ner, Scheib and Svirbely[15] and the freezing point determinations of Washburn and Reade[16] indicate that the system benzene–diphenyl approximates fairly closely to the ideal over a large range of temperature. Furthermore, determinations of the lowering of the freezing point of benzene by benzyl benzoate made by Kendall and Booge[17] indicate that the system benzene–benzyl benzoate remains approximately ideal at considerably lower temperatures than those of the present measurements.

The system ethyl acetate–benzyl benzoate shows small but definite positive deviations from Raoult's law which persist substantially unchanged over a considerable temperature range. Two factors appear to be of importance in this case. In the first place contacts will be largely between the alkyl groups of the ethyl acetate and the phenyl groups of the benzyl benzoate. It is probable that the fields of these would be dissimilar as the solubility[14] of diphenyl in heptane deviates greatly from the ideal. Second, the shielding of the polar ester group in ethyl acetate is less complete than in benzyl benzoate. It is probable that this group accounts for an appreciable portion of the attractive forces between ethyl acetate molecules themselves. When these are surrounded in part by benzyl benzoate molecules it would seem probable that the separation between the polar ester groups in the two molecules of unlike size would be greater and their mutual attractions smaller. As a consequence the ethyl acetate molecules would show a higher escaping tendency.

If this analysis of the situation in these systems is correct it would indicate that differences in the volume of the components of a system are of secondary importance as determining its deviation from Raoult's law in comparison with differences in the effective molecular fields. The effective fields will be those of the component atoms or groups in the molecules which are most frequently in contact.

Summary

The total vapor pressures of the systems benzene–diphenyl, benzene–benzyl benzoate and ethyl acetate–benzyl benzoate have been determined from 50 to 95° over limited ranges of concentration. The bearing of these measurements on the validity of Raoult's law as applied to these systems is discussed. The benzene–diphenyl and benzene–benzyl benzoate systems follow Raoult's law within the limits of the experimental error. The ethyl acetate–benzyl benzoate system shows deviations several times larger than the experimental error, indicating a slight, but real, positive deviation from Raoult's law.

DURHAM, N. C. RECEIVED MARCH 31, 1938

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(15) Warner, Scheib and Svirbely, *J. Chem. Phys.*, **2**, 591 (1934).

(16) Wasbburn and Reade, *Proc. Nat. Acad. Sci.*, **1**, 191 (1915).

(17) Kendall and Booge, THIS JOURNAL, **38**, 1712 (1916).

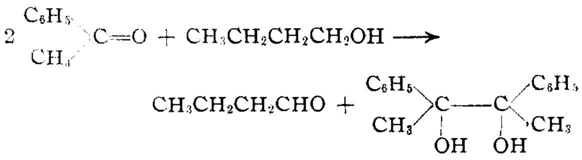
[CONTRIBUTION FROM THE DANIEL SIEFF RESEARCH INSTITUTE]

Photochemical Interaction between Ketones and Alcohols

BY CH. WEIZMANN, ERNST BERGMANN AND YEHUDA HIRSHBERG

Ciamician and Silber[1] were the first ones to observe that ketones and (primary or secondary) alcohols, under the influence of light, may undergo a process of mutual oxidation and reduction. But although the amount of available experimental material is not small,[2] the elementary photochemical processes, apparently, have not yet been elucidated. In connection with other experiments which will be referred to later on, we have started an investigation of the questions concerned, primarily of the reaction products in some typical cases

Acetophenone and butanol on irradiation with the mercury arc give the pinacol of the former substance, butanol being dehydrogenated to form butyraldehyde according to the scheme



$$2\,(C_6H_5)(CH_3)C{=}O + CH_3CH_2CH_2CH_2OH \longrightarrow CH_3CH_2CH_2CHO + (C_6H_5)(CH_3)C(OH){-}C(OH)(CH_3)(C_6H_5)$$

Fifty per cent. of the theoretical amount of the aldehyde could be traced by titration according

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(1) (a) Ciamician and Silber, *Ber.*, **33**, 2911 (1900); (b) **34**, 1537 (1901); (c) **36**, 1575 (1903); (d) **43**, 945 (1910); (e) **44**, 1280 (1911); (f) **45**, 1540 (1912); (g) **47**, 1806 (1914); (h) **48**, 190 (1915).

(2) (a) Baeyer and Co., German Patent 297,993 (1921); (b) Cohen, *Rec. trav. chim.*, **39**, 243 (1921); (c) Paternò, Chieffi and Perret, *Gazz. chim. ital.*, **44**, I, 151 (1914).

to Wagner.[3] It is interesting to note that both the diastereomerides of the pinacol, but to quite a different extent, are contained in surprisingly large yields in the solid product which is formed; their separation could be effected by fractional crystallization from light petroleum (b. p. 80–100°).

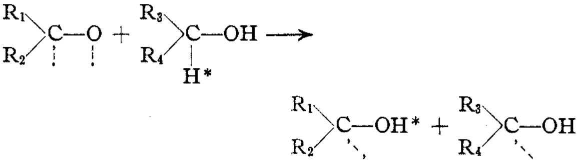
Acetophenone and cyclohexanol on irradiation gave the diastereoisomerides of acetophenonepinacol and cyclohexanone. Here, the cyclohexanone was determined in the mixture with excess cyclohexanol by Girard's reagent (trimethylammonium chloride acethydrazide)[4] which converts the ketone into a water-soluble, easily decomposable derivative. The amount of cyclohexanone found was as high as 80% of the theoretical yield.

In an analogous way acetophenone reacts with phenylmethylcarbinol to give the same mixture of pinacols. All these interactions parallel the known reaction between acetophenone and ethyl or isopropyl alcohol. In the same way, pinacol has been obtained from acetone and isopropyl alcohol.[2a]

The system cyclohexanone–cyclohexanol gives cyclohexanone pinacol only in poor yield. This substance[5] could not be obtained in an analytically pure state, but its identity has been proved by conversion into dicyclohexenyl.[6] Obviously, one cannot yet decide whether the above system is relatively inert or a complete exchange of two hydrogen atoms takes place, which would give again the original mixture of reactants.

Finally, the pair acetone–butanol was irradiated. Three substances have been isolated in pure state: two isomeric forms of *sym*-dipropylglycol, $C_3H_7CHOHCHOHC_3H_7$ (one liquid, one solid) as half-oxidation products of butyl alcohol and the trimeric form of butyraldehyde. In addition butyraldehyde and isopropanol were found in the first fractions of the reaction product. The question as to whether part of the acetone was converted into pinacol could not be decided, since no pure fraction consistent with its properties has been isolated. The balance of the concerned oxidation and reduction processes gave satisfactory results.

The characteristic feature of all these reactions is the reducing power of hydrogen H* on the carbon atom of a (primary or secondary) alcoholic group, $-CH^*OH$. That the hydrogen of the hydroxyl group itself is relatively insignificant may be concluded from the fact that ethers behave similarly toward ketones.[7] The primary step, however, in all these cases is most probably not the loosening of this hydrogen atom. This may be deduced from the following consideration. If irradiation would cause the loosening or dissociation of the C–H* bond—which is even for thermodynamical reasons highly improbable—then irradiation of an optically active secondary carbinol like phenylmethylcarbinol should lead to racemization, free radicals of the $C_6H_5CHCH_3$ type being configurationally unstable.[8] There is no change in rotation to be observed on irradiation of the optically active carbinol, but if a mixture of acetophenone and the carbinol is irradiated, the mixture of the epimeric acetophenone pinacols is found inactive, although one of them could have been formed in active state.[9] We therefore come to the conclusion that the first step in the irradiation of the above-discussed mixtures is the activation of the carbonyl compound, *e. g.*, leading to a diradical form.[10] This form reacts with the carbinol, splitting the C–H* bond and giving two radicals



which subsequently stabilize by symmetrical or unsymmetrical dimerization or by a second oxidation–reduction process. It is not easy to foresee which stabilization reaction will actually occur in a given case; here the relative stability of the intermediate radicals will play an important part.

It may well be that hemiacetal formation which takes place between carbonyl and hydroxyl compounds plays also a certain role in the course of the photocondensation, but it cannot be essential, since, according to the investigations of K. L.

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[3] Wagner, *Biochem. Z.*, **194**, 441 (1928).

[4] Girard and Sandulesco, *Helv. chim. acta*, **19**, 1095 (1936).

[5] Zelinsky, *Ber.*, **34**, 2801 (1901).

[6] De Barry-Barnett and Lawrence, *J. Chem. Soc.*, 1104 (1935).

[7] Ciamician and Silber, *Ber.*, **34**, 1541 (1901); **44**, 1554 (1911); **48**, 194 (1915); Paternò and Chieffi, *Gazz. chim. ital.*, **40**, II, 321 (1911); Bergmann and Fujise, *Ann.*, **483**, 65 (1930).

[8] Pauling and Wheland, *J. Chem. Phys.*, **1**, 362 (1933); Bergmann and Schuchardt, *Ann.*, **487**, 225 (1931).

[9] It is noteworthy that the part of the carbinol recovered unchanged from that experiment shows practically the original rotation, a slight decrease possibly being due to a certain complete hydrogen exchange between the ketone and the secondary alcohol.

[10] For this assumption, compare Bodenstein, *Sitzungsber. Preuss. Akad. Wiss.*, 73 (1931); *Z. physik. Chem.*, **B12**, 151 (1931); Farkas and Hirshberg, This Journal, **59**, 2450 (1937); Hirshberg and Farkas, *ibid.*, **59**, 2453 (1937).

Wolf and Herold,[11] some of our pairs of compounds are unable to form hemiacetals.

The photochemical mobilization of the hydrogen in an alcoholic group is of interest with regard to the mechanism of ergosterol irradiation. At variance with the assumption of Spring[12] that this important reaction involves primarily epimerization at C_3, Windaus and Dimroth[13] were able to demonstrate that the secondary hydroxyl group at C_3 is actually not influenced by irradiation, while in the presence of eosin, which acts as hydrogen "acceptor," the well-known conversion of ergosterol into ergopinacol occurs.[13b,14] This reaction, undoubtedly, is rather complex in nature but here too, the primary step appears to be the loosening of the H* atom in the secondary alcoholic group in the presence of the activated "acceptor" molecule.

Experimental Part

Acetophenone and Butanol.—The irradiation product was fractionated. In the first fraction (b. p. 110–120°) butyraldehyde has been determined, as described above. The main part of this fraction was unchanged butyl alcohol: 0.74 g. was heated with 1.93 g. of *p*-nitrophthalic anhydride and 5 cc. of toluene for twelve hours on the water-bath. The solid product was collected and recrystallized from 20% acetic acid: leaflets, m. p. 146°, which were identified by mixed melting point as butyl hydrogen *p*-nitrophthalate.

The second fraction (b. p. 80–110° at 20 mm.) consisted of acetophenone, the third one (b. p. 205–210° at 25 mm.) was a viscous oil, which crystallized immediately on trituration with light petroleum (b. p. 40–60°). The solid product on recrystallization from light petroleum (b. p. 80–100°) gave first prisms, m. p. 123°, which were identified as acetophenone pinacol[15] by mixed melting point and analysis. The mother liquor was treated with petroleum ether, and the precipitate (m. p. 85–95°) recrystallized from petroleum ether (m. p. 80–100°); diamond-shaped crystals, m. p. 122–123°. This substance was again identified as isomeric acetophenone pinacol[16] by mixed m. p. and analysis.

Cyclohexanone and Cyclohexanol.—After removal of cyclohexanone and cyclohexanol, a viscous residue was obtained, boiling at 130–131° (20 mm.), 90° (0.04 mm.). It was identified by analysis and conversion into dicyclohexenyl.[6]

Anal. Calcd. for $C_{12}H_{22}O_2$: C, 72.7; H, 11.0. Found: C, 72.5, 72.4; H, 10.2, 10.5.

Acetone and Isopropanol.—The pinacol formed distilled at 60–65° (2 mm.) and was identified as its crystalline hydrate, m. p. 50°.[17]

Acetone and Butanol.—The reaction product was divided into five fractions: (a) b. p. 50–70° (760 mm.) acetone. (b) b. p. 78–80° (760 mm.). This fraction contained 29.1% isopropanol, as found after oxidation with chromic acid by Messinger's method for the determination of acetone,[18] which would not be present in this fraction, and 45% butyraldehyde. (c) b. p. 95–120° (760 mm.). This fraction was mainly butyl alcohol, but still contained 2.7% isopropanol. (d) b. p. 110–115° (25 mm.). Liquid *sym*-di-*n*-propyl-glycol. *Anal.* Calcd. for $C_8H_{18}O_2$: C, 65.7; H, 12.3. Found: C, 65.2; H, 12.3. (e) b. p. 140–150° (25 mm.). This fraction immediately separated crystals, which could be isolated by trituration with ice-cold petroleum ether (b. p. 40–60°). From the same solvent leaflets, m. p. 121°, with some sublimation, were obtained. Analysis showed that this substance was a solid isomer of the foregoing one. *Anal.* Calcd. for $C_8H_{18}O_2$: C, 65.7; H, 12.3. Found: C, 65.0; H, 12.3.

The mother liquor of the crystals was again distilled *in vacuo*, the first portion being rejected as containing some more of the above crystals. The fraction b. p. 95° (0.3 mm.), $n^{11.5}D$ 1.4640, was analytically identified as *p*-butyraldehyde. *Anal.* Calcd. for $(C_4H_8O)_3$: C, 66.7; H, 11.1. Found: C, 66.4; H, 11.1.

Experiments with Optically Active Phenylmethylcarbinol.—An equimolecular mixture of phenylmethylcarbinol ($[\alpha]D$ +23.6°) and acetophenone (2 g. of each) was irradiated for about two hundred hours with a small mercury arc lamp and the mixture gradually turned yellow. Fractionation gave a mixture of the unchanged reactants (1.2 g.; b. p. 40–60° at 0.04 mm.) and a residue which crystallized on trituration with light petroleum (2.57 g.) and could be identified by the method of fractional crystallization indicated above[1] as mixture of the two acetophenone pinacols. While this mixture was optically inactive, the rotation of the liquid fraction amounted to αD 9.05°. Under the assumption that this liquid product was still an equimolecular mixture of acetophenone and phenylmethylcarbinol, the specific rotation of the latter substance would be $[\alpha]D$ +18.1°.

Irradiation of pure phenylmethylcarbinol for about two hundred hours failed to produce an appreciable decrease in rotation (19.2 ⟶ 18.6°), only a slight yellowish discoloration taking place.

Summary

The irradiation of the following pairs of compounds has been studied: acetophenone–butanol, acetophenone–cyclohexanol, acetophenone–phenylmethylcarbinol, cyclohexanone–cyclohexanol, acetone–butanol.

Optically active phenylmethylcarbinol is not racemized by ultraviolet light, but in the presence of acetophenone an optically inactive product is formed.

An activated ketone molecule reacts with the

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(11) K. L. Wolf and Herold, *Z. physik. Chem.*, **B5**, 124 (1929); **12**, 165, 194 (1931).

(12) Spring, *Chemistry & Industry*, **55**, **837** (1936).

(13) (a) Windaus and Dimroth, *Ber.*, **70**, 376 (1937). (b) Compare Dimroth, *ibid.*, **69**, 1123 (1936).

(14) Dehydroergosterol, lumisterol and dehydrocholesterol behave analogously. Windaus and Linsert, *Ann.*, **465**, 148 (1928); Urushibara and Ando, *Chem. Zentralbl.*, **109**, I, 2982 (1937).

(15) Beilstein, Vol. VI, p. 1011; Supplementary Vol. VI, p. 498.

(16) Ramart-Lucas and Salmon-Legagneur, *Bull. soc. chim.*, [4] **45**, 718 (1929).

(17) Beilstein, Volume I, Berlin, 1918, p. 488.

(18) Messinger, *Ber.*, **21**, 3368 (1888).

C–H bond of an alcoholic group, giving two configurationally unstable radicals. They stabilize by disproportionation or dimerization.

The significance of the results for the photochemical behavior of ergosterol is discussed.

REHOVOTH, PALESTINE RECEIVED MARCH 12, 1938

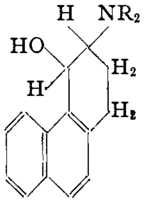
[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

Studies in the Phenanthrene Series. XVII. Amino Alcohols Derived from 9-Hydroxy-1,2,3,4-tetrahydrophenanthrene[1]

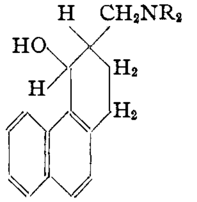
BY ALFRED BURGER

Some of the amino alcohols of types I and II derived from 1,2,3,4-tetrahydrophenanthrene[2] have been found to possess relatively favorable pharmacological properties.[3]

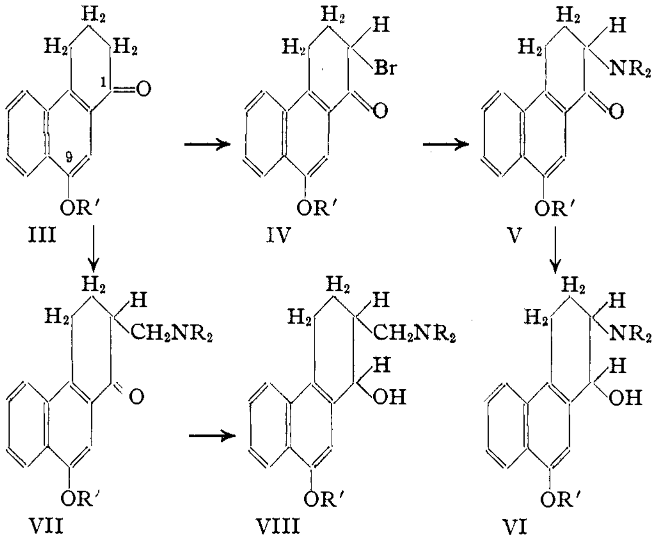
The 1,2,3,4-tetrahydroisoquinolino derivative of type I, for example, approaches codeine and pseudocodeine in analgesic action. The corresponding derivative of type II is weaker in analgesic effect, but does not exhibit any convulsant and emetic action. In morphine, the phenolic hydroxyl group is undoubtedly an important factor influencing the high analgesic effect of this alkaloid,[4] and therefore it appeared desirable to synthesize amino alcohols of types I and II carrying a phenolic hydroxyl group in one of the aromatic nuclei. The synthesis of the first group of amino alcohols with these structural features was planned as shown.



I



II



The starting materials for these syntheses, III ($R' = H, CH_3, CH_3CO$) are relatively easily accessible.[5]

The preparation of IV ($R' = H, CH_3$) did not offer any difficulties; only monobromo compounds were obtained. Attempts to exchange the bromine atom in IV ($R' = H$) with secondary amines were without success. With $R' = CH_3$, however, the reaction resulted in the expected amino ketones in yields that varied according to the secondary amine used. With piperidine the corresponding amino ketone V ($R_2 = C_5H_{10}$) was obtained in a yield of about 60%, while 1-hydroxy-9-methoxyphenanthrene appeared as a by-product. When diethylamine was used the amino ketone was formed in yields of about 30%; in this instance the formation of 1-hydroxy-9-methoxyphenanthrene by loss of hydrogen bromide and subsequent aromatization seems to be a main reaction, perhaps accompanied by the simultaneous formation of III.[6]

Unfortunately, catalytic hydrogenation under various experimental conditions did not furnish the corresponding amino alcohols VI, since the hydrogen absorption would not stop at this stage.

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[1] The work reported in this paper is part of a unification of effort by a number of agencies having responsibility for the solution of the problem of drug addiction. The organizations taking part are: The Rockefeller Foundation, the National Research Council, the U. S. Public Health Service, the U. S. Bureau of Narcotics, the University of Virginia and the University of Michigan.

[2] (a) Mosettig and Burger, THIS JOURNAL, **57**, 2189 (1935); (b) Burger and Mosettig, *ibid.*, **58**, 1570 (1936).

[3] Mosettig, Eddy and co-workers, "Attempts to Synthesize Substances with Central Narcotic and, in Particular, Analgesic Action," Supplement to the U. S. Public Health Reports, in press.

[4] Edmunds, Eddy and Small, *J. Am. Med. Assoc.*, **103** 1417 (1934).

[5] Kon and Ruzicka, *J. Chem. Soc.*, 187 (1936).

[6] Compare footnotes 5 and 6 of Ref. 2a.