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

Molecule	Measured	Chemical shift relative to orthophosphoric acid: 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] (δ = +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.*

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(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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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-

philic attack in aromatic complexes,[1] and to charge-transfer complexes generally.[2] Theory requires ions such as Ag^+, H^+, etc., to form asymmetric benzene complexes,[3] and this has been confirmed by the diffraction data for $AgClO_4$–benzene,[4] where the silver ion lies above the ring over one C–C link.

The results of recent physical and chemical studies on solutions of gallium "dichloride" in benzene[5] have shown this compound to be the ion-pair $Ga^+(GaCl_4)^-$, in which the Ga^+ ion is strongly solvated by benzene. Although it has been reported that Ga_2Cl_4 may be recrystallized from benzene,[6] the solid phase that separates is actually a rather stable benzene complex of $Ga(GaCl_4)$.

As expected, $Ga(AlCl_4)$[7] also forms a similar complex; $Tl(AlCl_4)$ apparently does not. These observations have called to our attention the fact that the previous theoretical argument as to the symmetry of benzene-ion complexes depends upon the configuration of the cation, and does not hold for the third group elements in their +1 oxidation state.

Consider an M^+-benzene complex with the cation on the benzene axis, and therefore of symmetry C_{6v}. The highest filled π-orbitals of the benzene ring belong to the irreducible representation e_1(doubly degenerate),[8] and the orbital of the cation must belong to the same representation in order to allow bonding by electron transfer from benzene to the cation. For ions such as Ag^+, H^+, etc., the lowest acceptor orbital is an s-orbital belonging to a_1, orthogonal to the upper filled π-orbitals of the ring. Charge transfer is then impossible without considerable electronic promotion, so that movement of the cation to a position of lower symmetry is necessary for bonding. However, for Ga(I), In(I) and Tl(I), the lowest acceptor orbitals available are the p-orbitals, where the degenerate pair, p_x, p_y, belonging to e_1, can accept the highest energy π-electrons from the benzene ring. Hence, a symmetry C_{6v} for the benzene-M^+ ion is by no means excluded in this case.

On the experimental side, crystals of $Ga(GaCl_4)$-benzene have been examined by X-ray diffraction. They are at least pseudohexagonal, with a = 11.89, c = 30.05 Å., and $Z \cong 12$. The very large unit cell makes this material unpromising for complete structure determination, and other similar complexes are being explored. $Ga(GaCl_4)$-benzene is not isomorphous with the $AgClO_4$-benzene complex, and the hexagonal structure at least does not discourage the view that the Ga^+-benzene ion may have hexagonal symmetry.

(1) L. J. Andrews, *Chem. Rev.*, **54**, 713 (1954), and papers referred to therein.

(2) R. S. Mulliken, THIS JOURNAL, **72**, 600 (1950).

(3) R. S. Mulliken, *J. Chem. Phys.*, **19**, 514 (1951); THIS JOURNAL, **74**, 811 (1952).

(4) R. E. Rundle and J. H. Goring, *ibid.*, **72**, 5337 (1950). Refinement of this structure is in its final stages.

(5) R. K. McMullan and J. D. Corbett, to be published.

(6) "Inorganic Syntheses," Vol. IV, J. C. Bailar, Jr., Ed., McGraw-Hill Book Co., Inc., New York, N. Y., 1953, p. 113.

(7) J. D. Corbett and R. K. McMullan, THIS JOURNAL, **78**, 2906 (1956).

(8) Notation of H. Eyring, J. Walter and G. Kimball, "Quantum Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1944, p. 387.

Work was performed in the Ames Laboratory of the U. S. Atomic Energy Commission.

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THE UTILITY OF β,δ-DIHYDROXY-β-METHYLVALERIC ACID (MEVALONIC ACID) IN EVALUATING POTENTIAL HYPOCHOLESTEROGENIC AGENTS

Sir:

Cholesterol accumulation in mammalian systems, and its implication in abnormal metabolic states, have focused experimentation on agents that may suppress cholesterol biosynthesis or its accumulation.

The very efficient incorporation of DL-β,δ-dihydroxy-β-methylvaleric acid into cholesterol by rat liver homogenates[1] suggests that mevalonic acid (MVA)[2] may be a natural precursor of cholesterol on the pathway from acetate to the sterol. Since the suppression of utilization of a more advanced intermediate in a reaction sequence should, on theoretical grounds, be subject to less difficulty of interpretation than would be the case with an earlier member of the sequence, we felt that mevalonic acid might be considerably more valuable than acetate as an aid in the search for hypocholesterogenic agents.

In order to test this hypothesis, we have compared two compounds, α-phenylbutyric acid and α-*p*-biphenylylbutyric acid, for their effectiveness in preventing cholesterol synthesis from labeled acetate, and from labeled mevalonic acid. The two substituted butyrates have been prominent in the recent literature. The former, α-phenylbutyric acid, was found to inhibit the incorporation of acetate into the non-saponifiable lipid fraction of rat liver slices.[3] The second compound, α-*p*-biphenylylbutyric acid, is known to inhibit, *in vitro*, the Coenzyme A-catalyzed acetylation of sulfanilamide,[4] and to reverse in great measure the hypercholesteremia and hyperlipemia produced in intact rats[5] by the administration of Triton.

We were further directed to the selection of these two compounds by the reports concerning their hypocholesteremic properties. Cottet[6] found that α-phenylbutyric acid (*ca.* 3 g. daily) produces up to a 40% decrease in the serum cholesterol levels of hypercholesteremic patients. Annoni[7] has re-

(1) P. A. Tavormina, M. H. Gibbs and J. W. Huff, THIS JOURNAL, **78**, 4498 (1956).

(2) The letters MVA, rather than the previously used DVA, will serve to designate DL-β,δ-dihydroxy-β-methylvaleric acid, which has been renamed "mevalonic acid"; D. E. Wolf, C. H. Hoffman, P. E. Aldrich, H. R. Skeggs, L. D. Wright and K. Folkers, THIS JOURNAL, in press.

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(6) J. Cottet, A. Mathivat and J. Redel, *Presse méd.*, **62**, 939 (1954).

(7) G. Annoni, *Farm. sci. e tec. (Pavia)*, **11**, 244 (1956).