120. *The Preparation and Bacteriostatic Properties of some Amines derived from Citral.*

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Aldimines obtained by condensation of citral with primary and secondary amines are hydrogenated to saturated secondary and tertiary amines using Raney nickel catalyst at 120° under about 140 atmospheres' pressure. The light absorption properties of the unsaturated aldimines, which are similar to those of the parent aldehyde, are discussed.

HYDROGENATION of citraloxime with Raney nickel catalyst in the presence of ammonia gives a 60% yield of tetrahydrogeranylamine (*hydrochloride*, m. p. 104—105°) and 30% of di(tetrahydrogeranyl)amine.

Aldimines from citral and *n*-butylamine and *cyclo*hexylamine have been prepared by a method similar to that of Campbell, Sommers, and Campbell (*J. Amer. Chem. Soc.*, 1944, **66**, 82) and it has been found that the hydrogenation of these aldimines with a Raney nickel catalyst at about 120° under pressures of 140 atmospheres proceeds readily and gives excellent yields of the saturated secondary amines (cf. Henze and Humphreys, *ibid.*, 1942, **64**, 2878).

The hydrogenation of the aldimine derived from *cyclo*hexylamine proceeds in two distinct stages. Under moderate conditions of temperature and pressure in *cyclo*hexane solution, cyclo*hexylcitronellylamine* (I) can be obtained in about 70% yield. It gives acetone (80% yield) on ozonolysis and, on hydrogenation under rather more vigorous conditions, yields the same saturated secondary amine as does the original aldimine when similarly treated. This resistance to hydrogenation of the terminal double bond in compounds of the citral series has been encountered by earlier workers (Skita, *Ber.*, 1909, **42**, 1634; Armstrong and Hilditch, *Proc. Roy. Soc.*, 1925, *A*, **108**, 121).

$$CMe_2{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CHMe{\cdot}CH_2{\cdot}CH_2{\cdot}NH{\cdot}C_6H_{11} \quad \text{(I.)}$$

Owing to the presence of the $C{=}C{-}C{=}N$ system, both of the aldimines mentioned above absorb intensely in the ultra-violet in the region of 2400 A. The aldimines, like the oximes (Evans and Gillam, *J.*, 1943, 565), therefore exhibit much the same light absorption properties as the parent carbonyl compounds and, generally speaking, the chromophores $C{=}C{-}C{=}C$, $C{=}C{-}C{=}O$ and $C{=}C{-}C{=}N$, appear to be very similar in their properties in so far as high-intensity absorption is concerned. The considerable bathochromic effects observed with the semicarbazones and thiosemicarbazones (Evans and Gillam, *loc. cit.*) cannot therefore be attributed, as considered by these authors, to the $C{=}C{-}C{=}N$ chromophore, and the suggestion that $C{=}C{-}C{=}N{-}NH$ chromophores are involved does not explain the difference between the semicarbazones and their thio-analogues. As has already been suggested (Braude and Jones, *J.*, 1945, 498) these effects must be connected with the marked bathochromic effects and conjugating power of nitrogen (Bowden, Braude, Jones, and Weedon, this vol., p. 45) and (in the thiosemicarbazones) sulphur atoms (unpublished observations), and extended chromophores such as $C{=}C{-}C{=}N{-}NH{-}C{=}O$ and $C{=}C{-}C{=}N{-}NH{-}C{=}S$ are probably involved in these cases. The similarity between the light absorption of the oximes and the aldimines is explained both by the absence of any chromophoric group attached to the second oxygen valency and by the almost negligible bathochromic effect and conjugating power of the oxygen atom.

Mannich, Handke, and Roth (*Ber.*, 1936, **69**, 2112) examined the condensation of αβ-unsaturated aldehydes with primary amines and found that ethylenic diamines [*e.g.*, $CHMe(NMe_2){\cdot}CH{:}CH{\cdot}NMe_2$] were initially formed. On heating, these eliminated a molecule of secondary amine giving aminobutadienes (Langenbeck, Gödde, Weschky, and Schaller, *Ber.*, 1942, **75**, 232; cf. Bowden, Braude, Jones, and Weedon, *loc. cit.*). It was observed by the original authors that the intermediate diamines cannot be isolated from condensations with the higher aldehydes, and we have found that condensation of citral with di-*n*-butylamine gives the triply unsaturated tertiary *amine* (II), hydrogenated to the saturated *amine* with a Raney nickel catalyst. The light absorption properties of this compound (maxima at 2820 and 2920 A.) are fully in accordance with expectations, in view of the bathochromic and hyperchromic effects already observed (Bowden, Braude, Jones, and Weedon, *loc. cit.*) when nitrogen atoms are attached to the terminal carbon atoms of olefinic or polyene systems.

$$CMe_2{:}CH{\cdot}CH_2{\cdot}CH{:}CMe{\cdot}CH{:}CH{\cdot}NBu_2 \quad \text{(II.)}$$

Bacteriostasis tests, against a variety of bacteria, on the hydrochlorides of the saturated amines described above, and also on the hydrochloride of the ethylenic amine (I), were kindly carried by Dr. A. T. Fuller of the National Institute for Medical Research, through the courtesy of the Director, Dr. C. R. Harington, F.R.S. The activities observed are roughly of the same order as those already reported for the straight chain amines (Fuller, *Biochem. J.*, 1942, **36**, 548) and, as was found with the latter, they are considerably diminished in serum-broth media.

EXPERIMENTAL.

Light absorption data obtained using alcoholic solutions.

Hydrogenation of Citraloxime with Raney Nickel Catalyst.—(Cf. Skita and Keil, *Ber.*, 1928, **61**, 1452, who employed colloidal platinum.) The oxime (20 g.), dissolved in alcohol (180 c.c.) containing ammonia (*d* 0·88; 15 c.c.), was hydrogenated at 100°/140 atm. for 12 hours using Raney nickel (4—5 g.). The product consisted of (*a*) tetrahydrogeranylamine (10·5 g.), b. p. 60—61°/5 mm., $n_{\mathrm{D}}^{16^\circ}$ 1·4382 (Wallach and Behnke, *Annalen*, 1912, **389**, 197, give b. p. 202—203°, $n_{\mathrm{D}}^{21^\circ}$ 1·4316), giving a *hydrochloride* which crystallised from acetone–light petroleum (b. p. 40—60°) in plates, m. p. 104—105° (Found: N, 7·4. $C_{10}H_{24}NCl$ requires N, 7·25%), and (*b*) di(tetrahydrogeranyl)amine (5·3 g.), b. p. 140°/5 mm., $n_{\mathrm{D}}^{16^\circ}$ 1·4516, hydrochloride, m. p. 140—141° (Skita and Keil, *loc. cit.*, give b. p. 192—193°/15 mm., hydrochloride, m. p. 141—142°).

n-*Butyltetrahydrogeranylamine* (n-*butyl*-3 : 7-*dimethyloctylamine*).—*n*-Butylamine (24·5 g.) was stirred at 0°, and citral (51·5 g.) was added during 2 hours. After stirring for a further hour the product was isolated with ether, the ethereal solution being dried (powdered KOH) at 0° for 20 hours. Evaporation and distillation from a little potassium hydroxide gave the *aldimine* (51·7 g.), b. p. 97—98°/4 mm., $n_{\mathrm{D}}^{18^\circ}$ 1·4879, as a colourless liquid which darkened rapidly in air (Found: C, 81·15; H, 12·05. $C_{14}H_{25}N$ requires C, 81·1; H, 12·15%). Light absorption: Maximum, 2400 A.; log ε = 4·35.

The aldimine (20 g.), dissolved in methyl alcohol (180 c.c.), was hydrogenated at 120°/140 atm. for 9 hours using Raney nickel (4—5 g.), giving n-*butyltetrahydrogeranylamine* (17·1 g.), b. p. 90—92°/4 mm., $n_{\mathrm{D}}^{20^\circ}$ 1·4384 (Found: C, 78·9; H, 14·4. $C_{14}H_{31}N$ requires C, 78·8; H, 14·65%). The *hydrochloride*, prepared with dry hydrogen chloride in ether and crystallised from acetone and from ethyl acetate, had m. p. 196—197° (Found : N, 5·65. $C_{14}H_{32}NCl$ requires N, 5·6%).

cyclo*Hexyltetrahydrogeranylamine* (cyclo*hexyl*-3 : 7-*dimethyloctylamine*).—(Cf. Skita and Keil, *loc. cit.*) The aldimine, prepared in 70% yield by the method described above, had b. p. 125°/4 mm., $n_{\mathrm{D}}^{15^\circ}$ 1·5101 (Found : C, 82·55; H, 11·45. Calc. for $C_{16}H_{29}N$: C, 82·35; H, 11·65%). Light absorption : Maxima, 2390 and 2490 A.; log ε = 4·34 in each case. Reduction of the aldimine (15 g.) in methyl alcohol (150 c.c.) with hydrogen at 120°/140 atm. for 7 hours using Raney nickel (4—5 g.) gave the saturated amine (11·3 g.) with b. p. 103°/4 mm., $n_{\mathrm{D}}^{20^\circ}$ 1·4612 (Found : C, 80·25; H, 13·6. Calc. for $C_{16}H_{33}N$: C, 80·25; H, 13·9%). The hydrochloride had m. p. 153—153·5° (Skita and Keil, *loc. cit.*, give m. p. 154—155°) (Found : N, 5·05. Calc. for $C_{16}H_{34}NCl$: N, 5·1%).

cyclo*Hexylcitronellylamine* (cyclo*hexyl*-3 : 7-*dimethyloct*-6-*enylamine*).—The crude but dried aldimine from *cyclo*hexylamine (26 g.) and citral (40 g.) was dissolved in *cyclo*hexane (85 c.c.) and hydrogenated at 100°/90 atm. for 10 hours in the presence of Raney nickel (4—5 g.). The agitation of the reaction mixture in this case was probably less efficient than in the hydrogenation described immediately above. Isolation in the normal manner gave cyclo*hexylcitronellylamine* (43·2 g.), b. p. 112—113°/4 mm., $n_{\mathrm{D}}^{16^\circ}$ 1·4780 (Found : C, 80·95; H, 12·85. $C_{16}H_{31}N$ requires C, 80·95; H, 13·15%). The *hydrochloride* crystallised from acetone–light petroleum (b. p. 40—60°) in micro-crystals, m. p. 125—126° (Found : N, 5·15. $C_{16}H_{32}NCl$ requires N, 5·15%).

Ozonolysis of cyclo*Hexylcitronellylamine*.—The amine (2 g.) was dissolved in AnalaR acetic acid (35 c.c.), and ozonised oxygen was passed into the solution until absorption ceased (*ca.* 4 hours). Water (150 c.c.) was added and the solution was distilled in steam. The first 30 c.c. of distillate yielded 1·6 g. (80% of theory) of acetone 2 : 4-dinitrophenylhydrazone, m. p. 123—124° undepressed on admixture with an authentic specimen, on treatment with 2 : 4-dinitrophenylhydrazine sulphate solution.

Hydrogenation of cyclo*Hexylcitronellylamine*.—A solution of the amine (25 g.) in methyl alcohol (200 c.c.) was hydrogenated at 100°/140 atm. for 9 hours using Raney nickel (4—5 g.) giving the saturated amine described above, b. p. 110—112°/5 mm., $n_{\mathrm{D}}^{23^\circ}$ 1·4597; the hydrochloride had m. p. 152·5—153°, undepressed on admixture with an authentic specimen.

Di-n-*butyl*-3 : 7-*dimethylocta*-1 : 3 : 6-*trienylamine*.—Citral (38 g.) was added during 25 minutes to stirred di-*n*-butylamine (49 g.) at 0° and stirring was continued for a further 1½ hours. The mixture was treated with anhydrous potassium carbonate and the product isolated with ether, the ethereal solution being dried at 0° for 16 hours (K_2CO_3). Distillation gave the tertiary *amine* (40·5 g.), as a pale yellow mobile oil, b. p. 144—145°/4 mm., $n_{\mathrm{D}}^{20^\circ}$ 1·5129 (Found : C, 82·45; H, 12·85. $C_{18}H_{33}N$ requires C, 82·05; H, 12·6%). Light absorption : Maxima, 2820 and 2920 A.; log ε = 4·37 in each case.

Di-n-*butyltetrahydrogeranylamine* (*di*-n-*butyl*-3 : 7-*dimethyloctylamine*).—The above unsaturated amine (20 g.), on hydrogenation in methyl alcohol (180 c.c.) at 120°/140 atm. with Raney nickel (5—6 g.) for 14 hours, gave the saturated tertiary *amine* (13·9 g.), b. p. 116—117°/4 mm., $n_{\mathrm{D}}^{18^\circ}$ 1·4431 (Found : C, 80·35; H, 14·6. $C_{18}H_{39}N$ requires C, 80·25; H, 14·6%).

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