Synthesis of Frontalin with Toluene as Solvent.—The same mixture as above was diluted with 2845.0 g (32.0 mol) of toluene and heated for 1.25 hr at 250°. Distillation yielded 6018.0 g of acetone, 356.0 g of methallyl alcohol, 2785.0 g of toluene, 376.0 g of frontalin, 270.0 g of high-boiling fraction, and 376.0 g of residue. The yield of frontalin based on reacted methallyl alcohol was 24.0%.

Synthesis of Frontalin Using 4-Hydroxy-2-butanone.—A mixture of 7.2 g (0.1 mol) of methallyl alcohol, 8.8 g (0.1 mol) of 4-hydroxy-2-butanone, and 46.0 g (0.5 mol) of toluene was heated in a sealed glass tube for 1 hr at 250°. The glc analysis (excluding the toluene peak) indicated the presence of 30.5% frontalin, 52.0% unreacted methallyl alcohol, and 12.4% higher boiling by-products.

Registry No.—Frontalin, 28401-39-0.

A Highly Stereoselective Synthesis of *meso-N,N'*-Dicarbethoxy-2,4-diaminopentane and *meso*-2,4-Diaminopentane

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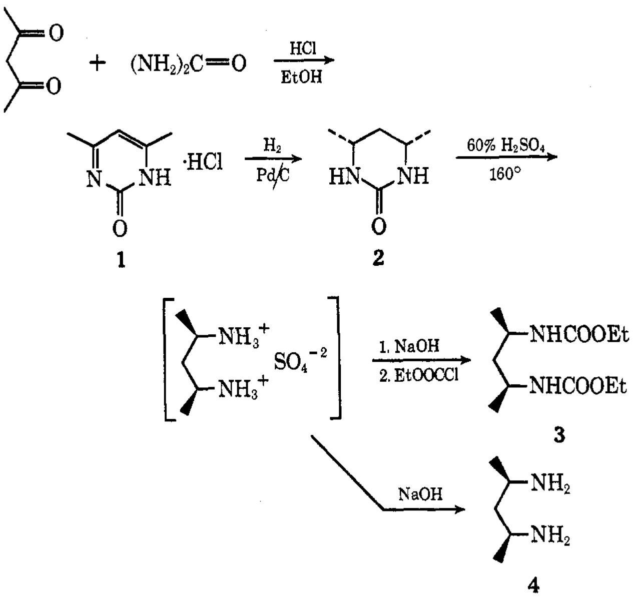
In the course of another study we required *meso*-2,4-diaminopentane. This note reports a unique, highly stereoselective synthesis of this material and its more conveniently isolated *N,N'*-dicarbethoxy derivative, which was also needed for further synthetic operations.

2,4-Diaminopentane has been prepared by reduction of 2,4-pentanedione dioxime by various methods,[1] the best of which was sodium in ethanol.[1] This procedure, which is inefficient and unwieldy, results in an 80% yield of product (as the dihydrochloride), only 30% of which is the meso diastereomer.[1] In addition, the meso and *dl* compounds must be separated, which is a tedious and yield-reducing process.[1] Our attempts to obtain a more favorable meso/*dl* ratio using other reducing agents did not meet with success. For example, aluminum hydride (an excellent reducing agent for oximes[2]) afforded a good yield of the diamine but the mixture contained only *ca.* 50% (by nmr) of the meso stereoisomer.

In order to obtain more conveniently the desired meso isomer, we devised a method in which the stereochemistry could be more easily controlled. The approach (outlined in Scheme I) involved establishing the proper atom arrangement within a readily formed pyrimidine ring (1) followed by catalytic hydrogenation[3] to the saturated cyclic urea 2 containing the correctly oriented *cis*-methyl groups. Hydrolysis then provided the desired meso diamine. The procedure takes advantage of the situation that any equilibration of 2 during hydrogenation should greatly favor the cis diequatorial disposition of the methyl groups and thus reinforce the predominance of the wanted stereoisomer.

SCHEME I



The reaction of acetylacetone with urea in refluxing acidic 95% ethanol[4] furnished a good yield (70–75%) of 2-hydroxy-4,6-dimethylpyrimidine hydrochloride (**1**). The 2-one tautomeric structure is suggested for **1** on the basis of ir and uv spectra. An aqueous solution of **1** was hydrogenated[5] using palladium on carbon[6] and the crude cyclic urea was obtained. Recrystallization gave diastereomerically pure **2**, which *required* sublimation in order to remove the solvent (mostly water). The cis cyclic urea **2** was hydrolyzed[7] in 60% sulfuric acid and the resulting diammonium salt was converted to the dicarbamate **3** in moderate yield (50–57%), or to the free diamine **4** in fair yield (25–30%).

The assignment of the cis configuration for the cyclic urea was made on the basis of nmr comparison with *cis*- and *trans*-2-phenyl-4,6-dimethyl-2-bora-1,3-dioxacyclohexane[8] and was consistent with a noninterconverting ring with diequatorial methyl groups. The nmr spectrum of the dicarbethoxy compound **3** is consistent with the presence of the vertical mirror plane contained in the meso isomer.

Experimental Section

Melting points and boiling points are uncorrected. Microanalyses were performed by Alfred Bernhardt Microanalytisches Laboratorium, West Germany. Infrared spectra were taken on a Perkin-Elmer Model 457 spectrophotometer. Nmr spectra were obtained on a Varian A-60 or HA-100 spectrometer using tetramethylsilane as an internal reference. Ultraviolet spectra were recorded on a Perkin-Elmer Model 402 spectrophotometer.

2-Hydroxy-4,6-dimethylpyrimidine Hydrochloride (1).—To acetylacetone (24.0 g, 0.24 mol) and urea (12.0 g, 0.20 mol) in 250 ml of 95% ethanol was added 50 ml of concentrated hydrochloric acid. The mixture was stirred under reflux for 2 hr, cooled in ice, and filtered. The colorless crystals were rinsed with ice-cold absolute ethanol and then with dry ether, and dried *in vacuo* to afford 20–22 g (70–75%) of colorless **1**, mp 260° dec

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[1] C. J. Dippel, *Recl. Trav. Chim. Pays-Bas*, **50**, 525 (1931), and references cited therein.

[2] N. M. Yoon and H. C. Brown, *J. Amer. Chem. Soc.*, **90**, 2927 (1968).

[3] Catalytic hydrogenation was anticipated to provide a predominance of the cis isomer. See (a) O. V. Bragin and A. L. Liberman, *Russ. Chem. Rev.*, **39** (12), 1017 (1970); (b) E. A. Mistryukov, E. L. Ilkova, and M. A. Ryashentseva, *Tetrahedron Lett.*, 1691 (1971).

[4] R. R. Hunt, J. F. W. McOmie, and E. R. Sayer, *J. Chem. Soc.*, 525 (1959); also see W. J. Hale, *J. Amer. Chem. Soc.*, **36**, 104 (1914).

[5] V. H. Smith and B. E. Christensen, *J. Org. Chem.*, **20**, 829 (1955).

[6] Use of activated Raney nickel as a catalyst under similar conditions resulted in complete recovery of the starting material (**1**) which was contaminated with Ni(II): J. J. Fox and D. Van Pragg, *J. Amer. Chem. Soc.*, **82**, 486 (1960).

[7] G. S. Skinner, R. H. Hall, and P. V. Susi, *ibid.*, **79**, 3786 (1957).

[8] We thank Dr. F. A. Davis and I. Turchi for nmr spectra of the boron heterocycles (to be published in *J. Org. Chem.*), which were chosen as models for comparison because of the expected geometric similarity of these rings to the corresponding cyclic ureas.

(sublimes). An additional 1–2 g of less pure product may be obtained from the filtrate: ir (KBr) ν_{max} 3420 (broad, w), 3030 (w–m), 1743 (s), 1625 cm^{-1} (s); nmr (D_2O) δ 2.63 (s, 6, methyls), 6.85 (s, 1, ring H); uv (H_2O) λ_{max} (log ϵ) 213 nm (3.97), 293.5 (3.79); uv (H_2O, pH > 7) λ_{max} (log ϵ) 226 nm (3.78), 289.5 (3.72), compare with 2-hydroxypyridine, uv (H_2O) $\lambda_{max}^{pH>7}$ (log ϵ) 230 nm (4.00), 295 (3.80),[9] which has a large contribution made to its structure by the 2-one tautomer.

Anal. Calcd for $C_6H_9ClN_2O$: C, 44.87; H, 5.65; Cl, 22.08. Found: C, 44.91; H, 5.61; Cl, 21.86.

***cis*-2-Oxo-4,6-dimethyl-1,3-diazacyclohexane (2).**—A mixture of the pyrimidine hydrochloride 1 (12.28 g, 0.076 mol) and 1.0 g of 10% palladium on carbon in 80 ml of distilled water containing a few drops of concentrated hydrochloric acid was hydrogenated (3–4 atm) in a Parr apparatus at room temperature until uptake of hydrogen had ceased (*ca.* 4 hr). The mixture was filtered as soon as possible and the filtrate was concentrated to dryness at reduced pressure to leave a colorless, clear, viscous oil which crystallized exothermically when kept under high vacuum. The crystalline mass was broken up and dried *in vacuo* overnight. The crude product (12.7 g) was recrystallized from a 1:1 mixture of ethyl acetate and tetrahydrofuran (THF) and dried *in vacuo*. The colorless, crystalline product (10.7 g), mp 110–118°, contained included solvent (10–15% solvent by weight) and was a single stereoisomer (nmr). Doubly sublimed material was clear, sparkling needles: mp 250–252° dec (strong sublimation); ir (KBr) ν_{max} 3220 (NH, s), 3075 (NH, m), 1670 cm^{-1} (C=O), s); nmr (acetone-d_6–D_2O) δ 1.32 (d, 6, methyls, J = 6.3 Hz), 1.37 (d of t, 1, axial H, J_{ab} = 13.4 Hz, J_{ax} = 11.0 Hz), 2.21 (d of t, 1, equatorial H, J_{bx} = 3.8 Hz), 3.80 (m, 2, methine), NH protons were absent due to deuterium exchange.

Anal. Calcd for $C_6H_{12}N_2O$: C, 56.22; H, 9.44. Found: C, 56.08; H, 9.25.

***meso-N,N'*-Dicarbethoxy-2,4-diaminopentane (3).**—The cyclic urea solvent-inclusion complex [29.4 g, 0.2 mol (*ca.* 25.6 g of pure urea)] was heated to reflux in 200 ml of 40% aqueous sulfuric acid (w/w). After reflux was attained (150° oil bath), five 22.0-ml portions of concentrated sulfuric acid (96–98%) were cautiously added at 30-min intervals through the top of the condenser. The mixture (*ca.* 60% in H_2SO_4) was heated at 160° for 4 days with stirring. It was cooled, diluted with 200 ml of 2-propanol, and poured into a mixture of *ca.* 3000 ml of THF and *ca.* 500 ml of dry ether.[10] The supernatant liquid was decanted and saved and the dense oil was rinsed with 200-ml portions of THF until it became a highly viscous, immobile deposit (usually two to five washings). The washings were combined with the supernatant solution and 200–300 ml of dry ether was added to force out more of the oil. Again the solvent was decanted and the oil was rinsed with THF (smaller portions). The crude diammonium salt was thus obtained and was not purified further. The cloudy oil was dissolved in 75 ml of distilled water and neutralized with *ca.* 9.0 g of sodium hydroxide (pH 8–9) with cooling and stirring. Ether (75 ml) was added, and to the stirred mixture kept at 10–15° was then added dropwise 36.0 g of ethyl chloroformate, followed by dropwise addition of 90 ml of 15% aqueous sodium hydroxide. The mixture was stirred for 1 hr at room temperature and diluted with 150 ml of ether, and the layers were separated. The aqueous phase was extracted with two 75-ml portions of ether and the combined ethereal extracts were washed with 25 ml of distilled water and dried ($MgSO_4$). Stripping of the solvent furnished 26–28 g (*ca.* 55%) of colorless dicarbamate, mp 94–95.5°. Recrystallization from hexane–ethyl acetate (prisms, mp 94–95.5°) followed by sublimation provided an analytical sample, mp 95–96°. Noteworthy is the fact that the dicarbamate, even before recrystallization, contained no detectable amount (<5%) of *dl* compound (nmr; also note melting point constancy), reinforcing the claim that the cyclic urea was stereochemically homogeneous: ir (KBr) ν_{max} 3325 (NH), 1682 cm^{-1} (C=O); nmr ($CDCl_3$) δ 1.17 (d, 6, methyls, J = 6.7 Hz), 1.22 (t, 6, ethoxy methyls, J = 7.0 Hz), 1.57 [1.43 (b), 1.70 (a)] (t of q_{ab}, J = 13.6 Hz, $J_{ax} \cong J_{ay}$ = 7.0–7.2 Hz, $J_{bx} \cong J_{by}$ = 6.5–6.8 Hz), 3.72 [d of d of d of q, methine, J (NH–CH) = 7.2–7.5 Hz], 4.12 (q, 4, ethoxy methylenes, J = 7.0 Hz), 4.80 (broad d, 2, NH, J = 7.2–7.5 Hz). The pattern for the methenyl and methinyl protons, excluding J (NH–CH) and J (CH_3–CH), represented an abxy system in which the chemical shifts of x and y were accidentally coincident. The *dl* dicarbamate prepared from predominantly *dl* diamine dihydrochloride[1] gave an nmr spectrum similar to that of **3**. The methylene resonance at 1.53 ppm, however, could be used to distinguish it from the meso isomer: nmr ($CDCl_3$) δ 1.17, 1.23, 1.53, 3.72, 4.12, 4.82.

Anal. Calcd for $C_{11}H_{22}N_2O_4$: C, 53.64; H, 9.00. Found: C, 53.54; H, 8.87.

***meso*-2,4-Diaminopentane (4).**—The diammonium salt, obtained as described above, was made strongly alkaline with *ca.* 25% aqueous sodium hydroxide (enough to dissolve most of the precipitated salts) and the resulting mixture was extracted with five equal volume portions of ether. The combined ethereal extracts were dried (Na_2SO_4, then $CaSO_4$) and carefully concentrated. The concentrate was dried over crushed KOH pellets overnight and carefully distilled at *ca.* 70 mm through a Vigreux column. After removal of a forerun, essentially pure[11] 4 distilled, bp 78–81° (70 mm) [lit.[1] bp 60–61° (22 mm)], n^{22}D 1.4388. The yield of diamine from 4.52 g of 2 was 0.9–1.0 g (25–30%). The *N,N'*-dibenzoyl derivative of 4 recrystallized from dilute ethanol had mp 194.5–195.5° (lit.[1] mp 193–194°). A sample of the diamine purified by preparative glc had the following properties: ir (thin film) ν_{max} 3360 (NH), 3285 (NH, d), 2965, 2930, 1600, 1457, 1376, 1142, 1060, 905, 870, 818 cm^{-1}; nmr ($CDCl_3$) δ 1.09 (d, 6, methyls, J = 6.5 Hz), 1.35 (t, 2, methylene, J = 6.8 Hz), 1.39 (s, 4, NH), 3.05 [hextet (d of d of q), 2, methine]. The nmr spectrum of chiefly *dl* diamine[1] was similar to that of 4, but clearly distinguishable by the fact that the methine protons resonated at 3.00 ppm: nmr ($CDCl_3$) δ 1.08, 1.32, 1.52, 3.00.

Registry No.—**1**, 34289-60-6; **2**, 34289-61-7; **3**, 34289-62-8; **4**, 29745-96-8.

Acknowledgment.—We thank Mrs. Carol Folk at the University of Pennsylvania for 100-MHz proton nmr spectra.

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[9] See R. M. Silverstein and G. C. Bassler, "Spectrophotometric Identification of Organic Compounds," Wiley, New York, N. Y., 1968, p. 168.

[10] (a) The object at this point in the preparation is to separate the salt as a viscous, dense oil. The exact amount of solvent in the mixture may be variable; thus it is recommended that only 150 ml of 2-propanol be used initially. If the dense phase is too voluminous, then more 2-propanol may be added. The oily deposit should not be very voluminous and should show signs of increased viscosity. (b) This *work-up* is a variation of a general one[7] in which acetone was employed. Use of acetone in our case resulted in only 24–30% yield of dicarbamate **3**. We found that this was due to the formation of the *gem*-diamine, 2,2,4,6-tetramethyl-1,3-diazacyclohexane (by rapid condensation of acetone with the disalt), which was isolated pure by preparative glc (after treating the mixture of diammonium salts with aqueous alkali and extracting with ether): ir (thin film) ν_{max} 3370 (broad NH), 3275 cm^{-1} (NH); nmr ($CDCl_3$) δ 0.95 (broad s, 2, NH), 1.05 (d, 6, methyls, J = 6.3 Hz), 1.31 and 1.35 (pair of s, 6, *gem*-methyls), 1.78 (d of t, methylene, possibly one-half of an ab pattern centered at 1.34 ppm with δ_{ab} = 26 ± 2 Hz, J_{ax} = 12 ± 2, J_{bx} = 2.7, and J_{ab} = 13 Hz), 3.00 [m (d of d of q), 2, methines, 11 lines were observed of the hypothetical 13-line pattern which would be expected if the above postulated parameters were valid with J_{ax} = 12 Hz]. Reaction of this compound with 2,4-dinitrophenylhydrazine reagent gave acetone 2,4-DNP which was identical with the authentic material. *Anal.* Calcd for $C_8H_{18}N_2$: C, 67.55; H, 12.76. Found: C, 67.68; H, 12.58.

[11] No contaminants other than water (*ca.* 3%) were present in the final product. The diamine is very hygroscopic and sensitive to carbon dioxide. A more lengthy purification, which supplies an anhydrous product, is provided in ref 1.

Photochemistry of 2-Phenyloxazolo[4,5-c]pyridine. Photoalkylation by Diethyl Ether

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Photoalkylation of various aromatic nitrogen heterocycles has been observed in a variety of alcoholic sol-