Action of Hydrogen Sulfide upon the Silver Salt of IV.—A suspension of 10 g. of powdered silver salt in 50 cc. of water was agitated and saturated with hydrogen sulfide for five hours at 40°. After removal of silver sulfide, the filtrate was concentrated at 30° in an atmosphere of hydrogen, and 1 g. of a white amorphous product (VI) separated. Purification of this white product was not practicable because of ease of decomposition. Product VI melted at about 122°, though not sharply; further heating caused color change to a bright red, with evolution of a gas.

Isatin, by the Oxidation of VI.—A suspension of 0.4 g. of product VI (obtained above) in 25 cc. of 3% hydrogen peroxide was agitated and warmed gently for three hours. The color changed from pale yellow to red. After cooling, acidification caused the slow separation of a red-brown substance which crystallized from alcohol in red needles, yield 80%, and was identified as isatin by melting point methods.

Summary

Isatin condenses with malonamide and with malonanilide, mole for mole, to give the corresponding iso-indigoid compounds. Diethyl malonate, however, yields the tetra-ethyl ester of 3,3-bis-(methane di-acid)-oxindole.

Malonic acid and isatin react in the presence of ammonia to give a product for which the formula of ammonium-3-(methylene di-acid)-oxindole, is suggested. Acid treatment of this compound causes the formation of known quinolones, but oxidation to yield isatin demonstrated its essential oxindole configuration.

NEW YORK, N. Y.
NEW HAVEN, CONN.

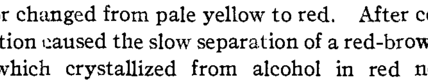
RECEIVED JANUARY 25, 1935

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE UNIVERSITY OF MICHIGAN]

The Cleavage of Unsymmetrical Ketones by Potassium Hydroxide. I

BY W. E. BACHMANN

A considerable number of two-way reactions have been investigated in order to obtain comparisons of chemical reactivities; these reactions have received ample discussion from von Braun,[1] Schönberg,[2] Adkins[3] and others. Among the methods is the cleavage of unsymmetrical ketones by potassium hydroxide; thus, a ketone R_1—CO—R_2 can react with the alkali in two ways



$$R_1\text{—CO—}R_2 \xrightarrow{\text{KOH}} \begin{cases} R_1\text{COOK} + R_2\text{H} \\ R_1\text{H} + R_2\text{COOK} \end{cases}$$

By determining the proportions of the two acids in the mixture that is produced the amount of cleavage at each of the two bonds, R_1—CO and R_2—CO, can be ascertained. Since the reactions are irreversible no equilibrium is attained; the relative rates at which two competing reactions take place are measured. As far as can be learned, no quantitative study of the cleavage of a single unsymmetrical aromatic ketone has been made. We have now undertaken an investigation of this reaction and at this time report the results obtained on eleven aromatic ketones. The method is simple, rapid and gives reproducible results; the method possesses a number of advantages over that of Schönberg, who employed sodamide to cleave unsymmetrical aromatic ketones.

Procedure.—A mixture of 0.005 gram mole of ketone and 1.5 g. of solid potassium hydroxide (85%) is heated in a 15-cm. Pyrex test-tube in a direct flame. During the heating the mixture is shaken in order to obtain an emulsion and the heating is carried out cautiously in order to avoid a violent reaction which occurs if the temperature is allowed to go too high. When the mixture thickens it is stirred with a glass rod as it is being heated; after five to ten minutes the reaction is at an end. The potassium salts of the acids are separated from the neutral products by solution in water and the proportion of each acid in the mixture is determined.[4] The results of several runs checked each other; thus, four runs on *p*-tolyl *p*-biphenyl ketone gave for the ratio of *p*-toluic acid to *p*-phenylbenzoic acid values of 53:47, 54:46, 53:47 and 52:48. With a little experience one can cleave the ketone to the extent of 90–100%; since the remainder was found to be unchanged ketone, the yields of acids were practically quantitative, an indication that the reaction RCOOK + KOH $\longrightarrow$ RH + K_2CO_3 did not take place under the conditions of the experiment. It is considered that the results are accurate within a few per cent.

Discussion of Results.—The results of the experiments are summarized in Table I.

On the basis of phenyl as unity, the groups can be assigned values which represent what might be termed the relative tenacity with which the groups are held to the carbonyl group; these values are shown in Table II.

---

[1] Von Braun, *Ber.*, **56**, 1573 (1923).

[2] Schönberg, *Ann.*, **436**, 205 (1924); *Ber.*, **58**, 580 (1925).

[3] Adkins, *J. Chem. Educ.*, **9**, 1865 (1932).

[4] The methods of analysis were those employed in the study of the pinacol-pinacolone rearrangement; see Bachmann and Moser, THIS JOURNAL, **54**, 1124 (1932); Bachmann, *ibid.*, **54**, 2112 (1932); Bachmann and Sternberger, *ibid.*, **56**, 170 (1934); Bachmann and Ferguson, *ibid.*, **56**, 2081 (1934).

TABLE I

CLEAVAGE OF KETONES, $R_1—CO—R_2$

R_1	R_2	R_1COOH % by moles	R_2COOH % by moles
Phenyl	*o*-Tolyl	82	18
Phenyl	*m*-Tolyl	48	52
Phenyl	*p*-Tolyl	42	58
Phenyl	*p*-Biphenyl	49	51
o-Tolyl	*p*-Biphenyl	16	84
m-Tolyl	*p*-Biphenyl	48	52
p-Tolyl	*p*-Biphenyl	52	48
Phenyl	1-Phenanthryl[a]	96	4
Phenyl	2-Phenanthryl[a]	56	44
Phenyl	3-Phenanthryl[a]	55	45
Phenyl	9-Phenanthryl[a]	95	5

[a] For the preparation of these ketones see Bachmann, *ibid.*, **57**, 555 (1935).

TABLE II

RELATIVE TENACITIES OF GROUPS

p-Tolyl	1.38	2-Phenanthryl	0.79
m-Tolyl	1.08	*o*-Tolyl	.22
p-Biphenyl	1.04	9-Phenanthryl	.05
3-Phenanthryl	0.82	1-Phenanthryl	.04

It is apparent that not only the nature of the group but also the position of attachment to the ring are of importance; this is especially evident from a comparison of the tenacities of the four phenanthryl groups: the 1- and 9-phenanthryl groups are rapidly separated from the carbonyl group while the 2- and 3-phenanthryl groups are held more firmly. Similarly, the *o*-tolyl group is easily separated from the carbonyl while the *m*- and *p*-tolyl radicals are not.

Knowing the values of the tenacities of two groups R_1 and R_2 with respect to the phenyl group, one can calculate the manner in which the unsymmetrical ketone $R_1—CO—R_2$ will cleave. Thus, from the value 0.22 for *o*-tolyl and 1.04 for *p*-biphenyl the ratio of *o*-toluic acid to *p*-phenylbenzoic acid in the cleavage reaction should be 17 to 83%. In Table III a comparison is shown of the predicted and the actual results that have been observed in the three cases that have been investigated.

TABLE III

COMPARISON OF PREDICTED AND ACTUAL RESULTS

R_1	R_2	Predicted, % R_1COOH	Predicted, % R_2COOH	Found, % R_1COOH	Found, % R_2COOH
o-Tolyl	*p*-Biphenyl	17	83	16	84
m-Tolyl	*p*-Biphenyl	51	49	48	52
p-Tolyl	*p*-Biphenyl	57	43	52	48

It is seen that in these three instances the predicted results are of the same order as the experimental results. We are now engaged in determining the relative tenacities of a large number of groups and in testing the values in the manner indicated.

Summary

Eleven unsymmetrical aromatic ketones have been cleaved by potassium hydroxide and the proportions of the two acids in the mixture have been determined.

Values representing the relative tenacity with which the groups are held to the carbonyl group have been determined for eight radicals.

ANN ARBOR, MICHIGAN RECEIVED JANUARY 25, 1935

[CONTRIBUTION FROM THE DEPARTMENT OF RESEARCH IN PURE CHEMISTRY, MELLON INSTITUTE OF INDUSTRIAL RESEARCH]

Cinchona Alkaloids in Pneumonia. II. Ketone Formation with Sodium Amide

BY ALICE G. RENFREW AND LEONARD H. CRETCHER

The preparation of α-aminopyridine from the action of sodium amide on pyridine is well known. In an attempt to prepare amino-cinchona alkaloids for use in chemotherapeutic investigations which have been under way in this Laboratory for some time, hydroquinine, quinine and cinchonine were treated with sodium amide. We were unable to isolate any amino-substituted alkaloid from the reaction mixture despite the patent claims of Chichibabin.[1] However, it was found that the alkaloid present in the reaction mixture had been transformed to the corresponding ketone in amounts equaling or exceeding the yield of ketone obtained in the usual method of oxidation by means of chromic acid.[2]

The conditions used in the present experiments were comparable with those employed by Chichibabin[3] for the amination of nicotine. Unchanged alkaloid was recovered, and varying amounts of ketone were formed—the latter involving a transformation of the secondary alcohol group of the

---

[1] German Patent 374, 291; *C. A.* **18**, 2176 (1924).

[2] Rabe, *Ann.*, **364**, 330 (1909).

[3] Chichibabin and Kirssanov, *Ber.*, **57**, 1163 (1924).