their sincere appreciation to Mr. F. A. MacKellar of the Upjohn Company for measurement and interpretation of n.m.r. spectra. In addition the authors thank Dr. D. S. Matteson and the Washington State University Department of Chemistry for the use of their Varian A-60 n.m.r. spectrometer.

Transmission of Substituent Effects in Bicyclo[2.2.2]octanes and Aromatic Analogs[1,2]

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A series of 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids and the corresponding aromatic acids have been synthesized and their dissociation constants determined potentiometrically in 50 vol.% ethanol-water. From these data σ'-, σ_p-, σ_m-, σ_R-, and σ_I-constants are derived. The results for charged substituents supplement existing data. The derived constants are examined in terms of the Kirkwood–Westheimer cavity model and attention is focused on the role of external dielectric constant in determining the apparent σ-constants of charged substituents.

An important problem of physical organic chemistry is the correlation of the effect of substituents on free-energy changes involved in rate processes and equilibria. Although this is fundamentally a quantum mechanical problem, in practice it is usually reduced to finding that set of simplified concepts and associated parameters that most accurately mirror the experimental results. Thus, substituent effects have been decomposed into various combinations of inductive, field, polarizability, and resonance effects.[4-8]

One of the most fruitful approaches available for understanding substituent effects in saturated systems is the Kirkwood–Westheimer cavity model. Although it has severe theoretical and practical limitations,[9,10] it appears to be the most basic model available[11] and is the only one that considers the solvent explicitly.

This paper presents pK data on a series of 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids and the corresponding *meta*- and *para*-substituted benzoic acids. These data, which supplement published data on the same system, are discussed in terms of inductive and resonance parameters and in terms of a simple Kirkwood–Westheimer model.

Results and Discussion

σ-Constants.—The thermodynamic dissociation constants of the substituted bicyclic and aromatic acids measured in this work (see Experimental for details) are recorded in Table I along with the statistically corrected constants. All of the constants were determined in 50 vol. % ethanol–water. It should be noted that the value reported for the parent bicyclic monoacid is based on the apparent pK of Roberts[12] with an added activity coefficient correction of +0.05, which is the estimated difference in pK between the apparent and thermodynamic pK values of benzoic acid. The internal consistency of the data validates this assumption. The deviations recorded in Table I represent the reproducibility of several determinations. While the absolute pK's recorded may be in error by as much as 0.1 pK unit, the ΔpK's of any two acids are presumably reliable to about the sum of their deviations, *i.e.*, to about ±0.04 pK units.

TABLE I

THERMODYNAMIC pK VALUES IN ETHANOL–WATER (50 VOL.%)

Benzoic acid substituent	Thermodynamic pK	Statistically corrected pK
H	5.80 ± 0.01	5.80
m-COOH	5.14 ± 0.02	5.44
m-COO$^-$	6.33 ± 0.01	6.03
p-COOH	4.90 ± 0.01	5.20
p-COO$^-$	6.27 ± 0.01	5.97
p-COOEt	5.20 ± 0.01	5.20
p-N(CH$_3$)$_3$I	4.46 ± 0.02	4.46
4-Substituted bicyclo[2.2.2]octane		
H	6.79[a]	6.79
COOH	6.07 ± 0.02	6.37
COO$^-$	7.27 ± 0.02	6.97
COOEt	6.38 ± 0.00	6.38
N(CH$_3$)$_3$$^+$	5.43 ± 0.02	5.43
NH$_3$$^+$	5.64 ± 0.03	5.64

[a] Calculated from Roberts[12] apparent pK of 6.74.

Where comparisons are possible the present results agree reasonably well with those of Holtz and Stock[13] and with those of Roberts.[12] The agreement of the data with those of Lewis and Ritchie[14] is unsatisfactory in the present solvent 50 vol.% ethanol–water but these authors have remarked that their indicator method is insensitive in this media. Their extensive data in less aqueous solvents can be correlated satisfactorily with our results.

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[2] Abstracted from the dissertation submitted by J. S. McIntyre to the Cornell Graduate School, June 1962, in partial fulfillment of the requirements of the Ph.D. degree.

[3] Cornell Fellow, 1958–1959.

[4] C. K. Ingold, *Chem. Rev.*, **15**, 225 (1934).

[5] R. W. Taft, Jr., "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, Chapter 13.

[6] M. J. S. Dewar and P. J. Grisdale, *J. Am. Chem. Soc.*, **84**, 3539 (1962).

[7] H. H. Jaffé, *J. Chem. Phys.*, **21**, 415 (1953).

[8] J. G. Kirkwood and F. H. Westheimer, *ibid.*, **6**, 506 (1938).

[9] C. Tanford, *J. Am. Chem. Soc.*, **79**, 5348 (1957).

[10] F. H. Westheimer, W. A. Jones, and R. A. Lad, *J. Chem. Phys.*, **10**, 478 (1942).

[11] A hierarchy of models can be envisioned in which the substituent and functional group are first embedded in an unvarying continuum, next in an environment divided into separately continuous solvent and substrate parts, and on to environments of increasingly higher degree of structure.

[12] J. D. Roberts and W. T. Moreland, *J. Am. Chem. Soc.*, **75**, 2167 (1953).

[13] H. D. Holtz and L. M. Stock, *ibid.*, **86**, 5188 (1964). We are indebted to Professor Stock for making a copy of his manuscript available to us in advance of its publication.

[14] C. D. Ritchie and E. S. Lewis, *ibid.*, **84**, 591 (1962).

In Table II are recorded the σ- and σ'-constants calculated from the data of Table I using Roberts value of 1.464 for ρ.[15]

TABLE II

COMPARISON OF σ- AND σ'-VALUES IN ETHANOL-WATER (50 VOL.%)

Substituent	σ'	σ_p	σ_m	σ_R	σ_I
H	0.0	0.0	0.0	0.0	0.0
COOH	0.29	0.41	0.25	0.12	0.17
COO^-	−0.12	−0.12	−0.16	0.00	−0.18
COOEt	0.28	0.41	0.33[a]	0.13	0.29
$N(CH_3)_3^+$	0.93	0.92[b]	0.96[c]	−0.01	0.98

[a] Taken from ref. 12. Since this is a ΔpK between acids of the same charge type no activity correction has been applied. [b] Roberts[12] found 1.02 based on apparent pK-values. An activity coefficient correction of −0.05 for the benzoate anion, −0.05 for the undissociated quaternary ammonium acid, and −0.01. for the zwitterion (see Experimental) gives the tabulated value. [c] Roberts[12] reports 0.88. With the same activity coefficient applied to the *meta* compound his data would yield a σ_p of 0.82.

Taft[5,16] following the suggestion of Roberts and Moreland[12] has equated $\sigma_p - \sigma'$ to σ_R', the resonance contribution to a substituent's σ-constant. These data show, as they should, that the COOH and COOEt groups have essentially the same resonance contribution and the same inductive effect. The observed σ_m of 0.25 for COOH seems low compared with the value reported for a *m*-COOEt and that observed for *m*-COOH. About half of the discrepancy can be dismissed as experimental uncertainty but the remaining difference of 0.04 σ-units suggests some systematic error in the determination of the pK values of isophthalic acid.

A satisfying aspect of the data is the identity of the σ_p- and σ'-values found for COO^-. This indicates, as expected for the cross-conjugated carboxylate anion, that it has a very small resonance contribution to σ_p and that it is an electron donor by induction. This suggests that COO^- should be an *ortho-para*-directing group in electrophilic substitution in contrast to the strong *meta*-directing character of the neutral and unsymmetrical COOH.[17] The *m*-COO^- constant, like the *m*-COOH constant, seems too negative by 0.05 σ-units although other data in the literature suggest that σ_m (COO^-) is more negative than σ_p (COO^-).[18]

The σ'- and σ_p-constants for the trimethylammonium ion observed in this work were identical within experimental error and were close to the σ_m-value determined by Roberts[12] when the latter was adjusted to include activity corrections. The essential identity of the σ_p- and σ_m-constants is in contrast to the significant difference of 0.1 σ-units found by Roberts[12] and parallels their identity in water.[19] Of some interest here is the lower value of 0.79 observed for a *p*-NH_3^+ group. A possible rationalization of this decrease will be considered in the next section.

Charton[20] has recently compiled values of σ_I for many substituents as derived from aliphatic dissociation constants. There is good quantitative agreement between his values and the present ones, particularly when the effect of solvent is considered (see below).

Kirkwood-Westheimer Cavity Model.—The experimental ΔpK values for the different substituents were compared with the theoretical values calculated for the Kirkwood-Westheimer cavity model[8] in order to assess the interplay between solvent dielectric constant and substituent charge type. The cavity was taken to be spherical and the depth, following Tanford,[9] was taken to be 1.5 Å. for the dipolar groups and 1.0 Å. for the charged groups COO^- and NH_3^+. The charge depth of the $N(CH_3)_3^+$ group should be greater than 1.0 Å. because of the added bulk of the methyls but because of the drastic distortion of the cavity shape by these methyls the effective depth is hard to estimate. Since the goal was to assess the effect of a change in the external dielectric constant, the problem was solved in reverse and the observed ΔpK's were equated with theoretical ΔpK's for spherical cavities of different depths. An apparent depth of 1.36 Å. was obtained. Since no change would be expected for the carboxyl end of the molecule, the effective depth of the $N(CH_3)_3^+$ is larger by approximately the difference, *i.e.*, a depth of 1.72 Å. Given the crude method of making this estimate, the result is in fair agreement with the depth of 2.55 Å. that is calculated by placing the hydrogen atoms of the methyls at the cavity boundary.

The variation in the depth of charge in the cavity can explain the smaller ΔpK obtained with NH_3^+ compared with $N(CH_3)_3^+$. The deeper the charge is placed in the cavity, the smaller the effective dielectric constant becomes. This handling of the Kirkwood-Westheimer model leads to the expectation that the inductive effect of an NH_3^+ group should increase with the number of methyls substituted for hydrogens. Such an order has been deduced[21] for the methylated glycines although it was ascribed to specific solvation rather than to variations in the effective interposed dielectric constant. Unfortunately, the poor analysis of the NH_3^+ compound (see Experimental) reduces the significance of this argument for the bicyclic cases.

The COO^- substituent was considered to possess two opposing effects. One was a negative potential field created by a point charge centered between the oxygens of the anion; the second was a positive potential field ascribed to the *dipole* of the COO^- group. The influence of the pole was calculated in the same manner as the NH_3^+ group. Although the magnitude of the dipole could have been estimated, it seemed preferable to again work backwards and use the consistency of the

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(15) D. H. McDaniel and H. C. Brown [*J. Org. Chem.*, **23**, 420 (1958)] have calculated the higher value of 1.522 using a more extensive set of data taken from several sources. Most of the difference can be ascribed to their use of absolute pK's without regard to the pK for benzoic acid reported by the different workers. When the same set of measurements was analyzed using the reported ΔpK's, a ρ' of 1.470 was obtained. The original value of 1.464 has been used in this paper because of the ambiguity of the best value and its use by Roberts in defining σ'-constants. The derived constants are changed little by use of the McDaniel-Brown value.

(16) R. W. Taft, Jr., *J. Am. Chem. Soc.*, **79**, 1045 (1957).

(17) This point has been made previously by Okamoto and Brown [*ibid.*, **80**, 4976 (1956)] and is supported by the chlorination and bromination products of the benzoate ion examined by J. C. Smith [*J. Chem. Soc.*, 213 (1934)].

(18) σ-Constants for a *p*-COO^- group vary from −0.4 to +0.4 depending on the solvent and type of reaction studied.

(19) See the reference cited in footnote 15. The σ_p- and σ_m-constants in water were determined by two different workers, which makes the comparison less significant. See also H. H. Jaffé, *Chem. Rev.*, **53**, 191 (1953), and D. H. McDaniel, *J. Org. Chem.*, **26**, 4692 (1961). Because of the large numerical value of these two constants, they have considerable statistical influence on any derived relation between inductive effects in the *meta* and *para* positions.

(20) M. Charton, *ibid.*, **29**, 1222 (1964).

(21 G. Branch and M. Calvin, "The Theory of Organic Chemistry," Prentice-Hall, Inc., New York, N. Y., 1941, p. 229. See also ref. 20.

result as an indication of its reliability. The calculated effect of the pole was subtracted from the observed ΔpK and the difference was set equal to the desired dipole effect. The apparent dipole of the COO^- group obtained in this manner was 3.2 D. The COO^- dipole moment would be reasonably expected to be larger than the dipole moment of a COOH group (1.68 D), where the OH bond acts in opposition to the CO dipole, and might be of the same order as the dipole moment of a NO_2 group (3.68 D.).

When the theoretical ΔpK's for the bicyclic acids bearing charged and dipolar substituents are plotted against the reciprocal of the solvent dielectric constant an instructive pattern emerges (see data in Table III).

Table III

Calculated Dependence of ΔpK on External Dielectric Constant

	External dielectric constant			
	20	40	60	∞
Substituent	Calculated ΔpK			
NH_3^+	1.69	1.15	0.92	0.53
$N(CH_3)_3^+$	2.11	1.55	1.27	0.88
CO_2^- (charge only)	−1.46	−0.95	−0.75	−0.39
CO_2^- (charge and dipole)	−0.78	−0.34	−0.16	0.14
CO_2H	0.31	0.28	0.27	0.24
CN	0.77	0.68	0.66	0.59
Br	0.61	0.55	0.52	0.48

First, the plots are essentially linear in $1/D_{\text{ext}}$ as required by the equations derived by Kirkwood and Westheimer[8] for the present spherical model (see eq. 1, where f_1 and f_2 are structural factors taken in good approximation to be independent of the external and internal dielectric constants).

$$\frac{1}{D_{\text{effective}}} = \frac{f_1}{D_{\text{external}}} + \frac{f_2}{D_{\text{internal}}} \tag{1}$$

Second, the lines for acids with charged substituents have strikingly different slopes from those for acids with dipolar substituents. Third, the ratio of the theoretical ΔpK's of all pairs of dipolar substituted acids is nearly constant over the normally studied range of D_{ext} of 20 to 80. This constancy arises from the low sensitivity of f_1 to changes in the length of the different dipolar substituents, which is the essential variant in this model. In contrast to the behavior of the dipolar acids the charged acids show a greater sensitivity to D_{ext}. Although the plots are also linear over the range of D_{ext} of 20 to 80, the ratio of the theoretical ΔpK of the $N(CH_3)_3^+$- or NH_3^+-substituted acids to the dipolar acids changes by a factor of about two over this same range. With the COO^--substituted acid the ratio changes even more because the theoretical ΔpK is composed of two opposing effects.

An observed set of ΔpK values can be equated empirically to $\rho\sigma$, where σ is associated with the substituent dependent variation in ΔpK and ρ is associated with the solvent and system dependent variations. Even the present simple model brings out the general adequacy of assigning constant σ-values to dipolar substituents (constant ratios of ΔpK's in different media) as well as the well-known inadequacy of constant σ's for charged substituents (variable ratio of ΔpK's when compared with dipolar acids, which are used to establish ρ). The model also provides a simple explanation of why the COO^- substituent with opposing polar and dipolar influences gives apparent σ-constants that show a marked trend to more positive values in solvents of high dielectric constant. The variation of σ of charged groups is customarily ascribed to specific solvent effects like varied hydrogen bonding. Although the present version of the Kirkwood–Westheimer model is certainly over-simplified, it does suggest that much of the variation in σ-values of charged groups results from a bulk dielectric constant effect. It is hoped that in the near future it will be possible to refine the model[11] so as to make more significant assessments of the general and specific solvent influence.

Experimental

Materials.—The 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids were prepared by the general approach developed by Roberts, *et al.*[22] The reduction of diethyl 2,5-dioxobicyclo-[2.2.2]octane-1,4-dicarboxylate to diethyl bicyclo[2.2.2]octane-1,4-dicarboxylate was carried out by a modified Clemmensen reduction using absolute ethanol saturated with dry hydrogen chloride gas. Conversion as high as 67% was obtained when a large excess of zinc was employed (weight ratio of zinc–diester, 7:1) with vigorous stirring.

4-Aminobicyclo[2.2.2]octane-1-carboxylic Acid Hydriodide.—A solution of 1 g. of ethyl 4-N-(carbethoxy)aminobicyclo[2.2.2]-octane-1-carboxylate[22] (0.0038 mole) and 5 ml. of hydriodic acid were heated at 100° for 10 hr. The hydriodic acid was removed on a flash evaporator and the residue was dried *in vacuo*. The residue was washed with a small quantity of acetone and then dissolved in 8 ml. of 1:1 ethanol–ethyl acetate followed by precipitation with 12 ml. of acetone. The resulting solid, m.p. above 360°, turned brown on standing.

Anal. Calcd. for $C_9H_{16}INO_2$: C, 36.38; H, 5.39; N, 4.72. Found: C, 42.96; H, 6.54; N, 5.54.

The ratio of the observed percentages to those calculated are 1.18, 1.21, and 1.19 for C, H, and N, respectively. This near constancy can be accounted for as a loss of HI during transportation for analysis.

4-Carbomethoxybicyclo[2.2.2]octane-1-trimethylammonium Iodide.—A solution of 1.47 g. of the hydriodide (0.005 mole), 2.15 g. of methyl iodide (0.015 mole), 1.25 g. of sodium bicarbonate, and 40 ml. of methanol was heated under reflux for 70 hr. At the end of 24 and 48 hr., 0.34-g. portions of methyl iodide were added. The methyl alcohol and excess methyl iodide were removed by evaporation on a steam bath and the residue was extracted with six 20-ml. portions of hot chloroform. After evaporation of the chloroform and recrystallization of the residue from ethanol, a solid, m.p. 285–288° dec., was obtained in about 65% yield.

Anal. Calcd. for $C_{13}H_{24}INO_2$: C, 44.21; H, 6.80; I, 35.96. N, 3.97. Found: C, 43.80; H, 6.92; I, 35.84; N, 4.02.

4-Carboxybicyclo[2.2.2]octane-1-trimethylammonium Iodide.—A solution of 0.4 g. of the above ester (0.0011 mole) and 2 ml. of 1 *N* HI was heated in a sealed tube at 100° for 10 hr. Upon cooling and filtering, 0.25 g. of product was obtained, which after recrystallization from 75% ethanol–water had a melting point of 299–300° dec.

Anal. Calcd. for $C_{12}H_{22}INO_2$: C, 42.49; H, 6.49; I, 37.44; N, 4.13. Found: C, 42.10; H, 6.51; I, 36.92; N, 4.00.

Method of p*K* Measurements.—The dissociation constants of both the mono- and diacids were determined potentiometrically in 50 vol. % ethanol–water using a glass electrode and a Beckman G pH meter with a saturated aqueous KCl calomel electrode as reference. In order to avoid the solvent errors noted by Grunwald, the glass electrode was stored in 50 vol.% ethanol–water and the meter was standardized in the same solvent. In order to be able to combine our results with those of Roberts, *et al.*,[12,23] this indirect calibration procedure was used. A 3.1×10^{-3} *M* solution of benzoic acid in 50% ethanol was half-neutralized and the meter was zeroed to 5.75, the apparent p*K* reported by Rob-

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[22] J. D. Roberts, W. T. Moreland, Jr., and W. Frazer, *J. Am. Chem. Soc.*, **75**, 637 (1953).

[23] At the time this work was done neither the results of Stock[13] nor those of Lewis and Ritchie[14] in 50 wt.% ethanol-water were available.

erts, *et al.*, for benzoic acid.[24] Insertion of the electrodes into 0.02 *N* potassium acid phthalate buffer in 50% ethanol gave a reading of 5.51 ± 0.01 for three titrations and duplicate buffer preparations. In subsequent runs the meter was standardized directly against phthalate buffer.[25]

All titrations were carried out in a 100-ml. three-neck flask maintained at 25.0 ± 0.1°. The two electrodes, fitted through rubber stoppers, were inserted into two of the necks and a 5-ml. buret (graduated in 0.01 ml.), into the third. The solutions were stirred with a magnetic stirring bar under a nitrogen atmosphere. While a pH reading was being taken, the stirrer and all current in the vicinity of the meter was shut off temporarily to avoid interference from a.c. fields.

Except for terephthalic acid, 100 ml. of 6.2×10^{-5} *M* stock solutions of the different acids in absolute alcohol were prepared; 25 ml. of this solution was titrated into the three-neck flask followed by addition of 25 ml. of water and 2.2 ml. of 50% ethanol (the latter to compensate for the contraction on mixing). For each acid duplicate stock solutions were used in the titrations. The base used in all titrations was 0.05 *N* sodium hydroxide in 50% ethanol and was prepared from carbonate-free water and base. Terephthalic acid precipitated on preparation of a 50% ethanol solution; so a partially neutralized solution was prepared by adding 10.0 ml. of the 0.050 *N* sodium hydroxide to a 1-l. flask followed by 200 ml. of 50% ethanol and 0.1024 g. of terephthalic acid. A glass stopper was wired on and the solution was stirred magnetically at 50° for 2 hr. This partially neutralized acid remained in solution when the flask was cooled to 25°. A 52.5-ml. sample of this solution was titrated as before; the initial pH corresponded to the addition of 2.5 ml. of base.

Calculation of p*K* Values.—The dissociation constants of the dicarboxylic acids were evaluated by the method of Speakman which takes into account explicitly the activity coefficients of the various species present as the solution is progressively neutralized. The activity coefficients of the species H_2A, HA^-, and A^{-2} are f_0, f_1, and f_2, respectively; f_0 was taken as unity; f_1 and f_2 were estimated from the Debye–Hückel limiting law using the value of 52.5 for the dielectric constant of 50% ethanol. The Speakman plots were drawn for measurements between 25% and 75% neutralization which in general represented about 14 different pH readings.

The dissociation constants of the monocarboxylic acids were evaluated in a similar fashion using a reduced Speakman expression in which the K_2 term had been set equal to zero. The activity coefficients of the zwitterions were evaluated by the simple[26] Ingold expression

$$-\log f_{\pm} = \frac{4\pi N e^4 z^2 d I}{2303 k^2 (DT)^2}$$

where *d* is the separation of the changes, *I* is the ionic strength, and the remaining symbols have their conventional meaning.

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[24] After the original work Roberts and Regan reported a value of 5.80 using different apparatus and materials.

[25] It should be emphasized that 5.51 is only a relative, apparent value that places the meter on the same scale used by Roberts. The work of Grunwald with benzoic acid suggests that our p*K*'s and those of Roberts may be high on an absolute scale by as much as 0.1 p*K* unit.

[26] Two other much more complicated equations have been presented by Kirkwood and Westheimer.[8] It can be shown that with reasonable values for their parameters appropriate to the present molecules that the Kirkwood–Westheimer expressions are, in fact, very nearly the same as the simpler Ingold expression. Numerically, the p*K* obtained using activity coefficients calculated from any of the three expressions would not vary by more than 0.01 units.

Medium-Ring Thiacycloalkanes. II.[1,2]

Long-Chain Dibromides and *gem*-Dimethyl-Substituted Dibromides

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A versatile synthesis of long-chain *gem*-dimethyl-substituted dibromides has been developed. The preparation of 6,6-dimethylundecanedioic acid (VI), a key intermediate in the preparation of several of these dihalides, has been substantially improved. Cristol and Firth's modification of the Hunsdiecker reaction has been extended to the synthesis of dibromides including 1,9-dibromo-5,5-dimethylnonane (XII). 1,11-Dibromo-6,6-dimethylundecane (IX) and 1,10-dibromo-5,5-dimethyldecane (XIII) were prepared and cyclized to 7,7-dimethylthiacyclododecane (XVIII) and 6,6-dimethylthiacycloundecane (XXI) in 23 and 22% yield, respectively. Identical procedures applied to 1,11-dibromoundecane and 1,10-dibromodecane yielded less than 3% of crude product in the former case and 13% of thiacycloundecane in the latter. Comparison of yields of the substituted and unsubstituted 10-, 11-, and 12-membered ring sulfides strongly implies operation of the *gem*-dimethyl effect in these ring closures. Certain cyclic sulfides were oxidized to sulfoxides and sulfones.

Earlier work[2] showed that 1,9-dibromononane and sodium sulfide in very dilute alcohol yield only 5.7% of thiacyclodecane, whereas the 5,5-dimethyl-substituted dibromide yields 34.5% of 6,6-dimethylthiacyclodecane. These results confirmed our belief that the *gem*-dimethyl effect would obtain in ring closures ininvolving sulfide ion nucleophilic substitution at a saturated carbon atom. However, we needed an improved synthesis of the *gem*-dimethyl dihalides required for the study of other medium ring thiacycloalkanes, the bishomologization procedure used for

$(C_2H_5O_2C)_2C(C_4H_8OCH_3)_2$ I

$(HOCH_2)_2C(C_4H_8OCH_3)_2$ II

1,9-dibromo-5,5-dimethylnonane[1,4] being prohibitively laborious for the preparation of higher homologs.

The preparation of dihalides *via* malonic ester failed; although I was prepared and reduced to II, the latter could not be converted to a dibromide completely nor could the two hydroxymethyl groups be changed to methyl groups *via* the ditosylate. However, we modified the ingenious work of Badger[5] (Scheme I). Badger's conversion of 2,2-bis(2-thienyl) propane (III) to V *via* 2,2-bis(5-acetyl-2-thienyl) propane (IV) was unsuitable for large-scale preparation as IV is difficult to isolate and oxidize, but III could be easily converted

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[1] Paper I in this series: P. Friedman and P. Allen, Jr., *J. Org. Chem.*, **27**, 1095 (1962).

[2] (a) Presented in part at the 142nd National Meeting of the American Chemical Society, Atlantic City, N. J., Sept. 1962; Abstracts, p. 70. (b) From a portion of the Doctoral Dissertation of P. Friedman, Stevens Institute of Technology, June 1963. (c) This work was supported by a grant from the U. S. Public Health Service, National Institutes of Health, Am-03649.

[3] Author to whom inquiries should be addressed.

[4] A. T. Blomquist, E. S. Wheeler, and Y. Chu, *J. Am. Chem. Soc.*, **77**, 6307 (1955). Thirteen steps were required in adapting this synthesis to the preparation of XII from δ,δ-dimethylglutaric acid.

[5] G. M. Badger, H. J. Rodda, and W. H. F. Sasse, *J. Chem. Soc.*, 4162 (1954).