for 10 days. After concentration of the reaction mixture *in vacuo*, the residue was purified according to the same procedure as described in a). Yield of **8c** was 263 mg (14%). This material was identical with an authentic sample prepared in a) by mixed melting point and IR comparison. The recovered **7a** was 320 mg.

c) From 2-Acetyl-3-methylamino-5,5-dimethyl-2-cyclohexen-1-one (**8a**): A solution of **8a** (204 mg) in methylene chloride (22 ml) was irradiated with a 450 W high pressure mercury lamp in a quartz vessel for 40 hr. After concentration of the reaction mixture *in vacuo*, the residue was purified according to the same procedures as described in a). Yield of **8c** was 20 mg (11%), and 44 mg of the starting material (**8a**) was recovered.

3-Acetamido-2-chloro-5,5-dimethyl-2-cyclohexen-1-one (**9**)——A solution of **7c** (2.1 g) in methylene chloride (1000 ml) was irradiated with a 450 W high pressure mercury lamp in a Pyrex vessel for 2 weeks. The rection mixture was concentrated *in vacuo* and the residual solid was submitted to the preparative TLC on alumina with $CHCl_3$ to give three bands. Extraction of the band of the second *Rf* value with $CHCl_3$ gave 0.330 g (13%) of crude **9**, which was recrystallized from pet-benzine to give colorless crystals, mp 130—131°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400, 1720, 1670, 1600. UV λ_{max}^{EtOH} $m\mu(\log \varepsilon)$: 291 (4.29). NMR (in $CDCl_3$) τ: 8.90 (6H, s, $2\times CH_3$), 7.75 (3H, s, $COCH_3$), 7.60 (2H, s, CH_2), 6.88 (2H, s, CH_2), 2.14 (1H, b-s, NH). Mass Spectrum *m/e*: 215 (M^+). Beilstein test was positive. *Anal.* Calcd. for $C_{10}H_{14}O_2NCl$: C, 55.68; H, 6.49; N, 6.49. Found: C, 55.78; H, 6.73; N, 6.32. From the band of the lowest *Rf* value the starting material **7c** was recovered and from that of the highest an unidentified compound was obtained.

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On the Air Oxidation of 5-Amino-1,3-dialkyl-5-methylhexahydropyrimidines[1]

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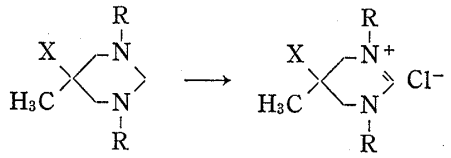
As a part of our studies on hexahydropyrimidines,[3,4] it has been reported in a previous communication[5] that the air oxidation of 5-amino- and 5-nitro-1,3-dialkyl-5-methylhexahydropyrimidine hydrochlorides (I and II) in the presence of palladium black gave the corresponding 3,4,5,6-tetrahydropyrimidinium chloride (III and IV), establishing the new method for the dehydrogenation of 2-methylene group of hexahydropyrimidines. Now the air oxidation of I in the absence of the catalyst was found to proceed in a different way with that of the palladium-catalyzed oxidation. This paper describes the air oxidation of 5-amino-1,3-dialkylhexahydropyrimidines.

Reflux of a solution of 5-amino-1,3-dibenzyl-5-methylhexahydropyrimidine (V) in 10% HCl for 30 hr afforded 5-amino-1-benzyl-5-methylhexahydropyrimidine (VI, in 2.4% yield), N^1-benzyl 2-methyl-1,2,3-propanetriamine (VII, 32%) and benzaldehyde (VIII, 19%) with a recovery of V in 39% yield. The reaction did not take place under nitrogen, suggesting the reaction to be the air oxidation. The structure



I: X=NH_2 II: X=NO_2 III: X=NH_2 IV: X=NO_2

Chart 1

1) This work was presented at the 92 th Annual Meeting of Pharmaceutical Society of Japan, Osaka, April 1972.
2) Location: *Mejiro-dai, Bunkyo-ku, Tokyo.*
3) T. Tsuji, *Chem. Pharm. Bull.* (Tokyo), **19**, 2551 (1971).
4) T. Tsuji and Y. Okamoto, *Chem. Pharm. Bull.* (Tokyo), **20**, 184 (1972).
5) T. Tsuji and M. Muraoka, *Chemistry Letters*, **1972**, 167.

of VI was assigned on the basis of the elementary analysis ($C_{12}H_{19}N_3$) and the nuclear magnetic resonance (NMR) spectrum, which are given in the experimental section. Reflux of VI with HCl gave VII without the formation of VIII. Compound VII was identical with the authentic sample of N^1-benzyl 2-methyl-1,2,3-propanetriamine.[6] Compounds VI and VII were further obtained from the hydrogenolysis of hydrochloride of V in the presence of palladium carbon.

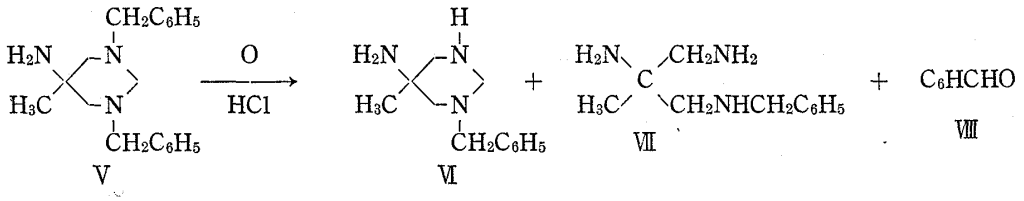


Chart 2

Reflux of a solution of 5-amino-1,3-di-*n*-hexyl-5-methylhexahydropyrimidine in 10% HCl for 30 hr gave hexanal in a poor yield (below 1%). Although the detection of other products was failed, this reaction might proceed very slowly in the similar manner with the oxidation of V in HCl. It is likely that the dehydrogenation of the active benzyl methylene group of V proceeds fast. The reaction course of the air oxidation of 5-amino-1,3-dialkyl-5-methylhexahydropyrimidines might be proposed to involve a process shown in Chart 3. The oxidation of the N-alkyl group will occur initially to form Schiff's salts (IX), which may be hydrolyzed into 1-alkyl-5-amino-5-methylhexahydropyrimidines accompanied with a liberation of aldehyde.

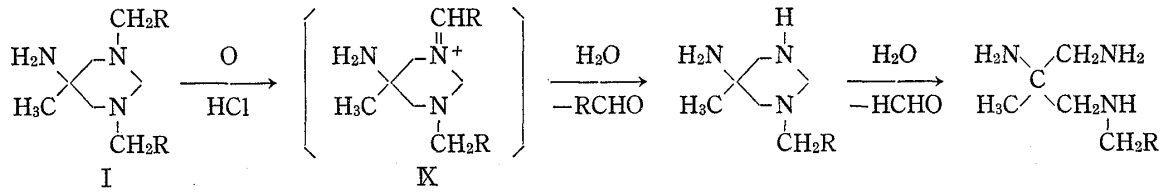


Chart 3

Taking into consideration the facts that the palladium-catalyzed oxidation of amines such as piperazine, piperidine and 1-methylpiperidine did not occur, but that the oxidation of alcohols took place to form aldehyde,[7] the possible reaction course of the palladium-catalyzed oxidation of I and II was presumed. As shown in Chart 4, the reaction may proceed through the formation of the open-chain compounds (X) by the hydration of I and II, followed by the oxidation of X into XI and the successive ring-closure into III and IV.

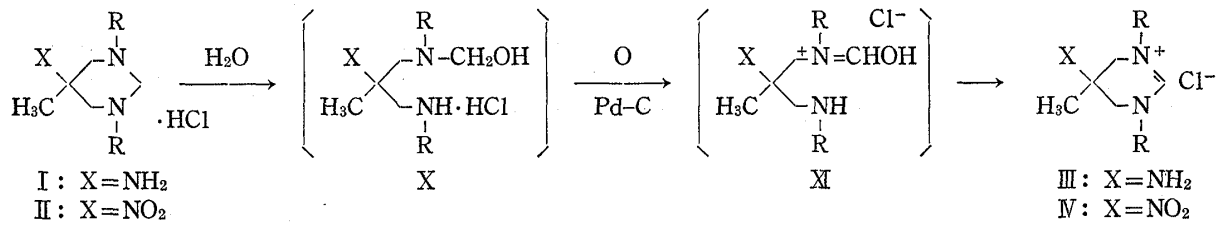


Chart 4

6) T. Tsuji, H. Momona and T. Ueda, *Chem. Pharm. Bull.* (Tokyo), **15**, 936 (1967).
7) E.M. Wise. "Palladium. Recovery, Properties, and Uses," Academic Press, New York, 1968, p. 172.

Experimental[8]

Air Oxidation of a Solution of 5-Amino-1,3-dibenzyl-5-methylhexahydropyrimidine in HCl (V)——A solution of 11.8 g of V[9] in 100 ml of 10% HCl was refluxed for 30 hr. Liberated benzaldehyde (0.8 g, 19% yield) was extracted with $CHCl_3$ from an aqueous sclution. Remained aqueous solution was evaporated to dryness in vacuum. The residue was dissolved in a small amount of water, basified with K_2CO_3, and the separate oil was extracted with $CHCl_3$. The extract was dried with anhyd. K_2CO_3, concentrated and distilled fractionally giving 2.4 g (32%) of N^1-benzyl-2-methyl-1,2,3-propanetriamine (VII), bp 136° (2 mmHg), and 0.2 g (2.4%) of 5-amino-1-benzyl-5-methylhexahydropyrimidine (VI), bp 140—143° (2 mmHg), with a recovery of V (4.6 g, 39%). The IR spectrum of VII was identical with that of the authentic sample.[6] Compound VI solidified after distillation and was recrystallized from petroleum ether to colorless needles, mp 72—74°: NMR ($CDCl_3$): 0.97 (3H, s, 5-CH_3), 1.80 (3H, s, NH and NH_2), 2.18 (2H, ABq, 6-CH_2), 2.56 (2H, s, 4-CH_2), 3.37 (2H, ABq, 2-CH_2), 3.41 (4H, s, $PhCH_2$), 7.33 (5H, s, C_6H_5). *Anal.* Calcd. for $C_{12}H_{19}N_3$: C, 70.20; H, 9.33; N, 20.47. Found: C, 69.98; H, 9.31; N, 20.35. Reflux of a solution of 0.5 g of VI in 20 ml of 10% HCl for 2 hr gave 290 mg of VII after treatment in a similar manner with that described above.

Air Oxidation of a Solution of 5-Amino-1,3-di-*n*-hexyl-5-methylhexahydropyrimidine in HCl——A solution of 14.2 g of 5-amino-1,3-di-*n*-hexylhexahydropyrimidine[9] in 150 ml of 10% HCl was refluxed for 30 hr. Liberated hexanal (40 mg, 0.8% yield) was extracted with $CHCl_3$ from an aqueous solution. Remained aqueous solution was treated in a similar manner with the procedure described above. However, it was failed to yield any product except the recovery of the starting material.

Hydrogenolysis of V in the Presence of Palladium Carbon——Compound V (29.5 g) was dissolved in 140 ml of 5% HCl and the solution was hydrogenated at 110° for 1 hr under pressure (100—120 kg/cm^2) in the presence of palladium carbon (Pd, 1 g). After removal of the catalyst by filtration, the filtrate was evaporated to dryness *in vacuo*. The residue was dissolved in a small amount of water and basified with K_2CO_3. The separate oil was extracted with $CHCl_3$. After removal of the solvent from the extract, the oil was distilled under diminished pressure to give VI (2.4 g, 12%), VII (1.5 g, 8%) and unreacted V (17 g, 58%).

8) Infrared (IR) spectra were recorded with a JASCO IR-S spectrophotometer. NMR spectra were taken at 60 MHz with a JEOL JNM-C-60H spectrometer using tetramethylsilane as the internal reference.
9) M. Senkus, *J. Amer. Chem. Soc.*, **68**, 1611 (1946).