tatively for the following hydrocarbons: methane, butene, butadiene, propylene, ethylene, higher hydrocarbons. The results lead to an interpretation of the mechanism of the decompositions.

(6) *Iso*propylethylene is stable toward diluted sulfuric acid but can be made to rearrange to trimethylethylene to a slight extent by the action of acid of such a concentration that polymerization does not take place appreciably.

(7) The boiling point, melting point, densities at various temperatures and index of refraction of trimethylethylene, pentene-2, *iso*propylethylene and tertiary amyl alcohol were redetermined with carefully purified material.

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[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, No. 18]

THE REACTIVITY OF ATOMS AND GROUPS IN ORGANIC COMPOUNDS. II. SECOND CONTRIBUTION ON THE RELATIVE REACTIVITIES OF THE HYDROXYL-HYDROGEN ATOMS IN CERTAIN ALCOHOLS

BY JAMES F. NORRIS AND FRANK CORTESE[1]

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In a former paper[2] from this Laboratory the results were given of the study of the rates at which certain alcohols react with *p*-nitrobenzoyl chloride, and it was shown that the rates, which varied greatly, could be taken as a measure of the relative reactivities of the hydroxyl-hydrogen atoms in these alcohols. As certain striking relationships were indicated from the results obtained with the eleven alcohols investigated, the work was continued and eighteen additional compounds were studied. The alcohols were so selected that the results would show the influence of structure on the reactivity of the hydroxyl-hydrogen atom, especially as this reactivity is affected by lengthening of the carbon chain and by the position of a side chain with reference to the hydroxyl group.

Sufficient data have been obtained from the investigation of these twenty-nine alcohols to warrant definite conclusions. The results are in accord with the well-known qualitative differences in chemical behavior between the several types of alcohols; but they have, in addition, a quantitative significance, and throw some light on the change in the atomic bonding between oxygen and hydrogen produced by changes in the structure of the radical with which the hydroxyl group is combined.

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[1] From the thesis of Frank Cortese, Grasselli Fellow in Chemistry, 1925–1926, presented in partial fulfilment of the requirement for the degree of Doctor of Philosophy, 1926.

[2] Norris and Ashdown, THIS JOURNAL, **47**, 837 (1925).

The effect of the substitution of a hydrogen atom by a methyl radical in a series of normal alcohols is noteworthy. For example, such replacement of an α-hydrogen atom in ethyl, propyl, butyl and amyl alcohols, respectively, caused a decrease in the reactivity of hydroxyl-hydrogen atom of the same order of magnitude in the four cases. Similar results were obtained when the methyl radical was in the beta, gamma and delta positions, although the percentage effect differed in the various positions.

Objections have been raised to the use of reaction velocities in the comparison of the chemical behavior of compounds. These objections are based upon the fact that the rate at which a reaction proceeds is markedly affected by conditions, some of which are not under control, such as, for example, the presence of unrecognized catalytic agents. The relationships indicated above were drawn from the results of the study of a large number of independent reactions and could not have been obtained if unrecognized factors that influenced the results were involved. An important deduction from the work is, therefore, that velocity constants when determined under fixed conditions can be used in the quantitative interpretation of chemical behavior.

All synthetic methods used in organic chemistry are based on the reactivities of the atoms involved in the changes which result in the desired syntheses. Quantitative measurements of these reactivities are largely lacking and any additional knowledge in this field will advance the science from the point of view of synthesis, and will be useful in enlarging our knowledge of bonding between atoms. The work described in this paper will make possible a more intelligent use of alcohols in syntheses involving the hydroxyl-hydrogen atoms of these compounds, and will be helpful in interpreting the effect of structure on the lability of the hydrogen-oxygen bond.

The methods used in the determination of the velocity constants of the alcohols were identical with those reported in the earlier communication.[2] The constant for *n*-butyl alcohol was redetermined in order to find out if the conditions of experimentation were identical with those used in the earlier investigation. The results checked the value previously obtained within the limit of accuracy of the work. In order to facilitate comparisons the constants of all the alcohols studied up to the present are given in Table I. The alcohols reported on in this paper are listed in Table II.

The study of the results given in Table I leads to the following conclusions.

(1) The lengthening of the carbon chain in normal primary alcohols results in a decrease in the reactivity of the hydroxyl-hydrogen in the first three members of the series; the constant increases progressively with the next three members and then decreases again.

TABLE I

SECOND ORDER VELOCITY CONSTANTS FOR THE REACTIONS BETWEEN ALCOHOLS AND *p*-NITROBENZOYL CHLORIDE

Temperature, 25°. Concentration of each reactant 1 mole in 1000 g. of ether taken as unity. Time in hours.

Normal primary alcohols	*k*	Secondary alcohols	*k*
Methanol	0.184	Propanol-2	0.010
Ethanol	.085	Butanol-2	.0074
Propanol-1	.066	Pentanol-2	.0059
Butanol-1	.074	Hexanol-2	.0065
Pentanol-1	.079	Pentanol-3	.0036
Hexanol-1	.085	Heptanol-4	.0027
Heptanol-1	.069	Tertiary alcohols	
Primary alcohols with a branched chain		Methyl-2-propanol-2	0.0027
Methyl-2-propanol-1	0.031	Methyl-2-butanol-2	.0025
Methyl-2-butanol-1	.036	Methyl-3-pentanol-3	.0014
Methyl-2-pentanol-1	.034	Aromatic alcohols	
Methyl-3-butanol-1	.073	Benzyl	0.017
Methyl-3-pentanol-1	.077	β-Phenylethyl	.040
Methyl-3-hexanol-1	.075	γ-Phenylpropyl	.020
Methyl-4-pentanol-1	.068	α-Phenylethyl	.00052
		α-Phenylpropyl	.00050
		α-Phenylbutyl	.00050

In the case of the secondary alcohols with the hydroxyl group in position 2 the constant decreases with the first three members of the series and then increases.

(2) The introduction of a methyl radical as a side chain in primary alcohols has a marked effect on the constant. This effect is greatest in position 1; it decreases as we pass to positions 2 and 3 and begins to increase in position 4. The alternations in this effect are similar to, though greater than, those brought about by lengthening the chain—the periodicity is in cycles of 3.

(3) The percentage reduction in the constant brought about by the replacement of a hydrogen atom in position 1 by a methyl radical is of the same order of magnitude whatever the length of the chain. The constant of *iso*propyl alcohol is 11.7% of the constant of ethyl alcohol; that of secondary butyl alcohol is 11.2% of the constant of *n*-propyl alcohol; the constant of pentanol-2 is 8% that of *n*-butyl alcohol; and the constant of hexanol-2 is 8.2% that of amyl alcohol.

(4) When a methyl radical replaces a hydrogen atom in position 2 its effect on the constant is much less. The constant of *iso*butyl alcohol is 46.9% of that of *n*-propyl alcohol; the constant of methyl-2-butanol-1 is 48.6% that of *n*-butyl alcohol; and the constant of methyl-2-pentanol-1 is 44.3% that of *n*-amyl alcohol.

(5) When a methyl radical replaces a hydrogen atom in position 3 the effect almost disappears. The constant of *iso*-amyl alcohol is 98%

that of *n*-butyl alcohol; and the constant of methyl-3-pentanol-1 is 97% that of *n*-amyl alcohol.

(6) When a methyl radical replaces a hydrogen atom in position 4 the effect now begins to increase. The constant of methyl-4-pentanol-1 is 86% that of *n*-amyl alcohol.

(7) The relationships between the constants of primary and secondary alcohols containing the same number of carbon atoms are as follows. The constant of the secondary alcohols containing 3, 4, 5 and 6 carbon atoms are, respectively, 15.8, 10.0, 7.5 and 7.6% those of the corresponding primary alcohols. In this case the effect increases with increasing molecular weight in the case of the first three members of the series.

(8) The relationships between the constants of tertiary and primary alcohols containing four and five carbon atoms are, respectively, 3.7 and 3.2%.

(9) The effect of the position of the hydroxyl group in a straight chain of carbon atoms is great. The constants of pentanol-1, pentanol-2 and pentanol-3 are in the ratio 1 to 0.075 to 0.045.

(10) In the case of the aromatic alcohols there is an alternation in the value of the constant as the phenyl radical is removed from the hydroxyl group. The depression of reactivity produced by the replacement of a hydrogen atom by phenyl is so great that the secondary alcohols containing this group in position 1 had the smallest constants measured.

The striking relationships between the constants of alcohols of similar structure indicate clearly that the results are significant in regard to the effect of the position of a substituent on the hydrogen bond in alcohols. It is hoped to interpret later the results in terms of the electronic theory of the bonding of atoms in organic compounds. Further work must be done, however, before this is attempted. The relationships indicated hold when the hydroxyl-hydrogen is replaced by the *p*-nitrobenzoyl radical. It is possible that they may be found to be different when another atom or group replaces this hydrogen atom. The speed with which two molecules interact depends at least in part on the tendency of the atoms eliminated to unite and the tendency of the radicals formed to combine with each other. It is interesting to note in this connection that the velocity constant of *iso*propyl alcohol is 11.7% of that of ethyl alcohol when measured by *p*-nitrobenzoyl chloride as a second order reaction in ethereal solution, and that the velocity constant of *iso*propyl alcohol is 9.4% of that of ethyl alcohol when measured as first order reactions by diphenylchloromethane dissolved in a large excess of the respective alcohols.

Work is now in progress on the study of rates at which alcohols react with sodium and with potassium. As the result of this type of reaction, hydrogen is eliminated and the hydroxyl-hydrogen is replaced by a strongly electropositive metal.

TABLE II
PREPARATION AND PROPERTIES OF THE ALCOHOLS USED[a]

Alcohol	Substances used in preparation	Crude alcohol % yield	Crude alcohol B. p. (°C. at 760 mm.)	G. of alcohol fractionated	G. of purified alcohol from final fractionation	B. p. (°C. at 760 mm.) of purified alcohol; b. p. in literature and references ( )	Density, 25°/4°; density in literature and references ( )	N_D^{25}; index in literature and references ( )
Pentanol-1	Butyl bromide							
	Trioxymethylene	47	134–144	300	52	138.0–138.1	0.8110	1.4077
						137.8–137.9(2)	.8106(2)	1.4114(15°)(3)
Hexanol-1	Butyl bromide			191	28	157.6–157.7	.8153	1.4162
	Ethylene oxide	68	150–160			157.3–157.6(2)	.8154(4)	
							.8129(2)	
Heptanol-1	From Eastman			100	24	175.8–176.2	.8187	1.4224
	Kodak Company		172.8–175.8			175.8(2)	.8185(5)	1.4222(5)
Methyl-2-butanol-1	Sec. butyl bromide			295	64	129.4	.8152	1.4087
	Trioxymethylene	59	124–135			129.4(11)	.8155(11)	
Methyl-2-pentanol-1				142	16	147.9–148.1	.8192	1.4180
	Sec. amyl bromide					147.9(16)	.8191(15)	1.4182 (at 19°)
	Trioxymethylene	70	143–150			147.8(15)		(17)
Methyl-3-butanol-1	*Iso*propyl bromide			129	26	132.0–132.1	.8044	1.4046
	Ethylene oxide	30	125–138			131.9(6)	d_0^0 .8238(6)	
Methyl-3-pentanol-1	Sec. butyl bromide			74	12	153.7–154.1	.8205	1.4177
	Ethylene oxide	36	149–157			154.1(18)	.8226(19)	
Methyl-3-hexanol-1	Sec. amyl bromide			82	8	171.7–172.7	.8245	1.4246
	Ethylene oxide	36	150–173			173(21)	d_4^{20} .8239(21)	1.4219(20°)(21)
Methyl-4-pentanol-1	*Iso*butyl bromide			155	12	151.8–152.8	.8110	1.4134
	Ethylene oxide	45	142–157			153(12)	d_4^{20} .8156(12)	1.5152(20°)(12)
Pentanol-2	From Standard			300	40	119.16–119.26	.8068	1.4048
	Oil Co.	35	118–120			119.2(10)	d_4^{20} .8088(10)	1.4043(9)
						119.5(9)	.8048(9)	

TABLE II (*Concluded*)

Alcohol	Substances used in preparation	Crude alcohol % yield	Crude alcohol B. p. (°C. at 760 mm.)	G. of alcohol fractionated	G. of purified alcohol from final fractionation	B. p. (°C. at 760 mm.) of purified alcohol; b. p. in literature and references ( )	Density, 25°/4°; density in literature and references ( )	N_D^{25}; index in literature and references ( )
Hexanol-2	Butyl bromide			90	8	140.0–140.4	0.8044	1.4136
	Acetaldehyde	28	133–142			140.1(13)	d_4^0 .8287(14)	1.4140(18°)(14)
							d_4^2 .8141(14)	
Pentanol-3	Ethyl bromide			92	24	115.8–116.0	.8154	1.4079
	Ethyl formate	52	112–118			115.6(9)	.8154(9)	1.4077(9)
Heptanol-4	Propyl bromide			150	32	155.9–156.0	.8156	1.4184
	Ethyl formate	64	150–158			155.4(9)	.8130(9)	1.4178(9)
Methyl-2-butanol-2	From A. D. Little, Inc. Prepared by Raymond Reuter(7)				600	101.7–101.8(7)	.80475(7)	1.4024
						101.5–102(8)	.80452(8)	
Methyl-3-pentanol-3	Ethyl bromide			116	28	122.8–123.0	.8233	1.4166
	Ethyl acetate	57	117–123			122.4–123.4(20)	.8194(20)	
α-Phenylethyl				57	16	94–95(12 mm.)	1.0119	1.5244
	Acetophenone	36	94–95(12 mm.)			94(12 mm.)(22)	d_4^{15} 1.008(23)	1.526(15°)(23)
α-Phenylpropyl	Ethyl bromide			209	100	106–108(15 mm.)	0.9915	1.5124
	Benzaldehyde	77	100–111(15 mm.)			63.2–63.4(0.5 mm.)	.9925(25)	1.5204
						108–110(15 mm.)(24)		
α-Phenylbutyl	Propyl bromide			195	64	78.0–78.2(0.5 mm.)	.9697	1.5191(13.7°)(26)
	Benzaldehyde	65	117–125(15 mm.)			113–115(10 mm.)(26)	d_4^{13} .9861(26)	

[a] Note: The values taken from the literature were the best ones found, the methods of preparation and purification always being taken as the criteria of purity. The figures in parentheses refer to the citations at the end of the table.

1. Brunel, Crenshaw and Tobin, This Journal, **43**, 574 (1921).
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3. Kaufmann and Adams, This Journal, **45**, 3029–44 (1923).
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5. Falk, This Journal, **31**, 93 (1909); extrapolated value.
6. Balbiano, *Gazz. chim. ital.*, **6**, 235 (1876); corrected value.
7. Norris and Reuter, This Journal, **49**, 2624 (1927).
8. Perkin, *J. prakt. Chem.*, [2] **31**, 510 (1885); d = recalculated value.
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10. Clough and Johns, *J. Ind. Eng. Chem.*, **15**, 1030 (1923).
11. Lieben and Zeisel, *Monatsh.*, **7**, 60 (1886); extrapolated and calculated value.
12. W. Longinow, *Chem. Zentr.*, I, 1054 (1916).
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15. Lieben and Zeisel, *Monatsh.*, **4**, 31 (1883); extrapolated and recalculated values.
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18. Van Romburgh, *Rec. trav. chim.*, **5**, 219 (1886); extrapolated value.
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21. Dewal and Weckering, *Bull. soc. chim. Belg.*, **33**, 495–504 (1924).
22. Klages and Keil, *Ber.*, **36**, 1632 (1903).
23. Vavon, *Ann. chim.* [9] **1**, 184 (1914).
24. Klages, *Ber.*, **36**, 621 (1903).
25. Wagner, *Ber.*, **17 R**, 317 (1884); extrapolated value.
26. Grignard, *Ann. chim. phys.*, [7] **24**, 466 (1901).

Experimental Details

A large proportion of the alcohols used were prepared by means of the Grignard reaction, according to the methods described in the literature. The amounts synthesized were sufficient to allow of fractionation with a column.

The general procedure of purification adopted for all the alcohols was as follows. The crude material was refluxed for five hours over 20% sodium hydroxide. After distillation and drying with potassium carbonate, it was given a preliminary fractionation, the boiling-point range being narrowed to 2 degrees. The resulting product was refluxed for five hours over anhydrous aluminum amalgam and redistilled. A distillation curve was made and a cut was taken representing the amount boiling within one degree or less. This fraction was redistilled from fresh anhydrous aluminum amalgam, a distillation curve made, and the final pure fraction selected from the curve. It boiled within the limits indicated in Table II. When redistilled in a four-bulb Ladenburg flask with the thermometer totally immersed, it boiled within the range last indicated by the curve.

It was not possible to obtain certain of the alcohols with a boiling range of 0.1°. In order to determine whether the trace of impurity present had an appreciable effect on the velocity constant, the value of the constant was determined for two samples of n-amyl alcohol, one of which boiled at 138.0–138.1° at 760 mm. and the other at 137.5–

138.1° at 760 mm. The average constant in the first case was 0.079 and in the latter 0.076. The difference between the two numbers is about twice the experimental error. It is probable that the small amounts of impurities present which cause the spread in the boiling points of certain of the alcohols used are of such a nature that they have very little effect on the value of the velocity constant.

Table II consists of a summary of the methods of preparation and physical properties of the alcohols reported on in this paper. The numbers in parentheses refer to the numbered references given at the end of Table II (p. 2646).

In Table III the results of the determination of the velocity constants are given. In the determination of the experimental data and in the calculations applied to the latter, the methods used were those explained in detail in the previous paper by Norris and Ashdown.[2] The degree of accuracy of the work can be judged from the duplicate determinations reported. The deviation of any single observation from the mean was of the same order of magnitude as that previously observed—from 2 to 10%.

TABLE III

SECOND ORDER VELOCITY CONSTANTS OF THE REACTIONS BETWEEN CERTAIN ALCOHOLS AND *p*-NITROBENZOYL CHLORIDE[a]

Concentration: 1 mole of alcohol, 1 mole of acyl chloride and 1000 gr. of ether taken as unity. Temperature, 25°. Time expressed in hours.

Alcohol	No. of observations	Time to last observation, hours	% Conversion at last observation	Greatest % deviation of any observation from mean	Constant	Average
Pentanol-1	6	6	30.3	5	0.079	
	6	6	30.5	5	.080	
	8	6	30.2	3	.078	0.079
Hexanol-1	7	7	34.4	5	.084	
	7	7	34.6	2	.085	.085
Heptanol-1	8	7	30.1	9	.068	
	8	7	30.0	9	.069	.069
Methyl-2-butanol-1	8	7	18.9	6	.035	
	10	10	24.3	5	.036	.036
Methyl-2-pentanol-1	9	11	26.1	3	.034	
	9	11	26.4	3	.033	.034
Methyl-3-butanol-1	6	6	25.8	7	.073	
	6	5	25.5	3	.072	.073
Methyl-3-pentanol-1	7	7	33.7	2	.077	
	7	7	33.6	4	.077	.077
Methyl-3-hexanol-1	7	7	32.2	6	.075	
	7	7	32.2	4	.074	.075
Methyl-4-pentanol-1	7	6	27.7	3	.068	
	7	7	30.0	4	.068	.068

TABLE III (*Concluded*)

Alcohol	No. of observations	Time to last observation, hours	% Conversion at last observation	Greatest % deviation of any observation from mean	Constant	Average
Pentanol-2	8	10	5.4	4	.0058	
	8	10	5.4	5	.0059	.0059
Hexanol-2	7	11	6.7	4	.0065	
	7	11	6.5	3	.0065	.0065
Pentanol-3	8	11	3.2	2	.0037	
	8	11	3.8	8	.0035	.0036
Heptanol-4	7	8	2.4	4	.0027	
	7	8	2.3	4	.0027	.0027
Methyl-2-butanol-2	6	10	2.6	0	.0025	
	6	10	2.5	4	.0025	.0025
Methyl-3-pentanol-3	7	11	1.5	7	.0014	
	7	11	1.5	0	.0014	.0014
α-Phenylethyl	7	169	7.4	8	.00052	
	7	169	7.5	4	.00052	.00052
α-Phenylpropyl	8	198	8.7	6	.00049	
	8	198	8.5	10	.00050	.00050
α-Phenylbutyl	8	220	10.1	6	.00050	.00050

[a] Note: The extent to which the reactions had proceeded at any time was determined by the titration of the hydrochloric acid produced. The values given above for the per cent. conversion have been corrected for the small amount of hydrochloric acid formed by hydrolysis from the acyl chloride during the titration.

It was found with these alcohols, as was the case with those studied earlier, that the velocity constant decreased slowly in value after a certain percentage of the alcohol had been converted into ester. The values given in Table III are calculated from the results obtained up to the time when the decrease in the constant began. It can be seen from the table that in the case of primary alcohols the reaction fulfilled the requirements of one of the second order up to from 20 to 35% conversion to ester. In the case of secondary alcohols the decrease in the constant began when from 4 to 7% conversion had taken place; and in the case of tertiary alcohols the change occurred at a lower conversion.

It is probable that the reaction may not be one of the second order—that a more complex mechanism is involved—but the results show that at the beginning of the reaction the requirements of the equation for a reaction of this type are fulfilled; and comparisons under these circumstances are justified. It should be noted that the method of calculating second-order velocity constants has been shown in the past to give real constants only when reactions are carried out at very low concentrations—

in certain cases as low as 0.02 normal. Further, constants calculated from results obtained at different concentrations do not agree except when the concentrations used are very small.

It was impossible to determine with a reasonable degree of accuracy the velocity constants of the reactions reported in this paper at lower concentrations than 0.2 *N*. The degree of accuracy of the analytical methods used and the sources of error that could not be eliminated made work at lower concentrations inadvisable.

In order to study the influence of change in concentration in the constants, experiments were carried out with four alcohols with solutions made by dissolving, respectively, 1, 0.5 and 0.2 moles of the alcohols in 1000 g. of ether. The values are given in Table IV.

TABLE IV

EFFECT OF CONCENTRATION ON THE VELOCITY CONSTANT OF THE REACTION BETWEEN ALCOHOLS AND *p*-NITROBENZOYL CHLORIDE DISSOLVED IN ETHER

Alcohol	Moles of each reactant in 1000 g. of ether	*k*
Methyl-2-butanol-1	1.0	0.036
Methyl-2-butanol-1	0.5	.019
Methyl-3-butanol-1	1.0	.073
Methyl-3-butanol-1	0.5	.032
Methyl-3-butanol-1	.2	.011
n-Amyl	1.1	.079
n-Amyl	0.5	.048
n-Amyl	.2	.034
n-Hexyl	1	.085
n-Hexyl	0.5	.054
n-Hexyl	.2	.035

The constants tabulated show in all cases that the values decrease rapidly with decreasing concentration. It is important to note, however, that the order in which the alcohols stand, as measured by the reactivity of their hydroxyl-hydrogen atoms, is the same irrespective of the concentration at which they are compared. The earlier results with methyl and ethyl alcohols led to the same conclusion.

The cause of the progressive change in velocity constant is being studied with the hope of elucidating the mechanism of the reactions involved. It is possible that the reactions are reversible or that the ester and hydrochloric acid formed react. If either is the case, the use of the usual expression for calculating a second-order velocity constant is warranted only in the early stages of the reaction before the secondary reaction becomes significant. The constants given are based on this assumption.

Summary

1. The second order velocity constants for the reaction between *p*-nitrobenzoyl chloride and the following alcohols have been determined:

pentanol-1, hexanol-1, heptanol-1, methyl-2-butanol-1, methyl-2-pentanol-1, methyl-3-butanol-1, methyl-3-pentanol-1, methyl-3-hexanol-1, methyl-4-pentanol-1, pentanol-2, hexanol-2, pentanol-3, heptanol-4, methyl-2-butanol-2, methyl-3-pentanol-3, α-phenylethyl, α-phenylpropyl and α-phenylbutyl alcohols.

2. The results obtained, together with those from an earlier investigation of the lower fatty alcohols, make possible definite conclusions as to the effect of structure on the reactivity of the hydroxyl-hydrogen atoms of alcohols.

CAMBRIDGE, MASSACHUSETTS

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY
No. 554]

RESEARCHES ON QUINAZOLINES. XXXVIII. THE SYNTHESIS OF SOME NEW ANALOGS OF CINCHOPHEN AND INTERMEDIATE PRODUCTS

BY MARSTON TAYLOR BOGERT AND EUGENE MILLER MCCOLM[1]

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Our knowledge of the pharmacodynamics of the quinazoline group is scattering, fragmentary and meager. It, therefore, seems to us worth while to endeavor to contribute something to this field, not only with the object of throwing additional light upon the connection between chemical constitution and physiological effects, but also in the hope of discovering new compounds of therapeutic value. In this undertaking we have been so fortunate as to enlist the valuable coöperation of two distinguished pharmacologists, Professors Arthur D. Hirschfelder, of the University of Minnesota, and Elbert W. Rockwood, of the State University of Iowa, whose investigations will be published in appropriate journals.

The syntheses recorded in this paper were for the purpose of obtaining quinazoline derivatives of cinchophen (atophan) type, carrying a carboxyl group in Position 4 and hydroxylated phenyls in Position 2, since the preliminary pharmacological examination of the di-ammonium salt of 2-phenylquinazoline-4,2′-dicarboxylic acid, synthesized by Bogert and Nabenhauer,[2] had given results which looked both interesting and promising.

From these carboxylic acids, ethyl esters also were prepared, giving compounds analogous to acitrin; while the 2-hydroxyphenyl-4-carboxylic acids are intermediate between our 4,2′-dicarboxylic acid and the well-known hexophan of the cinchophen series.

These 2-hydroxyphenylquinazolines were synthesized because Kalle and

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[1] This research was made possible by a generous grant from the Sigma Xi Foundation, for whose assistance we are most grateful.—M. T. B. and E. M. McC.

[2] Bogert and Nabenhauer, THIS JOURNAL, **46**, 1702 (1924).