solid was washed with methanol, weighed 0.33 g, and was a mixture of two very similar substances (tlc). Recrystallization from methanol–chloroform gave the major component **24**: mp 202–203° (lit.[10] mp 205–206°); nmr signals at 3.62 (methoxyl), 3.14 s (4 p, CH_2S), 1.17 (C-4 methyl), 0.98 d and 0.90 d (J = 7 cps, isopropyl), 0.84 (C-10 methyl). Concentration of the mother liquors gave a small quantity of **25**: mp 192–193°; $[\alpha]^{25}D$ −41° (c 0.776, $CHCl_3$); nmr signals at 3.62 (methoxyl), 3.13 s (4 p, CH_2S), 1.17 (C-4 methyl), 1.07 d and 1.05 d (J = 6 cps, isopropyl), 0.86 (C-10 methyl).

Anal. Calcd for $C_{23}H_{38}O_2S_2$: C, 67.29; H, 9.33. Found: C, 67.03; H, 9.10.

Desulfurization of 0.20 g of **24** in 60 ml of ethanol by refluxing with Raney nickel for 50 hr, filtering, and evaporating *in vacuo* gave 0.14 g, of a colorless oil. Although this material was homogeneous on tlc, it could not be induced to crystallize. Glpc (230°, 6-ft column of silicone rubber on Diatoport S, carrier gas helium, flow rate 70 ml/min) indicated that the product was mainly **5b** contaminated with a trace of **3b** and 13% of a third ester, presumably **6b**, since the retention time of the third compound indicated that it was not **4b**. The infrared spectrum of the ester mixture was identical with that of **5b**.

Thioketals from 22.—When 0.50 g of **22** was mixed with 0.6 ml of ethanedithiol in 2 ml of acetic acid containing 0.6 ml of boron trifluoride etherate and the product was worked up as described in the preceding paragraph, there was obtained 0.38 g of **25**. Thin layer chromatography of the material from the mother liquors (0.22 g) indicated the presence of equal parts of **24** and **25**. When the reaction was carried out in the absence of acetic acid, the only isolable product was **24**.

8β,9α,13αH-Abietanoic Acid (3a). A.—To a solution of 3.52 g of **10b** in 100 ml of diethylene glycol was added 8.4 g of 85% hydrazine hydrate. The reaction mixture was heated at 110° for 2 hr, 6.12 g of potassium hydroxide was added, and the temperature was raised to 200° for 2 hr at which time an additional 6.12 g of potassium hydroxide was added. After 2 more hr at reflux, the solution was poured into ice water, acidified, and extracted with chloroform. The organic layer was washed, dried, and evaporated; the weight of the residue was 2.54 g (76%), mp 197–199°. Recrystallization from acetone gave the analytical sample: mp 201–201.5°, $[\alpha]^{25}D$ +8° (c 0.67) (lit.[8] mp 202°, $[\alpha]$ +7°); nmr signals at 1.18 (C-4 methyl), 0.86 d (J = 6 cps, isopropyl), and 0.85 (C-10 methyl). The substance was identical with material prepared by hydrogenation of **19**.

Anal. Calcd for $C_{20}H_{34}O_2$: C, 78.38; H, 11.18. Found: C, 78.12; H, 11.23.

B.—Desulfurization of 0.25 g of **25** in 60 ml of ethanol with Raney nickel by heating at reflux for 50 hr, filtering, and concentrating *in vacuo* furnished 0.18 g of the methyl ester **3b** as a clear oil which was homogeneous by tlc and glc criteria. It crystallized after lengthy standing and was recrystallized from aqueous methanol: mp 75–77° (lit.[8] mp 77°); nmr signals at 3.71 (methoxyl), 1.19 (C-4 methyl), 0.88 (C-10 methyl), and 0.87 d (J = 7 cps, isopropyl). A solution of this material in 2.6 ml of collidine was refluxed with 1.5 g of lithium iodide for 16 hr, poured into excess 10% hydrochloric acid, and extracted with ether. The washed and dried ether layer was evaporated; the residue melted at 200–201° and was identical with **3a**.

Catalytic Reduction of 19.[8]—A solution of 1.0 g of **19** in 50 ml of acetic acid was hydrogenated with 0.2 g of prereduced platinum oxide at 3 psi for 24 hr, filtered, and diluted with water. The solid was washed and dried (1.0 g); its nmr spectrum showed it to be a mixture of **3a** (60%) and **4a** (40%). No starting material was present. A preliminary separation was effected by preparation and recrystallization of the *n*-amylamine salts, the salt of **4a** being less soluble. By regenerating the acid with dilute hydrochloric acid and recrystallizing several times, pure **4a** was obtained, mp 162–164°; mixture melting point with **4a** (*vide supra*) was 162–164°; infrared and nmr spectra were superimposable. Regeneration of the acids from the mother liquors of the salts gave a mixture which was considerably enriched in **3a**. Several recrystallizations from ethanol furnished pure **3a**; mixture melting point with **3a** (*vide supra*) was undepressed; nmr and infrared spectra were superimposable.

Oxidation of the Thioketals 24 and 25.—To a solution of 0.20 g of **24** in 25 ml of methylene chloride was added, with cooling, 0.40 g of *m*-chloroperbenzoic acid. The mixture was allowed to stand at room temperature for 15 hr, heated at reflux for 5 hr, cooled, washed with 5% sodium bisulfite and 5% sodium bicarbonate solution, and evaporated. Recrystallization of the residual white solid (0.20 g, 80%) from acetone furnished the disulfone which melted above 250°: infrared bands at 1715 (ester) and 1123 cm^{-1} (sulfone); nmr signals at 3.70 (methoxyl and $CH_2S\rightarrow O$), 1.19 (C-4 methyl), 1.01 d (J = 7 cps, isopropyl), and 0.92 g (C-10 methyl).

Anal. Calcd for $C_{23}H_{38}O_6S_2$: C, 58.21; H, 8.08. Found: C, 58.05; H, 8.05.

Oxidation of 0.08 g of **25** in the same fashion furnished 0.70 g (70%) of the corresponding disulfone, mp 211–212° after recrystallization from methanol: infrared bands at 1706 (ester) and 1120 cm^{-1} (sulfone); nmr signals at 3.73 ($CH_2S\rightarrow O$), 3.67 (methoxyl), 1.17 (C-4 methyl), 1.13 d (J = 7 cps, isopropyl), and 0.93 (C-10 methyl).

Anal. Calcd for $C_{23}H_{38}O_6S_2$: C, 58.21; H, 8.08. Found: C, 57.94; H, 8.08.

Derivatives of 2-Hydroxyalkylmalonic Acids. Participation by γ-Hydroxy Groups in Reactions of Nucleophiles with the Carboxylic Centers

PIER L. PACINI AND ROBERT G. GHIRARDELLI[1]

Duke University and the Army Research Office—Durham, both at Durham, North Carolina

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Hydrogenation of 4,5-dimethyl-2-oxo-2,5-dihydro-3-furonitrile leads to a mixture of 4,5-dimethyl-2-oxotetrahydro-3-furonitriles in which the isomer with *cis* methyl groups predominates over that with *trans* by a ratio of five to one. Both isomers have been prepared independently and each rearranges on treatment with ammonia or primary amines to give the corresponding 2-amino-2,3-dihydro-3-furamide. From the ultraviolet spectra it appears that the enamino tautomer (with endocyclic double bond) is favored in the case of the simple amino furamides, but the imino tautomer (exocyclic double bond) in the case of the homologs with both nitrogens monomethylated. As do simple lactones, these compounds undergo hydrolysis, ammonolysis, and aminolysis with relative ease. Much of the chemistry can be explained in terms of the establishment of equilibria among open-chain species (which can be considered derivatives of 2-hydroxyethylmalonic acid) and a collection of cyclic species wherein the hydroxy group, γ with respect to each carboxyl function, engages one or the other of them.

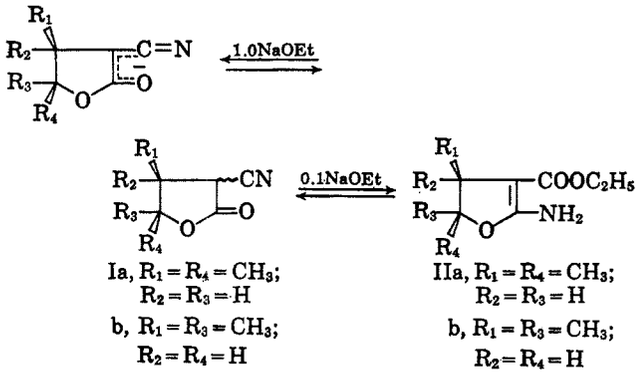
That the α-cyano-γ-butyrolactone system will readily (and reversibly) rearrange in the presence of strong base to give a molecule containing an enamine grouping was first reported by Glickman and Cope.[2] More recently, Korte and co-workers have, as part of a much broader study of related isomerizations,[3] confirmed the nature of the reactions: that in the presence of 0.1 molar equiv of sodium ethoxide in ethanol, various 3-cyano-2-oxotetrahydrofurans are transformed into

(1) To whom inquiries concerning this paper should be sent.

(2) S. A. Glickman and A. C. Cope, *J. Am. Chem. Soc.*, **67**, 1012 (1945).

(3) F. Korte and K. Trautner, *Ber.*, **95**, 281 (1962).

2-amino-3-carbethoxy-4,5-dihydrofurans; introduction of 1 full molar equiv of ethoxide ion favors a shift of this equilibrium toward the cyano lactone by formation of the conjugate anion of the latter.

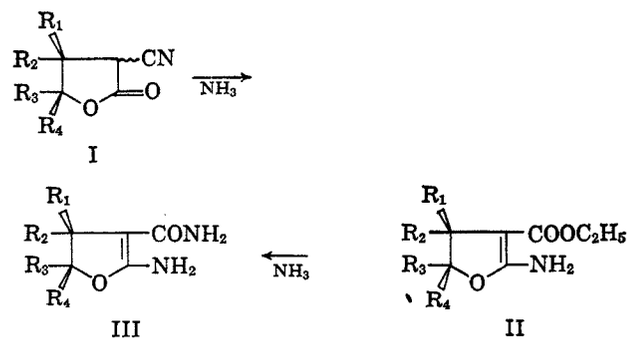


(in this study all compounds are racemic)

Observations

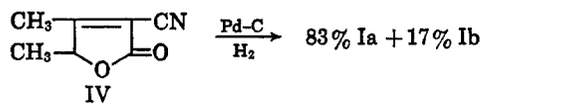
In the course of an investigation where an intermediate objective was the preparation of open-chain derivatives of 2-cyano-4-hydroxy-3-methylpentanoic acid, the cyano lactones Ia and Ib were obtained from ethyl sodiocyanoacetate and *trans*- and *cis*-2,3-dimethyloxirane, respectively. The assignment of configuration was made on the basis of the accepted *trans* mode of ring opening of oxiranes with similar carbanions.[4,5] An observation of possible diagnostic value can be made from the nmr spectra. In each case studied the signal (multiplet) for the proton on ring carbon number five was found, in isomers assigned the configuration with *cis*-methyl groups on ring carbons four and five, approximately 0.5 ppm downfield from its position in the corresponding *trans* isomer. From examining models it appears that interaction of the *cis*-methyl groups can augment the tendency to thrust the proton in question into a quasi-axial position, and thus closer to the periphery of any π bond based on carbon number two.

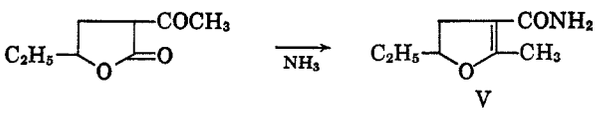
Treatment of the cyano lactones Ia and Ib with aqueous ammonia gave solid products; from spectral and analytical evidence the structure of these products was deduced to be represented by IIIa and IIIb, resulting from recyclization of the initially formed cyano amides. In a straightforward manner the same products could be obtained by treatment of the amino esters IIa and IIb with ammonia.



for *cis* isomers, a, $R_1 = R_4 = CH_3$; $R_2 = R_3 = H$
for *trans* isomers, b, $R_1 = R_3 = CH_3$; $R_2 = R_4 = H$

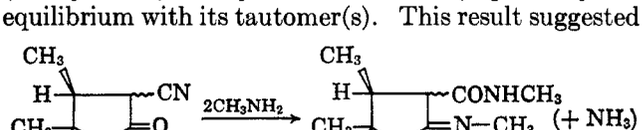
Compound I of undetermined stereochemistry was earlier prepared as an oil by Hori[6] who condensed acetoin with ethyl cyanoacetate to obtain the α,β-unsaturated cyano lactone IV which was then hydrogenated over palladium on charcoal. This work was repeated in the present instance following closely the published procedure, and the product mixture, which was partly crystalline, subjected to analysis by gas–liquid partition chromatography. It proved to be composed of 83 ± 2% of the compound with *cis*-methyl groups (Ia), and 17 ± 2% of the *trans* isomer (Ib). This result reflects the favored *cis* addition of hydrogen from the side of the double bond opposite the methyl group on the number five carbon of the ring.

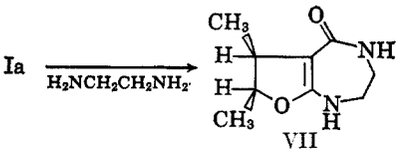




Similar rearrangements are evidently possible where the cyano group is replaced by an acyl function. Thus, when 3-acetyl-4-ethyl-2-oxotetrahydrofuran (obtained from the reaction of 2-ethyloxirane and ethyl sodioacetoacetate) was treated with aqueous ammonia in the same manner, 2-methyl-5-ethyl-4,5-dihydro-3-furamide V was produced. This general type of reaction was reviewed by Korte and Büchel,[7] who named it the acyllactone rearrangement. It is general under acidic conditions; since a dehydration step is involved, it is mildly surprising that it can occur under the conditions (*i.e.*, aqueous ammonia) employed in the present case.

Treatment of the cyano lactone Ib with an excess of methylamine led to the incorporation of two methylamino groups into the product, identified as VI, the methylamide of the corresponding 4,5-dimethyl-2-(methylimino)tetrahydro-3-furoic acid, probably in equilibrium with its tautomer(s). This result suggested the use of difunctional amines, and indeed the cyano lactone Ia was found to give, on treatment with 1,2-ethanediamine, a compound whose properties could most readily be explained in terms of the bicyclic structure VII.





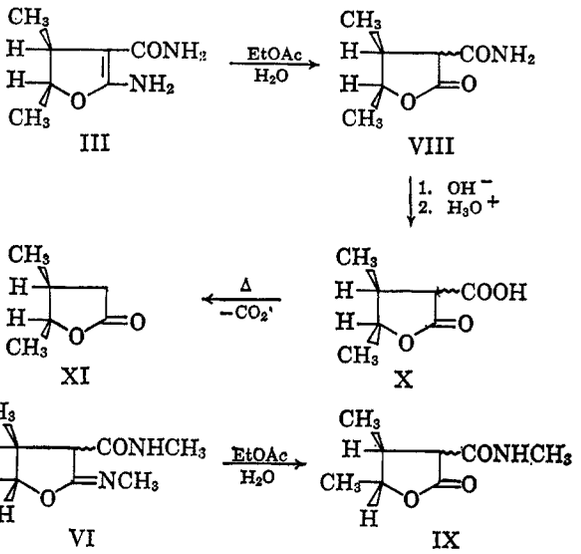
(4) W. E. Grigsby, W. E. Hind, J. Chanley, and F. H. Westheimer, *J. Am. Chem. Soc.*, **64**, 2606 (1942).

(5) The stereochemistry at ring carbon number three (α position) will be neglected in this discussion although the hydrogen there, which is quite mobile, is (in the tautomeric form where it resides on carbon) probably *cis* to the adjacent methyl group for steric reasons.

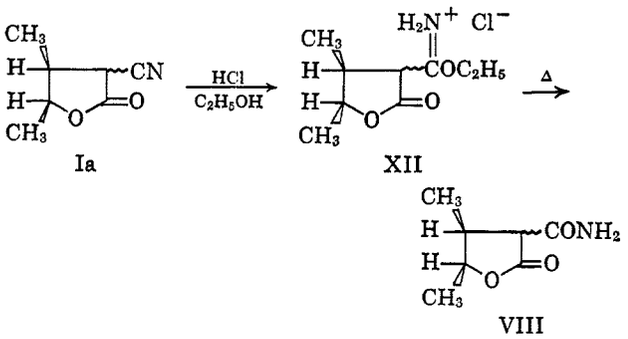
(6) I. Hori, *Sci. Papers Inst. Phys. Chem. Res.* (Tokyo), **56**, 178 (1962); *Chem. Abstr.*, **58**, 5508 (1963).

(7) F. Korte and K. H. Büchel, "Newer Methods of Preparative Organic Chemistry," Vol. III, W. Foerst, Ed., H. Birnbaum, Transl, Academic Press Inc., New York, N. Y., 1965, p 199.

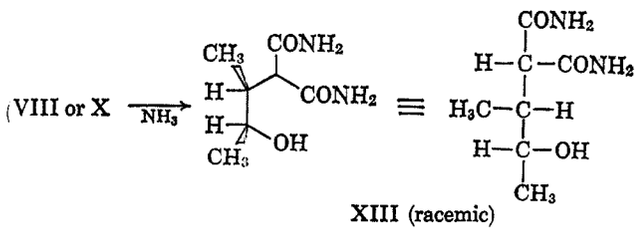
Hydrolysis of either amino amide (III or VI) under exceptionally mild conditions (refluxing with wet ethyl acetate) led to the formation of the corresponding carbamoyl lactones VIII and IX. Further hydrolysis



of VIII was effected rapidly in dilute aqueous sodium hydroxide solution at room temperature to give, after careful acidification, the carboxy lactone. This underwent the expected facile thermal decarboxylation to the simple lactone. The carbamoyl lactone VIII could also be prepared from the cyano lactone, through the intermediacy of the imido ester hydrochloride XII, subjected to thermolysis according to the procedure of Korte and Trautner.[3]



When the carbamoyl lactone VIII was treated with an excess of aqueous ammonia, there was produced the hydroxyalkyl malonamide XIII, representing the only acyclic derivative isolated in the present study. The same product (XIII) was obtained by ammonolysis of the carboxy lactone X.

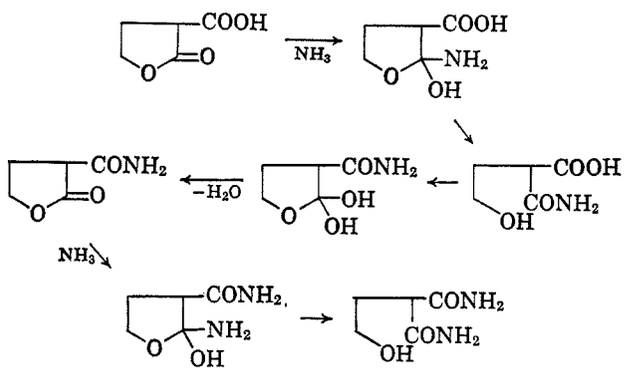


Discussion of Results

In any discussion of the path by which the above-described reactions take place it is reasonable (and obvious) to implicate acyclic intermediates generated by the attack of the nucleophile on the lactonic carbonyl group. The resulting alcoholic hydroxyl group is in a position γ with respect to each of the multiple (carbonyl or cyano) bonds; rearrangement occurs when it "switches its allegiance" to the cyano or carbonyl group to which it was not originally attached. The relative ease with which rings of this nature can open and close has been used to explain enhanced reactivity at carboxylic centers in the presence of a γ or δ substituent capable of participating (as a nucleophile) in the reaction.[8-10]

If the carbonyl functions are different it is possible for two isomeric cyclic species to be in equilibrium with the open-chain compound. One cannot draw any firm conclusions regarding relative stabilities from these experiments, since the products obtained may reflect such factors as the nature of the solvent, excess of nucleophile, and method of isolation, but two qualitative observations can be made: first, that in a hydroxylic solvent the cyano group is quite susceptible to attack by the γ hydroxyl (or its conjugate base); and, second, that the carbamoyl group is least likely of those studied to undergo a ring-closure reaction, and thus when acid functions are transformed into carbamoyl groups, the acyclic hydroxyalkylmalonamide (XIII in this study) is isolated.

The formation of this last compound from the carboxy lactone X also serves to illustrate the earlier comments regarding reactivity enhanced through the intermediacy of lactones. A reaction path such as the following could account for the experimental observations. (Methyl substituents and proton transfers to and from the solvent pool have been neglected.) That the last step is a realistic postulate was confirmed by the reaction of the carbamoyl lactone VIII with ammonia to give XIII.



Whether to represent compounds of the type of IIa and IIb as enamino (endocyclic double bond) or imino (exocyclic double bond) tautomers was investigated by Glickman and Cope,[11] who decided on spectral evidence that the enamine representation was the correct one. Our observations on the amides IIIa and IIIb are in agreement with this conclusion, whereas the N-methyl homolog VI presents a somewhat different picture. The ultraviolet carbonyl absorption of VI is, by two units (measured as log ϵ), weaker than the corresponding

(8) See the review by M. L. Bender, *Chem. Rev.*, **60**, 53 (1960).
(9) M. L. Wolfrom, R. B. Bennett, and J. D. Crum, *J. Am. Chem. Soc.*, **80**, 944 (1958).
(10) Rate studies of the hydrolysis of 2-phenyliminotetrahydrofuran have been carried out: see G. L. Schmir and B. C. Cunningham, *ibid.*, **87**, 5692 (1965).
(11) S. A. Glickman and A. C. Cope, *ibid.*, **67**, 1017 (1945).

absorption of IIIb, its homolog without N-methyl groups; this suggests that unlike IIIb the methylated amide exists *preponderantly* as the imino tautomer. At first inspection the nmr spectrum of VI appeared to be in conflict with this interpretation, since the signal (τ 7.07) assigned to the methyl protons of the 2-methylimino group was crowned by a twin peak, and no evidence was given of any signal attributable to a proton on the attached nitrogen. A shoulder on the above did reveal itself, however, centered at τ 6.93 and integrating close to one proton in value; it can most easily be attributed to hydrogen on carbon number three, and thus implicates the imino tautomer. A likely explanation for the twin peak of the N-methyl signal is therefore not coupling, but a difference in chemical shift owing to the attachment of the methyl group to sp^2 nitrogen in one tautomer and to sp^3 nitrogen in the other. A similar phenomenon, encountered in studies of enol–keto tautomerism by nmr, has been described and discussed in a standard text on the subject.[12]

Experimental Section[13]

Oxiranes.—The *cis*- and *trans*-2,3-dimethyloxiranes were prepared from the corresponding 2-butenes utilizing published procedures.[14] The Dow Chemical Co. kindly supplied the 2-ethyloxirane used.

***cis*-4,5-Dimethyl-2-oxotetrahydro-3-furonitrile (Ia).**—*trans*-2,3-Dimethyloxirane (72 g, 1.0 mole) and ethyl cyanoacetate (113 g, 1.0 mole) were allowed to react in the presence of sodium ethoxide (1.0 mole in 500 ml of absolute ethanol), utilizing a procedure similar to that employed by Glickman and Cope,[2] except that the reaction mixture was maintained at 60–65° for 18 hr. A product yield of 100 g (72%), bp 122–125° (1 mm), resulted and solidified on standing. Several recrystallizations from 95% ethanol gave an analytical sample: mp 63–64°; infrared lactone carbonyl at 1780 and cyano at 2270 cm^{-1}; nmr ($CDCl_3$) τ 8.81 (doublet, J = 6 cps, 3 H), 8.60 (doublet, J = 6 cps, 3 H), 7.09 (multiplet, 1 H), 5.97 (doublet, J = 8 cps, 1 H), 5.25 (multiplet, 1 H).

Anal. Calcd for $C_7H_9NO_2$: C, 60.42; H, 6.52; N, 10.07. Found: C, 60.12; H, 6.68; N, 10.05.

***trans*-4,5-Dimethyl-2-oxotetrahydro-3-furonitrile (Ib).**—The *trans* isomer was obtained in similar manner: yield 66%; bp 136–141° (3 mm); mp 48–49° (from 95% ethanol); nmr spectrum ($CDCl_3$) τ 8.70 (doublet, J = 6 cps, 3 H), 8.52 (doublet, J = 6 cps, 3 H), 7.50 (multiplet, 1 H), 6.50 (doublet, J = 12 cps, 1 H), 5.75 (octet, 1 H).

Anal. Found: C, 60.22; H, 6.46; N, 9.90.

4,5-Dimethyl-2-oxotetrahydro-3-furonitrile by Procedure of Hori.[6]—A solution of 13.7 g (0.100 mole) of 4,5-dimethyl-2-oxo-2,5-dihydro-3-furonitrile[6] [IV, bp 172–175° (6 mm)] in 60 ml of ethanol was hydrogenated at room temperature and low pressure in the presence of 2 g of palladium (10%) on charcoal, the uptake of hydrogen in 2 hr being 10% in excess of the theoretical. The catalyst was removed by filtration and the solvent was evaporated to give an oily residue. Partial crystallization gave 5.2 g (38%) of solid material which proved by comparative and mixture melting point determinations to be the isomer with *cis*-methyl groups described above (Ia). A sample representative of the entire reaction product was subjected to separation by gas–liquid partition chromatography (Wilkens Auto-Prep 700, silicone oil Si-30 on Chromosorb, 180°). It repeatedly analyzed, by comparative retention times and integration as 83 ± 2% *cis*-4,5-dimethyl-2-oxotetrahydro-3-furonitrile and 17 ± 2% the *trans* isomer. No evidence of unsaturated cyano lactone could be found.

Ethyl *cis*-4,5-Dimethyl-2-amino-4,5-dihydro-3-furoate (IIa).—*cis*-4,5-Dimethyl-2-oxotetrahydro-3-furonitrile (17 g, 0.13 mole) was treated with sodium ethoxide (0.013 mole) in 50 ml of absolute ethanol, in accord with published procedures.[3] Product representing a 63% yield, bp 125–128° (3 mm), resulted and solidified on cooling. Recrystallization from ethyl ether–pentane gave an analytical sample: mp 33–35°, $\lambda_{max}^{95\%\ EtOH}$ 272 mμ (log ϵ 4.29).

Anal. Calcd for $C_9H_{15}NO_3$: C, 58.38; H, 8.16; N, 7.56. Found: C, 58.04; H, 8.20; N, 7.92.

Ethyl *trans*-4,5-Dimethyl-2-amino-4,5-dihydro-3-furoate (IIb).—This was prepared in similar manner (66% yield) from *trans*-4,5-dimethyl-2-oxotetrahydro-3-furonitrile. It boiled at 116–119° (3 mm); $\lambda_{max}^{95\%\ EtOH}$ 272 mμ (log ϵ 4.32).

Anal. Found: C, 58.06; H, 8.09; N, 7.34.

***cis*-4,5-Dimethyl-2-amino-4,5-dihydro-3-furamide (IIIa). Method A.**—*cis*-4,5-Dimethyl-2-oxotetrahydro-3-furonitrile (5.0 g, 0.036 mole) was treated with 10 ml of concentrated aqueous ammonia. After standing overnight the resulting solid was filtered, washed with water, and dried to afford 5.3 g (93%) of product; recrystallization from methanol gave an analytical sample: mp 156.0–156.5°; $\lambda_{max}^{95\%\ EtOH}$ 278 mμ (log ϵ 4.31); the infrared spectrum was consistent with the structure assigned. The nmr spectrum at 60° in $(CD_3)_2SO$ (*vs.* external $(CH_3)_4Si$) showed τ 8.65 (doublet, J = 6 cps, 3 H), 8.33 (doublet, J = 6 cps, 3 H), 6.57 (multiplet, 1 H), 5.96 (singlet, 2 H), 5.11 (multiplet, 1 H), 3.71 (broad peak, 1 H), 2.95 (broad peak, 1 H).

Anal. Calcd for $C_7H_{12}N_2O_2$: C, 53.83; H, 7.74; N, 17.94. Found: C, 53.77; H, 7.68; N, 18.22.

Method B.—Ethyl *cis*-4,5-dimethyl-2-amino-4,5-dihydro-3-furoate (6.5 g, 0.035 mole) was treated with 20 ml of concentrated aqueous ammonia, the reaction mixture heated on a steam bath for 30 min and then cooled. The crystalline precipitate, after drying, weighed 2.3 g (55%) and showed an infrared spectrum essentially identical with that of the compound prepared by method A.

***trans*-4,5-Dimethyl-2-amino-4,5-dihydro-3-furamide (IIIb). Method A.**—This was prepared in 95% yield from *trans*-4,5-dimethyl-2-oxotetrahydro-3-furonitrile according to method A above. Repeated crystallizations from methanol gave an analytical sample: mp 151–152°; $\lambda_{max}^{95\%\ EtOH}$ 277 mμ (log ϵ 4.36); infrared spectrum consistent with structure assigned. The nmr spectrum in $(CD_3)_2SO$ (60°) showed τ 8.35 (two overlapped doublets, 6 H), 6.78 (multiplet, 1 H), 5.90 (singlet, 2 H), 5.46 (multiplet, 1 H), 3.63 (broad peak, 1 H), 2.76 (broad peak, 1 H).

Anal. Found: C, 54.28; H, 8.05; N, 17.49.

Method B.—*trans*-4,5-Dimethyl-2-amino-4,5-dihydro-3-furamide (IIIb) was also prepared by method B, ethyl *trans*-4,5-dimethyl-2-amino-4,5-dihydro-3-furoate (1.0 g, 5.4 mmoles) being allowed to react with 5.0 ml of concentrated aqueous ammonia. A yield of 0.45 g (53%) resulted, mp 145–148°. There was no depression of the melting point when mixed with a sample prepared by method A.

3-Acetyl-5-ethyl-2-oxotetrahydrofuran (α-Acetyl-γ-caprolactone).—Sodium metal (92 g, 4.0 g-atoms) was dissolved in 1600 ml of absolute ethanol, there was added 561 g (4.2 moles) of ethyl acetoacetate, and the resulting solution was cooled in a water bath. Over a 3-hr period 288 g (4 moles) of 2-ethyloxirane was added, and the solution was maintained at room temperature, with stirring, for a 6-day period. A crude fraction, bp 100–120° (2 mm) and weighing 332 g, was obtained on distillation; fractionation gave 311 g of product, bp 106–108° (2 mm), the infrared spectrum consistent with structure assigned.

2-Methyl-5-ethyl-4,5-dihydro-3-furamide (V).—Treatment of 15.5 g (0.100 mole) of 3-acetyl-5-ethyl-2-oxotetrahydrofuran with 40 ml of concentrated aqueous ammonia gave a precipitate (6.6 g, 42%) after stirring overnight at room temperature, then refrigerating. An analytical sample was recrystallized twice from benzene and attained a melting point of 88–90°.

Anal. Calcd for $C_8H_{13}NO_2$: C, 61.91; H, 8.44; N, 9.03. Found: C, 61.64; H, 8.11; N, 8.94.

***trans*-4,5-Dimethyl-2-methylimino-3-(N-methylcarbamoyl)tetrahydrofuran (VI).**—*trans*-4,5-Dimethyl-2-oxotetrahydro-3-furonitrile (1.39 g, 0.0100 mole) was treated with 3 ml of a 40% aqueous solution of methylamine, and the reaction mixture was allowed to stand for 1 hr at room temperature. The volatile materials were removed under reduced pressure and the oily

(12) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York N. Y., 1959, Chapter 17.

(13) Melting points and boiling points are uncorrected. Elemental analyses were carried out by Triangle Chemical Laboratories, Chapel Hill, N. C. Spectra were recorded as follows: infrared using Perkin-Elmer Model 137 and 237 Infracord spectrometers, ultraviolet using a Cary Model 14 spectrometer, and nuclear magnetic resonance using a Varian Model A-60. (All chemical shifts were determined *vs.* tetramethylsilane.)

(14) S. Winstein and H. J. Lucas, *J. Am. Chem. Soc.*, **61**, 1576 (1939); H. O. House and R. S. Ro, *ibid.*, **80**, 182 (1958).

residue recrystallized from *dry* ethyl acetate to afford 0.70 g (38%) of product, mp 103.0–103.5°. The infrared spectrum showed bands at 1730 and at 1650 cm^{-1}, indicating the presence of the imino and carbonyl groups; $\lambda_{max}^{95\% EtOH}$ 277 mμ (log ε 2.41). The nmr spectrum in $CDCl_3$ showed τ 8.72 (doublet, J = 7 cps, 3 H), 8.64 (doublet, J = 7 cps, 3 H), 7.73 (multiplet, 1 H), 7.19 (doublet, J = 5 cps, 3 H), 7.07 ("doublet," separation 2 cps for 0.25 of height with shoulder at τ 6.93, 4 H), 6.04 (multiplet, 1 H), 1.64 (broad peak, 1 H). Isotopic exchange with D_2O substantially diminished the peaks at τ 6.93 and 1.64, and transformed the signals attributed to the N-methyl groups into singlets at 6.95 and 7.10.

Anal. Calcd for $C_9H_{16}N_2O_2$: C, 58.67; H, 8.75; N, 15.21. Found: C, 58.28; H, 8.50; N, 14.83.

cis-6,7-Dimethyl-2,3,4,5,6,7-hexahydrofurano[2.3-*e*]-1,4-diazepin-5-one (VIII).—*cis*-4,5-Dimethyl-2-oxotetrahydro-3-furonitrile (2.78 g, 0.020 mole) was treated with 1,2-ethanediamine (1.80 g, 0.030 mole) in 5 ml of water, and the solution was allowed to stand at room temperature for 2 hr. The volatile materials were removed under vacuum and the oily residue crystallized from ethanol to give 1.10 g (31%) of colorless crystals, mp 168–171°. The ultraviolet spectrum showed a maximum at 279 mμ (log ε 4.42); nmr ($CDCl_3$) τ 9.00 (doublet, J = 7 cps, 3 H), 8.70 (doublet, J = 7 cps, 3 H), 7.0 (multiplet, 1 H), 6.40 (singlet, 4 H), 5.46 (multiplet, 1 H), 4.55 (broad peak, 1 H), 3.03 (broad peak, 1 H).

Anal. Calcd for $C_9H_{14}N_2O_2$: C, 59.32; H, 7.74; N, 15.37. Found: C, 59.21; H, 7.77; N, 15.27.

Hydrochloride of Ethyl *cis*-4,5-Dimethyl-2-oxotetrahydro-3-furimidate (XII).—A solution of *cis*-4,5-dimethyl-2-oxotetrahydro-3-furonitrile (20.8 g, 0.15 mole) and absolute ethanol (7.8 g, 0.17 mole) in 55 ml of anhydrous diethyl ether was treated with gaseous hydrogen chloride (7.70 g, 0.21 mole) while at ice–salt temperatures. The reaction mixture was stored in a refrigerator for 7 days, during which time two liquid phases developed, the more dense one finally solidifying. It was filtered, washed with dry ether, and dried to give 22.4 g (67%) of crude product. This was used in the following experiment without further purification.

cis-4,5-Dimethyl-2-oxotetrahydro-3-furamide (VIII). Method A.—Heating 30.7 g (0.14 mole) of the hydrochloride of ethyl *cis*-4,5-dimethyl-2-oxotetrahydro-3-furimidate to 120–130° for 90 min in accord with the published procedure[3] led to the evolution of 4.6 g of ethyl chloride. The residue was boiled twice with 25-ml portions of absolute ethanol, filtered from the ammonium chloride (4.8 g) formed, and concentrated to give 9.1 g (41%) of solid product. Recrystallization from ethanol gave an analytical sample, mp 117–119°, infrared spectrum consistent with the assigned structure.

Anal. Calcd for $C_7H_{11}NO_3$: C, 53.49; H, 7.05; N, 8.91. Found: C, 53.22; H, 6.72; N, 9.01.

Method B.—*cis*-4,5-Dimethyl-2-amino-4,5-dihydro-3-furamide (3.12 g, 0.020 mole) was refluxed in a solution composed of 2 ml of water in 15 ml of ethyl acetate for 9 hr. Concentration of the solution led to crystallization of the product (2.5 g, 80%), melting point and infrared spectrum essentially identical with those of the compound prepared by method A.

***trans*-4,5-Dimethyl-2-oxo-3-(N-methylcarbamoyl)tetrahydrofuran (IX).**—This was similarly prepared by hydrolysis of a partly purified sample of *trans*-4,5-dimethyl-2-methylimino-3-(N-methylcarbamoyl)tetrahydrofuran (VI), representing the product from 0.039 mole of cyano lactone Ib and excess methylamine. A reflux period of 24 hr, in 25 ml of 80% ethyl acetate–20% water, was utilized. Concentration gave 5.30 g (85% based on cyano lactone) of product, mp 116–119°, recrystallized from ethyl acetate to give an analytical sample. The infrared spectrum showed lactone carbonyl absorption at 1770 and the amide carbonyl at 1650 cm^{-1}, in addition to two N–H bands at 3350 and 3150 cm^{-1}. The nmr spectrum in $CDCl_3$ showed τ 8.75 (doublet J = 7 cps, 3 H), 8.58 (doublet, J = 7 cps, 3 H), 7.54 (multiplet, 1 H), 7.17 (doublet, J = 5 cps, 3 H), 6.89 (doublet, J = 12 cps, 1 H), 5.88 (multiplet, 1 H), 2.82 (broad peak, 1 H).

Anal. Calcd for $C_8H_{13}NO_3$: C, 56.12; H, 7.65; N, 8.18. Found: C, 56.05; H, 7.43; N, 8.11.

cis-4,5-Dimethyl-2-oxotetrahydro-3-furoic Acid (X).—*cis*-4,5-Dimethyl-2-oxotetrahydro-3-furamide in the amount of 1.57 g (0.010 mole) was stirred at room temperature with 15 ml of 2 *N* sodium hydroxide. The odor of ammonia was detectable immediately. After 3 hr the solution was cooled to 0°, slowly acidified with concentrated hydrochloic acid, and extracted with three 10-ml portions of chloroform. The combined extracts were dried over magnesium sulfate, filtered, and evaporated to approximately one-tenth of their original volume. Solidification occurred on cooling to give slightly more than 1 g of white product, soluble in water, capable of liberating carbon dioxide from sodium bicarbonate solution. It was recrystallized from chloroform–petroleum ether (bp 30–60°) to give an analytical sample, mp 85.5–86.5°. The infrared spectrum showed carbonyl bands at 1780 and 1735 cm^{-1}.

Anal. Calcd for $C_7H_{10}O_4$: C, 53.16; H, 6.37; Found: C, 52.91; H, 6.39.

cis-4,5-Dimethyl-2-oxotetrahydrofuran (XI).—Heating a sample of *cis*-4,5-dimethyl-2-oxotetrahydro-3-furoic acid to 120–140° led to the evolution of carbon dioxide and the formation of *cis*-4,5-dimethyl-2-oxotetrahydrofuran (XI): bp 64–67° (2 mm), carbonyl band (Nujol) at 1780 cm^{-1}.

Anal. Calcd for $C_6H_{10}O_2$: C, 63.13; H, 8.83. Found: C, 62.78; H, 8.72.

DL-*threo*-2-Carbamoyl-3-methyl-4-hydroxypentanamide (XIII). Method A.—*cis*-4,5-Dimethyl-2-oxotetrahydro-3-furamide (1.67 g, 0.0100 mole) was added to 10 ml of concentrated aqueous ammonia; after standing for 1 hr at room temperature the reaction mixture was cooled in ice, and the resulting precipitate was filtered off and dried to give 1.60 g (93%) of product, mp 193° dec. Recrystallization from methanol gave an analytical sample.

Anal. Calcd for $C_7H_{14}N_2O_3$: C, 48.26; H, 8.10; N, 16.08. Found: C, 47.93; H, 7.96; N, 16.21.

Method B.—The same compound resulted from *cis*-4,5-dimethyl-2-oxotetrahydro-3-furoic acid when the latter (0.40 g) was treated with excess of concentrated aqueous ammonia to give 0.45 g of product with properties (melting point, mixture melting point, and infrared and nmr spectra) essentially identical with those of the product prepared by method A.