and are corrected to constant temperature, solvent, and leaving group by standard techniques.

The existence of a linear free energy relationship between the reactivity and selectivity of this group of compounds is established by a plot of log k_t vs. log k_N/k_s and results in the rather extraordinarily good correlation line of Figure 1 with slope = 2.83 and intercept = -2.60. Note that compounds which vary in rate by over seven powers of ten are included in this correlation.

Table I. Rates and Selectivities of Alkyl Chlorides on Solvolysis in 80% Aqueous Acetone at 0° in the Presence of Sodium Azide

RCl	k_t, rel.	k_N/k_s
$(CH_3)_3CCl^a$	1.00	1.45×10^1
$(Ph)_2CHCl^b$	6.50×10^1	6.10×10^1
$PhCClHCH=CHCH_3^c$	9.40×10^2	2.10×10^2
$(CH_3)_2CClCH=CH_2^d$	1.17×10^3	3.90×10^2
$(p\text{-MePh})CClHCH=CHCH_3^c$	9.40×10^3	8.15×10^2
$(p\text{-MePh})_2CHCl^e$	3.72×10^4	8.70×10^2
$(Ph)_3CCl^f$	1.95×10^7	1.12×10^4

[a] L. C. Bateman, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 960 (1940). [b] M. G. Church, E. D. Hughes, and C. K. Ingold, *ibid.*, 969 (1940). [c] Original data for the *p*-nitrobenzoate ester: R. A. Sneen and A. M. Rosenberg, *J. Am. Chem. Soc.*, **83**, 900 (1961). [d] Unpublished work, P. S. Kay. [e] L. C. Bateman, M. G. Church, E. D. Hughes, C. K. Ingold, and N. A. Taher, *J. Chem. Soc.*, 979 (1940); L. C. Bateman, E. D. Hughes, and C. K. Ingold, *ibid.*, 974 (1940). [f] E. A. Hill, *Chem. Ind.* (London), 1696 (1965).

More significant perhaps than the correlation itself are deviations from it. Thus attempts to correlate the reactivity and selectivity of 2-octyl derivatives with those of Table I are unsuccessful; in fact the experimentally observed selectivity of 2-octyl mesylate[6,7] is *ca.* 3.1 powers of ten, 1250 times greater than predicted by the correlation. Similarly α-methylallyl chloride,[8] with $k_N/k_s = 6130$, deviates from the correlation by 3.49 log units, or is 3100 times more selective than predicted.

The rationale is both exciting and useful. The compounds of Table I share the common characteristic that the species attacked competitively by solvent and azide ion is almost certainly a dissociated carbonium ion while it has been established[7] that, at least in the case of 2-octyl mesylate, the species attacked competitively is an undissociated ion pair. It would thus seem that nonadherence to the relationship of Figure 1 can serve as a diagnostic for reaction at an ion-pair stage.

Several of the disturbing features of the chemistry of simple allyl chlorides, including the product spreads observed on solvolysis[9] as well as the unusual solvent dependence noted for the bimolecular reaction of allyl chloride with hydroxide ion by Vernon[10] (reaction faster in better ionizing solvents), would now seem to

It should be pointed out that the ratio calculated from this revised equation never deviates by more than a factor of two from the original equation which in practice was used to obtain first approximations.

(5) This has been recognized by E. A. Hill, *Chem. Ind.* (London), 1696 (1965).
(6) H. Weiner and R. A. Sneen, *J. Am. Chem. Soc.*, **87**, 292 (1965).
(7) R. A. Sneen and J. W. Larsen, *ibid.*, **88**, 2593 (1966).
(8) Unpublished work.
(9) R. H. DeWolfe and W. G. Young, *Chem. Rev.*, **56**, 794 (1956).
(10) C. A. Vernon, *J. Chem. Soc.*, 4462 (1954).

have simple and logical explanations in terms of ion-pair intermediates.[11]

(11) Perhaps it should be noted that this behavior is also observed for the reaction of 2-octyl mesylate with azide ion which is also faster in better ionizing solvents.[6,7] It becomes intelligible when it is recognized that the reaction is in fact a preequilibrium generation of ion pair (favored by better ionizing solvents) followed by attack by azide ion to produce product (disfavored by better ionizing solvents but apparently disfavored to a lesser extent than is the preequilibrium favored).
(12) Fellow of the Purdue Research Foundation, 1964–1965.

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Free Radicals Involving Phosphorus

Sir:

It has been known for several years that arylphosphines and phosphine oxides give colored solutions when treated with alkali metals in polar solvents.[1] However, very few esr studies have been made on these interesting systems.[2-5] Since conflicting results were reported[3,4] for the alkali metal reduction of triphenylphosphine, we have reinvestigated the corresponding reduction of triphenylphosphine oxide. We also wish to report on the effect of replacing the phenyl groups of $(C_6H_5)_3P(O)$ with other groups, and to describe a novel anion radical involving two phosphorus atoms.

The nature of the free-radical species derived from $(C_6H_5)_3P(O)$ depends on the alkali metal and the solvent. Like Hoffmann and Tesch[2] we were able to detect only the biphenyl anion radical (*via* phenyl–P cleavage) in the sodium reduction of $(C_6H_5)_3P(O)$ in 1,2-dimethoxyethane (DME). We obtained the same result with sodium reduction in tetrahydrofuran (THF). However, reduction of $(C_6H_5)_3P(O)$ with potassium in THF at $-10°$ resulted in a blue solution with a 28-line esr spectrum. By contrast, potassium reduction in DME resulted in a red-brown solution with a 10-line spectrum. The 28-line spectrum can be assigned to two sets of overlapping dectets (a 5.25-gauss doublet splitting by P^{31} and a 1.75-gauss dectet splitting from nine equivalent protons in three phenyl groups), each line of which is split into an overlapping set of four lines due to a 0.875-gauss potassium splitting.[6] This evidence suggests that the species in THF solution is $(C_6H_5)_3P(O)\cdot^-$. The 10-line spectrum has a very similar appearance to that reported for $(C_6H_5)_2P\cdot^-$ by Britt and Kaiser.[4] It consists of two sets of overlapping septets with a phosphorus splitting of 7.7 gauss and a 2.6-gauss splitting from six equivalent protons. Under high resolution an additional four-line splitting

(1) See, for example, F. Hein, H. Plust, and H. Pohleman, *Z. Anorg. Allgem. Chem.*, **272**, 25 (1953); F. Hein and H. Hecker, *Z. Naturforsch.*, **11b**, 677 (1956); and D. Wittenberg and H. Gilman, *J. Org. Chem.*, **23**, 1063 (1958).
(2) A. K. Hoffmann and A. G. Tesch, *J. Am. Chem. Soc.*, **81**, 5519 (1959).
(3) M. W. Hanna, *J. Chem. Phys.*, **37**, 685 (1962); M. I. Kabachnik, V. V. Voevodskii, T. A. Mastryukova, S. P. Solodovnikov, and T. A. Malenteva, *Zh. Obshch. Khim.*, **34**, 3234 (1964).
(4) A. D. Britt and E. T. Kaiser, *J. Phys. Chem.*, **69**, 2775 (1965).
(5) A. D. Britt and E. T. Kaiser, *J. Org. Chem.*, **31**, 112 (1966).
(6) The assignments were aided by calculating spin densities by the Hückel molecular orbital method (Table I). These calculations indicate that the spin densities are very small in the *meta* positions of phosphorus-substituted benzene rings, and, furthermore, that the spin densities of the *ortho* and *para* positions are approximately equal. However, unequivocal assignment must await deuteration experiments.
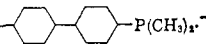
Table I. Calculated and Experimental Spin Densities of Phosphorus-Substituted Anion Radicals

Anion	Atom^a	a_i, gauss	ρ_i (obsd)^b	Q^c	ρ_i (calcd)^d
$(C_6H_5)_3P(O)K\cdot^-$	P	5.25			0.21
	2	1.75	0.076 ⎫		0.083
	3		⎬	23.0	0.00006
	4	1.75	0.076 ⎭		0.084
	K	0.875			
$(C_6H_5)_2P(O)K\cdot^-$	P	7.9			0.285
	2	2.6	0.108 ⎫		0.112
	3	.....	..... ⎪	24.0	0.0001
	4	2.6	0.108 ⎬		0.113
	K	0.4	..... ⎭		....
$[(CH_3)_2N](C_6H_5)_2P(O)\cdot^-$	P	7.2			0.233
	2	2.44	0.090 ⎫		0.091
	3	.....	..... ⎪		0.00007
	4	2.44	0.090 ⎬	27.0	0.091
	N	4.9	⎪		0.188
	CH$_3$	0.2	0.007 ⎭		....
$(C_6H_5)(CH_3)_2P(O)\cdot^-$	P	8.75			0.421
	2	3.50	0.118 ⎫		0.106
	3	.....	..... ⎪	29.5	0.0001
	4	3.50	0.118 ⎬		0.113
	CH$_3$	0.875	0.029 ⎭		....
$(CH_3)_2P$—⟨⟩—⟨⟩—$P(CH_3)_2\cdot^-$	P	5.7			0.194
	2	2.2	0.078 ⎫	28.0	0.077
	3	0.44	0.015 ⎬		0.022
	Na–K	0.88	..... ⎭		....

^{a} The numbering system is
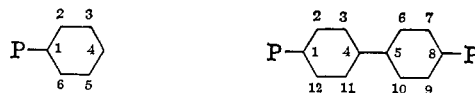
^{b} Based on the relationship $a_i = Q\rho_i$ (obsd): H. M. McConnell, *J. Chem. Phys.*, **24**, 764 (1956). ^{c} These Q values refer to protons only. ^{d} Based on Hückel molecular orbital calculations.

($\sim$0.4 gauss) is observed which is presumably due to potassium. These data would correspond to the $(C_6H_5)_2P(O)K\cdot^-$ anion radical. Both of these metalated phosphine oxide anion radicals are analogous to the well-known metal ketyls.

Sodium–potassium alloy reduction of dimethylaminodiphenylphosphine oxide in THF at ambient temperature gave a light brown solution with a 14-line spectrum. The spectrum corresponds to a 7.2-gauss P^{31} doublet, each component of which is split into three lines of equal intensity and spacing of 4.9 gauss due to the N^{14} nucleus. Each of the six lines is further split into a system of overlapping septets with a spacing of 2.44 gauss due to the interactions from six equivalent protons in two phenyl groups. Some additional splitting ($\sim$0.2 gauss) may be due to the CH$_3$ groups, but this is not certain at present. The free-radical species thus appears to be $[(CH_3)_2N](C_6H_5)_2P(O)\cdot^-$. The N^{14} coupling constant is quite large (4.9 gauss) and suggests considerable interaction between phosphorus and nitrogen.[7] The potassium-generated anion radical from bis(dimethylamino)phenylphosphine oxide gave a complex spectrum which has not yet been analyzed. The free-radical behavior of the mixed phenyldimethylaminophosphine oxides contrasts with Fraenkel, Ellis, and Dix's very interesting observation[8]

that $[(CH_3)_2N]_3P(O)$ solvates electrons when treated with alkali metals. The reaction of other dimethylamino-substituted phosphine oxides with alkali metals is currently being studied in an attempt to understand this solvation effect.

Anion radicals can also be obtained when one or two phenyl groups of $(C_6H_5)_3P(O)$ are replaced by other groups such as methyl. For instance, a 29-line spectrum with $a_p = 8.75$, $a_H(\text{ring})(3) = 3.5$, and $a_H(\text{methyl})$-(6) = 0.875 gauss corresponds to $(CH_3)_2(C_6H_5)P(O)\cdot^-$.

The new[9] bisphosphine I gave a green solution with a 57-line spectrum on reduction with Na–K alloy at

I
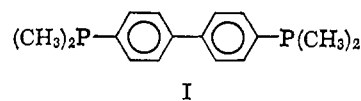
$-80°$. This spectrum could arise from a triplet P^{31} splitting with a spacing of 5.7 gauss, each component of which has a 2.2-gauss splitting from protons 2, 7, 9, and 12 (see Table I for numbering system). The other contributions are a 0.44-gauss quintet splitting from protons 3, 6, 10, and 12 and an alkali metal interaction of 0.88 gauss.

(7) p_π–d_π bonding between nitrogen and phosphorus has also been noted previously in nmr and chemical studies of aminophosphines: see, for example, R. R. Holmes and R. P. Carter, Jr., *Inorg. Chem.*, **2**, 1146 (1963); A. B. Burg and P. J. Slota, *J. Am. Chem. Soc.*, **80**, 1107 (1958); W. A. Hart and H. H. Sisler, *Inorg. Chem.*, **3**, 617 (1964); G. Ewart, D. S. Payne, A. L. Port, and A. P. Lane, *J. Chem. Soc.*, 3984 (1962); A. H. Cowley and R. P. Pinnell, *J. Am. Chem. Soc.*, **87**, 4454 (1965).

(8) G. Fraenkel, S. H. Ellis, and D. T. Dix, *ibid.*, **87**, 1406 (1965).

(9) Prepared in 78% yield by the reaction of 4,4'-dilithiobiphenyl with $(CH_3)_2PCl$ in $(C_2H_5)_2O$ solution using a similar procedure to that described by M. D. Curtis and A. L. Allred, *ibid.*, **87**, 2554 (1965).

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Computer-Aided Interpretation of High-Resolution Mass Spectra. II.[1] Amino Acid Sequence of Peptides[2]

Sir:

In a continuation of our efforts to make use of computers in the interpretation of complex mass spectrometric data[1] we have selected the determination of the amino acid sequence in peptides as a specific example. This problem seemed to lend itself particularly well to a complete solution even at this early stage because the structures of oligopeptides follow a few strict requirements which can be simply expressed in computer language.

In amino acids and peptides the CH–CO bonds as well as the CO–N bonds cleave relatively easily[3] with retention of the positive charge at the CH and CO groups, respectively, and the mass spectrum of an oligopeptide (I) thus always contains peaks due to "amine fragments" A_1, A_2, A_3, etc., and the molecular ion. The mass of ion A_1 must correspond to that of X–NH–CH plus the substituent at C_α of any one of the amino acids present in the peptide (H for glycine, CH_3 for alanine, etc.). There should also be an ion of mass A_1 plus CONHCH plus another α substituent, etc., and the molecular ion must be of mass A_n + COOH. Cleavage of the CO–NH bonds gives rise to a series of "amino-acyl fragments" B_1, B_2....B_n, differing from the above only by the addition of the mass of CO.

tion of polyfunctional amino acids leads sometimes to very intense peaks not fitting this simple scheme. N-Trifluoroacetyl peptide esters[3a,d] often have the tendency to eliminate the trifluoroacetyl group and require a detailed consideration of the mass spectrometric behavior of N-TFA peptides, of metastable ions, etc.[3b] The correct interpretation of conventional mass spectra of peptide derivatives of unknown sequence is thus quite tedious and time consuming. If the mass spectrometric technique is to be applied to the many small peptides produced in the course of the determination of the primary structure of polypeptides of biological interest, a much faster and objective approach is desirable.

A complete high-resolution mass spectrum[5] of a small peptide lends itself particularly well to automatic determination of the amino acid sequence, because the data represent the accurate mass (in the order of millimass units) of *all ions regardless of their relative abundance and significance. Thus, the elemental composition, a structurally unique parameter, becomes the criterion, rather than the more subjective abundances.* Given the exact mass of the N-terminal substituent X plus –NHCH<[6] (*e.g.*, 159.0320 for phthaloyl, 192.9931 for chlorophthaloyl, 125.0088 for trifluoroacetyl, 140.9793 for chlorodifluoroacetyl, 163.0633 for carbobenzoxy, etc.), the computer then adds the masses of the "side chain" of all possible amino acids (*e.g.*, 1.0078 for Gly, 15.0234 for Ala, *etc.*), each time comparing the sum (a possible A_1 fragment) with the masses found. By addition of the mass of CO (27.9949), ion B_1 is searched for. The next amino acid is identified by adding 56.0136 (the "backbone-unit" –CONHCH<) to the mass of ion A_1 plus the accurate masses of all possible "side chains," testing the data for a fit each time, etc., etc. For each fragment of type A found, 44.9977 (CO_2H) is added to test whether the C terminal

$$\begin{array}{ccccccccc}
 & R_1 & & & R_2 & & & R_3 & & & R_n \\
 & | & & & | & & & | & & & | \\
\text{X—NH—CH}\text{—CO}\text{—NH—CH—CO}\text{—NH—CH—CO}\ldots\ldots\text{NH—CH}\text{—COOH} \\
 & A_1 & & & A_2 & & & A_3 & & & A_n \\
 & & B_1 & & & B_2 & & & B_3 & & & B_n
\end{array}$$

I

While those peaks may be quite intense, they can easily be overshadowed by others arising from fragments that have lost the N-terminal.[3] It was suggested[3c] that one attaches a homologous pair of long acyl chains to the N-terminus (*e.g.*, N-heptadecanoyl and N-octadecanoyl) to shift the ions containing the N-terminal acid to high mass and relies on the expected high abundance of the amino-acyl ions. This holds for peptides containing uncomplicated, aliphatic amino acids,[4] but the tendency to side-chain fragmenta-

has been reached (59.0133 for methyl esters). Typical fragments (M − CO_2, M − H_2O, and M − CH_3OH) are tested to recognize peptides exhibiting no molecular ion.

Since secondary fragmentation processes may lead to ions of the same elemental composition as A or B ions (*e.g.*, loss of C_4H_8 or C_3H_6 from leucine leads to ions corresponding to the presence of glycine and alanine, respectively), for this reason the sequence representing the largest fraction (in terms of intensity) of the entire spectrum (*i.e.*, utilizing the more intense peaks of a given type) is considered the best result. Various sequence-specific fragment ions are then searched for as well (see Figure 1).

(1) Part I: K. Biemann and W. J. McMurray, *Tetrahedron Letters*, 647 (1965).

(2) This work was supported by grants from the National Institutes of Health (GM 05472 and GM 09352). The use of the facilities of the MIT Computer Center is gratefully acknowledged. We are indebted to Mrs. V. Beecher for writing the program.

(3) (a) E. Stenhagen, *Z. Anal. Chem.*, **181**, 462 (1961); (b) K. Biemann, "Mass Spectrometry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 294; (c) E. Bricas, *et al.*, *Biochemistry*, **4**, 2254 (1965); (d) F. Weygand, A. Prox, H. H. Fessel, and K. K. Sun, *Z. Naturforsch.*, **20B**, 1169 (1965).

(4) (a) M. Barber, P. Jolles, E. Vilkas, and E. Lederer, *Biochem. Biophys. Res. Commun.*, **18**, 469 (1965); M. Barber, *et al.*, *Tetrahedron Letters*, 1331 (1965); (c) G. Laneelle, J. Asselineau, W. A. Wolstenholme, and E. Lederer, *Bull. Soc. Chim. France*, (1965) 2133.

(5) Techniques for the automatic recording of accurate mass data in digital computer compatible form have been described previously (P. Bommer, D. Desiderio, W. J. McMurray, and K. Biemann, Twelfth Annual Symposium on Mass Spectrometry, Montreal, Ontario, Canada, June 1964).

(6) NCH for phthaloyl derivatives. An aromatic and/or halogenated substituent X results in a unique elemental composition of the A and B ions, assuring their unambiguous identification.