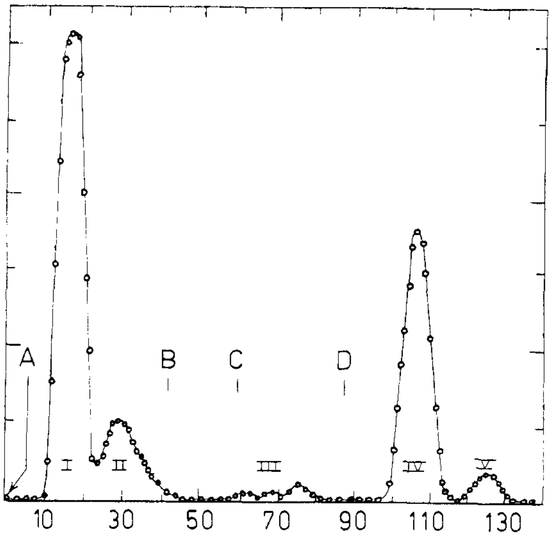

Fig. 1.—Elution diagram for crude crystalline elastase: buffers, A, *p*H 8.8, Na_2CO_3–HCl; B, *p*H 8.8, carbonate–0.15 *M* NaCl; C, *p*H 8.8, carbonate–0.2 *M* NaCl; D, *p*H 8.8, carbonate–0.23 *M* NaCl. See text for explanation of numerals I–V.

teins designated as III had no activity either on elastin or insulin; they disappeared on recrystallization of the crude material. Component IV showed no insulin-hydrolyzing activity, but did have a weak proteinase activity against albumin.

Pancreatic insulinase, isolated as indicated above, showed a single, symmetrical boundary during electrophoresis and ultracentrifugation. The electrophoretic mobilities at *p*H 8.8 and 4.0 were -4.9×10^{-5} and $+1.2 \times 10^{-5}$ cm.^{2}/sec./volt, respectively. The isoelectric point is therefore near *p*H 4.

Insulinase activity was measured, essentially according to the procedure of Mirsky, Perisutti and Dixon,[3] by following the degree of solubilization of radioactivity by enzyme treatment of I^{131}-labeled insulin. In a typical experiment with 200 μg. of insulin as substrate, 26 μg. of insulinase caused 50% hydrolysis of the insulin in 15 minutes. Carboxypeptidase is without action in the assay. Chymotrypsin produced a slight hydrolysis of insulin, but in rate and extent nowhere approached the activity of the new pancreatic insulinase.

We are indebted to Dr. N. G. Brink and Dr. G. E. Boxer for their many valuable suggestions, and we wish to thank Dr. D. E. Williams for the electrophoretic and ultracentrifuge studies.

[3] I. A. Mirsky, G. Perisutti and F. J. Dixon, *J. Biol. Chem.*, **214**, 397 (1955).

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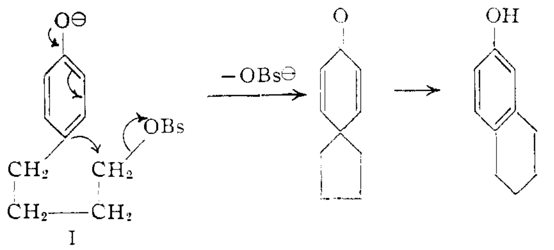
THE FORMATION OF DIENONES THROUGH Ar_1-PARTICIPATION

Sir:

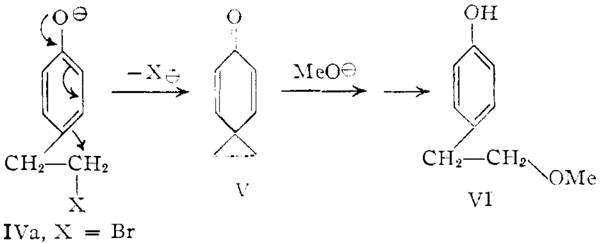
By proper selection of structure and reaction conditions, it is possible to arrange for the formation of dienones through Ar_1-participation[1] of a neighboring phenoxide-ion group.

Thus, Ar_1-5 assisted reaction may be made to dominate over anchimerically unassisted reactions by treatment of 4-*p*-hydroxyphenyl-1-butyl *p*-bromobenzenesulfonate (0.03 *M*) with a slight excess of potassium *t*-butoxide in anhydrous *t*-butyl alcohol. Under these conditions a first order rate of reaction of the ion I is observed, the first order rate constant being $4.85 \pm 0.08 \times 10^{-4}$ sec.$^{-1}$ at 50.00°. From this reaction was isolated a ketone, m.p. 34–35°, with a λmax. in the ultraviolet at 242 mμ and an ϵ of 16,000 in methanol, and with a strong band in the infrared for a conjugated carbonyl. That the ketone is *spiro*-(4:5)-deca-1,4-diene-3-one (II) is clear from the spectral evidence,[2] elementary analysis, quantitative hydrogenation (2.04 moles hydrogen absorbed), and quantitative dienone-phenol rearrangement[3] to 5,6,7,8-tetrahydro-2-naphthol (III), m.p. 60.5–61.0°.



The reaction is of value for the preparation of the dienone II, since the latter was obtained in a yield of greater than 50% on a small scale, without further exploration for optimal conditions.

With 2-*p*-hydroxyphenyl-1-ethyl derivatives it is relatively easy to arrange for essentially complete control of reaction by Ar_1-3 participation. Thus 0.03 *M* 2-*p*-hydroxyphenyl-1-ethyl bromide reacts by way of the ion IVa in 0.13 *N* sodium methoxide in absolute methanol at a rate which is initially faster than that of 2-*p*-anisyl-1-ethyl bromide by practically 10^3. Evidently the dienone, *spiro*-[2:5]octa-1,4-diene-3-one (V) is formed, but it reacts rapidly with methoxide ion and aryloxide ion. With sufficiently high methoxide ion concentration the product from IVa is predominantly 2-*p*-hydroxyphenyl-1-ethyl methyl ether (VI), m.p. 42–43°; the latter was isolated in 82% yield after ten half-lives of the ion IVa in 1 *N* methanolic sodium methoxide. With lower methoxide ion concentrations competition of aryloxide ion for the dienone



IVa, X = Br
b, X = I

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[1] S. Winstein, R. Heck, S. Lapporte and R. Baird, *Experientia*, **12**, 138 (1956).

[2] (a) R. H. Burnell and W. I. Taylor, *J. Chem. Soc.*, 3486 (1954); (b) E. A. Braude and E. R. H. Jones, *ibid.*, 498 (1945).

[3] A. L. Wilds and C. Djerassi, THIS JOURNAL, **68**, 1715 (1946).

V leads to the formation of higher molecular weight products in addition to the methyl ether VI.

The formation and destruction of the dienone V has been studied spectrophotometrically at 10^{-4}–10^{-5} *M* concentrations of the ions IVa and IVb. At these concentrations competition by aryloxide for the dienone V is negligible and the primary source of destruction of V is the excess base necessary to insure complete ionization of the phenols used. Thus, in methanol with 0.01 to 0.1 *M* methoxide ion, an absorption at 274 mμ, attributed to V, with an ϵ of 17,000 to 20,000 has been observed to increase with time and then to disappear. The resulting solution has the same ultraviolet spectrum as that of the basic salt of the methyl ether VI. From the spectral kinetics the rate of decay of the dienone V was found to be first order in both V and in methoxide ion, the second order rate constant being 9.3×10^{-2} l.-mole^{-1} sec.$^{-1}$ at 25.0°. Further, the first order rate constants for the formation of dienone V via the ion IV are 5.09×10^{-3} sec.$^{-1}$ for the iodide and 1.10×10^{-3} sec.$^{-1}$ for the bromide, the latter value agreeing with the titrimetric rate constant.

The dienone V is formed more rapidly and is more stable in *t*-butyl alcohol than in methanol. Even with *t*-butyl alcohol as solvent, however, attempts to isolate the dienone under preparative conditions have so far been unsuccessful.

[4] National Science Foundation Predoctoral Fellow, 1953–1955, 1956–1957.

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EQUATION RELATING CHEMICAL SHIFT WITH MOLECULAR CONSTANTS IN THE NUCLEAR MAGNETIC RESONANCE OF TRIPLY CONNECTED PHOSPHORUS

Sir:

In the paper[1] by Muller, Lauterbur and Goldenson on the nuclear magnetic resonance spectra of phosphorus compounds, an equation was given for relating the amount of unbalance in the p electrons with the chemical shift of phosphorus in those compounds in which the phosphorus atom is covalently bonded to three neighboring atoms. Unfortunately, this equation does not fit the available information presented in an earlier publication[2] and a recent paper[3] from our laboratories. I have modified Equation 4 of Muller, *et al.*, to read

$$D' = [(3/4) - \beta^2]\beta^2(1 - \epsilon) \qquad (1)$$

This equation is based on the assumption that the wave function asymmetry of the P atom in the PX_3 molecule is zero for both p^3 ($\beta^2 = 0$) and pure sp^3 ($\beta^2 = {}^3/_4$), so that the asymmetry is a maximum for a bond angle of 98° 13′.

Table I shows the values of X–P–X angles I have used for the computation of β^2 (Equation 2, Ref. 1) and hence *D* (Equation 4, Ref. 1) and *D′* (Equation 1).

TABLE I

VALUES OF X–P–X ANGLES

X	Angle in degrees
H	93[1]
Cl	100.5 ± 1.5[4]
Br	101.5 ± 1.5[4]
I	102 ± 2[4]
F	104 ± 4[4]

A semilogarithmic plot of chemical shift plus 230 *versus* *D′* is well represented by a straight line, which yields equation (2) relating the measured chemical shift, δ, with *D′*

$$\delta = -230 + (29.0 \times 10^3 e^{-46.0D'}) \qquad (2)$$

where δ is the chemical shift of the phosphorus nuclear magnetic resonance peak referred to 85% phosphoric acid in p.p.m. of the applied magnetic field and defined as $\delta = H_{\text{sample}} - H_{\text{standard}}/H_{\text{standard}} \times 10^6$. *D′* is the number of unbalanced p electrons in the phosphorus valence shell and defined by Equation 1.

In Table II, I have listed measured chemical shifts and compared them with values calculated from Equation 5 of Muller, *et al.*, and values calculated from Equation 2.

TABLE II

COMPARISON OF MEASURED AND CALCULATED PHOSPHORUS NUCLEAR MAGNETIC RESONANCE SHIFTS

		Chemical shift relative to orthophosphoric acid	
Molecule	Measured	Calculated from equation 4 of Muller, *et al.*	Calculated from equation 2 above
PH_3	+238[3]	+240	+230
PF_3	− 97[2]	−640	−114
PI_3	−178[2]	−100	−201
PCl_3	−219[1]	−215	−201
PBr_3	−227[1]	−230	−227

I have used Equations 1 and 2, the chemical shift[3] ($\delta = +62$ p.p.m.), the Pauling electronegativities of P and C, and Equations 2 and 3 of Reference 1 to compute the bond angle of trimethylphosphine. The calculated bond angle is 102.5° as compared to the measured value of 100° ± 4°.[5] Since Equations 1 and 2 fit all the available data including phosphorus trifluoride and trimethylphosphine, they should be substituted for Equations 4 and 5, respectively, in the article by Muller, *et al.*

[1] N. Muller, P. C. Lauterbur and J. Goldenson, THIS JOURNAL, **78**, 3557 (1956).

[2] H. S. Gutowsky and D. W. McCall, *J. Chem. Phys.*, **22**, 162 (1954).

[3] J. R. Van Wazer, C. F. Callis, J. N. Shoolery and R. C. Jones, THIS JOURNAL, **78**, 5715 (1956).

[4] P. W. Allen and L. E. Sutton, *Acta Cryst.*, **3**, 46 (1950).

[5] H. D. Springall and L. O. Brockway, THIS JOURNAL, **60**, 996 (1938).

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RECEIVED OCTOBER 12, 1956

CONCERNING THE SYMMETRY OF BENZENE-POSITIVE ION COMPLEXES; UNPOSITIVE THIRD GROUP IONS

Sir:

The nature of benzene-positive ion complexes has implications as to the mechanism of nucleo-