ml. of ether were added simultaneously, dropwise, to 100 ml. of ether while stirring and cooling during 30 min. A white solid separated. After the additions were completed, the mixture was stirred 30 min. longer, and then filtered. The white solid weighed 11.6 g. (90%), m.p. 114–115°. One recrystallization from water gave the analytical sample, m.p. 116–117°; infrared bands at 2.89, 2.98, 5.81, and 5.98 μ.

Anal. Calcd. for $C_{14}H_{18}N_2O_4$: C, 60.42; H, 6.52; N, 10.07. Found: C, 60.27; H, 6.53; N, 10.05.

N-(2-Aminoethyl)acetoacetamide Hydrobromide (IX).—The benzyloxycarbonyl group was removed from VIII using the method of Ben-Ishai and Berger.[17] A mixture of 27.8 g. (0.1 mole) of VIII and 200 ml. of 30–35% hydrogen bromide–acetic acid solution was allowed to stand at room temperature, with occasional shaking, for 1 hr., at which time the evolution of carbon dioxide had ceased. A large volume of ether was added, and the oil which separated was triturated with fresh portions of ether until it became a nearly white solid. This solid (IX) weighed 25.5 g. (quantitative). It was very hygroscopic and was stored in a vacuum desiccator until used in the next step without further purification.

7-Methyl-1,2,3,4-tetrahydro-1,4-diazepin-5-one (Xa).—A mixture of 9.0 g. (0.04 mole) of IX in 1000 ml. of chloroform was stirred as ammonia was bubbled through the mixture for 1 hr. Sodium sulfate was added, the mixture was filtered, and the filtrate was evaporated. The residue, a yellowish-white solid, wt. 4.7 g., was recrystallized from chloroform to give 1.8 g., m.p. 160–163.5°, of Xa as a white crystalline product. This solid gradually turned yellow on standing several days. The analytical sample was prepared by recrystallization from alcohol–ether, m.p. 163.5–165°. The infrared spectrum showed bands at 2.89, 3.05, 3.37, and 6.14 μ. The ultraviolet spectrum showed an absorption peak at 285 mμ (ε 15,900); addition of acid resulted in no absorption above 220 mμ.

Anal. Calcd. for $C_6H_{10}N_2O$: C, 57.11; H, 7.99; N, 22.21; mol. wt., 126. Found: C, 56.74, 56.92; H, 7.91, 8.11; N, 22.36; mol. wt., 126 (mass spectrometry) and mol. wt., 128 (isothermal distillation).

(17) D. Ben-Ishai and A. Berger, *J. Org. Chem.*, **17**, 1564 (1952).

The hydrochloride of Xa was prepared with alcoholic hydrogen chloride, m.p. 165–167° dec. The hydrochloride was hygroscopic.

Anal. Calcd. for $C_6H_{11}ClN_2O \cdot {}^1/_4H_2O$: C, 43.12; H, 6.94; Cl, 21.22; N, 16.76. Found: C, 42.94; H, 6.75; Cl, 21.15; N, 16.75.

The picrate of Xa was prepared in alcohol, m.p. 170.5–171° dec.

Anal. Calcd. for $C_{12}H_{13}N_5O_8$: C, 40.57; H, 3.69; N, 19.71. Found: C, 40.37; H, 3.79; N, 19.62.

Hexahydro-7-methyl-1,4-diazepin-5-one (IVa).—A solution of 5 g. (0.04 mole) of Xa, 100 ml. of ethanol, and 11 ml. (0.04 mole) of 3.9 *N* alcoholic hydrogen chloride was reduced with hydrogen at room temperature and 19 p.s.i. in the presence of 1.0 g. of platinum oxide. Within an hour the theoretical amount of hydrogen was absorbed. The catalyst was removed and the solvent was evaporated. The sticky residue was dissolved in chloroform and treated with ammonia. The mixture was filtered and the filtrate was evaporated. This gave 4.1 g. (80%) of IVa as a white solid. Two recrystallizations from chloroform–petroleum ether and one from ethyl acetate gave 2.9 g. of crystalline material, m.p. 105–108°. The analytical sample was obtained by dissolving a sample in ether, filtering to remove a trace of insoluble material, and evaporating the ether. This raised the m.p. to 109–111°. There was a strong band at 6.00 μ in the infrared spectrum and no absorption in the ultraviolet.

Anal. Calcd. for $C_6H_{12}N_2O$: C, 56.22; H, 9.44; N, 21.86. Found: C, 55.94; H, 9.13; N, 21.76.

The picrate of IVa was prepared in alcohol and recrystallized from water, m.p. 232–233° dec.

Anal. Calcd. for $C_{12}H_{15}N_5O_8$: C, 40.34; H, 4.23; N, 19.60. Found: C, 40.65; H, 4.19; N, 19.95.

Acknowledgment.—We wish to thank Mr. L. M. Brancone and associates for the analytical data and molecular weight determinations by isothermal distillation; Dr. A. Struck and associates for a molecular weight determination by mass spectrometry; and Mr. W. Fulmor and Dr. J. Lancaster and their associates for the determination and interpretation of the n.m.r. data.

Reductions with Ruthenium Catalyst. III. Hydrogenation of Nuclear Substituted Anilines

MORRIS FREIFELDER AND GEORGE R. STONE

Organic Chemistry Department, Research Division, Abbott Laboratories, North Chicago, Illinois

Received April 30, 1962

A study of the activity of ruthenium dioxide in the hydrogenation of substituted anilines is carried out. The effect of the catalyst on certain potentially hydrogenolyzable groups is reported along with the effect of substituents on reduction.

In the past we had prepared a few substituted cyclohexylamines as intermediates for compounds to be tested as sweetening agents. For the most part they were obtained by reduction of the corresponding anilines with ruthenium dioxide. Our continuing interest in the hydrogenation of nitrogen-containing compounds with this catalyst[1] led us to expand the series to cover a wide range of substituents.

Our purpose was not only to note the effect of substitution on hydrogenation, but also to see the effect of the catalyst on those groups which have a tendency to hydrogenolyze.

Alkyl substituents on the ring do not appear to have too profound an effect on the rate of hydrogenation under the conditions used in this work.

(1) M. Freifelder and G. R. Stone, *J. Am. Chem. Soc.*, **80**, 5278 (1958); M. Freifelder and G. R. Stone, *J. Org. Chem.*, **26**, 3805 (1961).

Branching as seen in compounds VI and X impeded the reaction somewhat, making a larger catalyst ratio or higher reaction temperature necessary for a more rapid uptake of hydrogen. It is interesting that in the preparation of I to XI, secondary amine was detected only in the hydrogenation of 4-(2-pentyl)aniline leading to VI, where it was the main product of reaction.

Except in the conversion of 2-butoxyaniline to XX, hydrogenolysis of the —OR grouping occurred during the preparation of compounds XII to XXIII. In each instance cyclohexylamine was identified. In the preparation of XXII a mixture of 2- and 5-methoxycyclohexylamine was obtained. Likewise, in preparing XXIII, the corresponding ethoxycyclohexylamines were obtained along with cyclohexylamine.

A comparison of the yields of 2-methoxy- and 2-ethoxycyclohexylamine shows a considerable increase of XV over XII. In addition, with XV a lesser amount of cyclohexylamine was obtained during hydrogenation. These results suggest that the size of the group in the 2-position has a considerable effect on the extent of hydrogenolysis. This was substantiated in the preparation of XX. The effect was not so dramatic in the other positions and did not show up until 4-butoxyaniline was converted to XXI, when less than 10% of cyclohexylamine was obtained. The mechanism by which hydrogenolysis takes place is not clear. However, it must occur during an intermediate stage of ring saturation, since an attempt to hydrogenolyze 4-ethoxycyclohexylamine under the conditions used for reduction resulted in recovery of unchanged product and absence of cyclohexylamine.

Extensive hydrogenolysis occurred during the conversion of the N,N-dialkyl substituted anilines to XXIV and XXV. A low yield of XXIV had been obtained by reduction of the corresponding aniline with a cobalt catalyst.[2] The yield of XXV did not compare with the 70% yield of the related N,N-diethylcyclohexane-1,4-diamine also obtained by ruthenium reduction.[2,3] In this same group the hydrogenation of 4-diethylaminoaniline was interrupted before uptake was complete. The results (see Experimental) suggest that as in the reduction of the alkoxyanilines, hydrogenolysis accompanies saturation of the ring.

In the only example of the hydrogenation of an N-monoalkylaniline, N-methylaniline was converted to N-methylcyclohexylamine with little accompanying hydrogenolysis. The ethyl ester of N-phenylglycine, another N-substituted product, was converted to the corresponding cyclohexyl compound in very good yield.

The hydrogenation of 4-aminoacetophenone to XXVI was uncomplicated despite a report that only 4-ethylcyclohexylamine was obtained when another catalyst was used.[4]

To successfully reduce 4-aminobenzoic acid and its ethyl ester to XXVII and XXVIII, respectively, it was necessary to use a higher catalyst ratio.

No serious attempt was made to separate *cis* and *trans* forms of the substituted cyclohexylamines Kirby[3] suggests that the *cis* isomer predominates as a result of hydrogenation of substituted anilines. The large amount of *cis* isomer obtained after the preparation of XXVII appears to substantiate his suggestion. Examination of the melting points of the hydrochloride salts listed in the table might in a number of instances point to only one isomer. However, the melting points of all the salts prepared from distilled amines, before recrystallization, would tend to indicate a mixture of isomers. Indeed, in preparing the salt of XXVIII, we were able to isolate and identify a second product.

The hydrogenation of some of these compounds with another catalyst will be investigated and reported at a later date.

Experimental

Except where noted in the table, substituted anilines were used as starting materials. Compound XXVI was prepared directly from 4-aminoacetophenone. All the intermediates are commercially available or their preparations are reported in the literature.

***n*-Propoxynitrobenzene.**—The method used is a modification of the literature preparation.[5]

A mixture of 29.5 g. (0.212 mole) *n*-nitrophenol, 28.3 g. (0.23 mole) of propyl bromide, 12.9 g. (0.23 mole) of potassium hydroxide, and 50 cc. of ethyl alcohol was heated in a 270-cc. rocker type bomb for 6 hr. at 170–180°. The suspension was filtered and washed with alcohol. The alcoholic solution was concentrated and the residue extracted with ether. The precipitate from the reaction mixture was dissolved in water and the solution extracted with ether. The ether solutions were combined and extracted with 4% sodium hydroxide solution to remove unchanged phenol. The ether extract was dried over magnesium sulfate, filtered, and distilled. The residue was fractionated and the portion distilling at 102° (1 mm.), $n^{25}D$ 1.5313, was collected in 74.5% yield.[6]

Anal. Calcd. for $C_9H_{11}NO_3$: C, 59.66; H, 6.12. Found: C, 59.61; H, 6.17.

In the preparation of *p*-propoxynitrobenzene the yield was much lower when sodium *p*-nitrophenolate was used. The product distilled 115–118° (1.1–1.2 mm.), $n^{25}D$ 1.5547; yield, 40.5%; described b.p. 285–287°.[5]

The following is an illustration of the conditions used to prepare the compounds listed in the table. Methyl or ethyl alcohol was a suitable solvent. The ratio of catalyst to starting material was 2% by weight. Any variation of these conditions will be found in the table.

Ethyl α-Aminocyclohexylacetate.—Ruthenium dioxide,[7] 1.0 g., was added to a solution of 53.7 g. (0.3 mole) of ethyl α-aminophenylacetate in 150 cc. of ethyl or methyl alcohol.

(2) L. C. Behr, J. E. Kirby, R. N. MacDonald, and C. W. Todd, *J. Am. Chem Soc.*, **68**, 1296 (1946).

(3) J. E. Kirby, U. S. Patent 2,606,925, August 12, 1952.

(4) E. Ferber and H. Bruckner, *Ber.*, **72**, 995 (1939), quote some unpublished work by the former.

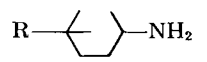
(5) L. Spiegel and S. Sabbath, *Ber.*, **34**, 1935 (1901).

(6) H. H. Hodgson and H. Clay, *J. Chem. Soc.*, **134**, 2097 (1931), report a solid melting at 28°.

(7) Supplied by Engelhard Industries, Newark, New Jersey.

TABLE I

CYCLOHEXYLAMINES



	R	Reaction time, hr.	Yield, %	Constants B.p., °C.	mm.	$n^{25}D$	Hydrochloride,[a] m.p., °C.	Formula	C Calcd.	C Found	H Calcd.	H Found	N Calcd.	N Found
I	2-CH_3	[b]	84	151	atm.[c]	1.4573		$C_7H_{15}N$						
II	3-CH_3	<1	73	150–151	atm.[d]			$C_7H_{15}N$						
III	4-CH_3	0.5	74	150	atm.[e]	1.4523		$C_7H_{15}N$						
				75–76	26									
IV	2-C_2H_5[f]	1[g]	81	170–171	746	1.4601[h]		$C_8H_{17}N$						
V	4-C_2H_5[f]	[b]	71.5	75–80	20	1.4600	234–247	$C_8H_{18}ClN$	75.52	75.29	13.47	12.98		
VI	4-$CH(CH_3)C_3H_7$	8[i,j]	11.5[k]	88–95	4.5–5.0	1.4674		$C_{11}H_{23}N$	78.03	78.01	13.69	13.20	8.28	8.27
VII	2,4-di-CH_3	<1[i]	87	60–65	18[l]	1.4523	193–200	$C_8H_{15}ClN$	58.70	58.70	11.08	10.94		
VIII	2,5-di-CH_3	0.5[j]	73	167	atm.[m]	1.4548	187–188	$C_8H_{18}ClN$	58.70	58.68	11.08	11.11		
				76–77	27									
IX	3,4-di-CH_3	2	84.5	178–183	746	1.4568	229–235	$C_8H_{18}ClN$	58.70	58.54	11.08	11.19		
X	2-CH_3-5-$CH(CH_3)_2$	<2[n]	81	209–214	atm.[o]	1.4638	206–207	$C_{10}H_{22}ClN$	62.61	62.60	11.57	11.81	7.31	7.32
XI	2,4,6-tri-CH_3	0.5[p]	66	69–75	13[q]	1.4541	279–280	$C_9H_{20}ClN$	60.82	60.78	11.34	11.10		
XII	2-OCH_3	2	42.5	173–174	atm.	1.4613	187–188[r]	$C_7H_{16}ClNO$	50.75	50.91	9.74	9.67	8.47	8.52
XIII	3-OCH_3	2	35.5	173–180	atm.[s]	1.4618	125–128	$C_7H_{16}ClNO$	50.75	50.81	9.74	9.90		
XIV	4-OCH_3	2	35	187	atm.[t]	1.4612	128–130	$C_7H_{16}ClNO$	50.75	51.01	9.74	9.70		
				84–87	30									
XV	2-OC_2H_5	1	78.7	180–182	751[u]	1.4529	200–201	$C_8H_{18}ClNO$	53.47	53.45	10.10	10.09	7.80	7.89
XVI	3-OC_2H_5	<1	53	195–200	755[u]	1.4602	165	$C_8H_{18}ClNO$	53.47	53.24	10.10	9.85	7.80	7.76
XVII	4-OC_2H_5	1	52.5	96	24[u]	1.4588	151–157	$C_8H_{18}ClNO$	53.47	53.39	10.10	10.16		
XVIII	3-OC_3H_7[f]	2	46.5	100–110	8–13	1.4620	145–146	$C_9H_{20}ClNO$	55.80	56.13	10.41	10.25	7.23	7.06
XIX	4-OC_3H_7[f]	3	55	212–215	755[w]	1.4588	184–185	$C_9H_{20}ClNO$	55.80	56.06	10.41	10.41	7.23	7.07
				120	30									
XX	2-OC_4H_9[f]	1.5	84.7	218	755	1.4532	190–193	$C_{10}H_{22}ClNO$	57.81	57.60	10.67	10.62	6.74	6.76
XXI	4-OC_4H_9[f]	1.0	76	128–130	32	1.4576		$C_{10}H_{21}NO$	70.14	70.28	12.36	12.19	8.18	8.28
XXII	2,5-di-OCH_3	6	32.5	83	1.7	1.4663	190–191	$C_8H_{17}ClNO_2$	49.10	49.30	9.27	9.50	7.16	7.23
XXIII	2,5-di-OC_2H_5	2.5[v]	35	111–117	11–12	1.4658	190–191	$C_{10}H_{21}ClNO_2$	53.92	53.53	9.52	9.28	6.30	6.29
XXIV	4-$N(CH_3)_2$	2	20	200–205	755[w]	1.4795								
XXV	2-CH_3-4-$N(C_2H_5)_2$	0.5	36	121–125	19	1.4782	160–165[x]	$C_{11}H_{26}Cl_2N_2$	51.35	51.20	10.19	10.45	10.89	10.60
XXVI	4-CHOHCH$_3$	<1[y]	72.5	245–248	755	1.4936	171–176	$C_8H_{18}ClNO$	53.47	53.69	10.14	9.95	7.79	7.93
XXVII	4-COOH	<2[z]	87.5[aa]											
XXVIII	4-$COOC_2H_5$	3-4[g]	82.5	105	5[bb]	1.4637	211–213[cc]	$C_9H_{18}ClNO$	52.51	52.62	8.73	8.71	6.74	6.68

[a] Since the alicyclic amines absorbed carbon dioxide rapidly, it was necessary to convert a portion of distilled base to the salt for identification. The salt was recrystallized once for analysis. [b] Uptake of hydrogen was complete when reaction temperature was reached. [c] Described 148–150°, 143 mm., J. Gutt, *Ber.*, **40**, 2061 (1907). [d] As reported, A. Skita and W. Berendt, *Ber.*, **52**, 1519 (1919). [e] See ref. *c*. [f] Prepared by low pressure hydrogenation of an alcoholic solution of nitro compound with Raney nickel or preferably 5% palladium on carbon and subsequent reduction after removal of catalyst. [g] In another run without solvent starting with 2-nitroethylbenzene, it was necessary to raise the reaction temperature to 140° before uptake of hydrogen was completed. [h] R. Willstatter, *et al.*, *Ber.*, **58**, 385 (1925), gives 170–171°, $n^{20}D$ 1.4682. [i] No solvent. [j] With solvent and a 5% catalyst ratio hydrogenation was complete in 1 hr. [k] In both instances, secondary amine was the major product, b.p. 190° (1.4 mm.), $n^{25}D$ 1.4880, yield 63%. *Anal.* Calcd. for $C_{22}H_{43}N$: C, 82.16; H, 13.48; N, 4.35. Found: C, 82.39; H, 13.29; N, 4.35. [l] A. Skita, *Ann.*, **427**, 255 (1922), gives 161–164.5° at atm. pressure. [m] 164–168°, atm. pressure, A. Skita, *Ber.*, **56**, 2241 (1923). [n] Reduction carried out at 125°, too slow at 90–100°. [o] O. Wallach and A. Herbig, *Ann.*, **287**, 371 (1895), report 210–212° for the *active* form and 211–212° for the *inactive* form. [p] Nitromesitylene was hydrogenated directly in alcoholic solution. Reaction was exothermic, temperature rising rapidly from 40 to 90°

TABLE I (*Continued*)

and then gradually to 103–105°. [v] Mentioned as an intermediate in British Patent 630,525, October 14, 1949. No constants given. [r] M. Mousseron and M. Canet, *Compt. rend.*, **233**, 484 (1951), report the preparation but give no constants except melting point of a picrate. [s] D. S. Noyce and D. B. Denny, *J. Am. Chem. Soc.*, **76**, 768 (1954), give constants for the *cis* form: 97–98° (45 mm.), n^{25}D 1.4610. [t] D. E. Cooper, U. S. Patent 2,578,641, December 11, 1951, 187–189°, atm. pressure. [u] L. Hartman and L. Panizzon, U.S. Patent 2,152,960 give boiling points of the following cyclohexylamines: 2-ethoxy, 55–60° (3 mm.); 3-ethoxy, 74–76° (3 mm.); 4-ethoxy, *cis*, 50–60° (5 mm.); *trans*, 60–62° (3 mm.); 4-propoxy, *cis*, 80–82° (4 mm.); *trans*, 114–116° (4 mm.). [v] A larger catalyst ratio used, 3.25–3.5%. [w] See ref. 2. [x] M.p. of dihydrochloride salt. [y] Uptake of hydrogen began at 60. Temperature rose to 85° and then gradually to 103–105° without heating. [z] Water used as solvent, catalyst ratio 5%. [aa] *cis* Acid, 78.5% yield, m.p. 286°. Calcd. for $C_7H_{13}NO{\cdot}0.25H_2O$: C, 57.00; H, 9.22; N, 9.47; O, 24.39. Found: C, 56.92; H, 9.10; N, 9.16; O, 24.58. *trans* acid, 9% yield, m.p. above 495° uncorrected. Calcd. for $C_7H_{13}NO{\cdot}0.5H_2O$: C, 55.24; H, 9.27; N, 9.21; O, 26.28. Found: C, 55.04; H, 9.41; N, 9.15; O, 26.16. J. P. Greenstein and J. Wyman, Jr., *J. Am. Chem. Soc.*, **60**, 2341 (1938) report 285° and 260° for *cis* acid dependent on method of preparation. G. Wendt, *Ber.*, **75**, 425 (1942) gives 304–305° and for the more soluble *trans* form 486–488°. [bb] S. I. Sergievskaya, *et al.*, *J. Gen. Chem. USSR*, **28**, 1839 (1958), give 125–135° (20 mm.), n^{21}D 1.4640. [cc] R. K. Patel and O. Gisvold, *J. Am. Pharm. Assoc.*, **42**, 321 (1953), give 193–194° for the *cis* form. In addition to the higher melting form shown in this table, a small amount of hydrochloride salt was obtained which melted at 133°. Compared to calculated values for XXVIII, the found values are C, 52.32; H, 9.10; N, 6.69.

The mixture was hydrogenated at 90–100° under 70–80 atm. Uptake of hydrogen was complete by the time the reaction temperature was reached. The contents of the bomb when cooled to room temperature were filtered through a light bed of carbon (to prevent the catalyst from going through). The catalyst was washed with alcohol and the filtrate and washings concentrated to dryness. The residue distilled at 106–109°, 4–5 mm. An 86.5% yield was obtained.

Anal. Calcd. for $C_{10}H_{19}NO_3$: C, 64.80; H, 10.34; N, 7.56. Found: C, 64.50; H, 10.63; N, 7.73.

Occurrence of Hydrogenolysis. 4-Dimethylaminocyclohexylamine (XXIV).—4-Dimethylaminoaniline, 68.1 g. (0.5 mole) was hydrogenated without the use of solvent. When hydrogen uptake came to a halt, the oily material was filtered from the catalyst and fractionated. About 23% of cyclohexylamine was obtained, identified by melting point of the hydrochloride salt and mixed melting point with an authentic sample. An intermediate fraction, a mixture of cyclohexylamine and product, was discarded. After the main fraction was collected, considerable residue remained.

Another reduction with 4-diethylaminocyclohexylamine was carried out in ethyl alcohol. The reaction was interrupted at about 50–60% of the theoretical hydrogen uptake and the solution submitted for vapor phase chromatography examination. The results indicated 8.5% of cyclohexylamine, 30% of the desired product and 58% of starting material.

N-Methylaniline was hydrogenated under the conditions described for the preparation of XXIV. A sample of the oil after removal of the catalyst was submitted for vapor phase chromatography. The result indicated the presence of 1–2% of cyclohexane. The material on distillation gave pure N-methylcyclohexylamine distilling at 147° (747 mm.),[8] n^{25}D 1.4523. Loss was mechanical, low boil, and residue amounting to less than 5%.

In the preparation of XXV the product of hydrogenolysis was 2-methylcyclohexylamine (24%), identified by melting point of the hydrochloride salt and analysis. As in XXIV, an intermediate fraction had to be discarded.

During the preparation of compounds XII to XIV, it was found necessary to redistill the main fractions to remove contaminating cyclohexylamine. Vapor phase chromatography of XV before distillation indicated only 7–8% of cyclohexylamine. With XVI and XVII, the 3- and 4-ethoxy compounds, it was also necessary to redistill the main fractions to remove contaminating cyclohexylamine, (shown to be present by vapor phase chromatography). Distillation of XVIII and XIX, the propoxy compounds, was simple because of the spread in boiling points between them and the contaminant, 26 and 31% of cyclohexylamine being obtained, respectively.

Examination of XX before distillation showed no cyclohexylamine present. During reduction of 4-butoxyaniline to XXI less than 10% of cyclohexylamine was obtained. In the hydrogenation of the anilines leading to XXII and XXIII a mixture of 2- and 5-alkoxycyclohexylamines was obtained in each case in addition to cyclohexylamine.

***cis*- and *trans*-4-Aminocyclohexanecarboxylic Acid.**—After the hydrogenation of *p*-aminobenzoic acid was complete, the reaction mixture was cooled to 25–50° and filtered from the catalyst. The catalyst was washed with water and the filtrate and washings concentrated to a thick paste. Absolute ethyl alcohol, 500 cc., was added and the slurry heated to boiling and filtered. The insoluble *cis* product was washed with some cold absolute alcohol and dried. The filtrate was cooled and a small amount of precipitate ob-

(8) As described, A. Skita and H. Rolfes, *Ber.*, **53**, 1242 (1920).

tained. The solution was then concentrated to about a third of the volume and cooled. Additional crystalline material was obtained. The solution was then concentrated to 50–75 cc. and treated with three volumes of anhydrous ether. Each of the precipitates did not melt below 495°.

Acknowledgment.—The authors are grateful to Messrs. E. F. Shelberg and O. Kolsto for microanalyses, P. Helgren for vapor phase chromatographic results, and to Mr. Y. H. Ng for technical assistance.

Ortho Substitution Rearrangement of 1,1-Dimethyl-2-phenylpyrrolidinium Ion by Sodium Amide. Ring Enlargement to Form a 2-Benzazocine[1]

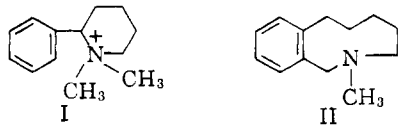
GLENN C. JONES AND CHARLES R. HAUSER

Department of Chemistry, Duke University, Durham, North Carolina

Received April 30, 1962

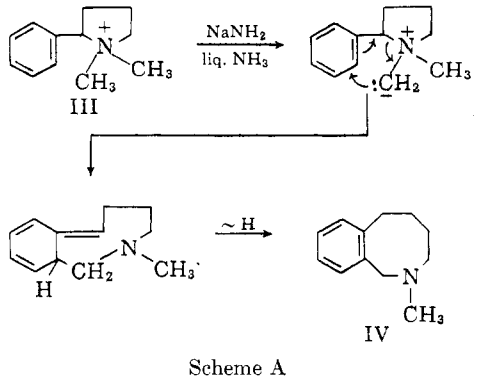
The 1,1-dimethyl-2-phenylpyrrolidinium ion (III) reacted with sodium amide in liquid ammonia to form 2-methyl-1,2,3,4,5,6-hexahydro-2-benzazocine (IV) and a polymer in about equal yields. The product IV was formed by an ortho substitution rearrangement involving the enlargement of a five-membered ring to an eight-membered ring. This reaction furnishes a new and convenient route to the synthesis of certain 2-benzazocine derivatives. The polymer evidently arose through an elimination reaction. The conformation of quaternary ion III appears to be less favorable for rearrangement than that of the earlier reported 1,1-dimethyl-2-phenylpiperidinium ion, which rearranges exclusively.

Recently[2] quaternary ammonium ion I was shown to undergo the ortho substitution rearrangement with sodium amide in liquid ammonia to form tertiary amine II in 83% yield. The rearrangement involves enlargement of a six-membered ring to a nine-membered ring. Although quaternary ion I had β-hydrogen, no appreciable elimination reaction was observed.



I II

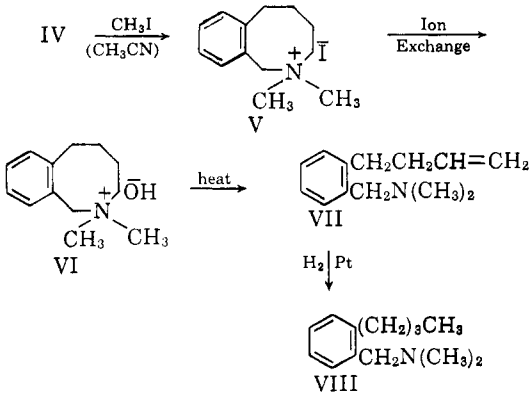
In the present investigation the related 1,1-dimethyl-2-phenylpyrrolidinium ion (III) reacted with sodium amide in liquid ammonia to afford tertiary amine IV and polymeric material in yields of 41 and 38%, respectively (see below). Amine IV arose through the ortho substitution rearrangement involving enlargement of a five-membered ring to an eight-membered ring (Scheme A).[3]



Scheme A

The distilled rearranged amine was indicated by vapor phase chromatography to consist essentially of a single substance. It was shown to be an *ortho* substitution rearrangement product by oxidation to form phthalic acid (51%). No benzoic acid was isolated; this acid should have been obtained has the original rearrangement involved a possible Stevens 1,2-shift.

Structure IV was established by a Hofmann degradation of hydroxide VI, which was prepared through methiodide V by ion exchange. The degradation afforded olefin-amine VII (not isolated), which was hydrogenated to give amine VIII (Scheme B).



Scheme B

The hydrogenation product was shown by vapor phase chromatography to be contaminated with a small amount of higher boiling material, which arose presumably through SN2 displacement at

(1) Supported by the National Institutes of Health, Grant No. CY-4455(C2).

(2) D. Lednicer and C. R. Hauser, *J. Am. Chem. Soc.*, **79**, 4449 (1958).

(3) The methyl carbanion in this scheme might arise through intermediate formation of a benzyl type carbanion; see ref. 7.