A STUDY OF THE RATE OF ENOLIZATION BY THE POLARISCOPIC METHOD

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It is a well-known fact that optically active ketones, esters and acids are racemized by alkaline reagents only if the alpha carbon atom is the center of the asymmetry and carries a hydrogen atom. The generally accepted explanation of this phenomenon is the formation of an inactive enol in very small quantities which then reverts to the optically inactive keto form. In particular the investigation of McKenzie[1] using ketones, esters and amides have provided us with numerous examples in support of this theory. Dakin[2] has shown that an hydantoin cannot be racemized unless there is a hydrogen atom on the asymmetric alpha carbon atom; the same is true of alpha amino acids.[3] The evidence is so overwhelming that there seems to be no escape from the conclusion that the phenomenon of racemization by alkaline reagents occurs only if the asymmetric carbon atom carries a hydrogen atom capable of enolization. If this is the case the rate of racemization may be considered as the rate of enolization and by the use of optically active substances a very convenient method is available for studying the latter process. It should be noted that the rate of enolization cannot be faster than the rate of racemization (whatever mechanism is assumed) since the enol must be an inactive compound because of its structure.

Before proceeding with the study of the rate of enolization of a series of ketones and esters by the polariscopic method, we decided to test once again the possibility of racemizing a ketone which had no hydrogen in the alpha position. In particular we wished to try more vigorous conditions than those we knew to be effective in causing rapid racemization of ketones having an alpha hydrogen. We therefore prepared d-campholyl phenyl ketone,[4]

$$C_6H_5COC \underset{\underset{CH_3}{|}}{\overset{\overset{CH_2-----CH_2}{\diagup}}{\diagdown}} \underset{C(CH_3)_2-CH(CH_3)}{\overset{|}{}} \quad \text{and } d\text{-methylphenylbutylacetophenone.} \quad \text{No}$$
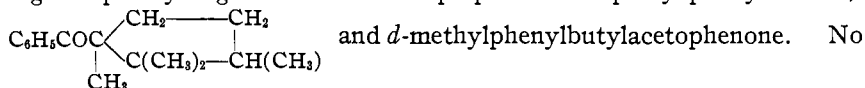
change of rotation took place when these compounds were dissolved in solutions of 1.3 M sodium butylate in butyl alcohol and allowed to stand for a week, or even when heated for three hours at 100° with a dilute solution (0.017 M) of the butylate (higher concentrations of catalyst caused so much discoloration at 100° that no measurements could be made). The
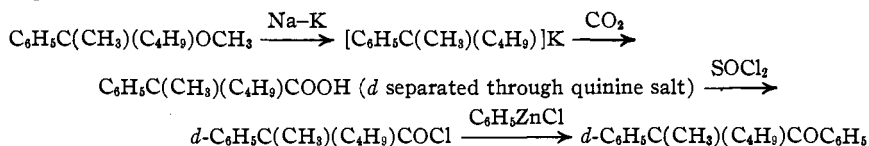
[1] McKenzie and Smith, *J. Chem. Soc.*, 121, 1348 (1922); McKenzie, Martin and Rule, *ibid.*, 105, 1585 (1914); McKenzie and Dennler, *Ber.*, 60, 222 (1927), and other papers. See also Wren, *J. Chem. Soc.*, 113, 210 (1918).

[2] Dakin, *Am. Chem. J.*, 44, 48 (1910).

[3] E. Fischer, *Ann.*, 406, 1 (1914).

[4] Rupe and Jäggi, *ibid.*, 428, 164 (1922).

d-methylphenylbutylacetophenone, which is new, was made by the following series of reactions

$$C_6H_5C(CH_3)(C_4H_9)OCH_3 \xrightarrow{Na-K} [C_6H_5C(CH_3)(C_4H_9)]K \xrightarrow{CO_2}$$

$$C_6H_5C(CH_3)(C_4H_9)COOH \ (d \text{ separated through quinine salt}) \xrightarrow{SOCl_2}$$

$$d\text{-}C_6H_5C(CH_3)(C_4H_9)COCl \xrightarrow{C_6H_5ZnCl} d\text{-}C_6H_5C(CH_3)(C_4H_9)COC_6H_5$$

The five compounds prepared for the study of their rates of enolization by the polariscopic method were phenylbenzylacetophenone, phenylmethylacetophenone, benzylmethylacetophenone, phenylbenzylacetomesitylene, phenylmethylacetomesitylene and the methyl ester of methylbenzylacetic acid. The ketones were all prepared from the corresponding optically active acids by the action of the aryl zinc halide on the acid chloride. Attempts to prepare optically active phenyltolylacetophenone by the same method failed because complete racemization occurred in the last step in spite of all precautions; this fact deprived us of the most interesting member of our intended series but indicated clearly the increased rate of enolization caused by the presence of two aryl groups on the alpha carbon atom.

Our final experiments with basic catalysts are given in Table I; in addition to these a number of preliminary experiments were carried out which gave essentially the same values but were discarded because the concentration of the catalyst was not sufficiently accurately controlled. The value of k (the monomolecular constant, time expressed in minutes) was determined graphically from a plot of the log of the rotation against the time; the best straight line was run through the points and the reciprocal of its slope multiplied by 2.30. These are the values given in column 5 of Table I. In all the experiments the points fell closely on a line corresponding to a monomolecular reaction; this was found to hold even up to 95% racemization, though in most cases the experiment was continued only to 50–70% conversion. The concentration of catalyst is given in column 3 and the catalytic constant obtained by dividing k by the concn. of catalyst is given in column 6. The initial concentration of optically active material was varied irregularly from 0.007 to 0.05 molar, since the rate was not dependent on this variable.

The constancy of the catalytic constant (Col. 6) within the various sections of Table I is a measure of the validity of the generalization that the rate is proportional to the concentration of the catalyst. This was tested over a ten-fold range in most cases and a twenty-fold range in a few. The proportionality was within the experimental error with sodium butylate, but in the case of sodium methylate an increase as great as 60% in the catalytic constant with a ten-fold increase of concentration occurred in two cases. Aside from these two cases one may conclude that the proportionality holds with the alcoholates within 25%. With piperidine the con-

TABLE I

SUMMARY OF RESULTS

(A) Catalyst, Sodium n-Butylate in n-Butyl Alcohol

Expt.	Substance	Concn. cat.	Temp., °C.	$k \times 10^2$	Catalytic constant	Activation energy in kg. cal.
1	l-Phenylbenzylaceto-	0.00157	22.5	0.246	1.56	14.0 (1, 2)
2	phenone	.00157	37.5	.784		
3		.0157	7.5	.630		14.2 (3, 5)
4		.0157	22.5	2.28	1.45	14.0 (3, 4)
5		.0157	38.0	7.76		14.4 (4, 5)
6	d-Phenylbenzylaceto-	.0157	23.0	0.491	0.31	
7	mesitylene	.0157	38.5	1.93		16.1 (6, 7)
8		.1297	8.0	1.25		
9		.1297	24.5	4.63	0.36	13.1 (8, 9)
10	d-Phenylmethylaceto-	.00129	22.0	0.407	3.16	
11	phenone	.0129	9.0	1.42		
12		.0129	22.5	4.51	3.50	14.2 (11, 12)
13		.0157	8.0	1.34		
14		.0157	22.5	5.10	3.24	15.1 (13, 14)
15	d-Phenylmethylaceto-	.00157	11.0	0.983		12.1 (15, 17)
16	mesitylene	.00157	23.0	2.56	16.3	13.3 (15, 16)
17		.00157	38.0	6.70		12.4 (16, 17)
18		.0157	23.0	28.8	18.3	
19	d-Methylbenzylaceto-	.0157	10.5	0.274		15.9 (19, 21)
20	phenone	.0157	22.5	0.800	0.51	14.9 (19, 20)
21		.0157	38.0	3.20		16.6 (20, 21)
22		.1593	24.5	9.16	0.575	

(B) Catalyst, Sodium Methylate in CH_3OH

Expt.	Substance	Concn. cat.	Temp., °C.	$k \times 10^2$	Catalytic constant	Activation energy in kg. cal.
23	l-Phenylbenzylaceto-	0.0144	23.0	0.601	0.42	16.6 (23, 25)
24	phenone	.0144	33.0	1.53		16.7 (23, 24)
25		.0144	38.0	2.36		16.4 (24, 25)
26		.0160	23.0	0.589	.37	
27		.0726	23.0	3.13	.43	
28		.1602	6.0	1.37		
29		.1602	22.5	7.50	.47	16.8 (28, 29)
32	d-Phenylmethylaceto-	.0144	7.5	0.320		
33	phenone	.0144	23.5	1.56	1.08	16.4 (32, 33)
34		.0160	24.5	1.79	1.12	
35	d-Phenylmethylaceto-	0.00144	7.5	0.238		
36	mesitylene	.00144	22.5	0.685	4.76	11.6 (35, 36)
37		.00144	24.5	0.770	4.68	11.4 (35, 37)
38		.0144	7.5	3.30		
39		.0144	22.5	11.2	7.77	13.4 (38, 39)
40	d-Methylbenzylaceto-	0.0144	25.5	0.181	0.09	
41	phenone	.0726	22.5	0.810	.11	
42		.1453	7.0	.364		
43		.1453	22.5	1.62	.11	16.4 (42, 43)

TABLE I   (*Concluded*)

(C)   Catalyst, Piperidine in Butyl Alcohol

Expt.	Substance	Concn. cat.	Temp., °C.	$k \times 10^2$	Catalytic constant
44	*l*-Phenylbenzyl-	0.963	24.0	0.094	0.97×10^{-3}
45	acetophenone	1.997	25.0	.234	1.18×10^{-3}
46		4.004	25.0	.458	1.14×10^{-3}
47	*d*-Phenylmethyl-	1.977	24.0	.509	2.57×10^{-3}
48	acetophenone	4.004	24.5	.956	2.39×10^{-3}
49	*d*-Phenylmethyl-	0.963	25.5	5.48	
50	acetomesitylene	1.977	24.0	8.46	
51		4.004	23.0	15.70	

(D)   Catalyst, Piperidine in Methyl Alcohol

54	*l*-Phenylbenzyl-	0.992	25.0	0.217	2.18×10^{-3}
55	acetophenone	2.005	23.0	.361	1.80×10^{-3}
56	*d*-Phenylmethyl-	0.992	25.0	.572	5.76×10^{-3}
57	acetophenone	2.005	23.0	.710	3.54×10^{-3}
58	*d*-Phenylmethyl-	0.992	22.5	7.67	7.74×10^{-2}
59	acetomesitylene	2.005	24.0	14.10	7.04×10^{-2}
60	*d*-Methylbenzyl-	0.992	25.0	0.062	6.25×10^{-4}
61	acetophenone	2.005	22.0	0.066	3.02×10^{-4}

centration was varied only four-fold and in most cases only two-fold, the catalytic constants showed divergencies of 20%, in some cases decreasing, in others increasing with concentration of catalyst. In spite of certain irregularities which seem to be greater than the experimental error, there seems to be no doubt but that the racemization (enolization) is a pseudo monomolecular reaction, the real reaction being bimolecular between the substrate and the catalyst, the differential expression being as follows where $C_{cat.}$ is the concentration of catalyst and $k_{cat.}$ the true bimolecular constant which is equal to the monomolecular constant divided by the concen-

$$\frac{dx}{dt} = k_{cat.} \, C_{cat.} \, (a - x)$$

tration of catalyst. On the whole this bimolecular equation seems to hold as well as in most organic reactions.

Only a few experiments were performed using acid catalysts, which were found to be much less effective than the alcoholates, but of the same order of effect as piperidine. Thus the catalytic constants at 26° with benzylphenyl-acetophenone were: H_2SO_4 in $CH_3OH < 1 \times 10^{-5}$; H_2SO_4 in acetic acid 2.7×10^{-4}; HCl in CH_3OH, 6.5×10^{-3}, as compared with 1.45 for sodium butylate and 1×10^{-3} for piperidine in butyl alcohol for the same compound. Two experiments in which the hydrochloric acid concentration in methyl alcohol was varied two-fold indicated that the rate was roughly proportional to the apparent catalyst concentration $k_{cat.} = 5.6 \times 10^{-3}$ and 7.1×10^{-3}. It seems clear that the phenomenon of enolization is a case of acid

and basic catalysis similar to the mutarotation of glucose studied by Brönsted and Lowry and the ideas of these investigators can be applied at least as a first approximation. A proton acceptor and a proton donor seem to be required for the reaction. With the alcoholates, the acid catalyst is the alcohol, the alcoholate ion the base; in acid catalysis in alcohol solution, there are probably a number of species of acid catalysts (the hydrated proton, undissociated acid, alcoholated proton, etc.), and the alcohol itself the base. The rate of enolization is at a minimum in "neutral solvents" where the concentrations of the acid and base are both very low.

In such complicated non-aqueous solvents with the solvent and catalyst both changing, only a qualitative application of Brönsted's ideas can be expected to hold. It is interesting, however, to note that the alcoholates of ethyl, n-propyl, n-butyl and $sec.$-butyl are all about the same in their effect ($k_{cat.}$ = 2.1 − 1.6 for phenylbenzylacetophenone) whereas with sodium methylate $k_{cat.}$ = 0.4 and with piperidine $k_{cat.}$ = 0.001. The catalytic constants thus parallel the basicity since the pK values[5] of C_2H_5OH and $C_6H_{11}NH^+$ are estimated as 19 and 11, respectively, and methyl alcohol would certainly be expected to be somewhat the strongest acid of the series of alcohols.

In Table II are collected the data of Table I and certain other experiments with other catalysts. For convenience the results are all expressed

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TABLE II

RELATIVE RATES OF ENOLIZATION AT 25°

(A) Acetophenone Derivatives

[XYCHCOC₆H₅]

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Substituents on α-carbon atoms (X.Y)	NaOCH₃ in CH₃OH	NaOC₄H₇ in C₄H₉OH	NaOC₃H₇(n) in C₃H₇OH(n)	NaOC₄H₉(n) in C₄H₉(OH)n	NaOC₄H₉($sec.$) in C₄H₉OH($sec.$)	NaOCH₃ in C₄H₉(OH)$tert.$	C₅H₁₀NH in CH₃OH	C₅H₁₀NH in C₄H₉OH	HCl in CH₃OH
I C₆H₅, C₆H₅CH₂	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
II C₆H₅, CH₃	3.0		3.0	2.3	2.3	2.1	2.6	2.2	
III C₆H₅CH₂, CH₃	0.26	0.31	0.67	0.35	0.34	0.40	0.29	0.06	7.0

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(B) Acetomesitylene Derivatives [XYCOC₆H₂(CH₃)₃]

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IV C₆H₅, C₆H₅CH₂ 0.35				0.21					
V C₆H₅, CH₃ 21	10.5	10.8	12.7	14.4	12.8	35.5	36.2		

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(C) Methyl Ester [XYCHCOOCH₃]

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VI C₆H₅CH₂, CH₃   0.003

The constants were determined with a concentration of catalyst of approximately 0.01 molar in the case of the alcoholates, about 2 M with piperidine and 2 M with hydrochloric acid. In each case the concentration of catalyst was accurately measured and this value used in determining the catalytic constant.

[5] Danner, THIS JOURNAL, **44**, 2841 (1922), gives $k = 7 \times 10^{-20}$ for C_2H_5OH in ethyl alcohol.

as rates relative to that of phenylbenzylacetophenone with the same catalyst.   It is clear from a brief inspection of the table that the relative rates are not independent of the catalyst.   Even with the series of closely related catalysts, the alcoholates, there are divergencies as much as 100% in a number of cases and 20 to 50% in many others; these divergencies seem to be beyond any possible experimental error.   When we turn to such different catalysts as piperidine and hydrochloric acid, enormous irregularities occur. For example, with piperidine in n-butyl alcohol, methylbenzylacetophenone is enolized only about one-twentieth as fast as the reference compound, whereas with most other alkaline catalysts the ratio of the two rates is about one-third.   With hydrochloric acid, the compound actually racemized faster than the reference substance, instead of more slowly.   When we consider the complicated nature of the reaction which involves the interaction of the ketone with a proton donor and a proton acceptor, the results are not at all surprising.   They show, however, *the impossibility of making any generalizations about the rate of enolization without regard to the solvent or catalyst*.   It is, of course, quite probable that the actual mechanism of proton transfer may be different under different conditions.

In view of the difficulties mentioned above, it is possible to compare the effect of substituent groups on the rate in only a very rough and approximate way.   Taking the average of the alcoholate results as a basis of comparison, it is clear that substitution of methyl or benzyl by phenyl increases the rate by three- to six-fold (III *vs*. I and III *vs*. II).   This increase in the rate of enolization parallels the greater degree of enolization caused by the introduction of a phenyl group in acetoacetic ester[6] ($K = 0.45$) as compared with α-methylacetoacetic ester ($K = 0.05$) or α-benzylacetic ($K = 0.06$, all equilibrium constants in dilute alcohol at 25°).   A similar parallelism with the free energy measurements is seen with the low rate of enolization of the ester (VI) compared to the corresponding ketone; here the ratio is about a hundred times.   The ratio of the equilibrium constants of acetoacetic ester and acetylacetone varies from 10 to 40 depending on the standard state chosen;[6] (though this is the best comparison available it is not very satisfactory as in the replacement of $COOCH_3$ by $-COCH_3$ a methyl and not a phenyl ketone is involved).   The difference caused by the replacement of a benzyl by a methyl group (I *vs*. II and IV *vs*. V) does not find its analogy in the free energy measurements, where the two groups are nearly equivalent.   The substitution of the phenyl group by the mesityl group in one series (I *vs*. IV) decreases the rate, in the other (V *vs*. II) it increases the speed of enolization by basic catalysts.

The irregularities exhibited in Table II are in part due to the small range between the most rapidly enolized and the least (only about 10^4).   Complications due to the effect of solvent would be expected to obscure relation-

[6] Conant and Thompson, THIS JOURNAL, **54**, 4039 (1932).

ships between compounds differing less than five-fold in the rate, for even if there were a parallelism between the equilibrium constant and the rate of enolization (due to the fact that the rate of ketonization was independent of structure), the solvent effects would amount to ± 500 cal.,[6] which corresponds to about two to three-fold difference in k. While there is, perhaps, some such general parallelism indicated by the discussion of the preceding paragraph, it is clear that there must be many disturbing factors. Unless one wishes to assume that entirely different forces are at work here than in the case of the substituted acetoacetic ester, one must conclude *that the relation between free energy of isomerization and structure is more regular than that between rate of isomerization and structure.*

The activation energy calculated from the temperature coefficient is given in the last column of Table I. The average value is about 14,000 cal.; it was not possible to obtain sufficiently accurate and reliable values to test the question of whether or not there was a relation between the rates and activation energies. By an extrapolation of the free energy measurements of diketones and keto esters,[6] one feels quite confident that $\Delta F > +$ 6000 for the acetophenone derivatives and ΔH is not far from this value (since ΔS for an isomeric change is small). This sets a lower limit to the values of ΔF and ΔH for the enolization; an upper limit can be placed on the value of ΔH by a consideration of the fact that the heat of activation of the ketonization cannot be less than zero and since $\Delta H = E_1 - E_2$, ΔH cannot be greater than $+14,000$ cal., the activation energy of enolization. These considerations are independent of the catalyst since approximately the same value of E was obtained with piperidine and with hydrochloric acid in methyl alcohol; they only depend on the correctness of two assumptions, (1) that the rate of racemization is a measure of the rate of enolization and (2) that there are not several consecutive reactions involved in the enolization. Since ΔF is probably within a thousand calories of ΔH for an isomeric change of this sort, we may place the value of ΔF for the enolization of acetophenone derivatives as between 6000 and 14,000 cal., which correspond to values of K of 10^{-5} to 10^{-10}. It seems worth while to set such limits since there seems to be no way of measuring ΔF or ΔH for this type of isomeric change (where the one isomer is in extremely small concentration at equilibrium) or calculating it from the third law. It is interesting that if one takes a figure nearer the upper limit of ΔF, say $K = 10^{-9}$ and assumes that the enol form is itself an acid of the strength of phenol, the value of K for the equilibrium ketone $\longrightarrow$ enol ion $+$ H$^+$ is $10^{-9} \times 10^{-10} = 10^{-19}$. The value of 10^{-20} was taken as a probable approximate value for the acidity constant of acetophenone from entirely other considerations in a recent paper from this Laboratory.[7] Preliminary experiments on the rate of racemization of the methyl ester of methyl-

[7] Conant and Wheland, THIS JOURNAL, **54**, 1212 (1932).

benzylacetic acid with sodium methylate gave values of 18,000 for the activation energy. The fact that this is larger than the average value for the ketones cannot be considered as significant without further work, but an upper limit for ΔH and ΔF of enolization can be set by the considerations just mentioned. Using such approximations, together with the quantitative information in the preceding paper[6] and the qualitative behavior of the compounds, the following table may be constructed to summarize our present information about enolization.

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TABLE III

ESTIMATED VALUES OF ΔF OF ENOLIZATION IN GASEOUS PHASE

ΔF for liquid phase or solutions may differ from these values by ± 0.7 kg. cal.

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Type of compound	ΔF in kilogram calories	Type of compound	ΔF in kilogram calories
$R_2CHCOOC_2H_5$	16–14	$CH_3COCHRCOCH_3$	
$R_2CHCOCH_3$	10–12	$CH_3COCH_2COOC_2H_5$	0
R_2CHCHO	10– 7	$CH_3COCH(C_6H_5)COOC_2H_5$	−1
$CH_2(COOC_2H_5)_2$	7	$CH_3COCH_2COCH_3$	−1.3
$CH_3COCHRCOOC_2H_5$	1	$(RCO)_3CH$	less than · 3

$(R = C_nH_{2n+1}$; if R = aryl, it is probable that ΔF of enolization will be about 1.5 kg. cal. more negative.)

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Experimental

(a) Preparation of Compounds

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Methylbutylphenylcarbinol.—A Grignard reagent prepared from 137 g. of n-butyl bromide and 24.3 g. of magnesium was treated at 0° with 120 g. of acetophenone dissolved in an equal volume of ether. The product of reaction was hydrolyzed with ice and sulfuric acid. The aqueous layer was extracted three times with ether and the ether extract washed with a concentrated sodium carbonate solution. The dried and filtered solution was evaporated and the residue vacuum distilled. The carbinol (110 g.) had the following physical properties: b. p. 129–130° at 4 mm., n_D^{20} 1.5091, d_{20} 0.9592; mol. ref. calcd., 55.54; found, 55.42.

Anal. Calcd. for $C_{12}H_{18}O$: C, 80.89; H, 10.18. Found: C, 81.09; H, 10.32.

Methyl (α-Methyl-α-phenyl-n-amyl) Ether.—A solution of 17.8 g. of the carbinol in 30 cc. of methyl alcohol containing 1 cc. of concentrated sulfuric acid separated into two layers on standing overnight. The product of reaction was dissolved in ether, washed with water and a sodium carbonate solution, dried and the ether distilled; the residue was distilled in a vacuum. Twelve grams of product was obtained having the following properties: b. p. 105–106° at 6 mm., n_D^{20} 1.4940, d_{20} 0.9275; mol. ref. calcd., 60.27; found, 60.27.

Anal. Calcd. for $C_{13}H_2O$: C, 81.25; H, 10.41. Found: C, 81.02; H, 10.38.

α-Methyl-α-phenyl-n-caproic Acid.—Five grams of methyl-(methylphenylamyl) ether was dissolved in 150 cc. of dry ether and treated with 5–6 cc. of liquid sodium–potassium alloy in an atmosphere of nitrogen. The reaction started immediately and proceeded without shaking. The red potassium derivative was treated with carbon dioxide until all color disappeared. Excess alloy was decomposed by adding moist ether and alcohol. The alcohol-ether solution was then extracted several times with water. The alkaline solution was acidified and the liberated acid extracted with ether. After drying over sodium sulfate the ether was distilled off and the residue combined

from two similar experiments vacuum distilled. The yield was 6.5 g.; b. p. 155° at 4 mm. In a larger run 40 g. of acid was obtained from 55 g. of ether.

Neutral equivalent. Calcd. for $C_{13}H_{18}O_2$: 206. Found: 194.7. *Anal.* Calcd. for $C_{13}H_{18}O_2$: C, 75.68; H, 8.78. Found: C, 75.83; H, 8.94.

α-Methyl-α-phenylmethylcaproate.—Four grams of α,α-methylphenylcaproic acid as the potassium salt was methylated with dimethyl sulfate at the temperature of the steam-bath. Two fractions of product were collected (1) 1.4 g., boiling point 112–113° at 1 mm.; (2) 1.85 g., b. p. 115° at 2 mm. The last fraction was odorless and had the following physical properties: n_D^{20} 1.4964, d_{20} 0.9938; mol. ref. calcd., 64.78; found, 64.70. Molecular weight by the freezing point method in benzene: mol. wt. calcd., 220; found, 206.

Anal. Calcd. for $C_{14}H_{20}O_2$; C, 76.36; H, 9.09. Found: C, 76.21; H, 9.13.

d-α-Methyl-α-phenylcaproic Acid.—Ten grams of methylphenylcaproic acid and 16 g. of quinine were dissolved in 75 cc. of hot alcohol and filtered. The filtrate was diluted with water until turbid and sufficient alcohol then added until the solution became clear. After three crystallizations the salt was decomposed by dilute sulfuric acid. The free acid gave the following value for the specific rotation in alcohol solution

$$[\alpha]_{5461} = 13.65° = \frac{0.70° \times 100}{2 \times 2.559}$$

To determine whether the ease of resolution was greater with some other alkaloid, 10 g. of the acid and 14.3 g. of cinchonidine were dissolved in 100 cc. of hot alcohol and the solution filtered. The filtrate was diluted with water and set aside to crystallize. After three crystallizations the salt was decomposed with dilute hydrochloric acid. The free acid in this case gave a slightly lower specific rotation in alcohol solution.

$$[\alpha]_{5461} = 10.68° = \frac{0.26° \times 100}{2 \times 1.219}$$

d-α-Methyl-α-phenylcaprophenone.—Five grams of thionyl chloride and 2.5 g. of d-α-methyl-α-phenylcaproic acid ($\alpha_{5461} = 13.65°$) were mixed in a 100-cc. Erlenmeyer flask attached to a reflux condenser provided with a calcium chloride tube. The reaction was completed by warming on the steam-bath for ten to fifteen minutes. Excess thionyl chloride was distilled off at the pressure of the water pump. The residual acid chloride was dissolved in 25 cc. of toluene and the flask tightly stoppered.

A Grignard reagent prepared in the usual manner from 0.3 g. of magnesium and 2 g. of bromobenzene was treated with 2 g. of freshly fused zinc chloride dissolved in a minimum quantity of ether. The phenyl zinc chloride formed separated from solution as a fine gray powder. Twenty-five cc. of toluene was added and the flask connected with the condenser set for downward distillation. Most of the ether was distilled from the zinc compound and replaced by an equal volume of toluene. The acid chloride previously prepared was added slowly to the suspension of the phenyl zinc chloride in boiling toluene. A rather vigorous reaction occurred and a gummy mass was formed which held the stirrer fast in some cases. After one hour, hydrolysis was effected by 50 cc. of a saturated ammonium chloride solution. The toluene layer was washed with water, a dilute sodium carbonate solution, and finally with dilute hydrochloric acid, dried and evaporated at the pressure of the water pump. The residue was dissolved in several solvents but showed no tendency to crystallize from any one even at low temperature. Attempts to crystallize the ketone were abandoned and after evaporating the solvent the residue was distilled in vacuum. The yield was 1.7 g. of ketone having a boiling point of 150–152° at 0.5 mm. specific rotation in alcohol solution

$$[\alpha]_{5461} = 30.78° = \frac{0.62° \times 100}{2 \times 1.008}$$

Anal. Calcd. for $C_{19}H_{22}O$: C, 85.66; H, 8.33. Found: C, 85.48; H, 8.55.

d-Methylbenzylacetophenone.—The acid chloride was prepared by the usual procedure from 7.2 g. of *d*-methylbenzylacetic acid ($[\alpha]_{5461} = 31.5°$ for the sodium salt) and 21 g. of thionyl chloride. A Grignard reagent prepared from 7.5 g. of bromobenzene and 1.2 g. of magnesium was treated with 6.6 g. of freshly fused zinc chloride dissolved in a minimum quantity of ether. The ether was replaced with toluene. The acid chloride prepared above was dissolved in toluene and added to the boiling toluene suspension of phenyl zinc chloride. After one hour the product was hydrolyzed by a saturated ammonium chloride solution and the toluene layer washed with a dilute sodium carbonate solution, dilute hydrochloric acid, and finally with water. The dried and filtered toluene solution was evaporated under diminished pressure and the residue vacuum distilled. The yield was 5.5 g. of ketone having a boiling point of 148–150° at 6 mm. When cooled the distillate was solid, but melted at room temperature. The solidified distillate was transferred to a small chilled porous cell and centrifuged at a high speed at the temperature of the cold room. In this manner 2.5 g. of white crystalline ketone of m. p. 42–43° was obtained. The ketone had the following specific rotation in alcohol solution

$$[\alpha]_{5461} = 87.5° = \frac{4.66° \times 100}{2 \times 2.669}$$

Anal. Calcd. for $C_{16}H_{16}O$: C, 85.67; H, 7.19. Found: C, 85.72; H, 7.45.

1-Phenylbenzylacetomesitylene.—A petroleum ether solution of 6 g. of 1-benzylphenylacetic acid ($[\alpha]_{5461} = -70.48°$) was treated with 10 g. of thionyl chloride at room temperature. The reaction was completed by warming on the water-bath; excess thionyl chloride was evaporated at reduced pressure and the residual acid chloride dissolved in 25 cc. of toluene.

A Grignard reagent prepared from 10.6 g. of mesityl bromide and 1.3 g. of magnesium was treated with 7.5 g. of freshly fused zinc chloride dissolved in a minimum quantity of ether. The ether was replaced by toluene and the hot suspension of mesityl zinc chloride treated with the solution of acid chloride previously prepared. After one hour the product was hydrolyzed with a saturated ammonium chloride solution and the toluene layer washed with dilute sodium carbonate, dilute hydrochloric acid, and finally with water. The dried and filtered solution was evaporated at reduced pressure. Mesitylene and mesityl bromide were distilled off at 2–3 mm. by immersing the flask in a metal bath maintained at 100° and the residue crystallized from methyl alcohol. Five grams of mesityl ketone of m. p. 113–114° was obtained. The ketone had the following specific rotation in acetone solution

$$[\alpha]_{5461} = -8.06° = \frac{-0.10° \times 100}{2 \times 0.620}$$

Anal. Calcd. for $C_{24}H_{24}O$: C, 87.75; H, 7.36. Found: C, 87.74; H, 7.60.

d-Phenylmethylacetomesitylene.—Twenty-five grams of thionyl chloride and 9.5 g. of the *d*-phenylmethylacetic acid ($[\alpha]_{5461} = 61.75°$ in alcohol) were mixed in the usual apparatus at room temperature. Excess thionyl chloride was evaporated off and the residual acid chloride dissolved in 25 cc. of toluene.

The acid chloride was added to a boiling toluene suspension of mesityl zinc chloride prepared as usual from 20 g. of mesityl bromide, 2.5 g. of magnesium, and 14 g. of freshly fused zinc chloride. After one hour the product was hydrolyzed with a saturated ammonium chloride solution and the toluene layer washed with a dilute sodium carbonate solution, dilute hydrochloric acid, and finally with water. The dried and filtered solution was evaporated at reduced pressure and the residue crystallized from methyl alcohol at −20°. The yield was 6.5 g. of mesityl ketone of m. p. 59–60.5°; specific rotation (in methyl alcohol)

$$[\alpha]_{5461} = 71.5° = \frac{1.88° \times 100}{2 \times 1.268}$$

Anal. Calcd. for $C_{15}H_{20}O$: C, 85.66; H, 7.99. Found: C, 85.39; H, 8.01.

l-Methylbenzylmethylacetate.[8]—The compound used in the rate measurements had the following rotation

$$[\alpha]_{5461} = -18.00 = \frac{-18.31°}{1 \times 1.0174}$$

1-Benzylphenylacetophenone.—The compound used in the final rate measurements was prepared from the chloride of the completely resolved acid by the action of phenyl zinc chloride. Some racemization must have occurred during the preparation as the m. p. was 115–116° and $[\alpha]_{5461} = -168.2° = (3.49° \times 100)/(2 \times 1.038)$ as compared with m. p. 121–121.5° and $[\alpha]_D = -268°$ recorded by McKenzie.[9]

d-Phenylmethylacetophenone.—The compound used in the rate measurements melted at 32–33° and had a rotation in methyl alcohol of $[\alpha]_{5461} = 242.1 = (5.06 \times 100)/(2 \times 1.045)$ as compared with m. p. 34–35° and $[\alpha]_{5461} = 260$ (in $CHCl_3$) recorded by McKenzie and $[\alpha]_D = 210.8$ in alcohol.[10] The analytical data for the compound were satisfactory.

(b) Measurements

The measurements were made with a Schmidt and Haensch polariscope which was read to 0.01°, a mercury arc light with suitable filters giving light of $\lambda = 5461$ was used. The polariscope tube was jacketed and the temperature kept constant by circulating water; the temperature was read on a thermometer immersed in the liquid in the polariscope tube itself. Anhydrous solvents were used throughout. The alcoholates were prepared by dissolving metallic sodium in the alcohol in question, the concentration being finally determined by titration of an aliquot sample with standard acid. The piperidine used in the final experiments was distilled from solid potassium hydroxide; thus prepared it was about 30% less effective than piperidine which had not been given this treatment. A number of experiments indicated that it was more difficult to obtain reproducible results with various samples of purified piperidine than with the alcoholates.

Summary

1. The rates of enolization of five optically active aryl ketones and one closely related ester were determined under a variety of conditions by noting the rate of racemization. The rate was found to be nearly directly proportional to the concentration of catalyst when the sodium alcoholates were used as the catalytic substances. The most effective catalyst was sodium methylate using tertiary butyl alcohol as the solvent; this catalyst was about 2000 times as effective as piperidine in methyl alcohol, which was the least effective base and 1000 times as effective as hydrogen chloride in methyl alcohol.

2. The relative rates of enolization depended on the catalyst and solvent although with all the alcoholates the relative rates only varied about 50%. Using these values as a basis for comparison, it was found that the ester enolized much more slowly than the ketones but that there was no clear regularity between the rate of enolization of the ketone and its structure.

[8] This Journal, **48**, 169 (1926).

[9] McKenzie, *J. Chem. Soc.*, **129**, 779 (1926).

[10] McKenzie, Roger and Wells, *ibid.*, **129**, 787 (1926).

3. The heat of activation of the enolization is about 14 ± 1 kg. cal. The free energy of enolization of the acetophenone derivatives is estimated to be between +5 and +14 kg. cal.

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THE REACTION BETWEEN TRIARYLMETHYL HALIDES AND PHENYLMAGNESIUM BROMIDE. I

BY C. S. SCHOEPFLE AND S. G. TREPP[1]

In a previous communication[2] the apparently abnormal reaction of tetraphenylethylene dichloride and phenylmagnesium bromide, which results in the formation of p-phenyltetraphenylethylene and tetraphenylethylene,[3] was explained on the assumption that the dichloride reacts in the para quinonoid form. Another Grignard reaction of this type has been described by Gilman and Jones,[4] who treated triphenylchloromethane with phenylmagnesium bromide and obtained a 47% yield of biphenyldiphenylmethane in addition to a small amount of the expected product, tetraphenylmethane. Again, as in so many other reactions of the triarylmethyl salts, the products of this reaction can be readily explained by a simple mechanism involving quinoidation of the triphenylchloromethane. If the quinonoid modification of triphenylchloromethane (I) reacts
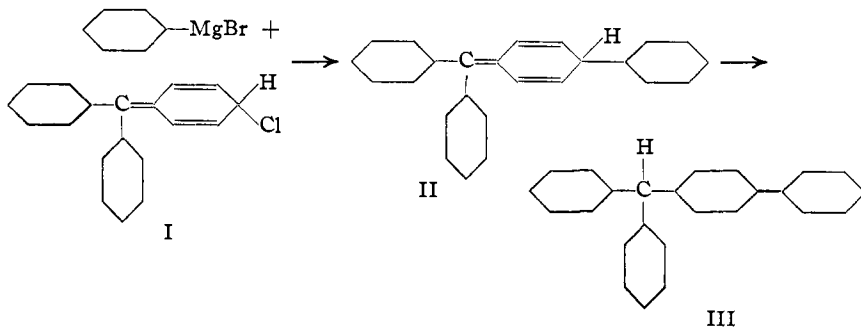
with the Grignard reagent, there will be formed an unstable intermediate product (II) which will rearrange to give biphenyldiphenylmethane (III); the benzenoid modification of the chloride of course gives tetraphenyl

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[2] Schoepfle and Ryan, THIS JOURNAL, 54, 3687 (1932).
[3] Norris, Thomas and Brown, Ber., 43, 2955 (1910).
[4] Gilman and Jones, THIS JOURNAL, 51, 2840 (1929).