α-chloronaphthalene (0.50 g.) over a 5-min. period. After allowing the mixture to cool, 2.0 g. of α-chloronaphthalene was removed by distillation and had b.p. 125° (12 mm.). The residue was triturated with petroleum ether (b.p. 30–60°), and the resulting solution was chromatographed on 120 g. of Alcoa F-20 activated alumina. The materials to come off the column were 10 mg. (5.8%) of sulfur, m.p. 119–120°; 835 mg. of α-chloronaphthalene (a total recovery of α-chloronaphthalene was 2.84 g., 81%); 200 mg. (15.2%) of 2,4-diphenylthiophene, m.p. 118–119°, lit.[15] m.p. 121.5–123°; and 31.2 mg. (3.7%) of a yellow oil–crystal mixture which had an infrared spectrum identical with that of authentic 1,1-naphthyl disulfide.

2-Hydroxycyclohexylhydrazines. I.[1] Synthesis, Acylation, Acyl Migration, and Dihydrooxadiazine Ring Formation

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DL-*trans*- and DL-*cis*-2-hydroxycyclohexylhydrazines (*trans*- and *cis*-I) were prepared. The *trans* isomer was correlated with DL-*trans*-2-aminocyclohexanol in two ways, confirming the configuration of *trans*-I and accordingly of *cis*-I. N-Monobenzoyl, N_1,N_2-dibenzoyl, and N_1,N_2,O-tribenzoyl derivatives were derived from I. The N-benzoylated derivatives were treated with hydrogen chloride in anhydrous ethanol (method A) and in water (method B). Method A converted both forms of DL-2-benzoyl-1-(2-hydroxycyclohexyl)hydrazine (VI) and DL-*cis*-1,2-dibenzoyl-1-(2-hydroxycyclohexyl)hydrazine (*cis*-V) to dihydrooxadiazine derivatives (*trans*-X, *cis*-X, and *cis*-IX) with retention. On the same treatment, each form of DL-1-benzoyl-1-(2-hydroxycyclohexyl)hydrazine (IV) was converted to DL-4a,5,6,7,8,8a-hexahydro-3-phenyl-1H-4,1,2-benzoxadiazine (X) with retention, which was identical with the product from VI. This indicated that the reaction involved $N_1 \rightarrow N_2$ acyl migration followed by cyclization reaction to X. This new mode of acyl migration from N_1 to N_2 was found and confirmed in treatments of IV by method B and also with 10% anhydrous ethanolic hydrogen chloride for less time than in method A.

A few studies[2] have been carried out on 2-hydroxyalkyl hydrazines, mainly for synthetic purposes, but nothing appears to be reported concerning the stereochemistry of diastereomeric 2-hydroxyalkyl hydrazines. This prompted us to investigate the stereochemical behavior of DL-2-hydroxycyclohexylhydrazines (I) in comparison with that of the DL-2-aminocyclohexanols which have been widely studied.

DL-*trans*-2-Hydroxycyclohexylhydrazine (*trans*-I) was prepared by the action of hydrazine on *meso*–*cis*-cyclohexene oxide in ethanol. The *trans* assignment was established by correlating it with DL-*trans*-2-aminocyclohexanol[3] in three ways, of which two are described below and the other will appear in the next paper.[4] Treatment with hydroxylamine O-sulfonic acid[2g] converted DL-*trans*-2-aminocyclohexanol to a hydrazine derivative which was identical with *trans*-I. *trans*-I was condensed with acetone to give the N_2-isopropylidene derivative (*trans*-II), the structure of which was supported by the ultraviolet and the infrared spectra: λ_{max}^{EtOH} 227 mμ (ε 8092) (C=N), ν_{max}^{Nujol} 1634 cm.$^{-1}$ (C=N). The Schotten–Baumann benzoylation converted *trans*-II to the N_1-benzoyl, N_2-isopropylidene derivative (*trans*-III) which gave DL-*trans*-2-benzamidocyclohexanol on treatment with sodium amalgam in acetic acid. Thus the results confirmed the configuration of *trans*-I.

Benzoyl derivatives of *trans*-I were prepared and characterized as follows. The N_1-benzoyl, N_2-isopropylidene compound (*trans*-III) underwent deacetonization to give DL-*trans*-1-benzoyl-1-(2-hydroxycyclohexyl)hydrazine hydrochloride (*trans*-IV·HCl) by adding ether as soon as dissolved in 20% anhydrous ethanolic hydrogen chloride in the cold.[5] Support for the structure of *trans*-IV was presented when the compound reverted to *trans*-III by condensation with acetone. Moreover, the infrared spectrum also supported the structure: ν_{max}^{Nujol} 1647 (–CON<) and 1610 cm.$^{-1}$ (–NH_2). *trans*-IV was further treated with benzoyl chloride in aqueous sodium hydroxide to afford a dibenzoyl derivative which was identified as DL-*trans*-1,2-dibenzoyl-1-(2-hydroxycyclohexyl)hydrazine (*trans*-V) by infrared spectrum determination (lack of the ester carbonyl bands). *trans*-V was converted to the N_1,N_2,O-tribenzoate (*trans*-VII) on heating with benzoyl chloride in pyridine; ν_{max}^{Nujol} 1692, 1292, and 1120 (ester), and 1684 and 1664 cm.$^{-1}$ (amide). On the other hand, acylation of *trans*-I with boiling ethyl benzoate gave rise to a monobenzoyl derivative which was identified as DL-*trans*-2-benzoyl-1-(2-hydroxycyclohexyl)hydrazine (*trans*-VI) because of nonidentity with the N_1-benzoyl derivative (*trans*-IV) and also with the O-benzoate (see below) by mixture melting point and infrared comparison. An alternative preparation of *trans*-VI concerns application of the acyl migration reaction described later. In the Schotten–Baumann benzoylation of *trans*-I with 1 equiv. of benzoyl chloride, reaction temperature was found to govern product formation. Room temperature favored the formation of *trans*-V, while chilling at 0–5° resulted in the formation of *trans*-IV accompanied by a small amount of *trans*-VI.

(1) Studies in Stereochemistry. XXXI. Part XXX, *Tetrahedron Letters*, **3**, 131 (1963).

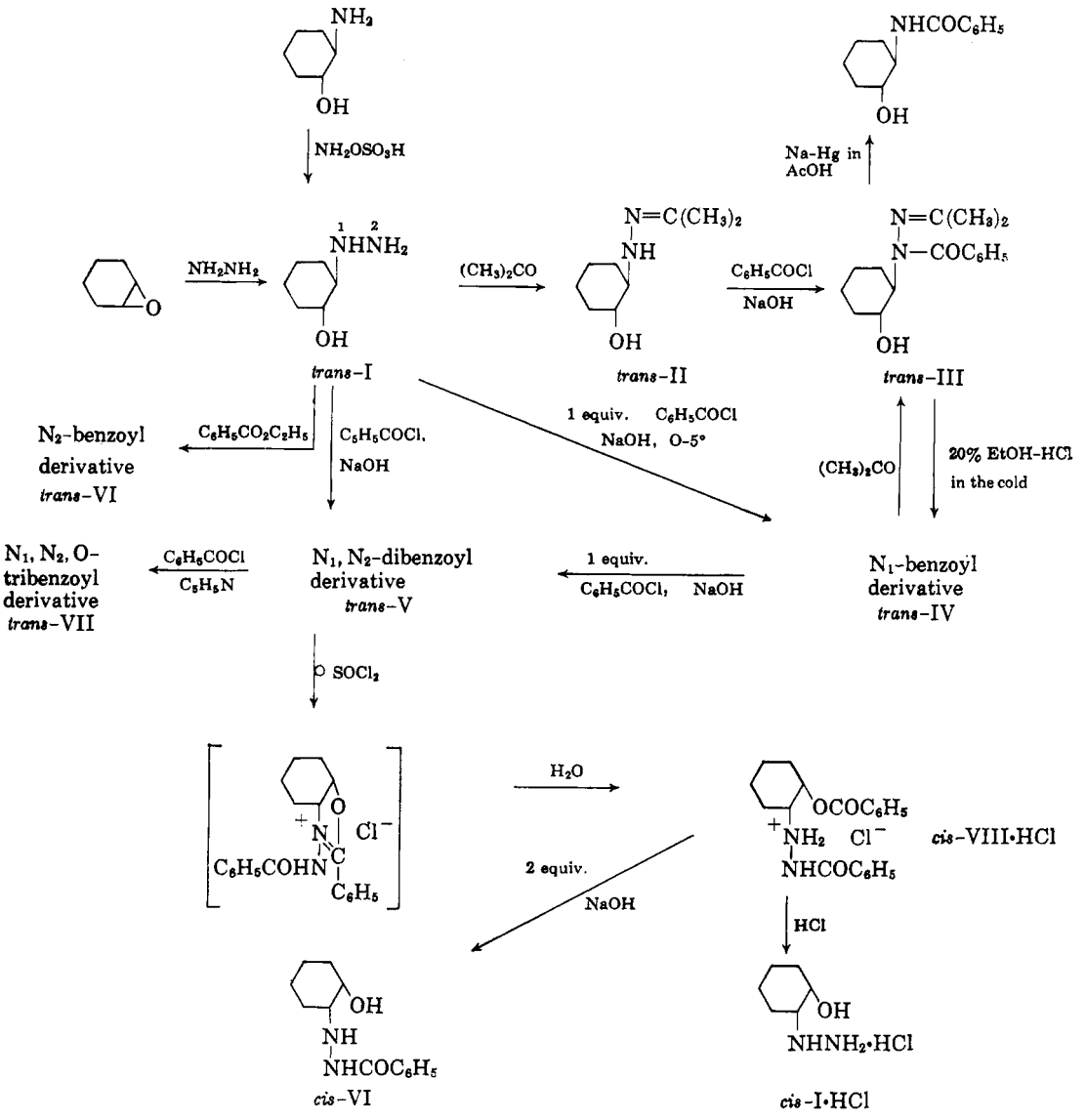
(2) (a) A. K. Plisov, *Ukr. Khim. Zh.*, **3**, 125 (1928); *Chem. Abstr.*, **22**, 3392 (1928); (b) S. Gabriel, *Ber.*, **47**, 3028 (1914); (c) G. Benoit, *Bull. soc. chim. France*, 242 (1947); (d) R. Gösl and A. Meuwsen, *Ber.*, **92**, 2521 (1959); (e) G. Gever, *et al.*, *Chem. Abstr.*, **48**, 12,168 (1954); (f) N. Rabjohn and M. S. Cohen, *J. Am. Chem. Soc.*, **76**, 1282 (1954); (g) G. Gever and K. Hayes, *J. Org. Chem.*, **14**, 813 (1949); (h) J. C. Howard, G. Gever, A. B. Neill, and P. H. I. Wei, *ibid.*, **26**, 1082 (1961).

(3) G. E. McCasland and co-workers, *J. Am. Chem. Soc.*, **71**, 637 (1949); **72**, 2190 (1950); W. S. Johnson and E. N. Schubert, *ibid.*, **72**, 2187 (1950); S. Winstein and R. Boschan, *ibid.*, **72**, 2311, 4699 (1950); T. Taguchi and M. Nakayama, *ibid.*, **73**, 5679 (1951).

(4) T. Taguchi, J. Ishibashi, T. Matsuo, and M. Kojima, *J. Org. Chem.*, **29**, 1104 (1964). The correlation was achieved by the conversion of *trans*-I to DL-*trans*-2-aminocyclohexanol through the deamination reaction.

(5) Treatment for a prolonged time or hot caused $N_1 \rightarrow N_2$ benzoyl migration affording *trans*-VI and the use of 10% anhydrous ethanolic hydrogen chloride hot caused ring closure to *trans*-X, as discussed later.

CHART I

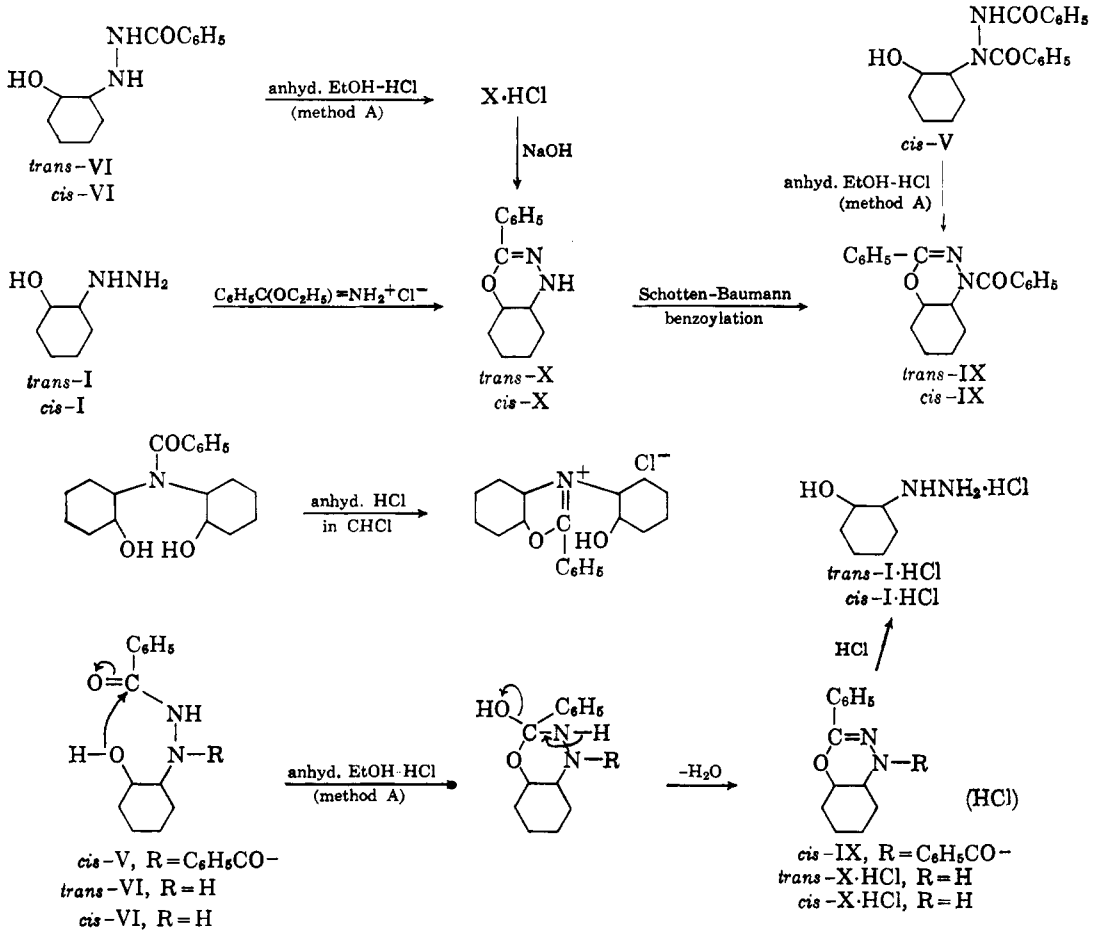


DL-*cis*-2-Hydroxycyclohexylhydrazine (*cis*-I) and its benzoylated derivatives were prepared as follows. The *trans*-N_1,N_2-dibenzoyl compound (*trans*-V) was treated with thionyl chloride to give a crystalline product, $C_{20}H_{22}N_2O_3 \cdot HCl$. Hydrolysis of the product in aqueous hydrochloric acid gave rise to the other DL isomer of 2-hydroxycyclohexylhydrazine hydrochloride which must be the *cis* form (*cis*-I·HCl). The compound, $C_{20}H_{22}N_2O_3 \cdot HCl$, was submitted to hydrolysis with 2 equiv. of sodium hydroxide to yield DL-*cis*-2-benzoyl-1-(2-hydroxycyclohexyl)hydrazine (*cis*-VI), an authentic sample of which was prepared as described later. This shows that one of two benzoyl groups in $C_{20}H_{22}N_2O_3 \cdot HCl$ attaches to N_2 and the existence in the salt form shows that the other combines with O, thus suggesting that the compound is DL-*cis*-2-benzoyl-1-(2-benzoyloxycyclohexyl)hydrazine hydrochloride (*cis*-VIII·HCl). In addition, the infrared spectrum, ν_{max}^{Nujol} 1733, 1280, and 1105 (ester), and 1694 cm.$^{-1}$ (secondary amide), agreed with it. The Walden inversion involved in the course from *trans*-V to *cis*-VIII seems to occur passing through an oxazolinium salt in analogy with the same treatment of DL-*trans*-2-benzamidocyclohexanol[3] (see Chart I). N_1-Benzoyl, N_2-benzoyl, N_1,N_2-dibenzoyl, and N_1,N_2,O-tribenzoyl derivatives of *cis*-I (*cis*-IV, -VI, -V, and -VII, respectively) were obtained and characterized by methods exactly similar to those used for the corresponding *trans* isomers (see Chart I).

Acyl migration in N-benzoyl derivatives of *trans*- and *cis*-I were carried out under two conditions: method A, boiling in twenty parts of 10% anhydrous ethanolic hydrogen chloride for 30 min.; method B, heating in 3 *N* aqueous hydrochloric acid on a water bath for 30 min.

Materials treated by method A and the resulting products are shown in Table I. As indicated in Table I and Chart II, of the N-benzoyl derivatives (IV, V, and VI) treated, only the *trans*-N_1,N_2-dibenzoyl compound (*trans*-V) underwent acyl migration, while the others suffered dehydrative ring closure. The migration product from *trans*-V was formulated as DL-*trans*-2-benzoyl-1-(2-benzoyloxycyclohexyl)hydrazine hydrochloride (*trans*-VIII·HCl) on the grounds that it exists in the salt form and was converted to the *trans*-N_2-benzoyl compound (*trans*-VI) on treatment with 2 equiv. of sodium hydroxide. The infrared spectrum also supported the identification. From *trans*- and

CHART II



cis-VI, respectively, was obtained DL-4a,5,6,7,8,8a-hexahydro-3-phenyl-1H-4,1,2-benzoxadiazine (X) of the same configuration, together with some starting material. The infrared spectra supported the structure of X (presence of C=N, -NH-, and C-O-C). The retention of configuration in the reaction was clear from the finding that hydrolysis of X gave I·HCl keeping the configuration. *cis*-V treated by method A also gave a dehydration product, $C_{20}H_{20}N_2O_2$, which was identified as DL-*cis*-1-benzoyl-4a,5,6,7,8,8a-hexahydro-3-phenyl-1H-4,1,2-benzoxadiazine (*cis*-IX), because the product was identical with the one formed by the introduction of a benzoyl group into *cis*-X by the Schotten-Baumann method; the infrared spectrum supported the structure (presence of C=N, -CON<, and C-O-C). *trans*-IX was also prepared by the Schotten-Baumann benzoylation of *trans*-X (see Chart II).

Condensation of ethyl benzimidate hydrochloride with *trans*- and *cis*-I gave compounds $C_{13}H_{16}N_2O$, which were identical with *trans*- and *cis*-X, respectively, thus indicating that the condensation occurred between the hydroxyl and the N_2-benzoyl groups with retention (see Chart II).

Previously, Taguchi and Hayashida[6] had reported that DL-(*trans*-*cis*-2,2′-dihydroxydicyclohexyl)benzamide with anhydrous hydrogen chloride caused ring closure giving DL-3-(*trans*-2-hydroxycyclohexyl)-2-phenyl-*cis*-4,5-cyclohexanooxazolinium chloride with retention. By analogy with this report, the formation of the 4a,5,6,7,8,8a-hexahydro-3-phenyl-1H-4,1,2-benzoxadiazines, *cis*-IX, *trans*-X, and *cis*-X, respectively from *cis*-V, *trans*-VI, and *cis*-VI, by method A seems to proceed through attack of the hydroxyl group to the carbon of the N_2-carbonyl followed by dehydration (see Chart II). However, it appeared strange that the N_1-benzoyl com-

TABLE I

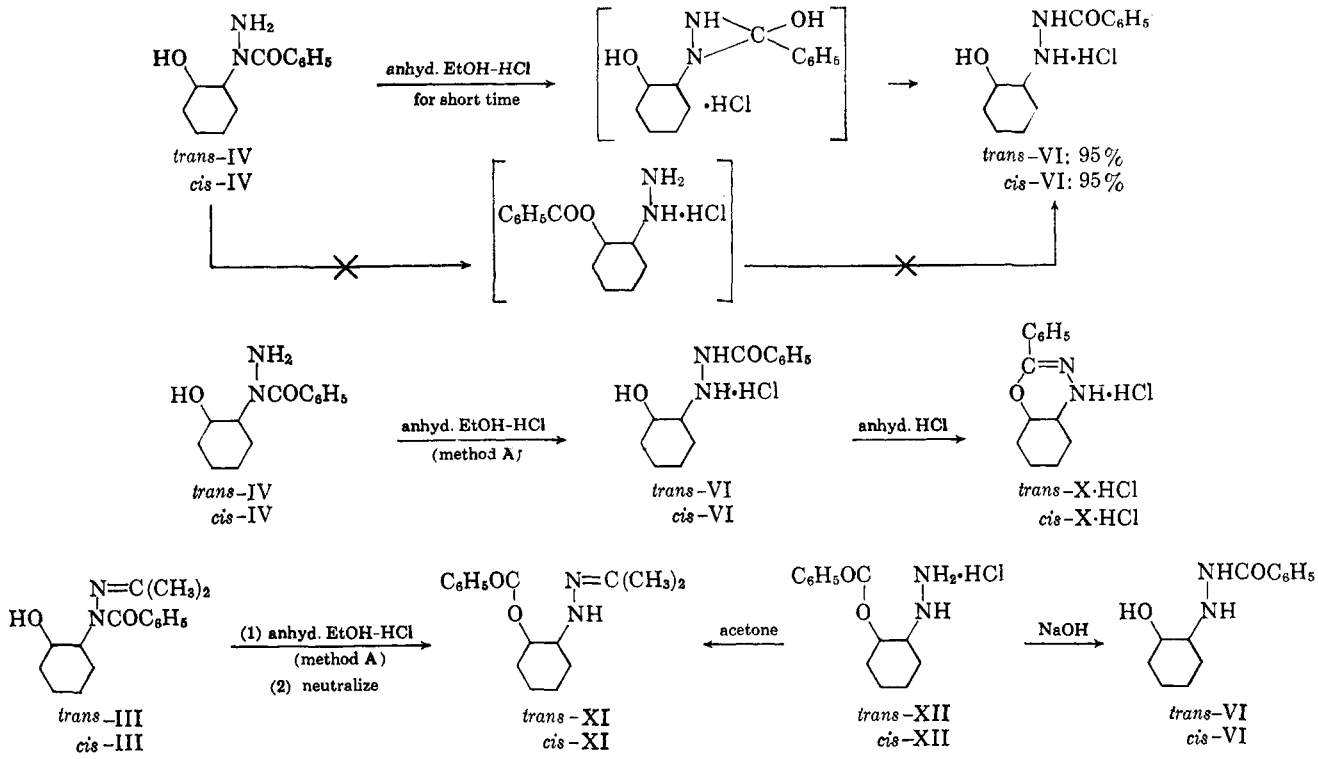
TREATMENT OF N-BENZOYLATED DL-2-HYDROXYCYCLOHEXYLHYDRAZINES WITH HYDROGEN CHLORIDE

Compound treated	Solvent (method)[a]	Product (yield, %)
trans-V	Anhyd. EtOH (A)	*trans*-VIII·HCl (71)
cis-V	Anhyd. EtOH (A)	*cis*-IX·HCl (87)
trans-VI	Anhyd. EtOH (A)	*trans*-X·HCl (54)[b]
	Water (B)	*trans*-XII·HCl (43)[b]
cis-VI	Anhyd. EtOH (A)	*cis*-X·HCl (56)[b]
	Water (B)	*cis*-XII·HCl (42)[b]
trans-IV	Anhyd. EtOH (A)	*trans*-X·HCl + *trans*-VI·HCl (48:52)[c]
	Water (B)	*trans*-XII·HCl + *trans*-VI·HCl (42:58)[c]
cis-IV	Anhyd. EtOH (A)	*cis*-X·HCl + *cis*-VI·HCl (63:37)[c]
	Water (B)	*cis*-XII·HCl + *cis*-VI·HCl (42:58)[c]
trans-III	Anhyd. EtOH (A)	*trans*-XI (52)
	Water (B)	*trans*-XII·HCl + *trans*-VI·HCl (73:27)[c]
cis-III	Anhyd. EtOH (A)	*cis*-XI (50)
	Water (B)	*cis*-XII·HCl + *cis*-VI·HCl (86:14)[c]

[a] See the text. [b] The formation ratio of product to the starting material recovered. [c] The formation ratio of products.

(6) T. Taguchi and K. Hayashida, *J. Am. Chem. Soc.*, **80**, 2522 (1958).

CHART III



pounds, *trans*-IV and *cis*-IV, treated by method A gave *trans*-X and *cis*-X, respectively, the products identical with those from the N_2-benzoyl compounds (*trans*-VI and *cis*-VI) by the same treatment. In addition, the reactions also caused the formation of VI·HCl with retention.

To throw light upon the case, the action of anhydrous hydrogen chloride was carefully examined. As soon as *trans*- and *cis*-IV were dissolved in 10% anhydrous ethanolic hydrogen chloride, ethanol was removed by vacuum distillation. The treatments afforded DL-*trans*- and DL-*cis*-2-benzoyl-1-(2-hydroxycyclohexyl)-hydrazines (*trans*- and *cis*-VI), respectively, which might be formed *via* $N_1 \rightarrow N_2$ acyl migration, in yields up to 95%. The other migration route, $N_1 \rightarrow O \rightarrow N_2$, is entirely excluded, because the acyl migration from O to N is improbable in an acidic medium, though $N \rightarrow O$ migration seems probable. This supports the direct migration of the benzoyl group from N_1 to N_2, a new mode of migration as shown in Chart III. Moreover, this also suggests that the first step of the reaction of IV, when treated by method A, is the formation of VI, which was then partially converted to X (see Chart III).

The compounds in which the 2-amino group of IV was blocked with acetone, *trans*- and *cis*-III, were also treated by method A, followed by neutralization. The reactions caused acyl migration to afford DL-*trans*- and DL-*cis*-2-isopropylidene-1-(2-benzoyloxycyclohexyl)hydrazines (*trans*- and *cis*-XI), respectively (see Chart III). Structural proof was provided for *cis*-XI by its identity with the condensation product of DL-*cis*-2-benzoyloxycyclohexylhydrazine (*cis*-XII) with acetone described below. This supported also the structure of *trans*-XI by analogy. Moreover the specific absorption bands in the infrared spectra, ν_{max}^{Nujo} 1698, 1271, and 1114 (*trans*-XI, ester), and 1718, 1285, and 1117 cm.$^{-1}$ (*cis*-XI, ester), confirmed the structure of XI. Hence the behavior of IV on treatment by method A reveals that $N_1 \rightarrow O$ acyl migration can occur only when the 2-amino group is blocked with the isopropylidene radical; otherwise, $N_1 \rightarrow N_2$ acyl migration preferentially occurs and favors formation of X.

In comparison with method A, method B (the treatment in aqueous hydrochloric acid) was applied to the N-benzoyl derivatives of I which are listed with products in Table I. Consequently, both forms of the N_2-benzoyl derivative (VI) underwent $N_2 \rightarrow O$ acyl migration with retention to give DL-2-benzoyloxycyclohexylhydrazine hydrochlorides (XII·HCl). Of the resulting O-benzoyl compounds (XII·HCl), the *cis* isomer was a liquid substance; therefore, it was condensed with acetone to a crystalline substance, which was identical with the *cis*-N_2-isopropylidene-O-benzoate (*cis*-XI). Treatment of *trans*- and *cis*-XII·HCl in alkaline media caused the reverse acyl migration, $O \rightarrow N_2$ not $O \rightarrow N_1$, to reproduce *trans*- and *cis*-VI with retention (see Chart III).

These findings and the infrared data supported the structures of the products (XII).

On treatment by method B, each form of the N_1-benzoyl derivative (IV) gave XII·HCl with retention in addition to the N_2-benzoyl derivative (VI) of the same configuration, a product resulting from $N_1 \rightarrow N_2$ acyl migration. As described above, this mode of migration was found also in the short treatment of IV with 10% anhydrous ethanolic hydrogen chloride (see Chart III). The N_1-benzoyl-N_2-isopropylidene derivative (III) showed the same behavior as IV toward method B treatment in the formation of products.

Experimental[7]

DL-*trans*-**2-Hydroxycyclohexylhydrazine** (*trans*-**I**). **A.**—To a solution of 7.0 g. of DL-*trans*-2-aminocyclohexanol[3] in 40 ml. of 3% aqueous potassium hydroxide was added an aqueous solution of 1.2 g. of hydroxylamine O-sulfonic acid in drops for 15 min. at 95–96°. After heating for 15 min. more and then chilling, 15 ml. of glacial acetic acid and 1.7 g. of benzaldehyde were added to the solution and stirred vigorously for 10 min. at 55°. The reaction mixture was extracted with ether and the ether layer was evaporated to dryness. To the residue was added 10 ml. of water containing 1.7 g. of oxalic acid, and it was steam distilled to remove benzaldehyde completely. The remainder was evaporated to dryness, washed with a small amount of ethanol, and recrystallized from ethanol to give colorless scales, m.p. 165° dec., yield 0.7 g. (5.2%).

Anal. Calcd. for $C_6H_{14}N_2O \cdot C_2H_2O_4$ (*trans*-I hydrogen oxalate): C, 43.63; H, 7.32; N, 12.72. Found: C, 43.59; H, 7.25; N, 12.47.

B.—To a mixture of cyclohexene oxide (78 g.) and 80% hydrazine hydrate (250 g.) was added ethanol (170 ml.) and the mixture was refluxed for 2.5 hr. After removal of ethanol and surplus hydrazine by evaporation, the residue was distilled under reduced pressure, b.p. 137° (8.5 mm.), and the distillate crystallized in the receiver and had m.p. 80°, yield 85 g. (83%). The crystals were hygroscopic and became colored on standing in air.

Hydrochloride.—On treatment with hydrochloric acid, *trans*-I gave a dihydrochloride, m.p. 160°.

Anal. Calcd. for $C_6H_{14}N_2O \cdot 2HCl$: C, 35.47; H, 7.94; N, 13.78. Found: C, 35.61; H, 7.95; N, 14.26.

The dihydrochloride changed to the monohydrochloride on recrystallization from ethanol and yielded colorless needles of m.p. 126°.

Anal. Calcd. for $C_6H_{14}N_2O \cdot HCl$: C, 43.24; H, 9.07; N, 16.81. Found: C, 43.22; H, 9.01; N, 16.68.

Hydrogen oxalate had m.p. 165° dec. A mixture melting point with an authentic sample prepared by A showed no depression.

DL-*trans*-**1-Benzoyl-2-isopropylidene-1-(2-hydroxycyclohexyl)hydrazine** (*trans*-**III**). **A.**—Twenty grams of *trans*-I was dissolved in acetone by heating on a water bath. It was freed of acetone and distilled *in vacuo* to give hygroscopic crystals of DL-*trans*-2-isopropylidene-1-(2-hydroxycyclohexyl)hydrazine (*trans*-II), b.p. 117–118° (2 mm.), m.p. 35–37°, yield 22 g. (85%), λ_{max}^{EtOH} 227 mμ (ε 8092) (C=N), ν_{max}^{Nujol} 1634 cm.$^{-1}$ (C=N). To a mixture of an ethereal solution of *trans*-II (22 g.) and 5% aqueous sodium hydroxide was added an ethereal solution of benzoyl chloride (18 g.) with ice cooling to cause precipitation. After filtration, recrystallization from methanol gave colorless plates, m.p. 132–134°, yield 19 g. (54%).

Anal. Calcd. for $C_{16}H_{22}N_2O_2$: C, 70.03; H, 8.08; N, 10.21. Found: C, 70.09; H, 8.06; N, 10.05.

B.—A solution of 0.3 g. of *trans*-IV (described below) in acetone was refluxed for 1.5 hr. and evaporated to dryness to leave colorless plates, yield 0.34 g. (97%), m.p. 133–134° after recrystallization from methanol, which were identical with a sample of *trans*-III prepared by A on a mixture melting point determination.

Treatment of DL-*trans*-**1-Benzoyl-2-isopropylidene-1-(2-hydroxycyclohexyl)hydrazine** (*trans*-**III**) **with Sodium Amalgam. The Formation of** DL-*trans*-**2-Benzamidocyclohexanol.**—To a solution of *trans*-III (1 g.) in ethanol (10 ml.) and glacial acetic acid (6 g.) was added, little by little, 2% sodium amalgam (22 g.) with stirring at 30–35°. The resulting reaction mixture was stirred for 30 min. more, and the precipitated mercury was removed and concentrated, furnishing a solid. Repeated recrystallization from ethanol gave colorless needles, m.p. 165–167°, yield 0.11 g. (12.4%), which were identical with DL-*trans*-2-benzamidocyclohexanol[3] by a mixture melting point determination.

DL-*trans*-**1-Benzoyl-1-(2-hydroxycyclohexyl)hydrazine** (*trans*-**IV**).—Immediately after *trans*-III (13 g.) was dissolved in 20% ethanolic hydrochloric acid at 0–5°, ether was added to the solution to cause precipitation of crystals, yielding 11.5 g. (90%) of colorless needles of m.p. 170.5° dec. after recrystallization from ethanol.

Anal. Calcd. for $C_{13}H_{18}N_2O_2 \cdot HCl$ (*trans*-IV·HCl): C, 57.67; H, 6.70. Found: C, 57.62; H, 7.18.

trans-IV·HCl was neutralized with sodium hydroxide in ethanol, the precipitated sodium chloride was filtered off, and the solution was evaporated to dryness to give colorless needles, m.p. 132–133° after recrystallization from benzene.

Anal. Calcd. for $C_{13}H_{18}N_2O_2$: C, 66.63; H, 7.74; N, 11.95. Found: C, 66.85; H, 7.81; N, 11.90.

DL-*trans*-**1,2-Dibenzoyl-1-(2-hydroxycyclohexyl)hydrazine** (*trans*-**V**). **A.**—To a benzene solution containing 0.2 g. of *trans*-IV and 0.13 g. of benzoyl chloride (1 equiv.) was added 5% aqueous sodium hydroxide while stirring until crystals ceased to deposit. Filtration, followed by recrystallization from ethanol, gave colorless needles of m.p. 218–218.5°, yield 0.27 g. (94%).

Anal. Calcd. for $C_{20}H_{22}N_2O_3$: C, 70.98; H, 6.55; N, 8.28. Found: C, 70.84; H, 6.77; N, 8.24.

B.—An aqueous solution of *trans*-I (50 g.) was mixed with an ethereal solution of 2 equiv. of benzoyl chloride (108 g.), and to the mixture was slowly added 5% aqueous sodium hydroxide with stirring and ice chilling until the precipitation of crystals ceased. After filtration, recrystallization from ethanol gave colorless needles, m.p. 218° alone and on admixture with authentic *trans*-V, yield 125 g. (96%).

The use of 1 equiv. of benzoyl chloride in the benzoylation reaction gave *trans*-V when the reaction was carried out at room temperature, yielding 24%.

DL-*trans*-**2-Benzoyl-1-(2-hydroxycyclohexyl)hydrazine** (*trans*-**VI**). **A.**—One gram of *trans*-I was combined with 3 g. of ethyl benzoate and heated at 130–150° for 5 hr. After cooling, the resulting precipitate was filtered and recrystallized from ethanol, yielding 0.27 g. (15%) of colorless needles, m.p. 155–156°. A mixture melting point with authentic *trans*-IV showed no depression.

Anal. Calcd. for $C_{13}H_{18}N_2O_2$: C, 66.63; H, 7.74; N, 11.95. Found: C, 66.43; H, 7.88; N, 12.16.

Hydrochloride.—Colorless needles had m.p. 189° dec., ν_{max}^{Nujol} 1695 and 1563 cm.$^{-1}$ (amide).

Anal. Calcd. for $C_{13}H_{18}N_2O_2 \cdot HCl$: C, 57.66; H, 6.67; N, 10.35. Found: C, 58.13; H, 7.19; N, 10.78.

B.—To a mixture of an aqueous solution (10 ml.) of *trans*-I (0.5 g.) and an ethereal solution (5 ml.) containing 1 equiv. of benzoyl chloride (0.54 g.) was added in drops 5% aqueous sodium hydroxide with stirring and cooling at 0–5° to deposit crystals. Filtration followed by recrystallization from ethanol gave colorless needles of m.p. and m.m.p. (with authentic *trans*-VI) 155°, yield 0.53 g. (59%). From the mother liquor a small amount of *trans*-IV was obtained.

C.—A solution of DL-*trans*-2-benzoyl-1-(2-benzoyloxycyclohexyl)hydrazine (*trans*-VIII, described below, 0.5 g.) in 15 ml. of aqueous ethanol containing 1 equiv. of sodium hydroxide (0.06 g.) was refluxed on a water bath for 30 min. and ethanol was evaporated. To the cooled residue was added 10% aqueous sodium hydroxide; it was extracted with ether and evaporated to dryness, yielding 0.3 g. (87%), m.p. 156° after recrystallization from ethanol and also on admixture with authentic *trans*-VI.

DL-*trans*-**1,2-Dibenzoyl-1-(2-benzoyloxycyclohexyl)hydrazine** (*trans*-**VII**).—A mixture of *trans*-V (1 g.), benzoyl chloride (0.42 g.), and pyridine (20 ml.) was heated at reflux for 5 hr. The reaction mixture was evaporated to dryness leaving crystals, and the crystals were recrystallized from ethanol as colorless plates of m.p. 181°, yield 0.64 g. (49%); ν_{max}^{Nujol} 1692, 1292, and 1120 (ester), 1684 and 1664 cm.$^{-1}$ (amide).

Anal. Calcd. for $C_{27}H_{26}N_2O_4$: C, 73.28; H, 5.93; N, 6.33. Found: C, 72.94; H, 6.31; N, 6.30.

The Action of Thionyl Chloride on *trans*-**V. The Formation of** DL-*cis*-**2-Benzoyl-1-(2-benzoyloxycyclohexyl)hydrazine** (*cis*-**VIII**).—To 1 g. of *trans*-V was added 1 ml. of thionyl chloride and set aside for 6–7 hr. at room temperature (25°). The reaction mixture was poured on ice to precipitate a gummy mass which crystallized slowly. Filtration followed by recrystallization from ethanol gave colorless needles of m.p. 168.5°, yield 1 g. (91%); ν_{max}^{Nujol} 1733, 1280, and 1105 (ester), and 1694 cm.$^{-1}$ (–CON<).

Anal. Calcd. for $C_{20}H_{22}N_2O_3 \cdot HCl$ (*cis*-VIII·HCl): C, 64.07; H, 6.18; N, 7.47. Found: C, 64.33; H, 6.29; N, 7.25.

The filtrate was made alkaline to afford an additional crop of *cis*-VIII (free base), yielding 0.05 g. Recrystallization from acetone–water gave colorless needles of m.p. 117–118°; ν_{max}^{Nujol} 1691, 1297, and 1114 (ester), 1668, and 1555 cm.$^{-1}$ (—CON<).

Anal. Calcd. for $C_{20}H_{22}N_2O_3$ (*cis*-VIII): C, 70.98; H, 6.55; N, 8.28. Found: C, 71.17; H, 6.60; N, 8.11.

(7) Melting and boiling points are uncorrected.

DL-*cis*-**2-Hydroxycyclohexylhydrazine** (*cis*-**I**).—A suspension of *cis*-VIII (70 g.) in 20% aqueous hydrochloric acid (1 l.) was vigorously refluxed to get a clear solution and then for an additional hour. The reaction time needed over-all was 7–8 hr. After cooling, the precipitated benzoic acid was filtered off, and the filtrate was evaporated to dryness. The residue was recrystallized from ethanol furnishing colorless needles of m.p 110–111°, yield 26 g. (84%).

Anal. Calcd. for $C_6H_{14}N_2O \cdot HCl$ (*cis*-I·HCl): C, 43.24; H, 9.07; N, 16.81. Found: C, 43.28; H, 9.03; N, 16.97.

cis-I, which was obtained by neutralization of *cis*-I·HCl with sodium hydroxide, boiled at 119° (4 mm.) and crystallized to colorless needles, m.p. 78°, which were hygroscopic and turned pale yellow on standing in air.

Alkaline Hydrolysis of *cis*-VIII·HCl with Two Equivalents of Sodium Hydroxide. The Formation of DL-*cis*-**2-Benzoyl-1-(2-hydroxycyclohexyl)hydrazine** (*cis*-**VI**).—To an ethanolic solution of *cis*-VIII·HCl (0.5 g.) was added an ethanolic solution containing 2 equiv. of sodium hydroxide (0.11 g.). The solution was refluxed on a water bath for 30 min.

To the reaction mixture freed of ethanol was added a small amount of 10% aqueous sodium hydroxide solution; the solution was extracted with ether and evaporated to dryness. The residue was recrystallized from ethanol as colorless needles, yielding 0.28 g. (89%), m.p. 162° alone and on admixture with authentic *cis*-VI (described below).

Benzoyl Derivatives of *cis*-I.—The following *cis* compounds were prepared analogously by the method applied to the corresponding *trans* isomer. (Headings A, B, and C correspond to those of methods in *trans* series.)

DL-*cis*-**1-Benzoyl-2-isopropylidene-1-(2-hydroxycyclohexyl)-hydrazine** (*cis*-**III**). **A.**—Colorless plates had m.p. 160–161° from methanol, and a 94% yield from the intermediate, DL-*cis*-2-isopropylidene-1-(2-hydroxycyclohexyl)hydrazine (*cis*-II).

Anal. Calcd. for $C_{16}H_{22}N_2O_2$: C, 70.03; H, 8.08; N, 10.21. Found: C, 69.88; H, 8.10; N, 10.12.

The intermediate (*cis*-II) had b.p. 110° (3 mm.), and deposited hygroscopic colorless needles m.p. 46–48°, in 87% yield; λ_{max}^{EtOH} 227 mμ (ε 9290), ν_{max}^{Nujol} 1629 cm.$^{-1}$ (C=N).

B.—The yield was 93%, m.p. 160–161° alone and on admixture with a sample prepared by A.

DL-*cis*-**1-Benzoyl-1-(2-hydroxycyclohexyl)hydrazine** (*cis*-**IV**), colorless needles, m.p. 134–135° from benzene, had a yield of 46%.

Anal. Calcd. for $C_{13}H_{15}N_2O_2$: C, 66.63; H, 7.74; N, 11.95. Found: C, 67.00; H, 7.78; N, 11.72.

The hydrochloride (*cis*-IV·HCl) did not crystallize.

DL-*cis*-**1,2-Dibenzoyl-1-(2-hydroxycyclohexyl)hydrazine** (*cis*-**V**), colorless needles, m.p. 201° from ethanol, had yields of (A) 90% and (B) 98%.

Anal. Calcd. for $C_{20}H_{22}N_2O_3$: C, 70.98; H, 6.55; N, 8.28. Found: C, 71.16; H, 6.61; N, 7.91.

DL-*cis*-**2-Benzoyl-1-(2-hydroxycyclohexyl)hydrazine** (*cis*-**VI**), colorless needles, m.p. 161.5–162.5° from ethanol, had yields of (A) 25%, (B) 67%, and (C) 89%.

Anal. Calcd. for $C_{13}H_{18}N_2O_2$: C, 66.63; H, 7.74; N, 11.95. Found: C, 66.74; H, 7.80; N, 11.89.

Hydrochloride, colorless needles, had m.p. 193° dec. from ethanol; ν_{max}^{Nujol} 1667 and 1546 cm.$^{-1}$ (amide).

Anal. Calcd. for $C_{13}H_{18}N_2O_2 \cdot HCl$: C, 57.66; H, 6.67; N, 10.35. Found: C, 57.70; H, 7.23; N, 10.30.

DL-*cis*-**1,2-Dibenzoyl-1-(2-benzoyloxycyclohexyl)hydrazine** (*cis*-**VII**), colorless needles, m.p. 212° from ethanol, had a 52% yield; ν_{max}^{Nujol} 1706, 1287, and 1112 (ester), and 1684, 1664, and 1527 cm.$^{-1}$ (amide).

Anal. Calcd. for $C_{27}H_{26}N_2O_4$: C, 73.28; H, 5.93; N, 6.33. Found: C, 73.10; H, 5.98; N, 5.95.

Treatments of N-Benzoyl Derivatives of I with Hydrogen Chloride by Two Methods. Method A.—The derivatives were refluxed in twenty parts of 10% anhydrous ethanolic hydrogen chloride on a water bath for 30 min. and concentrated.

(1). **The Formation of** DL-*trans*-**2-Benzoyl-1-(2-benzoyloxycyclohexyl)hydrazine Hydrochloride** (*trans*-**VIII·HCl**) **from** *trans*-**V.**—After treatment of *trans*-V·HCl (0.5 g.) by method, A, recrystallization from ethanol gave colorless needles, m.p. 169° dec., yield 0.42 g. (71%); ν_{max}^{Nujol} 1724, 1282, and 1109 (ester), 1672 and 1529 cm.$^{-1}$ (amide).

Anal. Calcd. for $C_{20}H_{22}N_2O_3 \cdot HCl$: C, 64.07; H, 6.18; N, 7.47. Found: C, 63.79; H, 6.15; N, 7.38.

The Free Base (*trans*-**VIII**).—Treatment of the hydrochloride with a 10% cold, aqueous solution of sodium hydroxide followed by extraction with ether and by evaporation furnished colorless needles, m.p. 151–152° after recrystallization from ethanol; ν_{max}^{Nujol} 1724, 1277, and 1110 (ester), 1642 and 1520 cm.$^{-1}$ (amide).

Anal. Calcd. for $C_{20}H_{22}N_2O_3$: C, 70.98; H, 6.55; N, 8.28. Found: C, 70.92; H, 6.72; N, 8.46.

(2). **The Formation of** DL-*cis*-**1-Benzoyl-4a,5,6,7,8,8a-hexahydro-3-phenyl-1H-4,1,2-benzoxadiazine** (*cis*-**IX**) **from** *cis*-**V.**—Method A followed by neutralization and recrystallization from ethanol converted 0.5 g. of *cis*-V to colorless needles, m.p. 163–164°, yield 0.41 g. (87%); ν_{max}^{Nujol} 1629 (C=N), 1624 (amide), and 1096 cm.$^{-1}$ (C–O–C).

Anal. Calcd. for $C_{20}H_{20}N_2O_2$: C, 74.97; H, 6.29; N, 8.75. Found: C, 74.99; H, 6.34; N, 8.42.

The product in 20% aqueous hydrochloric acid was refluxed for 10 hr. and cooled. The precipitated benzoic acid was filtered, and the filtrate was washed with ether and evaporated to dryness furnishing *cis*-I·HCl.

(3). **The Formation of** DL-*trans*-**4a,5,6,7,8,8a-Hexahydro-3-phenyl-1H-4,1,2-benzoxadiazine** (*trans*-**X**) **from** *trans*-**VI.**—Treatment of *trans*-VI (0.5 g.) by method A left a solid mass. The mass was combined with 10% aqueous sodium hydroxide solution and extracted repeatedly with ether. After evaporation of ether, the remainder was divided into two portions by extraction from ether. The soluble portion, 0.25 g. yield, was recrystallized from ethanol, m.p. 128–128.5°; ν_{max}^{Nujol} 1637 (C=N), 3322 (–NH), and 1092 cm.$^{-1}$ (C–O–C).

Anal. Calcd. for $C_{13}H_{16}N_2O$ (*trans*-X): C, 72.18; H, 7.45; N, 12.95. Found: C, 72.28; H, 7.52; N, 12.94.

Hydrochloride (*trans*-**X·HCl**).—Recrystallization from ethanol gave product with m.p. 208–209° dec.; ν_{max}^{Nujol} 2390, 2457, and 2525–2730 cm.$^{-1}$ ($-NH_2^+$).

Anal. Calcd. for $C_{13}H_{16}N_2O \cdot HCl$: C, 61.77; H, 6.78; N, 11.08. Found: C, 61.97; H, 6.70; N, 10.89.

The less soluble portion, yield 0.23 g., was converted to the hyrochloride and identified as *trans*-VI·HCl. The ratio of product to recovered material was 54:46. The acidic hydrolysis of *trans*-X, worked up as for *cis*-IX, furnished *trans*-I·HCl.

(4). **Formation of** DL-*cis*-**4a,5,6,7,8,8a-Hexahydro-3-phenyl-1H-4,1,2-benzoxadiazine** (*cis*-**X**) **from** *cis*-**VI.**—Method A converted 0.5 g. of *cis*-VI to a mixture of crystals, yield 0.24 g., and an oil, yield 0.30 g. The crystals were *cis*-VI·HCl. The oil was mixed with 10% aqueous sodium hydroxide, extracted with ether, and evaporated to dryness, leaving an oil again. The primary and the secondary oily products were identified as *cis*-X·HCl and *cis*-X, respectively, by the finding that the Schotten–Baumann benzoylation converted the secondary oily product to crystals, m.p. 163°, which were identical with *cis*-IX by a mixture melting point determination.

(5). **The Formation of** *trans*-**X and** *trans*-**VI from** *trans*-**IV.**—Treatment of *trans*-IV (0.25 g.) by method A furnished 0.27 g. of crystals. Fractional recrystallization from ethanol gave two compounds. Mixture melting point determinations indicated that one, m.p. 208–209° dec., 0.11 g. yield, was identical with *trans*-X·HCl and the other, m.p. 185–188° dec., 0.13 g. yield, was identical with *trans*-VI·HCl. The ratio of the compounds was 48:52.

(6). **The Formation of** *cis*-**X and** *cis*-**VI from** *cis*-**IV.**—*cis*-IV (0.20 g.) was submitted to treatment by method A furnishing a crystalline product, 0.04 g. yield, and an oily product, 0.17 g. yield. The ratio of products was 37:63. The crystals were recrystallized from ethanol as colorless plates, m.p. 191–192° dec., and identified as *cis*-VI·HCl by a mixture melting point determination. The oily product underwent the Schotten–Baumann benzoylation to form crystals as colorless needles, m.p. 163–164°, which were identical with *cis*-IX by a mixture melting point determination. The oily product was characterized as *cis*-X·HCl.

(7). **Formation of** DL-*trans*-**2-Isopropylidene-1-(2-benzoyloxycyclohexyl)hydrazine** (*trans*-**XI**) **from** *trans*-**III.**—An oily product from *trans*-III (1 g.) by method A was neutralized with 10% aqueous sodium hydroxide, extracted with ether, and the ether solution was evaporated to leave a solid residue, yield 0.52 g. (52%), as colorless needles, m.p. 107–108° after recrystallization from ethanol; ν_{max}^{Nujol} 1698, 1271, and 1114 cm.$^{-1}$ (ester).

Anal. Calcd. for $C_{16}H_{22}N_2O_2$ (*trans*-XI): C, 70.03; H, 8.08; N, 10.21. Found: C, 70.06; H, 8.11; N, 10.35.

(8). **Formation of** DL-*cis*-**2-Isopropylidene-1-(2-benzoyloxycyclohexyl)hydrazine** (*cis*-**XI**) **from** *cis*-**III.**—An oily product

obtained on treatment of *cis*-III (2 g.) by method A was neutralized with 10% aqueous sodium hydroxide, extracted with ether, and evaporated to dryness. Distillation of the residue, b.p. 174–176° (3.5 mm.), gave an oil which crystallized in the receiver as colorless needles, m.p. 78° after recrystallization from petroleum ether (b.p. 30–70°), yield 1 g. (50%); ν_{max}^{Nujol} 1718, 1285, and 1117 cm.$^{-1}$ (ester).

Anal. Calcd. for $C_{16}H_{22}N_2O_2$ (*cis*-XI): C, 70.03; H, 8.08; N, 10.21. Found: C, 70.18; H, 8.03; N, 10.00.

Method B.—The derivatives were heated in five parts of 3 *N* aqueous hydrochloric acid solution on a water bath for 30 min. and concentrated.

(1). **The Formation of DL-*trans*-2-Benzoyloxycyclohexylhydrazine Hydrochloride (*trans*-XII·HCl) from *trans*-VI.**—Treatment of *trans*-VI(0.5 g.) by method B left crystals. Fractional recrystallization from ethanol gave 0.27 g. of *trans*-VI·HCl unchanged and 0.20 g. of *trans*-XII·HCl as colorless granules, m.p. 173–174° dec.; ν_{max}^{Nujol} 1715, 1294, and 1117 cm.$^{-1}$ (ester). The ratio of *trans*-XII·HCl and *trans*-VI·HCl recovered was 43:57.

Anal. Calcd. for $C_{13}H_{18}N_2O_2$·HCl: C, 57.66; H, 6.67; N, 10.35. Found: C, 58.04; H, 7.11; N, 10.54.

The product was converted to *trans*-VI on treatment with alkali, as described below.

(2). **The Formation of DL-*cis*-2-Benzoyloxycyclohexylhydrazine Hydrochloride (*cis*-XII·HCl) from *cis*-VI.**—Treatment of *cis*-VI (0.5 g.) by method B afforded 0.25 g. of crystals, that were identical with *cis*-VI·HCl unchanged, and 0.18 g. of an oil. The oil was neutralized with 10% aqueous sodium hydroxide, extracted with ether, and evaporated to dryness leaving an oil again with ν_{max}^{Nujol} 1721, 1276, and 1110 cm.$^{-1}$ (ester). The secondary oily product was refluxed in acetone to yield crystals as colorless needles, m.p. 78° after recrystallization from petroleum ether, which were identical with authentic DL-*cis*-2-isopropylidene-1-(2-benzoyloxycyclohexyl)hydrazine (*cis*-XI) on a mixture melting point determination, thus indicating the secondary oily product to be *cis*-XII·HCl. The ratio of *cis*-XII·HCl and *cis*-VI·HCl recovered was 42:58.

(3). **The Formation of *trans*-XII·HCl and *trans*-VI·HCl from *trans*-IV.**—Treatment of *trans*-IV (0.25 g.) by method B left 0.25 g. of crystals. Fractional recrystallization from ether–ethanol effected the separation of the crystals to two compounds. One, m.p. 186–189° dec., 0.13 g. yield, was identical with authentic *trans*-VI·HCl and the other, m.p. 168–173° dec., 0.09 g. yield, was identical with authentic *trans*-XII·HCl. The ratio of *trans*-VI·HCl and *trans*-XII·HCl was 58:42.

(4). **The Formation of *cis*-XII·HCl and *cis*-VI·HCl from *cis*-IV.**—Treatment of *cis*-IV (0.20 g.) by method B left a mixture of crystals and an oil. The crystals, 0.03 g. yield, were recrystallized from ethanol furnishing colorless plates, m.p. 190–191.5° dec. alone and on admixture with authentic *cis*-VI·HCl.

The oily product, 0.15 g. yield, was neutralized with 10% aqueous sodium hydroxide, extracted with ether, and evaporated to dryness affording an oil, which then was refluxed in acetone to turn into a crystalline product, 0.02 g. yield, as colorless needles, m.p. 77.5–78° after recrystallization from petroleum ether. The condensation product with acetone was identical with authentic *cis*-XI by a mixture melting point determination, and accordingly the primary oily product was characterized as *cis*-XII·HCl.

(5). **The Formation of *trans*-XII·HCl and *trans*-VI·HCl from *trans*-III.**—Work-up of *trans*-III (0.5 g.) was exactly the same as 3, giving 0.30 g. of *trans*-XII·HCl and 0.12 g. of *trans*-VI·HCl which were the same as the products under 3. The ratio of *trans*-XII·HCl and *trans*-VI·HCl was 73:27.

(6). **The Formation of *cis*-XII·HCl and *cis*-VI·HCl from *cis*-III.**—Treatment of *cis*-III (0.5 g.) and identification of products were exactly the same as 4, affording 0.45 g. of *cis*-XII·HCl and 0.08 g. of *cis*-VI·HCl (ratio 86:14), which were same as the products under 4.

Short Treatment of DL-1-Benzoyl-1-(2-hydroxycyclohexyl)-hydrazines (IV) with Anhydrous Ethanolic Hydrogen Chloride at Room Temperature. A.—As soon as *trans*-IV (0.25 g.) was completely dissolved in 10% anhydrous ethanolic hydrogen chloride, ethanol was distilled *in vacuo*. The residue which was recrystallized from ethanol gave colorless needles, 0.28 g. yield (95%), m.p. 188–189° dec. alone and on admixture with authentic *trans*-VI·HCl.

B.—*cis*-IV was treated just like A, furnishing colorless plates which were recrystallized from ethanol, 95% yield, m.p. 193° dec. alone and on admixture with *cis*-VI·HCl.

Treatments of DL-2-Benzoyloxycyclohexylhydrazine Hydrochlorides (XII·HCl) with an Aqueous Sodium Hydroxide Solution. The Formation of VI *via* O → N_2 Migration. A.—*trans*-XII·HCl (0.5 g.) was neutralized with 10% aqueous sodium hydroxide, extracted with ether and evaporated to dryness. Recrystallization from ethanol gave colorless needles, 0.28 g. (64%) yield, m.p. 156° alone and on admixture with authentic *trans*-VI.

B.—*cis*-XII·HCl (0.5 g.) was treated exactly as in A, furnishing colorless needles which were recrystallized from ethanol, 0.35 g. (81%) yield, m.p. 162.5° alone and on admixture with *cis*-VI.

DL-*trans*-1-Benzoyl-4a,5,6,7,8,8a-hexahydro-3-phenyl-1H-4,1,2-benzoxadiazine (*trans*-IX).—To an ethereal solution (15 ml.) of *trans*-X (0.5 g.) and benzoyl chloride (0.33 g.) was added 5% aqueous sodium hydroxide until precipitation of crystals was complete. Recrystallization from ethanol afforded colorless needles, m.p. 135.5–136.5°, 0.65 g. (88%) yield, ν_{max}^{Nujol} 1664 (amide) and 1645 cm.$^{-1}$ (C=N).

Anal. Calcd. for $C_{20}H_{20}N_2O_2$: C, 74.97; H, 6.29; N, 8.75. Found: C, 75.01; H, 6.38; N, 8.70.

The Action of Ethyl Benzimidate Hydrochloride on DL-2-Hydroxycyclohexylhydrazines (I). The Formation of DL-4a,-5,6,7,8,8a-Hexahydro-3-phenyl-1H-4,1,2-benzoxadiazines (X). A.—An ethanolic solution (75 ml.) of *trans*-I (2.00 g.) and ethyl benzimidate hydrochloride (2.90 g.) was refluxed for 1 hr. and evaporated to dryness. The residue was mixed with water, extracted with ether, dried over anhydrous sodium sulfate, and evaporated to dryness, furnishing an oil which crystallized while cooling to yield 0.87 g. (26%). Recrystallization from ethanol gave colorless needles, m.p. 128–129° alone and on admixture with authentic *trans*-X.

B.—*cis*-I (1.20 g.) was treated exactly as described under A furnishing an oily product, 1.20 g. (60%) yield, which was identified as *cis*-X by the fact that the Schotten–Baumann benzoylation in pyridine converted it to *cis*-IX, m.p. 163–164°.

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