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Grignard Reaction and Products. VI.[1] The Reaction of Grignard Reagents with 2-Phenoxy- and 2-Benzyloxy-cyclohexanone Oximes

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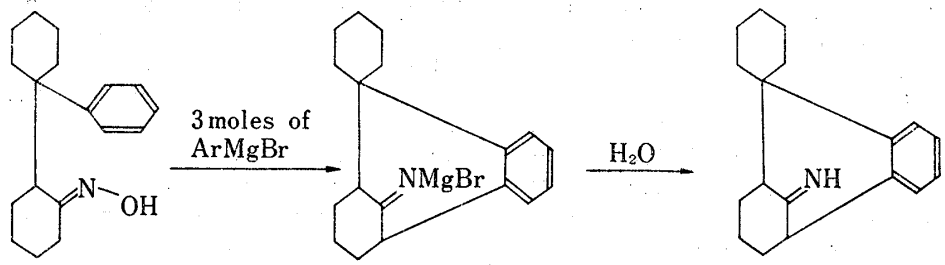
The reaction of *anti*-oxime (1) of 2-phenoxycyclohexanone was attempted in continuation of the former studies on the Grignard reactions of oximes.[1b,4] Consequently, it ended in a result entirely different from the Hoch-Campbell reaction and also the intramolecular ring-closure reaction which has been previously reported.[1b,4] causing the elimination of phenol and the productions of aniline and 2-phenoxycyclohexanone in main. The reaction pathway was discussed. Additionally, the government of reaction by both changes of 2-substituent on cyclohexanone oxime and Grignard reagent was preliminarily examined.

It has been well-known that the actions of Grignard reagents on oximes give rise usually to the Hoch-Campbell reaction.[5] However, Taguchi, *et al.*[4] revealed that the reaction of excessive arylmagnesium bromide with 2-(1-phenylcyclohexyl)cyclohexanone oxime caused intramolecular ring-closure to afford spiro[bicyclo[3.3.1]-3,4-benzononanyliden-9-imine-2,1′-cyclohexane] in good yield (Chart 1). Furthermore, it has been made clear that this kind of reaction occurs only in the treatment of cyclohexanone oxime substituted at C-2 by a tertiary carbon atom involving aryl group.



Ar=phenyl or *p*-tolyl

Chart 1

1) *a*) T. Taguchi, Studies in Stereochemistry, LIV; *b*) Part V; K. Imai, Y. Kawazoe, and T. Taguchi, *Chem. Pharm. Bull.* (Tokyo), **24**, 1083 (1976).
2) To whom inquiries should be addressed.
3) Location: *Maedashi, Higashi-ku, Fukuoka, 812, Japan.*
4) T. Taguchi, K. Miyano, Y. Shimizu, and Y. Kawazoe, *Tetrahedron Letters*, **1968**, 4105; K. Miyano and T. Taguchi, *Chem. Pharm. Bull.* (Tokyo), **18**, 1799 (1970); *ibid.*, **18**, 1806 (1970).
5) J. Hoch, *Compt. Rend.*, **198**, 1865 (1934); *ibid.*, **204**, 358 (1937); K.N. Campbell, *J. Org. Chem.*, **8**, 99, 103 (1943), *ibid.*, **9**, 178, 184 (1944); H. Henze and W.D. Compton, *J. Org. Chem.*, **22**, 1036 (1957).

These observations stimulated us to investigate the neighboring group effect on the Grignard reaction of oximes. As the reaction of 2-phenoxycyclohexanone oxime (**1**) with the Grignard reagent was examined as the first attempt, we wish to report the details of this reaction.

In the Hoch-Campbell reaction of acyclic ketoxime, *syn*- and *anti*- isomers give isomeric aziridines respectively,[6] but the situation is differrent in the alicyclic system.[7] Speaking on the basis of results from the reactions of 2-methylcyclohexanone and menthone oximes, *anti*-isomers give aziridines, but *syn*-isomers do not undergo the Grignard reaction remaining unchanged.[7] As these knowledges tell, it should be prerequisite of the present study to make clear the geometrical isomerism of 2-phenoxycyclohexanone oxime. For this purpose, nuclear magnetic resonance (NMR) spectral determination is useful, because the signal due to the methine of the *syn*- form shifts to lower field than the same signal of the *anti*-form by the shielding effect of the oxime-hydroxyl group.[8] Practically, NMR spectrum of a mixture of the *syn*- and *anti*-oxime shows signals at δ 4.82 and δ 5.65 which are attributable to methines of the *anti*- and the *syn*-oxime respectively. Repeated recrystallizations of the mixture from ethanol gave solely an isomer, mp 89—92°, which was characterized as the *anti*-form by NMR spectral determination of the methine group (δ 4.75) and supplied for the starting material of this study.

The *anti*-oxime (**1**) was treated with 5 molar equivalents of phenylmagnesium bromide in refluxing toluene and the reaction mixture was treated as usual with an aqueous solution of ammonium chloride. The toluene layer was extracted with 10% aqueous sodium hydroxide and then 10% hydrochloric acid to be separated into basic, acidic and neutral fractions. As major products, phenol was isolated from the basic fraction and aniline from the acidic fraction. Treatment of the neutral fraction gave minor products, 2-phenoxycyclohexanone (**6**) and 2-phenylcyclohex-2-enone (**7**) which were identified in the form of 2,4-dinitrophenylhydrazone by mixed mp determinations with authentic samples (Table I, Exp. No. I). Product dependence on the change of reaction condition is recorded in Table I.

Table I. Reaction of *anti*-2-Phenoxycyclohexanone Oxime (**1**) with Phenylmagnesium Bromide

Exp. No.	Reaction condition			Products (%)						
	Molar ratio PhMgBr/**1**	Solvent	Time (hr)	PhOH	$PhNH_2$	**8**	**9**	**6**	**7**[a]	**14**[a]
I	5	toluene	5	51	21	—	—	4[a]	trace	trace
II	2.5	toluene	5	30	26	—	—	20[a]	trace	trace
III	5	benzene	5	64	22	2	1	13		
IV	5	benzene	1.5	51	19	2	1	4		
V	5	ether	1.5	34	16	3	—	22[b]		

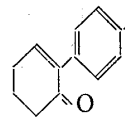
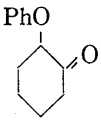
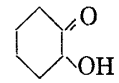
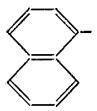
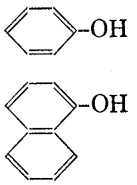
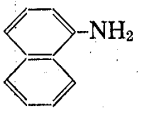
a) as 2,4-dinitrophenylhydrazone
b) recovery of **1**

When benzene or ether was used instead of toluene as solvent in the same reaction, 1-phenyl-2-phenoxy-7-azabicyclo[4.1.0]heptane (**8**, the Hoch-Campbell product) was produced in the both cases and 1-anilino-1-phenyl-2-phenoxycyclohexane (**9**) only in the case conducted in benzene besides the same products as those obtained in the reaction performed in toluene. The possible isolations of **8** and **9** seem to depend upon the reason that reaction temperatures

6) G. Alvernhe and A. Laurent, *Bull. Soc. Chim. France*, **1970**, 3003; A. Laurent and A. Muller, *Tetrahedron Letters*, **1969**, 759.
7) K. Miyano, Doctor's thesis, Kyushu University, **1968**.
8) A.C. Hutric, *J. Org. Chem.*, **32**, 1961 (1967).

in the both solvents are lower than in toluene enough to prevent further decomposition. Now, to know how are the major products, phenol and aniline, formed, reactions of the oxime (**1**) with *p*-tolylmagnesium bromide and with α-naphthylmagnesium bromide were tried. As a result, phenol was isolated as a major acidic product commonly and *p*-toluidine and α-naphthylamine as major basic products respectively in each of the reaction (Table II).

TABLE II. Reaction of *anti*-2-Phenoxycyclohexanone Oxime (**1**) with Arylmagnesium Bromide (ArMgBr)

ArMgBr Ar=	Products (%) Acidic	Basic	Neutral
CH_3-	-OH 34 CH_3--OH trace	CH_3--NH_2 8	 **10** trace[a]  **6** trace[a]  **14** trace[b]
	 34 trace	 6	

a) as 2,4-dinitrophenylhydrazone
b) as 2,4-dinitrophenylosazone

This finding indicates that in the reaction of the oxime (**1**) with phenylmagnesium bromide, aniline originates from the Grignard reagent, but the majority of phenol does not and is produced from the oxime (**1**) through elimination.

Considering these conclusions and the phenomenon above-stated that the aziridine (**8**, the Hoch-Campbell product) can be yielded in lower reaction temperature, the reaction pathway was presumably proposed as follows: The reaction course is divided into two routes (see Chart 2).[9]

Route A: Two moles of phenylmagnesium bromide react with the oxime (**1**) to form the Schiff base (**12**) through **11**. This conjecture is supported by the analogous finding which has been reported about the Grignard reaction of acetoxime by Alvernhe and Laurent.[10] On treatment with water, the schiff base (**12**) is hydrolyzed directly or *via* the enamine (**13**) formed by the work of another mole of the Grignard reagent to produce aniline and 2-phenoxycyclohexanone (**6**). On the other hand, when the enamine (**13**)-formation is followed by hydrolysis and then elimination of phenol, 2-hydroxycyclohexanone (**14**) and aniline are produced. Otherwise, if the schiff base (**12**) accepts arylation by the Grignard reagent, it converts into the amine (**9**).

Route B: This is a course where the aziridine (**8**) is formed by the usual way.[11] The aziridine is hydrolyzed to give 2-phenyl-3-phenoxycyclohexanone (**16**) *via* 2-amino-1-phenyl-6-phenoxycyclohexanol (**15**).[12] When the neutral fraction of the reaction mixture (see above)

9) Configurations of compounds (**8**, **9**, and **15** *etc.*) produced *via* azirine or ketimine can be deduced from the stereochemistry that the Grignard reagent approaches from less hindered site (steric approach control). However, the deduction is not supported by conclusive evidences.
10) G. Alvernhe and A. Laurent, *Tetrahedron Letters*, **1972**, 1007.
11) S. Eguchi and Y. Ishii, *Bull. Chem. Soc. Japan*, **36**, 1434 (1963).
12) It has been reported that the ring-fission of 2,2-disubstituted aziridine by hydrolysis proceeds *via* SN1 (V.B. Schatz and L.B. Clapp, *J. Am. Chem. Soc.*, **77**, 5113 (1955).) The formation of **15** from **8** may occur in analogous way. Hence, **15** seems presumably to have the configuration which permits *trans*-elimination of water to produce **16**.

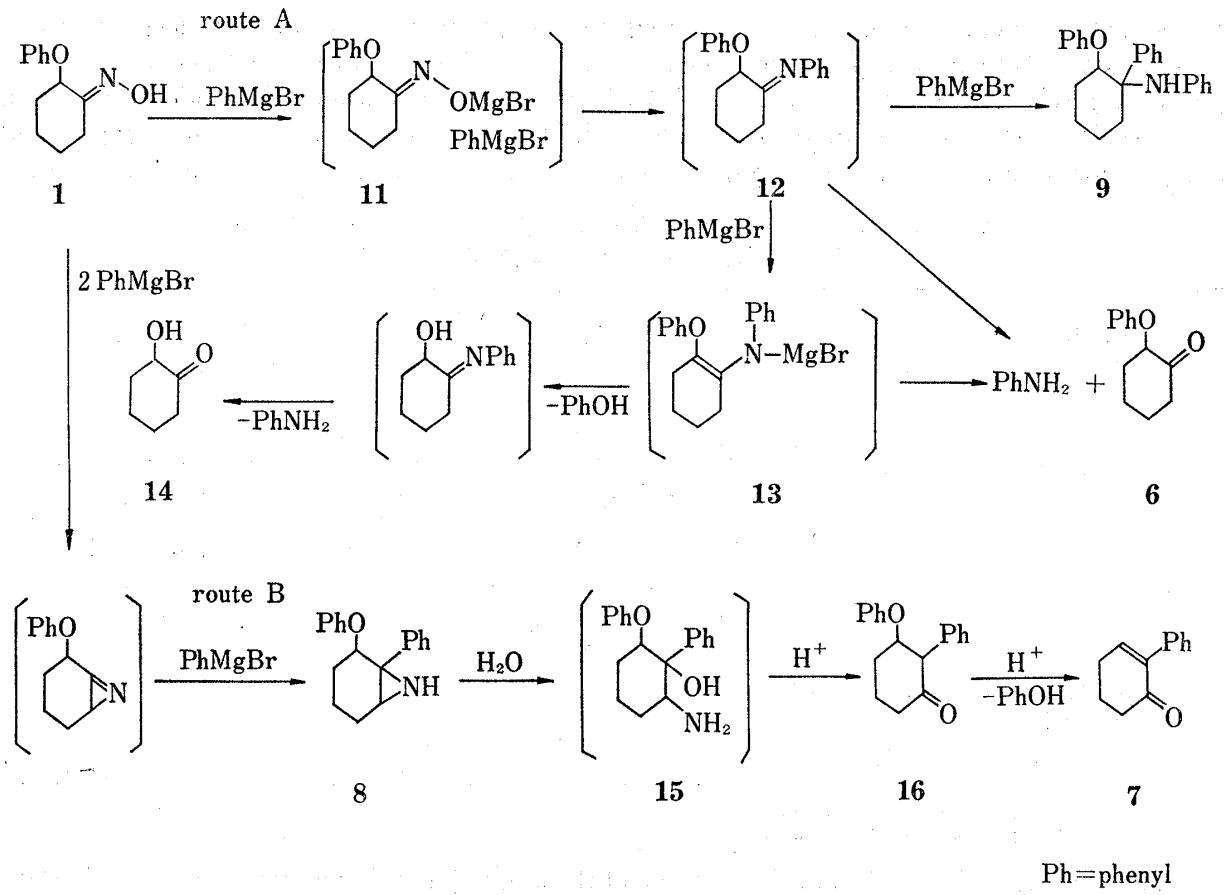


Chart 2

was treated with 2,4-dinitrophenylhydrazine in ethanolic phosphoric acid for the identification of **16**, 2-phenylcyclohex-2-enone (**7**) 2,4-dinitrophenylhydrazone was obtained besides the same derivative of **16**. Considering a report which describes the elimination of methanol producing cyclohexanone 2,4-dinitrophenylhydrazone on the occasion of the analogous treatment of 3-methoxycyclohexanone,[13] **7** seems probably to have been derived from **16** by elimination of phenol in the procedure where **16** is introduced to the 2,4-dinitrophenylhydrazone.

Thus, the reaction of cyclohexanone oxime holding the phenoxy group at C-2 with phenylmagnesium bromide showed a result entirely different from the known results reported on the Grignard reactions of alicyclic ketoximes.[1b,4,7] Hence in passing, influences upon the product formation by the change of the Grignard reagent from aromatic to aliphatic and also by the change of the substituent from phenoxy to alkoxy or others were preliminarily investigated.

Chart 3 shows results obtained when reactions of the oxime (**1**) with ethyl-, *t*-butyl- and cyclohexylmagnesium halide were performed in benzene. As can be seen there, the oxime (**1**) was recovered unchanged only in the use of *t*-butylmagnesium chloride. On the other hand, the other cases afforded aziridine derivatives through the Hoch-Campbell reaction accompanying the formation of phenol, but amines which may be resulted from N-alkylation by the Grignard reagents have not been found.

Chart 4 shows product formation in the reaction of *anti*-2-benzyloxy- and *anti*-2-cyclohexyloxycyclohexanone oxime (**2** and **3**) with phenylmagnesium bromide in benzene. In both cases, tendencies of the product formation were nearly similar to the case of the oxime (**1**), though cyclohexanol could not be detected in the case of the oxime (**3**). Investigations in

13) H. Adkins and A.G. Rossow, *J. Am. Chem. Soc.*, **71**, 3836 (1949).

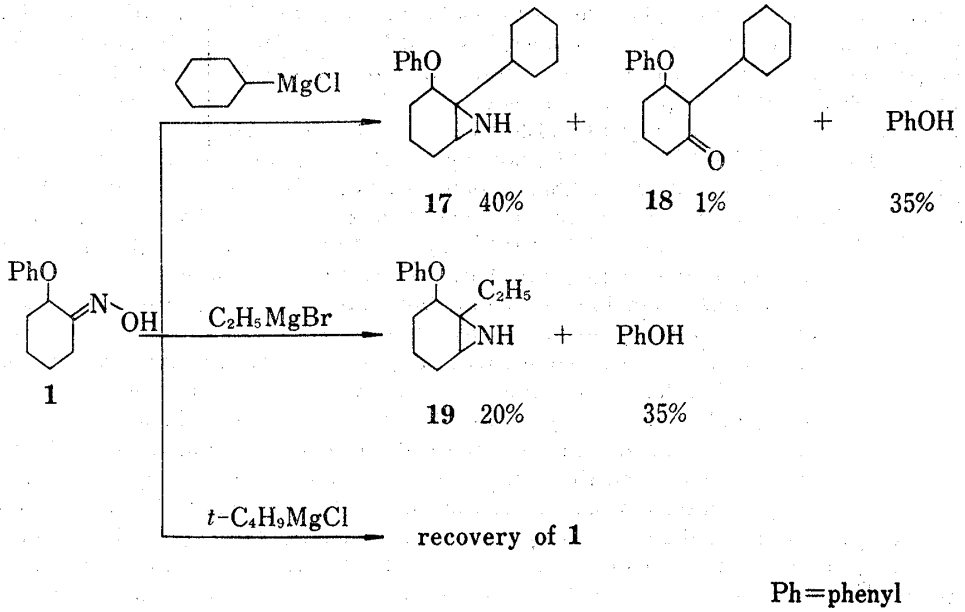


Chart 3

details were omitted for these reactions, because specificities of reactions were not found in comparison with the former analogous study of the oxime (**1**). Additionally, the reactions of *anti*-2-N-methylanilino- and *anti*-2-phenylthiocyclohexanone oxime (**4** and **5**) with phenylmagnesium bromide were pursued on trial. As a result, it was found that the Hoch-Campbell reaction proceeded originarily, therefore interests in further investigation were spoiled.

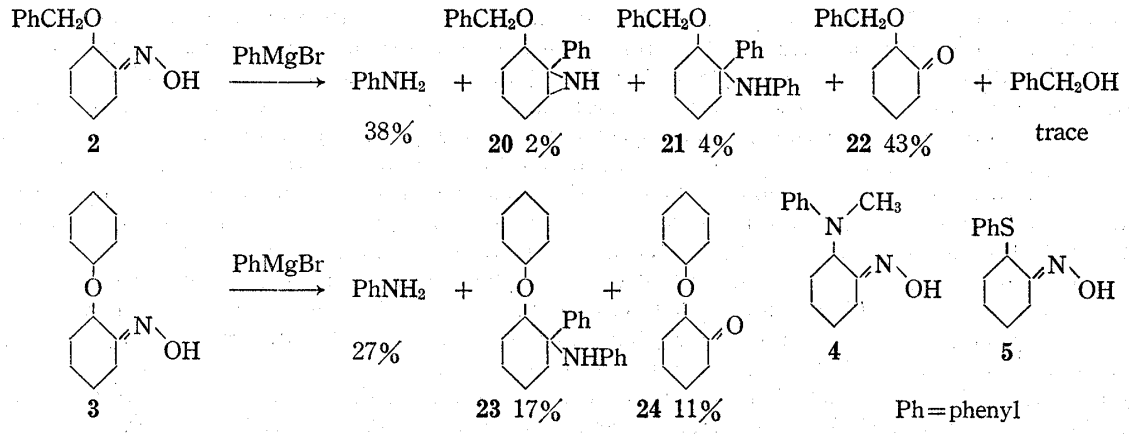


Chart 4

Experimental

Melting points were uncorrected. Infrared (IR) spectra were recorded with a JASCO DS-701G spectrometer. NMR spectra were obtained with Nihon Denshi C-60H spectrometer at 60 MHz using tetramethylsilane (TMS) as an internal standard. Gas chromatographic analyses were performed with a Shimadzu GC-4A gas chromatograph with a hydrogen flame ionization detector using a 5% SE-30 on Chamelite CK (60—80 mesh, 4 m × 3 mm) column. Mass spectra were recorded using JMS-01SG mass spectrometer.

Preparation of *anti*-Ketoximes——Treatment of 2-phenoxy-[14] and 2-benzyloxy[15] cyclohexanone with $NH_2OH \cdot HCl$ in ethanol–pyridine gave the corresponding oximes **1** and **2**. Also treatment of 2-cyclohexyl-

14) F. Winternitz, N.J. Antia, M. Tumlirova, and R. Lachazette, *Bull. Soc. Chem. France*, **1956**, 1817 [*C.A.*, **51**, 7345b(1957)]; L. Baczynskyj, S. Mizsak, and J. Szmuszkovicz, *J. Org. Chem.*, **37**, 4104 (1972).

15) Yu.A. Arbuzov, A.A. Kiryushkin, Yu.A. Ovchinnikov, and M.M. Shemyakin, *Z. Obshch. Khim.*, **34**, 1100 (1964) [*C.A.*, **61**, 1769g (1964)].

oxy-,[16] 2-N-methylanilino-,[17] and 2-phenylthio[14] cyclohexanone with $NH_2OH \cdot HCl$ in dilute ethanol containing CH_3COONa gave the corresponding oximes **3**, **4**, and **5**. *anti*-Oximes were obtained by repeated recrystallizations from ethanol, but *syn*-isomers were not obtained in pure state. *anti*-2-Phenoxycyclohexanone oxime (**1**): mp 89—92°. NMR (CCl_4) δ: 4.75 (broad, >CH–O). *anti*-2-Benzyloxycyclohexanone oxime (**2**): mp 62—64°. *Anal.* Calcd. for $C_{13}H_{17}O_2N$: C, 71.20; H, 7.82; N, 6.39. Found: C, 71.53; H, 7.84; N, 6.30. NMR (CCl_4) δ: 3.94 (broad, >CH–O). *anti*-2-Cyclohexyloxycyclohexanone oxime (**3**): mp 78—83°. *Anal.* Calcd. for $C_{12}H_{21}O_2N$: C, 68.21; H, 10.02; N, 6.63. Found: C, 68.28; H, 10.08; N, 6.50. NMR (CCl_4) δ: 3.95 (broad, >CH–O). *anti*-2-N-Methylanilinocyclohexanone oxime (**4**): mp 130—131°. *Anal.* Calcd. for $C_{13}H_{18}ON_2$: C, 71.52; H, 8.31; N, 12.83. Found: C, 71.50; H, 8.31; N, 12.81. NMR (CCl_4) δ: 4.10 (broad, >CH–N). *anti*-2-Phenylthiocyclohexanone oxime (**5**): mp 90—93°. NMR (CCl_4) δ: 3.90 (broad, >CH–S).

The Grignard Reaction of *anti*-Ketoximes (General Procedure)——A Grignard reagent was prepared as usual from Mg and aryl or alkylhalide dissolved in anhydrous ether of 2—3 times volume as much as the halide. After the formation of the reagent completed, ether was removed off by evaporation as much as possible. To the vessel was added dehydrated toluene (or benzene) of almost same volume as the residue. An *anti*-ketoxime dissolved in anhyd. toluene (or benzene) was added to the toluene solution containing the Grignard reagent at refluxing temperature under stirring and reflux was continued for additional some hours. After the reaction mixture was cooled and then hydrolyzed with sat. aqueous NH_4Cl at 0°, the hydrolysate was extracted with ether. The ether extract was treated with 10% aqueous NaOH and subsequently 10% HCl to be separated into basic, acidic and neutral fractions. After the basic and acidic fractions were neutralized respectively with conc. HCl and 30% aqueous NaOH, the solutions were extracted with ether. These ether extracts were washed with water, dried over $MgSO_4$ and concentrated *in vacuo* respectively to leave brown viscous liquids. The liquids were purified and separated into products by column chromatography over Al_2O_3 (Merck, activity II-III) or SiO_2 (Merck, 70—325 mesh).

Reaction of *anti*-2-Phenoxycyclohexanone Oxime (1) with Phenylmagnesium bromide——i) In Anhydrous Toluene Solution: a) Five g of the oxime (**1**) were reacted with C_6H_5MgBr (5eq)| prepared from Mg (3.1 g) and phenylbromide (20 g) for 5 hr in anhyd. toluene. Working up as the general procedure, the basic fraction gave phenol (bp 78—80° (20 mmHg)) in yield 51%. Isolated product from the acidic fraction was aniline exclusively, which was charcterized as N-*p*-tosyl derivative (mp 100—101°), although gas liquid chromatography (GLC) showed the existence of a very small amount of other products. The neutral fraction was treated with 2,4-dinitrophenylhydrazine in H_3PO_4(85%)–ethanol, the resulting 2,4-dinitrophenylhydrazones were purified by chromatography on SiO_2 as follows. 1) From elution with *n*-hexane–benzene (1: 1): 2-Phenylcyclohex-2-enone (**7**) 2,4-dinitrophenylhydrazone, mp 165—167° (ethanol) alone and on admixture with an authentic sample[18]; yield trace. 2) From elution with *n*-hexane–benzene (1: 2): 2-Phenoxycyclohexanone (**6**) 2,4-dinitrophenylhydrazone, mp 151—152° (ethyl acetate) alone and on admixture with an authentic sample.[14] 3) From elution with benzene: 1,2-cyclohexanedione 2,4-dinitrophenylosazone, mp 217—220° ($CHCl_3$–ethanol), yield trace. Mass Spectrum *m/e*: 472 (M^+). b) Product-formation is shown in Table I when 2.5 equimoles of phenylmagnesium bromide to the oxime (**1**) were used.

ii) In Anhydrous Benzene Solution: The operation was carried out by the general procedure using 5 molar equivalents of phenylmagnesium bromide. A mixture of crude products from the acidic fraction was steam-distilled to remove off aniline. The residue was purified by chromat. on Al_2O_3 as follows. 1) From elution with *n*-hexane–benzene (5: 1): 1-Anilino-1-phenyl-2-phenoxycyclohexane (**9**), mp 124—125° (petroleum ether), yield 1%. *Anal.* Calcd. for $C_{24}H_{25}ON$: C, 83.92; H, 7.34; N, 4.08. Found: C, 84.24; H, 7.42; N, 4.12. Mass Spectrum *m/e*: 343 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3415 (–NH–), 1230 (–O–). NMR (CCl_4) δ: 4.15 (triplet, >CH–O). 4.55 (singlet, –NH–). 2) From elution with benzene: 1-Phenyl-2-phenoxy-7-azabicyclo-[4.1.0]heptane (**8**), mp 95—96° (petroleum ether), yield 2%. *Anal.* Calcd. for $C_{18}H_{19}ON$: C, 81.47; H, 7.22; N, 5.28. Found: C, 81.54; H, 7.20; N, 5.42. Mass Spectrum *m/e*: 172(M^+–C_6H_5O). IR ν_{max}^{KBr} cm^{-1}: 2995 (>NH), 1232 (–O–). NMR (CCl_4) δ: 0.98 (singlet, >NH), 4.78 (broad, >CH–O). Products from the neutral fraction were separated by chromat. over SiO_2 as follows. From elution with benzene; 2-phenyl-3-phenoxycyclohexanone (**16**), mp 125—126° (ethanol), yield trace. Mass Spectrum *m/e*: 266 (M^+). IR ν_{max}^{KBr} cm^{-1}: 1720 (C=O), 1248 (–O–). NMR (CCl_4) δ: 3.52 (broad, >CH–Ph), 4.68 (broad, >CH–O).

iii) In Anhydrous Ether Solution: The reaction was operated just as (i) and (ii) by the general procedure. Table I, Exp. No. V shows reaction condition and product-formation.

Reaction of *anti*-2-Phenoxycyclohexanone Oxime (1) with *p*-Tolylmagnesium Bromide and α-Naphthylmagnesium Bromide Respectively——The reactions were operated just as (i) of the foregoing heading. Table II shows products in the both cases. 2-*p*-Tolylcyclohex-2-enone (**10**) was identified in the form of 2,4-dinitrophenylhydrazone, mp 174—177° (ethanol), yield trace: Mass Spectrum *m/e*: 266 (M^+).

Reaction of *anti*-2-Phenoxycyclohexanone Oxime (1) with Cyclohexylmagnesium Chloride——The oxime (**1**) (5 g) was treated along the general method with $C_6H_{11}MgCl$ (5eq) prepared from Mg(3.0 g) and cyclohexyl chloride (14.5 g) in anhydrous benzene for 1.5 hr. Treatment of the basic fraction gave phenol, yield 35%.

16) M. Mousseron, J. Jullien, and Y. Jolchine, *Bull. Soc. Chim. France*, **1952**, 757 [*C.A.*, **48**, 3273*g* (1954)].
17) E. Campaigne and R.D. Lake, *J. Org. Chem.*, **24**, 478 (1959).
18) D. Ginsburg and R. Pappo, *J. Chem. Soc.*, **1951**, 516.

Products from the acidic fraction were separated by chromat. on Al_2O_3 as follows. 1) From elution with petroleum ether–benzene (1: 1): 2-cyclohexyl-3-phenoxycyclohexanone (**18**), mp 107—109° (petroleum ether), yield 1%. *Anal.* Calcd. for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.45; H, 8.92. IR ν_{max}^{KBr} cm^{-1}: 1727 (C=O), 1240 (–O–). NMR (CCl_4) δ: 4.50 (broad, >CH–O). 2) From elution with benzene: 1-cyclohexyl-2-phenoxy-7-azabicyclo[4.1.0]heptane (**17**), mp 61—64° (petroleum ether), yield 40%. *Anal.* Calcd. for $C_{18}H_{25}ON$: C, 79.66; H, 9.29; N, 5.16. Found: C, 79.60; H, 9.28; N, 5.30. IR ν_{max}^{KBr} cm^{-1}: 3299 (>NH), 1232 (–O–). NMR (CCl_4) δ: 0.60 (singlet, >NH), 4.62 (broad, >CH–O).

Reaction of *anti*-2-Phenoxycyclohexanone Oxime (1) with Ethylmagnesium Bromide——The oxime (**1**) (5 g) was reacted by the general procedure with C_2H_5MgBr (5eq) prepared from Mg(2.4 g) and ethylbromide (10.6 g) in anhydrous benzene for 1.5 hr. Treatment of the basic fraction gave phenol, yield 35%. An oil isolated by treatment of the acidic fraction was distilled under reduced pressure (1 mmHg) at 110—120° (bath temp.) to give a yellow viscous liquid, which showed mainly two spots (*Rf* values, 0.8 and 0.6) on thin-layer chromatography (TLC) (Al_2O_3, $CHCl_3$). Further, the distillate was purified by preparative TLC using Al_2O_3 (Merck, G(Typ E)) and a solvent system of $CHCl_3$–CH_2Cl_2 (1: 1). The band (Rf=0.8)on TLC was scraped from the plate, collected, and extracted with ether. The ether extract was concentrated to leave a pale yellow viscous liquid of 1-ethyl-2-phenoxy-7-azabicyclo[4.1.0]heptane (**19**), yield 20%. IR $\nu_{max}^{liq.}$ cm^{-1}: 3300 (>NH), 1240 (–O–). NMR (CCl_4) δ: 0.65 (singlet, >NH), 4.50 (triplet, >CH–O). N-*p*-Tosylate: mp 91—93° (petroleum ether). *Anal.* Calcd. for $C_{21}H_{25}O_3NS$: C, 67.90; H, 6.78; N, 3.77. Found: C, 67.88; H, 6.78; N, 3.80.

Reaction of *anti*-2-Phenoxycyclohexanone Oxime (1) with *t*-Butylmagnesium Bromide——The reaction was carried out just as the case of C_2H_5MgBr above-stated by the general procedure, but the starting material (**1**) was recovered unchanged.

Reaction of *anti*-2-Benzyloxycyclohexanone Oxime (2) with Phenylmagnesium Bromide——The oxime (**2**) (5 g) was reacted by the general procedure with C_6H_5MgBr (5 eq) in anhyd. benzene for 1.5 hr. No product was found from the basic fraction except that the mixing of benzylalcohol in a very small quantity was observed on GLC. Steam distillation of substance from the acidic fraction gave aniline, yield 38%. The residue of steam distillation was separated by chromat. on Al_2O_3 as follows. 1) From elution with petroleum ether–benzene (1: 1): 1-anilino-1-phenyl-2-benzyloxycyclohexane (**21**). mp 116—118° (petroleum ether), yield 4%. *Anal.* Calcd. for $C_{25}H_{27}ON$: C, 83.99; H, 7.61; N, 3.92. Found: C, 84.17; H, 7.72; N, 3.88. IR ν_{max}^{KBr} cm^{-1}: 3446 (–NH–), 1070 (–O–). NMR (CCl_4) δ: 3.40 (broad, >CH–O), 4.45 (singlet, –NH–). 2) From elution with benzene: 1-phenyl-2-benzyloxy-7-azabicyclo[4.1.0]heptane (**20**), identified as N-*p*-tosylate: mp 157—158° (ethyl acetate). *Anal.* Calcd. for $C_{26}H_{27}O_3NS$: C, 72.02; H, 6.27; N, 3.23. Found: C, 72.03; H, 6.36; N, 3.16. NMR (CCl_4) δ: 3.50 (broad, >CH–O). Isolated product from the neutral fraction by chromat. on SiO_2 was 2-benzyloxycyclohexanone (**22**) exclusively, which was identified with an authentic sample by the comparison of GLC data and IR spectrum.

Reaction of *anti*-2-Cyclohexyloxycyclohexanone Oxime (3) with Phenylmagnesium Bromide——The oxime (**3**) (5 g) was treated by the general procedure with C_6H_5MgBr (5eq) in anhyd. benzene for 1.5 hr. Steam distillation of the substance isolated from the basic fraction gave aniline, yield 27%. The residue of steam distillation was separated by chromat. on Al_2O_3. The elution with petroleum ether–benzene (2: 1) gave 1-anilino-1-phenyl-2-cyclohexyloxycyclohexane (**23**). mp 110—113° (petroleum ether). yield 17%. *Anal.* Calcd. for $C_{24}H_{31}ON$: C, 82.47; H. 8.94; N, 4.01. Found: C, 82.52; H, 8.82; N, 4.13. IR ν_{max}^{KBr} cm^{-1}: 3440 (–NH–), 1090 (–O–). NMR (CCl_4) δ: 3.30 (broad, >CH–O), 4.40 (broad, –NH–). Chromatography over SiO_2 of the substance isolated from the neutral fraction gave 2-cyclohexyloxycyclohexanone (**24**), which was identifield with an authentic sample by the comparison of GLC data and IR spectrum.

Reaction of *anti*-2-N-Methylanilinocyclohexanone Oxime (4) with Phenylmagnesium Bromide——The oxime (**4**) (5 g) was treated by the general procedure with C_6H_5MgBr (5eq) in anhyd. benzene for 1.5 hr. Substances isolated from the acidic fraction were separated by chromat. on Al_2O_3. and then, crude products were eluted with benzene and distilled under reduced pressure (2 mmHg) at 150—160° (bath temp.) to give a pale yellow viscous liquid, yield 17%. The structure of the liquid was suggested by IR and NMR spectra to be 1-phenyl-2-N-methylanilino-7-azabicyclo[4.1.0]heptane (**25**). IR $\nu_{max}^{liq.}$ cm^{-1}: 3295 (>NH). NMR (CCl_4) δ: 1.08 (singlet, >NH), 1.3—1.9 (6H, multiplet, alipha. H), 2.10 (1H, broad, C_6-methine), 2.92 (3H, singlet, $-CH_3$), 4.20 (broad, >CH–N), 6.3—7.3 (10H, multiplet, arom.H). The liquid (**25**) was treated by Schotten-Baumann method with *p*-tosylchloride, but its N-*p*-tosylate was not obtained.

Reaction of *anti*-2-Phenylthiocyclohexanone Oxime (5) with Phenylmagnesium Bromide——The oxime (**5**) (5 g) was treated by the general procedure with C_6H_5MgBr (5eq) in anhyd. benzene for 1.5 hr. The substance obtained by treatment of the acidic fraction was purified by chromat. on Al_2O_3. The elution with benzene gave 1-phenyl-2-phenylthio-7-azabicyclo[4.1.0]heptane (**26**). mp 67—69° (ethanol), yield 10%. *Anal.* Calcd. for $C_{18}H_{19}NS$: C, 76.84; H, 6.81; N, 4.98. Found: C, 76.81; H, 6.82; N, 4.90. IR ν_{max}^{KBr} cm^{-1}: 3294 (>NH). NMR (CCl_4) δ: 0.85 (singlet, >NH), 3.60 (broad, >CH–S).

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