COMMUNICATIONS TO THE EDITOR

OXIDATIVE COUPLING OF BUTANES TO OCTANES

Sir:

The simplest method of converting low molecular weight paraffins into higher molecular ones would be a one-step synthesis consisting in the oxidative coupling of two paraffin molecules by means of molecular oxygen, in line with the over-all equation

$$2C_nH_{2n+2} + {}^1/_2O_2 \longrightarrow C_{2n}H_{4n+2} + H_2O \quad (1)$$

Unfortunately, all known methods of oxidation of paraffins lead, at best,[1] to oxidation products of the original paraffin containing the same number of carbon atoms. It was anticipated, however, that if paraffin molecules are pressed so tight that they cannot orient themselves and are forced to react with deficient amounts of oxygen in such close proximity to each other that successive oxidation of the same molecule would become highly improbable, *simply because of restrictions of geometry*, oxidative coupling of two close-lying paraffin molecules might occur. Under ideal coupling conditions the oxygen is forced to react with hydrogen atoms in its immediate vicinity and equal reactivities for primary and tertiary C–H-bonds are to be expected. Thus *isobutane* would couple to yield only: 2,5-dimethylhexane, 2,2,4-trimethylpentane and 2,2,3,3-tetramethylbutane, while *n-butane* would give only: *n*-octane, 3-methylheptane and 3,4-dimethylhexane. *Iso-* and *n-butane* were chosen for our experiments because any likely reaction products can be easily analyzed; furthermore they can be readily compressed to desired loading densities. It was assumed that favorable coupling conditions might prevail at pressures over 20,000 p.s.i. and at 300–350°, *i.e.*, below their thermal cracking range.

Isobutane (99.5+%) containing 4.4 mole % dissolved O_2, was heated in a 30-cc. Aminco Superpressure reactor at 325 ± 5° and at 23,000 p.s.i. pressure for 20–24 hours. It was found that over 80% of the O_2 reacted, forming only traces of CO_2 and CO; H_2O was formed in amounts corresponding to one-fourth of the O_2 consumed. Sixteen identical experiments yielded 9.0 g. of reaction products (b.p. > isobutane). They were divided into: (a) normal oxidation products of isobutane = 75 vol. % and (b) coupling products = 25 vol. %.

(a) consisted of ≃75 vol. % *t*-butanol and 25 vol. % of its degradation products, acetone and methanol.

(b) consisted of octanes, after removal of olefin traces. Microanalysis gave: 81.55% C, 15.17% H, or $CH_{2.22}$ (calcd. for C_8H_{18} = 2.25, for C_8H_{16} = 2.00). Infrared and mass spectra identified the following in vol. % of (b) *2,5-dimethylhexane* 40%, *2,2,4-trimethylpentane* 38%, *2,2-dimethylhexane* 8%, *2,2,3,3-tetramethylbutane present*, other octanes and octanes—possible traces. No masses above octanes were observed in the spectrum.

Identical conditions were used with *n*-butane; 25 vol. % of the product analyzed as follows: *n-octane* 10%, *3-methylheptane* 40–50%, *3,4-dimethylhexane* 30%; other paraffins and possibly olefins 10–20%.

Thus with each butane the three expected octanes were produced. They were also the *only* octanes observed, with the exception of 2,2-dimethylhexane. This abnormal octane is perhaps due to isomerization "*in statu nascendi.*" The amount of water found is also in agreement with equation 1.

The data presented indicate that under the conditions given the usual oxidation paths, although not eliminated, are sufficiently restricted so that the coupling reaction can be readily observed. No attempt to discuss possible mechanisms of this reaction will be made at this time.

The effect of highly restricted geometrical conditions, due to high pressure, on reaction paths, is, of course, not limited to paraffins and can be expected to yield interesting results with other types of compounds.

Acknowledgment is due to the Standard Oil Development Company for the support of this project and to Drs. R. F. Robey and B. E. Hudson, Jr., for mass and infrared analyses and to J. Snyder for some preliminary experiments.

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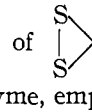
(1) Usually complete breakdown to CO, CO_2 and H_2O takes place.

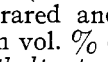
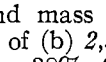
MECHANISM OF ENZYMATIC OXIDATIVE DECARBOXYLATION OF PYRUVATE

Sir:

The generation of active acetate (acetyl CoA[1]) from pyruvate by purified pyruvate oxidase preparations from bacterial[3] and animal[4,5] sources has been formulated as shown in reaction 1. TPN^+ will not replace DPN^+ in this reaction.[4]

$$\text{Pyruvate} + DPN^+ + CoA \longrightarrow \text{Acetyl CoA} + DPNH + CO_2 + H^+ \quad (1)$$

Studies[6] with soluble pyruvate apoöxidase preparations from an *Escherichia coli* mutant which cannot synthesize LTPP[7] reveal that reaction 1 does not proceed in the absence of  . An analysis of the role of this coenzyme, employing

(1) The following abbreviations are used: CoA or CoA-SH = coenzyme A; DPN^+, DPNH and TPN^+, TPNH = oxidized and reduced diphospho- and triphosphopyridine nucleotides, respectively;  and  = oxidized and reduced lipothiamide pyrophosphate (LTPP),[2] respectively; TPP = thiamine pyrophosphate.

(2) (a) L. J. Reed and B. G. DeBusk, THIS JOURNAL, **74**, 3964 (1952); (b) *J. Biol. Chem.*, **199**, 881 (1952).

(3) S. Korkes, *et al.*, *ibid.*, **193**, 721 (1951).

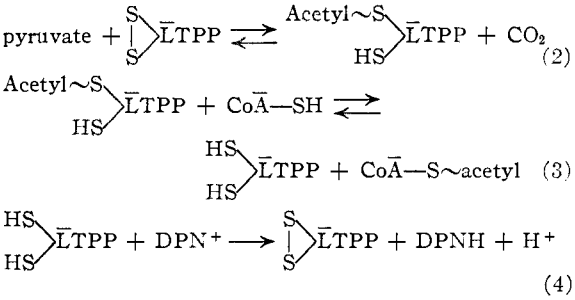
(4) J. W. Littlefield and D. R. Sanadi, *ibid.*, **199**, 65 (1952).

(5) R. S. Schweet and K. Cheslock, *ibid.*, **199**, 749 (1952).

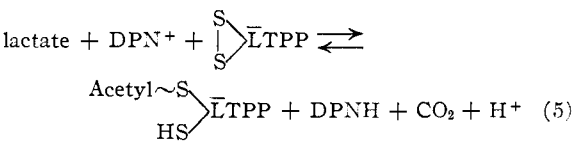
(6) L. J. Reed and B. G. DeBusk, unpublished results.

(7) L. J. Reed and B. G. DeBusk, THIS JOURNAL, **74**, 4727 (1952).

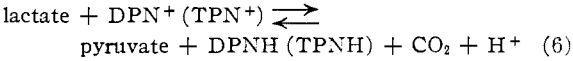
a purified pyruvate apoöxidase preparation from the mutant, shows that reaction 1 comprises reactions 2–4.



The stoichiometry of reaction 2 is demonstrated in Table I. Its reversibility has been demonstrated spectrophotometrically at 340 mμ by means of over-all reaction 5

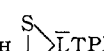


which requires lactic dehydrogenase and pyruvate apoöxidase, and is the sum of reactions 6 and 2.



Evidence for reaction 3 consists of the demonstration that the acetyl group generated in reaction 2 can be utilized for the synthesis of acetyl sulfanilamide in the presence of pyruvate apoöxidase, CoĀ–SH and the arylamine acceptor enzyme

TABLE I

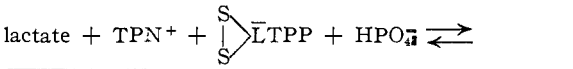
STOICHIOMETRY OF REACTION OF PYRUVATE WITH 

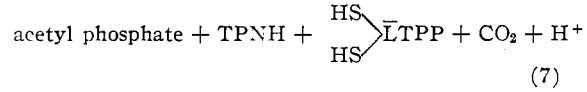
(Δ in micromoles)

Pyruvate	CO_2	−SH	Acetylmercaptan
−3.8	+3.88	+3.71	+3.29

The reaction mixture contained 150 units[8] of pyruvate apoöxidase (specific activity, 1500 units/mg.), 6.5 μmoles[8] of DL-  , 20 μmoles of potassium pyruvate, 10 μmoles of $MgCl_2$,[9] 60 μmoles of tris-(hydroxymethyl)-aminomethane buffer (*p*H 7.4). Final volume, 1.2 ml. Incubation, 10 min. at 25° in an atmosphere of N_2. Pyruvate was analyzed as the 2,4-dinitrophenylhydrazone,[10] –SH by the nitroprusside reaction,[11] and acetylmercaptan by the hydroxamic acid procedure.[12]

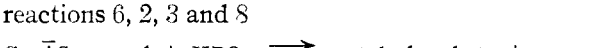
of pigeon liver.[13] The reversibility of reaction 3 has been demonstrated spectrophotometrically at 340 mμ by means of over-all reaction 7, which requires lactic dehydrogenase

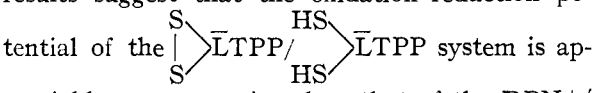


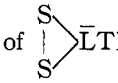
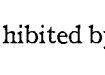


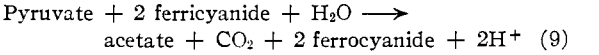
(7)

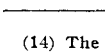
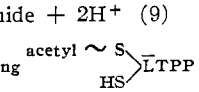
pyruvate apoöxidase, phosphotransacetylase and a catalytic amount of CoĀ–SH, and is the sum of reactions 6, 2, 3 and 8



A spectrophotometric demonstration of reaction 4[14] at 340 mμ, in the presence of pyruvate apoöxidase, has been obtained, but a net reversal of this reaction could not be demonstrated. These results suggest that the oxidation–reduction potential of the  system is appreciably more negative than that of the DPN^+/DPNH system, and therefore the equilibrium of reaction 4 is far to the right. TPN^+ will not replace DPN^+ in reaction 4.

It is to be noted that TPP does not function in the above reactions and actually inhibits the action of  . However, the pyruvate apoöxidase preparation can effect an oxidative decarboxylation of pyruvate as represented by reaction 9. TPP is required for this reaction and its action is inhibited by  .



(14) The  was obtained by treating  with aqueous mercuric acetate, which catalyzes hydrolysis of the thiol ester linkage.[15]

(15) F. Lynen, *et al.*, *Ann.*, **574**, 1 (1951).

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(8) 6.5 mg. of a 66% pure preparation.

(9) The pyruvate apoöxidase preparation exhibits a partial requirement for Mg^{++} in reaction 1. The role of this activator in reactions 2–4 will be the object of a separate study.

(10) T. E. Friedemann and G. E. Haugen, *J. Biol. Chem.*, **147**, 415 (1943).

(11) R. R. Grunert and P. H. Phillips, *Arch. Biochem.*, **30**, 217 (1951).

(12) F. Lipmann and L. C. Tuttle, *J. Biol. Chem.*, **159**, 21 (1945).

(13) T. C. Chou and F. Lipmann, *ibid.*, **196**, 89 (1952).

THE IDENTIFICATION OF THE ISOMERIC ADENYLIC ACIDS *a* AND *b* AS THE 2′- AND 3′-ADENOSINE PHOSPHATES, RESPECTIVELY[1]

Sir:

The location of the phosphate moiety in the first pair of isomeric nucleotides discovered and isolated in this Laboratory four years ago (adenylic acids *a* and *b*)[2,3] has generally been regarded as 2′ and 3′, but not necessarily, respectively.[4] The structures of the subsequently isolated isomeric pairs of guanylic,[3] cytidylic[5,6] and uridylic[5] acids have been assumed to be the same as the adenylic acid pair;

(1) Work performed under Contract No. W-7405-eng-26 for the Atomic Energy Commission.

(2) C. E. Carter, THIS JOURNAL, **72**, 1466 (1950).

(3) W. E. Cohn, *ibid.*, **72**, 1471 (1950); **71**, 2275 (1949).

(4) D. M. Brown and A. R. Todd, *J. Chem. Soc.*, 44, 52 (1952); D. M. Brown, D. I. Magrath and A. R. Todd, *ibid.*, 2708 (1952).

(5) W. E. Cohn, THIS JOURNAL, **72**, 2811 (1950).

(6) H. S. Loring, *et al.*, *ibid.*, **72**, 2811 (1950).