Proton Nuclear Magnetic Resonance Spectra of Substituted Succinic Anhydrides, Acids, Salts, and Esters[1]

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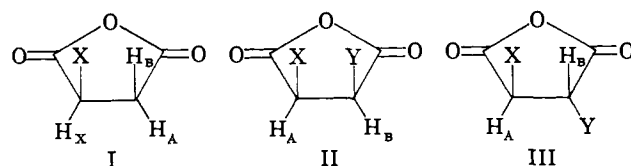Contribution from the Department of Chemistry, Grinnell College, Grinnell, Iowa. Received November 9, 1964

The proton n.m.r. spectra of three monosubstituted succinic anhydrides (I) and six disubstituted succinic anhydrides (II, III) and corresponding acids, salts, and esters have been analyzed. Proton–proton and C^{13}–proton spin-coupling constants and proton chemical shifts are reported. An unusually large solvent effect on $J_{H-H'}$ and $J_{C^{13}-H}$ for dl-dibromosuccinic anhydride is reported. Substituent effects on $J_{vicinal}$ for acyclic compounds are discussed in terms of equilibrium among rotational isomers. A simplified electrostatic model is used to account for the neutralization effects on $J_{vicinal}$ of the acids. Estimates of rotamer energies and relative steric effects of several groups are included. Chemical shifts are cited as evidence for the interpretations proposed to account for substituent and solvent effects. Dibromo and dichloro compounds have been found to have essentially equal shifts for both dl and meso anhydrides and for meso salts, where the geometry is virtually fixed.

Introduction

Ever since publication of Karplus' calculations of the dependence of $J_{HH'}$ on the dihedral angle, ϕ, for the H–C–C–H' fragment of ethane,[2] chemists have clung to the hope that spin-coupling constants obtained from n.m.r. spectra can be used to determine bond angles and conformations of organic molecules. Although subsequent work largely substantiated the general form of the ϕ-dependence ($J_{HH'} \sim 10$ c.p.s. for $\phi = 0$ and 180° with a decrease proportional to $\cos^2 \phi$ to ~ 0 at 90°) in several substituted ethanes and cyclic derivatives containing H–C–C–H' fragments, it soon became clear that indiscriminate application of the Karplus curve to highly substituted and cyclic compounds would readily lead to incorrect structural assignments. Karplus[3] has recently reviewed the problem and has critically discussed some of the other factors which might be expected to lead to deviations from the simple first-order calculation. The following factors were isolated by Karplus for discussion: (1) substituent electronegativity, (2) H–C–C' bond angle, and (3) C–C bond length. In view of the present inability to adequately handle all of these parameters theoretically, systematic accumulation of experimental data for a wide variety of simple systems must still provide bases for semiempirical generalizations which can be applied to structure determinations.
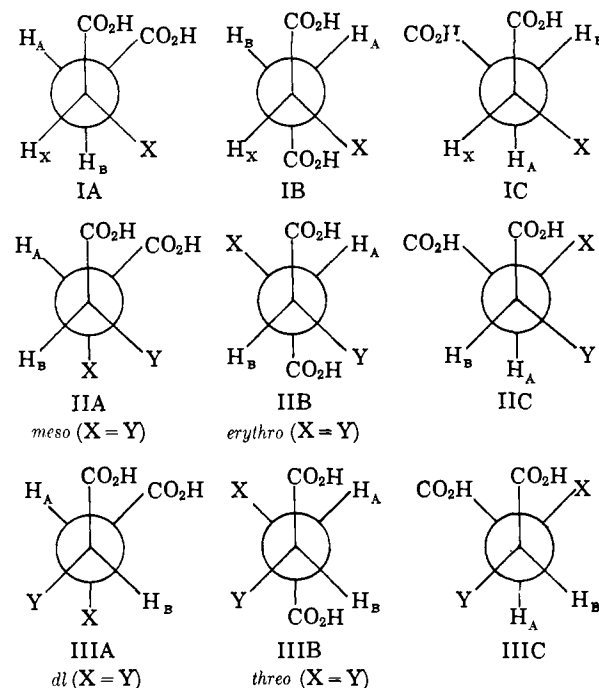
With that in mind, we undertook the investigation of several unsymmetric succinic anhydrides (I–III)

below where X = Cl, Br, OH; Y = H, Br, Cl) and the corresponding succinic acids and salts.

Subsequent recognition[4] that observation of C^{13} side bands could provide J_{AB} for symmetric compounds (X = Y) led us to expand the investigation to include dl- and meso-dihalosuccinic anhydrides. Several esters of the corresponding acids were also prepared, and their spectra were obtained. These compounds were chosen because they provided systems in which spin-coupling constants could be assigned without ambiguity. More important, drastic changes in the conformation of the H–C–C–H' moiety could be effected readily by opening the anhydride ring and neutralizing or esterifying the resultant acid.

Interpretation of the data obtained for the acyclic acids, salts, and esters, like that for other substituted ethanes, requires the recognition that the observed spectra are those of equilibrium mixtures of the three rotational isomers shown below (for the acids) for each different symmetry type.[5–8] On the basis of data

(1) This work was supported by grants from the Petroleum Research Fund (984-E8), National Science Foundation (URP Grant No. GE-3990), and Public Health Service (CA-06852).

(2) M. Karplus, J. Chem. Phys, 30, 11 (1959).

(3) M. Karplus, J. Am. Chem. Soc., 85, 2870 (1963).

(4) C. N. Banwell, A. D. Cohen, N. Sheppard, and J. J. Turner, Proc. Chem. Soc., 266 (1959).

(5) The general effects of rotational isomerism on n.m.r. parameters are treated by J. A. Pople, W. G. Schneider, and H. J. Bernstein in "High-Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959. Several papers most closely connected to this work are cited in ref. 6–8.

available for malic acid,[9] we expected to be able to account qualitatively for the changes occurring upon neutralization in terms of increased stabilization of conformation B for the divalent salt because of smaller electrostatic repulsion between the negative CO_2^- groups in B relative to A and C. We expected similarly that esterification of the carboxyl groups should stabilize B relative to A and C by increasing the effective size of that group. These expectations have been largely substantiated. By introducing simplifying assumptions, we have made some estimates of relative rotamer populations and, hence, energy differences between rotamers for some of these compounds.

Experimental

N.m.r. Spectra. Except for the malic anhydride and malic acid spectra,[10] all spectra were recorded on a Varian A-60 high-resolution spectrometer. Tetramethylsilane was included as an internal standard for chemical shift measurement in organic solvents; tetramethylammonium bromide was used in aqueous solutions (usually D_2O). Neat liquid samples or 1-2 M solutions were usually used.

In order to observe C^{13} side bands where such observations were made, 1 g. of solute was dissolved in 1 ml. of solvent. Chemical shifts at infinite dilution were obtained by extrapolation, but C^{13} side bands could not usually be observed at much lower concentrations.

Spectra of the acids and salts in D_2O were obtained as follows. A small amount of HCl was added to one sample to suppress ionization and ensure presence of the fully protonated species. A second sample was then titrated with NaOH (in D_2O) and the spectrum was recorded at intervals until neutralization was complete. In the case of *erythro*-2-chloro-3-bromosuccinic acid, J_{AB} was obtained by extrapolation of values obtained after a portion had been titrated, since the two protons have essentially equal chemical shifts in the acid, for which only a single line is observed.

Analysis of Spectra. Spin-coupling constants and chemical shifts were calculated by familiar procedures.[11]

The three protons of the monosubstituted derivatives yield typical ABX spectra. The assignment of A and B protons was made on the basis of the AX spectrum of malic anhydride-d_B, in which the two protons are known to be *cis*.[12] The vicinal spin-coupling constant obtained, 9.0 ± 0.1 c.p.s., identifies the larger of the two vicinal coupling constants of malic anhydride as being due to the *cis* protons. This further requires that the downfield methylene signal is from the proton *cis* to X.

Unsymmetric dihalo compounds yield AB spectra. For the symmetric dihalo compounds, J_{AB} and $J_{C^{13}-H}$ were obtained from the C^{13} satellites which appear as doublets on either side of the strong C^{12}–H proton peak.

The separation of the doublet components is just J_{AB}, and the separation of the centers of the doublets is $J_{C^{13}-H}$.

Solvents. Solvents used were reagent grade and were employed without further purification except for drying over molecular sieve.

Chlorosuccinic and Bromosuccinic Anhydrides. These were prepared by the method of Anshutz and Bennett.[13] Ten grams of fumaric acid in 35 g. of acetic acid was sealed in a pressure tube with 15-22 g. of acetyl halide. The mixture was heated 5-7 hr. at 120-130° and then concentrated to half its original volume by distilling off acetic acid and excess acetyl halide. The n.m.r. spectrum of the resultant mixture, which contained some unreacted fumaric acid and maleic anhydride (formed in the first step of the reaction), was obtained without any attempt to separate or purify the anhydride. Subsequent treatment with water produced the corresponding acid whose spectrum in acetic acid was also obtained. Upon standing, the acids precipitated from the supersaturated solution and were then separated by filtration and purified by recrystallization from chloroform; m.p. of bromosuccinic acid 161-162° (*vs.* lit.[13] 160-161°) and of chlorosuccinic acid 154-155° (*vs.* lit.[13] 153-154°).

Malic Anhydride. Malic anhydride was prepared from disilver malate by the action of thionyl chloride in anhydrous tetrahydrofuran (THF).[14] Silver chloride was removed from the reaction mixture by filtration, and part of the THF was removed under vacuum. The proton n.m.r. spectrum of the concentrated reaction mixture was obtained directly. Since subsequent addition of water produced malic acid, the previous presence of the anhydride was verified. All of the THF was removed from one of the anhydride samples, and the melting point of the unpurified material, 70-77° (*vs.* lit. 75-76°), provided additional confirmation of the identity of the anhydride.

The monodeuterio isomer, malic anhydride-d_B, was prepared from the corresponding acid in the manner described above. Malic acid-d_B was first prepared from fumaric acid by the stereospecific, fumarase-catalyzed addition of D_2O in heavy water.[12]

threo-2-Bromo-3-chlorosuccinic Anhydride. *threo*-2-Bromo-3-chlorosuccinic anhydride was prepared by the *trans* addition of BrCl to maleic anhydride in chloroform in the sunlight.[15] The BrCl was produced by bubbling dry chlorine gas into a solution of bromine in chloroform. The anhydride separated from the reaction mixture on standing and was recrystallized from chloroform. N.m.r. analysis showed that appreciable quantities of *dl*-2,3-dichlorosuccinic anhydride and a trace of 2,3-dibromosuccinic anhydride were also produced. Since the presence of the dichloro anhydride did not interfere with the analysis of the spectra, no great pains were taken to effect a complete separation of the two compounds. Addition of water to the anhydride and subsequent vacuum drying yielded *threo*-2-bromo-3-chlorosuccinic acid.

erythro-2-Bromo-3-chlorosuccinic Acid. *erythro*-2-Bromo-3-chlorosuccinic acid was prepared by the *cis*

(6) F. A. L. Anet, *J. Am. Chem. Soc.*, **84**, 747 (1962).
(7) A. A. Bothner-By and C. Naar-Colin, *ibid.*, **84**, 743 (1962).
(8) H. S. Gutowsky, G. G. Belford, and P. E. McMahon, *J. Chem. Phys.*, **36**, 3353 (1962).
(9) R. A. Alberty and P. Bender, *J. Am. Chem. Soc.*, **81**, 542 (1959).
(10) L. E. Erickson, Ph.D. Thesis, University of Wisconsin, 1959.
(11) J. D. Roberts, "An Introduction to Spin-Spin Splitting in High-Resolution Nuclear Magnetic Resonance," W. A. Benjamin, Inc., New York, N. Y., 1961.
(12) O. Gawron, A. J. Glaid, III, and T. P. Fondy, *J. Am. Chem. Soc.*, **83**, 3634 (1961); F. A. L. Anet, *ibid.*, **82**, 994 (1960).

(13) R. Anshutz and C. Bennett, *Ann.*, **254**, 155 (1889).
(14) W. S. Denham and H. Woodhouse, *J. Chem. Soc.*, **103**, 1870 (1913).
(15) P. Walden, *Ber.*, **30**, 2887 (1897).

Table I. Spin-Coupling Constants of Succinic Anhydrides, Acids, Salts, and Dimethyl Esters[a]

Parent compound	J_{ij}	Anhydride (solvent)	Acid (solvent)	Salt in D_2O	Dimethyl ester (neat)
(OH, H_B / H_X, H_A)		(THF)	(D_2O)		
	J_{AX}	8.6[b]	7.0	10.3	...
	J_{BX}	6.8[b]	4.4	2.8	...
	J_{AB}	18.2[b]	17.1	15.3	...
(Cl, H_B / H_X, H_A)		(Acetic acid)	(D_2O)		
	J_{AX}	9.0	7.3	10.8	...
	J_{BX}	5.7	5.7	3.4	...
	J_{AB}	19.1	17.5	15.6	...
(Br, H_B / H_X, H_A)		(Acetic acid)	(D_2O)		
	J_{AX}	8.7	7.1	8.9	8.1
	J_{BX}	4.9	7.1	6.1	6.7
	J_{AB}	19.8	17.5	15.8	17.0
	$J_{C^{13}-H}$	...	...	...	(148, 148)
(Br, H_B / H_A, Br)		(Neat)			
	J_{AB}	3.7	...	....	9.3
	$J_{C^{13}-H}$ (C–H)	170	...	...	163
	$J_{C^{13}-H}$ (CH_3)	...	...	...	149
(Br, H_B / H_A, Cl)		(Benzene)	(D_2O)		
	J_{AB}	6.6	5.8	4.2	...
(Cl, H_B / H_A, Cl)		(Several)			
	J_{AB}	8.0	...	...	6.0
	$J_{C^{13}-H}$ (C–H)	160	...	...	156
	$J_{C^{13}-H}$ (CH_3)	...	...	...	150
(Br, Br / H_A, H_B)		(Acetic anhydride)	(THF)		
	J_{AB}	7.0	11.9	11.3	11.0
	$J_{C^{13}-H}$ (C–H)	165	163	161	167
	$J_{C^{13}-H}$ (CH_3)	...	...	...	149
(Br, Cl / H_A, H_B)		(Acetic anhydride)	(THF)		
	J_{AB}		11.0	10.8	...
(Cl, Cl / H_A, H_B)		(Acetic anhydride)	(THF)		
	J_{AB}	7.0	9.0	8.9	9.2
	$J_{C^{13}-H}$ (C–H)	165	160	161	161
	$J_{C^{13}-H}$ (CH_3)	...	...	...	150

[a] Estimated accuracy: within ±0.2 c.p.s. for J_{AB}, ±1 c.p.s. for $J_{C^{13}-H}$. [b] L. Erickson, Ph.D. Thesis, University of Wisconsin, 1959.

addition of HBr to chlorofumaric acid in acetic acid.[16] Chlorofumaric acid was obtained (via chlorofumaric acid chloride) by the action of PCl_5 on meso-tartaric acid. The erythro acid separated on cooling the reaction mixture, m.p. 223–235° (vs. lit.[16] 235°); neut. equiv., 115 (vs. 115.7 for $C_4H_4O_4BrCl$).

dl-Dihalosuccinic Anhydrides and Acids. dl-Dichlorosuccinic anhydride and dl-dibromosuccinic anhydride were prepared by the addition of Cl_2 and Br_2, respectively, to maleic anhydride in chloroform in the sunlight.[17] The solid anhydrides precipitated upon removal of a portion of the solvent under vacuum and were recrystallized from carbon tetrachloride. Again, the corresponding acids were obtained by addition of water to the anhydrides; m.p. of dl-dichlorosuccinic acid 177–178° (vs. lit. 175°), dl-dibromosuccinic acid 170–171° (vs. lit. 166–167°).

meso-Dihalosuccinic Acids. These were obtained commercially from Eastman Kodak and K and K Laboratories and were used without further purification.
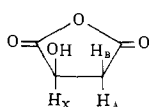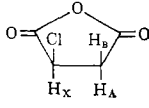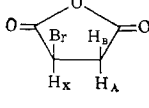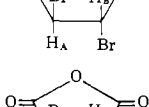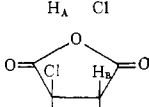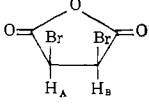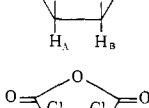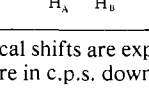
(16) W. K. Perkin, J. Chem. Soc., 53, 696 (1888).
(17) A. Michael, J. prakt. Chem., 52, 292 (1895).

meso-Dihalosuccinic Anhydrides. These compounds were obtained (and the spectra run) without isolation by adding 10 g. of the corresponding acid to 10 ml. of acetic anhydride and shaking at room temperature. Appearance of the acetic acid methyl peak (n.m.r.) and disappearance of the acetic anhydride methyl peak measured progress of the reaction as the acid slowly dissolved. At higher temperatures HX was apparently eliminated rapidly, and no anhydride was obtained. In one run with meso-dibromosuccinic acid containing fumaric acid, the conversion to anhydride appeared to be virtually quantitative, and HBr elimination was minimal. A small amount of fumaric acid was used in subsequent syntheses of both anhydrides, with a similar effect. Attempts to remove solvent by evaporation resulted in decomposition of the anhydride (loss of HX), so spectra were run on the reaction mixture and on solutions of the reaction mixture in various solvents.

Esters. All the esters whose spectra are included in this report and the method of synthesis, heating an excess of alcohol with acid in the presence of a mineral acid catalyst, are described in the literature.[18] Upon

Table II. Proton Chemical Shifts of Succinic Anhydride, Acids, Salts, and Dimethyl Esters at 60 Mc.

Parent compound	Proton	Anhydride[a] (solvent)	Acid[a] (solvent and concn.)	Acid[b] in D_2O	Salt[b] in D_2O	Dimethyl[a] ester
		(THF, 2 M)	(THF, 2 M)			
	H_X	290.0	265.5	90.5	67.2	
	H_A	192.2		−19.7	−49.2	
	H_B	169.1	(161.0)	−13.6	−31.2	
	CH_3	...	...	...	...	
		(CH_3CO_2H, 2 M)	(CH_3CO_2H, 2 M)			
	H_X	308.6	284.5	99.4	83.6	
	H_A	223.5		−2.8	−34.8	
	H_B	196.5	(186.7)	−0.7	−16.6	
	CH_3	...	...	...	...	
		(CH_3CO_2H, 2 M)	(CH_3CO_2H, 2 M)			(Neat)
	H_X	305.2	276.1	92.0	80.0	278
	H_A	227.7	185.0	−2.3	−26.8	182
	H_B	198.3	197.2	6.5	−9.6	194
	CH_3	...	...	...	...	222, 227
		(THF)	(THF)			(Neat)
	H	325	278	111.3	99.1	287
	CH_3	...	...	...	...	229
	H_A, H_B	325	285	123.5	(114.6, 108.7)	...
	CH_3	...	...	...	...	...
		(THF)	(THF)			(Neat)
	H	325	294	133.0	116.7	300
	CH_3	...	...	...	...	230
		(Acetic anhydride)	(THF)			(Neat)
	H	329	275	93.0	70.5	282
	CH_3	...	...	...	...	231
			(THF)			(Neat)
	H_A, H_B	...	...	99.9	(74.9, 69.0)	...
	CH_3	...	...	...	...	...
		(Acetic anhydride)	(THF)			(Neat)
	H	327	275	118	71	284
	CH_3	...	...	...	...	231

[a] Chemical shifts are expressed in c.p.s. downfield from internal TMS standard, extrapolated to infinite dilution except as noted. [b] Chemical shifts are in c.p.s. downfield from internal tetramethylammonium bromide. No significant concentration dependence was observed.

subsequent cooling, phase separation occurred. The ester phase was washed with water to remove unreacted alcohol and dried. Spectra were run on the neat liquids or supercooled liquids and on solutions in several solvents. The n.m.r. spectrum was used to verify the identity of each ester.

Results

Spin-coupling constants of all anhydrides, acids, salts, and dimethyl esters are listed in Table I; chemical shifts, in Table II. It should be noted that chemical shifts are measured in c.p.s. (at 60 Mc.) *downfield* from TMS or—in the case of aqueous solutions of acids and salts—tetramethylammonium bromide.[19] Table III summarizes the large solvent dependence observed for the n.m.r. parameters of the dihalo

anhydrides. Data for six dibromosuccinate esters are recorded in Table V.

Discussion

Anhydride Spin-Coupling Constants. Vicinal coupling constants summarized in Table I for substituted succinic anhydrides can be compared with data for similar compounds in the literature. In discussing the spin-coupling constants observed in cyclic derivatives of 2,3-disubstituted butanes, Anet[6] has cited n.m.r. data for several five-membered, heterocyclic ring compounds which are structurally similar to the substituted succinic anhydrides. These include cyclic carbonates and dioxolanes,[20] 2,3-dihydrofuran,[21] cyclopentanone,[22] and the camphors.[23] Vicinal coupling

(18) F. K. Beilstein, "Handbuch der organischen Chemie," Band II, 1st Ed., 1920, pp. 619–626.
(19) A. Loewenstein and J. D. Roberts, *J. Am. Chem. Soc.*, **82**, 2705 (1960); L. E. Erickson and R. A. Alberty, *J. Phys. Chem.*, **66**, 1702 (1962).

(20) R. V. Lemieux, *Can. J. Chem.*, **39**, 116 (1961).
(21) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press Inc., New York, N. Y., 1959, p. 87.
(22) F. A. L. Anet, *Can. J. Chem.*, **39**, 2316 (1961).
(23) F. V. Brutcher, Jr., T. Roberts, S. J. Barr, and N. Pearson, *J. Am. Chem. Soc.*, **81**, 4915 (1959).

constants have also been determined for cyclic, five-membered ring sulfites[24] and for the two products of HBr addition to acenaphthalene. Vicinal coupling constants for the three monosubstituted succinic anhydrides are in general agreement with these results; coupling between *cis* protons is greater (8.6–9.0 c.p.s.) than that between *trans* protons (4.9–6.8 c.p.s.), and all vicinal coupling constants are in the range 5–9 c.p.s. However, the relatively large effect of N-substituents on J_{cis} and J_{trans} for 2,3-dimethylindoline[25] shows that factors other than conformation can have large effects on vicinal coupling constants.

Careful studies of cyclopropanes,[26, 27] norbornenes,[28] and epoxides,[26] where conformational effects should be minimal, show that $J_{cis} > J_{trans}$ and that *both* J_{cis} and J_{trans} increase approximately linearly with decreasing substituent electronegativity when only one substituent at one position is varied. However, for the monosubstituted succinic anhydrides, J_{cis} is virtually independent of substituent while J_{trans} increases with increased substituent electronegativity for the three monosubstituted succinic anhydrides considered. This may reflect a significant steric effect of X on the conformation of what may be a rather flexible H_2C–CHX moiety of the anhydride. Similarly, for the anhydrides in the "*dl*" series (III), J_{AB} varies from 8.0 to 6.0–2.5 c.p.s. in going from X = Y = Cl to X = Y = Br. This trend is the same as that observed for the corresponding spin-coupling constant, J_{BX}, in the monosubstituted series (I).

On the basis of the data for the monosubstituted anhydrides, one might expect $J_{cis} > J_{trans}$ for disubstituted anhydrides. In fact, the observed coupling constants vary considerably with the nature of substituent and—in the case of *dl*-dibromosuccinic anhydride—with solvent. For the dichloro isomers, the *dl* compound (protons *trans*) has the larger J_{AB} (8.0 *vs.* 7.0). By contrast, for the dibromo isomers, the *meso* compound (protons *cis*) has a larger J_{AB} (7.0 *vs.* 6.0–2.5).

The geminal coupling constants observed for the three monosubstituted anhydrides are quite large (18.2–19.8 c.p.s.), as is the case in systems in which the CH_2 group is adjacent to a substituent with considerable π-bonding. Barfield and Grant[29] have discussed these data and the effect of π-bonding on geminal coupling constants in considerable detail. The sign of J_{AB} for these compounds was not determined by the ABX analysis, but current opinion favors a negative sign.

Following Muller and Pritchard's early lead,[30] $J_{C^{13}-H}$ has been used to estimate the percentage of s-character of the carbon orbital used in bonding to H. For the four symmetric disubstituted anhydrides considered here, $J_{C^{13}-H}$ varies from 160 to 172 c.p.s.,

indicating something close to sp^2 hybridization for the carbon orbital (34–36% s-character). Recent work by Karabatsos and Orzech,[31] however, suggests that the correlation between $J_{C^{13}-H}$ and the percentage of s-character of the carbon orbital is not as good as earlier results suggested.

It is of interest that $J_{C^{13}-H}$, like J_{cis} and J_{trans}, for these succinic anhydrides is very similar to values for corresponding substituted cyclopropanes. J_{gem}, however, is much smaller in the cyclopropanes, for which the attenuating effect of a C=O group is not present.

Anhydride Shifts. Anhydride chemical shifts are summarized in Table II. Like Williamson,[26,28] we find a fair correlation between internal chemical shift, $\nu_A - \nu_X$ and $\nu_B - \nu_X$, and substituent electronegativity for monosubstituted anhydrides. On the basis of only three compounds, we find a slope of about 45 c.p.s./electronegativity unit for $\nu_X - \nu_A$ and 30 c.p.s./ electronegativity unit for $\nu_X - \nu_B$. These values, based on Cavanaugh and Dailey's electronegativity scale,[32] are to be compared with 100 and 66 c.p.s./ electronegativity unit observed by Williamson for corresponding protons of substituted bicycloheptenes and 128 and 110 c.p.s. for 1,1-dichlorocyclopropanes. For all three systems, the proton *cis* to X is more sensitive to the nature of X, but the succinic anhydride chemical shifts are much less sensitive to substituent electronegativity than are either of the other two systems.

In each of the three monosubstituted anhydrides (I), the shift of the methylene proton *cis* to X, H_B, is upfield from the proton which is *trans*. Similar observations have been made for the cyclic compounds mentioned above and for bromocyclopropane.[33]

For the disubstituted anhydrides (Tables II and III) the following generalizations are significant. (1) All three of the *dl* anhydrides have essentially the same chemical shift; both *meso* anhydrides also have the same chemical shift. (2) *meso* anhydride chemical shifts are invariably larger (more downfield) than corresponding *dl* anhydride shifts. A combination of electronegativity (Cl > Br) and neighbor anisotropy (Br > Cl and directional dependent) effects can be invoked to account for these results. The magnitude of anisotropy effects that have been estimated are consistent with this interpretarion.[32,34]

Solvent Effects on Chemical Shifts and Spin-Coupling Constants of Disubstituted Anhydrides. Of the four dihalo anhydrides, *dl*-dibromosuccinic anhydride showed a large solvent dependence for J_{AB} and $J_{C^{13}-H}$ which was investigated in more detail. The results are summarized in Table III. Both J_{AB} and $J_{C^{13}-H}$ vary with the nature of the solvent. As J_{AB} increases, $J_{C^{13}-H}$ decreases. By contrast, J_{AB} and $J_{C^{13}-H}$ are both independent of solvent for *dl*-dichlorosuccinic anhydride over the whole range from chloroform to acetone (Figure 1).

The basicity of the solvent appears to be the property which is responsible for the large effects. For the

(24) J. G. Pritchard and P. C. Lauterbur, *J. Am. Chem. Soc.*, 83, 2105 (1961).

(25) F. A. L. Anet and J. M. Muchowski, *Chem. Ind.* (London), 81 (1963).

(26) K. L. Williamson, C. A. Lanford, and C. R. Nicholson, *J. Am. Chem. Soc.*, 86, 762 (1964).

(27) D. J. Patel, M. E. H. Howden, and J. D. Roberts, *ibid.*, 85, 3220 (1963).

(28) K. Williamson, *ibid.*, 85, 516 (1963); P. Laszlo and P. R. Schleyer, *ibid.*, 85, 2709 (1963).

(29) M. Barfield and D. M. Grant, *ibid.*, 85, 1899 (1963).

(30) N. Muller and D. E. Pritchard, *J. Chem. Phys.*, 31, 768, 1471 (1959).

(31) G. J. Karabatsos and C. E. Orzech, Jr., *J. Am. Chem. Soc.*, 86, 3574 (1964).

(32) R. J. Cavanaugh and B. P. Dailey, *J. Chem. Phys.*, 34, 1099 (1961).

(33) K. W. Wiberg and B. J. Nist, *J. Am. Chem. Soc.*, 85, 2788 (1963).

(34) J. H. Goldstein and G. S. Reddy, *J. Chem. Phys.*, 36, 2644 (1962); H. Spiesecke and W. G. Schneider, *ibid.*, 35, 722 (1961).

Table III. Solvent Effects on Spin-Coupling Constants and Chemical Shifts of Dihalosuccinic Anhydrides[a,b]

Compound		Acetone	Dioxane	Acetic anhydride	Acetic acid	Benzene	Neat	Chloroform
dl-Dibromosuccinic anhydride	J_{AB}	6.0	6.0	5.0	4.8	3.8	3.7	2.5
	$J_{C^{13}-H}$	166	165	167	168	170	170	172
	ν	342	317	315	316	211	308	291
dl-Dichlorosuccinic anhydride	J_{AB}	8.0	8.0	8.1	...	8.0	8.0	...
	$J_{C^{13}-H}$	160	160	160	...	160	160	...
	ν	340	318	318	316	216	...	291
meso-Dibromosuccinic anhydride	J_{AB}	...	...	6.9	...	...	...	...
	$J_{C^{13}-H}$	...	...	165	...	...	...	...
	ν	349	323	(329)		234	...	311
meso-Dichlorosuccinic anhydride	J_{AB}	...	...	7.0	...	...	...	...
	$J_{C^{13}-H}$	...	...	165	...	...	...	...
	ν	348	322	(327)		231	...	310

[a] Chemical shifts, ν, in c.p.s. downfield from internal TMS, extrapolated to infinite dilution in each solvent. [b] Estimated maximum uncertainties: J_{AB}, ± 0.2; $J_{C^{13}-H}$, ± 1; ν, ± 1 c.p.s.

most basic solvents used (dioxane, acetone, and tetrahydrofuran), J_{AB} is large (6.0 c.p.s.). For the least basic solvents (methylene chloride and chloroform), J_{AB} is small (2.5 c.p.s.). For more basic solvents than those listed (pyridine and dimethyl sulfoxide), the anhydrides decompose on contact. For less basic solvents (carbon tetrachloride and cyclohexane), the anhydrides are not soluble enough to obtain C^{13} side bands.
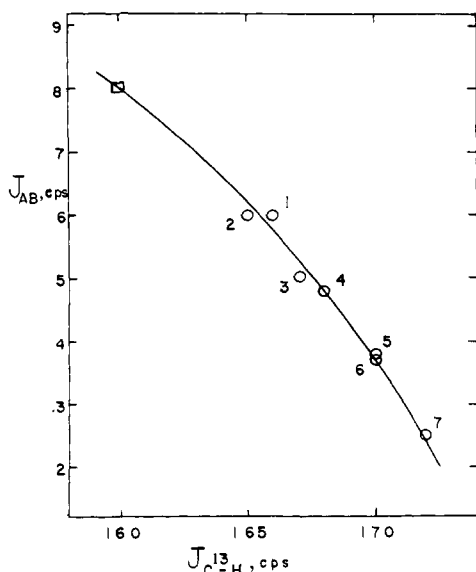

Figure 1. Solvent and substituent effects on J_{AB} and $J_{C-^{13}H}$ for *dl*-dihalosuccinic anhydrides. O, dibromo; □, dichloro. The numbered points correspond to solvents as given in Table III. The single point indicated for *dl*-dichlorosuccinic anhydride represents overlap of data for five solvents.

With the exception of benzene, where π-electron circulation effects produce huge upfield shifts for all of the anhydrides, there is a good correlation between chemical shift and J_{AB}. Solvents which increase J_{AB} relative to the neat liquid produce a downfield shift (less shielding), while those which decrease J_{AB} produce an upfield shift (more shielding). Surprisingly, solvent effects on the chemical shifts of the other three anhydrides, where there are no measurable effects on J_{AB} or $J_{C^{13}-H}$, closely parallel those for *dl*-dibromo-

succinic anhydride. Shaeffer and Schneider[35] attribute similar solvent effects on chemical shifts of protons *meta* to substituent X in *para*-substituted toluenes to specific hydrogen bonding of that proton to acceptor solvent molecules. The most basic solvents produce the most downfield shift (except for benzene).

In light of the similarity in hydrogen-bonding properties of the two *dl* anhydrides and the fact that $J_{C^{13}-H}$ changes invariably accompany J_{AB} changes, it seems unlikely that the solvent effect on J_{AB} for the dibromo anhydride is simply a result of significant conformational changes. Very likely, the much greater polarizability of bromine relative to chlorine is responsible for the difference. Since the single point obtained for the dichloro compound in several solvents lies along the extrapolated smooth curve obtained for the dibromo compound in the same solvents (Figure 1), the effect of both substitution and solvent might be simply to change the hybridization of the carbon orbital without changing the conformation of the $H_A-C-C-H_B$ fragment significantly.

Regardless of the origin of these effects, their significance is clear. In comparing data for different compounds, the possibility of large solvent effects on spin-coupling constants cannot be overlooked, even in cyclic compounds where the geometry of the molecule might be expected to be relatively fixed.

Vicinal Coupling Constants and Conformational Equilibria for Acyclic Derivatives. Relative populations of rotamers A, B, and C can be calculated from energy differences determined from the temperature dependence of J, provided that a value can be assigned to J_{gauche} and J_{trans} or that a sufficient temperature range can be investigated.[8] Attempts to measure these changes for some of the esters have not been particularly successful as the changes were quite small. In the case of the *meso* esters J_{AB} was found to be virtually insensitive to temperature from room temperature to 150°. A slight increase, 0.4 ± 0.2 c.p.s., was, in fact, noted for both *meso* esters. Since a temperature increase would be expected to lead to *increased* contribution from rotamers IIA and IIC, in which protons are *gauche* (small J), this result is somewhat surprising. We plan to investigate these temperature effects in more detail. Although exact values for rotamer energy

(35) T. Shaeffer and W. C. Schneider, *J. Chem. Phys.*, **32**, 1218 (1960).

differences cannot be derived from the data obtained, it can be shown that the data are consistent with a model which considers only *gauche* interactions between bulky groups and attributes the effect of neutralization to electrostatic repulsion between carboxyl groups considered as point charges. Figure 2, a schematic representation which shows the relative energies of the three rotamers for the three types of compounds and the effect of neutralizing the carboxyl groups, is provided as a convenient reference for the discussion which follows.

Estimates of relative rotamer energies were made on the basis of the following assumptions. (1) Only *gauche* CO_2H-X, CO_2H-CO_2H, or X-X interactions need be considered. (2) A value of 1000 cal./mole was assigned to *gauche* CO_2H-Br, Br-Br, and CO_2H-CO_2H configurations, and 500 cal./mole was assigned to *gauche* Cl-CO_2H and Cl-Br configurations. Equating CO_2H-Br, Br-Br, and CO_2H-CO_2H interactions can be justified by the fact that $J_{AX} = J_{BX} = 7.1$ c.p.s. for bromosuccinic acid. Since $J_{AX} = J_{BX}$ in conformation IA and the roles of H_A and H_B are reversed in IB and IC, IB and IC must contribute equally in order that $J_{AX} = J_{BX}$—hence, the equality of CO_2H-Br and CO_2H-CO_2H interactions. The assignment of 1000 cal./mole to the Br-Br interaction is supported by data for dibromethane.[36,37] To complete the calculations, we took $J_{trans} = 12$ c.p.s. and $J_{gauche} = 3$ c.p.s. The vicinal coupling constants were calculated for each compound by

$$J_{calcd} = f_A J_A + f_B J_B + f_C J_C =$$
$$f_A J_A + f_A e^{-(E_B - E_A)/RT} J_B + f_A e^{-(E_C - E_A)/RT} J_C \quad (1)$$

where f_i is the fraction in the ith rotamer, J_i is the corresponding vicinal coupling constant, and the exponential terms have the usual significance. For monobromosuccinic acid, $f_B = f_C$ so that $f_B = f_C = 1/(2 + e^{-1000/RT})$. This yields $J_{AX} = J_{BX} = 7.1$ c.p.s. at $25°$ (*vs.* observed 7.1 c.p.s.). For the two dibromo acids, the two high energy rotamers make equal contributions, so that $f_C = 1/(2 + e^{-1000/RT})$ and $J_{calcd} = 9.5$ c.p.s. at $25°$ (*vs.* observed 11.9 for *meso* in THF and 9.3 *for the dl ester*). Unfortunately, these values are rather insensitive to ΔE changes of a few hundred calories, and J_{AB} is not available for aqueous solutions. For chlorosuccinic acid a similar calculation, based on $E_A - E_C = 1000$ and $E_B - E_C = 500$ cal./mole, yields $J_{AX} = 8.0$ (*vs.* 7.3) and $J_{BX} = 6.1$ (*vs.* 5.7) c.p.s. The smaller value estimated for $E_B - E_C$ reflects the smaller steric effect of Cl relative to Br.

For calculating the additional electrostatic stabilization imparted to conformation B as a result of neutralization of the carboxyl groups, it was assumed that the negative charges of the carboxylate ion can be represented as point charges located along the extension of the methylene carbon–carboxyl carbon bond. Taking C–C = 1.54 and 2.14 Å. for the distance between the point charge and the nearest methylene carbon, the electrostatic energy for the carboxyl
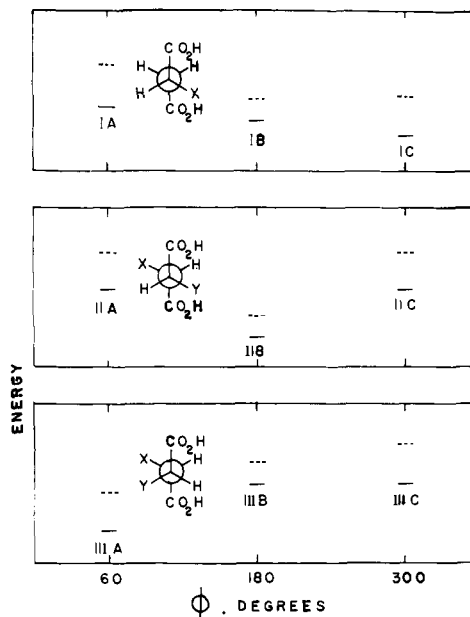
(36) S. Mizushima, "Structure of Molecules and Internal Rotation," Academic Press, New York, N. Y., 1954, p. 65.

(37) We feel that the energy difference between rotamers for CH_2-Br-CHBr$_2$, which should be very similar to bromosuccinic acid according to the above arguments, estimated by Gutowsky, *et al.*,[8] is unreasonably small.

Figure 2. Schematic representation of relative rotamer energies of substituted succinic acids (————) and salts (---------). The dihedral angle, ϕ, is taken to be that between CO_2H groups, so that the conformation shown corresponds to B ($\phi = 180°$) in each case.

groups for $\phi = 60°$ (*gauche*) and $180°$ (*trans*) based on Coulomb's law was calculated. This was added to the relative energies assumed above for the acids to obtain the relative rotamer energies and populations of the salts. Vicinal spin-coupling constants were then calculated for the salts using the same values for J_{trans} (12 c.p.s.) and J_{gauche} (3 c.p.s.) as were used for the acids. Results are given in Table IV. Initial calculations using the bulk dielectric constant of water (80) predicted neutralization effects which are somewhat smaller than those observed. By using a somewhat smaller effective dielectric constant as suggested by Kirkwood and Westheimer in their classic calculations of dissociation constants of organic acids,[38] neutralization effects on J_{AX} and J_{BX} for chlorosuccinic and bromosuccinic acids which gave somewhat better agreement with observed values were obtained. All values tabulated on Table IV are based on an effective dielectric constant of 60.

Although this model for calculating relative rotamer populations of the monosubstituted acids is admittedly relatively crude since it ignores dipole–dipole and charge–dipole interactions, it does predict correctly the approximate extent of neutralization effects. Furthermore, it predicts correctly both that J_{AX} should be more affected by neutralization than J_{BX} and that $J_{AX} + J_{BX}$ should be increased by neutralization.

These estimates and calculations were extended to the disubstituted acids (Table IV). Energy differences between rotamers were estimated as described earlier. For the *meso* salts, the agreement between theory and experiment is reasonably good. Unfortunately, we were able to obtain a high enough concentration of acids to observe C^{13} side bands only in THF. For the *dl* series, lower solubilities made it impossible to obtain data for any of the symmetric acids and salts.

(38) J. G. Kirkwood and F. H. Westheimer, *J. Chem. Phys.*, 6, 506, 513 (1938).

Table IV. Vicinal Proton Spin-Coupling Constants and Estimated Relative Rotamer Energies of Halogen-Substituted Succinic Acids and Salts

Compound	Form	$E_A - E_B$, cal./mole	$E_A - E_C$, cal./mole	Calcd.[a] J_{AX}	Calcd.[a] J_{BX}	Obsd. J_{AX}	Obsd. J_{BX}
Bromosuccinic	Acid	1000	1000	7.1	7.1	7.1	7.1
	Salt	1516	1000	9.0	5.5	8.9	6.1
Chlorosuccinic	Acid	1000	500	8.0	6.1	7.3	5.7
	Salt	1516	500	10.2	4.3	10.8	3.4
meso-Dibromosuccinic	Acid	1000	0	9.5	...	11.9 (THF)	...
	Salt	1516	0	10.7	...	11.3	...
meso-Dichlorosuccinic	Acid	500	0	7.7	...	9.0 (THF)	...
	Salt	1016	0	9.5	...	8.9	...
dl-Dibromosuccinic	Acid	−1000	−1000	...	9.5	...	9.3 for dimethyl ester
	Salt	−484	−1000	...	8.5	...	
dl-Dichlorosuccinic	Acid	0	−1000	...	7.0	...	6.0 for dimethyl ester
	Salt	516	−1000	...	5.5	...	

[a] Based on J_{trans} = 12 c.p.s. and J_{gauche} = 3 c.p.s. and relative energies tabulated.

The neutralization effect on J_{AB} for threo-2-bromo-3-chlorosuccinic acid (5.8 to 4.2 c.p.s.), however, is about that expected on the basis of the calculated values for the two symmetric acids (dibromo, 9.5 to 8.5; dichloro, 7.0 to 5.5 c.p.s.), but the absolute values are less than those calculated.

It was expected that esterification would produce effects on J_{AB} that could be accounted for by a similar analysis of the expected effects on steric interactions. These expectations have been approximately realized for dimethyl bromosuccinate and the three meso- and three dl-dibromosuccinates, whose n.m.r. parameters are summarized in Table V. The investigation included only esters of bromo acids where neglect of gauche H–H and X–H interactions would be expected to be a fair approximation.

Table V. Comparison of Chemical Shifts[a] and Spin-Coupling Constants[b] for Dibromosuccinate Esters

Ester	J_{AB}, c.p.s. Obsd.	J_{AB}, c.p.s. Calcd.[c]	$J_{C^{13}-H}$, c.p.s.	ν_H, c.p.s.
meso-Dimethyl	11.0	9.8	164	282
meso-Diethyl	11.3	...	165	279
meso-Diisopropyl	11.2	10.7	165	274
dl-Dimethyl	9.3	10.0	163	287
dl-Diethyl	9.7	...	162	279
dl-Diisopropyl	10.3	10.5	162	274

[a] In c.p.s. (±1) downfield from TMS at 60 Mc. for neat liquids.
[b] Estimated uncertainty: ±0.1 c.p.s. for J_{AB}; ±1 c.p.s. for $J_{C^{13}-H}$.
[c] Based on J_{trans} = 12 and J_{gauche} = 3 c.p.s. and model described in text.

For dimethyl bromosuccinate, the increase in J_{AX} and decrease in J_{BX} relative to the acid requires that conformation IB is somewhat more significant for the ester than for the acid. This additional stability could be attributed to increased steric interaction of CO_2R relative to CO_2H or to elimination of intramolecular hydrogen bonding. In any case, the observed increase in J_{AX} (from 7.1 for acid to 8.1 for ester) and decrease in J_{BX} (from 7.1 for acid to 6.7 for ester) can be accounted for almost exactly by assigning relative energies to unfavorable gauche configurations

and assuming J_{trans} = 12 c.p.s. and J_{gauche} = 3 c.p.s. as was done for the acids. In order to obtain the observed difference between J_{AX} and J_{BX} with this model, gauche $CO_2Me–CO_2Me$ configurations must contribute about 1400 cal./mole, and gauche CO_2Me–Br configurations, 1200 cal./mole while gauche Br–Br configurations remain at 1000 cal./mole. With these values, $E_A - E_B$ = 1400 cal./mole, $E_C - E_B$ = 200 cal./mole, J_{AX} = 8.0 c.p.s. (vs. 8.1 observed), and J_{BX} = 6.6 c.p.s. (vs. 6.7 observed). The calculated values for J_{AB} for the dibromo esters were based on gauche $CO_2R–CO_2R$ interactions of 1400 (R = CH_3) and 2000 (R = $CH(CH_3)_2$) and on CO_2R–Br interactions of 1200 (R = CH_3) and 1500 (R = $CH(CH_3)_2$) cal./mole (Table V).

This simple model predicts a somewhat greater increase in J_{AB} in going from R = CH_3 to R = $CH(CH_3)_2$ for the meso esters (0.9 c.p.s. vs. 0.2 observed) and a somewhat smaller increase for the dl esters (0.5 c.p.s. vs. 1.0 observed). Because the conformation with protons trans dominates in all of these dibromosuccinate esters, the system is not very sensitive to changes in the size of R. In particular, J_{AB} for the three meso esters varies only from 11.0 to 11.3 c.p.s. which might be taken as evidence that the size of R has little influence on rotational equilibria in these compounds. The model, however, predicts that the conformation with protons trans should make a greater contribution to J_{AB} as the size of R increases. The fact that J_{AB} values for both meso and dl esters increase and become more nearly identical as R increases is in accord with this prediction. Chemical shift data support this conclusion.

Chemical Shifts of Acyclic Compounds. The chemical shift data for the disubstituted compounds show three significant trends. (1) The three meso acids all have identical chemical shifts in THF; similarly, the three meso salts and dimethyl esters have essentially identical shifts. (2) The shifts for the dl isomers are invariably downfield from the corresponding meso isomers, with the difference being greatest for dichloro (19 and 16 c.p.s.) and smallest for dibromo (3 and 5 c.p.s.) acids and dimethyl esters. (3) The shifts of dimethyl esters are slightly downfield (6–9 c.p.s.)

from the corresponding acids for both *meso* and *dl* compounds.

For the disubstituted succinic anhydrides, the same equality of chemical shift for protons *trans* and *cis* to X for X = Cl and X = Br has already been noted. It is not surprising, therefore, to find the same chemical shifts for all three members of the acyclic *meso* series, *provided the same conformation* (IIB) *predominates in each case*, as is indicated by the vicinal coupling constants. Furthermore, the very small difference in shifts between *meso-* and *dl*-dibromosuccinic acids and esters adds weight to the hypothesis that IIB predominates for the *meso* isomer while IIIA predominates for the *dl* isomer. In both cases each proton is *gauche* to both CO_2R and Br. This is particularly apparent for R = $CH(CH_3)_2$ (Table V), for which $J_{AB} = 10.3$ and 11.2 c.p.s. and the shifts are equal. By contrast, the difference in chemical shifts of the dichloro compounds is greater since conformation IIB still predominates for the *meso* isomer, while IIIA and IIIB probably both make important contributions for the *dl* isomer. In IIIB, each proton is *trans* rather than *gauche* to a chlorine and is thereby shifted further downfield. This conclusion is again consistent with that based on vicinal coupling constants. A similar difference between *meso-* and *dl*-dibromobutane chemical shifts has been reported. As for the acids and esters, the *meso* shifts are upfield from *dl* shifts.[6,7] The effect of neutralization on chemical shifts of the acids can be accounted for on a similar basis. For example, all three of the *meso* salts, with both steric and electrostatic factors favoring conformation IIIB, should have almost identical chemical shifts as is observed (71 ± 1 c.p.s.).

Relative Steric Effects of Bromine Atom and Other Groups. On the basis of vicinal spin-coupling constants reported in this paper and those for other substituted dibromoethanes in the literature, it is possible to assign relative steric effects to several groups.

Confining the comparison to substituted dibromo-ethanes reduces the likelihood that electronegativity differences might be responsible for a significant part of the observed coupling constant differences. On the basis of two dibromoethanes, *erythro*-C_6H_5CHBr-CHDBr and *threo*-$(CH_3)_3CCHBrCHDBr$, Buza and Snyder[39] concluded that the steric effect of $(CH_3)_3C$ is greater than that of Br and that of C_6H_5 is less than that of Br. Similarly, the data of Anet[6] and Bothner-By and Naar-Colin[7] for *meso-* and *dl*-dibromobutane requires that $CH_3 <$ Br and $CH_3 < C_6H_5$. The close similarity between vicinal coupling constants (10.4 and 11.3 c.p.s.) for two dibromethanes studied by Gutowsky, *et al.*,[8] which differ only by replacement of CH_3 by C_6H_5 at one carbon, is consistent with an assignment of similar steric effects for CH_3 and C_6H_5. Unfortunately, the configuration of these compounds, CH_3CHBr-$CHBrCOC_6H_5$ and C_6H_5-$CHBr$-$CHBrCOC_6H_5$, is not known. However, a Br-COC_6H_5 *gauche* interaction of magnitude similar to that we have estimated for Br-CO_2CH_3 (1200 cal./mole) would result in the conformation with protons *trans* being more stable for either of the two possible *dl* pairs. In summary, these results and those discussed earlier suggest the following order for steric effects in substituted ethanes: $CO_2CH(CH_3)_2 > CO_2C_2H_5 > CO_2CH_3 > CO_2H=Br > C_6H_5 > CH_3$, Cl with $(CH_3)_3C$ and COC_6H_5 also > Br.

(39) M. Buza and E. I. Snyder, Abstracts, 148th National Meeting of the American Chemical Society, Chicago, Ill., Aug. 1964.

Electron Paramagnetic Resonance Study of Radicals Produced in Irradiated Amides[1,2]

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An e.p.r. study of the radicals produced by electron irradiation of a series of polycrystalline amides, N-alkylamides, and N,N-dialkylamides at low temperatures has been made. The isotropic hyperfine interactions with the protons usually permit identification of the radical species. For the N-alkyl- and N,N-dialkylamides the radiation damage consists of loss of a proton from the carbon atom of the alkyl group adjacent to nitrogen. In the amides and carboxylic acids a proton is lost from the carbon atom adjacent to the carbonyl group. When there are no hydrogen atoms on the carbons adjacent to nitrogen or carbonyl, other bonds may be broken. Thus, trimethylacetic acid and trimethylacetamide give the t-butyl radical. The hyperfine splitting constants tend to be lower when the radical site is adjacent to nitrogen, presumably as a result of some delocalization of the odd electron onto nitrogen.