

Strained Cyclic Molecules.

I. The Crystal and Molecular Structure of *trans*-3-*tert*-Butyl-4-cyanocyclohexanone: A Twist Conformation

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The crystal structure of *trans*-3-*tert*-butyl-4-cyanocyclohexanone, $C_{11}H_{17}NO$, has been determined by direct methods from three-dimensional diffractometer data. The unit cell is monoclinic, space group $P2_1/c$ with four molecules per unit cell and $a = 8.068$ (2), $b = 11.420$ (3), $c = 12.255$ (3) Å, $\beta = 106.42$ (2)°. The final R for 1696 independent reflections is 0.051. The molecular structure shows a twist conformation with a C_2 pseudo-symmetry axis through C(1) and C(4) which relieves the strong *gauche* interaction between the *tert*-butyl and the cyano groups. The main geometrical modifications and the strongest intramolecular non-bonded interactions are compared with those of similar molecules. The driving force of the molecular packing seems to be the strong electrostatic attraction between the close and antiparallel cyano groups.

Introduction

The influence of strong *gauche* interactions between vicinal substituents on the conformational behaviour of six-membered rings has been recently studied by diastereoisomer equilibria (Aycard & Bodot, 1973), by proton magnetic resonance (Aycard & Bodot, 1975; Lafrance, Aycard, Berger & Bodot, 1976) and vibrational spectroscopy (Monnier, Davidovics, Aycard & Bodot, 1977). In particular, it has been shown that *trans*-3-*tert*-butyl-4-cyanocyclohexanone presents a sharp conformational heterogeneity involving, besides the chair conformer, another conformer, the structure of which is difficult to determine with only PMR data.

In connection with the purposes of these research activities, we are starting a series of papers on the crystal and molecular structures of this kind of compound, the present paper being related to the general problem of non-chair conformations (Kellie & Riddell, 1974).

Experimental

A summary of the crystal data is given in Table 1. The preparation of this compound was described by Lafrance (1975).

The crystal used in the structure determination has a somewhat irregular form but may be described as a rectangular colourless prism of dimensions $0.40 \times 0.32 \times 0.22$ mm. It was mounted along **b** on a Lindemann-glass capillary.

All X-ray measurements were made at room temperature. X-ray oscillation, Weissenberg and precession photographs with the use of Ni-filtered Cu $K\alpha$ radiation taken about all three axes, showed a monoclinic system with well formed reflections.

The approximate cell dimensions thus obtained ($a = 8.07$, $b = 11.41$, $c = 12.21$ Å and $\beta = 106.2^\circ$) were in agreement with the diffractometer values determined subsequently and used in all calculations.

Table 1. Crystal and experimental data

Estimated standard deviations given in parentheses refer to the least significant digit. The cell parameters are the diffractometer-determined values.

Molecular formula $C_{11}H_{17}NO$	$a = 8.068$ (2) Å
FW 179.26	$b = 11.420$ (3)
m.p. 73°C	$c = 12.255$ (3)
Crystal system: monoclinic	$\beta = 106.42$ (2)°
Space group: $P2_1/c$	$V = 1083.1$ Å ³
Laue class: $2/m$	$\lambda(\text{Cu } K\alpha) = 1.54178$ Å
d_o (by flotation) = 1.11 (2) g cm ⁻³	$\mu(\text{Cu } K\alpha) = 5.55$ cm ⁻¹
d_c (with $Z = 4$) = 1.10	$F(000) = 392$
$Z = 4$	

The intensities were collected on an on-line four-circle Syntex $P2_1$ diffractometer, operating in the $\theta-2\theta$ scan mode and using graphite-monochromatized Cu $K\alpha$ radiation. 1804 reflections up to $\theta = 65^\circ$ were recorded including 108 systematic extinctions; hence, 1696 reflections were considered as observed. Two reference reflections were chosen and recorded at the beginning of the data collection and after every set of 30 readings. The intensities of the selected reflections were checked to confirm that the variance did not exceed 3.7% throughout the data collection and that there was no significant crystal decomposition due to X-ray exposure.

The usual correction was made for the Lorentz-polarisation factor, but an absorption correction was not applied because of the small size of the crystal and the low μ .

Structure determination and refinement

With Wilson's (1942) method, preliminary absolute scale ($K = 0.0382$) and overall temperature factors ($B = 4.63 \text{ \AA}^2$) were estimated.

The phases of the 325 largest normalized structure factors ($E > 1.3$) were determined by symbolic addition for a centred group (Karle & Karle, 1966) with the *LSAM* program system (Main, Woolfson & Germain, 1970). 331, 477 and 221 were used to fix the origin. The numerical phase values of three additional reflections were determined by the Hauptman & Karle (1953, 1959) method. The starting set of the phases is given in Table 2. From the various sets of the generated phases, that showing the highest absolute figure of merit was selected.

The Fourier synthesis calculated with the 325 reflections revealed seven non-hydrogen atoms. A new Fourier synthesis phased on these seven atoms yielded a further four non-hydrogen atoms. By repeating this method, all the remaining non-hydrogen atoms were located. The R value was then 0.20 for 908 reflections, with $R = \Sigma |KF_o - |F_c|| / \Sigma |KF_o|$.

The atomic parameters of these atoms were refined by the least-squares method first isotropically (three cycles) and then anisotropically (four cycles) with the Busing, Martin & Levy (1962) program with a full matrix. The weighted final R value was 0.051 with

Table 2. *Starting set of phases*

hkl	E	φ ($^\circ$)	
3 3 $\bar{1}$	2.97	0	} origin
4 7 $\bar{7}$	3.31	0	
2 2 1	2.52	0	
3 3 1	2.97	0	
4 8 0	3.41	180	
2 4 2	2.87	180	

Hughes's (1941) weighting scheme applied with $F_o \text{ min.} = 0.0$.

All the H atoms were located from a difference map. They were included in the last two stages of refinement but their parameters were not refined. Each H atom was assigned the mean isotropic thermal parameter of the C atom to which it is bonded.

The atomic scattering factors used for C, N and O were those of Doyle & Turner (1968). For H, the values given by Stewart, Davidson & Simpson (1965) were used.

The final positional and H isotropic thermal parameters are shown in Tables 3 and 4.*

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33084 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 3. *Final fractional coordinates ($\times 10^4$) for non-hydrogen atoms*

Standard deviations in parentheses refer to the last digit quoted.

	x	y	z
C(1)	4813 (2)	558 (2)	3560 (1)
C(2)	6540 (2)	1135 (1)	3730 (2)
C(3)	6803 (2)	2155 (1)	4583 (1)
C(4)	5336 (2)	3084 (1)	4141 (1)
C(5)	3778 (2)	2609 (2)	3211 (1)
C(6)	3330 (2)	1380 (2)	3466 (2)
C(7)	8650 (2)	2690 (1)	4871 (1)
C(8)	8792 (3)	3710 (2)	5697 (2)
C(9)	9091 (2)	3120 (2)	3804 (2)
C(10)	9962 (2)	1759 (2)	5459 (2)
C(11)	4721 (2)	3512 (1)	5094 (1)
N(12)	4191 (2)	3833 (1)	5812 (1)
O(13)	4639 (2)	-496 (1)	3507 (1)

Table 4. *Fractional coordinates ($\times 10^4$) and isotropic thermal parameters for hydrogen atoms*

	x	y	z	B (\AA^2)
H(21)	7432	550	3945	4.22
H(22)	6527	1442	2908	4.22
H(31)	6721	1820	5373	3.26
H(42)	5773	3812	3775	3.36
H(51)	2829	3175	3132	4.49
H(52)	4012	2641	2408	4.49
H(61)	3126	1300	4252	5.21
H(62)	2291	1071	2875	5.21
H(81)	9939	4016	5981	5.20
H(82)	8041	4393	5318	5.20
H(83)	8545	3436	6456	5.20
H(91)	10188	3537	4037	5.40
H(92)	9081	2487	3221	5.40
H(93)	8173	3741	3336	5.40
H(101)	11097	2081	5727	5.84
H(102)	9619	1406	6121	5.84
H(103)	10040	1114	4915	5.84

All calculations were carried out on the 370/145 IBM computer of the Office Central de Mécanographie of Abidjan.

Molecular structure

The molecular structure is illustrated in Fig. 1 and the bond lengths and the valency angles for non-hydrogen atoms are shown in Fig. 2. The C—H bond lengths are listed in Table 5. The torsion angles in the form of Newman projections are given in Fig. 3.

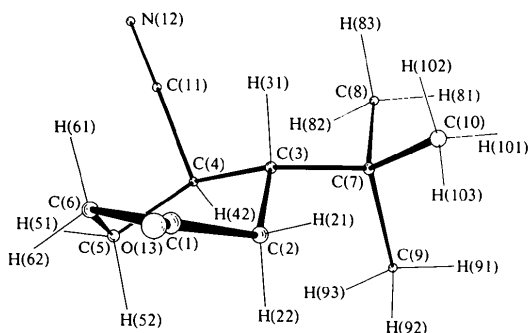


Fig. 1. The molecular structure, with the numbering scheme, projected along **b**.

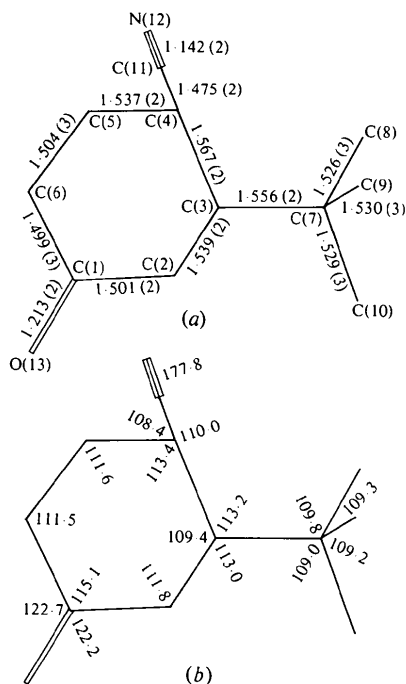


Fig. 2. Projection of the structure along **c** showing: (a) the bond lengths (Å) with their standard deviations given in parentheses to last digit quoted; (b) the valency angles (°); standard deviations near 0.2°. Hydrogen atoms are omitted for clarity. Angles not shown in the figure: C(3)—C(7)—C(9) 111.8, C(8)—C(7)—C(10) 107.8°.

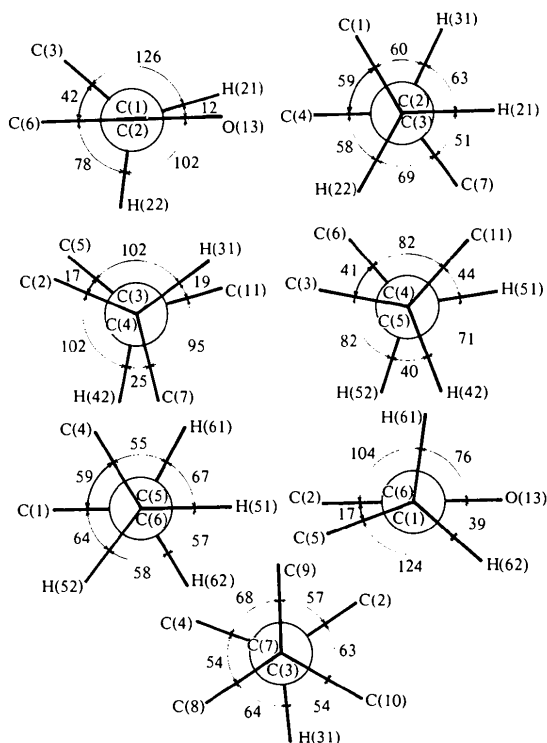


Fig. 3. Selected Newman projections (°).

The best planes through selected atoms show that C(1), C(2), C(6) and O(13) are coplanar within 0.002 Å; C(6) is 0.08 Å from the C(3), C(7), C(9) plane. The best *anti* relation between vicinal atoms is found with C(2), C(3), C(7), C(8), which are coplanar within 0.02 Å.

Ring conformation

From Figs. 1 and 3 it is obvious that, in the crystal, the molecule is not in the chair form (whose sign alternation of dihedral angles is shown in Table 6); the sequence of dihedral-angle signs is the same for our experimental data as those for the calculated twist and boat conformations (Bucourt, 1974). The values of the experimental dihedral angles are half-way between those for the two flexible conformations (Table 6).

Table 5. The C—H bond lengths (Å)

C(2)—H(21)	0.96	C(8)—H(81)	0.96
C(2)—H(22)	1.06	C(8)—H(82)	1.02
C(3)—H(31)	1.06	C(8)—H(83)	1.05
C(4)—H(42)	1.05	C(9)—H(91)	0.97
C(5)—H(51)	0.99	C(9)—H(92)	1.02
C(5)—H(52)	1.05	C(9)—H(93)	1.07
C(6)—H(61)	1.03	C(10)—H(101)	0.96
C(6)—H(62)	1.00	C(10)—H(102)	1.01
		C(10)—H(103)	1.01

As twist is associated with conformations presenting the C_2 pseudosymmetry axis, our molecule is very close to that with the axis through C(1) and C(4) which may be named twist-1,4; the pseudosymmetry is clearly shown by Fig. 4(a) and demonstrated by the near equalities $\varphi_{12} \simeq \varphi_{45}$, $\varphi_{23} \simeq \varphi_{56}$ and $\varphi_{34} \simeq \varphi_{61}$. Another C_2 pseudosymmetry axis goes through the centres of the C(2)—C(3) and C(5)—C(6) bonds (Fig. 4b).

For cyclohexanone itself, the twist-2,5 (Bucourt, 1974) or the twist-1,4 (Allinger, 1976) conformations are well known as the more stable among the flexible conformations. For our molecule, the relief of the strong *gauche* interaction is best achieved with a small

value of φ_{34} which allows the increase of the C(7), C(3), C(4), C(11) dihedral angle (95° for our molecule); hence, our molecule adopts the twist-1,4 conformation, the *tert*-butyl and the cyano groups being respectively pseudoequatorial (ψ_{ie}) and isoclinal (ψ_{ic}) according to the recent terminology (Bellucci, Berti, Colapietro, Spagna & Zambonelli, 1976).

cis-2,*trans*-3-Dibromo-*cis*-4-*tert*-butylcyclohexyl *p*-nitrobenzoate is the only case of a non-chair cyclohexane derivative studied by X-ray diffraction (Bellucci *et al.*, 1976); in spite of its complexity, this molecule adopts a conformation very similar to that of ours, which must be because the main driving force of the conformational adaptation is, in both molecules, the strong *gauche* interaction between a *tert*-butyl and a *trans* vicinal substituent.

Table 6. Endocyclic torsion angles (φ_{ij}) of *trans*-3-*tert*-butyl-4-cyanocyclohexanone and of model structures

	Experimental twist-1,4†	Calculated twist-2,5‡	Calculated boat‡	Experimental chair§
φ_{12}^*	42.	29.	50.	47.
φ_{23}	-59.	-60.	-50.	-52.
φ_{34}	17.	29.	0.	57.
φ_{45}	41.	29.	50.	-57.
φ_{56}	-59.	-60.	-50.	52.
φ_{61}	17.	29.	0.	-47.

* $\varphi_{12} = \varphi C(6)-C(1)-C(2)-C(3)$.

† This work; pseudo- C_2 axis through C(1) and C(4).

‡ Bucourt (1974); pseudo- C_2 axis through C(2) and C(5).

§ Lectard (1976); 4-*tert*-butylcyclohexanone.

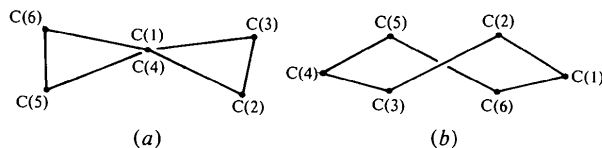


Fig. 4. Ring projections.

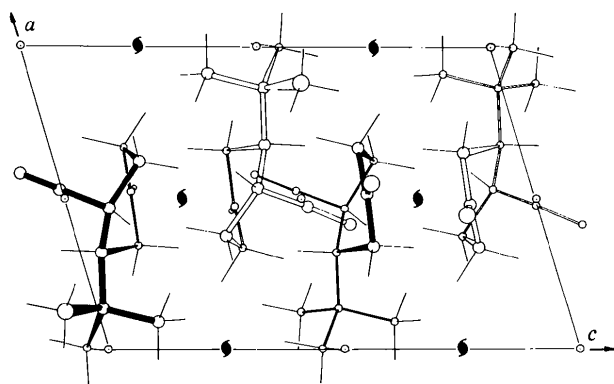


Fig. 5. The molecular packing viewed along *b*.

Geometrical modifications

The bond lengths (Fig. 2) are very similar to those of 4-*tert*-butylcyclohexanone (Lectard, 1976) except for C(3)—C(4) which is 0.05 Å longer, another way to minimize the *gauche* interaction; a similar increase has been observed with three *trans*-3-*tert*-butyl-4-*X*-cyclohexene derivatives (Viani, Lapasset, Aycard, Lafrance & Bodot, 1978).

Among the endocyclic valence angles (Fig. 2b) we observe a small pinching of C(2)—C(3)—C(4) (109.4°), always associated with the presence of the *tert*-butyl group (Lectard, 1976).

Other general features of this substitution, concerning exocyclic angles, are common to the chair conformation and to our twist molecule; the flattening of the pyramid, with C(2), C(4), C(7) as the base and C(3) as the top, increases the C(2)—C(3)—C(7) and C(4)—C(3)—C(7) angles ($\approx 113^\circ$). The inequality C(3)—C(7)—C(9) (111.8°) > C(3)—C(7)—C(8) (109.8°) and C(3)—C(7)—C(10) (109.0°) is also general, and it allows the decrease of the steric interaction between C(9), its H and H(22) and H(42). It is noticeable that C(3)—C(7)—C(8) and C(3)—C(4)—C(11) are not larger, as has been observed for similar cyclohexenes (Viani *et al.*, 1978), as a result of the interaction between the methyl C(8) and the cyano groups.

The exocyclic dihedral angles associated with C(3)—C(7) as a central bond (Fig. 3) correspond to $\Delta\varphi \simeq 5^\circ$, $\Delta\varphi$ being the mean deviation from the staggered conformation of the *tert*-butyl group; this is a little more than for compounds without a vicinal group, $\Delta\varphi \simeq 2^\circ$, (Lectard, 1976) but less than for the 3-*tert*-butyl-4-*X*-cyclohexenes: $7 < \Delta\varphi < 17^\circ$ (Viani *et al.*, 1978).

The uncommon C(8)—C(7)—C(4)—C(11) dihedral angle is notable for its deviation from a pure *syn*-1,3 situation between the methyl C(8) and the cyano groups; for our molecule (33°), it is far larger than in the cyclohexene series (between 7 and 17°).

Non-bonded interactions

As we are dealing with a strained molecule, there are many 'short distances' ($\leq d_0$) between non-bonded atoms, d_0 corresponding to a zero value for the non-bonded energy as it is parametrized in the molecular mechanical calculations (Allinger, 1976).

If we arbitrarily consider the 'very short distances' as corresponding to $\leq 0.9d_0$, the strongest interactions involve the H(*i*)–H(*j*) pairs (distances in Å): *ij* = 21–103 (2.20); 22–52* (2.38); 22–92 (2.32); 42–82 (2.33); 42–93 (2.15); which are very similar to non-bonded distances in six-membered-ring molecules with a *tert*-butyl substituent, but without a vicinal substituent.

The C(11)–C(8) (3.16 Å) and the C(11)–H(82) (2.80 Å) distances are significantly larger than the corresponding distances in the cyclohexene series, 2.98 and 2.58 Å respectively (mean values of six molecules). Hence, the twist cyclohexanone conformation is more efficient than the sofa cyclohexene in relieving the steric strain between two vicinal substituents.

Molecular packing

As shown in Fig. 5, the mean features of this molecular packing are the closeness of the cyano groups and their antiparallel orientations. The distance between these groups is about 3.43 Å which is less than the sum of the van der Waals radii (≈ 3.70 Å); the corresponding loss of attractive non-bonded energy may be counter-balanced by the strong electrostatic attraction between the large dipoles.

A similar situation has been observed with 7,7,8,8-tetracyanoquinodimethane–naphthalene (1:1) (Shaanan, Shmueli & Rabinovich, 1976), but the nearest cyano groups are 3.57 Å from each other. This difference from our result may be related to the decrease of the electrostatic attraction owing to the smaller dipole moments of the cyano groups bonded to the same sp^2 carbon.

Conclusion

Of the two conformers of *trans*-3-*tert*-butyl-4-cyano-cyclohexanone, it is the twist one which is present in the crystal; the ring conformation has a C_2 pseudo-symmetry axis [C(1)–C(4)].

The analysis of the molecular structure shows the usual interactions between a *tert*-butyl group and a six-membered ring; because of the large dihedral angle between the *tert*-butyl and cyano groups, the geometrical modifications are less than those observed in the

cyclohexene series where the *gauche* interaction is minimized by the adoption of a sofa conformation.

In solution, the chair and the twist conformations are equally populated; this may come from a balance between the energy requirement of the twist conformation, about 3 kcal mol⁻¹ (Bucourt, 1974), and the *gauche* interaction energy in the chair conformation. A crystallographic study of the latter would be of prime interest.

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References

- ALLINGER, N. L. (1976). *Adv. Phys. Org. Chem.* **13**, 1–82.
 AYCARD, J. P. & BODOT, H. (1973). *Can. J. Chem.* **51**, 741–747.
 AYCARD, J. P. & BODOT, H. (1975). *Org. Magn. Reson.* **7**, 226–236.
 BELLUCCI, G., BERTI, G., COLAPIETRO, M., SPAGNA, R. & ZAMBONELLI, L. (1976). *J. Chem. Soc. Perkin Trans. 2*, pp. 1213–1218.
 BUCOURT, R. (1974). *Top. Stereochem.* **8**, 159–224.
 BUSING, W. R., MARTIN, K. O. & LEVY, H. A. (1962). *ORFLS*. Report ORNL-TM-305. Oak Ridge National Laboratory, Tennessee.
 DOYLE, P. A. & TURNER, P. S. (1968). *Acta Cryst.* **A24**, 390–397.
 HAUPTMAN, H. & KARLE, J. (1953). *Solution of the Phase Problem. I. The Centrosymmetric Crystal*. ACA Monograph No. 3. Pittsburgh: Polycrystal Book Service.
 HAUPTMAN, H. & KARLE, J. (1959). *Acta Cryst.* **12**, 93–97.
 HUGHES, E. W. (1941). *J. Am. Chem. Soc.* **63**, 1737–1752.
 KARLE, J. & KARLE, I. L. (1966). *Acta Cryst.* **21**, 849–859.
 KELLIE, G. M. & RIDDELL, F. G. (1974). *Top. Stereochem.* **8**, 225–269.
 LAFRANCE, R. (1975). Thèse de Spécialité, Univ. de Provence, Marseille, France.
 LAFRANCE, R., AYCARD, J. P., BERGER, J. & BODOT, H. (1976). *Org. Magn. Reson.* **8**, 95–101.
 LECTARD, A. (1976). Thèse de Doctorat ès-Sciences Physiques. Univ. de Pau, France.
 MAIN, P., WOOLFSON, M. M. & GERMAIN, G. (1970). *LSAM. A System of Computer Programs for the Automatic Solution of Centrosymmetric Structures*, Univs. of York, England, and Louvain, Belgium.
 MONNIER, M., DAVIDOVICS, G., AYCARD, J. P. & BODOT, H. (1977). *J. Mol. Struct.* To be published.
 SHAANAN, B., SHMUELI, U. & RABINOVICH, D. (1976). *Acta Cryst.* **B32**, 2574–2580.
 STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.
 VIANI, R., LAPASSET, J., AYCARD, J. P., LAFRANCE, R. & BODOT, H. (1978). To be published.
 WILSON, A. J. C. (1942). *Nature (London)*, **150**, 151–152.

* These hydrogens are pseudo-axial ($\psi_{\tau a}$), and in relative positions which are less strained but similar to the well-known flagpoles of a boat conformation.