161. *A Convenient Method of Preparation of Certain Primary Amines.*

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Various primary amines, uncontaminated by the corresponding secondary and tertiary compounds, are readily obtained by condensation of *O*-methylhydroxylamine (1 mol.) with 2 mols. of alkylmagnesium chlorides or preferably bromides, but not with iodides. The yields vary from 40 to 90%. The reaction is also applicable to aliphatic dibromides; *e.g.*, cadaverine is obtainable in 68% yield from pentamethylene bromide.

An investigation requiring considerable quantities of *tert.*-butylamine led to an examination of its preparation on a moderately large scale. Van Erp (*Rec. Trav. chim.*, 1895, **14**, 16) and Brander (*ibid.*, 1918, **37**, 67) prepared it respectively by the Hofmann degradation of pivalic amide and by heating *tert.*-butyl chloride with ammonia, but in both cases the yields were extremely small. Coleman and Yager (*J. Amer. Chem. Soc.*, 1929, **51**, 567) obtained it in 60% yield by condensation of *tert.*-butylmagnesium chloride with chloroamine, but the instability of the latter rendered this method unsuitable for our purpose. Sheverdina and Kocheshkov (*J. Gen. Chem. Russia*, 1938, **8**, 1825), however, overcame this difficulty by replacing the chloroamine by the stable *O*-methylhydroxylamine, two mols. of Grignard compound being required.

$$2RMgCl + MeO{\cdot}NH_2 = RNH{\cdot}MgCl + RH + MeOMgCl$$

The experiments of Sheverdina and Kocheshkov (*loc. cit.*) were carried out on a very small scale (0·03 molar) and at such great dilution as to make larger-scale preparation impracticable, but suitable modifications have permitted an increase to 3-molar scale, the yield being 70% calculated on *O*-methylhydroxylamine.

A number of other halides have also been examined under the same conditions, the results being shown in the Table, together with comparative yields obtained by Sheverdina and Kocheshkov (*loc. cit.*) and by Coleman *et al.* (*loc. cit.* and *J. Amer. Chem. Soc.*, 1928, **50**, 1193; 1933, **55**, 3669; 1936, **58**, 27), all the work of the latter authors involving the use of chloroamine. In contrast to the experience of Coleman and his colleagues with chloroamine the yields with bromides were slightly better than when using the corresponding chlorides, but the result with *iso*amyl iodide confirms the conclusions of all previous investigators that the use of iodides in this type of reaction is to be avoided. No explanation of this phenomenon could be found, all attempts, for example, to correlate the yield of amine with the relative proportions of RMgX and R_2Mg in the Grignard solution being unavailing.

The method finally adopted and exemplified by *tert.*-butylamine in the experimental section is rapid and easy to operate, and permits the facile preparation of a number of primary amines which are otherwise difficult to prepare. A further advantage is that the products are free from secondary and tertiary amines, although ammonia always appears to be formed.

	% Yield R·NH_2.				% Yield R·NH_2.		
Halide.	Present authors.	Sheverdina and Kocheshkov.	Coleman *et al.*	Halide.	Present authors.	Sheverdina and Kocheshkov.	Coleman *et al.*
Ethyl bromide	81 *	66·6 *	27·7 *	*iso*Amyl chloride	60	80·1 *	55·2
n-Propyl bromide	85 *	—	27·0 *	*iso*Amyl bromide	71	—	—
n-Butyl chloride	58	—	58·9	*iso*Amyl iodide	Trace	5·3 *	10·9
n-Butyl bromide	63	—	27·2	*tert.*-Amyl chloride ...	48	—	66·2
*iso*Butyl bromide	90	—	—	Allyl bromide	40	—	—
tert.-Butyl chloride ...	70	73·6 *	60·2	Benzyl chloride	57	—	92
n-Amyl chloride	46	—	—	2-Phenylethyl chloride	68	—	74·0
n-Amyl bromide	65	—	—	Cinnamyl chloride ...	Trace	—	14

* Isolated as, and yields calculated on, hydrochlorides.

In addition to the mono-halides listed in the Table experiments were carried out with pentamethylene bromide, hexamethylene bromide, and decamethylene bromide. In agreement with the work of Hilper and Grüttner (*Ber.*, 1914, **47**, 178) and of Bygdén (*Ber.*, 1915, **48**, 1238) it was found that attempts to form the Grignard compounds under normal anhydrous conditions resulted in the formation of highly polymerised compounds

completely unreactive towards *O*-methylhydroxylamine which was recovered unchanged. When, however, a small quantity of water was present, as suggested by Bygdén (*loc. cit.*), the normal Grignard compounds were formed, and these reacted readily with *O*-methylhydroxylamine. The optimum quantity of water required in the ether was found to be 0·1%. Under these conditions the yields of cadaverine, hexamethylenediamine, and decamethylenediamine were respectively 68%, 51%, and 53% calculated on *O*-methylhydroxylamine; the method provides a convenient means of preparation of this type of compound.

Experimental.

tert.-*Butylamine*.—A solution of *O*-methylhydroxylamine (Traube, Ohlendorf, and Zander, *Ber.*, 1920, **53**, 1477) (141 g., 3 mols.) in anhydrous ether (300 c.c.) was added gradually with vigorous stirring to a solution of *tert.*-butylmagnesium chloride (from 609 g. of *tert.*-butyl chloride) in ether (3 l.), the internal temperature during the addition being maintained at −10° to −15°. After addition was complete the temperature was kept at −10° for a further ½ hour, then allowed to rise slowly to room temperature, and the reaction mixture finally refluxed for 2 hours. It was then cooled and treated at 0° with 5N- hydrochloric acid (3 l.), the layers were separated, and the aqueous solution was evaporated to small bulk under reduced pressure. The residue, containing *tert.*-butylamine hydrochloride, magnesium chloride, and a little ammonium chloride, was strongly basified with 50% aqueous potassium hydroxide and the *tert.*-butylamine distilled out, the fraction b. p. 35—70° being collected. The crude amine was dried (KOH) and redistilled. Yield, 153 g. B. p. 40—45°. The amine after several distillations had b. p. 44·4°, $d_4^{20°}$ 0·6951, $n_D^{20°}$ 1·3789. The following were prepared: N-*Benzoyl* derivative, needles from alcohol, m. p. 134° (Found: N, 7·8. $C_{11}H_{15}ON$ requires N, 7·8%). *Picrate*, prepared in benzene; needles from ethyl acetate–chloroform, m. p. 197—198° (Found: C, 39·7; H, 4·9; N, 18·4. $C_{10}H_{14}O_7N_4$ requires C, 39·7; H, 4·7; N, 18·6%). *Styphnate*, prepared in alcohol; rhombs from alcohol, m. p. 248—250° (decomp.) (Found: C, 43·0; H, 6·5; N, 17·9. $2C_4H_{11}N, C_6H_3O_8N_3$ requires C, 43·0; H, 6·4; N, 17·9%). *Picrolonate*, prepared in benzene; needles from ethyl acetate–alcohol, m. p. 260° (decomp.) (Found: C, 50·1; H, 5·9; N, 20·4. $C_{14}H_{19}O_5N_5$ requires C, 49·9; H, 5·7; N, 20·7%).

n-*Butylamine*.—The yield of amine, b. p. 77—78°, prepared as above, was 63% from *n*-butyl bromide, or 58% from the chloride. The *picrate* crystallised from ethyl acetate–benzene in needles, m. p. 145° (Found: C, 39·9; H, 4·7; N, 18·6. $C_{10}H_{14}O_7N_4$ requires C, 39·7; H, 4·7; N, 18·6%). The *picrolonate* separated from ethyl acetate in needles, m. p. 219—220° (Found: C, 50·0; H, 5·7; N, 20·7. $C_{14}H_{19}O_5N_5$ requires C, 49·9; H, 5·7; N, 20·7%).

iso*Butylamine*.—Prepared in 90% yield from *iso*butyl bromide. B. p. 68—69°. The *picrate* crystallised from ethyl acetate–benzene in needles, m. p. 150° (Found: C, 40·2; H, 4·7; N, 18·4. $C_{10}H_{14}O_7N_4$ requires C, 39·7; H, 4·7; N, 18·6%). The *picrolonate* crystallised from ethyl acetate in needles, m. p. 215—216° (Found: C, 49·5; H, 5·9; N, 20·6. $C_{14}H_{19}O_5N_5$ requires C, 49·9; H, 5·7; N, 20·7%).

n-*Amylamine*.—Prepared in 65% yield from *n*-amyl bromide or 46% from the chloride. B. p. 104°. The *picrate* crystallised from ethyl acetate–benzene in needles, m. p. 138—139° (Found: C, 42·0; H, 4·6; N, 17·4. $C_{11}H_{16}O_7N_4$ requires C, 41·7; H, 5·1; N, 17·7%). The *picrolonate* crystallised from ethyl acetate in needles, m. p. 198° (Found: C, 51·5; H, 6·1; N, 19·7. $C_{15}H_{21}O_5N_5$ requires C, 51·3; H, 6·0; N, 19·9%).

iso*Amylamine*.—Obtained in 71% yield from the corresponding bromide or 60% from the chloride. B. p. 95—96°. *Picrate*, needles from ethyl acetate–benzene, m. p. 137·5° (Found: C, 41·5; H, 5·3; N, 17·4. $C_{11}H_{16}O_7N_4$ requires C, 41·7; H, 5·1; N, 17·7%). The *picrolonate* crystallised from ethyl acetate in needles, m. p. 219° (Found: C, 51·6; H, 6·1; N, 19·6. $C_{15}H_{21}O_5N_5$ requires C, 51·3; H, 6·0; N, 19·9%).

tert.-*Amylamine*.—The yield from *tert.*-amyl chloride was 48%. B. p. 77—78°. The *picrate* crystallised from ethyl acetate–benzene in needles, m. p. 182—183° (Found: C, 42·0; H, 5·2; N, 17·4. $C_{11}H_{16}O_7N_4$ requires C, 41·7; H, 5·1; N, 17·7%).

Allylamine.—Allyl bromide gave a 40% yield of the amine, b. p. 58°. It was characterised as its picrate, m. p. 140° (Gabriel and Eschenbach, *Ber.*, 1897, **30**, 1125, give m. p. 140—141°).

Benzylamine.—The yield of amine, b. p. 90°/12 mm., prepared from the chloride by the above method was 57%. No reason could be found for this yield being so much lower than that obtained with chloroamine (Coleman *et al.*, *loc. cit.*). The amine was identified as its picrate, m. p. 194° (Moureu and Lazennec, *Bull. Soc. chim.*, 1906, **35**, 1183, give m. p. 194°).

2-*Phenylethylamine*.—The yield of this amine, b. p. 76—78°/10 mm., prepared from the chloride, was 68%. It was characterised as the picrate, m. p. 167° (Kolshorn, *Ber.*, 1904, **37**, 2484, gives m. p. 167—168°).

Cadaverine.—Pentamethylene bromide (23 g.) was added gradually with stirring to magnesium turnings (7·6 g.) in ether (150 c.c.) containing 0·1% of water. The mixture was cooled so that the ether was just refluxing, and when the reaction had moderated the reaction mixture was kept overnight at room temperature and then refluxed for 4 hours. It was then cooled to −15° and a solution of *O*-methylhydroxylamine (4·7 g.) in dry ether (15 c.c.) was added gradually with stirring, the temperature being maintained between −10° and −15°. After addition of the *O*-methylhydroxylamine was complete, the reaction mixture was allowed to attain room temperature and then refluxed for 2 hours. The complex was decomposed with 5N-hydrochloric acid at 0°, the aqueous layer separated and made alkaline with 40% aqueous sodium hydroxide, and the diamine steam-distilled out. The distillate was made acid with hydrochloric acid and evaporated to dryness under reduced pressure, and the residue extracted with alcohol containing a trace of water. Evaporation of the alcohol gave the cadaverine hydrochloride; the free amine was liberated by means of 50% aqueous potassium hydroxide, dried over solid potassium hydroxide, and distilled. B. p. 178—180°. Yield 68%. The dipicrate crystallised from water in needles, m. p. 237° (decomp.) [Baumann and Udránszky, *Z. physiol. Chem.*, 1889, **13**, 570, give m. p. 220—222° (decomp.)].

Hexamethylenediamine.—Prepared from hexamethylene bromide as for cadaverine. B. p. 204°. Yield, 51%. The picrate crystallised from water in needles, m. p. 220° (decomp.) [Ssolonina, *Bull. Soc. chim.*, 1896, **16**, 1880, gives m. p. *ca.* 220° (decomp.)].

Decamethylenediamine.—Prepared in 53% yield from decamethylene bromide in the same way as cadaverine. M. p. 60°. The *picrate* crystallised from water in needles, m. p. 134° (Found: C, 42·0; H, 4·5; N, 17·4. $C_{22}H_{30}O_{14}N_8$ requires C, 41·9; H, 4·8; N, 17·7%).

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