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

PREPARATION AND PROPERTIES OF SOME SUBSTITUTED JULOLIDINES¹

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Julolidine (I, R = H) is readily obtained from tetrahydroquinoline, for ex-



ample by the utilization of trimethylene chlorobromide (1) or β -chloropropionyl chloride (2). For various reasons these routes are not readily adaptable to the preparation of julolidines substituted on the aromatic ring, with the exception of the 9-methyl- and 9-methoxyl- derivatives (3). The similarity of julolidine to N,N-dimethylaniline suggested that the aromatic substitution reactions known to be successful with dimethylaniline might be used to prepare many previously unknown 9-substituted julolidines. Such an investigation interested us because the quinolizidine skeleton present in julolidine is a major part of the structures of an important group of alkaloids, and because the saturated rings in julolidine present interesting questions related to the effect of geometrical conformation on the properties of N,N-dialkylanilines. In this paper are reported some exploratory experiments in this field.

Nitrosation of julolidine has been reported by Pinkus (3) as an unsuccessful reaction which led to an unidentified red solid. We are able to confirm Pinkus' observation that no nitroso compound is formed, either with nitrous acid or N-nitroso-N-methylaniline, and we have furthermore inferred that the red substance formed is an oxidation product of 9,9'-bijulolidyl (II). Bijulolidyl can be



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obtained from the red substance by the action of reducing agents or by disproportionation in basic solution. Its structure has been inferred from its analysis, its molecular weight, and its formation from julolidine as well by other oxidizing but not necessarily nitrosating reagents, such as copper nitrate in acetic anhydride, aqueous copper sulfate, lead dioxide, potassium permanganate, and diazotized sulfanilic acid. The colored substance is developed from bijulolidyl even by carbon tetrachloride in daylight. A similar oxidative coupling has been observed with dimethylaniline, resulting in N, N, N', N'-tetramethylbenzidine (4, 5).

The very easy oxidation of juloidine in the (presumably) 9-position suggests an unusually great availability of electrons at that point. Previous discussions of the effect of *ortho*-substituents on N, N-dialkylanilines strongly suggest the opposite effect on electron-density by *ortho*-substituents, due to interference by the *ortho*-substituents with coplanarity of the N-attached atoms with the benzene ring (6, 7). Further examples of the behavior of juloidine and its derivatives which appears anomalous when the substances are considered as *ortho*-substituted dialkylanilines have been encountered in this work, and will be discussed together in a later section.

Bromination and thiocyanation of julolidine in glacial acetic acid solution were both successful. The 9-thiocyanojulolidine so obtained did not give satisfactory carbon and hydrogen analyses, although it melted sharply, but support for its identity was obtained by its nearly quantitative conversion to 9,9'dijulolidyl disulfide. In fact, it may be contamination with this product which was responsible for the poor analyses of the thiocyanate.

Although Friedel-Crafts acetylation and benzoylaton of julolidine were not successful, the Vilsmeier-Haack modification (8, 9), making use of N-methyl-formanilide, benzanilide, and o-toluanilide, led to 9-julolidinecarboxaldehyde, 9-benzoyljulolidine, and 9-o-toluyljulolidine (I, R = acyl) in satisfactory yields (75%, 70%, and 55%); attempted acetylation with acetanilide produced only tar, as it has been reported to do with dimethylaniline (10).

From 9-julolidinecarboxaldehyde a variety of compounds was made, as indicated schematically in the diagram. The conversion to 9-julolidinecarboxylic acid was accomplished indirectly through the nitrile which was made both by the Schmidt reaction on the aldehyde and by dehydration of the aldoxime. This acid was also obtained by a Cannizzaro reaction in 60% yield. As the ordinary Cannizzaro reaction fails with 9-julolidinecarboxaldehyde as it is known to do with *p*-dimethylaminobenzaldehyde (11), resort was made to the modification described by Pearl (12), whereby a silver catalyst is used in addition to alkali. It was presumably oxidation due to the presence of the silver which was responsible for the formation of more than the theoretical 50% yield of carboxylic acid, along with 9-julolidinemethanol isolated in reduced yield as its methiodide. 9-Julolidinemethanol was better prepared by reduction of the aldehyde with lithium aluminum hydride; it is unstable in air and was converted to its methiodide for characterization. The analogous 9-(aminomethyl)julolidine was prepared by lithium aluminum hydride reduction of the nitrile; it was obtained as an oil which was characterized as its acetyl derivative.



9-Benzovljulolidine was converted to a mixture of amides by the Schmidt reaction. Hydrolysis of the mixture gave benzoic acid in yields up to 46%, and an amphoteric acid, identical with the 9-julolidinecarboxylic acid obtained from the aldehyde, in varying yields. It is thereby established that the formylation and benzovlation attacked the same position on the julolidine ring. Furthermore, it is apparent that the Schmidt reaction inserted an NH moiety to a significant extent on either side of the carbonyl, in accord with previous results with psubstituted benzophenones (13). The aminojulolidine expected to accompany the acids in the products from the hydrolysis of the amide mixture proved to be difficult to isolate. It was, of course, accompanied by aniline, and, unexpectedly, by julolidine, whose formation by decarboxylation was apparently the reason for the erratic yields of 9-julolidinecarboxylic acid. In addition, aminojulolidine is readily oxidized (14) by air, as would be expected for a p-phenylenediamine derivative. It was obtained initially in small yield as a brown picrate, m.p. 140-148°, which on recrystallization became reddish black, assumed clean, crystalline character, and then melted at 165–168°. This is presumed to be a quinhydrone-like oxidation product of 9-aminojulolidine picrate; the change in carbon and hydrogen content due to loss of one hydrogen atom is too small to be surely detected by analysis.

In an attempt to obtain a more satisfactory preparation of 9-aminojulolidine, 9-o-toluyljulolidine was subjected to the Schmidt reaction, since o-methylbenzophenone had been found to give almost entirely o-toluanilide (15). Although a small amount of the picrate, m.p. 167–168.5°, was obtained, this approach was no more satisfactory. The yields in the several steps were poor, and the Schmidt reaction appeared to have given both isomeric amides, as well as some N-o-tolyl-N'-9-julolidylurea. The formation of such an unusual side product in a Schmidt reaction is discussed in another connection elsewhere (16).

Julolidine brominated readily in glacial acetic acid at room temperature, and a monobromo product was isolated in 50% yield. An attempt to prepare a Grignard reagent from it was unsuccessful, and an attempt to prepare bijulolidyl from it by a Wurtz-Fittig reaction led only to julolidine. An attempt was also made to synthesize 9-bromojulolidine from 6-bromotetrahydroquinoline and trimethylene chlorobromide; the product was mainly tar.

Sulfonation of julolidine by a method which succeeds with dimethylaniline (17) led only to a very small yield of an acidic product which appeared from its analysis and equivalent weight to be a dijulolidylsulfone disulfonic acid.

An attempt to run a Mannich reaction on julolidine with piperidine and formaldehyde produced only an insoluble, nearly infusible base, apparently polymeric and obviously not 9-piperidinomethyljulolidine.

A number of condensation reactions of 9-julolidinecarboxaldehyde were run, in addition to the formation of simple derivatives. An attempt to obtain a mixed benzoin condensation by reaction with benzaldehyde produced only benzoin itself, as does *m*-dimethylaminobenzaldehyde (18), in contrast to *p*-dimethylaminobenzaldehyde, which has been reported to react readily with benzaldehyde (19). The reaction of 9-julolidinecarboxaldehyde with acetone in the presence of aqueous sodium hydroxide led only to tar, under conditions where *p*-dimethylaminobenzaldehyde gives a clean product (20).

However, condensation of the aldehyde with α -picoline methiodide proceeded in 96% yield to give an intensely colored stilbazole dye (III). The absorption spectrum of this dye was compared to that of *p*-dimethylaminostilbazole meth-



iodide in the range 3000-5000 Å. The dye from julolidine showed a single, broad maximum at 4780 Å (ϵ 26,100), which is strongly shifted toward the red and is more intense compared to the maximum of the dimethylamino analog, which we found at 4370 Å (ϵ 25,300) [Phillips (7) reports a value of 4440 Å for this compound]. The effect of substituents ortho to a dialkylamino group in both benzenes (6) and in stilbazoles (7) is to cause a shift toward the blue and a lessening of the intensity of the absorption; these effects have been correlated with the degree to which the ortho-substituent interferes with coplanarity of the Nattached atoms with the benzene ring. That the opposite effects are observed in the julolidine system would, according to such interpretations, indicate that the fused-ring system actually favors coplanarity, rather than hindering it. In dimethylaniline there is perhaps some departure from coplanarity due to rotatory vibration about the nitrogen-benzene axis resulting from thermal collisions. An effect of cyclization to the ortho position similarly interpreted as due to favored coplanarity has recently been reported (14); the oxidation potential for semiquinone formation from 9-aminojulolidine shows an exceptional shift in the positive direction as compared to *p*-aminodimethylaniline, whereas substituents ortho to the tertiary amino group have the opposite effect.

A further effect which may derive from the favored coplanarity is the failure of 9-juloidinecarboxaldehyde to take part in the benzoin condensation. An

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unusually high electron density in the 9-position might so reduce the fractional positive charge on the carbonyl-carbon as to render reaction at that point by cyanide ion or the carbanion of a mandelonitrile, essential steps in the benzoin condensation (21), too improbable for effective result.

In addition, the spectra support the assignment of the 9-position for the substituents inserted by the electrophilic reagents used in this work. The stilbazole methiodide derived from 8-julolidinecarboxaldehyde would not show in such pronounced degree the auxochromic influence of the tertiary amino group, which would then be *meta* to the conjugated vinylene bridge, but should closely resemble the stilbazole methiodide from *m*-dimethylaminobenzaldehyde, whose absorption maximum at about 3700 Å (7) is over 1000 Å on the blue side of that of the julolidine dye we have prepared.

EXPERIMENTAL²

Attempted nitrosation of julolidine and formation of bijulolidyl. Treatment of 5.0 g. of julolidine "hydrohalide"³ in 20 ml. of cold, concentrated hydrochloric acid with an aqueous solution of 1.5 g. of sodium nitrite produced a blood-red solution and a small amount of red solid. The red color of the solid could be washed off with fresh, concentrated hydrochloric acid, but returned gradually on standing in air. Solution of the solid in water and alkalizing with sodium hydroxide gave a brown precipitate which became nearly colorless when recrystallized from acetone, and then melted at $207-208^{\circ}$. A larger quantity of this substance was obtained by alkalizing the original, red, acid filtrate; total yield, 0.7 g. It was subsequently identified with the product of the action of copper nitrate on julolidine, with which there was no depression of melting point, and which is believed to be 9,9'-bijulolidyl.

Anal.^m Calc'd for C₂₄H₂₈N₂: C, 83.68; H, 8.19; Mol. wt., 344.

Found: C, 83.28; H, 8.42, Mol. wt. (Rast), 330.

In another experiment, 2.5 g. of julolidine hydrohalide in 20 ml. of ethanolic hydrogen chloride at 0° was treated with 1.5 g. of N-nitroso-N-methylaniline in 100 ml. of dry ether. After 48 hours, the red solid which had separated was filtered off and treated with aqueous sodium hydroxide producing, after recrystallization of the product from acetone, 0.5 g. of bijulolidyl, m.p. 206° .

Attempted nitration of julolidine. Julolidine (2.0 g.) was dissolved in 10 ml. of acetic anhydride, and 3 g. of powdered copper nitrate trihydrate was added in portions with shaking, according to the method of Menke (22). When the mixture was then poured into 200 ml. of water a brown precipitate separated which, when recrystallized from aqueous ethanol, weighed 1.0 g. (50%), m.p. $207-208^{\circ}$.

Other nitrating conditions, using nitric acid in acetic acid or sulfuric acid solution, led mainly to tar, accompanied by some of the red material.

Attempt to couple julolidine with diazotized sulfanilic acid. To a cold solution of 1.5 g. of julolidine in 5 ml. of glacial acetic acid was added an aqueous solution of the diazonium salt, freed of nitrous acid by urea, prepared from 1.1 g. of sulfanilic acid, according to the procedure of Hickinbottom and Lambert (23) for coupling with diisoamylaniline. The solution turned red instantly, but an attempt to precipitate a potassium salt by the addition of base produced only 0.2 g. of bijulolidyl.

Treatment of acidic solutions of julolidine with copper sulfate, with potassium per-

² Melting points are uncorrected. Analyses are by Micro-Tech Laboratories, Skokie, Ill.^(m) or by Clark Microanalytical Laboratory, Urbana, Ill.^(c).

³ Mixed hydrobromide-hydrochloride, as obtained from tetrahydroquinoline and trimethylene chlorobromide (1). manganate, or lead dioxide also converted it to the red compound, which could be decolorized with sodium bisulfite, and decolorized and precipitated by ammonia or stronger bases.

9-Bromojuloidine. A 5% solution of bromine in acetic acid was added slowly to 5.0 g. of juloidine in 20 ml. of glacial acetic acid, until excess bromine was detectable with starchiodide external indicator. The resulting red slurry was diluted and alkalized with sodium hydroxide and extracted with ether. Distillation of the dried extracts gave 3.7 g. (50%) of 9-bromojuloidine, b.p. 135-136.5°/0.15 mm. It solidified when placed in a Dry Ice-acetone bath, and then melted at 36.5°. Because it discolored rapidly on standing, it was converted to the *picrate* in ether solution and recrystallized from ethanol for analysis.

Anal.^c Calc'd for C₁₈H₁₇BrN₄O₇: C, 44.92; H, 3.56.

Found: C, 45.57; H, 3.60.

9-Thiocyanojulolidine. To 4.0 g. of julolidine and 4.0 g. of ammonium thiocyanate in 50 ml. of glacial acetic acid was added dropwise with stirring over 20 min., 1 ml. of bromine in 5 ml. of glacial acetic acid while the temperature was kept between 10° and 20° [directions of Brewster and Schroeder for thiocyanation of dimethylaniline (24)]. Dilution with 800 ml. of water produced a solid which crystallized from aqueous ethanol as colorless needles, m.p. 93-94°, wt. 0.4 g. (64%).

Anal.^m Cale'd for C₁₃H₁₄N₂S: C, 67.78, H, 6.13.

Found: C, 69.28, H, 6.43.

Constant and more satisfactory analyses could not be obtained, and it was felt that the product may have been contaminated with dijulolidyl disulfide (see below).

9.9'-Dijulolidyl disulfide. When 2.0 g. of 9-thiocyanojulolidine was warmed with 20 ml. of 10% alcoholic potassium hydroxide, a yellow solid separated rapidly. After filtration and recrystallization from ethanol, the product formed yellow prisms, wt. 1.7 g. (96%), m.p. 185-186° d.

Anal.^m Calc'd for C₂₄H₂₈N₂S₂: C, 70.53; H, 6.90.

Found: C, 70.63; H, 6.87.

Sulfonation of julolidine. A mixture of 4.5 g. of julolidine "hydrohalide" and 5 ml. of concentrated sulfuric acid was heated for 4 hours at 180°, cooled, and poured into 50 ml. of water. The mixture was alkalized with ammonia and extracted with ether to remove the unreacted julolidine, and reacidified with hydrochloric acid. A small amount of solid formed when the solution was evaporated to a small volume; after recrystallization from water, it weighed 0.3 g. (ca. 5%), and showed no definite melting point, but charred on heating.

Anal.^m Calc'd for C₂₄H₂₈N₂O₈S₃: C, 50.68; H, 4.96; Neut. equiv., 284.

Found: C, 50.51; H, 4.94; Neut. equiv., 281.

9-Juloidinecarboxaldehyde. To a mixture of 6.0 g. of N-methylformanilide and 7 g. of phosphorus oxychloride cooled in an ice-bath was added slowly a solution of 6.0 g. of juloidine in a small amount of ether. After standing overnight, the mixture was decomposed with water, made alkaline, and steam-distilled to remove N-methylaniline. The aldehyde crystallized in the distilland on cooling, and was collected and recrystallized from aqueous ethanol; it formed colorless scales, wt. 5.2 g. (75%), m.p. 83°.

Anal.^m Cale'd for C₁₃H₁₅NO: C, 77.58; H, 7.51.

Found: C, 77.37; H, 7.64.

The oxime was obtained from aqueous ethanol as colorless platelets, m.p. 127-128°.

Anal.^m Calc'd for C₁₃H₁₆N₂O: C, 72.20; H, 7.48.

Found: C, 72.11; H, 7.38.

The p-nitrophenylhydrazone formed shining black crystals from ethanol, m.p. 254°.

Anal.^m Calc'd for C₁₉H₂₀N₄O₂: C, 67.84; H, 6.01.

Found: C, 67.51; H, 5.94.

9-Benzoyljulolidine. A mixture of 3.0 g. of benzanilide, 6.0 g. of julolidine, and 3 g. of phosphorus oxychloride was heated at 120° for one hour, according to the directions of Shah, Deshpanle, and Chaubal (25) for the benzoylation of dimethylaniline. The mixture was then boiled for a short time with 15 ml. of concentrated hydrochloric acid and diluted with 20 ml. of water. Upon partial neutralization a green oil separated and soon solidified;

after recrystallization from aqueous ethanol it was obtained as colorless prisms, m.p. $108-109^{\circ}$, yield 5.5 g. (70%).

Anal.^m Calc'd for C₁₉H₁₉NO: C, 82.26; H, 6.92.

Found: C, 82.30; H, 6.78.

The oxime was obtained as light yellow needles, m.p. 202-203°.

Anal.^m Calc'd for C₁₉H₂₀N₂O: C, 78.05; H, 6.91.

Found: C, 78.08; H, 6.90.

9-o-Toluyljulolidine. A mixture of 4.0 g. of julolidine, 3.0 g. of o-toluanilide, and 3 g. of phosphorus oxychloride was refluxed for $1\frac{1}{4}$ hours, and then boiled for a short time with 40 ml. of 1:1 hydrochloric acid. On partial neutralization with aqueous ammonia, a green oil separated and soon solidified, wt. 3.7 g. (55%). After two recrystallizations from aqueous alcohol it was obtained as greenish platelets, m.p. 124.5-126°, greatly depressed when mixed with o-toluanilide (m.p. 125°).

Anal.^m Cale'd for C₂₀H₂₁NO: C, 82.45; H, 7.26.

Found: C, 82.73; H, 7.33.

Schmidt reaction on p-dimethylaminobenzaldehyde. p-Dimethylaminobenzaldehyde (5.0 g.) was dissolved in 20 ml. of concentrated sulfuric acid, and 3.0 g. of sodium azide was added in portions with stirring while the temperature was kept below 10°. When the rapid nitrogen evolution had ceased, the mixture was diluted with 50 ml. of ice-water, neutralized with aqueous sodium hydroxide, and the resulting precipitate was collected and washed with water. After recrystallization from aqueous ethanol it was obtained as yellowish platelets, wt. 3.0 g. (61%), m.p. 75° [reported for p-dimethylaminobenzonitrile, 76° (26)].

9-Cyanojulolidine.—A. By the Schmidt reaction. To 2.5 g. of 9-julolidinecarboxaldehyde in 10 ml. of concentrated sulfuric acid kept at 5–10° was added 0.8 g. of sodium azide slowly with stirring. When the nitrogen evolution was over, the mixture was diluted with 30 ml. of ice-water and neutralized with 10% sodium hydroxide solution. The brown precipitate which formed was collected and recrystallized from ethanol; this gave 1.9 g. (77%) of golden platelets, m.p. 119–120°.

Anal.^m Calc'd for C₁₃H₁₄N₂: C, 78.76; H, 7.11.

Found: C, 78.23; H, 7.30.

B. By dehydration of the oxime. A mixture of 4.0 g. of 9-julolidinecarboxaldehyde oxime and 30 ml. of acetic anhydride was refluxed for 3 hours, following the method of Sachs and Steinert (26) for dehydrating p-dimethylaminobenzaldoxime. The mixture was then poured into 200 ml. of water, neutralized with aqueous ammonia, and left to stand overnight. The 9-cyanojulolidine which separated was recrystallized from ethanol; m.p. 119°, wt. 3.1 g. (85%).

Cannizzaro reaction and 9-julolidinecarboxylic acid. A mixture of 2.0 g. of 9-julolidinecarboxaldehyde, 40 ml. of 10% sodium hydroxide, 30 ml. of ethanol, and 1 g. of silver catalyst (27) was refluxed on a steam-bath for 48 hours. The ethanol was then evaporated, the silver catalyst was filtered off, and the solution was made slightly acid. The precipitate of 9-julolidinecarboxylic acid was recrystallized from aqueous ethanol, from which it was obtained as pale yellow prisms, m.p. 240-241°, wt. 1.3 g. (60%).

Anal.^m Cale'd for C₁₈H₁₅NO₂: C, 71.87; H, 6.95.

Found: C, 71.82; H, 6.97.

The filtrate was neutralized with sodium hydroxide and extracted with ether. Evaporation of the dried ether extracts left a white solid, m.p. 50° , which turned red readily on standing, especially in the presence of traces of acid. It was therefore treated immediately with methyl iodide in warm acetone for 1 hour. The resulting *methiodide* of *9-julolidinemethanol* was recrystallized from ethanol-ether, and formed colorless needles of m.p. 186°.

Anal.^m Calc'd for C₁₄H₂₀INO: C, 48.70; H, 5,85.

Found: C, 48.73; H, 5.81.

For comparison, a sample of 9-julolidinecarboxylic acid was prepared from the aldehyde through the nitrile. 9-Cyanojulolidine was prepared by means of the Schmidt reaction as described up to the dilution of the reaction mixture with water. At this point the solution was refluxed for three hours, and then partially neutralized, causing the precipitation of 9-julolidine carboxylic acid, m.p. 240° alone and when mixed with the product from the Cannizzaro reaction.

Attempted benzoin formation from 9-juloiidinecarboxaldehyde. An equimolar mixture of benzaldehyde and the 9-aldehyde was refluxed for 2 hours with an aqueous-alcoholic solution of potassium cyanide, according to the method of Staudinger (19) for p-dimethylaminobenzoin. The solid product which separated on cooling melted at $136-137^{\circ}$, alone and when mixed with benzoin. The filtrate appeared to contain only an oily mixture of benzaldehyde and 9-juloidinecarboxaldehyde.

Reduction of 9-julolidinecarboxaldehyde. To 2.0 g. of the 9-aldehyde in anhydrous ether was slowly added 0.2 g. of lithium aluminum hydride, and the mixture was refluxed for 4 hours while being protected from atmospheric moisture. After cooling, moist ether was added to decompose unused reagent, and the filtered solution was evaporated to leave a white solid, m.p. 50°, which readily turned red in air. The *methiodide*, prepared in refluxing acetone solution, after recrystallization from alcohol-ether melted at 186°, alone and when mixed with product obtained from the Cannizzaro reaction.

9-Acetamidomethyljulolidine. To 3.0 g. of 9-cyanojulolidine in 100 ml. of anhydrous ether, 1.0 g. of powdered lithium aluminum hydride was added slowly, and the mixture was then refluxed for 3 hours with exclusion of atmospheric moisture. A small amount of water was added to decompose the reaction mixture, which was then filtered. Evaporation of the ethereal filtrate left an oil which was immediately acetylated with acetic anhydride in the presence of 10% sodium hydroxide solution. The crude product was recrystallized from ether, forming colorless needles, m.p. 142.5°, wt. 2.2 g. (55%).

Anal.: Calc'd for $C_{15}H_{20}N_2O$: C, 73.74; H, 8.25.

Found: C, 73.88; H, 8.34.

Schmidt reaction on p-dimethylaminobenzophenone. The Schmidt reaction was run on 8.0 g. of p-dimethylaminobenzophenone in trichloracetic acid solution as described for other benzophenones (15). The mixed amides so obtained weighed 7.0 g. (82%). A 5-g. portion of the mixed amides was refluxed with 100 ml. of concentrated hydrochloric acid for 48 hours. The benzoic acid formed was collected from the cooled solution by filtration and extraction with carbon tetrachloride; the total weight was 1.1 g., m.p. 120-121°. The remaining solution was neutralized to pH 5, whereupon a green precipitate of p-dimethylaminobenzoic acid separated from the now pink solution; it weighed 1.3 g., and melted at 235-240°. Alkalization of the filtrate destroyed the pink color, and subsequent steam-distillation removed aniline. From the residue p-aminodimethylaniline was extracted with several portions of ether, and was acetylated with acetic anhydride for isolation; there was obtained 1.3 g. of p-dimethylaminoacetanilide, m.p. 120-125°.

From these results the original mixture of amides would appear to have been 47% benzop-dimethylaminoanilide and 53% p-dimethylaminobenzanilide.

Schmidt reaction on 9-benzoyljulolidine. To a mixture of 1.39 g. of 9-benzoyljulolidine, 15 g. of trichloroacetic acid, and 1.2 ml. of concentrated sulfuric acid at $55-60^\circ$ was added 0.5 g. of sodium azide in portions. Gas evolution was rapid and appeared to be complete in about 3 hours. When the mixture was poured into water and alkalized with ammonia, a greenish-yellow, putty-like solid separated, wt. 2.7 g. The precipitate was then refluxed for 48 hours with a mixture of concentrated hydrochloric and glacial acetic acids, and finally extracted repeatedly with carbon tetrachloride. Evaporation of the extracts left 0.28 g. (46%) of benzoic acid, m.p. 120-122°. The aqueous phase was then neutralized with sodium carbonate, but no precipitation of 9-julolidinecarboxylic acid occurred. Therefore the solution was extracted with four portions of benzene, and the combined extracts were fractionally steam-distilled. The benzene first came over, and the distillate soon turned pink, and then turned bright green as the distillation proceeded. These colors were discharged by small amounts of sodium borohydride, but not by sodium bisulfite, and were regenerated by standing in air. Soon after the removal of the benzene, a solid began to come over, which was identified as *julolidine* by its melting point, 41°, and that of its *picrate*, 180-181°. In another run, 0.5 g. of julolidine was thus obtained from 5.0 g. of 9-benzoyl-

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julolidine. The aqueous residue from the steam-distillation was associated with a tarry substance which was completely soluble in hydrochloric acid, and is believed to be crude 9-aminojulolidine. It was taken up in ether and precipitated with pieric acid as a black, intractable lump mixed with numerous, small brown needles, which weighed 0.25 g., m.p. 140-148°, after mechanical separation. Recrystallization of the needles from an ethanolbenzene mixture gave shining, purple-black needles, which melted with charring at 165-168°. This substance was only sparingly soluble in ethanol, giving an orange-red solution, but dissolved completely in aqueous ammonia with fading of the color to yellow. Whether it is partly or completely oxidized to a semiquinone, as would appear from its color, is not surely detectable by ultimate analysis.

Anal.^m Cale'd for C₁₈H₁₉N₅O₇: C, 51.80; H, 4.56.

Found: C, 51.74; H, 4.67.

Another experiment, utilizing 1.0 g. of 9-benzoyljulolidine, was run in the above manner with the exception that the time allowed for hydrolysis of the crude amides was reduced to only 2 hours. This change was made when it appeared that decarboxylation of 9-julolidine-carboxylic acid during the 48-hour hydrolysis might have been responsible for the formation of julolidine and the failure to isolate the acid. Neutralization of the hydrolysis mixture precipitated 0.1 g. (13%) of the acid, m.p. 242-244°, and julolidine was not present in sufficient amount to separate during the steam-distillation.

Attempted Schmidt reaction on p-aminobenzoic, p-dimethylaminobenzoic, and 9-julolidinecarboxylic acids. Each of these acids was treated with sodium azide while in concentrated sulfuric acid solution at $50-55^{\circ}$ under chloroform. After dilution with water and neutralization, the starting acids were precipitated in recovered yields of 77%, 81%, and 71%, respectively.

Schmidt reaction on 9-o-toluyljulolidine. To 1.5 g. of 9-o-toluyljulolidine in 15 ml. of concentrated sulfuric acid overlaid with 15 ml. of benzene was added 0.5 g. of sodium azide in portions with shaking. When gas evolution had ceased, the mixture was poured into 100 ml. of water, neutralized with aqueous ammonia, and the benzene was evaporated. The green solid which separated weighed 1.2 g. (<76%). In the hope that it might be nearly all 9-o-toluamidojulolidine, it was extracted with several portions of aqueous alcohol, and the residue was recrystallized from aqueous acetone; the least-soluble portion, amounting to about 0.6 g., was obtained as needlets, m.p. 215-216°, and is believed to be N-o-tolyl-N'-9-julolidylurea.

Anal.^m Cale'd for C₂₀H₂₃NO₃: C, 74.73; H, 7.21.

Found: C, 74.67; H, 7.47.

The more soluble material, in the alcoholic extracts, was never obtained completely pure, and the best sample, about 0.3 g., formed leaflets, m.p. 155-160°.

In another experiment starting with 1.7 g. of ketone, the crude amides were refluxed with 50 ml. of concentrated hydrochloric acid for 60 hours. From the cooled solution, 0.2 g. (43%) of o-toluic acid, m.p. 100-101°, was collected; extraction of the filtrate with carbon tetrachloride produced only a small amount of tar. Neutralization to pH 3 precipitated a small amount of tarry material from which a few crystals of 9-julolidinecarboxylic acid, m.p. 238-240°, were obtained by recrystallization from aqueous ethanol. Steam-distillation of the alkalized filtrate produced the usual pink and green colors in the distillate, from which a small amount (<0.1 g.) of julolidine was isolated as its *picrate*, m.p. 178-180°, undepressed with authentic material. A dark picrate, wt. 0.04 g., m.p. 167-168.5°, was obtained from an ethereal extract of the distilland, and appeared to be that of 9-aminojulolidine. The small yield is not indicative, however, as there was an appreciable accidental loss at this stage.

The stilbazole methiodide from ϑ -juloidinecarboxaldehyde. An alcoholic solution of 0.5 g. of the 9-aldehyde and 0.9 g. of α -picoline methiodide and two drops of piperidine was refluxed for two hours, according to the directions of Doja (28) for the corresponding reaction with *p*-dimethylaminobenzaldehyde. The red solid which formed on cooling was recrystallized from absolute ethanol, from which it was obtained as dark red needles, m.p. 251°, wt. 1.0 g. (96%).

Anal.^m Calc'd for C₂₀H₂₃IN₂: C, 57.42; H, 5.55.

Found: C, 57.60; H, 5.67.

The absorption spectra of this dye and of *p*-dimethylamino- α -stilbazole methiodide were determined in 0.0013% solution in water on a Beckman model DU instrument. Between 3000 and 5200 Å there was a single broad maximum in each case, having a peak at 4780 Å (ϵ 26,100) in the case of the dye from 9-julolidinecarboxaldehyde, and a peak at 4370 Å (ϵ 25,300) in the case of the dye from *p*-dimethylaminobenzaldehyde. For both compounds the absorption was beginning to climb on the shorter wave-length side.

SUMMARY

By direct substitution reactions on julolidine (I, R = H), 9-bromo-, 9-thiocyano-, 9-formyl-, 9-benzoyl-, and 9-o-toluyl-julolidine have been prepared. From these compounds a number of other new substances have been prepared by standard reactions. Oxidation of julolidine by nitrous acid and other oxidizing agents gave bijulolidyl. The absorption spectrum of the stilbazole methiodide from 9-julolidinecarboxaldehyde supports other evidence for the coplanarity of the C—N bonds in julolidine compounds.

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