Organic and Biological Chemistry

Studies in Magnetic Nonequivalence. Nuclear Magnetic Resonance Spectra of Some Three-Spin Systems

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Abstract: Results of nmr spectral analysis of 12 1,1,2-trisubstituted ethanes in two to seven solvents are reported. In all compounds the vicinal and geminal coupling constants are of opposite sign. Variation in the vicinal coupling constants with solvent was relatively small, in strong contrast to the behavior of the chemical-shift difference between nonequivalent methylene protons, indicating that the chemical-shift difference *per se* is an inadequate criterion of conformer distribution. Nonequivalent methylene protons were noted in an acyclic ethyl ester.

In a previous article we reported some data pertinent to the question of whether chemical shift differences between the nonequivalent protons in appropriate types of methylene groups were simply related to differences in population of the various rotational isomers (conformers), particularly as regards the change in chemical shift with solvent.[1] These results suggested that, at least for those systems, the chemical shift *per se* was not a reliable measure of conformational equilibria. It soon became apparent that more information on conformational equilibria is contained in three-spin systems of the type XCH_2CHYZ, where magnetic nonequivalence, if present, of the methylene protons permits measurement of both vicinal coupling constants. A quantitative relation between the difference in magnitude of the vicinal coupling constants and the conformational equilibrium constant would obtain in these systems if the couplings were a function solely of the dihedral angle between the spin-coupled protons and if the dihedral angles were known.

Roberts and co-workers[2] were perhaps the first to report a difference in the two vicinal coupling constants for three-spin proton systems, although Shoolery and Crawford had long ago noted similar behavior for fluorine couplings,[3] and clearly recognized its significance. Roberts also suggested that this inequality supported the thesis that nonequivalence arises from conformational effects.[4] (It seems to us that this observation of unequal vicinal coupling constants does not in any way preclude the possibility that nonequivalence in the chemical shift sense arises solely or in part from an inherent magnetic asymmetry associated with an asymmetric center near the methylene group,[5] although the conformational origin might ultimately be proved correct. Let us emphasize, however, that in three-spin systems of the type XCH_2CHYZ one uses the nonequivalence, *i.e.*, a nonzero chemical shift difference, of the methylene protons merely as a means by which to measure the two vicinal couplings so that the origin of such nonequivalence is irrelevant to arguments based on inequality of vicinal couplings. Efforts to relate vicinal coupling constants with an equilibrium conformational distribution have been hampered by the lack of reliable values for couplings between hydrogens *trans* and *gauche* oriented although the exit from this dilemma has been clearly outlined by Gutowsky and co-workers.[6]

In this paper we present the results of spectral analysis of several three-spin systems in two to seven solvents, and those characteristics which seem to be significant are discussed. In the following paper we present data which seem to unequivocally identify the major conformer in two dibromides. In the last of the present trio of papers we present a *crude, "zeroth-order" approximation* to the problem of determining conformational equilibria from the vicinal coupling constants of three-spin and related systems.

Experimental Section

Nmr Measurements. All measurements were performed on an A-60 spectrometer system. A sweep-width calibration, using a side band generated by an audiooscillator and measured with a frequency counter, was made sometime during every day the reported spectra were recorded. Corrections to the sweep width of greater than 0.2% were applied to the observed data. The good reproducibility in nmr parameters calculated from observed spectra of any one system recorded at widely differing times, and sometimes recorded by different operators (see Table I), suggests that errors in the coupling constants from this source is small. Differences in air and magnet temperature certainly resulted in different probe and sample temperatures. However, (unpublished) results of investigations into the temperature dependence of the vicinal couplings suggest a variation of about 0.1 cps per 10°, which is of the same order as the estimated error in couplings. Spectra were generally obtained from "40%" solutions (0.2 g of solute, 0.5 ml of solvent).

Materials. Commercially available compounds were purified by recrystallization from a suitable solvent or by distillation. The melting points of solids were checked against reported values; purity of liquids were determined by vpc examination. In no case

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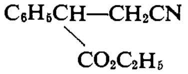
Table I. Nmr Parameters at 60 Mc for Various Three-Spin Systems

Solvent	ν_1[a]	ν_2[a]	ν_3[a]	J_{12},[b] cps	J_{13}, cps	J_{23}, cps	Av dev[c]	Max dev[d]	Method	No. of sweeps
$CH_2BrCHBrCO_2H$										
Benzene	8.62 (235)	39.63 (200)	66.16 (178)	10.93	4.47	− 9.92	0.013		NMRIT	
$CHCl_3$	8.70 (266)	43.62 (231)	57.03 (218)	11.31	4.38	−10.11	0.044	0.18	*e*	
CH_3CN	8.42 (274)	49.37 (233)	54.20 (228)	11.22	4.15	−10.21	0.051	0.13	NMRIT	
CH_3COCH_3	8.42 (279)	49.38 (238)	54.59 (232)	10.78	4.60	− 9.82	0.068	0.18	MODIT	
$CH_2BrCHBrCO_2C_2H_5$										
Benzene	8.89 (248)[f]	35.96 (221)	66.27 (191)	11.26	4.44	− 9.81	0.013	0.026	MODIT	2
	8.89[f]	35.71	66.15	11.26	4.40	− 9.73	0.015	0.033	MODIT	2
Neat	8.67 (270)	43.07 (236)	53.62 (225)	10.95	4.59	− 9.80	0.028	0.084	MODIT	2
CCl_4	8.99 (263)[f]	36.84 (235)	52.21 (220)	11.46	4.30	− 9.82	0.031	0.075	MODIT	3
	8.94[f]	36.76	52.15	11.42	4.33	− 9.84	0.021	0.056	MODIT	2
CH_3CN	8.43[g]	47.93	54.24	10.68	4.64	− 9.94			MODIT	3
	8.39[g]	47.86	54.31	10.56	4.71	− 9.91	0.034	0.075	MODIT	
CH_3COCH_3	8.41[g]	50.13	54.87	10.84	4.53	− 9.87			MODIT	4
	8.46[g]	50.38	54.93	10.99	4.34	− 9.93	0.033	0.085	MODIT	2
$C_6H_5NO_2$	8.55	42.82	55.34	10.77	4.63	− 9.90	0.055	0.24	MODIT	4
$CH_2ClCHClCO_2H$										
Benzene	7.24 (239)	37.72 (208)	50.43 (196)	8.01	5.26	−11.41	0.011	0.023	MODIT	5
$CHCl_3$	7.35 (272)	40.31 (239)	47.20 (232)	8.23	5.24	−11.31	0.026	0.060	MODIT	6
$CH_2ClCHClCO_2C_2H_5$										
Benzene	7.62 (245)	33.80 (219)	50.69 (202)	8.42	5.30	−11.14	0.020	0.048	MODIT	1
$CHCl_3$	7.64 (267)	35.91 (238)	44.87 (229)	8.39	5.36	−11.24	0.026	0.058	MODIT	2
CCl_4	7.96 (261)	32.41 (237)	43.40 (226)	8.90	5.29	−11.08	0.015	0.027	MODIT	4
Neat	7.25 (271)	39.85 (238)	45.95 (232)	7.78	5.52	−11.28	0.018	0.031	MODIT	2
CH_3CN	Too degenerate for analysis									
CH_3COCH_3	Too degenerate for analysis									
$CH_2BrCHBrC_6H_5$										
CCl_4	8.60 (298)	72.39 (235)	76.12 (231)	5.25	10.89	−10.26			NMRIT	
$CHCl_3$	8.60 (309)	72.63 (245)	75.89 (242)	5.58	10.60	−10.27			*e*	1
CH_3COCH_3	8.44 (278)	80.31 (205)	78.19 (207)	5.74	10.11	−10.47	0.089	0.30	*e*	
	8.45	80.29	78.20	5.54	10.31	−10.48	0.087	0.30	*e*	
Benzene[h]				5.25	10.70					
CH_3CN[h]				5.27	10.52					
$CH_2ClCHClC_6H_5$										
Benzene	7.53 (277)	71.67 (213)	75.91 (209)	6.52	7.74	−11.38	0.055	0.17	MODIT	5
CCl_4	7.63 (292)	67.64 (232)	71.91 (228)	6.39	8.06	−11.24	0.029	0.12	MODIT	5
MeCN	Too degenerate for analysis									
Neat	Too degenerate for analysis									
$CH_2BrCHOHC_6H_5$										
CH_3COCH_3	6.18 (299)	83.78 (221)	87.12 (218)	4.63	7.30	−10.32	0.010	0.025	MODIT	3
$CHCl_3$	6.50	66.23	70.37	3.94	8.37	−10.50	0.010	0.025	MODIT	3
Benzene	Too degenerate for analysis									
$CH_2OHCHIC_6H_5$										
$CHCl_3$	7.64 (306)	74.07 (240)	83.90 (230)	7.19	7.40	−12.06	0.047	0.085	NMRIT	3
CH_3CN	7.72 (314)	78.38 (244)	85.89 (236)	6.83	7.94	−11.93	0.024	0.065	MODIT	3
$CH_2BrCHBrC(CH_3)_3$										
Benzene	6.90 (228)	23.87 (211)	40.76 (194)	2.76	9.63	−11.54	0.018	0.040	MODIT	3
CCl_4	7.11 (241)	12.41 (236)	35.04 (213)	3.08	9.26	−11.37	0.025	0.095	MODIT	3
	7.10	12.42	35.02	3.08	9.26	−11.37	0.025	0.061	NMRIT	3
CH_3CN	7.11 (250)	11.22 (246)	39.59 (217)	2.42	10.07	−11.72	0.012	0.030	NMRIT, MODIT	3
CH_3COCH_3	7.22 (251)	8.95 (249)	39.51 (218)	2.64	9.91	−11.66	0.044	0.12	MODIT	3
	7.22	8.95	39.52	2.64	9.91	−11.66	0.043	0.12	NMRIT	3
$CH_2BrCHBrCN$										
Neat	11.69 (284)	63.16 (233)	66.61 (229)	6.11	8.37	−10.70	0.051	0.12	MODIT	4
Benzene	8.18 (210)	52.32 (166)	46.05 (172)	5.17	9.85	−10.51	0.044	0.17	MODIT	4
$CH_2ClCHClCN$										
Neat	6.43 (292)	59.93 (238)	63.06 (235)	5.39	6.81	−11.78	0.020	0.061	NMRIT	4
Benzene	6.90 (225)	49.50 (182)	51.71 (180)	7.55	5.33	−11.79	0.036	0.07	NMRIT	3
	6.90	49.53	51.68	7.51	5.37	−11.88	0.041	0.15	MODIT	3
CCl_4	Too degenerate for analysis									
CH_3COCH_3	6.00 (318)	75.55 (248)	80.25 (244)	4.82	6.73	−11.91	0.022	0.050	MODIT	5
CH_3CN	6.04 (302)	66.90 (241)	70.84 (237)	4.84	6.64	−11.87	0.036	0.17	MODIT	5

Table I (*Continued*)

Solvent	ν_1[a]	ν_2[a]	ν_3[a]	J_{12},[b] cps	J_{13}, cps	J_{23}, cps	Av dev[c]	Max dex[d]	Method	No. of sweeps
 $C_6H_5CH{-}CH_2CN$ with $CO_2C_2H_5$										
Benzene	7.94 (219)	70.28 (156)	85.81 (141)	7.81	7.25	−16.85	0.026	0.12	MODIT	3
CH_3CN	7.70 (240)	68.58 (179)	75.64 (172)	7.12	7.69	−16.89	0.032	0.06	MODIT	1
CH_3CN-C_6H_6										
85:15	7.78	68.58	75.83	7.19	7.57	−16.88	0.035	0.087	MODIT	2
7:3	7.73	68.30	76.10	7.36	7.43	−16.86	0.039	0.097	MODIT	3
4:6[i]										
3:7	7.99	69.43	79.70	7.83	7.09	−16.84	0.10	0.35	MODIT	2
2:8	7.88	69.85	81.31	7.87	7.10	−16.82	0.075	0.18	MODIT	3
1:9	7.87	69.84	82.95	7.84	7.17	−16.82	0.059	0.12	MODIT	3
$CHCl_3$	8.06 (234)	64.49 (178)	77.05 (165)	7.49	7.43	−16.75	0.094	0.42[j]	MODIT	2
CCl_4	7.90 (229)	65.97 (171)	78.94 (158)	7.54	7.44	−16.73	0.097	0.39		

[a] ν_i is the resonance frequency in cps of the *i*th proton relative to some arbitrary zero (usually the first strong spectral line). The number in parentheses is the resonance frequency relative to internal TMS. [b] J_{ij} is the coupling constant between nuclei *i* and *j*. [c] This represents the average deviation between calculated and observed frequencies. [d] This represents the maximum difference between calculated and observed line frequencies. [e] This solution was obtained by trial and error. [f] These two sets of spectral parameters are for spectra recorded 9 months apart. [g] Sets of parameters correspond to spectra recorded 3 months apart by different operators. [h] Although the spectrum was too degenerate for analysis, J_{12}, J_{13} could be determined from a mixture of $C_6H_5CHBrCH_2Br$ and *erythro*-$C_6H_5CHBrCHDBr$. (See accompanying paper by Buza and Snyder.) [i] The (perturbed) quartet of the ethyl group from the ester moiety coincided with the benzylic proton resonances, preventing analysis. [j] The large half-width (*ca.* 1.5 cps) of the benzylic proton made impossible resolution of the central line of the observed triplet; a separation of 0.7 cps is calculated from the data above.

were compounds of known purity of less than 95% used for spectral studies. The commercial samples were those of 2,3-dibromopropionic acid and its ethyl ester and ethyl 2,3-dichloropropionate.

2,3-Dichloropropionic acid was prepared by acid hydrolysis of its ethyl ester. Distillation from hydroquinone afforded a fraction, bp 85–88° (1.5 mm), which was recrystallized from pentane.

(1,2-Dibromoethyl)benzene, prepared by addition of bromine to styrene in carbon disulfide at 0°, was twice recrystallized from methanol, mp 73–74° (lit.[7] mp 74–74.5°).

(1,2-Dichloroethyl)benzene, from chlorination of styrene in chloroform at 0°, was distilled through a Widmer column. A fraction, bp 64–70° (1 mm), containing 7% $C_6H_5CH{=}CHCl$ by vpc was redistilled through a spinning-band column. The cut, bp 67° (1 mm), n^{20}D 1.5522, analyzing 98.7% pure by vpc (2 *m* silicone oil, 168°), was used for nmr samples.

(1-Iodo-2-hydroxyethyl)benzene was prepared as described,[8] mp 77–78° (lit.[8] mp 78.5°), and its nmr spectrum was recorded immediately after solution.

(1-Hydroxy-2-bromoethyl)benzene was prepared by sodium borohydride reduction of phenacyl bromide,[9] bp 111–114° (2–4 mm), n^{20}D 1.5786 (lit.[9] bp 109–110° (2 mm), n^{25}D 1.5751, n^{17}D 1.5800).

2,3-Dichloropropionitrile, from chlorination of acrylonitrile in chloroform at 0°, was distilled through a short Vigreux column. One fraction, bp 67–69°, n^{20}D 1.4655 (lit. bp 61° (13 mm), n^{20}D 1.4645;[10a] n^{26}D 1.4633[10b]), was homogeneous by vpc examination (2 *m* silicone oil, 130°).

2,3-Dibromopropionitrile, from bromination of acrylonitrile in chloroform at 0°, was purified by redistilling a fraction, bp 62–68° (1 mm), n^{20}D 1.5479–1.5503, through a Widmer column to give a fraction, bp 55° (0.7 mm), n^{20}D 1.5487 (lit. bp 108–110° (25 mm), n^{20}D 1.5410,[11a] 1.5580[11b]).

3-Ethoxycarbonyl-3-phenylpropionitrile was prepared as described,[12] bp 142–143° (1 mm), n^{20}D 1.5090 (lit.[12] bp 166–167° (9 mm)).

1,2-Dibromo-3,3-dimethylbutane was prepared by bromination of 3,3-dimethylbutene-1 in chloroform at −60°. Distillation through a Widmer column gave material, homogeneous on vpc examination, bp 52–53° (1 mm), n^{20}D 1.5076 (lit.[13] bp 73° (3 mm), n^{20}D 1.5054).

Results

All nmr spectra were analyzed by exact solution of the Hamiltonian using the iterative procedure of Swalen and Reilly[14] or using an empirical scheme (MODIT) developed by the author which also iterates on the observed line frequencies. Comparison of the results of these two methods shows that both lead to values which are experimentally indistinguishable. After convergence of the iterations had occurred to give a set of parameters which generated a spectrum whose line frequencies agreed closely with the observed line frequencies, the "acceptability" of the solution was checked by comparing calculated with observed intensities. This comparison was usually qualitative, but in some cases a quantitative comparison was made. The results of nmr analysis are summarized in Table I. Spectra of the following compounds in the indicated solvents were too degenerate for analysis: $C_6H_5C(CO_2H)HCH_2OH$ (acetonitrile), $C_6H_5C(OAC)HCH_2OAc$ (acetonitrile, acetone), $C_6H_5CHBrCH_2CO_2H$ (dioxane, dimethylformamide), $C_6H_5CHOHCH_2CN$ (benzene, acetonitrile, acetone). We note that usually chemical shift differences between magnetically nonequivalent methylenes in the systems $C_6H_5CHXCH_2Y$ were small (*cf.* $C_6H_5CHBrCH_2Br$, $C_6H_5CHClCH_2Cl$, $C_6H_5CHOHCH_2Br$), leading to spectral degeneracy in a number of systems (*vide supra*). This was unexpected in view of the known anisotropy of the phenyl group, and in fact these particular compounds were chosen because it was anticipated that the anisotropy of the aromatic ring would accentuate chemical shift differences. Where comparison with other groups is

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Table II. Nmr Parameters at 60 Mc for Three-Spin Olefinic System

Solvent	ν_1, cps	ν_2, cps	ν_3, cps	J_{12}, cps	J_{13}, cps	J_{23}, cps	Av dev	Max dev	Method	No. of sweeps
				$CH_2{=}CHCN$						
CH_3CN	12.70	20.84	41.31	0.87	18.01	11.87	0.016	0.034	NMRIT	4
$(CH_3)_2CO$	13.13	20.16	38.16	0.91	17.93	11.79	0.008	0.018	NMRIT	4
Benzene	12.31	26.48	44.01	0.90	17.95	11.77	0.017	0.053	NMRIT	3
$CHCl_3$	12.42	20.08	43.64	0.85	17.99	11.75	0.014	0.029	NMRIT	4
CCl_4	12.51	19.94	42.85	0.93	17.94	11.74	0.021	0.048	MODIT	4
				$CH_2{=}CHC_6H_5$						
Benzene	15.80	74.83	106.39	17.72	10.86	1.03	0.027	0.070	MODIT	4
$CHCl_3$	5.11	64.01	94.73	17.72	10.98	1.00	0.011	0.030	MODIT	3
CCl_4	15.80	74.51	104.64	17.68	10.94	1.03	0.014	0.032	MODIT	3
$(CH_3)_2CO$	15.82	73.82	107.31	17.67	10.96	1.03	0.012	0.022	MODIT	3

Table III

	$CH_2BrCHBrCO_2H$				$CH_2BrCHBrCO_2CH_3$			
% concn[a]	40	20	10	5	40	20	10	5
J_{12}, cps	10.93	10.93	10.86	10.97	11.15	11.21	11.24	11.24
J_{13}, cps	4.54	4.53	4.53	4.50	4.44	4.41	4.40	4.42
J_{23}, cps	−10.10	−9.96	−10.01	−10.03	−9.84	−9.86	−9.86	−9.86

[a] Weight solute per 100 ml of solvent (benzene).

possible (*viz.*, CO_2R, CN, *t*-butyl) the phenyl ring seems peculiarly ineffective in this respect.

Several features common to most, if not all, of the systems studied are evident from the data. Solvent variation in the vicinal coupling constants of any one compound is minimal; this point is discussed further below. All of the geminal coupling constants are negative with respect to the vicinal ones. A clear-cut difference between two sets of solutions containing different signs of the geminal coupling constant was possible for most compounds by comparing calculated and observed line intensities. Although this result is not novel—it presently seems to be the consensus of opinion that this represents the "normal" situation—the data do provide many additional examples where a negative geminal coupling constant in saturated acyclic systems has been demonstrated with some degree of reliability. In contrast to the results of our earlier investigation there seems to be no correlation between the chemical shift difference of the methylene hydrogens of compounds in Table I with those of the olefins from which they are formally derived. (Nmr data for the latter are presented in Table II.) This suggests that such correlations may be highly specific to the class of compounds previously used. Furthermore, evidence for solvent variation in geminal coupling constants is somewhat tenuous. In only two systems (CH_2Br-$CHBrCO_2H$ and $CH_2BrCHBrC(CH_3)_3$) was the variation significant (0.4 cps), whereas, in the remaining systems the variation was on the order of the combined limits of error (0.2 cps).

Reference to Table III shows that the vicinal coupling constants are sensitive to solvent changes. Since the vicinal couplings are intimately associated with the dihedral angle between coupled protons, solvent variation of the couplings indicate a solvent variation of the conformational equilibrium constant, as one might expect. However, we note that for many systems of the table the solvent dependence of the vicinal couplings is "small," similar to an observation previously made by Danyluk for benzylacetone,[15] but contrary to the reported solvent dependence of 2,3-dibromopropionic acid.[16] However, the latter compound is the first entry of Table III and a spread of only 0.5 cps is observed. Such "small" variation in coupling constants might result from the preponderance of one conformer in the equilibrium. Alternatively it might reflect an inherent insensitivity of the conformational equilibrium constant to the solvent, which is contrary to the results of previous work.[17] We shall return to this point in our concluding paper.

In contrast to the small variation of the vicinal couplings is the marked solvent dependence of the chemical shift difference between the methylene hydrogens. Because the former indicates little change in conformational population, the latter serves to demonstrate again[1] that chemical-shift differences between nonequivalent protons in a methylene group are *per se* unsuitable in deriving information about conformer distribution. An interesting example of this is provided by $C_6H_5CHBrCH_2Br$, where a "crossover" in chemical shift between the methylene hydrogens has been unequivocally demonstrated.[18]

In several systems the chemical shift between nonequivalent protons seems to vary inversely with the dielectric constant of the solvent.[19] Roberts has interpreted this to mean that the chemical shift accurately reflects conformational changes. Because these conformational changes[19] are quite different from those considered here, no conflict exists between these different observations.

Some of our conclusions might be critized on the basis that our solutions are so concentrated that the medium is less like the solvent than, *e.g.*, its dielectric constant would indicate. Finegold has recently observed that vicinal couplings of several dihalides are

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(19) G. M. Whitesides, J. J. Grocki, D. Holtz, H. Steinberg, and J. D. Roberts, *ibid.*, **87**, 1058 (1965).

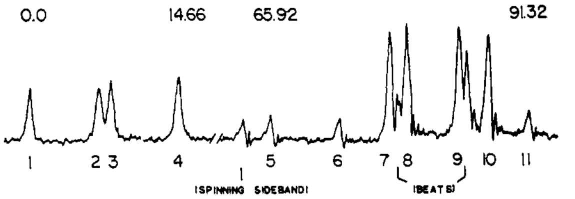


Figure 1. Spectrum of $C_6H_5CHICH_2OH$ (CH_3CN). Bottom numbers refer to line numbers (Table IV) and top are line positions in cps relative to an arbitrary zero.

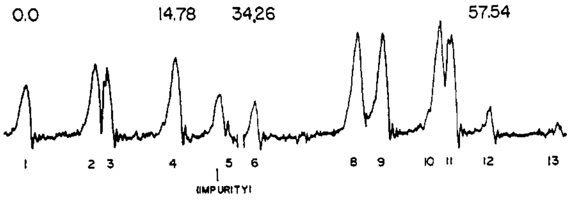
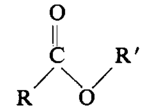


Figure 2. Spectrum of $CH_2BrCHBrCN$ (C_6H_6). Top and bottom numbers refer to line positions in cps and line numbers (Table V), respectively.

concentration dependent in the range of 0.1–0.2 mole fraction.[20] This is the same concentration range of many of our solutions. Accordingly, the solvent dependence of $CH_2BrCHBrCO_2H$ and its methyl ester in benzene solution was studied from 40 to 5% w/v concentration (0.13–0.017 mole fraction). The data[21] of Table III show that there is no significant variation in vicinal coupling constants with concentration. If these data are representative, then it seems our solutions are sufficiently dilute for solute to respond to differences in solvent properties.

The following section discusses spectral features more specific than the ones mentioned above.

2,3-Dibromopropionic Acid and Its Ethyl Ester. The acid has been shown by several types of double resonance experiments to have vicinal and geminal coupling constants of opposite sign.[22] Such an assignment gives good agreement between calculated and observed line intensities in both the acid and its ester. The spectral parameters for acid and ester are remarkably similar. The absence of any important change in coupling constants not only implies that hydrogen bonding between the carboxyl hydrogen and the β-bromine is unimportant insofar as determining conformation, but also suggests the lack of important interactions between the ester alkyl group and the acid side chain. Both of these are consistent with the carboxyl function residing predominantly in the *cis* conformation



which is generally regarded as the most stable one.[23]

2,3-Dichloropropionic Acid and Its Ethyl Ester. Line intensities were in harmony with opposite signs given to the geminal and vicinal couplings. Comments made above related to the configuration of the carboxyl group are equally applicable here.

(1-Iodo-2-hydroxyethyl)benzene. Using only line frequencies two sets of parameters were calculated differing only in the relative sign of J_{gem} and J_{vic}. Differentiation between the two assignments is possible on the basis of the relative intensity of certain pairs of lines belonging to the AB portion of the ABK spectrum. In both cases the relative intensities for the assignment with J_{gem} positive are line 5 < 6, 11 < 12, whereas for J_{gem} negative the calculated intensities are line 5 > 6, 11 > 12. The former assignment was qualitatively incompatible with observed spectra; intensity measurements for the 5–6 pair in acetonitrile solution quantitatively confirm the latter assignment. Unfortunately the intensity of line 12 was somewhat altered by a resonance signal from an unidentified impurity. Table IV and Figure 1 show the pertinent data and observations.

Table IV. Relative Sign Determination in $C_6H_5CHICH_2OH$ (Acetonitrile)

	Assignment A	Assignment B	Line no.	Calcd intensities[a] A	Calcd intensities[a] B
ν_1	7.72	7.73	1	0.817	0.818
ν_2	78.38	78.43	2	0.970	0.965
ν_3	85.89	85.82	3	1.000	0.979
J_{12}[b]	6.83	5.70	4	1.212	1.210
J_{13}[b]	7.94	9.07	5	0.158	0.099
J_{23}[b]	−11.93	11.86	6	0.148	0.213
			7	2.025	2.094
			8	2.054	2.083
			9	1.669	1.602
			10	1.640	1.605
			11	0.158	0.116
			12	0.148 (at 99.3 cps)	0.188 (at 99.3 cps)

[a] *Cf.* Figure 1. [b] *J* values given in cps.

2,3-Dihalopropionitriles. For both the bromo and chloro derivatives, examination of line intensities clearly favored the assignment where geminal and vicinal couplings were of opposite sign over the one where both were of the same sign. The pertinent data for the dibromo species are in Table V and Figure 2.

3-Ethoxycarbonyl-3-phenylpropionitrile. Spectra in various acetonitrile–benzene mixtures were obtained to ascertain if a crossover in chemical shift had occurred, similar to what has been observed for C_6H_5-$CHBrCH_2Br$. The smooth change in ν_2, ν_2, and their difference shows that none has occurred. The data do show very clearly a small solvent dependence of the vicinal coupling constants. They also demonstrate that little change occurs in vicinal couplings as acetonitrile is added to benzene until the solvent is at least 40% by volume acetonitrile. The chemical shift difference, $|\nu_3 - \nu_2|$, shows the opposite behavior, changing most rapidly as acetonitrile is added to benzene.

Most interestingly, the methylene protons of the ethyl group on the ester moiety give rise to a quartet whose members show additional fine structure. Figure 3

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[20] H. Finegold, *J. Chem. Phys.*, **41**, 1808 (1964).

[21] These data were obtained with the aid of Mr. A. Solomon, National Science Foundation Undergraduate Research Participant, 1964–1965.

[22] R. Freeman, K. A. McLauchlan, J. I. Musher, and K. G. R. Pachler, *Mol. Phys.*, **5**, 321 (1962); K. A. McLauchlan, D. H. Whiffen, *Proc. Chem. Soc.*, 144 (1962); R. Freeman and W. A. Anderson, *J. Chem. Phys.*, **37**, 2053 (1962).

[23] D. J. Millen, *Progr. Stereochem.*, **3**, 161 (1962).

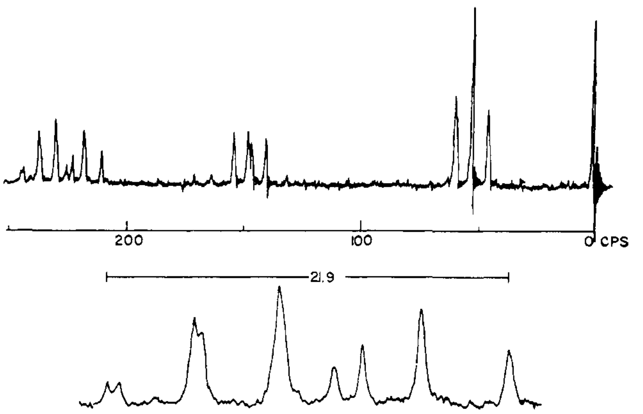


Figure 3. Spectrum of $C_6H_5CH(CO_2C_2H_5)CH_2CN(C_6H_6)$. Bottom shows CH_2 of ethyl group and benzylic proton triplet.

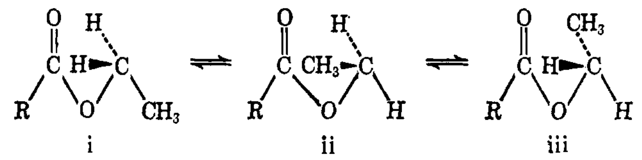
shows the lowest field member of the quartet split cleanly into a doublet. Because the resulting separation (1.0 cps) is considerably larger than that usually arising from second-order splittings in the ethyl group[24] and because it arises unsymmetrically—the high field members have no such fine structure—it seems likely that the fine structure is a consequence of nonequivalence of the methylene hydrogens. Computer calculations for an ABX_3 system with $|\nu_A - \nu_B|$, $|\nu_A - \nu_X|$, equal to 3 and 163 cps, respectively, and $J_{AB} = -10$ cps, $J_{AX} = J_{BX} = 7.1$ cps, result in a spectrum where the low-field line splits into a doublet of separation 0.9 cps. In contrast the highest field member of the "quartet" is a doublet of separation <0.01 cps.

Table V. Relative Sign Determination in $CH_2BrCHBrCN$ (Benzene Solution)

	Assignment			Calcd intensities[a]	
	A	*B*	Line no.	*A*	*B*
ν_1	8.18	8.08	1	0.677	0.686
ν_2	46.05	45.77	2	0.871	0.895
ν_3	52.32	52.71	3	0.937	1.011
J_{12}[b]	9.85	7.60	4	1.409	1.406
			5	0.087	
J_{13}[b]	5.17	7.36	6	0.344	0.195
J_{23}[b]	−10.51	10.22	(7)	0.011	0.145 (at 42.3 cps)
			8	2.089	2.223
			9	2.065	2.119
			10	1.624	1.437
			11	1.579	1.541
			12	0.233	0.183
			13	0.053	0.157

[a] *Cf.* Figure 2. [b] *J* values given in cps.

Nonequivalence of methylenes of ethyl groups in esters has recently been observed in the 10-carbethoxy-1,1-dimethyl-*trans*-decalin and $-\Delta^8$-octalin series.[25] Meyer and co-workers have ascribed the origin of nonequivalence in these systems to differences in conformer population of the ethyl group brought about by the *gem*-dimethyls. We have argued above that the close similarity in nmr parameters between other acids and their ester argues against any important steric interactions between the ethyl group and the carboxylic acid alkyl chain. Granted that the carboxylate group is also predominantly in the *cis* conformation in the ester under discussion, then it seems unlikely that the alkyl group could effect differences in conformer population. It might be argued that interactions with the carbonyl group itself will suffice to create an imbalance in conformer population. Assuming that the O–C bond is eclipsed with the C=O bond, analogous with the lowest energy state in acetaldehyde, propene, and other compounds with the structure aC(=X)Yb,[26] the conformational equilibrium would be



When the symmetry is ideal, ii and iii will be present in equal amounts. (They will be mirror images if R is symmetric.) It can then be seen that in cases where R is not symmetric, a *sufficient* condition that the ethyl methylene hydrogens be nonequivalent is that the concentrations of i and ii be different. Hence, nonequivalence could arise *via* conformational effects due to the carbonyl group, which are completely distinct from steric interactions involving the alkyl side chain.[27]

Spectra of the dibromides $C_6H_5CHBrCH_2Br$ and $(CH_3)_3CCHBrCH_2Br$ are treated in detail in the following paper.

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(24) See, *e.g.*, P. T. Narasimhan and M. T. Rogers, *J. Chem. Phys.*, 33, 727 (1960).

(25) W. L. Meyer and co-workers, *J. Am. Chem. Soc.*, 87, 1573 (1965).

(26) Reference 23, p 146.

(27) The author wishes to acknowledge fruitful correspondence with Dr. Meyer on this subject and to thank him for pointing out that the carbonyl group alone was capable of bringing about the conformational imbalance needed for nonequivalence.