TABLE I

METHYLMAGNESIUM IODIDE–AZOMETHINE ADDITION COMPOUNDS

Compound	Formula	N, % Calcd.	N, % Found	Mg, % Found	Mg, % Found	I, % Calcd.	I, % Found
Benzophenone anil[a]	$C_{20}H_{18}NMgI$	3.30	2.77	5.74	6.69	29.96	30.27
Benzylideneaniline[b]	$C_{14}H_{14}NMgI$	4.03	3.65	7.00	7.21	36.52	36.98
Benzylidenebenzylamine[c]	$C_{15}H_{16}NMgI$	3.87	3.00	6.72	6.45	35.11	35.18
Benzylidene-*n*-butylamine[d]	$C_{12}H_{18}NMgI$	4.27	3.47	7.43	7.04	38.75	39.23
Benzylidenecyclohexylamine[c]	$C_{14}H_{20}NMgI$	3.96	3.63	6.88	8.04	35.90	34.48
Benzylidene-ethylamine[d]	$C_{10}H_{14}NMgI$	4.68	4.26	8.12	8.33	42.38	43.88
Benzylideneisopropylamine[d]	$C_{11}H_{16}NMgI$	4.47	4.18	7.76	7.32	40.49	40.71
Butylidenebenzylamine[d]	$C_{12}H_{18}NMgI$	4.27	3.53	7.43	7.06	38.75	39.44

[a] Prepared by the method of G. Reddelien, *Ber.*, **43**, 2476 (1910). [b] Prepared as described in "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 80. [c] Prepared by the method of A. T. Mason and G. R. Winder, *J. Chem. Soc.*, **65**, 191 (1894). [d] Prepared by the method of H. Zauschirm, *Ann.*, **245**, 281 (1888).

hygroscopic nature of the compounds made analyses difficult.

A quantitative study of the reactions between certain azomethines and 2-substituted Δ^1-pyrrolines and methylmagnesium iodide using the Zerevitinov method[6] indicated that these compounds, all containing the >C=N— group, reacted with one mole of the reagent in butyl ether, while analyses of addition compounds of 2-phenyl-Δ^1-pyrroline pointed to the same conclusion.

In order to determine the exact nature of the compounds resulting when such reactions take place with azomethines, a series of methylmagnesium iodide–azomethine compounds was prepared and analyzed by a method similar to that of Sachs and Sachs, except that butyl ether was used as a solvent, a modification which enabled the compounds to be more easily separated and dried. The analytical data listed in Table I show that equimolar quantities of the azomethine and Grignard reagent had reacted to form the addition compound.

Experimental

The azomethines were prepared as described in the literature (see Table I). The methylmagnesium iodide solution was prepared in the usual manner from 62.7 g. of methyl iodide, 10.8 g. of magnesium and 250 ml. of anhydrous butyl ether. To 1 g. of the azomethine, dissolved in 25 ml. of the butyl ether, was added slightly more than the theoretical quantity of the methylmagnesium iodide solution. The ether was decanted from the tarry precipitate first formed (generally yellowish in color) and more butyl ether added. The precipitate was then rubbed until it separated out as a powder, whereupon it was removed by filtration and dried in a vacuum desiccator.

Benzylidene-*n*-butylamine and methylmagnesium iodide yielded an oil, which solidified eventually when immersed in an ice-bath.

When the procedure of Sachs and Sachs was used, namely, preparing the compound in ethyl ether, washing four times with fresh ether, and rubbing until the tar turned to powder, the compound was never obtained completely dry and the analyses were not satisfactory.

The reaction of benzophenone anil with the Grignard reagent in benzene as described by Short and Watt[7] was repeated, but although a gas was evolved, no separation of an addition compound was observed.

The data of Table I summarize the analytical results obtained for the addition compounds thus prepared. Magnesium was determined as the sulfate and nitrogen was determined by the Dumas method, both as described by Niederl and Niederl.[8] Iodine was determined gravimetrically as silver iodide.

(6) P. M. Maginnity with J. B. Cloke, THIS JOURNAL, **73**, 49 (1951).

(7) W. F. Short and J. S. Watt, *J. Chem. Soc.*, 2293 (1930).

(8) J. B. Niederl and V. Niederl, "Micromethods of Quantitative Organic Analysis," John Wiley and Sons, Inc., New York, N. Y., 1942.

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Preparatory Method for N-Vinyl-2-pyrrolidone

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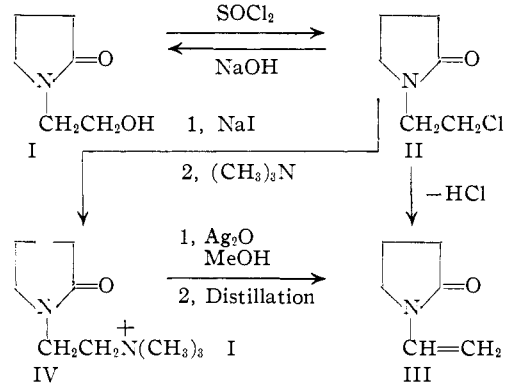
The present commercial process for the preparation of N-vinyl-2-pyrrolidone is based on the high pressure reaction of acetylene with 2-pyrrolidone.[1a,b] The extensive interest in the polymer, polyvinylpyrrolidone,[2] as a blood plasma extender[3] prompted us to consider alternative syntheses of the monomer avoiding the use of acetylene and pressure. Two such syntheses are outlined in the flow sheet.

The preparation of N-(β-hydroxyethyl)-2-pyrrolidone (I) by the passage of 2-aminoethanol and butyrolactone over dehydration catalysts has been reported.[1a,4] The corresponding chloro derivative, (β-chloroethyl)-2-pyrrolidone (II), was reported[1a] as being formed by the action of thionyl chloride on I. We have prepared I by heating a solution of butyrolactone in excess 2-aminoethanol to 180–190° so that the water liberated was entrained by the slowly distilling 2-aminoethanol. The yields

FLOW SHEET



(1) (a) J. W. Reppe, "Acetylene Chemistry," PB Report No. 18852-S, U. S. Department of Commerce, New York, N. Y., Charles A. Meyer & Co., Inc. (1949); (b) French Patent 865,354 (May 21, 1941).

(2) An excellent summary on polyvinylpyrrolidone is "PVP," General Aniline and Film Corporation, New York, March, 1951.

(3) PVP (Macrose) is the trade name for the Schenley Laboratories blood plasma extender.

(4) In this connection see C. Schuster and A. Seih, German Patent 694,043; E. Spath and J. Lintner, *Ber.*, **69**, 2727 (1936).

were 85–90%. Benzene solutions of the chloro compound (II) were dehydrohalogenated to N-vinyl-2-pyrrolidone (III) using potassium hydroxide, sodium amide or sodium methoxide. Using powdered sodium hydroxide a 76% yield of the alcohol (I) was obtained.

A less attractive method involved the conversion of the chloro compound (II) to the quaternary iodide (IV) with sodium iodide and trimethylamine in acetone. Treatment of a methanolic solution of the quaternary iodide with silver oxide and subsequent distillation afforded an 82% yield of III.

Experimental[5,6]

N-(β-Hydroxyethyl)-2-pyrrolidone (I).—A solution formed by adding 860.0 g. (10.0 moles) of butyrolactone to 750.0 g. (12.3 moles) of 2-aminoethanol was heated at a temperature of 180–190° so that over a period of 20 hours the excess 2-aminoethanol and the liberated water were distilled over. Distillation of the residue afforded 1,135 g. of I (88%), b.p. 142–143° at 2.3 mm.

Anal. Calcd. for $C_6H_{11}O_2N$: C, 55.81; H, 8.53. Found: C, 55.74; H, 8.64.

N-(β-Chloroethyl)-2-pyrrolidone (II).—To a cooled solution of 129.0 g. (1.0 mole) of I in 100 ml. of benzene was added 119.0 g. (1.0 mole) of thionyl chloride at such a rate that the temperature did not go higher than 35°. After the addition, stirring was continued for three hours at room temperature. The benzene was removed under vacuum and distillation of the residue gave 112 g. (76%) of a colorless product which slowly became yellow on standing; b.p. 118–119.5° at 7 mm.

Anal. Calcd. for $C_6H_{10}ClNO$: C, 48.64; H, 6.76; N, 9.46. Found: C, 48.68; H, 6.51; N, 9.42.

Dehydrohalogenation of the Chloro Compound (II) **to N-Vinyl-2-pyrrolidone** (III). **A.**—To a solution of 22.2 g. (0.15 mole) of II in a 100 ml. of benzene was added 9.0 g. (0.17 mole) of sodium methoxide. After stirring at room temperature for four hours, the mixture was filtered and the benzene was removed under vacuum. Distillation of the residue yielded 8.1 g. (48%) of III, b.p. 64–66° at 2.0 mm., m.p. 17°.

Anal. Calcd. for C_6H_9NO: C, 64.86; H, 8.11; N, 12.61. Found: C, 64.93; H, 7.88; N, 12.44.

B.—A mixture of 14.8 g. (0.1 mole) of II, 100 ml. of benzene and 3.9 g. (0.1 mole) of sodium amide was refluxed for five hours. After filtering and removing the benzene under vacuum, 6.1 g. (55%) of III was isolated by distillation.

C.—A mixture of 14.8 g. (0.1 mole) of II, 125 ml. of benzene and 6.7 g. (assay 85% KOH, corresponding to 0.1 mole) of potassium hydroxide was refluxed for 22 hours, while the liberated water was collected in a Dean and Stark receiver. The reaction mixture was filtered and concentrated. Distillation afforded 6.2 g. (56%) of III.

Polymerization to polyvinylpyrrolidone was effected by keeping a solution containing 1.0 ml. of III, 1.0 ml. of water, 0.01 ml. of Superoxol and 0.01 ml. of concentrated aqueous ammonium hydroxide at 70°. In a short time the temperature rose spontaneously and the solution became extremely viscous.

It was observed that distillation of II was accompanied by some decomposition losses. In order to obtain better over-all yields a benzene solution of I was treated with thionyl chloride as described above. At the end of the stirring an excess of solid sodium bicarbonate was added, the reaction mixture was filtered, and the conversion to III effected by the treatment with the theoretical amount of potassium hydroxide as described above under method C. In this manner 21.8 g. (49% over-all yield) of III was isolated from 51.6 g. (0.4 mole) of I.

Regeneration of I.—To 14.8 g. (0.1 mole) of N-(β-chloroethyl)-2-pyrrolidone (II) was added a suspension of 4.0 g. (0.1 mole) of finely powdered sodium hydroxide in 100 ml. of benzene and the reaction mixture refluxed for 12 hours. After filtering and removing the benzene, 9.8 g. (76% yield) of I was isolated by distillation.

Formation of the Quaternary, IV.—A solution containing 7.4 g. (0.05 mole) of II and 7.5 g. (0.05 mole) of sodium iodide in 120 ml. of acetone was refluxed for four hours. The resulting reddish solution was filtered and added to 120 ml. of acetone in a 500-ml. centrifuge bottle. To the resulting solution gaseous trimethylamine was introduced for 15 minutes and the bottle stoppered. Within ten hours separation of the quaternary appeared complete. The crystalline precipitate was collected by filtration; yield 7.9 g. (53%). An analytical sample of IV, white plates, m.p. 224–225°, was obtained by recrystallization from methanol.

Anal. Calcd. for $C_9H_{19}ION_2$: C, 36.24; H, 6.37; N, 9.39; I, 42.61. Found: C, 36.30; H, 6.42; N, 9.16; I, 42.94.

On standing for several days the quaternary became discolored.

Attempts were made after refluxing II with sodium iodide to isolate the corresponding iodo compound. After removal of the sodium chloride by filtration and the acetone by vacuum evaporation, careful distillation gave a yellow viscous oil, b.p. 125–127.5° at 0.5 mm., corresponding to a 74% conversion to the iodo compound. This freshly distilled product analyzed only closely for N-(β-iodoethyl)-2-pyrrolidone and on standing it assumed a deep red color. If the temperature of the bath on distillation was allowed to rise much over 150° considerable decomposition occurred as evidenced by the deepening color of the distillate. The analytical results reported are those obtained from a freshly redistilled sample.

Anal. Calcd. for $C_6H_{10}INO$: C, 30.13; H, 4.18; N, 5.86; I, 53.1. Found: C, 32.54; H, 4.43; N, 8.34; I, 50.89.

Decomposition of the Quaternary IV.—To a solution of 10.2 g. (0.034 mole) of IV dissolved in 100 ml. of absolute methanol was added 7.0 g. of silver oxide and the resulting mixture allowed to stand overnight in the dark. Filtration and evaporation in the cold gave an amber-colored residue. Distillation yielded 3.1 g. (81%) of III.

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(5) The melting points and boiling points are uncorrected.

(6) All microanalyses were performed by Clark Microanalytical Laboratory, Urbana, Illinois.

Hexahydroindolo[2,3-a]quinolizine[1]

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In a program carried out in these laboratories to investigate the relationship between curariform activity and chemical structure, a number of β- and γ-carbolinium salts were synthesized and found to exhibit weak curare activity.[2] It was felt that compounds approaching the structure believed at that time[3] to be present in the calabash curare alkaloids should be synthesized, and some compounds[4] prepared on this basis showed marked curare activity.

A continuation of this approach has led us to prepare the tetracyclic compound hexahydroindolo-[2,3-a]-quinolizine (II).

This compound was readily obtained by application of the Fischer indole synthesis to 1-ketoquinolizidine.[5] The synthesis of the latter by simplified

(1) Aided by a grant from the National Foundation for Infantile Paralysis, Inc.

(2) V. Boekelheide and C. Ainsworth, THIS JOURNAL, **72**, 2132 (1950).

(3) P. Karrer and H. Schmid, *Helv. Chim. Acta*, **29**, 1853 (1946). More recent work [H. Schmidt, A. Ebnöther and P. Karrer, *ibid.*, **33**, 1486 (1950)] indicates that the earlier ideas on the structure of the calabash curare alkaloids may require considerable modification.

(4) L. E. Craig and D. S. Tarbell, THIS JOURNAL, **71**, 462 (1949).

(5) G. R. Clemo and G. R. Ramage, *J. Chem. Soc.*, 437 (1931). An analogous synthesis of a benzo derivative of II was reported by G. R. Clemo and G. A. Swan, *ibid.*, 617 (1946).