane and points its ethereal chain towards the interior of the macroring partially filling the intramolecular cavity.

Table I.   Fractional atomic coordinates ($\times 10^4$, hydrogen $\times 10^3$), with standard deviations in the least significant digits in parentheses. Hydrogen atoms have the numbers of the carbon atoms to which they are attached.

	x/a	y/b	z/c		x/a	y/b	z/c
O(1)	2674(2)	1329(2)	5063(3)	H(9)3	402(10)	−128(5)	628(9)
C(1)	2879(3)	824(2)	5717(4)	H(10)1	222(6)	−89(5)	829(9)
C(2)	3312(3)	340(2)	5249(4)	H(10)2	283(6)	−49(5)	937(9)
C(3)	3500(3)	−155(2)	5925(5)	H(10)3	311(6)	−124(5)	909(9)
C(4)	3273(3)	−173(2)	7061(5)	H(11)1	414(6)	−28(6)	907(9)
C(5)	2816(3)	309(2)	7492(5)	H(11)2	504(6)	−32(6)	812(8)
C(6)	2608(3)	813(2)	6854(4)	H(11)3	465(6)	−97(6)	876(9)
C(7)	3598(4)	343(2)	4011(4)	H(12)1	362(4)	188(3)	588(6)
C(8)	3549(4)	−700(3)	7812(5)	H(12)2	399(4)	154(3)	464(6)
C(9)	3869(9)	−1221(5)	7158(9)	H(13)1	360(6)	264(4)	452(6)
C(10)	2884(6)	−823(5)	8713(9)	H(13)2	245(6)	240(3)	457(6)
C(11)	4448(6)	−547(6)	8420(10)	H(14)1	233(7)	200(4)	178(8)
C(12)	3418(4)	1749(3)	5033(5)	H(14)2	171(7)	224(3)	294(8)
C(13)	3131(6)	2275(3)	4336(6)	H(14)3	214(7)	151(4)	291(8)
O(2)	3127(4)	2154(3)	3148(5)	H(3′)	246(3)	−151(2)	146(4)
C(14)	2271(7)	1965(4)	2683(8)	H(5′)	456(3)	−63(2)	342(4)
O(1′)	1794(2)	252(2)	3128(3)	H(7′)1	82(4)	−28(2)	169(4)
C(1′)	2362(3)	−219(2)	2915(4)	H(7′)2	112(4)	−90(2)	89(5)
C(2′)	2068(3)	−692(2)	2232(4)	H(9′)1	328(5)	−227(3)	151(7)
C(3′)	2690(3)	−1142(2)	1989(4)	H(9′)2	441(5)	−242(3)	114(7)
C(4′)	3587(3)	−1139(2)	2426(4)	H(9′)3	382(5)	−181(3)	53(7)
C(5′)	3860(3)	−651(2)	3088(4)	H(10′)1	480(6)	−239(4)	329(8)
C(6′)	3271(3)	−193(2)	3336(4)	H(10′)2	365(5)	−217(3)	344(7)
C(7′)	1092(3)	−721(2)	1731(4)	H(10′)3	454(6)	−175(3)	407(7)
C(8′)	4250(3)	−1654(3)	2232(5)	H(11′)1	545(4)	−109(3)	255(7)
C(9′)	3924(5)	−2072(3)	1290(7)	H(11′)2	504(4)	−120(3)	115(7)
C(10′)	4338(5)	−2014(3)	3342(6)	H(11′)3	573(4)	−174(3)	183(7)
C(11′)	5203(4)	−1416(3)	1946(7)	H(12′)1	67(4)	−19(3)	374(4)
C(12′)	1147(3)	154(3)	3999(4)	H(12′)2	150(3)	2(3)	478(4)
C(13′)	639(4)	724(3)	4157(5)	H(13′)1	114(4)	106(3)	441(5)
O(2′)	168(3)	924(2)	3139(4)	H(13′)2	16(4)	67(3)	482(5)
C(14′)	−645(5)	604(4)	2876(9)	H(14′)1	−83(6)	78(4)	205(9)
O(1″)	−873(2)	−668(1)	1399(3)	H(14′)2	−118(6)	71(4)	346(9)
C(1″)	−510(3)	−1059(2)	2210(4)	H(14′)3	−57(6)	13(4)	283(9)
C(2″)	−1117(3)	−1389(2)	2836(4)	H(3″)	−122(2)	−205(3)	414(4)
C(3″)	−755(3)	−1783(2)	3652(4)	H(5″)	151(3)	−154(2)	336(4)
C(4″)	188(3)	−1849(2)	3851(4)	H(7″)1	−259(3)	−101(2)	296(4)
C(5″)	772(3)	−1503(2)	3218(4)	H(7″)2	−252(3)	−157(2)	191(4)
C(6″)	442(3)	−1103(2)	2410(4)	H(9″)1	110(7)	−322(3)	454(4)
C(7″)	−2155(3)	−1349(2)	2613(4)	H(9″)2	126(7)	−275(3)	338(7)
C(8″)	580(4)	−2310(2)	4699(5)	H(9″)3	16(7)	−303(3)	363(7)
C(9″)	793(7)	−2874(3)	4022(7)	H(10″)1	−25(6)	−206(3)	603(7)
C(10″)	−100(5)	−2467(3)	5606(5)	H(10″)2	25(6)	−277(3)	619(7)
C(11″)	1435(5)	−2054(4)	5343(5)	H(10″)3	−73(6)	−267(3)	529(7)
C(12″)	−779(4)	−850(3)	225(4)	H(11″)1	199(5)	−194(4)	480(7)
C(13″)	−1648(4)	−697(3)	−440(5)	H(11″)2	167(5)	−238(4)	596(7)
O(2″)	−2370(3)	−1051(3)	−157(4)	H(11″)3	122(5)	−166(4)	578(7)
C(14″)	−3195(5)	−876(4)	−746(7)	H(12″)1	−19(4)	−64(3)	−13(4)
H(3)	381(3)	−54(2)	555(5)	H(12″)2	−70(5)	−133(3)	20(4)
H(5)	261(3)	29(2)	836(5)	H(13″)1	−153(4)	−75(3)	−133(4)
H(7)1	434(4)	36(2)	401(4)	H(13″)2	−182(5)	−24(3)	−27(4)
H(7)2	332(4)	73(2)	360(4)	H(14″)1	−367(4)	−118(4)	−38(5)
H(9)1	314(9)	−119(5)	724(10)	H(14″)2	−318(5)	−95(4)	−165(7)
H(9)2	413(9)	−160(5)	764(10)	H(14″)3	−341(5)	−43(4)	−59(6)

Table II. Bond distances (Å), bond angles (°) and selected torsion angles (°) with standard deviations in parentheses.

|		′	″
O(1)—C(1)	1.400(6)	1.375(6)	1.390(5)
O(1)—C(12)	1.441(7)	1.438(6)	1.456(6)
C(1)—C(2)	1.384(6)	1.394(6)	1.389(7)
C(1)—C(6)	1.413(7)	1.399(6)	1.403(6)
C(2)—C(3)	1.391(7)	1.397(6)	1.398(6)
C(2)—C(7)	1.534(7)	1.522(6)	1.529(6)
C(3)—C(4)	1.394(8)	1.388(6)	1.394(6)
C(4)—C(5)	1.381(7)	1.398(6)	1.391(7)
C(4)—C(8)	1.526(8)	1.532(7)	1.537(7)
C(5)—C(6)	1.389(7)	1.381(6)	1.385(7)
C(7)—C(6′)	1.513(7)	1.529(7)	1.538(9)
C(8)—C(9)	1.489(14)	1.519(10)	1.538(9)
C(8)—C(10)	1.491(12)	1.541(9)	1.527(9)
C(8)—C(11)	1.511(12)	1.538(8)	1.547(9)
C(12)—C(13)	1.493(10)	1.497(9)	1.505(8)
O(2)—C(13)	1.428(9)	1.434(7)	1.372(8)
O(2)—C(14)	1.410(12)	1.411(9)	1.422(9)
C(1)—O(1)—C(12)	113.7(4)	115.4(4)	115.5(4)
O(1)—C(1)—C(6)	118.4(4)	118.2(4)	120.6(4)
O(1)—C(1)—C(2)	120.7(4)	121.4(4)	118.1(4)
C(2)—C(1)—C(6)	120.8(4)	120.2(4)	121.3(4)
C(1)—C(2)—C(7)	121.4(4)	121.4(4)	121.5(4)
C(1)—C(2)—C(3)	119.0(5)	119.0(4)	118.3(4)
C(3)—C(2)—C(7)	119.6(4)	119.6(4)	120.1(4)
C(2)—C(3)—C(4)	121.7(4)	122.0(4)	121.9(4)
C(3)—C(4)—C(8)	121.0(5)	122.1(4)	121.5(4)
C(3)—C(4)—C(5)	117.8(5)	117.2(4)	118.0(4)
C(5)—C(4)—C(8)	121.2(5)	120.7(4)	120.5(4)
C(4)—C(5)—C(6)	122.8(5)	122.6(4)	122.0(4)
C(1)—C(6)—C(7′)	121.3(5)	119.7(4)	120.1(4)
C(1)—C(6)—C(5)	117.8(4)	118.8(4)	118.8(4)
C(7)—C(6′)—C(5′)	120.8(4)	121.4(4)	121.4(4)
C(2)—C(7)—C(6′)	114.0(4)	114.2(4)	114.7(4)
C(4)—C(8)—C(11)	107.7(6)	110.4(5)	110.0(5)
C(4)—C(8)—C(10)	113.2(6)	107.7(5)	112.2(5)
C(4)—C(8)—C(9)	113.1(6)	113.3(5)	107.3(5)
C(10)—C(8)—C(11)	106.2(7)	108.8(5)	105.9(5)
C(9)—C(8)—C(11)	98.2(8)	108.4(6)	112.8(6)
C(9)—C(8)—C(10)	116.6(8)	108.0(5)	108.8(5)
O(1)—C(12)—C(13)	109.8(5)	107.4(4)	108.9(4)
C(12)—C(13)—O(2)	112.4(6)	112.9(5)	112.3(5)
C(13)—O(2)—C(14)	114.3(7)	113.3(6)	111.3(6)
C(1)—C(2)—C(7)—C(6′)	− 128.6(5)	− 97.2(6)	− 80.5(6)
C(3)—C(2)—C(7)—C(6′)	52.2(7)	84.0(5)	102.3(7)
C(1)—O(1)—C(12)—C(13)	− 179.0(5)	176.4(4)	140.1(5)
O(1)—C(12)—C(13)—O(2)	− 76.4(7)	58.7(6)	− 70.6(6)
C(12)—C(13)—O(2)—C(14)	93.0(8)	76.2(7)	176.6(6)
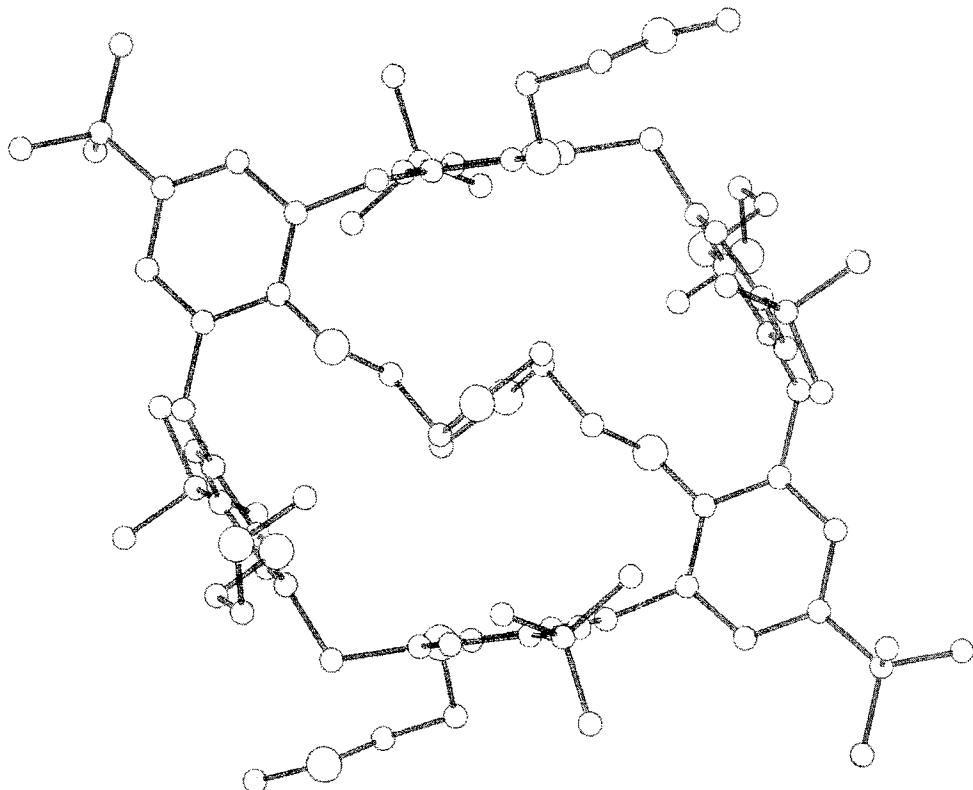
Fig. 1.   View of the molecule on the mean molecular plane.

This conformation is not found in solution at ambient temperature since the ¹H NMR spectrum (**3**) in CDCl₃ shows singlets for aromatic bridging methylene and *tert*-butyl protons, which in conformationally immobile calixarenes give more complex patterns [2,3].

By means of dynamic NMR measurements a barrier of 11.7 kcal mol⁻¹ has been estimated [12] for the inversion or 'pseudo' rotation process [13] for compound (**3**).

Therefore in the solid state and in the absence of any included ionic or neutral guest the macrocycle (**3**) assumes the observed topology in order to maximize the crystal density and to minimize the molecular volume. This condition, and the absence of intramolecular hydrogen bonds, because of the functionalisation of the phenolic OH groups, have significant consequences on some molecular parameters which have been observed both in cyclic [1] and linear [14, 15] phenol-formaldehyde oligomers. For example, the torsion angles involving the methylene carbon atoms which usually range around ± 90°. With these values the conformation of the molecule minimizes the steric interactions involving the methylene hydrogen atoms, the phenolic oxygens and the *tert*-butyl *para*-substituents. All the other geometrical parameters are comparable with the values reported for the calix[*n*]arenes or similar compounds studied up to now.

The ethereal chains show a large flexibility to adapt to the molecular packing as indicated by the torsion angles reported in Table II.

A [001] projection of the molecular packing is given in Figure 2. The contacts, compatible with van der Waals radii, are mainly due to the *tert*-butyl groups and to the oligoethereal chains and no channels or intermolecular cavities are evident.
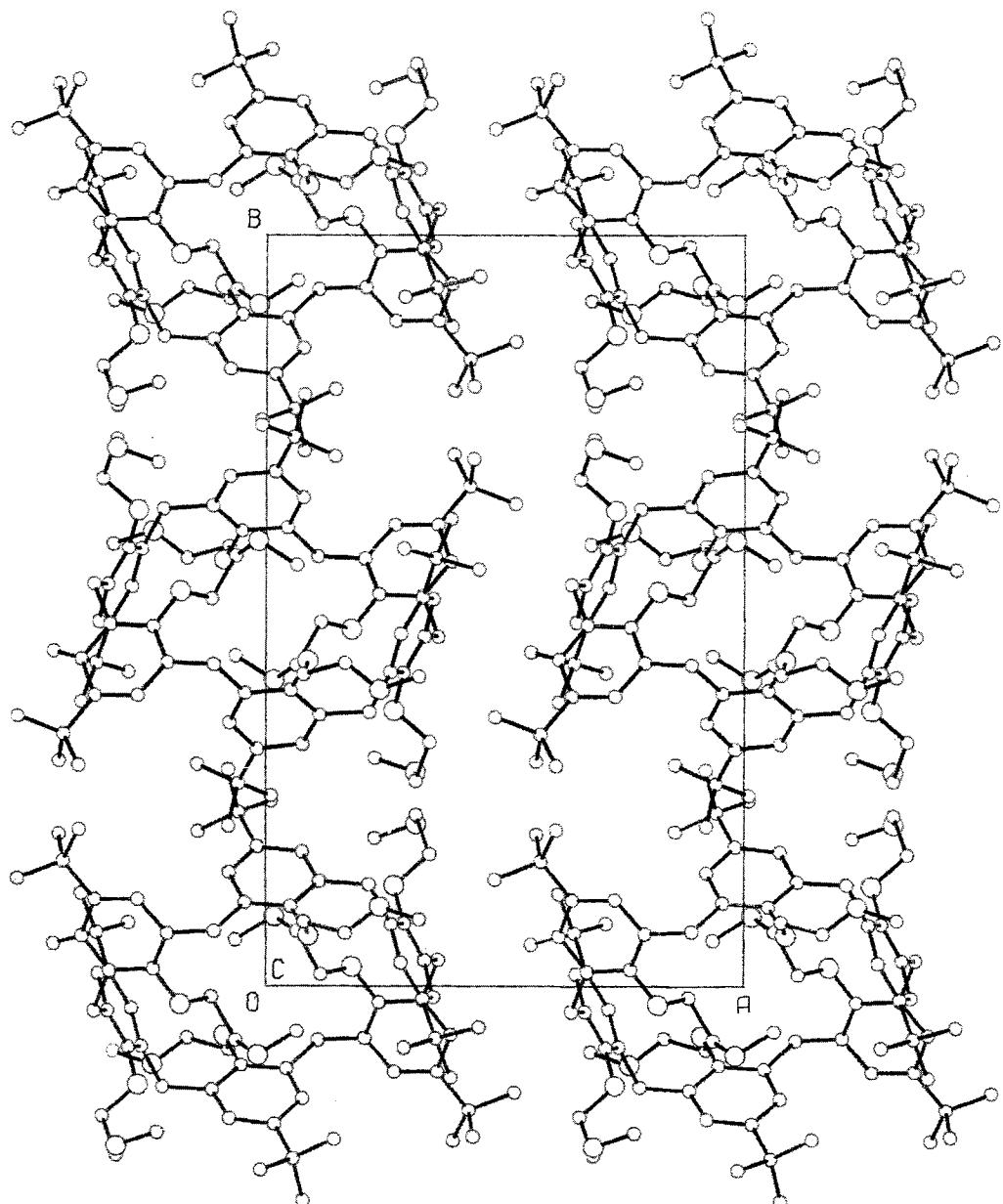
Fig. 2.   Molecular packing projected along [001].

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