Polarography of Organic Halogen Compounds. III.[1] Quantitative Correlation of the Half-Wave Potentials of Alkyl Bromides with Taft Polar and Steric Constants

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Previously, the reduction potentials of several alkyl bromides at the dropping mercury electrode were shown to be qualitatively related to their SN reactivity in the classic series of alkyl halides with substitution at the α- and β-carbon atoms.[1b] However, past attempts to correlate the reduction potentials of alkyl bromides with Taft's substituent constants have met with limited success. The quantitative correlation of the half-wave potentials of 24 alkyl bromides with the Taft polar (σ^*) and steric (E_s) constants is herein demonstrated. The influence of distant groups on electroreduction is indicated. Acceptable prediction of half-wave potentials is given by the equation, $E_{1/2}$ (in volts) $= 0.32^5\,\sigma^* + 0.12E_s - 2.16^5$. The results of this study support the mechanism involving formation of a negatively charged entity such as the anion radical (R–Br)$\cdot^-$, but *via* an attack which is perpendicular to the axis of the C–Br bond rather than by a simple "SN2-like" attack in the potential-determining step for the reduction of alkyl bromides.

Many publications have dealt with the quantitative relationships between fundamental structural characteristics of organic compounds and their half-wave potentials, $E_{1/2}$, when they are reduced at a cathode such as a dropping mercury electrode. Correlations of the $E_{1/2}$ with physicochemical parameters have included ultraviolet spectra, electron capture affinities, nmr data, and molecular orbital functions, among others.[2]

Especially widespread success has been achieved in relating the half-wave potentials of aromatic and heterocyclic compounds with the Hammett equation.[3] In extending this search for correlations, and because Hammett's constants are not applicable to aliphatic compounds, Zuman[4] has adapted the Taft equation to polarographic data and verified its validity for 60 reaction series and more than 260 substances. Elving and Markowitz[5] have also used the Hammett–Taft relation in successfully correlating the polarographic reduction potentials of several types of organic compounds with structural parameters.

However, in the polarography of aliphatic halogen compounds the methods of application and the success of the modified Taft equation are open to question. Zuman's line of correlation[6] has a unique slope of 4.95 v/σ^*; all other systems investigated by Zuman[3] have values of 0.02 to 1.8 v/σ^*. More conclusively, the line cannot include bromo compounds with positive values of σ^*, such as $Ph(CH_2)_3Br$ with a σ^* of 0.02 and $E_{1/2}$ of -2.18 v.[7]

In their pioneering work of correlating polarographic results with Taft–Hammett parameters, Elving and Markowitz[5] report their results with alkyl halides from which they derived a correlative line with a slope of 1.04 v/σ^*. However, butyl and isobutyl bromides lie even farther from the line than the large standard deviation of 0.12 v. They conclude: ". . . . in the alkyl bromides the Taft–Hammett relationship, when applied to half-wave potentials, breaks down for substituents larger than ethyl groups."

The present work was planned to clarify the application and the limitations of the Taft substituent constants to the polarographic reduction of substituted alkyl bromides. We believed that steric factors had not been properly assessed,[8] that the use of only three or four compounds with a small range of σ^* values was inadequate to establish a correlation, and that rigorously standardized conditions with nonaqueous solvents were essential for meaningful results.

Experimental Section

Materials.—Reagent N,N-dimethylformamide (Eastman) was distilled through a 30-cm glass-helix-packed column and the midfraction was redistilled to obtain material which gave no more than a 0.3-μa rise between -1.5 and -2.5 v (*vs.* a saturated calomel electrode) in a blank polarographic run with 0.01 *M* Eastman White Label tetraethylammonium bromide.

When required, commercially available reagents were purified until less than 2% of impurities were present as determined by vapor phase chromatography. Isoamyl bromide, isohexyl bromide, bromomethylcyclohexane, 1-bromo-3-fluoropropane, and (3-bromopropyl)benzene were obtained from Columbia Organic Chemicals Co.; octyl bromide and β-bromophenetole (2-phenoxyethyl bromide), from Eastman; methyl bromide, from Matheson; ethyl, propyl, butyl, amyl, hexyl, isopropyl, and isobutyl bromides, 3-bromopropanenitrile, 4-bromobutanenitrile, and ethyl 3-bromopropanoate, from Matheson Coleman and Bell; neopentyl bromide, from K and K Laboratories.

Elementary synthetic procedures were used in preparation of the remaining compounds (or as alternate sources to cross-check results from purchased materials). Bromomethylcyclohexane and isohexyl bromide resulted from PBr_3 treatment of cyclohexanemethanol (Eastman) and isohexyl alcohol (from isoamyl bromide *via* a Grignard reaction), respectively. 3-Phenoxypropyl and 4-phenoxybutyl bromides were made by the reaction of phenol in basic solution with the appropriate dibromoalkane (Columbia). Ethyl 4-bromobutanoate and ethyl 5-bromopentanoate were derived from the corresponding nitriles (Matheson Coleman and Bell) by acid hydrolysis in ethanol. Significant physical properties of the purified products corresponded with those in the literature.

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[1] (a) Part II: F. L. Lambert, A. H. Albert, and J. P. Hardy, *J. Am. Chem. Soc.*, **86**, 3155 (1964); (b) part I: F. L. Lambert and K. Kobayashi, *ibid.*, **82**, 5324 (1960).

[2] Leading references are cited in the review articles: D. J. Pietrzyk, *Anal. Chem.*, **38**, 278R (1966); S. Wawzonek and D. J. Pietrzyk, *ibid.*, **36**, 220R (1964); and by S. Wawzonek, *ibid.*, **34**, 182R (1962); **32**, 144R (1960); and **30**, 661 (1958). Earlier work is given by P. Zuman, *Chem. Listy*, **48**, 94 (1954).

[3] (a) P. Zuman has investigated some 44 different groups of compounds comprising 540 individual substances whose half-wave potentials fit the Hammett or modified Hammett equation: P. Zuman, D. Sc. Thesis, Czech. Acad. of Science, Prague, 1959, cited on p 3299 of ref 3b; (b) P. Zuman, *Collection Czech. Chem. Commun.*, **25**, 3255 (1960); (c) see ref 2 for other systems.

[4] See ref 3b, pp 3234 and 3241.

[5] P. J. Elving and J. M. Markowitz, *J. Org. Chem.*, **25**, 18 (1960).

[6] See ref 3b, p 3236. Also, P. Zuman, "Advances in Polarography," I. S. Longmuir, Ed., Pergamon Press Ltd., Oxford, 1960, Figure 2, p 817.

[7] $E_{1/2}$ value for $Ph(CH_2)_3Br$ from the present research under the conditions of Zuman.[6]

[8] If the corrections for steric effects ($0.04E_s$) are completely omitted from the plotted points of Zuman in ref 6, the resulting uncorrected half-wave values still fit a correlative line as adequately as with the corrections.

Apparatus and Procedure.—Initial work employed apparatus and methods previously described.[1b] However, comments of referees concerning the methods of *iR* correction for the high resistances encountered therein led to investigation of other electrode systems. The Ag–AgBr electrode of Sease[9] gave reproducible results over short periods of time, but not throughout a span of months. Standard three-electrode techniques employing Arthur's[10] *iR* compensator were not completely satisfactory because with it some substances gave anomalous drop-rate changes at very negative potentials.

For half-wave reproducibility, for interrupted periods of experimentation, and for the wide variety of compounds represented in this work, the best system proved to be one with a simple mercury pool anode whose potential could be monitored with a saturated calomel electrode (SCE) by means of a Corning Model 12 pH meter. In addition to its insertion as a monitor of the mercury pool potential, the SCE could be placed in the polarographic cell so that the agar–KCl tip of the SCE bridge was not more than 2 mm from the mercury drop as it formed on the dropping mercury electrode. Thus, the SCE could be used as the reference electrode in a standard three-electrode arrangement as additional corroboration of the results using a simple mercury pool system.

Current–potential curves were recorded with a Leeds and Northrup Type E electrochemograph. The resistance of the cell circuit was 3700 ± 100 ohms as measured on an Industrial Instruments RC conductivity bridge. Corrections for *iR* drop are included in the results reported. Capillary characteristics were m = 1.20 mg/sec and $t_{\max}$ = 4.9 sec (open circuit, Hg height = 66.1 cm), with the electrode immersed in 0.01 M tetraethylammonium bromide in N,N-dimethylformamide (DMF).

Except for the use of a mercury pool cell (a simple 34/28 ₸ cylindrical vessel into which the leg of the SCE bridge could be inserted and also fitted with electrode connection to the bottom pool), the procedure was very similar to that reported.[1b] The potential of the pool *vs.* the SCE was determined, after a run had been made, by inserting the SCE and applying the approximate half-wave potential between the dropping mercury electrode and the pool.

The waves were highly irreversible, diffusion controlled, and consisted of single steps. Methyl bromide gave an anomalous wave with a long, drawn-out rise just prior to the actual wave; the potential listed is that of the final wave only. (Methyl bromide has been shown to react with DMF.[11] Waves were recorded immediately after introduction of gas in the cell.) Maxima were present in the bromonitriles. With these three exceptions, all of the polarographic waves were of the same character with clean rises and plateaus and no pre- or postwaves. (The greater difficulty of reading the methyl bromide and bromonitrile records is indicated by the greater standard deviations of their half-wave potentials in Table I.)

Because one experiment with amyl bromide gave a different half-wave potential from previous work,[1b] all of the reductions of alkyl bromides of that research were repeated. The large number of determinations of some of the simple alkyl bromides in this present work is an indication of the use of different preparations or batches of the halide, of the supporting electrolyte, and of the DMF, as well as variations in cell geometry and mode of operation. The better-than-expected reproducibility shown in Table I for these organic systems is proof of the utility of the simple cell and apparatus, but it leaves unexplained the cause of the numerical differences from some of the half-wave potentials in the previous work. At least two "homemade" calomel electrodes were used in that research. Because in the past year we were surprised to find such a saturated calomel electrode to be in error by 30 mv, we hypothesize that one or more of the old electrodes may have been faulty. Any SCE employed in the current research was checked prior to use in polarography.

The essential electrochemical details of the experimental work are given in Table I.

Results and Discussion

The results of reduction of some organic bromo compounds at the dropping mercury electrode together with pertinent Taft constants and half-wave potentials corrected for steric influence are presented in Table II.

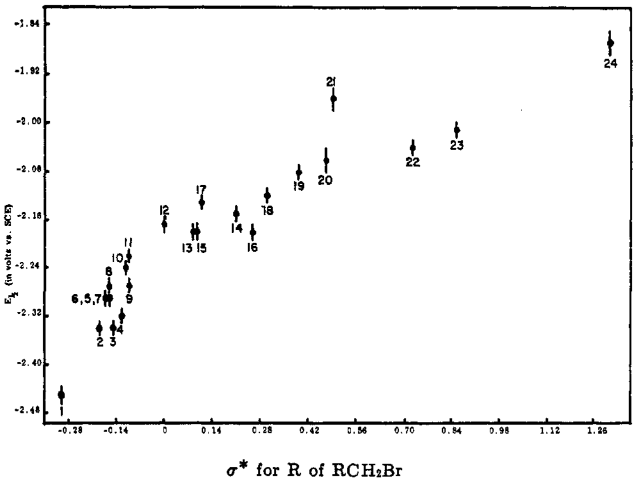

Figure 1.—Half-wave potentials of alkyl bromides against Taft polar constants, σ*.

Table I

Electrochemical Characteristics of Bromo Compounds, RCH_2Br[a]

Compd	RCH_2 radical name or formula	No. of detn[b]	Mean $E_{1/2}$[c]	Std dev of $E_{1/2}$	i_d/C, μa/mm l.
1	Neopentyl	5	−2.451	0.0038	4.9
2	*i*-Butyl	8	−2.339	0.0043	5.0
3	Cyclohexylmethyl	3	−2.339	0.0022	5.5
4	*i*-Amyl	5	−2.317	0.0028	5.8
5	*i*-Hexyl	9	−2.294	0.0045	5.8
6	Octyl	6	−2.291	0.0029	5.2
7	Hexyl	3	−2.288	0.0013	6.0
8	Amyl	12	−2.273	0.0026	5.9
9	*i*-Propyl	5	−2.271	0.0037	6.6
10	Butyl	4	−2.243	0.0016	6.5
11	Propyl	3	−2.218	0.0040	6.2
12	Ethyl	3	−2.167	0.0035	5.3
13	3-Phenylpropyl	3	−2.178	0.0030	5.6
14	2-Phenylethyl	4	−2.149	0.0012	5.7
15	$EtO_2C(CH_2)_3CH_2$	5	−2.180	0.0028	4.8
16	$EtO_2C(CH_2)_2CH_2$	3	−2.177	0.0031	3.8
17	4-Phenoxybutyl	3	−2.134	0.0026	4.3
18	3-Phenoxypropyl	3	−2.119	0.0017	5.1
19	$F(CH_2)_2CH_2$	4	2.084	0.0037	6.7
20	$NC(CH_2)_2CH_2$	6	−2.059	0.0066	4.6
21	Methyl	4	−1.964	0.0090	...
22	$EtO_2CCH_2CH_2$	4	−2.039	0.0041	4.5
23	2-Phenoxyethyl	3	−2.008	0.0014	6.6
24	$NCCH_2CH_2$	6	−1.865	0.0060	3.8

[a] Halide concentration of 2–4 × 10^{-4} M in anhydrous N,N-dimethylformamide with 0.01 M tetraethylammonium bromide as the supporting electrolyte; dropping mercury electrode at 25.0°, and other conditions as in Experimental Section. [b] Each determination consisted of two electroreductions, one with increasing and one with decreasing potential scan. [c] In volts *vs.* the SCE and corrected for *iR* drop in the cell.

Figure 1 is a plot of the half-wave potentials of the bromo compounds of this study, RCH_2Br *vs.* the σ* values of R. There is a general linear relationship over a range of 1.45σ* units, although the least sterically encumbered substances (methyl and ethyl bromide) and those classed in displacement reactions as the most sterically hindered compounds (neopentyl, isobutyl, and cyclohexylmethyl bromide) are clearly

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[9] J. W. Sease, P. Chang, and J. L. Groth, *J. Am. Chem. Soc.*, **86**, 3154 (1964).

[10] P. Arthur and R. H. VanderKam, *Anal. Chem.*, **33**, 765 (1961).

[11] J. L. Neumeyer and J. G. Cannon, *J. Org. Chem.*, **26**, 4680 (1961).

TABLE II

HALF-WAVE POTENTIALS OF BROMO COMPOUNDS, RCH_2Br[a]

Compd	RCH_2	$E_{1/2}$ of RCH_2Br[b]	σ^* for R[c]	E_s for RCH_2[c]	$E_{1/2} - 0.12E_s$
1	$(CH_3)_3CCH_2$	−2.45	−0.30	−1.74	−2.24
2	$(CH_3)_2CHCH_2$	−2.34	−0.19	−0.93	−2.23
3	$C_6H_{11}CH_2$	−2.34	−0.15	−0.98	−2.22
4	$(CH_3)_2CHCH_2CH_2$	−2.32	−0.125	−0.51[d]	−2.26
5	$(CH_3)_2CH(CH_2)_2CH_2$	−2.29	−0.16[e]	−0.47[d]	−2.23
6	$CH_3(CH_2)_6CH_2$	−2.29	−0.17[e]	−0.53[d]	−2.23
7	$CH_3(CH_2)_4CH_2$	−2.29	−0.16[e]	−0.44[f]	−2.24
8	$CH_3(CH_2)_3CH_2$	−2.27	−0.16[e]	−0.40	−2.22
9	$(CH_3)_2CH$	−2.27	−0.1[g]	−0.47	−2.21
10	$CH_3(CH_2)_2CH_2$	−2.24	−0.115	−0.39	−2.19
11	$CH_3CH_2CH_2$	−2.22	−0.10	−0.36	−2.18
12	CH_3CH_2	−2.17	0.00	−0.07	−2.16
13	$Ph(CH_2)_2CH_2$	−2.18	0.08	−0.51[d]	−2.12
14	$PhCH_2CH_2$	−2.15	0.215	−0.55[h]	−2.08
15	$EtO_2C(CH_2)_3CH_2$	−2.18	0.09[i]	−0.4[j]	−2.13
16	$EtO_2C(CH_2)_2CH_2$	−2.18	0.26[i]	−0.5[j]	−2.12
17	$PhO(CH_2)_3CH_2$	−2.13	0.11[i]	−0.4[k]	−2.08
18	$PhO(CH_2)_2CH_2$	−2.12	0.30[i]	−0.51[l]	−2.06
19	$F(CH_2)_2CH_2$	−2.08	0.39[i]	−0.4[k]	−2.03
20	$NC(CH_2)_2CH_2$	−2.06	0.47[i]	−0.5[k]	−2.00
21	HCH_2	−1.96	0.49	0.0	−1.96
22	$EtO_2CCH_2CH_2$	−2.04	0.72[i]	−0.9[j]	−1.93
23	$PhOCH_2CH_2$	−2.01	0.85	−0.87[d]	−1.91
24	$NCCH_2CH_2$	−1.87	1.30	−0.9[j]	−1.76

[a] Electroreduction as described in the Experimental Section. [b] In volts *vs.* the SCE and corrected for *i*R drop in cell. [c] Unless otherwise noted, values are from 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. [d] John E. Hiatt, Occidental College, results from acid hydrolyses at 25.00° in 70% acetone. [e] A. B. Hoelfelmeyer and C. K. Hancock, *J. Am. Chem. Soc.*, **77**, 4746 (1955). [f] G. Davies and D. P. Evans, *J. Chem. Soc.*, 339 (1940). [g] Value estimated from the σ^* of −0.10 resulting from replacement of the first hydrogen in CH_3 by a methyl group. [h] H. A. Smith and R. R. Meyers, *J. Am. Chem. Soc.*, **64**, 2362 (1942). [i] Derived from the Taft σ^* for the fundamental substituent[c] by multiplying its σ^* by 1/2.8 for each CH_2 group between the substituent and the CH_2Br root. [j] From hydrolysis rates by E. J. Salmi, *Ber.*, **72**, 1767 (1939). [k] Estimated from E_s value of four comparable pairs of esters of Salmi[j] and Hiatt.[d] [l] As in footnote *d*, by David L. McFadden.

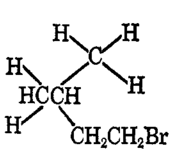
off such a line.[12] If the $E_{1/2}$ values of all the bromo compounds are plotted *vs.* the σ^* for RCH_2 rather than the σ^* for R, a much less acceptable linear relationship results.[13]

This loss in correlation is caused by decreasing the influence of the Taft polar parameter on the $E_{1/2}$ function; *i.e.*, adding a CH_2 group to an R reduces the radical's positive σ^* value by a factor of 0.385 and decreases the power of the σ^* parameters to act as operators in any function—in this series of compounds, by reducing their σ^* values from a total span of −0.30 to +1.30 to one of only −0.19 to +0.47.

Thus, it is clear that inductive or field effects as indicated by the Taft polar constants, σ^*, are a strongly determinative factor in the polarographic reduction of alkyl bromides at the DME. However, it is equally apparent that methyl bromide, ethyl bromide, and the compounds in which steric hindrance exists to conventional SN2 chemical displacement deviate most from the correlation line. Use of the Taft steric parameters, E_s, as a measure of steric influence on polarographic reduction corrects for these deviations remarkably well.

The best regression line which includes all points is shown in Figure 2 as $E_{1/2} = 0.32^5\sigma^* + 0.12E_s - 2.16^5$. The standard deviation for these 24 compounds is 0.023 v. The inclusion of substances with a σ^* range of 1.60 and an E_s variation of 0 to −1.74 over a half-wave span of 0.58 v certainly emphasizes the quantitative relationship of the polarographic reduction of alkyl bromides to both polar and steric effects.[14]

An unexpected, but potentially important, result appears upon examining the structure of the substances other than methyl bromide which deviate most from the line in Figure 2: isoamyl bromide (**4**), ethyl 4-bromobutanoate (**16**), and 4-phenoxybutyl bromide (**17**).



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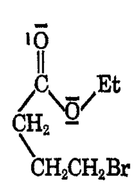

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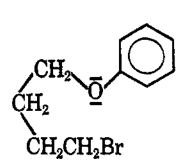

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After correction for steric influences by use of the E_s factor, the $E_{1/2}$ of **4** lies considerably below the line, as does **16**, whereas **17** lies an equal potential above the line.

It appears that we have evidence for a Newman "rule of six" effect,[15] considering the mercury drop as being at the 1 position attacking either the carbon

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[12] A least-squares analysis gives $E_{1/2} = 0.32^0\sigma^* - 2.23$ with a standard deviation of 0.049 v.

[13] $E_{1/2} = 0.66^8\sigma^* - 2.19$, with a standard deviation of 0.068 v.

[14] In comparison to the many electroreducible systems reported by Zuman,[3] the group of alkyl bromides presented here appears to comprise the organic class with the largest range in half-wave potentials and of σ^* values. No such wide variation in E_s values of affective groups has been successfully treated in previous polarographic–Taft constant studies.

[15] E. S. Gould, "Mechanisms and Structure in Organic Chemistry," Henry Holt and Co., New York, N. Y., 1959, p 323. M. S. Newman, *J. Am. Chem. Soc.*, **72**, 4783 (1950).

of the CBr as the 2 position or the antibonding orbital of CBr itself as the 2 position (*vide infra*). Alternatively, considering the influence of oxygen (or hydrogen in the case of **4**) on the carbon of the CBr bond (or the antibonding orbital itself) these three compounds demonstrate five-membered ring interaction in polarographic reduction.

The explanation for the off-curve location of isoamyl bromide is not profound; the deviation can be shown to be simply an artifact of the definition of the Taft steric constants.[16] Nevertheless, this seeming discrepancy emphasizes the steric importance to polarographic reduction of more than two or three hydrogen atoms which are located in the 6 position relative to the carbon of the CBr bond as the 2 position (or 5 position relative to carbon as in the 1 position, of course).

The behavior of **16** and **17** appears to represent another form of active participation in electroreduction by a group distant from the site of the reduction. However, hypotheses concerning the nature of the interaction of the phenoxy or carbethoxy group must be considered very tentative at this time.[17]

No three-membered ring participation is seen in the polarographic reduction of alkyl bromides **23** and **24** (or **14**). The normally large E_s values for esters which are substituted in the β position with electron-rich groups are adequately corrective for steric influences in these electrochemical reductions. This is not completely to be expected because the electron-rich nitrogen and oxygen in **23** and **24** might themselves be repelled by the DME and make the reduction more difficult than would be predicted by the inductive and steric effects measured by the Taft constants.

As shown here, electron-withdrawing groups aid polarographic reduction; our results therefore support the frequently mentioned mechanism involving formation of the radical anion, $(R{-}Br)\cdot^-$, in the potential-determining step for these compounds. But further, our quantitative evaluation of steric effects as modulating influences in these electroreductions appears to challenge Elving's[18] and our[1] case for strict application of electrostatics as the determining factor in orienting the RBr molecule in the transition state.

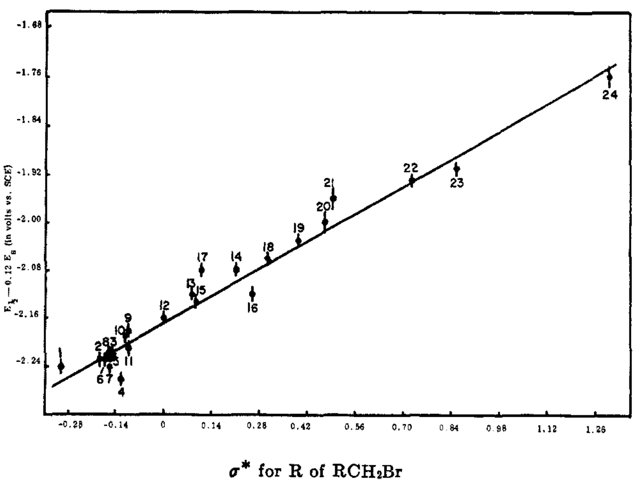

Figure 2.—Half-wave potentials of alkyl bromides corrected for steric factors ($E_{1/2} - 0.12E_s$) against σ^*.

We had maintained, after Elving, that the negatively polarized bromine in RBr would be repelled by the negative dropping mercury electrode. This should cause the RBr molecule to approach the electrode with the axis of the carbon–bromine bond normal to the electrode surface with the bromine directed away from the surface. Subsequently, the transition state should involve the same geometry with an electron being transferred from the electrode to the rear of the carbon holding the bromine. As in SN2 reactions, therefore, steric factors should be equally prominent in polarographic reduction because of the hindering effects of groups which block the rear of the CBr bond. This was qualitatively shown to be true in our early work[1b] and was used as a guide in interpreting more recent results.[1a]

However, the present study indicates far milder quantitative steric effects than are operative in normal SN2 chemical displacements. In such displacement reactions, methyl halides are an order of magnitude more reactive than ethyl or propyl halides which in turn are an order of magnitude more reactive than isobutyl and *ca.* 10^5 than neopentyl halides. This is not the difference present in the Taft steric parameters[19]—for the obvious reason that Taft constants are derived from ester hydrolyses where reaction occurs on the sp^2 carbonyl carbon rather than by displacement on an sp^3 carbon attached to the carbethoxy group. And yet, as shown by the regression line of Figure 2, the Taft constants furnish an excellent quantitative measure of the influence of steric factors on the polarographic reduction of alkyl bromides.

Thus, if the polarographic transition state does involve a direct attack of electrons from the cathode on the backside of the carbon in the CBr bond ("SN2-like"), the attack must be able to penetrate a screen of alkyl groups *more* readily than does a nucleophile

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[16] As demonstrated in this research, when there are more than three hydrogens either in the 5 or 6 position of the alkyl bromide (numbering the carbon attached to bromine as the 2 position and counting hydrogen atoms as in ref 15), polarographic reduction is unusually difficult; *e.g.*, neopentyl, isobutyl, cyclohexylmethyl, and isoamyl bromides. However, the Taft E_s parameter will be adequately corrective in the first three of these examples because the esters from which their E_s values are derived have the same number of hydrogens in the ester's 6 position (numbering the carbonyl carbon as the 2 position) as the alkyl bromides have in their 5 position. Only in the case of isoamyl bromide is there an anomaly in this pattern. In ethyl isocaproate, from which the E_s for isoamyl bromide is derived, there is only one hydrogen in the ester's 6 position (and two hydrogens in the 5 position). But there are six hydrogen atoms in isoamyl bromide's 6 position (and one hydrogen in the 5 position).

Therefore, the Taft E_s value for the isoamyl group inadequately corrects for the steric hindrance actually present in the polarographic reduction of isoamyl bromide. From the results of this research, a better value for the E_s of the isoamyl group would be 1.0 in polarographic work with comparable mechanisms. (With this correction, the standard deviation of the entire series is lowered to 0.020 v).

[17] The disparate behavior of **16** and **17** was made evident only by final plotting of curves as this research was being prepared for publication; further work to elucidate the extent and mechanism of the participation phenomenon is planned. A tenable hypothesis involves dispersal of the electron (or electrons) in the σ-antibonding orbital of $R(CH_2{-}Br)\cdot^-$ *via* the nonbonded electrons on the oxygen to the anti-bonding orbitals of carbon atoms in the benzene ring; a σ-star to π-star transition may play a part. Such broad electron and charge dispersal is not only impossible in **17** but in addition the electron clouds of two oxygen atoms could be significantly destablizing to a negative radical such as $R(CH_2{-}Br)\cdot^-$.

[18] P. J. Elving and B. Pullman, *Advan. Chem. Phys.*, **3**, 1 (1961), and Elving's earlier work.

[19] The steric parameters, E_s, for methyl (0.0), ethyl (0.07), propyl (0.36), isobutyl (0.93), and neopentyl (1.74) bear no discernible quantitative relation to the classic SN2 reactivity of the corresponding bromides, nor does any combination of the σ^* function modified by these E_s factors that we have been able to discover.

such as OH$^-$ or SCN$^-$[20] and precisely in the same quantitative order as the E_s constants indicate. This could conceivably be the case but in the absence of powerful evidence to support it, the simple picture of "SN2-like" attack in electroreduction of alkyl bromides must be discarded.

Alternatively, the attack may be as Sease has proposed for bridgehead bromides,[21] "head-on" to the bromine resulting in displacement of the R *from* the bromine. But in this process of attack from the bromine side, no conventional steric effects by R groups should be noted in polarographic reduction of RBr compounds; the $E_{1/2}$ values of our alkyl bromides should lie on a line *vs.* σ^* prior to any correction for steric factors. Thus, frontal attack on bromine is at variance with the experimental results in this paper.

A third possibility for the geometry of the transition state could involve attack on the alkyl bromide by electrons from the DME in a direction perpendicular to the axis of the CBr bond.[22] Certainly, this would be spatially consistent with addition of an electron to the σ-antibonding orbital. In such a process not only would steric effects of nearby alkyl groups be present but they should be roughly as effective as in the hydrolysis process from which the Taft steric constants were derived. In hydrolysis, the incoming group also attacks perpendicularly to the axis of the (>C=O) bond. The quantitative success of the E_s parameters in correlating the polarographic behavior of these widely differing alkyl bromides provides support for a mechanism involving side attack on the CBr bond.

Work is planned to explore the mechanism of the involvement of distant groups in electroreductions including the use of *p*-methylthiophenoxyalkyl bromides to indicate the extent of radical character in the activated intermediate.[23]

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[20] The *ad hoc* argument on p 5327 of ref 1b to explain the more negative reduction potentials of butyl and amyl bromides than propyl bromide invoked *more* hindrance to polarographic electron attack than SCN$^-$ attack because the dominant importance of polar substituent effects was not then seen.

[21] J. W. Sease, P. Chang, and J. L. Groth, *J. Am. Chem. Soc.*, **86**, 3154 (1964).

[22] A possibility suggested by Professor A. Streitwieser, Jr., Gordon Research Conference on Electrochemistry, Santa Barbara, Calif., Jan 1965.

[23] A. Streitwieser, Jr., and C. Perrin, *J. Am. Chem. Soc.*, **86**, 4938 (1964).

Synthetic Experiments in the Eudalene Group of Bicyclic Sesquiterpenes. II[1]

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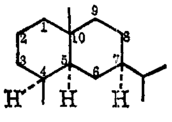
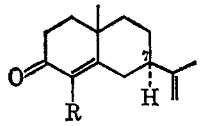
Some investigations on the application of the Robinson–Mannich annelation reaction to synthesis in the eudesmane group of sesquiterpenes are described. Epimerization at position 7 of the diketone XIV and the epoxide XV is easily effected by acid or base treatment. The possibility of using the major products of annelation reactions with (−)-dihydrocarvone in synthesis is thereby opened up.

The Robinson–Mannich and related annelation reactions have featured prominently in syntheses in the terpene and steroid fields. We describe here some preliminary experiments designed to extend the application of the reaction in syntheses in the eudesmane (I) group of bicyclic sesquiterpenes. Our attention has been focussed in particular on the stereochemical problems[5] involved in the use of the reaction as a starting point in synthesis in this family.



I



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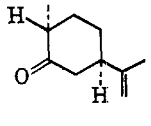
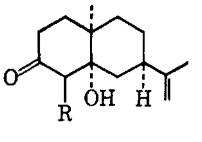


III



IV

In their synthesis of natural (+)-α-cyperone (II, R = CH_3) Howe and McQuillin[6] effected a Robinson–Mannich condensation between (+)-dihydrocarvone, of known absolute configuration[7] (III), and 1-diethylaminopentan-3-one methiodide. The major products were the ketol IV (R = CH_3) and the conjugated enone V (R = CH_3), in accordance with the established stereochemical course of the annelation reaction.[8] (+)-α-Cyperone (II, R = CH_3) was a minor product, but fortunately it was easily separated by chromatography and through the crystalline oxime. We anticipated that an analogous condensation of (+)-

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[1] Part I: A. R. Pinder and R. A. Williams, *J. Chem. Soc.*, 2773 (1963); *Chem. Ind.* (London), 1714 (1961).

[2] Abstracted from a thesis presented by D. C. Humber in partial fulfillment of the requirements for the Ph.D. Degree, University of Wales.

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[5] For a review of stereochemical relationships among eudesmane sesquiterpenes see W. Cocker and T. B. H. McMurry, *Tetrahedron*, **8**, 181 (1960). We have used these authors' numbering.

[6] R. Howe and F. J. McQuillin, *J. Chem. Soc.*, 2423 (1955).

[7] A. J. Birch, *Ann. Rept. Chem. Soc.*, **47**, 192 (1950), and references cited therein.

[8] (a) F. J. McQuillin, *J. Chem. Soc.*, 528 (1955); (b) T. A. Spencer, H. S. Neel, D. C. Ward, and K. L. Williamson, *J. Org. Chem.*, **31**, 434 (1966); (c) K. L. Williamson, L. R. Sloan, T. Howell, and T. A. Spencer, *ibid.*, **31**, 436 (1966); (d) T. A. Spencer, K. K. Schmiegel, and K. L. Williamson, *J. Am. Chem. Soc.*, **85**, 3785 (1963); (e) W. Cocker, *Ann. Rept. Chem. Soc.*, **51**, 210 (1954); (f) J. A. Marshall and W. I. Fanta, *J. Org. Chem.*, **29**, 2501 (1964).