be in considerable degree interpreted on the assumption that the initial process is the attachment of one water molecule to each polar amino-acid side chain. The data also indicate that peptide carbonyl and imido groups usually do not bind water, because of their mutual interaction by hydrogen-bond formation, but that water is bound by carbonyl groups which are not coupled by hydrogen bonds with imido groups. In salmin, in which most of the amino-acid residues are polar, these polar residues coöperate to attach one water molecule jointly to two polar groups in the initial process of hydration.

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[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMICAL ENGINEERING AND CHEMISTRY OF ILLINOIS INSTITUTE OF TECHNOLOGY]

# Catalytic Dehydration of 1-Hexanol and 1-Octanol

BY V. I. KOMAREWSKY, S. C. UHLICK AND M. J. MURRAY

The recent publication of Appleby, Dobratz and Kapranos[1] on vapor phase dehydration of 1-heptanol prompts us to report similar results on catalytic, vapor phase dehydration of 1-hexanol and 1-octanol. In line with the work of the above-mentioned authors, we have found that 1-hexanol and 1-octanol when dehydrated over aluminum oxide catalyst yield as a main product 1-hexene and 1-octene, respectively. The purity of the olefins was checked by boiling points, indices of refraction, specific gravities and Raman spectra. In addition, the hydrogenation to corresponding paraffins was carried out.

## Experimental Part

**Apparatus and Procedure.**—The apparatus consisted of a Pyrex glass reaction tube of 12-mm. diameter placed in a tubular, electrically heated, bronze block furnace with automatic temperature control (±1°). The catalyst bed was 40 cm. long. It was preceded by a layer of glass beads 5 cm. in length which served as a preheater. Alcohols were passed over the catalyst at a constant rate of 35 ml. per hour (space velocity, 0.5) at 350°. There was practically no gas evolution nor carbon deposition on the catalyst.

TABLE I

PHYSICAL CONSTANTS OF 1-HEXENE AND 1-OCTENE

| Olefin | | | 1-Hexene | 1-Octene |
|---|---|---|---|---|
| Present authors | B. p. | °C. | 62.8–63.1 | 121.1–121.4 |
| | | Mm. | 743 | 750 |
| | $n^{20}_D$ | | 1.3880 | 1.4095 |
| | $d^{20}_4$ | | 0.6740 | 0.7152 |
| Egloff[a] | B. p. | °C. | 63.5 | 122.5 |
| | | Mm. | 760 | 760 |
| | $n^{20}_D$ | | 1.3886 | 1.4103 |
| | $d^{20}_4$ | | 0.6747 | 0.7159 |
| Doss[b] | B. p. | °C. | 63.7 | 121.6 |
| | | Mm. | 760 | 760 |
| | $n^{20}_D$ | | 1.3880 | 1.4090 |
| | $d^{20}_4$ | | 0.6733 | 0.7150 |

[a] Egloff, Physical Constants of Hydrocarbons, Vol. 1, Reinhold Publishing Corporation, New York, N. Y., 1939.
[b] Doss, Physical Constants of the Principal Hydrocarbons, Technical and Research Division of the Texas Company, Third Edition, New York, N. Y., 1942.

**Alcohols.**—1-Hexanol, Carbon and Carbide Chemical Corporation; 1-octanol, E. I. du Pont de Nemours and Company: both alcohols were purified by careful distillation with a 100-plate Podbielniak column. Boiling points of the purfied alcohols were: 1-hexanol, 157°; 1-octanol, 192–193°.

**Catalyst.**—Alumina catalyst was prepared by precipitation of aluminum hydroxide from a clear solution of sodium aluminate by ammonium chloride. The precipitate was washed ion-free, dried at 105–110° in an oven, screened to 8–10 mesh particle size and finally dried in the catalytic tube in a slow stream of dry nitrogen at 350°.

**Analysis of the Product.**—The products, after separation of water and drying over anhydrous sodium sulfate, were distilled in a 100-plate Podbielniak column with heligrid packing. In each case more than 90% of the product boiled in the range of the 1-olefin. The distillation bot-

TABLE II

RAMAN SPECTRA OF 1-HEXENE AND 1-OCTENE

| 1-Hexene | | | | | | 1-Octene | | | |
|---|---|---|---|---|---|---|---|---|---|
| Present work | | | | | | | | | |
| Dehydration of 1-hexanol | | Synthetic | | Literature[a] | | Present work | | Literature[b] | |
| cm.$^{-1}$ | I[c] | cm.$^{-1}$ | I[c] | cm.$^{-1}$ | I | cm.$^{-1}$ | I | cm.$^{-1}$ | I[d] |
| 312 | 1 | 312 | 1 | | | 291 | 2 | 289 | 10 |
| 357 | 2 | 357 | 3 | 358 | 2 | | | | |
| 395 | 1 | 398 | 1 | | | 430 | 1 | 433 | vw |
| 626 | 1 | 627 | 1 | | | 633 | 1 | 633 | vw |
| 819 | 3 | 819 | 3 | 818 | 2 | 812 | 2 | 813 | 4 |
| 872 | 1 | 871 | 1 | 873 | 1 | 854 | 1 | 850 | 5 |
| 890 | 1 | 889 | 1 | | | 886 | 2 | 886 | 11 |
| 910 | 3 | 912 | 2 | 912 | 2 | 911 | 2 | 909 | 11 |
| | | | | | | 970 | 0 | 966 | vw |
| 984 | 1 | 984 | 0b | | | | | 989 | vw |
| | | | | | | 1013 | 1 | 1014 | 6 |
| 1056 | 3 | 1057 | 2 | 1056 | 2 | 1061 | 2 | 1067 | 12 |
| | | | | | | 1076 | 2 | 1079 | 13 |
| 1102 | 2 | 1102 | 2 | | | 1111 | 2 | 1114 | 8 |
| 1216 | 1 | 1216 | 0 | | | | | | |
| 1293 | 6 | 1293 | 7vb | 1296 | 7 | 1292 | 5 | 1293 | 94 |
| 1417 | 5 | 1416 | 5 | 1417 | 8 | 1416 | 4 | 1415 | 42 |
| 1449 | 6b | 1448 | 5b | 1448 | 7 | 1443 | 5 | 1440 | 79 |
| | | | | | | 1457 | 5 | 1456 | 63 |
| 1643 | 10 | 1641 | 10 | 1642 | 8 | 1644 | 7 | 1641 | 134 |
| | | | | | | 1671 | 0 | | |
| | | | | | | 2729 | 1 | 2727 | 4 |
| 2861 | 8b | 2863 | 8b | 2859 | 5 | 2856 | 10 | 2853 | 544 |
| | | | | 2876 | 8 | | | 2873 | 778 |
| 2911 | 9 | 2913 | 8 | 2909 | 8 | 2891 | 10 | 2899 | 1000 |
| 2935 | 6 | 2937 | 7 | | | 2934 | 8 | 2925 | 535 |
| 2963 | 4 | 2961 | 3 | 2963 | 5 | 2967 | 3 | 2961 | 98 |
| 3003 | 8 | 2999 | 9 | 3002 | 8 | 3006 | 5 | 2999 | 124 |
| 3081 | 5 | 3082 | 4 | 3076 | 5 | 3087 | 4 | 3078 | 23 |

[a] See ref. 2. [b] Forrest F. Cleveland, see ref. 4. Spectrum of an A. P. I. sample. [c] Intensity visually estimated on a scale of 10. [d] Intensity on a presumed scale of 1000.

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[1] Appleby, Dobratz and Kapranos, THIS JOURNAL, 66, 1938 (1944).

toms consisted of unreacted alcohols and probably some polymerization products. The properties of the obtained olefins, together with literature data, are presented in Table I. Raman spectra are listed in Table II.

Both olefins were hydrogenated to corresponding paraffins over nickel–alumina catalyst at 180°. The properties of the obtained paraffins were as follows: *n*-hexane, b. p. 68.7°, $n^{20}{}_D$ 1.3750; *n*-octane, b. p. 125.6°, $n^{20}{}_D$ 1.3976.

## Discussion

The Raman spectrum of the dehydration product of 1-hexanol agrees well, in general, with the literature[2] values for 1-hexene. The concurrence is much closer, however, with the more complete spectrum obtained on a sample of 1-hexene, b. p. 63.3–64.0°, synthesized in this Laboratory.[3] The strong line at 1643 cm.$^{-1}$ in the spectrum of the dehydration product is the only one in the olefinic region and this arises from the $R{-}CH{=}CH_2$ group.

The Raman spectrum of the dehydration product of 1-octanol is in excellent agreement with the spectrum reported by Cleveland[4] for an A. P. I. sample of 1-octene. Besides the strong olefinic line at 1644 cm.$^{-1}$ which arises from the $R{-}CH{=}CH_2$ group, the spectrum of the dehydration product has also a very weak line at 1671 cm.$^{-1}$. This line is not found on a comparable spectrogram[5] obtained from the A. P. I. sample and hence shows the presence of a small amount (of the order of 2%) of an impurity in the product.

The position of the line of the impurity permits one to eliminate as possibilities *cis*-$RCH{=}CHR'$ (1658 cm.$^{-1}$), $RR'C{=}CH_2$ (1650 cm.$^{-1}$), and with less certainty $RR'C{=}CCHR''$ (1678 cm.$^{-1}$) and $RR'C{=}CR''R'''$ (1678 cm.$^{-1}$). In each case the approximate frequency expected is given in parentheses. For the *trans*-octenes (2-, 3- or 4-) one should find a line at 1674, and this is within experimental error of the 1671 cm.$^{-1}$ value which was observed. The origin of the small amount of this olefin is uncertain.

Regardless of the status of the weak line discussed above, the Raman spectrum gives unambiguous evidence that the vapor phase dehydration by aluminum oxide of 1-hexanol and 1-octanol produces mainly the olefin expected in each case.

## Summary

The vapor phase dehydration of 1-hexanol and 1-octanol over alumina catalyst results in the production of the expected 1-olefin as the main product. The purity of the product in each case was checked not only by the usual physical constants but also by the Raman effect.

CHICAGO, ILLINOIS

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[2] Hibben, "The Raman Effect and Its Chemical Applications," Reinhold Publishing Corp., New York, N. Y., 1939, p. 162.

[3] Prepared by H. J. Taufen through the action of allyl bromide on *n*-propylmagnesium bromide: Taufen, Murray and Cleveland, THIS JOURNAL, **63**, 3500 (1941).

[4] Forrest F. Cleveland, *J. Chem. Phys.*, **11**, 1 (1943).

[5] Kindly lent by Dr. Cleveland.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

# The Mode of Action of Sulfonamides. Dissociation Constants of the Enzyme-Drug Complex

BY IRVING M. KLOTZ AND HELMUT R. GUTMANN[1]

Abundant evidence has been accumulated to show that the action of sulfonamides is to be attributed to their competition with various substrates associated with particular enzyme systems.[2,3,4] Recently it has been shown also that the inhibition of bacterial growth by sulfonamides may be accounted for quantitatively on the assumption that the action is due to a reversible combination between the basic form of the drug and an enzyme and that the law of mass action is applicable.[5] In this quantitative treatment, dissociation constants for the enzyme–drug complex were unavailable and had to be evaluated by indirect methods. A direct measurement of these equilibrium constants was considered desirable, both for their intrinsic value in describing the system as well as to substantiate some of the assumptions made in the theoretical approach.

Lineweaver and Burk[6] have modified and extended the original method of Michaelis and Menten[7] for the determination of dissociation constants of enzyme complexes and have derived convenient expressions for the evaluation of these constants. These equations have been applied by Wyss[3] to the inhibition of bacterial growth by sulfanilamide, but no attempt was made to evaluate the enzyme–drug dissociation constant. Dorfman and Koser,[4] on the other hand, have calculated equilibrium constants, but only for nicotinamide-stimulated respiration, and not for the growth-enzyme system associated with *p*-aminobenzoic acid. Data are presented in this paper which allow one to calculate the dissociation constants of the enzyme–drug complexes of sulf-

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[1] At present, Lieutenant, Medical Corps, U. S. Army.

[2] Woods, *Brit. J. Exp. Path.*, **21**, 74 (1940); Kohn and Harris, *J. Pharmacol.*, **73**, 343, 383 (1941); Jensen and Schmith, *Z. Immunitäts*, **102**, 261 (1942); *C. A.*, **38**, 3308 (1944); Sevag, Shelburne and Mudd, *J. Gen. Physiol.*, **25**, 805 (1942).

[3] Wyss, *Proc. Soc. Exp. Biol. Med.*, **48**, 122 (1941).

[4] Dorfman and Koser, *J. Infectious Diseases*, **71**, 241 (1942). This article lists many other pertinent references.

[5] Klotz, THIS JOURNAL, **66**, 459 (1944).

[6] Lineweaver and Burk, *ibid.*, **56**, 658 (1934).

[7] Michaelis and Menten, *Biochem. Z.*, **49**, 1333 (1913).