[CONTRIBUTION FROM THE LILLY RESEARCH LABORATORIES AND FROM THE WM. H. CHANDLER LABORATORY, LEHIGH UNIVERSITY]

Preparation and Reactions of Some 2-Amino Tetrahydrofurans

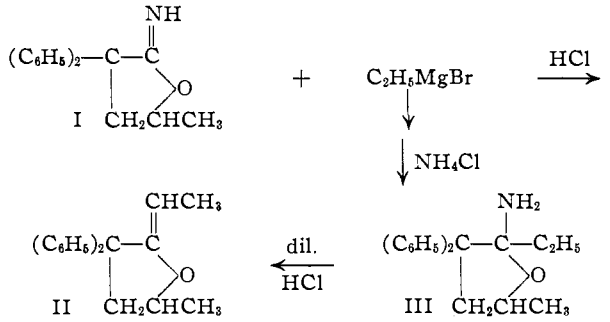
BY NELSON R. EASTON, CARL A. LUKACH, SAMUEL J. NELSON AND VELMER B. FISH

RECEIVED AUGUST 22, 1957

Treatment of 3,3-diphenyl-2-furanoneimines with Grignard reagents gives 2-amino-3,3-diphenyltetrahydrofurans. These compounds can be reduced with lithium aluminum hydride to give the corresponding γ,γ-diphenyl-δ-amino alcohols which in turn can be dehydrated to give 3,3-diphenylpyrrolidines. Treatment of the 2-amino-3,3-diphenyltetrahydrofurans with warm acid gives the 2-alkylidene-3,3-diphenyltetrahydrofurans.

The unexpected products obtained from the action of Grignard reagents on α,α-diphenylbutanolactones[1] prompted us to investigate the effect of Grignard reagents on the imines corresponding to these lactones.[2,3]

Treatment of 3,3-diphenyl-5-methyl-2-furanoneimine (I) with ethylmagnesium bromide, followed by decomposition with hydrochloric acid, gave good yields of 3,3-diphenyl-5-methyl-2-ethylidenetetrahydrofuran (II) identical with that obtained from the pyrolysis of Methadone methiodide[4] and that produced by the action of ethylmagnesium bromide on 3,3-diphenyl-5-methylbutanolactone.[1] However, when an ice-cold solution of ammonium chloride was used to decompose the reaction mixture, a different compound was obtained. This product formed a hydrochloride in ether and was soluble in dilute acid. The acid solution, on warming or standing, gave a white precipitate identical to II. The dry hydrochloride was unstable and decomposed at room temperature in a few days; however, it was stable enough to be analyzed. The base is a white solid and relatively stable at room temperature. Samples have been kept for several years with no obvious decomposition.



There are two alternative structures that would satisfy the chemical requirements: the aminotetrahydrofuran III and the imino alcohol IV. The infrared spectrum shows no OH bands and clearly indicates that III is the correct structure. Both I and its homolog, 3,3-diphenyl-2-furanoneimine, have been treated with other aliphatic Grignard reagents to give similar results.

A question exists as to whether the Grignard reagents react with the furanoneimine I or with the isomeric hydroxynitrile V or both. In the case when compound I was treated with methylmagnesium iodide at the reflux temperature of ether for two hours, the product was largely a non-basic nitrogen-containing compound which was identified as the hydroxynitrile V. Longer periods of reflux gave good yields of the desired amine. Similar results were obtained with the same Grignard reagent on 3,3-diphenyl-2-furanoneimine, but the hydroxynitrile was a liquid which was not purified. Since a good yield of II was obtained when I and ethylmagnesium bromide were refluxed for two hours and similar results were obtained with the higher Grignard reagents, a difference in activities of the methyl Grignard and its higher homologs is indicated. Although the intermediate was not investigated in the case of the ethyl and higher Grignard reagents, the rate of reaction would suggest that they probably reacted with the furanoneimine whereas the methyl reagent converts the furanoneimine to the hydroxynitrile. A further reaction of the hydroxynitrile with the excess Grignard reagent followed by a cyclization would give the aminotetrahydrofuran.

It can be seen from the structure of III that reductive cleavage of the tetrahydrofuran ring to the amino alcohol would give a primary amine closely related in structure to Methadol (VI). In this case the two functional groups, the amino and hydroxy, would be interchanged compared to those in VI. With this motive in mind, reduction of III was attempted. Only the starting material was isolated from a hydrogenation under low pressure at room temperature over Adams catalyst. Raney nickel as a catalyst did not give any basic material but did give a non-basic high boiling oil. When lithium aluminum hydride in boiling ether was used, only starting material was isolated. This reagent in boiling tetrahydrofuran caused cleavage of the starting material to 4,4-diphenyl-2-butanol, identical to that isolated[5] from the sodium–alcohol reduction of I. However, the use of lithium aluminum hydride in a mixture of benzene and ether gave good yields of the desired amino alcohol VII. This compound could be methylated with formic acid and formaldehyde to give the expected product VIII. Since the stereoisomers of Methadol differ greatly in their pharmacological activity,[6] and in

(1) N. R. Easton, C. A. Lukach, V. B. Fish and P. N. Craig, THIS JOURNAL, **75**, 4731 (1953).

(2) N. R. Easton, J. H. Gardner and J. S. Stevens, *ibid.*, **69**, 2941 (1947).

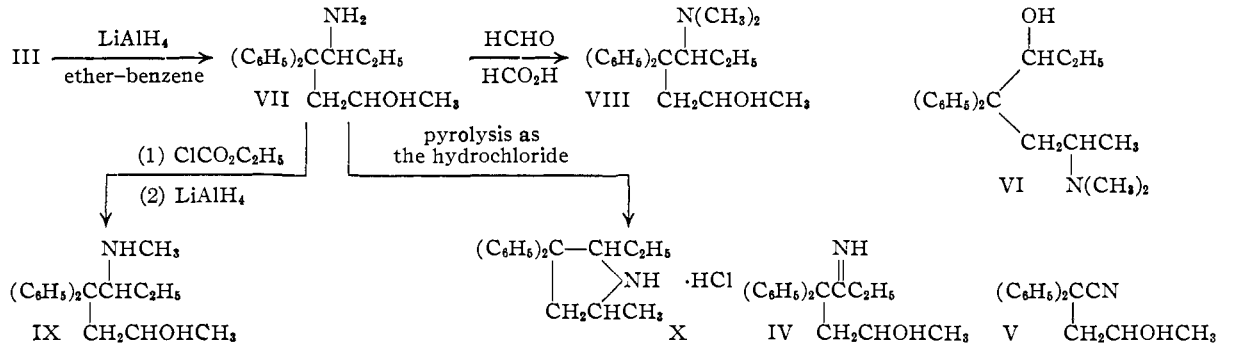
(3) E. M. Schultz, C. M. Robb and J. M. Sprague, *ibid.*, **69**, 2454 (1947).

(4) N. R. Easton, S. J. Nelson, V. B. Fish and P. N. Craig, *ibid.*, **75**, 3751 (1953).

(5) N. R. Easton and V. B. Fish, *ibid.*, **77**, 1776 (1955).

(6) (a) A. Pohland, F. J. Marshall and T. P. Carney, *ibid.*, **71**, 460 (1949); (b) M. E. Speeter, W. M. Byrd, L. C. Cheney and S. B. Binkley, *ibid.*, **71**, 57 (1949); (c) E. L. May and E. Mosettig, *J. Org. Chem.*, **13**, 459 (1948); (d) W. B. Eddy, E. L. May and E. Mosettig, *ibid.*, **17**, 321 (1952); (e) E. L. May and W. B. Eddy, *ibid.*, **17**, 1210 (1952).

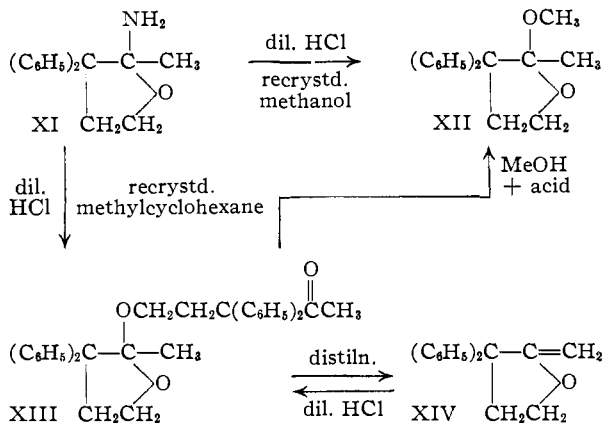
some cases the esterification of the hydroxy group greatly enhances the analgetic activity, a thorough study of the different forms of VIII and their ace-



tates was made. It was found that the two racemates of VII could be separated: the α-form as the maleate salt and the β-form as either the base or as the hydrochloride. Each of these forms was then carried through the sequence of reactions to give the corresponding acetate of VIII. None of these compounds showed any appreciable analgetic activity.

Heating of the hydrochloride of VII above its melting point proved a convenient method of obtaining the pyrrolidine X. The treatment of VII with ethyl chlorocarbonate and then reduction with lithium aluminum hydride was a convenient method of obtaining the monomethyl derivative IX. Several homologs of III, VII and X have been prepared.

Since the treatment of III with dilute hydrochloric acid readily gave the ethylidenetetrahydrofuran II and similar results were obtained with 2-amino - 2 - ethyl - 3,3 - diphenyltetrahydrofuran, 2 - amino - 2 - methyl - 3,3 - diphenyltetrahydrofuran XI was treated in a similar manner. However, the methylidenetetrahydrofuran[7] XIV was not obtained and different compounds were found depending on whether the product was recrystallized from methanol or from methylcyclohexane. The material obtained from the methylcyclohexane recrystallization has been assigned structure XIII. The molecular weight shows it to be of approximately dimeric nature and the empirical formula $C_{34}H_{34}O_3$ agrees with the analytical results. It



(7) S. J. Nelson, V. B. Fish and N. R. Easton, THIS JOURNAL, **77**, 1908 (1955).

shows carbonyl absorption in both the infrared and ultraviolet regions. In the ultraviolet spectrum the ratio of intensities of the phenyl band to the carbonyl band is approximately 2:1, whereas in 1-dimethylamino-3,3-diphenyl-5-pentanone this ratio is roughly 1:1. The infrared curve shows no OH absorption, and it does show the typical pattern of the diphenyltetrahydrofuran ring. The product obtained from the recrystallization from methanol was assigned the structure XII. This was based on the analytical results and the infrared and ultraviolet spectra.

The methylidene tetrahydrofuran XIV can be obtained from either XII or XIII by distillation at reduced pressure. Also XIV can be reconverted to XIII by treatment with dilute acid and to XII by reaction with methanol in the presence of an acidic catalyst.

Acknowledgment.—The authors wish to thank Mr. William Brown, Mr. Howard Hunter, Mr. George Maciak and Miss Gloria Beckmann for analytical data, and Dr. Harold Boaz, Mr. Donald Woolf, Mr. Leland Howard and Miss Martha Hofmann for the physical chemical data.

Experimental

2-Amino-2-ethyl-3,3-diphenyl-5-methyltetrahydrofuran (III).—To a solution of ethylmagnesium bromide prepared from 61 g. of ethyl bromide and 14.4 g. of magnesium, there was added a solution of 37.6 g. (0.15 mole) of 3,3-diphenyl-5-methyl-2-furanoneimine in benzene. The mixture was refluxed for 2 hours and decomposed with a solution of ammonium chloride. The organic layer was separated, washed with water, dried, and concentrated. The residue was taken up in ethanol and on scratching a solid came out (32.4 g.). After recrystallization from methanol it melted at 82–83°.

Anal. Calcd. for $C_{19}H_{23}NO$: C, 81.10; H, 8.24; N, 4.98. Found: C, 81.15; H, 8.36; N, 4.84.

The following were prepared in a similar manner:

2-Amino-3,3-diphenyl-2-methyltetrahydrofuran XI (refluxed 5 hours), m.p. 91–92° (methylcyclohexane). *Anal.* Calcd. for $C_{17}H_{19}NO$: C, 80.57; H, 7.56; N, 5.53. Found: C, 80.75; H, 7.54; N, 5.80.

2-Amino-3,3-diphenyl-2,5-dimethyltetrahydrofuran, m.p. 87–88° (methylcyclohexane). *Anal.* Calcd. for $C_{18}H_{21}NO$: C, 80.86; H, 7.92; N, 5.24. Found: C, 80.98; H, 8.03; N, 5.30.

2-Amino-3,3-diphenyl-2-propyl-5-methyltetrahydrofuran, m.p. 67–69° (MeOH–H_2O). *Anal.* Calcd. for $C_{20}H_{25}NO$: C, 81.31; H, 8.53; N, 4.74. Found: C, 81.55; H, 8.69; N, 4.69.

2-Amino-2-ethyl-3,3-diphenyltetrahydrofuran, m.p. 92–93° (ethanol).—*Anal.* Calcd. for $C_{18}H_{21}NO$: C, 80.86; H, 7.92. Found: C, 80.60; H, 8.07.

4-Amino-3,3-diphenyl-1-heptanol Hydrochloride.—A suspension of 48 g. of 2-amino-3,3-diphenyl-2-propyltetrahydrofuran and 10 g. of lithium aluminum hydride in a 50–50 mixture of ether and benzene was refluxed for 11 hours. It was

filtered and the organic layer was extracted with dilute hydrochloric acid. The water layer was neutralized with base and extracted with ether and the ether layer was separated and dried over magnesium sulfate. Addition of dry hydrogen chloride to the ether solution gave a solid melting at 191–192°.

Anal. Calcd. for $C_{19}H_{26}NOCl$: C, 71.34; H, 8.19. Found: C, 71.17; H, 8.00.

α- and β-5-amino-4,4-diphenyl-2-heptanol (VII) was obtained from 2-amino-2-ethyl-3,3-diphenyl-5-methyltetrahydrofuran. To the ether solution obtained as above there was added an alcoholic solution of maleic acid. The solid, which precipitated after being recrystallized from ethanol and melted at 187–189°, was **α-5-amino-4,4-diphenyl-2-heptanol maleate.**

Anal. Calcd. for $C_{23}H_{29}NO_5$: C, 69.15; H, 7.32. Found: C, 69.19; H, 7.33.

The mother liquors were concentrated at reduced pressure. The residue was made basic with dilute sodium hydroxide and extracted with ether. The ether layer was dried over magnesium sulfate and concentrated at reduced pressure. The residue was taken up in hot Skelly B; on cooling crystals formed which, after being recrystallized from Skelly B, melted at 90–91°. This was **β-5-amino-4,4-diphenyl-2-heptanol**; hydrochloride, m.p. 213–215°.

Anal. Calcd. for $C_{19}H_{25}NO$: C, 80.52; H, 8.89; N, 4.94. Found: C, 80.70; H, 8.89; N, 4.68.

The following were prepared in a similar manner:

5-Amino-4,4-diphenyl-2-hexanol hydrochloride was obtained from 2-amino-2,5-dimethyl-3,3-diphenyltetrahydrofuran, m.p. 108–110° (water). *Anal.* Calcd. for $C_{18}H_{24}NOCl$: C, 70.68; H, 7.91. Found: C, 70.44; H, 7.84.

4-Amino-3,3-diphenyl-1-hexanol hydrochloride was obtained from 2-amino-2-ethyl-3,3-diphenyltetrahydrofuran, m.p. 183–185° (ethyl acetate–ethanol). *Anal.* Calcd. for $C_{18}H_{24}NOCl$: C, 70.68; H, 7.91; Cl, 11.59. Found: C, 70.95; H, 7.82; Cl, 11.59.

Pyrolysis of the Amino Alcohols.—The amino alcohol hydrochlorides were pyrolyzed by heating them above their melting points until all evidence of decomposition ceased. The products were recrystallized from ethanol.

The following were prepared in a similar manner:

2-Ethyl-3,3-diphenylpyrrolidine hydrochloride was obtained from 4-amino-3,3-diphenyl-1-hexanol, m.p. 223–225°. *Anal.* Calcd. for $C_{18}H_{22}NCl$: C, 75.11; H, 7.71; N, 4.86. Found: C, 75.22; H, 7.89; N, 4.86.

α-2-Ethyl-3,3-diphenyl-5-methylpyrrolidine hydrochloride was prepared from α-5-amino-4,4-diphenyl-2-heptanol, m.p. 258–260°. *Anal.* Calcd. for $C_{19}H_{24}NCl$: C, 75.60; H, 8.01. Found: C, 75.63; H, 8.02.

β-2-Ethyl-3,3-diphenyl-5-methylpyrrolidine hydrochloride was synthesized from β-5-amino-4,4-diphenyl-2-heptanol, m.p. 231–233°. *Anal.* Calcd. for $C_{19}H_{24}NCl$: C, 75.60; H, 8.01; N, 4.64. Found: C, 75.42; H, 8.08; N, 4.60.

2,5-Dimethyl-3,3-diphenylpyrrolidine hydrochloride was formed from 5-amino-4,4-diphenyl-2-hexanol, m.p. 256–258° (water). *Anal.* Calcd. for $C_{18}H_{22}NCl$: Cl, 12.32; N, 4.87. Found: Cl, 12.45; N, 5.06.

3,3-Diphenylpyrrolidine hydrochloride was obtained from 4-amino-3,3-diphenyl-1-butanol, m.p. 234–236°. *Anal.* Calcd. for $C_{16}H_{18}NCl$: C, 73.97; H, 6.98; N, 5.39. Found: C, 74.11; H, 7.15; N, 5.66.

1,2-Dimethyl-4,4-diphenylpyrrolidine hydrochloride (by methylation of 2-methyl-4,4-diphenylpyrrolidine), m.p. 193–195° (acetone). *Anal.* Calcd. for $C_{18}H_{22}NCl$: C, 75.11; H, 7.71; N, 4.87; Cl, 12.32. Found: C, 75.28; H, 7.89; N, 4.88; Cl, 12.12.

2-Methyl-3,3-diphenylpyrrolidine hydrochloride was obtained from 4-amino-3,3-diphenyl-1-pentanol, m.p. 209–210°. *Anal.* Calcd. for $C_{17}H_{20}NCl$: C, 74.57; H, 7.36; N, 5.12. Found: C, 74.27; H, 7.49; N, 4.88.

2-Methyl-4,4-diphenylpyrrolidine hydrochloride was prepared from 5-amino-4,4-diphenyl-2-pentanol,[5] m.p. 262–263°.

Anal. Calcd. for $C_{17}H_{20}NCl$: C, 74.57; H, 7.36; Cl, 12.95. Found: C, 74.80; H, 7.12; Cl, 12.72.

β-5-Methylamino-4,4-diphenyl-2-heptanol.—To a well-stirred solution of 15 g. of β-5-amino-4,4-diphenyl-2-heptanol in 50 ml. of pyridine there was added slowly a 10% excess of ethyl chlorocarbonate. The mixture became warm and was stirred for two hours. It was concentrated at reduced pressure and water and ether were added to the residue. The ether layer was separated, washed successively with water, dilute hydrochloric acid, dilute sodium bicarbonate and was dried over magnesium sulfate. This solution then was added to a well-stirred suspension of 7 g. of lithium aluminum hydride in ether and the mixture was refluxed for six hours and then was decomposed with a solution of sodium hydroxide. The mixture was filtered and the ether solution dried over magnesium sulfate. To this solution dry hydrogen chloride was added. On scratching a solid came out and was recrystallized from a mixture of ethanol, ethyl acetate and diethyl ether, m.p. 208–210°.

Anal. Calcd. for $C_{20}H_{28}NOCl$: C, 71.94; H, 8.45; N, 4.20. Found: C, 71.84; H, 8.39; N, 4.11.

The following was prepared in a similar manner: α-form (base), m.p. 124–126°; *Anal.* Calcd. for $C_{20}H_{27}NO$: C, 80.76; H, 9.15; N, 4.71. Found: C, 80.99; H, 9.36; N, 4.63. Hydrochloride (from dil. HCl), m.p. 140°. (Calcd. as hydrate) $C_{20}H_{28}NOCl \cdot H_2O$: C, 68.26; H, 8.59; Cl, 10.08. Found: C, 68.16; H, 8.85; Cl, 9.95.

5-Dimethylamino-4,4-diphenyl-2-heptanol.—The oily product containing both isomers of 3-amino-4,4-diphenylheptanol was refluxed overnight with a 50–50 mixture of formalin and formic acid. The mixture was concentrated to dryness at reduced pressure. The residue was taken up in water, neutralized with base and extracted with ether. The ether solution was dried over magnesium sulfate and dry hydrogen chloride added. The oil which formed crystallized on scratching and after recrystallization from a mixture of ethanol and ethyl acetate gave the α-form melting at 197–199°.

Anal. Calcd. for $C_{21}H_{30}NOCl$: Cl, 10.19; N, 4.03. Found: Cl, 10.06; N, 3.89.

The β-form was isolated from the mother liquors as the free base, m.p. 138–140° (methylcyclohexane).

Anal. Calcd. for $C_{21}H_{29}NO$: C, 80.98; H, 9.39; N, 5.14. Found: C, 80.98; H, 9.65; N, 4.89.

β-5-Dimethylamino-4,4-diphenyl-2-heptanol hydrochloride, m.p. 202–203°; a mixed melting point of the two hydrochlorides was 178–185°. *Anal.* Calcd. for $C_{21}H_{30}NOCl$: Cl, 10.19; N, 4.03. Found: Cl, 9.88; N, 4.13.

4,4-Diphenyl-5-dimethylamino-2-acetoxyheptane.—A mixture of the amino alcohol, acetic anhydride and pyridine was heated on the steam-bath for several hours. The solution was then poured into water, extracted with ether and the ether layer washed with water, dried and concentrated; β-form, m.p. 111–113° (methanol).

Anal. Calcd. for $C_{23}H_{31}NO_2$: C, 78.14; H, 8.84. Found: C, 77.82; H, 9.15. α-Form, m.p. 85–86° (methanol–water). Found: C, 77.60; H, 8.98; α-hydrochloride, m.p. 188–189° (ethanol–ether); β-hydrochloride, m.p. 183–185° (ethanol–ether).

2,2-Diphenyl-4-hydroxypentanonitrile.—To a mixture of methylmagnesium iodide, prepared from 29 g. of methyl iodide and 5 g. of magnesium in 100 ml. of ether, there was added a solution of 25.3 g. of 3,3-diphenyl-5-methyl-2-furanoneimine in 110 ml. of benzene. The mixture was refluxed for two hours and then decomposed by pouring into cold ammonium chloride. The mixture was separated and the organic layer was washed with cold dilute hydrochloric acid and then with a cold solution of sodium bicarbonate, dried over magnesium sulfate and concentrated at reduced pressure. After recrystallization from methylcyclohexane, the product melted at 91–92°; infrared spectrum ($CHCl_3$ solution): 2.84 μ (OH), 4.2 μ (CN).

Anal. Calcd. for $C_{17}H_{17}NO$: C, 81.24; H, 6.82; N, 5.57. Found: C, 81.45; H, 6.91; N, 5.42.

Decomposition of 2-Amino-3,3-diphenyl-2-methyltetrahydrofuran (XI).—A sample (7 g.) of XI was dissolved in a small amount of concentrated hydrochloric acid and the solution diluted to about 70 ml. The mixture was warmed on a steam-bath for 30 minutes, cooled and extracted with ether. The ether layer was dried over magnesium sulfate and concentrated at reduced pressure. A portion of the residue, after being recrystallized from methylcyclohexane, melted at 135–137° (XIII); infrared spectrum, chloroform solution: 5.85, 8.67, 8.96, 9.33 and 9.70 μ; ultraviolet spectrum: A_m 257 = 956; A_m 292 = 491; for 1-dimethylamino-3,3-diphenyl-4-pentanone hydrochloride, A_m 258 = 466; A_m 295 = 414.

Anal. Calcd. for $C_{34}H_{34}O_3$: C, 83.23; H, 6.99; mol. wt., 490.6. Found: C, 83.16; H, 7.18; mol. wt., 561.

A second portion of the concentrate, after being recrystallized from methanol, melted at 93–95°; infrared spectrum chloroform solution: 8.65, 9.00, 931 and 9.66 μ, no OH, NH or C=O.

Anal. Calcd. for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.66; H, 7.30.

3,3-Diphenyl-5-methyl-2-ethylidenetetrahydrofuran.—The reaction was run as in the preparation of III. After the reaction had been completed the mixture was poured into 6 *N* hydrochloric acid. The mixture was extracted with ether, the ether layer washed with water and then with dilute sodium bicarbonate solution, dried over magnesium sulfate and concentrated. The residue was recrystallized from methanol, m.p. 79–80°; mixed m.p. with authentic sample[4] 79–80°.

INDIANAPOLIS, INDIANA
BETHLEHEM, PENNA.

[CONTRIBUTION FROM THE PHARMACEUTICAL INSTITUTE, MEDICAL FACULTY, UNIVERSITY OF KYUSHU]

Stereochemistry of the 2,2′-Dihydroxydicyclohexylamines. I[1]

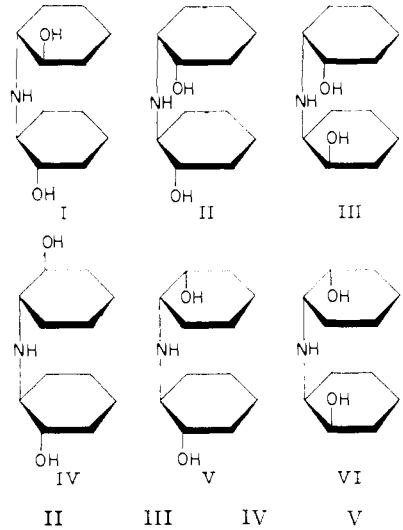
BY TANEZO TAGUCHI AND KEN HAYASHIDA

RECEIVED AUGUST 7, 1957

meso-trans-trans-2,2′-Dihydroxydicyclohexylamine (I) has been converted to the *dl-trans-cis*-epimer II *via* the Walden inversion of its N-benzoyl derivative VII by thionyl chloride; VIII, the N-benzoyl derivative of II, yields the *cis-cis*-epimer III upon similar treatment. In the reaction of the N-benzoyl *meso-trans-trans*-epimer VII with thionyl chloride, *dl*-3-(*trans*-2′-hydroxycyclohexyl)-2-phenyl-*cis*-4,5-cyclohexanoöxazolinium chloride (X) was isolated as an intermediate; X also was obtained by treatment of the N-benzoyl *dl-trans-cis*-epimer VIII with dry hydrogen chloride. It was found that N-benzoylation was inhibited in those dicyclohexylamines which contained a *cis*-hydroxy group.

Examination of the formula for 2,2′-dihydroxydicyclohexylamine reveals the possible existence of

CHART I



I II III IV V VI

I, *meso-trans-trans*-2,2′-dihydroxydicyclohexylamine
II, *dl-trans-cis*-2,2′-dihydroxydicyclohexylamine
III, *meso-cis-cis*-2,2′-dihydroxydicyclohexylamine
IV, *dl-trans-trans*-2,2′-dihydroxydicyclohexylamine
V, *dl-trans-cis*-2,2′-dihydroxydicyclohexylamine
VI, *dl-cis-cis*-2,2′-dihydroxydicyclohexylamine

six diastereoisomers,[2] of which two are *meso* and four racemic as shown in Chart I.

Of the six compensated isomers, two (m.p. 153° and 114°) were prepared by Brunel[3] on treatment of *meso-cis*-cyclohexene oxide with ethanolic ammonia. Much later Mousseron and his co-workers[4] repeated Brunel's work and suggested that these compounds were the *meso-trans-trans*- and *dl-trans-trans*-isomers on the basis of the known *trans* opening of the *cis*-oxide ring. They were unable to classify the two *trans-trans*-isomers by means of optical resolution. However, when *cis*-cyclohexene oxide reacted with either *d-trans*-2-aminocyclohexanol or its antipode, they obtained *d*- or *l-trans-trans*-2,2′-dihydroxydicyclohexylamine (m.p. 115°), respectively, and *meso-trans-trans* 2,2′-dihydroxydicyclohexylamine (m.p. 153°); thus the isomer of the m.p. 115° is the *dl*-form IV, and that of m.p. 153° is the *meso*-form I. We are investigating the other four stereoisomers which have not previously been reported, and have synthesized the *dl-trans-cis*- (II) and *meso-cis-cis*-epimer (III) from *meso-trans-trans*-2,2′-dihydroxydicyclohexylamine (I).

dl - *trans* - *cis* - 2,2′ - Dihydroxydicyclohexylamine (II) was prepared as follows; see Chart II. The N-benzoyl derivative VII of the *meso-trans-trans*-aminodiol I was obtained by the treatment of *meso-cis*-cyclohexene oxide with aqueous ammonia, followed by Schotten–Baumann benzoylation. This N-benzoyl derivative VII, m.p. 232°, was converted to VIII, m.p. 197°—the N-benzoyl derivative of another, 2,2′-dihydroxydicyclohexylamine—by reaction with thionyl chloride, followed by treatment with aqueous sodium hydroxide. The new N-benzoyl derivative VIII was converted to a free aminodiol II, m.p. 147°, *via* its hydrochloride IX. The same aminodiol II was obtained by the reaction of *meso-cis*-cyclohexene oxide with *dl-cis*-2-aminocyclohexanol. The stereospecificity of the latter reaction indicates that II is *dl-trans-cis*-2,2′-dihydroxydicyclohexylamine and, therefore, that VIII is the corresponding N-benzoyl derivative.

(1) Studies in Stereochemistry. XV.

(2) There exist two *dl-trans-cis*-isomers which are difficult to distinguish by the nomenclature adopted here. They are pictured in perspective formulas II and V as shown in Chart I. The molecules are drawn so that the average planes of the two cyclohexane rings are in the *syn*-relationship to C₁–N–C₁′ and at right angles to the plane of the paper; C₁, N, C₁′, C₄ and C₄′ are bisected by the plane of the paper. Then in II the two hydroxy groups are situated on the same side of the plane of the paper, while in V they are on different sides.

(3) L. Brunel, *Compt. rend.*, **137**, 199 (1903).

(4) M. Mousseron, R. Granger, G. Combes and V. A. Pertzoff, *Bull. soc. chim. France*, 859 (1947).