refluxing for six hours with stirring, the benzene layer was washed thoroughly until free of halide and mercuric ions. The nitrile was distilled from Raney nickel. The yield was 85%, based on the piperonyl alcohol.

Dihomopiperonylamine was isolated as the hydrochloride by dissolving the non-volatile residue from the Raney nickel catalyzed hydrogenation in dry ether and bubbling in dry hydrogen chloride. The hydrochloride, after recrystallizing twice from water and once from 95% ethanol melted at 261–262° with dec. *Anal.* Calcd. for $C_{18}H_{20}O_4NCl$: C, 61.82; H, 5.73; N, 4.00. Found: C, 62.08; H, 5.84; N (Dumas), 4.15.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF MARYLAND
COLLEGE PARK, MARYLAND   RECEIVED JANUARY 12, 1950

The Dipole Moment and Molecular Configuration of 1,6-Dichloro-1,5-cyclooctadiene

BY JOHN D. ROBERTS

The structure of the eight-membered ring dimer (I) of chloroprene (2-chloro-1,3-butadiene) has been established as 1,6-dichloro-1,5-cyclooctadiene (the product of "head-to-head" dimerization)[1] with probably the *cis–cis* configuration of double bonds.[2] Inspection of Fisher–Hirschfelder models reveals that this substance might be expected to exist in three strainless forms analogous to the boat and chair forms of cyclohexane.[3]

"Chair" form   "Skew" form   "Boat" form
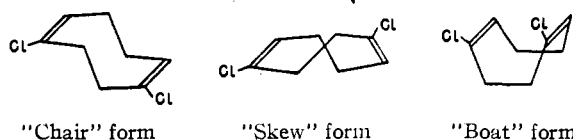
In the "chair" form of I, the C–Cl bonds (barring minor perturbations) lie within parallel planes with the projection of one bond on the plane of the other bond forming an angle of 120°[4] with the latter. If it is assumed that (a) only the C–Cl moments make important contributions to the dipole moment of the molecule and (b) the vector moment of each C–Cl is equal to 1.5D,[5] the calculated moment of this form is 1.5D. In the "skew" configuration the C=C—Cl groups lie in two intersecting planes inclined at about 45°, the line of intersection of the planes passing through the mid-points of each of the C=C bonds and perpendicular to them. The resultant of the C–Cl vectors in the skew form is 1.4D. In the "boat" configuration the C–Cl bonds lie within

the same plane at an angle of 40°. The value of the angle is readily obtained if the equivalence is recognized between this angle and the one formed by the extensions of the C1–C8 and C6–C7 bonds. The calculated moment for a 40° angle is 2.8D.

The dipole moment of pure I[1] in benzene solution was found to be 2.60D by the method previously described.[6] The data are given in Table I. The experimental value for the dipole moment is in good agreement with the value calculated for the boat configuration and indicates that this is the actual configuration for at least 85% of the molecules formed by the dimerization of chloroprene. The boat configuration could hardly have been expected *a priori* to be the most stable form since the dipole–dipole repulsions of the C–Cl bonds (operating across a medium of unit dielectric constant) would amount to about 500 cal./mole.

TABLE I

DIELECTRIC CONSTANTS, DENSITIES AND POLARIZATIONS IN BENZENE AT 25° OF 1,6-DICHLORO-1,5-CYCLOOCTADIENE

f_2	ϵ	d	P_2
0.00000	2.2760	0.87308	($P_1 = 26.697$)
.00596	2.3329	.87654	182.0
.01027	2.3756	.87882	183.4
.02562	2.5270	.88751	181.1
.05918	2.8716	.90496	178.0

$P_\infty = 183.0$, $MR_D = 48.15$, $\mu = 2.60D$

In order to test a provisional hypothesis, that (a) the forms might not be readily interconvertible and (b) the boat form is produced almost exclusively in the dimerization, approximate calculations have been made of the energy barriers to interconversion of the three forms. It was expected that the boat and chair forms should not be easily convertible since they correspond to the reported isomeric salicylides.[7] This expectation was not verified on calculation of the strain energy involved in the interconversion process. From inspection of scale models, the most energetically favorable interconversion route appeared to be that shown below with a transition state having C-3,4,5,6,7 and 8 lying in one plane. The strain
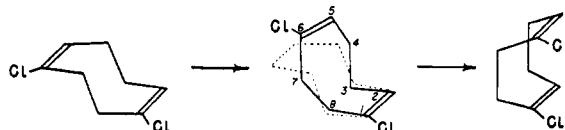
in this transition state results from changes in the valence angles of C-1,2,4,5,6 and 7. No particular strain seems to be involved in angles of C3 and 8 if free rotation exists around the C2-C3 and C1-C8 bonds.

(1) Cope and Schmitz. THIS JOURNAL. **72**, 3056 (1950).

(2) Cope, Stevens and Hochstein. *ibid.*, **72**, 2510 (1950).

(3) Baker, Banks. Lyon and Mann. *J. Chem. Soc.*, 27 (1945). have previously suggested the possibility of similar isomeric forms for the analogously constituted *sym*-dibenzocyclooctadiene. The X-ray crystallographic data were reported to indicate that *sym*-dibenzocyclooctadiene exists as a centro-symmetrical form.

(4) Throughout this paper the following values are assumed for the normal bond angles and bond lengths: ∠C–C–C, ∠C–C–H = 109.5°; ∠C=C–C, ∠C=C–Cl, ∠C=C–H = 120°; C–H = 1.09 Å.; C=C = 1.34 Å.; C–C = 1.54 Å., =C–Cl = 1.70 Å.

(5) This moment is obtained from the average moments (2.1D) of secondary alkyl chlorides in benzene and the 0.6D difference between ethyl chloride and vinyl chloride, Hugill, Coop and Sutton, *Trans. Faraday Soc.*, **34**, 1518 (1938).

(6) Rogers and Roberts, THIS JOURNAL. **68**, 843 (1946); Roberts, Armstrong. Trimble and Burg. *ibid.*, **71**, 843 (1949).

(7) *Cf.* Schönberg. *J. Chem. Soc.*, 891 (1948), for references and discussion. Note. however. that Baker, Ollis and Zealley, *Nature*, **164**, 1049 (1949), have very recently presented evidence that the β-salicylide is actually a trimer.

In the calculation of the strain energy of the transition state it was assumed that (a) only angular strain is involved, (b) the amount of strain at each of the positions 4, 5, 6 and 7 is equal and the same is true of positions 1 and 2, and (c) the energy for bond bending (calculated from the k_{δ_1}/l_2^2 force constant of ethylene)[8] is 13 cal./deg.^{2}/mole.[9] The following procedure was used in the calculation. The distance between C3 and C8, r, was computed as a function of the deviation, θ, of each of the angles of C-4,5,6 and 7 from their normal values[4] by the equation, $r = 1.34 + 3.08$ [sin(30° $+ \theta) - \sin(40.5° - 20°)$]. The deviations, ϕ, from the normal values of the angles of C1 and C2 corresponding to various r values were obtained from the equation, $\sin(\phi + 30°) = (r - 1.34)/3.08$. The values of θ and ϕ for given r's were used to calculate the strain energy of the transition state as a function of r (Fig. 1). The minimum value of the energy is about 9 kcal. and corresponds to a fairly rapid interconversion of the boat and chair forms at room temperature. It is probable that the calculated interconversion energy would be substantially lower if part of the strain were considered to be relieved by bond stretchings or compressions. No refinements of this sort were attempted since the purpose of the calculation was not to obtain a minimum activation energy but to show whether the barrier for some reasonable interconversion path would be low enough to permit establishment of equilibrium between the boat and chair at room temperature.

The interconversion of the skew and boat forms is hindered by steric repulsions between the hydrogen atoms located on C3 and C7 or C4 and C8. If all of the bond angles of the molecule are held at the normal values the nuclei of the hydrogen atoms in question attain a distance of 0.74 Å. in the interconversion transition state. This distance is well under the kinetic theory diameter for molecular or atomic hydrogen (2.4–2.5 Å.).[10] An approximate value for the repulsive forces in the transition state may be computed by considering C3 and C7 (or C4 and C8) to be colliding methane molecules and using the Morse potential energy curve for methane in conjunction with the closest distance of approach (2.47 Å.) of C3 and C7 during the interconversion process. From the data summarized by Hirschfelder, Bird and Spotz[11] the calculated value of the barrier is 3 kcal./mole which would correspond to very easy interconversion at room temperature between the boat and skew forms. In one sense, this value is a lower limit since the average orientation in the collisions of methane molecules may permit a closer ap-
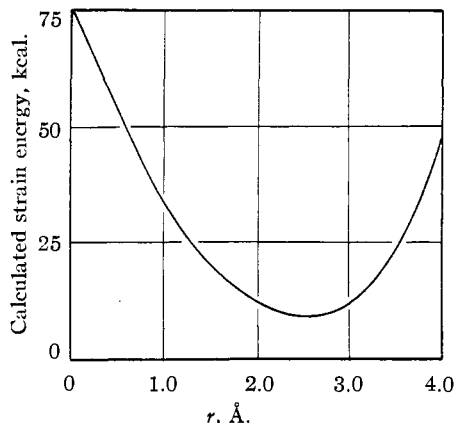

Fig. 1.

proach of carbon nuclei for a given potential energy than in the interconversion transition state. However, if the same value of r_0 (3.882 Å.) for the Morse curve is used as for methane but the colliding groups are considered to be as "hard" as helium ($\epsilon = 6.03$ as against 1.365 for methane)[11] the barrier is still not more than 14 kcal., which would permit interconversion at room temperature. Actually the barrier calculated by this method, regardless of its value, represents an upper limit since the repulsive forces could be reduced by bending and stretching of the bonds of the cyclooctadiene ring.

We conclude that the chair, boat and skew forms are likely to be easily interconvertible. The observed predominance of the boat configuration seems best accounted for by secondary valence forces, possibly similar to the "dispersion forces" suggested for molecular complexes,[12] which are powerful enough to overcome the unfavorable electrostatic repulsions between the C–Cl dipoles. Such secondary valence forces might also account for the apparent non-formation of the "head-to-tail" dimer by stabilizing the dimerization transition state involving two superimposed chloroprene molecules as shown
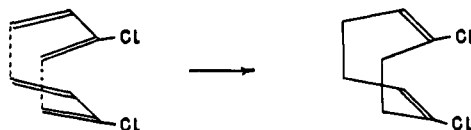
It is particularly interesting to note that "α"-disalicylide is reported to have a dipole moment of $6.27D$[13] showing that the boat-type configuration is most stable for this substance as well as for I.

Acknowledgment.—The 1,6-dichloro-1,5-cyclooctadiene was kindly supplied by Dr. Arthur C. Cope and Mr. William R. Schmitz. Mr. Schmitz also aided in the determination of the dipole moment. Drs. I. Amdur, Richard C.

(8) Herzberg, "Infrared and Raman Spectra of Polyatomic Molecules," D. Van Nostrand Company, New York. N. Y., 1945, p. 184.

(9) The force constants for bending of carbon single bonds are here assumed to be independent of whether the carbon is singly or doubly-bonded to other groups. The error so introduced should not amount to more than 10–20%.

(10) Amdur, J. Chem. Phys., 4, 339 (1936).

(11) Hirschfelder, Bird and Spotz, Chem. Rev., 44, 205 (1949).

(12) Cf. Dewar, "Electronic Theory of Organic Chemistry," Oxford University Press, London, 1949, pp. 184–185.

(13) Edgerly and Sutton, Nature, 144, 1050 (1949).

Lord, Jr., and D. H. R. Barton gave valuable advice for the theoretical part.

DEPARTMENT OF CHEMISTRY
MASSACHUSETTS INSTITUTE OF TECHNOLOGY
CAMBRIDGE 39, MASSACHUSETTS
RECEIVED JANUARY 16, 1950

Organic Salts of Benzylpenicillin. I. Aliphatic Amine Vasoconstrictors

BY H. W. RHODEHAMEL, JR.

During the preparation of a series of organic amine salts of benzylpenicillin, a number of crystalline combinations have been found. This note deals with the relatively water soluble crystalline benzylpenicillin salts of three useful aliphatic amine vasoconstrictors which have been of sufficient interest to suggest possible clinical application. Each is prepared in the same manner as follows: The free amine base in a convenient organic solvent, generally amyl acetate or diethyl ether, is added to an organic solution of free benzylpenicillin acid. The salt combination precipitates out as crystals immediately or after short standing with scratching or seeding.

The 2-Aminoheptane Salt of Benzylpenicillin.—White, needle-like crystals with a theoretical penicillin potency of 1270 Oxford units per mg.; m.p. (hot stage) 102–105° dec.; $[\alpha]^{25}D + 225 \pm 3°$ (c, 1 in H_2O). *Anal.* Calcd. for $C_{23}H_{38}O_4N_3S \cdot H_2O$: C, 59.09; H, 7.98; N, 8.99. Found: C, 59.99; H, 8.56; N, 8.89.

The 2-Amino-4-methylhexane Salt of Benzylpenicillin.—White, small, needle-like crystals with a theoretical penicillin potency of 1270 Oxford units per mg., m.p. (hot stage) 103–106° dec.; $[\alpha]^{25}D + 225 \pm 3°$ (c, 1 in H_2O). *Anal.* Calcd. for $C_{23}H_{35}O_4N_3S \cdot H_2O$: C, 59.09; H, 7.98; N, 8.99. Found C, 59.00; H, 7.87; N, 8.94.

The 1-Cyclopentyl-2-methylaminopropane Salt of Benzylpenicillin.—White, needle-like crystals with a theoretical penicillin potency of 1200 Oxford units per mg., m.p. (hot stage) 202–204° dec. *Anal.* Calcd. for $C_{25}H_{37}N_3O_4 \cdot S \cdot H_2O$: C, 60.70; H, 8.15; N, 8.50. Found: (ash free) C, 61.21; H, 6.36; N, 8.86.

Another commerically available aliphatic amine vasoconstrictor, 1-cyclohexyl-2-methylaminopropane, has given a water soluble, amorphous salt with benzylpenicillin, but efforts to induce its crystallization have to date been unsuccessful.

The author is indebted to Mr. W. L. Brown for microanalyses, to Dr. E. Rohrmann for supplying the amines used in this study, and to Miss Mary Stieff for technical assistance.

THE LILLY RESEARCH LABORATORIES
INDIANAPOLIS, IND.   RECEIVED FEBRUARY 18, 1950

The Trimer of o-Phthalonitrile[1]

BY SIDNEY D. ROSS AND MORTON FINEMAN

In the course of their work on magnesium phthalocyanine, Linstead and Lowe[2] isolated an acetic acid soluble by-product melting at 296° and analyzing correctly for a polymer of phthalonitrile, $(C_8H_4N_2)_x$. In a later publication Dent

and Linstead[3] showed by a molecular weight determination that this substance was a trimer, and that on hydrolysis with nitric acid it yielded phthalimide. On the basis of this evidence they assigned to the trimer a 2,4,6-tri-(o-cyanophenyl)-1,3,5-triazene structure. It is the purpose of the present communication to report a preparation of this trimer, some of its properties, and evidence confirming Linstead's structure assignment.

In connection with other work in these laboratories, we have observed that when o-phthalonitrile is heated at high temperature in the presence of a trace of acid or water, the trimer, reported by Linstead and Lowe, is formed. The trimer gives a yellow solution in sulfuric acid, from which phthalimide can be isolated after dilution with water.

The Linstead structure was confirmed by comparing the infrared spectrogram[4] of the trimer, mulled in nujol, with that of 2,4,6-triphenyl-1,3,5-triazene prepared by the method of Cook and Jones.[5] The o-phthalonitrile trimer (Figs. 1 and 2) shows the expected nitrile absorption at 4.53 microns, and the other absorptions can be attributed to the benzene ring, the triazene ring or the nujol vehicle. The spectrum of 2,4,6-triphenyl-1,3,5-triazene (Fig. 3) is shown for comparison.

All of the o-phthalonitrile trimer samples which we prepared were crystallized from acetic acid. Nevertheless, we observed that we obtained the product in two crystalline modifications, fine needles (Form A) and poorly defined clusters (Form B). Both crystalline forms melted at the same point and gave similar infrared spectrograms (Figs. 1 and 2). However, the two forms

TABLE I				TABLE II			
X-RAY DIFFRACTION LINES FOR 2,4,6-TRI-(o-CYANOPHENYL)-1,3,5-TRIAZENE (FORM A)				X-RAY DIFFRACTION LINES FOR 2,4,6-TRI-(o-CYANOPHENYL)-1,3,5-TRIAZENE (FORM B)			
#[a]	θ[b]	d[c]	I[d]	#	θ	d	I
1	4.35	10.1	V. S.	1	4.14	10.7	V. S.
2	5.90	7.49	M	2	6.38	6.92	W
3	7.10	6.25	S	3	7.68	5.75	M
4	8.96	4.94	M	4	9.12	4.85	W
5	11.30	3.92	S	5	9.87	4.49	W
6	12.7	3.50	S	6	10.6	4.19	W
7	13.5	3.30	V. S.	7	11.4	3.89	V. W.
8	15.0	2.96	W	8	12.0	3.70	W
9	16.0	2.79	W	9	13.6	3.27	V. S.
10	17.5	2.56	W	10	14.6	3.05	W
11	18.9	2.38	W	11	21.6	2.09	W
12	20.9	2.16	W	12	27.7	1.65	W
13	22.0	2.05	W				
14	22.8	1.98	W				
15	23.5	1.93	W				
16	26.6	1.72	W				
17	27.8	1.65	W				

[a] #, order in which lines found. [b] θ, Bragg angl. [c] d, interplanar spacing. [d] I, qualitative intensity.

(2) R. P. Linstead and A. R. Lowe. *J. Chem. Soc.* 1022 (1934).

(3) C. E. Dent and R. P. Linstead. *ibid.*, 715 (1938).

(4) The spectra were determined by Philip Sadtler of Samuel P. Sadtler and Son, Inc.

(5) A. H. Cook and D. G. Jones. *J. Chem. Soc.*, 278 (1941).