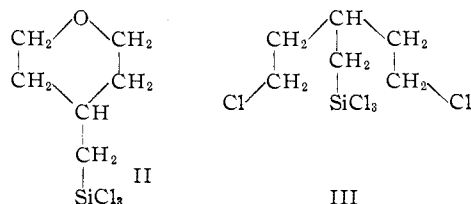


The Grignard reagent prepared from 4-bromomethyltetrahydropyran⁴ in tetrahydrofuran was added to excess silicon tetrachloride and gave 4-trichlorosilylmethyltetrahydropyran (II), b.p. 63.5° (2 mm.); *Anal.* Calcd. for C₆H₁₁SiOCl₃: Si, 12.0; Cl, 45.6. Found: Si, 11.9; Cl, 45.5. Treatment of II with boron trichloride followed by thionyl chloride gave 1,5-dichloro-3-trichlorosilylmethylpentane (III) in 50% yield, b.p. 131° (2 mm.). *Anal.* Calcd. for C₆H₁₁Cl₂Si: Si, 9.74; Cl (attached to Si), 36.9. Found: Si, 9.80; Cl (attached to Si), 36.9.



Reaction of III with 30% excess magnesium in ether gave a 45% yield of the bridgehead chloride (I), b.p. 54° (5 mm.), n_D^{20} 1.4956. *Anal.* Calcd. for C₆H₁₁SiCl: Si, 19.1; Cl, 24.2. Found: Si, 18.8; Cl, 23.9. The infrared spectrum of I showed the absence of Si-H, C=C, and Si-CH₃. Furthermore, the spectrum was rich in detail and contained eight strong and well-defined maxima characteristic of the bicyclic ring system in I which were also present in the two derivatives of I described below.

The bridgehead chloride (I) has an acrid odor, hydrolyzes rapidly in a stream of moist air to give the disiloxane (IV), and undergoes rapid quantitative titration of its Si-Cl bond with 0.1 *N* alkali. The disiloxane (IV), bis-(1-silabicyclo[2.2.1]heptyl) oxide, obtained in 70% yield from treatment of I with wet ether, is a white crystalline solid which sublimes readily and has m.p. 76°. The infrared spectrum, both solution and KBr block, shows the complete absence of Si-OH, has the Si-O-Si maximum at 9.5 μ , and also shows the eight maxima present in I. *Anal.* Calcd. for C₁₂H₂₂Si₂O: Si, 23.5; mol. wt., 238. Found: Si, 23.8; mol. wt. (cryoscopically in benzene), 235.

The bridgehead chloride (I) reacted readily with lithium aluminum hydride in ether at 0° and gave a 60% yield of 1-silabicyclo[2.2.1]heptane (V), b.p. 131° (732 mm.), m.p. 63°. *Anal.* Calcd. for C₆H₁₂Si: Si, 25.0; H (attached to Si), 0.90; mol. wt., 112. Found: Si, 24.9; H (attached to Si), 0.89; mol. wt., (cryoscopically in benzene), 113. The infrared spectrum showed the strong Si-H maximum at 4.65 μ and the eight maxima present in I and IV.

The above facts are in accord with a preliminary working hypothesis which includes the following three postulates: (1) Many nucleophilic displacements on silicon involve formation of an addition complex with the attacking reagent. (2) The geometry of the complex approximates that of a trigonal bipyramid (PCl₅ and PF₅ have this structure in the vapor state)⁵ and the bonding is dsp³. (3)

(4) A. Burger, L. B. Turnbull and J. G. Dinwiddie, *THIS JOURNAL*, **72**, 5512 (1950).

(5) For a discussion of the geometry and bonding of PCl₅ and PF₅ see T. Moeller, "Inorganic Chemistry," John Wiley and Sons, New York, N. Y., 1952, p. 626.

The entering group and the group which is ultimately displaced need not occupy the apices of the trigonal bipyramid. Instead of an angle near 180°, the entering group may form an angle near 90° with the group to be displaced and the central silicon atom.⁶

The high reactivity of I and the mechanism envisaged in the above hypothesis are attributed to the d-orbitals and large size of silicon relative to carbon.

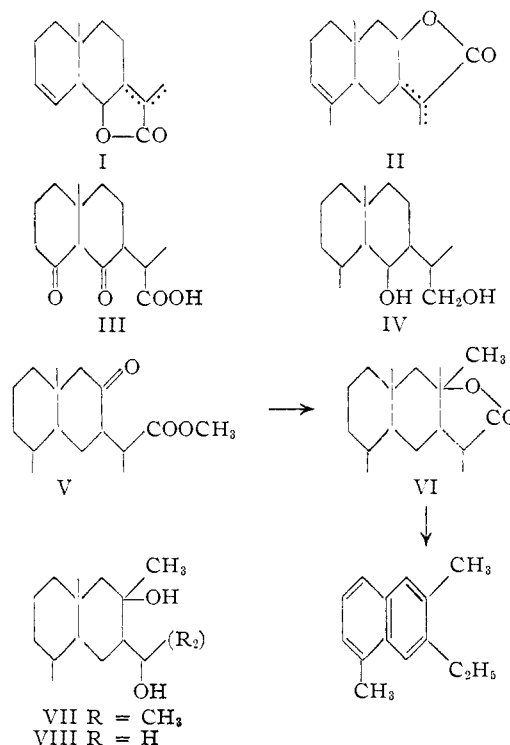
(6) Postulate (1) is at least 30 years old and has been in use up to the present time by chemists working with the organic and inorganic chemistry of silicon. See N. V. Sidgwick, "The Electronic Theory of Valency," Oxford University Press, London, 1927, pp. 159-160. Postulate (2) is an attempt to more closely define the geometry of the addition complex in terms of modern theory. Postulate (3) is completely new.

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ON THE STRUCTURE OF ALANTOLACTONE

Sir:

Attempts to correlate alantolactone with santonin which belongs to the eudalene group of sesquiterpenes have been entirely unsuccessful.¹⁻⁴ Iwai previously has reported the facts: (1) the diketacid III derived from the 4-ketolactone shows none of the characteristic properties of β -diketones,



III and IV are conventional formulae by Ruzicka, *et al.*

(1) K. Matsumura, I. Iwai and Ohki, (a) *J. Pharm. Soc. Japan*, **74**, 738 (1954); (b) **74**, 1029 (1954); (c) **74**, 1206 (1954); (d) **74**, 689 (1955).

(2) Mme. C. Asselineau, Mme. S. Bory, and E. Lederer, *Bull. soc. chim. France*, 1524 (1955).

(3) Ö. Kovács, V. Herout, M. Horák, and F. Sorm, *Collection Czechoslov. Chem. Commun.*, **21**, 225 (1956).

(4) L. Ruzicka and J. A. van Melsen, *Helv. Chim. Acta*, **14**, 397 (1931).

e.g., it gives no pyrazole derivative with hydrazine and no color with ferric chloride,^{1b} and (2) the diol IV produced by the action of lithium aluminum hydride on tetrahydroalantolactone affords a dibenzoate, but that obtained from desoxytetrahydro-santonin gives only a monobenzoate.^{1d}

These facts led us to question the position of the lactone ring in the formula (I) suggested by Ruzicka, *et al.*, for alantolactone.^{4,5} The following experiments have enabled us to conclude that alantolactone should be represented by II and not I.

The keto ester V,^{1b,6} b.p. 134–135° (0.05 mm.), $[\alpha]_D^{25} -26^\circ$ ($c = 5$, CHCl₃), was treated with methylmagnesium iodide to give 7-methyltetrahydroalantolactone (VI), in 44% yield, m.p. 99–100°, $[\alpha]_D^{25} -0.8^\circ$ ($c = 5$, CHCl₃), Calcd. for C₁₆H₂₆O₂: C, 76.75; H, 10.47. Found: C, 76.72; H, 10.54, together with VII, in 6% yield, m.p. 199–200°, $[\alpha]_D^{25} +7.0^\circ$ ($c = 2.9$, CHCl₃), Calcd. for C₁₈H₃₄O₂: C, 76.54; H, 12.13. Found: C, 76.16; H, 11.83. The structure of VI is based on analysis, infrared spectrum (ν_{\max} 1762 cm.⁻¹, γ -lactone), and the facts that it is converted to an acid by methanolic alkali and recovered unchanged in acidic medium, and that reduction with lithium aluminum hydride yielded a diol (VIII), m.p. 157–158°; calcd. for C₁₆H₃₀O₂: C, 75.53; H, 11.89. Found: C, 75.20; H, 11.84.

Dehydrogenation of VI with selenium gave a hydrocarbon which showed characteristic absorption for substituted naphthalenes in the ultraviolet region. Its picrate and styphnate melt at 102–103° and 149°, respectively. The infrared absorption spectrum of this hydrocarbon resembles closely that of 2,3,5-trimethylnaphthalene,⁷ so we have synthesized 2,5-dimethyl-3-ethylnaphthalene to compare with the above hydrocarbon.

o-Tolylacetyl chloride was condensed with ethylzinc iodide to give *o*-methylbenzyl ethyl ketone, b.p. 121° (10 mm.) (semicarbazone, m.p. 173–174°), which was converted, by condensation with ethyl α -bromopropionate, followed by dehydration and hydrogenation, into ethyl γ -*o*-tolyl- α -methyl- β -ethyl butyrate, b.p. 160–161° (12 mm.); calcd. for C₁₈H₂₄O₂: C, 77.37; H, 9.74. Found: C, 77.49; H, 9.43. Ring closure of the ester with sulfuric acid gave 2,5-dimethyl-3-ethyl-1,2,3,4-tetra-1-one, b.p. 169–170° (10 mm.) (2,4-dinitrophenylhydrazine, m.p. 205–206°; calcd. for C₂₀H₂₂O₄N₄: C, 62.81; H, 5.80; N, 14.65. Found: C, 63.15; H, 5.70; N, 14.66). The dimethylethyltetralone was reduced with lithium aluminum hydride to give 2,5-dimethyl-3-ethyl-1,2,3,4-tetra-1-ol, m.p. 101–102°; calcd. for C₁₄H₂₀O: C, 82.30; H, 9.87. Found: C, 82.40; H, 9.90, which was dehydrogenated with selenium to 2,5-dimethyl-3-ethylnaphthalene, b.p. 120–121° (1.5 mm.); calcd. for C₁₄H₁₆: C, 91.25; H, 8.75. Found: C, 91.28; H, 8.54. Picrate, m.p. 102–103°; calcd. for C₂₀H₁₉O₇N₃: C, 58.11; H, 4.36; N, 10.17. Found: C, 58.19; H, 4.55; N, 10.18. Styphnate, m.p. 149°; Calcd. for C₂₀H₁₉O₈N₃: C, 55.94; H, 4.46; N, 9.79. Found: C, 55.71; H, 4.42; N, 9.81.

(5) L. Ruzicka and P. Pieth, *Helv. Chim. Acta.*, **14**, 1090 (1931).

(6) T. Ukita and S. Nakazawa, *Pharm. Bull.*, **2**, 299 (1954).

(7) W. L. Mosby, *THIS JOURNAL*, **74**, 2564 (1952).

The synthetic hydrocarbon was identical with that obtained from III as shown by infrared absorption spectrum and by mixed melting points of their picrates and styphnates.

Alantolactone, isoalantolactone, and dihydro-isoalantolactone which are isolated from the roots of *Inula helenium* are catalytically hydrogenated to give the same tetrahydroalantolactone,^{4,5} and thus the last two lactones must also have oxygen at C₇.

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RECEIVED DECEMBER 28, 1956

OXIDATION STATE OF RESPIRATORY CARRIERS AND THE MECHANISM OF OXIDATIVE PHOSPHORYLATION

Sir:

To account for coupling of phosphorylation to the electron transport chain in mitochondria, it has been proposed that certain oxido-reduction steps lead to the formation of a "high-energy" linkage between a respiratory carrier and either phosphate or some other compound with which phosphate may exchange.^{1,2,3,4,5} Such a "high-energy" complex is postulated as the ultimate donor of phosphate to ADP.⁶ Thermodynamic considerations alone do not suffice to determine whether such a "high-energy" complex involves the oxidized or the reduced state of the carrier.⁵ In this communication is presented that the primary "high-energy" linkage generated during electron transport involves or is dependent upon the oxidized state of the respiratory carriers.

The experiments were carried out with a complex of enzymes which catalyzes electron transport from β -hydroxybutyrate to oxygen and the coupled phosphorylations.⁷ Such preparations also catalyze exchange of labeled inorganic phosphate with the terminal phosphate of ATP in the absence of *net* electron transport, a reaction which is a reflection of the activity of the coupling mechanisms.^{3,8} Under certain conditions the oxidation-reduction state of the carriers determines the rate of the ATP-P_i^{3,2} exchange. The exchange is maximal when the carriers are in the oxidized state and is greatly inhibited in the reduced state. Data in Table I show that when the enzyme complex is amply supplied with oxygen, in the absence of added oxidizable substrate, the incorporation of P_i^{3,2} into ATP is maximal; DNP⁶ completely inhibits the reaction. Insignificant *net* electron flux oc-

(1) E. C. Slater, *Nature*, **172**, 975 (1953).

(2) A. L. Lehninger, *Harvey Lectures*, **49**, 176 (1953–1954).

(3) C. Cooper and A. L. Lehninger, *J. Biol. Chem.*, in press (February, 1957).

(4) P. D. Boyer, A. B. Falcone and W. H. Harrison, *Nature*, **174**, 401 (1954).

(5) B. Chance and G. R. Williams, *Adv. in Enzymology*, **XVII**, 65 (1956).

(6) Abbreviations: ATP and ADP, adenosine tri- and diphosphate; P_i, inorganic orthophosphate; DNP, 2,4-dinitrophenol.

(7) C. Cooper and A. L. Lehninger, *J. Biol. Chem.*, **219**, 489 (1956).

(8) C. Cooper and A. L. Lehninger, *ibid.*, in press (February, 1957).