Chem. Pharm. Bull.
19(6)1178—1185(1971)

UDC 547.233.04 : 546.175.04

Deamination Reaction of Diastereomeric DL-2(1-Phenylcyclohexyl)cyclohexylamine with Nitrous Acid[1,2]

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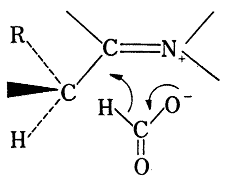
(Received January 16, 1971)

DL-*trans*-and DL-*cis*-2-(1-Phenylcyclohexyl)cyclohexylamine (*trans*- and *cis*-II) were prepared from DL-2-(1-phenylcyclohexyl)cyclohexanone (I) and submitted to deamination reaction with HNO_2 expecting steric government of 1-phenylcyclohexyl group as an extraordinarily bulky substituent. As a result, steric effect was observed more remarkably in the reaction of *trans*-II than of *cis*-II. On the way to completion of the reaction, *cis*-II nitrite was isolated as one of unusual examples. In addition, dehydration reaction of *trans*- and *cis*-alcohol derived from I and the Chugaev reaction of their xanthates were undertaken to prepare reference compounds for the identifications of products from the deamination reaction. All reactions involved in this study were mechanistically discussed.

As the previous papers have reported,[4] the reaction of 2-cyclohexylidenecyclohexanone with phenylmagnesium bromide yielded mainly DL-2-(1-phenylcyclohexyl)cyclohexanone (I). DL-Diastereomers of 2-(1-phenylcyclohexyl)cyclohexylamine (II) which can be derived from I are sterically characteristic in the aspect that so bulky a substituent as 1-phenylcyclohexyl group occupies strictly an e-position and consequently conformations of them might be stabilized. Because of this conformational feature, deamination reaction of II was examined in comparison with those of other 2-alkylated cyclohexylamines. Also investigations on dehydration reaction of DL-diastereomers of 2-(1-phenylcyclohexyl)cyclohexanol (III) and the Chugaev reaction of their xanthates were needed in this study to identify products from the deamination reaction.

The ketone (I) oxime was reduced with Na and EtOH to yield a mixture of *cis*- and *trans*-II, the formation ratio of which was established as 21.5: 78.5.[5] The mixture was separated into each component by derivation to *p*-tosylate salts followed by recrystallization from acetone and then hydrolysis. This result is consistent with the previous proposal[6] that a reduction passing through a carbanion intermediate produces a thermodynamically stable product in major. On the other hand, in the Leuckart reaction of I which was undertaken to obtain the amine (II), the product was indicated to consist of almost pure *cis*-II by the gas chromatographic analysis. The Leuckart reaction has been postulated to proceed through a critical step where an activated complex (quasi-ring type) is formed by the dipolar attraction of the immonium ion working on the formate ion[7-9] (See diagram V).



Va : R = methyl

Vb : R = 1-phenylcyclohexyl

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1) This forms, "Studies in Stereochemistry. XLV. Grignard Reaction and Products. III," by T. Taguchi.
2) Part II of this series: K. Miyano and T. Taguchi, *Chem. Pharm. Bull.* (Tokyo), **18**, 1806 (1970).
3) Location: *Katakasu, Fukuoka*; *a*) Present address: *Basic Research Laboratories, Toyo Rayon Co., Ltd., Tebiro, Kamakura*; *b*) To whom inquiries should be addressed.
4) *a*) K. Miyano and T. Taguchi, *Chem. Pharm. Bull.* (Tokyo), **18**, 1799 (1970); *b*) T. Taguchi, K. Miyano, Y. Shimizu and Y. Kawazoe, *Tetrahedron Letters*, **1968**, 4105.
5) Calculated from gas chromatographic peak areas.
6) D.H.R. Barton and C.H. Robinson, *J. Chem. Soc.*, **1954**, 3045.
7) D.S. Noyce and F.W. Bachelor, *J. Am. Chem. Soc.*, **74**, 4577 (1952).
8) N.J. Leonard and R.R. Sauers, *J. Am. Chem. Soc.*, **76**, 6210 (1957).
9) R.R. Sauers, *J. Am. Chem. Soc.*, **80**, 4721 (1958).

In this mechanism, the stereochemical specificity is explained in the view that hydrogen of the formate ion orientates to C–1 from the relatively unhindered side.7,9) For example, the preferential formation of the *cis*-amine in the Leuckart reaction of 2-methylcyclohexanone (IV) was attributed to the transition state7) shown as Va. In the present case, the reaction behaved more stereospecific than the case of IV to produce exclusively *cis*-II. This may arise from the transition state (Vb) where one side of the ring is much more hindered by the 2-substituent than Va.10) The assignment of *cis*- and *trans*-II were achived by conformational analysis of the deamination reaction described below.

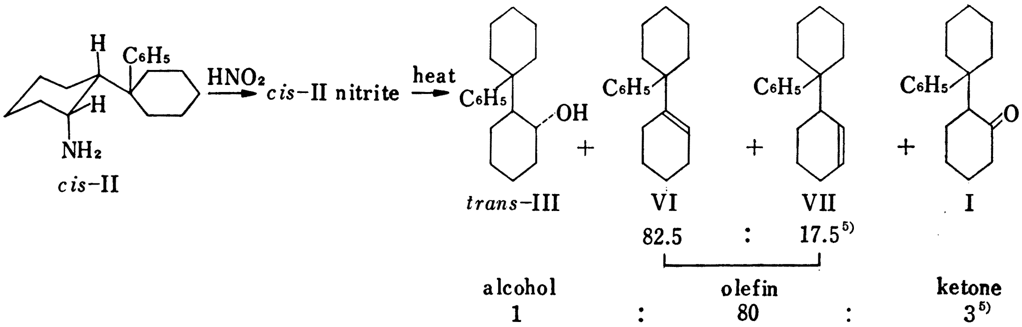

Chart 1

When *cis*-II was treated with $NaNO_2$ in 10% AcOH with ice–chilling, there appeared a precipitate which was thermally unstable and fairly soluble in H_2O. The precipitate was purified by adding ether to its cold ethanolic solution to afford colorless powder which decomposed at 118—119° evolving gas, yield 38%. The product showed a positive Liebermann test and specific bands due to $\nu_{NH_3^+}$ at 3474 and 2500 cm^{-1} in the infrared (IR) spectrum (Nujol). Morever, the product returned to *cis*-II on treatment with aqueous NaOH. These observations suggested *cis*-II nitrite for the structure of the product. This appears as one of unusual examples, because only a few primary amine nitrites have been isolated.11) When the same reaction was carried out at 30—40°, it caused deamination products of which were analyzed by the gas chromatography12) (See Chart 1). The products are classified into three species of compounds, alcoholic, olefinic and ketonic, which existed in a ratio of 1: 80: 3.5) DL-*trans*-2 (1-Phenylcyclohexyl) cyclohexanol (*trans*-III) and DL-2 (1-phenylcyclohexyl) cyclohexanone (I) were found to be sole products respectively as alcoholic and ketonic compound formed. The olefinic product consisted of 1-(1-phenylcyclohexyl)cyclohexene (VI) and DL-3-(1-phenylcyclohexyl)cyclohexene (VII) in a ratio of 82.5: 17.5.5,12)

On working up exactly as in the case of *cis*-II, *trans*-II suffered deamination reaction in the cold to afford three groups of products in a formation ratio of 1.9: 2.7: 1.0.5) The first group (alcoholic) consisted of *trans*-III 92% and *cis*-III 8% and the second group (hydrocarbonaceous) of VI 15%, VII 9%, 1-(1-phenylcyclohexylmethyl)cyclopentene (VIII) 39%, 6-(1-phenylcyclohexyl)bicyclo[3.1.0]hexane (IX) 29% and others 8%.5,12) The third group (ketonic) consisted only of I (See Chart 2).

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10) An alternative mechanism has been presented for the Leuckart reaction by A. Lukasiewicz, *Tetrahedron*, **19**, 1789 (1963).

11) O. Wallach, *Ann.*, **353**, 318 (1907).

12) Preparations of the reference compounds are described later.

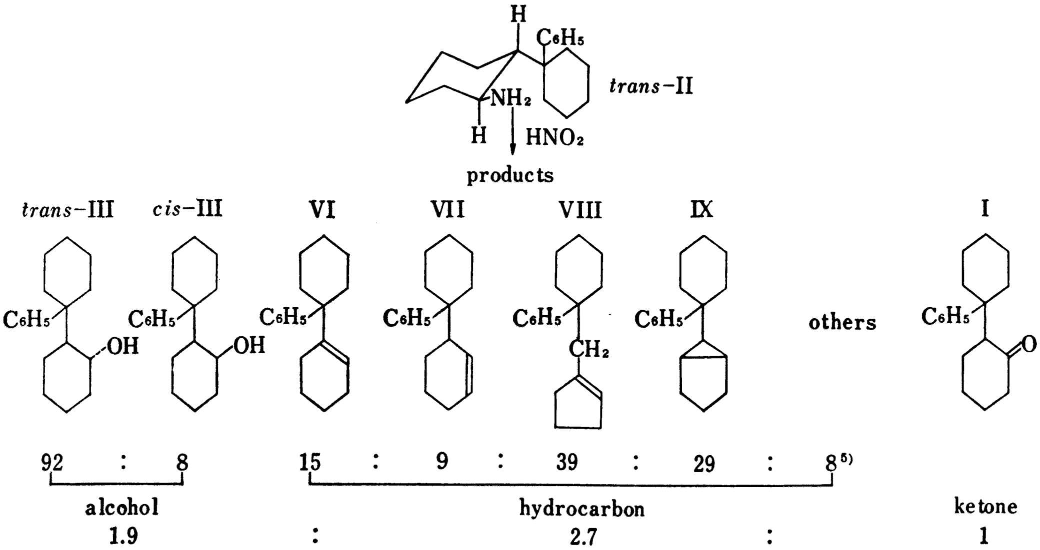

Chart 2

The generalization in stereochemistry of deamination reaction is that e-amines are converted by HNO_2 into alcohols of the same configuration, but a-amines yield mostly olefins with some inverted alcohols.[13] Chart 1 shows that *cis*-II behaved clearly as an a-amine in the light of the generalization, proving the validity of the configuration assigned to itself. The formation of the ketone (I) in a minor quantity, though ambiguous, may be due to air oxidation of *trans*-III catalyzed by nitrogen oxides. The deamination reaction of *trans*-II displayed the product distribution different to some extent from that of the usual e-amine (See Chart 2). At a glance, the formation of olefins is much more than usual and the formation of *trans*-III (S_{Ni}) is less. This may be explained by postulating a flattening in part of the chair form toward the flexible form in the transition state of the reaction. In the transition state of diazotization of *trans*-II, the two bulky substituents, 1-phenylcyclohexyl and diazonium group, tend to bend away from each other so as to release the steric compression transforming to the flexible form (See Chart 3). This bending away is much more facile in the *trans*-1,2- than the *cis*-1,2-disubstituted compound.[14] Thus, *cis*-II acted as usual in the deamination reaction and *trans*-II didn't. In the reaction of *trans*-II, olefins VI and VII appear to be products from the flexible form where the diazonium group has somewhat a-character and *trans*-III, VIII and IX, from the chair form. As the relationship between conformational government and product formation in the deamination reaction has been well-defined in the previous works,[13] additional explanation might be unnecessary to the fomations of these products except IX. IX was isolated from a mixture of hydrocarbonaceous products by removing olefinic VI, VII, and VIII by means of ozonization. The formation of IX can be comprehensible in analogy to the previous finding that cyclohexylamine was deaminated to give bicyclo[3.1.0]hexane.[15]

The structural assignment of IX was based on the following findings. IX agreed with an empirical formula, $C_{18}H_{24}$, which was found to have no olefinic double bond by ozonization,

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13) *a*) J.A. Mills, *J. Chem. Soc.*, **1953**, 260; *b*) A.K. Bose, *Experientia*, **9**, 256 (1953); *c*) D.H.R. Barton and W.J. Rosenfelder, *J. Chem. Soc.*, **1951**, 1048; *d*) W.G. Dauben, R.C. Twit and C. Mannerskantz, *J. Am. Chem. Soc.*, **76**, 4420, (1954); *ibid.*, **77**, 48 (1955) and references there cited; *e*) W. Hückel and G. Ude, *Ber.*, **94**, 1026 (1961).

14) For the reason, see E.L. Eliel, L.A. Pilato and J.C. Richer, *Chem. Ind.* (London), **1961**, 2007.

15) O.E.Edwards and M. Lesage, *Can. J. Chem.*, **41**, 1592 (1963).

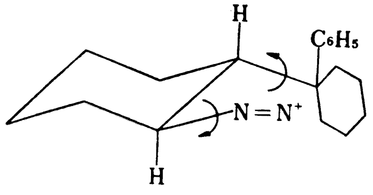
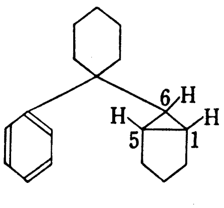
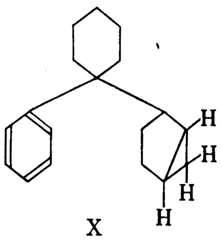


Chart 3



IX



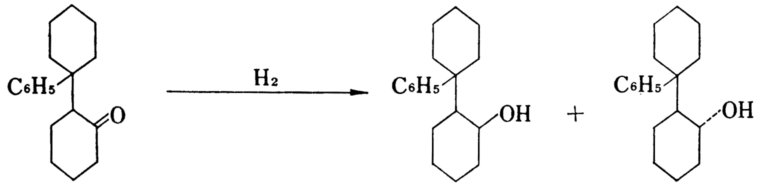
X

IR and nuclear magnetic resonance (NMR) spectra. The NMR spectrum exhibited protons at τ 2.7 (m, 5H), methine protons at τ 9.1 (m, 2H) and 9.5 (t, 1H). The latter two signals are attributable to 3H on the cyclopropane ring and the signal at τ 9.5 indicated the coupling of H on C-6 with magnetically equivalent 2H on C-1 and C-5 because it appeared as a fine triplet of an intensity ratio 1:2:1. These observations support the structural assignment of IX and an altern ative (X) was excluded.

Standing on conformational analysis, the results observed hitherto in the deamination reaction of II support the validity of *cis–trans* assignment given to diastereomers of II.

To obtain reference compounds for the gas chromatographic analyses of products resulted from the deamination reaction of II, dehydration reaction of DL-diastereomers of 2(1-phenylcyclohexyl)cyclohexanol(III) and the Chugaev reaction of their xanthates (*cis*- and *trans*-XI) were carried out. I was reduced to III by the Meerwein–Ponndorf method, $NaBH_4$ and Na in EtOH. A resulting mixture of *cis*- and *trans*-III was separated into each component by derivation to O-benzoates followed by recrystallization and then saponification. Results were shown in Table I.

TABLE I. Reduction of DL-2-(1-Phenylcyclohexyl)cyclohexanone (I) to DL-2-(1-Phenylcyclohexyl)cyclohexanol (III)



I

cis-III

trans-III

		Meerwein–Ponndorf	$NaBH_4$	Na+EtOH
Formation ratio[5]	*cis*-III	92.5	87	15
	trans-III	7.5	13	85

The supposed *cis* isomer of III was dehydrated with 50% H_2SO_4 or $ZnCl_2$ to afford exclusively an olefinic compound (VI). The ozonization of VI gave a ketocarboxylic acid which was identical with 6(1-phenyl)cyclohexyl-6-oxo-hexanoic acid (XII).[4] This tells us VI to be 1(1-phenylcyclohexyl)-cyclohexene.

The xanthate(*trans*-XI) derived from the supposed *trans* isomer of III was submitted to the Chugaev reaction at 220—230° to afford two olefinic compounds in a formation ratio of 76:24.[5] The major olefin was proven to be identical with VI on the gas chromatogram. As VI should be a product from *cis* elimination (the Chugaev reaction), the *trans* assignment to the alcohol used as a starting material was confirmed and accordingly the *cis* assignment was given to the other isomeric alcohol. Additionally, the olefin (VII) formed in minor from *trans*-XI was characterized as DL-3-(1-phenylcyclohexyl)cyclohexene because the Chugaev reaction has been well-known to proceed through *cis* elimination without any rearrangement.[16] *cis*-III(a-OH) did not give a xanthate by the treatment similar to the case of *trans*-III(e-OH). Analogously, *trans*-III(e-OH) reacted with phenylisocyanate to form the urethane derivative, while the *cis* isomer didn't. In view of the rule that an e-hydroxyl group is more easily esterified than an a-hydroxyl group,[17] these phenomena in both esterification reactions confirm further the configurational assignment to *trans*- and *cis*-III.

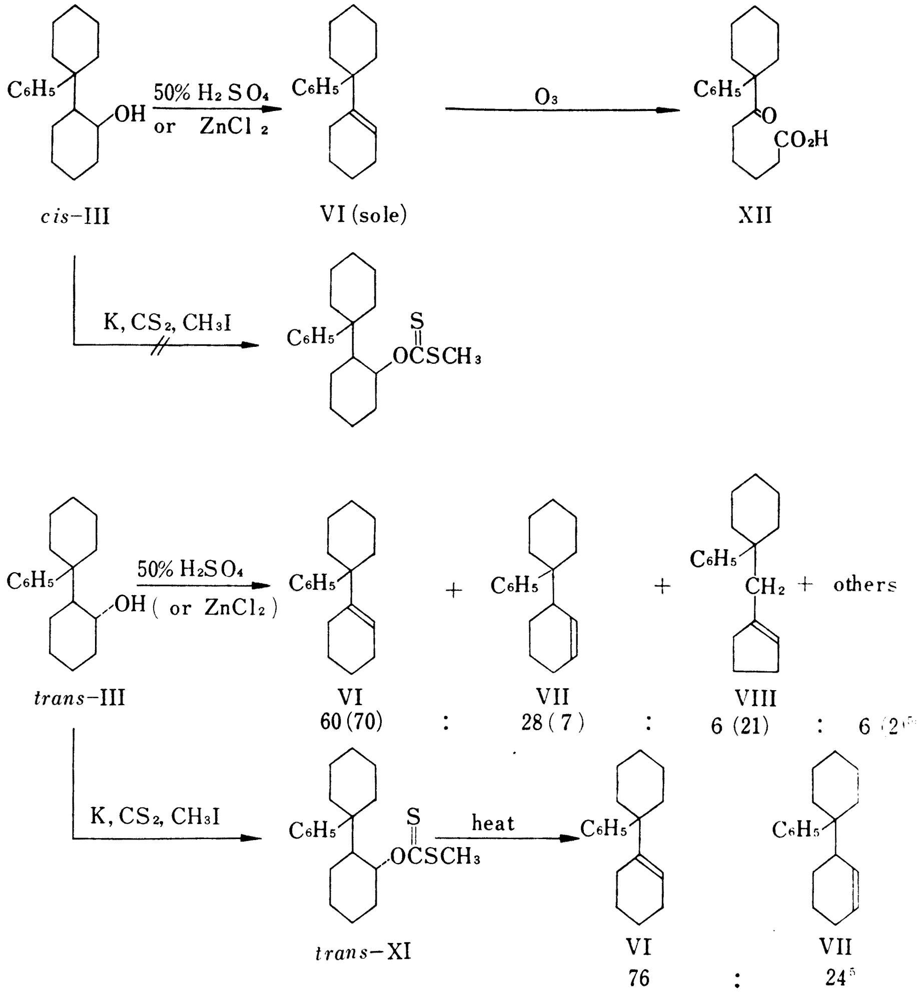


Chart 4

Next, *trans*-III was dehydrated similarly to the case of *cis*-III to afford three kinds of olefins, VI, VII and VIII as be shown in Chart 4. The structure of VIII formed in company with VI and VII of the established structures was deduced possibly to be 1(1-phenylcyclohexylmethyl)cyclopentene from the finding that an analogous olefin was formed in the dehydration reaction of DL-*trans*-2-cyclohexylcyclohexanol.[18]

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[16] D.J. Cram, "Steric Effects in Organic Chemistry," ed. by M.S. Newman, John Wiley and Sons, Inc., New York, N.Y., 1956, p.305.

[17] D.H.R. Barton and R.C. Cookson, *Quart. Rev.* (London), **10**, 60 (1956).

[18] W. Hückel and O. Neunhoeffer, *Ann.*, **477**, 106 (1930).

Experimental[19]

Gas Chromatography——It was carried out using Yanagimoto Gas Chromatograph GCG-2 equipped with an U-shape copper column (100 cm × 4 mm). The column was packed with 30% P.G. 6000 on celite 545 (80—100 mesh) and conditioned during analyses at 250° with H_2 flow at the rate of 65 ml/min, unless otherwise stated.

DL-2-(1-Phenylcyclohexyl)cyclohexanone[4] Oxime (I-Oxime)——To an ethanolic solution (1 l) of hydroxylamine hydrochloride (50 g) and I (50 g) was added KOH (200 g) and the mixture was refluxed for 3 hr. After cooling, the reaction mixture was poured into 9 liters of H_2O and the resulting precipitate was recrystallized as colorless cubes from EtOH, yield 48 g (90.5%), mp 127—128°. *Anal.* Calcd. for $C_{18}H_{25}ON$: C, 79.66; H, 9.26; N, 5.16. Found: C, 79.57; H, 9.28; N, 4.85.

DL-*trans*-2-(1-Phenylcyclohexyl)cyclohexylamine (*trans*-II)——To a solution of 10.6 g of I-oxime in 350 ml of boiling EtOH was added in portions 35.0 g of Na and the mixture was refluxed until Na disappeared almost. The solution was cooled and then H_2O added in excess after excluding completely unreacted Na by addition of a small quantity of aqueous EtOH. The mixture was extracted with ether and the ether layer was washed with H_2O, dried over fused Na_2SO_4 and evaporated to dryness. The residue was distilled *in vacuo* to yield 8.0 g of a colorless oil, bp 151—154° (3 mmHg) which was established by the gas chromatographic analysis to consist of 78.5% *trans*-II and 21.5% *cis*-II.

A solution of 9.4 g of the amine mixture (II) in 30 ml of ether was combined with a solution of 10.0 g of *p*-toluenesulfonic acid in EtOH–ether (10 ml : 50 ml) and refluxed on a water-bath for 10 min. While setting aside at room temperature, colorless crystals appeared and were collected by filtration. The crystals were added to 50 ml of acetone and heated on a water-bath for 10 min. After cooling, insoluble crystals were filtered and recrystallized from EtOH–acetone as colorless needless (*trans*-II *p*-tosylate), weight 10.5 g (67%), mp 181—183°. *Anal.* Calcd. for $C_{25}H_{35}O_3NS$: C, 69.77; H, 8.14; N, 3.26. Found: C, 70.09; H, 8.26; N, 3.30.

The filtrate (acetone solution) was evaporated to dryness and the residue was recrystallized from acetone–ether (or acetone only) as colorless needles, weight 2.5 g (16 %), mp 159—160° alone and on admixture with a sample of *cis*-II *p*-tosylate prepared by the Leuckart reaction of I (See the next).

Trans-II *p*-tosylate (10.5 g) was treated with 10% aqueous NaOH and extracted with ether. The ether layer was washed with H_2O, dried over fused Na_2SO_4 and evaporated to dryness to leave a colorless oil (*trans*-II), weight 5.4 g (86 %), bp 159—161° (4 mmHg). The N-benzoyl derivative was prepared by the Schotten–Baumann method, mp 223—225° (AcOH). IR ν_{max}^{Nujol} cm^{-1}: 3403 (NH), 1632, 1603, 1531 (CONH). *Anal.* Calcd. for $C_{25}H_3ON$: C, 83.05; H, 8.64; N, 3.87. Found: C, 83.02; H, 8.67; N, 3.73.

DL-*cis*-2-(1-Phenylcyclohexyl)cyclohexylamine (*cis*-II)——To a mixture of 10.0 g of I and 10 ml of formamide was added 12 ml of 89% formic acid while heating at 170—185° in an oil-bath for 10 hr. Heating was continued for additional 3 hr. After cooling, the mixture was extracted with ether, washed with H_2O, dried over fused Na_2SO_4 and evaporated to dryness. The residue was recrystallized from EtOH–H_2O as colorless needles (N-formyl derivative of *cis*-II), yield 8.8 g (79%), mp 129—131°. IR ν_{max}^{Nujol} cm^{-1}: 2978 (NH), 1667, 1642, 1522 (CONH). *Anal.* Calcd. for $C_{19}H_{27}ON$: C, 79.95; H, 9.54; N, 4.31. Found: C, 79.76; H, 9.74; N, 4.31.

A solution of 6.5 g of the product in 100 ml of 20% ethanolic KOH was refluxed on a water-bath for 12 hr. The solution was concentrated by distillation, H_2O added and extracted with ether. The ether layer was washed with H_2O, dried over fused Na_2SO_4, evaporated to dryness and distilled *in vacuo* to give a colorless oil of bp 150—151° (3 mmHg), yield 5.1 g (95%). The gas chromatographic analysis showed it to consist of *cis*-II solely. IR $\nu_{max}^{liq.}$ cm^{-1}: 3430, 3344 (NH). The following crystalline derivatives were prepared by usual methods. *p*-Tosylate salt: colorless needles of mp 159—160° (acetone). *Anal.* Calcd. for $C_{25}H_{35}O_3NS$: C, 66.96; H, 8.26; N, 3.14. Found: C, 66.91; H, 8.53; N, 3.13. N-Benzoyl derivative: colorless needles of mp 136—137° (EtOH). *Anal.* Calcd. for $C_{25}H_{31}ON$: C, 83.05; H, 8.64; N, 3.87. Found: C, 82.91; H, 8.67; N, 3.63.

DL-2-(1-Phenylcyclohexyl)cyclohexylamine Nitrite (*cis*-II Nitrite)——To a solution of 1.0 g of *cis*-II in 4.0 ml of 10% AcOH was added all at once a concentrated aqueous solution of $NaNO_2$ (0.4 g) with ice-chilling to cause precipitation of a colorless mass. The precipitate was recrystallized in cold by adding ether to its ethanolic solution to give 0.45 g (38%) of colorless powder, mp (decomp.) 118—119°, which was positive in the Liebermann test and also in a dye-formation test by reaction with a mixture of aniline and β-naphthol in AcOH. IR ν_{max}^{Nujol} cm^{-1}: 3474—, —2500 (broad, $-NH_3^+$). The product decomposed evolving N_2 gas on heating and on the other hand, reproduced *cis*-II on treatment with aqueous NaOH.

Deamination Reaction of *cis*-II with HNO_2——To a solution of 2.5 g of *cis*-II in 10 ml of 10% AcOH was added a conc. aqueous solution of 1 g of $NaNO_2$ at 30—40° while stirring and stirring was continued till N_2 gas ceased to evolve. The reaction mixture was extracted with ether, washed with 5% aqueous HCl, 5% aqueous NaOH and then H_2O and dried over anhydrous Na_2SO_4. The ether layer was evaporated to

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[19] All melting and boiling points were uncorrected.

dryness and the residue was purified by column chromatography over Al_2O_3 using petroleum ether, weight 1.65 g. The gas chromatographic analysis showed the product distribution as noted in Chart 1.

Deamination Reaction of *trans*-II with HNO_2——To 40 ml of 10% AcOH solution containing 10 g of *trans*-II was added a conc. aqueous solution of 4.0 g of $NaNO_2$ with ice-chilling and the mixture was stirred for 30 min. Additionally, stirring was continued at room temperature till N_2 gas ceased to evolve. After extraction with ether, the ether layer was washed with 5% aqueous HCl, 5% aqueous NaOH and H_2O, dried over fused Na_2SO_4 and evaporated to dryness, weight 7.8 g. The gas chromatographic analysis of the residue indicated the product distribution as noted in Chart 2.

6-(1-Phenylcyclohexyl)bicyclo[3.1.0]hexane (IX)——A mixture of products resulted from the deamination reaction of *trans*-II was submitted to fractional distillation and the distillate, 129—140° (3 mmHg), was gathered. The distillate (3.7 g) dissolved in $CHCl_3$ (20 ml) was ozonized with ice-chilling for 2 hr. After removing $CHCl_3$ by distillation, the residue was added to a mixture of AcOH (10 ml) and 30% H_2O_2 (4 ml) and warmed on a boiling water-bath for 9 hr. The reaction mixture was concentrated *in vacuo* and the residue was dissolved in ether. The ether layer was washed with 10% aqueous Na_2CO_3 and then H_2O, dried over anhydrous Na_2SO_4 and evaporated to dryness. No precipitate appeared after addition of a phosphoric acid solution of 2.4-dinitrophenylhydrazine to a trace quantity of the residue dissolved in EtOH. The residue was purified by column chromatography over Al_2O_3 using petroleum ether to give colorless scales, mp 68.5—70° after recrystallization from MeOH, yield 0.57 g. *Anal.* Calcd. for $C_{18}H_{24}$: C, 89.94; H, 10.06. Found. C, 89.76; H, 9.94. NMR τ: 2.7 (m, 5H, aromatic protons), 9.1 (m, 2H, methine protons on C-1 and C-5 of IX), 9.5 (t, 1H, methine proton on C-6 of IX). The intensity ratio of the last peak was calculated as 1:2:1.

Reduction of DL-2-(1-Phenylcyclohexyl)cyclohexanone (I)——a) To a solution of 4.0 g of I in 100 ml of EtOH was added Na as much as it was consumed and the mixture was heated on a water-bath for 2 hr. After cooling, the reaction mixture was neutralized with dil.HCl and extracted with ether. The ether layer was washed with H_2O, dried over fused Na_2SO_4 and evaporated to dryness to leave a colorless oil, yield 4.0 g. IR $\nu_{max}^{liq.}$ cm^{-1}: 3470 (OH). The gas chromatographic analysis indicated the composition of the product to be 85% *trans*-III and 15% *cis*-III.

b) To 1.2 g of $NaBH_4$ dissolved in 20 ml of MeOH was added dropwise a methanolic solution (40 ml) of 5.0 g of I while stirring at room temperature and stirring was continued for additional 2 hr. To 100 ml of 1% aqueous AcOH was added the reaction mixture and the solution was neutralized with $NaHCO_3$, extracted with ether, washed with H_2O, dried over fused Na_2SO_4 and evaporated to leave a colorless oil, weight 5.1 g. IR $\nu_{max}^{liq.}$ cm^{-1}: 3507 (OH). The composition of the product was indicated to be 13% *trans*-III and 87% *cis*-III by the gas chromatographic analysis.

c) A solution of I (6.0 g) and Al isoproxide (10 g) in iso-PrOH (100 ml) was heated in an oil-bath removing slowly produced acetone with iso-PrOH by distillation. During operation, 100 ml of iso-PrOH was supplimented. The production of acetone ceased after 9 hr and the total amount of distillate (acetone and iso-PrOH) came to 170 ml. After reaction was completed, the contents of the flask was concentrated, 100 ml of 5% aqueous HCl added and extracted with ether. The ether solution was washed with H_2O, dried over fused Na_2SO_4 and evaporated to leave a colorless oil, weight 5.7 g. IR $\nu_{max}^{liq.}$ cm^{-1}: 3507 (OH), 1715 (C=O). The composition of the oil was indicated by the gas chromatographic analysis to be 7% *trans*-III, 86% *cis*-III and 7% I.

DL-*trans*-2-(1-Phenylcyclohexyl)cyclohexanol (*trans*-III)——A mixture of *trans*- and *cis*-III (500 mg) obtained by reduction of I with Na and EtOH was dissolved in pyridine (8 ml), benzoyl chloride (250 mg) added and allowed to stand for 3 days. After addition of dil. HCl, the reaction mixture was extracted with ether and the ether layer was washed with dil. NaOH and then H_2O, dried over fused Na_2SO_4 and evaporated to dryness. Recrystallization of the residue from EtOH–H_2O was repeated to give colorless cubes of *trans*-III ester benzoate, mp 102—103°, weight 500 mg (71%). IR ν_{max}^{Nujol} cm^{-1}: 1718 (C=O), 1300—1250, —1101 (C–O). *Anal.* Calcd. for $C_{25}H_{30}O_2$: C, 82.83; H, 8.34. Found: C, 82.91; H, 8.39.

trans-III ester benzoate (3.6 g) was dissolved in 10% ethanolic KOH (60 ml) and refluxed for 2 hr. The reaction mixture was concentrated, H_2O added and extracted with ether. The ether layer was washed with H_2O, dried over fused Na_2SO_4 and evaporated to dryness. Recrystallization from EtOH–H_2O gave colorless cubes of *trans*-III, mp 75—76°, weight 2.5 g (quantitative). IR ν_{max}^{Nujol} cm^{-1}: 3470 (OH). *Anal.* Calcd. for $C_{18}H_{26}O$: C, 83.66; H, 10.14. Found: C, 83.90; H, 10.28. Phenylurethane: colorless needles of mp 157—159°. *Anal.* Calcd. for $C_{25}H_{31}O_2N$: C, 79.53; H, 8.28; N, 3.71. Found: C, 79.35; H, 8.46; N, 3.73.

DL-*cis*-2-(1-Phenylcyclohexyl)cyclohexanol (*cis*-III)——A mixture of *trans*- and *cis*-III (4.4 g) obtained by reduction of I with $NaBH_4$ was benzoylated just as described under the foregoing item. Recrystallization from EtOH was repeated to give colorless needles of *cis*-III ester benzoate, mp 91—92°, weight 4.2 g (70%). IR ν_{max}^{Nujol} cm^{-1}: 1718 (C=O), 1300—1250,—1101 (C-O). *Anal.* Calcd. for $C_{25}H_{30}O_2$: C, 82.83; H, 8.34. Found: C, 82.82; H, 8.39.

Saponification of *cis*-III ester benzoate (10 g) was also persued as described under the foregoing item to give an oil of *cis*-III, bp 161° (1.5 mmHg), weight 6.5 g (90.5%). *Anal.* Calcd. for $C_{18}H_{26}O$: C, 83.66; H, 10.14. Found: C, 83.23; H, 9.96. *cis*-III did not react with phenylisocyanate to give the phenylurethane.

Dehydration Reaction of *cis*-III——a) With H_2SO_4: To 5 ml of 50% H_2SO_4 was added 100 ml of *cis*-III and refluxed on direct fire for 2 hr. The resulting turbid solution was neutralized with aqueous Na_2CO_3, H_2O added and extracted with ether. The ether layer was washed with H_2O, dried over fused Na_2SO_4 and evaporated to dryness. The residual oil was purified by column chromatography over Al_2O_3 using petroleum ether to afford a colorless oil, bp 137—138.5° (3 mmHg), weight 90 mg (97%). The gas chromatographic analysis indicated it to consist of 100% 1(1-phenylcyclohexyl)cyclohexene (VI).

b) With $ZnCl_2$: One hundred and ten miligrams of *cis*-III was heated with 500 mg of $ZnCl_2$ at 180—190° in an oil-bath for 30 min. After cooling, to the mixture was added H_2O and extracted with ether. The ether layer was dried over fused Na_2SO_4 and evaporated to dryness. Purification was conducted just as (a) to obtain a colorless oil which was proven to consist of 100% olefin VI by the gas chromatographic analysis, weight 92 g (90%).

Dehydration Reaction of *trans*-III——a) With H_2SO_4: *trans*-III (500 mg) was treated exactly as described under (a) of the foregoing item to give a colorless oil, weight 450 mg. The gas chromatographic analysis showed it to consist of 60% 1(1-phenylcyclohexyl)cyclohexene (VI), 28% DL-3(1-phenylcyclohexy) cyclohexene (VII), 6% 1(1-phenylcyclohexylmethyl)cyclopentene (VIII) and 6% unknown.

b) With $ZnCl_2$: *trans*-III was treated just as described under (b) of the foregoing item to give a colorless oil which was shown to consist of 70% VI, 7% VII, 21% VIII and 2% unknown by the gas chromatographic analysis.

Thermal Decomposition (The Chugaev Reaction) of DL-*trans*-2-(1-Phenylcyclohexyl)cyclohexyl S-Methyl Xanthate (*trans*-XI)——To a solution of *trans*-III (1 g) in anhydrous benzene (10 ml) was added K (0.16 g) and refluxed for 3 hr to get a clear solution. After cooling, CH_3I (0.68 g) was added to the solution and stirred at room temperature for 6 hr. The resulting precipitate was filtered off and the filtrate was concentrated *in vacuo*. The remainder was decomposed by heating at 220—230° in an oil-bath for 8 hr. The decomposition product was purified by column chromatography over Al_2O_3 using petroleum ether and then distilled *in vacuo* gathering distillate at bp 129—131° (2 mmHg). The gas chromatographic analysis indicated the distillate to consist of 73% olefin VI and 27% olefin VII.

Ozonization of 1-(1-Phenylcyclohexyl)cyclohexene (VI)——To a solution of VI (525 mg) in 5 ml of $CHCl_3$ was introduced O_3 with ice-chilling till a spot of VI had disappeared on thin layer chromatogram. The reaction mixture was distilled *in vacuo* to remove $CHCl_3$, a mixture of AcOH (2 ml) and 30% H_2O_2 (1 ml) added and warmed at 80° while stirring for 3.5 hr. During warming, 1 ml of 30% H_2O_2 was supplimented. The resulting solution was evaporated *in vacuo* to remove AcOH, excess of 10% aqueous Na_2CO_3 added and washed with ether. The aqueous layer was neutralized with conc. HCl and allowed to stand overnight to complete the precipitation of crystals. After filtration, crystals were recrystallized from petroleum benzine to afford colorless needles, weight 200 mg (32%), mp 80—81° alone and on admixture with an authentic sample of 6(1-phenyl)cyclohexyl-6-oxo-hexanoic acid (XII).[4)]

Acknowledgement The authors are indebted to the staff of the analysis room of this faculty for elemental analyses and measurements of IR spectra and also to members of the analysis section of Sankyo Research Laboratories for determinations of NMR spectra.