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201. *The Reduction of Allylamines with Sodium in Liquid Ammonia.*

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The reduction by sodium in liquid ammonia in the presence of alcohol of eight tertiary amines containing a double bond in the allyl position to the nitrogen has been investigated. In no case did hydrogenolytic fission, such as occurs in the reduction of allyl ethers and alcohols, take place, but with three amines, *N*-allyl- and -methallyl-piperidine and diethylmethallylamine, reduction occurred to give the saturated compound. *N*-Crotyl-, -2-*tert*.-butylallyl-, -1-*cyclo*hex-2′-enyl-, -benzyl-, and -2 : 3 : 4 : 5-tetrahydrobenzyl-piperidine were unaffected by sodium in liquid ammonia. The above amines and the corresponding saturated derivatives have been characterised.

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THE reductive fission by sodium in liquid ammonia of allyl alcohols has been well investigated, but the similar reduction of allylamines has been little studied. In the case of the oxygen compounds it seems possible to make the generalisation that, if in the system $>\overset{1}{C}=\overset{2}{C}-\overset{3}{C}-O-R$ either of the atoms C_1 or C_3 carries H_2 or PhH, then reduction will take place with fission of the C_3–O link (see Birch, *Quart. Reviews*, 1950, **4**, 69). In no case has reduction of the double bond been reported unless this is conjugated with another olefinic link or with a phenyl substituent. The fission of allylamines under the action of potassium or sodium has been reported on two occasions; by Clayson (unpublished work, see Birch, *loc. cit.*) who has observed the fission of the heterocyclic ring in laudanosine, and by Clemo and King (*J.*, 1948, 1661) to account for the uptake of six atoms of hydrogen in the sodium–ammonia reduction of strychnine. Strychnine contains the group $-O-CH_2-CH=\overset{1}{C}-CH_2-N<$, and it was to confirm the possibility of hydrogenolytic fission in simple aliphatic tertiary allylamines that this work was carried out.

The first amine to be investigated was *N*-allylpiperidine prepared by reaction of allyl bromide with two equivalents of piperidine in benzene (Menschutkin, *J. Russ. Phys. Chem. Soc.*, 1899, **31**, 43; *Chem. Zentr.*, 1899, I, 1066). The purity of the product was checked by analysis and by quantitative catalytic hydrogenation. Reduction was carried out by using an excess of sodium in the presence of methanol as a proton source. All attempts to isolate piperidine or to detect its presence in the reaction mixture were unsuccessful, the product being a tertiary amine, characterised as the picrate and methiodide, and identified as *N*-propylpiperidine by comparison of these derivatives with the corresponding derivatives obtained from *N*-propylpiperidine prepared from piperidine and propyl iodide and by catalytic reduction of allylpiperidine. When only two equivalents of sodium were used in this reduction catalytic hydrogenation showed the presence of 45% of unsaturated material in the crude product, but when 5—6 equivalents of sodium were used less than 15% of the starting material remained unreduced. This result was very surprising, being so far as we know the only reported case of chemical reduction of a double bond unconjugated with another unsaturated centre.

To determine the influence of substituents on the course of the reduction the following amines were prepared (with the exception of the diethylamine derivative, in the preparation of which no solvent was used, by the standard procedure used for allylpiperidine) and subjected to the action of sodium in ammonia: diethylmethallylamine, *N*-methallyl-, *N*-crotyl-, *N*-*cyclo*hex-2-enyl-, *N*-2-*tert*.-butylallyl-, *N*-benzyl-, and *N*-2 : 3 : 4 : 5-tetrahydrobenzyl-piperidine.

A standard procedure was employed for the reduction of the amines and for the working up of the reaction mixture. In each case the crude product was isolated with ether and distilled with no attempt at fractionation. A portion of the total distillate was then subjected to quantitative catalytic reduction (not carried out with *N*-benzylpiperidine) and the remainder converted into the picrate and methiodide. Picrates and methiodides of the unsaturated amines and of the corresponding saturated compounds, made by catalytic reduction of the olefinic amine and sometimes also from the appropriate saturated halide, were also prepared for the purpose of comparison. Throughout the whole series we found it an invariable rule that the same derivative of both saturated and unsaturated amines having the same carbon skeleton did not show a depression of melting point when mixed. However, the actual melting points of the saturated and unsaturated compounds were usually very different and the routine

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quantitative hydrogenation carried out did not allow of any confusion between reduced and unreduced material.

Of the amines investigated only diethylmethallylamine, and allyl- and methallyl-piperidine were reduced under the conditions employed. With the remaining amines catalytic reduction of the product from the treatment with sodium in ammonia showed the presence of 98—101% of unsaturated material, *i.e.* a value indistinguishable from that obtained for the pure unsaturated compound. The non-reduction of *N*-crotylpiperidine, bearing so close a relationship to *N*-methallylpiperidine, would seem to indicate that reduction under the conditions investigated is confined to terminal double bonds. The failure of *tert.*-butylallylpiperidine to undergo reduction may be due either to the inductive effect of the *tert.*-butyl substituent or to steric effects.

Experimental.

Preparation of Amines.—The unsaturated bases and certain of the saturated bases were prepared by interaction of the appropriate halide with two equivalents of base in benzene as solvent. The halides used were methallyl chloride (commercial), crotyl bromide (Charon, *Ann. Chim. Phys.*, 1899, **17**, 233), 3-bromo*cyclo*hexene (Ziegler *et al.*, *Annalen*, 1942, **551**, 80), 2-*tert.*-butylallyl bromide [from 2-*tert.*-butylpropene (Edgar, Calingaert, and Marker, *J. Amer. Chem. Soc.*, 1929, **51**, 1483), and *N*-bromosuccinimide], benzyl chloride, 2-bromo-1-methylene*cyclo*hexane (Mousseron, Winternitz, and Jacquier, *Compt. rend.*, 1947, 1062), and 1-bromomethyl*cyclo*hexene. The last was prepared, in small yield, by the action of hydrobromic acid on the corresponding alcohol, which was readily obtained by lithium aluminium hydride reduction of *cyclo*hexene-1-carboxylic acid, prepared by acid (70% sulphuric acid) hydrolysis of the appropriate cyanide (Ruzicka and Brugger, *Helv. Chim. Acta*, 1926, **9**, 399). From the last two bromides only one tertiary amine was obtained, reaction of piperidine with 2-bromo-1-methylene*cyclo*hexane presumably being accompanied by an allylic shift.

With the unsaturated halides the initial reaction with the amine was vigorous and external cooling was usually required. When the reaction had subsided the mixture was heated on the steam-bath for 2 hours and then cooled, and the base hydrohalide removed by filtration and well washed with benzene. The combined filtrate and washings were finally distilled giving the amine. The bases were characterised as the picrates, prepared in ethanol and crystallised from aqueous ethanol, and as the methiodides, prepared in the absence of solvent and purified from acetone–ethyl acetate. *tert.*-Butylallylpiperidine methiodide had an unsatisfactory m. p., and the hydrogen oxalate was therefore also prepared.

Catalytic Reduction of the Unsaturated Bases.—Both analytical and preparative reductions were carried out quantitatively at room temperature and pressure, Adams's platinic oxide being used as catalyst and ethanol containing just more than one equivalent of hydrochloric acid as solvent. Reduction was rapid. In preparative reductions the products were isolated by evaporation of the solvent, treatment of the residue with aqueous sodium hydroxide (40%), and extraction of the liberated oil with ether followed by distillation. Yields of distilled base were in the range 80—90%, varying slightly with the solubility of the amine in aqueous sodium hydroxide. For characterisation picrates and methiodides were prepared.

Reduction of the Bases with Sodium in Ammonia.—(*a*) *N*-Allylpiperidine (Found: C, 76·6; H, 11·8. Calc. for $C_8H_{15}N$: C, 76·8; H, 12·0%) (1 g.) and methanol (1 c.c.) in ammonia (80 c.c.) in an unsilvered Dewar vessel were treated with successive small portions of sodium, with stirring between each addition until the blue colour was discharged. When 2 g. of sodium had been added the solution was poured into a beaker and the ammonia and methanol allowed to evaporate. Water (15 c.c.) was added to the solid residue, and the liberated oil taken up in ether and distilled, giving an oil (0·75 g., 75%), b. p. 148—150°, which on catalytic reduction showed the presence of 0·1 double bond per molecule. The picrate, m. p. 112° (Auerbach and Wolffenstein, *Ber.*, 1899, **32**, 2511, give m. p. 121°; Evans, *J.*, 1897; 524, gives m. p. 108°) (Found: C, 47·0; H, 5·5. Calc. for $C_8H_{17}N,C_6H_3O_7N_3$: C, 47·2; H, 5·6%), and methiodide, m. p. 185° (von Braun, *Ber.*, 1909, **42**, 2534, gives m. p. 181—182°) (Found: N, 4·8. Calc. for $C_9H_{20}NI$: N, 5·2%), were identical in appearance and m. p. with the derivatives obtained from propylpiperidine made both by catalytic reduction of allylpiperidine and by the reaction between propyl iodide and piperidine. The base hydrochloride was prepared from the picrate and purified by sublimation; it had m. p. 227°. Auerbach and Wolffenstein (*loc. cit.*) gave m. p. 212° for propylpiperidine hydrochloride, but an authentic specimen prepared by us, after crystallisation from acetone, had m. p. 226—227°.

(*b*) *N*-Methallylpiperidine and diethylmethallylamine were reduced as in (*a*). The crude product (72%) from the piperidine showed 0·15 double bond per molecule, and that from the diethylamine derivative (51%, low yield probably due to the greater solubility of this base in alkali) showed 0·13 double bond per molecule. Picrates and methiodides were prepared and corresponded with those obtained from the authentic saturated amines.

(*c*) The remaining unsaturated amines were entirely unchanged on attempted reduction under these conditions, or when more methanol and/or more sodium was employed. The substitution of ammonium chloride for methanol as the proton source was equally ineffective. The crude bases after attempted reduction gave on catalytic reduction 0·98—1·01 double bonds per molecule. (Benzylpiperidine was not subjected to catalytic reduction.)

Details of the amines and salts prepared in connection with this work are given in the table.

3-*Bromo*-2-tert.-*butylpropene.*—2-*tert.*-Butylpropene (Edgar *et al.*, *loc. cit.*) (9 g., 1 mol.) and *N*-

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bromosuccinimide (16·3 g., 1 mol.) in carbon tetrachloride (100 c.c.) were boiled under reflux for 4 hours. The solid was removed and the filtrate distilled, giving a fuming, cloudy liquid, b. p. 160—190°, which

Compound.	Yield,[a] %.	B. p. or m. p.	Cryst.[b] form.	Formula.	Found, %. C.	H.	N.	Required, %. C.	H.	N.
N-Allylpiperidine	67	148—151°	—	$C_8H_{15}N$	—	—	—	—	—	—
picrate		85	A	$C_{14}H_{18}O_7N_4$	—	—	15·7	—	—	15·8
methiodide		oily	—	$C_9H_{18}NI$	—	—	—	—	—	—
N-*Methallylpiperidine*	71	164	—	$C_9H_{17}N$	77·4	12·2	—	77·7	12·2	—
picrate		117—118	B	$C_{15}H_{20}O_7N_4$	49·2	5·5	15·5	48·9	5·4	15·2
methiodide		oily	—	$C_{10}H_{20}NI$	—	—	—	—	—	—
Diethylmethallylamine[c]	52	129	—	$C_8H_{17}N$	—	—	10·8	—	—	11·0
picrate		91—92	E	$C_{14}H_{20}O_7N_4$	47·1	5·3	—	47·2	5·6	—
methiodide		171	C	$C_9H_{20}NI$	40·1	7·4	—	40·2	7·4	—
N-*Crotylpiperidine*[d]	74	61/11 mm.	—	$C_9H_{17}N$	78·0	12·2	—	77·7	12·2	—
picrate		98—99	A	$C_{15}H_{20}O_7N_4$	49·4	5·3	—	48·9	5·4	—
methiodide		119	C	$C_{10}H_{20}NI$	43·1	7·2	—	42·7	7·1	—
N-cyclo*Hex*-2-*enylpiperidine*	88	105/10 mm.	—	$C_{11}H_{19}N$	80·3	11·2	—	80·3	11·5	—
picrate		108—109	A	$C_{17}H_{22}O_7N_4$	52·1	6·0	—	51·8	5·6	—
methiodide		160	D	$C_{12}H_{22}NI$	46·5	6·8	—	46·9	7·2	—
N-2-tert.-*Butylallylpiperidine*	71	95/12 mm.	—	$C_{12}H_{23}N$	79·9	12·6	—	79·6	12·7	—
picrate		104 (undried) 132 (dried) at 100°/12 mm.	A	$C_{18}H_{26}O_7N_4$	(on dried sample)		13·8	—	—	13·7
methiodide		148—155	D	$C_{13}H_{26}NI$	—	—	4·5	—	—	4·3
hydrogen oxalate		155	E	$C_{14}H_{25}O_4N$	—	—	5·0	—	—	5·2
N-2 : 3 : 4 : 5-*Tetrahydrobenzylpiperidine*	69	107/12 mm.	—	$C_{12}H_{21}N$	—	—	7·6	—	—	7·8
picrate		156	B	$C_{18}H_{24}O_7N_4$	52·7	6·1	—	52·9	5·9	—
methiodide		170	A	$C_{13}H_{24}NI$	48·6	7·6	—	48·6	7·5	—
N-Benzylpiperidine[e]	78	115/13 mm.	—	$C_{12}H_{17}N$	—	—	—	—	—	—
picrate		178—179	F	$C_{18}H_{20}O_7N_4$	—	—	14·2	—	—	13·9
*N-iso*Butylpiperidine[f]	62	161—163	—	$C_9H_{19}N$	—	—	—	—	—	—
picrate		144—145	D	$C_{15}H_{22}O_7N_4$	—	—	15·3	—	—	14·9
methiodide		197—198	D	$C_{10}H_{22}NI$	42·5	7·9	—	42·4	7·8	—
N-iso*Butyldiethylamine*	—	132	—	$C_8H_{19}N$	—	—	10·4	—	—	10·8
picrate		87—88	B	$C_{14}H_{22}O_7N_4$	47·3	6·2	15·5	46·8	6·15	15·3
methiodide		195	D	$C_9H_{22}NI$	40·1	8·4	—	39·9	8·1	—
N-2-tert.-*Butylpropylpiperidine*	—	95/10 mm.	—	$C_{12}H_{25}N$	78·3	13·7	—	78·6	13·7	—
picrate		135	B	$C_{18}H_{28}O_7N_4$	—	—	13·5	—	—	13·6
hydrogen oxalate		156	E	$C_{14}H_{27}O_4N$	—	—	5·3	—	—	5·1
N-cyclo*Hexylmethylpiperidine*	—	110/11 mm.	—	$C_{12}H_{23}N$	—	—	7·5	—	—	7·7
picrate		148—149	F	$C_{18}H_{28}O_7N_4$	53·2	6·7	—	52·7	6·4	—
methiodide		223—224	D	$C_{13}H_{26}NI$	47·8	8·1	—	48·3	8·05	—

(*a*) Refers to preparation from base and halide. (*b*) A = leaflets, B = prisms, C = tablets, D = needles, E = plates, F = fern-like clusters. (*c*) Made without solvent, reaction time 4 hours. (*d*) Mannich and Mangotte (*Ber.*, 1935, **68**, 273) describe a compound probably having this structure as its b. p. is 59—61°/12 mm. (picrate, m. p. 91°), no analyses were given. (*e*) Clarke (*J.*, 1912, 1807) gives b. p. 119°/13 mm. (*f*) Drake and McElvain (*J. Amer. Chem. Soc.*, 1933, **55**, 1156) give b. p. 160—161°.

was dried ($CaCl_2$) and redistilled under slightly reduced pressure; the pure *bromide* (6·5 g., 40%) had b. p. 140—145°/500 mm. (Found: Br, 44·6. $C_7H_{13}Br$ requires Br, 45·1%).

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