

large beaker and the benzene is evaporated on the water-bath, leaving a mixture of desoxybenzoin and desoxybenzoin pinacone. To this mixture 500 cc. of 80% alcohol is added and the beaker is heated on the steam-bath for one hour, while breaking up the lumps⁵ that are formed. After filtering through a hot water funnel and washing with a little alcohol, 30 g. of β -desoxybenzoin pinacone melting at 160–165° is obtained. The filtrate contains desoxybenzoin which can be recovered. One recrystallization from boiling alcohol yields β -desoxybenzoin pinacone⁶ melting at 172°.

Summary

Four methods of reduction of benzoin were studied and superior methods of preparation of stilbene, desoxybenzoin and β -desoxybenzoin pinacone developed.

⁵ Since desoxybenzoin is very soluble in alcohol and β -desoxybenzoin pinacone so very insoluble, a good separation can be made by this method provided the lumps are broken up to allow the alcohol to penetrate.

⁶ β -Desoxybenzoin pinacone was first made by Wislicenus and Blank [*Ann.*, **248**, 7 (1888)] together with the α -form and other products by the reduction of benzoin with zinc dust and acetic acid. Since then it has only been made by the prolonged action of light on an alcoholic solution of desoxybenzoin, Cohen, *Rec. trav. chim.*, **38**, 110 (1919).

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ELECTRON SHARING ABILITY OF ORGANIC RADICALS. VI. ALPHA-SUBSTITUTED PYRROLINES AND PYRROLIDINES

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The preceding paper by Craig and Hixon extended the studies¹ of this Laboratory on the electron sharing ability of organic radicals to the nitrogen heterocyclics. The data available have been increased in this paper by the preparation and measurement of a series of α -substituted pyrrolines and pyrrolidines.

The α -substituted pyrrolines were synthesized by the reaction of Cloke² as modified by Craig and Hixon.³ In using this reaction, it was found that the yields of the pyrrolines were markedly increased by avoiding the large excess of Grignard reagent recommended by Cloke. The yields obtained by using equimolar quantities of Grignard reagent and γ -chlorobutyronitrile are reported in Table I in comparison with yields by the original procedure as used by Craig.

The α -substituted pyrrolidines were prepared by the catalytic reduction of the corresponding α -substituted pyrrolines.

¹ I, Hixon and Johns, *THIS JOURNAL*, **49**, 1786 (1927); II, Allison and Hixon, *ibid.*, **50**, 168 (1928); III, Johns, Peterson and Hixon, *J. Phys. Chem.*, **34**, 2218 (1930); IV, Johns and Hixon, *ibid.*, **34**, 2226 (1930); V, Craig and Hixon, *THIS JOURNAL*, **53**, 4367 (1931).

² Cloke, *ibid.*, **51**, 1174 (1929).

³ Craig, Bulbrook and Hixon, *ibid.*, **53**, 1831 (1931).

TABLE I

Compound	Yield, %	Original yield, %
α -Benzylpyrroline	41	13
α -Phenylpyrroline	66	55
α -(<i>p</i> -Tolyl)-pyrroline	69	59

Preparation of Compounds

Trimethylene chlorobromide was prepared as described by Cloke.⁴

γ -Chlorobutyronitrile was prepared according to the directions found in "Organic Syntheses."⁵

α -Phenylpyrroline was prepared as reported by Craig,³ except that an equimolecular ratio of γ -chlorobutyronitrile and Grignard reagent was used. In calculating the amount of γ -chlorobutyronitrile required, the yield of phenylmagnesium bromide obtained was assumed to be within 5% of that reported by Gilman, Zoellner and Dickey.⁶ The boiling range was 120–130° (18 mm.) as reported by Craig. The melting point of the picrate checked that obtained by Gabriel and Colman at 198°. The compound was titrated electrometrically because the colorimetric end-point obtained with sodium alizarin sulfonate was indefinite.

Anal. Calcd. for $C_{10}H_{11}N$: neutralization equivalent, 145.1. Found: Fraction II, 145.8; Fraction III, 145.9.

α -Benzylpyrroline was prepared in much better yields than those reported by Craig.³ The reaction was carried out with the same modifications that were mentioned above in the preparation of α -phenylpyrroline. The compound boiled at 148–152° (34–36 mm.) or 110–114° (11–13 mm.). The chloroaurate melted at 125° as reported by Craig. The picrate prepared from an alcohol and ether mixture and recrystallized three times from alcohol and twice from an alcohol and ether mixture maintained a constant melting point at 111–112°. This compound was further identified by reduction to α -benzylpyrrolidine.

Anal. Calcd. for $C_{11}H_{13}N$: neutralization equivalent, 159.1. Found: Fraction I, 158.5; Fraction II, 159.3; Fraction III, 159.1.

α -Ethylpyrroline was prepared by the general method already mentioned and the separation of the compound was carried out according to Craig's directions. The compound boiled at 126° and the picrate melted at 87° as reported.

Anal. Calcd. for $C_8H_{11}N$: neutralization equivalent, 97.1. Found: Fraction I, 96.7; Fraction II, 96.7; Fraction III, 96.8.

α -(*p*-Tolyl)-pyrroline was prepared using the general method for the preparation of pyrrolines. The separation of the compound was carried out as in the preparation of α -phenylpyrroline; the compound is a solid melting at 60–61° and boiling at 125–132° (6–8 mm.) or 136–140° (16–18 mm.). A picrate was prepared from alcohol and recrystallized twice from a mixture of alcohol and water. It melted at 185–186°.

Anal. Calcd. for $C_{11}H_{13}N$: N, 8.80; neutralization equivalent, 159.1. Found: N, 8.65, 8.66; neutralization equivalent, 159.8, 159.9. Calcd. for $C_{11}H_{13}N \cdot HAuCl_4$: Au, 39.51. Found: Au, 39.77, 39.80.

The compound was further identified by reduction to α -(*p*-tolyl)-pyrrolidine.

α -Cyclohexylpyrroline was prepared by following the general procedure. The separation was similar to that for α -phenylpyrroline. The compound boils at 114–116°

⁴ Cloke, Anderson, Lachmann and Smith, *THIS JOURNAL*, **53**, 2791 (1931).

⁵ "Organic Syntheses," Vol. VIII, p. 52.

⁶ Gilman, Zoellner and Dickey, *THIS JOURNAL*, **51**, 1576 (1929).

(22–24 mm.) or 77–79° (4–6 mm.). A picrate was prepared in a mixture of alcohol and ether and recrystallized from alcohol. The melting point was 117°. It was difficult to obtain the base completely dry. The compound was reduced to α -cyclohexylpyrrolidine.

Anal. Calcd. for $C_{10}H_{11}N$: N, 9.26; neutralization equivalent, 151.2. Found: N, 9.36, 9.09; neutralization equivalent, Fraction II, 152.9; Fraction III, 151.9.

α -Benzylpyrrolidine was prepared from α -benzylpyrroline by the catalytic reduction method according to Craig.⁵ Adams and Shriner's platinum-oxide platinum black catalyst was used, with absolute alcohol acidified with hydrochloric acid as a solvent. The reduction was complete after two to three hours of shaking under 90 lb. of hydrogen pressure.

The compound boils at 129–131° (17–19 mm.) or 150–153° (44–46 mm.). The picrate was prepared and recrystallized twice in alcohol; m. p. 136–137°.

Anal. Calcd. for $C_{11}H_{13}N$: C, 81.85; H, 9.33; neutralization equivalent, 161.1. Found: C, 81.78, 81.30; H, 9.22, 9.40; neutralization equivalent, Fraction I, 160.8; Fraction II, 161.0; Fraction III, 161.0.

α -(*p*-Tolyl)-pyrrolidine was obtained from the corresponding pyrroline using the procedure mentioned for α -benzylpyrrolidine. The boiling points found were 128–130° (8–10 mm.) and 141–144° (23–25 mm.). A picrate was prepared and recrystallized in a 75% solution of alcohol. The melting point was 173°.

In 1901 Katzenellenbogen⁷ reported α -(*p*-tolyl)-pyrrolidine by the reduction of *p*-tolylpyridazine. The identity of the compound is questioned in the handbooks since the only evidence offered is the analysis of the picrate. The melting point of the picrate was reported as 150°, which does not check the picrate listed above.

The method of synthesis and analysis are sufficient evidence as to the identity of the compound.

Anal. Calcd. for $C_{11}H_{13}N$: C, 81.85; H, 9.33; neutralization equivalent, 161.1. Found: C, 81.50, 82.00; H, 9.29, 9.38; neutralization equivalent, Fraction I, 160.2; Fraction II, 161.7; Fraction III, 160.2.

α -Cyclohexylpyrrolidine was obtained by the addition of two hydrogen atoms to a molecule of α -cyclohexylpyrroline. The pyrroline contains but one double bond and in this case there is no doubt as to the position taken by the hydrogen atoms. The method of reduction is the same as that used previously and the reaction is perfectly definite. The theoretical amount of hydrogen being absorbed in two to three hours, gives practically a quantitative yield. The boiling point was 214–221°. When distilled under reduced pressure the boiling point was 84–87° (7–9 mm.) or 120–126° (39–41 mm.). The most satisfactory derivative prepared was the chloroaurate, which was recrystallized twice from benzene. The melting point is 105–106°. The compound is a strong base which forms a solid carbonate if allowed to stand in contact with the atmosphere.

Wibaut and DeJong⁸ have reported being able to obtain α -cyclohexylpyrrolidine by catalytic reduction of α -phenylpyrrole although Craig⁵ found that the catalytic reduction of α -phenylpyrroline gave an indefinite mixture containing some α -phenylpyrrolidine. Wibaut and DeJong identified the compound by analyzing the picrate for nitrogen. The boiling point given above, 214–221°, checks their value, 220–230°, but the melting point of the picrate given as 153° could not be confirmed.

Anal. Calcd. for $C_{10}H_{13}N$: C, 78.4; H, 12.53; neutralization equivalent, 153.2. Found: C, 78.8, 79.0; H, 12.31, 12.08; neutralization equivalent, Fraction II, 156.1;

⁷ Katzenellenbogen, *Ber.*, **34**, 3828 (1901).

⁸ Wibaut and DeJong, *Rec. trav. chim.*, **49**, 237 (1930).

Fraction III, 154.0. (The compound was difficult to obtain dry. Even though distilled from chips of sodium only the last fraction was completely dry.)

Measurement of Dissociation Constants.—The method used was that described by Carothers, Bickford and Hurwitz.⁹ The technique in measuring was that described by Craig¹ except for the α -(*p*-tolyl)-pyrroline which was a solid and could not be sealed in ampules for weighing. It was weighed in a watch glass as rapidly as possible.

The criteria of purity were constant boiling point, three fractions were collected within a range of 2°. Neutralization equivalents of each fraction were determined. In the case of α -cyclohexylpyrroline and α -cyclohexylpyrrolidine, where the first two fractions were not completely dry, the solutions were made up according to the amount of base titrated. The P_H of these solutions checked the P_H of the solutions made up from fractions that were completely dried. In all cases dissociation constants were

TABLE II

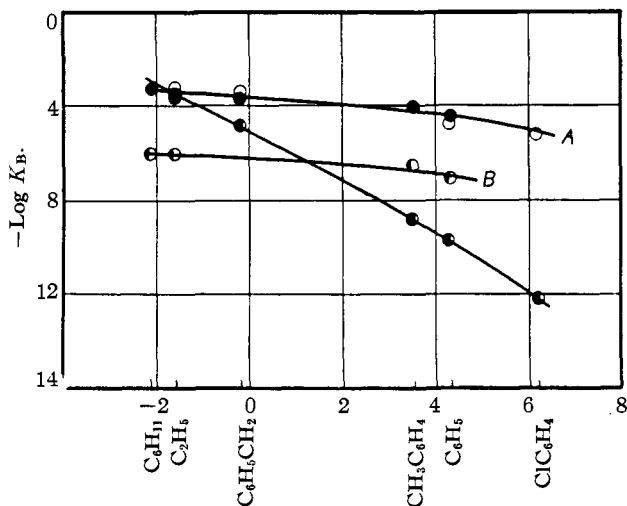
DISSOCIATION CONSTANTS OF α -SUBSTITUTED PYRROLINES AND PYRROLIDINES (25°)

Compound	E. m. f.	P_H	-Log K_B	
α -Ethylpyrroline	Fraction I	0.7133	7.91	6.09
	Fraction II	.7133	7.91	6.09
	Fraction III	.7138	7.92	6.08
α -Benzylpyrroline ^a	Fraction I	0.6648 ^a	7.08 ^a	6.92 ^a
	Fraction II	.6651	7.08	6.92
	Fraction III	.6693	7.16	6.84
α -(<i>p</i> -Tolyl)-pyrroline	Fraction I	0.6941	7.59	6.41
	Fraction II			
	Fraction III	.6942	7.59	6.41
α -Phenylpyrroline	Fraction I	0.6519	6.88	7.12
	Fraction II	.6428	6.73	7.27
	Fraction III	.6440	6.75	7.25
α -Cyclohexylpyrroline	Fraction I	0.7160	7.95	6.05
	Fraction II	.7159	7.95	6.05
	Fraction III	.7160	7.95	6.05
α -(<i>p</i> -Tolyl)-pyrrolidine	Fraction I	0.8381	10.02	3.98
	Fraction II	.8375	10.00	4.00
	Fraction III	.8343	9.95	4.05
α -(Benzyl)-pyrrolidine	Fraction I	0.8594	10.37	3.63
	Fraction II	.8583	10.34	3.66
	Fraction III	.8589	10.36	3.64
α -Cyclohexylpyrrolidine	Fraction I	0.8859	10.81	3.19
	Fraction II	.8838	10.78	3.22
	Fraction III	.8849	10.80	3.20

^a The values given represent the precision obtainable, but the voltage drifts and the values are probably too low. See discussion.

⁹ Carothers, Bickford and Hurwitz, THIS JOURNAL, 49, 2908 (1927).

measured on three fractions. The results are reported in tabular form (Table II) and are shown graphically in Fig. 1.



Electron sharing ability of radicals.

Fig. 1.—Relative magnitudes of the basic dissociation constants of substituted amines of the series RNH_2 (●); of the series RCH_2NH_2 (○); of the α -substituted pyrrolidines (●); and of the α -substituted pyrrolines (○). The drop from curve A for the α -substituted pyrrolidines to curve B for the α -substituted pyrrolines represents the influence of the introduction of one double bond in the pyrrolidine ring.

Discussion of Results

A satisfactory dissociation constant could not be obtained for α -benzylpyrroline. The value always drifted and was lower than the value which would be predicted on the basis of the curve for the pyrroline series. A solution of the base containing one-half equivalent of hydrochloric acid became colored after standing for eight hours. The voltage of the solution continued to drop from day to day, and after a month's time a total drop of 150 millivolts had been observed. The solutions became dark orange in color and deposited sediment at the bottom even though the solutions were less than 0.01 molar in concentration. In comparison, a solution of α -ethylpyrroline and one-half equivalent of hydrochloric acid showed no sign of turbidity and only a slight yellow color after twice the period of time. The drop in voltage was only 9 millivolts, which lowered the value for $-\log K_B$ by 0.16. These observations indicate that even though the α -ethylpyrroline is not stable indefinitely, it is stable enough to give a reliable dissociation constant by the half-neutralization method. The α -benzylpyrroline is relatively unstable and the method would probably

give results lower than the true values. Lipp and Widmann¹⁰ report that α -substituted pyrrolines react with water to give γ -aminopropyl substituted ketones. This would offer a possible explanation of the change observed.

The drift in e. m. f. of a half-neutralized benzylpyrroline solution is shown in Fig. 2, where the voltage of the solution is plotted against time,

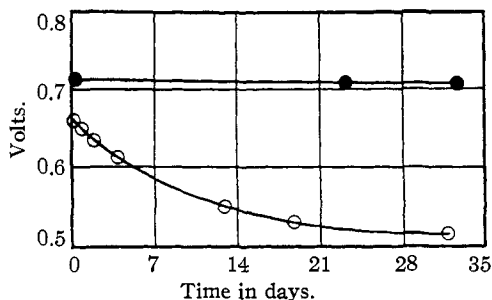


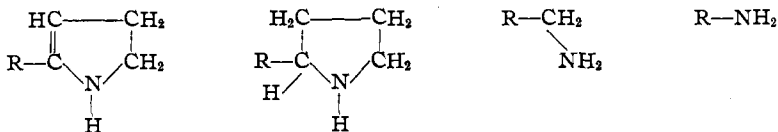
Fig. 2.—Comparison of the stability of an α -benzylpyrroline solution \odot with the stability of an α -ethylpyrroline solution \bullet as measured by the change in e. m. f. of half-neutralized solutions.

Similar values for the α -ethylpyrroline are also represented for comparison.

It was hoped that the α -benzylpyrroline might be more stable in the presence of an equivalent of hydrochloric acid. The solutions did not color and the voltage seemed to be more constant over periods of time, but the necessary precision was not obtained and the results were therefore discarded. The properties of this

compound should be more thoroughly investigated before a value for the dissociation constant is accepted.

The available dissociation constants of the four series of compounds



are compared graphically in Fig. 1 using the same magnitudes for the electron sharing ability of the various radicals R used in the previous publications. The results substantiate the working hypothesis actuating these studies; if the criteria for measuring chemical affinity are observed, the polar properties of any group may be expressed as a mathematical function of the electron sharing ability of the attached radical.

Summary

The general method for the preparation of α -substituted pyrrolines has been modified to improve yields.

α -(*p*-Tolyl)-pyrroline, α -cyclohexylpyrroline and α -benzylpyrrolidine have been described for the first time.

Dissociation constants of a few α -substituted pyrrolines and pyrrolidines have been measured.

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¹⁰ Lipp and Widmann, *Ann.*, **409**, 79 (1915).