glycol in a mixture of 12 ml. of absolute ethanol, 15 ml. of pyridine and 0.4 g. of hydroxylamine hydrochloride was refluxed for 1 hour and 40 minutes, after which the volume was reduced to about 10 ml. The addition of water until precipitation was complete gave 0.3 g. of a white solid. Crystallization twice from ethanol and once from ethanol-water yielded the pure oxime, m. p. 209–210° (dec.).

Anal. Calcd. for $C_{20}H_{15}N_3O$: C, 76.65; H, 4.82. Found: C, 76.74, 76.66; H, 5.25, 5.22.

Desoxyquinaldoin (V).—The glycol, 0.5 g., in 20 ml. of pyridine in which a small amount of hydrogen chloride had been dissolved was refluxed for 30 minutes, cooled and poured into 250 ml. of dilute ammonium hydroxide solution. The yellow to orange precipitate when dried weighed 0.4 g., m. p. 218°. Three crystallizations from carbon tetrachloride elevated the melting point to 221°.

Anal. Calcd. for $C_{20}H_{14}N_2O$: C, 80.52; H, 4.82; N, 9.36. Found: C, 80.62, 80.35; H, 4.78, 4.58; N, 9.54, 9.45.

The desoxyquinaldoin yielded an **oxime** when treated with hydroxylamine hydrochloride in absolute ethanol and pyridine. The white crystals, m. p. 208–209° (dec.), melted unchanged when mixed with the second oxime obtained from the glycol as described above.

Anal. Calcd. for $C_{20}H_{15}N_3O$: C, 76.65; H, 4.82. Found: C, 76.62, 76.49; H, 4.84, 4.74.

The desoxyquinaldoin in a mixture of dioxane and pyridine oxidized to **quinaldil**, m. p. 271–272°, when air was passed through the solution for 24 hours. This compound melted unchanged when mixed with the quinaldil obtained by the oxidation of the enediol.

Anal. Calcd. for $C_{20}H_{12}N_2O_2$: C, 76.92; H, 3.84. Found: C, 76.34, 76.64; H, 3.80, 3.98.

Summary

The benzoin condensation of quinaldehyde produces 1,2-di-2-quinolyl-1,2-ethenediol and its reduction product, 1,2-di-2-quinolyl-1,2-ethanediol.

A chelated ring formula is proposed to account for the high stability of the enediol.

The validity of Brown and Hammick's formula for the quinaldil obtained on the oxidation of 1,2-di-2-quinolyl-1,2-ethenediol is questioned since the compound responds to physical and chemical tests indicating the presence of the carbonyl group.

KNOXVILLE, TENNESSEE RECEIVED JULY 10, 1950

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF OKLAHOMA]

Ketimines. II. Diaryl Type[1]

BY P. L. PICKARD AND D. J. VAUGHAN[2]

The stability of *t*-butyl *o*-tolyl ketimine to hydrolysis[3] suggested that diaryl ketimines substituted in the *o,o'*-positions might also be stable. In view of the ease with which the alkyl-aryl ketimines were prepared, the synthesis of diaryl ketimines seemed feasible.

The synthesis of the six isomeric ditolyl ketimines has shown the hypothesis of stability to hydrolysis to be incorrect. All ketimines hydrolyzed slowly in 6 *N* hydrochloric acid. The only reaction products isolated during preparation were unsubstituted ketimines, even when 150% excess aryl halide was used in the preparation of the Grignard reagent. The products distilled cleanly, leaving no high-boiling residues. When the ratio of aryl halide to nitrile was 1:1, traces of unreacted nitrile were recovered, due to incomplete formation of Grignard reagent,[4] undoubtedly. The yield of ketimine was not lowered appreciably, however, and the reaction mixture was more easily worked up because of the smaller amount of inorganic material present.

Hydrolysis experiments failed to answer the question of relative stability of the *o,o'*-ditolyl ketimine as compared to its isomers. All the compounds were sufficiently stable to prevent complete hydrolysis to ketone in acid solution over a 4-hour period, but the amount of ketimine hydrolyzed was practically the same in each case.

Reduction of the ketimines to the corresponding primary amines was easily accomplished over pre-reduced Adams catalyst at atmospheric pressure. Relative reduction rates, as indicated in the experimental portion, were calculated by plotting volume of hydrogen absorbed against time. While hydrolysis experiments failed to show any inhibitory effect of the *o*-tolyl group, hydrogenation data indicates a very definite decrease in rate due to this group.

Absorption spectra were determined in alcoholic solution. The spectra of imines and ketones were found to be similar. With the exception of the di-*p*-tolyl compounds, an arrangement of compounds in order of increasing wave length of maximum absorption is the same for the two types of compounds. Absorption of amines was different from that observed for the other compounds. This was expected because of the elimination of conjugation of the aromatic nuclei with groups in the side chain. Data on the spectra obtained are shown in Figs. 1–3.

Experimental

Preparation of Ketimines.—The procedure previously reported[3] was used. The ratio of aryl halide to aryl nitrile was varied in each case from 3:1 to 1:1 with no appreciable change in the amount of ketimine recovered.

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[1] This work was done under a contract with the Office of Naval Research.

[2] Based on a portion of a thesis presented by D. J. Vaughan in partial fulfillment of the requirements for the degree of Doctor of Philosophy at the University of Oklahoma.

[3] Pickard and Vaughan, THIS JOURNAL, **72**, 876 (1950).

[4] H. Gilman, *ibid.*, **51**, 1576 (1929), reports the maximum yields of *o*-, *m*- and *p*-tolylmagnesium bromide as 92.7, 88 and 86%, respectively.

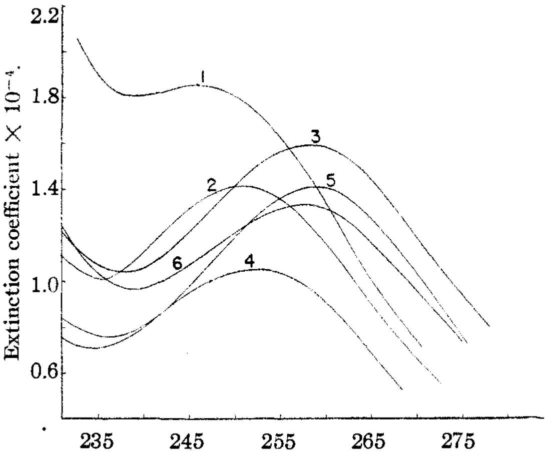

Fig. 1.—Absorption spectra of ketimines: 1, di-*o*-tolyl; 2, di-*m*-tolyl; 3, di-*p*-tolyl; 4, *o*-tolyl *m*-tolyl; 5, *o*-tolyl *p*-tolyl; 6, *m*-tolyl *p*-tolyl.

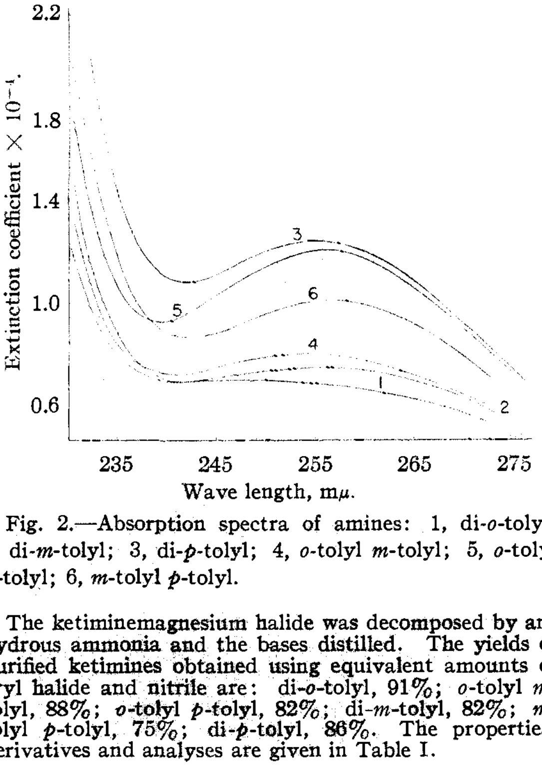

Fig. 2.—Absorption spectra of amines: 1, di-*o*-tolyl; 2, di-*m*-tolyl; 3, di-*p*-tolyl; 4, *o*-tolyl *m*-tolyl; 5, *o*-tolyl *p*-tolyl; 6, *m*-tolyl *p*-tolyl.

The ketiminemagnesium halide was decomposed by anhydrous ammonia and the bases distilled. The yields of purified ketimines obtained using equivalent amounts of aryl halide and nitrile are: di-*o*-tolyl, 91%; *o*-tolyl *m*-tolyl, 88%; *o*-tolyl *p*-tolyl, 82%; di-*m*-tolyl, 82%; *m*-tolyl *p*-tolyl, 75%; di-*p*-tolyl, 86%. The properties, derivatives and analyses are given in Table I.

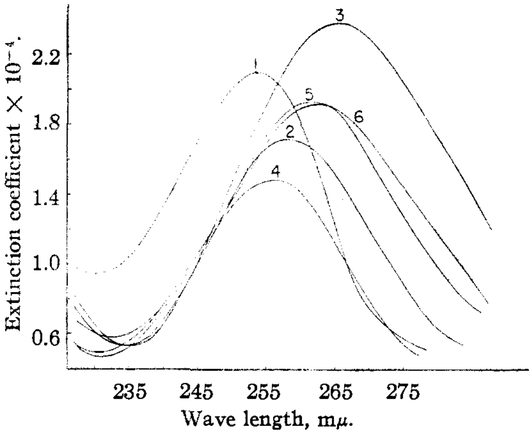

Fig. 3.—Absorption spectra of ketones: 1, di-*o*-tolyl; 2, di-*m*-tolyl; 3, di-*p*-tolyl; 4, *o*-tolyl *m*-tolyl; 5, *o*-tolyl *p*-tolyl; 6, *m*-tolyl *p*-tolyl.

Hydrolysis of Ketimines.—The ketimines were refluxed for 48 hours in 6 *N* hydrochloric acid and the mixtures allowed to cool. In each case crystals of hydrochloride precipitated. These crystals were filtered and washed with ether. The ether-water filtrate was separated and the ketones obtained by distillation of the ether layer. Additional amounts of ketimine hydrochloride were obtained by evaporation of the aqueous layer. All the ketimines were found to have hydrolyzed to the extent of about 40% based on ketone recovered, the remainder being recovered as hydrochloride. Properties, derivatives and analyses are given in Table II.

Hydrogenation of Ketimines.—A solution of 1.0 g. of ketimine in 40 cc. of methanol was reduced over pre-reduced Adams platinum catalyst at atmospheric pressure and 25°. The volume of hydrogen absorbed was the theoretical in each case. Relative reduction rates were calculated by determining the slope of a time *vs.* volume of hydrogen curve. The order of reduction, based upon the most difficultly reduced compound, di-*o*-tolyl ketimine, is: *o,o'*-1.00; *o,m'*-1.09; *o,p'*-1.32; *m,p'*-2.79; *m,m'*-2.99; *p,p'*-3.28.

The amines were recovered by distillation and characterized by physical constants and derivatives. These data are given in Table III.

Absorption Spectra.—The spectra of the ditolyl ketimines, ketones and methylamines were obtained using the Beckman-DU quartz spectrophotometer. Approximately 1 × 10^{-5} molar solutions in 95% ethanol of all compounds were found to give best results. The region 214–320 millimicrons was covered in 1–2 millimicron increments. The data obtained are shown in Figs. 1–3.

Summary

1. The six isomeric ditolyl ketimines have been prepared and characterized.

TABLE I

KETIMINES[a]

R_1—C(=NH)R_2 R_1 = Tolyl	R_2 = Tolyl	B. p., °C. 740 mm.	B. p., °C. 2 mm.	d^{20}_4	n^{20}_D	N,[b] %	Hydrochloride M. p., °C.	Hydrochloride N,[c] %	Picrate M. p., °C.	Picrate N,[d] %
o	*o*	313	135–137	1.0512	1.5975	6.70	273	5.81	175	12.71
o	*m*	315	136–137	1.0434	1.5962	6.65	243	5.65	148	12.85
o	*p*	318	138–140	1.0355	1.5961	6.69	236	5.80	153	12.79
m	*m*	321	137–138	1.0442	1.6005	6.68	222	5.78	160	12.73
m	*p*	335	140–142	1.0385	1.5937	6.66	234	5.73	249(d)	12.81
p	*p*	M. p. 81	160–162 (3 mm.)	1.0387	1.5969	6.69	215	5.67	197	12.83

[a] Benzenesulfonamides were oils. Theoretical values: [b] = 6.69; [c] = 5.72; [d] = 12.78.

TABLE II

KETONES

$R_1—CO—R_2$		B. p., °C.					2,4-Dinitrophenylhydrazone	
R_1 = Tolyl	R_2 = Tolyl	740 mm.	Red. p.	Mm.	d^{20}	n^{20}_D	M. p., °C.	N,[g] %
o	*o*[a]	310 (m. p. 75)	134–135	1			194	14.31
o	*m*[b]	319	135–136	1	1.0669	1.5895	208	14.41
o	*p*[c]	316	140–141	2	1.0586	1.5924	218	14.40
m	*m*[d]	329	141–142	1	1.0681	1.5926	223	14.29
m	*p*[e]	330 (m. p. 71)	150–152	3			215	14.36
p	*p*[f]	335 (m. p. 92)	150–152	2			220	14.38

[a] *Bull. soc. chim.*, **11,** 373 (1944), gives m. p. as 71°, b. p. as 308°; *Rec. trav. chim.*, 1109 (1940), gives 2,4-dinitrophenylhydrazone as 190°. [b] THIS JOURNAL, **63,** 1573 (1941), gives the 2,4-dinitrophenylhydrazone m. p. as 204–207°. [c] *Ber.*, **36,** 2025 (1903) gives b. p. as 316–318° and oxime m. p., as 122°; the oxime of our ketone melts at 121–122°. [d] *Rec. trav. chim.*, 1109 (1940), gives the 2,4-dinitrophenylhydrazone m. p. as 233°. [e] *Ber.*, **36,** 2025 (1903), gives the b. p. as 328–330° and semicarbazone m. p. as 183°. The semicarbazone of the ketone prepared in this investigation melts at 183°. [f] *Ber.*, **10,** 2174 (1877). gives the b. p. as 333° and m. p. as 92–95°. *Rec. trav. chim.*, **59,** 1109 (1940), gives the 2,4-dinitrophenylhydrazone m. p. as 220°. [g] Theoretical value, 14.35.

TABLE III

AMINES

$R_1 = CH(NH_2)R_2$		B. p., °C.						Benzenesulfonamide		Picrate	
R_1 = Tolyl	R_2 = Tolyl	740 mm.	Red. p.	Mm.	d^{20}_4	n^{20}_D	N,[a] %	M. p °C.	N,[b] %	M. p., °C.	N,[c] %
o	*o*	316	160–162	4	1.0449	1.5891	6.62	194	4.21	205	12.50
o	*m*	320	154–155	3	1.0380	1.5893	6.71	93	3.90	190	12.65
o	*p*	321	141–142	2	1.0286	1.5847	6.67	108	3.92	176	12.57
m	*m*	317	152–153	3	1.0264	1.5817	6.63	98	4.19	158	12.71
m	*p*	322	153–154	3	1.0297	1.5850	6.70	80	4.15	182	12.85
p	*p*[d]	318 M. p. 90°	140–141	2			6.68	128	4.11	178	12.65

[a] Theoretical values: [a] = 6.63; [b] = 4.00; [c] = 12.72. [d] *Ber.*, **24,** 2798 (1891), gives the m. p. as 93°; *Ber.*, **31,** 1773 (1898), gives b. p. as 318°.

2. The corresponding ketones were produced by hydrolysis of ketimines in 6 *N* hydrochloric acid.

3. Reduction of the ketimines at low pressure has resulted in the formation of the six dimethylbenzhydrylamines.

4. Relative rates of reduction have been determined and indicate a distinct hindrance in the case of ortho substituted ketimines.

5. Absorption spectra of the imines, ketones, and amines have been determined.

RECEIVED MARCH 15, 1950

[CONTRIBUTION FROM THE BIOCHEMISTRY DEPARTMENT AND THE MCARDLE MEMORIAL LABORATORY, UNIVERSITY OF WISCONSIN]

Chemical Preparation of Asymmetrically Labeled Citric Acid[1]

BY PHILIP E. WILCOX,[2] CHARLES HEIDELBERGER AND VAN R. POTTER

The classic investigations of Krebs[3] on the oxidation of carbohydrates and their metabolites in minces of pigeon breast muscle led him to formulate the metabolic cycle which is presented with only minor modifications in Fig. 1. Evans and Slotin[4] with pigeon breast muscle minces and Wood, *et al.*,[5] with pigeon liver minces independently discovered the β-carboxylation of pyruvic acid (Step 1) in animal tissues. When they introduced labeled carbon dioxide into the cycle by this step, they were able to isolate α-ketoglutaric acid which carried isotopic carbon (indicated by asterisks in Fig. 1). Analysis showed that all of the isotope was in the α-carboxyl group. Weinhouse, *et al.*,[6] performed a similar experiment, introducing acetate-1-C^{13} through Step 2 in rat kidney minces, and found that in this case the isotope was predominantly in the γ-carboxyl group of the α-ketoglutaric acid.

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(5) H. G. Wood, C. H. Werkman, A. Hemingway and A. O. Nier, *ibid.*, **142,** 31 (1942).

(6) S. Weinhouse, G. Medes, N. F. Floyd and L. Noda, *ibid.*, **161,** 745 (1945).