

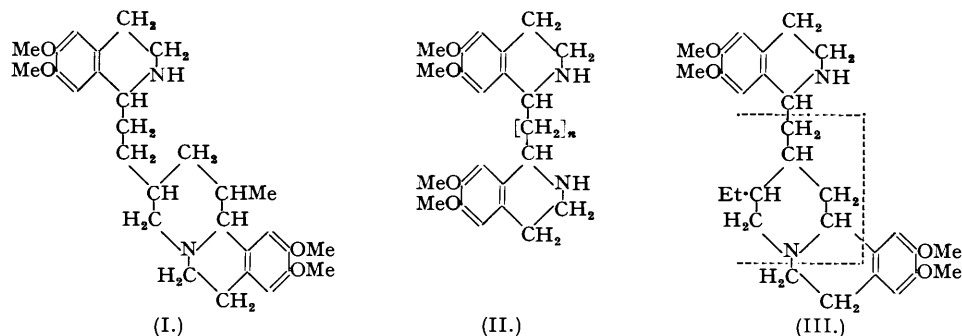
373. Structure and Amœbicidal Activity. Part I. Aliphatic Diamines.

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Fourteen aliphatic diamines of the type $\text{NH}_2 \cdot \text{CHR} \cdot [\text{CH}_2]_n \cdot \text{CHR} \cdot \text{NH}_2$ have been synthesised as their dihydrochlorides. Three of them with $n = 3$ and one with $n = 4$ are effective against *Entamœba histolytica* at a concentration of 1 in 10^5 . (Emetine is effective at a concentration of 1 in 5×10^5 .)

ATTEMPTS to dissect out that portion of the emetine molecule which might be responsible for the amœbicidal action of the alkaloid have so far met with little success. Thus, Child and Pyman (*J.*, 1929, 2010) basing their ideas on Pyman's emetine formula (I) (*J.*, 1927, 1067) prepared a series of compounds of the type (II), or closely related thereto, with $n = 4, 5$, or 8. None of the substances examined was active against *Entamœba histolytica* at dilutions of 1 in 5000, whereas emetine is effective at 1 in 500,000.

Later, however, Pyman (*Rep. Brit. Ass.*, 1937, 107, 57) reported some amœbicidal activity on the part of 1 : 10-bisdiamylaminododecane. Goodson, Gorvin, Goss, Kirby, Lock, Neal, Sharp, and Solomon (*Brit. J. Pharmacol.*, 1948, 3, 49) examined a considerable series of compounds, including some of the types $[\text{3 : 4 : 1-(OMe)}_2\text{C}_6\text{H}_3 \cdot \text{NH}]_2 > [\text{CH}_2]_n$ and $(n\text{-C}_8\text{H}_{17} \cdot \text{NH})_2 > [\text{CH}_2]_n$ and also the one primary diamine $\text{NH}_2 \cdot [\text{CH}_2]_{10} \cdot \text{NH}_2$.



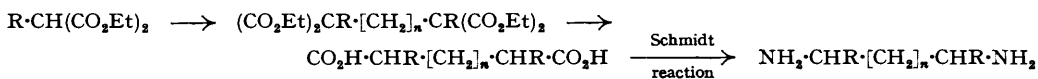
The correction of the formula for emetine to (III) (Robinson, *Nature*, 1948, 162, 524; Pailer and Porschinski, *Monatsh.*, 1949, 80, 94; Battersby, Openshaw, and Wood, *Experientia*, 1949, 5, 114; Battersby and Openshaw, *J.*, 1949, 3207) does not bear materially on the interpretation of the search for amœbicides outlined above. [It is interesting to note that the central portion—within dotted lines in (III)—of the emetine structure contains the features of a partly decyclised ethylquinuclidine.]

All the above compounds with the exception of the diaminododecane contain secondary or tertiary nitrogen atoms. In the present work a study has been made of long-chain diamines containing two *primary* amino-groups and having the general formula $\text{NH}_2 \cdot \text{CHR} \cdot [\text{CH}_2]_n \cdot \text{CHR} \cdot \text{NH}_2$. *In vitro* activities against *E. histolytica* found within the series are as high as 1 in 100,000.

As expected, simple polymethylene diamines of low molecular weight ($\text{R} = \text{H}$, $n = 1$ or 2) are inactive. With the introduction of alkyl groups having 4, 5, 6, or 8 carbon atoms, activity is consistently manifested when $n = 3$ (see Table). When $n = 4$ or 5 (see Table) the dystherapeutic effect of increasing molecular weight becomes evident and compounds 11 ($\text{R} = 2$ -ethylhexyl; $n = 4$) and 14 ($\text{R} = n$ -hexyl; $n = 5$) are inactive. This is an interesting result in view of the fact that the emetine molecule contains, apart from the methoxyl groups, a skeleton of 25 carbon atoms (compounds 11 and 14 have 22 and 19 carbon atoms, respectively). However, in emetine the two nitrogen atoms are separated by five carbon atoms, corresponding to $n = 3$ in our series.

The straight chain diamines are in several cases more active than the corresponding compounds with branched chains. Thus, the activities of compounds 1 ($\text{R} = \text{Bu}^n$; $n = 3$) and 3 ($\text{R} = n$ -amyl; $n = 3$) are reduced when R becomes *isobutyl* and *isoamyl*, respectively (compounds 2 and 4).

The diamines were prepared (in the form of their hydrochlorides) by the following general procedure :



All the compounds were tested as the water-soluble hydrochlorides.

In vitro amœbicidal activities of dihydrochlorides of $\text{NH}_2\cdot\text{CHR}\cdot[\text{CH}_2]_n\cdot\text{CHR}\cdot\text{NH}_2$.

Compound no.	Diamines of the pentamethylene series (n = 3).	R.	Activity.
1	5 : 9-Diaminotridecane	Bu ^a	1 in 10,000
2	4 : 8-Diamino-2 : 10-dimethylundecane	Bu ^t	1 in 1,000
3	6 : 10-Diaminopentadecane	<i>n</i> -amyl	1 in 100,000
4	5 : 9-Diamino-2 : 12-dimethyltridecane	<i>iso</i> amyl	1 in 10,000
5	7 : 11-Diaminoheptadecane	<i>n</i> -hexyl	1 in 100,000
6	7 : 11-Diamino-5 : 13-diethylheptadecane	2-ethylhexyl	1 in 100,000
Diamines of the hexamethylene series (n = 4).			
7	5 : 10-Diaminotetradecane	Bu ^a	1 in 10,000
8	6 : 11-Diaminohexadecane	<i>n</i> -amyl	1 in 10,000
9	5 : 10-Diamino-2 : 13-dimethyltetradecane	<i>iso</i> amyl	1 in 10,000
10	7 : 12-Diamino-octadecane	<i>n</i> -hexyl	1 in 100,000
11	7 : 12-Diamino-5 : 14-diethyloctadecane	2-ethylhexyl	inactive
Diamines of the heptamethylene series (n = 5).			
12	5 : 11-Diaminopentadecane	Bu ^a	1 in 10,000
13	4 : 10-Diamino-2 : 12-dimethyltridecane	Bu ^t	1 in 10,000
14	7 : 13-Diaminononadecane	<i>n</i> -hexyl	inactive

EXPERIMENTAL.

Microanalyses by Drs. Weiler and Strauss.

Ethyl Alkanetetracarboxylates and Derived Acids.—Normal procedure was adopted for condensing polymethylene dibromides with the sodio-derivatives of substituted malonic esters (compare Perkin and Prentice, *J.*, 1891, 59, 818). The following esters were thus prepared (yields are given in parentheses) and were hydrolysed to the tetracarboxylic acids by boiling them with alcoholic potassium hydroxide.

Ethyl tridecane-5 : 5 : 9 : 9-tetracarboxylate (25%), b. p. 198—202°/1 mm., 214—216°/4 mm., crystallised from methyl alcohol, melted at 35—37° (Found : C, 63.5; H, 8.6. C₂₅H₄₄O₈ requires C, 63.5; H, 9.3%). The derived *acid*, crystallised from water, had m. p. 149—151° (decomp.) (Found : C, 56.0; H, 7.8. C₁₇H₂₈O₈ requires C, 56.5; H, 7.8%).

Ethyl 2 : 10-dimethylundecane-4 : 4 : 8 : 8-tetracarboxylate (33%), crystallised from methyl alcohol, melted at 45—47°. Perkin and Prentice (*loc. cit.*) did not obtain a crystalline specimen. The derived *acid*, crystallised from aqueous acetic acid, had m. p. 148—150° (decomp.) (Found : C, 56.1; H, 7.8. C₁₇H₂₈O₈ requires C, 56.5; H, 7.8%). Perkin and Prentice (*loc. cit.*) prepared this acid but did not purify it or analyse it.

Ethyl pentadecane-6 : 6 : 10 : 10-tetracarboxylate (32.5%) had b. p. 234°/2 mm.; *n*_D^{18.5} 1.4492 (Found : C, 64.9; H, 9.2. C₂₇H₄₈O₈ requires C, 64.7; H, 9.6%). The derived *acid*, crystallised from dilute aqueous acetic acid, had m. p. 175.5° (decomp.) (Found : C, 58.4; H, 8.4. C₁₉H₃₂O₈ requires C, 58.7; H, 8.3%).

Ethyl 2 : 12-dimethyltridecane-5 : 5 : 9 : 9-tetracarboxylate (36%) had b. p. 225°/2 mm., *n*_D²⁰ 1.4480 (Found : C, 65.0; H, 9.5. C₂₇H₄₈O₈ requires C, 64.7; H, 9.6%). The derived *acid*, crystallised from aqueous acetic acid, had m. p. 196—197° (decomp.) (Found : C, 57.3; H, 8.4. C₁₉H₃₂O₈ requires C, 57.4; H, 8.3%).

Ethyl heptadecane-7 : 7 : 11 : 11-tetracarboxylate (39%) had b. p. 254°/5 mm., 270°/9 mm., *n*_D¹⁷ 1.4530 (Found : C, 65.9; H, 9.9. C₂₉H₅₂O₈ requires C, 65.8; H, 9.9%). The derived *acid*, crystallised from dilute aqueous acetic acid, had m. p. 175—177° (decomp.) (Found : C, 60.6; H, 8.5. C₂₁H₃₆O₈ requires C, 60.5; H, 8.7%).

Ethyl 5 : 13-diethylheptadecane-7 : 7 : 11 : 11-tetracarboxylate (28.5%) had b. p. 258°/3 mm., *n*_D¹⁸ 1.4569 (Found : C, 68.2; H, 10.3. C₃₃H₆₀O₈ requires C, 67.8; H, 10.3%). The derived *acid*, crystallised from aqueous acetic acid, had m. p. 167—168° (decomp.) (Found : C, 63.7; H, 9.3. C₂₅H₄₄O₈ requires C, 63.5; H, 9.3%).

Ethyl tetradecane-5 : 5 : 10 : 10-tetracarboxylate (70%), crystallised from light petroleum (b. p. 40—60°), melted at 31—32° (Found : C, 64.0; H, 9.6. C₂₆H₄₆O₈ requires C, 64.1; H, 9.5%). The derived *acid*, crystallised from benzene-acetic acid, had m. p. 194—197° (decomp.) (Found : C, 58.0; H, 8.2. C₁₈H₃₀O₈ requires C, 57.7; H, 8.0%).

Ethyl hexadecane-6 : 6 : 11 : 11-tetracarboxylate (42%) had b. p. 244—246°/2 mm., *n*_D²² 1.4495 (Found : C, 65.8; H, 9.9. C₂₈H₅₀O₈ requires C, 65.3; H, 9.8%). The derived *acid*, crystallised from aqueous acetic acid, had m. p. 189—191° (decomp.) (Found : C, 60.0; H, 8.7. C₂₀H₃₄O₈ requires C, 59.7; H, 8.5%).

Ethyl 2 : 13-dimethyltetradecane-5 : 5 : 10 : 10-tetracarboxylate (46%) had b. p. 242°/3 mm., *n*_D²⁷ 1.4465 (Found : C, 65.3; H, 9.7. C₂₈H₅₀O₈ requires C, 65.3; H, 9.8%). The derived *acid*, crystallised from

aqueous acetic acid, had m. p. 213° (decomp.) (Found : C, 59.3; H, 8.5. $C_{30}H_{34}O_8$ requires C, 59.7; H, 8.5%).

Ethyl octadecane-7 : 7 : 12 : 12-tetracarboxylate (45%) had b. p. 254—260°/5 mm., n_D^{21} 1.4510 (Found : C, 67.0; H, 10.3. $C_{30}H_{34}O_8$ requires C, 66.3; H, 10.0%). The derived acid, crystallised from aqueous acetic acid, had m. p. 194° (decomp.) (Found : C, 61.9; H, 8.7. $C_{22}H_{38}O_8$ requires C, 61.4; H, 8.8%).

Ethyl 5 : 14-diethyloctadecane-7 : 7 : 12 : 12-tetracarboxylate (50%) had b. p. 248°/1 mm., n_D^{20} 1.4562 (Found : C, 68.7; H, 10.5. $C_{34}H_{62}O_8$ requires C, 68.2; H, 10.4%). The derived acid, obtained as a glass which did not crystallise, gave a silver salt (Found : Ag, 46.9. $C_{26}H_{42}O_8Ag_4$ requires Ag, 47.2%).

Ethyl pentadecane-5 : 5 : 11 : 11-tetracarboxylate (70%), crystallised from light petroleum (b. p. 40—60°), melted at 44—46° (Found : C, 64.8; H, 9.5. $C_{27}H_{46}O_8$ requires C, 64.7; H, 9.6%). The derived acid, crystallised from aqueous acetic acid, had m. p. 169—171° (decomp.) (Found : C, 59.0; H, 8.3. $C_{19}H_{32}O_8$ requires C, 58.7; H, 8.3%).

Ethyl 2 : 12-dimethyltridecane-4 : 4 : 10 : 10-tetracarboxylate (70%), crystallised from light petroleum (b. p. 40—60°), melted at 63—65° (Found : C, 65.6; H, 9.2. $C_{27}H_{46}O_8$ requires C, 64.7; H, 9.6%). The derived acid, crystallised from benzene-acetic acid, had m. p. 153—155° (decomp.) (Found : C, 57.8; H, 8.4. $C_{19}H_{32}O_8 \cdot \frac{1}{2}H_2O$ requires C, 57.4; H, 8.3%).

Ethyl nonadecane-7 : 7 : 13 : 13-tetracarboxylate (50%) had b. p. 248—250°/2—3 mm., n_D^{18} 1.4550 (Found : C, 66.8; H, 9.7. $C_{31}H_{56}O_8$ requires C, 66.8; H, 10.1%). The derived acid, crystallised from benzene-acetic acid, had m. p. 174—176° (decomp.) (Found : C, 61.5; H, 8.8. $C_{23}H_{40}O_8$ requires C, 62.1; H, 9.1%).

Dicarboxylic Acids.—These were obtained in almost quantitative yield by heating the tetracarboxylic acids at a pre-determined optimum temperature which is given in parentheses immediately after the name of the acid

Tridecane-5 : 9-dicarboxylic acid (205°) crystallised from aqueous acetic acid in plates, m. p. 107—108° (Found : C, 66.7; H, 10.1. $C_{15}H_{28}O_4$ requires C, 66.1; H, 10.3%).

2 : 10-Dimethylundecane-4 : 8-dicarboxylic acid, crystallised from light petroleum (b. p. 80—100°), had m. p. 107—109° (Found : C, 66.7; H, 10.1. Calc. for $C_{15}H_{28}O_4$: C, 66.1; H, 10.3%) (Perkin and Prentice, *loc. cit.*, give m. p. indefinite, 82—84°).

Pentadecane-6 : 10-dicarboxylic acid (160°) crystallised from aqueous acetic acid in plates, m. p. 109—112.5° (Found : C, 67.9; H, 10.6. $C_{17}H_{32}O_4$ requires C, 67.9; H, 10.8%).

2 : 12-Dimethyltridecane-5 : 9-dicarboxylic acid (190°) crystallised from light petroleum (b. p. 60—80°) in shining plates, m. p. 140° (Found : C, 67.2; H, 10.6. $C_{17}H_{32}O_4$ requires C, 67.9; H, 10.8%).

Heptadecane-7 : 11-dicarboxylic acid (180°) crystallised from benzene in shining plates, m. p. 112—114° (Found : C, 70.0; H, 10.8. $C_{19}H_{36}O_4$ requires C, 69.4; H, 11.0%).

5 : 13-Diethylheptadecane-7 : 11-dicarboxylic acid (160°), obtained as an oil, gave a silver salt (Found : Ag, 36.1. $C_{23}H_{44}O_4Ag_2$ requires Ag, 36.0%).

Tetradecane-5 : 10-dicarboxylic acid (170°), crystallised from light petroleum (b. p. 40—60°), had m. p. 103—109° (Found : C, 66.9; H, 10.5. $C_{16}H_{30}O_4$ requires C, 67.1; H, 10.5%).

Hexadecane-6 : 11-dicarboxylic acid (190°), crystallised from light petroleum (b. p. 60—80°), had m. p. 99° (Found : C, 69.0; H, 10.7. $C_{18}H_{34}O_4$ requires C, 68.7; H, 10.9%).

2 : 13-Dimethyltridecane-5 : 10-dicarboxylic acid (190°), crystallised from light petroleum (b. p. 60—80°), had m. p. 119—121° (Found : C, 69.0; H, 10.9. $C_{18}H_{34}O_4$ requires C, 68.7; H, 10.9%).

Octadecane-7 : 12-dicarboxylic acid (165°) crystallised from light petroleum (b. p. 40—60°) and had m. p. 97° in a sealed tube (Found : C, 70.0; H, 11.2. $C_{20}H_{38}O_4$ requires C, 70.1; H, 11.1%).

5 : 14-Diethyloctadecane-7 : 12-dicarboxylic acid (175°), obtained as an oil, gave a silver salt (Found : Ag, 35.0. $C_{24}H_{44}Ag_2$ requires Ag, 35.2%).

Pentadecane-5 : 11-dicarboxylic acid (160°) crystallised from aqueous acetic acid in rods, m. p. 90—94° (Found : C, 67.7; H, 10.8. $C_{17}H_{32}O_4$ requires C, 67.9; H, 10.8%).

2 : 12-Dimethyltridecane-4 : 10-dicarboxylic acid (160°), crystallised from aqueous acetic acid, had m. p. 111—112° (Found : C, 67.5; H, 10.4. $C_{17}H_{32}O_4$ requires C, 67.9; H, 10.8%).

Nonadecane-7 : 13-dicarboxylic acid (175°), crystallised from light petroleum (b. p. 40—60°), had m. p. 72.5—75.5° (Found : C, 69.1; H, 11.1. $C_{21}H_{40}O_4 \cdot \frac{1}{2}H_2O$ requires C, 69.0; H, 11.3%).

Diamines.—Schmidt's reaction was used for the preparation of the diamines from the long-chain dicarboxylic acids. Up to the present it had been applied only to three aliphatic dicarboxylic acids : succinic, adipic, and dodecane-1 : 12-dicarboxylic acid. The following general conditions were used : the dibasic acid was dissolved in concentrated sulphuric acid and benzene added (3—5 c.c. of acid and 3—6 c.c. of benzene for each g. of dibasic acid). Powdered activated sodium azide (Nelles, *Ber.*, 1932, 65, 1345) was added (2—4 g.-mols. for 1 g.-mol. of dibasic acid) in small portions, with stirring at such a rate that the reaction mixture remained at a suitable temperature (usually *ca.* 30°). In a few cases the reaction mixture was subsequently warmed to a higher temperature to complete the reaction. Sodium hydroxide solution (30%) was added with strong cooling and the base extracted with benzene. Hydrogen chloride was passed into the dried extract and the precipitated hydrochloride separated.

5 : 9-Diaminotridecane was obtained as the hydrochloride (compound 1) from tridecane-5 : 9-dicarboxylic acid in 50—60% yield. The reaction was carried out at 35—45°. The *di(hydrogen oxalate)* crystallised from alcohol and had m. p. 198.5—199° (Found : C, 52.3; H, 8.2; N, 7.1. $C_{17}H_{34}O_8N_2$ requires C, 51.8; H, 8.7; N, 7.1%).

4 : 8-Diamino-2 : 10-dimethylundecane was obtained as the hydrochloride (compound 2) (decomp. above 225°) in 75% yield. The reaction mixture was heated to 45° to start the reaction but thereafter it proceeded smoothly at 30—32°. The *dipicrate* crystallised from aqueous ethyl alcohol in needles, m. p. 187—190° (Found : C, 44.9; H, 5.3; N, 16.5. $C_{25}H_{38}O_{14}N_8$ requires C, 44.6; H, 5.3; N, 16.6%).

6 : 10-Diaminopentadecane hydrochloride (compound 3) was obtained in 78% yield. The reaction was carried out at 25—30°. The *dipicrate*, crystallised from benzene-ethyl alcohol, had m. p. 130—133° (Found : C, 47.0; H, 5.4; N, 15.8. $C_{27}H_{40}O_{14}N_8$ requires C, 46.3; H, 5.7; N, 16.0%). The *diacetyl* derivative, crystallised from aqueous alcohol, had m. p. 179—180° (Found : N, 8.8. $C_{19}H_{38}O_2N_2$ requires N, 8.5%).

5 : 9-Diamino-2 : 12-dimethyltridecane hydrochloride (compound 4) was obtained in 80% yield. The reaction was carried out at 20—30°. The *dipicrate*, crystallised from benzene-ethyl alcohol, had m. p. 167—170° (Found : N, 15.9. $C_{27}H_{40}O_{14}N_8$ requires N, 16.0%).

7 : 11-Diaminoheptadecane hydrochloride (compound 5) was obtained in 75% yield, the reaction being carried out at 25—30°. The *dipicrate*, crystallised from benzene-ethyl alcohol, had m. p. 144—146° (Found : N, 15.2. $C_{29}H_{44}O_{14}N_8$ requires N, 15.3%). The *diacetyl* derivative, crystallised from aqueous ethyl alcohol, had m. p. 186° (Found : C, 70.9; H, 12.1; N, 7.7. $C_{31}H_{42}O_2N_2$ requires C, 71.1; H, 12.0; N, 7.9%).

7 : 11-Diamino-5 : 13-diethylheptadecane hydrochloride (compound 6) was obtained in 25—35% yield. The reaction was carried out at 25—30°. The *dihydrochloride* could only be isolated with water of crystallisation which it retained even after intensive drying *in vacuo*. It melted at 134—138° (Found : C, 60.4; H, 11.8; N, 6.8; Cl, 17.0. $C_{21}H_{46}N_2 \cdot 2HCl \cdot H_2O$ requires C, 60.4; H, 12.0; N, 6.7; Cl, 17.0%). The *dipicrate*, crystallised from benzene-ethyl alcohol, had m. p. 151—153° (Found : C, 50.3; H, 6.7; N, 13.8. $C_{33}H_{52}O_{14}N_8$ requires C, 50.5; H, 6.6; N, 14.2%).

5 : 10-Diaminotetradecane hydrochloride (compound 7) was obtained in 60% yield, the reaction being carried out at 25—30°. The *dipicrate*, crystallised from water, had m. p. 205—206° (Found : C, 45.8; H, 5.7; N, 16.5. $C_{26}H_{38}O_{14}N_8$ requires C, 45.4; H, 5.5; N, 16.3%).

6 : 11-Diaminohexadecane hydrochloride (compound 8) was obtained in 60% yield, the reaction being carried out at 25—30°. The *dipicrate*, crystallised from benzene-ethyl alcohol, had m. p. 155—158° (Found : C, 46.7; H, 5.7; N, 14.6. $C_{28}H_{42}O_{14}N_8$ requires C, 47.0; H, 5.9; N, 15.7%).

5 : 10-Diamino-2 : 13-dimethyltetradecane hydrochloride (compound 9) was obtained in 76% yield, the reaction being carried out at 25—30°. The *dipicrate*, crystallised from benzene-ethyl alcohol, had m. p. 205° (decomp.) (Found : C, 47.5; H, 5.8; N, 14.8. $C_{28}H_{42}O_{14}N_8$ requires C, 47.0; H, 5.9; N, 15.7%).

7 : 12-Diamino-octadecane (compound 10) was obtained as the picrate in 75—80% yield, the reaction being carried out at 25—30°. The *dipicrate*, crystallised from benzene-ethyl alcohol, had m. p. 176—180° (Found : C, 48.9; H, 6.1; N, 15.1. $C_{30}H_{46}O_{14}N_8$ requires C, 48.5; H, 6.2; N, 15.1%).

7 : 12-Diamino-5 : 14-diethyloctadecane hydrochloride (compound 11) was obtained in 70—87% yield, the reaction being carried out at 30—35°. The *dipicrate*, crystallised from benzene-ethyl alcohol, had m. p. 157—159° (Found : C, 51.1; H, 6.6; N, 14.0. $C_{34}H_{54}O_{14}N_8$ requires C, 51.1; H, 6.8; N, 14.0%). The *dihydrochloride* was prepared in benzene-carbon tetrachloride (Found : C, 64.1; H, 11.5; N, 6.6. $C_{22}H_{46}N_2 \cdot 2HCl$ requires C, 63.9; H, 12.1; N, 6.7%).

5 : 11-Diaminopentadecane hydrochloride (compound 12) was obtained in 79% yield, the reaction being carried out at 25—30°. The *dipicrate*, crystallised from aqueous ethyl alcohol, had m. p. 198—199° (Found : C, 46.3; H, 5.9; N, 15.8. $C_{27}H_{40}O_{14}N_8$ requires C, 46.3; H, 5.7; N, 16.0%).

4 : 10-Diamino-2 : 12-dimethyltridecane hydrochloride (compound 13) was obtained in 50—55% yield, the reaction being carried out at 20—25°. The *dipicrate*, crystallised from water, had m. p. 194—195° (Found : C, 46.5; H, 5.7; N, 16.1. $C_{27}H_{40}O_{14}N_8$ requires C, 46.3; H, 5.7; N, 16.0%).

7 : 13-Diaminononadecane (compound 14) was obtained as the hydrochloride (m. p. 188—189°) in 80% yield, the reaction being carried out at 20—25°. The *dipicrate*, crystallised from benzene-ethyl alcohol, had m. p. 157—159° (Found : C, 49.8; H, 6.1; N, 14.4. $C_{31}H_{46}O_{14}N_8$ requires C, 49.2; H, 6.3; N, 14.8%).

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