Chem. Pharm. Bull.
18(9)1806—1814(1970)

UDC 547.288.4.04 : 542.957.2

Grignard Reaction and Products. II. A Novel Intramolecular Cyclization in the Grignard Reaction of Alicyclic Ketoxime containing an Aromatic Nucleus[1)]

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(Received February 14, 1970)

A novel intramolecular cyclization reaction was found in the reaction of 2(1′-phenyl)-cyclohexylcyclohexanone oxime (I-oxime) with aromatic Grignard reagent, either phenyl- or *p*-tolylmagnesium bromide, which worked as a catalyst. The reaction required at least 3 equivalent moles of Grignard reagent. The structure of the cyclization product (II) was established as spiro[bicyclo[3.3.1]-3,4-benzononan-9-one-2,1′-cyclohexane]. The structural feature of oximes which suffer the cyclization reaction was preliminary discussed.

In the preceding paper,[1c)] it was described that the Grignard reaction of 2-cyclohexylidenecyclohexanone with phenylmagnesium bromide produced mainly 2(1′-phenyl)cyclohexylcyclohexanone (I) through 1,4-addition, accompanying a small amount of a ketoacid which was formed by the oxidative cleavage of I. This paper reports an intramolecular cyclization reaction of I-oxime by the catalytic action of Grignard reagents.

The reaction of I-oxime with more than three equivalent moles of phenylmagnesium bromide was carried out in absolute toluene at 110—120° and products were separated by alumina column chromatography to afford spiro[bicyclo[3.3.1]-3,4-benzononan-9-one-2,1′-cyclohexane] (II) (48%) and two other basic substances, namely, spiro[bicyclo[3.3.1]-3,4-benzononanyliden-9-imine-2,1′-cyclohexane] (III) (21%) and a diastereomer of 1-phenyl-2 (1′-phenyl) cyclohexyl-7-azabicyclo[4.1.0]heptane (IVb) (15.5%).

When, without use of alumina column chromatography for separation, the reaction mass was recrystallized from ethanol–ether, III·HCl was obtained in yield 71.8%. Hydrolysis of III·HCl in hydrochloric acid gave II.[1b)] Therefore, it can be concluded that a large portion of III was converted into II during a seperation process by the chromatography, and this transformation was also ascertained by use of thin–layer chromatography (TLC).

Hoch[4a)] and Campbell[4b)] have reported a reaction of Grignard reagent with aliphatic ketoxime as one of methods for the preparation of aziridine (Chart 2) and thereafter the reaction mechanism was corrected by Henze[5)] and Eguchi.[6)]

These reports suggest that the structure of the basic product, IV b, may be a kind of aziridine. In fact, infrared (IR) spectrum of IV b showed a characteristic weak band at 3357 cm^{-1} (>NH), which disappeared on tosylation. In addition, an elemental analysis and a result from hydrolysis of IV b, which gave V through IV′, agreed with the aziridine structure for IV (Chart 1).

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1) *a*) T. Taguchi, Studies in Stereochemistry. XLIV; *b*) Part of this work appeared as a communication: *Tetrahedron Letters*, **1968**(38), 4105; *c*) Part XLIII: K. Miyano, *Chem. Pharm. Bull.* (Tokyo), **18**, 1799 (1970).

2) Location: *Katakasu, Fukuoka*; *a*) Present address: *Faculty of Pharmacy, Fukuoka University, Nanakuma, Fukuoka.*

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4) *a*) J. Hoch, *compt. rend.*, **198**, 1865 (1934); *ibid.*, **204**, 358 (1937); *b*) K.N. Campbell, *J. Org. Chem.*, **8**, 99, 103 (1943); *ibid.*, **9**, 178, 184 (1944).

5) H. Henze and W.D. Compton, *J. Org. Chem.*, **22**, 1036 (1957).

6) S. Eguchi and Y. Ishii, *Bull. Chem. Soc. Japan*, **36**, 1434 (1963).

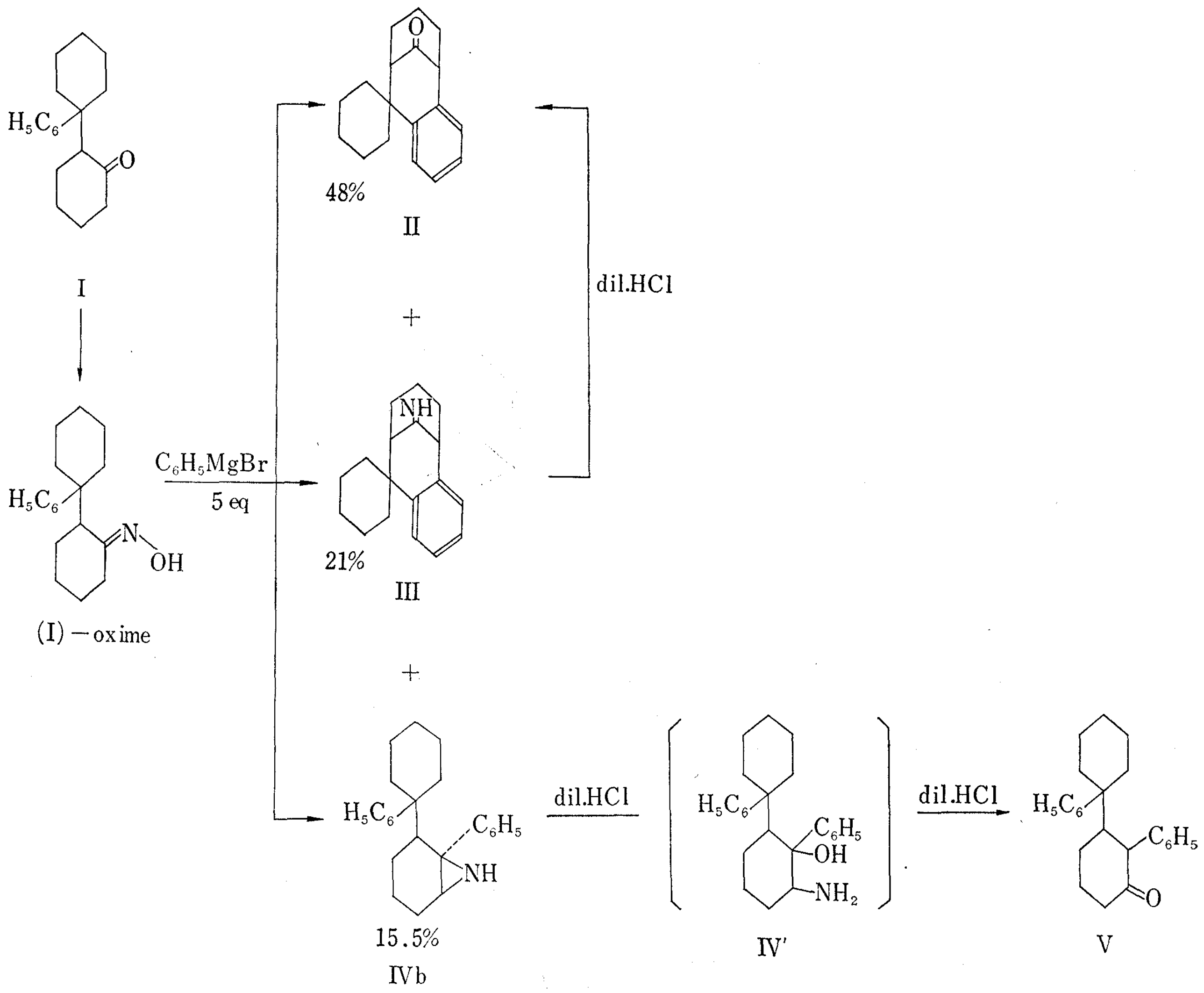

Chart 1

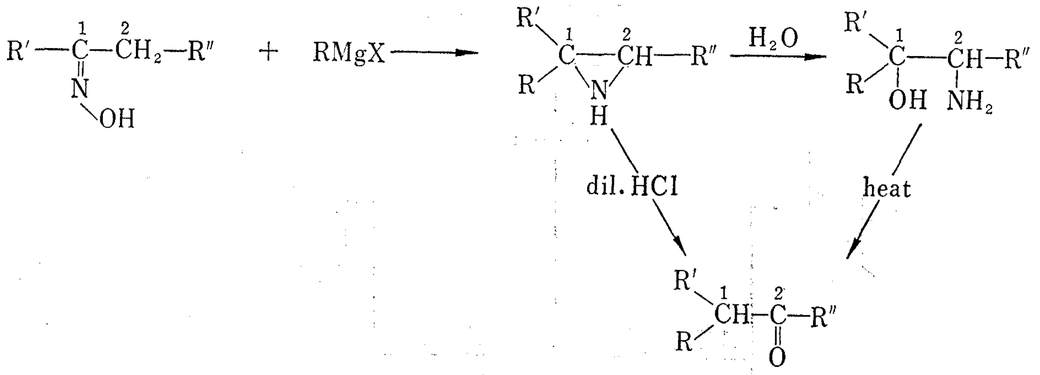

Chart 2

For determination of the structure of II, mass spectrum, nuclear magnetic resonance (NMR) spectrum and IR spectrum afforded significant informations. In mass spectrum, parent peak was recognized at *m/e* 254, which was also base peak. This fact suggested the very stable or rigid structure for II, which, as stated later, can account for the difficulty of deuteration of II. The molecular weight corresponds to that of dehydrogenation product of I less by one mole of hydrogen. However, the presence of double bond was denied by chemical tests and also by NMR spectrum, in which any signals due to usual olefinic protons did not appear at the lower field. On the other hand, the NMR spectrum (60 Mc, in CCl_4)

of II exhibited signals characteristic for benzene protons (2.85 τ, 4H, A_2B_2 type symm. m.), two methine protons (6.63 τ, 1H, 7.10 τ, 1H) and cyclohexane protons (7.80—8.80 τ, 16H, broad m.).

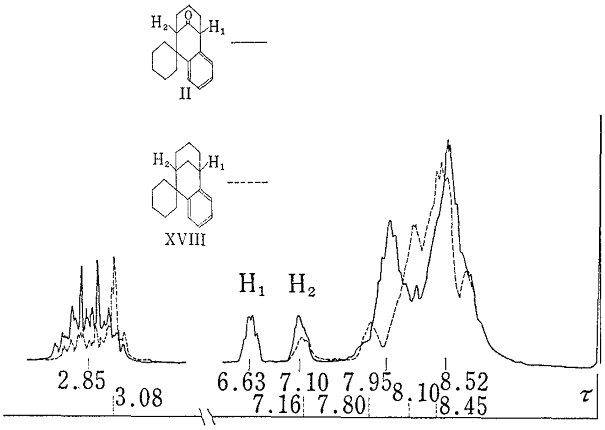

Fig. 1. NMR Spectra of II and XVIII (60 Mc, in CCl_4)

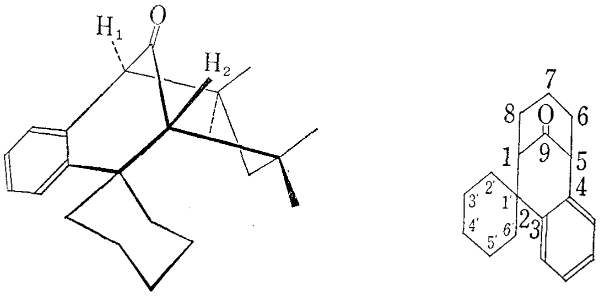

Fig. 2. Spiro[bicyclo[3.3.1]-3,4-benzononan-9-one-2,1'-cyclohexane]

In comparison of I with II in their IR spectra, bands at 739 and 704 cm^{-1} due to monosubstituted benzene existing in the case of I, shifted to a band at 753 cm^{-1} due to *o*-disubstituted benzene in the case of II. Therefore, as shown in Fig. 2, two methine signals in the NMR spectrum of II could be interpreted as bridgehead protons, H_1 and H_2. A signal at 6.63 τ is due to H_1 which is more deshielded than the other by the effect of benzene ring anisotropy.

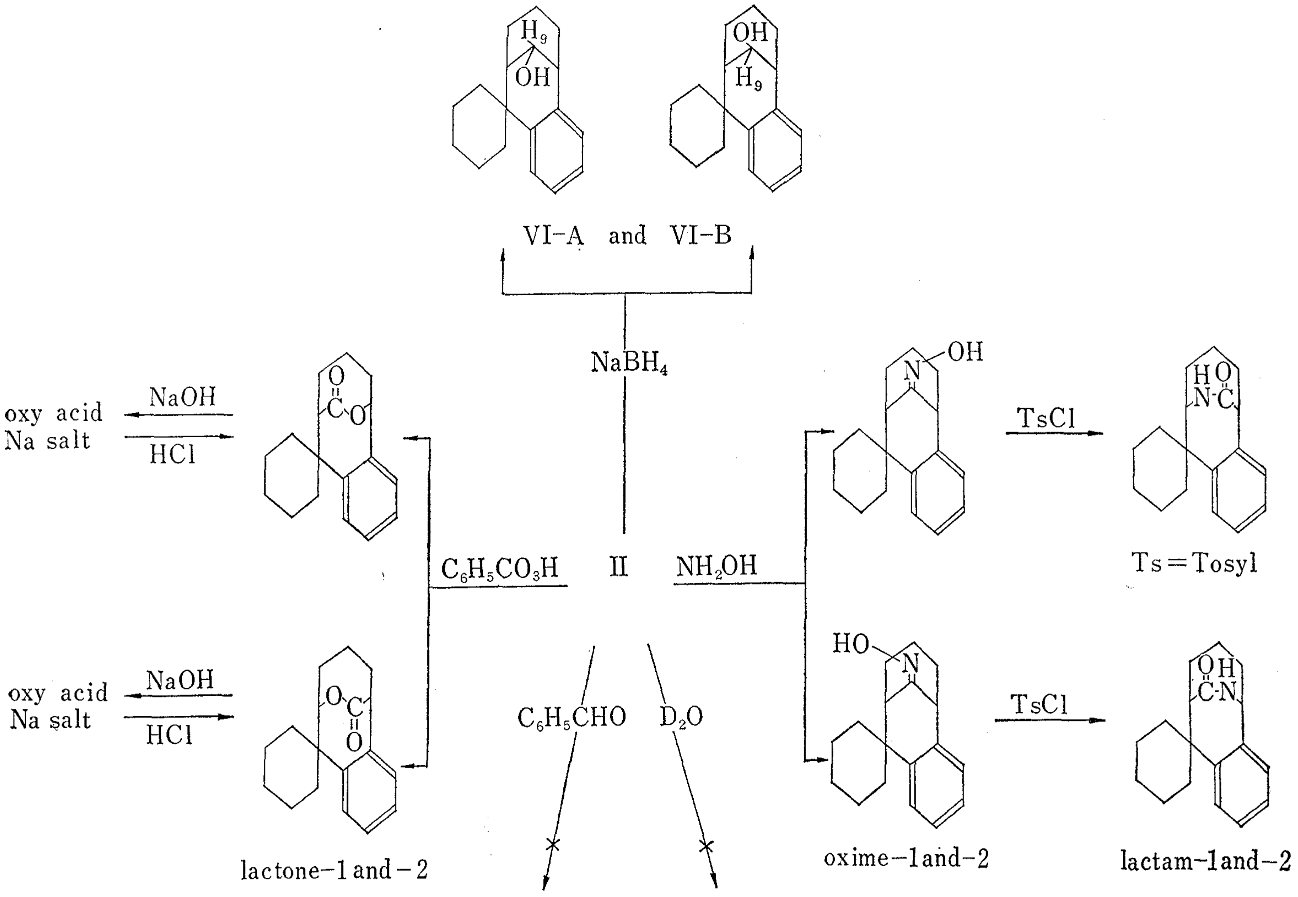

Chart 3

This assignment was supported in comparison of the observed value of the shift (σ) caused by benzene anisotropy with the value calculated by use of the McCornell's equation and the Bovey's table.7) Thus, all the data shown were in accordance with the postulated structure for II and consequently III was assigned to the corresponding ketimine which showed IR absorption bands at 1650 cm^{-1} (=NH) and 755 cm^{-1} (disubstd. benzene). In addition, the results of several chemical reactions tried were coinsistent with the structure postulated for II as follows.

a) Reduction of II by sodium borohydride gave two isomeric alcohols, (VI-A) and (VI-B), in 74% and 11.5% yields respectively. Of three methine signals in the NMR spectrum of VI-A, a signal at 5.93 τ (J=3.0 cps) shifted to 5.15 τ (J=3.45 cps) by derivation to O-tosylate and appeared as triplet. Thus, the signal is ascribable to H_9 on C_9 coupling with two methine protons on both sides. VI-A and VI-B resisted to dehydration reaction showing the government of the Bredt's rule. These observations support the basic skeleton of the mother compound II. b) II gave two isomeric oximes, oxime-1 and oxime-2, in 3.3/2 formation ratio. They were subjected to the Beckmann rearrangement giving lactams, *lactam*-1 and *lactam*-2, respectively. However, they did not accept hydrolysis. c) The Baeyer–Villiger reaction of II gave two lactones, lactone-1 and lactone-2, in 3.5/2 formation ratio. Each of them was easily hydrolyzed by alkali, but readily cyclized by acid. d) II did not undergo condensation with benzaldehyde, showing absence of an active methylene, while I easily condensed with it, giving α,β-unsaturated ketone (XIX). e) Deuteration reaction of II did not succeeded, while three deuterium was introduced into I under the same condition giving ($\mathrm{I}d_3$).

Subsequently, to seek a type of Grignard reagents promoting the cyclization, a few reagents were reacted with I-oxime.

Of those, only *p*-tolylmagnesium bromide induced the intramolecular cyclization to afford same products as the case of phenylmagnesium bromide. Interestingly, cyclohexylmagnesium chloride acted reductively to form a diastereomer of 1H-2(1′-phenyl)cyclohexyl-7-azabicyclo-[4.1.0]heptane (VIII b). However, in the other cases, the formation of diastereomeric azabicyclic compound8) (aziridine) predominated by the Hoch–Campbell reaction.4)

Generally, in the Grignard reaction of a ketone, it is postulated that reaction course is affected by steric structure of the Grignard reagent regardless of aromatic or aliphatic.9) In the reaction of organolithium reagent with ketoxime, it was found in a very few examples that reaction course was changed depending on the property of reagent, aromatic or aliphatic.10) In the present cyclization reaction, it seems to govern the reaction course whether the reagent is aromatic or not, but nothing is said about steric influence of the reagent on the basis of results obtained (see Chart 4).

Next, the Grignard reaction was performed with a variety of ketoxime more or less similar to I-oxime, using phenylmagnesium bromide as reagent, as shown in Chart 5.

Of those, only XVI and XVII gave cyclization products11) and other examples succeeded has already been shown in the preceding paper.1b) Generally summarizing the results, cyclization occurs only in the reaction of cyclohexanone oxime, which is substituted at 2-position by a tertiary carbon radical containing an aromatic ring. Thus, this cyclization reaction requires high specificity. As mentioned above, the cyclization reaction required more than

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7) C.E. Johnson and F.A. Bovey, *J. Chem. Phys.*, **29**, 1012 (1958).

8) Details of these reactions will be described in the following paper.

9) R.C. Fuson and R. Tull, *J. Am. Chem. Soc.*, **71**, 2543 (1949); R.C. Fuson, J.P. Freeman, and J.J. Looker, *J. Org. Chem.*, **26**, 4217 (1961); W.E. Ross and R.C. Fuson, *J. Am. Chem. Soc.*, **59**, 1508 (1937); F.C. Whitmore and C.E. Lewis, *J. Am. Chem. Soc.*, **64**, 1618, 1619 (1942); F.C. Whitmore and R.S. George, *J. Am. Chem. Soc.*, **64**, 1239 (1942); *ibid.*, **63**, 758 (1941); G. Vavon and C. Reviere, *compt. rend.*, **220**, 286 (1945); *ibid.*, **224**, 1435 (1947); J. Miller and L. Gilman, *J. Am. Chem. Soc.*, **58**, 937 (1936).

10) N.W. Gabel, *J. Org. Chem.*, **29**, 3129 (1964); H. Gilman, *J. Am. Chem. Soc.*, **74**, 1594 (1952); H.T. Fabrics, *J. Org. Chem.*, **32**, 2031 (1967).

11) K. Imai, Master's thesis.

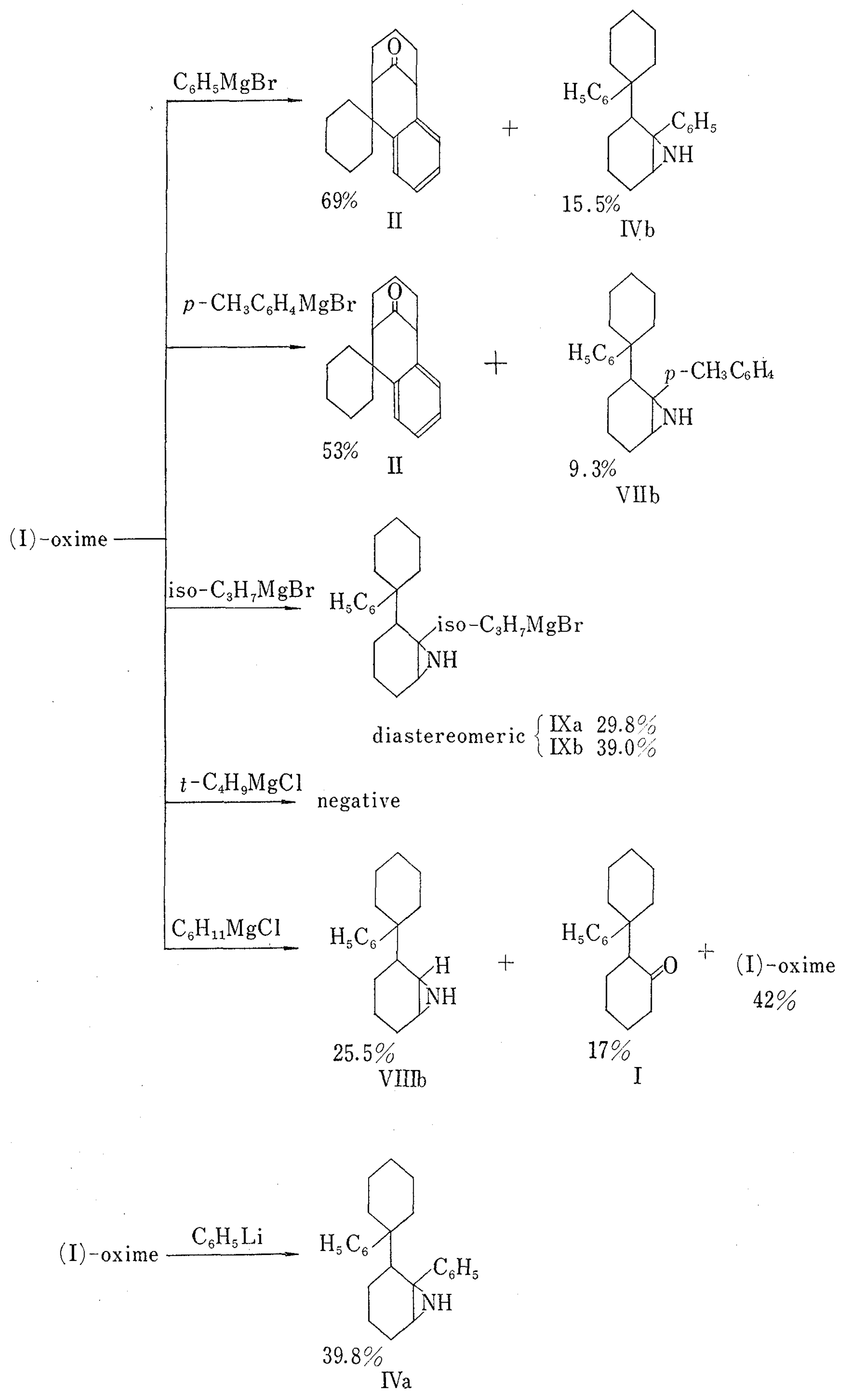

Chart 4

three moles of the Grignard reagent. The role of the reagent as a catalyst in relation to possible reaction mechanism has been discussed in the preceding paper.[1b] The paper suggested with some evidences that the reaction proceeded probably *via* an azirine intermediate as in *Hoch–Campbell reaction.*[4] However, as pointed out hitherto, some problems and questions remain unsolved. This needs further studies.

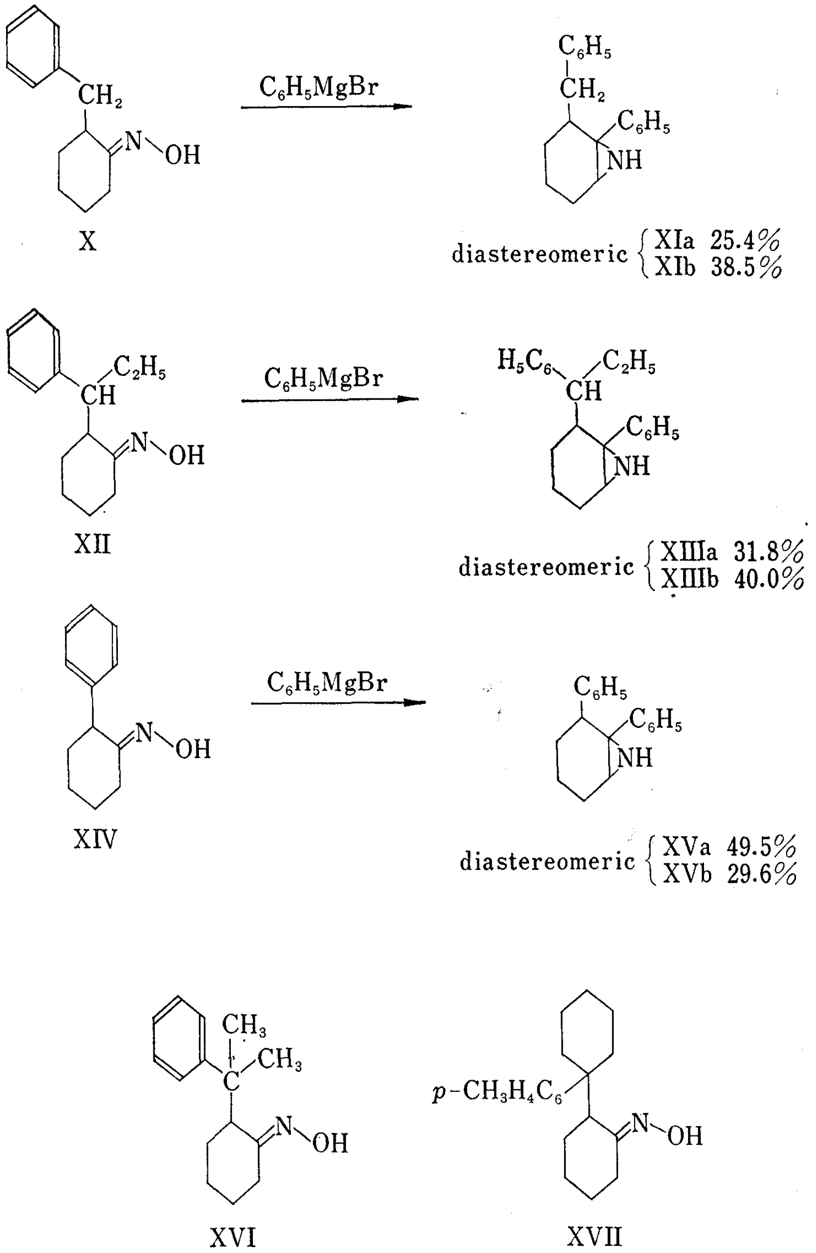

Chart 5

Experimental[12]

The Grignard Reaction of Ketoximes (General Method)——Grignard reagent was prepared as usual from Mg (5 eq) and a halide (5 eq) dissolved in 2—3 times volumes of absolute ether (abs. ether). After the formation of the reagent was completed, vessel temperature was raised gradually and ether was removed off as much as possible. To the vessel was added abs. toluene almost the same volume as the residue. An oxime (1 eq) in abs. toluene was added to the reagent solution at refluxing temperature under stirring, and reflux was continued for additional 0.5—1 hr. After the reaction mixture was cooled and then hydrolyzed with sat. aqueous NH_4Cl at 0—10°, the hydrolysate was extracted with ether. The ether extract was washed with water, dried over Na_2SO_4 and concentrated *in vacuo*. Isolation and purification of products were carried out by column chromatography over Al_2O_3 (Al_2O_3–chromat.).

The Grignard Reaction of 2(1′-Phenyl)cyclohexylcyclohexanone (I)-oxime with Phenylmagnesium Bromide——I-Oxime (7.5 g, 1 eq) was reacted by the general method with the C_6H_5MgBr (5 eq) prepared form Mg(3.0 g) and bromobenzene (19.5 g). Products were separated by Al_2O_3–chromat. as follows: 1) From

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[12] All melting and boiling points were uncorrected.

elution with benzene; colorless plates of spiro[bicyclo[3.3.1]-3,4-benzononan-9-one-2,1′-cyclohexane] (II), mp 78—79°, after recrystallization from petr. ether, yield 48%. *Anal.* Calcd. for $C_{18}H_{22}O$: C, 84.99; H, 8.72. Found: C, 84.68; H, 8.72. Mass Spectrum[13a] *m/e*: 254 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 1728 (C=O), 1490, 753 (bezene). NMR[13b] (in CCl_4) τ: 7.10 (1H, broad, bridgehead H), 6.63 (1H, quart., J_{ee}(apparent) = 2.6 cps, J_{ae}(apparent) = 5.0 cps, bridgehead H), 2.85 (4H, A_2B_2 type mult. arom. H). UV λ_{max}^{EtOH} mμ (ε): 214 (11500), 217 (11000), 253 (263), 261 (416), 267 (560), 274 (550). 2) From elution with benzene–$CHCl_3$; (a) colorless needles of spiro[bicyclo[3.3.1]-3,4-benzononanylidene-9-imine-2,1′-cyclohexane] (III), mp 101° after recrystallization from petr. ether, yield 21%. *Anal.* Calcd. for $C_{18}H_{23}N$: C, 85.32; H, 9.15; N, 5.53. Found: C, 85.14; H, 9.31; N, 5.67. IR ν_{max}^{Nujol} cm^{-1}: 3184 (=NH), 1670 (C=N). (b) Pale yellow viscous liquid of a diastereomer of 1-phenyl-2(1′-phenyl)cyclohexyl-7-azabicyclo[4.1.0]heptane (IVb),[8] n_D^{20}, 1.5780, yield 15.5%. *Anal.* Calcd. for $C_{24}H_{29}N$: C, 87.08; H, 8.83; N, 4.23. Found: C, 86.73; H, 9.39; N, 4.13. IR $\nu_{max}^{liq.film}$ cm^{-1}: 3357 ($\rangle$NH). NMR (in $CDCl_3$) τ: 7.32 (1H, broad, bridgehead H). *p*-Tostlate colorless needles, mp 194° (acetone). *Anal.* Calcd. for $C_{31}H_{35}O_2NS$: C, 76.70; H, 7.22; N, 2.89. Found: C, 76.56; H, 7.01; N, 2.71.

The Grignard Reaction of I-Oxime with *p*-Tolylmagnesium Bromide——I-Oxime (4.0 g) was reacted by the general method with *p*-$CH_3C_6H_4MgBr$ prepared from Mg (1.6 g) and *p*-bromotoluene (11.0 g). Products were separated by Al_2O_3-chromat. as follows: 1) From elution with petr. ether–$CHCl_3$ (3:1); colorless plates of II, identical with an authentic sample by a mixed mp determination and comparison of IR spectra, mp 78—79°, yield 53%. 2) From elution with petr. ether–$CHCl_3$ (1:3); colorless crystals of a diastereomer of 1-*p*-tolyl-2(1′-phenyl)cyclohexyl-7-azabicyclo[4.1.0]heptane (VIIb), mp 112—114° after recrystallization from petr. ether, yield 9.3%. *Anal.* Calcd. for $C_{25}H_{31}N$: C, 87.03; H, 9.06; N, 4.06. Found: C, 86.99; H, 9.15; N, 4.12. IR ν_{max}^{Nujol} cm^{-1}: 3357 ($\rangle$NH).

Reaction of I-Oxime with Phenyllithium——A phenyllithium ether solution prepared from Li (0.56 g), bromobenzene (6.4 g) and abs. ether (50 ml) was evaporated to replace the solvent with abs. toluene. A toluene solution of I-oxime (2.0 g) was added to the PhLi–toluene solution and refluxed for 1 hr. Products were chromatographed over Al_2O_3. 1) From elution with petr. ether–$CHCl_3$ (9:1); formation of II and IVb were recognized on TLC. 2) From elution with petr. ether–$CHCl_3$ (4:1); pale yellow viscous liquid of the other diastereomer of 1-phenyl-2(1′-phenyl)cycohexyl-7-azabicyclo[4.1.0]heptane (IVa), n_D^{20} 1.5642, which crystallized on standing for a long period, mp 90—92° (petr. ether), yield 39.8%. *Anal.* Calcd. for $C_{24}H_{29}N$: C, 87.08; H, 8.83; N, 4.23. Found: C, 86.42; H, 8.18; N, 4.08. IR ν_{max}^{Nujol} cm^{-1}: 3275 ($\rangle$NH). *p*-Tosylate: colorless needles, mp 178—179° (acetone). *Anal.* Calcd. for $C_{31}H_{35}O_2NS$: C, 76.70; H, 7.22; N, 2.89. Found: C, 76.68; H, 7.21; N, 3.01.

Reaction of I-Oxime with A Phenylmagnesium Bromide-LiAlH$_4$ Mixture——A toluene (40 ml) solution of I-oxime (3.0 g, 1 eq) was added to C_6H_5MgBr (2 eq) prepared from Mg (0.74 g) and bromobenzene (4.4 g) under refluxing. To the mixture was added a C_6H_5MgBr (3 eq)–$LiAlH_4$ (3 eq) mixture in abs. toluene. The latter mixture was prepared by mixing $LiAlH_4$ (0.3 g) with Grignard reagent obtained from Mg (1.2 g) and bromobenzene (7.2 g) in abs. toluene. After refluxing for 1 hr and cooling, products were separated by Al_2O_3–chromat. as follows: 1) From elution with petr. ether–$CHCl_3$ (9:1); (a) I, identical with an authentic sample by a mixed mp determination and comparison of IR and TLC data, yield 19%. (b) II, identical with an authentic sample by a mixed mp determination and comparison of IR and TLC data, yield 12.8%. 2) From elution with petr. ether–$CHCl_3$ (7:3); (a) IVb, the tosylate was identical with an authentic sample by a mixed mp determination and comparison of IR and TLC data, yield 3—4%. (b) Pale yellow liquid of a diastereomer of 1H-2(1′-phenyl)cyclohexyl-7-azabicyclo[4.1.0]heptane (VIIIa), yield 4.5% IR $\nu_{max}^{liq.film}$ cm^{-1}: ($\rangle$NH). *p*-Tosylate: colorless plates, mp 118—119° (MeOH). *Anal.* Calcd. for $C_{25}H_{31}O_2NS$: C, 73.41; H, 7.64; N, 3.42. Found: C, 72.91; H, 7.63; N, 3.29. (c) Pale yellow liquid of the other diastereomer of 1H-2(1′-phenyl)cyclohexyl-7-azabicyclo[4.1.0]heptane (VIIIb), $n_D^{17.5}$ 1.5650, yield 22.0%. IR $\nu_{max}^{liq.film}$ cm^{-1}: 3222 ($\rangle$NH). *p*-Tosylate colorless pillars, mp 142° (MeOH). *Anal.* Calcd. for $C_{25}H_{31}O_2NS$: C, 73.41; H, 7.64; N, 3.42. Found: C, 72.88; H, 7.73; N, 3.28.

Hydrolysis of III——One tenth gram of III was suspended in 2N HCl (10 ml) at room temperature. On allowing to stand, III·HCl (mp 259° (decomp.)) deposited. Heating the mixture for 1 hr on a steam bath, an oil liberated was extracted with ether. The ether layer was washed with water, dried over Na_2SO_4 and concentrated *in vacuo*. Crystallized residue was identified as II, by comparison of IR spectra and a mixed mp determination.

Hydrolysis of IVb——To a solution of 60% $HClO_4$ (0.4 ml) in water (2.6 ml) was added IVb (0.28 g) and the mixture was heated on a steam bath for 2.5 hr. An oil liberated was extracted with ether. The ether extract was washed with water, dried over Na_2SO_4 and chromatographed over Al_2O_3. Colorless crystals of 2-phenyl-3(1′-phenyl)cyclohexylcyclohexanone (V) were obtained, mp 69° (petr. ether), yield 72%. *Anal.* Calcd. for $C_{24}H_{28}O$: C, 86.82; H, 8.50. Found: C, 86.67; H, 8.54. IR ν_{max}^{Nujol} cm^{-1}: 1720 (C=O).

Spiro[bicyclo[3.3.1]-3,4-benzononane-9-one-2,1′-cyclohexane] Oxime——A raw product obtained by the reaction of I-oxime with C_6H_5MgBr was dissolved in EtOH, and added a large excess of $NH_2OH \cdot HCl$ and

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13) *a*) The same charts were obtained at both conditions, 40 & 70 eV of chamber voltage. *b*) $(CH_3)_4Si$ was used as an internal reference.

an equivalent mole of CH_3COONa dissolved in a small volume of water. The mixture was refluxed for 3 hr on a steam bath. After removal of EtOH, a large quantity of water was added to the remainder and a material liberated was extracted with ether. The ether extract was washed with water. Removal of ether left crystals, which were separated into two oximes through repeated recrystallizations. (1) Colorless needles of oxime-1, mp 175—177° (MeOH). *Anal.* Calcd. for $C_{18}H_{23}ON$: C, 80.25. H, 8.61; N, 5.20. Found: C, 80.45; H, 8.54; N, 5.40. IR ν_{max}^{Nujol} cm^{-1}: 3222 (OH), 1667 (C=N). (2) Colorless granules of oxime-2, mp 174—177° (MeOH). *Anal.* Calcd. for $C_{18}H_{23}ON$: C, 80.25; H, 8.61; N, 5.20. Found: C, 80.59; H, 8.75; N, 5.24. IR ν_{max}^{Nujol} cm^{-1}: 3301, 3204 (OH), 1685 (C=N). Products ratio: oxime-1/oxime-2=3.3/2. Mixed mp of them: 148—150°.

The Beckmann Rearrangement of Oxime-1 and -2——a) To an acetone (130 ml) solution of oxime-1 (2.0 g) was added 10% aqueous KOH (4.5 ml), and subsequently TsCl (1.5 g) in acetone (20 ml), maintaining a vessel temperature at 0°. Removing an ice-bath, stirring was continued for 10 min at room temperature and then concentrated *in vacuo*. An oil, separated by adding water to the residue, changed to crystals which gave colorless granules of lactom-1, after recrystallization from acetone, mp 194—195°, yield 65%. *Anal.* Calcd. for $C_{18}H_{23}ON$: C, 80.25; H, 8.61; N, 5.20. Found: C, 80.03; H, 8.41; N, 5.31. IR ν_{max}^{Nujol} cm^{-1}: 3222, 3316 (NH), 1663 (C=O, amide). b) Treating oxime-2(2.0 g) quite in the same way as a), gave colorless granules of lactom-2, mp 218—219° (acetone), yield 55%. *Anal.* Calcd. for $C_{18}H_{23}ON$: C, 80.25; H, 8.61; N, 5.20. Found: C, 80.07; H, 8.44; N, 5.03. IR ν_{max}^{Nujol} cm^{-1}: 3329, 3222 (NH), 1684 (C=O, amide). Both of lactams were not hydrolyzed even under drastic condition.

Reaction of II with Perbenzoic Acid——A mixture of II (2.0 g, 1 eq) and perbenzoic acid–$CHCl_3$ solution (containing 2 eq of peracid) was stood on a dark and cool place for 35 days with a catalytic amount of 10% H_2SO_4–AcOH. After removal of excess peracid with $FeSO_4$-d. H_2SO_4, the chloroform layer was washed with water and concentrated *in vacuo*. The remaining viscous liquid was treated with petr. ether to deposit lacton-1 which was separated on filter. Colorless needles of mp 182—183° after recrystallization from MeOH, yield 35.8%. *Anal.* Calcd. for $C_{18}H_{22}O_2$: C, 80.07; H, 8.21. Found: C, 79.66; H, 8.25. IR ν_{max}^{KBr} cm^{-1}: 1715 (C=O), 1160, 1030 (C–O–C). The filtrate was concentrated and chromatographed over Al_2O_3. In addition to recovered II (31%), colorless crystals of lacton -2 was obtained, mp 78—79° after recrystallization from ether–petr. ether, yield 20.2%. *Anal.* Calcd. for $C_{18}H_{22}O_2$: C, 80.07; H, 8.21. Found: C, 80.35; H, 8.41. IR ν_{max}^{KBr} cm^{-1}: 1728 (C=O), 1156, 1031 (C–O–C). Products ratio: lacton-1/lacton-2=3.5/2.

Both of lactons were hydrolyzed with 25% NaOH–EtOH on heating to reflux for 8 hr. However, starting lactones were recovered by acidifing the alkaline solution.

Spiro[bicyclo[3.3.1]-3,4-benzononan-2,1′-cyclohexane] (XVIII)——II (20 g) was refluxed with diethylene glycol (15 ml), NaOH (0.95 g) and hydrazine hydrate (2.0 ml) for 1 hr. Subsequently, water was drived out by distillation and then the reaction mass was heated at 195—200° for additional 3 hr. After cooling, the reaction mixture was acidified with dil. HCl, and extracted with benzene-ether. The organic layer was washed with water, dried over Na_2SO_4 and concentrated *in vacuo*. By Al_2O_3-chromat., colorless crystal were obtained from fraction eluted with petr. ether. Recrystallization from EtOH gave colorless needles of XVIII, mp 73°, yield 50.3%. *Anal.* Calcd. for $C_{18}H_{24}$: C, 90.08; H, 10.08. Found: C, 89.74; H, 10.09.

Spiro[bicyclo[3.3.1]-3,4-benzononan-9-ol-2,1′-cyclohexane] (VI) Tosylate——$NaBH_4$ (0.2 g) in MeOH (20 ml) was added to methanolic (20 ml) solution of II (2.5 g), under ice-cooling and stirring. After stirring for additional 3 hr at room temperature, MeOH was removed. The residue was dissolved in ether and dried over Na_2SO_4. After evaporation of the ether, the remainder was dissolved in abs. pyridine and added TsCl (2.1 g) under cooling. The reaction mixture was poured into a large volume of water, and the precipitate filtered was recrystallized from benzene giving colorless granules of VIa·tosylate, mp 113—115° (decomp.), yield 42.2%. *Anal.* Calcd. for $C_{25}H_{30}O_3S$: C, 73.23; H, 7.38. Found: C, 73.05; H, 7.28. NMR (in CCl_4) τ: 7.35 (1H, broad, bridgehead H), 7.03 (1H, broad, bridgehead H), 5.15 (1H, tripl., $J=3.45$ cps, $\underline{H}$COTs). The filtrate was concentrated *in vacuo* and the residual liquid was dissolved in MeOH, and allowed to stand in an ice-box. Crystals collected were recrystallized from MeOH giving fine needles of VIb, mp 130—133°, yield 11.5%. *Anal.* Calcd. for $C_{18}H_{24}O$: C, 84.45; H, 9.45. Found: C, 83.99; H, 9.49. IR ν_{max}^{KBr} cm^{-1}: 3318 (OH), 1017 (C=O). NMR (in CCl_4) τ: 7.78 (2H, singl., bridgehead H and OH), 5.85 (1H, broad tripl., $\underline{H}$COH). *p*-Tosylate: fine granules, mp 135—136° (decomp.) (EtOH–benzene), which was transformed into VIa·tosylate through repeated recrystallizations. The mother liquor, after filtration of VIb, was chromatographed over Al_2O_3 and was obtained pale yellow liquid which was identified as VIa, by derivation to tosylate and a mixed fusion with VIa·tosylate, yield 31%. IR $\nu_{max}^{liq.film}$ cm^{-1}: 3373 (OH). NMR (in $CDCl_3$) τ: 8.27 (1H, singl., OH), 7.52 (1H, broad, bridgehead H), 7.03 (1H, broad quart., bridgehead H), 5.93 (1H, tripl., $J=3.0$ cps, $\underline{H}$COH).

2(1′-Phenyl)cyclohexylcyclohexanone-2,6,6-d_3 (Id_3)——Under a stream of dry N_2, I (0.1 g) was stirred with the reagent[14] (10 ml) prepared by dissolving Na (50 mg) in abs. dioxane–D_2O (1:1) (4 ml), at 70° for 1 hr. After removal of the dioxane *in vacuo*, the residue was extracted with abs. ether. The ether extract

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14) E. Lund, H. Budzikiewiez, M. Wilson, and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 1528 (1963).

was washed once with a small amount of D_2O and dried over $MgSO_4$. Removal of the ether left colorless crystal, which were identified as I d_3 by mass spectra (M^+: m/e 259) and IR spectrum, mp 78—79°.

2(1′-Phenyl)cyclohexyl-6-benzalcyclohexanone (XIX)——To a solution of I (0.2 g) in EtOH (20 ml) was added benzaldehyde (0.6 g, 1.5 eq) and 10% NaOH–EtOH (20 ml) and stood for 5 days at room temperature under occasionally shaking. After evaporating most of EtOH, water was added to the residue and extracted with ether. The ether layer was washed with water and dried over Na_2SO_4. Isolation by Al_2O_3–chromat. gave pale yellow viscous liquid of XIX, yield 0.27 g. *Anal.* Calcd. for $C_{25}H_{28}O$: C, 87.28; H, 8.20. Found: C, 87.08; H, 8.54. IR $\nu_{max}^{liq.film}$ cm^{-1}: 1677 (C=C–C=O).

2(α-Phenyl)propylcyclohexanone Oxime (XI)——To a solution of EtMgBr prepared from Mg (1.3 g) and ethylbromide (5.9 g) was added 2-benzalcyclohexanone (8.0 g) and CuCl (200 mg) as catalyst under cooling. After refluxing for 2 hr, the reaction mixture was hydrolyzed with sat. aqueous NH_4Cl and extracted with ether. The ether layer was washed with water, dried over Na_2SO_4 and concentrated *in vacuo*. Isolation through Al_2O_3–chromat. gave 2(α-phenyl)propylcyclohexanone from a fraction eluted with petr. ether, bp 120—121° (2.0 mmHg), n_D^{20} 1.5293. XI: colorless viscous liquid, 154—161° (1.5 mmHg). *Anal.* Calcd. for $C_{15}H_{21}ON$: C, 77.89; H, 9.16; N, 6.06. Found: C, 77.89; H, 8.98; N, 6.04. IR $\nu_{max}^{liq.film}$ cm^{-1}: 3520—3080, 3200 (OH), 1600 (C=N). Semicarbazone: colorless crystals, mp 199—201° (EtOH–H_2O). *Anal.* Calcd. for $C_{16}H_{23}ON_3$: C, 70.39; H, 8.49; N, 15.39. Found: C, 70.39; H, 8.51; N, 15.37.