et al.:[33] bp 118–120° (0.9 mm). Methylation of **18a** with diazomethane yielded 79% of **18e**: mp 58–59.5°. The esters **18d,f–h** were prepared from **18b** and the corresponding alcohols in pyridine: **18d** (51%, mp 46.5–50°), **18f** (68%, bp 71–73° (0.04 mm)), **18g** (43%, bp 69–71° (0.04 mm)), **18h** (63%, bp 110–125° (0.03 mm)). Acylation of anisole with **18b** in CS_2 ($AlCl_3$) produced 43% of **18i**, mp 101–103°. Dimethylamine and **18b** reacted to give 68% of **18j**, mp 73–77°.

1-Bromochloromethyl-3,5,7-trimethyladamantane (18k). The procedure used to prepare **18k** is molded after that described by Taylor, *et al.*[34] One gram (3.7 mmol) of **18a** in 5 ml of petroleum ether was added to 0.92 g (3.7 mmol) of thallous ethoxide in 5 ml of petroleum ether. The thallous carboxylate was collected and recrystallized from 95% ethanol, giving 1.33 g (76%), mp 97–99°. The salt was added to a solution of 0.67 g of bromine in 5 ml of carbon tetrachloride, and the mixture was refluxed under nitrogen for 4 hr. Water was then added, the organic layer washed with sodium bicarbonate solution, and the solvent evaporated. The residue consisted of 50 mg of an oil which slowly crystallized, mp 72–73°. The mass spectrum shows a triplet for the molecular ions at *m/e* 304, 306, and 308 with an intensity ratio of about 36:50:14, which is consistent with the presence of one chlorine and one bromine atom in the molecule. The ir spectrum is devoid of carbonyl bands.

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The Origin of the Anisochronism of Geminal Groups in Conformationally Mobile Systems. II. Intrinsic and Conformational Contributions in Asymmetric Fluoroethanes

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Abstract: Fourteen asymmetrically substituted fluoroethanes were investigated by fluorine nmr spectroscopy (fmr) at ambient and low temperature. They include the ten compounds of the general formula $BrCF_2CXYZ$, where the substituents X, Y, Z correspond to all possible combinations of the five ligands hydrogen, fluorine, chlorine, bromine, and phenyl; the remaining four are $ClCF_2CHClPh$, $ClCF_2CHBrPh$, $ClCF_2CFClPh$, and $ClCF_2CHFI$. In 12 of the cases the fmr spectra of all three conformers could be detected at low temperature; for $BrCF_2CHBrPh$ and $BrCF_2CFBrPh$ only two conformers were found to be significantly populated. The simultaneous application of several empirical criteria led to the assignment of each fmr subspectrum to a particular conformer and of each fluorine chemical shift within a subspectrum to a particular fluorine atom in that conformer. With this information it is possible to calculate the magnitudes and absolute signs of the intrinsic and conformational contributions to the total time-averaged anisochronism of the geminal fluorine nuclei at low temperature. It is found that the magnitude of the intrinsic term is in most cases smaller than 1 ppm, whereas the total anisochronism at low temperature covers the range from about −5 to +16 ppm. In six of the cases the intrinsic and conformational terms have opposite signs, thus partially or completely canceling one another.

The only rigorous method for the determination of standard free energy differences between preferred conformations of molecules in solution consists in the *direct* measurement of the conformer concentrations (or strictly speaking, activities) at equilibrium, but conformational analysis would be in poor shape if it were limited by the applicability of this technique. The rapid progress in the alicyclic and heterocyclic field dates from the breakthrough in chemical equilibration studies made possible by the idea[3] of the remote holding group. Since no *indirect* chemical method of comparable power and reliability has so far become known for acyclic systems, the bulk of the information about conformer populations around carbon–carbon single bonds[4] stems from indirect investigations using a variety of physical techniques, among which nmr spectroscopy now occupies the dominant position. For substituted ethanes in which symmetry restricts the number of diastereomeric conformational isomers to two, the measurement of time-averaged vicinal spin–spin coupling constants seems to represent a fairly promising approach,[4,5] especially when combined with the sophisticated theory of solvent effects recently developed by Abraham,[6] which serves to reduce the remaining uncertainties concerning the validity of the various assumptions to an unavoidable, and sometimes perhaps insignificant, minimum.

Asymmetrically substituted ethanes, in which all

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three conformers differ in energy, contain the maximum in conformational information, but this information is also the most difficult to extract. It seems likely that nmr spectroscopy is virtually the only indirect tool available at present with which one can hope to tackle this problem with a fair chance of success, but the experience with an early attempt,[7] which was later shown[8,9] to have been a failure, appears to have discouraged quantitative work in this field.[10] In view of the potential importance of this kind of knowledge for the understanding of the conformational preferences of side chains in amino acids and polypeptides, we considered it worthwhile to reinitiate a systematic investigation.

We have chosen to start with model fmr studies on a series of asymmetric ethanes of the general formula RCF_2CXYZ, which for reasons to become clear in the succeeding paper[11] includes the ten compounds $BrCF_2CXYZ$ corresponding to all combinations of five different ligands. As a consequence of the relatively high barriers to internal rotation and the sensitivity of the fluorine nuclei to environmental effects, the reliability of our indirect nmr method[11] can in these cases be calibrated against unassailable conformational information obtained directly[12] at low temperature. In the present paper we shall in the main only be concerned with a single aspect of this work, namely the origin of the time-averaged anisochronism of the geminal fluorines, a problem whose intricacies are explained in the preceding paper.[13] Our approach is identical with that first applied by Raban[14] to the low-temperature data of Newmark and Sederholm[9] on $BrCF_2CHBrCl$ and $BrCF_2CFBrCl$. We have reinvestigated these two compounds and can now also report on the absolute signs of the (modified) numbers calculated by Raban.[14] Of the other quantitative information of general interest contained in our results, we shall here only make qualitative use insofar as we need it for making assignments.

Syntheses and Structure Proofs

The compounds **10**–**12** (for key, see Table I) were obtained by chlorine or bromine addition to α-chloro-β,β-difluorosytrene (**15**)[15] or α,β,β-trifluorostyrene (**16**). The schemes employed for the preparation of the other compounds not previously described are presented in Charts I and II, together with the chemical information that was important for establishing the structures of the products.[16]

Chart I

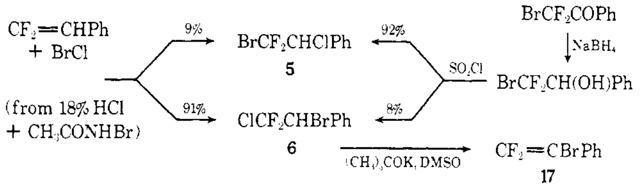
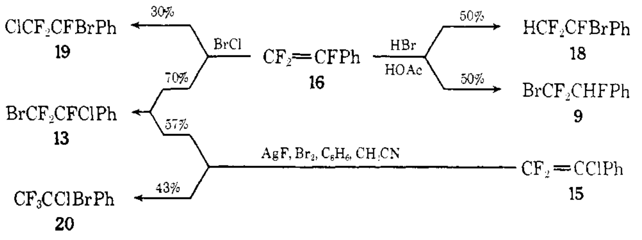


Chart II



The two routes shown in Chart I led to mixtures of **5** and **6**, from which the major component could in each case be obtained pure by preparative vpc. Structures **5** and **6** can be distinguished on the basis of the characteristic range of the geminal fluorine chemical shifts (Table I). Chemical proof was provided by dehydrohalogenation of **6** to **17**, which was identified by its fmr and mass spectra.

Hydrogen bromide addition to **16** (Chart II) yielded a 1:1 mixture of **9** and **18**, from which **9** was isolated by preparative vpc. The discriminating feature in the pmr and fmr spectra of the mixture is the geminal hydrogen–fluorine coupling constant in **18** and the vicinal in **9**. Bromine monofluoride, generated from silver fluoride and bromine, reacted with **15** to produce a mixture of **13** and **20**, in which the components could be distinguished on the basis of the fine structure in their fmr spectra. This reaction proceeded in low yields and was therefore not suitable for preparative purposes, but it provided the necessary structural information about the major product in the bromine monochloride addition to **16** (Chart II).

Spectra and Assignments

The fmr spectra were recorded using two different spectrometers, one operating at 56.4 MHz in the field sweep mode, the other at 94.1 MHz in the frequency sweep mode. Comparison of the two types of spectra permitted the resolution of ambiguities in the assignments of the lines; proton spectra, where applicable, provided additional checks. The results obtained on analysis of the ambient-temperature fmr spectra of **1**–**14** in two solvents are summarized in Table I. Owing to overlap of lines and technical difficulties associated with the maintenance of magnetic field homogeneity at the very low temperatures, the 56.4-MHz fmr spectra of the individual conformers could not always be fully analyzed. In Table II we therefore only list the parameters extracted from the 94.1-MHz low-temperature fmr spectra.

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(16) The yields indicated in Charts I and II are relative yields.

Table I. Ambient-Temperature Fmr Data of RCF_2CXYZ

Compd	R	X	Y	Z	Solvent (concn)[a]	Spectrometer frequency, MHz	Chemical shifts, ppm[b–d] δ_A	δ_B	δ_M	Coupling constants, Hz[b,c] $\|J_{AB}\|$	$\|J_{AM}\|$	$\|J_{BM}\|$	$\|J_{AQ}\|$	$\|J_{BQ}\|$	$\|J_{MQ}\|$
1	Br	H	F	Cl	$CH_2{=}CHCl$ (10% v/v)	94.1	−61.742	−65.571	−145.896	174.1	18.00	18.04	3.71	6.22	48.15
					$CFCl_3$ (0.4 *M*)	56.4	−61.725	−65.603	−146.051	173.3	18.1	18.1	3.6	6.2	48.4
2	Br	H	F	Br	$CH_2{=}CHCl$ (10% v/v)	94.1	−59.312	−63.490	−149.360	172.6	23.64	20.60	3.62	9.15	47.11
					$CFCl_3$ (0.4 *M*)	56.4	−59.358	−63.756	−149.155	172.5	24.0	20.6	3.4	9.1	47.5
3	Br	H	Cl	Br	$CH_2{=}CHCl$ (10% v/v)	94.1	−53.556	−56.853		162.0			5.98	8.44	
					$CFCl_3$ (0.4 *M*)	56.4	−53.603	−56.914		161.5			6.0	8.1	
4	Br	H	Br	Ph	$CH_2{=}CHCl$ (10% v/v)	94.1	−45.591[e]	−55.089[f]		157.9			5.28	17.26	
					$CFCl_3$ (0.4 *M*)	56.4	−45.676	−55.348		157.8			5.2	17.2	
5	Br	H	Cl	Ph	$CH_2{=}CHCl$ (10% v/v)	94.1	−51.584[g]	−56.499[h]		160.4			7.09	12.79	
					$CFCl_3$ (0.4 *M*)	56.4	−51.534	−56.406		159.5			6.9	12.6	
6	Cl	H	Br	Ph	$CH_2{=}CHCl$ (10% v/v)	94.1	−53.098[i]	−59.380[j]		161.0			6.24	14.09	
					$CFCl_3$ (0.4 *M*)	56.4	−53.357	−59.725		161.7			6.0	14.1	
7	Cl	H	Cl	Ph	$CH_2{=}CHCl$ (10% v/v)	94.1	−57.430[k]	−60.560[l]		162.6			7.21	10.75	
					$CFCl_3$ (0.4 *M*)	56.4	−58.165	−61.316		163.1			7.4	10.3	
8	Cl	H	F	I	$CH_2{=}CHCl$ (10% v/v)	94.1	−62.583	−65.020	−158.484	169.3	26.10	5.3	22.20	9.6	47.30
					$CFCl_3$ (0.4 *M*)	94.1	−62.813	−65.288	−158.387	169.4	26.12	5.1	22.16	9.44	47.35
9	Br	H	F	Ph	$CH_2{=}CHCl$ (10% v/v)	94.1	−59.634	−61.362	*m*	170.2	19.45	19.25	7.85	8.5	44.4
					$CFCl_3$ (0.4 *M*)	56.4	−59.662	−61.545	−183.662	170.5	19.5	19.4	7.9	8.2	44.4
10	Br	Cl	Br	Ph	$CH_2{=}CHCl$ (10% v/v)	94.1	−52.05[n]	−52.05[n]		*n*					
					$CFCl_3$ (0.4 *M*)	56.4	−52.22[n]	−52.22[n]		*n*					
11	Br	F	Br	Ph	$CH_2{=}CHCl$ (10% v/v)	94.1	−56.251[o]	−58.203[p]	−119.530	170.2	16.28	14.52			
					$CFCl_3$ (0.4 *M*)	56.4	−56.271	−58.308	−119.982	169.2	15.6	14.2			
12	Cl	F	Cl	Ph	$CH_2{=}CHCl$ (10% v/v)	94.1	−65.970[q]	−66.591[r]	−120.386	168.9	9.6	10.2			
					$CFCl_3$ (0.4 *M*)	94.1	−66.177	−66.757	−120.887	168.9	10.0	10.2			
13	Br	F	Cl	Ph	$CH_2{=}CHCl$ (10% v/v)	94.1	−59.835[s]	−60.298[t]	−118.409	170.4	11.58	12.17			
					$CFCl_3$ (0.4 *M*)	56.4	−60.430[u]	−60.430[u]	−118.711	*u*	12.0[u]	12.0[u]			
14	Br	F	Cl	Br	$CH_2{=}CHCl$ (10% v/v)	94.1	−59.085	−60.733	−69.160	167.8	13.85	13.79			
					CF_2Cl_2 (0.4 *M*)[v]	56.4	−59.066	−60.740	−69.082	167.7	13.7	13.8			

[a] For the spectra recorded at 94.1 MHz the solutions were diluted with 8% (v/v) of TMS; vinyl chloride solutions contained an additional 5% of $CFCl_3$ and 1–3 mg of 4-*tert*-butylcatechol. [b] Standard errors are equal to or smaller than 3 units in the last digit listed. [c] A and B refer to the downfield and upfield geminal fluorine chemical shifts, respectively, M to X (or Y) = F, and Q to X (or Y) = H. [d] Chemical shifts are in ppm relative to internal $CFCl_3$, with positive numbers to lower field. [e] ${}^{5(6)}J_{HF} = 0.58$ Hz. This long-range coupling gives rise to triplets, but whether it is caused by the ortho or meta protons of the phenyl ring has not been determined. [f] ${}^{5(6)}J_{HF} = 1.12$ Hz. [g] ${}^{5(6)}J_{HF} = 0.70$ Hz. [h] ${}^{5(6)}J_{HF} = 0.90$ Hz. [i] ${}^{5(6)}J_{HF} = 0.56$ Hz. [j] ${}^{5(6)}J_{HF} = 0.82$ Hz. [k] ${}^{5(6)}J_{HF} = 0.50$ Hz. [l] ${}^{5(6)}J_{HF} = 0.75$ Hz. [m] Not covered by the standard frequency sweep range of the spectrometer. [n] Broadened singlet. [o] ${}^{5(6)}J_{HF} = 0.72$ Hz. [p] ${}^{5(6)}J_{HF} = 1.23$ Hz. [q] ${}^{5(6)}J_{HF} = 0.80$ Hz. [r] ${}^{5(6)}J_{HF} = 0.75$ Hz. [s] ${}^{5(6)}J_{HF} = 0.89$ Hz. [t] ${}^{5(6)}J_{HF} = 0.92$ Hz. [u] A_2M spectrum. [v] The solvent served as internal standard; the chemical shifts were converted to the δ scale by adding −6.888 ppm, determined from an equal volume mixture of CF_2Cl_2 and $CFCl_3$, which is at variance with the value of −16.3 ppm reported by L. H. Meyer and H. S. Gutowsky, *J. Phys. Chem.*, **57**, 481 (1953).

Table II. Low-Temperature Fmr Data at 94.1 MHz[a]

Compd	Temp,[e] °C	Sub-spectrum	Rel area[f]	Chemical shifts, ppm[b–d]			Coupling constants, Hz[b,c]					
				δ_A	δ_B	δ_M	$\lvert J_{AB}\rvert$	$\lvert J_{AM}\rvert$	$\lvert J_{BM}\rvert$	$\lvert J_{AQ}\rvert$	$\lvert J_{BQ}\rvert$	$\lvert J_{MQ}\rvert$
1	−160	I	0.418	−56.98	−62.63	-146^{g}	181.0	11.3	17.8	$<4^{h}$	$<4^{h}$	*g*
		II	0.500	−60.94	−70.71	-146^{g}	174.9	21.6	15.6	$<4^{h}$	15.6	*g*
		III	0.082	-61.7^{i}	-74.5^{i}	$-146^{g,i}$	158^{i}	*h, i*	*h, i*	*h, i*	*h, i*	*g, i*
2	−160	I	0.21	−55.85	−62.04	-150^{g}	181.8	18	24.8	$<6^{h}$	$<4^{h}$	*g*
		II	0.73	−59.19	−65.85	-150^{g}	175.6	29.3	18	$<4^{h}$	18	*g*
		III	0.06	-61.9^{i}	-71.5^{i}	$-150^{g,i}$	160	*h, i*	*h, i*	*h, i*	*h, i*	*g, i*
3	−136	I	0.562	−46.81	−64.46		161.2			$<2^{h}$	19.5	
		II	0.212	−50.37	−65.83		160.5			$<2^{h}$	19.4	
		III	0.226	−52.17	−52.80		166.3			2.2	3.0	
4	−127	I	0.953	−43.23	−59.86		155.3			$<3^{h}$	23.6	
		II	0.047	−45.3	−48.17		164.6			$<5^{h}$	$<5^{h}$	
5	−139	I	0.747	−48.37	−65.16		155.5			$<3^{h}$	22.0	
		II	0.147	−48.11	−50.18		165.7			4.4	3.8	
		III	0.106	−46.78	−62.60		166.4			$<3^{h}$	22.5	
6	−140	I	0.856	−49.53	−64.65		156.2			$<3^{h}$	22.0	
		II	0.073	−51.93	−64.25		165.7			$<3^{h}$	20	
		III	0.071	−50.96	−53.98		163.8			3^{h}	3^{h}	
7	−141	I	0.647	−54.24	−69.65		156.7			$<3^{h}$	21.2	
		II	0.158	−53.04	−67.85		167.5			$<3^{h}$	20.8	
		III	0.195	−53.85	−55.34		166.5			4^{h}	4^{h}	
8	−160	I	0.771	−59.61	−63.22	−159.74	173.7	33.4	20.3	$<4^{h}$	18.8	46.5
		II	0.098	−67.25	−68.80	−157.33	152.8	20	20	$<4^{h}$	18	47.2
		III	0.131	−61.6	−63.4	−162.03	176	20.3^{j}	$<4^{h,j}$	$<4^{h}$	$<4^{h}$	47.6
9	−160	I	0.455	−52.16	−61.32	-188.2^{k}	177.3	9.3	19.5	$<4^{h}$	$<3^{h}$	*h, i, k*
		II	0.320	−58.92	−65.20	-183.5^{k}	178.4	21.0	17.1	$<4^{h}$	17.1	*h, i, k*
		III	0.225	−59.65	−73.20	-178.7^{k}	152.8	22.0	20.0	$<4^{h}$	20.0	*h, i, k*
10	−113	I	0.770	−51.54	−53.11		155.4					
		II	0.110	−53.31	−58.34		155.2					
		III	0.120	−53.70	−56.14		165.7					
11	−160	I	0.900	−55.03	−60.29	−122.32	169.8	19.3	13.2			
		II	0.100	−57.75	−60.55	−120.59	176.9	15.3	12.2			
12	−139	I	0.548	−66.46	−66.87	−122.61	169.8	12.1	7.9			
		II	0.367	−64.07	−66.09	−120.75	174.5	11.9	$<2^{h}$			
		III	0.085	-70.33^{l}	-70.33^{l}	-120.89^{l}	*l*	21.3^{l}	21.3^{l}			
13	−128	I	0.397	−57.94	−61.87	−118.14	176.6	13.7	5.3			
		II	0.563	−60.30	−63.08	−120.99	169.9	18.1	7.1			
		III	0.040	-65.74^{l}	-65.74^{l}	-120.39^{l}	*l*	21.4^{l}	21.4^{l}			
14	−119	I	0.691	−56.38	−60.73	−69.42	171.3	14.5	12.3			
		II	0.255	-61.82^{l}	-61.82^{l}	-70.46^{l}	*l*	13.1^{l}	13.1^{l}			
		III	0.054	−64.36	−68.01	−76.14	158.0	20.4	21.6			

[a–d] See Table I. [e] The precision of the temperatures is estimated to be ±2° at around −100°, and ±5° at around −160°. See also Experimental Section. [f] Standard errors are ≤0.006 if three digits are listed, and ≤0.02 if two digits are listed. [g] Overlapping lines; not analyzed. [h] Not completely resolved. [i] Exchange-broadened lines. [j] J_{AM} and J_{BM} may have to be interchanged; these couplings could only be extracted from the M part of the spectrum. [k] Extracted from 56.4-MHz spectrum. [l] A_2M pattern.

The assignments of the subspectra and of the individual geminal fluorine chemical shifts shown in Figure 1[17] are based on the simultaneous application of several empirical criteria. These criteria consist partly of reasonable premises, partly of evidence from the literature, and partly of conclusions drawn from the present study. Our reasoning is thus frequently of a cyclic nature and its strength rests on the feasibility of cross checks and on the absence of internal contradictions. The salient features of the criteria can be summarized as follows.

(1) A cursory examination of the data reveals that vicinal steric interactions alone, which may reasonably be expected to decrease in the sequence I > Br > Cl > F > H, cannot account for the trends in the conformer populations. A consistent picture can only be obtained if one includes the electrostatic interactions between the substituents, which correspond to the last term in the Scott–Scheraga equation[18]

$$U(\omega) = (U_0/2)(1 + \cos 3\omega) + \sum_{i<j}^{\text{vic}}[a_{ij}\exp(-b_{ij}r_{ij}) - c_{ij}/r_{ij}^{6} + d_{ij}/r_{ij}]$$

Although the numerical values[19] to be chosen for the parameters d_{ij} are open to doubt,[20,21] all previous

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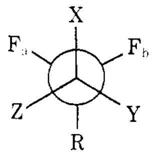
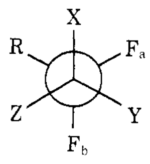
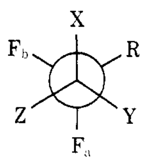
(17) In referring to the staggered Newman projections representing the idealized geometries of the three conformers α, β, γ and to the specific fluorine nuclei F_a and F_b in these conformers, we shall always adhere to the convention depicted in the following drawing, where the ligands X, Y, Z are arranged in decreasing order of priority in the Cahn–Ingold–Prelog sequence. Geminal fluorine chemical shift differences Δ_j and $\langle\Delta\rangle$ are defined as $\Delta_j = (\delta_a - \delta_b)_j$ and $\langle\Delta\rangle = \langle\delta_a - \delta_b\rangle = \langle\delta_a\rangle - \langle\delta_b\rangle$.



α



β



γ

(18) R. A. Scott and H. A. Scheraga, *J. Chem. Phys.*, **42**, 2209 (1965); **44**, 3054 (1966).

(19) We have used[20] $d_{ij} = \sqrt{d_{ii}d_{jj}}$ with $d_{FF} = 13.28$, $d_{ClCl} = 7.84$, $d_{BrBr} = 6.59$, $d_{II} = 4.42$ and $d_{HF} = -3.38$, $d_{HCl} = -2.60$, $d_{HBr} = -2.38$, $d_{HI} = -1.95$.

(20) R. J. Abraham and K. Parry, *J. Chem. Soc. B*, 539 (1970).

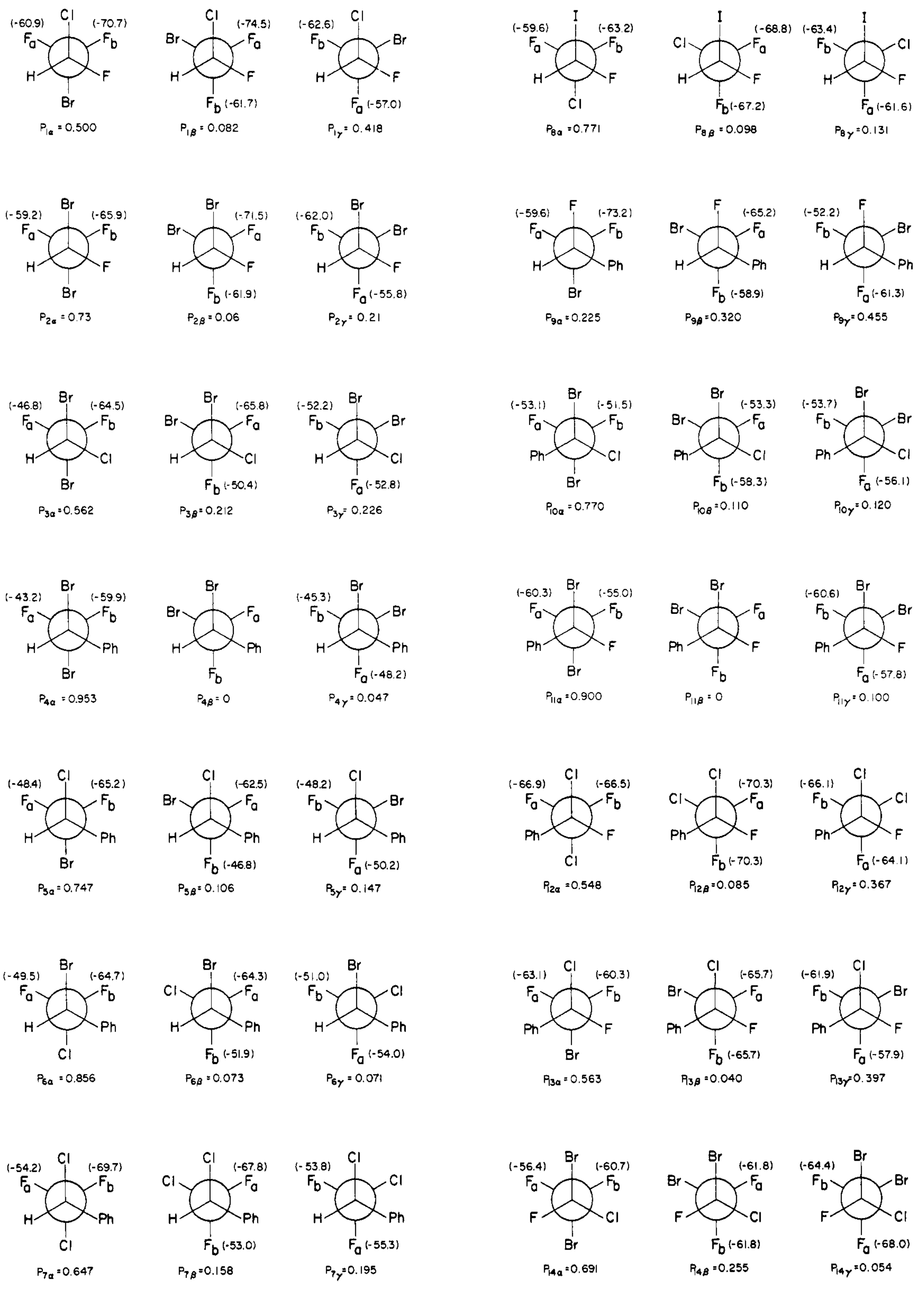


Figure 1. Assignments of fmr subspectra and individual fluorine chemical shifts.

treatments agree in assigning much larger values to electrostatic interactions involving fluorine, as compared to the other halogens, which is all that is needed for qualitative purposes.[23] Electrostatic effects involving the phenyl substituent are expected to be small and have been neglected. For assessing the steric requirements of a phenyl group in substituted ethanes the literature evidence is inconclusive. From an indirect nmr study of a series of neohexyl derivatives, Whitesides, *et al.*,[5c] concluded that phenyl should be slightly

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[21] The general principles underlying the Scott–Scheraga[18] approach have recently been criticized by Wolfe, *et al.*,[22] who felt justified in postulating a special attractive gauche interaction between polar bonds. This criticism, even if valid, need not concern us here, since the number of polar gauche relationships is always the same for the three conformers α, β, γ; see also ref 20.

[22] S. Wolfe, A. Rauk, L. M. Tel, and I. G. Csizmadia, *J. Chem. Soc., B*, 136 (1971).

[23] The quantitative results of molecular mechanics calculations on geometrically relaxed conformers will be published elsewhere.

"larger" than iodine, whereas the trans and gauche conformers of 1,2-diphenyltetrachloroethane are reported[24] to have approximately equal enthalpies. In concordance with the latter result we find that our data can be explained if we assume phenyl to be slightly "smaller" than chlorine.

(2) In **1**–**9** the vicinal hydrogen–fluorine coupling constants, whose dihedral angle dependence is well-established experimentally[25] and theoretically,[26] serve to distinguish the conformer with both vicinal fluorines gauche to the hydrogen from the other two conformers. By the same token, once one additional conformer has been identified by some other means, four fluorine nuclei out of the six can be assigned unambiguously on the basis of the magnitudes of $^3J_{\mathrm{HF}}$.

(3) In contrast to vicinal proton–proton and proton–fluorine coupling constants, the signs[27] and magnitudes of three-bond fluorine–fluorine couplings, especially their dependence on geometry and substituents, do not seem to be well understood at this time,[28] which precludes their use as diagnostic tools in the present study. However, it was found that the geminal fluorine–fluorine coupling constants of a given compound decrease in magnitude with increasing electronegativity of the substituent gauche to both fluorines. The same trend has recently been observed by Weigert and Mahler[12l] in an independent low-temperature fmr study of trifluoromethyl derivatives. Although the origin of this effect is not known, it provides an empirical consistency check of the conclusions drawn with the help of other criteria.

(4) The chemical shifts and coupling constants of the individual conformers determine the population-weighted time-averaged parameters at ambient temperature. Although such calculations can at present only be carried out approximately, since the entropies of the conformers and the temperature dependence of the static parameters have not yet been measured accurately, the preliminary information was frequently sufficient for distinguishing between alternative assignments. Additional evidence has in a few cases been obtained by measuring the time-averaged spectra at a number of different temperatures.

(5) Halogen substituent effects on fluorine chemical shifts have been attributed[29] to the time-averaged squares of electric fields arising from the electron distribution in the carbon–halogen bonds. Our preliminary attempts to apply this theory to the idealized staggered geometries of **1**–**14** led to self-contradictory results, with the exception of the qualitative behavior of shifts of fluorine gauche to chlorine or bromine in structurally homologous conformers, which survives as a useful diagnostic criterion.[12d,k] It is clear that a considerably more sophisticated approach is needed to account for all fluorine chemical shifts in these molecules theoretically. In agreement with an empirical observation already made by Roberts, *et al.*,[12k] we find that the fluorines in the conformers populated to less than 10% frequently exhibit abnormal upfield chemical shifts when compared with their structurally analogous counterparts in the more populous conformers. Since the origin of this effect remains obscure, we have only used it as a diagnostic tool in those cases where the other criteria are insufficient for making assignments.

To present our detailed reasoning for all individual compounds would require far too much space. We shall therefore restrict ourselves to illustrating the operation of the general principles by a few representative examples.[30]

The multiple relationships between the populations of the nine conformers of **1**–**3** illustrate the complex interplay between steric and electrostatic effects. For instance, it can be seen that the population differences between α and β for **1**–**3** are clearly controlled by steric effects, whereas the γ conformers are stabilized relative to the β conformers by one additional attractive gauche H–F interaction in γ and one additional attractive gauche F–F interaction in **1**β and **2**β. More complicated comparisons of relative population trends, such as in the series **1**$\alpha \rightarrow$ **2**$\alpha \rightarrow$ **3**α, **1**$\beta \rightarrow$ **2**$\beta \rightarrow$ **3**β, and **1**$\gamma \rightarrow$ **2**$\gamma \rightarrow$ **3**γ, convincingly bear out these principles. By the same token, it is easy to understand the "abnormally" high population of **1**γ and the near-equality of $p_{3\beta}$ and $p_{3\gamma}$. The large differences in the vicinal H–F coupling constants, where they could be observed (Table II), fully corroborate the assignments of the subspectra and in addition provide unambiguous assignments for 8 of the 18 fluorine chemical shifts. The operation of criterion 3 is demonstrated by the small values of $^2J_{\mathrm{FF}}$ in **1**β and **2**β, and comparisons of $\mathrm{F_a}^{1\beta}$ with $\mathrm{F_b}^{1\alpha}$, of $\mathrm{F_b}^{1\beta}$ with $\mathrm{F_a}^{1\gamma}$, of $\mathrm{F_a}^{2\beta}$ with $\mathrm{F_b}^{2\alpha}$, and of $\mathrm{F_b}^{2\beta}$ with $\mathrm{F_a}^{2\gamma}$ provide examples of criterion 5. Multiple comparisons of the relative magnitudes of the chemical shifts and chemical shift differences between fluorine atoms in similar environments, in combination with criterion 4, gave information sufficient for assigning the remaining chemical shifts. For instance, on the basis of the assignment chosen for **1** (Figure 1) one calculates an approximate value for $\langle\Delta\rangle$ at ambient temperature of $+3.52$ ppm, as compared with the observed value of ± 3.83 ppm, whereas reversing the shifts for $\mathrm{F_a}^{1\gamma}$ and $\mathrm{F_b}^{1\gamma}$ yields $\langle\Delta\rangle = -0.81$ ppm. The corresponding numbers for **2** are $+3.35$, ± 4.18, and -0.48 ppm. From the results on **1**–**3** we can draw the conclusion that fluorines gauche to hydrogen experience a large downfield shift, a trend which is consistently followed in all 26 observed conformers of **1**–**9** and which is in qualitative agreement with previous studies on time-averaged systems.[29] Furthermore, it transpires that a gauche fluorine causes a larger downfield shift than a gauche chlorine or bromine, a relationship that proved useful for some of the other compounds. The

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(24) L. H. L. Chia, K. K. Chiu, and H. H. Huang, *J. Chem. Soc. B*, 1117 (1969).

(25) K. L. Williamson, Y.-F. Li, F. H. Hall, and S. Swager, *J. Amer. Chem. Soc.*, **88**, 5678 (1966); K. L. Williamson, Y.-F. Li Hsu, F. H. Hall, S. Swager, and M. S. Coulter, *ibid.*, **90**, 6717 (1968); A. M. Ihrig and S. L. Smith, *ibid.*, **92**, 759 (1970).

(26) G. Govil, *Mol. Phys.*, **21**, 953 (1971); M. S. Gopinathan and P. T. Narasimhan, *ibid.*, **21**, 1141 (1971).

(27) Relative sign determinations for the coupling constants in Tables I and II are in progress.

(28) For recent attempts to shed light on this problem, see R. A. Newmark, G. R. Apai, and R. O.Michael, *J. Magn. Resonance*, **1**, 418 (1969); R. Ernst, *Mol. Phys.*, **16**, 241 (1969); R. K. Harris and V. J. Robinson, *J. Magn. Resonance*, **1**, 362 (1969); K. L. Williamson and A. Loh, Abstracts, 160th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1970, No. ORGN-054.

(29) J. W. Emsley, *Mol. Phys.*, **9**, 381 (1965); J. Feeney, L. H. Sutcliffe, and S. M. Walker, *ibid.*, **11**, 117, 129, 137, 145 (1966); J. Homer and D. Callaghan, *J. Chem. Soc. A*, 518 (1968); *J. Chem. Soc. B*, 247 (1969).

(30) For the full story, see ref 1.

Table III. Time-Averaged Geminal Anisochronism[a] and Gross Averages[a] at Low (LT) and Ambient (AT) Temperature[17]

Compd	$\langle\Delta\rangle^{LT}$	$\langle\Delta\rangle_i^{LT}$	$\langle\Delta\rangle_c^{LT}$	$\langle\Delta\rangle^{AT}$[b]	$\langle\langle\delta\rangle\rangle^{LT}$	$\langle\langle\delta\rangle\rangle_i^{LT}$	$\langle\langle\delta\rangle\rangle^{AT}$
1	6.19	0.9	5.3	3.829 (3.878)	−63.50	−64.6	−63.657
2	5.59	1.1	4.5	4.178 (4.388)	−62.02	−62.7	−51.401
3	6.50	0.52	5.98	3.297 (3.311)	−55.45	−55.41	−55.205
4	15.71			9.498 (9.762)	−51.32		−50.340
5	10.56	−0.37	10.93	4.915 (4.872)	−55.42	−53.53	−54.042
6	11.83	−0.07	11.90	6.282 (6.368)	−56.84	−65.88	−56.239
7	7.34	−0.30	7.64	3.130 (3.151)	−60.28	−59.00	−58.995
8	2.87	1.3	1.6	2.437 (2.475)	−62.21	−64.0	−63.802
9	−3.13	−0.63	−2.50	−1.728 (−1.883)	−60.62	−61.74	−60.498
10	−0.95	0.34	−1.29	0.0 (0.0)	−53.02	−54.32	−52.05
11	−4.45			−1.952 (−2.037)	−57.81		−57.227
12	0.52	0.54	−0.02	0.621 (0.580)	−66.40	−67.36	−66.281
13	0.00	0.38	−0.38	0.463 (0.0)	−61.14	−62.45	−60.067
14	2.81	0.23	2.58	1.648 (1.674)[c]	−59.80	−62.17	−59.909

[a] In ppm. [b] Values in parentheses refer to 0.4 *M* solution in $CFCl_3$. [c] From 0.4 *M* solution in CF_2Cl_2.

only assignment that remains somewhat uncertain in **1**–**3** is that of $F_a^{3\gamma}$ and $F_b^{3\gamma}$. The sign of the difference ($\delta_a^{3\gamma} - \delta_b^{3\gamma}$) is as expected from the gauche relationships to bromine and chlorine and its magnitude is consistent with the small difference between $F_b^{2\gamma}$ and $F_b^{1\gamma}$. Further tentative support is provided by the calculated ambient temperature value for $\langle\Delta\rangle$ of +3.27 ppm, as compared to +3.63 ppm predicted from the alternative assignment (see Tables I and III), but because of the near-equality of the numbers the empirical criteria are clearly not reliable enough to be conclusive. Fortunately, this residual ambiguity is also of minor importance for the conclusions to be drawn from the present study.

By an analogous line of reasoning one arrives at the assignments shown in Figure 1 for the other compounds containing a hydrogen ligand (**4**–**9**). In particular, the conclusion that the steric requirements of the phenyl substituent are indeed "smaller" than those of chlorine seems inescapable from the total body of data. As another valuable empirical correlation one observes that fluorines gauche to chlorine or bromine absorb at lower fields than corresponding fluorines gauche to phenyl. The strength of the arguments based on criterion 2 and the complete consistency of the data borne out by numerous cross checks lead us to believe that the assignments of all 36 fluorine chemical shifts in **4**–**9** are unimpeachable.

The complete assignments of all subspectra to the individual conformers of **10**–**14** follow in a straightforward manner from the multifarious evidence accumulated at this point in our discussion and require no further comments. The absence of hydrogen as a ligand introduces a higher uncertainty in the assignments of the individual chemical shifts, since the differential effects are smaller in **10**–**14** than in **1**–**9** and criterion 2 becomes inapplicable. Certain combinations of chemical shifts can be excluded by means of criterion 4 and a choice between the remaining possibilities can be made on the basis of the chemical shift trends referred to earlier, leading to the results shown in Figure 1. These conclusions are corroborated by criterion 3, and for **12**β, **13**β, and **14**γ also by criterion 5. It is clear, however, that the arguments based on rough chemical shift trends are somewhat weakened by their failure to account for the observed equalities $F_a^{12\beta} = F_b^{12\beta}$, $F_a^{13\beta} = F_b^{13\beta}$, and $F_a^{14\beta} = F_b^{14\beta}$. The possibility can therefore not be completely discounted that some of the assignments will have to be revised in the light of future evidence, especially those of $F_a^{12\alpha}$ and $F_b^{12\alpha}$.

Compounds **3** and **14** have previously been investigated at low temperature by Newmark and Sederholm[9] and **14** also by Dean and Lee.[12j,31] Our data are in good agreement with those reported, the small discrepancies of approximately 0.5 ppm or less in the chemical shifts presumably arising from solvent and/or concentration effects.[32] However, none of the previous authors succeeded in assigning individual fluorine chemical shifts. It should also be noted that our assignment of $F_a^{3\gamma}$ and $F_b^{3\gamma}$ is opposite to the chemical shift *combination* assumed previously.[9]

Anisochronism

We are now in a position to calculate the time-averaged geminal chemical shift differences, including their signs,[17] *at low temperature.* The intrinsic term $\langle\Delta\rangle_i^{LT}$ is obtained[13] by averaging the individual chemical shifts with a factor of $^1/_3$, the total anisochronism $\langle\Delta\rangle^{LT}$ corresponds to the population-weighted average, and the conformational term $\langle\Delta\rangle_c^{LT}$ is given by the difference $\langle\Delta\rangle^{LT} - \langle\Delta\rangle_i^{LT}$. The results are shown in Table III together with the observed ambient-temperature values of $\langle\Delta\rangle^{AT}$. Even though only two conformers could be observed for **4** and **11**, it is nevertheless possible to specify the signs of $\langle\Delta\rangle^{AT}$ in all cases. In addition we list the gross averages defined as $\langle\langle\delta\rangle\rangle^{LT} = (\langle\delta_a\rangle^{LT} + \langle\delta_b\rangle^{LT})/2$, $\langle\langle\delta\rangle\rangle_i^{LT} = \Sigma_j(\delta_a^j + \delta_b^j)/6$ and $\langle\langle\delta\rangle\rangle^{AT} = (\langle\delta_a\rangle^{AT} + \langle\delta_b\rangle^{AT})/2$.

The data in Table III lead to the following conclusions. (1) The gross averages consistently follow the qualitative trend expected on the basis of electric field theory,[29] according to which the more polarizable halogen substituent should cause a downfield shift. This can be seen by comparing **7** with **5**, **6** with **4**, **12** with **13**, and in the series **1** → **2** → **3**, **9** → **5** → **4**, and **13** → **11** → **10**. These observations sug-

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(31) A paper by Brey and Ramey[8] does not contain sufficient information for comparison.

(32) The chemical shift data and the assignments of two of the subspectra quoted for **3** in a recent review article[33] are incorrect.

(33) J. W. Emsley and L. Phillips, *Progr. Nucl. Magn. Resonance Spectrosc.*, 7, 1 (1971).

gest that distortions from idealized geometry are a major cause of the failure of electric field theory to account for the fluorine chemical shifts in the individual conformers. (2) The magnitude of the intrinsic term is in general small, albeit not negligible. As confirmed by the results of the preceding paper,[13] this situation appears to be the rule when structural constraints prevent the diastereotopic nuclei from making intimate contact with the asymmetric center. (3) In six cases the intrinsic and conformational terms were found to be of opposite sign, and in **13** they accidentally cancel one another exactly at low temperature. To infer[34] a vanishing intrinsic term from an observed accidental total isochronism is therefore a logical *non sequitur*. Furthermore, the magnitude of the total anisochronism cannot necessarily be assumed to exhibit a monotonic dependence on temperature; the extrapolation procedure[35] for determining the intrinsic term is therefore of questionable validity.[13] (4) A comparison of the corresponding numbers in columns 6–8 of Table III demonstrates that the gross chemical shift averages are not useful for obtaining quantitative conformational information on acyclic compounds of the type investigated in this study. It is equally clear, however, that the numbers in columns 2, 4, and 5 of Table III do not yield this kind of information on mere inspection either, not even qualitatively, although they are very sensitive to conformational effects. In the succeeding publication[11] we present a heuristic mathematical model designed to overcome this difficulty.

Experimental Section

Nmr Measurements. Ambient-temperature proton spectra were obtained on 10–15% solutions in $CFCl_3$ containing 2–5% TMS as internal standard, using a Varian A-60A spectrometer. Fluorine spectra were recorded on 0.4 *M* solutions in $CFCl_3$, using a Varian HR-60 spectrometer and standard audio-side-band techniques for calibration, and on 10% (v/v) solutions in CF_2Cl_2 or vinyl chloride, using a Varian XL-100-15 spectrometer, internally locked on the proton resonance of TMS (8%). Vinyl chloride solutions contained an additional 5% of $CFCl_3$ as internal fluorine standard and 1–3 mg of 4-*tert*-butylcatechol as polymerization inhibitor. The samples were degassed by three freeze–thaw cycles and the tubes sealed under reduced pressure. Temperatures were measured by substituting an open sample tube containing a copper–constantan thermocouple immersed in liquefied CF_2Cl_2 before and after recording a spectrum and were reproducible to within about 1°, except at the lowest temperatures (−160°) where random fluctuations amounted to about ±3°. Line positions, averaged over five upfield-sweep and five downfield-sweep spectra, were subjected to iterative LAOCN3[36] computations for patterns more complex than AB. The integrals were averaged over at least ten electronic integrations and were checked by manual planimetry.

All samples were purified by preparative vpc (Aerograph Chromatograph Models A-700 or A-90-P) using 15 ft × $^3/_8$ in. 20% Carbowax 20M on Chromosorb G or 10 ft × $^3/_8$ in. 10% UC-W98 on acid-washed Chromosorb W columns. The compounds not described in the following were either purchased or prepared according to literature procedures.

1,2-Dibromo-1-chloro-2,2-difluoro-1-phenylethane (10) was prepared in 96% yield by addition of 1.8 g (11 mmol) of bromine to a solution of 2.2 g (12 mmol) of α-chloro-β,β-difluorostyrene[15] in 20 ml of CCl_4 at 50° over a period of 30 min: pmr ($CFCl_3$) δ 7.5 (s).

Anal. Calcd for $C_8H_5ClBr_2F_2$: C, 28.74; H, 1.51. Found: C, 28.98; H, 1.59.

1,2-Dibromo-1,1,2-trifluoro-2-phenylethane (11) was obtained in analogy to **10** by bromine addition to α,β,β-trifluorostyrene: bp 69° (0.9 mm); pmr (vinyl chloride) δ 7.4 (s).

Anal. Calcd for $C_8H_5Br_2F_3$: C, 30.32; H, 1.59. Found: C, 30.33: H, 1.56.

1,2-Dichloro-1,1,2-trifluoro-2-phenylethane (12) was prepared by bubbling chlorine through a CCl_4 solution of α,β,β-trifluorostyrene: bp 53–55° (3 mm); pmr ($CFCl_3$) δ 7.5 (s).

Anal. Calcd for $C_8H_5Cl_2F_3$: C, 41.95; H, 2.20. Found: C, 42.10; H, 2.29.

1-Bromo-2-chloro-2,2-difluoro-1-phenylethane (6). To 22 ml of 18% hydrochloric acid were added in portions 3.95 g (28 mmol) of *N*-bromoacetamide and 4.04 g (28 mmol) of β,β-difluorostyrene[37] over a period of 20 min at −5° with stirring, after which time the reaction mixture was slowly (2 hr) warmed up to room temperature. The organic layer was filtered through sodium sulfate and then potassium carbonate and distilled under reduced pressure. A crude vpc purification yielded 3.1 g (40%) of a mixture consisting of 91% of **6** and 9% of **5** (see below), bp 33–39° (1–2 mm), from which **6** was obtained pure by repeated vpc: pmr ($CFCl_3$) δ 5.19 (dd, J = 6.6 and 13.8 Hz, 1), 7.35 (s, 5),

Anal. Calcd for $C_8H_6BrClF_2$: C, 37.61; H, 2.37. Found: C, 37.64; H, 2.45.

Hydrogen Halide Elimination from 6. A solution of 2.5 g of **9** and 1.2 g of potassium *tert*-butoxide in 10 ml of dry dimethyl sulfoxide was stirred at 50° for 4 hr; the reaction mixture was poured into water and extracted with ether. The extracts were washed with water and dried (Na_2SO_4); the ether was evaporated, the residue distilled under reduced pressure, and the distillate subjected to preparative vpc to yield 1.2 g of starting material and 200 mg of α-bromo-β,β-difluorostyrene: mass spectrum parent *m/e* 218, 220; fmr ($CFCl_3$) δ −79.39 (d, J = 32.0 Hz, 1), −85.82 (d, J = 32.0 Hz, 1).

2-Bromo-2,2-difluoro-1-phenylethanol. To a solution of 0.76 g (20 mmol) of sodium borohydride and 2 ml of 2 *N* NaOH in 5 ml of water was added 7.0 g (30 mmol) of α-bromo-β,β-difluoroacetophenone[38] in 5 ml of methanol at −10° over a period of 30 min. The reaction mixture was stirred for 1 hr, poured into 20 ml of 10% NaOH, and extracted five times with 20-ml portions of ether. Work-up by distillation under reduced pressure yielded 5.6 g (80%) of product: bp 104–106.5° (8 mm); ir (neat) 3413 cm^{-1}; pmr (neat) δ 4.87 (t, J = 8.9 Hz, 1), 5.14 (s, 1), 7.25 (s, 5); fmr ($CFCl_3$) δ −56.24 and −59.51 (AB part of an ABX pattern).

Anal. Calcd for $C_8H_7BrF_2O$: C, 40.54; H, 2.98. Found: C, 40.76; H, 3.11.

1-Bromo-2-chloro-1,1-difluoro-2-phenylethane (5). A mixture of 4.25 g (18 mmol) of 2-bromo-2,2-difluoro-1-phenylethanol, 2.35 g (20 mmol) of thionyl chloride, and 1 ml of pyridine was heated to 60° for 2 hr. Ether was added to the cold solution, the liquid decanted from the precipitated pyridine hydrochloride, washed with water, and dried (Na_2SO_4), the ether evaporated, and the residue distilled under reduced pressure to give 3.0 g (65%) of product, shown by fmr to consist of 92% of **5** and 8% of **6** (see above). Pure **5** was obtained by preparative vpc: bp 115–117° (22 mm); pmr (CCl_4) δ 5.08 (dd, J = 7.34 and 12.31 Hz, 1), 7.31 (s, 5).

Anal. Calcd for $C_8H_6BrClF_2$: C, 37.61; H, 2.37. Found: C, 37.80; H, 2.45.

Reaction of α,β,β-Trifluorostyrene with Hydrogen Bromide. A mixture of 5.0 g (32 mmol) of α,β,β-trifluorostyrene and 70 ml of 1.7 *N* HBr (119 mmol) in acetic acid was heated to 50° for 3 hr, to 80° for 11 hr, and to 110° for 22 hr, poured into 150 g of ice water, and extracted with ether. Work-up by distillation under reduced pressure yielded 4.1 g (55%) of a mixture, bp 93–108° (24 mm), shown by pmr and vpc to consist of approximately equal amounts of **9** and **18**: pmr ($CFCl_3$) δ 5.35 (ddd, J = 7.9, 8.2, and 44.4 Hz, 1, $\mathrm{BrCF_2C}H\mathrm{FC_6H_5}$), 7.39 (s, 5, $\mathrm{BrCF_2CHFC_6}H_5$), 5.70 (dt, J = 4.0 and 55.1 Hz, 1, $H\mathrm{CF_2CFBrC_6H_5}$), 7.32 (s, 5, $\mathrm{HCF_2CFBrC_6}H_5$). An fmr sample of chromatographically pure **9** was obtained by preparative vpc.

Reaction of α-Chloro-β,β-difluorostyrene with Bromine Monofluoride. Reaction of 1.25 g (7 mmol) of α-chloro-β,β-difluorostyrene[15] with bromine monofluoride, generated *in situ* from 8 g (16 mmol) of silver fluoride and 1.7 g (11 mmol) of bromine in a mixture of 25 ml of acetonitrile and 18 ml of benzene, produced,

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after work-up and crude separation by vpc, approximately 100 mg of a 57:43 mixture, whose 94.1-MHz fmr spectrum showed a singlet (43%) at δ −57.94 and an ABX pattern, the latter being identical with that of the major component in the bromine monochloride addition to α,β,β-trifluorostyrene (see below).

Reaction of α,β,β-Trifluorostyrene with Bromine Monochloride. To a mixture of 10 ml of 18% hydrochloric acid and 5.9 g (37 mmol) of α,β,β-trifluorostyrene was added, with stirring, 3.1 g of *N*-bromoacetamide at 0° over a period of 20 min. The mixture was allowed to warm up to room temperature over a period of 2 hr, added to 5 ml of 5% sodium bisulfite solution, and extracted with ether. Work-up by distillation yielded 4.4 g of a mixture, shown by fmr to consist of 70% of **13** and 30% of a second component, presumably **19**: bp 92° (11 mm). A pure sample of **13** was obtained by preparative vpc: pmr (CCl_4) δ 7.7 (s).

Anal. Calcd for $C_8H_5BrClF_3$: C, 35.13; H, 1.84. Found: C, 35.34; H, 1.95.

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Time-Averaged Geminal Anisochronism and Molecular Energetics in Acyclic Systems. A Heuristic Mathematical Model

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Abstract: An empirical relationship between the time-averaged anisochronism in asymmetric ethanes of the general formula RCG_2CXYZ and the free energy differences between the individual conformers is derived from heuristic arguments based on transformation properties and sum rules. The mathematical model is developed to first order in certain scalar quantities characterizing the ligands X, Y, and Z at the asymmetric center and applied to the experimental data of the preceding paper. It is found that the model correctly accounts for the qualitative trends in the populations of all 30 conformers of the 10 compounds $BrCF_2CXYZ$, in which the substitution pattern at the asymmetric center corresponds to all possible combinations of the five ligands hydrogen, fluorine, chlorine, bromine, and phenyl, and that the calculated ambient-temperature populations, obtained from the first-order model after scaling with the cubic root of the product of the free energy differences, agree with the experimental values to within an average precision of about 4%.

The work to be described in this paper was stimulated by an observation reported in 1965 by Ugi,[2] who found that the logarithms of the diastereomer ratios in two series of asymmetric syntheses could be fitted, with remarkable precision, to products of differences of scalar parameters characterizing the ligands at the asymmetric centers. An elaborate group-theoretical edifice has since been erected on this observation, culminating in a general algebraic theory of the chirality phenomenon in chemistry.[3] Fortunately, however, the salient features of this treatment relevant to the special case of interest in the context of the present paper are so simple and obvious that they can be derived and appreciated by inspection.

The geminal time-averaged anisochronism $\langle\Delta\rangle$ in molecules of the general formula RCG_2CXYZ is another example of a chirality observation describable by a chirality function, *i.e.*, a function χ satisfying the following two rigorous mathematical requirements: (1) χ must vanish identically if two of the ligands X, Y, or Z are the same; (2) χ must change sign, and sign only, if two ligands are interchanged. The latter of these two obvious properties of $\langle\Delta\rangle$ could previously not be fully exploited because all measurements have so far only yielded the magnitude of time-averaged geminal chemical shift differences. With the results of the preceding publication,[4] the missing piece of information is now available for 14 compounds, which include a complete set of 10 corresponding to the general formula $BrCF_2CXYZ$ where the ligands X, Y, and Z run through all combinations of five different substituents. It is of interest, therefore, to determine empirically the level of complexity in the chirality functions that is required to reproduce such experimental data to a desired degree of precision, and in particular to investigate whether a simple chirality product, involving only one scalar parameter per ligand, can give satisfactory results. In the latter case, as already stressed by Ugi[2] and Ruch,[3] the theory would yield nontrivial new information; only $n - 1$ measurements are needed in principle to fix the parameters for n (>3) different ligands, so that $\langle\Delta\rangle$ could be predicted for $n!/(3!(n-3)!) - (n-1)$ additional systems.

Apart from and beyond such a possibility we had reasons to believe that in the present series there was a finite chance of arriving at a physical interpretation of the ligand parameters, an effort that has so far not been attempted. Most importantly, the prospect of discovering an empirical relationship between time-averaged intensive quantities satisfying the required

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