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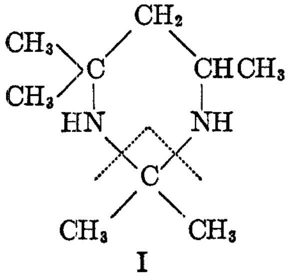
THE CONDENSATION OF 2,4-DIAMINO-4-METHYLPENTANE WITH CARBONYL COMPOUNDS

E. BERGMANN, D. HERMAN, and E. ZIMKIN

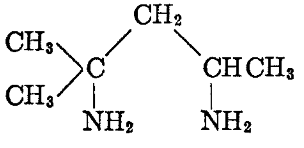
Received November 26, 1947

E. Matter (1) has recently described, as one product of interaction between acetone and ammonia, 2,2,4,6,6-pentamethyl-1,2,5,6-tetrahydropyrimidine, which could be reduced by means of sodium and alcohol to the corresponding hexahydro compound (I).[1] Its structure derives from the observation that both dilute hydrochloric acid and alcoholic sodium hydroxide solution decompose it into 2,4-diamino-4-methylpentane (II) and acetone, in the manner indicated in (I). Veer (3) had observed the same degradation, by acids, of the condensation products from 1,3-dianilinopropane and aldehydes, which he also considered as hexahydropyrimidines.

We wish to report in this connection that substances of the type (I) are obtained easily and in good yield, when a 1,3-diamine such as (II) is heated with a ketone in benzene solution in such a way that the water liberated is continuously removed in form of its azeotrope with benzene. Obviously, acetone which boils below that azeotrope (63°) cannot be condensed with (II) by this method; but 3-methyl-3-butanol-2-one (III) and cyclohexanone reacted in the desired manner. The same method can be applied advantageously to aldehydes boiling above 63°, *e.g.*, to benzaldehyde, 2-ethylhexanal or 2-ethyl-2-hexenal.



I



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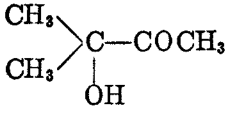

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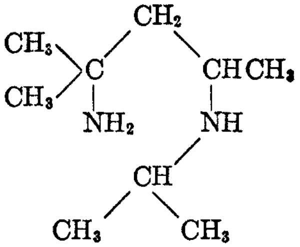

IV

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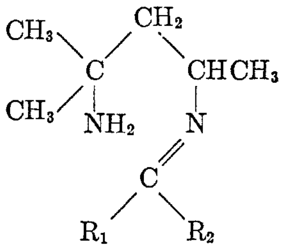
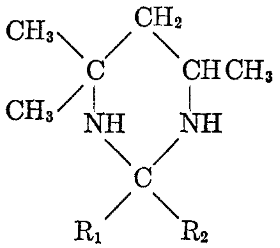
[1] Spaeth and von Szilagyi (2) have recently isolated a similar product from formisobutyraldol and ammonia.

Acetophenone and methylisobutyl ketone did not react appreciably in boiling benzene; the desired reaction could be achieved at 150°.

Theoretically, this condensation can lead to a Schiff base as well as to a hexahydropyrimidine, *e.g.*,





The molecular refractivity permits a decision between the two formulas.[2] Table I shows that is is in better agreement with the heterocyclic formula. The experimental values are usually even lower than the figures calculated for the heterocyclic compounds (average deviation, −0.54). This seems to be due to the presence of the heterocyclic ring, as already emphasized by Cope and Hancock (4, 5). We are trying at present to verify this conclusion by other methods.

TABLE I

Molecular Refractions

BASE	CARBONYL COMPOUND	MOL. REFRACT., FOUND	MOL. REFRACT., CALC'D FOR HETEROCYCLIC SYSTEM	SCHIFF'S BASE
2,4-Diamino-4-methylpentane	Methylisobutyl ketone	62.95	62.64	64.06
" "	3-Methyl-3-butanol-2-one (IV)	59.22	59.55	59.98
" "	Cyclohexanone	60.00	60.44	61.86
" "	Acetophenone	67.50	68.27	69.69
" "	Benzaldehyde	63.14	63.65	65.07
" "	2-Ethyl-2-hexenal	70.58	71.41	72.83
Ethylenediamine	Cyclohexanone	41.27	41.94	43.36

The reduction of (I) to (IV) which Matter has observed, is not in discord with the hexahydropyrimidine formula; it has been known that the rings in cyclic acetals (6) and oxazolidines[3] can be opened by catalytic hydrogenation.

In Table I, the condensation product of ethylenediamine and cyclohexanone has also been included. Whilst the condensation products of this base with

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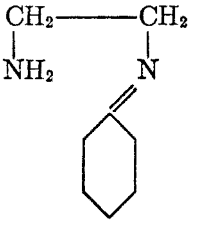
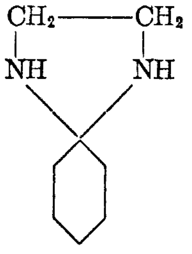
[2] For the application of this criterion to the condensation products of α-amino alcohols and aldehydes or ketones, see Cope and Hancock (4).

[3] See references (4) and (7). We have also calculated the molecular refractions of some of the more complicated oxazolidines described by Senkus: they are all heterocyclic compounds and not the isomeric Schiff's bases (No. 1, Found, 32.99; Calc'd for the oxazolidine, 33.19; for the Schiff's base, 34.64. No. 3, Found, 51.46; Calc'd, 51.63 and 53.08. No. 14, Found, 60.70; Calc'd, 60.42 and 61.87).

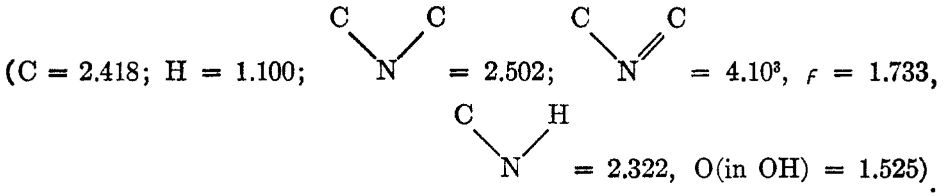
aldehydes have generally been assumed to be imidazolines (8), Pearson, Jones, and Cope (9) have recently condensed ethylenediamine with various ketones, without giving the products a definite structural formula. The molecular refractivity for the product from cyclohexanone is again in favor of the heterocyclic formula of a 2-(pentamethyleno)imidazoline (VI). The hydrogenation of the product to N-cyclohexylethylendiamine can be interpreted equally well as that of the double bond in (V) and as ring fission in (VI).



V



VI



$$(C = 2.418;\ H = 1.100;\ \overset{C\quad C}{\diagdown\!\diagup}\!\!\!\!\!\!\!\!\!\!\underset{}{N} = 2.502;\ C{-}N{=}C = 4.10^3,\ f = 1.733,\ C{-}N{-}H = 2.322,\ O(\text{in OH}) = 1.525).$$

EXPERIMENTAL

2-Phenyl-4,6,6-trimethylhexahydropyrimidine. A mixture of 23.2 g. of 2,4-diamino-4-methylpentane (II), 21.2 g. of benzaldehyde, and 50 cc. of benzene was heated until 3.6 cc. of water had collected in the azeotropic receiver. The product was distilled under 15 mm. pressure; it boiled at 155–156° and formed 33 g. of a yellowish, basic-smelling oil; d_4^{20}, 0.973; n_D^{20}, 1.5170$_5$.

Anal. Calc'd for $C_{13}H_{20}N_2$: C, 76.5; H, 9.8; N, 13.8.
Found: C, 76.3; H, 10.0; N, 14.0.

2-(α-Ethylpentyl)-4,6,6-trimethylhexahydropyrimidine. Thirty grams of the diamine (II), 33 g. of 2-ethylhexanal, 50 cc. of benzene; 5 cc. of water was liberated; b.p. 105–106°/5 mm.; yield, 53 g.

2-(α-Ethyl-Δ^α-pentenyl)4,6,6-trimethylhexahydropyrimidine. Eleven and six-tenths grams of the diamine, 11.6 g. of 2-ethyl-2-hexenal, 50 cc. of benzene; 1.8 cc. of water collected in the receiver; b.p. 125°/47 mm.; a considerable resinous residue remained; yield, 5 g., d_4^{20}, 0.880; n_D^{20}, 1.4664$_5$.

Anal. Calc'd for $C_{14}H_{28}N_2$: C, 75.0; H, 12.6; N, 12.5.
Found: C, 74.7; H, 12.6; N, 12.8.

2-Phenyl-2,4,6,6-tetramethylhexahydropyrimidine. Twenty-three and two-tenths grams of the diamine (II) and 24 g. of acetophenone in 50 cc. of benzene reacted only very slowly. The two components were, therefore, heated without diluent for 4 hours at 150° Even so, 40% of the starting materials (9.3 g.and 9.6 g., respectively) were recovered. The product, which was obtained in a yield of 26.2 g. (60% of the theory, calc'd on the total of the starting material) boiled at 155–160°/25 mm.; d_4^{20}, 0.975; n_D^{20}, 1.5191$_5$.

Anal. Calc'd for $C_{14}H_{22}N_2$: C, 77.1; H, 10.1; N, 12.8.
Found: C, 77.3; H, 10.4; N, 12.5.

2-Isobutyl-2,4,6,6-tetramethylhexahydropyrimidine. Eleven and six-tenths grams of the diamine (II) and 10 g. of methyl isobutyl ketone were boiled for 4 hours in a short column until the expected quantity of 1.8 cc. of water had collected in the receiver. The product boiled at 125°/50 mm.; yield, almost quantitative; d_4^{20}, 0.850; n_D^{20}, 1.4513_5.

Anal. Calc'd for $C_{12}H_{26}N_2$: C, 72.7; H, 13.1; N, 14.1.
Found: C, 72.7; H, 13.3; N, 14.0.

2-Pentamethyleno-4,6,6-trimethylhexahydropyrimidine. Thirty-two and two-tenths grams of the diamine (II), 20 g. of cyclohexanone, and 30 cc. of benzene were distilled azeotropically until 3.6 cc. of water had collected in the receiver; b.p. 82–83°/5 mm.; yield, 31.5 g.; d_4^{20}, 0.9356_5; n_D^{20}, 1.4845.

Anal. Calc'd for $C_{12}H_{24}N_2$: C, 73.2; H, 12.2; N, 14.6.
Found: C, 73.3; H, 12.5; N, 14.4.

2-(α-Hydroxyisopropyl)-2,4,6,6-tetramethylhexahydropyrimidine. Eleven and eight-tenths grams of the diamine (II), 11.2 g. of 3-methyl-3-butanol-2-one (10) (II), and 50 cc. of benzene; 1.8 cc. of water were liberated; yellowish oil of b.p. 144°/40 mm.; yield, 17 g.; d_4^{20}, 0.931; n_D^{20}, 1.4621_5.

Anal. Calc'd for $C_{11}H_{24}N_2O$: C, 66.0; H, 12.0; N, 14.0.
Found: C, 65.6; H, 12.2; N, 13.9.

2-Pentamethylenoimidazoline (VI). Twenty grams of freshly distilled ethylenediamine, 33 g. of cyclohexanone, and 50 cc. of benzene. The expected quantity of water was liberated within 15 minutes. The colorless reaction product boiled at 80–81°/8 mm.[4]; yield, 22 g., d_4^{20}, 0.988; n_D^{20}, 1.4960.

Anal. Calc'd for $C_8H_{16}N_2$: C, 68.6; H, 11.4; N, 20.0.
Found: C, 68.5; H, 11.9; N, 20.2.

REHOVOTH, PALESTINE
PHILADELPHIA, PA.

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[4] Pearson, Jones, and Cope (9) have not isolated their product, but subjected it directly to catalytic hydrogenation.