

for 20 min, during which period a heavy sublimate of iodine collected in the condenser. The solution was cooled and poured into water (50 mL), and the product was filtered off, washed with water (3 × 10 mL), and dried to give off-white crystals: 653 mg (81%); mp 281–282 °C dec (lit.^{17b} mp 279 °C); NMR (Me₂SO-*d*₆) δ 7.92 (s); mass spectrum (EI), *m/e* 191 + 193 (M⁺).

5-Bromo-1-methyl-4-nitroimidazole (30). A solution of 29 (160 mg, 0.83 mmol) in aqueous sodium hydroxide (1 M, 3 mL) was treated with dimethyl sulfate (100 μL, 1.05 mmol) and stirred at ambient temperature for 20 min. The product was filtered off, washed with ice-water (2 × 1 mL), and dried to give a white solid: 120 mg (70%); mp 175–178 °C (lit. mp (a)²⁴180 °C, (b)²⁵ 178 °C; lit.²⁵ mp (2-bromo-1-methyl-4-nitroimidazole) 155 °C); NMR (CDCl₃) δ 7.60 (s, 1 H), 3.70 (s, 3 H); mass spectrum (EI), *m/e* 205 + 207 (M⁺).

Crystallographic Data and X-ray Structure Analysis. A plate-shaped crystal (1.04 × 0.80 × 0.02 mm) of 4-[2-[(1-methyl-5-nitro-2-imidazolyl)thio]ethoxy]benzoic acid sodium salt was used for the X-ray structure analysis. Cell parameters were determined by a Philips PW1100 diffractometer using Mo Kα (λ = 0.7107 Å) radiation. Crystal data: C₁₃H₁₂N₂O₅Na monoclinic; space group C2/c; *a* = 50.547 (8) Å, *b* = 6.235 (5) Å, *c* = 9.318 (4) Å, β = 95.80 (3)°; *V* = 2921.6 Å³; *Z* = 8; *M* = 345.31; ρ_{calcd} = 1.569 g cm⁻³. Intensity data were measured by using Mo Kα radiation (λ = 0.7107 Å, θ_{max} = 25°). A total of 2499 reflections was collected; of these, 1685 which had *F* > 6 σ(*F*) were used in the analysis. The structure was solved by direct methods²⁶ and refined by full-matrix, least-squares procedures to *R*₁ = 0.067 and

(26) G. M. Sheldrick, SHELX 76 program, University of Cambridge, Cambridge, United Kingdom.

*R*₂ = 0.064. As a test that the atoms in the imidazole ring were correctly assigned, refinement was repeated by assuming N(2) to be carbon and C(12) to be nitrogen (see Figure 1 for numbering scheme); the apparent temperature factors then changed markedly to values substantially different from those of the other atoms and in a direction which shows that the original assignment was correct. In addition, the hydrogen atom on C(12) which did not appear clearly in the final synthesis was shown to be present in a difference synthesis using the low-angle reflections only (calculated by multiplying all the observed structure factors by exp[-2.31 sin² θ]). The bond lengths and angles obtained are, in general, closely similar to those found in related compounds.

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Registry No. 1, 53869-36-6; 2, 13369-87-4; 3, 17024-47-4; 4, 76529-46-9; 5, 41386-38-3; 8, 76529-47-0; 9, 76529-48-1; 10, 35681-63-1; 11, 13369-81-8; 12, 13369-86-3; 13, 76529-49-2; 14, 19198-80-2; 16, 15813-09-9; 17, 3034-62-6; 18, 76529-50-5; 22, 71759-89-2; 23, 76529-51-6; 24, 72946-56-6; 29, 6963-65-1; 30, 933-87-9; 2-iodo-1-methylimidazole, 37067-95-1; 4-[2-[(1-methyl-5-nitro-2-imidazolyl)thio]ethoxy]benzoic acid sodium salt, 64444-68-4.

Supplementary Material Available: Tables I-III listing positional parameters, thermal parameters, and bond lengths and angles with their estimated standard deviations, respectively (6 pages). Ordering information is given on any current masthead page.

Conformations of the 3,4-Dichloro- and 3,4-Dibromo-2,5-dimethylhexanes. A Test of the Gauche-Gauche' C-C-C-X Steric Exclusion

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The 3,4-dichloro- and 3,4-dibromo-2,5-dimethylcyclohexanes provide a good test case of the gauche-gauche' steric exclusion in C-C-C-X chain segments, analogous to established exclusions in five-carbon chains and in 1,3-dihalogenated three-carbon chains. If the exclusion holds, there should be only one conformation for the meso form and at most two for the (±) form. The two forms have very different dipole moments and NMR spectra, consistent with the conformations predicted. The vibrational spectra indicate the presence of only one conformation in each case, and the infrared-Raman coincidences, Raman polarizations, and frequency differences between symmetric and antisymmetric C-X stretches are consistent with the proposed exclusion. The data are shown to be inconsistent with several alternative possibilities for conformational mixtures.

In the study of the conformations of molecules undergoing internal rotation, steric effects have had an important place. In Pitzer's classic treatment of saturated noncyclic hydrocarbons¹ using tetrahedral angles and threefold barriers, he assumed that one type of five-carbon, four-bond segment was so unfavorable that it occurred only in those highly branched molecules where no alternative conformation existed. This steric exclusion, sometimes called the pentane effect, applies to that combination of two adjacent gauche rotations in which the first and fourth bonds would lie parallel, like opposite sides of a chair-form cyclohexane ring. The two terminal carbons of the segment are then separated by only 2.5 Å. Pitzer assigned

such conformations an infinite conformational energy and was able to make accurate and useful predictions of thermodynamic properties on this basis.

In halogen-substituted alkanes, two possible extensions of the pentane effect (hereafter called the C₅ exclusion) might occur: those involving C-C-C-C-X and X-C-C-C-X segments. These will be called the C₄X and C₃X₂ exclusions, respectively. Thompson and co-workers showed that the zero dipole moment of pentaerythryl chlorides, bromides, and iodides² could be explained by using the C₃X₂ exclusion and that the assumption was useful in treating other small halocarbons as well.³ Many

(1) Pitzer, K. S. *Chem. Rev.* 1940, 27, 39.

(2) Thompson, H. B.; Sweeney, C. C. *J. Phys. Chem.* 1960, 64, 221.

(3) Thompson, H. B.; Lawson, C. W. *J. Phys. Chem.* 1960, 64, 1788.

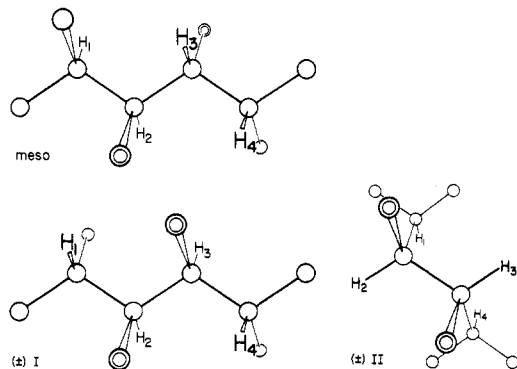


Figure 1. Conformations of 3,4-dihalo-2,5-dimethylhexanes allowed by assuming C_5 and C_4X exclusions (see text).

other examples have been found,⁴ and the C_3X_2 exclusion, when X is chlorine or a larger halogen, appears to be well established.

The C_4X exclusion is less thoroughly documented. Thompson and Hanson used this assumption in treating the dipole moments of dichlorides and dibromides of the type $X(CH_2)_nX$.⁵ Bonham, on the other hand, found a best fit to the electron diffraction pattern for 1-chlorobutane for a mixture containing the conformation in question as a major contributor (24%),⁶ although the same conformation is apparently absent in 1-bromobutane.⁷

Given the extensive evidence for the C_5 and C_3X_2 exclusions, the C_4X exclusion may seem a reasonable interpolation. A counterargument can, however, be made. The C_5 exclusion may result from the sheer size of the terminal methyl (or larger) groups. The C_3X_2 exclusion involves somewhat smaller terminal groups, but the steric effect may be augmented by an unfavorable dipole-dipole energy. In the C_4X case, on the other hand, there may be a favorable dipole-induced dipole interaction between the ends. Szasz⁸ proposed such an interaction as important in three-bond chains of the type C-C-C-Cl, and indeed, the gauche form of 1-chloropropane predominates (80%)⁹ in the vapor phase.

It thus seems most desirable to find test cases in which if the C_4X exclusion operates its consequences can be clearly and simply seen. The 3,4-dihalo-2,5-dimethylhexanes provide such a case. They exist in both meso and (\pm) modifications. In the meso form, of the 27 possible rotational positions about the three center carbon bonds, only one survives both exclusions (see Figure 1). The molecule should have C_i symmetry and thus possess a center of inversion. In the (\pm) form there should be two surviving conformations, both of C_2 symmetry. The C-X bonds should be anti to each other in the meso form and gauche in the (\pm) form. In the meso form and in conformation II for the (\pm) case the halomethine hydrogens (marked H_2 and H_3) should be mutually anti and gauche to the neighboring protons H_1 and H_4 . In (\pm) conformation I, H_2 and H_3 are mutually gauche and anti to H_1 and H_4 . However, if only the C_5 exclusion is effective, additional conformations, involving other symmetries and bond relationships, are available in both forms. We here report studies of the dipole moments and infrared, Raman, and

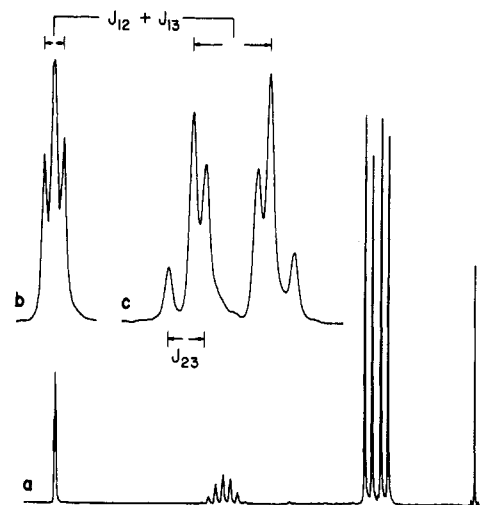


Figure 2. 1H NMR spectra of 3,4-dihalo-2,5-dimethylhexanes: (a) meso-dibromide, singlet at right is Me_4Si internal standard; (b) halomethine spectrum from part a expanded; (c) halomethine spectrum from the (\pm)-dichloride, on the same horizontal scale as spectrum b.

NMR spectra of the (\pm) and meso dichlorides and dibromides. The dibromides are known compounds, and their NMR has been studied.¹⁰ The dichlorides have not been previously reported.

Experimental Section

Compound Preparation. The dibromo compounds were prepared as described by Yates and McDonald.¹⁰ Crude products were recrystallized from methanol. (\pm)-3,4-Dibromo-2,5-dimethylhexane melted at 72–73 °C while meso-3,4-dibromo-2,5-dimethylhexane melted at 56–57 °C. Colorless dibromo crystals became slightly yellowish after sitting a short time at room temperature.

(\pm)-3,4-Dichloro-2,5-dimethylhexane was prepared in the following manner. A chlorine solution in chloroform (6.1 g/100 mL) was titrated into a solution containing 2.0 g of *cis*-2,5-dimethyl-3-hexene in 20.0 mL of chloroform until a faint yellow-green color persisted. The reaction was carried out in an ice bath under subdued light and with stirring. The reaction mixture was then washed with equal volumes of dilute solutions of Na_2CO_3 , $NaHSO_3$, and water and concentrated to yield the crude product. Vacuum sublimation produced a colorless solid: yield 29%; mp 48–49 °C.

meso-3,4-Dichloro-2,5-dimethylhexane was prepared similarly except that the starting material was *trans*-2,5-dimethyl-3-hexene: yield 30%; mp 21–22 °C.

Vibrational Spectra. Infrared spectra were obtained on a Perkin-Elmer 621 spectrometer utilizing a single beam and a CsI cell (thickness 0.075 mm). Samples were run as solutions in cyclohexane (15–25%). The observed range was 1000–400 cm^{-1} with a resolution of 3 cm^{-1} .

Raman spectra were obtained on an instrument described by Diem and Burow.¹¹ Samples were run as concentrated solutions (30–40%) in cyclohexane. Cells were capillary tube microspheres.

Dipole Moments. Guggenheim's method¹² was employed. The capacitance measuring circuit,¹³ procedure,¹⁴ and capacitance cell¹⁵ have been described previously. The solvent used was cyclohexane fractionally distilled from sodium. Solutions of the meso compounds ranged from approximately 0.50 to 2.0 wt %. Solutions of the (\pm) compounds ranged from 0.25 to 1.0 wt %.

NMR Spectra. Spectra were obtained on JEOL FX-90Q (Fourier transform) and Varian T-60A spectrometers. In all four

(4) See: Park, P. J. D.; Pethrick, R. A.; Thomas, B. H. In "Internal Rotation in Molecules"; Orville-Thomas, W. J., Ed.; Wiley: London, 1974, p 89 and references cited therein.

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(7) Bonham, R. A.; Momany, F. A.; McCoy, W. H. *J. Am. Chem. Soc.* 1963, 85, 3077.

(8) Szasz, G. J. *J. Chem. Phys.* 1955, 23, 2449.

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(10) Yates, K.; McDonald, R. S. *J. Org. Chem.* 1973, 38, 2474.

(11) Diem, M.; Burow, D. F. *J. Chem. Phys.* 1976, 64, 5179.

(12) Guggenheim, E. A. *Trans. Faraday Soc.* 1948, 45, 714.

(13) Thompson, H. B.; Rogers, M. T. *J. Chem. Educ.* 1955, 32, 20. See also ref 2, p 223.

(14) Thompson, H. B.; Ebersson, L.; Dahlen, J. V. *J. Phys. Chem.* 1962, 66, 1634. Thompson, H. B. *J. Chem. Educ.* 1966, 43, 66.

(15) Thompson, H. B.; Walmsley, J. A. *J. Chem. Educ.* 1979, 56, 837.

Table I. NMR Spectra, 3,4-Dihalo-2,5-dimethylhexanes^a

	meso		(±)	
	dichloro	dibromo	dichloro	dibromo
Coupling Constants (Hz)				
$J_{2,3}$ exptl	11.1 (3) ^b	11.6 (3) ^b	3.6 (1) ^c	3.6 (1) ^c
calcd ^d	9.1	9.1	3.7	3.6
$J_{1,2} + J_{1,3}$	2.0 (1) ^c	2.0 (1) ^c	7.7 (1) ^c	7.8 (1) ^c
$J_{1,2}$	2.2 (2) ^b	2.2 (2) ^b	7.9 (2) ^e	8.0 (2) ^e
$J_{1,3}$	-0.2 (2)	-0.2 (2)	-0.2 (1) ^e	-0.2 (1) ^e
$J_{1,Me}$	6.5, 6.8	6.3, 6.6	6.7, ^f 6.8 ^f	6.6, 6.4
J_{CH_2}	152.4 ^b	154.0 ^g		
Chemical Shifts (ppm)				
methyl	0.916	0.904	1.018 ^h	1.028
doublets	1.060	1.067	1.094 ^h	1.139
septet	2.606	2.523		
octet			2.18 ⁱ	2.18
(H ₂ , H ₃)				
multiplet	3.921	4.201	3.798 ⁱ	3.858 ⁱ
(H ₃ , H ₄)				
Assumed HCCH Central Dihedral Angle (Deg)				
	180	180	46 ^j	47 ^j

^a Values are as observed in the ¹H spectrum at 89.6 MHz by using a JEOL FX90Q Fourier transform NMR spectrometer unless otherwise noted. Figures in parentheses are estimated uncertainties in the last significant figure. See Figure 1 for the numbering of hydrogens. ^b Observed in ¹³C satellites in the ¹H spectrum. ^c Appears directly as a measured peak separation in the ¹H spectrum (see Figure 1). ^d From the Karplus equation¹⁷ using the listed dihedral angles. ^e Best simulated fit. ^f Observed at 60 MHz by using a Varian T-60 spectrometer (see note h). ^g Observed in both the ¹³C and the ¹H spectrum. ^h The methyl doublets overlap in the 90-MHz spectrum, producing an apparent triplet. The shifts are calculated from the positions of the outside lines of this triplet and the coupling constants observed at 60 MHz. ⁱ Taken as midway between the most intense two lines of the multiplet. ^j Taken as 60° - (φ_g - 60°), where φ_g is the XCCX dihedral angle in the corresponding 1,2-dihaloethane (see ref 18).

compounds, each of the two nonequivalent (diastereotopic) pairs of methyls gives a simple doublet. In the meso compounds, the halomethine hydrogens appear as a triplet: decoupling from the methyl hydrogens allows observation of the center peak as a just-resolved doublet (separation approximately 0.2 Hz). The ¹³C satellites of this feature consist of a doublet (11 Hz) of doublets (2 Hz). The isopropyl tertiary hydrogens appear as a septet. In the (±) compounds the halomethine hydrogens produce a multiplet consisting of two major and four minor lines (Figure 2c). The isopropyl tertiary hydrogens appear as an even multiplet with additional complex structure, which changes to a septet when decoupled from the halomethine hydrogens.

Simulations were performed on a Digital Equipment PDP-8/I minicomputer.¹⁶

Results and Discussion

NMR Spectra. The general features of the NMR spectra are described in the Experimental Section. Coupling constants and chemical shifts are given in Table I. The four numbered hydrogens in Figure 1 form an AA'BB' spin system. Coupling to the methyls greatly complicates the isopropyl tertiary hydrogen spectrum but merely broadens the individual lines in the halomethine region. We obtain coupling constants that agree in magnitude with those of Yates and McDonald¹⁰ for the dibromides. However, in the (±) case we assign to $J_{1,2}$ the value they

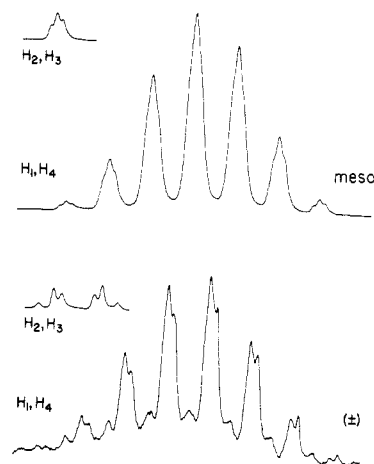


Figure 3. Isopropyl tertiary hydrogen NMR spectra in 3,4-dihalo-2,5-dimethylhexanes (meso spectrum is for the dibromide and (±) is for the dichloride). The corresponding halomethine spectrum, much reduced in height but on the same horizontal scale, is shown to the upper right of each for comparison.

assigned to $J_{2,3}$, and vice versa. Our basis for this assignment follows.

In the meso compounds H₂ and H₃ produce a triplet (Figure 2b) typical of a large $J_{2,3}$ coupling and a much smaller value for $J_{1,2} = J_{3,4}$. The precise value of $J_{2,3}$ is best measured in the ¹³C satellites. In the (±) compounds the complex six-line spectrum (Figure 2c) is typical of a small $J_{2,3}$ and a larger $J_{1,2} = J_{3,4}$. Simulated spectra obtained by using the coupling constants of Table I match experimental spectra closely. The assignment of Yates and McDonald yields a predicted spectrum for the (±) case that resembles Figure 2b rather than 2c. The H₁,H₄ features reinforce the above analysis. As the other half of the AA'BB' system, these hydrogens should, in the absence of coupling to the two nearby methyls, produce a feature which mirrors that for H₂,H₃. Figure 3 shows these lines, with a small image of the H₂,H₃ multiplet inset to the upper left of each. In the meso compounds, coupling to the methyls produces the expected septet, with each line mimicking the H₂,H₃ triplet. Thus $J_{1,2}$ is clearly much smaller than the H₁-methyl coupling. In the (±) compounds, the equivalent feature has the gross appearance of an even multiplet, describable as an octet from nearly equal coupling to the six methyl and one neighboring halomethine hydrogens. More precisely, the H₁,H₄ multiplet is a septet of overlapping images of the halomethine multiplet. Thus $J_{1,2}$ is clearly much larger in this case than in the meso case.

On the usual assumption that the larger coupling constants correspond to anti conformations, the NMR spectra are consistent with the meso conformation of Figure 1 and with (±) conformation I. Values of $J_{2,3}$ calculated on this basis from the Karplus equation¹⁷ are included in Table I for comparison. The H₂,H₃ dihedral angle is 180° in the meso conformation by symmetry. In the (±) case this angle was estimated from the geometries of the gauche 2,3-dihaloethanes.¹⁸

Dipole Moments. The results are summarized in Table II. The low moments for the meso compounds argue for a structure with opposed C-Br bonds, at least as the

(17) Karplus, M. *J. Am. Chem. Soc.* **1963**, *85*, 2870. The values in Table I were obtained using Karplus' parameterization. $J_{2,3}$ values obtained by using the parameters recommended by Bothner-By (*Adv. Magn. Reson.* **1965**, *1*, 195) are respectively 13, 13, 6.0, and 6.1 Hz.

(18) Kveseth, K. *Acta Chem. Scand., Ser. A* **1974**, *A23*, 482; **1975**, *A29*, 307. Fernholt, L.; Kveseth, K. *Ibid.* **1978**, *A32*, 63.

(16) The program used was a Lorentzian envelope modification of DEUCUS 8-194, from the program library of Digital Equipment Computer Users Society.

Table II. Dipole Moments for 3,4-Dihalo-2,5-dimethylhexanes

compd	S ^a	dipole moments, D ^b	
		exptl	calcd ^c
(±)-3,4-dibromo	50.4	2.71	2.66
(±)-3,4-dichloro	46.8	2.62	2.68
meso-3,4-dibromo	4.00	0.76	0.47
meso-3,4-dichloro	2.21	0.57	0.47

^a Best slope for $(\epsilon^2 - n^2)/(\epsilon^2 + 2)(n^2 + 2)$ vs. concentration (moles/milliliter) (see ref 13). ^b One debye = 3.336×10^{-30} coulomb meters. ^c Reference moment taken from 1,4-dihalocyclohexane (see text).

dominant conformation. It might be argued that since the observed moments are not zero, a small population of a highly polar conformation is present. However, some small moment is to be expected in a case of two opposed, very polar bonds. This may be treated as an abnormal atomic polarization. Coop and Sutton¹⁹ give the relation shown in eq 1, where μ_i is the magnitude of each of two opposing

$$P_a = 4\pi N\mu_i^2/9V' \quad (1)$$

moments, N is Avagadro's number, V' is a bending force constant for a mode which takes these moments out of opposition, and P_a is the resulting contribution to the atomic polarization. If such a contribution occurs, and is calculated as an orientation polarization (eq 2), then the

$$P_0 = 4\pi N\mu_a^2/9kT \quad (2)$$

apparent moment will be given by eq 3. Most probably,

$$\mu_a/\mu_i = (kT/V')^{1/2} \quad (3)$$

the largest P_a contribution will be from torsional motion about the central C-C bond. For this motion, V' will be approximately $9V_3/2$ if the barrier is a simple threefold one. For a 2650-cal/mol ethane-like barrier, assuming a bond moment of 2.1 D, this single mode would produce a μ_a value of 0.47 D. Given the approximate nature of this estimate and the presence of other vibrational modes that contribute to μ_a , the observed moments may well result from the meso structure of Figure 1 only. However, even if the difference between this predicted m_a and the experimental results were entirely due to a small population of a polar form of moment 2.7 D, the mole fractions of the polar forms would be 0.050 and 0.014 in the chloride and bromide, respectively.

Calculated dipole moments for the (±) compounds were obtained as follows. First, the moment for two C-X bonds at a 60° dihedral angle was taken as that for the corresponding *cis*-1,4-dihalocyclohexane.²⁰ (The 1,4-dihalocyclohexane was used rather than the 1,2-dihalocyclohexane because in the 1,4-compounds and in (±) conformation I all contributions from moments induced by the polar bonds in neighboring C-C bonds cancel by symmetry, while in the 1,2-compounds some C-C bond contributions will add to the total.) A moment for two bonds at a 74° dihedral angle was then estimated by multiplying the 60° moment by $\cos(74^\circ/2)/\cos(60^\circ/2)$. These moments are included in Table II. Given expected experimental uncertainties of 0.05 D and differences in solvent between our moments and the cyclohexane work, the agreement seems more than adequate. Thus the dipole moments are completely consistent with (±) conformation I but would

Table III. Infrared and Raman Spectra for 3,4-Dihalo-2,5-dimethylhexanes

compd	frequencies, cm ⁻¹ ^a		
	infrared	Raman	assignment
(±)-3,4-dibromo	570	566 dp	
		607 p	
	712	717 p	A _g } C-Br stretch
	725	730 dp	
(±)-3,4-dichloro	608	610 p	
	665	669 p	
	705	766 p	A _g } C-Cl stretch
	780 br	784 dp	
meso-3,4-dibromo	470	508	
	620	705	A _u } C-Br stretch
meso-3,4-dichloro	690	545	
		755	A _g } C-Cl stretch

^a Frequency range 450-800 cm⁻¹, resolution 3 cm⁻¹; p = polarized, dp = depolarized, br = broad.

not rule out the presence of conformation II.

Vibrational Spectra. The infrared and Raman results are summarized in Table III. The frequencies assigned to carbon-halogen stretching modes may be compared with the range of values for vicinal dihalocyclohexanes studied by Altona, Hageman, and Havinga.^{21a} Our C-X frequencies are uniformly within 15 cm⁻¹ of the upper end of the ranges for comparable cyclohexyl dihalides, except for the antisymmetric vibrations in the meso compounds. In the meso spectra, the C-X regions are very sparse, with no IR-Raman coincidences and only one pair of lines that seem likely candidates for the symmetric and antisymmetric stretches. The Raman spectra are particularly clean, with no other features in the region tabulated that are as much as 2% as intense as the assigned bands. The frequency differences between the A_u- and A_g-type lines are slightly smaller than those reported for the diaxial cyclohexyl dichlorides (67-94 cm⁻¹) and bromides (94-125 cm⁻¹). Thus both meso compounds appear to exist in only one conformation, and that conformation has a center of inversion.

The (±) compounds have richer spectra, and most lines, including all that we assign to C-X stretches, appear in both infrared and Raman spectra. In each case there is only one pair of lines with the correct Raman polarization and frequency difference to be the A and B symmetry C-X stretches. Thus we do not find separate features assignable to conformations I and II. This could be because only one conformation is present. However, in the (±) dichloride the high-frequency line is broad in the IR: it is possible that the lines for the two conformations are not resolved. It has been proposed^{21b} that a major determiner of the C-X frequency is the nature of the groups anti to this bond along the carbon chains. In both form I and form II, the C-X is anti to one hydrogen and one alkyl group.

Conclusions

It seems clear that the experimental data can be explained in terms of the C₅ and C₄X exclusions, with the resulting limitation of the meso compound to one conformation and the (±) compound to two, as shown in Figure 1. The vibrational spectra appear to show only one

(19) Coop, I. E.; Sutton, L. E. *J. Chem. Soc.* 1938, 1269.

(20) McClellan, A. L. "Tables of Experimental Dipole Moments"; W. H. Freeman Co.: San Francisco, 1963; pp 206-8.

(21) (a) Altona, C.; Hageman, H. J.; Havinga, E. *Spectrochim. Acta, Part A* 1968, 24A, 633; (b) *Ibid.* p 647.

Table IV. Conformational Populations under the C₅ Exclusion Alone

compd	weighting	gauche fractions for		
		H ₁ -H ₂	H ₂ -H ₃	X-X
meso	equal	0.73	0.18	0.27
	2G only ^a	0.50	0	0
	0.3/G ^b	0.61	0.10	0.12
(±)	equal	0.64	0.73	0.91
	2G only	0.50	1	1
	0.3/G	0.56	0.85	0.95
	C ₄ X exclusion, 0.3/G ^c	0.23	0.77	1

^a Only conformations with the lowest possible number (two) of gauche carbon segments counted. ^b Conformations given a weighting of 0.3/gauche carbon segment. ^c Assuming the C₄X exclusion also, with conformation II weighted 0.3 relative to conformation I.

conformation in the (±) case, and the NMR data indicate that this must be conformation I. Conformation I contains two gauche carbon segments while conformation II contains three: this might make the latter less stable by approximately 800 cal/mol, producing a mole fraction population of 0.2. Our vibrational spectra appear to weigh against the presence of this much II; however, our NMR $J_{1,2}$ values would fit such a population nicely.

A basic remaining question is as follows. While the C₅ and C₄X exclusions operating together adequately explain our observations, would those observations be equally well explained by the C₅ exclusion alone? To answer this question, it is necessary to examine the allowed conformations available to 2,5-dimethylhexane. There are five of these, two of symmetry C₂ and one each of symmetries C_{2h}, C_i, and C₁. (The C₂ and C₁ forms have, of course, two optical isomers each.) Upon introduction of the two

halogens, there result seven conformations in the meso case and eight in the case of either optical isomer of the (±) compound. Table IV gives local conformation (gauche-anti) populations for mixtures of these conformations under three different assumptions: (1) that all conformations contribute equally (i.e., with symmetry-number weighting only), (2) that only conformations with the smallest possible number (i.e., two) of gauche five-carbon segments contribute, and (3) that each gauche five-carbon segment present leads to a Boltzmann weighting factor of 0.3 (equivalent to a destabilization by about 700 cal/mol). In both compounds, the predicted gauche populations are at variance with the NMR results. In the meso case, a $J_{1,2}$ value of 2.2 Hz does not fit an anti population of 27-50%. In the (±) case, a $J_{1,2}$ of 7.9 Hz is equally poorly explained by a gauche population of 50-64%. The small number of infrared and Raman lines observed also weighs against the presence of any large number of conformations.

We conclude that the C₄X exclusion may be used with confidence in predictions of thermodynamic and equilibrium properties of conformational mixtures of chlorine- and bromine-substituted hydrocarbons.

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Registry No. meso-3,4-Dichloro-2,5-dimethylhexane, 76599-70-7; meso-3,4-dibromo-2,5-dimethylhexane, 40084-93-3; (±)-3,4-dichloro-2,5-dimethylhexane, 76599-71-8; (±)-3,4-dibromo-2,5-dimethylhexane, 40084-92-2; cis-2,5-dimethyl-3-hexene, 10557-44-5; trans-2,5-dimethyl-3-hexene, 692-70-6.

Facile Synthesis of 2-Deoxy-2-substituted-D-arabinofuranose Derivatives¹

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Several methyl 2-deoxy-2-substituted-D-arabinofuranosides (**4a-e** and **5b-e**) to be used as intermediates in the synthesis of 2'-substituted arabinonucleosides of biomedical interest were prepared by treatment of methyl 3,5-di-*O*-benzyl-2-*O*-(trifluoromethanesulfonyl)- α - and - β -D-ribofuranosides **2** and **3** with the lithium, sodium, or tetrabutylammonium salts of various nucleophiles (F⁻, Cl⁻, Br⁻, I⁻, N₃⁻). While the α anomer **2** could be readily converted into the desired arabinofuranosides **4a-e** in good yields, the β anomer **3** afforded the corresponding 2-substituted products **5b-e** only in modest amounts together with furfuryl ether **7** as the major product. A possible interpretation for the difference in the course of these reactions is discussed.

Previous studies in our laboratory on the synthesis of several (2'-halogeno-2'-deoxy-D-arabinosyl)pyrimidine nucleosides²⁻⁴ have afforded substances of biological interest. Thus, 1-(2'-deoxy-2'-fluoro- β -D-arabinofuranosyl)cytosine^{2,4} (2'-F-*ara*-C) exhibits pronounced inhibitory activity against the growth of L-1210 mouse leukemic cells in culture. 1-(2'-chloro-2'-deoxy- β -D-arabinofuranosyl)cytosine³ was

similarly active against several mouse leukemic cell lines in vitro. Finally, several 5-substituted (2'-deoxy-2'-fluoro- β -D-arabinofuranosyl)pyrimidines were shown to inhibit the replication of herpes simplex virus in vitro and in vivo.⁵

From these and other studies on pyrimidine nucleoside transformations, it is clear that direct introduction of a substituent in the 2' "up" (arabino) configuration of a preformed pyrimidine nucleoside may be difficult, if not impossible, because of the ease with which the 2-carbonyl

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