The Importance of Steric Inhibition of Resonance in the Mass Spectral Cleavage of Benzophenones

MAURICE M. BURSEY*[1] AND CHARLES E. TWINE, JR.

Venable Chemical Laboratory, The University of North Carolina, Chapel Hill, North Carolina 27514

Received June 5, 1970

The intensity of the benzoyl ion, *m/e* 105, in the mass spectra of some para-monosubstituted benzophenones was compared with the intensity of this ion in benzophenones where the para substituent is flanked by two bromo substituents in the 3 and 5 positions. Consideration of the scatter in the Hammett plot expected for multiple substitution does not alter the conclusion that the dimethylamino group acts very nearly the same in the presence and in the absence of two adjacent bromo substituents.

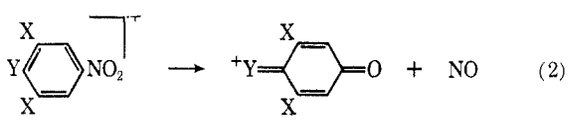
This study extends the analysis of substituent effects on ion intensities with a search for steric inhibition of resonance of the dimethylamino substituent by flanking groups. It was observed some years ago that relative intensities of the *m/e* 105 ion, presumably $C_6H_5CO^+$, in the spectra of singly substituted benzophenones can be correlated remarkably well with Hammett σ constants.[2] If the intensities of benzoyl ions in each spectrum [A^+], divided by the intensities of the molecular ions from which they are formed [M^+], are plotted as the ratio $Z = [A^+]/[M^+]$ against substituent constants, then eq 1 is obeyed very well, with a ρ value of

$$\log (Z/Z_0) = \rho\sigma \qquad (1)$$

1.01.[2] Other plots for data collected for other systems have been prepared;[3] sometimes a good correlation is obtained, sometimes not. More sophisticated arguments than the original kinetic interpretation[2] have now been advanced to explain these results,[4-8] and it now appears that the benzophenone system fits the Hammett equation so well because of the coincident magnitudes of many factors which influence reactivity in one of several ways: either the factors correlate well in Hammett plots, or else they are quite independent of Hammett constants and produce only a uniform influence on intensity, or else they have an effect tending to destroy the correlation but are insignificant when compared to the effects which tend to produce an overall correlation. Hence the benzophenone system should give a tight correlation because of an appropriate dependence of ionization potentials and appearance potentials on substituent constants, a proper distribution of ion energies after electron impact, and a lack of competing reactions which would tend to destroy the correlation, so that rates of processes and amounts of ions produced by decomposition reflect the fundamental effect of the substituents on electron density.

For singly substituted benzophenones the correlation is sufficiently good to be of excellent predictive value; ortho substituent effects derived from the mass spectra of ortho-substituted benzophenones[9] produce essentially the same Hammett-type constants as data for the same substituents obtained from gas-phase pyrolyses of esters.[10] Likewise, one can take advantage of the excellent correlation of singly substituted benzophenones to test the loss of correlation predicted for multiply substituted benzophenones as a result principally of the introduction of more reaction pathways competing with the formation of benzoyl ion.[11] It appears that, as expected, a loss of correlation does occur for doubly substituted benzophenones, but the standard deviation of points from the line does not increase so greatly as to preclude the extraction of information about fundamental substituent effects from an ion-intensity plot.

Consequently, it is possible to examine this well-behaved system for steric inhibition of resonance. Steric inhibition of resonance has been studied for another mass spectral reaction, eq 2, where the effect of



(2)

the para electron donor on the formation of the product ion is in keeping with stabilization of the daughter ion by resonance when X is H; the intensity of the ion increases markedly for Y = OH, OCH_3, NH_2, $N(CH_3)_2$.[12] On the other hand, when X is fairly large, a chloro or bromo substituent[13] or a methyl substituent[14] on either side of a very large para donor like the dimethylamino substituent should prevent stabilization of the product ion by resonance, since the electron donor should be twisted with respect to the plane of the ring, and, in fact, the relative intensity of the product ion is dramatically reduced for the hindered system.

It has been observed empirically that the stability of the product ion is a very important "driving force" in governing the intensities of product peaks in mass spectra.[5b,15] In the case of the nitrobenzenes, the substituents obviously play a very great role in this respect. We have now studied the benzophenone system, in which the stability of the product ion is not determined by a retained substituent in the ion. Thus we may ex-

(1) Research Fellow of the Alfred P. Sloan Foundation, 1969–1971. To whom correspondence should be addressed.

(2) M. M. Bursey and F. W. McLafferty, *J. Amer. Chem. Soc.*, **88**, 529 (1966).

(3) For a review, see M. M. Bursey, *Org. Mass Spectrom.*, **1**, 31 (1968).

(4) (a) R. P. Buck and M. M. Bursey, *ibid.*, **3**, 387 (1970); (b) M. M. Bursey and P. T. Kissinger, *ibid.*, **3**, 395 (1970); (c) M. M. Bursey and M. K. Hoffman, "Mass Spectrometry, 1970," G. W. A. Milne, Ed., Wiley, New York, N. Y., in press.

(5) (a) F. W. McLafferty, *Chem. Commun.*, 956 (1968); (b) F. W. McLafferty and M. M. Bursey, *J. Amer. Chem. Soc.*, **90**, 5299 (1968).

(6) (a) R. S. Ward, R. G. Cooks, and D. H. Williams, *ibid.*, **91**, 2727 (1969); (b) R. G. Cooks, I. Howe, and D. H. Williams, *Org. Mass Spectrom.*, **2**, 137 (1969).

(7) M. S. Chin and A. G. Harrison, *ibid.*, **2**, 1073 (1969).

(8) T. W. Bentley, R. A. W. Johnstone, and D. W. Payling, *J. Amer. Chem. Soc.*, **91**, 3978 (1969).

(9) K. K. Lum and G. G. Smith, *J. Org. Chem.*, **34**, 2095 (1969).

(10) G. G. Smith, K. K. Lum, J. A. Kirby, and J. Posposil, *ibid.*, **34**, 2090 (1969).

(11) M. M. Bursey and C. E. Twine, Jr., *ibid.*, **35**, 2012 (1970).

(12) M. M. Bursey and F. W. McLafferty, *J. Amer. Chem. Soc.*, **88**, 5023 (1966).

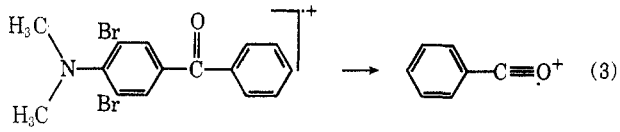
(13) M. M. Bursey, *ibid.*, **91**, 1861 (1969).

(14) M. M. Bursey and M. K. Hoffman, *ibid.*, **91**, 5023 (1969).

(15) F. W. McLafferty, "Interpretation of Mass Spectra," W. A. Benjamin, New York, N. Y., 1966, p 81.

pect that steric effects are likely to play a more subtle role than in the nitrobenzene system. For example, the removal of direct resonance interaction of the substituent and reaction site might limit the substituent effect approximately to its field or inductive effect. In this case, one might expect the substituent effect to resume that of the meta substituent, where the resonance effect is small and other interactions predominate.

The point of our experiment was to determine whether the regular ion intensity relationship for the *m/e* 105 ion observed in the mass spectrum of benzophenones[2,9,11] showed deviation from additivity when the dimethylamino group in the para position was blocked by ortho bromo substituents (eq 3). If there is signifi-



(3)

cant steric inhibition of resonance, it will be reflected in an *increase* in the production of *m/e* 105, for a decrease in electron-donor ability increases the amount of *m/e* 105 formed. The alteration in the substituent effect may be estimated by comparing the σ values of *p*-$N(CH_3)_2$ and *m*-$N(CH_3)_2$, -0.83 *vs.* -0.21, respectively.[16] Since substituent effects in this system are additive,[11] we may assume that the difference between these effects will hold irrespective of further substitution on the ring by the blocking groups. This is of course an oversimplification: the degree of resonance interaction of the dimethylamino group with the ring depends on the angle by which it is twisted out of the plane; the angle depends on the size of the blocking group. For our model, we assume a picture in which, as an extreme, the groups are sufficiently large to effectively remove the typical para resonance interaction.

Thus the alteration in intensities will be given by eq 4. The slope estimate from the correlation of mono-

$$\Delta \log (Z/Z_0) = \rho\Delta\sigma \quad (4)$$

substituted benzophenones is 1.01;[2] from disubstituted, 0.77.[11] Hence, for alteration of the substituent effect to something approximated by the meta effect, there should be an increase in log *Z* by 0.48–0.62 log unit.

This increase is predicated upon the accurate prediction of intensities by the Hammett correlation. As we have noted,[11] when there is multiple substitution the scatter increases because of the increase in the number of decomposition routes competing with the production of $C_6H_5CO^+$ from the molecular ion. The standard deviation of points from the line for doubly substituted compounds is 0.15 log unit against σ, 0.06 log unit against σ^+; the standard deviation for singly substituted compounds using the same substituents is 0.06 against σ, 0.07 against σ^+. Thus the expected value of the change in log *Z* is much larger than the error introduced by the assumption that the substituent effects which tend to destroy the correlation for this fragmentation process are not important. The magnitude of 95% of all deviations from the expected values is, according to statistics, less than twice the standard deviation; consequently, so large a change in log *Z*, if observed, can be ascribed with high confidence to an alteration in the substituent effect involving electron distribution (*e.g.*, the σ constant for the substituent), not to some other phenomenon such as the introduction of competitive processes, gross alteration of the distribution of energy states, and so forth. In short, interpretation of results is feasible.

(16) The σ values were taken from the tabulation of C. D. Ritchie and W. F. Sager, *Progr. Phys. Org. Chem.*, **2**, 323 (1964).

Experimental Section

Preparation of Benzophenones.—The compounds were either commercially available or else produced by literature procedures.[17-19] The only new compound was **3,5-dibromo-4-dimethylaminobenzophenone**, which was prepared by the methylation of 4-amino-3,5-dibromobenzophenone[17] with trimethyl phosphate at 60° for 8 hr,[20] and purified by column and thin layer chromatography, after which it had mp 97–98°. It tends to decompose on silica.

Anal. Calcd for $C_{15}H_{13}Br_2NO$: C, 47.04; H, 3.39; monoisotopic mol wt, 380.9363. Found: C, 46.97; H, 3.23; mol wt, 380.9361.

The purity of all samples was checked by agreement of their melting point with reported values and/or thin layer chromatographic homogeneity. If apparent decomposition on the tlc plate was observed (recovered single bands from tlc giving, on repeated chromatography, multiple bands identical with the previous chromatogram), the identity and purity of the desired band were checked by other means. The analytical sample of the 3,5-dibromo-4-dimethylaminobenzophenone was used for the mass spectra, since its purity was crucial.

Mass Spectra.—All the mass spectra were recorded on a Hitachi RMU-6E single-focusing instrument, using 75-eV electrons (emission current 80 μA). The source pressure was always in the range $5–10 \times 10^{-7}$ Torr, with a source temperature at 185 ± 5°. Samples were introduced by the direct-insertion probe, because the data for samples introduced by the heated inlet at 185 ± 5° gave indication of some thermal decomposition, especially for the dibromohydroxy and dibromomethoxy compounds.[21] The reproducibility of peak height ratios was at least 3% for quadruplicate determinations and usually much better (1%).

Results and Discussion

Our results for the "unblocked" and "blocked" compounds are listed in Table I. Their correlation with

TABLE I

RELATIVE INTENSITIES OF $C_6H_5CO^+$ (*m/e* 105) IN MASS SPECTRA OF SUBSTITUTED BENZOPHENONES

Substituent	Registry no.	Log Z/Z_0	$\Sigma\sigma$[a]	$\Sigma\sigma^+$[a]
4-OH	1137-42-4	−0.27	−0.37	−0.92
4-OCH_3	611-94-9	−0.33	−0.27	−0.78
4-NH_2	1137-41-3	−0.79	−0.66	−1.3
4-$N(CH_3)_2$	530-44-9	−0.47	−0.83	−1.7
3,5-Br_2-4-OH	26733-16-4	+0.29	+0.41	−0.12
3,5-Br_2-4-OCH_3	26733-17-5	+0.50	+0.51	+0.02
3,5-Br_2-4-NH_2	26733-18-6	−0.20	+0.12	−0.5
3,5-Br_2-4-$N(CH_3)_2$	26785-69-3	−0.68	−0.05	−0.90

[a] See ref 16.

substituent constants are illustrated in the figures. Figure 1 shows a plot of relative intensities *vs.* the sum of Hammett σ constants for both the monsubstituted

(17) L. Clarke and G. J. Esselen, Jr., *J. Amer. Chem. Soc.*, **33**, 1135 (1911).

(18) P. J. Montagne, *Recl. Trav. Chim. Pays-Bas*, **41**, 703 (1922).

(19) *Cf.* G. N. Vyas and N. M. Shah, "Organic Syntheses," Coll. Vol. IV, N. Rabjohn, Ed, Wiley, New York, N. Y., 1963, p 836.

(20) *Cf.* J. H. Billman, A. Radike, and B. W. Mundy, *J. Amer. Chem. Soc.*, **64**, 2977 (1942).

(21) There was a small variance in several data points for the disubstituted benzophenones introduced by the direct probe from values reported earlier.[11] The change in the position of points was just outside experimental error, no new trends for these points were noted, and the quantitative conclusions reached earlier[11] are still valid.

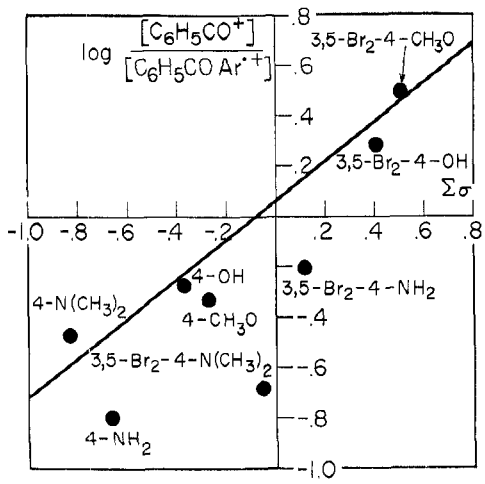


Figure 1.—Correlation of log (Z/Z_0) with σ and $\Sigma\sigma$ for the formation of $C_6H_5CO^+$ from unhindered and hindered benzophenones.

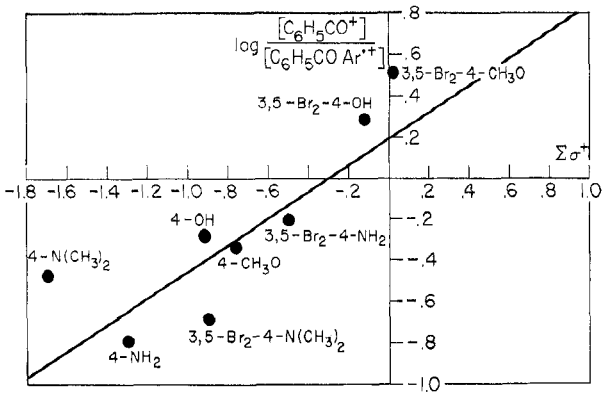


Figure 2.—Correlation of log (Z/Z_0) with σ^+ and $\Sigma\sigma^+$ for the formation of $C_6H_5CO^+$ from hindered and unhindered benzophenones.

and trisubstituted compounds; Figure 2 shows the same data points *vs.* the sum of σ^+ constants. We plot both monosubstituted and trisubstituted compounds in the same graph because the substituent effects are additive,[11] the bromo substituents affecting the orientation only of the dimethylamino group, and because we wish to illustrate at once the behavior of the key substituent, dimethylamino, when it is flanked by large substituents and when it is not. The correlation lines are determined with the exclusion of the point for the dibromodimethylamino compound; only compounds where there can be no steric effect influence the position of the line. Thus the line is not influenced by the dibromodimethylamino compound, the one point whose deviation from the line is the crux of this analysis.

For Figure 1, the plot *vs.* σ values, the slope is 0.78, the standard deviation of seven points from the correlation line is 0.17 log unit, and the correlation coefficient is 0.913. The slope is in reasonable agreement with the value of 1.01 for monosubstituted benzophenones and 0.77 for disubstituted benzophenones. The correlation coefficient is nearly the same as that found for the disubstituted compounds earlier, 0.918,[11] though it might be expected to decrease as a result of less sampling of data in this graph. The standard deviation is larger than the values of 0.09 and 0.15 obtained for monosubstituted and disubstituted compounds earlier.[11]

For Figure 2, the plot *vs.* σ^+ values, the slope is 0.63, the standard deviation of seven points from the correlation line is 0.24, and the correlation coefficient is 0.884. The value of the slope may be compared with values of 0.66 and 0.55 for the slopes of correlation lines found for the monosubstituted[2] and disubstituted[11] benzophenones plotted *vs.* σ^+ constants. As expected from the smaller sampling of data, there is a decrease in the correlation coefficient relative to that for the plot of disubstituted compound values *vs.* σ^+ (0.956) and an increase in standard deviations from previous[11] values (0.11, 0.06). Hence the deviation of data points from predicted values, *i.e.*, points on the correlation line, is in rather good accordance with what was expected.

We are now in a position to comment on the placement of the dibromodimethylamino point on these graphs. The deviation from the correlation line in Figure 1 is −0.70 log unit; in Figure 2 it is −0.29 log unit. The strong inhibition of resonance described earlier would have been expected to raise the point above the line by 0.48 to 0.62 log unit; one may even argue that since the log Z/Z_0 values for the single substituent *m*-Br is also above the correlation line for single substituents,[2] additivity of substituent effects requires that the point should actually be raised even more than 0.48 to 0.62 log unit. Quite obviously the deviation from the correlation line is not so positive as this picture predicts. To a first approximation, then, the picture is invalid.

Considering now the standard deviation of the data in these plots and others previously cited, we find it unlikely that the results can be explained away by two compensating effects, one an increase in the true substituent effect on the reaction in question and the other an opposite variation in intensity resulting from the introduction of new reaction pathways and distortion of energy distributions. The statistics argue strongly against so large a variation due to other causes. The amount by which log (Z/Z_0) would have to be lowered to compensate for so large an increase in the true substituent effect (0.48 to 0.62 log unit), and also lower the point to its actual position below the line, exceeds the standard deviation of the data by more than four times the standard deviation of data points for comparable systems, and must therefore correspond to a situation which exists less than one time in five thousand. The more reasonable picture is that there is in fact very little steric inhibition of resonance of the dimethylamino group by the bromo substituents flanking it in this system; if there is any change in the effect of the dimethylamino group, it is less than can be detected because of statistical problems. Thus more resonance interaction remains in the system than the meta-substitution analogy can approximate, and indeed the para-substitution analogy still predicts results fairly well.

We note that there is a parallel between these results, where the resonance effect of the dimethylamino group cannot be diminished by attempts at twisting it, and the previously reported case of the *p*-phenyl substituent in the benzophenone system.[2] A very strong resonance effect, greater than nearly all solution cases, was noted there in the formation of *m/e* 105, and it was attributed to the ability of the *p*-phenyl substituent to achieved coplanarity with the substituted ring in the molecular ion more easily, since blocking by ortho hydrogens was

apparently very easily overcome. We are continuing our studies by examining the effect of other, larger ortho substituents on the resonance effect of the *p*-phenyl substituent in benzophenones.

In comparison with the result for the hindered nitrobenzenes,[13,14] these two results are startling. In the nitrobenzenes, where one begins with a system without much resonance interaction between substituent and reaction center and produces an ion where resonance stabilization is important, steric inhibition of resonance is easily achieved by flanking groups. Now juxtaposed to this system we have a case where resonance demand is lost in the product ion, yet as measured by substituent effects flanking substituents seem unable to decrease resonance interaction substantially. This latter case is of course one in which the number of free rotors increases throughout the progress of the reaction, while the nitrobenzene rearrangement involves a decreasing number of rotors as the quinonoid ion is formed in the initial stages of the reaction. In the statistical treatment,[22] the energy dependence of rates (and therefore ultimately ion intensities) is then different for the two cases. Even so, it is difficult to draw a fully consistent picture. Apparently resonance effects remain important in spite of blocking in simple cleavages like the formation of *m/e* 105 in benzophenones, fast reactions on the average, but can be blocked in at least some rearrangements, like the nitrobenzene rearrangement, which are on the average several orders of magnitude slower. Perhaps this implies that steric inhibition of resonance takes time to become effective, as if ionization on the nitrogen atom in both systems (or the first transmittal of energy to this site of lowest energy) produces at first a nonequilibrium set of states in which there is enough vibrational energy associated with the dimethylamino group to force a more nearly planar configuration of the substituent and the ring, but then over several hundred vibrational periods equilibrium among vibrational modes over the whole molecule is achieved, and the substituent then no longer can so easily achieve such a small average dihedral angle with the ring.

(22) H. M. Rosenstock, *Advan. Mass Spectrom.*, **4**, 523 (1968), and references contained therein.

Acknowledgments.—We thank the University Research Council of the University of North Carolina at Chapel Hill for help in supporting this work.

Cleavage of α,α'-Dinitrocyclanones

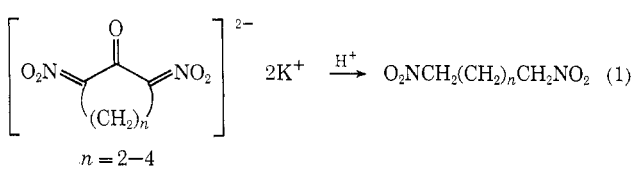
H. FEUER,* A. M. HALL, AND R. S. ANDERSON

Department of Chemistry, Purdue University, Lafayette, Indiana 47907

Received April 27, 1970

In aqueous medium at the appropriate pH, potassium salts of α,α'-dinitrocyclanones undergo ring cleavage to the corresponding α,ω-dinitroalkanes in high yield. In methanolic acetic acid, cleavage proceeds without decarboxylation to α,ω-dinitroalkyl methyl esters.

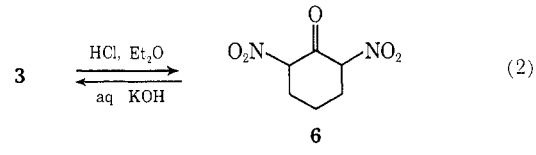
In a preliminary report,[1] we communicated a new ring-opening reaction of potassium 2-keto-3-nitrocycloalkanenitronates which provides a convenient route for the preparation of α,ω-dinitroalkanes. These salts were obtained directly from alkyl nitrate nitration mixtures[2] after acidification with glacial acetic acid and, therefore, were contaminated with potassium acetate. We are now reporting on the results of the reaction with the analytically pure salts, dipotassium 2-keto-1,3-cyclopentanedinitronate (**1**), potassium 2-keto-3-nitrocyclopentanenitronate (**2**), dipotassium 2-keto-1,3-cyclohexanedinitronate (**3**), potassium 2-keto-3-nitrocyclohexanenitronate (**4**), and dipotassium 2-keto-1,3-cycloheptanenitronate[3] (**5**) (eq 1). The purity of these



salts was conveniently determined by nonaqueous titration.[4]

The pure mononitronate salts **2** and **4** were obtained on acidifying aqueous solutions of the corresponding dinitronate salts[3] **1** and **3** at 0° with acetic acid. Compound **4** was also obtained on treating **3** with methanolic glacial acetic acid at 25°. This procedure was not applicable for the preparation of **2** because of its high solubility in methanol.

The high purity of **3** was demonstrated by the fact that it was converted in 93% yield to 2,6-dinitrocyclohexanone (**6**) upon treatment with hydrogen chloride in an ether suspension. Compound **6** was purified by sublimation *in vacuo* and, contrary to a previous report,[5] readily gave a 2,4-DNP derivative in 90% yield. **6** was reconverted into **3** on treatment with aqueous potassium hydroxide (eq 2).



α,ω-Dinitroalkanes.—The results of hydrolytic cleavage of compounds **1**–**6** leading to α,ω-dinitroalkanes are summarized in Table I. At about the same pH, the disalts **1** and **3** gave 1,4-dinitrobutane (**7**) and 1,5-dinitropentane (**8**), respectively, in the same yields as the monosalts **3** and **4**, except that 2 molar equiv of acid was required. However, a significant difference between **1** and **3** was observed on treatment with acetic

* To whom correspondence should be addressed.

(1) H. Feuer and R. S. Anderson, *J. Amer. Chem. Soc.*, **83**, 2960 (1961).

(2) H. Feuer, J. W. Shepherd, and C. Savides, *ibid.*, **78**, 4364 (1956).

(3) H. Feuer, A. M. Hall, S. Golden, and R. L. Reitz, *J. Org. Chem.*, **33**, 3622 (1968).

(4) H. Feuer and B. F. Vincent Jr., *Anal. Chem.*, **35**, 598 (1963).

(5) H. Wieland, P. Garbsch, and J. J. Chavan, *Justus Liebigs Ann. Chem.*, **461**, 295 (1928).