reaction, exhibits smooth pseudo-first-order behavior throughout virtually its entire course.

Differences in catalytic efficiency among the effective additives can be pictured as arising from differences in the equilibrium between the aggregated and the solvated ion pair species. The larger accelerations brought about by the best catalysts result from higher steady-state concentrations of the solvated species, which in turn derive from larger values of the equilibrium constants.[32]

Because the participation orders of the effective additives vary somewhat, and often exhibit nonintegral values (Table IV), mathematical interpretation of the mechanism of solvent action is not possible without employing many unwarranted assumptions. Nevertheless, further qualitative considerations indicate that some form of specific solvation must be operative.

In the first place, the best catalysts, among the fairly wide spectrum of polar compounds tested, are restricted to the two groups: disubstituted amides and coordinate covalent N-, P- and S-oxides; and in the second, not one of these substances displays a participation order less than one in any of the concentration experiments conducted. This means that whatever the mode of solvation may be, the effective additives interact with the aggregate in an average stoichiometric ratio of at least one molecule of additive per ion-pair.

A better understanding of the possible nature of these specific solvent effects can be reached by considering some of the known properties of electrolyte solutions in benzene. As already noted,[30] Kraus[31b] has shown that "the ion dipoles of all salts having one large and one small ion are all [*sic*] highly associated" in benzene solution. These are so-called type 2 electrolytes. In contrast, type 3 electrolytes, having two large ions, show little tendency to associate in benzene beyond the quadrupole stage (association number $\lesseqgtr 2$).

Now, according to Streitwieser[33] "anions and cations require different solvating characteristics: hydrogen-bonding solvents make good anion solvators; solvents containing atoms having unshared electron pairs such as oxygen and nitrogen make relatively good cation solvators." The effective catalysts of the present work all fall into the latter category. Therefore, it is reasonable to assume that they solvate the sodium ion preferentially thereby increasing its effective size The solvated sodio-derivative now contains two large ions. In short, specific solvation of the sodio-derivative by these additives transforms a type 2 to a type 3 electrolyte, which, whatever the reason may be, no longer can exist in its original highly associated form.[34]

This still does not explain why many other additives, also containing unshared electron pairs, exert little, if any, effect on the alkylation rate. The problem of structure–activity relationships among these additives is the subject of the following paper.

Acknowledgments.—The authors are indebted to Mr. Ross Robinson for the cryoscopic and nephelometric determinations, and to Mr. Timothy Wang for technical assistance. H. E. Z. wishes to thank Dr. Nathan Kornblum, Purdue University, Dr. D. S. Tarbell, University of Rochester, and Dr. Irving Klotz, Northwestern University, for many helpful discussions.

[32] This explains why dimethyl sulfoxide can accelerate the reaction despite an augmented activation energy. The extent of equilibrium shift, resulting from the unusually stable solvate with this substance,[22] more than compensates for any retardation of the rate-controlling step produced by an increase in its activation energy.

[33] A. Streitwieser. Jr., *Chem. Revs.*, **56**, 605 (1956).

[34] The possibility of the existence in these experiments of kinetically significant concentrations of free ions has been ignored for several reasons. According to Ingold[35] 'two univalent counter-ions attract each other in benzene, with an energy equal to the mean kinetic energy of either along a line, at a separation of 500 Å.; they haul each other in from such distances." Again, Grunwald[36] has shown from a consideration of the potential energy function of a uni-univalent electrolyte, that even in a dilute solution in a medium of dielectric constant as high as 20, ion-pairs possess considerable stability relative to the separately solvated ions: Brändström[20] has shown kinetically that even in alcoholic solutions of 1 *M* concentration the alkylation of the sodium derivative of acetoacetic ester by methyl iodide is nearly a pure ion-pair reaction. Finally, Zook and Rellahan[4] and Hauser and co-workers[5] have found evidence to indicate the virtual absence of free ions in ethereal solutions of sodio-ketones.

[35] C. K. Ingold, *Proc. Chem. Soc.*, 281 (1957).

[36] E. Grunwald, *Anal. Chem.*, **26**, 1696 (1954).

NORTH CHICAGO, ILL.

[CONTRIBUTION FROM ORGANIC RESEARCH DEPARTMENT, RESEARCH DIVISION, ABBOTT LABORATORIES]

Specific Solvent Effects in the Alkylation of Enolate Anions. II. Relationships between Structure and Physical Properties of Additives and Their Catalytic Efficiencies

BY HAROLD E. ZAUGG

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The ultraviolet behavior of N-methyl-2-pyridone in the presence of sodio-*n*-butylmalonic ester has been studied. Relative basicities of a number of additives have been estimated by titration with perchloric acid in acetic anhydride. Wave lengths of the infrared carbonyl-stretching bands of a group of amide additives have been determined. Molar refractions of a structural cross-section of the amides have been measured. These physical properties, taken together with currently available knowledge of the stereoelectronic nature of many of these additives, have been correlated with catalytic activity in the alkylation reaction. It appears that the presence of a region of high π-electron density is of critical importance in determining the accelerating action of an additive on the alkylation reaction.

In the accompanying paper,[1] evidence was presented which indicates strongly that acceleration of the rate of alkylation in benzene of sodiomalonic esters, by addition of small quantities of certain additives, is brought about, basically,[2] by specific solva-

[1] H. E. Zaugg, B. W. Horrom and S. Borgwardt, THIS JOURNAL, **82**, 2895 (1960).

[2] The double meaning is intended.

tion of the sodium cation. The question, why certain substances (*i.e.*, N,N-disubstituted amides and P-, S- and N-oxides) apparently act as good sodium ion solvators while many others (*i.e.*, ketones, nitriles, ethers. nitrocompounds, sulfones and even pyridine), also possessing available unshared electrons, do not, was left unanswered.

To study the nature of this anomaly, measurements of several physical properties of the additives and spectral examination of an additive-solute interaction were carried out. Specifically, the influence of varying concentrations of sodio-derivative on the ultraviolet spectrum of N-methyl-2-pyridone was studied. The relative basicities of many effective and ineffective additives, as measured by perchloric acid titration in acetic anhydride,[3] were examined. The wave lengths of the infrared carbonyl-stretching bands of most of the amide additives were compared. And, to estimate the importance of electron polarizability, molar refractions of a series of eight amides and one sulfoxide were determined.

These data are used, along with what is already known about the stereoelectronic nature of these substances, to develop a reasonable picture of additive action (see Discussion).

Experimental

Ultraviolet spectra were obtained using a 1-cm. cell in a Cary recording spectrophotometer, model 11. The diethyl sodio-*n*-butylmalonate solutions were prepared and handled as described previously,[1] but using spectro grade cyclohexane or isoöctane (2,2,4-trimethylpentane) as solvent in place of benzene.

Infrared spectra were taken in a Perkin–Elmer model 21 double-beam spectrometer calibrated using a polystyrene film (0.07 mm. thickness) at 6.238 μ.

For the determination of molar refractions, refractive indices were obtained using a Bausch and Lomb Abbe 56 refractometer at 25.0°. Each final value was an average of eight readings (4 readings were taken, the instrument was cleaned, and the procedure was repeated). The standard deviation of the instrument was calculated, using triply distilled water, and was found to be 1.8×10^{-4}. Density values were obtained at 25.0° using Gay–Lussac type pycnometers of approximately 5-ml. volume. Triply distilled water (assumed density at 25°, 0.997044 g./ml.) was used to calibrate the pycnometers. A weight loss–time curve was determined for each sample, with the weights being noted at 2-minute intervals from 5 to 15 minutes after removal from the thermostat. The weight at zero time was found by extrapolation and this value was used in calculating the density. A straight line relationship was found in all cases. Molar refractions were computed using the equation, $M_r{}^{25}\mathrm{D} = M(n^2-1)/d\cdot(n^2+2)$, where M is the molecular weight.

The perchloric acid titrations were performed in the same way as described elsewhere.[3] The compounds used in this study were obtained and purified as described previously.[1]

Results

In a high-resolution spectrophotometer, the ultraviolet absorption spectrum of N-methyl-2-pyridone in either cyclohexane or isoöctane consists of a broad band with two peaks at 308 mμ (ϵ 5000) and 319 mμ (ϵ 4500) of comparable intensities, and a shoulder at 334 mμ (ϵ 2300).[4] Table I shows the effect of the presence of increasing concentrations of sodio-*n*-butylmalonic ester on the molar extinction coefficients of the 319 mμ peak and the 334 mμ shoulder, at two concentrations of the pyridone and in two solvents. The 308 mμ peak could not be used in this experiment because it was completely masked by unexpectedly intense absorption (peak at 273 mμ) of the sodio-compound.[5]

TABLE I

ULTRAVIOLET ABSORPTION INTENSITIES OF N-METHYL-2-PYRIDONE

N-Methyl-2-pyridone $\times 10^4$ M	Na malonate $\times 10^3$ M	ϵ(319 mμ)[a]	ϵ(334 mμ)[a]
3.16	0	4580 (4440)	2310 (2250)
3.16	0.086	4580	2310
3.16	0.86	4360	2050
3.16	1.72	2560	1730
3.65	4.32	(3770)	1450 (1380)
3.65	8.64	(3690)	1240 (1180)
3.65	21.6	(3970)	1210 (1146)

[a] Numbers in parentheses are in isoöctane; others are in cyclohexane.

Clearly, interaction of the two compounds results in a decrease in absorptivity of the pyridone. The apparent reversal of the trend for the 319 mμ peak at the highest concentration (21.6×10^{-3} M) of sodio-derivative used is again due to interference from the 273 mμ band of the sodio-derivative. At this extreme concentration the 319 mμ peak appears only as a slight shoulder on a line running off the top of the recording paper.[6]

Results of the potentiometric titration of many effective and ineffective additives are given in Table II together with the relative rates of the alkylation (at 25°) in their presence (0.324 M concn.) (see Table II of paper I[1]). Because of the instability of the liquid junction potential in these titrations, reproducibility of half-neutralization potentials ($E_{1/2}$) was good only for a limited time. Each group in Table II comprises those compounds which were titrated during a period for which good reproducibility was established by regular checking. Comparisons of $E_{1/2}$ values, then, must be restricted to members within a group.

Streuli[7] has shown that, in similar titrations, the pK_a's of weak bases are inversely proportional to their half-neutralization potentials. Therefore, at least for qualitative purposes, it can be taken that the more basic substances in a comparable group of Table II possess the lower half-neutralization potentials. Those that show no break in the titration curves possess basicity too weak to be detected by this method.

The basicity of substances measured in this way probably does not represent basicity toward protons, but rather toward some other electrophilic species. Burton and Praill[8] have suggested that perchloric acid and acetic anhydride exist in equilibrium with acetyl perchlorate and acetic acid. What is being measured potentiometrically here

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(3) D. C. Wimer, *Anal. Chem.*, **30**, 77 (1958).

(4) Compare, L. C. Anderson and N. V. Seeger, THIS JOURNAL, **71**, 343 (1949).

(5) Investigation of this phenomenon is in progress.

(6) Further qualitative spectral evidence for mutual interactions between sodio-malonates and additives comes from unmistakable shifts in infrared bands. Bands at 6.05, 6.24, 8.99, 9.08 and 9.35 μ in the spectrum of an 0.1 M isoöctane solution of sodio-*n*-butylmalonic ester are shifted to 6.01, 6.13, 9.01, 9.13 and 9.37 μ, respectively, when dimethyl sulfoxide is added. When N-methyl-2-pyrrolidone is added, the last three bands are shifted even further to 9.04, 9.18 and 9.40, respectively.

(7) C. A. Streuli, *Anal. Chem.*, **30**, 997 (1958).

(8) H. Burton and P. F. G. Praill, *Analyst*, **80**, 9 (1955).

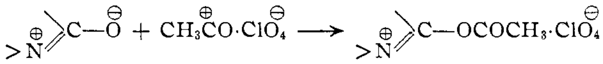
TABLE II

RELATIVE RATES, HALF-NEUTRALIZATION POTENTIALS[a] AND AMIDE I BANDS OF ADDITIVES

Compound	Relative rate[b]	$E_{1/2}$, mv.[c]	Amide I band, μ	
			Liquid	0.5% in CCl_4
	Group A			
$(CH_3)_2NNO$	1.9	No break		
$HCON(C_6H_5)_2$	3.0	No break		5.89
$HCON(CH_3)C_6H_5$	2.6	No break	5.95	5.92
$(CH_3)_2NCOOCH_3$	1.5[d]	No break	5.83	5.82
$(CH_3)_2NCN$	1.5[e]	623 (565)		
$(CH_3)_2NCON(CH_3)_2$	6.0[d]	546	6.06	6.04
$HCON(CH_3)_2$	7.0	625 (523)	5.96	5.93[i]
$CH_3CON(CH_3)_2$	8.7	530	6.07	6.02[j]
	Group B			
N-Acetylmorpholine	4.6	546		
N-Formylmorpholine	4.6	564	5.95	5.93
N-Formylpiperidine	6.0	553 (370)	5.97	5.95
N-Formylpyrrolidine	9.7	536 (325)	5.99	5.96
	Group C			
$CF_3CON(CH_3)_2$	1.7	No break	5.87	5.86
$(CH_3)_3CCON(CH_3)_2$	4.1	460 (514)	6.13	6.11
$C_6H_5CON(CH_3)_2$	6.2	438 (476)	6.12	6.08
N-Methyl-ε-caprolactam	7.5	374 (410)	6.08	6.05
N-Methyl-2-piperidone	9.9	344 (373)	6.08	6.05
N-Methyl-2-pyrrolidone	11.0	405 (443)[f]	5.92	5.89
N-Vinyl-2-pyrrolidone	3.0[e]		5.85	5.82
1,2,4,4-Tetramethyl-2-pyrroline-5-one	2.0[e]		5.80	5.79
	Group D			
$CH_3CON(CH_3)_2$	8.7	462	6.07	6.02[j]
$[(CH_3)_2N]_3PO$	54	450 (487)		
	Group E			
2,4-Dimethylsulfolane	1.5[e]	No break		
$(CH_3)_2SO$	15	476 (355)[f]		
$(CH_3)_3PO$	25[d]	431		
	Group F			
N-Methyl-2-pyridone	16	466[h]		
N-Methyl-4-pyridone	[g]	229[h]		

[a] Determined by potentiometric titration with perchloric acid in acetic anhydride by the method of Wimer.[3] [b] Based on the rate at 25° in the presence of 0.324 *M* additive. [c] The numbers in parentheses indicate the $E_{1/2}$ values measured on different days and usually with employment of different concentrations of $LiClO_4$ in the salt bridge. Parenthesized numbers within a given group represent results of determinations carried out on the same day and are mutually comparable. [d] Estimated from the relative rate observed[1] in the alkylation of sodio-1-methyl-butylmalonic ester with ethyl bromide. [e] Estimated from the relative rate at 0.648 *M* concentration. [f] Streuli[7] reported $E_{1/2}$ values for N-methyl-2-pyrrolidone as 676 mv. and for dimethyl sulfoxide as 605 mv. using a silver–silver chloride reference cell. [g] N-Methyl-4-pyridone was too insoluble in benzene to allow measurement of its effect on the alkylation rate. [h] Albert and Phillips[9] report pK_a values (in H_2O at 20°) for the N-methyl 2- and 4-pyridones as 0.32 (spectrophotometric) and 3.33, respectively. [i] Literature[10] reports 5.94 μ (1684 cm.$^{-1}$) for 0.01 *M* solution in CCl_4. [j] Literature[10] reports 6.02 μ (1662 cm.$^{-1}$) for 0.01 *M* solution in CCl_4.

may be the attack by acetyl perchlorate (or acetyl cation) of the negative oxygen atom of the dipole



In accord with this view, Davidson[11] has reviewed evidence showing that many reactions of amides with acid chlorides and anhydrides can be understood through initiatory reaction of the electrophilic reagent with the amide oxygen atom.[12] Whatever the reference acid may be here, proton or acetyl cation, it is certainly more electrophilic than the acid species (sodium ion) involved in the alkylation interactions.[13] It is no surprise, therefore, to find that there is no general correlation of basicities ($E_{1/2}$) with relative rates. However, one item of apparent significance deserves mention. Although one clearly ineffective additive (dimethylcyanamide) shows measurable basicity, there is not one clearly effective catalyst which does not exhibit basicity as determined by this method. In accord with the picture[1] of selective solvation of sodium ion by an electron-donor substance, it appears that basicity of some sort is a necessary requirement for appreciable catalytic action.

Table II also lists the wave lengths of the carbonyl stretching bands (amide I bands) of most of the amide additives, measured both on the pure liquid and in dilute carbon tetrachloride solution. Consistent slight increases in wave length on going from dilute solution to the liquid phase are indicative of some intermolecular interaction in these amides in the liquid state. However, others[14] have shown that, unlike the hydrogen-bonded mono- and unsubstituted amides, N,N-disubstituted amides do not associate in either benzene or carbon tetrachloride solution.

In Table III are listed eight amide additives in increasing order of efficiency in the alkylation reaction, together with the observed and calculated molar refractions, and the differences between them (exaltations). The last column gives the decreasing order of magnitude of the exaltations.

If the relative magnitudes of these exaltations can be viewed as rough indications of the relative electron polarizabilities of the amide groups in these substances, it is clear that there is no exact correlation of catalytic efficiency with polarizability. If any significance is to be attached to the numbers in the last column of Table III, it would indicate an approximate *inverse* correlation. The numbers are notably less than randomly distributed, as the first four amides (the poorer additives) all have higher exaltations than the last four.[15]

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(9) A. Albert and J. N. Phillips, *J. Chem. Soc.*, 1294 (1956).

(10) D. Cook, THIS JOURNAL, **80**, 49 (1958).

(11) D. Davidson, *Trans. N. Y. Acad. Sci.*, **20**, 316 (1958).

(12) Compare R. Huisgen and H. Brade, *Ber.*, **90**, 1432 (1957); and R. Huisgen, H. Brade, H. Walz and I. Glogger, *ibid.*, p. 1437. These workers measured base strengths of a number of amides by titration with perchloric acid in glacial acetic acid using other methods of end-point detection. They also concluded that proton (or electrophilic) attack occurs at the amide oxygen atom. Incidentally, it is interesting to note that the relative order of basicity, 6 > 7 > 5, observed by us for the three lactams (Table II, group C) is the same as that found by these workers for the corresponding unmethylated compounds.

(13) This is easily apparent from a consideration of the relative facility with which the three substances, $CH_3COOC_2H_5$, HOC_2H_5, and $NaOC_2H_5$, release ethoxide ion.

(14) (a) H. O. Chaplin and L. Hunter, *J. Chem. Soc.*, 1114 (1937); (b) A. M. Buswell, W. H. Rodebush and M. F. Roy, THIS JOURNAL, **60**, 2444 (1938).

(15) This apparent inverse relationship between catalytic efficiency and electron polarizability is borne out by a consideration of the electron group refractions of the CN, CO, SO and PO bonds in benzonitrile, acetonitrile, acetone, dimethyl sulfoxide and trimethylphosphine

TABLE III

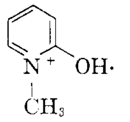
MOLAR REFRACTIONS OF AMIDES

Amide[a]	$n^{25}D$	d^{25}	Molar refraction Obsd.	Molar refraction Calcd.[b]	Exaltation	Order[c]
1,2,4,4-Tetramethyl-2-pyrroline-5-one	1.4810	0.9572	41.39	40.43	+0.96	1
N-Methylformanilide	1.5597	1.0918	40.01	39.49	+ .52	2
N-Formylmorpholine	1.4851	1.1468	28.78	28.68	+ .10	4
N-Formylpiperidine	1.4826	1.0155	31.80	31.66	+ .14	3
N,N-Dimethylformamide	1.4281	0.9440	19.93	20.01	− .08	6
N,N-Dimethylacetamide	1.4359	0.9372	24.30	24.62	− .32	8
N-Formylpyrrolidine	1.4780	1.0365	27.07	27.04	+ .03	5
N-Methyl-2-pyrrolidone	1.4680	1.0302	26.75	27.04	− .29	7

[a] Listed in increasing order of catalytic efficiency. [b] The values for electron group refractions given by C. P. Smyth, "Dielectric Behavior and Structure," McGraw-Hill Book Co., Inc., New York, N. Y., 1955, p. 409, were used. [c] Order of decreasing magnitude of exaltation.

Discussion

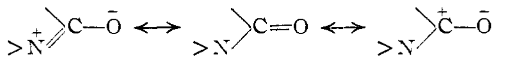
Amide Additives.—Comparison of the ultraviolet spectral behavior of N-methyl-2-pyridone in the presence of sodio-*n*-butylmalonic ester with that in aqueous solutions of varying *p*H is instructive. Albert and Phillips[8] measured the pK_a of N-methyl-2-pyridone by determining the *increase* in the molar extinction coefficient of the 300 mμ band with decreasing *p*H of its aqueous environment. The increase in absorption was ascribed to rising concentrations of the aromatic protonated species with



decreasing *p*H. The present observation that increasing concentrations of sodium ion donor in non-polar media *decrease* the intensity of this absorption is strong indication that sodium ion does not bond with the oxygen atom of the pyridone.

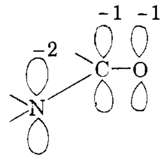
Neither is it likely that it bonds with the nitrogen atom, because the nitrogen lone pair in this substance is largely delocalized. According to recent molecular orbital calculations of Mason,[18] in the ground state of N-methyl-2-pyridone the nitrogen atom carries nearly a full (+0.857) positive charge, as the unshared pair is delocalized throughout the molecular orbital encompassing the oxygen atom and the heterocyclic ring. However, only part (−0.286) of the negative charge is in the ring. Most of it (−0.571) is re-localized in the π-orbital around the oxygen atom. The net result is a π-orbital containing a region of high electron density; in short, a strongly directed molecular orbital. This region of negative charge is of critical importance in effecting solvation of sodium ion by mutual electrostatic attraction. However, the more electrophilic proton[13] does not stop at this stage of interaction, but continues on to form a σ-bond with the oxygen atom. This accounts for the observed spectral contradiction between proton and sodium ion interaction with N-methyl-2-pyridone.[19]

This picture of π-solvation of sodium ion is qualitatively consistent with the observed variation with structure of the efficiency of amide additives in accelerating the alkylation reaction. Amides may be represented[11] as resonance hybrids of the three valence-bond structure:



I II III

In molecular orbital terms they are pictured[20] as



in which the oxygen, carbon and nitrogen 2pπ-atomic orbitals shown contain four electrons. These four electrons just suffice to fill the bonding molecular orbital embracing the NCO grouping and the N ↔ O non-bonding orbital. The net effect of this 2pπ-overlap is a decrease in π-bond order in the carbon–oxygen link (resonance form II) with a compensating increase in π-bond order in the carbon–nitrogen link (resonance form I). Furthermore, the bond orders of the carbon–oxygen and carbon–nitrogen links can vary in a continuous manner depending on the steric and electrical effects of substituents.

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oxide. The observed[16] molar refractions of the first three of these compounds are: C_6H_5CN, 31.58; CH_3CN, 11.09; and $(CH_3)_2CO$, 16.11. Subtracting from these the suitable multiples of the values for the appropriate electron group refractions (C—H, 1.705; C—C, 1.209; C=C, 4.15) assigned by Smyth (Table III, footnote *b*) leaves 5.77 for the CN group in benzonitrile, 4.77 for the CN in acetonitrile and 3.46 for the CO in acetone.

The observed molar refraction of dimethyl sulfoxide ($n^{25}D$ 1.4771, d^{25} 1.0958) is 20.15. Subtracting the values for the six C–H bonds (6 × 1.705) and Smyth's value of 9.18 for the C–S–C group, leaves only 0.74 as the refraction of the SO bond in dimethyl sulfoxide. Similarly, but more approximately, using Vogel's[17] assignments of *atom* refractions (H, 1.029; C. 2.591; P + O, 5.91), the calculated molar refraction for trimethylphosphine oxide is 22.94. Subtracting the *electron group* values for the nine C–H bonds and Smyth's value of 11.28 for the $(C)_3P$ group leaves −3.68 as the refraction of the PO bond in trimethylphosphine oxide.

Clearly, in these instances, a relatively low degree of electron polarizability of the polar bond accompanies heightened catalytic activity in the alkylation reaction. Conversely, a looser electronic system appears to characterize the polar bonds of the three additives which show little catalytic activity.

(16) A. I. Vogel, *et al.*, *J. Chem. Soc.*, 171 (1940); 674 (1948).

(17) A. I. Vogel, *ibid.*, 1833 (1948).

(18) S. F. Mason, *ibid.*. 1253 (1959).

(19) Assuming that the necessary geometric requirements can be met, it is conceivable that partial *covalent* solvation of sodium ion by the directed π-orbital can make small contributions to solvate stability. However, the almost total lack of electrophilicity in sodium ion precludes the characterization of this π-solvate as anything resembling the usual covalent π-complex.

(20) W. J. Orville-Thomas, *Chem. Revs.*, **57**, 1179 (1957).

Maximum overlap of the $2p\pi$-orbitals requires that the nitrogen atom and its two σ-bonded substituents be coplanar with the NCO group. It follows that any effect tending to inhibit this coplanarity will reduce the degree of the nitrogen lone pair delocalization and hence lower its catalytic effectiveness in the alkylation reaction. Conversely, any influence promoting coplanarity will increase catalytic activity. In accord with this view is the fact that relative alkylation rates increase in the order, dimethylpivalamide (4.1), dimethylacetamide (8.7), N-methyl-2-pyrrolidone (11.0).[21]

The degree of delocalization of the lone pair will also be influenced by the inductive effects of the nitrogen substituents. Electron-withdrawing groups will decrease and electropositive ones will increase the availability of the unshared pair for delocalization. This influence is illustrated by the catalytic excellence of N-methyl-2-pyrrolidone (11.0) as compared to the corresponding N-vinyl derivative (3.0) and the 1,2,2,4-tetramethyl-2-pyrroline-5-one (2.0). The superiority of dimethylformamide (7.0) over N-methylformanilide (2.6) and N,N-diphenylformamide (3.0) are also examples of this effect.

Finally, the substituent on the carbonyl carbon atom will also affect catalytic activity of amides. An electron-withdrawing group will have the effect of placing a relative positive charge on the carbonyl carbon. This will tend to move the π-orbital electron density away from oxygen and toward carbon, rendering it more diffuse and less prone to attract sodium ion. This effect is illustrated by the series, $CH_3CON(CH_3)_2$ (8.7) > $HCON(CH_3)_2$ (7.0) > $CF_3CON(CH_3)_2$ (1.7).[22] Likewise, lack of catalytic activity in methyl N,N-dimethylcarbamate [$(CH_3)_2NCOOCH_3$ (1.5)] is ascribable to the negative inductive effect of the methoxyl group, whereas the much better activity (6.0) of tetramethylurea can be understood in terms of the positive mesomeric effect of the second amino group compensating for its negative inductive effect.[23]

Other, more subtle electrical and steric effects undoubtedly influence the degree of delocalization of the amide lone pair. The significant variation in catalytic activity with ring size (5 > 6 > 7) in the series of lactams (Table II, group C), and the interesting difference between N-formylpyrrolidine and N-formylpiperidine (Table II, group B) are suggestive of this.[24] However, in the absence of more experimental information, detailed discussion of these effects would be premature.

As has already been indicated, for the reason that different acceptor species are involved, there is no reason to expect a broad correlation of catalytic activity with basicity as measured by potentiometric titration. Likewise, because amide substituents influence the force constant of the carbonyl group in a manner not necessarily parallel to their influence on the lone pair availability (see footnote 22), one cannot expect a perfect correlation of catalytic activity with the wave length of the amide I band. However, when amides posessing closely related structures are compared with each other, correlations are indeed observed. As can be seen by inspection of Table II, relative rates, basicities ($\sim E_{1/2}$) and amide I band wave lengths all increase in the same order in the following two groups: $CF_3CON(CH_3)_2 < HCON(CH_3)C_6H_5 < HCON(CH_3)_2 < CH_3CON(CH_3)_2$; and N-formylmorpholine < N-formylpiperidine < N-formylpyrrolidine. Likewise, the amide I band wave lengths increase with relative rates in the group, 1,2,4.4-tetramethyl-2-pyrroline-5-one < N-vinyl-2-pyrrolidone < N-methyl-2-pyrrolidone.

Finally, there is one physical property of acyclic amides which shows a good correlation with relative rates and indicates that the degree of nitrogen lone pair delocalization is indeed a prime factor. This is the magnitude of the energy barrier to rotation about the C–N bond. Increasing contributions of resonance form I are reflected in increasing resistance to rotation about the C–N bond. Using proton magnetic spectra, Gutowsky and Holm[26] have estimated this barrier for the three amides, $HCON(CH_3)C_6H_5$, $HCON(CH_3)_2$ and $CH_3CON(CH_3)_2$. They are, <1, 7 ± 3 and 12 ± 2 kcal., respectively. Within the fairly wide limits of error, these values are directly proportional to the catalytic efficiencies of these amides. Although more evidence of this kind, covering a wider structural range of acyclic amides, would be desirable, the semi-quantitative correlation achieved with these three amides is strong indication that the catalytic value of an amide depends on the extent to which the nitrogen lone pair is delocalized with consequent shift of electron density into the π-orbital around oxygen.

Coördinate Covalent Additives.—Contrasting the catalytic behavior, basicities and electron distributions of pyridine and pyridine N-oxide provides more evidence consistent with the π-solvation mechanism of acceleration of these alkylations. Figure 1 shows the calculated charge distributions for these two compounds recently reported by

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(21) Scale models show that exact coplanarity is easily attained in dimethylacetamide, but not in dimethylpivalamide. The catalytic superiority of N-methyl-2-pyrrolidone over all the other saturated amides is compatible with its geometry, which is fixed in a conformation most suitable for maximum π-orbital overlap.

(22) N,N-Dimethylpivalamide (4.1) is out of order in this series for reasons already discussed.[21] However, the long wave length of its amide I band (longer than any other in Table II) suggests that the positive inductive effect of the *t*-butyl group effectively stabilizes contributions of resonance form III to the ground state of the molecule, even though its bulk results in reduced contributions of resonance form I.

(23) Cook[9] has presented excellent spectral evidence to show that the unshared pairs on an alkyl oxygen of an ester group are delocalized to a lesser extent than is the nitrogen lone pair of an analogous amide. This is in agreement with the well-known reluctance of oxygen to acquire a positive charge.

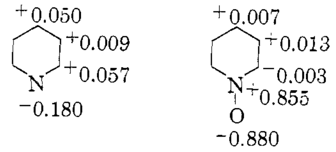
With two nitrogens feeding two unshared pairs into molecular orbitals involving the oxygen, one wonders why tetramethylurea isn't a much better catalyst. This may be due to its difficulty, clearly shown by models, in assuming the complete molecular planarity necessary for this process. This explanation is subject to a planned experimental test. N,N′-Dimethylethyleneurea, the completely planar analog of tetramethylurea, should be a better alkylation catalyst, even, than N-methyl-2-pyrrolidone.

(24) For example, the higher relative rate (9.7) for formylpyrrolidine as compared to formylpiperidine (6.0) may be a manifestation of 1-strain[25] rendering the lone pair more available to delocalization in the 5-membered ring because of energetically more favorable consequences arising from sp^2 hybridization of the nitrogen atom in the smaller ring.

(25) H. C. Brown, J. H. Brewster and H. Shechter, THIS JOURNAL, **76**, 467 (1954).

(26) H. S. Gutowsky and C. H. Holm, *J. Chem. Phys.*, **25**, 1228 (1956).

Barnes.[27] The corresponding calculated π- and σ-moments, experimental dipole moments, basicities and relative rates are also listed. Even though pyridine is a stronger base toward protons by a factor of 30,000, its catalytic activity compared to that of pyridine N-oxide is barely significant.[28] The distinguishing feature of pyridine oxide which accounts for its catalytic superiority is its high π-moment (5.7 D.). In short, like the amides, it possesses a region of high electron density in the molecular orbital around the oxygen atom.

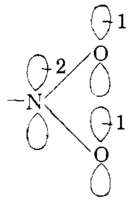


π-Moment, D.	1.23	5.7
σ-Moment, D.	0.85	−1.30
Exptl. moment, D.	2.21	4.28
pK_a	5.3	0.79
Rel. rate (0.324 M)	1.35	18.3

Fig. 1.—Pyridine and pyridine N-oxide.

Unfortunately, quantitative data of this type are not available for the coördinate covalent compounds of phosphorus and sulfur. However, according to Van Wazer,[29] 4-covalent compounds of phosphorus possess an sp^3-hybridized (tetrahedral) phosphorus atom, but in addition to the four σ-bonds there is present a varying amount of π-bonding, with an average of about one dπ-bond per phosphorus atom for most compounds in this class. Similar dπ-bonding was ascribed by Van Wazer to other sp^3 σ-bond base hybrids of the second row elements [*i.e.*, $(CH_3)_2SO$].[30] The effect of π-bonding in these compounds is to reduce the ionic character of the σ-bond. For example, based on the electronegativity difference between the atoms, the P–O bond [*i.e.*, in $(CH_3)_3PO$] should have about 70% ionic character. To stabilize this extreme charge separation, some of the negative charge on oxygen is delocalized into a π-orbital by what Van Wazer calls a "feedback mechanism." The net result, again, is a molecular orbital with a region of high electron density near oxygen.[31]

Ineffective Additives.—After what has gone before, to enumerate reasons why ketones, nitriles, ethers, ethanol and ethyl carbonate do not measure up to amides and coördinate covalent compounds as alkylation catalysts would be repetitive. However, the reason for lack of activity in compounds containing nitro and sulfone groups is less than obvious. Orville-Thomas[20] pictures the nitro group as



Here, π-delocalization of the nitrogen lone pair occurs as in the amide group. However, instead of relocalizing the charge in the molecular orbital near one oxygen, the nitro group divides it equally between two. Thus no region of the π-orbital possesses sufficient electron density to attract sodium ion to the degree that the amide group does. Similar considerations can be applied to the sulfone group as compared to the sulfoxide, except that the sulfone sulfur, unlike the nitro nitrogen, is sp^3-hybridized.[33]

Two inactive compounds, N,N-dimethylcyanamide and N,N-dimethylnitrosamine require individual attention. Although infrared data[34] indicate that the delocalized resonance form $(CH_3)_2\overset{+}{N}=\overset{-}{C}=N$ may contribute to the ground state structure of dimethylcyanamide, it seems unlikely (because of the unstable carbodiimide configuration) that it can be nearly so important as the corresponding form (resonance form I) for the amide group. The weak basicity observed (Table II, group A) for this substance may then be ascribed to a low order of amine (nitrogen) basicity.

At first glance, dimethylnitrosamine appears to have much in common with the amides. Its high dipole moment (3.98 D.) coupled with a very high energy barrier (23 kcal.)[35] to rotation about the N–N bond points to important contributions of the delocalized resonance form, $(CH_3)_2\overset{+}{N}=N-\overset{-}{O}$. Yet, the substance is a notably poor catalyst in the alkylation reaction. Very likely, its anomalous behavior is connected in some way with the presence of an extra unshared electron pair on the central nitrogen atom.[36] But whatever the reason may

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[27] R. Barnes, This Journal, **81**, 1935 (1959).

[28] Comparison of relative rates at unit concentration rather than at 0.324 *M*, would be even more striking. Although the participation order for pyridine oxide has not yet been determined, it is reasonable to assume that it will be much greater (1.5–2) than the fractional order displayed by pyridine (ref. 1, Table IV).

[29] J. R. Van Wazer, "Phosphorus and Its Compounds," Vol. I, Interscience Publishers, Inc., New York, N. Y., 1958, pp. 42–43, 57.

[30] O. Bastiansen and H. Viervoll, *Acta Chem. Scand.*, **2**, 702 (1948) have shown by electron diffraction studies that dimethyl sulfoxide is pyramidal and not planar as is acetone. Hence, it is analogous to the 4-covalent phosphorus compounds but with an unshared pair on sulfur in place of the fourth σ-bond on phosphorus.

[31] It is known that the aliphatic tertiary amine oxides possess more ionic character than the heterocyclic ones.[32] Indeed, even those with large lipophilic groups on nitrogen still have insufficient benzene solubility to permit testing as catalysts in the present alkylation studies. Unlike the sp^2-hybridized nitrogen in pyridine oxide, the sp^3-hybridized nitrogen in the aliphatic amine oxides cannot form a π-bond with the oxygen. This would require another orbital which is unavailable to first row elements. Thus, the "feedback mechanism" cannot operate in aliphatic amine oxides and the N–O bond keeps its ionic character.

[32] C. C. J. Culvenor, *Rev. Pure Appl. Chem.* (*Australia*), **3**, 91 (1953).

[33] This effect of delocalization without relocalization is further illustrated by the behavior of 1,3,5,5-tetramethylbarbituric acid and of N-methylsuccinimide as alkylation catalysts. In both of these substances, the nitrogen lone pair can be delocalized throughout a molecular orbital encompassing *two* adjacent carbonyl groups. The rate of the alkylation reaction in the presence of either of these compounds could not be measured. Although the reaction mixture appeared homogeneous, extremely wide variation of sodio-malonate concentration with time (as determined by titration of aliquots) indicated an increased rather than a decreased degree of heterogeneity in the system. These compounds behaved essentially as inhibitors.

[34] M. Davies and W. J. Jones, *Trans. Faraday Soc.*, **54**, 1454 (1958).

[35] C. E. Looney, W. D. Phillips and E. L. Reilly, This Journal, **79**, 6136 (1957).

[36] If, as is quite possible,[37] the lone pair commands much of the surface of the central nitrogen atom, it will interfere with development of the 2pπ-orbital on the same atom. This will have the effect of

be, there remains the comforting fact that dimethylnitrosamine also differs from the effective amide catalysts by being devoid of measurable basicity (Table II, group A).

Dipole Moments and Polarizabilities.—The present work has served to emphasize the primacy of linear π-bond moments (as compared to σ-bond moments) of polar substances in determining their ability to solvate sodium ions in nonpolar media and, consequently, to catalyze the alkylation reaction. Since the observed dipole moment of an unsaturated polar substance is the algebraic sum of its σ- and π-moments, it is not surprising that little connection between dipole moment and catalytic activity can be found. Table IV lists a number of reagents and additives used in this work together with their dielectric constants and dipole moments. As the additives are listed in roughly increasing order of activity, it is easy to see that, while the ineffective compounds may or may not possess strong dipoles, all of the effective additives do. This is compatible with the contention that a certain kind of dipole (due to a linear π-moment) is necessary for catalytic action.

TABLE IV

DIELECTRIC CONSTANTS AND DIPOLE MOMENTS OF REAGENTS

Compound	ϵ	μ, D.
C_6H_6	3	0
C_2H_5Br	9	1.8
$(C_2H_5O)_2CO$	3	0.9
CH_3CN	39	3.2
C_6H_5CN	26	3.9
$(CH_3)_2CO$	21	2.8
$(CH_3)_2NNO$		3.98
$C_6H_5NO_2$	36	4.0
C_2H_5OH	25	1.7
$(CH_3)_2NCON(CH_3)_2$		3.3
$HCON(CH_3)_2$	37	3.82
$CH_3CON(CH_3)_2$	38	3.87
$(CH_3)_2SO$	45	
Pyridine N-oxide		4.28

It is well known[38] that separation of charge stiffens or reduces the electron polarizability of a bond. Furthermore, π-electrons are usually more polarizable than σ-electrons and contribute more to the refractivity of an unsaturated group. That the group refractions (electron polarizabilities) of the PO and SO bonds are much smaller than those for the CO and CN groups is further indication that, in the former, the π-orbitals are more polarized in the ground state than they are in the latter. The trend discernible in Table III also betokens a similar variation of π-orbital polarization, roughly related to catalytic activity, within the series of amides. Judging from these observations, then, it appears that the burden of success in solvation rests with the additive. The importance of inductive polarization brought about by proximity of the positive sodium ion must be relatively small. Again, it is the π-electron density in the ground state of the additive that is critically important.[39]

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pinching the triatomic molecular orbital in the middle and of decreasing delocalization of the lone pair of the terminal nitrogen. The energy barrier must then be accounted for by overlap of the two lone pair orbitals and the dipole moment by the atomic dipole of the central nitrogen combined with the dipole of the N–O bond. The nitroso group thus resembles the nitro group of nitrobenzene more than the carbonyl group of an amide.

(37) Compare G. G. Stewart and H. Eyring, *J. Chem. Ed.*, **35**, 550 (1958).

(38) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 129–130.

(39) These views are consistent with Mason's[18] contention that in N-methyl-2-pyridone, the first electronically excited state is *less* polarized than the ground state.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, IOWA STATE UNIVERSITY]

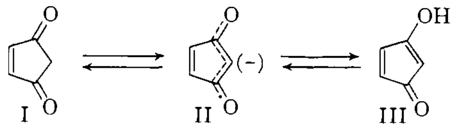
Cyclopentene-3,5-dione. III. Reactions of the Methylene Group[1,2]

BY C. H. DEPUY AND P. R. WELLS

RECEIVED NOVEMBER 2, 1959

Reactions of the active methylene group of cyclopentene-3,5-dione are reported. It has proved possible to condense it with benzaldehyde in acid solution, through the intermediacy of β-hydroxy-cyclopentadienone, as well as in basic solution. By reaction with aryldiazonium salts the arylhydrazones of cyclopentene-3,4,5-trione have been prepared. Some studies on the kinetics of the base-catalyzed polymerization of the dione are recorded and a mechanism for the polymerization is suggested.

Cyclopentene-3,5-dione (I) is a stable, highly reactive compound easily prepared by the oxidation of the commercially available diol.[3] Because so little is known about the synthesis and properties of highly unsaturated five-membered ring compounds, and because this enedione contains such a variety of reactive centers, we have been exploring the synthetic utility of this compound. Reductions, derivatizations and Diels–Alder reactions have already been reported.[1,3] In this paper we describe some reactions of the methylene group.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[1] Paper II in this series, C. H. DePuy and C. E. Lyons, THIS JOURNAL, **82**, 631 (1960).

[2] Supported by a grant from the National Science Foundation.

[3] C. H. DePuy and E. F. Zaweski, THIS JOURNAL, **81**, 4920 (1959).