tion products. In each case reduction was carried out by stirring an ethanolic solution of olefin and hydrazine hydrate in an oxygen atmosphere at 55° (camphene was reduced at 45°), and product composition was determined by analytical vapor phase chromatography (reproducibility $\pm 0.5\%$). The results of the diimide reductions are summarized in Table I, along with, for comparison purposes, product ratios observed in catalytic reductions of the same olefins. In cases where substrate steric features are clearly important factors (no. 1, 2, 6 and possibly 7), greater than 90% of the less stable stereoisomer appears, resulting from reagent approach from the less hindered side. Of the other examples, perhaps the most instructive is 4-*t*-butylmethylenecyclohexane, where the six-membered ring itself is—for all practical purposes—the only steric contributor in the reduction; here, axial and equatorial attack by diimide are just counter-balanced. It should be noted that in no reduction did more than 76% of the more stable product result.

Acknowledgment.—The authors are grateful to the Petroleum Research Foundation for financial support (Grant No. 589-C).

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF WISCONSIN
MADISON, WISCONSIN

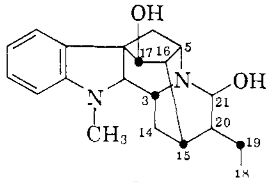
E. E. VAN TAMELEN
R. J. TIMMONS

RECEIVED FEBRUARY 8, 1962

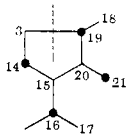
BIOSYNTHESIS OF THE NON-TRYPTOPHAN DERIVED PORTION OF AJMALINE[1]

Sir:

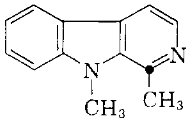
We have shown[2] previously that the administration of tryptophan-2-C^{14} to *Rauwolfia serpentina* plants leads to the formation of ajmaline-5-C^{14}, strongly suggesting that this amino acid or closely related metabolite is a precursor of the reduced β-carboline moiety of ajmaline. The origin of the residual carbons of ajmaline and related indole alkaloids has been the subject of much controversy. Discussion of the various hypotheses will be simplified if we confine our attention to ajmaline (I). Woodward[3] and Robinson[4] suggested that C_3 and carbons 14 to 20 are derived from 3,4-dihydroxyphenylalanine. Wenkert[5] proposed that these carbons are derived from prephenic acid. In both these hypotheses C_{21} is derived from a one carbon fragment and recent tracer studies[6] with sodium formate-C^{14} support this idea. In a third hypothesis independently conceived by Thomas[7] and Wenkert[5c] all the non-tryptophan derived carbons are considered to arise from a monoterpene having the carbon skeleton II. The cyclopentane ring is cleaved at the dotted line and the carbons



I



II



III

are numbered as they would be expected to appear in ajmaline. The extra carbon at C_{16} is absent in ajmaline but becomes the carbomethoxy group of serpentine, reserpine and related alkaloids.

We have tested these hypotheses by feeding various labeled compounds to *R. serpentina* plants by methods previously described.[2] Tyrosine is a known precursor of 3,4-dihydroxyphenylalanine and the administration of tyrosine-2-C^{14} would be expected to yield ajmaline-3-C^{14} if the Woodward–Robinson scheme were correct. However, the ajmaline, reserpine and serpentine obtained from the plant which had been fed this tracer (0.2 mc.) were completely inactive. The side chain of prephenic acid is derived from pyruvate,[8] which in turn can be formed rapidly from alanine by a transamination reaction. Thus if Wenkert's prephenic hypothesis were correct one would expect alanine-2-C^{14} to yield prephenic acid labeled on the ketone group which ultimately becomes C_3 of ajmaline. Administration of DL-alanine-2-C^{14} (0.36 mc.) led to the formation of radioactive ajmaline; however, the specific activity was quite low (2.9×10^4 d.p.m./mM.) and degradation indicated that there was only about 2% of the radioactivity located at C_3. Ajmaline isolated from the plant which had been fed mevalonic acid-2-C^{14} (0.1 mc.), an established precursor of terpenes,[9] was completely inactive. The administration of sodium acetate-1-C^{14} (3.25 mg., 0.2 mc.) yielded radioactive ajmaline (9.3×10^5 d.p.m./mM.). Kuhn–Roth oxidation of the ajmaline afforded radioactive acetic acid which on treatment with sodium azide and sulfuric acid yielded carbon dioxide assayed as barium carbonate (2.4×10^5 d.p.m./mM.) and inactive methylamine (assayed as the platinochloride). On heating the ajmaline with soda-lime harman (2.3×10^5 d.p.m./mM.) and N-(*ind*)-methylharman (III) (2.4×10^5 d.p.m./mM.) were obtained.[10] The acetic acid obtained by the Kuhn–Roth oxidation of III was subjected to the Schmidt reaction yielding barium carbonate (2.4×10^5 d.p.m./mM.) and inactive methylamine. These results indicate that approximately one half the total radioactivity of the ajmaline is located at C_3 and C_{19} and equally divided between these positions. These results are incompatible with the monoterpene hypothesis since acetate-1-C^{14} would produce mevalonate-1,3,5-C^{14} which would afford

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(1) This investigation was supported by a Research Grant MY-2662 from the National Institute of Mental Health, U.S. Public Health Service.

(2) E. Leete, *J. Am. Chem. Soc.*, **82**, 6338 (1960).

(3) R. B. Woodward, *Angew. Chemie*, **68**, 13 (1956).

(4) R. Robinson, *Festschrift Arthur Stoll*, Birkhäuser, Basel, 1957, p. 457.

(5) (a) E. Wenkert and N. V. Bringi, *J. Am. Chem. Soc.*, **81**, 1474 (1959); (b) E. Wenkert, *Experientia*, **15**, 165 (1959); (c) E. Wenkert, *J. Am. Chem. Soc.*, **84**, 98 (1962).

(6) P. N. Edwards and E. Leete, *Chemistry and Industry*, 1666 (1961).

(7) R. Thomas, *Tetrahedron Letters*, 544 (1961).

(8) J. G. Levin and D. B. Sprinson, *Biochem. and Biophys. Research Comm.*, **3**, 157 (1960).

(9) A. J. Birch, D. Boulter, R. I. Fryer, P. J. Thomson, and J. L. Willis, *Tetrahedron Letters*, No. 3, 1 (1959).

(10) F. A. L. Anet, D. Chakravarti, R. Robinson, and E. Schlittler, *J. Chem. Soc.*, **1242** (1954).

the monoterpene II labeled at the positions indicated by black dots.

However, our results do support a new hypothesis for the biosynthesis of ajmaline which is also adaptable to all the known indole alkaloids.[11] We suggest that the chain involving carbons 18, 19, 20, 15, 14, and 3 is formed by the linear condensation of three molecules of acetylcoenzyme A, C_{18} being the methyl end of the chain.[12] A one-carbon fragment is attached at C_{20} (a methylene position in the poly-β-ketoacid). At C_{15} condensation occurs with the methylene carbon of a molecule of malonylcoenzyme A. In ajmaline one of the carboxyl groups at C_{16} is lost, but in many other indole alkaloids, *e.g.*, macusine-A,[13] it is retained. We would thus expect the ajmaline derived from acetate-1-C^{14} to be labeled on carbons 3, 15, 17, and 19, indicated by black dots in formula I. Since only a small amount of radioactive ajmaline was at our disposal we were unable to carry out a more extensive degradation to locate the rest of the activity in the alkaloid. Feeding experiments will be carried out with malonic acid-1-C^{14} and larger amounts of acetate-1-C^{14}.

We thank Dr. W. I. Taylor of Ciba for the generous supply of ajmaline.

[11] This hypothesis was independently adumbrated by E. Schittler and W. I. Taylor, *Experientia*, **16**, 244 (1960). A. R. Battersby has also expressed similar ideas in private communications.

[12] It is probable that carboxylation of acetylcoenzyme A to malonylcoenzyme A will occur prior to condensation, *cf.* S. J. Wakil and J. Ganguly, *J. Am. Chem. Soc.*, **81**, 2597 (1960); R. Bentley J. G. Keil and D. S. Bhate, *ibid.*, **83**, 3716 (1961); R. Bentley, and J. G. Keil, *Proc. Chem. Soc.*, 111 (1961); A. J. Birch, A. Cassera, and R. W. Rickards, *Chemistry and Industry*, 792 (1961).

[13] A. T. McPhail, J. M. Robertson, G. A. Sim, A. R. Battersby, H. F. Hodson, and D. A. Yeowell, *Proc. Chem. Soc.*, 223 (1961).

SCHOOL OF CHEMISTRY
UNIVERSITY OF MINNESOTA
MINNEAPOLIS 14, MINNESOTA

EDWARD LEETE
SHIBNATH GHOSAL
PHILIP N. EDWARDS

RECEIVED FEBRUARY 19, 1962

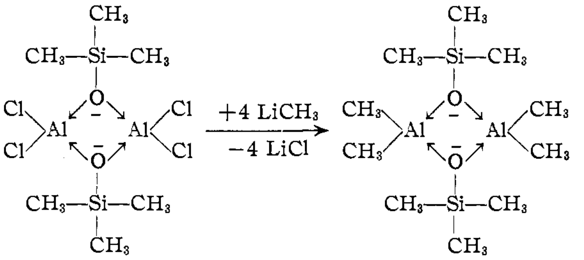
WEAKENING OF $d_{\pi}p_{\pi}$-BONDS BY COÖRDINATION

Sir:

In previous papers[1,2,3] we have reported some results of our current investigations on various types of alkyl-hetero-siloxanes containing elements of the IVb and Vb group. This communication now describes the synthesis of pentamethylsiloxalane, the first member of the *homologous* series of alkyl-alumino-siloxanes, and records our conclusions from physical studies on that new compound.

Both procedures for the preparation of alumino-siloxanes described in the literature are not applicable for the synthesis of pentamethylsiloxalane.[4,5] In the reaction of trimethylsiloxy-dichloro-alane (I), $Me_3SiOAlCl_2$,[6] with two moles of methyllithium in diethyl ether at 10°, we have found a simple method of preparation of the desired $Me_3SiOAlMe_2$. If the reaction is carried out in an atmosphere of dry nitrogen good yields of pentamethylsiloxalane (II) are recovered. By repeated vacuum distillation, fractional crystallization and sublimation *in vacuo* the pure compound is obtained in the form of dry, colorless crystals of several cm. length with m.p. +45.5°, which can be distilled without decomposition at b.p. +81.5° (10 mm.). The substance shows excellent solubility in all dry and proton-inactive organic solvents. Chemical analysis and assignment of the infrared spectrum confirm the composition and principles of structure, according to the formula $Me_3SiOAlMe_2$ (II).

Cryoscopic and dipole measurements of benzene solutions of the compounds I and II have shown, however, that both compounds are dimeric and have no dipoles within the experimental error of the apparatus. The dimerization demanded by these experiments takes place with formation of a planar four-membered ring, in which each siloxy-group forms coördinative bonds to two aluminum atoms



The unusual chemical and thermal stability of the inorganic four-membered ring II is evident from the facts that it cannot be split even by the strong donator trimethylamine at 30°, and that the compound can be distilled under ordinary pressure of dry nitrogen at about 200° with only slight decomposition.[7]

N.m.r. spectra[8] of I and II give rise to certain conclusions regarding the types of bondings in these compounds. Solutions of II in CCl_4 showed a spectrum with two singlet peaks, the areas of which are (in agreement with formula II) in the ratio 3:2. Using tetramethylsilane in CCl_4[8] as an external standard the protons of the Me_2Al-group appear at higher fields with a chemical shift of $\tau = 10.82$ p.p.m., suggesting a comparatively high electron-density at these partly negative carbon atoms. The protons of the silyl group, however, are in resonance at lower fields with a chemical shift of $\tau = 9.80$ p.p.m. Compared with hexamethyldisiloxane (chemical shift $\tau = 9.96$ p.p.m., as an additional internal standard of equal concentration) this chemical shift is considerably high.[9]

The unusual small deshielding effect of the protons in the transition $Me_4Si \rightarrow Me_3SiOSiMe_3$ must be ascribed to the strong $d_{\pi}p_{\pi}$-bonds in the latter,[9] which increase the electron density at the carbon atoms and are nearly compensating the electron withdrawing effect of the new substituent oxygen.

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[1] H. Schmidbaur and M. Schmidt, *Chem. Ber.*, **94**, 1138 (1961).

[2] H. Schmidbaur and M. Schmidt, *J. Am. Chem. Soc.*, **83**, 2963 (1961).

[3] H. Schmidbaur and M. Schmidt, *Angew. Chem.*, **73**, 655 (1961).

[4] W. A. Kriner, A. G. McDiarmid and E. Ch. Evers, *J. Am. Chem. Soc.*, **80**, 1546 (1958).

[5] H. Jenkner, *Z. f. Naturforschung*, **14b**, 133 (1959).

[6] N. F. Orlow, *Dokl. Akad. Nauk SSSR*, **114**, 1033 (1957); *C. A.*, **52**, 2742 (1958), and A. H. Cowley, F. Fairbrother and N. Scott, *J. Chem. Soc.* (London), 717 (1959).

[7] The analogous compound $[H_3SiOAlMe_2]_2$ slowly decomposes at room temperature, SiH_4 being formed.[4]

[8] Varian Associates 60, 60 Mc.; CCl_4 solutions with concentrations 5 ± 1%.

[9] M. P. Brown and D. E. Webster, *J. Phys. Chem.*, **64**, 698 (1960).