the rapid passage technique in order to observe the B^{11} resonance at +20 p.p.m. in the same medium.

The study of photochromism in mesomeric phosphonium salts and other organophosphorus compounds is continuing.

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THE PREPARATION, PYROLYSIS AND PHOTOLYSIS OF CHLORODIAZOMETHANE[1]

Sir:

Halogen derivatives of diazomethane are of interest as potential precursors of divalent carbon intermediates. Particularly, comparison of reactivities of halomethylenes derived from such diazocompounds with those of the formally identical carbenes generated by α-eliminations promises to give new insights into some problems of carbene chemistry.[2] We wish to report the preparation of solutions of chlorodiazomethane and some of their physical and chemical properties.

Reactions of *t*-butyl hypochlorite with dilute solutions of diazomethane in ether or hydrocarbons at −100° give solutions of a red compound which we believe to be chlorodiazomethane on the basis of the following observations: The electronic absorption spectrum in pentane exhibits a bathochromic shift relative to diazomethane with three maxima of about equal intensities at 485, 518 and 545 mμ (ϵ about 15),[3] respectively. The infrared spectrum shows a strong band at 2066 cm.$^{-1}$ attributed to the stretching vibration of a diazo group (*vs.* 2097 cm.$^{-1}$ for diazomethane). The solutions slowly decolorize with loss of nitrogen at temperatures above −40°. Reactions with carboxylic acids lead to rapid nitrogen evolution and decolorization. Chloromethyl acetate and chloromethyl propionate have been prepared in this way.

Confirming evidence for the structure of the chlorination product was obtained from the pyrolytic (−20°) and photolytic (−80°) decompositions of these solutions. Using olefins as solvents, satisfactory (30–40%) yields of chlorocyclopropanes were isolated. Thus, *trans*-2-butene reacted stereospecifically to give 1-chloro-*trans*-2,3-dimethylcyclopropane while *cis*-2-butene gave the two epimeric 1-chloro-*cis*-2,3-dimethylcyclopropanes in equal quantities. Similarly, with cyclohexene both 7-chloronorcarenes were formed in a 1:1 ratio.[4] From reactions in *n*-pentane the three possible carbon–hydrogen insertion products, 1-chlorohexane, 1-chloro-2-methylpentane and 1-chloro-2-ethylbutane, have been identified.[5] Vapor phase chromatographic analysis indicated a ratio of insertion into primary *vs.* secondary carbon–hydrogen bonds of 0.05 for both photolysis and pyrolysis.

The remarkable reactivity differences of chlorocarbene derived from the diazocompound and of the formally identical intermediate in α-elimination from methylene chloride[4] is noteworthy. The failure of the latter intermediate to insert into carbon–hydrogen bonds and its relatively high steric discrimination in additions to olefins[6] (*e.g.*, ratio of the two 1-chloro-*cis*-2,3-dimethylcyclopropanes resulting from the addition to *cis*-2-butene is 5.5)[6] suggests that in the α-eliminations a truly free carbene might be bypassed.[7]

(1) Supported by a grant from the Petroleum Research Fund, administered by the American Chemical Society.

(2) For a recent review see: W. Kirmse, *Angew. Chem.*, **73**, 161 (1961).

(3) Since a satisfactory method for assaying the chlorodiazomethane solutions has not yet been found, the ϵ value is based on an estimated yield of 50% and undoubtedly will be subject to revision.

(4) *Cf.* G. L. Closs and L. E. Closs, *J. Am. Chem. Soc.*, **82**, 5723 (1960).

(5) These compounds were isolated by v.p.c. and their infrared spectra were compared with those of authentic samples.

(6) G. L. Closs and G. M. Schwartz, *ibid.*, **82**, 5729 (1960).

(7) *Cf.* the similar observations for diphenylcarbene; G. L. Closs and L. E. Closs, *Angew. Chem.*, **74**, 431 (1962).

(8) A. P. Sloan Foundation Fellow, 1962–1964.

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ON THE MECHANISM OF ERGOT ALKALOID BIOGENESIS[1]

Sir:

Although the biogenetic origin of the C–8 substituted N-methylergoline skeleton of the ergot alkaloids has been established as arising from tryptophan,[2] mevalonate[2] and the S-methyl of methionine,[2] the mechanism of the biosynthesis is still unknown.

The association of mevalonic acid (I) with tryptophan (III) involves the bond formation of C–5 of mevalonate (I) with the C–4 and α-carbon of tryptophan (III), and the C-3′ of mevalonate (I) with the α-amino group of tryptophan (III), respectively. In order to obtain information on the mechanism of the formation of the new C–C linkages and of the biosynthetic route by which the different substituents appear at C–8 of the ergot alkaloids, the changes in the oxidation state at C–5 and C–2 of mevalonate were examined during its conversion into ergot alkaloids.

During the over-all biosynthetic reaction the T,C^{14} ratio of DL-mevalonic acid-2-C^{14}-5-T compared to the same ratio of the ergot alkaloid (festuclavine and pyroclavine) has been changed to a degree which indicates the net loss of 1 atom of hydrogen. The T,C^{14} ratio of DL-mevalonic acid-2-C^{14}-2-T did not change during its conversion into agroclavine, indicating that there is no change in the oxidation level at C–2 of mevalonate during the biosynthesis (Table I).

The loss of one atom of hydrogen from DL-mevalonic acid-2-C^{14}-5-T may be associated with the oxidation of the primary alcoholic group of mevalonate (I) into an aldehyde group before its bond formation with tryptophan. Another possibility which may exist is that the first bond formation occurs without any change in the oxidation

(1) Presented in part at the International Symposium on Organic Chemistry of Natural Products, Brussels, June 12–15, 1962. This work was supported by a grant, A-686, from the National Research Council of Canada.

(2) K. Bentley, *Ann. Rev. Biochemistry*, **31**, 618 (1962).

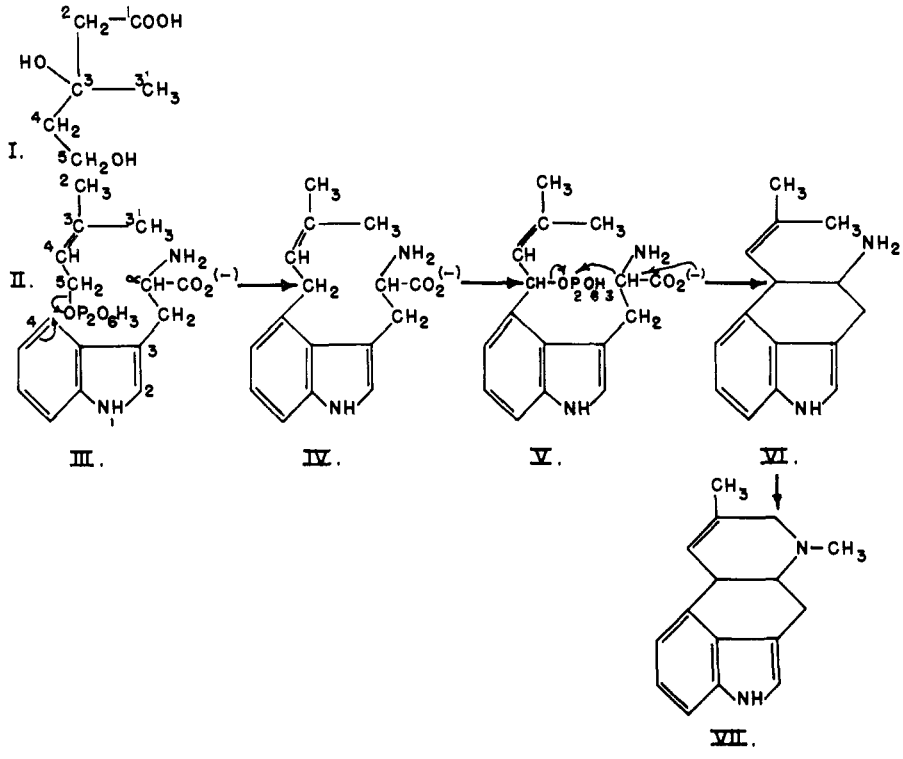

Fig. 1.

TABLE I

	C¹⁴, d.p.m.	T, d.p.m.	T/C¹⁴	Loss of T atom/mole
Mevalonic acid-2-C¹⁴-5-T	7.48×10^6	19.2×10^6	5.6	
Festuclavine and pyroclavine	2.78×10^3	7.42×10^3	2.6	1
Mevalonic acid-2-C¹⁴-2-T	2.92×10^6	18.6×10^6	6.37	
Festuclavine and pyroclavine	2.4×10^3	14.6×10^3	6.08	0

level at the C–5 with the loss of one atom of hydrogen being associated with the second bond formation. In light of the previous findings of Plieninger, *et al.*,[3] and ourselves[4] implicating one of the two mevalonate metabolites (isopentenyl pyrophosphate and dimethylallyl pyrophosphate) in the biosynthesis of ergot alkaloids we are inclined to prefer the second type of mechanism. One of the many possible variants of this type of mechanism which is not in conflict with the experimental data obtained in different laboratories is depicted in Fig. 1.

The bond formation between the active isoprene unit and C–4 of tryptophan may be formulated as the electrophilic attack of the C–5 of the active isoprene unit[5] (II) on the C–4 of tryptophan (III) by the loss of a pyrophosphate ion (II + III → IV).[6,7]

The subsequent step may be the oxidation of the $-CH_2-$ group (IV) into a tertiary alcoholic group, then phosphorylation or pyrophosphorylation (VI) resulting in the generation again of a potential electrophilic center. The electrophilic carbon formed by the fission of the phosphate ester may now attack the α-carbon of the tryptophan moiety, where the nucleophilic activation may take place by anionic decarboxylation (V → VI).

Thus agroclavine (VII) may arise subsequent to the above reactions by the formation of a bond between the C–3′ of mevalonate[4,8] with the amino group of tryptophan and by N-methylation *via* transmethylation. (The formation of the three bonds between tryptophan and the active isoprene unit as well as the N-methylation may not necessarily follow this reaction sequence[9]). That chanoclavine would be an obligatory intermediate of other ergot alkaloids as proposed by several authors[10,8a] seems unlikely, since the "biosynthetic"

(3) H. Plieninger, R. Fischer, G. Keilich and H. D. Orth, *Ann.*, **642**, 246 (1961).

(4) R. M. Baxter, S. I. Kandel and A. Okany, *Tetrahedron Letters*, 596 (1961).

(5) For the sake of simplicity we apply the usual numbering of mevalonic acid (I) to dimethylallyl pyrophosphate (II).

(6) J. W. Cornforth and G. Popjak, *Tetrahedron Letters*, 19 (1959).

(7) R. Robinson, "The Structural Relations of Natural Products," Clarendon Press, Oxford, 1955, p. 108.

(8) (a) S. Bhattacharji, A. J. Birch, A. Brack, A. Hofmann, H. Kobel, S. C. C. Smith and J. Winter, *J. Chem. Soc.*, 421 (1962); (b) R. M. Baxter, S. I. Kandel and A. Okany, *J. Am. Chem. Soc.*, **84**, 2997 (1962).

(9) Subsequent to our presentation of the above experiments and considerations[1] Dr. F. Weygand reported that the synthetically prepared tritium labeled compound (Fig. 3) incorporates into elymoclavine (incorporation % = 20 to 33), which assumes a modification in the sequence of the above proposed mechanism. In contrast to Weygand's findings are those from the Plieninger laboratory (H. Plieninger, R. Fisches and V. Liede, *Angew. Chem.*, **74**, 430 (1962), where the synthetically prepared dimethylallyl-tryptophan-C¹⁴ (IV) (previously proposed as an intermediate[8a]) proved to be a precursor of elymoclavine (incorporation % = "at least" 5) an observation which is not in conflict with the original sequence of our proposed mechanism.

(10) K. Mothes, F. Weygand, D. Groger and H. Grisebach, *Z. Naturforsch.*, **13b**, 41 (1958); (b) H. Rochelmeyer, *Pharm. Ztg.*, **103**, 1260 (1958); (c) D. Groger, *Arch. Pharm.*, **292**, 389 (1959).

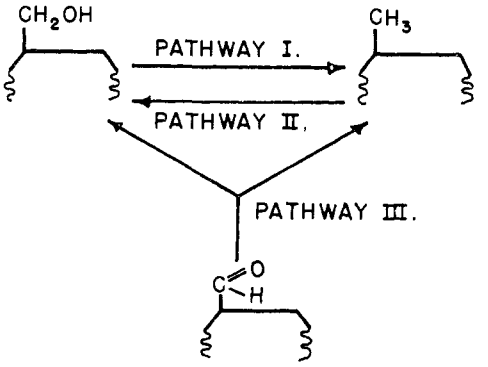

Fig. 2.

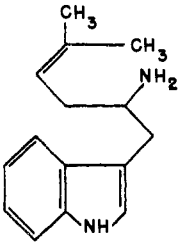

Fig. 3.

chanoclavine-C^{14} (biosynthesized from tryptophan-β-C^{14} by *Claviceps purpurea*) does not according to our findings,[11a] prove to be either the precursor or the metabolite of agroclavine. Rather agroclavine seems to be a common precursor of the other clavine-type ergot alkaloids,[12] which we have found to be converted into festuclavine, pyroclavine, setoclavine[11b] and isosetoclavine by *Claviceps purpurea*, a sequence which was proposed by Yamatodani and Abe.[13,11a]

Lastly our present finding that there is no change in the oxidation level at C–2 of mevalonate during its conversion into agroclavine (Table I) indicates that of the three possible pathways (Fig. 2) pathway II accounts for the appearance of the different substituents at C–8 (C–17 of ergot alkaloids) of ergot alkaloids. This finding is in good agreement with another observation in this laboratory, that chemically prepared lysergol-T and lysergene-T do not incorporate into agroclavine, thus ruling out the reaction sequence from elymoclavine into agroclavine through lysergol and lysergene as has been proposed[13] and confirming the report that agroclavine is converted irreversibly into elymoclavine.[12]

(11) (a) Similar interrelationships were established by S. Agurell and E. Ramstad, personal communication. (b) C. I. Abon Chaar, D. Groger, L. R. Brady and V. E. Tyler, Jr., *Lloydia*, **24**, 159 (1961).

(12) S. Agurell and E. Ramstad, *Tetrahedron Letters*, 501 (1961).

(13) S. Yamatodani and M. Abe, *Bull. Agr. Chem. Soc. Japan*, **20**, 95 (1956).

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SOLVENT EFFECT ON THE DISPROPORTIONATION OF MONOSODIUM TETRAPHENYLETHYLENE

Sir:

The sodium adducts of tetraphenylethylene (TPE) exhibit anomalous behavior in ethereal

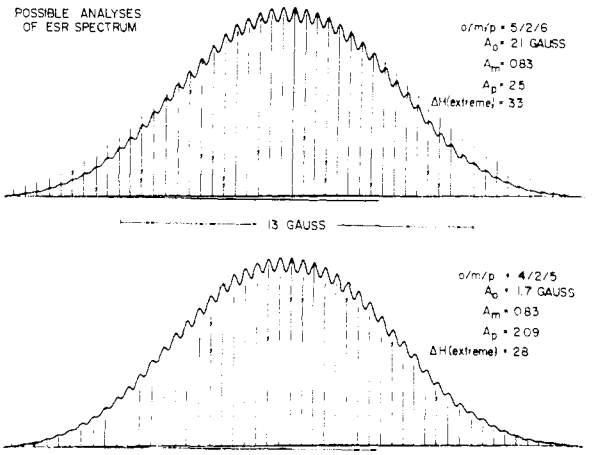

Fig. 1.—(a) Upper: Thirty-two lines of the calculated spectrum, all of intensities less than 3.2% of that of the central line, are not shown. (b) Lower: Twenty lines of the calculated spectrum, all of intensities less than 0.6% of that of the central line, are not shown.

solvents, in that the value of K appears to be abnormally large.[1–6] No e.s.r. signals have been

$$2\mathrm{ArH}^-, \mathrm{Na}^+ \overset{K}{\leftrightarrows} \mathrm{ArH} + \mathrm{ArH}^{-2}, 2\mathrm{Na}^+ \qquad (1)$$

detected in sodium–TPE solutions in dioxane or diethyl ether, even in the presence of a large excess of TPE.[7] The effects of anionic solvation,[2,6c] ionic aggregation,[6a] and possible changes in geometry[2,6b,6c,6d] all have been suggested as being responsible for this behavior.

We have observed that a change in solvent from diethyl ether to 1,2-dimethoxyethane changes the magnitude of $K_{TP\bar{E}}$ by a factor of at least 10^5 at room temperature (*ca.* 22° in our laboratories).

Dissolution of sodium in a TPE solution in 1,2-dimethoxyethane leads directly to a blue, paramagnetic solution with absorption maxima at 6350 ± 100 and 4900 ± 50 Å., the relative intensities of which vary with the amount of dissolved sodium.[8]

The e.s.r. spectrum[8a] of the blue solution exhibits the same hyperfine pattern whether the alkali metal employed is Li, Na, K, or Cs. Figure 1 shows an integrated version of the spectrum together with the spectra predicted from two possible coupling constant analyses, $A_o/A_m/A_p$ = 5/2/6 and 4/2/5, the best fits we have been able to find. These ratios are in reasonable agreement

(1) For leading references to work on alkali metal adducts of aromatic hydrocarbons see A. Streitwieser, Jr., "Molecular Orbital Theory," John Wiley and Sons, Inc., New York, N. Y., 1961, p. 159 ff.

(2) N. S. Hush and J. Blackledge, *J. Chem. Phys.*, **23**, 514 (1955).

(3) W. Schlenk, J. Appenrot, A. Michael and A. Thal, *Ber.*, **47**, 473 (1914); W. Schlenk and E. Bergmann, *Ann.*, **463**, 1 (1928).

(4) N. B. Keevil and H. E. Bent, *J. Am. Chem. Soc.*, **60**, 193 (1938).

(5) H. Gilman and R. V. Young, *J. Org. Chem.*, **1**, 315 (1936).

(6) (a) D. W. Ovenall and D. H. Whiffen, *Chemical Society Special Publication No. 12*, 1958, p. 139; (b) discussion of M. J. S. Dewar, *ibid.*, p. 164; (c) discussion of N. S. Hush, *ibid.*, p. 164; (d) discussion of P. Gray, *ibid.*, p. 166.

(7) (a) Solvent dioxane, reference 6a; (b) solvent diethyl ether, this work.

(8) (a) Preparation of a blue solution of sodium tetraphenylethylene in tetrahydrofuran by taking care to insure a large excess of TPE has been described recently. The authors attribute the blue color, as do we, to TPE^-. See A. G. Evans, J. C. Evans, E. D. Owen, B. J. Tabner and J. E. Bennett, *Proc. Chem. Soc.*, 226 (1962). (b) See also H. P. Leftin and W. K. Hall, *J. Phys. Chem.*, **64**, 382 (1960).